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A rodent model of metabolic surgery for study of type 2 diabetes and positron emission tomography scanning of beta cell mass

William B. Inabnet III, M.D.^{a,*}, Luca Milone, M.D.^a, Judith Korner, M.D., Ph.D.^b, Evren Durak, M.D.^a, Leaque Ahmed, M.D.^a, Jill Pomrantz, D.V.M.^c, Paul E. Harris, M.D.^b, and Marc Bessler, M.D.^a

^aDivision of Gastrointestinal and Endocrine Surgery, Department of Surgery, Columbia University College of Physicians and Surgeons, New York, New York

^bDivision of Endocrinology, Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York

^cInstitute of Comparative Medicine, Columbia University College of Physicians and Surgeons, New York, New York

Abstract

Background—Type 2 diabetes mellitus is a worldwide healthcare problem with major socioeconomic implications. Metabolic surgical procedures have been shown to improve diabetes, but the mechanism of action is poorly understood. The Goto-Kakizaki (GK) rodent is a type 2 diabetic animal model that is ideally situated for studying the effect of surgery on diabetes; however, the operative mortality is high. The aim of this study was to describe the operative technique, improvements in perioperative management, and the technique of micro-positron emission tomography (PET) scanning of the β -cell mass in GK rodents.

Methods—A total of 53 GK rats were divided into 1 of 3 operative groups: sham, sleeve gastrectomy, and duodenojejunal bypass. A subset of animals underwent micro-PET scanning with [11C]-dihydrotetabenazine to determine the vesicular monoamine transporter 2 binding index, an indicator of β -cell mass.

Results—The 30-day mortality in the sham and sleeve gastrectomy rodents was 0; however, 2 sleeve gastrectomy rodents developed enterocutaneous fistula and 1 developed an abscess. In the duodenojejunal bypass group, the initial mortality rate was close to 90%; however, refinements in the surgical technique and perioperative management (fluids, antibiotics, pain control) lowered the mortality rate to 60%. The surgical technique is discussed in detail. [11C]-Dihydrotetabenazine uptake in the pancreas was demonstrated on micro-PET scanning in the sham and duodenojejunal bypass rodents.

Conclusion—Intensive medical management in the perioperative period and attention to the operative technique lowered the mortality. [11C]-Dihydrotetabenazine micro-PET scanning is a feasible method for assessing the β -cell mass in GK rodents and could prove to be an important modality for evaluating β -cell performance in type 2 diabetes.

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*Reprint requests: William B. Inabnet, M.D., F.A.C.S., Division of Gastrointestinal and Endocrine Surgery, Department of Surgery, Columbia University College of Physicians and Surgeons, 161 Fort Washington Avenue, New York, NY 10032. wbi2102@columbia.edu.

Disclosures

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Keywords

Metabolic surgery; Diabetes mellitus; Goto-Kakizaki; Positron emission tomography; PET scanning; β -cell mass; Animal model

Type 2 diabetes mellitus (T2DM) is an international healthcare problem, with an estimated 197 million individuals throughout the world with impaired glucose homeostasis [1]. By 2030, the current projections predict that 420 million people will have glucose intolerance and the obesity-related metabolic syndrome [1].

In humans, weight loss surgery has been shown to be the most effective treatment modality for T2DM, in particular, procedures that surgically bypass the foregut, such as gastric bypass or duodenal switch [2,3]. In addition to the Centers for Medicare and Medicaid Services-approved weight loss surgical procedures (laparoscopic gastric banding, gastric bypass, and biliopancreatic diversion with and without duodenal switch), novel surgical procedures have been developed to treat the obesity-associated metabolic syndrome [4–6]. These procedures, which are still considered experimental, include sleeve gastrectomy (SG), ileal transposition, and duodenojejunal bypass (DJB), to name a few. After surgical alteration of the gastrointestinal tract, the resultant alterations in the enteral-insular axis are complex and poorly understood.

