researchsummit2021

UNIVERSITY OF WISCONSIN–MADISON | DEPARTMENT OF SURGERY

Virtual Summit | Tuesday, January 12, 2021

Reimagining Research

ABSTRACT BOOK

Welcome

Welcome to the 12th Annual University of Wisconsin Department of Surgery Research Summit – A Virtual Event

Every year, we come together as members of the Department of Surgery to share our visions for future investigation in the field of surgery and report on progress we have made in our current research so we can celebrate and learn from each other. This year, the Covid-19 pandemic created many disruptions, not only to our research endeavors, but also to our clinical practices and personal lives. The pandemic shines light on critical issues in our field, such as healthcare disparities, but it has also created opportunities due to the need for telehealth and telecommuting. In this highly challenging time, scientists had to reimagine how they conduct research, investigate novel challenges, and maintain successful research teams. Our scientists are keen innovators who leverage their expertise and confront adversity head-on, defying the odds when least expected. During the Covid-19 pandemic, meeting hardship with collective talent and dedication is exactly what we have done. Our response as a Department has built resiliency and brought our community together. We dedicate this year's Virtual Research Summit to all who focus our efforts, respond rapidly, and reimagine our daily lives in the face of the Covid-19 pandemic. ***Reimagining Research*** is therefore the theme of the 2021 Department of Surgery Research Summit. This Research Summit is a platform to highlight the inspiring and imaginative discoveries of our members as well as an opportunity to share our vision and collective knowledge. The contribution of each individual to our Department of Surgery team—from students, residents, and fellows, to administrative and research staff, to postdocs, researchers and scientists—will allow us to move forward together and continue to positively impact the health of the people of Wisconsin and beyond.

Our Research Summit will feature a discussion from a panel of experts who are front and center in the fight against the Covid-19 pandemic.

David Andes, MD
Dr. David Andes is a faculty member and chief of the Division of Infectious Disease within the Department of Medicine, and also has an appointment in the Department of Medical Microbiology and Immunology. He holds the William A. Craig Endowed Professorship, and directs the Wisconsin Antimicrobial Drug Discovery and Development NIH Center of Excellence. Dr. Andes is frequently acknowledged for his multidisciplinary research contributions in the areas of infectious disease and drug resistance. His study tactics span from the bench to the clinic, including identifying new resistance mechanisms, defining new antimicrobial drug targets, delineating the optimal dosing strategies for treatment of drug resistant infections, and clinical trial study of epidemiology of drug resistance epidemiology. Dr. Andes' research efforts have been continuously funded by the NIH since 2001.

William Hartman, MD, PhD
Dr. William Hartman is an anesthesiologist at UW Health and an assistant professor in the Department of Anesthesiology. He is the Medical Director for the UW Health Preanesthesia Assessment Clinic. Dr. Hartman's current research focuses on quick implementation of therapy trial protocols to expeditiously bring novel treatments from the laboratory to the patient. Dr. Hartman is the principal investigator on UW's clinical trial of AstraZeneca's investigational COVID-19 vaccine, as well as UW's study on using convalescent plasma to fight COVID-19.

Continued...

Richard L. Moss, PhD
Dr. Moss joined the UW in 1979 as Assistant Professor of Physiology and was promoted to Associate Professor in 1983 and to Professor in 1987. He served as department chair from 1988 to 2009. During this time, the Department grew from 10 to 23 faculty and became one of the leading research departments in the nation. Dr. Moss founded the UW Cardiovascular Research Center and the M.S. in Biotechnology degree program. He was an AHA Established Investigator, held an NHLBI Merit Award, and led two NIH program project groups. In 2007, Dr. Moss received an honorary Doctor of Medicine degree from Uppsala University, the first medical school in Sweden. In 2009, he was appointed SMPH Senior Associate Dean for Basic Research, Biotechnology, and Graduate Studies.

Dr. Moss's research focuses on the roles of myofibrillar proteins as modulators of myocardial function in health and in diseases such as heart failure and both acquired and heritable cardiomyopathies. He has authored more than 180 papers and has supervised over 20 graduate students and post-doctoral fellows who now hold positions in academic medical centers and research institutions around the world.

Betsy Nugent, MSPH, CCRP
For the past 30 years, Ms. Nugent has worked in clinical research in everything from drug discovery to epidemiology to all phases of clinical trials. For the past 15 years, she has focused on developing innovative methods to improve the efficiency and adaptability of clinical research operations. She consulted internationally on projects related to the worldwide opioid crisis for Health Canada, FDA and the World Health Organization. Most recently she worked at Kaiser Permanente to build a standards-based program for the conduct of clinical trials. She has testified before the legislature on issues related to clinical trials accessibility and patient advocacy. Currently Ms. Nugent is the Chief Clinical Research Officer at the University Of Wisconsin School Of Medicine and Public Health and UW Health where she is engaged in culture change, clinical integration and building a standards-based clinical trials program. Ms. Nugent is a Certified Clinical Research Professional through the Society of Clinical Research Associates. She holds a Bachelor's Degree in Zoology from Colorado State University and a Master's of Science in Public Health with a focus on Epidemiology and Biostatistics from University of Colorado.

Susan Thibeault, PhD, CCC-SLP
Susan Thibeault, PhD, CCC–SLP is the Medical Director of the Speech & Hearing Services at UW Health, the Diane M. Bless Endowed Professor in the Department of Surgery, Division of Otolaryngology-Head & Neck Surgery, at the University of Wisconsin-Madison. Dr. Thibeault is also the Vice Chair of Research in the Department of Surgery. She received her PhD from the University of Wisconsin-Madison. Her NIDCD funded research efforts are primarily in the areas of vocal fold mucosa biology encompassing regenerative medicine, immunology and development.

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Thank you for making space in your busy schedules to attend the 2021 Research Summit. We hope today's program will increase your awareness of the innovative research activities that take place every day in the Department of Surgery.

Welcome to the Summit.
Hau Le, MD and **Susan Pitt, MD, MPHS**
Program Co-Chairs
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Program

UNIVERSITY OF WISCONSIN DEPARTMENT OF SURGERY

12th Annual Research Summit: *Reimagining Research*

Tuesday, January 12, 2021

Virtual

AM

8:00 **Welcome and Opening Remarks**

Hau Le, MD, Program Co-Chair
Susan Pitt, MD, MPHS, Program Co-Chair

8:05 **Research Update** – Rebecca Minter, MD

8:30 **UW Department of Surgery Research Talks**

- Cynthia Kelm-Nelson, PhD (8:30-8:40)
  Outside the classical framework: Using a rodent model to decipher mechanisms, pathways, and novel treatments of vocal communication dysfunction in Parkinson's disease
- Jason Smith, MD (8:40-8:50)
  TBD
- Matthew Brown, PhD (8:50-9:00)
  Assessing the immunogenicity of allogeneic pluripotent stem cell-derived cardiovascular therapies

9:00 **Invited Speaker** – Ankit Bharat, MD
Pathogenesis of COVID-19 ARDS leading to double lung transplant

9:45 **Break**

10:00 **COVID-19 Research Panel**

Moderator: Hau Le, MD

Panelists:
- David Andes, MD – Professor, Department of Medicine
- William Hartman, MD, PhD – Assistant Professor, Department of Anesthesiology
- Richard Moss, PhD – Senior Associate Dean for Basic Research, Biotechnology and Graduate Studies, SMPH
- Betsy Nugent, MSPH, CCRP – Chief Clinical Research Officer, SMPH and UW Health
- Susan Thibeault, PhD, CCC-SLP – Professor and Vice Chair of Research, Department of Surgery

10:50 **Break**

11:00 **Top Abstract Talks – Breakout Rooms** (see detailed schedule on following pages)

11:50 Closing

Top Abstract Talks – Breakout Rooms | 11:00-11:50 am

Breakout rooms will run simultaneously. Attendees can select their preferred breakout room to attend.

Basic Science Breakout Room | Moderator: David Al-Adra, MD, PhD

- **11:00-11:10 am:** Marissa Ziolkowski
  Comparison of a Topical v. Systemic Dual PI3K/mTOR Inhibitor in Preventing Anal Cancer in Mice
  Authors: M Ziolkowski, T Moyer, L Gunder, M Keating, M Finlay, P Bertrang, EH Carchman

- **11:10-11:20 am:** Patrick Schwartz, MD
  Chronic Circadian Disruption Induces Sustained Phase Shift in the Pancreas
  Authors: Patrick B Schwartz, MD, Morgan Walcheck, BS, Gang Wu, PhD, Noah Carrillo, BS, Kristina A Matkowskyj, MD PhD, Sean M Ronnekleiv-Kelly, MD

- **11:20-11:30 am:** Elise DeRoo, MD
  Circulating RIPK3 is Elevated in Aortic Aneurysm and Promotes Coagulation
  Authors: Elise DeRoo MD, Mitri Khoury MD, Scott LeMaire MD, Ying Shen MD PhD, Bo Liu PhD

- **11:30-11:40 am:** Josh Verhagen
  Characterization of Lewis rat liver dendritic cells generated by FLT3L administration
  Authors: Josh Verhagen, Kristin Carlson, David Al-Adra

- **11:40-11:50 am:** Taylor Aiken, MD
  Short-course neoadjuvant intratumoral immunotherapy can establish immunologic memory in murine melanoma
  Authors: Taylor Aiken, David Komjathy, Arika Feils, Amy Erbe, Alexander Rakhmilevich, Paul Sondel

Clinical Science Breakout Room | Moderator: David Schneider, MD, MS

- **11:00-11:10 am:** Ton Doan
  Content and Use of Long Talk in Outpatient Surgical Consults
  Authors: Ton C. Doan, Nathan D. Baggett, Anne Buffington, Amy B. Zelenski, Elle L. Kalbfell, Fiona Ljumani, Bret Hanlon, Justin Clapp, Robert M. Arnold, Margaret L. Schwarze

- **11:10-11:20 am:** Alexander Idarraga
  Machine Learning Detects False Negative Benign Thyroid Nodule Diagnoses
  Authors: Alexander Idarraga, George Luong, Vivian Hsiao, David Schneider

- **11:20-11:30 am:** Annalise Panthofer
  Anatomic Eligibility for Endovascular Aneurysm Repair Preserved Over Two Years of Surveillance
  Authors: Annalise M. Panthofer, BS, Sydney L. Olson, BS, Brooks L. Rademacher, MD, Jennifer K. Grudzinski, BS, RT(R)(M), Elliot L. Chaikof, MD, PhD, Jon S. Matsumura, MD, for the N-TA3CT Investigators

- **11:30-11:40 am:** Gabriel Sobczak
  Cochlear Implant Outcomes and Tumor Characteristics in Patients with Neurofibromatosis Type 2 and Bilateral Vestibular Schwannoma
  Authors: Gabriel Sobczak, Wendy Marchant, G. Mark Pyle, Sara Misurelli, Joseph Roche

- **11:40-11:50 am:** Carol Soteropulos, MD
  Preoperative Immunonutrition Decreases Wound Complications in Immediate Breast Reconstruction
  Authors: Carol E. Soteropulos MD, Kylie M. Edinger MD, Kishan M. Thadikonda MD, Katherine M. Gast MD, MS

Health Services Research and Education Research Breakout Room | Moderator: Susan Pitt, MD, MPHS

- **11:00-11:10 am:** Megan Saucke, MA
  Scared Decision-Making: The Role of Emotions in Surgeon-Patient Treatment Decisions about Low-Risk Thyroid Cancer
  Authors: Megan C. Saucke, MA, Alexandra A. Rosser, BS, Benjamin R. Roman, MD, MSHP, Jennifer Hay, PhD, Corrine I. Voils, PhD, Susan C. Pitt, MD, MPHS

- **11:10-11:20 am:** Joanne Peters, PhD
  Post-operative Opioid Prescribing: How close is Wisconsin to Evidence-Based Guidelines?
  Authors: Joanne Peters, PhD; Gregory J Raupp; Jessica Schumacher, PhD; Tudor Borza, MD, MS; Dou-Yan Yang, PhD; Manasa Venkatesh, MS and Elise H. Lawson, MD, MSHS

- **11:20-11:30 am:** Christopher Stahl, MD
  Teaching Surgical Anatomy with Perceptual Fluency Interventions: A Randomized Controlled Trial
  Authors: Christopher C. Stahl MD, Jacob A. Greenberg MD, Martina Rau PhD

- **11:30-11:40 am:** Esra Alagoz, PhD
  Referring and Accepting Provider Communication during Inter-hospital Transfers of Emergency General Surgery Patients: Challenges and Opportunities
  Authors: Esra Alagoz, PhD, Megan Saucke, MA, Angela Ingraham, MD, MS

- **11:40-11:50 am:** Sarah Jung, PhD
  Multi-Disciplinary Assessment of the Entrustable Professional Activities of Surgery Residents
  Authors: Jung S, Stahl CC, Rosser AA, Kraut AS, Schnapp BH, Westergaard M, Hamedani AG, Minter RM, Greenberg JA

Translational Science Breakout Room | Moderator: Hau Le, MD

- **11:00-11:10 am:** Courtney Broadfoot, MS
  Tongue Strength and Vocal Communication Deficits Improve with Targeted Tongue and Laryngeal Exercises in a Pink1-/- Rat Model of Parkinson Disease
  Authors: Courtney K. Broadfoot, Jesse D. Hoffmeister, Sarah A. Lechner, Maryann N. Krasko, Emily Lambert, John Russel, John Szot, Tiffany Glass, Nadine P. Connor, Cynthia A. Kelm-Nelson, Michelle R. Ciucci

- **11:10-11:20 am:** Khang Huynh
  Cold atmospheric plasma: a novel and selective treatment for solid cancers
  Authors: Khang Huynh, Ha M. Nguyen, Bindu Anilesh Nair, Taylor J Aiken, Kevin Janeck, Song Kim, Paul Sondel, Mario Otto, J. Leon Shohet, Hau D. Le

- **11:20-11:30 am:** Weifeng Zeng, MD
  Beyond Adding The Core Suture: An Entirely New Approach To Tendon Repair
  Authors: Weifeng Zeng, MD, Nicholas J Albano, MD, Ruston J. Sanchez, MD, Ray Vanderby, PhD, Ronald Mccabe, PhD, Samuel O. Poore, MD, PhD, Aaron M. Dingle, PhD

- **11:30-11:40 am:** Linda Rowe, MS
  Respiratory-Swallow Coordination in a Rat Model of Chemoradiation
  Authors: Linda M Rowe, Nadine P Connor, John A Russell

- **11:40-11:50 am:** Christopher Little, MD
  Polymorphic P2X7 receptor activity drives Th17-dependent self- and alloreactivity in non-human primates
  Authors: Christopher Little, Jeremy Sullivan, William Burlingham, Dixon Kaufman

Acknowledgements

We would like to thank the following individuals who served on the **2021 Research Summit Organizing Committee** and made invaluable contributions to the planning of this event:

Lauren Ross-Hixson
Katie Dorst
Nicole Jennings, MA
Sarah Pavao
Lisa Werning
Karen Williams
Susan Thibeault, PhD

We also wish to recognize the **abstract reviewers** who served on our Program Committee. The following individuals generously donated their time to review the 76 abstracts that were submitted:

David Al-Adra, MD, PhD
Kathy Beck, PhD
Andi Donelly
Dawn Elfenbein, MD, MPH
Luke Funk, MD, MPH
Rachel Godbout, MS
Bridget Johnson, RN, BAN, CCRC
Sarah Jung, PhD
Cynthia Kelm-Nelson, PhD
Santosh Kumari, PhD
Elise Lawson, MD, MSHS
Hau Le, MD
Heather Neuman, MD, MS
Sudha Pavuluri Quamme, MD, MS
Samuel Poore, MD, PhD
Austin Scholp, MS
Jessica Schumacher, PhD
Nathan Welham, PhD, CCC-SLP
Lisa Werning
Dou-Yan Yang, PhD

Finally, we would like to acknowledge the **oral presentation judges** who worked to determine the award winners.

Julia Berian, MD, MS
Ankit Bharat, MD
Randi Cartmill, MS
Scott Chaiet, MD, MBA
David Foley, MD
Vlasta Lungova, PhD
Bridget Johnson, RN
Muhammed Murtaza, MD, PhD
Heather Neuman, MD, MS
Thomas Pasic, MD
Sudha Pavuluri Quamme, MD, MS
Susan Thibeault, PhD

List of Abstracts

Research Summit Poster Abstracts

Alphabetized by PI/Lab within each group. Number represents abstract number.

GROUP ONE: Basic Science

AL–ADRA

Anti-inflammatory cytokines delivered during normothermic ex vivo liver perfusion improve graft function and reduce immunogenicity; *Kristin Carlson, Juliana Pavan-Guimaraes, Joshua Verhagen, Feridoon Najmabadi, David Al-Adra*
Abstract Number: **B3**

Characterization of Lewis rat liver dendritic cells generated by FLT3L administration; *Josh Verhagen, Kristin Carlson, David Al-Adra*
Abstract Number: **B23**

BURLINGHAM

Maternal extracellular vesicles cross-dressing of cord blood antigen presenting cells is associated with graft allotolerance; *Diego Lema, Ewa Jankowska-Gan, Stacey McMorrow, Jeremy Sullivan, David Al-Adra, Sami Kanaan, Afsar Naqvi, J Lee Nelson, William Burlingham*
Abstract Number: **B15**

CARCHMAN

Comparison of a Topical v. Systemic Dual PI3K/mTOR Inhibitor in Preventing Anal Cancer in Mice; *M Ziolkowski, T Moyer, L Gunder, M Keating, M Finlay, P Bertrang, EH Carchman*
Abstract Number: **B25**

CIUCCI

Characterization of functional deficits along the aerodigestive and gastrointestinal tracts in the Pink1-/- rat model of Parkinson disease; *Maryann N. Krasko, Cynthia A. Kelm-Nelson, Michelle R. Ciucci*
Abstract Number: **B12**

CONNOR

Age influences the impact of stroke on bihemispheric motor cortex connectivity to the jaw and tongue muscles; *Miranda J. Cullins and Nadine P. Connor*
Abstract Number: **B4**

Bioenergetic evaluation of rat styloglossus muscle during fatigue; *Tiffany J. Glass, Linda M. Rowe, Jared Cullen, Nadine P. Connor*
Abstract Number: **B9**

DEY

MR1 overexpression is related with poor clinical prognosis in glioma; *Phillip Kubica, Mario Henriquez, Marpe Bam, Montserrat-Lara-Velazquez, Seema Sira, Irene Ong, Peng Liu, Raj Priya, Shahriar Salamat, Randy Brutkiewicz and Mahua Dey*
Abstract Number: **B13**

GIBSON

Bandage-like Nanogenerator-driven Electrical Stimulation Enhances Wound Healing in Human Skin; *Aiping Liu, Yin Long, Jun Li, Lily Meronek, Xudong Wang, Angela Gibson*
Abstract Number: **B16**

JIANG

Excised Modeling Supraglottic Pressure Project; *Nikita Menon*
Abstract Number: **B17**

Microstructural Differences Between Laryngeal Animal Models; *Jarett Jones, Jack Ersbo; BS, Jack Jiang; MD PhD*
Abstract Number: **B8**

KELM-NELSON

Thyroarytenoid muscle gene expression in a rat model of early Parkinson disease; *Sarah A. Lechner, Heidi Kletzien, Samantha E. Lettenberger, Taylor A. R. Kaldenberg, Natalie K. Pahapill, Amy Regenbaum, Stephen C. Gammie, Cynthia A. Kelm-Nelson*
Abstract Number: **B14**

LE

Development of cold atmospheric plasma jet device as a novel tool for cancer treatment; *Ha M. Nguyen, Khang Huynh, Bindu Anilesh Nair, Taylor J Aiken, Kevin C Janek, D. Benjamin, J. M. Blatz, F. A. Choudhury, Paul Sondel, Mario Otto, J. L. Shohet, Hau D. Le*
Abstract Number: **B18**

LIU

GSK2593074A Blocks Progression of Existing Abdominal Aortic Aneurysms; *Mitri K. Khoury, MD; Ting Zhou, PhD; Huan Yang, PhD, Samantha R. Prince, Kartik Gupta, MS; Amelia R. Stranz, Qiwei Wang, PhD; Bo Liu, PhD*
Abstract Number: **B19**

Circulating RIPK3 is Elevated in Aortic Aneurysm and Promotes Coagulation; *Elise DeRoo MD, Mitri Khoury MD, Scott LeMaire MD, Ying Shen MD PhD, Bo Liu PhD*
Abstract Number: **B5**

MCCULLOCH

Spectral Arc Length as a Method to Quantify Pharyngeal High-Resolution Manometric Curve Smoothness; *Austin J. Scholp; Matthew R. Hoffman; Sarah P. Rosen; Suzan M. Abdelhalim; Corinne A. Jones; Jack J. Jiang; Timothy M. McCulloch*
Abstract Number: **B20**

ODORICO

Islet microenvironment stimulates islet health and function in culture; *Dan Tremmel, Sara Dutton Sackett, Sam Mitchell, Austin Feeney, Sakar Gupta, Colin Steck, and Jon Odorico.*
Abstract Number: **B22**

POORE/DINGLE

Development of a clinically translatable osseointegrated neural interface in sheep.; *Zeeda H. Nkana, Kirsten A. Gunderson, Scott K. Odorico, Rashea L. Minor, Samuel O. Poore MD, Aaron M. Dingle, PhD*
Abstract Number: **B6**

Differential Gene Expression in Nerve Gap Repair via the Interrupted Epineural Suture Technique with Low versus High Tension: A pilot study; *Kasey Leigh Wood, BS and Marina I. Adrianzen Fonseca, BS (co-first authors), Kirsten A. Gunderson, BS, Zeeda H. Nkana, BS, Aaron M. Dingle, PhD, Jacqueline S. Israel, MD, Samuel O. Poore, MD, PhD.*
Abstract Number: **B1**

How the Local Environment Induces Differential Gene Expression in Regenerating Nerve After Neurotmesis – Implications for Neuroma Prevention and Neural Interfacing for Prosthetic Control; *Kasey Leigh Wood, BS, Marina I. Adrianzen Fonseca, BS, Kirsten A. Gunderson, BS, Zeeda H. Nkana, BS, Jacqueline S. Israel, MD, Samuel O. Poore, MD, PhD, Aaron M. Dingle, PhD*
Abstract Number: **B24**

Not All Controls are Created Equally: Differences in Cutaneous Gene Expression Among Control Groups Used in Breast Research; *Kirsten A. Gunderson, BS; Rebecca L. Farmer, MD, PhD; Sarah M. Lyon, MD; Jacqueline S. Israel, MD; Sandra Splinter BonDurant, MS; Zeeda H. Nkana, BS; Katherine M. Gast, MD; Samuel O. Poore, MD, PhD; John W. Siebert, MD*
Abstract Number: **B10**

RONNEKLEIV-KELLY

Chronic Circadian Disruption Induces Sustained Phase Shift in the Pancreas; *Patrick B Schwartz, MD1, Morgan Walcheck, BS1, Gang Wu, PhD2, Noah Carrillo, BS1, Kristina A Matkowskyj, MD PhD3, Sean M Ronnekleiv-Kelly, MD1*
Abstract Number: **B21**

SONDEL

Short-course neoadjuvant intratumoral immunotherapy can establish immunologic memory in murine melanoma; *Taylor Aiken, David Komjathy, Arika Feils, Amy Erbe, Alexander Rakhmilevich, Paul Sondel*
Abstract Number: **B2**

GROUP TWO: Clinical Science

DJAMALI

Sequential biopsies in renal transplant recipients with refractory chronic active antibody-mediated rejection: improvements in histopathology are delayed compared to the reduction in DSA; *Kenna R. Degner, PhD, Sandesh Parajuli, MD, Fahad Aziz, MD, Neetika Garg, MD, Maha Mohamed, MD, Didier A. Mandelbrot, MD, Sarah E. Panzer, MD, Nancy A. Wilson, Ph, Shannon R. Reese, MS, Kristin Van Hyfte, Weixiong Zhong, MD, Peter Nickerson, MD, Arjang Djamali, MD*
Abstract Number: **C3**

FIEDLER

Outcomes after LVAD Implantation by Bi-Thoracotomy versus Sternotomy Approach; *Elizabeth M. Stoeckl, BS; Jason W. Smith, MD; Ravi Dhingra, MD; Amy G. Fiedler, MD*
Abstract Number: **C17**

GAST

Preoperative Immunonutrition Decreases Wound Complications in Immediate Breast Reconstruction; *Carol E. Soteropulos MD, Kylie M. Edinger MD, Kishan M. Thadikonda MD, Katherine M. Gast MD, MS*
Abstract Number: **C15**

JIANG

Age and Sex Comparison of Aerodynamic Phonation Measurements using Noninvasive Assessment; *Jim R. Lamb, Austin J. Scholp, Jack J. Jiang*
Abstract Number: **C9**

LARSON

The Effects of Preoperative Anemia on Breast Reconstruction; *Jesse Kasim, Justin Davis, Jeffrey Larson*
Abstract Number: **C2**

LONG

One Bad Apple or the Whole Bunch: Patterns of Disease in non-MEN1 Familial Hyperparathyroidism; *Cassandra Crifase, David Schneider MD MS, Mariam Ali-Mucheru MD, Kristin Long MD MPH*
Abstract Number: **C1**

MATSUMURA

Anatomic Eligibility for Endovascular Aneurysm Repair Preserved Over Two Years of Surveillance; *Annalise M. Panthofer, BS, Sydney L. Olson, BS, Brooks L. Rademacher, MD, Jennifer K. Grudzinski, BS, RT(R)(M), Elliot L. Chaikof, MD, PhD, Jon S. Matsumura, MD, for the N-TA3CT Investigators*
Abstract Number: **C11**

Open partial conversion with endograft preservation for the treatment of persistent type II endoleaks; *Thomas Staniszewski, Reagan Beyer, Dr. Courtney Morgan, Dr. Jon Matsumura*
Abstract Number: **C16**

Predictors Of Volume Growth In Abdominal Aortic Aneurysms; *Sydney Olson, Annalise Panthofer, Michael Terrin, John Curci, Timothy Baxter, Fred Weaver, Jon Matsumura*
Abstract Number: C10

PURICELLI

International Pediatric Otolaryngology Group (IPOG) Consensus recommendations on the prenatal and perinatal management of anticipated airway obstruction: Micrognathia*; Michael D. Puricelli, MD*
Abstract Number: **C12**

Vestibulopathy; A sign of COVID-19?: First case report of pediatric patient presenting with vestibular neuritis as the sole sign of COVID-19 infection*; Cody J Falls BS, Zhang Yanchen MD, Michael D Puricelli MD*
Abstract Number: **C6**

Video Laryngoscopy for Intubation in Severe Pierre Robin sequence: A Retrospective Review*; Michael D Puricelli, Joseph D Peterson, Ahmed Alkhateeb, Richard JH Smith, Deborah SF Kacmarynski*
Abstract Number: **C13**

ROCHE

Cochlear Implant Outcomes and Tumor Characteristics in Patients with Neurofibromatosis Type 2 and Bilateral Vestibular Schwannoma*; Gabriel Sobczak, Wendy Marchant, G. Mark Pyle, Sara Misurelli, Joseph Roche*
Abstract Number: **C14**

SCHNEIDER

Risk Stratifying Indeterminate Thyroid Nodules with Machine Learning Using Available Electronic Health Record Data*; George Luong, BS, Alexander J. Idarraga, BA, Vivian Hsiao, MD, BA, BS, David F. Schneider, MD, BA, MS, FACS*
Abstract Number: **C8**

Machine Learning Detects False Negative Benign Thyroid Nodule Diagnoses; *Alexander Idarraga, George Luong, Vivian Hsiao, David Schneider*
Abstract Number: C7

What are the Drivers of Cost in Parathyroidectomy?*; Amanda R. Doubleday, DO, MBA; Christopher C. Stahl, MD; Rebecca S. Sippel, MD, FACS; Kristin L. Long, MD, MPH, FACS; Susan C. Pitt, MD, MPHS, FACS; Dawn M. Elfenbein, MD, MPH, FACS; David F. Schneider, MD, MS, FACS*
Abstract Number: **C5**

SCHWARZE

Content and Use of Long Talk in Outpatient Surgical Consults*; Ton C. Doan, Nathan D. Baggett, Anne Buffington, Amy B. Zelenski, Elle L. Kalbfell, Fiona Ljumani, Bret Hanlon, Justin Clapp, Robert M. Arnold, Margaret L. Schwarze*
Abstract Number: **C4**

GROUP THREE: EDUCATION

GREENBERG, J.

