

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

PROTOCOL TITLE: Magnetic Anastomosis for Glycemic Insulin Control (MAGIC): A pilot study of minimally invasive (endoscopic /laparoscopic) side-to-side duodeno-distal ileal anastomosis in pigs.

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:**

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Sus scrofa	12	12	12

2. **PROTOCOL TYPE / CHARACTERISTICS:** (Check all applicable terms in **EACH** column)

- | | | |
|--|--|--|
| <input type="checkbox"/> Training: Live Animal | <input type="checkbox"/> Medical Readiness | <input type="checkbox"/> Prolonged Restraint |
| <input type="checkbox"/> Training: non-Live Animal | <input type="checkbox"/> Health Promotion | <input type="checkbox"/> Multiple Survival Surgery |
| <input checked="" type="checkbox"/> Research: Survival (chronic) | <input type="checkbox"/> Prevention | <input type="checkbox"/> Behavioral Study |
| <input type="checkbox"/> Research: non-Survival (acute) | <input type="checkbox"/> Utilization Mgt. | <input type="checkbox"/> Adjuvant Use |
| <input type="checkbox"/> Other () | <input checked="" type="checkbox"/> Other (Treatment) | <input type="checkbox"/> Biohazard |

3. **PROTOCOL PAIN CATEGORY (USDA):** (Check applicable) C 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 No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.

Report Documentation Page

Form Approved
OMB No. 0704-0188

Public reporting burden for the collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to a penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.

1. REPORT DATE 17 OCT 2013	2. REPORT TYPE Final	3. DATES COVERED 01 NOV 2012 - 17 Oct 2013
--------------------------------------	--------------------------------	--

4. TITLE AND SUBTITLE FDG20130001A entitled Magnetic Anastomosis for Glycemic Insulin Control (MAGIC): A pilot study of minimally invasive (endoscopic/laparoscopic) side-to-side duodeno-distal ileal anastomosis in pigs	5a. CONTRACT NUMBER
	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S) Lt Col Kullada Pichakron, Capt Hilary Gallogly, Dr's Michael Harrison, E.J. Leeflang, D.A. Kwiat, and C.W. Iqbal	5d. PROJECT NUMBER FDG20130001A
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Clinical Investigation Facility David Grant Medical Center 101 Bodin Circle Travis AFB, CA 94535	8. PERFORMING ORGANIZATION REPORT NUMBER
---	--

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) Clinical Investigation Facility David Grant Medical Center 101 Bodin Circle Travis AFB, CA 94535	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
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.

15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT unclassified	b. ABSTRACT unclassified	c. THIS PAGE unclassified	UU	3	

Standard Form 298 (Rev. 8-98)
 Prescribed by ANSI Std Z39-18

ADDITIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, IACUC approval - Yes/No)

DELETIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, Effective date of deletion)

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).

~~Presented at the American Academy of Pediatrics National Conference in Washington D.C., 17-20 October 2009.~~ JCK

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^a, Leeflang EJ^b, Kwiat DA^b, Iqbal CW^b, Catalano KJ^b, Pichakron KO^{a,c}, Harrison MR^b

^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.

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 jejunem 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 ($48\% \pm 3$ vs $18\% \pm 14$). 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.



(PI / TC Signature)

10/8/2013

(Date)