

STATEMENT OF FUNDS

There are no pending external funds for this project. Needed funding in excess of the \$30,000 we are applying for in this grant will be from internal Department of Surgery funds.

SUMMARY

There is accelerated bone loss after bariatric surgery. The larger the malabsorptive component of the operation the more bone mineral density that is lost [1]. Historically operations like the jejunoileal bypass have resulted in significant osteoporosis and pathological fractures [2]. The most popular bariatric procedure in the United States today, Roux-en-Y gastric bypass, has been shown to decrease bone mineral density in the hip and femoral neck as early as one year after operation despite high dose vitamin D and calcium supplementation [3]. Yet, studies looking at purely restrictive bariatric procedures like the adjustable gastric band have shown little or no effect on bone mineral density [4, 5]. This may be explained by the reduced weight loss seen in adjustable gastric banding as compared to Roux-en-Y gastric bypass. Alternatively this may be due to the different changes in hormonal regulation of bone metabolism after bariatric procedure. There is increasing evidence that hormonal regulation of bone is significantly altered after bariatric surgery [6].

The number of sleeve gastrectomies being performed in the United States is increasing exponentially. While the weight loss achieved by sleeve gastrectomy is more similar to Roux-en-Y gastric bypass than adjustable gastric banding, the procedure is generally thought to be restrictive. How does sleeve gastrectomy change bone mineral density? There are no published studies to address this question. What is the appropriate bariatric procedure in a patient with increased risk of developing osteoporosis? **We hypothesize that sleeve gastrectomy reduces bone loss as compared to Roux-en-Y gastric bypass.** And therefore sleeve gastrectomy may be the preferred treatment for morbidly obese patients that have high risk factors for developing osteoporosis such as the postmenopausal female patient.

We propose to answer these questions by conducting a study that has two specific aims. First, compare the change in osteoclast and osteoblast activity in postmenopausal females one year after undergoing Roux-en-Y gastric bypass versus sleeve gastrectomy. Second, compare the changes in bone mineral density in postmenopausal females one year after undergoing Roux-en-Y gastric bypass versus sleeve gastrectomy. We anticipate that the patients undergoing sleeve gastrectomy will have a significant reduction in bone catabolism as compared to patients having Roux-en-Y gastric bypass and therefore have a decrease in changes in bone mineral density and osteoclast activity.

The research proposal is a prospective cohort study with a total of 30 subjects enrolled. The subjects will consist of class II and III obese postmenopausal females. This population of patients, postmenopausal females, is at high risk for accelerated bone loss and changes in their bone metabolism are readily apparent in their bone mineral density. Fifteen of the subjects will undergo Roux-en-Y gastric bypass for treatment of their morbid obesity while the other 15 patients will undergo sleeve gastrectomy. The groups will be matched as to have similar risk factors for osteoporosis and starting body mass index. The osteoclast activity, osteoblast activity, and the bone mineral density will be measured in all subjects preoperatively and 12 months postoperatively. All subjects will be treated with our standard dose vitamin D and calcium replacement to try and prevent bone mineral density loss.

BACKGROUND

1) The Problem

Bariatric surgery has been shown to be effective in long term weight loss and the reduction of associated comorbidities including diabetes, coronary artery disease, and nonalcoholic fatty liver disease [7]. Because of rising rates of obesity and the aforementioned comorbidities there are increasing numbers of patients undergoing bariatric surgery. One adverse effect of bariatric surgery is accelerated bone loss that can be measured as a decrease in bone mineral density as early as six months to a year after operation [3, 8]. The long-term effects from bariatric surgery on bone metabolism are unknown. These consequences will become increasingly important with an increasing population of aging postoperative bariatric patients as well as new patients with increased preoperative risks for bone loss including postmenopausal females, and in pediatric population that may have a lifelong accumulation of changes in bone metabolism.

Obesity is protective against osteoporosis in postmenopausal women [9] and the weight loss seen after bariatric surgery is associated with accelerated bone loss. Several prospective studies have shown a decrease in bone mineral density after bariatric surgery [8, 10, 11]. Malabsorptive procedures like the jejunioileal bypass, biliopancreatic diversion with or without duodenal switch have shown the greatest effect on loss of bone mineral density [1, 2, 12]. Roux-en-y gastric bypass has shown to decrease bone mineral density at the femoral neck and hip as early as one year postoperatively [3] despite aggressive vitamin D and calcium replacement. While adjustable gastric banding has shown to not exert a detectable decrease in bone mineral density one year after operation [5]. It is unknown if these differences are because of the change in hormones after restrictive versus malabsorptive operation or if it is the effect of differing amounts of total weight loss.

2) Significance

A literature search revealed that there are no published reports on the effects of sleeve gastrectomy on bone metabolism. To our knowledge this will be the first prospective trial comparing changes in bone density and bone metabolism after sleeve gastrectomy versus Roux-en-Y gastric bypass. It will be the first study looking at the change in bone metabolism and bone mineral density specifically in sleeve gastrectomy. The results of this study may alter the operation that we recommend for morbidly obese patients at high risk for osteoporosis, like the postmenopausal female, patients with an existing diagnosis of osteoporosis, pediatric patients that are likely to have changes in bone metabolism at a time when bone anabolism is favored.

