Stanford MEDICINE | Department of Surgery

THE 22nd ANNUAL
EMILE F. HOLMAN LECTURE
In Surgery

The 22nd Annual
Emile F. Holman Lecture In Surgery
and
12th Annual Resident Research Day

Friday, May 7, 2021

David and Joan Traitel Building
Hoover Institution I Stanford University

Poster Presentations
10:30 AM - 12: 00 PM
Hoover Tower Lawn

Lunch
12:00 PM - 1:00 PM
Fairweather Courtyard

Abstracts
1:00 PM - 5:00 PM
Fairweather Courtyard

Holman Lecture
5:00 PM - 6:00 PM
Fairweather Courtyard
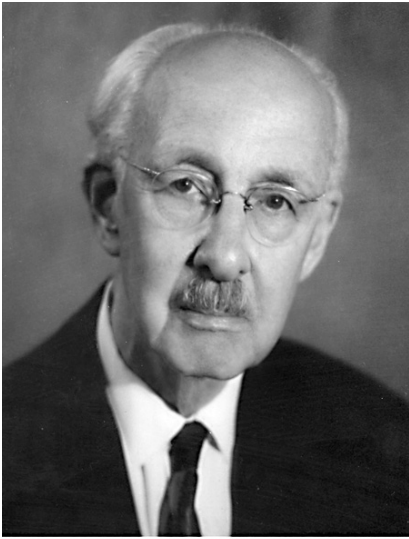
Holman Networking Hour
6:00 PM
Fairweather Courtyard

Stanford MEDICINE | Department of Surgery

Emile Frederic Holman, MD

August 12, 1890 to March 19, 1977
Founding Chair – Department of Surgery
Stanford University

Emile Frederic Holman, the son of a Methodist minister, was born in Missouri and then moved with his family as a teenager to southern California. He entered Stanford University as a math major in 1907; he dropped out for a semester to learn shorthand and typing in order to support himself. Upon his return, he performed stenographic work for Stanford's founding President, David Starr Jordan. After graduation, Holman stayed on as Secretary to President Jordan until 1914 when Holman went to Oxford as a Rhodes Scholar. Thereafter, began a key period of education at Johns Hopkins University.

Of some note, Sir William Osler wrote a letter recommending Holman for admission to The Johns Hopkins School of Medicine; Holman received his M.D. degree from Hopkins in 1918. He then became Assistant in Surgery in the Surgical Hunterian Laboratory, the research lab of the noted surgeon, William Stewart Halsted. He continued in Halsted's residency program until 1923, serving as the last resident surgeon at the time of Halsted's death in 1922. His loyalty to Professor Halsted was legendary; it was Holman who first brought the principles of the Halstedian residency to the west. In 1925 he returned to Stanford as Associate Professor of Surgery and in 1926 he was named head of the Department, a position he held for 29 years until his retirement from the faculty in 1955.

" … as a scholar, innovator, teacher and clinical surgeon, he pioneered a truly academic surgical program at a time when there were few others west of the Mississippi." — William P. Longmire, Jr

Dr. Holman is perhaps best known for his pioneering work in vascular surgery and, in particular, the physiology of arteriovenous fistulas. This research won him the coveted Samuel D. Gross prize from the Philadelphia Academy of Surgery in 1930 and the Rudolph Matas Medal in Vascular Surgery from Tulane in 1954. He was elected a member of The Johns Hopkins Society of Scholars in 1970. His co-authors over the years are a literal compendium of the substantial physicians and surgeons of the 20th century. Less well known were his fundamental ideas and observations on skin grafting. In 1924 he published a paper of his early work in the identification and characterization of the phenomenon of rejection of transplanted skin (from a parent to a child), particularly the accelerated rejection of second transplants from the same donor. These observations were not pursued, though many believe formed the basis for Medawar's work a quarter of a century later. His astute observations were recognized at the International Congress of The Transplantation Society in 1972 nearly 50 years after his paper was published.

Perhaps most importantly, Dr. Holman was a humanist as well as a scientist, devoted to the service of his fellow man. During World II his patriotism and selflessness were obvious during his volunteer time in the Pacific, though 51 at the time. His experiences in both World Wars made him a fervent critic of war; he did not hesitate to speak out against national policy or social injustice.

In all, he was perhaps the most Halsted-like graduate of any of the Halstedian residents.

"He was a man not easily forgotten. Yet it was not by bombast or power that he attracted attention. It was by his sharp and incisive mind, by his thoughtful and gentle demeanor and by his perpetual search for truth and excellence in science that we remember him." — James B.D. Mark, M.D

In his in memoriam tribute in the Journal of Thoracic and Cardiovascular Surgery, Frank Gerbode, in describing Dr. Holman's life and accomplishments, chose to quote William Shakespeare in King Lear: "We have seen the best of our time. We that are younger shall never see so much nor live so long." ■

Mary T. Hawn, MD, FACS

Professor and Chair
Emile Holman Professor in Surgery

The 2021 Emile F. Holman Lectureship and the Stanford Surgery Research Symposium had an unprecedented number and high caliber abstracts submitted this year. We're thrilled to continue the long tradition of showcasing the outstanding research by our trainees.   While the COVID-19 pandemic is not totally behind us, science has delivered highly effective vaccines at unprecedented speed! This remarkable accomplishment will allow us to convene safely, in person for this wonderful tradition. This year we are fortunate to be joined by John Alverdy MD, Professor of Surgery at the University of Chicago as our Holman Visiting Professor.

I'm grateful to Dr. Ardent Morris, Vice Chair for Research and the surgical research council respectively for their stewardship of this program and selection of the top abstracts for presentation.

Emile F. Holman was the first of the classically trained surgeons to move west, and for 29 years served as the founding Executive Head of the Department of Surgery. He established the tradition of an integrated research program, permeating every aspect of the surgical department, which continues to this day. We honor his legacy today.

A critical component of research within the department is the active participation of our residents under the mentorship of surgeons and scientists across our University. After the completion of a two year training core of surgery, our residents participate in a two year professional development program. The residents devote themselves to a project designed, first and foremost, to advance the field, but also to advance their own professional development and further forge their path in academic surgery. Basic science laboratories throughout the Department, the University and beyond are but one option, clinical research outcomes, education, device design and many others are options; advanced degrees are also possible.

I'm grateful to all of our faculty mentors and investigators for their commitment to this endless and exhilarating cycle of training the next generation of surgeon leaders. We're showcasing the abstracts that represent an enormous amount of work and preparation. We are proud of all their accomplishments! ∎

Arden M. Morris, MD, MPH

Professor and Vice Chair for
Research Department of Surgery
Director, S-SPIRE Center
Stanford University School of Medicine

Welcome to the 12th Annual Emile F. Holman Resident Research Day in Surgery!

In a year of firsts, Holman Day marks our first ever hybrid meeting and for nearly all of us who will attend in-person, our first opportunity to convene in the past year.

We are honored to host Dr. John Alverdy as our first Visiting Professor in over a year!

In spite of all we have been through, the Stanford Department of Surgery residents, post-docs, fellows and students once again have been more productive than ever before. This year, 69 individuals submitted a record 103 abstracts!

The best abstracts from each Department of Surgery trainee scientist are captured in this booklet. We invite you to read them all and hope you will share our appreciation of the diverse interests and disciplines represented within our department, from fundamental molecular biology to translational, clinical, bioinformatics, education, and health services research. Once more this year, we will return to the tradition of poster and podium presentations from our top-scoring trainee scientists. For the remaining abstracts, an online poster session is available at the Holman Day website https://surgery.stanford.edu/holman/2021.html. I encourage each of you to reach out for questions and discussion to those who describe work that particularly piques your interest.

Many thanks to Dr. Hawn and our spectacular Holman Day staff committee, Rachel Baker, Joseph Martinez, Julia Miranda, and Angelina Sepulveda for planning and operationalizing our first hybrid meeting! I would also like to recognize the heroic work of the Department of Surgery's Research Oversight Committee for abstract review and creation of the 2021 program—many thanks to each of you.

Clinical and Health Services Research Reviewers:
Catherine M. Curtin, MD, MPH
Arden M. Morris, MD, MPH
Sue Fu, MD
James R. Korndorffer, Jr., MD, MHPE
George R. Poultsides, MD,MS
Todd Wagner, PhD
Sherry Wren, MD
Marc Melcher, MD, PhD

Basic and Translational Research Reviewers:
James Dunn, MD, PhD
Stefanie Jeffrey, MD, MA
Sheri Krams, PhD
Nicholas Leeper, MD
Sakti Srivastava, MBBS, MS
Daniel J. Stoltz, MD
Derrick Wan, MD

Please join us in congratulating our trainees and colleagues in the Department of Surgery for the curiosity, enthusiasm, and systematic inquiry that they continue to apply to their scholarly work!

Sincerely,
Arden M. Morris, MD, MPH ◼

John C. Alverdy, MD

Sarah and Harold Lincoln Thompson Professor of Surgery
Executive Vice-Chair of the Department of Surgery and
Associate Director of NIH Digestive Disease Research
Center Core at the University of Chicago

Dr. is also a fellow of the Institute of Molecular Engineering at the University of Chicago. Dr Alverdy has been continuously RO1 funded by the NIH for over 20 years and has trained over 100 undergraduate students, graduate students, medical students and surgical research fellows in his laboratory. He studies the molecular pathogenesis of infection-related surgical complications such as sepsis, surgical site infections and anastomotic leak. He is past president of the Surgical Infection Society, past recipient of the Ravdin lectureship and Surgical Forum dedication from the American College of Surgery and recipient of the Flance-Karl Award from the American Surgical Association. He is co-founder and chief scientific officer of Covira Surgical which develops non-antibiotic polymer based anti-infective compounds to combat postoperative infection.

Dr Alverdy attended medical school at the Autonomous University of Guadalajara and Loyola University and received his surgical training at the University of Chicago affiliated Michael Reese Hospital. He completed a surgical research fellowship at the University of California San Francisco under the mentorship of Dr George Sheldon and Donald Trunkey. Dr Alverdy has an active practice involving minimally invasive/robotic surgery of esophagus, stomach and pancreatobiliary tree. ■

PROGRAM

Resident Research Day

Poster Presentations – Basic

Hoover Tower Lawn
10:30 AM – 12:00 PM

Title of Presentation	Presenter
Rescue of osteonecrosis by transplantation of intact blood vessel stem cell niches	Ling Zhao, MD
A New Spatial Single Cell Transcriptomics Method For Detecting Signaling Relationships In Stem Cell Niches	Yuting Wang, MD
Adipose Precursor Cell-Embedded Collagen Gels Attenuate Inflammation and Improve Tissue Perfusion in Cutaneous Wounds	Evan Fahy, MB BCh BAO, MCh
Disrupting Mechanotransduction Reduces Scar Formation and Restores Transcriptomic Cell Fates in a Large Animal Model of Skin Grafting	Kellen Chen, PhD
High RAS expression is associated with poor neuroblastoma patient survival and required for tumor formation in an orthotopic mouse model	Modupeola Diyaolu, MD
Identification of Genetic Variants Associated with Post-operative Atrial Fibrillation	Shaunak S. Adkar, MD, PhD
Wild-type mice dynamically alter fibroblast sub-populations to heal dorsal skin radiation wounds	Darren B. Abbas, MD
Novel genetic analysis of MRL mice reveals that complement inhibition by Factor H reduces scarring	Heather E. desJardins-Park

Poster Presentations – Clinical

Title of Presentation	Presenter
Sex-Based Differences in Self-Reported Post-Operative Pain Experience Following Common General Surgery Procedures	Alexis Doyle, MPP presented by Ashley Titan, MB BAO BCh MRCSI MD
Improving Tracheostomy Delivery for Trauma & Surgical Critical Care Patients: Timely Trach Initiative	Erin K. McShane, BS
Improvements and Gaps in Financial Risk Protection Among Veterans Following the Affordable Care Act	Charles Liu, MD, MS
Biliary Disease During the COVID-19 Pandemic	Andrea Fisher, BS
The Impact of Reconstructive Modality on the Severity of Postoperative Complications in Breast Reconstruction	Rachel Pedreira, MD
Postoperative Administration of Acetylsalicylic Acid Does Not Improve Clinical Outcomes after Microsurgical Breast Reconstruction	Farrah C. Liu
Geocoding Nationwide Trends and Disparities in High-Capability Trauma Center Access, 2013-2019	Jeff Choi, MD, MS
Prospective Study of Quality-of-Life One Year After Traumatic Rib Fractures	Suleman I. Khan, BA

Resident Research Day

Abstracts – Basic

Fairweather Courtyard
1:00 PM – 2:45 PM
Four minutes are allotted following each presentation for Q&A

Moderators:
Nick Leeper, MD
Geoff Gurtner, MD

	Title of Presentation	Presenter		Title of Presentation	Presenter
1:05 - 1:13	Cancer associated fibroblasts share highly-conserved phenotypes and functions across tumor types and species	Deshka S. Foster, MD, PhD, MA	**1:57 - 2:05**	Adipocytes in dermal wounds undergo conversion to pro-fibrotic fibroblasts that contribute to scar formation	Nicholas Guardino, BS
1:18 - 1:26	Integrated Spatial Multi-omics Reveals Fibroblast Fate During Wound Healing: A Novel Framework For The Study Of Complex Tissue	Michael Januszyk, MD, PhD	**2:10 - 2:15**	Regenerative skin healing through targeted modulation of Engrailed-1 expression	Shamik Mascharak,
1:31 - 1:39	Regenerating Articular Cartilage by Skewing the Skeletal Stem Cell Fate	Lauren S. Koepke, BS	**2:23 -2:31**	Transplantation of Skeletal Stem Cells and Wnt3a Prevents Re-synostosis Following Surgical Repair of Craniosynostosis in Coronal Sutures of Twist-1+/- Mice	Siddharth Menon, BS
1:44 - 1:52	NeuroStitch: Nanofabrication of a Biomimetic Peripheral Nerve Interface	Zeshaan Maab, MD, MSc	**2:36 - 2:44**	The mSSC response after tendon-to-bone injury is dampened with aberrant TGF-β Signaling	Ashley Titan, MB BAO BCh MRCSI MD
			2:50 - 3:00	BREAK	

For Q&A use slido

Resident Research Day

Abstracts – Clinical

Fairweather Courtyard
3:00 PM – 4:45 PM
Four minutes are allotted following each presentation for Q&A

Moderators:
Cindy Kin, MD
Cara Liebert, MD

	Title of Presentation	Presenter		Title of Presentation	Presenter
3:00 - 3:08	Racial Disparities in the Utilization of Parathyroidectomy among Patients with Primary Hyperparathyroidism: Evidence from a Nationwide Analysis of Medicare Claims	Wilson M. Alobuia, MD	**3:52 - 4:00**	Performance Assessment of Multimodal Cardiopulmonary Bypass Skills Assessment Within a High-Fidelity Simulation Environment	Calvin Perumalla, PhD
3:13 - 3:21	Comparing perioperative outcomes after noncardiac surgery across VA and non-VA hospitals	Elizabeth L. George, MD, MSc	**4:05 - 4:13**	Cost effectiveness of computed tomography versus ultrasound-based surveillance following endovascular aortic repair of intact abdominal aortic aneurysms	Vy T Ho, MD
3:26 - 3:34	Anemia: A Potential New Target For Preoperative Optimization In Heart Failure Patients Undergoing Elective Surgery	Charlotte M. Rajasingh, MD	**4:18 - 4:26**	Which AI Algorithms Best Define Surgical Workflow? A Look at Surgical Techniques and Instrument Use	Hossein Mohamadipanah, PhD; presented by Calvin Perumalla, PhD
3:39 -3:47	Insurance churn after traumatic injury: National evaluation among a large private insurance database	Sue Fu, MD	**4:31 - 4:39**	Impact of High Deductible Health Plans on Hernia Presentation	Kirbi Yelorda, MD
			4:45 - 5:00	BREAK	

5:00 PM – 5:45 PM
The 22nd Annual Emile F. Holman Lecture in Surgery

John C. Alverdy, MD

**"Microbiome Science to Understand and Prevent
the Worst of Our Surgical Complications"**

POSTER PRESENTATIONS

Rescue of osteonecrosis by transplantation of intact blood vessel stem cell niches

Liming Zhao, Holly Steininger, Yuting Wang, Malachia Hoover, Lauren Koepke, Thomas Ambrosi, Patricia Nguyen, Michael Longaker, Charles Chan

Introduction: Osteonecrosis is a common bone disease characterized by death of bone cells and collapse of bone structures. Whether restoring the blood supply to the affected bone could treat osteonecrosis is currently a hot topic of research. We have observed that vessels are composed of stem cell as well as niche populations, and co-transplanting vessel stem cells (VSCs) with niche cells results in formation of intact vessels cable of rescuing ischemic damage. We hypothesized that co-isolation and transplanting intact VSCs with niches will lead to optimal neovascularization and improvement of blood supply.

Methods: We established a new microfluidic based method (On-chip Sort) to purify intact VSCs clusters with niches and tested their ability to form vessels. We further tested transplanting of intact VSCs/Niches clusters in a mouse model of ischemic osteonecrosis. Laser Doppler was used to measure the blood flow of ischemic tissue, and uCT was used to assess changes to the bone structure. Histologic analysis was also performed to show the bone cell death and bone structure change.

Results: We observed that purified intact VSCs/Niches clusters gave rise to a higher frequency of host-derived intact vessel formation compared to VSCs along group. In addition, transplanting of VSCs/Niches clusters resulted in restoration of blood flow around the cauterized vessel to supply the distal tissue. Finally, the bone cell viability and bone structure in ischemic area were remarkably improved in the VSCs/Niches clusters transplanting group.

Conclusion: Our findings describe a new approach to rescue osteonecrosis by co-isolation and transplanting VSCs/niches units as their intact organization.
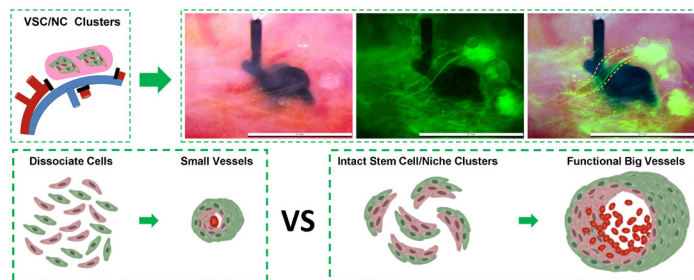
A New Spatial Single Cell Transcriptomics Method For Detecting Signaling Relationships In Stem Cell Niches

Ms Yuting Wang*,Dr liming Zhao, Ms Lauren S Koepke, Dr Thomas H Ambrosi, Ms Malachia Y Hoover, Dr Charles KF Chan.

Introduction: A thorough understanding of the regulatory mechanism within the stem cell niches is essential to develop efficient and specific strategies to stimulate stem cell medated regeneration in response to injury or disease. Here we introduced TESSERACT, a new spatial transcriptomic approach for profiling the 3 dimensional genetic changes within stem cell niches during regeneration.

Methods Intact clusters of regenerative tissues in rainbow mice were scanned by confocal to record the position of each cell before enzymatically dissociated and index sorted for single cell sequencing by high coverage Smart-seq2 scRNA-seq, and further analyzed for their precise cellular identity and signaling state. Confocal images were computationally quantified and matched back to cell index data by our matching algorithm, thus adding spatial information to scRNA-seq data and provided a dynamic spatial transcriptomic information at single cell level.

Results Up to 90% of the cell in the cluster scanned by confocal were detected by scQPCR. And by separately matching the index sort data with confocal image of the same cluster scanned from different angle, we verified that this approach can accurately record the spatial relationship in the cluster.

Conclusion We have developed a new spatial single cell transcriptomics method for detecting regulatory relationships in clusters of interacting cells, which provides a vital new tool for on-the-spot elucidation of cellular mechanisms and key niche signals in various tissue.

Adipose Precursor Cell-Embedded Collagen Gels Attenuate Inflammation And Improve Tissue Perfusion In Cutaneous Wounds

Evan J. Fahy, Darren B. Abbas, Michelle Griffin, Christopher V. Lavin, Michael T. Longaker, Derrick C. Wan

Introduction: Augmentation of wound tissue with progenitor-cell populations may provide a means to achieve tissue regeneration following injury. Collagen gels present a potential delivery method for biologic therapies such as these. Adipose precursor cells (APCs) have previously been defined by FACS and demonstrate the ability to generate adipocytes and potentially other cell types. The use of APCs in wound healing has not been previously explored.

Methods: CD1 nude mice underwent full-thickness excisional dorsal cutaneous splinted wounds. Adipose precursor cells(APCs) were identified and sorted from the harvested homogenized adipose depots of UBC/GFP+C57Bl/6 mice by FACS (Lin-, Sca1+, CD34+, PDGFRα+). Sorted APCs were embedded into collagen gels in 96-well plates(100k cells/well). Gels were placed into wound defects immediately following wounding. Gels without APCs and wounds without gels were employed as controls. Monitoring was carried out via photography and dermatoscopy, alongside scanning laser doppler flowmetry to assess perfusion between groups. Wounds were harvested for histological, cytokine and protein evaluation.

Results: APC-treated wounds exhibited a broadly reduced cytokine profile compared to control wounds (see figure for values). SLDF perfusion analyses demonstrated that the average perfusion of healed wounds was 80.40% of baseline in APC-gel treated wounds, compared to 62.25% in control gel wounds.

