UNIVERSITY OF WISCONSIN DEPARTMENT OF SURGERY

research summit 2024

FRIDAY, JANUARY 19, 2024 | THE MARQUEE AT UNION SOUTH

PROGRAM BOOK

Celebrating 15 Years of Innovation, Collaboration, and Discovery!

Welcome

Welcome to the 15th Annual University of Wisconsin Department of Surgery Research Summit!

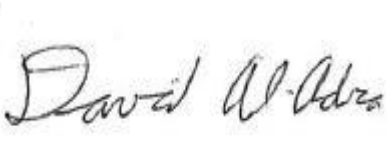
This academic year is not only a year in which the university celebrates its 175th anniversary of providing top-notch education, but also one for our department to mark 15 years of sharing the cutting-edge scientific achievements of our research faculty, staff, and trainees. Thus, "**Celebrating 15 Years of Innovation, Collaboration, and Discovery"** is the theme of the 2024 Department of Surgery Research Summit.

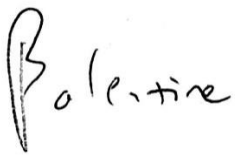
We are thrilled to have Dr. Katherine Gallagher join us as this year's keynote speaker. Dr. Gallagher is the Leland Ira Doan Professor of Surgery at the University of Michigan. She is also Vice Chair of Basic and Translational Science and holds a joint appointment as Professor of Microbiology and Immunology. A vascular surgeon-scientist, she is an expert in the molecular pathogenesis of wound repair and has contributed substantially to the understanding of epigenetics in immune cells associated with tissue repair, cardiovascular diseases, sepsis, and COVID-19. Dr. Gallagher is a successful and well-funded researcher, and her talk will address the surgeon-scientist career track, including how we learn from our failures, cope with self-doubt, and conquer the barriers we encounter.

Researchers across our 11 divisions are continuing to conduct rigorous and innovative basic, clinical, educational, and translational science that is transforming surgical care, improving patient outcomes, and enriching the training of the next generation of surgeons and surgeon-scientists. You will hear just a sampling of these projects during today's 14 oral presentations, and we hope you will take the time to learn even more by visiting the 62 posters during our poster session. The faculty, scientists, and trainees who are sharing their research with us today represent the astounding breadth and diversity of the science that is being conducted in the department.

Conversations about artificial intelligence (AI) have become ubiquitous in news cycles over the last year, and the field of medical research is by no means unaffected. We're very fortunate to have Dr. Pallavi Tiwari, Associate Professor in the UW Departments of Radiology and Biomedical Engineering, as a guest speaker during our afternoon session. Dr. Tiwari co-leads Machine Learning for Medical Imaging, a multi-disciplinary initiative that is intended to foster collaboration between machine learning experts and medical imaging researchers at UW. She will be discussing the opportunities that AI applications present for the advancement of precision medicine, using her own lab's work in the area of tumor biology as a case study.

Over the last 15 years, the Research Summit has allowed us to share with and learn from one another as we collectively work to advance the field of surgery. We look forward to continuing that journey today and over the many years to come.





David Al-Adra, MD, PhD Courtney Balentine, MD, MPH

Program Co-Chairs

KEYNOTE SPEAKER

Katherine A. Gallagher, MD

Katherine A. Gallagher, Professor of Surgery, Professor of Microbiology and Immunology, and the Leland Ira Doan Professor of Surgery at the University of Michigan, is internationally known for her innovative translational research on epigenetic regulation of immune cells during normal and pathologic tissue repair and other cardiovascular disease processes. She is an expert in the molecular pathogenesis of wound repair and has contributed substantially to the understanding of epigenetics in immune cells associated with tissue repair, cardiovascular diseases, sepsis, and most recently, COVID-19.

She is, most notably, an exceptionally well-funded researcher supported by multiple R01s and is a member of the National Academy of Medicine, American Society of Clinical Investigation, American Surgical Association, Society of Clinical Surgery, a James IV International Scholar, a Distinguished Fellow of the Society of Vascular Surgery, and a Taubman Scholar. Dr. Gallagher is also the Vice Chair of Basic and Translational Science in the Department of Surgery. Her work is distinguished for its high quality and impact and has established the connection between epigenetic reprogramming of immune cells in normal and pathologic tissue repair as well as other disease states (published in such journals as *Cell Immunity*, the *Journal of Experimental Medicine*, and the *Proceedings of the National Academy of Sciences*). She is the Chair of the Bioengineering, Technology, and Surgical Sciences NIH-study section and is an original member of the NIH-NIDDK Wound Consortium. She is a tremendous mentor to junior faculty and trainees in medical research and has trained many postdoctoral residents to be the next generation of scientists, each of whom has achieved NIH (F/K) and major society funding (AHA, ADA, ACS, AAS/SUS, SVS). She was awarded the 2022 Michigan Institute for Clinical & Health Research mentor of the year award for her translational science mentoring efforts at the University of Michigan.

Gallagher received a Bachelor of Science degree in physiology and neurobiology from the University of Maryland in 1998, graduating with Highest Honors. She was a Howard Hughes Fellow at the NIH for two years. She graduated summa cum laude from the University of Maryland School of Medicine in 2002. She pursued her general surgery training at the University of Maryland, followed by her vascular surgery training at Columbia University in New York. During her residency, she pursued a postdoctoral research fellowship at the University of Pennsylvania. She has been tenure track faculty at the University of Michigan since 2011.

Her clinical expertise is in complex peripheral arterial disease, having previously directed the Cardiovascular Center's multidisciplinary Peripheral Arterial Disease Clinic for many years. She currently runs a nationally known program for popliteal entrapment and other non-atherosclerotic pathologies associated with claudication/leg pain at the University of Michigan. She is also on the executive board for Vascular Cures and the Taubman Institute.

INVITED UW-MADISON CAMPUS SPEAKER

Pallavi Tiwari, PhD

Dr. Pallavi Tiwari is an Associate Professor in the Departments of Radiology, Biomedical Engineering, and Medical Physics at the University of Wisconsin-Madison and serves as the Co-Director of Imaging and Radiation Science at the UW Carbone Cancer Center. Dr. Tiwari's research interests lie in pattern recognition, data mining, and image analysis for automated computerized diagnostic, prognostic, and treatment evaluation solutions using radiologic imaging in oncology and neurological disorders. Her research has so far evolved into over 60 peer-reviewed publications, 50 peer-reviewed abstracts, and 13 patents (8 issued, 5 pending). Dr. Tiwari has been a recipient of several scientific awards, most notably being named as one of 100 women achievers by the Government of India for making a positive impact in the field of Science and Innovation. In 2018, she was selected as one of Crain's Business Cleveland Forty under 40. She has also been awarded the J&J Women in STEM (WiSTEM2D) scholar award in Technology, and the Honorary Early Career Achievement Award through the Society for Imaging Informatics in Medicine. Most recently, Dr. Tiwari was inducted as a senior member of the National Academy of Inventors. Dr. Tiwari's research is funded through the National Cancer Institute, Veterans Affairs, the Department of Defense, and various foundation and state grants.

Program

University of Wisconsin Department of Surgery

15th Annual Research Summit

Friday, January 19, 2024 | Union South

7:30 AM **Registration & Continental Breakfast, Varsity Hall**

8:00 AM **Welcome & Opening Remarks, The Marquee**
David Al-Adra, MD, PhD, Program Co-Chair
Courtney Balentine, MD, MPH, Program Co-Chair

8:15 AM **Keynote Address: "Navigating a Career as a Surgeon-Scientist: Overcoming Setbacks, Dealing with Imposter Syndrome and Learning from Failure", The Marquee**
Katherine Gallagher, MD
Leland Ira Doan Professor of Surgery
Professor of Surgery, Section of Vascular Surgery
Professor of Microbiology and Immunology, University of Michigan

9:15 AM **Break**

9:25 AM **Abstract Oral Presentations, The Marquee**
7 minutes + 3 minutes Q&A

- **Clayton Marcinak** - "Early Pancreas Cancer Death Despite Pancreaticoduodenectomy: Investigating the Futile Whipple"
- **Sarah Thornton -** "Risk Factors for Acute Intraoperative Bradycardia in Patients Undergoing Gender Mastectomy"
- **Manasa Kalluri** - "Treating Hydrocephalic Macrocephaly Using Reduction Cranioplasty: A Systematic Review Evaluating Surgical Outcomes"
- **Peter Chlebeck** - "Novel Nano-particle Therapy Attenuates Acute Kidney Injury After Ischemia-Reperfusion"
- **Benjamin Cher** - "Small Sample Size but Still Definitive: A Secondary Analysis of a Randomized Trial on Central Neck Dissection for Papillary Thyroid Cancer"
- **Peter Nicksic** - "Comparison of Rodent Forelimb Nerve Repair Following Intraoperative Electrical Stimulation and Trigeminal Nerve Stimulation by Histologic Analysis"
- **Dawda Jawara** - "Patient and Provider Perceptions About Social Support After Bariatric Surgery: A Qualitative Study "

10:45 AM **Break**

Program

10:55 AM **Poster Session, Varsity Hall**

- 11:00-11:30 AM Speed Dating

11:45 AM **Lunch, Varsity Hall**
*Voting ends for Surgery Science Image Contest at 2:15 PM

12:45 PM **Abstract Oral Presentations, The Marquee**
7 minutes + 3 minutes Q&A

- **Ruth Davis** - “Microbiome Disruption in Post-Intubation Laryngeal Injury”
- **Jack Bontekoe** - “Loss of RIPK3 in Vascular Smooth Muscle Cells Prevents Abdominal Aortic Aneurysm Rupture”
- **Sahand Eftekari** - “Double Mirror Array Stereomicroscope for Resident and Global Microsurgical Training: A Proof-of-Concept Microscope”
- **Tiffany Glass** - “Feeding Ability and Intrinsic Tongue Maturation in the Ts65Dn Mouse Model of Down Syndrome”
- **Vlasta Lungova** - “Streptococcus Pseudopneumoniae Contributes to Vocal Fold Epithelial Remodeling”
- **Julia Illiano** - “Targeting Protein Consumption After Sleeve Gastrectomy Can Influence Weight Loss and Metabolism”
- **David Barnett** - “Resveratrol and Celastrol Modify Synaptic and Inflammatory Genetic Expression in a Model of Parkinsonian Rat Midbrain Primary Neurons”

2:05 PM **Break**

2:15 PM **AI in Research: “Artificial Intelligence and Computational Imaging: Opportunity for Precision Medicine”, The Marquee**
Pallavi Tiwari, PhD
Associate Professor, Departments of Radiology and Biomedical Engineering
Co-Director of Imaging and Radiation Science at Carbone Cancer Center
University of Wisconsin

3:00 PM **Department of Surgery Research Update, The Marquee**
Rebecca Minter, MD
A.R. Curreri Distinguished Chair, Department of Surgery

3:45 PM **Awards & Closing Remarks, The Marquee**
David Al-Adra, MD, PhD, Program Co-Chair
Courtney Balentine, MD, MPH, Program Co-Chair

4:00 PM **Celebration of 15th Anniversary Reception, Varsity Hall**
Bar service and refreshments provided

Acknowledgements

We would like to thank the following individuals who served on the **2024 Research Summit Planning Committee** and made invaluable contributions to the planning of this event.

David Al-Adra, MD, PhD
Erin Alexander
Courtney Balentine, MD, MPH
Collin Brown
Hannah Clark
Jingyu Hao
Jessica Karls-Ruplinger, JD
Karen Lynch
Sarah Pavao
Susan Thibeault, PhD
Lee Wilke, MD
Jennifer Zellner, 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 80 abstracts that were submitted:

Kaleem Ahmed, MBBS, MS
David Al-Adra, MD, PhD
David Aufhauser, MD
Courtney Balentine, MD, MPH
Anna Beck, MD
Julia Berian, MD, MS
Daniel Cho, MD, PhD
Angela Gibson, MD, PhD
Rachel Godbout
Kirsten Gunderson, MD
David Harris, MD
Sarah Jung, PhD
Dixon Kaufman, MD, PhD
Cynthia Kelm-Nelson, PhD
Elise Lawson, MD, MSHS
Hau Le, MD
Aiping Liu, PhD
Brett Michelotti, MD
Muhammed Murtaza, MBBS, PhD
Heather Neuman, MD, MS
Manabu Nukaya, PhD
Samuel Poore, MD, PhD
Sudha Quamme, MD, MS
Patrick Schwartz, MD
Jacqueline Garonzik Wang, MD, PhD

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

Matthew Brown, PhD
Connie Chamberlain, PhD
Daniel Cho, MD, PhD
Michelle Ciucci, PhD, CCC-SLP
Luke Funk, MD, MPH
Angela Gibson, MD, PhD
David Harris, MD
Sarah Jung, PhD
Cynthia Kelm-Nelson, PhD
Mehreen Kisat, MBBS, MS
Hau Le, MD
Sandra Lin, MD
Vlasta Lungova, PhD
Brett Michelotti, MD
Courtney Morgan, MD
Muhammed Murtaza, MBBS, PhD
Sudha Pavuluri Quamme, MD, MS
Samuel Poore, MD, PhD
Tehseen Sarwar, MBBS
Linda Stafford, MPH
Nathan Welham, PhD, CCC-SLP
Lee Wilke, MD
Nabeel Zafar, MD, MPH

List of Abstracts

Alphabetized by PI/Lab within each group.

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

Group One: Basic Science and Translational Research

Carchman

Frequency of PI3K mutations in anal dysplasia and cancer; *Hillary Johnson, MD, Kirsten Dennison, Elise Dietmann, Evan Yao, Laura Gunder, Everlyne Nkadori, Stephanie McGregor, MD, PhD, Muhammed Murtaza, MBBS, PhD, Evie Carchman, MD*

Topical protease inhibitor, saquinavir, decreases eEF2 expression in a transgenic mouse model; *Sakura Haggerty, Evan Yao, Laura Gunder, Nathan Sherer, PhD, Evie Carchman, MD*

Ciucci

Pink1-/- rat model of Parkinson disease demonstrates abnormal swallowing of thin liquids in the prodromal stage of disease; *Maryann N Krasko, MS, Michelle R Ciucci, PhD, CCC-SLP*

Dingle

Can electrical stimulation prevent recurrence of keloid scars: A scoping review; *Robert George, MD, Caroline C. Bay, BA, Sarah Thornton, BA, Jessieka Knazze, BA, Nicole Kane, BS, Kip Ludwig, PhD, Samuel Poore, MD, PhD, Aaron Dingle, PhD*

Comparison of rodent forelimb nerve repair following intraoperative electrical stimulation and trigeminal nerve stimulation by histologic analysis; *Peter J. Nicksic, MD, D’Andrea T. Donnelly, BA, Weifeng Zeng, MD, Samuel O. Poore, MD, PhD, Aaron Suminkski, PhD, Aaron M. Dingle, PhD*

Osseointegrated neural interface: A proof-of-concept study in an ovine model; *Lucas Alan Sears, BS, Kirsten A. Gunderson, MD, Zeeda H. Nkana, BS, Robbie George, MD, Weifeng Zeng, MD, Danny Lazega, BS, James Morizio, PhD, Samuel Oliver Poore, MD, PhD, Aaron M. Dingle, PhD*

ROS scavengers addition to UW Solution extends hindlimb preservation times in advance of VCA; *Michael O. Sohn, Grant R. Seils, BS, Zeeda H. Nkana, BS, Weifeng Zeng, MD, Ellen C. Shaffrey, MD, Samuel O. Poore, MD, PhD, William E. Fahl, MD, Aaron M. Dingle, PhD*

Dingle & Poore

Advancements in rodent microsurgery: A novel 3D-printed microsurgery table with integrated heating pad, anesthesia delivery, and magnetic surgical instrument compatibility; *Rishi Mereddy, Weifeng Zeng, MD*

Garonzik-Wang

Characterizing the immunoglobulin repertoire in the nasal mucosa of transplant recipients with SARS-CoV-2 infection; *Pavan Bhimalli, BS, Max Bobholz, BS, William Vuyk, BS, Ava McCaw, Melanie Benito, BS, Alex Shipe, BS, Taylor Bradley, BS, Nancy Wilson, PhD, David O'Connor, PhD, Jacqueline Garonzik-Wang, MD, PhD*

Gibson

Evaluation of burn depth and reactive inflammation using perioperative fluorescence imaging; *Mary Junak, MD, Jocelyn Zajac, MD, Aiping Liu, PhD, Trevor Seets, MS, Sydney Jupitz, PhD, Tisha Kawahara, MS, Christie Lin, PhD, Adam Uselmann, PhD, Lauren Nosanov, MD, Lee Faucher, MD, Angela Gibson, MD, PhD*

The cytotoxic effect of CHG, Dial, and Johnson & Johnson on human burn wounds; *Rabia Ahmed, BS, Jocelyn Zajac, MD, Aiping Liu, PhD, Joana Pashaj, BS, Angela Gibson MD, PhD*

Glass

Feeding ability and intrinsic tongue maturation in the Ts65Dn mouse model of Down syndrome; *Erin Fisher, BS, Qiuyu Yang, MS, Kayla Hang, BS, Riley Brutto, Tiffany Glass, PhD*

Harris

Targeting protein consumption after sleeve gastrectomy can influence weight loss and metabolism; *Julia Illiano, BS, Grace Zhu, PhD, Luiz Lopez, Odin Schaepkens, Dudley Lamming, PhD, David A. Harris, MD*

Vertical sleeve gastrectomy reduces senescent signal in female mice; *Samuel Saghafi, Julia Illiano, Grace Zhu, PhD, Molly Mulcahy, PhD, RD, Maggie Stangis, MS, Dawn Belt Davis, MD, PhD, David A. Harris, MD*

Kelm-Nelson

Effect of site-specific resveratrol administration on Parkinsonian vocalization behavior and inflammatory gene markers in male Pink1-/- rats; *Monalyce Hamza, BA, David G.S. Barnett, MD, Sarah A. Lechner, BS, Cynthia A. Kelm-Nelson, PhD*

Resveratrol alters NF-κB signaling target mRNA profiles in Parkinsonian Pink1-/- rats; *Sarah A. Lechner, BS, David G.S. Barnett, MD, Stephen C. Gammie, PhD, Cynthia A. Kelm-Nelson, PhD*

Resveratrol and celastrol modify synaptic and inflammatory genetic expression in a model of Parkinsonian rat midbrain primary neurons; *David G.S. Barnett, MD, Sarah A. Lechner, BS, Cynthis A. Kelm-Nelson, MS, PhD*

Le

Assessing the therapeutic potential of cold atmospheric plasma (CAP) on glioblastoma: In vitro studies unveiling cellular responses; *Ligi Milesh, PhD, Bindu Nair, PhD, Ha M. Nguyen, PhD, J. Leon Shohet (Emeritus Professor), Hau D. Le, MD*

Liu

Loss of RIPK3 in vascular smooth muscle cells prevents abdominal aortic aneurysm rupture; *Jack Bontekoe, MD, Ting Zhou, PhD, Zulmari Silva-Pedraza, Michelle Conte, Huan Yang, PhD, Bo Liu, PhD*

Poore

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

Ronnekleiv-Kelly

Genetic knockout of clock repressors produces a less aggressive pancreatic adenocarcinoma phenotype; *Desmond L. Layne, MD, Matthew Shen, Patrick B. Schwartz, MD, PhD, Manabu Nukaya, PhD, Sean M. Ronnekleiv-Kelly, MD*

Thibeault

Effects of acute and chronic psychosocial stress on the laryngeal microbiome; *Anumitha Venkatraman, PhD, CCC-SLP, John Binns, BS, Katelyn Jacobs, Susan L. Thibeault, PhD, CCC-SLP*

RNA-sequencing of human vocal fold fibroblasts: Defining a scar genotype; *Michelle Bretl, MS, CCC-SLP, Lingxin Cheng, Christina Kendziorski, PhD, Susan Thibeault, PhD, CCC-SLP*

Streptococcus pseudopneumoniae contributes to vocal fold epithelial remodeling; *Vlasta Lungova, PhD, Madhu Gouda, BSc, Stephanie Bartley, BSc, Anumitha Venkatraman, PhD, Susan L. Thibeault, PhD*

Transcriptome dynamics during vocal fold injury and repair; *Kristy Wendt, Elliot Xie, Ted Lunga, MD, Chitrasen Mohanti, Christina Kendziorski, PhD, Susan Thibeault, PhD*

Group Two: Clinical Science and Health Services Research

Afifi

A systematic review of concomitant use of low-dose isotretinoin and energy-based therapies for acne vulgaris; *Caroline C. Bay, BA, Sarah M. Thornton, BA, Gina Krause, BS, Alessandro Preda, BS, Robert E. George, MD, Ahmed Afifi, MD*

Aufhaser

Takotsubo cardiomyopathy in orthotopic liver transplant: Single center experience; *Ekaterina Fedorova, MD, David Aufhaser, MD*

Balentine

Small sample size but still definitive: A secondary analysis of a randomized trial on central neck dissection for papillary thyroid cancer; *Benjamin A.Y. Cher, MD, MS, Alex Chiu, MD, Dawn M. Elfenbein, MD, MPH, Simon A. Holoubek, DO, Kristin L. Long, MD, MPH, Erin C. MacKinney, MD, David F. Schneider, MD, Rebecca S. Sippel, MD, Courtney J. Balentine, MD, MPH*

The risks of failed nonoperative management of appendicitis in older adults; *Nicole Lunardi, MD, MSPH, Elisa Marten, MS, Sherene Sharath, PhD, MPH, Panos Kougias MD, MSc, Thai H. Pham, MD, Courtney J. Balentine, MD, MPH,*

Cho

Detecting single suture sagittal, unicoronal, and metopic craniosynostosis: Evaluating the diagnostic accuracy of anthropometric measurements; *Manasa H. Kalluri, BS, Jessica D. Blum, MD, MSc, Kristine M. Carbuilldo, MD, Catharine B. Garland, MD, Daniel Y. Cho, MD, PhD*

Evaluating outcomes and complications following various maxillomandibular fixation techniques: A systematic review and meta-analysis; *Manasa H. Kalluri, BS, Armin Edalatpour, MD, Kishan M. Thadikonda, MD, Jessica D. Blum, MD, MSc, Catharine B. Garland, MD, Daniel Y. Cho, MD, PhD*

The association of neighborhood disadvantage with surgical outcomes and follow up adherence in patients with cleft lip and/or palate; *Daniel Y. Chu, BA, Jessieka T. Knazze, BA, Chloe Lam, BS, Alexandra D. Center, BA, Manasa H. Kalluri, BS, Caroline Bay, BS, Ellen C. Shaffrey, MD, Steven P. Moura, MA, Catharine B. Garland, MD, Daniel Y. Cho, MD, PhD*

Treating hydrocephalic macrocephaly using reduction cranioplasty: A systematic review evaluating surgical outcomes; *Manasa H. Kalluri, BS, Steven P. Moura, MA, Alexandra D. Center, BS, Jessica Blum, MD, MSc, Ellen C. Shaffrey, MD, Samuel Lee, BA, Jinggang J. Ng, MA, Bermans J. Iskandar, MD, Catharine B. Garland, MD, Daniel Y. Cho, MD, PhD*

Davis

Microbiome disruption in post-intubation laryngeal injury; *Ruth J. Davis, MD, Meghan H. Shilts, MS, MHS, Britton A. Strickland, PhD, Seesandra V. Rajagopala, PhD, Suman R. Das, PhD, Christopher T. Wootten, MD, Alexander Gelbard, MD*

De Roo

This is kind of a scary conversation: A qualitative analysis of patient-surgeon communication about rectal cancer treatment; *Melanie Fritz, MD, Joshua Sommovilla, MD, Elise Lawson, MD, Amy Zelenski, PhD, Margaret Schwarze, MD, Ana De Roo, MD*

Dingle

A narrative review exploring bacterial colonization and stoma complication management in osseointegrated prosthetics; *Mitchell J. Benyukhis, Michael O. Sohn, Sahand C. Eftekari, BS, Caden J. Lambie, BS, Nicole C. Kane, BS, D'Andrea T. Donnelly, BA, Samuel O. Poore, MD, PhD, Aaron M. Dingle, PhD*

The genetic landscape following neurorrhaphy: A narrative review; *Nicole Kane, BS, Molly Winchenbach, Sarah Thornton, BA, Anna Jesch, D'Andrea Donnelly, BA, Samuel Poore, MD, PhD, Aaron Dingle, PhD*

Trigeminal nerve stimulation: A systematic review of reported adverse events and future clinical applications; *Sarah M. Thornton, BA, D'Andrea T. Donnelly, BA, Peter J. Nicksic, MD, Samuel O. Poore, MD, PhD, Aaron M. Dingle, PhD*

Funk

Patient and provider perceptions about social support after bariatric surgery: A qualitative study; *Dawda Jawara, MD, Esra Alagoz, PhD, Kate V. Lauer, MD, Corrine I. Voils, PhD, Luke M. Funk, MD, MPH*

Garonzik-Wang

Length of stay following orthotopic adult liver transplant; *Ekaterina Fedorova, MD, Jacqueline Garonzik Wang, MD*

Gast

Regret after gender-affirming surgery: A comparison; *Sarah M. Thornton, BA, Armin Edalatpour, MD, Katherine M. Gast, MD, MS*

Trends in nipple reconstruction in gender-affirming mastectomies; *Sumin Yang, BS, Armin Edalatpour, MD, Jacqueline Israel, MD, Katherine Gast, MD, MS*

Gibson

Effect of a multidisciplinary approach in the management of patients with advanced stage pressure injuries; *Alyssa McClelland, BS, Jocelyn Zajac, MD, Molly Oberdoerster, DO, Cindy Schmitz, NP, Ambar Haleem, MD, Angela Gibson, MD, PhD*

Lautner

Axillary nodal staging in women undergoing upfront surgery for DCIS in Wisconsin; *Meeghan A. Lautner, MD, Chandler S. Cortina, MD, MS, Jessica R. Schumacher, PhD, Randi S. Cartmill, MS, Joseph J. Weber, MD, Jill Ties, MD, Joanne Pasiuk, MD, Adrienne N. Cobb, MD, MS, Subramanian Natarajan, MBBS, Barbara J.S. Boyer, MD, Elise Lawson, MD, Amanda L. Kong, MD, MS*

Lobeck

Changing the paradigm of congenital diaphragmatic hernia care - A tale of a two-hospital system; *Michael Stellon, MD, Devashish Joshi, MD, Sofia Nehring Firmino, BA, Molly Ryan, BA, Michael Beninati, MD, Ryan McAdams, MD, Inna Lobeck, MD*

Implications of social determinants of health in access to and outcomes of fetal surgery; *Devashish Joshi, MD, Michael Stellon, MD, Gabriella Mullally, BA, Linda Cherney Stafford, MPH, Glen Leverson, PhD, Michael Beninati, MD, Inna Lobeck, MD*

McCulloch

Coordination of oro-pharyngeal pressures during swallowing; *Tadeas Lunga, MD, Kazuhiro Hori, MD, Suzan Abdelhalim, MD, MPH, Timothy McCulloch, MD*

Michelotti

Patient-reported functional outcomes in operative versus non-operative treatment for traumatic hand and wrist injuries; *Elif Kurt, BS, Steven Moura, MA, Caroline Bay, BA, Armin Edalatpour, MD, Brett Michelotti, MD*

Odorico

Is it safe to import donation after cardiac death (DCD) organs for simultaneous pancreas and kidney transplant (SPK)?; *Riccardo Tamburrini, MD, PhD, Glen Leverson, Dixon B. Kaufman, MD, PhD, Nikole A. Neidlinger, MD, MBA, David P. Al-Adra, MD, PhD, David D. Aufhauser, MD, Carrie Thiessen, MD, PhD, Didier Mandelbrot, MD, Sandesh Parajuli, MD, Jon S. Odorico, MD*

Successful simultaneous en-bloc kidney and pancreas transplantation (SEBKP) from donors <25 kg; *Riccardo Tamburrini, MD, PhD, Jon S. Odorico, MD*

Poore

Surgical management of adult acquired buried penis syndrome: A systematic review of patient-reported outcome instruments; *Sarah M. Thornton, BA, Allison J. Seitz, MD, Armin Edalatpour, MD, Samuel O. Poore, MD, PhD*

Puricelli

Cleft spectrum perinatal airway management: A quantitative analysis; *Johanna Ellefson, Samantha Barr, Maya Matabele, Manasa Venkatesh, Michael Puricelli, MD*

Quamme

Declines in perioperative opioid prescribing to Wisconsin children, 2017-2022; *Randi Cartmill, MS, Manasa Venkatesh, MS, Tudor Borza, MD, MS, Christine Boxhorn, MD, Rebecca Busch, MD, Elise Lawson, MD, MSHS, Sudha Pavuluri Quamme, MD, MS, Jessica Schumacher, PhD*

Rao

Risk factors for acute intraoperative bradycardia in patients undergoing gender mastectomy; *Sarah M. Thornton, BA, Ellen C. Shaffrey, MD, Caroline C. Bay, BA, Joshua Verhagen, BS, Peter J. Wirth, MD, Armin Edalatpour, MD, Jacqueline S. Israel, MD, Katherine M. Gast, MD, Venkat K. Rao, MD, MBA*

Sanger

Access to HRA and colorectal surgery support identified as important facilitators to a successful Veterans Affairs anal cancer screening program; *Austin Hewitt, MD, Linda Cherney Stafford, MPH, Esra Alagoz, PhD, Cristina B. Sanger, MD*

Voils

A quasi-experimental comparison of engagement and outcomes from a weight management trial delivered in-person versus virtually; *Hisham Ahmad, Stephanie M. Carpenter, Armaan Shetty, Scott Hetzel, Katya Garza, Laura Porter, Kristen Gray, Ryan Shaw, Megan Lewis, Lu Mao, Heather Johnson, William S. Yancy Jr., Felix Elwert, Corrine I. Voils*

Assessment of patient and provider factors associated with pharmacogenomic testing: A partnered evaluation of the Veterans Affairs National Pharmacogenomics Program; *Abigail Silva, PhD, Deepak Voora, MD, R. Ryanne Wu, MD, MHS, Catherine Chanfreau, PhD, Brian Bartle, MS, Nina Sperber, PhD, Allison Hung, MPH, Corrine Voils, PhD*

Increasing participation of Black and African Americans in weight management research: A qualitative study; *Chloe Mayfield, Shubhangi Sneha, Jennifer M. Gierisch, Corrine I. Voils*

Zafar

An electronic health record-based data commons for pancreatic cancer; *Kaleem S. Ahmed, MBBS, MSAI, Clayton Marcinak, MD, Yonghe Yan, BS, Gabriel McMahan, BS, Thomas Callaci, PhD, Noelle LoConte, MD, Sharon Weber, MD, Majid Afshar, MD, MSCR, Matthew M. Churpek, MPH, PhD, Jomol Matthews, PhD, Syed Nabeel Zafar, MD, MPH*

Early pancreas cancer death despite pancreaticoduodenectomy: Investigating the futile Whipple; *Clayton T. Marcinak, MD, Kaleem S. Ahmed, MBBS, Patrick R. Varley, MD, MS, Kaitlyn J. Kelly, MD, MAS, Rebecca M. Minter, MD, Sharon M. Weber, MD, Sam J. Lubner, MD, Jeremy D. Kratz, MD, Noelle K. LoConte, MD, S. Nabeel Zafar, MD, MPH*

Machine learning driven prediction modeling to identify patients at risk for post discharge venous thromboembolism after pancreatectomy for pancreas cancer; *Kaleem S. Ahmed, MBBS, MSAI, Sheriff M. Issaka, Clayton Marcinak, MD, Majid Afshar, MD, MSCR, Matthew M. Churpek, MD, MPH, PhD, Syed Nabeel Zafar, MD, MPH*

Survival among South Asian Americans with colon cancer: A cross-sectional analysis of a national dataset; *Kaleem S. Ahmed, MBBS, MSAI, Clayton T. Marcinak, MD, Noelle K. LoConte, MD, John K. Krebsbach, BS, Sehar S. Virani, MBBS, Andrea M. Schiefelbein, MSPH, Patrick Varley, MD, MS, Margaret Walker, MD, Kulsoom Ghias, PhD, Muhammed Murtaza, MBBS, PhD, Syed Nabeel Zafar, MD, MPH*

Group Three: Education Research

Afifi

A call for contributions: The need for improved retirement benefits and financial education for plastic surgery residents; *Zeeda H. Nkana, BS, Kirsten A. Gunderson, MD, Ahmed M. Afifi, MD*

Cho

Navigating the plastic surgery in-service exam: Content patterns and accessibility; *Sarah M. Thornton, BA, Armin Edalatpour, MD, Sarah M. Lyon, MD, Jessica D. Blum, MD, Jeffrey D. Larson, MD, Daniel Y. Cho, MD, PhD*

Dingle

The current state of microsurgical training models: A framework for the field of plastic surgery; *Taylor Penn, Sahand Eftekari, D'Andrea Donnelly, Ellen Shaffrey, MD, Sarah Jung, PhD, Aaron Dingle, PhD*

Poore

Bucatini pasta, Japanese shirataki konjac noodles, and artificial vessels: In search of the ideal low-cost vessel simulator for microsurgical education; *Jessieka T. Knazze, BA, Sarah M. Thornton, BA, Stephan L. Blanz, BS; D'Andrea T. Donnelly, BS, Anna K. Jesch, Weifeng Zeng, MD, Aaron M. Dingle, PhD, Samuel O. Poore, MD, PhD*

Double mirror array stereomicroscope for resident and global microsurgical training: A proof-of-concept microscope; *Sahand C. Eftekari, BS, Ellen C. Shaffrey, MD, Weifeng Zeng, MD, Katherine D. Reuter Munoz, MD, Aaron Dingle, PhD, Samuel O. Poore, MD, PhD*

Livestreaming microsurgery education: An avenue to expand global plastic surgery; *Sahand C. Eftekari, BS, Weifeng Zeng, MD, Ellen C. Shaffrey, MD, Katherine D. Reuter Munoz, MD, D'Andrea T. Donnelly, BA, Aaron M. Dingle, PhD, Samuel O. Poore, MD, PhD*

Unmatched. What's next? Is a preliminary year of residency or research fellowship better for reapplicants to plastic surgery?; *Robert E. George, MD, Caroline C. Bay, BA, Sarah M. Thornton, BA, Tammy Zhong, BS, Lauren P. Feeley, Aaron M. Dingle, PhD, Samuel O. Poore, MD, PhD*

Abstracts for Presentation

Basic Science & Translational Research Abstracts

Frequency of PI3K mutations in anal dysplasia and cancer

Hillary Johnson, Kirsten Dennison, Elise Dietmann, Evan Yao, Laura Gunder, Everlyne Nkadori, Stephanie M. McGregor, Muhammed Murtaza, Evie Carchman

Purpose/Background: Incidence and mortality of anal cancer are increasing despite improvements in HPV vaccination and anal dysplasia screening. Although anal dysplasia is thought to be a precursor lesion, we have limited ability to identify which patients with dysplasia are at highest risk for progression to anal cancer. The most common recurrent driver mutations, detected in 20% of anal cancers, affect the catalytic subunit of Phosphatidylinositol (3,4,5)-trisphosphate Kinase (PI3K). We hypothesize that PI3K mutations are an early event in anal carcinogenesis that may help identify patients with anal dysplasia at highest risk of developing cancer. In the current study, we evaluated the frequency of PI3K mutations in anal dysplasia and cancer samples.

