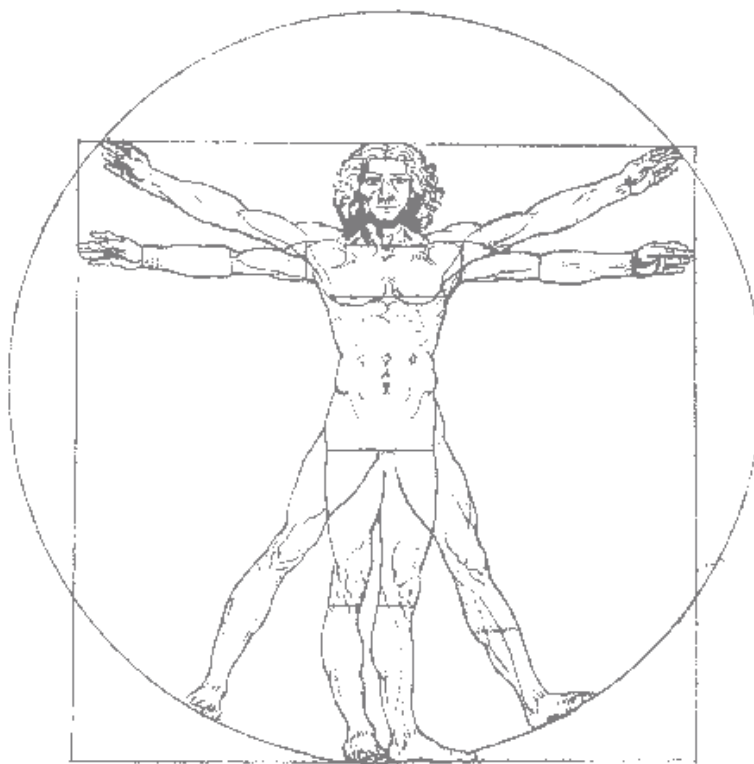


SURGICAL SCIENCES
Twenty-Ninth Annual
Residents' and Fellows'
RESEARCH DAY

WAKE FOREST SCHOOL OF MEDICINE



NOVEMBER 4, 2021

Research Day Chairperson

Reese Randle, MD



Wake Forest[®]
School of Medicine

In keeping with the mission of the School of Medicine to maintain extensive research programs, Surgical Sciences is proud to announce its 29th Annual Research Day. From its humble beginning in the early 1990's to the very large symposium of today, the Residents' and Fellows' Research Day has grown with the Surgical Sciences. This day is an opportunity to display and recognize the depth and breadth of research within Surgical Sciences; not only to our peers in the surgical departments, but to the entire population of the Medical Center.

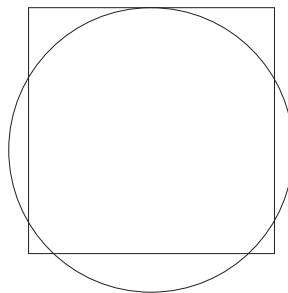
Students from both medical and graduate programs; residents, and fellows present data on activities, projects and applications which cover a broad spectrum ranging from the very basic to clinically applied research and the testing of innovative procedures or medications in patients. While the posters are presented by the trainees of Surgical Sciences, this is a celebration of the research carried out by residents, fellows, graduate students, medical students, Ph.D. researchers, surgeons and other dedicated research staff.



In recognition of the need to balance the dual goals of promoting effective scientific collaborations through open sharing of early stage results, on the one hand, and promoting commercialization in the public interest through intellectual property of research developments, on the other, the Surgical Sciences Research Day is conducted as a “closed meeting.” Accordingly, you acknowledge and agree that by participating in the event, you will receive and maintain any unpublished information or materials in confidence until such time as the information or materials are published or otherwise made publically available by the originating investigator.

SCHEDULE OF ACTIVITIES

- 11:30 am – 1:00 pm..... Set Up Posters
Commons Conference Rooms 1, 2, & 3
G and E Floor, Nutrition Center
- 1:00 pm – 2:00 pm..... Research Lecture
Rebecca Sippel, MD, FACS
“The Challenges of Running a Surgical
Clinical Trial: The Road to Success is an
Obstacle Course”
Babcock Auditorium
E Floor, Gray Building
- 2:00 pm – 4:00 pm..... Judging of Posters and Reception
Commons Conference Rooms 1, 2, & 3
G and E Floor, Nutrition Center



KEYNOTE SPEAKER



Rebecca Sippel MD, FACS
Professor of Surgery
Chief, Division of Endocrine Surgery
Vice Chair of Academic Affairs and Professional Development
University of Wisconsin-Madison

Rebecca Sippel, M.D., FACS, is a tenured Professor of Surgery, Chief of the Division of Endocrine Surgery, and Vice Chair of Academic Affairs and Professional Development at the University of Wisconsin. She is a nationally recognized leader in the field of endocrine surgery. She is currently serving as the program director for the Endocrine Surgery Fellowship at the University of Wisconsin. She is past Secretary of the American Association of Endocrine Surgeons and past President of Association for Academic Surgery. She has a highly productive clinical research program focusing on the diagnosis and management of patients with endocrine disorders and the outcomes of patients after surgery. She is currently PI on an R01 funded randomized controlled trial examining the utility of prophylactic central neck dissection for patients with clinically node negative thyroid cancer.

SURGICAL SCIENCES

DEPARTMENT CHAIRMEN:

- Edward H. (Ted) Kincaid M.D.Department of Cardiothoracic Surgery
J. Wayne Meredith, M.D.Department of General Surgery
Charles L. Branch, Jr., M.D.Department of Neurosurgery
Craig M. Greven, M.D.Department of Ophthalmology
L. Andrew Koman, M.D.Department of Orthopaedic
J. Dale Browne, M.D.Department of Otolaryngology
Lisa David, M.D.Department of Plastic and Reconstructive Surgery
Anthony Atala, M.D.Department of Urology
Matthew Edwards, M.D.Department of Vascular and Endovascular Surgery

RESEARCH DAY 2021 PLANNING COMMITTEE

HOST DEPARTMENT- GENERAL SURGERY

J. Wayne Meredith, M.D.Chair, Department of General Surgery
Reese Randle, M.D.Chairperson, Department of General Surgery
James Jordan, Ph.D.....Co-Chairperson, Department of Cardiothoracic Surgery

Committee Members

Lydia DurrHypertension & Vascular Research
Shanna J. Ellison.....Hypertension & Vascular Research
Jennifer Hinson.....Department of General Surgery
Kenya Little.....Hypertension & Vascular Research
Sarah P. Smith, C.A.P.....Hypertension & Vascular Research
Emily Southern.....Department of General Surgery
Pam Stafford.....Hypertension & Vascular Research

PAST KEYNOTE SPEAKERS

1993	Frank W. LoGerfo, M.D. Chief, Division of Vascular Surgery Harvard Medical School	2002	W. Randolph Chitwood, Jr., M.D. Professor and Chairman Department of Surgery East Carolina University School of Medicine
1994	James A. O'Neill, Jr., M.D. C. E. Koop Professor of Pediatric Surgery University of Pennsylvania School of Medicine	2003	L. D. Britt, M.D., M.P.H. Brickhouse Professor of Surgery Chairman, Department of Surgery Eastern Virginia Medical School
1995	James Patrick O'Leary, M.D. Isidore Cohn, Jr., Professor and Chairman, Department of Surgery LSU School of Medicine	2004	Arthur Kellermann, M.D., M.P.H. Professor and Chairman Department of Emergency Medicine Director, Center for Injury Control Rollins School of Public Health Emory University Atlanta, Georgia
1996	Joseph A. Smith, Jr., M.D. William M. Bray Professor and Chairman Department of Urologic Surgery Vanderbilt University School of Medicine	2005	James Urbaniak, M.D. Virginia Flowers Baker, Professor and Chair Emeritus Division of Orthopaedic Surgery Duke University Medical Center Durham, NC
1997	Robert Martuza, M.D. Professor and Chairman Department of Neurosurgery Georgetown University Hospital	2006	William D. Steers, M.D., F.A.C.S. Professor and Chairman Department of Urology University of Virginia Charlottesville, Virginia
1998	John M. Fredrickson, M.D. Professor of Otolaryngology Washington University School of Medicine	2007	Mitchell Berger, M.D. Professor and Chairman Department of Neurological Surgery Kathleen M. Plant Distinguished Professor Director, Brain Tumor Surgery Program University of California San Francisco
1999	Joseph E. Murray, M.D. 1990 Nobel Laureate in Medicine Professor Emeritus of Plastic Surgery Brigham and Women's Hospital Harvard Medical School	2008	Raphael Lee, M.D. Professor of Surgery (Plastic) Professor of Medicine (Dermatology) Professor of Organismal Biology and Anatomy Professor of Molecular Medicine University of Chicago Medical Center
2000	C. Thomas Caskey, M.D., F.A.C.P. President and C.E.O. Cogene Biotech Ventures		
2001	Elizabeth G. Nabel, M.D. Scientific Director, Clinical Research National Heart, Lung and Blood Institute National Institutes of Health		

PAST KEYNOTE SPEAKERS

2009	Alexander W. Clowes, M.D, Professor of Vascular Surgery V. Paul Gavor – Helen S. and John A. Schilling Endowed Chair in Vascular Surgery The University Washington	2017	Micheal T. Longaker, M.D, M.B.A., F.A.C.S. Deane P. and Louise Mitchell Professor and Vice Chair Co Director, Stanford Institute for Stem Cell Biology and Regenerative Medicine Director, Children’s Surgical Research Director, Program in Regenerative Medicine Professor, by Courtesy, of Bioengineering Professor, by Courtesy, Department of Materials Science and Engineering Stanford University School of Medicine Lucile Salter Packard Children’s Hospital
2010	Jonas T. Johnson, M.D. Professor of Otolaryngology Eugene N. Myers, M.D. Chair in Otolaryngology University of Pittsburg School of Medicine		
2011	Marco Zarbin, M.D., Ph.D., F.A.C.S. Professor of Ophthalmology & Visual Science The University of Medicine & Dentistry New Jersey Medical School	2018	Todd E. Rasmussen, M.D., F.A.C.S. Colonel USAF MC Harris B. Shumacker, Jr. Professor of Surgery Associate Dean for Research F. Edward Hébert School of Medicine Uniformed Services University
2012	Paul Sobotka, M.D., F.A.C.P., F.A.C.C. Professor of Medicine / Cardiology The Ohio State University Chief Medical Officer, Coridea-NC1		
2013	Vindo H. Thourani, M.D. Associate Professor of Surgery, Division of Cardidothoracic Surgery Department of Surgery Emory University School of Medicine.	2019	Andreas K. Lauer, M.D. Professor and Chair Department of Ophthalmology Oregon Health & Science Universtiy
2014	Regis J. O’Keefe, M.D., Ph.D. Professor and Chair Orthopaedic Surgery Washington University School of Medicine St. Louis, Missouri	2020	Ana H. Kim, M.D. Director, Cochlear Implant Program Associate Professor, Department of Otolaryngology/Head & Neck Surgery Columbia University Medical Center
2015	Ralph V. Clayman, M.D. Professor, Department of Urology Dean, Emeritus University of California, Irvine School of Medicine Irvine, California		
2016	Andres Lozano, M.D., Ph.D., FRCS, FRSC, FCAHS Professor and Chairman, Dan Family Chair in Neurosurgery RR Tasker Chair in Functional Neurosurgery Canadian Research Chair in Neuroscience (Tier 1) University of Toronto		

PREVIOUS AWARD RECIPIENTS

CLINICAL RESEARCH

GOLD MEDAL

1993 Tim Dersch, M.D.
Plastic and Reconstructive Surgery

1994 Raymond Poore, M.D.
Urology

1995 Preston R. Miller, M.D.
General Surgery

1996 L. Andrew Eskew, M.D.
Urology

1997 S. Iyer, Ph.D.
Hypertension Center

1998 Alan Burke, M.D.
Otolaryngology

1999 Charles J. Rosser, M.D.
Urology

2000 Gregory S. Cherr, M.D.
General Surgery

Dean DeRoberts, M.D.
Plastic Surgery
Resident

2001 Matthew S. Edwards, M.D.
General Surgery
Fellow

2002 Jonathan C. Hundley, M.D.
General Surgery
Resident

SILVER MEDAL

R. Bradley Thomasson, M.D.
General Surgery

Anthony Seaton, M.D., Ph.D.
Urology

L. Andrew Eskew, M.D.
Urology

John P. Little, M.D.
Otolaryngology

A. J. C. Burke, M.D.
Otolaryngology

Dom Coric, M.D.
Neurosurgery

Jonathon Deitch, M.D.
General Surgery

Todd R. Reulbach, M.D.
Otolaryngology

Sanford G. Duke, M.D.
Otolaryngology

Marc. M. Malek, M.D.
Plastic and Reconstructive Surgery

Steven D. Wray, M.D.
Neurosurgery
Resident

Tina Singh, M.D.
Ophthalmology
Fellow

Jeffrey McNeil, M.D.
CT Surgery
Fellow

CLINICAL RESEARCH continued

GOLD MEDAL

2002 Phillip S. Moore, M.D.
General Surgery
Resident

Claire Sanger, M.D.
Plastic and Reconstructive Surgery
Resident

James D. Maloney, M.D.
CT Surgery
Fellow

2003 J. A. Veys, M.D.
Urology
Resident

D. Wilson, M.D.
General Surgery
Fellow

2004 Catherine J. Rees, M.D.
Otolaryngology
Resident

Jeffrey A. Travis, M.D.
Cardiothoracic Surgery
Fellow

Annemarie Relyea-Chew, B.S.
Emergency Medicine
Student

2005 Dean DeRoberts, M.D.
Plastic and Reconstructive Surgery
Resident

Eric S. Gwynn, M.D.
Urology and Sticht Aging Center
Resident

Barnaby Dedmond, M.D.
Orthopaedics
Fellow

SILVER MEDAL

Michael R. Goins, M.D.
Otolaryngology
Resident

Matthew M. Mondy, M.D.
General Surgery
Resident

Jeffrey A. Travis, M.D.
General Surgery
Fellow

Jeffrey David Pearce, M.D.
General Surgery
Resident

David Cole, M.D.
Orthopaedics
Resident

Hiroshi Yokoyama, M.D.
Hypertension and Vascular Disease Center
Fellow

R. Shayn Martin, M.D.
General Surgery
Resident

Christina M. Plikaitis, M.D.
Plastic and Reconstructive Surgery
Resident

Graham Bundy, M.D.
Cardiothoracic Surgery
Fellow

CLINICAL RESEARCH continued

GOLD MEDAL

- 2006
Oliver Adrian Varban, M.D.
General Surgery
Resident
- Adrian Lata, M.D.
Cardiothoracic Surgery
Fellow
- 2007
Christina M. Plikaitis, M.D.
Plastic and Reconstructive Surgery
Resident
- Rajinder Singh, M.D.
General Surgery and Internal Medicine
Fellow
- Cheryl Onwuchuruba
Orthopaedics
Student
- 2008
Jeff Carter, M.D.
General Surgery
Resident
- Rajinder Pal Singh, M.D.
General Surgery
Fellow
- Joshua Matthew Cooper
Orthopaedic Surgery
Student
- 2009
Jeff Carter, M.D.
General Surgery
Resident
- Luke Neff, M.D.
General Surgery
Resident
- Phillip Moore, M.D.
Vascular and Endovascular Surgery
Fellow

SILVER MEDAL

- Daniel Barnes, M.D.
Emergency Medicine
Resident
- George D. Chloros, M.D.
Orthopaedic Surgery and Neurology
Fellow
- Matthew T. Cline
Orthopaedics
Student
- Ellen Chance Sanders, M.D.
Ophthalmology
Resident
- William Todd Stoeckel, M.D.
Plastic and Reconstructive Surgery
Resident
- Joe Gonzalez-Engle
Emergency Medicine
Student
- Christina M. Plikaitis, M.D.
Plastic and Reconstructive Surgery
Resident
- Rajinder Pal Singh, M.D.
General Surgery
Fellow
- Stephanie Lareau
Emergency Medicine
Student
- Jordan Wallin, M.D.
Otolaryngology
Resident
- Roche de Guzman, Ph.D.
Institute for Regenerative Medicine
Fellow

CLINICAL RESEARCH continued

GOLD MEDAL

- 2009 Kerry Danelson
Plastic Surgery
Student
- 2010 Robert D. Becher, M.D.
General Surgery
Resident
- Thomas Sarlikiotis, M.D.
Orthopaedics
Fellow
- Kevin Shamburg
Orthopaedics
Student
- 2011 Jade M. Nunez, M.D.
General Surgery
Resident
- Billy G. Chacko, M.D.
Vascular and Endovascular Surgery
Fellow
- W. Parker Abblitt, B.S.
Orthopaedic Surgery
Student
- 2012 Mark Witcher, M.D. / Ph.D.
Neurosurgery
Resident
- Billy G. Chacko, M.D.
Cardiology, Ophthalmology,
Cardiovascular Epidemiology
Fellow
- Richard Kao
Otolaryngology
Student

SILVER MEDAL

- Babak Yekta
Emergency Medicine
Student
- Jeffrey Carter, M.D.
General Surgery
Resident
- Jaehyun Kim, Ph.D.
Institute for Regenerative Medicine
Fellow
- Amber Campbell
Plastic Surgery
Student
- James T. O'Neil, M.D.
Otolaryngology
Resident
- Hamza Rana, M.D.
Vascular and Endovascular Surgery
Fellow
- Bronwyn Russell, B.S.
Orthopaedic Surgery
Student
- Tim Fife, M.D.
Otolaryngology
Resident
- JaNae Joyner, Ph.D.
Hypertension and Vascular Research Center
Fellow
- Wayne Chen
Orthopaedics
Student

CLINICAL RESEARCH continued

GOLD MEDAL

- 2013 Benjamin Schmidt, MD
Cardiothoracic
Resident
- Kelly Kempe, MD
Vascular and Endovascular
Fellow
- Ashley Wagoner, BS
Hypertension & Vascular Research Center
Student
- 2014 Andrea Doud, M.D.
General Surgery
Resident
- Alejandro Marquez-Lara, M.D.
Orthopaedics
Fellow
- Ashley Wagoner, B.S.
Hypertension and Vascular Research Center
Student
- 2015 Brian Bones, M.D.
Radiology
Resident
- Hany El-Hennawy, M.D.
Surgery - Transplant
Fellow
- Amber Carrier, Ph.D
Surgery - Transplant
Student

SILVER MEDAL

- Andrea Doud, MD
General Surgery
Resident
- Imran Choudhry, MD
Orthopaedics
Fellow
- Matthew Rohlfig, BS
Orthopaedics
Student
- Reese Randle, M.D.
General Surgery
Resident
- Mark Witcher, M.D.
Neurosurgery
Resident
- Hany El Hennawy, M.D.
General Surgery
Fellow
- Jia Hao Liang, B.S.
General Surgery
Student
- Ryan Rebowe, M.D.
Plastic and Reconstructive Surgery
Resident
- Bruce Chung, M.D.
General Surgery - Trauma
Fellow
- Ashley Wagoner, B.S.
Hypertension and Vascular Research
Student

CLINICAL RESEARCH continued

GOLD MEDAL

2016 Konstantinos Chouliaras, MD
General Surgery-Oncology
Resident

Nima Pourhabibi Zarandi, MD
Institute for Regenerative Medicine
Fellow

Hayden Holbrook, BS
Orthopaedic Surgery
Student

2017 Olivia Priest, MD
Plastic and Reconstructive Surgery
Resident

David Harriman, MD
General Surgery-Transplant
Fellow

Tyler Callese, BS
Radiology/Vascular and Interventional Radiology
Student

2018 Robert C. Siska, MD
Plastic and Reconstructive Surgery
Resident

David Harriman, MD
General Surgery-Transplant
Fellow

Mike C. Lin, BS
Cardiothoracic Surgery
Student

Lindsay Jones Allred, MD
Plastic and Reconstructive Surgery (Educational Science)
Resident

2019 Christine Velazquez, MD
Plastic and Reconstructive Surgery
Resident

SILVER MEDAL

Mija Khan, MD
Plastic and Reconstructive Surgery
Resident

Baha Alradawna, MD
General Surgery-Transplant
Fellow

Alexandra Goodwin, BS
Orthopaedic Surgery
Student

Konstantinos Chouliaras, MD
General Surgery-Oncology
Resident

Robert Ferguson, MD
Cardiothoracic Surgery
Fellow

Heather Barber, BS
Institute for Regenerative Medicine
Student

Konstantinos Chouliaras, MD
General Surgery-Oncology
Resident

Ioannis Kontopidis, MD
Cardiothoracic Surgery
Fellow

Tracey Pu, BS
Cardiothoracic Surgery
Student

Suman Medda, MD
Orthopaedic Surgery
Resident

CLINICAL RESEARCH continued

GOLD MEDAL

2019 Adam Campman Nelson, MD
General Surgery
Fellow

R. Andrew Hesse, BS
Surgery-Ophthalmology
Student

Thomas N. Steele, MD
Plastic and Reconstructive Surgery (Educational Science)
Resident

2020 Mija Khan, MD
Plastic and Reconstructive Surgery
Resident

Christine Velazquez, MD
General Surgery
Fellow

Vanessa Lukas, BA
General Surgery-Urology
Student

SILVER MEDAL

David Hobson, MD
Cardiothoracic Surgery
Fellow

Harper Wilson, BS/BA
Otolaryngology
Student

Jungwon Park, MD, PhD
Plastic and Reconstructive Surgery
Resident

Shiny Rajan, PhD
Institute for Regenerative Medicine
Fellow

Ishetta Madeka, BA
General Surgery-Oncology
Student

BASIC RESEARCH

GOLD MEDAL

- 1993 Dudley Hudspeth, M.D.
Cardiothoracic Surgery
- 1994 David Pollock, M.D.
Orthopaedic Surgery
- 1995 James Jordan, B.S.
Cardiothoracic Surgery
- 1996 Stephen Troum, M.D.
Orthopaedic Surgery
- 1997 David Major, M.S.
Plastic and Reconstructive Surgery
- 1998 Wade J. Sexton, M.D.
Urology
- 1999 Jung-Soo Kim, M.D.
Otolaryngology
Dickson Schaeffer, M.D.
Orthopaedic Surgery
- 2000 D. Nicole Deal, M.D.
Orthopaedic Surgery
- 2001 Claire Sanger, D.O.
Plastic Surgery and Reconstructive Surgery
Resident
- LioMar A. Alvarez, Ph.D.
Hypertension & Vascular Research Center
Fellow
- 2002 Cassandra A. Lee, M.D.
Orthopaedic Surgery
Resident
- Atsushi Sakima, M.D.
Hypertension & Vascular Disease Center
Fellow

SILVER MEDAL

- Ibrahim Benter, Ph.D.
Hypertension and Vascular Research Center
- Virginia Newman, M.D.
General Surgery
- Xiao Wei Lu, M.D.
Hypertension and Vascular Research Center
- Robert D. Riley, M.D.
General Surgery
- Zhongyu Li, M.D.
Orthopaedic Surgery
- Timothy Oskin, M.D.
General Surgery
- M. Todd Kirby, Ph.D.
Neurosurgery
- Cassandra Lee, M.D.
Orthopaedic Surgery
Resident
- Tina Singh, M.D.
Neurobiology & Anatomy
Fellow
- Jason A. Castle, M.D.
Orthopaedic Surgery
Resident
- Ojas Shah, M.D.
Urology
Fellow

BASIC RESEARCH continued

GOLD MEDAL

- 2002 Jason Hong
Hypertension & Vascular Disease Center
Student
- 2003 Cassandra Lee, M.D.
Orthopaedic Surgery
Resident
- R. Richmond, Ph.D.
Hypertension & Vascular Disease Center
Fellow
- P. Garabelli
Hypertension & Vascular Disease Center
Student
- 2004 Jian Shen, M.D., Ph.D.
Orthopaedic Surgery
Resident
- Anastasios Papadonikolakis, M.D.
Orthopaedic Surgery
Resident
- Michiya Igase, M.D.
Hypertension and Vascular Disease Center
Fellow
- David R. Soto-Pantoja, B.S.
Hypertension and Vascular Disease Center
Student