Multi-Disciplinary Assessment of the Entrustable Professional Activities of Surgery Residents*; Jung S, Stahl CC, Rosser AA, Kraut AS, Schnapp BH, Westergaard M, Hamedani AG, Minter RM, Greenberg JA*
Abstract Number: **E2**

JUNG

Mentored Clinical Research Experiences for High School Students: Reported Impacts on Career Trajectories*; Sarah Jung*
Abstract Number: **E1**

POORE

The Infused Pig Chest Wall "Sandwich" - A Novel Training Model for Internal Mammary Artery Preparation in Breast Reconstruction*; Weifeng Zeng MD, Ruston Sanchez MD, Kirsten Gunderson MS, Nicholas J Albano MD. Aaron M. Dingle PhD, Samuel O. Poore MD, PhD*
Abstract Number: **E4**

RAU

Teaching Surgical Anatomy with Perceptual Fluency Interventions: A Randomized Controlled Trial*; Christopher C. Stahl MD, Jacob A. Greenberg MD, Martina Rau PhD*
Abstract Number: **E3**

GROUP FOUR: HEALTH SERVICES RESEARCH

DIMUSTO

Acute Type B Aortic Dissection early in-hospital outcome at a Single Institution*; A.M. Um, F.C. Razalan-Krause, G. Tefera, C.W. Acher, P. DiMusto*
Abstract Number: **H7**

FUNK

Individual-level bariatric surgery barriers in the Veterans Health Administration: A Qualitative Study*; Jacqueline A Murtha, MD, MPH; Esra Alagoz, PhD; Catherine R Beuer, MS; Alex Finn, BS; Susan D Raffa, PhD; Corrine I Voils, PhD; Luke M Funk, MD, MPH*
Abstract Number: **H3**

INGRAHAM

Referring and Accepting Provider Communication during Inter-hospital Transfers of Emergency General Surgery Patients: Challenges and Opportunities*; Esra Alagoz, PhD, Megan Saucke, MA, Angela Ingraham, MD, MS*
Abstract Number: **H1**

Working Behind the Scenes: How Transfer Center Nurses Facilitate Interactions and Communication between Providers regarding Transfers of Emergency General Surgery Patients*; Ingraham A, Saucke M, Fernandes-Taylor S, Ljumani F, Alagoz E.*
Abstract Number: **H2**

LAWSON

Post-operative Opioid Prescribing: How close is Wisconsin to Evidence-Based Guidelines?*; Joanne Peters, PhD; Gregory J Raupp; Jessica Schumacher, PhD; Tudor Borza, MD, MS; Dou-Yan Yang, PhD; Manasa Venkatesh, MS and Elise H. Lawson, MD, MSHS*
Abstract Number: **H5**

PITT

Scared Decision-Making: The Role of Emotions in Surgeon-Patient Treatment Decisions about Low-Risk Thyroid Cancer*; Megan C. Saucke, MA, Alexandra A. Rosser, BS, Benjamin R. Roman, MD, MSHP, Jennifer Hay, PhD, Corrine I. Voils, PhD, Susan C. Pitt, MD, MPHS*
Abstract Number: **H6**

POORE

Investigation of racial disparities in postoperative outcomes of reconstructive breast surgery in Wisconsin*; Zeeda H. Nkana BS, Kasey Leigh Wood BS, Alison M. Karczewski BS, Kirsten A. Gunderson BS, Sarah M. Lyon MD, Aaron M. Dingle PhD, Samuel O. Poore MD PhD*
Abstract Number: **H4**

GROUP FIVE: TRANSLATIONAL RESEARCH

BROWN

Genomic and functional assessment of allogeneic immunogenicity in pluripotent stem cell-derived arterial endothelial cells*; Haynes WJ, Zhang J, Hermsen J, Perrin ES, Kumari S, Argus C, Bolin J, Steill J, Swanson S, Stewart R, Biermann M, Zhang J, Kamp TJ, Thomson JA, Brown ME*
Abstract Number: **T2**

CIUCCI

Tongue Strength and Vocal Communication Deficits Improve with Targeted Tongue and Laryngeal Exercises in a Pink1-/- Rat Model of Parkinson Disease*; Courtney K. Broadfoot, Jesse D. Hoffmeister, Sarah A. Lechner, Maryann N. Krasko, Emily Lambert, John Russel, John Szot, Tiffany Glass, Nadine P. Connor, Cynthia A. Kelm-Nelson, Michelle R. Ciucci*
Abstract Number: **T1**

KAUFMAN

Polymorphic P2X7 receptor activity drives Th17-dependent self- and alloreactivity in non-human primates*; Christopher Little, Jeremy Sullivan, William Burlingham, Dixon Kaufman*
Abstract Number: **T4**

LE

Cold atmospheric plasma: a novel and selective treatment for solid cancers*; Khang Huynh, Ha M. Nguyen, Bindu Anilesh Nair, Taylor J Aiken, Kevin Janeck, Song Kim, Paul Sondel, Mario Otto, J. Leon Shohet, Hau D. Le*
Abstract Number: **T3**

POORE/DINGLE

Beyond Adding The Core Suture: An Entirely New Approach To Tendon Repair*; Weifeng Zeng, MD1, Nicholas J Albano, MD1, Ruston J. Sanchez, MD1, Ray Vanderby, PhD2, Ronald Mccabe, PhD2, Samuel O. Poore, MD, PhD1, Aaron M. Dingle, PhD1*
Abstract Number: **T6**

RUSSELL

Respiratory-Swallow Coordination in a Rat Model of Chemoradiation*; Linda M Rowe, Nadine P Connor, John A Russell*
Abstract Number: **T5**

Abstracts

GROUP ONE

Basic Science

B3

Anti-inflammatory cytokines delivered during normothermic *ex vivo* liver perfusion improve graft function and reduce immunogenicity

Kristin Carlson, Juliana Pavan-Guimaraes, Joshua Verhagen, Feridoon Najmabadi, David Al-Adra

Submitter	Kristin Carlson
Phone	608-265-5088
Email Address	Kcarlson9@wisc.edu
Classification	Academic Staff
Division	Transplant
Lab	Al-Adra
Science Type	Basic Science
Keywords	Transplantation, Liver, Perfusion, Immunomodulation, Dendritic Cell

Abstract Starts on Page 2.

Introduction: Normothermic *ex vivo* liver perfusion (NEVLP) provides an exciting system for improved organ preservation and optimized therapeutic agent delivery to a donor liver prior to transplantation. An improved organ preservation method has been necessitated by the increasing use of marginal organs which poorly tolerate the standard static cold storage (CS) and which may benefit from clinical assessment and therapeutic intervention prior to transplantation. NEVLP maintains the donor liver at physiological temperature, restoring metabolic processes to allow both assessment of graft function and delivery of bioactive agents. These therapeutic agents may improve the graft condition or alter immunogenicity, such as through polarization of liver-resident immune cells to a regulatory phenotype. Anti-inflammatory cytokines IL-10 and TGF-β are known to maintain dendritic cells in an immature, tolerogenic phenotype and to induce regulatory T cell polarization. Our team found that normothermic *ex vivo* perfusion of the Lewis rat liver with anti-inflammatory cytokines IL-10 and TGF-β improved liver function and decreased immunogenicity.

Methods: Male Lewis rats (aged 8-12 weeks) were randomly divided into three experimental groups: Cold storage (CS) control for 4 hours at 4°C with reperfusion for 2 hours at 37°C (n=3), NEVLP for 4 hours at 37°C (n=5), and NEVLP for 4 hours at 37°C with 20ng/mL each IL-10 and TGF-β (NEVLP-Cyt) (n=5). Livers were procured in standard fashion, and machine perfusion was performed with a nutrient-supplemented, oxygenated perfusate. Perfusate samples were collected once per hour and later analyzed for liver damage and cytokine markers by multiplex ELISA. Following perfusion, liver lobes were partitioned for histological analysis and collagenase digestion. Non-parenchymal cells were isolated from collagenase digested liver lobes and stained for dendritic cell and regulatory T cell flow cytometry.

Results: NEVLP-Cyt livers demonstrated improved function during perfusion as evidenced by higher lactate clearance in comparison to NEVLP and CS livers. All treatment groups produced similarly low concentrations of liver damage markers in the perfusate with a trend toward a decrease in inflammatory cytokine production in NEVLP-Cyt livers when compared to NEVLP livers. Dendritic cell activation was in part ameliorated by anti-inflammatory cytokine treatment (**Fig 1),** as evidenced by lower MHC II median fluorescence intensity in NEVLP-Cyt livers (148,394.40 ± 5,360.06) compared to NEVLP livers (193,844.40 ± 10,191.83), $t(4) = 3.95$, $p < 0.01$, and a trend toward an increase in the percentage of dendritic cells expressing the co-inhibitory molecule PD-L1 (NEVLP vs. NEVLP-Cyt, 16.38 ± 5.69 vs. 26.41 ± 15.69, n.s.). Histopathological analysis of liver damage revealed similarly low damage levels in all treatment groups.

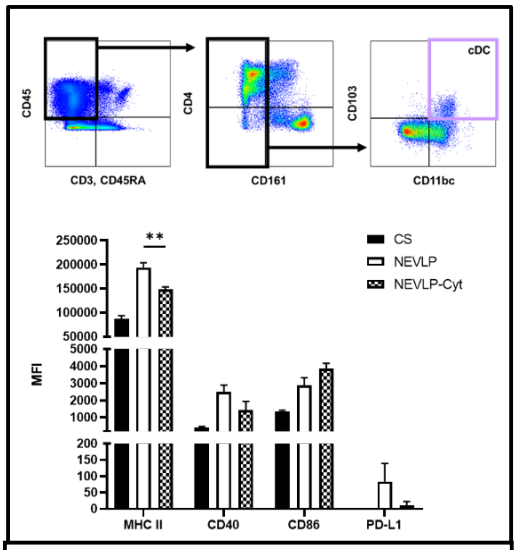


Figure 1. Anti-inflammatory cytokines decreased dendritic cell activation. NEVLP-Cyt liver dendritic cells expressed significantly lower levels of MHC II and trended toward lower CD40 expression in comparison to NEVLP livers.

Conclusions: Anti-inflammatory cytokines IL-10 and TGF-β improved liver function during normothermic *ex vivo* machine perfusion and in part ameliorated the inflammatory effects of perfusion. Reduction of immunogenicity during organ preservation may reduce incidence of allograft dysfunction and rejection following transplantation. Future studies will implement an allogeneic rat liver transplant model to further investigate the functional results of these treatments.

B23

Characterization of Lewis rat liver dendritic cells generated by FLT3L administration

Josh Verhagen, Kristin Carlson, David Al-Adra

Submitter	Josh Verhagen
Phone	920-819-6858
Email Address	jcverhagen@wisc.edu
Classification	Undergraduate Student
Division	Transplant
Lab	Al-Adra
Science Type	Basic Science
Keywords	Dendritic Cell, FLT3L, qRT-PCR, Flow Cytometry, Liver

Abstract Starts on Page 2.

Introduction: Dendritic cells (DCs) are potent antigen presenting cells that bridge the innate and adaptive immune systems and play a key role in allograft rejection. Conflicting reports have emerged demonstrating that the two major subsets of DCs, classical DCs (cDCs) and plasmacytoid DCs (pDCs), may play differing roles in episodes of allograft dysfunction and rejection. Due to this discrepancy, there is interest in characterizing the phenotype and functionality of tissue specific subsets of DCs. However, tissue specific DCs are hard to characterize as they compose a small cell population; therefore, DC yield can be increased by using FMS-like tyrosine kinase 3 ligand (FLT3L). The exact phenotype and function of dendritic cell subpopulations, specifically in the rat liver, has yet to be well characterized after FLT3L exposure. Our aim is to explore the effects of FLT3L on rat liver-resident cDC and pDC populations as well as further characterize the phenotype of these specific cell populations.

Methods: Female Lewis rats (aged 8-12 weeks) will receive intraperitoneal injections of saline or 10, 50, or 100µg FLT3L once daily for 10 days. On the eleventh day, the liver will be collected, digested, and tissue-resident immune cells will be isolated. Cells from the liver will be stained for multi-color spectral flow cytometry to determine cDC and pDC enumeration as well as MHC I, MHC II, CD40, CD80, CD86, and PD-L1 expression levels. cDC and pDC populations will be isolated by FACS and harvested into cell lysis buffer. mRNA will be isolated from lysed cells, reverse-transcribed to generate a cDNA library, and followed by quantitative real time PCR (RT-qPCR) to determine expression of maturation and phenotypic markers including toll-like receptors, cytokines, and antigen presentation machinery.

Results: FLT3L injection increased the frequency of cDCs within the liver (n=3; **Fig. 1**). In contrast, pDCs were not significantly changed by FLT3L injection. There was also increased expression of MHC II for the cDCs compared to the pDCs following the 100µg FLT3L injections (n=2).

Conclusions: The generation of DCs *in vivo* using FLT3L leads to expansion of primarily cDCs and increases their MHC II expression. Ongoing experiments with qRT-PCR and flow cytometry to determine costimulatory protein expression and pattern recognition receptor levels is necessary to understand the effect of FLT3L on dendritic cell populations. A better understanding of the liver-resident cDC and pDC immunobiology will be key to understanding their roles in allograft dysfunction and rejection.

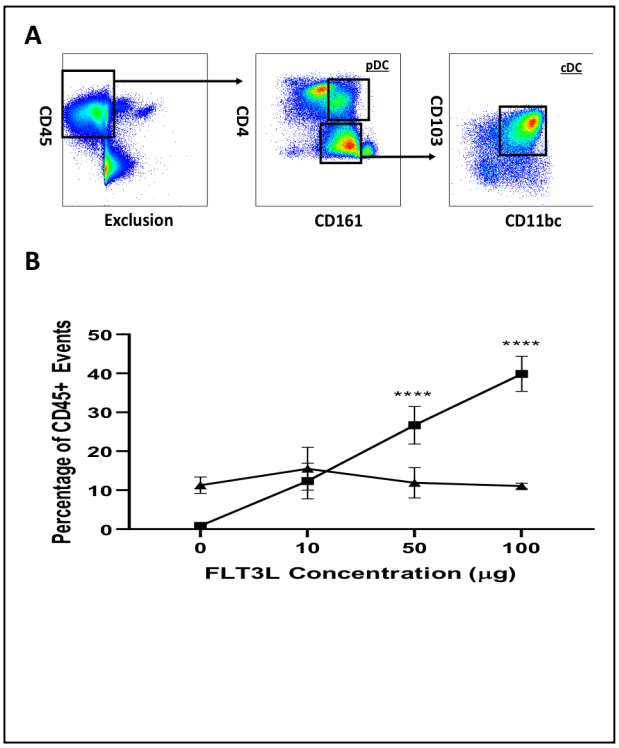


Figure 1. DC characterization.
A: A representative gating strategy for cDCs and pDCs. After gating on single live cells that were CD45+ and Exclusion–(CD3 and CD45RA),the cDCs are CD161 intermediate, CD4-, CD11bc+, CD103+ and pDCs are CD161+ and CD4+
B: Titration curves were established for several FLT3L concentrations, and a 2-way ANOVA followed by Tukey's multiple comparisons test revealed that cDC 50ug and 100ug are significantly different than cDC 0ug ($p<0.0001$).

Maternal extracellular vesicles cross-dressing of cord blood antigen presenting cells is associated with graft allotolerance

Diego Lema, Ewa Jankowska-Gan, Stacey McMorrow, Jeremy Sullivan, David Al-Adra, Sami Kanaan, Afsar Naqvi, J Lee Nelson, William Burlingham

Submitter	Diego Lema
Phone	608501939
Email Address	lema@surgery.wisc.edu
Classification	Graduate student
Division	Transplant
Lab	Burlingham
Science Type	Basic science
Keywords	Exosomes, extracellular vesicles, transplant, NIMA

Abstract Starts on Page 2.

Introduction: While transplantation remains the only therapeutic option available for many diseases, its success is hampered by immune rejection of the graft. The principal target of the donor immune system are mismatched HLAs, with the number of mismatched alleles generally correlating with the rate of rejection. However, if these HLA mismatches are non-inherited maternal antigens (NIMAs), i.e., HLAs present in the mother yet not in the offspring, graft outcomes improve. Preclinical studies in murine models have shown that maternally-derived cells cross the placenta during pregnancy and persist in the offspring for live. There, they secrete extracellular vesicles (EVs) that transport NIMAs that are acquired by the offspring's dendritic cells (DCs), "cross-dressing" them. In addition, they transport micro RNA (miRNA) that upregulates expression of the immune regulatory surface molecule PD-L1. Presentation of NIMA in PD-L1 expressing DCs results in T cell tolerance towards these antigens. However, these observations have not yet been made in humans.

Methods: We isolated immune cells from 12 cord blood of full-term, non-complicated pregnancies for which the mother and child were HLA-typed and NIMAs identified. We analyzed these cells for expression of NIMAs using multicolor flow cytometry and imaging flow cytometry. We performed qPCR to study the presence of maternal microchimeric cells in the cord blood. We isolated EVs from cord blood plasma using size exclusion columns and ultracentrifugation. Nanoparticle tracking assays, ELISA and qPCR were used to study cord blood expression of NIMAs and PD-L1 as well as miRNA affecting PD-L1 expression.

To translate these results to transplantation, we performed similar assays on graft-infiltrating immune cells isolated from explanted liver and kidney grafts with identified HLA mismatches that were NIMAs.

Results: We identified expression of NIMA in the surface of both myeloid (mDC; ~1.7%) and plasmacytoid (pDC; ~2.2%) populations of cord blood DC in half of our samples. While PD-L1 expression was low in non-cross dressed DCs, it was significantly higher in their cross-dressed counterparts (18% vs 60%, $p=0.0016$ for mDCs, 20% vs 60%, $p=0.0243$ for pDCs). Imaging flow cytometry showed a spotted, punctate expression of NIMA in cross-dressed mDCs and pDCs, consistent with an EV-mediated mechanism of acquisition of these molecules. PD-L1 was similarly distributed and co-localized with acquired NIMA, suggesting that, in contrast to mice, PD-L1 is transported in EVs together with NIMA (not a miRNA phenomenon). In kidney and liver grafts, we identified infiltrating host DCs cross-dressed with donor HLA (the NIMA mismatch). PD-L1 was negligible in non-cross dressed DCs but approached 100% in their cross-dressed counterparts, mirroring our observations in cord blood.

Conclusions: Cord blood DCs acquire NIMAs via EVs and present these antigens in the context of PD-L1, contributing to NIMA-specific allotolerance. This phenomenon is replicated in NIMA-mismatched transplants. Further characterization of the EVs mediating this phenomenon will shed light in the mechanisms involved and potential applications.

B25

Comparison of a Topical v. Systemic Dual PI3K/mTOR Inhibitor in Preventing Anal Cancer in Mice

M Ziolkowski, T Moyer, L Gunder, M Keating, M Finlay, P Bertrang, EH Carchman

Submitter	Marissa Ziolkowski
Phone	2624099571
Email Address	mziolkowski@wisc.edu
Classification	Undergraduate Student
Division	Surgery
Lab	Carchman Lab
Science Type	Basic Science
Keywords	HPV, anal cancer, dysplasia, autophagy, oncogenes

Abstract Starts on Page 2.

Introduction: Anal dysplasia and anal cancer are ever-growing health problems. Current treatments for anal dysplasia are poorly tolerated, with significant recurrence rates. We have previously shown the importance of the autophagy in the development of anal dysplasia and anal cancer. This study investigates the efficacy of autophagic induction, by use of a dual mTOR/PI3K inhibitor applied topically versus administered systemically, in preventing anal cancer in mice with established anal dysplasia.

Methods: This study used *K14E6/E7* mice, expressing HPV16 E6 and E7 oncogenes in all epithelial cells. To model patients with low-grade dysplasia, mice began treatment at 15 weeks of age; at 15 weeks of age, the majority of mice exhibit low-grade anal dysplasia. Mice were treated weekly with the topical carcinogen 7,12 dimethylbenz[a]anthracene (DMBA) to promote anal carcinogenesis. Mice were randomly assigned to treatment groups: no treatment, DMBA only, topical Samotolisib, DMBA with topical Samotolisib, systemic Samotolisib, and DMBA with systemic Samotolisib. Topical Samotolisib (1% w/v) was administered to the anus and systemic Samotolisib (4.5 mg/kg) was given via oral gavage daily for 20 weeks. Weekly observations were made to monitor tumor incidence. At 35 weeks of age, anuses were harvested. Tumor incidence was assessed using two-sided Fisher's t-test.

Results: None of the control mice or the mice treated systemically with Samotolisib alone developed overt tumors over 20 weeks. One of the 26 mice (3.85%) treated topically with Samotolisib alone developed an overt tumor. All 11 mice (100%) treated with DMBA alone developed overt tumors, whereas 7 of the 15 (46.67%) mice given topical Samotolisib with DMBA and 5 of the 13 mice (38.46%) treated with systemic Samotolisib with DMBA developed overt tumors. Differences in tumor incidence were significant between mice treated with topical Samotolisib with DMBA and DMBA only (p-value=0.000), as well as between mice treated with systemic Samotolisib with DMBA and DMBA only (p-value=0.0002). There was no significant difference between topical Samotolisib with DMBA and systemic Samotolisib with DMBA treatments (p-value=1.000).

Conclusions: Inhibition of PI3K/mTOR pathways using either a topical or systemic dual PI3K/mTOR inhibitor is effective in preventing anal cancer development in mice with established low-grade anal dysplasia.

B12

Characterization of functional deficits along the aerodigestive and gastrointestinal tracts in the *Pink1-/-* rat model of Parkinson disease

Maryann N. Krasko, Cynthia A. Kelm-Nelson, Michelle R. Ciucci

Submitter	Maryann N. Krasko
Email Address	krasko@surgery.wisc.edu
Classification	PhD Student
Division	Otolaryngology
Lab	Ciucci Lab – Michelle R. Ciucci, PhD., CCC-SLP
Science Type	Basic Science
Keywords	Parkinson disease, Swallowing, Gastrointestinal Tract, Rat

Abstract Starts on Page 2.

Introduction: Parkinson disease (PD) is a whole-body degenerative disorder with pathology in both the central nervous system (CNS) and in peripheral nerves and organs. Although the full etiology is not yet known, recent evidence suggests that early-onset pathology, such as misfolded alpha-synuclein, may spread from the gastrointestinal (GI) tract ascending to the brain. As such, many motor and non-motor deficits throughout the aerodigestive and GI tracts may serve as early disease biomarkers, including dysphagia, delayed gastric emptying, and constipation. However, because these deficits can also appear as common, non-specific, or a result of normal aging, they often go unreported, making the subsequent identification, treatment, and study of swallowing and GI dysfunction in the early stages of PD difficult in humans. Early-onset genetic animal models are a useful tool for studying the prodromal phase of disease. The *Pink1-/-* rat has thus far been promising, showing the progressive nature of salient early PD deficits such as vocal, chewing, and limb dysfunction. The aims of this study were to examine the progressive development of 1) swallowing and 2) GI deficits in this model of PD. We hypothesized that *Pink1-/-* rats would show early and progressive oropharyngeal dysphagia, delayed gastric emptying, and signs of constipation.

Methods: Thirty male rats were tested at 4 (*Pink1-/-* = 15, wildtype controls (WT) = 15) and 6 (*Pink1-/-* = 7, WT = 6) months of age. Videofluoroscopic images of rats ingesting a peanut-butter-barium mixture were taken at 30 frames/second. Mastication rate (cycles/second) and bolus area (mm^2) were measured. Videofluoroscopic images of rats post-oral gavage of 2 mL of liquid barium were also obtained to track barium contents at the stomach, small intestine, caecum, and colon at hours 0-6 post-barium gavage. Data including number of fecal emissions and average weight (grams) of fecal emissions over a 24-hour period were also collected. Two- and three-way mixed model ANOVAs were performed for swallowing and GI data, respectively ($\alpha<0.05$).

Results: Compared to WT controls, *Pink1-/-* rats showed slower rates of mastication ($p<0.001$) and swallowed larger boluses ($p<0.001$) at both 4 and 6 months of age. No differences were noted for gastric emptying ($p>0.05$). Two hours post-barium gavage, WTs began showing presence of contents in the colon while *Pink1-/-* rats did not. This was significant by hour 3; *Pink1-/-* rats had fewer contents within the colon compared to WTs ($p<0.01$). *Pink1-/-* rat cages also had a lower fecal pellet count and higher fecal pellet weight after 24 hours at 6 months of age ($p<0.01$).

Conclusions: The *Pink1-/-* rat model of PD showed functional deficits, occurring in early adulthood, within the aerodigestive and GI tracts. Specifically, *Pink1-/-* rats showed signs of oropharyngeal swallowing dysfunction as early as 4 months of age (this is younger than previously reported). This model also demonstrated delayed content transit to the colon and constipation-like signs. The presence of these early oropharyngeal and GI deficits in *Pink1-/-* rats is analogous to those observed in human PD and suggests that this model of PD may be useful in studying mechanisms underlying Parkinsonian GI pathology, including the spread of misfolded alpha-synuclein and inflammation, to ultimately advance identification and treatment.

B4

Age influences the impact of stroke on bihemispheric motor cortex connectivity to the jaw and tongue muscles

Miranda J. Cullins and Nadine P. Connor

Submitter	Miranda Cullins
Phone	N/A
Email Address	mcullins@wisc.edu
Classification	Postdoc
Division	Otolaryngology
Lab	Connor
Science Type	Basic
Keywords	Stroke, Dysphagia, Motor Cortex, Age

Abstract Starts on Page 2.

Introduction: Dysphagia commonly occurs after stroke, yet the mechanisms of corticobulbar plasticity after stroke are not well understood. Due to the bihemispheric control of swallowing, it has been suggested that plasticity of the contralesional (intact) cortex drives recovery of swallowing. Age may be an important factor in that stroke most commonly occurs in aged individuals, age is an independent predictor of dysphagia after stroke, and neuroplasticity may be reduced with age. We sought to determine the impact of unilateral stroke and age on cortical plasticity by examining the volume of the sensorimotor cortex that activates the jaw and tongue muscles in both hemispheres.

Methods: Using the middle cerebral artery (MCA) occlusion rat stroke model, intracortical microstimulation (ICMS) was used to map regions of sensorimotor cortex that activate tongue and jaw muscles in both hemispheres. Larger cortical maps suggest greater functional connectivity for muscles important in sensorimotor control of swallowing. Young adult (7 months) and aged (30 months) F344xBN rats underwent either a stroke via left middle cerebral artery occlusion or a control sham surgery, followed by ICMS mapping 8 weeks later. Preliminary data reflected in this abstract included the following sample sizes: 5 Aged Stroke, 5 Aged Sham, 4 Young Stroke, 3 Young Sham.

Results: The volume of ipsilesional sensorimotor cortex that activates both the jaw and tongue was reduced with stroke ($p < 0.001$). The jaw activating region of the contralesional cortex increased in the stroke group vs. sham ($p = 0.041$). Within the aged stroke group, the remaining region of ipsilesional cortex that activates the jaw and tongue was significantly smaller than in the young adult stroke group ($p = 0.007$).

Conclusions: MCA stroke is associated with a significant loss of functional connectivity between the sensorimotor cortex and the muscles of the jaw and tongue, which is greater with age. This reduced cortical input is likely to represent reduced volitional control of the swallowing musculature. An increase in the jaw representation in the intact hemisphere is in agreement with studies that have suggested a role for contralesional cortical plasticity in the recovery of oral-motor function after stroke.

B9

Bioenergetic evaluation of rat styloglossus muscle during fatigue

Tiffany J. Glass, Linda M. Rowe, Jared Cullen, Nadine P. Connor

Submitter	Tiffany Glass
Phone	651 343 6048
Email Address	glass@surgery.wisc.edu
Classification	Academic staff
Division	Otolaryngology
Lab	Connor
Science Type	basic
Keywords	Fatigue, rat, styloglossus, muscle

Abstract Starts on Page 2.

Introduction: Increased fatigue is a characteristic of aging muscle, and can occur after exercise. In skeletal muscle, glycolysis generates ATP from glycogen reserves stored in myofibers. Depleted glycogen stores contribute to muscle fatigue. When muscle bioenergetic substrates such as glycogen and ATP are depleted by exercise, transcription of genes involved in bioenergetic homeostasis is initiated. One of these genes, *Slc25a25,* (a mitochondrial *ATP*-$Mg^{2+/}$Pi solute transporter), is instrumental in use of mitochondrial ATP. It has previously been demonstrated in limb muscles that treadmill running to a state of fatigue results in reduced glycogen content, as well as increased abundance of *Slc25a25*. In this work, we tested the hypothesis that styloglossus (SG) muscle of the tongue would similarly demonstrate reduced glycogen content and increased expression levels of *Slc25a25* in this experimental fatigue condition.

Methods: Old male Fischer 344-Brown Norway rats were trained to undergo either a treadmill fatigue regimen (treadmill running) (n=5), or routine sedentary control conditions (n=5). Rats in the treadmill group ran until a state of fatigue, upon which they were promptly euthanized and muscles were isolated. Soleus (limb) muscles were analyzed to confirm limb muscle glycogen depletion in the fatigue group, and styloglossus (SG) muscles were analyzed for both glycogen content and gene expression levels. Muscle glycogen content was quantified with a colorimetric plate assay (Sigma MAK016), in samples run in duplicate. Muscle gene expression was quantified through qRT-PCR with Taqman primers, using *hprt* as a housekeeping control gene. Each biological sample was run in triplicate, and each set of triplicate reactions was repeated at least twice to confirm reproducibility. Data were analyzed by unpaired t-tests.

Results: There were significant reductions of muscle glycogen content in soleus muscles of the fatigue group as compared to control group ($p < .01$). SG muscles in the fatigue group also demonstrated significantly less glycogen content than SG muscles in the control group ($p<.05$). SG muscles in the fatigue group showed significantly increased relative expression of *Slc25a25* ($p = .001$) as compared to the control group.

Conclusions: These results demonstrate reduction in tongue muscle glycogen content and increased expression of a mitochondrial *ATP*-$Mg^{2+/}$Pi solute transporter in the tongue muscles of old rats immediately following a fatigue paradigm. These results constitute initial findings of a larger study designed to determine how tongue muscle fatigue is involved in age-related swallowing disorders, and how tongue muscle exercise may influence resilience to fatigue in the context of aging.

