

UNIVERSITY OF WISCONSIN



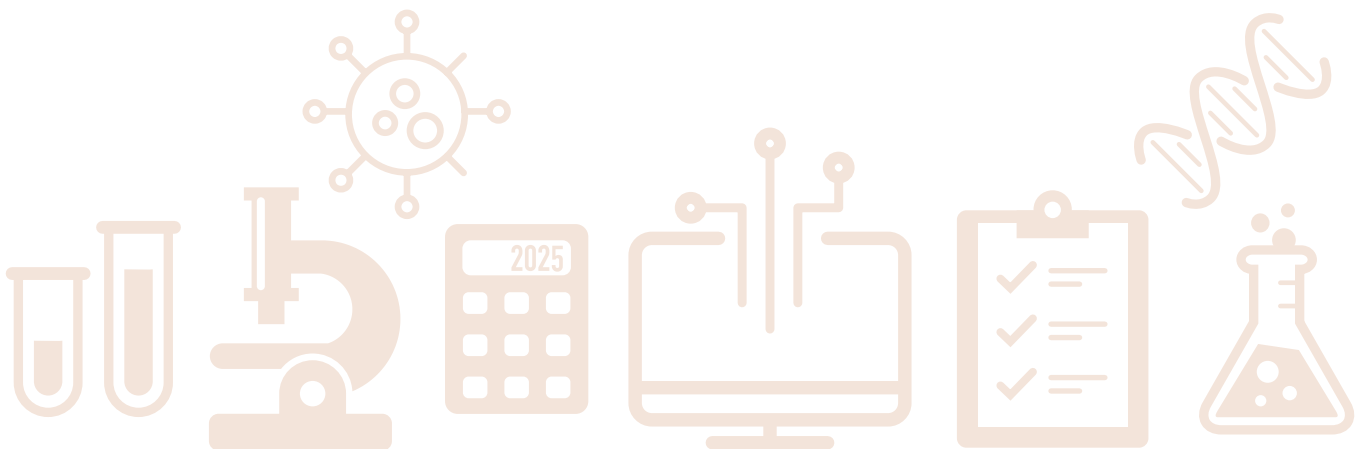
DEPARTMENT OF SURGERY

# research summit 2025

*Advances in Surgical Research and Innovation*

THURS JANUARY 9 2025 | HEALTH SCIENCES LEARNING CENTER (HSLC)

# program book





## **Welcome to the 16th Annual University of Wisconsin Department of Surgery Research Summit!**

The Department of Surgery recently wrapped up a year-long celebration of our founding 100 years ago. There is no question that surgical research, like surgical practice and education, has advanced light years since 1924. Thus, **“Advances in Surgical Research and Innovation”** is the theme of the 2025 Department of Surgery Research Summit, where we will learn about the cutting-edge scientific achievements of our research faculty, staff, and trainees over the last year alone.

We are honored to welcome Dr. Carla Pugh as this year’s keynote speaker. Dr. Pugh is the Thomas Krummel Professor of Surgery at Stanford Medicine. She is also the Director of the Technology Enabled Clinical Improvement Center, which aims to transform human health by advancing sensor technology at the point of care. As a surgeon-scientist with clinical focus in Acute Care Surgery, her research employs advanced engineering technologies, AI, and simulation to develop new approaches in how we assess and define technical mastery in surgery. Her presentation today will address applications of AI and wearable technologies.

We will be given a small snapshot of the innovative research that is being conducted in the department during the Abstract Oral Presentations. The eight talks featured during this session represent the range of basic, clinical, translational, and educational science that is being conducted in our department. The poster session in the HSLC Atrium at 11am will further highlight the breadth and depth of our department’s research.

The afternoon sessions will kick off with our Surgical Innovation panel discussion. We will hear from a unique and diverse group of panelists from within and outside of our department who will be highlighting how they have taken advantage of the unique infrastructure at the UW to conduct innovative research and product development. We’re fortunate to have Dr. Aimee Arnoldussen from Discovery 2 Product (D2P) join this panel. D2P is a partnership between the university and the Wisconsin Alumni Research Foundation that is focused on connecting researchers to the people, programs, and resources designed to help bring UW-Madison’s innovations to the marketplace.

The final session of the day will highlight how partnerships with patients, families, and other stakeholders play a critical role in advancing the research, clinical, and educational missions of our department. We will hear from several of our scientists who have formed valuable partnerships with donors to drive impactful research, improve the quality of clinical care, and find new ways to educate and train residents and students. We hope that their stories will increase awareness of the power of philanthropic partnerships to shape the future of medicine.

Innovation thrives on teamwork, where diverse perspectives and combined knowledge can generate creative solutions that might not be possible through individual efforts alone. We are immensely proud to showcase today the novel ideas and collaborative efforts of our colleagues in this department. The vision, ingenuity, and sheer talent exhibited by our research faculty, staff, and trainees is truly inspiring.

**Courtney Balentine, MD, MPH** and **Mehreen Kisat, MBBS, MS**

*Program Co-Chairs*



# Keynote Speaker



## **Carla Pugh, MD, PhD, FACS**

*Thomas Krummel Professor of Surgery*

*Director of the Technology Enabled Clinical Improvement (T.E.C.I.) Center*

*Stanford University School of Medicine*

Carla Pugh, MD, PhD, FACS is the Thomas Krummel [Professor of Surgery](#) at Stanford University School of Medicine and Director of the [Technology Enabled Clinical Improvement \(T.E.C.I.\) Center](#). Her clinical area of expertise is Acute Care Surgery and her research involves

the use of simulation, advanced engineering technologies, and artificial intelligence to develop new approaches for assessing and defining mastery in clinical procedural skills. Dr. Pugh is considered to be a leading, international expert on the use of sensors and motion tracking technologies for clinical performance measurement.

Dr. Pugh obtained her undergraduate degree in Neurobiology at U.C. Berkeley and her medical degree at Howard University School of Medicine. Upon completion of her surgical training at Howard University Hospital, she attended Stanford University to obtain her PhD in Education. Her graduate studies have given her a unique vision and the empirical skills necessary to forge a new and innovative path in using technology and metrics to bridge the gap between process and outcomes. Her goal is to forge a new path towards applied quality metrics in healthcare and to change the face of medical and surgical education through data analytics, data visualization and performance feedback.

Dr. Pugh holds multiple patents on the use of sensor and data acquisition technology to measure and characterize hands-on clinical skills. Currently, over two hundred medical and nursing schools are using one of her sensor-enabled training tools for their students and trainees. She is the Principal Investigator on eight active grants, including a National Institute of Health (NIH) R01 Grant, "Quantifying the Metrics of Surgical Mastery: An Exploration in Data Science," and a Scoliosis Research Society (SRS) award, "Leveraging Embedded Haptic Sensor Technology for Force Vector Mapping in Orthoses for Adolescent Idiopathic Scoliosis." Most recently, she was awarded a Wellcome LEAP SAVE (Surgery: Assess/Validate/Expand) contract for her proposal titled, "Advanced Quantification and Acquisition of Surgical Skills Using the Wearable Sensing System." Throughout her career, she has been awarded over 50 grants garnering over \$30 million in funding from government agencies, trusts and foundations, and educational institutions.

Her work has received numerous awards from medical and engineering organizations, including the [Presidential Early Career Award for Scientists and Engineers](#) from President Barack Obama at the White House in 2011. In 2014, she was invited to give a [TEDMED talk](#) on the potential uses of technology to transform how we measure clinical skills in medicine. Dr. Pugh was inducted into the [American Institute for Medical and Biological Engineering](#) (April 2018), the [American College of Surgeons Academy of Master Surgeon Educators](#) (April 2019), as well as the [American Board of Surgery Council](#) (February 2020). She was elected a member of the [National Academy of Medicine](#) in 2021 for "pioneering sensor technology research that helped to define, characterize and inspire new and innovative performance metrics and data analysis strategies for the emerging field of digital health care."



# Surgical Innovation Panelists

## **Aimme Arnoldussen, PhD**



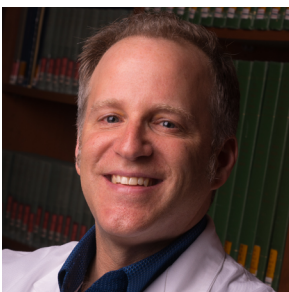
Aimee Arnoldussen is an Innovation Coach at UW Madison. After receiving her PhD in Neuroscience, she joined the WARF startup company Wicab Inc. where she developed and gained FDA 510(k) de novo clearance for the BrainPort vision device for those who are blind. Her research was awarded over \$6M in non-dilutive funding from the NIH and Department of Defense that led to venture fundraising exceeding \$7M. This expertise was tapped to manage a UW Health's technology assessment needs, providing evidence-based analyses of technologies to guide strategic organizational purchasing and investment decisions. With these experiences she gained insights for successful healthcare innovation deployment – understanding perspectives of patients, clinicians, hospitals, insurers and companies.

## **Aaron Dingle, PhD**



Dr. Aaron Dingle is a dedicated scientist specializing in patient-centered solutions for complex medical conditions. He is at the forefront of advancements in neuroprosthetics and vascularized composite allotransplantation, aimed at improving limb replacement outcomes. Dr. Dingle is deeply committed to promoting diversity in education, research, and medicine, ensuring inclusivity and equitable opportunities across the field. Committed to pushing the boundaries of medical science, he collaborates with multidisciplinary teams to translate cutting-edge research into practical therapies.

## **Joshua Mezrich, MD**



Dr. Joshua Mezrich is a Professor of Surgery and the Mark A. Fischer Chair in Transplantation at the University of Wisconsin School of Medicine and Public Health in Madison, WI, where he is the Surgical Director of the Living Donor Kidney Transplant program. His clinical interests include kidney and liver transplantation, and live donor kidney transplantation. He has a special interest in history, particularly medical history, ethics in medicine, and xenotransplantation. Dr. Mezrich has a federally funded laboratory investigating the role of the AHR as a sensor to environmental signals at organs at the interface with the outside world. He enjoys creative writing featuring his patients and their stories, and has written multiple articles in *The Atlantic*. His book, "When Death Becomes Life: Notes from a Transplant Surgeon" was released on January 15, 2019, and he is currently in the process of writing his second book.



# Surgical Innovation Panelists

## **Muhammed Murtaza, MBBS, PhD**



Dr. Muhammed Murtaza serves as the Director for Center Human Genomics and Precision Medicine and Associate Professor in Surgical Oncology at University of Wisconsin-Madison. He leads a research program focused on developing and translating multianalyte assays for early detection, minimal residual disease detection, and monitoring response to treatment for patients with cancer. Besides publications and NIH funding, this work has led to more than 12 intellectual property applications, an acquired startup company as well as a licensing agreement for commercial development. Dr. Murtaza holds a PhD from Cancer Research UK Cambridge Institute at the University of Cambridge, and an MBBS from Aga Khan University in Karachi, Pakistan. Prior to his current position, he was a faculty member at Translational Genomics Research Institute and at Mayo Clinic in Arizona.

## **Lee Wilke, MD, FACS**



Dr. Lee G Wilke is a Professor of Surgery in the University of Wisconsin School of Medicine and Public Health, the Senior Medical Director of Clinical Cancer Services for UW Health/Carbone Cancer Center and the Hendricks Chair in Breast Cancer Surgery Research. Dr. Wilke currently oversees the clinical operations for the UW Health/Carbone Cancer Center, which provides care for over 30,000 individuals with cancer annually. Dr Wilke is a founder of Elucent Medical, which developed the Envisio/Smart Clip technology for oncologic surgery. She is the Chair for Quality for the National Accreditation Program for Breast Centers, a member of the NCCN Board of Directors as well as an elected member of the Physician Clinical Leadership Initiative for the Association of American Cancer Institutes. Most importantly, Lee is the mother of two adult sons, enjoys traveling with her husband and spending time on her Peloton bike!

## **Carla Pugh, MD, PhD, FACS**



*See Keynote Speaker bio ...*



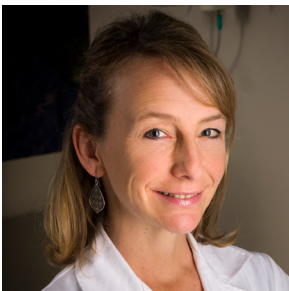
# Philanthropy-Funded Research Presenters

## **Luke Funk, MD, MPH, FACS**



Dr. Funk is a Professor of Surgery and Co-Vice Chair of Research in the Department of Surgery at UW-Madison and Chief of General Surgery at the William S. Middleton VA. His clinical practice includes minimally invasive and bariatric surgery. As a health-services researcher, his long-term goal is to optimize access and outcomes of obesity care for adults with overweight/obesity. His research team uses quantitative and qualitative research methods and conducts clinical trials aimed at improving utilization of obesity treatment for adults in the U.S.

## **Angela Gibson, MD, PhD, FACS**



Dr. Gibson is an Associate Professor of Surgery, Co-Vice Chair of Research in the Department of Surgery at UW-Madison and the Medical Director of UW Health Wound Healing Services. Her Acute Care Surgery practice includes Burn, Trauma, Emergency General Surgery and Surgical Critical Care. As a translational surgeon scientist, her focus is on understanding the burn wound microenvironment to improve healing prognostication and refine treatment options for burn survivors. Her research team uses basic science and clinical research methods in a bidirectional manner to improve the potential for translation of scientific findings and ultimately positively impact burn survivor outcomes.

## **James Maloney, MD**



Dr. Maloney is the Anthony J Arenas Professor in Lung Transplantation and a Board-certified Thoracic Surgeon, who specializes in general Thoracic Surgery and oncologic surgery. He is the Chief of Surgical Services at the Middleton Memorial VA, Fellow of COSECSA and active with the American College of Surgeons Global Health initiative.



# Philanthropy-Funded Research Presenters

## **Samuel Poore, MD, PhD**



Dr. Poore specializes in microvascular surgery with an emphasis on breast reconstruction, as well as general plastic and reconstructive surgery, including reconstruction of the hand, lower extremity and head and neck. He is the Chair of Plastic and Reconstructive Surgery at the University of Wisconsin, Madison and holds the Endowed Chair of Global Education in Plastic and Reconstructive Surgery. Dr Poore serves as co-director of the UW Microsurgery and Regenerative Medicine Laboratory (with Aaron Dingle, PhD). He has led and participates in global surgery programs focusing on microsurgical education in Vietnam, Egypt, Rwanda, South Africa and Nicaragua.

## **Sean Ronnekleiv-Kelly, MD, FACS**



Dr. Ronnekleiv-Kelly is an Associate Professor and surgeon-scientist in the Department of Surgery at UW SMPH, and the Kissinger Surgical Oncology Research Professor with a clinical expertise in liver, bile duct and pancreas cancers. He serves on the National Comprehensive Cancer Network guideline panel for bile duct and liver cancer. His research program focuses on understanding how misalignment of the circadian clock rewires tumor metabolism to promote pancreas cancer development and spread, in order to target the abnormally functioning clock in tumor cells. Furthermore, his lab has pioneered a model system that mimics rare forms of human bile duct and pancreas cancer caused by a unique gene mutation, and is using this model system to develop effective therapy for three separate rare and lethal cancers.



# Program

University of Wisconsin Department of Surgery

## 16th Annual Research Summit

*Advances in Surgical Research and Innovation*

**Thursday, January 9, 2025**

### AM

**7:30**     **Registration & Continental Breakfast**, HSLC Atrium

**8:00**     **Welcome & Opening Remarks**, 1306 HSLC

- **Courtney Balentine, MD, MPH**, Program Co-Chair
- **Mehreen Kisat, MBBS, MS**, Program Co-Chair

**8:15**     **Keynote Address**, 1306 HSLC

"Precision Learning & Data Sharing Through Wearable Technology. What's AI Got to Do With It?"

**Carla Pugh, MD, PhD, FACS**

*Thomas Krummel Professor of Surgery*

*Director of the Technology Enabled Clinical Improvement (T.E.C.I.) Center*

*Stanford University School of Medicine*

**9:15**     **Break**, HSLC Atrium

**9:30**     **Abstract Oral Presentations**, 1306 HSLC, 7 minutes + 3 minutes Q&A

• **Kaleem Ahmed**

"Predicting Real-world Overall Survival for Post-Operative Pancreatic Ductal Adenocarcinoma: An ASCO CancerLinQ Discovery Analysis"

• **John O'Connor**

"Who Gets Referred? Disparities in Access to Specialist Care for Hyperparathyroidism"

• **Deep Kappadia**

"Use of Islet Vascularized Extracellular Matrix Organoids (IVEO) to Improve Transplantation and Survivability of Islets"

• **Joshua Brady**

"Sublobar Resection is not Associated with Increased Risk of Recurrence in Stage I Non-Small Cell Lung Cancer with Lymphovascular Invasion"

• **Szu-Tsen Yeh**

"The Effect of B Cell Depletion Therapies On Preformed Xenoantibodies In Transplant Recipient"

• **Julia Illiano**

"Sleeve gastrectomy improves cognition and frailty in AD prone mice"

• **Mary Junak**

"A Bidirectional Translational Approach to Evaluate Perioperative Fluorescence Imaging for Burns"

• **Sydney Tan**

"Are Work Hours Actually Linked to Burnout in Residents?"





# Program cont'd

## AM cont'd

**10:50**     **Break**, HSLC Atrium

**11:00**     **Poster Session**, HSLC Atrium

## PM

**12:00**     **Lunch**, 3110 HSLC (3rd Floor)

**1:00**     **Surgical Innovation Panel Session**, 1306 HSLC

- **Aimme Arnoldussen, PhD**
- **Aaron Dingle, PhD**
- **Joshua Mezrich, MD**
- **Muhammed Murtaza, MBBS, PhD**
- **Lee Wilke, MD, FACS**
- **Carla Pugh, MD, PhD, FACS**

**2:15**     **Break**, HSLC Atrium

*\*\*Voting for the Surgery Science Image Contest ends at 2:30pm!\*\**

**2:30**     **Meaningful Contributions: The Power of Philanthropy-Funded Research**, 1306 HSLC

- **Samuel Poore, MD, PhD**
- **Luke Funk, MD, MPH**
- **Angela Gibson, MD, PhD**
- **Sean Ronnekleiv-Kelly, MD**
- **James Maloney, MD**

**3:45**     **Awards & Closing Remarks**, 1306 HSLC

- **Courtney Balentine, MD, MPH**, Program Co-Chair
- **Mehreen Kisat, MBBS, MS**, Program Co-Chair

**4:00**     **Reception**, HSLC Atrium



# Acknowledgements

We would like to thank the following individuals who served on the **2025 Research Summit Planning Committee** and made invaluable contributions to the planning of this event.

Courtney Balentine, MD, MPH	Jessica Karls-Ruplinger, JD
Hannah Clark	Kayden Louzada
Luke Funk, MD, MPH	Karen Lynch
Angela Gibson, MD, PhD	Bhabna Pati, MS
Sally Gray	Jennifer Zellner, PhD
Mehreen Kijat, MBBS, MS	

We also wish to recognize the **abstract reviewers** who served on our Program Committee. The following individuals generously donated their time to review the 114 abstracts that were submitted:

David Aufhauser, MD	Angela Gibson, MD, PhD	Heather Neuman, MD, MS
Courtney Balentine, MD, MPH	Rachel Godbout	Manabu Nukaya, PhD
Anna Beck, MD	David Harris, MD	Marziyeh Ostadi
Julia Berian, MD, MS	Sarah Jung, PhD	Sudha Pavuluri Quamme, MD, MS
Jason Brant, MD	Cynthia Kelm-Nelson, PhD	Apoorva Reddy, PhD, MS
Matthew Brown, PhD	Mehreen Kijat, MBBS, MS	Toria Rendell, MD
Connie Chamberlain	Elise Lawson, MD, MSHS	Tehseen Sawar
Daniel Cho, MD, PhD	Hau Le, MD	Amber Shada, MD
Dawn Elfenbein, MD, MPH	Vlasta Lungova, PhD	Greg Sigler, MD
David Foley, MD	David Melnick, MD, MPH	Lee Wilke, MD
Luke Funk, MD, MPH	Brett Michelotti, MD	
Jacqueline Garonzik Wang, MD, PhD	Muhammed Murtaza, MBBS, PhD	

Finally, we would like to acknowledge the **abstract oral presentation judges** and **poster session judges**, who worked to determine the winners of the Bernhardt, Kent, and Rikkers Awards.

David Al-Adra, MD, PhD	David Foley, MD	Brett Michelotti, MD
Courtney Balentine, MD, MPH	Luke Funk, MD, MPH	Muhammed Murtaza, MBBS, PhD
Anna Beck, MD	David Harris, MD	Sudha Pavuluri Quamme, MD, MS
Jason Brant, MD	Sarah Jung, PhD	Tehseen Sarwar, MBBS
Matthew Brown, PhD	Mehreen Kijat, MBBS, MS	Stephanie Savage, MD, MS
Connie Chamberlain, PhD	Anne Lidor, MD, MPH	Patrick Schwartz, MD
Daniel Cho, MD, PhD	Sandra Lin, MD	Linda Stafford, MPH
John Fechner	Vlasta Lungova, PhD	Lee Wilke, MD

# List of Abstracts



## **Alphabetized by PI/Lab within each group.**

Jump to any abstract by selecting “Ctrl” and clicking on the abstract title.

### **Group One: Basic Science and Translational Research**

#### **Al-Adra**

Sirtuin-6 and its Effects on Liver Inflammation during Normothermic ex vivo Liver Perfusion;  
*Brooke Miller, Slava Kuznietsov, PhD, Peter Chlebeck, Heather Jennings, Bret Verhoven, John Denu, PhD, David Al-Adra, MD, PhD*

#### **Aufhauser/Dominko**

The Effect of B Cell Depletion Therapies On Preformed Xenoantibodies In Transplant Recipient; *Szu-Tsen Yeh, MS, Tanja Dominko, PhD, David Aufhauser, MD*

#### **Birbrair**

Targeting CPXM1 in Fibroblasts as a therapeutic strategy to reduce Melanoma Metastasis;  
*Stephen Kim, Brajesh Kumar Savita, Debpali Sur, Taeho Lee, Alexander Birbrair, PhD*

#### **Brant**

A rodent model to probe central effects of chronic cochlear implant stimulation; *Gunnar Quass, PhD, Jason Brant, MD*

#### **Brown**

A humanized mouse model of tissue repair and transplant allograft rejection following myocardial infarction; *Jiwon Seo, BS, Liupei Huang, MD, Matthew E Brown, PhD*

Diminished Immune Cell Adhesion in Hypoimmune ICAM-1 Knockout Human Pluripotent Stem Cells; *Sayandeep Saha, MS, W. John Haynes, PhD, Natalia M. Del Rio, BS, Elizabeth E. Young, BS, Jue Zhang, PhD, Jiwon Seo, BS, Liupei Huang, MD, Alexis Holm, BS, Wesley Blashka, BS, Lydia Murphy, BS, Merrick J. Scholz, BS, Abigale Henrichs, Jayalaxmi Suresh Babu, BS, John Steill, BS, Ron Stewart, PhD, Timothy J. Kamp, MD PhD, Matthew E. Brown, PhD*

Evaluation of Thymus-Associated T Cell Gene Expression in mRNA-Vaccinated Humanized Mice; *Wesley Blashka; Liupei Huang; Jiwon Seo; Natalia Del Rio; Arista Whitson; McKeon Lucas; Zach Bromet; Abhiram Nettem; Abigale Henrichs; Matthew Brown*

## **Carchman**

The Topical Protease Inhibitor, Saquinavir, Modulates Translation Pathways in a Transgenic Mouse Model of Anal Cancer Prevention; *Sakura Haggerty, Evan Yao, Wei Zhang, Grace Hansen, Yun Zhou, Garrett Bartelt, Nathan Sherer, Evie Carchman*

## **Connor/Glass**

Swallowing characteristics with aging in Down syndrome: A preclinical study in the Ts65Dn mouse model; *Marziyeh Ostadi, MSc, Tiffany J Glass, PhD, Nadine Connor, PhD*

## **de Biasi**

A Quantitative Evaluation of Perioperative Hemodynamic Metrics in Mitral Valve Surgery Using 4D Flow MRI; *Leah Gober MD, Mackenzie Sloan, Mike Stellon MD, Alejandro Roldán-Alzate PhD, Andreas de Biasi MD*

## **Dingle**

The Effect of Cannabidiol (CBD) on Skin Flap Survival in a Rat Model; *Armin Edalatpour, MD, Molly Winchenbach, Peter Nicksic, MD, Robert George MD, Aaron Dingle, PhD, Ahmed Afifi, MD*

Optimizing Flexor Digitorum Profundus Tendon Repair: A Narrative Review; *Rishi Mereddy, Emily E Zona BS, Camille J Laliberte BS, Aaron Dingle PhD*

Osseointegrated Neural Interface: Preliminary Electrophysiological Observations in an Ovine Forelimb Model; *Rishi Mereddy, Ashlesha Deshmukh B.S., Lucas Sears B.S., Emily E Zona B.S., Kent N. Bachus PhD, James Morizio PhD, Samuel O. Poore MD PhD, Aaron M. Dingle<sup>1</sup> PhD*

## **Gibson**

A Bidirectional Translational Approach to Evaluate Perioperative Fluorescence Imaging for Burns; *Mary Junak, MD, Hector Garcia, PhD, Aiping Liu, PhD, Bailey Donahue, BS, Joana Pashaj, BS, Emily Klossowski, MS, Adam Uselmann, PhD, Lee Faucher, MD, Brian Pogue, PhD, Angela Gibson, MD, PhD*

A Protocol to Evaluate the Local Burn Wound Environment with Sequential Sampling; *E.T. Klossowski, MS, M. Junak, MD, B.A., Donahue, BS, A.L.F. Gibson, MD, PhD*

Protoporphyrin IX based- photodynamic therapy enhances burn wound healing in ex vivo human skin; *Aiping Liu, PhD, Marien I. Ochoa, PhD, Emily T. Klossowski, MS, Bailey A. Donahue, BS, Joana Pashaj, BS, Mary Junak, MD, Brian Pogue, PhD and Angela LF Gibson, MD/PhD*

## **Glass**

Evaluating Swallowing Dysfunction in Down Syndrome: Analysis of Df(17)2 and Df(16)8 Mouse Models; *Gaurav Singhal, PhD, Erin H. Fisher, Tiffany J. Glass, PhD*

Hypoglossal nucleus phenotypes of the Ts65Dn mouse model of Down syndrome through aging; *Lucille M Vue, MS, Tiffany J Glass, PhD*

Microanatomical Differences of Intrinsic Tongue Muscles in the Adult Ts65Dn Mouse Model of Down syndrome; *Jayde C. Sitko, Tiffany J. Glass, PhD*

## **Harris**

Sleeve gastrectomy improves cognition and frailty in AD prone mice; *Julia Illiano BS, Reji Babygirija MS, Michelle Sonsalla MS, Grace Zhu PhD, Luiz Lopez, Odin Schaepkens, Dudley Lamming PhD, David A. Harris MD*

The synergistic impact of resistance training and altered protein diets in sleeve gastrectomy; *Grace Zhu, Luiz Lopez, Leah N. Braucher, Szczepan Olszewski, Julia Illiano, Samuel Saghafi, Isaac Grunow, Adam R. Konopka, Dawn B. Davis, Dudley W. Lamming, David A. Harris*

## **Kisat**

Adjudication Instrument for Infection in Critically Injured Trauma Patients; *Mary Junak, MD, Meghana Peddoddi, Nicole Werner, MD, Patrick Shahan, MD, Laura Hammel, MD, Hilary Faust, MD, Christopher Saddler, MD, Ambar Haleem, MD, Mehreen Kisat, MD*

Plasma metagenomic sequencing in organ transplant donors; *Miraf Molla, BS, Haikun Zhang, PhD, Eddie Dominguez, PhD, Michael Sclarici, MD, Caitlin Pepperell, MD, Joshua Mezrich, MD, Mehreen Kisat, MD*

## **Le**

Enhanced Viability and Proliferation of Human Neural Progenitor Cells Using an Oil-Overlay and Autonomously Regulated Oxygen Microenvironment (AROM); *Ligi Milesch, PhD, Nai-Wen Liang, Chao Li, PhD and Hau D. Le, MD*

## **Murtaza**

Tumor DNA analysis in peritoneal fluid to detect and monitor peritoneal carcinomatosis; *Muhammad Talha Nawaz, MD, Muhammad Talha Waheed, MD, Kirsten Dennison, MS, Bradon McDonald, PhD, Stephanie McGregor, MD, Syed Nabeel Zafar, MD, Mustafa Raouf, MD, Muhammed Murtaza, MBBS, PhD*

## **Kelm-Nelson**

Vorinostat, a histone deacetylase inhibitor, increases key neuroprotective mRNA expression in early-stage Parkinsonian midbrain neurons; *Sarah A. Lechner, B.S., Jaden N. Morrison, and Cynthia A. Kelm-Nelson, Ph.D.*

## **Odorico**

The Beta Cell “Invisibility Cloak” – Developing Stem Cell Derived Pancreatic Beta Cells that are Protected from the Immune System; *Leavens C, Chamberlain CS, Abad Santos E, Palwasha Khan A, Brown M, Gumperz J, Baiu D, Sackett SD, Chlebeck P, Tremmel D, Raglin S, Wang X, Huangfu D, Odorico J*

Evaluation of NBSGW-RIP-DTR mouse strain as an inducible diabetes and humanizable model to study diabetic transplant therapies and allogeneic immune responsiveness; *Li Andrew R, Chamberlain CS, PhD, Kapadia D, BS Abad Santos E, BS, Gorski K, BS, Leavens C, BS, Sackett SD, PhD, Chlebeck P, BS, Brown M, PhD Zaeem M, PhD, Huang L, PhD, Odorico J MD*

Use of Islet Vascularized Extracellular Matrix Organoids (IVEO) to Improve Transplantation and Survivability of Islets; *Kapadia D, BS1 Tremmel DM, PhD2, Chamberlain CS, PhD1, Abad Santos E, BS1, Gorski K, BS1, Leavens C, BS1, Sackett SD, PhD1, Chlebeck P, BS1, Odorico J.*

## **Phillip**

Development of MRI-Compatible Kidney Perfusion System for Organ Assessment; *Daniel Rice, James Rice, M.S., Leah Gober, MD, Gregory Simchick, PhD, Diego Hernando, PhD, Alejandro Roldán-Alzate, PhD, Jennifer Philip, MD*

Validation of Intravoxel Incoherent Motion MRI using Perfused Explanted Human Livers; *Daniel Rice, Gregory Simchick, PhD, James Rice, M.S., Leah Gober, MD, Diego Hernando, PhD, Alejandro Roldán-Alzate, PhD, Jennifer Philip, MD*

## **Poore**

Generation of a small-diameter universal artery graft from pluripotent stem cells; *Weifeng Zeng<sup>1</sup>, John P. Maufort<sup>2</sup>, Robert George, Ellen Shaffrey<sup>1</sup>, Peter Nicksic<sup>1</sup>, Sarah Lyon<sup>1</sup>, Jue Zhang<sup>2</sup>, Dave Vereide<sup>2</sup>, James A. Thomson<sup>2</sup>, Samuel O. Poore<sup>1</sup>*

## **Ronnekleiv-Kelly**

*Modulation of RBP-1 Phosphorylation is a Novel Therapeutic Vulnerability in Fibrolamellar Carcinoma; Patrick Carney, MD, PhD, Manabu Nukaya, PhD and Sean Ronnekleiv-Kelly, MD*

## Group Two: Clinical/Outcomes Research

### Afifi

Psychiatric History and Multiple Chemical Sensitivity as a Marker of Somatization in Predicting Migraine Surgery Outcomes; *Keenan Fine, MS, Caroline Bay, BA, Robert George, MD, Ahmed Afifi, MD*

### Bentz

Exploring the Landscape of Cosmetic Surgery in Africa - A Survey; *Jessieka Knazze, MPH, Jasmine Craig, MD, MPH, Elizabeth WU, BS, Darius Balumuka, MD, Metasebia Worku Abeba, MD, Musunga Mulenga, MD, Ian Shyaka, MD, Amanda Gosman, MD Michael Bentz, MD*

### Berian

Timing of Urgent Colectomy for Cancer: A NSQIP Analysis; *Madhuri V Nishtala, MD, Kelsey Franklin, MD, MPH, Ben Zarzaur, MD, MPH, Julia R Berian, MD, MS*

### Chiu

Who Gets Referred? Disparities in Access to Specialist Care for Hyperparathyroidism; *John O'Connor, Rebecca Sippel, MD, Lily Stalter, Amy Kind, MD, PhD, Alexander Chiu, MD, MPH*

### Cho

Clefts and Contaminants: Investigating the Link Between Orofacial Clefts and PCB Pollution in Wisconsin; *Jessieka Knazze, MPH, Gina Krause, BS, Doruk Orgun, MD, Jessica Blum, MD, MSc, Jasmine N. Craig, MD, MPH, Catharine B. Garland, MD, Daniel Cho, MD, PhD*

From theory to practice: A systematic review of MRI's clinical applications in evaluating and treating cleft-associated velopharyngeal insufficiency; *Aidan O'Shea, ScB, Emily Zona, BS, Jasmine Craig, MD, MPH, Jessica Blum, MD, MSc, Catharine Garland, MD, Daniel Cho, MD, PhD*

Global Perspectives on Primary Cleft Repair in the Adult Patient: Navigating a Unique Reconstructive Challenge; *Emily E. Zona BS, Aidan W. O'Shea ScB, Sumin Yang, B.S., Jasmine Craig MD MPH, Catharine B. Garland MD, Daniel Y. Cho MD PhD*

The Impact of Socioeconomic Disadvantage on Craniosynostosis Care; *Manasa H. Kalluri, BS, Daniel Y. Chu, PhD, Aidan W. O'Shea, ScB; Gina Krause, BS; Jessica D. Blum, MD, MSc, Kristine M. Carbullido, MD, Catharine B. Garland, MD, Daniel Y. Cho, MD, PhD*



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Prevalence of Trapeziometacarpal Osteoarthritis Across Age Cohorts: A Retrospective Radiographic Analysis; *Camille LaLiberte, BS, Keenan Fine, MS, Brett Michelotti, MD*

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Five-year Outcomes of Recipients of Dual Kidney Transplantation are Better Compared to Single Kidney Transplantation with Comparable Early Post-transplant Complications; *Ekaterina Fedorova, MD, Sofia Nehring Firmino, MS3, David Foley, MD, Jacqueline Garonzik-Wang, MD, PhD, Dixon Kaufman, MD, PhD, Jon Odorico, MD, David Aufhauser, MD, Nikole A Neidlinger, MD, Carrie Thiessen, MD, PhD, Jennifer Philip, MD, Kelly M Collins, MD, Josh Mezrich, MD, David Al-Adra, MD, PhD, Brad Astor, PhD, Didier Mandelbrot, MD, Sandesh Parajuli, MBBS*

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Wound Complications After Breast Reconstruction: The Limited Role of HbA1c Compared to BMI; *Emily E. Zona, B.S., Doruk Orgun, M.D., Caroline C. Bay, B.A., Robert E. George, M.D., Sarah M. Thornton, B.A., M. Kristine Carbullido, M.D., Aaron M. Dingle, Ph.D., Samuel O. Poore, M.D., Ph.D.*

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A Day In The Life of a Surgical Instrument: The Cycle of Sterilization; *Robert E. George, MD, Caroline C. Bay, BA, Ellen C. Shaffrey, MD, Peter J. Wirth, MD, Venkat K. Rao, MD MBA*

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Factors Associated with Survival after Surgical Resection for Pancreatic Ductal Adenocarcinoma: A Systematic Review; *Muhammad Maisam Ali, MBBS; Kaleem S. Ahmed, MD, MSAI; Clayton T. Marcinak, MD; Noorain Ahmed, MBBS; Haider bin Khalid, MBBS; Kainat Fatima, MBBS; Ajia Syed, MD; Asra Siddiqui, MD; Syed Nabeel Zafar, MD, MPH, FACS*

Predicting Real-world Overall Survival for Post-Operative Pancreatic Ductal Adenocarcinoma: An ASCO CancerLinQ Discovery Analysis; *Kaleem S. Ahmed, MD, MSAI; Sheriff M. Issaka, BS; Benjamin Cher, MD; Clayton T. Marcinak, MD; Syed Nabeel Zafar, MD, MPH*

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Detecting Bias in Plastic Surgery Residency Application Letters of Recommendation using Natural Language Processing; *Nagar T, Jung S, Wirth P, Schappe A, Salyapongse AN*

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Continued Design and Development of a Novel 3D Printed Microsurgery Microscope; *Elizabeth P Wu, BS; Sahand Eftekari, MD; Weifeng Zeng, MD; Ellen Shaffrey, MD, Aaron Dingle, PhD; Samuel Poore, MD PhD*

Educational interventions to enhance medical student knowledge and interest in plastic surgery: A scoping review; *Aidan O'Shea, ScB, Keenan Fine, MS, Emily Zona, BS, Samuel Poore, MD, PhD*

Empowering Future Surgeon-Scientists: A Structured Approach to Involving Medical Students in Research Projects; *Emily E. Zona BS, Aidan W. O'Shea ScB, Keenan S. Fine MS, Armin Edalatpour, MD, Jacqueline S. Israel, MD, Samuel O. Poore MD PhD*

From Learner to Leader: The Impact of Training Novice Microsurgery Educators; *Emily E. Zona; James E. King; Maci Fulton; Nnadozie Uchegbu; Esther Wang; Weifeng Zeng, MD; Samuel Poore, MD, PhD; Aaron Dingle, PhD*

Innovative Solutions in Microsurgery: A Validation Study of the WiscVision™ Microscope for Education and Training; *Emily E. Zona, B.S., M. Kristine Carbullido, MD, Elizabeth P. Wu, B.S., Sahand Eftekari, MD, Ellen Shaffrey, MD, Weifeng Zeng, MD, Aaron M. Dingle Ph.D., Samuel O. Poore M.D., Ph.D.*

Livestreaming Microsurgery: An Avenue to Expand Global Plastic Surgery; *Weifeng Zeng MD1, Rishi Meredy BS. Sahand C. Eftekari MD, Ellen C. Shaffrey MD1, Katherine D. Reuter Munoz MD1, Aaron M. Dingle PhD1, Samuel O. Poore MD PhD1*

Preparing the Next Generation of Surgeons: A Tailored Microsurgical Training Curriculum for Undergraduate Students; *Nnadozie Uchegbu, MS, Weifeng Zeng, MD, Andi Donnelly, BS, Samuel O. Poore, MD, Ph.D., Aaron Dingle, Ph.D.*

**Schwarze**

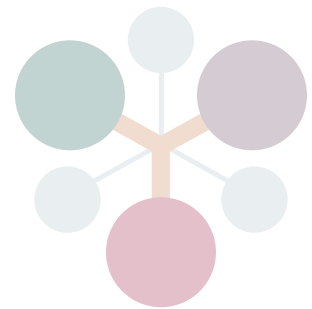
The Fundamentals of Communication in Surgery (FCS): Early Results from a Multisite Study; *C. Sobol, MD, L. Taylor, MD, K. Hill, MD, C. Morgan, MD, K. Kopecky, MD, E. Rivet, MD, A. Saad, MD, M. Kapadia, MD, A. Newcomb, MD, E. Strong, MD, R. Bynum, MFA, K. Bushaw, MA, ML. Schwarze, MD, A. Shada, MD*



# Abstracts for Presentation



# Basic Science & Translational Research Abstracts



## **Sirtuin-6 and its Effects on Liver Inflammation during Normothermic ex vivo Liver Perfusion**

Authors: Brooke Miller, Slava Kuznietsov, PhD, Peter Chlebeck, Heather Jennings, Bret Verhoven, John Denu, PhD, David Al-Adra, MD, PhD

**Introduction:** The demand for organs is increasing as the liver transplant waitlist continues to grow. Long-term success after organ transplantation is imperative and requires reliable methods to decrease the likelihood of organ rejection. Rejection occurs when damage associated molecular pattern (DAMP) signaling is initiated in response to a newly transplanted organ, overexpressing the TGF- $\beta$  pathway. This causes an increase in inflammation of the organ, which has a principal role initiating rejection. The TGF- $\beta$  pathway can be modulated by the enzyme Sirtuin-6 (SIRT-6). This study primarily investigates the efficacy of SIRT-6 upregulation in preventing the inflammatory response of an organ by modulation of the TGF- $\beta$  pathway prior to transplantation.

**Method:** Adult Lewis rat livers were procured and underwent normothermic ex vivo liver perfusion (NEVLP), an organ preservation method that allows for functional assessment of the liver and therapeutic modification of the graft prior to transplantation. Perfused livers were randomly assigned treatment groups: control (n=3) or experimental, containing SIRT-6 small molecule activators (n=3). Livers were perfused for four hours and functionality markers were recorded (lactate clearance, bile collection, pH). Following perfusion, the livers were reviewed for damage by Histology. Last, samples from the livers underwent inflammatory assays: flow cytometry and qRT-PCR.

**Results:** All livers were functional as indicated by lactate clearance in the last two hours of perfusion (2.5 mM/min/g), overall bile production (control=3000  $\mu$ L, experimental=1500  $\mu$ L), and final pH (7.35 pg/mL). Histology results showed no significant organ damage in the control or experimental groups. SIRT-6 perfused livers exhibited a decrease in antigen presenting cells (15%) and a less activated inflammatory phenotype when compared to the control. qRT-PCR results show an overall decrease in pro-inflammatory cytokine activity in the experimental group compared to the control.

**Conclusions:** Upregulation of SIRT-6 during NEVLP may be an opportunity to decrease inflammation of an organ prior to transplantation, promoting transplant acceptance. Future work will include additional inflammatory assays (LEGENDplex Rat Inflammation Panel Testing) and more trials with the SIRT-6 activators.

## The Effect of B Cell Depletion Therapies On Preformed Xenoantibodies In Transplant Recipient

Authors: Szu-Tsen Yeh, MS, Tanja Dominko, PhD, David Aufhauser, MD.

**Introduction:** Preformed xenoantibodies in humans are big barriers to xenotransplantation, and overcoming this challenge will greatly increase donor organ availability. Immunosuppressive treatments on B cell such as Rituximab, IVIg, and steroids have been widely used to reduce antibody-mediated rejection following transplantation. Our previous studies demonstrated that these B cell treatments significantly reduce human preformed xenoantibody binding to porcine cells. In this study, we further investigate the efficacy of these treatments in reducing antibody responses and explore the correlation between reductions in xenoantibodies binding, donor-specific antibodies (DSA), and patient-specific factors such as age, sex, and MHC Class I/II expression levels.

**Method:** We obtained plasma from patients (n=26) that were treated with Rituximab, IVIg, and steroids for renal transplantations at 1,3, and 6 months post-treatment. Plasma obtained immediately prior to treatment and transplantation was used as a baseline. Patient plasma was diluted at 1:100 in FACs buffer with 10%Fetal Bovine Serum and incubated with wild-type pig PBMCs, wild-type pig fibroblasts, or pig fibroblast knocked out of the pig carbohydrates genes CMAH, GGTA1, and  $\beta$ 4galNT2 orthologs genes for 30 minutes. The levels of antibody binding were assessed by flow cytometry. Additionally, patients were stratified by age groups ( $\leq 20$  years, 21-45 years,  $\geq 45$  years) and by sex. We performed correlation analyses to evaluate the relationships between anti-pig antibody binding, DSA levels, and MHC Class I/II expression in response to the B cell treatments.

**Results:** The level of IgG binding to wild-type porcine epithelial cells dropped to 0.79-fold at 3 months (n=10, p<0.05 vs. baseline), and 0.71-fold at 6 months (n=10, p<0.05 vs. baseline). Similarly, the IgM titer showed a continuous trend to decrease after initial B cell treatments the titer was reduced to 0.9-fold at 3 months (n=10, p<0.05 vs. baseline) and 0.74-fold at 6 months (n=10, p<0.005 vs. baseline). We also assessed the level of IgG and IgM binding to porcine epithelial cells knocked out of the porcine carbohydrates. Flow cytometry revealed that patients' plasma showed significantly lower IgG and IgM binding to knockout porcine cells compared to that of wild-type cells (n=10, p<0.005 KO vs. WT). Correlation analysis revealed a weak inverse relationship between reductions in anti-pig antibody binding and changes in DSA levels (slope=-0.3, R-square=0.1106). Furthermore, stratification by age and sex suggested that younger patients ( $\leq 20$  years) and females had more pronounced reductions in antibody binding and DSA levels, although these trends require further investigation.

**Conclusions:** This study demonstrates that pre-transplant B cell treatments, combined with genetically modified donor cells, can reduce humoral responses in patients undergoing xenotransplantation.

## Targeting CPXM1 in Fibroblasts as a therapeutic strategy to reduce Melanoma Metastasis

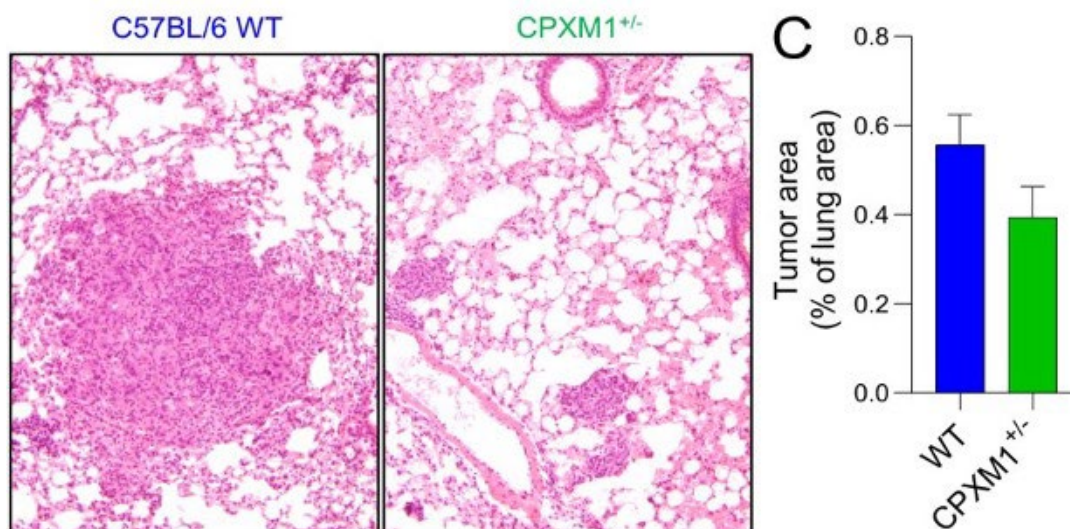
Authors: Stephen Kim, Brajesh Kumar Savita, Debpali Sur, Taeho Lee, Alexander Birbrair, PhD

**Introduction:** Malignant melanoma is one of the most lethal forms of skin cancer due to its aggressive nature and high potential for metastasis. Immune checkpoint inhibitors (ICIs) are the standard treatment for advanced-stage melanoma. However, nearly 50% of patients do not respond to these therapies. Furthermore, those who initially respond often develop resistance over time. This highlights an urgent need to identify novel therapeutic targets to enhance treatment efficacy and overcome resistance, ultimately slowing or preventing disease progression.

**Method:** To discover new potential targets for melanoma treatment, we utilized various approaches involving clinical data analysis, in vitro experiments, and mouse models. We screened tumor samples from patients with melanoma available in The Cancer Genome Atlas (TCGA) to identify genes secreted proteins associated with patient survival. Using a univariate Cox regression model, we stratified patients into groups with high or low gene expression levels. This analysis aimed to point out specific genes that could be linked to patient outcomes.

**Results:** Our screening identified CPXM1, which encodes Carboxypeptidase X, M14 family member 1 (a secreted collagen-binding N-glycoprotein involved in extracellular matrix remodeling) as significantly associated with an increased risk of death. CPXM1 was upregulated in melanoma tumors compared to healthy tissues. Single-cell RNA sequencing analysis revealed that CPXM1 is specifically upregulated in fibroblasts after infiltration within melanoma tumors. This suggests a potential role of CPXM1 in modulating fibroblast function during melanoma development and progression. Additionally, melanoma-bearing mice with decreased expression of CPXM1 developed fewer metastatic nodules, indicating that CPXM1 contributes to disease progression and metastasis. Following chart is the data collected from injecting  $1 \times 10^6$  D4M3 cell into the tail vein of C57BL6 WT or CPXM1<sup>+/-</sup> mice. Lungs were removed after 3 weeks for analyses. Representative microscopic images of lung sections from WT (left) and CPXM1<sup>+/-</sup> (right) mice are shown. The tumor areas were quantified and are presented in the accompanying chart.

**Conclusions:** Our findings suggest that CPXM1 is a promising therapeutic target for melanoma treatment. Targeting CPXM1 could enhance treatment efficacy and help overcome its resistance to current therapies. Future studies will focus on exploring the therapeutic potential of inhibiting CPXM1 in pre-clinical models of melanoma, with the goal of developing new strategies to slow or prevent Melanoma progression.



## A rodent model to probe central effects of chronic cochlear implant stimulation

Authors: Gunnar Quass, PhD, Jason Brant, MD

**Introduction:** Cochlear Implants (CI) are currently the best way to restore speech understanding for deaf individuals. However, there is a significant population of up to 10% poor performing patients for often unclear reasons, highlighting the urgent need for better understanding of CI stimulation. A high level of speech understanding positively impacts the quality of life of CI patients, connecting central brain activity directly to therapy outcome and patient well-being. Despite this significance, data about the differences in cortical brain activity between electric and acoustic hearing are scarce, since cortical activity cannot be measured directly in humans. Furthermore, most CI studies are conducted in larger anesthetized animal models like cats or guinea pigs, significantly limiting throughput and genomic tools. We established a rodent model for chronic cochlear implantation to overcome these limitations.

**Method:** We devised a novel cochlear implantation approach for rodents that allows for chronic cochlear implantation and enables large-scale cortical recordings during cochlear implant stimulation. We used a retro-auricular approach to implant custom-made CI through the round window of the cochlea during stereotaxic survival surgery. CI were fixed to the temporal bone and held in place with a mixture of glue and dental cement and guided to a headcap subdermally. 2 Mice were subsequently trained to detect CI stimulation in a head-fixed Go/NoGo paradigm days.

**Results:** Animals tolerated CI implantation well without any signs of distress. Impedances of CI electrodes stayed stable for at least 15 days, enabling reliable, chronic behavioral studies with physiological brain recordings in mice. In the behavioral experiment, mice learned to detect CI stimulation reliably after 4 days.

**Conclusions:** Our new small rodent model for chronic CI experiments enables investigations of brain activity over the course of chronic CI use in awake animals. In the future, this will allow us to compare novel technologies like optogenetics or  $\mu$ -TENNs ("living electrodes"), and different stimulation strategies for conventional stimulation, regarding brain activity and behavior. The model can further be expanded with high-density electrical recordings to investigate neural population activity during electric hearing, and with in-vivo 2-photon  $Ca^{2+}$ -imaging to probe cortical plasticity after CI implantation. (Disclosure: Some of these data have been recorded in the lab of Pierre Apostolides at the University of Michigan)

## **A humanized mouse model of tissue repair and transplant allograft rejection following myocardial infarction**

Authors: Jiwon Seo, BS, Liupei Huang, MD, Matthew E Brown, PhD

**Introduction:** Myocardial infarction (MI), also known as heart attack, is one of the leading causes of death in the United States. Heart transplantation remains the definitive treatment for MI-associated heart failure, yet it carries a significant risk of immune rejection. Induced pluripotent stem cell (iPSC) therapy has emerged as a promising approach for immune-tolerated cardiac repair. However, the role of the human immune system in cardiac repair, rejection mechanisms, and interactions with iPSCs following myocardial infarction is still unclear, as commonly used mouse models have substantial immunological differences from humans. Here, to understand human specific immune responses, we evaluated the NeoThy humanized mice for MI studies, including assessing human immune cells in heart and circulation, and via human cytokine profiling.

### **Method:**

- **Humanized Mouse with MI:** We humanized mice by implanting human neonatal thymic fragments, followed by transplantation with CD34+ hematopoietic stem cells derived from cord blood (NeoThy). Allowing about 6 months for human immune cell development, MI was induced via coronary artery ligation of mice hearts.
- **Luminex:** Serum was collected from NeoThy mice with MI at different time points. Both mouse and human cytokine panels were used for all cytokine quantification in NeoThy mice.
- **Flow Cytometry:** The whole blood was collected from NeoThy mice at different time points and quantified the number of human cells in circulatory.
- **Histology:** Hearts of NeoThy mice with MI were collected at different time points and Diaminobenzidine stained to visualize human immune cells.
- **Echocardiography:** The functional and morphological changes in the hearts of MI and non-MI mice were assessed post MI.

**Results:** The result of echocardiography showed functional changes in NeoThy hearts post-MI comparable to those observed in humans and mice. Additionally, NeoThy mice hearts collected exhibited similar cardiac hypertrophy as human post MI. Finally, human macrophages and regulatory T cells (Tregs) were observed in the NeoThy mice hearts following MI, with an increased infiltration of these cells into the cardiac tissue.

**Conclusions:** From this study, we demonstrated that humanized mice showed functional and morphological changes in their hearts comparable to humans and immunocompetent mice post-MI. Moreover, our histology data displayed a new finding of human macrophages and Tregs in the heart of a NeoThy/BLT-class humanized mouse. Particularly, the increased infiltration of these cells may suggest an active role of human immune cells in mouse hearts for the remodeling and repair process post MI. We will utilize this model in future studies of iPSC-derived therapies.

## Diminished Immune Cell Adhesion in Hypoimmune ICAM-1 Knockout Human Pluripotent Stem Cells

Authors: Sayandeep Saha, MS, W. John Haynes, PhD, Natalia M. Del Rio, BS, Elizabeth E. Young, BS, Jue Zhang, PhD, Jiwon Seo, BS, Liupei Huang, MD, Alexis Holm, BS, Wesley Blashka, BS, Lydia Murphy, BS, Merrick J. Scholz, BS, Abigale Henrichs, Jayalaxmi Suresh Babu, BS, John Steill, BS, Ron Stewart, PhD, Timothy J. Kamp, MD PhD, Matthew E. Brown, PhD.

**Introduction:** Hypoimmune gene edited human pluripotent stem cells (hPSCs) are a promising platform for developing reparative cellular therapies that evade immune rejection. Existing first-generation hypoimmune strategies have used CRISPR-Cas9 editing to modulate genes associated with adaptive (e.g., T cell) immune responses, but have largely not addressed the innate immune cells (e.g., monocytes, neutrophils) that mediate inflammation and rejection processes occurring early after graft transplantation. We identified a novel hypoimmune target--the adhesion molecule ICAM-1--that plays multiple critical roles in both adaptive and innate immune responses post-transplantation. In this study, we have used CRISPR/Cas9 to knock out ICAM-1 in hPSCs, then differentiated the cells into therapeutic cardiovascular cell types (endothelial cells, cardiomyocytes, cardiac fibroblasts) for downstream immunoassays.