Conclusion: APCs represent an intriguing cell-type worthy of further investigation in relation to biological capacity and potential in regenerative medicine. APC-embedded collagen gels may also lend themselves to bioengineering approaches whereby chemical or mechanical means to control APC fate may be applied ex- or -in vivo to alter cell progeny and tissue phenotype.
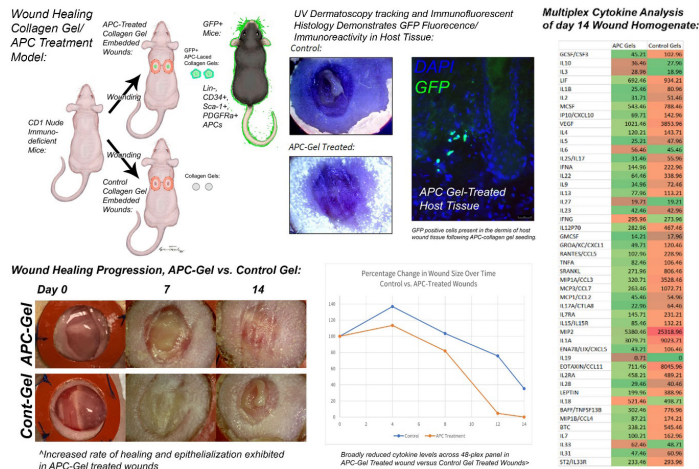
Disrupting Mechanotransduction Reduces Scar Formation and Restores Transcriptomic Cell Fates in a Large Animal Model of Skin Grafting

Kellen Chen PhD [1],, Dominic Henn, MD [1],*, Clark A. Bonham, BS [1], Chikage Noishiki, MD PhD [1], Janos A. Barrera, MD [1], Theresa C. Carlomagno, AS[1], Tara Shannon, BS[1], Chyna J. Mays[1], Artem A. Trotsyuk, BS[1], Jagannath Padmanabhan, PhD[1], Michael T. Longaker, MD, MBA[1], Michael Januszyk, MD, PhD[1], Geoffrey C. Gurtner, MD[1]*
[1]Hagey Laboratory for Pediatric and Regenerative Medicine, Division of Plastic and Reconstructive Surgery, Department of Surgery, Stanford University, Stanford, CA 94305, USA
[2]Institute for Stem Cell Biology and Regenerative Medicine, Stanford University, Stanford, CA 94305, USA
*contributed equally

Introduction: Humans and other large organisms heal wounds by fibrosis. The current standard-of-care for partial- and full- thickness soft tissue defects split-thickness skin grafting (STSG), which still result in scar formation.

Methods: We have developed the first large animal model of STSG using clinically relevant surgical techniques and established treatment protocols for postoperative wound care. Full-thickness excisional wounds were created on the back of red Duroc pigs. STSG were harvested and secured on the wound bed with skin staples, bolster dressings and either treated with focal adhesion kinase inhibitor (FAKI) hydrogels or standard dressings as controls. After 90 days, explanted tissue was processed for single cell RNA sequencing (scRNA-seq).

Results: All STSG showed a take rate >85%, undesirable aesthetics and a "meshed" appearance by 7 days, and substantial contracture and hypertrophy at 90 days (p<*0.05), indicative of a complex wound healed with fibrosis. From scRNA-seq, we identified pathways critical to driving scar formation, such as aberrant mechanotransduction signaling.

FAK inhibition significantly reduced contracture, fibrotic collagen deposition, and improved biomechanical properties. With scRNA-seq, we observed an increase in inflammatory cells in untreated scars which was reduced with FAKI. Moreover, fibroblast sub-populations in untreated scars showed an enrichment of chondrogenic differentiation fates, whereas FAKI drove fibroblasts toward pro- adipogenic differentiation states characteristic of unwounded skin.

Conclusion: Our findings indicate that FAKI-releasing patches provide an effective therapeutic strategy to mitigate fibrosis by restoring transcriptional differentiation fates. Our surgically relevant STSG model and translationally applicable therapy demonstrate promise for future human clinical use.

High RAS expression is associated with poor neuroblastoma patient survival and required for tumor formation in an orthotopic mouse model

Modupeola Diyaolu, Vinodh Rajagopalan, Jasmine Zeki, Lauren Wood, Rachel Greathouse, John O'Bryan, Bill Chiu

Introduction: MYCN-amplification predicts poor neuroblastoma (NBL) outcome but is only present in 22% of tumors, suggesting additional contributing pathways. Recently, RAS activity has been implicated in NBL. We hypothesize: 1) high HRAS expression results in poor patient survival, 2) RAS inhibition delays tumor formation. To test this, RAS monobody, NS1, was used to inhibit HRAS- and KRAS-mediated signaling.

Methods: GSE62564-dataset (498 patients) was divided according to MYCN-amplification, HRAS-expression, and overall survival. SK-N-FI cells (low-MYCN, high-HRAS) were infected with lentivirus encoding a doxycycline (DOX)-regulated NS1 expression construct that allowed for chemically regulated NS1 expression (SK-N-FINS1). Cells were treated with or without DOX to determine effects of RAS inhibition on cell proliferation and ERK-MAPK activity by Western blot for pERK levels. Orthotopic NBL xenografts were generated by injecting SK-N-FI-NS1 cells into the left adrenal gland of immunocompromised mice. Mice received fresh water +/- DOX every other day for 2 months. Tumors were tracked with ultrasound.

Results: NBL patients with low-MYCN can be divided into cohorts with high vs. low HRAS expression (p<0.0001). High-HRAS expression correlated with worse overall survival vs low-HRAS expression (p<0.001). DOX-induced NS1 expression in SK-N-FINS1 decreased RAS activity, pERK level, and proliferation. Mice injected with SK-N-FINS1 cells began to develop adrenal tumors at 13 days post injection however, treatment with DOX delayed tumor development to day 30. By day 34, all non-DOX-treated animals had developed tumor, while only 60% of DOX-treated animals did.

Conclusion: Patients with high-HRAS expression have worse overall survival. RAS inhibition delays NBL tumor formation suggesting that RAS-MAPK pathway may be potential therapeutic target for NBL treatment.

Identification of Genetic Variants Associated with Post-operative Atrial Fibrillation

Shaunak S. Adkar, Fudi Wang, Elsie G. Ross
Division of Vascular Surgery, Stanford University, Stanford, CA

Introduction: Post-operative atrial fibrillation (POAF) is a common complication after cardiac procedures associated with perioperative complications and mortality. Though etiology of POAF has been attributed to perioperative inflammation, adrenergic activation, and oxidative stress, whether an underlying genetic susceptibility exists has been unclear. Given the unique stressors of surgery, we hypothesized that new-onset POAF would be associated with genetic variants distinct from those previously associated with atrial fibrillation (AF).

Methods: The UK Biobank compiles phenotype data, genotype data, and inpatient hospitalization records for over 500,000 individuals. We stratified patients by presence of new onset AF after cardiac procedures, excluding patients with pre-operative AF. Categorical variables were compared using $c2$ tests and Mann-Whitney U tests were used for continuous variables. Genome wide association (GWA) analysis of post-operative and non-operative patients was performed using plink2.

Results: We identified 279 of 35138 (0.8%) patients diagnosed with new-onset POAF after cardiac procedures. Those with POAF were more likely to be male and have pre-operative hypertension, renal failure, CHF, and COPD (p<0.05). Patients undergoing CABG, aortic and mitral valve replacement were over-represented in the POAF cohort, while PCI and angioplasty were under-represented (p<0.05). GWA identified variants at chromosomes 6 (rs114931811, OR 3.2, CI 2.2-4.7, p < 5×10-8) and 8 (rs117682820, OR 2.9, CI 2-4.2, p<5×10-8) associated with POAF. These loci were not associated with AF in patients without surgery (Key Figure).

Conclusion: POAF is associated with distinct genetic variants compared with non-operative AF, suggesting a unique underlying predisposition to POAF in the setting of perioperative stressors from cardiac procedures.
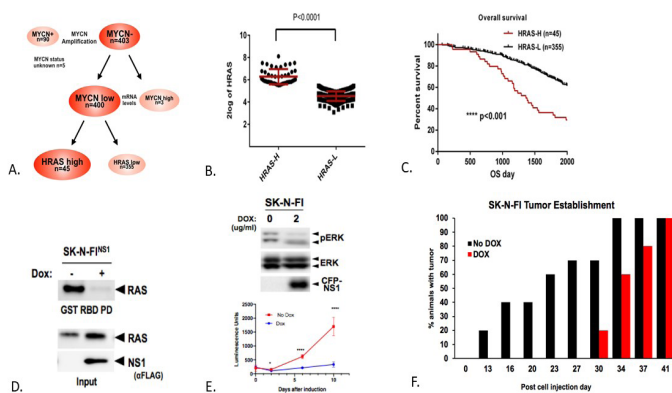

Figure 1. (A) Selection of patients from GSE62564 dataset with non-MYCN amplified, low MYCN and high HRAS expression NBL tumors. (B) Plot of log2 expression of *HRAS* in the MYCN-, low *MYCN* expression cohort. (C) Overall survival of the *HRAS* high vs *HRAS* low cohort. Patients with high *HRAS* expression exhibited significantly worse overall survival compared to those with low *HRAS* expression. (D) SK-N-FI cells with stable doxycycline (DOX)-inducible NS1 expression were treated +/-DOX for 2 days then lysed. Equivalent amounts of lysate were incubated with GST-RAF RBD to pulldown active RAS (top panel). Total RAS input and NS1 expression shown in bottom 2 panels. NS1 expression decreased RAS GTP levels. (E) Expression of NS1 inhibited pERK levels in SK-N-FI cells and NS1 expression reduced proliferation of SK-N-FI cells. (F) Days to tumor establishment, demonstrating longer time for tumor establishment in animals injected with SK-N-FI-NS1 cells and treated with DOX.

Wild-type mice dynamically alter fibroblast sub-populations to heal dorsal skin radiation wounds

Darren B. Abbas, M.D., Christopher V. Lavin, M.S., Evan J. Fahy, MB BCh BAO, MCh, Michelle Griffin, MBChB, Ph.D, Daniel K. Lee, M.D., Shamik Mascharak, B.S., Megan King, B.S., Michael Januszyk, M.D., Michael T. Longaker, M.D., M.B.A., Derrick C. Wan M.D.

Introduction: Radiation-induced skin fibrosis is a well-documented and burdensome sequela of radiation therapy, however the exact mechanism behind this effect is not well understood. We aim to better delineate the cellular mechanisms of acute and chronic radiation-induced skin fibrosis.

Methods: Thirty adult B6 mice underwent mechanical and chemical depilation of dorsal skin followed immediately by dorsal skin radiation with 5Gy every other day for 12 days, totaling 30Gy (A). At weeks 0, 1, 2, 4, and 8 after radiation, B6 skin was harvested and analyzed histologically. A machine learning algorithm was used to define collagen ultrastructure using polarized Picrosirius red images. Skin samples also underwent single-cell RNA sequencing to identify transcriptionally distinct subpopulations. Using GO analysis, genes were then cross-referenced with Enrichr to determine relevant biological pathways.

Results: Dermal thickness was noted to progressively increase from week 0 to 8. Dermal collagen deposition and linear organization also significantly increased throughout the experiment (B). CD31+ expression increased in the acute phase, but decreased below baseline levels by the chronic phase (C). Polarized picrosirius red images showed distinct clustering of time points as collagen fibers reorganize into a linear distribution (D). Five distinct fibroblast subpopulations were identified, and the genetic expression of these individual subpopulations demonstrated dynamic changes throughout the experiment (E).

Conclusion: Identification of these five fibroblast subpopulations and the dynamic gene expression during the healing process of irradiation wounds in wild-type mice is a novel finding and paramount to better understanding and treatment of radiation-induced skin fibrosis.
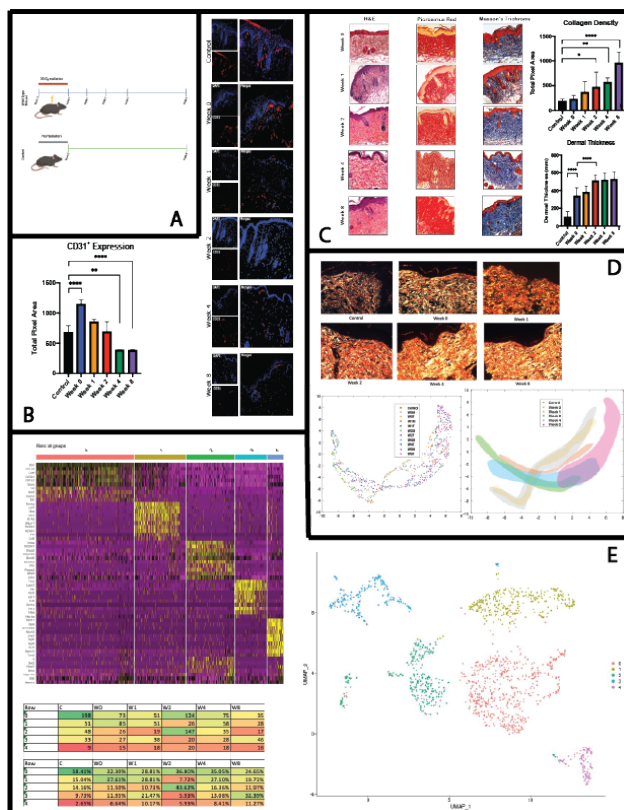
Novel genetic analysis of MRL mice reveals that complement inhibition by Factor H reduces scarring

Heather E. desJardins-Park,[1] Katya L. Mack,[2] Nicholas Guardino,[1] Michelle Griffin,[1] Michael F. Davitt,[1] Shamik Mascharak,[1] Derrick C. Wan,[1] Hunter B. Fraser,[2] Michael T. Longaker[1]
[1]Stanford School of Medicine, Stanford, CA, USA; [2]Department of Biology, Stanford University, Stanford, CA, USA.

Introduction: MRL mice regenerate ear punch wounds, while dorsal wounds scar. In recent Drosophila/fish studies, outbreeding a strain with a trait of interest and assessing offspring for spatial/tissue-specific differences in relative gene expression from the parent alleles (differential allele-specific expression; "diffASE") revealed genes underlying that phenotype. We hypothesized that diffASE could be applied to identify MRL pro-regenerative genes.

Methods: MRLxCAST offspring underwent dorsal excisional/ear punch wounding. POD7 dermal immune (CD45+), endothelial (CD31+), and fibroblast (Lin-) cells underwent FACS-isolation and RNA-sequencing. Reads were mapped to MRL/CAST genomes using strain-specific variants. Genes with significantly differing expression (FDR<5%) from MRL vs. CAST alleles and dorsal vs. ear wounds were identified.

Results: MRL ears regenerated by POD28, while MRL dorsum and CAST ear/dorsum scarred. Across cell types, substantially more genes in ear (vs. dorsum) had significantly different expression from MRL vs. CAST allele (e.g., immune cells: 2531 vs. 159 unique genes). Fibroblast diffASE genes were enriched for wound-related pathways (e.g., cell adhesion) and significantly overlapped with regions from a previous genomic study of MRL ear regeneration (*P=0.0094). Cfh (complement-inhibitory factor H) had MRL-specific upregulation in ear fibroblasts and was within a fine-mapped region. Treating MRL dorsal wounds with factor H (10mg/mL) yielded reduced scar thickness (*P=0.0050) and less-dense/-fibrotic ECM histologically.

Conclusion: In MRL/CAST hybrid mice, greater allele-specific gene expression occurred in ear (regenerative) than dorsal (scarring) wounds, consistent with ear-restricted phenotypic divergence. Integration with genomic regions previously functionally implicated in MRL regeneration revealed a potential role for complement factor H, suggesting a potential therapeutic approach to reduce scarring.

Sex-Based Differences in Self-Reported Post-Operative Pain Experience Following Common General Surgery Procedures

Alexis Doyle, MPP, Ashley Titan, MD, Kayla Pfaff, BS, Ioana Baiu, MD, Angela Lee, MD, Laura Graham, PhD, Andrew Shelton, MD, Mary Hawn, MD

Introduction: Given research reporting sex-based differences in sensitivity to pain and opioid analgesic response, we examined differences in self-reported experiences of postoperative opioid treatment between males and females.

Methods: A survey assessing opioid prescriptions, opioid use, and pain following surgery was sent to patients who underwent laparoscopic/open appendectomies, laparoscopic/open cholecystectomies, and laparoscopic/open inguinal hernia repair from January-June 2020. Bivariate analysis was conducted using χ^2 and fisher-exact tests for categorical variables and a student t-test for continuous variables.

Results: Among respondents, (n=139, 63.2% response rate), mean age was 49.3 years (SD 16.7) and 62 respondents (44.6%) were female. Females reported significantly higher levels of pain; both for worst pain level (6.0, SD 2.4 vs. 4.6, SD 2.3, p<0.001) and average pain level (3.9, SD 2.1 vs. 3.2, SD 1.9, p<0.05). Between males and females, there was a significant difference in those who reported sufficiently controlled pain (96.1% vs. 85.5%, p<0.05). There was no significant difference in number of opioid pills prescribed, amount of oral morphine equivalents (OMEs) prescribed, number of leftover pills, or opioid refill desire between males and females (Table 1).

Conclusion: Females reported significantly higher levels of pain overall during their recovery but were prescribed the same amount and had the same number of leftover opioids after surgery. These findings suggest that further exploration of patient-tailored postoperative pain regimens is warranted.

Table 1. Reported Pain Experience and Opioid Prescriptions by Sex of Survey Respondents.

	Male (n=77)	Female (n=62)	Difference in Means, Male-Female [95% CI]	p-value
Worst pain at surgical site following procedure (1-10), mean (SD)	4.61 (2.34)	6.00 (2.41)	1.39 [0.59, 2.19]	<0.001
Average pain at surgical site following procedure (1-10), mean (SD)	3.21 (1.94)	3.90 (2.13)	0.70 [0.01, 1.38]	0.04
Was your pain sufficiently controlled? (yes or no), n(yes) (%)	74 (96.10%)	53 (85.48%)	--	0.03
Number of leftover pills, mean (SD)	8.61 (4.24)	8.58 (6.64)	-0.02 [-2.41, 2.37]	0.98
Opioid refill desire (yes or no), n(yes) (%)	2 (2.56%)	3 (4.84%)	--	0.65
Number of pills prescribed, mean (SD)	12.28 (4.63)	12.78 (4.82)	0.49 [-1.16, 2.15]	0.55
Amount of OMEs prescribed, mean (SD)	91.58 (34.69)	93.02 (38.05)	1.43 [-11.26, 14.12]	0.82

Improving Tracheostomy Delivery for Trauma & Surgical Critical Care Patients: Timely Trach Initiative

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Introduction: Tracheostomy is recommended ≤7 days after intubation for patients with traumatic brain injury (TBI) or requiring prolonged mechanical ventilation. This quality improvement project aimed to reduce time-to-tracheostomy for eligible patients in the surgical intensive care unit (SICU).

Methods: Causes for delayed tracheostomy were determined through chart review at an American College of Surgeons Level 1 trauma center. We retrospectively analyzed two interventions: a July 2018 educational rollout for SICU residents and staff on the potential benefits and complications of early tracheostomy and a July 2019 digitally published workflow for early tracheostomy delivery for patients with TBI. Change in tracheostomy timing, hospital length of stay, ventilator-associated pneumonia, and peristomal bleeding rates were analyzed for three subgroups: patients with TBI, trauma patients, and all SICU patients.

Results: Following intervention, median time from intubation to tracheostomy decreased for all patients from 14 days (range: 4-57) to 8 days (range:1-32, p=<0.001) and median hospital length of stay decreased from 38 to 24 days (p<0.001, r=0.35). Tracheostomy timing for trauma patients improved after publication of the workflow (10 days [range: 3-21 days] to 6 days [range: 1-15 days], p=0.03). Among TBI patients, family meetings were held earlier for patients who underwent early vs. late tracheostomy (p=0.008).

Conclusion: We recommend regular educational meetings, enhanced by digitally published guidelines and strategic communication as effective ways to improve tracheostomy timing. Thorough, early meetings with patients or surrogate decision-makers are essential for early tracheostomy.
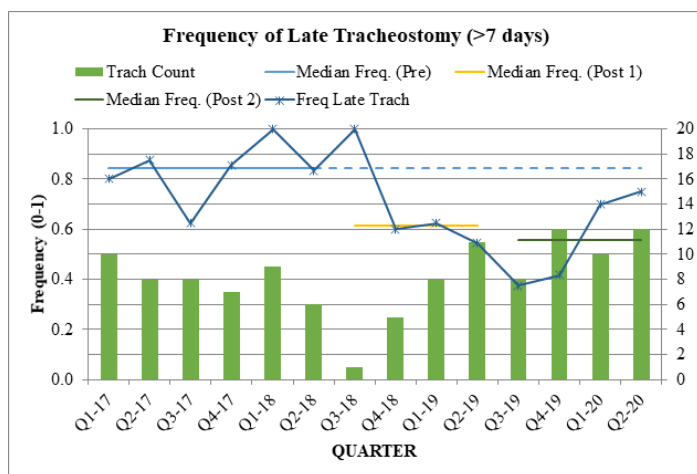
Figure 1: Frequency of late tracheostomy (left axis) and count of tracheostomies (right axis) for all patients. During the third quarter of 2018, informal bimonthly meetings began. During the third quarter of 2019, the early tracheostomy algorithm was published in the Trauma Guide App.

