10th annual

researchsummit

UNIVERSITY OF WISCONSIN • DEPARTMENT OF SURGERY

Pathways to Impact

Wednesday, January 16, 2019

Abstract Book

Welcome

Welcome to the 10th Annual University of Wisconsin Department of Surgery Research Summit.

Our theme this year is **Pathways to Impact**. Researchers take a wide array of roads—or pathways—to arrive at our research questions, to pursue the investigations that grow out of them, and finally, to implement the changes resulting from our work. The Research Summit is an opportunity to showcase the innovative questions, unique trajectories, and transformative effects of our Department's research efforts.

We are honored by the presence of two keynote speakers, both of whom embody the theme of Pathways to Impact. **Debra Houry, MD, MPH**, is Director of the National Center for Injury Prevention and Control at the Centers for Disease Control and Prevention in Atlanta, Georgia. Dr. Houry is currently leading the CDC's response to the opiate epidemic, and we look forward to her talk focused on helping us, as surgeons, to confront this public health epidemic. **Fred Lee Jr., MD, MPH**, is Professor of Radiology and Biomedical Engineering, The Robert A. Turrel Professor of Imaging Science, the past Chief of Abdominal Imaging, Oncologic Imaging, and past Senior Vice Chair at the University of Wisconsin Department of Radiology. While a Radiologic Society of North America Scholar, Dr. Lee developed an interest in minimally invasive tumor ablation therapy, leading him to establish the Tumor Ablation Laboratory at the University of Wisconsin in 1995, one of the first of its type in the world.

Five awards will be given in honor of individuals whose iconic contributions have made possible our research enterprise.

- The **Layton F. Rikkers, MD, Best Oral Presentation Award** is named in honor of one of our previous Department Chairs, who established the academic rigor and strength of our Department.
- The **K. Craig Kent, MD, Best Basic Science Poster Award** honors another previous Chairman, who led our department to its current national standing as a top-ranked, externally funded Department of Surgery.
- The **Charles N. Ford, MD, Best Translational-Clinical Poster Award** is named after our previous Otolaryngology Division Chairman, who built a world-class voice and laryngology enterprise within our Department.
- The **Debra A. Hullett, PhD, Best Basic Science Poster Award – Student** honors a beloved colleague who made important contributions as a leader and mentor to many in our Department.
- The **Louis C. Bernhardt, MD, Best Translational-Clinical Poster Award – Student** honors a man whose long-standing mentorship to our medical students and residents is legendary.
- A separate award will be given to the **top research-related image in our "Behind the Lens: Surgery Science Image Contest."**

Thank you for making space in your busy schedules to attend the 2019 Research Summit. We hope that today's program will increase your awareness of the innovative research activities that take place every day in the Department of Surgery.

Welcome to the Summit.

Robert R. Redfield III, MD and **Angela Ingraham, MD, MS**
Program Co-Chairs

Acknowledgements

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

Katie Dorst
Nicole Jennings
Sarah Pavao
Mary Marshall
Lisa Werning
Karen Williams

We would also like to recognize the **abstract reviewers** who generously donated their time to review the 128 abstracts that were submitted.

David Al-Adra, MD
John Fechner, MS
Luis Fernandez, MD
Luke Funk, MD, MPH
Angela Gibson, MD, PhD
Caprice Greenberg, MD, MPH
Bret Hanlon, PhD
Cynthia Kelm-Nelson, PhD
Elise Lawson, MD, MSHS
Glen Leverson, PhD
Anne Lidor, MD, MPH
Brett Michelotti, MD
Heather Neuman, MD, MS
Samuel Poore, MD, PhD
Sean Ronnekleiv-Kelly, MD
Sara Sackett, PhD
Jessica Schumacher, PhD, MS
Gretchen Schwarze, MD
Sarah Sullivan, PhD
Manasa Venkatesh, MS
Corrine Voils, PhD
Lisa Werning
Lee Wilke, MD
Dou-Yan Yang, PhD

Finally, we would like to acknowledge today's **onsite judges** who worked to determine the winners of the Bernhardt, Ford, Hullett, Kent, and Rikkers awards.

David Al-Adra, MD
Randi Cartmill, MS
Allison Dahlke, MPH
Seth Dailey, MD
Catherine Garland, MD
Angela Gibson, MD, PhD
Cynthia Kelm-Nelson, PhD
Bo Liu, PhD
Entela Lushaj, MD, PhD
Timothy McCulloch, MD
Bret Michelotti, MD
Sudha Pavuluri Quamme, MSc, MD
Samuel Poore, MD, PHD
Megan Saucke, MD
Jessica Schumacher, PhD, MS
Gretchen Schwarze, MD
Sarah Sullivan, PhD

Program

University of Wisconsin Department of Surgery

10th Annual Research Summit: *Pathways to Impact*

Wednesday, January 16, 2019

AM

7:30 **Coffee and Registration**

8:00 **Welcome and Opening Remarks, The Marquee**

Angela Ingraham, MD, MS, Program Co-Chair
Robert Redfield III, MD, Program Co-Chair

8:15 **UW Department of Surgery Research Talks**
Four 10-minute talks each followed by 5-minute Q&A

- **Jon Odorico, MD**
  "Strategies for overcoming immunological damage to Stem Cell Beta Cell Transplants"
- **Bo Liu, PhD**
  "Chemical Approaches to Manipulating Cell Death"
- **Sean Ronnekleiv-Kelly, MD**
  "Circadian Disruption in Pancreatic Cancer"
- **Heather Neuman, MD, MS**
  "Understanding Socioeconomic Disparities in the Receipt of Post-Mastectomy Breast Reconstruction"

9:15 **Coffee Break, Poster Viewing and Judging, Varsity Hall**
If you are presenting a poster, we encourage you to stand by your poster during this time to answer any questions that may arise.

10:15 **Invited Speaker, The Marquee**

Fred Lee Jr., MD
Robert Turrel Professor of Imaging Science
Chief of Abdominal Intervention
Department of Radiology, University of Wisconsin School of Medicine and Public Health
"Bench to Bedside in Action: A UW Story"

11:00 **Top Six Abstract Presentations**
7 minutes + 3 minutes Q&A

- **Matthew Kelly**
  "Tartrate-resistant acid phosphatase (TRAP)-positive macrophages in aneurysmal disease exhibit an enhanced proteolytic phenotype"
- **Sabrina Wang**
  "Effects of Age and Exercise on Lingual Muscle Regeneration"
- **Zach Rolfs**
  "In vivo Protein Turnover Rates Across the Proteome for Various Mouse Tissues"
- **Katherine Shaum**
  "Improving post-operative pain management in outpatient breast surgery with novel enhanced recovery after surgery protocol and pre-operative paravertebral block"
- **Adam Awe**
  "Maximum Axial Diameter is a Poor Surrogate for Volume and Surface Area of Small Pancreatic Cysts"
- **Chris Zimmerman**
  "Influence of system factors on surgeon inclination to offer non-beneficial surgery to older adults with life-limiting acute surgical conditions"

PM

12:00 **Lunch, Poster Viewing, and Judging, Varsity Hall**
If you are presenting a poster, we encourage you to stand by your poster during this time to answer any questions that may arise.

1:30 **Invited Speaker, The Marquee**

Debra Houry, MD, MPH
Director, National Center for Injury Prevention and Control
Centers for Disease Control and Prevention
"Addressing the Opioid Epidemic: Providers at the Frontlines of Medicine and Public Health"

2:30 **Coffee and Ice Cream Break**
If you are presenting a poster, we encourage you to stand by your poster during this time to answer any questions that may arise.

3:00 **UW Department of Surgery Research Talks**
Four 10-minute talks each followed by 5-minute Q&A

- **Ahmed Afifi, MD**
  "Qualitative outcome studies in migraine surgery"
- **Caprice Greenberg, MD, MPH**
  "An Overview of the Surgical Collaborative of Wisconsin"
- **Joseph Roche, MD**
  "When Hearing is Hard: The Influence of Binaural Hearing on Speech Intelligibility and Listening Effort"
- **Jonathan Kohler, MD**
  "Navel Gazing: Sometimes There Are Great Questions Hiding in Plain Sight"

4:00 **Research Update, The Marquee**

Rebecca M. Minter, MD
A.R. Curreri Distinguished Chair, Department of Surgery

4:45 **Closing and Announcement of Research Prize and Science Image Contest Winners**

YOU MUST BE PRESENT TO WIN AN AWARD.
There will be no exceptions. If you win an award but are not present, the award will be given to the runner-up.

5:00 **Reception, located in the lounge area just outside Varsity Hall at Union South**

List of Abstracts

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

GROUP ONE: Basic Science

AL–ADRA

Exploring the Effects of Cytokine Administration on Liver Allografts During Normothermic Ex-Vivo Liver Perfusion (NEVLP); *Obua A.U., Al-Adra D.P.*
Poster Number: **B24**

BURLINGHAM

Identification of PD-1-mediated Immune Regulation in NSCLC Patients Using the Trans-Vivo Delayed Type-Hypersensitivity Assay; *Lema D., Jankowska-Gan E., Burlingham W., Leal T.*
Poster Number: **B17**

CIUCCI

Vocal Communication Is Impacted by Social Isolation in a Parkinson Disease Rat Model; *Broadfoot C.K., Kelm-Nelson C.A., Ciucci M.R.*
Poster Number: **B2**

CONNOR

Central Versus Peripheral Contributions to Post Stroke Lingual Weakness in a Rat Model; *Miranda J. Cullins, John A. Russell, Linda M. Rowe, Nadine P. Connor*
Poster Number: **B3**

Effects of Age and Exercise on Lingual Muscle Regeneration; *Wang S, Kletzien H, Connor NP*
Poster Number: **B30**

GIBSON

Characterizing the Inflammation Response in Burn Tissue; *Glover C.R., Karim A.S., Wang Z., Kendziorski, C., Gibson A.L.*
Poster Number: **B8**

Development of a Humanized Murine Burn Model; *Karim A.S., Zhou Y., Ocotl E., Brown M., Gibson, A.L.*
Poster Number: **B12**

Establishing an Ex-Vivo Human Burn Model to Characterize Depth of Thermal Injury in Skin; *Edgar Ocotl; Angela Gibson*
Poster Number: **B25**

JIANG

An Aerodynamic, Acoustic, and Electroglottographic Investigation into Various Lengths of Straws in Straw Phonation Using Excised Canine Larynges; *Tangney, J.W., Kang, J., Scholp, A., Jiang, J.J.*
Poster Number: **B28**

Wound-Healing Effects of 635-nm Low-Level Laser Therapy on Primary Human Vocal Fold Epithelial Cells: An In Vitro Study; *Lou Z., Zhang C., Gong T., Xue C., Scholp A., Jiang J.J.*
Poster Number: **B18**

KELM-NELSON

Sensorimotor Control and Affect in the Pink1-/- Model of Female Parkinsonism; *Marquis, J., Ciucci, M.R., and Kelm-Nelson, C.A.*
Poster Number: **B20**

LE

A Model for Research on Ventilator-Induced Lung Injury by Negative versus Positive Pressure Ventilations; *Ha Nguyen, Sanjukta Shahu, Song Kim, Joshua Choe, Hau D. Le*
Poster Number: **B23**

Model for Studying the Effect of Mechanical Forces on Prenatal Lung Growth; *Ian Wolf, Dr. Hau Le, Ha Nguyen, Song Kim*
Poster Number: **B31**

LIU

Cell Autonomous Effect of Thrombospondin-1 on Macrophage Recruitment; *Yang H., Zhou T., Assa C., Liu B.K., Liu B.*
Poster Number: **B32**

Paracrine Functions of Smooth Muscle Cells in Supporting Endothelial Regeneration following Arterial Injury; *Vijaya S Pilli, Jun Ren, Ting Zhou, and Bo Liu*
Poster Number: **B26**

RIP3 as a Novel Regulator of Coagulation; *Khoury, MK; Pilli, S; Gupta; K; Liu, B*
Poster Number: **B14**

Targeting FOXM1 in Vascular Smooth Muscle Cells Induces Apoptotic Cell Death; *Franco S.R., Stranz A., Ljumani F., Urabe G., Stewart D, Chaudhary M, and Liu B.*
Poster Number: **B7**

MCCULLOCH

Pharyngeal Air Pressure During Vowels and with Semi-Occluded Vocal Tract: A Pilot Study with High-Resolution Pharyngeal Manometry; *Hoffmeister, J.D., Ulmschneider, C.L., Jones, C.A., McCulloch, T.M.*
Poster Number: **B10**

MEZRICH

Prolongation of Skin Allograft Survival via Indole-3-Carbinol Dietary Supplementation; *Fechner J.H., Afrazi A., Owens L., Mezrich J.D.*
Poster Number: **B5**

Tolerogenic Nanoparticles Targeting the Aryl Hydrocarbon Receptor; *Janek, K.C., Fechner, J.H., Mezrich, J.D.*
Poster Number: **B11**

NICHOL

Comparison Between Ubiquitous and Endoderm Derived Cell Fgfr2IIIb Invalidation; *Kowalkowski, A., Liebl, R., Rein, S., Nichol, P.F.*
Poster Number: **B16**

ODORICO

Investigating the Immunogenicity and Efficacy of the Syngeneically-Transplanted iPSC-Derived Pancreatic Î² Cells into Humanized NSG Mice; *Mitchell SA, Sackett SD, Tremmel DM, Brown ME, Zhou Y, Burlingham W, Odorico JS*
Poster Number: **B21**

Pancreatic ECM Co-Culture Enhances Phenotypic Maturity of Stem Cell-Derived Beta Cells; *Tremmel D.M., Sackett S.D., Curran A, Feeney A.K., Mitchell S.A., Jain V.S., Quirini N.Q., Odorico J.S.*
Poster Number: ***B29***

REDFIELD

BLyS Deficient Rats Inhibit Donor Specific Antibody (DSA) Production and B Lymphocyte Proliferation in Rodent Model; *Bath N.M., Verhoven B.M., Wilson, N.A., Redfield III R.R.*
Poster Number: **B1**

SMITH

In vivo Protein Turnover Rates Across the Proteome for Various Mouse Tissues; *Rolfs Z.J., Frey B.L., Shi X., Kawai Y., Welham, N.V.*
Poster Number: **B27**

THIBEAULT

Amniotic Fluid Assists in Separation of Murine Vocal Folds; *Lungova V., Lunga T., Thibeault S., L.*
Poster Number: **B19**

Characterizing Ontogeny of Yap in Proliferating and Differentiating Vocal Fold Epithelial Progenitors During Embryonic Development in a Murine Model; *Vidisha Mohad, Stephanie Bartley, Susan Thibeault*
Poster Number: **B22**

Cryotherapy Has Antifibrotic and Regenerative Effects on Human Vocal Fold Fibroblasts; *Gong T., Zhang C., Kang J., Lamb J., Jiang J.J.*
Poster Number: **B9**

Imaging and Quantifying Dehydration and Rehydration in Vocal Fold Tissue Layers; *King R.E., Steed K., Rivera A.E., Wisco J.J., Thibeault S.L.*
Poster Number: **B15**

Human vocal fold fibroblast genotype uniquely differentiated to maintain local biomechanical homeostatic fluctuations; Alexander Foote, Ziyue Wang, Christina Kendziorski, Susan L. Thibeault
Poster Number: **B6**

YAMANOUCHI

Characterization of Single Nanometer Ultrafine Oxygen Nanobubble Water; *Darwich B., Schoeller D.A., Yamanouchi D.*
Poster Number: **B4**

Tartrate-Resistant Acid Phosphatase (TRAP)-Positive Macrophages in Aneurysmal Disease Exhibit an Enhanced Proteolytic Phenotype; *Kelly, M.J., Igari, K., Yamanouchi, D.*
Poster Number: **B13**

GROUP TWO: Clinical Science

ABBOTT

Does Adjuvant Therapy Following Resection of Gastroenteropancreatic Neuroendocrine Tumors Improve Outcomes? An Analysis of the U.S. Neuroendocrine Tumor Study Group; *Barrett JR, Lopez-Aguiar, AG, Poultsides GA, Rocha FG, Crown A, Pawlik TM, Fields RC, Panni R, Idrees K, Cho CS Fisher AV, Weber SM, Maithel SK, Abbott* DE
Poster Number: **C4**

AFIFI

A New Approach to Migraine Surgery: The UW Flap; *Afifi AM., Carbullido MK., Israel JS., Sanchez RJ., Albano NJ.*
Poster Number: **C1**

Simplifying Prepectoral Reconstruction: A New Era in Alloplastic Breast Surgery; *Marks J.M., Afifi A.M.*
Poster Number: **C30**

AUDIOLOGY CLINIC

Effect of Tympanostomy Tubes on Distortion Product Otoacoustic Emissions (DP-OAEs); *Kate Tiefenthaler, AuD; Mackenzie Sinnen, BS; Sara M Misurelli, PhD*
Poster Number: **C41**

CONSTANTIAN

Emotional Facial Action Coding System Analysis of Primary and Secondary Rhinoplasty Patients; *Sanchez, R.J., Constantian, M.B.*
Poster Number: **C35**

DIMUSTO

Renal Function Changes Following Fenestrated Endovascular Abdominal Aortic Aneurysm; *Oberdoerster*, *Molly M., Tefera, Girma, Wynn, Martha M., DiMusto, Paul D.*
Poster Number: **C31**

DJMALI

The Effect of Pulse Steroids/IVIG/Rituximab on Circulating Lymphocytes and Cytokines in Kidney Transplant Recipients with Chronic Active ABMR; *Wilson N, Parajuli S, Redfield R, Aziz F, Garg N, Mandelbrot D, Muth B, Blazel J, Turk J, Mohamed M, Bath N, Verhoven B, Panzer S, Reese S, Djamali A*
Poster Number: **C47**

FUNK

Long-Term Dysphagia Resolution Following Poem Versus LHM in Patients with Achalasia; *Shea G.E., Davies K.D., Venkatesh M, Jolles S., Prout T.M., Shada A., Greenberg J.A., Lidor A.O., Funk L.M.*
Poster Number: **C37**

GARLAND

Feeding Outcomes Following Mandibular Distraction Osteogenesis in Pierre Robin Sequence; *Vik Patel MS2, Lisa Block M.D., Katherine Rose M.D., Delora Mount M.D., Catharine Garland M.D.*
Poster Number: **C32**

JIANG

Comparing the Exposure-Response Relationships of Physiological and Traditional Vocal Warm-Ups on Aerodynamic and Acoustic Parameters in Untrained Singers; *Kang J, Jiang J.J.*
Poster Number: **C19**

Comparing the Nonlinear Dynamic Acoustic Parameters of Healthy Adult and Pediatric Voices; *Adriana Chou, Colin Schrof, Evan Polce, Maia Braden, James McMurray, Jack Jiang*
Poster Number: **C9**

Lingering Effects of Straw Phonation Exercises on Aerodynamic, Electroglottographic, and Acoustic Parameters; *Kang J, Jiang J.J.*
Poster Number: **C20**

KOHLER

Physician Calls to Pediatric General Surgeons Foundational Data to Guide Future Interventions; *Timmel AE, Cartmill RS, Carrera-Valdez J, Rademacher B, Kohler JE*
Poster Number: **C42**

KOHMOTO

Dipyridamole Use May Reduce Gastrointestinal Bleeding in Patients Implanted with a Left Ventricular Assist Device; *Lushaj EB, Dhingra R, Lozonschi L, Kohmoto T*
Poster Number: **C23**

Donor Age Significantly Impacts Long Term Survival of Patients Undergoing Heart Transplantation; *Lushaj EB, Dhingra R, Osaki S, Johnson M, Lozonschi S, Kohmoto T*
Poster Number: **C25**

Evolution of Balloon-Expandable Devices for Transcatheter Aortic Valve Replacement: University of Wisconsin Experience; *Ujihira K., Kohmoto T., Jacobson K.M., Raval A.N., Gimelli G., Osaki S.*
Poster Number: **C44**

Impact of Distance from Implant Center on Mechanical Circulatory Device Patient Outcomes; *Park CJ, Murray M, Kohmoto T, Lushaj EB*
Poster Number: **C24**

Incidence, Etiology and Risk Factors of Unplanned Readmissions After Trans-Catheter Aortic Valve Replacement; *Kohmoto, TK, Osaki S, Ujihira K, Lushaj EB*
Poster Number: **C22**

Short and Long Term Predictors and Causes of Death Post Heart Transplant; *Lushaj E, Lozonschi L, Kohmoto T, Jaeger H, Johnson M, Dhingra R*
Poster Number: **C26**

The Impact of Conscious Sedation on the Outcomes After Transcatheter Aortic Valve Replacement; *Ujihira K., Kohmoto T., Jacobson K.M., Raval A.N., Gimelli G., Osaki S.*
Poster Number: **C43**

Three Case Reports of TAVR in Patients with Circumflex Coronary Artery Anomaly; *Ujihira K., Raval A.N., Wolff M.R., Osaki S.*
Poster Number: **C45**

LIEPERT

Outcomes of a Multidisciplinary Approach to Patients with Acute Necrotizing Pancreatitis; *Amy Liepert, Kyle Williams*
Poster Number: **C46**

LONG

In-Person Hemorrhage Control Training Effectiveness and Comprehension in Low-Resource Rural Settings; *El-Gabri D., McDow A., Sullivan S., Jung H.S.*
Poster Number: **C13**

LUBNER

Maximum Axial Diameter is a Poor Surrogate for Volume and Surface Area of Small Pancreatic Cysts; *V Adam Awe, Victoria Rendell, MD, Meghan Lubner, MD, and Emily Winslow, MD*
Poster Number: **C2**

MALONEY

MSSA Screening and Decolonization Among Non-Cardiac Thoracic Surgery Population; *Kurtz JL, Maloney JD, McCarthy DP, Decamp MM, Christopher Crnich C*
Poster Number: **C27**

Quality of Life and Survival: Comparing Treatment Options for Node-Positive Stage III Non-Small Cell Lung Cancer; *Decker-Palmer M, McCarthy DP, Maloney JD*
Poster Number: **C29**

MELNICK

Patterns of Opioid Use in Vascular Access Procedures; *Janek, K.C., Bennett, K.M, Imbus, J.R., Danobeitia, J.S., Phillips, J.L., Melnick, D.M*
Poster Number: **C17**

NEUMAN

Barriers to Breast Reconstruction for Women with Lower Socioeconomic Status; *Stankowski-Drengler TJ, Schumacher J, Hanlon B, Tucholka J, Amessoudji A, Venkatesh M, Yang D-Y, Neuman HB*
Poster Number: **C40**

ODORICO

Large Single Center Results of Simultaneous Pancreas-Kidney (SPK) Transplantation in Patients with Type 2 Diabetes (T2D) Compared to Type 1 Diabetes (T1D); *Pham P.H., Martinez E.J., Welch B., Leverson G., Marka N., Sollinger H.W., Kaufman D.B., Redfield R.R., Odorico J.S.*
Poster Number: **C33**

PEDIATRIC CARDIAC SURGERY

A Trick for an Old Dog: The Senning Procedure to Treat Atrio-Ventricular Discordance with Ventriculo-Arterial Concordance; *Hermsen JL, Okorie U, Srinivasan S, Anagnostopoulos PV*
Poster Number: **C14**

PITT

Overtreatment of Thyroid Cancer: A Qualitative Study of Surgeons and Endocrinologists; *Jensen C.B., Saucke M.C., Jennings J.L., Khokhar H.J., Voils C.I., Pitt S.C.*
Poster Number: **C18**

RAO

Improving Post-Operative Pain Management in Outpatient Breast Surgery with Novel Enhanced Recovery After Surgery Protocol and Pre-Operative Paravertebral Block; *Shaum K.M., Israel J.S., Hill M.K., King A., Warren M., Siebert J.W., Rao V.K.*
Poster Number: **C36**

REDFIELD

Alemtuzumab is Associated with Higher Rates of De Novo Donor Specific Antibody (DSA) in Patients with No Pre-transplant DSA; *Bath N.M., Djamali A., Parajuli S., Mandelbrot D., Leverson G., Ellis T., Hager D., Kaufman D.B.*, *Poster Number:* **C7**

Renal Autotransplantation Offers Pain Relief to Patients with Loin Pain Hematuria Syndrome; *N.M. Bath, T. Al-Qaoud, H.W. Sollinger, R.R. Redfield III*
Poster Number: **C6**

Renal Autotransplantation Results in Pain Resolution Following Renal Vein Transposition; *Natalie Bath, Talal Al-Qaoud, Hans Sollinger, Robert Redfield III*
Poster Number: **C5**

RICHARDS

The Utility of Urinalysis Prior to In-office Procedures: A Randomized Clinical Trial; *Katelyn Backhaus*
Poster Number: **C3**

ROCHE

Influence of Binaural Hearing on Speech Intelligibility and Listening Effort; *Snodgrass, E.; Litovsky, R.; Roche, J.*
Poster Number: **C39**

ROGUS-PULIA

Swallowing Biomechanical Analysis Following Lingual Strengthening Therapy in Patients with Post-Stroke Dysphagia; *Daggett S., Cullins M., Kletzien H., Hanson K., Pearson W., Rogus-Pulia N.*
Poster Number: **C10**

SCHNEIDER

Optimizing Levothyroxine Dose Adjustment After Thyroidectomy with a Decision Tree; *Chen S.S., Zaborek N, Doubleday A.R., Long K.L., Pitt S.C.; Sippel R.S.; Schneider D.F.*
Poster Number: **C8**

SCHWARZE

Influence of System Factors on Surgeon Inclination to Offer Non-Beneficial Surgery to Older Adults with Life-Limiting Acute Surgical Conditions; *Zimmermann C.J.,Taylor L.J.,Tucholka J.L.,Brasel K., Arnold B., Cooper Z., Schwarze M.L.*
Poster Number: **C48**

Surgeon Reflections on the Use of a Question Prompt List by Patients Considering High-Risk Operations; *Shogren S.L., Ballou J, Buffington A, Tucholka J.L., Senglaub S, Tufariello A, Brasel K.J., Cooper Z, Schwarze M.L.*
Poster Number: **C38**

SIPPEL

Does Extent of Surgery Impact Weight Changes after Thyroidectomy?; *Doubleday A.R., Chen S., Zaborek N., Long K.L., Pitt S.C., Schneider D.F., Sippel R.S.*
Poster Number: **C12**

Gender Disparities in Bone Density Testing of Patients with Hyperparathyroidism: A Bias Against Men; *Priya H. Dedhia, MD, PhD, Alexandria D. McDow, MD, Kristin L. Long, MD, Susan C. Pitt MD, MPHS, David F. Schneider, MD, MS, Rebecca S. Sippel, MD*
Poster Number: **C11**

Symptoms Reported by Thyroid Cancer Patients After Total Thyroidectomy for Papillary Thyroid Cancer; *Robbins, S.E., Macdonald, C.L., Connor, N.P., Sippel, R.S.*
Poster Number: **C34**

THIBEAULT
Correlations Among Upper Esophageal Sphincter Post-Swallow and Pharyngeal Pressures in Normal and Dysphagic Subjects; *Knigge M.A., Rosen S.P., McCulloch T.M., Thibeault S.L.*
Poster Number: **C21**

High-Resolution Pharyngeal Manometry in Pediatric Populations: A Systematic Review; *Hoffmeister, J.D., Braden, M.N., Broadfoot, C.K., Hooper-Lane, C., Jones, C.A., Thibeault, S.L.*
Poster Number: **C16**

Post-Extubation Dysphagia in Pediatric Populations: Incidence, Risk Factors and Outcomes; *Hoffmeister, J.D., Zaborek, N.A., Thibeault, S.L.*
Poster Number: **C15**

GROUP THREE: Education

FUNK
Motivations of Males with Severe Obesity Who Pursue Bariatric Surgery or Medical Weight Management; *Jolles, S.A., Alagoz, E., Voils, C.I., Shea, G.E., Liu, N., Funk, L.M.*
Poster Number: **E5**

GARLAND
Effective Educators and Constructive Mindsets for Optimal Surgical Training: Resident Perspectives; *Babchenko O. MD, Sullivan S. PhD, Frank S., Elmaraghi S. MD, Thiagarajasubramanian S. MD, Rendell V. MD, Nayar H. MD, Bentz M.L. MD, FAAP, FACS, Garland C.B. MD*
Poster Number: **E1**

GREENBERG, C.
What Makes a Good Surgical Coach?; *Vande Walle K, Pavuluri Quamme S, Wiegmann D, Ghousseini H, Dimick J, Greenberg C*
Poster Number: **E14**

GREENBERG, J.
Embodiment of Operative Instruction; *Godfrey, M., Sullivan, S., Rosser, S., Nathan, M.J., Greenberg, J.*
Poster Number: **E4**

JIANG
A Comparison of Phonosurgery Instrument Design: A Study in Surgical Novices; *Jessica Wang, Chris Ulmschneider, Adriana Chou, Jack Jiang*
Poster Number: **E15**

JUNG
A Gap Analysis of Surgical Simulation Training in Medical Education for Students with Physical Disabilities; *Patel, K.A., Jung, H.S., Sullivan, S.*
Poster Number: **E8**

An Analysis of Verbal Response Modes, Team Role, and Teamwork in Simulated Trauma Resuscitations; *Briana Statz, Ingie H Osman BS, Alexandra A Rosser BS, Sarah Sullivan PhD, Ryan Thompson MD, Hee Soo Jung MD*
Poster Number: **E10**

Automated Natural Language Processing of Closed Loop Communication in Trauma Resuscitations; *Alexandra A Rosser BS, Sarah Sullivan PhD, Ryan Thompson MD, Hee Soo Jung MD*
Poster Number: **E9**

LARYNGEAL/ PHYSIOLOGY LAB

The Prevalence and Risk Factors for Chinese Teachers in Middle School, Elementary School and Kindergartens; *Dehui Fu, ShanShan Huang, Yongwang Huang*
Poster Number: **E3**

MICHELOTTI

Development of a Regional Anesthesia Task-Sharing Model for Orthopedic Surgeons in Port-au-Prince, Haiti; *Brian Christie MD MPH, Pierre Marie Woolley MD, Brett Michelotti MD, George Dyer, MD*
Poster Number: **E2**

O'ROURKE

Beyond "Good Team Player": An Extended Clinic Experience with a Surgical Faculty Member Results in More Descriptive Narrative Clinical Evaluations; *Larson, S.L., Sullivan, S.A., O'Rourke, A.P.*
Poster Number: **E6**

POORE

Assessing Efficiency in Microsurgery Using Motion Tracking Technology; *Lyon S.M., Zeng, W., Albano N.J., Mohamadipanah H., Pugh C., Poore S.O.*
Poster Number: **E7**

Microsurgical Training Course Utilizing the "Blue-Blood" Chicken Thigh Model Significantly Enhances Comprehensive Resident Education; *Zeng W MD, Shulzhenko N.O. BA, Lyon S.M.MD, Albano N.J. MD, Dingle A.M PhD, Poore S.O. MD PhD*
Poster Number: **E16**

SULLIVAN

Addressing Gaps in Knowledge Sharing Within Trauma Teams-in-Training by Examining Team Process and Individual Empowerment; *Sullivan S, Rosser A, Thompson R, Jung H S.*
Poster Number: **E11**

Operating Room Preparation by General Surgery Residents: A Qualitative Analysis; *Goldwag J & Sullivan S*
Poster Number: **E12**

What Are Clinical Instructors Really Evaluated On? A Qualitative Study of Medical Student and Resident Comments on Evaluations of Teaching; *Sullivan, S., Greenberg, J., O'Rourke, A., Minter, R., Foley, E., Voils, C. I.*
Poster Number: **E13**

GROUP FOUR: Health Services

ABBOTT

Deficiencies in Postoperative Surveillance for Veterans with Gastrointestinal Cancer; *Lauren J. Taylor, MD; Kerui Xu, PhD, MPH; James D. Maloney, MD; Corrine I. Voils, PhD; Sharon M. Weber, MD; Luke M. Funk, MD; Daniel E. Abbott, MD*
Poster Number: **H14**

FUNK

Perioperative Cost Differences of Laparoscopic Sleeve Gastrectomy Versus Laparoscopic Roux-en-Y Gastric Bypass: A Single Institutional Review; *Svoboda D.C., Venkatesh M., Liu N., Johnson M., Greenberg J.A., Lidor A.O., Funk L.M.*
Poster Number: **H13**

Weight Loss for Patients with Severe Obesity: An Analysis of Long Term Electronic Health Record Data; *Liu N., Birstler J., Venkatesh M., Hanrahan L.P., Chen G., Funk L.M.*
Poster Number: **H7**

INGRAHAM

Effect of Transfer Status on Outcomes of Emergency General Surgery Patients; *Philip JL, Yang DY, Wang X, Fernandes-Taylor S, Hanlon BM, Schumacher J, Saucke MC, Havlena, J, Greenberg CC, Santry HP, Ingraham AM*
Poster Number: **H10**

KOHLER

Early Repair of Uncomplicated Pediatric Umbilical Hernias: Complications of Potentially Unnecessary Surgery; *Cartmill R.S., Yang D.-Y., Fernandes-Taylor S., Kohler J.E*
Poster Number: **H6**

Variation in Opioid Prescribing After Pediatric Umbilical Hernia Repair; *Cartmill R.S., Yang D.-Y., Fernandes-Taylor S., Kohler J.E.*
Poster Number: **H4**

LIEPERT

Surgeon Engagement in Surgical Health Policy Advocacy; *Beilke S.B, Alcantara J, Liepert A.E.*
Poster Number: **H3**

PITT

Treatment Recommendations for Low-Risk Thyroid Cancer: Are Patients' or Providers' Preferences More Important?; *Saucke M.C., Roman B.R., Brito J.P., Zaborek N., McDow A.D., Jensen C.B., Jennings J.L., Pitt S.C.*
Poster Number: **H11**

SCARBOROUGH

Safety in Allowing Residents to Independently Perform Appendectomy, a Retrospective Review; *Barrett J R, Drezdzon M, Monawer A, O'Rourke A P, Scarborough J E*
Poster Number: **H2**

TEFERA

Vascular Surgery Outcomes of Trauma Patients at TASH, Addis Ababa, Ethiopia; *Semma Y.Z., Getachew F., Tefera G., Abebe N.S.*
Poster Number: **H12**

WIEGMAN

Promoting Systemic Improvement Through a Human Factors Analysis of Patient Safety Reports; *Vande Walle K., Osadchuk T., Alagoz E., Greenberg C., Wiegmann D.*
Poster Number: **H15**

WILKE

Evaluation of Long-Term Satisfaction with Mastectomy vs Breast Conserving Surgery in Patients Treated for Ductal Carcinoma In Situ: A Population-Based Longitudinal Cohort Study; *Devon Livingston-Rosanoff, MD, PhD; John Hampton, MS; Polly Newcomb, PhD; Amy Trentham-Dietz, PhD; Lee G Wilke, MD*
Poster Number: **H9**

Time to Initiation of Neoadjuvant Chemotherapy for Breast Cancer Treatment Does Not Influence Patient Survival: A National Cancer Database Study; *Devon Livingston-Rosanoff, MD, PhD; Bret Hanlon, PhD; Nicholas Marka, MS; Kara Vande Walle, MD; Trista Stankowski-Drengler, MD; Jessica Schumacher, PhD; Caprice Greenberg, MD, MPH; Heather Neuman, MD; Lee G Wilke, MD*
Poster Number: **H8**

WINSLOW

The Impact of Diagnosis on Patient Satisfaction in a Large Sample of General Surgery Outpatients; *Bandealy N., Rendell V.R., LeRette K.A., Leaf M.A., Winslow E.R.*
Poster Number: **H1**

Understanding Communication Gaps in the Hospital Consultation Process; *Fischer C.L., Rendell V., Winslow E.*
Poster Number: **H5**

GROUP FIVE: Translational

BURLINGHAM

Assessing the Immunogenicity of Pluripotent Stem Cell Therapies; *Matthew E Brown, Jue Zhang, Elizabeth Perrin, Ying Zhou, Jack Hermsen, Timothy J. Kamp, John Steill, Scott Swanson, Ron Stewart, William J. Burlingham and James A. Thomson*
Poster Number: **T1**

CONNOR

Effects of Tongue Exercise Dose on Tongue Force, Mastication Rate, Bolus Size and Bolus Speed in a Rat Model; *Weycker, J.M., Krekeler, B.N., Connor, N.P.*
Poster Number: **T18**

Tongue Exercise Paired with Swallow Does Not Impact Thyroarytenoid Muscle Outcomes in a Rat Model of Aging; *Glass T.J., Bado M., Krekeler, B.N. Rowe L.M., Connor N. P.*
Poster Number: **T5**

FERNANDEZ

Treatment with Complement Blockade in Recipients of Brain-Death Donor Kidneys Defends Against Delayed Graft Function in Non-Human Primates; *Eerhart M.J., Reyes J.R., Blanton C.L., Danobeitia J.S., Chlebeck P.J., Zitur L.J., Coonen J., Capuano S., D'Allesandro A.M., Torrealba J., Yankol Y., and Fernandez L.A.*
Poster Number: **T3**

GUMPERZ

Modeling Human Hematopoietic Stem Cell Transplantation Outcomes in the Lab; *Nicholas J. Hess; Peiman Hematti; Jenny E. Gumperz*
Poster Number: **T6**

JIANG

Applied Chaos Level Test for Validation of Signal Conditions Underlying Optimal Performance of Voice Classification Methods; *Liu B., Polce E., Sprott J., Jiang J.J.*
Poster Number: **T8**

Application of Local Intrinsic Dimension for Acoustical Analysis of Voice Signal Components; *Liu B., Polce E., Jiang J.J.*
Poster Number: **T10**

An Objective Parameter to Classify Voice Signals Based on Variation in Energy Distribution; *Liu B., Polce E., Jiang J.J.*
Poster Number: **T9**

Measurement Reliability of Laryngeal Resistance and Mean Flow Rate in Pediatric Subjects; *Austin J. Scholp, BS; Calvin D. Hedberg, BS; Jim R. Lamb; Matthew R. Hoffman, MD, PhD; Maia N. Braden, MS, CCC-SLP; J. Scott McMurray, MD; Jack J. Jiang, MD, PhD*
Poster Number: **T16**

Measurement Reliability of Phonation Threshold Pressure in Pediatric Subjects; *Matthew R. Hoffman, MD, PhD ; Austin J. Scholp, BS; Calvin D. Hedberg; Jim R. Lamb; Maia N. Braden, MS, CCC-SLP; James Scott McMurray, MD; Jack J. Jiang, MD, PhD*
Poster Number: **T17**

Quantification of Voice Type Components Present in Human Phonation Using a Modified Diffusive Chaos Technique; *Liu B., Polce E., Raj H., Jiang J.J.*
Poster Number: **T7**

KAUFMAN

Induction of Tolerance to Kidney Transplants in Rhesus Macaque; *Post, J.L., Haynes, L.D., Haynes, W.J., Jankowska-Gan, E.,Bloom, D., Fernandez, L., D'Alessandro, T., Forrest, L., Hematti, P., Burlingham, W.J. and Kaufman, D.B.*
Poster Number: **T13**

ODORICO

Quantifying Pancreatic Lipid Content: Correlating Donor Data with Pancreas Quality; *Feeney A.K., Tremmel D.M., Mitchell, S.A., Sackett S.D., and Odorico J.S.*
Poster Number: **T4**

Towards In Vitro Maturation of Stem Cell-Derived Beta Cells Utilizing Pancreatic Matrix Hydrogel; *Quirini NQ, Tremmel DM, Sackett SD, Mitchell SA and Odorico JS*
Poster Number: **T14**

PANZER

MHC Class II Ligation on Glomerular Endothelial Cells Upregulates Adhesion Molecules and Chemoattractants: An In Vitro Model of Microvascular Injury; *Wilson Schlei, NA, Dylewski, J, Redfield III, RR, Djamali, A, Blaine, J, Panzer, SE*
Poster Number: **T19**

POORE

Beyond Adding the Cord Suture: An Entirely New Approach to Tendon Repair; *Weifeng Zeng, Ruston Sanchez, Samuel O. Poore, Aaron M. Dingle*
Poster Number: **T20**

Design and Manufacture of an Osseointegrated Neural Interface (ONI) for Chronic Electrophysiology in Rabbits Towards Improved Prosthetic Control; *Millevolte, A. X. T., Dingle, A. M., Ness, J. P., Novello, J., Zeng, W., Nemke, B., Sanchez, R., Lu, Y., Markel, M. D., Suminski, A. J., Williams, J. C., Poore, S. O.*
Poster Number: **T11**

Osseointegrated Neural Interface (ONI): A Chronic Neural Interface in Rabbits Complete with Osseointegrated Percutaneous Connections for Prosthetic Control; *Dingle, A. M., Ness, J. P., Novello, J., Zeng, W., Nemke, B., Sanchez, R., Lu, Y., Markel, M. D., Suminski, A. J., Williams, J. C., Poore, S. O*.
Poster Number: **T2**

WILLIAMS

Evaluation of Neural Interfaces for Electrical Stimulation of the Rat Trigeminal Nerve; *Ness J.P., Suminski A.J., Zeng W., Novello J., Brodnick S.K., Pisaniello J., Dingle A., Poore S.O., Lake W.B., Williams J.C.*
Poster Number: **T12**

WINSLOW

Direct Radiologic-Pathologic Correlation of Colorectal Liver Metastases with an MR-Compatible Sectioning and Localization Device; *Rendell V.R., Colgan T.J., Knobloch G, MÃ¼hler M.R., Loeffler A.G., Agni R., Reeder S.B., Winslow E.R.*
Poster Number: **T15**

Abstracts

GROUP ONE

Basic Science

B24

Exploring the Effects of Cytokine Administration on Liver Allografts During Normothermic Ex-Vivo Liver Perfusion (NEVLP)

Obua A.O., Al-Adra D.P.

Abstract Submitter	Andre Obua
Email Address	obua@wisc.edu
Classification	Medical Student
Principal Investigator	David P. Al-Adra MD PhD
Science Type	Basic Science
Keywords	Transplantation, Liver, N

Introduction: Liver transplant is the best treatment for liver failure. Normothermic Ex-Vivo Liver Perfusion (NEVLP) is an alternative to currently static cold storage techniques. Recently completed phase III trials have demonstrated that NEVLP perfused livers exhibit superior graft function and decreased early graft dysfunction when compared to cold stored livers. Additionally, NEVLP allows for the modification of the liver prior to transplant, which has potential to reduce graft rejection. Current immunosuppressant strategies have significantly decreased acute graft rejection, however chronic graft rejection remains a significant cause of morbidity in patients receiving liver transplants. Modification of the liver during NEVLP, through the addition of immunoregulatory cytokines, may provide a novel technique to decrease graft immunogenicity through the induction of donor regulatory T & dendritic (DC) cells. The objective of this experiment is to examine the effect of cytokine administration during NEVLP on donor allograft resident lymphocytes, and their effects on long term allograft survival.

Methods: Male and female 10-12 week old Lewis rat livers will be removed in the standard fashion, and placed on a small animal *ex-vivo* liver perfusion apparatus (Harvard Apparatus). Rat recombinant IL-2 (20ng/mL), IL-10 (40ng/mL) and TGFβ (5ng/mL) will be added to the perfusion solution, and livers will be perfused for 12 hours through the hepatic artery and portal vein. NEVLP perfused livers without cytokines, cold stored and fresh livers will serve as controls. The effect of NEVLP on donor lymphocyte populations will be assessed using flow cytometry. To assess the effect of cytokine administration on allograft rejection, livers will be cultured with Brown Norway responders in a mixed lymphocyte reaction.

Results: Due to delays in the delivery and installation of the NEVLP apparatus, we were not able to perform any experiments on NEVLP perfused livers during the allotted 10-week fellowship. During this time, we generated an 11-color flow cytometric protocol for assessing lymphocyte populations within the liver. Additionally, we optimized a protocol for the isolation and culture of primary rat hepatocytes for the mixed lymphocyte experiments.

Conclusions: NEVLP provides an attractive alternative to current cold storage techniques. We will continue to explore the utility of NEVLP and assess its potential to modify liver allografts by modifying the perfusate.

B17

Identification of PD-1-Mediated Immune Regulation in NSCLC Patients Using the Trans-Vivo Delayed Type-Hypersensitivity Assay

Lema D, Jankowska-Gan E, Burlingham W, Leal T

Submitter	Diego Lema
Phone	6085041939
Email Address	lema@surgery.wisc.edu
Classification	Research Assistant
Division	Transplantation
Lab	Burlingham
Science Type	Basic Immunology
Keywords	Checkpoint inhibitors, immunotherapy, non-small cell lung cancer, DTH

Introduction: The success of PD-1/PD-L1 inhibition in NSCLC immunotherapy is clearly dependent on optimal patient selection. Emerging evidence has shown a role for antigen-specific regulation in cancer, with the identification of CD4+ T cells specific for various tumor antigens that have suppressive function. Given the potentially detrimental impact regulatory responses can have, identifying individuals with these preexisting regulatory responses will be key to select those who are more likely to respond to PD-1 or PD-L1 inhibitors. Additionally, identifying whether patients with negative PD-L1 tumor expression also have regulatory responses may further clarify if these patients may also be candidates for immune checkpoint inhibitors or if combination therapies are warranted.

Methods: We performed the trans-vivo delayed-type hypersensitivity assay to identify the role of PD-1/PD-L1-mediated tumor-specific immune responses in a small cohort of patients with advanced NSCLC.

Results: We found that, while most patients have PD-1-mediated anergic immune responses towards their tumor antigens, a minority (2/6) further have active PD-1-mediated immune suppressive regulatory responses. These patients not only fail to respond to their own tumor antigens, but further have tumor antigen-specific regulatory cells capable of actively suppressing an immune response towards recall antigens. Furthermore, CTLA-4 did not play a role in anergy or immune suppression towards tumor antigens in any patient.

Conclusions: Thus, our results suggest that PD-1-mediated anergy is a common feature of NSCLC immune responses, whereas PD-1-mediated immune suppression is present only in a minority of patients. Additionally, we plan to study the role of exosomes in inducing PD-L1 expression by antigen presenting cells (ie. this immune escape mechanism).

B2

Vocal Communication Is Impacted by Social Isolation in a Parkinson Disease Rat Model

Broadfoot C.K., Kelm-Nelson C.A., Ciucci M.R.

Abstract Submitter	Courtney K. Broadfoot
Email Address	Ckuehn2@wisc.edu
Classification	Graduate Student
Principal Investigator	Michelle R. Ciucci, Ph.D.
Science Type	Basic Science
Keywords	Parkinson Disease, Vocal Deficits, Social Isolation

Introduction: Parkinson Disease (PD) is a complex, progressive neurodegenerative disease characterized by motor and non-motor features. Individuals with PD develop significant vocal communication deficits, social isolation, anxiety, and depression that are devastating to quality of life. The relationship between social environment, vocal function, and well-being in this population is not well understood. To investigate this complex problem, we use a well-established PD rat model (*Pink1* -/-) that shows sensorimotor dysfunction including early-onset vocal deficits and progressive pathology analogous to that in humans. The central hypothesis for this study is that social isolation contributes to rat vocal function degradation, decreased cognitive ability, and exacerbates anxiety and depression signs. Additionally, implementing a social enrichment intervention will attenuate these deficits. Finally, we hypothesize that neurotransmitter concentrations in key brain regions will be altered by these social conditions. With a better understanding of social environment on PD pathology, more targeted behavioral and pharmaceutical interventions can be developed.

Methods: Twelve, male *Pink1-/-* rats were randomly assigned into three experimental groups: 1) control, which were housed in pairs, 2) isolated, which were housed individually, and 3) socially enriched, which were housed in pairs and underwent an additional social enrichment intervention. Social enrichment involved grouping rats in a larger 'socialization' cage with another pair of cage mates for 1 hour, 5x per week. To measure acoustic and non-acoustic parameters of vocal communication abilities, ultrasonic vocalizations (USVs) were recorded at 2- (baseline), 4-, 6-, and 8-month time points. At the final time-point, all animals were assessed for cognitive function (novel object recognition test), anxiety levels (elevated-plus maze), and presence of anhedonia, an indicator similar to depression in humans (sucrose preference test). After final testing, brain tissue was harvested from the medial prefrontal cortex (mPFC), ventral tegmental area (VTA), and substantia nigra (SN). To quantify changes in neurochemical content in these targeted brain regions, HPLC-ECD was used to determine concentrations of dopamine, serotonin, norepinephrine and their respective metabolites. A two-way repeated measures ANOVA was used to analyze acoustic differences between groups across time. One-way ANOVAs were utilized to analyze behavioral tests and neurochemical concentrations.

Results: As illustrated in **Figure 1***, Pink1-/-* rats in social isolation demonstrated decreased loudness ($p<0.01$) compared to socially enriched animals. Socially enriched animals produced calls with significantly greater intensity ($p<0.05$) than controls after intervention. Isolated *Pink1-/-* rats produced calls of higher peak frequencies ($p<0.05$) when exposed to conspecific animals compared to controls and socially enriched animals, suggesting irregularity in their call profile and communicative function. There were no detectable differences in indicators of anhedonia (depression) between groups ($p<0.05$). Trends suggested decreased cognitive function ($p<0.10$) and higher presence of anxiety ($p<0.10$) in the isolated *Pink1-/-* rats compared to control and socially enriched animals. There were trends that revealed decreased levels of norepinephrine ($p<0.10$) and serotonin's metabolite, HIAA, ($p<0.10$) in the VTA in isolated *Pink1-/-* rats. There were no detectable differences in neurochemical content between groups in the mPFC or the SN at 8-months.

Conclusions: This data support our hypothesis that social isolation negatively impacts the progression of vocal characteristics and may contribute to cognitive function and anxiety in this PD model. Further, socialization rescues acoustic deficits and may be beneficial in maintaining cognitive abilities and indicators of well-being. With further study and increased sample size, we predict the neurochemistry findings may be linked to the acoustic and behavioral differences we observed. Overall, by developing a better understanding of PD progression, there is opportunity to translate these findings and develop clinical interventions to directly target these deficits.

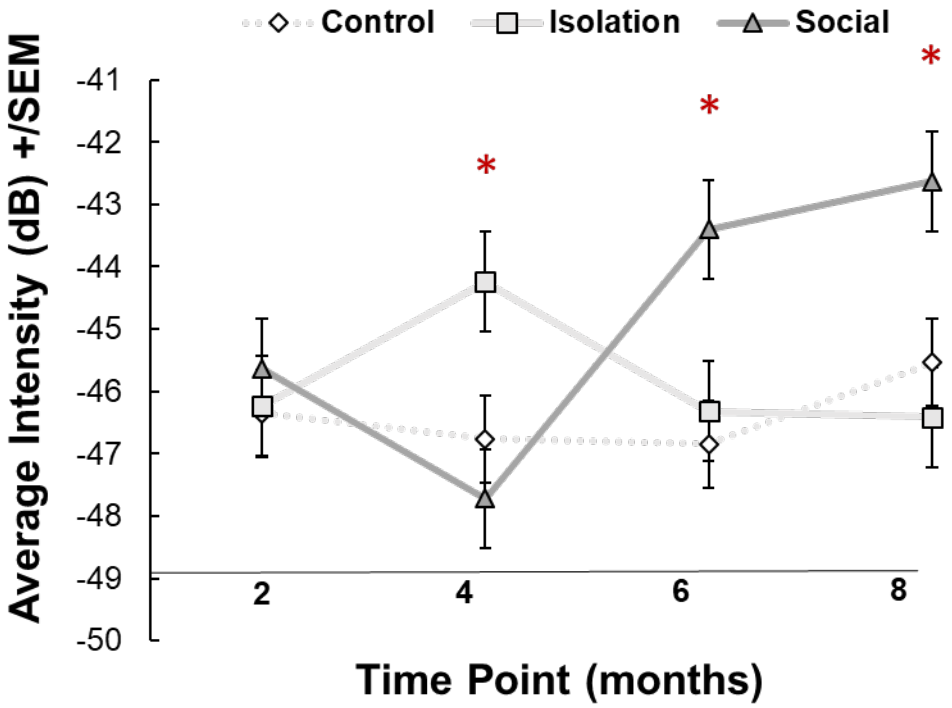


Figure 1. Average intensity (dB) across condition at 2-, 4-, 6-, and 8-months. After intervention, average intensity was greater in the social enrichment group compared to the isolation and control groups. Asterisk indicates significance ($\alpha < 0.05$).

B3

Central Versus Peripheral Contributions to Post Stroke Lingual Weakness in a Rat Model

Miranda J. Cullins, John A. Russell, Linda M. Rowe, and Nadine P. Connor

Submitter	Miranda Cullins
Phone	
Email Address	mcullins@wisc.edu
Classification	Postdoctoral Fellow
Division	Otolaryngology
Lab	Connor
Science Type	Basic
Keywords	Stroke, Dysphagia, Tongue

Introduction: Lingual weakness after stroke is associated with dysphagia and is often targeted by exercise interventions. Chronic weakness after stroke is attributed to both impaired ability to centrally activate target muscles and reduced force generating capacity within muscles. However, how these factors contribute to lingual weakness after stroke is not known. The middle cerebral artery occlusion (MCAO) rat model of post stroke dysphagia is associated with both chronic lingual weakness and deficits in swallowing function. We used this model to test the hypotheses that both reduced muscle force generating capacity (maximum *stimulated* force) and reduced ability to activate the muscle (Percent Voluntary Activation) contribute to lingual weakness (maximum *voluntary* force).

Methods: Six-week-old rats were randomly assigned to MCAO (N = 8) or sham (N = 9) surgeries and trained to press an instrumented disk with the tongue for a water reward. Maximum voluntary tongue force was determined prior to MCAO and at 8 weeks post-surgery, which represents the chronic phase of stroke in rodent models. At 8 weeks, bilateral stimulation of the medial hypoglossal nerve was used to determine maximum protrusive force generating capacity. Swallowing function was assessed by videofluoroscopy.

Results: Maximum stimulated force was not significantly different between groups (MCAO = 408.3 ± 184.1 mN, Sham = 327.9 ± 117 mN, $p = 0.147$). Percent Voluntary Activation (voluntary force/stimulated force) was significantly reduced in the MCAO group (MCAO = 26.7 ± 15.6 %, Sham = 41.9 ± 10.2 %, $p = 0.015$) and moderately correlated with mean bolus area (*Pearson's r* = 0.438, $p = 0.003$), a measure of swallowing function previously found to be reduced in the MCAO model.

Conclusions: These data suggest that the primary cause of chronic lingual weakness after stroke is an impairment in central control of muscle activation rather than a deficit of force generating capacity in lingual muscles. Percent Voluntary Activation deficits in the absence of muscle force deficits have also been reported in select hand and leg muscles. Further assessments of lingual muscle physiology in this stroke model, including muscle cross sectional area and fiber diameter, will augment this initial assessment of central and peripheral contributions to post stroke lingual weakness.

B30

Effects of Age and Exercise on Lingual Muscle Regeneration

Wang S, Kletzien H, Connor NP

Abstract Submitter	Sabrina Wang
Email Address	swang492@wisc.edu
Classification	Undergraduate Student
Principal Investigator	Nadine Connor
Science Type	Basic Science
Keywords	Aging, Swallowing Disorder, Regeneration

Introduction: By the year 2050, the number of individuals 60 years and older will increase to more than 2 billion world-wide. Age-related degeneration of lingual muscles contributes to swallowing disorders, but mechanisms remain elusive. Possible causal pathways include failure of the regenerative machinery in response to injury or disease. ***However,*** the regenerative capacity of muscle stem cells (satellite cells, SC) has never been studied in aging cranial muscles, nor have mechanisms of SC dysfunction been explored. The ***purpose*** of this research is to examine underlying cellular mechanisms of age-related decline and potential rescue by exercise in aging tongue muscles.

Methods: One hundred twenty-four young adult (n=62) & old (n=62) F344/BN rats were randomized into either: (1) tongue exercise or (2) no exercise, control conditions. Maximum voluntary tongue forces (MVTF; mN) were determined in rats undergoing tongue exercise at baseline, 2-wk, & 8-wk study endpoints. Videofluoroscopic swallow studies (VSS) were also performed to determine age-related alterations in swallow biomechanics & kinematic variables (bolus area, bolus velocity, mastication rate). Following the Baseline, 2-wk, or 8-wk study period, the genioglossus (GG), styloglossus (SG), hyoglossus (HG), intrinsic tongue (IT) muscles, & extensor digitorum longus (EDL) were extracted & immediately frozen for western blot (WB) analyses. Protein expression of Pax7, a marker of quiescent and activated satellite cells, will be determined in all muscle tissue homogenates at all time points and treatment conditions. Following immunodetection, the total amount of protein transferred will be determined for data normalization. Data will be expressed as a ratio of protein band relative to total protein.

Results: Preliminary results suggest that swallowing function & biomechanics are impaired with age. Bolus area significantly increased ($p=0.048$), and mastication rate significantly decreased with age ($p<0.001$). Aging accounted for 77.1% of the variance in swallow biomechanics (CV1: $D=1.907$, $p<0.0001$; Fig 1A), and 18.7% of the variance was associated with swallow phase (oral vs pharyngeal; CV2: $D=1.1835$, $p<0.0001$;). Post hoc discriminant function analysis suggested that with aging, tongue base retraction was reduced, masticatory movements were more variable, and increased head extension was observed in old rats compared to young rats during the swallow (Fig 1B).

Maximum Voluntary Tongue Forces significantly increased following exercise ($p<0.001$) at both 2-wk & 8-wk time points in young adult and old rats (Fig 1C). Preliminary data from the GG muscle suggests that Pax7 protein expression is upregulated following 2-wks of progressive resistance tongue exercise ($p=0.029$), and normalized back to baseline levels by the 8-wk time point.

Conclusions: Underlying cellular mechanisms that contribute to age-related changes in lingual muscle function and structure are unknown. The quantification of lingual muscle regeneration via satellite cells will have high impact due to the putative link with age-related swallowing disorders. Our preliminary data showing upregulated Pax7 protein expression after 2-wks of tongue exercise may be an indication of satellite cell proliferation and differentiation. A previous study has shown that most SCs downregulate after the initial upregulation before the cells begin to differentiate, which may explain the lower levels of Pax7 expression at the 8-wk time point. Understanding how these variables may be optimized with exercise therapy will be useful in directing treatment of swallowing disorders.

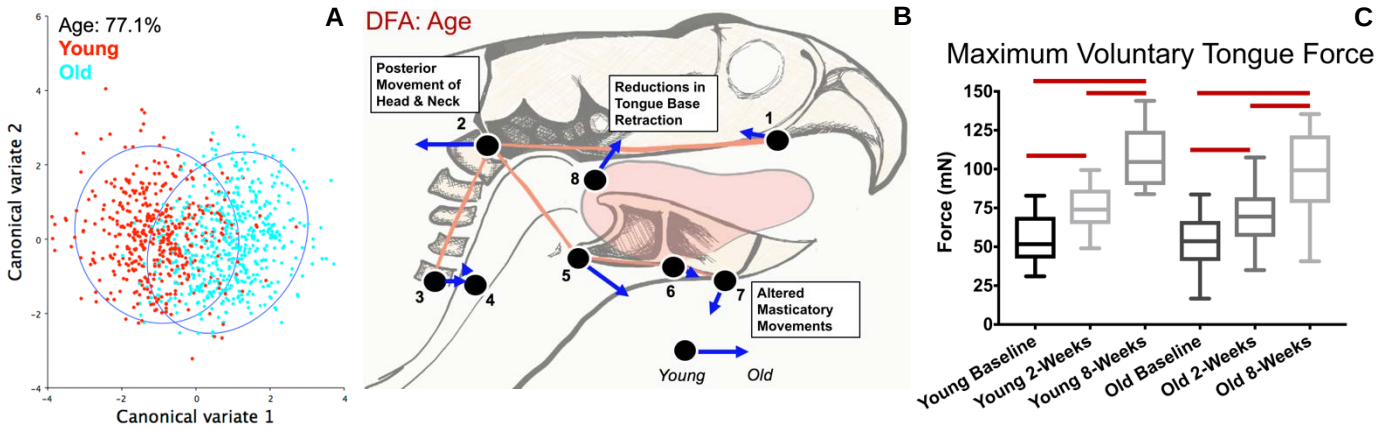


Fig. 1: Aging accounted for 77.1% of the variance in shape change during the oropharyngeal swallow (A). Overlaid are eigenvectors showing the magnitude and direction of shape change of young versus old swallowing biomechanics, and suggests reduced tongue base retraction (8), more variable masticatory movements (5,7), and compensatory head movements (2) with increasing age (B). Maximum Voluntary Tongue Forces increased following progressive resistance tongue exercise (C; lines denote significance).

B8

Characterizing the Inflammation Response in Burn Tissue

Glover C.R., Karim A.S., Wang Z., Kendziorski, C., Gibson A.L.

Abstract Submitter	Christopher Glover
Email Address	crglover@wisc.edu
Classification	Medical Student
Principal Investigator	Angela Gibson, MD, PhD, FACS
Science Type	Basic Science
Keywords	Burn wound, macrophages, RNA Sequencing

Introduction: The processes governing apoptosis, necrosis, inflammation, and regeneration in human burn wounds are not well understood. One cell type that we hypothesized could be a key regulator in the inflammatory/regenerative process is macrophages (MΦ). MΦ can undergo a change in phenotype between M1 (inflammatory) and M2 (anti-inflammatory), depending on cytokine and chemokine stimuli. How these two classes of MΦ behave in different burn depths has not been well studied. We hypothesized that the MΦ phenotype in deep partial thickness (DPT) and full thickness (FT) burns are different.

Methods: Biopsies from DPT and FT human burn tissue were obtained 5-10 days post burn at the time of excision, and control tissue samples (NRL) were collected from abdominoplasty procedures. These samples were submitted for RNA Seq, and differentially expressed (DE) genes were identified. Lists of genes associated with the M1 or M2 phenotype were constructed from the literature, and then compared to the list of DE genes from the RNA Seq data for DPT and FT sample types.

Results: Thirty-nine M1 phenotype genes were identified in the literature, and 19 were DE and upregulated (UR) in total from NRL in either DPT, FT or both (50%). UR genes were mostly involved in proinflammatory pathways resembling MΦ stimulated by lipopolysaccharide (LPS). There were 9 DE/UR genes expressed in DPT represented by Figure 1A (27%), and 2 were uniquely expressed genes (IL-6 and TLR3). There were 17 DE/UR genes expressed in FT represented by Figure 1B (44%), and 9 were uniquely expressed, of which 5 are involved in INFγ pathway activation.

Fifty-nine M2 phenotype genes were identified from the literature, and 21 were DE/UR in total from NRL in either DPT, FT or both (35%). UR genes were mostly associated with tissue repair and inflammatory resolving MΦ induced by IgG and IL-4. There were 15 DE/UR genes expressed in DPT represented by Figure 1C (25%), 2 of which were uniquely expressed genes (ARG1 and VEGFA). There were 21 DE/UR genes in FT represented by Figure 1D (35%), and 10 uniquely expressed genes, of which 6 are M2 cell surface markers.

Conclusions: Our data suggests there is a greater M1 and M2 response in FT compared to DPT up to 10 days post burn. These results also suggest that INFγ MΦ stimulation may be upregulated in FT compared to DPT burns.

Figure 1

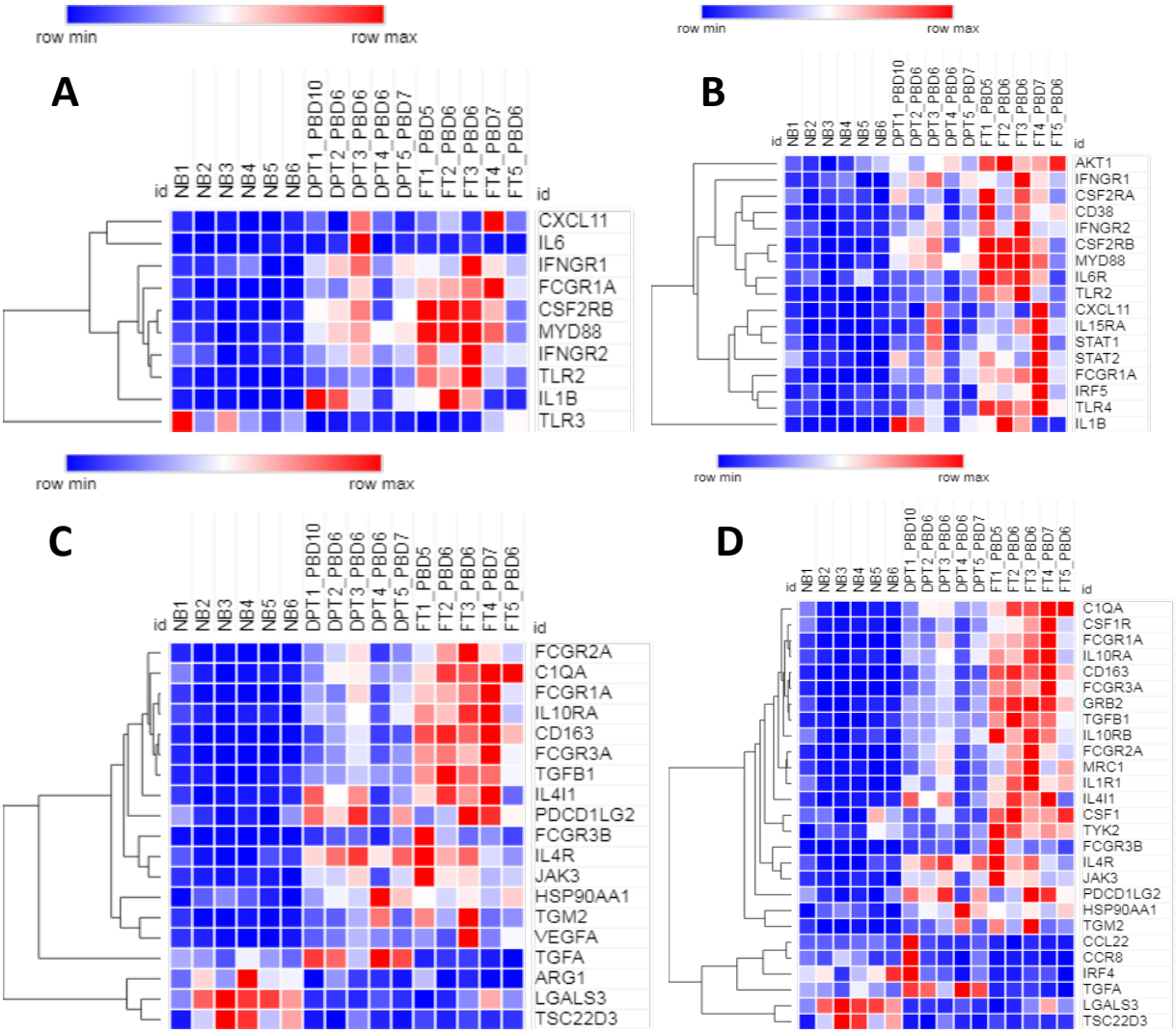


Figure 1. Gene specific heatmaps representing DE M1/M2 associated RNA gene expression in NRL, DPT, and FT samples. Analysis shown for (A) DE M1 associated genes in DPT (B) DE M1 associated genes in FT (C) DE M2 associated genes in DPT (D) DE M2 associated genes in FT.