### Method:

- Flow cytometry
- Immune cell binding assays
- Mixed lymphocyte reactions
- In vivo humanized mouse transplantation

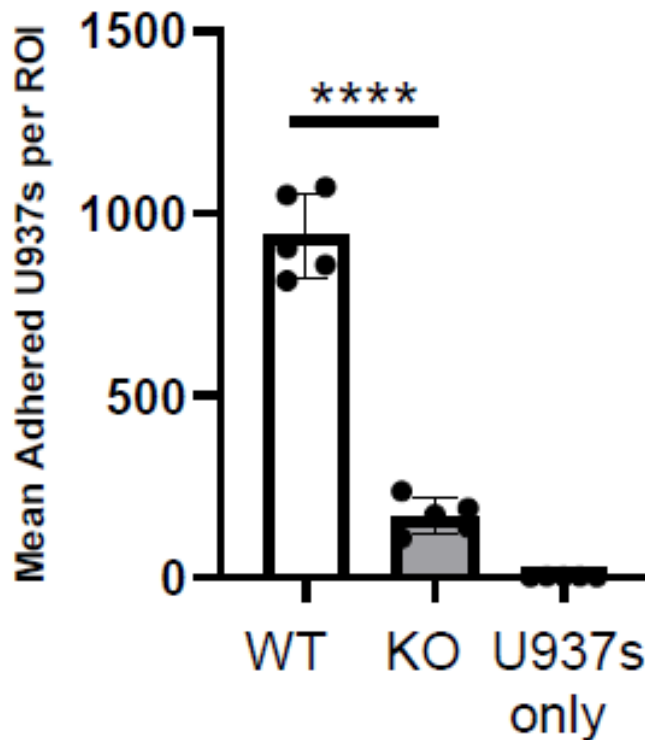
### Results:

- Antibody blocking of ICAM-1 on human pluripotent stem cell-derived cells inhibits immune cell adhesion
- CRISPR/Cas9 knock-out of ICAM-1 ablates surface and secreted ICAM-1 protein and inhibits immune adhesion
- ICAM-1 knock-out results in decreased T cell proliferative responses to human pluripotent stem cell-derived grafts in vitro, and resistance to immune-mediated graft loss in vivo
- Addition of ICAM-1 knock-out to first generation MHC knock-out human pluripotent stem cells confers protection against immune adhesion

**Conclusions:** In this study, we leveraged two critical technological advances (hPSCs and CRISPR/Cas9 gene editing) to precisely introduce ICAM-1 KO into hPSC-cardiovascular cell types. We showed that ICAM-1 KO has clear effects in diminishing binding of innate and adaptive immune cells and that evasion of in vitro and in vivo immune recognition is conferred by this editing approach. Future applications of ICAM-1 KO and related editing could include optimization of engineering strategies to attenuate, but not totally ablate, immune responses to balance diminishing allorecognition and graft loss with allowing for some amount of residual immunosurveillance capacity against malignant transformation and/or formation of viral (e.g., cytomegalovirus) reservoirs. Additionally, our ICAM-1 KO developed for use in hPSC therapeutics could also be a promising target for gene editing in xenotransplantation. Further progress in this area of research will ultimately improve the effective clinical translation of regenerative therapies for cardiovascular pathologies and other diseases.



## Leukocyte Adhesion (U937 Cells)



**Figure 1. Immune Cell Adhesion Assay with ICAM-1 Knock-Out (KO) Pluripotent Stem Cell (PSC)-Derived Endothelial Cells (ECs).** H9 wild type (WT) and ICAM-1 KO PSCs were differentiated into high-purity CD31+CD144+ ECs and stimulated with TNF $\alpha$  (10ng/ml) and IFN $\gamma$  (50ng/ml) for 48 hours. As in Figure 1, U937s were co-cultured with both cell types and washed. Images were acquired on ECHO Revolve | R4 microscope. \*\*\*\* p<0.0001, biological replicates=3. Statistical analysis was performed via Prism 10.2.2 software. ROI = Region of Interest.

## Evaluation of Thymus-Associated T Cell Gene Expression in mRNA-Vaccinated Humanized Mice.

Authors: Wesley Blashka; Liupei Huang; Jiwon Seo; Natalia Del Rio; Arista Whitson; McKeon Lucas; Zach Bromet; Abhiram Nettem; Abigale Henrichs; Matthew Brown

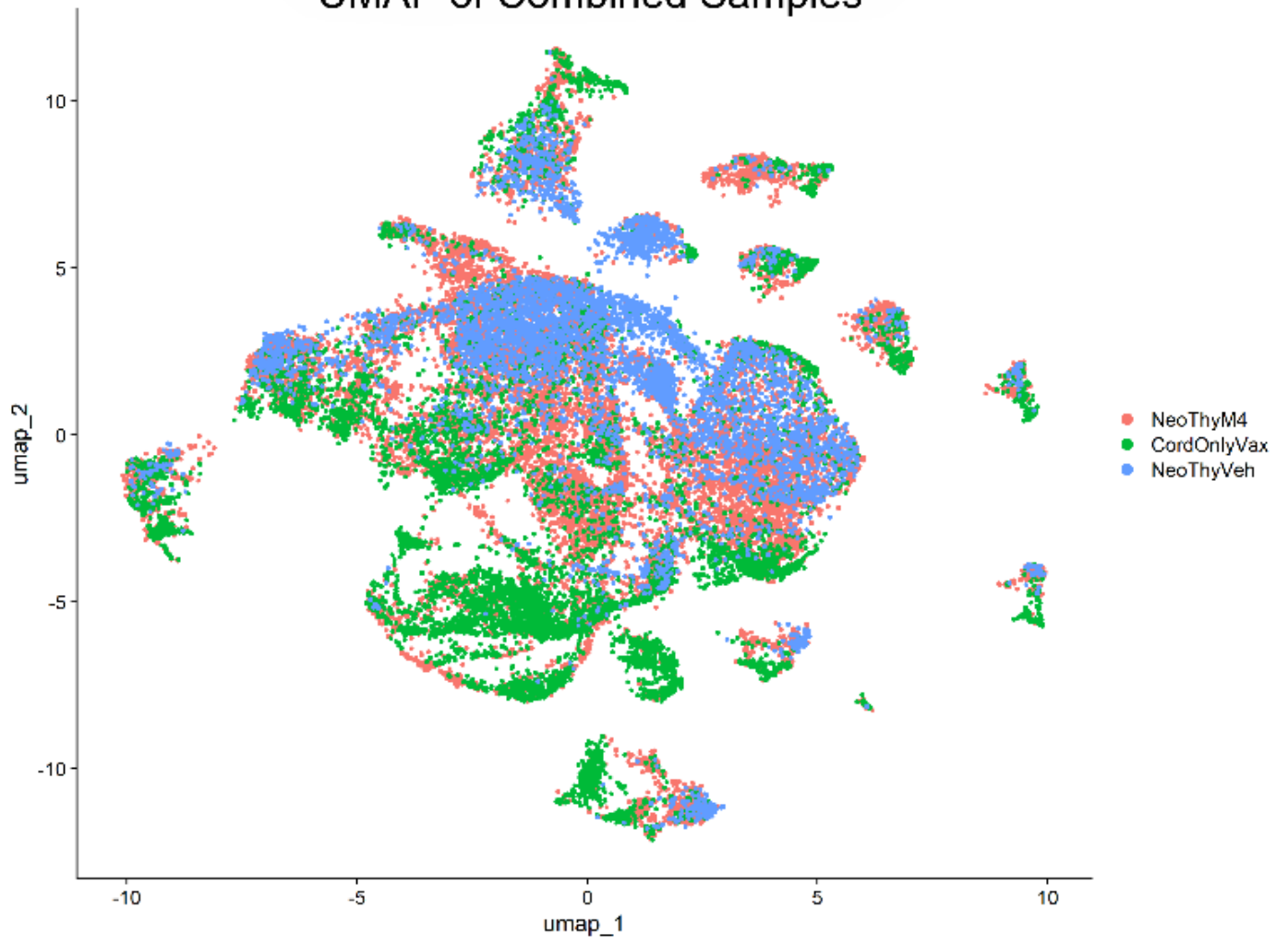
**Introduction:** Humanized mouse models are invaluable in immunological research for generating insights into in vivo human immune responses. This study evaluates the NeoThy model, which incorporates human thymus tissue to foster a more representative in vivo immune system, assessing its efficacy in mounting a controlled antiviral T cell reaction following mRNA SARS-CoV-2 spike vaccination. Its response is compared with the Cord-only humanized mouse model, which lacks thymic tissue and may therefore lack the necessary environment to create mature, competent T cells.

**Method:** We established four experimental conditions: vehicle-only NeoThy, vaccinated NeoThy, vaccinated Cord-only, and vaccinated human control. NeoThy and Cord-only mice were humanized with cells from the same cord-blood donor to reduce variability from donor-specific factors. Both vaccinated groups received a prime and boost dose six weeks apart, with samples collected one week post-booster. Human CD3<sup>+</sup> T cells were profiled using 10X Genomics BEAM-T (Barcode Enabled Antigen Mapping) technology to capture full-length paired T cell receptor (TCR) V(D)J sequences and whole transcriptome gene expression, offering an in-depth view of the models' immune profiles.

**Results:** Both vaccinated models displayed gene expression patterns indicative of immune activation. The NeoThy model uniquely upregulated IFITM2, a gene critical for antiviral response, along with negative regulators ZFP36, NFKBIA, and TNFAIP3, signaling a moderated immune response. The Cord-only model, in contrast, exhibited gene upregulation linked to potential immune dysfunction, including TOX, CD74, GZMK, and CST7. Additionally, the upregulation of PECAM1, a marker of recent thymic emigrants, suggests that Cord-only T cells may not have fully undergone the peripheral maturation processes necessary for optimal function. Analysis of the TCR repertoires revealed that clonal diversity was substantially elevated in both vaccinated conditions compared to the vehicle-only, underscoring vaccine-induced receptor variability. Notably, the vaccinated NeoThy model exhibited greater clonal diversity than the Cord-only model, suggesting a broader adaptive immune response.

**Conclusions:** Preliminary findings suggest that the NeoThy model's incorporation of human thymic tissue may be key to achieving regulated immune responses, positioning it as a promising platform for modeling human immune mechanisms and evaluating therapeutic interventions. While these results warrant further validation, the NeoThy model shows potential for advancing studies in immunology, highlighting its relevance in preclinical research aimed at understanding and refining human antigen-specific immune responses in multiple disciplines.

# UMAP of Combined Samples



## The Topical Protease Inhibitor, Saquinavir, Modulates Translation Pathways in a Transgenic Mouse Model of Anal Cancer Prevention

Authors: Sakura Haggerty, Evan Yao, Wei Zhang, Grace Hansen, Yun Zhou, Garrett Bartelt, Nathan Sherer, Evie Carchman

**Introduction:** Anal cancer is a growing health concern worldwide. It has been previously shown that a topical protease inhibitor, saquinavir (SQV), can decrease anal cancer development in K14E6/E7 transgenic mice. However, its mechanism of action is unknown, as previous work in vivo did not demonstrate changes in HPV E6 and E7 oncoprotein expression. Based on published literature showing that protease inhibitors affect translation, we examined SQV's effects on the phosphorylated inactivation of eukaryotic initiation factor 2 $\alpha$  (eIF2 $\alpha$ ) and eukaryotic elongation factor 2 (eEF2), proteins associated with the initiation and elongation stages of mRNA translation respectively. We hypothesized that eEF2 and eIF2 $\alpha$  phosphorylation would increase in mice treated with SQV at the ATZ.

**Method:** HPV16 transgenic mice, K14/E6/E7, were utilized in this study due to their potential for spontaneously developing high grade anal dysplasia by 25 weeks of age. Mice were randomized into four treatment groups with approximately equal numbers of males and females: no treatment (n=34), SQV (2.5%) only (n=41), 7,12-Dimethylbenz(a)anthracene (DMBA) only (n=37), and DMBA + SQV (n=45). DMBA, a carcinogen, was administered topically to two treatment groups to promote carcinogenesis. Treatment began at 25 weeks of age and concluded after 20 weeks of treatment. Anuses were harvested to be fixed and underwent immunofluorescent staining for phosphorylated eIF2 $\alpha$  or pEIF2 $\alpha$  (Cell Signaling, 3597), eEF2 (Cell Signaling, 2332S), and phosphorylated eEF2 or pEF2 (Cell Signaling, rabbit, 2331). An Ordinary one-way ANOVA with multiple comparisons test (Šídák's) was utilized for the analysis of quantitative IF values at the ATZ, and a Fisher's exact test was performed to compare pEF2 localized expression at the ATZ as well.

**Results:** There was a statistically significant decrease in pEIF2 $\alpha$  expression with SQV alone compared to no treatment ( $p = 0.0005$ ). There were no changes in the markers in overall quantification for eEF2 or pEF2, but there was an increase in localized staining of pEF2 at the anorectal transition zone (ATZ) in mice treated with SQV only compared to no treatment ( $p = 0.0090$ ).

**Conclusions:** In conclusion, our data provides evidence that the mechanism by which the topical protease inhibitor, saquinavir, decreases the development of anal dysplasia into anal cancer in our K14E6/E7 mice model may be related to its role in translational modulation via decreased eIF2 $\alpha$  phosphorylation and increased localized eEF2 phosphorylation at the ATZ.

## Swallowing characteristics with aging in Down syndrome: A preclinical study in the Ts65Dn mouse model

Authors: Marziyeh Ostadi, MSc, Tiffany J Glass, PhD, Nadine Connor, PhD

**Introduction:** Down syndrome (DS) occurs in approximately 1/700 births and is associated with difficulties in speech and swallowing. Aging is known to affect swallowing function, and deficits may be more pronounced in older adults with DS than in the general population. Furthermore, DS is associated with Alzheimer's disease (AD) and dysphagia is a significant comorbidity in AD. Swallowing phenotypes have been found in the Ts65Dn-mouse model of DS. This mouse model displays a number of phenotypes applicable to DS. The current study investigates the effect of aging on swallowing characteristics in 20-month-old adult Ts65Dn-mice, using videofluoroscopic swallow studies (VFSS).

**Method:** This study included 9 male and 7 female Ts65Dn mice and 13 male and 5 female euploids at 20-months old. The mice underwent VFSS to identify significant differences in swallowing measures including swallowing rate (SR), inter-swallow-interval (ISI: a measure of time elapsing between swallows, taken at an arbitrary timepoint during the meal), first ISI and last ISI of the imaging session (an indication of changes in swallowing function that occur through the course of a meal), jaw excursion rate (JER), and facial height (the vertical distance from the top of the skull to the alveolar process in the upper jaw). Preliminary data analysis was performed using two-way ANOVA, statistical significance  $\alpha \leq 0.05$ , to evaluate differences between genotypes, with GraphPad-Prism.

**Results:** The Euploid group exhibited a higher SR than the Ts65Dn group, with no significant effect from sex or the interaction between sex and genotype. The ISI analysis revealed Ts65Dn had significantly longer ISI than euploids, in the absence of a significant effect due to sex, and in the absence of significant interactions between sex and genotype. The comparison of First and Last-ISI measures showed a significant difference between genotype groups. At the start of the meal, the Euploid group exhibited shorter inter-swallow intervals (first-ISI), indicating a faster swallowing rate, progressively slowed by the meal's end, as shown by increased last-ISI. In contrast, the Ts65Dn maintained prolonged inter-swallow intervals consistently throughout the meal, with both first and last-ISIs remaining high.

**Conclusions:** While the Euploid group adapts its swallowing rate over the course of a meal, the Ts65Dn group maintains a consistently slower swallowing rate, possibly indicating differences in their neuromuscular control. The Euploid group has a higher SR than the Ts65Dn group, supporting the interpretation of improved swallow function in the Euploid. Sex does not impact these outcomes.

## A Quantitative Evaluation of Perioperative Hemodynamic Metrics in Mitral Valve Surgery Using 4D Flow MRI

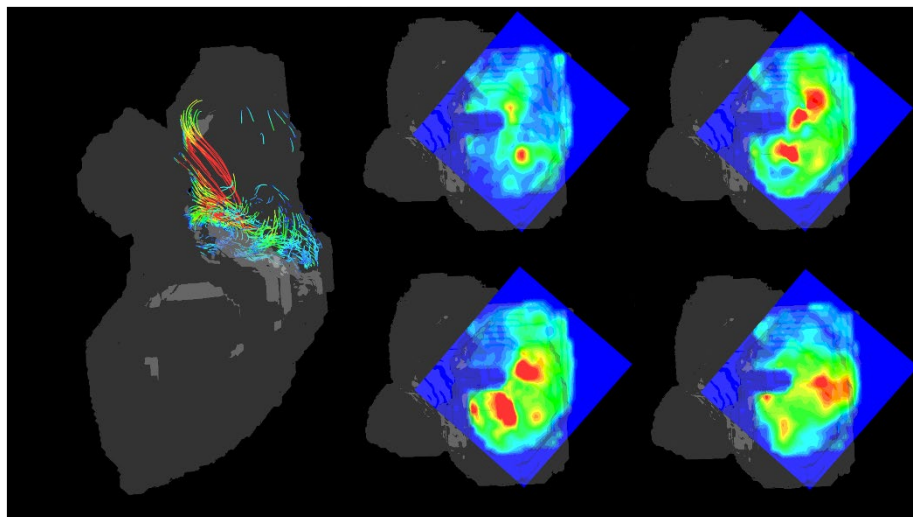
Authors: Leah Gober MD, Mackenzie Sloan, Mike Stellon MD, Alejandro Roldán-Alzate PhD, Andreas de Biasi MD

**Introduction:** Quantification of mitral regurgitation (MR) is complicated by the complex geometry and dynamic interaction between the leaflets, annulus, papillary muscles and left ventricle, however it plays a major role in decision making, and procedural planning. Clinically, echocardiography is the primary imaging modality used, despite its user-dependence and bias. We aim to use 4D Flow MRI derived metrics to define flow abnormalities and predict intraoperative “repairability” and/or the durability of successful intervention.

**Method:** The ultimate goal for this study is to involve pre- and post-operative acquisition of 4D Flow MRI in patients undergoing mitral valve surgery. At the time of submission, this study is in active recruitment and has obtained 2 healthy controls and 2 MR scans. Patients will be scanned on a 3.0T clinical system using a 4D Flow MRI sequence known as PCVIPR. Post-processing includes segmentation and quantification. Metrics are derived from planes placed in the ascending aorta and just distal to the mitral valve and include net flow, peak velocity and regurgitant fraction. Qualitative observations are made regarding flow regimens with the computation of pathlines.

**Results:** For both MR patients, scheduled for mitral valve repair, preoperative echocardiography and 4D Flow MRI had good quantitative agreeability. Metrics are averaged over multiple cardiac cycles and “net” or “peak” values are extracted from this averaged waveform. Compared to healthy controls, MR patients had similar net aortic flows (4.9 vs 4.8 L/min) with significantly decreased net mitral valve flow (5.8 vs 3.13 L/min). Peak velocity was higher in the healthy controls for the ascending aorta but not the mitral valve (135 vs 109 cm/s and 96 vs 139 cm/s, respectively). Regurgitant fraction was 0% for healthy controls and ranged from 39-45% in the MR group, indicating severe disease and correlating well with the clinical picture. Regurgitant jet was observed qualitatively, as depicted in Figure 1, and demonstrates an initial anterior leaflet jet, followed by a more severe posterior leaflet jet.

**Conclusions:** This study demonstrates the value of 4D Flow MRI in quantifying MR, through more direct, less invasive and less variable methods. Additionally, while echocardiography utilizes derivatives of derivatives for metric quantification, 4D Flow uses a single dataset of velocity vectors, thereby reducing the additive error across values. This novel method of studying MR has initial data that correlates well with echocardiography and contributes valuable qualitative visualization for surgical planning.



## The Effect of Cannabidiol (CBD) on Skin Flap Survival in a Rat Model

Authors: Armin Edalatpour, MD, Molly Winchenbach, Peter Nicksic, MD, Robert George MD, Aaron Dingle, PhD, Ahmed Afifi, MD

**Introduction:** Skin flaps are essential in plastic and reconstructive surgery to address various tissue defects; however, they often suffer from necrosis due to insufficient blood supply. The standard care for skin flap necrosis is application of nitroglycerin ointment, a vasodilator that widens blood vessels and increases blood flow. However, nitroglycerin can have side effects including headache, dizziness, and hypotension, limiting its use in certain patients. Cannabidiol (CBD), a major active compound in cannabis, may offer a viable alternative for skin flap necrosis as it promotes vasodilation through smooth muscle relaxation in the vascular endothelium. Previous human and rat studies have demonstrated the benefit of nitroglycerin ointment, but none examined the effect of CBD on skin flap necrosis. Therefore, we aim to assess the effect of topical CBD on necrosis in a skin flap model in rats.

**Method:** Thirty adult Sprague Dawley rats were randomized into three groups (N = 10 each): control, topical CBD, and topical nitroglycerin. A 3x10cm caudally based, dorsal, random pattern skin flap was raised on each rat, with a barrier placed to prevent healing of the flap to the wound bed. The nitroglycerin group received 0.5in (7.5mg) of 2% nitroglycerin ointment applied to each flap. The CBD group received 0.5in (10mg) of CBD ointment applied to each flap. The control group received 0.5in of unmedicated petroleum jelly applied to each flap. Ointments were applied immediately after flap elevation and daily for five days. The percentage of skin necrosis was assessed by five blinded evaluators at postoperative day (POD) 1, 3, 5, and 7.

**Results:** Percent skin necrosis was similar between the CBD and nitroglycerin groups on POD 1 (32.0% vs. 30.6%,  $p=0.971$ ). The CBD group demonstrated non-inferiority to the Nitroglycerin group on POD 3 (51.5% vs. 61.3%,  $p=0.272$ ), POD 5 (52.4% vs. 69.9%,  $p=0.070$ ), and POD 7 (52.5% vs. 69.5%,  $p=0.151$ ).

**Conclusions:** As states legalize cannabis for medical use, it is imperative for plastic surgeons to understand the safety and efficacy of cannabinoids in surgical patients. Our findings demonstrate that CBD achieved similar success in reducing skin flap necrosis as the current standard. Previous studies have demonstrated the vasodilatory effect of CBD on vessels. Our study supports the effectiveness and reveals the promising potential of CBD for enhancing skin flap survival without the adverse effects of nitroglycerin.

# Optimizing Flexor Digitorum Profundus Tendon Repair: A Narrative Review

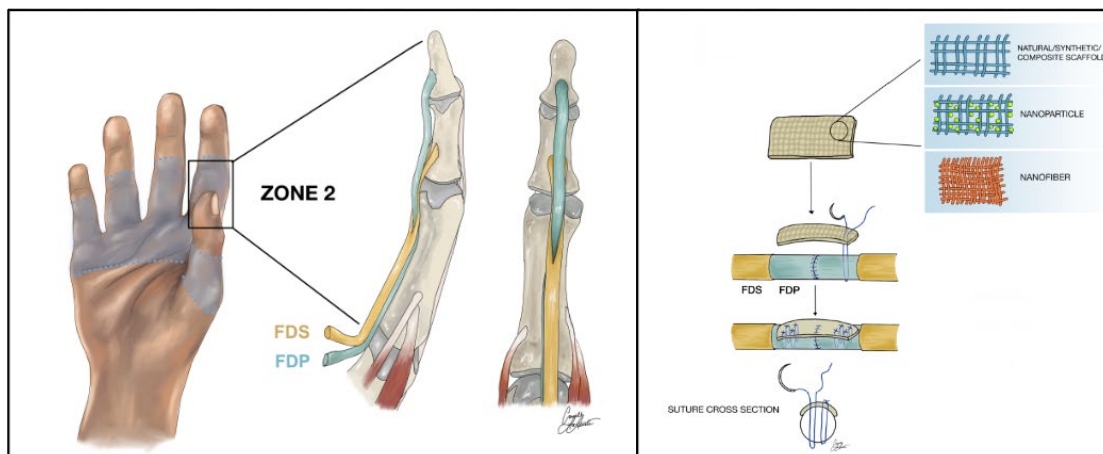
Authors: Rishi Mereddy, Emily E Zona BS, Camille J Laliberte BS, Aaron Dingle PhD

**Introduction:** Zone II flexor digitorum profundus (FDP) tendon injuries significantly impact hand function, presenting unique challenges due to the need for a repair that balances strength and flexibility. Traditional suture techniques risk complications such as adhesions and rupture, necessitating alternative approaches. This review explores Zeng et al.'s technique, which employs a flexor digitorum superficialis (FDS) tendon autograft to bolster FDP repair strength. Integrating biomaterials, particularly collagen-polycaprolactone (PCL) composites, offers further potential to enhance FDP tendon repair while preserving the FDS tendon.

**Method:** This narrative review utilized PubMed to search for systematic reviews published after 2020. Key search terms included “Biomaterials for tendon repair,” “Scaffolds for tendon repair,” and “Nanomaterials for tendon repair.” Three systematic reviews and one literary review were selected based on relevance to FDP tendon repair. Comparative analysis focused on biomaterials’ biomechanical properties, biocompatibility, degradation rates, and compatibility with suture techniques. Natural materials evaluated included collagen and silk fibroin, while synthetic options included polylactic acid, polyglycolic acid, and PCL.

**Results:** Among the materials evaluated, collagen-PCL composites provided an optimal combination of biocompatibility, mechanical strength, and controlled degradation, essential for FDP tendon regeneration. These composites also minimize repair bulk, reducing adhesion risks and enhancing range of motion. While nanofibers and nanoparticles offer benefits in cell proliferation and adhesion reduction, their manufacturing complexity limits their practical application. Silk fibroin (SF) demonstrated promise due to its tensile strength and adaptability in various scaffold forms, such as films and electrospun fibers, although its mechanical properties are generally inferior to synthetic materials. Synthetic options, particularly PCL, offered superior mechanical integrity and controlled degradation but required surface modifications for optimal cell adhesion. The combined analysis identified collagen-PCL as the most promising material, given its blend of mechanical strength and biocompatibility.

**Conclusions:** Collagen-PCL composite biomaterials appear highly promising for Zone II FDP tendon repair, balancing mechanical support with biocompatibility. This review underscores the potential of biomaterials to improve FDP repair without sacrificing FDS tendon tissue. Future directions should focus on testing these biomaterials in cadaver and animal models to confirm their efficacy in biological contexts, monitor tendon healing via imaging, assess functional outcomes, and conduct cost-effectiveness analyses. These insights may provide a foundation for refining biomaterial-based repairs for broader applications in tendon injury management.





## **Osseointegrated Neural Interface: Preliminary Electrophysiological Observations in an Ovine Forelimb Model**

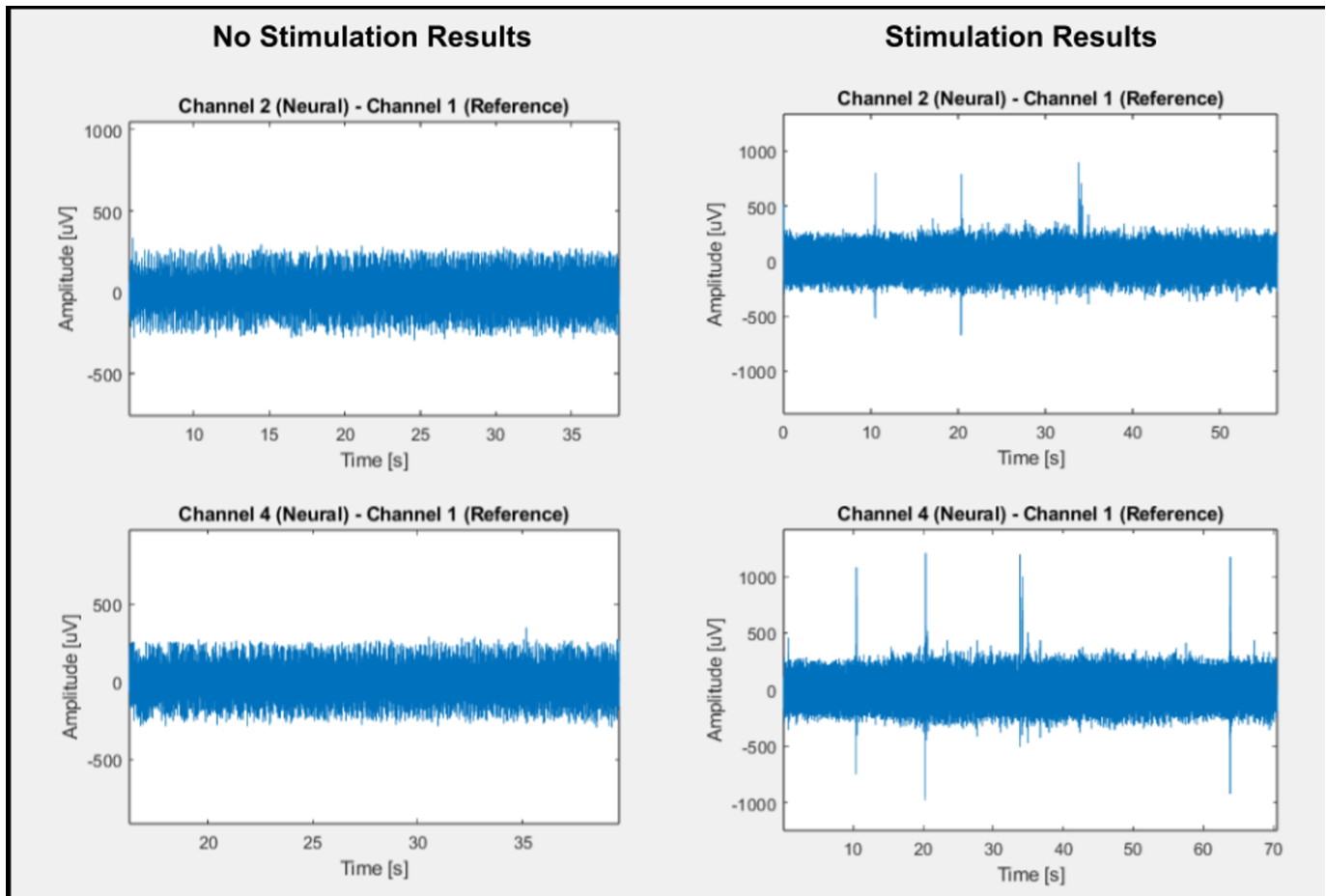
Authors: Rishi Mereddy, Ashlesha Deshmukh B.S., Lucas Sears B.S., Emily E Zona B.S., Kent N. Bachus PhD, James Morizio PhD, Samuel O. Poore MD PhD, Aaron M. Dingle<sup>1</sup> PhD

**Introduction:** The Osseointegrated Neural Interface (ONI) represents a novel approach to peripheral nerve interfacing, with the potential to enable closed loop control of prosthetic limbs. By implanting electrodes within the medullary canal of long bones, the ONI may provide a stable platform for recording neural signals and delivering stimulation. This study seeks to create a clinically translatable large animal model for chronic sensory input in a freely ambulating animal.

**Method:** One female adult sheep underwent a forelimb amputation followed by surgical implantation of the ONI system. Neural electrodes were implanted within the radial nerve. Channels 2 and 4 were assigned for neural recordings, Channel 1 served as the common reference, and Channel 5 was used to record the EMG signal. Following implantation, afferent electrical stimulation trials were performed to verify whether the ONI could evoke and record afferent compound nerve action potentials (CNAPs). Graded stimulation currents were applied, and data was collected with different frequencies and amplitudes. The electrophysiological signals recorded underwent processing to subtract the reference and EMG channels from the neural channels to isolate the neural activity.

**Results:** Afferent CNAPs were recorded from Channels 2 and 4 after 10 weeks post-op. Distinct changes in the neural signals were observed, more so after subtraction of the reference signal (channel 1) from the neural recordings (channels 2 and 4). This subtraction enhanced the view of the stimulation spikes as shown in Figure 1.

(See more on next page.)



**Conclusions:** These preliminary results indicated that ONI could deliver electrical stimulation that could be recorded by the proximal electrode (afferent CNAPs), a critical first step in demonstrating the potential of this system for use in sensory prosthetic control. While encouraging, especially given the limited number of trials, additional research is necessary to confirm consistency across more extensive trials and subjects. The capability of the system to detect CNAPs may eventually facilitate the creation of prosthetics that provide a more organic sense of control by translating neural signals into active output in prosthetic limbs. This work is ongoing. Future work will focus on replicating these findings in the same animal over a period of 6 months, refining stimulation parameters, and exploring the integration of sensory feedback to enhance prosthetic functionality.

## A Bidirectional Translational Approach to Evaluate Perioperative Fluorescence Imaging for Burns

Authors: Mary Junak, MD, Hector Garcia, PhD, Aiping Liu, PhD, Bailey Donahue, BS, Joana Pashaj, BS, Emily Klossowski, MS, Adam Uselmann, PhD, Lee Faucher, MD, Brian Pogue, PhD, Angela Gibson, MD, PhD

**Introduction:** The primary method to evaluate healing capacity of a burn wound is visual assessment; a subjective interpretation that risks over-excision. This ongoing study investigates the use of indocyanine green (ICG) fluorescence imaging to evaluate burn depth and healing potential. Early enrollment challenges encountered with the heterogeneity of human burn wounds, difficulty of patient recruitment early after a trauma, and variable timing of assessment post-injury led to the addition of a parallel translational pre-clinical swine model.

**Method:** Human subjects ( $n = 13$ ) and adult pigs ( $n = 2$ ) with burns of various depths received a 7 mg injection of ICG for angiography (ICGA) followed by a 5mg/kg intravenous (IV) infusion of ICG on post-burn day (PBD) 2 or 3. Second window indocyanine green (SWIG), a novel method of delayed fluorescence imaging, was performed the day after ICG injection on a region of interest (ROI) during wound care. A full thickness skin biopsy was taken from the center of the ROI and ICG microscopy and histologic staining was performed for tissue architecture and viability. MATLAB R2023b was used for data processing and GraphPad Prism 8.0 was used for statistical analyses.

**Results:** In patient samples, there was high interpatient variability between histologic cellular viability and perfusion as measured by ICGA peak fluorescence intensity when looking at the ROI ( $R^2 = 0.04$ ). Microscopically, the tissue exhibited intense inflammatory cell infiltrate at the interface of viable and nonviable tissue in some tissues without correlation to need for skin grafting. Patients had a wide range of SWIG fluorescence intensities and patterns. Qualitatively within patients, ICGA and SWIG signals exhibit inverse fluorescence intensities. In our pig model, there was a strong linear correlation between increasing burn depth and decreasing ICGA peak fluorescence intensity ( $R^2 = 0.84$ ). Additionally, samples with a burn depth  $\leq 50\%$  demonstrated significantly higher SWIG fluorescence intensity compared to those  $> 50\%$  ( $p = 0.003$ ).

**Conclusions:** Variability in perfusion and inflammation contributes to heterogeneity in the ICGA and SWIG parameters in patients. The experimental approach we have pivoted to given the known challenges with human subjects research, exacerbated in trauma and burn injury, represents a paradigm shift. This iterative, bidirectional approach using human subjects and animal models in parallel, allows more nimble experimental design modifications and data interpretation to ensure translational success.

## A Protocol to Evaluate the Local Burn Wound Environment with Sequential Sampling

Authors: E.T. Klossowski, MS, M. Junak, MD, B.A., Donahue, BS, A.L.F. Gibson, MD, PhD

**Introduction:** Burn wound progression is the process in which a superficial burn evolves into a deeper burn that may require surgical intervention. Several theories have been proposed for burn progression through preclinical animal studies including ischemia, reactive oxygen species, autophagy, and inflammation. Given the lack of human data on burn progression, we hypothesized that wound exudate may be a feasible biomarker to identify burn progression. Preliminary studies were conducted to assess feasibility of fluid protein collection.

**Method:** Ex vivo and in vivo approaches were utilized. Fluid samples were extracted from ex vivo human burn tissue after 24 hours in culture. Next, consent was obtained from an admitted burn patient and samples were collected during routine daily dressing changes using a non-stick gauze placed directly onto the burned region of interest (ROI over a three-day period). The gauze was collected 24 hours later during routine wound care. Protein concentrations were assessed via Modified Lowry Protein assay. The protein concentration of the standard of care polypeptide antibiotic ointment used in dressing changes was also assessed.

**Results:** Initial studies of wound exudate from an ex vivo tissue culture model using surgically excised burned human skin resulted in protein concentrations ranging from 1715.61 to 5362.75 ug/mL. In vivo, protein was present in the exudate of two burned Regions of Interest (ROI) daily for 3 days. Protein concentrations were consistent within each ROI, but a significant difference was noted between the ROIs, with higher levels of protein detected in ROI 1 (Arm) compared to ROI 2 (Chest). Protein concentrations of polypeptide ointment alone were much lower than patient samples. Slow patient enrollment prevented the collection of additional patient samples.

**Conclusions:** We report a noninvasive method to collect burn wound exudate as a potential biomarker for burn progression. We found that enrollment is challenging in the early period after a traumatic injury due to the acute stress of the event and inability to consent in a timely manner. Our preliminary studies suggest that our protocol is feasible to collect burn exudate for future analyses. Despite being a polypeptide, the standard of care ointment used in wound care has negligible impact on the total protein concentration obtained. Importantly, this allows us to maintain the standard of care of patients during our study. Future studies will utilize these methods to investigate how changes in specific protein expression in the wound environment correlates with burn wound progression in humans.

## Protoporphyrin IX based- photodynamic therapy enhances burn wound healing in ex vivo human skin

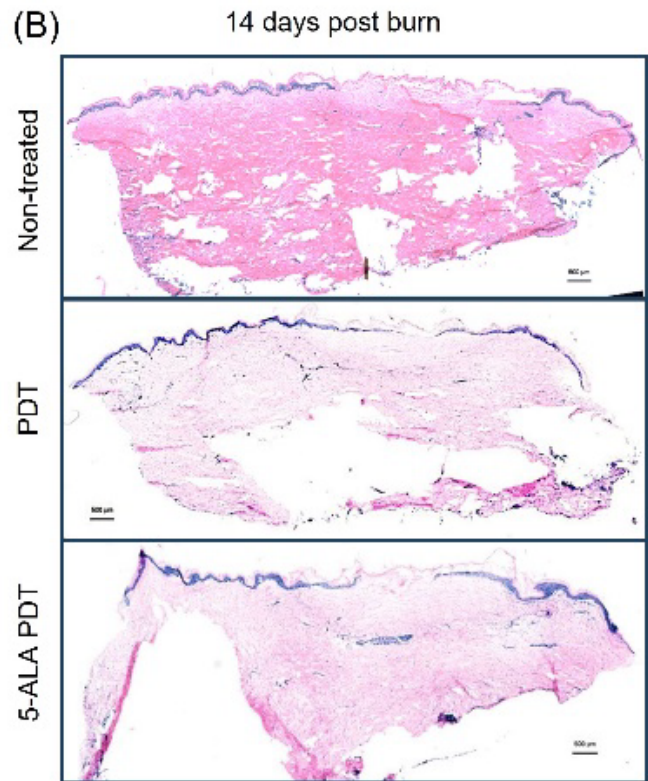
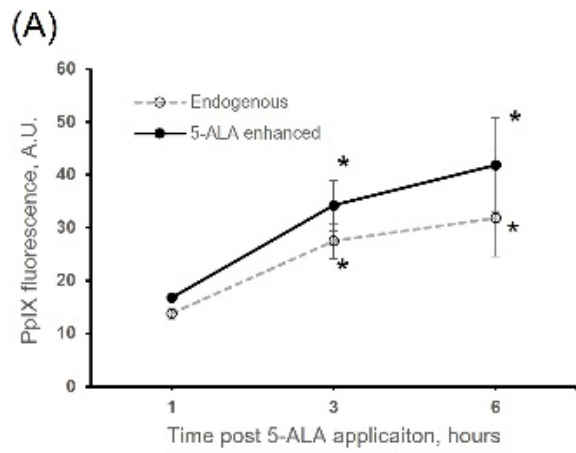
Authors: Aiping Liu, PhD, Marien I. Ochoa, PhD, Emily T. Klossowski, MS, Bailey A. Donahue, BS, Joana Pashaj, BS Mary Junak, MD, Brian Pogue, PhD and Angela LF Gibson, MD/PhD

**Introduction:** Photodynamic therapy (PDT) is widely used to treat skin tumors and infections where protoporphyrin IX (PpIX) is commonly used as the photosensitizer. PpIX is synthesized through the heme pathway from its precursor 5-aminolevulinic acid (5-ALA) endogenously and can be induced through topical application of 5-ALA. In contrast to traditional PpIX-PDT, low-dose PpIX-PDT utilizes lower concentrations of photosensitizer and/or irradiation doses to generate a lower level of ROS, which has been shown to promote burn wound healing in rodents. However, translation of this therapy in human burns remains unknown. This pilot study aimed to evaluate PpIX-PDT in human burn wound healing ex vivo.

**Method:** Partial thickness burns were created on ex vivo human skin using a customized burn device. Three 5-ALA application groups and three groups without 5-ALA were used to study the temporal production of PpIX. The 5-ALA groups had PpIX imaged at 1, 3 or 6 hours after topical application of 20% 5-ALA solution along with the corresponding groups without 5-ALA application. To study the effect of PpIX-PDT on burn wound healing, PDT with or without application of 5-ALA, and a non-treated group were evaluated. 3 hours after 20% ALA application, the PDT groups were illuminated by red light (630 nm) using a light-emitting diode lamp on the burn region at an energy density of 20 J/cm<sup>2</sup>. Tissue biopsies were then cultured for 14 days, processed for histology and stained for Lactase Dehydrogenase to evaluate cell viability and healing.

**Results:** PpIX fluorescence was significantly higher after 3 hours of 5-ALA application than that of 1 hour of application. PpIX fluorescence at 6 hours of 5-ALA application was not significantly different from that of 3 hours of application (Figure 1A). Interestingly, without 5-ALA application, PpIX was produced endogenously in burn wounds and increased with time. 20% 5-ALA application non-significantly enhanced PpIX production in burn wounds. After 14 days, both PDT groups demonstrated enhanced reepithelization in burn wounds without overt cytotoxicity compared to the non-treated control (Figure 1B). Healing after PpIX PDT treatment does not require exogenous 5-ALA application.

**Conclusions:** This pilot study demonstrated efficacy of PpIX-PDT in burn wound healing in human skin. In addition, our data showed that endogenously PpIX-PDT has similar effects as 5-ALA enhanced PDT in burn wound healing. We will further optimize PDT parameters such as increasing 5-ALA concentration, light dose and treatment scheme using this ex vivo human skin model of burn.



**Figure 1.** (A) Time course of endogenous and 5-ALA enhanced PpIX fluorescence produced in burn wounds. (B) Lactase Dehydrogenase images (blue = viable cells) of burn wounds in non-treated, PDT and 5-ALA enhanced PDT groups after 14 days post burn. Two-way ANOVA analysis was conducted to compared the averaged PpIX fluorescence over time in burns with/without 5-ALA application. \*,  $P < 0.05$  compared to 1 hour post 5-ALA application.

## Evaluating Swallowing Dysfunction in Down Syndrome: Analysis of Df(17)2 and Df(16)8 Mouse Models

Authors: Gaurav Singhal, PhD, Erin H. Fisher, Tiffany J. Glass, PhD

**Introduction:** Individuals with Down syndrome (DS) often experience significant swallowing challenges. Our previous work with the Ts65Dn mouse model of DS, which incorporates a partial trisomy of regions of mouse chromosomes 16 and 17 (syntenic to human chromosomes 21 and 6, respectively), revealed significantly slower swallowing rates as adults and reduced body weights at weaning on postnatal day 21 (P21), whereas the Dp(16)1Yey model of DS with a duplication of mouse chromosome 16 showed typical swallowing as adults and typical weights at P21. This study explores swallowing phenotypes in two additional mouse models, Df(17)2 and Df(16)8. We hypothesize that specific deletions in mouse chromosome 17 (Df(17)2) and mouse chromosome 16 (Df(16)8) will result in perturbations in swallowing functions, potentially impacting early postnatal body weights and oral-motor functions essential for normal swallowing.

**Method:** To assess early growth, the body weights of WT (7 males, 8 females) and Df(17)2 (9 males, 5 females), and WT (12 males, 19 females) and Df(16)8 (7 males, 17 females) mice were recorded at P21 and P22. Videofluoroscopic swallow study (VFSS) assessed swallowing function in WT (12 males, 2 females) and Df(17)2 (2 males, 4 females), and WT (6 males, 5 females) and Df(16)8 (9 males, 15 females) mice at 8-10 weeks. Key metrics included swallow rate (SR), jaw excursion rate (JER), interswallow interval (ISI), and jaw cycle swallow ratio (JSR). T-tests and two-way ANOVA were used to evaluate statistically significant differences at  $\alpha < 0.05$ .

**Results:** At P21, Df(17)2 mice exhibited significantly reduced body weights ( $p = 0.0004$ ), particularly in males ( $p = 0.0047$ ), with this difference persisting at P22 ( $p < 0.0001$ ). No significant differences in body weight were observed in Df(16)8 mice ( $p > 0.05$ ). VFSS results showed that Df(17)2 mice had a lower JER than WT ( $p = 0.0045$ ). Female WT mice showed a higher ISI ( $p = 0.0115$ ) and JSR ( $p = 0.0068$ ), but a lower SR ( $p = 0.0192$ ) compared to Df(17)2 females. In Df(16)8 mice, ISI ( $p = 0.0045$ ) and JSR ( $p = 0.0230$ ) were significantly lower, while JER was significantly higher ( $p = 0.0284$ ) when compared to WT. WT females displayed higher ISI ( $p = 0.0030$ ) and JSR ( $p = 0.0080$ ) than Df(16)8 females.

**Conclusions:** This study suggests the critical roles of specific regions on mouse chromosomes 16 and 17 in swallowing function. This lays the groundwork for understanding the genetic underpinnings of swallowing difficulties. Acknowledgements NIDCD R01DC019735 and NICHD R01HD104640

# Hypoglossal nucleus phenotypes of the Ts65Dn mouse model of Down syndrome through aging.

Authors: Lucille M Vue, MS, Tiffany J Glass, PhD

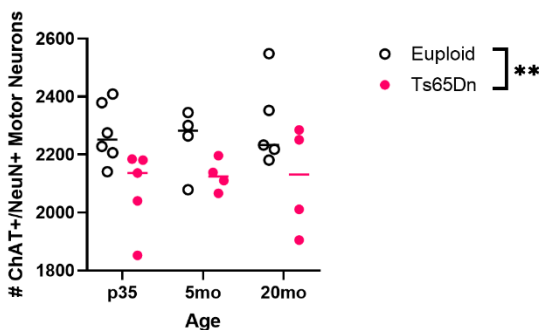
**Introduction:** Down syndrome (DS) is a developmental disorder in which atypical tongue movements contribute to impaired speech, breathing, swallowing and feeding. The tongue muscles are innervated by cholinergic motor neurons located in the hypoglossal nucleus. While a loss of cholinergic neurons has been reported to occur in Ts65Dn, it is currently unknown whether cholinergic motor neurons directing tongue movement are impacted, and whether this is impacted by age. Therefore, this study tested the hypothesis that the Ts65Dn mouse model of DS demonstrates significant biological differences of the hypoglossal cholinergic motor neurons at different ages relative to euploid sibling controls.

**Method:** Female Ts65Dn and euploid sibling controls (n=4-6 per group) were euthanized at postnatal days of age 35-36 (p35-36), 5 months (5mo) and 20 months (20mo), corresponding respectively to juvenile, mature adult and old adult ages. Brains were frozen on dry ice and serial cross sections extending throughout the hypoglossal nucleus were stained through immunofluorescence to identify hypoglossal cholinergic motor neurons expressing both neuronal nuclei (NeuN) and choline acetyltransferase (ChAT). A semi-automated image analysis protocol was created and used to quantify and characterize hypoglossal motor neurons in images of serial tissue sections. Dependent variables included motor neuron cell count (#) and density (# cells / mm<sup>2</sup>). Data were analyzed by 2-way ANOVA to detect significant effects of genotype and age, as well as significant interactions between genotype and age.

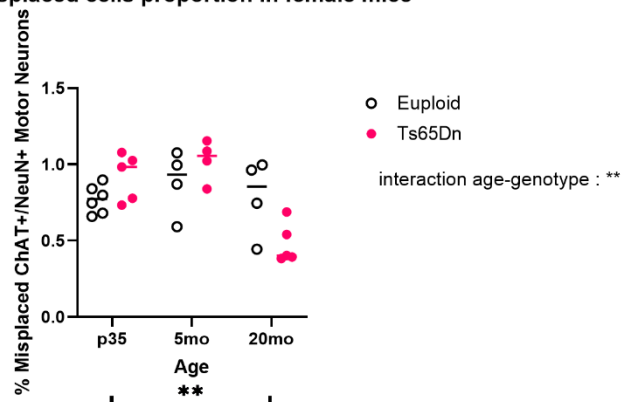
**Results:** Ts65Dn females show significantly fewer hypoglossal motor neurons than euploid sibling controls, and older mice present a lower neuronal cell density within the hypoglossal nucleus than juvenile mice. Ts65Dn mice have fewer hypoglossal motor neurons than euploid siblings [F(1,22)=11.53, p=0.0026] as evaluated through total numbers of hypoglossal motor neurons present. Aging induces a decrease in hypoglossal nucleus neuronal density as older mice have a lower count of motor neurons per mm<sup>2</sup> of tissue area [F(2,22)=12.72, p=0.0002].

**Conclusions:** While expansion of this study is ongoing, these early results suggest that significant phenotypes of the hypoglossal motor nucleus occur in the Ts65Dn model of DS. The use of mouse models to clarify hypoglossal nucleus phenotypes associated with DS and age will guide future research to ensure that therapies targeting tongue movement disorders are as biologically informed for patients with DS as they are for the general population.

Hypoglossal motor neuron counts in female mice



Misplaced cells proportion in female mice





## Microanatomical Differences of Intrinsic Tongue Muscles in the Adult Ts65Dn Mouse Model of Down syndrome

Authors: Jayde C. Sitko, Tiffany J. Glass, PhD

**Introduction:** Down syndrome (DS) is a developmental disability that may impact tongue muscle maturation, especially intrinsic tongue (IT) muscles which are essential for important oral motor tasks such as eating and swallowing. Individuals with DS typically encounter challenges involving tongue movement, however, the specific impact on IT muscles in adults with DS remains unclear. This study used the adult Ts65Dn mouse model which allows researchers to explore DS-related tongue muscle differences that would be difficult to study in humans. The hypothesis of this study is that the sizes of IT tongue structures and transverse tongue myofibers in Ts65Dn mice differ from the euploid controls.

**Method:** Male Ts65Dn mice (n=5), male euploid controls (n=11), female Ts65Dn mice (n=8), and female euploid controls (n = 5) were euthanized at five months of age, and the IT was collected, sectioned, and stained using immunofluorescence. One entire tongue section was imaged from each mouse. Transverse myofiber cross-sectional area (CSA) and minimum feret diameter, which are independent measures of myofiber size, were analyzed using MATLAB's Semi-automatic Muscle Analysis using segmentation of Histology (SMASH) application. Tongue length and specific IT muscle structures including areas of the superior longitudinal muscle (SL), inferior longitudinal muscle (IL), transverse/verticalis muscles (T/V), and whole IT section areas were measured through ImageJ. 2-way ANOVAs assessed whether the independent variables of genotype and sex significantly impacted measures of transverse myofiber CSA and minimum feret in the anterior, middle, and posterior regions of the IT, along with measures of IT muscle sizes and overall tongue section area size.

**Results:** Preliminary results show that Ts65Dn mice had significantly shorter tongues ( $p=.003$ ) and smaller IL ( $p=.007$ ), T/V ( $p=.001$ ), and whole IT section areas ( $p=.002$ ) than euploid controls. The Ts65Dn mice had significantly smaller myofiber cross-sectional areas in the anterior IT region compared to the euploid controls ( $p=.049$ ), although no significant differences were observed in minimum feret in the anterior IT region. No significant differences were found for sex, and there were no significant interactions between sex and genotype.

**Conclusions:** This study shows genotype-specific differences in IT size for five month old mice, which is a mature adult age. Adult Ts65Dn mice have smaller IT muscles than euploids. There may be region-specific differences in myofiber size, such that Ts65Dn may have smaller myofibers specifically in the anterior region of the IT, but work is ongoing to increase sample sizes, and verify reproducibility of these findings.

## Sleeve gastrectomy improves cognition and frailty in AD prone mice

Authors: Julia Illiano BS, Reji Babygirija MS, Michelle Sonsalla MS, Grace Zhu PhD, Luiz Lopez, Odin Schaepekens, Dudley Lamming PhD, David A. Harris MD

**Introduction:** Obesity is a major risk factor for Alzheimer's disease (AD). Sleeve gastrectomy (SG; bariatric surgery) effectively treats metabolic diseases. In humans, SG improves metabolic health and cognition, but the effect of SG on AD is understudied. We hypothesized that SG would slow cognitive decline and improve metabolic health in AD prone mice.

**Method:** We employed a triple transgenic (3xTg) mouse model prone to both diet induced obesity and AD via accumulation of A $\beta$  plaques and tau tangles. Twenty 3xTg female mice were preconditioned on western diet (WD). They were weight matched to sham or SG surgery and continued WD after recovery. Metabolic phenotyping, indirect calorimetry, body composition, frailty, weight, and food intake were tracked longitudinally. Cognition and memory were assessed with validated behavioral assays including Novel object recognition (NOR) and Barnes maze (BM). Mice were sacrificed 12 months post-operatively. AUC, one-way ANOVA with Dunnett corrections, t-tests, and Chi-squared were used, where appropriate.

**Results:** Despite consumption of WD, SG mice had greater percent weight loss than shams with no differences in food intake. SG improved glucose tolerance( $p=0.016$ ) and lowered fasting blood glucose( $p=0.002$ ) at 1-month post-op, but not at later timepoints. This was independent of insulin sensitivity, which was not different. At 2 months, SG mice had decreased fat mass( $p=0.022$ ), increased lean mass( $p=0.021$ ), and increased glucose utilization (RER; $p=0.005$ ). Energy expenditure did not differ. SG mice had consistently lower frailty scores than shams( $p=0.04$ ). At 10 months, SG mice showed significantly improved short- and long-term memory during BM testing. Three-quarters of SG mice could complete memory tasks versus one sham.

**Conclusions:** SG induces short term improvements in metabolic health and sustained improvements in frailty and cognition in 3xTg mice, despite prolonged exposure to a pathologic diet. We will assess AD pathology and autophagy markers to understand how SG affects disease progression. Future studies will explore SG in male 3xTg mice. SG may be an effective intervention for patients with obesity prone to AD.