3) Prior or Concurrent studies conducted

The decrease in bone mineral density after bariatric surgery has been measured on dual-energy x-ray absorptiometry (DEXA) scan. Fleischer et al. have documented a decrease in bone mineral density as measured on DEXA scan of 9.2% in the femoral neck and 8.0% in the total hip one year after Roux-en-Y gastric bypass [3]. Vilarrasa et al. documented a change in bone mineral density of 10.2% at the femoral neck and 3.2% in the lumbar spine one year after Roux-en-Y gastric bypass surgery [8]. Bone mineral density as measured on DEXA scan is most decreased in the hip, femoral neck and lumbar spine after gastric bypass surgery. The long term effects of bariatric surgery on bone mineral density are unknown.

Estrogen is known to have protective effects on bone density. Menopause is a significant risk factor for developing osteoporosis. Like estrogen, obesity has a protective effect against bone loss [9]. This protective effect is now thought to be mediated through different adipocyte hormones. Adipocytes likely play a role in bone metabolism through endocrine hormones including leptin, adiponectin, visfatin, TNF-alpha, IL-6, and resistin [6, 13].

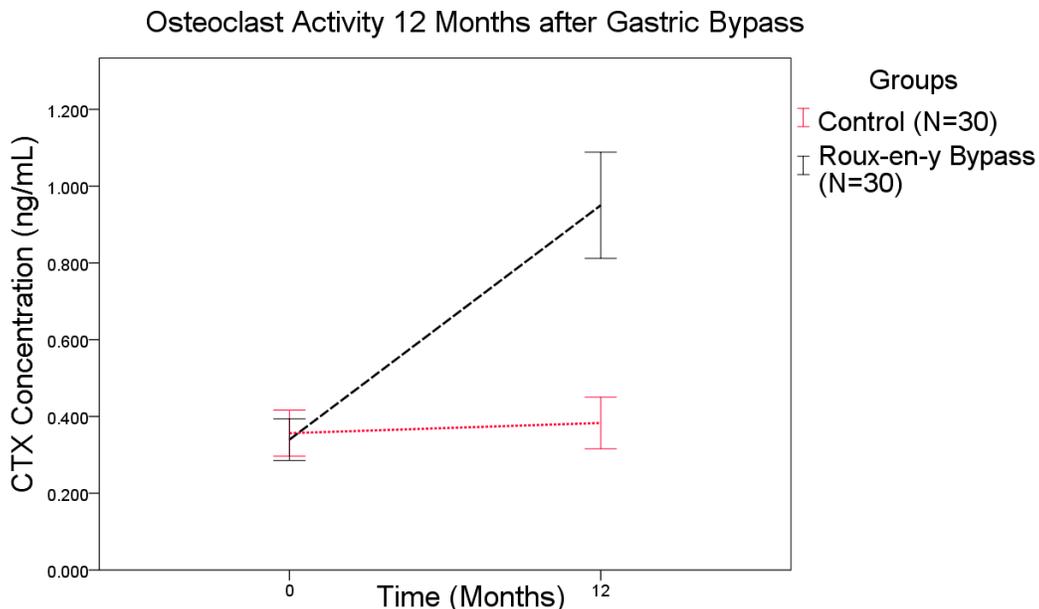
These changes in hormones may be different depending on the type of bariatric surgery. Studies looking at bone density of gastric banding patients have shown no difference in bone density after one year of operation [4, 5]. It is unknown if these different changes are the result of different hormone changes after differing bariatric surgeries or correlate more to overall weight loss.

Studies looking at osteoclast and osteoblast function after Roux-en-Y gastric bypass have shown a substantial increase in osteoclast and osteoblast function 6, 12, and 18 months after surgery [13]. It is unknown if these changes are seen in patients undergoing sleeve gastrectomy.

4) Preliminary Data

We conducted a prospective cohort study looking at the change of osteoclast activity after Roux-en-Y gastric bypass surgery compared to a matched control group with 30 subjects in each group. Serum was collected from each subject at time point zero and 12 months. The two groups were not statistically different when comparing age, gender, and enrolment body mass index. At twelve months the treatment group had a significant decrease in body mass index (31.2 kg/m^2 versus 40.4 kg/m^2 , $p < 0.001$).

We used Serum CrossLaps® ELISA to measure the c-terminal telopeptides of type I collagen (CTX) which is a marker for osteoclast activity [14]. At baseline both the control group and the gastric bypass group had a similar starting CTX concentration (0.356 ng/ml versus 0.340 ng/ml , $P = 0.685$) which is in the population range for healthy individuals as provided by the company (0.294 to 0.439 ng/ml) [15]. CTX concentrations twelve months after Roux-en-Y gastric bypass surgery were significantly increased compared to the control group (0.383 ng/ml versus 0.950 ng/ml , $P < 0.001$).



