MAGNETIC MINI-MOVER DEVICE
TO CORRECT PECTUS EXCAVATUM

Tracked
Supplemental Information
INVESTIGATIONAL DEVICE EXEMPTION (IDE)
APPLICATION (#G090006/S013)
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Michael R. Harrison, M.D.
Professor Emeritus of Surgery, Pediatrics, and Obstetrics, Gynecology & Reproductive Sciences
Director, UCSF Pediatric Device Consortium
University of California, San Francisco

Contact Information:
Division of Pediatric Surgery
University of California, San Francisco
513 Parnassus Avenue, HSW-1601
San Francisco CA 94143-0570
Tel (415) 476-4086; Fax (415) 476-2314
e-mail: michael.harrison@ucsfmedctr.org
http://www.pedsurg.ucsf.edu/
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§1. Name and Address of Sponsor:

Michael R. Harrison, M.D.
Professor Emeritus of Surgery, Pediatrics, and Obstetrics,
Gynecology and Reproductive Sciences
University of California, San Francisco
Department of Surgery, Division of Pediatric Surgery
513 Parnassus Avenue, Room HSW-1601
San Francisco CA 94143-0570
(415) 476-4086 (primary) or 476-4914 (secondary); Fax (415) 476-2314
e-mail: michael.harrison@ucsfmedctr.org
§2. Report of prior investigations

2.a. Relevant Bibliography

- Tenforde TS. Magnetically induced electric fields and currents in the circulatory system. Progress in Biophysics and Molecular Biology 2005;87:279-288.

2.b. Background

Pectus excavatum (PE) is one of the most common major congenital anomalies, and has a significant impact on patients' lives.\(^1\)\(^-\)\(^7\) The excavatum defect is characterized by a deep depression of the sternum, usually involving the lower half or two thirds of the sternum, with the most recessed area at the junction of the chest and the abdomen. The lower costal cartilages dip backward abnormally to increase the deformity or depression and push the sternum posteriorly. In many of these deformities, there is also an asymmetric rotation of the sternum along its axis. The entire defect also pushes the midline structures so that the lungs and heart (specifically the right ventricle) are compressed and displaced. The pectus excavatum deformity has measurable and often significant effects on lung volume and cardiac performance, which can be reversed by repair.\(^6\)\(^-\)\(^14\)

There are several approaches to repair—all involve a major surgical reconstruction with significant morbidity and cost. The gold standard for repair has been the Ravitch procedure, which has been modified many times over the past several decades.\(^1\)\(^-\)\(^5\) This requires exposure of the cartilage/sternal junction, removal of abnormal cartilage, and fixation of the sternum to the normal position with a bar or pin. Despite the numerous modifications, inherent disadvantages exist as it requires a major operation, is demanding technically to the surgeon, requires a large incision, may be associated with blood loss and pneumothorax, and requires 3-7 days of hospitalization for pain control and a long recovery at home. Furthermore, the Ravitch procedure does not address correction of asymmetric defects.

An alternative approach has evolved which is considered to be minimally invasive. The Nuss procedure uses small incisions on the chest wall through which a camera and instruments are inserted to allow placement of the bar under the depressed sternum. The bar is then flipped, pushing the sternum outward to anatomical position, and secured into place. Advantages of this approach are that the sternum is elevated without requiring cartilage resection and is less technically demanding. However, due to the abrupt elevation of the sternum under great force, it still requires general anesthesia and regional anesthesia (epidural) for 3-7 days in the hospital for pain control.\(^16\)\(^-\)\(^17\) There can be significant complications such as injury to the heart from passage of the metal bar under the sternum, and there is a significant failure rate. Additionally, several more weeks of moderate to severe discomfort are typical. Also, it is necessary to leave the bar in place for a year or more (usually two years), and requires another procedure for removal. Like the Ravitch procedure, the Nuss bar does not correct asymmetry. Total cost usually reimbursed by third party payers ranges between $80,000-$85,000. Despite the numerous modifications and attempts at more minimally invasive techniques, the current standard of care for PE repair continues to be associated with a considerable complication rate of between 15-20%\(^17\)\(^,\)\(^18\)
We believe that substantial improvement can be achieved in what is currently the standard of care in the treatment of PE. We have developed a procedure that is safer, easier, and less expensive. We believe this new approach could drastically improve our patients’ lives, improve respiratory and cardiovascular capacity, and improve their self-image. Our approach would replace a major surgical reconstruction with a minimally invasive, gradual reformation of the chest wall.

2.c. Economic Impact

Pectus excavatum is the most common chest wall birth defect, occurring in 1 in approximately 300-400 births in the US, UK, Europe, and to a slightly lesser degree in Japan. Thus, 10,000 cases per year occur in the US; of these, less than 2000 undergo surgical correction. Pectus excavatum is more common in males by a 3:1 margin.

The deformity worsens during the onset of puberty until about the age of 18. The most significant measurable physiologic effects are decreased lung volume and impaired cardiac filling due to atrial compression. Physical symptoms include: 1) inability to take a deep breath, 2) shortness of breath and lack of stamina during limited exercise, 3) anterior chest pain, and 4) variety of respiratory complications. Psychological symptoms, often overlooked, range from mild self-conscious behavior, to loss of motivation, anxiety and other social problems.

Non-surgical treatments, for example, the vacuum bell, are ineffective. Current methods of surgical correction are effective in most cases, but are very morbid and expensive. Costs for these standard procedures average more than $80,000 and include a major operation requiring general anesthesia, post-operative regional (epidural) anesthesia for 3-5 days in the hospital, and a second operation under general anesthesia to remove the metal bar 1-2 years after the first procedure. The cost can double if a second procedure is necessary because the initial one fails (~10%).

About a fifth of all pectus excavatum patients (approximately 2000) undergo surgery at an average cost of $80,000, resulting in costs of $160 million per year. The Magnetic Mini-Mover procedure (implant and explant) and provision of the Magnimplant device cost an average of $46,000. If 50% of patients now having the standard procedure underwent the new 3MP, the savings of $34,000 per procedure would result in approximately $34 million of benefit per year.

Due to the substantial lower cost and lower morbidity of the new procedure, it is possible that additional surgeries may be performed on those patients who previously desired one but found the cost prohibitive and/or the treatment morbid.

2.c.1. Insurance Coverage of Pectus Excavatum Surgeries

Medical insurance providers cover correction of pectus excavatum when deemed medically necessary, generally when the defect causes cardiopulmonary effects and the Pectus Severity Index (PSI) is greater than 3.25.

Pectus Severity Index: Pectus Severity Index (PSI) has long been accepted as a means to determine the severity of pectus excavatum. In most cases we and others have found a majority of the patients displaying a Pectus Severity Index well beyond 3.25. Yet, the insurance industry remains steadfast in that none of the major carriers will fund surgery for pectus excavatum if the PSI is below 3.25. The Healthcare Cost & Utilization Project (HCUP) statistics for insurance coverage for Nuss and Ravitch coverage is seen in Table 1.
Table 1. Insurance Coverage for Pectus Excavatum Surgeries (ICD-9-CM 754.81)\textsuperscript{23}

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Medicare</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Medicaid</td>
<td>102 (12.58%)</td>
<td>96 (7.20%)</td>
<td>176 (10.94%)</td>
<td>161 (10.70%)</td>
</tr>
<tr>
<td>Private</td>
<td>637 (78.53%)</td>
<td>1,204 (90.47%)</td>
<td>1,322 (81.97%)</td>
<td>1,217 (80.6%)</td>
</tr>
<tr>
<td>Other</td>
<td>58 (7.20%)</td>
<td>0</td>
<td>94 (5.86%)</td>
<td>0</td>
</tr>
<tr>
<td>Uninsured</td>
<td>*</td>
<td>*</td>
<td>*</td>
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Source: HCUP; *Statistics suppressed as unreliable

Nothing differentiates our patient population from those requiring surgical intervention using present techniques. The 3MP as opposed to the Nuss or Ravitch may potentially be much safer (deaths have occurred with both of these procedures), as well as less morbid (an outpatient procedure versus a 3-7-day hospital stay), and less expensive because there is no expected hospital stay. We chose a PSI > 3.5 to be even more stringent about having a significantly severe defect than that defined by clinicians and all insurance companies today, that is, a pectus severity index (PSI) greater than 3.25.

2.d. Other
Success with this procedure and device will set the platform for development of magnetic implant treatments for other orthopedic muscular-skeletal deformities such a scoliosis. For scoliosis, 38,000 patients annually undergo spinal fusion and another 30,000 children are treated conservatively with full torso orthotic braces. Many orthopedic and pediatric surgeons are closely following this project; some are beginning to work with us in the application of the technology for other indications.

2.e. Preliminary Studies
Two years ago we reported the development of the Magnetic Mini-Mover Procedure (3MP) for correction of pectus excavatum, including development, design, and simulations for feasibility and safety.\textsuperscript{24} Four years before this application, we worked with Laurence Derose, President and CEO, and Dale Clough, Engineering Projects Manager, both of Texcel, LLC, on the development, design, and fabrication of the Magnimplant, designed to be implanted in the sternum in a brief outpatient procedure. Specifically, we encased a 1½-in diameter neodymium-iron-boron magnet and a ferromagnetic focus plate inside a 2-in diameter titanium cylinder, and designed the device as a “button” or rivet, with a threaded-screw stem that went through the sternum and attached and threaded to a small-nut plate on the underside of the sternum.

We then developed the Magnatract, the external orthotic device molded specifically to each patient’s anterior chest deformity. The external magnet suspended in this orthosis incorporates two special properties: 1) the patient adjusts by simply screwing and unscrewing the can that houses the magnet and thus changing the distance between magnets; and 2) we incorporated a data-logging device that allows pressure and temperature measurements to be recorded every 10 minutes and downloaded at each patient visit. This turned out to be an excellent monitor of compliance.
Of particular concern was the possibility of any ill effect from a magnetic field close to the heart. As part of our first IDE application, we studied the literature for possible biologic effects of static magnetic fields, and consulted with two experts in the field:

- Dr. Thomas F. Budinger, Professor of Bioengineering, UCB/UCSF and in the Department of Functional Imaging, Lawrence Berkeley National Laboratory, and

- Dr. Thomas Tenforde, President, National Council on Radiation Protection and Measurements

All the available evidence suggests there is no measurable effect from static magnetic fields less than 4 tesla on living tissue. Some studies actually tested field strengths above 4 tesla without ill effect. Both Dr. Budinger and Dr. Tenforde believe that the magnetic field generated by the Magnimplant (0.4 tesla at the surface of the magnet, 0.1 tesla at 2 cm from the surface, which is the closest the outside surface of the heart could come to the implanted magnet) will have no measurable ill effect (Figure 1).

We then tested this device and further developed the design in animals, and simulated and measured the magnetic field strength it generated in order to prove the safety of a static magnetic field near the heart. Finally, under FDA approval (IDE G050196), IRB approval, and funding from the Office of Orphan Products Development Grant Program (R01FD003341), we conducted a proof-of-concept study to confirm the safety and probable efficacy of this procedure in 10 otherwise healthy patients, age 8-14, with Pectus Severity Index > 3.5 (normal = 2.56).

WHAT WE LEARNED FROM THE TRIAL:

2.e.1. Procedure to implant Magnimplant

As expected, the surgical procedure to attach a titanium-enclosed Magnimplant to the sternum evolved through our experience with the initial 10 patients. We used the same Magnimplant described in our previous work in all 10, but the surgical procedure and instruments improved.

In each patient, the Magnimplant was implanted through a 2-inch incision made at the xiphoid-sternal junction. The xiphoid was separated from the lower sternum with electrocautery and blunt dissection, and a space was created under the sternum and over the sternum by blunt...
finger dissection. In the first patient, the hole to affix the implant was created in the most depressed part of the sternum using an orthopaedic drill, but later found that a punch anvil was much more efficient at piercing and removing the plug of sternum easily, quickly and safely [Figure 2].

![Punch Mechanism](image1)

![Punch Sternum](image2)

**Figure 2**: (a) Sternal punch device; (b) Sternal punch device engaged with sternum.

We also developed several tools to place the posterior fixation disk with its standing female thread through the hole on the underside of the sternum and then to manipulate the external Magnimplant male thread to engage and then tighten. This maneuver to find the punched hole was more difficult than anticipated because it was performed blindly through a very small incision. Various ratchet devices held in place by the magnet itself proved useful but problematic because they allowed over-tightening of the implant to the sternum. In one case, the implant had to be loosened to relieve persistent discomfort. Two other patients required replacement when the device uncoupled. Clearly this was mis-crossthreaded initially—both patients could feel it pop loose, one a week after the procedure when he was exercising and the other about two months after implantation. The solution was a flexible, braided, stainless steel wire (ASTM F138) that screws into the female component of the posterior plate (Figures 3 and 4).

The flexible wire tool has evolved and proven so effective that a grasper is no longer necessary. The description of the flexible wire tool is as follows: A 10/24 threads-per-inch (TPI) stainless steel rod (ASTM F138), 9/16” in length, is attached to a stainless steel flexible cable (ASTM F138) by a silver braze, 18” length. The flexible cable is passed through the hole punched in the sternum. The wire is screwed into the female connector on the backplate. The backplate is then drawn into the retro-sternal space, and the female end is guided into the punched hole. The flexible guide wire is then unscrewed and the male stem of the magnet device is screwed into the backplate. This mechanism greatly simplifies the procedure and allows us to complete the entire procedure more quickly.
Figure 3: Implant guide wire used to affix Magnimplant to the sternum.

Figure 4: Stainless steel (ASTM F138) guide wire device for 3MP.
Operating time decreased as techniques and instruments improved as described above (mean = 71 min; range = 43-105 min). Nine of our 10 patients went home the same day; one was admitted for observation.

Three of ten patients required evacuation of retained pleural air postoperatively. There was no damage to the pleural structure, but air entered the cavity during the procedure and was evacuated with a simple procedure under local anesthesia. This is a common complication of thoracic procedures when operating in or near the pleural cavity. This problem was addressed by obtaining a chest x-ray to evaluate for entrained air on the operating table before the patient is awakened.

Although these changes were made to make the device easier for implant and explant, we ultimately found a new way to attach the encased magnet to the sternum by using a cerclage method. We present these design improvements and attachment method below.

2.e.2. Magnimplant design improvements

Improvements to the Magnimplant are presented in Figure 5 below along with a pictorial image of the device (see Figure 5a). The drawings are provided by Hayes Manufacturing Services, Inc. Due to the complications with the prior implant with regards to implant and explant using a screw mechanism, we developed a cable system to allow for easier implant and explant of the device by the surgeon. The anterior plate is maintained with the N55 rare earth magnet and carbon steel focusing cup encased in titanium as before, but no screw female connector. Both versions 2 and 3 anterior cups have the magnet sitting in a carbon steel cup (1.75” diameter with sides 0.26” deep (pictured in Figure 5b item 2) which is placed in the titanium can (1.95” diameter and 0.328” deep). The carbon steel cup was added in our version 2 design and maintained in the version 3 design to focus the magnetic field outward from the patient. Since the dimensions did not change and titanium is not ferromagnetic the magnetic field will not change. The anterior can has wings on either side of the can in which the set screws reside (1” x 0.325”, see Figure 5b item 1).

The new backplate is rectangular-shaped to accommodate for the wings on the anterior cup. This shape also ensures centering of the anterior cup and backplate for even distribution of pressure. The diameter of the generation 2 backplate was 1.25” compared to the generation 3 back plate dimensions of 1.8” x 1” giving only an additional 0.275” of length on either side of the version 2 backplate. (NOTE: Maintaining the backplate at 1.25” in length would result in easy off-centering as well as pressure and damage to the sternum). This small increase in the backplate, which is positioned directly under the sternum, should not cause additional pressure or potential damage to the surrounding structures. The generation 3 backplate is 1/8” in thickness as a safety measure to encase the cables and to keep the cables in place so they don’t move around or cause damage to the sternum by cutting through it (see Figure 5c). The 2nd generation backplate suffers from high stress concentrations, as did the first generation backplate, which broke in 3 patients during the pilot clinical trial. The third generation backplate with the cable design does not suffer from these stress concentrations, as confirmed by fatigue testing (see section 2.e.4.iv).

The set screws are used to secure a titanium cable in place (see Surgical Manual for implant schematic). The titanium cable wire is configured of titanium alloy (Ti-6Al-4V ELI) of 7 wire strands wrapped into a cable then 7 cables each 0.0065” are wrapped together to given a woven cable of 0.05940” and 15.875” in length. The ends of the cable are beaded to protect...
from fraying (see Figure 5D). A torque wrench preset to 0.3N-m is used to tighten the set screws to prevent over or under tightening. Finally, this next generation backplate also contains a small hook for the surgeon to hold on to in order to place or remove the back plate. This is in comparison to the previous backplate, which had no physical hook for the surgeon to grasp, making it very cumbersome to place or remove. In the pilot study, we experienced difficulty finding and grasping the backplate in order to remove it.

Figures 5 (A-D): Next Generation Magnimplant – Assembly drawings by Hayes Manufacturing Services, Inc.

**Figure 5A:** The 3rd generation Magnimplant

**Figure 5B:** Anterior plate. The anterior plate contains an N55 magnet set in a focusing cup.
**Figure 5C:** Posterior plate. The posterior plate design includes channels for running the cable through.
2.e.3. Improvements to the external magnetic orthosis (Magnatract)

The design of the external brace and magnet housing mechanism evolved significantly throughout the initial trial. Key to this evolution was patient feedback at monthly check-ups that gave us insight into reengineering the device throughout the trial. The device evolved from a simple suspend magnet holder in a polypropylene custom brace to a magnet caddy system encompassing three novel functions: (1) the applied magnetic force is completely adjustable by the patient; (2) the force exerted on the implant is measured by a force sensor; and (3)
measured force and temperature data is recorded at 10-minute intervals and stored in a data logger which is downloaded at each follow-up visit.

In the pilot study, we observed that brace wear compliance was directly related to brace design, brace functionality and perceived sense of correction. We learned that patients liked having control over the strength with which the brace pulled on their sternum. The patients enthusiastically participated in reengineering improvements in the device. They also found it motivating to see the read-out of the force-sensing device, which outlines their activity over the last month.

The improved design features are as follows:

1) Incorporating a high-density steel focusing cup optimizes the configuration of the external neodymium magnet (Figure 6c). This focusing cup increases the magnetic force (applied by the external magnet) toward the internal magnet by shielding the force facing away from the brace. To assess this relationship, we tested various external magnet configurations coupled to an implant in an Instron mechanical testing machine and generated force-versus-displacement profiles for each setup. These data values allowed us to determine the configuration that generates adequate levels for force and reduces the weight and profile of the brace. The addition of the focusing cup increased the force between 6-8%.

2) We identified the maximum size constraints of an external housing unit that both completely houses the external magnet, focusing cup, FSR and data logger, and reduces the overall

![Figure 6: Improved Magnatract device. (a) Force sensing resistor (FSR) to measure magnetic coupling of the implant and external magnet; (b) FSR in Magnatract cup; (c) external magnet in magnetic focusing steel cup; (d) internal components of Magnatract cup; (e-f) assembled Magnatract assembly with cup and ring.](image-url)
diameter and height of the can (Figure 6e). A reduction in the overall dimensions of the can improves brace aesthetics and increases patient satisfaction with a slightly more discrete brace.

3) We incorporated a conical dimension to the side of the housing unit facing the patient. This is an important design element because it allows access to much deeper defects and accommodates female patients with developing breasts, without touching the skin.

4) The modified Magnatract can was engineered to improve ease-of-use and comfort (Figure 7 a-f): 1) The design is such that it allows user adjustability by a simple screw device containing the magnet, focusing cup, FSR and data logger. 2) The material used is PVC with a smooth finish. 3) The thread pitch on the outer can allows smooth screwing by the user while maintaining a good mechanical advantage. 4) A low-profile handle was engineered into the anterior face of the screw. By simply twisting the handle, the patient can move the can closer and farther from the internal magnet, therein adjusting the magnetic force.

5) The force sensors originally used in the device were too large and sensitive to shock loads for our application. After modifying the sensors, we incorporated low-profile force sensing resistors (FSRs) into the device (Figures 6a and 6b). FSRs are able to withstand high shock loads (e.g., as observed when a brace drops) and fit easily within the screw housing.

6) Initially, we used an off-the-shelf data logger to measure and record the interval force and temperature. This device was crude, did not allow for customization, and was limited by its dimensions, poor durability, internal memory, battery life, software, and hardware. Therefore, we designed a smaller, more robust device that will accurately measure force and temperature data over extended periods of time that can be easily downloaded from a micro SD card in the data logger.

7) The can evolved to a completely self-contained and sealed unit, but with a micro SD card in the data logger that when removed and plugged into a USB connector to the computer allows the doctor to download the data to a computer. The design specifications for the device are presented in Figure 8.
Figure 7 (a-f): Engineering drawings of the Magnatract can assembly

Figure 7a.

Figure 7b.
Figure 7e.

Figure 7f.

Figure 8: Design specifications for Magnatract can with FSRs and data logger
2.e.4 Characterization of the next generation Magnetic Mini-Mover

The next generation Magnimplant has been optimized in terms of its strength—an N55 magnet versus N42 in the original design. The N55 magnet is custom-manufactured for the investigators. The Magnimplant has also been reconfigured to include a front plate containing the magnet and a flat back plate with channels which cables can be passed through. The device is then attached to the sternum using cable wires.

To address concern about the safety of the magnetic fields generated by the latest version of our investigational device, we characterize the Magnetic Mini-Mover by providing:

i. A force versus displacement curve for the N55 magnet, with and without use of the focusing cups, to demonstrate maximum forces on the sternum (Figures 9 and 10 and Tables 2 and 3);

ii. A magnetic field map across the transverse plane of the highest magnetic intensity with and without use of the focusing cup under normal conditions (Figures 11 and 12 and Tables 4 and 5);

iii. A magnetic field map across the transverse plane of the highest magnetic intensity with and without use of the focusing cup under worst-case conditions (Figures 13 and 14 and Tables 6 and 7);

iv. Magnetic isobars that characterize the highest magnetic field strength experienced by the heart under normal and worst-case conditions.

In addition, because the magnetic field strength of the next generation Magnetic Mini Mover versus the previous device is crucial to assessing risk, also included below are data from magnetic field testing of both versions.