## The synergistic impact of resistance training and altered protein diets in sleeve gastrectomy

Authors: Grace Zhu, Luiz Lopez, Leah N. Braucher, Szczepan Olszewski, Julia Illiano, Samuel Saghafi, Isaac Grunow, Adam R. Konopka, Dawn B. Davis, Dudley W. Lamming, David A. Harris

**Introduction:** Sleeve gastrectomy (SG) is one of the most effective treatments for obesity. Surgery itself and the resulting substantial weight loss often leads to improvements in many obesity-related conditions such as type 2 diabetes and metabolic dysfunction associated fatty liver disease. Following SG, patients are told to consume a protein preserving diet to retain lean skeletal muscle mass and prevent protein malnutrition. However, there's inadequate evidence to evaluate the effect of dietary protein on lean mass loss. Our previous study on protein restriction after SG in mice revealed that diet heavily influenced body weight and glucose homeostasis. Low protein intake was associated with energy expenditure and weight loss. In this study, we explored the interplay of diet and exercise in mice after SG to investigate whether routine resistance exercise training modified the physiologic response of low and high protein intake after SG.

**Method:** C57BL/6J mice were preconditioned on western diet for 12 weeks and subjected to SG or sham surgery. Mice were then switched to a high (36%) or a low protein (7%) diet. Four weeks after the surgery, mice were further divided into the resistance training group or the sedentary group. Body weight, food consumption, and body composition were monitored. Metabolic phenotyping, indirect calorimetry, and muscle strength assay were performed.

**Results:** No significant difference in adiposity between the exercise and sedentary groups was observed, although the exercise mice weighed slightly less than the sedentary mice while on a 7% protein diet for both SG and sham groups ( $p = 0.04$  and  $0.05$  for SG and sham, respectively). All the exercise groups pulled similar weight when normalized to body weight and showed improved muscle strength and flexor digitorum longus muscle weight compared to their respective sedentary counterparts ( $p = 0.04$  and  $0.05$  for 36% and 7% protein diets, respectively). While there was no difference in glucose tolerance between exercise and sedentary mice on the low protein diet, exercise trended to improve glycemic control in SG mice on the high protein diet.

**Conclusions:** Routine resistance exercise is sufficient to maintain lean mass while further driving weight loss in SG mice on low protein. While mice on a high protein diet generally had worse glycemic control than those on a low protein diet, exercise seemed to improve glucose tolerance after SG in high protein fed mice. More studies are needed on the safety and efficacy of low protein diets in humans after SG to improve outcomes.

## Adjudication Instrument for Infection in Critically Injured Trauma Patients

Authors: Mary Junak, MD, Meghana Peddoddi, Nicole Werner, MD, Patrick Shahan, MD, Laura Hammel, MD, Hilary Faust, MD, Christopher Saddler, MD, Ambar Haleem, MD, Mehreen Kijat, MD

**Introduction:** Approximately one in four trauma patients admitted to the Intensive Care Unit (ICU) develop an infection resulting in 20% mortality. Severe traumatic injuries cause a systemic inflammatory response manifested by tachycardia, fever, leukocytosis, and ultimately end-organ dysfunction. In trauma patients, many of the Sepsis-3 criteria for organ dysfunction are present due to injury which makes it difficult to distinguish the systemic inflammation due to injury from infection. The lack of gold-standard makes it difficult to evaluate biomarkers to diagnose infection in trauma patients. We developed and piloted an adjudication instrument to determine infection status in critically injured trauma patients.

**Method:** We formulated an adjudication instrument consisting of clinical data abstraction and an infection status form. We summarized the abstracted clinical data in case report forms (CRF) including history of presentation and injuries, operations, vital signs, laboratory data, imaging, culture results, and antimicrobial administration during the first 10 days of hospitalization. The infection status form includes likelihood of infection on a Likert scale (not infected, unlikely, possible, probable, definite), site of infection, infection type, hospital day of clinical suspicion of infection, and day of anti-infective therapy. Next, we formed an adjudication committee of six clinical experts who were trained on the adjudication instrument. We randomly assigned two adjudicators to independently review the CRF and complete the infection status form. If both adjudicators provided concordant responses, consensus was achieved. If there was a discrepancy in responses, a third adjudicator was assigned for an independent review, using agreement between two of the three adjudicators as the final response. If a discrepancy remained, a committee meeting was held.

**Results:** Of the 115 patients enrolled in this study, 8 have undergone adjudication of infection status. Concordance between the two primary adjudicators for infection status was found in 87.5% (7/8) of the cases. Of these, infection was identified in 28.6% (2/7). In both cases, adjudicators assessed a lung source of bacterial infection and chose to initiate anti-infective therapy. In the one case where adjudicators disagreed on infection status, adjudicator 1 chose “unlikely,” while adjudicator 2 chose “probable” for infection status and need for anti-infective therapy. This case will be reviewed by a third adjudicator.

**Conclusions:** In the absence of a gold standard for the diagnosis of infection in critically injured trauma patients, an adjudication instrument that can be used by a clinical adjudication committee can be an effective way to standardize the assessment of study endpoint.

## Plasma metagenomic sequencing in organ transplant donors.

Authors: Miraf Molla, BS, Haikun Zhang, PhD, Eddie Dominguez, PhD, Michael Sclarici, MD, Caitlin Pepperell, MD, Joshua Mezrich, MD, Mehreen Kisat, MD.

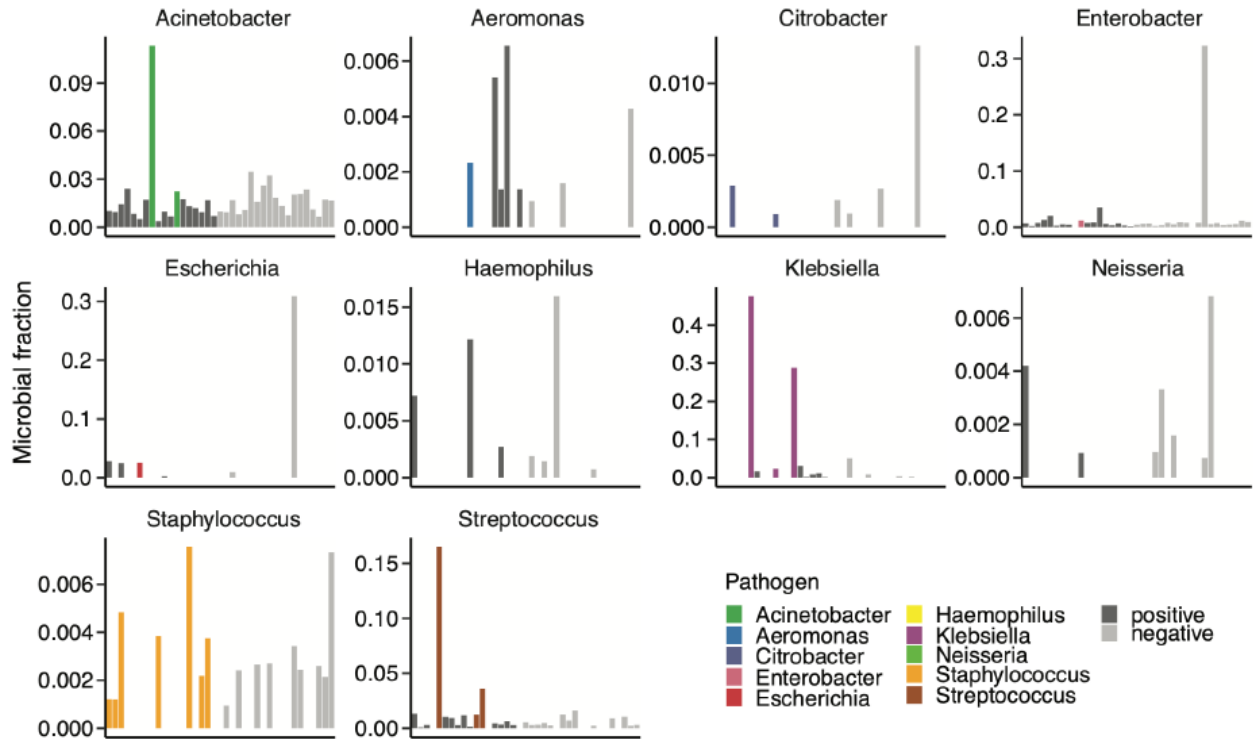
**Introduction:** Organ transplantation is the treatment of choice for many patients with end-stage disease. Most organs are donated from patients after brain death (BD, irreversible cessation of all brain functions). In critically ill patients, the length of time from BD to organ recovery is variable and can range from two to five days. During this time, the BD donor is at risk of infection which can be transmitted to potential recipients. Microbial cultures are the standard-of-care, but they fail to identify any pathogen in 30-60% of patients with infections. We hypothesize that analysis of microbial DNA (mDNA) in plasma can identify the presence of infection in donors.

**Method:** We prospectively enrolled 37 donors and collected blood samples at the time of organ recovery. We extracted plasma DNA, prepared single-stranded DNA libraries (ssDNA), and applied size selection to exclude fragments  $>110$  bp (to preferentially recover mDNA from the pool of cell-free DNA). Following sequencing, we performed taxonomic classification and evaluated pathogen detection rate using plasma metagenomic sequencing as compared to standard microbiology. Correlation between mDNA fraction and cell-free DNA (cfDNA) was assessed using a Pearson's correlation test. Differences in mDNA fractions between samples were evaluated using Mann-Whitney U test. A pathogen was considered detectable by plasma metagenomic sequencing if the observed genus-level mDNA fraction was at least 2.5 median absolute deviations away from the median across the set of samples from culture negative patients.

**Results:** We analyzed 37 plasma samples from 37 donors. Of these, 18 (49%) had 23 positive microbiology cultures between BD and organ recovery. These included 18 respiratory (bronchoalveolar lavage, tracheal aspirate, sputum), 2 blood, 1 urine, and 2 cerebrospinal fluid cultures. 8 out of the 23 (35%) cultures were polymicrobial. mDNA fraction was negatively correlated with cfDNA yield ( $p = -0.782$ ). mDNA fractions were not significantly different between culture-positive and culture-negative patients ( $p = 0.707$ ; median mDNA fractions 0.0164% and 0.0161%, respectively). We detected pathogen-specific DNA in 72% (13/18) of culture positive donors (Figure1).

**Conclusions:** Our results demonstrate that pathogen-specific DNA is detectable using plasma metagenomic sequencing in donors. This can enable early recognition of infection and treatment of donors before organ recovery.

### ssDNA size selected



## **Enhanced Viability and Proliferation of Human Neural Progenitor Cells Using an Oil-Overlay and Autonomously Regulated Oxygen Microenvironment (AROM)**

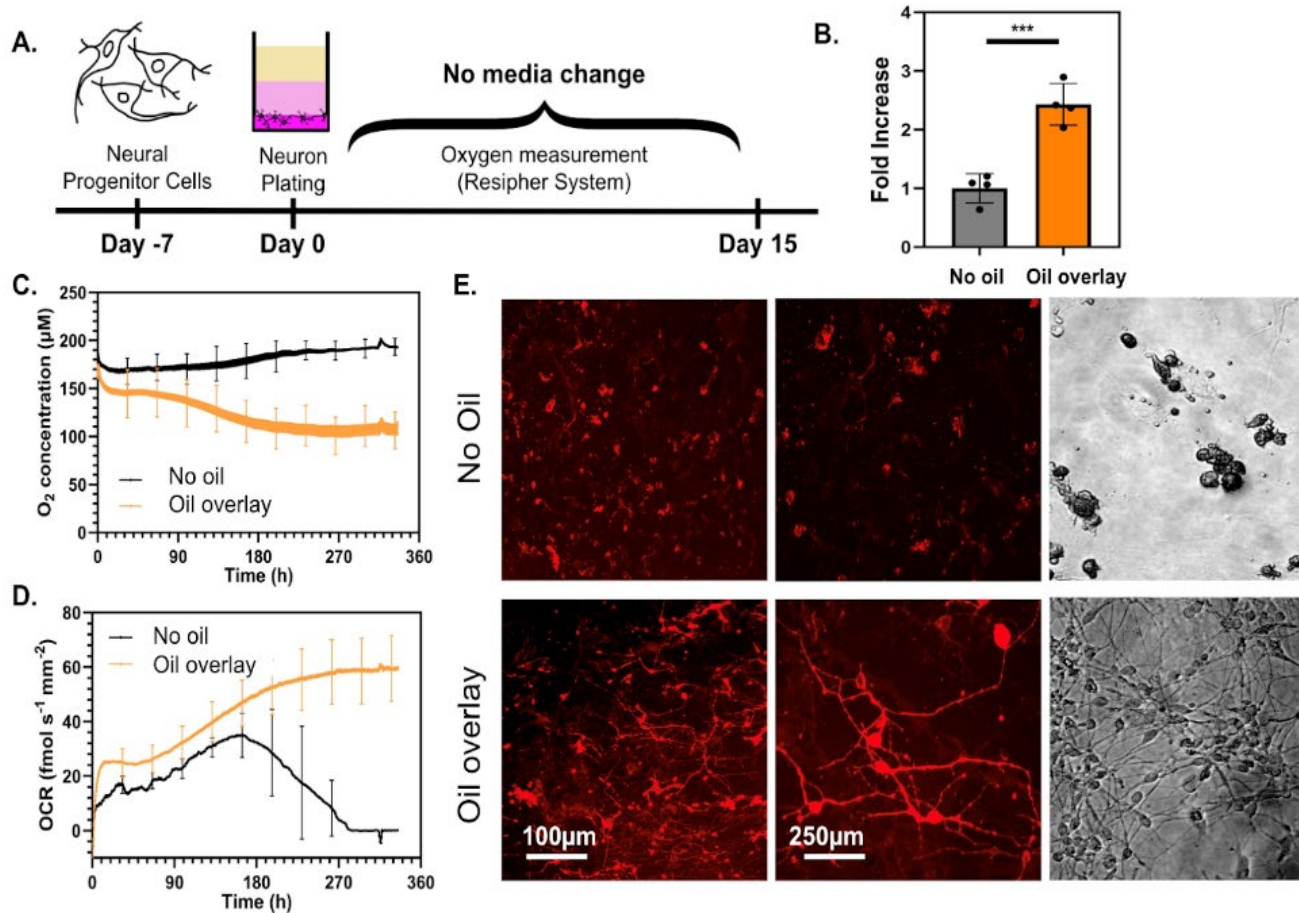
Authors: Ligi Milesh, PhD, Nai-Wen Liang, Chao Li, PhD, Hau D. Le, MD

**Introduction:** Culturing human neural progenitor cells (NPCs) *in vitro* faces challenges related to specific media requirements and frequent media changes, limiting the stability and viability of long-term studies. This study introduces an autonomously regulated oxygen microenvironment (AROM) using an oil-overlay method to stabilize oxygen levels and support NPC culture over extended periods without media changes, mimicking *in vivo* conditions.

**Method:** NPCs were cultured with and without an oil overlay for 15 days without any media change. The oil-overlay system created a self-regulating oxygen environment, enhancing cell viability and reducing apoptosis. Cell viability was assessed using fluorescence microscopy, and cell cycle progression was analyzed via flow cytometry. Oxygen consumption rate (OCR) and oxygen concentration (OC) were measured using the Resipher system to monitor oxygen dynamics. Cell counts and viability were compared between oil and no-oil conditions.

**Results:** After 15 days, NPCs cultured under the oil overlay exhibited high viability (88.86% healthy cells) compared to the no-oil cultured group (11.43%), with a 4.6-fold increase in total cell count (44,805 vs. 9,719 cells). The oil overlay stabilized oxygen levels and supported balanced cell cycle progression, with 85.39% of NPCs in the Go/G1 phase, indicating robust metabolic activity. In contrast, the no-oil cultured group showed high apoptosis and disrupted cell cycle progression due to environmental stress. Microscopic images post-experiment further supported these findings, illustrating enhanced cell integrity in the oil-overlay cultures.

**Conclusions:** The AROM oil-overlay method effectively supports NPC viability and stability over extended culture periods without media changes, mimicking *in vivo* conditions by autonomously regulating oxygen kinetics and providing a self-sustained stable culture environment, suitable for long-term NPC culture. The autonomous oxygen regulation provided by the oil-overlay system promotes a self-sustained environment, reducing the need for frequent media interventions and supporting stable cellular proliferation and differentiation. Additionally, this approach shows potential for supporting organoid culture, advancing disease modeling and cancer treatment options *in vitro*.



**Figure 1: Improved growth of hiPSC-derived NPCs in under-oil AROM.** (A) Experimental Flow. Cells were cultured with or without oil overlay (n=4 wells), with no media change for 15 days. (B) Quantification of neurite outgrowth in NPC culture, with and without oil overlay. Data was normalized to no oil control (n=4, p<0.001). (C, D) Average POC (C) and OCR (D) kinetics for NPC culture, measured by the Resipher system. Cell cultures under oil showed more physiological levels of oxygen concentration as well as sustained oxygen consumption. (E) Fluorescent and bright field images of NPCs. Cells were stained with Red Cytoplasmic Membrane dye to visualize neurites. Cells under oil overlay showed more neurite growth and healthier morphologies.



## **Tumor DNA analysis in peritoneal fluid to detect and monitor peritoneal carcinomatosis**

Authors: Muhammad Talha Nawaz, MD, Muhammad Talha Waheed, MD, Kirsten Dennison, MS, Bradon McDonald, PhD, Stephanie McGregor, MD, Syed Nabeel Zafar, MD, Mustafa Raoof, MD, Muhammed Murtaza, MBBS, PhD

**Introduction:** Gastrointestinal (GI) cancers often metastasize to the peritoneum. Current diagnostic tools for peritoneal carcinomatosis (PC) show limited accuracy. Reliable biomarkers to detect and monitor treatment response for PC are urgently needed. While circulating tumor DNA in plasma is a promising cancer biomarker, contribution of tumor DNA from PC into blood is minimal. We hypothesize that peritoneal fluid tumor DNA (ptDNA) may be useful for PC detection and response monitoring. Currently, there are no established laboratory methods for ptDNA analysis. In this study, we evaluate the feasibility of two DNA extraction methods using peritoneal fluid (PF) samples.

**Method:** We first evaluated the performance of two cell-free DNA extraction kits based on magnetic beads (MagMax) or silica columns (QIAamp) using commercially-obtained PF from two individuals, at 1 mL and 4 mL starting volumes. Based on these results, we evaluated the optimal method further using PF samples from 8 patients with PC from GI cancers (biliary tract, appendiceal, and colorectal primary) undergoing surgery or paracentesis at City of Hope National Medical Center. PF samples were collected prior to therapy. We extracted DNA using 4 mL inputs, eluted in 30  $\mu$ L buffer, and assessed using electrophoresis (TapeStation) and fluorometry (Qubit).

**Results:** In commercially obtained samples, adequate DNA yield and quality was obtained using both kits. Compared to QIAamp, mean DNA concentration was slightly lower using MagMax (24.88 ng/mL [range 13.90 - 35.85] vs. 25.66 ng/mL [range: 16.08-35.25;  $p=0.905$ ]). Similarly, mean fragment length was also shorter using MagMax compared to QIAamp (287.5 bp [range 202–350] vs. 294.3 bp [range: 239–348;  $p=0.80$ ]). In contrast to our prior experience with plasma DNA, ptDNA was observed at higher concentrations (3.7-fold higher) and longer fragment lengths. Based on these results and processing considerations, we selected MagMax kit to evaluate patient PF samples. We observed similar fragment lengths (mean: 293 bp, range: 266–342), with concentrations ranging from 4.02 ng/mL to 105 ng/mL in PF (mean: 27.73 ng/mL).

**Conclusions:** Our results demonstrate the feasibility of ptDNA analysis using PF samples in patients with PC. Furthermore, the yield and quality of DNA extracted is adequate for downstream molecular analyses. We were able to detect differences in PF vs. plasma DNA and observe inter-patient variability potentially related to heterogeneity in PC burden. We are now using this optimal PF DNA extraction method to expand our study and evaluate detection and quantification of peritoneal tumor-specific DNA as a biomarker for PC detection and monitoring.

## **Vorinostat, a histone deacetylase inhibitor, increases key neuroprotective mRNA expression in early-stage Parkinsonian midbrain neurons**

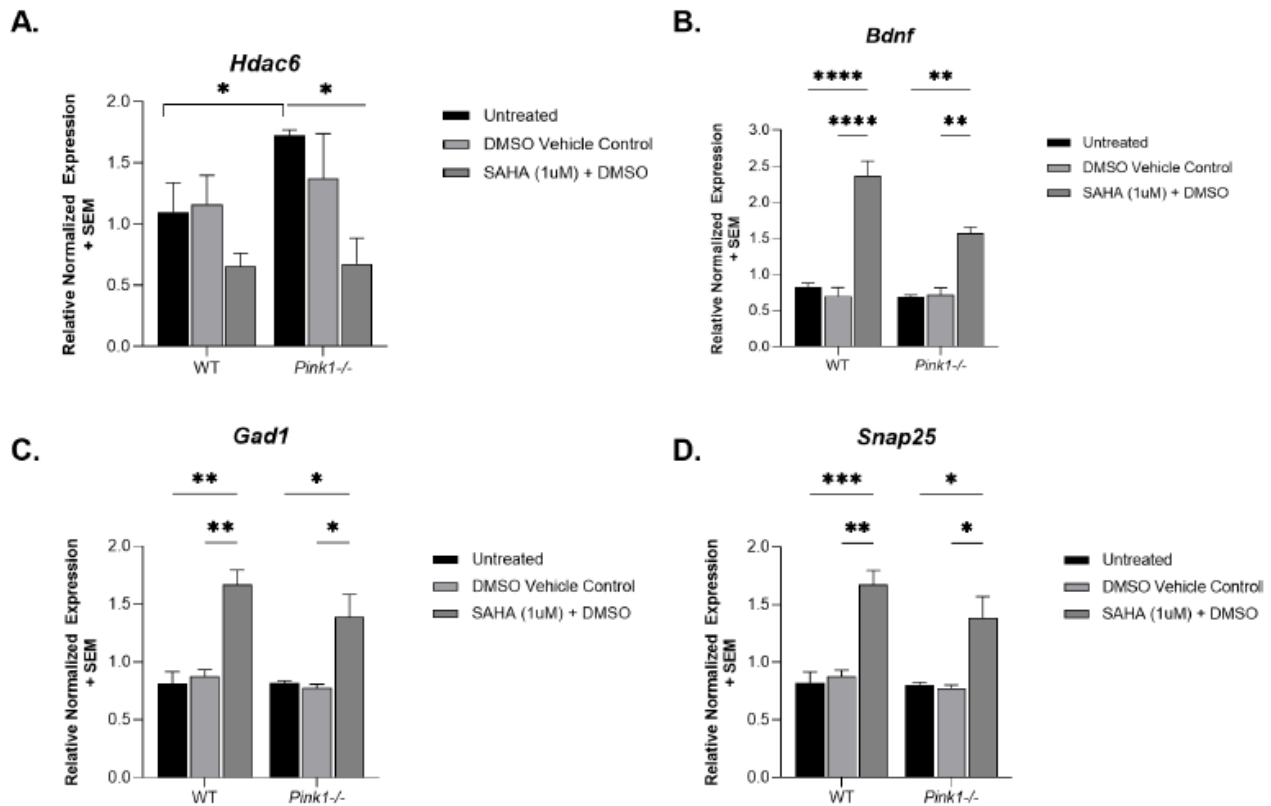
Authors: Sarah A. Lechner, B.S., Jaden N. Morrison, and Cynthia A. Kelm-Nelson, Ph.D.

**Introduction:** Parkinson disease (PD) is the fastest growing neurodegenerative disorder. Current treatments alleviate some symptoms but do not halt disease progression. The development of disease-modifying drugs is critical for optimizing patient treatments but remains challenging due to an incomplete understanding of the disease's etiology. The Pink1<sup>-/-</sup> rat model mimics the genetic, familial form of PD. Our previous RNA sequencing and bioinformatics analyses revealed that both male and female Pink1<sup>-/-</sup> rats exhibit significantly upregulated neuroinflammatory gene networks, strongly influenced by histone deacetylases, in the brainstem. Epigenetic alterations, specifically histone modifications, are implicated in human PD and PD animal models also show that HDAC6 plays a role in the pathogenesis of PD. Therefore, histone deacetylase inhibitors (HDACi), such as Vorinostat (suberoylanilide hydroxamic acid; SAHA), may be a promising therapeutic. SAHA is an epigenetic-modifying class I/ class II HDACi and specific HDAC6 inhibitor that is neuroprotective, reduces CNS inflammatory responses, and induces epigenetic reprogramming. Therefore, we hypothesized that SAHA would cause significant increases key genes such as neuronal growth (Bdnf), GABAergic transmission (Gad1), and synaptic transmission (Snap25), as well as decrease Hdac6 expression in Pink1<sup>-/-</sup> neurons.

**Method:** Midbrains were dissected and processed according to our established protocols that achieve significant neuronal predominance. Cells were either: (1) untreated, (2) complete medium supplement with DMSO vehicle, or (3) medium supplemented with SAHA dissolved in DMSO vehicle (1  $\mu$ M, Selleck Chemical). After 48 hours, cells were harvested, and total RNA was extracted. Gene expression was determined using real-time qPCR analysis following the MIQE guidelines and then analyzed with one-way ANOVA with Tukey post-hoc comparisons. All statistical analyses were conducted with SigmaPlot®; level of significance was set a priori at 0.05.

**Results:** Under normal conditions, Pink1<sup>-/-</sup> cells have significantly increased Hdac6 compared to wildtype-controls (Figure 1 A); but do not show differences in Bdnf, Gad1, or Snap25. SAHA significantly increased (>2-fold) Bdnf, Gad1, and Snap25 gene expression (Figure 1 B-D). These effects were observed to be significant in both genotypes, with WT cell cultures showing an even greater increase with SAHA compared to Pink1<sup>-/-</sup>. Additionally, SAHA decreased Hdac6 gene expression in Pink1<sup>-/-</sup> culture.

**Conclusions:** This is the first study to suggest that SAHA reduces the upregulated Hdac6 expression in Pink1<sup>-/-</sup> neurons and increases expression of genes that play a critical role in neuroprotection. This is significant because these data suggest that altering gene expression could mechanistically lead to inhibition of neurodegeneration through inducing transcription factors and genes.



**Figure 1.** SAHA increases mRNA expression in midbrain primary neuron cell cultures. (A) *Hdac6* (Histone deacetylase 6) is increased in *Pink1*<sup>-/-</sup> cells compared to WT and then was statistically decreased with SAHA drug administration in *Pink1*<sup>-/-</sup> cell culture. (B) *Bdnf* (brain-derived neurotrophic factor), (C) *Gad1* (glutamate decarboxylase 1), and (D) *Snap25* (synaptosomal-associated protein 25) mRNA expression was significantly increased with SAHA administration in compared to normal and vehicle treated cell culture in both wildtype (WT) cultures and *Pink1*<sup>-/-</sup> midbrain cultures. Asterisks with bars show levels of significance between groups (\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ ) between cell treatments in each genotype. Black bars: untreated cell culture; Light Gray: DMSO vehicle treated cell culture; Dark Gray: SAHA (1 $\mu$ M) + DMSO treated cell culture. X-axis is cell conditions in the two cell culture genotypes (wild-type, WT; PTEN-induced putative kinase1, *Pink1*<sup>-/-</sup>). Y-axis is relative normalized mRNA expression + standard error of the mean (SEM). Cell culture experiments were performed simultaneously in triplicate and normalized using the Pfaffl method to two reference genes (*Hsp90*, *Gapdh*).

## The Beta Cell “Invisibility Cloak” – Developing Stem Cell Derived Pancreatic Beta Cells that are Protected from the Immune System

Authors: Leavens C, Chamberlain CS, Abad Santos E, Palwasha Khan A, Brown M, Gumperz J, Baiu D, Sackett SD, Chlebeck P, Tremmel D, Raglin S, Wang X, Huangfu D, Odorico J.

**Introduction:** Type 1 diabetes is an autoimmune disorder that destroys pancreatic beta cells leading to insulin deficiency and hyperglycemia. While pancreas and islet cell transplantation are effective in controlling glycemia, challenges exist, including the need for life-long immunosuppression to prevent allograft rejection and autoimmune reoccurrence. We have genetically engineered a human embryonic stem cell (hESC) line that is devoid of immunostimulatory HLA Class I and II expression (double knockout, DKO) and expresses doxycycline-inducible T cell inhibitors, CTLA4Ig (iC) and PD-L1 (iP). We hypothesize these DKO;iCP hESCs can be differentiated to phenotypic and functional stem cell-derived islet-like clusters (SCILCs) and have the ability to avoid immune system detection and destruction.

**Method:** DKO;iCP hESCs were differentiated to SCILCs based on an established protocol. Differentiated SCILCs were then used in an in-vitro assessment analyzing HUES8 SCILCs (control) and DKO;iCP SCILCs ability to avoid detection from the immune system via incucyte analyses.

**Results:** Here we report that DKO;iCP hESCs can be successfully differentiated into SCILCs with similar morphology and function to human cadaver islets. DKO;iCP SCILCs were further analyzed via flow cytometry and IF staining for confirmation of PD-L1 and CTLA4Ig overexpression. Incucyte analysis via four effector cell types (NK,  $\gamma\delta$  T cells, CD8, CD4 T cells) reveal that human islets are targeted by NK cells,  $\gamma\delta$  T cells, and less so, at least in the short term by CD8+ T cells. Strikingly, DKO;iCP SCILCs are not targeted by any of the four effector cell types used in the assay, regardless of PD-L1 and CTLA4Ig expression.

**Conclusions:** Our results demonstrate the ability to differentiate genetically modified hESCs to functional SCILCs. Incucyte analyses reveal that SCILC DKO;iCPs go undetected by the four effector immune cells used in the assay. While these results are promising, they lacked a comparison to wild-type hPSC derived SCILCs. We plan to perform additional repeats and gather more allogeneic sourced cells to establish more generalizability of this data. We also plan to examine the ability of these grafts to evade the immune system using a humanized mouse model. These genetically modified SCILCs may provide a scalable cell source for therapeutics that can reverse diabetes while preventing immune rejection.

## **Evaluation of NBSGW-RIP-DTR mouse strain as an inducible diabetes and humanizable model to study diabetic transplant therapies and allogeneic immune responsiveness**

Authors: Li Andrew R, Chamberlain CS, PhD, Kapadia D, BS Abad Santos E, BS, Gorski K, BS, Leavens C, BS, Sackett SD, PhD, Chlebeck P, BS, Brown M, PhD Zaeem M, PhD, Huang L, PhD, Odorico J MD.

**Introduction:** Humanized mice have been developed to study in vivo human immune responses but current models are hampered by several factors including high rates of graft versus host disease reducing the effective therapeutic window. These shortcomings are exacerbated when applying humanized mice to study diabetes therapies because of the generalized toxicity that accompanies streptozotocin-induced hyperglycemia. To address the challenges of current humanized models, our team developed a humanizable NBSGW strain that when backcrossed with the NSG-RIP-DTR mouse, results in a humanizable NBSGW-RIP-DTR mouse model with facile diabetic induction. The NSG-RIP-DTR strain is immunodeficient and expresses the human diphtheria toxin receptor (DTR) under control of the rat insulin promoter (RIP). NBSGW mice are also immunodeficient and contain a hypomorphic mutation in the c-kit gene that provides an environment for hematopoietic expansion while obviating the requirement for irradiation. Using the new NBSGW-RIP-DTR mouse strain, we previously demonstrated the ability to induce diabetes via diphtheria toxin (DT). The goal of the current study is to evaluate the NBSGW-RIP-DTR mouse model in its ability to accept human islet grafts leading to correction of diabetes, and once humanized, stimulate allograft rejection.

**Method:** Following diabetic induction (blood glucose (BG) > 300 mg/dL x 3 days), NBSGW-RIP-DTR mice were transplanted with 2000 IEQ human islets via kidney subcapsule to assess engraftment of human islets and diabetes reversal. To assess the in vivo allogeneic response to islets, NBSGW-RIP-DTR mice were humanized via delivery of neonatal human thymus fragment transplants and umbilical cord blood i.v. Chimeric mice were transplanted with human islets. Grafts were collected at 8- and 12-weeks post-transplant and tissue sections were stained for immune cell infiltration.

**Results:** Female diabetic non-humanized NBSGW-RIP-DTR mice returned to normoglycemic levels after human islet transplants as indicated by the reduction in fed blood glucose levels and an increase in human serum C-peptide. Though males remained hyperglycemic, elevated C-peptide levels suggested engraftment of human islets. Diabetes reversal was similar to the NSG-RIP-DTR mice. Staining of the islet grafts in humanized NBSGW-RIP-DTR mice demonstrated immune infiltration of human cells within 8 weeks post-transplant, and was similar to the infiltration observed in humanized NBSGW mice.

**Conclusions:** The NBSGW-RIP-DTR mouse model represents a powerful platform for preclinical testing of human diabetes therapies and elucidating mechanisms involved in human allograft rejection and immunity.

## Use of Islet Vascularized Extracellular Matrix Organoids (IVEO) to Improve Transplantation and Survivability of Islets

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**Introduction:** Type I diabetes (T1D) is an autoimmune disease, resulting in beta cell function and loss. While donor islet transplantation offers a viable method to replace lost beta cells, critical survival, and vascularization signals are missing, thereby limiting post-transplant function and survival. We have generated 3-D islet organoids comprised of human donor islets and endothelial cells embedded into a native decellularized pancreatic extracellular matrix (ECM) hydrogel as a method to deliver islets more effectively. We hypothesize that transplantation of these Islet Vascularized ECM Organoids (IVEOs) into a diabetic mouse model can promote engraftment and post-transplant survival in a minimally invasive manner.

**Method:** IVEO constructs were generated by embedding 1000 IEQ human pancreatic islets isolated from donor pancreata and human umbilical vein endothelial cells (ECs) into human pancreatic ECM hydrogel (hp-HG) droplets. After gelation, constructs were cultured with a medium containing bFGF, SDF1 $\alpha$ , and VEGF growth factors. Vascular network formation within the IVEOs was monitored over 3 days via immunofluorescence and microscopy. Then the ability to reverse T1D after IVEO transplantation was assessed using an in vivo transgenic NSG RIP-DTR (NOD.Cg-Prkdcscid Il2rgtm1Wjl Tg(Ins2-HBEGF)6832Ugfm/SzJ) diabetic mouse model. After three days in culture, the IVEO-supplemented growth factor (IVEO+GF) constructs were subcutaneously transplanted. Blood glucose and serum C-peptide levels of the transplanted mice were monitored over 12 weeks to evaluate IVEO construct-mediated T1D rescue. Results were compared to diabetic mice transplanted with IVEO constructs without growth factor (IVEO without GF), islets embedded in hpHG without EC (HG+Islets), and naked islets.

**Results:** In vitro results indicated that vascular network formation, as determined via F-actin staining, was evident throughout the IVEO+GF constructs. Few to no vascular networks were apparent in the IVEO without GF constructs or HG+Islets. In vivo results demonstrated that diabetic mice transplanted with IVEO+GF constructs showed significantly reduced fasted blood glucose and increased serum human C-peptide levels over 12 weeks compared to mice transplanted with IVEO without GF, HG+Islets, and naked islets.

**Conclusions:** Islet vascularized ECM organoids offer a localized, minimally invasive delivery alternative that augments islet engraftment, survival, and function in vivo. The use of these islet organoids may overcome biological and transplant site limitations associated with currently available beta cell transplantation strategies for patients with T1D.

## Development of MRI-Compatible Kidney Perfusion System for Organ Assessment

Authors: Daniel Rice, James Rice, M.S., Leah Gober, MD, Gregory Simchick, PhD, Diego Hernando, PhD, Alejandro Roldán-Alzate, PhD, Jennifer Philip, MD

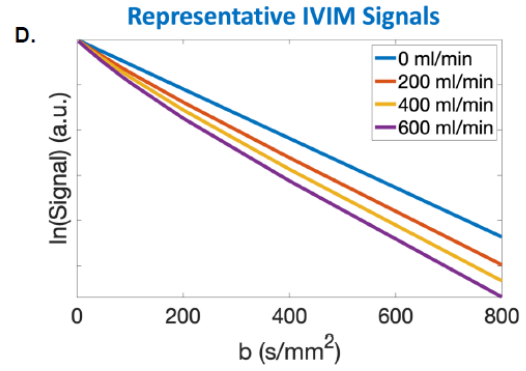
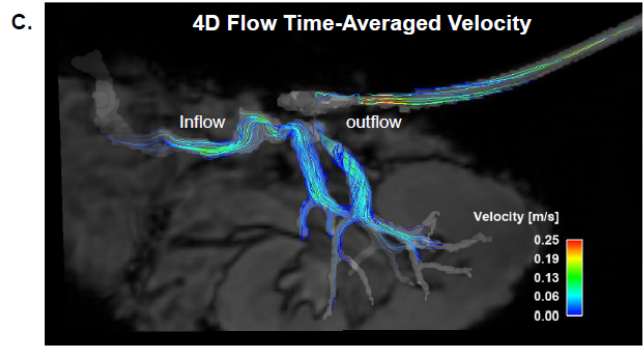
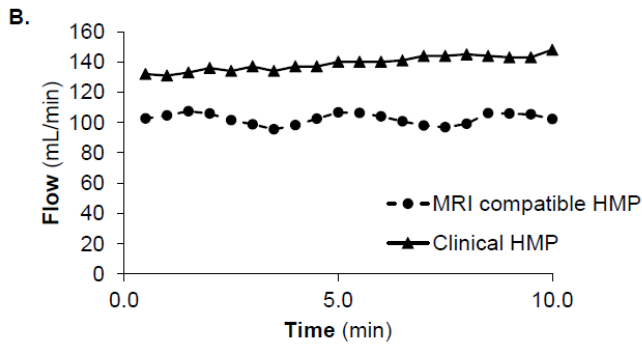
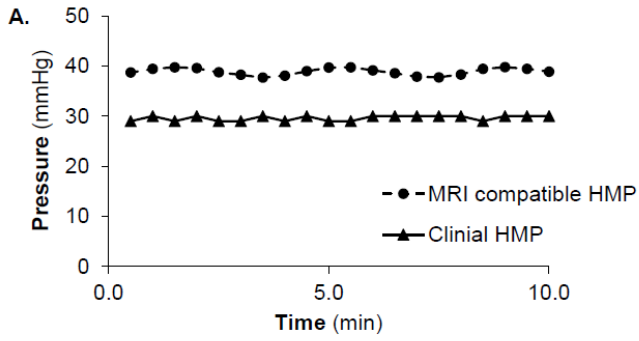
**Introduction:** There is a high and increasing rate of discards of deceased donor kidneys. This is in part driven by growing numbers of donation after cardiac death donors, older donors, and donors with medical comorbidities. Recent efforts have focused on developing strategies to improve evaluation of organs to increase utilization. Donor kidneys are typically perfused under hypothermic conditions prior to transplantation providing an opportunity of organ assessment. Novel and complementary MRI-techniques could potentially be used to evaluate deceased donor kidneys during preservation. We sought to develop an MRI-compatible ex vivo perfusion system to assess deceased donor kidneys using advanced MRI techniques of 4D Flow and Intravoxel incoherent motion (IVIM).

**Method:** Deceased donor kidneys that had undergone hypothermic machine perfusion (HMP) were placed on an MRI-compatible mock circulatory loop. Perfusion parameters between the clinical HMP and MRI-compatible systems were compared. Kidneys were imaged using a 3.0T clinical MRI system using constant flow at 150ml/min for 4D-Flow MRI and flow ranging from 0-600ml/min for IVIM acquisitions.

**Results:** MRI-compatible perfusion system reproduced clinical HMP conditions (Figure 1 A&B). In 4D-Flow sequences, velocity can be resolved in both inflow and outflow (Figure 1C). Inflow volumetric flow rate computed 4D Flow MRI differed from pump control flow rate by 10.1% (165.2 mL/min vs 150 mL/min, respectively). A change in the IVIM signal curve is observed with changes in flow rate, showing IVIM signal dependence on flow (Figure 1D). Perfusion signal fraction F was approximately 0 for the no flow case and increased dramatically for the 600 mL/min case. Increases in the diffusion coefficient in the kidney was also observed for the 600 mL/min flow state relative to no flow.

**Conclusions:** In this study, an MRI-compatible ex vivo kidney perfusion system was demonstrated to replicate the clinically used HMP system. With this system, 4D Flow MRI can be used to assess total renal perfusion and determine the spatial variations in flow of the macro-vasculature. IVIM can be used to assess microvascular perfusion for better understanding of how kidneys may respond to changes in flow. Future efforts will focus on coupling 4D Flow MRI derived metrics to perfusion metrics obtained from IVIM with the goal of improving deceased donor kidney assessment.

**Figure 1**



**Figure 4:** Evaluation of renal perfusion during preservation using MRI compatible HMP system. A&B. Clinical HMP pressure-flow profile is replicated in the MRI compatible HMP system. Longer tubing needed for MRI compatible system is likely responsible for small differences in pressures and flow. C. 4D flow image with anatomical overlay illustrates ability to quantify perfusion within renal vasculature. D. An effect of flow rate on the IVIM signal was observed. Shown are the natural logarithm of representative IVIM signal decay curves for multiple flow rates.



## Validation of Intravoxel Incoherent Motion MRI using Perfused Explanted Human Livers

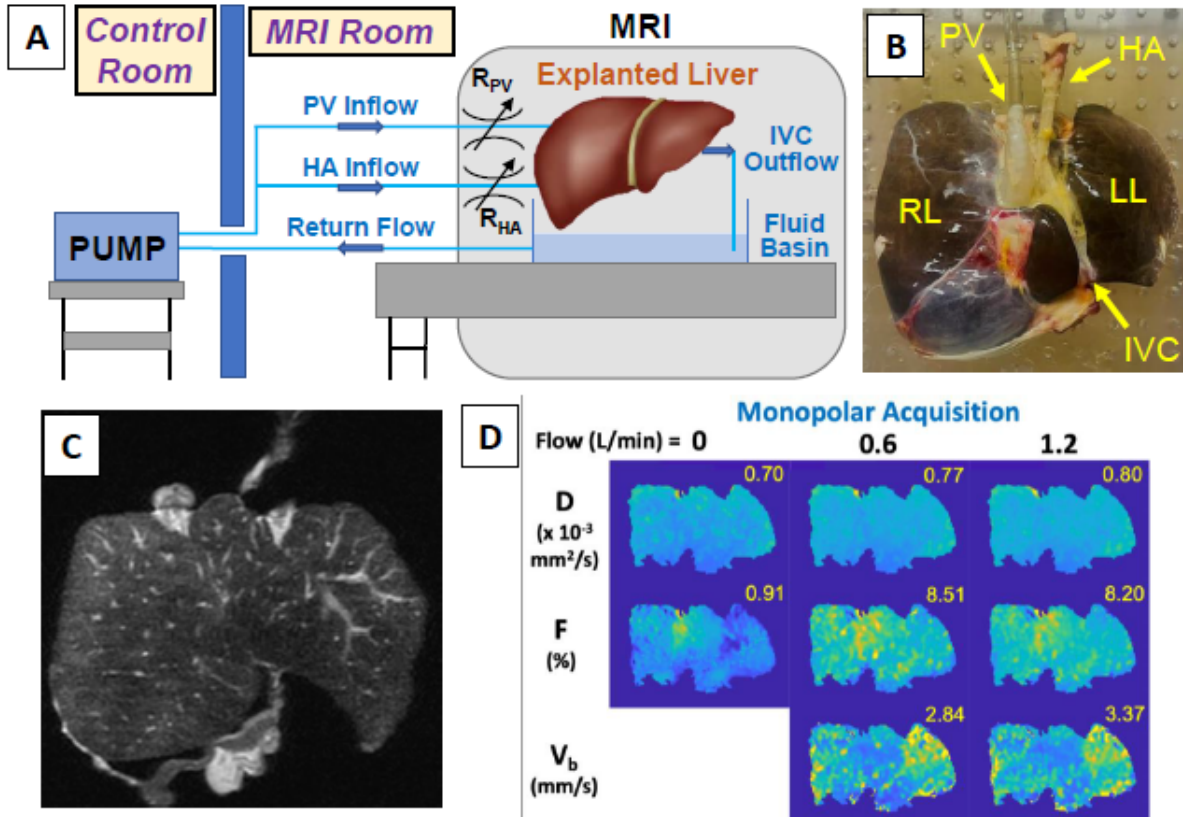
Authors: Daniel Rice, Gregory Simchick, PhD, James Rice, M.S., Leah Gober, MD, Diego Hernando, PhD, Alejandro Roldán-Alzate, PhD, Jennifer Philip, MD

**Introduction:** Imaging techniques are limited in ability to detect liver pathology leading to a reliance on invasive biopsies for diagnosis of pathology. Intravoxel incoherent motion (IVIM) is a promising technique for evaluation of diffusion and microvascular perfusion with the potential aid in detection of liver disease including cirrhosis and steatosis. Despite recent technical developments, systematic validation of IVIM remains challenging due to a lack of histologic and phantom studies. Phantoms have limitations, including not accurately mimicking biological microstructure and microvascular geometry and/or not containing two distinct perfusion and diffusion compartments. Use of explanted deceased donor organs may provide a platform for validation that overcomes these limitations. Therefore, the purpose of this work was to evaluate the use of perfused deceased donor human livers for validating IVIM.

**Method:** Deceased donor livers unable to be used for transplantation were preserved with UW organ preservation solution and cannulated for ex vivo perfusion. Dual inflow lines branching from a single peristaltic pump were connected to the portal vein and hepatic artery. Donor livers underwent MR imaging protocols at flow rates ranging from 0 to 1.2 L/min. IVIM parameter maps were made of each liver in order to determine the perfusion and diffusion coefficients.

**Results:** Dual hepatic and portal perfusion was able to be obtained in the MRI-compatible ex-vivo perfusion system (Figure 1). IVIM acquisitions are shown in Figure 1D showing flow dependent and independent variables. As expected, the diffusion coefficient ( $D$ ) remained relatively constant across varying flow rates; perfusion signal fraction ( $F$ ), was zero for no flow and relatively constant during flow at any rate; blood velocity standard deviation ( $V_b$ ) demonstrated logarithmic increase with flow rate increase.

**Conclusions:** This study demonstrates the feasibility of utilizing perfused explanted human deceased donor livers for validation of IVIM. This has important application in both disease detection in living patients and in evaluation of donor organs for viability and damage during ex vivo machine perfusion prior to transplantation. Future work will include evaluating IVIM results across a spectrum of liver pathology and comparison of imaging findings with histology.



**Figure 1:** (A) Experimental MRI setup consisting of dual inflow lines for the portal vein (PV) and hepatic artery (HA). Each inflow line included a resistive valve (R) to constrain the inflow ratio. The inferior vena cava (IVC) outflow was collected in a fluid basin. (B) Image of explanted liver and flow connections. (C) T2-weighted MRI image of explanted liver. (D) Representative explanted liver IVIM parameter maps of the diffusion coefficient ( $D$ ), perfusion signal fraction ( $F$ ), blood velocity standard deviation ( $V_b$ ). Estimates for each parameter are given in the upper right corner of each map.

## Generation of a small-diameter universal artery graft from pluripotent stem cells

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**Introduction:** Cardiovascular disease is the leading cause of death worldwide. Vascular bypass procedures are widely used for occlusive heart and peripheral vascular disease. Current vascular bypass options include both autologous and synthetic materials; however, each graft presents specific limitations. Engineering artificial small diameter arteries with vascular cells derived from pluripotent stem cells (PSCs) could provide a useful therapeutic solution. Personalized vein grafts that combined expanded polytetrafluoroethylene (ePTFE) vascular grafts and autologous endothelial cells from patients significantly improved the long-term patency in clinical trials. However, the patency rates remain inferior to arterial grafts, manufacturing is costly and time consuming, and some patients lack suitable vessels to culture endothelial cells. In addition, synthetic and tissue-engineered grafts have yet to show clinical effectiveness in arteries smaller than 5 mm in diameter.

**Method:** To address these challenges, 3mm universal arterial grafts were developed by lining ePTFE vascular grafts with arterial endothelial cells (AECs) derived from pluripotent stem cells. In this study, we optimized AEC generation, cell adhesion to ePTFE, in vitro perfusion of vascular grafts, and assessed patency of our engineered small-diameter arterial grafts in a rhesus macaque model for lower extremity arterial bypass.

**Results:** Unexpectedly, grafts lined with major histocompatibility complex wild-type (MHC-WT) AECs were able to maintain 100% patency for six months, outperforming arterial grafts lined with MHC class I/II double knockout (MHC-DKO) AECs. Further investigations demonstrated that MHC-WT-AECs are less immunogenic than MHC-DKO-AECs.

**Conclusions:** This study provides the first evidence that PCS-derived MHC-WT artery grafts can be used as an off-the-shelf, universal vascular graft for allogeneic arterial bypass.

## Modulation of RBP-1 Phosphorylation is a Novel Therapeutic Vulnerability in Fibrolamellar Carcinoma

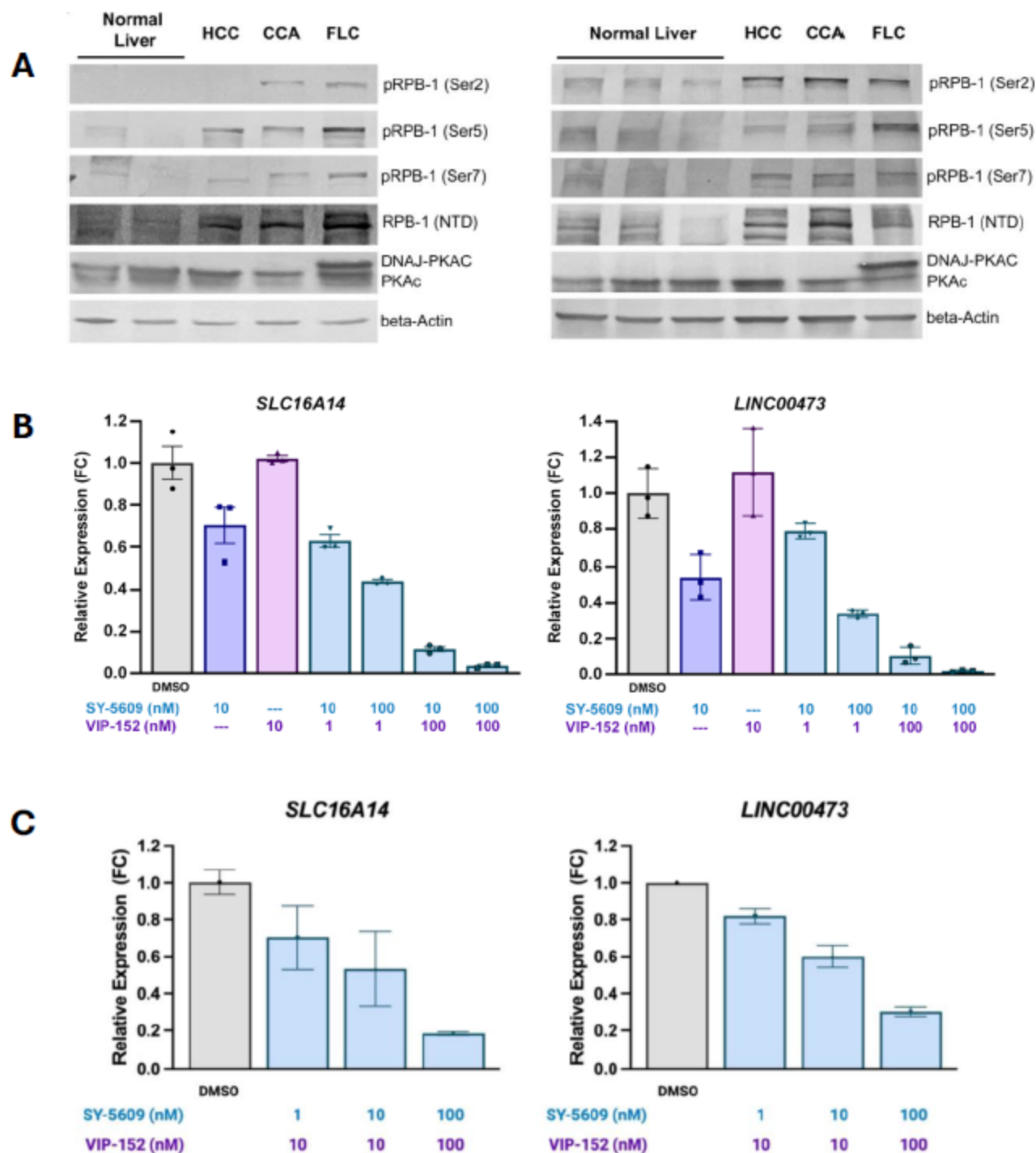
Authors: Patrick Carney, MD, PhD, Manabu Nukaya, PhD and Sean Ronnekleiv-Kelly, MD

**Introduction:** Fibrolamellar carcinoma (FLC) is a rare cancer that is highly lethal and disproportionately affects young individuals without known genetic or environmental predisposition. Unfortunately, only 30-45% of patients survive beyond 5 years and the lack of effective systemic therapy options is a major barrier to long-term survival. A unique gene fusion between heat shock protein 40 (DNAJB1) and the catalytic subunit alpha of protein kinase A (PRKACA) causes FLC and results in the production of an oncoprotein (DNAJ-PKAc). DNAJ-PKAc causes epigenetic remodeling and emergence of FLC specific super enhancers that drive high levels of FLC-specific gene expression. RNA Polymerase II (RBP-1) is highly enriched at super enhancers and aberrantly active in cancers that manifest a 'transcriptional addiction'. We identified in human FLC samples that this aberrant activity is characterized by serine-5 phosphorylation. Notably, serine-5 is the molecular target of cyclin dependent kinase 7 (CDK7) and CDK7 inhibitors have emerged as drugs of interest for treating advanced solid malignancies. Consequently, we hypothesized that CDK7 represents a therapeutic vulnerability in FLC.

**Method:** Human FLC, HCC, CCA and matched normal liver samples were evaluated for presence of the DNAJ-PKAc oncoprotein and for phosphorylated RBP-1 protein at serine-2, -5 and -7 residues (Western blot). Phosphorylation of RBP-1 serine residues is regulated by CDK7 (preferential target serine-5) and CDK9 (serine-2). A CDK7 specific inhibitor (SY-5609) and a CDK9 specific inhibitor (VIP-152) were evaluated in our engineered cell line expressing DNAJ-PKAc and in FLC organoids to assess FLC specific gene expression and synergy of these compounds.

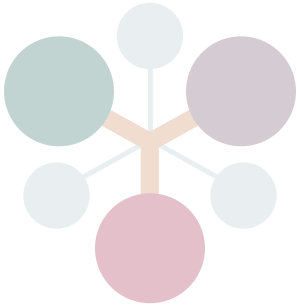
**Results:** Human FLC tumor tissue samples show increased phosphorylation of RBP-1 serine-5 residue as compared to human HCC, CCA and normal liver samples. Treatment of DNAJ-PKAc expressing cells and FLC patient derived organoids with SY-5609 and VIP-152 showed suppression of FLC specific super enhancer driven genes in a dose dependent manner (Figure 1).

