

# SURGERY UPDATE LEADING THE WAY

SUMMER 2015 • VOLUME 7, NUMBER 2



## We Will Miss You: Congratulations to the Department of Surgery Chief Residents



Drs. Annabelle Butler, Rebecca Rentea, Ryan Groeschl, Paul Jeziorczak, Kathleen O'Connell, Caitlin Patten, and Jacob Peschman.

The featured picture in this issue of *Leading the Way* pays tribute to our departing Chief Residents as we prepare for the annual Eberbach banquet in their honor. We are extremely fortunate to host Dr. Michael Sarr as this year's Eberbach Visiting Professor. Dr. Sarr is an Emeritus Professor of Surgery in the Department of Surgery at the Mayo Clinic, editor of the journal *Surgery*, and an internationally renowned surgeon.

Congratulations to the graduating Chief Residents. We greatly appreciate their many extra efforts in the care of our patients and all they have done to advance the missions of MCW and our department.

### CHIEF RESIDENTS (and their fellowship positions)

**Annabelle Butler, MD**

Fellowship in Minimally Invasive Surgery, Indiana University School of Medicine in Indianapolis, IN

**Rebecca Rentea, MD**

Fellowship in Pediatric Surgery, Missouri University Kansas City at Children's Mercy Hospital in Kansas City, MO

**Ryan Groeschl, MD**

Fellowship in Hepatopancreatobiliary Surgery, Mayo Clinic in Rochester, MN

**Paul Jeziorczak, MD, MPH**

Fellowship in Pediatric Surgery, Washington University School of Medicine/St. Louis Children's Hospital in St. Louis, MO

**Kathleen O'Connell, MD**

Fellowship in Critical Care and Masters in Public Health, University of Washington, Seattle in Seattle, WA

**Caitlin Patten, MD**

Fellowship in Breast Oncology, Carolinas Medical Center in Charlotte, NC

**Jacob Peschman, MD**

Fellowship in Critical Care, Mayo Clinic in Rochester, MN United States Navy Reserves Medical Corps

### FELLOWS (and their staff positions in July)

**Hepatopancreatobiliary Fellowship**

**Amir Fathi, MD**

University of California San Francisco

**Endocrine Surgery Fellowship**

**Diana Ortiz, MD**

Bay Surgical Group, Miami, Florida

**Minimally Invasive Surgery Fellowship**

**Harish Nirujogi, MD**

Practice plans in-process

**Pediatric Surgical Critical Care Fellowship**

**Jack Schneider, MD**

University of Oklahoma

**Vascular Surgery Fellowship**

**Rishi Subbarayan, MD**

McKenzie-Willamette Medical Center, Eugene, Oregon

**Pediatric Surgery Fellowship**

**Henry Chang, MD**

Practice plans in-process

**Surgical Critical Care Fellowship**

**Hani Hasan, MD**

Medical College of Wisconsin

**Surgical Critical Care Fellowship**

**Michael Mount, DO**

Mercy Health St. Elizabeth Hospital Youngstown, Ohio

### IN THIS ISSUE:

Complex Aortic Interventions – Endovascular Technology Transforms ..... 2

Endovascular Repair of Ruptured Aortic Aneurysms ..... 6

New Technology Provides Clinical Options for Treatment of Varicose Veins ..... 7

Welcome New Residents ..... 7

Hybrid Operating Room – Provides Imaging for Complex Integrated Vascular Surgery ..... 8

American College of Surgeons Clinical Congress... 9

Beyond Surgical Resection – Understanding the Role for Liver-Directed Therapies in Neuroendocrine Tumors..... 10

Personalized Therapy for Biliary Tract Cancers: The Emerging Role of Molecular Profiling to Identify New Treatment Options..... 12

Dr. Webb to Lead Curriculum at MCW..... 13

Center for Advanced Care – New Home for Many Department of Surgery Programs..... 14

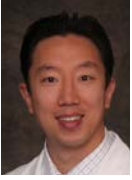
Jonathan B. Towne, MD, Visiting Professor Lectureship ..... 15

History Corner: The Connell Stitch..... 16

Awards and Appointments ..... 18

Faculty Listing ..... 19

# Complex Aortic Interventions—Endovascular



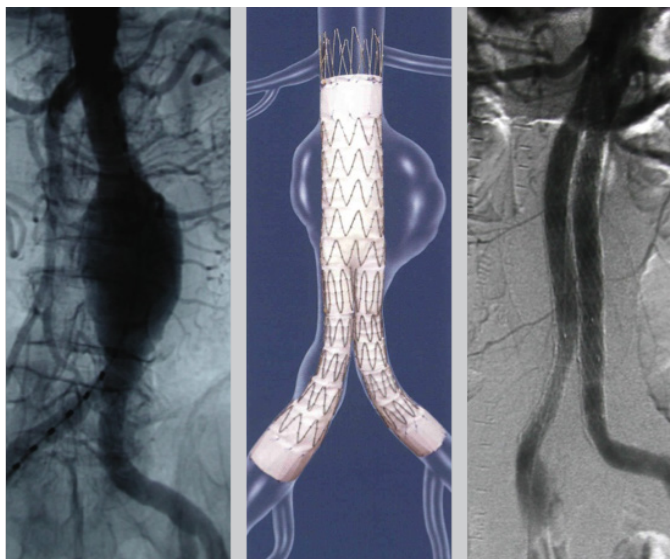
**CHEONG J. LEE, MD**  
Division of Vascular Surgery



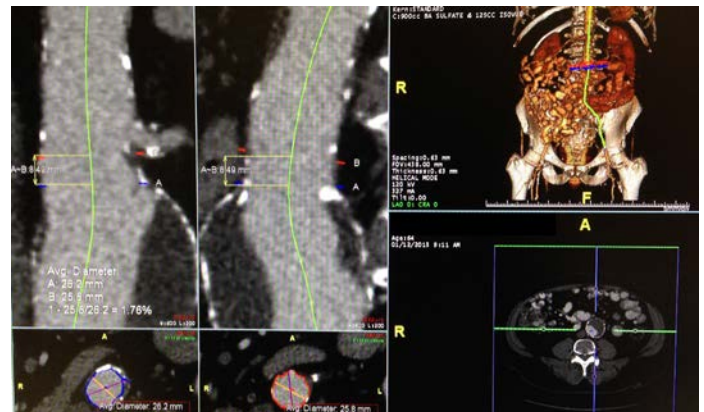
**MICHAEL J. MALINOWSKI, MD**  
Division of Vascular Surgery

Considerable advancements have been made in the treatment of abdominal aortic aneurysms the past two decades. In 1990, Dr. Juan Parodi and his team in Buenos Aires, Argentina treated the first patient with a device to exclude an aortic aneurysm using an endovascular technique, which involved delivering a fabric covered framework in a catheter system to exclude the aneurysm from within the blood vessel (Figure 1). This technology, combined with sophisticated and miniaturized delivery systems, has evolved to treating the entire diseased aorta with endovascular techniques. The primary reason the scope of endovascular therapy has been limited is due to involvement of visceral aortic branches, namely juxtarenal and thoraco-abdominal pathology – where the blood flow to the arterial branches must be maintained while excluding the aneurysmal disease.

The majority of aneurysm pathology involves the infrarenal aorta, however up to 30% of abdominal aortic aneurysms (AAA)



**FIGURE 1:** Angiogram of infrarenal abdominal aortic aneurysm extending to aortic bifurcation (left) with fabric covered endovascular stent graft with suprarenal fixation bridging the aneurysmal segment (middle). Completion angiography (right) confirms the aneurysmal segment has been excluded by the device.