B12

Development of a Humanized Murine Burn Model

Karim A.S., Zhou Y., Ocotl E., Brown M., Gibson, A.L.

Abstract Submitter	Aos S. Karim, MD
Email Address	Karim@surgery.wisc.edu
Classification	Resident
Principal Investigator	Angela Gibson, MD, PhD, FACS
Science Type	Basic Science
Keywords	Burn, Model Development, Standardization

Introduction: The translation of burn research has suffered from the lack of an appropriate animal model due to the anatomical and wound healing differences in animals compared to humans. Several factors, such as tissue characteristics and thermal injury methods, influence the depth of burn injury. A standardized model of human burn injury to study the mechanisms underlying burn wound progression, inflammation and regeneration is crucial for the successful translation of bench research to humans. In this study we sought to develop and characterize a murine model that allows the study of human burn wound healing.

Methods: De-identified normal human skin excised during reconstructive operations was obtained using an IRB exempt protocol. A 1 cm x 2 cm full thickness piece of human skin tissue was grafted onto the dorsal flank of 6-8 weeks old NOD.Cg-*Kit*^{W41J} *Tyr*+ *Prkdc*^{scid} *Il2rg*^{tm1Wjl}/ThomJ (NSGW) mice (n=5). Punch biopsies were taken of the human skin 1 and 2 weeks after grafting. Mice were sacrificed at week 3 post-grafting and the entire graft including the biopsy sites and a small amount of surrounding mouse skin was harvested for downstream analysis. The tissue was divided into two halves longitudinally for frozen and paraffin embedding. Slides were stained for Hematoxylin and Eosin (H&E), human mitochondrial (Mito), lactate dehydrogenase (LDH), and human CD31 (hCD31).

Results: Visual inspection of the graft at 1 week after grafting revealed pale but adherent human skin. There was no gross evidence of superficial sloughing to indicate complications such as ischemia or rejection at the 2 or 3 week evaluations. Upon histologic examination of the samples, there was successful engraftment as early as 1 week and persisting through 3 weeks post grafting. However, over the first 2 weeks, epidermolysis indicative of tissue stress was microscopically evident in the biopsy samples (Figure A1, A2). This finding was resolved by week 3, as demonstrated by healthy proliferative epidermis (Figure A3). Despite early evidence of epithelial stress at 2 weeks, positive staining for hCD31 was present at the interface between the graft and the underlying mouse muscle (Figure B3; arrows point to staining at interface).

Conclusions: We demonstrate successful engraftment and regeneration of human skin using the immunocompromised NSGW mouse. The epidermolysis was likely a result of tissue hypoxia during the transition of inosculation to neovascularization of the graft. This is a known phenomenon observed clinically in full thickness grafts initially. The transition likely happens sometime around week 2 when neovascularization occurs between the human tissue and the underlying mouse muscle. Our next steps in model development include optimizing the method and timing of thermal injury creation and evaluation. Future development of our human burn wound model will include the humanization of the mouse using donor lymphocytes isolated from the donor skin or donor peripheral blood to more closely recapitulate the processes underlying inflammation and regeneration in humans. Our ultimate goal is to conduct mechanistic studies using this model to better understand the processes that guide burn progression and wound healing.

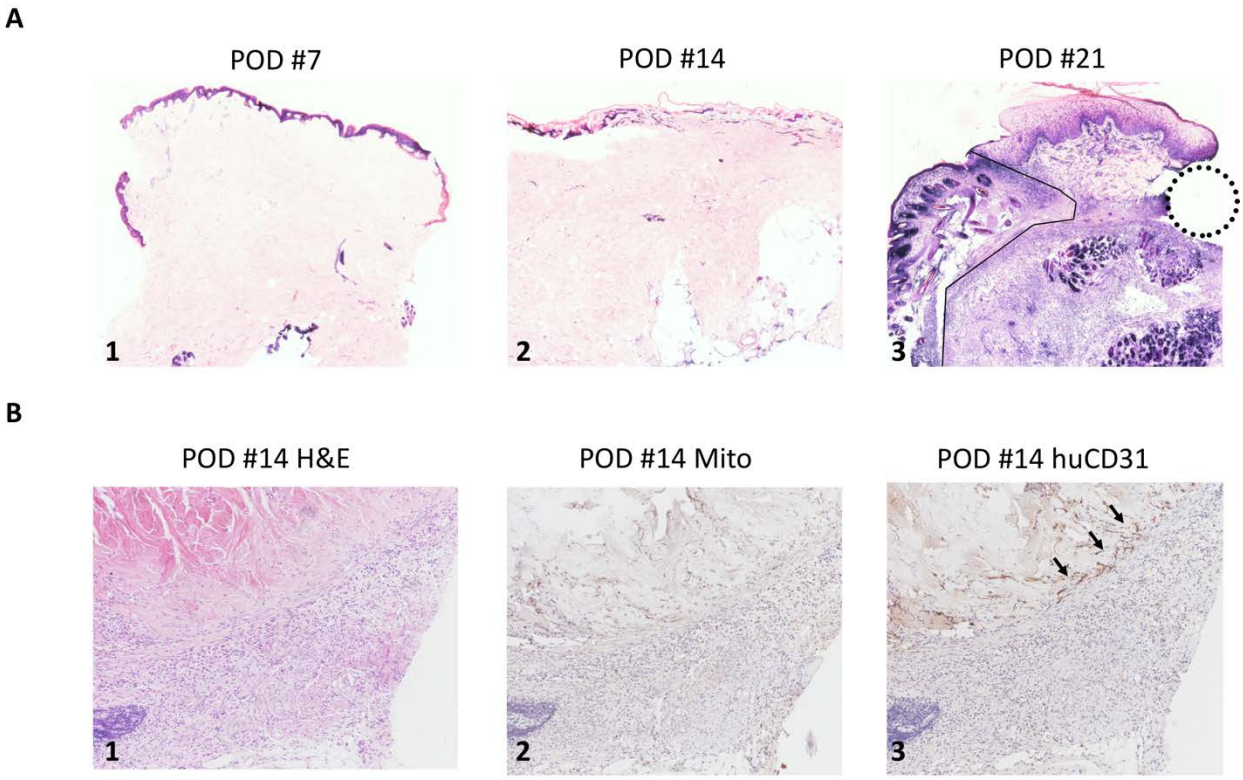


Figure: Human skin is viable and has regenerative capacity after grafting onto an immunocompromised mouse. Panel A 1, 2 and 3 shows LDH staining of the epidermal layer of the skin graft on postoperative day (POD) 7, 14, and 21 after grafting (LDH stains viable cells blue). In A3, the line denotes the interface between the human and mouse tissue, while the dotted circle denotes a biopsy site. Panel B shows interface between the mouse and human skin graft 2 weeks after grafting. H&E (B1), human mitochondrial (B2) and human CD31, a marker of vascular tissue (B3). In B2 and B3, positive staining is brown.

B25

Establishing an Ex-Vivo Human Burn Model to Characterize Depth of Thermal Injury in Skin

Ocotl E.W., Gibson A. L.

Abstract Submitter	Edgar Ocotl
Email Address	ocotl@wisc.edu
Classification	Academic staff
Principal Investigator	Angela Gibson
Science Type	Basic Science
Keywords	Wound-healing model, burn, skin

Introduction: Clinically relevant models are necessary for understanding the mechanisms of human wound healing and for evaluation of prospective medical treatments. The field of burn wound healing is lacking reproducible human skin models that accurately replicate the different classifications of burn injury necessary to characterize human burn wound healing. Inaccurate models lead to the inability to properly translate observations made in the laboratory to patients in a clinical setting. Therefore, the development of a reproducible thermal injury model in human skin is essential to standardizing research related to the proper identification, treatment, and prevention of burn injuries. Our aim is to develop an ex-vivo human burn model that adequately simulates thermal injury sustained in patients.

Methods: Unidentified discarded tissue was obtained from patients undergoing elective cosmetic procedures under an IRB exempt protocol. Skin tissue was obtained from various body sites including abdomen (n=12), thigh (n=1), arm (n=1), and unspecified sites (n=8). Several burning methods were tested to determine the ideal method that would create reproducible injuries. Contact, flame, and scald thermal injury methods were tested. A customized burn device was then created based upon the contact method of heat transfer for subsequent studies. Burn wounds were generated by applying standardized pressure with the spring-loaded device at 100°C for 15s. Samples were harvested immediately or placed into tissue culture and harvested after one and four days of culture. A cell viability assay (Lactate Dehydrogenase) and hematoxylin and eosin staining were utilized to determine the extent of burn injury. Qualitative observations were made based on tissue architecture, morphology of cells, and presence or lack of viable skin appendages that remained after burn damage.

Results: Burns generated with the copper bar contact method or the flame method resulted in the most variability in depth of injury. Moreover, in multiple samples the depth of injury for both the copper and flame burns increased over time in culture. The most consistent method to create a deep partial thickness burn was found with the contact device set at 100°C and in contact with the skin for 15s. A reproducible full thickness burn was generated using a submersion scald method which demonstrated denaturation of the collagen throughout the tissue and complete loss of cellular viability. Burn depth quantification was challenging due to reproducibility in processing of the tissue. Interestingly, in those tissues placed into culture, re-epithelialization was observed as early as 1 day in culture. Additionally, burn and non-burned tissue was found to remain viable for up to 14 days in culture.

Conclusions: Reproducible human burn models are necessary to improve the translation of basic science discoveries to patients. Variability was diminished with the development of a burning device to generate a contact burn. The ability to accurately measure depth of thermal injury and progression of necrosis over time is limited by the tissue alterations, such as compression, that occur with processing. It is unknown if inter-individual differences in skin composition might also contribute to the variations. The presence of re-epithelialization identified in this simple model, suggests it may have utility to test therapeutic interventions. Future studies will focus on further optimizing this model to understand the mechanisms surrounding the early phases of burn wound healing and evaluate potential interventions that may enhance wound healing in humans.

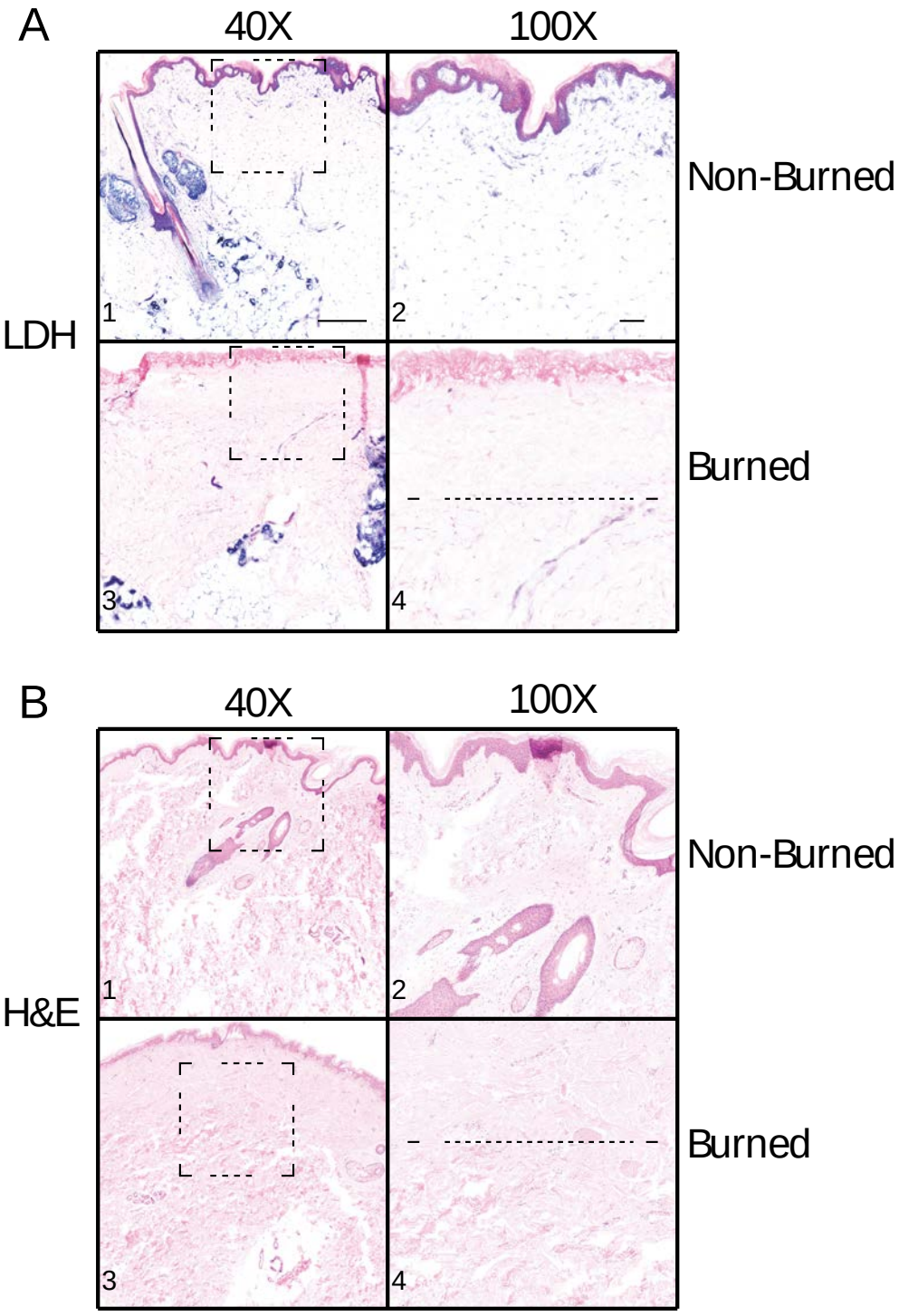


Figure 1: Viability and morphological changes of thermally injured human skin. Representative images of burned and non-burned samples stained for (A) LDH (blue staining) on frozen sections and (B) H&E on paraffin sections from the same tissue sample. The dotted box in images A1, A3, B1, and B3 represent areas enlarged in images A2, A4, B2, and B4, respectively. The dotted line in A4 and B4 represents the approximate level of thermal injury. Scale bar represents 500 microns in A1 for all 40X images and 100 microns in A2 for all 100X images.

B28

An Aerodynamic, Acoustic, and Electroglottographic Investigation into Various Lengths of Straws in Straw Phonation Using Excised Canine Larynges

Tangney J.W., Kang, J., Scholp, A., Jiang J.J.

Submitter	Jacob Tangney
Phone	612-719-4655
Email Address	tangney2@wisc.edu
Classification	Undergraduate Student
Division	Otolaryngology-Head & Neck Surgery
Lab	Laryngeal Physiology Lab (Jiang Lab)
Science Type	Basic Science
Keywords	Excised larynges, straw phonation, SOVT

Introduction: Straw phonation is a well-established method of vocal exercises, started over one hundred years ago. However, some basic questions about best practices remain, including how long the straw should be, and what role the extension of the vocal tract itself plays in the benefits of straw phonation. This study aims to answer those questions by looking at straws of varying length which do not include a semi-occlusion of the vocal tract, thereby keeping other variables controlled. A simulated vocal tract and excised model were used to facilitate the collection of many data points which are difficult to collect in humans.

Methods: Four straws with lengths of 5, 25, 50 and 75 centimeters were used. They attached to the end of a simulated vocal tract which was then affixed to an excised canine larynx. The canine larynx was attached to an apparatus which simulated the human respiratory system. The larynges were brought to phonation, then aerodynamic, acoustic, and electroglottographic data were collected.

Results: There was a significant decrease in the phonation threshold pressure using the 5 and 25 cm straws. With the longer two lengths of 50 and 75 cm, there was a significant increase in supraglottal pressure. The phonation threshold flow and closure quotient all saw insignificant changes.

Conclusions: It is theorized that the increased inertive reactance helped decrease the phonation threshold pressure. By controlling for all other variables, the effects of the length of the straw were able to be looked at in isolation, our results can help efforts to identify an optimal length of straw.

B18

Wound-Healing Effects of 635-nm Low-Level Laser Therapy on Primary Human Vocal Fold Epithelial Cells: An In Vitro Study

Lou Z., Zhang C., Gong T., Xue C., Scholp A., Jiang J.J.

Abstract Submitter	Zhewei Lou
Email Address	zheweilou@163.com
Classification	Undergraduate student
Principal Investigator	Zhewei Lou and Jack J. Jiang
Science Type	Basic Science
Keywords	Low-level laser therapy, Vocal fold epithelial cells, Wound healing

Introduction: Low-level laser therapy (LLLT) has been promoted for its beneficial effects on tissue healing and pain relief for skin and oral applications. However, there is no corresponding literature reporting on vocal fold wound healing. Our purpose was to assess the potential wound-healing effects of LLLT on primary human vocal fold epithelial cells (VFECs).

Methods: In this study, normal vocal fold tissue was obtained from a 58-year-old male patient who was diagnosed with postcricoid carcinoma without involvement of the vocal folds and underwent total laryngectomy. Primary VFECs were then cultured. Cells were irradiated at a wavelength of 635 nm with fluences of 1, 4, 8, 12, 16, and 20 J/cm^2 (50 mW/cm^2), which correspond to irradiation times of 20, 80, 160, 240, 320, and 400 s, respectively. Cell viability of VFECs in response to varying doses of LLLT was investigated by the Cell Counting Kit-8 (CCK-8) method. The most effective irradiation dose was selected to evaluate the cell migration capacity by using the scratch wound-healing assay. Real-time polymerase chain reaction (RT-PCR) was used to detect the gene expression of TGF-β1, TGF-β3, EGF, IL-6, and IL-10.

Results: Irradiation with doses of 8 J/cm^2 resulted in 4% increases in cell proliferation differing significantly from the control group ($p < 0.05$). With subsequent doses at 48 and 72 h after irradiation, the differences between the experimental and the control groups became greater, up to 9.8% ($p < 0.001$) and 19.5% ($p < 0.001$), respectively. It also increased cell migration and the expression of some genes, such as EGF, TGF-β1, TGF-β3, and IL-10, involved in the tissue healing process.

Conclusions: This study concludes that LLLT at the preset parameters was capable of stimulating the proliferation and migration of human vocal fold epithelial cells in culture as well as increase the expression of some genes involved in tissue healing process. Additionally, successive laser treatments at 24 h intervals have an additive beneficial effect on the healing of injured tissues.

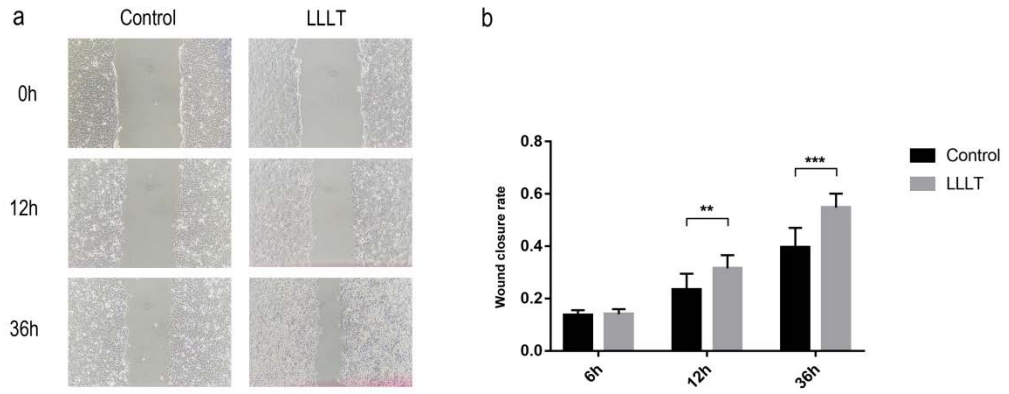


Fig. 3 Cell migration ability was increased by LLLT using scratch wound-healing assay. **a** Scratches were made immediately after treatment, and representative images were obtained immediately, 12, and 36 h after scratch. **b** LLLT increased the wound closure rate of VFECs. *p <0.05; **p <0.01; ***p < 0.001 versus control. LLLT, low-level laser therapy; VFECs, vocal fold epithelial cells

Table 1 Sequences of Primers Used for Real-Time Polymerase Chain Reaction

Target	Oligo	Sequence	Gene Bank ACC
GAPDH	Forward primer	5’-TGAAGGTCGGAGTCAACGGATT-3’	NM_001289746.1
	Reverse primer	5’-TTGACGGTGCCATGGAATTTGC-3’	
TGF-β1	Forward primer	5’-CGACTCGCCAGAGTGGTTAT-3’	NM_000660.6
	Reverse primer	5’-TAGTGAACCCGTTGATGTCCA-3’	
EGF	Forward primer	5’-GCCATGCTCCAGCAAAATCAA-3’	NM_001963.5
	Reverse primer	5’-GTGCAGGACCCACACAAGTAG-3’	
IL-6	Forward primer	5’-CATCCTCGACGGCATCTCAG-3’	NM_000600.4
	Reverse primer	5’-AGCTCTGGCTTGTTCCTCAC-3’	
IL-10	Forward primer	5’-TACGGCGCTGTCATCGATTT-3’	NM_000572.3
	Reverse primer	5’-TAGAGTCGCCACCCTGATGT-3’	
TGF-β3	Forward primer	5’-ATGACCCACGTCCCCTATCA-3’	NM_003239.4
	Reverse primer	5’-CAGACAGCCAGTTCGTTGTG-3’	

B20

Sensorimotor Control and Affect in the *Pink1-/-* Model of Female Parkinsonism

Marquis, J.M., Ciucci, M.R., and Kelm-Nelson, C.A.

Submitter	Julia M. Marquis
Phone	608-262-6122
Email Address	jmmarquis@wisc.edu CAKelm@wisc.edu
Classification	Graduate Student
Division	Otolaryngology
Lab	Kelm-Nelson/Ciucci
Science Type	Basic Science
Keywords	Parkinson disease; female; Pink1

Introduction: Parkinson disease (PD) is a progressive neurodegenerative disease that affects millions of people worldwide. In addition to later-stage limb motor impairment, individuals with PD also exhibit early-onset (preclinical) signs including communication dysfunction (dysarthria, dysphonia) and anhedonia. To treat these signs, a deeper understanding of the onset, progression, and pathology is necessary. To study brain-behavior relationships, our lab employs a rat model of PD (*Pink1*-/-). Rats in this model show progressive sensorimotor deficits and pathology analogous to that of human PD. Basic research, including that from our lab, has used male-only subjects as estrous cycle causes day to day behavioral variability. However, it is vital to study both sexes because PD signs and symptoms vary according to sex in humans. In this study, we hypothesized that female *Pink1*-/- rats would show limb and vocalization deficits and anhedonia compared to age-matched wildtype (WT) controls and these assays would vary according to estrous phase.

Methods: A total of 20 female (n=10 *Pink1* -/-; n=10 WT) long Evans rats were used in this study (SAGE™). Longitudinal behavioral testing was completed at 2, 4, 6, and 8 months of age. Analysis is ongoing and full data set will be presented. In this abstract, we report on the 6-month timepoint. Traditional rodent behavioral tests of (**1**) limb motor function (hindlimb and forelimb movement aka 'cylinder test'), (**2**) cranial sensorimotor function (ultrasonic vocalization acoustics), and (**3**) anhedonia (sucrose preference test) were analyzed. Statistical analyses were conducted with SigmaPlot® 12.5 (Sys-tat Software). Student's t-tests were used to analyze genotype differences for limb motor variables. A repeated measures ANOVA was used to evaluate the acoustic and sucrose differences between genotype (*Pink1* -/- and WT) and estrous phase (estrous, no estrous). Fishers LSD was used for post-hoc analysis and critical level of significance was set *a priori* to 0.05.

Results:

(1) Limb Motor Function: At 6 months of age, *Pink1*-/- females made significantly fewer hindlimb movements ($t(18)=1.75$, $p=0.048$) and rears/lands ($t(18)=1.68$, $p=0.05$) in the cylinder limb motor test compared to WT. There was no significant difference in forelimb movements ($t(18)=1.11$, $p=0.14$). These data are consistent with the presentation/onset of limb motor deficits at a mid-stage timepoint in males.

(2) Ultrasonic Vocalizations: There was a significant interaction between genotype and estrous stage for the number of calls produced during the 2 minute testing period ($F(1, 8)=19.263$, $p=0.002$). Specifically, all animals produced more calls when in estrous ($p<0.001$) and *Pink1*-/- animals produced more calls compared to WT ($p=0.05$). There were no significant interactions or main effects for genotype and estrous for call complexity, average duration of the call, average bandwidth of the call or loudness (intensity) at the 6 month timepoint ($p>0.05$).

(3) Anhedonia: At 6 months, there was no significant main effect or interaction between genotype and estrous for sucrose consumption ($F(1, 15)=0.793$, $p=0.39$).These data suggest that anhedonia may not be an early-onset sign in this model.

Conclusions: This is the first study of Parkinsonian deficits in a female genetic rat model of PD. These findings establish estrous-related differences in behavioral sensorimotor and affect assays in the *Pink1*-/- model, with the goal of quantifying a model to improve translatability to human health. Relationships among genotype and estrous cycle over time as well as preliminary brain tissue analyses will be presented.

B23

A Model for Research on Ventilator-Induced Lung Injury by Negative Versus Positive Pressure Ventilations

Ha Nguyen, Sanjukta Shahu, Song Kim, Joshua Choe, Hau D. Le

Abstract Submitter	Ha Nguyen
Email Address	Mnguyen5@wisc.edu
Classification	graduate student
Principal Investigator	Hau D. Le
Science Type	Biomedical Engineering
Keywords	Ventilator-induced Lung Injury, Negative Pressure Ventilation, Positive Pressure Ventilation, Medical Device

Introduction: Lung injury can be an adverse consequence of mechanical ventilation, which is one of the most practiced interventions in the pediatric intensive care unit. This injury is called ventilator-induced lung injury (VILI) and can result in pulmonary edema, barotrauma, and worsening hypoxemia that can prolong mechanical ventilation, lead to multi-system organ dysfunction, and increase mortality. Thus, adopting a ventilator strategy that reduces VILI is an important goal in ventilator management. The hypothesis that a negative pressure ventilation (NPV) causes less lung injury than its positive pressure ventilation (PPV) counterpart has been investigated over decades. However, research outcomes have been very contradictory. This might partially be due to lacking a VILI model that fairly compares the setting conditions for both NPV and PPV modes.

Methods: We develop a VILI model that fairly compares the NPV and PPV waveforms whose absolute values are approximately identical under the statistical analysis of our waveforms data. This model consists of two components. Firstly, a pressuring system of a sensor and an actuator interfaced with a computer using an Arduino microcontroller. This pressuring system can switch between the NPV and PPV modes with a desired preset waveform, which is controlled and logged by a LABVIEW program. Secondly, a pressurized artificial thorax, which is a disposable plastic cell culture flask (T25), is used to house an isolated lung. The control, NPV, and PPV groups (n=3) of 3-week males of the same C57BL/65 litter weighed 9-11 g are randomized for lung isolation and cannulation with a 23G needle. The thorax with the isolated lung is ventilated for 30 minutes in 37^{o}C cell culture incubator with 5% CO_2 gas. We use sinusoidal waveforms with frequency 60 breaths/minute and pressure varies from 10 mmHg to 15 mmHg for PPV mode and -15 mmHg to -10 mmHg for NPV mode in this report for our “proof-of-concept” purpose, where hematoxylin and eosin staining is used for histology.

Results: Our injury model is proved to work in the way that NPV and PPV pressure waveforms is fairly compared. This is evidenced from our statistical analysis of waveform data. Our histology images for the three groups show qualitatively that lungs in the NPV and PPV models are visibly injured with the latter being more injurious.

Conclusions: Our VILI eliminates the inherent bias of previous VILI models such as ion lung-based models. As a result, it would be used to resolve the controversy of whether or not NPV is capable of reducing lung injury caused by mechanical ventilation. Qualitatively, our preliminary result suggests that NPV is less injurious than PPV. However, our experiments need to be improved in order to have high quality samples of lung slides for further quantitative lung morphology analysis using lung stereology techniques. Firstly, 37^{o}C is not a proper temperature for ventilation. Rather, 4^{o}C should be chosen to avoid a fast degradation of proteins. Secondly, high static pressure (~20-25 cm H_2O) should be used for lung fixation. Lastly, the parameters of the waveforms (frequency and the range of pressure variation) should be optimized in order to reduce the time of injury exposure. These improvements will be performed as our future work.

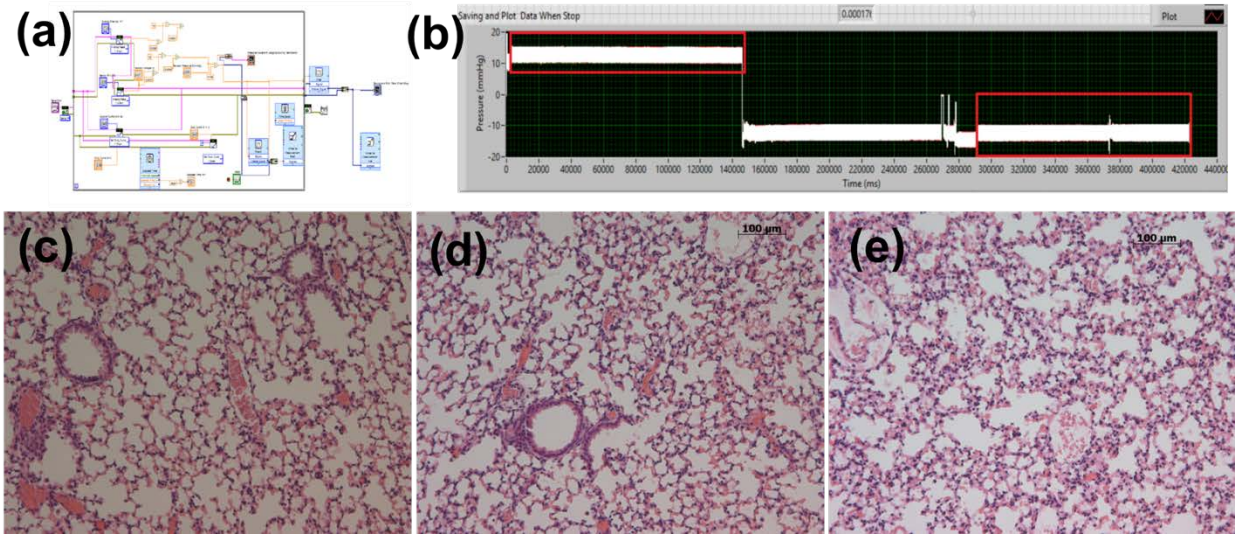


Fig 1. Preliminary results. (a) Block diagram of LABVIEW program. (b) Negative and positive pressure waveforms logged by LABVIEW program. H&E histological images for (c) control, (d) NPV, and (e) PPV

B31

Model for Studying the Effect of Mechanical Forces on Prenatal Lung Growth

Ian Wolf, Dr. Hau Le, Ha Nguyen, Song Kim

Submitter	Ian Wolf
Phone	920-585-2854
Email Address	iwolf@wisc.edu
Classification	Other
Division	Pediatric Surgery
Lab	Dr. Hau Le's Lab, Fab Lab at the Morgridge Institute
Science Type	Basic Science
Keywords	Mechanical Stress, Morphogenesis, Lung Development, Prenatal Development, Live Imaging

Introduction: Congenital diaphragmatic hernia (CDH) is a complex disorder that occurs in utero in which a defect in the diaphragm allows abdominal content to migrate into the chest cavity and press on the growing lungs, preventing them from developing properly. As a result, it leads to severe pulmonary hypoplasia, hypoxemia, and pulmonary hypertension after birth. Children born with CDH still suffer a significant mortality rate, especially those born with very small lung volume, prompting investigation into inducing lung growth before and after birth. Mechanical forces have been shown to play an important role in cell growth and development. However, there is currently no effective model to study the effects of mechanical forces exerted by the thorax during fetal development. We're building a model that can generate a dynamic and tightly controlled negative trans-pulmonary pressure to fetal murine lungs in ex-vivo culture to study the effects of mechanical forces on fetal lung development.

Methods: The trans-pulmonary pressure is applied to the lung by controlling the relative pressure between two media-filled chambers in a customized PDMS microfluidic device. Chamber 1, containing the lung, is exposed to a negative pressure environment inside of a sealed bioreactor using an air-over-water method; Chamber 2 is opened to an atmospheric pressure. The two chambers are joined by a glass micro-needle embedded in the wall that is used to cannulate the trachea. The negative pressure environment is established by a pneumatic micro-pump and monitored by a pressure transducer attached to the chamber. By changing the pressure applied to the lung using an air-over-water method, a large range of pressure profiles can be applied to the lung that are able to change dynamically on a short timescale.

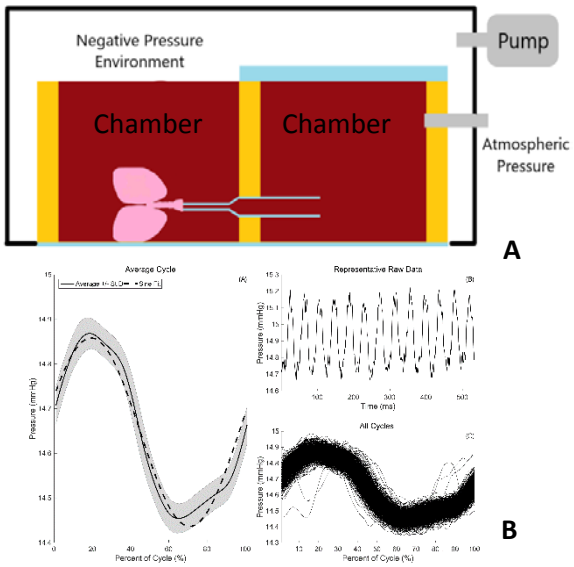


Figure 1A: Side-view of the model. The microneedle is inserted into a wall between two wells and the PDMS structure (yellow) is bonded to cover glass. Another piece of glass is bonded to the top right well to seal it off from the negative pressure environment, so it can be vented to atmosphere.
Figure 1B: Statistical analysis of pressure waveform demonstrating precise control of the pressure environment inside the chamber

Results: We have fabricated four generations of the device and the most recent iteration has demonstrated the ability to control the transmural pressure across the lung in both a static and dynamic fashion. A transmural pressure can be generated between -18mmHg and +18mmHg and can produce sine-waveforms at frequencies and amplitudes up to 2Hz and 3mmHg respectively. Embryonic mouse lungs harvested at day 11.5 of gestation were able to grow for up to 48 hours inside of the device based on assessment from brightfield images and live/dead staining of the tissue.

Conclusions: The experiments conducted have shown that this model is a reliable and effective way to study the effect of mechanical forces on prenatal lung development. The data from previous experiments is being analyzed and further experiments are being conducted to assess the difference in lung growth using this model. The number of airway branches formed, diameter of these branches, lobe development, and lung surface area will be used as metrics to assess lung growth. In future experiments, qRT-PCR will be used to assess the expression of genes involved in mechanotransduction such as CELA-1, TRPV4, PIEZO1, and PIEZO2 in response to various static and dynamic transmural pressures.

B32

Cell Autonomous Effect of Thrombospondin-1 on Macrophage Recruitment

Yang H., Zhou T., Assa C., Liu B.K., Liu B.

Abstract Submitter	Huan Yang
Email Address	yangh@surgery.wisc.edu
Classification	Postdoc
Principal Investigator	Bo Liu
Science Type	Basic Science
Keywords	Thrombospondin-1, Macrophage, Aneurysm

Introduction: Thrombospondin-1 (TSP1) is a large matricellular protein with a diverse array of functions that has been implicated in numerous cardiovascular disease states. Our previous work demonstrates that mice lacking TSP1 are protected from developing abdominal aortic aneurysm (AAA), a highly lethal disease characterized by ECM destruction, smooth muscle depletion and vascular inflammation. The objective of the current study is to explore how *Thbs1* gene deficiency inhibits inflammation associated with aortic aneurysm.

Methods and Results: Using fluorescent *in situ* hybridization, we evaluated which cell types express *Thbs1* in developing mouse AAAs. We induced AAA by perivascular application of 0.5M calcium phosphate, and we chose day 4 as our time point for sacrifice. Sham-treated aorta controls expressed very low levels of *Thbs1* mRNA and these transcripts were largely restricted to the endothelium. In contrast, developing AAAs from the calcium phosphate treated group had significantly higher *Thbs1* expression, expressed predominantly by $CD68^+$ macrophages. It is unclear how *Thbs1* expression is upregulated in AAA, however, our *in vitro* data show that challenging macrophages with LPS stimulates *Thbs1* expression**.** Besides, we found no significant difference in basal levels of circulating monocytes or other myeloid cells, indicating that lacking TSP1 does not disrupt homeostasis these cell lineages.

To explore whether TSP1 in macrophages important for macrophage infiltration, we harvested bone marrow cells from $Thbs^{+/+}$ and $Thbs1^{-/-}$ mice and differentiated them into macrophages. Flow cytometry data showed that lacking TSP1 did not affect macrophage differentiation. In a 3D inverted Matrigel infiltration assay, $Thbs1^{-/-}$ macrophages showed a ~53% reduction in Matrigel infiltration compared to the wildtype control. Interestingly, the presence of $Thbs^{+/+}$ macrophages was unable to rescue the migratory defect of $Thbs^{-/-}$ cells, suggesting that TSP1 functions in a cell-autonomous manner.

Despite their reduced ability to migrate, $Thbs^{-/-}$ bone marrow derived macrophages exhibited no alterations in ability to express pro-inflammatory cytokines IL1β and IL6 upon LPS stimulation, or phagocytic capacity (using fluorescence labeled Zymosan particles to track phagocytosis). Using the thioglycolate elicited peritoneal inflammation model, we found a ~25% reduction in peritoneal infiltration of $F4/80^+/CD11b^+$ macrophages in $Thbs^{-/-}$ mice, suggesting TSP1 may contribute to macrophage recruitment in other inflammatory states in addition to AAA.

Conclusions: Taken together, our results demonstrate that TSP1 is integral for vascular inflammation in a mouse AAA model and necessary for macrophage recruitment.

B26

Paracrine Functions of Smooth Muscle Cells in Supporting Endothelial Regeneration following Arterial Injury

Vijaya S Pilli, Jun Ren, Ting Zhou, and Bo Liu

Abstract Submitter	Vijaya, Pilli
Email Address	
Classification	Postdoc
Principal Investigator	Liu
Science Type	Basic Science
Keywords	

Introduction: Intercellular communication, through direct contacts, secreted molecules or extracellular vesicles, is an important mechanism contributing vascular homeostasis. Protein kinase C-delta (PKCδ) plays a complex role in arterial injury responses by regulating smooth muscle cell (SMC) apoptosis as well as production of chemokines. By using an adenoviral vector driven by the SM22 promoter, our lab recently showed that SMC-specific overexpression of PKCδ accelerated endothelial regeneration in balloon injured rat carotid arteries. We hypothesized that SMCs promote endothelial regeneration through a PKCδ-mediated paracrine mechanism.

Methods and Results:
Conditioned media from PKCδ-overexpressing SMCs promoted endothelial cell (EC) migration in scratch assay as well as transwell assay. Using a chemokine expression array, we identified multiple chemokines including CXCl1 and CXCL7 whose expression was upregulated in injured arteries in a PKCδ-mediated fashion. We further showed similar PKCδ-dependent paracrine functions in SMCs stimulated with TNFα or UV. Next, we tested whether CXCL1 or CXCL7 are primary effectors through which SMCs promote EC migration. Administration of a CXCL7 neutralizing antibody inhibited endothelial cell migration, whereas, neutralizing CXCL1 produced no significant effect. These results indicate CXCL7 as a key molecule in the SMC-EC communication. In the rat carotid artery balloon injury model, knocking down PKCδ in SMCs using a shRNA containing lentivirus under the control of SM22 impaired re-endothelialization of denuded carotid artery. This anti-endothelial effect of PKCδ-shRNA was rescued by supplementation of CXCL7 cDNA, which further underscores the role of PKCδ-CXCL7 pathway in regulation of the endothelial repair process.

Conclusions:
SMCs promote endothelial cell migration and re-endothelialization through a mechanism involving PKCδ-mediated expression of CXCL7.

B14

RIP3 as a Novel Regulator of Coagulation

Khoury, M.K., Pilli, S., Liu, B

Abstract Submitter	Khoury, M.K
Email Address	khoury@surgery.wisc.edu
Classification	Basic Science
Principal Investigator	Bo Liu
Science Type	Basic Science
Keywords	RIP3, Necroptosis, Coagulation, Thrombus

Introduction: Necroptosis is a form of caspase-independent cell death that has been recently discovered. Receptor Interacting Protein Kinase 3 (RIP3) mediates this process via phosphorylation of Mixed Lineage Kinase Domain-Like (MLKL) protein. However, emerging evidence suggests that RIP3 is also involved in cell death unrelated processes. This study looks to evaluate RIP3's functional role in thrombosis along with the clinical implications on thrombus formation in regards to its' inhibition.

Methods: Platelet-poor plasma was prepared from mouse and human peripheral blood by centrifugation. Thrombin generation in platelet-poor-plasma (PPP) using thrombin generation assays (TGA). The Inferior Vena Cava (IVC) Ligation Model was performed on both *Rip3* wildtype (WT) and knockout (KO) mice by ligating the IVC just inferior to the renal veins. All side branches from the left renal vein to the bifurcation were ligated or cauterized. The IVC and thrombus were harvested after 48 hours.

Results: The endogenous thrombin potential (ETP) was significantly higher in the WT versus the RIP3 KO PPP. With the addition of recombinant RIP3, the ETP was able to be restored in the RIP3 KO PPP. Furthermore, the addition of recombinant RIP3 to WT PPP was able to enhance its' ETP. Using the RIP3 inhibitor GSK'843, the ETP of the WT PPP was significantly reduced compared to the untreated plasma. There was no change in the ETP when RIP3 inhibitors were used on RIP3 KO PPP. Human PPP was also subjected to treatment with RIP3 inhibitor GSK'843. Untreated human PPP had significantly higher ETP than treated human PPP. In addition, we used our novel RIP3 inhibitor, code name C9, and found that this also inhibited human PPP at a much lower concentration.

The *in vivo* effects of RIP3 on coagulation was evaluated via the use of the Inferior Vena Cava Ligation Models. The thrombus weight (TW) of WT mice (n=3) was larger compared to the RIP3 KO mice (n=2); however, this is currently not statistically significant (p=0.06). WT mice treated with C9 (n=4) versus DMSO (n=3) showed a significant reduction in TW (p=0.04).

Conclusions: RIP3 appears to have a functional role in thrombus formation. The TGA assays using PPP suggest that RIP3 has a functional role in coagulation outside of the cell, a novel finding. In addition, the IVC ligation models suggest that the absence and inhibition of RIP3 is capable of reducing thrombus formation *in vivo*. RIP3 KO mice do not have a bleeding phenotype, suggesting that targeting RIP3 for its anticoagulative properties may be safer than current pharmaceutical treatments today.

B7

Targeting FOXM1 in Vascular Smooth Muscle Cells Induces Apoptotic Cell Death

Franco S.R., Stranz A., Ljumani F., Urabe G., Stewart D, Chaudhary M, and Liu B.

Abstract Submitter	Franco, S.R.
Email Address	srfranco@wisc.edu
Classification	Postdoctoral research associate
Principal Investigator	Bo Liu
Science Type	Basic
Keywords	Smooth muscle cell, intimal hyperplasia, apoptosis, FOXM1

Introduction: Vascular smooth muscle cell (VSMC) proliferation and survival are key contributors to the initiation and progression of vascular diseases including restenosis. Forkhead Box M1 (FOXM1) is a proliferation-associated transcription factor shown to play a role in a variety of biological processes including cell cycle progression, cell survival, and apoptosis in many cell types. However, the role of FOXM1 in VSMC phenotypic transformation as a result of vascular injury following balloon angioplasty has not been studied. We hypothesize that FOXM1 modulates VSMC response by enhancing pro-proliferative and pro-survival signaling following vascular injury.

Methods: The rat carotid artery balloon injury was used to model vascular injury. Immunofluorescence staining was carried out on sections from injured carotid arteries or uninjured controls collected at 3, 7, or 14 days post injury using FOXM1, PCNA, and SMA specific antibodies. Serum deprivation/reintroduction and double thymidine block were used to synchronize rat aortic smooth muscle cells (A-10 cell line) and protein samples were collected to detect levels of FOXM1 via western blot. To inhibit FOXM1 *in vitro*, we utilized thiostrepton and FDI-6 (two chemical inhibitors of FOXM1) or siRNA-mediated knockdown of FOXM1. Smooth muscle cell viability was measure by CCK-8 assay, 7-AAD/Annexin V flow cytometry, and western blotting to detect cleaved caspase 3. Immunohistochemistry was utilized to characterize morphological changes induced by FDI-6.

Results: We observed that FOXM1 expression was up-regulated in injured arteries at day 7 and 14 post-injury**.** Expression of FOXM1 in injured arteries co-localized with PCNA, a marker of proliferation. The up-regulation of FOXM1 protein was replicated in cultured rat VSMCs by serum stimulation. We also observed that FOXM1 expression followed a cell cycle specific pattern *in vitro*. More detailed immunocytochemistry analysis revealed that FDI-6 treated VSMCs exhibit disorganized microtubule networks. Furthermore, FDI-6 treatment decreased expression of Eg5, a motor protein essential for microtubule orientation and critical for mitosis execution. Additionally, FOXM1 inhibition decreased levels of beta catenin, a known activator of cell cycle-related genes and proliferation.

Conclusions: In conclusion, our data suggest FOXM1 is critical to VSMC viability and may modulate VSMC proliferation and survival via regulation of important cell cycle and pro-proliferative proteins. Our results show FOXM1 inhibition leads to VSMC apoptosis and therefore may serve as a novel therapeutic target to prevent VSMC pathophysiology in the context of restenosis.

B10

Pharyngeal Air Pressure During Vowels and with Semi-Occluded Vocal Tract: A Pilot Study with High-Resolution Pharyngeal Manometry

Hoffmeister, J.D., Ulmschneider, C.L., Jones, C.A., McCulloch, T.M.

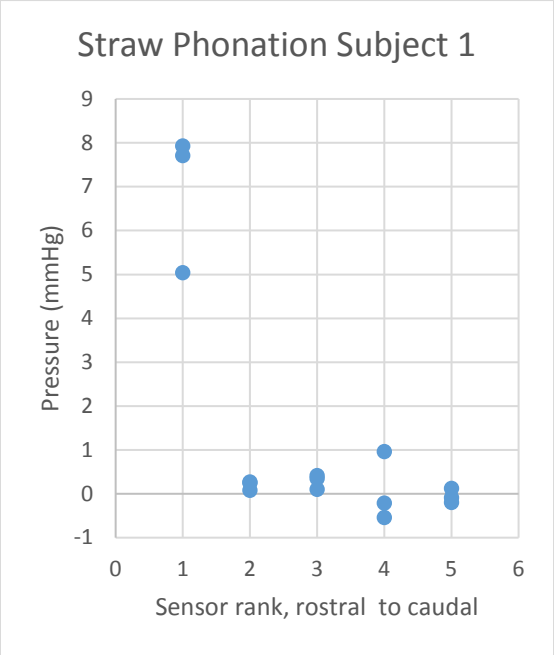
Abstract Submitter	Jesse Hoffmeister, M.S., CCC-SLP
Email Address	hoffmeister@surgery.wisc.edu
Classification	Graduate Student, Voice T32 Pre-doctoral Trainee
Principal Investigator	Timothy McCulloch, MD
Science Type	Basic Science
Keywords	Voice, Pressure, Manometry

Introduction: Semi-occluded vocal tract (SOVT) therapy is commonly used in voice training and the treatment of voice disorders. The theoretical rationale behind the use of SOVT therapy revolves around the creation of optimal resonant chamber shapes in the vocal tract. Voice therapy with SOVT therapy is thought to teach individuals to subtly modify the shape of supraglottic structures to create an epilaryngeal tube. This modification allows glottal impedance to match input impedance to the vocal tract, ultimately leading to vocal economy and efficient voice production. While several studies have measured intraoral pressure, made estimates of tracheal pressure, and directly measured subglottal and transglottal pressures during SOVT therapy, the role of laryngopharyngeal, oropharyngeal and nasopharyngeal pressures during SOVT therapy has not been explored. High-resolution pharyngeal manometry (HRPM) is a procedure used to measure pressures from the velum to the proximal esophagus during swallowing. HRPM has also been shown to accurately measure changes in pharyngeal air pressure with the use of expiratory muscle strength training (EMST) devices. The goals of this proof-of-concept pilot study were: 1) to determine whether air pressure differentials during different SOVT exercises could be detected, 2) to determine whether these differ from pressure measurements taken from the anterior oral cavity reported in other studies. We hypothesized that: 1) HRPM will acurrately measure pressure across multiple regions of the pharynx, and 2) HRPM will be able to distinguish pressure differences between open resonant vowels and various SOVT exercises.

Methods: Two healthy adult males underwent pharyngeal manometry using a high-resolution manometer with 36 circumferential pressure sensors (each 4 mm in length) spaced 1 cm apart. After catheter insertion, participants performed the following tasks: (1) sustained /a/ vowel at a comfortable loudness for 5 seconds, (2) straw blowing without phonation, (3) straw phonation, (4) lip trill and (5) voiced bilabial fricative. Pressure data was analyzed in a customized MATLAB program (MathWorks, Inc., Natick, MA). The pharyngeal area of interest was defined as the five rostral-most sensors located caudal to the velum and rostral to the UES. Mean pressure and standard deviations were calculated for each of the five sensors contained in the area of interest over a three second time interval. Pressure differences between sensors were observed, but were averaged to facilitate comparison to other studies in the literature. Pressure data from this study were then compared to that reported by Maxfield and Titze (2015).

Results: HRPM was generally well-tolerated by both subjects with no adverse events. Lowest average pressure during a phonatory task was measured on sustained /a/ for both subjects (-1.19 mmHg, SD 0.667 for Subject 1 and 0.515 mmHg, SD 0.760 for subject 2). Highest average pressure during voicing was measured during the voiced bilabial fricative (3.45 mmHg, SD 2.72 for Subject 1, and 7.40 mmHg, SD 0.956 for Subject 2). Both subjects produced pressures during straw phonation that were within the 95% confidence interval calculated from Maxfield and Titze (2015) (CI 0.666 to 3.53). Subject 1 produced pressures during voiced bilabial fricative that were within the Maxfield and Titze (2015) 95% confidence interval (CI -0.112, 7.10).

Conclusions: This study demonstrates that changes in air pressure at multiple levels in the pharynx can be consistently measured during voicing tasks with HRPM. Interestingly, both subjects showed a patern of increased pressure on a single, rostrally-located sensor, which did not appear to be an artifact of contact with a pharyngeal structure. While data obtained from HRPM during SOVTE is similar to that obtained from the anterior oral cavity as reported in the literature, it is not identical. This may represent pressure differentials between the anterior oral cavity and the pharynx during SOVTE. Future studies will perform both tasks simultaneously and with larger sample sizes.



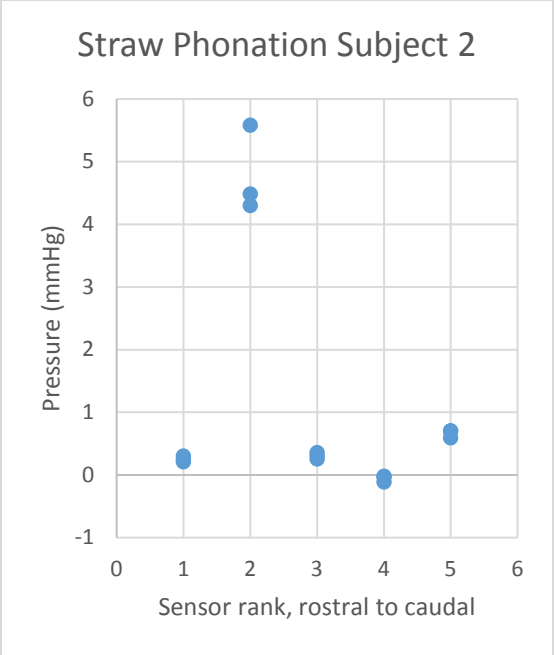


Figure 2. Pressures obtained from each of 5 sensors labeled 1-5, rostral to caudal respectively. Blue dots represent repetitions of a trial.

B5

Prolongation of Skin Allograft Survival via Indole-3-Carbinol Dietary Supplementation

Fechner J.H., Afrazi A., Owens L., Mezrich J.D.

Abstract Submitter	John Fechner
Email Address	fechner@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Joshua Mezrich
Science Type	Basic Science
Keywords	Transplantation, Diet, T Lymphocyte

Introduction: The role of the diet has been implicated in a number of biological processes including immune cell development and gut inflammatory responses. In this study, indole-3-carbinol (I3C), a dietary proligand of the aryl hydrocarbon receptor (AhR) shown to have efficacy in reducing GI-disease in rodent models, is assayed for modulatory effects in a minor antigen mismatched skin graft model.

Methods: Recipient female B6 mice were maintained on a synthetic, semi-purified diet, AIN-76A, devoid of AhR ligands (Diet) or on a diet replete with I3C (Diet + I3C) for three weeks prior to and after engraftment with a skin graft from a male B6. Graft survival time was determined, and immune response to graft was characterized.

Results: Median graft survival time was significantly prolonged for female mice maintained on Diet + I3C compared to animals maintained on Diet (42d vs 18d respectively). This was AhR-dependent. Ex-vivo production of IFNγ in response to the male antigen by Diet + I3C splenocytes or lymph nodes cells was not reduced compared to control. However, the frequency of some T cells subsets within the graft and other sites was significantly different between the two groups. Notably, IFNγ-producing CD4 T cells infiltrating the grafts of Diet + I3C fed mice on day 13 post-transplant was markedly reduced compared to control mice.

Conclusions: Addition of a dietary AhR ligand to synthetic diet devoid of AHR ligands significantly prolonged the survival of male B6 skin grafts transplanted to female B6 recipients in an AhR-dependent fashion. Prolongation of graft survival appears to be mediated via altered cell trafficking rather than immune suppression. The findings provide clues to a potential role for diet in clinical organ transplantation.

B11

Tolerogenic Nanoparticles Targeting the Aryl Hydrocarbon Receptor

Janek, K.C. [1], Fechner, J.H.[1], Mezrich, J.D.[1]

[1]University of Wisconsin School of Medicine and Public Health, Division of Transplant, Department of Surgery, Madison, WI

Abstract Submitter	Kevin Janek
Email Address	kjanek@uwhealth.org
Classification	Resident
Principal Investigator	Josh Mezrich, MD
Science Type	Basic science
Keywords	Transplant, nanoparticles, aryl hydrocarbon receptor

Introduction: Current immunosuppressive strategies after transplantation rely on non-specific global suppression of the immune system. There is a need for a novel, targeted approach to extend graft survival, reduce side-effects, and avoid global immunosuppression. The aryl hydrocarbon receptor (AHR) has been shown to have a central role in the ability of DCs to direct differentiation of Tregs from naïve T cells, and have been utilized to prolong murine skin grafts with intraperitoneal, oral or inhaled AHR ligands. Nanoparticles (NPs) have been extensively investigated for targeted drug delivery to treat various major diseases, and can significantly enhance the stability and solubility of the payloads and deliver the payloads more specifically to the targeted tissues/cells. It has recently been shown that NPs loaded with a ligand of the AHR can promote the generation of Tregs by DCs and reduce disease in murine models of EAE and diabetes. We propose the use of these tolerogenic nanoparticles (tNPs) in models of allogenic transplant as a novel method of targeted immunosuppression via the aryl hydrocarbon receptor.

Methods: PLA/PEG nanoparticles approximately 50 nm in size were designed and manufactured by the Gong lab in the Wisconsin Institute for Discovery and loaded with 2-(1H-Indol-3-ylcarbonyl)-4-thiazolecarboxylic acid methyl ester (ITE), an aryl hydrocarbon receptor ligand. Nanoparticles were also co-loaded with peptide antigen to the alpha chain of I-E (Eα-peptide) or ovalbumin to evaluate for antigen-specific response. BMDCs generated from AHR+/- and AHR-/- mice were exposed to free ITE, NP-ITE, NP-peptide/ITE. Cells were evaluated for uptake into DCs by flow cytometric analysis of Cy5.5-labeling of NP, and ability to activate AHR determined by RT-PCR expression of CYP1A1 and IDO1. Dendritic cells isolated from OT-II splenocytes were generated and exposed for 4 days to ova, NP-Ova, NP-Ova/ITE for evaluation of proliferative response and effect on cytokine production of IL-17 and IFN$\boldsymbol{\gamma}$. NPs were utilized in-vivo by injecting CFSE-labeled OT-II splenocytes IV into B6 mice, treating the following day with ova peptide or NP, and performing flow cytometric analysis of proliferation after 3 days.

Results: BMDCs cultured with NP-Ea/ITE had reliable uptake of NPs by CD11c+ cells and a subsequent 4-6 fold increase in CYP1A1 expression of AHR+/- mice over untreated control. OT-II splenocytes incubated with NP-Ova or NP-Ova/ITE had markedly suppressed generation of IL-17 or IFN$\boldsymbol{\gamma}$ compared to exposure to ova peptide alone. In-vivo experiments demonstrated significant reduction in proliferation of NP-Ova/ITE treated mice compared to NP-Ova treated mice.

Conclusions: Nanoparticles containing the aryl hydrocarbon receptor ligand ITE have been generated and used in preliminary experiments demonstrating the ability to be taken up by dendritic cells, activate the AHR, and decrease inflammatory cytokines IL-17 and IFN$\boldsymbol{\gamma}$ upon antigen stimulation in-vitro, and decrease proliferative response to stimulation in-vivo. Ongoing studies focusing on NP optimization and allogenic transplantation aim to demonstrate tolerogenic effects of these nanoparticles by targeted delivery of AHR ligand to antigen-presenting cells with greater efficiency and less toxicity than free ligand.

B16

Comparison Between Ubiquitous and Endoderm Derived Cell Fgfr2IIIb Invalidation

Kowalkowski, A., Liebl, R., Rein, S., Nichol, P.F.

Abstract Submitter	Anna Kowalkowski
Email Address	akowalkowski@wisc.edu
Classification	Graduate Student
Principal Investigator	Peter Nichol, MD, PhD
Science Type	Basic Science
Keywords	Atresia, Fgfr2IIIb, Endoderm

Introduction: *Fibroblast growth factor receptor 2IIIb (Fgfr2IIIb)* is a transmembrane receptor thought to be restricted to the intestinal epithelium during organogenesis. Homozygous mutation of this gene at conception results in 100% incidence rates of atresias of the distal colon. If this receptor is truly located only within the endodermal cell lineage, then we hypothesize that an endoderm specific mutation of this receptor would have the same intestinal phenotype as ubiquitous invalidation of the receptor.

Methods: All mice were bred on a C57B6 background. To induce a whole embryo recombination of *Fgfr2IIIb,* female *Fgfr2IIIb*$^{rec/+}$*; Hprt*$^{Cre/+}$ animals were breed with *Fgfr2IIIb*$^{flox/flox}$ males. To recombine *Fgfr2IIIb* in only the endodermal lineage, *Fgfr2IIIb* $^{flox/flox}$ animals were mated to *Fgfr2IIIb* $^{rec/+}$; *Shh* $^{cre/+}$ animals. Embryos were harvested at E18.5.

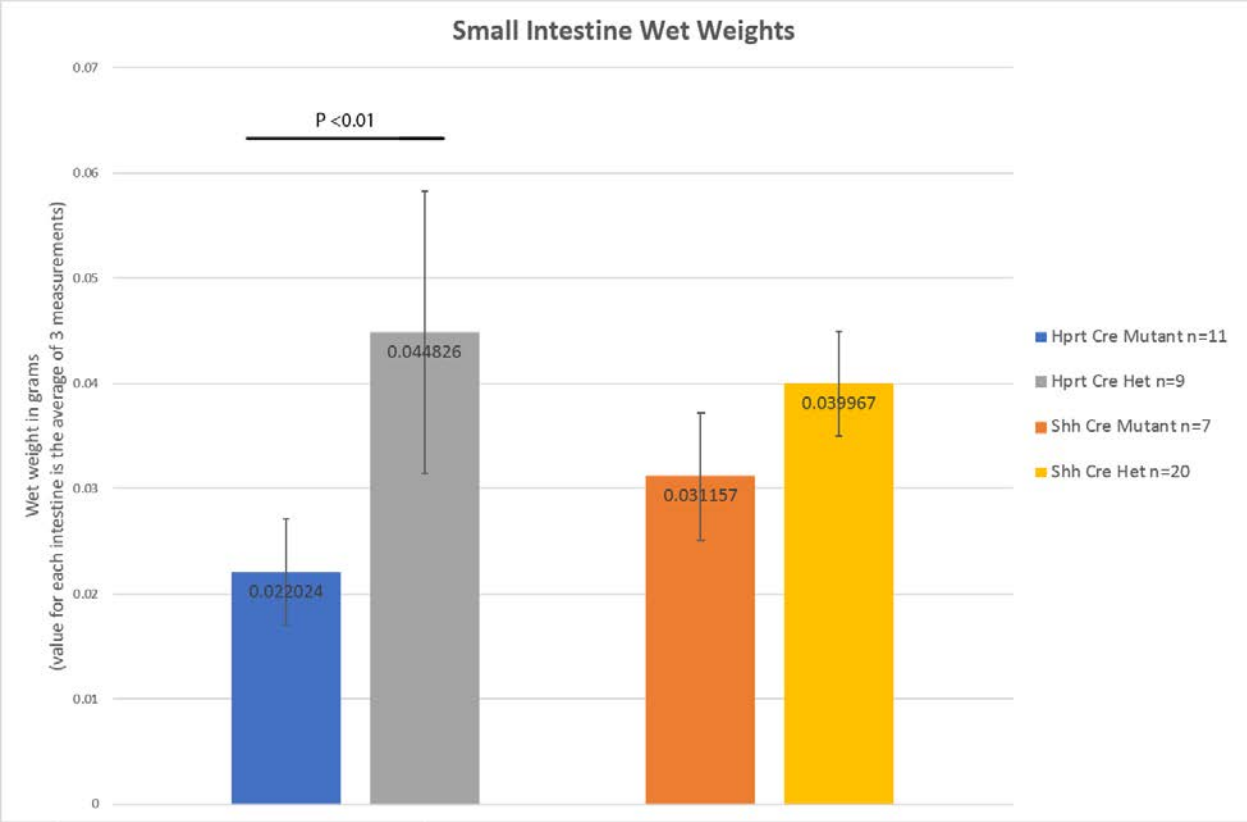
Embryos were fixed in 4% paraformaldehyde and stored in phosphate buffered saline. Intestines were dissected to determine atresia incidence rates and intestinal wet weights. Other embryos were fixed in 4% paraformaldehyde, placed into phosphate buffered saline, dehydrated, embedded in paraffin, and sectioned at 7μm for hematoxylin and eosin staining. These samples were used for villus height, villus number, and intestinal diameter measurements. A one-way ANOVA was run on the resulting measurements.

Results: Both a whole embryo or endodermal cell lineage specific knockout of *Fgfr2IIIb* lead to a 100% incidence rate of colonic atresias. However, the general phenotype of *Shh* cre (endodermal lineage) mutants is not as severe as that observed with the *Hprt* cre mutation. The loss of limbs, thin skin, and staggering size decrease seen when using an *Hprt* cre are not present in the *Shh* cre mutants.

Additionally, when examining small intestinal wet weights, villus heights, intestinal diameter, and average villus numbers between regions the two groups show distinct differences. In general, these values measured in the mutants versus phenotypically normal heterozygous littermates are significantly decreased in *Hprt* cre mutants but not in the *Shh* cre mutants.

Conclusions: Shh expression is restricted to the intestinal epithelium during intestinal organogenesis. *Shh* Cre invalidation of *Fgfr2IIIb* results in a 100% colonic atresia rate similar to that seen in the ubiquitous *Hprt* cre mutation. However, other intestinal deficits are diminished in the *Shh* Cre animals.

This leads to a question of FGFR2IIIb location of during intestinal organogenesis. If the receptor is also found in the mesoderm throughout organogenesis then this could lead to a more severe intestinal phenotype in the *Hprt* cre mutants than in the *Shh* cre mutants.


Small Intestine Wet Weights
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
P <0.01
Wet weight in grams
(value for each intestine is the average of 3 measurements)
0.022024
0.044826
0.031157
0.039967
Hprt Cre Mutant n=11
Hprt Cre Het n=9
Shh Cre Mutant n=7
Shh Cre Het n=20

B21

Investigating the Immunogenicity and Efficacy of the Syngeneically-Transplanted iPSC-Derived Pancreatic β Cells into Humanized NSG Mice

Mitchell SA, Sackett SD, Tremmel DM, Brown ME, Zhou Y, Burlingham W, Odorico JS

Abstract Submitter	Mitchell SA
Email Address	samitchell@wisc.edu
Classification	Academic Staff
Principal Investigator	Odorico JS
Science Type	Basic
Keywords	Diabetes, stem cells, immunogenicity

Introduction: Diabetes and its complications still claim the lives of millions of people despite continuing advances in insulin delivery technology primarily because insulin fails to achieve perfect glycemic control. Induced pluripotent stem cells (iPSCs), cells reprogrammed with defined factors to a pluripotent embryonic stem cell (ESC)-like state from somatic cells, hold great therapeutic promise for patients with debilitating, degenerative diseases, such as diabetes.

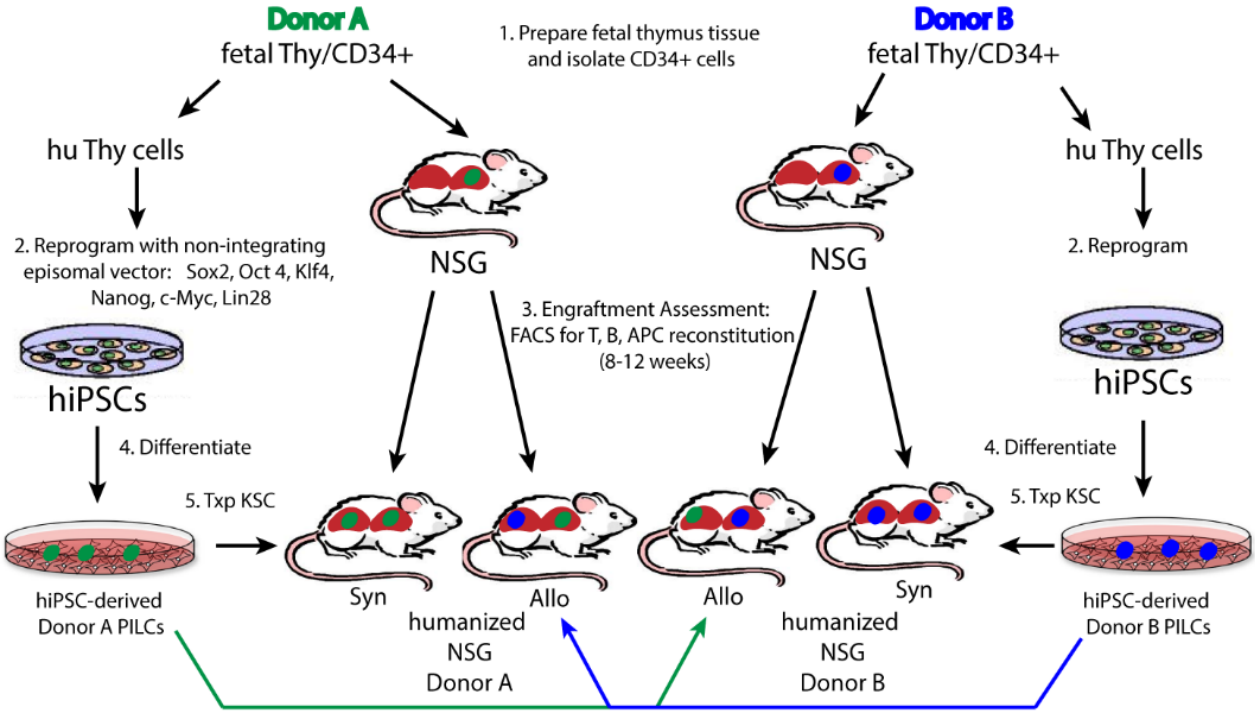
Significant progress is being made in deriving functional insulin-producing tissues from human pluripotent stem cells which can control diabetes in mouse models. We have demonstrated that both hESCs and hiPSCs have the capacity to differentiate into insulin^{+} cells *in vitro.* Consequently, human iPSC-derived pancreatic tissue grafts are a suitable test graft to address the question of whether iPSC-derived cells/tissues will be truly autologous or would be rejected by a syngeneic human immune system. The goal of this study is to elucidate the immune response evoked upon syngeneic engraftment of hiPSC-derived pancreatic progenitors (PILCs) into humanized NSG mice. We **hypothesize** that mice harboring a syngeneic human immune system will accept the iPSC derived cell grafts, while the allogeneic, non-self-derived cells will be rejected.