**Conclusions:** Aberrant activation of RBP-1 has been shown to cause emergence of cancer-specific super enhancers and drive expression of genes important for cancer cell survival. These genes (e.g., SLC16A14 and LINC00473) are actively being investigated as therapeutic targets in FLC. We targeted the upstream driver (i.e., abnormal phosphorylation of RBP-1) with a CDK7 specific inhibitor (SY-5609) and identified a synergistic partner (CDK9 specific inhibitor (VIP-152)) to suppress RBP-1 phosphorylation and cause downregulation of FLC specific genes. Our data shows that abnormally increased RBP-1 phosphorylation is a clinically relevant target in FLC and appears to be driven by aberrant CDK7 activity.



**Figure 1. (A)** Individual patient normal liver, HCC, CCA and FLC samples (NC1, NC2, NC3, HCC3, CCA2, FLC109 and NC4, NC5, HCC6, CCA6, FLC55) were evaluated for phosphorylated RPB-1 (Ser-2, -5, -7). The presence of the DNAJ-PKAc oncoprotein was confirmed in FLC samples but not in normal liver, HCC or CCA. **(B)** Expression of the FLC specific genes *SLC16A14* and *LINC00473* were decreased in a dose dependent manner in response to dual CDK7 and CDK9 inhibitor treatment in *DNAJB1-PRKACA* expressing human HCC cells and **(C)** FLC patient derived organoids.

# Clinical Science & Health Services Research Abstracts



# Psychiatric History and Multiple Chemical Sensitivity as a Marker of Somatization in Predicting Migraine Surgery Outcomes

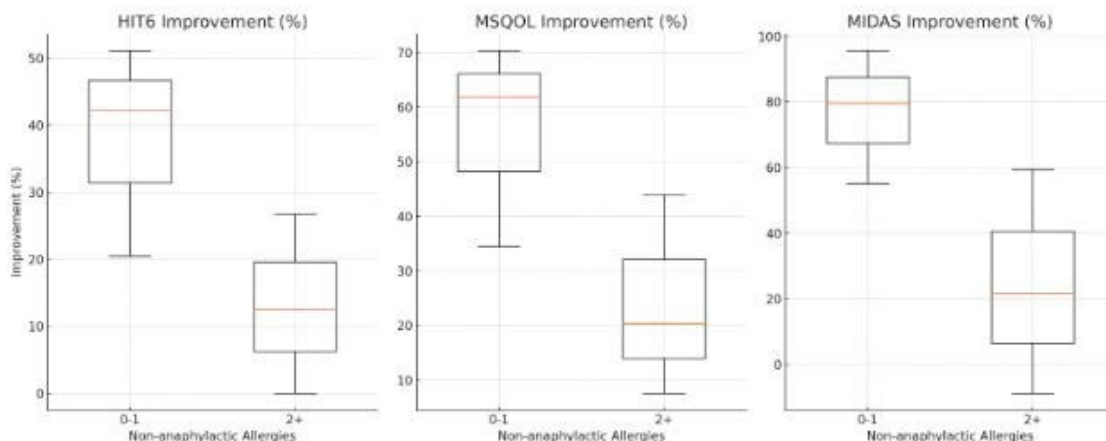
Authors: Keenan Fine, MS, Caroline Bay, BA, Robert George, MD, Ahmed Afifi, MD

**Introduction:** Mood and anxiety disorders has been shown to negatively affect patient-reported outcomes (PROs) after surgery. Somatic symptom disorder (SSD) is also linked to poorer outcomes and is often underdiagnosed. Research shows a strong link between polyallergy (or multiple chemical sensitivity) and SSD, as well as a significant connection between somatization and migraines. This study aims to examine whether mood or anxiety disorders impact the effectiveness of migraine surgery and whether polyallergy, as a marker for SSD, influences PRO improvements.

**Method:** A retrospective cohort study was conducted on patients who underwent migraine surgery by a single plastic surgeon between May 2012 and July 2017. Patient data, including psychiatric diagnoses, non-anaphylactic allergies, and surgical PROs, were collected and analyzed. Preoperative and postoperative outcomes were assessed using the HIT-6, MSQOL, and MIDAS scores. Subgroup analyses were performed based on a history of mood disorders, a history of anxiety disorders, and the number of non-anaphylactic allergies (0-1 vs. 2+), with the latter serving as a proxy for somatization. Percentage improvements in each metric were calculated, and Mann-Whitney U tests were used to compare outcomes between subgroups.

**Results:** Significant improvements were observed in HIT6, MSQOL, and MIDAS scores across all subgroups, except patients with a history of an anxiety disorder with MIDAS scores. Patients with an anxiety disorder had less improvement across all 3 measures than those without but the differences were not statistically significant. There were no differences in improvement between those with and without a history of a mood disorder. Patients with 2+ non-anaphylactic allergies experienced significantly less improvement compared to patients with 0-1 allergies in HIT-6 (12.5% vs. 42.3%,  $p=0.002$ ), MSQOL (20.4% vs. 61.9%,  $p=0.007$ ), and MIDAS (21.8% vs. 79.6%,  $p=0.018$ , Figure 1).

**Conclusions:** Migraine surgery significantly improved PROs as measured by HIT-6, MSQOL, and MIDAS scores. However, individuals with a history of anxiety disorders showed less improvement, though this difference was not statistically significant, potentially due to the small sample size. Patients with 2+ non-anaphylactic allergies, serving as a proxy for somatization, experienced significantly worse outcomes compared to those with fewer allergies. These findings suggest that somatization, indicated by polyallergy, may negatively impact the effectiveness of migraine surgery in improving PROs. This underscores the importance of recognizing somatic symptom burden when evaluating surgical outcomes and highlights the potential to use existing patient chart data to predict surgical success without requiring a formal diagnosis.



## Exploring the Landscape of Cosmetic Surgery in Africa - A Survey

Authors: Jessieka Knazze, MPH, Jasmine Craig, MD, MPH, Elizabeth WU, BS, Darius Balumuka, MD, Metasebia Worku Abeba, MD, Musunga Mulenga, MD, Ian Shyaka, MD, Amanda Gosman, MD Michael Bentz, MD

**Introduction:** There is a dire need for plastic and reconstructive surgery care in Africa. The burden of untreated traumatic injuries, burns, malignancies, and congenital anomalies greatly contribute to life years lost and disability in the region. An estimated 2 million disability adjusted life years are lost annually due to burns. Another study cites Africa as having one of the greatest proportions of surgically amenable burden for cleft lip and palate at 68%. Sustainable plastic surgery infrastructure is challenging due to a shortage of plastic surgeons, limitations in specialty training, and lack of resources, including funding. In analyzing financing plastic surgery infrastructure, various countries generate revenue for their infrastructure through cosmetic surgery. Unfortunately, it is not clear how cosmetic surgery is viewed in Africa or how much is being performed nor by whom. A comprehensive understanding of the current attitudes, training, and revenue surrounding cosmetic surgery will allow us to evaluate if strengthening of cosmetic infrastructure is a viable solution to sustain plastic, reconstructive, and aesthetic surgery care within the cultural framework of African countries.

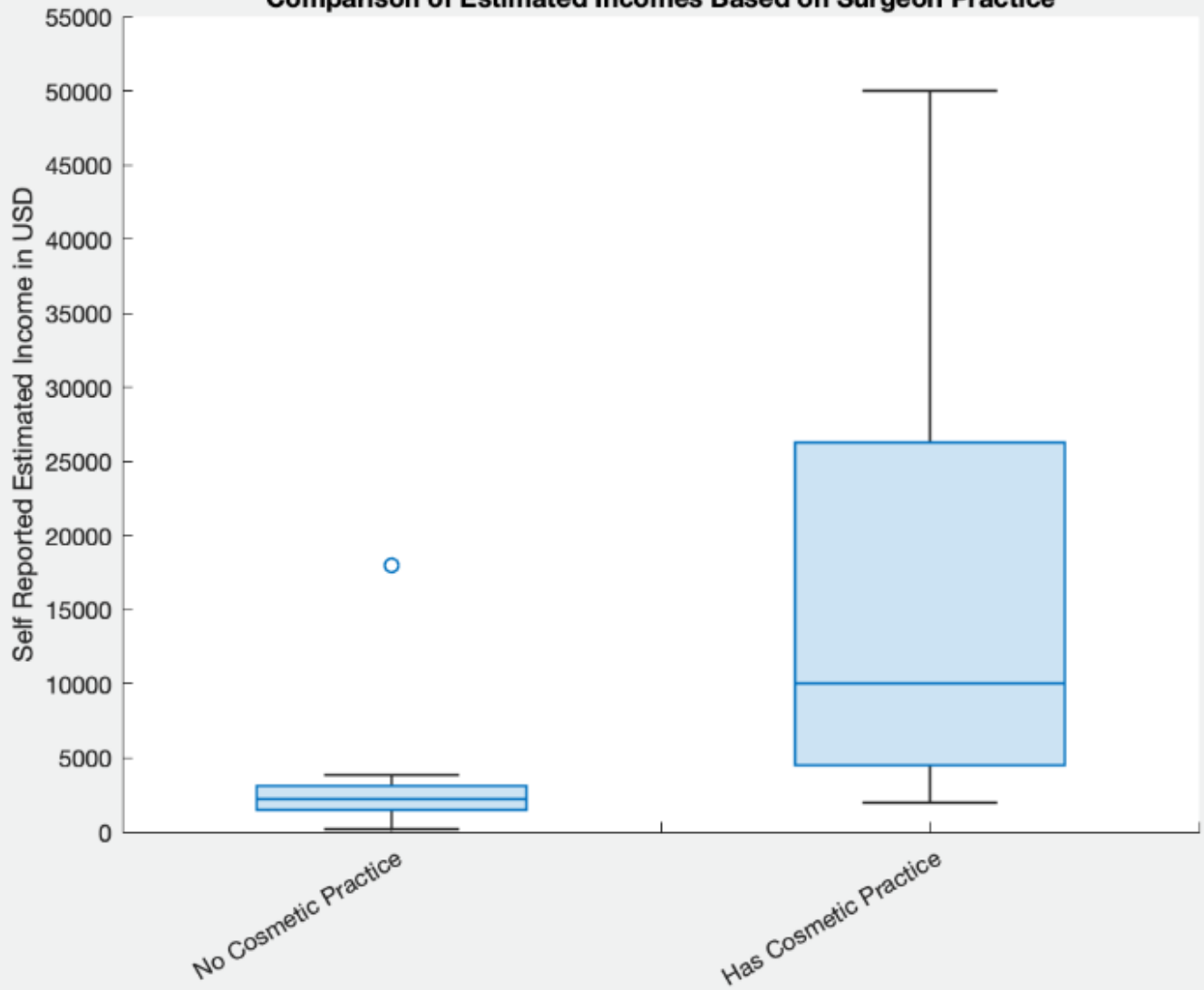
**Method:** A comprehensive survey was designed with input from several leaders in plastic surgery, including surgeons currently practicing in Africa. The secure Research Electronic Data Capture (REDCap) platform was used to create the online survey. The survey captures the perspectives of surgeons who are practicing cosmetic surgery and surgeons who are not. Participants were identified through email and professional organizations. Survey responses were aggregated and analyzed to identify trends. MATLAB and open source Python software were used for data visualization.

**Results:** 51 surveys were collected, of which 35 were fully complete. Most of the respondents completed residency in Ethiopia and currently practice plastic surgery in Eastern Africa. Cosmetic surgery is performed by 61.7% of respondents, the majority of whom learned in residency or fellowship training. Many of the surgeons dedicate less than 25% of their time to cosmetics, with abdominoplasty most frequently performed. Regarding surgeons who do not perform cosmetic surgery, nearly 100% agree additional training would be beneficial and many of them cite lack of training and supply chains as the main barriers to performing cosmetic surgery. Those who perform cosmetic surgery have higher incomes compared to their counterparts ( $p=0.035$ ).

**Conclusions:** Increased cosmetic training is needed and desired by African surgeons. There are several positively perceived benefits of increasing cosmetic surgery. Strengthening cosmetics can offset the cost of vital reconstructive surgery and generate increased revenue in local economies.



**Comparison of Estimated Incomes Based on Surgeon Practice**



## Timing of Urgent Colectomy for Cancer: A NSQIP Analysis

Authors: Madhuri V Nishtala, MD, Kelsey Franklin, MD, MPH, Ben Zarzaur, MD, MPH, Julia R Berian, MD, MS

**Introduction:** The timing of urgent surgery variably affects surgical outcomes: in common emergency general surgery procedures, delayed operations correlate with increased mortality and morbidity. However, for certain indications in colon surgery, e.g., diverticulitis and appendicitis, observation may be safe. We sought to examine patterns in time to surgery for urgent colectomy in cancer cases, where malignancy may influence risk profiles. We aimed to determine if surgical delays in emergency colectomies for colorectal cancer impact 30-day mortality and morbidity. We hypothesize that delays may not increase risk, as they could be warranted for staging or recent chemotherapy.

**Method:** This retrospective cohort study used NSQIP Procedure Targeted Colectomy data from 2015–2021, including patients aged  $\geq 18$  who underwent non-elective colectomy for confirmed colon cancer. Surgery timing was categorized as early ( $\leq 48$  hours) or late ( $> 48$  hours). The primary outcome was 30-day mortality; secondary outcomes included any and serious complications. A multivariable logistic regression adjusted for confounders like age, race/ethnicity, comorbidities, frailty, disseminated cancer, and other clinical factors.

**Results:** 8049 patients (mean age 68.3 years, 49.3% male, 50.7% White) underwent urgent colectomy. The mean time to surgery for the cohort was 1.5 days  $\pm$  2.05 (mean  $\pm$  std dev) with 67.2% categorized as early operation. The most common indications for surgery included obstruction (57.6%), perforation (26.9%), and bleeding (6.4%). The mean time to surgery was significantly greater for bleeding (3.5 days  $\pm$  2.53) than obstruction (1.57  $\pm$  1.95) and perforation (1.00  $\pm$  1.79). Compared to early operation, patients with late operation were older (67.7 years  $\pm$  14.7 vs 69.7  $\pm$  15.1  $p < .0001$ ), with  $\geq 2$  comorbidities (22.6% vs 17.5%,  $p < .001$ ), but fewer had preoperative sepsis (22.6% vs 41.9%,  $p < .001$ ) or disseminated cancer (22.0% vs 25.6%,  $p = .0005$ ). Late operations had increased risk for any complications (53.6% vs 48.7%;  $P < 0.001$ ) and serious complications (58.6% vs 53.4%;  $p < 0.001$ ). There were no differences in unadjusted 30-day mortality (91.1% vs. 90.2%;  $p = 0.19$ ). After adjusting for age, race, ethnicity, comorbidities, sepsis, frailty, disseminated cancer, and transfer status, late operation did not increase risk for 30-day mortality (odds ratio [OR], 1.158; 95% CI, 0.970-1.380), any complications (OR, 1.014; 95% CI, 0.916-1.123), or serious complications (OR, 1.042, 95% CI, 0.939-1.156).

**Conclusions:** Time to urgent colectomy in colorectal cancer patients was not significantly associated with 30-day mortality or complications after adjusting for clinical factors. This should provide reassurance and support surgeons in using clinical judgment to individualize time to surgery for colectomy in cancer patients.

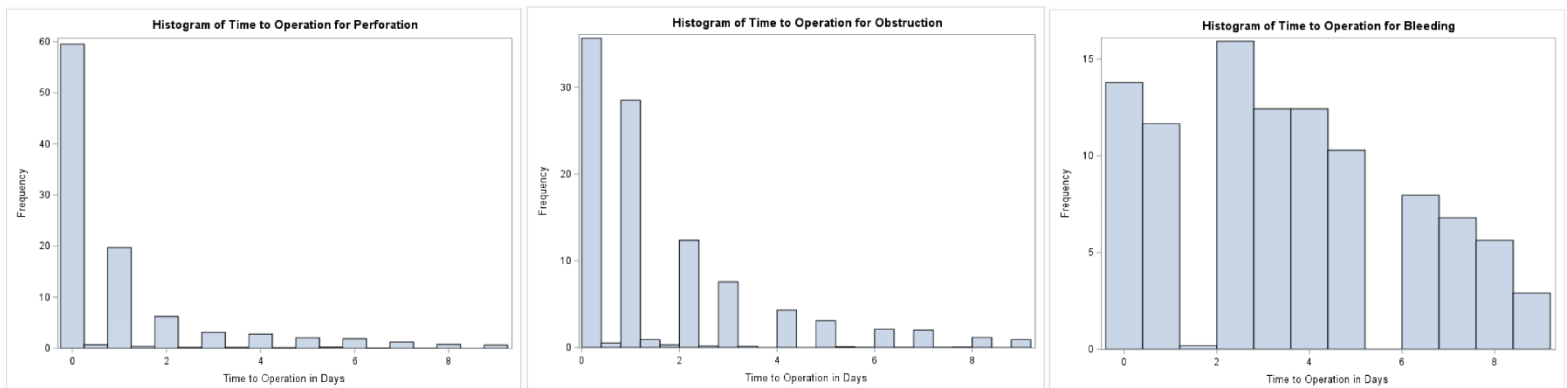


Figure 1: Time to Operation According to Indication for Surgery

## Who Gets Referred? Disparities in Access to Specialist Care for Hyperparathyroidism

Authors: John O'Connor, Rebecca Sippel, MD, Lily Stalter, Amy Kind, MD, PhD, Alexander Chiu, MD, MPH

**Introduction:** Primary hyperparathyroidism (PHPT) affects approximately 1% of adults in the United States. Untreated PHPT is associated with osteopenia/osteoporosis, nephrolithiasis, and cardiovascular events. Currently, the only curative therapy for PHPT is parathyroidectomy. Although the procedure is safe and cost-effective, it remains underutilized, particularly among disadvantaged populations. We sought to understand the association social determinants, as measured by neighborhood advantage, have on PHPT evaluation and referral for treatment.

**Method:** Retrospective analysis was performed on all adult patients with an elevated calcium value ( $>10.2$  mg/dl) in our academic healthcare system between 1/1/2021 and 1/1/2023. Patient demographic (age, gender, race, nine digit zip-code, and insurance status) and laboratory information (initial and subsequent calcium levels, and PTH) were abstracted. Exclusion criteria included patients with kidney failure, secondary or tertiary HPT, prior renal transplant, or prior parathyroidectomy. Patients were grouped into likely ( $>65$  pg/mL), possible (30-65 pg/mL), or unlikely ( $<30$  pg/mL) PHPT based on PTH values. Patients' neighborhood advantage was stratified using the Area Deprivation Index (ADI) to create three cohorts — disadvantaged, moderate, advantaged. The primary outcome was specialist referral for PHPT management. Multivariate logistic regression was performed to evaluate factors associated with referrals.

**Results:** Hypercalcemia was identified in 6,562 patients and 3,543 (54.0%) met inclusion criteria. The study cohort was 91.4% White, 60.2% female, 84.7% privately insured, and 54.5% under 65 years of age. PTH levels were recorded in 959 (27.1%) patients and 530 (55.3%) were determined to likely have PHPT. There were no significant differences for rate of PTH workup ( $p = 0.26$ ) or likely PHPT by neighborhood advantage ( $p = 0.70$ ). However, patients in disadvantaged communities were significantly less likely to receive specialist referral compared to those from advantaged communities (OR 0.72, CI 0.52 - 0.98), especially for patients in disadvantaged neighborhoods likely to have PHPT (OR 0.49 vs. advantaged, CI 0.26 - 0.92).

**Conclusions:** Overall, significant specialist referral disparities exist for PHPT management based on neighborhood advantage. Interventions addressing both individual and community level barriers, particularly in transition from primary care to specialists, are needed to increase access to parathyroidectomy and health equity.

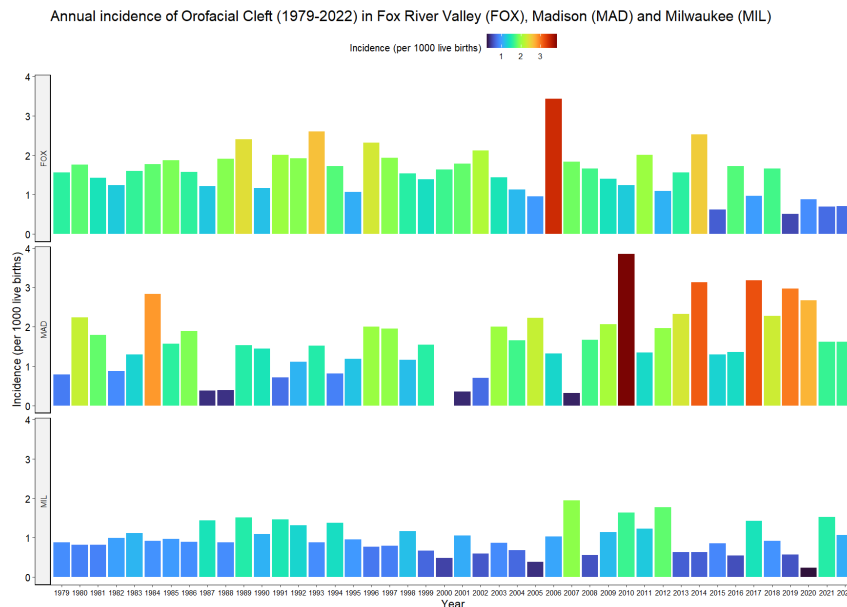
# Clefts and Contaminants: Investigating the Link Between Orofacial Clefts and PCB Pollution in Wisconsin

Authors: Jessieka Knazze, MPH, Gina Krause, BS, Doruk Orgun, MD, Jessica Blum, MD, MSc, Jasmine N. Craig, MD, MPH, Catharine B. Garland, MD, Daniel Cho, MD, PhD

**Introduction:** In the 1950s and 60s, the Fox River Valley (FRV) region of Wisconsin was known for its paper mills that lined the Fox River. During this time, the mills used the river as a disposal site for waste, which included polychlorinated biphenyls (PCBs) used in the production of carbon copy paper. The non-biodegradable properties of PCBs led to the contamination of 39 miles of river sediment, affecting both the local water ecosystem and Lake Michigan. This contamination is concerning as experimental studies have shown PCBs to be correlated with orofacial cleft (OFC) formation. Fortunately, the United States Environmental Protection Agency mandated cleanup of the Fox River which took place between 2004-2020. With this case study in mind, the aim of this study was to investigate incidence rates of OFC in FRV before, during, and after PCB remediation compared to more densely populated Madison (MAD) and Milwaukee (MIL).

**Method:** Vital records from the Wisconsin Department of Health Services were obtained on all births with a congenital anomaly from 1979 to 2022. The maternal zip codes of children with an OFC were plotted. The average OFC incidence per 1000 births each year was calculated for MAD, MIL and FRV. Incidence rates were calculated for three time points: inception of vital records data in 1979 to 2003, before PCB remediation (T1), the duration of remediation from 2004 to 2020 (T2), and after remediation in 2021 to the most recent vital records data in 2022 (T3).

**Results:** From 1979-2022, a total of 2762 children were born with an OFC in Wisconsin. In MAD, the average OFC incidence per 1000 births was 1.28 in T1, 2.09 in T2, and 1.62 in T3. In MIL, the average OFC incidence per 1000 births was 0.986 in T1, 0.951 in T2, and 1.30 in T3. In FRV, the average OFC incidence per 1000 births was 1.72 in T1, 1.48 in T2, and 0.704 in T3. FRV incidence rates were significantly different ( $p < 0.05$ ) from MAD and MIL for all three time points.



**Conclusions:** FRV OFC incidence rates were significantly higher before remediation and significantly lower after remediation compared to MAD and MIL. The trend of OFC incidence rates appears to be decreasing in FRV after remediation, however it has increased in MAD. Long-term surveillance continues and will be crucial in investigating relationships between PCBs and OFC development. 75

## **From theory to practice: A systematic review of MRI's clinical applications in evaluating and treating cleft-associated velopharyngeal insufficiency**

Authors: Aidan O'Shea, ScB, Emily Zona, BS, Jasmine Craig, MD, MPH, Jessica Blum, MD, MSc, Catharine Garland, MD, Daniel Cho, MD, PhD

**Introduction:** Magnetic resonance imaging (MRI) has gained significant attention in the last two decades for its use in evaluating velopharyngeal insufficiency (VPI). Initially, the use of MRI for VPI was largely restricted to research settings to establish normative reference data and refine protocols. However, more recently, there has been growing interest in its broader clinical deployment. This systematic review aims to evaluate the evidence base for the clinical application of MRI in the management of VPI, in particular in patients with clefts.

**Method:** A systematic review was conducted according to PRISMA guidelines. Studies involving the clinical use of MRI in cleft-associated VPI care were included. Case reports and cleft syndrome-specific studies were excluded. Studies were categorized by MRI's role in diagnosis, postoperative monitoring, or comparison to other imaging modalities. Relevant data were extracted and analyzed.

**Results:** The search identified 1,054 unique studies and 32 met inclusion criteria. Eighteen studies reported the use of MRI for diagnostic evaluation and/or treatment planning for VPI. MRI frequently demonstrated utility in objective evaluation of the severity and nature of VPI, helping to inform personalized treatment plans. This considered, 4 studies found that MRI measurements did not always correlate with clinical severity at initial presentation, highlighting the complexity of the factors influencing velopharyngeal function in patients with clefts. MRI was used to assess postoperative changes following surgical intervention for VPI in 15 studies. It proved to be particularly useful in procedures such as pharyngeal flap surgery or augmentation palatoplasty for which it can assess changes over time that can impact function, such as tissue atrophy or migration of injected materials or implants. Two studies identified specific MRI measurements associated with speech outcomes following surgery for VPI. However, 4 studies found that MRI measurements did not always correlate with or predict speech outcomes following surgery for VPI. Five studies allowed for direct comparison of MRI with other imaging modalities. Of these, 1 early study demonstrated good results with a combination of MRI and nasoendoscopy, while 4 studies showed that MRI is generally equally as reliable as traditional modalities and in some cases can provide additional clinically meaningful detail.

**Conclusions:** MRI shows significant promise in evaluating and managing VPI, particularly in patients with clefts. Expanding its clinical use may not only enable better outcomes and more patient-centered care, but will also strengthen the evidence base on its optimal application in VPI care.

## **Global Perspectives on Primary Cleft Repair in the Adult Patient: Navigating a Unique Reconstructive Challenge**

Authors: Emily E. Zona BS, Aidan W. O'Shea ScB, Sumin Yang, B.S., Jasmine Craig MD MPH, Catharine B. Garland MD, Daniel Y. Cho MD PhD

**Introduction:** Adults with unoperated cleft lip and palate (CL/P) represent a unique patient population with their own clinical and surgical challenges. While it is rare to encounter these adults in developed countries – owing in part to medical advancements, resources, and patient awareness – untreated CL/P still affects a significant number of adults in developing nations, with potential impacts on their speech, function, economic productivity, and quality of life. The purpose of this review is to examine the current literature on the primary repair of untreated CL/P in adult patients.

**Method:** We queried three databases (Embase, PubMed, and Web of Science) using relevant keywords (e.g., “adult” AND “cleft lip” OR “cleft palate”) for studies published since 2000. Our initial search identified 1,825 studies. Of these, 25 English-language articles with 1,143 adult patients discussed the primary repair of untreated CL/P and represented data from seven countries. A qualitative thematic analysis was conducted to identify recurring themes related to primary repair of untreated CL/P. Quantitative analysis included counts and percentages.

**Results:** Most studies focused on the surgical repair of CL/P in adults living in developing countries (ten articles), the elderly patient population (two articles), or specific surgical techniques of primary repair in adults (eight articles). Notably, the definition of adulthood varied, with some studies considering individuals over 12 or 13 years of age as adults. Five articles emphasized local anesthesia as a safe and reliable option for CL repair, particularly valuable in developing countries with limited access to equipment and personnel for general anesthesia. In all five studies, local anesthesia did not increase perioperative complications and, in some cases, resulted in greater patient satisfaction and shorter hospital stays compared to general anesthesia. Three studies described the distinct anatomy of clefts in adults, which are often significantly larger in three dimensions due to patient growth and maxillary expansion. This anatomy poses challenges for surgical repair, necessitating greater soft-tissue dissection and possibly the use of biomaterials. Additionally, some articles noted that the tissues in adults are bulkier and stiffer, requiring special handling during the procedure. Despite these challenges, all studies reported satisfactory outcomes, including improvements in speech, appearance, or quality of life.

**Conclusions:** We describe the current outcomes data regarding adults undergoing primary CL/P repair. Key takeaways include the use of local anesthesia in CL repair, the anatomical challenges associated with unoperated clefts in adults, and the satisfactory outcomes of repair from functional and psychosocial perspectives. This will enhance our understanding of the unique needs and considerations for this patient population as we strive to provide evidence-based surgical

## The Impact of Socioeconomic Disadvantage on Craniosynostosis Care

Authors: Manasa H. Kalluri, BS, Daniel Y. Chu, PhD, Aidan W. O'Shea, ScB; Gina Krause, BS; Jessica D. Blum, MD, MSc, Kristine M. Carbullido, MD, Catharine B. Garland, MD, Daniel Y. Cho, MD, PhD

**Introduction:** Surgical treatment of craniosynostosis can be performed via a minimally invasive or open approach. While emerging evidence points toward significant advantages of early minimally invasive surgery, this procedure is generally only available to patients presenting before 5 months of age and typically requires postoperative helmet therapy or additional surgery to remove cranial expansion devices. These requirements may pose access challenges. This study aims to assess the relationship between surgical approach, age at surgery, and total number of surgeries with neighborhood-level socioeconomic deprivation, as assessed by the Area Deprivation Index (ADI).

**Method:** A retrospective chart review of patients with nonsyndromic craniosynostosis at American Family Children's Hospital between 2016 and 2023 was performed. Patient addresses were used to calculate a state-based ADI quintile using the University of Wisconsin's Neighborhood Atlas. Sex, ethnicity, race, age at primary surgery, operative technique, and number of required surgeries were collected. Patients with non-Wisconsin home addresses were excluded. Descriptive statistics and univariate analyses were used to analyze binary variables and ANOVA and Spearman-ranked correlation for continuous variables.

**Results:** Of 155 patients (58 male, 97 female), 27% came from the least disadvantaged quintile while 11% came from the most disadvantaged quintile. Mean age at initial surgery was  $9.31 \pm 13.65$  months; age was not significantly associated with ADI quintile ( $p=0.136$ ). A higher ADI quintile, indicating greater disadvantage, was associated with an increased likelihood of undergoing open surgery ( $p=0.015$ ). Total number of surgeries was not associated with ADI quintile ( $p=0.055$ ).

**Conclusions:** Greater socioeconomic disadvantage was associated with a higher likelihood of receiving open surgery in our patients, but not with age at initial surgery. This suggests that factors beyond age at initial surgery contribute to the choice of surgical approach in patients from more disadvantaged areas. Open surgery is known to be associated with increased blood loss, longer hospital stays, and less aesthetically favorable results. Emerging evidence suggests that it may also be associated with inferior neurocognitive outcomes and increased reoperation rates. However, a relative benefit of open surgery over minimally invasive surgery is that it does not require additional postoperative treatment such as regular helmet therapy appointments or a second surgery for device removal, which can add burdens to caregivers. Further advocacy efforts to improve equitable access to minimally invasive surgery and the interventions that make its outcomes most optimal are likely to help alleviate socioeconomic disparities in perioperative and long-term outcomes for patients with craniosynostosis.

## Uncovering the Link: Investigating the Role of Environmental Contaminants in Orofacial Cleft Development

Authors: Jessieka Knazze, MPH, Jessica Blum, MD, MSc., Jasmine Craig, MD, MPH, Gina Krause, BS, Caroline Bay, BA, Sarah Thornton, BA, Nnadozie Uchegbu, MA, Tyler R. Dorobek, BS, Catharine Garland, MD, Daniel Cho, MD, PhD

**Introduction:** There is little known about specific environmental contaminants that lead to orofacial clefts (OFC); thus the objective of this review is to identify environmental contaminants with the strongest associations to OFC development for further investigation so that the mechanisms of OFC development due to environmental contaminants can begin to be elucidated.

**Method:** Preferred Reporting Item for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to conduct a systematic review. A search was conducted of the following databases: PubMed, Embase, Web of Science, and Agriculture & Environmental Science collection Database. Select study and demographic characteristics were extracted and analyzed.

**Results:** Studies were published between the years 1982-2023. Case-control studies accounted for 62% of studies followed by cohort designs at 17%, ecological studies at 6.2% and the remaining 14.8% a combination of retrospective case series, case-crossover, and other designs. Included studies represent 17 countries including China, Taiwan, Indonesia, France, Italy, Sweden, Denmark, Norway, Iran, South Africa, Mexico, Mongolia, Australia, Netherlands, the United Kingdom, Finland and the United States. The majority of authors were in the field of epidemiology (45%) with reproductive/maternal and child health being second (20%). One author was within the field of plastic surgery. Studies initially revealed over 125 contaminants that were potentially associated with OFC. Approximately 74% of studies showed a statistically significant association between the contaminant(s) and OFC formation, indicated by an Odds ratio  $>1$ . Nearly all studies (97%) mentioned a mode of transmission and geographic location. Regarding contaminant exposure, 95% reported a comprehensive exposure assessment, 83% reported a dosage/concentration of contaminant(s), and 71% listed a duration of exposure. Of all identified contaminants, 81 have demonstrated a statistically significant association to OFC development in at least one included paper. These contaminants were transmitted via occupational settings 26% of the time, 22% were ubiquitous in the environment and therefore transmitted via any combination of modes including diet and soil routes, via water sources 21% of the time, via an overlap of air and occupational modes 19% of the time, and via only air 11% of the time. Nitrites, per the included study, were transmitted through diet alone (1% of significant contaminants) (Table 1).

Mode	Major Contaminants
Water	Disinfection by-products: trihalomethanes, haloacetic acids, nitrates
Air	Particulate Matter < 2.5 & 10 $\mu$ m, NO <sub>2</sub> , CO
Occupational	Glycol ethers, aliphatic alcohols
Ubiquitous	Lead, cadmium, barium, arsenic

Table 1. Major Contaminants Identified Stratified by Mode of Transmission



**Conclusions:** Environmental contaminants associated with OFC are diverse and have various modes of transmission and mechanisms of action. Understanding the relationships of environmental contaminants with OFC will enhance our ability to care for all patients with OFC here in Wisconsin.

## The Art of Upper Limb Replacement: A Systematic Review of Upper Limb Replacement Interventions and Techniques

Authors: Jusuf Ademi, Lance Johnson, Lucas Sears, B.S., Samuel O. Poore, M.D., Ph.D., Aaron M. Dingle, Ph.D.

**Introduction:** Individuals that experience upper limb loss struggle to reacclimate to their new reality along with the functional implications associated with their specified rehabilitative intervention. The primary rehabilitative implications for these patients concern issues regarding prosthetic control, dexterity, and sensation—hoping to maximize rehabilitative outcomes while minimizing functional complications. The objectives of this review are to provide a highly-detailed and neutral description of each clinically available upper limb prosthetic device while also consolidating clinical knowledge of upper limb replacement interventions and techniques.

**Method:** Article acquisition began with a general literature survey with the purpose of identifying specific interventions of upper limb rehabilitation. With the information gathered in the initial literature survey, a comprehensive literature survey was conducted; motivated by the trends observed in the general literature survey. Inclusion criteria consisted of systematic reviews of clinically implemented upper limb interventions published after 2018. PubMed was the only database utilized.

**Results:** Of the 278 articles generated by the search, 107 reviews were consistent with inclusion criteria. The accumulated interventions comprised Cosmetic Prosthesis, Body-Powered Prosthesis, Electrically-Powered Prosthesis [Myoelectric, Brain-Computer Interface, or Peripheral – expressed via socket or osseointegration] Hybrid Prosthesis, Activity-Specific Prosthesis, Vascularized Composite Allograft (VCA), and Replantation.

**Conclusions:** Body-powered prostheses are the clinical standard for the upper limb due to their durability and low cost. While electrically-powered devices demonstrate promising advancements in sensation and degrees of freedom, the combined high cost and often low durability limits their practicality as a viable intervention. Hybrid prostheses offer injury specificity by combining both body-powered and electrically-controlled components, mitigating disadvantages of individual components. Cosmetic prosthesis may be a viable option for patients who may choose to prioritize cosmetic rather than functional outcomes. Activity-specific prostheses serve as specific iterations of a prosthetic device meant for a particular activity. VCA and replantation are surgical interventions for upper limb loss where tissue (foreign or native respectively) is integrated into the limb maximizing cosmetic and functional outcomes. Replantation is only suggested if the replanted structure will restore function at least as well as a prosthetic, but patients will often concede greater functional outcomes for preservation of tissue. VCA may present substantial functional and cosmetic outcomes, but this intervention is rather inaccessible as it requires multiple prerequisites for it to be an option. The recipient must be physiologically and immunologically consistent with the donor, and only after all these prerequisites have been met can patients be added to a waitlist similar to organ donation.

## Exploration of Anaplastology Methods for Microtia Prosthetics: Improving Access to Care

Authors: Lauren Feeley, Eli Wu B.S., Sarah Hu, Aaron M. Dingle Ph.D., Samuel O. Poore M.D., Ph.D.

**Introduction:** In Vietnam, there is a high prevalence of patients with microtia and a demand for reconstruction. The gold standard is autologous rib reconstruction which requires multiple stages and patients can be lost to followup. Anaplastology is a field in which prosthetics are constructed for patients. Prosthetic application can involve one minimally invasive surgery for osseointegration, or a non surgical option with the use of glue for application. However, the field of Anaplastology is small and the work remains largely unpublished in plastic surgery journals. The primary objective of this study is to develop a low-cost, accessible, and satisfactory treatment for microtia using anaplastology technique to improve its access worldwide.

**Method:** Alginate is used to create an ear mold of unaffected contralateral ear as an inexpensive alternative to silicone. The mold is filled with plaster to create a cast of the contralateral ear. The cast of the contralateral ear is then scanned using smartphone 3D scanning technology (Polycam). The scanned virtual model is mirrored using free open source software. This virtual model can be mirrored to create a mold to produce an ipsilateral ear reconstruction. Various methods for creating an ipsilateral reconstruction mold have been tested (one part 3D printed mold filled with silicone, alginate mold filled with silicone, and direct 3D printed reconstruction).

**Results:** Out of the methods we tested for creating the molds, those constructed out of silicone are the most realistic. A one part 3D printed mold is currently the most promising, but further development is needed to optimize results.

**Conclusions:** Further development is needed to create an ear that minimizes imperfections and maximizes durability. Exploration of different options for creating the ear mold is intended, such as considering a three-part mold. The use of wax would also improve moldability and reduce computer requirements and technological skill. Additionally, bubbles in silicone products can be minimized by mixing the silicone with an additive to alter the texture of the product. Lastly, color theory can be explored to mimic differences in skin coloring, and the addition of details to make the ear more realistic can also be used.

## **Perspectives from Surgeons who Meditate: How Training the Mind Influences Well-being and Practice**

Authors: Sydney Tan, MD, Vasu Rishi, BS, Bhabna Pati, MS, Esra Alagoz, PhD, Dawn M Eifenbein, MD, MPH

**Introduction:** Training the mind by meditating can improve surgeon well-being, concentration, and non-technical skills. Current research on how meditation influences surgeon well-being focuses on interventions for novice meditators. Little is known about the effects of meditation on surgeons who already meditate. We conducted a qualitative study to describe how meditation influences surgeon well-being and surgical practice in established meditation practitioners.

**Method:** Semi-structured interviews were conducted with practicing or retired surgeons nationwide who self-identified as meditators. Participants were recruited through word of mouth and surgery network email lists. The interview guide was developed using the established Awareness, Connection, Insight and Purpose (ACIP) well-being framework to explore well-being domains influenced by meditation. Four researchers iteratively developed the codebook based on ACIP domains and created new codes for constructs specific to surgery (e.g. operating room performance, surgeon identity) and meditation (e.g. challenges for meditation practice). We coded the data using thematic analysis, identifying influences of meditation on surgeon well-being and surgical practice.

**Results:** We interviewed 12 participants. Participants were 50% male and included three obstetrics-gynecologists, two acute care surgeons, two endocrine surgeons, two otolaryngologists, one general pediatric surgeon, one transplant surgeon, and one urologist. Participants identified meditation influencing all four ACIP domains: Awareness, Connection, Insight, and Purpose. Surgeons found meditation developed awareness in the operating room through focus and concentration. Outside of the operating room, surgeons practiced awareness by being present in daily life and noticing negative self-talk or reactions. Furthermore, surgeons identified improved connection with patients, colleagues, and operating teams through emotion regulation and increased compassion. Connection intersected with Purpose in that fostering purpose was tied to helping others. We found Awareness and Insight overlapped with surgeons developing self-awareness of their vulnerabilities which created tension with their identity as a surgeon. Challenges to meditation practice included time and stigma in the surgical community.

**Conclusions:** Meditation plays a transformative role in the well-being and work of surgeons with established meditation practices. However, stigma and community perceptions of meditation were challenges to meditation practice even for experienced meditators. Addressing these barriers and integrating meditation training into surgeon development and surgical workflows can promote well-being.

## Performance of Machine Learning Weight Gain Prediction Models Using Electronic Health Record and Survey Data

Authors: Kate V. Lauer MD, Dawda Jawara MD, Manasa Venkatesh MS, Lily N. Stalter MS, Bret M. Hanlon PhD, Matthew M. Churpek MD, MPH, PhD, Carson Gehl BS, Anai N. Kothari MD, MS, Luke M. Funk MD, MPH

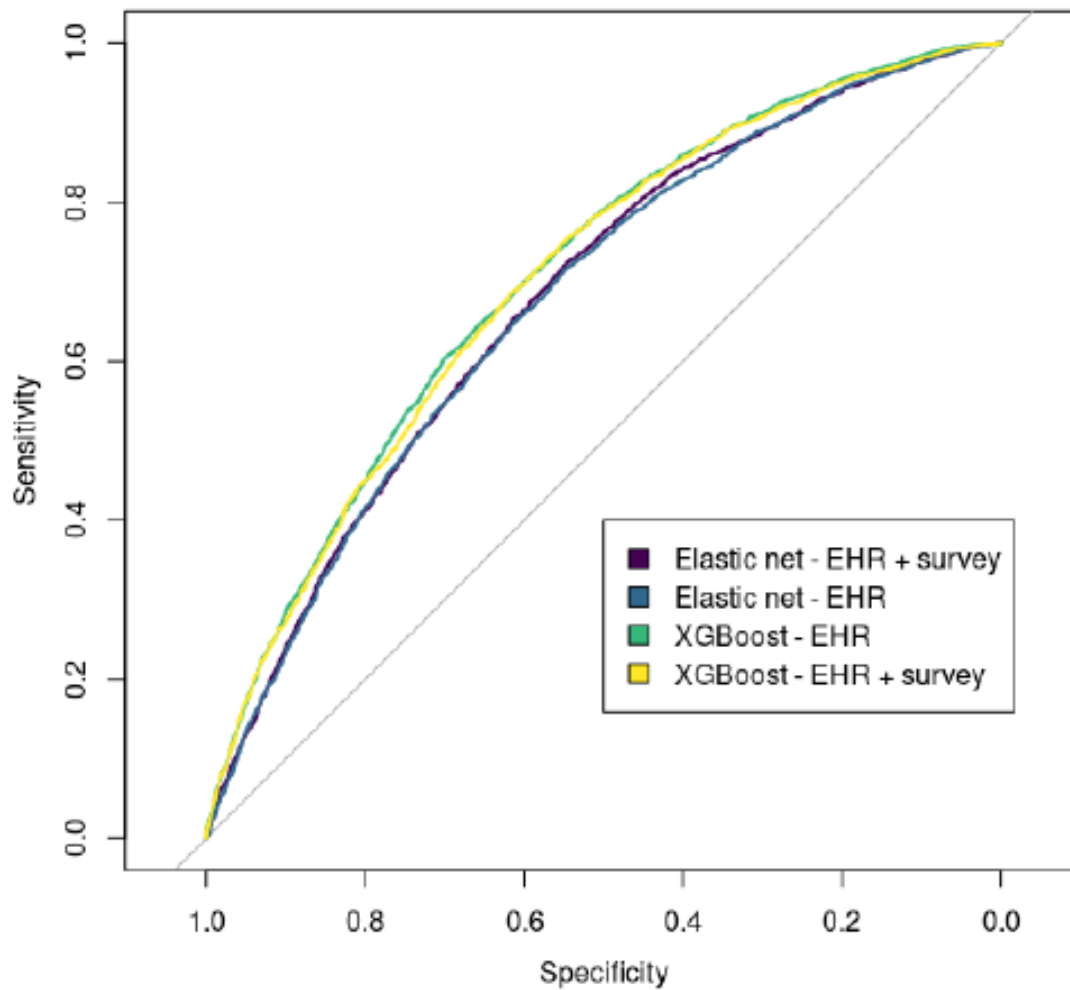
**Introduction:** Obesity, defined as a body mass index (BMI) of  $\geq 30$  kg/m<sup>2</sup>, is a major public health concern in the United States. More than 40% of adults meet BMI criteria for obesity. Addressing obesity using behavioral treatment, medications, and/or bariatric surgery is effective for patients who utilize these evidence-based treatments, but they have not reversed the rise in obesity prevalence. Preventative approaches are essential to curbing the obesity epidemic. However, they are limited by an inability to accurately predict individuals at highest risk of weight gain. Our study objective was to develop accurate machine learning weight gain prediction models using the All of Us dataset. We hypothesized that machine learning algorithms, including elastic net logistic regression (EN) and XGBoost, would have higher performance in weight gain prediction with the inclusion of patient behavioral survey data.

**Methods:** Our study utilized the racially representative NIH-funded All of Us dataset. Adults age 18-70 years old with weight measurements two years apart between 2008 and 2022 were selected. Exclusion criteria included a history of cancer, bariatric surgery, or pregnancy during the study interval. Predictors used in the models included demographics, vital signs, laboratory results, comorbidities, and survey data (Alcohol Use Disorder Identification Test [AUDIT-C], Patient-Reported Outcomes Measurement Information System [PROMIS] physical and mental health scores). The primary outcome was  $\geq 10\%$  total body weight (TBW) gain at two years. EN and XGBoost machine learning models were developed with and without survey data. The data was split into a training sample (60%) and a testing sample (40%), and parameters were tuned using 10-fold cross validation. Model performance was compared using area under the receiver operating characteristic curves (AUCs).

**Results:** Our cohort consisted of 34,715 patients (mean [SD] age 50.9 [13.4] years); 45.7% White; 55.3% female). Over a two-year span, 10.4% of the cohort gained  $\geq 10\%$  TBW. AUCs for EN and XGBoost models were 0.663 [95% confidence interval 0.648-0.677] and 0.716 [0.702-0.729], respectively. Incorporation of survey data did not improve performance, with AUCs of 0.667 [0.653-0.682] and 0.715 [0.702-0.729].

**Conclusions:** Incorporation of AUDIT-C and PROMIS physical and mental health scores did not improve the performance of EN and XGBoost machine learning weight gain prediction models. The addition of other All of Us variables, including genomic data, may be informative in future studies.

**Figure 1: Area under the receiver operating characteristics curves for weight gain prediction models with and without survey data**



Area under the receiver operating characteristic curves (AUCs) for elastic net and XGBoost models based on electronic health record (EHR) data with and without survey data. Survey data did not improve model performance. XGBoost with and without survey data had slightly higher performance compared to elastic net.

## Longitudinal Assessment of Solid Organ Transplant Recipients with SARS-CoV-2

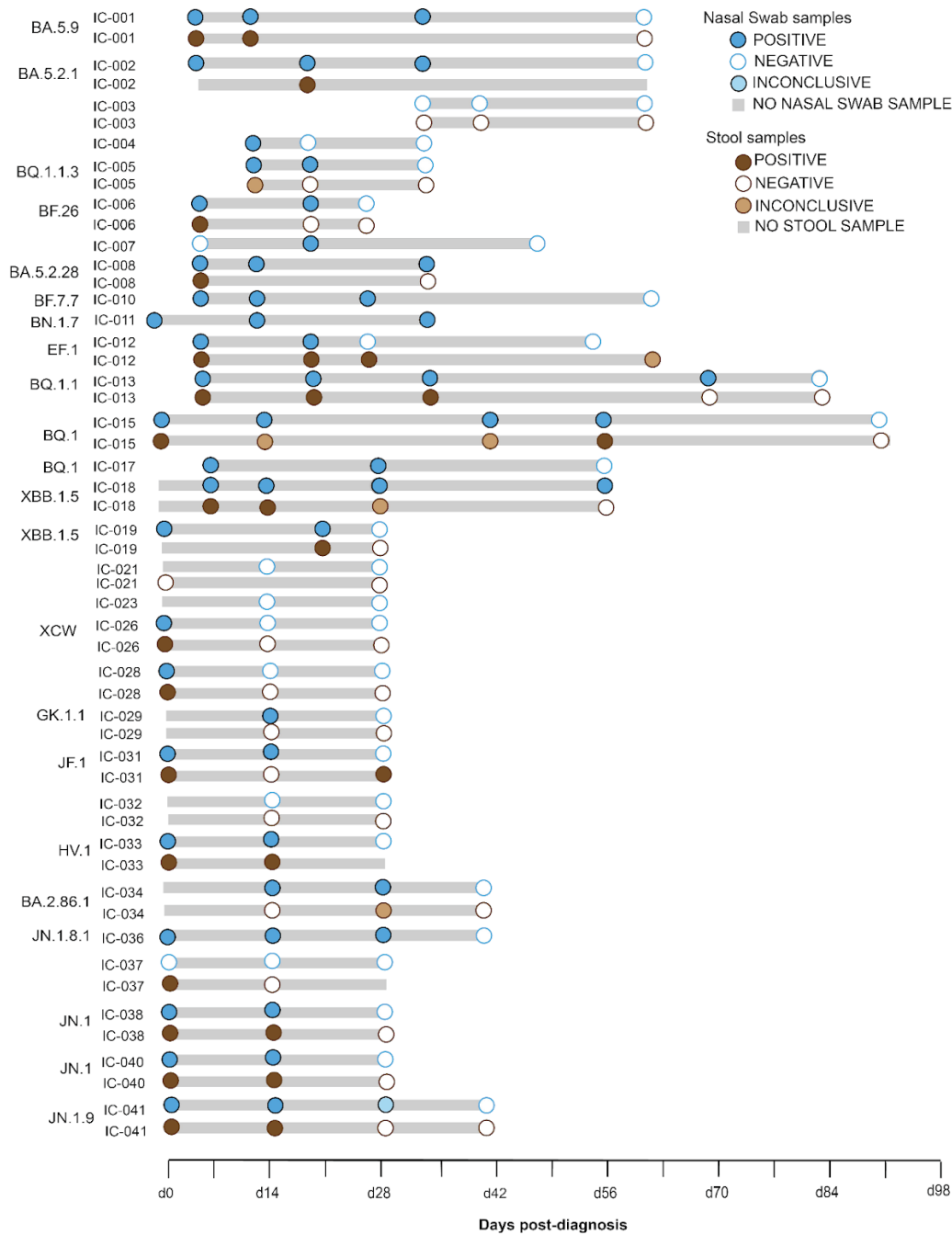
Authors: Bradley, T. BS, Garonzik-Wang, J. MD-PhD, O'Connor, D., PhD, Friedrich, T., PhD, Wilson, N., PhD, Smith, J., MD, Gifford, A. MA, Mohamed, R. MBBS, Shipe, A. BS, Benito, M. BS, Bhasin, M. BS, VanSleet, G. BS, DePachter, C. BS, Richardson, A. BS, Weiler, A. MS, BS, Wei, W. BS, Machkovech, H. MD-PhD, Ries, H. BS, Bhimalli, P. BS, Minor, N. MS, BS, Lail, A. BS, Emmen, I. BS, Bobholz, M. BS, Vuyk, W. BS

**Introduction:** Immunocompromised individuals are more likely to experience prolonged SARS-CoV-2 infection, however there is limited knowledge about risk factors for and duration of infection in solid organ transplant recipients (SOTs). As there are broader public health implications associated with prolonged SARS-CoV-2 infection, we prospectively followed SOTs to determine the prevalence and duration of prolonged SARS-CoV-2 shedding. When possible, we evaluated viral variants among those with persistence to compare against when variants peaked within the community.

**Method:** SOT recipients who tested positive for SARS-CoV-2 infection were enrolled and provided baseline nasal and optional stool samples. Prospective samples were collected on day 7, day 14, day 28, and monthly thereafter for up to 2 years after COVID diagnosis. We utilized RT-qPCR to determine if stool and nasal samples contained SARS-CoV-2. Where possible, we sequenced the viral genome. Participants were removed from the study once they tested negative for SARS-CoV-2 by both nasal swabs and stool samples. Participants could also complete optional surveys at each time collection point, and researchers conducted chart reviews on each participant.

**Results:** A third (11) of the 29 enrolled SOTs tested positive at or beyond day 28 from their initial positive SARS-CoV-2 test result. Three of the 29 participants tested positive in nasal swabs out to 56+ days post-infection, and one stool sample also tested positive at day 56 (Figure 1). One participant had a high viral load ( $Ct < 30$ ) at 28d post infection, with continued detection out to 54 days post infection even after receiving antiviral medications and vaccinations.

**Conclusions:** 30% of the enrolled SOT recipient cohort had viral persistence at and beyond 28 days post-infection. These findings suggest some SOT recipients continue to test positive for SARS-CoV-2 well beyond the 20d recommended isolation guidelines. There was no association between length of viral shedding and viral lineage, immunosuppression, or time from transplantation to infection. Further exploration of prolonged SARS-CoV-2 infections is warranted to better understand ongoing SARS-CoV-2 viral evolution and variants in immunocompromised individuals and the impact on general population health.



**Figure 1. Kinetics of viral RNA positivity in SOT recipients.** Blue (filled-in) dots signify a **positive** nasal swab result. The light blue-filled dot indicates an **inconclusive** test. White (with a blue outline) dots indicate a **negative** result. Dark brown circles indicate **positive** results from stool samples. Light brown circles indicate **inconclusive** results, meaning that of the 3 gene targets used in the assay, we detected at least one of the genes but not all three replicates for each gene. White circles (with brown outline) indicate **negative** results. Stool and nasal swab samples were taken on the same day. If sequencing was possible, the lineage is shown to the left of the ID. The \* indicates the one patient who was a persistent shedder, defined as having samples that tested positive after 28 days of infection, and who had a high viral load at this time point, with a Ct <30. Subjects whose nasal swabs and stool samples both tested negative for SARS-CoV-2 on or before day 28 were removed from the study and no further samples were collected from these subjects.



## Using a centralized normothermic machine preservation and assessment service to rescue hard-to-place kidneys

Authors: Gifford A, Bradley T, Holzner ML, Goggins W, Guerra G, Philip JL, van Leeuwen LL, Shapiro R, Leuvenink HGD, Jaynes CL, Garonzik-Wang JM

**Introduction:** Normothermic machine perfusion (NMP) may allow for improved preservation and assessment of donor kidneys. This presentation reports the initial results of using the 34 Lives (West Lafayette, Indiana) preservation service with brief NMP to rescue hard-to-place kidneys for transplant.