**FIGURE 2:** Computer-generated images provide center line lengths and precise intraluminal diameters to measure dimensions for graft constructions and treatment design. The exact three-dimensional orientation is required when evaluating the visceral blood flow adjacent to the aneurysmal segment to insure accurate deployment and exclusion of the aneurysmal disease.

cannot be treated with standard endovascular stent grafts. This technology has rapidly evolved, from physician-modified devices to industrial-custom manufactured devices. The use of parallel grafting (placing visceral stent grafts in juxtaposition to a main aortic stent graft to seal para-visceral anatomy) technique for visceral artery preservation is an alternative to prefabricated branched or fenestrated endovascular aortic repair.

For complex aortic pathology, CT images are analyzed with sophisticated radiologic imaging software that allows precise measurements of the involved segments of the abdominal or thoracic aorta which are close to the area of aneurysmal disease (Figure 2).

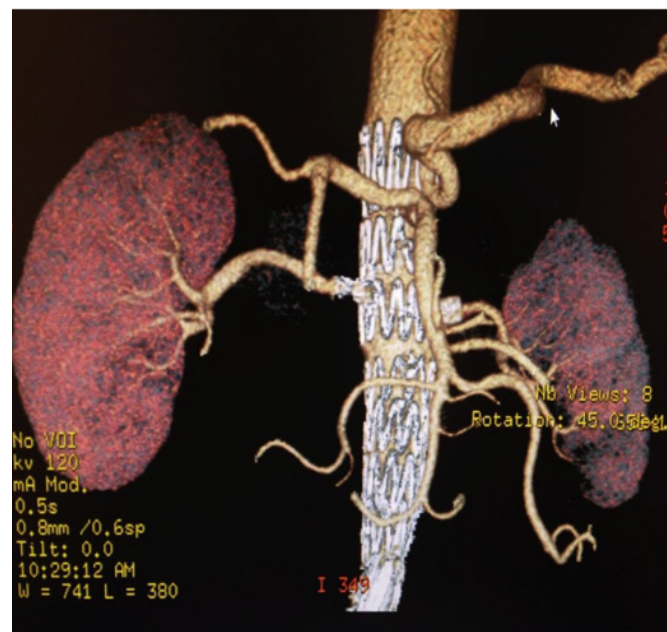
Following precise measurement and analysis, the best treatment modality is selected from options including a fenestrated graft, branched grafts, parallel grafts, traditional endografts, hybrid repair (requiring open and endovascular components) or traditional open repair techniques. The historical experience with open aneurysm repairs and familiarity with the technical features of specific devices play a major role in the success of a durable and safe outcome.

# Technology Transforms Vascular Surgery Care

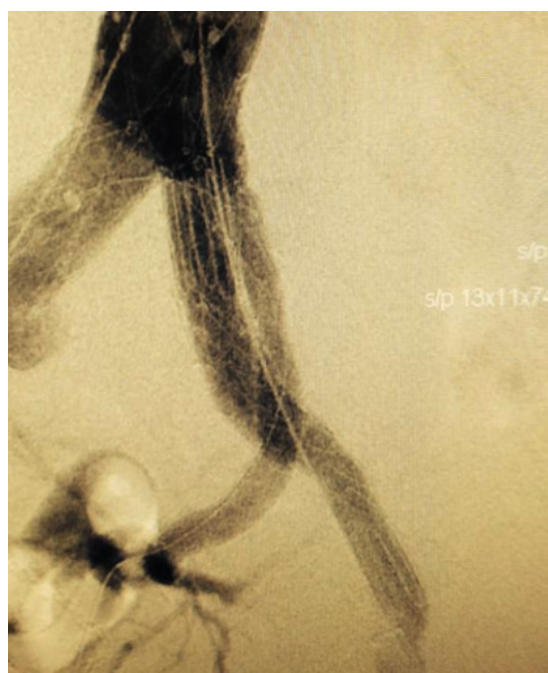
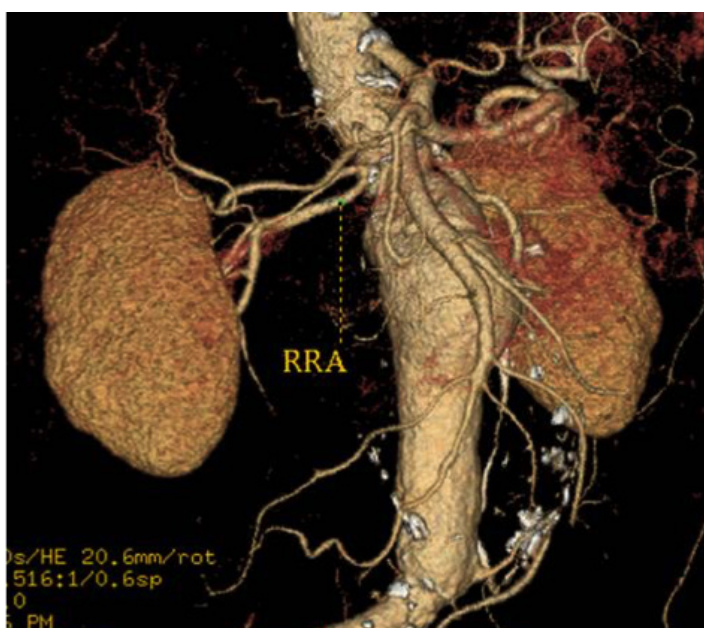
Although each patient requires a precisely configured aortic device, the current technique involves creating fenestrations in the graft fabric to preserve flow to the visceral vessels supplying the kidneys, bowel and other abdominal organs (Figure 3).

The US clinical studies, started in January 2005 for fenestrated endografts, have shown comparable surgical outcomes for aortic anatomy that previously would have been repaired with open aortic surgery. Endovascular techniques require individually constructed grafts that are specific to the individual patient's anatomy, allowing

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**FIGURE 3:**  
**ABOVE:** Postoperative CT angiogram showing the completed endovascular repair with renal stents.  
**LEFT:** 3-D rendering of a Juxtarenal Aortic Aneurysm.

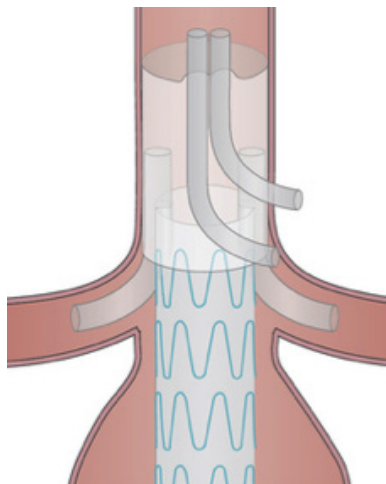


**FIGURE 4:**  
**LEFT:** Angiogram of a large common iliac artery aneurysm, involving the internal iliac artery (A) which is responsible for maintaining blood flow to the pelvic organs, and the external iliac artery (B).  
**RIGHT:** Sandwich technique using parallel running stents to seal the aneurysm and preserve flow to the left leg and internal iliac artery, similar to the technique used in the Gore Iliac Branched Device. It is placed through the fenestrations in the main aortic endograft.

## Complex Aortic Interventions continued from page 3

the graft to be positioned more proximal with apposition and fixation to healthier areas of the aorta to seal the aneurysm. Fenestrated grafting deploys the device adjacent to the origin of the branch arteries to which critical blood flow must be preserved. Small covered stents are delivered into the celiac, superior mesenteric and renal arteries through these fenestrations both to maintain flow into the branch artery and seal flow from reaching the aneurysmal segment of the aorta.

