Note from the Chair

In terms of individual and team accomplishments, this has been an eventful six months. First and foremost, the Department has excelled in its clinical mission, receiving two tremendous honors in the fall acknowledging our high-quality patient care. First the MGH was recognized for achieving Meritorious Outcomes on the General Surgical and Vascular Surgical services by the American College of Surgeons National Surgical Quality Improvement Program (ASC-NSQIP). A few weeks later, the Cardiac Surgical team was recognized by the Society of Thoracic Surgery for receiving “Three Stars” (their top rating) in four of the five listed procedures. These outcomes were exceeded by only three hospitals across the entire United States. Congratulations to all of the surgeons, residents and fellows, nurses, and other members of the healthcare team for continuing this tremendous level of patient care.

Not “forgetting” our academic mission, a record number of faculty received HMS promotions over the last year. Most significant has been the promotion of four outstanding women — Sareh Parangi, Laurence Rahme, Colleen Ryan, and Barbara Smith – to the rank of Harvard Professor. These surgeons join Pat Donahoe, promoted to Professor “just a few years ago,” giving the MGH the highest number (5) of female Professors of Surgery throughout Harvard Medical School.

Finally, we have had the usual “comings and goings” as new residents, fellows, and faculty have now acclimated to the MGH family and all of our finishing chief residents have lined up fellowships for next summer.

Most prominent among the new recruits has been the addition of Matt Eagleton, MD, as Chief of the Division of Vascular and Endovascular Surgery. Matt and his wife, Sunita Srivastava, MD, also a vascular surgeon, have joined the Department as of January 1, 2018, and his impact is already being felt.

The issue contains numerous other clinical and research articles, including a closer look at the clinical activities of our surgical subspecialty teams in the General and GI Division, but you’ll have to read the entire issue to learn more.

Please enjoy the Newsletter and help us celebrate the success of this department. I thank all of you for your contributions.

Keith D. Lillemoe, M.D.
Chair, Department of Surgery
Surgeon-in-Chief
Massachusetts General Hospital
Ott Lab Creates Functional Stem Cell-Derived Small Bowel Segments

Investigators from the Division of Thoracic Surgery and Center for Regenerative Medicine have used human induced pluripotent stem cells (hiPSCs) to successfully bioengineer functional segments of small intestine that can mature and deliver nutrients into the bloodstream when implanted in rats. The groundbreaking achievement was published in the online journal *Nature Communications* (PMID: 29018244).

“The significance of this breakthrough” senior author Harald C. Ott explains, “is that it bridges the gap between the differentiation of single cells and the generation of tissue with a higher level of function, in this instance vascular perfusion and nutrient absorption.” Although previous studies have reported successful differentiation of small millimeter units of tissue from hiPSCs, the present technology enables those units, or organoids, to form larger scale grafts that someday could be used as replacement organs for patients with short bowel syndrome, who are unable to sustain life by enteral intake alone.

Serious gastrointestinal diseases, including Crohn’s disease, may require resection of all or part of the small intestine, leading to insufficient absorption of nutrients. Patients with short bowel syndrome sometimes can be treated with special diets, but many must rely on intravenous nutrition. While small bowel transplantation is a feasible treatment option, the availability of suitable organs is limited. Although 127 small bowel intestine transplants were performed in the U.S. in 2015, as of October 4, 2017, 273 patients remain on the waiting list.

The technology that supports this breakthrough begins with perfusion decellularization, a technique developed by Dr. Ott’s research team in 2008. A detergent solution is used to strip the living cells from a donor organ, leaving a scaffold of denuded extracellular matrix (ECM). The matrix is then repopulated with patient-derived, organ-appropriate hiPSCs.

In previous work, Dr. Ott’s team has decellularized animal kidneys, lungs, and hearts; they have generated functional rat kidneys and lungs; and last year they regenerated functional heart muscle from decellularized human hearts.

Repopulating the decellularized 4-cm small bowel segments for the present study was a complex process, requiring the delivery, engraftment, and maturation of two different cell types – epithelial cells for the intestinal lining and endothelial cells for the blood vessels – in the right locations. According to Ott, “The next steps will be to further mature the grafts and to scale the construct to a human size, so that someday we may be able to provide a more accessible alternative to small bowel transplantation for patients with short bowel syndrome – ideally growing ‘on-demand’ patient-specific grafts that would not require immunosuppressive drugs.”

Kentaro Kitano, MD, a research fellow in the Department of Surgery, and Dana M. Schwartz, MD, an MGH general surgery research resident, are co-lead authors of the *Nature Communications* paper. The study was supported by a National Institutes of Health Director’s New Innovator Award DP2 OD008749-01, the Charles and Sara Fabrikant MGH Research Scholar Award, and a grant from the Mendez National Institute of Transplantation Foundation.
Understanding How Gastric Bypass Surgery Effects Weight Loss and Reversal of Insulin Resistance

In a significant step toward understanding how gastric bypass surgery triggers weight loss and reversal of insulin resistance, researchers from the Center for Engineering in Medicine have developed a novel method for quantifying human organ perfusion dynamics, which could lead to the discovery of new drugs for treating obesity, type II diabetes, and other metabolic disorders. The research team, led by Nima Saeidi PhD, Principal Investigator on the project, published their first paper on this technological advancement, termed Metabolic Modularity Analysis (MMA), in the journal *Metabolites* (PMID: 29137180).