Animal models of T2DM that permit the study of therapeutic interventions on glucose homeostasis are of paramount importance to permit translation of basic science data to the clinical realm. The Goto-Kakizaki (GK) rodent is an ideal animal model for investigating the effects of surgery on T2DM; however, to date, no studies have been published on the high mortality in GK rodents undergoing metabolic surgical procedures [7–11]. The GK rodent model was established by selectively inbreeding Wistar rats to achieve glucose intolerance [12]. Because GK rodents are not obese yet have progressive glucose intolerance and hyperlipidemia, investigators can study the effects of surgical alteration of the gastrointestinal tract on glucose homeostasis (i.e., the anatomy of the operation), removing weight loss as a confounding factor. GK rodents have been used extensively to study the effects of surgery on glucose homeostasis; however, the fragility and high operative mortality of GK rodents have not been previously reported. The first aim of this study was to report our initial experience with metabolic surgery in GK rodents, paying particular attention to the operative technique and the implementation of a comprehensive perioperative treatment protocol to decrease the operative mortality.

The second aim of this study was to describe the technique and feasibility of [^{11}C]-dihydrotrabenazine (DTBZ) micro-positron emission tomography (PET) scanning in GK rodents, a new promising technique for measuring the β -cell mass. An imaging study that permits quantitative measurement of the β -cell mass and function would be a great advance in the management of T2DM. The current markers for monitoring the severity of DM, such as glycosylated hemoglobin and C-peptide, provide information on the effectiveness of a treatment from the preceding 4 weeks to 3 months. An imaging study that permits a point-of-care assessment of β -cell performance, such as [^{11}C]-DTBZ PET scanning, would be invaluable to the diabetologist for monitoring the effectiveness of treatment, whether medical or surgical, in real time. Micro-PET scanning has been shown to be an accurate method for measuring the β -cell mass in a type 1 diabetic rodent model [13,14]. We hypothesized that micro-PET scanning would also be feasible and accurate in the GK rodent model of T2DM.

Methods

Rodents

The Institutional Animal Care and Use Committee of the Columbia University College of Physicians and Surgeons approved the study protocol. A total of 53 male GK rats (Taconic Laboratory, Hudson, NY) were used for this study. On arrival at the Animal Care Facility of Columbia University, the rats were 10–12 weeks old and weighed 290–320 g. The rats were housed 2 per cage in a 12-hour dark/light cycle room that was maintained at a temperature of 26°C. The rodents were allowed to acclimate for 7 days before starting the protocol and had ad libitum access to house water and a special diabetic rat chow (Purina 5008, Purina Mills, St. Louis, MO).

Blood sampling

Two methods of taking blood samples were used. The first and preferred method was to take blood from the tail vein. For this method, an awake rodent was placed into a special “cone” that allowed safe, humane restraint of the rodent but access to the tail. The tail vein was then cannulated with a 25-gauge butterfly needle and 1.5 mL of blood was aspirated. If the tail vein was not accessible, the orbital venus plexus was used. Under general anesthesia, the rat was held on its side with its head pressed firmly against the table surface to minimize movement of the head. A 100- μ L capillary tube was positioned at the inner corner of the eye, then gently moved a few millimeters forward along the side of the orbit to the orbital venus plexus. The blood vessels of the orbital sinus are extremely fragile and rupture on contact with the tube. Once blood started to flow, the head was tilted so that the capillary tube faced downward, and the blood was allowed to drip into the collecting tube.

Preoperative preparation and anesthesia

At 12 hours before surgery, the rodents had nothing by mouth except for ad libitum water. At 1 hour before the induction of anesthesia, 5 mg/kg enrofloxacin (Baytril) was administered subcutaneously. The rats were transported to the animal surgical suite in a covered cart to minimize stress. An induction dose of 4% isoflurane and 2.5 L/min oxygen was infused for 2 minutes, after which the rodent was placed in the supine position on a covered T-Pad temperature therapy pad (Gaymar Industries, Orchard Park, NY). The mouth and nose were covered by a rodent anesthesia mask for maintenance anesthesia, which consisted of 2% isoflurane and oxygen 2–4 L/min.

Surgical procedures

After the induction of general anesthesia, the rodents were randomized to 1 of 3 surgical groups: sham, SG, or DJB. The abdomen was shaved and prepared with chloroxedine. A 3-cm midline incision was made in the epigastric region, and the abdomen was entered under direct vision.

Sham operation—For the sham operation, the small bowel and stomach were manipulated with surgical forceps and the surgeon’s fingers for 20 minutes and the abdomen was then closed: The peritoneum was closed with a continuous Vicryl 3-0 suture and the skin with a running Prolene 3-0 suture with a straight needle.