2.e.4.i. Magnimplant v.1 vs. v.2: Force vs Displacement for N55 Magnet

Comparing Magnimplant version 1 (v.1) with version 2 (v.2), the maximum improvement measured with the new implant is 7.90% over the working range of the Magnatract, this correlates to a force of 44.66 N. Both versions 2 and 3 anterior cups have the magnet sitting in a carbon steel cup (1.75" diameter with sides 0.26" deep as pictured in Figure 5b item 2 of the mechanical drawing in the IDE), which is placed in the titanium can (1.95" diameter and 0.328" deep). The carbon steel cup was added in the v.2. design and maintained in the v.3 design to focus the magnetic field outward from the patient. Since the dimensions did not change between the two versions, the magnetic field will not change. The next change on the anterior can are the wings on either side of the can in which the set screws reside (see Figure 5b item 1). Each wing is 1” long and 0.325” wide with a thickness of 0.328”. Although this design change adds 0.325” of length along one axis of the can, this does not change the magnetic field because we are using titanium. Titanium is non-ferromagnetic. Therefore, changes to the titanium can do not change the magnetic field or the exposure to the patient. In the discussion that follows, Magnimplant v.2 is interchangeable with v.3 with regard to the magnet studies for the reasons cited above.
Figure 9 (above): Force versus displacement curve for Magnimplant v.1 (blue) and Magnimplant v.2 (green) coupled with a 2” x 1” N55 NdFeB disc magnet.

<table>
<thead>
<tr>
<th>Blue Implant</th>
<th>Magnimplant v.1</th>
<th>d [mm]</th>
<th>Magnimplant v.1 F [N]</th>
<th>Magnimplant v.2 F [N]</th>
<th>Percent difference</th>
</tr>
</thead>
<tbody>
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<td>Backing -</td>
<td>20</td>
<td>41.13</td>
<td>44.66</td>
<td>7.90%</td>
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<tr>
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<td>29.5</td>
<td>31.41</td>
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<tr>
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<tr>
<td>Strength N42</td>
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<td>16.44</td>
<td>2.49%</td>
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<tr>
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<tr>
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<td>7.21</td>
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</tr>
<tr>
<td>Green Implant</td>
<td>Magnimplant v.2</td>
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<td>5.93</td>
<td>5.81</td>
<td>2.03%</td>
</tr>
<tr>
<td>Backing Focusing cup</td>
<td>60</td>
<td>4.62</td>
<td>4.57</td>
<td>1.20%</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: (top left) Experimental setup for Test 1. (top right), Measured force data in N and calculated % improvement using Magnimplant v.2.

Magnimplant v.2 with (green) and without (purple) the use of a steel focusing cup on the “internal” magnet. The maximum improvement measured with the new implant is 7.90% over the working range of the Magnatract, this correlates to a force of 44.66 N. Maximum force at this point without a magnetic focusing cup is 38.39 N.
Figure 10: Force versus displacement curve for Magnimplant v.2 with (green) and without (purple) a magnetic focusing cup coupled with a 2" x 1" N55 NdFeB disc magnet.

![Force versus displacement curve](image)

### Table 3:

<table>
<thead>
<tr>
<th>Green</th>
<th>Implant</th>
<th>Magnimplant v.2</th>
<th>d [mm]</th>
<th>Cup F [N]</th>
<th>No Cup F [N]</th>
<th>Percent difference</th>
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<tr>
<td></td>
<td>Backing</td>
<td>Focusing cup</td>
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<td>44.66</td>
<td>38.39</td>
<td>14.04%</td>
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<td>Orientation</td>
<td>Symmetric</td>
<td>25</td>
<td>31.41</td>
<td>27.66</td>
<td>11.93%</td>
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<td></td>
<td>Magnet</td>
<td>2&quot; x 1&quot;</td>
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<td>20.46</td>
<td>9.02%</td>
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<tr>
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<td>11.81</td>
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<td></td>
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<td>Setting</td>
<td>Straight</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Table 3: (a) Experimental setup for Test 2. (b) Measured force data for Test 2 in Newton and calculated % improvement using a magnetic focusing cup.

**Magnetic Field Mapping:** Magnetic field maps were generated by measuring the magnetic field for varying configurations of the current Magnimplant (v.1) and the proposed second generation Magnimplant (v.2). Magnetic field was measured in Gauss using a standard Gaussmeter at 0.5 cm intervals along a transverse plane behind the posterior face of the implant. Transverse planes were measured at 0.5 cm intervals from the posterior plate of the implant.

Included are plots of the magnetic field lines behind the posterior face of the implant. These magnetic field maps depict isobars at 0.01 Tesla intervals. The x-axis is in line with the transverse plane along the radius of the Magnimplant with the zero point centered at the implant’s center. Data points were measured in 0.5 cm intervals. The y-axis is the distance from...
the posterior face of the Magnimplant. Raw data accompany all graphs within the range of interest.

### 2.e.4.ii. Magnimplant v.1 vs. v.2: Magnetic Field Map Across Transverse Plane of the Highest Magnetic Intensity w/ and w/o Focusing Cup – Normal Conditions (Experiments 1 and 2)

#### Experiment 1: Magnimplant v.1

Magnetic field is posterior to Magnim-plant v.1 without the external Magna-tract magnet. The maximum strength of the magnetic field on the soft tissue is 0.06 T. The maximum strength of the magnetic field at the level of the heart (2 cm) is 0.02 T.

![Figure 11: Magnetic field map for Magnimplant v.1.](image)

Table 4: Raw data for magnetic field strength (tesla) of Magnimplant v.1.

<table>
<thead>
<tr>
<th>Implant radius (cm)</th>
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<th>0.5</th>
<th>1.0</th>
<th>1.5</th>
<th>2.0</th>
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</table>
Experiment 2: Magnimplant v. 2

Magnetic field is posterior to Magnimplant v.2 without the external Magnatract magnet. The maximum strength of the magnetic field on the soft tissue is 0.06 T. The maximum strength of the magnetic field at the level of the heart (2 cm) is 0.02 T.

**Figure 12:** Magnetic field map for Magnimplant v.2.

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<th>Distance from back of implant (cm)</th>
<th>Implant radius (cm)</th>
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</table>

**Table 5:** Raw data for magnetic field strength of Magnimplant v.2 (measured in teslas.)
2.e.4.iii. Magnimplant v.1 vs. v.2: Magnetic Field Map Across the Transverse Plane of the Highest Magnetic Intensity w/ and w/o Focusing Cup – Worst-case Conditions (Experiments 3 and 4)

**Experiment 3: Magnimplant v.1 with Maximum Magnetic field.** Magnetic field posterior to Magnimplant v.1 with a 2" x 1" N50 NdFeB external magnet separated 1 cm. This is the maximum possible configuration for the Magnimplant v.1 coupled system. The maximum strength of the magnetic field on the soft tissue is 0.20 T. The maximum strength of the magnetic field at the level of the heart (2 cm) is 0.08 T.

**Figure 13:** Magnetic field map for Magnimplant v.1 coupled w/ 2" x 1" N50 NdFeB external magnet with three backing plates separated 1 cm.

### Table 6: Raw data for magnetic field strength (tesla) of Magnimplant v.1 coupled with 2" x 1" N50 NdFeB external magnet separated 1 cm.

<table>
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<tr>
<th>Distance from back of implant (cm)</th>
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<th>1.5</th>
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</tbody>
</table>

*Figure 13: Magnetic field map for Magnimplant v.1 coupled w/2" x 1" N50 NdFeB external magnet with three backing plates separated 1 cm.*
Experiment 4: Magnimplant v.2 with Maximum Magnetic field – (Figure 16)

Magnetic field posterior to Magnimplant v.2 with a 2” x 1” N50 NdFeB external magnet separated 1 cm. This is the maximum possible configuration for the Magnimplant v.2 coupled system. The maximum strength of the magnetic field on the soft tissue is 0.27 T. The maximum strength of the magnetic field at the level of the heart (2 cm) is 0.09 T

**Figure 14**: Magnetic field map for Magnimplant v.2 coupled with 2” x 1” N50 NdFeB external magnet with 3 backing plates separated 1 cm.
Implant radius (cm)

<table>
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<td>0.03</td>
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</tr>
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<td>0.06</td>
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<tr>
<td>4.5</td>
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<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Table 7: Raw data for magnetic field strength (tesla) of Magnimplant v.2 coupled with 2” x 1” N50 NdFeB external magnet separated 1 cm.

2.e.4.iv. Magnimplant v. 2 vs v.3: Load-to-Failure Tensile Strength Testing

Dr. Jenni Buckley, Director of The Taylor Collaboration for Orthopaedic Research, Education, and Innovation at St. Mary’s Medical Center in San Francisco, and previously Mechanical Engineer and Research Director at the Biomedical Testing Facility at San Francisco General Hospital, performed axial load test analysis on the Magnimplant v.2 (single machined back plate). She found that the device failed at the female connector at 4210N, which is 67 times the physiologic load (60N). Magnimplant v.3 underwent load-to-failure and cyclic fatigue testing at Empirical Testing, Corp. The first test performed was a static axial tension test (n=3). The device was fixed in a rig (see appendix 1 for pictorial representation) and placed in an INSTRON device, where the anterior plate was displaced at a rate of 0.2 mm/sec. Under these conditions, the device failed at an initial peak load of 1353 ± 408 N, with failure defined as slippage of the cable at the level of the set screws (20 times physiological load). Axial load continued until there was complete failure of the device at the peak load of 1546 ± 368N where the cables were frayed and/or broke. However, given the loss of integrity that occurred at the initial peak load, we designated this value to be our device failure load. It is unclear if the cable frayed at the initial peak load, as the testing continued and the cable was not examined other than in the jig at the initial peak load testing result.

The second testing scenario was cyclic fatigue testing. The device (n=3) was subject to a sinusoidal load of 30-60N over 15,000,000 cycles to simulate breathing at a rate of 15 breaths per minute for two years. All three devices ran out the 15,000,000 cycles without failure. There was no failure of the device during the fatigue testing. The cable wire was noted to have only the imprint of the set screws from initial hand. However, there was no fraying or destruction of the cables (see Figure 15 a-c). The sinusoidal load was based on literature and studies from Dr. Buckley’s research team as described in Appendix 1. Dr. Buckley’s interpretation of the testing results from Empirical Testing, Corp., which state the above, are included in Appendix 1.
Figure 15 (a-c, below). Pictorial images of titanium cable wire following fatigue testing. Note the indentation in the cable from the set screw, but there is no fraying, breakage, or other damage. The scale of the cable appears to vary below which is due to imaging technique as all cables were the same size of 7 x 7 x 0.0065” wrapped together to a diameter of 0.0594”. Figures 15a, b, c are images taken from testing on devices MI3004, MI3005, and MI3006, respectively.

To avoid under or over-tightening by the surgeon, we tested five more devices using a set torque value of 0.3N-m (equal to hand-tightening) to tighten all 4 set screws in each device and then subject each device to the same axial load testing pattern as before (see Appendix 2 for results and images). We found that this set of 5 devices had a peak load range of 1305 ± 132 N, which is within range of the prior 3 devices tested. The same failure also occurred with slippage which when examined in the jig showed no damage to the cable but upon removal revealed fraying of the cable (see Appendix 2). We have demonstrated that 8 devices can withstand up to 20 times the physiological load with failure of the device as slippage and fraying of the cable. The anterior and back plates of the devices had no identifiable damage (ie, break, bending, degradation, etc). In regards to the fatigue testing, version 2 suffers from high stress concentrations in the back plate, which would lead to premature failure and low fatigue life due to the shape of the male post on the back plate. Version 3, with the cable design, does not suffer from the same stress concentrations and our fatigue testing has proved that it has an acceptable fatigue life as mentioned previously.

To summarize the results of this testing:

a. The maximum increase of the field strength of the Magnimplant alone (i.e., without the Magnatract) at the level of the skin is 4.5%, while field strength is 0.02 tesla in the first generation device and 0.02 tesla in the next generation device. At 2 cm, the field strength decreases by 8.4% (0.0015 tesla) in the next generation Magnimplant. Maximum increase/decrease by percentage is variable across the map. Given the change in the anterior plate of Magnimplant v.3 was only in the shape of the titanium casing and titanium is not ferromagnetic, this had no effect on altering the magnetic field between versions 2 and 3.

b. The maximum field strength of the Magnimplant and Magnatract together (i.e., when the patient is wearing the Magnatract) is 0.08 tesla in version 1 and 0.09 tesla in version 2.

c. No matter what configuration is tested, the maximum increase in magnetic field strength exposure from version 1 to version 2 is 0.071 T. If we define the “worst-case” conditions to be an external magnet (N50, 2” x 1” disc with three steel focusing plates) at a distance of 1 cm, then the worst-case scenario exposure to magnetic field increases by 26.4% or 0.071 T in version 2 compared with version 1 at the level of the skin, and by 15.5% or 0.014 T at 2
This increase in exposure is insignificant because maximum exposure is still orders of magnitude below the level where there is any measurable effect of a static magnetic field on any biologic system (4 T or greater). If the external magnet is off-centered to treat asymmetric cases, then the maximum magnetic field decreases 11.6% or 0.023 T in an asymmetrical setting compared to symmetric at the level of the skin, and decreases by 7.6% or 0.006 T at 2 cm.

d. The Magnimplant using the cable attachment system withstands load strengths at least 20 times that of physiological load levels (60N) or the load between the internal and external magnet pulls (80N). The failure of the device was slippage of the cables at the level of the set screws with fraying. The fatigue testing demonstrated that the device could withstand physiologic conditions over at least a two-year period without any sign of fatigue failure.

In short, the maximum magnetic field exposure of the worst-case configuration of the Magnimplant and Magnatract (implant and 2”x1” N50 external magnet with three focusing plates) is 0.27 T at the surface of the magnet and 0.09 tesla at the level of the heart. Both are many-fold below the level of 4 teslas where any biologic effect of a static magnetic field is detectable. The slight increase in magnetic field strength in version 2 versus version 1 (<4.7%) poses no significant increased risk because the levels are far below 4 teslas.

### 2.6.5. Qualitative assessment of pectus excavatum severity and correction

As noted above, we tried all published and several novel methods of assessing severity of the pectus deformity and found none of them satisfactory or reliable. The standard method of measuring pectus severity is by calculating a Pectus Severity Index from CT scan. While this method was adequate for defining our inclusion criteria, measurement post-implantation was difficult because of magnetic scattering (Figure 16). Moreover, repeat measurement by CT scan is not appropriate due to high doses of radiation.

![Figure 16: Postoperative CT scan to measure Pectus Severity Index with image scatter due to implant.](image)
Chest x-ray as a primary modality to measure PSI in pectus patients has been reported in the recent literature.\textsuperscript{25} We used this method with the intention of developing a trend over the course of each patient’s pectus correction. But, in addition to the supporting literature, there are several reasons to use X-ray rather than CT as long as the PSI can be measured with comparable accuracy: i) CT scan is 200 times the radiation exposure of a chest X-ray, and there is growing concern from pediatric radiologists about long-term cancer risk; ii) Chest X-ray is approximately one-fifth the cost of CT scan; iii) Because of the lower radiation risk, the anatomy of the chest can be documented by X-ray more frequently. However, this technique is limited by several factors, including variation in subject positioning relative to two-dimensional image and variation in patient’s respiratory cycle between visits (altering thoracic dimensions).

Our experience with the ten patients in the current study persuades us that neither CT nor chest x-ray provide adequate assessments of the degree of pectus severity. We discuss this further in the Study Endpoints Section.

Similar to radiographic techniques, documentation of pectus correction by photography was not an adequate method of assessing pectus correction. While the deformity was visibly improving, this was difficult to document with two-dimensional photographs and does not yield quantitative data (Figure 17).

![Figure 17: Postoperative photographs to document sternal position.](image)

We developed a depth gauge to measure the improvement in sternal position by measuring the external improvement in sternal position. This method also had numerous inherent variables in
it, including differences in measurements due to respiratory cycle, difficulty in consistent positioning of the measuring gauge, and no method of normalizing the data to account for patient growth.

While these methods of assessing the improvement in sternal positioning proved to be inadequate for our therapy, our experience has shown that a simple PA and lateral chest x-ray may be as good a method as any for documenting the Pectus Severity Index before treatment starts (i.e., to meet inclusion criteria) and when treatment ends after explantation of the sternal magnet. Other methods of assessing severity are similarly subject to variation with positioning and respiratory cycle. Perhaps the best assessment is that of the patient and their family on a very subjective basis, but this is reflected in the compliance.

2.e.5.i. Measuring brace wear compliance

Success of the 3MP may be dictated by three factors: pectus severity, patient growth maturity, and brace wear compliance, of which patient compliance may carry the most impact. This is simply because if an adolescent patient does not perceive improvement, he or she will not comply with wearing the external device as recommended. It therefore became important to have an accurate measure of compliance, rather than the patient’s verbal report.

We thought that one way to validate the subjects’ self-reporting of brace wear would be to ask them to keep a diary in which they would record brace wear time, as well as describe pain and discomfort, and note their feelings and concerns about study participation. We would review the diary contents at each subject’s monthly follow-up visit. However, the diary failed at being a record of compliance: the medium did not mean anything to patients, as they already talk to their parents and the study investigators. In addition, parents are comfortable e-mailing us with questions or problems. As a result, a data-logging device was developed to record force and temperature information at ten-minute intervals during brace wear. When the patient wears the brace, a force sensor measures the magnetic attraction force between the Magnimplant and external magnet. Within the data logger, a thermistor measures the increase in temperature around the brace due to proximity to patient body heat. These data can then be used to calculate brace wear compliance (Figure 18).

![Figure 18: Force (blue) and temperature (red) data for one month period. Data shows periods of brace wear.](image-url)
In the near future, the patients will plug the data logger into the USB port of a home computer to upload data to our secure web portal system and allow the clinicians to assess their progress from afar rather than only at the monthly visits. In addition, as we have found with our pilot study, the patients are interested in following their own compliance.

2.e.5.ii. Compliance with wearing the external brace
All patients in the first study have been able to wear the brace during day and nighttime activities, including sleep. As mentioned above, compliance was measured objectively with a data logger. Brace wear compliance varies greatly between patients (Table 9). In general, all the patients wear their appliance the majority of the day. We find this remarkable for pre-teen and teenagers who often have many ongoing activities, including school and sports. We also found that wear time increased as the Magnatract itself evolved to become smaller, lighter, easier to hold in place with magnetic force alone, easier to adjust, and easier to use the data logger.

Table 9. Mean brace wear compliance and percent correction at end of treatment.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Total Months in Study</th>
<th>Mean Compliance Over Total Months (%)</th>
<th>Pectus Severity Index (PSI) by CT at Enrollment</th>
<th>Pectus Severity Index (PSI) by CT at One-Month Post Explant</th>
<th>Percent Correction (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>S0001</td>
<td>18</td>
<td>48.8</td>
<td>4.3</td>
<td>3.48</td>
<td>78.1</td>
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<tr>
<td>S0002</td>
<td>17</td>
<td>86.2</td>
<td>3.71</td>
<td>3.55</td>
<td>34.8</td>
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<tr>
<td>S0003</td>
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<td>60.5</td>
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<td>4.24</td>
<td>-182.86</td>
</tr>
<tr>
<td>S0004</td>
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<td>6.1</td>
<td>6.37</td>
<td>-9.5</td>
</tr>
<tr>
<td>S0005</td>
<td>25</td>
<td>61.5</td>
<td>3.96</td>
<td>3.01</td>
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<tr>
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<td>16</td>
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<td>4.19</td>
<td>3.66</td>
<td>56.4</td>
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<tr>
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<td>67.6</td>
<td>7.3</td>
<td>8.12</td>
<td>-20.2</td>
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<tr>
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<td>4.86</td>
<td>3.45**</td>
<td>87.6</td>
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<td>65.6</td>
<td>5.66</td>
<td>7.65</td>
<td>-62.6</td>
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</tbody>
</table>

*Achieved % of ideal correction is defined as: \((\text{PSI}_{\text{pretreatment}} - \text{PSI}_{\text{current}})/(\text{PSI}_{\text{pretreatment}} - \text{PSI}_{\text{cutoff}})\)*100, where PSI_{cutoff} = 3.25 (cut-off value that differentiates normal control from pectus excavatum patient population)*

** S0008 post-treatment PSI was based on a chest x-ray rather than CT scan, as the parents had concerns about additional significant radiation exposure and refused a CT scan, given the amount of radiation exposure the patient had already experienced since the beginning of treatment. S0008 was withdrawn from the study on 5/21/2009, but continued treatment under FDA- and IRB-approved Compassionate Use designation.

References:

2.e.6. Choosing the optimum time for repair

We are learning a great deal about the best time to use the Magnetic Mini-Mover procedure. For the first trial we chose the age range 8 to 14 years of age because that is the most common time when other types of pectus repairs are performed. Experience with 3MP confirms the general impression that most surgeons who perform pectus repairs believe the ideal time of repair is more related to the onset and duration of the rapid growth spurt of puberty than to chronologic age. Repairing pectus too early risks relapse when the patient later goes through the rapid growth spurt. Repairing pectus too late is more difficult because the chest wall and the deformity have already stabilized. Decreased compliance makes the repair extremely difficult.

Our strong impression from our first 10 patients is that the ideal time of repair is at the onset of the rapid growth spurt of puberty, and the ideal time to end treatment and remove the magnet is when the chest stabilizes at the end of the rapid growth spurt of puberty (Tables 10a and b). Until now it has been difficult to predict when this occurs. However, we have consulted with pediatric orthopaedic surgeons treating scoliosis to determine the optimum time for intervention and treatment, whether bracing or surgery, is just at the beginning of the rapid growth spurt. Pediatric orthopaedic surgeons have devoted a great deal of effort to trying to define the onset of puberty, even before maturation changes such as the tannin index or hormonal changes. Fortunately, they have developed a simple, safe, reliable method, which is the Digital Skeletal Age. From a simple X-ray of the left hand, using a detailed analysis of the relation of the epiphyses to the metaphysis of the proximal phalanges, called Tanner-Whitehouse-III staging system [Sanders JO et al. Predicting scoliosis progression from skeletal maturity: a simplified classification during adolescence. J Bone Joint Surg Am 2008;90(3):540-53].

<table>
<thead>
<tr>
<th>Table 10a.</th>
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</thead>
<tbody>
<tr>
<td>Age at Implant (years)</td>
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<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>11</td>
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<td>12</td>
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Table 10b. (below)

Tables 10a and 10b. The youngest (pre- and early pubertal) patients had the best response to treatment. 3MP works best in this subset of patients whose cartilaginous chest walls are deformed, but are still compliant. However, 3MP does not work in patients who have gone through the pubertal growth spurt and have deformed, but now non-compliant, cartilaginous chest walls. The average correction seen in children who were older at the time of implant was clearly worse. The proposed second trial will use the more reliable bone age, rather than highly variable chronologic age, as entry criteria.
It has been suggested that biochemical indicators of puberty, such as LH, FSH, and sex hormones be added to the radiological evaluation of the left wrist. Certainly, biochemical markers of puberty would be useful if the actual timing of puberty were required to make the decision about the initiation of the pectus repair. But gonadotropin and sex hormone levels are variable even within any given Tanner stage. In addition, for this study, knowing exactly where the patient is in puberty is not the point. Rather, what is needed for this treatment is an assessment of skeletal maturation, not puberty; they are not the same thing, although they are usually highly correlated. The process of skeletal maturation involves the lengthening, then the fusing of the epiphyses of the long bones in response to estrogen; this will occur at the same time in either the phalanges (Tanner-Whitehouse) or in the ribs. Since the degree of skeletal maturation is what is in question here, the bone age is a better indicator of the phenomenon we are trying to time. Thus, we can use serial bone age radiographs (every 6 months) to assess the degree of epiphyseal maturation in order to plan the timing of the surgery. In fact, better markers of puberty would be Tanner staging on physical exam and the patient’s height velocity (as these measure sex hormone effect, not levels), which will occur concurrently with the bone age radiographs.