Methods: NSG mice were conditioned with sub-lethal levels of radiation prior to administration of human tissues and cells. Introduction of the human immune system is achieved through transplantation of human fetal thymus into the left kidney capsule of mice (6–10 weeks), immediately followed by intravenous injection of autologous isolated CD34+ cells. Engraftment is confirmed via FACS analysis for immune cell populations. Syngeneic and allogeneic iPSCs were generated via nucleofection with pluripotency-inducing episomal vectors to deliver transcription factors OCT4, SOX2, LIN28, KLF4, c-Myc and Nanog to human cells (CD34+, thymus epithelial cells). Immunohistochemistry was performed to confirm expression of pluripotency markers.

The hiPSCs are differentiated into pancreatic progenitor cells according to our differentiation protocol and transplanted under the right kidney capsule of the humanized mice. Human immune cell engraftment from blood and kidney grafts were analyzed postmortem at 8 and 12 weeks post-transplant. Kidney sub-capsule grafts were fixed and sectioned for immunofluorescence (IF) to identify immune infiltration (CD3/4/8/FoxP3) and graft development. Humanized mouse spleens were removed at the experiment end point for a T cell proliferation assay. Isolated splenic T cells were incubated with CFSE proliferative dye and CD3/CD28 activator for 72hr. Cells were collected and stained for flow cytometry to examine subsequent T-cell generations.

Results: Circulating human immune cell numbers increased over the course of the experiments showing that the mice remained humanized throughout the time course. Preliminary results suggest that syngeneic grafts are not rejected and further analysis of these populations is ongoing. IF staining of kidney sub-capsule grafts containing allogeneic cells showed an increased presence of CD3+ cells and very few insulin positive cells, whereas the syngeneic grafts contained insulin positive grafts. Syngeneic grafts also contain CD3 (T cells), however with further analysis, many of these cells were also positive for FoxP3 (Regulatory T cell) staining, which may indicate a protective capacity. Quantification of these populations is ongoing. The CFSE assay showed that the humanized mouse splenic T cells were capable of activation in a functional assay.

Conclusions: In this study, we seek to clarify the adaptive immune response to *human* iPSC-derived cells using pancreatic beta cell grafts in an established humanized mouse model, an essential step before translation to the clinic. A more detailed analysis of the immune populations is required to understand the complex response to iPSC grafts.



Controls

1. HFP graft Donor A (syn)
2. Human isolated islets (allo)
3. HFP graft Donor B (allo)
4. Non-humanized NSG (neg)

Readouts

1. serum human C-peptide
2. serum glucose
3. metabolic profile: GTT
4. graft histology

B29

Pancreatic ECM Co-Culture Enhances Phenotypic Maturity of Stem Cell-Derived Beta Cells

Tremmel D.M., Sackett S.D., Curran A, Feeney A.K., Mitchell S.A., Jain V.S., Quirini N.Q., Odorico J.S.

Abstract Submitter	Daniel M Tremmel
Email Address	tremmel@wisc.edu
Classification	Graduate Student
Principal Investigator	Jon Odorico
Science Type	Basic Science
Keywords	Extracellular matrix, stem cells, beta cells

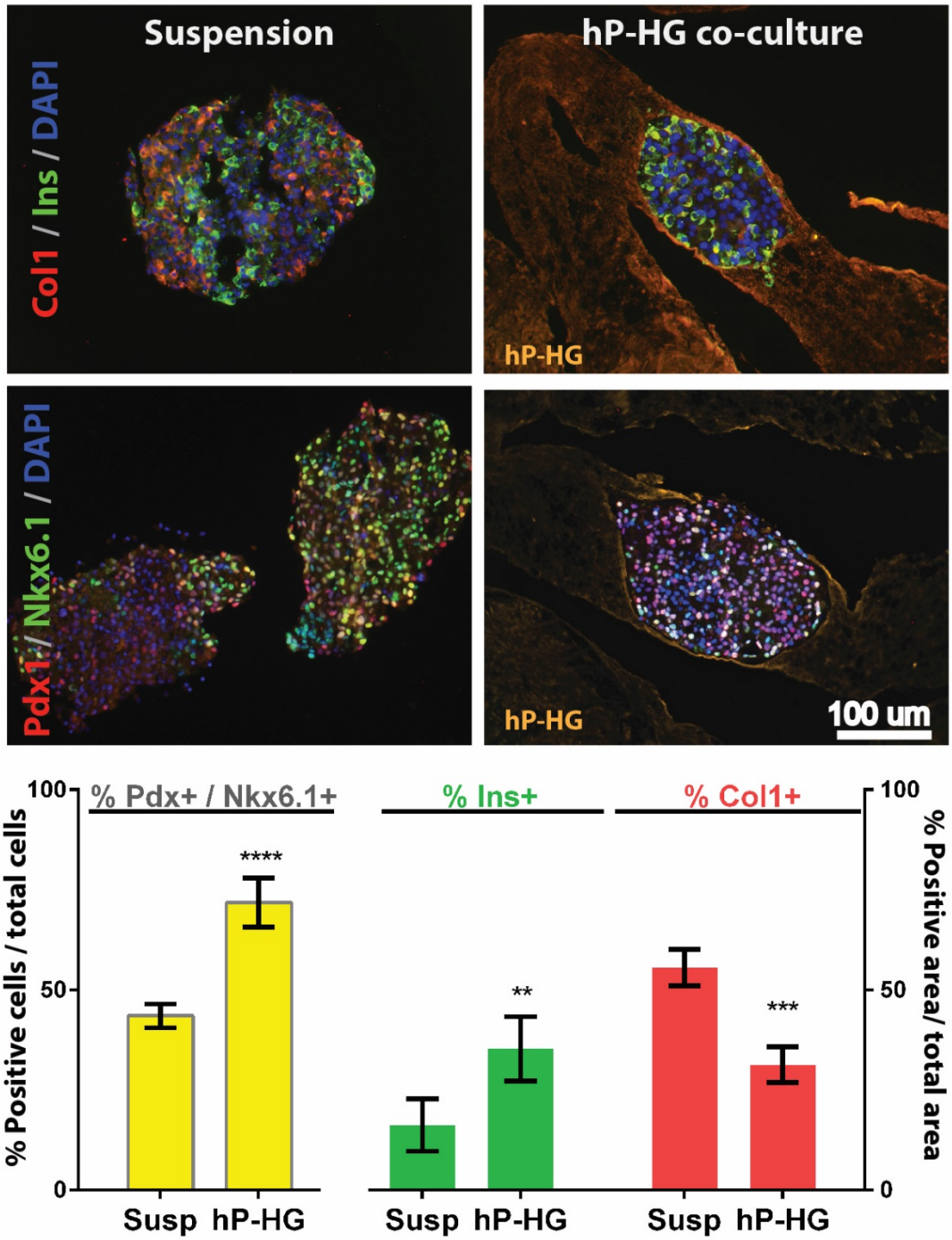
Introduction: Stem cell-derived β cells (SCβCs) could provide an abundant supply of insulin-producing cells for diabetic patients. Despite remarkable progress in SCβC differentiation, fully mature phenotypes have not been consistently achieved *in vitro*. Extracellular matrix (ECM), the tissue-specific scaffold in which cells differentiate *in vivo*, provides chemical signals to developing cells. No studies to date have explored the potential of using human pancreatic ECM (hP-ECM) to enhance the differentiation of SCβCs. Our lab has produced a novel hydrogel scaffold from decellularized hP-ECM, which retains many of the native ECM molecules and is cytocompatible in 3D tissue culture. We hypothesize that co-culture of hP-ECM hydrogel (hP-HG) with SCβCs will enhance β cell maturation, reflected in increased β cell-specific gene expression and function of the cells.

Methods: In four biological replicates, hESCs were differentiated into SCβCs following a 28-day differentiation protocol. On day 11 or day 18, cells were embedded into 10 uL hP-HG droplets and cultured through the remainder of the 28 day protocol. In parallel, cells were cultured in suspension in the absence of added ECM, as per the standard differentiation protocol. On the final day of differentiation, hydrogel constructs and suspension culture controls were collected for comparative analysis. Immunofluorescent (IF) staining was performed and quantified using ImageJ to assess expression of Pdx1 and Nkx6.1, which are uniquely co-expressed in pancreatic β cells. Insulin and Urocortin 3 expression, indicative of β cell maturation, were also assessed. RNA was collected to assess gene expression through QPCR. A panel of 17 key islet endocrine genes was tested, comparing the control group to the hydrogel treatment to assess enhancement of expression. All groups were normalized to undifferentiated human stem cells and compared to isolated human islets.

Results: Following hP-HG co-culture, insulin, somatostatin, urocortin-3 (Ucn3), glucose transporter 2 (Glut2), NeuroD1 and IAPP gene expression was significantly upregulated in SCβCs compared to suspension controls. Through IF staining, cell clusters co-cultured with hP-HG contained 34.9% Ins^+ area, while suspension cultured contained only 16.2%. Co-expression of the critical beta cell transcription factors Pdx1 and Nkx6.1 was found in 72.1% of hP-HG cultured cells, while only in 43.5% of suspension cultured cells. Furthermore, 54.7% of total cellular area was Col1+ in suspension, while only 31.6% of the area was $Col1^+$ in the hP-HG embedded cell clusters, suggesting that hydrogel culture may reduce the need for the differentiated cells to produce their own Collagen 1 (Figure 1).

Conclusions: These results suggest pancreatic ECM may improve the efficiency of differentiation toward a more mature β cell fate. This is reflected in a higher percentage of Pdx1/Nkx6.1 co-positive cells, as well as improved gene expression of a variety of endocrine genes. Future studies testing β cell survival and function following hP-HG co-culture will be necessary to verify improvement in β cell differentiation.

Figure 1:


Suspension
hP-HG co-culture
Col1 / Ins / DAPI
hP-HG
Pdx1 / Nkx6.1 / DAPI
hP-HG
100 um
% Pdx+ / Nkx6.1+
% Ins+
% Col1+
% Positive cells / total cells
% Positive area/ total area
100
50
0
****
**
***
Susp
hP-HG
Susp
hP-HG
Susp
hP-HG

B1

BLyS Deficient Rats Inhibit Donor Specific Antibody (DSA) Production and B Lymphocyte Proliferation in Rodent Model

Bath N.M., Verhoven B.M., Wilson, N.A., Redfield III R.R.

Abstract Submitter	Natalie Bath
Email Address	nbath@wisc.edu
Classification	Resident
Principal Investigator	Robert Redfield
Science Type	Basic science
Keywords	Alloantibody, B cells, antibody mediated rejection, kidney transplant

Introduction: APRIL (A proliferation inducing ligand) and BLyS (B Lymphocyte Stimulator) are two critical survival factors for B lymphocyte maturation and plasma cells, the main source of alloantibody. We generated rats deficient in APRIL and BLyS to characterize the effects of targeting these cytokines in our established rodent model of antibody mediated rejection (AMR) in kidney transplant. Here we report our initial phenotyping and response to alloantigen in these novel rodents.

Methods: Using CRISPR/Cas9 we engineered APRIL$^{-/-}$ and BLyS$^{-/-}$ Lewis rats. Collected tissues were analyzed using flow cytometry, ELISPOT, and immunohistochemistry (IHC). APRIL$^{-/-}$ and BLyS$^{-/-}$ rats were sensitized with Brown Norway (BN) blood (complete MHC mismatch). Flow cross match and a 3 day mixed lymphocyte reaction (MLR) was performed with wild type (WT), APRIL$^{-/-}$, and BLyS$^{-/-}$ rats to assess DSA (Donor Specific Antibody) production and cell proliferation, respectively. Anti-PAX5 antibody was used to stain for B lymphocytes in sectioned spleens.

Results: When challenged with alloantigen, sensitized BLyS$^{-/-}$ had significant decreases in DSA when compared to WT and APRIL$^{-/-}$. MLR demonstrated a significant decrease in BLyS$^{-/-}$ cell proliferation when challenged by BN splenocytes compared to APRIL-/- and WT ($p<0.02$). Additionally, BLyS$^{-/-}$ significantly depleted antibody secreting cell production of IgM and IgG in all tissues compared to WT and APRIL$^{-/-}$ ($p<0.04$). BLyS$^{-/-}$ demonstrated a significant reduction of splenic marginal zone B lymphocytes detected by anti-PAX5 compared to both WT and APRIL$^{-/-}$ ($p<0.0001$) (Figure 1).

Conclusions: BLyS$^{-/-}$ produced fewer alloantibodies and demonstrated a significant reduction in cell proliferation when challenged with alloantigen. Antibody secreting B lymphocytes and splenic germinal centers are also depleted in BLyS$^{-/-}$, which translates into a reduction of alloantibody production. Future studies will characterize rodents deficient in both APRIL and BLyS and apply this to kidney transplant model as a method to prevent AMR.

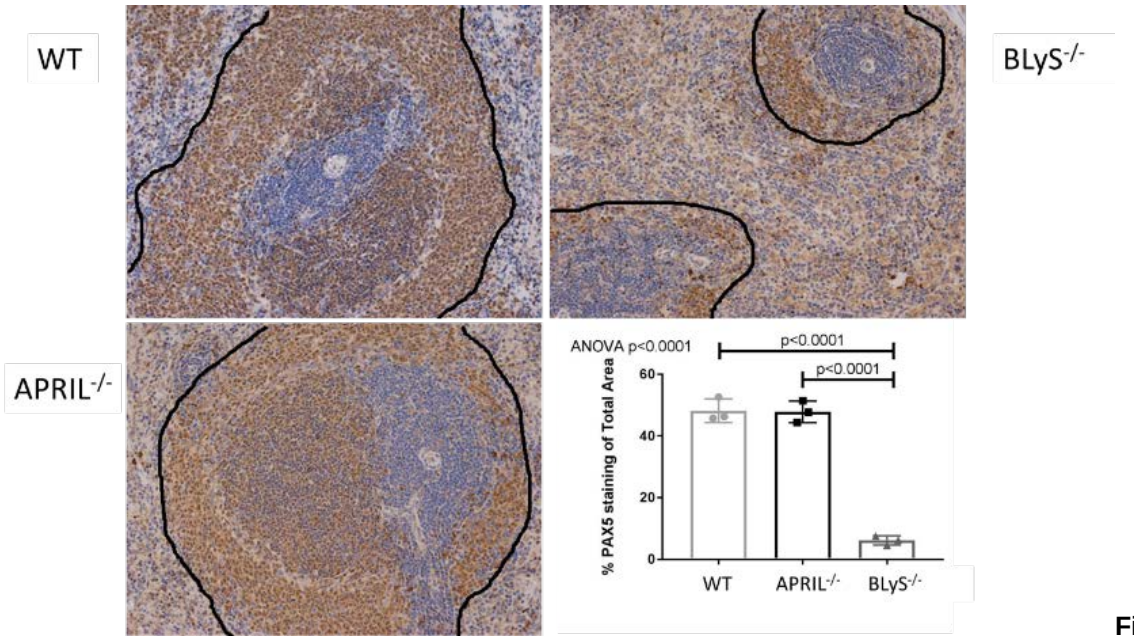


Figure 1: BLyS$^{-/-}$ demonstrated significant disruption of marginal zone B lymphocytes in spleen compared to WT and APRIL$^{-/-}$. Germinal centers outlined in black. Brown staining represents marginal zone B lymphocytes stained with anti-PAX5 antibody.

B27

In vivo Protein Turnover Rates Across the Proteome for Various Mouse Tissues

Rolfs Z.J., Frey B.L., Shi X., Kawai Y., Welham, N.V.

Abstract Submitter	Rolfs Z.J.
Email Address	zrolfs@wisc.edu
Classification	Graduate student
Principal Investigator	Welham N.V.
Science Type	Basic Science
Keywords	Protein turnover rates, quantitative proteomics, extracellular matrix

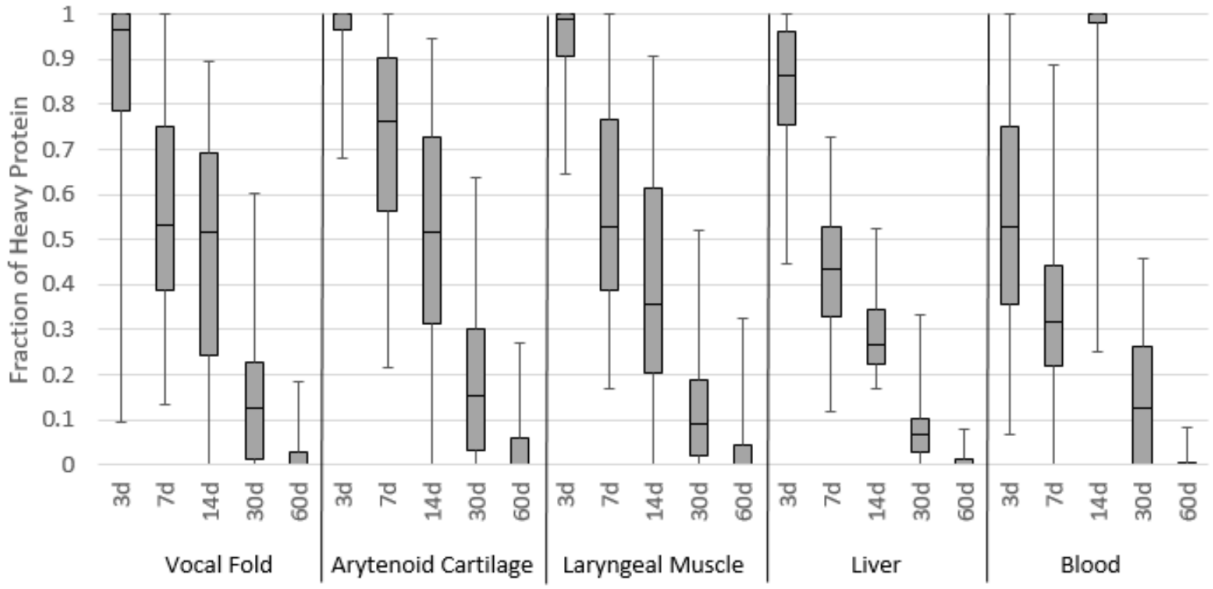
Introduction: Protein turnover is critical for the regulation of cellular processes. The unique rates of protein synthesis and degradation for each protein are defining features of each tissue type, and these differences result in widely varying tissue functions. Using stable isotope labeling, we have determined the *in vivo* protein turnover rates for thousands of proteins in several mouse tissues. This has resulted in the generation a reference table for wild type protein synthesis and degradation rates that could be used as a control resource when studying protein turnover rates under varied conditions, such as in response to stress or therapeutic treatments.

Methods: NSGW mice were supplied a lysine depleted diet and supplemented with heavy lysine (+8 Da) over three generations, such that 99% of all lysines in the mice were heavy lysines. After determining near complete heavy incorporation, the mice were switched to a light lysine diet. Mice were sacrificed at 3, 7, 14, 30, and 60 days after switching to the light lysine diet, with five mice for each timepoint. Surgically-dissected tissue samples were homogenized, and proteins were extracted, prepared, digested with LysC, and analyzed by mass spectrometry. FlashLFQ in MetaMorpheus was used to quantify the identified peptides, search for the complementary heavy and light peptides, and match peptides between runs.

Results: We were able to identify and quantify roughly 3000 proteins in each tissue. The half-life of protein turnover was on the order of days, with substantial tissue-specific and protein-specific variations. After 60 days, most proteins had been completely turned over. Some tissues, such as vocal folds, had much slower overall turnover rates in comparison to other tissue types like liver. Interestingly, most proteins were identified in multiple tissues and exhibited different turnover rates in the different tissues. Therefore, the differences between tissues may depend more on the turnover rates of shared proteins than on the presence of unique, tissue-specific proteins. We additionally observed evidence of amino acid “recycling”, wherein a single peptide contained both a heavy and a light lysine, suggesting that the original parent protein was synthesized after switching to light food, but that the synthesis partially incorporated heavy lysine from previously degraded heavy proteins.

Conclusions: Stable isotope labeling has been used to investigate *in vivo* protein turnover for several tissues in mice. We determined the protein synthesis and degradation rates for thousands of proteins and observed substantial differences in those rates across the various tissues. The data generated through this study serve as a resource for tissue-specific protein turnover rates in mice.

Fraction of Original Protein Remaining Over Time



B19

Amniotic Fluid Assists in Separation of Murine Vocal Folds

Lungova V., Lunga T., Thibeault S., L.

Abstract Submitter	Vlasta Lungova
Email Address	lungova@surgery.wisc.edu
Classification	Faculty staff
Principal Investigator	Susan Thibeault
Science Type	Basic Science
Keywords	Amniotic fluid, Epithelial Lamina, Remodeling

Introduction: Amniotic fluid is found inside the amniotic sac in mammals. It is produced by the fetal lungs and kidneys, it is taken up with fetal swallowing and sent across the placenta to the mother's circulation. Too much or too little amniotic fluid is associated with abnormalities in development and pregnancy complications. These abnormalities are mainly associated with defects of the gastrointestinal, respiratory and renal tracts. Because the larynx sits at the crossroad between respiratory and digestive tracts, we assume that amniotic fluid will also affect the formation of vocal folds. Based on these findings we hypothesize that 1) amniotic fluid assists in VF separation and 2) amount of the amniotic fluid affects the shape of the vocal folds.

Material and Methods: Five pregnant females at day 15.5 of the gestation period underwent surgery. The peritoneum was opened and embryos were removed. Depending on the size of the litter, two to four embryos underwent a puncture of the amniotic sac with a 21G needle. Remaining embryos were left as controls. Embryos were then returned to their initial position in utero. The peritoneum was flushed with saline and closed with sutures; skin was closed with clips. Tissue collection was performed day 1 and 2 post-surgery. Neck regions of dissected embryos at embryonic (E) day E16.5 and E17.5 were fixed with 4% paraformaldehyde overnight at 4^0C, rehydrated, treated with xylene, embedded in paraffin and cut into serial sections (5 m). Section samples were stained with hematoxylin-eosin (H&E) to assess morphology. Staining for Cytokeratin (K) 8, p63 and Collagen 1 (Col1) was performed to investigate remodeling of the epithelial cell layer and the lamina propria.

Results: At E16.5, in controls, the vocal folds were typically separated. In contrast, in drained embryos, vocal folds were partly fused with apical K8+ cells detached from the cell layers beneath. At E17.5, in drained embryos, the vocal folds fully separated. Polyp-like structures appeared in the vocal fold mid-membranous region. Notably, these polyps were covered with K8+ epithelium without a clearly defined p63+ progenitor basal layer. On the other hand, in controls, the epithelium was composed of two cell layers, a p63+K8- basal and p63- K8+ suprabasal layer, rather cuboidal in shape. We further observed downregulation of Col1 in the lamina propria in drained embryos at E17.5 as compared to controls.

Conclusion: In summary, drainage of amniotic fluid causes delayed vocal fold separation accompanied with structural changes of the vocal fold epithelium and lamina propria. The presence of amniotic fluid is an important factor in the development of normal structure.

B22

Characterizing Ontogeny of Yap in Proliferating and Differentiating Vocal Fold Epithelial Progenitors during Embryonic Development in a Murine Model

Mohad V., Bartley S., Thibeault S

Abstract Submitter	Vidisha Mohad
Email Address	mohad@wisc.edu
Classification	Doctoral Candidate
Principal Investigator	Susan Thibeault
Science Type	Basic Science
Keywords	Vocal folds, Hippo pathway, development

Understanding molecular genetic mechanisms during embryogenesis is relevant in advancing the knowledge of basic biology of vocal fold (VF) development, and to biomedical research efforts utilizing progenitors and stem cells for therapeutic interventions for VF disorders. In this study we have, for the first time assessed the expression of Hippo pathways downstream effector Yap, alluding to its function in VF epithelial progenitors during development. We analyzed expression patterns of Yap and phosphorylated Yap (p-Yap) in VF epithelial development. By describing the overall temporal and spatial patterning of Yap expression, we have now begun to understand the importance of Yap and the Hippo pathway in VF epithelial morphogenesis. Using a murine model, we hypothesized that Yap regulates the proliferation and differentiation of epithelial progenitors in developing VFs. As Yap controls the balance between cellular proliferation and differentiation, we hypothesize that the VF epithelial morphogenesis will be primarily caused by increased cellular proliferation during the early embryonic stages (E10.5 through E15.5). Utilizing wild type FVB/N mice, tissue was harvested from embryonic larynges. Pregnant females were sacrificed at E10.5, E11.5, E13.5, E15.5, E16.5, E18.5 and pups were sacrificed at P0, P1, P2, P4, P6 weeks and adult (8 weeks). Embryos were fixed, processed to form paraffin-embedded sections. Immunofluorescence was completed at each time point using mouse anti-Yap, rabbit anti-phospho-Yap antibodies and co-staining of Yap and phospho-Yap. Cell proliferation assay was performed to by using thymidine analogue Edu into newly synthesized DNA. We found prominent expression of Yap in earlier developmental stages specifically E10.5, through E15. In these time points IF analysis of total Yap revealed a markedly distinct subcellular distribution in the epithelial cells compared to the developing mesenchyme. Total yap is ubiquitously distributed but appeared to be strongest in the VF epithelium. In epithelial cells, we observed both nuclear and cytoplasmic Yap expression however; the nuclear Yap expression is strongest in stages E10.5 through E15.5, indicating that Hippo Pathway is off during these developmental stages. Through E16.5 to adulthood Yap remains in phosphorylated form in the cytoplasm suggesting that in these stages the Hippo pathway activity is on. A comparison of the staining patterns of total Yap and phosphorylated Yap (pYap) revealed a pattern as reported in other contexts. We also discovered that epithelial cells are in high proliferative stage during E10.5, E11.5 and E13.5 time points with a noteworthy decrease after these time points This increase in Yap activity during early time points alludes to the correlation between Hippo pathway and cell proliferation. Presence of nuclear Yap suggests local activation of Yap-mediated transcriptional program controlled by inactivity of Hippo pathway during morphogenesis. We propose that knowledge of the Yap expression during morphogenesis is the first crucial step in uncovering the critical role of the Hippo-YAP pathway in VF epithelial development and understanding epithelial disorders such as VF epithelial hyperplasia and cancer. This proposed work has implications beyond development and can potentially advance future investigations in epithelial development, epithelial cancer and regeneration.

B9

Cryotherapy Has Antifibrotic and Regenerative Effects on Human Vocal Fold Fibroblasts

Gong T., Zhang C., Kang J., Lamb J., Jiang J.J.

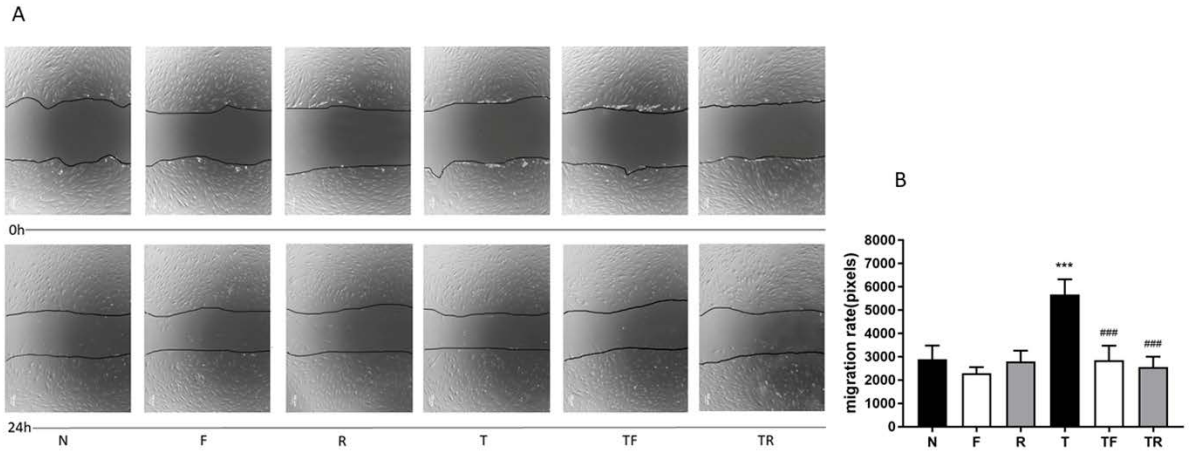
Abstract Submitter	Gong Ting
Email Address	kagomegong@163.com
Classification	faculty
Principal Investigator	Gong T., Zhang C., Kang J., Lamb J., Jiang J.J.
Science Type	Basic Science
Keywords	Cryotherapy, vocal fold fibroblasts, extracellular matrix, antifibrotic, regenerative

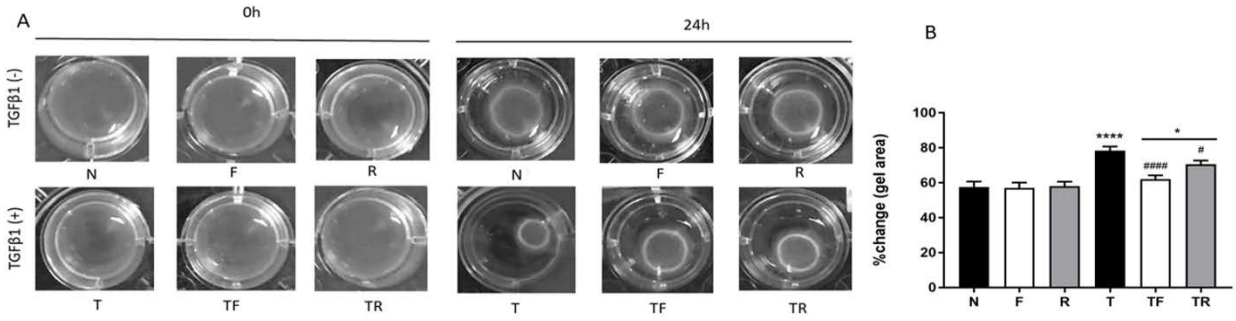
Introduction: Vocal fold scarring remains a major treatment challenge, and scar prevention without residual lesions remains a dilemma. Cryotherapy has shown cosmetic outcomes on skin lesions with minimal scarring. The aim of this study was to clarify the beneficial effects of cryotherapy for the prevention and the treatment of vocal fold scarring.

Methods: Primary cultures of human vocal fold fibroblasts (VFFs) were used in this study. Myofibroblast differentiation was stimulated by transforming growth factor β1 (TGF-β1). We mimicked the cryotherapy effect on vocal fold healing in vivo by freezing VFFs ± TGF-β1 in vitro. The influence of freezing on cell viability, proliferation, migration, and contractile properties were analyzed. The expression of collagen I, collagen III, fibronectin, TGF-β1, matrix metallopeptidase 1 (MMP1), hyaluronan synthase 1 (HAS1) were investigated by real-time polymerase chain reaction (RT-PCR), and the expression of alpha smooth muscle actin (α-SMA) and decorin were investigated by RT-PCR and Western blot.

Results: Freezing was found to modify extracellular matrix (ECM) synthesis and differentiation of VFFs. Expression of collagen I, collagen III, fibronectin, α-SMA, and TGF-β1 was downregulated, and MMP1 was upregulated in VFFs + TGF-β1 (myofibroblast) by freezing. HAS1 and decorin were upregulated in both VFFs ± TGF-β1 by freezing. Freezing VFFs + TGF-β1 (myofibroblast) with fast thawing had a lower expression of α-SMA when compared with slow thawing. Freezing reduced the migration and collagen contraction of VFFs + TGF-β1 (myofibroblast).

Conclusions: Cryotherapy induces antifibrotic and regenerative ECM alterations in VFFs. These data provide insight into the prevention and the treatment of vocal fold scarring with cryotherapy in phonomicrosurgery.


A
0h
24h
N
F
R
T
TF
TR
B
migration rate(pixels)
8000
7000
6000
5000
4000
3000
2000
1000
0
***
###
###
N
F
R
T
TF
TR


A
0h
24h
TGFβ1 (-)
TGFβ1 (+)
N
F
R
T
TF
TR
B
%change (gel area)
100
80
60
40
20
0
****
####
*
#
N
F
R
T
TF
TR

B15

Imaging and Quantifying Dehydration and Rehydration in Vocal Fold Tissue Layers

King R.E., Steed K., Rivera A.E., Wisco J.J., Thibeault S.L.

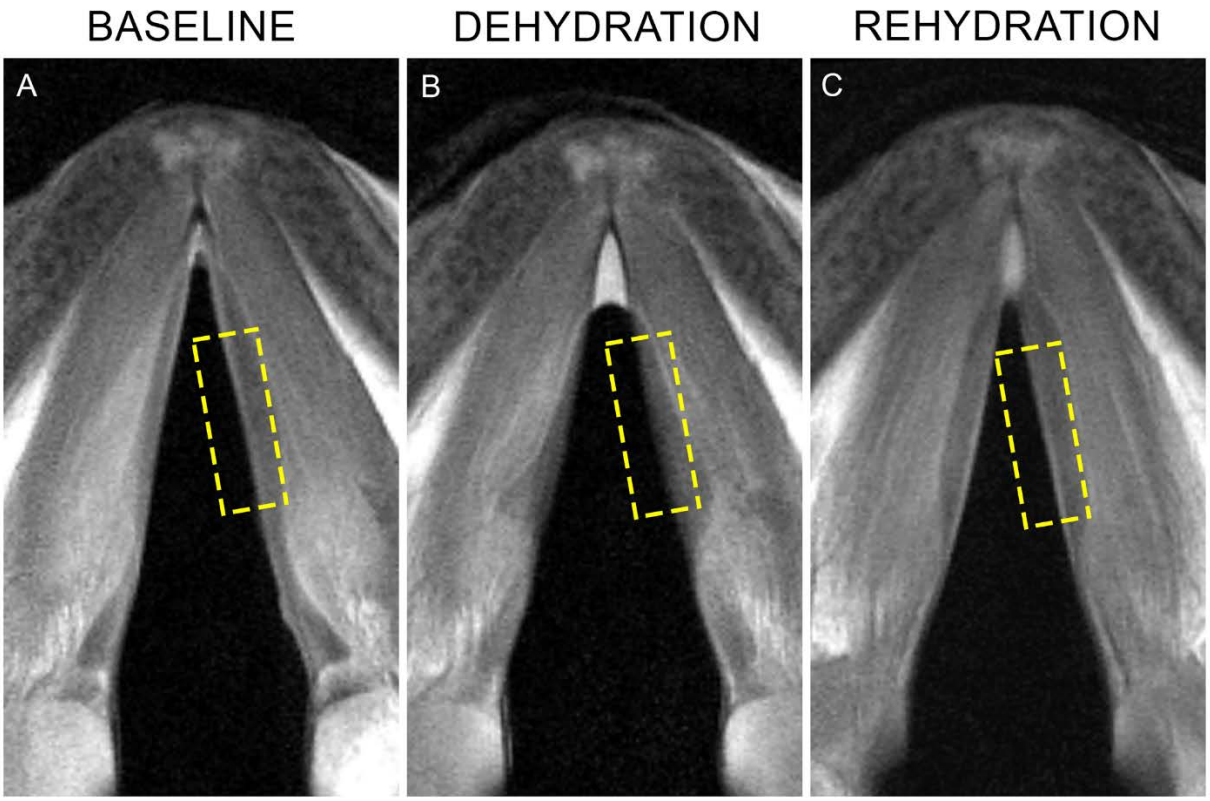
Abstract Submitter	Renee King
Email Address	kingr@surgery.wisc.edu
Classification	Graduate Student
Principal Investigator	Susan Thibeault
Science Type	Basic Science
Keywords	voice, hydration, laryngeal imaging

Introduction: Clinicians commonly recommend increased hydration to patients with voice disorders. However, effects on clinical voice outcome measures have been inconsistent. Hydration-induced change within different layers of vocal fold tissue is currently unknown. Magnetic resonance imaging (MRI) is a promising method of noninvasively measuring water content in vocal folds *in vivo*. The objective of this study was to image and quantify changes in water content within separate vocal fold tissue layers after dehydration and rehydration.

Methods: Excised porcine larynges (N = 30) were imaged using proton density-weighted MRI (PD-MRI) (1) at baseline and (2) after immersion in one of five hypertonic, isotonic, or hypotonic solutions or in dry air. Larynges dehydrated in hypertonic solutions or dry air were rehydrated and imaged a third time. Normalized signal intensity was measured in vocal fold mucosa and thyroarytenoid muscle.

Results: Scans revealed fluid-rich vocal fold mucosa that was distinct from muscle at baseline. Baseline normalized signal intensity in mucosa and muscle varied by left vs. right vocal fold ($p < 0.01$) and by anterior, middle, or posterior location ($p < 0.0001$). Intensity changes in the middle third of vocal fold mucosa differed by solution after immersion ($p < 0.01$). Hypertonic solutions dehydrated the middle third of mucosa by over 30% ($p < 0.001$). No difference from baseline was found in anterior or posterior mucosa or in muscle after immersion. No association was found between intensity change in mucosa and muscle after immersion. After rehydration, intensity did not differ by solution in any tissue, and was not different from baseline, but post-rehydration intensity was correlated with post-immersion intensity in both mucosa and muscle ($p < 0.05$).

Conclusions: PD-MRI can be used to visualize large mammalian vocal fold tissue layers and to quantify changes in water content within vocal fold mucosa and thyroarytenoid muscle independently. Degree of change in vocal fold water content induced by hypertonic solutions *ex vivo* persists after rehydration.



PD-MRI scans of *ex vivo* porcine vocal folds. Representative images of slices through vocal folds of the same larynx at different timepoints. (A): Baseline. (B): After dehydration in 30% NaCl. (C): After rehydration in H2O. Dashed boxes highlight mucosa at the vocal fold edge.

B6

Human vocal fold fibroblast genotype uniquely differentiated to maintain local biomechanical homeostatic fluctuations

Alexander Foote, Ziyue Wang, Christina Kendziorski, Susan L. Thibeault

Submitter	Alexander Foote
Phone	716-706-9322
Email Address	foote@surgery.wisc.edu
Classification	Predoctoral graduate student
Division	Otolaryngology
Lab	Dr. Susan Thibeault
Science Type	Basic Science
Keywords	Vocal fold biology, human vocal fold fibroblast, functional gene expression, transcriptome profiling, mechanobiology

Abstract Starts on Page 2.

Introduction: Numerous physiological and pathophysiological aspects of vocal fold fibroblast (VFF) function remain poorly understood, however it is becoming established that physical forces, such as mechanical stress, are essential for tissue homeostasis and influence gene expression of these cells. The purpose of this study was to compare the VFF genotype with their cellular counterparts at various anatomic locales to identify differences in functional gene expression profiles.

Methods: In vitro. We compared seven normal human fibroblast primary cell lines from healthy cadavers, which included: vocal fold, trachea, lung, abdomen, scalp, upper gingiva, and soft palate. Primary cultures were validated with a subtractive immunocytochemical methodology for confirmation of fibroblast lineage with next generation RNA-sequencing performed. DESeq2 was applied for identification of differentially expressed gene programs and a functional enrichment analysis was completed.

Results: Unsupervised gene expression analysis yielded 3999 genes differentially expressed. Hierarchical cluster analysis revealed fibroblast grouping based on anatomic site origin rather than cells from the same donor, suggesting global phenotype heterogeneity. Sex and age-related effects were negligible. Functional enrichment analyses based on post-hoc comparisons revealed several functional themes related to transcription factors for signaling pathways regulating pluripotency of stem cells as well as extracellular matrix components such as cell signaling, migration, proliferation, and differentiation potential.

Conclusions: Human fibroblasts display a phenomenon of global topographic differentiation, which is maintained in isolation via in vitro assays. Epigenetic mechanical influences on vocal fold tissue may play a role in uniquely modeling and maintaining the local environmental cellular niche during homeostasis with VFFs distinctly specialized related to their anatomic positional and developmental origins established during embryogenesis.

B4

Characterization of Single Nanometer Ultrafine Oxygen Nanobubble Water

Darwich B., Shriver T., Igari K., Kelly M.J, Schoeller D.A., Yamanouchi D.

Abstract Submitter	Banan Darwich
Email Address	darwich@wisc.edu
Classification	Academic Staff
Principal Investigator	Dr. Dai Yamanouchi
Science Type	Basic Science
Keywords	Ultrafine Nanobubble, Nanobubble O_2, Bubble Stability

Introduction: Nanobubbles are nanoscopic gaseous pockets in aqueous solutions whose diameters are less than 1µm. They are preferred to microbubbles as they are stable for long periods of time in solution, and because they can flow through the smallest of capillary vessels in vivo.

Creation of nanobubbles can be achieved in a number of ways; most use the cavitational properties of ultrasonic waves to create nanobubbles. However if not stabilized with a surfactant, the bubbles would burst upon removal of the ultrasonic source. Thus an amphipathic molecule such as phospholipids is added to generate stabilized nanobubbles. However such procedure is very complex and most stabilizing compounds are non-biocompatible and toxic. The current smallest nanobubble size achieved is 20nm.

In our lab, in collaboration with the inventors, we have the only ΣPM–5 device in the U.S. It produces nanobubbles with diameters lying within the single nanometer range as tested with cryo-transmission electron microscopy and dynamic light scattering. These nanobubbles are stable for weeks after production without the use of a stabilizing agent. We hypothesize that O_2 nanobubble water has the ability to increase the intracellular oxygen concentration and protect the cells from hypoxic injury which is a common feature of many heart diseases and malignancies.

Methods: Formation of Oxygen NBs by ΣPM–5 device: Water and oxygen were mixed at 0.4MPa. The collision force of two opposing streams of the water/gas mix as it gets pushed out at very high velocity creates the NBs.

Analysis of the gaseous content of the NB water: Water was loaded in Helium flushed vacuatiners®. Headspace gas content was analyzed using Finnigan Delta Plus® Isotope ratio mass spectrometer. Sample introduction was done via the dual inlet.

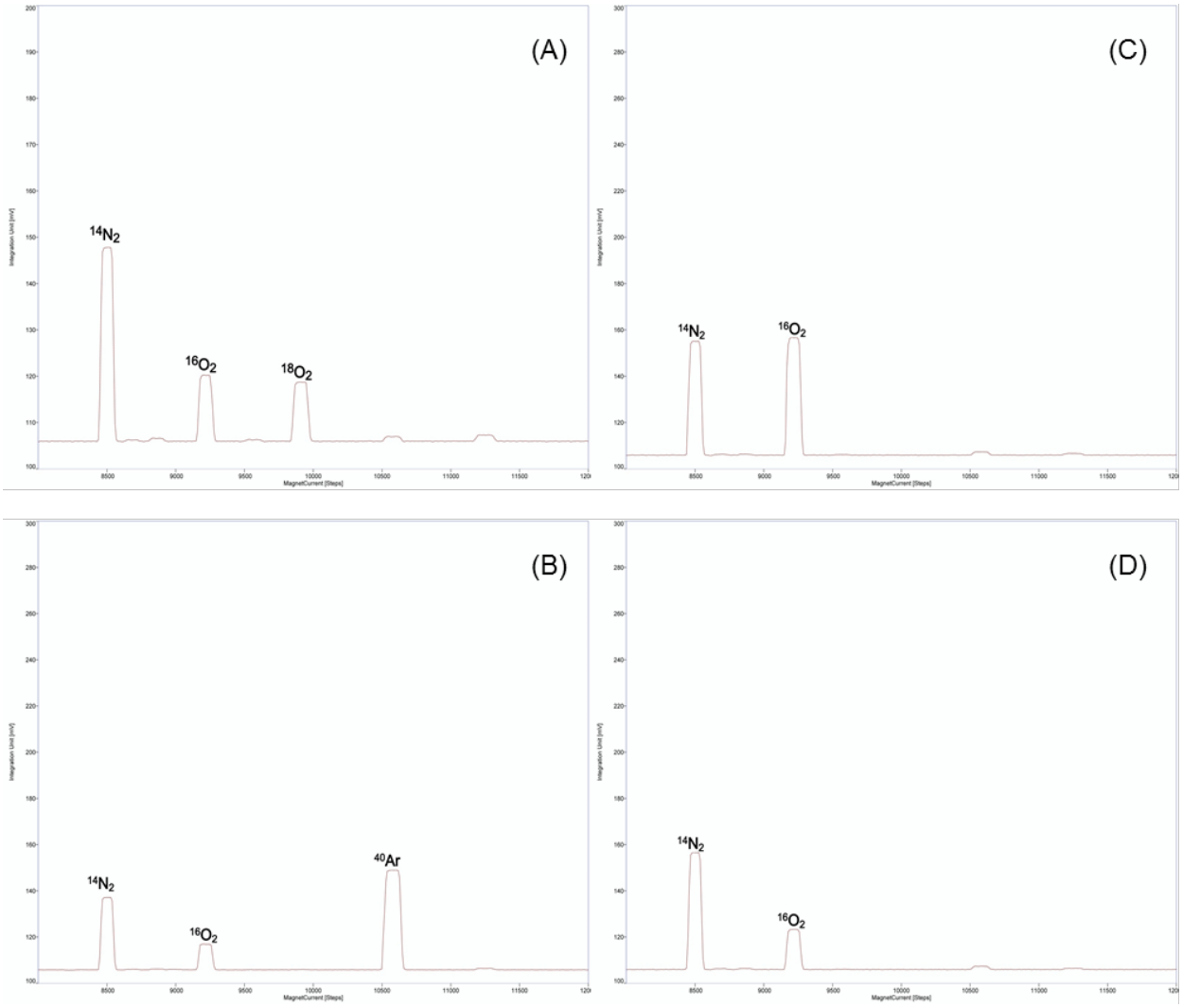
We have used Argon and two stable Oxygen isotopes ($^{16}O_2$ and $^{18}O_2$) to determine the longevity and utility of the nanobubbles under different storage conditions. Using Argon and $^{18}O_2$ (natural abundance=0.2%) to generate the NBs, we were able to exclude room air contamination (21% O_2 & 78% N_2). However $^{18}O_2$ is very expensive to obtain and Argon is not actively utilized in cellular metabolism. In order for us to be able to use the less expensive $^{16}O_2$ in our studies, we used Nitrogen as an internal contamination reference to calculate the tested water oxygen content.

Results: Using Helium flushed Vacutainers®; we have successfully established a method to analyze the gas content of NB water.

$^{18}O_2$ NB water was found to be stable for more than 4 months at 4ºC when stored in aluminum coated spout packs. They have also sustained rough shipping conditions from overseas.

$^{16}O_2$ NB water retained significantly higher levels of O_2 as compared to the control deionized water for periods exceeding 7 weeks when stored at room temperature despite repetitive opening and closure of the spout pack.

Conclusions: Using the ΣPM–5 device, we were capable of producing long lived nanobubbles whose diameters lay within the single nanometer range without any additives.



Representative results of the headspace mass spectra of: **A)** $^{18}O_2$ NB water, **B)** ^{40}Ar NB water, **C)** $^{16}O_2$ NB water and **D)** Control DI water.

B13

Tartrate-Resistant Acid Phosphatase (TRAP)-Positive Macrophages in Aneurysmal Disease Exhibit an Enhanced Proteolytic Phenotype

Kelly, M.J., Igari, K., Yamanouchi, D.

Abstract Submitter	Matthew Kelly
Email Address	mjkelly@wisc.edu
Classification	Postdoctoral Trainee
Principal Investigator	Dai Yamanouchi
Science Type	Basic Science
Keywords	Aneurysm, TRAP-positive macrophages (TPM), Proteases

Introduction: Abdominal aortic aneurysm (AAA) is among the top 20 leading causes of death in the United States. There is a great need for non-invasive therapeutic strategies for AAA since invasive surgical repair, by open or endovascular surgery, is still the gold standard for AAA therapy. Calcification of the artery was once thought to be a passive and degenerative process, but now is considered to be regulated by catabolic (bone resorption by osteoclasts) and anabolic (bone formation by osteoblasts) processes similar to the bone. AAA is more closely associated with catabolic degradation of the artery, rather than the anabolic processes of calcification of the artery. One of the markers of osteoclastogenic macrophage activation is the expression of TRAP. Furthermore, osteoclasts secrete catabolic enzymes such as MMP-9 and cathepsin K which are involved in the degradation of bone matrix. We have reported the presence of TRAP-positive macrophages (TPMs) in human aneurysmal tissue, and in the calcium phosphate ($CaPO_4$) and angiotensin II (AngII)-induced mouse models of AAA. The aim of this study was to examine the expression of the degradative enzymes MMP-9 and cathepsin K by TPMs found in mouse and human aneurysmal tissues.

Methods: The $CaPO_4$ mouse aneurysm model was produced in C57Bl/6 mice through sequential perivascular application of $CaCl_2$ and PBS to the carotid artery. Mice were sacrificed after 7 days. Treated and contralateral carotid arteries were resected for digestion or sectioning. The mouse AngII aneurysm model was produced in retired male breeder $ApoE^{-/-}$ mice via subcutaneous administration of 1000 ng/kg AngII via mini osmotic pump. Mice were sacrificed after 28 days. Aortas of control (PBS) and AngII-treated mice were resected for digestion or sectioning. All mouse and human tissue samples were minced and enzymatically digested for flow cytometry. Dissociated tissues were first blocked with mouse IgG, and subsequently stained for CD11b and viability. Cells were then fixed, permeabilized, stained intracellularly for TRAP, MMP-9, and cathepsin K, and analyzed on an Attune NxT flow cytometer. For immunofluorescence staining, mouse and human tissue sections were blocked, stained for CD11b, permeabilized, blocked, and stained for TRAP and DAPI.

Results: Confirming our previous studies, we identified an increase in TPMs in aneurysmal tissues. We quantified TPMs as the percentage of live cells double-positive for CD11b and TRAP, and found significant increases in TPMs compared to controls in the mouse $CaPO_4$ model (Control: 0.01043 ± 0.004556 vs. $CaPO_4$-treated: 1.145 ± 0.1756, $p<0.01$), mouse AngII model (Control: 0.19 ± 0.01732 vs. AngII-treated: 1.125 ± 0.1194, $p<0.001$), and human arterial disease (carotid plaque: 0.02036 ± 0.01515 vs. AAA: 5.287 ± 1.535, $p<0.05$). Further, we found that TPMs from aneurysmal tissues express more cathepsin K and MMP-9 than TRAP-negative macrophages in the mouse $CaPO_4$ model (Cathepsin K – macrophage: 1324 ± 123.4 vs. TPM: 4594 ± 955.2, $p<0.05$; MMP-9 – macrophage: 1739 ± 168.1 vs. TPM: 6477 ± 1381, $p<0.05$), mouse AngII model (Cathepsin K – macrophage: 1331 ± 340.6 vs. TPM: 4161 ± 739.1, $p<0.01$; MMP-9 – macrophage: 2536 ± 427.2 vs. TPM: 5851 ± 465.1, $p<0.001$), and human AAA (Cathepsin K – macrophage: 5675 ± 1542 vs. TPM: 33604 ± 7540, $p<0.05$; MMP-9 – macrophage: 5444 ± 1891 vs. TPM: 27830 ± 5823, $p<0.05$).

Conclusions: These data demonstrate that TPMs produce significantly more of the proteases MMP-9 and cathepsin K than TRAP-negative macrophages. MMP-9 and cathepsin K are known to be involved in bone and aortic degradation, therefore, TPM activation may be an attractive target for non-surgical suppression of aneurysm formation.

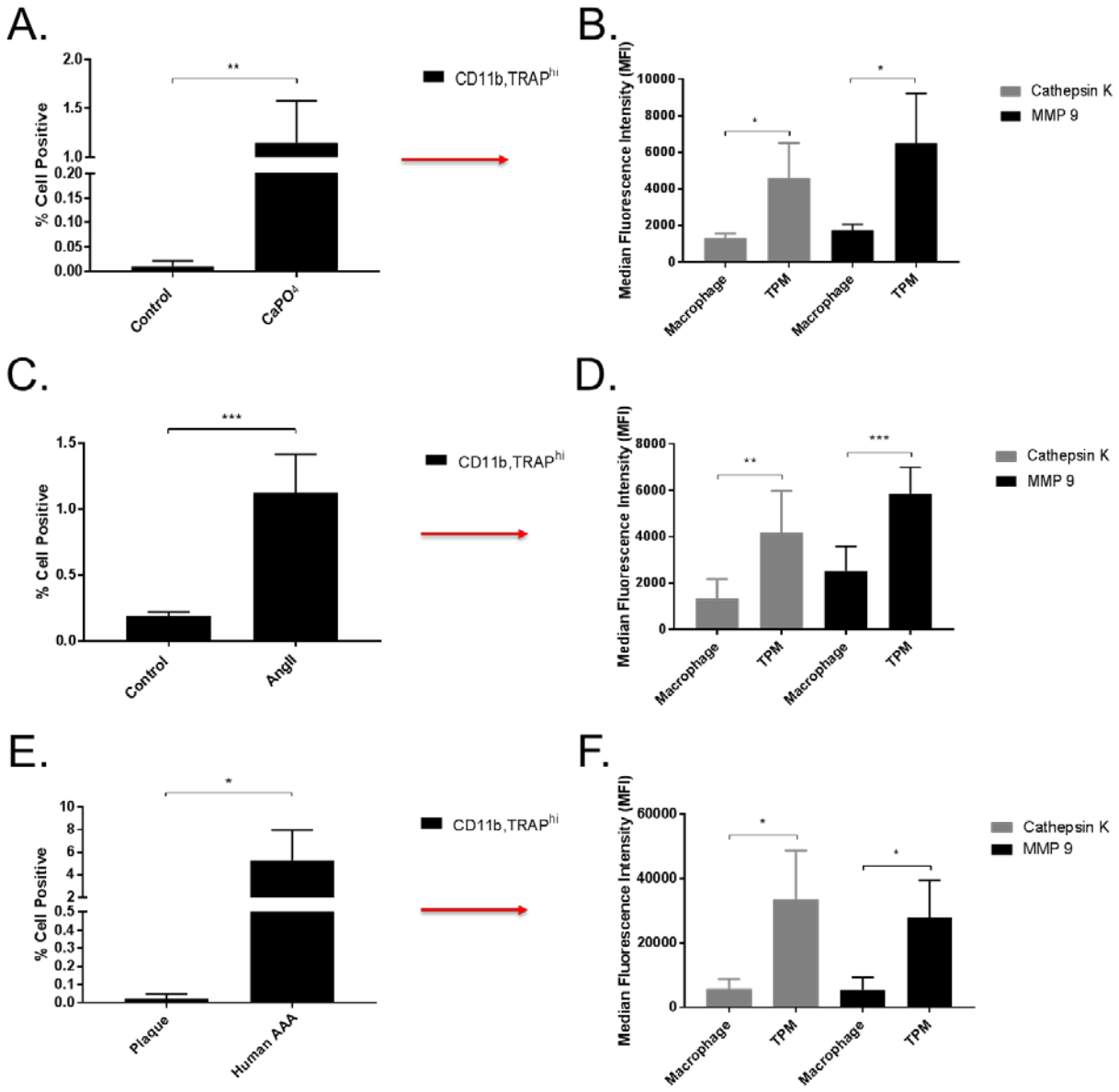


Figure 1

Flow cytometric analysis of TPMs in mouse and human aneurysmal disease. The extent of TPM activation is represented by the percentage of live cells co-expressing CD11b and TRAP in mouse $CaPO_4$ (A), mouse AngII (C), and human (E) aneurysmal tissue. Cathepsin K and MMP-9 expression are compared between macrophages (CD11b+) and TPMs (CD11b+, TRAP+) from mouse $CaPO_4$ (B), mouse AngII (D), and human (F) aneurysmal tissue. * $p<0.05$, ** $p<0.01$, *** $p<0.001$

GROUP TWO

Clinical Science

C4

Does Adjuvant Therapy Following Resection of Gastroenteropancreatic Neuroendocrine Tumors Improve Outcomes? An Analysis of the U.S. Neuroendocrine Tumor Study Group

Barrett JR, Lopez-Aguiar, AG, Poultsides GA, Rocha FG, Crown A, Pawlik TM, Fields RC, Panni R, Idrees K, Cho CS Fisher AV, Weber SM, Maithel SK, Abbott DE

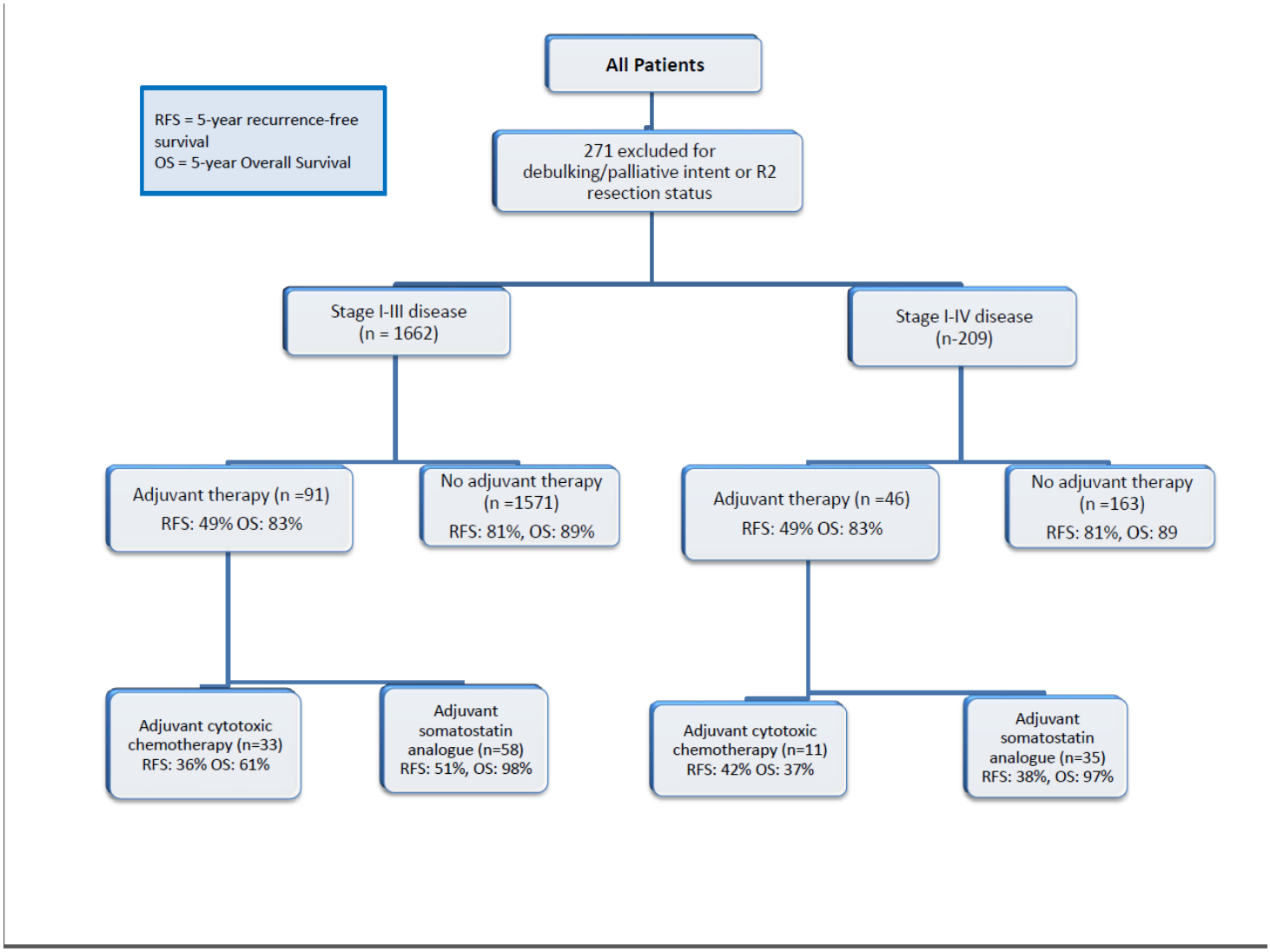
Abstract Submitter	James Barrett
Email Address	Jbarrett2@uwhealth.org
Classification	Resident
Principal Investigator	Dan Abbott
Science Type	Clinical
Keywords	Neuroendocrine tumors, adjuvant therapy, cancer outcomes

Introduction: Lack of high-level evidence supporting adjuvant therapy for patients with resected gastroenteropancreatic neuroendocrine tumors (GEP NETs) provides an opportunity to evaluate its non-standard of care use. Data from the US Neuroendocrine Tumor Study Group were used to evaluate adjuvant therapy and recurrence-free (RFS) and overall (OS) survival in this population.

Methods: Patients with primary GEP NETs who underwent curative-intent resection at eight institutions between 2000 and 2016 were identified; those with residual disease were excluded. 91 patients (of 1,662) received adjuvant therapy. RFS and OS were estimated and compared between adjuvant cytotoxic chemotherapy and somatostatin analogue cohorts.

Results: In resected patients, 33 received cytotoxic chemotherapy, and 58 received somatostatin analogues. 5-year RFS/OS was 49% and 83%, respectively. In contrast, patients not receiving adjuvant therapy demonstrated higher 5-year RFS/OS of 81% and 89%, respectively ($p<0.001$). On subset analysis, cytotoxic chemotherapy RFS/OS was 36% and 61%, respectively, lower than the no therapy cohort ($p<0.001$). RFS with somatostatin analogue therapy (compared to none) was lower ($p<0.001$), while OS was not different. Multivariable analysis demonstrated that adjuvant cytotoxic therapy was negatively associated with RFS/OS after controlling for patient comorbidities and tumor-specific characteristics (RFS $p = 0.001$, OS $p<0.003$).

Conclusions: Our data, reflecting the largest reported experience to date, demonstrate that adjuvant therapy for resected GEP NETs is negatively associated with RFS/OS. Selection bias enriching our treatment cohort for individuals with unmeasured high-risk characteristics likely explains some of these results; future studies should focus on subsets of patients who may benefit from adjuvant therapy.


RFS = 5-year recurrence-free survival
OS = 5-year Overall Survival
All Patients
271 excluded for debulking/palliative intent or R2 resection status
Stage I-III disease (n = 1662)
Stage I-IV disease (n-209)
Adjuvant therapy (n =91) RFS: 49% OS: 83%
No adjuvant therapy (n =1571) RFS: 81%, OS: 89%
Adjuvant therapy (n =46) RFS: 49% OS: 83%
No adjuvant therapy (n =163) RFS: 81%, OS: 89
Adjuvant cytotoxic chemotherapy (n=33) RFS: 36% OS: 61%
Adjuvant somatostatin analogue (n=58) RFS: 51%, OS: 98%
Adjuvant cytotoxic chemotherapy (n=11) RFS: 42% OS: 37%
Adjuvant somatostatin analogue (n=35) RFS: 38%, OS: 97%

C1

A New Approach to Migraine Surgery: The UW Flap

Afifi AM., Carbullido MK., Israel JS., Sanchez RJ., Albano NJ.

Abstract Submitter	Nicholas J. Albano, MD
Email Address	nalbano@uwhealth.org
Classification	Resident
Principal Investigator	Ahmed M. Afifi, MD
Science Type	Clinical
Keywords	Migraine; Greater occipital nerve; fat flaps

Introduction: The most common surgical approach for occipital headache surgery was first described by Guyuron, with later studies demonstrating long-term efficacy and encouraging results reported by multiple authors. Briefly, through a vertical midline incision the greater occipital nerve (GON) is decompressed along six potential compression points. A fat flap, based inferiorly, is then passed under the nerve bringing it to a subcutaneous position. The lesser occipital nerve (LON) is then approached through a separate incision. We believe that a transverse incision has distinct advantages, and that wrapping the decompressed nerves can further improve outcomes. In this work we describe the use of a single transverse incision with modified fat flaps to decompress both the greater and lesser occipital nerves.

Methods: We performed a retrospective review of all patients undergoing occipital nerve decompression at our institution. The incision is designed 2.5 centimeters caudal to the external occipital protuberance and extends, for bilateral cases, from the posterior edge of one SCM to the other. The skin is then elevated cephalically and caudally in the plane just deep to the hair follicles, sparing the deep fat over the trapezius fascia. This deep fat is then raised as a rectangular flap off of the trapezius fascia, leaving the base of the flap attached medially to the deeper tissues over the nuchal ligament. The GON is identified and decompressed. The fat flaps are then used to wrap the GON. The flap is passed deep, then lateral, then superficial to the nerve, using the distal edge of the flap to cover the nerve as it crosses the nuchal ridge.

Results: This technique was used in 71 patients between 2014 and 2017. There was one case of wound infection, but no cases of seroma or alopecia. Thirty-two patients (30 bilateral, 2 unilateral) had greater than 6 months of follow up with complete records for evaluation of their outcomes. The mean duration of migraine symptoms prior to their surgery was 21 years, and mean follow up was 8 months. Average Migraine Headache Index (MHI) was 191 preoperatively and 55 postoperatively ($p = 0.004$, SD = 130.7) with a mean improvement of 70%. Mean Headache Impact Test (HIT-6TM) score was 67 preoperatively and 57 postoperatively ($p<0.0001$, SD = 10.6) with a mean improvement of 15%.

Conclusions: The vertical approach to GON decompression has the longest track record, making it the standard of care. However, we believe our described modification to be easy, reproducible, and safe. Our results provide further evidence supporting the surgical principles for occipital nerve surgery, and that it is an effective headache treatment in properly selected patients.

C30

Simplifying Prepectoral Reconstruction: A New Era in Alloplastic Breast Surgery

Marks J.M., Afifi A.M.