Improvements and Gaps in Financial Risk Protection Among Veterans Following the Affordable Care Act

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Introduction: Most of the nearly 20 million US veterans receive healthcare outside the Veterans Health Administration (VHA) and are thus vulnerable to burdensome out-of-pocket healthcare spending. Moreover, it remains unclear how recent reforms have affected veterans' financial burdens. We evaluated changes in veterans' risk of catastrophic health expenditures after implementation of the Affordable Care Act (ACA) and characterized drivers of their catastrophic spending post-ACA.

Methods: We evaluated a nationally-representative sample of 13,030 veterans aged 18+ from the 2010-2017 Medical Expenditure Panel Survey. Using multivariable linear probability regression, we examined changes in likelihood of catastrophic health spending, defined as out-of-pocket spending exceeding 10% of family income, after ACA implementation in 2014, stratifying by age (18-64 vs 65+), household income tercile, and payer (VHA vs non-VHA). Among veterans with catastrophic spending post-ACA, we evaluated sources of out-of-pocket spending.

Results: Among veterans aged 18-64, ACA implementation was associated with a 26% decrease in likelihood of catastrophic health expenditures (absolute change, -1.4 percentage points [pp]; p=0.03), which fell from 5.4% pre-ACA to 3.9% post-ACA. This was driven by a 38% decrease in catastrophic spending among veterans with non-VHA coverage (absolute change, -1.8pp; p=0.003). In contrast, catastrophic expenditure rates among veterans aged 65+ remained high, at 13.0% pre- and 12.5% post-ACA. Major drivers of veterans' spending post-ACA include dental care, prescription drugs, and home care.

Conclusions: ACA implementation was associated with reduced catastrophic health expenditures for younger but not older veterans. Potential policy solutions include establishing a veterans' dental benefit and improving prescription drug coverage.

Figure. Sources of out-of-pocket spending among veterans with catastrophic spending in post-ACA period (2014-2017), by age group and primary payer

VHA = Veterans Health Administration. Non-VHA includes Medicare, Medicaid, private insurance, and Tricare. ED = emergency department. Other includes durable medical equipment. Uninsured not shown for veterans aged 65+ due to small cell sizes.

Biliary Disease During the COVID-19 Pandemic

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Introduction: The COVID-19 pandemic has impacted hospital policies and influenced patient decision-making. Preliminary findings suggest patients were more likely to delay care for acute conditions during the pandemic, presenting later and with more severe disease. We investigated the effects of the pandemic on presentation, management, and outcomes of patients who developed gallbladder disease.

Methods: We retrospectively compared patients diagnosed with acute cholecystitis or symptomatic cholelithiasis who presented to Stanford University Medical Center emergency departments between March and June, 2020 to those in the same months of 2019. The primary outcome was overall incidence of disease; secondary outcomes included presentation, management, complications, and 30-day-re-presentation rates.

Results: 313 patients were identified: 152 in 2019 and 161 in 2020. The duration of symptoms prior to presentation was longer during the pandemic compared to control (mean [SD]: 4.2 [12.7] days in 2020 vs. 2.9 [5.8] days in 2019; p=0.21). Proportionally more patients in the COVID-19 cohort presented with acute cholecystitis (50% vs. 35%; p=0.01). Patients also presented with more severe cholecystitis in 2020 as indicated by higher mean Tokyo Criteria Scores (1.39 [0.56] vs. 1.16 [0.44]; p=0.02). Hospital admission was more likely in 2020 (65% vs. 50%; p=0.02), although no significant differences were observed in length of hospital stay or operative rate (Table 1).

Conclusion: During the pandemic, more patients presented with acute cholecystitis of higher severity, suggesting delays in treatment until progression of symptomatic cholelithiasis or worsening of cholecystitis. The COVID-19 pandemic has had far-reaching implications for health outcomes in non-COVID related illnesses.

Table 1 Presentation, Severity, and Treatment of Acute Cholecystitis and Symptomatic Biliary Colic Pre- and Post-COVID-19

	2019 (n =152)	2020 (n = 161)	P Value
Duration of Symptoms Prior to Presentation, mean (SD)	2.9 (5.8)	4.2 (12.7)	0.21
Patients with Cholecystitis (%)	53 (35%)	80 (50%)	0.01
Tokyo Grading for Acute Cholecystitis, mean (SD)	1.16 (0.44)	1.39 (0.56)	0.02
Antibiotics Administered, n (%)	61 (47%)	98 (61%)	0.10
Admitted to the hospital, n (%)	76 (50%)	104 (65%)	0.02
Surgery Performed, n (%)	61 (40%)	83 (52%)	0.06

The Impact of Reconstructive Modality on the Severity of Postoperative Complications in Breast Reconstruction

Rachel Pedreira, MD; Ruth Tevlin, MB BAO BCh MRCSI MD; Michelle Griffin, MBChB MRCS PhD; Derrick Wan, MD; Arash Momeni, MD

Background: Shared decision making is paramount in breast reconstruction. While large multicenter studies have broadly purported that autologous breast reconstruction (ABR) is associated with higher complication rates, few studies have investigated the rate and severity of complications following ABR and implant-based breast reconstruction (IBR) in matched cohorts. The aim of this study was to examine the impact of reconstructive modality on the severity of postoperative complications in matched patients undergoing ABR versus IBR.

Methods: A retrospective analysis of a prospectively maintained database of consecutive patients undergoing breast reconstruction was performed. Only patients who underwent nipple-sparing mastectomy with immediate breast reconstruction were included in the study. IBR consisted of staged expander/implant-based breast reconstruction in all cases. ABR consisted of immediate unilateral or bilateral free tissue transfer (including ms-TRAM, DIEP and PAP flaps). Major complications were those requiring inpatient admission and/or reoperation. Minor complications were those requiring intervention that did not meet major complication criteria. Multivariable logistic regression and propensity score match analyses were performed. A P-value of <0.05 was considered significant.

Results: 152 patients underwent nipple sparing mastectomy followed by ABR or IBR. 87 patients (n=143 breasts) underwent ABR and 65 patients (n=107 breasts) underwent IBR. The rate of total postoperative complications was not significantly different between reconstructive modalities (p = 0.61). However, there were significantly more major post-operative complications following IBR relative to ABR (p = 0.0043), whereas ABR was significantly associated with the development of minor complications relative to IBR (p = 0.0003). Propensity score matched analysis (PSM) of cohorts confirmed these significant findings (Table 1).

Conclusions: In conclusion, while there was no significant difference in overall complication rate between ABR and IBR in a matched cohort, IBR was associated with a higher rate of major complications. In contrast, ABR was associated with a higher rate of minor complications. These findings are relevant to pre-operative patient centered decision-making as they provide further granularity beyond total complication rates and address the important issue of severity of complications.

Table 1: Overall Rate, Major, and Minor Postoperative Complications Following Breast Reconstruction. PSM = Propensity Score Matching.

	Type of Breast Reconstruction	Frequency of Complication	Frequency of No Complications	P Value (X^2)	P Value (PSM)
Overall Complication Rate	Autologous	36	51	0.61	0.71
	Implant Based	24	41		
Rate of Minor Complications	Autologous	25	62	< 0.01	< 0.01
	Implant Based	4	61		
Rate of Major Complications	Autologous	8	79	< 0.01	0.01
	Implant Based	18	47		

Postoperative Administration of Acetylsalicylic Acid Does Not Improve Clinical Outcomes after Microsurgical Breast Reconstruction

Farrah C. Liu, MD; Travis J. Miller, MD; Dominic Henn, MD; Dung Nguyen, MD; Arash Momeni, MD

Background: Despite significant improvements in microsurgical technique, microvascular thrombosis in autologous breast reconstruction with resultant flap loss remains a devastating complication. While many surgeons prescribe acetylsalicylic acid (ASA) postoperatively with the intent to prevent microvascular thrombosis, clinical evidence supporting this practice remains insufficient. The aim of our study was to investigate the impact of postoperative ASA administration on clinical outcomes following microsurgical breast reconstruction.

Methods: A prospectively maintained database of two surgeons (A.M. and D.N.) was queried to identify patients who had undergone microsurgical breast reconstruction. Patients were categorized based on whether they had received postoperative ASA for 30 days (group 1) or had not received ASA (group 2). Patient demographics as well as reconstructive outcomes, complications, and transfusion requirements were collected.

Results: 136 patients with a mean age of 49.5 years and a mean BMI of 28.5 kg/m2 who had undergone a total of 216 microsurgical breast reconstructions were included. No significant differences were noted with regard to patient demographics with the exceptions of increased rates of neoadjuvant chemotherapy and delayed reconstruction in group 1. There were no significant differences in the rates of postoperative complications including breast hematoma, mastectomy skin flap necrosis, partial flap necrosis, seroma, and deep venous thrombosis between patients who did or did not receive ASA postoperatively. Similarly, no difference was noted regarding postoperative blood transfusion rates (group 1: 9.9% vs. group 2: 9.1%; P = 0.78). Finally, patients in group 1 had significantly longer hospital stays (P = 0.0003).

Conclusion: Postoperative ASA administration is not associated with improved postoperative clinical outcomes. The use of ASA routinely after autologous breast reconstruction should not be encouraged.

Table 1: Patient characteristics

	Group 1 (ASA) n=81	Group 2 (No ASA) n = 55	P-value
Mean (range)			
Age	48.6 (29-72)	50 (24-78)	0.44
BMI	28.5 (17.6-40.6)	29 (20.4-42.7)	0.55
n (%)			
Any comorbidity present	48 (59.3%)	39 (70.9%)	0.20
Neoadjuvant chemotherapy	43 (53.1%)	17 (30.9%)	0.01
Immediate	51 (62.9%)	51 (92.7%)	<.0001
NSM	49 (60.5%)	34 (61.8%)	1
Bilateral	49 (60.5%)	31 (56.4%)	0.72
Follow up time (months)	23.3	11.1	<.0001
Length of stay (days)	4.95	4.35	0.0003

Table 2: Postoperative Complications

	Group 1 (ASA), n=81	Group 2 (No ASA), n = 55	P-value
n (%)			
Any Complication	43 (53.1%)	25 (45.5%)	0.48
Breast seroma	1 (1.2%)	0 (0.0%)	1
Breast hematoma	3 (3.7%)	2 (3.6%)	1
Mastectomy skin necrosis	15 (18.5%)	15 (27.3%)	0.29
Partial flap necrosis	3 (3.7%)	2 (3.6%)	1
DVT/PE	1 (1.2%)	1 (1.8%)	1
Delayed abdominal wound healing	18 (22.2%)	5 (9.1%)	0.06
Abdominal bulge/hernia	1 (1.2%)	0 (0.0%)	1
Clostridium difficile infection	1 (1.2%)	0 (0.0%)	1

Geocoding Nationwide Trends and Disparities in High-Capability Trauma Center Access, 2013-2019

Jeff Choi MD MS & S Karr MS; Arjun Jain; Taylor C. Harris BS; Janelle C. Chavez BS; David A. Spain MD

Introduction: Injury management at high-capability trauma centers (American College of Surgeons verification Level I/II) is associated with improved outcomes, yet how many Americans have timely access to these trauma centers is unknown. We aimed to evaluate nationwide trends and disparities in high-capability trauma center access over the most recent decade.

Methods: American Trauma Society's Trauma Information Exchange Program provided addresses and verification levels of trauma centers between 2013 and 2019. Google Maps Application Programming Interface geo-coded population centers of 201,651 census block groups and addresses of Level I/II trauma centers. ArcGIS calculated ground transport times from each population center to the nearest trauma center, accounting for each unique road's speed limit and average driving time. We derived demographic data from US Census Bureau 2013-2019 statistics. We defined timely access as ground transport time <60 minutes.

Results: As of 2019, 32.3% of Americans live <20 minutes, 25.2% between 20-40 minutes, 12.2% between 40-60 minutes, and 30.3% >60 minutes from Level I/II trauma centers. Census block groups with higher per capita income have faster access to trauma centers. Thirty-two percent of uninsured Americans (age 19-64 years) do not have timely access to trauma centers. Among racial groups, American Indians have the poorest access to trauma centers. Between 2013 and 2019, 0.4% more Americans gained timely access to Level I/II trauma centers; largest gains were among American Indians and Native Hawaiian/Pacific Islanders (+1.1%).

Conclusion: Ground transport access to high-capability trauma center has improved, yet access disparities remain. National effort to expand trauma center access is critically needed.

Prospective Study of Quality-of-Life One Year After Traumatic Rib Fractures

Suleman I Khan, BA, Jeff Choi MD, MS, Nicholas Hakes, Garrison Carlos MD, Layla Aboukhater BS, Dina Sheira BS, David A Spain MD

Introduction: Long-term quality-of-life (QoL) of patients who suffer traumatic rib fractures remain under-studied. In this continuation of our prospective study on short-term QoL after rib fractures, we hypothesized rib fractures continue to be associated with suboptimal QoL one year after discharge.

Methods: We prospectively enrolled adult patients at our Level I trauma center with rib fractures between July 2019 and January 2020. We assessed QoL one year after discharge using the Revised Trauma Quality of Life questionnaire (RT-QoL) and 17 additional questions. RT-QoL assessed three QoL domains on a 5-point Likert scale (1-worst, 5-optimal QoL).

Results: Among 113 patients surveyed, 65% (N=73; average age 67 years) completed one-year follow-up. Patients had an average 4.5 rib fractures and moderate overall injury burden (Injury Severity Score [mean±SD]: 12.1±6.3). One year after discharge, 38% (N=28) of patients reported persistent chest wall pain; 4% (N=3) reported occasional narcotic medication use for this pain. One-third of patients (N=23) reported longer than expected convalescence, and 26% of patients who had been working prior to injury (N=9/26) had not returned to pre-injury working capacity. Patients reported near-optimal ability to perform daily functional activities (RT-QoL [mean±SD]: 4.6±0.7) and emotional wellbeing (RT-QoL [mean±SD]:4.3±1.0) but continued to **experience suboptimal physical wellbeing (RT-QoL [mean±SD]: 3.2±0.5).**

Conclusion: Many patients who suffered rib fractures report persistent pain and suboptimal physical wellbeing one year after discharge. Tracking long-term outcomes is needed to inform convalescence expectations and strategies to improve QoL beyond hospitalization.

ABSTRACTS

Cancer associated fibroblasts share highly-conserved phenotypes and functions across tumor types and species

Deshka S Foster, Michael Januszyk, Kathryn E Yost, Malini Chinta, Alan T Nguyen, Austin R Burcham, Ashley L Titan, Ankit Salhotra, Michelle Griffin, Khristian E Bauer-Rowe, R Ellen Jones, Oscar da Silva, R Chase Ransom, Kellen Chen, Dominic Henn, Irene L Wapnir, Geoffrey C Gurtner, Derrick C Wan, Howard Y Chang, Jeffrey A Norton, Michael T Longaker

Introduction: Cancer associated fibroblasts (CAFs) are one of the most abundant cell types in desmoplastic solid tumors such as breast and pancreas cancer, and are known to interact extensively with other cells in the tumor microenvironment. However, CAFs have yet to become a treatment target in mainstream cancer therapy. This is likely, at least in part, because CAF heterogeneity and their roles in solid tumors remain incompletely understood.The extent to which CAF subpopulations and functional profiles are recapitulated across solid tumor types and species has yet to be elucidated.

Methods: Here, we conducted a comprehensive investigation, considering single cell gene expression and chromatin accessibility in conjunction with spatial transcriptomics, of CAFs across multiple solid tumor types (breast and pancreatic cancers) and species (mouse and human),with the aim of identifying commonalities among these fibroblasts that may represent promising therapeutic targets.

Results: We discovered that CAF heterogeneity is conserved across both solid tumor types and species, and that the identified subpopulations fall into two broad functional categories – mechanoresponsive and immunomodulatory (Fig. 1a-c). These categories are governed by specific changes in chromatin accessibility and are spatially-distinct. Selective disruption of underlying immuneormechanical force signaling results in predictable shifts in cell subpopulation distributions.

Conclusions: Collectively, this research defines the spatial dynamics of the CAF biology in solid tumors. We identified fundamental CAF-related factors to consider in multi-modal solid tumor treatment protocols, unveil CAF-specific treatment targets for further investigation, and provide a multimodal -omics framework for understanding CAF biology in the tumor stroma niche.

Figure 1

Figure 1. **a)** Mouse breast cancer associated fibroblast (CAF) single cell RNA-sequencing (scRNA-seq) shows 6 CAF clusters - these can be characterized into mechanoresponsive and immunomodulatory subpopulations (left panel); UMAP plot showing integrated mouse breast CAF scRNA-ATAC (right panel); **b)** Integrated scRNA-seq and spatial transcriptomics of mouse breast cancer tissue shows distinct spatial distribution of cytokine-signaling characteristic of immunomodulatory CAFs and Mgp expression characteristic of mechano-responsive CAFs; **c)** Projection of mouse breast CAF clusters to integrated human breast-pancreas CAF clusters.

Integrated Spatial Multi-omics Reveals Fibroblast Fate During Wound Healing: A Novel Framework For The Study Of Complex Tissue

Michael Januszyk, Deshka S Foster, Malini S Chinta, Kathryn E Yost, Gunsagar S Gulati, Alan T Nguyen, Austin R Burcham, Dominic Henn, Kellen Chen, Heather E desJardins-Park, Shamik Mascharak, Derrick C Wan, Aaron M Newman, Jeffrey A Norton, Geoffrey C Gurtner, Howard Y Chang, Michael T Longaker

Introduction: The goal of regenerative healing has remained elusive in part because principles of fibroblast programming and their adaptive response to injury remain incompletely understood.

Methods: We describe a novel multimodal -omics framework for the comprehensive study of cell populations through integration of paired single-cell RNA- and ATAC-seq time course data with high-resolution spatial -omics assays to track cellular subgroups across time and space. This platform was applied to study murine excisional wound healing using locally-induced Rosa26VT2/GK3 ("Rainbow") mice (Figure 1a). Fibroblasts were FACS-isolated from wound tissue at key timepoints and underwent single cell (sc) sequencing (Figure 1b). scRNA-seq and scATAC-seq data were integrated using the ArchR epigenomic toolkit (Figure 1c). Wound tissue from paired animals was harvested, flash-frozen in OCT media, and processed for spatial transcriptomics using the 10X Visium platform (Figure 1d). Putative single-cell population constructs were projected onto time-matched spatial tissue sections using a modified label-transfer approach (Figure 1e).

Results: We identified four injury-responsive fibroblast subpopulations with distinct RNA/ATAC temporospatial distributions (Figure 1f). Notably, one putatively mechano-sensitive subpopulation demonstrated a strong pattern of radial proliferation associated with activation of pro-fibrotic transcriptional programming and loss of transcriptional diversity (Figure 1g). Clear trajectories of differentiation were observed moving from the wound edge inward (Figure 1h-i). Abrogation of mechanical signaling through genetic knockout of Ptk2 disrupted these changes and limited proliferation of mechano-responsive fibroblast subpopulations (Figure 1j).

Conclusion: This work represents the first integration of paired scRNA-seq and scATAC-seq analyses with next-gen spatial -omics and provides a framework for future studies in tissue repair.
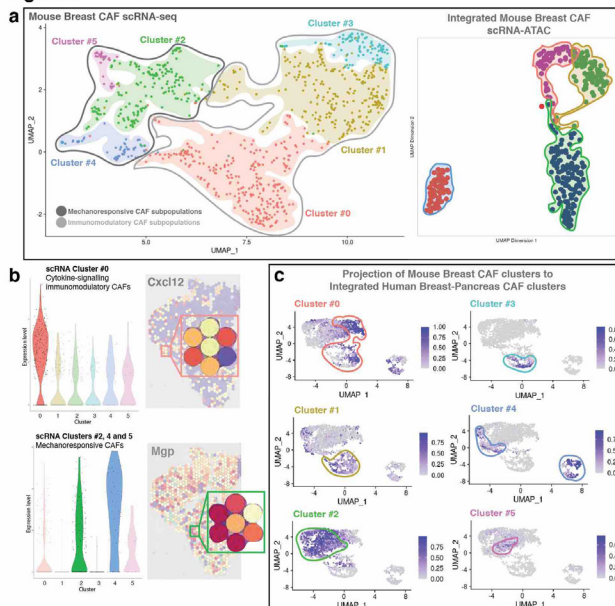
## Regenerating Articular Cartilage by Skewing the Skeletal Stem Cell Fate

Lauren S Koepke, BS; Matthew P Murphy, MD; Thomas Ambrosi, PhD; Yuting Wang, MD; Malachia Hoover, MS; Holly Steininger, BS; Irv Weissman, MD; Michael T Longaker, MD; Charles Chan, PhD

Introduction: Osteoarthritis (OA) is a degenerative disease resulting in progressive destruction of articular cartilage. The etiology involves a variety of factors, including genetic predisposition, acute injury, and chronic inflammation. Here we investigated the ability of resident mouse and human skeletal stem cell (SSC) populations to regenerate cartilage in conjunction with established and novel treatments.

Methods: We utilized FACS, proliferation and differentiation assays, histology, functional assays, and single cell analysis to determine SSC response to the normal aging process and to microfracture (MF) surgery alone and with localized co-delivery of BMP2 and soluble VEGFR1 (sVEGFR1), a VEGF receptor antagonist. These analyses were performed in both mouse and human xenografted mice models.

Results: We show that greater maturity is associated with progressive loss of SSC and diminished chondrogenesis in the joints of both mice and humans. However, MF triggers a local expansion of SSC at the chondral surface. While MF-activated SSC tend to form fibrous tissues, localized co-delivery of BMP2 and sVEGFR1 can differentiate MF-activated SSC towards generation of stable articular cartilage. This articular cartilage tissue is present at a 16-week timepoint in mice. Collagen 2 and aggrecan positive cartilage was also generated in our human xenograft model.