Other specially constructed devices are designed to maintain pelvic blood flow when aneurysms involve the distal aorta or iliac arteries (Figure 4). Successful treatment must provide blood flow to both the lower extremity and pelvic organs. A branched endoprosthesis is designed to preserve blood flow to the internal iliac artery during repairs of common iliac artery aneurysms.

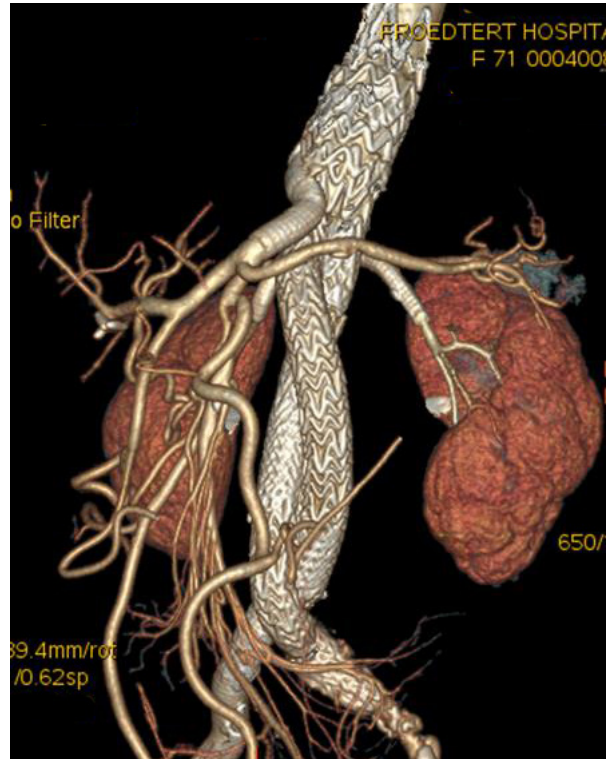


**Figure 5A:** Schematic of parallel grafting technique.

The technique of parallel grafting sandwiches multiple stent components together, running adjacent to each other between the aortic wall and the main body of the graft (Figure 5). Similar to fenestrated grafts, this strategy increases the area of coverage to the paravisceral aorta while preserving blood flow to vital visceral vessels. The parallel grafting technique places a conduit in the axillary artery to serve as a portal for deployment of stents into the renal and mesenteric arteries. These stents extend from the branch artery along the wall of the aorta to receive forward blood flow. With this technique, the grafts running parallel along the aorta raise the orifice of the target vessel above the aneurysmal aortic segment enabling blood to flow into the visceral structures without allowing blood into the aneurysm sac. Blood flow to the lower extremities follows the course of the main body of the graft.

Other hybrid techniques utilize components of both endovascular and traditional open surgery to successfully

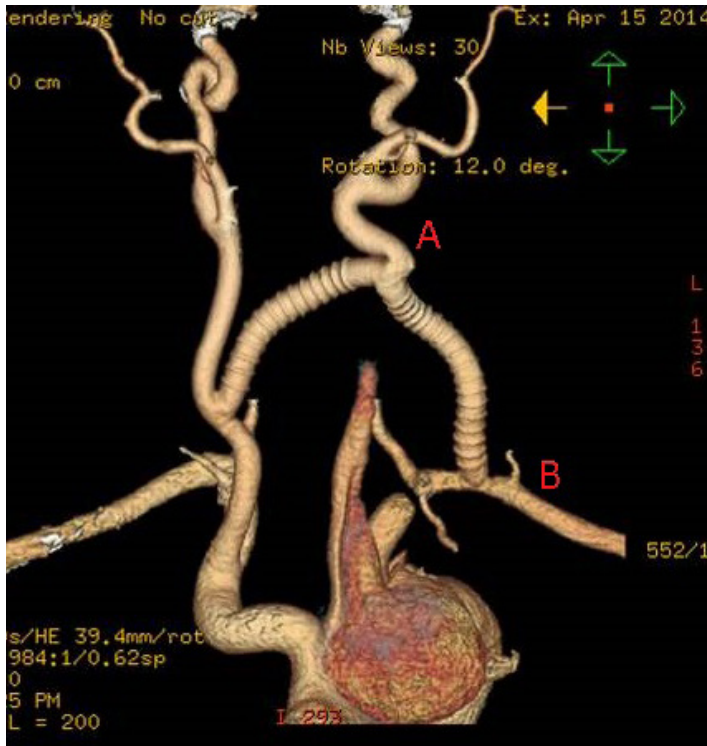
The technique of parallel grafting sandwiches multiple stent components together, running adjacent to each other between the aortic wall and the main body of the graft (Figure 5). Similar to fenestrated grafts, this strategy increases the area of coverage to the paravisceral aorta while preserving blood flow to vital visceral vessels. The



**Figure 5B:**  
**Top:** Volume rendered image of treated visceral segment aortic aneurysm demonstrates patent grafts to superior mesenteric and renal arteries.  
**Left:** Follow-up cross section CT scan of aorta demonstrates three parallel stent grafts (arrow) sandwiched between aortic wall and endovascular graft.

preserve intra-abdominal organ blood flow while providing durable surgical repair to prevent aortic aneurysm ruptures. “Debranching” involves traditional vascular bypass techniques in the chest and abdomen or in extra-anatomic fashion together with aortic stents. This hybrid approach allows treatment of the aortic disease while avoiding the risks of direct aortic clamping (Figure 6).

Taken together, these techniques have allowed treating patients with complex aortic disease with options that a



**Figure 6:** Hybrid repair of a thoracic aortic dissection with aneurysmal degeneration to preserve left hemispheric cerebral (A) and left arm (B) perfusion followed by thoracic stent graft placement.

decade ago were not available. Collaborative programmatic alliances between the Medical College of Wisconsin Divisions of Vascular Surgery and Interventional Radiology have contributed to our success in advancing treatments for aortic disease. Multidisciplinary planning and care conferences allow the evaluation of new techniques while seeking the optimal treatments for individual patients.

For those patients with conditions or anatomy that cannot be durably treated by the latest technology in endovascular commercial or investigational graft design options, the Division of Vascular Surgery remains committed to providing excellence in traditional open aortic surgery that dates back to operations invented by Drs. DeBakey, Crawford and Cooley in the 1950s — techniques that have become all but extinct at many institutions. Our advances in open surgical techniques, perioperative

anesthesia care and postoperative intensive care allow us to excel as part of a dedicated surgical team.

Recently we performed a retrospective analysis of the cross-sectional National Inpatient Sample (2000-2010) to evaluate patient characteristics and outcomes related to endovascular aneurysm repair and traditional open aneurysm repair for both unruptured and ruptured abdominal aortic aneurysms.<sup>1</sup> There were 101,978 patients in the sample with aneurysm repairs, open or endovascular, performed over the 11-year span of this study. The average age was 73 years, 21% were women, and 90% were white. Overall in-hospital mortality rate was 7%, with a median length of stay (LOS) of 5 days and median hospital charges of \$58,305. In-hospital mortality rate was 13 times greater for patients with ruptured aneurysms, with a median LOS of 9 days and median charges of \$84,744. For both unruptured and ruptured patients, endovascular interventions were associated with a lower in-hospital mortality rate (4% vs. 1% for unruptured and 41% vs. 27% for ruptured;  $P < .001$  for each), shorter median LOS (7 vs. 2 days; 9 vs. 6 days;  $P < .001$ ) but a 27%–36% increase in hospital charges.