Abstract Submitter	Jacob Marks, MD
Email Address	jmarks2@uwhealth.org
Classification	Resident
Principal Investigator	Ahmed Afifi, MD
Science Type	Clinical research
Keywords	Breast, Reconstruction, Prepectoral

Introduction: Prepectoral breast reconstruction has gained a lot of popularity over the last few years with encouraging outcomes reported. While most authors use some form of acellular dermal matrix (ADM), there is currently no consensus on the best method to wrap the prosthesis or suture the ADM. The most common method is an off-label wrapping of the prosthesis with the ADM on the back table, creating one construct that is then placed into the mastectomy pocket. This technique allows for suturing with relative speed and ease, as well as aesthetic shaping of the ADM-prosthesis construct. Drawbacks to this approach include a potential need for capsulotomies with exchange procedures, which may compromise long-term implant support. The alternate technique is to suture the ADM directly to the chest wall at the borders of the mastectomy defect. While this technique allows more precise matching of the breast footprint and decreases the need for capsulotomy, it may be more technically demanding and it can be difficult to achieve 3-dimensional shaping of the ADM. In this article we describe a technique that combines the advantages of both the above techniques by an in vitro shaping of the ADM and in vivo suturing.

Methods: The dimensions of the mastectomy pocket are measured in order to determine the appropriate expander size. The expander is brought into the mastectomy pocket and the locations of the expander tabs are marked on the chest wall (we prefer a smooth expander with 5 tabs). The expander is then brought to the back table where the ADM is placed on the expander. The dog-ears are then gathered and excised at the 6 o'clock position, with the excision site left open. Any extra mesh is then removed superiorly to match the exact height of the mastectomy pocket. Inferiorly the ADM is marked at the lower edge of the expander, and the extra length of ADM is preserved to act as a hammock along the inframammary folded. The locations of the tabs on the expander are marked on the ADM. For a direct-to-implant reconstruction, or a switch of a previous submuscular implant to a new prepectoral pocket, we use a shaped sizer for this back table portion of the procedure. The "anatomically shaped" ADM can then ensure the correct shape of the round implant. The ADM is then brought to the mastectomy pocket and easily sutured to the chest wall by matching the markings on the ADM and the chest wall (where the expander tabs will be). The central slit in the ADM where the dog-ear was removed is now used for two purposes. First, the extra length of ADM at the IMF is turned over and sutured to the chest wall creating an additional suture line to support the IMF. Second, the prosthesis is inserted into the pocket through this opening. This is much easier than placing the prosthesis through the ADM-chest wall junction, as the approximation of the ADM to itself in this central location is much easier and safer than suturing it to the chest wall, especially with an implant in place.

Results: Between 2015 and 2018, 64 reconstructions were performed in 38 patients. There were 12 unilateral and 19 bilateral reconstructions. 7 patients underwent conversion from submuscular to prepectoral implant placement. There were two cases of implant loss due to overlying mastectomy flap necrosis and one case of loss due to infection. One implant was removed due to residual cancer identified in the breast.

Conclusions: We describe a technical modification to simplify prepectoral reconstruction, and to allow the surgeon to have improved control over the shape of the ADM. This technique is especially helpful for direct-to-implant reconstruction, as it 1) allows the round implant to assume a nice anatomic shape, and 2) is easier and safer as the implant is only placed into the pocket after the ADM has been sutured to all the boundaries of the mastectomy pocket.

Figure 1. Patient 3 months after prepectoral direct-to-implant reconstruction (*above left*). 3 months after prepectoral expander to implant exchange (*above right*). Preoperative (*below left*) and 1 year postoperative (*below right*) after conversion from submuscular to prepectoral implants.

C41

Effect of Tympanostomy Tubes on Distortion Product Otoacoustic Emissions (DP-OAEs)

Kate Tiefenthaler, AuD; Mackenzie Sinnen, BS; Sara M Misurelli, PhD

Submitter	Kate Tiefenthaler, AuD, CCC-A
Phone	608-263-4048
Email Address	tiefenthaler@surgery.wisc.edu
Classification	Clinical/Academic Staff
Division	Otolaryngology
Lab	General Audiology
Science Type	Clinical
Keywords	Tympanostomy tubes, Distortion-Product Otoacoustic Emissions, Clinical Audiology

Introduction: Chronic otitis media, or middle ear infection, is prevalent among young children and, if untreated, can potentially cause decreased hearing sensitivity and delays in speech and language development. Tympanostomy tube placement is a common surgical procedure to aid in the prevention of middle ear effusion and reduce the recurrence of otitis media. Audiometric testing is recommended pre-operatively and post-operatively in order to verify hearing sensitivity; however, a subset of this population can be difficult to test behaviorally. For these individuals, especially young children, an objective measure of hearing sensitivity is necessary and considered best practice.

Distortion product otoacoustic emissions (DP-OAEs) are a well-known audiology tool used to objectively evaluate hearing sensitivity. The presence of DP-OAEs relies heavily on a healthy middle ear status. Several studies have investigated the effect of tympanostomy tubes on OAEs in the past; however, most have focused on transient evoked OAEs (TE-OAEs). TE-OAEs use a broad-frequency click stimulus, while DP-OAEs are recorded at frequency-specific intervals. The aim of the current study is to explore factors that may affect presence or absence of these frequency-specific DP-OAEs following tympanostomy tube placement.

Methods: A retrospective chart review study was completed for each patient, age 0-18 years old, that has had a tympanostomy tube placement procedure and who also had DP-OAEs scanned into their medical records over 5 years. A total of 53 charts were reviewed, 37 of which had data that could be used from right, left, or both ears, yielding a total of 59 ears. The following variables were recorded: gender, right vs left ear, days between surgery and DP-OAE procedure, type of tympanostomy tube placed, equivalent ear canal volume recorded during tympanometry, and the distortion product (DP), noise floor (NF), and DP-NF difference for each of 7 frequencies (1031Hz, 1453Hz, 2016 Hz, 2859 Hz, 3984Hz, 5672Hz, 8016Hz).

Results: Regression analyses were used to explore the relationship between each DP-OAE frequency and the aforementioned variables. Preliminary results suggest that there is a significant relationship between the presence of DP-OAEs and days between surgery and recording of DP-OAEs. Data will be further explored to assess if there are any additional factors that contribute to the absence of DP-OAEs at each frequency.

Conclusions: Our results add to the literature, indicating that there is a statistically significant relationship between DP-OAE responses and the number of days post-operative, suggesting that the more time between surgery and DP-OAE recording, the more likely DP-OAEs are to be present. Clinically, this information will help to determine when and whether further audiologic testing should be recommended.

C35

Emotional Facial Action Coding System Analysis of Primary and Secondary Rhinoplasty Patients

Sanchez, R.J., Constantian, M.B.

Abstract Submitter	Ruston J. Sanchez, MD
Email Address	Rsanchez@uwhealth.org
Classification	Resident
Principal Investigator	Mark B. Constantian, MD
Science Type	Clinical Research
Keywords	Rhinoplasty, FACS, facial expression

Introduction: There is a high prevalence of body dysmorphic disorder symptoms in patients with psychiatric history undergoing revision of aesthetic rhinoplasty. Causative links may exist between history of abuse and neglect, depression, body image disorders, and obsessive plastic surgery. Facial expression analysis software is becoming an increasingly popular and effective research tool for studying neuropsychiatric disorders, neuroscience of cognitive and social behavior, and doctor-patient interactions. We hypothesized that there were objective, measurable differences in facial expression within a subset of rhinoplasty patients during clinical encounter.

Methods: Facial expression recognition software was used to analyze preoperative and postoperative photographs of 172 rhinoplasty patients. Images were categorized by gender, patient engagement during clinical interview, preoperative vs postoperative setting, and primary vs. secondary presentation. Statistical analysis was conducted using paired t-test for equality of means with conventional statistical significance of $p \leq 0.05$.

Results: Engaged patients displayed significant increases in happiness and valence postoperatively, while there were no changes postoperatively within the disengaged group. Disengaged patients displayed higher neutral faces and lower valence with a trend towards lack of eye contact. There was significantly more happy facies among men in the engaged group and overall. Alternatively, there was significantly higher fear and surprise in the female disengaged group and overall. Lastly, primary and secondary disengaged patients were much more significantly likely to request revisions postoperatively.

Conclusions: This is the first documented use of computerized facial action coding system software to analyze facial emotions in a population of aesthetic surgery patients. Such powerful image or video analysis may serve a role in psychological analysis of rhinoplasty surgical patients.

C31

Renal Function Changes Following Fenestrated Endovascular Abdominal Aortic Aneurysm Repair (fEVAR)

Oberdoerster, Molly M., Tefera, Girma., Wynn, Martha M., DiMusto, Paul D.

Abstract Submitter	Oberdoerster, Molly M.
Email Address	moberdoerster@uwhealth.org
Classification	Resident
Principal Investigator	DiMusto, Paul D.
Science Type	Clinical
Keywords	Fenestrated Endovascular Repair

Introduction: Fenestrated endovascular abdominal aortic aneurysm repair (fEVAR) has been approved for clinical use since 2012. One possible complication of this repair is impairment in renal function. We sought to assess the clinical outcomes related to renal function over time in patients undergoing fEVAR at the University of Wisconsin Hospital.

Methods: A retrospective review was conducted of prospectively collected data on all patients undergoing fEVAR at our institution between 2012 and 2017. Patient characteristics, procedural variables, laboratory values, and imaging characteristics were collected. Serum creatinine was measured preoperatively, and at 1 month, 6 months, 1 year and yearly thereafter. Estimated glomerular filtration rate was calculated using the Cockcroft Gault equation.

Results: A total of 58 patients were included: 42 men and 16 women with an average age of 75 years. The average follow up time was 469 days; 6 patients were lost to follow up. A total of 111 out of 116 main renal arteries were successfully revascularized. Only one main renal artery that was planned for revascularization was not due to the inability to place a stent intraoperatively. The other four were above the graft and did not require revascularization. There were 11 accessory renal arteries that were covered with the aortic graft.

Eighteen patients (31%) had advanced chronic kidney disease (CKD) prior to the repair; 17 stage III, 1 stage IV. Nine patients (15.5%), including 3 of the 18 who had CKD prior to the repair, had an increase of at least 30% from baseline creatinine over two or more follow up visits. All nine had evidence of post-operative renal insult including infarct, renal artery stenosis, or occlusion. Four patients (7%) with no prior history of CKD progressed to stage II, 13 (22%) patients progressed from stage II to III, and 3 patients (5%) progressed from stage III to stage IV over the follow up period. Only the patient with stage IV CKD at the time of the repair went on to require dialysis 8 months after his procedure.

Eight patients (13.7%) developed stenosis in one of the renal artery stents. Five of these patients had worsening of their renal function with progression by one CKD stage. Two patients had an intervention due to the stenosis, but only one was successful. Four additional patients developed a renal artery occlusion, three of which had a progression of CKD by one stage. None of these patients went on to dialysis. A total of 24 patients (41%) developed renal infarction on imaging over the follow up period. Nine of these patients had progression of their CKD stage, however none went on to dialysis.

Conclusion: Our review demonstrates that while kidney dysfunction can occur over the long term following fEVAR, rates of worsening renal function are relatively low. Additionally, in patients with pre-operative CKD, fEVAR remains safe and effective with low rates of progression to dialysis.

C47

The Effect of Pulse Steroids/IVIG/Rituximab on Circulating Lymphocytes and Cytokines in Kidney Transplant Recipients with Chronic Active ABMR

Wilson N, Parajuli S, Redfield R, Aziz F, Garg N, Mandelbrot D, Muth B, Blazel J, Turk J, Mohamed M, Bath N, Verhoven B, Panzer S, Reese S, Djamali A

Abstract Submitter	Nancy Wilson Schlei
Email Address	nawilson@medicine.wisc.edu
Classification	Academic staff
Principal Investigator	Arjang Djamali
Science Type	Clinical
Keywords	Antibody mediated rejection, cABMR, rituximab

Introduction: There is no information on the effect of combination therapy with pulse steroids/IVIG/Rituximab on circulating T-cell and B-cell phenotypes and cytokines in kidney transplant recipients (KTR) with chronic active antibody mediated rejection (cABMR).

Methods: We examined this questions in 13 KTR with cABMR who underwent follow up evaluation with a repeat protocol biopsy within approximately 3 months of the initial diagnosis. PBMC subsets were identified using flow cytometry. Plasma was analyzed using Luminex 45-plex assay for cytokines. Paired Wilcoxon rank sum test was utilized to assess the effect of therapy on pre and post samples. Pre-treatment samples were also compared to a group of 11 healthy volunteers matched for age, gender, and race.

Results: Median age at the diagnosis of cABMR was 42 years. The diagnosis was made at a median of 8.2 years post-transplant. Median Scr and urine PC at biopsy were 1.8 mg/dL and 0.9 g/g.).

Compared to controls, KTR had significantly lower lymphocytes, memory B cells, Tregs and CD4+ T cells, but increased numbers of monocytes and basophils. Circulating fractaline, IL-15, TRAIL and VEGF levels were significantly increased ($p<0.01$ for all).

Treatment with pulse steroids/IVIG/Rituximab was associated with decline in ptc and mvi Banff scores at the three-month protocol biopsy, but was not statistically significant. Similarly, all B cell subsets, including mature, memory and plasmablasts were significantly reduced ($p<0.003$). Treatment was associated with an increase in CD4+ T cells and Tregs, which was not significant. Treatment was associated with a significant reduction in DSA to MHC I and MHC II ($p<0.005$), and an increase in circulating BAFF/APRIL, Flt3-ligand, IL-13, IL-15 and VEGF ($p<0.01$).

KTR could be stratified into two groups – responders and non-responders as determined by improvement in kidney function. Responders had a significant increase in kidney function ($p=0.03$), whereas non-responders experienced a decrease in function ($p=0.01$). At time of diagnosis, responders had significantly higher DSA ($p=0.01$) and significantly worse ($p=0.01$) kidney function.

Conclusions: In conclusion, KTR with ABMR have significantly different circulating B cell and cytokine profiles than healthy volunteers. Short term therapy with Pulse steroids/IVIG/Rituximab effectively inhibits disease activity in cABMR in 50% of KTR. We identified several potential biomarkers or therapeutic targets.

C37

Long Term Dysphagia Resolution Following Poem Versus LHM in Patients with Achalasia

Shea G.E., Davies K.D., Venkatesh M, Jolles S., Prout T.M., Shada A., Greenberg J.A., Lidor A.O., Funk L.M.

Abstract Submitter	Shea G.E.
Email Address	shea@surgery.wisc.edu
Classification	Graduate student
Principal Investigator	Dr. Luke M. Funk
Science Type	Clinical Research
Keywords	achalasia, POEM, Heller

Introduction: Laparoscopic Heller myotomy (LHM) has historically been considered the gold standard treatment for achalasia. However, peroral endoscopic myotomy (POEM) is a less invasive procedure and offers a quicker recovery. Although some studies have compared short-term outcomes of LHM to POEM, the strongest predictors of long-term dysphagia resolution are unclear. The objective of this study was to evaluate patient-reported outcomes for achalasia patients who underwent either POEM or LHM and had at least one year of follow-up.

Methods: Data from our single academic institutional foregut database were used to identify achalasia patients who underwent LHM or POEM over a 9-year period. Postoperative outcomes were assessed via telephone for patients with at least one year of follow-up using Eckardt dysphagia scores. Electronic health record data were reviewed to extract patient characteristics and operative data. Patient age, sex, type of operation, and length of follow-up were included in a multivariable linear regression model with Eckardt score as the outcome.

Results: Our cohort included 125 patients (93 LHM and 32 POEM). Sixty-four patients completed a phone survey at the one year or greater time interval (response rate=51%). Mean Eckardt scores were 2.95 and 1.85 at a median follow-up of 48 and 12 months for LHM and POEM patients, respectively (an Eckhardt score ≤ 3 is considered a successful myotomy). On multivariable analysis, operative approach was not associated with a statistically significant difference in dysphagia outcomes.

Conclusions: POEM and laparoscopic Heller myotomy were associated with similar rates of dysphagia resolution for achalasia patients at a median of 3 years of follow-up. Both procedures should be considered durable treatment options for achalasia treatment.

Table 1. Bivariate and Multivariate Predictors of Postoperative Dysphagia

Variable		Bivariate Analysis*	Multivariate Analysis*
		β-coeff (p-value)	β –coeff (p-value)
Sex (N, %)		0.14 (0.81)	-0.20 (0.74)
Male	36 (56.3)	-	
Female	28 (43.8)	-	
Age (mean, SD)	56.2 (16.9)	0.01 (0.65)	0.01 (0.48)
Procedure Type (N, %)		1.10 (0.07)	1.21 (0.09)
POEM	21 (32.8)	-	
LHM	43 (67.2)	-	
Follow-up interval (months)	29.5	0.01 (0.54)	0.0001 (0.99)
POEM	12		
LHM	48		

LHM, laparoscopic Heller myotomy; POEM, per oral endoscopic myotomy

*The reference group consisted of male sex and POEM as an operative approach.

C32

Feeding Outcomes Following Mandibular Distraction Osteogenesis in Pierre Robin Sequence

Patel V MS2, Block L M.D., Rose K M.D., Mount D M.D., Garland C M.D.

Submitter	Vik Patel, MS2
Phone	
Email Address	vbpatel2@wisc.edu
Classification	Medical Student
Division	
Lab	Dr. Catharine Garland
Science Type	Clinical
Keywords	Pierre Robin Sequence, mandibular distraction osteogenesis, feeding outcomes

Background and Purpose: Newborn feeding difficulties are commonly associated with Pierre Robin Sequence (PRS). Mandibular distraction osteogenesis (MDO) is well-described as a treatment for the airway obstruction associated with PRS, but fewer data is available regarding feeding outcomes for infants after MDO. The purpose of this study was to evaluate short and long term feeding outcomes after infant MDO.

Methods: A retrospective study of infants who underwent MDO between 2012 and 2018 for a diagnosis of PRS under the age of 12 months was conducted. Demographic variables included gestational age at birth, associated pathology including cleft palate and other airway lesions, and associated genetic syndromes. Surgical variables included age at MDO surgery, age at removal of mandibular hardware, distraction distance, and duration of time the infant was intubated after surgery. Feeding-related variables included preoperative and postoperative feeding method, preoperative and postoperative reflux symptoms and use of reflux medications, and preoperative and postoperative weight percentile.

Results: 30 patients were identified who underwent MDO for Pierre Robin Sequence. 10 (33%) patients had an identified genetic syndrome. 24 (80%) patients had a cleft palate. Preoperatively, only 40% of patients were feeding completely orally. The majority had a nasogastric tube. 3 patients had a preoperative surgical gastrostomy tube (G-tube) placed. In the early postoperative period, patients were intubated for a median of 7 days (range 4-14 days), took their first oral feeding attempts at a median of 9 days, and 60% of the patients had transitioned to full oral feeds at discharge, a median of 14 days after surgery. Ultimately, 70% were able to progress to full oral feeding after discharge to home with a nasogastric tube in place. Mean weight percentile dropped from preoperatively (15.8%) to the time of distractor hardware removal (8.2%), but had increased significantly at the time of most recent follow up (25.7% at a median of 4.6 years). 33.3% of patients were on reflux medications preoperatively, compared with 53.3% on reflux medications post-operatively at hospital discharge.

After MDO, an additional 6 patients underwent G-tube placement for a total of 30% with a G-tube at any point. Patients who required G tubes were more likely to have an associated syndrome (55%) and only 1/9 patients were feeding orally preoperatively. Mean weight percentile was lower in this group preoperatively, at the time of hardware removal, and at the most recent follow up.

Conclusions: After MDO, patients were more likely to feed orally and long term follow up weight percentile increased, suggesting that MDO for PRS improves feeding and growth outcomes. Patients who required gastrostomy tube placement were more likely to have an associated genetic syndrome and lower weight percentiles. This data may help to predict which patients will require additional feeding support.

C19

Comparing the Exposure-Response Relationships of Physiological and Traditional Vocal Warm-Ups on Aerodynamic and Acoustic Parameters in Untrained Singers

Kang J, Jiang J.J.*

Abstract Submitter	Kang J
Email Address	229272620@qq.com
Classification	Laryngology
Principal Investigator	Kang J, Jiang J.J.* (Corresponding Author)
Science Type	Original Article
Keywords	Semioccluded vocal tract–Straw phonation–Vocal warm-up–Aerodynamics–Acoustics.

Introduction: Vocal warm-up, an essential aspect of singing training, is believed to protect against vocal fold injury in both untrained and professional singing and speaking voice users. Leading the intrinsic laryngeal muscles through a series of vocal warm-ups facilitates contraction and efficiency, subsequently preventing or delaying symptoms of vocal fatigue. The aim of this study was to quantify the effects of traditional and physiological warm-up exercises and to determine the optimal duration of these methods using acoustic and aerodynamic metrics.

Methods: Twenty-six subjects were recruited to participate in both straw phonation exercises (physiological vocal warm-up) and traditional singing exercises (traditional vocal warm-up) for 20 minutes each, 24 hours apart. Phonation threshold pressure (PTP), fundamental frequency, jitter, shimmer, and noise-to-harmonics ratio were measured before the intervention (m0), as well as after 5 minutes (m5), 10 minutes (m10), 15 minutes (m15), and 20 minutes (m20) of intervention.

Results: PTP decreased significantly after straw phonation and reached a minimum value at 10 minutes ($P < 0.001$) and remained stable in traditional singing exercises. There were significant differences in fundamental frequency and shimmer from m0 to m15 and m20 in the traditional singing group ($P = 0.001$, $P = 0.001$, $P = 0.001$, and $P = 0.002$, respectively). No significant changes in acoustic parameters were observed after straw phonation.

Conclusions: Both straw phonation exercises and traditional singing exercises are effective for voice warm-up. Straw phonation improves the subjects' fatigue resistance and vocal economy, resulting in a reduced PTP, whereas tradition- al singing exercises focus on technical singing skills, leading to an improvement of acoustic variables.

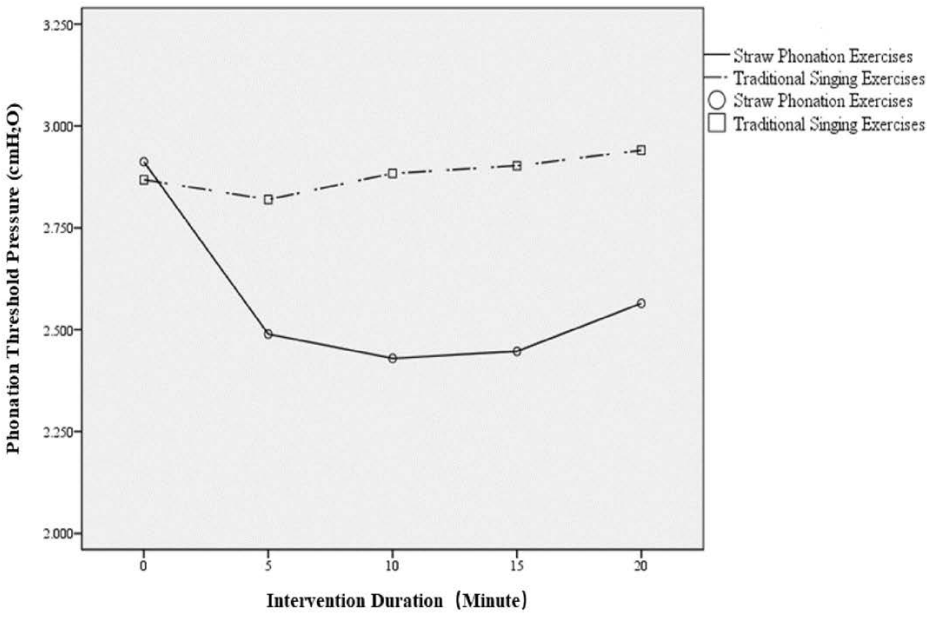


FIGURE 1. Comparison of PTP after straw phonation exercises and traditional singing exercises.

C9

Comparing the Nonlinear Dynamic Acoustic Parameters of Healthy Adult and Pediatric Voices

Adriana Chou, Colin Schrof, Evan Polce, Maia Braden, James McMurray, Jack Jiang

Submitter	Adriana Chou
Phone	510-378-7746
Email Address	Achou3@wisc.edu
Classification	
Division	Otolaryngology
Lab	Jiang
Science Type	
Keywords	Pediatric voice, Spectral Convergence Ratio (SCR), Rate of Divergence (ROD), Acoustic voice evaluation, Turbulence

Introduction: Digital acoustic analysis allows clinicians to objectively measure the amount of disorder in a recorded voice sample, and thus evaluate the subject's vocal health and functioning. Two novel analytic measures are Spectrum Convergence Ratio and Rate of Divergence. These were established using adult voice samples and have not yet been used in the pediatric setting. Our objective is to compare non-dysphonic adult and pediatric voices using linear and nonlinear acoustic parameters and evaluate the ability of adult Spectrum Convergence Ratio (SCR) and Rate of Divergence (ROD) reference values to correctly identify a pediatric voice type as periodic or aperiodic.

Methods: 20 adult and 36 pediatric non-dysphonic voice samples were collected and analyzed using linear and nonlinear acoustic parameters. Absence of voice disorder was confirmed with perceptual acoustic and spectral analysis. Mean values for jitter, shimmer, SCR, and ROD were compared between adults and children, across specific age groups, and within genders. Using adult reference values for SCR and ROD, samples were classified as primarily periodic or aperiodic, and typed using spectral

Results: Overall, jitter and shimmer were similar among the adult and pediatric age groups. ROD was significantly different between the 3 pediatric and 1 adult groups; the pediatric age groups are similar to each other. Adult SCR was also significantly different than all of the pediatric age groups. In adult males, ROD and SCR were significantly different from all of the pediatric age groups; the pediatric age groups were similar to each other. In females, ROD was significantly different between all age groups. The ROD and SCR reference values were significantly better at categorizing adult voice types compared to pediatric voice types.

Conclusions: In healthy subjects, SCR and ROD have discriminatory power for identifying adult versus pediatric voices, while jitter and shimmer cannot differentiate between the two groups. However, age- and gender-specific pediatric reference values must be determined to accurately classify voice types using SCR and ROD.

C20

Lingering Effects of Straw Phonation Exercises on Aerodynamic, Electroglottographic, and Acoustic Parameters

Kang J, Jiang J.J.*

Abstract Submitter	Kang J
Email Address	229272620@qq.com
Classification	Laryngology
Principal Investigator	Kang J, Jiang J.J.* (Corresponding Author)
Science Type	Original Article
Keywords	Semi-occluded vocal tract–Straw phonation–Contact quotient–Aerodynamics–Acoustics.

Introduction: Semi-occluded vocal tract exercises (SOVTEs), characterized by a reduction in the cross-sectional area of the distal part of the vocal tract while voicing, have been widely used in voice training and voice rehabilitation. This study aimed to investigate the duration of straw phonation effects using aerodynamic, electroglottographic, and acoustic metrics.

Methods: Twenty-four participants were recruited to perform both a 5-minute and a 10-minute straw phonation exercise. Upon completion of the exercises, phonation threshold pressure (PTP), mean airflow, contact quotient, fundamental frequency, jitter, shimmer, and noise-to-harmonics ratio were measured over a 20-minute time frame. Parameters were measured before the intervention (baseline), immediately after the intervention (m0), 5 minutes (m5), 10 minutes (m10), 15 minutes (m15), and 20 minutes (m20) after the intervention.

Results: PTP significantly decreased immediately after 5 minutes of straw phonation and returned to initial state within 5 minutes. PTP remained decreased over 5 minutes after 10 minutes of straw phonation. Mean airflow increased immediately after both 5 minutes and 10 minutes of straw phonations and remained improved for 20 minutes. No significant changes were obtained for contact quotient and acoustic parameters over the intervention period.

Conclusions: The results extended our knowledge of proper clinical application of straw phonation regarding the duration of exercise. This study confirmed that 10 minutes of straw phonation lead to optimal and relatively continuous effects in PTP and mean airflow. Although straw phonation did show lingering effects in aerodynamics, repeated practices were recommended to obtain optimum and therapeutic effects.

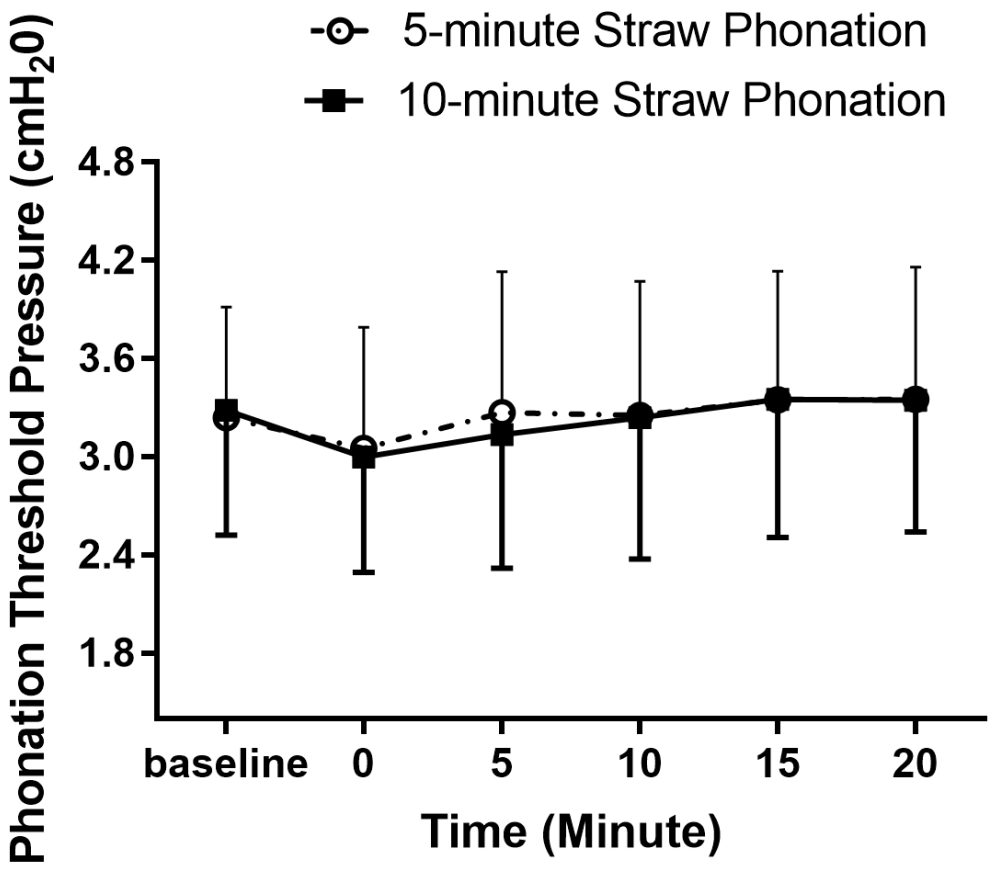


FIGURE 1. Comparison of PTP in 5-minute straw phonation and 10- minute straw phonation before and after intervention.

C42

Physician Calls to Pediatric General Surgeons – Foundational Data to Guide Future Interventions

Timmel AE, Cartmill RS, Carrera-Valdez J, Rademacher B, Kohler JE

Abstract Submitter	Timmel A.E.
Email Address	aetimmel@wisc.edu
Classification	Medical Student
Principal Investigator	Kohler J.E., MD MA
Science Type	Clinical
Keywords	Pediatric general surgery, interfacility transfers, quality improvement

Introduction: Many tertiary care hospitals have implemented central call centers to triage patient transfers, facilitate interdisciplinary phone consults, and expedite referrals. The type of calls received and decisions made based on these phone calls have not been well described. At our facility, the "Access Center" is a toll-free phone line that is staffed 24/7 by registered nurses who specialize in acute care and connect providers calling in with appropriate specialists to discuss treatment and transfer options. The goal of this study was to characterize calls received by the Pediatric Surgery service at a single tertiary care children's hospital, and to use that date to guide future educational outreach interventions.

Methods: A retrospective chart review was completed for all call encounters directed to Pediatric Surgery documented in the EMR between March 2014 and March 2017. Data collected included call location, call diagnosis, patient age, and call decision (treat at referring facility vs. transfer). Additional information was collected for patients that were transferred to the childrens' hospital, including days admitted and interventions performed.

Results: 870 patients met inclusion criteria. Of these, 39% of patients remained at the calling location and received care at the calling facility, 24% of patients were directly admitted to a children's hospital inpatient unit, 23% of patients were seen in the children's hospital emergency department (ED) and later admitted, and 14% of patients were seen in the ED then discharged home. Of patients that were admitted to the hospital (either directly or via the ED), the average admission was 3.15 days and 80.2% of patients had an operation during that admission. Of the 122 patients seen at the children's hospital ED but not admitted, 26.2% were evaluated for generalized abdominal pain and 19.7% for suspected appendicitis. Suspected intussusception (11.5%) and g-tube complications (8.2%) were also commonly evaluated in the ED only.

Conclusions: Many patients (39%) remained at the referring location, while admitted patients had operations 80.2% of the time, illustrating generally effective use of telephone consults. 14% of patients were transferred to the children's hospital, sometimes from great distances, but were discharged from the ED. These patients represent opportunities for intervention to better facilitate patients staying in their home communities. Further analysis of imaging, bedside procedures, and specialty consults associated with diagnoses that frequently were not admitted after transfer to the children's hospital will inform intervention development.

Table 1 Top Diagnoses for PGS Access Call Center Calls Between March 2014 and March 2017

Diagnosis	Percent of Calls
Appendicitis	21.81%
Abdominal pain	10.91%
Post-op complication (including infection, fever, abscess, pain, bleeding)	5.51%
Intussusception	5.05%
Inguinal hernia	4.25%
Pyloric stenosis	3.78%
Oost-op care	3.67%
SBO	3.56%
Abscess	3.32%
Congenital malformation or deformity	3.10%
G-tube complications	4.02%
Emesis (including bilious and bloody)	2.64%
Pulmonary (hemoperitoneum, pneumothorax, pneumomediastinum)	2.64%
Anorectal (includes bleeding, prolapse, hemorrhoids, fistula, polyp)	2.18%
Foreign body	1.15%
Constipation	1.03%
G-tube consult	1.03%
Gynecological (ovarian abscess, cyst, or torsion; labial laceration)	1.03%
Umbilical hernia	1.03%
Central line complication	0.80%

Table 2Top ED-only diagnoses. These diagnoses are areas for reducing unnecessary transfers though improved outreach education and tele-consults.

Diagnosis	% of all calls with same diagnosis
abdominal pain	33.7%
appendicitis	12.6%
intussusception	31.8%
G-tube complications	28.6%
abscess	20.7%
inguinal hernia	13.5%

C23

Dipyridamole Use May Reduce Gastrointestinal Bleeding in Patients Implanted with a Left Ventricular Assist Device

Lushaj EB, Dhingra R, Lozonschi L, Kohmoto T

Abstract Submitter	Entela Lushaj
Email Address	lushaj@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Kohmoto
Science Type	Clinical
Keywords	Outcomes, Dipyridamole, GI Bleed

Objective: Dipyridamole (DPY) is used in left ventricular assist device (LVAD) patients with thrombosis for its inhibitory effect of platelet aggregation. But DPY also impacts intestinal microcirculation by blocking adenosine uptake thus inhibiting the opening of the precapillary sphincters and counteracting regional hypoxia, vasodilation and angiodisplasia. Few LVAD patients experience both GI bleeding and thrombosis complications and we hypothesized that DPY may impact the GI bleeding rate.

Methods: We retrospectively reviewed 20 patients who had episodes of GI bleeding after LVAD implantation between 2011-2016. Out of these, 9 (45%) patients were treated with DPY for hemolysis (group 1). GI bleeding events after starting DPY were recorded and compared to those of patients not having hemolysis (DPY free; group 2). Hemolysis was defined as LDH 3x normal value and pfHb>40.

Results: The two groups were comparable with regard to age (54±11 vs. 50±21; p=0.51), gender (males: 100% vs. 90%; p=0.89) and BMI (29±6 vs. 26±5; p=0.74). In the DPY group, 7 (70%) patients were implanted with HMII and 2 patients were implanted with Heartware. All patients in group 2 were implanted with HMII. Median follow up time was 17 months

(Interquartile range: 7-28). Five (56%) of the 9 patients in group 1 did not have any more GI bleeding episodes after treatment with dipyridamole. The other 4 (44%) patients had only 1 episode of GI bleed after DPY for the duration of the study. Group 2 had an average of 4 GI bleeding episodes for the duration of the study follow-up.

Conclusions: Even though DPY's has been mainly used for the treatment of LVAD thrombosis it may also affect GI bleeding rates in LVAD supported patients. This latter effect deserves further investigations.

C26

Donor Age Significantly Impacts Long Term Survival of Patients Undergoing Heart Transplantation

Lushaj EB, Dhingra R, Osaki S, Johnson M, Lozonschi L, Kohmoto T

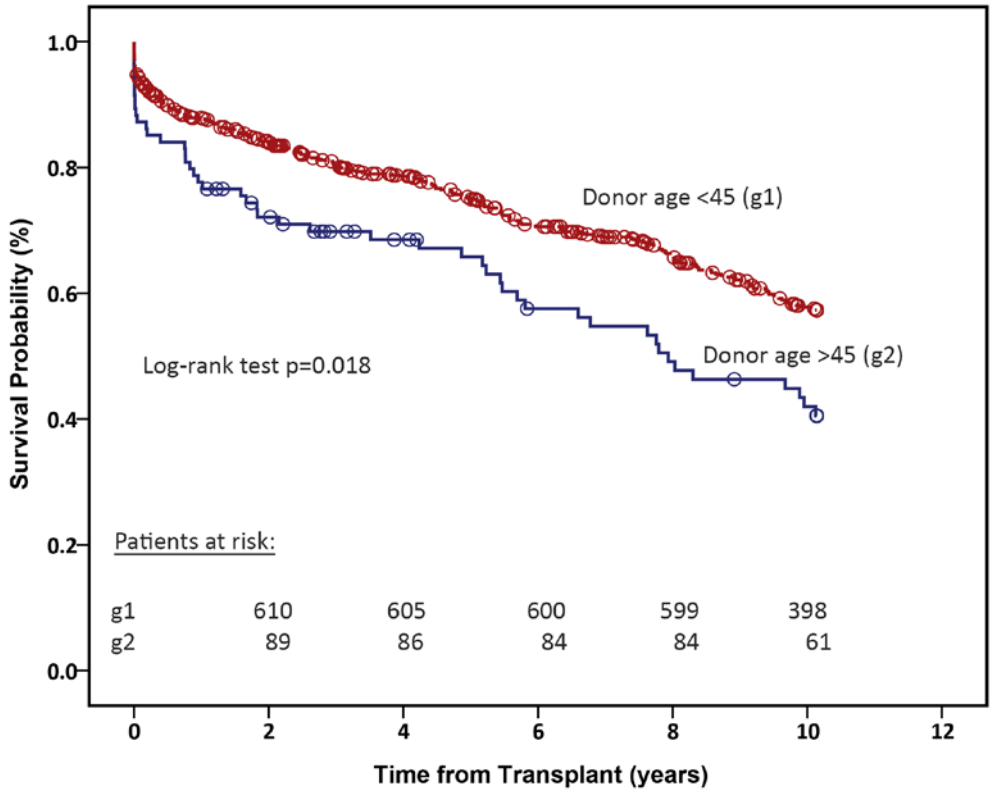
Abstract Submitter	Entela Lushaj
Email Address	lushaj@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Entela Lushaj
Science Type	Clinical Research
Keywords	Heart Transplant, Outcomes, Donor

Background: The scarcity of donors has led to use of older donor hearts for transplantation (HT). The impact of donor age on patient survival after heart transplant does not usually impact short to medium range survival. We analyzed the association of donor age with long-term patient survival after HT.

Methods: We retrospectively reviewed 755 patients undergoing HT at our institution from 05/1984 to 07/2018. Kaplan-Meier curves and Cox proportional hazard models were created to compare survival among patients who received hearts from donors <45 years old (group 1 [g1]; *n*=637) to those who received hearts from donors ≥ 45 years old (group 2 [g2]; *n*=118).

Results: The 2 groups were comparable with regard to recipient's age, gender and ischemic time. Median donor age for g1 was 24 years (Interquartile range [IQR]: 19-33) and for g2 was 50 years (IQR: 48-52). During follow up, (median 7 years; IQR 2-9.5), 229 (36%) patients died in g1 and 49 (52%) patients died from g2. Survival of patients receiving hearts from donors ≥45 years old was significantly lower compared to patients receiving hearts from younger donors (*p*=0.018; Figure 1). In multivariate Cox models using donor age as a continuous variable, risk of recipients' death was significantly higher with increasing donor age (HR 1.02, CI 1.01-1.02; *p*<0.001) even when adjusted for recipients' age, BMI and donor ischemic time. Reasons for death included cardiovascular events (21%), infection (16%) and malignancy (14%).

Conclusions: Higher donor age was associated with greater risk of recipients' death after cardiac transplant. Careful selection of older donor hearts to selected recipients may ameliorate the differences in long term survival.


1.0
0.8
0.6
0.4
0.2
0.0
Survival Probability (%)
Donor age <45 (g1)
Donor age >45 (g2)
Log-rank test p=0.018
Patients at risk:
g1 610 605 600 599 398
g2 89 86 84 84 61
0 2 4 6 8 10 12
Time from Transplant (years)

C44

Evolution of Balloon-Expandable Devices for Transcatheter Aortic Valve Replacement: University of Wisconsin Experience

Ujihira K.[1], Kohmoto T.[1], Jacobson K.M.[2], Raval A.N.[2], Gimelli G.[2], Osaki S.[1].

Abstract Submitter	Ujihira Kosuke
Email Address	ujihira@surgery.wisc.edu
Classification	Other (research scholar)
Principal Investigator	Devision of cardiothoracic surgery
Science Type	Clinical
Keywords	transcatheter aortic valve replacement, balloon expandable device

Introduction: Since transcatheter aortic valve replacement (TAVR) was launched at UW in 2012, a balloon-expandable device for TAVR has been advanced; first-generation (SAPIEN, 2012-2014), second-generation (SAPIEN-XT, 2014-2016), and third-generation (SAPIEN-3, 2015-present). The newer device offers a lower delivery profile and modifications to reduce para-valvular regurgitation. The aim of this study was to evaluate how the SAPIEN-3 valve improved the clinical outcomes.

Methods: From January 2012 to December 2017, SAPIEN (S1) was implanted in 74 patients, SAPIEN-XT (S2) in 80 patients, and SAPIEN-3 (S3) in 213 patients in UW. Outcomes of interest included in-hospital complications and all-cause mortality, cardiac complications, and para-valvular regurgitation at 12 months.

Results: Patients' background and pre-operative cardiac function were similar in 3 groups. The overall in-hospital complications were less in S3 (S1: 24%, S2: 36%, S3: 13%, $p<0.05$), typically the vascular complications (S1: 11%, S2: 7.5%, S3: 3.8%, $p<0.05$). Follow-up echocardiography at 12 months was conducted for 95% patients in total. Moderate or more para-valvular regurgitation was detected 6.0% in average, and this was not significantly different in 3 groups (S1: 8.6%, S2: 4.5%, S3: 6.3%). The average of survival rate at 12 months was 88% and escape of cardiac event was 80%, which were also similar in 3 groups.

Conclusions: S3 was resulted in lower in-hospital complications than previous generations. The clinical outcome at 12 months was acceptable, but long-term follow-up is expected to validate the efficacy of newer generation devices.

C24

Donor Age Significantly Impacts Long Term Survival of Patients Undergoing Heart Transplantation

Lushaj EB, Dhingra R, Osaki S, Johnson M, Lozonschi L, Kohmoto T

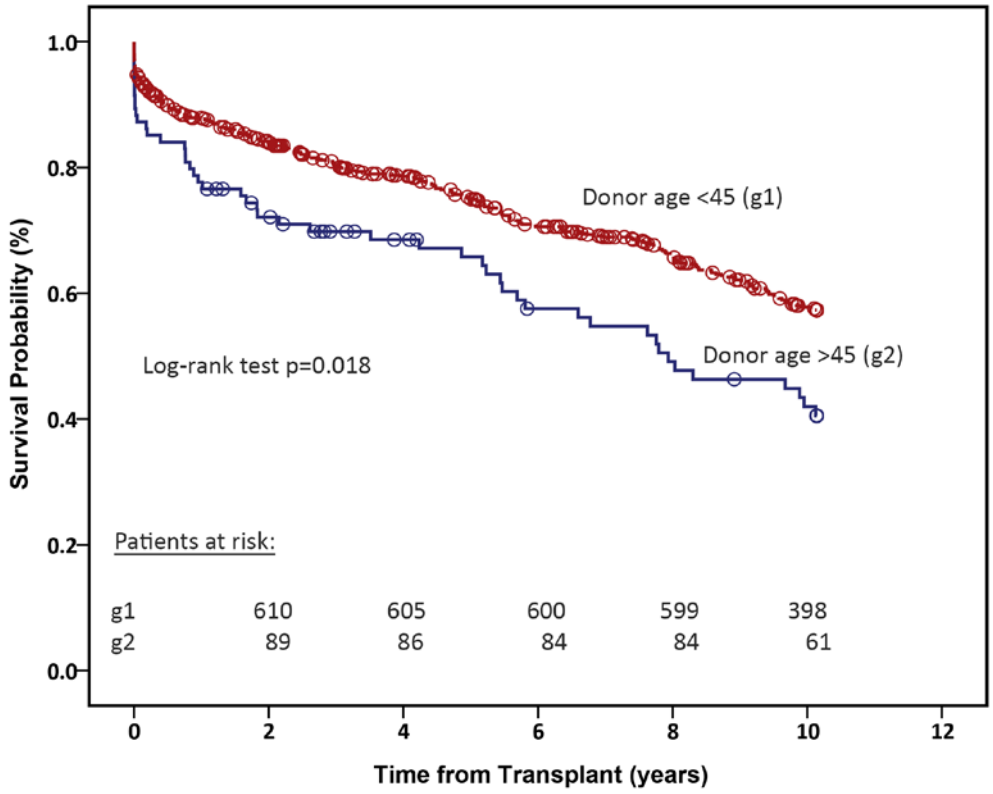
Abstract Submitter	Entela Lushaj
Email Address	lushaj@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Entela Lushaj
Science Type	Clinical Research
Keywords	Heart Transplant, Outcomes, Donor

Background: The scarcity of donors has led to use of older donor hearts for transplantation (HT). The impact of donor age on patient survival after heart transplant does not usually impact short to medium range survival. We analyzed the association of donor age with long-term patient survival after HT.

Methods: We retrospectively reviewed 755 patients undergoing HT at our institution from 05/1984 to 07/2018. Kaplan-Meier curves and Cox proportional hazard models were created to compare survival among patients who received hearts from donors <45 years old (group 1 [g1]; *n*=637) to those who received hearts from donors ≥ 45 years old (group 2 [g2]; *n*=118).

Results: The 2 groups were comparable with regard to recipient's age, gender and ischemic time. Median donor age for g1 was 24 years (Interquartile range [IQR]: 19-33) and for g2 was 50 years (IQR: 48-52). During follow up, (median 7 years; IQR 2-9.5), 229 (36%) patients died in g1 and 49 (52%) patients died from g2. Survival of patients receiving hearts from donors ≥45 years old was significantly lower compared to patients receiving hearts from younger donors (*p*=0.018; Figure 1). In multivariate Cox models using donor age as a continuous variable, risk of recipients' death was significantly higher with increasing donor age (HR 1.02, CI 1.01-1.02; *p*<0.001) even when adjusted for recipients' age, BMI and donor ischemic time. Reasons for death included cardiovascular events (21%), infection (16%) and malignancy (14%).

Conclusions: Higher donor age was associated with greater risk of recipients' death after cardiac transplant. Careful selection of older donor hearts to selected recipients may ameliorate the differences in long term survival.


1.0
0.8
0.6
0.4
0.2
0.0
Survival Probability (%)
Donor age <45 (g1)
Donor age >45 (g2)
Log-rank test p=0.018
Patients at risk:
g1 610 605 600 599 398
g2 89 86 84 84 61
0 2 4 6 8 10 12
Time from Transplant (years)

C22

Incidence, Etiology and Risk Factors of Unplanned Readmissions After Trans-Catheter Aortic Valve Replacement

Kohmoto, TK, Osaki S, Ujihira K, Lushaj EB

Abstract Submitter	Entela Lushaj
Email Address	lushaj@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Entela Lushaj
Science Type	Clinical Research
Keywords	Outcomes, Trans-Catheter Aortic Valve, Readmission

Introduction: Unplanned readmissions after initial hospitalization are frequent, significantly affecting clinical outcomes and patient quality of life. We analyzed the incidence, causes, and predictors of unplanned hospital readmissions after trans-catheter aortic valve replacement (TAVR). Methods:

We retrospectively reviewed 470 high risk patients (mean STS risk score 10±8) undergoing trans-aortic valve replacement therapy (TAVR) at our institution from 01/2012-04/2018. Eighty eight VA patients were excluded. Median follow-up time was 12 (IQR: 5, 18) months. Scheduled readmissions were excluded.

Results: 206 pts were readmitted for a total of 484 readmissions (2.3 readmissions/pt) for the duration of follow-up. On multivariate analysis, OR time, ICU and hospital length of stay, in-hospital postoperative events, and previous cardiac surgery were risk factors associated with unplanned readmissions. Age, gender, BMI, STS risk score and TAVR access were not found to be risk factors for readmission. Fifty-nine (29%) of the readmissions were within 30-days and 155

(75%) were within one-year post-discharge. Overall causes for readmission included cardiac

(32%), respiratory (8%), neurological (8%) and infection (8%). Leading causes for 30-day readmissions included cardiac (27%), respiratory (11%) and pain (11%). Median time-to-first readmission was 79 (IQR): 7-197) days. Median hospital length of stay at readmission was 3

(IQR: 1, 6) days. The 1-, 2-, 3- and 4-year freedom from first readmission was 74%, 60%, 51% and 51% respectively. Patients with unplanned readmissions had a significantly lower long term survival (p=0.014).

Conclusions: Unplanned readmissions are common during the first year after TAVR and nearly one third of them they are cardiac related. Readmissions were associated with lower long-term survival of patients after TAVR.

C26

Short and Long Term Predictors and Causes of Death Post Heart Transplant

Lushaj E, Lozonschi L, Kohmoto T, Jaeger H, Johnson M, Dhingra R

Abstract Submitter	Entela Lushaj
Email Address	lushaj@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Entela Lushaj
Science Type	Clinical Research
Keywords	Heart Transplant, Outcomes, Survival

Background: We analyzed our institutional data to assess the short and long term survival, causes, and predictors of mortality after heart transplant (HT).

Methods: We retrospectively compared patients who underwent HT at our institution between 1/2003- 5/2016 (*n*=250) and died within one year (group 1 [g1] of HT to those who survived more than 1 year (group 2 [g2]) after HT.

Results: Median follow-up time was 4 (Interquartile range [IQR]: 1-9) years. Mean age of patients was 54±10 years; 82% were males. During follow up, 24 (40%) deaths occurred within the first year after HT and 36 (60%) deaths occurred after the first year. Pre-HT cardiovascular risk factors such as age, diabetes, hypertension or smoking history, donor age and ischemic time, pre-operative creatinine values, history of LVAD and perioperative characteristics such as cardiopulmonary bypass time, renal failure, post-operative complications were similar between the 2 groups (p>0.05 for all). Overall, common reasons for death were infection (13%), malignancy (20%), cardiac complications (18%), gastrointestinal (7%) and neurological (5%) events. Primary graft failure accounted for 27% of cardiac related deaths. Infection was the major cause of deaths within 1 year (75% vs. 25%; p=0.055) whereas, malignancy was the leading cause of death beyond the first year (0% vs. 5%; p=0.004).

Conclusion: Even though long term survival rates after heart transplant at our institution were better than national average, deaths within the first year were more common due to infections and cardiac complications. After the first year, malignancies were the primary reason for deaths. None of the pre-HT cardiovascular risk factors were predictive of death post-HT.

C43

The Impact of Conscious Sedation on the Outcomes After Transcatheter Aortic Valve Replacement.

Ujihira K.[1], Kohmoto T.[1], Jacobson K.M.[2], Raval A.N.[2], Gimelli G.[2], Osaki S.[1].

Abstract Submitter	Ujihira Kosuke
Email Address	ujihira@surgery.wisc.edu
Classification	Other (research scholar)
Principal Investigator	Devision of cardiothoracic surgery
Science Type	Clinical
Keywords	Transcatheter aortic valve replacement

Introduction: Transcatheter aortic valve replacement (TAVR) is typically performed under general anesthesia (GA). However, with advancing the device technology, the safety of performing TAVR under conscious sedation (CS) has been reported. The aim of this study was to evaluate the impact of CS on the outcomes after TAVR.

Methods: In our institution, TAVR under GA was started from January 2012, and CS was from October 2014. A retrospective analysis of consecutive patients who underwent TAVR from 2012 to 2017 was performed. Immediate and mid-term results were assessed.

Results: The number of patients in each group was 235 in GA and 204 in CS. The average age was 79±9.6 years old in GA and 80±9.9 years old in CS. The severity of aortic stenosis and preoperative cardiac function were similar in 2 groups. The patients background was also similar except for the number of prior cardiac surgery (34% in GA vs 23% in CS, $p=0.017$). The length of stay in hospital (2.3±1.8 days vs 4.6±2.9 days, $p<0.001$) and ICU (10±17 hours vs 37±34 hours, $p<0.001$) was significantly shorter in CS, and the in-hospital complications was also less in CS (14% vs 29%, $p<0.001$). During this follow-up period, all-cause mortality and the number of cardiac events were similar.

Conclusions: CS was a safe and effective option for TAVR to shorten the length of stay in hospital and ICU, and this could be one of the factors to decrease the in-hospital complications.

C45

Three Case Reports of TAVR in Patients with Circumflex Coronary Artery Anomaly

Ujihira K.[1], Raval A.N.[2], Wolff M.R.[2], Osaki S.[1]

Abstract Submitter	Ujihira Kosuke
Email Address	ujihira@surgery.wisc.edu
Classification	Other (research scholar)
Principal Investigator	Devision of cardiothoracic surgery
Science Type	Clinical
Keywords	Transcatheter aortic valve replacement, anomalous coronary artery

Introduction: The most common coronary anatomic variation is the anomalous left circumflex artery (LCx), which can be found in approximately 0.17% of all patients who coronary angiography was performed. This anomaly could be a procedural risk during transcatheter aortic valve replacement (TAVR), however, best management for the TAVR patients with this anomaly has not been clarified.

Methods: We experienced 3 patients of severe aortic valve stenosis with the anomalous origin of LCx from right sinus of Valsalva, who underwent TAVR. The anomaly was confirmed by preoperative coronary angiography and enhanced CT. All 3 patients were octogenarian and considered to be high-risk for conventional surgical aortic valve replacement. We used Sapien-3 aortic valve for all these cases.

Results: For the first patient, as an LCx protection from the orifice occlusion or vessel stenosis, percutaneous placement of a coronary guidewire plus balloon was performed prior to deploy the aortic valve stent. TAVR was successfully completed without any complications, and no additional intervention was required as angiography revealed no stenosis within the LCx. For the second and third patients, no protection for LCx was placed, and their procedures were also completed safely. The post-operative course was uneventful, and no complications occurred till one-year follow-up.

Conclusions: From our experience, TAVR for patients with the LCx anomaly could be performed safely without protection or additional intervention.

C46

Outcomes of a Multidisciplinary Approach to Patients with Acute Necrotizing Pancreatitis

Liepert, A. E, M.D., Williams K. E, B.S

Abstract Submitter	Kyle Williams
Email Address	Kewilliams8@wisc.edu
Classification	Medical student
Principal Investigator	Amy Liepert
Science Type	Clinical
Keywords	Necrotizing pancreatitis, Multidisciplinary, Outcomes

Introduction: Acute necrotizing pancreatitis develops in 20% of the 240,000 patients diagnosed with acute pancreatitis each year in the US. Necrotizing pancreatitis often has a clinical course marked by sepsis and end organ failure with a mortality rate of 20-40%. Historical treatment with open necrosectomy carried a similar mortality rate of up to 40% along with a high risk of complications including pancreatic insufficiency. In recent years, minimally invasive techniques including percutaneous or endoscopic drainage and Video Assisted Retroperitoneal Drainage (VARD) have been shown to significantly improve mortality and complication rates when used in a “step-up” approach. It has been advocated to be adopted as the best treatment. However, this requires use of a multidisciplinary clinical approach. The initiation and development of multidisciplinary care is not well described, particularly for acute benign disease. In November 2015 University of Wisconsin Hospital and Clinics (UWHC) developed a multidisciplinary group called: UW PANC: Pancreatitis Acute Necrotizing Complex Multidisciplinary Workgroup in order to coordinate both inpatient and outpatient care of these complex patients.

Methods: A retrospective review based upon the UW PANC database of patients with necrotizing pancreatitis was carried out. Number of procedures performed, number of operative interventions, length of stay, and readmissions were reviewed. Workgroup records were also reviewed for specialty member attendance, volume of referrals, number of patients reviewed, and review of conference minutes to identify implementation challenges and evaluation for other themes

Results: A retrospective review was completed and a RedCap Database was developed using this patient information. Statistical analysis will be performed on data obtained.

Conclusions: Patients with necrotizing pancreatitis can be medically complicated and treatment historically has been associated with high morbidity and mortality. Treatment with a “step-up” approach with utilization of a multidisciplinary team has been shown to improve outcomes. With this research we hope to assess the outcome of this approach undertaken by the UW-PANC workgroup.

C13

In-Person Hemorrhage Control Training Effectiveness and Comprehension in Low-Resource Rural Settings

El-Gabri D., McDow A., Sullivan S., Jung H.S, Long K.

Abstract Submitter	Deena El-Gabri
Email Address	elgabri@wisc.edu
Classification	Medical student
Principal Investigator	Kristin Long
Science Type	Education
Keywords	Trauma; bleed; Low-resource

Introduction: The American College of Surgeons Committee on Trauma developed the Stop the Bleed (STB) program in 2015 as a mechanism to prepare the public for response to life-threatening bleeding or mass casualty incidents. Assessments of STB in the United States (US) have shown the training's effectiveness in improving comfort and skill in aiding a trauma victim. While the program continues to spread throughout the US, to the best of our knowledge, it has not been conducted and evaluated in low or middle-income countries, nor have there been assessments of its effectiveness in an international setting. Kenya has a high burden of injuries and violence accounting for 88.4 deaths per 100,000 people. Addressing this burden is a healthcare priority in the country. STB training represents a potential intervention that could reduce trauma morbidity and mortality in a country with limited healthcare resources. The purpose of this study was to assess the effectiveness and retention of STB training in Kenya.

Methods: This quasi-experimental study assessed differences between a STB intervention post-test conducted in the US and in Kenya. The two populations consisted of volunteer participants with no medical background. The population of interest was recruited in Migori Kenya (n=19), the comparison population in Wisconsin, United States (n=12). Each group received the same STB training course in July 2018 by instructors from the same US institution. After completing the course, each group received the same 5-question post-test, designed to assess effectiveness and comprehension of the material. The quizzes were voluntary, anonymous and not marked with any individual identifiers. The quiz mean scores between each group were compared with Mann-Whitney U-Test.

Results: There is a statistically significant ($p=0.04$) difference in the mean quiz scores between the US (n=12) and Kenya population (n=18). The Kenyan and US mean scores were 3.9 and 4.7 out of a possible 5, respectively. If one quiz question is excluded from analysis there is no significant difference between the two group's quiz scores ($p=0.41$). The individual question that significantly lowered the mean score among the population was: "What is the first step when approaching an injured, bleeding person?", which may identify a difference in interpretation of the material.

Conclusions: In general, both populations studied demonstrated good comprehension of the STB core concepts. In detailed review of the post-test scores, only one question was significantly different in answers among the Kenya and US populations. Additional studies to assess long-term retention of these concepts will be necessary in both populations. Understanding the discrepancies between the assessments in differing populations may contribute to validation and utility of this STB post-intervention evaluation.

C2

Maximum Axial Diameter is a Poor Surrogate for Volume and Surface Area of Small Pancreatic Cysts

Awe, A.M., Rendell, V.R., Lubner, M.G., and Winslow, E.R.

Abstract Submitter	Adam Awe
Email Address	aawe@wisc.edu
Classification	Medical student, UWSMPH
Principal Investigator	Meghan G. Lubner, M.D. Emily R. Winslow, M.D.
Science Type	Clinical Research
Keywords	Pancreatic cysts, Radiology, Volumetric analysis

Introduction: Pancreatic cystic lesions can be difficult to accurately and reproducibly characterize radiographically, which presents a challenge for clinical management. Current guidelines use maximum axial diameter (MAD) thresholds and growth criteria, but the correlation between cyst size and malignant potential has been variable. Particularly with non-spherical cysts, employment of MAD metrics may fail to accurately risk-stratify patients and capture cyst evolution. The aim of this study is to determine whether MAD is an appropriate surrogate measure for volume and surface area of pancreatic cysts.

Methods: We conducted a single-institution retrospective analysis of patients with radiologically confirmed PCs ≥1cm on a contrast-enhanced CT or MR scan. Patients with two scans ≥1 year apart were included in rate of change analyses. Patients with a pancreatic pseudocyst, surgical history pertaining to cyst of interest, or underlying pancreatitis were excluded. MAD, volume, surface area, and sphericity data were collected using HealthMyne, a novel lesion detecting software. Pearson's correlations were determined between volume-MAD and surface area-MAD for the entire patient data set, and within size groupings from the Fukuoka pancreatic cyst guidelines criteria. The absolute value of the percent difference of volume change was calculated using MAD-dependent volume estimation and measured volume. Pancreatic cysts were then stratified by high and low cyst sphericity and compared using chi-square analysis.

Results: In total, 202 patients were included in the volume-MAD and surface area-MAD correlation analyses. Pancreatic cyst MAD ranged from 1.0-7.5 cm and volume from 0.3-104.3 cm^3. Cyst volume as a function of MAD overall had a strong correlation (r=0.94). However, when grouped by Fukuoka criteria size correlations varied: r=0.78, 0.53, and 0.90 for 1-2 cm (n=87), 2-3 cm (n=61), and >3 cm (n=54) pancreatic cysts, respectively. Based on volume alone, 95 cysts (47%) overlapped Fukuoka size groups. Pancreatic cyst surface area ranged from 0.2-126.2 cm^2. Cyst surface area as a function of the MAD overall had a strong correlation (r=0.96). When grouped by Fukuoka criteria size, correlations varied: r=0.80, 0.56, and 0.92 for 1-2 cm (n=87), 2-3 cm (n=61), and >3 cm (n=54) pancreatic cysts, respectively. Based on surface area alone, 77 cysts (38%) overlapped Fukuoka size groups. A subset of 153 patients were included in the rate of change analyses. The average change in MAD/year was 1.0mm/year (SD 2.5mm/year) and volume/year was 0.88 cm^3/year (SD 2.5 cm^3/year). For 60 (39%), the actual volume change was larger than the estimated volume change based on MAD, and 64 (42%) had a >100% absolute difference in volume change between estimated and actual volumes. Pancreatic cysts with high sphericity (≥0.80) had greater concordance between estimated and actual volume changes (p=0.02).

Conclusions: Despite overall strong correlations between pancreatic cyst volume-MAD and surface area-MAD, grouping PCs based on Fukuoka criteria size reveals poor correlations for small cysts. MAD also poorly predicts changes in volume for pancreatic cysts, particularly for cysts with low sphericity. Overall, these findings suggest that volume may be a useful adjunct metric to characterize and monitor smaller pancreatic cysts.

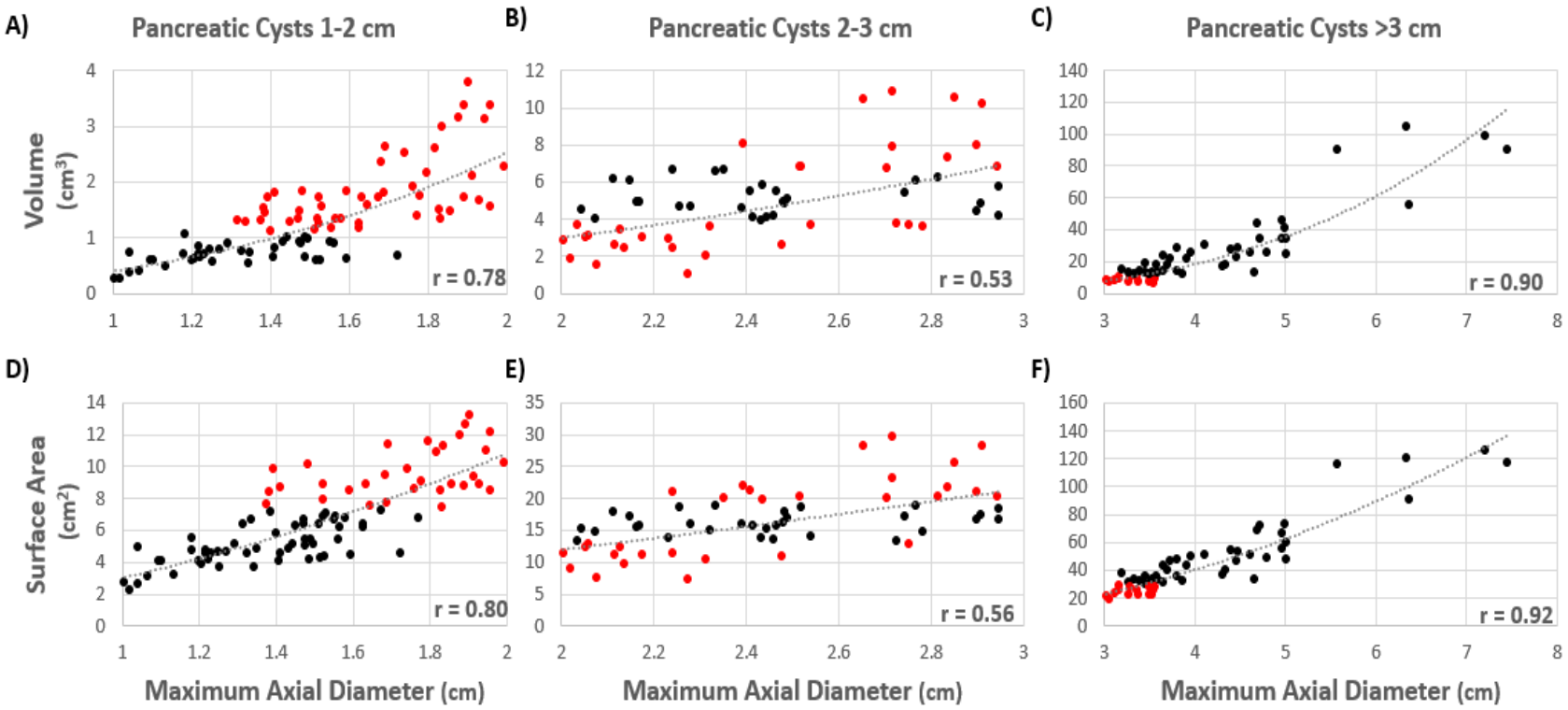


Figure 1. Volume-MAD and surface area-MAD are poorly correlated for small pancreatic cysts. 202 patients with radiologically confirmed pancreatic cysts are represented on scatterplots of cyst volume (cm^3) as a function of maximum axial diameter (MAD; cm) for 1-2 cm cysts (r=0.78; n=87), 2-3 cm cysts (r=0.53; n=61), and >3 cm cysts (r=0.90; n=54) (A-C). Patient data is also represented on scatterplots of surface area (cm^2) as a function of MAD (cm) for 1-2 cm cysts (r=0.80; n=87), 2-3 cm cysts (r=0.56; n=61), and >3 cm cysts (r=0.92; n=54) (D-F). Pancreatic cyst volume and surface area values that overlap between adjacent size subgroupings are indicated in red and non-overlapping data are indicated in black.