B13

MR1 overexpression is related with poor clinical prognosis in glioma

Phillip Kubica, Mario Henriquez, Marpe Bam, Montserrat-Lara-Velazquez, Seema Sira, Irene Ong, Peng Liu, Raj Priya, Shahriar Salamat, Randy Brutkiewicz and Mahua Dey

Submitter	Phillip Kubica
Phone	608-609-6703
Email Address	pkubica@wisc.edu
Classification	Medical Student
Division	Department of Neurological Surgery
Lab	Mahua Dey, M.D.
Science Type	Basic Science
Keywords	MR1, MAIT cells, glioblastoma, glioma, survival

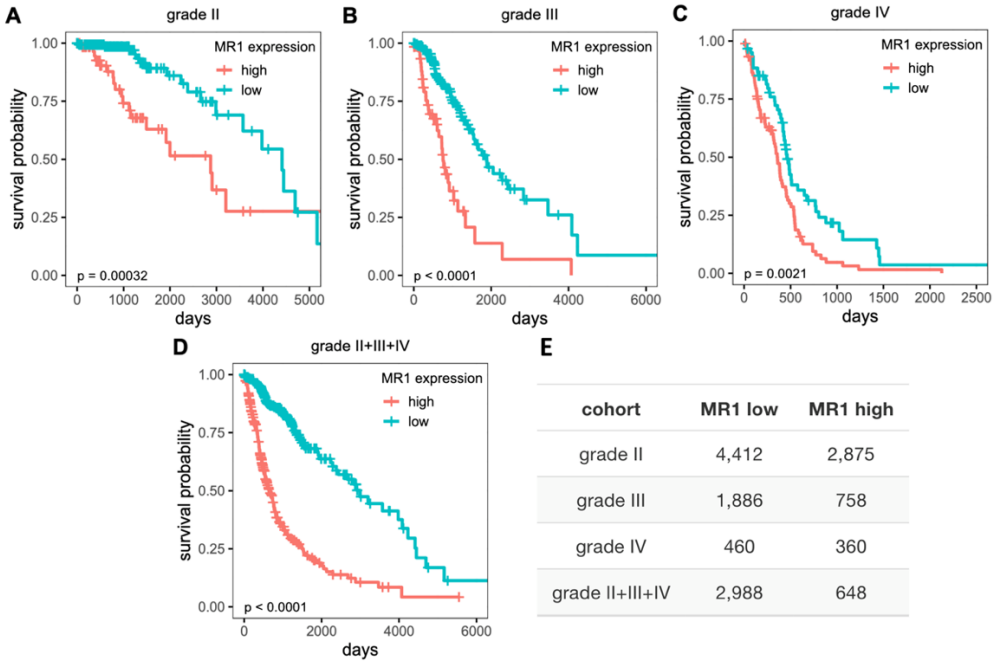
Abstract Starts on Page 2.

Introduction: Glioblastoma is the most common and aggressive brain tumor with near universal fatality. It is known to evade the immune system by generating an immunosuppressive state. Additionally, major histocompatibility complex (MHC) class I molecules are important mediators of CD8 activation and can be downregulated by cancer cells to escape immune surveillance. MR1 is a non-classical MHC class I-like molecule responsible for the activation of mucosal associated invariant T (MAIT) cells. Although high levels of MR1 expression should enhance cancer cell recognition, various cancers demonstrate MR1 overexpression with unknown implications. Here, we study the role of MR1 in glioma malignancy.

Methods: Using multi-omics data from The Cancer Genome Atlas (TCGA), we studied MR1 expression patterns, their impact on survival in solid tumors, gene expression profiles, methylation levels, and transcription factor (TF) expression.

Results: We observed that MR1 is overexpressed in glioma and other solid tumors (breast, renal, and thyroid) when compared to normal tissue. However, only glioma specifically had a negative correlation with survival and demonstrated global dysregulation of genes in an MR1-dependent manner. Epigenetically, high MR1-expressing tumors had decreased MR1 methylation and an upregulation of 4 predicted TFs.

Conclusions: For the first time, we show that MR1 expression is a predictor of clinical outcome in glioma patients showing a strongly negative correlation in survival and unique genetic profiles related to immune dysregulation. Given our data, MR1 should be considered as a novel prognostic marker to help direct patient treatment and could eventually be implemented in immunotherapeutic approaches for brain tumors.



E

cohort	MR1 low	MR1 high
grade II	4,412	2,875
grade III	1,886	758
grade IV	460	360
grade II+III+IV	2,988	648

Figure 1. MR1 expression in grade II, III, and IV gliomas and correlation with survival.

(A-D) High MR1 expression is linked with decreased overall survival in low (II) and high (III,IV) grade gliomas. Cutpoint was identified through maximally selected rank statistics. **(E)** Median survival for glioma patients according to MR1 expression levels.

B16

Bandage-like Nanogenerator-driven Electrical Stimulation Enhances Wound Healing in Human Skin

Aiping Liu, Yin Long, Jun Li, Lily Meronek, Xudong Wang, Angela Gibson

Submitter	Aiping Liu
Phone	608-262-9712
Email Address	Aliu26@wisc.edu
Classification	Scientist
Division	Surgery
Lab	Angela Gibson, MD, PhD
Science Type	Basic Science
Keywords	Wound Healing, Electrical Stimulation, Nanogenerator, Human Skin, Re-epithelialization

Abstract Starts on Page 2.

Introduction: Acute and chronic wounds affect 8.5 million patients in the US alone; to combat the escalating costs, effective, safe, and easy-to-use approaches to wound care are highly desired. Electrical stimulation has been shown to promote wound healing and regeneration, however, clinical applications are limited by cumbersome external power. We have developed a bandage-like wearable nanogenerator (NG), which is self-powered by body movements to deliver electric stimulation (ES). This NG-ES bandage is highly effective in rodent wound healing. Considering the inherent differences in healing between rodents and humans, the objective of this study was to test the efficacy and tissue-level effects of NG-driven ES on human skin wounds using a xenograft mouse model of human skin wound healing established in our lab.

Methods: Partial thickness human skin (2 cm x 2 cm in size) procured from elective surgeries was grafted onto immunocompromised nude mice. Full thickness excisional wounds were created in the human skin graft using a 3-mm biopsy punch eight weeks after grafting to allow for human skin engraftment on mouse wound bed prior to wounding. Mice were bandaged around the torso with or without NG-driven ES treatment (**Figure 1A**). Wounds were observed grossly throughout the healing process. On Day 4 and the day of wound closure (Day 7), tissues were harvested and processed for H&E staining to evaluate for re-epithelialization and tissue architecture. Various IHC stains were also performed on the tissue to identify critical cellular processes in wound healing.

Results: The earliest observable differences in the wound healing between ES and control wounds were visualized grossly on Day 2. Complete wound closure was identified in the ES treated mice on Day 7, compared to unhealed control wounds (**Figure 1 B**). Microscopic evaluation confirmed that ES wounds are fully re-epithelialized, in contrast to the control wound (Figure 1C). In addition, we found that more neutrophils accumulate at the ES wounds compared to the non-treated wounds on Day 4. This robust response resolves in the ES treated wounds on Day 7 compared to the non-treated wounds where neutrophil abundance persists. By day 7, ES increased vasculature as indicated by CD31 positive cells on the wound edges compared to the non-stimulated wounds.

Conclusions: We have developed a clinically relevant model system of human skin wound healing to test the efficacy and underlying tissue-level effects of NG-driven ES. ES enhances the rate of wound healing in human skin, largely through re-epithelialization. ES influences cell behaviors associated with an increase in angiogenesis, and early inflammatory response and resolution in the wound. *In vitro* experiments on dermal and epidermal cells are warranted to identify the contribution of each cell type to support the *in vivo* findings and together will provide a comprehensive understanding of the effect of electrical stimulation on the underlying cellular processes of wound healing.

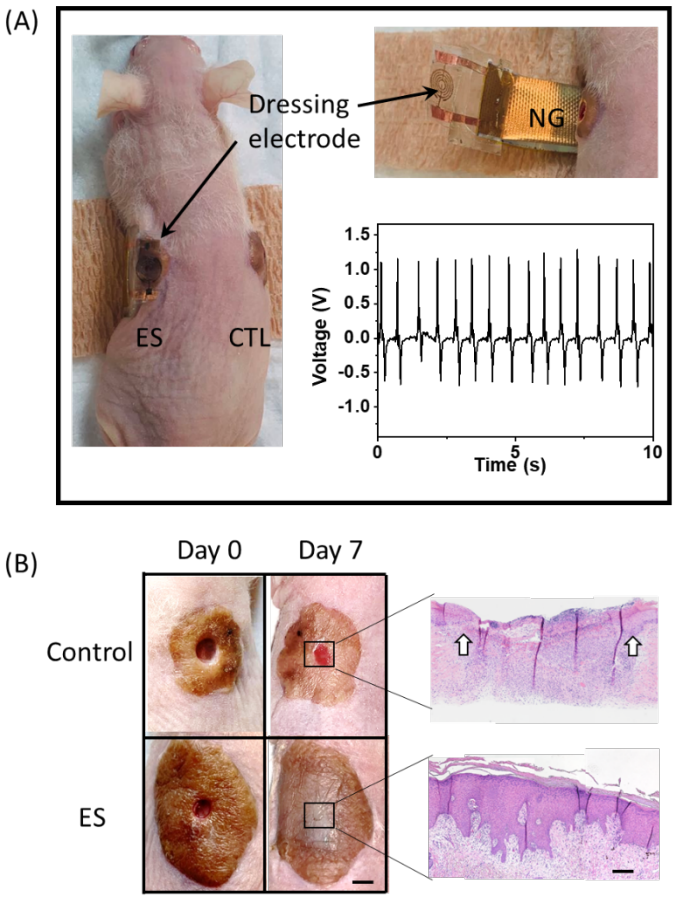


Figure 2. **Wearable-NG ES increases the healing rate of excisional wounds in human skin xenograft on mice.** (A) The NG ES device on mice with human skin xenograft and the voltage output obtained from respirations, (B) gross photograph of wound healing after 7 days with or without ES treatment, and H&E stain demonstrating complete re-epithelialization in ES treated wounds. Arrows indicate the gap in the leading edges of neo-epidermis in non-treated wound. The scale bars in the gross photograph= 3 mm and in the histological image = 200 µm.

B17

Excised Modeling Supraglottic Pressure Project

Nikita Menon

Submitter	Nikita Menon
Phone	612-701-4552
Email Address	nmenon@wisc.edu
Classification	Otolaryngology
Division	Straws Team
Lab	Dr. Jack Jiang (UW Laryngeal Physiology Lab)
Science Type	Basic Science
Keywords	Supraglottal Pressure, Larynx, Therapy, Phonation

Abstract Starts on Page 2.

Introduction: Phonation into a resonance tube, is a well-known practice that has been used in voice therapy to improve vocal economy by increasing supraglottal pressure and acoustic impedance in the vocal tract[1,2]. Straw phonation therapy, a specific therapy, involves vocal exercises performed into a tube that artificially creates a semi occluded vocal tract (SOVT)[1]. SOVTs have shown beneficial results. Increased supraglottal pressure reinforces vocal fold (VF) vibration which increases vibratory amplitude and aids in reaching a resonant voice. Previous studies have found that lower values of phonation threshold pressure (PTP), the minimum amount of lung pressure required for the onset of VF oscillation, and phonation threshold flow (PTF) are both good indicators of phonation ease[3]. A decrease in PTP and PTF is directly attributable to increased supraglottal pressure and impedance of the vocal tract[4]. Assessing how supraglottal pressure affects vocal economy will provide a better grasp of how it impacts the phonating larynx and the VFs, as no detailed analysis on this has been done. Previous studies have found that straw phonation therapy increases acoustic impedance, but no studies have separated supraglottal pressure from impedance, nor has the optimal supraglottal pressure level for vocal economy been determined. We hypothesize that the increase in supraglottal pressure would create an abducted glottal setup which would result in low impact VF oscillation and better vocal economy as measured by a decrease in PTP and PTF.

Methods: Studies have analyzed the effects of vocal extensions or constrictions and altering airflow on straw therapy using an excised larynx bench apparatus, indicating the excised larynx bench apparatus provides simulation for altering supraglottal pressures[2]. 20 canine larynges will be mounted on a bench apparatus following specifications by Jiang and Titze[4]. To measure vocal economy, PTP and PTF will be measured. The apparatus is in a sound attenuated room to minimize background noise and allows for stability of humidity and temperature. The larynx will be attached to a pseudo lung output via a hose clamp and tightened so air cannot escape. VF adduction and elongation will be constant across all larynges.

Each larynx will be subject to a pre control trial in which the larynx will be brought to phonate with the air valve with no added pressure. Further, the larynx will be exposed to five experimental trials, with pressure conditions of 4cm H2O, 8cm H2O, 12cm H2O, 16cm H2O, and 20cm H2O using a pressure transducer. The constant pressure source will be passed through a flowmeter, followed by two humidifiers in series which will connect to the pseudo lung[2]. The pressure will be measured directly below the larynx, via a digital pressure meter. Each larynx will undergo 5 phonations at each experimental condition. A five-minute rest period will occur in between each trial to eliminate any lingering effects with hydration via water applied periodically to ensure the larynges do not dehydrate. Last, the larynges will be subject to a post control trial in which no external pressure is applied, but this will test the effects of fatigue. This will be repeated on ten larynges to get consistent data, and the results will be analyzed after.

Results: Currently, our results are still pending as data collection is ongoing. It is expected that the optimal supraglottal pressure is 20cmH2O from the pressure values we are testing. The higher supraglottal pressure creates an abducted glottal setup which would result in low impact VF oscillation and better vocal economy which will be indicated by a decrease in PTP and PTF.

Conclusions: Our conclusions will be drawn after data collection is complete; however, our results will pave the way to improve and yield more effective straw phonation therapies in the clinical setting. This will help modify the most beneficial pressures for voice therapy in humans to improve vocal economy.

B8

Microstructural Differences Between Laryngeal Animal Models

Jarett Jones, Jack Ersbo; BS, Jack Jiang; MD PhD

Submitter	Jarett Jones
Phone	715-498-5541
Email Address	Jdjones8@wisc.edu
Classification	Undergraduate Student
Division	Division of Otolaryngology-Head & Neck Surgery
Lab	Jack Jiang – Laryngeal Physiology Lab
Science Type	Basic Science
Keywords	Larynx, Vasculature, Collagen, Tissue-Clearing, Animal-Model

Abstract Starts on Page 2.

Introduction: There are clear anatomical and physiological differences between a human laryngeal model and respective animal models; these differences are well characterized. Less well characterized, but equally important are the microstructural differences between various animal models. Selecting the proper animal model for vocal research is an important step in the experimental design. Phonation studies have revealed that different animal models have different phonation ranges under various positive/negative elongations. Furthermore, accurate characterization of the microstructure of several animal models in terms of vascular density, vascular branching, collagen density, and collagen organization will help researchers select the proper animal model for a specific experimental application. Tissue clearing utilizing the novel CLARITY procedure can aid in these characterizations of various excised animal larynges.

Methods: Dog, Pig, and Rabbit animal models will be analyzed and characterized by their microstructural properties. 3 Larynges from each animal model will have their vocal folds excised en bloc. The vocal folds will undergo tissue clearing using the CLARITY procedure. Following clearing, the vocal folds will be fluorescently labeled for collagen and blood vessels. After labelling, the vocal folds will be imaged using fluorescent microscopy. An observational measurement will be taken to determine collagen organization and collagen density will be determined by measuring the number of fibers per unit volume of the relevant tissue area. Vascular branching will be determined measuring the number of branches per unit volume of the relevant tissue area.

Results: Results will consist of both quantitative and qualitative data regarding the microstructural components mentioned in the introduction. Results will be able to characterize and potentially differentiate between animal models.

Conclusions: Based on the results section, quantitative and qualitative, conclusions will be drawn regarding which characteristics of each animal model make that particular model advantageous for specific applications. Conclusions about specified microstructural components may speak to the phonatory capabilities of the model or the stiffness of the tissue. This knowledge is important to have when selecting the right animal model for vocal experimentation.

B14

Thyroarytenoid muscle gene expression in a rat model of early Parkinson disease.

Sarah A. Lechner, Heidi Kletzien, Samantha E. Lettenberger, Taylor A. R. Kaldenberg, Natalie K. Pahapill, Amy Regenbaum, Stephen C. Gammie, Cynthia A. Kelm-Nelson

Submitter	Sarah A. Lechner
Phone	608-262-6122
Email Address	slechner@wisc.edu
Classification	Research Associate
Division	Otolaryngology
Lab	Kelm-Nelson
Science Type	Basic
Keywords	Parkinson disease; rat; ultrasonic vocalization; thyroarytenoid, total RNA sequencing; WGCNA; bioinformatics

Abstract Starts on Page 2.

Introduction: Voice disorders in Parkinson disease (PD) manifest in preclinical stages of the disease and negatively impact quality of life in 90% of individuals. However, the muscle pathology that contributes to laryngeal and voice dysfunction is poorly understood. Complete loss of function in the PTEN-induced kinase 1 gene (*Pink1*) causes an early-onset, autosomal recessive form of PD. Modeled after the human inherited mutation, the translational *Pink1*-/- rat shows cranial sensorimotor deficits including: declines in ultrasonic vocalization variables, negative impacts on the social vocal function, and alterations to thyroarytenoid (TA) muscle structure. Recent data demonstrate increased incidence of centrally nucleated myofibers as well as an increased proportion of the 2L myosin heavy chain isoforms and is suggestive of TA myopathy. The aim of this study was to identify differentially expressed genes in the TA of male *Pink1-/-* rats that may contribute to reported myopathy and muscle dysfunction compared to age-matched wildtype controls. We hypothesized that loss of *Pink1* from the TA muscle: (1) will produce significant changes in expression of genes that directly interact with *Pink1*, (2) alter biological pathways involved in disease mechanisms, and (3) produce a list of significant genes that also overlap between PD and other degenerative disorders.

Methods: Eight-month-old Long Evans rats (n=4 per genotype; *Pink1*-/- and WT) were deeply anesthetized and rapidly decapitated. Whole TA muscles were dissected, total RNA extracted, and the Illumina® Total RNA-Seq TruSeq platform was used to profile differential expression of genes between genotypes. Reads were mapped to the annotated *Rattus Norvegicus* genome in Ensembl. **Statistics**: Gene analysis was performed with the GLM using the EdgeR Bioconductor Package. The *p* value cutoff was set to 0.05; the master list of differentially expressed genes was assigned a NCBI gene otology category. Weighted gene correlation network analysis (WGCNA) was used to construct gene co-expression networks and modules from the dataset including where *Pink1* was a central node. Briefly, data were log 2 transformed, low expression genes were removed, and WGCNA was run using R software. Using a weighted network of genes and expression correlates, correlations were raised to a soft thresholding power β of 12. Unsupervised hierarchical clustering for WGCNA included: minimum module size of 30 genes, signed mode, deepSplit parameter set to 2, mergeCutHeight parameter set to 0.15, and a threshold setting for merging modules of 0.25. The ENRICHR tool was used for functional gene enrichment analysis.

Results: This work generated a list of differentially expressed genes (n=134, $p<0.05$ cutoff) in the TA muscle and highlights several gene pathways implicated in: Parkinson's disease (*Casp7, Pink1*), Parkin-Ubiquitin proteasome degradation (*Psmd12, Psmd7*), MAPK signaling (*Casp7, Ppm1b, Ppp3r1*), and inflammatory TNF-α, Nf-kB Signaling (*Casp7, Psmd12, Psmd7, Cdc34, Bcl7a, Peg3*). We also identified several differentially expressed genes (*Mx1*, *Cxcl9*, *Klk6*, and *Fabp5*) that are also reported to be dysregulated in Alzheimer's disease, ALS, and muscle dystonia.

Conclusions: These data are congruent with previous findings demonstrating changes in the TA muscle, and will provide a scaffold for future therapeutic interventions targeting these genes and pathways to improve vocal function in PD. Further, these data are consistent with our hypothesis that differences in peripheral muscle biology influence the early pathogenesis of vocalizations observed in patients with PD.

B18

Development of cold atmospheric plasma jet device as a novel tool for cancer treatment

Ha M. Nguyen[1,2], Khang Huynh[2], Bindu Anilesh Nair[2], Taylor J Aiken[2], Kevin C Janek[2], D. Benjamin[1], J. M. Blatz[1], F. A. Choudhury[1], Paul Sondel[3,4], Mario Otto[3], J. L. Shohet[1], Hau D. Le[2,3,5]
[1]Department of Electrical and Computer Engineering, [2]Department of Surgery, [3]Department of Pediatrics, [4]Department of Human Oncology, [5]Department of Biomedical Engineering

Submitter	Ha Nguyen
Phone	608-332-7883
Email Address	Mnguyen5@wisc.edu
Classification	Graduate student
Division	Pediatric Surgery
Lab	Le Lab
Science Type	Basic Science
Keywords	Cold atmospheric plasma, cancer, oncology, treatment

Abstract Starts on Page 2.

Introduction: Cold atmospheric plasma (CAP) is a type of room-temperature atmospheric-pressure gaseous electric discharge that can generate a variety of plasma species: ions, electrons, photons, and reactive atomic and molecular species. Over the past few decades, CAP has been demonstrated as a promising and effective treatment for a number of diseases including cancer. Among the reactive oxygen and nitrogen species (RONS) produced by CAP, hydroxyl radicals ($OH^{\cdot}$) are considered one of the most active species. However, the depth of penetration into the living tissue is limited, thus limiting its application for solid cancer treatment. Here, we report our progress in developing a CAP device in the form of a plasma jet (or CAP-jet) to use as an adjunct surgical treatment for positive surgical margin (PSM), neurosurgery, and beyond.

Methods: The development of our CAP-jet device was based on the principles of a dielectric-barrier discharge. The wall of a cylindrical quartz tube (inner diameter of 5 mm, outer diameter of 9 mm, and length of 80 mm) plays the role of a dielectric barrier to separate two electrodes: (1) a needle-like metallic high-voltage electrode that coincides with the tube axis and (2) a ring-like grounded metallic electrode that surrounds the tube. The discharge is ignited when a high-voltage source with a chosen waveform (e.g., sine, square, or triangle waveform) having a peak-to-peak voltage in the range from 0 to 20 kV and a frequency in the range from 0 to 23 kHz is applied between the two electrodes. These parameters can cover a wide range of dielectric-breakdown voltages for different feed gases including argon, helium, air, nitrogen, *etc*. A mixture of different feed gases can be employed to optimize the chemistry of the relevant reactive species. The flow rate of feed gas through the quartz tube can be adjusted in the range from 0 to 5 lpm. In addition, the distance between the CAP jet nozzle to the treated surface can also be varied. Plasma discharge and nozzle location can be controlled using a LABVIEW program, from which the voltage, frequency and treatment time can be set. Device portability, versatility, robustness, and user-friendliness are required for both for *in vitro* and *in vivo* experiments. Here, we report our CAP jet's functionality and quantification of hydroxyl radical free radical measurement using optical and chemical methods, and pH measurements, etc.

Results: The ultraviolet-visible (UV-Vis) emission spectra measured for the CAP-jet using air or argon as the feed gas show that the intensity of the emission of $OH^{\cdot}$ at 309 nm is higher (thus, higher $OH^{\cdot}$ content) for an argon CAP jet than for an air CAP jet. Argon gas also does not considerably change the pH of the media of interest (culture medium, 1% PBS, and ID water). The $OH^{\cdot}$ content characterized by the UV-Vis emission spectroscopy is in agreement with $OH^{\cdot}$ measurement using either coumarin or terephthalic acid as an $OH^{\cdot}$ fluorescent probe. CAP jet device kills significantly more cancer cells (NSX2, 9464D, GL261) than normal cells (NIH/3T3), with direct relationship to the duration of time exposure up to 120s. Also, *in vivo* application of CAP jet device showed no ill effects on the mice treated up to 5 minutes. Preliminary data also showed reduced recurrence of tumor in mice treated with CAP jet after underwent partial tumor resection, compared to untreated mice.

Conclusions: A functional CAP jet was constructed and operated and can produce hydroxyl radicals in addition to other RONS. The device demonstrated its effectiveness against both cancer cell lines and residual cancer in a murine model. Future work will be focused on controlling the number and type of radical species produced by CAP-jet, their fluxes and the device's optimal parameters to produce the most benefit on cancer-killing without harming normal tissues.

B19

GSK2593074A Blocks Progression of Existing Abdominal Aortic Aneurysms

Mitri K. Khoury, MD; Ting Zhou, PhD; Huan Yang, PhD, Samantha R. Prince, Kartik Gupta, MS; Amelia R. Stranz, Qiwei Wang, PhD; Bo Liu, PhD

Submitter	Samantha Prince, MS3
Phone	608-609-9931
Email Address	sprince2@wisc.edu
Classification	Medical Student
Division	Department of Surgery, Vascular Surgery
Lab	Dr. Bo Liu, PhD
Science Type	Basic Science
Keywords	Abdominal aortic aneurysm, macrophages, vascular smooth muscle cells, necroptosis, vascular inflammation

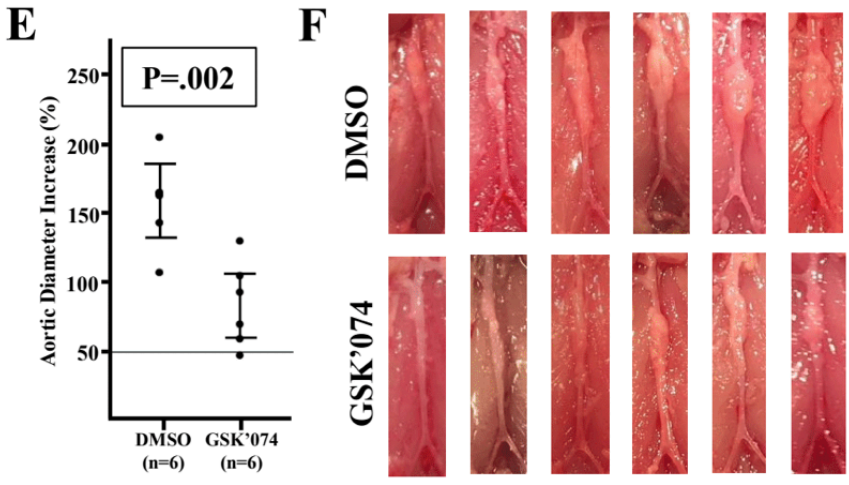
Abstract Starts on Page 2.

Introduction: Receptor interacting proteins kinase 1 and 3 (RIPK1 and RIPK3) have been shown to play essential roles in the pathogenesis of abdominal aortic aneurysms (AAAs) by mediating necroptosis and inflammation. We previously discovered a small molecular inhibitor GSK2593074A (GSK'074) that binds to both RIPK1 and RIPK3 with high affinity and prevents AAA formation in mice. In this study, we evaluated whether GSK'074 can attenuate progression of existing AAA in the calcium phosphate model.

Methods: C57BL6/J mice were subjected to the calcium phosphate model of aortic aneurysm generation. Mice were treated with either GSK'074 (4.65 mg/kg/day) or DMSO-controls starting 7 days after aneurysm induction. Aneurysm growth was monitored via ultrasound imaging every 7 days until harvest on day 28. Harvested aortas were examined via immunohistochemistry. The impact of GSK'074 on vascular smooth muscle cells and macrophages were evaluated via flow cytometry and transwell migration assay.

Results: At the onset of treatment, mice in both control (DMSO) and GSK'074 groups showed similar degree of aneurysmal expansion. The weekly ultrasound imaging showed a steady aneurysm growth in DMSO-treated mice. The aneurysm growth was attenuated by GSK'074 treatment. At euthanization, GSK'074-treated mice had significantly reduced increases in aortic diameter from baseline as compared to the DMSO-treated mice (83.2% SEM $\pm$ 13.1% versus 157.2% SEM $\pm$ 32.0%, P<.01). In addition, aortas in the GSK'074 group were protected from negative remodeling as demonstrated by reduced macrophages (F4/80, CD206, MHCII), less gelatinase activity, higher level of smooth muscle cell-specific myosin-heavy chain, and better organized elastin fibers compared to DMSO controls. *In vitro*, GSK'074 inhibited necroptosis in mouse aortic smooth muscle cells; whereas it was able to prevent macrophage migration without affecting *Il1b* and *Tnf* expression.

Conclusions: GSK'074 is able to attenuate aneurysm progression in the calcium phosphate model. The ability to inhibit both vascular smooth muscle cell necroptosis and macrophage migration makes GSK'074 an attractive drug candidate for pharmaceutical treatments of aortic aneurysms.



B5

Circulating RIPK3 is Elevated in Aortic Aneurysm and Promotes Coagulation

Elise DeRoo MD, Mitri Khoury MD, Scott LeMaire MD, Ying Shen MD PhD, Bo Liu PhD

Submitter	Elise DeRoo
Phone	203-912-6527
Email Address	ederoo@wisc.edu
Classification	Resident
Division	Vascular Surgery
Lab	Dr. Bo Liu
Science Type	Basic Science
Keywords	Aorta, Aneurysm, Receptor Interacting Protein Kinase (RIPK), Coagulation

Abstract Starts on Page 2.

Introduction: Aortic thrombus is invariably present in aortic aneurysm. Proposed mechanisms by which intraluminal thrombus contributes to aneurysm progression include increased vessel wall hypoxia and local inflammation, however, exactly how the local aortic environment promotes thrombus formation remains elusive. Previous work from our lab demonstrated that receptor interacting protein kinase 3 (RIPK3), a protein that interacts with receptor interacting protein kinase 1 (RIPK1) to mediate a form of cell death known as necroptosis, promotes abdominal aortic aneurysm (AAA) by causing lytic death of aortic smooth muscle cells. *Ripk3*$^{-/-}$ mice are relatively protected from experimentally induced AAA compared to *Ripk3*$^{+/+}$ mice. The current study sought to test the hypothesis that circulating RIPK3 is elevated in aortic aneurysm patients and that extracellular RIPK3 stimulates thrombus formation through interactions with the clotting cascade.