HYPOTHESIS

What is the appropriate bariatric procedure in a patient with increased risk of developing osteoporosis? **We hypothesize that sleeve gastrectomy reduces bone loss as compared to Roux-en-Y gastric bypass.** Thus, sleeve gastrectomy would be favored in a patient population that is at increased risk for osteoporosis like the postmenopausal female.

To test this hypothesis, we propose the following specific aims:

Aim 1: Compare the change in osteoclast and osteoblast activity in postmenopausal females one year after undergoing Roux-en-Y gastric bypass versus sleeve gastrectomy.

Aim 2: Compare the changes in bone mineral density in postmenopausal females one year after undergoing Roux-en-Y gastric bypass versus sleeve gastrectomy.

METHODS

1) Enrollment of Subjects

The hypothesis will be tested using a prospective cohort study with a total of 30 postmenopausal female subjects. The two groups will be case matched using a propensity score to have similar body mass index, age, visceral adiposity (measured by waist circumference), prevalence of type II diabetes, and number of years since starting menopause.

Group A includes 15 postmenopausal female subjects with class II and III obesity that will undergo laparoscopic roux-en-y gastric bypass.

Group B includes 15 postmenopausal female subjects with class II and III obesity that will undergo laparoscopic sleeve gastrectomy.

The subjects will be recruited from the Duke University Center for Metabolic and Surgical Weight Loss. Patient accrual is considered feasible given the annual number of new patients exceeds 1000. And while menopausal status has not routinely been documented, the number of female patients over the age of 50 receiving laparoscopic Roux-en-Y gastric bypass or sleeve gastrectomy exceeded 200 patients last year. It is expected that subjects will reflect the center's population, which is 85% Caucasian, 15% African American, and 5% Hispanic.

Inclusion Criteria

- 1) Postmenopausal women as determined by having a history of no menstrual bleed for greater than one year [16].
- 2) Body mass index $\geq 35 \text{ kg/m}^2$ and stable weight for the previous 3 months.

Exclusion Criteria

- 1) A documented history of osteoporosis or currently receiving medical treatment for osteoporosis with bisphosphonates, teriparatide, raloxifene, or denosumab.
- 2) Weight greater than 400 pounds as this is the weight limit for our Dual-energy X-ray absorptiometry machine.
- 3) Current or past (less than 1 year from enrolment) usage of estrogen hormone replacement therapy.
- 4) Any history of thyroid dysfunction including hypothyroidism, hyperthyroidism, currently or previous use of levothyroxine, or thyroidectomy.
- 5) Active smoker or use of tobacco products within the last year of enrollment.
- 6) Any history of glucocorticoid use greater than one year in duration or current use of glucocorticoids.

2) Anthropometric Data, Laboratory Data, and Specimens Collection

Height and weight will be measured to the nearest 0.1 cm and 0.5 kg respectively and body mass index (kg/m^2) will be calculated. As a standard of practice at the time of initial evaluation for bariatric surgery the postmenopausal female will have standard blood work including calcium, 24-OH Vitamin D, and phosphate which is also checked at their 6 month and one year follow-up appointment. This data will be collected by reviewing the chart of the subject. For the study, preoperatively and 12 months postoperatively the patient will have 30 ml of blood drawn from a venipuncture site in the arm. Using a centrifuge the serum will be extracted and stored in a freezer at -75 degrees Celsius. These samples will be used to measure osteoclast and osteoblast function.

3) Dual-energy X-ray Absorptiometry (DEXA)

A total-body narrow fan-beam scanner (Lunar iDXA; GE Healthcare, Madison, WI) will be used. The instrument has a high weight limit of 400 pounds and a wide scanning space that is designed to accommodate obese subjects. Scan analysis will be performed using GE Encore 11.10 software. This software allows for adjustment of regions of interest including the sagittal line, which controls the left-right body distribution of tissue. Measurements obtained by DEXA scan will include total body bone mineral density, site specific bone mineral density including the skull, cervical, thoracic, and lumbar spine, distal radius, femoral neck, and total hip. The total body bone mineral density will be used to calculate a t-score and z-score for each patient. T-score is calculated by comparing the patient's bone mineral density to internationally standardized values obtained from healthy 30 year-old women. A value of less than -2 is diagnostic for osteoporosis. A Z-score is calculated by comparing the total bone mineral density to internationally standardized values obtained from subjects with a similar age, weight, ethnicity, and gender. DEXA will also measure the change in total fat and lean mass.

4) Enzyme-Linked Immunosorbent Assay (ELISA)

After all serum samples from the study have been collected they will be analyzed using protein specific ELISA. Each ELISA kit comes in a 96 well plate with standardized controls. Each plate will analyze 40 samples. We will use 2 plates for each desired test to accommodate our 60 samples. To measure osteoclast function we will measure C-terminal telopeptides of Type I collagen which is the product of bone catabolism from osteoclasts. C-terminal telopeptide of Type I collagen has been well-established as a measure of osteoclast activity [17]. To measure osteoblast activity we will measure osteocalcin which is solely produced by osteoblasts. This has been a well-established measure of osteoblast activity [18]. These ELISA kits are commercially available.