**Method:** Recovered kidneys that exhausted standard UNOS allocation were transported to a third-party preservation service via hypothermic machine perfusion (HMP). Grafts underwent 2 hours of NMP at 35°C with an acellular perfusate for further assessment. Parameters assessed during NMP included flow, resistance, urine output, lactate, and Hosgood scores. Following NMP, accepted kidneys were placed on an oxygenated HMP device and transported to recipient centers. Early post-transplant outcomes were examined.

**Results:** 15 hard-to-place kidneys were transplanted after undergoing NMP. Kidneys were declined for a combination of biopsy findings, donor history, and poor preservation on HMP. Mean donor age, KDPI, and terminal serum creatinine (SCr) were 47.4 years, 64%, and 2.9 mg/dL, respectively (see Table 1 for detailed donor and graft characteristics). The median initial cold ischemia time (CIT) from cross-clamp to start of NMP was 19 hours (IQR 16-22 hours). Median flow and resistance after 2 hours of NMP were 680 ml/min and 0.11. At the conclusion of NMP, median urine output and lactate were 15ml (4-24 ml) and 2.2 mmol/L, respectively. Flow and resistance on HMP significantly improved following NMP (mean resistance on HMP pre-NMP 0.39 vs. 0.15 post-NMP; mean flow on HMP pre-NMP 84 ml/min vs. 138 post-NMP). The median total out of body time (cross-clamp to reperfusion) was 37 hours (IQR 32-44 hours). 11 recipients had immediate graft function (73%) while four (27%) had delayed graft function (DGF). Mean SCr and eGFR at 30-days were 2.0 mg/dL and 39, respectively.

**Conclusions:** These early results support utilization of centralized NMP to rescue hard-to-place kidneys with low rates of DGF. NMP can provide additional information for the assessment of marginal deceased donor kidneys, may improve discard rates, and may increase utilization rates.

**Table 1. Hard-to-place kidney and donor characteristics**

Kidney	Age	Donor type	Reason for decline	KDPI	Admit Cr	Peak Cr	Terminal Cr	1 <sup>st</sup> HMP resistance/flow	DGF
1	52	DBD	Biopsy results (re-biopsied)	70%	1.67	2	1.89	0.35/94	No
2	46	DCD	Biopsy results	68%	1.33	1.92	1.92	0.37/82	No
3	46	DCD	Biopsy results (re-biopsied)	68%	1.33	1.92	1.92	0.36/95	Yes
4	53	DBD	Biopsy results	61%	0.78	1.46	0.79	0.37/43	No
5	36	DBD	Creatinine/CRRT	29%	1.81	11.09	1.85	0.27/94	No
6	63	DCD	Biopsy results	79%	1.86	1.86	0.97	0.08/142	No
7	62	DBD	Donor history	87%	0.85	3.11	0.82	0.21/119	No
8	62	DBD	Donor history	87%	0.85	3.11	0.82	0.2/106	No
9	34	DBD	HMP parameters/CRRT	28%	1.2	5.5	5.5	0.68/48	Yes
10	34	DBD	HMP parameters/CRRT	28%	1.2	5.5	5.5	0.68/48	No
11	56	DCD	Biopsy results	93%	1.9	3.3	3.1	0.23/77	No
12	46	DCD	Biopsy results (re-biopsied)	53%	2	2.2	2.2	0.21/125	No
13	53	DCD	History/HMP parameters/creatinine	86%	1.22	3.6	3.6	1.03/33	Yes
14	53	DCD	History/HMP parameters/creatinine	86%	1.22	3.6	3.6	0.35/88	Yes
15	15	DBD	HMP parameters/creatinine	33%	10.9	10.9	8.6	0.52/71	No

# Mitigating Intraoperative Hypothermia in Plastic Surgery: The Need for Multimodal Warming Protocols to Optimize Surgical Outcomes

Authors: Keenan Fine

**Introduction:** Maintaining normothermia during surgery is essential to prevent SSIs, coagulopathy, and delayed discharge from PACU. This study investigates intraoperative temperature changes and development of hypothermia in plastic surgery and highlights the need for multimodal warming strategies to prevent hypothermia in different procedures.

**Method:** This retrospective analysis examined intraoperative temperature changes in 4,165 patients who underwent surgical procedures under general anesthesia at an academic institution from July 2021 to June 2024. Preoperative and postoperative temperature data were collected, and multivariable linear regression was used to assess the relationship between procedure type and temperature change, adjusting for surgery length and inpatient versus outpatient status. The proportion of patients with postoperative temperatures below 36°C, 35°C, and 34°C was also compared across procedure types.

**Results:** Plastic surgery procedures (n=2194) showed a mean temperature change of  $-0.34 \pm 1.85^\circ\text{C}$ , compared to an increase of  $0.06 \pm 1.80^\circ\text{C}$  in non-plastic surgery procedures ( $p < 0.001$ ). Multivariate regression analysis revealed that body contouring ( $p=0.020$ ), pedicled breast reconstruction ( $p=0.004$ ), revision breast reconstruction ( $p < 0.001$ ), and tissue expander breast reconstruction ( $p=0.009$ ) were associated with temperature decreases. These same procedures also experienced a significant increase in the proportion of patients with a body temperature of  $< 36^\circ\text{C}$  from pre- to postoperation. Gender mastectomy ( $p=0.056$ ) and non-reconstructive breast surgery ( $p=0.075$ ) approached significance. Longer surgeries ( $p < 0.001$ ) and outpatient procedures ( $p=0.006$ ) were associated with a lower likelihood of intraoperative temperature decreases.

**Conclusions:** Intraoperative hypothermia remains prevalent across many plastic surgery procedures, despite current warming practices and consistent use of a bair hugger device. The significant temperature drops observed in specific procedures, particularly implant-based breast reconstruction, as well as significant proportions of patients with initial body temperature  $< 36^\circ\text{C}$  indicate a need of multimodal operative warming techniques (foil caps, heat moisture exchangers, warm IV fluids, plastic wrap of extremities) to maintain normothermia.

**Table 1: Proportion of Patients with Pre- and Postoperative Temperature  $< 36^\circ\text{C}$**

Procedure Group	N	Preop Temp $< 36^\circ\text{C}$ (%)	Postop Temp $< 36^\circ\text{C}$ (%)	P-value
Blepharoplasty	22	86.4	40.9	0.006
Body Contouring	287	36.9	44.3	0.036
Elective Hand	31	38.7	38.7	1.000
Face and Nose	391	73.9	44.5	$< 0.001$
Free Flap Breast Reconstruction	116	55.2	21.6	$< 0.001$
Gender Mastectomy	58	34.8	43.3	0.060
Mastectomy	889	51.5	35.9	$< 0.001$
Non-reconstructive Breast	131	35.9	42.7	0.005
Pedicled Breast Reconstruction	38	57.9	47.4	0.503
Revision Breast Reconstruction	49	38.2	71.2	$< 0.001$
Tissue Expander Breast Reconstruction	203	24.1	62.1	0.007

## **Effect of Deployed Cardiothoracic Surgeons on Clinical Outcomes in United States Service Members with Thoracic Trauma in Operation Iraqi Freedom**

Authors: Timothy Guenther, MD, Michael Moulton, MD, Malcolm DeCamp, MD, Joshua Gustafson, MD

**Introduction:** Conflicts related to Operation Iraqi Freedom (OIF) led to nearly 32,000 wounded US service-members, with thoracic injuries seen in 8.6% of casualties. At various points throughout the conflict, surgical subspecialist were deployed in theater to care for wounded casualties. Our aim was to determine the effects of deployed cardiothoracic surgeons.

**Method:** A retrospective analysis of Department of Defense Trauma Registry data was performed. Inclusion criteria included US service members with thoracic trauma (as defined by ICD-9 codes) that sought care at the Role 3 hospital at Balad Iraq from 2004-2011 during OIF. Patients with isolated inhalation injuries without other thoracic trauma were excluded. Deployment timelines were established to determine when a United States Air Force cardiothoracic surgeon was present at Balad. Patients that met inclusion criteria were divided into two cohorts based on the presence of a cardiothoracic surgeon. Clinical outcomes such as patient demographics, injury type, injury severity score (ISS), type of thoracic trauma, thoracic procedures performed (as defined by ICD9-CM codes), blood product administration, transfer times, and mortality were assessed and compared between the 2 cohorts.

**Results:** One hundred and nine patients met inclusion criteria; 93.6% (n=102) of these patients were treated at Balad when a cardiothoracic surgeon was present and 6.4% (n=7) when a cardiothoracic surgeon was not present. Ninety eight percent of all patients from both cohorts were male and the most common mechanism of injury was penetrating (58.7%, n=64). Average Injury Severity Score (ISS) of patients when a cardiothoracic surgeon was present was 27.6 and when one was not was 29.4 (p value 0.73). The mean time between injury and presentation to Balad was 697 min when a cardiothoracic surgeon was present compared to 294 min when on was not present. (p-value 0.34). The most common injury observed between both cohorts was a pneumothorax and the most common thoracic procedure performed at Balad was bronchoscopy followed by chest tube placement. (Table 1) A mortality rate of 9.8% was observed in the cohort where a cardiothoracic surgeon was present and 14.3% in the cohort where a cardiothoracic surgeon was not present (p-value 0.70).

**Conclusions:** A USAF cardiothoracic surgeon was present at Balad for a large percentage of the time during OIF. The severity/distribution of patient injury and clinical outcomes appeared similar when a cardiothoracic surgeon was present/not present. A deeper understanding of the effects of deployed surgical subspecialist may aid in future conflicts.

		Number of Patients When a CT Surgeon was Present (% total)	Number of Patients When a CT Surgeon was not Present (% total)	
Thoracic Injury	Pneumothorax	n=60 (58.8)	n=6 (85.7)	
	Pulmonary contusion	n=52 (51.0)	n=3 (42.9)	
	Hemothorax	n=39 (38.2)	n=4 (57.1)	
	Rib Fractures (without flail chest)	n=33 (32.4)	n=2 (28.6)	
	Diaphragm Laceration	n=19 (18.6)	n=0 (0)	
	Burn of trachea/larynx/lung (inhalation injury)	n=15 (14.7)	n=1 (14.3)	
	Tracheal/bronchial injury	n=9 (14.7)	n=2 (28.6)	
	Chest wall contusion	n=7 (6.9)	n=0 (0)	
	Thoracic aorta/great vessel/PA/PV injury	n=7 (6.9)	n=1 (14.3)	
	Open chest wound	n=6 (5.9)	n=0 (0)	
	Rib Fractures (with flail chest)	n=4 (3.9)	n=0 (0)	
	Pulmonary laceration	n=4 (3.9)	n=2 (28.6)	
	Larynx injury	n=3 (2.9)	n=0 (0)	
	Cardiac injury	n=3 (2.9)	n=0 (0)	
	Thoracic trauma not otherwise specified	n=2 (2.0)	n=0 (0)	
	Sternal fracture	n=2 (2.0)	n=0 (0)	
	Pericardium laceration/injury	n=2 (2.0)	n=0 (0)	
	Esophageal injury	n=2 (2.0)	n=0 (0)	
	Procedure Performed at Balad	Bronchoscopy with concomitant thoracic trauma	n=78 (76.5)	n=6 (85.7)
		Chest tube placement	n=68 (66.7)	n=4 (57.1)
Esophagogastroduodenoscopy		n=17 (16.7)	n=0 (0)	
Diaphragm repair		n=16 (15.7)	n=0 (0)	
Exploratory thoracotomy		n=11 (10.8)	n=2 (28.6)	
Tracheostomy		n=10 (9.8)	n=0 (0)	
Lung resection/repair		n=8 (7.8)	n=2 (28.6)	
Repair of trachea		n=5 (4.9)	n=0 (0)	
Pericardial window		n=5 (4.9)	n=0 (0)	
Repair cardiac injury		n=3 (2.9)	n=0 (0)	
Chest Wall Repair		n=3 (2.9)	n=0 (0)	
Esophageal repair		n=2 (2.0)	n=0 (0)	
Repair of larynx		n=1 (1.0)	n=0 (0)	
Re-opening thoracotomy		n=1 (1.0)	n=0 (0)	
Great vessel repair	n=1 (1.0)	n=0 (0)		

## Cancellations in Congenital Heart Disease Surgery

Authors: Connor Cook, M.D., Jacob Switzer, B.S., Joshua Hermsen, M.D., Xiao Zhang, PhD., Natasha Hendrickson, P.A., John Hokanson, M.D.

**Introduction:** Short-term cancellation of surgical procedures has been demonstrated to negatively impact patient outcomes and increase healthcare costs. Although recognized as common, quantification of the frequency of cancellations in patients with congenital heart disease has not been previously described.

**Method:** Patients with congenital heart disease scheduled for surgical repair at the University of Wisconsin from January of 2018 through December of 2023 were reviewed. For patients with multiple scheduled procedures, only the principal surgery was included. Subsequent non-cardiac procedures were excluded. Patients' age at surgery and the STAT score (a measure of operative risk) were recorded. Cancellations were categorized into patient factors and institutional factors. Patient factors included viral illness, other illness, abnormal labs, and additional imaging required. Institutional factors included emergent surgical case taking priority, no bed available, no surgeon available, no operating room available, and insurance issues. Patients who had surgeries cancelled due to viral symptoms were counted as a viral illness, even if viral testing was not obtained. Patients with positive PCR and home antigen tests were considered confirmed COVID infections and other viral confirmations were confirmed with viral pathogen panel testing.

**Results:** A total of 729 cases were analyzed. Of these, 220 (30%) were cancelled with 145 (66%) cancelled due to patient factors and 68 (31%) cancelled due to institutional factors. The most common patient factor contributing to cancellation was a suspected or confirmed viral illness (69/145, 48%). The most common viral etiology for cancellation was rhinovirus (27/76, 36%), followed by SARS-COV-2 (17/76, 22%) with 15/76 (20%) symptomatic patients not having viral testing done. The most common institutional factor was an emergent case taking priority (33/68, 49%). As a single procedure may have been cancelled multiple times, the total number of cases scheduled (729) exceeds the total number of cases performed (682). Unsurprisingly, cancellations were least common in neonates and STAT 5 procedures but were similar across all other age groups and STAT categories. Cancellations did not show a notable seasonal variation.

**Conclusions:** The most common cause for cancellation of a congenital heart disease surgeries is a viral illness. Although neonates and patients needing STAT 5 procedures were the least likely to be cancelled, the rate of cancellation was similar across the other age and STAT categories. In a cohort including the COVID 19 pandemic, there was no obvious seasonal variation in cancellations.

Table 1: Cancellation Rates by Age and STAT Score

	Total Cases	Percent Cancelled
STAT Score		
1	393	25.2%
2	127	32.3%
3	74	24.3%
4	44	29.5%
5	44	4.5%
Age		
0-30 days	99	5.1%
1-6 mo	166	20.5%
6-12 mo	68	41.2%
1-9 yrs	148	37.2%
9-18 yrs	78	16.7%
>18 yrs	123	30.9%
Total	682	25.4%

## **Navigating Anticancer Treatments: Recommendations for Surgical Planning in Breast Reconstruction**

Authors: Sarah M. Thornton, B.A., Emily E. Zona, B.S., Ellen C. Shaffrey, MD, Mark E. Burkard, MD, PhD, Brett F. Michelotti, MD, Samuel O. Poore, MD, PhD, Meeghan A. Lautner, MD, Jacqueline S. Israel, MD

**Introduction:** Adjuvant anticancer agents are often prescribed to patients with breast cancer to reduce the risk for recurrence and improve outcomes. Advancements in targeted therapies have led to the need to integrate these treatments with surgical planning for breast reconstruction. This study aims to review literature on recommendations, side effects, and risks associated with anticancer agents during elective, medically-necessary breast reconstruction, and to present expert multidisciplinary consensus recommendations from a single center.

**Method:** Following the PRISMA 2020 guidelines, we queried three databases for relevant keywords (e.g., “breast reconstruction” AND “anticancer agent”). Inclusion criteria encompassed studies on anticancer agents and breast reconstruction; non-English articles and reviews were excluded. Perioperative recommendations were developed based on systematic review findings and multidisciplinary expert consensus.

**Results:** The initial query identified 1,188 papers, which narrowed to 19 included articles involving 5,793 patients. Included studies discussed tamoxifen (18), aromatase inhibitors (8), trastuzumab (2), and pertuzumab (1). No studies examined the effects of other agents like GnRH agonists or pembrolizumab. We created guidelines on when to hold medications preoperatively. Expert consensus indicated that most do not need to be held, though preoperative lab tests for leukocytes and/or platelets are advised in some cases.

**Conclusions:** Plastic surgeons play a crucial role in the care of patients with breast cancer who undergo reconstruction. Rapid research advancement makes it challenging for plastic surgeons to be well-versed in the impact of anticancer agents on perioperative risk and surgical outcomes. While ever-changing, these guidelines can help plastic surgeons with medication management for these patients.

## Acoustic Analysis of Blues, Country, Folk, Italian Opera, and Rock Singing

Authors: Grayson Bienhold, Owen Wischhoff, BS, Taylor Chumbley, Elise Moreira, Jack Jiang, MD

**Introduction:** This study investigates the distinct vocal characteristics of five music genres – blues, country, folk, Italian opera, and rock – by applying nonlinear acoustic analysis. Each genre is also compared to healthy speech phonation. The aim is to determine Cepstral Peak Prominence (CPP) and Correlation Dimension (D2) values and develop a comprehensive Voice Type Component Profile (VTCP) for each genre. This research seeks to quantify the levels of chaos and aperiodicity in singing voices across these genres, providing insights into the acoustic makeups unique to each singing style.

**Method:** 50 voice samples of the vowel /i/ from the Saarbrücken Voice Database were collected and analyzed. 29 voice samples from blues song “Call It Stormy Monday”, 29 samples from country song “Jolene”, 24 samples from folk song “City of New Orleans”, 23 samples from Italian Opera song “Nessun Dorma”, and 29 samples from a rock song “Man in the Box” were randomly selected from YouTube and analyzed for CPP, D2, and VTCP.

**Results:** Preliminary results show that rock singing exhibited significantly higher D2 values and lower CPP values compared to blues, country, and folk singing. Blues had significantly lower CPP values than the other genres. VTCP analysis revealed that rock singing had the lowest proportion of periodic Type 1 signals and the highest proportion of chaotic Type 3 signals. Folk singing contained the highest amount of VTC1 signals. Blues singing contained the greatest proportion of Type 4 signals, whereas rock singing displayed the smallest proportion of such signals.

**Conclusions:** The findings highlight the unique vocal demands and potential dysphonia associated with each genre. The results show rock singing displays greater levels of aperiodicity and low levels of stochastic noise. The high VTC4 proportion in blues singing may be attributed to its use of expressive techniques like growling or rasps to achieve its soulful and emotional sound. Folk singing appears to be the most similar to healthy speech phonation, likely due to the storytelling characteristics of the genre. Understanding acoustic differences can inform vocal training and health strategies, particularly for genres sharing similar traits with rock singing that exhibit higher levels of chaos.



## Early Experience with Proximal Gastrectomy with Double Tract Reconstruction in the U.S.

Authors: Greg Sigler, MD; Brittany Walker, BSc; Kaitlyn Kelly, MD, MAS

**Introduction:** Proximal gastric cancer has historically been treated with total gastrectomy (TG). Proximal gastrectomy (PG) with double-tract reconstruction (DTR) is an alternative procedure, which involves removal of the cardia and preservation of the distal stomach, pylorus, and duodenum with numerous purported benefits.

**Method:** We performed a single-institution review of patients who underwent PG and DTR and compared this cohort patients who underwent TG for proximal gastric cancer in the same time period.

**Results:** We began to offer PG-DTR at our institution in 2022 and have offered the procedure to 10 patients. The median age was 65 years (range 35-85). The median BMI was 29.3 (range 25.5-39.3). The diagnosis was gastric adenocarcinoma in 8 (80%), GIST in 1 (10%), and NET in 1 (10%). Tumors were in the gastroesophageal junction (GEJ) or cardia and all patients underwent baseline EUS confirming localized disease in the proximal stomach. The operative approach was laparoscopic in 8 (80%) and open in 2 (20%). One patient required conversion to TG due to positive distal margin on frozen section. For the 9 who had PG-DTR, median operative time was 480 minutes (range 360-540) and EBL was 100ml (range 50-700). All patients had a margin negative (R0) resection and the median number of lymph nodes examined was 17.0 (range 11-27). When D2 dissection was performed, the median number was 25 (range 22-27). The median length of hospital stay was 6 days (range 4-8). 30-day minor morbidity occurred in 2 patients (22%) and major morbidity occurred in 2 patients (22%). No patient died during or after surgery. In comparing short-term outcomes of these 9 patients who had PG-DTR to 9 who had TG in the same time period, all were similar (Table).

**Conclusions:** Here we report patient selection criteria and short-term outcomes for PG-TGR at a U.S. center. These data suggest that PG-DTR is a reasonable alternative to TG for carefully selected patients with proximal gastric malignancy in the U.S., including locally-advanced and poorly-differentiated adenocarcinoma. Margins should be assessed intraoperatively by frozen section.

**Table. Demographics and Short-term Outcomes**

	<b>PG-DTR (n=9)</b>	<b>TG (n=9)</b>
Age	65 (25-85)	69 (51-80)
BMI	29.3 (25.5-39.3)	25.3 (19.7-35.4)
Female Gender	1 (10)	3 (30)
White Race	9 (100)	9 (100)
Histology		
GIST	1 (11)	1 (11)
NET	1 (11)	0
Adenocarcinoma	7 (78)	8 (89)
Tumor location		
GEJ	4 (44)	2 (22)
Cardia	5 (56)	2 (22)
Body	0	4 (44)
Diffuse	0	1 (11)
Neoadjuvant Therapy	8 (89)	7 (78)
Approach		
Laparoscopic	7 (78)	5 (56)
Open	2 (22)	4 (44)
Operative Time (min)	480 (360-540)	360 (240-510)
EBL (ml)	100 (50-700)	150 (50-1000)
Node retrieval	17 (11-27)	21 (5-45)
R0 Margin	9 (100)	9 (100)
Length of Stay (days)	6 (4-9)	6 (5-78)
30-day Minor Morbidity	2 (22)	2 (22)
30-day Major Morbidity	2 (22)	3 (30)
30-day Return to OR	0	0
30-day Readmission	4 (44)	1 (11)

## Gastric Cancer in the United States: How Can We Do Better?

Authors: Greg Sigler, MD; Brittany Walker, BSc; Kaitlyn Kelly, MD, MAS

**Introduction:** The United States (U.S.) is a low-incidence country for gastric cancer and screening is not performed. As a result, patients most commonly have advanced-stage disease at diagnosis. We evaluated a comprehensive U.S. dataset to assess patient presentation and identify opportunities for earlier diagnosis.

**Method:** We reviewed all gastric cancer diagnoses at a single academic center over the past 11 years (2013 – 2024) and reviewed demographics, presenting signs and symptoms, diagnostic evaluations, stage at diagnosis, and outcomes.

**Results:** We identified 249 patients with gastroesophageal junction (GEJ) or gastric adenocarcinoma. The median age at diagnosis was 66 years (range 19 to 95). 216 patients (86%) were white, 12 (5%) were Asian, 13 (5%) were African American, and race was not reported for 8 (3%). 133 patients (53%) had a family history of cancer and 7 (2%) had a predisposing germline mutation. 41 patients (17%) had stage I disease at diagnosis, 109 (43%) had stage II/III, and 99 (40%) had stage IV. The presence of GI-related symptoms at diagnosis was statistically-significantly associated with more advanced disease ( $p < 0.001$ ), and symptoms differed across stages. The most common presenting symptoms for stage I patients were reflux, GI bleed, abdominal pain, and unintentional weight loss (Table). For all patients, the median self-reported duration of symptoms prior to first endoscopy was 2 months (range 0 to 35). 185 patients (74%) were participating in colon cancer screening. 181 (73%) had undergone a recent colonoscopy and 9 patients (4%) had a Cologuard test within 3 years of the gastric cancer diagnosis. 4 (45%) of these 9 had a positive Cologuard result with negative colonoscopy. 2 of these 4 patients (50%) had stage I gastric cancer on endoscopy to work up the positive Cologuard result. The median survival (MS) of the entire cohort was 23.0 mo [95% CI 14.4, 31.6] and was not reached for stage I patients. MS was 47 mo [24.3, 69.7] for stage II, 23.0 mo [19.9, 26.3] for stage III, and 11.0 mo [6.6, 15.4] for stage IV; ( $p < 0.001$ ).

**Conclusions:** The presence of symptoms is not a reliable indicator of early-stage gastric cancer. 74% of patients in this cohort were participating in colon cancer screening and in 2 asymptomatic patients, stage I gastric cancer was able to be detected by a stool-based DNA assay. Novel protocols such as more comprehensive GI cancer screening with addition of endoscopy to colonoscopy, or broader use of a DNA-based stool assay, should be investigated.

**Table. Percentage of Gastric Cancer Patients with Symptoms at Diagnosis Across Stage Groups**

Symptoms	Stage I (%) N=41	Stage II (%) N=86	Stage III (%) N=23	Stage IV (%) N=99	P
Any	65.9	88.4	100.0	94.9	<0.001
Nausea / vomiting	14.6	19.8	13.0	27.3	0.237
Reflux	19.5	24.4	39.1	19.2	0.209
GI Bleed	19.5	14.0	21.7	11.1	0.446
Anemia	14.6	17.4	8.7	11.1	0.556
Abdominal pain	19.5	38.4	65.2	58.6	<0.001
Dysphagia	9.8	31.4	13.0	33.3	0.010
Weight loss	19.5	52.3	59.1	69.7	<0.001

## Enrichment of microbial DNA in plasma to improve pathogen detection in sepsis

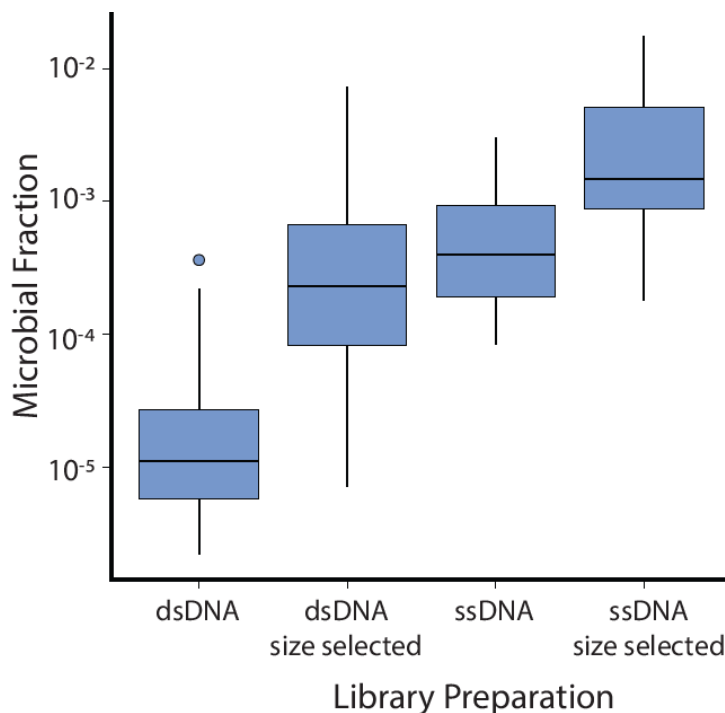
Authors: Eddie G. Dominguez, PhD, Bradon R. McDonald, PhD, Haikun Zhang, PhD, Michelle D. Stephens, BS, Elise C. Dietmann, BS, Megan Nedden, MD, Nicole Byington, BS, Sydney Thompson, BS, Mary Junak, MD, Caitlin S. Pepperell, PhD, Mehreen T. Kisat, MBBS, MS

**Introduction:** Diagnosis of sepsis and timely identification of pathogens in critically-ill patients remains challenging. Plasma metagenomic sequencing to detect microbial cell-free DNA (mDNA) has shown promise, but low abundance of mDNA in plasma limits sensitivity and necessitates high sequencing depth. mDNA is shorter and more fragmented than human cell-free DNA. Here, we evaluated whether combining single-stranded DNA (ssDNA) sequencing library preparation and size selection can enrich mDNA and improve pathogen detection.

**Method:** We prospectively enrolled 48 trauma patients and collected daily blood samples during the first 10 days of ICU admission. For patients with culture-proven infections, we extracted plasma DNA, prepared double-stranded DNA (dsDNA) and ssDNA sequencing libraries, and applied size selection to exclude fragments  $>115$  bp. Following sequencing, we performed taxonomic classification, and evaluated differences in mDNA fraction and in sensitivity for pathogen detection (compared to background noise).

**Results:** We analyzed 46 plasma samples from 5 patients who developed culture-proven infections, including 17 samples coincident with positive microbial cultures. Size-selected ssDNA libraries showed total mDNA fraction 235-fold higher on average, than conventional dsDNA libraries ( $p < 0.0001$ ). However, for pathogen-specific DNA (at the genus level), the highest sensitivity was observed in size-selected dsDNA (82%), compared to dsDNA (41%), ssDNA (71%), and size-selected ssDNA (35%) library preparations.

**Conclusions:** Our results demonstrate that combining ssDNA library preparation together with fragment size selection improves microbial DNA yield, potentially reducing sequencing requirements. However, at the genus level, this combination also increases background noise which limits sensitivity for pathogen detection.



## Sentinel Lymph Node Biopsy Utilization in Wisconsin Women Undergoing Breast Conserving Surgery for DCIS

Authors: Meeghan Lautner, MD, MSc, FACS, Jessica Schumacher, PhD, MS, Randi Cartmill, MS, Manasa Venkatesh, MD, Joseph Weber, MD, FACS, Elise Lawson, MD, FACS, Amanda Kong, MD, MS, FACS, Chandler Cortina, MD, MS, FACS

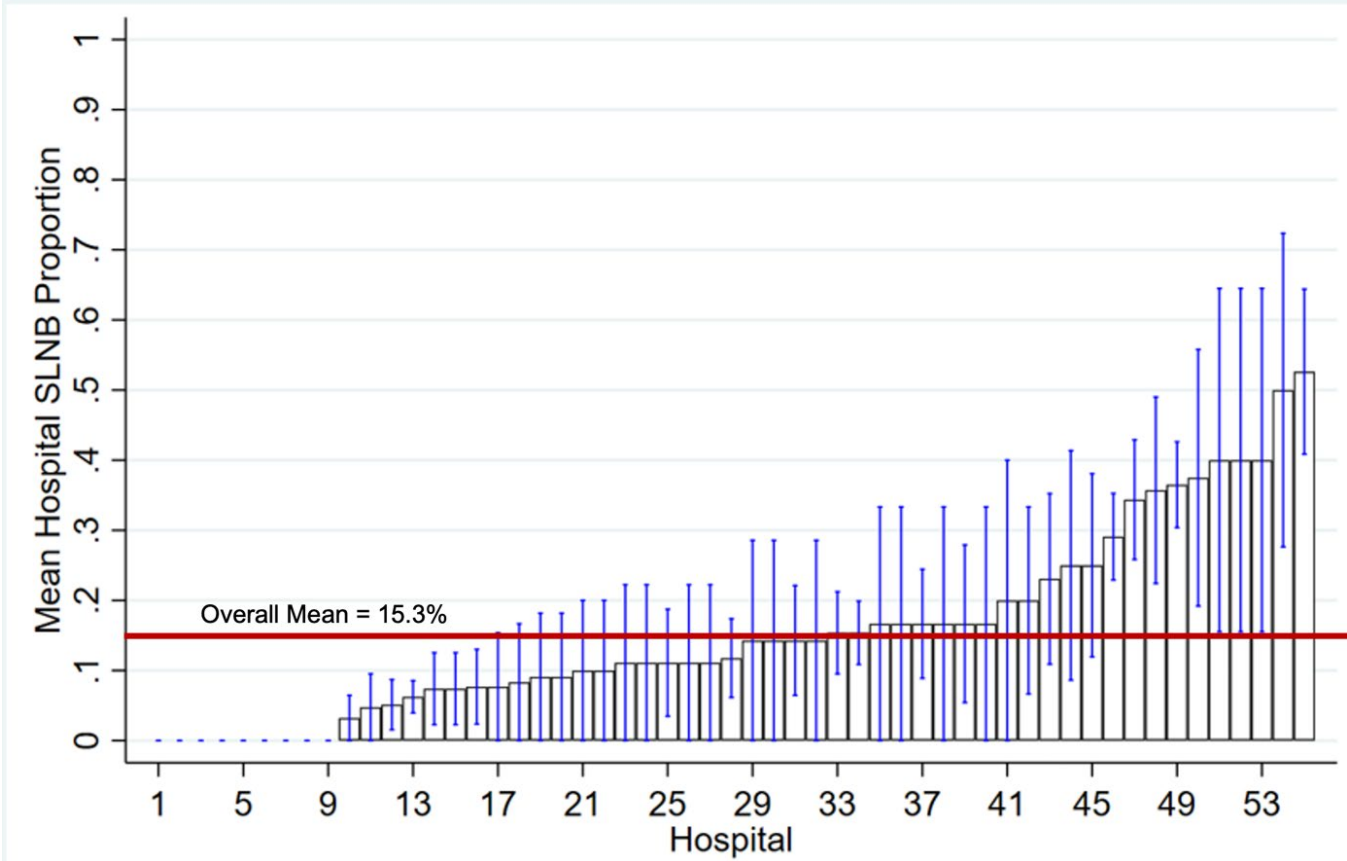
**Introduction:** Modern management of ductal carcinoma in situ (DCIS) includes surgical excision, adjuvant radiation therapy after undergoing breast conserving surgery (BCS), and risk-reducing endocrine therapy for hormone-receptor positive disease. Contemporary guidelines recommend against routine sentinel lymph node biopsy (SLNB) with BCS for DCIS. The aim of this study was to determine the statewide SLNB rate for Wisconsin women undergoing BCS for DCIS and assess facility-level SLNB variation.

**Method:** Wisconsin Hospital Association discharge data from January 2017 - June 2023 were used to identify women who underwent BCS for DCIS. Women with microinvasive disease, history of BCS in the previous 12-months, and those with invasive disease coded during the same encounter as the index surgery were excluded. CPT codes were used to identify SLNB and axillary injection/mapping. SLNB rates were examined annually over the period to assess trends. Facility-level rates were examined for facilities that treated  $\geq 5$  DCIS cases annually and were ranked by SLNB rate. Data for 2023 was only available for January-June 2023 at the time of analysis.

**Results:** During the study timeframe 6,215 women underwent surgery for DCIS: 78.65% (n=4,888) underwent BCS while 21.35% (n=1,327) underwent mastectomy. The rate of SLNB in patients undergoing BCS overall was 16.96% and this down trended over time from 23.97% in 2017 to 14.11% in 2023 (Table 1). In facility-level data, the range of patients undergoing SLNB at the time of BCS ranged from 0-52.63% during 2022–23 (median facility rate = 15.3%) (Figure 1). Individual facility rates across the state revealed that the 25th percentile for SLNB rates across all years was  $\leq 5\%$  for years prior to 2021. In 2021 and 2022–2023 the 25th percentile was 6.67 and 7.41, respectively. Facilities that ranked in the 75th percentile for performing SLNB with BCS had SLNB rates  $\geq 20\%$  across all years, except for 2019 when the rate was 16.67%.

**Conclusions:** Between 2017–2023, nearly 17% of Wisconsin women with DCIS undergoing BCS received SLNB. Despite a slight downward trend over time, there is opportunity for surgical de-escalation given the wide facility-level variation in SLNB utilization. Therefore, a statewide educational initiative developed through the Surgical Collaborative of Wisconsin will inform surgeons on evidence-based guidelines for surgical nodal management for DCIS through semi-annual virtual case discussions, a peer support network, and didactics. Efforts will support de-escalation of axillary surgery and ensure all women diagnosed with DCIS in Wisconsin receive evidence-based care that minimizes morbidity, regardless of treating facility.

**Figure 1.** Mean proportion of Wisconsin Women Undergoing SLNB at time of BCS for DCIS by individual facility (2022–2023\*).



\*=quarter 1-2 data only for 2023

## Single institution re-excision rates using multiple electromagnetic seed localizations for ipsilateral breast cancer

Authors: Patrick Carney, MD, PhD, Anna Beck, MD, Laura Bozzuto, MD, MS, Nicci Owusu-Brackett, MD, Lee Wilke, MD, Ashley Woodfin, MD, Mai Elezaby, MD and Meeghan Lautner, MD, MSc

**Introduction:** Breast conserving therapy (BCT) has equivalent survival to mastectomy for the treatment of invasive or in situ breast malignancies. Several non-wire localization technologies have emerged which increase operative day efficiency and improve patient comfort. The ACOZOG Z11102 study reinforced the oncologic safety of BCT for multiple ipsilateral breast cancers. Previous studies have shown comparable accuracy of percutaneous single wireless electromagnetic seed localization (“SmartClip”™, SC) and use of the EnVisio Navigation System compared to wires for breast conserving surgery (BCS). Our single institution retrospective review evaluates our unique high volume experience with multiple SmartClip localization and/or bracketing of ipsilateral tumors. We hypothesize the re-excision rate after localization with 2 SmartClips is similar to national average of 20% which allows for breast preservation in large volume or multicentric disease that historically required mastectomy.

**Method:** An IRB approved, retrospective review of an existing Radiology billing database (1/2019-9/2024) from a Multidisciplinary Breast Center in a large Midwestern academic institution was performed, identifying cases with multiple SC. Imaging data collected included localization modality and number and type of lesions localized. Surgical data collected included surgical pathology, margin status, and need for re-excision; re-excision surgical pathology when available was reviewed. Inclusion criteria were invasive or in situ disease on final pathology and breast conservation surgery with 2 preoperative SC localizations in the ipsilateral breast.

**Results:** During the study period there were 139 patients who underwent placement of 2 SC to localize and/or bracket in situ or invasive disease. Of the 139, 19.4% had initial re-excision as indicated by the SSO/ASCO/ASTRO consensus statement for invasive (no tumor on ink) and DCIS (2mm margin). The re-excision rate for invasive pathology was 17% as compared to DCIS alone which was 37.5%. The re-excision rate for invasive disease following neoadjuvant therapy was 3.7% as compared to primary surgery which was 23.3%.

**Conclusions:** This data demonstrates that the re-excision rate using 2 SmartClips to localize and/or bracket multicentric breast cancer in our institutional experience is non-inferior to the widely accepted national average of 20%. Importantly, we also show the rate of re-excision of invasive carcinoma using multiple SCs is lower than the national average. Our data also suggests significantly lower re-excision rates using multiple SCs in patients who underwent neoadjuvant treatment which supports multidisciplinary care to facilitate breast conservation.

<b>Overall Re-excision</b>	<b>27 (19.4%)</b>
Invasive Carcinoma Re-excision	21 (17%)
DCIS Re-excision	6 (37.5%)
Neoadjuvant Re-excision	1 (3.7%)
Upfront Re-excision	26 (23.2%)

**Table 1: Re-Excision Rates** Overall re-excision rate shown, re-excision rates shown for invasive carcinoma vs DCIS and Neoadjuvant vs Upfront treatment.

## Ergonomic practices and associated injuries among pediatric surgeons

Authors: Sydney F. Tan, MD, Michael Stellon, MD, Devashish Joshi, MD, Jessica Hellner, Mehul V. Raval, MD, Erin E. Perrone, MD, Romeo C. Ignacio, MD, Kyle J. Van Arendonk, MD, PhD, Barrie S. Rich, MD, Kevin P. Moriarty, MD, Danielle S. Walsh, MD, Jason C. Fisher, MD, Kenneth W. Gow, MD, Hau D. Le, MD

**Introduction:** Ergonomic injuries pose significant risks to surgeons, negatively impacting health, productivity, access to care, and retirement age at retirement. Despite unique challenges in pediatric surgery, including a wide range of patient sizes and operative variety, little is known about ergonomics specifically in pediatric surgeons. This study aimed to assess ergonomic practices and associated injuries among pediatric surgeons.

**Method:** A cross-sectional survey was distributed to the American Pediatric Surgical Association regular members and fellows. Data collected included demographics, physical health, surgical practices, operating habits, discomfort, injuries, interventions, and outcomes. Associations with injury were analyzed using Fisher's exact test, Pearson's Chi-squared test, and Wilcoxon rank-sum tests.

**Results:** Among 117 (11%) pediatric surgeons and fellows who responded, 53% were male with a median of 15 years in practice (IQR 6-25). Regarding operating habits, 76% did not take regular breaks, 48% double-gloved, and 51% used loupes regularly. Notably, 90% experienced discomfort or pain, and 30% sustained injuries from operating, primarily affecting the neck and cervical spine (53%). Pediatric surgeons who identified as white (80%) reported significantly more ergonomic injuries than other races ( $p < 0.01$ ). Only 18% of respondents received ergonomic training. Ergonomics training and operating with a resident or co-surgeon were associated with less injury ( $p < 0.05$ ). Among those experiencing discomfort or injury, 13% underwent a procedure, 63% experienced sleep disturbance, 74% reported contribution to burnout, and 88% used medications for pain.

**Conclusions:** Ergonomic-related discomfort and injuries occur in nearly 90% of pediatric surgeons who responded. Few have ergonomic training to mitigate injury and most report an impact on well-being. Modifiable ergonomic factors for pediatric surgeons, along with targeted interventions to reduce injuries, can significantly improve surgeon well-being.



## **Prophylactic surgical drain placement with irrigation reduces abscess formation in patients with severe, uncontained, perforated appendicitis.**

Authors: Michael A Stellon, Devashish S Joshi, Russell Herberg, Brittany Walker, Jessica Hellner, Kevin M Riggle, Hau D Le

**Introduction:** 20-25% of perforated appendicitis cases are complicated by abscess formation. This study assesses whether prophylactic closed-suction surgical drain (SD) placement after irrigation can decrease postoperative abscess formation in patients with extensively contaminated, perforated appendicitis.

**Method:** A multicenter retrospective review was performed on pediatric patients with uncontained perforated appendicitis from January 1, 2020, to August 1, 2023. Limited irrigation was performed. All SDs were oriented towards the pelvis. Data were analyzed in 4 groups: G1) SD and irrigation, G2) only SD, G3) only irrigation, G4) neither SD nor irrigation.

**Results:** 115 patients (44 in G1, 3 in G2, 21 in G3, 47 in G4) were included. The abscess rate was 5.1% (G1), 33.3% (G2), 33.3% (G3), and 37.0% (G4) ( $p = 0.001$ ). No interventional radiology (IR) drains were placed in G1 and G2. SD duration was 4.1 $\pm$ 2.1 days in G1 and 2.7 $\pm$ 0.6 days in G2. IR drain duration was 14 $\pm$ 10.7 days in G3 and 8.3 $\pm$ 3.9 days in G4 ( $p < 0.001$ ). There were no significant differences in total length of stay and antibiotic duration.

**Conclusions:** Irrigation with prophylactic SD placement may prevent postoperative abscesses in patients with severe, uncontained, perforated appendicitis, but prospective data are needed.

## Current referral patterns and pitfalls pertaining to the treatment of esophageal perforation

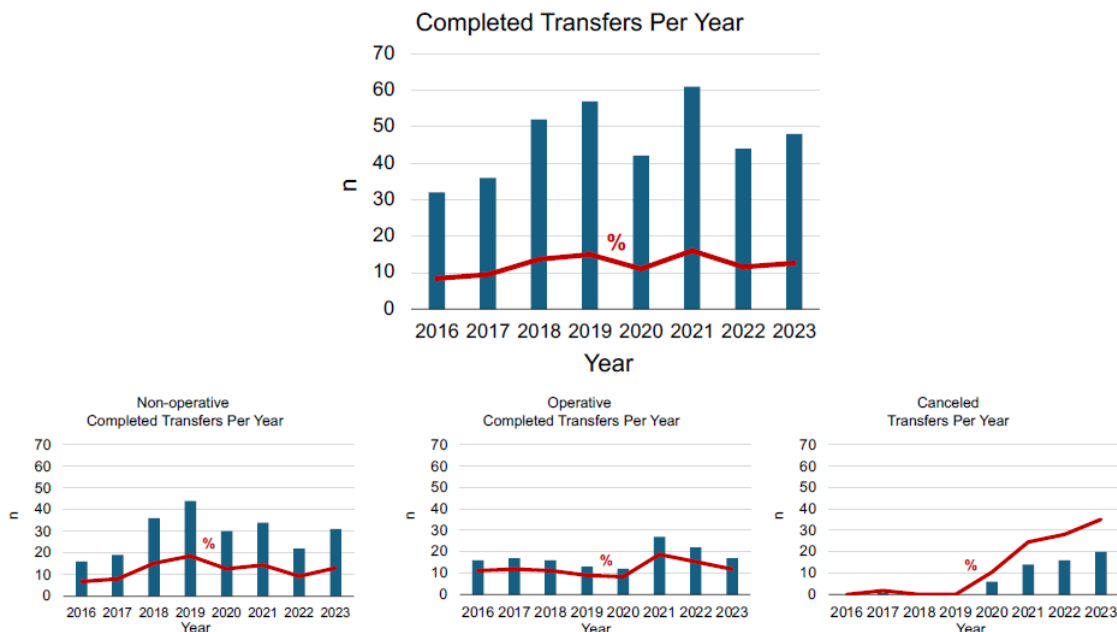
Authors: Madison B Argo, MD, MSc; Connor J Maloney, BS; James D Maloney, MD

**Introduction:** Esophageal perforation is one of the most feared and detrimental hollow viscous pathologies. It warrants prompt recognition and treatment to minimize morbidity and mortality. As both medical technologies and healthcare specialization progress, care for complex illnesses such as suspected esophageal perforation has transition to tertiary referral centers. We sought to determine the referral patterns and if operative management was pursued for all forms of suspected esophageal perforation to a tertiary care center, including the length of time to treatment and geographic distance of the referral.

**Method:** Using the University of Wisconsin Hospital and Clinics institutional administrative database, inter-hospital referral requests and hospital encounter records for esophageal perforation pathologies were queried from October 2015 to December 2023. Of the 455 individual records, data regarding timing and location of referral center as well as hospital admission and procedural timing were collected. Analyses were performed to compare non-operative and operative groups as well as geographic region and proximity to other hospitals with resuscitation capabilities.

**Results:** The pattern of the percentage of completed transfers was noted to be similar from 2016 to 2023; however, the number of canceled transfers gradually increased in the most recent years. Data demonstrated that the majority of patients arrived to the tertiary center the same day of referral and that most were treated non-operatively (62%). However, for those that were treated operatively, only 32% of patients (n=26) underwent operative intervention within 24 hours of their referral request with 42% (n=34) receiving their intervention  $\geq 2$  days after their referral request. The geographic catchment area spanned 77,500 square miles and there was overlap between referral centers and nearby local hospitals with resuscitation capabilities.

**Conclusions:** The desire to receive specialized care for suspected esophageal perforations must be balanced with the need to initiate prompt treatment and consideration of resource utilization. Early triage of patient acuity, initiation of non-operative treatment when deemed appropriate, and temporizing interventions and strategies at hospitals in closer proximity by general or cardiothoracic surgeons are encouraged to minimize delays in care.



## The Economic Impact Of Length Of Stay Variability In DIEP Flap Reconstruction: Insights For Healthcare Optimization:

Authors: Keenan Fine, MS, Armin Edalatpour, MD, Brett Michelotti, MD

**Introduction:** Length of Stay (LOS) is a pivotal factor in hospital management, impacting healthcare delivery efficiency and financial performance. Following Deep Inferior Epigastric Perforator (DIEP) flap procedures for breast reconstruction, LOS protocols exhibit substantial variation, often influencing costs, charges, and reimbursement rates. This study aims to examine the financial implications of LOS for patients undergoing DIEP flap reconstruction at a single-institution academic hospital.

**Method:** A retrospective review of financial data was conducted for DIEP flap breast reconstructions performed from 2021 to 2023. Only cases with LOS of 3, 4, or 5 days were included due to low case volumes outside this range. The primary financial metrics—operating margin, total charges, and estimated reimbursements—were analyzed by LOS and payer type (capitated, commercial, Medicaid, Medicare). Statistical analysis employed descriptive statistics, linear regression, and ANOVA to identify significant differences among LOS groups and cost components.

**Results:** A total of 202 DIEP flap procedures met inclusion criteria. Results indicated a significant increase in total charges by LOS, which averaged \$227,157, \$251,560, and \$278,769 for 3, 4, and 5-day stays, respectively ( $p=0.002$ ). Similarly, estimated reimbursements increased with LOS, averaging \$77,676, \$81,258, and \$87,491 ( $p=0.721$ ). Costs per stay increased with LOS, averaging \$55,453, \$60,453, and \$67,123 for 3, 4, and 5 days, respectively ( $p=0.035$ ). However, operating margins demonstrated no significant variation across LOS groups (\$42,153, \$41,582, and \$44,564 for LOS of 3, 4, and 5 days, respectively;  $p=0.986$ ), indicating that while charges and reimbursements increase with LOS, the profitability does not reflect these increments. Margins for Medicare patients were notably lower, averaging -\$20/day, compared to an average margin of \$12,000/day for other payer types (Medicaid, capitation, and contracted). Cost analysis per day revealed that personnel expenses, especially physician fees, constituted the largest portion of total costs, representing approximately 25% across all LOS groups. Nursing and non-clinical support personnel represented roughly 18% of the costs across all LOS. Linear regression modeling suggested that reducing LOS by one day could reduce total costs by an estimated \$818,400 across the study period.

**Conclusions:** The financial analysis underscores the critical need for optimized LOS management in DIEP flap breast reconstruction. While charges and reimbursements rise with extended hospital stays, operating margins remain largely unaffected, highlighting a potential area for cost containment without compromising patient outcomes. Streamlining discharge protocols and enhancing efficiency in patient flow may offer a balanced approach to improve financial sustainability and clinical outcomes.

## Equitable and Responsible Opioid Prescription Practices for Distal Radius Fractures: Age, Demographic, and Insurance Influences

Authors: Keenan Fine, MS, Camille Laliberte, BA, Brett Michelotti, MD

**Introduction:** Amid the opioid crisis, understanding patterns of opioid prescribing for common injuries like distal radius fractures (DRFs) is crucial for promoting safe pain management practices. This study investigates opioid prescription rates among DRF patients, examining variations by age, sex, race, and insurance type to identify demographic factors that may influence prescribing habits.

**Method:** This study analyzed patients with DRFs treated at a single academic institution from 8/2022-12/2023. Key variables included age (<18 vs. ≥18), sex, race, and insurance type. Chi-squared tests assessed opioid prescription differences between subgroups. A logistic regression model was used to evaluate the influence of sex, race, and insurance type on opioid prescription likelihood.

**Results:** In this cohort of 548 patients, 33.9% received opioid prescriptions. Patients <18 years had significantly lower prescription rates (11.4%) than those ≥18 ( $p<0.001$ ). No significant difference was observed by race ( $p=0.205$ ). Male patients under 18 were more likely to receive opioids (14.4% vs. 6.5%), but was not statistically significant ( $p=0.096$ ). Among patients ≥18, those with Medicaid had a lower prescription rate (38.9%) compared to Medicare (53.7%) and private insurance (52.7%) but did not differ statistically. Logistic regression showed no association between sex, race, or insurance type and opioid prescription likelihood.

**Conclusions:** This study shows that opioid prescription rates for distal radius fractures are significantly lower in patients under 18 compared to adults, with no notable differences in prescriptions by sex, race, or insurance type among adults. Further research is needed to identify other factors affecting opioid prescription rates in DRFs to improve pain management during the opioid crisis.

**Table 1:** Opioid Prescription Rate by Sex, Race, and Insurance Type

Category	Subgroup	< 18 Opioid Prescription Rate (n=245)	< 18 p-value	> 18 Opioid Prescription Rate (n=303)	> 18 p-value
Sex	Female	6.5%	0.065	53.2%	0.661
	Male	14.4%		49.3%	
Race	Non-White	7.1%	0.433	47.6%	0.512
	White	12.3%		53.1%	
Insurance Type	Medicaid	3.3%	0.331	38.9% (18-64)	0.565 (18-64 v Private)
	Private	11.4%		51.9% (18-64), 60.0% (65+)	—
	Medicare	—	—	53.7% (65+)	0.764 (65+ v Private)

## Prevalence of Trapeziometacarpal Osteoarthritis Across Age Cohorts: A Retrospective Radiographic Analysis

Authors: Camille LaLiberte, BS, Keenan Fine, MS, Brett Michelotti, MD

**Introduction:** Arthrosis of the trapeziometacarpal (TMC) joint is common with aging. Previous research found it rare in those under 50. With increased smartphone and computer use, higher rates in younger people might be expected. This study examines the prevalence of TMC osteoarthritis across the lifespan.

**Method:** We performed a retrospective chart review of the TMC joint in patients who presented to a single academic hospital for a distal radius fracture (DRF) between 8/2022-12/2023. Reliability testing was performed to ensure intra-rater reliability of radiographs. One rater assessed the degree of TMC OA on a scale of grade I (no arthritis), II (mild to moderate arthritis), or III (complete joint destruction) on radiographs. Continuous variables are represented as mean  $\pm$  standard deviation. Student t-tests were used to detect significant differences for continuous variables, while Chi-squared test of independence was used for categorical variables. P-values  $\leq$  0.05 were considered statistically significant.

**Results:** A total of 417 patients were included in the analysis. The most represented age groups were 0-10, 11-20 and 61-70 years old and 62.7% of the cohort was female. We had substantial agreement for intra-rater reliability with reliability testing (Cohen's Kappa = 0.713,  $p < 0.001$ ). The radiographic prevalence of Grade II and III arthrosis increased with age but stabilized above 90% when aged  $> 60$  years old. However, the proportion of patients with Grade III arthrosis continued to increase with age (Figure 1). 10.9% of patients between the age of 11-20 showed evidence of mild/moderate arthrosis. The mean age for Grade II arthrosis was  $56.8 \pm 18.6$  years and  $71.5 \pm 8.2$  years for Grade III. Compared to the reference group (Grade I arthrosis), the odds of history of thumb pain were 5.9x higher for patients with Grade II arthrosis [CI 95% = 2.7-12.6,  $p < 0.001$ ] and 15.9x higher for patients with grade III arthrosis [CI 95% = 6.1-41.2,  $p < 0.001$ ].

**Conclusions:** The results of this study suggest that there may be an increasing prevalence of arthrosis on plain radiography in younger patient populations, possibly due to increased repetitive thumb use from modern technology. The findings are consistent with past research that shows increases in the prevalence of TMC arthrosis with advancing age. Prospective research is needed to explore the potential influence of smartphone and computer usage on the earlier onset of TMC arthrosis.