MMA is a novel experimental and computational workflow. It represents the first use of rodent gastric bypass models, state-of-the-art mass spectrometry, and an array of bioinformatics tools to unravel the mechanism(s) by which gastric bypass surgery leads to weight loss and resolution of type II diabetes. Selecting human liver perfusion dynamics as their initial target, the team utilized mass spectrometry to quantify thousands of metabolites and proteins to obtain clues about how the liver reprograms itself after bariatric surgery. Utilizing a state-of-the-art SWATH proteomics workflow, the team discovered approximately 100 proteins in rat livers that were significantly elevated after Roux-en-Y gastric bypass (RYGB), including proteins involved in iron transport, lipid metabolism, and bile acid conjugation, all of which could be targeted by drugs using a liver-specific version of the gene silencing technology RNAi.

To date, gastric bypass surgery has been the only effective treatment for achieving permanent weight loss in individuals with metabolic disease. Our goal, Dr. Saeidi explains, “is to reverse engineer the weight loss and resolution of blood sugar control without having to perform such an invasive procedure.” Emphasizing the multi-disciplinary nature of the research, co-corresponding author, Dr. Martin Yarmush, director of the Center for Engineering in Medicine, pointed out that “Investigators in the field have long sought after this type of multi-omic analysis on a rodent gastric bypass model to study metabolic disease, but the work requires expertise in rodent surgery, multi-omics analytics, and computational biology.” Lead author, Dr. Sridharan adds “We have finally reached a stage in biomedical research where we can interrogate complex in vivo systems by cost effectively acquiring large scale mRNA, protein, and metabolite data. The challenge remains in the interpretation of these high-dimensional data to provide biological insight into how tissue-specific metabolic and signaling pathways are triggered by the surgery.” According to the authors, “developing network-based algorithms to handle time-series ‘omics’ data will be requisite to unraveling complex cause and effect relationships, such as the impact of post-surgery plasma hormone levels on tissue transcriptional reprogramming.”

Dr. Saeidi is an assistant professor of surgery at Harvard Medical School. Dr. Yarmush is professor of surgery and founding director of the Center for Engineering in Medicine. The study was supported by National Institutes of Health grants DK095558, DK103947 and DK103500.

Research Activities

*(The following represent federal grants in excess of $450,000 awarded between April and October 2017)*

**Mustafa Korkut Uygun** (Center for Surgery, Science & Engineering) received funding to develop a novel cryostasis cocktail for high subzero banking for human organs (DoD: 04/01/2017).

**Irit Adini** (Center for Surgery, Science & Engineering) received R01 funding to elucidate the regulation of angiogenesis by melanocytes in age-related macular degeneration (NIH: 6/30/2017).

**Joren C. Madsen** (Transplant Surgery) received funding to study donor kidney cointransplantation as a requirement to induce mixed chimerism tolerance in heart recipients (NIH–NIAID: 06/30/2016).

**Ronald G. Tompkins** (Center for Surgery, Science & Engineering) received funding to enable Big Data using the Glue Grant Databases EDGE (U.S. Navy: 06/30/2017).

**David Pepin** (Pediatric Surgery) received funding for GalT-KO gene therapy using a novel engineered MIS to treat ovarian cancer (U.S. Army: 06/30/2017).

**Patricia K. Donahoe** (Pediatric Surgery) received funding for gene mutation and rescue in human diaphragmatic hernia (NIH: 07/31/2017).

**Mehmet Toner** (Center for Surgery, Science & Engineering) received R01 funding to elucidate the regulation of angiogenesis by melanocytes in age-related macular degeneration (NIH: 6/30/2017).

**Curtis Cetrulo** (Plastic Surgery) received funding for GaIT-KO porcine nerve xenograft for reconstruction of large nerve gaps. (U.S. Army: 09/30/2017).

**Ronald G. Tompkins** (Center for Surgery, Science & Engineering) received R01 funding to study high subzero preservation of liver for transplantation (NIH: 07/31/2017).

**Curtis Cetrulo** (Plastic Surgery) received funding for GaIT-KO porcine nerve xenograft for reconstruction of large nerve gaps. (U.S. Army: 09/30/2017).

**Nima Saeidi** (Center for Surgery, Science & Engineering) received R01 funding to study a cell-free approach to the engineering of corneal stroma (NIH:09/30/2017).

**Mustafa Korkut Uygun** (Center for Surgery, Science & Engineering) received funding to develop a supercooled limb preservation protocol (U.S. Army: 09/30/2017).

**Martin Yarmush** (Center for Surgery, Science & Engineering) received R01 funding to study recellularization of liver bioscaffolds (NIH: 09/30/2017).
Clinical News

Spotlight on General and GI Surgery

The Division of General and Gastrointestinal Surgery (DGGIS) is the largest division in the Department of Surgery. While members of the division are capable of treating a wide variety of conditions, they tend to focus their clinical practices on subspecialty interests. There continues to be a strong relationship with the MGH Cancer Center, and surgeons in this division operate on the majority of gastrointestinal malignancies seen in the center. Multidisciplinary cancer clinics are held twice per week at the Wang 4 office suite and clinical trials are offered through this practice.

As the division aims to provide “right care in the right location,” there has been a strong collaboration with Newton-Wellesley Hospital (NWH). Recent hires in the Department of Surgery at NWH are also members of the DGGIS, with the vision of being able to perform cases of the appropriate complexity at optimal locations. The division was recently recognized by U.S. News & World Report as one of the leading centers for adult GI surgery in the country, but with subspecialty programs in gastroesophageal, colorectal, endocrine, liver, pancreas and biliary, and bariatric and metabolic surgery, the division has so much more to report.

Gastroesophageal Surgery Program
David W. Rattner MD, Director

The gastroesophageal surgery team was the first clinical team in Boston to perform per oral endoscopic myotomy (POEM), a new endoscopic treatment for achalasia. This procedure has now been successfully performed in over 80 patients and is rapidly overtaking open myotomy as the preferred treatment modality for this condition. GE Surgery boasts the largest foregut surgery program in the Northeast based on number of cases and referrals. It also serves as a regional referral center for complex re-operative surgery of the foregut. Nearly half of the procedures performed by this group are done in patients with previous failed anti-reflux operations or hiatal hernia repairs. The GE surgical team is comprised not only of general surgeons, but also of thoracic surgeons and surgical oncologists. Indeed, multidisciplinary care with gastroenterologists and thoracic surgeons has been an important key to their success in managing even the most complex and difficult cases.