Methods/Interventions: Archived tissue samples with known anal dysplasia and anal cancer were obtained through our institutional biobank. DNA was extracted from formalin-fixed, paraffin-embedded (FFPE) slides using the QIAamp DNA FFPE Advanced Tissue kit. Digital PCR (dPCR) assays for three of the most common PI3K mutants, E545K, H1047R, and H1047L (Qiagen dPCR LNA mutation assays), were utilized to test each sample with 20ng of template DNA on the QIAcuity microfluidic dPCR system. After correcting for loading concentration, the dPCR results are reported as total valid partitions and positive partitions (positive for wild-type and mutated DNA). Taking into account assay background, we required greater than or equal to 10 positive partitions for a sample to be considered positive for mutation.

Results/Outcomes: We have analyzed 88 samples so far in this study and unblinded them for data analysis. We found 10 patient samples (11.4%) positive for E545K mutation and no H1047R or H1047L mutants detected. Across the different stages of carcinogenesis, E545K mutation was detected in one patient (1/32, 3.1%) with pathologic low-grade dysplasia, six patients (6/52, 11.5%) with high grade dysplasia, and three patients (3/4, 75%) with anal cancer.

Conclusion/Discussion: Our results demonstrate that PI3K mutations can be detected in a fraction of patients with anal dysplasia, with increasing frequency of mutations in later stages of anal carcinogenesis. Further research is needed to determine if patients with anal dysplasia and associated PI3K mutations may be at an increased risk of progression to anal cancer.

Topical protease inhibitor, saquinavir, decreases eEF2 expression in a transgenic mouse model

Sakura Haggerty, Evan Yao, Laura Gunder, Nathan Sherer, PhD, Evie Carchman, MD

Background: Anal cancer, although rare, is a growing health concern worldwide as its prevalence has been increasing for the last decade. It has been previously determined that a topical protease inhibitor, Saquinavir (SQV), has the ability to decrease anal cancer development. However, the molecular mechanism by which it acts is unknown. This study was conducted to understand if SQV decreases the expression of eukaryotic elongation factor 2 (eEF2), an elongation factor known to promote cancer development when overexpressed, through phosphorylation. We utilized a transgenic mouse model of anal disease treated with or without SQV and analyzed eFF2 inactivation by measuring peEF2. We hypothesized that peEF2 would increase in mice treated with SQV.

Methods: HPV16 transgenic mice*, K14/E6/E7,* were utilized in this study due to their potential for spontaneously developing high grade anal dysplasia by 25 weeks of age. Mice were randomized into four treatment groups with approximately equal numbers of males and females: no treatment (n=25), SQV (2.5%) only (n=26), 7,12-Dimethylbenz(a)anthracene (DMBA) only (n=31), and DMBA + SQV (n=23). DMBA, a carcinogen, was administered topically to two treatment groups to promote carcinogenesis. Treatment began at 25 weeks of age and concluded after 20 weeks of treatment. Anuses were harvested to be fixed and underwent immunofluorescent staining for peEF2 (Cell Signaling, rabbit, #2331). A Fisher's exact test was performed to compare peEF2 expression at the anal transition zone (ATZ).

Results: 6 out of the 25 mice with no treatment had localized peEF2 staining at the ATZ while 14 out of the 26 mice treated with SQV had localized peEF2 staining at the ATZ. There was a statistically significant increase in peEF2 staining when mice were treated with SQV compared to mice that received no treatment (p=0.0448). 9 out of the 31 mice treated with DMBA had localized peEF2 staining at the ATZ while 11 out of the 23 mice treated with both DMBA and SQV had localized peEF2 staining at the ATZ. This difference was not statistically significant (p=0.2542).

Conclusions: peEF2 staining at the ATZ increased in mice treated with SQV alone compared to mice with no treatment, indicative of decreased eEF2 expression as a consequence of SQV treatment. Additional studies may be necessary to further analyze how SQV prevents anal cancer development, and if eEF2 inactivation can be used as a means of anal cancer prevention.

Pink1-/- rat model of Parkinson disease demonstrates abnormal swallowing of thin liquids in the prodromal stage of disease

Maryann N. Krasko, Michelle R. Ciucci

Introduction: Dysphagia is common in Parkinson disease (PD), and affects over 80% of individuals with PD. It has significantly adverse effects on health, quality of life, and mortality. The swallowing of thin liquids requires rapid, precise, and coordinated movement of the swallow mechanism. Given how swiftly thin liquids travel through the oropharynx, they can be challenging for individuals with PD. While the severity of dysphagia worsens as the disease advances, changes to swallowing occur years before a formal diagnosis is made. Therefore, signs of dysphagia could potentially serve as early indicators of the disease. However, because they are not specific and can be attributed to aging, they often go unreported, making it difficult to study changes in swallowing in the early or prodromal stages of PD. To address this, we used the validated early-onset genetic *Pink1* knockout (*Pink1-/-*) rat. Our prior research focused on their ability to ingest semi-solids and revealed oromotor and swallowing deficits, including increased oropharyngeal bolus speed. In this study, we hypothesized that *Pink1-/-* rats would show early oropharyngeal and esophageal dysfunction with thin liquids.

Methods: In this study, twelve male rats (*Pink1-/-* = 6, wildtype (WT) control = 6) were tested at 4 months of age. Videofluoroscopy (at 60 frames/sec) of rats ingesting a thin liquid–barium mixture was used to measure percent oropharyngeal stasis, oropharyngeal bolus accumulation, oropharyngeal residue, percent esophageal stasis, esophageal residue, esophageal retrograde flow, and gastric retrograde flow. Statistical analyses included paired t-tests to compare genotypes for swallowing outcomes (alpha 0.05).

Results: *Pink1-/-* rats showed a greater percentage of oropharyngeal (p=0.003) and esophageal residue (p=0.0002) across thin liquid trials compared to WT controls. Esophageal (p=0.023) and gastric retrograde flow (p=0.011) occurred in *Pink1-/-* rats significantly more times than in WT controls.

Conclusions: This study was the first to assess swallowing of thin liquids in *Pink1-/-* rats. Findings revealed that oropharyngeal and esophageal swallowing dysfunction occurs in *Pink1-/-* rats at 4 months of age during the prodromal stage of disease. The presence of swallowing deficits in *Pink1-/-* rats is analogous to that observed in human PD, suggesting that this model could be useful in studying the underlying mechanisms of early Parkinsonian pathology to advance identification and treatment.

Can electrical stimulation prevent recurrence of keloid scars: A scoping review

Robert George, MD, Caroline C. Bay, BA, Sarah Thornton, BA, Jessieka Knazze, BA, Nicole Kane, BS, Kip Ludwig, PhD, Samuel Poore, MD, PhD, Aaron Dingle, PhD

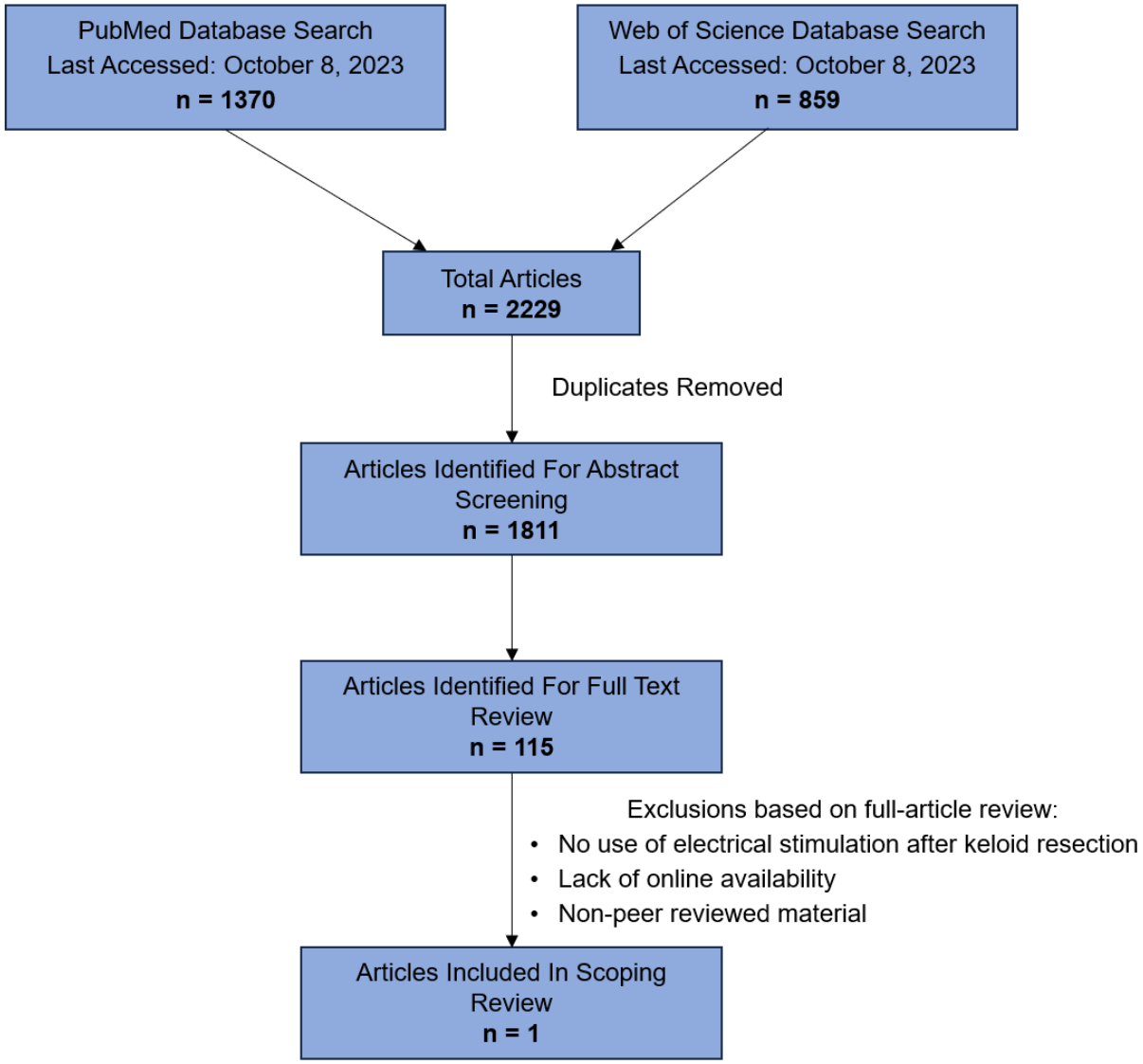
Introduction: Keloids represent an aberrant healing process, resulting in raised and discolored skin growths that expand beyond the initial injury. These lesions lead to discomfort, itchiness, psychological distress, and aesthetic concerns. The etiology is diverse, and treatment is difficult due to high recurrence rates, which span from 55-100% in certain cases. While no single theory explains keloid development, many treatments exist. Given their prevalence in both the developed and developing world, a treatment that provides a recurrence rate of 0% after excision would decrease the global burden of disease. Electrical stimulation (ES) has demonstrated interesting findings that could signify its utility in reducing the recurrence rate of keloids after resection. Therefore, the aim of this study is to conduct a scoping review to investigate ES as an adjuvant therapy for decreasing global keloid recurrence after excision.

Methods: A detailed scoping review was performed using PubMed and Web of Science databases in line with PRISMA guidelines. The search strategy encompassed terms linking keloids and various aspects of electrical stimulation. We did not apply any filters.

Results: Our search yielded 2229 articles, which, after removing duplicates, resulted in 1811 abstracts for full text review. 115 articles were analyzed as full text. After excluding all studies that did not use ES as adjuvant therapy after keloid resection, 1 article met inclusion criteria. In this article, 1 patient with a new wound after debulking of a “hypertrophic/keloid” scar was treated with ES. Keloid recurrence was not a measured outcome. Despite this, ES has demonstrated other evidence that suggests its utility. ES has been shown to counter keloidic features by reducing Mast cell counts, shifting wound composition from M2 to M1 macrophages, promoting angiogenesis, and, perhaps most importantly, controlling fibroblast orientation and location. Fibroblasts will orient themselves perpendicular to a current. While a direct current will make them migrate towards the anode, an alternating current will maintain their orientation, but they will not migrate. As a result, an alternating current is an inexpensive way to provide organization the wound bed of a disease characterized by disorganized fibroblasts.

Conclusions: ES could potentially serve as a multifaceted adjuvant treatment after keloid excision, steering the healing process away from keloid-associated characteristics. Its cost-effectiveness means it could be adopted globally, providing a strategy to mitigate the burden of keloids irrespective of other available treatments or economic conditions.

Figure 1. Search methodology



Comparison of rodent forelimb nerve repair following intraoperative electrical stimulation and trigeminal nerve stimulation by histomorphological analysis

Peter J. Nicksic, MD, D'Andrea T. Donnelly, BA, Weifeng Zeng, MD, Samuel O. Poore, MD, PhD, Aaron Suminkski, PhD, Aaron M. Dingle, PhD

Introduction: Peripheral nerve injuries are a common problem that incur significant morbidity and loss of function to patients. One method to improve outcomes in nerve regeneration is electrical stimulation (ES), which has been shown to improve motor and sensory functional outcomes when administered directly to the repaired nerve. Trigeminal nerve stimulation has also been shown to improve functional outcomes of nerve injury, but little is known about the mechanism of this therapy. The aim of this study is to compare the histologic architecture of repaired nerves in a rodent forelimb model to gain better insight on the mechanism of this therapy.

Methods: After being trained to proficiency in a reach and grasp task, 45 Lewis rats were randomized into 4 groups: (1) sham injury, (2) nerve injury with sham ES, (3) nerve injury with peripheral ES, and (4) nerve injury with trigeminal ES. The rats were then retrained on the reach and grasp task, and the median and ulnar nerves were harvested for analysis at 12 weeks post-injury. The nerves were Trichrome stained and compared qualitatively and quantitatively for ratios of total section area and total fascicle area.

Results: The sham injury and the peripheral ES groups maintained naive nerve architecture with organized fascicles. The sham ES and the trigeminal ES groups demonstrated loose fascicular architecture and abundant intrafascicular collagen. The cross-sectional fascicular area of the sham injury group was 61.50%. The repaired nerve cross-sectional fascicular area was 46.01%, 47.02%, and 53.57% for the sham ES, peripheral ES, and trigeminal ES, respectively. There was not statistical difference between groups for fascicular area ($P > 0.05$).

Conclusions: Cross-sectional fascicular area did not correlate with functional outcomes in this study. Qualitative histologic analysis demonstrated that the trigeminal ES group appeared to be more similar to the sham ES group, offering evidence that the improved functional outcome seen with this therapy is not acting directly on the peripheral nerve. These findings warrant further inquiry into the mechanism of trigeminal ES and support the hypothesis that this therapy is acting centrally, inducing targeted neuroplasticity at the level of the motor cortex.

Osseointegrated neural interface: A proof-of-concept study in an ovine model

Lucas Alan Sears, BS, Kirsten A. Gunderson, MD, Zeeda H. Nkana, BS, Robbie George, MD, Weifeng Zeng, MD, Danny Lazega, BS, James Morizio, PhD, Samuel Oliver Poore, MD, PhD, Aaron M. Dingle, PhD

Introduction: The Osseointegrated Neural Interface (ONI) is an innovative peripheral nerve interface that houses a transected nerve and coupled electrical components within long bones for eventual prosthetic control. Before the ONI can enter clinical testing, it must demonstrate longitudinal durability in an animal model analogous to the human anatomy. Similar in weight, and bone structure to adult humans, adult sheep are the standard model for osseointegrated prosthetic research, cementing them as the premier choice for the ONI. Despite their viability as an animal model, lack of information regarding nerve topography distal of the carpal and tarsal joints motivated the analysis of six thoracic limbs from mature, non-lactating female sheep. The anatomical data generated informed the construction of an Ovine ONI capable of stimulating and recording a sheep's major nerve. This study investigates the anatomy, surgical methodology, and electrophysiological data that will substantiate the ONI's move toward clinical trials.

Methods: Microsurgical dissection and radiological screening elucidated the topographical anatomy of major nerves, bone length, cortical bone thickness, and intramedullary canal diameter. Our surgical procedure saw one sheep undergo amputation followed by the insertion of an osseointegrated abutment. After osseointegration, we escorted the target nerve with electrodes attached into the medullary canal via corticotomy. Finally, we implanted the transmitter and receiver capsule into the sheep's shoulder. Now intact, the ONI system could receive programmed electrical stimulation patterns and transmit continuous recordings of the stimulated major nerve and EMGs from nearby muscles.

Results: The thoracic limb nerves consisted of one dorsal and three ventral nerves, with an average circumference of 5.14 (±2.00) mm and 5.05 (±1.06) mm at the midpoint, respectively. The average metacarpal length was 15.0 (±0.0) cm, respectively. The average cortical bone thickness of the forelimbs was 3.23 (±0.91) mm. Analysis of neural recording data identified stimulation artifacts with a frequency and pulse width of 32 Hz and 200 μs, respectively, verifying our neural interface system can remotely stimulate and continuously record from a major nerve.

Conclusions: Our investigation elucidates the critical anatomy and surgical approach used to create an ONI Ovine model. We also explore the functional specifications, benchtop test results, and 3D printing and coating processing steps for the capsule. In addition, we will cover electrophysiology data with various *in-vivo* stimulation patterns and post-processing data analysis used to validate the ONI.

ROS scavengers' addition to UW Solution extends hindlimb preservation times in advance of VCA

Michael O. Sohn, Grant R. Seils, BS, Zeeda H. Nkana, BS, Weifeng Zeng, MD, Ellen C. Shaffrey, MD, Samuel O. Poore, MD, PhD, William E. Fahl, MD, Aaron M. Dingle, PhD

Introduction: Ischemia-reperfusion injury (IRI) allows for tissue damage which might limit the success of vascularized composite allotransplantation (VCA), and reactive oxygen species (ROS) are integral to this injury which contributes to the inability of the current standard for tissue preservation, cold-ischemic (CI) storage with UW organ preservation solution, to sustain large VCAs for more than 6 hours prior to transplantation. We hypothesize that the addition of PrC-210, a ROS-scavenging compound triggered by ischemic reperfusion, to UW solution might reduce CI-induced myocyte injury and tissue damage during storage preceding VCAs, and our study investigates the efficacy of PrC-210 in this domain.

Methods: To test PrC-210's efficacy in reducing CI damage, Lewis rats underwent bilateral transfemoral amputation after receiving systemic perfusion, and both hindlimbs were then stored in 40mL of the same perfusate for 48h at 4°C. This perfusate was either the current standard UW solution alone (0mM PrC-210) or UW solution with PrC-210 at concentrations of either 10mM, 20mM, 30mM, or 40mM. Punch biopsies were taken at 0h, 4h, 8h, 24h, and 48h post-amputation, and these samples were used to test for CI-induced muscle cell death via activated Caspase-3,7 activity, free Cytochrome C levels, and qualitative histological analysis.

Results: Whereas the addition of UW solution alone resulted in significant increases relative to baseline in activated caspase-3,7 activity ($P=0.012$) and free cytochrome C levels ($P<0.0001$) by 8 and 24h, respectively, as well as the appearance of substantial myocyte injury in histological samples, the addition of 30mM PrC-210 was correlated with a significant reduction relative to control in both caspase-3,7 activity and free CytC levels ($P<0.01$ and $P<0.02$, respectively) as well as near-identical histological sample appearance to baseline at 0h and 8h (**Figure 1**). A single, 15-second perfusion of UW solution containing PrC-210 immediately prior to amputation was substantial enough to yield these dose-dependent rates of CI reduction, and the concentration of 2mM was determined to be sufficient for complete prevention of ROS-induced mitochondrial lysis.

Conclusions: These data illustrate the ability of PrC-210 to enhance the feasibility and cost-effectiveness of current organ transplantation procedures by reducing CI injury and extending preservation time. These findings are encouraging and suggest that PrC-210 warrants future development so it might one day be used to suppress IRI in VCA. Inspired by our initial results, we have since begun investigating the success of living VCA recipients following prolonged preservation either in the presence or absence of PrC-210.

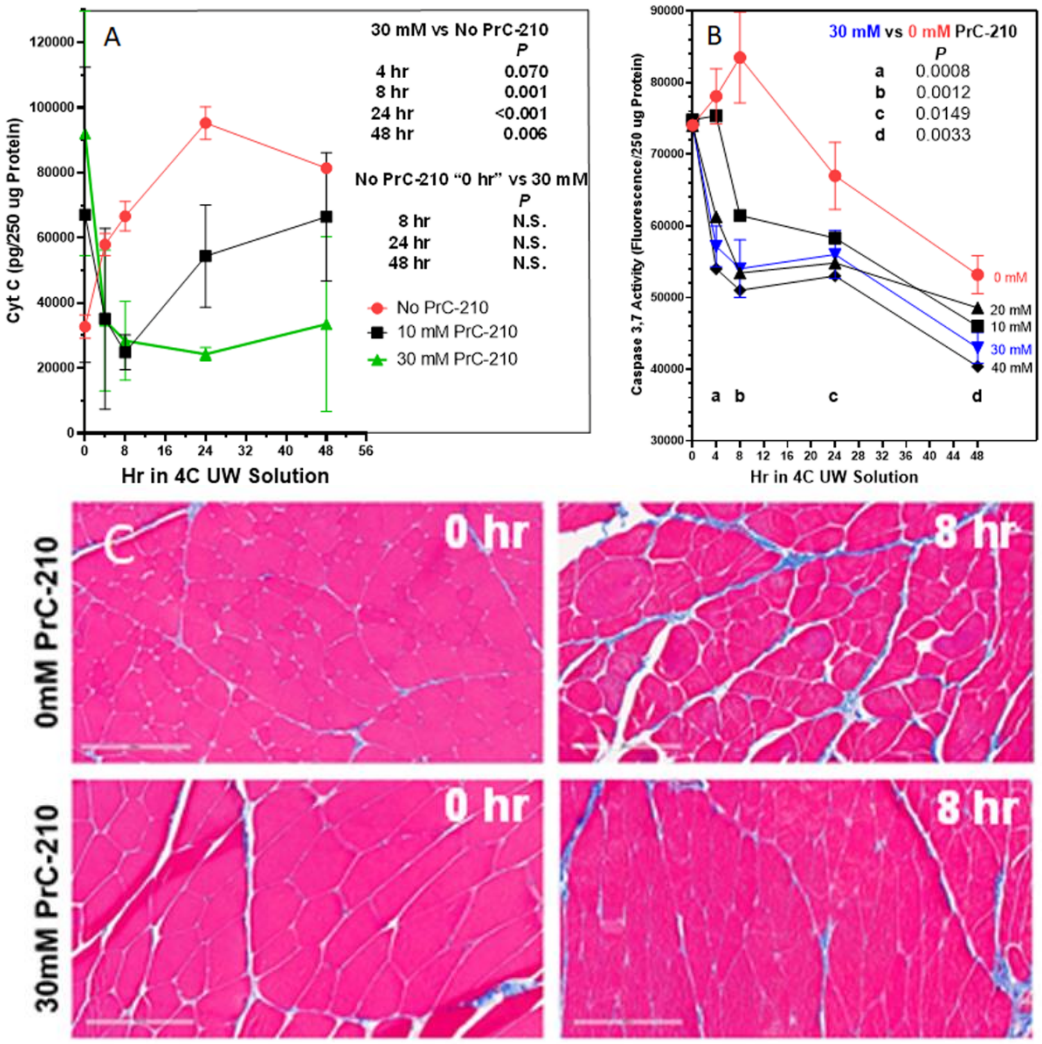


Figure 1 - The top plots illustrate that the addition of PrC-210 allows for decreased levels of cytochrome C and caspase-3.7 activity in a dose-dependent manner, and the bottom histological samples support this observation in their comparison of muscle tissue with or without the addition of PrC-210.

Advancements in rodent microsurgery: A novel 3D-printed microsurgery table with integrated heating pad, anesthesia delivery, and magnetic surgical instrument compatibility

Rishi Mereddy, Weifeng Zeng, MD

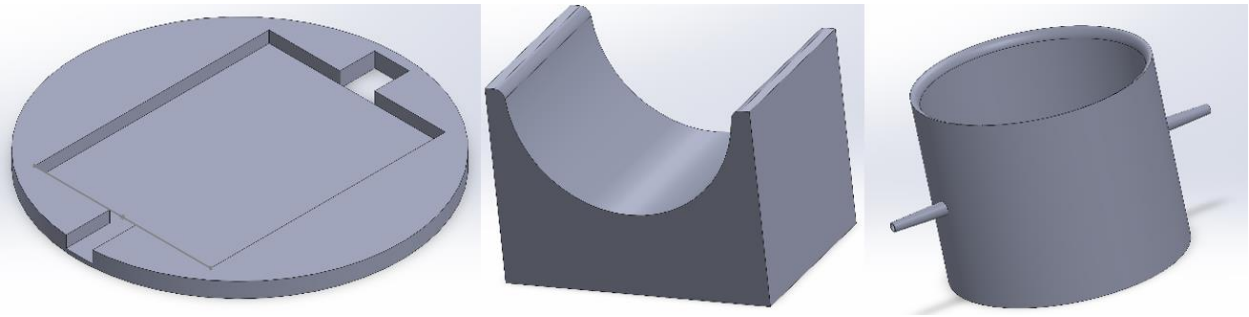
Introduction: Rodent models have long been invaluable in medical research, particularly in the fields of microsurgery and regenerative medicine. This abstract introduces a novel 3D-printed microsurgery table designed to enhance the rodent surgery environment and outcomes. The need for such a solution arises from challenges in controlling temperature and anesthesia delivery during rodent surgeries.

Methods: Our innovative microsurgery table incorporates an animal heating pad for maintaining rodent physiological stability and a modular nose cone for precise anesthesia delivery, minimizing the risk of leaks during movement, and ensuring a stable anesthetized state during surgeries. Additionally, the design features metal plates, enabling the use of magnetic surgical hooks for improved instrument control and greater ease of use for the operator.
1. Design Process: The 3D-printed microsurgery table was designed using SolidWorks, a computer-aided design (CAD) software. The design process involved conceptualization, material selection, and an iterative design.
2. Prototyping: Prototypes of the microsurgery table, nose cone holder and nose cone were 3D printed, out of PLA and resin respectfully, to verify the design's functionality and compatibility with rodent microsurgery needs.
3. Manufacturing: The final microsurgery tables and nose cones will be fabricated using 3D printing technology, ensuring consistency across multiple units.

Results: This project primarily focuses on the development and design of the 3D-printed microsurgery table with integrated features displayed in Figure 1. At this time no specific experimental data has been acquired. The primary purpose of this work is to introduce the novel design and highlight its potential benefits for the field of rodent microsurgery. Future studies will be conducted to evaluate the practical outcomes and performance improvements associated with the use of this table in rodent surgical procedures.

Conclusion: This 3D-printed microsurgery table offers various advantages for researchers, including enhanced surgical conditions and adaptability to a wide range of rodent species and sizes. It reduces the need for multiple specialized tables, thus promoting versatility and affordability. Moreover, the inclusion of magnetic surgical hook compatibility facilitates precise instrument control and greatly improves the surgeon’s quality of life. Researchers and educators can utilize this innovative design to improve rodent surgery techniques and provide comprehensive training for aspiring surgeons, ultimately advancing the fields of microsurgery and regenerative medicine. This novel solution addresses critical challenges in rodent microsurgery, contributing to the refinement of surgical procedures and fostering innovation in medical research.

Figure 1: SolidWorks CAD Designs of Microsurgery Table, Nose Cone Holder, and Nose Cone



Characterizing the immunoglobulin repertoire in the nasal mucosa of transplant recipients with SARS-CoV-2 infection

Pavan Bhimalli, BS, Max Bobholz, BS, William Vuyk, BS, Ava McCaw, Melanie Benito, BS, Alex Shipe, BS, Taylor Bradley, BS, Nancy Wilson, PhD, David O'Connor, PhD, Jacqueline Garonzik-Wang, MD, PhD

Introduction: The nasal mucosa is one of the primary entry sites for SARS-CoV-2 (SCV2). IgA is a main contribution of the adaptive immune system at the mucosal barriers. However, the relative contributions of different immunoglobulin (Ig) isotypes for mucosal host defenses, particularly in the context of immunocompromised patients, are poorly understood.

Methods: This observational study followed 20 immunocompromised patients who tested PCR positive for COVID-19. Patients were removed from the study upon testing negative. 17 patients had multiple positives over three or more different time points. Nasal swabs were collected from each patient on days 7, 14, and 28, then monthly thereafter, following a positive PCR test. Nasal swab fluid was diluted 1:100 and added to an Isotyping Panel and SCV2 Spike Panel. Ig concentrations were determined on MESO Workbench, with further analysis performed on Prism using paired t-testing for direct comparisons between IgGs and IgAs. Cycle quantification threshold (Cqt) values were determined by PCR to determine the amount of virus. Correlations were performed with Cqt values paired with Ig concentrations using two-tailed Person's r testing. If concentrations at a particular time point were unable to be calculated, both IgG and IgA concentrations were omitted.

Results: In the nasal mucosa, the levels of IgA were significantly higher than IgG ($p=.0024$), but the levels of spike-specific IgGs were significantly higher than IgAs for both wild-type (WT) ($p<.0001$) and several Omicron sublineages. However, Cqt values and anti-WT Ig concentrations were positively correlated with IgA levels ($p=.0066$) compared to IgG levels, where there was no correlation ($p=.9906$). This trend of IgA having a stronger correlation with Cqt values was observed with several Omicron sublineages.

Conclusions: In this study, we determined that IgG potentially confers a greater protective effect against infection due to its higher SCV2-specific concentrations relative to IgA. However, IgA may play a role in acute infection control, as IgA concentrations had a stronger correlation with the amount of virus present, as indicated by Cqt, compared to IgG. A better understanding of mucosal immunity can offer valuable insight into the frontline of infection and toward novel approaches to protecting vulnerable populations.

Evaluation of burn depth and reactive inflammation using perioperative fluorescence imaging

Mary Junak, MD, Jocelyn Zajac, MD, Aiping Liu, PhD, Trevor Seets, MS, Sydney Jupitz, PhD, Tisha Kawahara, MS, Christie Lin, PhD, Adam Uselmann, PhD, Lauren Nosanov, MD, Lee Faucher, MD, Angela Gibson, MD, PhD

Introduction: Early determination of burn depth is essential for guiding proper treatment of burn injuries. The primary technique used to evaluate burn depth is visual assessment, relying heavily on subjective interpretation while risking over-excision. Second window indocyanine green (SWIG) is a novel method of delayed fluorescence imaging with possible utility in burn surgery, as indocyanine green (ICG) persists in burn wounds 24 hours after intravenous injection. The objective of this study is to correlate intraoperative SWIG florescence with burn depth as evaluated by lactate dehydrogenase (LDH) staining. Additionally, given inflammation is thought to impact the progression of a burn, we investigated the relationship between SWIG florescence signal and reactive inflammation.

Methods: Consented patients with indeterminate depth burns received a 5 mg/kg ICG infusion during their third daily burn care after admission or 24-hours prior to surgery. SWIG was performed 24 hours after ICG injection on a region of interest (ROI) during wound care or during burn excision. A full thickness skin biopsy was taken from the center of the ROI and processed for ICG microscopy and staining. Burn depths were scored using LDH-stained sections. To investigate the relationship between SWIG and inflammation, nude mice underwent a full thickness contact burn or received endotoxin to induce inflammation. Mice were injected with ICG at 5mg/kg and SWIG signal was captured at the non-burned control, burned, and inflamed ROIs 24 hours after injection. Signal-background ratio (SBR) was calculated using the ratio between the averaged ICG intensity in the burned or inflamed ROI and the control ROI.

Results: There was no correlation between the raw SWIG fluorescence value of the ROI in vivo and burn depth as determined by LDH staining. Furthermore, when the fluorescence value of the ROI was normalized to the SWIG intensity of the overall image and the SWIG intensity of non-burn control skin, there was no correlation to burn depth. In mice, SWIG SBR was significantly higher in the burned region (3.2±0.5) compared to the endotoxin induced inflamed regions (1.6±0.1).

Conclusions: There is heterogeneity in the intraoperative fluorescence signal when compared to burn depth. This variability in fluorescence signal could be attributed to the effects of local inflammation on the burn wound microenvironment as animal studies have shown that ICG signal is present in non-burn inflamed tissue. Further studies are warranted to discern the role of inflammation on burn wound progression and fluorescence signal in humans.