# Quantifying Pain and Functional Improvement in Thumb CMC Arthritis: A Meta-Analysis Across Six Surgical Techniques

Authors: Keenan Fine, MS, Caroline Bay, BA, Brett Michelotti, MD

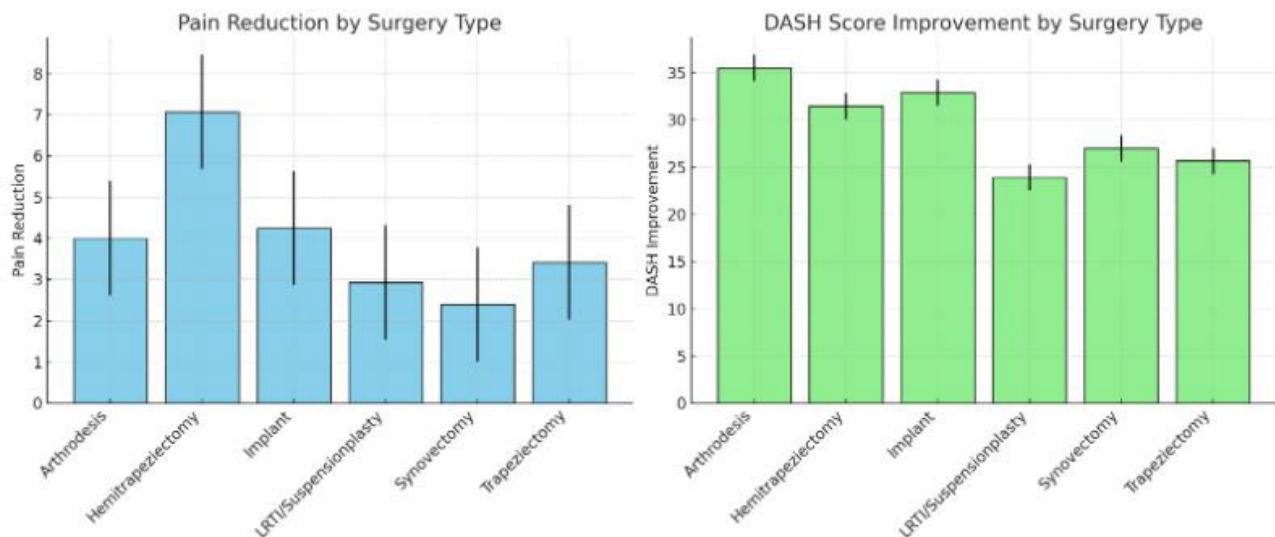
**Introduction:** Various surgical interventions exist for managing arthritis at the thumb carpometacarpal (CMC) joint. This meta-analysis aimed to quantify pain reduction and Disabilities of the Arm, Shoulder, and Hand (DASH) score improvement across different surgical techniques.

**Method:** A meta-analysis was conducted on studies reporting pain and DASH score changes following thumb CMC joint surgeries. The overall effect sizes for pain (measured by VAS 0-10) and DASH score changes were calculated. Subgroup analyses were performed across six surgery categories: arthrodesis, hemitrapeziectomy, implant arthroplasty, ligament reconstruction with tendon interposition (LRTI)/suspensionplasty, synovectomy, and simple trapeziectomy. Pairwise comparisons between surgery types assessed differences in outcomes.

**Results:** The pooled analysis indicated a significant overall pain reduction (mean improvement: 5.45, 95% CI: 5.20-5.70) across all surgical interventions. Pain reduction was significantly greater with hemitrapeziectomy compared to all other procedures ( $p < 0.001$ ). The pooled analysis for DASH showed an improvement of 29.4 points [95% CI: 28.2-30.7]. DASH improvement was significantly greater in arthrodesis compared to all other surgery types (mean improvement: 35.5, 95% CI: 34.9-36.1). Hemitrapeziectomy and implant arthroplasty also demonstrated significantly more improvement in DASH than LRTI/Suspensionplasty, synovectomy, and simple trapeziectomy.

**Conclusions:** This meta-analysis shows significant pain and DASH improvements across all thumb CMC surgeries, with hemitrapeziectomy providing the most pain relief and arthrodesis the highest DASH improvement. Hemitrapeziectomy and implant arthroplasty outperformed other techniques in functional outcomes, indicating potential superiority in managing thumb CMC arthritis.

**Figure 1:** Pain Reduction and DASH Improvement by Surgery Type



## Evaluation of a Standardized Protocol for Treatment of Acute Type B Aortic Dissections: A Single Center Review

Authors: 2Richmond E, 1Gober L, 2Liu S, 1Bontekoe J, 1Sobol C, 1Telma K, 1Tefera G, 1DiMusto P, 1Morgan C  
1University of Wisconsin, Department of Surgery, Division of Vascular Surgery 2University of Wisconsin, School of Medicine and Public Health

**Introduction:** The mainstay treatment for acute type B aortic dissection (TBAD) remains medical management, however recent literature has suggested early surgical intervention to reduce future complications. Acute aortic protocols, adopted in the mid 2000's, consist of aggressive anti-hypertensive regimens and ICU-level monitoring. In a review of our institutional acute aortic protocol, we sought to better understand its role surrounding patient outcomes in the acute TBAD population.

**Method:** A retrospective chart review was performed on patients who presented with acute TBAD over a 15-year period, with the intention to compare two groups: (1) pre-protocol and (2) post-protocol implementation. Acute TBAD was defined as a new dissection on imaging with  $\leq 2$  weeks of symptoms, excluding chronic dissections, intramural hematomas or ulcers. Primary outcomes included in-hospital morbidity, in-hospital mortality and progression to surgery. Secondary outcomes included ICU LOS, antihypertensive medications on discharge and readmission rates. Categorical variables were analyzed using chi-square.

**Results:** A total of 177 patients admitted with acute TBAD were identified: 97 pre-protocol implementation and 80 post-implementation. After adoption of a protocol-driven medical management approach to acute TBAD, there was an overall decrease in the incidence of surgical intervention (40 vs 20%,  $p < 0.01$ ) without notable differences observed across in-hospital mortality, morbidity, or readmission rates ( $p > 0.05$  for all) between the two groups. Furthermore, post-protocol patients had shorter average ICU stays ( $3.3 \pm 4.7$  vs  $5.4 \pm 4.1$  days,  $p < 0.05$ ) and were discharged on fewer outpatient antihypertensives ( $3.2 \pm 1.6$  vs  $3.8 \pm 1.6$ ,  $p < 0.05$ ).

**Conclusions:** Introduction: Method: Results: Conclusions: Implementation of a standardized protocol resulted in reduced ICU LOS, lower incidence of surgery and fewer antihypertensives required on discharge without a difference in in-hospital mortality, morbidity or 30- and 90-day readmission rates. This data, from a highly selective patient population, suggests that standardizing medical management of acute aortic syndromes may have resource utilization benefits without compromising patient outcomes.

## Breast Surgeons' Perspectives of Telemedicine Visits in Breast Clinic

Authors: Dickerson F, Wiener AA, Breuer C, Schumacher JR, Bozzuto LM, Wilke LG, Lautner MA, Neuman HB

**Introduction:** The COVID-19 pandemic provided an opportunity to advance the use of telehealth for medical care. Many specialties have continued to use telehealth visits due to the ability to provide patients easier access with reduced travel and the opportunity to perform the visit from home or work. However, breast surgeons have cited concerns regarding the lack of a physical exam. As restrictions for in-person care have lifted, it is not known how surgeons currently use and plan to use telehealth. The objective of this study was to assess breast surgeons' use and perspectives of synchronous audio/visual telehealth.

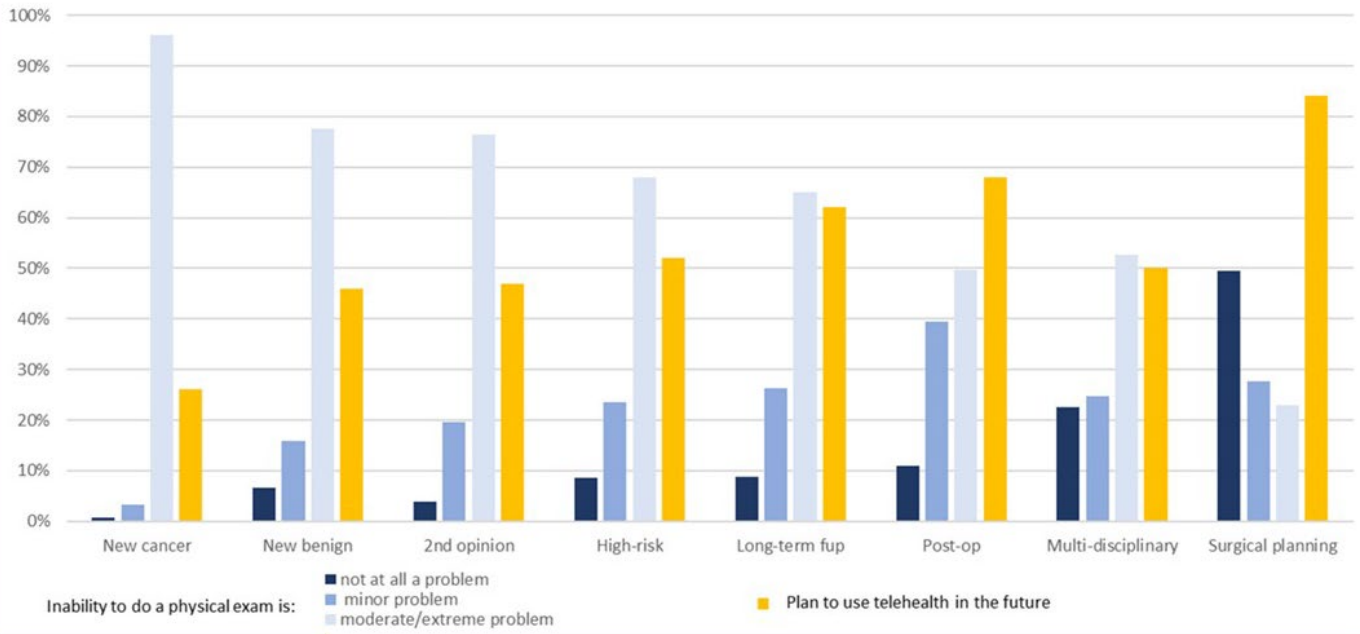
**Method:** Surgeon members of the American Society of Breast Surgeons were invited via email to anonymously complete an electronic REDCap survey (5/25/2023-7/14/2023). The survey elicited surgeon characteristics (categorical responses), and experience with telehealth (current and future use). Questions also assessed whether the inability to perform a physical exam with telehealth poses a problem (not at all, minor, moderate/extreme) and whether that perception differs by visit type (e.g., new benign, new malignant, new high-risk, new second opinion, surgical planning, post-operative, long term follow-up, and multidisciplinary). Descriptive statistics summarized surgeon factors. Chi-square tests were used to assess the association between use of telehealth and surgeon characteristics, and between perceived importance of physical exam and telehealth use (for each visit type).

**Results:** Of the 267 surgeons that opened the survey, 17 did not answer any questions and 1 only answered surgeon characteristics, leaving a final sample size of 249. The majority were in practice 20+ years (53%) and 83% reported their practice was >80% breast surgery. Most had experience with telehealth (82%). Surgeons who did not use telehealth (n=45) were more likely to be older (42% of non-users were >65 years versus 12% of users,  $p<0.001$ ). Surgeons were most likely to use telehealth for surgical planning (64%), post-op (61%), and long-term follow-up visits (60%); they were least likely to use telehealth for multi-disciplinary (8%), 2nd opinion (25%), and new malignant visits (30%). Surgeons reported that the inability to perform a physical exam was a moderate/extreme problem for most visit types, ranging from 23% for decision-making follow-up to 96% for new cancer visits (Figure). Perceived importance of a physical exam was significantly associated with planned use of telehealth in the future (Figure,  $p<0.05$  for all visit types).

**Conclusions:** Although surgeons who treat breast cancer are utilizing telehealth, the inability to perform a physical exam was perceived to be a significant limitation. Breast surgeons perceived that telehealth may have a role for visits where physical exam is deemed less necessary, such as surgical planning or post-operative visits. However, surgeons felt strongly that telehealth had a limited role when the physical exam was perceived to be important (e.g., new cancer and new benign visits). Telehealth can improve access for patients who cannot physically travel to a clinic due to transportation, weather, and/or work/family limitations.



Surgeon Perceptions of Importance of Physical Exam and Association with Telehealth Use



## Surgeon Recommendation Drives Receipt of Sentinel Lymph Node Biopsy in Women 70 and Over

Authors: Neuman HB, Breuer C, Dickerson F, Hanlon BM, Schumacher JR

**Introduction:** Sentinel lymph node biopsy (SLN) for women  $\geq 70$  years of age with early-stage breast cancer (SLN  $\geq 70$ ) has been identified as low-value care, making it appropriate for deimplementation. However, rates of SLN  $\geq 70$  have remained relatively unchanged over time. A critical gap toward supporting deimplementation of SLN  $\geq 70$  is our understanding of how decisions are made within the patient-surgeon interaction. The objective of this study is to identify patterns of surgeon-patient interactions that are associated with deimplementation of SLN  $\geq 70$ .

**Method:** We identified patients aged 70 or older that participated in clinical trial Alliance A231701CD (n=132) from 6/2019-12/2021. Patients were eligible for this post hoc analysis if they underwent breast surgery, were clinically node negative, did not have neoadjuvant treatment, and had hormone receptor positive/her2 negative breast cancer (n=67). We coded transcripts of the audio from initial patient-surgeon consultations to assess shared decision making (OPTION-5, range 0-100, Elwyn et al.) and for patient-surgeon interactions (using a taxonomy to assess who initiates topic, primary decision maker, strength of recommendation, and how patient responds, Stivers et al.). We summarized patients' demographic characteristics and performed logistic regression to identify factors associated with SLN  $\geq 70$ . We then described the interactional patterns that led to the decision for SLN  $\geq 70$  and summarized the justifications surgeons used to support the decision.

**Results:** The median participant age was 74 years (range 70-90). The majority had T1 cancers (75%), were grade 1 (50%), and underwent breast conservation (79%). Overall, 51/67 (76%) patients underwent SLN. Older age was associated with a lower likelihood of undergoing SLN (OR=-0.20 [95% CI-0.33- -0.58], p=0.01) with no association with OPTION-5 score (p=0.10), clinical size (p=0.09) or grade (p=0.9). Most consults (42/67) did not discuss the option of forgoing a SLN. For patients discussing SLN (n=24), interactional patterns were similar for patients who did and did not undergo SLN (Figure), with most conversations initiated by the surgeon, most recommendations presented as pronouncements, and the surgeon being the decision maker. For patients who underwent SLN (n=51), the most common justifications were that this was a standard part of staging (n=45), would impact radiation decisions (n=23), and/or would impact chemotherapy decisions (n=12). Conversely, surgeons used age (n=12), low impact on chemotherapy (n=8), and low risk of disease in nodes (n=4) to support forgoing SLN. Surgeons emphasized the importance of multi-disciplinary buy-in when justifying the role for SLN  $\geq 70$ .

**Conclusions:** Decision making for SLN  $\geq 70$  is largely based on strong surgeon recommendation, with minimal shared decision making with the patient. Although age is associated with receipt of SLN over 70, surgeons cite the perceived value of SLN for staging and treatment decision making when making their recommendation. Our findings suggest that ongoing surgeon education and support in framing conversations about SLN  $\geq 70$  may be valuable in supporting deimplementation.

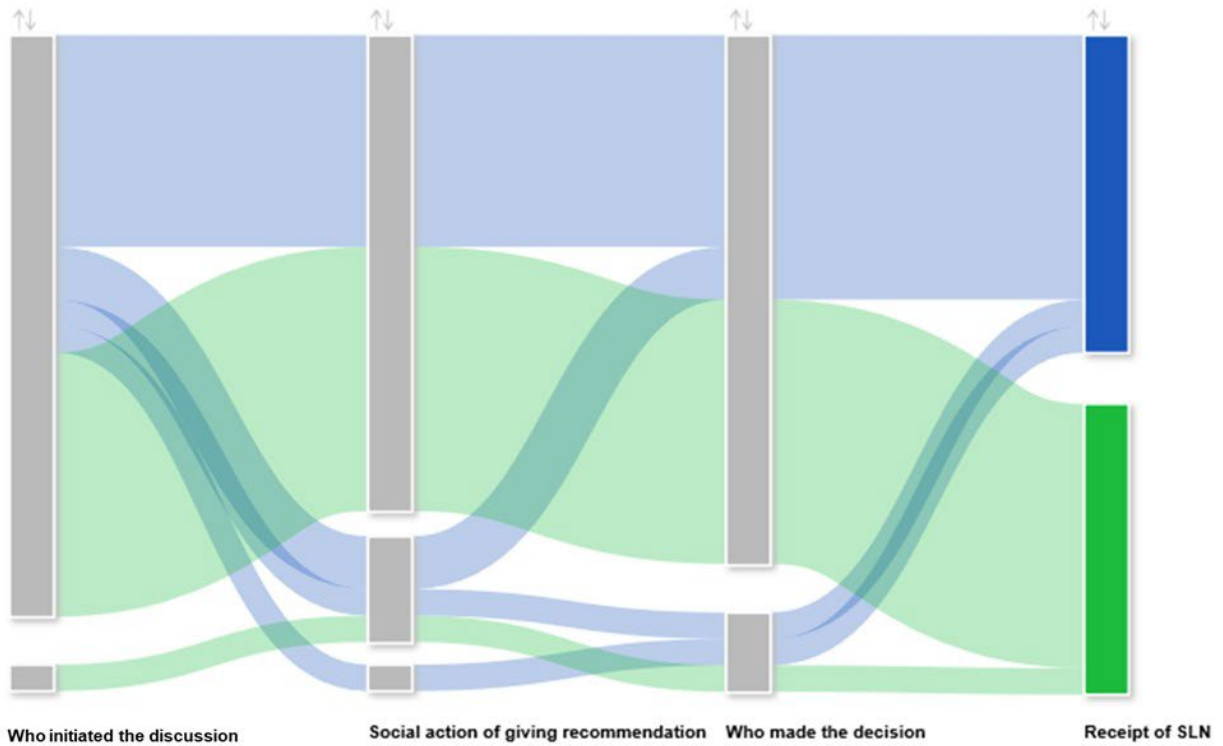


Figure. Sankey Diagram of Patient-Surgeon Interaction, including who initiated the discussion, the social action used to provide a recommendation, who was the decision maker, and whether SLN was received. Cohort includes 23 of 24 patients who discussed the option of forgoing a SLN (one excluded due to missing audio-recording)

## The Association of 25-Hydroxyvitamin D Levels with BK Viremia and Nephropathy in Kidney Transplant Recipients

Authors: Suseela Raj, BS, Angela Zhou, BA, Ekaterina Fedorova, MD, Zhongyu Yuan, MMed, Didier A. Mandelbrot, MD, Brad C. Astor, PhD, MPH, Sandesh Parajuli, MD

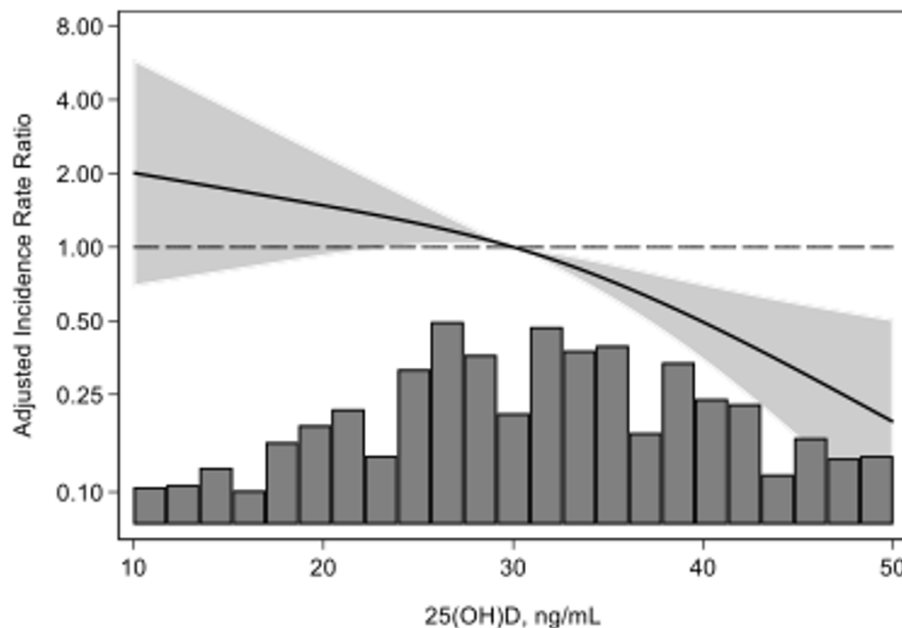
**Introduction:** BK viremia (BKV) and nephropathy (BKN) are significant causes of morbidity and mortality in kidney transplant recipients (KTRs). Vitamin D supports immune function, yet low 25-hydroxyvitamin D [25(OH)D] is common among KTRs. The association between 25(OH)D and BKV and BKN in KTRs remains undefined.

**Method:** The association between serum 25(OH)D, measured 61 days to 2 years post-transplant, and subsequent incident BKV and BKN was examined in 2938 and 3308 KTRs without previous BKV or BKN, respectively. Recipients received kidney-only transplants from 2010 to 2019.

**Results:** Out of 3308 KTRs, 399 (12%) were vitamin D deficient [25(OH)D  $\leq$ 20 ng/mL] and 916 (27.7%) were insufficient [25(OH)D 21-29 ng/mL]. A total of 184 KTRs developed BKV and 44 developed BKN. The incidence rate (/100 person-years) of BKV was 2.88 in the 25(OH)D sufficient group, 2.22 in the insufficient group, and 2.37 in the deficient group. Vitamin D deficiency or insufficiency was not significantly associated with incidence of BKV after adjustment for baseline characteristics. In contrast, the incidence rate of BKN was 0.30 in the 25(OH)D sufficient group, 0.75 in the insufficient group, and 1.28 in the deficient group. 25(OH)D deficiency (adjusted hazard ratio [aHR] compared to 25(OH)D sufficiency: 3.92; 95% CI: 1.66-9.23) and insufficiency (aHR: 2.22; 95% CI: 1.11-4.45) were significantly associated with increased risk for BKN in adjusted models (Figure 1).

**Conclusions:** Low 25(OH)D is associated with an increased risk of BKN but not BKV. Further studies are needed to explore the effects of vitamin D supplements to mitigate complications associated with BKN.

Figure 1. Incidence of BKN decreased with increasing 25(OH)D.



## **Delayed Graft Function in Simultaneous Pancreas Kidney Transplant Recipients is Associated with an Increased Risk of Urinary Tract Infection and Kidney Rejection**

Authors: Sofia Nehring Firmino, MS3, Ekaterina Fedorova, MD, Eman A. Alshaikh, MBBS, Dixon Kaufman, MD, PhD, Jon Odorico, MD, Didier Mandelbrot, MD, Brad C. Astor, PhD, Sandesh Parajuli, MBBS.

**Introduction:** Kidney delayed graft function (K-DGF) is associated with various detrimental outcomes among simultaneous pancreas and kidney (SPK) transplant recipients. However, its potential risk associated with specific infections and graft rejection remains unclear.

**Method:** We compared recipients with K-DGF to those without K-DGF among all adult SPK recipients transplanted at our center between 01/2010 and 12/2022 who had pancreas graft survival of more than 2 weeks. Outcomes of interest included urinary tract infections (UTI) and pneumonia, along with pancreas and kidney graft rejections, within one-year post-transplant.

**Results:** 543 SPK recipients were included, of whom 47 (8.6 %) developed K-DGF. A total of 89 recipients had UTI, 33 had pneumonia, 77 had pancreas rejection and 21 had kidney rejection within one-year post-transplant. Recipients with K-DGF experienced a higher incidence of UTI. This association remained after adjustment for baseline characteristics (adjusted Hazard Ratio [aHR]: 3.06; 95% CI: 1.46-6.42; p=0.003). Similarly, K-DGF was associated with increased risk for kidney rejection in an unadjusted and adjusted models (aHR: 5.47; 95% CI: 1.98-15.1, p=0.001). K-DGF was not associated with pneumonia or pancreas rejection.

**Conclusions:** K-DGF among SPK recipients is associated with an increased risk for UTI and kidney allograft rejection, likely related to dysregulation of the immune system. Close monitoring and appropriate management are warranted in this unique patient population.

## **Five-year Outcomes of Recipients of Dual Kidney Transplantation are Better Compared to Single Kidney Transplantation with Comparable Early Post-transplant Complications**

Authors: Ekaterina Fedorova, MD, Sofia Nehring Firmino, MS3, David Foley, MD, Jacqueline Garonzik-Wang, MD, PhD, Dixon Kaufman, MD, PhD, Jon Odorico, MD, David Aufhauser, MD, Nikole A Neidlinger, MD, Carrie Thiessen, MD, PhD, Jennifer Philip, MD, Kelly M Collins, MD, Josh Mezrich, MD, David Al-Adra, MD, PhD, Brad Astor, PhD, Didier Mandelbrot, MD, Sandesh Parajuli, MBBS

**Introduction:** Dual kidney transplant (DKT) an uncommonly performed technique, provides a unique opportunity to utilize higher risk kidneys that may otherwise be discarded. We compared post-transplant outcomes between DKT, and single kidney transplants (SKT) performed at our institution.

**Method:** We analyzed all adult recipients of deceased donor kidney-alone transplants at our center between 2001-2020 (DKT N=100/SKT N=3125). All recipients of the pediatric en-bloc kidney transplants were excluded. Outcomes of interest included delayed graft function (DGF), post-transplant length of stay (LOS), re-hospitalization within 30 days of discharge, and re-operation (OR) due to transplant surgical complications, biopsy-proven acute rejection (AR), death-censored graft failure (DCGF), uncensored graft failure (UCGF) and death with functioning graft (DWFG) within 5 years post-transplant.

**Results:** In comparison to SKT, DKT had a similar risk of DGF (aOR 1.25; 95% CI 0.76-2.08); LOS (linear coefficient 0.42; -0.9-1.7); reoperation (aOR: 0.73; 95% CI: 0.21-2.51) or re-hospitalization (aOR 0.98; 95% CI: 0.55-1.74). However, long term, DKT was associated with lower AR (aIRR0.28; 95% CI 0.12-0.64); DCGF (aIRR0.30; 95% CI 0.13-0.68), and UCGF (aIRR0.53; 95% CI 0.33-0.86), and similar DWFG (aIRR0.83; 95% CI 0.46-1.53).

**Conclusions:** In selected recipients, DKT delivered superior long-term outcomes compared to SKT without increased short-term complications. DKT can mitigate concerns that limit the use of medically complex donor kidneys, increase organ utilization, and increase access to transplantation.

## **Pretransplant Hypoalbuminemia Is Not Associated with Worse Outcomes among Simultaneous Pancreas and Kidney Transplant Recipients**

Authors: Ekatarina Fedorova, MD, Sofia Nehring Firmino, MS3, Brad Astor, PhD, Didier Mandelbrot, MD, Dixon Kaufman, MD, PhD, Jon Odorico, MD, Sandesh Parajuli, MBBS

**Introduction:** Hypoalbuminemia is a well-known independent risk factor predictive of worse outcomes in surgical patients. Nonetheless, the role of pre-transplant hypoalbuminemia and its impact on post-transplant outcomes in patients undergoing simultaneous kidney-pancreas (SPK) transplantation remains unclear.

**Method:** We retrospectively analyzed all SPK recipients at our center from 2001-2022, who had at least 2 weeks of pancreatic graft survival. Serum albumin levels measured within 6 weeks or closer to transplant were included. Recipients were categorized based on pre-transplant albumin level normal ( $\geq 4.0$  g/dL, N = 222), mild ( $\geq 3.5$  -  $< 4.0$  g/dL, N = 190), or moderate ( $< 3.5$  g/dL, N = 120). Multivariable logistic regression and Cox proportional hazard models were used to analyze associations with the length of stay (LOS), kidney delayed graft function (DGF), re-hospitalization within 30 days after discharge, and need for return to the operating room (OR) related to transplant surgical complications, along with acute rejection and uncensored and death-censored graft failure, within the first-year post-transplant.

**Results:** A total of 532 SPK recipients were included, 42% had normal serum albumin, 36% had mild, and 23% had moderate hypoalbuminemia. The mean pre-transplant albumin level was 4.3 g/dL in the normal, 3.7 g/dL in the mild, and 3.0 g/dL in the moderate group. After adjustment for multiple variables, with reference to normal pre-transplant albumin level, mild or moderate hypoalbuminemia were not associated with either increased or decreased risk for LOS, DGF, re-hospitalization or return to the operating room. Also, mild and moderate hypoalbuminemia were not associated with risk for either graft rejection or graft failure

**Conclusions:** Among SPK recipients, pre-transplant hypoalbuminemia is not associated with worse outcomes. Pre-transplant albumin level should not be the determining factor in offering or rejecting these life-saving organs.

## **Type of Deceased Donor Doesn't Significantly Differ Early Post-Kidney Transplant Outcomes of Delayed Graft Function**

Authors: Angela L. Zhou, BA, Suseela Raj, BS, Ekaterina Fedorova, MD, Jacqueline Garonzik-Wang, MD, PhD, Didier Mandelbrot, MD, Brad C. Astor, PhD, Sandesh Parajuli, MD

**Introduction:** Delayed graft function (DGF) after kidney transplantation (KT) is less common in donation after brain death (DBD) vs. circulatory death donors (DCD). To better understand the benefits and consequences of using DBD vs DCD kidneys, we compared the risk factors and outcomes significantly associated with DGF between both groups, from our center.

**Method:** We analyzed all adult deceased donor kidney transplant recipients (DDKTR) at our center between 2005-2019, stratified by donor type (DBD vs. DCD). We assessed risk factors for DGF, acute rejection (AR), and graft failure (GF).

**Results:** Among 2543 DDKTRs, 804 (31%) were from DCD donors. 20.9% of DBD and 46.6% of DCD recipients experienced DGF. Older donor age, higher recipient BMI, and receipt of a depleting induction agent were associated with greater risk for DGF in both DBD and DCD recipients, while female recipient and preemptive transplant was associated with reduced risk. Additional risk factors in DBD, but not in DCD recipients, included higher donor terminal serum creatinine, higher KDPI, right donor kidney, and prolonged cold ischemia time (CIT). Female donors were associated with a reduced risk of DGF only in DCD. DGF was linked to higher AR and GF risk, with no significant differences between DBD and DCD groups (AR: aHR 2.22 vs 2.37, p-interaction=0.65; GF: 3.04 vs 2.56; p-interaction=0.47).

**Conclusions:** Despite higher DGF rates in DCD-KTs, early adverse outcomes after DGF were similar between deceased donor types. Higher DGF rates alone should not deter the utilization of DCD kidneys.



## A Global Health Epidemiology Survey on Microtia in Vietnam

Authors: Sarah Hu (1), Elizabeth P. Wu, B.S. (1), Emily E. Zona, B.S. (1), Lauren Feeley (1), Jusuf Ademi (1), Samuel O. Poore, M.D., Ph.D.(1), Aaron M. Dingle, Ph.D.(1) (1) Division of Plastic and Reconstructive Surgery, Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA

**Introduction:** While autologous cartilage reconstruction is widely accepted as the gold standard treatment for microtia, there are complications such as donor site morbidity or infection. It also requires multiple stages that must be spaced at least three months apart to allow for healing. Several other techniques are widely used in the United States, such as using a porous polyethylene (Medpor) scaffold, or prosthesis. Prosthesis may be adhered with glue or osseointegrated magnets. In Vietnam, patients with microtia who elect for autologous cartilage reconstruction may be lost to follow-up. The primary objective of this study is to characterize available and desired treatments for patients with microtia in Vietnam by surveying Vietnamese surgeons regarding reconstructive options.

**Method:** An IRB approved survey was created to focus on surgeons' opinions and includes questions regarding the importance of microtia treatment in relation to other prevalent plastic surgery demands, the types of treatments most commonly requested and performed, and surgeon awareness of other techniques. Demographic questions are added to gauge specialty, level, and years of experience in the medical field. In addition, another survey will be created to better understand the needs and preferences of patients with microtia and their families. Surveys will be administered in March of 2025 during the microsurgery education course in Vietnam.

**Results:** Results will be collected in March of 2025 in Vietnam.

**Conclusions:** The surveys will allow for first-hand insight on microtia treatments from the different perspectives of providers and patients. It will highlight the significance of microtia in comparison to other conditions that require surgical reconstruction, which can aid in resource allocation for research efforts. Furthermore, if the survey helps identify knowledge gaps, subsequent global health trips can be geared towards providing education to plastic surgeons who may lack access to training on specific reconstruction methods. The study will also provide information on cultural acceptability of prosthetics and potential for global collaboration in the prosthetic field of anaplastology. Ultimately, a better understanding of microtia treatment preferences will improve patient outcomes and satisfaction.

## Wound Complications After Breast Reconstruction: The Limited Role of HbA1c Compared to BMI

Authors: Emily E. Zona, B.S., Doruk Orgun, M.D., Caroline C. Bay, B.A., Robert E. George, M.D., Sarah M. Thornton, B.A., M. Kristine Carbullido, M.D., Aaron M. Dingle, Ph.D., Samuel O. Poore, M.D., Ph.D.

**Introduction:** Although hemoglobin a1c (HbA1c) and body mass index (BMI) are routinely evaluated before both alloplastic and autologous breast reconstruction to assess postoperative complication risk, evidence-based guidelines are limited regarding accepted cutoffs of these measures. The primary objective of this study was to elucidate the associations between HbA1c levels or BMI with wound complications following reconstructive breast surgery.

**Method:** This retrospective cohort study utilized the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database to assess 30-day wound complications among patients who underwent autologous or alloplastic breast reconstruction after mastectomy for breast cancer between January 1, 2021 to December 31, 2022. Wound complications included wound dehiscence, superficial incisional surgical site infections (SSI), deep incisional SSI, or organ space SSI. Statistical analyses including multivariable Cox regression and Kaplan-Meier curve comparisons were performed based on the distribution of HbA1c or BMI in the study cohort.

**Results:** A total of 2,809 patients underwent autologous or alloplastic breast reconstruction for breast cancer with preoperative HbA1c measurement. Among these, 2,025 (72.1%) underwent alloplastic reconstruction while 784 (27.9%) underwent autologous breast reconstruction. For the entire cohort, the median age was 54, the median HbA1c was 5.7 (IQR: 5.3-6.4), and the median BMI was 29.4 kg/m<sup>2</sup> (IQR: 25.5-33.9). The 30-day complication rate (cumulative incidence) in the autologous group and alloplastic group were 11.7% and 7.5%, respectively. Kaplan-Meier curves for the comparison of absolute risk of 30-day wound complications showed no significant differences between HbA1c quartile curves (log-rank p-value=0.46). For BMI, compared with the first BMI quartile, the third (median BMI of 31.5 kg/m<sup>2</sup>) and fourth (median BMI of 37.3 kg/m<sup>2</sup>) BMI quartiles had over double the rate of any complication (Q1: 5.0%; Q2: 7.3%; Q3: 11.1%; Q4: 11.4%; p<0.001), which was confirmed by the comparison of Kaplan-Meier curves between the quartiles (plog-rank<0.001). With the first BMI quartile as reference, the adjusted hazard ratio estimates of 30-day complication risk were 1.83 (95%CI: 1.21-2.77; p=0.004) for the third BMI quartile, and 1.80 (1.18-2.76; p=0.007) for the fourth BMI quartile.

**Conclusions:** In conclusion, this study demonstrates that higher BMI is associated with wound complications after breast reconstruction. In the alloplastic group, the patients in BMI quartile 4 (taking the first BMI quartile as reference) had a 75% increased risk of wound complications while for patients in the autologous group, the risk increased more than 1.4 fold. On the other hand, no similar associations were observed with HbA1c levels.

## A Day In The Life of a Surgical Instrument: The Cycle of Sterilization

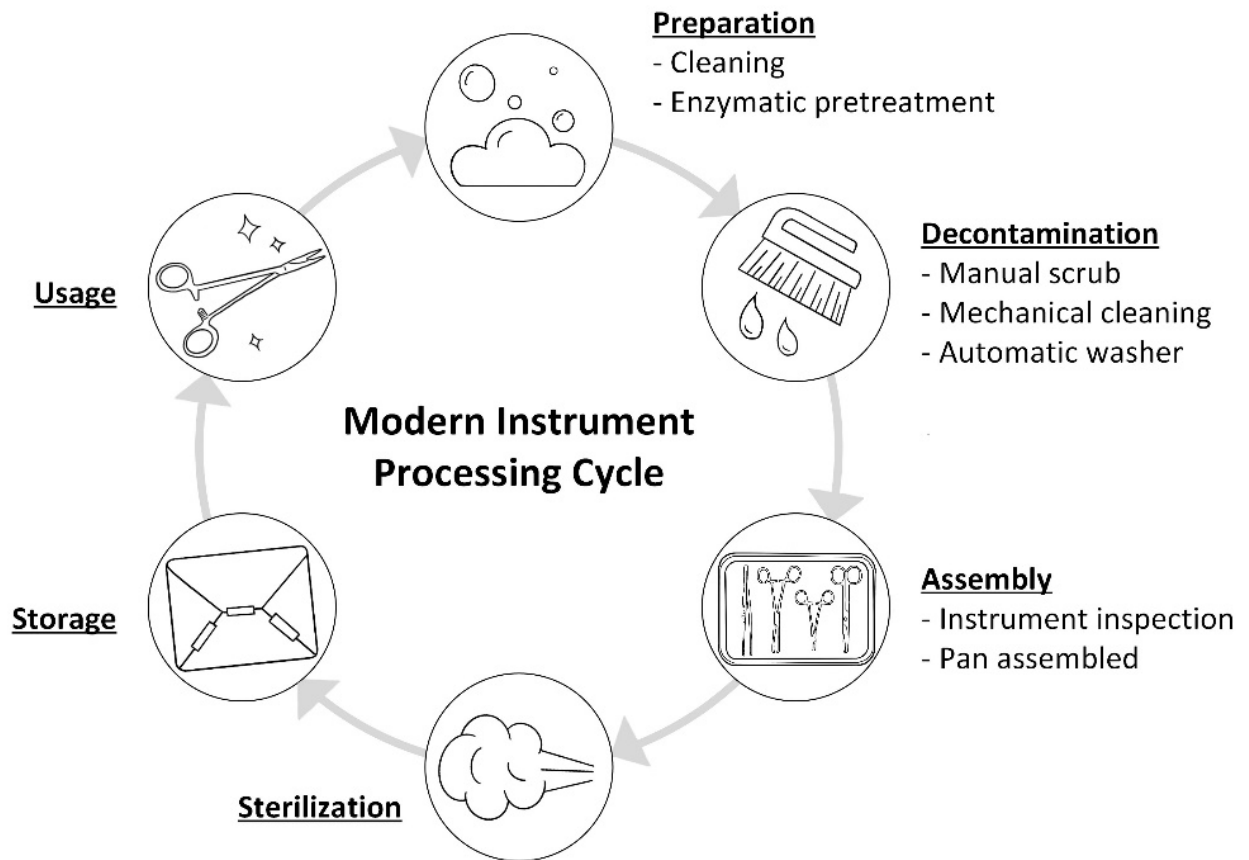
Authors: Robert E. George, MD, Caroline C. Bay, BA, Ellen C. Shaffrey, MD, Peter J. Wirth, MD, Venkat K. Rao, MD MBA

**Introduction:** Surgeons must be confident that the instruments they use do not pose risk of infection to patients due to bioburden or contamination. Despite this importance, surgeons are not necessarily aware of the steps required to ensure that an instrument has been properly sterilized, processed, and prepared for the next operation.

**Method:** This was a narrative review.

**Results:** Modern decontamination defines cleaning, disinfection, and sterilization as technical terms. Sterilization is the highest level of decontamination and begins at the end of an operation. Instruments must first be grossly cleaned by the scrub technician to remove blood, tissue, and other material. Prompt cleaning to decrease contact time with blood and using sterile water rather than saline decreases risk of instrument corrosion. Another important step is the use of an enzymatic transport gel or foam. This pretreatment facilitates cleaning in the sterile processing unit and significantly decreases the burden of cleaning for the sterilization technicians. The instruments are then transported to the sterile processing unit where they are decontaminated. This starts with manual scrubbing with nylon brushes and then a form of mechanical cleaning. A common variation of this is an ultrasonic cleaner. Following decontamination, instruments are then brought to the assembly area where pans are assembled and instruments are inspected to ensure functionality, lack of corrosion, and absence of gross contamination. The sterility of instruments is determined by the Sterility Assurance Level (SAL), which is the probability of finding a single microbe on an instrument after it has been sterilized. SALs of  $10^{-6}$  are typical for surgical sterilization. There are several ways to successfully sterilize instruments. These can be categorized as high temperature or low temperature methods. Within high temperature sterilization, dry or moist heat can be used. Heat sterilization can be used for many materials, but for heat sensitive materials, low temperature sterilization should be used. Low temperature sterilization consists of either chemical or radiation-based methods. Lastly, the usage rate of sterilized instruments room typically ranges from 13.0% to 21.9% and the number of instruments in a tray is inversely proportional to the usage rate. Importantly, a 70% reduction in excessive sterilization would correspond to an estimated savings up to \$2.8 million.

**Conclusions:** This review highlights the intricacies of the sterile processing of surgical instruments.



## Ventral Hernia Repairs in Wisconsin: Current State and Targets for Quality Improvement

Authors: Victoria Rendell, MD, Randi Cartmill, MS, Manasa Venkatesh, MS, Elise Lawson, MD MSHS, Matthew Goldblatt, MD

**Introduction:** Ventral hernia repairs (VHR) are among the most common general surgery procedures. Despite recent advances with rising use of minimally invasive approaches, recurrence rates remain high, ranging from 15-40% in recent studies without improvement over time. No previous research has quantitatively described the current practices for VHR in Wisconsin, which limits the ability to develop targets for quality improvement. The Surgical Collaborative of Wisconsin (SCW), a surgeon-led practice change community comprising over 400 surgeons and quality leaders statewide, aims to improve patient outcomes and the quality of care by developing a data-informed quality improvement initiative on VHR.

**Method:** All encounters for outpatient and inpatient VHR performed in Wisconsin Jan.-Dec. 2023 were examined using Wisconsin Hospital Association (WHA) discharge records. Surgeries designated by CPT codes and ICD-10 procedure codes were quantified. Outpatient VHR CPT codes include hernia size and status as a recurrent operation while ICD-10 codes describe only approach and use of mesh. Descriptive analyses compared VHR occurrence across patient demographics and facility location. Rates of VHR by region were adjusted for population.

**Results:** In 2023, 11,626 VHR were performed; 8771 were performed in the outpatient setting and 2855 as inpatient. The majority (58%, n=5117) of outpatient repairs were performed for <3cm non-recurrent hernias, of which 69% (n=3512) were performed in men. For outpatient and inpatient repairs, 68% (n=5830, n=2054) were performed for patients between 45-75 years of age. Patients over 75 years represented 8% of outpatient and 18% of inpatient repairs. Recurrent hernia repairs represented 6% of outpatient repairs (n=523), and 50% (n=263) were performed in women. In the inpatient setting, mesh-based repairs represented 52% of the cases (n=1493), and 58% (n=863) were performed in women. Minimally invasive approaches were used in 947 inpatient VHRs (33%), of which 525 (55%) were performed in women. All types of VHR were performed in each region of the state (Figure 1).

**Conclusions:** Larger and recurrent hernias are repaired outpatient at similar rates across the state without concentration in urban centers. Although women represent the minority of patients undergoing small, primary VHR, they represent the majority of patients undergoing more complex VHR (i.e., recurrent or requiring inpatient stays). SCW quality improvement efforts for VHR will aim to reach surgeons statewide and target improving recurrence rates, particularly for female patients. The SCW initiative will include further analysis of current VHR practice across the state and education initiatives for best practices in VHR.

Wisconsin Analysis Areas	Ventral Hernia Repairs Performed in the State of Wisconsin in 2023									
	Wisconsin Analysis Areas									
	Ventral Hernia Repairs-Rate per 100,000 population									
	1	2A	2B	3	4	5A	5B	6	7	
<i>Population in thousands</i>	1213	1122	941	639	652	515	283	476	148	
<b>Outpatient, First Repair</b>	123.6	144.9	102.4	<b>159.6</b>	<b>153.0</b>	100.6	118.2	<b>171.9</b>	97.3	
<b>Outpatient, Recurrent Repair</b>	7.3	6.8	6.8	<b>12.8</b>	<b>9.7</b>	7.8	5.7	<b>12.0</b>	8.8	
<b>Inpatient, Non-Mesh Repair</b>	20.9	<b>23.4</b>	<b>28.6</b>	<b>21.3</b>	20.2	15.7	17.7	19.1	8.1	
<b>Inpatient, Mesh-Based Repair</b>	18.6	<b>27.6</b>	<b>35.5</b>	23.8	<b>24.4</b>	11.3	17.3	20.8	10.8	
Minimally Invasive w/ synthetic mesh	9.4	<b>14.3</b>	11.7	<b>12.7</b>	<b>14.4</b>	7.2	7.4	10.9	7.4	
Open w/ synthetic mesh	7.2	<b>10.5</b>	<b>19.7</b>	<b>8.6</b>	7.7	3.3	7.8	8.4	2.7	

**Figure 1. Ventral hernia repair (VHR) rates per 100,000 people performed in the state of Wisconsin in 2023 are categorized by analysis areas.** Rates of outpatient and inpatient VHR were separately determined with outpatient recurrent repair and inpatient mesh-based repair denoting more complex repairs. The three highest rates of VHR for each operation category are indicated by bolding and shading

## A Comparison of Anal Cancer Risk Among Veterans with HIV Who Undergo Initial Anal Evaluations With Screening Versus Diagnostic Assessments

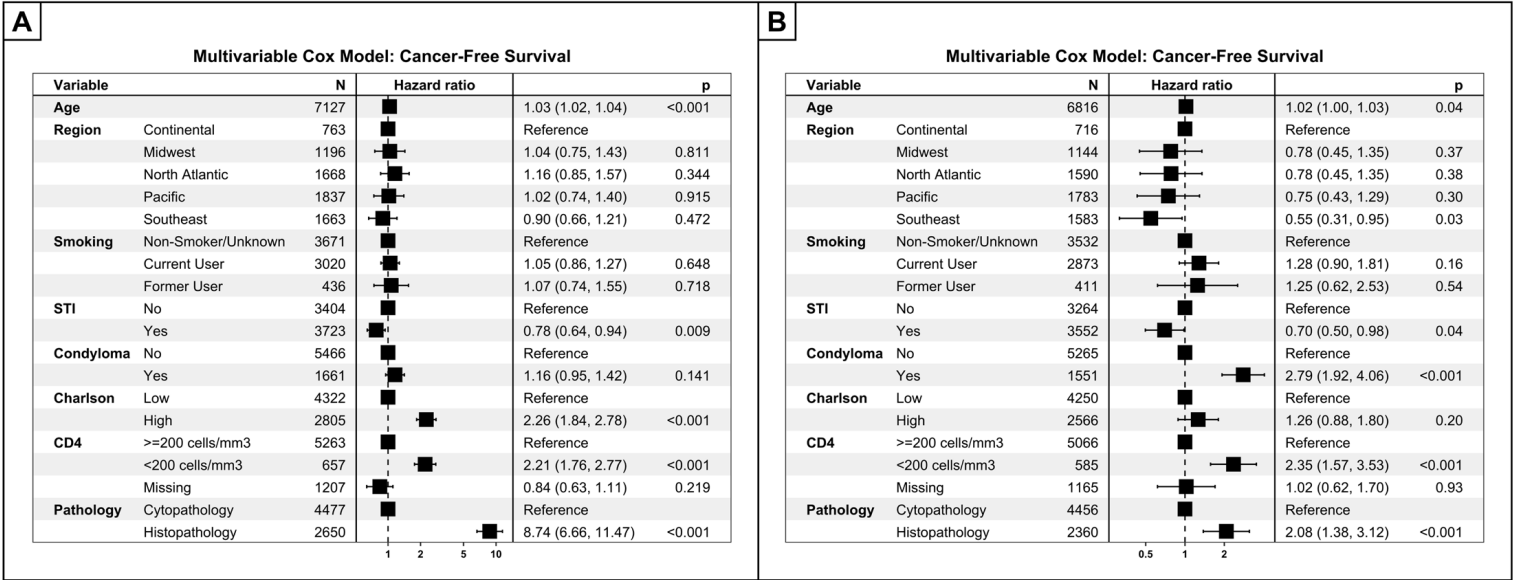
Authors: Austin Hewitt, MD, Matthew Freeman, MD, Evie Carchman, MD, Marin Schweizer, PhD, Cristina Sanger, MD

**Introduction:** Anal squamous cell carcinoma (ASCC) disproportionately affects specific populations, such as people with HIV (PWH). Detection of ASCC can occur in different ways, including as part of a routine screening algorithm or after a symptomatic clinical presentation. Initial pathologic assessments performed for screening protocols generally involve cytologic evaluations. Conversely, patients with symptomatic complaints often receive histologic evaluations without a preceding cytologic test. The primary objective of this study is to compare the risk of ASCC development between PWH who undergo initial anal pathologic evaluations via screening assessments with cytopathology versus diagnostic assessments with histopathology.

**Method:** This is a national retrospective cohort analysis of veterans with HIV between 1999-2023. We divided patients into two groups based on their first-ever VA anal pathology evaluation: 1) assessment with cytopathology and 2) assessment with histopathology. We analyzed anal cytopathology and histopathology reports. Kaplan-Meier methods were used to estimate rates of ASCC-free survival from time of first-ever anal pathology result. We evaluated factors associated with ASCC development using Cox proportional hazards models. As a sensitivity analysis, we removed patients with ASCC within 6 months of their first-ever anal pathology result.

**Results:** 7,127 veterans with HIV who had at least one anal pathology result were included for analysis. The majority were male (98%) with a mean age of 52 years and follow-up of 8 years. First-ever anal pathologic assessments were cytopathology in 4,477 (63%) and histopathology in 2,650 (37%). We identified 455 patients with ASCC. 5-, 10-, and 15-year ASCC-free survival rates for the cytopathology and histopathology groups were 98.9%, 98.1%, 97.3%, and 86.6%, 84.6%, 83.2% ( $p < 0.001$ ), respectively. Cox regression showed an increased risk of ASCC in the histopathology group (HR 8.74, 95% CI: 6.66-11.47,  $p < 0.001$ ) (Fig 1A). After removing patients for the sensitivity analysis ( $n=311$ ), 6,816 remained. Initial pathologic evaluations were cytopathology in 4,456 (65%) and histopathology in 2,360 (35%). ASCC free-survival rates for the cytopathology and histopathology groups were 99.4%, 98.6%, 97.8%, and 97.2%, 95.0%, 93.4% ( $p < 0.001$ ), respectively. Cox regression showed an increased risk of ASCC in the histopathology group (HR 2.08, 95% CI: 1.38-3.12,  $p < 0.001$ ) (Fig 1B).

**Conclusions:** In this national analysis of veterans with HIV, 6.4% of veterans with anal pathology results were diagnosed with ASCC. About two-thirds (68%) of ASCC diagnoses were made within 6 months after first-ever anal pathology evaluations. We observed an increased risk of ASCC and shorter ASCC-free survival among patients whose initial anal evaluation was histology rather than screening cytology.



**Figure 1.** A) Multivariable Cox regression model for risk factors associated with development of anal cancer. B) Multivariable Cox regression model for risk factors associated with development of anal cancer after removing patients with cancer <6 months after their first anal pathology evaluation.



## **Best Case/Worst Case-ICU (BC/WC-ICU): A National Implementation Study in Trauma Intensive Care Units (ICU)**

Authors: Melanie Fritz, MD, Alexandra Hernandez, MD, Amy Zelenski, PhD, Jenna Nitkowski, PhD, Carly Sobol, MD, Kristine Kwekkeboom, PhD, Margaret Schwarze, MD

**Introduction:** Older adults with a serious injury often undergo a significant change in their overall health trajectory, face multiple treatment decisions, and experience a major change in long-term functional status. In this setting, advanced communication techniques that support patients and families are needed to understand prognosis and promote goal-concordant treatment plans. The objective of this study was to implement BC/WC-ICU, a communication tool utilizing scenario planning and a graphic aid (GA), at 8 trauma centers and describe the implementation outcomes.

**Method:** We implemented BC/WC-ICU at Shock Trauma, Rhode Island Hospital, Lehigh Valley Health Network, Grady Memorial Hospital, University of Alabama, Froedtert Hospital, Harborview Medical Center, and University of California-Davis. We delivered training to attendings and fellows, residents and advanced practice providers, and nursing staff. We performed weekly audits of the BC/WC-ICU GAs and used audits to monitor adherence and provide feedback. We measured fidelity to the intervention by scoring GAs with an 8-point checklist and performed open-ended interviews with clinicians to assess effectiveness, barriers, and facilitators. We used the RE-AIM framework to summarize implementation outcomes.

**Results:** We reached 177 attending physicians and fellows with one-on-one training, representing 66-100% of trauma team leaders, 96% of whom were trained to competence. ICU team members effectively used the BC/WC-ICU tool with patients and families to communicate prognosis and change in clinical status over time. They reported that families better understood prognosis: “they really seem to get it now, how sick grandpa is.” BC/WC-ICU effectively supported team communication by ensuring consistent messaging and encouraging trainees to consider the big picture. Most trauma centers adopted the intervention with strong adherence. Six centers had an average adherence of 82.25% (range 62.1-100%), while two sites demonstrated lower uptake (25.5%, 50.3%). Implementation fidelity was high: GAs scored a mean of 6.5 of 8 points on a fidelity checklist. Implementation barriers identified by clinicians included high patient volume, perceived burdens of GA completion, and competing priorities on rounds. Maintenance of the intervention past 6 months was facilitated by leadership buy-in, site champions, a small, consistent group of ICU attendings/fellows, and the ability to integrate BC/WC-ICU into existing workflows.

**Conclusions:** We successfully implemented the BC/WC-ICU intervention across 8 trauma centers to effectively leverage team communication to consistently convey prognosis and changing health trajectories of seriously injured older adults. Long term use of BC/WC-ICU will require ongoing promotion efforts and successful integration of the tool into ICU practice and culture.