Conclusion: These data suggest that following MF, there is a therapeutic window to skew MF-activated SSC differentiation fate towards robust formation of de novo cartilage for treating localized chondral disease in OA. Our findings provide a new stem cell paradigm for regenerating cartilage that is validated in both mouse and human tissues.
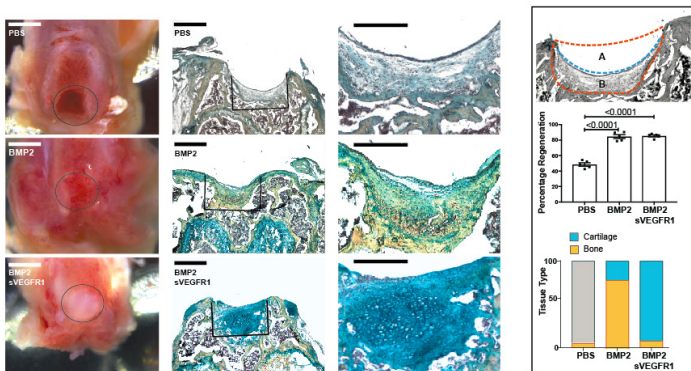
NeuroStitch: Nanofabrication of a Biomimetic Peripheral Nerve Interface

Zeshaan Maan MD, MSc; Eric Zhao MA; Janos Barrera MD; Dominic Henn MD; Jagannath Padmanabhan PhD; Kellen Chen PhD; Nicholas Melosh PhD; Geoffrey Gurtner MD

Introduction: Over a million people suffer limb loss annually. Existing prostheses are cumbersome and tiring, with a limited capacity to recapitulate natural hand motion, resulting in significant abandonment. There is need for a stable, high-fidelity neural interface for 2-way communication between robotic prostheses and the patient's neural circuitry. Existing neural interfaces are limited in both resolution and longevity. Application of semiconductor processing technology permits fabrication of biomimetic electrodes that are the same size as natural axons.

Methods: Ultra-small and flexible electrodes of the same dimensions, compliance and spatial distribution as human axons were fabricated. A 'needle and thread' approach was used to implant the ultra-flexible devices, allowing the electrodes to interface directly with individual axons. Using histology, 2-photon imaging, and the Sciatic Functional Index (SFI), we assessed the neural injury and foreign body reaction associated with the device. The Intan system was used to stimulate and record.

Results: SFI demonstrates resolution of the initial neuropraxia to baseline by 2 weeks post-implantation. The foreign body reaction at 6 months is minimal. Sparse action potentials were recorded within 30 minutes of device insertion. The ultra-small size of the electrodes and their proximity to individual axons permitted extremely local stimulation — down to a single toe.

Conclusions: We have developed the Neurostitch, a biomimetic intraneural electrode capable of single neuron recording and high selectivity stimulation. This device represents a step forward in the development of a high-resolution, stable man/machine interface for next-generation neuroprostheses.

Adipocytes in dermal wounds undergo conversion to pro-fibrotic fibroblasts that contribute to scar formation

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Introduction: Recent studies have suggested that adipocytes and fibroblasts interconvert in the wound environment. However, lineage dynamics and molecular properties of wound-resident adipocytes remain undefined. We hypothesized that mature adipocytes directly participate in pro-fibrotic wound repair via conversion into fibroblasts, contributing to scarring.

Methods: In AdipoqCre;ROSA26mTmG mice, mature adipocytes and their progeny express GFP, and other cells express RFP. AdipoqCre;ROSA26mTmG mice underwent splinted dorsal excisional wounding and were harvested at POD7 and 14. Wound sections underwent immunofluorescent staining for fibroblast and adipocyte markers and confocal imaging. Wound cells were stained for fibroblast subtype markers and analyzed via FACS. To achieve local adipocyte ablation, AdipoqCre;ROSA26mTmG;R26tm1(HBEGF)Awai mice were wounded, and diphtheria toxin was injected into the wound base.

Results: Using our AdipoqCre;ROSA26mTmG lineage-tracing model, we identified significantly greater number of GFP+ cells within wounds compared to unwounded skin. Compared to typical adipocytes, the GFP+ cells that infiltrated the injury site exhibited upregulation of fibrotic/fibroblast markers and downregulation of adipocyte markers, indicating conversion into wound fibroblasts. These GFP+ fibroblasts expressed fibroblast subpopulation markers indicative of a hypodermal/lipo-fibroblast identity. Ablation of subcutaneous adipocytes was confirmed by the absence of GFP+ cells in wounds; these wounds exhibited reduced dermal scarring compared to control wounds.

Conclusion: Our findings suggest that mature adipocytes in the skin undergo conversion to pro-fibrotic fibroblasts in the wound environment. Local adipocyte ablation resulted in reduced scarring, suggesting that adipocyte-derived fibroblasts are important contributors to wound fibrosis. Identification of the molecular cues driving adipocyte-to-fibroblast transdifferentiation may reveal novel strategies to target scarring/fibrosis.

Regenerative skin healing through targeted modulation of Engrailed-1 expression

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Introduction: Embryonically derived Engrailed-1 (En-1) lineage-positive fibroblasts (EPFs) drive dorsal skin fibrosis. More recently, we showed that En-1-lineage negative fibroblasts (ENFs) activate En-1 expression within wounds, and that blocking this conversion with verteporfin (YAP inhibitor) yields ENF-mediated skin wound regeneration. This observation presented a unique opportunity to study the molecular events differentiating skin regeneration from scarring.

Methods: We compared regenerating (verteporfin) and scarring (PBS) excisional wounds in mice at post-operative days (POD) 0 (unwounded), 2, 7, 14, and 30 (n = 5 mice/timepoint). Wounds were compared in a multi-"omic" fashion using single-cell RNA sequencing (scRNA-seq), timsTOF bulk proteomics, and a novel algorithm quantifying 294 extracellular matrix parameters.

Results: Pseudotime analysis of pooled scRNA-seq data revealed that fibroblasts followed two distinct transcriptional trajectories, one characterized by mechanical activation (EPFs, "fibrotic" trajectory) and the other characterized by developmental and regenerative pathways (ENFs). Cross-platform data integration confirmed that the fibrotic trajectory correlated with myofibroblast proteomic signatures and scar ECM. In contrast, the regenerative trajectory was instead associated with basket-weave ECM indistinguishable from unwounded skin. Comparison of scars and regenerated wounds by multiplexed in situ hybridization (RNAScope) using a custom image analysis pipeline revealed that ENF-mediated healing in YAP-inhibited (low Ank1) wounds yielded hair follicle regeneration through Wnt pathway activation (Rspo1, Trps1).

Conclusions: YAP inhibition unlocks wound regeneration through Wnt-active ENFs. Transcriptional divergence between the default, pro-fibrotic transcriptional trajectory (EPFs) and this regenerative trajectory occurs as early as POD 2, with proteomic and matrix signatures of skin regeneration following on POD 7 and 14.

Transplantation of Skeletal Stem Cells and Wnt3a Prevents Re-synostosis Following Surgical Repair of Craniosynostosis in Coronal Sutures of Twist-1+/- Mice

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Introduction: Cranial sutures are fibrous joints that comprise two approaching osteogenic bone fronts separated by intervening proliferative mesenchymal tissue. They represent the major sites of cranial morphogenesis and grow in close coordination with the rapidly developing brain. A delicate balance between cell proliferation, differentiation, migration, and apoptosis regulates the cranial sutures. Insufficient proliferation or accelerated differentiation results in premature cranial suture fusion, known as craniosynostosis. Previous studies have indicated that cranial suture closure versus patency is governed by canonical Wnt (cWnt) signaling. Fueled by our prior isolation of mouse SSCs from long bone, we aimed to examine cranial suture biology through the lens of the SSC.

Methods: SSCs are prospectively isolated by FACS from physiologically fusing and patent sutures, in addition to cranial sutures harvested from animal models of syndromic and non-syndromic craniosynostosis. SSCs in combination with recombinant Wnt3a protein were transplanted into a surgical ablated coronal suture of Twist-1+/- mouse to prevent refusion.

Results: We identify that aberrancies in SSC equilibrium may underlie both physiologic suture closure and pathologic craniosynostosis. Furthermore, we demonstrate that cWnt activation increases SSC frequency, prevents suture fusion, and ultimately rescues the craniosynostosis phenotype. These findings suggest that SSCs and Wnt3a may provide a combined cellular/molecular intervention to treat or even prevent craniosynostosis

Conclusion: BTaken together, the findings stemming from this study shift our focus towards viewing skeletal stem cells through a novel lens magnifying SSCs as an appealing tool suitable for preventing bone formation. Moreover, the findings from this study may lay the foundation for novel therapeutic options using SSCs coached with effectors of cWnt signaling as an early intervention therapy for craniosynostosis.
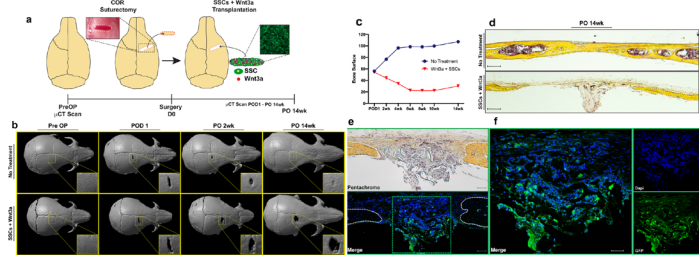
Transplantation of SSCs and Wtn3a Prevents Re-synostosis Following Surgical Repair of Craniosynostosis a, Schematic representation of experimental procedure for COR suture ablation experiments. pN16 Twist1+/- COR suture synostosis was confirmed by preoperative micro-CT scans. Fused COR sutures were excised using a 0.3mm drill and replaced by wild-type SSCs (3x105 cells) and recombinant Wnt3a protein (200ng) loaded onto a collagen scaffold sponge, thus engineering a "suture mesenchyme". An empty suturectomy was used as control. The extent of re-fusion was evaluated over a 14-week period by micro-CT and histological analysis. Abbreviations: POD, post-operative day; PO, post-operative. **b,** Time-course micro-CT analysis of treated and untreated COR suturectomies over a 14-week period. **c,** Quantification of COR suturectomy re-fusion by micro-CT over a 14-week period measuring image intensity in a standardized ROI. **d,** Movat's pentachrome staining of sagittal sections of COR suturectomies at 14-weeks showing fusion of the untreated suturectomies compared to suturectomies treated with SSCs and Wnt3a protein (n=2). Experiments were performed two independent times. Magnification 5x, scale bars: 200μm. **e,** wild-type GFP+ SSCs (3x105 cells) with Wnt3a protein were transplanted as above to monitor their presence within the ablated COR suture at 10-week post-operative. (top panel), Movat's pentachrome staining of a COR suturectomies sagittal section. Magnification 10x, scale bar: 100μm. (bottom Panel), confocal micrograph of a sister slide of COR suturectomies sagittal section. Fluorescence indicates the presence of SSCs within the ablated suture. Magnification 10x, scale bar: 100μm. **f,** Magnification at 20X of the boxed area in panel e, suggests that transplanted SSCs participate in the newly forming suture mesenchyme by recruiting neighboring cells (n=2). Experiments were performed two independent times. Magnification 20x, scale bar: 50μm.

The mSSC response after tendon-to-bone injury is dampened with aberrant TGF-β Signaling

Ashley Titan, Michael Davitt, Deshka Foster, Siddharth Menon, Ankit Salhotra, Kellen Chen, Evan Fahy, Austin Burcham, Michael Lopez, R Ellen Jones, Ioana Baiu, Michael Januszyk, Geoffrey Gurtner, Paige Fox, Charles Chan, Natalina Quarto, Michael Longaker

Introduction: The mouse skeletal stem cell (mSSC) has been shown to participate in tendon-to-bone interface (TBI) healing and to down-regulate TGF-β signaling pathway elements after injury. We interrogated if functional modulation of TGF-β alters mSSC response and TBI healing.

Methods: Thirty-six C57BL/6 and 12 transgenic Fibrillin-1 mice (known to have endogenously increased levels of active TGF-β), were used in this study. All procedures were approved by Stanford's APLAC. To test Achilles healing, we created a partial laceration at the Achilles TBI, while sham surgery was performed contralaterally. Mice were treated with one of the following: saline, DMSO, exogenous TGF-β, or SB43154 (a TGF-β inhibitor). Mice were euthanized 7 days after injury. Gross evaluation was performed to evaluate healing, while mSSC profiles in the Achilles TBI were measured using fluorescence-activated cell sorting (FACS).

Results: In C57BL/6 mice, a two-fold increase in mSSCs was seen 7 days after injury in the saline control group. Exogenous application of TGF-β post-injury prevented this mSSC response and resulted in impaired healing with significant inflammation. The use of SB43154, however, potentiated the mSSC response, leading to a three-fold increase in mSSCs (Figure 1A and 1B). Using a transgenic Fibrillin-1 mouse, we observed a repressed mSSC injury response and poor wound healing, similar to that seen with exogenous TGF-β. This phenotype is rescued by post-injury application of the small molecule TGF-β inhibitor SB43154 (Figure 1B and 1C).

Conclusion: We have identified that mSSCs increase in frequency following TBI injury. This response is dampened by TGF-β, while TGF-β inhibition rescues mSSC response.
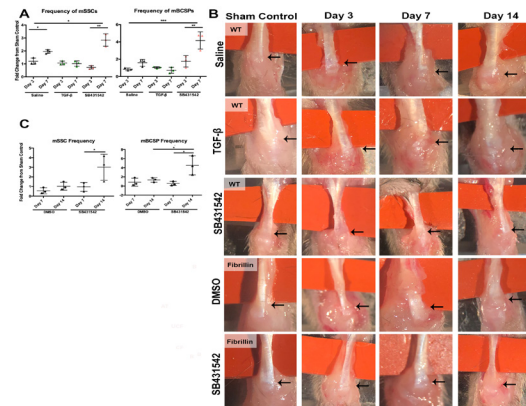

Figure 1: FACS Analysis and Gross Imaging after TBI Injury. A, Quantification of cellular frequency of FACS isolated mSSC demonstrating a significantly reduced response of mSSC and mBCSP post-injury after administration of exogenous TGFβ1 compared to saline administration, and a significantly increased response with SB431542 treatment (n = 2 pooled, with 3 replicates). B, Representative gross images of either wild type mice (first three panels) or Fibrillin-1 transgenic mice (bottom two panels) at post injury day 3, 7, and 14 treated with saline control (top panel), TGFβ (second panel), SB431542 (third panel) DMSO (fourth panel), or SB431542 (fifth panel). TBI injury identified with an arrow. C, Quantification of cellular frequency of FACS isolated mSSC demonstrating a significantly increased response with SB431542 treatment in wild-type mice. Data and error bars shown as mean ± STD. *P < 0.05, **P < 0.01, unpaired two-tailed t-test.

Racial Disparities in the Utilization of Parathyroidectomy among Patients with Primary Hyperparathyroidism: Evidence from a Nationwide Analysis of Medicare Claims

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Introduction: Among patients with primary hyperparathyroidism (PHPT), parathyroidectomy offers a chance of cure and mitigation of disease-related complications. The impact of race/ethnicity on referral and utilization of parathyroidectomy is unknown.

Methods: Population-based, retrospective cohort study using 100% Medicare claims from beneficiaries with PHPT from 2006-2016. The associations of race with disease severity, surgeon evaluation, and subsequent parathyroidectomy were analyzed using adjusted multivariable logistic regression models.

Results: Among 210,206 beneficiaries with PHPT, 63,136 (30.0%) underwent parathyroidectomy within 1 year of diagnosis. Black patients were more likely than other race/ethnicities to have stage 3 chronic kidney disease (10.8%) but had lower prevalence of osteoporosis and nephrolithiasis at diagnosis. Compared to White patients, Black and Hispanic patients were more likely to have been hospitalized for PHPT-associated conditions (White 4.8%, Black 8.1%, Hispanic 5.8%; p<.001). Patients who were White and met operative criteria were more likely to undergo parathyroidectomy than Black, Hispanic or Asian patients (White 30.5%, Black 23.0%, Hispanic 21.4%, Asian 18.7%; p<.001). Black and Hispanic patients had lower adjusted odds of being evaluated by a surgeon (ORs 0.71 [95%CI 0.69-0.74], 0.68 [95%CI 0.61-0.74], respectively) and undergoing parathyroidectomy if evaluated by a surgeon (ORs 0.72 [95%CI 0.68-0.77], 0.82 [95%CI 0.67-0.99]). Asian race was associated with lower adjusted odds of being evaluated by a surgeon (OR 0.64 [95%CI 0.57-0.71]), but no difference in odds of parathyroidectomy.

Conclusion: Racial/ethnic disparities exist in the management of PHPT among older adults. Determining the factors that account for this disparity require urgent attention to achieve parity in the management of PHPT.

Comparing perioperative outcomes after noncardiac surgery across VA and non-VA hospitals

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Background: Recent legislation facilitates Veterans' ability to receive non-VA surgical care. However, contemporary data comparing the quality and safety of VA and non-VA surgical care are lacking.

Methods: National cohort study of patients ≥18 years old who underwent noncardiac surgery recorded in the VA Surgical Quality Improvement Program (VASQIP) or the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) registries (2015-2018). Multivariable log-binomial modeling was used to evaluate the association between VA vs. private-sector care settings and 30-day mortality. Unmeasured confounding was quantified using the E-value.

Results: Overall, rates of 30-day mortality, complications, and failure to rescue were 0.8%, 9.5%, and 0.6% in NSQIP (N=3,174,274 operations) and 1.1%, 17.1%, and 0.8% in VASQIP (N=736,477), respectively (all p < 0.001). Veterans were more frequently male (VASQIP 92.1% vs. NSQIP 47.2%) and frail (60.0% vs. 21.3%) (both p<0.001). Relative to private-sector care, VA surgical care was associated with a lower risk of perioperative death (adjusted Relative Risk (aRR) 0.59 [95% CI 0.47-0.75]). This finding was robust in multiple sensitivity analyses performed among patients that were frail and non-frail, with or without complications, and undergoing low and high physiologic stress procedures. An unmeasured confounder (present disproportionately in NSQIP data) would require a RR of 2.78 to obviate our main finding.

Conclusions: VA surgical care is associated with lower perioperative mortality and decreased failure to rescue despite Veterans having higher-risk characteristics. Given the unique needs and composition of the Veteran population, health policy decisions and budgetary appropriations should reflect these important differences.

Figure 1. Serial modeling and subgroup analysis of the association between surgical care setting (i.e., VA vs. private sector) with risk of 30-day perioperative mortality. E-values quantifying the minimum strength of association that an unmeasured confounder would need to have with both the exposure and the outcome to eliminate the statistical significance of the observed main effect are also presented.

	Model	Favors VASQIP	Favors NSQIP	Relative Risk with 95% CI	E-value
Primary Analysis	Unadjusted			1.33 (1.04, 1.70)	1.99
	Adjusted for RAI			0.52 (0.43, 0.62)	3.26
	Adjusted for RAI and OSS			0.59 (0.50, 0.70)	2.78
	Adjusted for RAI, OSS and Urgency			0.68 (0.61, 0.76)	2.30
	Adjusted for RAI, OSS, Urgency and Complications			**0.59 (0.47, 0.75)**	**2.78**
Operative Stress Score	Adjusted for RAI, Urgency and Complications, restricted to OSS 1-3			0.52 (0.41, 0.66)	3.26
	Adjusted for RAI, Urgency and Complications, restricted to OSS 4-5			0.76 (0.69, 0.84)	1.96
Frailty	Adjusted for OSS, Urgency and Complications, restricted to RAI < 30			0.83 (0.69, 1.00)	1.70
	Adjusted for OSS, Urgency and Complications, restricted to RAI ≥ 30			0.64 (0.52, 0.79)	2.50
Failure to Rescue	Adjusted for RAI, OSS and Urgency, restricted to without Complications			0.71 (0.53, 0.95)	2.17
	Adjusted for RAI, OSS and Urgency, restricted to with Complications (i.e., failure to rescue)			0.55 (0.44, 0.68)	3.04

Abbreviations: NSQIP, National Surgical Quality Improvement Program; OSS, Operative Stress Score; RAI, Risk Analysis Index; VASQIP, Veterans Affairs Surgical Quality Improvement Program.

Anemia: A Potential New Target For Preoperative Optimization In Heart Failure Patients Undergoing Elective Surgery

Charlotte M Rajasingh, Beth A Martin, Sherri Rose, Sherry M Wren

Introduction: Heart failure (HF) patients have increased postoperative mortality. Current preoperative optimization focuses on medication optimization. We hypothesized that moderate preoperative anemia is associated with increased mortality in HF patients undergoing elective surgery.

Methods: National VA retrospective cohort study of HF patients undergoing elective, non-cardiac surgery in the VASQIP database from 2009-2016. Moderate anemia was defined as a preoperative hematocrit < 30% within 30 days of procedure; 90-day mortality is reported.

Results: A total of 44,212 HF patients were identified: 4,847 (11.0%) had Hct <30 and 39,365 (89.0%) had Hct >=30 (Table 1). The median Hct in each group was 27.5% and 39.7%, respectively. 90-d postoperative mortality in anemic patients was 14.7% as compared to 4.0% in patients with a Hct >=30 (p<0.001). After adjusting for patient and operative characteristics, the mortality odds in anemic patients compared to non-anemic patients was 3.05 (95% CI:2.75-3.39; Figure 1).