C27

MSSA Screening and Decolonization Among Non-Cardiac Thoracic Surgery Population

Kurtz JL, Maloney JD, McCarthy DP Decamp MM, Crnich C

Abstract Submitter	James Maloney
Email Address	maloney@surgery.wisc.edu
Classification	Faculty
Principal Investigator	James Maloney
Science Type	Clinical Research
Keywords	Thoracic, MSSA, Surgery

Background: Surgical site infections (SSI) are associated with poor surgical outcomes and increased heath care costs. Pre-operative MRSA (methicillin-resistant Staphylococcus aureus) and MSSA (methicillin-susceptible Staphylococcus aureus) screening and decolonization prior to Orthopedic and Cardiac Surgery is associated with decreased SSIs. Data describing this among patients undergoing (Non-Cardiac) Thoracic Surgery is lacking. Our facility implemented a quality improvement (QI) project to pre-operatively screen patients for MSSA and decolonize carriers.

Methods: This QI project utilized a descriptive design with a consecutive series of patients undergoing Thoracic Surgery at a single VA institution. Those excluded were inpatients and patients undergoing a procedure without an incision. Previously, Thoracic Surgery patients were pre-operatively screened for MRSA. Carriers were prescribed a decolonization protocol. With this enhanced protocol, pre-operative MSSA screening and decolonization was added. MRSA and MSSA carriers were prescribed a five day course of intranasal mupirocin ointment and chlorhexidine wipes.

Results: Between November 2015 and June 2018, 178 unique patients who were scheduled to undergo Thoracic surgical procedures. There was an additional 37 cases performed during this period that were excluded from the data due to either inpatient status or lack of incision. Of those, 178/178 (100%) were screened for MRSA and MSSA, 40 (22.4%) were MSSA carriers, 6 (3.4%) were MRSA carriers. All of the MRSA carriers were also MSSA carriers. One hundred percent of patients who screened positive were prescribed the decolonization protocol.

Discussion: While the benefit of MSSA screening and decolonization has been demonstrated in some surgical subspecialties, it has not been described among Thoracic Surgery patients. The small sample size limits the ability to demonstrate a statistically significant change in SSIs. Future analysis should include data on patient compliance with the decolonization protocol. Implementation of MSSA screening and decolonization could improve surgical outcomes and does not impose risk to patients.

C29

Quality of Life and Survival: Comparing Treatment Options for Node-Positive Stage III Non-Small Cell Lung Cancer

Decker-Palmer M, McCarthy DP, Maloney JD

Abstract Submitter	James Maloney
Email Address	maloney@surgery.wisc.edu
Classification	Faculty
Principal Investigator	James Maloney
Science Type	Clinical Research
Keywords	Thoracic, Quality of life, Cancer

Background: Conflicting evidence from clinical trials has led to uncertainty about which treatment strategy maximizes quality-adjusted life expectancy for survivors of node-positive Stage III non-small cell lung cancer (NSCLC). This study addresses this uncertainty by comparing the survival benefits as well as the quality-adjusted life expectancy attributable to each strategy. We hypothesized that the strategy that maximizes survival differs from the strategy that maximizes quality-adjusted life expectancy.

Methods: Systematic review of the literature was conducted to identify clinical trials for node-positive Stage III NSCLC, and lung cancer utility studies. The meta-analysis was organized by treatment strategies, which included: neoadjuvant chemoradiation + surgery

(NCR + S), neoadjuvant chemotherapy + surgery (NC + S), surgery + chemotherapy (S+ C), surgery + chemoradiation (S + CR). A Markov cohort model was constructed to estimate survival benefits and quality-adjusted life expectancy for each strategy.

Results: Five clinical trials comprised the meta-analysis. S + C is the strategy with the greatest survival benefit (S + C > NCR +S > NC + S > S + CR), with an additional 6.4 ± 1.4 months more life expectancy than NCR +S. S + C is also estimated to lead to the greatest quality-adjusted life expectancy, with an additional 5.2 ± 1.1 months more quality-adjusted life expectancy than NCR + S. The strategy with the lowest survival benefit and the worst quality-adjusted life expectancy is S + CR, with 1.4 ± 1.1 fewer months of survival benefit and 1.9 ± 0.7 months lower quality-adjusted life expectancy than NC + S (10.8 ± 1.7 months and 8.5 ± 1.1 quality-adjusted months less than S + C).

Conclusions: Surgery followed by chemotherapy for node-positive Stage III NSCLC is estimated to maximize survival, and it is projected to have the greatest health benefits in terms of quality-adjusted life expectancy.

C17

Patterns of Opioid Use in Vascular Access Procedures

Janek, K.C. [1], Bennett, K.M[1], Imbus, J.R. [1], Danobeitia, J.S., Phillips, J.L. [1], Melnick, D.M[1]

[1]University of Wisconsin School of Medicine and Public Health, Department of Surgery, Madison, WI

Abstract Submitter	Kevin Janek, MD
Email Address	kjanek@uwhealth.org
Classification	Resident
Principal Investigator	David Melnick, MD
Science Type	Clinical
Keywords	Opioid, vascular access, fistula

Introduction: Over-prescription of opioids following surgical procedures is recognized as important contributor to opioid misuse. Dialysis access procedures are commonly performed outpatient surgery with little information to guide prescription pain management practices. We sought to investigate opioid pain medication use following dialysis access surgery to inform quantity and duration of appropriate opioid prescriptions.

Methods: Following IRB approval, a retrospective review of 23 patients who underwent surgical dialysis access procedures from July through September of 2018. Patient-reported opioid use information was available from routine follow-up clinic or phone calls recorded in the electronic medical record. Information collected included procedure, type of intraoperative anesthesia/analgesia, and post-op prescription provided, as well as patient factors including age, sex, dialysis type, history of chronic pain, and history of chronic opioid or benzodiazepine use.

Results: We identified 16 patients in this study time-frame who underwent dialysis access procedures, including radiocephalic fistula or graft (1), brachiocephalic fistula or graft (8), brachiobasilic fistula or graft (5), or peritoneal dialysis [PD] catheter placement (2) who reported opioid use post-operatively (mean time to follow-up 20 days, range 4-60). All patients were provided with an opiate prescription of 5 mg oxycodone or hydrocodone 5 mg/acetaminophen 325 mg, with an average quantity of 9 +/- 3.4 pills, with the highest quantity given for basilic vein operations (12 +/- 2.74, range 10-15). Although 38% of patients took no pills, opiate use averaged 2.56 +/- 3.42 pills among all surgeries and taken for 1.5 +/- 1.4 days, and use was highest among PD catheter placement or revision and lowest for Stage 1 BVT.

Conclusions: Prescription practices following surgical dialysis access procedures has tendency to over-prescribe, resulting in left-over pain medication which is vulnerable to opioid misuse. Prescriptions given for upper extremity procedures for more than 4 pills are unlikely to be used in the immediate post-operative period.

Procedure	N=	# opiate pills provided	# of opiate pills used	Days taken
Elbow	6	7.16 +/- 3.125	2.33+/-2.30	2.16 +/-1.47
PD catheter	2	10 +/- 0	15 +/-7.07	4 +/- 1.41
Stage 1 BVT	2	12.5 +/- 3.54	0.5 +/- .707	0.5 +/- .707
Stage 2 BVT	2	10 +/- 0	2.5 +/- 3.54	1 +/-1.41
Upper Arm Graft	1	15 +/- 0	0	0
Wrist	1	4 +/- 0	0	0

Figure 1: Procedure-specific opioid prescription practices and patient-reported use

C40

Barriers to Breast Reconstruction for Women with Lower Socioeconomic Status

Stankowski-Drengler TJ, Schumacher J, Hanlon B, Tucholka J, Amessoudji A, Venkatesh M, Yang D-Y, Neuman HB

Submitter	Trista Stankowski-Drengler
Phone	612-308-0325
Email Address:	tstankowski-drengler@uwhealth.org
Classification:	Resident
Division:	General Surgery
Lab:	Heather Neuman (GEAR Lab)
Science Type:	Clinical Research
Keywords:	Breast Cancer, Health Disparities, Reconstruction

Introduction: Disparities in post-mastectomy breast reconstruction exist for women with lower socioeconomic status (SES). Understanding factors that influence reconstruction may identify actionable changes to reduce disparities. Key informants have suggested that finding surgeons that accept Medicaid and travel time to a plastic surgeon are key factors. Our objective was to assess the relationship between these factors and reconstruction for low SES women in Wisconsin.

Methods: We identified women <75 years of age with stage 0-III breast cancer who underwent mastectomy between 2009-2014 using the Wisconsin Cancer Reporting System. Area deprivation index, a census block-based composite measure, was calculated as a surrogate for SES. Women were categorized by tertiles and the lowest tertile comprised our cohort. Geocoding determined turn-by-turn drive time from a woman's home to the nearest accredited Commission on Cancer or National Accreditation Program for Breast Centers. Multivariable logistic regression determined the relationship between reconstruction and Medicaid and travel time, controlling for variables known to impact receipt of reconstruction.

Results: Our cohort consisted of 1756 primarily white women (82%) with early stage breast cancer (52% stage 0/I). The median age was 55 and 18% had Medicaid. 37% of women underwent reconstruction. On multivariable regression (Table), low SES women with Medicaid *vs*. any other insurance were significantly less likely to receive reconstruction (OR 0.56, 95% CI 0.4-0.7). Longer travel time was also significantly associated with lower odds of reconstruction (OR 0.99, 95% CI 0.99-1.0). This translates to an adjusted predicted probability of 38% *vs*. 33%, depending on whether a woman lives within 10 *vs.* 50 minutes of an accredited center.

Conclusion: In our cohort of low SES women living in Wisconsin, having Medicaid and living further from an accredited center remain important predictors of reconstruction, even after controlling for clinical variables. Further work will explore opportunities to improve access to reconstruction for women with Medicaid. This is particularly challenging and may require low SES women to travel further to receive care.

Table: Likelihood of Breast Reconstruction Attributable to Patient and Clinical Variables			
	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Medicaid	0.56	0.42-0.74	<0.0005
Travel time to Accredited Center	0.99	0.99-1.0	0.007
Age <40	Reference		<0.0005
40-50	0.72	0.54-0.96	
50-60	0.30	0.22-0.41	
60-70	0.11	0.07-0.16	
Stage 0	Reference		0.002
1	0.70	0.44-1.11	
2	0.50	0.31-0.83	
3	0.31	0.16-0.60	
Bilateral mastectomy	2.13	1.68-2.70	<0.0005
Radiation	0.90	0.66-1.23	0.525
Chemotherapy	0.84	0.62-1.14	0.261
*Also controlled for Estrogen/Progesterone receptor, Her2neu status, and Year of diagnosis			

C33

Large Single Center Results of Simultaneous Pancreas-Kidney (SPK) Transplantation in Patients with Type 2 Diabetes (T2D) Compared to Type 1 Diabetes (T1D)

Pham P.H., Martinez E.J., Welch B., Leverson G., Marka N., Sollinger H.W., Kaufman D.B., Redfield R.R., Odorico J.S.

Abstract Submitter	PHUOC HUY PHAM
Email Address	PPHAM3@WISC.EDU
Classification	MEDICAL STUDENT
Principal Investigator	JON ODORICO, MD
Science Type	CLINICAL RESEARCH
Keywords	SPK, DIABETES, OUTCOMES

Introduction: Compared to T1D, in which pancreas transplantation (PTx) is an established effective treatment, there are only a few studies addressing SPK outcomes and patient selection criteria for SPK transplantation in T2D patients. These studies not only found similar transplant outcomes including patient, kidney graft, and pancreas graft survival between T1D and T2D SPK recipients, but also suggested that SPK transplantation might be associated with improved patient and kidney survival compared to kidney transplantation alone. However, few data are available regarding the effect of recipient factors such as age, BMI, or pre-transplant insulin requirements on such outcomes, specifically for T2D recipients. Questions therefore remain as to which type of T2D patient is best suited for PTx.

In this study, we assessed the effects of recipient pre-transplant BMI and insulin requirement on the outcomes of SPK transplantation in T2D patients, and compared these to the impact of those parameters on T1D SPK recipients. The results of this study will not only contribute to the understanding of PTx in T2D recipients, but will also better inform patients and physicians in the decision-making process regarding treatment options.

Methods: A total of 323 patients who underwent SPK at the University of Wisconsin Hospital between 2006-2017 were assessed for recipient pre-transplant BMI and insulin requirements (Pre-IR). Outcome assessed were post-transplant diabetes (PTDM) (defined by post-transplant return to an oral hypoglycemic agent (OHA) and/or return to any insulin for > 3 consecutive months) and graft failures (GF) (as reported for resumption of insulin, pancreatectomy, or death). Minimum follow-up was 1 year except patients underwent pancreatectomy or failed <90 days, or expired <1 year after transplant. Recipient factors were analyzed to categorize patients as T1D or T2D. Additional variables controlled for included: Donor: age, race, gender, BMI, type (DBD vs. DCD), KDPI, CIT; and Recipient: age at time of transplant, gender, race, donor-recipient CMV/EBV status and induction therapy. Data collection was completed using UW Transplant Database and EHR (EPIC).

Results: SPK transplants for T2D increased from 1 per year (3.1% all SPK/year) (2006) to 12 (29.3%) per year (2016). The 323 patients were categorized into 284 T1D and 39 T2D patients based on several clinical parameters. During the follow-up period, 52 patients (16.1% [49 T1D and 3 T2D]) resumed insulin for > 3months, 23 patients (7.1%, all T1D) initiated OHA use post-transplant. Overall, 59 patients (18.2%) experienced GF (pancreatectomy: 18 T1D, 1 T2D; resumption of insulin: 37 T1D, 3 T2D). In T2D patients, BMI and Pre-IR were not significantly associated with GF (p_{BMI} = 0.71; $p_{pre\text{-}IR}$= 0.30) or PTDM (p_{BMI} = 0.58; $p_{pre\text{-}IR}$= 0.54). In T1D patients, neither BMI nor Pre-IR was significantly associated with GF (p_{BMI} = 0.12; $p_{pre\text{-}IR}$= 0.16) or PTDM (p_{BMI} = 0.14; $p_{pre\text{-}IR}$= 0.16).

Conclusions: Despite clinical concerns that high BMI and Pre-IR would be associated with poor results, we could not identify a significant association between these pre-transplant parameters and graft failure in general, or PTDM specifically, in T2D SPK recipients. These observations could inform a less restricted approach in T2D recipients.

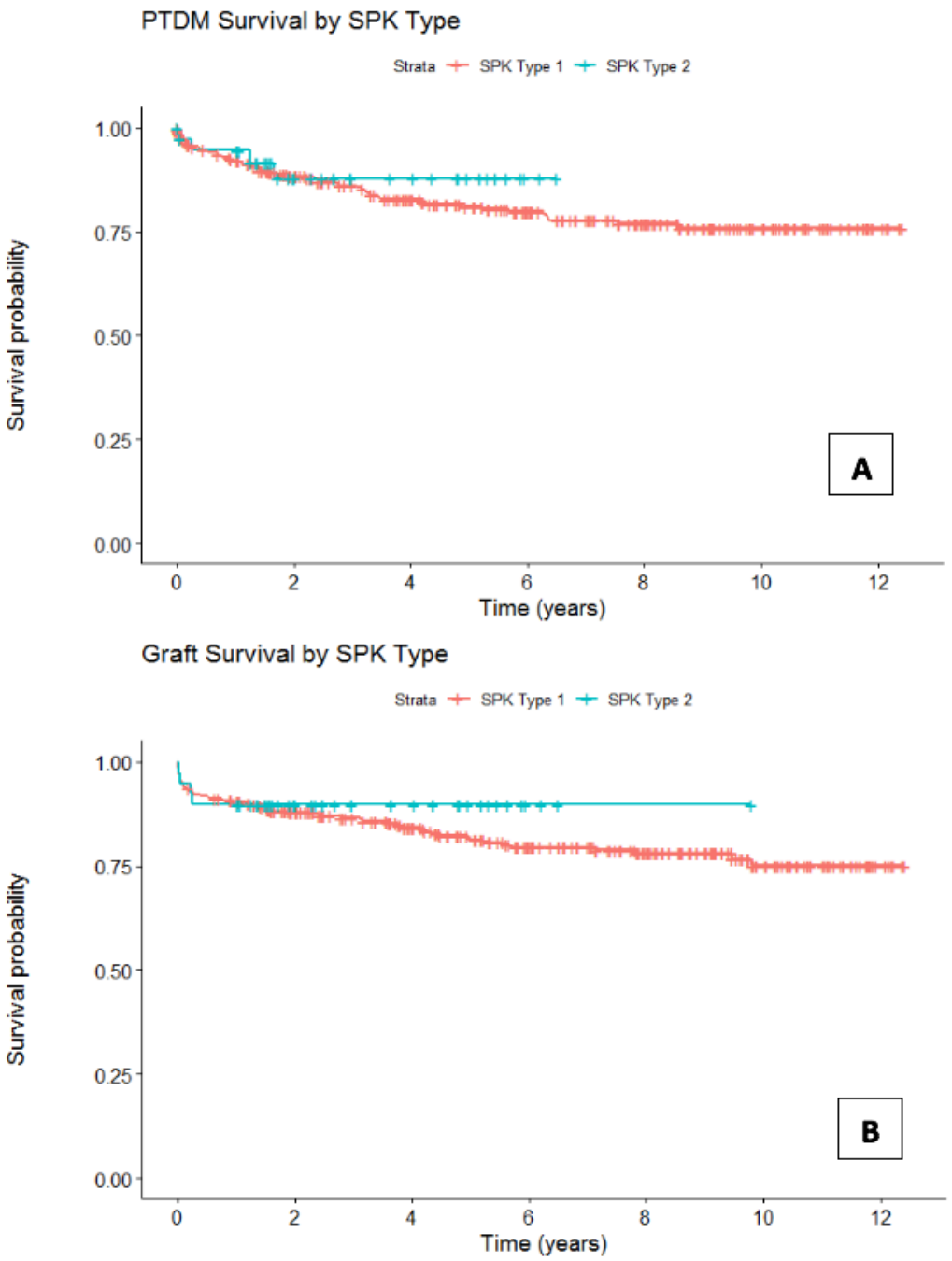


Figure. Kaplan Meier shows that survival from outcome (PTDM in curve A and Graft Survival in curve B) was not statistically different between the two groups (Type 1 diabetes mellitus and Type 2 diabetes mellitus) at the 0.05 significance level.

C14

A Trick for an Old Dog: The Senning Procedure to Treat Atrio-Ventricular Discordance with Ventriculo-Arterial Concordance

Hermsen J.L., Okorie U., Srinivasan S., Anagnostopoulos P.V.

Abstract Submitter	JL Hermsen
Email Address	hermsen@surgery.wisc.edu
Classification	clinical
Principal Investigator	Hermsen
Science Type	n/a
Keywords	Congenital heart disease, cyanosis, atrioventricular discordance, Senning

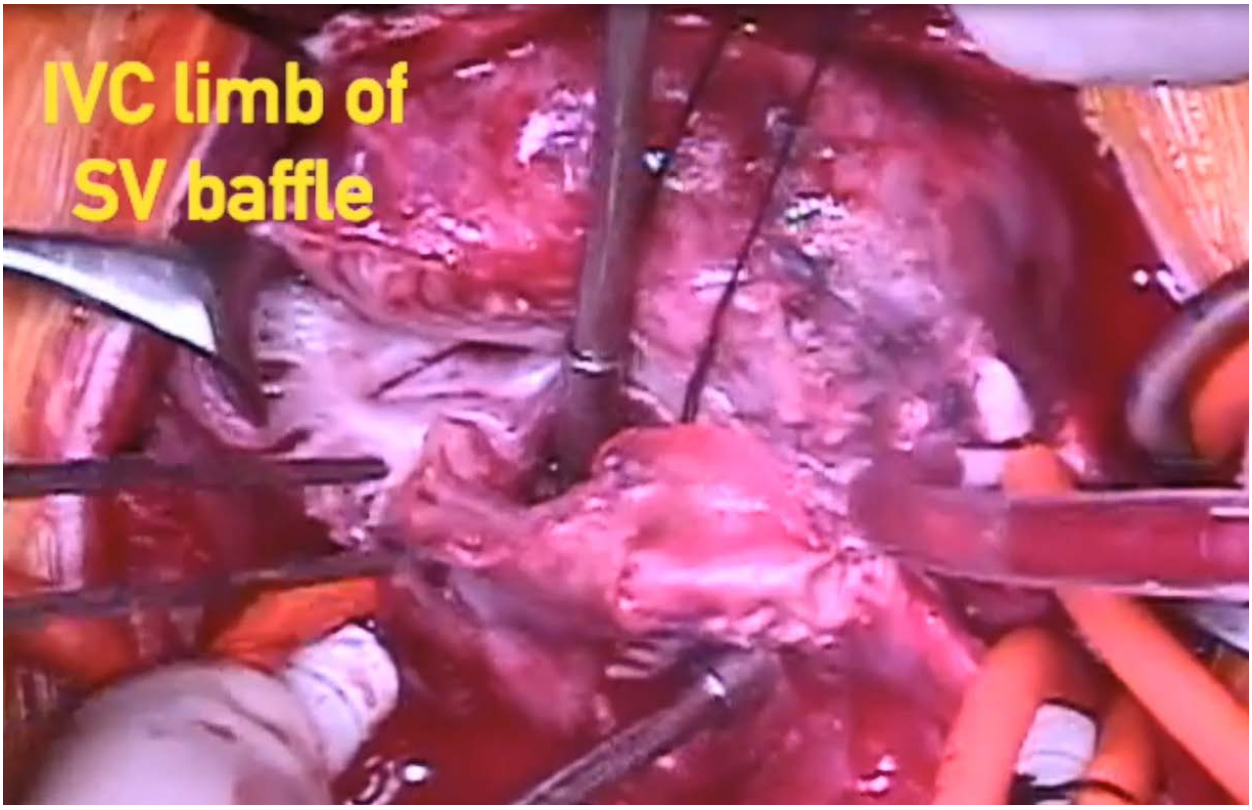
Introduction: Atrioventricular discordance (AVD) with ventriculoarterial concordance (VAC) and ventricular septal defect (VSD) is an extremely rare congenital heart lesion in which closing the VSD would create D-transposition of the great arteries and performing an arterial switch and VSD closure would produce congenitally corrected transposition of the great arteries. As such, it is the only lesion for which an isolated atrial switch is the preferred correction. The Senning procedure, a type of atrial switch first performed in 1958, was the first “corrective” operation used to treat D- transposition of the great arteries.

Methods: The patient is a term baby girl born with AVD/VAC, a large ventricular septal defect, and situs inversus totalis who developed heart failure in the neonatal period and was palliated with atrial septostomy to allow for optimal mixing and pulmonary artery banding to control symptoms of heart failure and protect the pulmonary vasculature. At 8 months of age she underwent complete repair with a Senning atrial switch procedure, VSD closure, and pulmonary artery debanding with pulmonary arterioplasty.

Results: The patient underwent corrective surgery with patch closure of the VSD, and the Senning atrial switch procedure resulting in correct assignment of the morphologic left ventricle, mitral and aortic valves to the systemic circulation and the morphologic right ventricle, tricuspid and pulmonic valves to the pulmonary circulation. The patient was discharged on post-operative day 6 with normal saturations.

Conclusions: The atrial switch procedure is very rarely used in the modern era as the outcomes in the setting of transposition of the great arteries is inferior to the arterial switch operation. However for AVD with VAC it remains the procedure of choice resulting in a physiologically normal biventricular circulation.

Intra-operative photograph showing portion of the Senning procedure redirecting the systemic venous blood to the right ventricle.



C18

Overtreatment of Thyroid Cancer: A Qualitative Study of Surgeons and Endocrinologies

Jensen C.B., Saucke M.C., Jennings J.L., Khokhar H.J., Voils C.I., Pitt S.C.

Abstract Submitter	Catherine Jensen
Email Address	cjensen22@wisc.edu
Classification	Medical Student
Principal Investigator	Susan Pitt MD, MPHS
Science Type	Clinical
Keywords	overtreatment, overdiagnosis, thyroid cancer

Introduction: Overtreatment of thyroid cancer is a significant problem in the United States. With the increasing incidence of this malignancy, it is essential to understand providers' views on overtreatment in order to reduce the unnecessary morbidity that results. Therefore, we aimed to better understand the attitudes and beliefs of surgeons and endocrinologists about overtreatment of patients with very low-risk thyroid cancer.

Methods: We conducted semi-structured interviews with 24 providers (12 high-volume surgeons and 12 endocrinologists) from all regions of the United States who treat patients with thyroid cancer. Interviews were conducted at the 2016 American Thyroid Association (ATA) meeting and prompted providers to discuss: (1) management of a patient with a very low-risk papillary thyroid cancer and (2) changes in the ATA guidelines made because of concerns about overtreatment. We used content analysis to identify themes related to overtreatment and created concept diagrams to map observed relationships between themes.

Results: Providers were 70.8% male and 87.5% white. In addition, 87.5% practiced at academic institutions. In the interviews, providers discussed overtreatment of very low-risk thyroid cancer as resulting directly from overdiagnosis and being difficult to prevent. They described diagnosis as an event that lets "the cat out of the bag" or "opens Pandora's box." Providers believed that overdiagnosis is commonly initiated by the incidental finding of a thyroid nodule on imaging studies and acknowledged that ordering of these tests by primary care and other providers is out of their control. Providers saw subsequent biopsy of the nodule as a habitual action driving overdiagnosis and pivotal step where they could intervene. Factors providers identified as influencing the reflex to biopsy included lack of adherence to or knowledge of guidelines, recommendations by radiology, patient expectations, and the desire of patients and their providers to minimize diagnostic uncertainty (Table). Providers also described how a cancer diagnosis provoked an instinctive desire by patients and surgeons to proceed with surgery. Most providers believed that it is easier to prevent overdiagnosis than subsequent overtreatment. Strategies suggested for avoiding overdiagnosis included education of patients and providers; unification of guidelines across specialties; re-classifying low-risk malignancies; changing reimbursement models; and resetting patients' expectations by both reframing the diagnostic-treatment paradigm and engaging mass media (Table).

Conclusions: Surgeons' and endocrinologists' attitudes and beliefs about overtreatment focus on the automaticity of overdiagnosis and the established path that exists from incidental discovery of a thyroid nodule to potentially unnecessary surgery. Providers suggest that the seemingly inevitable process of overdiagnosis can be interrupted with educational and behavioral interventions. Further studies are needed to identify effective interventions that prevent the harms of overtreatment.

Table. Surgeons' and Endocrinologists' Views on Overdiagnosis and Overtreatment		
Theme	**Subtheme**	**Example quote**
Factors that contribute to overdiagnosis	Lack of adherence to or knowledge of guidelines	*"… the guidelines are telling us not to biopsy anything less than a centimeter regardless of what it looks like, but then we're still getting referred patients that have eight-millimeter thyroid carcinomas."*
	Recommendations by radiology	*"Some radiology reports I get now it says that there's a half a centimeter nodule in the right lobe, recommend biopsy, and they send it to the patient."*
	Patient expectations	*"Patient expectations are a tricky thing when you're thinking of whether or not to biopsy a nodule."*
	Need to minimize diagnostic uncertainty	*"The majority of patients do not want to go around with the idea that they might have something that looks like cancer but without ever biopsying."*
Strategies to prevent over-diagnosis and overtreatment	Education of patients and physicians	*"...education, both at the patient level and the provider level with the surgeons and the endocrinologists. Um, through continuing education obviously."*
	Unification of guidelines across specialties	*"There are radiology guidelines, there are ATA guidelines, there will be AAES guidelines…There are lots of different people having opinions, so having a multidisciplinary approach…is important."*
	Re-classification of these low-risk malignancies	*"Finding a better name for this. I understand it's a cancer from the biology standpoint. But it is not a cancer the way the U.S. uses this word."*
	Changing reimbursement models	*"Insurance carriers, Medicare, etc. need to stop reimbursing for biopsies done on—asymptomatic patients with nodules less than 1 cm."*
	Engaging mass media	*"I mean people pay attention to social media. They pay attention to the news. We can get the message out there--if we carefully word it."*

C36

Improving Post-Operative Pain Management in Outpatient Breast Surgery with Novel Enhanced Recovery After Surgery Protocol and Pre-Operative Paravertebral Block

Shaum K.M., Israel J.S., Hill M.K., King A., Warren M., Siebert J.W., Rao V.K.

Abstract Submitter	Katherine Shaum
Email Address	Kshaum@uwhealth.org
Classification	Resident
Principal Investigator	Venkat Rao
Science Type	Clinical
Keywords	Pain management, paravertebral block

Introduction: Postoperative pain, nausea and vomiting are frustrating sequelae of elective breast surgery (e.g. breast augmentation or reduction). The opioid epidemic has made decreasing perioperative opioid use imperative. Enhanced recovery after surgery (ERAS) protocols and regional blockade have shown benefit in gastrointestinal and oncologic breast surgery. To date, ERAS protocols have not been studied in elective breast surgery. This study's purpose is to develop a protocol optimizing perioperative pain and postoperative recovery using paravertebral block (PVB) and a novel breast-specific ERAS protocol in patients undergoing elective breast surgery.

Methods: Beginning with literature review of regional blockade techniques for oncologic breast surgery and ERAS protocols for gastrointestinal surgery, we created a protocol using multidisciplinary collaboration (anesthesiology, nursing, surgery center administration, plastic surgery). After determining PVB to be the optimal regional blockade for this population, we provided additional training in this technique for the care team. A prospective, randomized clinical trial was then initiated to study the effects of the developed ERAS protocol and pre-operative PVB in a population of elective breast surgery patients.

Results: A breast-specific ERAS protocol was developed and approved by the Institutional Review Board. Components of the protocol include: (1) Preoperative: standardized verbal and written counseling; oral acetaminophen, meclizine and gabapentin in the pre-op holding area; (2) Intraoperative: IV ketorolac, dexamethasone, ondansetron with limitation of IV fluids as possible; (3) Postoperative: scheduled oral ondansetron, acetaminophen and ibuprofen for 5 days, as-needed low dose opioid. Patients undergoing elective breast surgery are prospectively randomized to either ERAS or non-ERAS (e.g. current clinical practice) groups. To independently study the effects of PVB on postoperative recovery, a second group is randomized to either preoperative PVB or sham block. Outcomes of all groups are assessed using validated pain surveys, the Quality of Recovery (QOR-40) survey, and medication quantitation for 7 days. To date, 32 patients have enrolled in the prospective randomized trial. Preliminary data demonstrates trend toward improved post-operative pain control in patients receiving pre-operative paravertebral block and improved patient satisfaction for those patients enrolled in the ERAS protocol, as demonstrated by QOR-40.

Conclusions: Enhanced recovery protocols may facilitate recovery after elective breast surgery. We have developed and pilot tested a multimodal ERAS protocol. Next steps include completion of a prospective randomized clinical trial of this protocol and preoperative PVB for patients undergoing elective breast surgery. Preliminary data indicates that these modalities will reduce perioperative opioid requirements, improve patient satisfaction and optimize recovery following elective breast surgery.

C7

Alemtuzumab is Associated with Higher Rates of De Novo Donor Specific Antibody (DSA) in Patients with No Pre-Transplant DSA

Bath N.M., Djamali A., Parajuli S., Mandelbrot D., Leverson G., Ellis T., Hager D., Kaufman D.B., Redfield III R.R.

Abstract Submitter	Natalie Bath
Email Address	nbath@wisc.edu
Classification	Resident
Principal Investigator	Redfield
Science Type	Clinical
Keywords	Alloantibody, induction therapy, kidney transplantation

Introduction: Basiliximab, alemtuzumab, and thymoglobulin are the most commonly used induction agents in the US. While many centers use depleting antibody induction therapy in patients with DSA, the optimal induction for patients without pre-transplant DSA is not completely understood. The goal of this study is to compare the incidence of de novo DSA (dnDSA) and outcomes between induction therapies in patients with no pre-transplant DSA.

Methods: A retrospective chart review was performed which identified 1,147 adult patients undergoing kidney transplantation at a single high-volume institution between January 2013 and May 2017. Patients receiving multiple or no induction agents were excluded. 782 patients were identified as having a negative virtual cross match (VXM) (absence of DSA) and were included in this study. Kaplan-Meier analysis was used to assess the incidence of dnDSA and allograft survival between induction therapies in this group. DnDSA is defined as the development of new post-transplant DSA, at any MFI level.

Results: All 782 (68%) patients with a negative VXM were included in this study. Induction therapy included alemtuzumab (n=88, 11.3%), basiliximab (n=522, 66.2%), and thymoglobulin (n=173, 22.5%). Patients were followed for mean of 2.4 years after transplant. As expected, 1-year graft survival was excellent and similar between the three groups (alemtuzumab 100%, basiliximab 98.2%, thymoglobulin 98.8%). Likewise, the incidence of acute rejection at one year was less than 2% and not different between the three groups. Thymoglobulin was associated with the highest incidence of CMV viremia (38.4%) compared to alemtuzumab (36.6%) and basiliximab (22.3%) at 1 year ($p<0.0003$). However, alemtuzumab was associated with the highest incidence of dnDSA at 14.5% compared to 5.4% and 8.9% in the basiliximab and thymoglobulin groups at 1 year, respectively ($p=0.009$). In multivariate regression analyses, alemtuzumab retained its significant association with dnDSA HR 2.5 (95% CI 1.51-4.25, $p=0.0004$).

Conclusions: Alemtuzumab is associated with significantly higher rates of dnDSA in patients with no pre-transplant DSA when compared to basiliximab and thymoglobulin but had no impact on kidney allograft outcomes. Additional controlled analyses and long-term follow up are needed to more completely understand this finding.

C6

Renal Autotransplantation Offers Pain Relief to Patients with Loin Pain Hematuria Syndrome

Bath N.M., Al-Qaoud T., Sollinger H.W., Redfield III R.R.

Abstract Submitter	Natalie Bath
Email Address	nbath@wisc.edu
Classification	Resident
Principal Investigator	Redfield
Science Type	Clinical
Keywords	Loin pain hematuria syndrome, renal autotransplantation

Introduction: Loin Pain Hematuria Syndrome (LPHS) is a rare clinical entity in which patients typically present with severe loin pain. This pain is often debilitating to the point that patients require narcotics for pain control and are often unable to continue employment. Renal autotransplantation is a potential treatment although results are varied. This highlights the importance of patient selection. In order to improve patient selection, we developed the UW-LPHS Test. Here we describe our initial results.

Methods: A retrospective chart review was performed which identified 15 patients with LPHS who underwent renal autotransplantation at a single institution between January 2017 to May 2018. In order to identify patients with LPHS who would likely benefit from autotransplantation, patients underwent bupivacaine injection into the ureter via cystoscopy, known as the UW-LPHS Test. Patients who report pain relief following the UW-LPHS Test are then deemed to benefit from renal autotransplantation. Pre-operative length of pain, pain medications taken pre-operatively, resolution of pain following the UW-LPHS Test, post-operative complications, and return to normal lifestyle were among data points collected.

Results: All patients had previously undergone extensive work-up to determine the etiology of their pain. Nutcracker Syndrome (NCS) was identified as the cause of LPHS in 60% of patients (n=9) with 55.5% of NCS patients (n=5) having undergone previous operative interventions which failed to resolve their pain. Of the 15 patients identified, 93.3% (n=14) underwent the UW-LPHS Test with near or complete resolution of their pain. Two patients not included in this cohort did not have pain relief following the UW-LPHS Test and were later diagnosed with interstitial cystitis. All patients report near complete or complete resolution of their pain post-operatively. 73.3% of patients (n=11) no longer require narcotics for pain control, and 26.7% of patients (n=4) are weaning their narcotic usage. 80% of patients (n=12) have returned to school or employment with 6.7% (n=1) planning to return in the coming months.

Conclusions: Renal autotransplantation for Loin Pain Hematuria Syndrome has been shown to reliably provide pain relief in this patient population; however, it is imperative to properly identify patients who will benefit from autotransplantation. The UW-LPHS Test appears to be an accurate predictor of successful outcomes following renal autotransplantation. Future studies are needed to further clarify the long-term outcomes in patients with LPHS who have undergone renal autotransplantation.

C5

Renal Autotransplantation Results in Pain Resolution Following Renal Vein Transposition

Bath N.M., Al-Qaoud T., Sollinger H. W., Redfield III R. R.
Please list in LastName First Initial.Middle Initial., format (e.g. Smith J.S.,).

Abstract Submitter	Natalie Bath
Email Address	nbath@wisc.edu
Classification	Resident
Principal Investigator	Robert Redfield
Science Type	Clinical
Keywords	Renal Autotransplantation, Loin Pain Hematuria Syndrome, renal vein transposition

Introduction: Left renal vein (LRV) transposition is often the preferred treatment for Nutcracker syndrome (NCS), which frequently is characterized by flank pain and hematuria. Here we report our initial results of renal autotransplantation (AT) in patients with persistent flank pain despite a previous renal vein transposition.

Methods: Four patients underwent renal AT following a LRV transposition for NCS from December 2016 to May 2018. All had prior LRV with persistent flank pain despite a patent LRV transposition (Figure 1). Importantly, patients underwent bupivacaine injection into the ureter via cystoscopy, known as the UW-LPHS Test which our team developed, in order to identify who would likely benefit from renal AT. Patients who report pain relief following the UW-LPHS Test are deemed to likely benefit from renal AT. Pain resolution and post-operative narcotic usage were among data points collected.

Results: All patients (n=4) had previously been diagnosed with NCS and had undergone LRV transposition only to have their pain recur. 75% (n=3) underwent the UW-LPHS test and reported significant improvement in their pain. All patients report near or complete resolution of their flank pain post-operatively. All patients are weaning (75%, n=3) or are no longer requiring narcotics (25%, n=1).

Conclusions: Renal autotransplantation after LRV transposition for NCS yields excellent results. More study is needed to determine the optimal treatment option for NCS. Additionally, the UW-LPHS Test may be an important diagnostic maneuver to determine which patients may benefit from an autotransplant.

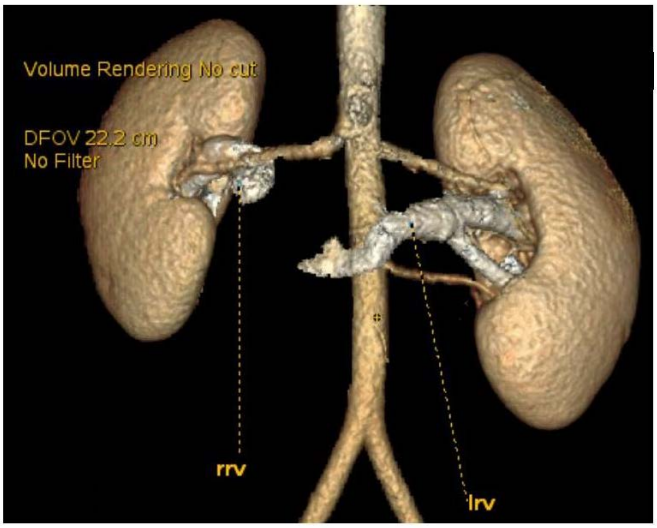


Figure 1: Pre-operative imaging demonstrating patent left renal vein. 3-D reconstruction performed prior to patient's renal autotransplant shows that left renal vein is patent; however, patient continued to experience severe loin pain. Lrv- left renal vein. Rrv- right renal vein.

C3

The Utility of Urinalysis Prior to In-Office Procedures: A Randomized Clinical Trial

Backhaus, K.B.

Abstract Submitter	Katelyn Backhaus
Email Address	kbackhaus@wisc.edu
Classification	Medical Student
Principal Investigator	Kyle Richards MD
Science Type	Clinical Science
Keywords	Health Services/ QI

Introduction: All Bacille Calmette Guerin (BCG) patients undergo urinalysis (UA) before their procedures in order to reduce rates of UTI. Retrospective studies have suggested that there is no difference in the rates of UTI in people who were administered UA tests before BCG treatments versus people who were not administered UA tests before treatment. Additionally, a study found that the risk of symptomatic UTI is 4.5% in patients, therefore most patients do not benefit from UA or preventative antibiotics. Additionally, the cost of every UA is around $4.24, which for the course of our study alone would amount to over $1300. Furthermore, results of UA tests can lead to delays in procedures. Delays are cumbersome and can cause a delay in a more serious diagnosis.

Methods: A total of 664 patients will be enrolled in a randomized clinical trial over the course of a year. Patients will be blindly randomized. There will be two primary cohorts in the study. The control cohort will receive a UA prior to their scheduled in-office urological procedure and will be treated with current standard of care. For the experimental cohort, a UA will be obtained and a UC as needed. The treating physician will not have access to the results of the UA/UC and will proceed with the treatment as planned. The UC will be monitored by research staff so that if a patient develops a UTI, treatment can be initiated immediately. The primary outcome of the study is to assess the number of UTI occurrences within the study period.

Results: Enrolling patients.

Conclusions: The current guidelines for in-office urological procedures may be hindering patient care instead of improving it. Nearly, 2.5% of patients who receive UA/ UC prior to their procedures have their treatments delayed. Despite delay of treatment, there is no improvement in rates of UTI development. Additionally, current practice may promote antibiotic resistance, as positive results prompt the use of antibiotics even though use of UA/UC have not been shown to improve outcomes.

C39

Influence of Binaural Hearing on Speech Intelligibility and Listening Effort

Snodgrass, E.; Litovsky, R.; Roche, J.

Abstract Submitter	Snodgrass, Ellen
Email Address	snodgrass@surgery.wisc.edu
Classification	Faculty
Principal Investigator	Roche, J. P.
Science Type	Clinical
Keywords	Binaural Hearing; Listening Effort; Pupillometry

Introduction: Binaural hearing can improve speech intelligibility performance when sound sources are spatially separated. Additionally, binaural hearing may reduce the effort required to complete a listening based task. However, the influence of binaural hearing abilities on listening effort remains poorly understood. Pupil dilation can be used to measure listening effort and engagement during listening tasks. Large pupil sizes indicate high effort during the task, and small pupil sizes indicate low effort. We used pupillometry to investigate the effect of spatially separating target speech from competitors. We hypothesized that pupil dilation will be reduced in conditions where target and competitors are spatially separated compared to the co-located conditions.

Methods: Normal hearing adult subjects participated. During testing participants listened to, and repeated target stimuli (male voiced IEEE sentences) in the presence of competing signals (male voiced AZ-Bio sentences). Pupil size was measured concurrently. Target sentence were presented at 0°azimuth and competing sentences were presented at either 0°azimuth (Co-located) or to the right and left at 90°azimuth (Symmetric) configurations. The symmetric configuration was selected to maximize use of binaural cues. Target and masker presentation levels were varied to signal-to-noise ratios (SNR) of -12 to +9 in 3 dB steps. The overall sound level was held constant 65dBA. A total of 32 sentences per condition were presented across 2 blocks of 8 sentences during each of 2 sessions. Speech intelligibility was measured as the number of correctly repeated keywords. An Eyelink 1000 infrared camera focused on one eye measured the area of the pupil over time starting 2 seconds prior to stimulus onset and continuing for 7 seconds after the stimulus offset.

Results: Speech intelligibility scores reached approximately 95% correct responses at 0 dB SNR with percent correct scores decreasing with decreasing SNR in both stimulus configurations. Pupillary response waveforms were averaged for each SNR/stimulus configuration and the peak pupil response was determined. Analysis of peak pupil responses indicate that pupil dilation systematically increased when Target SNR decreased, and pupil dilation was greater in Co-located conditions than Symmetric conditions at the same SNRs from -12 to 0 dB.

Conclusions: These preliminary findings provide further evidence regarding the interaction of speech intelligibility and listening effort in normal hearing adults, and the role of binaural hearing.

C10

Swallowing Biomechanical Analysis Following Lingual Strengthening Therapy in Patients with Post-Stroke Dysphagia

Daggett S.[1], Cullins M.[2], Kletzien H.[2,3], Hanson K.[1], Pearson W.[4], Rogus-Pulia N.[1,2,5]

Abstract Submitter	Sarah Daggett
Email Address	smdaggett@wisc.edu
Classification	Academic staff
Principal Investigator	Dr. Nicole Pulia
Science Type	Clinical
Keywords	Dysphagia, stroke, biomechanics

Introduction: Dysphagia affects up to 76% of acute post-stroke patients. Lingual strengthening therapy is a potential treatment modality, but the effects on the biomechanics of pharyngeal swallowing are not well understood. Using Computational Analysis of Swallowing Mechanics (CASM) with videofluoroscopic swallow study (VFSS) images, our purpose was to assess the biomechanical changes of swallowing-related structures following device-facilitated lingual strengthening as compared to usual care in a group of patients with post-stroke dysphagia.

Methods: VFSS images from 20 patients within 6 months of stroke onset were analyzed before and after treatment. Nine patients (6 male, 3 female) were randomized to usual care and eleven patients (7 male, 4 female) to lingual strengthening facilitated by the SwallowStrong® device. The lingual strengthening group performed 10 press repetitions at front and back tongue locations against sensors embedded in a custom-fit mouthpiece 3 times per day, 3 days per week for 8 weeks. Multivariate morphometric analyses of VFSS images were performed to assess the effects of lingual strengthening in comparison to usual care on swallowing biomechanics in post-stroke patients.

Results: Biomechanics of the pharyngeal phase of the swallow were significantly altered following 8 weeks of lingual strengthening in post-stroke patients compared to baseline ($CV1 = 64.9\%$; $D = 1.67$, $p < .0001$) and compared to those who received 8 weeks of usual care ($CV1 = 52.5\%$; $D = 4.66$, $p < .0001$). Posthoc discriminant function analyses suggest improvements in pharyngeal biomechanics following lingual strengthening therapy. More specifically, we observed increased laryngeal elevation, hyoid excursion, and tongue base retraction with 8 weeks of lingual strengthening.

Conclusions: These results suggest that pharyngeal swallowing biomechanics in patients with post-stroke dysphagia are positively influenced by a lingual strengthening protocol as compared to usual care. Future studies will apply this analysis to determine relationships among pharyngeal biomechanical changes post-treatment and swallowing-related outcomes, such as airway invasion and pharyngeal residue.

C8

Optimizing Levothyroxine Dose Adjustment After Thyroidectomy with a Decision Tree

Chen S.S., Zaborek N, Doubleday A.R., Long K.L., Pitt S.C.; Sippel R.S.; Schneider D.F.

Abstract Submitter	Stephen Chen
Email Address	Sschen3@wisc.edu
Classification	Medical Student
Principal Investigator	Dr. David F Schneider
Science Type	Clinical
Keywords	Levothyroxine, Machine Learning, Dosage Adjustments

Introduction: After thyroidectomy, patients require Levothyroxine (LT4), and it may take years of dose adjustments to achieve euthyroidism. During this time, patients encounter undesirable symptoms associated with hypo- or hyperthyroidism. Currently, providers adjust LT4 dose by clinical estimation, and no algorithm exists. The objective of this study was to build a decision tree that estimates LT4 dose adjustments and reduces the time to euthyroidism.

Methods: We performed a retrospective cohort analysis on 320 patients who underwent total or completion thyroidectomies at our institution between 2008 and 2016 and required one or more dose adjustments from their initial postop LT4 dose before attaining euthyroidism. Using the Classification and Regression Tree (CART) algorithm, we built various decision trees from patient characteristics that estimated the dose adjustment to reach euthyroidism. We evaluated tree accuracy with repeated 10-fold cross validation. The most accurate decision tree was developed on a training set of 214 patients, with the remaining 106 patients making up the evaluation set. We compared the accuracy of the decision tree to the actual dose adjustments made by an expert provider and to a naïve system that increased or decreased the dose by 12.5 mcg based on patient TSH.

Results: In our study cohort, an expert provider adjusted LT4 doses, and achieved euthyroidism after one dose adjustment for 156 patients (48.8%), two dose adjustments in 90 patients (28.1%), and three or more dose adjustments in 74 patients (23.1%). Figure 1 shows the most accurate decision tree using TSH values at first dose change (mean absolute error = 13.0 mcg). In comparison, the naïve system had an absolute error of 17.2 mcg, and the expert provider had an absolute error of 11.7 mcg. In the evaluation dataset (106 patients), the decision tree correctly predicted the dose adjustment within the smallest LT4 dose increment (12.5 mcg) 79 of 106 times (75%, CI = 65% - 82%). In comparison, expert provider estimation correctly predicted the dose adjustment 76 of 106 times (72%, CI = 62% - 80%).

Conclusion: A decision tree predicts the correct LT4 dose adjustment with an accuracy exceeding that of a completely naïve system and comparable to that of an expert provider. Since this tree-based algorithm approximates an expert provider's accuracy in adjusting LT4 doses, it can assist providers inexperienced with LT4 dose adjustment.

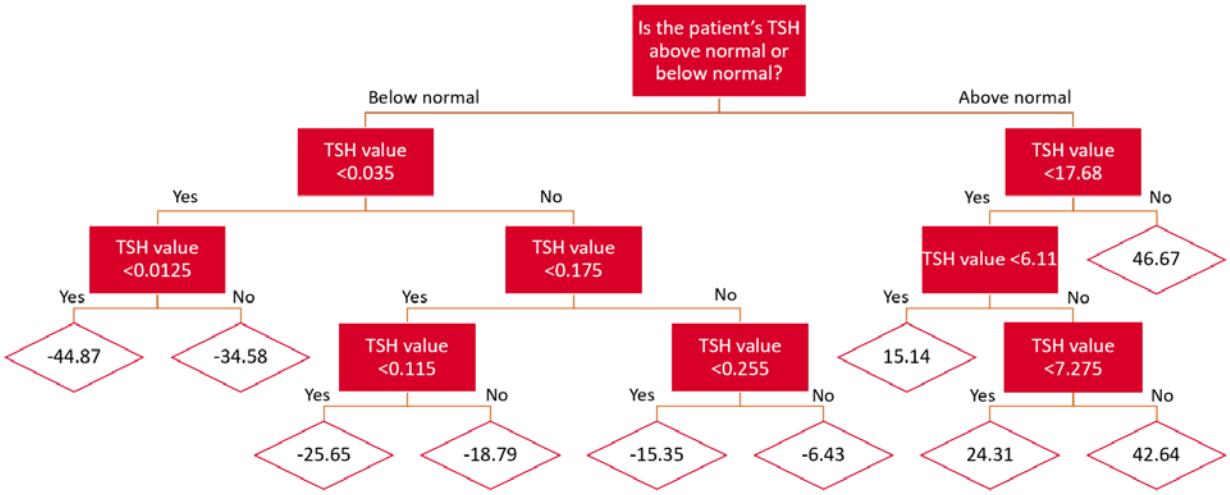


Fig 1: Decision Tree with LT_4 dosing recommendations based on TSH value. *This decision tree was generated using the CART algorithm, a recursive partitioning method. The decision tree is based on TSH values (U/mL) at first dose adjustment, and can be interpreted by starting at the top, and moving down the branches until a final LT_4 dose adjustment recommendation (change in mcg contained within the diamonds) is reached.*

C48

Influence of System Factors on Surgeon Inclination to Offer Non-Beneficial Surgery to Older Adults with Life-Limiting Acute Surgical Conditions

Zimmermann C.J.,Taylor, L.J.,Tucholka, J.L., Brasel K., Arnold B., Cooper Z., Schwarze M.L.

Abstract Submitter	Christopher Zimmermann
Email Address	czimmermann@uwhealth.org
Classification	PGY-3 General Surgery, 2nd year WiSOR Research Fellow
Principal Investigator	Margaret Schwarze
Science Type	National survey
Keywords	Non-beneficial surgery, end-of-life, palliative care

Introduction: Use of burdensome intensive treatments near the end of life is increasing. More accurate predictive models and interventions to improve surgeon-patient communication are proposed solutions, yet the impact of systems factors may be an important driver of non-beneficial treatment. Using a national survey of practicing surgeons, the objective of this study is to describe factors that promote non-beneficial surgical interventions and assess surgeon inclination to offer surgery to older adults with life-limiting acute surgical conditions.

Methods: We developed a self-administered 15-item survey with a clinical vignette using a 2 by 2 factorial design to test the effect of patient (co-morbid illness) and system factors (influence of other clinicians) on the inclination to offer surgery to an older patient with comorbid illness for whom surgery was unlikely to confer short or long-term survival. We mailed paper surveys to 2800 surgeons in the United States randomly selected from the American College of Surgeons member database. We used Pearson's chi squared tests to analyze the association between the likelihood of offering surgical treatment and patient and systems factors in the clinical vignette. We used univariate models to describe the association between surgeon reports about the importance of specific patient, practice and system factors on their likelihood of offering surgery. We selected relationships of statistical significance ($p<0.05$) for inclusion in a multivariable model to determine factors independently associated with offering surgery.

Results: A total of 1319 eligible surgeons responded (adjusted response rate 63%). For an 87-year-old patient with fulminant colitis, 35% of surgeons reported they would be somewhat or very likely to offer an operation to remove the patient's colon while 58% were somewhat or very likely to offer comfort-focused care only. On univariate analysis, surgeons who received a vignette describing a patient with stage IV lung cancer were significantly more likely to offer surgery than surgeons presented with a vignette describing a patient with advanced dementia. This finding persisted on adjusted analysis, and was enhanced by the systems factor that the consulting intensivist supported surgical intervention (OR 1.48, 95% CI 1.05-2.01 and 1.74, 95% CI 1.24-2.45). Surgeons who reported that the availability of an on-call operating room team and the family member requests "everything done" were more likely to offer an operation, regardless of the patient's functional status or comorbidity.

Conclusions: System factors play an important role in surgeons offering procedures to acutely ill older surgical patients near the end of life. Interventions for reducing non-beneficial surgery will need to consider these systems factors in conjunction with improvements in predictive modeling and communication.

Table 4: Interaction of patient comorbidity and functional status with elements of clinical momentum on the surgeons' inclination to offer an operation to a seriously-ill, older adults with an acute surgical condition

Environmental factor	**Somewhat or very likely to offer an operation, N (%)**	**P value**	**Interaction of patient comorbidity with environmental factors**	**Somewhat or very likely to offer an operation, N (%)**	**P value**
Availability of OR time and personnel		<0.001	*Comorbidity; OR availability*		
Not important	264 (27.3)		Dementia; not important	128 (24.9)	<0.001
Important	186 (62.4)		Dementia; important	65 (59.4)	
			Cancer; not important	136 (30.0)	<0.001
			Cancer; important	110 (64.7)	
Time required to discuss non-operative treatments		<0.001	*Comorbidity; time to discuss non-operative treatment*		
			Dementia; not important	125 (27.8)	<0.001
			Dementia; important	80 (40.8)	
Not important	278 (32.1)		Cancer; not important	153 (36.7)	0.058
Important	171 (42.8)		Cancer; important	91 (44.6)	
Family member requests "everything done"		<0.001	*Comorbidity; family request*		
			Dementia; not important	24 (13.7)	
			Dementia; important	178 (38.2)	<0.001
Not important	94 (24.4)		Cancer; not important	70 (33.3)	
Important	352 (40.4)		Cancer; important	174 (42.9)	0.022
Desire to preserve referral relationships		0.093	*Comorbidity; preserve referral relationships*		
			Dementia; not important	162 (30.8)	0.405
Not important	362 (34.5)		Dementia; important	40 (34.8)	
Important	84 (40.6)		Cancer; not important	200 (38.2)	0.081
			Cancer; important	44 (47.8)	

C38

Surgeon Reflections on the Use of a Question Prompt List by Patients Considering High-Risk Operations

Shogren S.L., Ballou J, Buffington A, Tucholka J.L., Senglaub S, Tufariello A, Brasel K.J., Cooper Z, Schwarze M.L.

Submitter	Sophie Shogren
Phone	612-269-0218
Email Address	sshogren@wisc.edu
Classification	Medical Student
Division	Department of Surgery
Lab	Schwarze Lab
Science Type	Clinical Research
Keywords	Question prompt list, high-risk operations, decision-making

Introduction: For older adults considering high-risk surgery, the decision to pursue surgery can be complicated and confusing. The Question Prompt List (QPL) is a brochure—designed by patients and families—that provides questions to help patients consider options, understand expected outcomes, and prepare for possible complications. The QPL is mailed to patients prior to their preoperative clinic visit to prepare patients for participation in a decision-making conversation. The objective of this study is to characterize surgeons' attitudes about use of the QPL with patients.

Methods: We performed a multi-site, randomized clinical trial involving 444 patients and 40 oncologic and vascular (cardiac, peripheral, neuro) surgeons at five sites—Oregon Health Sciences University, Rutgers University Hospital, Brigham and Women's Hospital, the University of California San Francisco, and the University of Wisconsin. Upon completion, we performed face-to-face interviews with 33 surgeons. We asked the surgeons to describe how the QPL impacted preoperative conversations with patients—specifically, how the QPL may or may not have assisted patients with participation in decision-making. We audio recorded and transcribed each interview. Two investigators coded each transcript inductively using constant comparison. We created construct tables to facilitate comparison of the transcripts and characterize surgeons' perceptions of the QPL.

Results: Surgeons reported that the QPL empowered patients to ask questions they otherwise may not have asked. *"[Patients] may not be aware that they have the right to ask those questions, you know, and so I think this gives them the license to do that."* Surgeons were divided about whether the QPL changed patient decision-making about surgery. One surgeon reported, *"There are patients that decided not to proceed with surgery because of the pamphlet, because of the in-depth conversation that we have regarding the procedure."* Others had different experiences, noting the QPL allowed patients to identify their goals and values. *"I don't think it changed their decision to have the surgery. I believe the list was good in that it gave the patients questions to think about, and in some cases, they wanted to wait to make a decision 'til after they went home and decided, you know, if it was right for them or not… It just gave them a useful platform to go back and sort of look at what might be important to them."* Some surgeons worried the questions were redundant and time consuming, but noted repetition was helpful to patients. *"So it became less of a hindrance than I thought it would be and more of a reaffirmation of what we said."*

Conclusions: Surgeons were typically supportive of the QPL and their patients' use of the brochure during preoperative conversations. Although surgeons had concerns about the questions extending their visits with patients, they praised the QPL for giving patients confidence to ask questions and consider how surgical intervention may or may not help them meet their goals.

C12

Does Extent of Surgery Impact Weight Changes After Thyroidectomy?

Doubleday A.R., Chen S., Zaborek N., Long K.L., Pitt S.C., Schneider D.F., Sippel R.S.

Abstract Submitter	Amanda R. Doubleday
Email Address	doubleday@surgery.wisc.edu
Classification	Clinical Research Postdoctoral Fellow
Principal Investigator	Dr. Rebecca Sippel
Science Type	Clinical
Keywords	Thyroid, Weight, Thyroid Stimulating Hormone (TSH)

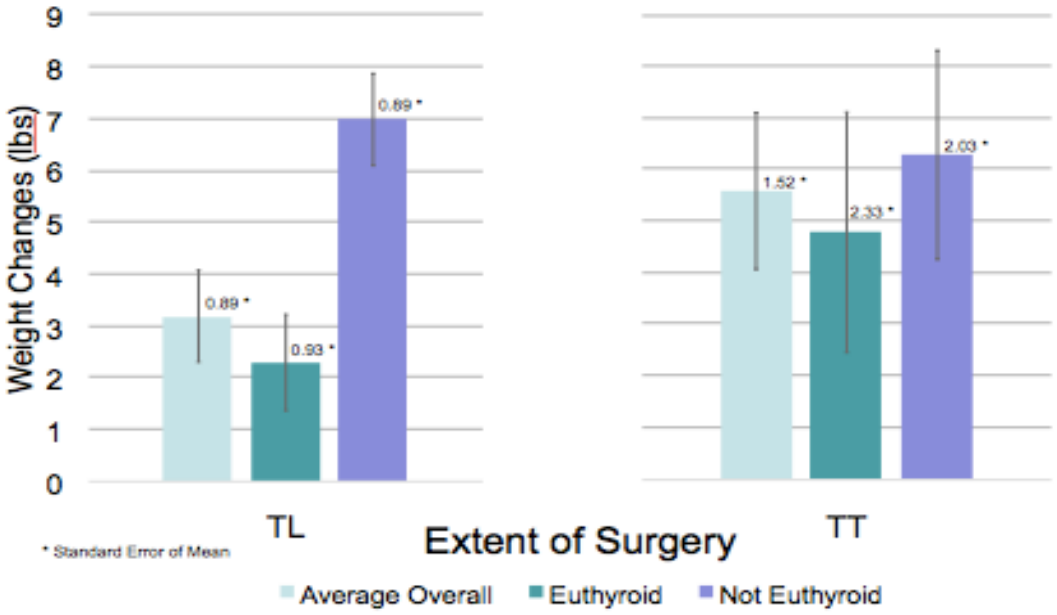
Introduction: Patients often report weight gain after thyroid surgery, and many express significant concern about this possibility pre-operatively. Patients with thyroid nodular disease frequently have a choice between a thyroid lobectomy (TL) and a total thyroidectomy (TT). The purpose of this study was to determine if there is a difference in postoperative weight changes among patients undergoing either a TL or TT for benign disease, and to investigate if postoperative thyroid stimulating hormone (TSH) changes correlated with weight changes.

Methods: We conducted a retrospective review of 205 patients who underwent TL (116) or TT (89) for benign disease from January 2015 to December 2016. Six week postoperative TSH changes and 1-year postoperative weight changes were recorded. Patients were classified as either euthyroid (TSH in the normal range) or non-euthyroid (TSH above or below normal) at 6-weeks postoperatively. Group mean weight changes were compared using the unpaired student's t-test, and Pearson's correlation coefficient tested the association between TSH and weight changes.

Results: Overall, patients gained an average of 4.2±0.83 lbs in the first year after either type of thyroid surgery, while 37.6% of patients gained >5 lbs. Weight gain was higher in patients undergoing a TT vs. TL (5.6±1.52 vs. 3.2±0.89, p=0.167), but this was not statistically significant. Patients that achieved or maintained a euthyroid status at 6 weeks had less weight gain than those non-euthyroid at 1 year after a TL (2.3±0.93 lbs vs. 7.0±2.32 lbs, p=0.069), but that difference was not seen after a TT (4.8±2.33 vs. 6.3±2.03 lbs, p=0.634). There was no correlation between change in TSH shortly postoperatively and 1-year postoperative weight changes for either TL (r=-0.05) or TT (r=0.13).

Conclusions: Weight changes are common after thyroidectomy. Weight gain was lowest in patients undergoing a thyroid lobectomy who are able to maintain a euthyroid status at 6 weeks. Unfortunately for patients undergoing a total thyroidectomy, achieving a euthyroid state shortly after surgery post-operatively did not impact total weight gain at one year.

Figure 3: Group Mean Weight Changes at 1-year post-op



C11

Gender Disparities in Bone Density Testing of Patients with Hyperparathyroidism: A Bias Against Men

Dedhia P. H., McDow A. D., Long K. L., Pitt S. C, Schneider D. F., Sippel R. S.

Abstract Submitter	Priya Dedhia
Email Address	Dedhia2@wisc.edu
Classification	
Principal Investigator	Rebecca Sippel
Science Type	ClinicalFellow
Keywords	Endocrine, hyperparathyroidism, osteoporosis

Introduction: Primary Hyperparathyroidism can lead to osteoporosis. Guidelines recommend that all patients with primary hyperparathyroidism should undergo a DEXA scan to evaluate for the presence of bone disease. While osteoporosis is more common in women, we sought to determine if there were gender differences in the presence or the evaluation of bone disease in female and male patients with primary hyperparathyroidism.

Methods: This is a retrospective review of a prospective surgical database of 3608 patients with primary hyperparathyroidism who underwent surgical exploration between 2000 and 2018 at a single institution. Clinical characteristics, DEXA scan evaluation, mean t-scores, and the presence of osteopenia or osteoporosis were studied.

Results: Of the 3608 patients with hyperparathyroidism who underwent surgical exploration, 78% (n=2818) were female and 29% (n=790) were male. Female patients were significantly more likely to have a history of either fractures or osteopenia or osteoporosis compared to the male patients (65% vs. 15%, $p<0.0001$). Furthermore, female patients were also significantly more likely to undergo a DEXA scan during their pre-operative evaluation than male patients, 49% versus 28% ($p<0.00001$).

In looking at only those patients who underwent a DEXA scan, 86% of women versus 77% of men had osteopenia or osteoporosis as indicated by a t-score of <1.0 ($p=0.0008$). A diagnosis of osteoporosis was present in 32% of women versus 22% of men ($p=0.0035$). Mean t-score was -1.71 for women compared to -1.92 for men ($p=0.07$). Interestingly, men without a history of bone disease or fractures were just as likely to have osteopenia or osteoporosis on DEXA scan as women without history of bone disease or fractures, 54% compared to 61% ($p=0.27$).

Conclusions: Men with primary hyperparathyroidism are less likely to undergo DEXA scans compared to women. However, our work shows that men and women with no history of bone disease or fractures are equally likely to have osteopenia or osteoporosis on a DEXA scan. These data suggest that the incidence of osteopenia and osteoporosis is likely higher in men than current literature indicates, and that men with a diagnosis of primary hyperparathyroidism without history of bone disease or fractures would benefit from evaluation by DEXA scan.

C34

Symptoms Reported by Thyroid Cancer Patients After Total Thyroidectomy for Papillary Thyroid Cancer

Robbins, S.E., Macdonald, C.L., Connor, N.P., Sippel, R.S.

Submitter	Sarah Robbins
Phone	265-9138
Email Address	robbins@surgery.wisc.edu
Classification	Academic staff
Division	General surgery
Lab	Sippel/Connor
Science Type	Clinical
Keywords	Papillary thyroid cancer, total thyroidectomy, thyroid cancer

Introduction: Total thyroidectomy (TT) is a recommended treatment for papillary thyroid cancer (PTC). However, the complications of this procedure and side effects of thyroid hormone replacement required after surgery can be profound and persist for one year after surgery. This study analyzed symptoms reported by patients with PTC in the first year after TT.

Methods: PTC patients were evaluated at five time points: before TT (n=57) and at 2 weeks (n=50), 6 weeks (n=47), 6 months (n=40), and 1 year after TT (n=33). At each time point, patients reviewed a collection of index cards showing a range of symptoms experienced by PTC patients. Symptom cards were developed based on input from pilot interviews with TT patients at various stages of recovery. Patients sorted the cards based on which symptoms they had and how much these symptoms bothered them.