Endovascular techniques for aneurysm repair have become common during the past 10 years (5.2% to 74% of the total number of AAA repairs), even though the total number of AAAs remains stable at 45,000 cases per year. In-hospital mortality rates for patients with both ruptured and unruptured cases have fallen by more than 50% during this time period. For patients with suitable arterial anatomy, endovascular techniques are the preferred management for aneurysm repair. •

**FOR ADDITIONAL INFORMATION** on this topic, see reference below, visit [mcw.edu/surgery](http://mcw.edu/surgery), or contact Dr. Lee at 414-805-9160, [cjlee@mcw.edu](mailto:cjlee@mcw.edu), or Dr. Malinowski, 414-805-9160, [mmalinowski@mcw.edu](mailto:mmalinowski@mcw.edu).

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# Endovascular Repair of Ruptured Aortic Aneurysms: Out with the old, in with the new, back in with the old?



**PETER ROSSI, MD**  
Division of Vascular Surgery

The treatment of ruptured aortic aneurysms, both thoracic and abdominal, has undergone the same transformation over the last decade as has the elective treatment of aortic aneurysms. Nationally, hospitalization for ruptured aneurysms has steadily decreased as hospitalization for elective endovascular aneurysm repair (EVAR) has increased. Importantly, the overall mortality rate for repair of ruptured aneurysms has decreased for both open and endovascular techniques.<sup>1</sup>

Nationwide, there has been a trend toward increasing use of EVAR for ruptured aneurysms. This trend has been mirrored at the Medical College of Wisconsin, where we have been repairing ruptured aneurysms primarily with an endovascular technique since 2008, with our first endovascular case being performed in 2005. Our hybrid operating theater provides an ideal location for application of these extremely advanced techniques; patients with ruptured aneurysms can be immediately stabilized with an aortic occluding balloon delivered by a transfemoral approach, and imaging can subsequently be obtained on-table to determine whether the patient would be best served by an open or endovascular repair. We are then able to immediately convert between endovascular and open surgical repair as needed.

Recently, data have been published that call into question the benefit of an endovascular-first approach to repair of ruptured aortic aneurysms.<sup>2</sup> At the Medical College of Wisconsin, we are in the process of reviewing all patients from the last 20 years to determine whether a survival benefit has been realized from implementation of the newest technology available. We continue to push the therapeutic envelope with an endovascular-first approach, and we are the only major center in southeast Wisconsin routinely applying these techniques to the ruptured aorta. •

**FOR ADDITIONAL INFORMATION** on this topic, please visit [mcw.edu/surgery](http://mcw.edu/surgery), or contact Dr. Rossi at [prossi@mcw.edu](mailto:prossi@mcw.edu), 414-805-9160.

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2. Grieve R, Gomes M, Sweeting MJ, *et al.* Endovascular strategy or open repair for ruptured abdominal aortic aneurysm: one-year outcomes from the IMPROVE randomized trial. *Eur Heart J.* 2015 Apr 7. pii: ehv125. [Epub ahead of print]



**Figure 1:** Ruptured abdominal aortic aneurysm in a Jehovah's witness with hemoglobin of 7.0 g/dl and hemodynamic collapse.



**Figure 2:** Successful endovascular exclusion of aneurysm.



**Figure 3:** CT scan 3 years post-operatively reveals aneurysm sac collapse around endograft and resolution of periaortic hematoma. Patient doing well clinically and living independently in community.

# New Technology Provides Clinical Options for Treatment of Varicose Veins



**KELLIE R. BROWN, MD**  
Division of Vascular Surgery  
Co-Director, MCW Comprehensive Vein Clinic

The most common underlying abnormality causing varicose veins is saphenous venous insufficiency. Traditionally, symptomatic varicosities have been treated with stripping of the vein, which typically involves multiple incisions in a surgical operation performed under general anesthesia. New technology has largely replaced operative vein stripping to treat saphenous insufficiency using endogenous techniques – treating the abnormal vein with a catheter directed into the vein through a small percutaneous canula. The Comprehensive Vein Clinic at the Medical College of Wisconsin is a multi-disciplinary clinic that offers the latest endovenous treatments for venous insufficiency and varicose veins.

Venous insufficiency is diagnosed based on a focused history and physical examination and confirmed with b-mode ultrasound performed in conjunction with an outpatient clinic visit. With the patient standing, venous blood flow is evaluated and the anatomic abnormalities are mapped with analysis of flow characteristics. Reflux and valvular incompetence is evaluated with velocity spectral analysis to measure reflux time.

Laser ablation, a technique that is performed in the clinic under ultrasound guidance and utilizing local anesthetic, allows for endovenous placement of a laser fiber via a micro-incision, achieving successful ablation of the saphenous vein for 97% of patients presenting for treatment. This procedure provides equivalent efficacy, a rapid recovery and less pain than traditional stripping. Other minimally invasive, office-based techniques are performed to treat venous tributaries, including microphlebectomy (surgical excision under local anesthesia) and sclerotherapy (chemical ablation of varicosities with needle injection). New, non-thermal technologies that promise even less invasive techniques for saphenous ablation will become available for our patients. •

**FOR ADDITIONAL INFORMATION** visit [mcw.edu/surgery](http://mcw.edu/surgery), or contact Dr. Brown at 414-805-9160, [krbrown@mcw.edu](mailto:krbrown@mcw.edu)

## Welcome Residents

The Department of Surgery welcomes the incoming 2015–2016 PGY1 General Surgery Residents:

**Adam Aronson**  
Washington University in St. Louis  
School of Medicine

**Christina Bence**  
Georgetown  
University School of Medicine

**Kelly Boyle**  
University of Wisconsin School of  
Medicine and Public Health

**Michael Cain**  
Medical College of Wisconsin

**Johnathan Doolittle**  
University of Texas Medical School  
at Houston

**Kathryn Haberman**  
Medical College of Wisconsin

**Dustin Hang**  
Case Western Reserve University  
School of Medicine

**Katherine Hu**  
University of Iowa Roy J. and  
Lucille A. Carver College of  
Medicine

**Christopher Johnson**  
Medical College of Wisconsin

**Kaleb Kohler**  
University of Cincinnati College  
of Medicine

**Rebecca Mitchell**  
University of Wisconsin School  
of Medicine and Public Health

**Joshua Piotrowski**  
Mayo Medical School

**Erin Strong**  
University of Michigan Medical  
School

**Chase Tobin**  
Eastern Virginia Medical School

**Keegan Zuk**  
University of Kansas School  
of Medicine

# Hybrid Operating Room Provides Imaging for Complex Integrated Vascular Surgery



**GARY SEABROOK, MD**  
Division of Vascular Surgery

A hybrid operating room combines state-of-the-art, high-resolution angiographic capability in a traditional operating room environment, affording the versatility of combining traditional open anatomic surgical exposure with endovascular catheter techniques. The Froedtert Hybrid OR is equipped with a multi-directional floor mounted robotic c-arm with 18 degrees of freedom, allowing sophisticated vascular imaging during surgical procedures.

When vascular patients are treated with catheter-directed therapy, integration of live radiological imaging is required during surgery. With angiographic capabilities in a hybrid OR, treatment devices can be guided and deployed precisely within human vascular anatomy from remote catheter-directed access. With ultrasound assessment of the arterial access site, micro-catheter entry techniques, and the use of arterial closure devices, percutaneous delivery of endovascular devices can be performed. Intra-vascular ultrasound (IVUS) is employed as an adjunct to evaluate luminal wall characteristics, assess the origins of branch vessels and measure the internal diameter of vessels to precisely select and position endovascular grafts.

Pre-operative digital and angiographic imaging is integrated on the surgical field via a 60-inch multi-panel high resolution video display. CT imaging, physiological data, and televised images of the operative field are integrated with reference and live angiography. In a glass-enclosed radiological control room adjacent to the hybrid OR, imaging acquisition is performed and archived. On-table three-dimensional CT imaging provides roadmaps and reconstruction assessment for complex vascular interventions.