SILVER MEDAL

- Jing Li
General Surgery
Student
- Matt Camp
Plastic Surgery
Student
- G. A. Elsaidi, D.O.
Orthopaedic Surgery
Resident
- A. Sakima, M.D.
Hypertension & Vascular Disease Center
Fellow
- Stevco Stefanoski
Otolaryngology
Student
- L. Anton
Hypertension & Vascular Disease Center
Student
- Jill Wykosky, B.S.
Neurosurgery
Resident
- Liliya M. Yamaleyeva, M.D.
Hypertension and Vascular Disease Center
Fellow

BASIC RESEARCH continued

GOLD MEDAL

- 2005
- Matthew Bolinger, M.D.
Otolaryngology
Resident
- Yagna Jarajapu, Ph.D.
Regenerative Medicine
Fellow
- Jill Wykosky, B.S.
Neurosurgery
Student
- Steven J. Newton
Hypertension and Vascular Disease Center
Student
- Benjamin C. Wood
Plastic and Reconstructive Surgery
Student
- 2006
- Patrick William Whitlock, M.D., Ph.D.
Orthopaedic Surgery and
Wake Forest Institute for
Regenerative Medicine
Resident
- Pedro Miguel Baptista, M.D.
Wake Forest Institute of
Regenerative Medicine
Fellow
- Jyotsana Menon
Hypertension and Vascular Disease Center
Student
- Jill Wykosky
Neurosurgery and Radiation Oncology
Student

SILVER MEDAL

- Cassandra Lee, M.D.
Orthopaedic Surgery
Resident
- Normann B. Cabrera, M.D.
Orthopaedic Surgery
Fellow
- William Frazier, M.D.
Otolaryngology and
Wake Forest Institute for
Regenerative Medicine
Resident
- Tao Xu, M.D.
Wake Forest Institute of
Regenerative Medicine
Fellow
- Maxwell Kenneth Langfitt
Orthopaedics
Student

BASIC RESEARCH continued

GOLD MEDAL

- 2007
- Peter J. Apel, M.D.
Orthopaedics
Resident
- Enzo S. Palma, M.D.
Neurosurgery and Radiation Oncology
Fellow
- Jill Wykosky
Neurosurgery
Student
- 2008
- Patrick W. Whitlock, M.D.
Orthopaedic Surgery
Resident
- Pedro M. Baptista, M.D.
Regenerative Medicine
Fellow
- Hetal Pandya
Neurosurgery
Student
- 2009
- Hossam Shaltout, Ph.D.
Hypertension & Vascular Research Center
Resident
- Benjamin Corona, Ph.D.
Regenerative Medicine
Fellow
- Kyle Binder
Regenerative Medicine
Student

SILVER MEDAL

- Katheryne J. Stabile, M.D.
Orthopaedics and WFIRM
Resident
- George Chloros, M.D.
Orthopaedics
Fellow
- Jyotsana Menon
Hypertension
Student
- Andy Stevens, M.D.
Neurosurgery, Infectious Disease & Pathology
Resident
- Bryan Tillman, M.D.
Regenerative Medicine &
Vascular & Endovascular Surgery
Fellow
- David Ricardo Soto-Pantoja
Hypertension & Vascular Research Center
Student
- Luke Neff, M.D.
Regenerative Medicine
Resident
- TanYa Gwathmey, Ph.D.
Hypertension & Vascular Research Center
Fellow
- Katherine Cook
Hypertension & Vascular Research Center
Student

BASIC RESEARCH continued

GOLD MEDAL

- 2010 Sandeep Mannava, M.D.
Orthopaedics
Resident
- Roche de Guzman, Ph.D.
Regenerative Medicine
Fellow
- Carla Maria Lema Tome, Ph.D.
Neurosurgery
Fellow
- Hetal Pandya
Neurosurgery
Student
- 2011 Kyle David Wood, M.D.
Urology
Resident
- Wenhong Chen, M.D., Ph.D.
Neurosurgery
Fellow
- Van T. Nguyen
Neurosurgery
Student
- 2012 Austin Stone, M.D.
Orthopaedic Surgery
Resident
- Christopher MacNeil, Ph.D.
Plastic and Reconstructive Surgery
Fellow
- Elizabeth Miller
Cardiothoracic Surgery
Student

SILVER MEDAL

- Luke Neff, M.D.
General Surgery
Resident
- Manisha Nautiyal, Ph.D.
Hypertension & Vascular Research Center
Fellow
- Shantaram Bharadwaj, Ph.D.
Institute for Regenerative Medicine
Fellow
- Van Nguyen
Neurosurgery
Student
- Charles Peyton, M.D.
Institute for Regenerative Medicine
Resident
- Christopher M. MacNeill, Ph.D.
Plastic and Reconstructive Surgery
Fellow
- Amanda Beauchamp
Neurosurgery
Student
- Reese Randle, M.D.
General Surgery
Resident
- Norihito Moniwa, M.D.
Hypertension and Vascular Research Center
Fellow
- Tabitha Rosenbalm
Plastic and Reconstructive Surgery
Student

BASIC RESEARCH continued

GOLD MEDAL

- 2013 Mark Witcher, M.D., Ph.D.
Neurosurgery
Resident
- Sara Ferluga, Ph.D.
Neurosurgery
Fellow
- Rui Wang
Plastic and Reconstructive Surgery
Student
- 2014 Austin Stone, M.D., Ph.D.
Orthopaedics
Resident
- Tabitha Rosenbalm, Ph.D.
Plastic and Reconstructive Surgery
Fellow
- Elizabeth Graham, B.S.
Plastic and Reconstructive Surgery
Student
- 2015 Alejandro Marquez-Lara, M.D.
Orthopaedic Surgery
Resident
- Hooman Sadri-Ardekani, M.D., Ph.D.
Wake Forest Institute for Regenerative Medicine
Fellow
- Eleanor McCabe-Lankford, B.S.
Plastic and Reconstructive Surgery
Student

SILVER MEDAL

- Daniel Bracey, M.D.
Orthopaedics
Resident
- Christopher MacNeil, Ph.D.
Plastic and Reconstructive Surgery
Fellow
- Alison Arter
Hypertension and Vascular Research Center
Student
- Cara Lorentzen, M.D.
Orthopaedics
Resident
- Ian Hutchinson, M.D.
Orthopaedics
Fellow
- Bryce Robinson, B.S.
Cardiothoracic Surgery
Student
- W. Keith Ballentine III, M.D.
Urology
Resident
- Joao Paulo Zambon, M.D., Ph.D.
Wake Forest Institute for Regenerative Medicine
Fellow
- Guorui Deng, B.S.
Hypertension and Vascular Research
Student

BASIC RESEARCH continued

GOLD MEDAL

- 2016 Benyam Yoseph, MD
Institute for Regenerative Medicine
Resident
- Guillermo Galdon, MD
Institute for Regenerative Medicine
Fellow
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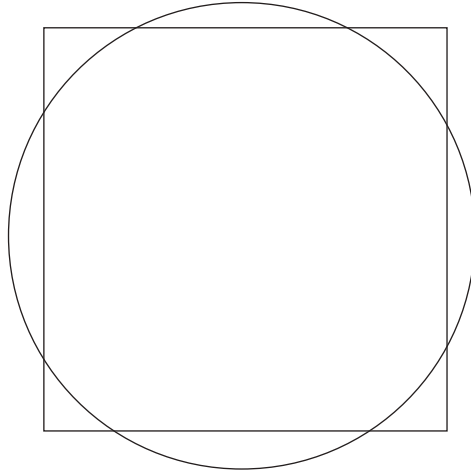
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1. Endocrine-Targeted Therapy and Diet Interactions on Gut Permeability and the Microbiome

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Background: Studies implicate the gut microbiome as a risk factor for estrogen receptor-positive (ER+) breast cancer and a factor modifying therapeutic response. Alterations in gut microbial composition associated with obesity result in increased intestinal permeability and elevated LPS bioavailability. We propose oral endocrine-targeting therapies may differentially affect gut microbiome populations in mice consuming a healthy or western diet to affect intestinal permeability mediating chronic low-grade inflammation, leading to tumor recurrence. Methods: 6-week-old female C57BL/6 mice were placed on a healthy control (HC; 21% kcal from fat derived from olive oil and fish oil) or a Western diet (45% kcal from fat derived from corn oil, lard, milk-fat) for 6 weeks. They were randomized based on body fat composition into 6 groups: HC, HC+tamoxifen (TAM; 37 ppm tamoxifen citrate), HC+aromatase inhibitor (AI; 5 ppm letrozole), Western diet, Western+TAM and Western+AI. Body weight measurements, glucose tolerance test (GTT), intestinal permeability assays, plasma LPS ELISA, immunohistochemistry (IHC) and fecal metagenomics sequencing were performed. Results: Increases in body weight and body fat composition were significantly different across groups. In the GTT, Western+AI had higher fasting blood glucose and area-under-the-curve. Intestinal permeability measurements indicate endocrine therapies alter intestinal permeability, with plasma LPS and FITC dextran displaying decreasing trends with endocrine therapy. Ultrasound colon thickness measurements were increased in Western plus endocrine therapy. Differences in microbiota and phage populations with endocrine therapy demonstrate oral endocrine therapies differentially shift *Lactobacillus* and *Lactococcus* populations. Conclusions: Our study indicates oral endocrine therapies affect the gut microbiome and intestinal permeability that are sensitive to dietary-influenced baseline microbiota populations, which result in differential drug metabolic outcomes. Future studies modifying gut *Lactobacillus* abundance in ER+ tumor bearing mice will be performed to determine relevance of this population modifying anti-cancer tamoxifen efficacy.

2. Harnessing the Microbiome to Impact Chemotherapeutic Responsiveness in Triple Negative Breast Cancer

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Triple negative breast cancer (TNBC) is highly aggressive subtype with a 5-year survival rate significantly worse when compared to other breast cancers types. Furthermore, there are no targeted therapy options, limiting these patients to cytotoxic chemotherapy regimens. Increasing evidence show the strong correlation between gut microbiota and the development of many diseases including breast cancer. Moreover, gut microbiota populations are highly plastic, shifting in response to diet changes, drug administration, and geographical location. The purpose of our study was to determine whether chemotherapy modifies the gut microbiota populations and whether ablation of the microbiome modifies drug responsiveness. To do so, 8-week old female BALB/c mice were injected with 4T1-luciferase TNBC cells into the mammary fat pad. Once tumors reached 100 mm³, mice were either untreated (control group), treated with 1x weekly 2.5 mg/kg doxorubicin (Dox) for 4 weeks, or treated with Dox + antibiotics (mixture of streptomycin, ampicillin, and colistin in the drinking water to ablate the microbiome) and the fourth group are treated with only antibiotics cocktail in their drinking water. Fecal samples were collected at T0 (before treatment) and T4 (after treatment). Mice from Dox +antibiotics group displayed reduced tumor weight and decreased lung metastatic burden, suggesting presence of gut microbiome modifies chemotherapy efficacy. Metagenomics analysis of fecal samples showed no bacterial microbiome detected in antibiotics treated groups. Doxorubicin treatment modulated the diversity and abundance of many bacterial species including increase in *Akkermansia muciniphila*, *Alistipes shahii*, *Prevotella copri*, and *Bacteroides vulgatus*. Doxorubicin treatment affected some bacterial species that were used as probiotics including reduced *Bacteroides uniformis*, *Lactobacillus johnsonii* and increased *Bifidobacterium longum* abundance. Furthermore, doxorubicin only treated group was stratified into responders and non-responders according to tumor growth over time, and metagenomics data showed elevated proportional abundance in *Alistipes shahii*, *Bacteroides vulgatus* in responders post treatment. On the other side, non-responders showed increase in *Enterococcus faecalis* and reduction in *Bacteroides cellulosilyticus* bacterial species post treatment.

These modulations in gut microbiota were associated with intestinal inflammation changes in villi length, muscularis layer thickness and goblet cells counts. Taken together, our data demonstrates that ablation of gut microbiota using antibiotics along with chemotherapy treatment may show better outcomes than using doxorubicin. Moreover, systemic treatment with chemotherapeutic agents can modulate gut microbiota composition suggesting that fecal microbiota populations could be used as a predictive biomarker of chemotherapeutic responsiveness and modulation of the gut microbiota through dietary, antibiotics or probiotic interventions may affect therapeutic efficacy.

3. Frontal bossing is the longest standing descriptor of the morphology of patients with sagittal craniosynostosis

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PURPOSE: Frontal bossing is the longest standing descriptor of the morphology of patients with sagittal craniosynostosis. Attempts have been made to objectively quantify bossing; however, none have used imaging that can be easily obtained without radiation exposure. As a result, most clinical descriptions of preoperative and postoperative frontal bossing remain subjective.

METHODS: Clinical computed tomographic scans and 3D stereophotograms of 415 patients with sagittal craniosynostosis and 220 normal patients ranging in age from 0 to 72 months taken between 2013-2019 were used to create 3D models. Ten equidistant axial and sagittal planes were created for each individual, and a Cartesian grid was created from the intersection of these planes across the cranial surface. The distances between the 42 points of intersection found to overlay the forehead and the mid-coronal plane were analyzed in order to quantify the difference in forehead protrusion between the two populations.

RESULTS: In patients with sagittal craniosynostosis, increased protrusion was seen at all points on the forehead with the greatest differences present at the superior and lateral aspects. By using the point of maximum protrusion and the change in protrusion in the superior and horizontal directions an objective frontal bossing index can be measured.

CONCLUSIONS: The frontal bossing index (FBI) will allow for objective quantification frontal severity in patients with sagittal craniosynostosis using only 3D photography or surface laser scanners, making the FBI available to nearly all clinicians. This will guide surgical decision making and allow for greater accuracy in analyzing and comparing operative outcomes.

4. Balloon Occlusion Cholangiography and Sphincteroplasty Catheter-An Novel Device for Performing Laparoscopic Balloon Sphincteroplasty

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Background: Choledocholithiasis can be managed safely by either laparoscopic cholecystectomy (LC) with pre-/post-operative endoscopic retrograde cholangiopancreatography (ERCP) or LC with intraoperative laparoscopic common bile duct exploration (LCBDE). LC + LCBDE has the advantage of being a one-step, one-anesthetic process. This technique has decreased in utilization over the past decade in the United States. At Wake Forest, we have piloted a stepwise technique to perform balloon sphincteroplasty as a simple LCBDE adjunct. This has prompted adoption by both the acute care surgery and pediatric surgery services. Implementation of the technique has allowed for identification of opportunities for improvement and innovation. In response to this, a novel device was designed by the surgical team to allow for both balloon occlusion cholangiography and balloon sphincteroplasty with a singular catheter. After a prototype was built, a proof of concept trial was performed in a pig animal model. **Methods:** The balloon occlusion cholangiography and sphincteroplasty prototype was designed by the surgical team. Beacon Launch Partners produced the prototype. The catheter allows for a cholangiogram to be performed through the lumen of the catheter for the identification of common bile duct stones. The advantage of this system is that the distal tip of the catheter has a round balloon which can be inflated to seal the common

bile duct. This allows for pressurization of the bile duct distally when performing the cholangiogram and attempting to flush stones forward. If pressurized flushing is unsuccessful, the distal balloon can be deflated and the proximal elongated proximal balloon can be advanced to straddle the sphincter. Once the proximal balloon is in position, it can be inflated to dilate the sphincter which should facilitate stone clearance. After dilation, the smaller distal balloon can once again be utilized to seal the duct and flush stones forward into the duodenum. All of these steps can be performed sequentially without the need for any device exchange. This prototype device was tested in a pig animal model in which peanuts were inserted into the common bile duct to act as common bile duct stones. Clearance of the duct was attempted with the novel device. Results: Initial fluoroscopy demonstrates the “stones” (peanuts) in the common bile duct of the animal. The common bile duct is sealed with the distal balloon and a subsequent cholangiogram is performed with pressurized flushing. The sphincter is dilated by the more proximal elongated balloon. After dilation the proximal balloon is deflated and the catheter is withdrawn. The distal balloon re-creates a seal for final cholangiogram/power flushing. The “stones” have been noted to flush forward into the duodenum. Conclusions: The balloon occlusion cholangiography and sphincteroplasty catheter is a novel device that allows for performing a cholangiogram, pressurized flushing of the CBD, and dilation of the sphincter without any instrument changes. It has been determined to be successful in clearance of common bile duct stones in an animal model and may prove to be helpful in an operative setting.

5. A Novel Suturing Trainer for Medical Students

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Purpose:

Suture training is a critical component of the medical school curriculum, as it serves as the first opportunity to learn proper technique. For those students who enter surgical specialties such as plastic surgery, early and repetitious practice is crucial in developing competence for residency. Currently, the majority of medical schools in the United States utilize suture training tools such as porcine feet or sponges to simulate human tissue. At our institution, satisfaction survey data has indicated dissatisfaction with the accessibility, quality, and longevity of these materials. Herein, the purpose of this project is to devise a novel tool for suture training using medical grade silicone and a three dimensional (3D) printed stencil to create life-like, standardized tissue defects.

Methods:

Using 3D printing, a 10cm x 5cm x 2cm mold was developed. Via Blender software, tissue defects of varying depths, shapes, and sizes were included in the design. Different textures of silicone were poured into the mold and dyed with pigment to simulate the layers of skin, fat, and muscle. Plastic surgeons were consulted on material textures and layer depths. Study outcomes included a thirty-question survey given to fourth year medical students following a thirty minute practice session with the silicone device. Questions measured texture characteristics and similarity of suture material to human tissue on a scale from 1 to 5 (5 being identical to human tissue). Additionally, the survey assessed limitations with current suture training models, and impression of this novel device’s educational utility.

Results:

Twenty five fourth years participated in the study. All (n=25) had sutured on human tissue an average of 46.0 (SD: 66.0) times. Additionally, all participants had sutured on porcine feet and sponges. The most common barriers to self-directed suturing practice were accessibility to material (n=23) and material longevity (n=20). The mean score for the silicone pad’s tissue layers (4.20, SD: 0.5) and “feel” (4.36, SD: 0.64) was significantly higher (p<.0001) than those for porcine feet (2.52, SD 1.00 and 2.48, SD: 0.87 respectively) and sponges (1.21, SD: 0.51 and 1.38 SD 0.65, respectively). Upon assessment of varying suturing techniques on each material, the mean score for the silicone pad’s interrupted sutures (4.56, SD: 1.411) running sutures (4.30, SD 0.62), and knot tying (4.44 SD: 0.711) was significantly higher (p<.0001) than those for porcine feet (3.08, SD: 1.04; 2.16, SD: 0.85; and 3.36, SD: 0.95 respectively) and sponges (1.75, SD: 0.85; 1.66, SD: 0.816; and 2.04, SD: 0.99 respectively). All (n=25) participants stated that the silicone suture pad was the best tool to practice suturing, and 92% (n=23) stated that their suture skills would be better or much better if the silicone pads replaced porcine feet and sponges.

Conclusion:

Preliminary survey data demonstrate that the silicone suture pad generated with a 3D printed stencil serves as a mobile, cost-effective, and realistic training tool. This suturing training device has been introduced into the Wake Forest surgical training curriculum, and an IRB has been submitted to follow longitudinal student improvement as a result of exposure to this suturing device over time.

6. A Cost analysis of Transmetatarsal Amputation Postoperative Wound Complications

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Background: The purpose of the current study is to identify the cost associated with transmetatarsal amputation (TMA) flap healing complications. Methods: Utilizing CPT codes, all TMAs performed in the Wake Forest Baptist Medical Health System (WFBHS) between January 1, 2015 and January 1, 2020 were identified. Inclusion criteria includes TMAs which achieved an entirely closed skin envelope at time of surgery. Exclusion criteria include TMAs without adequate follow up or those which underwent fluorescence angiography. Costs were calculated by analyzing the facility location, number of days hospitalized, reoperation rates, additional procedures performed, and prosthesis costs in 1 year from index TMA. Results: 87 patients and 90 TMAs met criteria for enrollment in this cohort. Of the 90 TMAs performed, 43% (39/90) healed with intact skin envelope at 1 month postoperatively. Of the TMA patient population 21% (19/90) had a partial thickness wound and 33% (30/90) had a full thickness wound at 1 month postoperatively. Patients with a healed TMA at one month postoperatively were admitted for an average of 6.5 days in the one year following a TMA including index admission. Patients with full thickness postoperative wounds were admitted for an average of 22.6 days in the same one-year period. Patients with healed TMA at one month postoperatively had 0 reoperations. Patients with full thickness postoperative wound healing complications experienced an average of 1.3 revision procedures. The average 1 year cost of TMA was 25,745 USD. The average cost of a TMA which healed at the one-month mark was 15,914 USD. The average 1 year cost of TMA with a full thickness wound was \$44,015 ($p < 0.00001$). Conclusion: Complications from transmetatarsal amputations are common and significant causes of patient morbidity and mortality. In our data set full thickness wound dehiscence increases the likelihood of readmission and reoperation. The authors theorize efforts to reduce wound healing complications associated with TMA may decrease postoperative complications and cost to the healthcare system through fewer readmissions and fewer limb salvage procedures.

7. Blockade of CD47/Thrombospondin-1 signaling Modulates Cellular Energetics as a Protective Mechanism from Chemotherapy-Induced Cardiac Injury

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Advances in early detection and treatment have led to a decrease in cancer-related mortality; consequently, by the year 2030, there will be over 20 million cancer survivors in the United States. Anthracycline-based treatment regimens are currently essential for managing triple-negative breast cancer. Patients treated with doxorubicin (DOX) often exhibit cardiovascular morbidity due to cumulative dose-dependent cardiotoxicity. Novel strategies are needed to overcome anthracycline-induced cardiotoxicity in the increasing number of breast cancer survivors. Activation of the CD47/Thrombospondin-1 (TSP1) signaling axis impacts the progression of heart failure with reported increased TSP1 levels following myocardial infarction. Therefore, we examined the potential of CD47 blockade as a strategy to prevent cardiac injury as a consequence of cancer chemotherapy. CD47 is a transmembrane protein that plays a role in cell fate during cellular stress through its interaction with TSP1 (Figure 1). Our data in a syngeneic orthotopic breast cancer model shows that CD47 blockade using an in vivo anti-sense phosphodiesterase morpholino (PMO) preserved ejection fraction, fractional shortening, and cardiac output when compared to DOX treatment. RNA sequencing was performed on the hearts of control and CD47 PMO-treated mice to determine a potential cardioprotective mechanism. Gene set enrichment analysis (GSEA) showed significant positive enrichment for metabolic pathways including pyruvate metabolism (NES= 2.3, $p < 0.002$), fatty acid oxidation (NES= 2.53, $p < 0.003$), oxidative phosphorylation (NES=2.0, $p < 0.01$) while negative enrichment was observed in

pathways related to cytokine receptor interaction (NES= -2.2, p<0.002) and extracellular matrix receptor (ECM) interaction (NES= -2.6, p<0.05). During cardiac insult, metabolic flexibility of cardiomyocytes results in metabolic reprogramming from fatty acid oxidation to a glycolytic mechanism to overcome injury. Thus, DOX-associated cardiotoxicity may be mediated by an increase in TSP1 and a decrease in glycolysis, leading to the inability to overcome acute cellular stress. In-vitro cellular bioenergetics analysis revealed that TSP1 caused a dose-dependent reduction in glycolytic flux and glycolytic capacity in cardiac cells. This analysis, coupled with preserved cardiac cell viability in cells treated with CD47 PMO in the presence of DOX, suggests that TSP1 may act through CD47 to prevent cardiac cell metabolic reprogramming needed to overcome injury. Overall, our studies suggest that the TSP1/CD47 axis may be central to the interplay of ECM proteins and metabolism to preserve cardiac tissue integrity; thus, targeting this pathway may prevent the onset of chronic cardiac disease due to chemotherapy in cancer patients.

