

# Research Publication Series

October 2019



knowledge changing life



## About the Research Publication Series:

The Medical College of Wisconsin is a major national research center and the second-largest research institution in Wisconsin. Basic science, clinical, and translational researchers thrive in the unique setting of an academic medical center. The innovative work of our scientists leads to groundbreaking discovery that impacts healthcare and saves lives. The Research Publication Series is a sampling of recent publications by faculty, staff, and student investigators.



MCW Collaborative Highlights, indicated with the puzzle piece icon, call out articles that are produced by multidisciplinary teams. These articles represent collaborative efforts between researchers from different departments, centers, divisions, or fields of study.



knowledge changing life

## Research Publication Series:

# October 2019

---

### Christina L. Wichman, DO

“Co-located perinatal psychiatry clinic: impact of adding a psychologist on clinical quality improvement metrics”

---

### Andreas M. Beyer, PhD, FAHA

“Detrimental effects of chemotherapy on human coronary microvascular function” 

---

### Meena Bedi, MD

“Does Vacuum-assisted Closure Reduce the Risk of Wound Complications in Patients With Lower Extremity Sarcomas Treated With Preoperative Radiation?” 

---

### Sadie E. Larsen, MA, PhD

“A pilot randomized trial of a dual n-back emotional working memory training program for veterans with elevated PTSD symptoms”

---

### Rachel K. Harrison, MD

“Peripartum infectious morbidity in women with preeclampsia” 

---

### James J. Miller, PhD

“Rats deficient in alpha-galactosidase A develop ocular manifestations of Fabry disease” 

---

### Nathan J. Smith, MD

“Minimally invasive single-vessel left internal mammary to left anterior descending artery bypass grafting improves outcomes over conventional sternotomy: A single-institution retrospective cohort study”

---

### Saman Shabani, BS, MD

“AOSpine Global Survey: International Trends in Utilization of Magnetic Resonance Imaging/Computed Tomography for Spinal Trauma and Spinal Cord Injury across AO Regions” 

---

### Katherine Flynn-O'Brien, MD, MPH

“Health outcomes and the healthcare and societal cost of optimizing pediatric surgical care in the United States”

---

### Meinuo (Mei) Chen, BS

“Sequential compression device compliance in pregnant women requiring antepartum admission”

---

### Andrew Montoure, MD

“Great Hospitals in North America: The Medical College of Wisconsin Neurological Surgery”

---

### Rachel Schlaak, BS

“Mapping genetic modifiers of radiation-induced cardiotoxicity to rat chromosome 3” 

---

All rights reserved. Contents are the property of the authors and/or journals cited.

Cover Image from “Great Hospitals in North America: The Medical College of Wisconsin Neurological Surgery”



## Christina L. Wichman, DO

Professor

Department of Psychiatry

Department of Obstetrics & Gynecology

Medical Director, The Periscope Project

Director, Women's Mental Health

Program Director, Consultation-Liaison

Psychiatry Fellowship

I am a Professor of Psychiatry and Obstetrics and Gynecology at MCW. I completed my residency in Adult Psychiatry and a fellowship in Psychosomatic Medicine at Mayo Clinic. Clinically, I created and direct a co-located perinatal psychiatric service, embedded within the Department of Obstetrics and Gynecology, and I am the Director of Women's Mental Health at MCW. I am the Medical Director of The Periscope Project, a provider to perinatal psychiatrist teleconsultation service. I am also fellowship director for the Consultation-Liaison Psychiatry Fellowship. My research pursuits have been within the realm of women's mental health, and I have published and lectured extensively regionally and nationally.

## “Co-located perinatal psychiatry clinic: impact of adding a psychologist on clinical quality improvement metrics”

Pawar D, Huang CC, Wichman C. *Journal of Psychosomatic Obstetrics and Gynaecology*. 2019;40(2):123-127.

Perinatal mental disorders are common and can affect the well-being of mother and baby. Integration of obstetric and mental health care can promote early detection and treatment and improve quality of care. The purpose of our study was to describe the impact of adding a psychologist (intervention) to a colocated perinatal psychiatry clinic (PPC) in terms of effects on clinical quality improvement (QI) metrics. Compared to pre-intervention, post-intervention the psychiatrist saw a greater number of unique patients, mean wait time to new visits with a physician decreased, and no-show rates for established visits decreased. By adding a psychologist to the PPC, we improved quality of perinatal mental health care by improving efficiency, timeliness, and patient-centered care. A psychologist could be a valuable addition to a PPC.