The 900-square-foot operating room allows space for the robotic angiographic arm's "fly zone"







and the supporting equipment for complex arterial interventions including anesthesia equipment, transfusion support, patient warming devices, blood salvage, intra-operative echocardiography, intravascular ultrasound, and radiation protection equipment for staff. The floating surgical table is linked with the robotic c-arm to maintain exact orientation of the patient's arterial anatomy and the digital angiographic images acquired during the procedure.

In addition to vascular surgery procedures, the hybrid OR is used by other services for procedures requiring high-resolution imaging and anesthesia care including TIPS for portal decompression,

chemo-embolization treatment, neurological vascular interventions, deployment of cardiac assist devices, laser-lead extraction of cardiac electrophysiological hardware, and intravascular coil deployment for gastrointestinal bleeding. With growth in volume of vascular interventions, and increasing complexity and length of procedures, Froedtert is planning for installation of a second hybrid OR. •

**FOR ADDITIONAL INFORMATION** on this topic, visit [mcw.edu/surgery](http://mcw.edu/surgery), or contact Dr. Seabrook at [gseabrook@mcw.edu](mailto:gseabrook@mcw.edu), 414-805-9160.

## PLEASE JOIN US

### RECEPTION AT AMERICAN COLLEGE OF SURGEONS CLINICAL CONGRESS

**October 5, 2015 | 6–8 p.m. | The University Club of Chicago, 76 E. Monroe Street, Chicago, Illinois**

Plan to join us at the MCW Department of Surgery / Alumni Association reception during the American College of Surgeons Annual Clinical Congress on Monday, October 5, 2015.

The reception will be held 6–8 p.m. at The University Club of Chicago, 76 E. Monroe Street.

# Beyond Surgical Resection – Understanding Neuroendocrine Tumors



**JOSEPH ZECHLINSKI, MD**  
Department of Radiology



**WILLIAM RILLING, MD**  
Department of Radiology



**KATHLEEN CHRISTIANS, MD**  
Department of Surgery

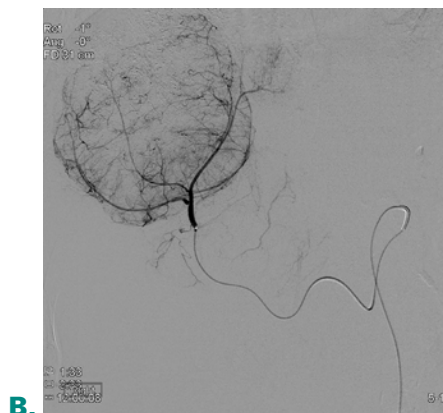
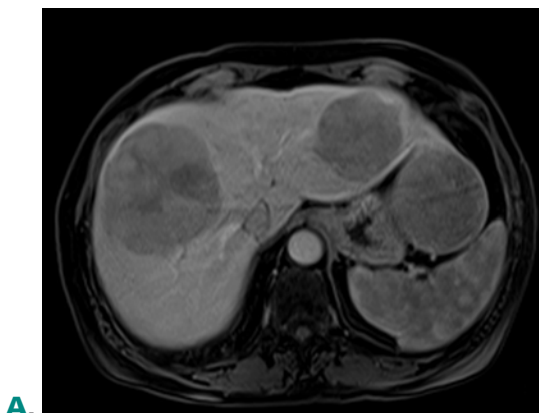
**N**euroendocrine tumors (NETs) are a heterogeneous family of tumors with a complex spectrum of clinical behavior. They may grow slowly or more rapidly without symptoms, or they may cause hormone hypersecretion associated with characteristic symptoms (flushing, wheezing, cramping, or diarrhea – known as carcinoid syndrome). Recent epidemiologic data have revealed that their incidence has increased substantially in the past 30 years, with no significant change in survival.<sup>1,2</sup> NETs arising within the abdomen are classically divided into endocrine pancreatic tumors and carcinoid tumors depending on whether they originate in the pancreas or intestinal tract, with the term carcinoid historically implying a more indolent nature although modern classification systems more clearly define lesion aggressiveness.<sup>3</sup>

Pancreatic NETs represent approximately one third of gastroenteropancreatic NETs, of which 50% are functional and classified by the predominant hormone secreted (insulin, gastrin, glucagon, or vasoactive intestinal peptide). In 2010, the World Health Organization developed a clinically relevant staging system based on tumor grade and Ki-67 proliferation index to discern well-differentiated from poorly differentiated tumors.<sup>3</sup> These tumor characteristics are now used to guide multimodality, multidisciplinary treatment strategies. Aggressive primary tumor resection and macroscopically complete (R0/R1) resection of liver metastases are considered curative, offering the best chance for overall survival (60-80% at 5 years).<sup>4</sup> Unfortunately, a large proportion of patients present with advanced disease and are prone to recurrence (frequently within the liver), such that other treatment approaches are necessary.<sup>5</sup>

Cytotoxic chemotherapy has a limited role for NET with disease control lasting only 8-10 months for conventional agents, although response rates are dependent on the primary tumor site and histologic grade.<sup>6</sup> Several targeted molecular and hormonal therapies are available, most notably octreotide (a somatostatin analogue commonly given as a monthly injection), as well as newer agents including everolimus (an mTOR inhibitor) and sunitinib (a tyrosine kinase receptor inhibitor), which have been shown to control disease progression in phase III clinical trials.<sup>7-9</sup>

In addition to systemic therapies, several other novel approaches are utilized to treat liver-predominant, nonresectable NET. Known collectively as liver-directed therapies, these can be broadly divided into two general categories: percutaneous ablation and intra-arterial therapy (IAT).

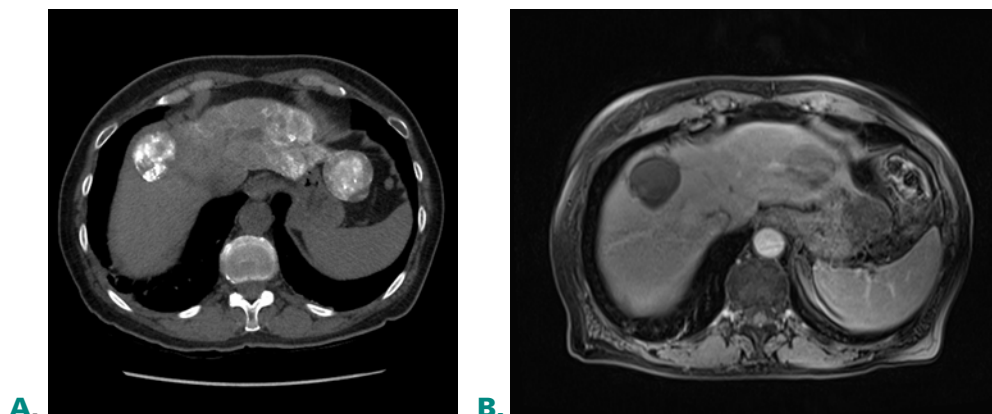
Percutaneous ablation offers a minimally invasive means of disease control and is commonly performed using radiofrequency or microwave probes. This approach is best suited to those patients with a limited number of hepatic lesions which are not amenable to surgical resection and/or intraoperative ablation.



**FIGURE 1:** A woman with crampy abdominal pain found to have metastatic neuroendocrine tumor with bulky liver metastases (A). The patient was referred for liver-directed therapy. Marked tumor hypervascularity is evident on subselective hepatic angiography (B).