Milestones in Gastroesophageal Surgery
1991     First laparoscopic anti-reflux operation performed in Boston.
2003     First advanced GI/MIS fellowship in Boston.
2012     First LINX procedure in Boston.
2013     First per oral endoscopic myotomy (POEM) for achalasia performed in New England.

The members of the surgical team, Ozanan Mereiles, Christopher Morse, John Mullen, and David Rattner, work closely with multidisciplinary care providers in the Swallowing and Heartburn Center within the Digestive Healthcare Center as well as the Tucker Gosnell Center for Gastrointestinal Cancers within the Mass General Cancer Center.
Established in 2007, the goal of the Colorectal (CR) Program has been to promote excellence in clinical care, research, technology development, and training opportunities for future colorectal surgeons. The program works closely with the Mass General Cancer Center, the Digestive Healthcare Center, and the Pelvic Floor Disorders Center. The members of the surgical team are David Berger, Liliana Bordeianou, James Cusack, Richard Hodin, Todd Francone, Hiroko Kunitake, David Rattner, Rocco Ricciardi, and Paul Shellito.

The program is noted for implementing the first ERAS pathway in colorectal surgery. Dr. Liliana Bordeianou, who assumed leadership of the program in 2014, spearheaded the painstaking process of reviewing the literature for best clinical practices, developing a viable protocol, and securing the cooperation of multiple groups within MGH, including surgeons, anesthesiologists, nurse practitioners, and nutritionists among others. This tremendously successful effort not only streamlined the patient’s path to recovery, but also reduced complications, wound infections (1.1 percent versus 6 percent prior to implementation), and overall length of hospital stay by one full day. In recognition of this effort, Dr. Bordeianou and her team received the Bowditch Prize in 2017. As a result of her significant outcomes, Partners HealthCare adopted ERAS as the foundation for a system-wide colorectal collaborative, which has included the use of a standardized pre-surgery kit with all medications and bowel prep material to ensure patient compliance with the protocol and better outcomes after surgery.

Several CR team members have been active in clinical guidelines and curriculum development at the national level through the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES).

Innovative Clinical Practices

Novel surgeries offered to patients with colorectal cancer include the transanal total mesorectal excision (taTME). This procedure was developed in large part when Dr. Patricia Sylla was the advanced GI/MIS fellow. While total mesorectal excision (TME) by open approach remains a standard technique, laparoscopic approaches (laTME) have been increasingly favored and have produced excellent outcomes in recent clinical trials, particularly with regard to short and long-term results. However, the utility of laTME is limited in patients with mid- and low colorectal cancers, where the risk of leaving a positive circumferential resection margin is high. The sphincter-sparing TaTME procedure has produced excellent clinical outcomes at MGH.
Recent additions to the clinical team include Drs. Rocco Ricciardi, Todd Francone, and Hiroko Kunitake. Dr. Ricciardi was hired in 2017 to lead the newly created Section of Colorectal Surgery, which will encompass both the MGH and Newton-Wellesley Hospital (NWH) campuses. Dr. Ricciardi is an experienced colorectal surgeon who was recruited from the Lahey Clinic. He holds a a senior leadership position within the CR group. Dr. Francone, another recruit from Lahey, practices at NWH under Dr. Ricciardi’s leadership. Finally, Dr. Kunitake is a specialist in inflammatory bowel disease and geriatric surgery. She is developing a geriatric ERAS pathway for the CR program.

Milestones in Colorectal Surgery

2008  Established the first Pelvic Floor Disorder Center in Boston.
2012  World’s first Natural Orifice Proctectomy with TaTME (with the Barcelona Surgical Group).
2016  First colorectal ERAS pathway implemented at MGH and adopted system-wide by Partners Healthcare.

The Endocrine Program

Richard A. Hodin MD, Director

Endocrine disorders are exceedingly common in the U.S., and surgical care of the thyroid, parathyroid, and adrenal disorders is complex. Thyroid cancer alone has increased exponentially and is currently the 5th most common cancer in women. The DGGIS has established a multidisciplinary Advanced Thyroid Cancer program that includes endocrine surgeons, endocrinologists, medical oncologists, radiation oncologists, and laryngologists. The clinic meets monthly and takes care of the small subset of patients with advanced forms of thyroid cancer. These aggressive cancers are difficult to treat and complex in their presentation. The advanced thyroid cancer program is one of the few in the U.S. The team’s monthly Endocrine Oncology Conference is directed by Dr. Sareh Parangi and has become a very successful educational and clinical venue that brings together specialists from inside and outside the MGH.

The endocrine program is comprised of 8 surgeons: Randall Gaz, Richard Hodin, Carrie Lubitz, Vinod Narra, Sareh Parangi, Roy Phitayakorn, Gregory Randolph, and Antonia Stephen. The surgery team works closely with multidisciplinary care specialists from the Center for Endocrine Tumors within the MGH Cancer Center and the MGH Endocrine Division.

Rich Hodin in OR with past endocrine surgery fellow, Dana Lin.

An endocrine surgery clinical fellowship was started approximately 10 years ago and is widely regarded as one of the premier programs in the country. The endocrine fellows have had uniformly stellar credentials, adding significantly to the clinical, research, and educational components of the endocrine surgical service. The MGH fellows have gone on to wonderful positions in the world of academic endocrine surgery, including at top notch institutions throughout the US (Johns Hopkins, Stanford, Mayo Clinic, University of Pennsylvania). Two of the graduates of the program are on the MGH faculty - Carrie Lubitz and Roy Phitayakorn.