References:


With this reliable way to predict the onset of puberty, we have a simple, safe way to estimate the optimal time to implant the Magnimplant. We thus propose to enroll patients in our study anytime after the age of 8 (but before the age of 15) with the onset of pubertal growth as seen through hand x-ray read by Dr. Lustig and using the Tanner-Whitehouse-III staging system.

2.e.7. Defining success or failure of the treatment: Study endpoints

The primary endpoint is, of course, anatomic correction. We have developed a formula to express percent (%) improvement that will allow us to quantify how much the PSI has moved toward normal (see below). This equation will allow us to relate compliance measures as percent wear time with anatomic improvement measured as % improvement in PSI. Our predefined criterion for the success of this study will be a 50% improvement in PSI, as measured by CT scan pre-implantation and post-explantation, making this study the first to use any objective criteria for success. The final degree of correction may or may not be better than the Ravich or Nuss procedures due to neither reporting a PSI after repair and never being studied in a proper trial. There is no evidence that these procedures achieve 100% correction, especially in patients with a high PSI.

But we must also recognize the limitations of PSI measurements. Perhaps the most surprising thing we have learned from our experience so far is that our attempts to quantify pectus severity and, therefore, document the results of treatment are unsatisfactory. While Pectus Severity
Index measured by x-ray is equivalent to that measured by CT, both are inaccurate. Variability in measurement by chest x-ray and CT is due to the effects of the respiratory cycle and patient position, which we cannot control. For instance, although we tried to standardize the chest x-ray procedure by having a single radiologist, a study consulting radiologist, read the films, the variability is significant. A central conclusion from this experience is that it is very difficult to standardize Pectus Severity Index measurements, even within individual patients.

This conclusion can be further illustrated from the literature. Nakagawa et al performed the only large-scale study in which they examined CT index (CTi) before and after Nuss repair. The authors studied 150 patients, comparing pre-operative CT with post-removal of the Nuss bar CT. Their study shows a wide range of CT values. Of particular interest is PSI in control patients, which ranges from 1.92 to 3.70, suggesting that some of these random, supposedly normal patients have a pectus deformity.

**Table 1.** Findings of pre- and post-CTi and control CTi in the Nakagawa et al** study.

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-CTi</td>
<td>5.97 ± 3.31</td>
<td>2.63-33.3</td>
</tr>
<tr>
<td>Post-CTi</td>
<td>3.08 ± 0.64</td>
<td>1.96-6.25</td>
</tr>
<tr>
<td>CTi of control</td>
<td>2.47 ± 0.32†</td>
<td>1.92-3.70</td>
</tr>
</tbody>
</table>

* P < .001 compared with pre-CTi.
† P = .17 compared with post-CTi.

At this point in the present study of ten patients, we have learned that a measurement of correction will be the comparison of pre-treatment PSI (by CT) to the post-treatment PSI, which is what we propose to do in next trial. The calculation of percent correction follows the formula:

$$Percent\text{Correction} = \frac{\text{PSI}_{\text{Post-treatment}} - \text{PSI}_{\text{Cut-off}}}{\text{PSI}_{\text{Post-treatment}} - \text{PSI}_{\text{Cut-off}}} \times 100 \%$$

where \( \text{PSI}_{\text{Cut-off}} = 3.25 \)

This is how we will report the results of the present and next study. We must recognize that the variability in the single measurement is such that large differences can be reliably detected over years rather than month-to-month. In the future trial, we propose doing interval chest x-rays primarily for safety (i.e., to confirm the position and integrity of the Magnimplant) and secondarily for calculating interval PSI. The primary outcome will be reported as percent correction over the entire treatment period, with 50% improvement the criterion for success of the treatment.

The secondary endpoint is patient satisfaction with both cosmetic result and any physiologic improvement. This endpoint will be assessed with a questionnaire administered at the beginning and end of treatment (one month and one year post-explantation). Physiologic improvement is the major reason for surgical intervention of any type. But, the cost of redoing the studies by Fonkalsrud, Beisner, and Nuss correlating PSI and physiologic effect is prohibitive. Therefore, we make the claim based on clinical intuition that by achieving the same anatomic correction (as with the Nuss or the Ravitch) we will achieve comparable physiologic improvement. This has proven to be the case in our present trial, where interim analysis reveals...
significant self-reported symptomatic and exercise tolerance improvement with the gradual remodeling of the chest. Kelly et al also suggest that surgical repair of pectus excavatum can significantly improve the body image difficulties and limitations on physical activity experienced by patients.27

Finally, we believe the answers patients provide in the Quality of Life questionnaire administered after treatment may provide additional insight. Subjects in the pilot study were administered Quality-of-Life questionnaires at the beginning (one month post-implant) and end of treatment (one month post-explant). In brief, one patient was very satisfied with the correction, four patients were satisfied, one was unsure, two were very dissatisfied and two chose not to answer this question.

2.e.8. Cost effectiveness of the treatment
We have demonstrated that the 3MP can be accomplished in a relatively short procedure (< 1 hour) in an outpatient setting and that it does not require hospitalization for pain management. This is in stark contrast to both the Ravitch and Nuss procedures. In the pilot study, these factors contributed to a significant cost savings in healthcare dollars, as well as to the ease and speed with which our patients returned to normal activities, including sports and dance. Standard treatment for PE costs, on average, $80,000; the 3MP averaged $46,000.

In summary, what we have learned so far from our Phase II study using the first generation Magnimplant:
1. **Implant Procedure**: Operating time decreased from 105 to 43 minutes as implant techniques evolved.
2. **Brace Wear Compliance**: Wear-time increased as brace design evolved.
3. Our results to date suggest that the Magnetic Mini-Mover Procedure is a safe, outpatient, minimally-invasive, and cost-effective treatment for pectus excavatum; and patients are increasingly compliant in wearing the external magnet throughout the day and night.

2.f. References


§ 3. Investigational Plan

3.a. Purpose, Specific Aim, and Duration of the Investigation:

**Purpose:** Our ongoing FDA-sponsored phase I-II study of 10 patients, ages 8-14, with a Pectus Severity Index > 3.50, establishes a safety record for the 3MP and allows proof of concept. This study has also led to design improvements in both the Magnimplant and external Magnatract (the components of the Magnetic Mini-Mover Procedure) and method of manufacturing of the next generation device. Additional data that demonstrates sufficient safety and probable benefit is necessary to support an application for Humanitarian Device Exemption (HDE). Therefore, we will study the second-generation 3MP (under IDE #G090006) in 15 additional patients.

Nothing differentiates our patient population from those requiring surgical intervention using present techniques. The 3MP as opposed to the Nuss or Ravitch may potentially be much safer (deaths have occurred with both of these other procedures), as well as less morbid (an outpatient procedure versus a 3-7-day hospital stay), and less expensive because there is no expected hospital stay. We chose a PSI > 3.5 to be even more stringent about having a significantly severe defect than that defined by clinicians and all insurance companies today, that is, a pectus severity index (PSI) greater than 3.25.

We believe that data from this device will be poolable with the data from the previous generation of 3MP because the design improvements on the new implant are minor, the change in magnetic field strength is non-significant at less than 4.7 %, and the changes in the Magnatract device do not increase risk to the subjects. In addition, patients in the first study have been the beneficiaries of ongoing refinements and improvements in the Magnatract, the configuration of which is carried over as the next generation Magnatract.

Finally, we expect the variability in compliance will affect the effectiveness of the treatment. The improved monitoring system consisting of a data sensor/data logger may allow better documentation of the degree of compliance, that is, percentage wear time, continuously. In a total of 10, 15, or 25 patients, it may be difficult to correlate effectiveness, i.e., movement of the sternum, with the time of wear and the amount of pressure applied, as these subjects, although they all meet the same inclusion criteria, represent variability amongst themselves with regard to defect severity, skeletal maturity, brace size, external magnet type/size. We can attempt to perform statistical stratification on all data time points, and certainly analyze within-patient changes using established statistical methods, including calculation of means, comparisons by Student's paired t test, etc.

**Specific Aims:**

1. **To establish the optimal age and duration of treatment:** The initial results of the first trial suggest that treatment is best started and completed during the pubertal growth spurt. We will use biological markers of puberty (wrist bone maturation on x-ray or growth velocity) with the goal of starting treatment before the pubertal growth spurt (generally, ages 8-11 in females and ages 9-12 in males), and explanting after the chest wall stabilizes at the end of the growth spurt. We will continue to use a Pectus Severity Index of > 3.50 even though the industry standard for payment for repair using any method is a Pectus Severity Index > 3.25.

2. **To assess optimal outpatient management and follow-up:** We will replace interval CT scans (high radiation) with simple chest x-ray to measure pectus severity and will study compliance by monthly downloads of recorded data on a SIM card from the re-engineered Magnatract device.
3. To assess effectiveness of the treatment, we will compare PSI obtained by CT scan pre-implantation to PSI obtained by CT scan post-explantation.

4. To assess clinical site variability and reproducibility of results of the 3MP: Enrollment, treatment, and follow-up will occur at UCSF and two other collaborating centers.

Duration: Duration of the investigation will be 48 months, with patient enrollment occurring in the first 12 months. Implant time will be 18-24 months to accommodate patients who take longer to finish puberty and achieve chest growth stabilization. We will conduct long-term follow-up, seeing the patients at six-month intervals for two years post-explantation. However, we will propose a possible fifth year of investigation, if needed.

3.b. Protocol

In a multicenter Phase III-IV trial, we will further test the safety and efficacy of the second generation magnetic Mini-Mover in correcting pectus excavatum in 15 patients. A rare earth magnet encased in FDA-approved titanium as described above will be implanted securely on the outer surface of the lower end of the sternum in 15 patients with pectus excavatum. This is accomplished as an outpatient procedure, under brief general anesthesia.

We will base patient selection on the following inclusion/exclusion criteria (also see page:

**Inclusion Criteria:**
1. Otherwise healthy male/female with pectus excavatum
2. Age 8-14 years*
3. Pectus severity >3.5
4. Ability to read, speak and understand English
5. Onset of rapid pubertal growth documented by hand/wrist x-ray
6. Early to mid-puberty§ (Bone age F: 7-13 y; M: 9-14 y) from hand/wrist x-ray

**Exclusion Criteria:**
1. Other congenital anomalies (including significant skeletal anomalies-scoliosis, bony fusion of cervical vertebrae, etc) not directly related to pectus excavatum
2. Bleeding disorders
3. Heart disease (including arrhythmia)
4. Persons with active implantable medical devices (AIMD) - pacemakers
5. Persons living in the household with an implanted pacemaker
6. Persons with arteriovenous malformations
7. Chest deformity more complicated than pectus excavatum (eg. Poland syndrome)
8. Persons for whom an implantable foreign body would be harmful (eg. immunodeficiency)

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Note:
* - This age range is specific to the patient’s chronological age
§ - Within the chronological age of 8-14 years, patients will be screened based on their bone age on hand-wrist x-ray, with enrollment at early puberty based on bone age (F 7-13 years and M 9-14 years). Additionally, patients will be enrolled not only based on their chronological and bone age but also secondary sex characteristics and growth spurt
9. Persons at increased risk for general anesthesia (eg. malignant hyperthermia)
10. Respiratory conditions that have required steroid treatment (eg prednisone) in last 3 years
11. Pregnancy
12. Inability to understand or follow instructions
13. Refusal to wear the external brace
14. Refusal to undergo monthly chest x-rays
15. Inability or refusal to return to trial institution biweekly then monthly for clinic appointments for 24 months
16. Inability to obtain pre-approval (authorization) from the patient’s insurance carrier
17. Hand/wrist x-ray:
   a. Pre-puberty (Bone age F: <7y; M<9y)
   b. Late puberty/post-puberty (Bone age F: >13y; M>14y)

For patients ages 8-14, we will use the following surgical technique. A 2-inch transverse skin incision is made at the junction of the sternum and the xiphoid, and the space in front and behind the sternum dissected bluntly. The titanium can containing the magnet is securely fixed to the sternum by a cable around the sternum which is placed through a titanium plate behind the sternum and the cable is brought forward and up through the sternum to be secured by set screws in the titanium can. The procedure takes about one hour, and the patient can go home the same day.

After allowing at least two weeks for healing of the small skin incision, an external orthotic device “Magnatract” is fitted specifically to the patient’s chest wall deformity. A calibrated meter in the external device measures the force applied between the two magnets. When the patient and family are comfortable with the device, the measurement of force is operational, and the assessment of comfort and skin condition is suitable for wearing the Magnatract, the patient will be allowed to take the external device home and begin the process of gradually advancing the sternum forward as the abnormal costal cartilage is reformed. The patient will be seen bi-weekly during the first month after surgery to implant the device.

After the first month after surgery to implant the Magnimplant, the patient will be seen at least every month to assess comfort and skin condition. However, the patient will be seen at any time if indicated by symptoms or signs of a problem.

The endpoints are anatomic correction and patient satisfaction. The change in chest wall shape in response to the Magnetic Mini-Mover Procedure will be assessed by visual appearance (photographs) at one-month intervals, and by chest CT measurement of Pectus Severity Index at one month post-explant. An outcome variable will be the amount of time necessary to reach this endpoint. The number of chest x-rays and CT scans performed per patient are:

<table>
<thead>
<tr>
<th></th>
<th>Enrollment</th>
<th>Monthly post-implant (1-24 months)</th>
<th>One-month post explant</th>
<th>Total images performed per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest CT</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>0</td>
<td>24</td>
<td>0</td>
<td>24</td>
</tr>
</tbody>
</table>

We learned that the only meaningful measurement of correction is the comparison of pre-treatment PSI to the post-treatment PSI, both by CT scan. We will express percent improvement, which will allow us to quantify how much the PSI has moved toward normal, as follows:
The equation relates compliance measured as percent wear time with anatomic improvement measured as percent improvement in PSI. We will use a 50% improvement in the PSI as our pre-defined criterion of success of the treatment. We must recognize that the variability in the single measurement is such that large differences can be reliably detected over several months or yearly rather than month-to-month.

Secondary outcome measures are related to safety, comfort, and stability of the correction long-term. The secondary endpoint of patient satisfaction will relate to both cosmetic result and any physiologic improvement. This endpoint will be assessed with a questionnaire administered at the beginning and end of treatment. While physiologic improvement is the major reason for surgical intervention of any type, the cost of redoing the studies by Fonkalsrud, Beisner, and Nuss correlating PSI and physiologic effect is prohibitive. Therefore, we hypothesize, based on clinical intuition and experience, that by achieving the same anatomic correction (as with the Nuss or the Ravitch) the 3MP will achieve comparable physiologic improvement. This proved to be the case in the pilot study, where interim analysis revealed significant self-reported symptomatic and exercise tolerance improvement with the gradual remodeling of the chest. Kelly et al also suggest that surgical repair of pectus excavatum can significantly improve the body image difficulties and limitations on physical activity experienced by patients.27

Finally, we will conduct 6, 12, 18 and 24-month post-explantation follow-up visits to evaluate the patient for worsening or recurrence of the chest wall defect.

With regard to safety, all adverse reactions will be recorded and reported to the IRB and the FDA, including complications from implantation of the device, complications from application of the external device over time including discomfort and changes in skin.

At the conclusion of the study of 15 patients, the results will be reported in peer-reviewed medical literature.

3.b.1. STOPPING RULES

The study will be stopped if any of the following events occur:

- Patient death related to the treatment; or
- Development of mediastinitis and/or severe pulmonary complications related to treatment; or
- Any cardiac event that could be related to the treatment. (Note: Any cardiac event that can be related to the treatment will be viewed as serious.)

3.c. Risk Analysis and Patient Population

3.c.1. RISK ANALYSIS: Surgical Procedure to Place (and Later Remove) the Magnimplant Device.

The outpatient surgical procedure to attach the titanium “Magnimplant” to the sternum requires general anesthesia (approximately 60 minutes), a 2-inch substernal incision, and blunt dissection of the lower end of the sternum.
• There is a risk of injury from general anesthesia. An anesthesiologist will monitor patients throughout the procedure. Postoperatively, the patients will remain at the Post-Anesthesia Care Unit (PACU) until they are deemed stable to return home.

• There is a risk of significant injury from drilling the hole in the sternum to place the magnetic button device and from removing the piece of costal cartilage. This risk will be minimized by putting a stainless steel malleable retractor under the sternum before the drill is passed or the piece of cartilage is removed.

• There is a risk of injury to surrounding structure(s) and/or air/fluid in the pleura cavity. There is a small chance (less than 1%) of injury to the surrounding structures, but a likely possibility that some air gets into the sac surrounding the lung (entrained air or "pneumothorax"), or fluid gets in the sac around the lung (hydrothorax), and/or blood gets in the sac around the lung (hemothorax). This risk is associated with thoracic surgery in general, including the 3M procedure as well as the Nuss or Ravitch repair procedures for pectus excavatum [Kelly RE et al. Prospective multicenter study of surgical correction of pectus excavatum: design, perioperative complications, pain, and baseline pulmonary function facilitated by internet-based data collection. J Am Coll Surg 2007;205;205-16]. This risk will be minimized by performing intra-operative imaging to detect this complication and routine evacuation of entrained air to either prevent or remedy this complication in the operating room. Long-term efforts will include modification of surgical technique and either modification of shape or reduction of size of device.

• The usual risk of bleeding and infection are equivalent to the risk of any surgical intervention. However, if infection develops, treatment with antibiotics would ensue and possible removal of the device (less than 1%).

• There is a risk of prolonged or persistent pain. If pain persists (>2 weeks) due to the implant pulling on the sternum, either the strength of the external magnet will be adjusted and/or wear-time of the external brace will be reduced. To prevent prolonged or persistent pain due to the implant being secured too tightly to the sternum, the surgeon will hand-tighten the screws rather than use a ratchet wrench.

• There is a possibility that a seroma could develop around the device or in the space following extant of the device. Most seromas are reabsorbed back into the body in about a month or less. If the area becomes painful, infected or the seroma does not improve, it can be drained and antibiotic treatment may be initiated for infection.

• The procedure to remove the implant when the correction is complete is similar in magnitude and risks to the initial procedure.

3.c.2. RISK ANALYSIS: Risk of Injury from a Magnet Encased in Titanium

The Magnimplant contains a rare earth magnet, which, if exposed to the body, would pose an unknown risk. However, the potential risk is minimized by proper isolation of the magnet from the body tissue and fluid.

The Magnimplant is constructed in a manner that uses materials and methods used in many existing FDA approved medical devices. The material for the hermetic enclosure and attachments is titanium. Hermeticity is assured by means of encapsulation with a Helium/Argon atmosphere for subsequent testing through gross and fine leak test methods. The design principles have been adopted from those used in the manufacture of implantable CRM (cardiac...
Detailed information regarding performance standards, sterilization, manufacturing, validation procedures, and sterility assurance level has now been included in the Appendix of this application.

3.c.3. RISK ANALYSIS: Safety of a Static Magnetic Field on Human Tissue.

Magnetic fields have been extensively studied in relation to human health and effect on human tissue, both at a gross and microscopic level. A particular concern is the establishment of a magnetic field in close anatomic proximity to the heart and to blood flow through the heart (see below). Fortunately, these risks have been well studied by biophysicists interested in establishing the effects of electrical and magnetic fields, usually for the purposes of diagnostic imaging procedures such X-ray, computer tomography (CT), and particularly magnetic resonance imaging (MRI). The upshot of these extensive analyses is that there is no detectable effect on tissues from exposure to magnetic field strength below those generated by the supermagnets used in MRI. In general, that field strength is approximately above 4 teslas (T) and usually above 7T. The implantable magnet in our procedure has a maximum field strength at the outer surface of the magnet of 0.04T and the field strength, of course, falls off rapidly with distance from the magnet. The closest the heart could come to the implanted magnet is at least 2 cm, since the magnet is on the outside surface of the sternum. We have measured the field strength of magnets in the proposed configurations. We were concerned that the magnetic field might increase when the second, external magnet is placed on the outside of the chest in front of the sternum. However, the tesla field strength, while it might increase between the magnets, actually diminishes on the back of the magnets by their interaction with each other. Our measurements show that the tesla field strength deep to the internal magnet can never exceed 0.04 tesla, no matter what the interaction with the external magnet, and the maximum field strength 2 cm from the underside of the implanted magnet (i.e., the closest to the outside surface of the heart) cannot exceed 0.02 tesla. Although the Magnimplant titanium can housing the magnet has changed in configuration, titanium is not ferromagnetic so the magnetic field is not altered by the new configuration and poses no further risk than what has already been described.

3.c.4. RISK ANALYSIS: Safety of a Static Magnetic Field on the Beating Heart

A particular concern is the theoretical possibility that the small magnetic field adjacent to the internal implanted magnet might have an effect on the heart by virtue of blood flow through this magnetic field. A very particular concern is whether blood flow through a magnetic field could generate current that could possibly affect the conduction system of the heart and cause arrhythmias. Fortunately, this concern has been addressed by Thomas S. Tenforde in studies reviewed in his article “Magnetically induced electric fields and currents in the circulatory system” (Progress in Biophysics and Molecular Biology 2005;87:279-288). Dr. Tenforde, after reviewing the literature and all available studies, concludes, “...The results of many studies in cardiovascular performance during exposure to static magnetic fields up to 2 T have not shown significant effects on either cardiac function or the dynamic properties of blood flow.”

The safety of our patients is our most important consideration. That is why we re-designed our device so that the magnet itself was in a subcutaneous position on the outer side of the sternum (rather than inside the chest attached to the underside of the sternum). We then measured that the maximum field strength at the surface of the heart and found it to be no greater than 0.02 T.
We have combed the rather extensive scientific literature and found that static magnetic fields less than 4 T (or 200x the field strength at the surface of the heart) have no measurable effect on living tissue in extensive animal experiments conducted over a relatively short time (< two weeks). Like the FDA, we were concerned that there could still possibly be some effect from exposure from the longer duration necessary to correct the pectus deformity (3 to 12 months). We asked two experts, Dr. Tenforde as well as Dr. Thomas Budinger, who spent their careers studying the biologic effects of magnetic fields, whether there could be biologic effects from long-term exposure, even though there is no demonstrable effect from shorter-term exposure.

- **Studies on long-term exposure of workers to electromagnetic fields.** We have studied five reports of very carefully conducted research examining large populations of workers exposed to high magnetic field strengths for long periods of time in electric transmission and aluminum plants. In these very large population-based studies involving many thousands of workers, both in the United Kingdom and the U.S., there was no demonstrable ill effects in the incidence of cardiac disease or arrhythmias, nor in the development of tumors, particularly hematopoietic tumors, i.e., leukemia.