# the Role for Liver-Directed Therapies in

**FIGURE 2:** After multiple conventional TACE procedures, dense Lipiodol retention is seen within liver metastases on noncontrast CT, which have significantly decreased in size (A). No appreciable contrast enhancement is seen on T1-weighted postcontrast MRI, indicating a favorable response to therapy (B). The patient ultimately underwent hepatic resection and was found to have 95% tumor necrosis on final pathology, with negative surgical margins.



Conversely, IAT is preferred for patients with higher volume hepatic disease, encompassing several modalities including: transarterial bland embolization (TAE), chemoembolization (TACE), and yttrium-90 radioembolization (Y-90). Owing to the dual blood supply of the liver, IAT is intuitively attractive because neuroendocrine liver metastases (NELMs) derive a disproportionately greater amount of blood supply from the hepatic artery compared to the portal vein, offering an effective means of concentrating embolic, chemoembolic, or radioembolic material within hypervascular tumor (Figures 1 and 2). IAT is particularly effective in achieving excellent rates of symptom control in patients with unresectable disease,<sup>10</sup> and in select situations may be more appropriate than surgical resection, with similar outcomes observed in asymptomatic patients with high disease burden (>25% hepatic tumor involvement). The optimal timing of IAT for asymptomatic patients, however, remains controversial.<sup>11</sup>

For patients with pancreatic NETs presenting with liver metastases, timing of therapy is particularly important as a colonized biliary tree (either from a biliary-enteric anastomosis or presence of a biliary stent) carries an attendant risk of hepatic abscess when ablative or intraarterial therapies are performed. In such cases, a staged algorithm beginning with liver-directed therapy (such as Y-90 or TACE) followed by primary tumor resection, or combined resection of the primary tumor and hepatic metastases should be considered.<sup>12</sup> Factors such as these emphasize the need for multidisciplinary care of patients with NETs, as tumor biology varies widely and multiple treatment modalities may be employed. Frequently these approaches are combined to optimize quality of life and oncologic outcomes for patients with neuroendocrine cancer. •

**FOR ADDITIONAL INFORMATION,** please visit [mcw.edu/surgery](http://mcw.edu/surgery), or contact Dr. Rilling at [wrilling@mcw.edu](mailto:wrilling@mcw.edu), 414-805-3125 or Dr. Christians at [kchristi@mcw.edu](mailto:kchristi@mcw.edu), 414-805-9720.

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# Personalized Therapy for Biliary Tract Cancers: of Molecular Profiling to Identify New Treatments



**T. CLARK GAMBLIN, MD, MS**  
Division of Surgical Oncology



**JOHN MIURA, MD**  
General Surgery Resident



**MARY POTKONJAK**  
Second-year medical student

**I**ntrahepatic cholangiocarcinoma (ICC) and gallbladder adenocarcinoma (GC) are frequently considered a similar disease in treatment planning. Although rare, incidence of ICC has been increasing in the United States, and GC is the most common malignancy of the biliary tract. An R0 surgical resection is the only potentially curative treatment for both diseases; however, few patients present early enough to be considered surgical candidates. For many patients diagnosed with ICC and GC, chemotherapy is the only treatment option.

According to the National Comprehensive Cancer Network (NCCN), first line regimens for both ICC and GC are interchangeable and consist of fluoropyrimidine-based, gemcitabine-based, or gemcitabine/cisplatin combination therapy for advanced or unresectable disease.<sup>1</sup> The use of gemcitabine/cisplatin therapy is the only treatment option backed by category 1 evidence, based on a phase III clinical trial, which demonstrated that gemcitabine/cisplatin increased median progression-free survival from five months to eight months for advanced biliary tract cancers, compared to gemcitabine alone.<sup>2</sup> However, suboptimal response rates, evidenced by a median survival of less than a year, underscore the need for more effective treatment regimens.

While research into the molecular pathogenesis of both ICC and GC has revealed potential mechanisms contributing to tumorigenesis such

as EGFR activation in the setting of chronic inflammation; KRAS and IDH1 mutations in the development of ICC; and mutations in KRAS, p53, increased COX2, and decreased adhesion molecules in the development of GC; much is unknown about the molecular profiles of these two diseases.

Chemotherapeutic agents, however, have been extensively studied. Molecular characteristics of tumors have provided insight into the most effective therapeutic interventions and have identified potential resistance to standard therapy. Clinical susceptibility to fluoropyrimidines is associated with low expression of thymidylate synthase (TS), susceptibility to gemcitabine is associated with low expression levels of ribonucleotide reductase subunit M1 (RRM1), and susceptibility to platinum agents, such as cisplatin, are associated with low expression of excision repair cross complementation group 1 (ERCC1); conferring potential theranostic value to the expression levels of these biomarkers.

Biomarker analysis of actionable targets known to convey susceptibility to specific drugs has been purported to be an effective method of tailoring existing chemotherapeutic agents to exploit the specific weaknesses in individual tumors. This showed promising results in a prospective study.<sup>3</sup>

This study sought to differentiate the molecular profiles of ICC and GC by a panel of biomarkers to evaluate the potential efficacy of current chemotherapy regimens and to potentially refine current treatment strategies. 245 surgical specimens—217 ICC and 28 GC patients—were referred to Caris Life Sciences, a commercial referral diagnostic laboratory, where they underwent specific testing by immunohistochemistry for 17 different biomarkers. The frequency that the expression of each biomarker was found to be actionable across the entire cohort and by subgroup was analyzed.

Consistent with NCCN recommendations, the three biomarkers most frequently actionable across the entire cohort were TS (96%), RRM1 (82%), and ERCC1 (74%), inferred susceptibility to fluoropyrimidines, gemcitabine, and platinum agents, and supported their use as first line agents. Furthermore, the high frequency that ERCC1 was actionable provides further support for the efficacy of gemcitabine/oxaliplatin demonstrated by several phase II clinical trials. Non-NCCN compendium drugs found to be actionable at a high frequency in the entire cohort include MGMT (50%) and SPARC monoclonal (34%) which have been associated with susceptibility to temozolomide and nab-paclitaxel and suggest alternative treatments that should be further explored in a clinical setting.

Comparative analysis by tumor type found a differential expression pattern in 6 of the 17 biomarkers analyzed. TS (99% vs. 72%;  $p < 0.01$ )

# The Emerging Role of Targeted Therapy Options

as well as RRM1 (85% vs. 64%;  $p=0.021$ ) were significantly decreased in GC as compared to ICC suggesting that there is a large subgroup of patients who may not respond to the recommended first line therapies. In contrast, the most frequently actionable target for GC was TOPO1 (76%), which is associated with a susceptibility to irinotecan. This would suggest that its use in the treatment of GC could prove beneficial and provides further support for the phase II clinical trials looking into its use in various combinations. The differences in the molecular profiles of ICC and GC suggest that response rates to first line agents can be variable and support a more targeted therapeutic approach to these diseases.

In conclusion, ICC and GC continue to carry a poor prognosis, thereby highlighting the need for more effective treatment regimens. The use of molecular profiling to guide treatment has shown promising results in other tumor types and warrants further investigation. While our analysis supports the use of fluoropyrimidines, gemcitabine, and cisplatin as first line agents to treat ICC and GC, we also identified agents, such as irinotecan, that could be beneficial in subsets of patients unresponsive to first line drugs. The molecular characteristics described, in addition to the differential expression pattern found between ICC and GC, provides compelling evidence that future investigations should approach these diseases independently. •

**FOR ADDITIONAL INFORMATION** on this topic, see references below, visit [mcw.edu/surgery](http://mcw.edu/surgery), or contact Dr. Gambelin at 414-805-5020, [tcgambelin@mcw.edu](mailto:tcgambelin@mcw.edu).