5) Study Intervention

The subjects will be treated at Durham Regional Hospital or Duke Raleigh Hospital by Duke University Medical Center bariatric surgeons. The operative technique amongst the group of Duke bariatric surgeons is standardized. Postoperatively all patients will be placed on 800 IU of vitamin D daily and 1,200 mg of calcium carbonate daily to prevent bone loss attributed to malabsorption of vitamin D and calcium.

Group A: Laparoscopic Roux-en-Y Gastric Bypass

The procedure is done laparoscopically with standard multiport placement. A 15 mL proximal gastric pouch is formed, an ante-colic, retro-gastric Roux-en-Y gastrojejunostomy with linear stapled technique is performed. A 100 cm Roux-limb, and a 40 cm bilipopancreatic limb is fashioned, and a stapled end-side enteroenterostomy is performed.

Group B: Laparoscopic Sleeve Gastrectomy

The procedure is done laparoscopically with standard multiport placement. A 36 French bougie is used to guide the formation of a standardized gastric pouch. Using linear staplers the greater curve of the stomach is resected along the edge of the preplaced bougie.

6) Research Design

Aim 1: Compare the change in osteoclast and osteoblast activity in postmenopausal females one year after undergoing Roux-en-Y gastric bypass versus sleeve gastrectomy.

Hypothesis: Osteoclast activity will be significantly increased in subjects one year after operation and this increase will be greater in subjects who underwent Roux-en-Y gastric bypass as compared to subjects that received sleeve gastrectomy. As well there will be an increase in osteoblast activity seen in both groups one year after operation.

To test this hypothesis, we will collect serum samples preoperatively and 12 months after operation. The samples will be analyzed using a C-terminal telopeptide of type I collagen ELISA (Serum CrossLaps®, Immuno Diagnostic System, Scottsdale, AZ). This is a measure of osteoclast activity. We will also analyze the samples using an ELISA specific for osteocalcin (hOST-EASIA, GenWay, San Diego, CA) which is a specific measure of osteoblast activity.

Anticipated results: We expect that in Group A (subjects undergoing Roux-en-Y gastric bypass) that the level of C-terminal telopeptide of type I collagen will more than triple compared to their preoperative value. This is based on our preliminary work. The measured osteoclast activity of Group B (subjects undergoing sleeve gastrectomy) is expected to be at least 50% less than the measured difference in Group A.

Aim 2: Compare the changes in bone mineral density in postmenopausal females one year after undergoing Roux-en-Y gastric bypass versus sleeve gastrectomy.

Hypothesis: There will be a greater decrease in bone mineral density in subjects undergoing Roux-en-Y gastric bypass compared to sleeve gastrectomy.

To test this hypothesis, subjects in group A and B will have dual-energy X-ray absorptiometry (DEXA) scans performed preoperatively and 12 months postoperatively. DEXA scan will record total body bone mineral density as well as regional site specific bone mineral density including the femoral neck, total hip, cervical, thoracic, and lumbar spine.

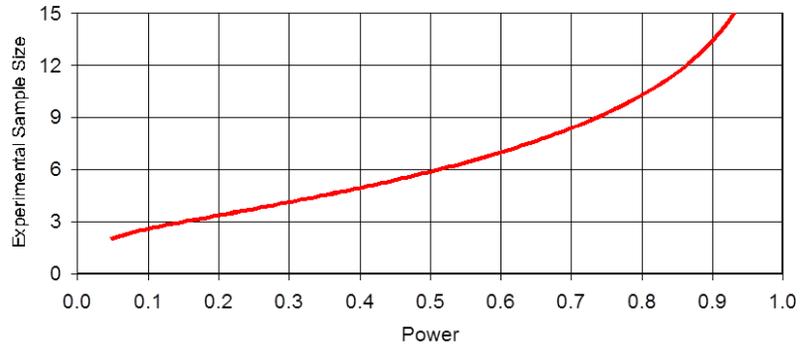
Anticipated results: There will be a statistically significant decrease in bone mineral density in the femoral neck, lumbar spine, and hip in patients undergoing Roux-en-Y gastric bypass that will not be seen in patients having sleeve gastrectomy. The 1 year decrease in total hip bone mineral density in subjects undergoing Roux-en-Y gastric bypass will be approximately 8% loss and a 9% loss at the femoral neck as compared with previous studies [3, 8].

7) Statistical Analysis and Sample Size

Aim 1: Our primary endpoint is change in osteoclast activity as measured by C-terminal telopeptide of type I collagen. This is a continuous variable and given our small sample size we will use a nonparametric Wilcoxon rank-sum test to compare the difference in one year change of osteoclast activity between the 15 patients in Group A versus Group B.