**Table I: Number of unique patients seen by provider, pre- and post-intervention**

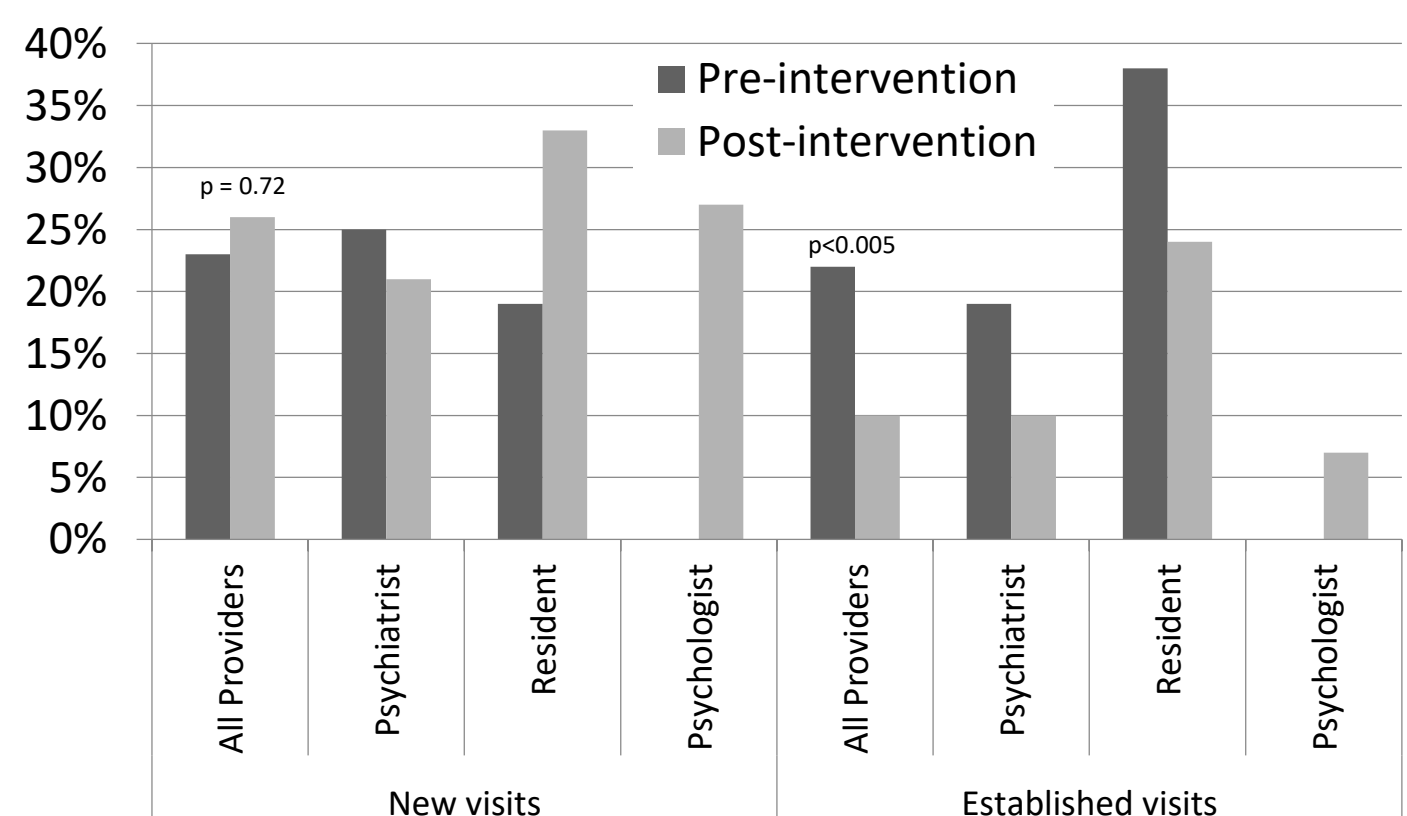
Provider	Pre-intervention	Post-intervention
Psychiatrist*	90	118
Resident	22	23
Psychologist	-	99
All providers	110 <sup>a</sup>	193 <sup>b</sup>

\*p=0.06

a Two patients were seen by both psychiatrist and resident

b One patient was seen by both psychiatrist and resident; one patient was seen by all providers, and 44 patients were seen by a physician (psychiatrist or resident) and psychologist