Methods: RIPK3 levels were measured by ELISA in plasma from 8-12 week old C57BL/6 mice that underwent an AAA inducing surgery ($CaCl_2$ model), sham surgery, or no surgery, from *Ripk3*$^{+/+}$ and *Ripk3*$^{-/-}$ mice without AAA, and in human subjects with thoracic aortic aneurysms (TAA) and healthy controls. Thrombin generation was assessed by a thrombin generation assay (TGA) in these groups, and in plasma from *Ripk3*$^{+/+}$ and *Ripk3*$^{-/-}$ mice without AAA. Recombinant RIPK3, with or without heat inactivation, and inhibitors of the necroptosis pathway (RIPK3 inhibitor GSK'843 &, RIPK1 inhibitor Necrostatin-1s) were introduced in TGAs to better define the interaction of RIPK3 with the clotting cascade.

Results: Plasma RIPK3 and thrombin generation were significantly elevated in mice with AAA at 4 days post-operatively (Figure 1A, B). Thrombin generation was reduced in *Ripk3*$^{-/-}$ mice without aneurysm compared to *Ripk3*$^{+/+}$ mice without aneurysm. Recombinant RIPK3 restored thrombin generation in a dose-dependent fashion in *Ripk3*$^{-/-}$ plasma (data not shown). In patients with TAA, a positive correlation was found between plasma RIPK3 level and the TGA endpoints peak height & velocity index (Figure 1C, D). In plasma from healthy humans, a dose dependent decrease in thrombin generation was observed after treatment with GSK'843 but not Necrostatin-1s. Conversely, addition of recombinant human RIPK3 increased thrombin generation in a dose-dependent fashion. Heat inactivation of RIPK3 abrogated the effects of RIPK3 on thrombin generation (data not shown).

Conclusions: Together these findings suggest that elevated circulating RIPK3 may contribute to a procoagulant state associated with aortic aneurysm. Aside from its classic role in necroptosis, RIPK3 stimulates thrombin formation, independent of RIPK1. The current findings are an important step toward better understanding how the local aortic environment promotes thrombus formation in aortic aneurysmal disease.

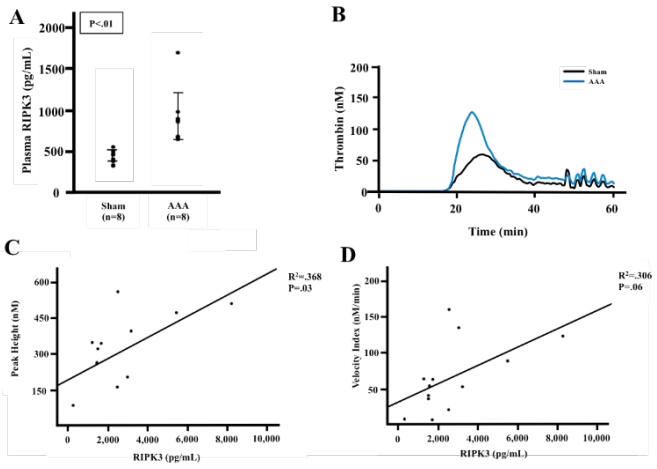


Figure 1. Plasma RIPK3 is elevated in aortic aneurysm and promotes coagulation. (A) Plasma RIPK3 levels in mice with or without AAA. (B) Thrombin generation in plasma from mice with or without AAA (4 days post treatment). (C, D) Correlation of thrombin peak height (nM) and velocity index (nM/min) with plasma RIPK3 levels in patients with TAA.

B20

Spectral Arc Length as a Method to Quantify Pharyngeal High-Resolution Manometric Curve Smoothness

Austin J. Scholp, MS; Matthew R. Hoffman MD, PhD; Sarah P. Rosen, MD; Suzan M. Abdelhalim, MD, MPH; Corinne A. Jones, PhD; Jack J. Jiang, MD PhD; Timothy M. McCulloch, MD

Submitter	Austin Scholp
Phone	815-474-5403
Email Address	scholp@wisc.edu
Classification	Academic Staff
Division	Otolaryngology
Lab	McCulloch HRM Lab
Science Type	Basic Science
Keywords	pharyngeal high-resolution manometry; swallow; spectral arc length; stroke; dysphagia.

Abstract Starts on Page 2.

Introduction: Pharyngeal high-resolution manometry (HRM) has emerged over the last decade as a valuable instrumented assessment for oropharyngeal dysphagia. Data analysis thus far has focused primarily on measures of pressure and duration within key anatomic regions. We apply spectral arc length (SPARC), a dimensionless metric for quantifying smoothness felt to indirectly reflect neuromuscular coordination, as a new method of describing manometric curves. We then use it to distinguish swallows from healthy subjects and those with dysphagia related to stroke.

Methods: Previously collected pharyngeal HRM data from eight subjects with history of stroke and eight age- and sex-matched controls were reviewed. Receiver operating characteristic (ROC) analysis was used to optimize SPARC inputs. SPARC was then computed for the velopharynx, tongue base, hypopharynx, and upper esophageal sphincter (UES) and the values were compared between the two subject groups.

Results: Optimized parameter settings yielded an ROC curve with area under the curve (AUC) of 0.953. Mean SPARC values differed between control and stroke subjects for the velopharynx ($t=3.25$, $p=0.0058$), tongue base ($t=4.77$, $p=0.0003$), and hypopharynx ($t=2.87$, $p=0.0124$). Values were similar for the UES ($t=0.43$, $p=0.671$).

Conclusions: In this preliminary study, SPARC analysis was applied to distinguish control from post-stroke subjects. Considering alternative methods of analyzing pharyngeal HRM data may provide additional insight into the pathophysiology of dysphagia beyond what can be gleaned from measures of pressure and duration alone.

B22

Islet microenvironment stimulates islet health and function in culture

Dan Tremmel, Sara Dutton Sackett, Sam Mitchell, Austin Feeney, Sakar Gupta, Colin Steck, and Jon Odorico.

Submitter	Dan Tremmel
Phone	262-347-9814
Email Address	tremmel@wisc.edu
Classification	Graduate Student
Division	Transplantation
Lab	Odorico
Science Type	Basic Science
Keywords	Islets, Tissue Culture, Architecture, Microenvironment, Function

Abstract Starts on Page 2.

Introduction: Pancreatic islets contain the endocrine cells that regulate blood glucose levels in the body. Islets can be isolated from the pancreas through a combination of enzymatic digestion and density gradient, resulting in purified islet clusters that can be cultured in suspension for a short period of time and are suitable for various *ex vivo* studies. Isolated human islets are considered the gold standard for studying islet function, to which novel therapies for treating diabetes are compared, such as stem cell-derived beta cells (SCBCs).

Primary islet culture is limited *in vitro* partially due to anoikis-mediated apoptosis in the absence of extracellular matrix (ECM) and other supportive elements of the islet microenvironment, which is damaged during the harsh isolation process. Furthermore, long-term reversal of diabetes following clinical islet transplantation is reduced due to low islet survival throughout the isolation, culture, and transplantation process. To study the role of ECM on islet survival and function, our lab has derived a human pancreas ECM hydrogel (hP-HG) from decellularized human pancreas tissues.

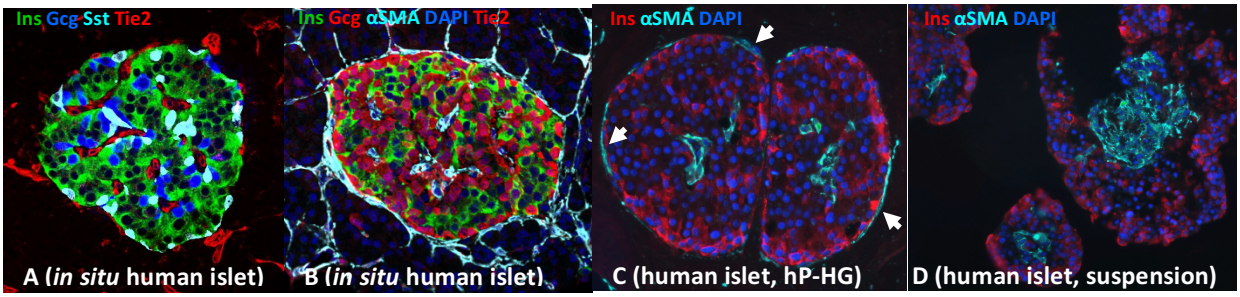
Methods: Isolated human islets were cultured in suspension or hP-HG for up to 7 days, and survival was assessed with an MTS assay every other day. On Day 0, 2 and 7 of culture, islet function was measured through a glucose stimulated insulin secretion assay (GSIS) and protein expression through immunofluorescent (IF) staining. Antibodies against insulin (Ins, β cells), glucagon (Gcg, α cells), somatostatin (Sst, δ cells), Tie2 (endothelial cells), αSMA (mural cells) and a variety of ECM proteins were used to detect and quantify protein expression.

Results: Human islets had improved survival and function in hP-HG culture compared to standard suspension culture. GSIS was found to be 4.7 fold higher in hP-HG culture compared to suspension, with 2.7x increased survival at day 7. Further, we observed an architectural rearrangement of the endocrine cells (α, β, δ) in suspension culture, with the majority of β cells moving to the outside of the clusters; this was significantly reduced in hP-HG culture. Interestingly, the arrangement of non-endocrine cell types and *ex vivo*-ECM expression was dysregulated in islets in suspension (Fig 1D), compared to islets *in situ* (Fig 1A-B), or in hP-HG culture (Fig 1c), in which the αSMA^{+} mural cells form a capsule surrounding the islets (Fig 1C, white arrows).

Conclusions: Human islets cultured in hP-HG have improved survival and function compared to islets cultured in suspension. Furthermore, the architecture and microenvironment of the islets differed among the two culture conditions over time, suggesting that replacement of the ECM leads to retention of islet integrity. Recent insights into synchronized endocrine cell function and endocrine crosstalk with surrounding cell types suggests that cell-cell and cell-ECM interactions are important for regulating islet function. This model may provide a context for studying these mechanisms *ex vivo*, as well as studying islet biology and function in a more *in vivo*-like environment.

Future directions for this study involve culturing SCBCs with hP-HG to test for improved differentiation, maturation, and function, as well as co-transplantation with hP-HG to assess the impact of recapitulating the islet environment at the transplant site on graft survival and function.

Figure 1:


Ins Gcg Sst Tie2
A (*in situ* human islet)
Ins Gcg αSMA DAPI Tie2
B (*in situ* human islet)
Ins αSMA DAPI
C (human islet, hP-HG)
Ins αSMA DAPI
D (human islet, suspension)

B6

Development of a clinically translatable osseointegrated neural interface in sheep.

Zeeda H. Nkana, Kirsten A. Gunderson, Scott K. Odorico, Rashea L. Minor, Samuel O. Poore MD, Aaron M. Dingle

Submitter	Aaron Dingle
Phone	608.509.1778
Email Address	dingle@surgery.wisc.edu
Classification	Associate Scientist
Division	Plastics and Reconstructive
Lab	Poore/Dingle
Science Type	Basic
Keywords	Amputation, prosthesis, prostheses, neural interface

Abstract Starts on Page 2.

Introduction: The use of large animals as preclinical models is a key step in biomedical research yet are underrepresented in the field of neural prosthetic control. Ovine (sheep) models for osseointegrated prosthesis research are well established, but do not consider future implications for neural control of advanced prosthesis. Adult sheep share a similar size, weight, and bone structure to adult humans; however, their anatomy differs significantly. The standard ovine model for osseointegration consists of a metacarpal amputation of the thoracic limb as an analogy for trans-tibial amputation in humans. With recent technological advances in methods of neural interfacing such as the Osseointegrated Neural Interface (ONI), the validity of these new technologies to provide chronic and stable communication between native nerves and advanced prosthetics is required but remains unexplored. This objective requires longitudinal studies in a robust, clinically translatable large animal model, such as the sheep, which already serves as the gold standard model for osseointegration research. While there are generalized topographical maps of the nerves of the thoracic and pelvic limbs of sheep, more granular information, particularly distal to the carpal and tarsal joints where the amputation is often performed, is lacking. The objective of this study is to provide a detailed anatomic description of the major nerves in the thoracic and pelvic limbs distal to the carpal and tarsal joints, identifying anatomical variations towards creating a chronic osseointegrated neural interface for prosthetic control in sheep for clinical translatability to humans.

Methods: Six pelvic and six thoracic cadaveric limbs from mature female, non-lactating sheep (mixed breeds) were collected for anatomical study. Each limb was radiographed allowing measurements of metatarsal and metacarpal bone length, cortical bone thickness, and intramedullary space. Microsurgical dissection was performed to determine the overall topography of the major nerves of the pelvic (superficial fibular, deep fibular, and tibial) and thoracic limbs (superficial radial, dorsal ulnar, deep ulnar, and median) along the metatarsus and metacarpus, respectively. The locations of branch points of each nerve were noted. Circumferences of each nerve were measured at three sites along the metatarsus or metacarpus: the most proximal point, the midpoint, and the most distal point. Illustrations of the variations in nerve branching patterns were made. Histological analysis is currently being performed on nerve sections stained with Gomori's trichrome to identify epineurial thickness and number of fascicles.

Results: Building on current clinically translatable ovine models for osseointegration, we studied the topography of ovine nerves distal to the carpal and tarsal joints in order to design and create an ONI suitable for chronic testing in sheep. Thoracic limb nerves consisted of one dorsal and three ventral nerves, with an average circumference of 5.6 mm and 5.0 mm at the midpoint, respectively. Pelvic limb nerves consisted of one dorsal and two ventral nerves, with an average circumference of 5.3 mm and 7.1 mm at the midpoint, respectively. Bone measurements demonstrate an average metacarpal length of 15.0 cm and an average metatarsal length of 19.5 cm. The average cortical bone thickness for the limbs was 3.685 mm at the midpoint. The average intramedullary canal diameter for the limbs was 9.5 mm at the midpoint. These anatomic data inform the manufacture of a sensory ONI for chronic testing in awake, freely ambulating animals for future clinical translation.

Conclusions: Nerves located below the carpal and tarsal joints were sensory in nature, demonstrating only cutaneous innervation. Nerves were adequate in both length and circumference to allow transposition into the medullary canal and subsequent neural interfacing. Creation of an osseointegrated neural interface in sheep is best suited to the metacarpal bone, in line with current osseointegration models.

B1

Differential Gene Expression in Nerve Gap Repair via the Interrupted Epineural Suture Technique with Low versus High Tension

Kasey Leigh Wood, BS[1] and Marina I. Adrianzen Fonseca, BS,[1] Kirsten A. Gunderson, BS,[1] Zeeda H. Nkana, BS,[1] Aaron M. Dingle, PhD[1], Jacqueline S. Israel, MD,[1] Samuel O. Poore, MD, PhD,[1]

Submitter	Marina I. Adrianzen Fonseca
Phone	415-717-0534
Email Address	adrianzenfon@wisc.edu
Classification	Medical Student
Division	Plastic and Reconstructive Surgery
Lab	Samuel O. Poore, Aaron M. Dingle
Science Type	Basic Science
Keywords	Nerve Regeneration, Nerve Repair, Surgical Nerve Repair, Epineural Suture Techniques, Low, High, Tension, RNA sequencing, Differential Gene Expression

Abstract Starts on Page 2.

Introduction: Reparation of nerves under high tension has proved unfavorable to nerve regeneration given localized ischemia and abnormal wound healing. This study aims to understand the effect of post-repair differential gene expression of nerves repaired under minimal and high tension when compared to its contralateral naïve nerve. Our study investigates differential gene expression using next-generation RNA sequencing of nerves repaired under minimal or high tension. Gaining an understanding of genetic and biomolecular mechanisms can help us find potential drug therapeutics that target differentially expressed genes and improve pathologic nerve repair.

Methods: Sciatic nerve transection was performed on 17 male Lewis rats under isoflurane anesthesia. The nerves were repaired under minimal (n=8) or high (9 mm excision [n=9]) tension with 9-0 nylon sutures using the interrupted epineural suture technique. Nerve samples from both tension groups of the injured limb and the uninjured contralateral limb were collected from the repair site 14 weeks postoperatively and subjected to RNA-sequencing analysis using Illumina HiSeq 2500.

Results: Utilizing hierarchical clustering, we noted that the control, minimal tension, and high-tension groups were each clustered together (Figure 1). We noted 37 differentially expressed genes. Under high tension,17 genes were upregulated while 18 genes were downregulated. Compared to the control group, both the high tension and the minimal tension groups had similar gene expressions. However, the high-tension group had a higher z-score=3 for upregulated genes involved in DNA binding, telomere stability, protein degradation and absorption, cancer, and epithelioid conversion of fibroblasts. Similarly, the high tension group had a lower z-score=-2.33 for the downregulated genes involved in NOTCH signaling pathway (p=0.05), Hedgehog signaling (p=0.04), cholesterol metabolism (p=0.05), signal transduction, neurodegenerative disease, immune system antigen processing, protein metabolism, and ferroptosis (p=0.04) among others.

Conclusions: Our analysis found that in high tension nerve repair, gene expressions were impacted differentially compared to minimal tension nerve repair and the naïve control. This study has implications for future studies using RNA-sequencing in mitigating the effects of high-tension procedures. This may have clinical applications such as minimizing gliomas, neuromas, and other neurological or cancer disorders. These findings can guide currently used targeted drug interventions or aid in developing new genetically targeted drug therapeutics to prevent postoperative damage and neurological disorders.

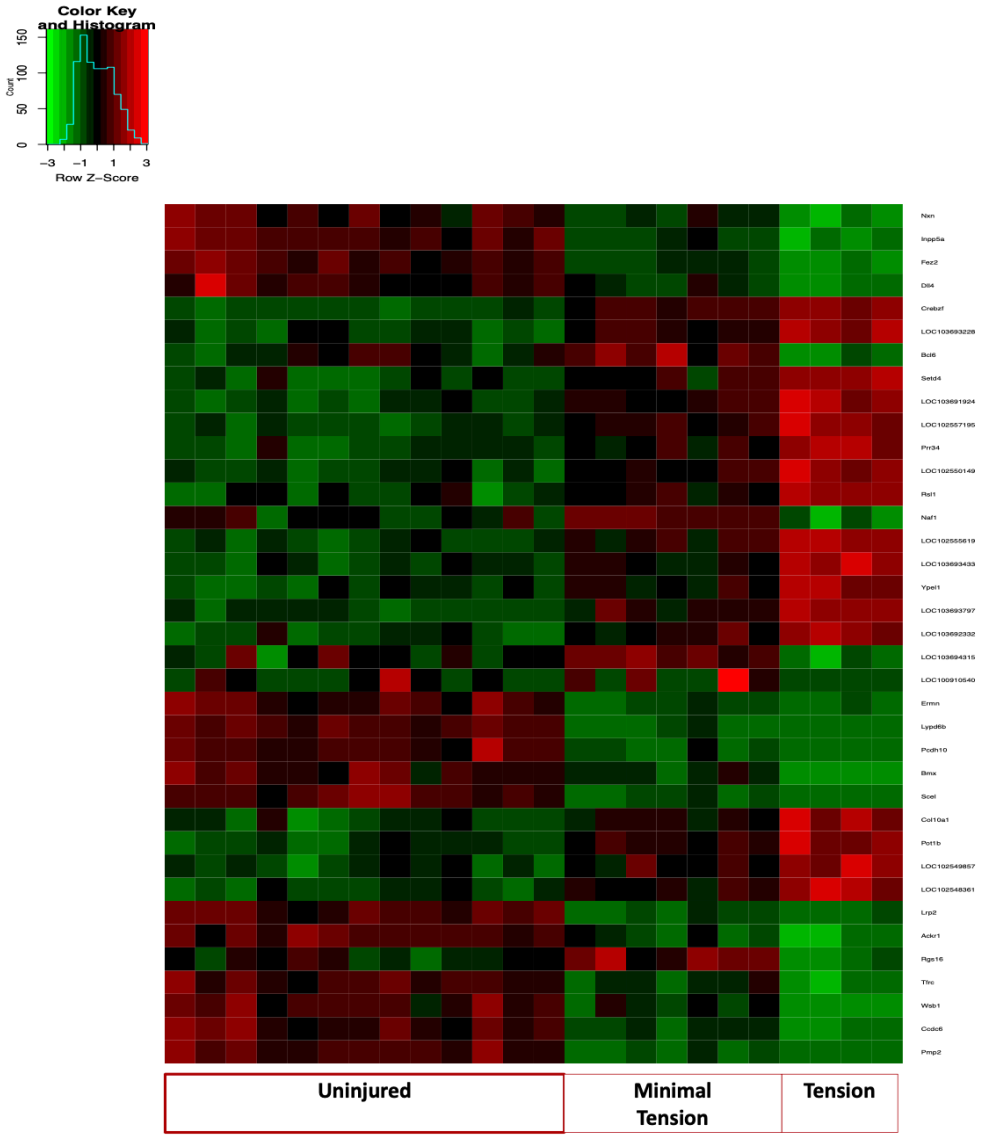


Figure 1: Heatmap of Differential Gene Expression of the control (uninjured), minima tension and high-tension groups.

B24

How the Local Environment Induces Differential Gene Expression in Regenerating Nerve After Neurotmesis – Implications for Neuroma Prevention and Neural Interfacing for Prosthetic Control

Kasey Leigh Wood, BS, Marina I. Adrianzen Fonseca, BS, Kirsten A. Gunderson, BS, Zeeda H. Nkana, BS, Jacqueline S. Israel, MD, Samuel O. Poore, MD, PhD, Aaron M. Dingle, PhD

Submitter	Kasey Wood
Phone	(914) 473-0772
Email Address	Kwood4@wisc.edu
Classification	Medical Student
Division	Plastic Surgery
Lab	Poore/Dingle Lab
Science Type	Basic Science
Keywords	Amputation; Neuroma; Neurotmesis; Nerve Repair; RNA-sequencing

Abstract Starts on Page 2.

Introduction: Approximately 80% of major limb amputations are complicated by painful neuromas. While there is no gold standard management, methods include nerve translocation into bone and implantation into skeletal muscle grafts. Beyond preventing and treating neuromas, these approaches to peripheral nerve management have facilitated the development of regenerative neural interfaces, which may enable creation of prosthetics with motor and sensory abilities. However, molecular-level differences between nerves in these environments have not been investigated. This study aimed to elucidate the physiology of regenerating nerves in different settings by assessing gene expression.

Methods: New Zealand white rabbits underwent transfemoral amputation with sciatic nerve transposition into the femur or tacked to skeletal muscle. At five weeks, RNA-sequencing of samples of distal nerve terminating in bone or muscle and nerve of the contralateral limb (naïve, control) identified differentially expressed genes (DEGs) and biochemical pathways (a=0.05).

Results: Three samples of nerve housed in bone, four of nerve tacked to muscle, and seven naïve controls were analyzed. Relative to naïve nerve, nerve housed in bone had distinct gene expression with little within-group variation and 13,028 DEGs, and nerve tacked to muscle had dramatic within-group variation and 12,811 DEGs. These samples demonstrated upregulation of the following pathways: lysosome, phagosome, antigen processing/presentation, and cell adhesion molecule. Relative to nerve housed in bone, nerve tacked to muscle had 12,526 DEGs, demonstrating upregulation of pathways of B cell receptor signaling, focal adhesion, NK cell mediated cytotoxicity, leukocyte transendothelial migration, and ECM-receptor interactions.

Conclusion: Nerve housed in bone has a more predictable molecular profile than does nerve tacked to muscle. Thus, the intramedullary canal may provide a more reliable setting for neuroma prevention and neural interfacing. As neural interfacing technologies advance, edging closer to the generation of prosthetics with bi-directional feedback ability, these molecular-level changes will become increasingly important considerations.

B10

Not All Control are Created Equally: Differences in Cutaneous Gene Expression Among Control Groups Used in Breast Research

Kirsten A. Gunderson, BS; Rebecca L. Farmer, MD, PhD; Sarah M. Lyon, MD; Jacqueline S. Israel, MD; Sandra Splinter BonDurant, MS; Zeeda H. Nkana, BS; Katherine M. Gast, MD; Samuel O. Poore, MD, PhD; John W. Siebert, MD

Submitter	Kirsten A. Gunderson
Phone	608-225-1005
Email Address	Kagunderson2@wisc.edu
Classification	Medical Student
Division	Plastic Surgery
Lab	Samuel O. Poore and John W. Siebert
Science Type	Basic Science
Keywords	Gene expression profiling, transcriptomics, breast, controls, study design

Abstract Starts on Page 2.

Introduction: In breast cancer research, it is common practice to define a control group as any non-cancerous breast tissue. A variety of tissue sources have been used throughout the literature to serve as controls, including the contralateral, unaffected breast in cancer patients, prophylactic risk-reducing mastectomy specimens, and tissue from patients undergoing elective, non-oncologic breast procedures. The purpose of this study was to define the gene expression profiles of commonly used control groups in breast cancer research and to assess for major differences in the activity of particular biologic pathways.

Methods: Full thickness skin samples were collected from patients undergoing non-oncologic breast procedures (i.e., breast reduction or breast augmentation) or prophylactic, risk-reducing mastectomy. Additionally, samples were taken from the contralateral breast of breast cancer patients who chose to have simultaneous risk-reducing mastectomy of the unaffected breast. Patients with known inflammatory or immunologic conditions were excluded. All samples were analyzed using RNA-Seq technology to determine their cellular transcriptome. Gene expression was then analyzed via hierarchical clustering to identify biologic pathways that showed differing levels of activity between the three groups.

Results: A total of 81 skin samples were included for analysis, including 20 non-oncologic breast procedure samples, 26 risk-reducing mastectomy samples, and 35 samples from the unaffected breast of breast cancer patients. Analysis showed distinct differences between the gene expression profiles of each group. Several pro-oncologic and inflammatory pathways were found to be up-regulated in patients undergoing prophylactic mastectomy, including TNF, PI3K-Akt and JAK-STAT, when compared to non-oncologic samples. Similarly, MAPK and Ras signaling pathways were found to be upregulated in the unaffected breast in breast cancer patients as compared to both benign controls and those undergoing prophylactic mastectomy.

Conclusions: We have demonstrated that there are significant, fundamental differences in the cutaneous gene expression profiles of healthy patients, patients known to be at increased risk of breast cancer, and the unaffected breast of breast cancer patients. These findings suggest that control groups for breast cancer research must be carefully chosen in order to eliminate confounding variables due to baseline differences in gene expression.

B21

Chronic Circadian Disruption Induces Sustained Phase Shift in the Pancreas

Patrick B Schwartz, MD, Morgan Walcheck, BS, Gang Wu, PhD, Noah Carrillo, BS, Kristina A Matkowskyj, MD PhD, Sean M Ronnekleiv-Kelly, MD

Submitter	Patrick B Schwartz
Phone	8122901046
Email Address	pbschwartz@wisc.edu
Classification	Postdoctoral Fellow/Resident
Division	Surgical Oncology
Lab	Ronnekleiv-Kelly
Science Type	Basic Science
Keywords	Circadian, Pancreas, Metabolism, Rhythmicity, Carcinogenesis

Abstract Starts on Page 2.

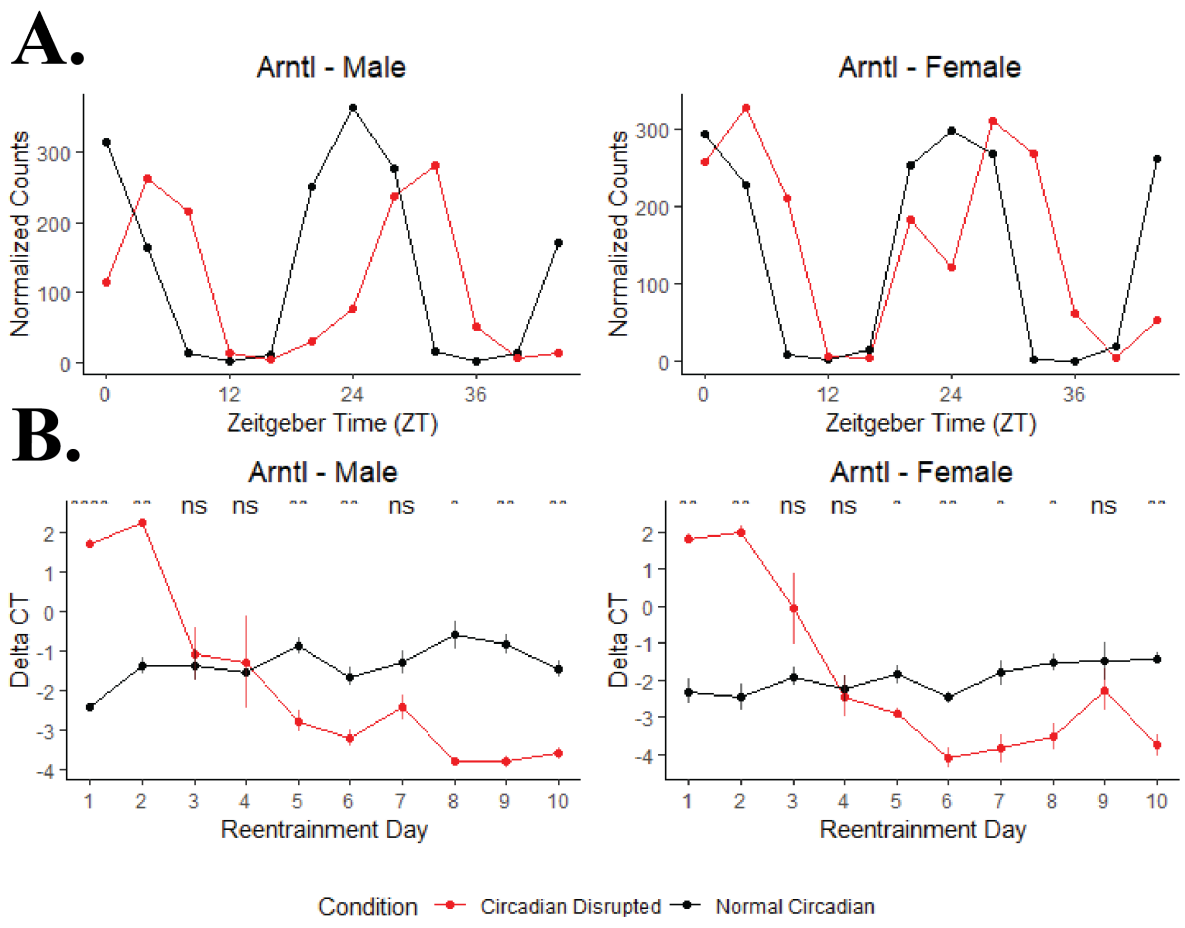
Introduction: Circadian rhythms control several homeostatic processes from metabolism to immune cell function, including in the pancreas. Disruption of the clock is known to lead to organ dysfunction, such as obesity, diabetes, and carcinogenesis. We sought to determine the effects of long-term circadian disruption on the pancreas, through a series of transcriptomic experiments on wild-type C57B6/J mice (WT). Analogous experiments of circadian disruption in the liver demonstrated complete obliteration of hepatic clock rhythmicity, which resulted in severe metabolic dysfunction and pre-cancerous steatohepatitis. We hypothesized pancreatic clock gene expression may become similarly arrhythmic following disruption, and such effects would be resistant to re-entrainment (or normalization of gene expression).