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## Dr. Webb to Lead Curriculum at MCW



**Travis Webb, MD, MHPE,** Associate Professor of Surgery (Trauma and Critical Care), has been appointed the Associate Dean for Curriculum at MCW.

Dr. Webb will be responsible for administrative oversight of the medical school curriculum and provide leadership for curriculum development and implementation, monitoring curriculum quality, and advancing the curriculum to meet student educational needs. Dr. Webb replaces Dr. Redlich who served in this position since 2003.



# Center for Advanced Care – New Home for Many Department of Surgery Programs



**GARY SEABROOK, MD**  
Division of Vascular Surgery

In October 2015, Froedtert Hospital will open the **Center for Advanced Care**, which is now in the final phases of construction on the south border of the medical center campus on Doyme Avenue. A two-story skywalk will connect the new building with the adjacent Cancer Center. This 12-story facility, which includes three levels of underground parking for patients receiving care in the center, will be the new home of the General Surgery outpatient clinics, Heart & Vascular Center, Transplant Center, and the front door to a new integrated surgical and intervention platform for surgery, interventional radiology and cardiac catheterization services.

The General Surgery Outpatient Clinic on Level 2 will be the new home for clinic services for the Division of Minimally Invasive and GI Surgery, benign Colorectal Surgery, and Trauma Surgery. The Transplant Center, also on Level 2, will provide a single site of care for the Solid Organ Transplant program and provide facilities for pre-transplant assessment, consolidation of support for transplant coordinators and organ procurement, and outpatient clinic space for post-operative care.

Level 3 of the Center for Advanced Care will become the new front door for all patients scheduled for surgery, interventional radiology procedures, or cardiac catheterization and electrophysiology interventions. Patients will arrive at a single registration desk and be admitted for procedural preparation in this unit.

For patients scheduled for outpatient procedures, anesthetic recovery and discharge will also occur from this unit, providing continuity of nursing care through the continuum of the patient experience. An outpatient pharmacy on this platform will allow patients to be discharged with new prescriptions. A large family waiting area with floor-to-ceiling windows spans the entire south exposure of the building, providing views of the ponds and natural habitat extending to Wisconsin Avenue. The Pre-procedural Evaluation Center, previously called pre-admission testing (PAT), will also be moved to Level 3 – providing perioperative risk assessment, pre-operative anesthesiology planning and coordination of patient education in preparation for procedures. Patients visiting the Pre-procedural

Evaluation Center will have the opportunity to become familiar with the logistics of traffic and parking, navigating the building, and locating the check-in area, thereby reducing anxiety associated with arrival of the day of their procedure.

The Heart & Vascular Center will occupy the entire geography of Level 4. Outpatient clinics for Cardiovascular Medicine, Cardiothoracic Surgery, Vascular Surgery, Interventional Radiology, Vascular Medicine, and the Wound Care Program will be organized in coordinated clinical pods. Services for echocardiography, electrophysiology monitoring and device interrogation, and non-invasive vascular testing facilities will be located adjacent to clinic space.

As outpatient clinics relocate to the Center for Advanced Care, all current clinic space on Level 3 in the West Clinics Building and the Specialty Clinics Building will be vacated and reconstructed as operating rooms and interventional treatment suites. Working in phases, the original Froedtert operating room space will be replaced with larger specialty equipped rooms. This platform will provide a geographic concentration for all Froedtert ORs (currently split between two buildings) and complex imaging for vascular, cardiac, oncologic, neurological, and musculoskeletal diseases, addressing the current and future demand for efficient, integrated care. The platform will encourage cross-specialty fertilization and innovative techniques to deliver state-of-the-art care. Design teams are now planning innovations for the remodeled space including operating rooms for laparoscopic and video-assisted minimally invasive surgery, robotic surgery, procedures performed with computer-guided imaging, and emerging technology in surgical and interventional therapy. •



# Jonathan B. Towne, MD, Visiting Professor Lectureship

by Meg M. Bilicki, Director of Development for the Department of Surgery

Endowments are established to live in perpetuity. Endowed lectureships are part of the robust academic culture in the Department of Surgery at the Medical College of Wisconsin, and we greatly cherish the appearances by nationally regarded clinicians and scientists. The lectureships are supported by resident and medical school alumni, faculty and staff, as well as generous members of the community.

Jonathan B. Towne, MD, Professor and Chief Emeritus for the Division of Vascular Surgery retired June 30, 2007, after 30 years at MCW. Dr. Towne helped develop a multidisciplinary model of care for vascular disease at MCW, Froedtert Hospital, and the Zablocki VA Medical Center. This model required a high level of cooperation between Vascular Surgery and Interventional Radiology through commitment, education and collaboration that forever changed the treatment of vascular disease at these institutions. Dr. Towne dedicated his career to inspiring and educating students and physicians whose interests lie in healing through education and collaboration.

To perpetually commemorate his dedicated years of surgical, academic and professional leadership, the **Jonathan B. Towne, MD, Visiting Professor Lectureship endowed fund** was established to provide an annual award paying tribute to the life and career of Dr. Towne, one of the most respected surgeons at MCW. The fund presents a meaningful vehicle to carry on his legacy, while also impacting future generations of physicians. The ultimate beneficiaries are patients and their families, who would benefit from improved treatments for injury and disease.

Proceeds from this fund generate support of the annual lecture by a distinguished surgeon in the field of vascular surgery. It also provides our alumni with a forum for an annual collegial reunion, in the setting of a lecture of clinical significance to them as well as our residents and medical students. Visiting professors are provided with an honorarium and travel expenses, and sometimes feted with a reception or dinner with colleagues.



Jonathan B. Towne, MD

Establishing a steady revenue stream to support the costs associated with these activities is an important goal of the Department of Surgery as it seeks to build a vibrant and intellectually challenging residency program. It also benefits resident and physician education, and helps MCW recruit talented candidates for the program in the future.

Please consider joining your fellow alumni and current department faculty in making a contribution to support the Jonathan B. Towne, MD, Visiting Professor Lectureship endowed fund. For more information, please contact Meg Bilicki at [mbilicki@mcw.edu](mailto:mbilicki@mcw.edu) or (414) 805-5731. •

**To refer a patient or request a transfer/consultation, please use the references below:**

## **Froedtert & the Medical College of Wisconsin**

### **All non-cancer requests**

Referrals: 800-272-3666

Transfers/Consultations:

877-804-4700

[mcw.edu/surgery](http://mcw.edu/surgery)

### **Clinical Cancer Center**

Referrals: 866-680-0505

Transfers/Consultations:

877-804-4700

## **Children's Hospital of Wisconsin**

Referrals/Transfers/

Consultations: 800-266-0366

Acute Care Surgery:

414-266-7858

## HISTORY CORNER

# The Connell Stitch: A Two-Generation

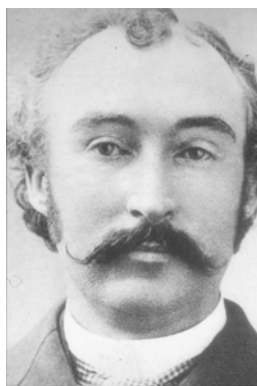
By T. Clark Gamblin, MD, MS, Department of Surgery; and Rachel Lundberg, MPAS, PA-C, Department of Medicine, Division of Hematology-Oncology

Amidst the flashing lights of ambulances, the throngs of construction vehicles and steady rotation of “closed road” signs, Connell Avenue cuts through the heart of the Milwaukee Regional Medical Complex. This small, unassuming street hints at the hospital’s history, reflecting upon the family of physicians whose legacy continues to influence surgery.