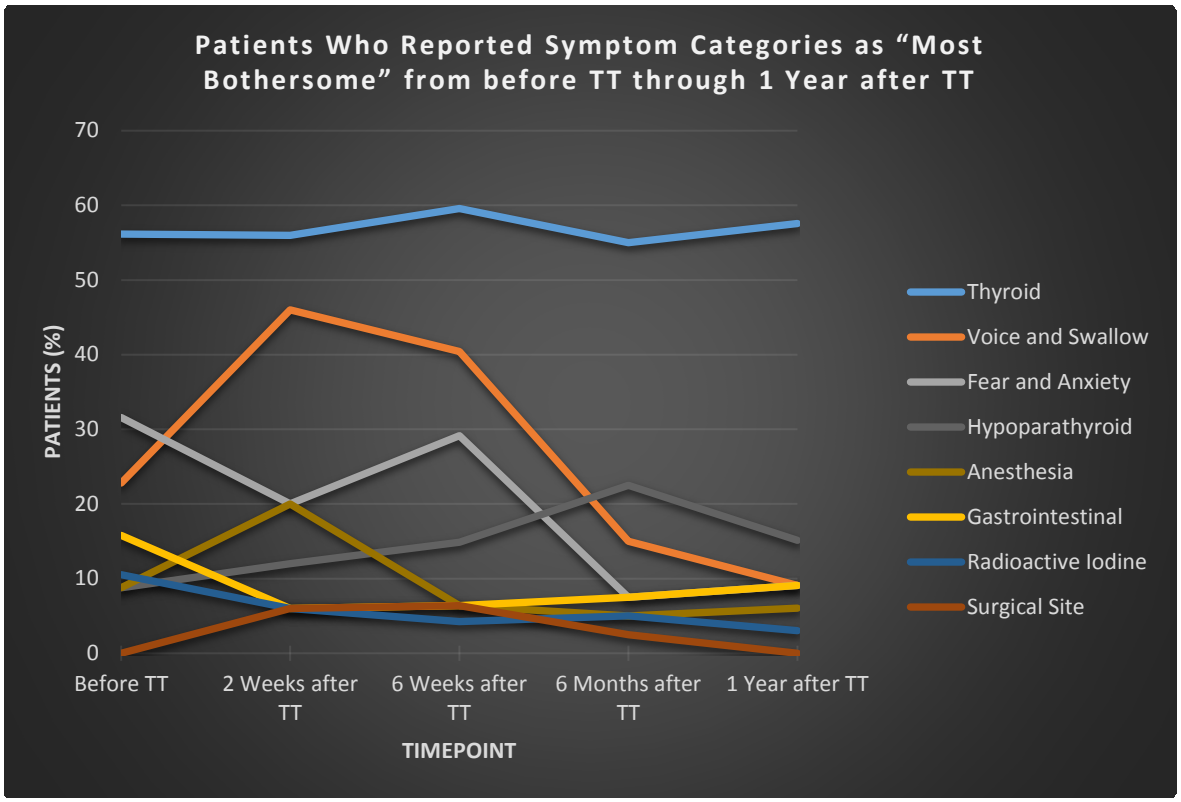
Results: Before TT, 31.6% (n=18) of participants ranked fear and anxiety symptoms as “most bothersome.” These issues were largely resolved at 1 year after TT (9.1%, n=3) with the exception of one peak at 6 weeks after TT (29.79%, n=14).

Thyroid-related symptoms were ranked “most bothersome” by the most patients before TT and at one year after TT (56.1%, n=32 vs. 57.6%, n=19). However, only 14% (n=8) of all participants reported these symptoms as most bothersome at both time points. This indicates that different patients ranked thyroid symptoms as “most bothersome” before and after TT, i.e. one set of patients described distress from thyroid-related symptoms prior to surgery and seemed to improve after surgery, while a distinct second set did not rank those symptoms as most bothersome prior but became bothered by them later.

Of the participants who reported most bothersome thyroid symptoms before surgery, 12.9% (n=4) had history of thyroid hormone replacement, 6.5% (n=2) had abnormal TSH and 25.8% (n=8) also reported most bothersome thyroid symptoms at 1 year after TT. Of the participants who reported most bothersome thyroid symptoms 1 year after TT, 15.8% (n=3) of these had an elevated TSH and 5.3% (n=1) had an undetectable TSH.

Within the thyroid symptom category, low energy and weight gain were most frequently ranked as most bothersome symptoms. 26.3% (n=15) of participants ranked low energy as most bothersome before TT vs. 33.33% (n=11) at 1 year. 25.5% (n=14) of participants ranked weight gain as most bothersome before TT vs. 30.3% (n=10) at 1 year after TT.

Conclusions: While thyroid related symptoms are major issues for PTC patients after TT, similar complaints were present prior to surgery for many. Interestingly, patients who considered possible thyroid related symptoms most bothersome before TT were not the same people who reported these issues at 1 year after TT. More than half of participants reporting thyroid symptoms as most bothersome at one year after TT did not experience these before surgery. Further investigation into factors causing these changes is warranted in order to improve the patient experience and outcome after TT.


Patients Who Reported Symptom Categories as “Most Bothersome” from before TT through 1 Year after TT
70
60
50
40
30
20
10
0
PATIENTS (%)
Before TT
2 Weeks after TT
6 Weeks after TT
6 Months after TT
1 Year after TT
TIMEPOINT
Thyroid
Voice and Swallow
Fear and Anxiety
Hypoparathyroid
Anesthesia
Gastrointestinal
Radioactive Iodine
Surgical Site

C21

Correlations Among Upper Esophageal Sphincter Post-Swallow and Pharyngeal Pressures in Normal and Dysphagic Subjects

Knigge M.A., Rosen S.P., McCulloch T.M., Thibeault S.L.

Abstract Submitter	Knigge M.A.
Email Address	knigge@surgery.wisc.edu
Classification	Graduate student
Principal Investigator	Susan Thibeault
Science Type	Clinical
Keywords	Dysphagia, high-resolution manometry, upper esophageal sphincter

Introduction: Manometric post-swallow pressures represent muscular contraction and caudal movement of the upper esophageal sphincter (UES) returning to its rest position. Little is understood about how these high-amplitude pressures relate to the pharynx. This study examined relationships among pharyngeal and UES post-swallow pressures generated during swallowing tasks in healthy and dysphagic subjects.

Methods: High-resolution manometry data were extracted for 63 adult patients with dysphagia (mean age 66±15 years) from the UW Madison Voice & Swallow Outcomes database. Age- and sex-matched healthy controls were evaluated for comparison. For 10ml swallow tasks, correlations were calculated among maximum nasopharyngeal, tongue base region, and UES post-swallow pressures in both the normal and dysphagic groups.

Results: Post-swallow pressures were positively correlated with both nasopharyngeal ($r=0.525$, $p<0.001$) and tongue base regions ($r=0.415$, $p=0.001$) in healthy subjects. Nasopharyngeal and tongue base region pressures showed a significant correlation in both healthy ($r=0.406$, $p=0.001$) and dysphagic ($r=0.377$, $p=0.002$) subjects. In contrast, post swallow pressures generated in patients with dysphagia showed no significant correlation with nasopharyngeal or tongue base region pressures ($p>0.05$).

Conclusions: Pharyngeal and UES post-swallow pressures are correlated in healthy subjects. However, the loss of this relationship in patients with dysphagia indicates that UES post-swallow pressures may be influenced by factors independent of pharyngeal contractile force and bolus-related sensory feedback.

C16

High-Resolution Pharyngeal Manometry in Pediatric Populations: A Systematic Review

Hoffmeister, J.D., Braden, M.N., Broadfoot, C.K., Hooper-Lane, C., Jones, C.A., Thibeault, S.L.

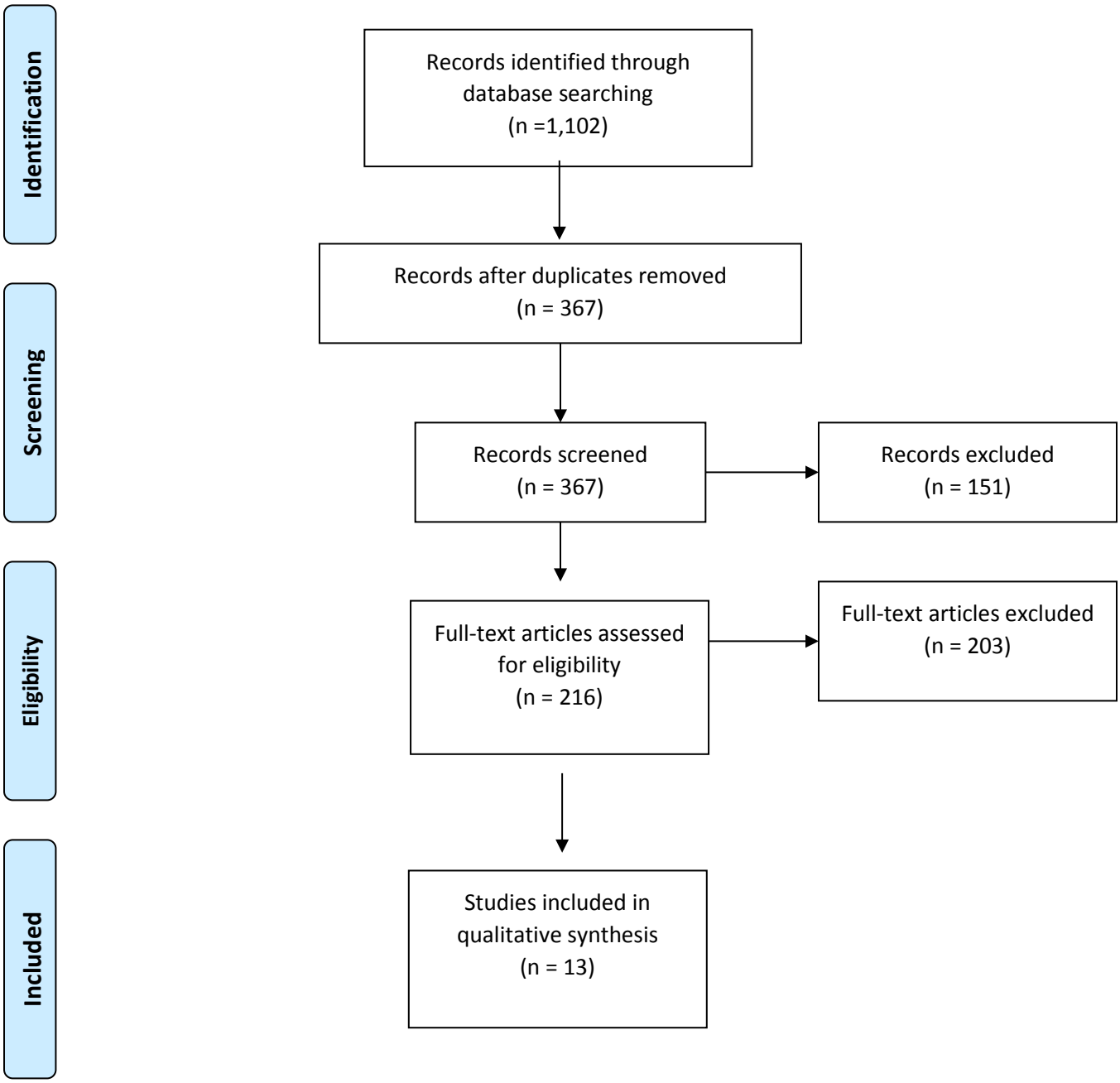
Abstract Submitter	Jesse Hofflmeister, M.S., CCC-SLP
Email Address	hoffmeister@surgery.wisc.edu
Classification	Graduate Student, Voice T32 Pre-doctoral Trainee
Principal Investigator	Susan Thibeault, PhD, CCC-SLP
Science Type	Clinical
Keywords	Manometry, Systematic Review, Pediatrics

Introduction: High-resolution pharyngeal manometry (HRPM) objectively measures pressures in the pharynx during swallowing, contrasting with more-subjective analysis of videofluoroscopy and endoscopy. Recently, the role of HRPM in pediatric swallowing has been investigated. Implementation of pediatric HRPM in clinical practice remains challenging due to a lack agreement on which measures to take, how to take them, and normative values. The purpose of this study was to systematically review peer-reviewed literature on HRPM in pediatrics to describe common measures, protocols, and to synthesize normative data.

Methods: A multi-engine electronic search was conducted on 6/5/17 and updated on 6/11/18 in accordance with standards published by the Preferred Reporting for Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA). Full-text articles were included if they reported high-resolution manometric data from the pharynx and upper esophageal sphincter (UES) in subjects aged 0-17 years. The query was conducted with terms related to “high resolution”, “manometry” and “pediatrics.”

Results: The search yielded 367 articles; following screening of abstracts and titles, 216 full text articles were inspected and 30 reviewed in full. Thirteen met inclusion criteria. Case Controls and Case Series were the most common study types. Across studies, more than 25 HRPM measures were reported. The most frequent were pharyngeal peak pressure (PP) and UES resting pressure. Studies varied in age, diagnostic population, protocol, and level of detail provided in measure definitions. Subsequently, results of measures taken varied widely. In nondysphagic populations across ages, measures of central tendency for PP ranged from a mean of 22 to a median of 165mmHg, and for UES resting pressure from a mean of 13 to a median of 55.2mmHg. HRPM often differentiated groups with and without dysphagia.

Conclusions: HRPM in pediatric populations is valuable in objectively describing swallowing function, and has the potential to contribute significantly to decision-making in dysphagia management. Measures, methods and normative data are inconsistent between studies. There is a need for definition of standard measures that should be obtained during HRPM, and for normative data for interpretation of these measures specific to age and diagnostic population.


Identification
Screening
Eligibility
Included
Records identified through database searching (n =1,102)
Records after duplicates removed (n = 367)
Records screened (n = 367)
Records excluded (n = 151)
Full-text articles assessed for eligibility (n = 216)
Full-text articles excluded (n = 203)
Studies included in qualitative synthesis (n = 13)

C15

Post-Extubation Dysphagia in Pediatric Populations: Incidence, Risk Factors and Outcomes

Hoffmeister, J.D., Zaborek, N.A., Thibeault, S.L.

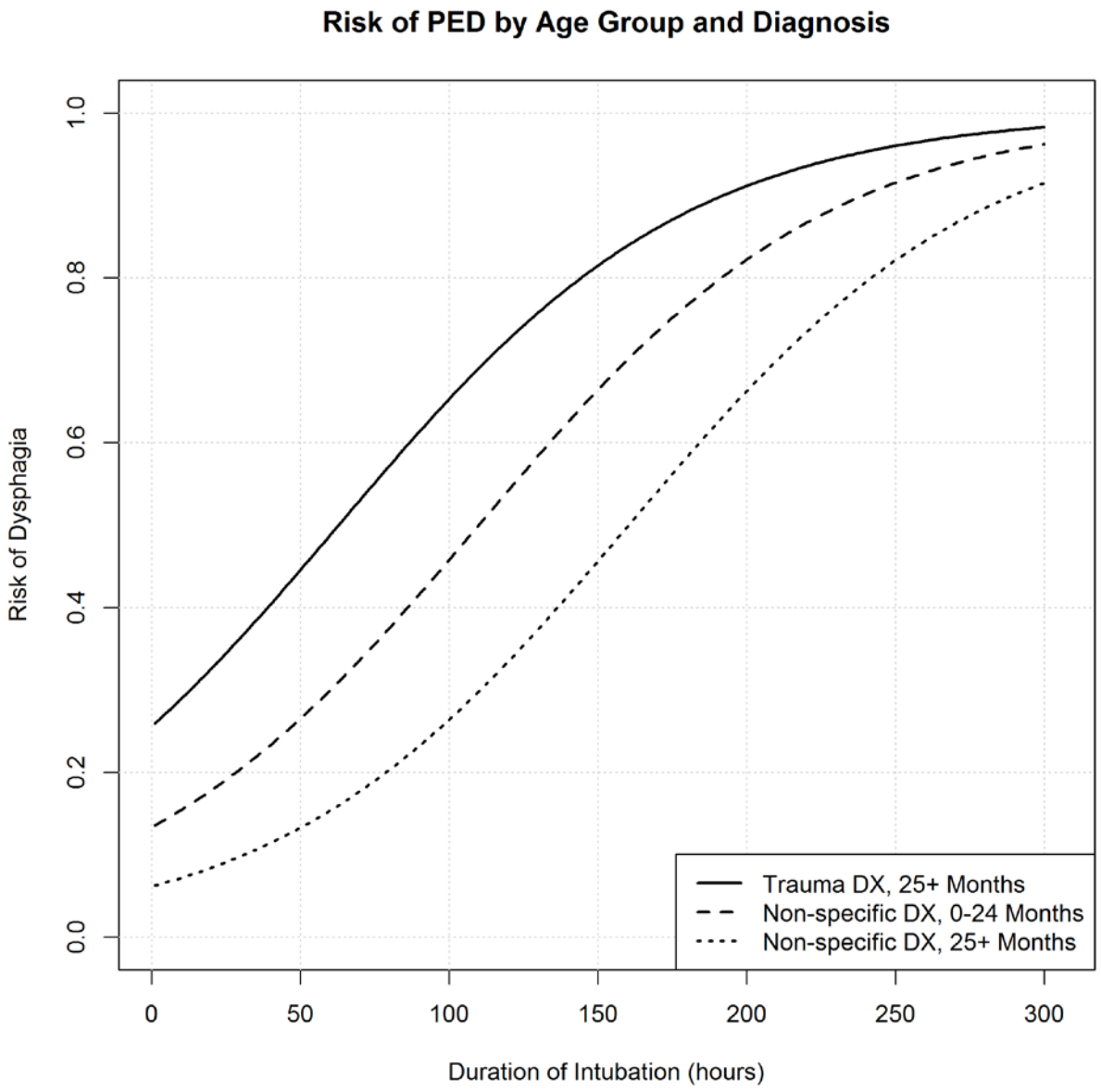
Abstract Submitter	Jesse Hoffmeister, M.S., CCC-SLP
Email Address	Hoffmeister@surgery.wisc.edu
Classification	Graduate Student, Voice T32 Pre-doctoral Trainee
Principal Investigator	Susan Thibeault, PhD, CCC-SLP
Science Type	Clinical
Keywords	Extubation, Dysphagia, Pediatrics, Swallowing, Outcomes

Introduction: Post-extubation dysphagia (PED) is common and associated with negative outcomes in adults. PED in pediatric populations remains unexplored despite differences in anatomy and physiology of airway protection. We hypothesized that incidence of PED in pediatrics would approximate or exceed that in adults, age and duration of intubation would increase risk for PED, and presence of PED would negatively impact patient outcomes.

Methods: We performed a retrospective, observational cohort study of patients aged 0-16 admitted between 2011 and 2017. Patients were included if they were extubated in the ICU and fed orally within 72 hours. Records were reviewed to determine dysphagia status and assess the impact of patient factors on risk of PED. The impact of PED on patient outcomes was then assessed.

Results: Following application of inclusion and exclusion criteria, sample size was 372 patients. PED was observed in 29% of patients. For every day of intubation, risk of PED increased by approximately 50% ($p<.0001$). Age of <25 months increased risk of PED more than two-fold ($p<.05$). When controlling for age, diagnosis, number of complex chronic conditions and dysphagia status, patients with dysphagia had an increase in total length of stay of 10.95 days ($p<0.0001$). PED increased risk of gastrostomy or nasogastric tube at time of discharge ($p<.0001$).

Conclusions: This study is the first to systematically describe incidence, risk factors, and outcomes of PED in pediatrics. PED is associated with increased time between extubation and discharge and with risk of gastrostomy or nasogastric tube at time of discharge.



Risk of Dysphagia increases by 1.7% for every hour of intubation (50% per day). Risk is increased for patients aged 0-24 months versus 25+ months, and is further-increased for patients with a primary diagnosis of Trauma (there were no patients aged 0-24 months with a primary diagnosis of Trauma in this study).

GROUP THREE

Education

E5

Motivations of Males with Severe Obesity Who Pursue Bariatric Surgery or Medical Weight Management

Jolles, S.A., Alagoz, E., Voils, C.I., Shea, G.E., Liu, N., Funk, L.M.

Abstract Submitter	Sally Jolles
Email Address	jolles@surgery.wisc.edu
Classification	Academic staff
Principal Investigator	Luke Funk
Science Type	Health Services
Keywords	**Bariatric Surgery, Weight Loss, Motivations**

Introduction: Obesity is associated with serious health conditions including cardiovascular disease and type 2 diabetes. The main treatments for weight loss are medical weight management (MWM) and bariatric surgery. Both MWM and bariatric surgery are significantly underutilized, particularly by males. Roughly 27% of participants in MWM programs are male and only 20% of patients undergoing bariatric surgery are men.The motivations of males who pursue either MWM or bariatric surgery are unclear.

Methods: We conducted a secondary analysis of 25 semi-structured interviews with males with severe obesity (BMI $\geq$35) who participated in a VA weight loss program to identify their motivations for pursuing bariatric surgery (n=14) or MWM (n=11). The interviewer asked participants to describe why they pursued bariatric surgery or MWM. All interviews were audio-recorded, transcribed, and uploaded to NVivo for data management and analysis. Five coders iteratively developed a codebook and used inductive content analysis to identify relevant themes. We utilized theme matrices organized by type of motivation and treatment pathway to conduct generate higher-order themes.

Results: Participants were 58.7 (SD 8.6) years old on average, and 24% were non-white. Motivations for pursuing either treatment pathway included a desire to improve physical health, psychological health, and quality of life. Patients seeking bariatric surgery were motivated by the fear of death and by the belief that they had exhausted all other weight loss options**.** Patients who pursued MWM felt like they had more time to pursue other weight loss options, despite meeting criteria for bariatric surgery.

Conclusions: Males with severe obesity who pursued obesity treatment were motivated by their desire to improve their health and have longer, higher-quality lives. Patients pursuing MWM were unaware they qualified for bariatric surgery and many had not taken weight management medications, despite wanting to try them. These anecdotes suggest that patients lack information on available weight loss treatments. Introducing patients to a targeted educational intervention with available treatment options would increase awareness and utilization of obesity treatment options.

Table 1: Themed quote matrix of patients pursuing medical weight management (MWM) or bariatric surgery

Themes	MWM Group	Bariatric surgery Group
Improving physical health	"I wanted to have control of my diabetes and I wanted to make sure that I had a better handle on my blood pressure and on heart disease" (68 years old)	"I don't wanna have to constantly be a slave to insulin." (57 years old)
Improving psychological health	"I was very depressed and uncomfortable and I couldn't, my quality of life had almost, ultimately deteriorated to nothing and I was a couch potato and then when I went to bed, I hated to go to bed at night cause I knew I couldn't sleep" (64 years old) "I got bigger and bigger and it wasn't making no sense. And then my clothes didn't fit no more so I was mad at that." (59 years old)	I guess, I kinda started slipping on it, you know just activities of daily living you know. I wasn't showering as often, just wasn't motivated as far as personal hygiene." (39 years old)
Improving quality of life	"I was in the store and I saw this really fat lady, and I was like you know, what, she couldn't even walk, and I'm like, that's not going to be me. And then that's really what kind of motivated me to kinda take matters and get things going" (54 years old) I've always worked with athletic type things outside. I love outdoor and indoor sports. So I wanted to get back to doing some of those things that I once did." (64 years old)	I couldn't walk up and down the steps in my house. I have a basement where my grandkids play and they, I got a lot of things set up there. And I wasn't able to go up and down the steps for over a year." (68 years old) "I can't do the things I used to do. And I think most of it's based on my weight. You know. Going hiking and things like that, it's difficult when you're carrying another pack that's not a pack, you know." (40 years old) I miss being active. I used to rock climb, scuba dive, I was in the Marines. You know, I mean I enjoyed that. Now, I'm exhausted, can't play with my kids, you know I mean that's ten and six, that's the greatest time to be a kid." (40 years old)
Fear of death	None	At the rate I was gaining weight, I couldn't see living very much longer, 'cause I was probably going to end up having a heart attack." (67 years old)
Exhausted all other weight loss options	"I could control the weight if I just applied myself, rather than depending on something like (surgery) as an intervention." (68 years old)	"I knew if I continued down the path that I had, I wasn't going to be around. I knew I was in trouble. I wasn't getting better. I was doing worse all the time. And there was nothing I was doing that was doing better for me. So I needed [surgery]." (68 years old)

E1

Effective Educators and Constructive Mindsets for Optimal Surgical Training: Resident Perspectives

Babchenko O. MD, Sullivan S. PhD, Frank S., Elmaraghi S. MD, Thiagarajasubramanian S. MD, RendellV. MD, Nayar H. MD, Bentz M.L. MD, FAAP, FACS, Garland C.B. MD

Submitter	Oksana Babchenko, MD
Phone	
Email Address	obabchenko@uwhealth.org
Classification	
Division	Plastic and Reconstructive Surgery
Lab	Catharine B. Garland, MD. Plastic Surgery Faculty.
Science Type	Educational
Keywords	Surgical culture, Education, Educational psychology

Background: The operating room (OR) educational milieu – including faculty-resident interactions, residents' internal states (e.g. confidence, mindset, emotion), and faculty's influence on those internal states – has not been thoroughly examined in a surgical training context. Negative faculty-resident interactions can function as distractors that hijack working memory away from the operation[1,2] and are primary drivers of resident attrition.[3] Education research has demonstrated that teachers' feedback approaches can affect students' self-perceptions and thus impact confidence, performance, and future responses to challenges.[4] The goal of this study was to solicit resident perspectives on these subtle, though important, influencers of resident training.

Methods: An 11-question, open-ended survey was distributed to all surgical residents at our institution. Residents were asked to describe teaching methods and personal mindsets that were conducive vs. obstructive to learning. Recurring themes were identified utilizing line-by-line content analysis by 2 coders per question.

Results: Thirty-six of 134 residents (26.8%) completed the full survey, and 6 completed parts of it. Inter-coder reliability was 91-96%.

Recurring themes were (*percentage of residents that stated a given theme is in parenthesis):*

Effective educators were identified to possess humane qualities (62%), including patience (36%), prioritize teaching (49%), and allow resident autonomy (26%). Ineffective educators were described to have an inadequate focus on education (56%), including inadequate allowance of autonomy (22%). They were also described as impatient (27%) and short-tempered (20%).

Almost all residents (97%) affirmed that there were certain mindsets that helped them excel in the OR, including positivity/optimism (54%) and confidence (34%). Almost all (97%) residents affirmed that faculty/senior residents influenced those mindsets. When asked about what promotes their constructive mindsets, the top themes were positive faculty mood/behaviors (38%) and one's own preparation (34%). Factors contributing to poor OR performance were identified as inadequate preparation (49%) and negative interactions with faculty (34%).

Conclusion: Residents overwhelmingly felt that faculty influence their confidence and mindset during surgical training. Effective educators exhibit humane qualities and prioritize teaching. Poor preparation and discouraging interactions with faculty may have negative effects on resident learning and performance.

E14

What Makes a Good Surgical Coach?

Vande Walle K, Pavuluri Quamme S, Wiegmann D, Ghousseini H, Dimick J, Greenberg C

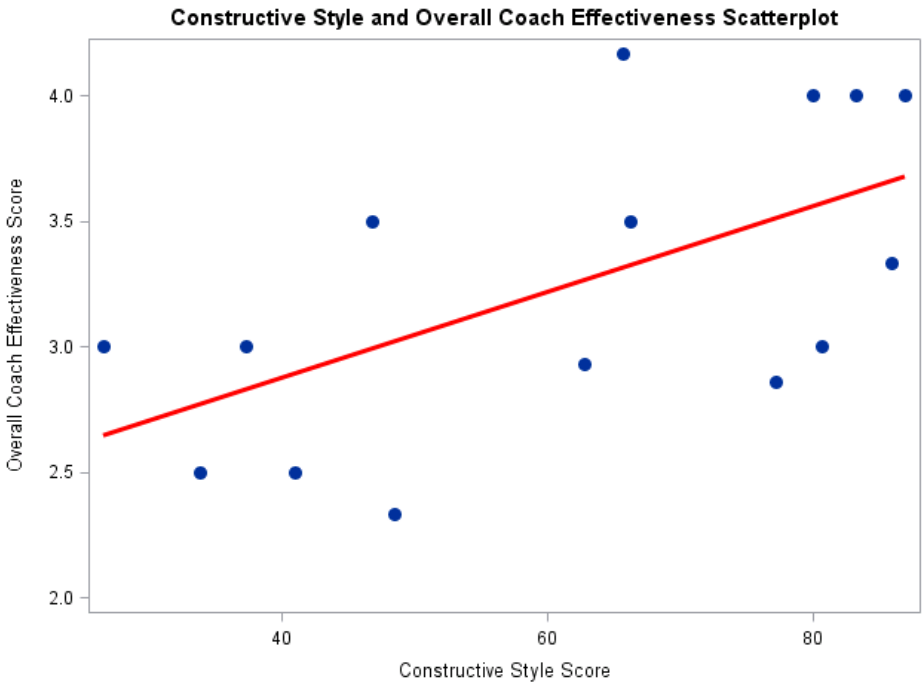
Abstract Submitter	Kara Vande Walle
Email Address	kvandewalle@uwhealth.org
Classification	Resident
Principal Investigator	Caprice Greenberg
Science Type	Education
Keywords	Coaching, Life Styles Inventory, Professional Development

Introduction: Surgical coaching programs have shown promise as a method for facilitating continuous professional development. However, there is currently no objective way to identify surgeons who will make effective coaches. The purpose of this study was to determine if the Myers-Briggs Type Indicator (MBTI)® and the Life Styles Inventory (LSI)™ can identify characteristics of effective surgical coaches.

Methods: Surgeon coaches in the Wisconsin Surgical Coaching Program (WSCP) and Michigan Bariatric Surgery Collaborative (MBSC) coaching program were administered the MBTI and LSI. Coaching sessions were audio recorded and transcribed. An overall coach effectiveness score (1-5) for each session was generated by a minimum of 2 blinded raters using a validated tool. The four dichotomies of the MBTI (extraversion/introversion, sensing/intuition, thinking/feeling, judging/perceiving) were rated on a continuous scale. The 12 thinking styles of the LSI were grouped into 3 clusters: constructive passive/defensive, and aggressive/defensive. Cluster scores were calculated by averaging the 4 LSI style scores included in each cluster. A Pearson correlation coefficient was calculated between each MBTI dichotomy and LSI style/cluster with the overall coach effectiveness score.

Results: 18 coaches were included in the MBTI and 15 were included in the LSI analysis. 9/18 (50.0%) coaches preferred extraversion, 13/18 (72.2%) preferred sensing, 12/18 (66.7%) preferred thinking, and 12/18 (66.7%) preferred judging. The Pearson correlation coefficients for each MBTI dichotomy and overall coach effectiveness were < 0.4 and not statistically significant. The mean score on the LSI (out of 100) was 61.5 for constructive, 58.1 for passive/defensive, and 44.8 for aggressive/defensive. A higher LSI constructive score correlated with a higher overall coach effectiveness ($r=0.59$, $p=0.02$) while passive/defensive scores and aggressive/defensive scores did not correlate with overall coach effectiveness ($r=-0.04$, $p=0.88$; $r=-0.01$, $p=0.98$). The mean overall coach effectiveness scores for the highest and lowest LSI constructive score tertiles were 3.7 and 2.9, respectively. Two of the four styles in the constructive cluster also correlated with overall coach effectiveness (self-actualizing $r=0.60$, $p=0.02$; humanistic-encouraging $r=0.58$, $p=0.02$).

Conclusions: This is the first study to propose a quantifiable assessment to identify effective surgical coaches. A higher LSI constructive score correlated with an increase in overall coach effectiveness. This suggests the LSI constructive score may be used to identify the most effective surgical coaches and training to increase an individual's constructive behaviors may lead to more effective coaching.


Constructive Style and Overall Coach Effectiveness Scatterplot
Overall Coach Effectiveness Score
4.0
3.5
3.0
2.5
2.0
40
60
80
Constructive Style Score

E4

Embodiment of Operative Instruction

Godfrey, M., Sullivan, S., Rosser, S., Nathan, M.J., Greenberg, J.

Abstract Submitter	Martha Godfrey
Email Address	godfrey@surgery.wisc.edu
Classification	Resident
Principal Investigator	Jacob Greenberg
Science Type	Education
Keywords	Teaching, Embodiment, Gesture

Introduction: Embodiment theory posits that cognition happens not only through computation in the brain, but is also grounded in action. Thus, gestures in other educational contexts have been shown to convey information to students that is not apparent through verbal communication. This pilot work explores the role of embodiment in intraoperative educational practices by studying how attending surgeons use gesture to instruct surgical trainees during a laparoscopic case.

Methods: One surgical attending and one surgical resident were video recorded while performing mesh placement during a laparoscopic inguinal hernia repair. Video was collected from a head-mounted GoPro camera situated on the attending's forehead and from the laparoscope. Video was transcribed and attending gesture was coded for four different types of gestures: beat, indexical (e.g. pointing), iconic, and metaphoric. Verbal communication along with accompanying gesture was evaluated in the context of the surgical procedure to determine the overall function of the gesture.

Results: All four types of gestures were used. The predominant gesture used was indexical while instructing the resident to move the mesh. During the case the laparoscope functioned as a camera, but also as a laparoscopic instrument to manipulate mesh position. The attending used iconic gesture of the laparoscope for both uses and the resident was able to understand the attending's instruction for the dual use of the laparoscope when it went immediately from one use to another. However, later the attending used the same iconic gesture intended to represent the laparoscopic instrument, not the laparoscope, and the resident was unable to discern which tool was indicated to use. Figure 1.

Conclusions: While the attending used all four types of gestures, iconic gestures were ambiguous. Gestures serve communication, but also enhance thinking. By using hands to replicate movements of laparoscopic instruments, these gestures may carry instructional value not in showing the resident what to do, but rather in assisting the attending to verbalize the procedure. This study demonstrates the need to explore who intraoperative gesture is created for and how to develop intentional gestures that promote intraoperative learning.

Figure 1 Iconic Gesture – hand as tip of tool

	
“use your scope to bring it up and in, right in the middle of the mesh” Hand representing the laparoscope being used as a laparoscopic instrument	“now go in and kind of lift, no, with your instrument” Hand representing the tip of the laparoscopic instrument being used to manipulate the mesh

E15

A Comparison of Phonosurgery Instrument Design: A Study in Surgical Novices

Wang J., Ulmschneider C., Chou, A., Jiang, J.

Abstract Submitter	Jessica Wang
Email Address	jwang765@wisc.edu
Classification	Undergraduate Student
Principal Investigator	Jack Jiang, MD, PhD
Science Type	Education
Keywords	phonosurgery, tracking, instrument design

Introduction: Phonomicrosurgery is a technically demanding specialty requiring extensive practice to achieve proficiency. Practical surgical exposure is limited in residency programs due to reductions in working hours and time in operating rooms. Thus, the efficiency of phonomicrosurgical training must be maximized to ensure resident competency. Through determining the impact of secondary surgical parameters, such as instrument design, on surgical performance, we can optimally apply these findings to residency programs, ensuring quicker and easier skill acquisition. However, the effect of instrument design on phonomicrosurgical training efficiency has not been thoroughly studied, warranting a comparison of microinstrument design. Traditional microsurgery instruments are finger-driven, or forward-action, in that flexion of the fingers approximates the handle. An alternative to traditional microinstruments, the Benninger Microlaryngeal Instruments (Medtronic Xomed Instrumentation, Saint Aubin Le Monial, France) are thumb-driven, or reverse-action, in contrast to traditional instruments. Thus, the thumb can more easily manipulate the handle without rotating the wrist. This design reduces the physical effort necessary for instrument stabilization and decreases the chance of undesirable tissue damage. While the benefits of a reverse-action design may be negligible for experts in phonomicrosurgery, it will most likely be more evident in novices. Therefore, application of Benninger, or reverse action, instruments in phonomicrosurgery residency programs may allow residents to achieve competency more quickly and easily. The goal of this study is to assess the use of reverse-action and traditional microinstruments in novices. We hypothesize that the use of Benninger microinstruments will result in greater instrument stability and less involuntary movement, thus leading to a better task outcome.

Methods: 30 novice subjects performed a simulated surgical task using both standard and Benninger instrument designs. The instrument design trial order was randomized. The simulated surgical task involved cutting two outlined ovals from a piece of paper using microforceps and microscissors. For each trial, instrument position data for both instruments were collected using a video-based instrument tracking system (Figure 1a). Instrument position was triangulated and used to calculate instrument motion metrics: time to task completion, path length, depth perception, orientation smoothness, and motion smoothness. As in prior motion tracking studies, these metrics serve as an objective assessment of surgical performance. In addition, task outcome was calculated for each trial based on the accuracy of the subject's cut. Task outcome and motion metric values were analyzed to determine if there was a significant difference between use of traditional microinstruments and Benninger microinstruments.

Results: While all data has been collected, motion metrics and task outcome analysis is ongoing. Preliminary data from a small subset of subjects suggests that there may be no significant difference between use of traditional and Benninger microscissors in novices. However, we will be able to make justified final conclusions after data analysis.

Conclusions: Upon completing data analysis, we will be able to determine if there is a significant difference due to use of Benninger or traditional microinstruments. Thus, this information can be optimally applied to phonomicrosurgery residency programs such that skill acquisition can proceed more easily and quickly.

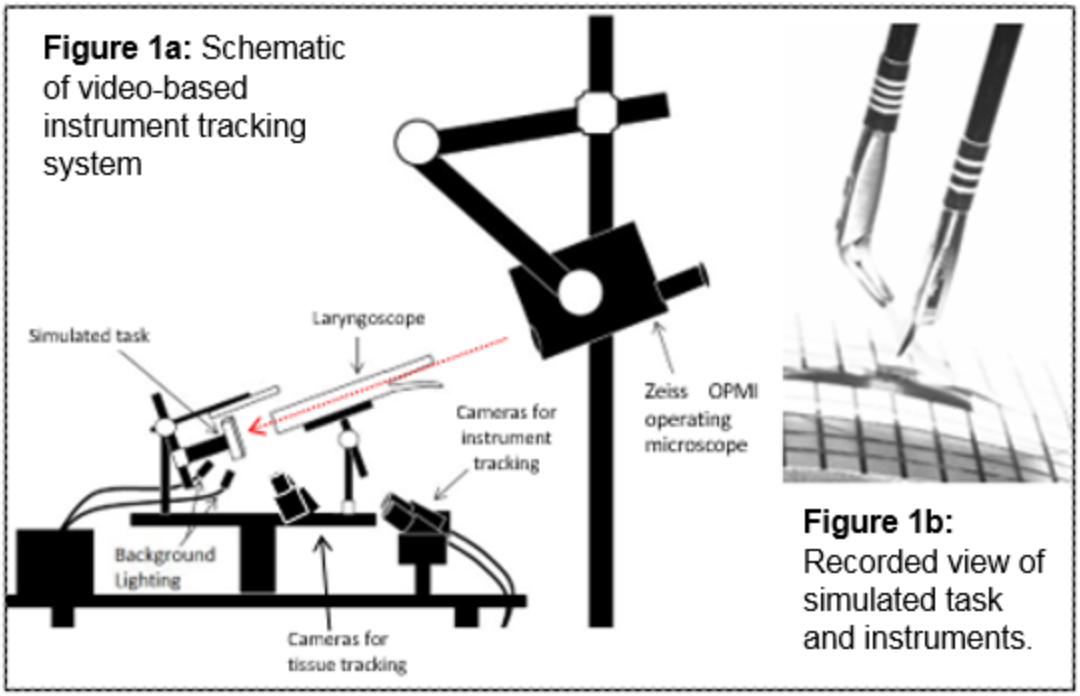


Figure 1b: Recorded view of simulated task and instruments.

E8

A Gap Analysis of Surgical Simulation Training in Medical Education for Students with Physical Disabilities

Patel, K.A., Jung, H.S., Sullivan, S.

Abstract Submitter	Kush Patel
Email Address	kapatel4@wisc.edu
Classification	Medical Student
Principal Investigator	Dr. Hee Soo Jung, M.D.
Science Type	Education
Keywords	Disability, simulation, accommodations

Introduction: Within the past decade, medical schools are admitting an increasing number of students that are physically disabled. These students are finding success in adapting to the rigorous demands of medical school education and are establishing professional careers in numerous specialties. At the same time, according to an Association of American Medical Colleges (AAMC) survey in September 2011, simulation has become one of the most prominent innovations in medical education over the past 15 years. Most hospitals and health profession training institutions have a simulation center, simulation equipment or simulation-based education programs. These technologies are used for teaching, practice and assessment of medical students. While there are tools and information developed to help institutions accommodate physically disabled students, there is no published information regarding the best practices of how medical schools can accommodate these students within their simulation-based curriculum, assessments, and evaluations. There is also very little described about how simulation can be used to assist learning for students with physical disabilities. Our research goals are to (1) develop a survey instrument that is approved by the ASE Surgery Clerkship Directors Committee targeted to surgical clerkship directors; (2) provide a description of how surgical clerkships accommodate physically disabled students within their simulation-based curriculum, assessments, and evaluations; and (3) to identify ways in which simulation is currently being used to enhance the learning of physically disabled students.

Methods: In order to facilitate survey construction, we interviewed key stakeholders at the University of Wisconsin School of Medicine and Public Health, including the medical student program manager for surgery, the technical standards director, and the simulation center manager. The content of the interview transcriptions was reviewed to identify salient themes. These themes were used to categorize and develop a survey tool that will be sent to all surgical clerkship directors as identified by the AAMC. The survey was piloted with clinical the simulation manager at the University of Wisconsin School of Medicine and Public Health.

Results: Review of interview transcriptions revealed themes that were used to develop a survey tool which features the following categories: structure of the program, simulation curriculum, simulation infrastructure, types of accommodations provided, attitudes and perceptions of clerkship directors, and barriers and limitations***.*** Currently, our survey is in the final stages of editing and will be sent to all surgical clerkship directors once approved.

Conclusions: The implementation of our survey instrument and the expected results will help inform medical education curriculum to the current strengths and challenges that all surgical clerkship programs face.

E10

An Analysis of Verbal Response Modes, Team Role, and Teamwork in Simulated Trauma Resuscitations

Statz B, Osman IH, Rosser AA, Sullivan S, Thompson R, Jung H

Abstract Submitter	Alexandra Rosser
Email Address	rosser@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Hee Soo Jung
Science Type	education
Keywords	simulation, trauma, education

Introduction: We sought to understand if role or gender affected the way team members spoke during trauma resuscitations and if those differences impacted trauma team performance.

Methods: Communication in 27 interdisciplinary trauma simulations was transcribed. Three physicians (trauma chief resident, trauma junior resident, emergency medicine resident) and two nurses (emergency medicine) participated in each simulation. Team performance was assessed using the Team Emergency Assessment Measure (TEAM) scale.

Speech was coded with Verbal Response Modes (VRM). VRM is a taxonomy that describes the relationship dynamics present in conversation by how the speech acts relate to the speaker or the person whom the speech targets. VRM codes can be classified into three dimensions: *Attentive* vs. *Informative*, *Presumptuous* vs. *Unassuming*, and *Directive* vs. *Acquiescent*. All utterances concerning another's experience are considered *Attentive*, whereas utterances concerning the speaker's experience are considered *Informative*. When an utterance presumes knowledge about the other person, it is considered *Presumptuous.* If no such presumption is made, the utterance is *Unassuming*. Finally, *Directive* utterances use the speaker's frame of reference in order to guide conversation, while *Acquiescent* utterances allow the other's viewpoint to determine the course of the conversation.

Ratios of speech acts in the three VRM dimensions for each team member were examined**.** We aggregated these proportions to compute mean VRM dimension ratios for each role and gender within the trauma team. Multiple regression and cluster analysis were performed to investigate relationships between VRM, team role (all physicians, trauma chief, nurses), gender, and TEAM score.

Results: T-tests of VRM dimension ratios demonstrated significant differences between physicians and nurses in how they spoke within simulated trauma resuscitations. Nurse speech was more attentive and unassuming than that of physicians. However, both physicians and nurses used equally directive speech. Trauma teams whose leaders used unassuming speech acts more than presumptuous speech acts had higher TEAM scores ($p=0.039$). Team member gender did not correlate with differences in speech acts or team performance.

Conclusions: Physicians and nurses speak differently within trauma resuscitations. Teams with leaders who communicate in an unassuming manner perform better. Based on VRM, the relationships between team members and the ways they spoke to one another did not correlate with gender.

E9

Automated Natural Language Processing of Closed Loop Communication in Trauma Resuscitations

Rosser AA, Sullivan S, Thompson R, Jung H

Abstract Submitter	Alexandra Rosser
Email Address	rosser@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Hee Soo Jung
Science Type	Education
Keywords	simulation, trauma, education

Introduction: Previous studies have shown that closed loop communication (CLC) improves task completion and patient outcomes in trauma resuscitations. In this study, we set out to develop an automated approach to measuring CLC in trauma resuscitations.

Methods: 27 simulated resuscitations were performed by interdisciplinary trauma teams including a surgery chief resident, a surgery resident, an emergency medicine resident and two emergency medicine nurses. Teamwork performance was assessed using the validated Team Emergency Assessment Measure scale. Trauma team communication was transcribed. Transcripts were then coded using an automated algorithm which captured patterns of discourse indicative of closed and open loops. Closed loops were parameterized as directions or requests that were subsequently acknowledged or acted upon. Open loops were directions or requests that received no such acknowledgment or action. Finally, we compared higher- and lower-performing teams by the proportional ratios of loop closure and overlap.

Results: An automated algorithm to analyze trauma team communication was developed. The automated coding algorithm was validated against a trained human rater's coding of the transcripts ($K > 0.83$, $rho < 0.05$). Regression analyses revealed significantly positive relationships between loop closure and performance ($p = 0.004$), as well as loop overlap and performance ($p = 0.001$). In other words, higher-performing teams used closed loop communication both more often and with a greater degree of parallelism, or multitasking ability.

Conclusions: CLC in trauma resuscitations can be identified by automated natural language processing. Our findings confirm that educational interventions focused on CLC and parallel workflow are likely to improve interdisciplinary team performance and patient care. More importantly, they demonstrate an important first step in developing automated, real-time feedback tools for trauma team communication.

E3

The Prevalence and Risk Factors for both Male and Female Chinese Teachers in Middle School, Elementary School and Kindergartens

Dehui Fu, ShanShan Huang, Yongwang Huang

Submitter	Dehui Fu
Phone	6089774325
Email Address	Dfu33@wisc.edu
Classification	Visiting scholar
Division	Otolaryngology
Lab	Laryngeal physiology lab
Science Type	Clinic
Keywords	Teachers; Voice Disorders; Vocal folds hemorrhage; Vocal folds hypertrophy; Vocal folds polyps; Vocal folds nodules

Introduction: The objective of this program was to investigate the prevalence and the risk factors of voice disorders for middle school, elementary school and kindergartens teachers in Tianjin, China.

Methods: There are 47796 teachers involved in this study. Questionnaires were collected; an integrated physical exam of ENT and the strobolaryngoscope were performed on the teachers. Logistic regression was used to find risk factors and effects of voice disorders for teachers.

Results: The prevalence rate of voice disorders was high, up to 33.81% in teachers. The most common diseases were vocal folds hypertrophy (9456, 19.80%), vocal fold hemorrhage (7064, 14.79%), glottis insufficiency (3174, 6.64%), vocal folds nodules (1234, 2.58%), and vocal folds polyps (920, 1.93%). According to the regression coefficients, OR, and 95%C.I. for OR, the distinct, gentle, teaching years, daily teaching hours, class capacity, speech loudness, smoke were the mainly risk factors for teachers voice disorders.

Conclusions: The studies have revealed that Chinese teachers had a higher occupational risk for voice disorders. These results imply the need for a preventive voice care program for teachers.

E2

Development of a Regional Anesthesia Task-Sharing Model for Orthopedic Surgeons in Port-au-Prince, Haiti

Christie, B.M., Woolley, P.M., Michelotti, B.M, Dyer, G.

Abstract Submitter	Brian Christie
Email Address	bchristie@uwhealth.org
Classification	Resident
Principal Investigator	Brian Christie
Science Type	Education
Keywords	Global surgery, task-sharing, capacity building

Introduction:
Trauma costs the global population up to 300 million years of healthy life every year, causing 11% of disability- adjusted life years (DALYs) worldwide. Orthopedic trauma, often from motor-vehicle accidents, contributes significantly to this burden, and treatment of open extremity fractures is considered a standard procedure 2,3, capacity for which is necessary in order to ensure delivery of emergency and essential surgical care. Adequate and timely surgical treatment, however, depends on a confluence of capacitive factors including access to safe regional or general anesthesia. Many upper and lower extremity long-bone fractures can be treated appropriately under regional anesthesia alone, but limited access to skilled practitioners for admission of regional techniques can delay care. Use of regional anesthesia requires knowledge of relevant anatomy and skillful use of ultrasonography. While orthopedic surgeons possess the former, teaching of ultrasonography and safe use of regional anesthetics to orthopedic surgeons has not been systematically performed.

Methods:
This study aimed to conduct a systematic needs assessment of extremity trauma needs in Hôpital Universitaire de la Paix (HUP/MSPP) and Hôpital Université d'état d'Haiti (HUEH/MSPP), Port-au-Prince, Haiti. We hypothesized that anesthesia faculty with expert knowledge in regional anesthesia are severely limited. Lack of access to anesthesia faculty limits use of regional anesthesia in orthopedic extremity trauma cases in HUP and HUEH and causes surgical delays. Furthermore, we aimed to measure utilization of regional anesthesia techniques before and after implementation of regional anesthesia teaching to anesthesia and orthopedic faculty. We hypothesized that utilization of regional anesthesia techniques will increase significantly following implementation of a regional anesthesia teaching course. Lastly, we aimed to compare outcomes and admission-to-surgery times before and after implementation of regional anesthesia teaching to anesthesia and orthopedic faculty. We hypothesized that surgical outcomes will remain unchanged, and surgical delays will be reduced following regional anesthesia treatment.

Results:
In January 2018, a needs assessment was carried out at Hôpital Universitaire de la Paix and Hôpital Université d'état d'Haiti, using the Harvard Medical School Program in Global Surgery and Social Change National Surgical, Obstetric and Anaesthesia Planning (NSOAP) Semi-structured Hospital Interview Tool. Orthopedic and anesthesia faculty, as well as orthopedic and anesthesia residents from both hospitals were interviewed and queried regarding key factors affecting the surgeon and anesthesiologists ability to provide safe, affordable and timely surgical care, relating to organizational infrastructure, workforce, service delivery, financing, and information management.

The results of the needs assessment identified multiple bottlenecks contributing to delays in surgical treatment of orthopedic trauma across all dimensions. Challenges to the delivery of timely, safe, and affordable surgical care related to infrastructural inconsistency, inadequate supply provision, and workforce shortages, coupled with high out-of-pocket spending and unreliable information management systems.

Conclusions:
Access to safe, affordable, and timely surgical care at two university hospitals in Haiti is impacted by multiple bottlenecks. Ongoing development of a regional anesthesia task-sharing model for orthopedic surgeons in the practice of extremity trauma surgery has promise in addressing some, but not all, of these obstacles.

E6

Beyond “Good Team Player”: An Extended Clinic Experience with a Surgical Faculty Member Results in More Descriptive Narrative Clinical Evaluations

Larson, S.L., Sullivan, S.A., O’Rourke, A.P.

Abstract Submitter	Sarah Larson
Email Address	larsonsa@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Ann O’Rourke, MD
Science Type	Education
Keywords	narrative evaluation, medical student, longitudinal clinic

Introduction: Clinical evaluations, with narrative content, aim to provide learners with more targeted and individualized assessments. Students perceive narrative evaluations as an indicator of their academic performance and competitiveness on residency applications, yet students are often dissatisfied with the quality of narrative comments received on surgical evaluations. We proposed assigning students a mentor through a three-month continuity clinic, which encourages longitudinal one-on-one faculty and student interaction, would result in an effective evaluation of performance. Our objective was to compare narrative evaluations given to students in a surgical continuity clinic (CC) program to those given on another surgical rotation (No-CC) in the same clerkship.

Methods: The clinical performance of medical students was assessed using a combined rating scale and comment-based evaluation from January-October 2018. The Professionalism-Reporter-Interpreter-Manager-Educator (PRIME) evaluation framework was used to code narrative assessments. PRIME was adapted to the surgical context by adding a domain for Skills assessment (S-PRIME). We conducted a content analysis of narrative comments from 81 CC and 81 No-CC evaluations to compare quality based on word count, S-PRIME competency domains, and reinforcing or corrective content. Differences were compared between CC and No-CC evaluations using the chi-square test, $p<0.05$ was considered significant.

Results: Reinforcing comments significantly differed in the domains of Interpreter (16% vs 8%) and Manager (8% vs 3%) between CC and No-CC. Corrective comments significantly differed in the domains Interpreter (36% vs 17%) and Manager (16% vs 5%). There was no significant difference between CC and No-CC corrective comments in the domains Skills, Reporter, or Educator. The CC program elicited more narrative comments. In both groups, faculty gave significantly more reinforcing comments than corrective.

Conclusions: As evidenced by significant differences in the domains Interpreter and Manager, extended contact between faculty and students in a CC setting allows faculty to give improved and focused comments on student abilities to interpret H&P data, formulate differential diagnoses, and determine a patient plan. Although corrective comments increased among CC preceptors, all faculty struggle with applying corrective feedback. These findings present an opportunity for education and development for faculty within the CC program to focus on providing effective corrective feedback.

E7

Assessing Efficiency in Microsurgery Using Motion Tracking Technology

Lyon S.M., Zeng, W, Albano N.J., Mohamadipanah H., Pugh C., Poore S.O.

Abstract Submitter	Lyon S.M.
Email Address	Slyon@uwhealth.org
Classification	Resident Physician
Principal Investigator	Poore
Science Type	Education
Keywords	Microsurgery, Education, Efficiency

Introduction: A high level of precision as well as controlled, efficient motions are important components of microsurgical technique and success. The current Halstedian model of resident microsurgical education confers this expertise in the operating room wherein residents acquire skills while operating on patients with the supervision and guidance of an experienced attending.

The goal of this study is to capture and to compare motion patterns of microsurgeons in various career stages in a lab-based anastomosis model. We employ a motion tracking technology to analyze hand and instrument motion to identify critical areas for trainee improvement. Ultimately, we aim to improve in vitro microsurgical education, decrease operative times and improve resident microsurgical skill and efficiency in the lab setting prior to performing anastomoses in the operating room.

Methods: Plastic surgeons with varying levels of microsurgical experience performed end-to-end microsurgical anastomoses in a laboratory setting. A blue blood chicken thigh model was used in which the femoral artery of a chicken was dissected and the proximal end was connected via an angiocatheter to blue-died saline.

The microsurgeon and an assistant were equipped with motion-tracking sensors which connected to standardized positions on their hands and to the microsurgical instruments. Vessel branches measuring less than 3 mm were transected and anastomosed using an end-to-end technique. The integrity of the anastomosis was interrogated by instilling blue saline into the vessel.

From the data collected, metrics such as the total anastomosis time, total path length and bimanual dexterity will be abstracted and analyzed.

Results: Two fellowship trained microsurgeons, one senior (PGY4) plastic surgery resident and one junior (PGY1) plastic surgery resident participated in the study. A total of 4 anastomoses were completed and saved for analysis.

Conclusions: With the implementation of resident work hours and the new focus on competency-based training, there is an increasing need for validated laboratory-based methods for microsurgical education. Our study uses a novel application of motion tracking technology to assess motion patterns in microsurgery using a lab-based chicken thigh model. We plan to apply this data to improve microsurgical technique and efficiency in trainees by identifying and reducing redundant or unproductive motion. Ultimately, we hope this will improve the microsurgical education experience for residents and attendings alike by reducing anastomosis time and optimizing operative flow.

E16

Microsurgical Training Course Utilizing the “Blue-Blood” Chicken Thigh Model Significantly Enhances Comprehensive Resident Education

Zeng W MD, Shulzhenko N.O. BA, Lyon S.M.MD, Albano N.J. MD, Dingle A.M PhD, Poore S.O. MD PhD

Abstract Submitter	Weifeng Zeng
Email Address	Wzeng28@wisc.edu
Classification	Academic staff
Principal Investigator	Samuel O. Poore MD PhD
Science Type	Education
Keywords	Resident education, resident training, simulation, microsurgery

Introduction: Microsurgical training curriculum and models are essential in helping trainees develop their skill. The curriculums and models used in different training program are various. An actual simulation on a microscope with handling the real tissue is still an ideal method to learn the microsurgical techniques. Identifying the improvement of microsurgical skill and awareness associated with the teaching method and models could optimize the result of training. A day-long multidisciplinary course in microsurgery with didactic and practical components was developed in our lab. We aimed to assess the efficacy of a microsurgical curriculum and that of the blue-blood chicken thigh model in the education of microsurgery.

Methods: *Course Design:* The course itinerary was comprised of both didactic and practical components. The course includes faculty-led lectures within plastic and reconstructive surgery, otolaryngology, and urology. And two practicing sessions utilizing a "LifeLike" Biomet Microsurgery Simulators and "blue-blood" chicken thigh simulators. All participants were free to work alone, in pairs, or with an instructor on microscopes. *Course Survey:* We developed questionnaires for the trainees attending our course. A pre-course survey was administered before any programming began and after. Questions included the level of anxiety and confidence of performing microsurgery, the value of the simulator, and the influence to the awareness of the value of microsurgery in their specialties, skill improvement, and career development, and general descriptive information (e.g. department, training level, etc.) was recorded as counts within categories. Median Likert Scores (MLS) ± Median Absolute Deviation (MAD) are used to calculate the level of the accessed domains. Inferential statistics between pre- and post-survey responses were performed using the non-parametric Wilcoxon signed-rank test.

Results: A total of nineteen residents attended a day-long microsurgical training course on two occasions (N = 10 and 9, respectively). A total of three surgical subspecialties were represented from PGY-2 to PGY-7, including Plastic and Reconstructive Surgery (N = 10), Urology (N = 6), and Otolaryngology (N = 3). A quarter of participants had never performed an anastomosis prior to attending the course and about half had performed less than five. A total of 114 anastomoses were performed: 82 end-to-end, 24 end-to-side, and eight coupler-assisted. On average, each participant performed 4.3 end-to-end, 1.3 end-to-side, and 0.4 coupler-assisted anastomoses. Post-course surveys revealed trainees reported significant improvement in nearly all assessed domains of microsurgery including: operating a microscope($P = 0.019$), handling microsurgical instruments ($P < 0.001$), handling tissues ($P < 0.001$) and performing end-to-end ($P < 0.001$) and end-to-side anastomosis ($P < 0.001$) and using coupler as well.

All participants believed the "blue-blood" vessels were at least somewhat more realistic as compared to Biomed vessels, with 7 (36.8%) believing them to be "very much," and 5 (26.3%) believing them to be "incredibly." Additionally, all but two respondents believed the course to have improved their awareness of the value of microsurgery in other specialties "very much," with six respondents believing it to have been improved "incredibly" (MLS ± MAD: 3.74 ± 0.34). All participants except one believed the course "very much" or "incredibly" improved what they would able to gain from future operative experiences from both the knowledge (MLS ± MAD: 3.86 ± 0.39) and skills (MLS ± MAD: 3.92 ± 0.44) they learned and practiced in the course.

Conclusions: This one-day-long condensed education course is a good curriculum for the residents from different training levels to learn the knowledge and practice the basic technique and advanced technique with the one-on-one opportunity with the supervision and instruction of attending surgeons. Our "blue-blood" chicken thigh model offers a significantly more realistic training experience than the Biomet simulator. The curriculum and the "blue-blood" chicken thigh model are efficacious and these translates to improved confidence and competence in trainee skills.

E11

Addressing Gaps in Knowledge Sharing within Trauma Teams-in-Training by Examining Team Process and Individual Empowerment

Sullivan S, Rosser A, Thompson R, Jung H S

Abstract Submitter	Sarah Sullivan
Email Address	sullivans@surgery.wisc.edu
Classification	Faculty
Principal Investigator	Sarah Sullivan
Science Type	Education
Keywords	medical education, non-technical skills, communication, simulation, debriefing

Introduction: Unintentional injury and violence are the leading causes of death in people aged 1 to 44 in the United States. Due to the time-sensitive, high-risk, and complex nature of treating critically injured patients, non-technical skills such as teamwork, communication, and leadership skills are imperative. This study investigate the use of an interdisciplinary trauma simulation for teaching non-technical skills. Specifically, this work looked at the role of the facilitator in the simulation debriefing.

Methods: Trauma resuscitation simulations are conducted at a medical education simulation center in order to provide an opportunity for training in non-technical teamwork skills for teams of five trauma learners. These learners include two surgery residents (a trauma chief and junior resident), a junior emergency medicine resident, and two nurse residents or trainees. Three faculty members conduct the simulations. Post simulation debriefings are performed by the simulation facilitators: a trauma surgeon, emergency medicine physician, and emergency department nurse. The audio from the debriefing sessions was recorded and transcribed.

Videos from 28 debriefings collected as part of 14 one-hour simulation sessions during one academic year were transcribed. The transcripts were examined for instances of discussion related to developing a shared team understanding of the patient's situation in the scenario by sharing information and ideas with the team. Of interest were 1) whether T-NOTECHS scores assigned by the facilitators captured differences in information sharing effectiveness 2) how learners approached this topic in debriefing and 3) how the debriefing facilitators provided support to learners on this issue. After these instances were identified, T-NOTECHS scores were compared between teams in which the sharing of knowledge had been identified as an issue (N = 8) and teams in which it was not (N = 20, See Table 1).

Results: Of the 28 debriefing sessions that were analyzed, eight (28.57%) contained instances of participants discussing issues with providing information that was needed by the team to develop a shared understanding of the patient's condition. Scores on the T-NOTECHS were compared across groups in which a lack of shared information was discussed during debriefings (N = 8) versus those in which this was not discussed (N = 20) using t-tests. With a threshold of alpha = .05, comparison of the domains of the T-NOTECHS scores indicated that there were no significant differences in scores on any of the domains between the two groups.

Conclusions: Using the T-NOTECHS global assessment tool, facilitators were not able to capture information-sharing nuances in team process and communication that might affect the provision of effective patient care. Facilitators were able to address these nuances in the debriefings and encouraged learners to feel empowered to share information with their teams. However, when discussing empowerment during debriefings, facilitators did not discuss or elicit strategies for developing empowerment with learners. Unfortunately, the inherent status differences between trauma members, which may result from their individual characteristics, varying levels of training, and roles in the trauma team, may render this discussion ineffective without structured inclusion of trainee perspectives and development of specific interventions.

Table 1: T-NOTECHS means (standard deviations)

Content of Debriefing	N	Leadership	Cooperation	Communication	Assessment	Awareness
Discussion of sharing information	8	3.98 (.40)	4.12 (.53)	4.00 (.51)	3.91 (.41)	3.87 (.54)
No discussion of sharing information	20	3.78 (.60)	3.99 (.56)	3.52 (.61)	3.63 (.65)	3.61 (.56)

E12

Operating Room Preparation by General Surgery Residents: A Qualitative Analysis

Goldwag J & Sullivan S

Abstract Submitter	Sarah Sullivan
Email Address	sullivans@surgery.wisc.edu
Classification	Faculty
Principal Investigator	Sarah Sullivan
Science Type	Education
Keywords	OR preparation, resident education, interviews, qualitative analysis

Introduction: There are growing concerns that graduating surgical trainees are not fully prepared to practice independently. With the implementation of policy changes, increased attending supervision, and duty hours, time in the operating room (OR) is limited. This leaves residency programs the challenge of optimizing trainee OR experiences to produce competent surgeons. In order for residents to fully utilize their OR training time, they must be prepared for the cases in which they participate. However, research is lacking on preparation strategies to best activate relevant knowledge that can then be applied in the case. We aim to explore how residents prepare for the OR by investigating how they learned to prepare, what factors impact their preparation, what resources they use, and what qualities make resources desirable.

Methods: We conducted a qualitative study using conventional content analysis. We invited surgery residents of all PGY levels at one institution to participate in semi-structured interviews. Each Interview's audio was recorded and transcribed verbatim. Two researchers inductively examined the transcriptions independently to generate themes.

Results: Fourteen residents elected to participate: Four PGY-1, Three PGY-2, Two PGY-3, One PGY-4, Two PGY-5, and two research residents. All participants similarly defined six topics they should know prior to a case: the patient, the pathophysiology, the anatomy, the indications, the procedural steps, and the common complications. Eight total themes emerged in our four areas of interest. Learned preparation: (1) acquired through "trial and error". Factors affecting preparation: (2) available time, (3) attending "quirks", (4) perceived potential autonomy. Resources used: (5) variation within each topic of preparation, (6) variation per PGY level, (7) occasional difficulty finding appropriate resources. Resource qualities: (8) high yield, meaning resources were: concise, easily available, comprehensive, and clear.

Conclusions: Although surgical residents similarly defined topics for operating room preparation, they use a variety of different resources to achieve this, even at one institution. Residents overwhelmingly reported learning to prepare through "trial and error," defined time as the most significant limiting factor in preparation, and stated it was often difficult to find an appropriate resource. Further investigation should define optimal preparation strategies and resources.

E13

What Are Clinical Instructors Really Evaluated On? A Qualitative Study of Medical Student and Resident Comments on Evaluations of Teaching

Sullivan, S., Greenberg, J., O'Rourke, A., Minter, R., Foley, E., Voils, C. I.

Abstract Submitter	Sarah Sullivan
Email Address	sullivans@surgery.wisc.edu
Classification	Faculty
Principal Investigator	Sarah Sullivan
Science Type	Education
Keywords	Teaching evaluations, medical students, residents, qualitative analysis

Introduction: The Accreditation Council for Graduate Medical Education (ACGME) has recently released new guidelines for faculty development that stress annual and continuous development as educators. While teaching is integral to academic surgery, few surgeons have formal training in education. To inform faculty development interventions, it is essential to understand the content of trainees' evaluations.

Methods: All trainees have the opportunity to provide open-ended comments on the program and faculty on completion of each rotation at our Midwestern academic hospital. Open-ended comments (N=716) from residents to faculty and from medical students to residents and faculty over one academic year were analyzed. All comments were open-coded.

Results: Content analysis revealed four higher-order themes. *Leadership* encompassed creating an atmosphere that prioritized learning, viz. feeling respected, remaining professional, and managing a team. *Communication* encompassed positive or negative verbal interactions, viz. communication skills, particularly related to providing feedback. *Teaching* encompassed teaching skills and approach, viz. direct teaching, involving medical students, and fostering autonomy. *Clinical skills* encompassed skill and approach to clinical practice, viz. engaging in evidence-based practice, being efficient, and providing appropriate patient care. Medical students focused on being involved in meaningful patient care and time for direct teaching. Residents focused on opportunities for appropriate autonomy and actionable feedback. Residents commented on faculty members' clinical skills when evaluating their teaching.

Conclusions: Our findings suggest that faculty development efforts in surgical education should target leadership, communication, teaching, and clinical skills. Future efforts are needed to implement and evaluate appropriate interventions to address these four content areas.

GROUP FOUR

Health Services

H14

Deficiencies in Postoperative Surveillance for Veterans with Gastrointestinal Cancer

Taylor LJ, Xu K, Maloney JD, Voils CI, Weber SM, Funk LM, Abbott DE

Abstract Submitter	Lauren Taylor, MD
Email Address	Ltaylor2@uwhealth.org
Classification	Resident
Principal Investigator	Dan Abbott, MD
Science Type	Health services
Keywords	cancer survivors, guideline concordance, gastrointestinal cancer

Introduction: Surveillance has been recognized as an essential component of survivorship care for patients with cancer. National guidelines for gastrointestinal cancers offer surveillance algorithms to facilitate detection of recurrent disease, yet rates of guideline adherence are unknown. We sought to characterize postoperative surveillance patterns for Veterans with gastrointestinal cancer at a tertiary care Veterans Affairs Hospital.