The cytotoxic effect of CHG, Dial, and Johnson & Johnson on human burn wounds

Rabia Ahmed, BS, Jocelyn Zajac, MD, Aiping Liu, PhD, Joana Pashaj, BS, Angela Gibson MD, PhD

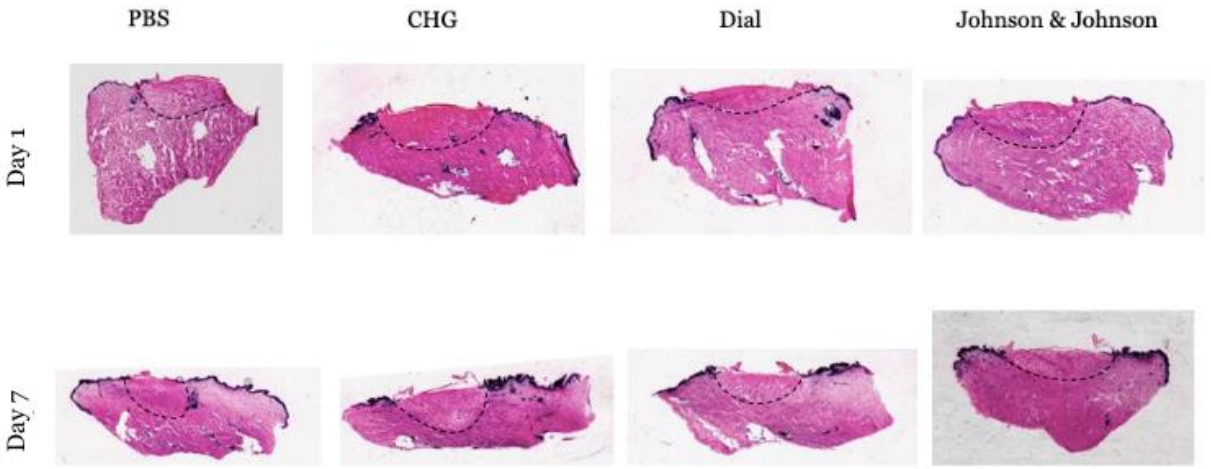
Introduction: Chlorhexidine gluconate (CHG) and soaps are commonly used to prevent burn wound infections in patients. However, it is thought that these antiseptic reagents may be cytotoxic to human skin. We have previously shown profound cytotoxicity of CHG in excisional wounds using an ex vivo human skin model. The purpose of this study was to observe the effects of CHG, Dial, and Johnson & Johnson (J&J) baby soap on cytotoxicity using an ex vivo human skin model of burn.

Methods: Skin samples were given partial thickness burns using a customized burn device at 150°C for 6 seconds (n =3 per condition per time point). The burn wounds were treated daily using a cotton tipped application for 20 seconds with either CHG, Dial, J&J, or PBS (phosphate buffered saline), then aspirated and rinsed using 1 milliliter of PBS 3 times. The tissue samples were cultured for 7 days in 37°C with 5% CO2. PBS was used as positive control for cell viability and full thickness boiled samples as negative control for 100% cell death. The cytotoxicity of CHG, Dial, J&J, was measured using lactate dehydrogenase (LDH) staining and an MTT viability assay on days 1 and 7. A two-way ANOVA statistical test was performed on the MTT with Tukey post-hoc analysis between time and treatment.

Results: In this ex vivo human skin model, we observed progressive loss of viability of PBS treated burn wounds indicative of burn progression. For better comparison among groups, in the MTT, we corrected for weight and normalized to PBS. We found a significant difference in viability between CHG and PBS on day 7 (p=.0388). In the samples stained with LDH: CHG, Dial, J&J, and PBS all show visible viable tissue on day 1. On day 7, CHG and Dial have a visible decrease in cell viability surrounding the burn region. However, there were no significant differences in the overall amount of viable tissue between days or treatment groups.

Conclusions: This study shows that CHG is toxic to the human skin starting from day 1 and leads to loss of viable skin cells extending outside of the original burn by day 7. J&J is less cytotoxic than Dial when applied for up to 7 days. Additionally, this model may be utilized to study burn wound progression in isolation of perfusion to identify non-vascular mechanisms of burn wound progression.

LDH Images



Feeding ability and intrinsic tongue maturation in the Ts65Dn mouse model of Down syndrome

Erin Fisher, Qiuyu Yang, Kayla Hang, Riley Brutto, Tiffany J. Glass

Introduction: Down syndrome (DS) is associated with developmental delays and difficulties with feeding during infancy and childhood. Weaning, or transitioning from nursing to independent deglutition, requires developmental change in movements of the tongue. However, little is known about whether tongue maturation is impacted in DS. This study tested the hypothesis that DS is associated with developmental delays in maturation of the tongue muscle system at weaning.

Methods: The Ts65Dn DS mouse model and controls were evaluated at 7 days of postnatal age (p7) (nursing), p21 (weaning), and p35 (mature deglutition) (n = 8-16 male and 8-16 female mice per group). Feeding, drinking, and body weight changes were quantified in p21 and p35 mice over 24 hours. Tongues were sectioned and stained to quantify myofiber size and expression of Myosin Heavy Chain isoform (MyHC) 2a and MyHC 2b. Transverse intrinsic tongue muscles were evaluated for myofiber size measures (average myofiber cross sectional area (CSA), CSA of MyHC 2a+ fibers, CSA of MyHC 2b+ fibers, Minimum Feret fiber diameter), and MyHC measures (%MyHC 2a+ fibers, and %MyHC 2b+ fibers). Weight and feeding data were analyzed by 3-way ANOVA to evaluate impacts of genotype, age, sex, and interaction effects. Preliminary tongue muscle data were evaluated with a univariate linear regression model to evaluate impacts of genotype on outcome measures in each anatomical region (anterior, middle, and posterior tongue), and a multivariate regression model was used to evaluate muscle measures with age, genotype and sex as covariates.

Results: There was a significant interaction effect between genotype and age in body weight changes (p=.0002), such that during 24 hours after weaning (p21), the Ts65Dn group lost between 6.1% - 8.5% of total body weight, compared to 1.7% - 2.6% loss of total body weight in the control group. However, Ts65Dn did not show weight loss relative to controls when evaluated over 24 hours at p35. The Ts65Dn group also consumed less food than the control group (p = .006). Preliminary analyses of tongue measures suggest Ts65Dn had differences predominately in myofiber size measures rather than MyHC measures, including significantly smaller CSA in the anterior tongue (p=.017) and middle tongue (p=.004), but not in the posterior tongue (p=.385) (**Figure 1**).

Conclusions: Weaning may be particularly susceptible to oromotor delays in DS, and Ts65Dn is useful for studying these delays. The Ts65Dn group showed differences in feeding efficacy at weaning, but did not show these differences two weeks later.

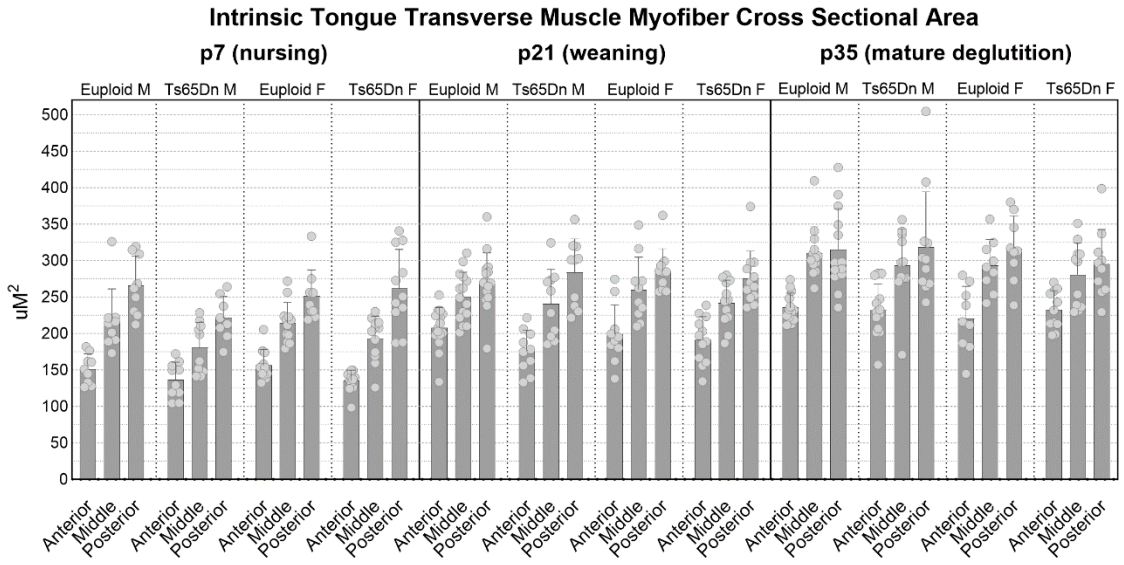


Figure 1. Myofiber cross sectional area (CSA) is one of several myofiber size measures of the anterior, middle, and posterior regions of the intrinsic tongue transverse muscle. Bars show mean and standard deviation. Each data point represents the average of several hundred myofibers in one muscle section of one mouse. Euploid = control, M = male, F = female.

Targeting protein consumption after sleeve gastrectomy can influence weight loss and metabolism

Julia Illiano, BS, Grace Zhu, PhD, Luiz Lopez, Odin Schaepkens, Dudley Lamming, PhD, David A. Harris, MD

Introduction: Following sleeve gastrectomy (SG) the added therapeutic potential of diet on obesity and T2D is understudied. Patients tend to increase protein consumption after surgery, however, protein restriction improves metabolic health and extends lifespan across species. We hypothesized that reducing protein intake following SG would improve post-operative weight loss, glucose tolerance, and metabolism.

Methods: Sixty-four C57BL/6J mice were preconditioned on western diet (WD) and weight-matched to SG or sham surgery. Mice were then placed onto high (36%), medium (21%), or low (7%) protein, or were continued on WD. Weights and food intake were tracked. Metabolic phenotyping, indirect calorimetry, body composition, and strength (cling assay) were measured. Untargeted metabolomics and whole tissue RNAseq were performed on liver and analyzed with MetaboAnalyst and EnrichR, respectively. AUC, one-way ANOVA with Dunnett corrections, and t-tests were used.

Results: SG induced weight loss compared to respective Shams except in the 7% group. 7%SG mice had increased weight loss compared to all SG groups despite increased food intake (Fig. A, B). 36%SG had reduced fat mass and elevated lean mass and lean mass in 7% and 21%SG was equivalent (Fig. C,D). All SG mice had improved glucose tolerance. 7%SG mice trended toward improved glucose tolerance and fasting glucose, independent of insulin sensitivity (Fig. E,F,G). Energy expenditure increased in 7% compared to 36% protein. Strength did not differ.

Across protein diets, metabolites were altered in SG compared to shams. There was no single metabolic pathway change across diets. In 36%SG there was an upregulation of the pentose phosphate pathway with a diversion of energy influx to NADPH to balance oxidative stress and create biosynthetic building blocks for repair and purine metabolism. In 7%SG, hepatic lipid metabolism and steroid biosynthesis pathways were upregulated. Combined increases were found in purine metabolism in 36% and 7%SG and inositol metabolism in 21% and 7% SG, suggesting improved glucose regulation (Fig. H, I). Interestingly, whole liver RNAseq revealed major perturbations between SG and sham animals across diet groups except for 7%, despite the metabolite changes. However, there were 2370 gene changes between 36 and 7% SG groups suggesting that diet can drive post-SG hepatic physiology.

Conclusions: Metabolism after SG can be heavily influenced by diet, Protein restriction enhances weight loss and improves T2D control after SG, which may largely be diet driven. SG protects against toxicity from excess protein. Targeting protein intake after SG may help patients realize their metabolic goals.

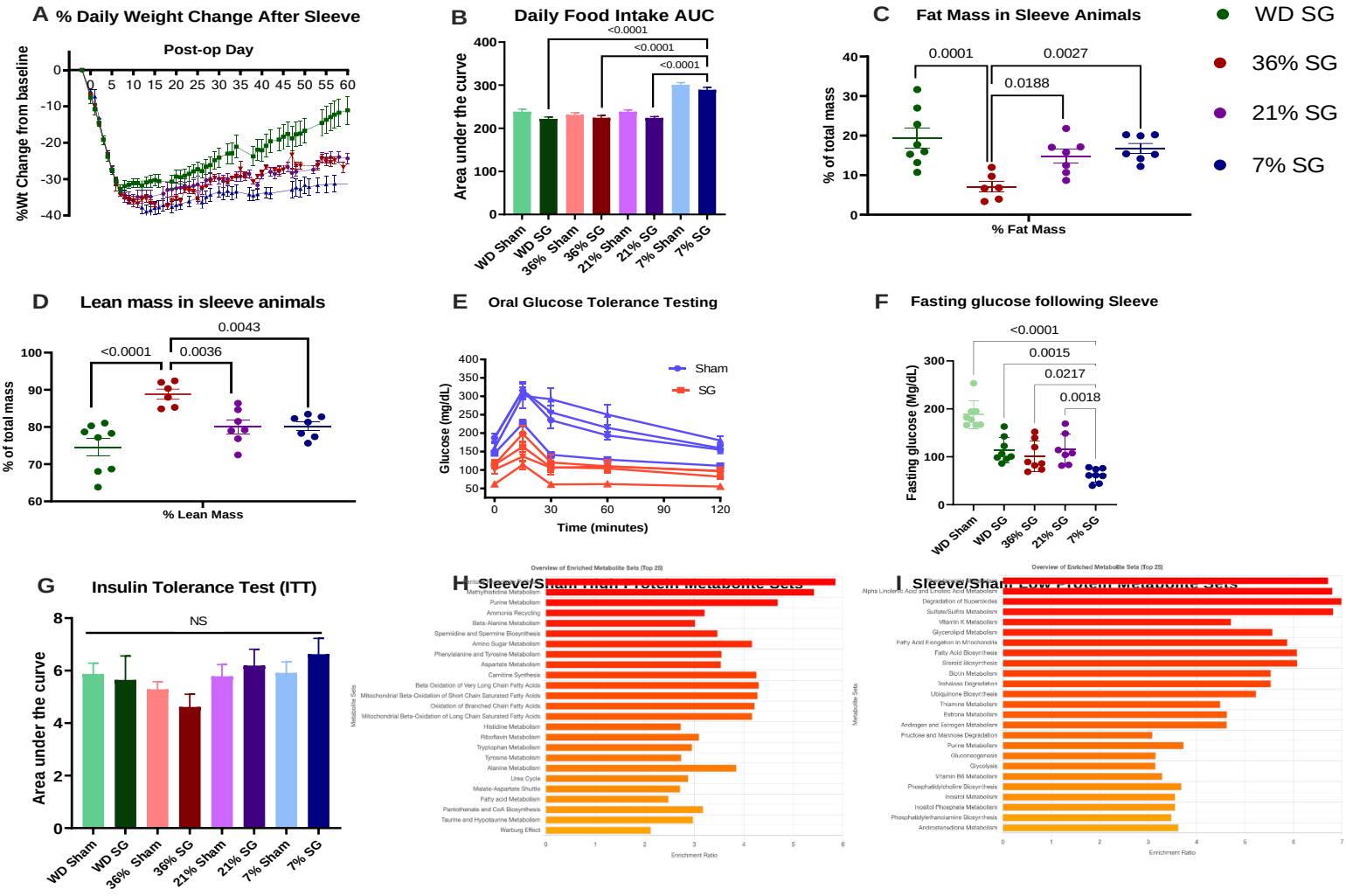


Figure 2: SG animals in all groups except those preconditioned and continued on post-operative normal chow diet had persistently reduced weight following surgery. SG animals on 7% protein (blue) have reduced weight overall (A), despite their increased food consumption (B). Animals on 36% percent protein (red) have reduced fat mass (C) and increased lean mass compared to other SG groups and specifically animals on 7% protein (D). All SG animals (red) have improved glucose tolerance compared to Shams (blue). Those on 7% protein have reduced fasting glucose levels (G). These changes occur without changes in insulin sensitivity (E). Hepatic Metabolomics analysis showed up and downregulation of several pathways in sleeve mice compared to sham mice across both high protein (H) and low protein (I) diets. Liver Western Diet Sham (n=8), WD SG (n=8), 36% protein Sham (n=6), 36% SG (n=8), 21% Sham (n=8), 21% SG (n=7), 7% Sham (n=8), 7% SG (n=8), Normal chow diet Sham (n=6), NCD SG (n=7). Comparisons represented one-way ANOVA with Dunnett corrections.

Vertical sleeve gastrectomy reduces senescent signal in female mice

Samuel Saghafi, Julia Illiano, Grace Zhu, Molly Mulcahy, Maggie Stangis, Dawn Davis, David A. Harris

Introduction: Bariatric surgery is currently the most effective treatment for obesity and Type 2 Diabetes (T2D). Vertical Sleeve Gastrectomy (VSG) is the most commonly performed bariatric surgery where approximately 70% of the stomach is removed. Patients often experience dramatic weight loss and remission of chronic conditions like T2D, kidney disease, and NAFLD. The exact mechanisms for these improvements remain unclear. Recent studies have identified pancreatic beta cell and adipose tissue senescence as an important factor in the pathophysiology of T2D. Since VSG decreases adiposity and chronic inflammation, and improves beta cell function we investigated the link between bariatric surgery and senescence. The cell cycle inhibitor, p16, was used as a marker for senescent cells.

Methods: A p16 luciferase reporter mouse was used to quantify cellular senescence *in vivo* following VSG and sham operations. Mice were preconditioned on Western Diet (WD; 42% kCal from fat; 30% sucrose by weight) for 25 weeks to induce obesity and T2D. They were weight matched to undergo VSG or sham surgeries, maintained on WD, and subjected to a panel of metabolic tests. After injection of coelenterazine, a luminescent substrate of luciferase, mice were imaged to measure luminescent signal coming from p16 expressing cells. *In vivo* imaging was done 1 week prior, and 2 and 5 weeks after surgery to quantify senescence over time.

Results: VSG mice maintained greater weight loss and had enhanced glucose tolerance compared to shams. *In vivo* imaging revealed no difference in luminescent signal in male mice, but did show a significant reduction in senescent signal in female VSG mice at 5 weeks after surgery. Fasting and post-prandial serum was collected and will be used to measure insulin excursion. Tissues were harvested and either flash frozen in liquid nitrogen or formalin fixed and paraffin embedded. qPCR, western blot, and immunofluorescent imaging will be done to assess the presence of senescent cells in a tissue specific manner.

Conclusions: VSG reduced the overall senescent signal in female mice as seen in the *in vivo* imaging, suggesting a possible mechanism by which VSG improves glucose tolerance. Senescence is known to contribute to aging and tissue disfunction. This study may reveal one possible mechanism by which VSG is able to improve organ health.

Effect of site-specific resveratrol administration on Parkinsonian vocalization behavior and inflammatory gene markers in male Pink1-/- rats

Monalyce Hamza, BA, David G.S. Barnett, MD, Sarah A. Lechner, BS, Cynthia A. Kelm-Nelson, PhD

Introduction: Parkinson disease (PD) is a neurodegenerative disorder that affects approximately 10 million people globally and the prevalence is rapidly increasing. Vocal deficits, including hypophonia, are present in 90% of individuals with PD and manifest during early stages of disease. These progressive vocal deficits do not respond to traditional PD therapies that target dopaminergic pathways. Thus, testing new treatments that target the brainstem vocal pathways may rescue or prevent vocal dysfunction in the early stages of PD. This study measured the therapeutic effect of resveratrol, a natural anti-inflammatory phenol, on PD vocal deficits using the validated *Pink1*-/- rat model of mitochondrial dysfunction. We hypothesized that a four-week, chronic resveratrol infusion into the lateral periaqueductal gray (LPAG) will increase the intensity of vocalizations and reduce inflammatory gene expression in the LPAG of *Pink1*-/- rats.

Methods: 12-month-old male Long-Evans rats (n = 6 Pink1-/-, n = 8 wildtype (WT) controls) underwent a 10-day acclimation. PD progression and LPAG projections influence multiple behaviors, thus, we quantified assay at baseline and 4 weeks post-treatment: ultrasonic vocalizations, spontaneous limb motor activity, and assessment of thermal nociception. After baseline testing, all rats underwent unilateral cannulation targeting the LPAG. Resveratrol (0.03 mg/ml at 0.11 µl/h) was administered unilaterally via an implanted glass cannula connected to a subcutaneous osmotic pump. Finally, an RT-qPCR gene panel for inflammatory markers was used to determine changes in whole blood between timepoint and genotypes.

Results: All rats produced more calls post-treatment. WT, but not Pink1-/- rats, had a significant increase in call intensity. There was a genotype difference regarding spontaneous limb motor activity, where Pink1-/- rats moved less; this is consistent with past work. Nociception was not affected by resveratrol treatment, which corroborated proper cannula placement. QIAGEN RT2 Profiler PCR array for NF-κB pathway targets showed systemic inflammation markers CD40, CD74, and CD83 were downregulated in Pink1-/- rats relative to WT who received resveratrol treatment.

Conclusions: This pilot study is the first to demonstrate that site-specific resveratrol administration into the LPAG can increase vocal loudness in the rat. Future studies should evaluate different age groups, duration of dose, increased numbers of sham surgeries as controls, and sex as a biological variable.

Resveratrol alters NF-κB signaling target mRNA profiles in Parkinsonian Pink1-/- rats

Sarah A. Lechner, BS, David G.S. Barnett, MD, Stephen C. Gammie, PhD, Cynthia A. Kelm-Nelson, PhD

Introduction: Parkinson disease (PD) is the fastest growing neurodegenerative disease. Identifying early-stage pathology and gene signatures is necessary for the development of novel and effective disease-modifying treatments. The *Pink1-/-* rat, a mitochondrial dysfunction model of prodromal PD, demonstrates the early-stage deficits in cranial motor (vocal) function with significant upregulation of inflammatory signaling pathways in the vocal fold as well as caudal brainstem vocal motor nuclei. Using CNS transcriptomic data and a drug repurposing approach, we first identified therapeutic candidates that could reverse pathologic gene expression patterns in the *Pink1-/-* model. The top match, resveratrol, has anti-inflammatory, antioxidant, and anti-apoptotic properties and in previous work has demonstrated a therapeutic effect in humans with PD. This study then tested the hypothesis that systemic resveratrol administration will ameliorate vocalization deficits and decrease inflammation-related transcription profiles in *Pink1-/-* rats, via whole blood measurement of readily-accessible blood biomarkers.

Methods: This study was performed at 4- and 10-months of age on two separate groups of male *Pink1-/-* rats (total $N = 40$). Rats were randomly assigned into drug condition groups, vehicle ($n = 10$) or resveratrol (20 mg/kg dose; $n = 10$) and were given a 4-gram sugar cookie + resveratrol daily for 8 weeks. Vocalization testing was done at three timepoints: baseline, 4-, and 8-weeks. The RT^2 Profiler PCR Array for NF-κB Signaling Targets was used to analyze whole blood mRNA expression changes after the 8 weeks of treatment. RM-ANOVAs were used to analyze differences in vocalization variables between timepoints and drug condition. Fisher's LSD was used for post-hoc comparisons; level of significance was set *a priori* at 0.05.

Results: There were no interactions between timepoint and treatment for any vocalization variables at 4-months; however, at 10-months, resveratrol increased the average duration and average peak frequency, a socially-motivated acoustic parameter, of all calls. Rats receiving resveratrol had significant beneficial transcription changes including downregulation of *Myd88* (microglial activation), *Bcl2a1* and *Irf1* (apoptosis), and upregulation of *Ifnb1* (anti-inflammatory).

Conclusions: This is the first study to suggest that resveratrol acts to reduce systemic inflammation in the *Pink1-/-* rat but did not change vocalizations. We hypothesize the lack of vocal deficit amelioration may be due to nonideal blood brain penetration or insufficient/subtherapeutic concentrations within the CNS. Our lab is presently testing this hypothesis with direct *in vivo* administration of resveratrol to brain parenchyma via stereotaxic microcannulation.

Resveratrol and celastrol modify synaptic and inflammatory genetic expression in a model of Parkinsonian rat midbrain primary neurons

David G.S. Barnett, Sarah A. Lechner, Cynthia A. Kelm-Nelson

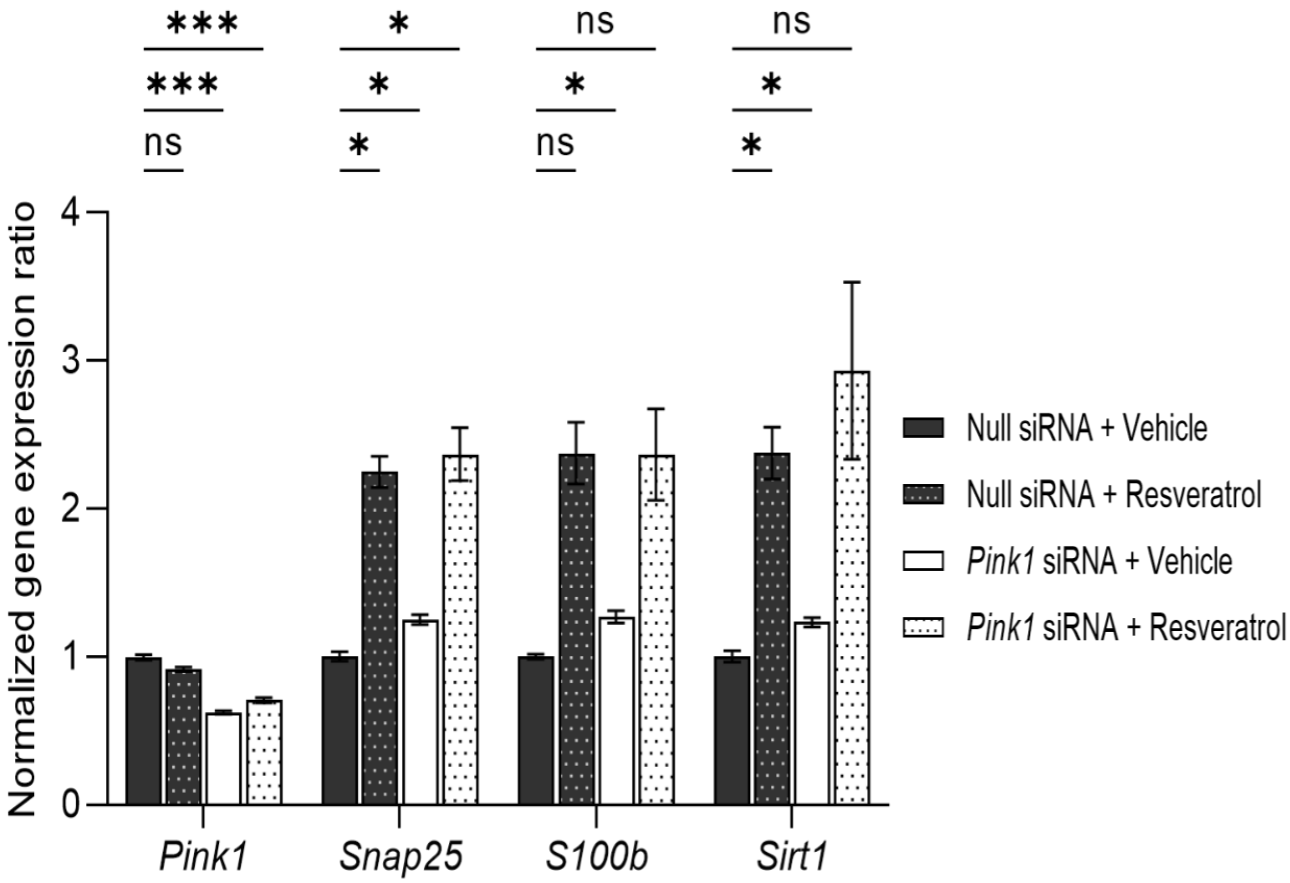
Introduction: Parkinson disease (PD) is highly prevalent and lacks disease-modifying therapies. Prompt treatment of the earliest manifestations of brainstem pathology are ideal to halt progression of disease. We have previously identified early-stage altered gene expression in caudal CNS nuclei, independent of nigrostriatal pathology, in the *Pink1-/-* rat model of prodromal PD. We used these transcriptomic data to power a drug repurposing technique designed to identify therapeutic candidates capable of reversing altered genetic expression due to loss of *Pink1*. The top results included naturally occurring resveratrol and celastrol. To screen the efficacy of these drugs in primary midbrain neurons germane to our previous work, we developed a relatively brief and inexpensive in vitro siRNA knockdown model. After validation, we tested the hypotheses that resveratrol and celastrol will reverse gene expression changes in midbrain neurons due to reductions of *Pink1* in vitro.

Methods: Midbrains were dissected from wild-type E18 Long-Evans rats. Each midbrain yielded approximately 0.5 – 1 x 10^6 cells with > 90% viability and cells were plated on either poly-D-lysine coated culture plates for qPCR, or chamber slides for immunocytochemistry (ICC). After treatment with siRNA directed against *Pink1* or control sequences, cells were treated with either resveratrol (10 µM in EtOH), celastrol (0.5 µM in EtOH), or vehicle followed by RNA harvest or ICC.

Results: We achieved significant neuronal predominance (microtubule associated protein [Map] expression, beta-III tubulin ICC) with few astrocytes (aldehyde dehydrogenase 1 member L1 [Aldh1l1] expression, glial fibrillary acidic protein [Gfap] ICC). Levels of *Pink1* siRNA knockdown were significant compared to control. Resveratrol treatment led to significant increases in genes necessary for normal synaptic function (*Snap25*, *S100b*) and activation of the transcription factor *Sirt1*, all decreased in the *Pink1-/-* rat. Celastrol similarly increased *S100b* and *Sirt1*, although not significantly. This study remains underway with addition of E18 *Pink1-/-* rat midbrain cultures for further validation of the in vitro model in a complete knockout.

Conclusions: Here, we highlight the utility of validating drug candidates prior to relatively lengthy and costly in vivo testing. These data support investigation of in vivo resveratrol and celastrol in the *Pink1-/-* rat and corroborate our previous in silico drug repurposing efforts. The nimble primary midbrain neuron culture model described can be quickly optimized or altered to address novel hypotheses while reducing animal subjects and reliance on immortalized cell lines with adulterated phenotypes.

Figure. Resveratrol treatment causes differential gene expression in a cultured primary midbrain neuron model of Parkinson disease



There was a significant effect of siRNA knockdown on *Pink1* expression. When treated with resveratrol and with *Pink1* siRNA and vehicle, *Snap25* gene expression significantly increased. *S100b* expression increased when treated with resveratrol and with *Pink1* knockdown, but the increase was only significant with *Pink1* siRNA and vehicle. *Sirt1* expression increased significantly with null siRNA and resveratrol and with *Pink1* siRNA and vehicle, expression also increased with *Pink1* siRNA and resveratrol. Data are normalized to a housekeeping gene (*Hsp90*, Heat shock protein 90) and presented as mean ± SEM relative to the control condition (Null siRNA + Vehicle) expression. $n = 3$ per gene per condition. **ns = not significant;** $* = P < .05$**;** $** = P < .01$**;** $*** = P < .001$**.** 2-way ANOVA with Sidak multiple comparisons test was performed.

Assessing the therapeutic potential of cold atmospheric plasma (CAP) on glioblastoma: In vitro studies unveiling cellular responses

Ligi Milesh, Bindu Nair, Ha M. Nguyen, J. Leon Shohet, Hau D. Le

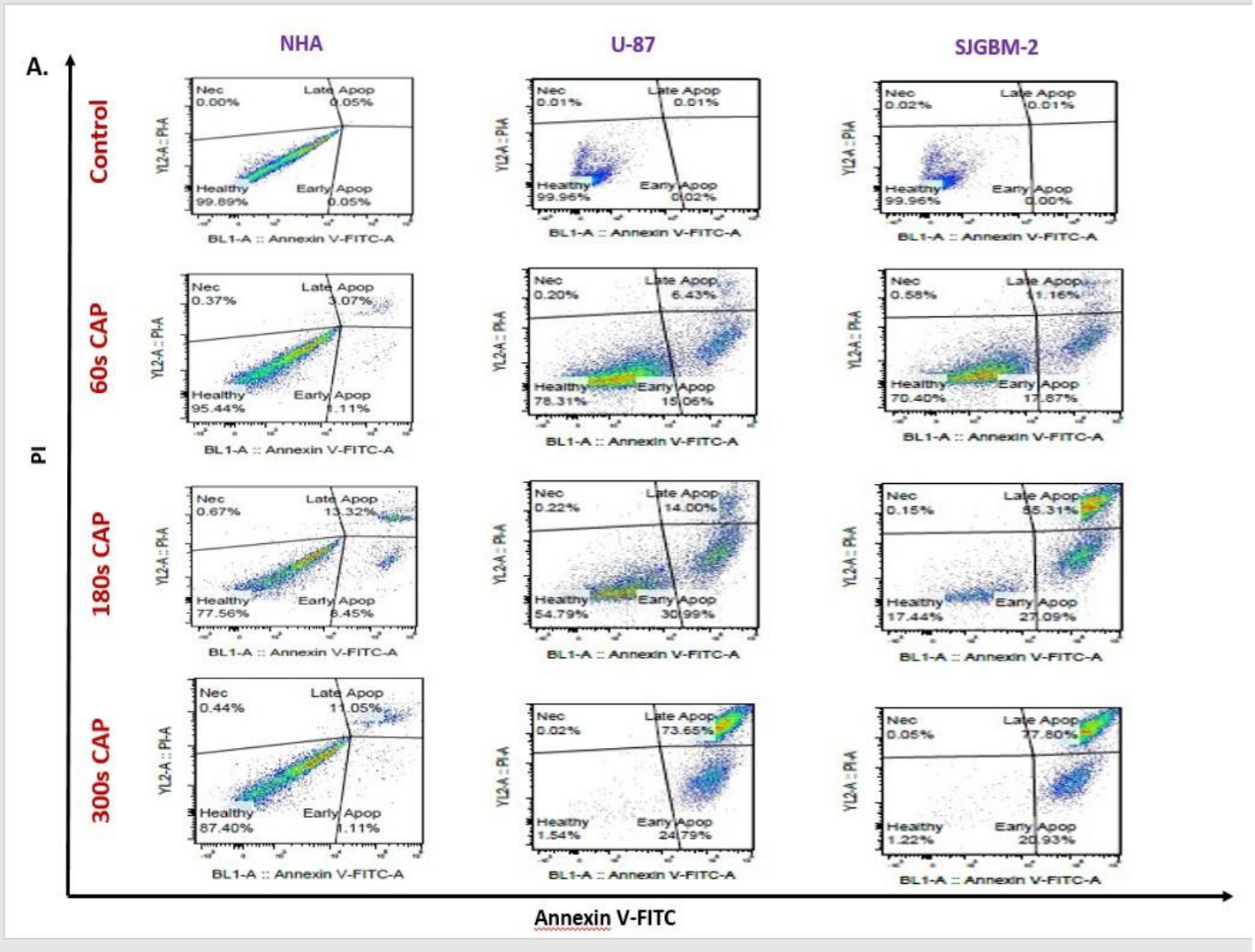
Introduction: Glioblastoma, the most aggressive form of primary brain tumor, poses significant challenges in terms of effective therapeutic interventions. Conventional treatment options have shown limited efficacy, necessitating the exploration of novel approaches. Cold Atmospheric Plasma (CAP) has emerged as a promising treatment modality for glioblastoma, offering potential advantages over conventional therapies. CAP generates various reactive species and electric fields that can induce multiple biological cellular responses in cancer cells thus modulating cellular signaling pathways. However, the differential effects of CAP on glioblastoma cells compared to normal cells and the underlying mechanisms remain to be elucidated. To assess the dose dependent therapeutic potential of CAP on glioblastoma, the present In-vitro treatment strategies were designed and performed.