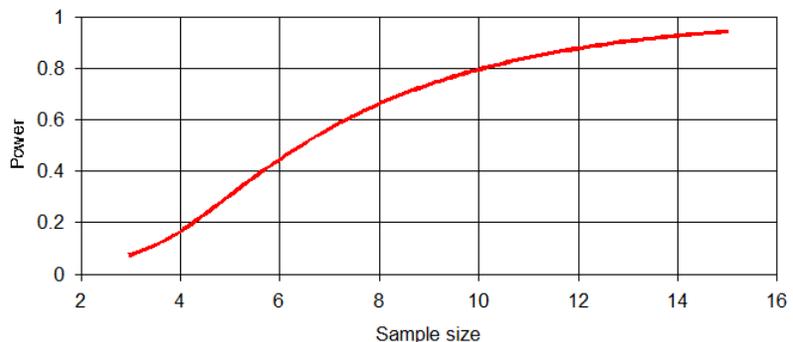
To calculate a power analysis for the study we used our preliminary data of change in C-terminal telopeptide of type I collagen at one year in patients undergoing Roux-en-Y gastric bypass. In the research literature there is no data available for changes in osteoclast activity after sleeve gastrectomy. We assumed at least a 30% difference between changes in osteoclast activity in the two study groups.

In our preliminary data the response within the group was normally distributed with a standard deviation of 0.23. If the true difference in the experimental and control means is 0.3, we will need to study 13 experimental subjects and 13 control subjects to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0.9. The Type I error probability associated with this test of this null hypothesis is 0.05. A sample population of 15 patients will power the study to a value approaching 1.0.



Aim 2: Our primary endpoint is change in bone density one year after operation. Again this is a continuous variable and given our small sample size we will use a nonparametric Wilcoxon rank-sum test to compare the difference in bone mineral density before and one year after surgery in the two groups.

There is no published data on changes in bone mineral density after sleeve gastrectomy. We used the data from Vilarrasa et al [8] a study looking at bone mineral density measured before and one year after Roux-en-Y gastric bypass. Based on their data we conducted a power analysis of number of patients needed to show a significant decrease in the bone mineral density in the femoral neck one year after Roux-en-Y gastric bypass. The Type I error probability associated with this test of this null hypothesis is 0.05. A sample population of 15 patients will power the study to a value of 0.97.



8) Potential Pitfalls

A difference may not exist between the bone metabolisms in subjects one year after Roux-en-Y gastric bypass as compared to sleeve gastrectomy. Therefore sleeve gastrectomy may not reduce bone loss as compared to Roux-en-Y gastric bypass. This would be an equally significant result as finding a difference. There is no study in the literature comparing the results of bone mineral density loss and osteoclast activity after Roux-en-Y gastric bypass versus sleeve gastrectomy. This would add to our knowledge of the changes in bone metabolism after bariatric surgery.

Another potential pitfall is that the follow-up of one year is not long enough to detect a significant difference between the two treatment groups. And with only one year follow-up the long term effects of changes in bone metabolism will not be assessed. The grant restricts the research to one year; we plan to continue to follow these patients out for at least three years from surgery. And our hope is that this research will serve as a pilot study for future grant submissions in the area of changes in bone metabolism after bariatric surgery.

SAGES RESEARCH GRANT APPLICATION BUDGET SHEET

Detailed budget for 12 month period from June, 1st 2013 through May 31st, 2014.

Dollar amount requested (Omit cents) \$30,000

Total for the grant request may not exceed \$30,000.

* Salary funds should be used for staff required to execute the study, but should not be used for salary support for the primary investigator. If salary support exceeds 50% of the project budget, then specific justification is required.

**Funds requests for travel for the presentation of a SAGES funded study should be limited to \$1,000.

NAME	POSITION TITLE	TIME/EFFORT		SALARY	FRINGE BENEFITS	SUB-TOTALS
		%	Hrs/ Week			
1. Lawrence Tabone, MD	Principal Investigator*	20	12			
2. Alfonso Torquati, MD	Co-Investigator	5	3			0
3.						
4.						
5.						
CONSULTANT COSTS	Biostatatician provided by the department of surgery					0
EQUIPMENT (List all Items&Total Equipment Cost)	pipets, vials, specimen boxes, labels, gloves, venopuncture kits					500
SUPPLIES (List all Items&Total Supplies Cost)	Assays for osteoclast activity (Serum CrossLaps® \$1850 for two plates), osteocalcin (hOST-EASI \$800 for two plates), Intact PTH ELISA kit (hPTH-EASIA \$650)					3,300
TRAVEL**	P.I. travel expenses to present at SAGES meeting.					1,000
PATIENT CARE COSTS	Dual-energy x-ray absorptimetry (\$410 per DEXA x 60 tests), Patient reimbursement for travel expenses for DEXA scan (\$10 per visit x 60 visits)					25,200
CONSORTIUM/CONTRACTUAL COSTS						
OTHER EXPENSES (List all Items & Total Cost)	Items					Subtotal
TOTAL DIRECT COSTS						30,000

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LOCAL / INSTITUTIONAL REVIEW BOARD

IRB approval is pending at the time of this grant submission.

AVAILABLE RESOURCES

Laboratory:

We occupy a laboratory space (700 sq. ft.) in the Stedman Metabolic Center Labs area. This space provides us with access to shared equipment in the Research Core labs and includes a cold room and common equipment areas. Available equipment includes: real-time RT-PCR, refrigerated and non-refrigerated centrifuges, microcentrifuges, spectrophotometer, gel electrophoresis equipment for protein, DNA and RNA, -80 C ultrafreezer, freezers, refrigerators, water baths, incubators, s shakers, orbital shaker, inverted contrast-phase microscope with digital acquisition, microplate and reader photometer for ELISA assays.