**Figure I: Percentage no-shows for new and established visits, by provider, pre- and post-intervention**





## Andreas M. Beyer, PhD, FAHA

Associate Professor of Medicine and Physiology  
Cardiovascular Research Center

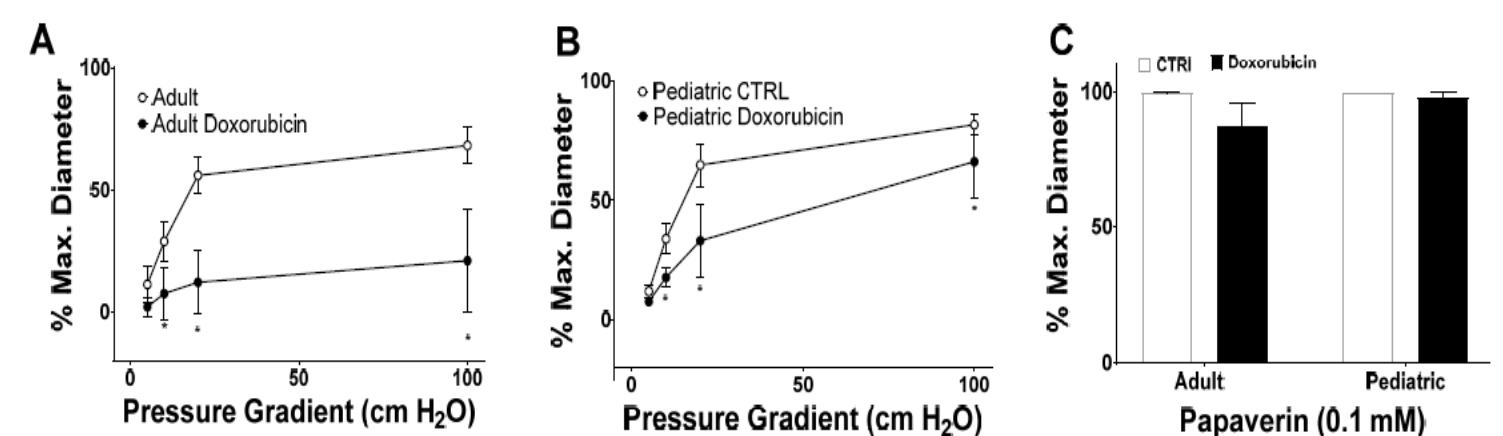
I am an Associate Professor of Medicine and Physiology with training in genetics, and a passion for physiology. My lab uses human tissue samples and rodent models in a reverse translation fashion to ascertain the underlying mechanism of microvascular function in health and disease. More specifically we study the role of endothelial cell function and its contributions to development of chronic cardiovascular maladies. Due to its established predictive value for development of future cardiovascular disease we have begun for the first time to define the negative impact of systemic anti-cancer therapy on the circulatory system. Understanding the underlying mechanisms by which anti-cancer therapy damages the microcirculation is a key component to understanding and developing ways to prevent adverse side effects of cardiovascular nature.

## “Detrimental effects of chemotherapy on human coronary microvascular function”

Hader SN, Zinkevich N, Norwood Toro LE, et al. *American Journal of Physiology. Heart and Circulatory Physiology*. 2019;317(4):H705-H710.

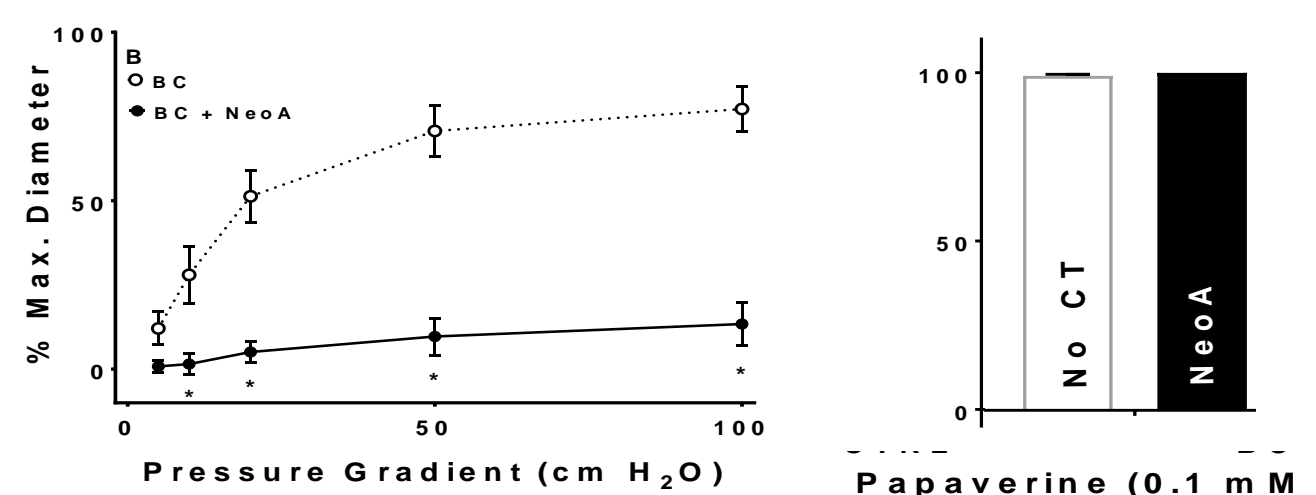
With improvements in anti-cancer therapy (CT), cardiovascular-toxicity has become a significant clinical problem leading to cessation of life-saving therapy. Despite extensive evidence that CT induces cardiac damage, little is known on the effect of CT on the vascular endothelium, particularly in the microcirculation, which is highly predictive for cardiovascular events. Our study, for the first time, evaluated the impact of doxorubicin (Dox) on human coronary microvascular function. In arterioles from adults, treatment with Dox significantly decreased endothelial function, whereas vessels from pediatric subjects showed only marginal impairment. Similarly, microvascular function from breast cancer patients (BC) with previous exposure to anti-cancer therapy impaired microvascular endothelial function while smooth-muscle function was not impacted. This finding might explain delayed onset of future CV events in children versus adults after CT.