Methods: In this study, we aim to investigate the cellular responses elicited by CAP treatment for glioblastoma using U-87 and SJGBM-2 (cancer cell lines) and normal human astrocytes (NHA) as control non-cancer cells. A dose-dependent experiment was performed in which the cells were subjected to CAP treatment at various durations (60s,180s and 300s). The cell viability through apoptotic stages was analyzed using microscopic imaging and flow cytometry. Furthermore, cell cycle analysis using flow cytometry was performed to understand the alterations in the cell cycle distribution of treated cells.

Results: The study's findings demonstrate a significant contrast in cellular responses to CAP treatment after 24 hours. Normal cells (NHA) maintained high viability, with a healthy population of 99.89% in the control group, while cancer cells (U-87 and SJGBM-2) had lower baseline viability (99.96% in control) and exhibited a substantial decline in cell viability following CAP treatment, especially after 300 seconds, where U-87 showed just 1.54% healthy cells, and SJGBM-2 had 1.22%. Moreover, NHA cells exhibited a more controlled cell cycle distribution, with 86.62% in the G0/G1 phase during the control, in contrast to cancer cells, which showed disrupted cell cycle patterns with an increase in S and G2/M phase populations, particularly after 300 seconds of CAP treatment. These results emphasize the differential responses of normal and cancer cells to CAP treatment, highlighting its potential in cancer therapy.

Conclusion: Our findings demonstrate the multifaceted advantages of employing dose dependent CAP treatment on glioblastoma showing higher cell viability percentage in normal cells when compared to cancer cells thus providing an advanced cancer treatment approach for glioblastoma. Further research is required to better comprehend the underlying mechanisms and to optimize treatment strategies for clinical applications.

Apoptosis result using flow cytometry



Loss of RIPK3 in vascular smooth muscle cells prevents abdominal aortic aneurysm rupture

Jack Bontekoe, MD, Ting Zhou, PhD, Zulmari Silva-Pedraza, Michelle Conte, Huan Yang, PhD, Bo Liu, PhD

Introduction: Pathologic remodeling of the aortic wall is a prominent feature of abdominal aortic aneurysm (AAA) and involves loss of vascular smooth muscle cells (VSMC) within the medial layer. Our prior research discovered human aneurysm tissues express high levels of Receptor Interacting Protein Kinase-3 (RIPK3), a key mediator of the proinflammatory programmed cell death pathway known as necroptosis, particularly among VSMCs. In murine AAA models, pharmacologic inhibition or total body gene deletion of RIPK3 protects against aneurysm, while even modest upregulation of *Ripk3* expression exacerbates AAA. RIPK3, however, may have functions beyond necroptosis, as suggested in disease models of kidney fibrosis and arterial stenosis. Therefore, the functional extent of RIPK3 in the aneurysmal aortic wall remains unknown. We hypothesize that reducing RIPK3 specifically within VSMCs promotes positive aortic wall remodeling, thereby reducing AAA burden.

Methods: We developed mice with specific loss of *Ripk3* expression within smooth muscle cells by crossing *Ripk3-gfp*$^{fl/fl}$ floxed mice with inducible SMMHC-Cre^{ERT2} transgenic mice. To better mimic human aneurysms, we adopted a surgical AAA model which combines periadventitial application of elastase to the infrarenal abdominal aorta with beta-aminopropionitrile (BAPN) supplemented drinking water. At 18-20 weeks of age, *Ripk3-gfp*$^{fl/fl}$-SMMHC-Cre^{ERT2} knockout (KO), heterozygous (Het) and wild-type (WT) mice underwent sham surgery or AAA induction, and were followed for 14-, 21-, and 56-days. Aortic tissues were analyzed by bulk-RNA sequencing (14-days) and histochemistry.

Results: Surgical aneurysm modeling (>50% increase in aortic diameter) was successful in all mice. Survival from AAA rupture was significantly different among genotypes (p=0.0134), despite no differences in aortic diameter or percent change (compared to pre-surgery). At 56-days, WT mice survival was only 47.06%, compared to 90.00% and 100.0% of Het and KO mice, respectively. Preliminary histological analysis of select samples reveals the average medial layer thickness of the AAA wall is significantly greater among Het (p=0.0103) and KO (p=0.0190) mice compared to WT rupture mice. Immunofluorescence demonstrates KO and Het aneurysm walls have higher medial layer cellularity compared to WT, as well as increased intensity of the cell proliferation marker, Ki67. Bulk-RNA sequencing of 14-day aortic tissue, additional histology, and in-vitro analysis of VSMCs is ongoing.

Conclusions: Loss of *Ripk3* expression within VSMCs appears to provide protection against AAA rupture through enhanced compensatory remodeling. Our preliminary findings reveal a novel role of RIPK3 in VSMC proliferation. Our next step is to test whether pharmacologically inhibiting RIPK3 is capable of stabilizing AAA and reducing rupture.

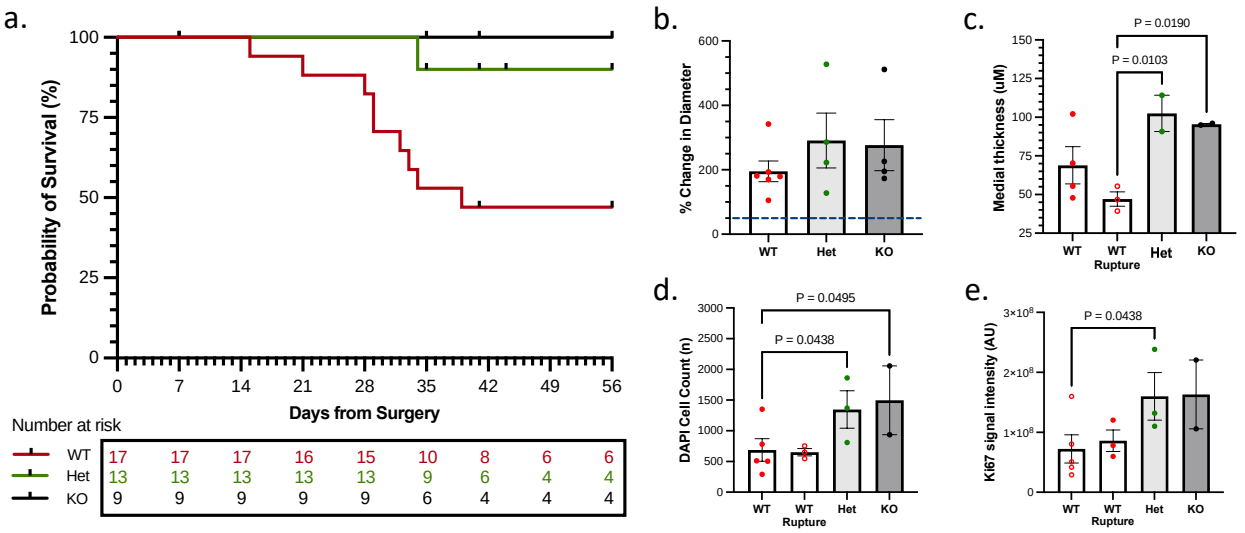


Figure 1. Analysis of SMC-specific RIPK3 mice at 56-days post-surgery. **(a)** Survival of WT mice is significantly reduced. Necropsy confirmed all deaths resulted from AAA rupture. **(b)** Percent change in aortic diameter from pre-surgery did not differ among genotypes. **(c)** Analysis of H&E-stained AAA segments revealed significantly increased average medial thickness in Het and KO aortas compared to WT ruptures. Immunofluorescence revealed **(d)** DAPI cell count of the medial layer is higher in Het and KO mice, as well as **(e)** total wall Ki67 signal intensity.

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

Weifeng Zeng, John P. Maufort, Robert George, Ellen Shaffrey, Peter Nicksic, Sarah Lyon, Jue Zhang, Dave Vereide, James A. Thomson, Samuel O. Poore

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

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

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

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

Genetic knockout of clock repressors produces a less aggressive pancreatic adenocarcinoma phenotype

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Introduction: The circadian clock functions to maintain organ homeostasis by coordinating essential biologic processes (*e.g.*, metabolism, cell division) with the 24-hour day/night cycle. The molecular clock achieves this through transcriptional-translational autoregulatory feedback loops comprised of transcriptional activators (positive arm) and repressors (negative arm). Disruptions in the circadian clock have been implicated in the development of various cancers, including pancreatic adenocarcinoma (PDAC). In previous work, we found that circadian clock disruption manifested by *Arntl* (*Bmal1*) dysregulation have led to a more aggressive PDAC phenotype *in vitro* and *in vivo*, confirmed by other investigators. The mechanism by which *Bmal1* dysregulation forms a more aggressive PDAC phenotype remains uncertain. We thusly investigated the extent that dysregulation of the reciprocal arm of the clock affects PDAC progression via knockout of *Period 1 (Per1)* and *Period 2 (Per2)* (circadian repressors).

Methods: CRISPR/Cas9 was utilized to mutate *Per1* and *Per2*, causing functional knockout of both genes in a cell line derived from an aggressive PDAC mouse model (*Kras*$^{G12D/+}$ *Tp53*$^{-/-}$ *Pdx-1* Cre (KPC). An abolished circadian clock in the *Per1/Per2* double knockout clones (DKO) was assessed by RTqPCR by isolating mRNA from cells every 4 hours for 24 hours. DKO, KPC, and *Bmal1* knockout (BKO) cells were injected into the right flank of C57BL/6J male mice at a concentration of 100,000 cells / 25µL. Tumors were harvested on day 28 and clock function assessed via RTqPCR after RNA isolation from harvested tissue.

Results: Circadian clock was confirmed to be disrupted in DKO cells by RTqPCR demonstrating arrhythmic expression of core clock genes (*e.g.*, *Bmal1*). Heterotopic tumor evaluation showed DKO tumors were siginificantly smaller in volume and weight compared to BKO tumors (Figure 1). Confirmation of an abolished circadian clock in the DKO tumors and BKO tumors *in vivo* was achieved by our novel heterotopic tumor approach.

Conclusions: Our aim was to evaluate how abolishing the circadian clock through knockout of negative arm components, *Per1* and *Per2,* impacted PDAC progression. With a confirmed abolished circadian rhythm, the DKO cells did not produce a similarly aggressive phenotype of PDAC to the BKO cells. This finding suggests that perturbation of different arms of the clock (i.e., *Bmal1*/positive arm vs *Per1/Per2*/ negative arm) may produce significant differences in core biologic processes that facilitate tumor growth. In future work, we will confirm these findings via an orthogonal approach, and will subsequently begin to dissect how dysregulation of *Bmal1* (positive arm) causes a more aggressive PDAC phenotype.

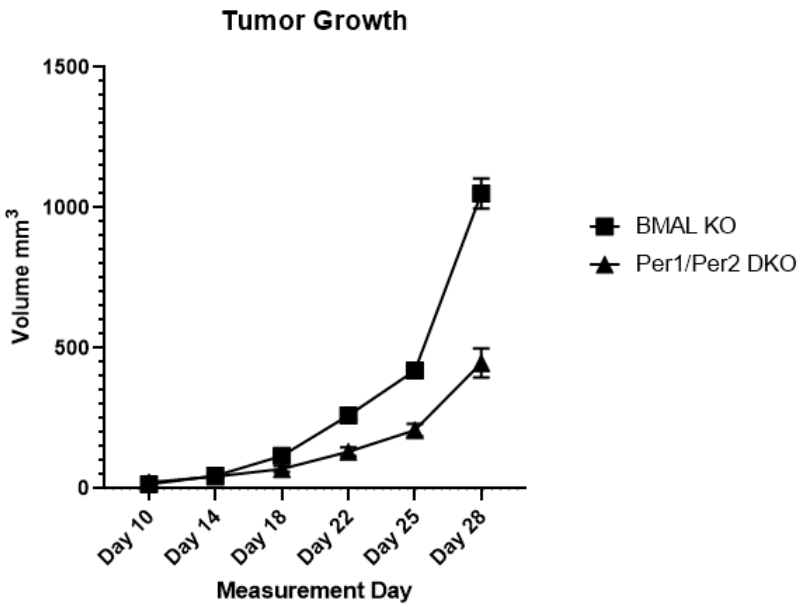

Figure 1: Heterotopic Tumor Growth

Effects of acute psychosocial stress on the laryngeal microbiome

Anumitha Venkatraman, John Binns, Katelyn Jacobs, Susan L. Thibeault

Introduction: Psychosocial stress and laryngeal physiology are circularly and inextricably linked. Whereas 25% of individuals with voice problems report concurrent psychosocial stress, a single exposure to stress can result in acoustic voice changes, and intrinsic laryngeal muscle activation patterns. However, little is known on the underlying biological mechanisms of psychosocial stress, in laryngeal physiology. The microbiome is a key mediator of the psychosocial stress response in other organs such as the gut, vagina and brain, resulting in reduced microbial diversity and abundance. Laryngeal microbiology is an emerging area of research that may shed light on the elusive role of psychosocial stress in laryngeal physiology.

Purpose: To delineate the effects of two psychosocial stress protocols (acute and chronic) on laryngeal microbiota. We hypothesize that both acute and chronic psychosocial stress will result in reduced microbial diversity and abundance in the larynges of stressed mice when compared to control animals.

Methods: Sixty C56BL/7 mice (6-10 weeks of age, 30 F, 30 M) were evenly divided into acute stress, chronic stress, and control groups (10M, 10 F per group). Animals in the acute stressed group experienced restraint stress for 6 hours a day for 7 days, whereas those in the chronic stress group experienced the same for 6 hours a day for 14 days. Corticosterone assays were performed on plasma samples collected from blood before and following each protocol to confirm stress induction. Following each psychosocial stress protocol, bacterial DNA were extracted from the larynx and amplified for 16S RNAseq. QIIME2 and R studio were used for bioinformatic analysis of 16S RNAseq data to obtain measures of microbial abundance (taxa bar plots), alpha and beta diversity and PICRUSt analysis.

Results: Acute psychosocial stress results in reduced alpha diversity in females not males. On the other hand, bacteria of low abundance are distinct in males (not females) following acute psychosocial stress (per beta diversity). No significant effects of acute psychosocial stress were observed on measures of microbial diversity, abundance of PICRUSt analysis when sexes are combined. Bioinformatic analysis of chronic psychosocial stress are currently ongoing and will be included in the final presentation.

Conclusions: Seven days of restraint stress may not be sufficient to see significant microbial changes in the larynx. Psychosocial stress-induced microbial changes in the larynx resulting from 14 days of restraint stress could lay the groundwork for identifying future probiotic therapeutic targets.

RNA-sequencing of human vocal fold fibroblasts: Defining a scar genotype

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Introduction: Vocal fold fibroblasts (VFF) are key players in the wound healing response and yet, little is known about their normal genotypic expression compared to diseased expression. Given the challenge of obtaining VFF from pathological vocal folds, normal VFF (nVFF) treated with TGF-β1 is a model commonly used to represent changes seen in scarred vocal folds. This study aimed to define a genotype of scarred VFF (sVFF) compared to nVFF, as well as compare the "scar-like" genotype from TGF-β1 treated VFF (tVFF) to sVFF.

Methods: nVFF cell lines from a 21-year-old male (N21), 41-year-old female (N41), 58-year-old male (N58), 59-year-old female (N59), and a sVFF cell line from a 56-year-old female (S56) were used in this study. nVFF were used as control and were also treated with 10ng/mL of TGF-β1 for 5 days to induce scar-like differentiation into myofibroblasts. sequencing was conducted to obtain gene expression data. Subsequently, differentially expressed genes were identified between nVFF and tVFF or sVFF, while the most similar co-upregulated genes between tVFF and sVFF groups were defined. Using these DE genes, enrichment analyses were performed, and comparisons were made across cell groups.

Results: The sVFF- and tVFF-specific co-upregulated genes are enriched in the actin binding pathway. sVFF should have differentiated into myofibroblasts due to the injury, and tVFF experienced induced differentiation following TGF-β1 treatment, so an increased expression of cytoplasmic and α-smooth muscle actin is likely present in myofibroblasts. When compared to nVFF, sVFF demonstrated upregulation of a cell-cell adhesion pathway, which may inform cell function and behavior in injury. In scarring, cell-cell adhesion plays a crucial role in wound contraction and scar development, which would not be seen in nVFF. Finally, tVFF genes that are most enriched are associated with the fibronectin binding pathway. Fibronectin deposition in the extracellular matrix has been reported to be increased in scarred vocal folds, so this enriched pathway indicates that the TGF-β1-treated cells can successfully represent a scar-like model, as least as it pertains to the vocal folds.

Conclusions: While differences are present, sVFF and tVFF groups show key similarities that may allow for identification of targets in the genome, either genes or pathways, for the treatment of scar. Given the differentiation of sVFF and tVFF in myofibroblasts, it would be prudent to identify a target or pathway that may induce de-differentiation to reduce wound contraction and other detrimental effects on voice production.

Streptococcus pseudopneumoniae contributes to vocal fold epithelial remodeling

Vlasta Lungova, Madhu Gouda, Stephanie Bartley, Anumitha Venkatraman, Susan L. Thibeault

Introduction: In this study, we focused on understanding the relationship between *S. pseudopneumoniae (SP),* a dominant bacterial species associated with benign lesions, and *S. salivarius (SS)*, a commensal bacterium, with human VF epithelial cells in our three-dimensional model of human VF mucosa. *SP* has been recognized as an opportunistic pathogen that can damage the epithelium and promote mucosal inflammation via the release of extracellular products like pneumolysin and metalloproteinases, such as HtrA. Both products can compromise the epithelial integrity as pneumolysin perforates cell membranes, and HtrA, cleaves E-cadherin, a cell adhesion protein. In contrast, *SS* has a probiotic effect, inhibits the action of pathogens and can modulate the host's immune responses.

Methods: Engineered human VF mucosae were inoculated with bacterial suspensions of (1) *SP* only, (2) *SS* only, (3) *SS/SP* co-cultures and plain culture medium for controls (4) for 24 and 48 hours at a low dose of 10:1 multiplicity of infection (MOI). We evaluated epithelial integrity and bacterial colonization using transmission electron microscopy, a biotin permeability assay and Fluorescent in Situ Hybridization (FISH) for a 16S rRNA probe in combination with anti-E-cadherin (cell junction marker). Then we assessed expression levels of bacterial metalloproteinase HtrA, pneumolysin and the host-related inflammatory cytokines (IL6 and IL8).

Results: Our data show the progression in VF epithelial damage and dilation of intercellular spaces in human VF mucosae inoculated with *SP,* with the most prominent pathological changes observed 48h post-inoculation. At this time point, E-cadherin was cleaved in apical epithelial layers which correlated with detection of HtrA and pneumolysin, leading to a compromised epithelium with increased permeability. Epithelial damage was diminished using *SS* that robustly attached to the epithelium in the presence of *SP* and induced desquamation of infected cells likely via MMP2. *SS* also significantly reduced expression of IL6 and IL8 secreted by mucosal cells in *SS/SP* co-cultures.

Conclusions: These findings extend our understanding of how pathogenic bacteria contribute to the disrupted epithelium and how commensal bacteria may neutralize the effect of pathogens and/or prevent infection.

Transcriptome dynamics during vocal fold injury and repair

Kristy Wendt, Elliot Xie, Ted Lunga, Chitrasen Mohanti, Christina Kendziorski, Susan Thibeault

Introduction: Voice disorders are the most common communication disorder across the lifespan and are caused by changes to the epithelium and lamina propria (LP) in the vocal fold (VF) resulting from injurious stimuli, including phono-, mechanical, and chemical trauma. The overall goal of this work is to elucidate subpopulations of cells that contribute to VF injury response and repair in a murine abrasion injury model.

Methods: VF are dissected, and single cells isolated from a murine abrasion injury model at longitudinal timepoints 12 hr, 24 hr, 3 days, 7 days, 14 days, and 21 days post-injury (PI) corresponding to established injury and repair stages of inflammation, re-epithelialization/proliferation, and remodeling, as well as from an uninjured control group. Transcriptional dynamics are characterized by single cell RNA sequencing analysis (scRNA-Seq) to identify cell subpopulations described in terms of differential gene expression during injury and repair. Complementary longitudinal analysis of epithelial and lamina propria morphological changes in the VF of the murine abrasion model is achieved by hematoxylin and eosin (H&E) and trichrome staining, as well as immunohistochemistry (IHC).

Results: Murine abrasion model is defined by epithelial denuding and disrupted LP at early timepoints 12-24 hrs PI by H&E, with epithelial proliferation confirmed by IHC by day 3 PI. Heterogenous cell subpopulations are described by principal component analysis and functional profiling via GO/KEGG accompanied by discussion of diagnostic significance.

Conclusions: Findings from study provide new insights into cell population heterogeneity during VF injury and repair.

Clinical Science & Health Services Research Abstracts

A systematic review of concomitant use of low-dose isotretinoin and energy-based therapies for acne vulgaris

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Introduction: Uneven skin tone and texture is often a sequela of severe acne and can cause severe psychosocial distress. For these individuals lasers and other such energy-based therapies (EBT) offer effective resurfacing options for improved aesthetics. However, current guidelines state patients must wait six to 12 months after discontinuing isotretinoin—a mainstay treatment for severe acne—before pursuing EBT or risk complications like keloids and delayed wound healing. Despite this, several studies in the literature have reported safe, effective treatment of acne vulgaris with concomitant use of EBT and low-dose isotretinoin. This systematic review aims to characterize the effectiveness and safety profile of this treatment combination as well as the quality of existing studies in the literature.

Methods: A search of PubMed, Scopus, and Web of Science databases was performed to identify journal articles related to concomitant use of low-dose isotretinoin and EBT published from database conception to October 2023. A total of 12 studies met inclusion criteria. The Newcastle-Ottawa Quality Assessment Scale (NOQAS) and Jadad Scale were used to appraise seven observational studies and five randomized trials, respectively, to determine the quality of the studies.

Results: Isotretinoin doses across the studies ranged from 5 mg to 30 mg daily. EBTs investigated include ablative and non-ablative fractional lasers, pulsed dye laser, fractional radiofrequency microneedling, delicate pulsed light, fluorescent light energy, and erbium-doped fiber laser. The quality of the data included an average NOQAS score of 6.4 (out of 9) and Jadad score of 2.8 (out of 5). Most observational studies using Agency for Healthcare Research and Quality criteria were considered the highest level of quality at “good” quality. A majority of studies (66.7%) included patient reported outcomes.

Conclusions: The results of this systematic review suggest that the concomitant use of low-dose isotretinoin and EBT is a safe and effective treatment combination for acne vulgaris in contrast to current guidelines. This review provides a collection of relatively good quality studies as evidence for practitioners to refer to when treating severe acne patients.

Takotsubo cardiomyopathy in orthotopic liver transplant: Single center experience

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Introduction: Takotsubo cardiomyopathy (TC) presents with a transient regional left ventricular (LV) systolic dysfunction in the absence of obstructive coronary artery disease and often mimics myocardial infarction. Patients undergoing orthotopic liver transplant (OLT) are particularly vulnerable to Takotsubo due to high catecholamine requirement to maintain hemodynamic stability intraoperatively and rapid increases in systemic vascular resistance with correction of liver failure. To date, only 56 cases have been reported describing TC phenomenon in OLT recipients. The aim of this study is to identify and study the outcomes of patients who developed TC after OLT at University of Wisconsin.

Methods: We retrospectively identified 12 patients who developed TC after adult OTL at University of Wisconsin (UW) from 2008 until 2017 using UW Database. Donor, recipient and post-operative outcomes were summarized.

Results: 83% of patients who developed TC underwent OLT alone and 17% also underwent simultaneous kidney transplant. Mean age was 61 years old (SD 6.5). Sex was equally distributed between male and female (50% each). Cirrhosis was due to Alcoholic Liver Disease (ALD) in 75% of cases and mean allocation MELD score was 25.7 (SD 11.2). 42% of patients required dialysis prior to transplant. Only one patient had diagnosed coronary artery disease prior to transplant. Mean % EF prior to TXP was 60% (SD 0.5). Mean ejection fraction (EF) at the time of TC diagnosis was 30% (SD. 0.7). Mean EF at recovery was 60% (SD. 0.7). 50% of patients were treated with beta blockers alone, with 33% of patients who had full recovery without any interventions. Median admission length of stay (LOS) was 32.5 days (10 – 326). Median time from TXP to diagnosis of TC was 4.5 days (1 – 124). Median time from diagnosis of TC to recovery was 11 days (4 – 1731). Liver graft loss at 90-days and 1-year was 0%, respectively. Patient survival at 90-days and 1-year was 100%, respectively (Table 1).

Discussion: TC is a relatively common after liver transplantation. It is associated with extended LOS, but long-term outcomes are excellent with no patient deaths or graft loss at 1yr and with recovery of EF in all patients. Large, multi-institutional study of TC after OLT may help identify risk factors and effective management strategies.

Table 1: Clinical characteristics and outcomes

	n=12
Age	61 (SD 6.5)
Sex	
- Male	6 (50%)
- Female	6 (50%)
Underline Liver Disease:	
- NASH Cirrhosis	1 (8.3%)
- ALD Cirrhosis	9 (75%)
- HCV Cirrhosis	1 (8.3%)
- Benign tumor:	
o Polycystic Liver Disease	1 (8.3%)
Dialysis Prior to TXP	5 (42%)
Creatinine Prior to TXP	1.7 (SD 1.1)
MELD at TXP	25.7 (SD 11.2)
Recipient Cardiac History	1 (8.3%)
% EF Prior to TXP	60% (SD 0.5)
% EF at Diagnosis of TC	30% (SD. 0.7)
% EF at Recovery of TC	60% (SD 0.7)
Troponin Elevation post-TXP	5 (42%)
Reason for ECHO post-TXP	
- Volume Overload	12 (100%)
ECHO Results post-TXP	
- Low EF with multiple wall motion abnormalities	12 (100%)
Cardiac Angiogram	1 (8.3%)
Treatment	
- None	4 (33%)
- Beta Blockers Alone	6 (50%)
- Beta Blockers + ACE Inhibitors	2 (17%)
Type of TXP:	
- Liver only	10 (83%)
- Simultaneous Liver Kidney	2 (17%)
Donor Type	
- DCD	2 (17%)
- DBD	10 (83%)
Liver Cold Ischemia Time (Hours)	8.4
Kidney Cold Ischemia Time (Hours)	12.1
Induction Agent	
- Basiliximab	11 (91.7%)
- Thymoglobulin (ATG)	1 (8.3%)
Admission Length of Stay (LOS) (Days)	32.5 (10 – 326)
Time from TXP to TC (Days)	4.5 (1 – 124)
Time from TC onset to Recovery of TC (Days)	11 (4 – 1731)
Duration of Follow up post TXP (Years)	4.9 (SD 2.6)
90-days Graft Loss	
- Liver	0 (0 %)
- Kidney	0 (0%)
1-year Graft Loss	
- Liver	0 (0 %)
- Kidney	0 (0 %)
90-days Patient Survival	12 (100 %)
1-year Patient Survival	12 (100 %)

Small sample size but still definitive: A secondary analysis of a randomized trial on central neck dissection for papillary thyroid cancer

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Introduction: We previously published results of a randomized trial that showed total thyroidectomy (TT) plus prophylactic central neck dissection (CND) did not reduce recurrence of papillary thyroid cancer compared to TT alone. However, the trial was criticized for being underpowered, therefore lacking sufficient external validity. Consequently, the purpose of this study was to evaluate whether repeating the trial with a larger or more diverse population would be likely to change the trial result and show that prophylactic CND reduces recurrence.

Methods: The original trial randomized 30 patients to TT and 31 to TT plus CND, with 24 TT patients (80%) and 21 CND patients (81%) classified as low-risk for recurrence ($p = 1$). We used simulation and Bayesian methods to assess whether repeating the trial with a larger sample size or different populations of patients and surgeons would be likely to show an advantage to prophylactic CND. We also used Bayesian methods to estimate the probability that the original trial reached an incorrect conclusion about the potential benefits of CND.

Results: Over 1,000 simulated repetitions of the study, we found >99% showed no significant difference between groups, and that the risk of recurrence in the CND group would have to decrease by 20% to show a significant advantage over the TT group. Using Bayesian methods, we calculated that the study results would only change if the true effect of CND were a 100% reduction in recurrence relative to TT alone. Bayesian methods also suggested that if we were to repeat the trial 10 times with a larger sample size, we would expect 7 out of 10 to show no difference in recurrence between groups.

Conclusions: Using methods that account for smaller sample sizes and differences in surgical skill and patient populations, we found that the conclusion from our randomized trial that CND does not reduce the risk of recurrence is highly robust to plausible levels of change. This strongly supports the conclusion that repeating the trial with a larger sample size is unlikely to offer a different result and that prophylactic CND is unnecessary for most patients with papillary thyroid cancer.

The risks of failed nonoperative management of appendicitis in older adults

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Introduction: The consequences of failed nonoperative management of appendicitis in patients ≥65 years old have not been evaluated. The purpose of this study is to compare outcomes of nonoperative failure versus success in older and younger adults.

Methods: This is a retrospective cohort study of the 2004-2017 National Inpatient Sample. We included 32,469 patients <65 years old and 11,265 ≥65 years old admitted with acute, uncomplicated appendicitis treated nonoperatively. The primary outcome was morbidity. Secondary outcomes included length of stay, inpatient costs, and discharge to skilled facilities. Differences were estimated using median and logistic regression models, as well as inverse probability weighting of the propensity score.

Results: Nonoperative management failed in 38% of patients <65 years old and ≥65 years old. For patients <65, nonoperative failure was associated with a 7% increase in morbidity (95% confidence interval (CI) 6.9%-8.1%), 3-day increase in length of stay (95% CI 3-4 days), $9,015 increase in costs (95% CI $8,216- $9,446), and 1% increase in discharges to skilled facilities (95% CI 0.9%-1.6%) when compared to nonoperative success. The differences were larger among patients ≥65, with a 14% increase in morbidity (95% CI 13.6% - 16.2%), 6-day increase in length of stay (95% CI 5-6 days), $15,964 increase in costs (95% CI $15,181- $17,708), and 12% increase in discharges to skilled facilities (95% CI: 10.0%-13.3). Results were robust to bias from unmeasured confounding.

Conclusions: Nonoperative management of appendicitis should be approached cautiously for older adults, given the significant consequences of failure.

Keywords: Acute appendicitis, Nonoperative management, Treatment failure

Abbreviations:
NIS: National Inpatient Sample
ICD: International Classification of Disease
RAI: Risk Analysis Index
NSQIP: National Surgical Quality Improvement Program
RIR: Robustness of Inference to Replacement

Table 1. Comparison of morbidity, length of hospitalization, costs, and risk of discharge to skilled facility after nonoperative failure versus success for older and younger patients.

	Patients < 65			Patients ≥ 65		
	Non-Operative Failure	Non-operative Success	Difference (95% CI)	Non-Operative Failure	Non-operative Success	Difference (95% CI)
Incidence of any hospital complication	1,642 (10%)	436 (3%)	7% (6.9%-8.1%)[ɬ]	1,007 (18%)	202 (4%)	14% (13.6% - 16.2%)[ɬ]
In-Hospital Mortality	340 (2%)	-		630 (11%)	-	
Length of Stay (Days) (SD)	8 (9.7)	5 (7.8)	3 (3-4) [ɬ]	12 (10.3)	6 (7.0)	6 (6-6) [ɬ]
Cost ($) (SD)	20,450 (29,724)	11,435 (23,741)	9,015 (8,216-9,446) [ɬ]	29,307 (34,586)	13,343 (20,427)	15,964 (15,181-17,708) [ɬ]
Discharge to Skilled Facility	536 (3%)	347 (2%)	1% (0.9%, 1.6%)[ɬ]	1,499 (30%)	917 (18%)	12% (10.0%-13.3%)[ɬ]

[ɬ]Difference reached statistical significance with p<0.001

Detecting single suture sagittal, unicoronal, and metopic craniosynostosis: Evaluating the diagnostic accuracy of anthropometric measurements

Manasa H. Kalluri, BS, Jessica D. Blum, MD, MSc, Kristine M. Carbuilldo, MD, Catharine B. Garland, MD, Daniel Y. Cho, MD, PhD

Introduction: Craniosynostosis is the premature fusion of one or more cranial vault sutures. If left untreated, consequences include craniofacial deformities, increased intracranial pressure, and developmental delays. This demonstrates the importance of early diagnosis and intervention. Anthropometric measurements have previously been used to compare normal pediatric craniofacial morphology to cranial anomalies. However, there are currently no diagnostic anthropometric measurements for sagittal, unicoronal and metopic craniosynostosis. The objective of this study is to develop anthropometric measurements for accurate craniosynostosis risk stratification in infants up to 12 months of age based on characteristic craniofacial deformities. These measurements will be incorporated into a smartphone application to provide a risk assessment for primary care providers when assessing patients with head shape differences to promote early referrals to specialists.

Methods: We performed a retrospective chart review of patients evaluated for craniosynostosis at the Children's Hospital of Philadelphia and the American Family Children's Hospital between 2016 and 2023. Clinical photos and demographic information were gathered. Photos of age-matched patients without craniofacial differences were used as controls. Anthropometric measurements were collected from these photos. Statistical analysis was performed using ANOVA and Receiver Operating Characteristic Curve analyses, with statistical significance of $p<0.05$.

Results: Our cohort included 177 patients with sagittal, 53 with metopic, and 23 with unicoronal craniosynostosis. For sagittal synostosis, we developed an angle between the cranial vertex, nasion, and opisthocranion (VNO) in profile view. The mean VNO angle was 54.7°±3.8° for the synostosis group (mean age 9.5±11.1 months) and 41.1°±3.7° for controls (mean age 8.4±2.4 months) ($p<.001$). Diagnostic sensitivity and specificity of an angle >50° were 96.6% and 99.2%. This demonstrates that the VNO angle is an accurate screening tool to help diagnose sagittal craniosynostosis. A similar analysis is currently underway to develop anthropometric measurements for children with unicoronal and metopic craniosynostosis, with results forthcoming.