The endocrine surgery program has continued to increase its surgical case volume and to spread its wings in regard to providing care at multiple sites beyond the walls of the MGH, i.e., Danvers/NSMC, MGH West, NWH, Mt. Auburn Hospital, Mass Eye and Ear Infirmary, and the Pentucket Medical Group in Merrimack Valley.

The program is academically productive with 3 NIH-funded investigators. Much of the research focuses on understanding the biology of various endocrine tumors, including aggressive thyroid cancers, with the hope of devising new tools for prevention and early treatment.

Members of the team are active in national organizations, including the American Association of Endocrine Surgeons (AAES), where Dr. Parangi is Treasurer, Dr. Lubitz is on the Program Committee, and Dr. Phitayakorn is on the Education Committee.
Milestones in Endocrine Surgery

2007  MGH Endocrine Surgery Tissue Repository established. The repository contains over 1000 annotated tissue and blood specimens from patients with endocrine tumors, serving as a resource for basic and translational researchers nationwide interested in developing biomarkers for endocrine tumors.

2005  MGH Endocrine Surgery Database established.

2008  MGH Thyroid Cancer Research Lab established. Since inception, the lab has been at the forefront of translational research efforts on mutation-directed therapeutics.

2007  MGH Endocrine Surgery Fellowship started.

2007  Recurrent laryngeal nerve monitoring techniques introduced to help identify nerve injury during thyroid and parathyroid surgery.

2015  Novel blood-based biomarker assay developed to identify patients with the high risk BRAFV600E mutation. This assay has the potential to serve as a marker of prognosis and to assist in the assessment of treatment response.

Metabolic and Bariatric Surgery Program
Matthew M. Hutter MD, Director

The Metabolic and Bariatric Surgery Program was founded in 1998. It is accredited both as an adult and adolescent surgery program through the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP). The MGH Weight Center is a multidisciplinary team that specializes in the treatment of patients with obesity. It includes 4 surgeons, 7 obesity medicine specialists, 4 registered dieticians, and 4 clinical psychologists. Offices are located at the MGH Main Campus and the Danvers facility. This multidisciplinary approach to the treatment of obesity is rather unique, and others view it as a model for how the treatment of obesity should be provided in the future. Matt Hutter is the Director of this multidisciplinary group, which sees over 1200 new patients and performs almost 400 bariatric operations annually. Drs. Denise Gee, Oznan Meireles, Elan Witkowski, and Matthew Hutter comprise the surgical team. Dr. Janey Pratt, who helped to found and build the program, left the MGH for Stanford Medical Center in 2016. Operations include the laparoscopic Roux-en-Y gastric bypass, the laparoscopic sleeve gastrectomy, and reoperative procedures. Intragastric balloons, which are placed and removed endoscopically, are also offered.

An advanced laparoscopic and bariatric fellowship was
established in 2002. The program graduates one fellow each year. All graduating fellows have achieved certificates for Metabolic and Bariatric Surgery from the American Society of Metabolic and Bariatric Surgery (ASMBS).

Surgeons at the Weight Center are actively engaged in many national surgical societies. For SAGES, this includes positions on the Board of Governors, the Education Committee, the Program Committee, the Telementoring Committee, the Endoluminal Bariatric Committee, as well as chair or co-chair of the Technology and Value Assessment Committee, the Bariatric Surgery Committee, and the Outcomes Committee. Other positions include a Fellowship Council Board Member and Chair of the Healthcare Quality and Outcomes Committee for the SSAT. For the ASMBS, team members hold positions on the Executive Council, the Chair of the Research Committee, the Surgical Quality Alliance Representative, and the Access to Care Committee. Dr. Hutter is president elect of the ASMBS. His term will run from 2019 to 2020.

The newest surgeon to join the program, Dr. Elan Witkowski, came on board in 2016 to perform general and bariatric surgery. He completed his surgical training at the University of Massachusetts and was the Advanced MIS/Bariatric Surgical Fellow in 2016 before joining the staff.

Innovative Practices

Dr. Hutter has been the steward and architect of the National Data Collection Program for Metabolic and Bariatric Surgery since it started in 2006. He was instrumental in the design and development of the accreditation program for bariatric surgery – the MBSAQIP. The current program has over 800 participating sites and captures ~95% of all bariatric operations performed in the U.S.
Liver Surgery Program
Cristina R. Ferrone MD, Director

Liver operations are high risk procedures that require advanced surgical expertise and experienced pre-, intra-, and postoperative teams. The liver surgery (LS) program at MGH performs operations for primary cancers (hepatocellular carcinoma and cholangiocarcinoma), metastatic disease, and non-cancerous lesions. The liver is one of only two organs capable of regeneration, allowing skilled surgeons to remove up to 80% of the entire liver. The MGH has one of the busiest surgical liver practices in the Northeast. Over 630 hepatectomies have been performed in the last 5 years with over 130 just last year. It is also the largest minimally invasive liver practice in New England and has performed more than 200 major and minor hepatectomies (Villani V, et al. “Idealized” vs. “True” learning curves: the case of laparoscopic liver resection. HPB. 2016 Jun;18(6):504-509. PMID: 27317954). Additionally, in 2017, a robotic hepatic resection program was implemented by Dr. Motaz Qadan.