8. Pre-Pectoral Breast Reconstruction Learning Curve: A Single Institution Retrospective Study

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Introduction and Background We hypothesize a learning curve exists with pre-pectoral breast reconstruction technique. This study aims to compare the outcomes of pre-pectoral breast reconstructions at our institution.

Methods After IRB approval, we completed a retrospective analysis of all pre-pectoral breast reconstructions. Breasts were divided into first 75 and last 75 completed pre-pectoral reconstructions. Statistical measures were used to compare means and categorical variables.

Results From 2016 to 2020, 92 patients, and 164 breasts underwent mastectomy and subsequent pre-pectoral breast reconstructions. Pre-pectoral breast reconstruction has become utilized more frequently in our practice. Age, BMI, comorbidities, and mastectomy techniques were not different between groups. Pre-pectoral techniques involved placement of ADM.

We significantly increased the amount of direct to implant reconstructions performed (p<0.0005)

When comparing prosthetic failure, in the first group of 75 breasts there was an expander loss rate of 19.7% and implant loss rate of 14.5%. In the last group of 75 breasts, expander loss rate 14.5% and implant loss rate 9.2%, not statistically significant between groups

Conclusions: Our data suggest that there is a learning curve effect present in our ability to identify patients suitable for immediate or delayed direct to implant reconstruction. Additionally, there is a trend toward reduction in prosthetic failure. We demonstrated significant practice transition to pre-pectoral breast reconstructions with improving complication profile.

9. Impact of COVID-19 Pandemic On Breast Cancer Screening and Operative Treatment

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The COVID-19 pandemic has impacted many areas of healthcare and had significant impact on care delivery. On March 26, 2020, a joint statement by the American Society of Breast Surgeons (ASBrS) and American College of Radiology (ACR) recommended that all medical facilities postpone all breast screening exams immediately due to concerns of mortality of coronavirus outweighing any potential mortality from a delay in screening. To better understand the changes to detection and treatment of breast cancer at our institution, Wake Forest Baptist Health (WFBH), we analyzed mammogram rates (screening as well as diagnostic) and breast cancer operations between 2019 to 2020. From 2019 to 2020, we analyzed retrospective data of mammograms from the Radiology Department as well as breast cancer operations at WFBH. Due to potential overlap between the two samples with regards to mammography, comparative analysis with relative and absolute differences were utilized. Proportion comparison with Z-score was utilized based on NC Census data for women eligible for mammogram screening (age 40-74) in Forsyth County, NC. For comparison of breast cancer stage, a breast

cancer stage severity score was formulated and statistical analysis was performed with Mann-Whitney U-test (two-tail, $p < 0.05$). Proportion analysis was compared to overall WFBH operative volume per public quarterly reports. Data obtained from mammography revealed a relative decline from 2019 to 2020 in breast cancer screening. Screening mammograms decreased by 44% or 1558 fewer screening mammograms ($Z = 4.75$, $p < 0.00001$) and by 21% or 771 fewer for diagnostic mammograms ($Z = 2.16$, $p = 0.03$). With regards to breast cancer operations, we did not identify a statistically significant difference in number of new breast cancer operations at WFBHMC with 340 in 2020 as compared to 384 in 2019 ($p = 0.9905$). We compared a breast cancer stage severity score (weighted by stage at time of operation) which did not reveal statistically significant difference in stage of breast cancer at time of operation ($p = 0.71$, $U = 28$). Mammography was impacted more than breast surgery cases by the COVID-19 pandemic in our current analysis. More data needs to be collected in order to evaluate future impact on morbidity and mortality related to breast cancer operations. Future analysis examining impact over time will look at any persistent disparities related to delay in breast cancer care due to COVID-19.

10. Trabeculectomy Revision via Needling Augmented with Sub-conjunctival Mitomycin

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Purpose / Relevance:

Trabeculectomy has been a common glaucoma surgery for many years. As such, the glaucoma specialist sees many patients who have had trabeculectomy which has failed over the years due to scarring. In these patients, low IOP may be obtained by a relatively non-invasive needling technique, re-opening an outflow pathway through scar tissue. This study suggests that needling may be preferable to more invasive, higher-risk surgical options.

Methods:

This is a retrospective chart review of all patients who had trabeculectomy revision via needling augmented with sub-conjunctival mitomycin as a stand-alone procedure during the years 2018-2020. Demographic data extracted included age, race, type of glaucoma. Historical surgical data included prior ocular surgery, bleb status, time between initial trabeculectomy and revision, pre-operative IOP, and number of glaucoma medications. Post-operative data included IOP at post-op day 1, week 1, month 1, 3, 6, and number of glaucoma medications at the same time points.

Results:

The medical records of 59 patients met study criteria. The average pre-operative IOP ($n = 59$) was 23.8 mmHg on an average of 3 topical glaucoma medications. On post-op day 1 ($n = 58$), average IOP was 11.8 on 0.5 glaucoma meds. On post-op week 1 ($n = 58$), month 1 ($n = 56$), month 3 ($n = 53$), month 6 ($n = 48$), the average IOP was 13.0, 13.4, 15.0, 13.7 respectively, with an average number of glaucoma meds of 0.7, 0.7, 1.0, 1.1. Wilcoxon-ranked signed tests showed the difference between pre-op IOP and post-op IOP at months 1, 3, 6 to be significant ($Z = -6.1$, $p < 0.001$; $Z = -5.6$, $p < 0.001$; $Z = -5.4$, $p < 0.001$), and the difference in pre-op and post-op number of glaucoma medications to be significant ($Z = -6.1$, $p < 0.001$; $Z = -5.1$, $p < 0.001$; $Z = -5.2$, $p < 0.001$).

Discussion:

A common scenario for the glaucoma specialist is the patient who has had trabeculectomy which has failed. At that point, commonly considered surgical options include tube shunts and ciliary photocoagulation. These surgeries carry significant risk of complications, and often have a prolonged recovery requiring a robust medicinal regime. This study suggests that an attempt to improve the function of the trabeculectomy should not be overlooked. The needling option is relatively non-invasive, does not require an incision, and requires minimal surgical time and anesthesia. In this study needling proved highly effective at significantly lowering IOP and medication burden.

Conclusion:

Glaucoma specialists should consider needling among the treatment options in patients who have failed trabeculectomy. In this study of patients undergoing needling, the average IOP was 42% lower than pre-op and the patient's medication burden was significantly less.

11. Examining the impact of exogenous lactate isoform administration on breast cancer cell proliferation and metabolic pathways

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Obesity is a prevalent health condition in the United States and has been found to serve as a modifiable risk factor for breast cancer development in postmenopausal women. As poor diet, like one high in fats and sugars, is a major contributing factor for the development of obesity and subsequent breast cancer, it is essential to maintain a healthy dietary lifestyle as a way to prevent breast cancer development. Balanced diets can also maintain essential intestinal and gut health by maintaining the symbiotic relationships between the microbes found there, but may also play a role on microbes found in distal organs and tissues, like the breast. Using a nonhuman primate (NHP) model, our lab performed metabolomics on mammary glands from *M. fascicularis* NHPs fed a Western or Mediterranean diet for 2.5 years. With the animals separated in groups based on body fat composition, we were able to look at the impact of adiposity within dietary patterns on mammary gland (MG) metabolism. Comparing metabolites identified from these MGs, NHP with the highest body fat composition displayed decreased lactate concentrations when compared with lean NHP breast tissue levels. In addition to the increased levels of lactate found in these MGs independent of diet, elevated proportional abundance of lactate-producing bacteria were present in lean NHP breast tissue, suggesting a potential role of the microbiome in the regulation of gland-specific lactate. C57BL/6 mice demonstrate susceptibility to dietary induced obesity. When analyzing protein levels of lactate dehydrogenase (LDH) enzyme isoforms responsible for converting pyruvate to lactate, LDHA (L-lactate isoform specific) and LDHD (D-lactate isoform specific), LDHA and LDHD were higher in MG tissue of low-fat control diet-fed mice compared to Western diet-fed mice. These data suggest the regulation of lactate metabolism by obesity within the mammary gland compartment may be mediated through repression of enzyme activity. In opposition to our findings, the overproduction of lactate is often associated with cellular stress and as a metabolic waste product. In a stressful cellular environment, like that lacking oxygen and/or uncontrolled proliferation, there is a shift in the glycolytic pathway to produce more lactate from pyruvate. As rapid proliferation is a hallmark of cancer cells, we aimed to investigate the impact of lactate administration on cell proliferation. When analyzing cell proliferation in vitro of non-neoplastic and breast cancer cells treated with exogenous doses of L- and D-lactate isoforms, data showed differential regulation in cell proliferation in the presence of D-lactate. Western blot analysis of matching protein samples taken at 24 hours post treatment, begin to also show differential protein expression of LDHA, LDHD and proliferating cell nuclear antigen (PCNA) in the presence of L- and D-lactate. These data begin to suggest the potential regulation of lactate metabolism regarding enzyme activity in breast cancer cells and subsequent impact on cell proliferation. Our lab aims to continue to investigate how diet, obesity and the microbiome mediate breast cancer risk and development. Future goals of the study include to investigate the impact of L-lactate and D-lactate isoforms on obesity-mediated breast cancer risk, breast metabolic pathways, and localized gland inflammation. Moreover, we plan to further explore the effect of the breast microbiome on regulating localized lactate levels within the MG to potentially modify breast cancer risk.

12. #Who: Investigation of Who Creates Laryngology Content posted on Instagram

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Introduction: Social media use is rising in medicine with both patients and providers developing a larger presence on networking platforms. Data suggests that many patients utilize social media to discern information regarding diagnosis and modalities of care. Therefore, it is important that information circulated on social media is accurate. A recent study in dermatology, through the analysis of hashtags (#), reported that many of the dermatology posts queried on Instagram were not entries created by dermatologists. This raises concern regarding the validity and accuracy of content viewed by people seeking information. Currently, there is no literature regarding the quality of laryngology social media posts and this study aims to raise awareness to mediate that gap between patients and providers. Methods: Fellowship-trained laryngologists were surveyed to obtain the most common encountered diagnoses and procedures. Hashtags were queried on Instagram over a set time period and the type of influencer was recorded into a category. Analysis was conducted to determine the

accounts involved in sharing laryngology content and further subcategorized into physician, speech language pathologist (SLP), and other. Results: Fellowship-trained laryngologists suggested top diagnoses and procedures. Many of the laryngology hashtags utilized on Instagram are from non-laryngologists. Discussion: With the growth of the online presence of information in laryngology, it is important that laryngologists remain on the forefront of sharing and teaching social media users to ensure the distribution of reliable information.

13. IMPACT OF PRE-OPERATIVE METABOLIC EQUIVALENT STATUS ON SURGICAL OUTCOMES IN HEAD AND NECK CANCER PATIENTS

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Importance: The association between functional status and postoperative complications in cancer surgery is well-described in the literature; however, utilization of pre-operative screening tools to predict post-operative outcomes in head and neck cancer patients are lacking. Objective: The aim of this study is to determine if there is an association of low functional status, using metabolic equivalents (METs), with post-operative adverse events and/or increased length of stay (LOS) among head and neck cancer patients who underwent surgical resection. Design, Setting, and Participants: This was a retrospective medical chart review of 221 patients with squamous cell carcinoma (SCC) of the aerodigestive tract, from 2014 through 2020, who underwent surgical resection and completed a standardized MET questionnaire during their pre-operative visit. Main Outcomes and Measures: METs is the objective measure of the ratio of the rate at which a person expends energy, relative to the mass, while performing various physical activities. METs are measured on a scale from 1-10, where one MET is equivalent to the energy expended when sitting quietly. The MET measurements were divided into three groups: METs > 10-7 is group 1; METs 6-4 is group 2; METs 4-1 is group 3. LOS and post-operative adverse events (systemic and wound-related complications) were identified in the cohort in attempt to determine a correlation with MET status. Statistical analysis was carried out via Welch t-test comparison and p value of 0.05 was considered statistically significant. Results: 48% of the total patients experienced post-operative adverse events. 20% of these patients were located in MET group 3, 75% were located in MET group 2, and 8% were located in MET group 1. 20.8% of patients had a performance equivalent to 4 or less METs, 64.7% 4-6 METs, and 14% of patients had more than 7 METs. MET group 1 (n=32) mean LOS was 5.56 days while MET group 2 (n=143) mean LOS was 8.69 days (p=0.005). MET group 2 (n=143) mean LOS was 8.69 days while MET group 3 (n=46) mean LOS was 12.67 days (p=0.06). MET group 1 (n=32) mean LOS was 5.56 days while MET group 3 (n=46) mean LOS was 12.67 days (p=0.002). The logistic regression adjusted r² was 65.29% for predicting adverse events and LOS duration from MET status. Conclusion: Low MET status was found to be associated with an increased LOS and 96% of adverse events were in patients who were in MET groups 2 and 3. Given these findings, MET status could be utilized to counsel patients regarding their chances of post-operative adverse events and increased LOS.

14. Assessment of CT-based Muscle and Adipose Phenotypes for Prediction of Peri-operative Outcomes in Head and Neck Cancer

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Importance Although body mass index, albumin, and prealbumin may inform nutritional status, these measures are subject to alterations unrelated to nutrition. Sarcopenia (substantial loss of muscle mass and function) is associated with many adverse health outcomes, including mortality. Automated abdominal CT-based muscle measurements are a widely accepted sarcopenia biomarker and may better inform peri-operative risk than historical nutritional markers. Objective We hypothesize an association of sarcopenia with peri-operative complications and increased length of stay among head and neck cancer patients undergoing surgical resection. The goal of this study is to test our hypothesis through retrospective chart review and image analysis. Design, Setting, and Participants Retrospective chart review of 165 patients with squamous cell carcinoma (SCC) of the oral cavity, oropharynx, hypopharynx, or larynx who underwent staging PET/CT followed

by surgical resection between 2010 and 2014. Main Outcomes and Measures Patients were analyzed separately by sex. From each patient's PET/CT, a single axial CT image at the L3 vertebral level was selected for automated muscle and adipose cross-sectional area (CSA) analysis (Slice-O-Matic software; TomoVision). Hounsfield unit (HU) thresholds (-29 to +150 HU for muscle; -190 to -30 HU for fat) were utilized. All automated L3 CSA outputs were reviewed by an attending radiologist, and manual adjustments were performed when necessary (3D Slicer; <https://www.slicer.org/>). Post-operative complications included both systemic complications (e.g., stroke, myocardial infarction) and wound-related complications. Length of stay (LOS) was divided into the following two groups: group 1 (LOS 1-10 days); group 2 (LOS 11-15 or more days). Results The following statistics were derived by utilizing a student t-test with the adjusted r^2 being 63.82% for predicting adverse events and LOS duration from mean L3 CSA. Males (n=129): Patients experiencing adverse post-operative events (n=99) had a mean L3 CSA of 148.07 cm² compared to 154.21 cm² among patients without complications (n=30) (p=0.05). LOS group 1 (n=89) mean L3 CSA was 150.69 cm² while LOS group 2 (n=40) mean L3 CSA was 141.22 cm² (p=0.055). Females (n=36): Patients experiencing adverse post-operative events (n=21) had a mean L3 CSA of 107.41 cm² compared to 107.71 cm² among patients without complications (n=15) (p=0.16). LOS group 1 (n=22) mean L3 CSA was 111.40 cm² while LOS group 2 (n=14) mean L3 CSA was 101.46 cm² (p=0.133). There were no significant associations between assessed adipose tissue phenotypes (total, visceral, subcutaneous, intermuscular) and outcomes. Conclusion Sarcopenia (as determined by L3 muscle CSA) was associated with increased complications and LOS among males in our cohort. The same associations were not observed in females, though small sample size may have an influence. L3 muscle CSA may have a role to inform patient counseling regarding adverse event risks and estimated LOS prior to head and neck cancer surgical resection.

15. Assessment of CT-based Cervical Spine Muscle Cross-sectional Area for Prediction of Peri-operative Outcomes in Head and Neck Cancer

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Introduction: Lumbar sarcopenia, defined as substantial loss of muscle mass and function at L3, is associated with many adverse health outcomes, including mortality. Many patients who are diagnosed with head and neck cancer undergo Neck CT scans for staging and treatment planning. The purpose of this study is to examine the potential for association of automated cervical spine, CT-based measurements with peri-operative complications and increased length of stay (LOS) among head and neck cancer patients undergoing surgical resection. Methods and Materials: A retrospective review of prospectively collected data from 61 patients with squamous cell carcinoma (SCC) of the oral cavity, oropharynx, hypopharynx, or larynx who underwent staging PET/CT followed by surgical resection between 2010 and 2014. Statistical analysis was carried out using a student t-test with the adjusted r being 64% for predicting adverse events and LOS duration from mean C3 CSA. Outcomes and Measures: Patients were analyzed separately by sex. From each patient's PET/CT, a single axial CT image at the C3 vertebral level was selected for automated muscle cross-sectional area (CSA) analysis (Slice-O-Matic software; TomoVision). Hounsfield unit (HU) thresholds (-29 to +150) were utilized. All automated C3 CSA outputs were reviewed by an attending radiologist and manual adjustments were performed when necessary. Post-operative complications included both systemic complications (e.g. stroke, myocardial infarction) and wound-related complications. LOS was divided into the following 4 groups: group 0 (LOS <5 days); group 1 (LOS 5-10 days); group 2 (11-15 days); group 3 (>15 days). Discussion: Figure 1: Males (n=48): LOS 0 (n=3) mean C3 was 40.96cm². LOS 1 (n=31) mean C3 was 41.54cm². LOS 2 (n=5) mean C3 was 39.59cm². LOS 3 (n=9) mean C3 40.92cm². Figure 2: Females (n=13): LOS 0 (n=0). LOS 1 (n=9) mean C3 was 32.83cm². LOS 2 (n=2) mean C3 was 25.57cm². LOS 3 (n=2) mean C3 was 39.11cm². The studies utilizing L3 data is promising for an avenue to help predict increased LOS and adverse peri-operative outcomes. The decision to analyze C spine stems from the CT scans available for head and neck patients. The C3 area did not decrease with increased LOS and was not found to be statistically significant in any LOS groups, males or females. The limitations of the study are likely due to the small power of the study; however, repeat analysis of an increased number of patients is to come. Conclusion: Sarcopenia (as determined by C3 muscle CSA) does not appear to be associated with increased LOS or peri-operative events amongst males or females in our cohort. However, small sample size may be a significant limiting factor.

16. The Effects of Prolonged Intraoperative Hypothermia on Patient Outcomes in Immediate, Implant-Based Breast Reconstruction

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Introduction: Maintenance of normothermia has been an important factor in limiting post-operative complications that has been well established in the general surgery literature. Implant-based breast reconstruction (IBBR) after mastectomy consistently has higher rates of infection than other (non-breast) implant based procedures or even autologous breast reconstruction. Additionally, hypothermia causes vasoconstriction, significantly decreasing subcutaneous oxygen tension resulting in poor wound healing. This study aims to evaluate the implications of extended intraoperative hypothermia on post-operative complications. **Methods:** A retrospective review of patients that underwent immediate breast reconstruction following mastectomy was performed. Patients were organized into a majority normothermic (NT) group if >50% of the operative time was spent $\geq 36^{\circ}\text{C}$ or a majority hypothermic (HT) group if $\geq 50\%$ of the operative time was spent $< 36^{\circ}\text{C}$. Patient demographics, comorbidities, surgical techniques, and postoperative complications were recorded. Univariate and multivariate statistics were utilized to assess for significant relationships. **Results:** There were 329 total patients that met inclusion criteria with 174 in the NT group and 155 in the HT group, yielding 302 and 264 total breasts, respectively. There was no significant difference in rates of infection ($p=1.0$), seroma ($p=0.27$), hematoma ($p=0.61$), or wound dehiscence ($p=1.0$). However, patients in the HT group had significantly more ischemic complications ($p=0.009$). After controlling for tobacco use, body mass index, mastectomy pattern, radiation, and mastectomy weight, multivariate analysis showed a 54.5% increased risk for ischemic complications in the HT group ($p=0.04$). **Conclusion:** IBBR continues to have higher rates of complications relative to their autologous counterparts. Prolonged intraoperative hypothermia can increase the risk for the development of ischemic wounds such as tissue necrosis or eschar formation. While there are many contributing factors, core body temperature can be easily augmented to reduce ischemic complications.

17. Modeling Pheochromocytoma & Paraganglioma Responses to Systemic Therapy in Patient-Derived Tumor Organoids

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Introduction

Pheochromocytomas (PCC) and paragangliomas (PG) are rare neuroendocrine tumors, with an incidence of ~ 0.8 per 100,000. Surgery is the only curative treatment option for patients with localized disease. However, patients with advanced disease lack effective treatments and the rarity of metastatic disease creates challenges in treatment advancements. This study aimed to evaluate the feasibility of patient-derived tumor organoids (PTOs) as a pre-clinical platform to explore treatments for these rare tumors.

Methods

After IRB approval, tumors were obtained from patients with PCC or PG who underwent operative resection. Tumors were processed to isolate tumor cells for incorporation into PTOs utilizing a collagen-based hydrogel. Blood was also obtained from patients to isolate peripheral mononuclear immune cells to create immune-enhanced PTOs (iPTOs). Organoids underwent treatment with chemotherapy, immunotherapy, or small molecule inhibitors. Cell viability was determined using multiple assays.

Results

Five PCC and two PG tumor samples were obtained from December 2020 – September 2021. Viable tumor organoids

were successfully generated from six tumors (6/7, 85.7%) for treatment studies. PCC and PG PTOs displayed high histological fidelity compared to primary tumor tissue. PCC and PG PTOs demonstrated sensitivity to cytotoxic agents and small molecule inhibitors. Sunitinib demonstrated significant treatment efficacy with an average post-treatment viability of 16.8%. Cabozantinib and Pazopanib also demonstrated efficacy with average post-treatment viabilities of 39.2% and 42.5%, respectively. One iPTO set demonstrated sensitivity to Ipilimumab/Nivolumab (1/6, 16.7%).

Conclusion

PTOs are a feasible platform to study PCC and PG and their response to treatments. Our results highlight the utility of small molecule inhibitors in the treatment of PCC and PG.

18. Targeting Inositol-requiring enzyme-1 (IRE1) signaling impacts triple-negative breast cancer chemotherapy sensitivity and prevents chemotherapy-related cardiotoxicity

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Triple-negative breast cancer (TNBC) is one of the most highly aggressive breast cancer types that predominately affect young and minority women. TNBC is ER-negative, PR-negative, and HER2 normal, accounting for 10-20% of all breast cancer cases. Unfortunately, there are no targeted therapeutic options, limiting TNBC patients to more severe toxic chemotherapy regimens associated with cardiac dysfunction, primarily myocardial ischemia and bradycardia. Due to the clinical benefit of chemotherapy, it is now essential to find novel strategies to ameliorate side effects. Another issue compounded in the risk of developing cancer and chemotherapy-related toxicities is obesity. Obesity is associated with worse overall survival in women with TNBC. Inositol-requiring enzyme-1 (IRE1) is an arm of the unfolded protein response (UPR) pathway that plays a crucial role in tumor development. IRE1 signaling is the most evolutionary conserved branch of the UPR. It has been shown that IRE1/XBP1 protein levels are upregulated in TNBC. Preliminary work demonstrates that high-fat diets increased IRE1 levels in the DMBA tumor model. However, whether diet differentially stimulates IRE1 on TNBC is unknown.