**Figure 1. Doxorubicin impairs microvascular endothelial dilator function.**



Endothelial dependent flow-mediated (FMD) dilation was compared in isolated atrial microvessels from adults age >18 yr (left) with and without coronary artery disease and children age 0–18 yr (center). Endothelium-independent smooth muscle-mediated dilation to papaverine (right). \*P < 0.05 two-way ANOVA repeated-measures Tukey’s post hoc analysis, N = 4–12 Adapted from PMID: 31397169

**Figure 2. Neoadjuvant Anti-Cancer Therapy Induce Endothelial Dysfunction in Human Microvessels.**



Left) Endothelial function of adipose arterioles was significantly decreased in breast cancer (BC) patients with anti-cancer therapy about one month after cessation of therapy vs. BC patients without previous treatment. Right) Smooth muscle dependent dilation to papaverine was not impaired. \*P<0.05 vs. CTRL/BC. N= 3-6. Unpublished Beyer lab



## Meena Bedi, MD

Associate Professor of Radiation Oncology, Surgery, Orthopaedic Surgery, and the Graduate School of Biomedical Sciences  
Sarcoma Program Leader  
Sharon K. Wadina Endowed Chair in Sarcoma Research

I joined the MCW faculty in 2013 and am an Associate Professor in the Departments of Radiation Oncology, Surgery, Orthopaedic Surgery and Graduate School of Biomedical Sciences. My interest in sarcoma was ignited early on in residency training, as I was exposed to the high-level of multidisciplinary care provided to each patient by the musculoskeletal oncology team. Since this time, my research endeavors have been fostered by this strong collaboration and I am proud to now serve as the Sarcoma Program Leader.

## “Does Vacuum-assisted Closure Reduce the Risk of Wound Complications in Patients With Lower Extremity Sarcomas Treated With Preoperative Radiation?”

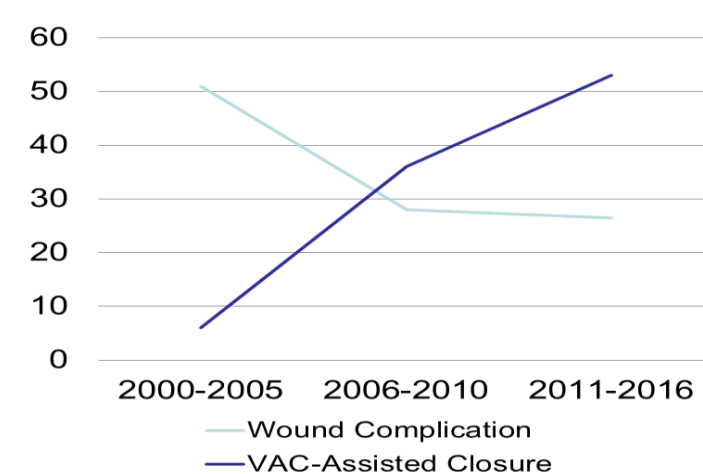
Bedi M, King DM, DeVries J, Hackbarth DA, Neilson JC. *Clinical Orthopaedics and Related Research*. 2019;477(4):768-774.

Soft tissue sarcomas (STS) are commonly treated with pre-operative radiation (RT) followed by wide local excision. There are many advantages of delivering radiation in a pre-operative manner, however, one disadvantage is the propensity for post-operative wound complications (WC). In this study we sought to assess the effect of vacuum-assisted closure (VAC) on the development of WC, local control and distant metastasis in proximal lower extremity STS. A retrospective review was performed on all patients with STS of the proximal lower extremity who underwent pre-operative RT. Both multivariate and univariate analyses revealed that the use of VAC-assisted closure in patients led to a decreased incidence of WC (Table 1) without compromise in local control or distant metastasis. In addition, an inverse relationship between the use of VAC-assisted closure and WC was revealed in this study (Fig 1). Although proximal lower extremity STS treated with pre-operative RT are at a high risk of post-operative WC, VAC-assisted closure may be associated with lower WC with uncompromised rates of local control and distant metastasis.