Established in 2007, the liver team works closely with the Mass General Cancer Center, the Digestive Healthcare Center, and Mass General Transplant Center. Multiple multidisciplinary clinics (surgical, medical, radiation oncology, transplant surgery, hepatology, gastroenterology, and interventional radiology) are conducted weekly to evaluate new and existing patients, creating an outstanding environment for comprehensive, state-of-the-art patient care. While the liver team handles a multitude of pathologies, each member has a special focus of expertise. Cristina Ferrone specializes in cholangiocarcinoma and metastatic disease to the liver. Kenneth Tanabe focuses on hepatocellular carcinoma (HCC) and metastatic disease to the liver. Motaz Qadan focuses on metastatic disease to the liver and cholangiocarcinoma. James Markmann and Nahel Elias, from the transplant team, focus on HCC and cholangiocarcinoma.

Innovative Clinical Practices

The liver program offers a number of innovative approaches designed to make “unresectable” liver masses resectable. For example, the Associating Liver Partition and Portal Vein Ligation for Staged (ALPPS) hepatectomy
operation is performed in two stages to permit resection of patients with tumors too large to resect with traditional approaches. Another approach to handling burdensome tumor loads is performed in collaboration with surgical colleagues from the Transplant Center, who remove the entire liver from the body for ex vivo resection by the liver team, after which the organ is reimplanted in the patient.

While surgery is the best chance for cure for most, the program offers other innovative strategies for patients who may not be the best surgical candidates. In conjunction with the interventional radiology team, they perform microwave ablation or irreversible electroporation of liver lesions. MGH was one of the first two institutions in the U.S. to offer proton beam therapy. As a consequence, the team has developed a deep experience with this technology, which has translated into cutting edge treatments for "unresectable" cancers.

For patients with synchronous colorectal cancers and liver metastases, the program offers simultaneous laparoscopic or open resection. This eliminates the need for a second operation, permitting patients to regain their quality of life sooner than if they had to undergo two successive operations.

**Basic science and translational research**

The basic and translational research efforts by this group are unparalleled and provide additional support to the clinical program. Drs. Cristina Ferrone, Kenneth Tanabe, and James Markmann all have a significant laboratory effort.

Dr. Ferrone is studying the immune response and genetics of cholangiocarcinoma and colorectal cancer metastases. She works in collaboration with Drs. David T. Ting and Nabeel El-Bardeesey. They were the first group to identify albumin as a definitive diagnostic marker for intrahepatic cholangiocarcinoma (IHCC). Before this marker was discovered, IHCC was largely a diagnosis of exclusion. Patients had to undergo multiple tests, such as colonoscopy, upper gastrointestinal endoscopy, mammogram, and positron emission tomography, to rule out a primary. Using the novel technology of branched DNA-enhanced albumin RNA in situ hybridization, they were able definitively diagnose IHCC, which has revolutionized and greatly benefited patient care. (Ferrone et al. Ann Surg Oncol. 2016 Jan;23(1):290-6) PMID: 25519926.)

Dr. Ferrone’s team was also the first to extensively outline the immune response to IHCC. This effort formed the basis for a large pharmaceutical trial. (Sabbatino et al. Clin Cancer Res. 2016 Jan 15; 22(2):470-8. PMID: 26373575).

Drs. Ferrone and El-Bardeesey developed the first mouse model for cholangiocarcinoma (Saha et al. Nature 2014 Sep 4;513(7516):110-4. PMID: 25043045). Their efforts have also yielded one of the largest repositories of patient tumor-derived cholangiocarcinoma cell lines and xenografts, which is used worldwide to support genetic research.

Dr. Tanabe, in collaboration with Dr. Bryan Fuchs, has extensively studied the molecular subtypes of hepatocellular carcinoma (HCC) and their drug sensitivities. They have also generated an animal model for cirrhosis-generated HCC.

Dr. Markmann’s research spans basic, translational, and clinical research. His basic research lab focuses on approaches to gain transplantation tolerance that will allow graft survival without immunosuppression. Currently, his team is investigating a population of regulatory lymphocytes that can prevent graft rejection without traditional immunosuppressive medications. An Immune Tolerance Network/NIAID sponsored clinical trial will begin in the Spring in collaboration with Eva Guina at Dana-Farber Cancer Institute in which purified regulatory T cells specific for the donor are administered to liver transplant recipients 3-4 months post transplant followed by gradual weaning of all immunosuppression. This will be the first of its kind trial and has the potential to alleviate the morbidity and mortality that accompanies traditional immunosuppressive approaches.

In other studies, in collaboration with the bioengineering team headed by Dr. Korkut Uygun, he is using ex vivo perfusion of livers as a means to assess performance, improve their function, and explore novel interventions to reduce immunogenicity and perhaps evoke regeneration ex vivo. These studies complement an ongoing clinical trial of ex vivo perfusion that allowed the team to perform the first clinical application of warm, oxygenated ex vivo liver perfusion in the US using the novel perfusion technology.

A more recent line of investigation centers on the application of newly developed gene editing tools to render xenografts suitable for transplantation to humans. Working collaboratively with a new startup company in Cambridge, eGenesis, the MGH team will evaluate organs from CRISPR modified lines of pigs to assess their function in preclinical transplant models. It is hoped that this work will lead rapidly to relevant clinical application.
Pancreas and Biliary Surgery Team: (From left) Cristina R. Ferrone MD, Carlos Fernandez-del Castillo MD, Keith D. Lillemoe MD, and Motaz Quadan MD.

Clinical News

Clinical News

Milestones in Liver Surgery

2002 Established the Liver Tissue Bank.
2008 Performed first laparoscopic liver resection.
2009 Performed first combined laparoscopic liver resection and colorectal resection.
2017 First combined robotic liver and colorectal resection.

Milestones in Liver Surgery

Clinical Trials

In keeping with its commitment to multidisciplinary care, the program has multiple ongoing investigator-initiated and pharma-initiated clinical trials for patients with cholangiocarcinoma, metastatic colorectal cancer, and hepatocellular carcinoma. For patients with colorectal cancer liver metastases, the program offers a postoperative vaccine made from the patient's own liver metastases combined with granulocyte macrophage-stimulating factor.