To investigate the role of Obesity and IRE1 targeting chemotherapy response and prevention of therapy-related cardiac toxicity, we obtained female BALB/c mice placed on control and western diets at 3-weeks of age 5 weeks. At 8-weeks of age, mice were injected with 4T1-luciferase breast cancer cells in the left inguinal fat pad. Primary tumor growth was monitored by IVIS and calipers weekly for 21 days. Primary tumors were then surgically resected, and IVIS imaging was performed to confirm complete tumor removal. One week after tumor resection, mice received 3.3 mg/kg doxorubicin (DOX) I.V. for 3 weeks. Tumor recurrence and metastases were monitored by IVIS. Cardiac function was measured by Vevo ultrasound. These studies demonstrated that the western diet stimulates primary breast tumor growth, decreased DOX responsiveness, and potentiated cardiac dysfunction compared with control diet consuming mice. Also, western diet affected the development of DOX-induced cardiac dysfunction by increasing cardiac fibrosis in response to therapy.

Also, we developed a syngeneic model of murine breast cancer by injecting female BALB/c mice consuming a control diet with 4T1-luc in the mammary gland. Once tumors developed mice were treated with the anthracycline doxorubicin with or without anti-sense morpholino to IRE1. We found that a combination of targeting IRE1 with doxorubicin (DOX) enhanced chemotherapy responsiveness in the 4T1 breast cancer model. Furthermore, we found that DOX alone reduces fractional shortening and ejection fraction but this effect was prevented by targeting IRE1. Also, IRE1 blockade reduces interstitial fibrosis in combination with DOX and reduces vimentin also known as fibroblast intermediate filament in combination with DOX. Also, 4T1 TNBC cell line conditioned media significantly upregulated IRE1 protein levels and decreased p-JNK (54kDA) in H9C2 rat cardiac myoblast cells. Overall results suggested that systemic suppression of IRE1 protected cardiac tissue in mice treated with doxorubicin while enhancing anthracycline-mediated tumor killing.

19. Application of Patient Derived Organoids in Modeling Merkel Cell Carcinoma

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Introduction

Merkel cell carcinoma (MCC) is a rare neuroendocrine cancer, with an estimated 0.3 cases per 100,000. Systemic therapy is often utilized as an adjunct to surgery, but a consensus treatment is yet unidentified. This study aimed to evaluate the feasibility of patient-derived tumor organoids (PTOs) as a pre-clinical platform to evaluate treatments for these tumors.

Methods

Tumor tissue from MCC patients was processed to isolate unsorted tumor cells, which were further suspended in an ECM based hydrogel. Patient blood and lymph tissue was also collected and incorporated into immune enhanced organoids (iPTOs) Organoids and tissue were compared using histology to determine PTO fidelity. Organoids were treated with chemotherapy or immunotherapy agents and cell viability was determined to determine efficacy of treatment regimens.

Results

Seven tissues were provided from six patients from December 2018-June 2021. Six tissues (5/6, 83.3%) provided sufficient viable cells to create PTOs, with patient matched iPTOs created in 4/6 (66.6%) patients. Histology on matched patient tissues and PTOs correlated expression of MCC markers. PTOs demonstrated variable responses to chemotherapy regimens between patients, with combinational therapy of cisplatin and doxorubicin demonstrating the highest rate of response (5/6, 83.3%). Immunotherapy did not demonstrate efficacy in four patients tested, although iPTOs demonstrated increased immune cell activity when treated.

Conclusion

PTOs are a feasible model for exploring new treatment regimens for this rare primary. PTOs have the potential to predict individualized patient responses to a variety of treatments, which could aid in achieving greater treatment efficacy with currently available drugs.

20. Peritoneal Mesothelioma Organoid Response to HIPEC

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Introduction

Peritoneal mesothelioma (PM) is a rare malignancy (2 patients per million) with poor prognosis, representing about 10-15% of all mesothelioma cases per year. We previously reported on the feasibility of generating PM patient-derived tumor organoids (PTOs). Herein we present the application of PM PTOs in elucidating personalized response to HIPEC.

Methods

After IRB approval, tumor samples were obtained from patients with PM undergoing cytoreductive surgery with HIPEC at Wake Forest. PTOs were fabricated with tumor cells suspended in a collagen-based hydrogel and treated with HIPEC regimen mimicry. Viability, live/dead imaging, and IHC analysis were performed post-treatment. Treatment efficacy was defined as killing at least 50% of organoid cells.

Results

Seven anatomically spatially specimens were processed from 4 patients from October 2020 through June 2021, with 3 specimens coming from the same patient. All underwent successful organoid fabrication, with 6/7 (86%) sites undergoing comparative 37° and 42° HIPEC treatments with cisplatin and MMC. Response to HIPEC was patient and site specific. Hyperthermia enhanced the cytotoxicity of both drugs which average post treatment viability drop of 27.1% and 19.4% respectively compared to normothermia. Heated cisplatin displayed the greatest cytotoxicity with an average post-treat-

ment viability of 45.5%. Overall, heated cisplatin demonstrated efficacy in 4/6 (66.7%) tumors, with statistically significant superiority in 3/6 (50%) PTOs when compared to mitomycin C. Mitomycin C demonstrated efficacy in only 1/6 (16.7%) of specimens, which was not responsive to cisplatin in the hyperthermic condition.

Conclusions

Peritoneal mesothelioma PTOs treated with HIPEC, exhibit patient and site specific response to treatment. Cisplatin exhibits superior cytotoxic activity over MMC. Organoids have the potential to personalize efficacious HIPEC regimens for PM patients.

21. The Microbiome Mediates Carcinogenic Alterations of the Mammary Gland in the Context of Obesity

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Obesity increases the relative risk for breast cancer incidence. Several obesity-linked molecular mechanisms are demonstrated to drive breast cancer progression, however, if and how obesity contributes to breast cancer initiation is poorly understood. Obesity alters adipose tissue structure and signaling, immune cell activity, and shifts the microbiome in ways that could potentially increase breast cancer risk. Our preliminary experiments with a mouse mammary carcinogenesis model indicate that diet-induced obesity alters the microbiome in the gut and the mammary gland that leads to decreased tumor-free survival, reduced tumor latency, and increased tumor multiplicity. Microbial-associated molecular pattern (MAMP)-proteins and metabolites such as lipopolysaccharide (LPS), a toll-like receptor 4 (TLR4)-agonist, could directly affect breast epithelial cell signaling. LPS was found to be elevated in the plasma and mammary glands of obese mice. Experiments in a 3D culture model of breast glandular units (acini) show that LPS disrupts the tight junctions (TJs) that maintain apical polarity. The loss of apical polarity is a known functional biomarker of breast cancer risk. Other biomarkers of risk include DNA damage and oxidative stress which were shown to be elevated by LPS treatment. Preliminary data show that LPS activates the nuclear factor-kappa B (NFκB) pathway by binding to the TLR4 receptor leading to an increased expression of inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α). The outcomes of our study underscore the importance this under-appreciated component of the tumor microenvironment, the microbiome, in the prevention of breast cancer. In conclusion, we show that obesity-modulated gut microbiome increases breast cancer risk, at least partly, through the involvement of microbiome metabolites such as LPS.

22. Laparoscopic Common Bile Duct Exploration: A Model in Surgical Innovation and Intraoperative Education

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Background: Today, there are increased efforts to promote surgical trainee and faculty competency and performance. One-stage laparoscopic common bile duct exploration (LCBDE), in comparison to laparoscopic cholecystectomy with pre- or post-cholecystectomy endoscopic retrograde cholangiopancreatography (ERCP), for treatment of choledocholithiasis is an ideal model for surgical innovation and intraoperative education while developing valuable skills. To that end, we describe our process of surgical technique conception, implementation, multiple surgical service adoption, and refinement.

Methods: In 2018, surgeons at Wake Forest conceived a technique to treat common bile duct stones during laparoscopic cholecystectomy for adult and pediatric patients. With initial success with the technique, we sought to create an efficient and accessible framework for acute care surgery (ACS) and pediatric surgery services to facilitate implementation. We initiated three phases to promote early adoption and implementation. First, we created an interactive pathway. Next, we defined the exact steps of the procedure, created an educational video, and constructed an intraoperative cart housing all necessary equipment along with just-in-time access to online educational material displayed on the cart via QR code. We then engaged in a targeted educational campaign to pediatric and ACS surgeons and surgical residents to drive adoption. To ensure quality outcomes, we created a prospective observational registry for continuous analysis of our progress.

As a final additional step, we designed a surgeon feedback survey to engage in continuous learning and near real-time feedback to correct and refine steps in the pathway with an emphasis on patient safety, user-experience, and efficiency.

Results: The number of LCBDE cases performed by the ACS service per year are as follows: 9 cases in 2019, 21 cases in 2020, and 22 cases to date in 2021. The rate of successful LCBDE on the ACS service from 2019 to present were the following: 55.6% in 2019, 90.5% in 2020, and 87.4% currently in 2021. Data suggests that through our efforts to create an interactive pathway and implement it in an intentional manner, we have increased the success of treating common bile duct stones intraoperatively.

Conclusions: Diffusion of innovative surgical techniques within a health system requires a multi-modal approach to promote efficient adoption and refinement with the ultimate goal of quality outcomes. Creative teaching methods integrating technology (QR codes to educational materials including videos, creation of intraoperative pathways, and a REDCap QA survey) drive innovation. Our next steps include tracking feedback and continuing our prospective observational registry to foster targeted pathway and phase-of-care refinement.

23. Characterizing Vascular Endotheliopathy Associated With Partial Versus Full REBOA In A Hemorrhagic Shock Model

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Intro: Shock induced endotheliopathy is a growing concern within the field of hemorrhagic shock and resuscitation, where shedding of the endothelial glycocalyx results in altered coagulopathy and endothelial dysfunction. While this phenomenon has been well described within trauma populations, less is known about how resuscitative endovascular occlusion of the aorta (REBOA) impacts the vascular endothelium. REBOA is known to significantly alter the hemodynamics within the aorta and results in profound ischemia reperfusion injury distal to the occlusion. Thus, we hypothesize that the altered hemodynamics imposed by REBOA may also contribute to significant changes to the integrity of the endothelial glycocalyx. Towards this goal, we performed a pilot study to quantify the extent of endotheliopathy in a hemorrhagic shock swine model, subjected to either partial (pREBOA) or full REBOA (fREBOA) with the hypothesis that pREBOA will exert less endothelial damage compared to fREBOA.

Methods:

Yorkshire swine were subjected to 20% hemorrhage followed by pREBOA versus fREBOA (n=4 per group) for 20 minutes and subsequently resuscitated with a standardized critical care protocol (vasopressor support along with fluid and blood resuscitation) for 6 hours. Serum samples were obtained at 5 time points: baseline (T0), end of hemorrhage (T30), end of aortic occlusion (T60), 10 minutes post-occlusion / initiated resuscitation (T75), and at the end of study (T310). All animals included in this analyses survived the study period. An enzyme-linked immunosorbent assay (ELISA) was used to quantify serum levels of key endothelial glycocalyx components, including hyaluronic acid (HA) and syndecan-1 (SDC-1). Descriptive statistics was used to determine differences between groups in terms of SDC-1 and HA levels.

Results:

Baseline vitals were similar between the fREBOA and pREBOA groups. We observed changes in SDC-1 and HA over time consistent with the hemorrhagic shock model. Pigs undergoing fREBOA had nearly double the levels ($11.4 \text{ ng/ml} \pm 4.99$ vs. $6.27 \text{ ng/ml} \pm 2.89$) of SDC-1 at baseline compared to those undergoing pREBOA. Furthermore, SDC-1 levels were elevated at T30, T60, and T75 for fREBOA in comparison to pREBOA ($8.80 \text{ ng/ml} \pm 2.80$ versus $5.57 \text{ ng/ml} \pm 1.44$, $5.32 \text{ ng/ml} \pm 1.63$ vs $5.10 \text{ ng/ml} \pm 0.93$, and $7.11 \text{ ng/ml} \pm 4.54$ versus $5.81 \text{ ng/ml} \pm 1.19$, respectively). The pREBOA group demonstrated lower HA levels, compared to those experiencing fREBOA, especially at T60 and T75 ($787.85 \text{ ng/ml} \pm 207.41$ versus $915.76 \text{ ng/ml} \pm 499.03$ and $682.73 \text{ ng/ml} \pm 225.09$ versus $1253.74 \text{ ng/ml} \pm 524.03$). This suggests that there is less endothelial glycocalyx damage imposed by pREBOA.

Conclusion:

In our preliminary study, swine treated with fREBOA displayed higher circulating levels of both SDC-1 & HA during aortic

occlusion (T60) and post occlusion (T75). This initial study suggests greater endothelial dysfunction with full aortic occlusion compared to partial aortic occlusion, which may inform the conduct of endovascular resuscitative efforts for patients in hemorrhagic shock. Future studies are needed to determine the relationship between the altered hemodynamics from REBOA and circulating biomarkers of endotheliopathy to improve the implementation of aortic occlusion interventions and resuscitation post-REBOA.

24. Achilles Heel No Longer: Marked Decline in Early Relaparotomy and Allograft Pancreatectomy Rates following Simultaneous Kidney-Pancreas Transplantation in the Contemporary Era

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Background: Technical complications requiring early relaparotomy (relap) and allograft pancreatectomy (AP) have long been the Achilles heel of simultaneous kidney-pancreas transplantation (SKPT). Methods: Single center retrospective review of all SKPTs from 11/1/01 - 8/12/20 with T-cell depleting antibody, tacrolimus, MMF, and steroids. Anticoagulation other than ASA 81 mg was not routinely used and all patients were managed by standardized protocols including enteric exocrine drainage. Early relap was defined as occurring within 3 months of SKPT. Patients (pts) were stratified into 2 sequential eras: Era 1 (E1): 11/1/01 - 5/30/13; Era 2 (E2) 6/1/13 - 8/12/20. Results: During the period of study, 255 SKPTs were performed (E1, n=165; E2, n=90) with an overall mean follow-up of 8.1±5 years. Recipient age and donor and recipient ethnicity, gender, and BMI were comparable between eras. E1 pts received organs from older donors (E1 27 vs. E2 23 years, P<0.001) with longer pancreas graft cold ischemic times (CIT) (E1 16 vs. E2 13 hours, P=0.04). E2 pts received more imported organs (E1 16% vs. E2 27%, P=0.04). E1 pts had a higher early relap rate (E1 43% vs. E2 14%, P<0.001) and were more likely to require AP (E1 10.3% vs E2 2.2%, P=0.019). E2 pts underwent systemic venous drainage more frequently (E1 8% vs. E2 29%, P<0.001). The most common indications for early relap in E1 were pancreas thrombosis (12%), abscess/infection (12%), bleeding (4%), and leak (4%) whereas in E2 were for abscess/infection (3%), small bowel obstruction (3%), and thrombosis (2%), P=0.001. Pancreas venous drainage technique did not affect either early relap or AP rates. Actuarial death-censored pancreas graft survival rates are shown in Table 1. Mean transplant volume was 14/year for E1 and 13/year for E2; mean transplant volume in the past 3 years of E2 was 18/year. Conclusions: Maximizing donor quality (younger donors) and minimizing CIT are paramount for reducing complications requiring either early relap or AP and for optimizing long-term pancreas graft survival following SKPT. Considering that the pancreas is the only organ for which supply exceeds demand, this can be achieved without compromising transplant volume by judicious use of imported organs.

25. Perioperative Chemotherapy for Resectable Colorectal Liver Metastases: Analysis from the Colorectal Operative Liver Metastases International Collaborative

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Background: Perioperative chemotherapy has been increasingly used with surgery as multimodality treatment for resectable colorectal-liver metastases (CLM). There is paucity of clinical data addressing optimal timing of chemotherapy administration relative to surgery. We examined outcomes of patients undergoing neoadjuvant and adjuvant chemotherapy in an international multicenter database of surgically-managed CLM. Methods: Data from 897 patients were obtained from a collaborative of CLM hepatectomy cases from five hepatobiliary institutions between 2000-2018. Overall survival (OS) was measured from time of hepatectomy for patients receiving: surgery alone, neoadjuvant chemotherapy, adjuvant chemotherapy, and neoadjuvant-plus-adjuvant chemotherapy. Kaplan-Meier analysis was performed to detect differences in OS between treatment groups. Single- and multi-variable analysis with Cox proportional hazards were run for OS between groups. Results: 164 patients (18.28%) received surgery, 132 (14.72%) received neoadjuvant-only, 249 (27.76%)

received adjuvant-only, and 352 (39.24%) received neoadjuvant-plus-adjuvant chemotherapy; with median OS of 40.1, 43.6, 56.0, and 49.1 months, respectively. Median OS for adjuvant-only was significantly longer compared to neoadjuvant-only ($p=0.047$) and surgery ($p=0.004$), and similar to neoadjuvant-plus-adjuvant ($p=0.104$). There were no significant differences in comorbidities between groups, based on Charlson-Deyo scores ($p=0.941$). There were significant differences in number of lesions ($p<0.0001$) and maximum tumor size ($p=0.0008$) between groups. On multivariate analysis, extra-hepatic disease ($p=0.0002$), intraoperative transfusion ($p<0.0001$), number of lesions ($p<0.0001$), and treatment algorithm ($p<0.0001$) were independent predictors of OS. Discussion: Despite group differences, adjuvant chemotherapy for CLM was independently associated with improved OS compared to other chemotherapeutic approaches. For patients with resectable disease, upfront surgery should be considered.

26. Skin Organoids: Tissue-Specific Self-Organization and Injury Model

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Ex vivo fabricated skin tissue constructs such as 3D skin organoids are becoming an alternative to fully replace animal models and traditional 2D cell cultures. A complex structure of 3D skin organoids allow for physiological cell-cell/cell-matrix interactions and enable them to serve as a model for drug testing and disease. Currently, the mostly used skin models on the market are reconstructed human epidermis and bioprinted skin. However, both are time and labor intensive. Furthermore, they require an air-liquid interface for maturation that is difficult to incorporate into body-on-a-chip platforms in contrast to spherical skin organoids.

In this study, we created human skin organoids containing multiple skin cell types in order to recreate the skin microarchitecture including authentic cell interactions. Seeding combinations of keratinocytes, melanocytes, dermal fibroblasts pre-adipocytes and follicle papillae cells in Low Attachment 96 Well Plates supported self-organization into spherical organoids, that maintained long-term viability (>30 days). Visual observation showed maturation of the skin organoids by obtaining uniform pigmentation and decreasing their size significantly by day 21 in culture. Anatomical analysis including histology, scanning electron microscopy and immunohistochemistry revealed skin-specific layer organization within the organoids, with the surface layer formed by epidermal cells (keratinocytes, melanocytes) and the central core formed by dermal (fibroblasts and follicle dermal papillae cells) and hypodermal (pre-adipocytes) cells. In addition, capillary-like structures composed by endothelial cells were observed inside the skin organoids, as well as high production of extracellular matrix proteins such as collagen III, and laminin.

To test the response of the skin organoids to external insults, they were exposed to UVB light and to skin irritating chemicals. The organoids developed endoplasmic reticulum (ER)-stress response and apoptosis upon UVB exposure and decreased cell viability and disruption of normal skin anatomy in response to skin irritating chemicals.

Taken together, these novel multicellular skin organoids are less technical demanding and are more reproducible compared to other 3D skin models. Ultimately, this technique could provide a reliable in vitro model of skin for investigation of dermato-pathologies and screening of treatments and counter measures.

27. The Demographics of Patients Presenting for Laryngological Care at an Academic Medical Center

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Objectives: Few studies address the demographics/epidemiology/socioeconomic status of patients presenting to a laryngologist at a tertiary care center for treatment. In order to identify any possible disparities in voice, airway and swallowing care, we sought to analyze the aforementioned data for new patients presenting to the voice center at an academic medical center. Methods: This is a retrospective cohort study of prospectively collected data from an institutional database of 4,623 new adult patients presenting for laryngological care at a tertiary care, academic medical center from 2015-2020. Demographic data were analyzed. Results: Of 4,623 patients 62.8% were female and 37.2% were male with ages ranging

from 19-99 years (Avg-59.51, SD-15.83). Patients were 81.8% white, 13% black, and 5.2% other, compared with 56.3% white, 34.8% black, 20% other in the local municipality from US Census Data. Payer mix included 46.98% Medicare, 42.59% commercial insurance, 3.22% Medicaid, 5.19% other, and 2.01% uninsured/self-insured. Patient demographics based on primary diagnosis codes were also examined. A majority of patients presented with voice related complaints. Conclusion: Understanding the demographics of those with laryngological disorders will help to develop targeted interventions and effective outreach programs for underrepresented patient populations. Future multi-center studies could provide further insight into the distribution of healthcare disparities in laryngology.

28. Normative Value for the Laryngopharyngeal Measure of Perceived Sensation

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Objectives: The Laryngopharyngeal Measure of Perceived Sensation (LUMP) is a recently validated patient-reported outcome measure (PROM) aimed at evaluating the symptom severity of patients with globus pharyngeus. The objective of this study was to define the normative values for the LUMP questionnaire. **Methods:** The LUMP questionnaire was completed by eighty-eight subjects. Individuals without throat related symptoms such as dysphagia, dysphonia, or cough were provided LUMP. The results of the eight-item questionnaire were analyzed for standard error of the mean (SEM), mean and standard deviation (SD). **Results:** Review of the eighty-eight LUMP questionnaires elucidated a mean of 0.42 (SEM = 0.10, SD = 0.96) in the normative population. By gender, the female (n=50) mean was 0.24, SD = 0.66, SEM = 0.09; for males (n=38), the mean was 0.66, SD = 1.21, SEM = 0.20. **Conclusion:** This study provides normative data for the LUMP, a recently established PROM useful in patients with globus pharyngeus. A LUMP score greater than, or equal to 3 should be considered abnormal, and warrants additional attention.

29. Characterizing Safety and Efficiency of Umbilical Hernia Repair on the Resident Run Surgical Service

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Background: The chief resident service provides final-year surgical trainees with a supervised experience in independence, responsibility and decision-making like they will face after graduation. Residents are entrusted to determine their personal preferred operative techniques while being supervised by an attending physician. The graduated independence this service provides is reliant on if it is safe for patients and cost effective for the institution. **Hypothesis:** We hypothesized outcomes and operative cost of umbilical hernia repairs to be equivalent between the chief resident service and the standard academic service. **Methods:** We matched each adult undergoing umbilical hernia repair from 07/2016-06/2019 on the chief resident service to two standard academic service patients based on operative indication, sex, and age. We compared demographics, surgical complications, operative time, 30-d complications and operative costs. **Results:** This study included 90 patients undergoing open umbilical hernia repair (30 chief service patients and 60 standard academic service patients). Chief service patients had less comorbidities on average (Charlson Comorbidity Index 0.5 vs 1, P = 0.05), but mean body mass index (31.8 vs 31.6, P = .55) and fascial defect size (1.6cm vs 1.8cm, P = 0.85) were similar between the chief resident and standard academic services, respectively. The overall complication rate was similar (10.0% chief resident, 10.0% standard, P= 1.0) Additionally, there were no significant differences in recurrence (6.7% chief resident and 1.7% standard, P = 0.23) infection (0.0% chief resident versus 5.0% standard, P= 0.12), seroma (3.3% chief resident versus 1.7% standard, P= 0.62) or hematoma (0.0% chief resident, 1.7% standard, P= 0.37) between services. Procedure-related ED visits were similar (10.0% chief resident versus 5.0% standard, P= 0.38) and no patients on either service required readmission or reoperation within 30 days. The chief resident service averaged longer operating times (38±22 vs 26±16 min, P < 0.01) as well as more time spent in the operating room (88±34 vs 70±21 min, P <0.01) versus the standard academic service, respectively. More time in the operating room translated into higher time-based cost for chief resident's service (\$763vs \$609, P < 0.01), but mean cost for materials was similar (\$203vs \$231, P= 0.52) between the chief resident and standard service, respectively. **Conclusions:** The chief resident service provides safe operations for patients undergoing umbilical hernia repair with outcomes similar to those on the standard academic service. Although operative times are longer on the chief resident service, residents spend no more on materials than faculty when operating according to their preferences.