As one of the first superintendents of the Milwaukee County Hospital in 1887, Dr. ME Connell worked to meet the needs of a rapidly growing city, while encouraging physicians to utilize the facilities for scientific research.<sup>1</sup> He collaborated with Dr. Nicholas Senn, Wisconsin’s most famous surgeon, whose animal research investigating the integrity of gastrointestinal anastomoses revolutionized enteric surgical procedures.<sup>2</sup> Anna Connell, ME’s wife, was among the first women in Wisconsin to hold an MD. She established Wisconsin’s first nursing school on the Milwaukee hospital’s grounds.<sup>3</sup>

Their son, F. Gregory Connell, grew up in this medical environment and was highly influenced by Dr. Senn and the scientists visiting his research laboratories. As a child, Greg would collect autographs of these physicians, and spent his free time observing and even working in Senn’s lab. He graduated from Wauwatosa High School in 1892, after which he studied at UW-Madison, followed by Rush Medical College. While training in Chicago, he prepared anatomic dissections for medical students studying in Dr. Christian Fenger’s lab. Dr. Fenger’s partner at this time was Dr. Clarence Hemmingway, the father of the famous American writer Ernest Hemmingway. Dr. Connell maintained a life-long correspondence with the writer, who was said to have valued Dr. Connell’s literary critique of his work.<sup>4</sup>

Dr. F. Greg Connell remained in Chicago on the faculty of the University of Illinois Medical School and as an attending at Cook County Hospital until he fell ill with what was thought to be tuberculosis. He relocated, hoping that the mountain air of Colorado would ease his respiratory illness. His relentless work ethic made rest elusive. He served as a railroad physician and published over 20 papers in the next five years. During this time he met and married Isabella Stickney, an artist from Milwaukee, who illustrated his medical articles.



ME Connell, MD



Anna Gregory Connell, MD

In 1907, Dr. F. Greg Connell returned to Milwaukee to work in a one-year association with another student of Dr. Senn’s, Dr. Charles W. Oviatt. He was hesitant to partner in a group, saying “Get engaged, but never married,” referring to his medical practice. During this time, Dr. Connell improved upon a technique that his father had pioneered years before, the “Connell Stitch,” a continuous right-angle stitch penetrating all layers of the bowel wall with knots buried within, but not completely perforating the mucosa.<sup>5</sup> Dr. Connell altered the stitch slightly from his father’s original design, inverting the knot to nullify the seton action. At a time when surgeons were known by their signature suture techniques, the Connell Stitch and their successes in bowel closures put the Milwaukee native on the map, making his name recognizable to surgeons around the world and to those in training for years to come.

Throughout his career, Dr. F. Greg Connell maintained an academic interest with a wide breadth of academic pursuits, publishing in topics ranging from peptic ulcer disease and the acute abdomen to protozoan infections and neuro-psychiatry. When he became the first acting president of the Wisconsin Surgical Society in 1923, one of his presidential goals was to advocate for this type of broad scholarship. In his induction speech, he said the role of the society should be to “emphasize the distinction between a surgeon and an operator, to prevent surgery from degenerating into merely a technical service.”<sup>6</sup>



# Contribution to GI Surgery



Dr. F. Gregory Connell (1875-1968)

Dr. F. Greg Connell guided the Wisconsin Surgical Society to become an organization that honored medical research and encouraged in-depth critical evaluation in all of Wisconsin's surgeons. When challenged on the overwhelmingly "medical" nature of some of the Wisconsin Surgical Society conferences, Dr. Connell responded, "No one can be a good physician who has no knowledge of operative surgery. Likewise, a surgeon is nothing if he is ignorant of medicine. Knowledge of both branches is essential... One must always remember, until the surgeon can make the diagnosis, he must, of necessity, be an internist."<sup>7</sup>

Both ME and Greg Connell's passion for medical advancement and education helped to transform a small county hospital into a nationally respected academic medical center. Both physicians nurtured medical curiosity in their colleagues and students

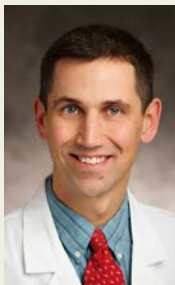
while infusing their respective organizations with a deep respect for scientific progress. Their legacy is honored not only in the name of that street cutting through the heart of the medical complex, but through the research, medical advancement, and collaboration between Wisconsin's physicians. •

*The authors thank Stuart Wilson, MD, for providing materials on the Connells and the literature review. Photos courtesy of the Ellison Library Archives.*

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## AWARDS and APPOINTMENTS



Brian Lewis, MD



Amy Leisten, MS



Hani Hasan, MD



Philip Redlich, MD PhD



Ryan Groeschl, MD

At the 2015 Annual Association for Surgical Education meeting, the Department of Surgery was well represented for educational excellence. **Brian Lewis, MD**, Associate Professor of Surgery (Vascular Surgery) was awarded the Philip J. Wolfson Outstanding Teacher Award in recognition of teaching excellence and educational contributions for student teaching. **Amy Leisten, MS**, Medical Education Coordinator II, was awarded the first annual Surgery Clerkship Recognition Award for her excellence in support and coordination of third- and fourth-year student surgery rotations. **Hani Hasan, MD**, General Surgery Resident, received a Surgical Education Research Fellowship certificate for completing all of the requirements of the program including an educational scholarly project.

At MCW, **Philip Redlich, MD, PhD**, *Gerald L. Schmitz MD Professor of Surgery*, was one of four winners of the 2015 T. Michael Bolger Standing Ovation Award presented by the Student Assembly. In addition, **Andrew Kastenmeier, MD**, (General Surgery) was one of the nominees. This award recognizes individuals who enhance the quality of campus life for students by providing exemplary educational, social or organizational improvements.

During commencement activities, **Brian Lewis, MD**, was selected by the senior class for the 2015 Ernest O. Henschel Clinical Teaching Award in recognition of clinical teaching excellence. **Kelli K. Pettit, MD**, Assistant Clinical Professor of Surgery – General and site director for the surgery clerkship at Waukesha Memorial Hospital, received the Milwaukee Academy of Medicine Award for Excellence in Teaching which is presented to a community physician for exemplary teaching and role modeling for students. **Ryan Groeschl, MD**, General Surgery Chief Resident, received the MCWAH Housestaff Award for Excellence in Teaching, which is presented to a resident who has made outstanding contributions to medical student education.

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Kathleen Simon, MD  
Abby Wochinski, MD

\* Also participates in Community Surgery/Off-campus locations.

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## MARK YOUR CALENDARS

### Upcoming Events

**June 12: Michael Sarr, MD – 55th Annual Carl W. Eberbach Visiting Professor**

**June 19-20: MCW & University of Texas M. D. Anderson Cancer Center Endocrine Surgery Symposium—Harley-Davidson Museum®**

**August 28: Multidisciplinary Approach to Complex Abdominal Wall Reconstruction and Inguinal Hernia Symposium—Medical College of Wisconsin**

**September 18: 2015 Fall Pancreatic Cancer Symposium—Milwaukee Yacht Club**

**September 25: Management of Esophageal Carcinoma Symposium**  
—Medical College of Wisconsin

**September 30: Pierre Alain Clavien, MD – 29th Annual C. Morrison Schroeder Visiting Professor**

**October 10: Get Your Rear in Gear, Run/Walk for Colon Cancer Prevention**  
—Hart Park, Wauwatosa

**October 22: Vascular Access Symposium—Medical College of Wisconsin**

*Please contact Heidi Brittnacher (hbrittna@mcw.edu) for more information on any of these events.*

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