Conclusion: Anemic HF patients undergoing elective surgery face a substantially increased risk of mortality compared to non-anemic patients, even at a hematocrit of 30%. HF is highly associated with iron deficiency anemia, a potentially modifiable risk factor. Preoperative optimization of iron stores warrants further investigation as a strategy to decrease mortality.

Table 1:

	Hct<30%	Hct>=30%
Total (n, %)	4,847 (11.0%)	39,365 (89.0%)
Hematocrit (median %, IQR)	27.5% (25.8-28.9)	39.7% (35.9-43.0)
90-d Mortality*	714 (14.7%)	1558 (4.0%)
Operative complexity*		
Standard	2,756 (56.9%)	20,997 (53.5%)
Intermediate	2,091 (43.1%)	18,368 (46.7%)
Anesthesia Type*		
General Anesthesia	3,722 (76.8%)	31,721 (80.6%)
Other (ex: epidural, MAC, local)	1,124 (23.2%)	7,640 (19.4%)
Ejection Fraction*		
Preserved (LVEF>50%)	2,879 (59.4%)	23,649 (60.1%)
Mildly reduced (40-49%)	748 (15.4%)	6,300 (16.0%)
Moderately reduced (30-39%)	637 (13.1%)	4,952 (12.6%
Severely reduced (<30%)	476 (9.8%)	3,385 (8.6%)

*p<0.01

Figure 1:

Adjusted* Odds Ratios for 90-d Mortality
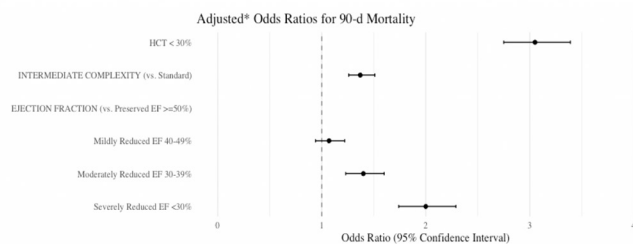
*Adjusted for variables as above, sex, age, BMI, and preoperative comorbidities (alcohol use, hypertension, atrial fibrillation, diabetes, coronary artery disease, stroke, chronic obstructive pulmonary disease, peripheral vascular disease, ESRD on dialysis, and preoperative renal function).

Insurance churn after traumatic injury: National evaluation among a large private insurance database

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Introduction: Traumatic injury can lead to significant disability, with injured patients often requiring substantial healthcare resources to return to work and baseline health. Inability to work can result in loss of employer-based insurance coverage, which in turn may significantly impact healthcare access and outcomes. Among privately insured patients, we hypothesized worsening instability in coverage based upon severity of injury.

Methods: Patients presenting to a hospital with traumatic injury were evaluated for insurance churn using Optum Clinformatics® Data Mart private-payer claims. Insurance churn was defined as cessation of enrollment in an Optum health insurance plan. Kaplan-Meier analysis was used to compare time to insurance churn by ISS category. Cox proportional-hazards regression was used to estimate hazard ratios for insurance churn.

Results: Among 788,163 privately insured hospitalized trauma patients, 62% dropped insurance within 1 year after injury. Compared to patients who remained on their insurance plan, patients who dropped insurance were younger and more likely non-white. The median time to insurance churn was 11.0 months for those with mild traumatic injury, 10.8 months for moderate and severe injuries, and 9.6 months for those with profound injuries (log rank p<0.001 [Figure]). In multivariable analysis, all ISS categories had increasingly higher rates of insurance churn compared with mild injury.

Conclusion: Increasing severity of traumatic injury is associated with higher levels of health coverage churn amongst the privately insured. Lack of access to health services may prolong recovery and further aggravate the medical and social impact of significant traumatic injury.

Figure: Probability of continuing insurance coverage following injury
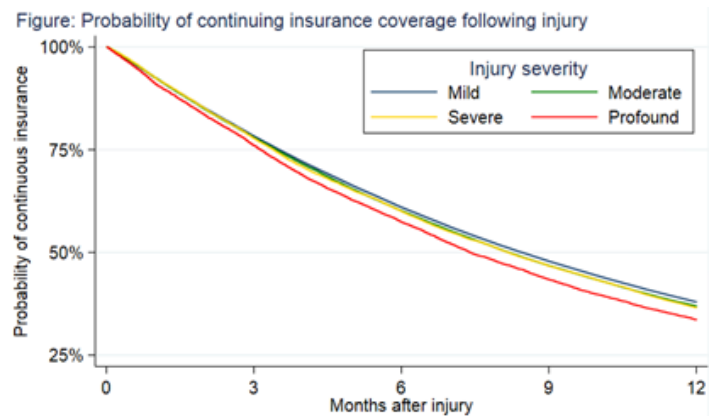
Performance Assessment of Multimodal Cardiopulmonary Bypass Skills Within a High-Fidelity Simulation Environment

Calvin Perumalla, PhD, Joshua L. Hermsen, MD, Hossein Mohamadipanah, PhD, Su Yang, BS, Brett Wise, BS, Amy Fiedler, MD, Paul DiMusto, MD, and Carla Pugh, MD, PhD

Introduction: A high-fidelity simulator that uses a perfused porcine heart, cannulae, and tubing is shown to be a useful training adjunct. We hypothesized that multimodal assessment of cardiopulmonary bypass (CPB) skills within this simulated environment could discern expert from trainee performance.

Methods: Three fellows (postgraduate year 6-8) and 3 attending surgeons each performed 3 aortic cannulations. The third sequence included venous cannulation, commencement of CPB, and placement of a cardioplegia catheter and aortic cross-clamp. Performance across 20 cognitive and 21 technical domains was evaluated. Surgeon and assistant hand movements and economy of motion were assessed by electromagnetic motion sensors worn under sterile gloves.

Results: Analysis showed significant difference in cognitive (6.7 ± 2.3 vs 4.6 ± 2.7, P [.03) but not technical (6.2 ± 2.5 vs 5.8 ± 2.2, P [.7) scores favoring experts. Moreover, experts showed higher efficiency by spending 64 ± 14 seconds to construct a nonpledgeted aortic purse-string suture and secure it with a Rummel. Trainees spent 82 ± 30 seconds completing the task (P [.03). Motion analysis revealed similar path-lengths for both group for cannulation and CPB but significantly shorter path-lengths for experts in cross-clamp (47.5 ± 15.5 m vs 91.9 ± 20.3 m, P [.04)

Conclusion: Multimodal assessment using cognitive, technical, and motion analysis of CPB tasks using a simulation environment is a valid system to measure performance and discriminate experts from trainees. This may allow for development of "competence thresholds" with implications for training and certification in cardiothoracic surgery.
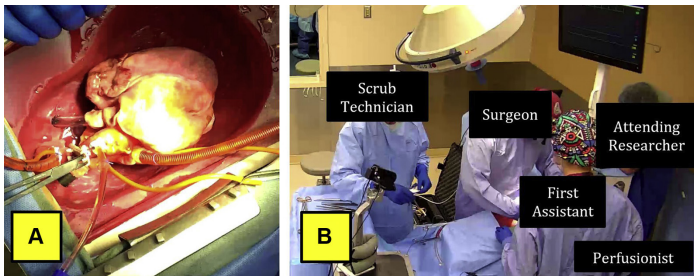

Figure 1. (A) The top view of the high-fidelity cardiac simulator using a porcine heart. (B) The simulation setting, including the presence of the surgeon, first assistant, scrub technician, attending researcher, and perfusionist.

Cost effectiveness of computed tomography versus ultrasound-based surveillance following endovascular aortic repair of intact abdominal aortic aneurysms

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Introduction: Expert guidelines recommend annual surveillance with computed tomography angiography (CTA) or ultrasound after endovascular aortic repair (EVAR). The differential costs, risks, and diagnostic utility of CT angiogram (CTA), color duplex ultrasound (CDU), and contrast enhanced ultrasound (CEU) merit cost-effectiveness analysis.

Methods: A decision tree with nested Markov models compared five annual strategies: CTA-only, CDU-only, CEU-only, CTA at 3first year followed by CDU, and CTA at first year followed by CEU. Literature review was undertaken for model parameters including test sensitivity, specificity, risk of acute kidney injury following CTA, mortality, and costs. The model was implemented on a monthly cycle over a 30-year time horizon for a 74-year old male, with a willingness-to-pay threshold of $50,000 per quality-adjusted life year (QALY) and 3% annual discount.

Results: Under base case assumptions, the hybrid CTA-CDU strategy is cost-effective with a lifetime cost of $77950 for 7.74 QALYs (Figure 1). In sensitivity analyses, the hybrid CTA-CDU strategy was cost-effective when CEU specificity was less than 95%, and up to a 20% incidence of acute kidney injury following CT scan. At sensitivities below 75% for CEU and 55% for CDU, a yearly CTA strategy maximized QALYs.

Conclusion: An EVAR surveillance strategy in which CTA ordered in the first postoperative year with CDU thereafter is cost-effective. Sensitivity analyses favor this strategy up to a 20% risk of contrast-induced nephropathy, after which a CDU-only approach is cost-effective. Conversely, if the sensitivity of CEU and CDU are lower, a yearly CT approach is reasonable.

Figure 1. Cost-effectiveness diagram demonstrating the relative costs and QALYs associated with each strategy. The blue strategies maximize QALY and minimize costs, with CTA/CDU being cost-effective per the willingness to pay threshold.
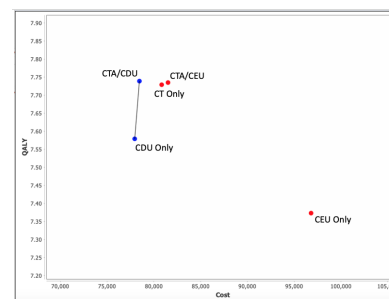
Strategy	Cost (USD)	QALY	ICER
CDU Only	77950	7.58	---
CTA/CDU	78460	7.739	3100.00
CT Only	80170	7.738	Strongly Dominated
CTA/CEU	81500	7.735	Strongly Dominated
CEU Only	96800	7.373	Strongly Dominated

## Which AI Algorithms Best Define Surgical Workflow? A Look at Surgical Techniques and Instrument Use

Calvin Perumalla, PhD Hossein Mohamadipanah, PhDa, LaDonna Kearse, MDa, Anna Witt, BSa, Brett Wise, BSa, Su Yang, BSa, Cassidi Goll, BAa, Carla Pugh, MD, PhD, FACSa

Introduction: Surgical videos are now being used for performance review and educational purposes; however, broad use is still limited due to time constraints. To make video review more efficient, we implemented Artificial Intelligence (AI) algorithms to detect surgical workflow and technical approaches.

Methods: Participants (N = 200) performed a simulated open bowel repair. The operation included two major phases: 1) Injury Identification and 2) Suture Repair. Accordingly, a phase detection algorithm (MobileNetV2+GRU) was implemented to automatically detect the two phases using video data. In addition, participants were noted to use three different technical approaches when running the bowel: 1) use of both hands, 2) use of one hand and one tool, or 3) use of two tools. To discern the three technical approaches, an object detection (YOLOv3) algorithm was implemented to recognize objects that were commonly used during the Injury Identification phase (hands vs. tools).

Results: The phase detection algorithm achieved high precision (recall) when segmenting the two phases: Injury Identification [86+9% (81+12%)] and Suture Repair [81+6% (81+16%)]. When evaluating three technical approaches in running the bowel, the object detection algorithm achieved high average precisions (Hands [99.32%] and Tools [94.47%]). The three technical approaches showed no difference in execution time (Kruskal-Wallis Test: p=0.062) or injury identification (not missing an injury) (Chi-squared: p = 0.998).

Conclusion: The AI algorithms showed high precision when segmenting surgical workflow and identifying technical approaches. Automation of these techniques for surgical video databases has great potential to facilitate efficient performance review.
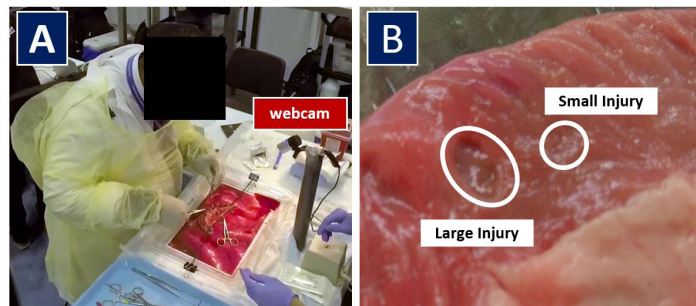
Impact of High Deductible Health Plans on Hernia Presentation

Kirbi Yelorda MD, Liam Rose PhD, M. Kate Bundorf PhD, Arden Morris, MD MPH

Introduction: The CDC reports 47% of persons under 65 with private insurance were enrolled in high-deductible health plans (HDHP) in 2018. While these plans entail substantially higher out-of-pocket costs and sometimes delayed care for patients with chronic medical conditions, their impact on potential delays among surgical patients who require short-term, episodic care is poorly understood. This study aims to determine the association between HDHP enrollment and presentation with a complex abdominal wall hernia.

Methods: We performed a retrospective cohort analysis of privately-insured patients using Optum, a deidentified commercial insurance claims database. We included patients aged 18-63 who underwent ventral or groin hernia operations from January 2016 to June 2019. We dichotomized into high and low deductible health plans using the I\RS HDHP cutoff and used multivariate analysis to assess presence of an incarcerated or strangulated hernia.

Results: Among 83,127 patients who underwent a hernia operation, 23.8% were enrolled in a HDHP and 25.6% had an incarcerated or strangulated hernia. The mean annual deductible was significantly higher for the HDHP group (unadjusted mean [SD], $706 [$760] vs. $3,620 [$2,055]; adjusted, -$2871, P <0.001). HDHP enrollees were slightly but statistically significantly more likely than traditional insurance enrollees to have an incarcerated or strangulated hernia (adjusted OR 1.11; 95% CI, 1.07-1.15; P <0.001).

Conclusion: HDHP enrollment was associated with higher odds of complex hernia presentation, an urgent or emergent condition that may result from delayed care. If other common surgical conditions among HDHP enrollees follow a similar diagnosis/treatment pattern, a review of HDHP plans including large scale clinical outcomes and comprehensive resource consumption is warranted.

VIRTUAL POSTER SESSION

Holman21 received a record number of abstracts. However, due to COVID-19, only the top eight posters from each category will be able to present in person. Thanks to the magic of technology though we are able to offer a virtual poster session.

In addition to the posters featured today on the Hoover Tower Lawn the following 36 abstracts can be viewed online at https://surgery.stanford.edu/holman/2021.html

Resident Research Day

Virtual Poster Session – Basic

Title of Presentation	Presenter	Title of Presentation	Presenter
Cost-effectiveness of Dapagliflozin for Non-Diabetic Chronic Kidney Disease	Thomas Handley	Mechanical activation of inflammation at the implant-tissue interface underlies pathological foreign body response	Jagannath Padmanabhan
Dermal Iron Chelation Reduces Indirect Radiation Injury	Christopher Lavin	Topical Antibiotic Elution in a Collagen Rich Hydrogel for Healing of Infected Wounds	Uriel Sanchez Rangel
Patient-specific changes in aortic hemodynamics is associated with thrombotic risk after fenestrated endovascular aneurysm repair with large diameter endografts	Kenneth Tran	Where there is fat there is fibrosis: Elucidating the mechanisms of creeping fat-driven stricture formation.	Khristian Bauer-Rowe
Single cell RNA sequencing reveals fibroblast heterogeneity across mouse and human embryonic origins	Michelle Griffin	Post-Engraftment Sciatic Neurectomy Slows Peripheral Sarcoma Growth	Michael Davitt
Adipose-Derived Stromal Cell Subpopulation with Adipogenic Capabilities Increase Fat Grafts in Irradiated Tissue	Nestor Diaz Deleon	Spatial Fidelity of Microvascular Perforating Vessels as Perceived by Augmented Reality Virtual Projections	David Cholok
BMP2 surrogate using bispecific nanobodies for effective cartilage regeneration	Eri Takematsu	The Value of Scientific Publications in Surgical Device Innovation	Alfred Song
The Effect of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) on Skeletal Stem Cell Functionality	Holly Steininger	Promoting Breast Health Awareness: Can a sensor-enabled training system help?	Cassidi Goll
Osteoskeletal regenerative ability of exosomes derived from adipose-derived stem cells upon inhibition of Transforming Growth Factor-β-signaling	Julika Huber		

Resident Research Day

Virtual Poster Session – Clinical

Title of Presentation	Presenter	Title of Presentation	Presenter
The Impact of Reconstructive Modality on the Severity of Postoperative Complications in Breast Reconstruction	Arhana Chattopadhyay, MD	Central Line Training Requires Deliberate Practice and Deliberate Training	Ingrid Schmiederer
Effect of Meteorological Conditions and Seasonality on Surgical Site Infection Prevalence in the United States	Raymond Liou	Feasibility and Interest in Establishing a Longitudinal Surgical Skills Performance Database	Brett Wise
Assessing Entrustment and Achievement of American Board of Surgery Entrustable Professional Activities (EPAs) for Graduating Residents	LaDonna Kearse	Preoperative β-Lactam Antibiotic Prophylaxis is Superior to Bacteriostatic Agents: Analyzing Outcomes in Immediate Breast Reconstruction with Acellular Dermal Matrix	Travis Miller
The omental fat-augmented free flap: minimizing post-operative pain in autologous breast reconstruction	Peter Deptula	Lasting improvements of a surgical infection prevention program: the sustainability of Clean Cut	Nichole Starr
Establishing Procedural Metrics for Scoliosis Bracing	Kayla Huemer	Pilot testing of a fit-for-purpose surgical headlight in Ethiopia	Muaad Hussien
Botox Produces Diagnostic and Therapeutic Benefit for Breast Reconstruction Pain and Animation Deformity	Halley Darrach	Clean & Confident: Impact of Sterile Instrument Processing Workshops on Knowledge and Confidence in Five Countries	Constance Harrell Shreckengost
Mental Health Outcomes in Pediatric Asthma Patients	Katelyn Chan	Surgical Lighting In Liberian ORs: Using Human-Centered Design To Close A Critical Patient Safety Gap	Nina Capo-Chichi
Infection with two multidrug-resistant organisms in solid organ transplant patients is associated with increased mortality and prolonged hospitalization	Siqi Cao	Lymphatic Microsurgical Preventive Healing Approach (LYMPHA) for Lymphedema Prevention After Axillary Lymph Node Dissection – A Single Institution Experience and Feasibility of Technique	Kelsey Lipman
Home-Time and Health-Related Quality of Life: A Mixed Methods Study of Veterans after Surgery	Ashley Langston		
Impact of COVID-19 on Presentation, Management, and Outcomes of Acute Appendicitis	Giselle Gomez		

Cost-effectiveness of Dapagliflozin for Non-Diabetic Chronic Kidney Disease

Thomas Handley, Rebecca Tisdale, Marika Cusick, Kelly Aluri, Alice Kate Joyner, Glenn Chertow, Doug Owens

Introduction: In the US, chronic kidney disease (CKD) affects 1 in 7 adults and costs over $100 billion annually. The DAPA-CKD trial found dapagliflozin, an SGLT2 inhibitor, to be effective in reducing kidney decline and mortality in patients with diabetic and non-diabetic CKD. Reducing this incidence could be important for preventing the number of people who go on to develop end stage renal failure and require surgical transplantation or dialysis. Currently, using SGLT2 inhibitors are not considered standard of care for non-diabetic CKD patients.

Methods: We used a deterministic Markov model that simulates patient progression through CKD stages, and modelled the effect of Dapagliflozin plus the current standard of care versus the standard of care on CKD stage progression.

Results: We found that distributing dapagliflozin to all 3.4 million diagnosed CKD patients in the United States would result in saving 4.8 million quality-of-life years and 370 billion U.S. dollars over the lifetime of the patients treated. This result was robust to a wide range of sensitivity checks; in all but early-CKD-stage elderly patients (over the age of 90), the dapagliflozin strategy strongly dominates usual care.

Conclusion: The study findings support the use of dapagliflozin in addition to ACE inhibitors or ARBs in non-diabetic CKD patients. The addition of this medication to current treatment plans could reduce the number of patients who go on to need either a kidney transplant or dialysis.
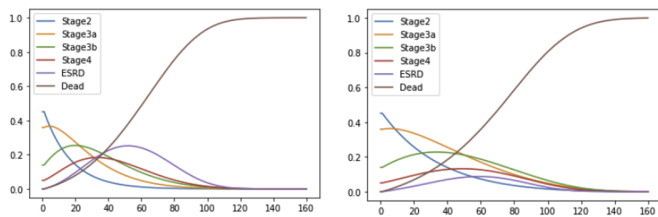

Figure 1. CKD stage prevalence of standard of care cohort (left) vs. dapagliflozin cohort (right) for individuals starting at age 60.

## Dermal Iron Chelation Reduces Indirect Radiation Injury

Christopher Lavin, MS; Evan J. Fahy, MD; Darren B. Abbas, MD; Michelle Griffin, MBChB, PhD; Daniel Lee, MD; Nestor M. Diaz Deleon, BS; Geoffrey C. Gurtner, MD; Michael T. Longaker, MD, MBA; Derrick C. Wan, MD

Introduction: Indirect oxidative damage is more injurious to tissues than the preceding direct DNA damage caused by ionizing radiation. In studying deferoxamine's (DFO) effect on radiation-induced fibrosis (RIF) of the skin, much of the focus has been on HIF-1α stabilization and healing through neovascularization. DFO's antioxidant conserving effects have been under-elucidated, even though reactive oxygen species (ROS) production is a well-known cause of local inflammation and fibrosis. Ferric iron is a reactant for Fenton-based chemistry and subsequent ROS generation. This study sought to investigate the effects of removing this reactant via chelation of labile dermal iron prior to irradiation (IR).