Methods: A total of 144 WT mice (age 4 weeks) were subjected to either normal circadian (NC) conditions with a 12-hour light-dark (LD) cycle or circadian disrupted (CD) conditions with a 12-hour LD cycle phase-shifted forward 8 hours every 2-3 days. After 4 weeks, mice were placed back under normal conditions and then serially sacrificed at 4-hour intervals (12 mice/time point) for 48 hours, and the pancreas dissected. Pancreas samples were then subjected to bulk RNA-sequencing. Rhythmicity testing was completed with Metacycle and those genes with a false discovery rate of < 0.1 were considered rhythmic. Differential rhythmicity testing was completed with DODR and CircaCompare. To test time to re-entrainment after disruption, an additional 96 WT mice (age 4 weeks) were subjected to NC or CD conditions. After 4 weeks, mice were shifted back to NC conditions. Mice were then sacrificed at 24-hour intervals (12 mice/time point) for 10 days and pancreatic RNA isolated. Gene expression of two core-clock genes, *Arntl* and *Per2*, were measured to assess for re-entrainment. Pairwise t-tests were used for the time until statistical equivalency between NC and CD gene expression ($p > 0.05$).

Results: Under NC conditions, 945/17448 (5.42%) of pancreatic genes were found to exhibit circadian-dependent rhythmic gene expression, demonstrating a substantial number of genes controlled by the circadian clock. Under CD conditions, this decreased to 616 (3.58%) genes. When split by sex, there was a differential response, whereby the number of rhythmic male genes increased from 1565/18488 (8.46%) to 1718 (9.63%) and female genes decreased from 1865/18236 (10.23%) to 1305 (7%) genes. While there were significant changes in the number of rhythmic genes with circadian disruption (i.e., became non-rhythmic), many genes remained rhythmic despite CD conditions. This included many of the core-clock genes (CCGs) (Fig. 1a) which drive the circadian clock. Thus, we performed differential rhythmicity testing to determine differences in these genes that remained rhythmic. This revealed that 97.9% of male (328/335) and 96.97% of female (288/297) rhythmic genes experienced a statistically significant phase-shift. Consequently, aberrancies in peak gene expression relative to the time of day occurred, a finding that could lead to an inability for an organism to coordinate organ function. Therefore, we assessed the time for gene expression to normalize following our disruption protocol (re-entrainment). After placing CD mice back under NC conditions, we found that gene expression remained aberrant and did not normalize within 10 days (Fig. 1b).

Conclusions: Contrary to our original hypothesis, we found there was not complete obliteration of the pancreatic clock, as has been shown in the liver. Instead, most of the CCGs remained rhythmic following our disruption protocol. Notably, we found the protocol produced statistically significant phase shifts in nearly every rhythmic transcript. These shifts caused mistiming of gene expression, especially in genes important for lipid metabolism. We found that these effects were long-lasting, with the pancreas failing to return to normal gene expression patterns by 10 days. These results suggest a possible mechanism for circadian disruption-related pancreatic pathologies, such as the metabolic syndrome. Future experiments will explore how the dysregulated pancreatic lipid metabolism we found leads to pathologic states.

Figure 1:


A.
Arntl - Male
Arntl - Female
Normalized Counts
Zeitgeber Time (ZT)
B.
Arntl - Male
Arntl - Female
Delta CT
Reentrainment Day
ns
Condition
Circadian Disrupted
Normal Circadian

B2

Short-course neoadjuvant intratumoral immunotherapy can establish immunologic memory in murine melanoma

Taylor Aiken, David Komjathy, Arika Feils, Amy Erbe, Alexander Rakhmilevich, Paul Sondel

Submitter	Taylor Aiken
Phone	417-860-1897
Email Address	taiken@uwhealth.org
Classification	Resident
Division	Human Oncology, Pediatrics
Lab	Sondel
Science Type	Basic Science
Keywords	Melanoma, Neoadjuvant, Immunotherapy, Tumor Immunology, Tumor Vaccine

Abstract Starts on Page 2.

Introduction: GD2 is disialoganglioside preferentially expressed in neuroblastoma and melanoma and anti-GD2 directed therapies are used clinically in neuroblastoma, with ongoing clinical trials in melanoma. We are currently developing an *in situ* vaccination approach using intratumoral (IT) delivery of an immunocytokine (IC) consisting of IL-2 linked to an anti-GD2 monoclonal antibody. While IT-IC monotherapy does not cure mice bearing established B78 melanoma tumors, it is effective when combined with local radiation therapy (RT). Here, we tested whether short course IT-IC monotherapy prior to surgical resection could result in a robust adaptive immune response preventing tumor recurrence following rechallenge after surgery.

Methods: Mice bearing 50-100mm^3 GD2-expressing melanoma (B78) tumors were treated with a 5-day course of 50μg IT-IC and complete surgical resection was performed 3 days following the final treatment. Mice that underwent RT received 12Gy external beam radiation in a single fraction 5 days prior to start of IT-IC. The immune infiltrate of resected tumors was assessed by flow cytometry. Mice were then rechallenged with $2x10^6$ B78 cells 40 days following surgical resection to assess immunologic memory preventing engraftment of a rechallenge tumor.

Results: IT-IC and RT + IT-CT treated tumors had fewer viable tumor cells, increased cluster of differentiation 8 (CD8) T-cells, and an improved CD8: Treg ratio compared to mice treated with RT or surgery alone. Rejection of rechallenge was observed in 60% (6/10) and 80% (4/5) of mice treated with IT-IC or RT + IT-IC, compared to 0% (0/4) and 10% (1/10) in mice treated with RT or surgery alone.

Conclusions: While ineffective in B78 melanoma as monotherapy, the 60-80% of mice receiving neoadjuvant IT-IC developed robust immunologic memory preventing recurrence. IT-IC, either as monotherapy or in combination with RT, should be further investigated as a neoadjuvant therapy for preventing recurrence in high-risk settings.

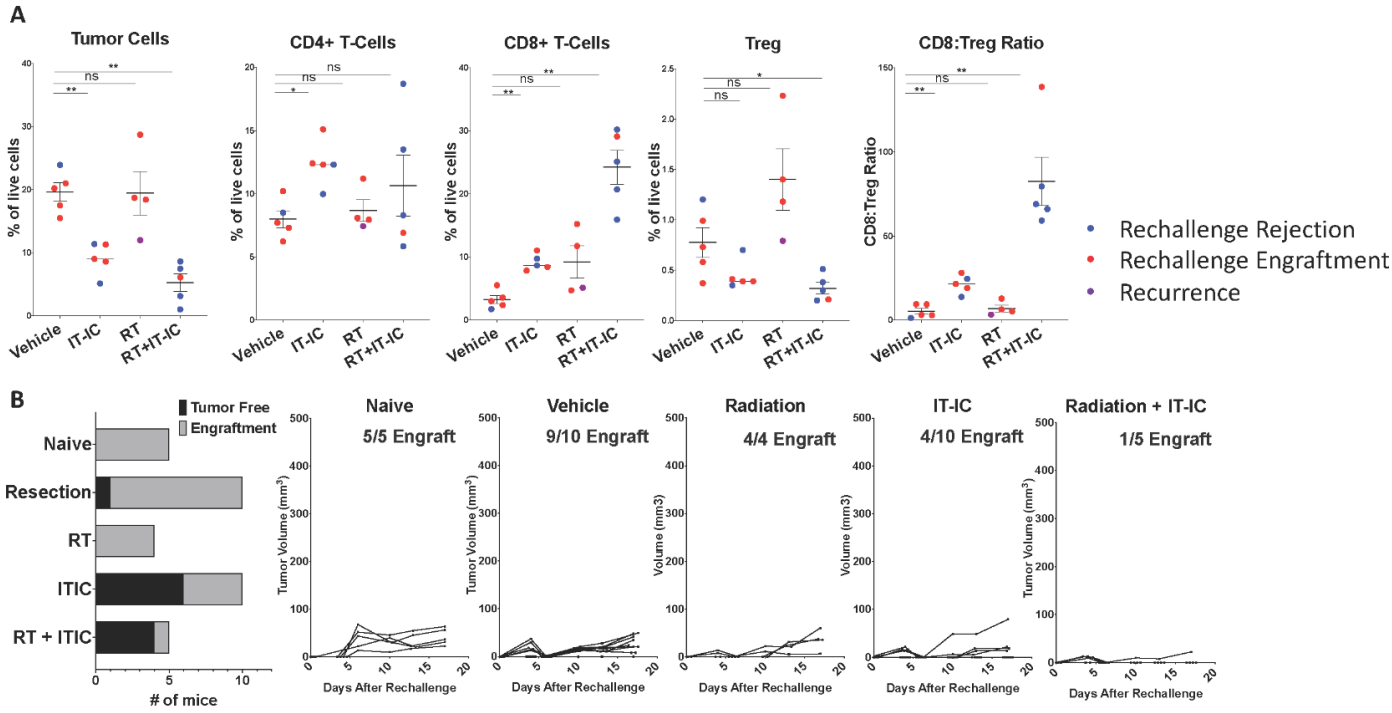


Figure 1. Neoadjuvant IT-IC immunotherapy in B78 melanoma. A) Immune infiltrate of treated tumor as assessed by flow cytometry. Mice that eventually developed immunologic memory (blue), rechallenge engraftment (green), or recurrence prior to rechallenge (red) are indicated. (B) Rechallenge of mice cured with resection +/- immunotherapy compared to engraftment in naïve mice.

GROUP TWO

Clinical Science

C3

Sequential biopsies in renal transplant recipients with refractory chronic active antibody-mediated rejection: improvements in histopathology are delayed compared to the reduction in DSA

Kenna R. Degner, PhD, Sandesh Parajuli, MD, Fahad Aziz, MD, Neetika Garg, MD, Maha Mohamed, MD, Didier A. Mandelbrot, MD, Sarah E. Panzer, MD, Nancy A. Wilson, Ph, Shannon R. Reese, MS, Kristin Van Hyfte, Weixiong Zhong, MD, Peter Nickerson, MD, Arjang Djamali, MD

Submitter	Kenna Degner
Phone	(715) 520-2304
Email Address	kdegner@wisc.edu
Classification	Post-doctoral fellow
Division	Transplant Surgery/Nephrology
Lab	Djamali
Science Type	Clinical
Keywords	Kidney, transplantation, cABMR, DSA, histopathology

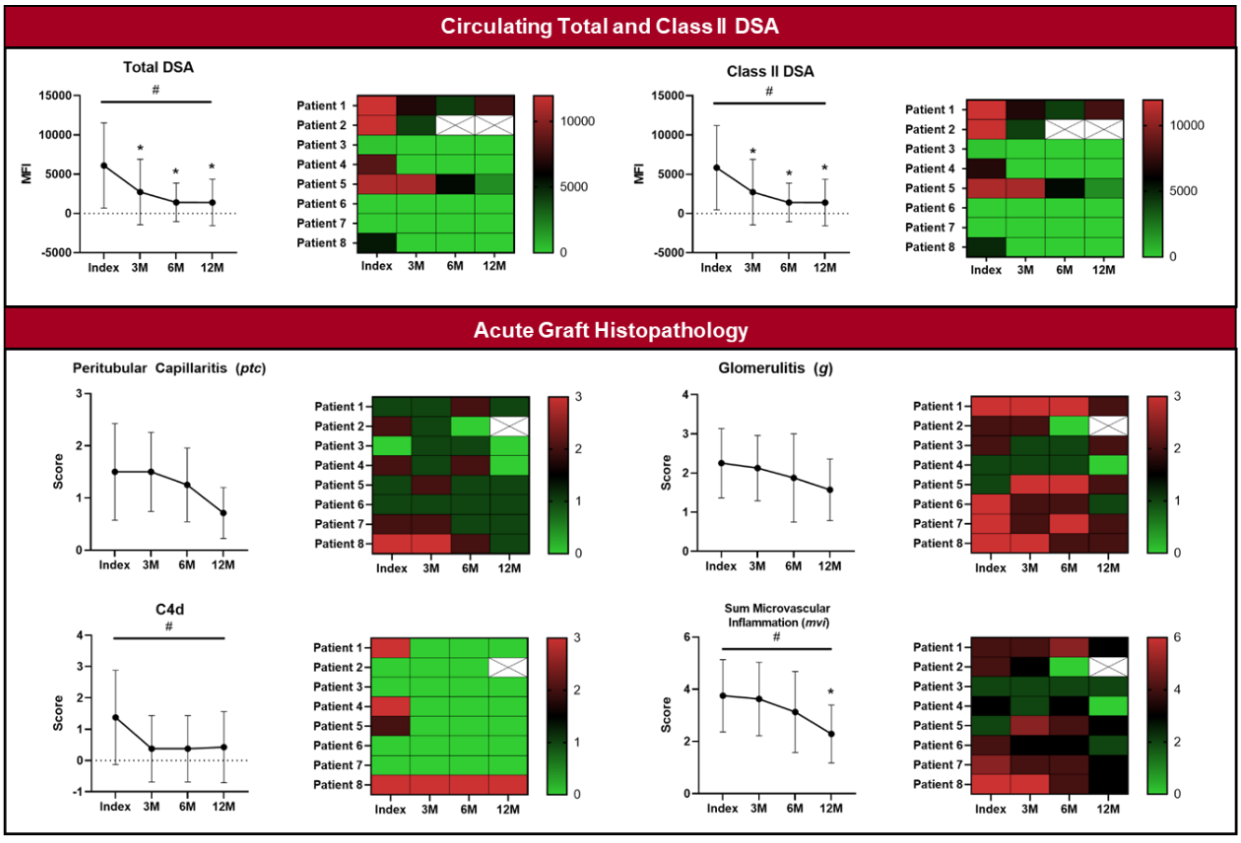
Abstract Starts on Page 2.

Introduction: There are limited options for the treatment and management of refractory chronic antibody mediated rejection (cABMR) after kidney transplantation.

Methods: Herein, kidney transplant recipients (n=8) with refractory cABMR, defined as persistent rejection despite treatment, underwent serial biopsies at diagnosis, three, six, and 12 months. Banff 2017 pathology, donor-specific antibodies (DSA), and renal function were assessed at each biopsy.

Results: One patient lost their allograft during the 12-month follow up period due to ongoing rejection. Otherwise, renal function was stable in the remaining seven. Total (6,093±5,424 vs. 2,731±4,172, p=0.04) and Class II DSA (5,845±5,366 vs. 2,731±4,172, p=0.04) declined within three months after treatment in parallel with C4d staining (1.6±1.5 vs. 0.4±1.1, p=0.03). Banff *mvi* (3.7±1.5 vs. 2.3±1.1, p=0.05) score decreased significantly at 12 months, but not sooner. The *g* and *ptc* scores followed a similar trend but were not statistically significant. Chronic allograft pathology (ct, ci, cv, cg scores) remained stable.

Conclusions: In patients with refractory cABMR, the decline in DSA precedes improvements in disease activity, suggesting that a subgroup of these patients may benefit from sequential biopsies and therapy.



C17

Outcomes after LVAD Implantation by Bi-Thoracotomy versus Sternotomy Approach

Elizabeth M. Stoeckl, BS; Jason W. Smith, MD; Ravi Dhingra, MD; Amy G. Fiedler, MD

Submitter	Elizabeth Stoeckl
Phone	(262) 470-1284
Email Address	estoeckl@wisc.edu
Classification	Medical Student
Division	Cardiothoracic Surgery
Lab	Fiedler
Science Type	Clinical
Keywords	Left ventricular assist devices, operative approach, sternal-sparing

Abstract Starts on Page 2.

Introduction: Left ventricular assist devices (LVAD) are standardly implanted via full sternotomy. Non-sternotomy approaches are gaining popularity, but potential benefits of this approach have not been well-studied. We hypothesized that LVAD implantation by bi-thoracotomy (BT) would demonstrate smaller and more consistent inflow cannula and better postoperative outcomes compared to sternotomy.

Methods: Charts of patients who underwent LVAD implantation between June 2018 and June 2020 at a single academic institution were retrospectively reviewed. Patient age, sex, cardiac surgery history, surgical approach (sternotomy vs. BT), past medical history, preoperative right heart catheterization, preoperative ejection fraction, INTERMACS profile, need for preoperative hemodynamic support, and postoperative hospital course were studied. The inflow cannula angle was measured on the first chest radiograph available postoperatively relative to the horizontal line.

Results: Of 40 patients studied, BT approach was used in 17 (42.5%). Comparing BT and sternotomy patients, there was no difference in rates of preoperative hemodynamic support (76.5% vs. 82.6%, p=0.32), preoperative ejection fraction (16.6% vs. 17.8%, p=0.28), or preoperative INTERMACS score (3.0 vs. 2.6, p=0.18), though more BT patients were planned as destination therapy (DT) than sternotomy (88.2% vs. 52.17%, p=0.005). There was no difference in intraoperative blood loss between the two approaches (143.8 mL vs. 277.5 mL, p=0.11). Mean inflow cannula angles were smaller in BT patients (24.2 vs. 35.6, p=0.02) and had a smaller standard deviation (14.44 vs. 20.56). Excluding patients who went on to receive heart transplant or passed away in the same hospitalization, there was no difference in average length of hospital stay after surgery (19.5 days vs. 23.2 days, p=0.21). However, BT patients required fewer days of postoperative inotrope support (5.2 vs. 11 days, p=0.02).

Conclusions: Our data suggest inflow cannula angles are smaller and more consistent with the BT approach, which has been associated with improved patient outcomes. Patients who underwent BT were more likely to be DT compared to bridge-to-transplant. Further research is needed to identify meaningful differences in postoperative outcomes compared to sternotomy.

C15

Preoperative Immunonutrition Decreases Wound Complications in Immediate Breast Reconstruction

Carol E. Soteropulos MD, Kylie M. Edinger MD, Kishan M. Thadikonda MD, Katherine M. Gast MD, MS

Submitter	Carol E. Soteropulos
Phone	310-245-3514
Email Address	soteropu@gmail.com
Classification	Resident
Division	Plastic and Reconstructive Surgery
Lab	Katherine M. Gast MD, MS
Science Type	Clinical
Keywords	Breast Reconstruction, Autologous Breast Reconstruction, Alloplastic Breast Reconstruction, Immunonutrition, Preoperative Nutrition, Wound Healing

Abstract Starts on Page 2.

Introduction: Recent literature in various surgical specialties has shown the use of enteral immunonutrition prior to major surgery to reduce infectious complications, length of stay and overall morbidity[1,2]. To date, no studies have examined the use of immunonutrition within plastic and reconstructive surgery. The purpose of this study is to evaluate the impact of preoperative immunonutrition supplementation on the outcomes of immediate breast reconstruction.

Methods: All patients undergoing immediate autologous or alloplastic breast reconstruction at the University of Wisconsin, Madison beginning February 2018 were contacted and offered enrollment in this study. All patients who consumed Impact Advanced Recovery for 5 days prior to surgery were reviewed (n=59, 36 autologous, 23 alloplastic). This group was compared with a retrospective control group (n=106, 40 autologous, 66 alloplastic) of patients who underwent surgery prior to February 2018. No other major changes in perioperative care or operative technique were made within the timeframe of the retrospective or prospective collection period. Chart review was performed on all patients in a 30-day (autologous, direct-to-implant) or 90-day (expander) postoperative window. The rates of surgical site infection, wound dehiscence, seroma, and mastectomy skin flap necrosis were analyzed individually and combined to form an aggregate “wound complication rate”.

Results: Aggregate wound complication rate was reduced from 49.06% to 32.20% after intervention (p=0.0361). Specifically, the rate of mastectomy skin flap necrosis was reduced from 24.53% to 8.47% (p=0.0114), and the rate of wound dehiscence was reduced from 15.09% to 1.69% (p=0.0067) in the cohort who received preoperative immunonutrition supplementation. The rates of infection, unplanned return to the operating room, and aborted reconstruction were not significantly different between the control and interventional cohorts.

Conclusions: Based on the initial results of this ongoing trial, preoperative immunonutrition supplementation with Impact Advanced Recovery may significantly improve wound complication rate in patients undergoing immediate autologous and alloplastic breast reconstruction.

Citations

1. Hegazi RA, Hustead DS, Evans DC. Preoperative standard oral nutrition supplements vs immunonutrition: results of a systematic review and meta-analysis. *Journal of the American College of Surgeons.* 2014;219(5):1078-1087.
2. Xu J, Sun X, Xin Q, et al. Effect of immunonutrition on colorectal cancer patients undergoing surgery: a meta-analysis. *International journal of colorectal disease.* 2018;33(3):273-283.

C9

Age and Sex Comparison of Aerodynamic Phonation Measurements using Noninvasive Assessment

Jim R. Lamb, Austin J. Scholp, Jack J. Jiang

Submitter	Grace Morley
Phone	952-769-7428
Email Address	gmorley@wisc.edu
Classification	Undergraduate student
Division	Otolaryngology Head-Neck Surgery
Lab	Laryngeal Physiology Lab, Dr. Jack Jiang
Science Type	Clinical
Keywords	Mechanical interruption; labial interruption; Aerodynamic measurement; Noninvasive assessment; Adults and children

Abstract Starts on Page 2.

Introduction: The goal of this study is to present vocal aerodynamic measurements from pediatric and adult participant pools. There are a number of anatomical changes involving the larynx and vocal folds that occur as children age and become adults. Data were collected using two methods of non-invasive aerodynamic assessment: mechanical interruption and labial interruption.

Methods: A total of 154 participants aged 4-24 years old took part in this study. Ten trials were performed for both methods of airway interruption. To perform mechanical interruption, participants phonated /ɑ/ for ten second trials while a balloon valve interrupted phonation five times. For labial interruption, participants said /pɑ/ five times at comfortable and quiet volumes. Aerodynamic measures included subglottal pressure, phonation threshold pressure, mean airflow, laryngeal resistance, and others.

		ANOVA			Regression		
		Age	Sex	Age*Sex	Male	Female	Total
Mechanical Interruption	mPs				-		-
	mPTP	X			-		-
	mMFR	X			+	+	+
	mPW					+	+
	mLR	X			-	-	-
	mSPL						
	mVE						
Labial Comfortable	cPs					-	-
	cMFR	X			+	+	+
	cPW				+		+
	cLR	X		X	-	-	-
	cSPL				+		
	cVE			X			
Labial Quiet	qPTP				-	-	-
	PTF	X			+	+	+
	PTW						+
	qLR	X			-	-	-
	qSPL						
	qVE	X	X	X			
	Hysteresis					+	

Table 3. Summary of results of the statistical tests. Blank boxes had non-significant results. Total regression is linear regression performed with the entire subject pool with respect to subject age. Pediatric regression used only subjects ages 4-17. A significance level of $\alpha = 0.05$ was used for statistical testing.

X indicates a significant result in the ANOVA testing

+ indicates a significant increasing trend with respect to age

- indicates a significant decreasing trend with respect to age

Results: 101 participants (51 females) successfully completed testing with both methods. 8 out of 20 measurements were found to have a statistically significant effect of participant age on measurements. Sex alone had a significant effect on vocal efficiency for the labial quiet method.

Conclusions: The data discussed here can be used to view age and sex trends in vocal aerodynamic measurements. When using either method of mechanical or labial interruption, participant age needs to be taken into account to properly interpret several aerodynamic parameters. A participant's sex is not as important when using these methods.

C2

The Effects of Preoperative Anemia on Breast Reconstruction

Jesse Kasim, Justin Davis, Jeffrey Larson

Submitter	Justin Davis
Phone	972-302-3222
Email Address	jdavis@uwhealth.org
Classification	Resident
Division	General Surgery
Lab	Jeffrey Larson
Science Type	Clinical Research
Keywords	Anemia Breast Reconstruction

Abstract Starts on Page 2.

Introduction: Within plastic surgery, studies have explored the effect of preoperative anemia in a variety of surgical populations including microvascular reconstruction[7], body contouring[8], hand, and cosmetic surgery[9].

Rates of anemia among patients with breast reconstruction range 41-82% reported in the literature[15]. Given the lack of clarity of the impact of anemia on surgical outcomes in these patients, the goal of this study is to characterize risk factors for preoperative anemia in patients undergoing primary breast reconstruction, investigate the work-up and optimization of anemia prior to surgery, and quantify the impact of preoperative anemia on 90-day complication rates.

Methods: After review and approval by the Health Sciences Institutional Review Board (IRB) of the University of Wisconsin (IRB #2018-1563), a retrospective chart review was performed on patients undergoing breast reconstruction at the University of Wisconsin Hospital and Clinics between January 1, 2015 and December 31, 2018. Data collected included preoperative hemoglobin and mean corpuscular volume (MCV), neoadjuvant therapies within six months of surgery, any treatments for anemia (including iron, folate, and B12), procedure performed, timing of procedure with respect to mastectomy, and any complications in 90 days following surgery.

Results: Anemic and non-anemic patients were not significantly different in prevalence of diabetes, smoking status, BMI, or ASA physical status classification. There was no difference in timing of reconstruction (immediate vs delayed), the laterality of the procedure (unilateral vs bilateral), or the time between measurement of preoperative hemoglobin and procedure. Overall, there was a significantly increased incidence of seromas in anemic patients (15% in anemic patients vs 7% in nonanemic patients, ($p = 0.042$). Nonanemic patients had a higher incidence of wound dehiscence (9% vs 2%, $p = 0.042$) and a longer average length of stay. This increased incidence of wound dehiscence and longer average length of stay in nonanemic patients were not significant when comparing patients within the autologous or alloplastic subgroups.

Conclusions: In conclusion, this study demonstrates that anemia is prevalent in patients undergoing breast reconstruction, especially those who underwent neoadjuvant chemotherapy. Preoperative anemia was not associated with increased incidence of medical or surgical complications except seroma in autologous reconstruction. The authors of this paper did not find a difference between preoperative anemia and complications in our sample of patients.

C1

One Bad Apple or the Whole Bunch: Patterns of Disease in non-MEN1 Familial Hyperparathyroidism

Cassandra Crifase, David Schneider MD MS, Mariam Ali-Mucheru MD, Kristin Long MD MPH

Submitter	Cassandra Crifase
Phone	(630)363-0332
Email Address	ccrifase@wisc.edu
Classification	Medical Student
Division	Department of Surgery, Division of Endocrine Surgery, University of Wisconsin School of Medicine & Public Health
Lab	Kristin Long, MD, MPH, FACS; Assistant Professor
Science Type	Clinical
Keywords	Parathyroid; hyperparathyroidism; genetics; genetic endocrinopathy; endocrine surgery

Abstract Starts on Page 2.

Introduction: Family history of primary hyperparathyroidism is commonly seen in the setting of genetic disorders such as multiple endocrine neoplasia 1 (MEN-1). Diagnosed genetic endocrinopathies presume multi-gland hyperplasia. Many patients, however, present with a clear family history of primary hyperparathyroidism and no other identifiable genetic syndrome and are successfully cured with single-gland excision. We sought to evaluate the patterns of disease seen in non-MEN-1 familial hyperparathyroidism (FHPT).

Methods: With institutional review board approval, we performed a retrospective review of a prospectively maintained database of patients treated surgically for primary hyperparathyroidism at the University of Wisconsin from 2000-2020. Diagnostic and clinical variables of interest were identified within the database and confirmed via chart review. Patients with a family history of hyperparathyroidism but no confirmed genetic parathyroid disease were compared to patients with a family history of hyperparathyroidism as well as diagnosis or family history of MEN-1.

Results: 268 patients with a reported family history of parathyroid disease were surgically treated for primary hyperparathyroidism at a tertiary referral center with high-volume endocrine surgeons over the last twenty years. Of these patients, 123 had a family history of hyperparathyroidism without an identifiable/confirmed genetic condition, 40 had a family history of hyperparathyroidism with clinical or genetically confirmed MEN-1, and 105 were excluded from analysis for missing or insufficient information. 54 patients (44%) with FHPT underwent single-gland excision, compared to 11 (28%) with MEN-1. 59 FHPT patients (48%) had a pathologically confirmed adenoma, while only 10 (25%) MEN-1 patients were reported to have an adenoma on pathologic examination. For the patients with complete data available, 63 (51%) of the FHPT patients demonstrated lasting biochemical cure past 6 months. 8 (7%) FHPT patients had concern for persistent disease.

Conclusions: This study suggests that not all cases of familial hyperparathyroidism present with multi-gland parathyroid hyperplasia. A large percentage of patients with FHPT were treated with single-gland excision and demonstrated durable biochemical cure. Clearly, a combination of careful family history, preoperative surgeon-performed ultrasound, intraoperative parathyroid hormone monitoring, and extensive preoperative counseling are necessary for patients with a family history of parathyroid disease.