A phase II trial that utilizes high-dose radiation to treat unresectable HCC and cholangiocarcinoma has provided sufficient data to support a large multi-institutional phase III trial.

The Pancreas and Biliary Program

Carlos Fernandez-del Castillo MD, Director

For over 50 years, the Department of Surgery at MGH has been at the forefront of clinical care for patients with surgical diseases of the pancreas. This institutional recognition began with Dr. George Nardi in the 1960s and was greatly expanded by Dr. Andrew Warshaw during his tenure as chief of the division of gastrointestinal surgery and later as department chair. Given his trajectory at Johns Hopkins, and then as chairman of surgery in Indiana, where he created one of the busiest pancreas surgery programs in the Midwest, the arrival of Dr. Keith Lillemoe in 2001 as Chief of Surgery further highlighted the MGH as one of the top centers in the country for pancreatic surgery. The program's reputation goes beyond the U.S. Indeed, worldwide the MGH is well-known for its high clinical volume and its numerous contributions to the literature.
Dr. Carlos Fernandez-del Castillo, the current director, along with Keith Lillemoe, Cristina Ferrone, and Motaz Qadan comprise the surgical team. The care of patients with acute pancreatitis is now under the leadership of Dr. Peter J. Fagenholz, from the division of trauma and acute care surgery. Dr. Fagenholz was responsible for developing the minimally invasive surgical techniques used at MGH, which have been widely accepted as the preferred approach to patients with necrotizing pancreatitis. Dr. Fagenholz coordinates the multidisciplinary team of endoscopists and radiologists who also participate in this effort.

In 2017, the program performed 192 pancreatic resections. Although fewer in number compared with procedures performed a decade ago, before similar programs were created at other local hospitals, MGH still performs the largest volume of pancreatic resections in New England, and the numbers have increased over the last 4 years despite insurance constraints (i.e., plans that do not allow patients to come to our hospital for care).

The bulk of pancreas resections at MGH are pancreaticoduodenectomies and the surgical outcomes are consistently rated amongst the best in the country based on traditional benchmarks of mortality (1.6% over the last 10 years), pancreatic fistula, length of stay, and readmissions. According to Dr. Fernandez, “A study we presented at the American Surgical Association in 2017 showed excellent long-term quality of life (i.e., more than 5 years) after a Whipple procedure.” This landmark study was conducted by an MGH resident under the direction of Dr. Ferrone. It dispelled many wrongly held assumptions about the long-term digestive and endocrine derangements purported to follow this operation.

**Innovative Clinical Practices**

Distal pancreatectomy is now increasingly performed via minimally invasive surgery (MIS). More than half of the procedures performed at MGH utilize MIS techniques without any apparent compromise in quality or complication profiles, and with some tangible advantages in terms of length of hospital stay. The team also performs a number of middle pancreatectomies. This operation was championed by Dr. Warshaw over 20 years ago and is not routinely offered at other centers. MGH also performs total pancreatectomy with islet cell autotransplantation, one of the few centers in the Northeast to offer this procedure.

In 2015, the pancreas team published a paper demonstrating the feasibility of downstaging locally advanced and borderline resectable tumors with FOLFIRINOX and radiation, a combination chemotherapy that has shown improved survival in patients with metastatic pancreatic cancer. Recently rated as one the most cited articles in *Annals of Surgery* (Fong et al. doi: 10.1097/SLA.0000000000000867, see *Peers in Press*), this was the first paper to highlight that changes around the major vasculature of the pancreas no longer serve as a reliable indicator of tumor involvement of vessel after neoadjuvant treatment, warranting surgical exploration for potential resection in this setting. The results also showed the operation could be done with good perioperative outcomes, making long-term survival for those who undergo resection possible, and potentially better compared with patients without locally advanced tumors who go directly to surgery. A fast-moving field, it is possible that, within a few years, most patients with pancreatic cancer will undergo neoadjuvant treatment before going to surgery, as is the case for patients with esophageal and rectal cancer.

The MGH was recently awarded $2.6 million by “Stand Up to Cancer” to evaluate the effects of neoadjuvant FOLFIRINOX, radiation, and Losartan (a common antihypertensive that reduces desmoplasia, i.e., tumor stroma density) to enhance drug delivery to tumors. MGH also continues to use intraoperative radiation therapy as a backup for patients with locally advanced pancreatic cancer who undergo surgical exploration after treatment (in those deemed unresectable at surgery), or for those undergoing resection that have close or positive margins.

Once considered a rare problem, cystic tumors of the pancreas, in particular, intraductal papillary mucinous neoplasms (IPMNs), represent one of the most common diagnoses in practice, and in fact, represent 15% of the pancreatic resections done annually at MGH. The management of IPMNs continues to evolve and is a source of heated controversy around the world. The pancreas group, together with outstanding colleagues in endoscopy, radiology, and pathology, is at the forefront of this problem. In a recent analysis of the literature, MGH ranked second worldwide as a leading the source of publications on this topic.

The pancreas program at MGH is also active in translational and basic research. The pancreas surgery laboratory, established by Dr. Warshaw 40 years ago, is now directed by Andrew Liss, PhD, who is studying the epigenetics of pancreatic cancer, as well as tumor/stromal interactions. The laboratory is also the seat of the Pancreas Biobank. This repository holds over 2700 patient samples, including tumor, blood, and fluid specimens, as well as over 100 live-
MGPO QI Incentive Program
by Donna M. Antonelli

Surgery performed with excellence on the MGPO QI Bonus measures. The measurement period for Term 2, CY 2017, ran from July through September 2017. Payments of $2500 were distributed to eligible clinicians in December.