## **Clinical momentum in the care of older adults with advanced dementia: What evidence is there in the medical record?**

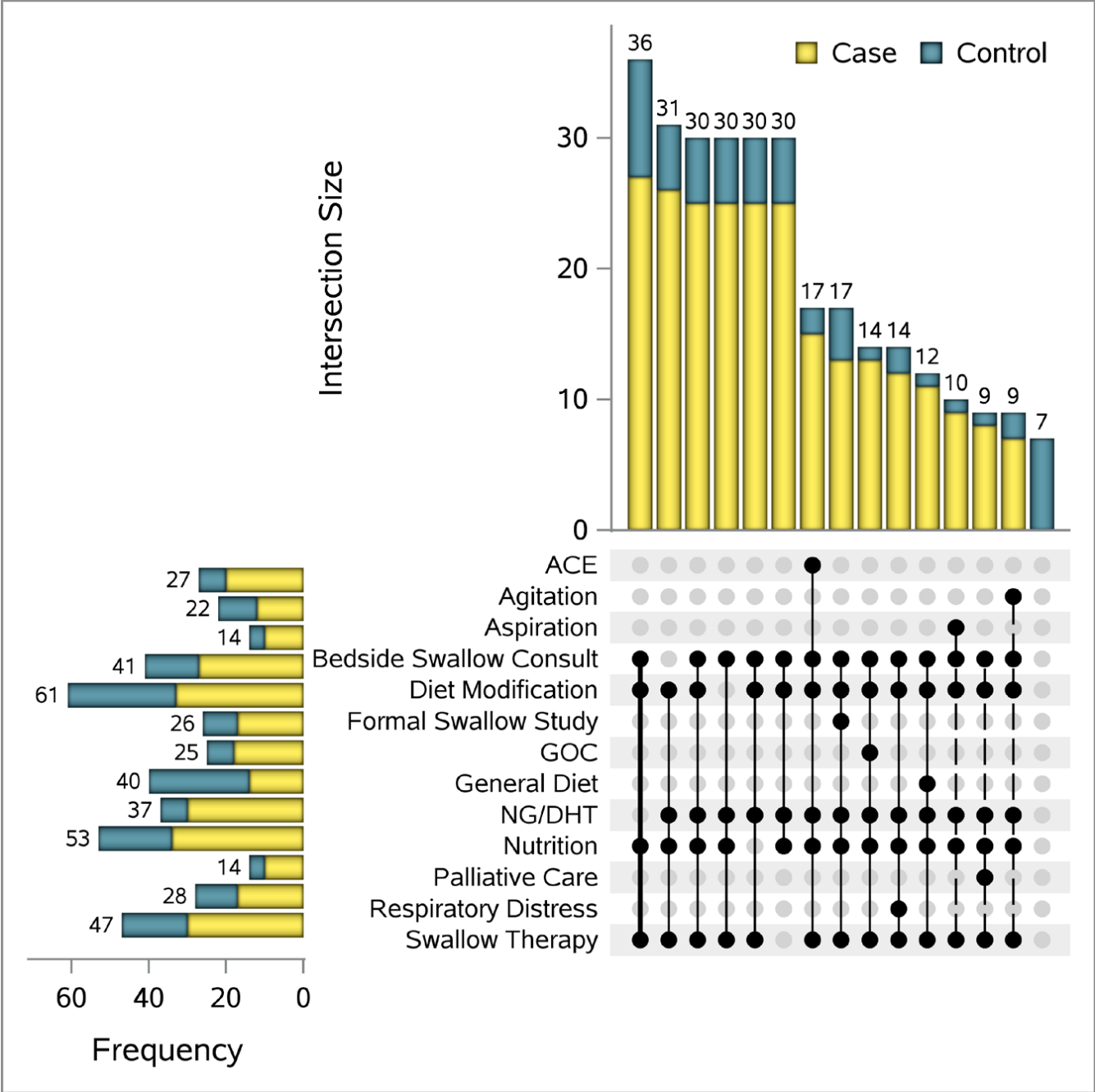
Authors: Lily N Stalter, MS, Bret M Hanlon, PhD, Kyle J Bushaw, MA, Taylor Bradley, BS, Anne Buffington, MPH, Karlie Zychowski, MD, Alex Dudek, RN, BSN, Sarah I Zaza, MD, Melanie Fritz, MD, Kristine Kwekkeboom, PhD, RN, FAAN, Margaret L Schwarze, MD, MPP

**Introduction:** Overtreatment at the end of life contributes to poor quality of life, is often discordant with patient preferences, and strains healthcare systems. “Clinical momentum” is a conceptual model to describe the latent, systems-level forces that create an inevitable trajectory toward intervention. Feeding tube placement in patients with advanced dementia is a clear example of overtreatment at the end of life, given the associated harms and limited benefits. This study aims to identify previously characterized markers of clinical momentum in the Electronic Health Record (EHR).

**Method:** We conducted a retrospective, single-center, matched case-control study. We used an EHR search to identify all hospitalized older adults (age  $\geq 65$ ) with a dementia diagnosis and activated health care agent during an unplanned admission of  $\geq 3$  days between January 2015 and December 2022. The case group included patients who received a permanent feeding tube (i.e., Gastrostomy, Gastrojejunostomy, or Jejunostomy tube). We 1-1 matched controls, patients who did not receive a permanent feeding tube, with cases based on age, sex, and admitting diagnosis. We cataloged hospital trajectories and the frequency of event combinations leading to permanent feeding tube placement for cases and death or discharge for controls, displayed via UpSet Plot.

**Results:** We identified 34 cases and 34 matched controls. The mean age (SD) was 80.2 (8.7), and 34 (50%) were male. The median (IQR) length of stay was 21.5 (15-43) days among cases and 5 (4-9) days among controls. At the median, feeding tubes were placed on day 15 (7-18) of admission. On average, case patients experienced 9.0 (2.2) unique hospital events before feeding tube placement, while control patients experienced, on average, 4.9 (2.5) events during their admission. We found higher rates for all events among case patients (Figure 1). Notably, 18 (52.9%) cases and 7 (20.6%) controls had a “goals of care” meeting, while 10 (29.4%) cases and 4 (11.8%) controls received a palliative care consult. Twenty-seven (79.4%) cases and 9 (26.5%) controls received a bedside swallow consult, diet modification, nutrition consult, and swallow therapy, the most common combination for both groups. Twenty-five (73.5%) cases and 5 (14.7%) controls received a nasogastric tube with this combination.

**Conclusions:** These results suggest momentum increases the longer patients stay in the system, leading to additional tests and interventions that are difficult to withdraw once they are in place. Future efforts to measure clinical momentum at scale may reveal novel targets to improve end-of-life care.



## Creating an MRI Classification System for Hip Abductor Musculature Atrophy

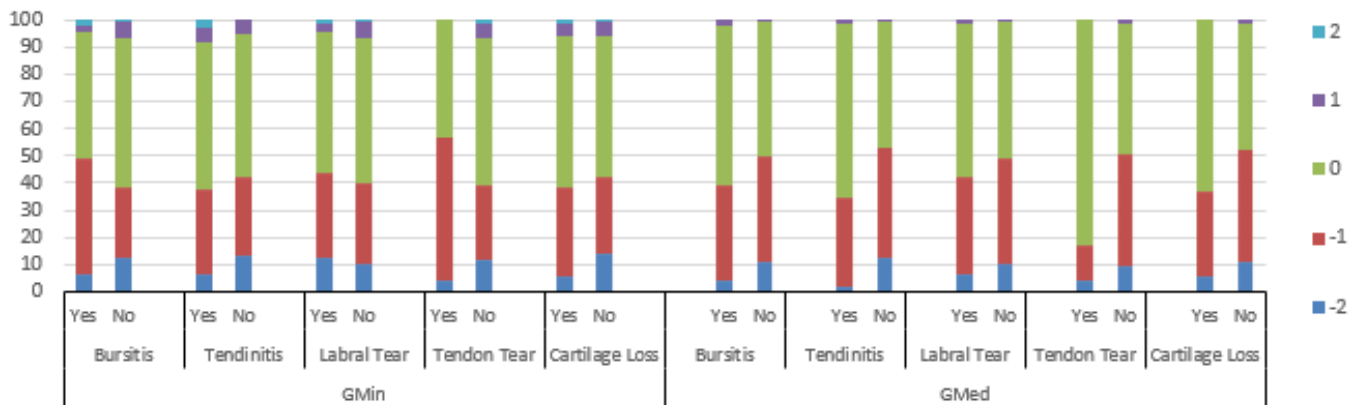
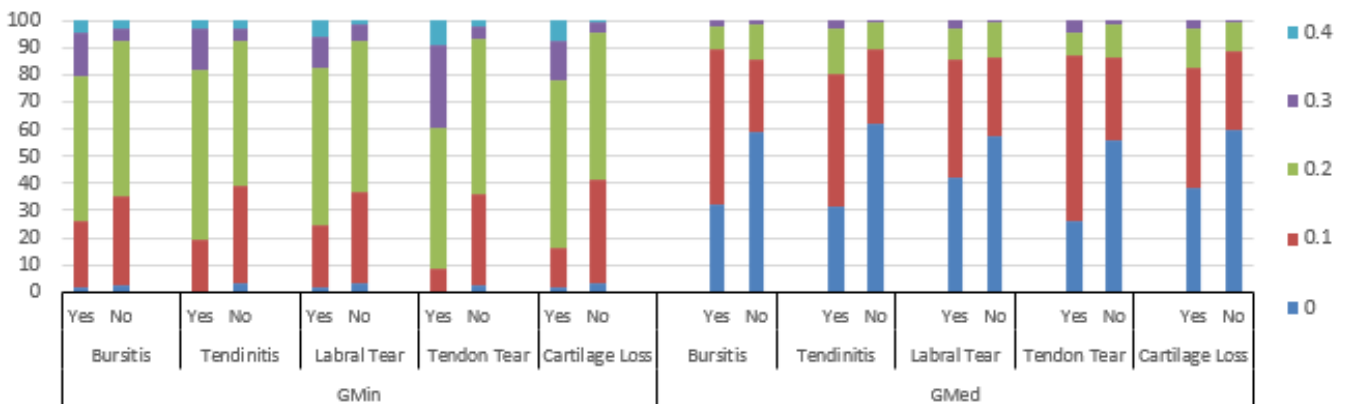
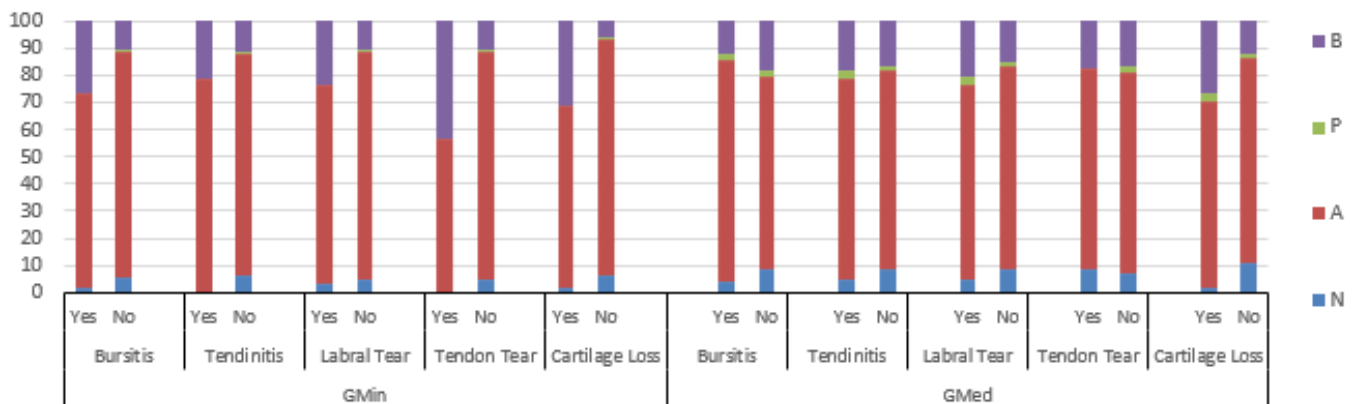
Authors: Megan N Baughman, BS, Donna G Blankenbaker, MD, Samuel J Mosiman, MS, Reagan SH Beyer, BS, Anchal P Dhawan, BS, Ariel H Kim, BA, Andrea M Spiker, MD

**Introduction:** No standardized classification system exists for fatty infiltration of hip abductors, though preoperative fatty infiltration correlates with postoperative outcomes in abductor tendon repairs. We aimed to create a simple, reliable, and reproducible MRI classification system for fatty infiltration specific to hip abductor anatomy and examine the correlation between fatty infiltration grades and hip pathology.

**Method:** We retrospectively identified 100 patients who underwent bony pelvic MRI with no infection, fracture, tumor, or prior history of hip surgery. Using these images, fatty infiltration of the gluteus medius (GMed) and gluteus minimus (GMin) of both hips were graded according to the new system we created. Grades consisted of a whole number (-2 to 2) corresponding to muscle thickness with respect to average, a decimal number (0-0.4) representing the ratio of fat-to-muscle cross-sectional area, and a letter (A, P, or B) indicating location of fat within the muscle. To increase ease of use of the system, we created an open access, online calculator for grade determination. Demographic information and details of hip pathology were collected for each patient, and descriptive data was compiled. Wilcoxon rank sums were used to determine if grade values were significantly different for those who did and did not have certain hip pathologies.

**Results:** Interquartile ranges for muscle thickness and fatty atrophy were [-1,0] and [0.1,0.2] for GMin and [-1,0] and [0,0.1] for GMed, respectively. Muscle thickness was significantly greater in males than females for both GMin ( $p=0.0027$ ) and GMed ( $p<0.0001$ ). Female GMin had 9% greater fat content than male GMin ( $p=0.002$ ), and fat content increased with age. Fat was most often localized to the anterior portion of the muscle in both the GMed and GMin. Fat located in the posterior portion or throughout the GMin was ubiquitously associated with pathology. Higher grades for fat content in the GMin and GMed correlated with tendon tear, tendinitis, and intra-articular hip cartilage loss (GMin:  $p<0.0001$ ,  $p=0.0017$ ,  $p<0.0001$ ; GMed:  $p=0.0248$ ,  $p=0.0001$ ,  $p=0.005$ ). Higher fat content grades in the GMin were separately associated with labral tear ( $p=0.0251$ ), while the same relationship was found between the GMed and greater trochanteric bursitis ( $p=0.0154$ ). Analysis of muscle thickness displayed a positive association between width of the GMed and incidence of tendon tear, tendinitis, and cartilage loss ( $p=0.0055$ ,  $p=0.0064$ ,  $p=0.0473$ ).

**Conclusions:** This classification system offers a simple way to grade fatty atrophy in hip abductor muscles and proved to correlate with various hip pathologies.

**A****Distribution of Muscle Thickness Scores Based on Presence or Absence of Pathology****B****Distribution of Fat Content Scores Based on Presence or Absence of Pathology****C****Distribution of Localization Scores Based on Presence or Absence of Pathology**

## Lessons Learned from the Interprofessional Mindfulness Practices Advancing Cancer Teamwork (IMPACT) Study

Authors: Sydney Tan, MD, Faith Dickerson, MD, Tanya Kroll, MBA, Amber Bradley, RN, Sherry Chesak, PhD, RN, Lee G Wilke, MD

**Introduction:** Mindfulness-based interventions (MBIs) can decrease burnout and improve well-being, however, the majority of MBI research focuses on the individual rather than the interprofessional team. We used an MBI focused on team resilience to train interprofessional oncology teams to address burnout and improve teamwork. We hypothesized that a team-focused MBI would improve teamwork and well-being while also being feasible and acceptable for oncology teams.

**Method:** At a single-institution cancer center, we conducted a prospective cohort study with interprofessional oncology team members in Breast, Gynecologic, and Gastrointestinal Oncology. Participants underwent a team resilience MBI involving four monthly, one-hour training sessions offered during the lunch hour by a team resilience expert. Sessions were hybrid (in-person and virtual), synchronous, and recorded. Participants completed pre- and post-intervention surveys on teamwork, burnout, stress, resilience, and flourishing. Acceptability, appropriateness, feasibility, and short-answer feedback was collected post-intervention. Paired t-tests compared pre and post outcomes. Descriptive statistics analyzed feasibility, acceptability, and appropriateness, while thematic analysis evaluated qualitative feedback.

**Results:** Out of 135 invited, 21 (16%) participants enrolled, consisting of clinic nurses, nurse managers, social workers, advanced practice providers, pharmacists, radiation oncologists, and surgical oncologists. The majority (57%) were 22-54 years of age with varied years of work experience (36% with >20 years). At baseline, participants scored high on team psychological safety (mean 5.16, SD 1.02) measured by Edmonson's Psychological Safety Scale. 31% of participants had burnout on the Maslach Burnout 2-Item. Follow-up was low with 6 respondents (29%) completing the post-intervention survey. Session attendance also diminished with 12 people attending the 1st session with 6 online views, to 1 person in attendance with 1 online view for the last session. There were no significant differences ( $p > 0.05$ ) when comparing pre- and post- teamwork, stress, burnout, resilience, and flourishing. Measures of Acceptability (mean 4.38, SD 0.38), Appropriateness (mean 4.33, SD 0.52), and Feasibility (mean 4.04, SD 0.62) of Intervention were high. In feedback, participants reported improved mindfulness, increased knowledge regarding building work relationships, and desiring more colleague participation.

**Conclusions:** Participants from interprofessional oncology teams had high team psychological safety at baseline and almost a third were burnt out, consistent with reported burnout ranges in oncology. We anticipated higher retention based on prior studies, however, our implementation approach requires re-evaluation. This study highlights the need to focus on population-specific factors when implementing and studying MBIs for optimal engagement. Further research is necessary to understand the best implementation approach for team-specific MBIs in multiprofessional oncology teams.

## Feasibility of Continued Impella 5.5 Support Following Bridge to Simultaneous Heart-Kidney Transplant

Authors: Angela Kristo, BS, Max Frenkel, PhD, Vyacheslav Lenkov, MD, Paul Tessman, MD, PharmD, Veli Topkara, MD, MSc, Joshua Hermsen, MD, Yu Xia, MD, MS

**Introduction:** Since the new heart allocation policy in 2018, the Impella 5.5 is increasingly used as a bridge to heart and simultaneous heart/kidney transplant (SHKT). Up to 40% of SHKT patients require renal replacement therapy (RRT) within 30 days of transplant. In our initial experience of three patients bridged to SHKT with Impella 5.5, the device was explanted at the time of heart transplant but all required post-operative dialysis. We present the outcomes of two other cases where the Impella 5.5 was left in place for temporary mechanical support following heart transplant with the goal of reducing post-transplant RRT.

**Method:** We present 5 patients who were bridged to SHKT with the Impella 5.5 at the University of Wisconsin between 2022 and 2024. Three patients had their Impella 5.5 explanted at the time of heart transplant. In two patients, the device driveline was included in the aortic crossclamp. Following recipient cardiectomy, the device was inspected, flushed with heparinized saline, and repositioned across the aortic valve in the transplanted heart. It was then used for temporary mechanical support during and after the kidney transplant. Post-operative RRT, vascular complications, strokes, and hemolysis were examined.

**Results:** All patients were male. In the Impella-explanted group, the patients were aged 44-51 years, dialysis-dependent, and two had ischemic cardiomyopathy while one was a re-transplant with cardiac allograft vasculopathy. Impella bridge duration were 9, 19, and 32 days. They all required RRT post-operatively due to delayed kidney graft function, but none were discharged on dialysis. One patient had brain imaging consistent with stroke but did not have any focal neurologic deficits. In the group where the Impella was continued, the patients were older (ages 60 and 65), not dialysis dependent (eGFR 20 and 30, respectively), and supported for 31 and 35 days with the Impella 5.5 before SHKT. These two patients had immediate production of urine without the need for RRT. The Impellas were both explanted on post-transplant day 4. There were no strokes, vascular complications, or hemolysis post-transplant and they were discharged on post-transplant days 15 and 16, respectively.

**Conclusions:** In patients bridged to SHKT transplant with the Impella 5.5, it is feasible to leave the device in place and may mitigate the risk of delayed graft function in the kidney. In our very limited sample, there were no complications related to leaving the device in place. Further investigation is necessary to study the safety and efficacy of this approach.

Patient	Impella Retained Post-Transplant	Age	Gender	Primary Diagnosis	Pre-Transplant Impella Duration (days)	Preoperative Dialysis	Preoperative eGFR (mL/min/1.73 <sup>2</sup> )
A	Yes	65	M	Amyloid	31	No	20
B	Yes	60	M	Ischemic	35	No	30
C	No	46	M	Idiopathic Dilated	9	Yes	CVVH
D	No	44	M	Ischemic	19	Yes	CVVH
E	No	51	M	Ischemic	32	Yes	CVVH

Post-transplant Length of Stay (days)	Postoperative Dialysis	Peak Creatinine (mg/dL)	Discharge Creatinine (mg/dL)	Stroke	Hemolysis Post-Transplant	Vascular Complications
15	No	2.09	0.88	No	No	No
16	No	2.4	1.05	No	No	No
97	Yes	2.24	1.14	No	No	No
10	Yes	2.14	0.8	No	No	No
16	Yes	2.79	1.17	Yes	No	No

## Factors Associated with Survival after Surgical Resection for Pancreatic Ductal Adenocarcinoma: A Systematic Review

Authors: Muhammad Maisam Ali, MBBS; Kaleem S. Ahmed, MD, MSAI; Clayton T. Marcinak, MD; Noorain Ahmed, MBBS; Haider bin Khalid, MBBS; Kainat Fatima, MBBS; Ajia Syed, MD; Asra Siddiqui, MD; Syed Nabeel Zafar, MD, MPH, FACS

**Introduction:** Pancreatic ductal adenocarcinoma (PDAC) is the third-leading cause of cancer-related deaths in the United States. Only 20% of patients present with resectable disease, while 30% present with borderline resectable or locally advanced PDAC. Surgical resection, combined with systemic therapy, offers the best chance for long-term survival, yet up to 80% of patients experience recurrence within 5 years, and the 5-year survival rate remains at 13%. This systematic review aims to evaluate the literature on survival following surgical resection for PDAC and characterize studied prognostic factors.

**Method:** This review was conducted according to PRISMA guidelines, including studies from January 1990 to January 2023. A comprehensive literature search was performed on PubMed, Embase, Scopus, and CINAHL. Eligible studies included observation, quasi-experimental, qualitative, health surveys, ecological, and basic science studies, randomized control trials (RCTs), and case series with 5 or more patients. Studies reported on factors associated with overall survival following surgical resection for PDAC. Data extraction and synthesis focused on demographics, clinical, genetic, molecular, radiomics, laboratory parameters, tumor characteristics, and treatment. A conceptual framework was developed to map the relationships between the domains and sub-categories across the care continuum.

**Results:** 1253 studies were included, the majority of which were cohort studies (n=1095) and a total of 1,904,583 patients studied across all groups. Adjuvant chemotherapy was identified as a positive predictor of survival in 89 of 373 studies. Neoadjuvant chemotherapy also showed favorable outcomes in 26 studies. Tumor size, number of positive lymph nodes, and margin status were extensively studied, with tumor size negatively impacting survival in 195 cases. Perineural invasion and clinical stage were also critical determinants. CA 19-9 levels were widely investigated, correlating with poorer outcomes in 93 studies. Genetic markers, such as KRAS and SMAD4 mutations, showed mixed prognostic significance. Age and gender were frequently studied, with older age associated with worse survival in 101 instances, while socioeconomic factors like income and hospital type had varying effects. The neutrophil-to-lymphocyte ratio (NLR), a laboratory parameter, was associated with negative outcomes in 17 studies. Radiology parameters such as SUVpeak and peripancreatic invasion were investigated, with metabolic activity frequently linked to poorer prognosis.

**Conclusions:** This review highlights the need for reliable prognostication in PDAC to improve patient management and inform clinical trials. The proposed framework facilitates a holistic understanding of PDAC prognosis, in an effort to personalize treatment strategies and refine clinical trial design.



## Predicting Real-world Overall Survival for Post-Operative Pancreatic Ductal Adenocarcinoma: An ASCO CancerLinQ Discovery Analysis

Authors: Kaleem S. Ahmed, MD, MSAI; Sheriff M. Issaka, BS; Benjamin Cher, MD; Clayton T. Marcinak, MD; Syed Nabeel Zafar, MD, MPH

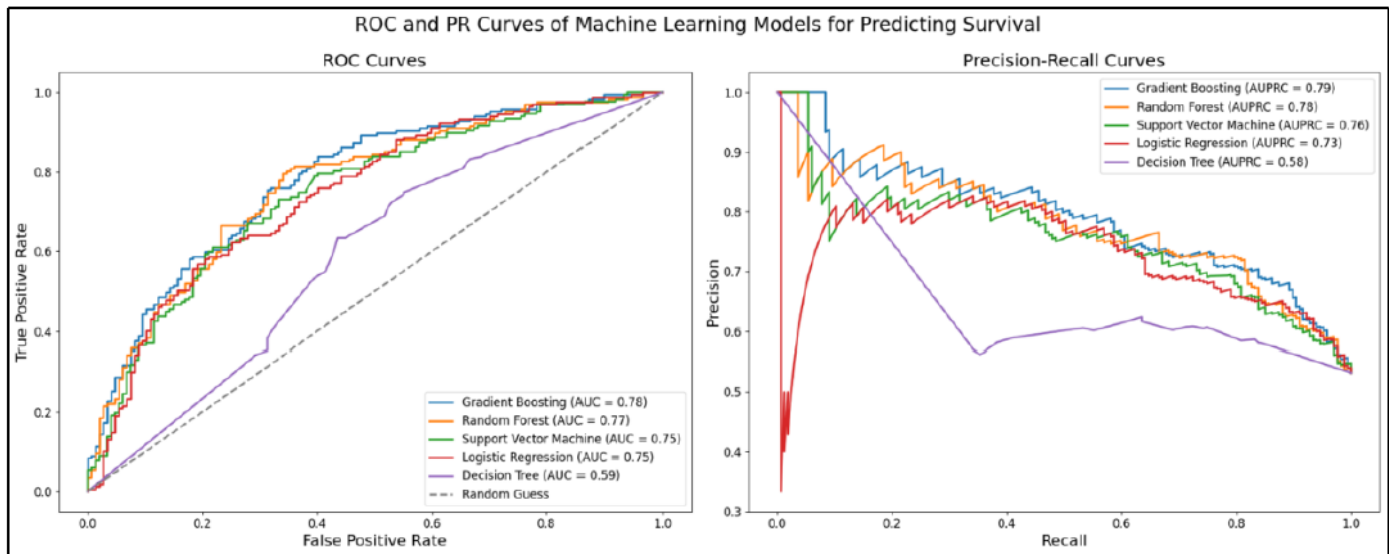
**Introduction:** Pancreatic ductal adenocarcinoma (PDAC) is the second leading cause of cancer-related deaths in the US. There is a need to improve risk-stratification of patients to facilitate treatment decisions. Novel datasets such as the American Society of Clinical Oncology (ASCO)'s CancerLinQ Discovery (CLQD) combined with machine learning (ML) methods provide an opportunity to generate new insights from "real-world data" (RWD) to study patient outcomes. The objective of this study was to develop an ML model using RWD to predict 1-year survival (1YS) for patients undergoing pancreatectomy for PDAC.

**Method:** Using the CLQD database, we identified patients diagnosed with PDAC who had undergone surgical resection between July 1998 and May 2021. Patients with complete data on procedure and tumor characteristics were included. Patients lost to follow-up within 12 months of surgery were excluded. We developed and compared five machine learning models: Gradient Boosting (GB), Random Forest (RF), Support Vector Machine (SVM), Logistic Regression (LR), and Decision Tree (DT). We employed a stratified data split of 80% training and 20% testing to ensure representative sampling across outcome classes. Model performance was assessed using multiple metrics, including Area Under the Receiver Operating Characteristic curve (AUROC), Area Under the Precision-Recall Curve (AUPRC), Positive Predictive Value (PPV), Negative Predictive Value (NPV), sensitivity, specificity, precision, recall, and F1 score. To interpret the models and identify the most significant predictors, we utilized SHAP (SHapley Additive exPlanations) values.

**Results:** Of the 1567 patients analyzed, 870 (55.5%) survived at least 1 year post-operatively. The mean age at time of the index surgery was 70.5 (SD 10.0) years, and 43.2% were male. Of the five types of ML models evaluated (Figure 2), tree-based models had the best performance with the GB models having the highest mean discrimination score (best AUC = 0.78, mean AUC = 0.71 [95% CI = 0.66-0.77]) in predicting 1YS (Figure 1). The best-performing GB model also achieved an AUPRC of 0.79, sensitivity of 90% with a corresponding specificity of 44%, PPV of 0.65 and NPV of 0.80.

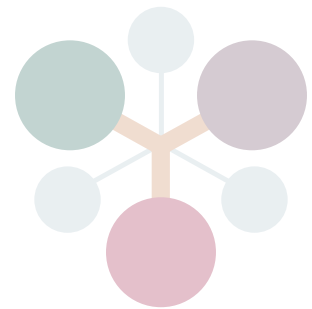
**Conclusions:** Our machine learning models predicted 1-year survival after pancreatectomy for pancreatic ductal adenocarcinoma using a large, real-world, and multicenter dataset with greater accuracy than prior models. Our study demonstrates both the value of, and analytic challenges with, real-world multicenter EHR based datasets. Our findings are useful for pre-operative counseling, and we highlight an important opportunity for improvement in patient selection for surgery because post-resection remains low.

**Figure: Area Under The Receiver Operator Curves (AUROC) and Area Under The Precision-Recall Curves (AUPRC) Showing Model Performance**



The plot displays the AUROC and AUPRC curves for five machine learning models: Gradient Boosting, Random Forest, Support Vector Machine, Logistic Regression, and Decision Tree. The AUROC curves show each model's ability to distinguish between positive and negative classes, plotting True Positive Rate against False Positive Rate, with higher curves indicating better performance. The AUPRC curves illustrate the trade-off between Precision and Recall, with higher curves reflecting improved precision and recall balance. Each model's performance is assessed across these metrics to facilitate comparison and highlight strengths in class separation and prediction accuracy.

# Education Research Abstracts



## The Changing Landscape of American Craniofacial Fellowships

Authors: M. Kristine Carbullido, MD, MAS, Caroline Bay, BS, Gina Krause, BS, Aidan O'Shea, ScB, Jasmine Craig, MD, MPH, Jessica Blum, MD, MS, Catharine B. Garland, MD, Daniel Cho, MD, PhD

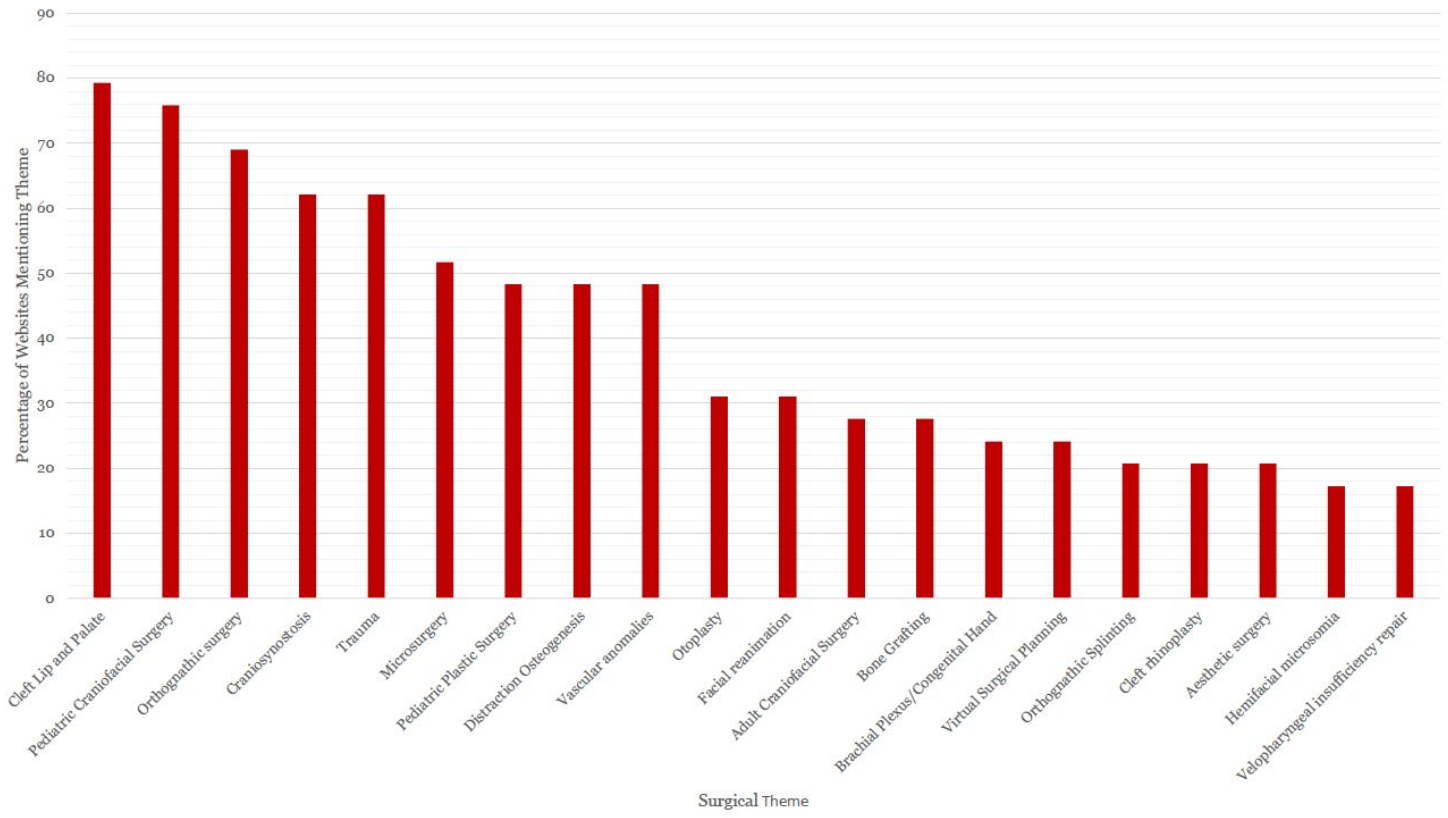
**Introduction:** Craniofacial surgery specializes in treatment of the craniomaxillofacial skeleton and soft tissues. Historically, fellowship programs in craniofacial surgery have most often focused on the treatment of pediatric congenital anomalies, as well as trauma and treatment of secondary deformities. However, current graduates of craniofacial fellowships have highly variable practices, with a recent study reporting a majority of respondents have practices which include craniofacial trauma reconstruction (92%), aesthetic surgery (61.5%), microsurgery (57.7%), and cleft lip and palate repair (53.8%). Less than 50% of recent graduates have practices which include craniosynostosis, microtia, and orthognathic surgery. Applicants to craniofacial fellowships often research programs through fellowship websites. They come from different training backgrounds and may have different goals following the completion of their training. The purpose of this study is to evaluate the types of patients and procedures advertised in craniofacial fellowship websites.

**Method:** In November of 2023 the American Society of Craniofacial Surgeons' Fellowship (ASCFS) Directory was used to identify officially endorsed craniofacial fellowships in the United States of America. Each website was evaluated for medical conditions and surgical procedures that trainees would be exposed to during fellowship training.

**Results:** A total of 32 ASCFS endorsed fellowships were identified. Twenty-nine programs had a website available, of which, four did not list any surgical procedures that their fellows are exposed to during training. In the remaining 25 fellowships, 43 themes were elucidated. The top 10 themes include cleft lip and palate (79.3%), pediatric craniofacial surgery (75.8%), orthognathic surgery (69.0%), craniosynostosis (62.1%), trauma (62.1%), microsurgery (51.7%), pediatric plastic surgery (48.3%), distraction osteogenesis (48.3%), vascular anomalies (48.3%), and otoplasty (31.0%). Gender surgery (3.4%), non-cleft rhinoplasty (3.4%), and adolescent breast (6.7%) are amongst the least reported procedures. Exposure to aesthetic surgery in craniofacial fellowships is 20.7%.

**Conclusions:** There is a discrepancy between the training advertised on ASCFS endorsed program websites and what recent craniofacial fellowship graduates report practicing. Increasing exposure to non-pediatric craniofacial surgery may better prepare graduates to an evolving landscape of craniofacial surgery.

Top 20 Themes in Craniofacial Fellowship Websites in Percentage of all Fellowships



## Are Work Hours Actually Linked to Burnout in Residents?

Authors: Sydney Tan, MD, Hana Siddiqui, BA, Bridget Paur, BA, Kaitlin Tetreault, MB, Guanhua Chen, PhD, Dawn Effenbein, MD, MPH, Vincent Minichiello, MD, Bruce Barrett, MD, PhD, Richard Davidson, PhD, Simon B. Goldberg, PhD

**Introduction:** Burnout is prevalent among residents, especially in frontline specialties. Identifying factors that contribute to or mitigate burnout is crucial for reducing burnout. The impact of work hours on burnout and well-being remains unclear, particularly post-pandemic, with no nationwide studies across specialties. We aimed to assess the relationship between work hours and burnout among residents in high-burnout specialties, and moderators of that relationship. We hypothesized that longer work hours would be associated with higher stress and burnout, and that higher levels of meaning and purpose would moderate the relationship between work hours and burnout.

**Method:** A nationwide cross-sectional survey was conducted as part of a randomized clinical trial evaluating a mental skills training intervention among residents in high-burnout specialties (surgery, obstetrics and gynecology, family medicine, internal medicine, and emergency medicine). The survey assessed burnout and well-being outcomes. Multiple regression models examined the associations between work hours, burnout, and well-being, controlling for demographic variables, with model selection based on the Akaike information criterion (AIC).

**Results:** A total of 544 residents responded, with 241 (44%) in a surgical specialty, 357 (66%) women, and 356 (65%) White representing 40 states. Mean levels of stress (16.9, SD 6.8), burnout in the subscales of depersonalization (6.6, SD 4.4), and emotional exhaustion (10.9, SD 4.3) were moderate-high range. Longer work hours in the last week was associated with higher perceived stress when controlling for specialty, gender, race, post-graduate level, relationship status, and geographic location ( $p < 0.05$ ). However, there was no association between average work hours and burnout in depersonalization and emotional exhaustion subscales. Furthermore, longer average work hours were associated with less burnout in the personal accomplishment scale ( $p < 0.01$ ). Mindfulness was the only study variable that significantly moderated the relationship between work hours and burnout, such that longer hours worked with increased mindfulness was associated with decreased burnout ( $p < 0.01$ ).

**Conclusions:** This study reveals that longer work hours were associated with reduced burnout in personal accomplishment, indicating that work hours alone do not explain burnout levels. These results highlight the potentially complex drivers of burnout and well-being and challenge the notion that restriction of work hours alone is a solution to burnout in residents. Future interventions could address factors such as mindfulness to better support resident well-being. Limitations include the self-report bias and the selection bias of the study population, which may affect generalizability.

## Effect of High Fidelity Emergency ICU Re-Sternotomy Simulation at a Low Volume Cardiac Center

Authors: Timothy Guenther, MD, Khloe Imig, RN, Darcy Christian, APNP, James Maloney, MD, Andreas de Biasi, MD

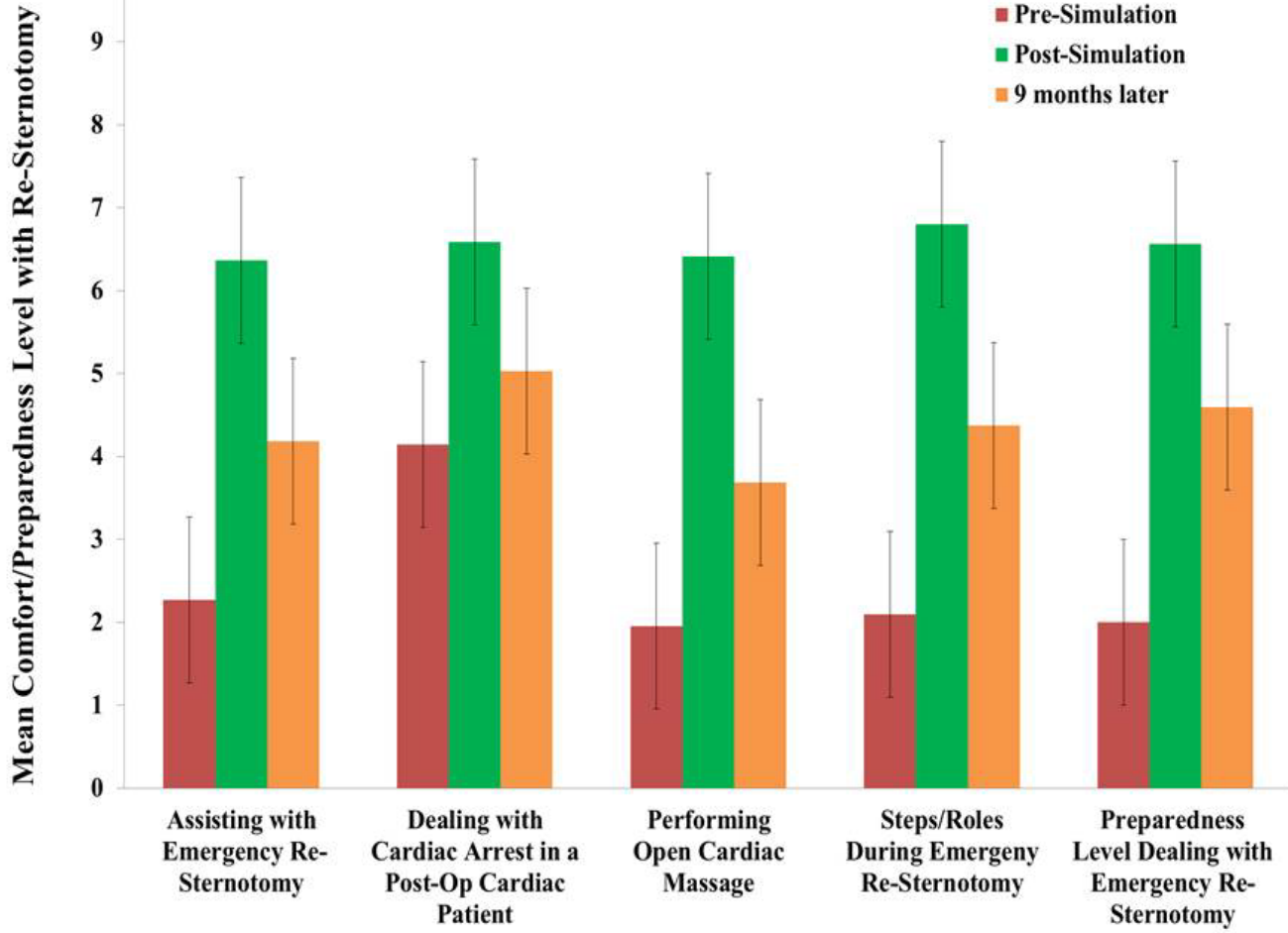
**Introduction:** Emergency re-sternotomy in a post-operative cardiac surgery patient is a rare, potentially lifesaving intervention that requires training and practice to improve the chances of a successful outcome. Although formal courses for re-sternotomy education exist (Cardiac Surgery Advanced Life Support Course), these can be associated with cost and difficulties with time away from patient care. We sought to develop an inexpensive, practical, yet effective way to improve knowledge and comfort regarding re-sternotomy at our low volume cardiac center.

**Method:** Re-sternotomy training sessions were performed with groups of 3-5 ICU RNs. These sessions included: 1) pre-simulation questionnaire assessing baseline knowledge and comfort with re-sternotomy 2) baseline hands on mannequin based simulation 3) debrief and educational session 4) repeat hands on simulation and 5) final questionnaire reassessing knowledge and comfort with re-sternotomy. During each initial and repeat simulation, times were recorded from the decision to perform re-sternotomy and the retractor being placed into the mannequin sternum. Retention was then assessed 9 months later.

**Results:** The re-sternotomy training simulation sessions took place on 12 occasions with a total of 41 RN participants. The average improvement in knowledge of re-sternotomy was 24.6% (p value < 0.001). Improvements were observed in all five areas of comfort related to re-sternotomy assessed (Figure 1, all areas p value < 0.001). Average time between decision to perform re-sternotomy and placement of retractor was 556 minutes for the baseline simulation and 411 minutes for the repeat simulation (p value < 0.001). Seventy six percent of nurses (31/41) participated in the repeat simulation 9 months later. The mean score on the 9 month follow up knowledge assessment was 89.7% (median 90.0%, SD 9.7). When compared to the post-simulation knowledge assessment 9 months prior, a p value of 0.057 was observed. Decreases were observed in all 5 areas of subjective self-assessment related to re-sternotomy that were assessed when compared to the post-simulation assessment 9 months prior. The mean time between the decision to perform re-sternotomy and retractor placement was 438 seconds compared to 411 seconds during the repeated simulation 9 months prior (p value 0.016)

**Conclusions:** This simple high fidelity training simulation led to improvements in knowledge, comfort, and time efficiencies related to emergency ICU re-sternotomy. Mannequin based re-sternotomy training simulation serves as an important role in team education and maintenance of skills, especially at low volume centers where this emergency procedure occurs infrequently.

## Comfort Level with Aspects of Re-Sternotomy





## Mapping Diversity, Equity, and Inclusion in Academic Plastic Surgery: A Scoping Review of Current Literature

Authors: Emily E. Zona, B.S., Manasa H. Kalluri, B.S., Rachel M. Smith, MD, Jacqueline S. Israel, MD

**Introduction:** In this scoping review, the authors critically examine current publications regarding diversity, equity, and inclusion (DEI) and the plastic surgery pipeline (medical students, trainees, and faculty) using the Kilbourne framework for advancing disparities research. Despite interest in improving representation of diverse populations among plastic surgery trainees, faculty, and leaders, the problem of homogeneity persists. Using the Kilbourne framework, an epidemiologically-based research roadmap for detecting, understanding, and reducing disparities, we categorized current publications according to each phase to better understand the current landscape of DEI research specific to workforce diversity and identify where future efforts should be directed to potentiate change.

**Method:** We queried the PubMed and Embase electronic databases using relevant keywords (e.g., “plastic surgery” AND “diversity” OR “disparities”) on September 16, 2024. Our initial search identified 3,198 studies. Of these, 134 English-language, US-based articles were included. A qualitative thematic analysis was conducted to classify articles according to the Kilbourne framework (detecting, understanding, reducing), and to identify recurring themes related to DEI. Quantitative analysis included counts and percentages.

**Results:** Of the 134 articles included in the review, 60 (44.8%) were classified as detecting, 36 (26.9%) as understanding, and 12 (9.0%) as reducing, according to the Kilbourne framework. The remaining 26 articles (19.4%) were categorized as other. Publication years also varied: only 14 articles (10.4%) were published between 2007 and 2019, while the majority, 120 articles (89.6%), were published from 2020 to 2024. Additionally, 92 articles (68.7%) were retrospective or cross-sectional studies, with the rest being mostly editorials or perspective articles. Regarding specific DEI topics, 62 articles (46.3%) discussed race/ethnicity, 83 (61.9%) examined gender, 5 (3.7%) focused on LGBTQ issues, 6 (4.5%) addressed socioeconomic status, and 15 (11.2%) were nonspecific.

**Conclusions:** The majority of publications reviewed remain in the detecting phase with very few moving forward to the intervention phase and even less to the reducing phase. Future work, funding, resources, and publishing priority should be directed towards studies that seek to understand determinants of plastic surgery pipeline disparities and those that intervene on them.

## Comparison of the Quality of Feedback from Faculty and Self-Reflections from Residents on General Surgery Entrustable Professional Activities

Authors: P. Prabaharasundar, A. Krumm PhD, N. Ly MD, F. Ocoko BS, S. Jung PhD

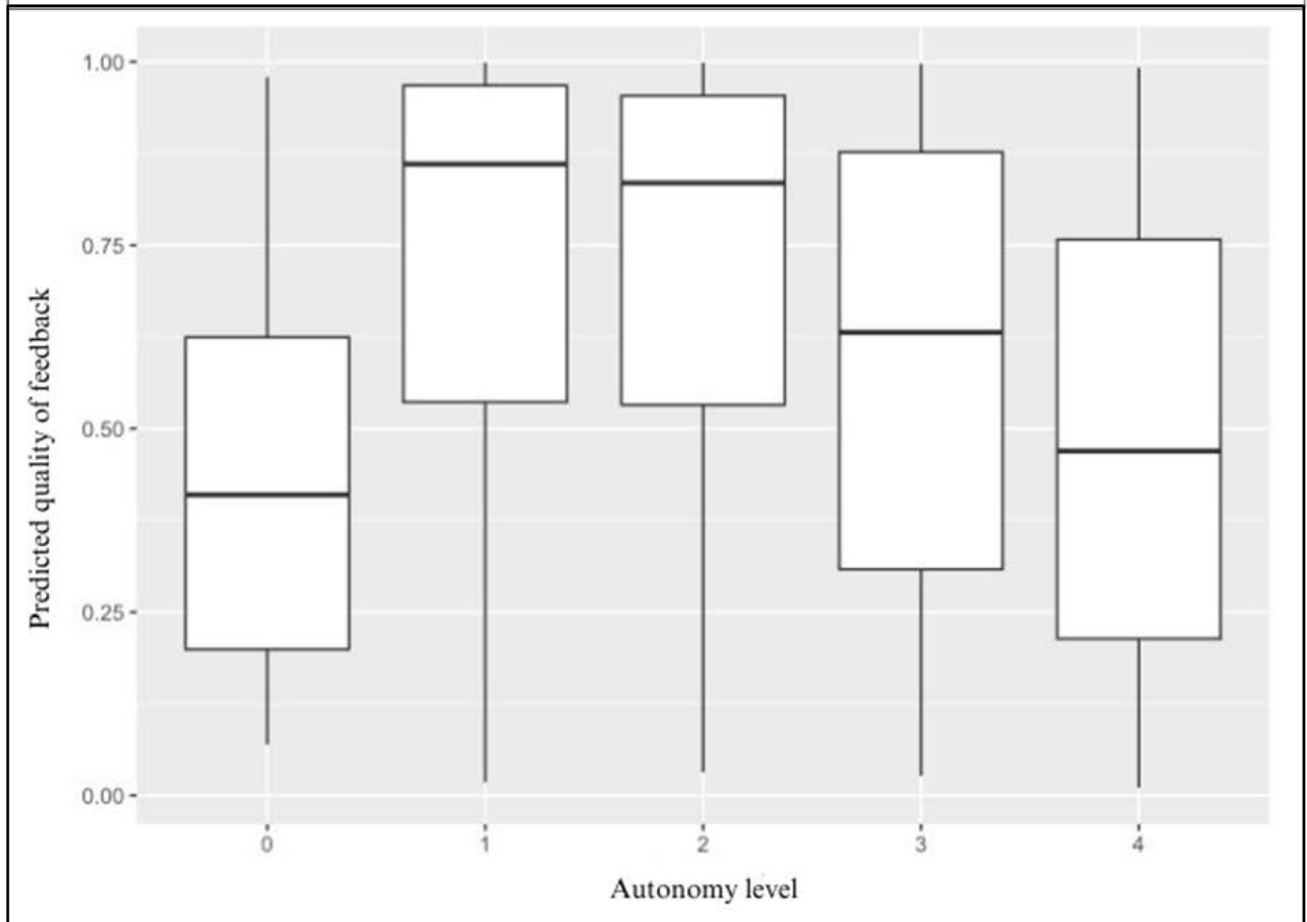
**Introduction:** Quality feedback is essential for the training and development of excellent surgeons. Coupled with this, medical education is experiencing a paradigm shift towards competency-based training. The successful implementation of the Entrustable Professional Activities (EPAs) assessment framework into many surgical training residency and fellowship programs allows for a broad focus on utilizing not only quality feedback but also trainees' self-reflections as tools to ensure readiness for autonomous practice. This study comprehensively investigates the quality of EPA feedback and self-reflections for General Surgery (GS) EPAs implemented within a GS residency program.

**Method:** A mobile application, SEPA, designed by a Midwestern academic department of surgery was used by the residents and faculty members from the department at a single tertiary care center. Entrustment levels and free text feedback were collected from July 2018 to November 2021 from four GS EPAs, right lower quadrant pain, gallbladder disease, inguinal hernia repair, and care for a traumatically injured patient. We applied a previously developed natural language processing (NLP) model that was validated using SIMPL OR narrative feedback to generate probabilities that an instance of feedback in SEPA could be classified as "high quality." We then analyzed predicted probabilities by different features of an EPA: rater, procedure, perioperative stage, and autonomy level earned by trainee.

**Results:** The quality of feedback and self-reflection did not vary between faculty and resident ratings. However, feedback quality did differ based on perioperative stage for which feedback was given and the level of autonomy at which the resident was assessed. Intraoperative feedback was of higher quality than pre- and post-operative feedback. Feedback based on autonomy level showed a rainbow shaped curve as shown in Figure 1, with the lowest and highest autonomy levels receiving the lowest quality feedback.

**Conclusions:** Residents' self-reflections and faculty's feedback on behaviors related to EPAs were similar in quality. To improve the equal and consistent provision of quality feedback to resident trainees, this study's results suggest that focus must be placed on how to improve the quality of pre- and post-operative feedback and feedback given to trainees assessed at the lowest and highest levels of autonomy.

Figure 1: Relationship between trainee autonomy (0=observation only to 4=teaching others) and quality of feedback given by faculty



## Detecting Bias in Plastic Surgery Residency Application Letters of Recommendation using Natural Language Processing

Authors: Nagar T, Jung S, Wirth P, Schappe A, Salyapongse AN

**Introduction:** The shift to pass/fail grading by many medical schools and the USMLE Step 1 exam has reduced availability of measures often used for evaluating residency applicants. Thus, the weight of subjective letters of recommendation (LORs) has increased multifold. While all measures are susceptible to bias, LORs may be especially prone to implicit bias. Fortunately, advances in Natural Language Processing allow for the systematic investigation of potential bias with the goal of making recommendations to mitigate its impact. This study investigates implicit biases in LoRs in plastic surgery residency applications using linguistic analysis and statistical methods.

**Method:** The dataset comprised 5,679 plastic surgery residency applications submitted via the ERAS system to a midwestern academic medical center over a six-year period, 2017-2022. A series of Python scripts were employed for anonymization of LORs, utilizing Part-of-Speech tagging, Named Entity Recognition software, and applicant-specific data to ensure the removal of all personal identifiers. The research team iterated on a 400-word dictionary containing descriptive attributes of applicants, such as academic performance, personality traits, and professional skills. These words were organized into 24 categories via discussion and team consensus. These categories were then compared based on applicant identified gender and race or ethnicity using a two-way MANOVA.

**Results:** There was a statistically significant interaction between gender and race/ethnicity on combined dependent variables,  $F(96,22596)=1.453$ ,  $p=.003$ , Pillai's Trace=.025. Given the significant multivariate interaction, significance tests for individual dependent variables were examined. There were significant univariate interactions for different categories. Men of multiple races were more likely to have activity comments,  $F(4,5669)=2.819$ ,  $p<.001$ , or were more likely described as Inventive or Curious,  $F(4,5669)=.495$ ,  $p=.034$ . Women of multiple races were more often described Sensitive or Nervous,  $F(4,5669)=.005$ ,  $p<.001$ , with descriptors such as Solitary or Reserved,  $F(4,5669)=.092$ ,  $p=.008$ , used more often for Asian and Black or African American women applicants. There was a significant main effect of gender for Gendered Terms,  $F(1,5669)=.038$ ,  $p<.001$ , with gendered language more often used for men, and Technical Skill,  $F(1,5669)=.007$ ,  $p=.002$ , with comments more often on technical skills of women. There were no significant main effects for race/ethnicity.