**Effect of Magnetic Field Exposure on Human Tissue**
5. Sommer AM et al. (38 weeks) The risk of lymphoma in AKR/J mice does not rise with chronic exposure to 50 Hz magnetic fields (1 micro T and 100 micro T). Radiat Res 2004;162(2):194-200.

**Use of Magnets for Medical Therapy**

**3.c.5. RISK ANALYSIS: Safety of a Static Magnetic Field on Patient's Environment**
To evaluate whether a magnetic mini-mover device could be a danger to the environment, we considered two situations.

First, the implanted magnet alone (i.e., without the external device): In this case, we have measured the flux fields produced outside the patient by the implanted magnet. The outer surface of the magnet will be 1 to 3 cm from the skin, depending on body habitus. In the worse case scenario, the flux field at the level of another person in very close contact, for instance, hugging, would be **0.07 T**. Of course, the force field drops off rapidly so that anything less than a tight hug would yield less than **0.02 T**. Six inches from the skin there is **minimal (0.0005 T)** measurable field. So there is no danger of triggering any device that is no closer than 6".

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Second, the outer magnet brace with the other magnet in place: We have measured the magnetic force fields facing out from the other surface of this brace, with and without a metal shield (Figure 20). The design of the brace requires an additional 1 cm distance from the face of the magnet and the outer lid of the can. Since the inner and outer magnets are symmetrical in configuration, the same force fields face outward as inward in this configuration. Thus, at the surface of the device, the measured force field is 0.075 T. We then added a thin ferromagnet metal shield to the outside of the external brace, and measured the force field at 0.063 T at the surface of the device and 0.033 T at 3 cm from the surface of the device.

Figure 20: Using the Gaussmeter, actual measurements of the magnetic field without (150 Gauss) and with (10 Gauss) the shield in place.

We have then consulted the literature, bioengineers, and device companies about the safety of various implanted devices with magnetic fields. Most implanted devices with reed switches will not be affected in magnetic fields less than 1 μT. It is possible to reach this level with close contact, such as might be achieved in a tight hug in which the magnet in the external brace happened to line up with the implanted device in the other person’s chest or abdomen. Of course, this is no different than any magnet (e.g., refrigerator magnet), but certainly requires vigilance to avoid proximity to vulnerable devices by the patient and their families. We will have a warning label on the external device itself about close contact with individuals with pacemakers and nerve stimulators. In addition, we will place warnings in the insert and of course educate the patients and families about the possibility of interaction with someone else’s device.

3.c.6. RISK ANALYSIS: Risk of Injury from the Magnimplant Breaking while Implanted

There is a risk that the magnet implant could break into two or more parts, which will require surgery to remove the device. In three of ten patients in the previous study, the backplate separated from the post that holds the magnet in place. It is important to note that the Magnimplant broke in the same place in all three patients. The events were found on chest x-ray taken during a scheduled follow-up visit. In the re-engineered device, a cable is wrapped around the sternum to hold it in place. We have performed static and fatigue testing that revealed the Magnimplant generation III will hold up to 20 times physiologic conditions with failure as slippage of the titanium cable at the set screw point. The fatigue testing subjected the device to sinusoidal loads of 30N to 60N over a 2 year period (15,000,000 cycles) and no failure was noted of the device (see Appendix for testing results and full report analysis). Our preclinical studies of Magnimplant generation III reveals a device that should not break. However, we will continue to perform monthly chest x-rays to monitor the integrity of the device and if it does break, it will be promptly removed.
**Plan for surgical revision/rescue and failed treatment when device breaks:** To ensure the Magnimplant remains intact and in place, all chest x-ray requisitions will include a request to the radiologist to evaluate and report on the integrity of the implanted magnet within 72 hours. Furthermore, the PI or one of the surgical Co-Investigators will personally review all chest x-rays at each patient’s visit, report the findings to the patient and family, and include the findings in the dictated note.

Should the Magnimplant break or uncouple, the device will be explanted (even though the previous broken implants have been found to be encased in a fibrous capsule and not causing apparent harm). The device will be explanted using the same surgical explant manual as used in the planned 18-to-24-month explant procedure. In our current study, our follow up protocol for scheduled explant is an appointment one-month following explant which includes a CT scan of the thorax, a quality of life questionnaire and an EKG performed. The one-year post-explant follow up is a clinic visit and a second quality of life questionnaire. We will perform this same follow up procedure for patients who are explanted due to device failure, a cause other than a scheduled explant, or a scheduled explant.

In the multicenter trial the follow up plan for a scheduled explant is a one-month post explant clinic visit followed by 6-month interval (6, 12, 18, and 24-months) clinic visits. Again, patients who undergo explant for reasons other than a scheduled explant will follow the same follow up plan as a scheduled explant in the multicenter trial: a one-month post-explant visit which includes a chest x-ray, EKG and quality of life questionnaire, followed by a clinical assessment at 6, 12, 18 and 24-months post-explant, and a quality of life questionnaire at the 12-month follow up. If a patient were to undergo revision and not removal of the explant in the multicenter trial, the patient will continue with treatment as outlined in the study protocol: monthly clinic visits until explant; EKG and chest CT at one month post-explantation; QOL questionnaire at one month and one year post-explantation; and post-explantation visits at six-month intervals for two years.

Patients and their parents will be instructed to contact us immediately if there is any problem, unusual symptom or changes in the child’s health, whether or not it seems related to the 3MP treatment, including wound issues or any symptom related to the sternum. We will recommend the patient come see us the same day or within 1-3 days, with the appropriate steps taken to diagnose and treat the problem.

**3.c.7. RISK ANALYSIS: Metal Objects Being Attracted to the Device**

Because there is a magnetic field outside the body over the magnet, individuals with an implanted magnet will be made aware that ferromagnetic materials, like iron or another magnet, could be attracted to the implanted device if brought close enough. Any object that is attracted and stays in place on the skin over the implanted magnet could cause pain and even damage to the skin. These objects should be carefully avoided or quickly removed.

**3.c.8. RISK ANALYSIS: Skin Damage**

Application of the external component of this device, Magnatract, applies pressure to the skin and soft tissue over the ribs around the defect, and may cause damage to these tissues. Tissue damage is signaled by pain, tenderness, and redness where the Magnatract device contacts the skin.

Damage to skin will be avoided by adjusting the strength with which the Magnatract pulls on the internal magnet. This is done by adjusting the position of the external magnet in the Magnatract device. Individuals wearing the external device must be vigilant about tissue damage. This is signaled by pain, tenderness, and redness where the Magnatract device contacts the skin.
3.c.9. RISK ANALYSIS: Other People with Pacemakers

Individuals with implanted cardiac pacemakers or nerve stimulation devices are aware that they should not come in contact with magnetic fields that could affect their devices. Likewise, persons with a magnet implanted on the chest and persons with an implanted magnet and the external magnet brace in place must be aware to not come in close contact with other individuals with those devices. The following statement will be provided in writing and discussed with patients.

*The safe distance from your magnet to an implanted device in another person is six (6) inches. Therefore, you should never have your chest wall magnet any closer than 6 inches from another device. In other words, never embrace or hug someone with a device that is sensitive to magnetic fields.*

3.c.10. RISK ANALYSIS: MRI

There is a risk of injury from any strong magnetic field such as a magnetic resonance imaging (MRI) machine. Persons using the Magnetic Mini-Mover will be advised that they should never have an MRI or come close to an MRI machine, until the device is removed. For the study, we provide the patients with a MedicAlert wristband or dog tag that states "No MRI".

3.c.11. PATIENT SELECTION/ENROLLMENT

Residents of the United States with previously diagnosed pectus excavatum who are referred for evaluation and treatment will be considered for the study. Only patients with moderate to severe pectus excavatum who meet all the inclusion criteria will participate. The patient and family will be fully counseled and consented about the risks and benefits of participation in the study, and will be asked to sign an informed consent reviewed and approved by the institutional review board overseeing human subjects research.

**Inclusion Criteria**

The inclusion criteria for the trial are, in brief, as follows:
1. Otherwise healthy male or female with pectus excavatum deformity.
2. $8 < \text{Age} < 14$ years of age
3. Pectus Severity Index $> 3.5$ (normal 2.56)
4. Ability to read, speak, and understand English
5. Onset of rapid growth of puberty documented by hand x-ray

Dr. Robert Lustig, Professor of Clinical Pediatrics and Chief of Pediatric Endocrinology at UCSF, has particular expertise interpreting hand x-rays to determine the pubertal growth spurt. The Radiology Department at UCSF refers the interpretation of hand x-rays for growth spurt analysis to him. Both he and we recognize that biochemical indicators of puberty, such as LH, FSH, and sex hormones, could be added to the radiological evaluation of the left wrist, as they would be useful if the actual timing of puberty were required to make the decision about the initiation of the pectus repair. But gonadotropin and sex hormone levels are variable even within any given Tanner staging [Albertsson-Wikland et al. J Clin Endocrinol Metab 1997; 82:541-549]. In addition, for this study, knowing exactly where the patient is in puberty is not the point. Rather, what is needed for this study is an assessment of skeletal maturation, not puberty; they are not the same thing, although they are usually highly correlated. The process of skeletal maturation involves the lengthening, then the fusing of the epiphyses of the long bones in response to estrogen; this will occur at the same time in either the phalanges (Tanner-Whitehouse) or in the
ribs [Tanner M et al. Clin Endocrinol Metab. 1986;15:411-51]. Because the degree of skeletal maturation is what is in question here, the bone age is a better indicator of the phenomenon we are trying to time. Thus, we can use bone age radiographs to assess the degree of epiphyseal maturation in order to plan the timing of the surgery.

Second, inclusion criteria based on lung capacity are not included because we are not measuring the lung capacity. Physiologic parameters have been correlated with the Pectus Severity Index, which we are measuring as the primary outcome variable.

Third, rather than an inclusion criterion that the patient must have a normal EKG, we include a statement about abnormal EKG in the exclusion criteria. We do not have an objective measure of cardiac performance and cannot justify echocardiograms, which are more invasive procedures in asymptomatic patients. Thus, we rely on symptoms and EKG to rule out significant cardiac impairment. We recognize that some impairment of the inflow filling is part of the pectus complex

**Exclusion Criteria**

The exclusion criteria for the trial are as follows:

1. Other congenital anomalies (included significant skeletal anomalies such as scoliosis, bony fusion involving the cervical vertebrae) not directly related to pectus excavatum
2. Bleeding disorders
3. Heart disease (including arrhythmia) and/or abnormal EKG
4. Persons with active implantable medical devices (AIMD) such as pacemakers
5. Persons with a relative(s) or close family friend(s) living within their households and having a pacemaker
6. Persons with arteriovenous malformations
7. Chest deformity more complicated than pectus excavatum (e.g., Poland syndrome)
8. Persons for whom a foreign body implant would pose a risk (e.g., immunodeficiency)
9. Persons at increased risk for general anesthesia (e.g., history of malignant hyperthermia)
10. Respiratory conditions that have required steroid treatment (e.g., prednisone in the last 3 years)
11. Pregnancy
12. Inability to understand or follow instructions
13. Refusal to wear the brace
14. Inability or refusal to return to the study site for all postoperative follow-up visits
15. Inability or refusal to undergo monthly chest x-rays
16. Inability to obtain pre-approval (authorization) from the patient’s insurance carrier
17. Hand/wrist x-ray:
   a. Pre-puberty (Bone age F: <7y; M<9y)
   b. Late puberty/post-puberty (Bone age F: >13y; M>14y)

**Enrollment**

Residents of the United States with previously diagnosed pectus excavatum deformities who are referred to participating study centers for evaluation and treatment will be considered for the study. Study centers which reach enrollment cap may refer patients to other study centers.

Study candidates will be screened by the site study coordinator prior to a clinic consultation. At the initial office visit, after all treatment options, including the 3MP, will be discussed in detail. To minimize adverse events, noncompliance, and loss to follow-up, patients who appear unwilling to accept any portion of the research study will not be considered eligible for study participation.
and will be counseled only with regard to appropriate standard pectus excavatum repair procedures (e.g., modified Ravitch or Nuss procedure). Patients who are interested in study participation will further review the consent and assent forms with the study coordinator. All patients and parents will be advised of study criteria. The consent and assent forms will be reviewed in detail and discussed with the patient and parents/guardians. At the conclusion of this session, if the patient and family decide to enroll, the study coordinator will obtain signed informed consent and assent, as well as a signed HIPAA Research Subject Authorization form.

Because the UCSF Conflict of Interest Advisory Committee (COIAC) identified a possible area of conflict of financial interest, the COIAC requires that Dr. Harrison cannot conduct the informed consent visit, but other site PIs may be involved in the process.

Upon signed informed consent and assent, preoperative studies will be obtained prior to the enrollment (CT to measure pectus severity; hand x-ray to measure bone maturity). Once it has been determined that the patient meets all inclusion criteria (i.e., PSI >3.5 and onset of puberty) and has none of the exclusion criteria, the PI and study nurse will discuss the study in great detail, including study requirements with the parents/guardians and the patient. Patients who meet all inclusion criteria will be invited to participate in the study. The patient and family do not have to make a decision regarding enrollment at the initial office visit and may call the study staff or come in for an additional consultation prior to enrollment.

There is a demonstrated tendency on the part of patients to overestimate potential benefits and underestimate the risks of new surgical procedures. Inflated expectations of benefit are a potential impediment to realistic decision-making and valid consent to become a study participant. It is not sufficient that teaching about the risks and benefits occur in a non-directed manner. More positively, each patient and his/her family must be assisted to reach a level of understanding that matches the complexity indicated by the ramifications of the surgery, including risks of the implanted device, general anesthesia, etc. The site PI and study coordinator will extensively discuss these aspects with the patient and family to ensure that they fully understand the information provided to them. Whether presenting the Nuss, Ravitch, or the Magnetic Mini-Mover procedure, to assess that the family’s expectations of the operation are reasonable, the study investigator will ask specifically what they think the patient will look like in 2 weeks after the procedure? After 6 months? After one year?

Once enrolled, the subject will be casted by the site orthotist. The cast of the preoperative pectus excavatum defect will be used to create a custom-fitted orthotic brace for the patient (Magnatract). The patient will be schedule for a brief, outpatient operation to implant the Magnimplant on the patient’s sternum.

Following the operation, the patient will return to the study site two weeks postoperatively. At this follow-up visit, the site PI will see the patient for a routine postoperative visit. The surgical site will be inspected and site management will be discussed. A chest x-ray to evaluate implant security and measure PSI will be obtained. At this visit, the patient will be fitted with their orthotic brace by the site orthotist. The orthotist will discuss in detail how to operate the device and a wear regimen will be prescribed to the patient to wean them into brace wear. The subject will begin to wear the brace approximately one month after implantation.

Patients will return to the study site at least monthly. At each scheduled follow-up visit, the patient will be seen by the site orthotist, PI, and study nurse and/or coordinator for evaluation. Modifications for the brace will be made at the visit as necessary.

Darrell Christensen, CO, one of the study investigators, performs all the orthotics work for our patients, helps design the orthotics, and contributes to all the improvements, including those in...
the second generation Magnatract. For this second study, we have also made arrangements to allow the potential Sacramento-area and Northern California patients to have their orthotic needs met on-site by Greg Aaron, CO, at the Shriners Hospital for Children (Site 2) or at the University of California, Davis Medical Center (UCDMC) (Site 3), both in Sacramento. Mr. Christensen and Mr. Aaron are professional acquaintances and will share uniform techniques through pre-trial visits between UCSF and the other sites and through ongoing communication at the investigators’ meetings.

Study treatment will last between 18-24 months or until the chest wall has reached satisfying correction and the patient is fully mature, whichever comes sooner. Interval assessment of chest correction will be done by visual documentation (photographs) and radiographically (chest x-ray). Chest x-ray will also confirm integrity of the implant.

Once the study endpoint is reached, the patient will undergo a brief, outpatient operation to remove the implant. The patient will return to the study site for a postoperative follow-up one month after the explantation. The patient will have a physical examination by the site PI and have an EKG and a CT scan to document pectus severity index. At that time, the patient will complete a questionnaire assessing the patient’s physical and mental health. At 6, 12, 18 and 24 months post-explantation, the patient will return for follow-up primarily so the investigators can assess whether there is a worsening or recurrence of the pectus defect.

### 3.c.11.i. Protocol for Device Failure and Breakage and Surgical Revision/Rescue

To ensure the Magnimplant has not failed and/or remains coupled, all chest x-ray requisitions will include a request to the radiologist to evaluate and report on the integrity of the implanted magnet within 72 hours. Furthermore, the PI or one of the surgical Co-Investigators will personally review all chest x-rays at each patient’s visit, report the findings to the patient and family, and include the findings in the dictated note.

1. **Device Failure/No Revision:** Should the Magnimplant break, the device will be explanted. Explantation of failed components will be carried out in the same manner as the planned 18- to 24-month explant procedure. Patients who fail the initial primary treatment will receive follow-up in the same fashion as those who complete treatment. That is, in addition to a postoperative office visit, they will have an EKG and chest CT at one month post-explant, and a QOL questionnaire administered at one month and one year post-explant.

2. **Device Failure/Revision:** Should the Magnimplant break or uncouple, and the study subject wishes to undergo revision, and the study surgeon and clinical team believe it is safe and clinically sound to do so, then the failed device will be explanted and replaced. Explantation of the failed component will be carried out in the same manner as the planned 18- to 24-month explant procedure. However, revision patients will continue with treatment which will be the same as for other patients in this study: monthly clinic visits until device removal at 18-24 months; at post-explantation, office visits at one month, 6, 12, 18 and 24 months; EKG and chest CT at one month post-explantation; and QOL questionnaire at one month and finally at one year post-device removal.

Patients and their parents will be instructed to contact us immediately if there is any problem, unusual symptom or changes in the child’s health, whether or not it seems related to the 3MP treatment, including wound issues or any symptom related to the sternum. We will recommend the patient come see us the same day or within 1-3 days, with the appropriate steps taken to diagnose and treat the problem.
3.c.12. Multicenter Study Monitoring

UCSF is the coordinating center for this study. Study personnel at Shriners and UCDMC will report to UCSF. All sites must have IRB approval in order to begin subject enrollment; UCSF will maintain copies of each site’s active IRB approval.

Prior to enrollment of study patients, UCSF will provide the study sites with regulatory binders, a sample patient binder, and all protocol information for review. Drs. Harrison and Hirose, the UCSF study nurse and study coordinator will provide a one-day training session (Initial Site Visit) at each site on the study protocol. During this session, they will review the protocol with the site’s study staff, review device storage and tracking requirements, and conduct an inspection of the facilities.

Each site will maintain study patient data. Each patient binder will include case report forms, screening documents, operative documents, radiology reports, physician reports, adverse event and protocol violation and incident logs, and other pertinent documents. Site personnel will maintain source documents and send copies to UCSF. It should be noted that, although Shriners and UC Davis Medical Center share an IRB and their staff have dual appointments, each institution is able to separate and maintain all HIPAA and regulatory requirements to protect each institution, as well as individual subject PHI. Electronic PHI is maintained on separate networks; any hard copy PHI is maintained in separate files. Study sites will submit quarterly reports to UCSF detailing enrollment status, subject events, and adverse event information. Site PIs are responsible for reporting protocol violations and deviations as well as adverse events to their IRBs and UCSF. The Study Director will report this information to the UCSF IRB and the FDA immediately and other study site PIs.

UCSF will be responsible for any protocol modifications and conveyance of important information to the other sites. Study personnel will hold joint clinic weekly meetings via teleconference. In-person investigator meetings will be held quarterly, with all study personnel present. These meetings will alternate between sites so that the burden of travel is shared and attendance is assured. In addition, UCSF will be in contact by phone (even teleconference), fax, and e-mail to share safety updates or other information, including protocol and/or consent document modifications that may impact risks to the subjects or others. With regard to protocol and consent documents, the PI or study coordinator (nurse or fellow) will provide a written summary of changes and a copy of the appropriate modified documents. The other sites will be responsible for submitting the changes to their own IRBs in a timely manner, and then providing a copy of their approval letter.

As the coordinating center, UCSF will oversee the study activity at all participating institutions and will conduct periodic site visits including prior to patient enrollment, at time of device implant and explant and at the close of the study. At each site visit, the Study Director and/or the Study Nurse and Coordinator will review subject binders, the research database and regulatory documentation. In addition, the UCSF representative will conduct an inspection of the sites facilities (e.g., surgery clinic, orthotics facility, storage of implants). Any and all deficiencies noted at the time of the site visit will be detailed in a report that will be prepared and sent to the participating site no later than one month from the date of the visit.

3.c.12.i Data and Safety Monitoring
Safety monitoring will be performed throughout the study. All adverse events (AEs) (regardless of causality or severity), protocol violations, and protocol incidents will be recorded on CRFs and, if necessary, appropriate medical intervention will be provided to the subject.

The purpose of the Data and Safety Monitoring Plan (DSMP) is to ensure subject safety and the validity and integrity of the data. In addition, the DSMP allows for the monitoring of study data to determine if early termination of a study is warranted for safety or efficacy reasons.

Assessment of Risk: The extent of monitoring required for this study is dictated by the assessment of the level of risk this study presents. As 3MP trial presents a relatively moderate to higher degree of risk (e.g., study involves an intervention/invasive procedure with substantial risk; the study is an investigator-initiated multicenter Phase III trial; the study involves a vulnerable population), the PI will solicit qualified staff, colleagues and/or experts in the area of study, who are independent from the research, to form a DSMB to monitor the safety and probable efficacy of the study. Formation of this DSMB should address any concern that this is a study that presents moderate to high risk to subjects for which monitoring by the PI does not confer adequate safety for the participants.

Monitoring Overview: Monitoring of the study will be done at several levels.

1. The site investigator will be responsible for monitoring at his/her specific institution;
2. The PI/Sponsor and study coordinator will be responsible for onsite monitoring of all sites (with the frequency of visits to other sites to be arranged);
3. The DSMB will provide independent monitoring of the study, with their responsibilities and frequency of their meetings as described elsewhere in this application.
4. It is possible that the FDA Office of Regulatory Affairs will initiate its own audit of the study.

Data and Safety Monitoring Board (DSMB). An enhanced DSMP is desirable. Therefore, the study PI recruited an independent DSMB of capable individuals from within and outside UCSF who have expertise on DSMBs and who are completely independent of the trial team.