Clinic:

We have access to the Clinical Research Unit at the Duke Center for Living Campus. This location has exam and procedure rooms available for clinical studies as well as a laboratory room with refrigerated and non-refrigerated centrifuges and freezers.

Principal Investigator (Last, First, Middle): Tabone, Lawrence, Edward

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Lawrence Edward Tabone		POSITION TITLE Postdoctoral Research Fellow	
eRA COMMONS USER NAME (credential, e.g., agency login)			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Illinois, Urbana, IL	B.S.	05/2000	Biochemistry
Boston University – School of Medicine	M.A.	5/2003	Medical Sciences
Loyola University – Stritch School of Medicine	M.D.	6/2007	Medicine
Loyola University Medical Center	Resident	2007 to 2012	General Surgery
Duke University	Fellow	2012 to 2014	Bariatric/MIS Surgery

A. Personal Statement

I am interested in pursuing a career in academic surgery with interest in research that advances our understanding of metabolic and weight loss surgery. I am currently doing a two year bariatric fellowship at Duke University in the division of Metabolic and Surgical Weight Loss. I am serving as a postdoctoral research fellow under the mentorship of Dr. Alfonso Torquati. I am interested in studying the changes in bone metabolism after bariatric surgery.

B. Positions and Honors

Employment

July 2007 to June 2008 – General Surgery Internship, Loyola University Medical Center, Maywood, IL
July 2008 to June 2012 – General Surgery Residency, Loyola University Medical Center, Maywood, IL
July 2011 to June 2012 – Chief General Surgery Resident and Administrative Educational Chief
July 2012 to Present – Postdoctoral Associate and Bariatric Fellow, Duke University, Durham, NC

Honors

Dr. James J. Feeney Memorial Scholarship (Academic year 2003/2004 and 2004/2005)
University of Illinois Leadership Scholarship

Membership in Professional Societies:

SAGES candidate member
American College of Surgeons resident member

C. Selected Peer-reviewed Publications

Tabone, LE, Sarker S, Fisichella PM, Conlon M, Fernando E, Yi S, Luchette FA. To 'gram or not'? indications for intraoperative cholangiogram. Surgery 2011;150:810-819

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Alfonso Torquati		POSITION TITLE Associate Professor of Surgery	
eRA COMMONS USER NAME torquaa			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Rome, Tor Vergata, SOM, Italy	M.D.	1982-1988	Medicine
University of Rome, Tor Vergata, SOM, Italy	Residency	1988-1993	General Surgery
Oregon Health and Science University, Oregon	Residency	1996-2000	General Surgery
Vanderbilt University, SOM, Nashville, Tennessee	Fellowship	2002-2004	Laparoscopic Surgery
Vanderbilt University, SOM, Nashville, Tennessee	M.S.C.I.	2001-2003	Master Clinical Investigation

B. Positions and Honors.**Employment**

1988-1993 General Surgery Resident, Department of Surgery, University of Rome "Tor Vergata", Italy.
1993 Visiting Scholar, Department of Surgery, Stanford University.
1993-1995 Assistant Professor, Department of Surgery, University of Rome "Tor Vergata", Rome, Italy.
1995-1996 Post-Doctoral Research Fellow in Surgery, Department of Surgery, Oregon Health & Science University, Portland, Oregon.
1996-1999 General Surgery Resident, Oregon Health & Science University, Portland, Oregon.
1999-2000 General Surgery Chief Resident, Oregon Health & Science University, Portland, Oregon.
2000-2001 Staff Surgeon Good Shepherd Hospital, Hermiston, Oregon
2001-2004 Instructor of Surgery, Department of Surgery, Vanderbilt University, Nashville Tennessee
2004-2007 Assistant Professor of Surgery, Department of Surgery, Vanderbilt University, Nashville TN
2007- Associate Professor of Surgery, Director of Obesity Research, Duke University, Durham NC
2010-2012 Director of Duke Endosurgery,
2010-2011 Co-Director of Duke Center for Metabolic and Weight Loss Surgery
2012- Chief, Division of Metabolic and Weight Loss Surgery, Duke University,

Honors

2001 Master of Science in Clinical Investigations, Vanderbilt University School of Medicine, Full Tuition Award
2003 Society of American Gastrointestinal Endoscopic Surgeons (SAGES) Research Grant Award: Role of the RUNX3, a Tumor Suppressor Gene, in Barrett's Esophagus: Does Laparoscopic Nissen Fundoplication Reverse RUNX3 Gene Inactivation?
2003 Society of American Gastrointestinal Endoscopic Surgeons (SAGES) Poster of Distinction Award: MII improves the evaluation of esophageal motility disorders in patients undergoing antireflux surgery for GERD.
2004 Society of American Gastrointestinal Endoscopic Surgeons (SAGES) Poster of Distinction Award: 200 consecutive laparoscopic gastric bypasses: lessons learned with 3 different gastro-jejunostomy techniques.