30. Intra-arterial delivery of immunotherapy for treatment of patients with refractory head and neck cancers

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Background: Patients with head and neck squamous cell carcinoma (HNSCC) have poor prognosis and few treatment options. In clinical studies, immunotherapy checkpoint inhibitors such as Pembrolizumab has demonstrated efficacy in solid tumors, though only 20% of HNSCC patients respond to monotherapy and only up to 45% respond to dual therapy. Immune cell infiltration into the tumor microenvironment is necessary for successful tumor eradication. Pre-clinical evidence of intra-arterial (IA) and IV delivery shows that IA delivery significantly increased T-cell tumor infiltration over IV therapy, due to local T cell activation. Further research is critical to discern the clinical benefit of IA immunotherapy administration in the treatment of head and neck cancer patients.

Hypothesis/Objectives: Intra-arterial infusion of Pembrolizumab in treatment naïve Head and Neck Squamous Cell Carcinoma patients is feasible and accelerates intratumoral T cell activation and infiltration without increased risk of adverse effects.

Methods: This is a proof-of-concept feasibility pilot study in which 5 patients with newly diagnosed HNSCC will be treated with fluoroscopic-guided intra-arterial injection of 200mg Pembrolizumab as their first dose of immunotherapy, followed by conventional IV treatment at three-week intervals. We will enroll a second matched cohort (n=5) who will undergo conventional IV Pembrolizumab therapy at the same dose and administration schedule, without a first IA booster dose. In both groups, prior to the second dose, an outpatient tumor biopsy will be performed and assessed with immunohistochemistry for quantification of activated T cells. Levels of immune-regulatory plasma microRNA will be quantified using PCR to assess response rates as per existing pembrolizumab protocols. Volume of the target HNSCC tumor will be calculated on computed tomography with contrast before treatment and after 4 total doses. All adverse effects over 90 days will be recorded.

Results: This proposal has been ratified by the Head and Neck DOT. We anticipate that >80% participants enrolled in this study will be able to undergo IA administration of pembrolizumab, and that serious adverse effects (including but not limited to bleeding, stroke, inpatient admission, rash, neurologic deficit) will be no higher in the IA group compared to the IV group. Using descriptive statistics, tumor T cell infiltration and tumor volume between groups will be compared using chi square tests for proportions and t-tests or ANOVA for continuous variables. Independent outcome predictors will be identified using regression analysis and other inferential statistical analysis will be performed as indicated.

Conclusion: Intra-arterial infusion of Pembrolizumab in treatment naïve HNSCC patients is likely a feasible treatment to potentiate increased immune cell infiltration and improve response rates to checkpoint inhibitors.

31. Early Outcomes with the Vantage Total Ankle Prosthesis

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Background: The Vantage total ankle replacement is a modern prosthetic design not well established in the literature. The aim of the present study was to analyze the early outcomes and complications of the Vantage total ankle system. **Methods:** Twenty-two Vantage total ankle implants were included in the study. Survivorship, complication rate, patient satisfaction, postoperative brace use, and pain levels were evaluated. **Results:** At a mean follow up of 24.6 month, there was a 4.5% (1/22) overall complication rate and 100% implant survivorship. Patient-reported pain scores decreased from an average 7.4 preoperatively to 0.66 postoperatively. Only 9% (2/22) of patients required a brace postoperatively, and there was a 100% patient-reported satisfaction rate. **Conclusion:** The Vantage total ankle system was associated with a low complication rate and positive early outcomes in terms of pain improvement and patient-reported satisfaction.

32. A Single Institution Comparison of Complications After Autologous vs Alloplast Cranioplasty

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Introduction and Background

Cranioplasty is a standard neurosurgical procedure used to reconstruct skull defects which may arise secondary to infection, congenital defects, trauma, or following tumor resection. Cranioplasty may be performed using either native bone (autograft) or foreign material (alloplast). Though often performed and well-studied, cranioplasty still presents a clinical challenge in minimizing negative outcomes that may lead to graft removal and revision. We hypothesized that the use of alloplastic graft material is associated with a lower rate of complications, and that comorbidities traditionally associated with poor wound healing (e.g., diabetes, prior radiation, smoking) would lead to a higher rate of complications.

Methods

A retrospective chart review of patients that underwent cranioplasty between 2000-2019 at Wake Forest Baptist Medical Center was performed. Three hundred and seventy-five adult cranioplasty patients treated from 2000-2019 were studied retrospectively. Demographics, comorbidities, and graft materials were assessed. Graft complication was defined as events requiring surgical revision or removal.

Results

The overall complication rate was 19.5% (n=73). Head and neck (HENT) radiation and use of autograft were associated with an increased risk of complications (p=0.028 and p=0.004, respectively). The rate of complications differed by indication for surgery, with tumor resection having the highest rate at 38.5% (p=0.003). Equal numbers of alloplast (50.9%) and autograft (48.0%) were used. Smokers were more likely to have an autograft (47.1%, p=0.021). After controlling for smoking in multivariate analysis, autograft was no longer an independent risk factor for complications. Fifty-nine patients (15.7%) had a revisionary operation. Graft-related complication was the most common indication for revision. We found no statistically significant association between indication for surgery and indication for revision. In multivariate analysis, HENT radiation alone increased odds of a graft complication by 15.63 fold (p=0.007). No other variables were statistically significant.

Conclusions

In our cohort, previous head and neck irradiation was associated with an increased risk of complication after cranioplasty. Although patients with autologous reconstruction had a higher incidence of complication, this difference was no longer significant when controlling for the higher rate of smoking among those who had autologous reconstruction. Finally, when controlling for all tested variables (MOI, age, smoking, HENT radiation, graft type), HENT radiation was found to significantly increase the odds of having a graft complication by a factor of 15.63. MOI had no influence on odds of graft complication.

33. Limitations of Neurobehavioral Testing in Rat Models of Intracerebral Hemorrhage

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Background: The incidence of spontaneous intracerebral hemorrhage (ICH) has been alarmingly high in the United States since the early 1980's, without any significant medical advancements in treatment. With case fatality rates up to 50%, new treatment strategies are critically needed. The majority of ICH research has been conducted in young, healthy male mice, which do not mirror the human ICH population. We have developed a rat model of ICH with concomitant cardiometabolic

comorbidities, which more closely align with the human ICH population in order to improve chances for successful identification of translational therapeutic targets. However, efficient neurobehavioral measurements have not been well-validated in rat models. In murine models, the Garcia score and Corner Turn tests are two measures of neurobehavioral change; however, there is significant variation in the amount of time and effort required to complete these two tests and the Garcia score measure has not been validated in rat models. Hypothesis: The Garcia score will have higher sensitivity in detecting neurobehavioral changes in rats than the Corner Turn test and will be more efficient in terms of completion time. Methods: The Garcia score and Corner Turn test were performed on 11 male Sprague Dawley rats at 7-8 weeks old for baseline measurements. Following this, small volume (50 μ L) autologous-injection ICH (n=6) and large volume (150 μ L) autologous-injection ICH (n=5) was performed per the standard Diz/Wolfe ICH lab protocol. Behavioral measures were performed at baseline and repeated at 24- and 72-hours post-surgery by the same technicians on all rats with video capture to document and standardize scoring. Results: Correlation is significant at 1-day post-ICH between Garcia and Corner Turn, but not significant at baseline (BL) or 3-day. Mann Whitney U tests demonstrate that at each timepoint, there are no significant differences between volumes for both tests. Friedman's test was used to test whether behavioral test scores differed between timepoints. For Garcia, 1-day is significantly different from BL ($p < .001$) and from 3-day ($p = .023$). For Corner Turn, 1-day is significantly different from BL ($p = .017$) and from 3-day ($p = .009$). Percent change between timepoints in Garcia and Corner Turn scores was calculated for both hematoma volumes. Garcia and Corner Turn both show a decrease in average performance from BL to 1-day, and an improvement in average performance from 1-day to 3-day. This trend is the same in both volume groups. For both Garcia and Corner Turn, the small volume group shows a greater improvement in average performance from 1-day to 3-day than the large volume group. Conclusions: The Garcia score and the Corner Turn test both effectively demonstrate neurobehavioral changes 24 hours post-ICH in a rat model. However, neither test was able to detect behavioral changes from baseline at 72 hours. Both models also lacked the sensitivity to detect behavioral differences between the 50 μ L and 150 μ L hematomas. Moreover, both tests showed the same trends in percent changes between different timepoints. With this information, we are more aptly able to understand the limitations of these measures and interpret the data they produce more carefully. Additionally, we can have confidence in the fidelity of the Garcia score and use this method alone rather than the Corner Turn test in order to conserve time and effort. Lastly, our data shows that deficits are significant 1-day post-ICH, but there is improvement in behavioral performance at day 3 compared to day 1, more so for the small volume group. This provides evidence of the initiation of recovery from hematoma in the rat model and that smaller hematomas confer a greater likelihood of restoration of neurological function. An important limitation to our experiment is lack of power in sub-groups due to small sample size. Funding: This work was supported by a pilot grant from the Wake Forest Cardiovascular Sciences Center.

34. Wide-awake Local Anesthesia with No Tourniquet: An Updated Review

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Background: The wide-awake local anesthesia with no tourniquet (WALANT) technique has become popularized for various hand/upper extremity procedures. Before surgery, patients receive local anesthetic, consisting of lidocaine with epinephrine, and remain awake for the entire procedure. The purpose of this review was to investigate the advantages, diverse application, outcomes, cost benefits, use in challenging environments, patient considerations, and contraindications associated with WALANT.

Methods: A comprehensive review of the literature on the WALANT technique was conducted. Search terms included: WALANT, wide-awake surgery, no tourniquet, local anesthesia, hand, wrist, cost, and safety.

Results: The WALANT technique has proven to be successful for common procedures such as flexor tendon repair, tendon transfer, trigger finger releases, Dupuytren disease, and simple bony procedures. Recently, the use of WALANT has expanded to more extensive soft-tissue repair, fracture management, and bony manipulation. Advantages include negating preoperative evaluation and testing for anesthesia clearance, eliminating risk of monitored anesthesia care, removal of anesthesia providers and ancillary staff, significant cost savings, and less waste produced. Intraoperative evaluations can be performed through active patient participation, and postoperative recovery and monitoring time are reduced. WALANT is associated with high patient satisfaction rates and low infection rates.

Conclusions: The WALANT technique has proven to be valuable to both patients and providers, optimizing patient satisfaction and providing substantial healthcare savings. As its application continues to grow, current literature suggests positive outcomes.

35. Analysis of Bedside Eyelid Laceration Repair from January 2014- November 2020

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Introduction: Wake Forest Baptist Medical Center (WFBMC) is a Level 1 Trauma center and eye injuries, especially eyelid lacerations, are a common consult for the Ophthalmology service. Precise anatomic tissue realignment during primary eyelid laceration repair can minimize complications and reduce the need for secondary repairs. The potential complications of lid repair surgery include functional and cosmetic complications. Currently, there is no comparative data in the literature that analyzes complication rates following primary eyelid laceration repair at the bedside in the emergency department setting. The goals of this study were threefold: to measure complication rates following primary eyelid laceration repair performed at the bedside in the WFBMC Emergency Department at the time of consultation from January 2014 to November 2020, to evaluate if the WFBMC practice pattern for managing eyelid trauma is resulting in low complication rates and desirable outcomes, and finally, to assess any need for quality improvement. Objectives: The primary objective was to determine the complication rates of primary eyelid laceration repair performed at bedside in the WFU ED. The secondary objective was to analyze the need for secondary eyelid repairs following a primary repair performed at the bedside. Methods The study was a retrospective chart review from January 2014 - November 2020 using ICD9 and ICD10 codes for eyelid laceration. Results: A total of 124 patients met inclusion criteria. Of those 124 patients, 86 (69%) were males and 38 (31%) were females. 102 patients were adults and 22 were children. The most common mechanism of eyelid laceration was motor vehicle collision (37%), blunt trauma (20%), fall (15%), assault (13%), animal scratch or bite (8%), followed by miscellaneous (7%). Of those 124 patients, 91 patients had at least one post-operative visit and were included in the final analysis of the data. 33 patients were lost to follow up and were not included in the final analysis of the data. 6 patients were identified as having a functional complication, which resulted in an overall functional complication rate of 6.6%. 8 patients were identified as having a cosmetic complication, which resulted in an overall cosmetic complication rate of 8.8%. None of the patients who had a cosmetic complication require secondary repair. Therefore, there was an overall rate of need for secondary surgical repair of 2.2%. The functional complication rate per year was 0.97%. The cosmetic complication rate per year was 1.3%. The infection rate per year was 0.16%. The yearly rate of secondary repair was 0.32%. Conclusion: There is no comparative data in the literature that specifically analyzes complications rates following primary eyelid laceration repair at that bedside in the emergency department. Overall, there are low complication rates following primary eyelid laceration repair at the bedside. The WFBMC practice pattern for managing eyelid trauma at the bedside resulted in good outcomes from January 2014 - November 2020.

36. Cost-Consciousness of General Surgery Residents During Laparoscopic Cholecystectomy and Open Inguinal Hernia Repair

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Background: General surgical chief residents are entrusted with the task of choosing the necessary equipment to perform common core operations according to their preferences on the chief resident service. To determine if residents are cost-conscious when selecting the materials needed to perform these operations, we aimed to compare operative costs between the chief resident service and standard academic service (SAS) for two common procedures, laparoscopic cholecystectomy and open inguinal hernia repair. Hypothesis: We hypothesized that chief residents will not incur higher material costs than general surgery faculty on standard academic services when they are entrusted to direct laparoscopic cholecystectomies and open inguinal hernia repairs according to their preferences. Methods: We matched adults undergoing laparoscopic cholecystectomy and unilateral open inguinal hernia repair without additional procedures from 07/2016-06/2019 on the chief resident service to the SAS (1:1) by CPT, age, and sex. We compared material and time-based operative costs between the services. Results: For laparoscopic cholecystectomy (n=120), body mass index (mean 31.9 versus 32.6, P=0.42), Charlson comorbidity index (mean 0.78 versus 0.98, P=0.69), and previous abdominal surgery (55% versus 63.3%, P=0.35) were similar between the chief service and SAS, respectively. Time in the operating room was greater for the chief service versus SAS (158.55 versus 134.70 minutes, P=0.001), and consequently, time-based costs

were greater on the chief service (\$1380.97 versus \$1173.24, $P=0.001$). However, material-based costs were lower on the chief service by an average difference of \$70.33 (\$490.69 versus \$561.02, $P=0.063$). Relatedly, residents used fewer disposable clip appliers (3 clip appliers on the chief service versus 13 clip appliers on the SAS, $P=0.006$), for an average cost savings of \$26.68 per case ($P=0.007$). The total operative cost (material and time-based costs) difference per laparoscopic cholecystectomy was only \$137.40 (\$1871.66 for the chief service versus \$1734.26 for the SAS, $P=0.04$). For open inguinal hernia repair ($n=100$), body mass index (mean 27.4 versus 25.8, $P=0.24$), Charlson comorbidity index (mean 1.3 versus 1.5, $P=0.35$), and previous abdominal surgery (44% versus 56%, $P=0.23$) were similar between the chief service and SAS, respectively. Use of mesh was almost unanimous between services (100% on chief service versus 98% on SAS, $P=0.24$); however, the residents used less costly mesh on average (\$155.40 versus \$199.30, $P=0.01$). The chief service had greater operating room time (163.80 versus 99.72 minutes, $P<0.001$), time-based costs (\$1426.7 versus \$868.56, $P<0.001$), and total cost (\$1709.56 versus \$1205.69, $P<0.001$), respectively. However, chief residents spent significantly less (\$282.86 versus \$337.13, $P<0.001$) on materials. Conclusions: Chief residents are seemingly cost-conscious, as evidenced by their relatively low material-based operative costs for common general surgery operations like laparoscopic cholecystectomy and open inguinal hernia repair. Differences in time-based costs between the chief service and the SAS are offset by lower material-based costs on the chief resident service.

37. Making Common Duct Exploration Common-Balloon Sphincteroplasty as an Adjunct to Transcystic Laparoscopic Common Bile Duct Exploration for Pediatric Patients

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Background:

Definitive management of choledocholithiasis with laparoscopic common bile duct exploration (LCBDE) at the time of cholecystectomy can avoid ERCP and decrease length of stay (LOS). However, pre- or post-operative ERCP is often employed, and this practice pattern may arise from the perceived complexity of LCBDE. To simplify LCBDE, we refined a 4-step technique for over-the-wire balloon dilation of the Sphincter of Oddi. We reviewed our initial experience with balloon sphincteroplasty on a pediatric surgery service and compared it to standard transcystic LCBDE methods.

Methods:

We retrospectively reviewed the records of patients who underwent LCBDE with balloon sphincteroplasty compared to previously described methods (flushing, wire baskets) on the pediatric surgery service at a single tertiary care center over a 36-month period. Age, fluoroscopy time, operative time, complications, and outcomes were compared.

Results:

The balloon sphincteroplasty technique was utilized exclusively for LCBDE in 15 patients ages 11-18 over the last 16 months. Prior to that, 14 patients underwent LCBDE utilizing more standard techniques (flush, crush, basket retrieval). All common bile ducts were successfully cleared in the balloon sphincteroplasty group, compared to 11/14 of patients undergoing standard methods. Those 3 that failed required postoperative ERCP. Average fluoroscopy time (minus ERCP) was similar amongst the two groups (292 ± 150 seconds with balloon sphincteroplasty, 326 ± 228 seconds without; $p=0.47$). Average operative time and LOS were similar ($p<0.05$). No postoperative complications were noted at 30-day follow up in either group.

Conclusion:

Balloon sphincteroplasty is a simple and safe adjunct to LCBDE. This simplicity may drive adoption of LCBDE amongst pediatric surgeons and increase the opportunity for them to provide the full spectrum of choledocholithiasis management for their patients.

38. Development and Delivery of Renal Progenitor Organoids for Rapid Kidney Tissue Integration and Functional Recovery

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Over 50% of patients with renal failure do not have access to the life-saving treatments of dialysis and transplantation due to a lack of transplantable organs and the high costs of maintenance care. This gap in care is predicted to grow dramatically in the next decade as the incidence of its highest causative factors, diabetes and hypertension, increases worldwide-especially in countries that lack the infrastructure for current treatments. To address this gap, we aim to develop a clinically feasible cell-based renal regeneration strategy capable of developing functional nephron structures by delivering scaffold-encapsulated progenitor-derived organoids into renal parenchyma. We modified well-established renal organoid formation protocols using an aggrewell culture system to increase yields for enhanced reconstitution of renal structures. In vitro analyses of these organoids assessed proper differentiation and maturation. In following in vivo studies using athymic mice, we encapsulated human renal progenitor organoids in a 0.2% collagen-based scaffold and implanted them into renal parenchyma. Contralateral kidneys were harvested as normal controls in addition to acellular vehicle-only controls. Assessment of morphological and biochemical parameters in vitro and in vivo demonstrated cell viability and proper upregulation of renal markers followed by renal structure formation. In vitro results show the expression of renal markers at 2 weeks and the formation of kidney-like structures at 4 weeks in culture. In vivo results show that acellular scaffolds alone induce tissue regeneration unseen in normal controls; and the integration of implanted cells into nephron-like structures by 2 weeks in organoid delivery groups. These findings show that delivery of renal progenitor organoids forms renal structures and facilitates rapid kidney tissue integration in vivo. This regeneration strategy may bridge the current gaps in care in patients with renal failure.

39. Investigation of fat embolism etiopathogenesis

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Introduction and Background Fat embolism syndrome (FES), a rare clinical syndrome involving the triad of respiratory distress, cerebral dysfunction, and petechial rash, is a feared complication of soft tissue trauma including liposuction and lipoinjection. Despite having been initially described in 1861, the pathogenesis of FES remains poorly understood. Several theories of fat embolism exist, and all presuppose venous injury as mode entry of fat emboli into the venous system. In light of recent evidence gleaned from a single patient experience, we postulate a novel description of the source fat emboli and their mode of injury in FES. We hypothesize that patients with clinically diagnosed FES more commonly demonstrate lipid droplets in lung parenchyma rather than arterial occlusion with fat tissue. At present, the treatment of FES is merely supportive, as clinical efforts are blunted by our poor understanding of this disease process. Elucidation of FES etiopathogenesis may enable clinicians to develop targeted therapies for treating this life-threatening condition. Given that liposuction and fat grafting are becoming ever more popular procedures, an improved understanding of these associated complications is urgent. **Methods** Retrospective analysis of documented cases of fat embolism at our institution was completed. By chart review, the pathology reports of deceased patients will be reviewed for detailed description of presence, location (intra-arterial vs parenchymal), and composition (fat tissue versus lipid aggregate) of fat emboli. **Results** Following IRB approval, patients diagnosed with fat embolism from 2006 through and July 2021 were identified by ICD code. In total 37 patients were identified. Patient charts were reviewed to determine the context of their fat embolism diagnosis, and the presence of autopsy records that could allow reanalysis of histopathology. Of the 37 patients, 9 were deceased. MRNs for these patients were cross-referenced with autopsy records. No patients had autopsy records available. **Conclusions:**

Data obtained from chart review yielded insufficient pathology reports to characterize etiopathogenesis of fat embolism. Further study is needed, ideally with larger sample size, in order to adequately characterize this syndrome.

40. Nephron Sparing Surgery for Ureteral Urothelial Cancer with Oncologic Outcomes and Follow-up

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INTRODUCTION AND OBJECTIVE

Upper urinary tract masses have primarily been managed with radical nephroureterectomy leaving the patient with a solitary kidney and consequences thereof. Robotic-assisted surgery allows for nephron-sparing approaches with the option for segmental ureterectomy or excision of the distal ureter with partial cystectomy with concurrent ureteral reconstruction by uretero-ureterostomy or ureteroneocystostomy with Boari's flap. Presented here is one of the largest single surgeon, single-center series with long-term reconstructive and oncologic efficacy data.

METHODS

A single-surgeon, retrospective review of patients undergoing surgical management of ureteral masses from 2008 to 2021 was conducted. Patient demographics, intraoperative data, pathologic results, and oncologic follow-up were reviewed.

RESULTS

22 patients were identified with a mean age of 71 ± 11 years. The distribution of the ureteral masses locations was varied with 68.2% distal, 18.2% mid, 4.5% proximal, and 9.1% in the renal pelvis. The primary tumor pathology was urothelial cell carcinoma (UCC, 81.8%, n=18); additionally, there were two cases of renal cell carcinoma (RCC, 9.1%), one case of non-Hodgkin diffuse-type B-cell lymphoma (4.5%), and one case without malignancy only chronic and granulomatous inflammation with associated necrosis (4.5%). Of those with UCC, 66.7% had high grade pathology (n=12), 16.7% had low grade pathology (n=3), and 16.7% were unknown (n=3). The operative management comprised of 50.0% ureteroneocystostomy (n=11), 18.2% ureteroureterostomy (n=4), 4.5% ileal conduit (n=1), 22.7% nephroureterectomy (n=5), and 4.5% partial cystectomy (n=1). A median follow-up of 30 months from surgery was observed with a median of 24 months of recurrence-free follow-up. 3 patients died of cancer-related deaths a median of 15 months from surgery. 8 patients exhibited disease recurrence: 4 with low-grade UCC, 2 with high-grade UCC, and 2 with RCC with metastasis. Of those with disease recurrence, 2 cases had known positive margins at the time of surgery (1 high-grade UCC and 1 RCC).