QI Bonus Measures this term included:

- Physician Satisfaction Survey, sent out by the MGPO (hospital-wide measure) – 97% of surgeons completed the survey.
- Implementation of Surgery’s Opioid Plan and completion of an MGPO Opioid Quiz, (hospital-wide measure for each Department) – 100% of surgeons completed the implementation, thanks to Dr. Kaafarani and a strong effort by the Division Quality Directors.
- eCare Training – HealthStream modules or in-person training sessions (hospital-wide measure) – 96% of surgeons achieved the measure.
- Tactics to Avoid Preventable 30-day Returns, especially involving the Emergency Department (department measure) – 100% of surgeons achieved the measure.

Quality Dashboards

The Codman Center continues to produce a wide variety of dashboards for Surgery, the most recent release was the sixth edition of the individual surgeon dashboards.

Annual Quality Report and Grand Rounds

The eighth edition of Surgery’s Annual Quality Report has been published. The report continues to feature all the great work being done to improve the quality, safety, and clinical effectiveness of surgical care provided at MGH. The Annual Quality Grand Rounds was held on January 25, 2018. Presentations by each of the Division Quality Directors were well received.

Quality and Safety Efforts

In addition to division-based projects, the department is focusing on the following high priority efforts – and is actively involving residents at each PGY level.

ED Capacity Project - Reducing ED length of stay for admitted Surgery patients;

Sepsis Campaign; Opioid Education, Culture Change, and Implementing Opioid Guidelines for Surgery;

IPASS – Improve Handoffs and Communication; and Root Cause Analysis – integrating patient safety into all of Surgery’s efforts.

Announcements

Honors & Awards—Faculty

Congratulations to faculty members and surgical teams in General and Vascular Surgery who were recognized for meritorious outcomes in surgical patient care by the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP). This recognition reflects the outstanding performance of the hospital’s surgical teams in providing patient care at many levels. This distinction goes to only approximately 10 percent of the 680 participating hospitals that entered data into NSQIP in 2016 and represents the first time MGH has reached this status.

In exciting news from the MGH-MIT Artificial Intelligence Collaboration, Ozanan R. Meireles (General and GI Surgery) and Daniela Rus (MIT) were recently informed that Olympus Tokyo has agreed to enter into formal negotiations to collaborate as a corporate sponsor and R&D partner in developing an artificial intelligence system to analyze laparoscopic surgical video in real-time.

Liliana G. Bordeianou MD was awarded the American College of Surgeons Traveling Fellowship to Japan for 2019.

Cristina R. Ferrone MD assumed the role of Secretary of the Society of University Surgeons.

Tawakalitu O. Oseni MD (Surgical Oncology) has been invited to participate in the Society of Black Academic Surgeons (SBAS) Leadership and Faculty Development Institute, April 26, 2018.

Noelle N. Saillant MD (Trauma, Emergency Surgery, Surgical Critical Care) won the Bullfinch award for Best Teacher in a Clerkship across the entire MGH and received a “thank you note” signed by her trainees.

MGH Faculty Teaching awards were granted to three individuals in the Department of Surgery: Noelle N. Saillant MD and Dana A. Stearns MD (Trauma, Emergency Surgery, Surgical Critical Care), and Antonia E. Stephen MD (Surgical Oncology).

Kenneth Tanabe MD (Surgical Oncology) was recognized as the inaugural incumbent of the ESSCO/Slater Family Endowed Chair in Surgical Oncology. This chair is made possible by Kenneth and Ellen Slater and the ESSCO-MGH Breast Cancer Research Fund.
Announcements

Michael T. Watkins MD (Vascular Surgery) was named to the list of 50 Most Influential People of Color in Healthcare and Life Sciences by Get Konnected, Neighborhood Health Plan, Partners Healthcare, and Boston Business Journal.

Jonathan M. Winograd MD (Plastic Surgery) was recently elected president of the Massachusetts Society of Plastic Surgeons in 2017 and named Historian for the American Society of Peripheral Nerve. Historian is the first level of leadership, leading to presidency in five years.

Cameron D. Wright MD (Thoracic Surgery) received the Society of Thoracic Surgery Distinguished Service Award for his many contributions to the specialty of thoracic surgery and to our country.

Honors & Awards—Residents

MGH was well represented at the Academic Surgical Congress in Jacksonville, FL (Jan 30-Feb 1). This combined meeting of the Society of University Surgeons and the Association of Academic Surgery is always successful, and was especially so this year. On opening night, two surgical residents, Cristy Cauley and Sophia McKinley, represented MGH in a game of “Surgical Jeopardy.” On day 2, Allan Goldstein MD (Pediatric Surgery) represented MGH in the Congress Poker Tournament, a new fundraising event. Allan began the tournament with more chips than anyone else because he raised more contributions than anyone else in support of the meeting. At the meeting, Sophia K. McKinley MD EdM (Research Resident) was awarded the AAS/AASF Training Research Fellowship Award for her project “A Mixed-Methods Study of General Surgery Inpatient Satisfaction with Surgical Resident Care.” Her mentor for this project was Roy Phitayakorn MD. She received her award just as last year’s recipient, Jarod Predina MD, another MGH Research Resident, gave his final report.

Yanik Bababekov MD MPH (Research Resident) attended the American Association for the Study of Liver Disease (AASLD) meeting (October, 2017) with support from the association’s Ambassador Award for Emerging Liver Scholars Program. He was also appointed to serve on the Liver Transplantation and Surgery Steering Committee for 3 years as a trainee member. Most recently, he received the Sherilyn Gordon Memorial Travel Award to attend the American Society of Transplant Surgeons (ASTS) Winter 2018 meeting. Congratulations are extended to his mentors, Drs. David Chang and Heidi Yeh, as well.