Sleeve gastrectomy—For the SG, the stomach was identified, and then the fundus was mobilized by incising the attachments at the junction of the greater curvature and the esophagus. A small gastrotomy was made on the greater curvature of the stomach to permit evacuation of the gastric contents. It was our experience that when the rats were fasted, they were more likely to eat bedding or feces from the cage, and, therefore, the stomach was

never empty, and evacuation was necessary. A linear stapler with 2 loads of a white cartridge 30-2.5 (Covidien, Norwalk, CT) was used to perform the SG. The previously created gastrostomy was included in the resected specimen. Because the organs are very small, it was also important to avoid any unnecessary traction when firing the staplers to prevent esophageal damage. Gentle pressure was applied for hemostasis, and the staple line was not oversewn. To assist with postoperative hydration, 5 mL of sterile room temperature normal saline was introduced into the peritoneal cavity.

Duodenojejunal bypass—For the DJB, the pylorus was identified, and then the duodenum was transected immediately distal to the pylorus. The duodenal stump was closed with 5-0 polyglactin sutures.

The ligament of Treitz was identified by following the duodenal sweep, and then the jejunum was divided 5 cm distal to the ligament of Treitz. The distal end of the divided jejunum was elevated in an antecolic direction and the duodenojejunostomy was fashioned in an end-to-end manner using 5-0 polyglactin sutures. The anastomosis was created with 2 running sutures (1 anteriorly and 1 posteriorly), paying attention not to narrow the lumen. Mesenteric alignment was ensured to prevent a twist. The mesenteric spaces were not closed, because the mesentery itself is paper thin. An end-to-side jejunojejunostomy was created 25 cm distal to the proximal anastomosis to create the Roux-en-Y configuration. To assist with postoperative hydration, 5 mL of sterile normal saline was introduced into the peritoneal cavity.

Pain control

At the end of the procedure but before anesthesia recovery, 0.05 mg/kg of buprenorphine was injected intraperitoneally. Additional doses were administered every 8 hours for 48 hours. Carprofen (Rimadyl) 5 mg/kg daily was also administered to some rodents subcutaneously for additional analgesia based on the individual animal assessments by the veterinary team. No antibiotics were administered postoperatively.

Evolution of perioperative management

After experiencing a remarkably high mortality in the DJB arm of the study (see the “Results” section), an intense perioperative management protocol was implemented and the surgical technique was refined (Fig. 1).

PET scanning protocol

The radioligand, [^{11}C]-DTBZ, has a high affinity for vesicular monoamine transporter type 2 (VMAT2), which is expressed on β -cells in the pancreas. (+)- α -[^{11}C]-DTBZ was synthesized by [^{11}C] methylation of the appropriate precursor to a specific activity of >2000 mCi/ μmol at the end of synthesis. The rats were sedated for the imaging study with isoflurane 2% and oxygen 2.5 L/min. After a transmission scan of the area of interest, the radioligand [^{11}C]-DTBZ was administered (0.5–1.0 $\mu\text{Ci/g}$) in saline as a bolus injection by way of the penile vein. PET scans of the rodents were acquired dynamically from 0 to 90 minutes after injection. The PET data were processed using an attenuation correction matrix obtained by the transmission scans. The images were reconstructed using micro-PET manager software (CTI Molecular Imaging, Knoxville, TN). The regions of interest were placed on reconstructed images across the image planes manually for the determination of the time–activity curves. The renal cortex does not accumulate the radioligand and provided a reference region. Decay-corrected time–activity curves for [^{11}C]-DTBZ uptake in the regions of interest were obtained from the tissues of interest (i.e., pancreas, right hepatic lobe, and renal cortices). The comparison of pancreatic [^{11}C]-DTBZ uptake among all rodents studied was performed by calculating a binding index. The binding index was

calculated from the area under the time activity (0–90 min) curve (AUC) for the pancreas and kidney reference region using the following equation: binding index = (AUC pancreas – AUC kidney)/AUC kidney.

Results

Surgery

Of the 53 rodents, 10 underwent a sham operation, 10 SG, and 33 DJB. No morbidity or mortality occurred in the sham group. In the SG group, 2 rodents developed an enterocutaneous fistula that responded to conservative management. One developed an abdominal wall abscess that did not respond to incision and drainage and antibiotics; this rodent was euthanized 32 days after surgery. At necropsy, multiple small abscesses in the peritoneal cavity were visualized.