CONCLUSIONS

Improved understanding of the surgical management of ureteral masses is imperative to balancing the goals of oncologic control and sparing renal function. This study is large compared to the other cases series exploring outcomes of ureteral neoplasm. It is unique for its inclusion of multiple ureteral tumor locations, both high- and low-grade pathology, and both segmental and radical surgical management. Future directions include using

genomic markers to determine the biologic behavior of these tumors to better inform the optimal surgical management and the role of neoadjuvant or adjuvant chemotherapy

41. Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Management of colorectal Cancers with Peritoneal Dissemination: 30 Years of Experience at a Single Institution

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CLINICAL SCIENCE – Resident

Introduction Cytoreductive surgery (CRS) is at the forefront of treatment for colorectal cancer with peritoneal metastasis (CRC-PM) with HIPEC as a promising adjunct. We report outcomes of the operative management of CRC-PM at a single center. Methods We retrospectively reviewed our prospectively managed database at a single center from 1991-2020. Kaplan-Meier method was used to estimate survival. Proportional hazards regression and multivariable models were used for assessments. Results This included 331 patients with mean age 53.6 years. In multivariate analysis, performance and resection status were independently associated with overall survival (OS) ($p < 0.001$). Within R0/R1 group, adverse impact

on OS was found with increasing PCI >13 (HR=2.44; CI:1.36-4.39, p= 0.003); the most significant increase at PCI >18 (HR=5.84; CI:2.23-15.3, p <0.001). Incomplete resection (R2) had significantly worse OS compared with complete CRS [R0/R1: 32.1 months (n=194) vs. R2a: 16.3 months (n=78), p <0.001]. When stratified by PCI for R0/R1 group, median OS for PCI<10, 10-15, and >15 was 34.4, 17.0, and 15.5 months, respectively (p=0.012 comparing PCI <10 and >15). Longitudinal analysis revealed improvement over time, mainly in patients with incomplete CRS starting in 2001 (HR=0.62; CI:0.43-0.90, p=0.013). Outcomes of R0/R1 subgroup remained largely stable (HR 1.36; CI 0.80-2.31, p=0.26). Clavien-Dindo complication (>3) rate was 22.1%. Conclusions CRS improves outcomes for CRC-PM compared to historic outcomes with nonoperative management. This benefit is greatest with R0 resection with lower disease burden. Results of CRS (+/-HIPEC) are improving over time, and surgery for CRC-PM should be routinely considered.

42. Oral Ascorbic Acid Supplementation Does Not Reverse Radiation-Induced Bone Loss in a Rat Model of Extremity Soft-Tissue Sarcoma Radiotherapy

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Introduction L-ascorbic acid (AA) exerts an anabolic effect on bone by promoting osteoblast differentiation and osteoclast apoptosis in vitro. Its safety profile and antioxidant properties make for an ideal therapeutic to prevent radiation-associated bone loss. The purpose of this study was to elucidate the in vitro and in vivo effects of AA using a clinically relevant model of sarcoma radiotherapy. Methods Osteoclast (RAW 264.7) and osteoblast (MC3T3-E1) precursors were cultured in conditions of increasing AA doses, then irradiated at 2-Gy after 24 hours. Cell differentiation and resorption activity was quantified. An in vivo study was performed in 68 adult female Sprague-Dawley rats divided into four groups: irradiated (n=18), non-irradiated (n=15), irradiated+AA treatment (n=17), and non-irradiated+AA treatment (n=18). AA supplementation (2mg/mL) was provided in drinking water to animal subjects for the entire study duration. The right hindlimbs were irradiated and harvested four weeks after irradiation for biomechanical (four-point bend test) and micro-computed tomography (microCT) analyses. Results Osteoclast differentiation (p=0.013) and resorption (p<0.01) significantly increased after radiation, which recovered with AA treatment in a dose-dependent fashion. Osteoblast mineralization was significantly lower after radiation in untreated control (p=0.002) and low-dose AA groups (p=0.049). Higher doses of AA resulted in similar mineralization between irradiated and non-irradiated cells. Neither radiation nor AA treatment exerted an effect on cortical bone biomechanical properties. Trabecular number significantly decreased on microCT after radiation (p<0.001), but did not recover in AA-treated rats. Conclusions Ascorbic acid attenuated the effects of radiation on mineralization, osteoclastogenesis, and bone resorption. Conversely, early prophylactic AA treatment in rats was not effective in reversing deleterious effects of radiation on trabecular bone compared to non-irradiated controls. The in vitro efficacy of AA treatment did not translate in rats receiving prophylactic AA treatment prior to hindlimb radiation.

43. Anti-CD47 Immunotherapy as a Therapeutic Strategy for the Treatment of Breast Cancer Brain Metastasis

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Triple-negative breast cancer (TNBC) is a highly aggressive subtype of breast cancer characterized by a lack of specific targets and a 35% incidence of brain metastasis. There is no targeted treatment for managing brain metastasis associated with TNBC; therefore, new strategies are urgently needed to overcome disease mortality. The presence of cell surface protein CD47 allows cancer cells to evade innate and adaptive immune surveillance resulting in metastatic spread. CD47 binds to and activates SIRP α on the surface of myeloid cells, inhibiting their phagocytic activity. On the other hand, CD47 binds the matricellular protein Thrombospondin-1, limiting T cell activation. Thus, blocking CD47 is a potential therapeutic strategy for the prevention of brain metastasis. To test this hypothesis, breast cancer patient biopsies were stained with antibodies against CD47 to determine differences in protein expression. An anti-CD47 antibody was used in a syngeneic model of orthotopic triple-negative breast cancer, and CD47 null mice were used in a breast cancer brain metastasis

model by intracardiac injection of the E0071-Br-Luc cell line. Brain metastatic burden was measured by the in vivo imaging system (IVIS) and quantified by luciferase luminescence. Immunohistochemical analysis was performed to quantify tumor-infiltrating macrophages, and gene expression analysis of tumors was carried out by RNA-sequencing. Immunohistochemical staining of patient biopsies revealed an 89% increase in CD47 expression in metastatic brain tumors compared to normal adjacent tissue ($p \leq 0.05$). Anti-CD47 treatment in mice bearing brain metastatic 4T1br3 orthotopic tumors reduced tumor volume and tumor weight by over 50% compared to control mice ($p \leq 0.05$) and increased F4/80 macrophage marker 5-fold in tumors compared to control ($p \leq 0.05$). CD47 null mice had a 60% increase in survival ($p \leq 0.05$) and an 89% decrease in metastatic brain lesions ($p \leq 0.05$) compared to control mice in a brain metastasis model. Additionally, RNA sequencing revealed 318 uniquely expressed genes and a significant reduction of genes related to extracellular matrix organization in tumors treated with an anti-CD47 antibody. Thus, CD47 blockade may be an effective therapeutic for triple-negative breast cancer brain metastasis.

44. Unmasking the Confounder - Inherent Physiological Variability in Swine During Automated Ischemia-Reperfusion Injury

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Background: Swine are often used in translational research of shock and resuscitation. To fully understand the effects of a given intervention, external variability must be minimized. The purpose of this study was to determine the magnitude of the inherent inter animal variability when external factors are minimized by automating a porcine experimental protocol of shock. Materials & Methods: Swine underwent a 30-minute controlled hemorrhage of 30% blood volume, followed by 30 minutes of complete REBOA to create an ischemic insult (ischemic phase). Automated reperfusion (REBOA modulated to maintain target proximal MAP of 65mmHg) occurred over five minutes and shed blood was transfused to produce the ischemia-reperfusion shock state. Physiologic parameters were collected and plasma was stored for later analysis. The variance between time points was analyzed retrospectively using an F-test ($p < .001$) and differences between gender or weights were measured with a t-test ($p < .05$). Results: There was no difference in baseline physiology. Proximal blood pressure trends showed that variability within groups increased slightly from baseline to the hemorrhagic phase, followed by a large increase in inter animal variability from the hemorrhagic phase to the ischemic phase and a drastic decrease from the time points after the balloon wean within the reperfusion phase. Variability in distal pressures generated by the automated REBOA catheter increased slightly from baseline to the hemorrhagic phase, followed by a steep decline during the ischemic phase, and a sudden increase and plateau after balloon weaning. Conclusion: Despite leveraging automation to minimal external variability, we noted that the greater the physiologic derangement, the greater the inter-animal hemodynamic variability. Given the significant role of swine in resuscitation research, the increasing inter-animal variability increasing physiologic compromise that we observed warrants further investigation.

45. Improving Access to Care: 3D printed nasal prostheses after subtotal rhinectomy

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Background: Carcinoma of the nose and paranasal sinuses may present at a locally advanced stage, either due to insidious growth or longstanding neglect. Surgical excision is the gold standard, with up to 82.5% obtaining loco-regional control with or without radiotherapy. Large nasal defects are severely disfiguring, and nasal reconstruction may be delayed. Nasal prostheses may be used while awaiting reconstruction or as a long-term solution.

Prostheses are traditionally created by anaplastologists, which can be prohibitively expensive and unavailable in certain areas. 3D printing provides a potential solution to create a low-cost prosthetic for patients.

Learning Objectives: To understand the feasibility, cost and logistics of 3D printed nasal prosthetics.

Study Objective: To create 3D printed nasal prostheses after subtotal rhinectomy. To analyze process and cost of 3D printed

prosthetics.

Method: Prospective study of rhinectomy patients who received a 3D printed prosthesis. Outcomes include the time to prosthetic creation, cost, and fit of the prosthetic.

Results: 3D printed nasal prostheses take 2-10 weeks to create compared to 10 weeks by local anaplastologists. 3D printed prostheses cost \$350-400 compared to around \$12,000.

Conclusion: Nasal appearance significantly affects self-image and defects contribute to poor quality-of-life after curative treatment. Reconstruction after rhinectomy improves quality-of-life, but may be delayed or not feasible in certain circumstances. The availability of 3D printed prostheses offer a faster, low-cost alternative as 3D printing capabilities become more widespread.

46. 3D printed ceramic scaffolds to reconstruct calvarial defects: a non-human primate model

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Background: Calvarial defects are a commonly encountered clinical problem. The gold standard for their repair is autologous bone (split calvarial graft or rib), however their use is limited to smaller defects. Larger defects require placement of custom alloplastic materials such as Medpor or PEEK, which carry a lifelong risk of infection, as they are not incorporated. An ideal solution is to repair these defects with a bone substitute that is rigid to protect the brain initially, and that has osteoinductive properties so that it is fully incorporated and replaced with healthy, living bone.

Methods:

8 Skeletally mature non-human primates were used for this study due to the similarity of skull anatomy when compared to humans. A 5cm calvarial defect was made in the top of the skull. 2 of the primates received treatment with no ceramic scaffold, 2 of the primates received a naked scaffold, 2 of the primates received a scaffold that was doped with dipyridamole, and 2 of the primates received a scaffold that was doped with BMP. The primates were followed for 2 months and received a CT scan to assess bone growth.

Results: using Mimics software, 3D models were created using the post operative CT scans and bone volume around the area of the defect was measured. At 2 months the primates with no ceramic scaffold had no appreciable boney ingrowth into the defect. The primates with the naked scaffold had minimal boney ingrowth, NS1 1667 mm³ NS2 1948 mm³. The primates with dipyridamole had more boney ingrowth, D1 2157 mm³ and D2 2128 mm³. The primates with the BMP had the most boney ingrowth B1 2423 mm³ B2 2516 mm³.

Conclusion: 3d printed scaffolds can safely be placed in cranial defects for a durable skull repair and encourage bone growth over 2 months. 5cm cranial defects are critical defects in our non-human primate model and do not regrow bone without scaffolding material. The addition of dipyridamole or BMP further stimulates bone growth. Longer follow up is required for to assess for integration of the scaffold

47. Use of Fetal Bovine Acellular Dermal Matrix to Treat Tunneling Diabetic Foot Wounds

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Introduction

Diabetic foot ulcers are difficult to heal, but tunneling infected wounds are particularly troublesome especially when they tunnel into joints or connect with a separate ulcer on a different part of the foot. Multiple treatments including NPWT have been suggested but such tunnels may delay time to closure. Fetal bovine acellular dermal matrix (FBADM) has the ability to generate robust granulation tissue and may be an adjunct to standard of care in managing tunneling wounds.

Methods

Patients treated at our wound care center or inpatient consult team with tunneling wounds, and in particular communicating with a second wound, were chosen for fetal bovine acellular dermal matrix application. The patients underwent sharp debridement of their wounds followed by fetal bovine acellular dermal matrix application. Negative pressure wound therapy was used until the dermal matrix was integrated. They were followed until wound or tunnel closure.

Discussion

We have encountered four patients whose diabetic limb wounds tunneled, two of which communicated with a second, separate wound, for a total of 6 external wounds. The two non-communicating wounds had exposed bone and one with exposed joint capsule. Patients followed for a mean of 6 months. All wound tunnels had closed, and three of the six wounds had closed. One patient went on to split thickness skin graft and the others healed or are healing by secondary intention.

Conclusion

Acellular fetal bovine dermal matrix promotes granulation tissue generation in tunneling wounds including those that tunnel to a separate defect. This product can promote closure of complex tunneling and communicating wounds. While reassuring, more controlled studies are needed to evaluate the matrix-assisted closure versus standard of care.

48. The Effects of Mechanical Tissue Resuscitation (MTR) for Treatment of Ischemia Reperfusion Injury in a Swine Model of Acute Myocardial Infarction

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Background: Heart disease is the leading cause of death in the US and worldwide. For those who suffer from heart attack, reperfusion of ischemic cardiac tissue is the primary objective. While necessary, reperfusion promotes various inflammatory processes that may ultimately lead to cardiomyocyte injury and death, otherwise called ischemia-reperfusion injury (IRI). Modern pharmacological interventions attempt to reduce the extent of damage by targeting specific and selective biochemical pathways. Yet due to the broad spectrum of mediators that contribute to IRI, these therapies have proven unsuccessful. Presently, no pharmacological treatment effectively attenuates IRI. Mechanobiology is an alternative intervention that involves physical manipulation of living tissues to elicit a biological change. Specifically, prior research directed toward reducing IRI has demonstrated that application of a uniform, negatively pressurized vacuum to ischemic tissue, or area at risk (AAR), mitigates inflammatory processes and the amount of necrosis within the AAR. This study aims to find the most effective length of MTR treatment - 60min (MTR-60), 120min (MTR-120), or 180min (MTR-180) - at a pressure of -125mmHg. **Hypothesis:** Preliminary work with MTR has indicated that moderation is necessary for effective treatment. In other words, balancing vacuum pressure and duration of treatment is essential for reducing IRI. For this reason, it is hypothesized that MTR-120 will provide the best therapeutic effect. **Methods:** A cohort of 34 Yorkshire swine were randomized to one of four groups: control (no treatment), MTR-60, MTR-120, or MTR-180. Each animal was placed under general anesthesia before instrumentation. Pressure catheters were inserted into the right femoral artery and left femoral artery for pressure monitoring. The right external jugular was isolated, and a catheter was placed for fluid administration. Next, a sternotomy was performed, and monofilament sutures were placed, but not secured, around several branches of the LAD. The left atrium was cannulated for microsphere administration to allow for measurements of regional myocardial blood flow. Ischemia was induced by securing rubber tourniquets around the selected LAD branches. The tourniquets were removed to allow for reperfusion after 70min, and the MTR device was applied to the AAR for the designated time. Hemodynamic, blood gas, and blood flow data were collected at regular time intervals throughout the five-hour study. After completion of the reperfusion phase, differential staining of the heart was performed to discriminate ischemic from non-ischemic tissue. The animal was then euthanized, the heart extracted, and further staining completed to help quantify non-necrotic ischemic tissue from necrotic tissue. **Results:** There were no statistically significant differences in the AAR among the control group, MTR-60, MTR-120, and MTR-180 (16.86±0.7%, 15.86±0.6%, 16.40±0.4%, 14.29±0.6% respectively). MTR-60 (41.90±5.6%) and MTR-120 (44.20±5.0%) reduced the AN relative to the control (56.72±3.4%), though neither group reached statistical significance. However, infarct size was significantly reduced in MTR-180 (37.90±4.5%; p<0.05). **Conclusions:** Based on these findings, MTR-180 is the most effective option for reducing infarct size in the setting of IRI. This suggests that longer treatment times are necessary to obtain optimal benefits. It is suspected that over the course of reperfusion, the sustained vacuum helps clear edema and eliminate inflammatory mediators. While these results support

MTR as a viable treatment for IRI, it will be crucial to perform survival studies in the future to further characterize long term therapeutic benefits of MTR. Source of Funding: Cheek Foundation Endowment of the Department of Plastic & Reconstructive Surgery, Wake Forest Department of Cardiothoracic Surgery, Groskort (Lois I.) Heart Research

49. Dietary Intervention with Probiotics and Muscadine Grape Extract Shifts Western Diet-Associated Metabolic, Microbial, and Inflammatory Parameters to Reduce Breast Tumor Growth

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Background: Western diet (WD) consumption is associated with increased risk and poor prognosis for breast cancer (BC) due to altered inflammation, metabolism, and microbial colonization. This study will determine whether intervention with probiotics (prbx) and muscadine grape extract (MGE) reduces WD-induced risk. Methods: Female C57BL/6 mice were fed either control diet (CD) or WD (45% fat and 25% sugar) and randomized into six groups per diet: diet alone, antibiotics (abx), prbx, MGE, MGE + abx, and MGE + prbx (n=8). Prbx groups received 1x10⁵ CFU of a 10-strain probiotic 3x weekly. MGE (0.1 phenolics/mL) and abx (5 mg/mL streptomycin, 1 mg/mL ampicillin, 1 mg/mL colistin) were administered in drinking water. Female BALB/c mice consuming either CD or WD, were injected with 1.0 x10⁶ 4T1 triple negative breast cancer cells into the R4/5 mammary fat pad. Tumors progressed to 100 mm³ prior to treatment with MGE, prbx, or combined MGE + prbx. Size was monitored with calipers for 21 days. Results: MGE + prbx administration in WD-fed mice resulted in reduced body weight. All intervention groups displayed reduced visceral adiposity and mammary gland (MG) weight compared to WD-fed mice. Significant intervention-mediated gut microbial alterations were observed by fecal 16S sequencing and included changes in proportional abundance of Bacteroidetes, Lactococcus, Lactobacillus, and Bifidobacterium taxa. Interventions modulated inflammatory markers in the visceral adipose tissue and MG as observed by immunohistochemistry (MCP-1 and CD68). Dietary intervention with MGE, prbx, and MGE + prbx reduced 4T1 tumor growth rate in WD-fed mice, but not in CD-fed mice. Conclusions: Our data suggests that MGE + prbx modulates diet-induced metabolic, inflammatory, and microbial factors. Further analysis of tumor tissue will determine whether MGE + prbx altered the tumor microenvironment to improve WD-associated BC prognosis.

50. Immune-enhanced tumor organoid (iTO) model for the testing of oncolytic immunotherapy

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Introduction: Despite recent advances in therapeutics, cancer remains one of the leading causes of mortality in the United States. Immunotherapies are a new class of medication that have demonstrated great promise in treating many different types of cancer, of which one promising subclass are oncolytic immunotherapies, based on the use of viral strains that selectively lyse tumor cells and induce antitumor immune activation. The development of oncolytic immunotherapies, as with many cancer therapies, is limited by a lack of in vitro models that effectively mirror the in vivo tumor microenvironment and host physiology, however, tumor organoids, based on growth of tumor cells alongside other cell types in a 3-dimensional, physiologically relevant extracellular matrix (ECM), represent a potential solution to this problem.

Methods: Tumor organoids have recently been engineered to include different immune cell types, representing a potential avenue for testing of immunotherapy. Here we develop and subsequently test an immune-enhanced tumor organoid (iTO) model for the testing of oncolytic immunotherapy. The model consisted of the CT-26 murine colorectal cancer cell line and BALB/c splenocytes embedded in a MatrigelTM matrix. This model was found to best support infection by the M51R-GFP strain of vesicular stomatitis virus (VSV) and subsequent immune activation due to its host compatibility.

Results: This model demonstrated profuse tumor cell-selective infection peaking at 24 hours and gradually declining through 96 hours after viral incubation. This resulted in increased levels of apoptosis and decreased tumor cell viability in the iTOs as assessed by immunofluorescence and ATP assay, respectively. Multiple signs of immune activation were also demonstrated consistent with the expected immunotherapeutic mechanism of action, including marked upregulation of IL-6 and enrichment in immune cell populations expressing antigen presenting cell and T cell markers.

Conclusions: The iTOs developed here effectively support infection with oncolytic immunotherapy and demonstrate core facets of the immunotherapeutic mechanism of action. This model represents a basis for the development of future oncolytic immunotherapies and ultimately a platform for personalized medicine through incorporation of human patient-specific tumor cells.

51. Using a Crowdsourcing Platform to Determine the Preferred Cephalic Index of Infants

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The cephalic index (CI), the width divided by the length of the head, is commonly used to assess head shape, particularly in children. In infants, it is used to diagnose abnormal head shapes, in particular positional plagiocephaly or scaphocephaly (long head). A recent study (Phelan et al. 2021 Plast Reconstr Surg), recorded the CI of children without any craniofacial disorders, and found that the normative CI values had increased significantly over the last 40 years, presumably due to the Back-to-Sleep campaign. Interestingly, to date there are no studies that have determined what is considered the ideal CI, and it is not known if it is the same as the normative CI. We used Amazon Mechanical Turk (mTurk), a crowdsourcing platform, to distribute an IRB-approved survey designed to determine the preferred CI. The survey included 9 questions in which four 3D surface images of heads of patients from age 3-6 months having different CI were presented, and the respondent was asked to choose a preferred head shape; based on this we were able to calculate each respondent's preferred CI. There were 1020 responses to the survey, 58% female, 77% white, and 39% college graduates. The overall mean preferred CI was 81.8 (standard deviation 2.5) compared to the normative CI of 85.4 from Phelan et al. There were no significant differences in preferred CI related to age of the respondent. In a subgroup analysis of respondents of different ethnicities, the mean preferred CI of white respondents was 81.7, while it was 82.3 and 82.7 for Asian and black respondents, respectively (Anova, $p = 0.00062$). There were no significant differences in mean preferred CI in subgroup analysis of level of education, medical literacy, or working with children. This is the first study that attempts to determine the preferred CI in infants 3-6 months of age, which will help craniofacial surgeons compare their outcomes to the preferred CI.

52. Preoperative Activity Status Predicts Postoperative Head and Neck Wound Complications

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Introduction: Preoperative functional activity status (PFAS) is a key component of frailty, a known risk factor for postoperative complications. The association between PFAS and incidence of postoperative wound complications, however, has not been well described in head and neck (H&N) literature. The current study investigates if PFAS as measured by metabolic equivalents (METs) impacts wound complication incidence after H&N cancer surgery Methods: IRB-approved, retrospective review of patients from 2014-20 who underwent resection of non-esophageal, aerodigestive tract Squamous Cell Carcinoma at a single tertiary care center. A standardized MET calculation questionnaire was utilized. METs measure energy cost of activities compared to basal metabolic rate. One (1) MET equates to energy used when sitting. Ten (10) METs correspond to energy used with vigorous activity. Patients were divided into 3 MET groups: 7-10 (Group 1), 5-6 (Group 2), or 1-4 (Group 3). Chart-documented wound complications included flap failure, dehiscence, infection, incisional breakdown, hematoma, and chyle leak. Wound complication incidences were compared to discern if low (<4) MET subgroup patients developed more complications than higher MET subgroup patients. Statistical analysis was done via Welch t-test. A p value <0.05 comprised statistical significance Results: Out of 233 patients, 46 (19.7%) had <4 METs (Group 3), 145 (62.2%) had 5-6 (Group 2), and 42 (18%) had >7 METs (Group 1). Wound complications occurred in 24.4% of patients. Of these, 12.2% were in Group 1, 66.6% in Group 2, and 21.0% in Group 3. Group 1 (METs >7) patients had a significantly lower wound complication incidence compared to Group 2 or 3 ($p=0.02$). The difference remained significant after adjusting for tobacco or alcohol use, preoperative albumin, and prior chemoradiation Conclusion: Patients with high PFAS (METs >7) had significantly lower incidence of postoperative wound complications compared to patients with METs <7 after adjusting for common risk factors. Functional status, defined by METs, may predict wound complications after H&N cancer surgery

53. Initial Evaluation & Risk Stratification of Orbital Fractures

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Purpose: To evaluate demographic characteristics, clinical and radiographic signs, symptoms, concomitant injuries and management of patients with acute orbital fractures in order to determine the degree to which initial evaluation of orbital fractures by ophthalmologists in the emergency department (ED) setting resulted in significant change of management and to explore the possibility of creation of a risk stratification tool **Methods:** A retrospective chart review of 2019 ED visits with initial orbital fractures involving ophthalmology consultation. Fracture details, imaging, comorbid ocular injuries, surgical reports, and management recommendations by ophthalmology were gathered and analyzed. **Results:** Intervention was recommended by ophthalmology in 27.9% of patients with orbital fractures. Ruptured globe, lateral canthotomy, and concern for entrapment being the most common associated injuries requiring emergent intervention. Several variables (decreased visual acuity ($p < 0.0001$), extraocular motility deficit ($p < 0.0084$), retrobulbar hemorrhage ($p < 0.0011$), and eyelid laceration requiring repair ($p < 0.0001$)) were associated with increased risk of concomitant, serious ocular injury. Retrospective application of these four variables as part of a risk stratification tool appears to effectively screen patients without compromising patient safety. **Conclusions:** The majority of orbital fractures seen by ophthalmology required no intervention. Application of a four-variable risk stratification tool by non-ophthalmology providers may result in safely risk stratifying patient consultation/visits safely decreasing unnecessary consultations in the ED.