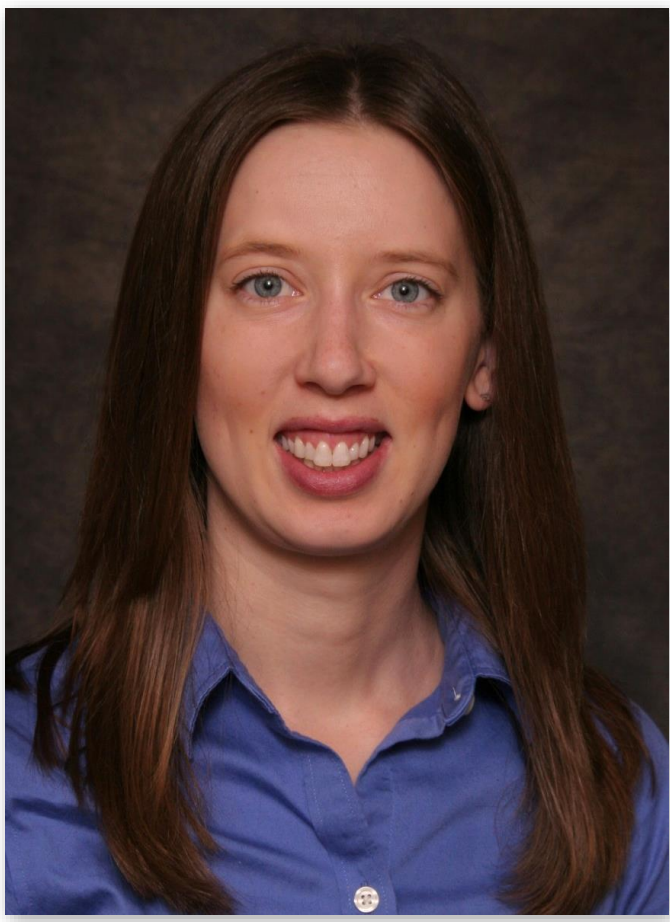
**Table 1. Incidence of Wound Complications**

Location	WC	P-value
<b>Proximal lower extremity STS</b>		
VAC	9%	<0.0001
No VAC	43.5%	
<b>Medial Compartment STS</b>		
VAC	8%	0.005
No VAC	45%	
<b>Proximal lower extremity STS</b>		
Incisional VAC	8%	<0.0001
No Incisional VAC	47%	
<b>Medial Compartment STS</b>		
Incisional VAC	9%	0.001
No Incisional VAC	46%	

**Figure 1. Proximal Lower Extremity STS**



Year	VAC-Assisted Closure	WC
2000-2005	6%	51%
2006-2010	36%	28%
2011-2016	53%	26.5%



## Sadie E. Larsen, MA, PhD

Associate Professor  
Department of Psychiatry

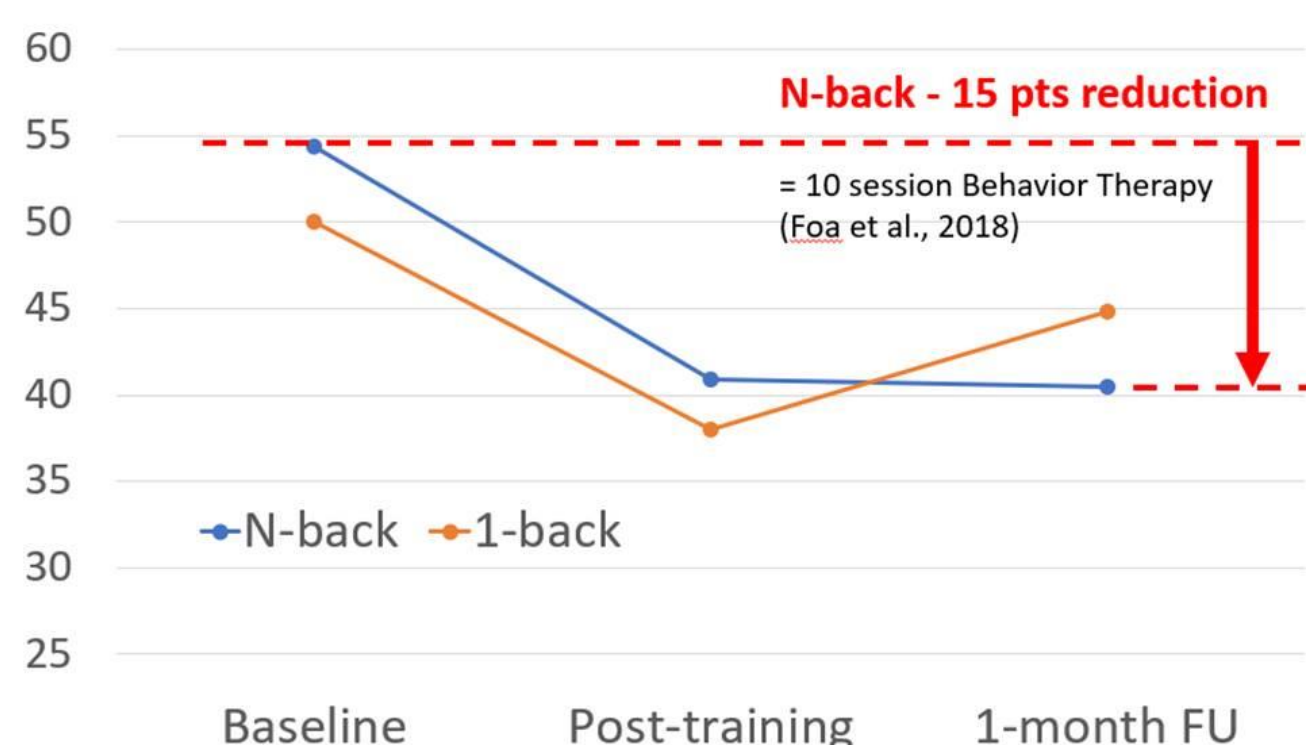
I am a psychologist who works at MCW and the Milwaukee VA. I conduct evidence-based psychotherapy with people recovering from trauma. Likewise, I conduct research on posttraumatic stress disorder, especially among veterans and survivors of violence. I examine what makes treatment helpful for those with PTSD, how the process of treatment works, and whether we can prevent the onset of PTSD.