C11

Anatomic Eligibility for Endovascular Aneurysm Repair Preserved Over Two Years of Surveillance

Annalise M. Panthofer, BS, Sydney L. Olson, BS, Brooks L. Rademacher, MD, Jennifer K. Grudzinski, BS, RT(R)(M), Elliot L. Chaikof, MD, PhD, Jon S. Matsumura, MD, for the N-TA 3 CT Investigators

Submitter	Annalise Panthofer
Phone	608-719-8499
Email Address	panthofer@surgery.wisc.edu
Classification	Medical Student, Associate Research Specialist
Division	Vascular
Lab	AortaCore Aortic Imaging Lab (PI: Jon Matsumura)
Science Type	Clinical
Keywords	Endovascular Procedures; Aortic Aneurysm, Abdominal; Surgical Procedures, Minimally Invasive; Disease Management; Decision-Making, Shared

Abstract Starts on Page 2.

Introduction: Endovascular aneurysm repair (EVAR) is a widely used option for patients with suitable vascular anatomy who have a large infrarenal abdominal aortic aneurysm (AAA). Patients with small AAAs are managed with careful surveillance and it is a common concern that their anatomy may change with AAA growth, and their option for EVAR may become limited. Device innovation has resulted in expanded ranges of anatomy that may be eligible for EVAR. This study sought to identify changes in anatomic eligibility for repair with contemporary endovascular devices in AAA patients, monitored by computed tomography over the course of two years.

Methods: Subjects from the Non-Invasive Treatment of Abdominal Aortic Aneurysm Clinical Trial (N-TA 3 CT, NCT01756833) were included in this analysis. Females had baseline AAA maximum transverse diameter (MTD) between 3.5-4.5 cm, and males had baseline MTD between 3.5-5.0 cm. Subjects were included in this analysis if they completed pre-enrollment and two-year follow-up CT imaging. Pertinent anatomic measurements were performed on a post-processing workstation in a centralized imaging core laboratory. EVAR candidacy was determined by measuring proximal aortic neck diameter, AAA length, and infrarenal neck angulation. Patients were considered to be eligible for EVAR if they qualified for at least one of the 7 studied devices' Instructions for Use (IFU) at baseline and at two years. Paired t-test analysis was used to detect differences in aortic measurements over two years, and McNemar test was used to compare eligibility over two years.

Results: 192 subjects were included in this analysis, 168 male and 24 female. 85% of patients were eligible for EVAR at baseline and 85% after two years of follow-up (P = 1.00, [95% CI, -0.034 - 0.034]). Of the 164 EVAR candidates at baseline, 160 (98%) remained eligible over two years of surveillance. Insufficient neck length was the most common reason for both ineligibility at baseline (18 of 28 subjects) as well as loss of candidacy over two years (3 of 4 subjects).

Conclusions: The majority of patients eligible for EVAR when entering a surveillance program for small AAA remain eligible after two years. Substantial changes in AAA neck anatomy resulting in loss of EVAR treatment options, are infrequent. Patients with anatomical AAA progression beyond EVAR eligibility remain candidates for complex EVAR and open repair.

C16

Open partial conversion with endograft preservation for the treatment of persistent type II endoleaks.

Thomas Staniszewski, Reagan Beyer, Dr. Courtney Morgan, Dr. Jon Matsumura

Submitter	Thomas Staniszewski
Phone	(414) 416-3336
Email Address	staniszewski@neurosurgery.wisc.edu
Classification	Academic Staff
Division	Department of Neurosurgery and Vascular Surgery
Lab	AortaCore Aortic Imaging Lab – Dr. Matsumura
Science Type	Clinical
Keywords	Endovascular Aneurysm Repair, Abdominal Aortic Aneurysm, Endograft

Abstract Starts on Page 2.

Introduction:

Type II endoleak after endovascular aneurysm repair (EVAR) can cause persistent sac growth requiring re-interventions. We sought to describe our technique of open partial conversion for the treatment of type II endoleaks. We also compared this technique with endograft explant to evaluate the benefits of endograft preservation.

Methods:

We performed a retrospective chart review of 784 patients who underwent surgical repair of an abdominal aortic aneurysm (AAA) from 2008 to 2018 at our institution. Seven patients were identified who underwent open exploration for treatment of persistent type II endoleak with sac expansion after EVAR. These patients were categorized based on the conversion technique: partial conversion with endograft preservation (n=5) or endograft explant (n=2). Our partial conversion procedure involved open aortic exposure with banding of the proximal neck using a felt strip to secure the endograft neck, opening the sac to oversew contributing vessels, and imbricating the sac over the endograft. The primary outcome of this study was 30-day mortality.

Results:

The average sac diameter at the time of open conversion was 8.7cm with a mean time from EVAR of 5.33 years and sac size increase of 2.8cm. All patients except one underwent at least one prior intervention for endoleak. When comparing the techniques, open partial conversion procedures had significantly reduced aortic clamp time (P=0.013) with cross clamping avoided entirely in three of the five procedures. Partial conversion patients trended toward a decreased total OR time, decreased mean estimated blood loss, and shorter hospital stays, though these outcomes did not reach statistical significance. No 30-day mortality was reported in either cohort. In-hospital morbidity of open partial conversion procedures was 40% due to one report each of acute kidney injury (AKI) and prolonged intubation. Open partial conversion patients with available follow-up computed tomography (n=3), reported complete resolution of type II endoleak.

Conclusions:

This study further demonstrates the safety of the open partial conversion procedure with endograft preservation for the treatment of type II endoleak. This technique is an important option to consider when planning intervention for patients with a persistent type II endoleak.

C10

Predictors Of Volume Growth In Abdominal Aortic Aneurysms

Sydney Olson, BS; Annalise M Panthofer, BS; Michael Terrin, MD MPH; John A Curci, MD; Timothy T Baxter, MD; Fred A Weaver, MD; Jon Matsumura, MD; Non-Invasive Treatment of Abdominal Aortic Aneurysm Clinical Trial Investigators

Submitter	Sydney Olson
Phone	651-492-8520
Email Address	olsons@surgery.wisc.edu
Classification	Medical student
Division	Vascular Surgery
Lab	AortaCore Imaging Lab- Jon Matsumura
Science Type	Clinical
Keywords	Aorta, CT imaging, aneurysm, growth prediction, abdominal aortic aneurysm

Abstract Starts on Page 2.

Introduction: Current management of abdominal aortic aneurysm (AAA) involves serial imaging surveillance of maximum transverse diameter (MTD). Other measurements, such as volume and tortuosity, may have a role in characterizing and predicting AAA progression. This study sought to evaluate possible predictors of AAA volume growth.

Methods: Subjects from the Non-invasive Treatment of Abdominal Aortic Aneurysm Clinical Trial were included in this analysis if they received ≥ 2 computed tomography scans (n=250). MTD, volume, and tortuosity were used to model growth. Univariate least squares regressions were used to assess associations with volume growth.

Results: Mean volume growth rate was 10.4 cm^3/year SD 8.8. Baseline MTD accounted for 43% of baseline volume variance ($p<0.001$) (Figure 1). Baseline volume accounted for 30% of volume growth variance ($p<0.001$) (Figure 2). More tortuous aneurysms at baseline had significantly greater volume growth rates ($p<0.001$) (Figure 3). Angiotensin receptor blocker use (regression coefficient -3.4, R^2 0.02, $p = 0.02$) and history of diabetes mellitus (regression coefficient -2.8, R^2 0.02, $p = 0.04$) were predictive of reduced volume growth.

Conclusions: MTD and volume are moderately correlated. Baseline AAA volume and tortuosity may help predict AAA growth rates. These findings may inform optimal AAA surveillance and mechanisms of AAA progression.

C12

International Pediatric Otolaryngology Group (IPOG) Consensus recommendations on the prenatal and perinatal management of anticipated airway obstruction: Micrognathia

Michael D. Puricelli, MD

Submitter	Michael Puricelli, MD
Phone	636-751-0770
Email Address	mpuricelli@wisc.edu
Classification	Faculty
Division	Otolaryngology
Lab	n/a
Science Type	Clinical
Keywords	Perinatal airway obstruction, Attended Delivery, Ex Utero Intrapartum Treatment, Fetal Intervention, Micrognathia

Abstract Starts on Page 2.

Introduction: Neonatal delivery with compromised airway presents a risk to life and long-term neurological function. At present, there are no published guidelines to support recommendations for ex utero intrapartum treatment (EXIT).

Methods: Recommendations are based on expert opinion by members of the International Pediatric Otolaryngology Group (IPOG). A two-iterative Delphi method questionnaire was distributed to all members of the IPOG and responses recorded. The respondents were given the opportunity to comment on the content and format of the survey, which was modified for the second round. “Consensus” was defined by >80% respondent affirmative responses, “agreement” by 51–80% affirmative responses, and “no agreement” by 50% or less affirmative responses.

Results: Twenty-seven responses were received from experts in eight countries. Recommendations are provided regarding etiologies of perinatal airway obstruction, imaging evaluation, adjunct evaluation, multidisciplinary team and decision factors, micrognathia management, congenital high airway obstruction syndrome management, head and neck mass management, attended delivery procedure, and delivery on placental support procedure. Micrognathia management is discussed in this submission.

Conclusions: Thorough evaluation and thoughtful decision-making are required to optimally balance fetal and maternal risks/benefits.

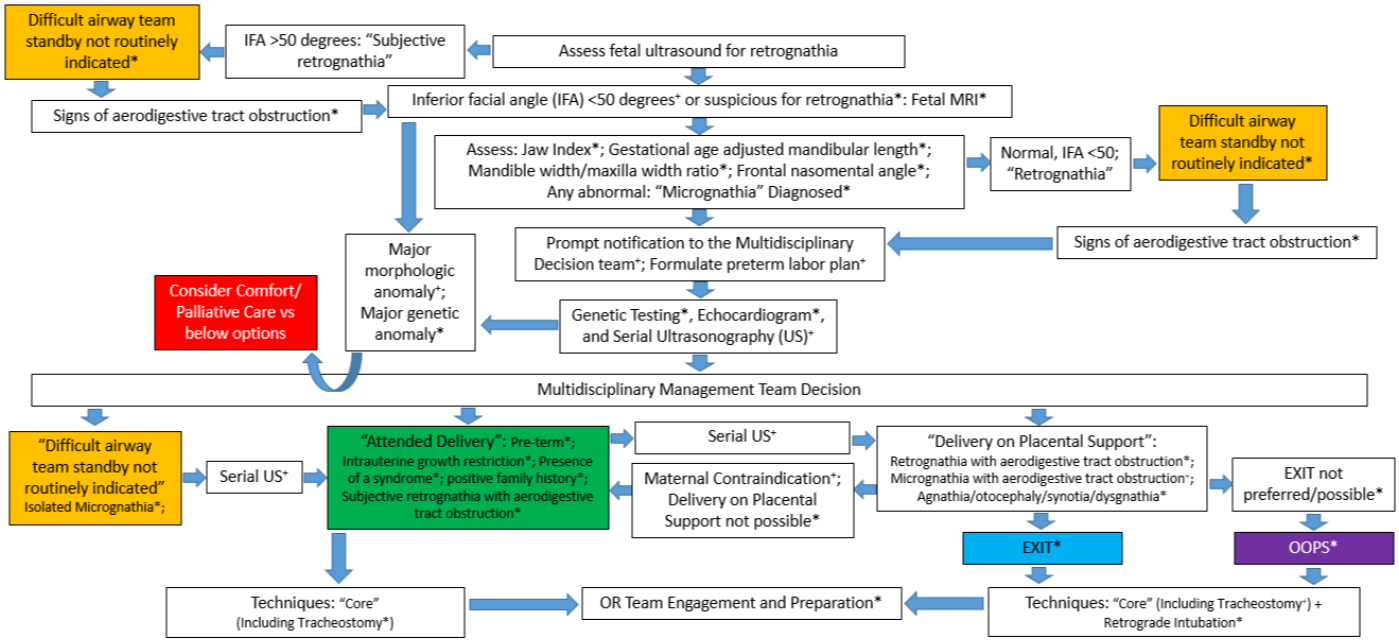


Figure 2: Fetal Micrognathia. + >80% Consensus Reached; * Majority Agreement;
"Core" Techniques: Resuscitation (NICU)+; Video laryngoscopy+; Operative laryngoscopy+; Seldinger-Assisted Videotelescopic Intubation+; Rigid Ventilating Bronchoscopy+; Transnasal Fiberoptic Intubation+; Fiberoptic Intubation via LMA+; Tracheostomy*/+

C6

Vestibulopathy; A sign of COVID-19?: First case report of pediatric patient presenting with vestibular neuritis as the sole sign of COVID-19 infection

Cody J Falls BS, Zhang Yanchen, MD, Michael D Puricelli, MD

Submitter	Cody J Falls
Phone	7707711723
Email Address	cfalls@wisc.edu
Classification	Medical student
Division	Department of Otolaryngology
Lab	Dr. Puricelli
Science Type	Clinical
Keywords	COVID-19, vestibular neuritis, pediatric

Abstract Starts on Page 2.

Introduction: Here we present a case of vestibular neuritis as the sole presenting sign of COVID-19 infection. This is significant as it indicates a need to implement proper protocols when treating patients presenting with vestibular neuritis in order to avoid unnecessary spread of the virus. Furthering the importance of this topic, vomiting/gagging are extraordinarily common in vestibular neuritis patients, especially during bedside maneuvers used in diagnosis, creating a potential source of widespread aerosolization of viral particles if proper precautions are not taken.

Methods: Case report.

Results: A 16-year-old male with no pertinent past medical history developed intractable nausea, vomiting, and dizziness after a family member was diagnosed with COVID-19. He was subsequently found to be suffering from vestibular neuritis and tested positive for COVID-19. His symptoms resolved with anti-emetics and corticosteroid treatment.

Conclusions: To our knowledge, this is the first reported pediatric case of vestibular neuritis as the sole presenting sign of COVID-19 infection.

C13

Video Laryngoscopy for Intubation in Severe Pierre Robin sequence: A Retrospective Review

Michael D Puricelli, Joseph D Peterson, Ahmed Alkhateeb, Richard JH Smith, Deborah SF Kacmarynski

Submitter	Michael D. Puricelli
Phone	6367510770
Email Address	mpuricelli@wisc.edu
Classification	Faculty
Division	Otolaryngology
Lab	n/a
Science Type	Clinical
Keywords	Pierre Robin Sequence, Micrognathia, Difficulty Intubation, Video laryngoscopy, Pediatric airway management

Abstract Starts on Page 2.

Introduction: The anatomy of children with severe Pierre Robin sequence can present a challenge for direct laryngoscopy and intubation. Advanced techniques including flexible fiberoptic laryngoscopy intubation have been described but require highly specialized skill and equipment. Rigid video laryngoscopy is more accessible but has not been described in this population.

Methods: A retrospective review was completed at a tertiary care center of all children between January 2016 to March 2020 with Pierre Robin sequence who underwent a mandibular distraction osteogenesis procedure. Intubation events were collected, and a descriptive analysis was performed. A univariate logistic regression model was applied to direct laryngoscopy and flexible fiberoptic laryngoscopy with rigid video laryngoscopy as a reference.

Results: Twenty-five patients were identified with 56 endotracheal events. All patients were successfully intubated. Direct laryngoscopy was successful at first intubation attempt in 47.3% (9/19) of cases. Six cases required switching to another device. Rigid video laryngoscopy was successful at first intubation attempt in 80.5% (29/36) of cases. Two cases required switching to another device. Flexible fiberoptic laryngoscopy was successful at first intubation attempt in 88.9% (8/9) of cases. Direct laryngoscopy was 4 times more likely to fail first intubation attempt when compared to rigid video laryngoscopy ($p<0.05$). There is no significant difference between rigid video laryngoscopy and flexible fiberoptic laryngoscopy for intubation.

Conclusions: For children with Pierre Robin, sequence rigid video laryngoscopy should be considered as a first attempt intubation device in the operating room and for emergent situations.

Table 1. Intubation According to Technique

	First Attempt Success	Subsequent Attempt Success	Instrument Switch	Odds Ratio for First Attempt Failure	95% CI	P Value
Direct Laryngoscopy	47.3% (9/19)	21.1% (4/19)	31.6% (6/19)	4.028	1.221-13.281	0.022
Video Laryngoscopy	80.5% (29/36)	13.8% (5/36)	5.5% (2/36)	[Reference]	[Reference]	[Reference]
Flexible Fiberoptic Laryngoscopy	88.9% (8/9)	11.1% (1/9)	0.0% (0/9)	0.453	0.049-4.178	0.485

C14

Cochlear Implant Outcomes and Tumor Characteristics in Patients with Neurofibromatosis Type 2 and Bilateral Vestibular Schwannoma

Gabriel Sobczak, Wendy Marchant, G. Mark Pyle, Sara Misurelli, Joseph Roche

Submitter	Gabriel Sobczak
Phone	(608) 712-5703
Email Address	gsobczak@wisc.edu
Classification	Medical Student
Division	Otolaryngology
Lab	Division of Otolaryngology
Science Type	Clinical
Keywords	Neurofibromatosis type 2, bilateral vestibular schwannoma, cochlear implant

Abstract Starts on Page 2.

Introduction: The bilateral vestibular schwannomas (VS) seen in a vast majority of patients affected by neurofibromatosis type 2 (NF2) present a challenge for physicians and patients when making decisions about disease management. Both the natural history of bilateral VS in NF2 and potential treatments carry significant risk of profound bilateral hearing loss, and treatment planning must incorporate auditory rehabilitation strategies. Traditionally, the only treatment available for an ear with profound hearing loss in NF2 patients was an auditory brainstem implant (ABI). Recent literature suggests that cochlear implantation (CI) is a viable alternative to ABI in patients whose cochlear nerve is anatomically preserved. CI carries several advantages over ABI, both in terms of more aggressive management options for bilateral VS and in reduction of surgical complexity and intraoperative risks. The present study seeks to expand the literature about the viability of CI for hearing rehabilitation in patients with NF2 to aid in clinical decision making and counseling for these patients.

Methods: This study is a retrospective case series of 5 patients with NF2 and bilateral VS who underwent cochlear implantation to treat bilateral profound sensorineural hearing loss. Specific variables reviewed included patient demographics, CI electrode type, VS dimensions, duration of hearing loss, treatment modality for VS ipsilateral and contralateral to CI, pre-operative and post-operative pure-tone averages (PTA) and speech reception scores (sentence and word scores). Daily CI use, telephone use, and any subjective comments from the patient were also reviewed.

Results: Five patients (3 female, 2 male) underwent unilateral cochlear implantation over the last nine years. The mean age at implantation was 54 years (range 36 – 78 years). Two patients did not undergo treatment in the implanted ear, and three underwent treatment in the implanted ear (tumor resection and/or radiation therapy). The mean ipsilateral duration of hearing loss was 103 months and all patients had profound hearing loss bilaterally at time of implantation. The mean ipsilateral VS dimensions at time of implantation were 14 mm x 7.2 mm x 6.1 mm (mediolateral x anteroposterior x craniocaudal). All patients experienced an average ipsilateral pure-tone average improvement of 63 dB (pre-activation PTA minus post-activation PTA) following implantation. All achieved enhanced open-set speech recognition in quiet (mean of 10% pre-activation and 57% post-activation). All patients reported improved lip-reading skills and increased environmental sound awareness. Four out of five patients continue to use their CI daily, demonstrating improved open-set speech recognition, compared to pre-CI, at the time of their last evaluation.

Conclusions: In patients with NF2 and bilateral VS in which the cochlear nerve is anatomically preserved following treatment, cochlear implantation can be a viable treatment option for hearing rehabilitation. This study revealed that all patients benefitted from their CI, in both objective and subjective audiometric performance measures. PTA and Az-Bio scores improved, and all patients reported enhanced lip reading and environmental sound awareness.

This research is funded by the American Otological Society Fellowship Grant and The Department of Surgery / Division of Otolaryngology.

C7

Machine Learning Detects False Negative Benign Thyroid Nodule Diagnoses

Alexander Idárraga, BA, George Luong, BS, Vivian Hsiao, MD, David Schneider, MD, MS, FACS

Submitter	Alexander Idarraga
Phone	4146406727
Email Address	idarraga@wisc.edu
Classification	Medical student
Division	Department of Endocrine Surgery
Lab	David Schneider, MD, MS, FACS
Science Type	Informatics
Keywords	Machine Learning, thyroid nodules, Bethesda II, benign, false negative

Abstract Starts on Page 2.

Introduction: Thyroid nodules are remarkably common - high-quality ultrasound will detect nodules in nearly two-thirds of US adults, and 95% of these nodules are benign. However, a false negative diagnosis delays cancer treatment and can be psychologically devastating to patient and provider. The purpose of this study is to use machine learning to develop a predictive model which can identify falsely benign thyroid nodule biopsies based on available clinical data.

Methods: We conducted a retrospective medical record review at one academic and one community center. ICD-9 codes identified patients with thyroid nodular disease; clinical information and notes were extracted from the electronic health record. Included patients were those with thyroid nodules evaluated by ultrasound, having received Bethesda II (benign) diagnosis following fine needle aspiration. We previously developed and validated natural language processing systems to extract nodule features from text cytology, ultrasound, and pathology reports. Features included nodule size, ultrasound features and TSH levels, and demographic data such as age and biological sex. A nodule was considered benign if either all pathology reports were benign or all follow-up cytology reports were benign. Missing values were imputed using a Random Forest based iterative method (missingpy, Python 3.8). The large class imbalance between cancerous and non-cancerous outcomes was corrected using synthetic oversampling with ADASYN (imbalanced-learn, Python 3.8). Tree-based, rule-based, and Bayesian models were generated with Sci Kit Learn (Python 3.8) using 10-fold cross validation and tested for predictive accuracy. Hyperparameter selection was accomplished using an automated iterative approach to maximize model specificity and area under the receiver operating characteristics curve (AUC ROC). We tested several thresholds of suspicion based on the probability of cancer assigned to each nodule by the algorithm.

Results: A total of 603 subjects met inclusion criteria; 6.25% were ultimately diagnosed with cancer. Of all algorithms tested, a Random Forest method was able to achieve the best AUC ROC (0.992) when predicting nodules as either cancerous or benign. A threshold of suspicion 0.7 or greater showed a false positive rate of 3.1%, a false negative rate of 14.1%, a positive predictive value (PPV) of 97.3%, and a negative predictive value (NPV) of 87.2%. A threshold of 0.8 resulted in a false positive rate of 0.005%, but markedly increased the rate of false negatives to 22.8% (PPV = 99.2%, NPV = 77.8%). A threshold of 0.6 returned a more balanced distribution of false positives (2.8%) and false negatives (7.2%)(PPV = 97.2%, NPV = 92.9%).

Conclusions: Machine learning can accurately identify falsely benign thyroid nodules. A Random Forest model performed well using readily available data obtained via standard clinical evaluation of thyroid nodules. Increasing the degree of suspicion required to classify a nodule as cancerous can reduce the false positive rate to nearly 0, a clinically desirable attribute to avoid unnecessary surgery. Future studies will prospectively evaluate the model's performance.

C8

Risk Stratifying Indeterminate Thyroid Nodules with Machine Learning Using Available Electronic Health Record Data

George Luong, BS, Alexander J. Idarraga, BA, Vivian Hsiao, MD, BA, BS, David F. Schneider, MD, BA, MS, FACS

Submitter	George Luong
Phone	(323)979-7367
Email Address	gluong@wisc.edu
Classification	Medical student
Division	Endocrine Surgery
Lab	David Schneider, BA, MS, MD, FACS
Science Type	Clinical
Keywords	machine learning, electronic health record, bioinformatics, thyroid nodule, diagnosis

Abstract Starts on Page 2.

Introduction: Up to 30% of thyroid nodules are classified as indeterminate after fine needle aspiration biopsy. These indeterminate thyroid nodules (ITNs) require surgical pathology for definitive diagnosis. Molecular testing provides additional cancer risk stratification but adds expense and invasive testing. The purpose of this study is to utilize a machine learning algorithm to predict malignancy of ITNs using available data from the electronic health record (EHR).

Methods: We conducted a retrospective study using records from two centers: an academic center and a community hospital. Clinical information and notes were obtained from the EHR; ICD-9 codes identified patients with thyroid nodules from 2005 to 2016. We extracted structured data (demographics, TSH values) and unstructured text reports from the EHR. Using a previously reported natural language processing system, we extracted nodule features from text cytology, ultrasound, and pathology reports. Malignancy was defined as cancer greater than one centimeter in size from pathology reports. To predict cancer on pathology, we tested tree-based and Bayesian methods for accuracy using 10-fold cross validation. All models were evaluated by area under the receiver operating characteristic curve (AUROC) and precision and recall scores.

Results: A total of 279 subjects had an ITN on cytology. Of these, 99 (35.4%) were ultimately diagnosed with cancer. For the entire ITN cohort, Random Forest performed the best, producing an AUROC of 0.83, positive predicative value of 70%, and negative predictive value of 81%.

Conclusions: In conclusion, machine learning methods can predict, with moderate accuracy, malignancy of thyroid nodules based on information from non-invasive, and inexpensive diagnostic tests. When combined with expert judgement, machine learning may be a cost-effective tool for triaging indeterminate nodules to the appropriate treatment.

C5

What are the Drivers of Cost in Parathyroidectomy?

Amanda R. Doubleday, DO, MBA; Christopher C. Stahl, MD; Kristin L. Long, MD, MPH, FACS; Dawn M. Elfenbein, MD, MPH, FACS; Susan C. Pitt, MD, MPH, FACS; Rebecca S. Sippel, MD, FACS; David F. Schneider, MD, MS, FACS

Submitter	Amanda R. Doubleday
Phone	262-490-2838
Email Address	doubleday@surgery.wisc.edu
Classification	Post doctorate Fellow
Division	Endocrine Surgery
Lab	Dr. David Schneider
Science Type	Clinical Research
Keywords	parathyroidectomy, health system costs, preoperative imaging, minimally invasive parathyroidectomy, bilateral neck exploration

Abstract Starts on Page 2.

Introduction: Variation exists in the workup and management of primary hyperparathyroidism. Current literature suggests that preoperative imaging allows for minimally invasive parathyroidectomy (MIP) but increases cost, and that bilateral neck exploration (BNE) mandates admission overnight. This study uses a matched cohort of patients undergoing parathyroidectomy to compare health system costs.

Methods: All patients that underwent parathyroidectomy from 2015-2019 at a single institution were identified by CPT code from the electronic health record (EHR). Actual cost data was obtained from a prospectively maintained institutional database and merged with the EHR patient data. Coarsened exact matching was used to create matched cohorts of patients that underwent a MIP or BNE. Weighted multiple linear regression was used to identify significant cost drivers.

Results: The matched data set included 560 patients; 281 patients underwent MIP, within that group a sub-analysis revealed 85 underwent MIP converted to bilateral exploration (MIPc), and 194 underwent BNE. The MIPc group had the longest average operative time, followed by BNE, then MIP (MIPc:105 minutes, BNE:101 minutes, MIP:68 minutes). Transient nerve injury remained low (MIP:0.4%, MIPc:2.4%, BNE:3.6%) while readmission rates were <1.1% for all. Of the patients who had documented imaging, 74.5% had only 1 preoperative imaging study, while 25.5% had 2 or more imaging studies. The average total cost of preoperative imaging was highest in MIPc, followed by BNE, then MIP (MIPc: $152.50, BNE: $140.20, MIP: $102.00, p=0.16). Same-day discharge was feasible for most regardless of extent of surgery (MIP:93.2%, MIPc:88.2%, BNE:89.2%, p=0.19). On multiple linear regression analysis after controlling for confounding variables, BNE added a total cost of $609.00 compared to MIP. Overall, same-day discharge saved a total cost of $2,333.50 per patient.

Conclusions: Contrary to previous literature, here we demonstrate that same-day discharge after parathyroidectomy is feasible and the most cost-saving variable regardless of imaging or extent of surgery. More imaging adds cost without necessarily the benefit of less invasive surgery.

C4

Content and Use of Long Talk in Outpatient Surgical Consults

Ton C. Doan, Nathan D. Baggett, Anne Buffington, Amy B. Zelenski, Elle L. Kalbfell, Fiona Ljumani, Bret Hanlon, Justin Clapp, Robert M. Arnold, Margaret L. Schwarze

Submitter	Ton Doan
Phone	(773) 971-8889
Email Address	tcdoan@wisc.edu
Classification	Medical Student
Division	Vascular Surgery
Lab	Schwarze Lab
Science Type	Clinical
Keywords	Shared decision making, informed consent, communication, long talk, consultation

Abstract Starts on Page 2.

Introduction: Collaborative decision making before major surgery is critical to support patient autonomy. It is well known that physician talk consumes most of the discussion as they work to provide information. What surgeons say and how they say it impacts a patient's ability to participate, but little is known about the length and content of typical surgeon talk in consultations. The objective of this study is to quantitate the length and categorize the content of long talk by surgeons during conversations about major surgery.

Methods: We performed secondary analysis on audio-recorded outpatient surgical consults between 43 surgeons and patients 60 years and older considering major vascular or oncologic surgery at 5 medical centers (UCSF, OHSU, UW, Brigham and Women's, Rutgers). We randomly selected 4 transcripts from each surgeon in the cohort. Each uninterrupted block of speech, or utterance, was quantitated by character length and content coded by at least 2 of 6 coders with discrepancies adjudicated through social moderation. The codes tagged utterances with typical elements of preoperative communication, e.g., risks, explanation of disease. We characterized long utterances as those in the top 5% of character length: >562 characters, roughly 108 words or 30 seconds.