54. Characterizing Blood Transfusion on Distal Aortic Blood Flow during Supraceliac Complete Aortic Occlusion in Swine Animal Model

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Background: Resuscitative endovascular balloon occlusion of the aorta (REBOA) is an endovascular procedure that can be used to provide hemodynamic support to hemorrhagic shock patients with non-compressible truncal hemorrhage. During REBOA, patients often receive blood transfusions to improve hemodynamics and correct hypovolemia before definitive surgical hemostasis. As cardiac output and aortic pressure increase in response to aortic occlusion and fluid and blood transfusion, aortic diameter will increase as a function of aortic compliance. This may result in unintended flow around the aortic balloon. To date, this leakage phenomenon has not been fully characterized and must be mitigated by progressive balloon inflation to maintain complete occlusion and to avoid ongoing hemorrhage. **Hypothesis:** We hypothesized that unintended blood flow around the REBOA balloon would occur following the initial establishment of aortic occlusion and during resuscitation, requiring continued inflation of the balloon to maintain complete aortic occlusion (AO). **Methods:** Yorkshire swine were anesthetized and instrumented to collect proximal mean arterial blood pressure (pMAP), distal MAP (dMAP), balloon pressure (bP), balloon volume (bV), and aortic flow (AF). A 7 Fr compliant aortic balloon was positioned in the supra-celiac aorta via femoral arterial access. Animals underwent 30% total blood volume hemorrhage over 30-min (T0-T30). At T30, the balloon was inflated to complete AO, defined by distal aortic flow of $<100\text{ml/min}$. Automated balloon inflation occurred from T30-T60 when downstream flow was detected. At T55, blood was transfused over 18-min (T55-T73). At T60, automated balloon deflation ensued to maintain a pMAP $>65\text{ mmHg}$ over 15 minutes. P values were calculated using a Mann-Whitney U test. **Results:** Hemodynamics were analyzed for 10 animals (weight $72.94\pm 5.36\text{ kg}$). At T30, T50, T55, and T60 the mean pMAP was $31.29\pm 7.86\text{ mmHg}$, $91.10\pm 21.20\text{ mmHg}$, $89.20\pm 19.60\text{ mmHg}$, and $129.54\pm 15.08\text{ mmHg}$. During complete AO and ongoing blood transfusion (T55-T60), mean pMAP was $108.5\pm 16.17\text{ mmHg}$ and mean dMAP was $12.44\pm 2.79\text{ mmHg}$. The mean AF at T30, T50, T55, and T60 was $15.53\pm 7.53\text{ mL/min/kg}$, $0.90\pm 0.79\text{ mL/min/kg}$, $0.95\pm 0.71\text{ mL/min/kg}$, and $2.00\pm 0.90\text{ mL/min/kg}$. During steady state complete AO (T35-55) mean AF was $0.84\pm 0.60\text{ mL/min/kg}$. This increased statistically significantly to $1.57\pm 0.77\text{ mL/min/kg}$ during T55-T60 ($p=0.035$). Mean bV at T30, T50, T55, and T60 was $0.00\pm 0.00\text{ mL}$, $5.57\pm 1.61\text{ mL}$, $5.61\pm 1.65\text{ mL}$, and $7.00\pm 1.52\text{ mL}$. During steady state AO, mean BV was $5.49\pm 1.57\text{ mL}$, which increased to $6.11\pm 1.56\text{ mL}$ ($p=0.353$) during AO with concurrent transfusion (T55-T60). The mean bP at maximum AO during blood transfusion was $253.53\pm 62.54\text{ mmHg}$. During T55-T60, there were 21 balloon inflations

among the 10 animals analyzed compared to 5 inflations during the preceding 15-min of steady state AO. Conclusions: Our data demonstrated that during REBOA with concurrent blood transfusion, progressive balloon inflation was required to maintain aortic occlusion due to increasing pMAP and AF. In clinical practice, following initial establishment of AO in the context of hemorrhagic shock, progressive balloon inflation may be required to maintain AO in response to intrinsic and transfusion mediated increases in cardiac output, blood pressure, and aortic diameter. This is particularly important when definitive hemostasis has not been achieved, as loss of aortic occlusion with blood flow beyond the balloon may result in ongoing hemorrhage and hemodynamic collapse. Funding Source: Funding for this study was provided by the US Army Medical Research and Development Command. Award Number: W81XWH-18-0072. Funding was also provided by The Dubie H. Holleman Fund for Cancer and Heart Research.

55. #Laryngology: A Standardized Hashtag Ontology

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Background: In the past decade, there has been a rise in social media applications and usage among individuals in the otolaryngology community. Hashtags (#), used to identify posts relating to similar topics, are utilized by patients and providers to search medical information, build a network, find providers, and discuss research. Previous otolaryngology literature includes a standard ontology, or list of hashtags, developed for otology. To date, the ontology of laryngology hashtags has not been created. The objective of this study is to propose a standardized ontology to use when discussing topics in laryngology on social media to maximize reach and effect. **Methods:** Using a combination of previously published techniques, along with some laryngology specific adjustments, the authors developed a list of suggested hashtags. An initial list was systematically culled from laryngology Instagram accounts including academic programs, professional societies, conferences, and expert social media laryngologists (fellowship-trained laryngologists with publically available professional accounts with greater than 500 followers). The list was narrowed down using current rate of use, specificity, and expert opinion. These were then categorized to include general terms, diseases and diagnoses, and treatment strategies

Results: Across all culled Instagram posts, there were 242 unique laryngology hashtags used and 1145 total hashtags were applied. The authors derived unique terms to be included in the ontology for laryngology by expert opinion of fellowship-trained laryngologists. **Conclusion:** Laryngology is in the early stages of utilization of social media. Developing a specific ontology of hashtags will optimize the reach and connections of term specific searches.

56. Quantifying the Hemodynamic Impact of REBOA vs. P-REBOA During Hemorrhagic Shock Using CFD

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Introduction: Traumatic injuries account for 5 million deaths per year globally, with hemorrhage responsible for 30-40% of all trauma-related fatalities [1]. In particular, non-compressible torso hemorrhage (NCTH) contributes to 34% of early fatalities, necessitating rapid lifesaving interventions. To address this problem, Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA), has been developed to mitigate internal bleeding by inflating balloon catheters to create a temporary aortic occlusion. While successful at augmenting pressure and perfusion proximal to the balloon, REBOA is associated with various distal complications including ischemia-reperfusion injury (IRI) and multi-organ failure [2]. To reduce collateral injury, partial inflation of the balloon (i.e., p-REBOA) has been recommended [3,4]. Yet, there remains no optimized implementation of p-REBOA. Towards this goal, we aimed to utilize computational fluid dynamic (CFD) models of the aorta to assess the hemodynamic impact of varying degrees of p- REBOA.

Materials and Methods: A three-dimensional (3D) anatomically representative geometry of a porcine thoracic aorta was constructed from CT scans within CRIMSON® (v1.4.5 Ann Arbor, MI). Varying degrees of aortic occlusion with a REBOA balloon catheter were modelled, ranging from 50-100% occlusion. The aortic geometry was thereafter discretized, generating meshes ranging from 2.9-4.7 million elements for each simulation. Pressure and flow boundary conditions were

set based on porcine experimental values during phases of baseline, hemorrhagic shock, and aortic occlusion. Cardiac output was prescribed as the inlet aortic velocity while three-element Windkessel models were prescribed to simulate the systemic vascular resistance and compliance at each arterial outlet. For all models, flow was assumed to be steady, Newtonian, and incompressible with a no-slip condition prescribed at all walls. Additionally, arterial walls and the REBOA device were assumed to be rigid.

Results and Discussion: Average blood pressure dropped from 75 mmHg to 54 mmHg during hemorrhage, corresponding to a 43% reduction in velocity. During 100% REBOA, pressure rose to 129 mmHg with areas of high recirculation proximal to the occlusion site. At 90% p-REBOA, significant pressure gradients (101/2 mmHg) were observed across the balloon, with an average flow of 0.12 L/min to the descending aorta. Meanwhile, 50% p-REBOA displayed an average pressure relatively similar to hemorrhage values but presented greater distal flows (an average of 2.08 L/min to the descending aorta). High wall shear stress (WSS) and shear rate, greater than 10 Pa and 8000 s⁻¹, respectively, were observed during 100% REBOA and 90% p-REBOA at the site of occlusion and in the brachiocephalic artery. 90% p-REBOA displayed not only the largest magnitude of WSS (>20 Pa), but also the largest WSS gradient across the balloon, potentially contributing to vascular endothelial damage.

Conclusions: This study resulted in the first in silico model simulating altered hemodynamics during various physiologic stages of hemorrhagic shock, and the impact of REBOA implementation. The resultant hemodynamic descriptors allow us to compare the impacts of varied percent occlusions under steady state conditions. During 90% p-REBOA, elevated WSS was observed around the site of occlusion; however, during a lower gradient partial occlusion (50%), WSS was observed to be near baseline values. These data suggest that optimal partial occlusion may be between 50 and 90%. Future work is needed to validate these simulations and to incorporate the shear-mediated physiologic response to REBOA with the ultimate goal to optimize REBOA implementation clinically.

57. Monitoring Early Postoperative Mobility at Scale

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Background: Early mobilization is considered an important component of postoperative recovery in the hospital; however, a large portion of patients fail to ambulate during their hospitalization, even with mobility initiatives and dedicated mobility aides. Real-time system-wide objective monitoring of patient mobility could play a central role in evaluating mobility programs and identify patients at higher risk for postoperative complications due to low mobility. The current study aimed to evaluate the feasibility of large-scale posture monitoring and the role of posture in measuring of postoperative mobility. Hypothesis: We hypothesized that existing continuous vital sign patient monitoring (VISI Mobile®) technology can objectively characterize the postural behavior of patients in the early postoperative period and identify patients at risk for adverse postoperative outcomes, like readmission. Methods: In this study, the accuracy of VISI Mobile in recording patient posture was evaluated and the feasibility of monitoring posture data at scale was evaluated. To evaluate VISI posture data (lying, reclining, upright) accuracy in detecting change in posture, five patients were monitored at fixed intervals over five hours comparing observed posture to VISI monitor real-time posture data. VISI monitor posture position was also recorded for 11 patients during ambulatory events. Retrospective accelerometer-based posture data from a cohort of postoperative patients between January and November 2019 was analyzed. Patients who had undergone major cancer surgery, were monitored for at least 24 hours, and had a length of stay longer than 24 hours were included. VISI Mobile posture was recorded and evaluated over the patient's postoperative recovery. Duration of upright posture was compared with postoperative outcomes including 30-day readmission. Results: 562 patients (60.7 mean age, 40.6% female) were identified with posture monitoring. The majority of patients monitored were ENT (26.0%) or Surgical Oncology (20.5%) patients with mean length of stay of 6.9 days (SD 6.1 days). Mean duration of posture monitoring was 77 hours (SD 49 hours) with mean number of posture changes being 18,495 (SD 11,692). VISI monitoring data recorded mean time spent upright per day of 206.2 minutes (SD 190.1 minutes) representing only 14.3% (SD 13.2%) of the observation period. Without adjusting for type of operation or other factors, no significant difference in the upright duration was identified between patients who were readmitted and those who were not ($p > 0.05$). During in-room posture change, VISI recorded posture was identical to observed posture with sensitivity and specificity of 1.0. During out-of-room ambulation, VISI monitoring was less reliable with accurate record of upright posture in 84% of ambulatory events. Conclusion: Real-time posture data from continuous vital sign patient monitoring (VISI Mobile®) technology was shown to be valuable for monitoring patients' mobility after surgery on a large scale.

58. The Impact of Autoimmune and Peripheral Vascular Disease on Sympathectomy Outcomes- An Update

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Purpose: To compare outcomes between autoimmune and non-autoimmune peripheral vascular disease (PVD) patients following periarterial sympathectomy (PAS). **Methods:** A retrospective review of patients with autoimmune disorders or PVD who underwent PAS from 1997-2017 was performed. Primary outcomes included non-healed digital ulcers, recurrent digital ulcers, amputations and a composite outcome of total adverse events. **Results:** During the study period, 123 hands in 88 patients were identified. Mean age was 54 ± 14 years and median follow-up was 9 months. There were 65 patients (97 hands) with autoimmune disorders and 23 patients (26 hands) with PVD. There was a significantly higher rate of vaso-occlusive disease in PVD patients, occurring in 100% of PVD patients and 54% autoimmune patients. PAS with revascularization was performed in 12% (N=8) of autoimmune patients and 39% (N=9) of PVD patients. Autoimmune patients had a significantly higher rate of bilateral disease requiring bilateral PAS, occurring in 49% (N=32) autoimmune patients and 13% (N=3) of PVD patients. On univariate analysis, there were no significant differences in the primary outcomes between the two groups. Total adverse events occurred in 42% (N=27) of autoimmune patients and 13% (N=3) of PVD patients. Symptomatic improvement was comparable, with 18% of autoimmune and 16% PVD patients experiencing persistent symptoms. Multivariate analysis was performed and controlled for disease state, presence of revascularization and bilateral hand PAS. This demonstrated that PVD patients had a lower likelihood of having postoperative adverse events in comparison to autoimmune patients. **Conclusion:** In comparison to autoimmune patients, PVD patients are at a lower risk of developing adverse postoperative events including non-healing ulcers, recurrent ulcers and amputations.

59. Donor Derived Cell Free DNA Monitoring in Kidney and Kidney Pancreas Transplant Recipients- Initial Wake Forest Experience

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Donor-derived Cell-free DNA monitoring In Kidney and kidney Pancreas Recipients - Initial Wake Forest experience Berjesh Sharda, MD, Matthew Garner MD, Alan C Farney, MD, PhD, Jeffrey Rogers, MD, Giuseppe Orlando, MD, PhD, Colleen Jay, MD,, Robert J Stratta, MD **Abstract:** ***Purpose:** Percutaneous renal allograft biopsy is the current gold standard for detecting acute rejection after kidney transplantation (KT). Noninvasive tests such as plasma-based donor-derived cell-free DNA (dd-cfDNA) assays have been proposed as an alternative to biopsy. We sought to examine the value of dd-cfDNA testing at one month following KT in different donor and recipient categories. ***Methods:** We performed a single center retrospective review of all adult KT and simultaneous pancreas-KT (SPKT) patients (pts) who underwent dd-cfDNA testing between January 2018 and September 2020. The diagnosis of acute rejection was based on histopathology obtained from percutaneous, ultrasound-guided, needle biopsies. Our center's standard practice included dd-cfDNA testing and performing surveillance kidney biopsies at 1 month following KT. The dd-cfDNA test was considered elevated if $>1.0\%$. ***Results:** During the study period, 3157 dd-cfDNA tests were performed in 695 de novo pts; only 2% of samples were unacceptable. Higher mean 1-month values (range 0.72-2.2%); 22-44% of patients have 1-month values $>1.0\%$ seen in: - Highly sensitized patients (panel reactive antibody level $\geq 98\%$) - Retransplants - Patients with early re-operations - SPK transplant recipients Lower mean 1-month values (0.45-0.56%); 7-14% have 1-month values $>1.0\%$ seen in: Primary kidney alone transplant recipients (standard criteria donor (SCD) expanded criteria donor (ECD), donation after cardiac death (DCD), living donor (LD), dual KT (DKT), acute kidney injury (AKI) donors, \pm delayed graft function (DGF). n 58 primary KT pts with negative 1-month surveillance biopsies, corresponding mean 1-month dd-cfDNA levels were 0.49 ± 0.4 . In 10 pts with positive 1-month surveillance biopsies, corresponding mean 1-month dd-cfDNA levels were 1.5 ± 1.8 . In 26 pts with a 1-month dd-cfDNA level >1.0 , the subsequent incidence of acute rejection was 27%; in 22 pts with a 1-month dd-cfDNA level ≥ 2.0 , the subsequent incidence of acute rejection was 50% (mean follow-up 14 months). ***Conclusions:** We noted a bimodal distribution of 1-month dd-cfDNA levels. Higher mean 1-month dd-cfDNA levels (range 0.72-2.2) were associated with retransplants, high PRA pts, SPKTs, and pts with early reoperations; 22-44% of pts in these categories had 1-month

dd-cfDNA levels >1.0. Conversely, primary KT alone pts (DCD, living donor, AKI donor, SCD, ECD, dual KT, those with DGF) had lower 1-month dd-cfDNA levels (range 0.45-0.56) and only 7-14% had 1-month dd-cfDNA levels >1.0. One-month surveillance biopsy results correlated with corresponding dd-cfDNA levels. Elevated 1-month dd-cfDNA levels occur in pts at a higher risk for acute rejection, suggesting that these pts need to be monitored more closely.

60. Immuno-Reactive Cancer Organoid Models to Examine Microbiome Metabolite Effects on Immune Checkpoint Blockade Efficacy

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Introduction: As the number of available immunotherapies for solid tumors increase, their prevalence in the clinic continues to rise as well. While the results are promising and immunotherapies have benefits over traditional chemotherapeutics, a sizable percentage of patients are non-responders to all types of immunotherapy as a treatment option. These differences in sensitivity can be either innate or acquired. It is well accepted that specific diets have a significant impact on our health including effects on different therapies for cancer and other diseases. Although much progress was made recently in developing models of cancer, there has been limited in vitro models to assess tumor immune-reactivity. Such models would be ideal for isolating specific molecular mechanisms that dictate cell behavior and interactions. We have recently created tumor organoid model containing cancer cells paired with cytotoxic T-cells in order to model immune checkpoint blockade (ICB) efficacy. Our goal is to use this model to examine novel microbiome-ICB interactions that were shown to alter therapeutic response levels in patients. **Methods:** We created tumor organoids consisting of matched tumor and immune cells, embedded in extracellular matrix (ECM)-like hydrogels. Organoids were treated with therapeutic equivalent doses of anti-PD-1 and anti-CTLA-4. The organoids were also exposed to physiologic concentrations of metabolites 3-indolepropionic acid derived from the bacterial species *Clostridium sporogenes*, hippurate derived from *Clostridiales*, *Faecalibacterium prausnitzii*, and *Eubacterium*, pyocyanin derived from *Pseudomonas aeruginosa*, butyrate derived from *Faecalibacterium prausnitzii*, and inosine derived from *Bifidobacterium pseudolongum*. Each of these bacterial species and the associated metabolite represent a likely effector of host immune function described in literature and therefore a potential effector of ICB response. Organoids were analyzed with cell viability assays, flow cytometry, RT-qPCR, and immunohistochemistry staining to determine the effects of the metabolites on ICB response. **Results and Discussion:** We showed that ICB therapy stimulated internally localizing T-cells, inducing T-cell-mediated tumor cell killing. ICB treated samples resulted significant loss of viability with corroborating readings from the other methods of characterization. RT-qPCR and flow cytometry demonstrated the cellular changes due to bacterial metabolite co-administration. These results include increased expression of CD-8 T-cell co-receptor, increased cytokine production, and increased effector T-cell viability. **Conclusion:** We have created an ex-vivo tumor immune-reactive organoid model for studying immunotherapy. We are working to elucidate the effects of microenvironment factors, such as microbiome metabolites, and observe their impacts on immunotherapy efficacy to better understand what conditions are conducive or detrimental to successful ICB treatment.

61. A1 Pulley Tenderness as a Modification to Tenderness along the Flexor Sheath in Diagnosing Pyogenic Flexor Tenosynovitis

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Background: Pyogenic flexor tenosynovitis (PFT) is frequently diagnosed by physical examination according to the Kanavel signs. However, these signs have had varying sensitivity and specificity for PFT. This study proposes a modification of the Kanavel sign “tenderness over the course of the flexor sheath” by including palpation of the A1 pulley to increase specificity. **Methods:** A retrospective review was performed over eight months for patients in the emergency department who received a consult to hand surgery to rule out PFT. Two cohorts, non-PFT infections and PFT infections, were studied for the presence or absence of the four Kanavel’s signs, as well as specifically over the A1 pulley on the affected digit(s) or T1 pulley of the thumb. **Results:** There were a total of 33 patients in the two cohorts (21 non-PFT, 12 PFT) with statistically

significant differences with regards to the presence of all the Kanavel signs. A1 pulley tenderness had the greatest odds ratio, positive predictive value, specificity, and accuracy when compared to all Kanavel signs. When used in conjunction with each Kanavel sign, there was an increase in specificity in all four signs. Receiver Operating Characteristic (ROC) analysis revealed increased area under the curve (AUC) with A1 pulley tenderness added, indicating improved ability to classify hand infections as PFT vs. non-PFT. Conclusions: While the classic Kanavel signs have shown reliable clinical utility, this study finds that tenderness at the A1 pulley can be a useful specification of “tenderness over the course of the flexor sheath.”

62. Feasibility of Deep Learning Combined with Multispectral Imaging for Intra-Operative Guidance in Burn Excision Surgery

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Purpose: In burn surgery the goal is to accurately excise the non-viable burned tissue to expose a healthy wound bed for skin grafting. The surgeon must estimate the required depth of excision and evaluate the viability of the wound bed prior to grafting. Currently, clinician judgment is the only method used to delineate viable from non-viable tissue. We investigated the effectiveness of a non-invasive multispectral imaging system to aid clinician judgment in a porcine model of burn excision. **Methods:** Multispectral imaging data was obtained from serial tangential excisions of thermal burn injuries and used to train two deep learning algorithms. One algorithm was developed to identify the location of non-viable tissue in the wound bed, the other was to estimate the depth of non-viable tissue. Histology of the excised tissue was used as the gold standard for determining the presence and depth of non-viable tissue. Following algorithm development, we studied the ability of two surgeons to estimate burn depth and wound bed viability both unaided and aided by the device. **Results:** The Deep Learning algorithm significantly improved the surgeons' abilities to determine the viability of the wound bed by 25%. In addition, when the surgeons updated their initial estimates of burn depth after seeing the device output, there was an 85% probability that the new estimate would be more accurate. **Conclusions:** This investigation shows the feasibility for image guided burn excision that involves understanding how clinician judgment would be impacted when aided by a device during surgery. This initial work shows promise for a real-time imaging system in burn surgery.

63. The Virtual Interview Experience: Advantages, Disadvantages, and Trends in Applicant Behavior

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Introduction: Residency programs and applicants were forced to hold virtual interviews during the 2020-2021 application cycle. Inability to evaluate a program and/or applicant in person has intangible drawbacks. However, there are obvious advantages: cost, convenience, and comfort. Do the advantages outweigh the disadvantages? How have applicant behaviors changed to learn about programs in a virtual-only interview process?

Methods: A survey was distributed to 302 applicants to a single plastic surgery residency program during the 2020 application cycle. Demographics, social media presence and utilization, and experience with the virtual application and interview process were analyzed. A 2018 survey from our institution was compared to a subset of questions for longitudinal analysis.