## “A pilot randomized trial of a dual n-back emotional working memory training program for veterans with elevated PTSD symptoms”

Larsen SE, Lotfi S, Bennett KP, Larson CL, Dean-Bernhoft C, Lee HJ. *Psychiatry Research*. 2019;275:261-268.

Anxiety is characterized by high attention to threatening information, leading to impaired working memory (WM) performance. Individuals with PTSD show particular difficulty with WM in emotional contexts. In a pilot randomized trial, we assigned Veterans with elevated PTSD symptoms to an online emotional WM training, either adaptive (n-back; n=11) or a less potent training (1-back; n=10). Overall, both groups showed significant decreases in PTSD symptoms. The n-back group showed a trend of outperforming the 1-back group in improving reexperiencing symptoms. This population anecdotally found the intervention quite challenging, which may be why even the less potent 1-back was still helpful. These preliminary findings justify the effort for developing new WM-focused PTSD intervention for complex, vulnerable populations, particularly as online training can improve accessibility.

### PCL-5 Total Score Change



## “Peripartum infectious morbidity in women with preeclampsia”

Harrison RK, Egede LE, Palatnik A. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2019 Jun 19:1-6.

Background: Preeclampsia is a common complication of pregnancy that leads to significant maternal and neonatal morbidity. The goal of our study was to investigate the association between the diagnosis of preeclampsia and ensuing risks of maternal peripartum infectious morbidity related to delivery. We hypothesized that the heightened chronic inflammatory state of preeclampsia increases the risk for maternal peripartum infection. Results: 6.3% of women in our large US cohort were diagnosed with preeclampsia. Women of non-Hispanic black race, with diabetes, higher BMI, older age, and multiple pregnancies were affected at higher rates than their counterparts. We found that women with preeclampsia did not have an increased risk of peripartum infection and that they were actually at lower risk of chorioamnionitis than women without preeclampsia.

### Rachel K. Harrison, MD

Maternal-Fetal Medicine Fellow, PGY-7  
Department of Obstetrics & Gynecology



### James J. Miller, PhD

Medical Student, MSTP  
Department of Biochemistry

## “Rats deficient in alpha-galactosidase A develop ocular manifestations of Fabry disease”

Miller JJ, Aoki K, Reid CA, Tiemeyer M, Dahms NM, Kassem IS. *Scientific Reports*. 2019;9(1):9392.

Fabry disease is an X-linked lysosomal disease caused by  $\alpha$ -galactosidase A deficiency. Patients develop ocular findings, such as corneal hazing, cataracts, and retinal vascular tortuosity, which serve as important diagnostic markers. We evaluated ocular phenotypes in a Fabry disease rat model. We found that Fabry rats develop corneal and lenticular opacities to a statistically greater degree than WT rats. However, we observed no major differences in retinal vasculature morphology. Because Fabry rats recapitulate many ocular phenotypes observed in patients, they can be used to study disease pathogenesis and determine whether ocular findings serve as noninvasive indicators of therapeutic efficacy.



## “Minimally invasive single-vessel left internal mammary to left anterior descending artery bypass grafting improves outcomes over conventional sternotomy: A single-institution retrospective cohort study”

Smith NJ, Miles B, Cain MT, Joyce LD, Pearson P, Joyce DL. *Journal of Cardiac Surgery*. 2019;34(9):188-795.

Minimally invasive coronary artery bypass grafting (MICABG) is a less invasive alternative to the treatment single vessel coronary artery disease. Study of this technique has been limited to large volume centers and potential benefits or detriments are unclear. We evaluated our institutions experience with this technique through use of a national database and found patients were in the hospital for a shorter period of time, suffered fewer postoperative complications, and had a mortality benefit at long term follow up. These findings support the benefit of a minimally invasive approach to the surgical treatment of single vessel disease.

### **Nathan J. Smith, MD**

Resident Physician, General Surgery  
Department of Surgery



### **Saman Shabani, BS, MD**

Resident, PGY-6  
Department of Neurosurgery

## “AOSpine Global Survey: International Trends in Utilization of Magnetic Resonance Imaging/Computed Tomography for Spinal Trauma and Spinal Cord Injury across AO Regions”

Shabani S, Kaushal M, Soliman HM, et al. *Journal of Neurotrauma*. 2019 Jun 21  
<https://doi.org/10.1089/neu.2019.6464>.