Composition:

We propose Dr. Mohammad Diab from UCSF and non-UCSF personnel, Gary Hartman, MD (Stanford), Steven Yedlin, MD (Children’s Hospital & Research Center, Oakland CA), and Susan Harwell, RN, MSN (independent) to serve as board members. The DSMB in the first trial was satisfactory to the CDRH, the OOPD, and UCSF IRB. Ms. Harwell is the Clinical Research Associate of TRIA (formerly SpectraGenics) in Dublin, California. She is an experienced data monitor who will be responsible for auditing the study records, including source documents, the study database and regulatory documents. In addition, she will review our Standard Operating Procedures, including general quality assurance and quality control procedures, and patient recruitment and device tracking logs. In addition, she will coordinate the meetings of the DSMB, draft, distribute and finalize the reports of the Board’s findings and be responsible for providing the reports to the UCSF Coordinating Center. Dr. Diab is Professor of Orthopedic Surgery and Chief of Pediatric Orthopedics, who specializes in treating musculoskeletal conditions in children and teenagers. His special areas of interest are spinal deformities, including scoliosis, and spondylolysis. In the course of monitoring safety in the pilot study regarding entrained air and pneumothorax, it was Dr. Diab who recommended intraoperative chest x-ray to minimize these risks in our patients. The two non-UCSF pediatric surgeons, with extensive expertise with pediatric chest wall correction, who have agreed to take on the responsibilities of the DSMB are...
1) Gary E. Hartman, MD, a board-certified general and pediatric surgeon at Lucile Packard Children's Hospital at Stanford University. He has extensive experience with pectus excavatum standard repair; and 2) Steven Yedlin, MD, a board-certified general and pediatric surgeon, who is presently part of the Children First Medical Group where he is Chief Medical Officer. All three surgeons will be responsible safety monitoring with regard to the surgical and orthotic procedures, any complications related or unrelated to treatment, and review all adverse events and unanticipated problems related to the implantation/explantation of the magnet or use of the external prosthesis.

**Independence:** The DSMB members will not participate in the study as investigators, and will not have conflicts of interest regarding the study, the study sponsor, or the device being studied.

**Data:** The DSMB will review the CRFs for completeness, important information that may affect the safety or welfare of the participants, and data validity and integrity; data for primary or secondary endpoints (i.e., pre-implant compared to post-explant PSI, one-month post-implant and one-month post-explant QOL questionnaires); data for early termination (stopping rules); and adverse events and AE reporting. The DSMB will not perform formal interim analyses.

**Frequency of Review:** The board will meet based on the number of subjects enrolled, using particular study milestones to schedule their monitoring. Specifically, the board will meet when approximately half the patients are enrolled (total of 7 or 8, all sites), when 15 patients are enrolled, when approximately half the patients are explanted (total of 7 or 8, all sites), when 15 patients have been explanted and have had their one-month post-explant follow-up, and when all patients have had their one year post-explant follow-up visit---a minimum of five meetings. The board may meet more frequently, if the members deem it necessary to review, for example, unanticipated problems, subject withdrawal, or use of the stopping rules.

**Authority:** The DSMB will have authority to recommend changes in the study, including discontinuation if there are unresolvable concerns about safety. Changes may include changes to the study design, operative technique, and study CRFs. The DSMB will report their findings, including recommendations for study modifications, in a formal report distributed to the study investigators, the CHR, and the FDA CDRH and OOPD. The DSMB will not perform formal interim analyses.

**Stopping Rules** for the study at all sites will be the occurrence of any one of the following events at any one site: death related to treatment; development of mediastinitis and/or any pulmonary complication related to treatment; any cardiac event related to treatment.
§4. Description of the methods, facilities, and controls used for the manufacture, processing, packing, storage, and installation of the device.

4.a. **Sterilization, Labeling, and Packaging**

4.a.1. **STERILIZATION AND PACKAGING: Investigational Device**

**Sealed magnet housing**

The rare earth magnet with its ferromagnetic backing disk is encased in titanium in a FDA-registered facility. All housing components will be machined from Titanium alloy 6Al 4V. This is commonly used in the manufacture of implantable ventricular assist devices, artificial heart components and cardiac rhythm management products. The hermetic housing will be fabricated using laser-welding methods based on glovebox welding systems used commonly for the production of implantable medical electronics such as pacemakers, defibrillators and neurostimulators. The glovebox laser welding system provides a clean, dry oxygen-free environment for the joining of titanium. Prior to laser welding of the encapsulated magnet assembly the components will be subjected to a vacuum bake-out cycle (time & temp TBD) to drive out any residual moisture before sealing. The welded device will have an internal atmosphere of 75% Argon & 25% Helium for subsequent leak testing.

The leak testing after welding will be in accordance with methods used in the production of implantable medical electronics such as cardiac rhythm products and blood pumps. A gross and fine leak test procedure is performed to ascertain leak rates are less than 10 to the minus 8 std CC/sec of Helium.

Bonding of the magnet sub-assembly will be by means of a Nusil brand of medical adhesive similar to that used in the attachment of molded headers to the top of cardiac rhythm products and neurostimulators.

**Sterilization**

The devices will be packaged in a backer card, inside a double Tyvek pouch. The packaged device will then be sterilized by gamma radiation at the Nutek Corporation in Hayward California under the guidance of Hantel Technologies, Inc.

- Sterility-Assurance level (SAL): $10^{-6}$
- Minimum radiation dose: 25 kGy
- Maximum dose: Determined by validation process
- Validation method: VD-Max method
- No claims regarding pyrogenicity

**External Magnet Prosthesis**

Fabrication of the external magnet prosthesis ("Magnatract") is under the direction of Darrell Christensen, certified orthotist of the UCSF Orthotic and Prosthetic Center, Richard Fechter, Senior Developmental Clinical Engineer of the UCSF Clinical Engineering Department., and Greg Aaron, CO, of Shriners' Hospital and Kaiser Sacramento. Hayes Manufacturing Services in Santa Clara, CA, is responsible for the pectus can assembly.

The sponsor/investigators conform to **Good Laboratory Practice (GLP)** as defined under 21 CRF 58. In addition, the manufacturer, Hantel Technologies Inc., and irradiation facility, Nutek Corporation, conform to GLP standards. Hantel Technologies and Nutek are FDA-registered facilities.
4.a.2. STERILIZATION AND PACKAGING: Labeling

Provided below is a draft label which includes the device name, manufacturer name and address, device materials, method of sterilization, expiration date, and the Investigational Device Cautionary Statement.

Label for package

Stickers for external brace and brace canister


Manufactured by:
University of California, San Francisco
400 Parnassus Avenue, A123
San Francisco, California 94143-0570
Device material(s): Rare Earth Metals
4.a.3. STERILIZATION AND PACKAGING: Package Insert

MAGNETIC MINI-MOVER for PECTUS (3MP)

The Magnetic Mini-Mover to correct pectus excavatum uses two magnets.

Description:

I. Magnimplant
The Magnimplant consists of a rare earth magnet and ferromagnetic plate enclosed within a hermetically-sealed titanium case that is implanted on the abnormally placed sternum (breastbone). The disk-shaped case has four holes which one titanium cable will pass through one hole, through the back plate channels and come back up through the sternum where it is laced through another hole and the set screws are tightened down. This is repeated for the second cable. The back plate acts as a protection barrier for the sternum from the titanium cables. Once the cables are cinched down the set screws are tightened and the cables are cut flush with the anterior plate edge.

II. Magnatract:
The second magnet is housed in an adjustable canister fastened to an external brace. The lightweight external brace with foam pads is worn on the chest and held in place by the attraction of the internal (implanted) magnet and the external magnet. The amount of pull or attraction is adjusted by manipulating the canister and changing the distance between the internal and external magnets. The patient can make this adjustment. The size (depth) of the magnet retainer can be adjusted to the patient’s needs.

Intended Use: The device is intended to correct pectus excavatum deformity in otherwise healthy males or females. Age: Greater than 8 years but less than 15 years of age, with a Pectus Severity Index greater than 3.5 (normal 2.56).

Contraindications: 1) Other congenital anomalies, including skeletal anomalies not directly related to pectus excavatum; 2) Bleeding disorders; 3) Heart disease, including arrhythmia, and/or an abnormal EKG; 4) Persons with Active Implantable Medical Devices (AIMD) such as pacemakers; 5) Persons with A-V malformation; 6) Chest deformity more complicated than pectus excavatum, e.g., Poland’s syndrome; 7) Persons for whom a foreign body implant would pose a risk, e.g., immunodeficiency; 8) Persons at increased risk for general anesthesia, e.g., history of hyperthermia; 9) Pregnancy

Sterilization Parameters: The Magnimplant device will be packaged in a backer card, inside a double-Tyvek pouch at Hantel Technologies, and the packaged device will be sterilized by gamma radiation at:

Nutek Corporation
30958 San Antonio St
Hayward CA 94544

- Sterility-Assurance level (SAL): $10^{-6}$
- Minimum radiation dose: 25 kGy
- Maximum dose: Determined by validation process
- Validation method: VD-Max method
- No claims regarding pyrogenicity
**Warnings and Precautions:** "CAUTION - Investigational Device. Limited by Federal law to investigational use."

Use of this device exposes human tissue around the device to a magnetic field that is strongest at the surface of the device and decreases with distance away from the device. Although there is no scientific evidence of any ill effect on biologic tissues from magnetic fields up to 400 times as powerful as this device, long-term exposure could still have some cumulative effect on tissue.

Because there is a magnetic field outside the body over the magnet, individuals with an implanted magnet will have to be aware that ferromagnetic materials, like iron or another magnet, could be attracted to the implanted device if brought close enough. Anything that could be attracted by a magnetic, such as metallic toys, iron bars, or other magnets, should be carefully avoided. Any object that is attracted and stays in place on the skin over the implanted magnet could cause pain and even damage to the skin, and should be carefully avoided or quickly removed if this occurs.

Application of the external component of this device, Magnattract, applies pressure to the skin and soft tissue over the ribs around the defect. Damage to these tissues must be avoided by adjusting the strength with which the Magnattract pulls on the internal magnet. This is done by adjusting the position of the external magnet in the Magnattract device. Individuals wearing the external device must be vigilant about tissue damage. This is signaled by pain, tenderness, and redness where the Magnattract device contacts the skin.

The external magnetic field might be a danger to others such as individuals with implanted cardiac pacemakers or nerve stimulation devices. Those individuals will be aware that they should not come in contact with magnetic fields that could affect their devices. Likewise, persons with a magnet implanted on the chest and persons with an implanted magnet and the external magnet brace in place must be aware to not come in close contact with other individuals with those devices. The following statement will be provided and discussed with patients.

*The safe distance from your magnet to an implanted device in another person is six (6) inches. Therefore, you should never have your chest wall magnet any closer than 6 inches from another device. In other words, never embrace or hug someone with a device that is sensitive to magnetic fields.*

There is a risk of injury from any strong magnetic field such as a magnetic resonance imaging (MRI) machine. Persons using the Magnetic Mini-Mover should never have an MRI or come close to an MRI machine.

The device’s magnetic field could interact with security systems, like electronic surveillance devices or metal detectors. The patient should be aware of these possible interactions and carry a document explaining the presence of the implanted magnet.
4.a.4. STERILIZATION AND PACKAGING: Patient Instructions for Use (Package Insert)

INSTRUCTIONS FOR PATIENTS USING THE MAGNETIC MINI-MOVER METHOD TO CORRECT PECTUS EXCAVATUM

Overview: The Magnetic Mini-Mover Device is made up of two pieces. The first piece is a magnet in a titanium case (the "Magnimplant") that has been implanted on your breastbone (sternum) where it is deformed by the pectus excavatum. The disk-shaped case can be palpated (or felt) under the skin. The second piece is an external brace (the "Magnatract") that has been specifically fitted to your chest wall deformity. When you wear the brace, the external magnet pulls on the implanted magnet and gradually pulls the sunken chest wall out to correct the deformity.

The strength and duration of pull can be adjusted to your comfort and lifestyle. It is desirable to have the device pull as hard as is comfortable and safe for your skin, and for as long as possible, preferably 22-24 hours a day. In practice, of course, the device can be taken off at any time to relieve discomfort, to take a shower, or to do special activities. It would be desirable to leave the device on at night while you sleep. There is a monitor, called a force sensor, built into the Magnatract that will keep a continuous record of the strength of pull and the amount of time the brace is worn. At each clinic visit, we will download the data from your brace monitor.

General instructions:

- For the four weeks after your surgery, while the skin incision heals, you will not wear the Magnatract.
- At your first return appointment in two weeks, the treatment team members will fit you with the Magnatract device and adjust the strength of pull. At one month (four weeks after surgery) you will then start wearing the brace and the treatment team will teach you how to adjust and remove the device and how to position it when it is replaced. The magnetic attraction between the implanted magnet and the external device will hold the device in place, but the elastic back-straps will help keep it in place at night and during activity.
- Remove the brace one hour or less to shower or relieve discomfort. Any soreness or skin redness (if any) should be relieved after the brace is removed. If the redness persists, call the treatment team at (415) 476-2538 (choose option 1 on the selection menu after hours and on weekends).
- You will return to the Pectus Study Clinic and the UCSF Orthotics and Prosthetics Center twice for the first month. After the first month, you will be seen once a month until maximum correction is achieved or until the study is ended. At each visit, the strength of the pull on your chest will be measured and adjusted if necessary. The treatment team will take a picture of your chest and read the force sensor log to see how much you wore the brace and the amount of force used since the last visit.

Adjusting the Magnatract:

- Decreasing the pull: Once you start wearing the Magnatract regularly, slight aches and pains may be common. Tylenol or Advil should help you, but if the discomfort is great or if you need stronger medicine, then call Dr. Harrison, Dr. Hirose or the study nurse during the daytime at 415-502-0173 or (415) 476-2538 (choose option #1 after hours and on weekends). Or you can call the orthotist, Darrell Christensen, at (415) 476-1788, Monday through Friday, 8AM to 5 PM.
The treatment team member may adjust the external magnet away from your skin by changing the cup which will contain a decreased number of magnets. This will decrease the strength of pull and should relieve your discomfort. When you feel the Magnatract is set comfortably the new brace adjustment will be recorded.

- **Increasing the pull**: If the brace feels like it is not pulling hard enough to stay attached and pull on the breastbone, a member of the treatment team will increase the strength of pull changing the cup to one with an increased number of magnets.

  CAUTION: The suspended magnet should never be so close that it touches your skin. When you feel the Magnatract is set comfortably, then the treatment team member will record the adjustment.

### Precautions when using the Magnetic Mini-Mover Device

- **Risks to others with electronic implants**: The magnets in your device may be dangerous to other people who have heart pacemakers or nerve stimulation devices or similar electronic implants. A safe distance from your magnet to an implanted electronic device in another person is 6 inches or more (≥6”). As long as you wear the Magnatract brace, it will be safe to stand or walk by other people with implanted electronic devices, but better not to hug them.

- **MRI**: With the Magnimplant and/or Magnatract in place, you can be seriously injured from having an MRI or being near any strong magnetic field like an MRI machine. Therefore, you **may not have an MRI** while the Magnimplant is in place. You will be given a bracelet or dog tag to wear at all times that says you cannot have an MRI while the magnet is implanted in your chest.

- **Video/TV screens and computer hard drives**: Your magnets can damage any kind of video/TV screen, laptop or desktop computers, cell phones, or iPod-type devices. Therefore, stay at least 12” (one foot) away from all computer hard drives, monitors, watches, and televisions.

- **Skin injury and discomfort**: The pressure of the Magnatract may cause a rash or irritation to your skin. This problem can be easily remedied by relieving where the brace is digging in, or by decreasing the pull of the magnets (that is, increasing the distance between them). If you and your parent/guardian cannot make the adjustment at home, then the treatment team can do this at UCSF—you **do not** have to wait for your next scheduled weekly or monthly appointment. Just call and arrange to see Dr. Harrison, Dr. Hirose, the study nurse, or Mr. Christensen. Also, daily cleaning of the brace and your skin using soap and water should help control skin problems.

- **Sharp metal objects**: If you are not wearing the brace, the Magnimplant and the Magnatract can attract small metal objects. Objects such as razor blades, pins, thumbtacks, nails, or other magnets can attach to the Magnimplant and, therefore, could bruise or cut your skin and create an infection. When you are taking a break from wearing the corrective brace, stay away from sharp metal objects and keep your Magnatract brace away from metal objects and electronic devices.

- **Metal screening devices**: Metal screening devices, such as those found in airport security areas, will detect your implanted magnet. The Magnetic Mini-Mover’s magnetic field could also interact with electronic surveillance devices. You will be given a letter from the UCSF Pectus Study team that explains you have an implanted metallic device.

### IMPORTANT REMINDERS...

- **No MRIs!**
• The magnets contained in the Magnetic Mini-Mover are powerful and could be dangerous. 
   *Always wear both components of the Magnatract: the magnet cup screwed in to the protective cover piece and the custom holding frame.* Using both components will protect you from getting hurt by small sharp metal objects, protect video and television screens, and prevent anyone else who wears a medical device from getting hurt.

• Do not let your magnets get closer than 6 inches to someone else’s electronic implant.

• Clean your brace once a day by wiping the inside padding of the brace with a washcloth, soap, and water.

• Take a shower or bath everyday.

• The device should be used only for treatment of your pectus deformity and for nothing else. When not worn by you, the brace should be kept in a safe place (like a closet) away from metal objects or other magnets, and out of the reach of children or friends.

If you have questions or experience problems wearing the Magnatract brace, you should immediately call the treatment team. If you are not feeling well for any reason, call Dr. Michael Harrison or Dr. Shin Hirose, the clinical fellow and study nurse. They are available everyday, 24 hours a day, at (415) 476-2538. The orthotist, Darrell Christensen, can be reached at (415) 476-1788, Monday through Friday, 8AM to 5 PM.

Important Phone Numbers:

- Pediatric Surgery Practice (Michael Harrison and Shin Hirose)
  - 415-476-2538 Option 1 After hours, Weekend and Holidays
- Study Nurses (Tamara Ryan and Jill Imamura-Ching)
  - 415-502-0173
- Darrell Christensen (Orthotist)
  - 415-476-1788

Fax:
- Pediatric Surgery Practice  415-476-2929
- Orthotic Practice  415-476-7003

Email:
- PectusTrial@ucsfmedctr.org

Web:
4.a.5.  STERILIZATION AND PACKAGING: Surgical Technique Manual (Draft)

Surgical installation of the device will be under the auspices of Dr. Michael Harrison, Professor of Surgery and Pediatrics, and the Director of the UCSF Fetal Treatment Center. All procedures and devices will be approved by the institutional review board overseeing research involving human subjects.
4.a.5.i. SURGICAL TECHNIQUE MANUAL: IMPLANTATION

Step 1.
Thirty to 60 minutes prior to incision, cefazolin (dosed by patient weight) should be given for antibiotic coverage (or clindamycin if patient is allergic to cefazolin or penicillin). Under general anesthesia and with the patient supine, prep and drape the anterior chest.

Step 2.
Make a 2-inch transverse skin-line incision at the junction of the xiphoid and the inferior border of the sternum (see Fig. 1). This incision may be converted to a vertical incision to provide better surgical approach and cosmetic scar.

Figure 1. Transverse skin incision at junction of xiphoid and inferior border of sternum.

Step 3.
Carry the dissection down to the junction and separate the xiphoid from the lower sternum with an electrocautery, taking care to cauterize blood vessels that frequently run on the underside of that junction (Fig. 2).

Figure 2

Step 4.
Carry out blunt dissection under the sternum, pushing the pleura away on both sides and pericardium away posteriorly. In this maneuver, air may become entrained around the lung, which is a likely risk that will be addressed with closure of the incision. There is also a risk of damage to the lung itself or the sac around the heart. Visualization and laying a flat, metal, malleable plate retractor over the tissues to act as a hard protective barrier should guard against damage to these tissues and organs. Once the underside of the sternum is completely free, use sharp and blunt dissection to free the outer side of the sternum, so that a subcutaneous pocket is created over the top of the sternum.
Step 5.
Once the underside and outer side of the sternum are completely free, place a cable into one of the holes on the anterior cup with the ball flush or 1 mm above the top of the anterior cup wing. Hand-tighten the set screw using the preset (0.3N-m) torque wrench until a click is heard. The click indicates the set screw has been tightened adequately. Repeat this step with a second cable for the second hole on the same side of the anterior cup (see Figure 3).

**Figure 3.** Placement of the first set of set screws using a preset torque wrench (0.3N-m).

Step 6.
Place the cable needle guide behind the sternum and punch through the sternum at the superior location to position the device at the deepest portion of the defect (see Figure 4). Feed one of the cable ends through the cable needle guide and capture it under the sternum with forceps. Then, remove the cable needle guide and reposition it on the opposite superior side of the posterior sternum, guide the second cable through and pull it out of the incision (see Figure 5 and 6). The use of the cable needle guide from the posterior portion of the sternum reduces the risk of injury to the heart and/or lungs by keeping the sharp needle end away from vital organs.

**Figure 4.** Cable needle guide comes from behind sternum and protrudes up through sternum.
Figure 5. Cable wire passes through cable needle guide.

Figure 6. Pulling and straightening cable wires to exit through the incision towards surgeon.

Step 7.
Feed the titanium cables through the channels of the back plate (see Figure 7). Position the back plate behind the sternum and center it with the anterior can by pulling the cables and cinching the back plate into place.

Figure 7. Guiding of the back plate over the cable wires to center under the anterior cup.

Step 8.
Place the cable needle guide behind the sternum and punch through the sternum to create a hole in the inferior sternum. The hole in the sternum should align with the corresponding inferior hole on the Magnimplant wing. As the cable needle guide is withdrawn from the hole, use a clamp to trail into the hole keeping the hole patent and act as a grasper for the cable wire. Once the clamp is through the hole, use the clamp to grasp the titanium cable and bring the cable through the hole. Then, feed the cable through the screw hole in the Magnimplant wing (see Figure 8). This procedure is repeated for the second cable for the corresponding hole in the Magnimplant wing.
Figure 8. Pulling cable wire up through pre-made holes and lacing through holes in anterior cup.

Figure 9. Tighten final two set screws with preset torque wrench until click heard (0.3N-m) and then cut cables flush to anterior cup wing.

Step 9.
Cinch the cables together and center and secure the back plate and anterior cup with each other. Tighten the final two set screws into place using the preset torque wrench until the click is heard (0.3N-m). Cut the cables flush or 1mm above the top of the anterior cup wing using a cable cutter (Figure 9).

Step 10.
Prior to complete closure, obtain a chest x-ray to assess for any entrained air.

If there is no entrained air, reattach the xiphoid to the lower end of the sternum and close the subcutaneous tissue with absorbable suture. Then, reapproximate the incision with subcuticular absorbable suture (Fig. 10). Inject Xylocaine around the site and irrigate the wound with antibiotic solution.