Conclusions: We demonstrate the development of anthropometrics such as the VNO angle for identifying craniosynostosis. This allows for increased accuracy in diagnosing children with craniosynostosis and promotes early referral to craniofacial centers, improving patient outcomes.

Evaluating outcomes and complications following various maxillomandibular fixation techniques: A systematic review and meta-analysis

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Introduction: Several methods of achieving maxillomandibular fixation (MMF) are currently available, all with the goal of immobilizing the maxilla and mandible to restore occlusion and promote healing, each with unique operative considerations and resulting patient outcomes and complications. Currently in the literature, patient outcomes are compared between two to three techniques of MMF, but not between all available MMF techniques. The goal of this study is to address this gap and review the literature to evaluate all MMF methods and compare their respective patient outcomes and complications for treatment of facial fractures. Conventional Erich arch bars were compared to various alternative interventions including modified arch bars such as hybrid arch bars, screw-based interventions such as MMF screws, and wire-based interventions such as eyelet interdental wiring.

Methods: A systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Included studies reported quantitative patient outcomes data for patients who underwent MMF for the treatment of facial fractures. Excluded studies were those that included patients who were treated for facial fractures without MMF, and those that did not report patient outcomes. Postoperative outcomes data was analyzed and compared between the different MMF techniques used. A random-effects meta-analysis was used to determine the mean differences, as well as 95% confidence intervals (CIs), with a statistical significance of $p<0.05$. RevMan Web Software 5.4 (Cochrane IMS) was used for statistical analysis.

Results: Our search yielded 4,234 articles, of which 24 studies were included. Seventeen of these included studies were able to be meta-analyzed. Included studies were randomized clinical trials, retrospective cohort studies, and prospective cohort studies. Time to achieve MMF (pooled mean difference -43.38 minutes; 95% CI, -58.20 to -28.56; P<0.001), total operative time (pooled mean difference -30.33 minutes; 95% CI, -61.05 to 0.39; P=0.05), incidence of needlestick injuries and glove perforations (pooled odds ratio 0.11; 95% CI, 0.04 to 0.30; P<0.001), and incidence of poor oral hygiene (pooled odds ratio 0.08; 95% CI, 0.02 to 0.28; P<0.001) were lower for alternative MMF interventions compared to conventional Erich arch bars.

Conclusions: Alternative MMF techniques resulted in a shorter operative time to achieve MMF, a shorter total operative time, and a decreased incidence of glove perforations, when compared to conventional Erich arch bars. If a patient is a candidate for MMF, the presented alternative MMF techniques should be considered depending on clinical context and availability of institutional resources.

The association of neighborhood disadvantage with surgical outcomes and follow up adherence in patients with cleft lip and/or palate

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Introduction: Social determinants of health can have a profound impact on the care provided to patients with cleft lip and/or palate (CLP). There is limited data on how neighborhood-level disadvantage may affect surgical outcomes in patients with CLP. The area deprivation index (ADI) is a novel measure of socioeconomic disadvantage, incorporating 17 United States census indicators of poverty, education, housing, and income with higher ADI scores representing greater neighborhood disadvantage. The purpose of our study is to elucidate whether neighborhood-level disadvantage is associated with worse cleft repair outcomes and patient follow-up adherence.

Methods: A retrospective chart review was conducted. Pediatric patients diagnosed with CLP who underwent surgery from 01/01/2013 to 01/01/2023 were included. State ADI scores, represented as deciles, were determined based on patients' full residential addresses or 9-digit zip codes. Demographics including sex, age, race, and ethnicity were collected. Clinical variables collected include post-operative opioid and antibiotic prescriptions at discharge, complications, emergency department (ED), pediatric intensive care unit (PICU), and hospital readmissions within 30 days of discharge, clinic visit no shows, and cancelled appointments. Univariable logistic regressions were used to assess the association of ADI with each binary variable listed above.

Results: A total of 414 patients (248 Male; 166 Female; average age of 5.35 ± 4.81 years at procedure) met inclusion criteria. Interventions included primary cleft lip repair (14%), primary cleft palate repair (19%), cleft rhinoplasties (18%), cleft lip revisions (12%), cleft palate revisions (11%), alveolar bone grafts (14%), speech surgeries (5%), and oronasal fistula revisions (7%). Univariable logistic regression revealed that higher ADI scores were correlated with fewer antibiotic prescriptions at discharge [OR 0.94, 95% CI [0.88-0.99], p=0.026], and with more postoperative ED visits [OR 1.24, 95% CI [1.07-1.43], p=0.005], hospital readmissions [OR 1.20, 95% CI [1.085 – 1.333], p<0.001], missed clinic appointments [OR 1.33, 95% CI [1.80-1.634], p=0.007], and postoperative complications [OR 1.12, 95% CI [1.05-1.19], p<0.001] within 30 days of discharge. ADI was not predictive of opioids prescriptions at discharge or PICU admissions.

Conclusions: Neighborhood disadvantage may impact cleft repair management and outcomes. Overall, our preliminary results demonstrated associations between ADI and antibiotic prescriptions, postoperative ED visits, hospital readmissions, presence of complications, and clinic visit no shows. Future work will further evaluate the correlation between ADI and clinical outcomes and follow up. Understanding how neighborhood disadvantage impacts cleft repair outcomes is crucial to clinical care, policy making, and eliminating health disparities for our patients.

Treating hydrocephalic macrocephaly using reduction cranioplasty: A systematic review evaluating surgical outcomes

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Introduction: Hydrocephalic macrocephaly can result in poor psychosocial development, positioning difficulties, skin breakdown, and poor cosmesis. Although reduction cranioplasty (RC) is a means of addressing these sequelae, the postoperative outcomes, complications, and risk for mortality of RC are not well understood given the rarity of hydrocephalic macrocephaly. Therefore, the primary objective of this systematic review is to evaluate the surgical outcomes of RC for the treatment of hydrocephalic macrocephaly.

Methods: A systematic review was performed using PubMed, Scopus, and Web of Science databases while following the Preferred Reporting Items for Systematic Review and Meta Analysis (PRISMA) guidelines. Inclusion criteria consisted of English and Spanish language publications reporting postoperative outcomes of patients with hydrocephalic macrocephaly following reduction cranioplasty. Two independent reviewers screened 350 studies; 27 studies met the inclusion criteria. Data on study design, patient demographics, operative details, and surgical outcomes were collected.

Results: There were a total of 65 reduction cranioplasties in the 27 included studies, representing 65 patients. Eighteen (66.7%) studies presented level V evidence, 7 (25.9%) presented level IV evidence, and 2 (7.4%) presented level III evidence. Following RC, improved postoperative head positioning was reported in 85.2% of studies, improved postoperative aesthetics was reported in 81.5% of studies, and improved postoperative neurologic functioning was reported in 74.1% of studies. In the 19 studies that reported both preoperative and postoperative head circumference measurements, the median relative difference in head circumference was a 15.1% reduction (range, 3.0% - 31.5%). Shunt revisions were the most common complication, reported in 9 (14.7%) of the 19 studies that evaluated complications. The median estimated blood loss was 633 mL (range, 20 - 2600). Of the 65 patients, there was a mortality rate of 6.2% (N = 4).

Conclusions: The majority of the included studies reported improvement in head size, head positioning, cranial cosmesis, and global neurologic functioning. However, the high risk of blood loss, complications, and mortality indicates the need for a serious discussion of surgical indication, an experienced team, and thorough perioperative planning to perform these complex surgeries.

Microbiome disruption in post-intubation laryngeal injury

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Introduction: Acute laryngeal injury (ALgI) occurs in over half of patients after intubation and mechanical ventilation and is associated with worse breathing and voice outcomes months later. ALgI results from endotracheal tube pressure on the posterior glottis, leading to ischemic mucosal injury that can progress to fibrotic cricoarytenoid joint contracture and severe reduction in airway caliber. While bacterial biofilms and microbiome alterations have been associated with mature post-intubation laryngotracheal stenoses, this study is the first to characterize the microbiology of acute post-intubation laryngeal injuries, with a goal of understanding how early bacterial shifts after mechanical epithelial barrier disruption may impact the pathogenesis and functional outcomes after post-intubation ALgI.

Methods: This cross-sectional study included 20 patients with ALgI who underwent early endoscopic intervention with tissue culture within 45 days of extubation, 20 patients with idiopathic subglottic stenosis (iSGS) who underwent tissue culture during routine endoscopic intervention, and 3 control patients who underwent mucosal swab culture during vocal fold injection augmentation in the operating room. Patients with pre-existing tracheostomy at the time of intervention were excluded due to potential for contamination. Scanning electron microscopy (SEM) was performed on one endotracheal tube in a patient with ALgI at the time of extubation to evaluate for biofilm.

Results: Demographic data and postoperative complications were compared. 15 (70%) of the ALgI patients had a positive culture compared to 1 (5%) of the iSGS patients ($p<0.001$) and none of the controls ($p=0.03$). The most identified microbes isolated from ALgI patients included *Staphylococcus* species in 6 patients (30%) and *Streptococcus* species in 5 (25%). 19 (95%) of iSGS patient cultures grew normal oropharyngeal flora or had no growth, and 3 (100%) of the normal control cultures grew normal oropharyngeal flora. SEM of the outer surface of an endotracheal tube at the time of extubation demonstrated biofilm formation.

Conclusions: The high rate of pathologic bacterial infiltration into post-intubation laryngeal wounds supports efforts to reduce bacterial colonization of endotracheal tubes and highlights the role of culture-directed antibiotic therapy as a part of early intervention to improve outcomes for patients with ALgI.

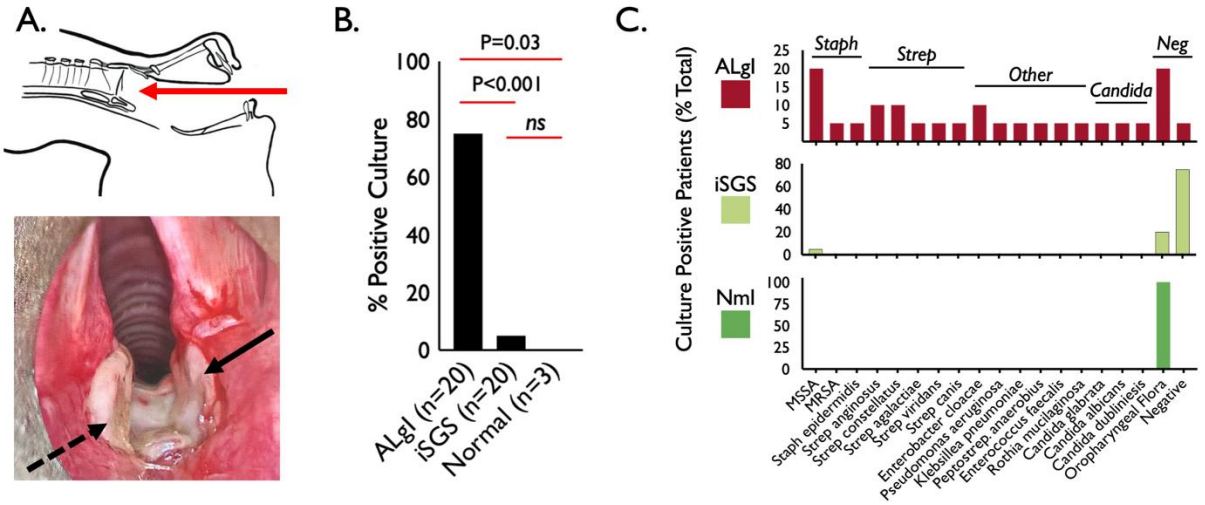


Figure 1: Microbiology of Acute Laryngeal Injury
(A) Posterior glottic ulceration in post-intubation acute laryngeal injury (ALgI). Dashed arrow: exposed cartilage; solid arrow: mucosal eschar. (B) Culture positivity (iSGS: idiopathic subglottic stenosis). (C) Cultured organisms.

“This is kind of a scary conversation”: A qualitative analysis of patient-surgeon communication about rectal cancer treatment

Melanie Fritz, Joshua Sommovilla, Elise Lawson, Amy Zelenski, Margaret Schwarze, Ana De Roo

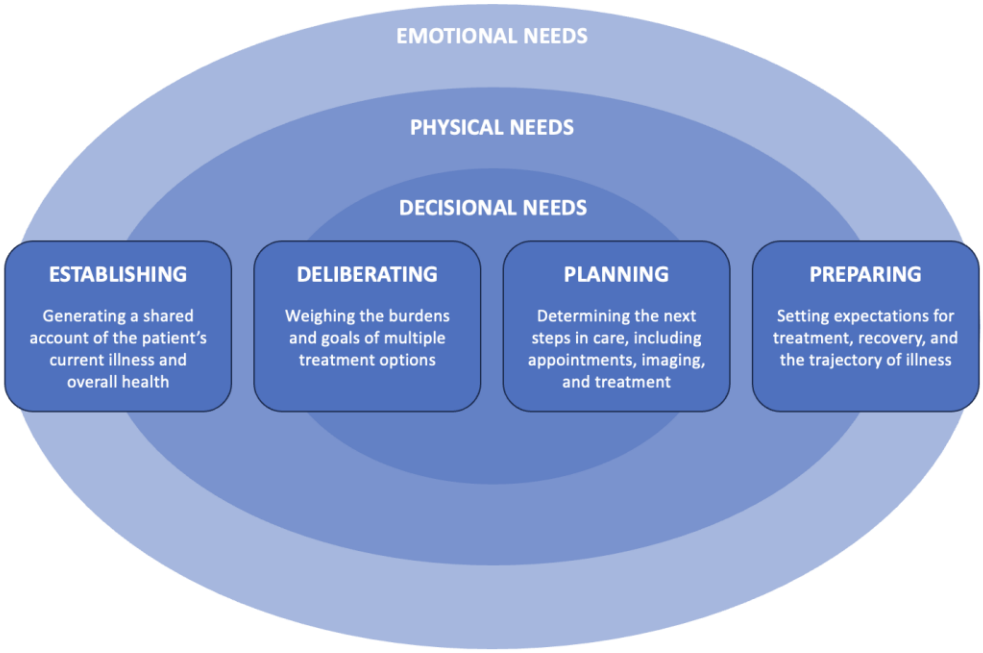
Introduction: Patients with rectal cancer face a potentially life-limiting disease with a substantial symptom burden, requiring consideration of multi-modal treatment options with possible trade-offs between survival and quality of life. Surgical consultations provide a critical moment to support patients as they navigate care. This study aims to characterize communication during clinic visits to identify: (1) unique challenges for patients with rectal cancer and (2) opportunities to optimize serious illness communication.

Methods: We performed secondary analysis of audio recorded clinic visits of patients with rectal cancer, and their families, with colorectal surgeons at 5 academic centers. The cohort included 18 patients seen by 8 surgeons. Four coders with backgrounds in surgery, communication, education, and palliative care used an inductive approach to assign codes to constructs as they arose in the data. We iteratively revised the taxonomy via group consensus. We pursued higher level analysis aided by MIRO, an online software program for concept mapping, to ensure the results faithfully represented the data. We characterized the relationship between tasks surgeons pursue during the visit and specific patient domains including physical symptoms, emotional concerns, and inclusion of priorities within a treatment plan.

Results: Surgeons have four key tasks to accomplish during the clinic visit: establishing a shared account of the patient’s current illness and overall health, deliberating about treatment options, planning treatment, and preparing patients for the experience of treatment and recovery. Figure 1 illustrates how, as surgeons address each task, patients express a range of needs: emotional (distress around illness progression, prognosis, and hygiene-related social isolation), physical (current and future symptom management), and decisional (incorporation of patient priorities into treatment planning). Surgeons attend to patients’ needs, often effectively, yet the overall objective of the clinic visit, multiple competing tasks, and complexity of treatment options can shift the focus of the conversation away from the patient’s needs, towards highly technical information.

Conclusions: Colorectal surgeons encounter patients with rectal cancer at a time in the disease course when patients are encumbered by intense emotional, physical, and decisional needs. This encounter requires surgeons to balance two agendas: addressing patients’ needs and accomplishing the specific tasks to guide patients through treatment. A more intentional conversational framework and the use of advanced communication techniques might support colorectal surgeons in integrating both agendas to improve care for patients with rectal cancer.

FIGURE 1. Tasks for surgeons to accomplish during the clinic visit and overlapping expression of patients' needs.



A narrative review exploring bacterial colonization and stoma complication management in osseointegrated prosthetics

Mitchell J. Benyukhis, Michael O. Sohn, Sahand C. Eftekari, BS, Caden J. Lambie, BS, Nicole C. Kane, BS, D'Andrea T. Donnelly, BA, Samuel O. Poore, MD, PhD, Aaron M. Dingle, PhD

Introduction: Osseointegration (OI), a direct skeletal attachment of a transcutaneous implant, is a propitious alternative providing increased sensation and quality of life whose limited research prevents clinical use. This study sought to understand the complications related to the stoma, the implant exit site, and possible interventions to minimize the occurrence of various obstacles. The stoma is the most common location resulting in the failure of the OI procedure, yet its research is still extremely underdeveloped.

Methods: A comprehensive literature review was conducted across multiple databases, including PubMed, Springer Link, Wiley, and MEDLINE. The review evaluated the capabilities and limitations of OI and the creation and maintenance of the stoma. Search terms such as osseointegration, amputation, arthroplasty, bacteria, infection, prosthesis, rehabilitation, and stress were employed. Limitations during the review included conflicting sources, insufficient information, and the need for further review. Key information on stoma creation and maintenance was cross-examined with complication rates, and the effectiveness of various techniques was assessed.

Results: Out of 51 articles reviewed, 40 met the inclusion criteria and were deemed suitable for the investigation. The findings support OI as a viable alternative; however, several complications hinder its widespread use. Common complications include infection, periprosthetic fracture, marsupialization, and avulsion. Mitigation techniques to minimize postoperative revision include specific material selection, precise porous coating, accurate sizing, and strategic soft tissue manipulation. The review suggests that titanium alloy encourages bone tissue repair, while a 50-400 micropores layer facilitates proper bony and tissue ingrowth. Likewise, accurate sizing is crucial to prevent periprosthetic fractures and soft tissue manipulation allows for drainage of the implant cavity, thereby reducing complication rates.

Conclusions: These promising findings establish the need for OI-centered clinical trials focusing on materials and procedures to mitigate bacterial colonization. The existing literature lacks studies that comprehensively test implants combining optimal material, porosity, sizing, and soft tissue manipulation. This study summarizes effective strategies and techniques, paving the way for future research to develop refined implant alternatives. Enhanced understanding of prosthesis sensation enables patients to receive the most advantageous solutions for lower extremity amputation.

The genetic landscape following neurorrhaphy: A narrative review

Nicole Kane, BS, Molly Winchenbach, Sarah Thornton, BA, Anna Jesch, D'Andrea Donnelly, BA, Samuel Poore, MD, PhD, Aaron Dingle, PhD

Introduction: Peripheral nerve injuries (PNI) are a common injury as they comprise 3% of trauma cases (Althagafi & Nadi, 2023). The prognosis of PNI varies from patient to patient, and in some cases, quality of life is diminished as loss of feeling can persist indefinitely (Zhang, et al., 2022). The primary treatment for a PNI is the surgical fixation of the severed nerve endings, also known as Neurorrhaphy. Neurorrhaphy is the first-line protocol for treatment and only has a success rate of 64.3% (Haninec, et al., 2007). This study sought to find the role genetics may play in promoting nerve regeneration in hopes of increasing success rates of Neurorrhaphy.

Methods: A broad narrative review was conducted using Pub-Med. The review evaluated genes associated with nerve regeneration following injury. The primary search terms included "Human", "Genetics", "Nerve Regeneration", "Neurorrhaphy", "Axonal recovery". The inclusion criteria were papers written within the past 10 years, written in English, and human models. The original search yielded 21,385 papers, 102 papers met our criteria, 48 papers were then analyzed based on their titles, and 19 papers were subjected to inclusion after full-text readings. Full-text readings analyzed genes associated with nerve regeneration, and a summarizing table was used to compare results.

Results: Five out of the 19 articles (26%) mentioned the MAPK signaling pathway. Four of the 19 articles (21%) mentioned the Sox2 gene positively correlated to nerve regeneration. Four out of the 19 (21%) articles mention the MTOR pathway having a substantial influence on nerve maturation. Other articles mentioned specific genetic pathways and mutations such as the CREB, SOD1, NF-K2, BASE1, DLK, ADCYAP1, PEDF, but they were not reflected throughout the literature.

Conclusions: These findings show great potential as they provide genetic pathways to target and promote positive nerve regeneration following injury. Previous literature lacks a comprehensive review of human genes corresponding to nerve regeneration following injury, as most research focuses on animal models. This review provides extensive resources for future research to establish human clinical trials upregulating these pathways in hopes of increasing the success rate following neurorrhaphy.

Trigeminal nerve stimulation: A systematic review of reported adverse events and future clinical applications

Sarah M. Thornton, BA, D'Andrea T. Donnelly, BA, Peter J. Nicksic, MD, Samuel O. Poore, MD, PhD, Aaron M. Dingle, PhD

Introduction: Trigeminal nerve stimulation (TNS) is a promising intervention that is gaining momentum in medicine. It is commonly compared to vagus nerve stimulation, which has demonstrated efficacy across a broad range of indications, including peripheral nerve regeneration. Vagus nerve stimulation requires surgical implantation of a cuff electrode deep in the neck, adjacent to critical structures in the carotid sheath. Contrarily, the superficial location of the trigeminal nerve offers a convenient site for non-invasive stimulation. This cranial nerve originates in the pons and offers projects to multiple deep brain nuclei, similar to the vagus nerve. Given these similarities, there may be opportunities for broader clinical application of TNS. In this systematic review, we focus on reported adverse effects of TNS that may help drive the exploration of novel clinical applications.

Methods: We queried Medline, SCOPUS, and Web of Science databases on Oct. 3, 2023, for relevant keywords ("trigeminal nerve stimulation" AND "epilepsy" OR "migraine" OR "ADHD") in accordance with PRISMA guidelines. Inclusion criteria were human studies that utilized TNS for the therapeutic benefit of an FDA-approved indication and mentioned adverse effects. Exclusion criteria were animal studies, review papers, stand-alone abstracts, and papers that did not mention side effects. Information was extracted regarding demographics, devices used, stimulation parameters, adverse effects, attrition, and efficacy.

Results: 367 records were identified on initial query. After abstract screening and inclusion and exclusion were applied, 1,009 patients across 17 studies were included. The indications for TNS included treatment of epilepsy (19.6%), migraine (66.8%), and ADHD (13.6%). All studies utilized capacitively coupled transcutaneous electrodes to interface with either the supraorbital, supratrochlear, or infraorbital nerve. Stimulation parameters varied between studies with a median of 115.4 Hz (range 100-120 Hz), 9.6 mA (range 2-25 mA), and consistent pulse width of 250 μs. There were no serious adverse events recorded, and minor adverse effects included skin irritation (6.3%), headache (5.7%), sleep disturbance (3.5%), skin/teeth tingling (3.2%), fatigue (2.2%), anxiety (0.7%), and pain (0.7%). Seven patients (0.7%) withdrew from the included studies due to inability to tolerate stimulation.

Conclusion: Trigeminal nerve stimulation, an FDA-approved intervention, offers a non-invasive approach utilizing simple electrodes. This systematic review underscores the favorable risk profile of TNS, coupled with a low rate of patient attrition. Encouraging advances exploring the effect of TNS on neuroplasticity, a key component to motor relearning required in nerve/tendon transfer and peripheral nerve repair, are underway.

Patient and provider perceptions about social support after bariatric surgery: A qualitative study

Dawda Jawara, MD, Esra Alagoz, PhD, Kate V. Lauer, MD, Corrine I. Voils, PhD, Luke M. Funk, MD, MPH

Introduction: Bariatric surgery is the most effective evidence-based obesity treatment. Social support is a critical part of the recovery process and weight loss maintenance following bariatric surgery. A limited number of studies have assessed both patient and provider perceptions about the role of social support after bariatric surgery. Our objective was to identify and understand patient and provider perceptions about the influence of social support on weight loss after bariatric surgery.

Methods: We reported a secondary analysis of qualitative data acquired from semi-structured interviews conducted from April-November 2020 with bariatric surgery patients and providers including primary care providers (PCP), health psychologists (HP), registered dietitians (RD), and bariatric surgeons (BS). Patients who had at least one-year of follow-up after their bariatric procedure were eligible for inclusion. A hybrid of Andersen's Behavioral Model of Health Services and Torain's Framework for Surgical Disparities was utilized to design the interview guides that were used to assess post-operative experiences regarding dietary habits, physical activity, and follow-up care. Using conventional content analysis, our study team members generated codes which were grouped into themes. A secondary analysis was performed to generate themes about social support pertaining to dietary habits, physical activity, and follow-up care.

Results: Forty-five participants were interviewed, including 24 patients (83% female; 79% white; mean age 50.6 ±10.7 years) and 21 providers (6 PCPs, 4 HPs, 5 RDs, 6 bariatric surgeons). **Table 1** summarizes four themes relating to social support facilitators and barriers: 1) culture and family dynamics impacted patient adherence to diet after surgery; 2) engagement in activities with partners/friends helped patients find pleasure in their daily exercises; 3) help with transportation to appointments by family members or friends provided patients with reassurance about getting to their providers for follow-up; and 4) Life stressors that patients experienced at home were related to poor social support.

Conclusions: Continued assessment of interpersonal factors, especially culture and family dynamics and life stressors that patients experience after bariatric surgery is crucial. The cultural backgrounds of patients can influence the types of food that are available at family gatherings, which can include non-recommended foods after surgery. Additionally, life stressors such as living with family members who have poor health conditions can limit the social support that patients need to enhance their weight loss after surgery. Providing individualized care by addressing these barriers and reinforcing the facilitators may help with maintenance of weight loss after bariatric surgery.

Table 1: Patient and provider themes regarding social support facilitators and barriers after bariatric surgery

Themes	Facilitators	Barriers
Culture and family dynamics	"Even now, all these years later, they [family members] make sure there are things that I can eat at family events. They are not weird if I do not feel like eating, or when I'm just having water or something because I already ate." (Patient #1)	"My mom lives in Chicago, and they make tamales when we go there. After my surgery, I could not eat the tamales they specially made for us, and that was a big thing. Like culturally speaking, I think that it is even a barrier for some of my patients to consider even starting with the bariatric process sometimes because they felt like their family members will not accepted it." (Primary Care Provider #2)
Engagement in activities with partners/friends	"I walk with my boyfriend because if I struggle or I fall, then he's there. I like to talk a lot, and he gets me talking about things or asking me like, 'what kind of flower is that?' And all of a sudden we'd walk much further than I ever intended." (Patient #1)	"If I had an active social life and if I had an active physical life, I would've thoroughly enjoyed my weight loss and would've wanted to keep going. But all I did was sit at home." (Patient #62)
Help with transportation to appointments	"That was not really an issue because I drove myself there and back. If I was not able to drive, my sister was very supportive. However, she has been out of town for about a year now due to work. But I have neighbors that would bring me if I needed it." (Patient #15)	"I have had some patients who lived in rural areas, and they think driving in the city is like, 'Oh my god, that's so scary, like I can't believe I am driving in the city.' So, the only way that they'll come to see the doctor is if they can get their son or husband or someone else to drive them. That can be limiting for them if that person is not available to take them in because they're too afraid to drive in." (Bariatric Surgeon #1)
Life stressors at home	"Stress essentially impacts everything. So, for our patients who have low health literacy or cognitive concerns, we have seen that having a supportive partner or someone who lives with them and is there to keep them on track can really make a huge difference. So, social support is key for everyone, especially for those patients who are cognitively not able to understand." (Health Psychologist #1)	"Often there are a lot of family members that have identical stressors [diabetes, depression, and anxiety]. So, then that person is part of a family unit where it's not just their own stressors, it's the stressors of the family. This is just a constant stressor for my patient." (Primary Care Provider #5)

Length of stay following orthotopic adult liver transplant

Ekaterina Fedorova, MD, Jacqueline Garonzik Wang, MD

Introduction: While liver transplantation (LT) can be lifesaving, it is one of the most resource-intensive interventions. Length of stay (LOS) after LT is a consistent benchmark for resource utilization and an independent predictor of survival. We sought to explore factors associated with LOS, and its effects on graft survival (GS) and overal patient survival (OS).

Methods: We retrospectively identified 1,287 patients who underwent adult liver-only transplantation at University of Wisconsin from 2002-2021. Median LOS was 12 days. Chi-squared and Wilcoxon rank sum tests were used to establish associations between factors and LOS > 12. Multivariable logistic regression and Cox proportional hazard models were used to analyze associations with GS and OS.

Results: LDLT (aOR=3.6, P=.013); length of surgery (aOR=1.1, P=.007); poor functional status (aOR=5.8, P=.001); postoperative ventilatory support (aOR=2.1, P=.001); CIT (aOR=1.1, P=.001) and postoperative dialysis (aOR=3.8, P=.001) were independent risk factors for LOS > 12 days. LOS > 12 days was an independent risk factor for GS (aHR=1.5; P=.001) and OS (aHR=1.3; P=.008). Postoperative ICU admission and LOS > 12 days effect interaction negatively affected GS (aHR=1.16, P=.004) and OS (aHR=1.06, P=.01). The effect of LOS on OS and GS was not modified by other patient or donor factors.

Conclusion: Understanding the relationships between pre-operative, intra-operative and post-operative variables that impact LOS after LT can help clinicians to mitigate risks and implement early therapeutic interventions, ultimately improving graft and patient overall survival.

Regret after gender-affirming surgery: A comparison

Sarah M. Thornton, BA, Armin Edalatpour, MD, Katherine M. Gast, MD, MS

Introduction: Regret after gender affirming surgery (GAS) is a complex and controversial issue that has been extensively researched. Comparing regret after GAS to regret after plastic surgery operations and other major life decisions, both surgical and non-surgical, is a novel approach that can provide insight into the magnitude of this issue. Importantly, this paper does not seek to equate gender affirming surgery to other elective surgeries or life decisions, but instead aims to provide a framework to understand regret after gender affirming surgery.

Methods: A systematic review of three databases was conducted to investigate the rate of regret after common plastic surgery operations. We queried Medline, SCOPUS, and Web of Science databases for relevant keywords ("regret" AND one of the following: breast reconstruction, breast reduction, breast augmentation, mastopexy, facelift, neck lift, abdominoplasty, blepharoplasty, brow lift, rhinoplasty, liposuction, thighplasty, and buttock lift) in accordance with PRISMA guidelines. Information regarding percentage of patients experiencing regret, Decision Regret Scale scores, and any quantitative information was extracted. Separately, three separate literature reviews on regret after GAS, regret after elective surgical operations, and regret after other major life decisions were performed.

Results: 295 records were identified on initial query. After abstract screening and inclusion and exclusion were applied, a total of 55 articles examining regret after plastic surgery were included. The Decision Regret Scale was commonly used to report regret, and scores ranged from 3.8-41.9. The percentage of patients reporting regret after plastic surgery operations ranged from 0-72%. Rate of regret after GAS is widely reported to be approximately 1%. Other major life decisions, such as tubal sterilization surgery, elective hernia repair, having children, and getting a tattoo have regret rates of 28%, 11%, 7%, and 16.2%, respectively.

Conclusion: Overall, when comparing regret after GAS to regret after other plastic surgeries and other major life decisions, the percentage of patients experiencing regret is minor. The next essential step in the study of regret after gender-affirming surgery is to implement interventions to minimize post-operative regret.

Trends in nipple reconstruction in gender-affirming mastectomies

Sumin Yang, BS, Armin Edalatpour, MD, Jacqueline Israel, MD, Katherine Gast, MD, MS

Introduction: Gender-affirming surgeries have been shown to improve the psychosocial functioning, mental and physical health of transgender and non-binary people. Many transmasculine and non-binary patients who experience chest dysphoria that impacts their daily functioning choose to pursue masculinizing top surgery, also known as gender-affirming mastectomy. One aesthetic option available to patients is to forgo nipple preservation with nipple grafting during surgery to create a smooth flat chest with no nipples. We hypothesize that in the last few years, more non-binary compared to transmasculine patients have chosen to forgo nipple-areola complex (NAC) preservation with nipple grafts in gender-affirming mastectomy surgery and testosterone use is associated with preservation of a NAC for a more traditionally masculine chest.

Methods: A chart review of 443 transgender patients who underwent gender-affirming mastectomies at UW Health between the years 2017-2023 was completed. A Pearson Chi-Square test was run on categorical data while an independent sample t-test was run on continuous data.

Results: In recent years, patients who chose to have nipple grafts declined steadily from 90.7% in 2019 to 77.8% in 2022. Patients who identified with genders outside the binary (e.g. nonbinary, agender, gender expansive) comprised the majority of those that opted out of receiving nipple grafts. In contrast, most of the patients who chose to receive nipple grafts identified as transmasculine. We found that the statistically significant factors in deciding to forego nipple grafts were a patient's gender identity, pronouns, and absence of prior testosterone therapy. Factors that were not associated with nipple preservation were race, age, BMI, time from social transition to surgery, time from medical transition to surgery, chest binding history, marital status, and employment history.

Conclusions: Patients who identified outside the gender binary and did not pursue testosterone therapy were more likely to choose a flat chest with no nipples. The steady increase among all transgender patients to forego nipple preservation with grafts affirms the need for constant adaptation in transgender healthcare. Future research should evaluate patient decision-making and aesthetic goals prior to gender affirming chest surgery.

Effect of a multidisciplinary approach in the management of patients with advanced stage pressure injuries

Alyssa McClelland, BS, Jocelyn Zajac, MD, Molly Oberdoerster, DO, Cindy Schmitz, NP, Ambar Haleem, MD, Angela Gibson, MD, PhD

Introduction: Pressure injuries (PI) affect approximately 2.5 million admitted patients each year in the United States incurring an annual cost of $26.8 billion. Management of PIs is multidisciplinary, requiring treatment for pre-existing comorbidities, complex wound care, comprehensive offloading plan and optimization of nutrition. In 2019, our hospital established a multidisciplinary approach for the management of PIs coordinated by our Wound Service. Prior to 2019, no standardized workflow existed. The purpose of this study was to evaluate the effectiveness of the multidisciplinary PI team approach with regards to resource utilization, coordination of management practices and patient outcomes.