The study was conducted to determine the current trends in MRI and CT utilization for spine trauma. A survey was conducted across six different continents. It was sent to 5813 surgeons and had a 9.6% response rate. The use of a particular imaging modality across different continents appeared to be influenced by the patient’s neurological status upon admission and the presence of neurological deficits post-surgery. Type of residency and fellowship training did not have an influence on choosing the appropriate imaging modality. It is unclear whether MRI accessibility would change surgeons' attitude in obtaining MRI in spine trauma.

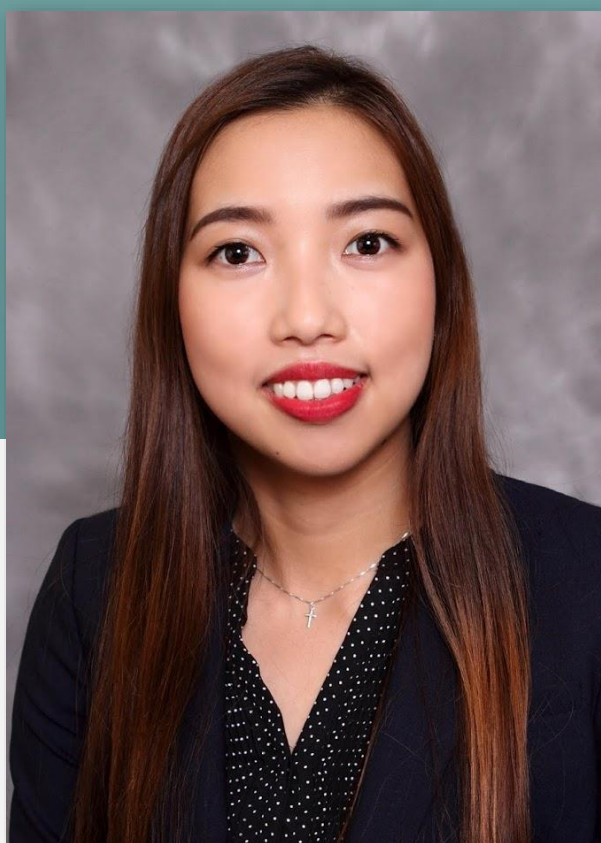
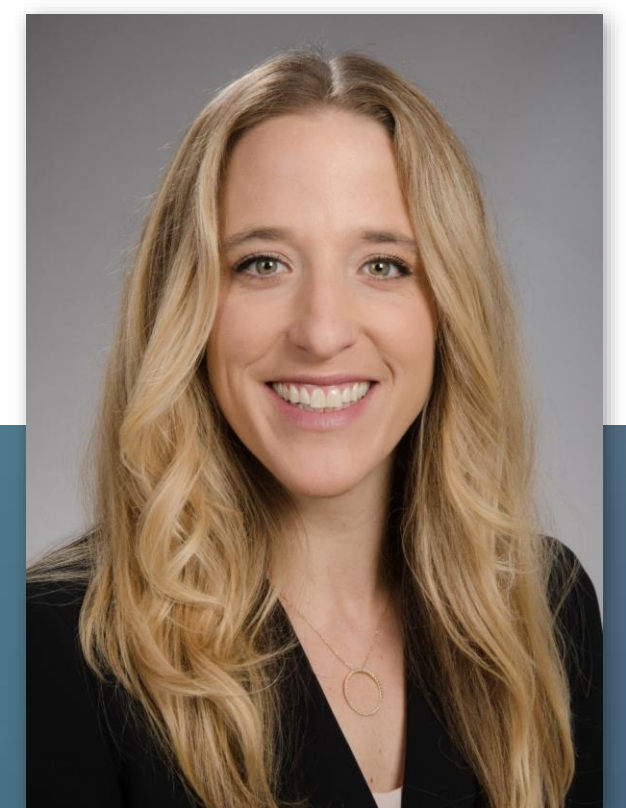
## “Health outcomes and the healthcare and societal cost of optimizing pediatric surgical care in the United States”

Flynn-O’Brien KT, Richards MK, Wright DR. *Journal of Pediatric Surgery*. 2019;54(5):621-627.

There is a movement to ensure that pediatric patients are treated in appropriately resourced hospitals through the ACS Children's Surgery Verification (CSV) program. The objective of this study was to assess the potential difference in care provision, health outcomes and healthcare and societal costs after implementation of the CSV program. In this study, all 2011 inpatient admissions for selected complex pediatric patients warranting treatment at a hospital with Level I resources were evaluated across 6 states. Multivariate regressions were used to analyze differences in healthcare outcomes (postoperative complications including death, length of stay, readmissions and ED visits within 30 days) and costs by CSV level. Recycled predictions were used to estimate differences between the base case scenario, where children actually received care, and the optimized scenario, where all children were theoretically treated at Level I centers. 8,006 children (mean age 3.06 years, SD 4.49) met inclusion criteria, with 45% treated at Level I hospitals, 30% at Level II and 25% at Level III. No statistically significant differences were observed in healthcare outcomes. Readmissions within 30 days were higher at Level II compared to Level I centers (adjusted IRR 1.61; 95% CI 1.11, 2.34), with an estimated 24 avoidable readmissions per 1000 children if treatment were shifted from Level II to Level I centers. Overall, costs per child were not significantly different between the base case and the optimized scenario. In conclusion, many complex surgical procedures are being performed at Level II/III centers. This study found no statistically significant increase in healthcare or societal costs if these were performed instead at Level I centers under the optimized scenario. Ongoing evaluation of efforts to match institutional resources with individual patient needs is needed to optimize children's surgical care in the United States.