Methods: CD-1 nude mouse dorsal skin (1.5x2cm area) was irradiated, mimicking fractionated clinical regimens (six sessions of 5Gy, totaling 30 Gy over two weeks). Mice received daily DFO (3mg) covering the area, prior to and during radiation therapy. DFO was administered as a transdermal patch or a direct injection.

Results: DFO treatment chelated free iron in the dermis. The transdermal patch was more effective than direct injection, and IR alone did not affect dermal iron content (*$p<0.05$, ****$p<0.0001$). IR increased 8-Isoprostane staining, while DFO mitigated this increase. Again, the patch was more effective than injection (****$p<0.0001$). Oxidized:reduced glutathione ratios were increased in response to IR, and DFO spared active antioxidant enzyme levels compared to control. Apoptotic activator Bcl-2-associated protein levels followed the same trend. The patch was more effective than injection for both of these protein assays (****$p<0.0001$).

Conclusion: Iron chelation reduces radiation-induced ROS production in the dermis, evidenced by decreased oxidative damage biomarkers, preserved antioxidant stores, and decreased apoptotic protein quantities. This mechanism protects against expected indirect radiation injury and plays a role in DFO's antifibrotic treatment effect.
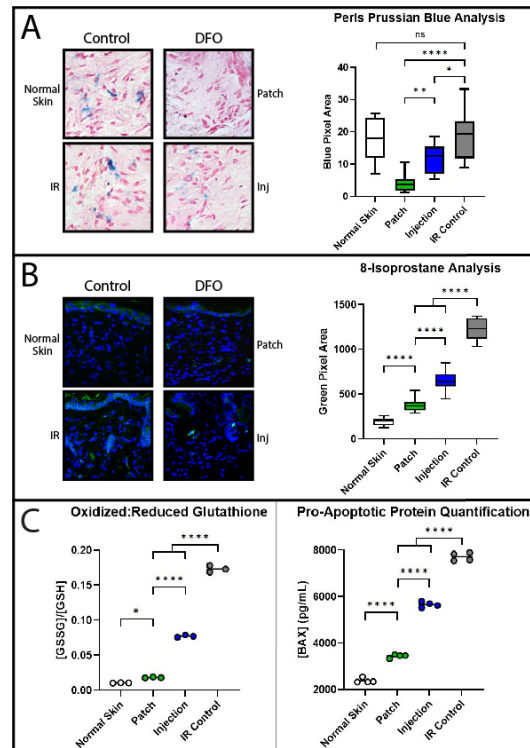
Patient-specific changes in aortic hemodynamics is associated with thrombotic risk after fenestrated endovascular aneurysm repair with large diameter endografts

Kenneth Tran MD1,2, Kyle Feliciano BS3, Weiguang Yang PhD2,4, Alison L. Marsden PhD2,3,4, Ronald L. Dalman MD1,2, Jason T. Lee MD1,2
1Division of Vascular Surgery, Stanford University, 2Cardiovascular Institute, Stanford University, 3Department of Bioengineering, Stanford University, 4Department of Pediatrics (Cardiology), Stanford University

Introduction: This study utilized computational fluid dynamic (CFD) modelling to investigate whether endograft diameter-dependent alterations in aortic hemodynamics can predict thrombotic events after fenestrated endovascular aneurysm repair (fEVAR)

Methods: A retrospective study was performed on patients undergoing fEVAR for juxtrarenal aortic aneurysms (JAAs). Patients were stratified into large (34-36mm) and small (24-26mm) diameter endograft groups. Patient-specific flow simulations were performed using 3D paravisceral aortic models with allometrically-scaled inflow and outlet boundary conditions. Aortic time-averaged wall shear stress (taWSS) and residence time (RT) were computed and correlated to future renal stent occlusion and intra-luminal graft thrombus.

Results: A total of 36 patients (14 small endograft; 22 large endograft) were included in this study. Patients treated with large endografts had a higher incidence of thrombotic complications compared to those with small endografts (45.5 vs 7.1%, p=0.016). In the large endograft group, a ≥0.39 dynes/cm2 reduction in aortic taWSS demonstrated discriminatory power to predict thrombotic complications (AUC 0.77). Increased aortic RT of ≥0.05s had similar accuracy for predicting thrombotic complications (AUC 0.78). Odds of thrombotic complications were significantly higher if patients met hemodynamic threshold changes in aortic taWSS (7.0 [1.1-45.9]) and RT (8.0 [1.13-56.8]). 3D visualization of areas of low post-operative aortic taWSS (<0.2 dynes/cm2) identified the location of maximum thrombus deposition in the majority (72%) of thrombotic events (Figure).

Conclusion: Post-operative reduction in aortic taWSS and increased RT correlate with future thrombotic events in patients treated with large diameter fenestrated endografts. Patient-specific simulation of aortic hemodynamics provides a novel method for thrombotic risk stratification after fEVAR.

Single cell RNA sequencing reveals fibroblast heterogeneity across mouse and human embryonic origins
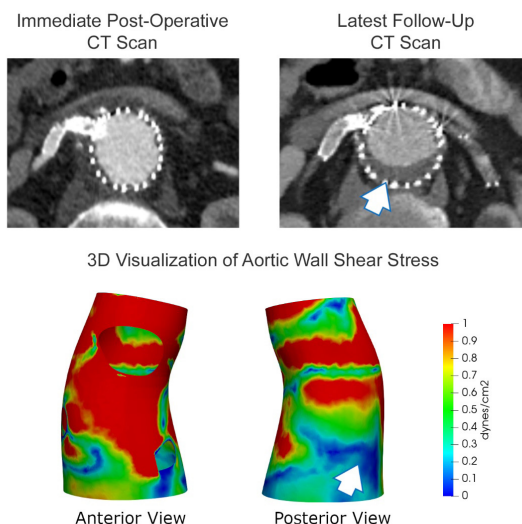
Michelle Griffin, MD, PhD, Megan King, BSc, Kellen Chen, PhD, Heather desJardins-Park, AB, Shamik Mascharak, BS, Evan Fahy, MD, Nicholas Guardino, BS, Chris Lavin, BS, Darren Abbas, MD, Michael Januszyk, MD PhD, Derrick Wan, MD, Michael Longaker, MD, MBA, FACS.

Introduction: Human skin scarring varies according to anatomical location, with the face healing at differing rates to scalp, ventrum and dorsum. Fibroblasts are the key cells involved in wound healing originating from four embryonic origins. Fibroblasts from the face, scalp, ventrum and dorsum originate from the neural-crest, cephalic mesoderm, lateral plate mesoderm and somite mesoderm, respectively. Here, we use single-cell RNA sequencing to understand fibroblast heterogeneity across embryonic origins.

Methods: Stented excisional wounds were created in the facial, scalp, ventrum and dorsum regions in C57/BL6J mice. Wounds were harvested at post-operative day (POD)-7 (midday through healing) and POD-14 (wound re-epithelialization), with unwounded skin serving as controls. Fibroblasts were then processed for droplet based microfluidic single-cell RNA analysis (scRNAseq).

Results: Facial wounds derived from the neural-crest displayed significantly accelerated wound closure and decreased scar thickness, compared to dorsal, ventral and scalp wounds (7 vs 14,*P<0.05) (n=10). We identified 6 distinct clusters of fibroblasts at POD-14. Two subpopulations were abundant in facial derived fibroblasts enriched for CD200, Ncam1, and Jag1. Pathway analysis using gene set enrichment analysis showed upregulation of known neural-crest signalling pathways including Wnt canonical-signalling, transforming growth factor-β regulation and hedgehog signalling in facial clusters, indicating that the embryonic origins of fibroblasts contributed to the outcome of skin scarring

Conclusion: Our study shows there is a high degree of fibroblast heterogeneity across embryonic regions, which may contribute to the diversity in skin scarring across the body. Identification of distinct scarring fibroblast subpopulations will allow us to develop targeted antifibrotic treatments to overcome skin fibrosis.

Immediate Post-Operative CT Scan

Latest Follow-Up CT Scan

3D Visualization of Aortic Wall Shear Stress

Anterior View Posterior View

*White arrow depicts location of intraluminal graft thrombus

Adipose-Derived Stromal Cell Subpopulation with Adipogenic Capabilities Increase Fat Grafts in Irradiated Tissue

Nestor M. Diaz Deleon, Sandeep Adem, Darren B. Abbas, Christopher V. Lavin, Mimi R. Borrelli, Abra H. Shen, Evan J, Fahy, Daniel K. Lee, Michael T. Longaker, and Derrick C. Wan.

Introduction: Effective cancer treatment requires the use of radiotherapy which remains costly as overlying tissue is permanently damaged. Autologous fat grafts that have been enriched with ASC subpopulations have been shown in improve retention and augmentation of skin fibrosis. A specific subpopulation of ASCs that are identified as CD34+BMPR1A+, have been shown to express an increase of adipogenic growth factors that may improve fat graft retention and reduce fibrosis in irradiated skin.

Methods: Immunodeficient mice were irradiated at the scalp with 30 Gray and allowed to rest for 4 weeks. Mice were grafted with five different treatment groups: fat only, fat enriched with unfractionated CD34+ ASCs, fat enriched with isolated CD34+BMPR1A+ ASCs, fat enriched with CD34+BMPR1A- ASCs, and no fat. After 8 weeks of grafting along with micro-CT scans biweekly, skin and fat were harvested and analyzed for histology.

Results: Fat grafts enriched with CD34+BMPR1A+ ASCs were scored significantly higher for integrity of fat grafts and Micro-CT scans demonstrated improved fat graft retention when compared to CD34+BMPR1A- and fat only grafts (p < 0.05).

Conclusion: Radiotherapy ablates cells of the target area, leaving behind damaged tissue and skin that heals with deposition of collagen. Fat grafts enriched with CD34+BMPR1A+ ASCs subpopulation of ASCs, which express high amounts adipogenic growth factors, improve retention capabilities of autologous fat grafts in irradiated tissue. Further studies will observe how subpopulations of ASCs may interact to provide a clearer understanding of the mechanisms of ASCs within fat.

BMP2 surrogate using bispecific nanobodies for effective cartilage regeneration

Eri Takematsu, Liming, Zhao, Sicong Wang, Yuting Wang, Elizabeth Arouge, Michael Longaker, Charles Chan

Introduction: The most common type of musculoskeletal disorder is osteoarthritis (OA), which afflicts 15% of the adult population with a lifetime risk of 40%. Damaged articular cartilage has no ability to regenerate, often necessitating invasive joint replacements. Stem cell therapy to regenerate damaged articular cartilage would be a highly attractive alternative to invasive joint replacement surgery. Recently, we identified that the combination of BMP2 and soluble VEGF receptor facilitated efficient regeneration of articular cartilage. BMP2-VEGFR protein therapy is very effective, however the efficiency of the BMP2 is still low, requiring high dosage. To overcome this limitation, we developed BMP2 surrogate made of two nanobodies (NBs) which have strong affinity to BMP2 receptors, bringing the two receptors in the optimal signalling configuration.

Methods: To generate the BMP2 surrogate, we first synthesized the extracellular domain of BMPR1a and BMPR2, then use them as templates for yeast nanobody selection. After screening the several candidate NBs, they were conjugated by peptide linker, varying the distance between BMPR1a and BMPR2 for the optimal BMP2 signaling configuration.

Results: Purified BMPR1a and BMPR2 were confirmed by western blot and Coomassie blue, indicating that vast majority was monomer with some dimer population (Fig.1.a,b). Activity of BMPR1a and BMPR2 on skeletal stem cells were confirmed by qPCR. In comparison to BMP2 alone treatment, BMPR1a and BMPR2 blocked BMP2 activity, reducing APL and Grem1 gene expression (Fig.1.c,d).

Conclusion: Our BMP2 surrogate will serve as an alternative for the conventional BMP2 with better functional activities, ultimately reducing the dosage of protein for cartilage regeneration.

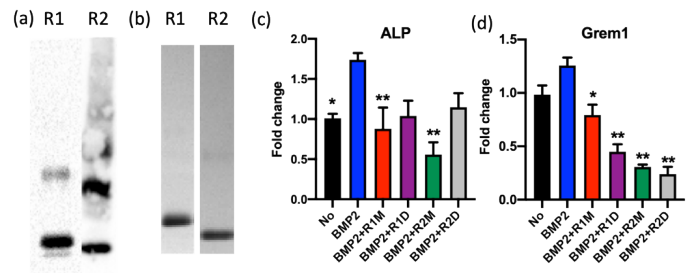**Fig.1.** (a) Western blot of BMPR1a and BMPR2. (b) Coomassie blue of BMPR1a and BMPR2. (c) Skeletal stem cells were treated with 100ng/ml of BMP2 or BMP2+BMPRs for 24 hours, and ALP gene expression was measured by qPCR. (d) Grem1 gene expression was measured. R1M: BMPR1a monomer, R1D: BMPR1a dimer, R2M: BMPR2 monomer, R2D: BMPR2 dimer. * p<0.05 compared to BMP2 group. ** p<0.01 compared to BMP2 group.

The Effect of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) on Skeletal Stem Cell Functionality

Holly Steininger BS, Thomas Ambrosi PhD, Henry Goodnough MD PhD, Malachia Hoover MS, Michael Bellino MD, Julius Bishop MD, Michael Gardner MD, Michael Longaker MD, Charles Chan PhD

Introduction: The use of non-steroidal anti-inflammatory drugs during fracture healing remains controversial. Our lab has identified a skeletal lineage tree with a skeletal stem cell (SSC) at the apex in both mouse and humans that allowed us to analyze this controversy at the cellular and molecular level.

Methods: Human and mouse SSCs were isolated from fractures by fluorescence-activated cell sorting. Purified SSCs were cultured in the presence or absence of five common NSAIDs and analyzed subsequently for colony-forming units (CFU-F). Osteogenic and chondrogenic differentiation capacity was quantified by Alizarin Red and Alcian Blue using spectrophotometry. Additionally, freshly isolated and cultured SSCs were collected for microarray analysis and expression of pathway related factors confirmed by immunofluorescence and qPCR.

Results: Cyclooxygenase-2 (COX-2), the enzyme through which NSAIDs are thought to control inflammation, can be detected in freshly isolated mouse and human SSCs at the gene and protein level. In line with previous studies in rodents, we find that NSAIDs (ibuprofen, ketoprofen, and indomethacin) significantly impair in vitro chondrogenesis (cartilage formation) in mouse SSCs, while only indomethacin impairs in vitro osteogenesis (bone formation). In contrast, human SSCs display no functional decline in response to NSAID treatment when tested during expansion and differentiation, even with the highly COX-2 selective inhibitor Celecoxib.

Conclusion: We propose that, opposite to mice, human SSC differentiation is independent of COX-2 signaling suggesting that NSAIDs may be safe for use in the context of orthopedic surgery.

Osteoskeletal regenerative ability of exosomes derived from adipose-derived stem cells upon inhibition of Transforming Growth Factor-β-signaling

Huber, Julika, MD, Dr.med.; Menon, Siddharth, BS; Longaker, Michael T, MD, MBA; Quarto, Natalina, PhD

Introduction: Reconstruction of bone defects represents a major challenge due to its poor self-regenerating capabilities. Mesenchymal stem cells (MSC) have been shown to have bone growth enhancing effects in vitro and in vivo. Recently, there has been a paradigm shift implying the MSC-derived secretome to be the key player in tissue engineering, rather than the differentiation potential of MSCs. MSC-derived microvesicles (MV) have been shown to enhance osteogenic function in vitro and in vivo, via transfer of osteogenic miRNAs and proteins.

Methods: MVs were isolated from osteogenically induced human adipose tissue-derived MSCs (hASCs), treated with or without small molecule SB431542, an TGF-ß-inhibitor. MVs were characterized using Western Blot and Nanoparticle Tracking Analysis. hASCs were cultured with MVs-derived from SB431542-treated hASCs (MV-hASCs[+]SB) and untreated hASCs (MV-hASCs[-]SB) to assess bone differentiation in vitro. In ongoing experiments, "cargo" of MVs is currently being assessed by miRomic and proteomic analyses. Potential osteoinductive factors/molecules unveiled from these analyses will be tested by gain and loss of function experiments both in vitro and in vivo.

Results: A significant enhanced in vitro mineralization has been shown in hASCs treated with MV-hASCs[+]SB compared to hASCs treated with MV-hASCs[-]SB. Current analyses on the MVs "cargo", such as proteomic and miRomics profiling, will unveil key factors playing a role in enhancing osteoskeletal regeneration.

Conclusions: Given that MVs are non-teratogenic and less immunogenic, they can be used for targeted therapy at the injury site and could potentially replace cell-based therapy and thus circumvent the risk of neoplastic transformation associated with MSC-transplantation.

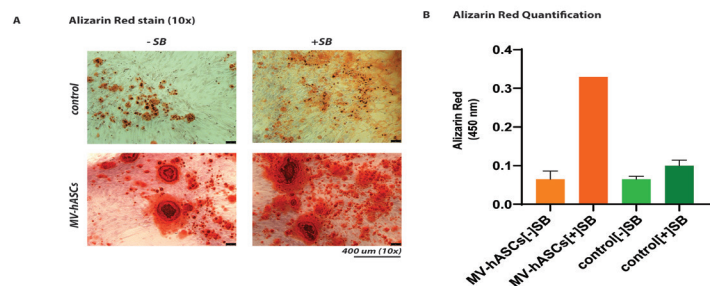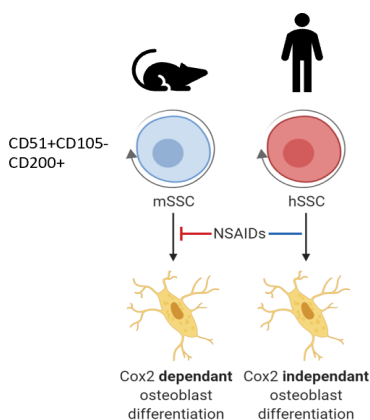**Figure 1:** (A) Top panel, Alizarin Red staining of in-vitro osteogenically induced hASCs with and without 10 μM SB431542-treatment (control +/- SB); Bottom panel, Alizarin staining of hASCs treated with MVs derived from SB431542-treated hASCs (MV-hASCs +/-SB). Magnification 10x. (B) Alizarin Red quantification (wavelength 450 nm) of osteogenically induced hASCs +/- SB and hASCs + 20 μl/ml MV-hASCs+/-SB

Mechanical activation of inflammation at the implant-tissue interface underlies pathological foreign body response.

Jagannath Padmanabhan[1], Kellen Chen[1], Clark A. Bonham[1], Britta A. Kuehlmann[1,3], Teruyuki Dohi[1], Dominic Henn[1], Zachary A. Stern-Buchbinder[1], Peter A. Than[1], Hadi S. Hosseini[2], Noah J. Magbual[1], Mimi R. Borrelli[1], Dharshan Sivaraj[1], Artem A. Trotsyuk[1], Sun Hyung Kwon[1], Zeshaan N. Maan[1], Michael Januszyk[1], James Dunn[2] , Lukas Prantl[3], Geoffrey C. Gurtner[1].*
[1] Division of Plastic and Reconstructive Surgery, Department of Surgery, School of Medicine, Stanford University, Stanford, CA.
[2] Division of Pediatric Surgery, Department of Surgery, Stanford University, School of Medicine, Stanford, CA.
[3] Department of Plastic and Reconstructive Surgery, University Hospital Regensburg, 93053 Regensburg, Germany

Introduction: The foreign body response (FBR) to implantable medical devices is characterized by sustained inflammation at the implant-tissue interface leading to poor implant-tissue integration and eventual implant failure. Elucidating and targeting these inflammatory mechanisms are crucial in order to develop durable, next-generation medical devices.

Methods: We analyzed the mRNA from a unique, large volume human tissue library consisting of breast implant capsules with different degrees of FBR. Further, we developed a new small animal mechanically stimulating implant (MSI) model to directly examine the effect of mechanical stimulation alone on subsequent FBR. We compared the fibrous capsules formed around standard implants and MSIs in mice using histopathology and single cell sequencing, and compared the results with human implant capsules.

Results: Analysis of the human tissue library implicated mechanical signaling as the prime driver of inflammation in pathological FBR. By varying only mechanical stimulation, we were able to recreate a human-like pathologic FBR at the molecular, cellular and tissue level in mice. Specifically, we found that increased local mechanical stress leads to a human-like FBR capsule architecture in mice, characterized by the sustained activation of unique subpopulations of inflammatory myeloid cells that upregulate of a pattern of gene expression identical to that found in the pathological human (Baker IV) capsules.

Conclusion: The current prevailing hypothesis is that the FBR is primarily a reaction to the chemical composition of implantable materials. Here we show for the first time that mechanical signaling alone is sufficient to drive the biology of FBR, independent of material chemistry.

Topical Antibiotic Elutionina Collagen Rich Hydrogel for Healing of Infected Wounds

Uriel Sanchez Rangel1,2, Zhen Wang1,2, Hiroki Oda1,2, Jung Gi Min1,2, Jack Akerman1,2, James Chang1,2, Paige Fox1,2
Division of Plastic and Reconstructive Surgery, Department of Surgery, Stanford University School of Medicine, 770 Welch Road,Suite 400,Palo Alto, CA, 94304,
Division of Plastic and Reconstructive Surgery, Department of Surgery, Veterans Affairs Palo Alto Health Care System, 3801 Miranda Ave., Palo Alto, CA, 94304

Introduction: Biofilm challenged wounds have an impaired healing response. Biofilms require 10-1000x antibiotic concentrations for treatment. Collagen-rich hydrogel (CHG) is simple to manufacture, has strong biocompatibility, and enhances neovascularization. This study examined a ciprofloxacin/collagen-richhydrogel (CHG-ABX) preparation for the treatment of Pseudomonas aeruginosa challenged wounds in vivo.