Methods: Patients admitted between January 2014 and June 2022 with initial documentation of a stage 3 or 4 pressure injury were included. One hundred patients were randomly selected from 2014 through December 2016, the period before the establishment of the multidisciplinary wound team (Pre-Group); and 100 patients were randomly selected from April 2019 through June 2022, the period during which the multidisciplinary team was operational (Post-Group). The 200 patient charts were manually reviewed to obtain information regarding PI details and time course, overall management course, patient outcomes and resource utilization.

Results: There were significant differences in the number of inpatient consults ($p < 0.01$) and the time elapsed from first documented record of PI and death ($p < 0.01$) between the two groups. No significant differences were found in the number of blood cultures, wound cultures or imaging obtained between the two groups ($p>0.05$). In the post group, 26 patients underwent palliative wound care with no intention to heal their pressure injury in contrast to 14 patients in the pre-group ($p = 0.05$). A discussion on the patients' underlying comorbidities directly contributing to their overall prognosis was undertaken more frequently in the post-group (n=44) compared with the pre group (n=30).

Conclusions: The implementation of a multidisciplinary team approach to the management of patients with PI resulted in improved hospital resource utilization, including fewer consults requested. Although we did not find a significant difference in patient outcomes, there was a clinical trend in palliative approaches to PI management with increased focus on patient comfort and symptom management as opposed to aggressive wound care in patients with significant comorbidities and expected poor prognoses.

Axillary nodal staging in women undergoing upfront surgery for DCIS in Wisconsin

Meeghan Lautner, MD, Chandler Cortina, MD, Jessica Schumacher, PhD, Randi Cartmill, MS, Joseph Weber, MD, Jill Ties, MD, Joanne Pasiuk, MD, Adrienne Cobb, MD, Subramanian Natarajan, MD, Barbara Boyer, MD, Elise Lawson, MD, Amanda Kong, MD

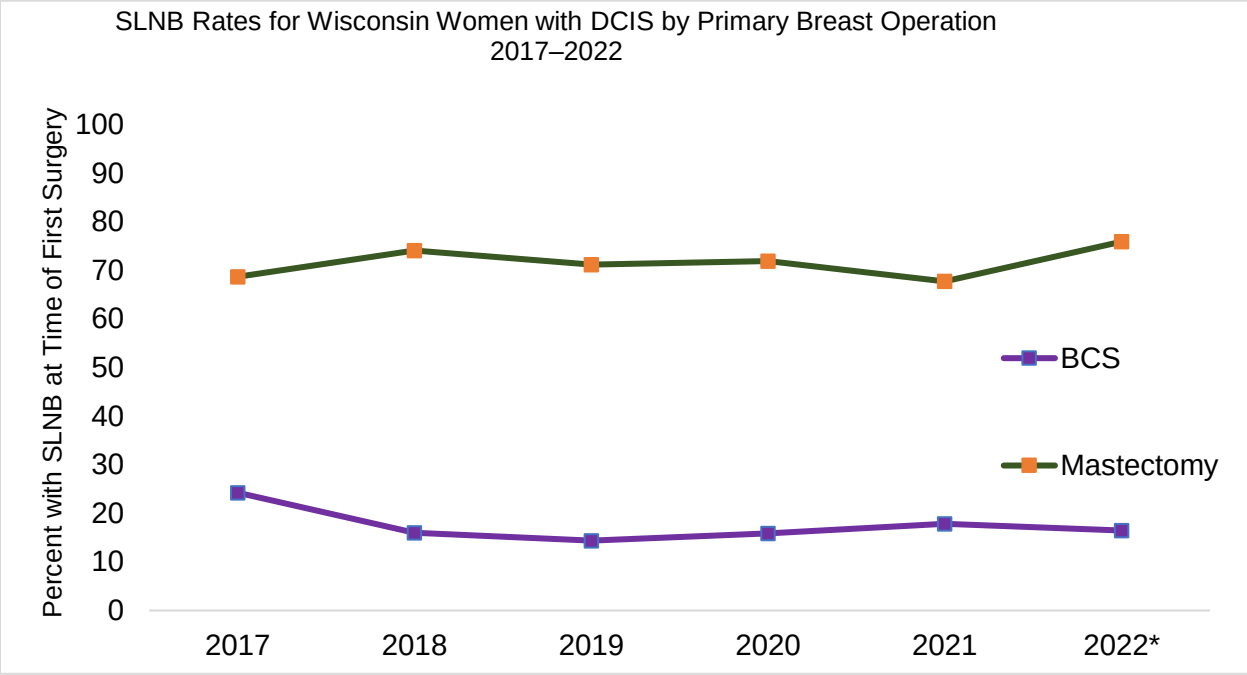
Introduction: Ductal carcinoma in situ (DCIS) is a precursor to invasive breast cancer. Modern treatment for DCIS is surgical excision, adjuvant radiation therapy for those who undergo breast-conserving surgery (BCS), and endocrine therapy. Guidelines do not recommend sentinel lymph node biopsy (SLNB) at the time of BCS for DCIS, but it may be considered for mastectomy patients. This research examines the statewide SLNB rate for Wisconsin women undergoing upfront surgery for DCIS and facility-level variations in SLNB rates for these patients.

Methods: In Wisconsin Hospital Association discharge data from 2017–2022, we identified adult females who underwent upfront BCS or mastectomy for DCIS, excluding those with microinvasive DCIS or a history of BCS in the previous 12 months. We examined rates of nodal staging using CPT codes for SLNB and axillary injection/mapping and compared rates by primary operation and over time. Hospital facility-level rates were calculated for patients undergoing BCS in facilities that treated ≥5 cases annually. Notably, data availability restricts 2022 data to January-September.

Results: From 2017-2022, 5,687 women met study inclusion. The majority (78.7%, n=4,476) underwent BCS while 21.3% (n=1,211) underwent mastectomy. The age distributions for patients were 13.58% of BCS patients aged <50 (30.64% mastectomy), 56.81% aged 50-69 (51.7%), and 29.6% aged ≥70 (17.67%). The rate of SLNB in patients undergoing BCS was 24.3% in 2017 and trended down to 16.5% in 2022 (Figure 1). For mastectomy, the SLNB rate trended slightly upward from 68.7% in 2017 to 75.9% in 2022. When examining facility-level data, the range of patients undergoing SLNB at the time of BCS ranged from 0-80%.

Conclusions: Between 2017–2022, >15% of Wisconsin women with DCIS who underwent BCS received SLNB, indicating overtreatment. Additionally, wide facility-level variation in SLNB utilization for BCS patients was also observed. Given these findings, future action by the Surgical Collaborative of Wisconsin aims to provide statewide educational opportunities on evidence-based guidelines for nodal staging for DCIS through webinars, regular state-wide tumor boards, and online educational content. These efforts will ensure women diagnosed with DCIS in Wisconsin receive evidence-based care that minimizes the morbidity of unnecessary axillary surgery, regardless of treating facility.

Figure 1.



*Quarter 1 through quarter 3 data only

Changing the paradigm of congenital diaphragmatic hernia care – A tale of a two-hospital system

Michael Stellon, Devashish Joshi, Sofia Nehring Firmino, Molly Ryan, Michael Beninati, Ryan McAdams, Inna Lobeck

Introduction: Infants born with a congenital diaphragmatic hernia (CDH) may require rapid escalation of care. Many centers employ a two-hospital system with separate birthing and children's hospitals with variable levels of care, requiring early transfer of some infants. Our objective is to determine the effectiveness of protocolization of CDH care in a two-hospital system and analyze the implications of transfer time on patient-related outcomes.

Methods: A single-institution 10-year retrospective chart review was performed on patients prenatally diagnosed with CDH. Patients that were not transferred, terminated prenatally, or elected palliative care at birth were excluded. Information collected included prenatal findings, data surrounding interhospital transport, details of care and post-natal complications. In 2017, a standardized protocol for CDH was implemented and pre- and post-protocolization was compared.

Results: 22 patients met inclusion criteria. 12 (55%) were born prior to initiating the CDH protocol. There were 6 deaths prior to protocol initiation (50%) and one after (10%, $p = 0.04$). Five patients were classified as mild, 12 moderate, and 5 severe. There was 1 death among mild cases, 4 in moderate cases, and 2 in severe cases. 22.7% required ECMO support (n=1 mild, n=4 moderate). The average times from birth to transfer call and call to transport were 232.5 minutes and 101.4 minutes, respectively. However, for patients who presented with more severe physiology (those who died or required ECMO), the average time from birth to transfer call was shorter (164.6 minutes). There were no significant differences between time from birth to transfer call ($p = 0.59$), call to transport ($p = 0.07$), and birth to arrival ($p = 0.54$) before and after protocol implementation. Two patients died prior to transfer.

Conclusions: Introducing a standardized postnatal protocol for the care of CDH patients in a two-hospital system improves survival. In this system, the sickest infants transferred earlier. Despite this, transfer may still be delayed and prenatal severity prognostication cannot be definitively relied upon for postnatal risk of deterioration. The remedy and safest delivery system is a high-risk delivery center where all infants with CDH may be born and treated with the highest level of care.

Implications of social determinants of health in access to and outcomes of fetal surgery

Devashish Joshi, Michael Stellon, Gabriella Mullally, Linda Cherney Stafford, Glen Leverson, Michael Beninati, Inna Lobeck

Introduction: Fetal surgery is a highly specialized field, offered at relatively few institutions, thus limiting access to fetal interventions. No data exist evaluating the impact of social determinants of health (SDoH) in fetal surgery. This study aims to investigate how SDoH affect fetal surgery access, outcomes, and healthcare utilization.

Methods: A single institution ten-year retrospective analysis was performed on expectant mothers with the fetal diagnoses of twin-to-twin transfusion syndrome (TTTS), open neural tube defect (ONTD), and congenital diaphragmatic hernia (CDH). Patient demographics including area deprivation index (ADI), healthcare, economic, social, environmental and educational data were collected, and outcomes compared between groups with variable SDoH. ADI was analyzed in two groups: 1-6 (less disadvantaged neighborhoods) and 7-10 (highly disadvantaged neighborhoods). Diagnosis specific information was collected to assess eligibility for referral. Fetal surgery accessibility and disease-specific outcomes were analyzed considering SDoH using Fisher's Exact test.

Results: 31 TTTS, 19 CDH, and 59 ONTD patients were reviewed. All TTTS, 16 moderate/severe CDH, and 55 ONTD patients qualified for referral to a fetal surgery center for potential intervention. Within the TTTS cohort, patients from ADI 7-10 presented with more severe stage TTTS (p=0.026), but were less likely to receive or attend a referral as compared to ADI 1-6, though this did not reach significance (**Table 1**). 32 ONTD patients were referred. 16 (55.1%) white patients attended the referral versus no non-white patients. 72.4% of children with ONTD in an ADI 1-6 neighborhoods were ambulatory by 18 months versus 46.1% in an ADI 7-10 (p=0.16). There were 3 postnatal deaths before discharge, all within the ADI 7-10 group (p=0.02). Three CDHs (18.75%) received a referral but two were unable to attend due to insurance or cost. Post-natal mortality for CDH was 20% and 50%, for ADI 1-6 and 7-10, respectively (p=0.27).

Conclusions: ADI affects access to fetal surgical services, outcomes, and healthcare utilization for patients. Patients from highly disadvantaged neighborhoods are less likely to be referred or attend referrals and more likely to experience worse outcomes. Multi-institutional studies are warranted to increase power and understand further the implications of SDoH in fetal surgery.

	Outcome	ADI 1-6 n (%)	ADI 7-10 n (%)	p-value
TTTS	Received referral	24 (88.9)	2 (50)	0.1117
	Completed referral	21 (77.8)	2 (50)	0.2683
	Cincinnati stage at diagnosis ≤2	20 (74.1)	1 (25)	0.0266
Open Neural Tube Defect	Received referral	22 (56.4)	10 (62.5)	0.7689
	Completed referral	13 (33.3)	3 (18.7)	0.3435
	Ambulatory at 18 months	21 (72.4)	6 (46.15)	0.1635
	Neonatal death Before Discharge	0 (0)	3 (20)	0.0247
CDH	Received referral	2 (15.4)	1 (33.3)	0.4893
	Completed referral	1 (50.0)	0	

Table 1: ADI-related outcomes and access to fetal surgery

Coordination of oro-pharyngeal pressures during swallowing

Tadeas Lunga, MD, Kazuhiro Hori, MD, Suzan Abdelhalim, MD, MPH, Timothy McCulloch, MD

Introduction: Swallowing is a complex process requiring precise coordination of pressure and timing across multiple structures. Recent advancements in pressure measurement methods have opened investigational avenues. Bolus volume and viscosity require swallow adaptation. However, the role of oral pressures modifications remains unclear. This study aims to investigate the role of tongue to palate pressures in swallow adaptation. Including anterior (AT) and lateral tongue (LT) pressures, velopharyngeal (VP) pressure, and base of the tongue (TB) pressure.

Methods: Seventeen healthy volunteers participated. Tongue and pharyngeal pressures were measured using a sensor sheet system and pharyngeal high-resolution manometry. Signals from both systems were synchronized for data analysis. The tongue pressure sensor sheet was attached to the palatal mucosa. Participants completed three swallows of different volumes (5 cc, 10cc, and 20cc) and viscosities (thin, nectar, honey). Maximum pressure magnitudes were recorded. Descriptive statistics and a TWO-WAY-ANOVA were used for analysis.

Results: Effect of Volume (5cc, 10cc, 20cc), regardless of Viscosity:
AT pressures: 54 mmHg (SD = 34), 63 mmHg (SD = 35), 59 mmHg (SD = 37).
LT pressures: 87 mmHg (SD = 52), 91 mmHg (SD = 55), 87 mmHg (SD = 48).
VP pressures: 117 mmHg (SD = 35), 124 mmHg (SD = 34), 133 mmHg (SD = 33)
TB pressures: 121 mmHg (SD = 36), 121 mmHg (SD = 39), 125 mmHg (SD = 41)
Effect of Viscosity (thin, nectar, honey), regardless of Volume:
AT pressures: 52 mmHg (SD = 34), 59 mmHg (SD = 37), 65 mmHg (SD = 34).
LT pressures: 79 mmHg (SD = 45), 90 mmHg (SD = 49), 97 mmHg (SD = 58).
VP pressures: 124 mmHg (SD = 33), 125 mmHg (SD = 36), 125 mmHg (SD = 36)
TB pressures: 121 mmHg (SD=38), 123 mmHg (SD=40), 124 mmHg (SD=39).
No significant effects of viscosity, volume, or their interaction were observed.

Conclusions: This study, the first to synchronously measure tongue and pharyngeal pressure using a sensor sheet system and high-resolution manometry, reveals some key observations. Pressures at the anterior and lateral tongue tend to increase with thicker liquids, requiring more pressure to initiate flow. Velopharyngeal pressures tend to increase with greater volume, ensuring a tight seal at the velopharynx when swallowing a large bolus to prevent nasal regurgitation. Some trends may have reached significance with additional data; other adaptive behaviors may have superseded changes in pressure generation.

Patient-reported functional outcomes in operative versus non-operative treatment for traumatic hand and wrist injuries

Elif Kurt, BS, Steven Moura, MA, Caroline Bay, BA, Armin Edalatpour, MD, Brett Michelotti, MD

Introduction: While objective surgical outcomes for traumatic hand and wrist injuries have been studied extensively, there is a paucity of research comparing patient-reported outcomes between operative and non-operative treatment. This study aimed to compare Patient Reported Outcomes Measurement Information System (PROMIS) scores for physical function, social function, and sleep disturbance between operative and non-operative patients with traumatic hand and wrist injuries.

Methods: We retrospectively reviewed all patients ≥ 18 years old with prospectively collected PROMIS scores from Nov 2022 – May 2023 treated operatively or non-operatively for traumatic hand and wrist injuries by the senior author at our institution. Data on patient demographics, treatment, and initial and final follow-up visit PROMIS scores were collected. Patients were followed for approximately three months after their initial consult.

Results: Among the 134 patients (45 operative, 89 non-operative), non-operative patients had significantly higher physical function scores than operative patients at the initial visit ($p=0.019$). However, there was no significant difference between the two groups at the final visit ($p=0.429$). Non-operative patients had significantly higher social function scores at the final visit compared to the initial visit ($p<0.001$) and significantly higher social function scores than operative patients at the final visit ($p=0.0074$). Additionally, non-operative patients had significantly lower sleep disturbance scores at the final visit compared to the initial visit ($p<0.001$) and had significantly lower sleep disturbance scores than operative patients at the final visit ($p=0.002$).

Conclusions: Although non-operative patients have greater physical function at initial follow-up visits, there is no significant difference in physical function between operative and nonoperative treatment at final follow-up. However, the higher social functioning and lower sleep disturbance scores in non-operative patients at the final visit suggest that non-operative patients have higher quality of life than operative patients for the duration of their treatment period.

Is it safe to import donation after cardiac death (DCD) organs for simultaneous pancreas and kidney transplant (SPK)?

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Introduction: Simultaneous pancreas and kidney (SPK) transplantation is among the best treatment options for diabetic patients with end stage renal disease. Donation after cardiac death (DCD) donors are becoming more common, and increasingly pancreatic grafts are being offered to non-local transplant centers; however, they are sometimes discarded due to anticipated longer cold ischemia times, fear of poor outcomes and other logistical factors. In this study we review our experience with importing and transplanting DCD SPK grafts.

Methods: 108 primary DCD SPK transplants were performed between 2000 and 2018. Recipient outcomes were included and analyzed based on the source of the graft: local donor service area (DSA) and import status. Primary outcomes were death censored-graft survival (DC-GS) and patient survival stratified by import status. Kaplan-Meyer analyses were performed; p-values <0.05 were considered statistically significant.

Results: Out of 108 recipients of SPK DCD grafts, 93 (86%) were locally procured and 15 (14%) were imported. Similar pancreatic DC-GS rates were noted at 5 years post-transplant (82% local vs 78% import, p=0.72) as well as patient survival (84% local vs 87% import, p=0.67). All patients became insulin independent immediately post-transplant.

Conclusions: DCD SPK donors are increasingly being used to expand the donor pool. Import criteria varies among transplant centers and depend on multiple factors. Importing DCD pancreata is safe; however, more detailed studies are needed to delineate screening criteria and to justify the economic cost.

DCD Pancreas Transplant	Total	Local	Import	p-value
Simultaneous Pancreas and Kidney	108 (100%)	93 (86%)	15 (14%)	
Death Censored Pancreas Graft Survival at 5 years (%)		82	78	0.72
Death Censored Kidney Graft Survival at 5 years (%)		89	77	0.40
Patient Survival at 5 years (%)		84	87	0.67

Successful simultaneous en-bloc kidney and pancreas transplantation (SEBKP) from donors <25kg

Riccardo Tamburrini, MD, PhD, Jon S. Odorico, MD

Introduction: Small pediatric donors are generally underutilized for simultaneous pancreas and kidney transplantation (SPK) due to the fear of inadequate islet mass and higher technical complications due to small vessels. Pediatric donors lower limit of age and weight are not well-defined criteria. In this study, we analyzed our experience with performing simultaneous en-bloc kidney and pancreas transplants (SEBKP) using very small pediatric donors.

Methods: Eight patients received a SEBKP transplant between 1997 and 2018; SEBKP transplant related outcomes were analyzed. En-bloc kidney transplants were all performed intraperitoneal and contralateral to the pancreas grafts; all pancreatic grafts were enterically drained with systemic venous drainage.

Results: Out of the 8 SEBKP recipients 5 were affected by Type I DM and 3 by Type II DM. The average recipient age was 46.6±12.8 years with average BMI of 25.2±3.8 kg/m^2. Seven grafts were from donation after brain death (DBD) and 1 from donation after cardiac death (DCD). Mean donor age was 5.0±1.7; donor weight was 19.8±4.8 and donor BMI was 15.8±3.7. All patients became insulin independent immediately; delayed kidney function was reported for one recipient, insulin resistance was also reported for one recipient; there were no graft thrombosis reported. Postoperative creatinine, glucose and c-peptide reflected good graft function. No graft loss was detected during the study period.

Conclusions: SEBKP transplantation is a safe technique and can be utilized to increase the donor pool. Organ allocation of <25 kg donors should incorporate algorithms for offering the organs for SPK transplantation.

Recipient N.	Length of Hospital Stay	Delayed Graft Function	Preoperative Creatinine	1 Month Postoperative Glucose	1 Month Postoperative C-Peptide	5 Years Postoperative Creatinine	5 Years Postoperative Glucose	5 Years Postoperative C-Peptide	Graft Thrombosis
1	12	-	6.0	91	NA	1	109	NA	No
2	10	-	7.1	89	NA	NA	NA	NA	No
3	32	Kidney	8.8	132	13.7	1.2	83	1.7	No
4	46	-	6.9	92	5.2	0.9	90	2.7	No
5	7	-	9-0	98	3.4	0.76	82	1.5	No
6	7	-	3.8	85	6.1	0.95	74	4.3	No
7	8	Pancreas	5.4	120	4.2	0.92	97	NA	No
8	5	-	11.9	90	4.7	1.56	111	7.71	No

Surgical management of adult acquired buried penis syndrome: A systematic review of patient-reported outcome instruments

Sarah M. Thornton, BA, Allison J. Seitz, MD, Armin Edalatpour, MD, Samuel O. Poore, MD, PhD

Introduction: Adult acquired buried penis (AABP) is a morbid condition with surgical intervention as a mainstay treatment. It is important to appropriately measure patients' symptoms pre- and postoperatively in order to understand how AABP affects the patients' quality of life, verify the efficacy of the surgical intervention, and practice patient-centered care. There is no universal, validated, standardized patient-reported outcome instrument specific to the evaluation of AABP. In this study, we aim to systematically examine the literature regarding patient-reported outcome instruments following surgical repair of AABP. In order to better understand the need for an AABP outcomes instrument, the goal of this systematic review was to establish which patient-reported outcomes are commonly reported, and which patient-reported outcome instruments are used.

Methods: A systematic review of three databases was conducted to investigate the use of patient-outcome instruments in AABP. We queried Medline, SCOPUS, and Web of Science databases for relevant keywords (e.g., buried penis repair") in accordance with PRISMA guidelines. Inclusion criteria were studies discussing surgical management of AABP with patient-reported outcomes. Pediatric and congenital cases were excluded. Information collected included study design, level of evidence, number of participants included in the study, etiology of buried penis, surgical technique, preoperative patient-reported outcomes, postoperative patient-reported outcomes, and patient-reported outcome instrument used.

Results: 998 records were identified on initial query. After abstract screening and inclusion and exclusion were applied, a total of 19 articles with 440 patients were included. Of the 19 included studies, 11 did not use a patient-reported outcome instrument and instead asked patients discrete, relevant questions about pre- and postoperative symptoms. 8 studies implemented patient-reported outcome instruments. The International Index of Erectile Dysfubnction-5 and Likert satisfaction scales were used most frequently, utilized in 4 and 3 studies, respectively. None of the employed instruments were specific to AABP surgical intervention, rather they were generic patient-reported outcome measures. While all instruments were validated, none were validated in the specific context of AABP surgical intervention.

Conclusions: Presently, there is a wide variety of surgical techniques utilized to treat AABP, and there is significant heterogeneity within the literature regarding patient symptomatology, postoperative complications, and patient-reported outcomes. The results of this study emphasize the need for a validated patient-reported outcome measure to examine how AABP repair influences patient satisfaction and health-related quality of life. This will promote patient-centered care and guide the surgical decision-making process.

Cleft spectrum perinatal airway management: A quantitative analysis

Johanna Ellefson, Samantha Barr, Maya Matabele, Manasa Venkatesh, Michael Puricelli, MD

Introduction: Cleft spectrum anomalies may increase the risk of airway obstruction at birth. Delivery at a more resourced facility or predelivery mobilization facilitates faster initiation of advanced treatment, but there is insufficient data examining the need in patients with cleft lip (CL), cleft palate (CP), or cleft lip and palate (CLP). This study aims to compare birth hospitalization data to inform delivery planning in individuals diagnosed prenatally with cleft spectrum anomalies.

Methods: Birth hospitalization data were extracted from the Healthcare Cost and Utilization Project (HCUP) Kids' Inpatient Database between 2000 and 2019. Individuals were segregated into unaffected, CL, CP, and CLP. Epidemiology, perinatal airway procedure performance, airway procedure performance according to gestational age, complications, and survival were examined. The Rao-Scott chi-square test was used for statistical comparison.

Results: The mean weighted incidence of cleft spectrum anomalies was 127 per 100,000 birth visits. Perinatal airway intervention was performed in 1.70% of unaffected individuals, 2.60% with CL, 5.16% with CLP, and 6.46% with CP. The most frequent intervention was intubation, while surgical airway was performed only in the group with CP. Compared to unaffected individuals, the odds of receiving cardiopulmonary resuscitation were 6-fold greater in CP and 3-fold greater in CLP. Among individuals receiving airway interventions, hypoxic complications or mortality were more frequent in patients with CP or CLP. Preterm delivery occurred more frequently among patients with cleft spectrum anomalies but did not account for the elevated rate of airway intervention. Survival occurred in 99.7% of unaffected, 98.44% with CL, 97.12% with CP, and 95.80% with CLP.

Conclusions: Individuals with cleft spectrum anomalies have an increased rate and complexity of perinatal airway intervention. Outcomes for individuals with CP and CLP are poorer than unaffected individuals. These benchmark data support delivery planning and informed decision making.

Declines in perioperative opioid prescribing to Wisconsin children, 2017-2022

Randi Cartmill, MS, Manasa Venkatesh, MS, Tudor Borza, MD, Christine Boxhorn, MD, Rebecca Busch, MD, Elise Lawson, MD, Sudha Pavuluri Quamme, MD, Jessica Schumacher, PhD

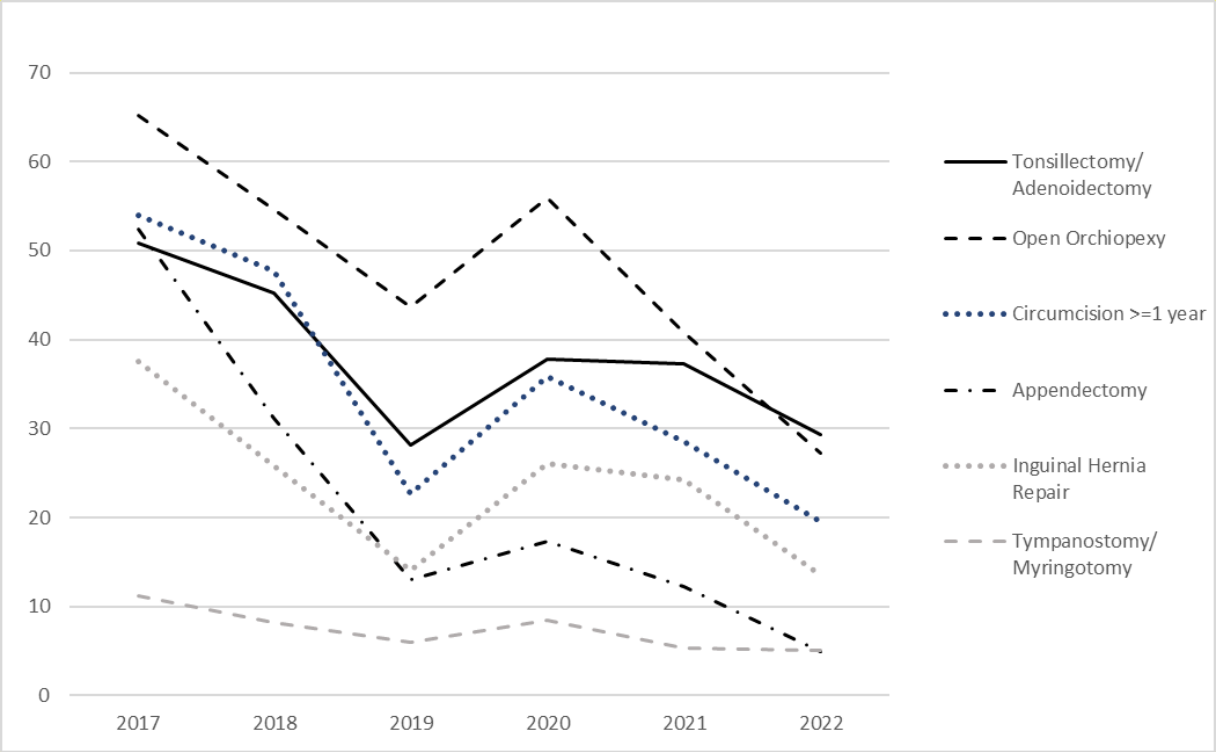
Introduction: Perioperative opioid pain medications are overprescribed to American children. National best practices encourage smaller prescriptions and non-opioid pain management techniques, and guidelines recommend zero opioids be prescribed to children undergoing appendectomy, inguinal hernia repair, open orchiopexy, circumcision and myringotomy. In this study, we examined trends in perioperative opioid fills for opioid-naïve children undergoing common outpatient surgical procedures in Wisconsin 2017-2022. We also examined perioperative codeine and tramadol fills to children under age 12, as the FDA released a “black box” warning in 2017 indicating that they are contraindicated.

Methods: We extracted data on perioperative opioid fills for children >12 from the Wisconsin Health Information Organization (WHIO) claims database, which includes ~75% of medical claims. We examined common outpatient procedures for which guidelines recommend zero postoperative opioids: laparoscopic appendectomy, circumcision, inguinal hernia repair, open orchiopexy, and tympanostomy/myringotomy. For comparison, we also examined fills for tonsillectomy/adenoidectomy, which has varying prescribing guidelines. Outpatient prescription fills were identified 3 days prior to 14 days after the surgical procedure. Patients were excluded if they filled an opioid prescription in the 30 days prior or underwent additional surgical procedures on the same day. We restricted our analysis of circumcisions to those at ≥1 year.

Results: The declines in perioperative opioid fills varied by procedure (Figure 1). The largest decline was for appendectomy (from 52% filling an opioid prescription in 2017 to 5% in 2022), with lesser but still significant declines for open orchiopexy (65% to 27%), circumcisions aged >1 (54% to 19%), and tonsillectomy/adenoidectomy (51% to 29%). Perioperative codeine and tramadol prescribing was relatively rare for children under age 12 and declined from 110 fills in 2017 (3.3% of all opioid fills) to 3 fills in 2022 (0.2%).

Conclusions: The rates at which Wisconsin children >12 filled a perioperative opioid prescription for minor surgeries declined substantially from 2017 to 2022. These declines are encouraging, but guidelines for many of the procedures recommend prescribing no postoperative opioids. Perioperative fills of the contraindicated medications codeine and tramadol were rare in 2017 for Wisconsin children >12 and almost zero by 2022. This is encouraging news for the safety of pediatric patients and suggests that surgical prescribers are heeding the FDA black box warning released in 2017. Further reducing opioid prescribing for these and other surgical procedures could substantially reduce the opioid exposure of young children in Wisconsin and decrease availability of excess opioids for misuse or diversion.

Figure 1: Percent of surgical patients under age 12 with perioperative opioid fills, by procedure



Risk factors for acute intraoperative bradycardia in patients undergoing gender mastectomy

Sarah M. Thornton, BA, Ellen C. Shaffrey, MD, Caroline C. Bay, BA, Joshua Verhagen, BS, Peter J. Wirth, MD, Armin Edalatpour, MD, Jacqueline S. Israel, MD, Katherine M. Gast, MD, Venkat K. Rao, MD, MBA

Purpose: The incidence of gender-affirming surgery continues to increase with a majority of patients undergoing top surgery. Within this population, the development of cardiac arrhythmias has been reported in the literature; however, the etiology of these arrhythmias has yet to be elucidated. At our institution, there has been a noticeable occurrence of acute intraoperative bradycardia in patients undergoing gender-affirming mastectomies that can require anesthetic intervention or halting of surgery. The aim of this study was to describe the frequency of acute intraoperative bradycardia in patients undergoing gender-affirming mastectomies and identify potential risk factors that could be contributing to its occurrence.

Methods: A retrospective review was performed for all patients who underwent gender-affirming mastectomy by two surgeons at a single institution. Demographic, comorbidity, and intraoperative data were collected. History of hormone or antidepressant therapy was also recorded. Intraoperative data included anesthetic interventions such as induction agents, if regional blocks were performed, and administration of atropine or glycopyrrolate. Surgical interventions were collected, including type of top surgery and if liposuction was performed. Patients were then further separated into those who did and did not develop acute intraoperative bradycardia. The definition of intraoperative bradycardia was any patient who experienced an acute change in heart rate that dropped below 60 beats per minute. Logistic regression was performed to determine which variables were predictive of intraoperative bradycardia.

Results: Three hundred and thirty-seven patients underwent gender-affirming mastectomy between January 2018 and January 2023. Of these patients, 144 (42.7%) experienced acute intraoperative bradycardia, with 97 (67.4%) requiring anesthetic intervention and 5 (3.5%) requiring halting of surgery. Two patients (1.4%) underwent compressions due to progression to asystole. Fluoxetine, a selective serotonin reuptake inhibitor (SSRI) (OR: 2.63, p= 0.011), and harvest of a nipple graft (OR: 2.77, p= 0.018) were associated with a significantly increased risk of developing acute intraoperative bradycardia. The use of an SSRI was significantly associated with the development of hypotension during the episode of bradycardia (OR: 3.33, p= 0.015).

Conclusions: Acute intraoperative bradycardia may be a unique phenomenon in patients undergoing gender-affirming mastectomies due to variables specific to this patient population. A future study comparing patients undergoing gender-affirming top surgery to those undergoing elective breast surgeries is forthcoming to assess further contributing risk factors.

Access to HRA and colorectal surgery support identified as important facilitators to a successful Veterans Affairs anal cancer screening program

Austin Hewitt, MD, Linda Cherney Stafford, MPH, Esra Alagoz, PhD, Cristina B. Sanger, MD

Introduction: Anal cancer disproportionately affects people living with HIV (PLWH). The Department of Veterans Affairs (VA) is the largest single provider of healthcare to PLWH in the United States and recommends all veterans living with HIV be screened for anal cancer annually. There are barriers to developing successful anal cancer screening programs and screenings within VA have been underutilized. A recently completed randomized controlled trial demonstrated treatment of high-grade anal neoplasia compared to monitoring led to a reduction of anal cancer in PLWH. These findings highlight the need to identify neoplastic lesions, which can be accomplished through screening. We hypothesized that there are healthcare provider perceived facilitators that can increase the uptake of VA anal cancer screening programs.