A total of 33 animals underwent DJB. Of the initial 28 animals undergoing DJB, only 3 survived (89.2% mortality rate). When the rodents displayed signs of irreversible stress (e.g., labored breathing, ruffled hair, loss of appetite, lethargy), they were humanely euthanized. All mortality occurred within 24 hours of surgery. Nine underwent necropsy, revealing a distended stomach and bowel in 7, pleural effusion in 7, and small bowel infarction in 2, suggestive of intestinal ischemia. The pleural effusion from 3 rodents was submitted for aerobic and anaerobic culture and was positive for *Enterococcus* in all 3 samples and positive for α -hemolytic streptococcus in 1 of 3 samples. In consultation with the veterinary team from the Institute of Comparative Animal Medicine, an intensive perioperative management protocol was implemented (Fig. 1). Five additional animals underwent DJB after implementation of this protocol. Two survived (mortality rate 60%).

PET scanning

PET scans were performed 45 days after the DJB or sham operations. Two animals (1 sham and 1 DJB) underwent micro-PET scanning. No complications developed from micro-PET scanning. In the sham rodent, the VMAT2 binding index was 0.51 compared with 2.38 in the DJB rodent. These data have demonstrated an increased concentration of VMAT2 in the pancreas, which could be associated with an increased β -cell mass in the rodent undergoing DJB.

Discussion

T2DM is a chronic disease for which there is no medical cure. Medical treatment of T2DM centers on dietary modification, increased physical activity, and administration of oral pharmaceutical agents and/or insulin or a combination of these interventions. In a randomized controlled trial comparing dietary, sulfonylurea, metformin, and insulin treatment for T2DM, only 25% of patients were able to achieve a glycosylated hemoglobin <7% at 9 years after treatment initiation [15]. It has long been observed clinically that subtotal gastrectomy and gastric bypass ameliorate DM and lead to a durable improvement in glucose homeostasis [2,3,16]. In most of these cases, the improvement in glycemic control has begun soon after the operative intervention and before significant weight loss, raising the strong possibility that bypassing the proximal intestine, in addition to caloric restriction, is involved in DM amelioration.

Despite these longstanding clinical observations, the mechanism of action of improved glucose homeostasis after gastric bypass is poorly understood. A reproducible animal model of T2DM would be invaluable to any investigator with an interest in DM pathophysiology, and the GK rodent model is one such model. GK rodents were first developed in the late 1970s by selectively inbreeding Wistar rats to achieve a state of impaired insulin secretion,

decreased β -cell mass, hyperlipidemia, and moderate insulin resistance in the peripheral tissue [7,12]. Because GK rodents are not obese, they are ideally suited for the study of the effects of intestinal manipulation (i.e., proximal intestinal bypass, ileal interposition, and SG) on glucose homeostasis. Because GK rodents typically maintain, or even gain, weight after these procedures, weight loss does not influence the alterations in the pancreatic-insular axis. Numerous investigators have used the GK rodent model to study the effects of metabolic surgery on DM; however, no investigator to date has included data on mortality or the perioperative management in this fragile animal model [7–12,17,18].

Our initial experience with DJB in GK rodents resulted in an extremely high mortality rate (close to 90%). In contrast, the sham and SG procedures were well tolerated. It was thought that the presence of DM might have contributed to the high DJB operative mortality in GK rodents, because other investigators have experienced much lower mortality in a nondiabetic obese rodent model of gastric bypass [19]. The implementation of a comprehensive perioperative treatment strategy led to a substantial reduction in mortality in the GK rodents undergoing DJB. To optimize the rodents before surgery, the enhanced protocol mandated that the rodents receive 7 days of antibiotics and hydration, as well as insulin on the day of surgery if the glucose level was >120 mg/dL. The intraoperative changes included decreasing the operative time, a smaller incision size, gentle handling of the intestines, and the use of very fine sutures for the bowel anastomoses. Because the mesentery of the rodents is paper thin, extremely gentle handling and alignment is critical to avoid mesenteric compromise. Postoperatively, the rodents were admitted to the “rodent intensive care unit” for continuous monitoring and intensive therapy by a member of our team. After implementation of the new protocol, not only did the mortality decrease, but the rodents seemed to return to normal behavior more quickly. However, we do not know which of these alterations led to the improved outcomes.