**Conclusions:** Significant differences were detected based on combinations of gender and race or ethnicity, as well as gender alone highlight the need to consider intersectionality of identities when examining for bias. These differences are important to consider and further explore, as they may impact evaluations of applicants' qualifications for plastic surgery residency programs.

# A Survey-Based Assessment of Attending Surgeons' Experiences with Intervening Against Discrimination Toward Surgical Trainees

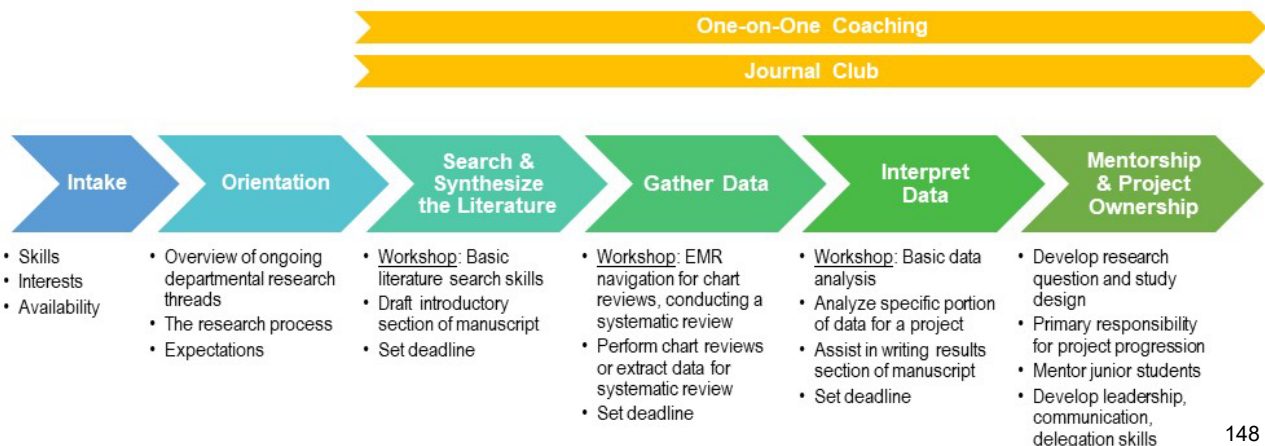
Authors: Jung S, Iding N, Prabahasundar P, Garcia J, Cooper A, Sanchez SE, Dorsey C, Rogers S, Lawson E, Cannon S.

**Introduction:** Discriminatory behaviors against surgical trainees have been documented in surgical learning environments. These experiences have major impacts on career satisfaction and progression, including attrition from training, which impacts patient care. Teaching support for attending surgeons typically focuses on areas such as clinical skill development, but rarely focuses on ways to be allies to trainees. Our objective was to explore attendings' experiences of witnessing discrimination, knowledge of strategies for intervening when witnessing discrimination, intervention behaviors, and facilitators and barriers to such intervention.

**Method:** A survey was developed to gather information on whether respondents have witnessed discrimination against surgical trainees, types of intervention behaviors, reasons for their decisions to intervene or not, responses to discriminatory scenarios, preferences for training in intervention strategies, experiences with training, and demographics. Pilot testing and cognitive interviews were conducted. Survey completion took approximately 15 minutes. The survey was distributed via email to attending surgeons across four institutions for a total of 355 survey invitations.

**Results:** We received 102 responses (29% response rate). Respondents witnessed discriminatory behaviors against trainees primarily from patients, but also from medical staff and other attendings (Figure 1). Most respondents reported that they were only somewhat or a little knowledgeable about strategies for intervening when discrimination is witnessed (66.7%) and only somewhat or a little confident in their ability to enact these strategies (66.7%). Reasons for not intervening included fears of intervening incorrectly or being viewed negatively (12%), increasing harm in the situation (8%), lack of support from leadership or the institution (7%), and fear of retaliation (6%). Only 30% of respondents reported engaging in education programs that explicitly taught intervention strategies, and participants expressed interest in interactive programs that cover multiple scenarios and contexts.

**Conclusions:** Education on intervening when witnessing discrimination against trainees is needed for attending surgeons, specifically in confident use of effective intervention behaviors. Based on these results, we will develop and pilot an upstander education program specifically adapted for the surgical environment to support knowledge and application of intervention strategies through an interactive program with a focus on enhancing self-efficacy and addressing fears that act as barriers to intervening.



## AI or Not? The Challenge of Discerning AI Contributions in Academic Medical Writing

Authors: Keenan S. Fine, MS; Emily E. Zona, BS; Aidan W. O'Shea, ScB; Ellen C. Shaffrey, MD; Samuel O. Poore, MD, PhD

**Introduction:** The increasing use of artificial intelligence (AI) in academic writing has raised concerns about the integrity of scientific manuscripts. This study aims to evaluate the ability of medical professionals and online AI-detector tools to detect AI involvement in manuscript passages.

**Method:** This study evaluated eight manuscript passages across four topics, with four of the passages on plastic surgery topics. The passages were either entirely human-written, human-written and AI-edited, or fully AI-generated. Ten raters, comprising medical students, residents, and attending physicians, were asked to classify each passage based on its origin (human-written, AI-edited, or AI-generated). Fleiss' kappa was used to measure interrater reliability among the reviewers. Additionally, the passages were analyzed using three different online AI detection tools to compare the accuracy of human assessments with automated detection. Intraclass correlation coefficients (ICC) were calculated to assess the agreement among the detection tools; these tools identify AI-generated content within the passages in terms of percentage generated by AI.

**Results:** Human raters accurately predicted the origin of the passages only 25% of the time, with a mean of  $2 \pm 1.63$  passages correctly identified. There was no difference in accuracy between plastic surgery and non-plastic surgery topics. For the four AI-generated passages, raters correctly identified them as AI-generated only 27.5% of the time, while entirely human-written passages were correctly identified 20% of the time. Interrater reliability among the raters, calculated using Fleiss's Kappa, was 0.304, indicating "fair agreement." AI detection tools incorrectly classified human-written content as more than 50% AI-generated in two-thirds of ratings. The ICC across the three online AI detection tools was 0.097, indicating "poor agreement" in determining the proportion of AI-generated content. The ICC was -0.162 for AI-generated passages and -0.370 for human-written and AI-edited passages.

**Conclusions:** The findings of this study highlight the significant challenges faced by both medical professionals and AI detection tools in accurately identifying AI involvement in manuscript passages. Human raters demonstrated poor accuracy, correctly identifying only 25% of the passages, with fair interrater agreement. Similarly, AI detection tools often misclassified human-written content as AI-generated, with poor agreement across the tools. These results suggest that neither human raters nor current AI detection tools can reliably distinguish between human and AI-generated content, highlighting the need for improved methods to ensure the integrity of scientific writing.

## Continued Design and Development of a Novel 3D Printed Microsurgery Microscope

Authors: Elizabeth P Wu, BS; Sahand Eftekari, MD; Weifeng Zeng, MD; Ellen Shaffrey, MD, Aaron Dingle, PhD; Samuel Poore, MD PhD

**Introduction:** Microsurgery is considered the top innovation in plastic surgery in the last 100 years, allowing for reconstruction of multiple body parts including limbs, breast and head and neck. However, the cost of training and equipment presents a barrier to adoption, particularly in low-resource countries. Our lab has invented a low-cost stereovision microscope (WiscVision™) to bridge the gap. These microscopes have been used to teach the first microsurgery courses in Vietnam and Rwanda. The objective of this research is to use engineering principles to improve microscope focus and provide modular dual head functionality, allowing for a surgical assistant.

**Method:** The novel microscopes were designed in AutoCAD Fusion and 3D printed in lab with polylactic acid on a Bambu X1C printer. Five mirror types under \$10 were tested for focus and clarity. A laser cut device was invented to determine the optimal mirror angle and optimal microscope angle. A dual head system was engineered to be affixed with a magnetic connection.

**Results:** Second surface mirrors were determined to have the best optical quality (0mm deviation; focus achieved). The optimal mirror angle was determined to be 22 degrees. Optimal angle for dual head functionality was 7.3 degrees from vertical. Optimal focal length for dual head functionality was 339 mm. This data was used to produce a complete dual head microscope while retaining the modular characteristics allowing for the microscope to be used by a single user. These newly designed microscopes were utilized by OhanaOne for microsurgical education in Mozambique. They were also used to teach microsurgery during the UW Annual Microsurgery Training Course.

**Conclusions:** In this project, a mirror-based WiscVision™ microscope was optimized for use in global microsurgery education settings. These microscopes will be used in upcoming microsurgery courses in Vietnam and Rwanda. The implication of these microscopes is improved access to microsurgical reconstructive care worldwide.



## **Educational interventions to enhance medical student knowledge and interest in plastic surgery: A scoping review**

Authors: Aidan O'Shea, ScB, Keenan Fine, MS, Emily Zona, BS, Samuel Poore, MD, PhD

**Introduction:** It has been well-documented that medical students harbor significant misperceptions of the scope and nature of plastic surgery. Despite numerous concerns over the consequences of these misperceptions for the diversity of the plastic surgery pipeline and the general plastic surgery knowledge of future physicians, few studies address interventions to reshape these perceptions. This scoping review aims to synthesize the current literature describing educational interventions designed to enhance medical students' knowledge of, and potentially interest in, plastic surgery.

**Method:** A comprehensive literature search was conducted using terms such as "medical student," "medical school," and "plastic surgery." Articles were screened for relevance, and those meeting inclusion criteria were categorized by type of educational offering, including one-time events, simulation opportunities, online modules, and formal curricular additions.

**Results:** The search identified 1,601 articles, of which 33 met the inclusion criteria. Nine articles detailed one-time events, such as career nights, mentorship events, and skill-based workshops designed to introduce students to plastic surgery's scope. Ten articles focused on simulation-based learning, such as emergency burn simulations, computer-assisted skin flap teaching, and 3D-printed models for craniosynostosis repair. Six articles described online offerings, including a virtual plastic and reconstructive surgery curriculum, a case-based learning series, and a collection of intraoperative videos. Five studies described formal medical school curricular additions, such as a clinically applied anatomy course taught by plastic surgeons and a core plastic surgery curriculum for fourth-year students. Additional interventions included a shadowing program and a student-run free clinic, aimed at offering direct clinical exposure. Importantly, among studies reporting pre- and post-intervention data on medical students' knowledge and interest, interventions reliably increased students' understanding of plastic surgery but less consistently increased their interest in pursuing plastic surgery as a career.

**Conclusions:** This scoping review highlights diverse educational approaches to introducing the specialty of plastic surgery to medical students. While single-day events, simulations, and online modules can be effective and may be more easily implemented, formal curricular integration may provide the most lasting impact. These findings underscore the need to address two essential goals: (1) fostering a foundational understanding of plastic surgery among all medical students, equipping future physicians with a basic competence in the field, and (2) inspiring select students to consider plastic surgery as a career path. More longitudinal studies are needed to assess these interventions' impacts on long-term knowledge retention and to identify strategies that may consistently increase interest in pursuing plastic surgery.



# Empowering Future Surgeon-Scientists: A Structured Approach to Involving Medical Students in Research Projects

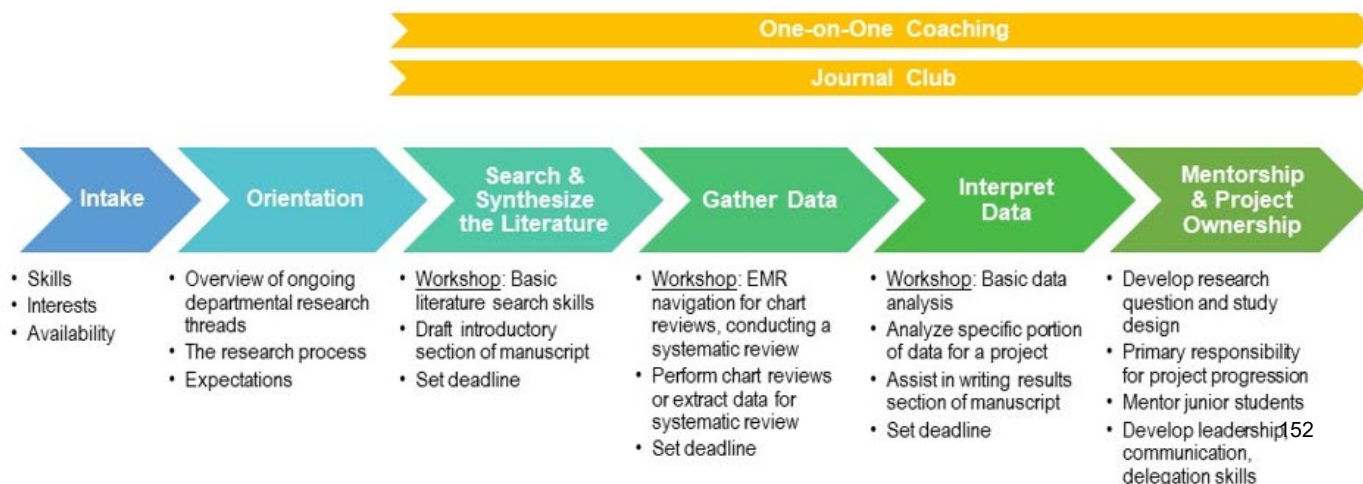
Authors: Emily E. Zona BS, Aidan W. O'Shea ScB, Keenan S. Fine MS, Armin Edalatpour, MD, Jacqueline S. Israel, MD, Samuel O. Poore MD PhD

**Introduction:** The increasingly competitive nature of the plastic surgery residency match process has raised the bar for research productivity among medical students. As a result, many aspiring plastic surgeons choose to take one or more research years to bolster their application, lengthening their medical education and incurring additional expenses in the process. For many, the high barrier of entry into plastic surgery research—owing to the specialized nature of the field and limited research opportunities—makes it difficult for them to gain experience earlier on in medical school. To address these challenges, we developed a structured research curriculum that can be implemented by plastic surgery research fellows, residents, and faculty to lower this barrier by progressively involving junior medical students in research projects and cultivating their skills.

**Method:** The curriculum serves as a blueprint for research fellows, residents, and faculty to engage medical students in ways that maximize their contributions, prevent delays in research progress, and promote successful collaborative partnerships [Fig. 1]. The curriculum is organized into several key steps and built around a graduated model. First, an intake assessment allows students to provide information on their previous research experience and skills, specific interests in plastic surgery, and available time commitment. Next, students progress through a series of workshops and project-based learning experiences. Following these workshops, students engage in essential research activities such as data collection, data analysis, and manuscript revision. In the later stages, students undertake independent projects, applying the skills they have acquired throughout the curriculum. Each phase builds on the previous one, emphasizing increasing responsibilities and a strong focus on coaching and mentorship.

**Results:** Since its implementation, 12 first- and second-year medical students are participating in the program. Of the 16 trainees who completed the curriculum, 2 (12.5%) are early-career faculty, 10 (62.5%) are residents/fellows, and 4 (25%) are fourth-year medical students. The average number of publications is 40 for faculty, 17 for residents/fellows, and 8 for medical students. Key insights from initial implementation of the curriculum include the importance of clear communication, effective task management, assessing time commitments, providing necessary resources and training, setting achievable goals and deadlines, and cultivating resilience.

**Conclusions:** Our initiative aims to establish a standardized curriculum that provides a scaffolded approach to research participation. By cultivating a supportive and structured research environment, we can better prepare the next generation of plastic surgeons to contribute meaningfully to the field.



## From Learner to Leader: The Impact of Training Novice Microsurgery Educators

Authors: Emily E. Zona; James E. King; Maci Fulton; Nnadozie Uchegbu; Esther Wang; Weifeng Zeng, MD; Samuel Poore, MD, PhD; Aaron Dingle, PhD

**Introduction:** Microsurgery, a complex subspecialty of plastic and reconstructive surgery, often has limited exposure prior to residency, and a standardized curriculum is lacking. This study aims to evaluate the effectiveness of training novice microsurgery educators to deliver a standardized microsurgery curriculum.

**Method:** The study comprised three stages. In the first stage, an undergraduate student (MF) with no surgical knowledge underwent a one-on-one microsurgical training course developed by the Microsurgery and Regenerative Medicine (MSRM) Lab (1). Supervised by a microsurgical educator (WZ), the curriculum consisted of six hours of training per week over six weeks. Techniques culminating in end-to-end (ETE) anastomoses, utilizing both the two-stay and back-wall-first methods, were performed on synthetic vessels (1mm, 2mm, and 3mm). MF's skills were evaluated by the supervising educator. In the second stage, a medical student (NU) with no prior surgical experience completed the same training and subsequently taught portions of the curriculum to naive undergraduate students. Their confidence and knowledge were assessed using pre- and post-training surveys. In the third stage, another undergraduate student (EW) repeated the process and taught high school and undergraduate students. Their skills were evaluated using pre- and post-training surveys, including assessments of vessel patency. Currently, we are onboarding another undergraduate student (JK) and validating our microsurgery training curriculum with a larger cohort of undergraduate and medical students through surveys.

**Results:** Results from this multistage research study are as follows: In the first stage, undergraduate student MF achieved a microsurgery skill level equivalent to that of a third-year surgical resident, successfully performing patent anastomoses on synthetic vessels (1mm, 2mm, and 3mm). Her time for tying three knots decreased from 2.53 minutes to 19 seconds, and her time for completing an ETE anastomosis on a 3mm synthetic vessel decreased by 5.13 minutes. In the second stage, students exhibited significantly increased confidence in five microsurgery techniques: identifying microsurgical instruments, handling synthetic vessels, placing stitches on synthetic vessels, tying knots on synthetic vessels, and performing two-stage ETE anastomoses. In the third stage, students reached a skill level comparable to junior residents, demonstrating enhanced confidence and reduced time for ETE anastomoses on 3mm synthetic vessels. Results from the fourth student are currently underway.

**Conclusions:** This study demonstrates that novice educators can effectively learn and subsequently teach a standardized microsurgery curriculum. The insights gained are vital for advancing microsurgical education and improving access to this specialized knowledge for trainees and practicing surgeons.

## **Innovative Solutions in Microsurgery: A Validation Study of the WiscVision™ Microscope for Education and Training**

Authors: Emily E. Zona, B.S., M. Kristine Carbullido, MD, Elizabeth P. Wu, B.S., Sahand Eftekari, MD, Ellen Shaffrey, MD, Weifeng Zeng, MD, Aaron M. Dingle Ph.D., Samuel O. Poore M.D., Ph.D.

**Introduction:** Microsurgery is a critical component of plastic and reconstructive surgery. However, the high costs associated with training and equipment pose significant barriers to its adoption, especially in low- and middle-income countries. To address these challenges, the WiscVision™ microscope was developed by the Microsurgery and Regenerative Medicine Lab within the Division of Plastic Surgery at the University of Wisconsin. This 3D-printed microscope has already been utilized for microsurgery education and training both in the United States and internationally. The primary objective of this study was to validate the use of WiscVision™ microscopes in microsurgery training and education by surveying surgical residents and attending surgeons about their experiences using this tool relative to traditional magnification methods (e.g., surgical loupes, benchtop microscopes).

**Method:** An anonymous survey was administered to otolaryngology and plastic and reconstructive surgery residents, fellows, and attending surgeons following their use of the WiscVision™ microscope to perform at least one end-to-end anastomosis on a blue-blood chicken thigh model in October 2024. The survey collected demographic information (e.g., level of training), microsurgery experience, and user feedback on various aspects such as quality and ease of use.

**Results:** Among the participants (n=26), 10 (38.5%) were attending surgeons, 2 (7.7%) were fellows, and 14 (53.8%) were residents. Of the respondents, 79.2% (19/24) reported that performing the end-to-end anastomosis was either easier or equivalent under the WiscVision™ microscope compared to using surgical loupes. All participants expressed a willingness to use the WiscVision™ microscope for microsurgery teaching and practice, citing its adequate quality and educational value. Additionally, 92.3% (24/26) believed that access to WiscVision™ microscopes would enhance their capacity to teach microsurgery at their institutions, and 96.0% (24/25) agreed it would improve their ability to teach microsurgery in other settings, such as global surgery trips. Comments provided in the survey reflected overwhelmingly positive feedback, with suggestions for enhancements including a height adjustment mechanism for the double-headed microscopes and the addition of a warmer LED light.

**Conclusions:** This validation study of the WiscVision™ microscopes supports the continued development and refinement of the design based on expert and trainee insight. Implementing these improvements will optimize the microscope's utility in both local and global microsurgery education courses, ultimately expanding access to microsurgery training worldwide.

## **Livestreaming Microsurgery: An Avenue to Expand Global Plastic Surgery**

Authors: Weifeng Zeng MD1, Rishi Meredy BS, Sahand C. Eftekari MD, Ellen C. Shaffrey MD1, Katherine D. Reuter Munoz MD1, Aaron M. Dingle PhD1, Samuel O. Poore MD PhD1

**Introduction:** Microsurgery is a highly technical subspecialty within the field of plastic surgery that is often not accessible in many hospital systems. Trainees around the world often have access to microscopes but lack the guidance to complete the complex maneuvers associated with microsurgical operations. Here, we propose a novel method to livestream microsurgical education over popular online platforms in order to lift the current barriers associated with microsurgical education.

**Method:** A three-camera system was developed to provide a complete view of the microsurgical field, instruments, and microsurgeon for livestreaming. These included a camera tethered to a cam link for a direct view of the microsurgical field, a second camera to view the microsurgeon's hands and instruments, and a third camera to view the microsurgeon's face. A microphone was also placed near the microsurgeon to enable clear audio during the operation. Open Broadcasting Software was used to compile this system onto one page to share over any streaming platform.

**Results:** 118 microsurgical livestreams were completed at the University of Wisconsin-Madison over Zoom and Instagram platforms. A total of 400 surgeons and trainees tuned into the livestreams representing 38 countries worldwide.

**Conclusions:** Microsurgery education is a highly complex and specialized field within plastic surgery that is often overlooked due to lack of proper equipment and training opportunities. Here, we propose an accessible and low-cost method to deliver virtual microsurgery education in order to overcome many of the educational barriers associated with this field.

## Preparing the Next Generation of Surgeons: A Tailored Microsurgical Training Curriculum for Undergraduate Students

Authors: Nnadozie Uchegbu, MS, Weifeng Zeng, MD, Andi Donnelly, BS, Samuel O. Poore, MD, Ph.D., Aaron Dingle, Ph.D.

**Introduction:** The demand for effective microsurgery training has grown, given the specialized skills required and the need for interdisciplinary education. In an effort to develop an enhanced mentorship program and to engage undergraduate students in the field of plastic surgery, we designed a hands-on microsurgery course aimed at fostering engagement and inspiration. This study evaluates the adaptation of the course to assess its impact on students' perspectives towards pursuing medicine, specifically in the field of plastic surgery.

**Method:** A 3-hour course integrated didactic lectures, case presentations, and practical sessions using hydrogel microvessels and the Blue Blood Chicken Thigh Model (BBCTM). Pre- and post-course surveys evaluated participants' self-reported comfort and confidence in microsurgical domains, teaching these microsurgical domains, and their interest in medicine and the surgical field.

**Results:** Four undergraduate students attended the course. After the course, participants reported increased comfort and confidence in identifying different types of instruments, handling a synthetic vessel, placing a stitch on a synthetic vessel, tying a knot on a synthetic vessel, and performing two-stage end-to-end (ETE) anastomoses ( $p < 0.05$ ). The participants also had increased confidence in teaching, particularly with teaching types of instruments, how to manipulate a suture needle, how to place a stitch on a synthetic vessel, how to tie a knot on a synthetic vessel, and how to perform a stage two-stage end-to-end (ETE) anastomosis.

**Conclusions:** After training in the brief course, participants significantly increased their confidence in 11 areas of the questionnaire. The course also increased the participants' interest in becoming surgeons, more specifically microsurgeons. Multispecialty microsurgery training is beneficial and underutilized, highlighting the potential for adapting similar courses for undergraduate students interested in plastic and reconstructive surgery. Longitudinal assessment of this small student cohort will shed further light on the long term impact of this course on the pursuit of medicine and plastic surgery.

## **The Fundamentals of Communication in Surgery (FCS): Early Results from a Multisite Study**

Authors: C. Sobol, MD, L. Taylor, MD, K. Hill, MD, C. Morgan, MD, K. Kopecky, MD, E. Rivet, MD, A. Saad, MD, M. Kapadia, MD, A. Newcomb, MD, E. Strong, MD, R. Bynum, MFA, K. Bushaw, MA, ML. Schwarze, MD, A. Shada, MD

**Introduction:** Advanced communication skills are essential to all surgical practices given the need to engage patients and families in decisions about surgery, and help them navigate burdensome treatments and unwanted postoperative events. The FCS is a 5-year curriculum centered on attending to emotion, supporting patients in deliberation, and managing uncertainty. With support from CESERT, the Macy Foundation, and the AAS we commenced a phase II ORBIT model multisite study to test the feasibility, acceptability, and fidelity of FCS delivery to assess scalability and impact on trainee outcomes.

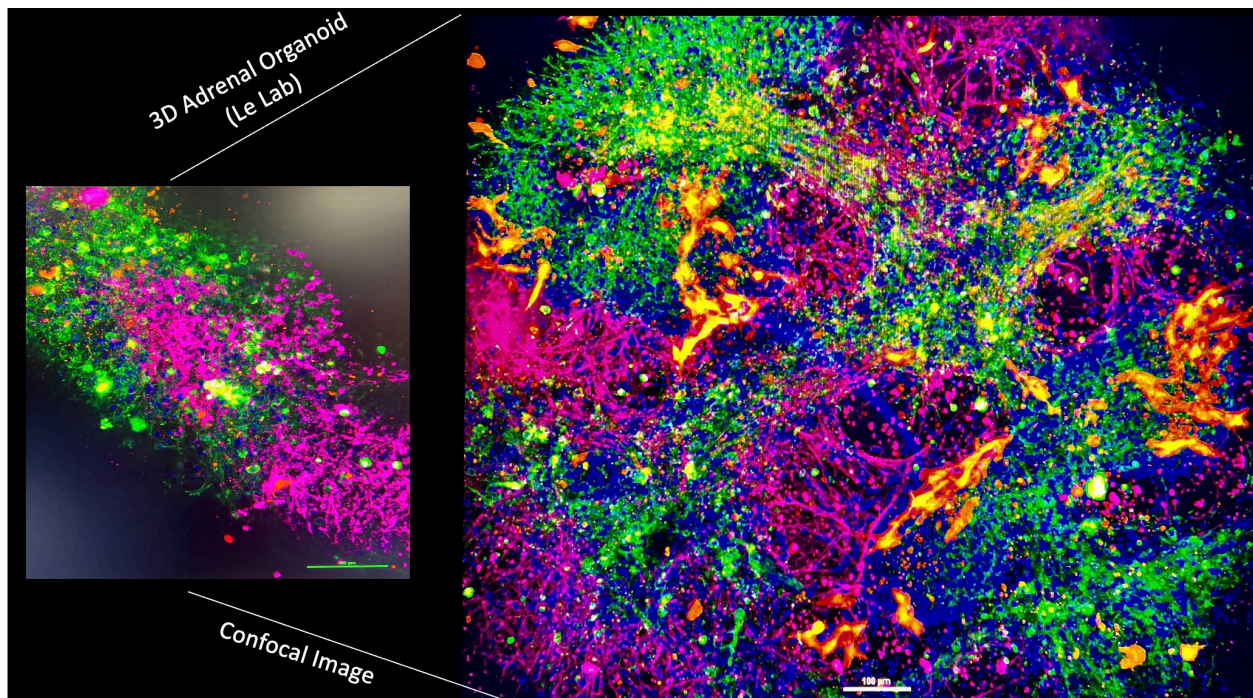
**Method:** The University of Wisconsin IRB declared this study exempt. After mailing physical and electronic materials to 5 pilot sites, including trainer and learner guides, PowerPoint videos, and props for skills activities, we conducted virtual train-the-trainer (TTT) sessions. We anticipate 175 resident learners will participate in academic year 2024-25. Data collection includes attendance, direct observation utilizing the Dane implementation fidelity framework, scoring rubrics, pre-post learner surveys, and stakeholder interviews. We used descriptive statistics and qualitative methods to analyze the data.

**Results:** All 15 trainers completed 4 hours of TTT. To date, 41 residents (93% attendance) have received one 2-hour FCS session. Residents reported the curriculum was worth their time and successfully met stated goals. Residents intended to apply what was learned when talking with patients and families, score mean  $4.08 \pm 0.4$  (max score 5). Trainers believed this was essential training and the curriculum was easy to teach. For example, “[FCS] doesn’t try to do 20 things, it narrows it down to really important basics.” As scored by peers, learners performed 97% of skills on the rubric during role play. The curriculum was delivered with fidelity. Specifically, trainers followed the training guides, participants engaged with intended content, and the FCS imprint was readily apparent. We estimate 134 additional residents will receive FCS this academic year.

**Conclusions:** The FCS curriculum is feasible, acceptable, and can be delivered with fidelity. We will use the data from this study to iteratively revise the curriculum and expand the cohort to 10 study sites in the 2025-26 academic year. We anticipate FCS will ultimately be accessible to all surgical trainees.

# Surgery Science Images





### Advancing Neuroblastoma Research with 3D Adrenal Organoids in Le Lab

**Caption:** This confocal image (make: Nikon) showcases a 3D adrenal organoid, a lab-grown model of human adrenal tissue developed in Le Lab. The organoid is a complex assembly of various cell types, including endothelial cells, pericytes, neural progenitor cells, macrophages, fibroblasts, microglia, and adrenal chromaffin cells, each tagged with specific antibodies to fluoresce in different colors under distinct wavelengths. This multi-color fluorescence allows for a detailed view of the organoid's structure and the interactions between different cell types.

**Interesting fact:** Our 3D adrenal organoid provides a powerful, animal-free model that closely mimics *in vivo* conditions, allowing researchers to study neuroblastoma, a severe pediatric cancer, in an environment that replicates real human tissue. By eliminating the need for animal models, this approach addresses ethical concerns while offering a more accurate platform for observing cancer behavior and testing treatments. This innovative model has the potential to significantly advance neuroblastoma research, accelerating the development of effective, targeted therapies that could ultimately improve outcomes for young patients.

**Credit Line:** Ligi Milesch, PhD, and Hau D. Le, MD, Le Lab, Department of Surgery, SMPH





### **Science as Art: A Blown Glass Anatomical Lung Model**

**Caption:** The image depicts a model made using scientific glassblowing techniques. The left lung has to accommodate the heart by wrapping around it. Because of this, when people aspirate an object, it usually takes the straighter path through the right lung. This model demonstrates this phenomenon when a pebble is dropped into the model trachea. This was made in appreciation for the beauty of the human body, and dedicated to the amazing anatomy professors here at UWSMPH.

**Interesting Fact:** I was taught scientific glassblowing by UW Madison's Tracy Drier of the Chemistry Department!

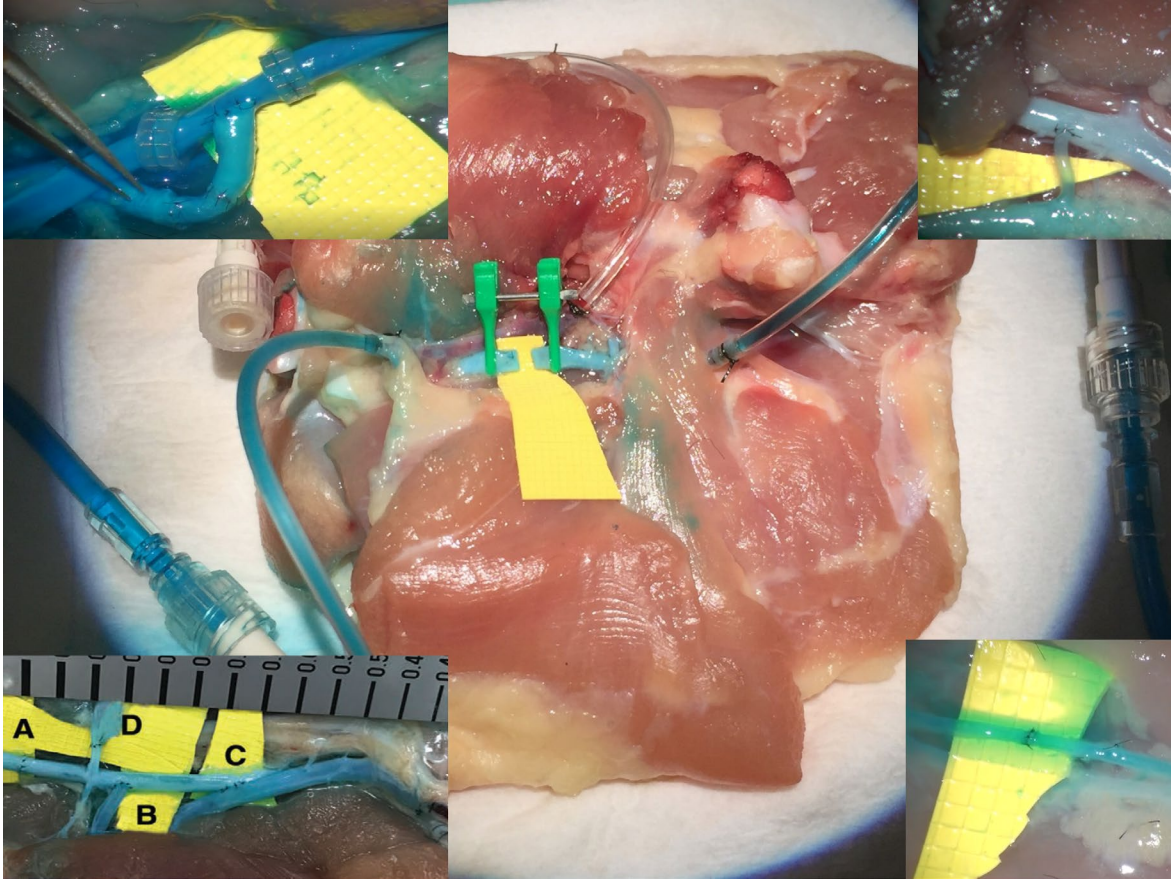
**Credit Line:** Elizabeth Wu, Microsurgery and Regenerative Medicine Lab, Medical Student (2nd year)



### **Pups in a Hut**

**Caption:** Three-week old Lewis rat pups taking a nap in their hiding spot. Lewis rats play a pivotal role in transplantation research, where their unique genetic uniformity provides a reliable and consistent graft rejection model. In the Al-Adra lab, Lewis rats are used for both kidney and liver transplantation immune tolerance studies aimed at reducing the need for long term immunosuppressive drugs.

**Credit Line:** Bret Verhoven, Al-Adra Lab



### **World-Famous Chicken Thigh Model Helping Microsurgery Education Around the World**

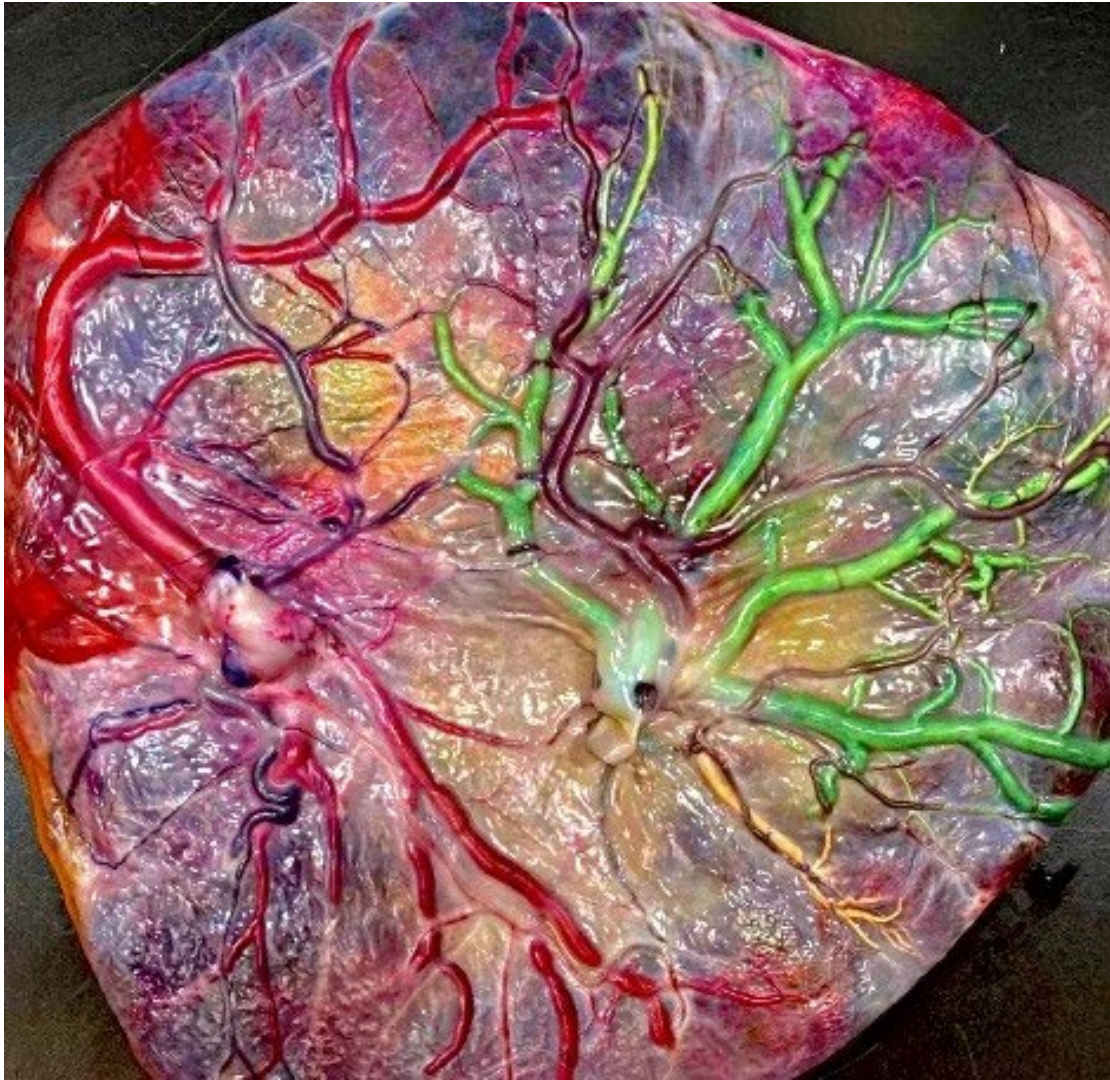
**Caption:** The image shows the Blue-Blood Chicken Thigh Model used for practicing various microsurgical techniques like artery and vein anastomosis, crucial for procedures such as finger replantation and organ reconstruction and transplantation.

Captured in a training setting, the model is prepared with artificial-colored Saline to simulate real surgical conditions, allowing visualization and manipulation of blood vessels. The model closely mimics human tissue and vascular structures, providing a realistic surgical experience for trainees. The trainees can practice supermicrosurgery in vessels as small as  $D = 0.3\text{mm}$ .

This model is vital for microsurgery education globally, especially in resource-limited countries. It is a major tool in UW-Madison's global microsurgery education mission. It offers cost-effective, accessible training, improving surgeons' skills and patient outcomes while the UW team teaching a course in like regions like Egypt, South Africa, Rwanda, and Vietnam.

**Credit Line:** Weifeng Zen, M.D., Sarah Hu, Jusuf Ademi, Aaron Dingle Ph.D., Samuel Poore, M.D. (Microsurgery and Regenerative Medicine Lab)

**Specific Roles:** Undergraduate Contributors (Sarah Hu and Jusuf Ademi), Weifeng Zeng, M.D. (Director of Microsurgery Education), Aaron Dingle, Ph.D. and Samuel Poore M.D. (Lab Directors)—All within the division of Plastic and Reconstructive Surgery



### **Separated Before Birth**

#### **Caption:**

#### **What does the image depict?**

A monochorionic-monoamniotic (MoMo) placenta following in-utero laser ablation for twin-to-twin transfusion syndrome (TTTS). Post-natal evaluation included dye injection of the umbilical vessels to evaluate their connections and the efficacy of surgery.

#### **How was the image taken?**

Pathologic evaluation

**What is an interesting fact about the object or phenomenon?**

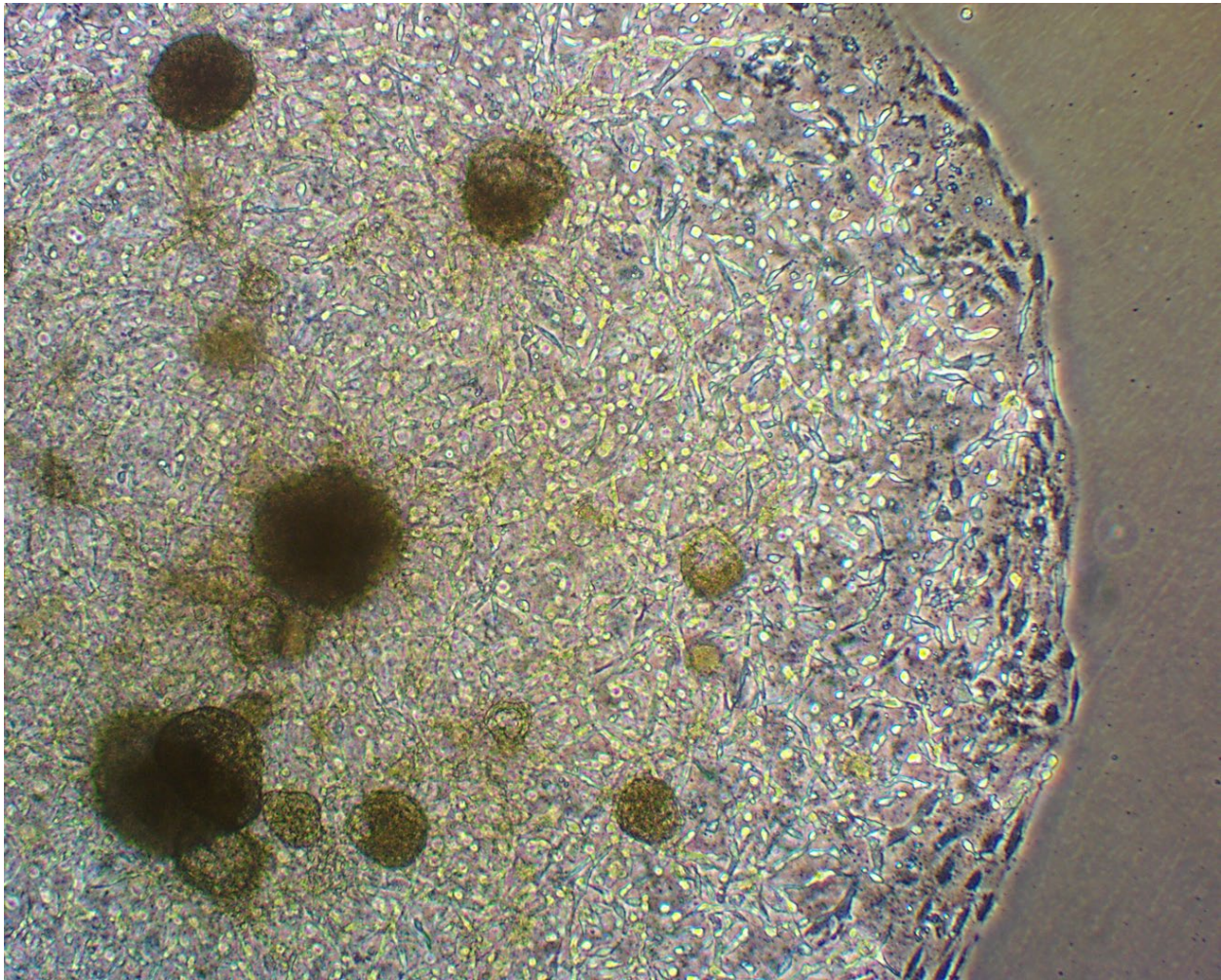
MoMo twins rarely present with TTTS requiring fetoscopic surgery and this was the first such case in the state of Wisconsin. The twins delivered safely at 34 weeks are doing well in the newborn period.

**How is this object, phenomenon, and/or method of image-making important to your research or discipline?**

TTTS is the most common indication for fetal surgery at UW and abroad. Dye injection of placental vessels is a uniquely beautiful way to assess the effectiveness of this type of surgical intervention.

**Credit line:** Michael Beninati, MD; Inna Lobeck, MD and the fetal surgery team

**Specific role :** Director of UW Health Fetal Diagnosis and Treatment Center (joint venture between departments of Ob-Gyn, SURGERY, and Pediatrics). Further, I am a member of the DOS division of acute care surgery.



### **A Cure for Diabetes**

This image showcases an islet organoid composed of pancreatic islet cells, endothelial cells, and de-cellularized pancreatic tissue. The circular, darkened cells towards the center represent the islets, and around them, you can see the developing vasculature, which is supported by the endothelial cells that naturally form the lining of blood vessels. Within the islet cells are beta cells, which produce insulin—a crucial function often impaired or destroyed in diabetes. Captured under a light microscope at 4X magnification, the image highlights the pancreatic islet cells with the formation of blood vessels all encapsulated within pancreatic hydrogel. These are key features that will enable these cells to function and survive after transplantation. Currently, islet transplants often fail due to poor engraftment and lack of oxygen, leading to cell death. However, these organoids could hold the promise for a new future in islet transplantation and potentially a cure for diabetes.

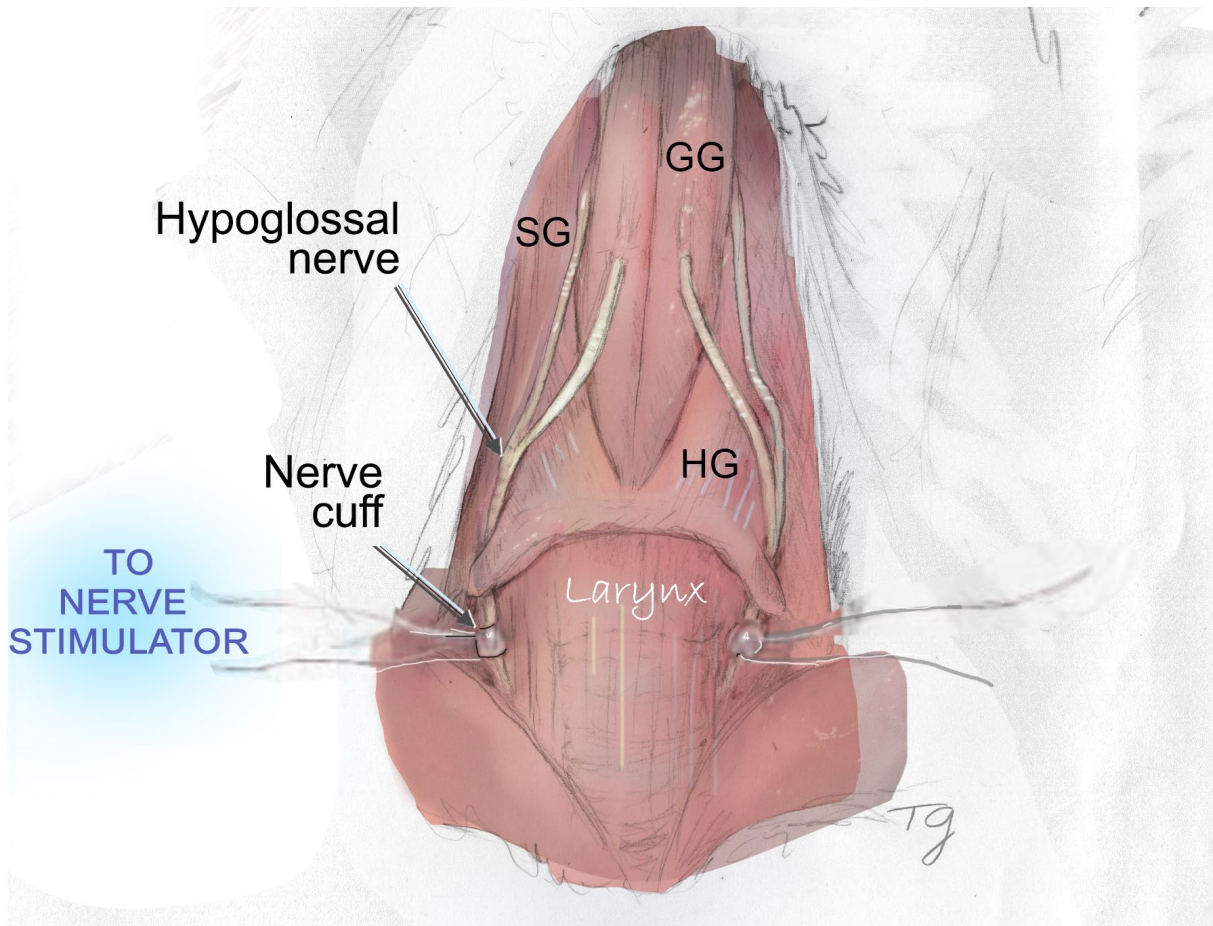
**Credit Line:** Caterra Leavens, Odorico Lab, Graduate Student, UW Department of Surgery, Transplant Division



### **The WiscVision: A Novel Low-Cost Stereovision Double Head Microsurgery Microscope**

**Caption:** This is a 3D printed microscope that has magnetic attachments so it can be broken down for travel. It has been used to teach the first plastic surgery microsurgery courses in Vietnam and Rwanda. It can also be used as a single head microscope. The Microsurgery and Regenerative Medicine Lab has patented the double mirror design used to keep the materials at an accessible price point for trainees.

**Credit Line:** Elizabeth Wu, Microsurgery and Regenerative Medicine Lab, Medical Student (2nd year)



**Hypoglossal nerve stimulation to evaluate tongue muscle contractile properties in a mouse model of Down syndrome.**

**Caption:** This is an illustration depicting the extrinsic tongue muscles and experimental stimulation of the hypoglossal nerve, prepared for a manuscript reporting results from a study using hypoglossal nerve stimulation in a mouse model of Down syndrome (DS). This image was prepared by first using a surgical microscope to photograph the anatomical preparation in a euthanized mouse. Pencil and paper were used to draw the illustration, using photographs as a reference. The pencil drawing was digitized, and Adobe Photoshop CS was used to apply color, shading, and labels. Down syndrome is a developmental disorder in which challenges involving tongue movement and positioning can impact speech, breathing, and swallowing. The experimental paradigm of hypoglossal nerve stimulation in animal models of DS may ultimately inform and support advances in clinical research using hypoglossal nerve stimulation to help patients with DS.

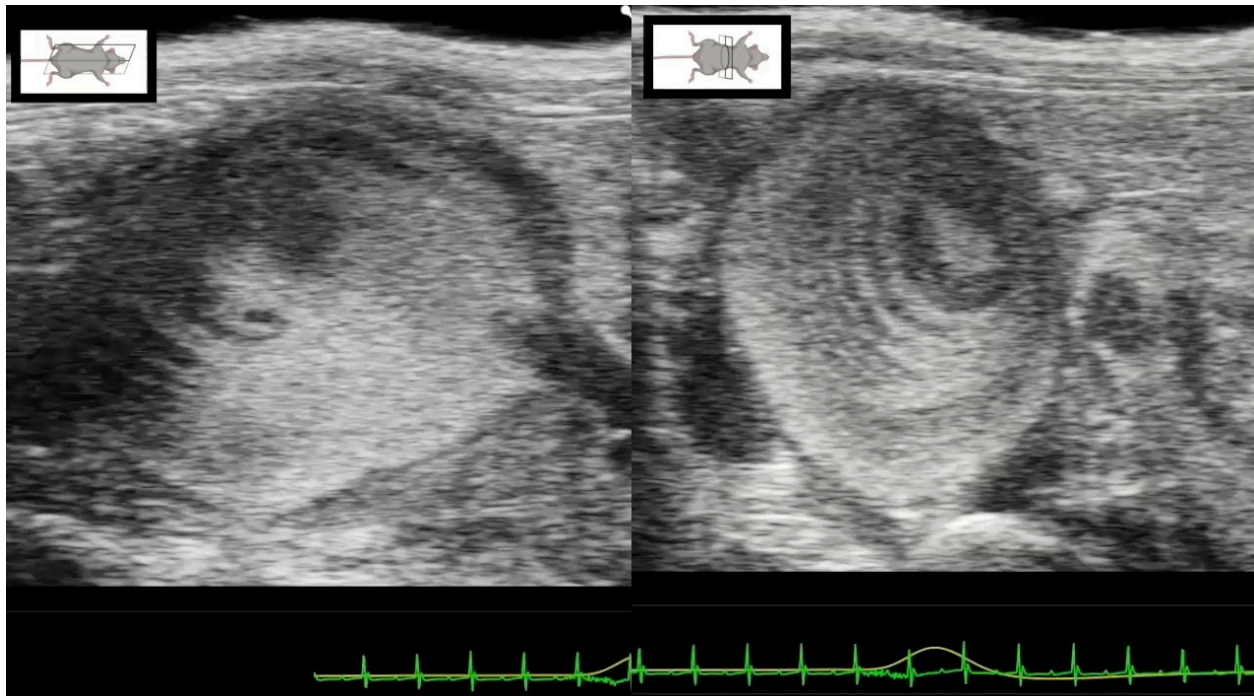
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**Citation:** Glass TJ, Russell JA, Fisher EH, Ostadi M, Aori N, Yu YE and Connor NP (2024) Altered tongue muscle contractile properties coincide with altered swallow function in the adult Ts65Dn mouse model of down syndrome. *Front. Neurol.* 15:1384572. doi: 10.3389/fneur.2024.1384572

**Credit:** Tiffany J. Glass, Connor Lab, PI & Scientist II, Division of Otolaryngology, Head & Neck Surgery



### **Non-laminar Blood Flow within an Abdominal Aortic Aneurysm of a Female Mouse**

**Caption:** Abdominal aortic aneurysms (AAA) can be induced in mice using a surgical model and monitored by abdominal ultrasonography. We highlight a large AAA in a female mouse 3 weeks after surgical induction, in longitudinal (left) and transverse (right) views. Laminar arterial blood flow within the proximal healthy aorta is disrupted upon reaching the dilated aneurysm sac, captured here as the mixing and swirling patterns seen with each cardiac cycle. This non-laminar flow results in the formation of intraluminal thrombus found in nearly all AAAs. In this optimized mouse model, we are able to investigate and replicate many of the behaviors and properties of human AAAs, such as intraluminal thrombus and sex differences. Ultrasound images courtesy of Ashley Weichmann.

**Name:** Jack Bontekoe, MD, Vascular Surgery Resident, Division of Vascular Surgery

**Lab:** Bo Liu, PhD



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