Congratulations to Rajshri Mainthia MD (Research Resident) for her poster on malpractice claims after cholecystectomy and the factors associated with plaintiff payout, which won Best Clinical Poster at the Massachusetts Chapter of the American College of Surgeons. Rajshri was mentored in this work by Elizabeth Mort MD MPH from the MGH Lawrence Center for Quality and Safety.

Thomas O’Donnell MD (Research Resident) won the 2018 Peter B. Samuels Award Competition sponsored by the Society for Clinical Vascular Surgery. His paper “Association of Aneurysm Sac Behavior with Long-Term Survival Following EVAR” will be presented and recognized at the society’s upcoming meeting. Tom, who also won the award last year, is mentored by Dr. Mark Schermerhorn and is supported by the Harvard Vascular Surgery NIH Training Grant.

Charles Rickert MD PhD (Research Resident) was elected to serve as a resident member of the Massachusetts Chapter of the American College of Surgeons Council.

Additions to the Faculty

Matthew J. Eagleton MD, the new Chief of Vascular and Endovascular Surgery, joined the Department on January 1, 2018, along with his wife, Sunita Srivastava MD, also a vascular surgeon.

Promotions

To Professor of Surgery

G. W. (Jay) Austen, Jr., MD, Chief of Plastic & Reconstructive Surgery and Chief of Burn Surgery
Laurence Rahme, PhD, Director of the Molecular Surgical Lab
Colleen M. Ryan, MD, Burn Surgery

To Associate Professor of Surgery

David D’Alessandro, MD, Cardiac Surgery
Haytham Kaafarani, MD, MPH, Trauma, Emergency Surgery, Surgical Critical Care
David King, MD, Trauma, Emergency Surgery, Surgical Critical Care
Sara I. Pai, MD, PhD, Surgical Oncology
Rocco Ricciardi, MD, MPH, General and GI Surgery
 Parsia Vagefi, MD, Center for Transplantation Sciences
Jonathan Winograd, MD, Plastic & Reconstructive Surgery
Heidi Yeh, MD, Transplant Surgery

To Assistant Professor of Surgery

Branko Bojovic, MD, Plastic & Reconstructive Surgery
Heather Faulkner, MD, Plastic & Reconstructive Surgery
Peers in Press

Selected publications between May and December 2017 with active links to PubMed.

Burns


Cardiac Surgery


Cardiac Surgery


Laryngeal


Pediatric Surgery


*This paper represents a collaboration between Pediatric Surgery and Plastic Surgery.*


Plastic Surgery


*This paper represents a collaboration between Pediatric Surgery and Plastic Surgery.*
Peers in Press


**Surgical Oncology**


**Thoracic**


**Transplant**


**Trauma**


**Vascular**


Send us your news!

CALENDAR

Graduation Dates
“Senior Class Graduation Ceremony and Dinner”
Wednesday, June 20, 2018
“Final Grand Rounds”
Thursday, June 21, 2018
“Change Show”
Friday, June 22, 2018

Surgical Grand Rounds Highlights
“Biologically Driven Risk-Based Therapy for Wilms Tumor”
Thursday, March 22, 2018, 8:30 A.M.
Robert C. Shamberger, MD
The Patricia K. Donahoe Visiting Professorship in Pediatric Surgery
Chief of Surgery, Children’s Hospital, Boston, MA
Robert E. Gross Professor of Surgery, Harvard Medical School

“The Future of Cancer Care”
Thursday, April 5, 2018, 8:30 A.M.
Nipun Merchant, MD
Alan S. Livingstone Endowed Chair in Surgical Oncology
Professor of Surgery, Vice Chair of Surgical Oncology Services
Chief of the Division of Surgical Oncology in the Department of Surgery at University of Miami Miller School of Medicine

“Translational Cancer Research—A Surgeon’s Role”
Thursday, April 12, 2018, 8:30 A.M.
Jeffrey Drebin, MD, PhD
Ferguson-Ottinger Visiting Professor Lecture Chair, Department of Surgery
Memorial Sloan Kettering Cancer Center

“Pushing the Limits of Oncologic Liver Surgery”
Thursday, April 26, 2018, 8:30 A.M.
The MGH/Johns Hopkins International Visiting Professor
Eduardo de Santibañes MD, PhD
Professor and Chairman of the Hospital Italiano

Send us your news!
We appreciate your input regarding important milestones of staff and faculty achievement, vital department statistics, demographics, scholarly publications, and reports of important clinical, research, and educational initiatives. Please send your news to kwilliams12@partners.org.

Follow us on Social Media
Department of Surgery Twitter: http://www.twitter.com/MGHSurgery/
Mass General Facebook Page: http://www.facebook.com/massgeneral
Mass General Twitter: http://www.twitter.com/MassGeneral

General Surgical Service
Buenos Aires, Argentina

“Surgery”
Thursday, May 17, 2018, 8:30 A.M.
Richardson Memorial Visiting Professor
Gerard M. Doherty, MD
Moseley Professor of Surgery, Harvard Medical School
Crowley Family Distinguished Chair
Department of Surgery
Brigham and Women’s Hospital

“Terminal Heart Failure (CARL, LVR, LVAD, TAH, HTX)”
Thursday, June 14, 2018, 8:30 A.M.
Professor Dr. Friedhelm Beyersdorf, MD, PhD, FECTS
Mortimer J. Buckley Visiting Professorship in Cardiac Surgery
Department of Cardiovascular Surgery
University Heart Center Freiburg
University of Freiberg, Germany

Keith D. Lillemoe, MD, Editor in Chief; Ann S. Adams, Editor, Contributing Writer, Design and Composition