If there is entrained air, insert a red rubber catheter into the pleural space to evacuate the air around the lungs. Reattach the xiphoid to the lower end of the sternum and close the subcutaneous tissue with absorbable sutures. Once the wound is nicely sealed, place the red rubber catheter underwater. The anesthesiologist should provide Valsalva airway pressure to visualize evacuation of any air entrained in the pleural space. Remove the red rubber catheter and approximate and close the skin with a subcuticular absorbable suture (Fig. 10). Inject Xylocaine around the site and irrigate the wound with antibiotic solution. Obtain a chest x-ray prior to patient awakening to assess appropriate removal of the entrained air. Persistent entrained air may require observation or further treatment.
Figure 10. Incision closed with absorbable sutures.
Operative Day Care

- Pt. managed intraoperatively by anesthesiologist

Maracaine injected by surgeons in OR
Ketorolac given IV by anesthesiologist

- Pt. enters PACU

Nurse & anesthesiologist assess pt. every 15-30 min

Pain orders per PACU (IV opioids as needed)

3-4 hours

Once Food Tolerated

Give oral narcotics (Tylenol #3) or Vicodin (5/500mg)

Pain assessment (0-10 scale; 0=no pain, 10=high pain)

- Pain > 5
  - Consult attending pediatric surgeon to admit patient.

- Pain < 5
  - Meet all discharge criteria on Pediatric PACU Orders
    - Discharge home on Tylenol #3 2 tabs po q 4 hrs prn pain or Vicodin (5/500mg) 1-2 tab PO q4h prn pain

When pain managed and vital signs stable
4.a.5.ii. Surgical Technique Manual: Explantation

Step 1.
Thirty to sixty minutes prior to incision, cefazolin (dosed by patient weight) should be given for antibiotic coverage (or clindamycin if patient is allergic to cefazolin or penicillin). Under general anesthesia and with the patient supine, prep and drape the anterior chest.

Step 2.
Make a 2-inch transverse skin-line incision at the junction of the xiphoid and the inferior border of the sternum over the original incisional scar (see Fig. 1). This incision may be converted to a vertical incision if that was performed as the original incision. Postoperatively, the incision and the area around it may feel numb due to cut nerves. The feeling in this area may come back but could take up to a year.

Figure 1. Incision through the original incisional scar.

Step 3.
Dissection is carried down to the implant, taking care to cauterize blood vessels that frequently run in that area (Fig. 2). Due to a foreign body being in the body, a fibrous capsule may have formed around the magnet, which will need to be dissected out in order to visualize the magnet for removal.

Figure 2

Step 4.
Blunt dissection is carried out under the sternum, pushing the pleura away on both sides and pericardium away posteriorly. In this maneuver, air may become entrained around the lung, which is a likely risk that will be addressed with closure of the incision. There is also a risk of damage to the lung itself or the sac around the heart. Damage to these tissues is guarded against with visualization and using a malleable (metal flat plate retractor) that lies over the tissues and acts as a hard protective barrier. Once the underside of the sternum is completely free, the outer side of the sternum is dissected free using sharp and blunt dissection, until the entire anterior portion of the device is visible.
Step 5.
Once the anterior implanted device is visible, the titanium cable is cut using a cable cutter on the inferior cables seen at the incision opening (see Figure 3).

![Figure 3. Wire cutters used to cut titanium cable for removal.](image)

Step 6.
Using the hook tag, the back plate can be removed. The anterior cup with the attached cables in the superior holes can then be removed (see Figure 4).

![Figure 4. Grasp hook tag on back plate with grasper instrument to facilitate removal.](image)

Step 7.
Prior to closure, a chest x-ray is taken to assess for entrained air. If there is no indication of entrained air, the incision is approximated and closed with subcuticular absorbable suture and xylocaine injected around the incision site for post-operative pain control. If there is entrained air, a red rubber catheter is inserted into the pleural space to evacuate any entrained air around the lungs. The xiphoid is reattached to the lower end of the sternum with absorbable sutures and the subcutaneous tissue is closed with absorbable sutures. Once the wound is nicely sealed the red rubber catheter is placed underwater and Valsalva airway pressure is provided by the anesthesiologist to visualize evacuation of any air entrained in the pleural space. The red rubber catheter is removed and the skin is approximated and closed with a subcuticular absorbable suture (Fig. 5). Xylocaine is then injected around the site. Chest x-ray obtained prior to patient awakening to assess entrained air removal. Persistent entrained air may require observation or further treatment.
Figure 5. Closure of the incision with absorbable sutures.
Operative Day Care

Pt. managed intraoperatively by anesthesiologist

Marcaine injected by surgeons in OR
Ketorolac given IV by anesthesiologist

Pt. enters PACU

Nurse & anesthesiologist assess pt. every 15-30 min

Pain orders per PACU (IV opioids as needed)

Once food tolerated

Give oral narcotics (Tylenol #3 or Vicodin)

Pain assessment (0-10 scale; 0=no pain, 10=high pain)

Pain > 5
Consult attending pediatric surgeon to admit patient.

Pain < 5
Meet all discharge criteria on Pediatric PACU Orders

When pain managed and vital signs stable

Discharge home on Tylenol #3 2 tabs po q 4 hrs prn pain
Or
Vicodin (5/500mg) 1-2 tab PO q4-6h prn pain
4.a.6. STERILIZATION AND PACKAGING: Magnatract Casting and Fabrication Manual (Draft)

CASTING PROTOCOL

During this casting visit, the orthotist will take a plaster and fiberglass impression of the patient’s chest which will be used to fabricate the custom orthotic brace. This requires the following materials:

- “T shirt” style stockinette
- 3 sets of 5 ply 5” or 4” plaster splints, long enough to cover the entire anterior chest
- two rolls of 4" fiberglass casting tape
- cutting strip
- cast saw or scalpel
- weak rod magnet(s)

Step 1: Put the stockinette on the patient. Identify and mark the inferior costal margins with marking pencil. Mark outline of implant and any points of rib flaring.

Step 2: Lay the plaster splints completely across and into the patient’s anterior chest wall, from the sternal notch to the inferior costal margins. Carefully mold the wet plaster into the full depth of the depressed sternum torso and around the implanted magnet to get an accurate impression of the defect (Fig. 1). There will still be some swelling around the Magnimplant, so be gentle close to the surgery site. Place the cutting strip on the patient’s back and wrap the fiberglass casting tape circumferentially over the plaster splints. Carefully mold the fiberglass around the full depth of the sternum.

Figure 1: Wet plaster cast of defect with Magnimplant.

Step 3: Use weak rod magnets to locate and mark the center of the implanted magnet. This point will be used later to center the Magnatract device over the Magnimplant (Fig. 2).
**FABRICATION PROTOCOL**

**Step 1:** Carefully drill a \( \frac{1}{4} \)" hole through your center mark on your cast of the implanted magnet.

**Step 2:** Seal, pour, and strip the positive mold.
Step 3: Mark the four areas of contact: the two superior pectoral areas (~2” in diameter) and the two inferior costal margins. Also retain the center magnet mark (Fig. 4).

Figure 4: Positive mold of the patient’s torso with four key contact points clearly marked

Step 4: Use a long shoe nail and put it at the center mark.

Step 5: The orthosis will be built up around the center of the implanted magnet to allow clearance. To determine the height of the build up, allow for \(\frac{1}{6}\)” minimum clearance from the plastic magnet container and the cast (Fig. 5). Put the top of the nail even with the inside surface of where the aliplast liner will eventually lay (~\(\frac{5}{16}\)” below the lip of the magnet can). Make the center nail the same height.

Figure 5: Magnatract screw mechanism with centering nail on positive cast.

Step 5: Add plaster build up to the level of the center nail. A plastic ring holds the container which suspends the external magnet. Make the diameter of the build up the same size as the ring (Fig. 6).
**Step 6:** With the exception of the four contact areas, build up all other areas \( \approx \frac{1}{2} \)" (Fig. 7).

**Step 6:** Mold the liner using \( \frac{1}{4} \)" aliplast or equivalent low-density foam. Wrap the cast with stockinette and place end caps onto the cast. Staple the liner. Cut four lengths of Ottobock prepreg (reinforcement) to span from the ring edge to the four contact points. Vacuum form 3/16" polypropylene over the four heated reinforcement strips with minimum stretch.

**Step 7:** After completely cooling, cut out the plastic shell and finish the edges. Trace the outline of the magnet can and cut out the center hole. Drill two holes in the ring and speedy rivet the ring to the plastic shell. Screw in the can, and the brace is completed (Fig. 8).
§5. An example of the agreement to be signed by the investigators and a list of the names and addresses of all investigators.

Agreement to Develop and Test a New Method to Repair Pectus Excavatum

“The undersigned agree to the following: 1) To participate in a study to test the safety and efficacy of a new method to correct pectus excavatum; 2) To abide by all the conditions and oversight established by the UCSF Committee on Human Research (CHR) and individual site IRBs for this study, including full disclosure of all risks and benefits; 3) To report all adverse events within a ten-day period to the site-specific IRB and FDA; and 4) To perform the procedure and conduct the study only at UCSF and its designated sites and, furthermore, only by designated study investigators.”

Michael R. Harrison, MD
406 Pacheco Street
San Francisco CA 94116
harrisonm@surgery.ucsf.edu

Shinjiro Hirose, MD
2322 – 39th Avenue
San Francisco CA 94116
Shinjiro.hirose@ucsfmedctr.org

Darrell Christensen, CO
1038 Hidden Valley Drive
Petaluma CA 94954
Christensen@orthosurg.ucsf.edu

Richard Fechter
684 Las Colindas Road
San Rafael CA 94903
richard.fechter@ucsfmedctr.org

Tamara Ryan, RN
39 Cobblestone Lane
San Carlos CA 94070
Tamara.Ryan@ucsfmedctr.org

Jill Imamura-Ching, RN, BSN
83 Diablo View Drive
Orinda, CA 94563
Email: Jill.Imamura-Ching@ucsfmedctr.org

Dillon Kwiat
351 Panorama Dr.
San Francisco CA 94131
Dillon.Kwiat@ucsfmedctr.org

Diana Farmer, MD, FACS, FRCS
Pearl Stamos Stewart Professor and Chair
Department of Surgery, UC Davis School of Medicine
Surgeon-in-Chief, UC Davis Children’s Hospital, UC Davis Health System
2221 Stockton Blvd, Suite 3112, Sacramento, CA 95817
Phone: 916-734-3190 Fax: 916-734-5119
diana.farmer@ucdmc.ucdavis.edu.
§6. Certification that all investigators have signed the agreement, that the list of investigators includes all investigators participating in the study, and that new investigators will sign the agreement before being added to the study.

The study sponsor certifies that all investigators participating in this study have read the above agreement (§5), agree to its terms and conditions, and have signed and dated the document to this effect. Additionally, the sponsor certifies that all new investigators will concur and sign the agreement before being added to the study as key personnel.

Michael R. Harrison, MD
Study Director and Sponsor

January 9, 2012
§7. A list of the names, addresses, and chairpersons of all IRBs that have or will be asked to review the investigation and a certification of IRB action concerning the investigation (when available).

University of California, San Francisco
The address for the UCSF Office of Research is as follows:

Office of Research
University of California, San Francisco
3333 California Street, Suite 310
San Francisco CA 94118
General Office: (415) 476-1814; Facsimile: (415) 502-1347
e-mail: chr@ucsf.edu

Committee on Human Research

POLICY ANALYSTS
John Heldens, CIP
Director, Human Research Protection Program RPP
(415) 476-9840
john.heldens@ucsf.edu

Richard M. Wagner, MA, CIP
Assistant Director, Human Research Protection Program RPP
(415) 476-1172
richard.wagner@ucsf.edu

Lisa Voss, MA, CIP
Assistant Director, Quality Improvement Unit (QIU)
(415) 514-2152
lisa.voss@ucsf.edu

CHR COMMITTEE CHAIRS
Victor I. Reus, M.D. – Chair (Parnassus)
Carol S. Viele, RN, MS. – Vice Chair (Parnassus)
Daniel S. Weiss, Ph.D. – Vice Chair (Parnassus)
Reese Jones, M.D. - Chair (Laurel Heights)
Charles B. Cauldwell, M.D. - Vice Chair (Laurel Heights)
Diane W. Wara, M.D. Vice Chair (Laurel Heights)

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)
Telephone: 415-476-2197; Fax: 415-502-7991
Email: iacuc@ucsf.edu
Web site: http://www.iacuc.ucsf.edu
Shriners Hospital for Children and UC Davis Health System

Institutional Review Board
CTS Building
University of California, Davis Medical Center
2921 Stockton Blvd., Suite 1400, Room 1429
Sacramento CA 95817

Ahmad Hakim-Elahi, Director
ahakimelahi@ucdavis.edu
(916) 703-9157

Lody Tarango, Assistant Director
elodia.tarango@ucdmc.ucdavis.edu
(916) 703-9154

Donald Orescanin, Assistant to the Director
donald.orescanin@ucdmc.ucdavis.edu
(916) 703-9152

IRB Clinical Committee A
Jefferson Lee, Analyst
jefferson.lee@ucdmc.ucdavis.edu
(916) 703-9164

IRB Clinical Committee B
Mihaela Harris, Analyst
mihaela.harris@ucdmc.ucdavis.edu
(916) 703-9165

Approval and Renewal Notices
John Leiken, Coordinator
john.leiken@ucdmc.ucdavis.edu
(916) 703-9163

Kaiser Permanente Medical Center – Sacramento
Institutional Review Board – Biomedical Panel
Division of Research Administrative Offices
2000 Broadway
Oakland CA 94612
(510) 891-3400
§8. The name and address of any institution (other than those above) where a part of the investigation may be conducted.

None.

§9. The amount, if any, charged for the device and an explanation of why sale does not constitute commercialization.

The internal device (implanted magnet): $79,126 (55 devices)
External device (external magnet prosthesis): $13,566 (30 braces)

These amounts represent the cost of development and fabrication, with no profit to the investigators and/or the institution.

§10. Environmental assessment

There is no environmental impact expected. The internal magnet will be retrieved in every case, after the chest wall deformity is corrected. All magnets will be sanitized and demagnetized after removal. Internal magnets may be kept by investigator or given to patient.

§11. Copies of all labeling for the device

a. Sample of letter for patients/parents/guardians with medical certification/explanation of implanted magnet for the purposes of going through security checkpoints.

To whom it may concern:

My patient, __________________________, UCSF ID # ________________________, born __________________________, has a metal magnet implanted on the breast bone (sternum) in the middle of the chest. It may trigger a metal detector. It can be seen by X-ray. This patient also has an external orthotic device, which can be removed at any time.

Michael R. Harrison, M.D.
Professor Emeritus of Surgery, Pediatrics, and OB/GYN & Reproductive Sciences
Director, Pediatric Device Consortium
Division of Pediatric Surgery, Department of Surgery
University of California, San Francisco

[Signature]

Vilma Zarate 1/13/12 11:24 AM
Deleted: Program
b. Draft label

**MAGNIMPLANT** – magnetic implant set

**CAUTION:** Investigational device. Limited by Federal law to investigational use.

**DO NOT STEAM sterilize** or expose to temperatures above 80°C.

Manufactured by:
Hantel Technologies, Inc.
703 Sandoval Way
Hayward, CA 94544
Ph 510-487-1561

Set includes:
1 Magnimplant serial number: __________
1 Backing plate serial number: __________
2 Titanium cable wires

Device materials: Titanium
Method of sterilization: Gamma radiation

---

Stickers for external brace and brace canister

**DANGER!**

**CAUTION:** Investigational Device. Limited by Federal Law to Investigational Use.

Manufactured by:
University of California, San Francisco
400 Parnassus Avenue, A123
San Francisco, California 94143-0570

Device material(s): Rare Earth Metals
§12. Copies of all informed consent forms and all related information materials to be provided to subjects.

(See informed consent for parents and assent forms for children beginning on the next page.)
Study Title: *Phase III Multicenter Trial of Magnetic Alteration of Pectus Excavatum (G090006)*

*This is a medical research study. You and your child have already met with a pediatric surgeon from the UCSF Department of Surgery, Division of Pediatric Surgery, and he or she has referred you to us for more information about this study. The study doctor, Shinjiro Hirose, M.D., the study nurse, and the research assistant from the UCSF Department of Surgery, Division of Pediatric Surgery, will explain this study to you and your child. If you and your child decide to participate in the study, you will meet with the lead study doctor, Michael R. Harrison, M.D., from the UCSF Department of Surgery, Division of Pediatric Surgery, and the study orthotist, Darrell Christensen, C.O., from the UCSF Department of Orthopaedic Surgery.*

Medical research studies include only people who choose to take part. Take your time to make your decision about allowing your child to participate. You may discuss your decision with your child, your family and friends, and with your health care team. If you have any questions, you may ask Dr. Harrison, Dr. Hirose (or any of the other the study doctors), and the study nurse coordinator.

Your child is being asked to take part in this study because your child has a congenital pectus excavatum (sunken chest) deformity for which your child and you are seeking corrective surgery. You have already been counseled about this condition and you know that the standard ways to repair this deformity are with operations that change the shape of your child’s chest and/or hold it in place with a metal bar. Dr. Harrison and his associates are testing a method to gradually repair the deformity by placing a magnet on the sternum (breastbone) and then applying an external magnetic force that will pull the sternum outward gradually. The Food and Drug Administration (FDA) has not approved the device but has given Dr. Harrison and his associates permission to test the magnet device in humans.

This treatment using magnets is an experimental procedure that has previously been tested in only a group of ten patients. None of these patients had a bad effect from the magnet device and none had serious medical problems or wound infections after the magnet was placed on the sternum or during the treatment. We evaluated the effectiveness of the treatment by calculating the Pectus Severity Index or PSI from your child’s pre- and post-treatment CT scan. The Pectus Severity Index is a numerical measure of how severe the chest is sunken. In our test of ten patients, some of the patients had no change between the pre- and post-treatment PSI, (that is, no measurable improvement in the defect), while three had a lower PSI (or measurable improvement), and four had a higher PSI (or worsening of the defect).

The design of the device that will be used in this study has been modified to try to reduce some of the risks seen in the pilot study of ten patients. Like the pilot study, this trial is being funded by the Food and Drug Administration.

Why is this study being done?
The purpose of this study is to test what effects, good and/or bad, placing an external/internal magnetic device has on correcting pectus excavatum deformity in children, and the safety of using such a device for treatment.

Dr. Harrison owns Magnets-In-Me, the company that developed the magnetic implant device and the Magnetic Mini-Mover Procedure [or 3MP]. Dr. Harrison has a substantial personal and financial interest in the device and will benefit financially, if the device does what they hope it will do. UCSF may also benefit financially. The Food and Drug Administration (FDA) has granted the study investigators permission to use this investigational device (IDE #G090006).

How many people will take part in this study?

A total of 15 children and adolescents at three different hospitals between the ages of 8 and 14 years will take part in this study. Five people will take part at UCSF.

What will happen if my child takes part in this research study?

If you agree to allow your child to participate in this study, then the following will happen:

Before your child begins the main part of the study...

- **CT scan of the Chest:** As part of the evaluation of your child’s chest wall deformity, a CT scan will be done and the Pectus Severity Index calculated. The Pectus Severity Index is a measure of how severe the chest is sunken. If your child has had previous CT scan done within the past year, then another procedure may not need to be done. You can bring a copy of the images to the study doctors’ clinic office, so the studies can be examined by a radiologist at UCSF.

- **Most insurance carriers require that a CT be done prior to providing authorization for the operation.** If this is the case, one will need to be ordered by your pediatrician or surgeon. During the CT scan your child will need to lie still on a table with his/her chest inside a large doughnut-shaped machine. The table will move and the machine will make clicking and whirring noises as the pictures are taken. The CT scan will take about 15 minutes to half an hour.

- **Hand/wrist X-rays:** Radiographs of the hand will be obtained to assess your child’s bone age and project his/her proximity to puberty. This hand x-ray is needed to evaluate whether your child is ready to enroll in the study now. If your child is enrolled, then this hand x-ray will be performed again at two other time points during treatment (12 and 24 months after implantation).

- **Electrocardiogram (EKG):** Also, as part of the evaluation, your child will have an electrocardiogram done to measure heart activity before a magnet is put on the breastbone and your child wears the outside brace containing a second magnet.
**Creation of a Plastic Mold:** If your child is eligible to enroll in the study, he/she will have a soft plastic mold made of his/her chest wall deformity. This will be made of a putty-like material which, when hardened, produces an exact copy of your child’s particular deformity. Dr. Harrison and his associates will use this mold to create a brace fitted exactly to your child’s chest. This external brace will contain a magnet, which your child will wear on the front of his/her chest. If wearing this brace is acceptable to your child and you, then your child can go on to have the internal magnet implanted. If your child does not like or want to wear this brace, then he/she should not be in the study.

**During the main part of the study...**

If your child wants to participate in this study, then your child will have the following procedures done.

- You will be given a standard consent form for surgery and anesthesia to read and sign before the surgery is done to implant the magnet.

- Your child will have a magnet, encased in titanium and 2 inches in diameter, attached to his/her sternum (breast bone). This will likely be accomplished in an outpatient procedure (your child does not have to stay in the hospital overnight) under general anesthesia. While your child is asleep, Dr. Harrison or Dr. Hirose will make a 2-inch incision near the bottom of the breastbone and attach the magnet to the breastbone. The operation will take about one hour. Your child will likely go home a few hours after the surgery, and can resume normal activity the next day provided he or she is feeling well. However, we will monitor your child closely in the recovery room and only discharge him/her once pain has been adequately addressed. Very rarely, outpatient procedures require admission to the hospital for monitoring.

- While your child has the magnet in place, he/she will be required to wear a medical alert identification bracelet or dog tag that states, “** Implanted magnet - NO MRI**”. This alerts a physician, emergency department personnel, any health care provider, or the police or firefighters of your child’s condition even if he or she cannot explain it. The study team will provide the bracelet or dog tag, or you can choose to provide your own as long as the warning language states, “Implanted magnet - NO MRI”.

- **After the incision has healed (two weeks), your child will be fitted with the external brace. Adjustments may be made to the brace, if necessary, to improve fit and comfort. At about four weeks after surgery, your child may start to wear the previously fitted brace. The magnetic brace must be worn as much as possible. Wearing the brace should not interfere with your child’s activities. It should be worn while sleeping at night. The brace is easily removed for bathing and relieving any discomfort.**

- For the first month after the procedure, your child will see Drs. Harrison and Hirose at two weeks and four weeks after the surgery. The study nurse and the clinical research fellow will also be present at these visits. Also, they will see your child more than once a week, if your child is experiencing discomfort and/or pain during the first month after the procedure.
The number of visits to the Chest Wall Deformities clinic office will depend on how your child is feeling.

After the first month, your child will have monthly visits with the study investigators who will assess the progress of the treatment, and make sure there is no difficulty such as discomfort or skin problems. Your child will have these monthly visits until the deformity has been corrected. The amount of time it takes to correct the deformity varies with each patient and is not precisely known for your child’s situation, but is likely to be 18 months to 24 months.

- One month after the magnet has been placed and every month after that until the magnet is removed, your child will have a plain x-ray of the chest (from the front and side). The chest x-rays are done for safety reasons, as they are the only way we can detect if the implanted magnet is broken or unattached.

- After the magnet has been placed, your child will have x-rays of the wrist/hand (from the front and side) at 12 and 24 months to measure bone maturity.