Results: Seventy-six respondents (25.2%) completed the survey. Most applicants (88.2%) spent less than \$1000 during the interview and application cycle. Over half (56.6%) did not receive letters of recommendation from outside their home program. A significant minority (27.6%) of applicants attended more than one interview in a single day. Compared to 2018, applicants in 2021 were significantly more likely to access alternative digital resources (forums/discussion boards, social media, and podcasts) when learning about programs. Average number of interviews remain in the range of pre-COVID studies, but the percentage of interviews attended increased.

Conclusion: Applicants spent substantially less money on interviews and relied on alternative digital sources to learn about residency programs. This study objectively quantifies the advantages of virtual interviews. Disadvantages include inability to assess “fit” and lack of non-verbal communication.

64. CD47 Blockade Limits Immunosuppressive Checkpoint Molecules in the Tumor Microenvironment to Sensitize Triple-Negative Breast Cancer Tumors to Immune Checkpoint Blockade Therapy

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Triple-negative breast cancer (TNBC) lacks druggable targets and has high metastatic incidence. Immune checkpoint blockade (ICB) antibodies are FDA approved for TNBC treatment, but therapeutic response and biomarkers are limited. Therefore, additional therapeutic targets and biomarkers are needed to sensitize TNBC tumors to immune checkpoint blockade therapies and improve patient response. CD47 is an integral membrane protein overexpressed on cancer cells that alters anti-tumor immunosurveillance, resulting in tumor progression. CD47 is involved in metabolic reprogramming but whether CD47 is a marker of progression and its role in ICB response for TNBC remains unknown. Human TNBC biopsies were subjected to immunohistochemical analysis to determine CD47 role in TNBC progression. Human matched primary, and metastatic TNBC biopsies increased immunoreactivity to CD47, signifying a potential therapeutic target. To determine CD47 impact on tumor burden, a carcinogen-induced TNBC model was performed in female wild type (WT) and cd47 null (cd47^{-/-}) C57Bl/6 mice. CD47 deficiency in the carcinogen-induced DMBA model decreased tumor incidence, weight, and area compared to WT. Since CD47 can regulate metabolism, tumors underwent metabolomic analysis. Principal component analysis displayed differentially regulated metabolites between WT and cd47^{-/-} tumors. Decreased carnitine conjugated fatty acids and ketone bodies were observed in cd47^{-/-} tumors compared to WT, suggesting decreased fatty acid availability and/or metabolism. TNBC cell respiratory measurements validated that targeting CD47 shifted metabolic dependency from fatty acid oxidation to glycolysis. Kynurenine/tryptophan pathway metabolites, which catabolize Indoleamine-2,3-dioxygenase (IDO1) and are involved in anti-PD-1/PD-L1 resistance, were decreased in cd47^{-/-} tumors compared to WT. To evaluate immune infiltrate signaling, tumors underwent spatial tissue proteomics by multiplexing photo-cleavable antibodies in Formalin-Fixed Paraffin-Embedded samples. Spatial proteomic analysis determined that cd47^{-/-} tumors had elevated immune cell infiltration (CD45⁺, CD3⁺), suggesting CD47 absence enhances tumor immunogenicity and immune-mediated tumor ablation. Multiplexing of photo-cleavable antibodies increased protein expression of immune checkpoint molecules (PD-L1, VISTA, B7-H3, BatF3) and immunosuppressive cell types (CD11b⁺, Ly6c⁺) in WT tumors compared to cd47^{-/-}, suggesting CD47 absence limits immunosuppressive signaling. Since anti-PD-L1 therapies are approved to treat TNBC and WT tumors from our DMBA model show PD-L1 upregulation, we examined how targeting CD47 would impact tumor burden of mice receiving anti-PD-L1 therapy through an orthotopic EMT-6 murine TNBC model. Targeting CD47 or PD-L1 as monotherapy decreased tumor burden; however, in combination it further reduced tumor burden compared to anti-PD-L1 treatment due to increased intratumoral granzyme B secreting cytotoxic T cells. Our data indicate that CD47 may serve as a marker of anti-PD-L1 response, and targeting CD47 enhances immunogenicity and decreases immunosuppressive molecules, sensitizing TNBC tumors to anti-PD-L1 therapy to reduce tumor burden.

65. Volumetric Analysis of Sagittal Synostosis Surgical Outcomes Using Three-Dimensional Stereophotogrammetry

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Craniosynostosis is the premature fusion of one or more cranial sutures with the most common being sagittal craniosynostosis that effects 1 in 4000 live births. These patients present with abnormal head shape (scaphocephaly) characterized by frontal bossing, sagittal ridging, bitemporal narrowing and occipital bulging. The sequela of untreated craniosynostosis include skull deformity, cranial growth restriction and delayed neurocognitive development. Operative interventions can largely be divided into strip craniectomy and cranial vault remodeling. Strip craniectomy with the utilization of spring dis-

traction (termed Spring assisted suturectomy, SAS) was a further modification popularized in the United States by our own Dr. Lisa David.

Cephalic index is a measurement of cranial head-shape and over time the use of this objective scale has been called into question due to its limitation of calculation from two-dimensional measurements. CT scans in the past have been available for the calculation of volumetric changes in craniofacial surgery; however, use has largely fallen out of favor due to unnecessary exposure to radiation in the infant. This has opened the door to increasing use of noninvasive three-dimensional stereophotogrammetry allowing surgeons to draw more definitive conclusions about calvarial shape and outcomes. Prior literature quantifying these volumetric differences between surgical techniques is largely based on CT scans and portable 3D imaging.

Our institution now routinely obtains non-invasive three-dimensional stereophotogrammetry on all patients presenting to our clinic with abnormal head shape or clefting allowing us a large collection of data. Our purpose is to analyze the volumetric differences in head shape between cranial vault remodeling, spring assisted suturectomy and endoscopic strip suturectomy with helmeting, using three-dimensional stereophotogrammetry.

Since 2018, we have had 46 patients undergo surgery for sagittal craniosynostosis including pre-operative and post-operative imaging with the 3dMDface System. Early analysis of imaging strengthens previous results from our own institution suggesting spring assisted suturectomy results in greater improvement in total cranial volume as opposed to frontal volume which translates to improvement in overall head shape that can be not be fully appreciated from cephalic indices alone. Our hope is the results of our study will further elucidate the volumetric impact of sagittal craniosynostosis intervention and will further the movement towards non-invasive three-dimensional stereophotogrammetry as the gold standard of measurement in craniofacial surgery.

66. Salvage Resections for Oropharyngeal Cancer in the HPV-Era

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Introduction The incidence of oropharyngeal squamous cell carcinoma (OPSCC) has risen in the last decade with a majority of new cancers now attributed to human papillomavirus infection (HPV). If initial management of a primary tumor fails, salvage surgery is the mainstay of treatment. Before the onset of the HPV-era, previous studies have shown a poor prognosis for salvage surgeries in oropharyngeal carcinoma. In this study, we aim to identify prognostic factors for patients treated with salvage surgery for OPSCC, specifically that of HPV-positive status. **Methods** A retrospective review of all definitive resections performed at our institution for OPSCC between 2010-2018 was conducted. Thirty-two patients were identified who had previously undergone radiation or chemo-radiation for OPSCC and later required salvage surgery at Atrium Health Wake Forest Baptist Hospital. Data on demographics, prior therapy, surgery, pathology findings, and outcomes were collected. Cox proportional hazard regression models were used to assess the association between independent measures with overall survival and time to recurrence. **Results** Smaller tumors were associated with improved overall survival and disease-free interval ($p=0.0082$, $p=0.011$). The ability to perform endoscopic or transoral surgery was also associated with improvement in survival and lack of recurrence ($p=0.0044$, $p=0.017$). Just over half of the cancers were HPV-positive ($n=17$, 53%); HPV-status was not associated with improvement in survival or disease-free interval. Fifteen patients recurred after surgery salvage surgery: six with distant metastases and local recurrence, eight with only local recurrence, and one with only distant metastases. Of these, only three remain alive. **Conclusions** Previous studies have demonstrated that tumors that survive initial chemo-radiation therapy have an especially aggressive biology (1). The two-year survival rate ranges greatly in prior studies, from 27-49% (2-3). At 47%, this study demonstrates a survival rate at the upper-limit of this range, though this outcome is still grim. While HPV-positive primary tumors tend to be associated with better outcomes, we found no impact in HPV-status and outcomes of salvage surgery. Because of the high morbidity and poor functional outcomes that can arise with salvage surgery, patients must be carefully selected.

67. Resident and Medical Student Perspectives on Future Training in Otolaryngology during the Covid-19 Pandemic

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Objective: To survey the attitudes of medical students on their decision to apply to otolaryngology residency, and otolaryngology residents on their decision to apply to fellowships in light of the Covid-19 pandemic. **Methods:** A cross-sectional survey was sent to medical students and current otolaryngology residents via otomatch.com and through distribution via email by residency program coordinators from July 2020 to August 2020. **Results:** 36 medical students and 24 residents completed the survey. For medical students, 6 of 36 (17%) respondents indicated that the Covid-19 pandemic changed their decision to apply for an otolaryngology residency. The change in the application process and changes at their home medical school were cited as the most common reasons for not applying. For residents, only 1 (4%) respondent indicated the Covid-19 pandemic had changed their decision to apply for fellowship due to the large number of aerosolized cases. **Conclusion:** There appears to be a portion of medical students who have either delayed their decision to apply to residency or applied to other specialties due to the changes in the application process in the 2020-2021 cycle caused by the Covid-19 pandemic. This may impact the future application process as students apply with later cycles or apply to other fields due to lack of exposure. Residents applying to fellowship do not appear to have been impacted though.

68. Shear-Wave Elastography of the Testis in Pediatrics, Establishing the Standard Values

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Introduction/Background Shear-wave elastography (SWE) is a technique that measures sonographic quantification of tissue elasticity. Previous studies provide evidence of apparent structural and histological differences in testicular tissue elasticity for certain testicular diseases. SWE provides a noninvasive investigation of the stiffness of the testicular tissue as a primary diagnostic tool for certain testicular disorders with the potential to replace biopsies and exploratory surgical procedures. While studies are investigating normal shear wave elastography values for testis in adult men, no studies have provided standardized normal range values for shear wave elastography for the pediatric testis. The purpose of this study is to establish the normal threshold ranges of shear-wave velocity in pediatric patients (0 - 18 years). **Methods/Materials** Patients from one clinic location were screened for the study, excluding those with a known history of testicular diseases, sex chromosome abnormalities, or testicular surgery. Fifty-four volunteers (mean age: 6.12 ± 4.57 , range: 3 months - 18 years) were chosen and underwent routine B-mode sonography and simultaneous multi-frame shear-wave elastography of both testes. Patients were divided into two age groups: 3 months - 9 years and 10 - 18 years ($n = 40$ and $n = 14$ respectively). The volume of each testis and the shear-wave velocity at the testis' superior, center, and inferior poles were measured and collected. **Results** The mean shear-wave velocity for the patients under and over 10 years old was 1.24 ± 0.035 m/s and 1.098 ± 0.074 m/s respectively ($p = 0.0654$). However, when age groups were analyzed by anatomical pole, a statistically significant decrease in the shear-wave velocity was found between groups at the inferior, central, and superior pole with p -values of 0.0317, 0.0006, and 0.024, respectively. **Conclusions** From the 54 patients, preliminary data to determine normal shear-wave velocities for a pediatric testis population was collected. Significant decreases in shear-wave velocities found between the age groups at each anatomical pole may indicate tissue elasticity differences as the testes mature and grow. We will continue to enroll more patients to better define standards for comparison.

69. Short Term Outcomes with Early Weightbearing Utilizing Willits Protocol Following Haglund's Surgery

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Background: Insertional achilles tendinopathy is a common foot and ankle condition that can cause severe, debilitating pain. When conservative treatment fails, surgical options are offered to patients. While literature has been published regarding surgical techniques for insertional achilles tendinopathy, there has been little published regarding postoperative protocol following surgery. We hypothesize that the Willits protocol will allow for early mobilization and decreased postoperative complications in regards to pain and reoperation rate. Methods: A retrospective chart review was conducted of 7 patients who underwent surgical treatment for insertional achilles tendinopathy with Haglund's deformity by a single foot and ankle surgeon. Following surgery, Willits protocol was initiated for early mobilization. Results: The patients had an average decrease in pain from 7 to 3 postoperatively. One patient or 14% required reoperation. There were no postoperative ruptures or avulsion fractures. No patients required a brace long term. Conclusion: The Willits protocol, though initially created for achilles tendon ruptures, provides an early mobilization protocol for patients after insertional achilles tendinopathy procedures. Our study found low reoperation rate and improved pain level while allowing patients to mobilize earlier than previously reported in literature.

70. Intermediate to long-term Follow up of the Salto Talaris Fixed Bearing Total Ankle Prosthesis

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Background: Total ankle arthroplasty is an alternative procedure for end-stage ankle arthritis. We hypothesize with exacting patient selection, the Salto Talaris arthroplasty will demonstrate as a favorable alternative to an ankle arthrodesis at a long term follow up. Methods: In this retrospective study, intermediate- to long-term outcome measures (VAS pain scale, survival rate, postoperative use of brace and patient satisfaction) of 19 consecutive fixed bearing Salto Talaris total ankle arthroplasties between August of 2009 and August of 2018 were analysed and compared before and after surgery. Medical records and radiographs were reviewed. Results: The average follow up in our study was 6.9 years. Our study showed a 21% complication rate according to the Glazebrook classification system. The reoperation rate was low at 10.5% with a 100% survivorship of the total ankle implant. Sixteen percent reported using a brace postoperatively. The average pain decreased from 9.1 preoperatively to 2.6 postoperatively. Patients reported a 95% satisfaction rate. Conclusion: The Salto Talaris arthroplasty provides a good alternative to ankle arthrodesis with low complication and reoperation rates and high survivorship. We believe with stringent patient selection, the Salto Talaris system shows great promise at a long term follow up.

71. Breast Cancer Organoids as a Model for Testing Personalized Therapies

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Introduction: Breast cancer is one of the most frequently diagnosed cancer in women with a high mortality rate. More than 20 different subtypes of breast cancer are identified. Advancement in patient-derived organoid technology makes it possible to preserve cellular, structural, and tissue microenvironment which mimics the tissue in vivo.

Method: We developed patient derived breast organoids both from normal and cancer biopsies recapitulate the structure of breast tissue. Breast biopsies were enzymatically digested to yield a single cell suspension. About 1x10⁵ cells were

encapsulated in a 3:1 collagen I (Col I) and hyaluronic acid (HA) mixture. For breast tumor immune enhanced organoids (iTOs), 2 x 10⁵ patient matched PMBCs were mixed with the breast cancer cells and encapsulated as described above.

Results: Histological analyses of the breast organoids shows the characteristics of the breast tissue with well-defined acini in H&E. In tumor organoids acini were somewhat perturbed compared to normal breast organoids. Immuno-fluorescence staining shows the expression of breast biomarkers including EGF receptor 2 (HER2), Progesterone receptor (PR), Estrogen receptor (ER). Zona occludin 2 and keratin 19 expression in luminal cells and expression of Keratin 14 and P63 in basal cells suggested correct polarization in the organoids. Immunofluorescence staining of (iTOs), with T cell markers including CD3, CD4, and CD8 indicated that immune cells remained viable in the iTOs. Drug responses to Doxorubicin, Paclitaxel and a combination of Doxorubicin-Paclitaxel showed significant inhibition of cell growth in normal and tumor organoids ($p < 0.04$) except for Paclitaxel failed to inhibit tumor cell growth. Immunotherapy with nivolumab (anti PD-1) immune check point inhibitor showed no significant effect on cell growth.

Conclusions: Breast cancer organoids recapitulate the histological features of breast tissue in culture and response to chemotherapies. In the future, patient-derived tumor organoids can provide a platform for personalized medicine.

72. Can Old Imaging Alter the Preoperative and Operative Course of Patients Undergoing Parathyroidectomy for Primary Hyperparathyroidism?

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Introduction Surgical intervention provides the only definitive treatment for primary hyperparathyroidism (PHPT). Although imaging plays no role in diagnosis, it is essential for preoperative localization when a focused parathyroidectomy is planned. We hypothesized that identification of enlarged parathyroid glands on imaging obtained prior to the diagnosis of PHPT has the ability to impact the preoperative evaluation and intraoperative course of patients undergoing parathyroidectomy. Methods The study included adult patients with a diagnosis of PHPT who underwent parathyroidectomy between 10/2015 and 10/2020 and had contrast-enhanced CT imaging of the lower neck and upper chest prior to diagnosis for unrelated indications. A neuroradiologist retrospectively viewed these prior scans blinded to the operative findings, and a surgeon compared the imaging findings to preoperative notes and operative reports to determine whether and how information derived from prior imaging might have impacted the preoperative work-up and intraoperative course of these patients. Results We identified at least one visibly enlarged parathyroid gland on a prior contrast-enhanced CT in 30 (75%) of 40 included patients. The average time between the oldest scan where an enlarged parathyroid was visible and parathyroidectomy was 4.6 years (range 0.9 to 11.4). Despite old imaging enabling correct localization, 16 of these 30 (53.3%) underwent a sestamibi scan and 2 (6.7%) underwent a parathyroid CT prior to parathyroidectomy. Additionally, knowledge of the enlarged parathyroid(s) on prior imaging might have allowed a more focused approach in 3 (10.0%) and prevented 1 unnecessary thyroid lobectomy performed in search of disease. Similarly, localizable disease on old imaging might have prompted a more thorough exploration in 4 (13.3%) and possibly prevented missed disease and failure to cure in 3 (10.0%). We determined that viewing prior imaging could potentially change the preoperative evaluation in 70.0% of patients with localizable disease on old imaging and the operative course in 23.3%. When considering the entire cohort with relevant old contrast-enhanced imaging available, conservative estimates indicate reviewing these scans might alter the preoperative work-up in 52.5% of patients presenting with PHPT and the operative course in 17.5%. Conclusion The identification of enlarged parathyroid glands on imaging that predates a diagnosis of PHPT has the potential to impact the preoperative evaluation and intraoperative course of patients undergoing parathyroidectomy. When available, prior contrast-enhanced CT imaging should be reviewed prior to obtaining additional imaging or planning the operative approach.

73. Pulsed Electromagnetic Field Therapy is Effective for Pain Reduction and Symptom Improvement in Patients with Interstitial Cystitis/Bladder Pain Syndrome

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Introduction: Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic pelvic pain condition (bladder and beyond) that affects millions of (mostly) women in the United States. Despite the wide range of available treatment options for IC/BPS, effective pain management continues to be a significant clinical challenge for these patients. Recent evidence suggests that an alternative novel strategy, pulsed electromagnetic field (PEMF) therapy, proven to be effective for pain reduction in other related chronic pain conditions, may provide pain relief in some IC/BPS patients. Therefore, the primary objective of this pilot study was to evaluate the efficacy of PEMF therapy for pain management in women with IC/BPS.

Methods: Women 18-80 years old with a confirmed diagnosis of non-bladder-centric IC/BPS (i.e., with an anesthetic bladder capacity >400cc) and a numeric rating scale (NRS) score for pelvic pain ≥ 6 were recruited for this prospective interventional trial. Following their initial study visit and training, participants were sent home with a PEMF device consisting of: (1) a central console pre-programmed to deliver the same therapeutic dose each session, (2) a whole-body mat, and (3) a long "belt" for targeted therapy over the pelvic region. Participants were instructed to use the device twice daily (8 minutes per pre-programmed session), once in the morning and evening - at least 8 hours apart - over the 4-week treatment period. Patient assessments occurred at enrollment and 1-day post-treatment period. The primary outcome measure was a change in the NRS score for pelvic pain; a change of ≥ 2 points was considered significant improvement. Secondary outcome measures were assessed by validated IC/BPS questionnaires including the O'Leary Sant Interstitial Cystitis Symptom and Problem Indices (ICSI/ICPI), Pain and Urgency/Frequency (PUF) Patient Symptom Scale, Female Genitourinary Pain Index (F-GUPI), and the Short Form-36 (SF-36) Quality of Life Questionnaire. In this proof-of-concept study, all participants (N = 10) received the full therapy (i.e., no sham control). Median difference in outcomes were assessed by the Wilcoxon signed rank test and $p < 0.05$ was considered significant.

Results: Of 10 enrollees, 8 women completed the 4-week therapeutic regimen and were eligible for analysis. Based on the primary outcome measure, 7/8 patients (87.5%) reported a significant reduction in pelvic pain; no participants reported an increase in pain. Significant improvement based on secondary outcomes were apparent from a decrease in mean scores for nocturia (2.38 to 1.75; $p=0.025$), and mean symptom scores including ICSI (13.88 to 8.00; $p=0.011$), ICPI (13.00 to 9.13; $p=0.046$), PUF (25.50 to 18.25; $p=0.02$), and GUPI scores (35.25 to 23.44; $p=0.012$). Additionally, patients showed a significant increase in mean SF-36 quality of life sub-scores including energy/fatigue (34.38 to 60.16; $p=0.018$), social functioning (45.31 to 73.43 $p=0.042$), and pain (38.44 to 63.13; $p=0.028$). Finally, mean urinary frequency scores decreased numerically but did not reach statistical significance (2.5 to 1.75; $p=0.059$). No adverse events were reported.

Conclusion: This proof-of-concept interventional trial evaluating the efficacy of PEMF therapy for pain management and symptom improvement in IC/BPS found measurable benefit in 7 of the 8 patients that completed the study. Randomized, sham-controlled trials in a larger cohort are necessary to validate these findings.

74. Differential Gene Expression Analysis to Elucidate the Mechanism of Testicular Fibrosis in Klinefelter Syndrome

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BASIC SCIENCE – Resident

Introduction/Background Klinefelter's Syndrome (KS) is characterized by widespread testicular fibrosis, germ cell loss, and seminiferous tubule degeneration during puberty. The exact mechanism of this process is unknown. However, alterations of the blood-testis barrier, loss of contractile function in peritubular myoid cells, and derangement in testicular blood flow have all been proposed as possible mechanisms. Macrophages and mast cells are increased in KS testes relative to normal testes, suggesting that inflammation may contribute to the fibrotic process. This study aimed to characterize changes in gene expression underlying testicular fibrosis in human KS testes. **Methods/Materials** Total RNA was extracted from homogenized, age-matched (patients aged 8-38 years old), paraffin-embedded testicular biopsies from five KS and four control (46XY) patients and analyzed with the NanoString nCounter Fibrosis Panel, which included 770 genes. Raw data was analyzed through R-based software. Change in gene expression was significant if the absolute fold change was >1.4 or <0.7 with a p -value <0.05 . Using Ingenuity Pathways Analysis (IPA) software, we analyzed the identified up- and down-regulated transcripts to map functional activity and gene networks. IPA generated p -values <0.05 indicated statistically significant, non-random association, and z -scores >2 and <-2 indicated activation or deactivation of a functional process,

respectively. Weighted gene correlation network analysis (WGCNA) was applied to find co-expressed gene modules. Results The NanoString analysis found 19 genes differentially expressed in KS testes compared to controls, with 17 upregulated and 2 downregulated. WGCNA identified six modules of co-expressed genes. 14/17 upregulated genes clustered in the “blue” module, which included 109 genes with significant membership ($p < 0.05$). “Blue” module hub genes included PNPLA3, ELOVL6, and EGFR. IPA showed that key functional categories of differentially expressed genes in KS testes were cellular function/maintenance, immunological disease, hematological system development/function, and inflammatory response. The most highly activated functional processes in KS testes involved vascular development and mobilization of immune cells. Conclusions This study indicates that the development of testicular fibrosis in Klinefelter’s syndrome is a complex process that involves immune cell mobilization and vascular development. Inflammation may contribute to the derangement of the testis microenvironment in KS, leading to hypogonadism and infertility. Further understanding of this process may help prevent or treat testicular dysfunction in KS patients.