Principal Investigator/Program Director (Last, First, Middle): Torquati, Alfonso

- 2004 Society of American Gastrointestinal Endoscopic Surgeons (SAGES) Poster of Distinction Award: Prevalence of non-acid reflux following medical and surgical treatment of Barrett's esophagus.
- 2004 Vanderbilt Clinical Research Scholars Program Award
- 2005 Paper Selected for Mosby's Year Book of Surgery 2005: RUNX3 inhibits cell proliferation and induces apoptosis by reinstating transforming growth factor beta (TGF- β) responsiveness in esophageal adenocarcinoma cells. Surgery 136:310-316, 2004
- 2006 Expression of RUNX3 in Barrett's metaplasia after Nissen Fundoplication. Abstract Selected for the "Best of the Best" Plenary Session at the 2006 meeting of the Society of American Gastrointestinal Endoscopic Surgeons (SAGES).
- 2006 Invited Grant Reviewer for Diabetes UK research initiative - a £3 million call for research to improve the Care and Treatment of people with diabetes –
- 2007 Grant Reviewer for NIH Clinical and Integrative Cardiovascular Sciences [CICS] Study Section
- 2007 Grant Reviewer for NIH Health of Populations [HOP-D] Study Section
- 2008 Grant Reviewer for NIH Special Emphasis Panel: ancillary studies to the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS).
- 2009 Society of University Surgeons: Faculty Research Award

National Committees:

- 2004-2012 Research Committee, Society of American Gastrointestinal Endoscopic Surgeons
- 2005-present Endoscopy Committee, Society of American Gastrointestinal Endoscopic Surgeons
- 2005-2010 Delphi Project Taskforce, Society of American Gastrointestinal Endoscopic Surgeons
- 2006-present Invention Innovation Special Interest Group American Society for Gastrointestinal Endoscopy
- 2006-present Research Committee, Natural Orifice Surgery Consortium for Assessment and Research
- 2008-present Continuing Medical Education Committee, American Society for Metabolic and Bariatric Surgery
- 2008-2011 Co-Chair Research Committee, Society of American Gastrointestinal Endoscopic Surgeons
- 2009-present Research Committee, American Society for Metabolic and Bariatric Surgery

C. Selected Relevant Peer-Reviewed Publications (selected from 51 peer reviewed publications)

- 1) **A Torquati**, R Lutfi, N Abumrad, WO Richards. Is Roux-en-Y Gastric Bypass Surgery the Most Effective Treatment for Type 2 Diabetes Mellitus in Morbidly Obese Patients? Journal of Gastrointestinal Surgery 9: 1112-1119, 2005.
- 2) RE Lutfi , **A Torquati**, N Sekhar, WO Richards. Predictors of Success after Laparoscopic Gastric Bypass: A Multivariate Analysis of Socioeconomic Factors. Surgical Endoscopy 20(6):864-7, 2006.
- 3) N Sekar, **A Torquati**, RE Lutfi , WO Richards. Endoscopic Evaluation Of The Gastrojejunostomy In Laparoscopic Gastric Bypass: A Series Of 340 Patients Without Post-Operative Leak. Surgical Endoscopy 20:199-201, 2006.
- 4) E Hansen, **A Torquati**, N Abumrad Metabolic Consequences of Bariatric Surgery and Liposuction. Annual Review of Nutrition, 26:481-511, 2006.
- 5) A Eckhauser, **A Torquati**, Y Youssef, J Kaiser, WO Richards. Internal Hernia: Postoperative Complication of Roux-en-Y Gastric Bypass Surgery. American Surgeon 72:581-585, 2006.
- 6) H Silver, **A Torquati**, G Jensen, W Richards. Weight, dietary and physical activity behaviors two years after gastric bypass. Obesity Surgery, 16:859-864, 2006.
- 7) B. Berch, **A Torquati**, RE Lutfi , WO Richards. Experience with the Optical Access Trocar for Safe and Rapid Entry in Performing the Laparoscopic Gastric Bypass. Surgical Endoscopy 20(8):1238-41, 2006.

