60th Medical Group (AMC), Travis AFB, CA
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

FINAL REPORT SUMMARY
(Please type all information. Use additional pages if necessary.)

PROTOCOL #: FDG20130001A                                      DATE: 8 October 2013
PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Lt Col Kullada Pichakron
DEPARTMENT: Surgery                                           PHONE #: 423-5188
INITIAL APPROVAL DATE: 1 Nov 2012    LAST TRIENNIAL REVISION DATE: N/A
FUNDING SOURCE: AF Surgeon General’s Office

1. RECORD OF ANIMAL USAGE:

<table>
<thead>
<tr>
<th>Animal Species:</th>
<th>Total # Approved</th>
<th># Used this FY</th>
<th>Total # Used to Date</th>
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<tr>
<td>Sus scrofa</td>
<td>12</td>
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2. PROTOCOL TYPE / CHARACTERISTICS: (Check all applicable terms in EACH column)
   - Training: Live Animal
   - Training: non-Live Animal
   - Research: Survival (chronic)
   - Research: non-Survival (acute)
   - Other ( )
   - Medical Readiness
   - Health Promotion
   - Prevention
   - Utilization Mgt.
   - Other (Treatment )
   - Prolonged Restraint
   - Multiple Survival Surgery
   - Behavioral Study
   - Adjuvant Use
   - Biohazard

3. PROTOCOL PAIN CATEGORY (USDA): (Check applicable)    C    X   D   E

4. PROTOCOL STATUS:
   *Request Protocol Closure:
   - Inactive, protocol never initiated
   - Inactive, protocol initiated but has not/will not be completed
   - Completed, all approved procedures/animal uses have been completed

5. FUNDING STATUS: Funding allocated: $5,565.00   Funds remaining $0.00

6. PROTOCOL PERSONNEL CHANGES:

Have there been any personnel/staffing changes (PI/CI/AI/TC/instructor) since the last IACUC approval of protocol, or annual review?    Yes    X  No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.
MAGIC (Magnetic Anti-Glycemic Ileal Conduit) I: Jejunal-Ileal Magnetic Compression Anastomosis Corrects Insulin Resistance in Diabetic Pigs. PURPOSE: Bariatric surgery corrects insulin resistance independent of weight loss, possibly through enterokine signaling pathways. We hypothesize that a Magnetic Anti-Glycemic Ileal Conduit (MAGIC) anastomosis created with magnetic compression between the proximal jejunum and distal ileum corrects insulin resistance. METHODS: Yucatan mini pigs (n = 12) received a high fat diet for 3 months to induce insulin resistance. Animals were randomly assigned to 4 groups (n=3). Baseline intravenous glucose tolerance tests (IVGTT) were performed in fat-fed pigs and one pig as a control. Eight animals underwent the MAGIC procedure using either 23 mm (n=3) or 17 mm diameter (n=5) magnets. Four animals underwent sham operation. Groups were survived for 2, 4, 8 or 12 weeks, at which points IVGTTs were repeated to assess changes in insulin sensitivity. Plasma glucose and serum insulin by ELISA was measured (n=8). Animals were euthanized and the anastomosis procured for histology.

RESULTS: Baseline insulin resistance was confirmed in fat-fed pigs versus control (Insulin area under the curve normalized to weight [AUC]: 0.330 ± 0.206 vs 0.053, p < .005). Insulin sensitivity improved by 2 weeks in animals after MAGIC treatment compared with sham (AUC: 0.169 ± 0.098 vs 0.382 ± 0.30, p < 0.005). While animals with 23 mm magnets experienced excessive weight loss (>25%) observed by 4 weeks, this was ameliorated in pigs with 17 mm magnets (48% ± 3 vs 18% ± 14). No anastomotic leaks or strictures were observed in any animals. All animals took liquids on the day of surgery and were tolerating solids on POD Two animals had diarrhea that abated, but none required supplements or TPN.

CONCLUSION: MAGIC jejunal-ileal bypass may be an effective treatment for insulin resistance and the metabolic syndrome, with the potential for an outpatient minimally invasive procedure.
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<th>15. SUBJECT TERMS</th>
<th>16. SECURITY CLASSIFICATION OF:</th>
<th>17. LIMITATION OF ABSTRACT</th>
<th>18. NUMBER OF PAGES</th>
<th>19a. NAME OF RESPONSIBLE PERSON</th>
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<td>b. ABSTRACT  unclassified</td>
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Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std Z39-18
7. **PROBLEMS / ADVERSE EVENTS:** Identify any problems or adverse events that have affected study progress. Itemize adverse events that have led to unanticipated animal illness, distress, injury, or death; and indicate whether or not these events were reported to the IACUC.

None.

8. **REDUCTION, REFINEMENT, OR REPLACEMENT OF ANIMAL USE:**

**REPLACEMENT (ALTERNATIVES):** Since the last IACUC approval, have alternatives to animal use become available that could be substituted in this protocol without adversely affecting study or training objectives?

No.

**REFINEMENT:** Since the last IACUC approval, have any study refinements been implemented to reduce the degree of pain or distress experienced by study animals, or have animals of lower phylogenetic status or sentience been identified as potential study/training models in this protocol?

No.

**REDUCTION:** Since the last IACUC approval, have any methods been identified to reduce the number of live animals used in this protocol?

No.

9. **PUBLICATIONS / PRESENTATIONS:** (List any scientific publications and/or presentations that have resulted from this protocol. Include pending/scheduled publications or presentations).


10. Were the protocol objectives met, and how will the outcome or training benefit the DoD/USAF?

Yes. Research residents received valuable training in intestinal surgery and conducting scientific studies while completing this protocol.

11. **PROTOCOL OUTCOME SUMMARY:** (Please provide, in "ABSTRACT" format, a summary of the protocol objectives, materials and methods, results - include tables/figures, and conclusions/applications.)

**MAGIC (Magnetic Anti-Glycemic Ileal Conduit) I: Jejunal-Ileal Magnetic Compression Anastomosis Corrects Insulin Resistance in Diabetic Pigs.**

Gallogly HB, Leeftlang EJ, Kwiat DA, Iqbal CW, Catalano KJ, Pichakron KO, Harrison MR

aDepartment of Surgery, University of California, Davis, Sacramento, CA 95817, USA.
bDepartments of Pediatric Surgery and Obstetrics, Gynecology & RS, University of California, San Francisco, San Francisco, CA 94143-0570, USA.
cDepartment of Surgery, David Grant Medical Center, Travis Air Force Base, CA 94535, USA.

department: Bariatric surgery corrects insulin resistance independent of weight loss, possibly through enterokine signaling pathways. We hypothesize that a Magnetic Anti-Glycemic Ileal Conduit (MAGIC) anastomosis created with magnetic compression between the proximal jejunum and distal ileum corrects insulin resistance.

**METHODS:** Yucatan mini pigs (n = 12) received a high fat diet for 3 months to induce insulin resistance. Animals were randomly assigned to 4 groups (n=3). Baseline intravenous glucose tolerance tests (IVGTT) were performed in fat-fed pigs and one pig as a control. Eight animals underwent the MAGIC procedure using either 23 mm (n=3) or 17 mm diameter (n=5) magnets. Four animals underwent sham operation. Groups were survived for 2, 4, 8 or 12
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