The second aim of this study was to demonstrate the safety and feasibility of micro-PET scanning for measuring the β -cell mass. The concept of functional imaging is not new to the endocrine surgeon, because imaging modalities such as metaiodobenzylguanidine and PET scanning are currently used to provide quantitative information of the tumor burden and responsiveness to treatment in patients with neuroendocrine tumors [20]. A functional imaging study that permits point-of-care measurement of the β -cell mass would allow DM investigators to determine the responsiveness of the β -cells to a given treatment. Such information could provide real-time prognostic information that might alter a chosen therapy all together, well before changes in glycosylated hemoglobin or C-peptide levels become apparent.

[^{11}C]-DTBZ is a radioligand that is currently used for PET scanning in patients with neurologic disorders such as Parkinson’s disease, Tourette syndrome, and Huntington’s disease [14]. It was discovered incidentally that VMAT2 is expressed, not only in the central nervous system, but also on β -cells in the pancreas. In the present study, the feasibility and safety of measuring the β -cell mass in the GK rodent model of T2DM using [^{11}C]-DTBZ micro-PET scanning was demonstrated (Fig. 2). In addition, the results of this study suggest that DJB may augment the β -cell mass as demonstrated by an increase in the VMAT2 binding index compared with the sham operation. Increasing the β -cell mass could help explain why DJB leads to improved glucose homeostasis [10].

Conclusion

The GK rodent model of T2DM is well suited for the study of metabolic surgery. However, GK rodents are extremely fragile and must be handled with great care. A comprehensive perioperative management protocol can help lower the operative mortality. [^{11}C]-DTBZ

micro-PET scanning is feasible in rodents with T2DM; however, additional study is needed to determine the accuracy of this functional imaging modality.

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References

1. Hossain P, Kawar B, El Nahas M. Obesity and diabetes in the developing world—a growing challenge. *N Engl J Med*. 2007; 356:213–5. [PubMed: 17229948]
2. Pories WJ, Swanson MS, MacDonald KG, et al. Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. *Ann Surg*. 1995; 222:339–52. [PubMed: 7677463]
3. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA*. 2004; 292:1724–37. [PubMed: 15479938]
4. Depaula AL, Macedo AL, Rassi N, et al. Laparoscopic treatment of metabolic syndrome in patients with type 2 diabetes mellitus. *Surg Endosc*. Epub 2008 March 18.
5. Vidal J, Ibarzabal A, Nicolau J, et al. Short-term effects of sleeve gastrectomy on type 2 diabetes mellitus in severely obese subjects. *Obes Surg*. 2007; 17:1069–74. [PubMed: 17953241]
6. Cohen RV, Schiavon CA, Pinheiro JS, et al. Duodenal-jejunal bypass for the treatment of type 2 diabetes in patients with body mass index of 22–34 kg/m²: a report of 2 cases. *Surg Obes Relat Dis*. 2007; 3:195–7. [PubMed: 17386401]
7. Movassat J, Bailbe D, Lubrano-Berthelie C, et al. Follow-up of GK rats during prediabetes highlights increased insulin action and fat deposition despite low insulin secretion. *Am J Physiol Endocrinol Metab*. 2008; 294:E168–75. [PubMed: 17986628]
8. Patrity A, Aisa MC, Annetti C, et al. How the hindgut can cure type 2 diabetes. Ileal transposition improves glucose metabolism and beta-cell function in Goto-Kakizaki rats through an enhanced proglucagon gene expression and L-cell number. *Surgery*. 2007; 142:74–85. [PubMed: 17630003]
9. Pacheco D, de Luis DA, Romero A, et al. The effects of duodenal-jejunal exclusion on hormonal regulation of glucose metabolism in Goto-Kakizaki rats. *Am J Surg*. 2007; 194:221–4. [PubMed: 17618808]
10. Rubino F, Marescaux J. Effect of duodenal-jejunal exclusion in a non-obese animal model of type 2 diabetes: a new perspective for an old disease. *Ann Surg*. 2004; 239:1–11. [PubMed: 14685093]
11. Patrity A, Facchiano E, Annetti C, et al. Early improvement of glucose tolerance after ileal transposition in a non-obese type 2 diabetes rat model. *Obes Surg*. 2005; 15:1258–64. [PubMed: 16259883]
12. Goto Y, Kakizaki M, Masaki N. Production of spontaneous diabetic rats by repetition of selective breeding. *Tohoku J Exp Med*. 1976; 119:85–90. [PubMed: 951706]
13. Souza F, Simpson N, Raffo A, et al. Longitudinal noninvasive PET-based beta cell mass estimates in a spontaneous diabetes rat model. *J Clin Invest*. 2006; 116:1506–13. [PubMed: 16710474]
14. Simpson NR, Souza F, Witkowski P, et al. Visualizing pancreatic beta-cell mass with [11C]DTBZ. *Nucl Med Biol*. 2006; 33:855–64. [PubMed: 17045165]
15. Turner RC, Cull CA, Frighi V, Holman RR. for the UK Prospective Diabetes Study (UKPDS) Group. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). *JAMA*. 1999; 281:2005–12. [PubMed: 10359389]
16. Friedman MN, Sancetta AJ, Magovern GJ. The amelioration of diabetes mellitus following subtotal gastrectomy. *Surg Gynecol Obstet*. 1955; 100:201–4. [PubMed: 13238177]
17. Rubino F, Forgione A, Cummings DE, et al. The mechanism of diabetes control after gastrointestinal bypass surgery reveals a role of the proximal small intestine in the pathophysiology of type 2 diabetes. *Ann Surg*. 2006; 244:741–9. [PubMed: 17060767]