Methods: 68 mice were divided into four groups: no infection and no CHG, infection without CHG, infection with CHG alone, and infection with ciprofloxacin-enriched CHG. 5mm skin excisions on the dorsum were stented open with silicone rings. On post-operative day (POD) 2, infection groups were inoculated with Pseudomonas aeruginosa. On POD-4, 2% CHG, with or without 2mg/ml ciprofloxacin elution, was applied. Wound dressings and hydrogel were replaced on alternating days until POD 7, 10, 12, 14, or 17.Healing was compared via wound photography and hematoxylin-eosin staining.

Results: On average, wound healing occurs on POD-10 +/- 1, 18 +/- 3, 12 +/-2, 16 +/- 2 for control, infection only, infection with cHG + ciprofloxacin and cHG only, respectively. By microscopy, the CHG+ABX group was more healed than the infection only group at POD7 46.2%±7.5% vs 16.8%±5.3% healed (p=.0007),POD-1067.2% vs 24.1%(p= 0.0003), and POD-14,95.0 ± 9.9 vs 34.8±2.5 (p= 0.00065).

Diagnostic labs showed normal renal and liver function for all CHG+ABX mice. Blood cultures showed no growth of P. aeriginosa growth in CHG+ABX mice.

Conclusion: Antibiotic impregnated collagen hydrogel demonstrated efficacy in vivo for the treatment of P.aeruginosa challenged biofilms.

## Where there is fat there is fibrosis: Elucidating the mechanisms of creeping fat-driven stricture formation.

Khristian E. Bauer-Rowe BS, Michelle Griffin MD, PhD, Deshka S. Foster MD, PhD, Shamik Mascharak BS, Heather desJardins-Park BS, Jeffrey A. Norton MD, FACS, Jeong H. Hyun MD, Michael T. Longaker MD, MBA,FACS.

Introduction: Crohn's disease (CD) is a subtype of inflammatory bowel disease (IBD) characterized by transmural inflammation and creeping fat formation. Thirty percent of CD patients develop strictures, eighty percent of which will require surgery. Creeping fat (CF) forms adjacent to strictures, but whether it promotes stricture formation is unclear. Here, we present a novel surgical model of intestinal fibrosis and show by lineage tracing and selective fat ablation studies that creeping fat may drive fibrosis by contributing to fibroblasts.

Methods: We developed a novel surgical model of CD fibrosis by creating anti-mesenteric colotomies. We performed lineage tracing of mature adipocytes in mice and characterized adipocyte-derived cells by immunostaining. Lastly, we selectively ablated CF adipocytes and assessed histological features such as collagen deposition and bowel wall thickness.

Results: Our surgical model phenocopies clinical features of human strictures (Figure1A-F). Lineage tracing of mature adipocytes in Adipoq-Cre; mTmG mice revealed adipocyte-derived cells that lose adipocyte markers and acquire fibroblast markers at the colotomy site (Figure 1G, H). Selective ablation of CF adipocytes led to reduced collagen deposition and bowel wall thickness compared tou nablated controls (Figure 1J,K).

Conclusions: Our colotomy model represents a novel approach to study intestinal stricture formation and CF without the long-term use of caustic agents. Lineage tracing demonstrates that CF adipocytes convert to fibroblasts that infiltrate the bowel wall (Figure 1L). CF ablation is sufficient to ameliorate stricture formation. Taken together, these findings suggest that CF may drive intestinal fibrosis in part through the contribution of CF-derived fibroblasts.
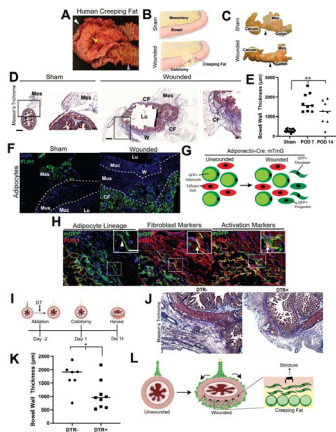
Creeping fat drives stricture formation partly through the conversion of adipocytes to fibroblasts. (A) Gross histology of human stricture (white arrowhead), creeping fat (yellow arrow), and normal colon (gray arrowhead) (adapted from L. Zhang et al. Surgical Pathology of Non-Neoplastic Gastrointestinal Disease, 2019). (B) The creation of anti- mesentericcolotomies.(C) Representativegrosshistologyofcolonsaftershamandcolotomy(wounded)surgeriesonpost- operative day (POD) 7. Arrowheads indicate colotomy site in wounded and an anatomically similar location in shamcolon.

(D) Masson's trichrome of sham (left) and wounded (right) colon on POD 7. Dotted line indicates colotomy site. (E) Bowel wallthickness(serosatomucosa).n=3biologicalreplicates.(F)ImmunostainforPLIN1insham(left) andwounded(right) colon on POD 7. (G) Adipoq-Cre; mTmG system. (H) Immunostain for adipocyte marker PLIN1 (left), fibroblast marker αSMA (middle), and collagen (right) in Adipoq-Cre; mTmG mice on POD 14. (I) Mesenteric white adipose tissue ablation studies in Adipoq-Cre; mTmG; DTR mice. (J) Masson's trichrome after administration of diphtheria toxin to Adipoq-Cre; DTR- (left) and Adipoq-Cre; DTR+ (right) mice on POD 14. (K) Bowel wall thickness after administration of diphtheria toxin on POD 14. n = 3 biological replicates. (L) Model of CF-derived fibroblasts instrictures.

Abbreviations:Mes=mesentery,CF=creepingfat,Lu=lumen.Muc=mucosa,Mus=muscularis,W=wound. Scalebars: 300µm(D(far left,middleright)),250µm(D(middle left,farright), J),75µm(F), 25µm(H) *P< 0.05,**P< 0.01.

Post-Engraftment Sciatic Neurectomy Slows Peripheral Sarcoma Growth

Michael Davitt, MD, Deshka Foster, MD, Shamik Mascharak, BS, Heather Elizabeth. desJardins-Park, BA and Michael T. Longaker, MD MBA FACS. Stanford University, Stanford, CA

Introduction: Recent investigations into interactions between visceral solid tumors and the autonomic nervous system have demonstrated positive feedback loops encouraging tumor growth and neural invasion. However, there has been little interrogation of 1) peripheral somatic neuron involvement in solid tumor progression or 2) sarcoma-nerve cross-talk. The significant heterogeneity in nerve-tumor signaling across different tissue types highlights the importance of clarifying relevant molecular signaling pathways specific to somatic nerve and peripheral sarcoma interactions, which could point towards new potential therapeutic targets.

Methods: Murine fibrosarcoma cells transfected with Firefly luciferase-GFP lentivirus were injected into mouse hindlimbs either before or after sciatic neurectomy or sham surgery, creating 4 groups. Weekly tumor measurements were taken using In Vitro Imaging Systems (IVIS). After 3 weeks of growth, tumors were collected, weighed, and compared to the unaffected hind limb. Tumors were also digested and are in process for bulk RNA-seq.

Results: We found that sciatic neurectomy after intramuscular sarcoma cell implantation results in slower tumor growth when compared to sham surgery performed before implantation, as measured by IVIS and confirmed by final gross tumor weights (Fig. 1). A trend towards significance was also detected between mice who received tumor cell implantation after neurectomy and after sham surgery.

Conclusion: Neurectomy appears to slow established tumor progression, but has less impact on tumor engraftment, suggesting a role for postoperative inflammation in disrupting tumor growth. Expanding the understanding of nerve-sarcoma interactions may uncover untapped therapeutic approaches which could mitigate the morbidity of surgical intervention, simplify reconstruction efforts, and reduce recurrence.
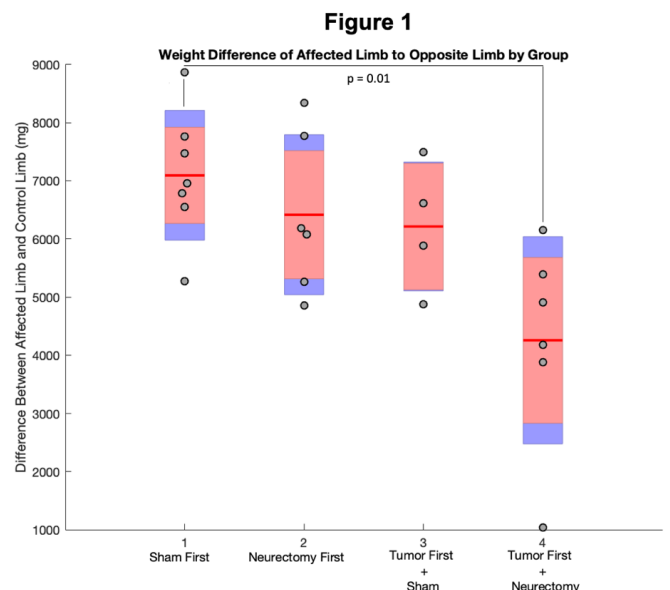
Figure 1

Weight Difference of Affected Limb to Opposite Limb by Group

p = 0.01

Spatial Fidelity of Microvascular Perforating Vessels as Perceived by Augmented Reality Virtual Projections

David Cholok, MD; Marc Fischer; Cristoph Leuze, PhD; Michael Januszyk, MD PhD, Bruce Daniel, MD; Arash Momeni, MD

Introduction: Autologous breast reconstruction yields improved long-term aesthetic results as reported by patients but requires increased resources of practitioners and hospital systems. Augmented reality affords the opportunity to superimpose relevant imaging on a surgeon's native field of view, potentially facilitating dissection of anatomically variable structures. To validate the spatial fidelity of Augmented Reality (AR) projected anatomic models of deep inferior epigastric perforator flap (DIEP) relevant anatomy, comparisons of 3D models and their virtual renderings were performed by four independent observers. Measured discrepancies between the real and holographic models were evaluated.

Methods: 3D-printed models of DIEP relevant anatomy were fabricated from CTA data from 19 de-identified patients. The corresponding CTA data was similarly formatted for the Microsoft Hololens to generate corresponding visual projections. Anatomic points were initially measured on 3D models, after which, the corresponding points were measured on the Hololens projections from two separate vantages. Statistical analyses, including Generalized Linear Modeling, were performed to characterize spatial fidelity regarding translation, rotation, and scale of holographic projections.

Results: Amongst all participants, the median translational displacement at corresponding points was 9.0 mm, 12.1 mm, and 13.5 mm between the real 3D model and V1, 3D model and V2, and between V1 and V2, respectively.

Conclusion: Corresponding points, including topography of perforating vessels for the purposes of breast reconstruction can be identified within millimeters, but there remain multiple independent contributors of error, most notably the participant and location at which the holographic projection is perceived.

The Value of Scientific Publications in Surgical Device Innovation

Alfred Song, Stefano E. Rensi, Abigail G. Tarquinio, Eli Cahan, Vivian Emmely de Ruijter, and James Kennedy Wall.

Introduction: In the course of medical technology innovation, a significant fraction of technology must be assessed in clinical trials. These clinical trials often impact the trajectory of a technology and the company attempting to bring the technology to the patient's bedside. Although the utility of publication is clear when it comes to regulatory and reimbursement activities, it is unknown how the publication foot print or signal affects venture capital valuation of a company and its technology. We set out to identify what associations may exist between the valuation of a technology and the number of publication records associated with that technology.

Methods: We queried Pitchbook from June 2019 to May 2020 with the following parameters: Deal Dates from January 1, 2010 to January 1, 2020. Deal options included Search on Full Transaction, Exclude deals without a deal size. Deal Types: Early stage VC, Later stage VC, Restart early stage VC, Restart later stage VC, By strategic acquirers, IPO, Distress. Ownership Status: Privately held, In IPO registration, Publicly held, Acquired/Merged, Out of Business. Backing Status: VC backed. Business Status: All business statues, Search current business status, Include active positions. Location: United States. Industries: Surgical Devices

Inclusion & Exclusion Criteria

Each company from the pitchbook database was evaluated by a surgeon for surgical product focus by evaluating company literature available on their website.

Companies with the following characteristics were included: Produces one or more medical devices. The device is used by surgeons in the care of their patients. The device is an implantable device which is implanted by either a surgeon or an interventionist including interventional cardiologists, vascular surgeons or cardiac surgeons with endovascular training.

Companies with the following characteristics were excluded: Devices implanted by interventional radiologists on behalf of a primary service. Companies whose sole product was a biologic or pharmaceutical. Companies that produced materials used in various devices, but not marketed directly for the care of a specific patient population. Companies that produce products used in advanced endoscopy managed by gastroenterologists, dentists or oral maxillofacial surgeons, podiatrists. Companies whose business model was that of a distributor.

Results

Pitchbook Dataset

The initial query of the Pitchbook database yielded a list of 222 companies and 535 deals. On average there were 2.4 +/- 1.6 deals per company. Table 1 shows high level statistics describing the companies and deals in our dataset stratified by deal series.

	# of Companies	Number of Deals	Median Deal Size ($M US)	Median Post Valuation ($M US)
Series A	118	156	3.45	13.16
Series B	80	93	5.68	25.51
Series C	40	48	10.28	38.74
Series D	17	17	11.00	50.00
Series E	11	12	10.27	36.58
Series F	6	7	12.72	107.07
Series G	2	2	91.00	196.00
Series H	2	2	25.56	156.89
Unknown	117	195	2.35	14.36

Table 1. Breakdown of Pitchbook dataset by deal series, queried between June 2019 to May 2020. Unknown series appear to represent Early Stage VC investment such as seed rounds based on their Deal Size and Post Valuation. Details of the query available in supplemental materials.

OpenFDA

We found 578 registrations associated with companies in our database. On average each company had 5.5 +/- 7.0 registrations with FDA. Figure 2 shows

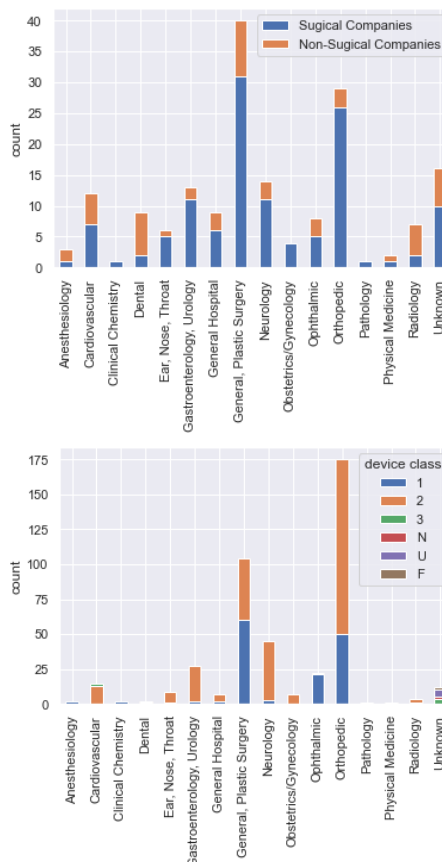**Figure 1.** (a) The number of surgical and non-surgical companies for each medical specialty. (b) The number of registrations associated with surgical companies in each risk class for each product specialty. Most registrations associated with surgical device startups are class I or class II devices. Cardiovascular (n=2) and Unknown medical specialty (n=4) device startups accounted for all class III, HDE, and unclassified devices.

Literature Search

A literature search was performed using the Dimensions (Digital Science) database. Our search was performed between July 2020 to December 2020 with the final analysis taking place on December 4, 2020. We programmatically searched for journal articles associated with surgical device companies in our Pitchbook database using the Dimensions Search API provided by Stanford University.

Data Analysis

Specialty	Company	Device Class	Series	Articles (Log)	Post Valuation (Million USD)
Cardiovascular	Saranas, Inc.	2	Series C	1.10	$32.80
	Micro Interventional Devices, Inc.	2	Series D	3.40	$50.00
	Clozex Medical, Inc.	1	NA	0.69	$19.48
	Saphena Medical	2	Series C	2.30	$20.77
	Lexington Medical, Inc.	2	Series A	1.61	$21.00
General, Plastic Surgery	Fluoptics SAS	1	NA	1.39	$21.63
	ReLIGN Corporation	2	Series B	0.00	$26.60
	Precise Light Surgical	2	Series B	1.10	$33.59
	ClearFlow, Inc.	1	Series D	3.14	$70.55
	Applied Medical Resources	2	Series F	6.63	$96.00
Neurology	Anuncia, Inc.	2	Series D	1.39	$12.00
	Augmedics Inc.	2	Series A	1.10	$18.13
	NICO Corporation	1	Series B	4.74	$122.51
Ophthalmic	Orbit Biomedical, Inc.	1	Series A	0.69	$15.00
	Sight Sciences, Inc.	1	Series C	3.55	$132.73
	Siesta Medical, Inc.	1	Series B	1.79	$7.30
	Figure 8 Surgical, Inc.	1	Series C	0.69	$9.67
Orthopedic	Shoulder Innovations, Inc	2	Series A	1.10	$10.13
	Hydrocision, Inc.	2	NA	3.09	$18.51
	Integrated Endoscopy, Inc.	2	Series A	0.69	$40.72
	OrthAlign, Inc	1	Series D	4.04	$50.00
	IlluminOss Medical Inc.	2	Series A	3.22	$51.68
	Vertos Medical Inc.	2	Series B	4.26	$61.78
	Benvenue Medical	2	Series F	5.02	$112.14
Unknown	NeoChord, Inc	N	Series C	5.38	$50.00
	Tryton Medical Inc.	3	Series A	4.14	$54.00
	Intact Vascular, Inc.	3	Series C	2.83	$115.00

Table 2. Surgical startups companies grouped by medical specialty and sorted by their most recent post money valuation. For device class N denotes a device that has not yet been classified. For series, NA indicates that the type of funding round is unknown. Number of publications appears to track with current post money valuation.
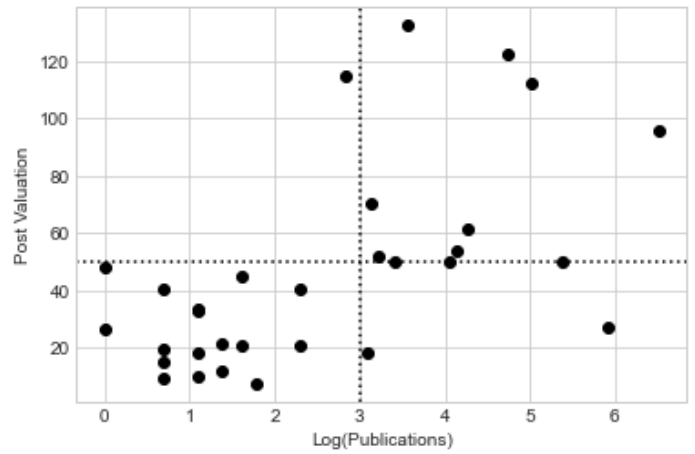
Figure 3. Scatter plot of publications vs current post money valuation in millions of US dollars for VC funded surgical device startups. Companies with an extensive track record of publication have higher valuations. Regression analysis shows a significant correlation between publications and most recent post money valuation (p = 0.004, r = 0.59). Dotted lines indicate thresholds of 20 publications and $50M USD valuation. Fisher's exact test indicates that companies with 20 or more publications are significantly more likely to be valued at $50M or higher (OR=93.5, p=1x10-5).

Conclusion: In this work, we demonstrate that for surgical device companies competing for venture funding, the number of publications correlate with the median deal size. We speculate that the relationship is multifactorial in nature and present four factors that could explain this association. Future work should be directed towards clarifying the characteristics of clinical evidence strategies that provide greater value to the development of new surgical technologies.

Promoting Breast Health Awareness: Can a sensor-enabled training system help?

Authors: Cassidi Goll, BA, Hossein Mohamadipanah, PhD, Anna Witt, BA, Brett Wise, BA, Su Yang, BA, Pamela Ratliff, MPA, Carla Pugh, MD, PhD

Introduction: According to a 2009 study published in the Journal of Clinical Oncology, 79% of women age ≤40 (N=222) diagnosed with breast cancer reported that they identified their cancers through breast self-exam (BSE).[1] Further, a 2011 study published in the Journal of Women's Health indicated that 25% of women survivors detected their breast cancer using the breast self-examination (N=361).[2] However, the U.S. Preventative Services Task Force does not require clinicians to teach women how to perform BSE.[3]

Methods: To address this grave challenge, our team at the Technology Enabled Clinical Improvement (TECI) Center has developed a mobile, sensor-enabled training system to teach women proper BSE technique. To validate the efficacy of the training system, our team deployed a data collection at the Stanford Cancer Institute's 2019 Breast Cancer and African Americans (BCAA) event where survey, sensor, and anecdotal data was collected from 61 participants. The breast used in this study had a single, hard mass embedded in it.

Results: Our previous work revealed that practitioners who use less than 10N of force are 70% more likely to miss a lesion.[4] Participants at the BCAA event were able to successfully identify the mass 65% of the time and used an average force of 7.2N. When looking at participants' confidence in their abilities to perform BSE, only 10% of respondents answered "very confident" pre-training whereas post-training, the reporting for "very confident" jumped to 66% (p<.01).