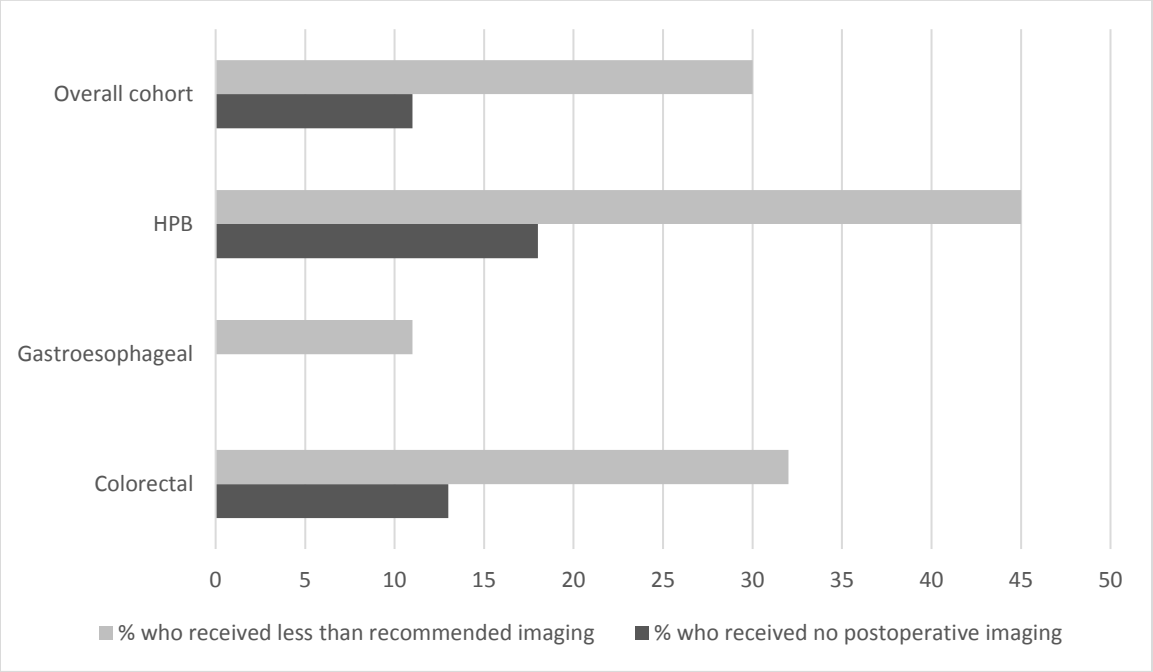
Methods: A single-center retrospective cohort study identified all patients who underwent surgical resection for colorectal, gastroesophageal or hepatopancreaticobiliary malignancy between 2010 and 2016. For each patient, we calculated the annual rate of cancer-directed clinic visits and abdominal imaging obtained during the surveillance period. We used National Comprehensive Cancer Network guidelines as a benchmark by which to assess adequate surveillance.

Results: Ninety-seven patients met inclusion criteria. Colorectal cancer was the most common diagnosis, representing 70% of the cohort. Median surveillance time was 1,203 days. Overall, 44% of patients had insufficient surveillance. Specifically, 11% received no postoperative imaging and 7% had no cancer-directed clinic visits during the surveillance period. An additional 30% received less than recommended surveillance imaging and 12% attended fewer than recommended clinic visits. By disease site, insufficient imaging was most common for patients with hepatopancreaticobiliary cancer (63%), while inadequate clinic follow-up was highest for veterans with colorectal cancer (24%).

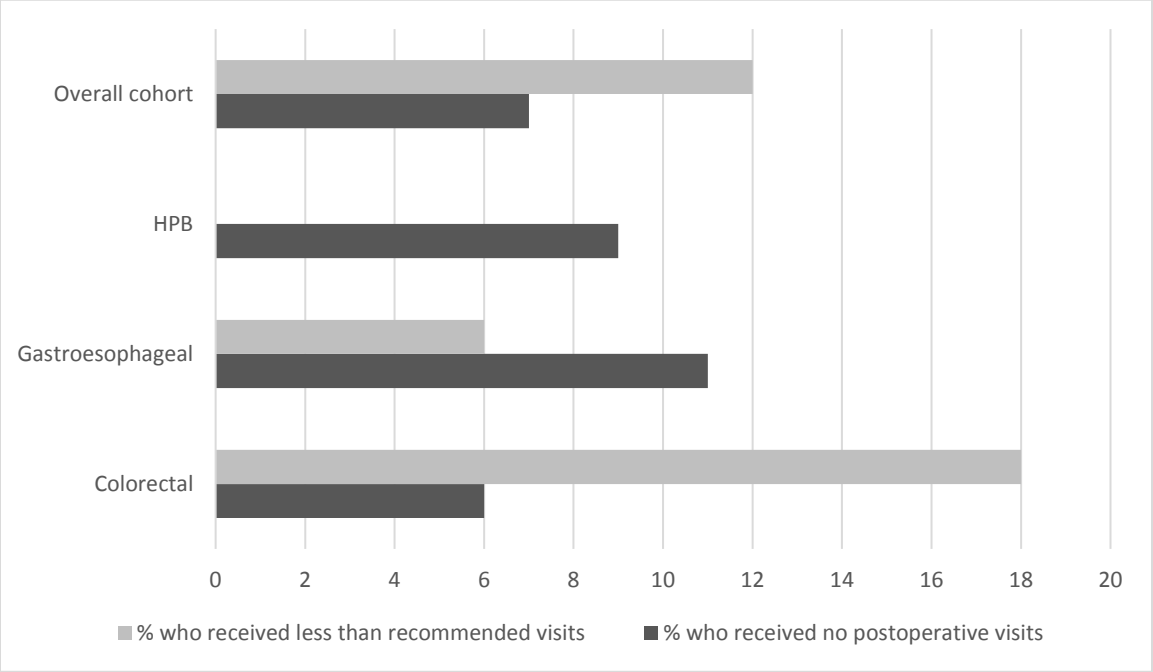
Conclusions: A significant proportion of veterans with gastrointestinal cancer received either no postoperative surveillance or inadequate follow-up based on national guidelines. This deficiency in surveillance utilization represents an opportunity for improvement through targeted efforts, including telemedicine and education of patients and providers.

Figure 1 A) Receipt of surveillance imaging and B) receipt of cancer-directed clinic visits by disease site

A



B



H13

Perioperative Cost Differences of Laparoscopic Sleeve Gastrectomy Versus Laparoscopic Roux-en-Y Gastric Bypass: A Single Institutional Review

Svoboda D.C., Venkatesh M., Liu N., Johnson M., Greenberg J.A., Lidor A.O., Funk L.M.

Abstract Submitter	Dillon C Svoboda
Email Address	dcsvoboda@wisc.edu
Classification	Medical Student
Principal Investigator	Luke Funk, MD, MPH, FACS
Science Type	Health Services
Keywords	Bariatric, surgery, cost

Introduction: Nearly 20% of the U.S. population is affected by severe obesity (body mass index ≥35). Bariatric surgery is the most cost-effective treatment for severe obesity, but differences in cost exist for the two most commonly bariatric procedures: laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB). Our group previously reported that laparoscopic sleeve gastrectomy patients incurred higher costs during the 1-year period that included surgery, but the etiology of this cost difference was unknown. The objective of this study was to compare operative costs and charges between LRYGB and LSG patients.

Methods: Adult bariatric surgery patients who underwent either LSG or LRYGB between June 2012 and June 2017 at a single institution were identified using our institution's bariatric surgery database. Operative costs and charges, defined as those incurred on the day of surgery, were obtained through billing data and linked to all patients in the study cohort. Each perioperative cost and charge was placed into 1 of 43 categories and subsequently combined to generate total costs and charges for each patient. Student's T tests were used to compared costs and charges overall and within each category for LSG and LRYGB patients.

Results: 559 bariatric surgery patients were included in the study cohort (234 patients who underwent LSG and 316 who underwent LRGYB). There was no statistically significant difference in the mean operative costs for the two procedures ($9,038 for LSG vs. $9,414 for LRYGB, p=0.15). However, there was a statistically significant difference in average total charges between the two procedures, with LRYGB patients incurring a greater mean charge compared to LSG patients ($42,815 vs. $39.662; p=0.02). The largest contributors to surgical costs for both procedures were staplers (19.9% of total costs for LSG vs. 25.1% for LRYGB), followed by staple loads (7.8% for LSG vs 6.7% for LRYGB), and OR time (7.5% for LSG vs 8.4% for LRGYB).

Conclusions: While overall operative costs between LSG and LRYGB patients were similar, LRYGB patients incurred higher total charges compared to LSG patients. This difference was primarily due to longer OR times and increased use of stapler equipment for bypass patients. These findings suggest that previously reported cost differences between sleeve and bypass patients are related primarily to costs generated outside the operating room, including costs related to subsequent emergency department visits and postoperative care. While minimizing operative costs remain paramount, they do not appear to be the main driver of cost differences between these two groups of patients.

H7

Weight Loss for Patients with Severe Obesity: An Analysis of Long Term Electronic Health Record Data

Liu N, Birstler J, Venkatesh M, Hanrahan LP, Chen G, Funk LM

Abstract Submitter	Natalie Liu
Email Address	nliu@uwhealth.org
Classification	Resident
Principal Investigator	Luke M. Funk, MD, MPH, FACS
Science Type	Health Services
Keywords	Obesity, weight loss, electronic health record

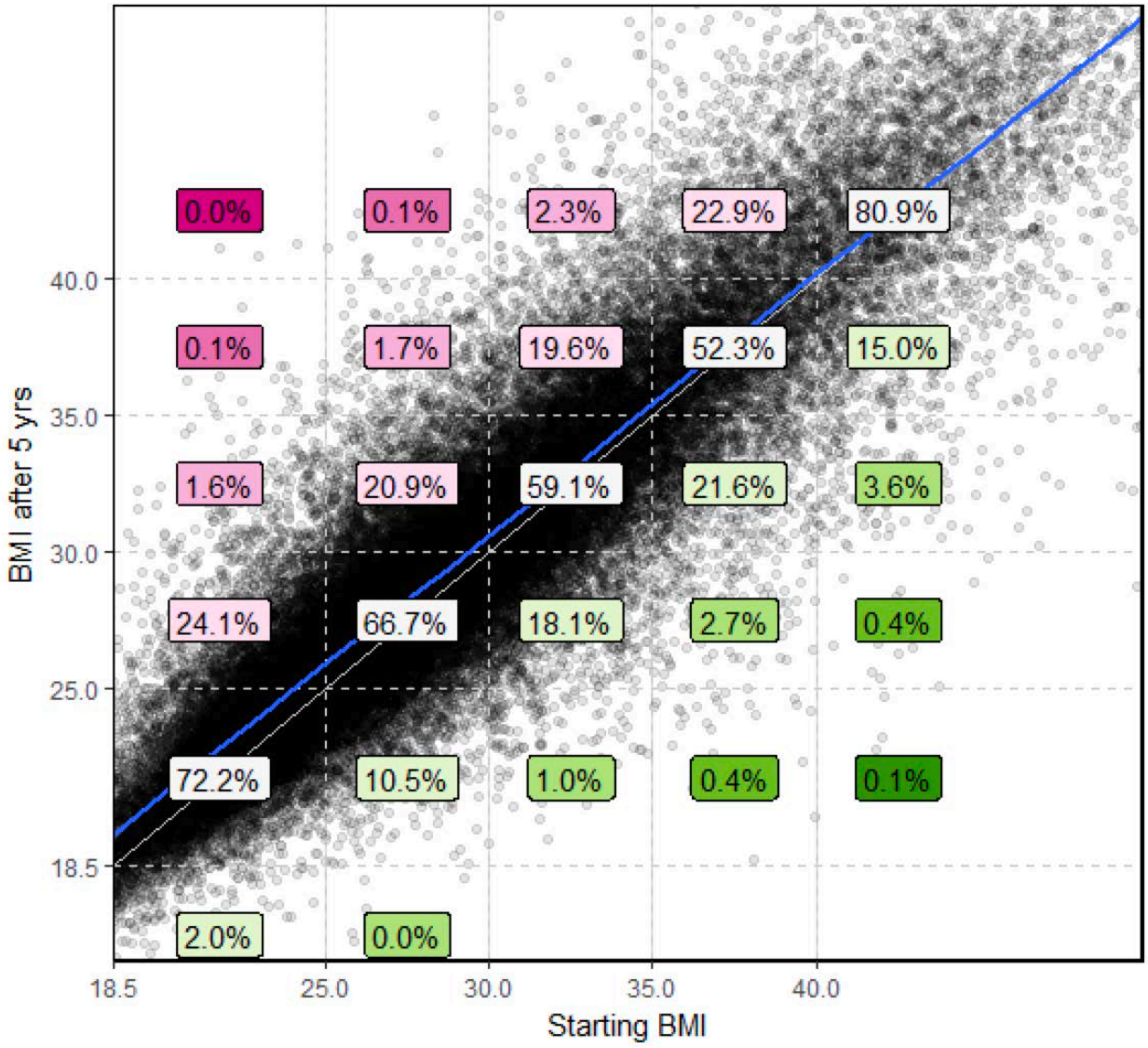
Introduction: Obesity is a widespread health problem in the US, affecting one-third of all US adults. Numerous studies have reported that losing as little as 5% of one's total weight can result in improved comorbidities, specifically cardiovascular health. However, for adults with severe obesity, 5% total body weight (TBW) loss rarely results in resolution of comorbidities. The objective of this study was to quantify clinically significant weight loss over a 5-year period for patients with severe obesity who had not undergone bariatric surgery. We defined clinically significant weight loss as achieving a BMI <30 kg/m^2. We hypothesized that less than 10% of our patient would achieve clinically significant weight loss.

Methods: All 18-75 year old patients at a single institution academic center who had 2 height and weight measurements at least 5 years apart between 2008 and 2016 were identified from the electronic health record (EHR). We excluded all underweight (BMI ≤ 18.5 kg/m^2), pregnant, and cancer, and bariatric surgery patients using ICD-9 and -10 codes. We categorized patients by their initial BMI measurement: normal (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), class 1 (30.0-34.9 kg/m^2), class 2 (35.0-39.9 kg/m^2), and class 3 (≥ 40.0 kg/m^2) obesity. BMI changes from initial to end date were plotted. Within each BMI group, we identified patients who lost ≥5% TBW.

Results: 59,816 patients met our study inclusion criteria. 17.1% were severely obese (class 2 or 3). 24.2% of class 2 obesity patients, and 27.8% of class 3 patients lost ≥5% TBW; 15.6% and 20.8% of overweight and class 1 patients, respectively, lost ≥5% TBW. Most patients with severe obesity (52.3% and 80.9% for class 2 and 3, respectively) remained in the same BMI category (**Figure 1**). 24.8% of class 2 and 19.1% of class 3 patients lost enough weight to drop down at least 1 obesity class. Only 3.2% and 0.5% of class 2 and 3 patients, respectively, achieved clinically significant weight loss.

Conclusions: Although patients with severe obesity were more likely to lose at least 5% of their total weight compared to overweight and class 1 obesity patients, weight loss into a non-obese weight class was exceedingly rare over a 5-year period. The vast majority of patients with severe obesity either remained in the same obesity class or increased classes. This pattern of ongoing weight gain for the most obese patients is concerning and requires solutions at societal and health systems levels.

Figure 1. Change in BMI over 5 year period



H10

Effect of Transfer Status on Outcomes of Emergency General Surgery Patients

Philip JL, Yang DY, Wang X, Fernandes-Taylor S, Hanlon BM, Schumacher J, Saucke MC, Havlena, J, Greenberg CC, Santry HP, Ingraham AM

Abstract Submitter	Philip JL
Email Address	jphilip@uwhealth.org
Classification	Resident
Principal Investigator	Ingraham AM
Science Type	Health Services Research
Keywords	Interhospital transfer, emergency general surgery, national inpatient sample

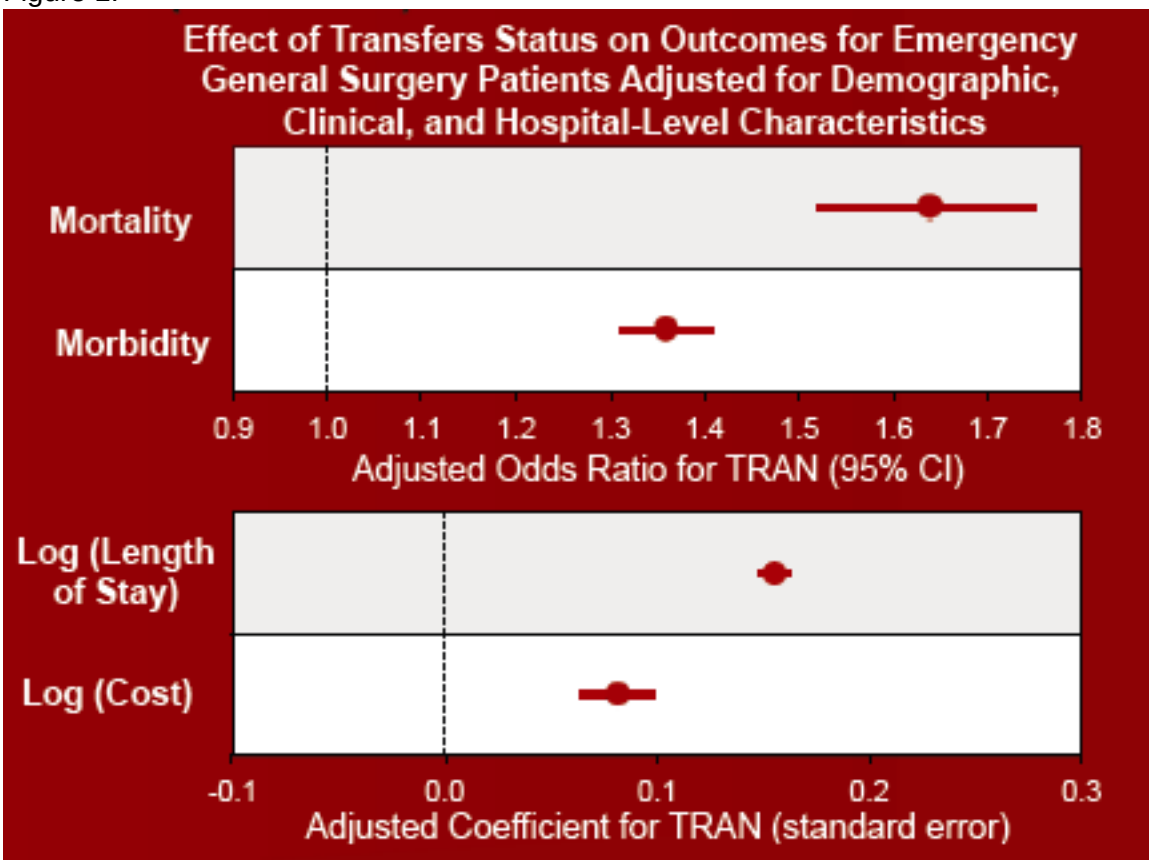
Introduction: Transferred emergency general surgery (EGS) patients are a vulnerable, high acuity population. Outcomes among transferred (TRAN) vs directly admitted (DA) patients have primarily been studied using single institution or hospital system data limiting generalizability. We evaluated outcomes among these EGS patients using a large national dataset

Methods: We identified patients aged ≥18 years with an American Association for the Surgery of Trauma-defined EGS diagnosis in the 2008-2013 Nationwide Inpatient Sample (NIS). Multivariable regression analyses determined if transfer status independently predicted in-hospital mortality (by logistic regression), morbidity (presence of any complication, among those who survived to discharge; by logistic regression), cost (by log-linear regression), and length of stay (LOS; among those who survived to discharge; by log-linear regression) accounting for NIS sampling design.

Results: We identified 274,145 TRAN and 10,456,100 DA patients. On univariate analysis, TRAN patients were more likely to have a higher Charlson comorbidity index, Medicare insurance, and a lower median household income compared to DA patients ($p<0.0001$). Mortality was significantly higher in the TRAN vs DA groups (4.4% vs 1.6%; $p<0.0001$). Morbidity (presence of any complication) was also higher among TRAN patients (38.8% vs 26.1%; $p<0.0001$). Morbidity among TRAN patients was primarily due to urinary- (13.7%), gastrointestinal- (12.9%), and pulmonary-related (13.3%) complications. Median LOS was 4.3 days for TRAN vs 3.0 days for DA ($p<0.0001$) patients. Median cost was higher for TRAN patients ($8,935 vs $7,167; $p<0.0001$). Regression analyses determined that TRAN patients after adjustment had significantly higher mortality, morbidity, cost, and longer length of stay. (Figure)

Conclusions: Interhospital transfer of EGS patients is associated with increased morbidity, mortality, length of stay, and cost. As the EGS population grows and ages while the EGS workforce declines, identifying risk factors associated with worse outcomes among transferred EGS patients can inform the design of specific performance improvement initiatives.

Figure 1:


Effect of Transfers Status on Outcomes for Emergency General Surgery Patients Adjusted for Demographic, Clinical, and Hospital-Level Characteristics
Mortality
Morbidity
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
Adjusted Odds Ratio for TRAN (95% CI)
Log (Length of Stay)
Log (Cost)
-0.1
0.0
0.1
0.2
0.3
Adjusted Coefficient for TRAN (standard error)

H6

Early Repair of Uncomplicated Pediatric Umbilical Hernias: Complications of Potentially Unnecessary Surgery

Cartmill R.S., Yang D.-Y., Fernandes-Taylor S., Kohler J.E.

Abstract Submitter	Kohler, JE
Email Address	kohler@surgery.wisc.edu
Classification	Faculty
Principal Investigator	Kohler, JE
Science Type	Health services
Keywords	Umbilical herniorrhaphy, pediatric surgery, patient age

Introduction: Umbilical hernia repairs are one the of the most common pediatric general surgery operations. It is estimated that 15-23% of newborns have a diagnosis of umbilical hernia, but up to 90% of these hernias close spontaneous by age 4. Common practice among many children's hospitals is to wait to repair uncomplicated hernias until age 4 or older. Complications of pediatric umbilical hernias are extremely rare, and risks of anesthesia and surgery are higher for young children. We characterize the age at which umbilical hernia repairs are performed in American children, and the total cost of repair by age.

Methods: We used the Truven Health Analytics Marketscan ® Research Database, a national database of employer-based insurance claims, from July 2012 to September 2015. Patients were included if they were under 18 years old at the time of repair of an uncomplicated umbilical hernia (ICD-9 procedure code 53.41, 53.42, 53.43 or 53.49, or CPT procedure code 49580 or 49585). Patients were excluded if they had any diagnosis code associated with an incarcerated or strangulated hernia (ICD-9 diagnosis codes 551.1 or 552.1 or CPT procedure codes 49582 or 49587). Patients were also excluded if they had another surgical procedure on the day of their hernia repair, as some umbilical hernia repairs may be performed incidental to other operations, or if their umbilical hernia repair was coded as having occurred during their newborn admission. We performed descriptive analyses of patient age and geographic regional variation. We further compared post-operative costs and outcomes up to 30 days post-operatively.

Results: We identified 7,882 children who underwent an umbilical hernia repair between July 2012 and September 2015. A total of 363 (4.6%) were excluded for a diagnosis or procedure code associated with acute complication or incarceration. Another 27.4% (2,158 cases) were excluded for having more than one surgical procedure on the day of the umbilical hernia repair, and 1% (73 cases) were excluded for having an umbilical hernia repair coded during their newborn admission, which we believe represents miscoding of repair of other abdominal wall defects, such as gastroschisis or omphalocele. A total of 5,288 children undergoing single-procedure, uncomplicated umbilical hernia repair were included in the analysis.

The age of repair for umbilical hernias varied widely. Nationally, 9.5% of umbilical hernias were performed in children under 2 years old, 17.7% were performed in children aged 2-3, 33.9% were performed in children age 4-5, and 38.9% were performed in children age 6 or older. Repairs performed under the age of 2 varied significantly by census region (see Figure 1), from a high of 14% in the west to a low of 6% in the Northeast ($p<0.001$).

Estimated median cost of single uncomplicated umbilical hernia repair is $5825. The cost is likely higher for children under age 2 because they are more likely to have inpatient surgery and to have postsurgical complications. The total estimated cost of umbilical hernia repairs in children under age 2 is over $2.95 million.

Conclusions: Children often undergo uncomplicated umbilical hernia repairs at ages when spontaneous closure remains possible. Though the natural history of uncomplicated umbilical hernias remains poorly described, they are thought to have a high likelihood of closing spontaneously until at least age 4. Although umbilical hernia repair is a technically straightforward operation with a low complication rate, the long-term risks of anesthesia in young children remain uncertain, and recent guidance from the Food and Drug Administration and pediatric anesthesia literature suggest that general anesthesia should be avoided when possible in children under 3.

Our data demonstrate that the percentage of children having umbilical hernia repair very young (under age 2) varies substantially across regions of the US. This supports the idea that delaying repair to age 4 could become a standard practice. Doing so would prevent unnecessary surgery and save over $5800 in medical costs per repair.

H4

Variation in Opioid Prescribing After Pediatric Umbilical Hernia Repair

Cartmill R.S., Yang D.-Y., Fernandes-Taylor S., Kohler J.E.

Abstract Submitter	Cartmill, RS
Email Address	cartmill@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Kohler, JE
Science Type	Health Services
Keywords	Umbilical herniorrhaphy, pediatric surgery, opioid analgesia

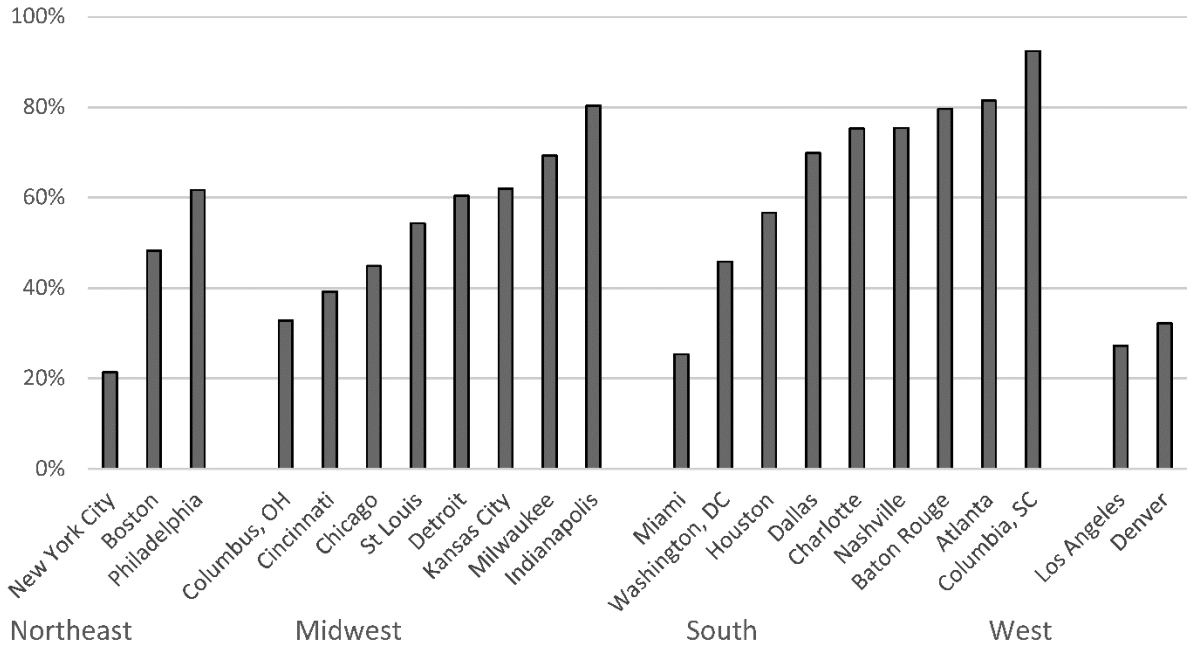
Introduction: Pediatric umbilical hernia repair is a common procedure that requires minimal tissue disruption. We examined variation in opioid prescription fills following repair of uncomplicated umbilical hernias to characterize the types and doses of opioid medication used, as well as persistent post-surgical use.

Methods: Using the Truven Health Analytics MarketScan© Research Database for June 2012 - September 2015, we identified pediatric patients undergoing umbilical hernia repair. We excluded patients with obstruction, gangrene, a prior repair or a concurrent surgical procedure, and those without available pharmacy claim data. Analyses describe filled outpatient prescriptions by age, geographic region, drug type, quantity, and second prescriptions/refills.

Results: Of 4,407 procedures performed, 2,292 patients (52%) filled a prescription for postoperative opioids. Opioid prescribing varied significantly by age (0-1 years: 21.6%, 2-3 years: 51.5%, 4-5 years: 54.3%, 6 years or older: 57.9% ($p < .0001$)). In the Northeast US, 42% of patients filled narcotic prescriptions, compared with 59% of patients in the South ($p < .0001$). The rate of prescribing also varied substantially across metropolitan areas in each region. Hydrocodone/acetaminophen was most commonly prescribed (51%), followed by codeine/acetaminophen (30%). Durations were ≤ 3 days (50%), 4-10 days (46%), and >10 days (4%). 6% of patients filled a second opioid prescription within 30 days.

Conclusions: Although many patients do not require opioids for umbilical hernia repair, most pediatric patients fill opioid prescriptions, including for prolonged courses and refills. Guidelines for appropriate opioid prescribing after common, simple procedures such as umbilical hernia repair could improve the quality of care for children and impact the US epidemic of opioid abuse.

Figure 1: Rate of opioid prescribing after uncomplicated umbilical hernia repair, by metropolitan area



H3

Surgeon Engagement in Surgical Health Policy Advocacy

Beilke S.B., Alcantara J., Liepert A.E.

Abstract Submitter	Sarah Beilke
Email Address	sbeilke@wisc.edu
Classification	Medical student
Principal Investigator	Dr. Amy E. Liepert
Science Type	Health services
Keywords	Helath policy, advocacy, survey

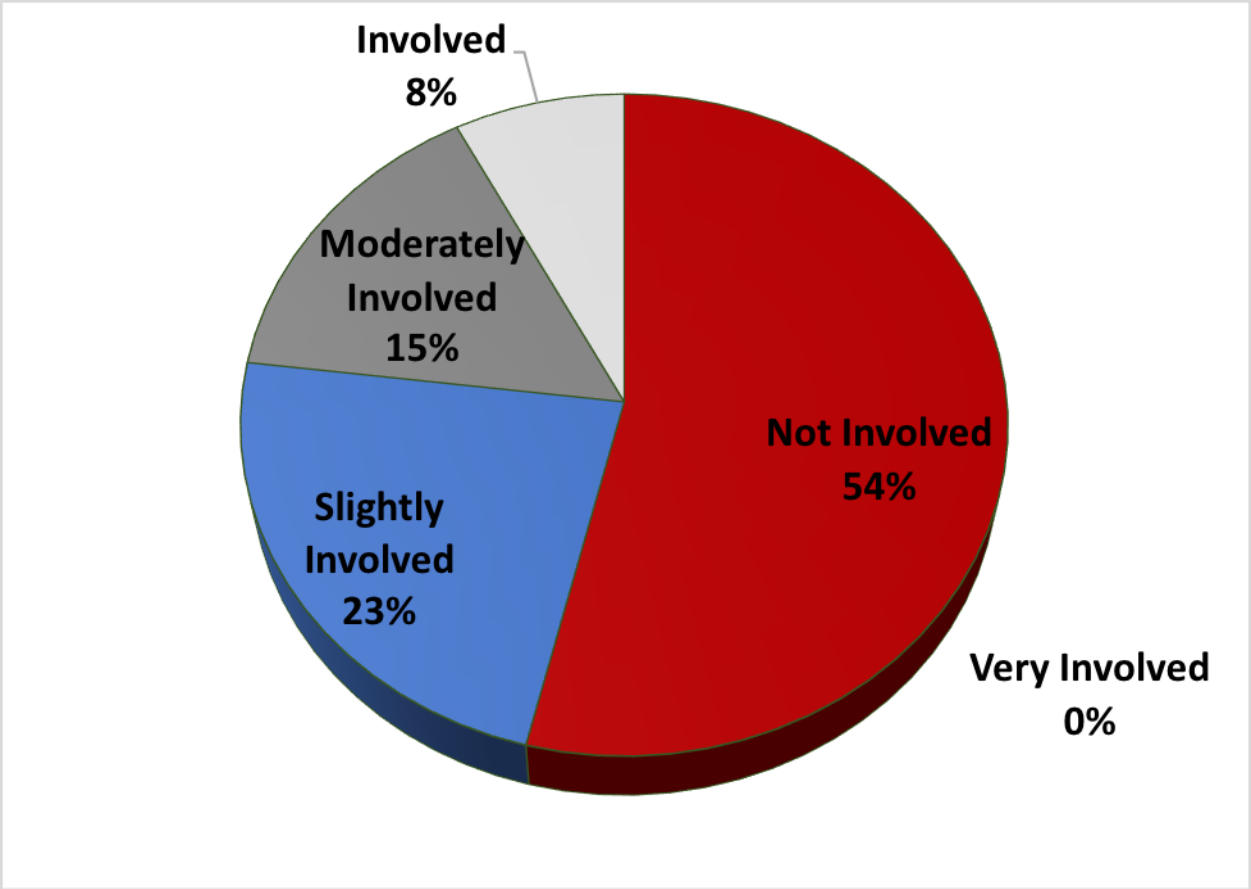
Introduction: Health policy decisions influence aspects of patient care including access to health care, physician reimbursement, and scope of practice. Physicians are uniquely equipped to participate in health policy advocacy due to their knowledge of medicine and health systems, their professional title which grants easier access to policymakers, and the trust the public places in physicians. Little is known about physicians' level of engagement in Health Policy Advocacy. We conducted a pilot survey of surgeons to assess current levels of engagement in Surgical Health Policy Advocacy (SHPA) and to identify barriers and benefits of involvement. We hypothesized surgeons have low involvement in SHPA due to time restrictions and perceived inability to participate.

Methods: This is a pilot study based upon a previously published and validated survey. It was modified to assess surgeon engagement in SHPA. The survey consisted of 21 questions administered to 20 surgeons participating in a Wisconsin Surgical Society board meeting. Items included self-reported involvement in public policy and SHPA, barriers to engagement, benefits of SHPA involvement, and demographics. Question types included multiple response items and Likert Scales. Statistical analysis was completed using SAS 9.4.

Results: Thirteen of the twenty surveys (65%) administered were completed. Demographics were: 100% Caucasian, 91% Male, Average Age of 48 years, 91% were General Surgeons, 54% worked in an urban setting, and 54% worked in an academic setting. SHPA items responses were: 54% reported no involvement in SHPA and another 23% reported being only slightly involved. The most common barriers were lack of time (69%) and other priorities (54%). 84% of respondents perceived some benefit in SHPA. The most frequent perceived benefits were improving the surgical health of the public (69%) and improving a situation or issue (62%). 73% of respondents received SHPA training and the most common sources of training were professional colleagues (46%) and sessions at a conference (46%).

Conclusions: This pilot study showed low participation rates in SHPA by surgeons. The identification of barriers presents possibilities to make participation in SHPA feasible. Additional study of a larger and more diverse population is needed.

Self-Reported Involvement in Surgical Health Policy Advocacy:



H11

Treatment Recommendations for Low-Risk Thyroid Cancer: Are Patients' or Providers' Preferences More Important?

Saucke M.C., Roman B.R., Brito J.P., Zaborek N., McDow A.D., Jensen C.B., Jennings J.L., Pitt S.C.

Abstract Submitter	Saucke M.C.
Email Address	saucke@surgery.wisc.edu
Classification	Academic staff
Principal Investigator	Pitt S.C.
Science Type	Health services research
Keywords	Overtreatment, thyroid cancer, survey, preferences

Introduction: Significant concern exists about overtreatment of patients with small, low-risk thyroid cancer, yet little is known about why surgeons and endocrinologists recommend treatment that has no survival benefit and may lead to unnecessary harm. We sought to identify factors associated with providers recommending overtreatment for this indolent cancer.

Methods: We conducted a web-survey of members of 3 national organizations: the American Thyroid Association, American Association of Endocrine Surgeons, and American Head & Neck Society. We developed 11 case scenarios to assess providers' recommendations for 1 of 4 treatment options ranging from active surveillance to total thyroidectomy. Scenarios examined clinical factors and patient preference for each treatment option. We also assessed providers' preference for their own treatment if they had a small, low-risk thyroid cancer, their beliefs about what influences patients' treatment preferences, and risk tolerance. Respondents were randomized 1:1 to receive information about active surveillance prior to taking the survey. We conducted multivariable logistic regression to identify factors associated with recommending total thyroidectomy.

Results: 345 physicians completed the survey: 99 endocrinologists and 246 surgeons. Significant overlap in membership precludes calculation of response rate. Respondents were 68.4% male, 69.1% white, and in practice on average 14.3±12.4 years. The majority (63.7%) practiced at academic, tertiary centers. The table summarizes the regression model. The factor most associated with recommending overtreatment was the providers' preference to receive total thyroidectomy if they were diagnosed with a small, low-risk thyroid cancer [OR 12.3]. Patient preference for total thyroidectomy also had a significant, albeit smaller impact on the recommendation [OR 2.2]. Surgeons were more likely than endocrinologists to recommend overtreatment [OR 2.4]. Female respondents and those who believe patients prefer to avoid a second surgery (if only half of the thyroid is removed initially) also had a propensity to over treat. Providing information about active surveillance decreased the odds that respondents recommended total thyroidectomy, though this was not significant (p=0.06).

Conclusions: Multiple factors are associated with surgeons and endocrinologists recommending overtreatment for patients with small, low-risk thyroid cancer. While patients' preferences influence the decisional process, providers' own preference for treatment appears to have the greatest impact on their recommendations. In order to avoid potentially unnecessary harm to these patients, providers' biases need to be addressed.

Table of Factors Associated with Surgeons and Endocrinologists Recommending Overtreatment for Patients with Small, Low-risk Thyroid Cancer

Respondent Characteristics	***Odds Ratio***	***95% C.I.***	***p-value***
Provider preference (respondent would choose TT for self)*	12.28	4.12 - 36.59	<0.0001
Patient preference (respondent recommends TT if patient prefers it)*	2.17	1.27 - 3.73	0.005
Surgeon	2.39	1.32 - 4.33	0.004
Female (sex of respondent)	1.90	1.11 - 3.25	0.02
Respondent believes patient preferences are strongly influenced by desire to avoid completion thyroidectomy**	1.99	1.14 - 3.44	0.02
Respondent received information about active surveillance	0.62	0.38 - 1.01	0.06
Academic-tertiary practice setting	0.61	0.36 - 1.03	0.07
Respondent agrees that they rarely take risks in their own life**	1.42	0.80 - 2.52	0.24

*TT=total thyroidectomy
**Agrees quite a bit or a great deal

H2

Safety in Allowing Residents to Independently Perform Appendectomy, a Retrospective Review

Barrett J R, Drezdzon M, Monawer A, O'Rourke A P, Scarborough J E

Abstract Submitter	James Barrett
Email Address	Jbarrett2@uwhealth.org
Classification	Resident
Principal Investigator	John Scarborough
Science Type	Health Services/clinical
Keywords	Resident autonomy, intra-abdominal infection, antibiotic duration, appendicitis

Introduction: In an era of competency-based education and concern about graduating resident readiness for practice, early resident autonomy is becoming increasingly important. In this study we aimed to understand the effect of two residents performing appendectomy on outcomes.

Methods: A single-center retrospective review of 500 consecutive patients from May 2016 to December 2017 who underwent appendectomy with the University of Wisconsin Hospital system. We examined how two residents (compared to one resident with an attending) attempting a case affect op time, SSI rate, or conversion to open rate while controlling for age, perforation, BMI, prior lower abdominal surgery, and ASA class.

Results: A total of 303 cases were performed with a single resident, 190 with two residents, and 7 cases were excluded that were performed with no resident present. We performed chi square analyses and logistic regression on the following outcomes: postoperative SSI (superficial or organ space) 1.40 (0.64, 3.03) p=0.40, long operation 1.44 (0.91, 2.27) p = 0.12, and conversion to open 1.72 (0.52, 5.69) p = 0.38. Our results demonstrated there was no statistically significant difference in outcomes.

Conclusion: As we push to promote early resident autonomy, allowing senior residents to take junior residents through an appendectomy is not associated with increased risk to patients. These results support the implementation of the EPA “Evaluate a patient with right lower quadrant pain and manage appendicitis” and programs should encourage faculty to allow residents to manage appendicitis as independently as possible.

H12

Vascular Surgery Outcomes of Trauma Patients at TASH, Addis Ababa, Ethiopia

Semma Y.Z., Getachew F., Tefera G., Abebe N.S.

Abstract Submitter	Yoseph Semma
Email Address	ysemma@wisc.edu
Classification	Observational
Principal Investigator	Dr. Girma Tefera and Dr. Nebyou Seyoum
Science Type	Health Sciences
Keywords	Surgery Outcomes, Vascular surgery, Ethiopia

Introduction: The field of vascular surgery is a relatively new surgical practice in Ethiopia. Currently, there is only one trained vascular surgeon practicing at Tikur Anbesa Specialized Hospital (TASH) in Addis Ababa, the major referral hospital in the country. The vascular surgery program at TASH was fully implemented two years ago. No previous study has been done to look at the impact of this new surgical field and the outcomes of trauma patients that have undergone vascular surgery procedures at TASH.

Methods: A list of all vascular procedures performed in the TASH emergency department over the past two years were identified. Of the identified cases, the surgical outcomes were analyzed for trauma patients whose paper charts were available.

Results: Of the 89 total vascular procedures that were identified to have been performed over the two year period, patient paper charts were located for 40. Of these, 32 of the procedures were cases related to trauma – penetrating (81.21%), blunt (6.25%), and crush injuries (9.37%). The primarily affected vessels were the popliteal and femoral artery, accounting for 43% of the cases. Of the 26 patients whose duration of symptom was recorded for, 73% presented at TASH 12 hours past the onset of symptoms or injury and were referred to the ED by general practitioners and surgeons at other hospitals. The most common presenting symptoms were bleeding (87%), absent or weak pulses (50%), and loss of sensation of the affected limb (25%). 50% of these patients were operated upon within 12 hours of admission and 76% were within two days of admission. Of the procedures performed, direct repair and ligation were the top two procedures accounting for 36% and 27% of the procedures respectively. The most common postoperative complications were infection (31.25%), amputation (9%), surgical site bleeding (9%), and compartment syndrome (6%). At discharge, 71% of the patients were near full functional capacity, 9.7% had mild loss of function, and 19.3% had severe loss of function. There was one death (3.2%) during inpatient stay due to severe sepsis over 30 days after surgery.

Conclusions: Although the study was limited in terms of the number of cases charts were found for, it does show that vascular surgery outcomes of trauma patients at TASH are relatively good, reflected by the near full functional capacity of 71% of the patients at discharge. Several factors affect the outcomes of these procedures including delay between onset of symptoms and surgery. These results highlight the effectiveness of the vascular surgery training at TASH and call for further exploration of its impact and outcomes in the elective surgery setting as well as the emergency department over all.

H15

Promoting Systemic Improvement Through a Human Factors Analysis of Patient Safety Reports

Vande Walle K., Osadchuk T., Alagoz E., Greenberg C., Wiegmann D.

Abstract Submitter	Kara Vande Walle
Email Address	kvandewalle@uwhealth.org
Classification	Resident
Principal Investigator	Doug Wiegmann
Science Type	Health Services
Keywords	patient safety, human factors, content analysis

Introduction: Patient safety reporting systems have become a widespread intervention with the goal of decreasing medical error by learning from past patient safety events. However, patient safety reporting systems are often ineffective at driving the systemic change needed to improve patient care. The purpose of this study was to understand if a human factors analysis could be applied to patient safety reports and identify areas for systemic improvement.

Methods: Patient safety reports in General Surgery at a single institution from July 2016 to June 2017 were included. The patient safety reports included outpatient, inpatient, and intraoperative events. A report was considered patient safety related if there was potential harm to the patient. Directed content analysis of the patient safety report narratives using the Human Factors Analysis and Classification System – Healthcare (HFACS-Healthcare) was performed to classify the causal factors contributing to the patient safety events. Compensatory factors were identified using an adapted form of HFACS-Healthcare. The first 60 patient safety reports were consensus coded in a group consisting of 3 researchers with clinical or human factors experience. Subsequent reports were coded independently by 2 coders with conflicts resolved as a group. Frequencies of each HFACS-Healthcare code were calculated.

Results: Coding has been completed for 173 patient safety reports. 20 (11.6%) patient safety reports were excluded for not meeting the definition of a patient safety related event. 125 (81.7%) of patient safety reports were able to be mapped to at least one causal factor in HFACS-Healthcare with a total of 160 causal factors identified. A compensatory factor was identified for 117 (76.5%) of patient safety reports with a total of 130 compensatory factors identified. The majority of causal factors were in the categories of preconditions for unsafe acts (45.6%) and unsafe acts (44.4%) with a minority in the categories of organizational influences (5.0%) and supervisory factors (5.0%). The most common causal factors were skill-based errors (23.8%), tools/technology (23.1%), decision errors (13.1%), and communication (12.5%). The majority of compensatory factors were team factors (67%) or situational factors (21.5%). Few compensatory factors were individual acts (7.7%), organizational influences (3.8%), or supervisory factors (0%).

Conclusions: The majority of patient safety reports described patient safety events and both the causal and compensatory factors were able to be classified using HFACS-Healthcare. While causal factors were most often skill-based errors and tools/technology, the compensatory factor was most often team factors. A human factors approach can be used to classify patient safety reports and can identify high frequency causal and compensatory factors which can serve as targets for system improvements to prevent future patient safety events.

HFACS Category	**Causal Factor Total *(%)***
Organizational Influences	
Organizational Culture	0 *(0%)*
Operational Process	4 *(2.5%)*
Resource Management	4 *(2.5%)*
Supervisory Factors	
Inadequate Supervision	4 *(2.5%)*
Planned Inappropriate Operations	0 *(0%)*
Failure to Correct Known Problem	4 *(2.5%)*
Supervisory Violation	0 *(0%)*
Preconditions for Unsafe Acts	
Situational Factors	
Task	2 *(1.3%)*
Tools/Technology	37 *(23.1%)*
Physical Environment	7 *(4.4%)*
Individual Factors	
Mental State	2 *(1.3%)*
Fitness for Duty	0 *(0%)*
Physiological State	0 *(0%)*
Team Factors	
Leadership	0 *(0%)*
Communication	20 *(12.5%)*
Coordination	5 *(3.1%)*
Unsafe Acts	
Errors	5 *(3.1%)*
Decision Errors	21 *(13.1%)*
Skill-based Errors	38 *(23.8%)*
Perceptual Errors	3 *(1.9%)*
V*iolations*	
Routine Violations	3 *(1.9%)*
Exceptional Violations	1 *(0.6%)*
Total	160

H9

Evaluation of Long-Term Satisfaction with Mastectomy vs Breast Conserving Surgery in Patients Treated for Ductal Carcinoma In Situ: A Population-Based Longitudinal Cohort Study

Livingston-Rosanoff, D; Hampton, J; Newcomb, P; Trentham-Dietz, A; Wilke, L.G.

Abstract Submitter	Devon Livinston-Rosanoff
Email Address	Dlivingston-rosanoff@uwhealth.org
Classification	Resident
Principal Investigator	Lee Wilke
Science Type	Health Services
Keywords	DCIS, patient satisfaction, breast reconstruction, mastectomy, breast conserving surgery

Introduction: Breast conserving surgery (BCS) and mastectomy have similar long-term survival outcomes for DCIS treatment. Thus, surgical decision making is often able to take patient preference into account. There are limited data evaluating patient satisfaction with their decision to undergo breast conserving surgery (BCS) vs mastectomy for treatment of DCIS.

Methods: Women treated for DCIS were enrolled in a population-based in situ cohort from 1997-2006. Participants were surveyed about their satisfaction with their decision to undergo BCS or mastectomy and reconstruction following mastectomy. Women who experienced recurrence between study enrollment and completion of satisfaction questions were excluded from analysis. Multivariable logistic regression modelling was used to calculate odds ratios (OR) and 95% confidence intervals (CI) examining the relationship between type of surgery or reconstruction and patient satisfaction. Education, household income, age at diagnosis and time since diagnosis were also included in the models.

Results: 1537 women were surveyed on average 2.9 years following their DCIS diagnosis, 1019 underwent BCS, 250 mastectomy without reconstruction and 267 mastectomy with reconstruction. Overall greater than 90% of all women surveyed reported they were somewhat or very satisfied with their treatment decision (BCS 96%, mast no recon 93%, mast w/recon 91%). Women who underwent mastectomy followed by reconstruction were more likely to report lower levels of satisfaction than women who underwent BCS or mastectomy alone. Greater than 80% of all women who underwent mastectomies reported satisfaction with their reconstruction decision (No recon 89%, Tissue 89%, Implant + tissue 87%, Implant 82%). Women who had implants as part of their reconstruction were less likely to be very satisfied than women who had tissue-based reconstruction or did not undergo reconstruction.

Conclusions: Regardless of their surgery, women treated for DCIS are overall quite satisfied with their treatment decision, although mastectomy patients who underwent reconstruction report lower satisfaction. Following mastectomy most women are satisfied with their reconstruction decision, however women with implants reported lower satisfaction.

Table 1: Multivariable analysis examining relationship between patient satisfaction and surgical or reconstruction decision*

		Somewhat Satisfied vs Very Satisfied	Neutral or Dissatisfied vs Very satisfied	
		OR (95% CI)	OR (95% CI)	p-value
Satisfaction with surgery type, n=1536				
Surgery	BCS	1 (ref)	1 (ref)	0.0003
	Mast no recon	1.57 (0.97, 2.55)	1.97 (1.04, 3.74)	
	Mast w/recon	1.97 (1.26, 3.07)	2.56 (1.41, 4.62)	
Age at Diagnosis	<50	1 (ref)	1 (ref)	0.19
	50-60	0.77 (0.50, 1.18)	0.87 (0.51, 1.50)	
	60-70	0.89 (0.55, 1.43)	0.41 (0.20, 0.85)	
	>70	1.24 (0.65, 2.36)	0.88 (0.38, 2.06)	
Diagnosis to survey	< 2y	1.40 (0.96, 2.03)	1.08 (0.67, 1.75)	0.2
	≥2y	1 (ref)	1 (ref)	
Satisfaction with reconstruction, n=517				
Recon Type	No recon	1 (ref)	1 (ref)	0.004
	Implant	3.86 (1.87, 7.96)	2.5 (1.08, 5.80)	
	Tissue	1.41 (0.72, 2.75)	1.05 (0.49, 2.22)	
	Implant + Tissue	2.87 (1.28, 6.43)	1.54 (0.54, 4.44)	
Age at Diagnosis	<50	1 (ref)	1 (ref)	0.39
	50-60	1.04 (0.59, 1.84)	1.22 (0.61, 2.44)	
	60-70	0.51 (0.23, 1.12)	0.72 (0.29, 1.77)	
	>70	0.59 (0.19, 1.81)	0.32 (0.07, 1.58)	
Diagnosis to survey	< 2y	1.38 (0.83, 2.29)	0.7 (0.39, 1.26)	0.18
	≥2y	1 (ref)	1 (ref)	

*Other variables included in the model: household income and education

H8

Time to Initiation of Neoadjuvant Chemotherapy for Breast Cancer Treatment Does Not Influence Patient Survival: A National Cancer Database Study

Livingston-Rosanoff, D; Hanlon, B; Marka, N; Vande Walle, K; Stankowski-Drengler, T; Schumacher,J; Greenberg, C; Neuman, H; Wilke, L.G.

Abstract Submitter	Devon Livinston-Rosanoff
Email Address	Dlivingston-rosanoff@uwhealth.org
Classification	Resident
Principal Investigator	Lee Wilke
Science Type	Health Services
Keywords	Breast cancer, neoadjuvant chemotherapy, NCDB

Introduction: Delays in the initiation of adjuvant chemotherapy or radiation therapy are associated with worse outcomes in patients undergoing treatment for breast cancer. However, the impact of the time to initiation of neoadjuvant chemotherapy (NAC) on patient outcomes has not been previously studied. This question has gained clinical importance as more women undergo NAC. The purpose of this study was to determine if delays in NAC initiation impacts patient survival and/or complete pathologic response (pCR).

Methods: We queried the National Cancer Database for women >18 years old who underwent NAC for stage 1-3 invasive breast cancer from 2010-2011 and had known ER, PR and Her2 receptor status. Patients with ER/PR+ Her2- disease or who started NAC more than 180 days following their diagnosis were excluded from the study. Patients were stratified by Her2 status for analysis. We dichotomized time to NAC based on a covariate-adjusted optimal cutpoint method, searching over three, four and five weeks. Cox proportional hazard modeling was used to evaluate the relationship between time to NAC, sociodemographic, diagnosis, and treatment factors with patient survival. Mutivariable logistic regression models using the same variables were used to evaluate the impact on pCR.

Results: The median age of the 12,080 women included in this study was 52 (range 21-90) with 51% presenting with stage 2 disease. 6,448 women had triple negative and 5,632 had Her2+ cancers. The median time to starting NAC was 4 weeks (range 0-26). Based on the optimal cutpoint method, the cutoff for time to NAC was set to four weeks for triple negative and five weeks for Her2+ cancers. The overall pCR rate was 19.4% (18.8% for triple negative and 20.0% for Her2+). Women with triple negative cancer who started NAC more than four weeks after diagnosis were less likely to experience a pCR (OR 0.81, CI 0.68-0.94) while no effect was observed for Her2+ patients at the five week cutoff (OR 0.94, CI 0.80-1.11). Time to NAC initiation was not associated with a difference in survival in triple negative or Her2+ cancers.

Conclusions: Delays in starting NAC are associated with decreased pCR rates for women with triple negative cancers but not those with Her-2/neu positive disease. However, there was no effect of time to NAC on patient survival for either biologic subtype. This study demonstrates that the majority of women in the modern era start NAC in a timely fashion, and that delays in starting NAC do not impact long-term patient outcomes.

Table 1: Cox proportional hazard model of the association between time to NAC initiation and patient survival[*].

		Her2+ (cutoff 5 wk)		Triple Negative (cutoff 4 wk)	
		HR (95% CI)	p-value	HR (95% CI)	p-value
T to NAC[**]		0.91 (0.74, 1.12)	0.368	1.10 (0.97, 1.24)	0.153
Clinical T Stage	1	Ref		Ref	
	2	1.00 (0.72, 1.40)	0.983	1.09 (0.88, 1.36)	0.419
	3	1.36 (0.94, 1.96)	0.098	1.60 (1.27, 2.02)	<0.001
	4	1.70 (1.20, 2.41)	0.003	2.4 (1.90, 3.03)	<0.001
Clinical N Stage	0	Ref		Ref	
	1	1.38 (1.09, 1.75)	0.008	1.89 (1.63, 2.20)	<0.001
	2	1.83 (1.33, 2.53)	<0.001	2.22 (1.82, 2.72)	<0.001
	3	1.83 (1.23, 2.71)	0.003	3.11 (2.51, 3.87)	<0.001
ER/PR-		Ref			
ER/PR+		0.59 (0.48, 0.71)	<0.001		

[*] Other variables measured at the time of diagnosis and included in the model were: age, race, ethnicity, comorbidities, education, income, insurance type, facility type, geographic location and tumor grade

H1

The Impact of Diagnosis on Patient Satisfaction in a Large Sample of General Surgery Outpatients

Bandealy N., Rendell V.R., LeRette K.A., Leaf M.A., Winslow E.R.

Abstract Submitter	Bandealy N.
Email Address	nbandealy@wisc.edu
Classification	Medical Student
Principal Investigator	Winslow E.R.
Science Type	Health Services
Keywords	Surgery, satisfaction, diagnosis

Introduction: Growing emphasis on Value Based Purchasing and patient-reported outcomes has increased interest in drivers of patient satisfaction. While demographic and other patient-related factors are known to impact satisfaction, the role of disease-related factors, specifically primary diagnosis, is not well studied. We aimed to determine if primary diagnosis affects satisfaction scores in the surgical outpatient setting.

Methods: Primary diagnosis was examined in relation to patient experience scores as reported in Medical Practice Survey responses of general surgery patients seen in an outpatient setting from July 2016-2018. Diagnoses with similar presentations, treatments, and prognoses were merged into groups prior to viewing survey results to ensure unbiased sorting. Groups with fewer than 50 surveys were excluded. Chi squared univariate analyses compared the percentage of top box responses to three key survey questions regarding provider and overall clinic evaluation across patient, clinic, provider, and survey-related variables. Multivariate logistic regression was performed to determine factors associated with top box responses.

Results: Survey results were extracted for 1,262 patients across 6 clinical groups: breast cancer (n=411), benign gallbladder disease (n=83), hernias (n=285), thyroid/parathyroid hormonal disorders (n=161), and hormonally inactive thyroid masses and cancer (n=225). On univariate analyses, female patients had higher percent top box scores for question 1 (Time spent with provider) and question 3 (Likelihood of recommending the clinic) ($p<0.05$). Female providers had higher percent top box scores for question 1 and question 2 (Likelihood of recommending provider) ($p<0.05$). Responses to questions 2 and 3 differed by clinic location ($p=0.01$ and $p=0.04$, respectively) and by diagnosis group ($p=0.001$ and $p=0.02$, respectively). On multivariate analyses, only diagnosis group remained significant for all three questions (**Table 1**). Patients in the breast cancer group were more likely to recommend the clinic than patients in all but one diagnosis group. They were also more likely to recommend their provider than the thyroid/parathyroid hormonal disorders group. Clinic location was significant for the amount of time provider spent and likelihood of recommending clinic, but was not significant for the likelihood of recommending the provider.

Conclusions: For general surgery outpatients, breast cancer patients have higher satisfaction scores compared with patients with several other examined diagnoses on multivariate analyses. This suggests diagnosis alone may influence outpatient patient satisfaction survey results. Institutions should consider the role diagnosis plays when evaluating provider performance.

Table 1: Multivariate analysis of percent top box score responses to patient satisfaction survey questions after outpatient general surgery visits.

	Question 1: Amount of time the care provider spent with you.		**Question 2:** Likelihood of your recommending this care provider to others.		**Question 3:** Likelihood of your recommending our clinic to others.	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Diagnosis Group						
Breast Cancer	Ref		Ref		Ref	
Thyroid/Parathyroid Hormonal Disorders	0.39 (0.14-1.11)	0.08	0.26 (0.09-0.79)	**0.02**	0.20 (0.05-0.83)	**0.03**
GI and Pancreas Cancer	0.27 (0.08-0.91)	**0.04**	0.33 (0.09-1.26)	0.11	0.16 (0.03-0.75)	**0.02**
Benign Gallbladder Disease	0.31 (0.11-0.90)	**0.03**	0.49 (0.15-1.61)	0.24	0.29 (0.07-1.27)	0.10
Hernias	0.39 (0.15-1.03)	0.06	0.39 (0.14-1.13)	0.08	0.20 (0.05-0.79)	**0.02**
Hormonally Inactive Thyroid Masses & Cancer	0.43 (0.16-1.19)	0.10	0.50 (0.16-1.49)	0.21	0.21 (0.05-0.85)	**0.03**
Clinic Location						
Clinic Location 1	Ref		Ref		Ref	
Clinic Location 2	0.20 (0.05-0.83)	**0.03**	0.49 (0.09-2.56)	0.40	0.16 (0.03-0.98)	**0.05**

Not shown above due to non-significance: Patient Sex, Patient Age, Patient County of Residence, Provider Sex, Survey Mode, Time to Return Survey, and Clinic Locations 3-6; GI: Gastrointestinal

H5

Understanding Communication Gaps in the Hospital Consultation Process

Fischer C.L., Rendell V., Winslow E.

Abstract Submitter	Cristina Fischer
Email Address	Clfischer3@wisc.edu
Classification	Medical Student
Principal Investigator	Emily Winslow, MD, FACS
Science Type	Health Services
Keywords	Consultation, Communication, Quality Improvement

Introduction: Consultations are common, with nearly 50% of inpatients receiving at least one medical consult over the course of their hospitalization. However, greater numbers of consultative services seeing a patient was found to be the most significant factor contributing to patient dissatisfaction over the course of a prolonged hospital stay. Effective communication is essential for coordination of care, a process that is integral to inpatient consultations. Weakness within this process allow communication gaps to develop, which have been tied to medical errors, treatment delays, and patient dissatisfaction. The hospital consultation process is particularly vulnerable to communication gaps, but these gaps have not been well studied. We aimed to evaluate which specific communication issues lend weaknesses to the consult process from the perspective of providers and patients.

Methods: As part of an existing quality improvement project at our institution, we evaluated inpatient communication event reports from clinicians and staff from February 2017 to January 2018. Semi-structured interviews of inpatients who had received either a medical oncology (MO) or general surgery (GS) consult were conducted, and detailed notes and data from the interviews were transcribed. We performed qualitative content analysis of the event reports and interviews to uncover themes illustrating consult communication challenges. Themes were numerated, and percentages determined out of total event reports or total interviews as appropriate.

Results: Of the 782 event reports reviewed, 59 (9%) were directly related to physician-physician communication during consultations and were categorized into six main groups: 1) inadequate verbal communication between providers (73%); 2) inadequate verbal communication between the provider(s) and the patient and/or their family (10%); 3) inadequate chart documentation from providers (10%); 4) delays in communication (3%); 5) inappropriate communication (2%); and 6) not accepting a consult (2%). Inadequate verbal communication was further categorized by setting: ED (23%), inpatient (47%), and peri-procedural (30%).

Interviews of 63 inpatients, 42 with GS consults and 21 with MO consults were conducted between June and August 2018. Five major patient-perceived issues with provider communication were identified with sub-themes detailed in Table 1: 1) inadequate verbal communication between provider(s) and the patient/family; 2) poor communication between physicians; 3) communication with the patient before consensus on a plan has been reached; 4) use of excessive medical terminology; and 5) inadequate non-verbal communication. Only patients with GS consults reported use of excessive medical terminology.

Conclusions: Inadequate verbal communication between providers is frequently identified as problematic in the inpatient consult process by both clinicians and patients. The peri-procedural setting represents a sizeable portion of these verbal communication issues. In order to improve communication within the hospital consultation process, strategies that target the quality of provider-to-provider and provider-to-patient communication, particularly in the peri-procedural setting, are likely to be most productive.

Table 1

Theme	Sub-Themes	Example
Inadequate verbal communication between provider(s) and the patient/family (GS: 38%, MO: 45%)	• Need for a better explanation of the plan/changes to the plan • Need family present for discussions • Need to communicate clearly to patient which team has primary responsibility	• "There may be an assumption that one medical team is communicating with the patient, when they are not. It needs to be clear between the teams, who is communicating what with the patient." • "Nothing was making sense to me, I needed to get my kids involved" • "I am not really sure who is in charge, because there are so many teams involved"
Perceived poor communication between physicians (GS: 13%, MO 2%)		• "The consulting team is not talking with the primary team" • "Everyone comes in and ask the same questions… it makes it seem as if they are not communicating"
Communication with the patient before consensus on a plan has been reached (GS: 4%, MO 10%)		• "Everyone was giving their own opinion on things, and sometimes this opinion would differ, which was confusing"
Use of excessive medical terminology (GS: 2%, MO: 0%)		• "Things could have been confusing due to use of acronyms and medical [terminology], however I made sure to ask questions"
Inadequate non-verbal communication (GS: 3%, MO: 4%)		• "When I am not feeling well, it is hard for me to understand things, so a document would be helpful, so I could review it when I am feeling better"

GS: Patient with a General Surgery consult; MO: Patient with a Medical Oncology consult

GROUP FIVE

Translational

T1

Assessing the Immunogenicity of Pluripotent Stem Cell Therapies

Brown M.E., Zhang J., Perrin E., Zhou Y., Hermsen J., Kamp, T.J., Steill J., Swanson S., Stewart R., Thomson J.A., and Burlingham W.J.

Abstract Submitter	Dr. Matthew E. Brown
Email Address	brownm@surgery.wisc.edu
Classification	Postdoctoral Research Fellow
Principal Investigator	William J. Burlingham and James A. Thomson
Science Type	Translational
Keywords	Humanized Mouse, Pluripotent Stem Cells, Transplant Immunology

Introduction: Translation of pluripotent stem cell (PSC) therapies to the clinic will require consistent and effective prevention of immune-mediated graft destruction, ideally, in the absence of immunosuppressive drugs. The transplantation immunology field has a wealth of empirical knowledge and a variety of well-characterized assays useful for understanding and manipulating the mechanisms of rejection and tolerance of allogeneic tissues. The work presented here applies various *in vitro* assays to assess the T cell and B cell-mediated immune responses to PSC-derived endothelial cells and cardiomyocytes. Additionally, the NeoThy humanized mouse model is used to assess *in vivo* graft immune cell infiltration. Rigorous *in vitro* and *in vivo* investigation of immune responses to PSC therapies will enable more effective clinical trial designs and increase the likelihood of realizing the potential of these promising therapies.

Methods: *Donor-Specific Antibodies Assay* Blood serum samples were collected and thawed fresh on the day of assay. PBMCs were collected and cryopreserved until they were thawed on day of the assay. Dead cells were excluded with BD Horizon™ Fixable Viability Stain 700, then stained and gated for T cells i.e. CD3+ CD20- for DSA analysis. *Mixed lymphocyte Reaction (MLR)* Target and effector cells were co-cultured at a 1:1 ratio for 5d in 96 well plates. Viable singlet CD3+ cells were analyzed for CFSE dilution. *Humanized Mice* Humanized mice were generated in 6-10-week-old immune-compromised NSG-W host animals. Cryopreserved CD34-enriched HSCs were injected (i.v.) into anesthetized mice, coinciding with cryopreserved thymus fragment implantation surgery into the kidney capsule. Mice also received i.v. αhCD2 antibody (100 µg) at days 0 and 7 post-surgery.

Results: MLR assays demonstrated an allogeneic T cell and NK immune response to primary and iPSC-derived endothelial cells. DSA assays demonstrated that a DSA response generated by primary organ transplant is also reactive to iPSC-derived endothelial cells. NeoThy mice created in NSG-W hosts using autologous thymus and HSCs, or with thymus and allogeneic HSCs, and in multiple donors with varying degrees of human leukocyte antigen (HLA) matching all robustly engrafted with human $CD45^+$, $CD19^+$, and $CD3^+$ cells. *Ex vivo* engagement of T cell receptors with αhCD3, αhCD28, and rhIL2 stimulated T cell proliferation, indicated by blast-like clustering, dilution of CSFE dye in both $CD4^+$ and $CD8^+$ T cell populations, and production of Th1 cytokine interferon γ. NeoThy mice reconstituted with human B and T cells also produced immunoglobulin G (IgG) and IgM antibodies, indicating a functional T helper role of $CD4^+$ T cells as well as functional B cells. NeoThy mice engrafted with allogeneic iPSC-CMs showed macroscopic and histological retention of implanted cells (3/3) at the terminal time point and were infiltrated by human $CD4^+$ and $CD8^+$ T cells.