- One month after the magnet has been placed, your child will also have a second EKG done.

- One month after the magnet has been placed, your child will complete a questionnaire. The questionnaire will help the study team find out how your child’s physical and mental health has been affected by wearing the magnet device and brace. Your child will be asked to complete this questionnaire again, after the magnet is removed. Completing the questionnaire should take 1/2-hour.

- At each monthly visit, the study nurse or research assistant will take photographs of your child’s chest and brace to document any changes. These photographs will be from the side and front of the chest and will not include your child’s face. For female patients, only a female practitioner (the study nurse or clinical fellow) will take the photographs.

- During the study, your child and you will be able to make adjustments to the magnetic housing of the brace to either decrease the pull, or increase the pull. Your child can turn the magnet housing unit counterclockwise away from his/her chest (decreasing pull), or clockwise toward his/her chest (increasing pull). In any situation, the suspended magnet should never be so close that it touches your child’s skin. On the other hand, only the study investigators will be allowed to adjust and/or alter the brace itself, if it is uncomfortable or causing any skin damage.

If after adjusting the pull and/or taking Tylenol™ or Advil™ to relieve pain, your child is still experiencing discomfort, then he/she will need to see the study team who will exchange the magnet housing for one with less magnetic strength. Or, if after adjusting the magnet housing unit, your child still feels the pull is not enough, then he/she will be seen by a member of the treatment team who will increase the strength of pull by exchanging the magnet housing unit for one with increased magnetic strength. When the Magnatract brace is set comfortably, then the treatment team member will record the new magnet housing unit and adjustment.
During the study, at the office visits, Dr. Harrison or Hirose or the study nurse will download information from the data sensor attached to the brace to monitor the your child’s compliance with wearing the brace. The number of hours each day your child wears the brace is recorded by the data sensor. Your child does not have to download this information at home. The data sensor records the wear-time of the brace by recording the strength of the pull on your child’s chest. The study team will review the data at least monthly at your child’s follow-up visits, and discuss the results with your child and you. They will review the data more frequently, if there is a problem with the correction or if your child reports a problem.

At the end of the study period (no more than 24 months) the magnet will be removed from your child’s sternum in an operation like the one used to place the magnet. Your child will have general anesthesia, and Dr. Harrison or Dr. Hirose will use the same incision to remove the magnet. The procedure will take about 30 minutes to one hour, and your child is expected to go home the same day and may resume full activity the next day. Very rarely outpatient procedures require admission to the hospital for monitoring.

One month after the magnet is removed...

- Your child will have an office visit with Dr. Harrison or Dr. Hirose and the study staff.
- Your child will have another EKG taken. If the EKG reveals an abnormality or change from prior EKG, then another EKG may need to be performed or an echocardiogram (ultrasound of the heart). 
- Your child will have a CT scan taken so the study investigators can calculate the Pectus Severity Index after pectus correction.
- Your child will be asked to complete a questionnaire. This is the same questionnaire that your child completed one month after the magnet was implanted, and will help Dr. Harrison and his colleagues find out how your child’s physical and mental health have been affected by wearing the magnet device and brace. Your child will be asked to complete this questionnaire again, one year after the magnet is removed. Completing the questionnaire should take 1½–hour.

Every six months for two years (at 6, 12, 18 and 24 months) after the magnet has been removed....

- Your child will have an office visit with Dr. Harrison or Dr. Hirose and the study staff.
- At the one year visit, your child will be asked to complete a questionnaire. This is the same questionnaire that your child completed one month after the magnet was implanted and one month after it was removed. Your child’s and your answers will help Dr. Harrison and his colleagues find out how your child’s physical and mental health have been affected by wearing the magnet device and brace. Completing the questionnaire should take 1½–hour.

Where will the study take place?

- **Study location:** The study will take place in the following locations:
  
  1. **Pediatric Surgery/Chest Wall Deformities** Clinic Office ACC 2nd Floor (400 Parnassus Avenue) 
     - Initial consultation: 1 hour x 2
Two visits during the month after the surgery: 20-30 minutes
Monthly visits until magnet removal: 20-30 minutes x 18-24 visits
Five visits after the magnet is explanted: at 1 month and then 6, 12, 18 and 24 months post-explant

2. Pediatric Cardiology ACC 2nd Floor (400 Parnassus Avenue)
- EKG preoperatively, one month and 1 year post operatively

3. Moffitt/Long Operating Suites
- Implant magnet: 1 hour operation
- Remove magnet: 1 hour operation

4. Orthotics and Prosthetics Center (C39, 521 Parnassus Avenue):
- One visit for casting preoperatively
- One visit two weeks after the surgery
- At least 18-24 monthly visits x 0.5-hr each until the magnet is explanted.

5. Radiology (3rd Floor, ACC or 3rd Floor Moffitt/Long)
- One visit pre operatively
- At least 18-24 monthly visits x 0.5-hr each beginning one month after the magnet is implanted and then throughout treatment.
- Three visits after the magnet is explanted: at one month and at one year and 2 years post-explant

How long will my child be in the study?

Participation in the main part of the study will take 18 months to 24 months, depending on how long it takes to correct your child’s pectus excavatum defect. Each clinic visit while the implant is in place will take on average 1.5 hours. After the magnet is removed from your child’s sternum, the study doctor will ask you to visit the office for follow-up exams. Participation in this study will also involve long-term follow-up (two years at six-month intervals) with potential for up to a five year follow up. Your child will be asked to complete a questionnaire at one month and again at one year after the magnet is removed. Each long-term follow up visit will take an average of 15 minutes.

Can my child stop being in the study?

Yes. You and your child can decide to stop at any time. Tell Dr. Harrison, Dr. Hirose, the study nurse, or any of the other study personnel if you and your child are thinking about stopping or decide to stop.

Dr. Harrison and Dr. Hirose may stop your child from taking part in this study at any time if he believes it is in your child’s best interest, if your child does not follow the study rules, or if the study is stopped.

What side effects or risks can my child expect from being in the study?
Participation in research involves the risk of a loss of privacy. Qualified personnel of the UCSF Institutional Review Board and/or the Food and Drug Administration may review patient/study records. There are laws that require that research records that will have your child’s name on them be shown to people who make sure that the research is being done the way it should be.

The risk of the operation to place the magnet on the breastbone (and later to have it removed) is small, but does require outpatient surgery under general anesthesia, similar to having an inguinal hernia repaired. The first Magnimplant device used in the pilot study for which many of the risks are taken from is different from the Magnimplant generation III device used in this multicenter clinical trial. The devices differ by the attachment method to the sternum in which a cable wire is used to secure the device onto the sternum rather than punching a hole in the sternum and screwing the front and back plates. The device change was made to make the Magnimplant generation III more safe for your child. We have performed extensive testing on this device to prove its integrity and greatly reduce the risk of breaking or becoming unattached while implanted. The medical risks involved in undergoing this type of treatment and participating in this study are the following:

**Radiation**

1) As a result of participating in this study, your child will receive a small amount of radiation. The amount is similar to that received in many standard X-ray procedures, but is far more than your child would receive from natural daily exposure and carries at least a theoretical risk. If you are especially concerned with radiation exposure, you may wish to discuss this with the investigators. In addition, this study requires up to two CT scans. Radiation is necessary to obtain CT images. It is known that high levels of radiation may cause cancer. CT scans result in a low-level exposure, but there is a slight chance of increasing your child’s risk of developing cancer in the future from excessive exposure to radiation. Every effort is made to limit the amount of radiation your child may receive from a CT scan. One measure is to restrict the area scanned as much as possible and to "fine tune" the CT settings based on the reason for the exam, the body area being examined, and your child's size. The radiologists at UCSF generally attempt to use the lowest radiation dose that will provide the needed information. If you are especially concerned with radiation exposure, you may wish to discuss this with the investigators.

**Surgery to Implant the Magnet**

2) There is a small chance (less than 1%) of injury to the surrounding structures, and a likelihood (at least a 50% chance) of getting some air into the sac surrounding the lung (entrained air or pneumothorax), getting fluid in the lung (hydrothorax), and/or blood in the lung (hemothorax). In the Phase II study, five of ten patients were treated for air and/or fluid in the chest due to surgical technique, but not due to injury to surrounding structures. Although the device configuration has changed since the pilot study, we are still operating in the same area so the risk of entrained air still exists.

In five patients, evacuation of pleural air and/or fluid using a needle occurred intraoperatively or immediately postoperatively. Of these five patients, one patient was admitted and underwent further evaluation using a catheter, another patient underwent further evacuation with a catheter as an outpatient, and a third patient was admitted and observed without intervention.
3) There are the risks associated with the surgery itself to implant a titanium-encased magnet to your child’s sternum. These include a small risk from the general anesthesia (about one hour), a 2” incision, punching a \( \frac{3}{8} \)” hole in the deformed sternum, and attaching the magnet encased in titanium to your child’s sternum. The side effects of general anesthesia may include nausea and vomiting, aspiration (inhaling material into the lung), or the inability to maintain normal breathing requiring placement of a breathing tube into the trachea (windpipe).

4) There is a chance of pain and tenderness at the incision and on the sternum that will require treatment with pain medication for 1-2 weeks. The pain could be due to the implant pulling on the sternum or being secured too tightly to the sternum. There is a chance that this pain may not improve with pain medications and may require an additional procedure to loosen, replace or rarely, remove the magnet.

   This happened to one of ten patients in the first trial. This patient had re-operation to loosen the magnet and went on to complete treatment.

5) There is a small risk of infection or bleeding that can occur with any invasive procedure. If an infection develops while the magnet is implanted, the magnet may need to be removed and/or replaced. There is a small risk of infection after the magnet has been removed which may require antibiotics. An infection at the surgical site occurred in two of ten patients in the first study after the implant was removed.

6) There is a risk that your child may require additional treatment to address any operative complications. This may include additional chest X-rays, a CT scan(s), or another surgical procedure.

**Magnet Implanted in the Body**

7) There is a risk that the magnet device could break or become unattached while implanted in your child. If this happens, the implant would have to be removed. In three of ten patients in the pilot study, the backplate separated from the post that holds the magnet in place. It is important to note that the Magnimplant failed in the same place in all three patients. The magnet separation was found on chest x-ray taken during a scheduled follow-up visit. One subject, who completed 17+ months of treatment, underwent outpatient surgery to remove the failed device. The second child, who completed nine months of treatment, underwent outpatient surgery to remove the broken magnet and had a new device implanted under CHR- and FDA-approved Compassionate Use designation. The third child, who completed 16 months of treatment, had the device removed in an outpatient surgery.

   Two additional patients had device separation between the magnet and the threaded post/back plate, likely due to incomplete threading of the device at the time of implant. Both patients (and their parents) chose to have surgery to replace the device and continue treatment.

   The study doctors emphasize the importance of your child having the monthly chest x-rays. Besides allowing us to measure changes to your child’s chest wall, the chest x-rays are done for safety reasons, as they are the only way we can detect if the implanted magnet is broken.
8) There is a possibility of fluid accumulating in the sac surrounding the heart (pericardial effusion). In the Phase II trial, one patient developed a build up of fluid in the sac surrounding the heart (pericardial effusion), which required hospitalization and percutaneous drainage of the fluid. However, it is unclear whether the pericardial effusion was related to the implant since it occurred 16 months after implantation and did not recur with the same implant still in place. There was no indication of injury to the pericardial sac on imaging that could have caused the pericardial effusion.

9) There is no known risk of having a magnet or any static (“unchanging”) magnetic field in your child’s body, even close to the heart. While magnetic fields changing rapidly [for example, magnetic resonance imaging (MRI)] can induce weak electric fields that can have minor biologic effects, static magnetic fields do not.

10) There is a possibility that fluid (seroma) could accumulate around the magnet as your child’s body becomes used to the implanted magnet. This should resolve in 1-2 weeks but may take up to a month. There is a possibility of a seroma developing at the surgical site after the magnet is removed. This may drain on its own or be reabsorbed by your child’s body and may require treatment with antibiotics.

**Injury to the Skin and Discomfort**

11) The risk of wearing the external magnetic brace may be discomfort or even injury if it is allowed to pull too hard. It is possible to pull hard enough to cause damage to the skin over the sternum. It is also possible to cause bruising, swelling or marks on the skin over the implant from contact with the brace. Damage to the skin and soft tissue may be caused by the surgical procedure itself. This complication was seen in one of ten patients and the wound was monitored for disruption or signs of infection. In another instance, a patient did have the magnets in the external housing device dislodge and attach directly to the patient’s chest. However, in this study, this risk is very low because the external magnet housing is now made from a single piece of plastic, unlike the housing unit used in the pilot study. The strength with which the external magnet pulls on the magnet on the sternum is adjustable. In addition, the strength can be accurately measured using the gauges built into the device. This is intended to allow Dr. Harrison and his associates to adjust the device for comfort and to avoid injury to the skin from pulling too hard. If a small skin blister or discoloration of the skin develops directly under the magnet-housing on the brace the wear-time and the magnet housing in the brace may need to be adjusted.

**Attracting Metal Objects**

12) There is a small danger that metal objects would be attracted to the device and stick on your child’s skin overlying the magnet in the lower chest. Your child will have to be careful around small metal objects and particularly other magnets.

**Interference with Electronic Devices**

13) There is a possibility that the implanted magnet or external brace may interfere with electronic devices, such as iPods, computers, television sets or cellular phones. Your child will have to be careful around these devices.
Photographs of Chest
14) There is a chance that your child may be uncomfortable with having photographs taken of his or her chest at monthly visits. However, these photographs are part of the study and your signed consent to this document gives permission for the study team to take pictures of your child’s chest to document correction.

Metal Screening Devices
15) There is a potential problem with having any implanted metal device in that it might be detected by metal screening devices, such as those found in airport security. The Magnetic Mini-Mover’s magnetic field could interact with security systems like electronic surveillance devices. You and your child will be given a letter to keep that explains that your child has an implanted metallic device.

Risks from Magnetic Resonance Imaging (MRI)
16) There is a risk of injury from having magnetic resonance imaging (MRI). Your child is not to have any MRI or be near any strong magnetic field like an MRI machine.

Risks to Others with Pacemakers or Other Medical Devices
17) There is a risk that the external magnet might be a danger to others such as people who use heart pacemakers or nerve stimulation devices. Those people will already be aware that they should not come into contact with magnetic fields that could affect their devices. Likewise, your child’s magnets (both implanted and outside) could affect another person’s device. So, you and your child must be aware that he/she and the brace must not come in close contact with other people with those devices.

18) A safe distance from your child’s magnet to an implanted device in another person is six inches (6”). Therefore, your child should never have his/her chest wall magnet any closer than 6” from another device.

Failure to Correct the Deformity or asymmetry of deformity
19) There is a risk that the pull on the sunken breast bone will not be strong enough to correct the deformity or the direction of the deformity completely in the time that your child is willing to wear the magnetic brace. If this proved to be the case, you could always choose another form of treatment.

Surgery to Remove the Magnet
20) There is the same small risk from the procedure to remove the magnet from the sternum as with the procedure to place the magnet. This again should be accomplished as an outpatient procedure under a general anesthesia of the same magnitude and with the same risks as mentioned above for implanting the magnet.

Unknown Risks
21) This experimental treatment may involve unforeseeable risks to your child. Or, should your child become pregnant, this treatment may have unforeseeable risks to the embryo or fetus.
22) The experimental treatment may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

For more information about risks and side effects, ask your child’s study doctor. It is very important that you and your child tell Dr. Harrison, Dr. Hirose, or the study nurse about any side effects, any unusual symptoms, or any changes in health your child experiences while taking part in the study, even if the symptoms do not seem related to the treatment.

**Are there benefits to taking part in the study?**

There may or may not be direct benefit to your child by participating in this study. However, information gained from this study may help other patients with this same problem. There may be a benefit from the treatment itself in that your child may have the sunken chest deformity corrected without having to undergo the major surgery and hospitalization required for methods of repair presently available (Nuss or Ravitch type repairs).

**What other choices does my child have if he/she does not take part in this study?**

Your child’s other choices may include:

- To decide not to participate in this study. The decision to not participate in this study will not affect your child’s care.
- To decide to stop participation in the study at any time;
- To receive no treatment;
- To receive standard treatment for your child’s condition without being in a study. Your child can undergo other surgical treatments that are considered standard (e.g., Nuss procedure or the modified Ravitch procedure). The advantage and disadvantages of these presently available procedures have been explained to you and your child.

**Will my child’s medical information be kept private?**

We will do our best to make sure that the personal information in your child’s medical record is kept private. Your child’s records may be reviewed by qualified personnel of the University of California, San Francisco Institutional Review Board and/or from the Food and Drug Administration (FDA). Your child’s personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your child’s name and other personal information will not be used.

Participation in research may involve a loss of privacy, but information about your child will be handled as confidentially as possible. A medical record will be created because of your child’s participation in this study. Your consent form, your child’s assent form, and some of your child’s research test results will be included in this record. Therefore, your child’s other doctors may become aware of your child’s participation. Hospital regulations require that all health care providers treat information in medical records confidentially.
**What are the costs of taking part in this study?**

The cost of office visits, surgery, and standard tests described above may be billed to you or your insurance carrier. The study doctors will not perform this experimental procedure unless pre-approval from your insurance company has been obtained. However, insurance companies and other carriers sometimes refuse to pay the costs of treatment retroactively or when individuals are participating in research. If this happens, you will be responsible for your child’s fees.

You or your insurance carrier will not be billed for any procedures or tests during the study that are done for research purposes only, such as monthly chest x-rays, hand x-rays and post-operative EKGs. In this study, few procedures, tests or study visits will be done for research purposes only, as most are all clinically necessary in the course of repair of pectus excavatum.

In addition, as described previously, there is a risk that this new procedure may fail to correct the chest wall deformity completely in the time that your child is willing to wear the magnetic brace. If this proved to be the case, you could always choose another form of treatment. However, there is the possibility that your insurance carrier will refuse to pay for the standard surgical repair if the experimental device fails. The likelihood that your insurance company will not pay for a second standard operation is low. However, there is a potential financial risk to you. We recommend that you discuss this possibility with your insurance carrier before your child enrolls in the study.

**Will my child be paid for taking part in this study?**

Your child will not be paid for taking part in this study.

**What happens if my child is injured because he/she took part in this study?**

It is important that you tell your child’s study doctors, Dr. Michael Harrison or Dr. Shin Hirose, or any member of the study team, if you feel that your child has been injured because of taking part in this study. You can tell the doctor in person or call him/her at 415 476-2538 (24 hours a day/7 days a week).

**Treatment and Compensation for Injury:** If your child is injured as a result of being in this study, treatment will be available. The costs of the treatment may be covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415-476-1814.

**What are my child’s rights if he/she takes part in this study?**

Taking part in this study is your child’s and your choice. You and your child may choose either to take part or not to take part in the study. If you and your child decide to take part in this study, your child may leave the study at any time. No matter what decision you make, there will be no penalty to your child and your child will not lose any of his/her regular benefits. Leaving the study will not affect your child’s medical care. Your child can still get your medical care from our institution.
We will tell you about new information or changes in the study that may affect your child’s health or your child’s willingness to continue in the study.

In the case of injury resulting from this study, you and your child do not lose any legal rights to seek payment by signing this form.

**Who can answer my questions about the study?**

You and your child can talk to your child’s study doctor and the study nurse coordinator about any questions or concerns you or your child have about this study. Contact your child’s study doctors, Dr. Michael Harrison or Dr. Shin Hirose, or the study nurses at (415) 476-2538, any time of the day or night.

For questions about your child’s rights while taking part in this study, call the office of the Committee on Human Research, UCSF's Institutional Review Board (a group of people who review the research to protect your child’s rights) at 415-476-1814.

For questions about the magnetic device used in this study, call the office of the Center for Devices and Radiological Health Food and Drug Administration at 301-796-5699 or located at WO66 Room 5428, 10903 New Hampshire Avenue, Silver Spring, MD 20993.

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**CONSENT – Part A**

You have been given copies of this consent form and the *Experimental Subject's Bill of Rights* to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about your child.

**PARTICIPATION IN RESEARCH IS VOLUNTARY.** You and your child have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which your child is otherwise entitled.

The person being considered for this study is unable to consent for himself/herself because he/she is a minor. By signing below, you are giving your permission for your child to be included in this study.

Date ____________________________
Parent or Legal Guardian

Date ____________________________
Parent or Legal Guardian

Date ____________________________
Person obtaining consent

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CONSENT – Part B

Your child has completed the extended work-up consisting of the chest CT scan, EKG, and hand/wrist x-ray. He/She has met all the inclusion criteria and no exclusion criteria apply to your child. By signing this consent again, you are giving permission for your child to continue in the study now that he/she has met all the inclusion criteria.

Date Parent or Legal Guardian

Date Parent or Legal Guardian

Date Person obtaining consent
What is this study about?
Michael R. Harrison, MD, Shinjiro Hirose, MD, Darrell Christensen, CO, and their associates from the UCSF Departments of Surgery (Division of Pediatric Surgery), Orthopedic Surgery, and Clinical Engineering are doing a research study. The study will test a new method to correct pectus excavatum (“sunken chest”) deformity to see if it is effective and safe for children and adolescents. Dr. Harrison and his associates have developed a method to gradually repair the deformity by placing a magnet on the sternum (breastbone) and then applying an outside magnetic force that will pull the sternum outward gradually.

The study doctors hope this method will help young people with pectus excavatum, but they don’t know if it will for sure. That’s why they’re doing the study.

Because you have a pectus excavatum, the doctors are asking if you want to be in this study.

How many people will take part in this study?
Fifteen (15) children and adolescents (8 to 14 years old) will be in this study. Five of them will participate at UCSF.

What will happen if you decide you might want to be in this research study?
First, your parents will be asked if they give their permission for you to be in this study. They will also be asked if they agree to participate themselves, by doing some things like answering questions about you. If your parents don’t agree, you cannot be in the study.

If your parents do agree, and you agree too, here’s what will happen next:

Before you begin the study:
1. The study doctor will ask your parents some questions about you.
2. The study doctor will ask you questions about your health.
3. You will have a CT scan done. These tests will allow the study doctors to measure how severe your chest is sunken. If you have had a CT scan done previously, then you may not need to have this pre-study CT scan. You and your parents can bring a copy of the CT scan to Dr. Harrison’s office.
4. You will have hand/wrist x-rays taken to evaluate your growth stage and to find out if you are beginning or are in puberty.
5. You will have an electrocardiogram (EKG) done to measure your normal heart activity before a magnet is put on your breastbone and before you wear an outside brace containing a second magnet.
6. You will have a soft plastic mold made of your chest wall deformity. This mold will be made of a putty-like material which, when it hardens, makes an exact copy of your deformity. Dr. Harrison and his associates will use this mold to create a brace to fit your chest exactly. They will also use this mold to create an outside (external) brace containing a magnet, which you will wear on the front of your chest. If you and your parents agree, then you will have a magnet implanted on your sternum. If you do not like wearing this brace, then you and your parents do not have to continue with this study.