Methods: VA providers who care for veterans living with HIV were invited to participate in 30-minute, semi-structured virtual interviews. Study participants included infectious disease providers and colorectal surgeons. Providers were asked to discuss factors that influence anal cancer screenings. Three researchers collaboratively reviewed interview transcripts and used thematic analysis to identify patterns in the data. Using the Theoretical Domains Framework (TDF), an established implementation science framework, the main themes in our data were mapped to TDF domains and characterized as facilitators to adopting anal cancer screening programs in VA.

Results: A total of 23 providers (21 infectious disease providers, 2 colorectal surgeons) were interviewed with representation from all major U.S. geographical regions and 11 of 18 VA regional care systems. The facilitators (themes) to successful screening programs that emerged from participant interview data were mapped to 15 unique behavior-influencing constructs and categorized into six TDF domains: (1) Environmental Context and Resources, (2) Professional Role and Identity, (3) Goals, (4) Knowledge, (5) Skills, and (6) Social Influences. Facilitators identified by providers included access to high resolution anoscopy (HRA) and colorectal surgery support. Being or having an advocate with programmatic goals supported by buy-in from institutional leadership and collaborating clinics were also identified as helpful facilitators.

Conclusions: Our study demonstrates facilitators identified by providers significant to successful anal cancer screening programs within VA. Identified facilitators map to six TDF domains including environment/resources, professional roles, goals, knowledge, skills, and social factors. Access to HRA and colorectal surgeons are identified as integral components of a successful program. The results of this study provide a framework for improving anal cancer screenings using evidenced-based interventions incorporating the facilitators identified and highlights the importance of colorectal surgeons to VA.

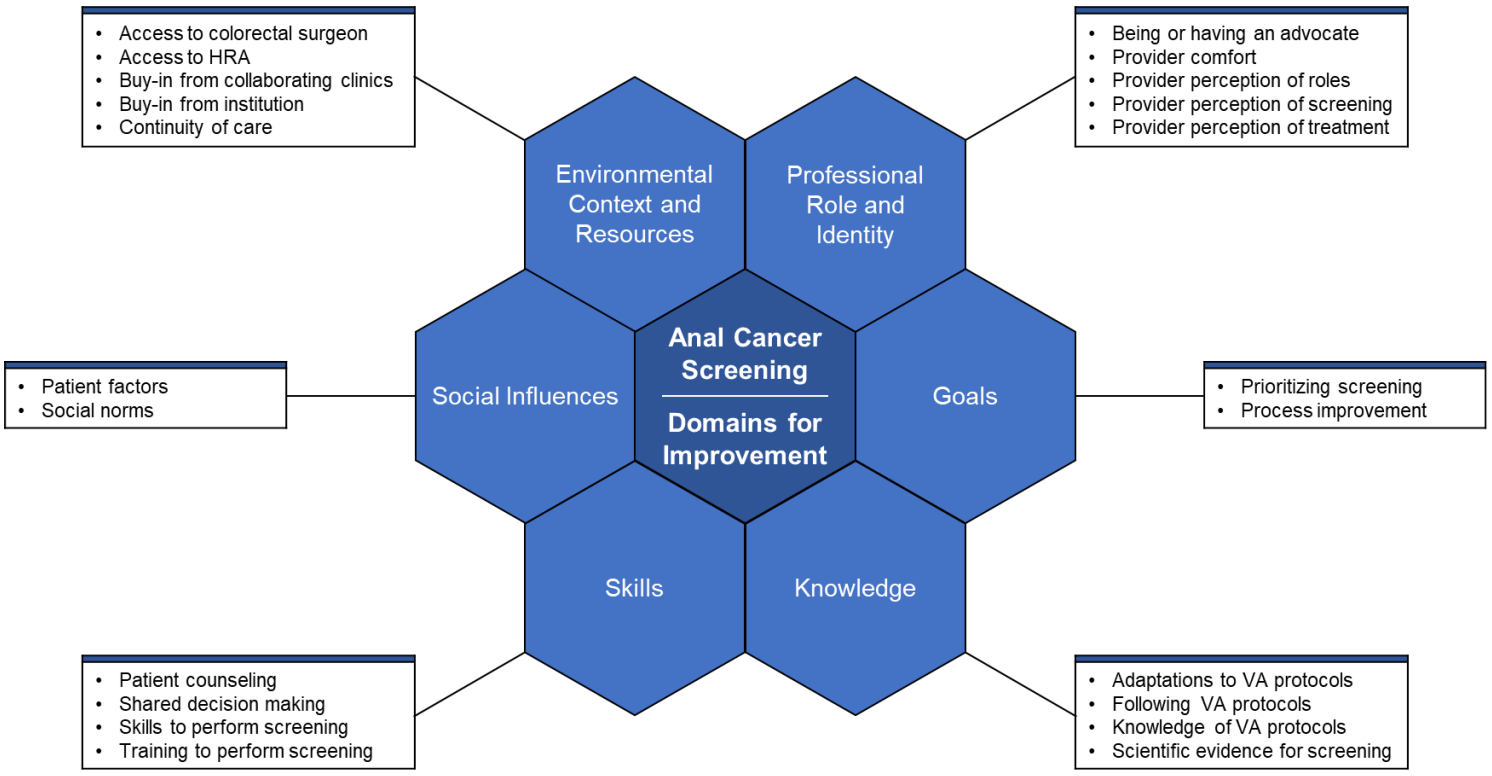


Figure 1. Facilitators (themes) for a successful anal cancer screening program mapped to validated domains of an established implementation science framework (Theoretical Domains Framework)

A quasi-experimental comparison of engagement and outcomes from a weight management trial delivered in-person versus virtually

Hisham Ahmad, Stephanie M. Carpenter, Armaan Shetty, Scott Hetzel, Katya Garza, Laura Porter, Kristen Gray, Ryan Shaw, Megan Lewis, Lu Mao, Heather Johnson, William S. Yancy Jr., Felix Elwert, Corrine I. Voils

Introduction: Excess body weight, defined by a body mass index of at least 27 kg/m^2, affects over 70% of US adults and poses significant health risks and economic burdens. While efficacious behavioral weight-loss programs exist, sustaining engagement remains a challenge. The COVID-19 pandemic prompted behavioral weight management interventions to shift from operating predominantly in-person to virtual videoconferencing. However, engagement remains a challenge, as people tend to abandon the use of virtual interventions over time. Virtual modalities may also not replicate in-person intervention experiences in terms of investment and connection with others.

Method: The current study presents a quasi-experimental comparison of engagement patterns and weight change in a weight-management program delivered to two cohorts who participated in-person (N=97) prior to the onset of COVID-19 versus three cohorts who participated virtually (N=134) due to COVID-19 restrictions. The program involved group sessions led by a dietitian every two weeks for 6 months, followed by three group sessions and nine individual phone calls decreasing in frequency for another 12 months. The last 6 months involved no contact from the interventionist. Primary and secondary outcomes were assessed at baseline and 6, 12, 18, and 24 months. Outcomes analyzed herein include attendance at group sessions, individual counseling calls, and retention for outcome assessments; self-reported daily caloric intake; daily steps assessed by accelerometer; and weight change.

Results: Cohorts who received virtual intervention post-COVID-19 had similar demographic composition (predominately white and female) compared to pre-COVID-19 cohorts who attended sessions in-person. Results indicate greater attendance at videoconference classes in the post COVID-19 cohorts (median [IQR]: 13 [10, 15]) who received the intervention virtually, compared to the in-person cohorts (11 [5, 14]; $p<0.001$). All other outcomes were comparable ($ps>0.05$), regardless of whether the intervention was delivered in-person or virtually.

Conclusions: While outcomes were similar regardless of delivery mode, engagement decreased over time in all participants. Understanding how best to measure and promote engagement in weight management interventions is crucial and warrants careful consideration in future research.

Assessment of patient and provider factors associated with pharmacogenomic testing: A partnered evaluation of the Veterans Affairs National Pharmacogenomics Program

Abigail Silva, PhD, Deepak Voora, MD, R. Ryanne Wu, MD, MHS, Catherine Chanfreau, PhD, Brian Bartle, MS, Nina Sperber, PhD, Allison Hung, MPH, Corrine Voils, PhD

Introduction: The VA National Pharmacogenomics Program provides pre-emptive, multi-gene, multi-drug pharmacogenomic (PGx) testing at VA medical centers (VAMCs). The objective is to identify patient- and provider-level factors associated with PGx ordering.

Methods: A retrospective matched study design was used. Cases (test ordered) and controls (no order) were matched 1:1: on encounter visit date (+/- 15 days), VAMC, and clinic type. Logistic regression was employed to determine patient sociodemographic attributes, clinical factors, and provider characteristics associated with receiving a PGx order. We queried data for all Veterans who had a clinical encounter between November 1, 2020 and July 21, 2022.

Results: A total of 19,626 cases and controls were identified across 23 VAMCs. Mean age was 59 and most patients were male (82.3%), White (76.8%) and married (54.3%). Patient characteristics positively associated with having a PGx order were female, Black race, younger age, receipt of pre-appointment PGx educational mailing, documented allergy to PGx-targeted medications, higher number of active prescriptions for PGx-targeted medications, and specialty care visits in year prior (all p-values <0.0001). Urban residence and inpatient stay within 1 year were negatively associated with having an order (p<0.001). Compared to being seen by a physician, patients seen by pharmacists were more likely to receive PGx while those seen by a nurse practitioner/physician assistant were less likely (p<.0001). Patients seen by providers who were older or with higher patient caseloads were less likely to receive an order (p<.0001).

Conclusions: Patients with prescriptions or prior negative reactions to PGx-targeted medications and those interacting with pharmacists are more likely to receive PGX testing. Despite the availability of pre-emptive PGx testing, providers may find more value with targeted testing. Pharmacists may be uniquely positioned to deliver PGx within the VA.

Increasing participation of Black and African Americans in weight management research: A qualitative study

Chloe Mayfield, Shubhangi Sneha, Jennifer M. Gierisch, Corrine I. Voils

Introduction: Log2Lose is a weight management behavioral clinical trial at the University of Wisconsin-Madison and Duke University. We conducted interviews with Black and African American study participants and community members to identify strategies to improve the representation of Black and African American people in weight management studies. The primary goal of the qualitative interviews is to identify strategies to recruit more Black and African Americans and to make the content more culturally appropriate and inclusive.

Methods: Qualitative interviews were conducted by a team member who identifies as Black and African American of 1) Community members from Madison, WI who are involved with the Black and African American community through organizations or work 2) Log2Lose trial participants who identified as Black or African American and had completed the trial. Interview guides were informed by the Cumulative Model of Patient Complexity by Shippee and colleagues. This model focuses intervention engagement through the lens of patient workload and patient capacity. Questions addressed community barriers may face regarding weight management. Other questions related to making the intervention more appealing to others in the community by assessing goals, values, and interests. Data were content-analyzed by three team members. Codes were informed by the Shippee model and emergent. Queries were generated for each code, from which thematic statements were created.

Results: Community members (n=11), study participants (n=20). Participants indicated that Black and African Americans desire evidence-based programs to assist them with weight management. Some individuals desired to manage weight primarily through exercise, whereas others desired to focus on changing eating habits. Participants highlighted the importance of programs offering accountability to an expert, social support from other participants, and long-term maintenance of healthy behaviors. Participants suggested paying participants for their time and making weight management programs enjoyable through music selection and community-building activities. Recommendations for enhancing recruitment of Black and African Americans included participating in community events and increasing racial representation on the study team. Participants also highlighted the need to be sensitive to historical exploitation of the Black and African American community by medical researchers.

Conclusion: Black and African Americans in Madison see weight management as a priority and desire to participate in evidence-based programs. Increasing representation of Black and African Americans will help increase trust and bring ideas to make programs more enjoyable.

An electronic health record-based data commons for pancreatic cancer

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Introduction: Pancreatic cancer (PC) is the second leading cause of cancer deaths in the United States. Clinical research in PC has been limited due to a lack of granularity of data in locoregional and national datasets. Linked electronic health record (EHR) data containing demographic, socioeconomic, clinicopathologic, laboratory, molecular, radiomic and genomic data have the potential to tremendously impact research for PC. Our aim was to create a novel EHR-based data commons for patients with PC.

Methods: The index cohort were adult patients at our institution who presented between January 1st 2010 and December 31st 2022 with a primary diagnosis of PC using International Classification of Disease for Oncology diagnosis codes C25.0-25.9. The PC Data Commons (PCDC) includes six linked data sources: (1) institutional EHR data retrieved from our Clinical Data Warehouse; (2) cancer-specific data from the North American Association of Central Cancer Registries (NAACCR); (3) surgical outcomes data from the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) for patients who had a pancreatectomy; (4) population census and community level data; (5) national mortality data, and (6) Area Deprivation Index (ADI). Data-use agreements were executed with the privacy-preserving record linkage software, Datavant®. The institutional honest broker served as the escrow for linkage to provide patient-level data with deidentified relational keys. The dataset was stored on an internal HIPAA-secure and National Institute of Standards and Technology (NIST) security compliant server.

Results: The PCDC contains data on 3236 patients from our institutional EHR, of which have 2799 have been linked to NAACCR, and 434 surgical patients to ACS-NSQIP along with socioeconomic data. Mean age at presentation was 72.8 (23-106) years, 1748 (54.0%) were male, 2953 (92.0%) were white race, and had median ADI of 51 (36-65). About half (1652, 51.1%) of patients are currently alive. From the linked cohort, the median follow-up time is 11.8 (3.7-28.3) months and with a median overall survival from diagnosis to be 16.7 months.

Conclusions: The PCDC is a centralized resource that solves the disconnect in PC research. The ability to securely link, store and analyze protected patient data is a strategic step towards enhancing clinical research and optimizing care for patients with PC. Our future work includes: (1) mapping our data extraction and linkage process to the Observational Medical Outcomes Partnership Common Data Model; and (2) obtaining data from several other high volume academic centers for multi-center integration into a data-commons specific to PC.

Early pancreas cancer death despite pancreaticoduodenectomy: Investigating the futile Whipple

Clayton T. Marcinak, Kaleem S. Ahmed, Patrick R. Varley, Kaitlyn J. Kelly, Rebecca M. Minter, Sharon M. Weber, Sam J. Lubner, Jeremy D. Kratz, Noelle K. LoConte, S. Nabeel Zafar

Introduction: Pancreaticoduodenectomy (PD), the only surgical option for right-sided pancreatic ductal adenocarcinoma (PDAC), carries significant morbidity and may not result in a survival advantage for certain patients when compared to non-surgical treatment options. We sought to identify the rate of futile Whipple surgery and its associated factors in a large national cohort.

Methods: We performed a retrospective analysis using the 2020 National Cancer Database (NCDB) participant user file, including all patients who underwent a PD or total pancreatectomy for non-metastatic PDAC between 2004 and 2020. Surgery was defined as futile if the patient died within 12 months of diagnosis. Patients with less than 12 months of follow-up and those who underwent resection past 12 months of diagnosis were excluded. Multivariable logistic regression was used to identify demographic, oncologic, and treatment factors associated with higher odds of futility.

Results: A total of 66,326 patients were analyzed, of whom 16,772 (25.3%) underwent a pancreatectomy that met criteria for futility. A higher percentage of patients in the futile group did not receive any systemic therapy compared to those in the non-futile group (42.4% vs. 16.9%, $p < 0.0001$). On multivariable regression, macroscopically positive margins (odds ratio [OR], 2.86; 95% confidence interval [CI], 2.36 – 3.47; $p < 0.0001$), poor tumor differentiation (OR, 2.44; 95% CI 2.25 – 2.6; $p < 0.0001$), and N2 nodal stage (OR, 2.09; 95% CI 1.98 – 2.20; $p < 0.0001$) were associated with greatest relative odds of futility. Meanwhile, receipt of any systemic therapy (OR 0.33; 95% CI 0.31 – 0.34; $p < 0.0001$), receipt of any radiation (OR 0.60; 95% CI 0.57 – 0.63; $p < 0.0001$), and receipt of neoadjuvant systemic therapy (OR 0.62; 95% CI 0.57 – 0.66; $p < 0.0001$) were associated with the lowest relative odds of futility.

Conclusions: In this national dataset, PD was futile in about one quarter of patients. Similar analyses on more granular datasets holds promise to more accurately identify patients who may not benefit from a complex operation. These findings have important implications for shared decision-making and optimizing care for patients with PDAC.

Machine learning driven prediction modeling to identify patients at risk for post discharge venous thromboembolism after pancreatectomy for pancreas cancer

Kaleem S. Ahmed, MBBS, MSAI, Sheriff M. Issaka, Clayton Marcinak, MD, Majid Afshar, MD, MSCR, Matthew M. Churpek, MD, MPH, PhD, Syed Nabeel Zafar, MD, MPH

Introduction: Post-discharge venous thromboembolism (pdVTE) remains a life-threatening complication following resection for pancreatic cancer (PC). 1/3rd of VTE events are diagnosed in the post-discharge setting after resection and are an independent predictor of diminished response to therapy and decreased survival. National guidelines from the National Comprehensive Cancer Network (NCCN), American College of Chest Physicians (ACCP) and the American Society of Clinical Oncology (ASCO) recommend extended chemoprophylaxis for up to 28 days for high-risk patients following abdominal or pelvic resection for malignancy. However, extended chemoprophylaxis prescription rates range from as low as 1.5% to 44%. Predicting and screening for a patient's pdVTE risk would enable tailored extended chemoprophylaxis regimens based upon individual risk, thus avoiding the cost and risks of overtreatment

Methods: We analyzed data from patients undergoing pancreatectomy for PC using the American College of Surgeons' National Surgical Quality Improvement Program database between 2014 and 2021. We trained predictive models using 80% of the dataset and 230 input variables including demographics, clinical, laboratory, cancer and operation specific variables. A "K-Nearest Neighbors" model was used to impute missing values. Classical machine learning models included Logistic Regression (LR), Multi-Layer Perceptron (MLP), Decision Tree (DT), Random Forest (RF) and Gradient Boosting (GB) Classifiers. We also introduced Anomaly Detection Models including Isolation Forests (IF) and Elliptical Envelope (EE), which have only recently been utilized in healthcare research. All models were finetuned using a grid-search and 2-fold cross-validation. To measure the performance of these models on a 20% hold-out dataset, we utilized area-under-the-curve (AUC) scores, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). We compared the AUC scores of the models using the f1-statistic.

Results: A total of 53,757 patients were analyzed. The mean age was 63.7 ± 12.8 years, 50.3% were male, and 38.0% underwent Whipple procedures. A total of 1775 (3.3%) developed a pdVTE. Multi-tree-based models such as GB and RF outperformed the other models with AUC scores of 0.777 and 0.775 respectively (Figure 1). The top predictive factors identified were length of stay, operative time, post-operative organ space infection, post-operative pneumonia, and pre-operative levels of serum Platelets, INR and Bilirubin.

Conclusions: Machine learning models can reliably screen and identify patients undergoing pancreatectomy for PC who are at high risk for pdVTE. Such models can be used to inform prescription of extended VTE prophylaxis at the time of discharge.

Survival among South Asian Americans with colon cancer: A cross-sectional analysis of a national dataset

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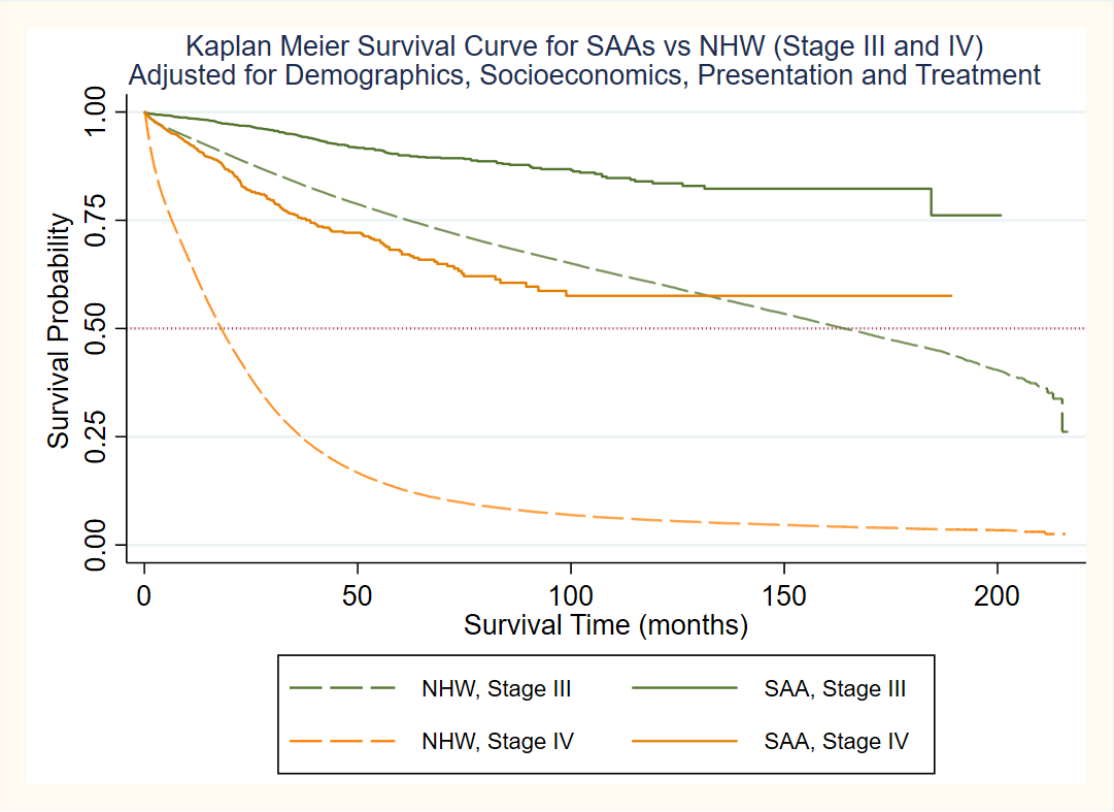
Introduction: Colon cancer (CC) is the fourth most common malignancy diagnosed in the United States (US), with an estimated incidence of over 150,000 in 2023. It is the second leading cause of cancer-related deaths, with a 5-year survival rate of 63%. CC disproportionately impacts vulnerable populations who face significant barriers to colon cancer screening and disparities in treatment. Examination of disparities among racial and ethnic minority groups has revealed differences in stage at presentation, treatment access, and survival amongst Asian Americans (AA). In addition, AAs have lower rates of screening for CC compared to other American racial groups (46.9% vs 72.4%). However, existing studies often fail to adequately capture the diversity within these groups such as South Asian Americans (SAA), who represent the fastest-growing immigrant subgroup in the US. The objective of this study was to measure differences in risk-adjusted survival amongst SAAs with CC compared to non-Hispanic whites (NHW) using a representative national dataset from the United States.

Methods: A retrospective analysis of all adult patients with CC in the National Cancer Database (2004-2020) was performed. Differences in presentation, management, median overall survival (OS), 3-year survival (3YS) and 5-year survival (5YS) between SAAs and NHWs were compared. Kaplan-Meier analysis and multivariable Cox regression were used to assess differences in survival outcomes, adjusting for demographics, presentation, and treatments received.

Results: Data from 2,873 SAA and 639,488 NHW patients with CC were analyzed. SAAs were younger at diagnosis (62.2 vs 69.5 years, $p<0.001$), higher stage (stage III [29.0% vs 26.2%, $p=0.001$] or Stage IV [21.4% vs 20.0%, $p=0.001$]), and experienced delays to first treatment (SAA 5.9% vs 4.9%, $p=0.003$). SAAs with CC had higher OS (median not achieved vs 68.1 months for NHWs), 3YS (76.3% vs 63.4%) and 5YS (69.1% vs 52.9%). On multivariable Cox regression, SAAs with CC had a lower risk of death across all stages (HR: 0.64, $p<0.001$).

Conclusions: In this national study, SAA patients with CC presented at younger ages, with more advanced disease, and may experience delays in treatment as compared to NHW patients. Despite these differences, SAAs had better adjusted OS than NHW, warranting further exploration of tumor biology and socioeconomic determinants of cancer outcomes in SAAs.

Figure: Adjusted Kaplan-Meier Curve Showing Survival for Stage III and IV Colon Cancer



Education
Research Abstracts

A call for contributions: The need for improved retirement benefits and financial education for plastic surgery residents

Zeeda H. Nkana, BS, Kirsten A. Gunderson, MD, Ahmed M. Afifi, MD

Introduction: Contributions to retirement savings throughout Plastic Surgery residency is fundamental to achieving financial independence. Residency is often an ideal period for individuals to leverage post-tax (Roth) contribution plans and employer contributions; however, most institutions do not consider residents “long-term” employees, resulting in ineligibility for various retirement benefits. Therefore, residents are limited in their ability to enact optimal financial advice. Further, literature demonstrates a lack of financial literacy and wellness amongst Plastic Surgery residents, highlighting a need for formal financial education. This study aims to evaluate the current state of retirement benefits and financial literacy education offered across Integrated Plastic Surgery Residency Programs in the United States.

Methods: The websites of all accredited Integrated Plastic Surgery Residency Programs were reviewed by two authors to determine: 1. Provision of information regarding retirement benefits, 2. Availability of retirement account options, 3. Availability of post-tax retirement contributions, 4. Provision of employer contributions, 5. Availability of financial advising, and 6. Provision of a formal resident financial literacy education curriculum.

Results: Eighty-eight program websites were analyzed. A mere 41 (46.6%) contained any level of information regarding retirement benefits offered. Of these programs, 68.3% offered 403b plans, 22.0% offered 401k plans, 34.1% offered 457 plans, 12.2% offered 401a plans, and 2.4% offered IRA plans. Only 61.0% of programs offered post-tax contribution plans, and fifteen (35.6%) programs offered employer contribution. Five (12.2%) programs advertised financial advising services, and only one program advertised a formal financial literacy program.

Conclusions: There is a considerable lack of transparency of retirement benefits across Integrated Plastic Surgery Residency Programs and a paucity of intentional financial education for residents. Given employment for six clinical years, Plastic Surgery residents should be considered long-term employees with broadened retirement benefit eligibility, including post-tax and employer contribution options, to promote overall financial wellness.

Navigating the plastic surgery in-service exam: Content patterns and accessibility

Sarah M. Thornton, BA, Armin Edalatpour, MD, Sarah M. Lyon, MD, Jessica D. Blum, MD, Jeffrey D. Larson, MD, Daniel Y. Cho, MD, PhD

Introduction: The plastic and reconstructive surgery (PRS) in-service examination is an annual, written exam designed to evaluate a resident's knowledge across all PRS topics. Success on this examination is correlated with success on the American Board of Plastic Surgery Written Exam. With busy schedules and limited time for studying, it is difficult for PRS residents to know what to prioritize when studying for the in-service examination. This study aims to investigate which PRS topics are most heavily represented on the PRS in-service examination, which references are most commonly cited, and how accessible these references are.

Methods: Plastic surgery in-service examination questions and answers from 2012-2022 were accessed through the American Council of Academic Plastic Surgeons website. Data extracted for each question included category, number of associated references, year of publication for each reference, journal for each reference, and whether the reference was accessible via PubMed.

Results: Data analysis revealed 2441 total references and 1161 unique references. The 5 most common plastic surgery references were Plastic and Reconstructive Surgery (80.9%), Journal of Hand Surgery (15.8%), Annals of Plastic Surgery (7.6%), Aesthetic Surgery Journal (6.1%) and Plastic Surgery (5.6%). The 5 most common non-plastic surgery references were New England Journal of Medicine (1.8%), World Journal of Surgery (1.8%), Journal of Bone and Joint Surgery (1.6%), Journal of the American Academy of Dermatology (1.5%), and Journal of the American Academy of Orthopedic Surgery (1.5%). Of the 49 categories of questions, the 5 most frequently represented were local anesthetics (4.7%), breast reconstruction (4.7%), hand, fingertip amputation, dupuytren's, vascular (4.5%), cosmetic liposuction/abdominoplasty (4.4%), and chest wall/abdominal wall (4.0%). 84.9% of references were available through PubMed.

Conclusions: The annual PRS in-service examination tests residents' knowledge of their field. This study demonstrated that some PRS topics are represented more heavily than others, just as some references are cited more than others. Question writers should be encouraged to reference resources that are free and accessible to residents.

The current state of microsurgical training models: A framework for the field of plastic surgery

Taylor Penn, Sahand Eftekari, D'Andrea Donnelly, Ellen Shaffrey, MD, Sarah Jung, PhD, Aaron Dingle, PhD

Objective: Microsurgery is utilized in various medical specialties, including plastic surgery. Due to the steep learning curve present to acquire microsurgical skills, the opportunity for training outside of the operating room has become increasingly important. While the gold standard for simulation is the live animal model, their implementation has numerous downsides, including high cost and ethical considerations. These barriers have driven innovation for new methods to establish and maintain foundational microsurgical skills, resulting in many physical and virtual models. This study aims to analyze existing non-living physical and virtual microsurgery simulation models to inform microsurgical curriculum development.

Methods: PubMed and Google Scholar searches were performed. All relevant articles available in the English language since January 2017 underwent an abstract review. Papers that discussed current, unique, non-living microsurgical education, training, or simulation models were included.

Results: After the initial literature search and article review, forty-two studies were included for full-text analysis. Microsurgical simulation models can be divided into the following two domains: physical and virtual. The physical domain comprises non-living, non-animal, non-living, animal, and non-living, human models, ranging from the use of synthetic vessels to chicken thighs or human placenta. Virtual models use any form of technology to facilitate the learning process and are either non-immersive or immersive (e.g., virtual reality headset).

Conclusions: Microsurgical simulation is crucial for trainees to build proficiency before the operating room. Although live animals remain the gold standard, many physical and virtual models have been described to offer benefits for a trainee. While there still exists room for advancement of these models in realism, accessibility, and cost, microsurgical education should involve a wide array of physical and virtual models to provide broad-based experience in various settings.

Bucatini pasta, Japanese shirataki konjac noodles, and artificial vessels: In search of the ideal low-cost vessel simulator for microsurgical education

Jessieka T. Knazze, BA, Sarah M. Thornton, BA, Stephan L. Blanz, BS, D'Andrea T. Donnelly, BS, Anna K. Jesch, Weifeng Zeng, MD, Aaron M. Dingle, PhD, Samuel O. Poore, MD, PhD

Introduction: Microsurgical education is expensive and complex, requiring significant exposure and practice with training materials. Several models, including silicone vessels, chicken thighs, and live rat models, have been used for simulation training. However, these materials are costly, difficult to acquire or assemble, and require substantial animal care costs, particularly in resource-limited countries. The Japanese shirataki konjac noodle is an inexpensive and readily available alternative for microsurgical education and outreach. For example, a 228 g bag of konjac noodles costs approximately $2 and enables trainees to perform around 100 anastomoses. Bucatini pasta is another economical alternative with the potential for microsurgery outreach, although remains unexplored. This study assesses low-cost, readily available materials for microsurgical education and outreach locally and globally. We hypothesize that both konjac and bucatini noodles can hold sutures and pass a patency check, making them feasible and cost-effective materials for microsurgical education and outreach.

Methods: This study utilized bucatini pasta boiled for either 9 or 11 minutes, precooked konjac noodles, and a silicone vessel. Using a digital caliper under the microscope, the diameter, lumen, and wall thickness of each noodle/vessel were measured. Microsurgery scissors were used to cut the noodles and vessel into two parts. For the konjac noodle, an 18-gauge needle was passed longitudinally through the center to create a lumen. Next, a complete end-to-end anastomosis was attempted on each material using an 8-0 nylon suture. An IV line/bag containing blue dye was attached to the noodle/vessel to assess patency. We compared both types of noodles to one another and a standard silicone vessel.

Results: The lumen of the bucatini pasta became smaller after cooking, while the diameter became larger. Bucatini pasta strands were unable to hold a suture. Therefore, a complete anastomosis was not completed on the bucatini, and patency was not assessed. The precooked konjac noodle was able to hold the 8-0 nylon suture, and a complete end-to-end anastomosis was performed. The repaired konjac noodle was patent. Similarly, the silicone vessel held a suture and was patent (Table 1).

Conclusions: The need for affordable and accessible materials in microsurgical education is evident, especially on a global scale. The Japanese shirataki konjac noodle is an excellent option for microsurgery outreach, with the added advantage of being less expensive than silicone vessels. Future research will involve further validation by multiple evaluators with varying microsurgery experience to further establish the utility of these materials.

Table 1. Assessing Potential Teaching Materials for Microsurgery Education & Outreach - Quantitative and Qualitative Measures

Noodle Type	Time Cooked (Minutes)	Diameter (mm)	Lumen (mm)	Wall Thickness (mm)	Hold a Suture (Y/N)	Patency (Y/N)
Bucatini	0	3.0	1.0	1.0	No	n/a
Bucatini	11	5.0	0.72	2.14	No	n/a
Bucatini	9	3.92	0.88	1.52	No	n/a
Konjac	Precooked	3.24	1.23	2.0	Yes	Yes
Silicone Vessel	N/A	3.0	2.27	0.24	Yes	Yes

Double mirror array stereomicroscope for resident and global microsurgical training: A proof-of-concept microscope

Sahand C. Eftekari, BS, Ellen C. Shaffrey, MD, Weifeng Zeng, MD, Katherine D. Reuter Munoz, MD, Aaron Dingle, PhD, Samuel O. Poore, MD, PhD

Introduction: Microsurgery is an intricate and specialized field within plastic surgery that has significant constraints due to the high resources needed for training and operation. One significant constraint is the unavailability of surgical microscopes within healthcare systems both in the United States and on the global scale. This leaves trainees with a lack of access to surgical microscopes to practice and develop their microsurgery competence. Despite prior investigations attempting to overcome this scarcity of microscopes using iPhones and Virtual Reality Systems, there remains a gap in having high fidelity microscopes for training purposes. This investigation presents a novel prototype that utilizes low-cost materials to produce a high fidelity, highly adaptable, and travel friendly surgical microscope for microsurgery training.

Methods: Binocular objective lenses were modified for near field viewing and coupled with a double mirror array to produce a stereoscopic microscope that does not require prisms or calibration. This system was housed within a low-profile 3D printed chassis to produce the correct orientation for a top-down view of a microsurgical field. A microscope light source was built into the chassis that may be powered either with standard 120-240V outlets or battery powered in case of resource limited environments.