18. Patrìti A, Facchiano E, Donini A. Effect of duodenal-jejunal exclusion in a non-obese animal model of type 2 diabetes: a new perspective for an old disease. *Ann Surg.* 2004; 240:388–91. [PubMed: 15273570]
19. Meguid MM, Ramos EJ, Suzuki S, et al. A surgical rat model of human Roux-en-Y gastric bypass. *J Gastrointest Surg.* 2004; 8:621–30. [PubMed: 15240001]
20. Pacak K, Eisenhofer G, Goldstein DS. Functional imaging of endocrine tumors: role of positron emission tomography. *Endocr Rev.* 2004; 25:568–80. [PubMed: 15294882]

- **Pre-op**
 - **7 days before surgery**
 - Lactated Ringers or 0.9% normal saline 5mls of SQ QD
 - Antibiotic 0.1mL of amoxicillin trihydrate/clavulanate potassium (Clavamox) 6.25mg PO BID
 - Place gel pack in cage
 - **Night before surgery**
 - Remove the bedding and keep the rats on a blue-pad
 - **Day of surgery**
 - Lactated Ringers or 0.9% normal saline 5mls SQ
 - Antibiotic (Ampicillin 22mg/kg SQ, Enrofloxacin 5mg/kg SQ)
 - If glucose is >120: 0.1 unit of regular insulin SQ
- **Intra-operative**
 - Incision size shortened to 1.5cm
 - Bowel not eviscerated
 - Bowel moistened with normal saline at 5 minute intervals
 - 6.0 sutures used for anastomosis (rather than 5.0)
- **Post-op**
 - For the first 24 hours, keep the rats on a blue pad to prevent ingestion of bedding
 - Buprenorphine (0.05mg/kg) SQ before anesthesia recovery
 - Buprenorphine (0.05mg/kg) every 8-12 hours SQ for the first 48 hours
 - Check glucose: immediately post-op and every 12 hours for the first 4 days
 - If glucose is >120: insulin glargine (Lantus) 0.1 unit subcutaneously
 - Give 5mls of Lactated Ringers or 0.9% normal saline SQ QD
 - If dehydration noted, give BID
 - Place a gel pack in the cage
 - Place some of the food in the bottom of the cage. Maintain body temperature using Thermacare (Gaymar Industries, NY, US) for the first 24 hours
 - Antibiotic (Ampicillin 22mg/kg SQ BID-TID, Enrofloxacin 5mg/kg SQ QD) then 6.25mg of Clavamox until 7 days post-operatively + Enrofloxacin PO 0.1mg/ml

Fig. 1.
Comprehensive perioperative treatment protocol.

Fig. 2.
[^{11}C]-DTBZ micro-PET scan demonstrating uptake in pancreas (white arrow).