Conclusions: The NeoThy mouse is a robust model for investigating the human T cell-mediated immune response to pluripotent stem cell-derived cell therapies. The NeoThy has similar immune engraftment phenotype as conventional fetal tissue based models, and the immune cells display similar functional attributes. Additionally, there are advantages of using more mature and abundant neonatal tissues, especially with regard to rigor and reproducibility of the model. *In vivo* data from the NeoThy can be used in conjunction with *in vitro* MLR and DSA assays to give an in depth profile of the allogeneic immune response. These *in vitro* and *in vivo* assays can be used to inform the design of more effective clinical trials for iPSC-based cell therapies.

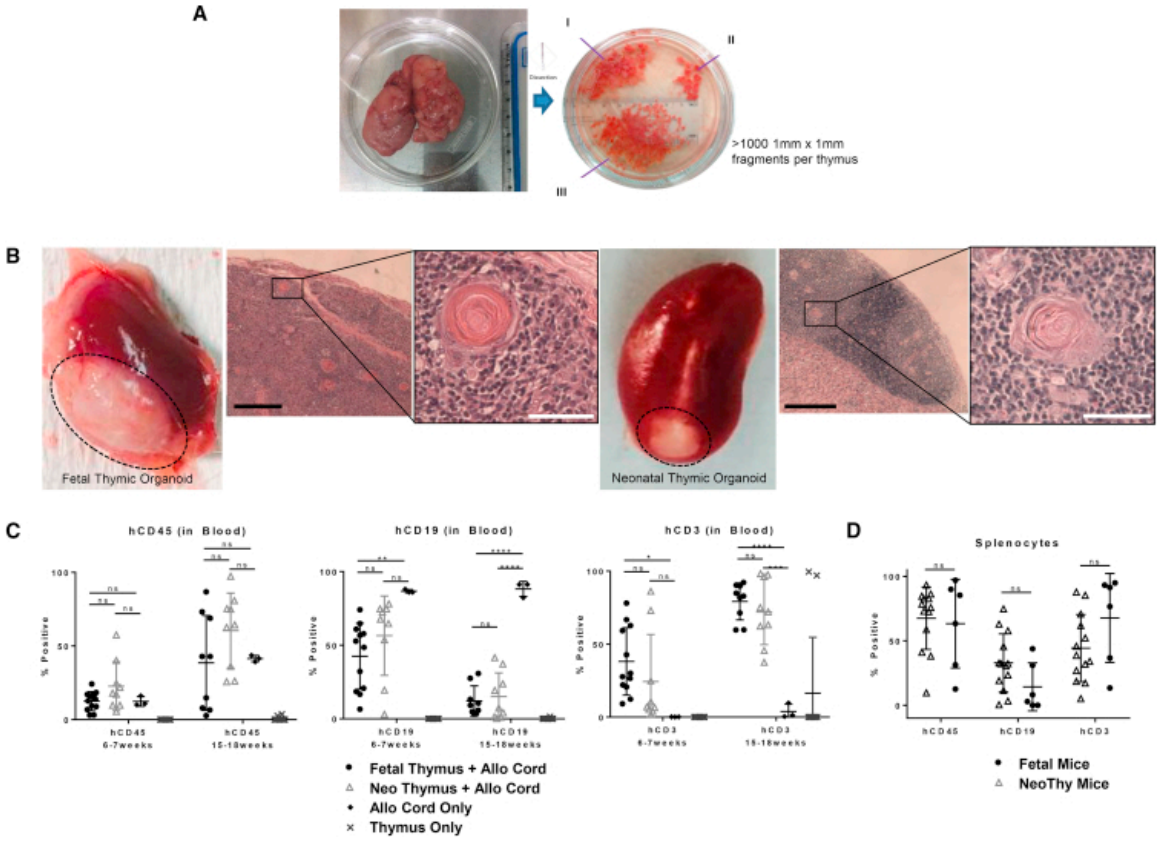


Figure 1

Engraftment of Human Thymus Tissue and Immune Cells

(A) Human neonatal thymus is abundant (e.g., 14.75 g, shown). Membrane, adipose, and blood vessels were removed and tissue processed into large (I), then medium (II), then 1 × 1 mm fragments (III) for cryopreservation. More than 1,000 fragments suitable for transplantation can be obtained from a single thymus.

(B) Implanted thymus fragments develop into organoids under the kidney capsule when co-transplanted i.v. with hCD34$^+$ cells, +/− αhCD2 antibody depletion (second- and first-generation mice, respectively). Histological analysis of first-generation fetal humanized mouse (NSG) (left) and second-generation neonatal (NSG-W) (right) thymic organoids, including Hassall's corpuscles, are shown (4× scale bar, 500 μm; inset is 10× scale bar, 100 μm).

(C) Humanized mice were generated from various human tissue samples in irradiated NSG mice w/o αhCD2 antibody depletion (first generation) and compared for human immune cell engraftment (hCD45$^+$), including B cells (hCD45$^+$hCD19$^+$) and T cells (hCD45$^+$hCD3$^+$) at early (6–7 weeks post-surgery) and late (15–18 weeks) time points. In four independent experiments, n = 12 animals received fetal thymus and allogeneic cord blood CD34$^+$ cells (Fet Thymus + Allo Cord), n = 9 animals received neonatal thymus and allogeneic cord (Neo Thymus + Allo Cord), n = 3 allogeneic cord only (Allo Cord Only) and n = 12 neonatal thymus alone from 3 donors (Thymus Only). The Thymus Only condition did not receive hCD34 $^+$ cells. The Allo Cord Only condition received hCD34$^+$ cells only.

(D) Splenocytes from fetal (n = 6) and neonatal tissue-derived (n = 13) first- and second-generation mice, using both NSG and NSG-W strains (seven independent experiments), were compared for human engraftment markers as in (C). Statistics were conducted using ANOVA, analyzed with GraphPad Prism 7.00. The Thymus Only control was included for comparison and was not analyzed for significance.

$^{****}p < 0.0001$, $^{***}p = 0.0001$, $^{**}p < 0.01$, $^{*}p < 0.05$; ns, not significant; no bar, not analyzed.

T18

Effects of Tongue Exercise Dose on Tongue Force, Mastication Rate, Bolus Size and Bolus Speed in a Rat Model

Weycker, J.M., Krekeler, B.N., Connor, N.P.

Submitter	Jacqueline M Weycker
Phone	
Email Address	weycker@wisc.edu
Classification	Graduate student
Division	
Lab	Nadine P Connor
Science Type	Translational Research
Keywords	tongue, aging, rat

Introduction: Aging can affect the function of muscles involved in swallowing (deglutition) which can contribute to impaired swallowing (dysphagia). Dysphagia is associated with reductions in quality of life and other health complications, including aspiration pneumonia. One known treatment for patients with dysphagia is tongue strengthening exercise. We have developed a rat model of tongue exercise in our laboratory. By studying the effects of aging and tongue exercise on deglutition in a rat model, a hypothesis can be developed that could lead to human clinical studies and finally evidence-based treatments. In our laboratory, we use a rat model to study the effects of age, training condition, and dose on tongue muscles and deglutition function. The purpose of this study is to explore the effect of varied dosing of tongue exercise on tongue force, mastication rate, bolus size, and bolus speed by using a videofluoroscopic swallow study before and after tongue exercise paradigms. We hypothesize that tongue exercise will significantly alter these deglutition characteristics and will be different between age groups.

Methods: A total of 52 male Fischer 344 Brown Norway rats were used in this study. There were 28 old rats (32-months) and 24 young rats (9-months). They were randomized into one of four conditions: 1 day, 3 days, 5 days/week exercise, or sham exercise. Rats were housed in pairs in a reverse light-dark cycle (12:12-hours) which allowed for tongue exercise when they were most active. The rats received 8 weeks of tongue exercise after a learning period to acclimate to the apparatus with a force operandum disk and water reward. Each exercise session included 100 tongue presses greater than or equal to the rat's individual target threshold for that particular session and received a water reward for pressed forces that were greater or equal to their target values. Additionally, videofluoroscopic swallow studies (VFSS) were performed prior to and following the 8-week exercise program. VFSS were recorded at the University of Wisconsin-Madison Wisconsin Institute of Medical Research prior to and following the 8-week exercise paradigm for each animal. The videos were recorded in IMA format at 30 frames/second and each video was calibrated manually via measurement of a dime shot for that particular VFSS date to ensure that videofluoroscopic settings were the same for each animal's pre- and post-videos. Each animal's pre-exercise and post-exercise video was blinded and analyzed using a protocol developed by our laboratory. Three swallows were analyzed from both the pre- and post-exercise conditions which included bolus speed, area, and mastication measurement for each swallow. The analysis was performed using ImageJ, a public domain Java image processing program inspired by NIH Image to calculate speed and area of pixel value statistics. Bolus speed was determined by using the "Multi-point Tool" to calculate the speed between points from bolus initiation or transit of the bolus through the pharyngeal phase of the swallow until the bolus met the Upper Esophageal Sphincter (UES) by following the head of the bolus and marking a point for each frame in which the bolus moved forward. Bolus area was measured using the "Freehand Selections" tool to mark around the entire bolus area in the frame prior to the bolus entering the UES. Finally, mastication rate was calculated by dividing five mastications by the number of frames within that time-point of the video near the time of that particular swallow.

Results: A two-way ANOVA comparing age x exercise dose demonstrated significant differences in tongue force based on training dose ($F=35.63$, $p<0.001$), however, age had no effect ($F=0.494$, $p=0.486$). In LSD pairwise comparisons, largest increase in tongue force from baseline occurred in the 5 day/week exercise dose condition ($p\leq0.001$) as compared to all other dose conditions; 1 day/week, 3 day/week, and 5 day/week exercise dose conditions all resulted in significantly increased tongue force as compared to the sham control exercise group ($p<0.001$). When looking at swallowing characteristics, two-way ANOVA comparing age x exercise dose showed no group differences for change in mastication rate (age - $F=0.233$, $p=0.632$; dose – $F=1.074$, $p=0.371$) or change in bolus size (age - $F=1.28$, $p=0.263$; dose – $F=1.09$, $p=0.365$) (change measured from pre- to post-training). However, bolus speed did show

an interaction effect between age and exercise dose ($F= 5.41$, $p=0.003$). Posthoc LSD comparisons showed that 5 day/week old rats had faster bolus speed rates after training as compared to all other conditions ($p<0.05$) except the 3 day/week young adult rats ($p=0.122$).

Discussion: We anticipated that there would be significant differences in deglutition including bolus speed, bolus size, and mastication rates for old and young rats with different training conditions following tongue exercise. Exercise for each of the groups demonstrated a significant difference based on their training dose. In order to translate these results to humans, clinical trials should be conducted to see if dose of exercise has an effect on tongue force, bolus speed, area, and mastication rate.

T5

Tongue Exercise Paired with Swallow Does Not Impact Thyroarytenoid Muscle Outcomes in a Rat Model of Aging

Glass T.J., Bado M., Krekeler, B.N. Rowe L.M., Connor N. P.

Abstract Submitter	Tiffany Glass
Email Address	glass@surgery.wisc.edu
Classification	Academic Staff
Principal Investigator	Nadine Connor
Science Type	Translational Research
Keywords	Thyroarytenoid muscle, Myosin Heavy Chain isoforms, Rat

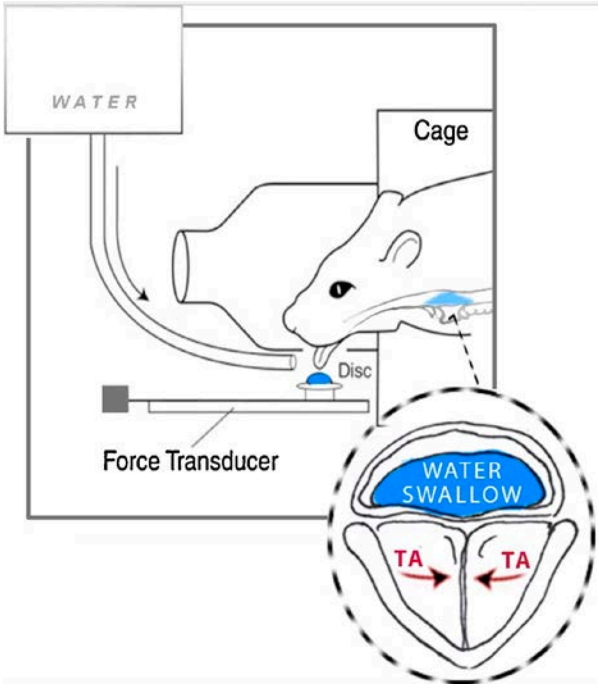
Introduction: Swallowing and voice disorders frequently occur in elderly adults and have a negative impact on overall health and quality of life. The thyroarytenoid muscle (TA) plays a critical role in both voice production and airway protection during swallowing. Prior work from this laboratory using a rat model of tongue exercise paired with a water swallow found impacts in muscles of the tongue and better maintenance of vocal intensity after 8 weeks of tongue exercise. These findings indicated possible cross-over effect of tongue training on the TA. Although there is activation of both the tongue and the TA muscle in this paradigm (Figure 1), it is not yet known how the muscle biology of the TA may be affected by tongue exercise. To address this question, we evaluated the impact of a tongue exercise regimen on TA muscle histology in a rat model of aging. This study included three age groups (young, middle age, and old) to determine whether exercise and age impact: 1) TA muscle fiber size (Minimum Feret's diameter), and 2) TA myosin heavy chain isoform (MyHC) profiles.

Methods: Male Fischer 344/Brown Norway rats underwent an 8-week regimen of tongue exercise paired with water swallow. Following this, rats were euthanized and TA muscles were isolated and embedded in OCT for sectioning. Tissue sections of 10 µm were stained for muscle laminin to label myofibers,and imaged at 40x magnification to permit TA myofiber size analysis through the semi-automated MatLab application SMASH. The two main divisions of the TA muscle, the extrinsic division (TA-Ex) and the vocalis division (TA-V), were analyzed separately. Following TA image acquisition, the remainder of each TA muscle was micro-dissected from cartilage attachments and embedding medium and homogenized to extract total protein. MyHC protein isoforms for each sample were separated through SDS-PAGE gels and bands visualized through silver staining. Staining intensity of each isoform band was quantified using UN-SCAN-IT gel analysis software (Silk Scientific). Final sample sizes were n=8-12/group for TA MyHC analysis, and 5-7/group for TA myofiber size analysis. Data were analyzed through 2-way ANOVA.

Results: Analysis of TA-Ex myofiber size indicated no significant main effects for either age or tongue exercise. Similarly, the TA-V also showed no significant main effects for either age or tongue exercise. MyHC analysis revealed a predominance of the IIX, IIB, and IIL isoforms, as previously reported. While TA muscle from young rats showed slightly elevated proportions of MyHC IIL relative to other age groups ($p=0.124$), MyHC profiles demonstrated no significant main effects for either age or exercise condition.

Conclusions: We hypothesized that tongue exercise may impact TA myofiber size and MyHC profiles in aging rats. To the contrary, no significant exercise or age effects of TA (MyHC or myofiber size) were found. This suggests that tongue exercise does not impact TA biology as measured in this study. The technical approach employed in this study conferred both strengths and limitations. While sectioning of the TA muscle prior to protein extraction permitted myofiber and MyHC measures to be evaluated in identical tissue, this approach differed from prior studies of the TA muscle in that MyHC protein samples were not comprised of protein from the entire muscle. This approach also reduced sample sizes due to incidental loss and artifact associated with processing. These limitations notwithstanding, results are compatible with the interpretation that this tongue exercise paradigm demonstrates limited, if any, cross-training impacts on TA muscle. These findings are broadly congruent with outcomes of prior work reporting that this rat paradigm of tongue exercise with swallow predominately influences measures of tongue function, with comparatively limited impacts on measures of vocal function.

Figure 1. Cross-activation of TA during tongue exercise paired with a water swallow. *Image from: Schaser AJ, Ciucci MR, Connor NP. Cross-activation and detraining effects of tongue exercise in aged rats. Behav Brain Res 2016*



T3

Treatment with Complement Blockade in Recipients of Brain-Death Donor Kidneys Defends Against Delayed Graft Function in Non-Human Primates

Eerhart M.J., Reyes J.R., Blanton C.L., Danobeitia J.S., Chlebeck P.J., Zitur L.J., Coonen J., Capuano S., D'Allesandro A.M., Torrealba J., Yankol Y., and Fernandez L.A.

Abstract Submitter	Dr. Michael Eerhart
Email Address	eerhart@surgery.wisc.edu
Classification	Postdoctoral fellow
Principal Investigator	Dr. Luis Fernandez
Science Type	Translational research
Keywords	Delayed graft function, complement, kidney transplant

Introduction: Delayed graft function (DGF), the need for dialysis within the first week of renal transplantation, can occur in up to 40% of kidney transplants. This is a result of ischemia-reperfusion injury leading to inflammation, complement activation, cytokine release, and acute kidney injury. This can be exacerbated by donor factors, specifically during brain death, including systemic inflammation, recruitment and activation of donor immune cells, and release of reactive oxygen species. To combat these donor risk factors for DGF, we have previously found that C1-inhibitor donor treatment of rhesus macaques using our brain death model followed by prolonged cold ischemia reduced the incidence of DGF in recipients. Our study evaluated the effects of recipient treatment with C1-INH compared to untreated recipients of renal allografts.

Methods: Fully mismatched rhesus macaques were used for both donors and recipients. Recipients were divided into vehicle (n=6) and treatment (n=8) groups. Bilateral nephrectomy was performed after brain death and kidneys were kept in static cold storage for at least 44 hours until transplantation. Upon arterial reperfusion, C1-INH 500U/kg plus heparin 40U/kg was given and the dose was repeated every 12 hours for a total of 3 doses in the treatment group. Standard immunosuppression was given postoperatively. Labs were performed the first seven days and twice weekly thereafter. Scheduled biopsies were performed roughly every two weeks. Outlier test was performed on creatinine values and one animal was excluded. DGF incidence was analyzed by chi-square test and comparison of groups compared with t-test, two-way ANOVA and Wilcoxon signed rank test evaluated Kaplan Meier survival.

Results: The vehicle group donors were statistically older ($p=0.0003$) compared to the treatment group, however recipient age, weight and cold ischemia time were similar ($p>0.05$). In the treatment group, 1/8 (14.3%) of animals met DGF criteria compared to the vehicle group where 4/6 (66.7%) of animals met DGF criteria ($p=0.036$). Creatinine was comparable between the two groups for the first 5 days postoperatively ($p>0.05$). Creatinine of treated recipients was reduced in the treatment group on postoperative days 6 and 7 when compared to the vehicle group ($p<0.05$). Four treated recipients who completed the study trended to delayed progression of antibody-mediated rejection (ABMR) when compared to vehicle animals on survival analysis ($p=0.1797$), three animals are still pending completion of the study.

Conclusions: Our study has shown a reduction in the incidence of DGF in kidney recipients who were treated with C1-INH starting at the time of transplantation. The effect of this was seen in post-operative days 6 and 7 creatinine values, which were lower in the recipient treatment group when compared to the vehicle group. Rates of ABMR trend towards being delayed in the treatment group, however, there are three animals who have not yet completed the study. In order to elucidate the mechanisms leading to the reduced rate of DGF, we plan to evaluate markers of renal injury, levels of circulating complement and cytokine levels, delayed-type hypersensitivity and a histopathological analysis of the transplanted kidneys. C1-INH has reduced the incidence of DGF when recipients are treated starting at the time of transplantation with a reduction in post-operative creatinine levels.

T6

Modeling Human Hematopoietic Stem Cell Transplantation Outcomes in the Lab

Hess, N.J.; Hematti, P.; Gumperz, J.E.

Abstract Submitter	Nicholas J. Hess
Email Address	njhess@wisc.edu
Classification	Postdoctoral fellow
Principal Investigator	Jenny Gumperz
Science Type	Translational research
Keywords	GVHD, Humanized Mice, Hematopiesis

Introduction: Cancers and autoimmune diseases, which affect 1.6% and 4.9% of the U.S. population respectively (CDC), arise because the immune system is not functioning properly. If chemotherapy and/or medications aren't able to control the disease, the result is often death if not for one more treatment option, a hematopoietic stem cell transplantation. Unfortunately, the biology behind these transplants has remained unclear leading to numerous complications with the mainstream application of this procedure. Our research aims to investigate the deeper biology behind hematopoietic stem cell transplants by utilizing a humanized mouse model that can recapitulate the biology of human transplants.

Methods: In our NSG and NSG-W mouse models, we mimic a non-myeloablative conditioning regimen where the mice have not received any irradiation or chemotherapy drugs but remain conducive to hematopoietic transplant due to their severe genetic immunodeficiency. Human cells from either peripheral blood, cord blood, mobilized blood or bone marrow is then intravenously injected into these mice which are continuously monitored for engraftment and GVHD for 12 weeks.

Results: Our results show that in a dose-dependent manner, each stem cell source has a differential capacity to cause GVHD and engraft in our humanized mouse model. As is seen in the clinic, bone marrow has the highest GVHD potential on a per-cell basis while cord blood had the least. This is compared to their engraftment potential, which is similar between bone marrow and cord blood but with mobilized blood having the lowest hematopoietic engraftment potential. These results imply that there are fundamental differences in the T cell and myeloid cell populations between different stem cell sources that act either as promoters or controllers of GVHD and engraftment. Furthermore, we have detected three areas of interest that are beginning to unravel the differences between the different stem cell sources. In the clinic, the total dose of cells given to each patient is dependent on the percentage of CD34+ cells but what is not well characterized is the percentage and impact of the other cell types within the graft that are also given to the patient. We have characterized the input populations and have found drastic differences in the cell populations present in the different stem cell sources. Additionally, we have measured the expression of several co-stimulatory receptors present on Tc and myeloid cells. This has led to some interesting differences such as bone marrow myeloid cells being highly enriched for the B7 complex. Lastly, the different stem cell sources have a differential capacity to produce various cytokines when activated by either TCR ligation or TLR stimulation. These results suggest that the biology within each of the different stem cells sources is different and contribute differently to GVHD and engraftment.

Conclusions: Each stem cell source is unique in both their collection method and in their biology. Understanding their biology is fundamentally important in understanding the pros and cons of each stem cell source to better treat the patient. Currently, we are investigating the role of each cell type within the graft to understand which cell types are the key contributors to GVHD and engraftment. We hope that this research will better inform clinicians on what stem cell source is the best option for hematopoietic stem cell transplantations.

T8

Applied Chaos Level Test for Validation of Signal Conditions Underlying Optimal Performance of Voice Classification Methods

Liu B., Polce E., Sprott J., Jiang J.J.

Submitter	Boquan Liu
Phone	608-265-9854
Email Address	bliu243@wisc.edu
Classification	Academic staff
Division	Dept. of Surgery
Lab	Laryngeal Physiology Lab
Science Type	Translational Research
Keywords	Acoustics, Voice, Voice disorders

Introduction: The purpose of this paper is to introduce a chaos level test to evaluate linear and nonlinear voice type classification method performances under varying signal chaos conditions without subjective impression.

Methods: Voice signals were constructed with differing degrees of noise to model signal chaos. Within each noise power, 100 Monte Carlo experiments were applied to analyze the output of jitter, shimmer, correlation dimension (D2), and spectrum convergence ratio (SCR). The computational output of the four classifiers was then plotted against signal chaos level to investigate the performance of these acoustic analysis methods under varying degrees of signal chaos. A diffusive behavior detection based chaos level test was used to investigate the performances of different voice classification methods. Voice signals were constructed by varying the signal-to-noise ratio to establish differing signal chaos conditions.

Results: Chaos level increased sigmoidally with increasing noise power. Jitter and shimmer performed optimally when the chaos level was less than or equal to 0.01, whereas D2 was capable of analyzing signals with chaos levels less than or equal to 0.0179. SCR demonstrated proficiency in analyzing voice signals with all chaos levels investigated in this study.

Conclusions: The results of this study corroborate the performance relationships observed in previous studies and, therefore, demonstrate the validity of the validation test method. The presented chaos level validation test could be broadly utilized to evaluate acoustic analysis methods and establish the most appropriate methodology for objective voice analysis in clinical practice.

T10

Application of Local Intrinsic Dimension for Acoustical Analysis of Voice Signal Components

Liu B., Polce E., Jiang J.J.

Submitter	Boquan Liu
Phone	608-265-9854
Email Address	bliu243@wisc.edu
Classification	Academic staff
Division	Dept. of Surgery
Lab	Laryngeal Physiology Lab
Science Type	Translational Research
Keywords	Voice disorders, acoustic analysis, intrinsic dimension

Introduction: The overall aim of this study was to apply a *k*-nearest neighbor algorithm for local intrinsic dimension (*D*i) estimation of voice signal recordings. It was predicted that continuous dimensional analysis throughout the entire time series would generate comprehensive descriptions of voice signal components, called voice type component profiles (VTCP).

Methods: One hundred thirty-five voice recording samples of the sustained vowel /a/ were obtained from the Disordered Voice Database Model 4337 and spectrographically classified into the voice type paradigm. The *D*i and correlation dimension (*D*2) were then used to objectively analyze the voice samples and compared based on voice type differentiation efficacy.

Results: The *D*2 exhibited limited effectiveness in distinguishing between the four voice type signals. For *D*i analysis, significant differences were primarily observed when comparing voice type component 1 (VTC1) and 4 (VTC4) across the four voice type signals ($P<0.001$). The four voice type components (VTCs) significantly differentiated between low-dimensional, type 3 and high-dimensional, type 4 signals ($P<0.001$).

Conclusions: The *D*i demonstrated improvements over *D*2 in two distinct manners: enhanced resolution at high data dimensions and comprehensive description of voice signal elements.

T9

An Objective Parameter to Classify Voice Signals Based on Variation in Energy Distribution

Liu B., Polce E., Jiang J.J.

Submitter	Boquan Liu
Phone	608-265-9854
Email Address	bliu243@wisc.edu
Classification	Academic staff
Division	Dept. of Surgery
Lab	Laryngeal Physiology Lab
Science Type	Translational Research
Keywords	Chaos, Nonlinear energy difference ratio, Voice signal classification

Introduction: The purpose of this paper is to introduce an iterative nonlinear weighted method based on the variation in spectral energy distribution present in a voice signal to differentiate between four voice types: type 1 voice signals are nearly periodic, type 2 voice signals have strong modulations and subharmonics, type 3 signals are chaotic, and type 4 signals are dominated by stochastic noise.

Methods: A total of 135 voice signal samples of the sustained vowel /a/ were obtained from the Disordered Voice Database and then individually categorized into the appropriate voice types based on the classification system described in Sprecher et al (2010). Voice samples were analyzed using the nonlinear methods of spectrum convergence ratio, rate of divergence, and nonlinear energy difference ratio (NEDR) to investigate classifier efficacy. An iterative nonlinear weighted method based on the derivative of instantaneous frequency and Fourier transformations is applied to calculate spectral energy distributions. The distribution is then used to calculate the NEDR to classify voice signal types.

Results: Statistical analysis revealed that NEDR effectively differentiated between all four voice types ($P < 0.001$). Subsequent multiclass receiver operating characteristic analysis demonstrated that NEDR (area under the curve [95% CI] = 0.99 [0.96–1.0]) possessed the greatest classification accuracy relative to spectrum convergence ratio and rate of divergence.

Conclusions: NEDR was shown to be an effective metric for objective differentiation between all four voice signal types. NEDR calculations occurred approximately instantaneously, constituting a substantial improvement over the tedious computational time required for calculation of previous nonlinear parameters. This metric could assist clinicians in the diagnosis of voice disorders and monitor the efficacy of treatment through observation of voice acoustical improvement over time.

T16

Measurement Reliability of Laryngeal Resistance and Mean Flow Rate in Pediatric Subjects

Scholp A.J., Hedberg C.D., Lamb J.R., Hoffman M.R., Braden M.N., McMurray J.S., Jiang J.J.

Abstract Submitter	Austin Scholp
Email Address	Scholp@wisc.edu
Classification	Graduate Student
Principal Investigator	Jack Jiang
Science Type	Translational
Keywords	Laryngeal resistance; pediatric; aerodynamic, subglottal pressure; voice; airflow interruption.

Introduction: Mean flow rate (MFR) and laryngeal resistance (R_L) are sensitive to changes in glottal configuration and biomechanics. There is little reported on aerodynamic parameters in children. We conducted a pilot study to evaluate MFR and R_L measurement reliability in a pediatric population using labial and mechanical interruption methods.

Methods: 39 subjects aged 4-17 performed ten trials per method. For labial interruptions, subjects produced five labial plosives at a comfortable amplitude. For mechanical interruptions, subjects maintained a steady /ɑ/ while a balloon valve interrupted their airflow five times for 250 ms each. MFR was measured as the flow through the interruption device between interruptions. R_L was calculated by dividing subglottal pressure (P_s) by MFR.

Results: Mean R_L ($p<0.01$) was higher for mechanical interruption while there were no significant differences in mean MFR ($p=0.066$) and mean P_S ($p=0.100$) between techniques. Intra-subject coefficients of variation were higher for the labial technique for both MFR ($p<0.01$) and R_L ($p<0.001$) while there was no difference in P_S ($p=0.468$). Mean MFR and R_L were related to age for both the labial (MFR: $r=0.578$, $p<0.001$; R_L: $r=0.487$, $p=0.002$) and mechanical trials (MFR: $r=0.525$, $p=0.001$; R_L: $r=0.551$, $p<0.001$).

Conclusions: Differences in means and intra-subject variation are likely due to differences in task and measurement timing. Precision of MFR and RL measurement in pediatric subjects was higher for mechanical interruption; further exploration of this method and its clinical utility is warranted. Measurement of aerodynamic parameters may be a useful addition to pediatric voice assessment.

T17

Measurement Reliability of Laryngeal Resistance and Mean Flow Rate in Pediatric Subjects

Hoffman M.R., Scholp A.J., Hedberg C.D., Lamb J.R., Braden M.N., McMurray J.S., Jiang J.J.

Abstract Submitter	Austin Scholp
Email Address	Scholp@wisc.edu
Classification	Graduate Student
Principal Investigator	Jack Jiang
Science Type	Translational
Keywords	Phonation threshold pressure; pediatric; aerodynamic; subglottal pressure; voice; airflow interruption.

Introduction: Phonation threshold pressure (PTP), the minimum subglottal pressure (Ps) required for phonation, is sensitive to changes in laryngeal biomechanics and is often elevated with pathology. Little is reported on PTP in children; challenges with task performance and measurement reliability represent barriers to routine clinical assessment.

Methods: Twenty-two subjects aged 4 to 17 years (10.7 ± 3.9 years) participated. Ten trials were performed for each method; task order was randomized. For labial interruption, subjects produced /pɑ/ five times at softest (onset PTP) and comfortable amplitude. For mechanical interruption, subjects produced a sustained /ɑ/ while a balloon valve interrupted phonation five times for 250 ms each; mechanical interruption was performed with a mouthpiece and mask. PTP was recorded as the difference between Ps and supraglottal pressure at phonation cessation (offset PTP). Mean PTP and Ps and intrasubject coefficients of variation were compared. Correlations with age were evaluated.

Results: Mean PTP ($P < .001$) and Ps ($P = .005$) were higher for labial interruption. Intrasubject coefficients of variation for PTP ($P = .554$) and Ps ($P = .305$) were similar across methods. Coefficient of variation was related to age for mechanical-mask trials only ($r = -0.628$, $P = .00175$).

Conclusions: Differences in means are likely related to differences in task and PTP hysteresis effect. Reliability is comparable with all methods; using a mouthpiece may be preferable to a mask for mechanical interruption. Measurement of PTP is noninvasive, reliable, and may be a useful adjunct in pediatric voice assessment.

T7

Quantification of Voice Type Components Present in Human Phonation Using a Modified Diffusive Chaos Technique

Liu B., Polce E., Raj H., Jiang J.J.

Submitter	Boquan Liu
Phone	608-265-9854
Email Address	bliu243@wisc.edu
Classification	Academic staff
Division	Dept. of Surgery
Lab	Laryngeal Physiology Lab
Science Type	Translational Research
Keywords	acoustic analysis, diffusive chaos, voice disorders

Introduction: The purpose of this study was to apply a modified diffusive chaos methodology to disordered voice samples, in order to conduct objective acoustic analysis. It was predicted that continuous calculation of the diffusive chaos parameter throughout the voice sample would allow for construction of comprehensive voice type component profiles (VTCP).

Methods: One hundred thirty-five voice samples of sustained /a/ vowels were randomly selected from the Disordered Voice Database Model 4337 and classified according to the voice type paradigm using spectrogram analysis. All voice samples were then analyzed using the diffusive chaos method, and VTCPs were generated to show the distribution of voice type components.

Results: The proportions of voice type component 1 (VTC1), VTC2, and VTC4 varied significantly between the majority of the traditional voice types ($P<0.001$). The VTCs of type 3 voices were all significantly different from the VTCs of type 4 voices ($P<0.001$).

Conclusions: Thus, the diffusive chaos method demonstrated proficiency in generating comprehensive VTCPs for disordered voices with varying severity. Diffusive chaos analysis has the potential to improve the assessment of voice disorders and treatment outcomes by providing an objective and quantitative description of the voice.

T13

Induction of Tolerance to Kidney Transplants in Rhesus Macaque

Post, J.L., Haynes, L.D., Haynes, W.J., Jankowska-Gan, E.,Bloom, D., Fernandez, L., D'Alessandro, T., Forrest, L., Hematti, P., Burlingham, W.J. and Kaufman, D.B.

Abstract Submitter	Post, J. L.
Email Address	post@surgery.wisc.edu
Classification	Other
Principal Investigator	Dixon Kaufman
Science Type	Translational Research
Keywords	Hematopoietic stem cells, chimerism, tolerance

Introduction: Solid organ transplantation is the current treatment for many end stage diseases, but long-term use of immunosuppressive medications negatively impacts quality of life. Tolerance is the state where transplant recipients are able to maintain good graft function in the absence of immunosuppression. We have established a large animal model to induce tolerance using a post-renal transplant immuno-depletion therapy followed by an infusion of donor hematopoietic stem cells (HSC), allowing investigation of mechanisms underlying tolerant acceptance of both HSC and renal allografts. This protocol is based on experimental treatments developed at Stanford University. Establishment of chimerism has been a challenge in this Rhesus model with approximately 30% of recipients developing chimerism. We therefore modified our protocol to increase radiation, inhibition of B cells with Obinutuzumab or the addition of Belatacept.

Methods: 8 Rhesus Macaques received HSC derived from peripheral mobilized apheresis product or bone marrow with or without splenic cells 11 or 15 days post treatment initiation. Animals also received 5 days of anti-thymocyte globulin, 9-10 doses of total lymphocyte irradiation with some also receiving one dose of total body irradiation (TBI) using tomotherapy. TBI was given at day 14. 2 animals received infusions of Obinutuzumab at 25 mg/kg on days 0, 7, 14 and 21 and 3 animals received infusions of Belatacept at 10 mg/kg on days 11, 14 and 18 and 5 mg/kg on day 25. Maintenance immunosuppression consisted of mycophenolate mofitil and tacrolimus. Recipients are monitored for cell reconstitution and donor chimerism.

Results: 3 of the 8 animals achieved chimerism and all 3 of these animals had also received Belatacept infusions as described above. Neither the Obinutuzumab nor the additional TBI radiation alone resulted in chimerism. Two of the 3 animals over engrafted with one diagnosed case of Graft vs. Host Disease in a model that traditionally had protected from GVHD.

Conclusions: Belatacept appears to assist with cell engraftment, resulting in a chimeric state in the recipient. The results are being confirmed with decreased cell infusion to minimize GVHD. In addition, the protocol will be replicated with the addition of a kidney transplant to determine if the level and type of chimerism established with Belatacept creates conditions for long-term, immunosuppression free survival of the transplanted kidney.

T4

Quantifying Pancreatic Lipid Content: Correlating Donor Data with Pancreas Quality

Feeney A.K., Tremmel D.M., Mitchell, S.A., Sackett S.D., and Odorico J.S.

Abstract Submitter	Austin Feeney
Email Address	afeeney@wisc.edu
Classification	Graduate Student
Principal Investigator	Jon S. Odorico
Science Type	Translational
Keywords	Pancreas, Transplantation, Diabetes

Introduction: The overall pancreatic graft quality is considered a critical factor that is associated with outcomes of pancreatic transplants. One of the key visual criteria for suitability for transplant is the amount of fatty infiltration or steatosis, which is felt to correlate with poor outcomes. In an effort to characterize the transplantability of donor pancreata accurately, several clinical factors of the donor are assessed. Although parameters such as older age and higher BMI have been correlated with poor outcomes, these may not have a direct correlation to the pancreata quality and lipid content. Consequently, there is a high discard rate of potentially transplantable pancreata, and many grafts from older and overweight donors could be successfully transplanted. The present study sought to determine how well BMI and other donor parameters correlate with actual lipid content in pancreata.

Methods: 38 donor pancreata were ethically obtained from the Organ Procurement Organization (OPO) at the University of Wisconsin, separated into male (n=21; ages:21-61) and female (n=17; ages:45-71) subgroups and analyzed for lipid content using a modified version of the Folch method. The pancreata were immediately prepared by dissecting the parenchyma from non-parenchymal tissues, such as the duodenum and vessels, and cut into 1cm cubes before freezing at -80^{o}C. 30mg lyophilized cubes were treated with a 1:3 chloroform/methanol solution for one hour for lipid extraction. Following centrifugation, the liquid was transferred to a new tube and brought to a 2:1 chloroform/methanol ratio to separate the lipid phase. The lipids were then placed in a new tube to air-dry for 4-7 days to quantify the dry weight of lipids relative to the dry weight of tissue. Technical replicates (n=3-5) were collected for each donor. Donor clinical parameters were collected from the OPO records and cross-referenced to the extracted lipid content for each donor.

Results: We observed a wide range of lipid content in this cohort of pancreata (Average=29.2%; Range=12.1-70.2%). When we analyzed all pancreata for Age versus BMI or %Fat using Pearson's correlation, we found no correlation. However, we found that %Fat and BMI are significantly correlated (R^2=0.1936; p=0.005). After stratifying by sex and examining %Fat and Age, there was a slightly positive correlation for the male subgroup (R^2=0.1269; p=0.111), but a slightly negative correlation (R^2=0.1234; p=0.164) in the female subgroup. %Fat and BMI were significantly correlated for the male subgroup (R^2=0.1855; p=0.05), and somewhat correlated in the female subgroup (R^2=0.2000; p=0.07). Additional relationships involving %Fat and amylase, HbA1c, and lipase yielded no significant correlations among these select donors.

Conclusions: Differences in pancreatic graft quality related to lipid content do exist. Currently, BMI is used as a surrogate marker in transplant practice for intraparenchymal lipid content and pancreas quality. The present study confirms that BMI correlates well with %Fat quantified via the Folch method. Additionally, these data indicate that older age may also be associated with higher %Fat for the male subgroup, which highlights potential differences in organ quality pertaining to sex. Outliers in the dataset where BMI and %Fat do not align well highlight the need to examine other clinical measurements which may better correlate with pancreatic lipid content.

T14

Towards In Vitro Maturation of Stem Cell-Derived Beta Cells Utilizing Pancreatic Matrix Hydrogel

Quirini NQ, Tremmel DM, Sackett SD, Mitchell SA and Odorico JS

Abstract Submitter	Nicholas Quirini
Email Address	nquirini@wisc.edu
Classification	Undergraduate
Principal Investigator	Jon S Odorico
Science Type	Translational
Keywords	Human pancreatic extracellular matrix, stem cell-derived beta cells, human embryonic stem cells.

Introduction: Although current beta cell replacement therapy has the capacity to restore normoglycemia in patients with type 1 and type 2 Diabetes Mellitus, this treatment is limited by donor shortage and the requirement for lifelong immunosuppressant therapy. Human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs) have the potential to become any cell type in the human body. Also, they have the capability to generate cells useful for regenerative medicine and disease treatment. A major limitation of current diabetes research is generating mature cell types *in vitro* comparable to those found *in vivo.* Our lab aims to improve the differentiation of mature stem cell-derived pancreatic islet-like clusters (PILCs). These clusters are formed through a 7 stage, 28-day, stepwise differentiation protocol and resemble the morphology of the Islets of Langerhans found in the human pancreas. Several studies have shown that PILCs become more mature after transplantation into an *in vivo* environment, suggesting that factors within the *in vivo* milieu aids in this maturation. Our lab has generated an extracellular matrix (ECM) scaffold derived from the human pancreas which houses cells at either stage 4 or stage 6 of their differentiation. We **hypothesize** that the co-culture of PILCs with human pancreatic-ECM (hP-ECM) *in vitro* will promote maturation towards a human islet phenotype.

Methods: To assess PILC maturation in hP-ECM co-culture, hESCs were differentiated toward a PILC fate, and embedded into hP-ECM at either Stage 4 or 6 of culture. Protein expression of the pancreatic endocrine markers Pdx1, Nkx6.1, insulin, and the beta cell maturation marker Urocortin 3 (Ucn3) were then quantified across two separate experiments using immunofluorescent staining. Collagen 1 was measured for all experiments and conditions in order to assess whether ECM co-culture affects cellular Col1 production. Area positive for insulin expression was quantified in PILCs co-cultured with ECM compared to those cultured in suspension. PILCs were also assessed for co-expression of Pdx1/Nkx6.1, indicative of beta cell fate, in co-culture conditions as compared to suspension controls. ImageJ was employed for quantification and calculation of total cell areas, and area of positive protein stains for each marker in reference to the total cell area.

Results: Preliminary experimental data displayed trends towards increased protein expression for cells cultured in hP-ECM compared to suspension culture controls. Cells cultured in hP-ECM at the stage 4 time point in the first experiment had a mean insulin expression percentage of 20.61%. Suspension culture control cells for this experiment had a mean insulin expression percentage of 13.51%. Results from the second experiment with cells seeded into hP-ECM at stages 4 and 6 had mean insulin expression percentages of 45.40% and 15.89%, respectively. Conversely, suspension culture control cells mean insulin expression percentage was 31.52%. Pdx1/Nkx6.1 co-expression data gathered from this experiment found mean expression percentages for stage 4 cells and stage 6 cells of 47.20% and 50.50%, respectively. Suspension culture control cells mean co-expression percentage was 33.70%.

Conclusions: These results suggest that the presence of hP-ECM improves the protein expression of insulin and co-expression of Pdx1/Nkx6.1 in PILCs. Results from the cells seeded at stage 4 suggest that earlier exposure to ECM improves the production of insulin positive cells. Further, hP-ECM co-culture may also reduce the need for PILCs to express Col1 and other ECM proteins. More cell area will need to be gathered before conclusive statements can be made and further experiments will have to confirm this data.

T19

MHC Class II Ligation on Glomerular Endothelial Cells Upregulates Adhesion Molecules and Chemoattractants: An *In Vitro* Model of Microvascular Injury

Wilson Schlei, NA, Dylewski, J, Redfield III, RR, Djamali, A, Blaine, J, Panzer, SE

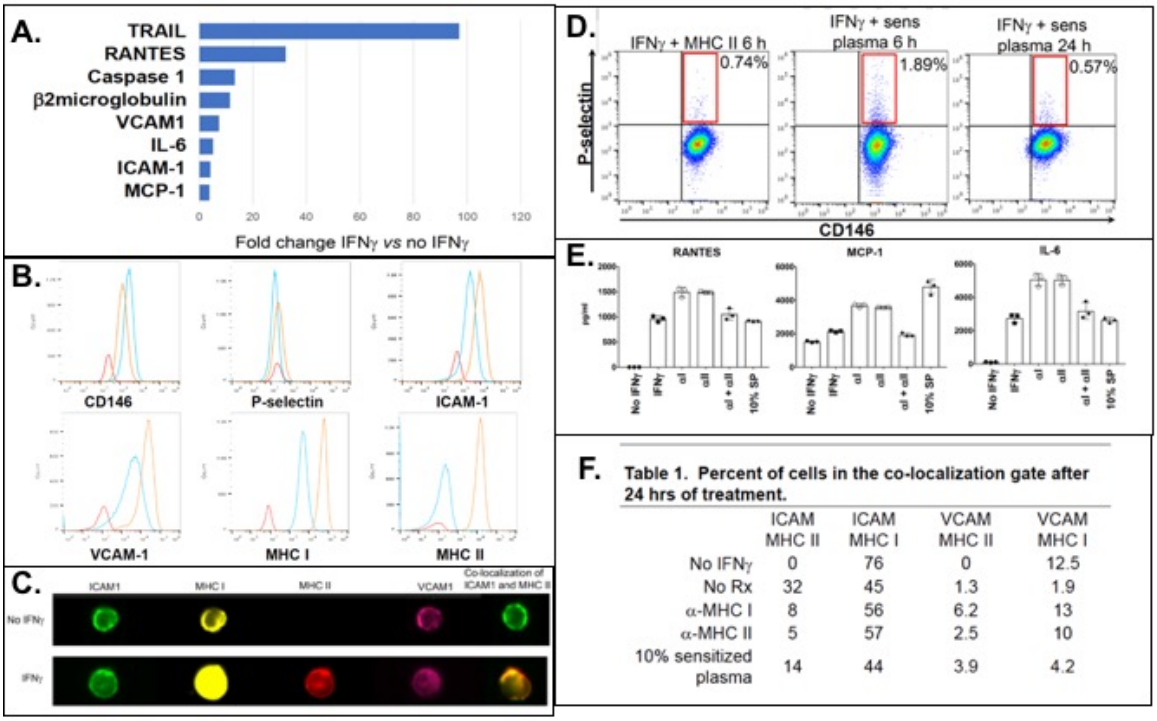
Abstract Submitter	Nancy Wilson Schlei
Email Address	nawilson@medicine.wisc.edu
Classification	Academic staff
Principal Investigator	Sarah Panzer
Science Type	Basic
Keywords	Endothelial, glomerular, chemoattractants, adhesion molecules

Introduction: Microvascular injury and leukocyte margination across glomerular endothelial cells are key pathologic processes in kidney allograft rejection. Intragraft leukocytes are associated with graft failure; however, the mechanisms of glomerular endothelial cell injury and leukocyte infiltration remain unclear. We hypothesize MHC class II ligation on glomerular endothelial cells will result in upregulation of adhesion molecules and chemoattractants.

Methods: A Bl/6 mouse glomerular endothelial cell line (Mouse GEndoC) was maintained at 33°C with a temperature sensitive large T antigen and had a fibroblast-like morphology. After shifting to 37°C for 7 days, the cell line developed into mature endothelial cells with typical cobblestone morphology. Mouse GEndoC were stimulated with IFNγ for 48 hours, and upregulated MHC class I and II. Mouse GEndoC were then incubated with anti-MHC class I or II antibodies, or sera from balb/c mice sensitized with Bl/6 splenocytes. Expression of CD146, MHC class I and II, ICAM1, VCAM1 and P-selectin were assessed by flow cytometry. Gene expression was measured by RT2 profiler. Cytokine expression was analyzed in culture supernatants with LegendPlex. Co-localization was determined using ImageStream.

Results: Mouse GEndoC stimulated with IFNγ upregulated gene expression of TRAIL, RANTES, MCP-1, caspase1, β2microglobulin, Vcam1, IL-6 and Icam1 (**A**). IFNγ stimulation of Mouse GEndoC increased surface expression of MHC class I, MHC class II, VCAM1, and ICAM1; but not P-selectin **(B)**. Expression was confirmed on Image Stream, which also determined that MHC Class I and MHC class II molecules co-localize with ICAM1 **(C)**. Subsequent ligation with MHC class II antibody transiently increased surface expression of P-selectin at 6 hours. Further enhanced surface expression of P-selectin was elicited using 10% sensitized plasma**,** which persisted at 24 hours (**D**). Mouse GEndoC secretion of chemoattractants (MCP-1 and RANTES) increased with IFNγ stimulation and was further enhanced with MHC II ligation (**E**). Adhesion molecules and MHC class I and II are up regulated with IFNγ and co-localize on the cell surface (**F**).

Conclusions: MHC II crosslinking on Mouse GEndoC resulted in an upregulation of P-selectin as well as the chemoattractants MCP-1 and RANTES. MHC molecules and adhesion molecules are co-localized on the endothelial cell surface. Maintaining the integrity and functionality of the glomerular endothelium is necessary to ensure survival of the allograft. Future studies will examine therapeutic targets to attenuate glomerular endothelial cell injury, such as inhibitors of mTOR (inhibition of ICAM1 clustering) and Nox4 (TRAIL pathway).



F. **Table 1. Percent of cells in the co-localization gate after 24 hrs of treatment.**

	ICAM MHC II	ICAM MHC I	VCAM MHC II	VCAM MHC I
No IFNγ	0	76	0	12.5
No Rx	32	45	1.3	1.9
α-MHC I	8	56	6.2	13
α-MHC II	5	57	2.5	10
10% sensitized plasma	14	44	3.9	4.2

Figure 1. MHC class II ligation results in upregulation of adhesion molecules and chemoattractants. A. The top fold increased transcripts after stimulation with IFNγ. **B**. While MHC I and II, ICAM1, VCAM1 are upregulated by IFNγ stimulation, P-selectin is not. **C.** Image Stream analysis indicates that adhesions molecules and MHC molecules co-localize. **D.** P-selectin was upregulated after short stimulation with MHC II crosslinking or sensitized plasma. **E.** Chemoattractants are upregulated by IFNγ and further increased with MHC I or II crosslinking. **F.** Image stream shows that ICAM and MHC I are co-localized, but not MHC II or VCAM.

T20

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

Zeng W, Sanchez R.J., Poore S.O., Dingle A.M

Abstract Submitter	Weifeng Zeng
Email Address	Wzeng28@wisc.edu
Classification	
Principal Investigator	Aaron M. Dingle, Samuel O. Poore
Science Type	Translation
Keywords	Tendon repair, repair strength, biomechanics, hand, flexor tendon

Introduction: The methods of Zone II flexor tendon repair in fingers remains limited, and the outcomes unpredictable. Decades of research have focused on applying stronger suture material and increasing the number of core sutures, ultimately creating a bulky repair site, prone to external adhesions, core suture rupture or suture pull out and ultimately repair failure. Despite the increased strength and number of core sutures, unpredictable outcomes remain.

This study utilizes the discarded or not-repaired tendon tissue and novel suture techniques to enhance the strength and redistribute the forces to a regeneration tendon, to ultimately prevent adhesion formation and rupture.

Methods: Pieces of flexor digitorum superficialis tendons (FDS) in zone II otherwise resected or not repaired were utilized to repair flexor digitorum profundus tendons (FDP) with two novel techniques: 1) Circumferential repair (CR): a whole segment of the FDS is wrapped around the repaired tendon. Five sutures anchor points are placed through the segment of FDS and FDP either side of the repair site, to secure the segment of FDS and provide strength. 2) Asymmetric repair (AR): ulnar/radial side of the FDS is resected and secured across the repair site by eight interrupted anchor points; 4 either side of the repair site that pass through the FDS pieces and FDP.

Results: We applied circumferential repair and asymmetric repair in 10 pig's feet, as the structure of flexor tendon of the second and third digitorums are similar to human. In Zone II, all the FDS can provide a complete segment for CR (where FDS is completely severed), or a piece of FDS from ulnar/radial side for AR (where FDS is partially severed). The transverse 5-anchor-points suture technique and the transverse 4-anchor-points suture technique can be performed simply through the FDS pieces and FDP in either side of the repair site. The preliminary test shows the native reclaimed FDS tissue is intended to take the brunt of the force, redistributing the force away from the repair site. The FDS pieces covering the repair site will act as isolation to prevent adhesion forming between the regenerating tendon and the surrounding tissues.

Conclusions: The FDP injury in Zone II usually combines with the FDS complete/partial injury. These entire new approaches using the autologous tendon tissue from FDS are achievable. Both CR and AR are currently undergoing qualitative static linear strength testing and cyclical testing to compare the novel methods with conventional methods.

T11

Design and Manufacture of an Osseointegrated Neural Interface (ONI) for Chronic Electrophysiology in Rabbits Towards Improved Prosthetic Control

Millevolte, A. X. T., Dingle, A. M., Ness, J. P., Novello, J., Zeng, W., Nemke, B., Sanchez, R., Lu, Y., Markel, M. D., Suminski, A. J., Williams, J. C., **Poore, S. O**.

Submitter	Augusto X. T. Millevolte
Phone	608-212-7766
Email Address	millevolte@wisc.edu
Classification	Legend
Division	Plastic Surgery
Lab	Poore, S. O.
Science Type	Translational Research
Keywords	Peripheral nerve, neural interface, osseointegration

Introduction: Advances in body armor and military medicine have dramatically increased the survival rate of traumatic amputations. (Casper, 2013) This growing community of veteran amputees face a multitude of post amputation challenges. Neuropathic pain from amputation neuromas frequently precludes the use of traditional prostheses. Current prosthetics lack the controllable degrees of freedom to enable patient desired grasping and object manipulation functionality. Better understanding the characteristics of peripheral nerve regeneration will facilitate the use of traditional prostheses while building towards the improved neuroprosthetic feedback and control required for more naturally dexterous prosthetic integration, this investigation requires chronic implantation of neural interfaces.

The **osseointegrated neural interface (ONI)** leverages the medullary cavity of bone to provide mechanical stability, electrical insulation, and the stem cell rich environment potentially acting as a suitable bioreactor for peripheral nerve regeneration. The objective of this research is to build towards improved bidirectional neural interfacing for prosthetic control through the design of both form and function required to create an ONI in rabbits.

Methods: The osseointegrated neural interface was built to contain three main components- neural interface, osseointegrated endoprosthetic attachment and percutaneous connector. Two independent cuff electrodes serve as the interface, stainless steel M4 cup point grub screws serve as the endoprosthesis and percutaneous connectors on the distal end of the endoprosthesis were hardwired to the cuff electrodes for chronic electrophysiology. The ONIs were implanted in a rabbit transfemoral amputation model, whereby the sciatic nerve is transposed into bone via a corticotomy. The distal electrode was placed on the terminal end of the nerve within the bone and the proximal electrode placed outside the bone proximal to the corticotomy. The endoprosthetic was inserted into the medullary canal and secured with bone cement. Animals were observed over 12 weeks, with chronic electrophysiological recordings and radiographs at weeks 3, 5, 8 and 12 post-operatively.

Results: The initial ONI implant successfully interfaced, with read/write latency and stimulation threshold decreasing as the implant matured. Mechanically, several design improvements were identified. The initial endoprosthesis was shortened to reduce leverage pressure placed on the bone during ambulation after fracture occurred in two animals. The first percutaneous connector proved easily broken by normal rabbit ambulation, due to inherent circuit board fragility and the particular mechanical arrangement. The second percutaneous connector managed to rectify ambulatory related breakages, but proved susceptible to intentional destruction (chewing).

Conclusions: Chronic implantation of the ONI successfully demonstrated the ability to write sensory information into the nervous system from nerves transposed into bone. In general, the neural signals achieved at peripheral nerve-electrode interface became stronger over time, with shorter response latency and lower stimulation thresholds. ONI is a feasible approach to chronic electrophysiology investigations, providing the stable interface required to explore late stage peripheral nerve regeneration interaction with implanted electrodes. Improving on mechanical stability with a more precise clinical approach, and properly protecting the percutaneous connector will provide a stable chronic interface, facilitating investigations into somatosensory evoked potentials, increasing the range and applicability of the neural interface.

T2

Osseointegrated Neural Interface (ONI): A Chronic Neural Interface in Rabbits Complete with Osseointegrated Percutaneous Connections for Prosthetic Control.

Dingle, A. M., Ness, J. P., Novello, J., Zeng, W., Nemke, B., Sanchez, R., Lu, Y., Markel, M. D., Suminski, A. J., Williams, J. C., **Poore, S. O**.

Abstract Submitter	Aaron M. Dingle
Email Address	Dingle@surgery.wisc.edu
Classification	Associate Scientist
Principal Investigator	Samuel O. Poore
Science Type	Translational Research
Keywords	Peripheral nerve, neural interface, osseointegration

Introduction: Todays advanced prosthesis hold great potential for restoring function and improving quality of life for amputees. The patient's ability to control these devices with ease and precision is constantly improving; however, seamless control with sensory feedback remain futuristic goals. We have previously demonstrated proof of principal for interfacing with nerves transposed to the medullary canal of long bones to create an Osseointegrated Neural Interface (ONI). This method builds on the clinical translocation of nerves into bone to treat symptomatic amputation neuromas. **The objective** of our current research is to create a novel ONI, complete with percutaneous osseointegrated abutment for chronic bi-directional electrophysiology in rabbits

Methods: Above knee amputation was performed in New Zealand white rabbits. Briefly, the sciatic nerve was isolated and severed above the point of trifurcation. The femur was amputated at the midpoint and the nerve passed through a corticotomy. The terminal end of the nerve was sutured into a bipolar cuff electrode, and pressed back into the medullary canal. A second bi-polar cuff electrode was secured proximal to the corticotomy in order to stimulate and record efferent and afferent signals between the proximal and distal electrodes respectively. Both electrodes were connected to independent printed circuit boards (PCBs), which were intern secured to a stainless steel screw. The stainless steel screw served as both the osseointegrated and percutaneous portion of the ONI device. The muscle and skin were closed over the femur. Animals underwent electrophysiological recordings of compound nerve action potentials (CNAPs) at weeks 3, 5, 8 and 12 weeks under anesthesia, as well as terminal recordings of somatosensory evoked potentials (SSEPs) at week 12.

Results: Efferent signals can be generated from the proximal electrode and recorded from by the distal electrode from week 3 through to week 12. Moreover, efferent signals improve over the 12 week period, indicated by higher peak amplitudes achieved from lower stimulation over time. Afferent signals generated within the bone and recorded proximal to the corticotomy are not achieved prior to week 8, and improve at week 12. The writing of sensory information via an ONI is demonstrated by the ability to record SSEPs.

Conclusions: Chronic implantation of an ONI is entirely achievable and repeatable. Furthermore, physiological function of nerves transposed into bone improve over a 12 week period, including the ability to generate sensory signals to the cortex via an ONI.

T12

Evaluation of Neural Interfaces for Electrical Stimulation of the Rat Trigeminal Nerve

Ness J.P.[1], Suminski A.J.[1,2], Zeng W.[3], Novello J.[1], Brodnick S.K.[1], Pisaniello J.[1], Dingle A.[3], Poore S.O.[3], Lake W.B.[2], Williams J.C.[1,2]

Abstract Submitter	Jared Ness
Email Address	jness2@wisc.edu
Classification	Academic Staff
Principal Investigator	Justin Williams
Science Type	Translational Research
Keywords	Trigeminal Nerve Stimulation

Introduction: Over the past decade, electrical stimulation of various cranial nerves has been shown to be an effective adjunctive therapy for many diseases including epilepsy and depression. Furthermore, these techniques hold great promise to treat other conditions and modulate cognitive functions such as learning, memory and decision-making. While the vagus nerve has traditionally been the target of these therapies, recent preclinical data suggests that the trigeminal nerve may present an alternative option due to is superficial course and integration with the sympathetic and parasympathetic nervous systems. However, the mechanism of action trigeminal nerve stimulation (TNS) remains in question. In this work, we describe the development and evaluation of a neural interface targeting the rat trigeminal nerve with the goal of enabling future mechanistic research on TNS.

Methods: Fifteen (n=15) Lewis rats we used in experiments designed to: 1) identify the best stimulation target(s) for TNS in the rat and 2) evaluate the ability of a cuff electrode to stimulate the nerves. To evaluate the methodology to engage the branches of the trigeminal nerve, Lewis rats were anesthetized with isoflurane (1-2.5%) and implanted with a custom bipolar cuff electrode on the infraorbital nerve distal to the infraorbital foramen (1.5mm ID, 0.05mm wire diameter; n=5) or supraorbital nerve (0.75mm ID, 0.05mm wire diameter; n=5). Electrical stimulation was performed using single, monophasic or biphasic (cathode leading) pulses (50-800uA, 100-300us per phase) initiated at pseudorandom intervals (varying between 3-4 seconds). We measured changes in cortical activity in the barrel cortex elicited by infraorbital stimulation using a custom 16 channel uECoG array (200um site diameter, 500um inter-electrode spacing). Similarly, we measured changes in the orbicularis oculi electroromyogram elicited by infraorbital stimulation to verify engagement of the supraorbital nerve.

Results: Using fresh cadavers (n=5), we investigated the course and measured the size of each branch of the trigeminal nerve. We found that both the V1 (supraorbital) and V2 (infraorbital) branches were the best candidates for a neural interface to their accessibility and size (0.57 +/- 0.14 mm and 2.83 +/- 0.22 mm diameter, respectively). Stimulation in both the infraorbital and supraorbital nerves increased evoked activity monotonically until saturation with increases in stimulation current, while activation thresholds decreased with increases in phase duration.

Conclusions: These preliminary results suggest that supraorbital and infraorbital nerve interfaces are suitable candidates for examining the neural mechanisms of TNS in the rat.

T15

Direct Radiologic-Pathologic Correlation of Colorectal Liver Metastases with an MR-Compatible Sectioning and Localization Device

Rendell V.R., Colgan T.J., Knobloch G, Mühler M.R., Loeffler A.G., Agni R., Reeder S.B., Winslow E.R.

Abstract Submitter	Rendell, V.R.
Email Address	vrendell@uwhealth.org
Classification	Resident
Principal Investigators	Winslow, E.R Reeder, S.B.
Science Type	Translational
Keywords	Radiologic-Pathologic Correlation, Colorectal Cancer, *Ex vivo* imaging

Introduction: Patients with colorectal cancer liver metastases derive a significant survival benefit from resection. However, small (<1cm) radiologically-indeterminate lesions are problematic for surgical planning. Precise radiologic-pathologic correlation of small lesions would improve their radiologic characterization but has proved challenging. We aimed to establish the feasibility of our magnetic resonance (MR) imaging compatible sectioning device for precise correlation of radiologic lesions in resected liver specimens following intraoperative gadoxetic acid contrast administration.

Methods: Patients undergoing liver resection at UW Hospital were assigned to one of three gadoxetic acid contrast doses for *ex vivo* contrast optimization: 1) none; 2) 0.025 mmol/kg; and 3) 0.05 mmol/kg. Contrast was administered intraoperatively prior to vascular inflow ligation. Once removed, the liver specimen was stabilized in the sectioning device and transported to a 3T MR scanner where high-resolution T1-weighted fast spoiled gradient echo and T2-weighted fast-spin-echo MR images were acquired using a single channel quadrature head coil. Radiologic lesion coordinates were provided to pathology to guide sectioning, and a final histopathologic diagnosis was prepared for all lesions. Accuracy of lesion identification using this method was calculated.

Results: Ten patients enrolled in the study, of whom six have undergone liver resection with the following contrast doses administered intraoperatively: no contrast (n=1), 0.025 mmol/kg (n=2), and 0.05 mmol/kg (n=3). The patients who underwent resection had diagnoses of colorectal cancer (n=4), mucinous cystic neoplasm (n=1), and adrenocortical carcinoma (n=1). In total, 25 lesions were identified radiologically, of which 17 were <1cm. Overall, 24/25 (96%) of radiologically identified lesions corresponded to lesions identified pathologically. **Figure 1A-D** demonstrates the precise correlation during gross sectioning of a 0.3cm lesion identified on MR. Interestingly, three radiographically identified lesions were not identified at the time of gross sectioning but were subsequently identified histologically, one of which is shown in **Figure 1E-H**. All three of those lesions were <1cm. Contrast enhancement was visible for all specimens where contrast was administered, with 5 hours, 38 minutes as the longest time interval between contrast administration and MR imaging (minimum: 1 hour 59 minutes). With an average of 43min between contrast administration and inflow ligation, the 0.05 mmol/kg gadoxetic acid dose provided the best SNR and CNR averages (37 and 25, respectively).

Conclusions: Our *ex vivo* MR radiologic-pathologic correlation method is feasible and accurate for small liver lesion localization when incorporated into the clinical environment for liver resections. Intraoperative administration of gadoxetic acid resulted in adequate liver parenchymal enhancement on *ex vivo* imaging several hours later. This method can be used in further work to improve radiologic characterization of small indeterminate hepatic lesions in patients with colorectal cancer.

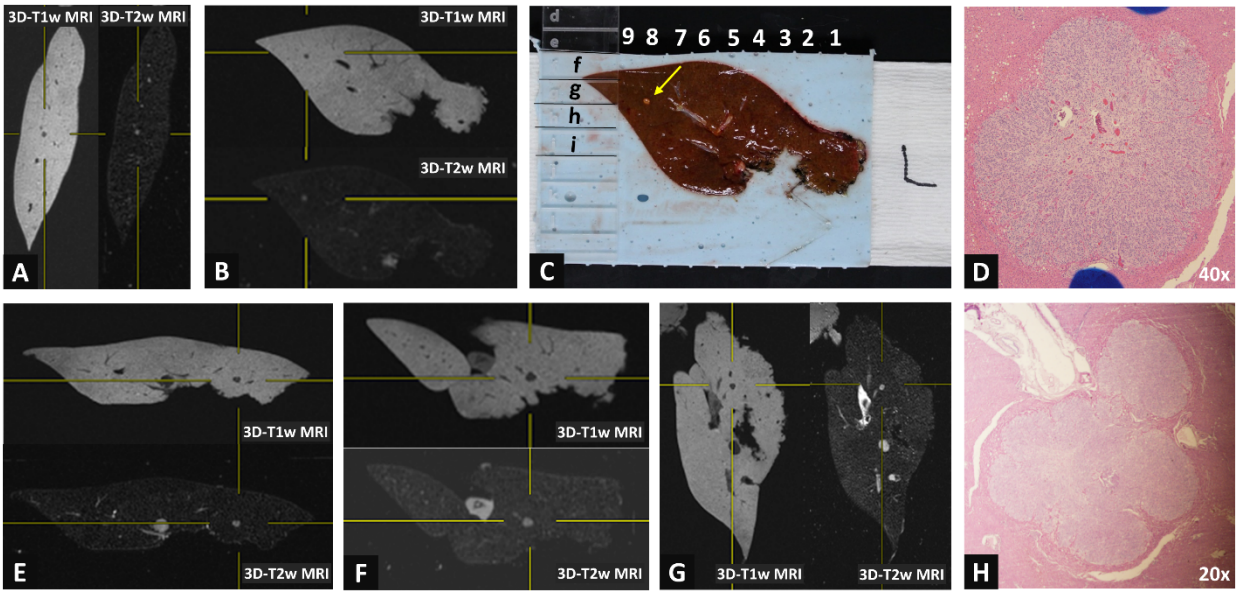


Figure 1. Accurate radiologic-pathologic correlation of small lesions using MR-compatible sectioning device. 3D T1- and T2-weighted MR images of a liver specimen stabilized in the study sectioning device following intraoperative administration of 0.05 mmol/kg gadoxetic acid (**A-B**) demonstrate a T1 hypointense and T2 hyperintense 0.3cm lesion located in radiologic coordinates L-M, f-g, 8-9, which was identified on gross sectioning (**C**) and by histological analysis (Haemotoxylin and Eosin staining shown in **D**). In the same patient, a 0.4 x 0.4 x 0.5cm lesion identified on sagittal (**E**), axial (**F**), and coronal (**G**) 3D T1- and T2-weighted MR images was not identified at the time of gross sectioning. However, on subsequent histological analysis of tissue corresponding to the radiographic coordinates, a 0.4cm lesion was identified (**H**). Both lesions were determined to be metastatic adrenocortical carcinoma.