During the study:

7. You will have a magnet that is encased in titanium (a metallic material) and is 2 inches wide attached to your sternum (breastbone). This is accomplished in an outpatient procedure under general anesthesia. We do not expect that you will have to stay in the hospital overnight, but it is possible. When you are asleep, Dr. Harrison and Dr. Hirose will make a small (2") incision near the bottom of your breastbone and attach the magnet to the breastbone. Once the magnet is attached, a chest x-ray will be done in the operating room to detect any air in the sac surrounding your lungs ("pneumothorax"). That is, a chest x-ray is done intraoperatively to minimize the risk of pneumothorax to you. The operation takes about one hour. We expect you and your parents can go home a few hours after the surgery, depending on your recovery. You can go back to your normal activity the next day, depending on how you are feeling.

8. After your incision has healed (about two weeks), you will be fitted with the brace that was made for you. About one month (approximately four weeks) after surgery, you may start wearing the brace, as long as it does not cause you serious discomfort. The magnetic brace must be worn as much as possible, but it should not interfere with your activities. You should wear the brace at night while you are sleeping. However, the brace can be easily taken off when you take a bath or shower, or if you feel uncomfortable. If correction has been achieved, then you may need to wear the brace only at night as a "retainer" to maintain correction.

9. After the surgery, you will need to visit the clinic every other week for one month after surgery to see Dr. Harrison, Dr. Hirose, and the study nurse. You can see them more often, if you need to because of discomfort or problems with your skin. After the first month, you will visit the clinic once a month so that Dr. Harrison, Dr. Hirose and their associates can determine the progress of the repair of your chest wall deformity. They will also make sure that you have no problems with discomfort or your skin. The amount of time it takes to correct the deformity will be different for each child and adolescent in the study. The study team does not know how much time will be needed to correct your situation, but it is likely to take 18 to 24 months.

10. Every month after the magnet has been placed until the magnet is removed, you will have an x-ray of the front and side of your chest done so that Dr. Harrison, Dr. Hirose and their associates can measure how well the treatment is working.
11. You will have an x-ray of your wrist/hand to evaluate your growth stage at 12 and 24-months.

12. One month after the magnet has been placed, you will have a second EKG done at the same time you have your chest X-ray.

13. One month after the magnet has been placed, you will be asked to fill out a questionnaire. Your answers to the questions will help Dr. Harrison find out how your physical and mental health have been affected by wearing the magnet device and brace. Completing the questionnaire should take \( \frac{1}{2} \)-hour.

14. During the study, at each monthly appointment, the study nurse or Dr. Hirose will take a photograph of the front and side of your chest so we can compare how your chest looks from visit to visit. These photos will not show your face. Your mother or father can stay in the room with you, if you want them to.

15. During the study, the study team will download information from your data sensor at each monthly visit in their clinic, so that they can measure the number of hours per day you are wearing your brace. Neither you nor your parents have to download this information from home. This wear-time is called “compliance.” The study team can also look at the data, if you report there is a problem or there is no correction. They will talk to you about your compliance once a month when you visit them in their office.

16. During the study, you may make adjustments to the pull of the magnet either by turning the magnet housing unit counterclockwise away from your chest (decreasing pull), or clockwise toward your chest (increasing pull). However, you will not be able to change or adjust the brace itself—only the study team can do this. Whether you increase or decrease the pull, the suspended magnet should never be so close that it touches your skin. If you unable to adjust the brace to your liking, then you will be seen by a member of the treatment team who may exchange the magnet housing for a new one. The study team may exchange the magnet housing if there is a problem with the data sensor.

17. During the study, you will wear a dog tag or a bracelet that says “No MRI”. When you cannot explain it yourself, this tag or bracelet will let doctors, nurses, police and firefighters know that you cannot have an MRI.

18. When the deformity is corrected, the magnet will be removed from your breastbone in an operation like the one used to place the magnet. You will have general anesthesia to make you sleep. Dr. Harrison and Dr. Hirose will use the same incision to remove the magnet. The procedure will take about one hour. We expect you will feel well enough to go home with your parents a few hours after the surgery, but there is a chance you will have to stay overnight. We expect you will feel well enough to go back to your normal activity the next day.

When the study ends, one month after the magnet is removed:

19. You will have another EKG taken one month after the magnet is removed.

20. You will also a CT scan done to document the results from using the magnet device.
21. You will be asked to answer a questionnaire. This is the same questionnaire you filled out before that will help Dr. Harrison, Dr. Hirose and the study nurse find out how you felt physically and emotionally while wearing the magnet device and brace.

22. You will visit the clinic every six months for two years so that Dr. Harrison and his associates can assess the repair of your chest wall deformity.

One year and two years after the magnet is removed:

23. You and your parents will answer the same questionnaire that you completed when the magnet was taken out.

Will any parts of this study hurt or have other risks?

**Surgery to place the magnet**

There are risks associated with the surgery to place the magnet on your breastbone or to remove it. For example, the general anesthesia that makes you sleep may make you feel nauseous and vomit or you can inhale material into your lung, or, if you are unable to breathe normally, the anesthesiologist may need to put a breathing tube into your windpipe.

There is a likelihood of risk of injuring surrounding structures around the breastbone when the magnet is placed or removed from your breastbone.

The first Magnimplant device used in the pilot study is different from the Magnimplant generation III device used in this study. The devices differ by how it attaches to your breast bone or sternum. The device change was made to make the Magnimplant generation III more safe for you. We have performed extensive testing on this device to prove its integrity and greatly reduce the risk of breaking or becoming unattached while implanted.

There is at least a 50% chance that some air, fluid, or blood might get into the sac surrounding your lung(s) that will need to be drained. In the Phase II study, five of ten patients were treated for air and/or fluid in the chest because of the surgical technique, but not due to injury to surrounding structures. In five patients, we removed air and/or fluid in the chest using a needle during the surgery and immediately after the surgery. Of these five patients, one patient was admitted to the hospital and underwent further evaluation using a catheter, another patient underwent further removal of air or fluid with a catheter as an outpatient, and a third patient was admitted to the hospital, monitored, but did not have a procedure done.

There is a chance that your incision and breastbone will hurt for 1-2 weeks following the surgery. This pain could be from the surgery and how the magnet is attached to your breastbone. We will give you pain medicine to treat this. This happened to one of ten patients in the first trial. This patient had re-operation to loosen the magnet and went on to complete treatment.

You may lose a little bit of blood when you have the magnet put in or when it is taken out, but this should not be a problem. There is also a very small risk of significant blood loss, but this rarely happens.
There is a chance that we may have to do other examinations to learn about a problem that can develop during or after surgery. This may be more x-rays or other procedures. There is also a chance that we have to do another surgery to correct these problems and make you feel better.

**Magnet Implanted in the Body and Wearing the Brace**

Once you have the magnet implanted and you are wearing the brace, it is very important that you tell your parents and the study doctors if you aren’t feeling well or you’re experiencing unusual symptoms. Even if you don’t think this is related to the treatment, you should tell your parents and us. A member of the study team may ask your parents to bring you to our office so that we can examine you and do other tests if we need to.

Some risks from having the magnet implanted in you and wearing the brace are the following:

1. There is a risk that your implant could break inside of your body. If this happens, you will have an operation to remove the broken implant. It is very important that you have monthly chest x-rays because this is the only way the study doctors can detect if the implant breaks. In three of ten patients, the backplate separated from the post that holds the magnet in place. It is important to note that the Magnimplant broke in the same place in all three patients. We learned that the device had broken on chest x-ray taken during a scheduled follow-up visit. One subject, who completed 17+ months of treatment, underwent outpatient surgery to remove the failed (broken) device. The second child, who completed nine months of treatment, had outpatient surgery to remove the broken magnet and had a new device implanted. The third child, who completed 16 months of treatment, had the device removed in an outpatient surgery.

2. There is a risk that the implant becomes separated but does not break inside of your body. If this happens, you will need an operation to remove or replace the implant. Two patients had the device separate between the magnet and the post/back plate. Both patients (and their parents) chose to have surgery to replace the device and continue treatment.

3. There is a risk that fluid may develop around your heart that will need to be treated by a heart specialist. You will need to stay in the hospital for this treatment. In the Phase II trial, one patient developed a build up of fluid in the sac surrounding the heart (pericardial effusion), which required hospitalization and drainage of the fluid. However, it is unclear whether the pericardial effusion was related to the implant.

4. There is a risk an infection may develop because of the treatment. If you do have an infection, Dr. Harrison will give you antibiotics. If the infection does not go away, Dr. Harrison and Dr. Hirose may have to remove the magnetic device. You may need to stay in the hospital for this treatment.

5. There is a risk that an infection may develop after the magnet is removed. If you do have an infection, Dr. Harrison or Dr. Hirose will give you antibiotics. If the infection does not go away, they may have to remove the magnetic device. You may need to stay in the hospital for this treatment.
6. There is a chance that some fluid could collect around your magnet after your surgery, after long periods of wear or (in the area of where the magnet was) after removal of the magnet. This is normal and should absorb naturally back into the body after a few weeks to a month. Or else, the fluid may drain on its own through the incision.

7. There is a possibility that your implant or brace might interfere with electronic devices, such as iPods, laptops, televisions, and cellular phones. You should be careful to keep these electronic devices away from your magnets to avoid damage.

8. There is no known risk of having a magnet in your body, even if it is close to your heart.

9. Wearing the outside magnetic brace may be uncomfortable or may cause injury to your skin if it pulls too hard. One patient developed a small blister and red mark on the skin that went away after remodeling the brace and reducing the amount of time wearing the brace. The strength with which the external magnet pulls on the magnet on your breastbone is adjustable to make it more comfortable for you and to prevent skin injury.

*Failure to correct the deformity*

10. There is the risk that the pull of the magnets on your sunken chest may not be strong enough to correct the deformity completely in the time you are willing to wear the magnetic brace. If this is the case, then you and your parents can always choose to have another form of treatment.

*Magnetic Resonance Imaging (MRI)*

11. There is a risk of being injured from having a magnetic resonance imaging (MRI) test. So, while you have the magnetic device implanted, you are not allowed to have an MRI or be near any strong magnetic field like an MRI machine or other devices that contain powerful magnets. The dog tag or bracelet that says “No MRI” will tell others that you cannot have an MRI in case you cannot explain it yourself. This must be worn at all times.

*Metal screening devices*

12. There may be a problem with having an implanted metal device that might be detected by metal screening devices, like those at the airport. The device could interact with these types of security systems. You and your parents will be given a letter from Dr. Harrison that explains that you have an implanted metallic device for medical reasons.

*Attracting metal objects*

13. There is a small risk that metal objects might be attracted to the device and stick to your skin that is over the magnet in your lower chest. You will have to be careful around small metal objects and particularly other magnets.

*Risks to other people using heart pacemakers or other medical devices*

14. There is a risk that the magnetic field might be a danger to others such as people who use heart pacemakers or other medical devices. Those people may already be aware that they should not come in contact with magnetic fields that could affect their devices. Likewise, your magnets (both implanted and outside) could affect another person’s device. So, you
and your external magnetic brace must not come in close contact with other people with those devices.

A safe distance from your magnet to an implanted device in another person is six (6) inches. You should never have your chest wall magnet any closer than 6 inches from another device. So, you should never hug someone with a device that is sensitive to magnetic fields.

**Other Risks**

15. There is a chance that you might feel uncomfortable when we take pictures of you at your appointments. If you want them to your parents can be present for these pictures to make you feel better.

**Removing the magnet**

16. There is the same small risk from the procedure to remove the magnet from your breastbone as with the procedure to place the magnet. The magnet will be removed in an outpatient procedure under general anesthesia. So, the risks are the same as mentioned above for implanting the magnet.

**Unknown risks**

17. This is a new treatment, so there may be risks that Dr. Harrison and his associates cannot predict.

**Will you get better if you are in this study?**

We don’t know if this study will correct your chest wall deformity. Your chest wall deformity may get a little better by being in this study, or it may stay the same.

**What if you have questions?**

You can ask Dr. Harrison, Dr. Hirose, or any of the people who work with them any questions you have about the study. You can ask your questions now or later, any time you like. You can also ask your parents to ask questions for you.

**What are your choices?**

If your parents agree, you can be in this study if you want to. But you don’t have to be in it if you don’t want to. Nobody will get mad at you if you don’t want to do this.

If you don’t want to be in the study, you can choose another form of treatment or no treatment at all.

If you decide to be in the study now and you change your mind later, that’s okay, too. You just have to tell the study doctor or the study staff as soon as you change your mind, and you will be taken out of the study.

**********************************************************************************
If you don’t want to be in this study, just say so, and don’t sign this form.

If you want to be in this study, please sign your name below.
If you sign here, it means you agree to participate in this study.
The doctor will give you a copy of this form to keep.

__________________________________   _______________ _____
Adolescent’s Signature     Date   Age

__________________________________
Adolescent’s Name (print)

________________________________   _______________
Signature of Person Conducting Assent Discussion  Date

________________________________
Name of Person Conducting Assent Discussion (print)
Why are we meeting with you?

We want to tell you about a research study we are doing to see if a new device will fix your chest. A research study is when doctors collect a lot of information to learn more about how to treat a health problem. Dr. Michael Harrison and the study team of specialists are doing a research study to treat children with a health problem called "sunken chest" deformity or pectus excavatum. After we tell you more about it this research study, we will ask if you’d like to be in this study or not.

Why are we doing this study?

We want to try to repair the sunken chest deformity with a small operation instead of a big one. So, we are trying a new treatment using two magnets and a brace on boys and girls like you.

In this study, there will be 15 children with a sunken chest who will volunteer to get the new treatment.

What will happen to you if you are in this study?

Only if you agree, the following things will happen:

1) You will have chest CT scan done so that Dr. Harrison can find out how much your chest is sunken. A CT scan — also called CT or computerized tomography — is an X-ray procedure where a high-speed computer is used to make multiple images or pictures of your body. You and your parents will receive information on how to get ready for this procedure. During the procedure, special lights may be used to make sure that you are placed properly. You may hear only slight buzzing, clicking and whirring sounds as the CT scanner moves around you.

2) You will have a hand and wrist x-ray to evaluate your growth stage. If you agree to be in the study, then you will have a hand and wrist x-ray two more times during the treatment.

3) You will have a test done called an electrocardiogram or EKG. This test will make a picture of your heartbeat.
4) You will have a soft plastic mold made of your chest wall deformity. This mold will be made from something like putty. This mold will be used to make a brace to fit your chest exactly. This brace will hold a magnet. You will be wearing this brace in front of your chest. If you do not like wearing this brace, then you do not have to go on with this study.

5) If you want to wear the brace and want to continue in the study, then Dr. Harrison will do a little operation to put a magnet under your skin and attach it to the sunken chest bone (sternum). This will be done in a special place called an operating room. You will get medicine that will prevent you from feeling pain during the operation and put you to sleep. You will be at the hospital until you feel good and are OK to go home. This might be a few hours or a day.

6) During the operation, after you have been put to sleep, Dr. Harrison or Dr. Hirose will make a small cut (about 2- inches) on your chest and attach the magnet to your chest bone. The magnet is about 2 inches wide.

7) During the operation, you will have a chest x-ray to make sure there is no air in the sac surrounding the lung (this is called “pneumothorax”).

8) When you wake up and are feeling well, you can go home. We do not expect you will need to stay in the hospital overnight, but this is possible. You can do your normal activity the next day, if you are comfortable.

9) After you have the magnet put in, you will wear a bracelet/wristband or dog tag that says “No MRI”. This dog tag or bracelet lets other doctors and nurses and even police and firefighters know you cannot have a certain medical test called an MRI.

10) When the small cut on your chest is healed, you will be fitted with the brace that was made for you. About a month after your operation, you can start wearing the brace. You and your parents will see Dr. Harrison, Dr. Hirose and the study team twice during the first month after your operation, and then once every month until your treatment ends. This way, the study team can make sure that you do not have a problem because of the treatment, including the magnet in your chest and your brace. If you have problems because of the treatment, or if you are not feeling well, you and your parents should call Dr. Harrison, Dr. Hirose, or any of the study team, as often as you need to. You and your parents should call them, if you are not feeling well for any reason, even unrelated to the treatment. If you have problems because of the brace, you and your parents may call or see the study doctors and the study team as often as you need to.

11) You should wear the brace as much as you can. The more you wear the brace, the more effective the treatment is. If possible, the brace should be worn all the time (day and night). If correction has been achieved, then you may wear the brace only at night as a “retainer” to maintain the correction.
The brace should not bother you when you are doing your normal activities, like walking, sitting, and playing. When you and your parents see the study doctors and the study team at their office for your monthly visit, they will adjust the magnets so that the brace remains comfortable.

12) You can rotate the magnet housing on the brace to either increase or decrease the pull, but neither you nor your parents can adjust the shape of the brace. Only the study team can adjust or change the shape of the brace. If after you have tried to increase or decrease the pull, the brace is still uncomfortable or not pulling hard enough, then you will be seen the treatment team who may change the magnet housing. The suspended magnet should never be so close that it touches your skin.

13) One month after you have the magnet put in, you will have another EKG done so that Dr. Harrison and the study team can make sure the treatment is safe for you.

14) One month after you have the magnet put in, you will have chest X-rays done, so that Dr. Harrison can make sure that the magnet is not broken. You will have a chest X-ray every month until the magnet is taken out.

15) One month after the magnet is put in, you will be asked some questions about how you feel about having the treatment.

16) At each appointment after you have the magnet put in, the study nurse or Dr. Hirose will take a picture of the side and front of your chest, so that Dr. Harrison can see if the treatment is working.

17) During the study, Dr. Harrison, Dr. Hirose and the study team will download the information from the data sensor that is in the magnet housing of your brace. This will be done every month at the clinic visit. You and your parents do not have to download this information at home. The information will help us measure how many hours each day you are wearing the brace. The study team will talk to you about your wear-time, when you visit them in the office.

18) After 18-24 months of treatment, Dr. Harrison and Dr. Hirose will take out the magnet. Just like when the magnet was put in, you will be given a medicine that will make you sleep and not feel any pain. When you wake up and are feeling well, then you can go home. We do not expect you will need to stay in the hospital overnight, but this is possible. You can do your normal activity the next day, if you are comfortable.

19) When the magnet is taken out, you will have another EKG done.

20) When the magnet is taken out, you will have a CT scan, just like at the beginning of the study.
Also, when the magnet is taken out, you will be asked some questions about how you felt about having the treatment. These are the same questions you answered when you first had the magnet put in. You will be asked the same questions next year.

You and your parents will see the study doctors and study team every six months for two years so they can see how the treatment is working.

**Will this study hurt?**

1) When you have the magnet put inside you or taken out, then the drug that makes you sleep may make you feel sick. This usually goes away overnight.

2) You may hurt where the magnet was attached to your breastbone and from the cut Dr. Harrison or Dr. Hirose made to put it in. We will give you medicine to make this feel better.

3) If the medicine can't fix these problems, then the study doctors or another specialist may have to operate to loosen the magnet and make you feel better. You may have to stay in the hospital for a few days until you feel better.

4) You may lose a little bit of blood when you have the magnet put in or when it is taken out. This is a very small problem.

5) You might have an infection because of the treatment. If you have an infection, Dr. Harrison or Dr. Hirose will give you medicine. But if the infection does not go away, the study doctors have to take out the magnet. If you have an infection after the magnet is removed, the study doctors may have to give you medicine or do an operation to remove the infection. You may need to stay a few days in the hospital to heal and feel better.

6) You might have fluid build up around your heart during treatment. If this happens, then we may have to do other tests to learn about the problem. There is also a chance that we have to do another procedure to drain the fluid and make you feel better. You will have to stay in the hospital a few days until you feel better.

7) There is a chance air could leak into your chest during the operation to place or remove the magnet. This is called a pneumothorax. This may need to be drained with a tube or may go away on its own.

8) There is a chance some fluid could collect around your magnet after surgery to put in or remove the magnet or during long periods of brace wear. This will usually go away on its own but may drain through the incision.
9) You can continue to play sports and do normal activities, even if they are rough. But, if you are playing rough, your chest might hurt. We will give you medicine to make this feel better.

10) There is a chance that the magnet inside of you could break. If this happens, you will have it taken out in another surgery like the operation to put it in.

11) There is a chance that the magnet may separate into two pieces. If this happens, you will have it taken out or replaced with another magnet in another surgery like the operation to put it in.

12) The outside brace may make you feel uncomfortable or hurt your skin. Your parents can call Dr. Harrison or Dr. Hirose, if your brace is uncomfortable. We can fix the brace so that it is more comfortable. Your parents can always call the study doctors or anyone on the study team when there is a problem with your brace.

13) The magnet in your chest might attract other metal objects. You and your parents will have to be careful around small metal objects and other magnets.

14) There is a chance that the magnet in your chest or brace could affect electronic devices, like your iPod, computer or TV. You should try to keep these away from your magnets.

15) There are some people who wear other medical devices. One example of an "other medical device" is an implanted defibrillator, a battery-operated device that monitors heart rate by sending electrical signals to a heart that beats too slow (similar to a pacemaker). You should not get too close to these other people so that your magnet does not act with their devices. For example, you should not hug them. A safe distance is 6 inches between you and someone who wears a medical device.

16) You may not feel comfortable about having the study nurse or Dr. Hirose take a picture of our chest. If you want them to, your mom and/or dad may stay with you in the room.

It is very important that you tell your parents and the study doctors if you are not feeling well for any reason. This is the only way that we can help you feel better.

**Will you get better if you are in this study?**

This study may make you feel better by fixing your chest. But if the magnet works or does not work, the doctors might find out something that will help other children like you.
Do you have any questions?
You can ask questions any time. You can ask now or you can ask later. You can talk to Dr. Harrison, Dr. Hirose or the study nurse, or you can talk to someone else.

Do you have to be in this study?
No, you don’t. No one will be mad at you if you don’t want to do this. If you don’t want to be in this study, just tell us. Or if you do want to be in the study, tell us that. And, remember, you can say yes now and change your mind later. It’s up to you.

If you don’t want to be in this study, just tell us.

If you want to be in this study, just tell us.
The doctor will give you a copy of this form to keep.

*************************************************************************
SIGNATURE OF PERSON CONDUCTING ASSENT DISCUSSION
I have explained the study to ______________________________ (print name of child here) in language he/she can understand, and the child has agreed to be in the study.

__________________________________   _______________
Signature of Person Conducting Assent Discussion   Date

_________________________________
Name of Person Conducting Assent Discussion (print)
§13. Any other relevant information that FDA requests for review of the IDE application.

None

§14. APPENDIX

1. E-mail from Dr. Diana Farmer confirming UC Davis Health System’s participation as a study site.
2. E-mail from Mary Beth Lawless MS, RN, Director of Research Operations, UC Davis Data Coordinating Center, confirming separation of data and PHI between UC Davis and Shriners.