### Katherine Flynn-O’Brien, MD, MPH

General Surgery Fellow  
Department of Pediatrics



### Meinuo (Mei) Chen, BS

4th year Medical Student  
Department of Obstetrics & Gynecology

## “Sequential compression device compliance in pregnant women requiring antepartum admission”

Chen M, Sarnoski KA, Jacques LH, Klatt T, Palatnik A. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2019 Jun 4:1-7.

Background: A quality improvement study done at the Medical College of Wisconsin between 2014 and 2016 demonstrated that, at baseline, sequential compression devices (SCD) were ordered for 46.0% of admitted antepartum women. In response, provider education and a prechecked SCD order in the electronic antepartum admission order set were implemented. Objective: To examine the effect of these interventions on SCD compliance during antepartum admissions. Conclusion: A prechecked antepartum order set for SCD increased the rate of provider compliance with SCD. However, this increase did not result in high patient compliance with SCD among antepartum women requiring admission for longer than 24 hours.

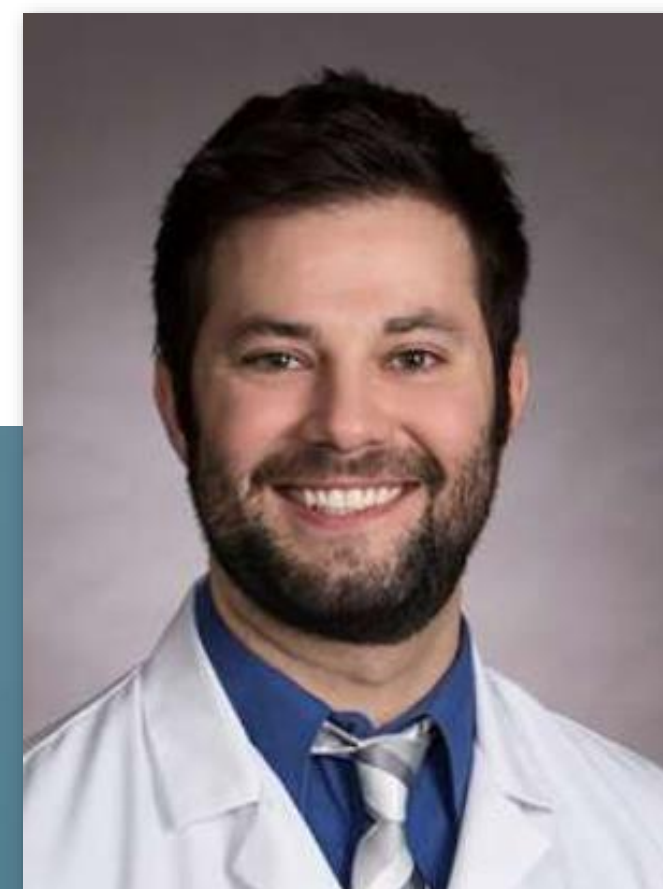
## “Great Hospitals in North America: The Medical College of Wisconsin Neurological Surgery”

Montoure A, Janich K, Cusick JF, Kurpad SN, Wang MC. *World Neurosurgery*. 2019;125:55-66.

Neurosurgery has a rich history at the Medical College of Wisconsin, including having the nation's first ever spine fellowship. This paper is a look at the creation and growth of the Department of Neurosurgery from its humble beginnings to its nationwide recognition today, and more importantly to focus on the individuals who made this possible.

### Andrew Montoure, MD

Resident, PGY5  
Department of Neurosurgery



### Rachel Schlaak, BS

Graduate Student  
Department of Pharmacology & Toxicology

## “Mapping genetic modifiers of radiation-induced cardiotoxicity to rat chromosome 3”

Schlaak RA, Frei A, Schottstaedt AM, et al. *American Journal of Physiology. Heart and circulatory physiology*. 2019;316(6):H1267-H1280.

Radiation therapy is used by over 50% of all cancer patients to reduce risk of recurrence and improve survival. Unfortunately, doses can be limited by toxicity in multiple organs, including the heart. This study reveals heritable genetic factors have the potential to modify cardiac sensitivity to radiation. Specifically, genetic variants on rat chromosome 3 greatly alter the severity of radiation-induced cardiac damage. We are genetically mapping these variants as well as using gene expression analysis to identify critical mediators of these differences. Identifying targets that alter radiation-induced cardiotoxicity may lead to personalized radiation treatments with less cardiovascular side effects.