Results: The initial proof of concept and working prototype produce a fixed magnification of either 6.5X that enables trainees to complete end-to-end anastomoses on a 2mm vessel. This investigation remains ongoing to compare the utility of this microscope against a state-of-the art surgical microscope.

Conclusions: Microsurgical education and practice are often hampered by the high cost and inaccessibility of surgical microscopes. Our novel stereomicroscope aims to alleviate these barriers and promote better accessibility to residents and trainees on a global scale. By providing a low cost, portable solution that does not compromise the quality of the stereoscopic image, this innovation has the potential to transform the field of microsurgical education and practice.

Livestreaming microsurgery education: An avenue to expand global plastic surgery

Sahand C. Eftekari, BS, Weifeng Zeng, MD, Ellen C. Shaffrey, MD, Katherine D. Reuter Munoz, MD, D'Andrea T. Donnelly, BA, Aaron M. Dingle, PhD, Samuel O. Poore, MD, PhD

Introduction: Microsurgery is a highly technical and resource-intensive subspecialty within the field of plastic surgery that is often not accessible in many hospital systems. This lack of accessibility is particularly prevalent in foreign nations which do not have access to expert microsurgical training. Surgeons and trainees around the world often have access to microscopes but lack the microsurgical guidance to complete the complex maneuvers associated with operations such as free flaps and peripheral nerve repairs. Here, we propose a highly accessible and low-cost method to livestream microsurgical education over popular online platforms in order to lift the current barriers associated with microsurgical education.

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

Results: Six microsurgical livestreams were completed at the University of Wisconsin-Madison over Zoom and Instagram platforms. These events were shared one day prior on Facebook and Instagram. A total of 96 surgeons and trainees tuned into the livestreams representing 28 countries worldwide.

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

“Unmatched. What’s next? Is a preliminary year of residency or research fellowship better for reapplicants to plastic surgery?”

Robert E. George, MD, Caroline C. Bay, BA, Sarah M. Thornton, BA, Tammy Zhong, BS, Lauren P. Feeley, Aaron M. Dingle, PhD, Samuel O. Poore, MD, PhD

Introduction: Matching into a plastic and reconstructive surgery residency remains a challenging task. The number of applicants has steadily increased in the last several years, outpacing the creation of new residency positions. Moreover, the match rate has continued to decline since 2018, with a match rate of ~55% in 2022. As a result, many people are left with the difficult decision of what the best course of action is after not matching. For applicants who wish to reapply, two common options include pursuing a preliminary year of residency (PY) or a research fellowship (RF). This study investigated which option is more likely to lead to a successful match for reapplicants.

Methods: This retrospective study included all applicants to an integrated plastic surgery residency from 2015-2023. Two cohorts based on reapplication strategy (RF or PY) were created. Demographic data and applicant variables including AOA status, induction into the Gold Humanism Honor Society, number of first author publications, non-first author publications, poster presentations, oral presentations, Step scores, and number of application attempts were included. Match year and specialty data were collected. Pearson’s Chi-squared or Fisher’s exact testing was performed for categorical data. Wilcoxon rank sum testing was conducted for continuous data. An α of 0.05 was selected for statistical significance.

Results: 125 reapplicants were included. 71 (57%) and 29 (23%) pursued a PY or RF, respectively. Compared to PY reapplicants, RF reapplicants had a greater mean number of first author publications (8.8 vs 3.2, $p<0.001$), non-first author publications (11.0 vs 6.0, $p=0.021$), poster presentations (9.7 vs 6.0, $p=0.028$), and oral presentations (12 vs 6, $p<0.001$). RF reapplicants were more likely to match into plastic surgery than PY reapplicants, with 21 (72%) RF reapplicants matching into plastic surgery vs 28 (39%) PY reapplicants ($p=0.003$). When comparing only RF and PY reapplicants who matched into any specialty, RF reapplicants were again more likely to match into plastic surgery compared to PY reapplicants (84% vs 54%, $p=0.010$).

Conclusions: This study found that RF reapplicants are more likely to successfully match into a plastic surgery residency compared to PY reapplicants. There were no confounding demographic variables. RF reapplicants demonstrated greater metrics of research productivity with no other statistically significant differences with respect to applicant data between cohorts. The rate of RF reapplicants matching into a plastic surgery residency was almost double the rate of PY applicants.

Table 1. Match Data

Characteristic	Preliminary year of residency, N = 71[1]	Research Fellowship, N = 29[1]	p-value[2]
Matched Into PRS	28 (39%)	21 (72%)	0.003
Matched (Any Specialty)	52 (73%)	25 (86%)	0.2
PRS Match (Of Those Who Matched)	28 (54%)	21 (84%)	0.010
Match Year			>0.9
2019	4 (7.7%)	2 (8.0%)	
2020	2 (3.8%)	1 (4.0%)	
2021	15 (29%)	8 (32%)	
2022	16 (31%)	7 (28%)	
2023	15 (29%)	7 (28%)	

[1] n (%)

[2] Pearson's Chi-squared test; Fisher's exact test

Surgery Science Images

Brain in a Dish- 3D Brain Organoid

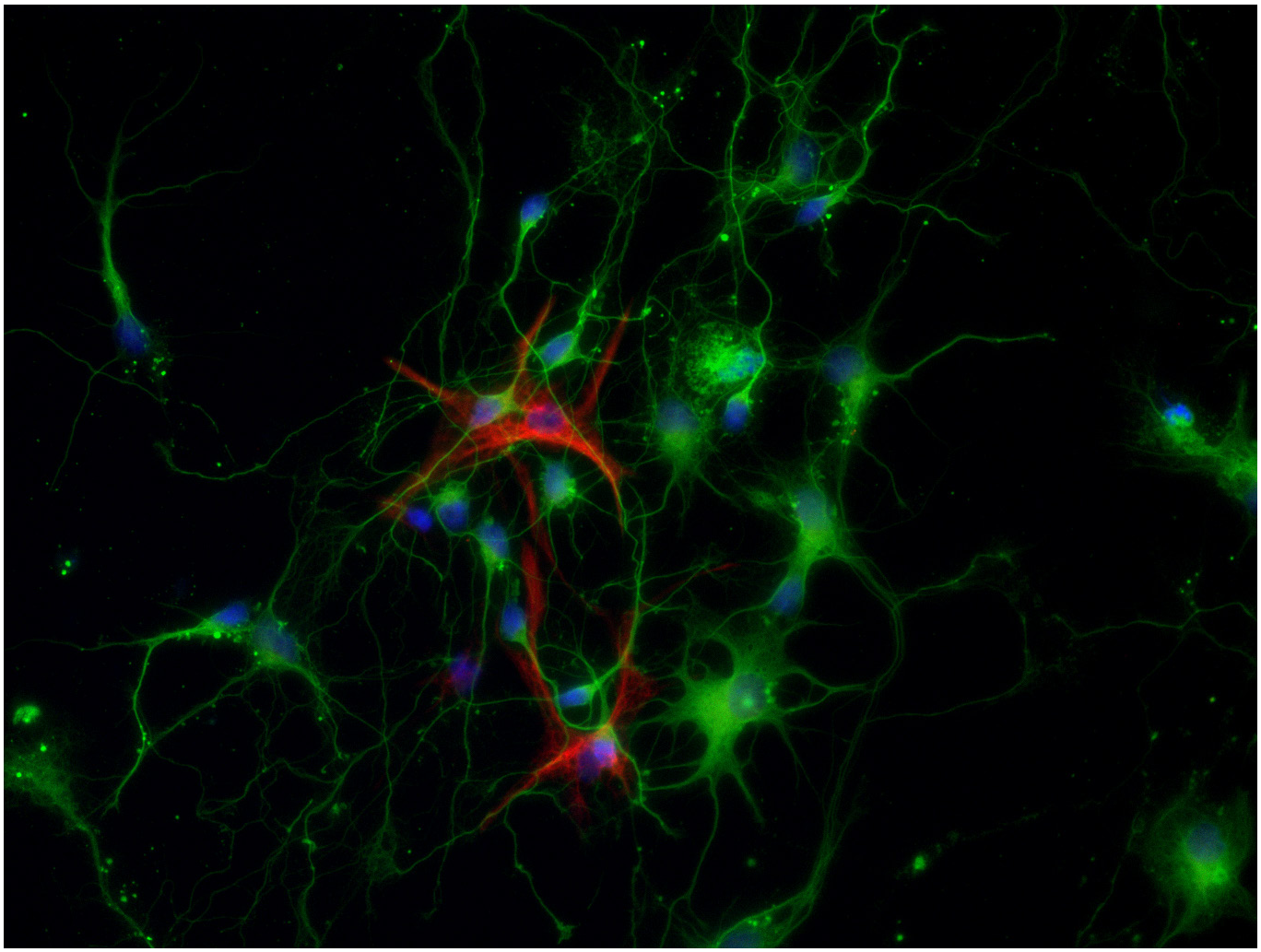
Ligi Milesh, *Research Specialist*
Le Lab, Division of Pediatric Surgery

What does the image depict?
The art depicts 'Brain in a Dish - 3D Brain Organoid' portrayed in artistic way.

How was the image taken?
The art was hand drawn and colored. The organoid image is the real image converted into artistic way. The vibrant colors shown in the organoid represent different types of cells arranged themselves as a tissue and combined together to form an organoid in a dish.

What is an interesting fact about the object or phenomenon?
The credit for providing the idea of generating the 3D organoid should be given to my PI (Dr. Hau D. Le). Our lab basically works for generating precise cancer treatment strategies using novel cold atmospheric plasma (CAP). At present, cancer therapies are currently limited to surgery, radiation, and chemotherapy. All three methods risk damage to normal tissues or incomplete eradication of the cancer. Our research technique allows normal cells to be unharmed and thus allowing cell's natural microenvironment to be maintained. 3D organoid will mimic the natural brain microenvironment and would help our treatment strategies using CAP. This will also help the researchers to reduce the usage of animals for the research in future.

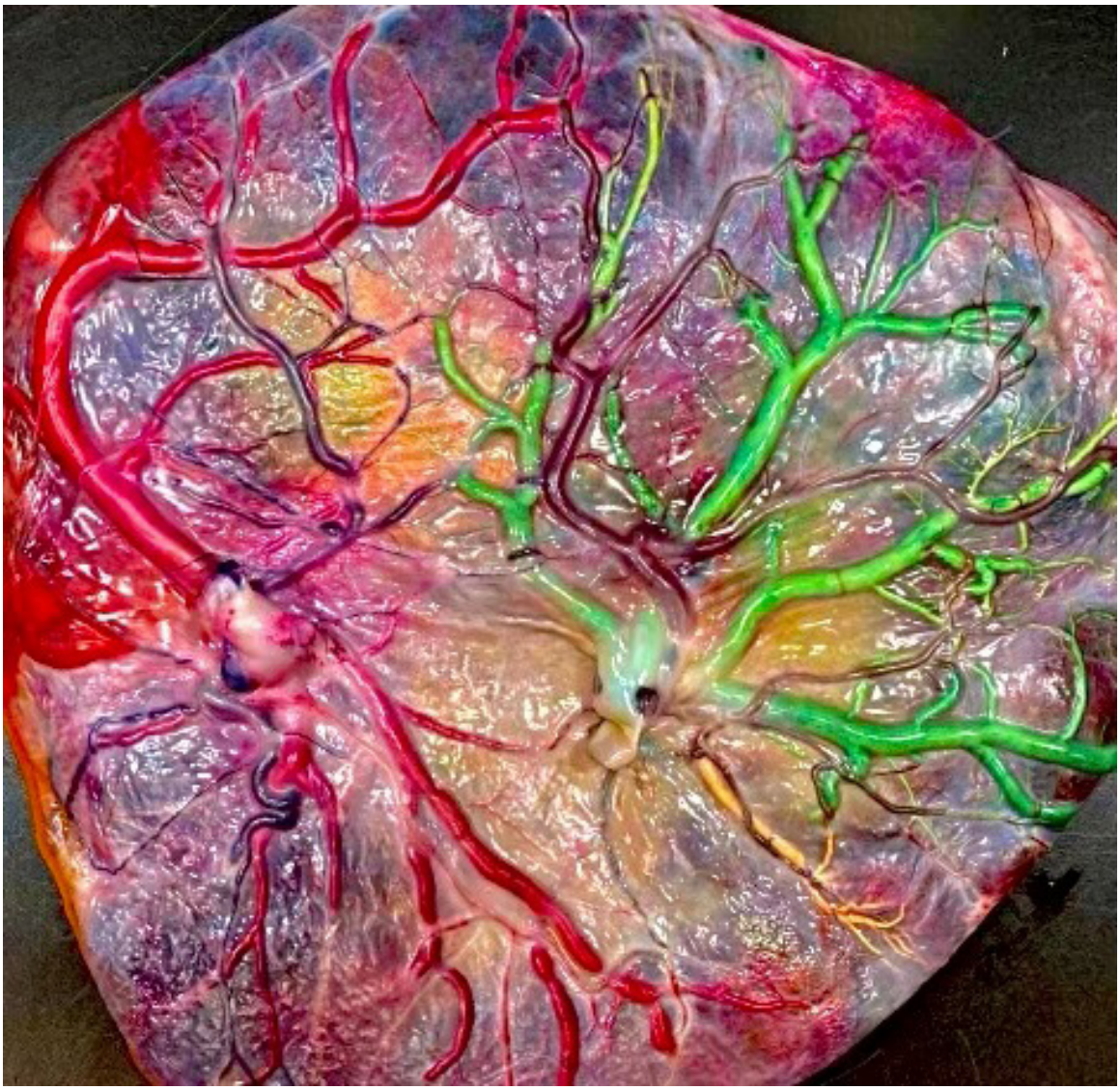
How is this object, phenomenon, and/or method of image-making important to your research or discipline?
The art shows the team efforts in generating 'Brain in a dish (3D Organoid)'. The main backbone of the research has always been Dr. Le. The main reason to showcase this art was to make an awareness that research can be made fun and easy yet can be very practical. This model will be the turning point to various treatment strategies available at present. The methods involves the expertize of invitro techniques mimicking the invivo environment thus closely relatable to human beings which will further help us to design our treatment possibilities using CAP for treating various types of cancers without killing the normal cells.



Unlocking the Mysteries of Parkinson Disease: Astrocyte-Neuron Crosstalk in Focus

Sarah Lechner, *Researcher*
Kelm-Nelson Lab, Division of Otolaryngology-Head and Neck Surgery

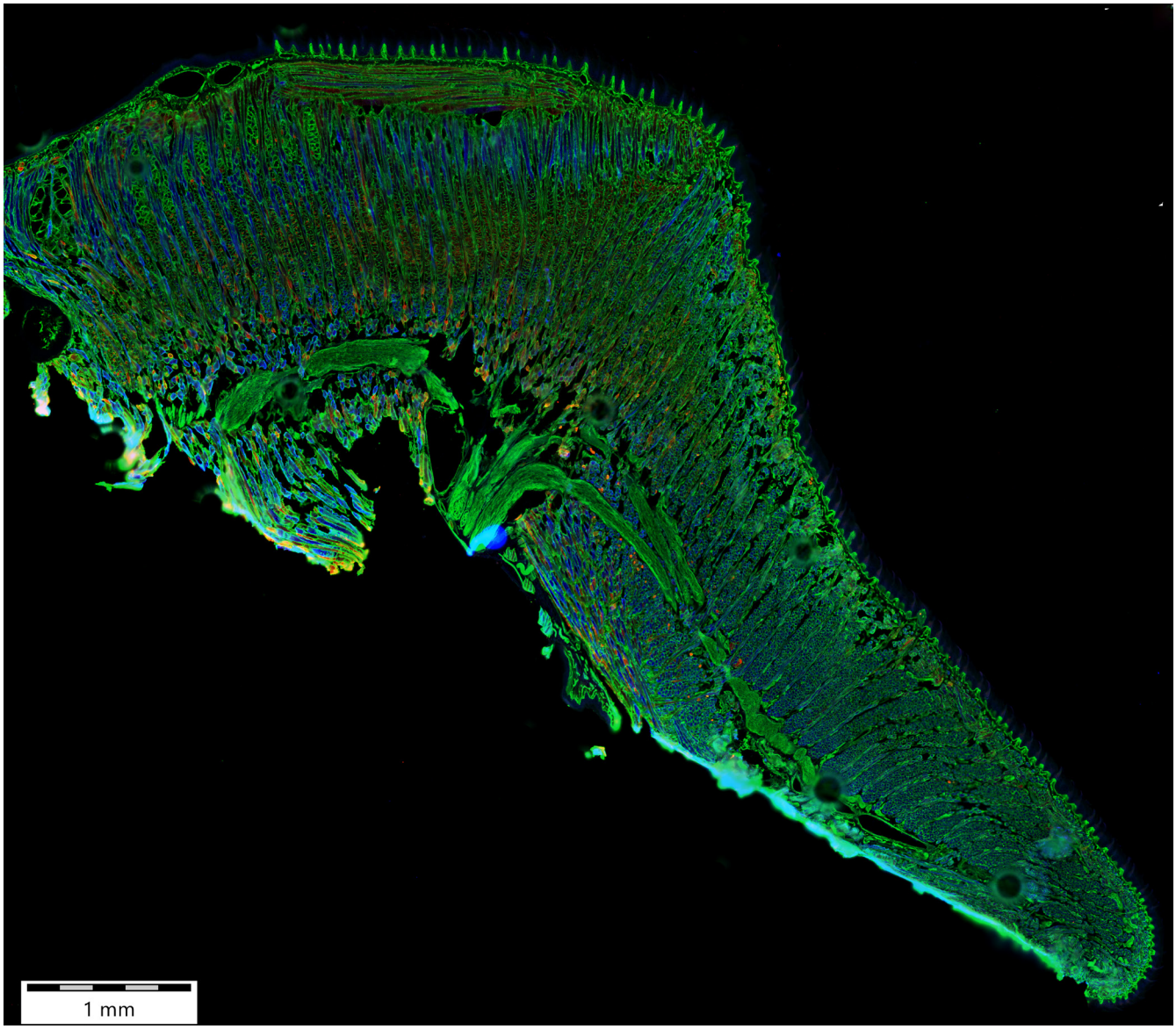
This immunofluorescence microscopy image of a brainstem cell culture, taken at 20X, is used to examine early changes associated with early-onset Parkinson disease (PD). The intricate crosstalk between neurons (labeled in green using β-III tubulin) and astrocytes (labeled in red using GFAP) is essential for maintaining and supporting CNS homeostasis. Astrocyte-neuron metabolic signaling is disrupted in PD and other neurodegenerative disorders leading to an increase in neuroinflammation. Analyzing brainstem cell cultures derived from a genetic rat model of PD allows us to explore disruptions in astrocyte-neuron interactions as well as investigate the specific effects of novel drug treatments on these cell cultures.



The Bond Before Birth

Inna Lobeck, *Pediatric and Fetal Surgeon*, Division of Pediatric Surgery
Michael Beninati, Maternal Fetal Medicine and Fetal Surgery
Jessica Gulliver, Pathology

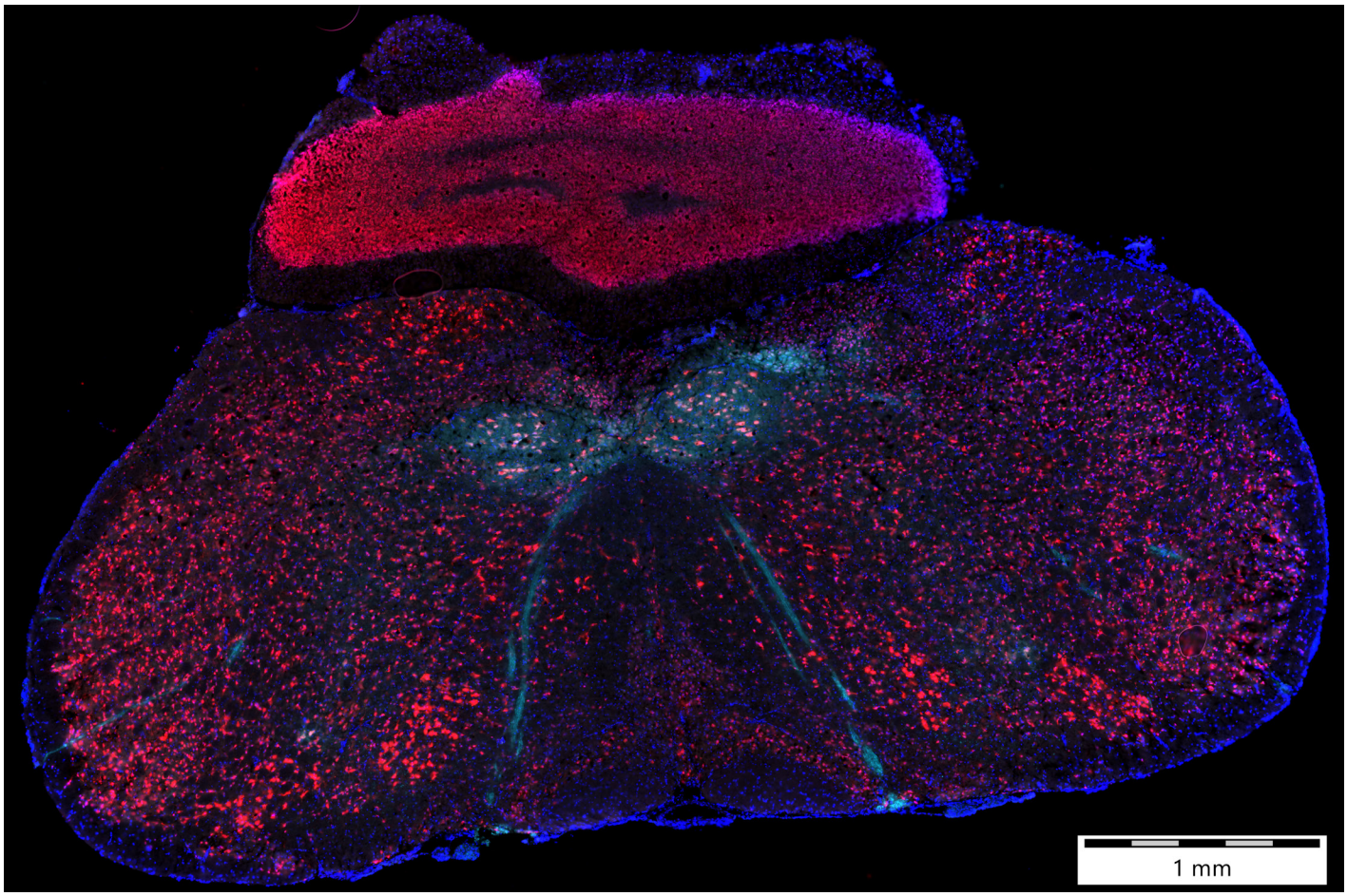
Twins who share a placenta also share blood vessels. Most of the time, these connections are harmless. However, in 10-15%, blood is directed away from one twin and towards another. Without fetal surgery, the mortality is 100%. This photograph of a placenta demonstrates the blood flow of both twins, dyed with red (vein) and blue (artery) in the donor connecting to green (vein) and yellow (artery) in the recipient. Multiple laser burns can be seen, closing these connections and allowing for delivery of two healthy babies. Through postnatal injection of these vessels, we are able to perform a 'quality check' of our fetal intervention to ensure all connecting vessels were closed, and better understand the pathology that was underlying the fetal illness. In this case, the twins not only shared a placenta but also a sac. This is only the seventh case ever reported of successful laser in monoamniotic-monochorionic twins.



Intrinsic Tongue of Ts65Dn Down Syndrome Mouse

Kayla Hang, *Research Specialist*
Jayde Sitko, *Undergraduate Researcher*
Connor Lab, Division of Otolaryngology-Head and Neck Surgery

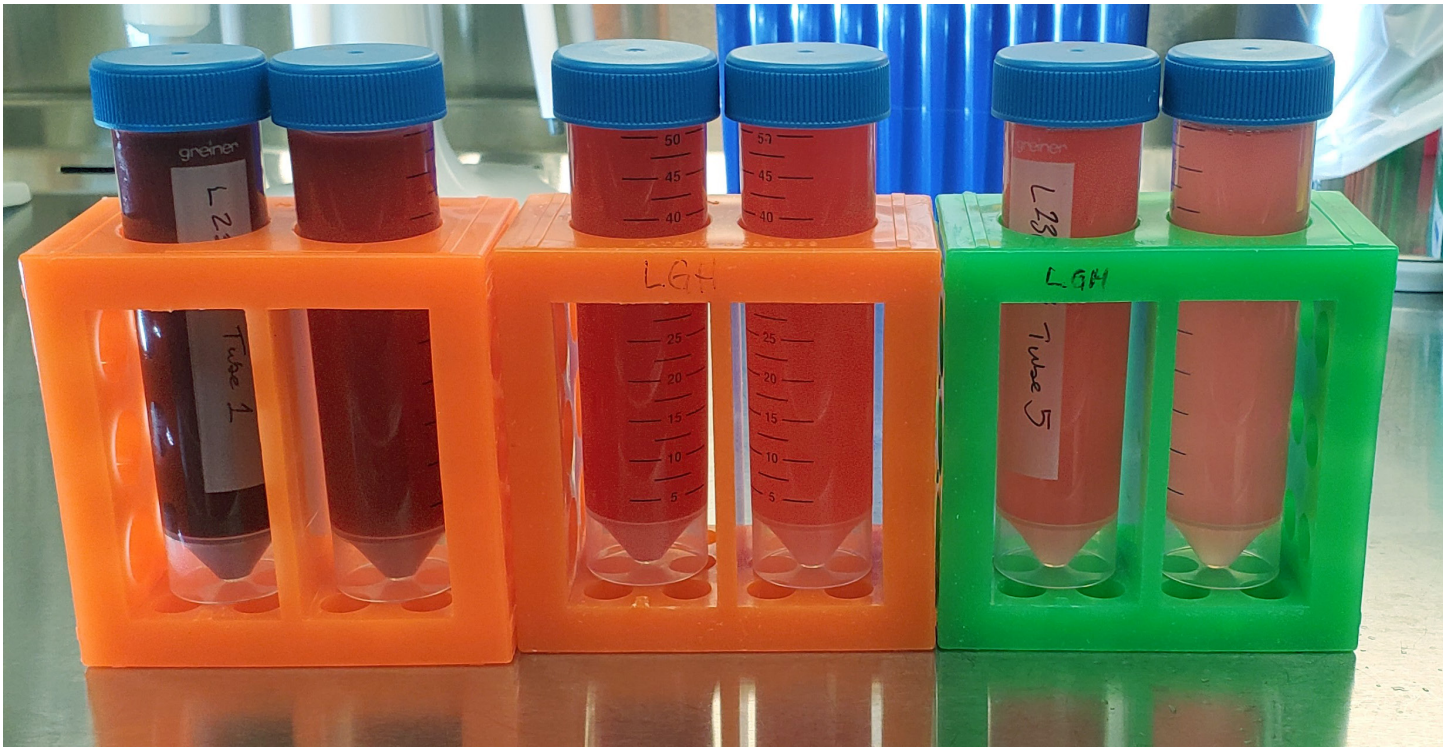
This image shows the intrinsic tongue muscles of a 22-day old Ts65Dn mouse model of Down syndrome. Taken with an Olympus epifluorescence microscope, this image shows fast tongue myofibers in blue (MyHC 2b), and relatively slower myofibers in red (MyHC 2a). The image is from a project using quantitative analysis to study postnatal development of transverse muscle fibers within the tongue. This research allows for a better understanding of how tongue muscles mature in this mouse model, which can ultimately assist our understanding of developmental differences of tongue function in Down syndrome.



The Mouse Hypoglossal Nucleus

Lucille Vue, *Research Specialist*
Connor Lab, Division of Otolaryngology-Head & Neck Surgery

Cell bodies of motor neurons innervating the tongue muscles are located in the brainstem, in the hypoglossal nucleus. This image shows the hypoglossal nucleus comprised of neurons forming the cyan butterfly shaped area in the center of the brainstem. This photograph of an immunofluorescence stain of a mouse brainstem tissue section was taken with an Olympus Bx53 epifluorescence microscope. Neuronal cell bodies throughout the tissue section are labeled with NeuN-Cy3 (red); cell nuclei are stained with Dapi (blue) and cholinergic neurons are stained with an antibody to Choline Acetyltransferase (ChAT)-AF633 (cyan). This image is part of a larger project to study the hypoglossal nucleus in mouse models of Down syndrome. The objective is to gain a better biological understanding of how Down syndrome impacts swallowing and tongue movement.

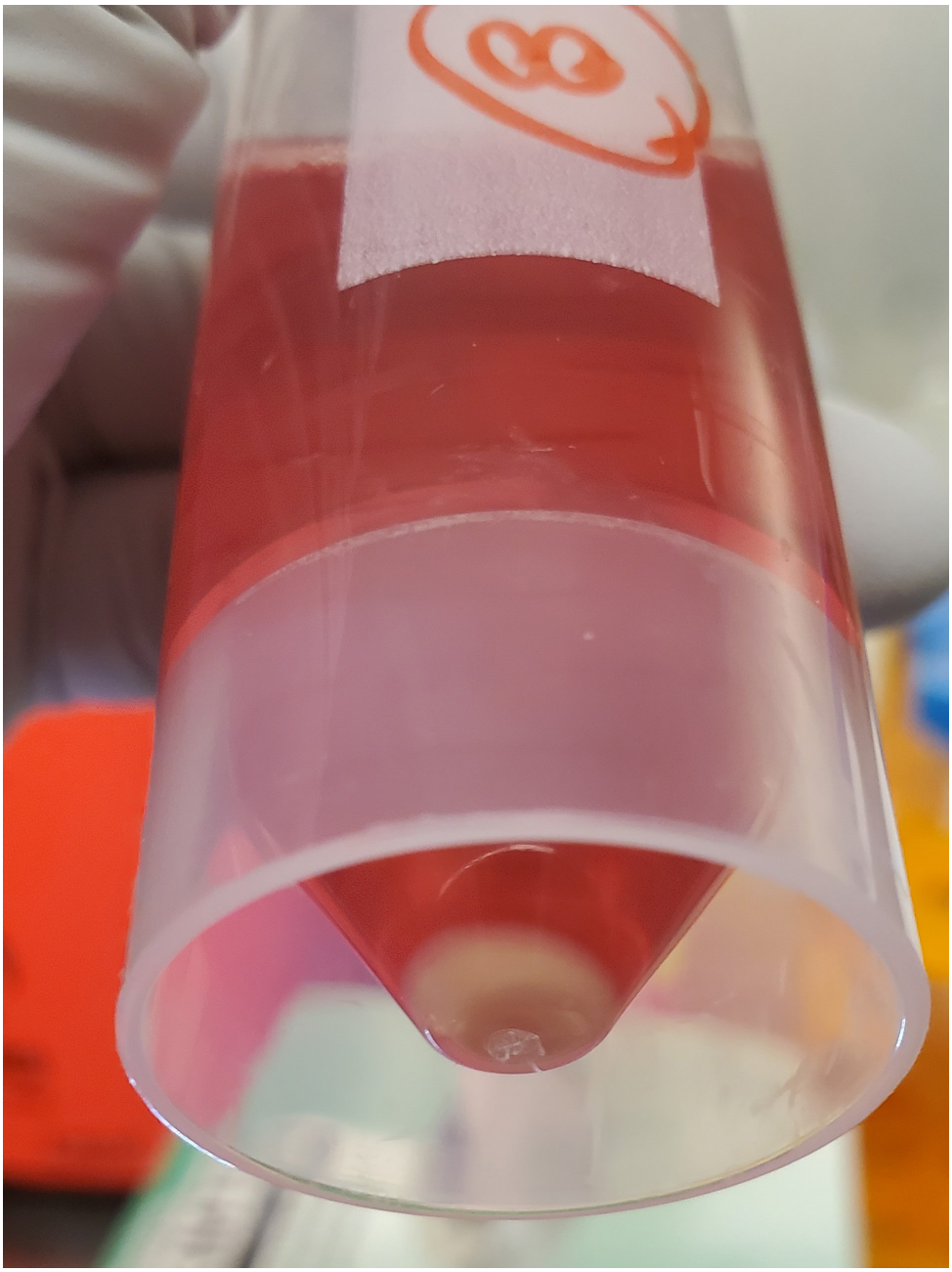


Bye-Bye RBCs, Hello WBCs!

Megan A. O'Neill, MSc, *Associate Researcher/Lab Manager*
Hidalgo Lab, Division of Transplantation

This image beautifully captures the colour gradient, from dark to light, that I see when I collect cells from human blood that has been put through a special filter after someone donated blood to the American Red Cross. Normally, these special filters are simply thrown away as biomedical waste. But our lab studies immune cells (WBCs, White Blood Cells), and these special filters are just FULL OF THEM! We get filters from the Red Cross, and then I wash out all of the precious immune cells! The more liquid I push through the filter, the more and more the filter gets flushed, and we can see less and less Red Blood Cells (RBCs) in each tube. Here's the secret – all of the tubes are chock full of WBCs, even though there are less RBCs! I like that we turn biomedical waste into something useful for our research on transplant rejection.

Image Capture Method & Credit(s): This image was taken using a Samsung Galaxy S10 phone, camera model SM-G973U, on May 24, 2023. The photographer is Megan O'Neill who is an Associate Researcher & Lab Manager in Dr Luis Hidalgo's lab in the Division of Transplantation.



Target Cells Acquired!

Megan A. O'Neill, MSc, *Associate Researcher/Lab Manager*
Hidalgo Lab, Division of Transplantation

This picture shows all of the White Blood Cells (WBCs) at the bottom of my tube. Notice the liquid above it sort of looks a bit like red Kool-Aid? This is because I added a special chemical to the blood that targets the Red Blood Cells (RBCs) and makes them explode! The colour of the liquid is from all the teeny, tiny pieces of the RBCs after they have exploded (science term is "lysed", but exploded sounds much cooler!). All of the precious WBCs that I need to use for my experiments are not harmed AT ALL by the special chemical, so that is why I am able to collect them at the bottom of the tube. We get the blood from filters that are normally thrown away as biomedical waste, and I like that we get to turn that into something useful for our research on transplant rejection.

Image Capture Method & Credit(s): This image was taken using a Samsung Galaxy S10 phone, camera model SM-G973U, on June 7, 2023. The photographer is Megan O'Neill who is an Associate Researcher & Lab Manager in Dr Luis Hidalgo's lab in the Division of Transplantation.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