Results: We analyzed 169 transcripts (median length 21 min, range 5 to 61 min). Three surgeons had only 3 transcripts appropriate for inclusion. Long utterances ranged from 562 to 10,322 characters (roughly 30 sec to 9.2 min). Forty-one of 43 (95%) surgeons engaged in long talk in at least one consultation and 84% used long talk in at least half of their consultations. The range of long talk was 3 to 46 utterances per surgeon and 1 to 18 utterances per transcript. There was no association between surgeon specialty or location with long talk. Long utterances primarily contained descriptions of the patient's disease and treatment and rarely included options or tradeoffs (Figure). Surgeons often covered multiple topics in their long talks (44% of long utterances covered 3 or more topics) without pause to let the patient or family contribute or ask questions. Within these long utterances, some surgeons used highly consistent phrasing among all patients while others broached a range of topics without recognizable patterns.

Conclusions: In this multi-specialty, multi-site sample, most surgeons talk in an uninterrupted fashion at times during surgical consultation; however, the frequency of use of long talk varies between individuals. These long talks most often delivered technical information about disease and treatment. Although surgeons were engaging in information transfer, this presentation may make it difficult for patients and families to identify the salient issues related to surgical decision making.

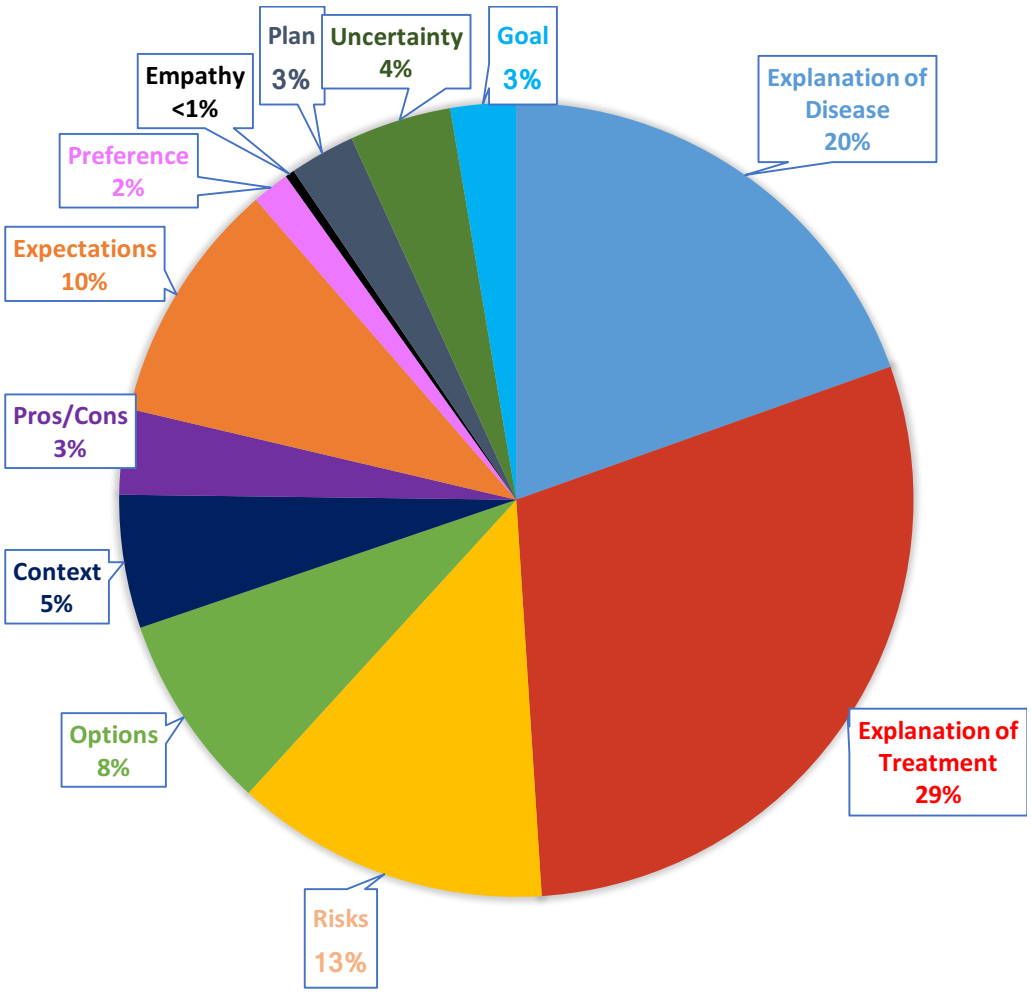


Figure. Content of long utterances in surgical consultations.

GROUP THREE

Education

E2

Multi-Disciplinary Assessment of the Entrustable Professional Activities of Surgery Residents

Jung S, Stahl CC, Rosser AA, Kraut AS, Schnapp BH, Westergaard M, Hamedani AG, Minter RM, Greenberg JA

Submitter	Sarah Jung
Phone	608-695-9448
Email Address	jungs@surgery.wisc.edu
Classification	Faculty
Division	Education
Lab	Jacob Greenberg
Science Type	Education
Keywords	Entrustable Professional Activities, Residents, Multi-Disciplinary, Assessment, Feedback

Abstract Starts on Page 2.

Introduction: Medicine is practiced in an increasingly collaborative and interdisciplinary manner. However, medical training and assessment remain largely isolated in traditional departmental silos. Two Entrustable Professional Activities (EPAs) developed by the American Board of Surgery, General Surgical (GS) Consultation and Trauma, are multidisciplinary in nature and offer a unique opportunity to study the potential advantages of interdisciplinary assessment.

Methods: EPA microassessments were collected from Surgery and Emergency Medicine (EM) faculty between July 2018 and May 2020 using both a locally-developed smartphone application and paper forms. Differences in feedback provided by faculty were assessed using natural language processing (NLP) techniques, (1) automated algorithms to capture qualitative themes related to performance; and (2) topic modeling. Summative content analysis was used to identify themes in our corpus of text feedback. We developed automated coding algorithms for these codes using regular expressions. Topic modeling was performed using latent Dirichlet allocation.

Results: 549 assessments were collected for two EPAs: 198 for GS Consultation and 351 for Trauma. 27 EM and 27 Surgery faculty provided assessments for 71 residents. Summative content analysis produced six themes: 1) Clinical Performance, 2) Communication, 3) Personality, 4) Skill Level, 5) Areas for Improvement, and 6) Timeliness. Both summative content analysis and topic modeling showed important differences between the feedback given by EM and Surgery faculty. EM faculty were significantly more likely than Surgery faculty to submit feedback qualitatively coded as *Communication*, *Personality*, and *Timeliness,* (all chi-square test p-values <0.01). No significant differences were found for *Clinical Performance*, *Skill Level*, or *Areas for Improvement*. Similarly, topic modeling indicated that assessments submitted by EM faculty focused on communication, timeliness, and interpersonal skills (“prompt”, “family”, “recommendations”, “communication”, “nice”, “calm”), while those submitted by Surgery faculty focused on the residents’ ability to effectively gather information and correctly diagnose the underlying pathology (“appropriately”, “history”, “complete”, “imaging”, “management”, “recognized”).

Conclusions: Feedback from EM and Surgery faculty differed significantly based on multiple NLP analyses. EPA assessments should stem from multiple sources to avoid assessment gaps and represent a more holistic picture of performance to ensure that trainees are prepared to practice in the collaborative modern medical environment.

E1

Mentored Clinical Research Experiences for High School Students: Reported Impacts on Career Trajectories

Sarah Jung, PhD

Submitter	Sarah Jung
Phone	608-695-9448
Email Address	jungs@surgery.wisc.edu
Classification	Faculty
Division	Education
Lab	Sarah Jung
Science Type	Education
Keywords	Mentoring, High School Students, Research Careers, Medicine, Underrepresented Students

Abstract Starts on Page 2.

Introduction: The goal of the Doris Duke Charitable Foundation's Clinical Research Continuum: High School to College Program (CRCP) was created to increase diversity of the biomedical workforce by exposing students (high school and early college) from underrepresented groups (URS) to mentored experiences with careers in clinical research and practice. This work reports a subset of evaluation results from eight program sites in the USA.

Methods: Between February 25, 2020 and April 1, 2020, a survey was sent to alumni who participated in the CRCP between 2012-2019. 269 (54%) alumni out of 499 responded to the survey. Descriptive statistics were calculated for responses to Likert-scale questions and responses to open-ended questions were organized by themes.

Results: The mode age was 19 (range 18-26). 232 (86%) students said the CRCP prepared them for their college experience. 123 (46%) said it impacted their college attendance plans; 137 (51%) said it impacted their chosen major; and 153 (57%) said it impacted their future professional goals either "Quite a Bit", or "A Great Deal". 87 (32%) students said the CRCP made them much more confident to pursue a career in clinical research; 92 (34%) said it made them much more confident to pursue a career in medicine; and 113 (42%) said the program made them much more confident to pursue a career in a STEM field.

There were 10 areas in which CRPC alumni felt particularly impacted: 1) Learning about research/the research process; 2) Engaging in hands-on learning; 3) Experiencing mentorship from researchers, clinical practitioners, and others, such as graduate and medical students; 4) Developing communication skills related to science 5) Developing confidence in skills/ability to pursue careers of interest; 6) Having a unique opportunity with advantages and challenges; 7) Working in a lab; 8) Exploring careers; 9) Experiencing data collection and analysis; and 10) Experiencing clinical work.

Conclusions: The CRCP influenced program alumni by increasing the number of professions in which they could see themselves, their confidence to pursue those professions, and their perceived skills relevant to those fields. These are important impacts supporting URS to enter clinical and research fields in surgery and other areas of medicine.

E4

The Infused Pig Chest Wall “Sandwich” - A Novel Training Model for Internal Mammary Artery Preparation in Breast Reconstruction

Weifeng Zeng MD, Ruston Sanchez MD, Kirsten Gunderson MS, Nicholas J Albano MD. Aaron M. Dingle PhD, Samuel O. Poore MD, PhD

Submitter	Weifeng Zeng
Phone	3194995006
Email Address	Wzeng28@wisc.edu
Classification	Academic staff
Division	Plastic surgery
Lab	Poore Lab
Science Type	Education
Keywords	Internal mammary artery, Breast reconstruction, Free flap

Abstract Starts on Page 2.

Introduction: Preparation of the internal mammary artery (IMA) as a recipient vessel is crucial in free flap breast reconstruction. Practicing the procedure using live laboratory pigs reportedly provides realistic simulation but is expensive and inconvenient. We aimed to develop a simple, inexpensive, and effective simulator for IMA preparation.

Methods: Chest walls were harvested from adult Wisconsin mini pigs at the termination of other projects. This included the sternum and ribs 1-7 bilaterally. Skin and fat above the pectoralis muscle were removed. The proximal and distal ends of the IMA were cannulated with angiocatheters. The proximal IMA was attached with tubing to a “blue blood” infusion bag (500mL fluids mixed with 1cc blue food dye) and placed at gravity to mimic real-time blood flow. A collection bag was placed below the field and connected with tubing to the distal IMA. A chest wall “sandwich” was assembled by placing the infused pig rib cage between two mannequin shells. Specifically, the rib cage was placed on the surface of one mannequin, covered with a layer of yellow sponge, and then sandwiched by a second identical mannequin shell with cut out windows exposing the parasternal area of ribs 3, 4, and 5 bilaterally. To perfuse, running the drip at approximately ten drops per minute was efficacious.

Results: This infused pig chest wall “sandwich” IMA preparation simulator could be set-up in any microsurgical suite. Residents can practice IMA preparation including elevating the perichondria, removing cartilage, dissecting the IMA, and anastomosing the IMA. With the perfusion of “blue-blood”, the model provides immediate feedback on the quality of anastomosis.

Conclusion: This novel model can provide highly realistic simulation of IMA preparation. The effect of applying this model on improving the proficiency and confidence of plastic surgery residents will be studied in the upcoming educational study.

E3

Teaching Surgical Anatomy with Perceptual Fluency Interventions: A Randomized Controlled Trial

Christopher C. Stahl MD, Jacob A. Greenberg MD, Martina Rau PhD

Submitter	Christopher C. Stahl
Phone	608-263-8500
Email Address	cstahl@uwhealth.org
Classification	Education
Division	General Surgery
Lab	Learning, Representations, and Technology Lab
Science Type	Education
Keywords	Visual Skills, Perceptual Fluency, Sense-Making

Abstract Starts on Page 2.

Introduction: Transitioning from the preclinical world of cadavers and stylized atlases to living, “surgical” anatomy is difficult, and not currently supported by medical training programs. Novel educational approaches using visual representations may help with transfer between these domains. The study of learning using visual representations highlights two common competencies trainees use to interpret visual representations: perceptual fluency (PF) and sense-making (SM). Formal training programs that teach surgical anatomy using PF and SM may improve trainee ability to recognize intraoperative anatomic structures.

Methods: Videos of laparoscopic inguinal hernia repairs were used to create PF and SM interventions designed to teach visual recognition of the hernia sac (peritoneum). The PF intervention consisted of 30 “anatomic flashcards” in which trainees were instructed to click on the peritoneum and provided feedback. The SM intervention consisted of a 6-minute instructional video describing verbally how one can recognize the hernia sac.

Participants were block randomized into two groups by experience level. All participants underwent a pre- and post-test of their ability to recognize the hernia sac, along with PF training. One group underwent the SM intervention in addition to PF training. Results were analyzed using mixed ANOVA.

Results: Forty-two medical students and residents completed the study; 22 were randomized to PF training alone while 20 were randomized to SM + PF. The intervention led to improvements in recognition of the hernia sac on the post-test in all comers (57% vs 81%, $p = 6x10^{-7}$). However, there was no difference between the two arms (PF vs SM + PF) of the intervention (56% vs 81%, 58% vs 80%, $p = 0.91$). Experience was significantly associated with outcome, with improvements in performance coming primarily from the less experienced trainees (MS2-PGY2 49% vs 79%, PGY3-5 84% vs 88%, $p = 1x10^{-5}$).

Conclusions: Surgical anatomy can be taught efficiently outside of the operating room. Perceptual fluency training was sufficient to achieve these learning gains. As sense-making tends to benefit those with low prior knowledge, the anatomy training participants received in medical school may have lessened its effect.

GROUP FOUR

Health Services

H7

Acute Type B Aortic Dissection early in-hospital outcome at a Single Institution

A.M. Um, F.C. Razalan-Krause, G. Tefera, C.W. Acher, P. DiMusto

Submitter	Andrea Um
Phone	605-929-2599
Email Address	Asherman3@uwhealth.org
Classification	Resident
Division	Vascular Surgery
Lab	Dr. DiMusto
Science Type	Clinical outcomes
Keywords	Aortic dissection, early outcome

Abstract Starts on Page 2.

Introduction: Acute type B aortic dissection (ATBAD) is a life-threatening condition that requires early diagnosis and management. The objective of this study is to better understand the current in hospital outcomes of patients with ATBAD.

Methods: This is a retrospective chart review of patients admitted with the diagnosis of ATBAD over a period of 10 years (May 2010 to March 2020). All patients with the diagnosis of ATBAD are generally admitted to the vascular surgery service. Patients who presented with acute symptoms and had evidence of a type B aortic dissection on Computed Tomographic Angiography (CTA) were included in the study while patients who presented with acute type A aortic dissection, intramural hematoma or penetrating aortic ulcer were excluded. Initial management for all patients included beta blockade and vasodilation. Surgical intervention was performed for malperfusion, persistent pain with refractory hypertension, rupture, and progressing dissection on CT. Demographics, clinical presentation, radiologic findings, hospital course, length of stay and mortality were recorded for analysis.

Results: There were 59 consecutive patients. The average age of the patients was 61 years and 70% were male. Eighty one percent of the patients had history of hypertension and they presented with an average systolic pressure of 183 mmHg. The most common presenting symptoms were back pain (76%) and chest pain (72.3%) while abdominal pain (52.5%) and extremity pain (13.6%) were less frequent. Twenty two percent of the patients presented with complications, visceral malperfusion (10) and rupture (3). These patients required emergency surgery. The remaining 46 patients were initially medically managed however 21 of these patients subsequently required intervention within 30 days. Of these 21, 6 developed malperfusion after presentation, 12 had refractory pain and hypertension, 2 had progressive dissection changes on CTA, and one had concern for associated symptomatic aneurysm. During the first 30 days, 58% of all the patients underwent required surgery, primarily Thoracic Aortic Endograft in 26 patients. There were three deaths within the first 30 days, rupture in 1, retrograde dissection after stent graft in 1 and a third patient died the day of discharge probably due to rupture. The average length of stay was 10.6 days (range 1 to 43). Patients who required intervention averaged a length of stay of 13.2 days compared to patients without intervention averaging 6.4 days.

Conclusions: ATBAD remains a serious condition. While the initial medical management is successful in many patients, over 50% ultimately required surgical intervention during the initial 30 days.

H3

Individual-level bariatric surgery barriers in the Veterans Health Administration: A Qualitative Study

Jacqueline A. Murtha, MD, MPH; Esra Alagoz, PhD; Catherine R. Breuer, MS; Alex Finn, BS; Susan D. Raffa, PhD; Corrine I. Voils, PhD; Luke M. Funk, MD, MPH

Submitter	Jacqueline Murtha, MD, MPH
Phone	678-689-5897
Email Address	jmurtha@uwhealth.org
Classification	Resident
Division	Minimally Invasive, Foregut and Bariatric Surgery
Lab	Luke Funk, MD, MPH
Science Type	Health Services
Keywords	Bariatric surgery; obesity; barriers to care; qualitative research; Veterans Health Administration system

Abstract Starts on Page 2.

Introduction: Bariatric surgery is the most effective weight loss treatment for individuals with severe obesity (defined as a body mass index [BMI] ≥35 kg/m^2), but <1% of U.S. adults and <0.1% of U.S. Veterans who meet BMI criteria undergo it. We previously characterized 8 barriers to bariatric surgery care at the health system level. Our objective in this study was to identify patient and provider perceptions of individual-level barriers to undergoing bariatric surgery within the Veterans Health Administration (VHA).

Methods: We conducted semi-structured interviews with Veterans with severe obesity and providers, including primary care physicians (PCPs), registered dieticians (RDs), health psychologists and bariatric surgeons. Veterans were from two Midwest VA medical centers (VAMCs) and had either been referred for bariatric surgery or were participating in the VHA's behavioral weight management program. PCPs, RDs and health psychologists were recruited from three VAMCs in the VA Great Lakes Health Care System, and bariatric surgeons were recruited from all 21 VHA bariatric surgery programs. Participants were asked to describe their experiences with obesity care treatment within VHA. Conventional content analysis identified individual-level barriers within Anderson's Behavioral Model of Health Services Use, which describes how service utilization is influenced by an individual's need, health behaviors, and predisposing beliefs or social structure.

Results: Thirty-three veterans and 40 providers (15 PCPs, 13 bariatric surgeons, 6 RDs and 6 health psychologists) were interviewed. Nearly 50% of Veterans had an annual household income less than $50,000 and 40% were disabled. We identified six individual-level barriers to undergoing bariatric surgery (**Table 1**): lack of social support, fear of surgery and its outcomes, fear of change, difficulty adhering to required dietary changes, the patients' perception that weight had not reached its "tipping point," and patient characteristics influencing provider referral.

Conclusions: Patient and provider education is needed to address patient fears of surgery and the lifestyle changes that are essential after surgery. Furthermore, patients must be empowered by providers to change their personal health practices.

Table 1. Individual barriers to bariatric surgery from provider and patient perspectives within Anderson's Behavioral Model of Health Services Use

Individual determinant	Theme	PCP	Bariatric surgeon	Registered dietitian	Health psychologist	Veteran
Social	1. Lack of social support	X			X	X
Beliefs	2. Fear of surgery and its potential outcomes	X	X	X		X
	3. Fear of change	X	X	X		X
	4. Patient characteristics influencing provider referral	X		X	X	X
Need	5. Perception that weight had not reached its "tipping point"	X	X	X		X
Personal Health Practices	6. Difficulty adhering to dietary changes	X	X	X		X

X indicates the barrier was identified as a theme during interviews with that type of study participant

H1

Referring and Accepting Provider Communication during Inter-hospital Transfers of Emergency General Surgery Patients: Challenges and Opportunities

Esra Alagoz, PhD, Megan Saucke, MA, Angela Ingraham, MD, MS

Submitter	Esra Alagoz
Phone	608-320-9495
Email Address	ealagoz@wisc.edu
Classification	Academic staff
Division	Wisconsin Surgical Outcomes Research
Lab	Ingraham lab
Science Type	Health services outcomes research
Keywords	Emergency general surgery, communication, inter-hospital transfers, qualitative research

Abstract Starts on Page 2.

Introduction: Transferred emergency general surgery (EGS) patients experience worse outcomes than directly admitted patients. Improving communication during transfers is a potential strategy to enhance patient care. However, little is known about inter-hospital provider communication. To this end, we examined the descriptions of the communication between providers during EGS transfers to a tertiary care hospital **(Figure)**.

Methods: We interviewed 17 transfer center nurses (TCNs) at an academic medical center regarding (in)efficient and (in)effective communication between referring (RP) and accepting (AP) providers. The in-person interviews were recorded, transcribed, and managed in Nvivo. We developed a codebook based on the Relational Coordination Framework and created new codes to capture emergent themes. Three or more researchers co-coded each transcript and met regularly to build consensus, discuss themes, and resolve differences. We used data matrices to perform constant comparisons and arrive at higher-level concepts.

Results: TCNs' descriptions of ideal communication from RPs consistently included a concise, accurate report describing the patient condition, a "complete work-up" (images, labs, etc.), and a reason for transfer. TCNs described APs as ideally being respectful and patient, without interrupting. Challenges to ideal communication centered around (1) appropriateness and completeness of information, (2) efficiency of communication, and (3) the degree of consensus about the course of action.

RPs provided incomplete information when they (1) lacked the infrastructure or personnel to complete the work-up, (2) were stretched too thin, (3) were unfamiliar with sending images to the accepting hospital, and (4) feared rejection of the transfer request based on information provided. In response, APs asked RPs to conduct additional tests or requested to speak to surgeons or other sub-specialists at referring hospitals to decide if transfers were necessary for optimal patient care.

Inefficiencies regarding the amount and order in which information was shared were another challenge. Excessive, irrelevant details during some RPs' presentations created challenges. Inefficient presentations were due to a lack of familiarity with and inconsistencies in the amount and content of information expected by APs. Notably, during a time crunch (e.g., APs operating), RPs were able to tease out the necessary details and tell a concise story. Finally, communication failed when RPs and APs disagreed about the need for transfer. RPs often expected APs to automatically accept their patient, and some grew frustrated when APs refused transfer. APs tried to diffuse tension during disagreements by (1) embracing the role of a "coach," (2) negotiating "wait-and-see" agreements with the RPs, (3) providing explanations of why they thought transfers were unnecessary, and (4) acquiescing to transfer requests to avoid confrontations.

Conclusions: TCNs at an academic medical center described numerous challenges to provider communication regarding transfers. Opportunities for improvement included sharing appropriate and complete information, ensuring communication is efficient, and reaching consensus about the course of action. The next phase of this study will examine AP and RP perspectives on communication and inform the development of interventions to improve inter-hospital communication.

Figure:

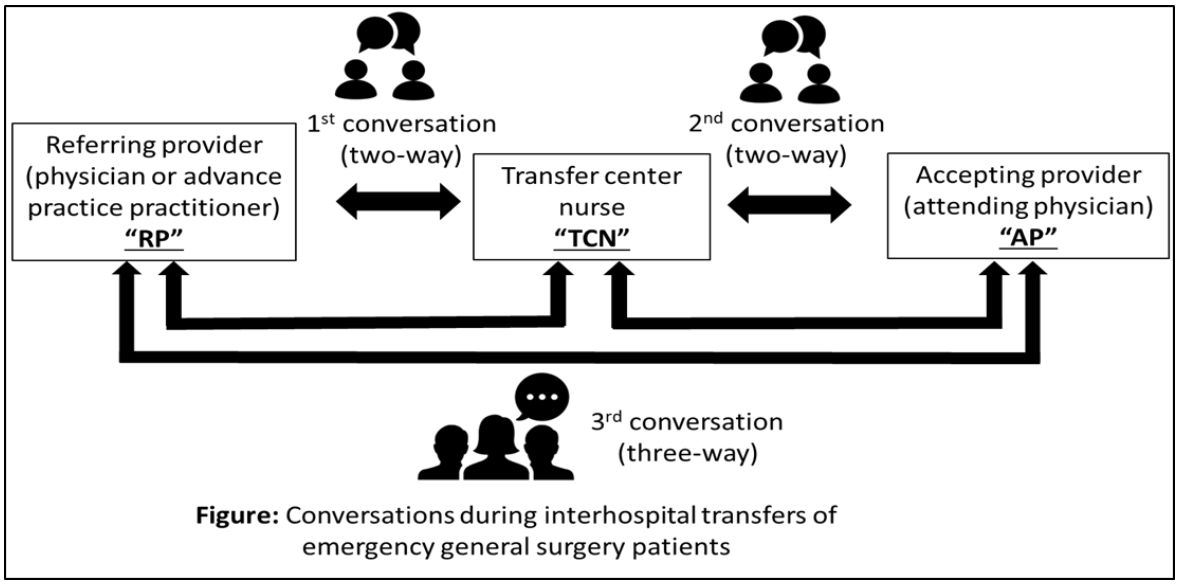


Figure: Conversations during interhospital transfers of emergency general surgery patients

H2

Working Behind the Scenes: How Transfer Center Nurses Facilitate Interactions and Communication between Providers regarding Transfers of Emergency General Surgery Patients

Ingraham A, Saucke M, Fernandes-Taylor S, Ljumani F, Alagoz E.

Submitter	Angela Ingraham
Phone	513-833-5205
Email Address	ingraham@surgery.wisc.edu
Classification	Academic staff
Division	Acute Care and Regional General Surgery
Lab	Ingraham
Science Type	Health Services
Keywords	Emergency general surgery, interhospital transfer, communication, transfer center, clinical outcomes

Abstract Starts on Page 2.

Introduction: Emergency general surgery (EGS) patients transferred between acute care hospitals experience worse outcomes than directly admitted patients. Breakdowns in communication between referring and accepting providers may contribute to this disparity. We describe barriers to care coordination by characterizing how transfer center nurses (TCNs) work to facilitate communication between providers.

Methods: We conducted semi-structured interviews with TCNs (n=17) at one tertiary, academic medical center, asking participants to describe their work arranging surgical transfers. We performed qualitative content analysis applying codes based on the Relational Coordination Framework and generating emergent codes. Codes were then organized within higher-order themes.

Results: When providers were unaware of hospitals' capabilities or processes (e.g., imaging availability at referring hospitals, which services treat specific conditions at accepting hospitals), TCNs provided the missing information required to facilitate timely care. Because referring providers struggled to describe, work-up, or diagnose patients' problems in a manner expected by the accepting provider, TCNs supplemented the conversation with critical or missing information, in particular the transmission of images. When providers expressed frustrations over transfer requests or delays in being connected with providers, TCNs helped providers manage their emotions. When providers struggled to multi-task (i.e., arranging transfers while simultaneously attending to other patients or duties), TCNs provided contextual information regarding providers' competing demands prior to connecting the providers on the call.

Conclusions: TCNs recognize and mitigate challenges providers face when transferring EGS patients. These threats may not be readily apparent to providers but may be targets for future initiatives to facilitate optimal patient outcomes.

H5

Post-operative Opioid Prescribing: How close is Wisconsin to Evidence-Based Guidelines?

Joanne Peters, PhD; Gregory J. Raupp; Jessica Schumacher, PhD; Tudor Borza, MD, MS; Dou-Yan Yang, PhD; Manasa Venkatesh, MS & Elise H. Lawson, MD, MSHS

Submitter	Joanne Peters, PhD
Phone	(608) 327-9820
Email Address	petersjo@surgery.wisc.edu
Classification	Associate researcher
Division	WiSOR
Lab	Elise Lawson & Tudor Borza
Science Type	Quantitative secondary data analysis regarding post-op patient opioid use
Keywords	Opioid-naïve, opioid-sensitized, Michigan OPEN prescribing guidelines, overprescribing, and surgeons

Abstract Starts on Page 2.

Introduction: There is substantial evidence that surgeons overprescribe opioids to patients after surgical procedures in the United States. Overprescribing has significant consequences as ~5% of opioid-naïve patients (defined as those not exposed to opioids in the 6 months prior to surgery) will continue taking opioids up to 12 months after the first postoperative prescription. Given the serious consequences of opioid abuse, judicious opioid prescribing to prevent persistent opioid use among surgical patients is critical. In 2018 and again in 2020, the Opioid Prescribing Engagement Network (OPEN) published evidence-based guidelines for postoperative opioid prescribing following common surgical procedures. The objective of our study was to determine how closely Wisconsin surgeons follow the OPEN guidelines for postoperative opioid prescribing after appendectomy, laparoscopic cholecystectomy, and hernia repair and to compare the difference in prescribing between opioid-naive and opioid-sensitized patients.

Methods: This study was a retrospective cohort study using secondary administrative data provided by the Wisconsin Health Information Organization (WHIO). We included adult patients (≥18 years old) who underwent an appendectomy, laparoscopic cholecystectomy, or hernia repair in Wisconsin between January - December 2017. Patients were excluded if they did not have continuous health insurance coverage in the 6 months before through 1 month after their surgical procedure. Opioid prescriptions filled within 7 days of the procedure were reported and normalized to Morphine Milligram Equivalents (MME). Analyses were conducted using STATA 15. Pearson chi-square tests were used to identify statistically significant differences among categorical variables. T-tests and Mann-Whitney U tests were used to identify statistically significant differences among continuous variables.