Principal Investigator/Program Director (Last, First, Middle): Torquati, Alfonso

- 8) **A Torquati**, R Lutfi, WO Richards. Predictors of Early Quality of Life Improvement after Laparoscopic Gastric Bypass Surgery. *American Journal of Surgery*, 193:471-5, 2007.
- 9) Y Youssef, N Sekhar, Joan Kaiser, WO Richards, N Abumrad, A Spagnoli, **A Torquati**. Risk of Secondary Hyperparathyroidism after Laparoscopic Gastric Bypass Surgery in Obese Women. *Surgical Endoscopy*, 21:1393-6. 2007.
- 10) N Sekhar, **A Torquati**, Y Youssef, JK Wright, WO Richards. A Comparison between 399 Open and 568 Laparoscopic Gastric Bypasses performed during a 4 year period. *Surgical Endoscopy* 2007;21:665-8
- 11) **A Torquati**, K Wright, W Melvin, WO Richards. Effect of Gastric Bypass Surgery on Framingham and Actual Risk of Cardiovascular Events in Class II-III Obesity. *Journal of American College of Surgeons* 204:776-82, 2007.
- 12) JA Talarico, **A Torquati**, EM McCarthy, S Bonomo, RE Lutfi. Pre-Lap-Band group education in Medicaid population: does it really make a difference? *Surg Obes Relat Dis.* 6:356-360, 2010.
- 13) Evans S, Pamuklar Z, Rosko J, Mahaney P, Jiang N, Park C, **Torquati A**. Gastric bypass surgery restores meal stimulation of the anorexigenic gut hormones glucagon-like peptide-1 and peptide YY independently of caloric restriction. *Surg Endosc.* 2011 Nov 2. [Epub ahead of print]
- 14) Z. Pamuklar, J. Chen, M Muehlbauer, A Spagnoli, **A. Torquati**. Insulin-sensitizing effects of gastric bypass surgery are mediated through neclin-e2f4 interaction. *Surgery for Obesity and Related* 2011, Nov 7. [Epub ahead of print].
- 15) J Cheregi J, F. Tiesenga, **A. Torquati**. R. Lutfi. Initial Learning Experience of Laparoendoscopic Single Site (LESS) Gastric Banding: Finding Predictors of Success. *Obesity Surgery*, 22:433-36, 2012.
- 16) J. Chen, Z. Pamuklar, **A. Torquati**. Serum leptin levels are inversely correlated with omental gene expression of adiponectin and are markedly decrease after laparoscopic gastric bypass surgery. *Surgical Endoscopy*, 26:1476-80, 2012.
- 17) J. Chen, A. Spagnoli, **A. Torquati**.. Omental gene expression of adiponectin correlates with degree of insulin sensitivity before and after gastric bypass surgery. *Obesity Surgery*, 22:472-7, 2012.
- 18) J. Chen, A. Spagnoli, **A. Torquati**. Adipogenic differentiation of adipose tissue-derived human mesenchymal stem cells: effect of gastric bypass surgery. *Surgical Endoscopy*, May 31 [Epub ahead of print], 2012.
- 19) A. Mor, E. Keenan, D. Portenier, **A. Torquati**. Case-matched analysis comparing outcomes of revisional versus primary laparoscopic Roux-en-Y gastric bypass. *Surg Endosc.* 2012 Jul 18. [Epub ahead of print].

D. Research Support

Ongoing Research Support:

Society of University Surgeons: Faculty Research Award

Torquati, Alfonso (PI)

Funded 12/1/2011- 11/30/2013

Completed Research Support:

The effect of laparoscopic gastric bypass surgery in combination with omentectomy on glucose metabolism of patients with type 2 diabetes: a randomized trial.

NIH K-12: K12 RR017697

Torquati Alfonso (Vanderbilt Clinical Research Scholar: salary and laboratory support)

Funded 8/01/2004-8/31/2006

Role of the RUNX3, a Tumor Suppressor Gene, in Barrett's Esophagus: Does Laparoscopic Nissen Fundoplication Reverse RUNX3 Gene Inactivation?

Society of American Gastrointestinal Endoscopic Surgeons (SAGES) Research Grant Award;

Principal Investigator/Program Director (Last, First, Middle): Torquati, Alfonso

Torquati, Alfonso (PI)
Funded 4/1/2004 – 3/31/2006

Acid Clearance Physiology after Collis-Nissen Gastroplasty, Nissen Fundoplication, and In Healthy Individuals.

Society of American Gastrointestinal Endoscopic Surgeons (SAGES) Research Grant Award
Torquati, Alfonso (PI)
Funded 4/1/2005 – 9/31/2007

Role of the Omentum in the Treatment of Morbid Obesity

NIH-NIDDK - R01 DK070860
Naji Abumrad (PI)
Role:Co-Investigator
Funded 4/1/2005-10/31/2007

Endoscopic plication of the gastroesophageal junction for gastroesophageal reflux disease: a randomized, sham versus control trial.

NDO plicator Inc.
Torquati, Alfonso (PI)
Funded: 4/1/05-9/31/08

Assessment of Cardiovascular risk factor after gastric bypass surgery.

NIH-NIDDK - 1 K23 DK075907
Torquati Alfonso (PI)
Funded 9/01/2006-8/31/2011

Role of renin-angiotensin system in the adipogenic differentiation of mesenchymal stem cells.

Society of American Gastrointestinal Endoscopic Surgeons (SAGES) Research Grant Award;
Torquati, Alfonso (PI)
Funded 4/1/2008 – 3/31/2011

PARTICIPATION IN SAGES

Lawrence Tabone has been a candidate member since 2009. He has attended the SAGES courses including the basic residents' workshop in April of 2009 at the Endo-surgery Institute in Cincinnati, Ohio. And more recently the SAGES Flexible Endoscopy Surgery Course for MIS fellows at Methodist Institute for Technology, Innovation and Education (MITIE) in Houston, Texas in 2012. He has submitted an abstract for presentation at the upcoming SAGES 2013 annual meeting titled "Improved insulin sensitivity after gastric bypass correlates with decreased total body fat, but not with changes in free fatty acids".

Alfonso Torquati is a long-standing member of SAGES and has been extensively involved with the society for many years.