Results: Of the 9,807 patients included in the study, 63.3% (n = 6,208) filled a postoperative prescription for opioids and 81.8% of patients filling a prescription were classified as opioid-naïve (n = 5,076). Opioid-sensitized patients were more likely to fill a prescription than opioid-naïve patients (77.7% vs. 60.8%, $p<0.001$). On average, opioid-sensitized patients were prescribed 207.4 (SD = 296.4) after surgery, while opioid-naïve patient received an average of 153.4 MME (SD = 70.91) ($p<0.0001$). Both groups substantially exceed OPEN's maximum recommendations for postoperative prescribing of 75 MME (the equivalent of 10 tablets of 5mg oxycodone). Setting aside outliers, the median prescription fill in the opioid-naïve group was 150 MME (IQR: 100-200), which doubles the maximum recommendation from OPEN.

Conclusion: Surgeons in Wisconsin overprescribe opioids after common surgical procedures, with over half of filled prescriptions doubling the maximum recommendation from OPEN. Further, large standard deviations point to substantial variation in prescribing, especially among opioid-sensitized patients. Overall, these results indicate the need for additional education and training of surgeons regarding postoperative opioid prescribing. Development of additional guidance, however broad, regarding prescribing for opioid-sensitized patients may also help to reduce the substantial variance in prescribing practices. Efforts to describe the opioid-sensitized patient population may inform these efforts. Finally, additional research using national data is needed to support generalizability of the aforementioned results.

H6

Scared Decision-Making: The Role of Emotions in Surgeon-Patient Treatment Decisions about Low-Risk Thyroid Cancer

Megan C. Saucke, MA, Alexandra A. Rosser, BS, Benjamin R. Roman, MD, MSHP, Jennifer Hay, PhD, Corrine I. Voils, PhD, Susan C. Pitt, MD, MPHS

Submitter	Megan Saucke
Phone	608-265-2458
Email Address	saucke@surgery.wisc.edu
Classification	Academic staff
Division	WiSOR
Lab	Pitt
Science Type	Health services
Keywords	Thyroid cancer, decision-making, emotions

Abstract Starts on Page 2.

Introduction: Emotions such as anxiety and worry influence patients' treatment choices and how they interpret information about non-thyroid malignancies. Research about emotions in decision-making for thyroid cancer is lacking. This study aimed to characterize the emotional content of surgeon-patient communication during decision-making about treatment for low-risk thyroid cancer.

Methods: We audio-recorded conversations about treatment choice between patients (n=30) with low-risk thyroid cancer or biopsy suspicious for thyroid cancer and their surgeons (n=9) in two diverse health networks between 2018 and 2020. We used inductive and deductive content analysis guided by Lowenstein's *Risk as Feelings* model to explore the emotional content of verbatim transcripts.

Results: Patients were 20-71 years old. Most were white (86.7%) and female (80.0%). Surgeons had been in practice 2-50 years; 66.7% were male and 66.7% white. During the decision-making conversations, emotions focused on two central aspects of care: diagnosis and outcomes. With respect to diagnosis, patients commonly expressed fear, worry, and uncertainty about "*the C-word*." In terms of treatment outcomes, patients often worried about cancer growing or spreading if it was not removed; few expressed fears about surgery itself. Many surgeons responded to patients' emotions with validation, education, and reassurance, acknowledging that a cancer diagnosis can be "*scary*" and highlighting the "*slow-growing*" nature and excellent prognosis of thyroid cancer compared to other malignancies. Some surgeons missed opportunities to provide empathy and rarely asked patients how they were feeling or coping. Regardless of whether patients expressed emotions about treatment, surgeons often described treatment alternatives in terms of their emotional outcomes or benefits. For example, some surgeons described thyroidectomy as providing "*peace of mind*" or a "*sense of completeness*." When describing less extensive treatment options, these surgeons warned that cancer or thyroid tissue remaining in the body might "*worry*" or "*bother*" patients. In contrast, surgeons who encouraged active surveillance often highlighted that surgery remained an option if the cancer grew, spread, or the patient experienced excessive anxiety. Surgeons also supported deliberation by emphasizing that are "*two right answers"* and *"no rush"* to make a decision.

Conclusions: Surgeons and patients both openly acknowledge patient fear and anxiety in response to diagnosis and as a reason to choose thyroidectomy. Peace of mind that comes from removing the cancer appears to be both a patient-centered and a surgeon-centered outcome. Active surveillance was not framed as providing psychological benefits. Emotionally supportive interventions are needed to provide peace of mind and reduce overtreatment in patients with low-risk thyroid cancer.

H4

Investigation of racial disparities in postoperative outcomes of reconstructive breast surgery in Wisconsin

Zeeda H. Nkana BS, Kasey Leigh Wood BS, Alison M. Karczewski BS, Kirsten A. Gunderson BS, Sarah M. Lyon MD, Aaron M. Dingle PhD, Samuel O. Poore MD PhD

Submitter	Zeeda Nkana
Phone	970.985.5422
Email Address	nkana@wisc.edu
Classification	Research Assistant
Division	Plastic Surgery
Lab	Samuel O. Poore and Aaron M. Dingle
Science Type	Health Sciences
Keywords	Racial disparities, postoperative outcomes, breast cancer, breast reconstruction, Wisconsin

Abstract Starts on Page 2.

Introduction: Breast cancer is one of the most common forms of cancer in females in the United States. Evidence demonstrates that non-white racial minority populations exhibit a higher risk of mortality and more advanced or aggressive presentations of the disease at the time of diagnosis, citing a racial disparity in access to preventative care and treatment as contributing factors. Further, breast reconstruction following mastectomy is known to elicit improvements in the quality of life of patients; however, females of non-white race are less likely to undergo reconstruction than their white counterparts. Although these disparities witnessed on a national level are evident in the state of Wisconsin as well, little is known about these effects on outcomes of breast reconstruction. Therefore, the present study used data from a single institution to evaluate the presence of racial disparities in postoperative outcomes of breast reconstruction following mastectomy in Wisconsin.

Methods: An IRB-exempt retrospective study was performed using the University of Wisconsin Hospitals and Clinics Authority Adult National Surgical Quality Improvement Program Registry to identify patients who underwent a reconstructive breast surgery following mastectomy from 2009 to 2020. Demographics, as well as preoperative, operative, and postoperative covariates, were recorded for each patient. Patients who underwent mastectomy without reconstruction, were of unknown or not reported race, and non-female were excluded. Univariate analysis and propensity score matching were performed to evaluate incidence of postoperative outcomes in relation to self-reported race.

Results: A total of 1,140 patients met the inclusion criteria, including 1,092 patients of white race, 29 patients of black or African American race, 7 patients of American Indian or Alaska Native race, 10 patients of Asian race, and 2 patients of Native Pacific Islander race. Patients of non-white race demonstrated a higher incidence of the preoperative covariates of morbid obesity (4.4% of white race versus 12.5% of non-white race, $p=0.010$) and existence of a bleeding disorder (0.3% of white race versus 4.2% of non-white race, $p<0.001$) than white patients. No association was found between patient self-reported race and incidence of postoperative complication on univariate analysis and propensity score matching.

Conclusions: The present study did not reveal an association between patient self-reported race and incidence of postoperative complication at an institution in Wisconsin. Analysis revealed an apparent lack of non-white patients who underwent breast reconstruction at the institution, which is not representative of the demographic distribution of the surrounding area. These findings warrant further research into the underlying causes that perpetuate inequities in access to care.

GROUP FIVE

Translational

T2

Genomic and functional assessment of allogeneic immunogenicity in pluripotent stem cell-derived arterial endothelial cells

Haynes WJ, Zhang J, Hermsen J, Perrin ES, Kumari S, Argus C, Bolin J, Steill J, Swanson S, Stewart R, Biermann M, Zhang J, Kamp TJ, Thomson JA, Brown ME.

Submitter	Matthew E. Brown, Ph.D
Phone	608-263-1727
Email Address	brownm@surgery.wisc.edu
Classification	Assistant Professor
Division	Transplantation
Lab	Brown
Science Type	Translational
Keywords	RNAseq, Pluripotent stem cell, arterial endothelial cell, cardiomyocyte

Abstract Starts on Page 2.

Introduction: Autologous and allogeneic pluripotent stem cells (PSCs) have the potential to enable curative, patient-specific cell therapies for cardiovascular pathologies and other vascular diseases affecting millions of Americans. Crucially, these cell therapies must maintain their function *in vivo* while evading destruction by recipient immune cells. Research to date has shown that, similar to traditional organ transplants, allogeneic PSC-derived cells, e.g., cardiomyocytes, can be swiftly rejected when transplanted into immune-competent hosts in the absence of immunosuppressive drugs.(Shiba et al, Nature 2016) Arterial endothelial cells (AECs) made from PSCs are a promising cell therapy for peripheral vascular disease and coronary bypass applications. However, in-depth studies of the molecular mechanisms mediating the immune response to PSC-AECs are lacking. In this study, we examine the immunogenicity-associated transcriptome of PSC-AECs using RNA sequencing (RNAseq). We also assess allogeneic immunogenicity in functional assays of cell proliferation and cytolysis.

Methods: RNAseq data was generated on an Illumina HiSeq2500 using the Ligation Mediated RNA sequencing (LM-Seq) protocol.(Hou et al, Sci Rep 2015) Differential Expression analysis was performed using count data with either the START App(Nelson et al, Bioinf. 2016) or DESeq2 followed by Gene Set Enrichment Analysis as implemented by GenePattern cloud-based servers. (Reich et al, Genetics 2006) Comparisons of select gene sets was done using TPM normalized data. Heat maps were generated using the web browser-based Morpheus.R widget from the Broad Institute. Mixed lymphocyte reactions (MLR) were performed by co-culturing PSC-AECs in the presence of allogeneic PBMCs. Cellular proliferation was measured by CFSE dilution in various immune subsets by flow cytometry. MLR supernatants were analyzed for cytokines via the Luminex 35-plex panel, on a MAGPIX xMAP system. Cytolysis was assessed using the CytoTox 96 Non-Radioactive Cytotoxicity Assay (Promega).

Results: Multiple gene sets were upregulated in PSC-AECs compared to PSC-cardiomyocytes (CMs) from the same PSC donor, including genes involved in cholesterol biosynthesis and VEGFA targets. Additionally, multiple immune-associated genes were upregulated with an FDR of less than 0.05, including NK cell mediated cytotoxicity, neutrophil degranulation, IL7 pathway, TNFa signaling, induced T cell and NK cells, IL8-CXCR2 pathway, plasma cells, and IL2RB pathway. Upon immune encounter in MLR assays, multiple ENDAT (rejection associated, Sis et al, AJT 2016) genes were expressed in PSC-AECs, including CAV1, CDH5, EDN1, and SELE. IL1B, TNFa, IL6, IL8 and other inflammatory cytokines and chemotactics were detected in the supernatants of MLR co-cultures. Finally, cytolysis was demonstrated in two allogeneic PBMC donors.

Conclusions: We have characterized an immunogenicity-associated transcription profile in PSC-AECs, including expression of genes previously shown in solid organ transplant patient biopsies to be associated with allorejection. In functional analyses (MLR and CytoTox assay), we show induction of inflammation-associated gene expression changes in PSC-AECs and that allogeneic PBMC donors mount a proliferative immune response to co-cultured PSC-AEC targets, including production of inflammatory cytokines and initiation of cell lysis.

Identification of gene expression patterns associated with allorejection will enable future approaches for genetically engineering PSC cellular therapies capable of evading recognition by transplant recipients' immune cells. (Deuse et al, Nat. Bio. 2019) Additionally, modeling the mechanisms of allorejection via experimental interrogation of purified populations of PSC-AECs and HLA-disparate donor PBMCs may offer novel insights into effective therapeutic design for preventing rejection/encouraging tolerance in traditional organ transplant patients.

T1

Tongue Strength and Vocal Communication Deficits Improve with Targeted Tongue and Laryngeal Exercises in a *Pink1-/-* Rat Model of Parkinson Disease

Courtney K. Broadfoot, Jesse D. Hoffmeister, Sarah A. Lechner, Maryann N. Krasko, Emily Lambert, John Russel, John Szot, Tiffany Glass, Nadine P. Connor, Cynthia A. Kelm-Nelson, Michelle R. Ciucci

Submitter	Courtney K. Broadfoot
Phone	920-737-5768
Email Address	Ckuehn2@wisc.edu
Classification	PhD Candidate
Division	Otolaryngology
Lab	Dr. Michelle R. Ciucci
Science Type	Translational Research
Keywords	Parkinson disease, exercise, voice, swallowing, *Pink-/-* rat

Abstract Starts on Page 2.

Introduction: Parkinson disease (PD) is a degenerative condition that devastates cranial sensorimotor functions, including vocal communication and swallow function. While the neuropathology of limb motor deficits is relatively well-understood, the progression and underlying neuropathology of cranial sensorimotor deficits remain poorly defined. Initial assays have suggested the noradrenergic-locus coeruleus (LC) system is likely to be involved in the early break-down of vocal communication and swallowing in PD. Previous work from our lab has revelated a relationship between norepinephrine (NE) concentration in the LC and vocal call complexity. Further, the LC demonstrates early and progressive neural degradation in Parkinson disease. Voice and swallowing exercises have been implemented to alleviate some aspects of dysfunction, however, the incomplete understanding of the mechanism of disease stymies treatment optimization. To investigate this problem with increased experimental control, we use a genetic rat model of PD (*Pink1*-/-) that shows early-onset vocal and swallow deficits and progressive pathology analogous to humans. The primary aims of this study were to: (1) determine how vocal and lingual exercise contribute to vocalization and tongue force behaviors, and (2) identify neurobiological mechanisms of disease progression and in response to exercise. Specifically, we hypothesized that targeted tongue and vocal exercise would increase tongue strength and increase loudness and complexity of vocal calls in *Pink1-/-* exercised rats compared to non-exercised rats. Additionally, we hypothesized that LC Tyrosine hydroxylase immunoreactivity (Th-ir), an indicator for NE synthesis, would be reduced in *Pink-/-* rats when compared to WT control rats, but increased as a function of exercise.

Methods: *Pink1-/-* rats (n=26) were randomly assigned either to an exercise or non-exercise condition. Wildtype (WT) rats (n=12) were assigned to a third control (non-exercise) group. Targeted exercises of the larynx and tongue were completed 5x per day for 8 weeks. Non-exercise rats underwent behavioral reinforcement procedures without vocal or lingual training. Ultrasonic vocalizations, tongue force, and timing behaviors were measured at pre- (2 months of age) and post-exercise (or control) timepoints (4 months of age). After the completion of the behavioral experiment, staining for tyrosine hydroxylase (TH) immunoreactivity was completed, and unbiased stereology was used to compare the number of TH-immunoreactive cell bodies in the locus coeruleus (LC) between treatment groups. To determine impact of exercise on tongue strength, timing behaviors, and vocal outcomes, a repeated measures analysis of variance (2x3 ANOVA) was carried out with factors of timepoint (pre/post-exercise) and condition (*Pink1-/-* exercise, *Pink1-/-* non-exercise, and wildtype non-exercise control). The number of TH immunoreactive cell bodies in the LC was compared among conditions using a one-way ANOVA. Post hoc analysis was performed with Fisher's Least Significant Difference Method. The critical level for significance was set at 0.05 for all testing.

Results: Exercise significantly increased maximum tongue forces (p<0.001) and vocal intensity (loudness) (p<0.05) in Pink1-/- exercised rats compared to the non-exercise Pink1-/- and WT control rats. There were no significant differences in number of TH immunoreactive cell bodies in the locus coeruleus as a function of exercise.

Conclusions: This work demonstrates benefits of targeted exercise to the larynx and tongue in a PD rat model. Future work stemming from these findings may uncover critical biological modifications occurring after exercise treatment that will provide a better understanding of the source driving these changes. Developing this foundational knowledge will support the advancement and refinement of clinical intervention targets.

T4

Polymorphic P2X7 receptor activity drives Th17-dependent self- and alloreactivity in non-human primates

Christopher Little, Jeremy Sullivan, William Burlingham, Dixon Kaufman

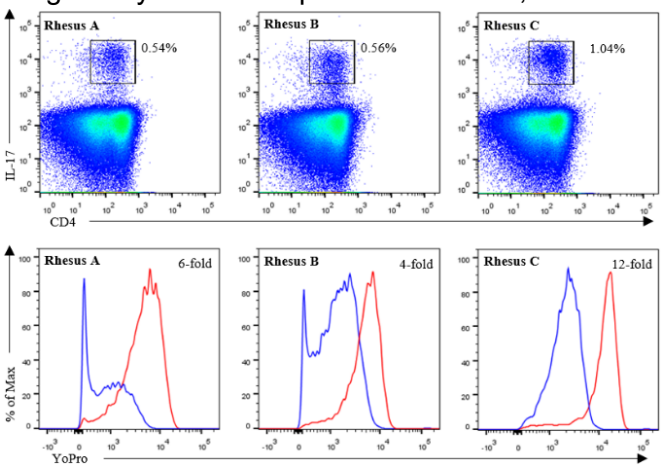
Submitter	Christopher Little, MD
Phone	920-277-8053
Email Address	little@surgery.wisc.edu
Classification	Resident
Division	Transplantation
Lab	Kaufman
Science Type	Translational
Keywords	Transplant, immunology, rejection, tolerance, primate

Abstract Starts on Page 2.

Introduction: Recent data has found the ATP-dependent P2X7 receptor (P2X7R) to be obligatorily involved in the cellular response to select self- and alloantigens. Notably, P2X7R activation has been implicated in Th17-dependent reactivity to collagen V (Col V), kα1-tubulin, and vimentin; antigens known to be exposed in ischemia/reperfusion injury and involved in allograft rejection. Such reactivity is normally suppressed by regulatory T-cells (Tregs); however, this effect can be lost. Accordingly, neutralization of Treg effector molecules, TGF-β and CD39, uncover Th17-mediated responses to these conserved antigens, thus implicating CD39+ Treg function and P2X7R activity as key components of immune equilibrium. Importantly, when antigen-specific tolerance is lost, P2X7R inhibition has been shown to abrogate Th17-mediated reactivity while maintaining Th1-based immunocompetency. In transplantation, there is evidence of increased lymphocytic P2X7R expression during acute rejection of cardiac and islet allografts, which is complemented by findings of prolonged graft survival after P2X7R antagonism in small animal models. Furthermore, P2X7R inhibition suppresses tv-DTH responses to alloantigen in cardiac and renal transplant recipients suffering acute and chronic rejection. Taken together, these studies underscore the importance of P2X7R activation and Th17 polarization in the pathogenesis of acute and chronic allograft rejection.

Methods: This study was carried out in rhesus macaques enrolled in the renal tolerance induction protocol through the Wisconsin National Primate Research Center
- Trans-vivo delayed type hypersensitivity assay (tv-DTH): Rhesus-to-mouse transfer of PBMC and specific antigen (with or without inhibitory agents) into the footpads of naïve mice
- YO-PRO-1 dye uptake assay: Flow cytometric analysis of YO-PRO-1 uptake through the P2X7 receptor after selective stimulation with BzATP
- Th17 polarization assay: Flow cytometric analysis of IL-17 production by stimulated T-cells

Results: As observed in humans, we demonstrated that TGF-β neutralization or restriction of extracellular ATP degradation via CD39 ATPase inhibition uncovered marked inflammatory responses to Col V, kα1-tubulin, and vimentin in rhesus macaques. We repeated this assay after CD4+CD25+ Treg depletion in lieu of molecular neutralization, which similarly unmasked reactivity to these antigens. Importantly, each of these approaches unveiled inflammatory responses, which were fully abrogated when performed in the presence of the P2X7R inhibitor, AZD9056. Having established its function in unregulated self-reactivity, we then turned our attention to the role of the P2X7R in transplant alloreactivity and tolerance induction. First, we characterized variant pore activity in rhesus macaques to validate their rigor as a translatable preclinical model for P2X7R-targeted immunoregulatory trials. Compared to humans, we revealed similar population-level frequencies of high and low P2X7R pore activity. Furthermore, we found that high pore activity was associated with increased Th17 polarization, as demonstrated by enhanced IL-17 production by CD4+ T-cells, which is known to be involved in alloreactivity. We therefore hypothesize that low pore activity may be associated with operational tolerance and that the P2X7R could therefore serve as a target for tolerance induction protocols. To address this question, studies are ongoing within



our current renal transplant tolerance model comparing P2X7R pore activity and T-cell polarization between tolerant and rejecting animals.

Conclusions: The P2X7R is an important component of Th17-mediated self- and alloreactivity that can serve as an immunoregulatory target for tolerance induction and anti-rejection therapy.

T3

Cold atmospheric plasma: a novel and selective treatment for solid cancers

Khang Huynh[1], Ha M. Nguyen[1,2], Bindu Anilesh Nair[1], Taylor J Aiken[1], Kevin Janeck[1], Song Kim[1], Paul Sondel[3,4], Mario Otto[3], J. Leon Shohet[2], Hau D. Le[1,3,5]

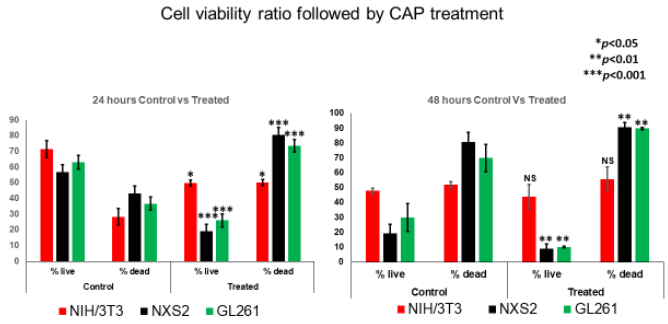
[1]Department of Surgery, [2]Department of Electrical and Computer Engineering, [3]Department of Pediatrics, [4]Department of Human Oncology, [5]Department of Biomedical Engineering

Submitter	Khang Huynh
Phone	678-708-5357
Email Address	knhuynh@wisc.edu
Classification	Medical student
Division	Pediatric Surgery
Lab	Le Lab
Science Type	Basic/Translational
Keywords	Cancer, oncology, pediatrics

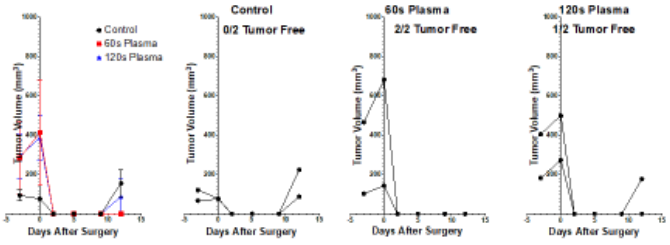
Abstract Starts on Page 2.

Introduction: Surgery is one of the main components in the multidisciplinary approach to solid cancer treatment. Among the top 10 most common solid cancers, 8.9% of the surgical resections result in incomplete resection. In some pediatric solid cancers such as high-risk neuroblastoma, complete resection is almost impossible due to the proximity and involvement of the tumor with vital organs, nerves or blood vessels. Tumor that remains after resection, either macroscopically or microscopically, is called positive surgical margin (PSM), and can lead to decreased survival, more morbid, intensive, and costly treatments. Current strategies against PSM have limited efficacy when further resection is not feasible. Cold atmospheric plasma (CAP) produces multiple radical oxygen and nitrogen species (RONS) which have been shown to be effective against many types of cancer. We ***hypothesize*** **that CAP can effectively and selectively target cancer cells and residual cancer in a murine model of PSM surgical margin.**

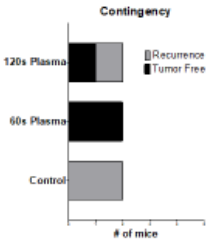
Methods: A cold atmospheric plasma jet was designed and constructed in collaboration with the College of Engineering, which produces higher proportion of hydroxyl radicals. A neuroblastoma cancer cell lines (NXS2) and a glioblastoma cell line (GL261) were used for *in vitro* experiments. A fibroblast cell line (NIH/3T3) was used as a control normal cell line. Cells are treated with CAP at various duration (0 – 120 s). Cell death was analyzed using trypan-blue method or CCK8 assay. A PSM was done using B78 melanoma cell line. Subcutaneous tumors were allowed to grow until approximately 300mm^3. To simulate PSM, the bulk of tumor was resected, leaving approximate 5% of tumor volume behind. Mice were then randomized into 2 groups: treatment group received CAP treatment, and control group without CAP treatment. Mice were then monitored for tumor recurrence.



Results: CAP treatment significantly produced more cell death to all cancer cells in comparison to normal fibroblast cells. The result suggests a relationship between degree of cell death and exposure time. In the PSM model, mice treated with CAP tolerated the treatment well without complications. Two weeks after treatment, 25% of mice in the CAP-treated group had recurrent tumor, compared to 100% of mice in the control group.



Conclusion: These early results demonstrate that CAP is both selective and effective in various *in vitro* tumor cell lines and an *in vivo* model of PSM. Future studies are needed to investigate the mechanism of tumor cytotoxicity and to further optimize the effectiveness of CAP in preclinical experiments.



CAP treatment *in vivo*

T6

Beyond Adding the Core Suture: An Entirely New Approach to Tendon Repair

Weifeng Zeng, MD[1], Nicholas J Albano, MD[1], Ruston J. Sanchez, MD[1], Ray Vanderby, PhD[2], Ronald Mccabe, PhD[2], Samuel O. Poore, MD, PhD[1], Aaron M. Dingle, PhD[1]

Submitter	Weifeng Zeng
Phone	3194995006
Email Address	Wzeng28@wisc.edu
Classification	Academic staff
Division	Plastic and reconstruction
Lab	Poore
Science Type	Translation
Keywords	Tendon repair, Flexor digitorum profundus

Abstract Starts on Page 2.

Introduction: Despite significant improvements to zone II flexor tendon over the last two decades, function-limiting complications persist. This article describes two novel techniques utilizing flexor digitorum superficialis (FDS) autografts to buttress the flexor digitorum profundus (FDP) repair site without the use of core sutures. The hypothesis being that the reclaimed FDS tendon autograft will redistribute tensile forces away from the FDP repair site, increasing overall strength and resistance to gapping in Zone II flexor tendon injuries compared to the current clinically utilized techniques.

Methods: Two novel FDP repair methods utilizing portions of FDS are described: 1) Asymmetric repair (AR), and 2) Circumferential repair (CR). Ultimate tensile strength and cyclical testing were used to compare novel techniques to current clinical standard repairs: 2-strand (2St) and 4-strand (4St) modified Kessler methods and 6-strand (6-St) M-Tang method. All repairs were performed in sheep tendons (n=10/group) by a single surgeon.

Results: Ultimate tensile strength testing demonstrated that both AR and CR techniques were comparable in strength to 6-St repairs, all of which were able to tolerate significantly stronger loads than the 2-St and 4-St repairs ($p<0.0001$). Cyclical testing demonstrated that AR and CR were able to withstand significantly more cumulative force ($p<0.001$ and $p=0.0064$ respectively) and tolerated significantly greater force to 2mm gap formation ($p=0.022$ and $p=0.026$) than the 6-st repair.

Conclusions: Incorporating FDS as an autologous graft for FDP repair provides at least equivalent ultimate tensile strength and significantly greater cumulative force to failure and 2mm gapping than a traditional 6-St repair.

T5

Respiratory-Swallow Coordination in a Rat Model of Chemoradiation

Linda M. Rowe, Nadine P. Connor, John A. Russell

Submitter	Linda Rowe
Phone	215 764 7428
Email Address	rowel@surgery.wisc.edu
Classification	Graduate Student
Division	Otolaryngology
Lab	Russell
Science Type	Translational
Keywords	respiration, dysphagia, chemoradiation, rat

Abstract Starts on Page 2.

Introduction: Safe deglutition requires the coordination of swallowing and respiration with a protective exhale-swallow-exhale pattern, which may be disrupted in people with head and neck cancer (HNC). Specifically, there are reports of post-swallow inhale events that elevate risk of penetration/aspiration. The effects of chemoradiation treatment (CRT) on the physiological mechanisms of swallow-respiratory phase relationships are not well understood. This gap in knowledge is largely due to challenges in isolating the specific effects of CRT versus other patient factors, and the invasive nature of biological assays. The purpose of this study was to assess the validity of a rat model for investigating the effect of CRT on respiratory-swallow coordination to allow future studies correlating functional changes with underlying biology.

Methods: Ten Sprague-Dawley rats received CRT (3mg/kg Cisplatin, followed by 10 fractions of 4.5 Gy/day of radiotherapy to an 8mm X 12mm area at the base of tongue). Ten additional control rats did not receive CRT. Videofluoroscopic swallow studies (VFSS) were performed at the 3-month time point in all rats. Diaphragm displacement was tracked as an indicator of respiratory phase. We examined the effect of CRT on swallow apnea durations, diaphragm movement, and bolus kinematics across the oropharyngeal (OP) and pharyngoesophageal (PE) phases of the swallow.

Results: Swallow-respiratory coordination patterns in all control rats were consistently characterized by exhalation after the swallow. However, CRT rats exhibited both post-swallow inhalation (CRT-IN), and post-swallow exhale (CRT-EX) patterns. The CRT-IN subgroup (n=4) had significantly longer swallow apnea durations (p=<.0001), faster PE bolus speed (p=.014), initiated the swallow at lower diaphragm displacements (p=<.0001), and inhaled post-swallow to higher diaphragm displacements (p=<.0001) than the control group and CRT-EX subgroup. The CRT-EX subgroup (n=6) took significantly smaller boluses than the control group (p=.039).

Conclusions: The rat CRT model exhibits altered respiratory-swallow coordination consistent with clinical HNC findings. Simultaneous VFSS diaphragm and bolus tracking in rat CRT model is a useful and valid tool for examining correlation between functional swallowing outcomes and underlying biological and physiological changes imposed by CRT in future studies.