Conclusion: The integration of sensors into the BSE training system allowed for objective, evidence-based assessment of hands-on skill. In addition to teaching women proper BSE technique, this training aims to empower women to be informed advocates in their breast health journey.

1   K. J. Ruddy, S. Gelber, R. Tamimi, L. Schapira, S. Come, S. Kereakoglow, N. U. Lin, E. P. Winer, A. H. Partridge. *Presentation of breast cancer in young women.* Journal of Clinical Oncology. 2009 27:15_suppl, 6608-6608

2   M. Y. Roth , J.G. Elmore, J.P. Yi-Frazier, L.M. Reisch, N.V. Oster & D.L. Migliorett (2011). Self-detection remains a key method of breast cancer detection for U.S. women. Journal of Women's Health (2002), 20(8), 1135–1139. https://doi.org/10.1089/jwh.2010.2493

3   USPTF Am Fam Physician. *Screening for Breast Cancer: Recommendation Sheet.* 2010 Sep 15;82(6):672-676.

4   NEJM Laufer, S., Cohen, E.R., Kwan, C. D'Angelo, A.L., Pugh, C., et al. *Sensor technology in assessments of clinical skill* [published correction appears in N Engl J Med. 2015 Mar 19;372(12):1182]. N Engl J Med. 2015;372(8):784-786.

The Effect of TAP Blocks on Conversion to Chronic Opioid Use in Patients Undergoing Autologous Breast Reconstruction

Arhana Chattopadhyay MD, Jennifer Shah, Vy Thuy Ho MD, Pooja Yesantharao MS, Clifford Sheckter MD, Rahim Nazerali MD

Background: The transversus abdominus plane (TAP) block is used to reduce postoperative donor site pain in patients undergoing autologous breast reconstruction with an abdominally-based free flap. The goal of this study was to determine the effect of TAP blocks on postoperative opioid prescriptions and the rates of conversion to chronic opioid use.

Methods: The ClinformaticsTM Data Mart (OptumInsight, Eden Prairie, MN) is a de-identified national claims database from a private insurer. From 2003-2019, adult patients within a 1-year continuous enrollment period were queried. Common procedural terminology codes for autologous breast reconstruction with an abdominally-based free flap and for placement of an intraoperative TAP block were used. Patients who underwent additional procedures within 180 days after their index surgery were excluded. Patients were considered opioid-naïve if they did not fill a narcotic prescription from 1 year to 30 days prior to surgery. Morphine milligram equivalents (MME) were calculated for postoperative prescriptions which were filled within 30 days after surgery. Chronic opioid use (COU) was defined as receiving 4 unique prescriptions or a 60-day supply between 30 and 180 days after surgery. Chi squared and Mann-Whitney-Wilcoxon tests were used for statistical analysis.

Results: Of 4091 patients meeting criteria (100% female, mean age 51.2 ± 9.0 years), 181 (4.4%) had a TAP block placed. There was no statistically significant difference in length of stay between patients who received a TAP block vs. those who did not (p= 0.266). Postoperative COU did not decrease in patients who received a TAP block (p = 0.192). Statistically significant predictors of conversion to COU included younger age, Elixhauser comorbidity index score greater than 3, filling a psychiatric or mood-adjusting medication prescription during the study period, and filling a benzodiazepine prescription during the study period.

Conclusion: In patients undergoing autologous breast reconstruction with free flap reconstruction, TAP blocks do not decrease length of stay or conversion to chronic opioid use. These data suggest that intraoperative TAP block placement may be a low-yield opioid-reduction strategy.

Effect of Meteorological Conditions and Seasonality on Surgical Site Infection Prevalence in the United States

Raymond Liou, BS, Joseph D Forrester, MD MSc

Introduction: Meteorological variables may represent a neglected group of risk factors for surgical site infections (SSI). We investigate whether increases in temperature, humidity, and precipitation increases SSI rate.

Methods: Records of surgical encounters and follow-ups within National Healthcare Safety Network-designated surveillance windows (30 or 90 days) were extracted from MarketScan® databases from 2007-2014. Data extracted included age, sex, procedure date, ICD-9 codes, and metropolitan statistical area (MSA) where procedures occurred. Average daily maximum temperature, specific humidity, and precipitation in associated MSAs were extracted from the Gridded Surface Meteorological dataset and standardized. SSI risk was analyzed with a multinomial model including environmental and previously identified risk factors with outcomes being 1) no SSI 2) SSI diagnosed during admission and 3) SSI diagnosed during follow-up. Seasonality of SSI was analyzed with Lomb-Scargle periodogram and regression fitting of a sinusoidal equation.

Results: A total of 7,862,418 patient records were extracted from 382 MSAs. Overall SSI rate was 1.57%, with 81.6% diagnosed at follow-up and 18.4% diagnosed during surgical admission. For every standard deviation increase in humidity, there was a 4.1% relative risk increase of SSI during admission ($p=0.03$) and 2.8% increase of SSI during follow-up ($p=0.003$). For every standard deviation increase in temperature, there was a 3.2% increase in SSI during follow-up ($p<0.001$). Lomb-Scargle analysis showed a ~12 month SSI periodicity ($p<0.05$), with peak incidence occurring in late July ($p<0.001$) (Figure 1).

Conclusion: Development of SSIs may be influenced by meteorological variables. Further investigations into relationships between climate and SSI may help inform future SSI prevention strategies.

Assessing Entrustment and Achievement of American Board of Surgery Entrustable Professional Activities (EPAs) for Graduating Residents

Kearse, LE, Schmiederer, IS, Anderson, TN, Dent, D., Payne, D., Korndorffer Jr, JR.

Introduction: Establishing competency-based medical education (CBME) has become a major goal in medical education, with Entrustable Professional Activities (EPAs) as one measure to assess and entrust competence. In 2018, the American Board of Surgery (ABS) began a 2-year pilot with preselected EPAs to shift general surgery residency toward CBME. As the pilot was at limited institutions, little is known about entrustment in these EPAs nationally. However, we hypothesize that postgraduate year 5 (PGY5) residents are achieving entrustment in the selected EPAs.

Methods: Following the 2020 ABS In-Training Examination, surgical residents completed a survey and indicated how often their assessments and operative plans were modified in the prior 6 months for 4 of the 5 ABS-selected EPAs. A Resident Entrustability Index (REI) score (1-5) was then developed to ascertain PGY5's levels of entrustment.

Results: 1049 of 1367 PGY5 residents responded. Residents achieved an average REI of 4, indicating rare modification of assessments and operative plans. Median REI for inguinal hernias and penetrating abdominal trauma was 5, indicating complete entrustment. A minority of residents were deemed to have a lack of entrustment, demonstrated by REI of 3 or less.

Conclusion: Of the EPAs evaluated, PGY5 residents are achieving appropriate levels of entrustment in evaluation and management. Although this is the case for a vast majority of PGY5 residents, there is still work to be done to ensure that all PGY5 residents are attaining entrustment prior to graduation. Our study also suggests that the surgical EPAs selected were appropriate to assess levels of entrustment in PGY5 residents.

Surgical EPAs	1	2	3	4	5	N/A	Mean (STD)	Median (IQR)
Assessment of RLQ pathology	7	11	103	504	424	318	4.27 (0.73)	4 (4,5)
Operative plan of RLQ pathology	6	13	95	495	439	319	4.29 (0.73)	4 (4,5)
Assessment of inguinal hernia	6	14	71	415	532	329	4.40 (0.73)	5 (4,5)
Operative plan of inguinal hernia	7	11	71	397	552	329	4.42 (0.73)	5 (4,5)
Assessment of biliary stone disease	6	15	99	519	407	321	4.25 (0.73)	4 (4,5)
Operative plan of biliary stone disease	6	14	101	524	401	321	4.24 (0.73)	4 (4,5)
Operative plan of penetrating abdominal trauma	6	13	77	357	473	441	4.38 (0.75)	5 (4,5)
Operative plan of blunt abdominal trauma	6	12	99	398	398	454	4.28 (0.76)	4 (4,5)

1: Always, 2: Frequently, 3: Occasionally, 4: Rarely, 5: Never

NA excluded in calculating mean, median

The omental fat-augmented free flap: minimizing post-operative pain in autologous breast reconstruction

Authors: Peter Deptula MD, Yulia Zak MD, Monica Dua MD, Irene Wapnir MD, Dung Nguyen MD PharmD

Introduction: The omental fat-augmented free flap (O-FAFF) is a recently developed technique for autologous breast reconstruction. We assess the O-FAFF donor site morbidity in terms of postoperative pain and narcotic use.

Methods: A retrospective analysis of patients undergoing O-FAFF from 2019-2021 was performed. Patients were evaluated for demographic data, operative time, complications, mean pain scores and narcotic pain medication use during their hospital course. We compared outcomes to a control group of patients who underwent breast reconstruction with free abdominal tissue transfer.

Results: A total of 14 patients (23 breasts) undergoing O-FAFF were identified. Average pain scores on POD1, POD2 and POD3 were 3.1 (±0.28), 2.8 (±0.21) and 2.1 (±0.35), respectively. The average narcotic use by patients in oral morphine equivalents (OME) on POD1, POD2 and POD3 are 24.3 (±5.5), 21.9 (±4.6) and 6.2 (±2.4), respectively. Total narcotic use during hospital stay was 79.4 (±11.1) mg. No patients required the use of a PCA (0.0%). Average pain scores and narcotic use are significantly lower when compared to a previously published cohort of patients who underwent autologous breast reconstruction with free abdominal tissue transfer (p<0.05) (Table 1).

Conclusion: The O-FAFF is proven to be a viable method of autologous breast reconstruction. Early series of patients undergoing O-FAFF reconstruction suggest a lower donor site morbidity as demonstrated by lower postoperative pain scores and lower consumptions of narcotic pain medications.

Table 1

Post-operative pain and narcotic use after autologous breast reconstruction

	O-FAFF Mean (SEM)	Control* Mean (SEM)	p-value
Pain score (1-10)			
POD1	3.1 (0.3)	4.8 (0.4)	0.019
POD2	2.8 (0.2)	5.4 (0.3)	0.0001
POD3	2.1 (0.35)	5.0 (0.3)	0.0001
Narcotic use (OME)			
POD1	24.3 (5.5)	81.9 (8.6)	0.0003
POD2	21.9 (4.6)	69.3 (8.8)	0.003
POD3	6.2 (2.4)	46.1 (5.7)	0.0002
Total narcotic use (OME)	79.4 (11.1)	197.4 (18.4)	0.0005

*Control group is a previously published cohort of patients (n= 40) who underwent autologous breast reconstruction with free abdominal tissue transfer.

Hunter C, Shakir A, Momeni A et al. Transversus Abdominis Plane Block and Free Flap Abdominal Tissue Breast Reconstruction: Is There a True Reduction in Postoperative Narcotic Use? Ann Plast Surg. 2017 Mar;78(3): 254-259.

SEM – Standard Error of Mean

Establishing Procedural Metrics for Scoliosis Bracing

Kayla Huemer, Grant Wood, Dr. John Vorhies, Su Yang, Dr. Carla Pugh

Introduction: Adolescent idiopathic scoliosis (AIS) is a condition involving deformity of the spine that impacts millions of children globally. Without effective treatment, severe scoliosis can progress to chronic back pain and decreased health-related quality of life. The current gold standard of non-operative management is to design a custom-fitted rigid orthosis. However, orthosis design and adjustment are largely guided by qualitative methods, resulting in high variability of success and ambiguity in treatment duration. Our aim is to develop specific and objective metrics to quantify success of custom orthoses.

Methods: We are currently designing textile-sensors to capture the dynamic in-brace forces present throughout a patient's treatment. In order to generalize to the myriad of bracing techniques, we began with a t-shirt style design to map the pressures across the entire torso. In characterizing the range of pressures and how it differs between bracing techniques, this will inform regions of interest to study longitudinally across the child's treatment with respect to the bracing technique.

Results: The pressure sensor in development is a variable resistor matrix-array. The external fabric is a water-proof material and internal layers are made of conductive and resistive fabric to create a conformable sensor. We are currently in the calibration and hysteresis-testing phase of development and plan to conduct patient observation once testing is complete.

Conclusion: Unpredictable adverse events associated with bracing and variable patient compliance remain barriers to standardizing bracing techniques. Quantitatively assessing the brace can augment a clinician's understanding of the mechanics of spinal correction, mitigate adverse events, and inform treatment duration.

Botox Produces Diagnostic and Therapeutic Benefit for Breast Reconstruction Pain and Animation Deformity

Halley Darrach MD, Pooja Yesantarao MS, Irene T Ma, MD, Jennifer G Seither NP, Jeff J Kim MD, Philip S Brazio MD, Dung H Nguyen, MD, PharmD

Introduction: Breast reconstruction is most commonly performed using implants, however patients with subpectoral implant placement can experience pain and animation deformity. Due to minimal literature describing the use of botulinum toxin (BTX-A) treatment of pain related to the manipulation of the pectoralis major and/or latissimus dorsi muscle (LD) in implant-based reconstruction, we report our outcomes for this patient population.

Methods: A retrospective chart review of breast reconstruction patients for a single surgeon was performed. Patients who underwent BTX-A injection for muscular pain, spasm, or animation deformity were identified and outcomes reviewed.

Results: 11 patients and 19 breasts were identified. All patients had a submuscular pectoralis pocket and/or a pedicled latissimus dorsi flap present, Baker grade 3 capsular contracture due to muscle spasms, and had not witnessed improvement with physical therapy. 25-100 units of BTX-A were delivered per breast (average 60) on average 11 months after last breast surgery. 82% of patients reported improvement or resolution of their pain and/or animation deformities (p=0.0002), as well as softening of their capsular contracture to grade 1-2 (p=0.02). Patients noted symptomatic relief for an average of 10 months. No patients reported adverse effects related to BTX-A therapy.

Conclusion: Implant-based reconstruction using the pectoralis major and/or latissimus dorsi muscles can be plagued by pain, spasm, and animation deformities. The use of BTX-A is a diagnostic and therapeutic modality for these post-breast reconstruction patients with the majority of patients having resolution of symptoms without the need for additional surgery.

## Mental Health Outcomes in Pediatric Asthma Patients

Katelyn Chan, Julia Chandler, Ryan Han, Stephanie Chao

Introduction: Asthma is the most common chronic childhood illness in the United States, accounting for significant morbidity and health care utilization. Prior research suggests a correlation between childhood asthma diagnoses and poor mental health outcomes. However, there are few population-based studies assessing this risk.

Methods: The IBM MarketScan private insurance claims database was used to identify children (5-18yo) admitted for asthma, traumatic injury, and appendicitis between 2007 and 2016. Time-to-event analysis was performed to compare mental health outcomes of PTSD, depression, anxiety, and adjustment disorder among children admitted with asthma to those admitted with traumatic injury and appendicitis.

Results: 68,024 children with admissions for asthma, traumatic injury, and appendicitis were identified in the database. Among the 20,958 children with asthma-related hospital admissions, 2.9% developed a subsequent mental health diagnosis of PTSD, depression, anxiety, or adjustment disorder. Children admitted for asthma were at increased risk of developing a mental health diagnosis compared to those admitted for traumatic injury (n= 25,549, HR 1.30, p<0.0010) as well as those admitted for appendectomy (n=21,517, HR 1.38, p<0.0010). There was no significant difference in risk between children admitted for trauma compared to those admitted for appendicitis (HR=0.98, p=0.741).

Conclusion: Children admitted to the hospital for asthma are at increased risk of developing mental health conditions compared to patients admitted for traumatic injuries or appendicitis. Early identification of children at risk for mental health conditions has the potential to enable appropriate intervention and treatment.
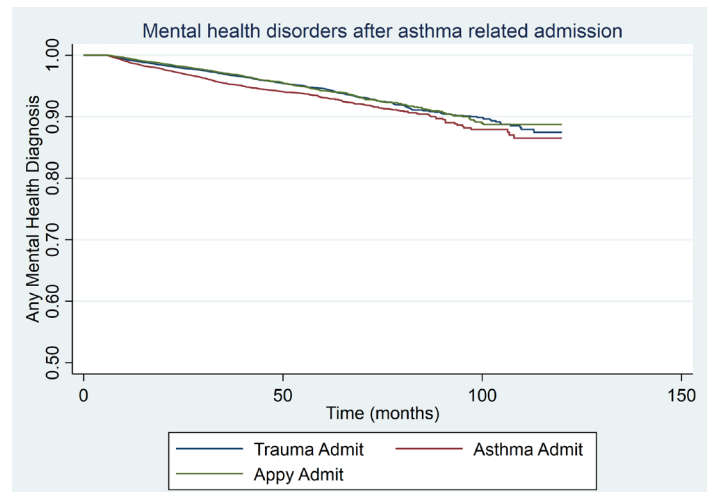
Infection with two multidrug-resistant organisms in solid organ transplant patients is associated with increased mortality and prolonged hospitalization

Siqi Cao BS, Lakshika Tennakoon MSc MPhil, Aleah L. Brubaker MD PhD, Joseph D. Forrester MD MSc

Introduction: Solid organ transplant patients may be at greater risk of multidrug-resistant (MDR) infections due to immunosuppression, invasive procedures and prolonged hospitalizations. While single-organism MDR infections have been reported to increase morbidity and mortality, little is known about the added risk of multiple-organism MDR infections among transplant patients.

Methods: To assess mortality and hospitalization associated with these infections, we analyzed 31,105 admissions records for liver, kidney, heart, lung and pancreas transplant recipients in the United States. Multidrug-resistant infections were defined by ICD-10 CM code. Outcomes of interest included hospital length of stay and death. Weights were applied in accordance with survey methodology. Variables were compared using Chi2, Wilcoxon rank-sum or Fisher's exact test as appropriate, with Bonferroni correction to the P-value. Outcomes were assessed by multivariate regression analysis adjusting for covariates.

Results: Of the 166 patients diagnosed with two MDR infections, 15% died (n=25) compared with 3% (40 of 1491) diagnosed with one MDR infection and 1% (355 of 29,451) of patients with no MDR infections. Diagnosis of two MDR infections was associated with an increased odds of death (OR = 9.6, 95% CI 3.3-27.9) and prolonged duration of hospitalization (beta = 41 days, 95% CI 34-49). Diagnosis of one MDR infection was associated with prolonged hospitalization (beta = 20 days, 95% CI 17-22) but not increased odds of death (OR = 1.2, 95% CI 0.5-2.5).

Conclusions: Strategies to decrease perioperative MDR infection may improve survival and decrease duration of hospitalization for solid organ transplant patients.

Home-Time and Health-Related Quality of Life: A Mixed Methods Study of Veterans after Surgery

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Introduction: Home-time, time spent at home after discharge, is emerging as a novel, patient-oriented outcome in stroke recovery and end-of-life care. Longer home-time is associated with lower mortality and higher patient satisfaction. However, a knowledge gap exists in the understanding of "home-time" in the surgical population and its association with postoperative recovery and quality of life (QOL).

Methods: A prospective mixed-methods explanatory sequential study in Veteran patients >65 years-of-age who underwent major surgery at VA Palo Alto within the past year. Home-time was standardized as a percentage of total time at home from surgery to survey. We surveyed participants (N=152) measuring (1) QOL: VR-12; CASP-19; Decisional Regret Scale and (2) Function: Activities of Daily Living (ADLs); Instrumental ADLs (IADLs). Associations of home-time with QOL and function were analyzed using Pearson correlation. We then conducted 12 interviews about home-time in postoperative recovery. We coded and thematically analyzed qualitative data and integrated with quantitative data using joint displays.

Results: Median home-time was 97.8% (IQR [94.6%, 98.6%]; range [22.2%, 99.5%]). Higher home-time was associated with higher ADL (r=0.21; p=.01) and IADL scores (r=0.21; p=.01) and physical QOL in VR-12 (r=0.34; p<.001). CASP-19 Control subscale was weakly correlated with home-time (r=0.14; p=.08). Home was perceived as "a sanctuary"–safe and familiar environment accelerating recovery.

Conclusion: Increased home-time in the first year after major surgery was associated with improved function and physical QOL. Interviewees considered transitioning home an indicator for recovery, making home-time a promising, patient-oriented quality outcome measure for surgical recovery that warrants further study.

Impact of COVID-19 on Presentation, Management, and Outcomes of Acute Appendicitis

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Introduction: COVID-19 has significantly impacted patient care but the specific impact on non-related surgical management and outcomes are still unknown. We assessed the impact of the COVID-19 pandemic on the presentation, management, and outcomes of patients with acute appendicitis.

Methods: We performed chart review using the Stanford Research Repository (STARR), gathering information on patients presenting with acute appendicitis to Stanford Emergency Departments (ED) between March–June in 2019 and 2020. We collected data involving patient demographics, symptoms, severity, perforation status, treatments, and post-operative courses. Relationships between variables were assessed by calculating r correlation coefficients and performing student T-tests and Chi-squared tests as appropriate.

Results: We identified 361 patients presenting to the ED with acute appendicitis, 182 (50.4%) and 179 (49.6%) patients in the 2019 and 2020 time periods, respectively. At presentation, more patients were diagnosed with a ruptured appendix in 2020 than in 2019 (20% vs. 16%, p=0.02). Patients in 2020 also presented with more severe cases, characterized by their ED severity scores (p<0.001), than those in 2019. Post-operatively, we found that a greater number of patients were discharged on antibiotics in 2020 than in 2019 (29% vs. 19%, p=0.04) and that representation rates increased in 2020 compared to 2019 (13% vs. 4%, p<0.01).

Conclusion: During the COVID-19 pandemic, patients who presented to our institution with acute appendicitis had higher severity scores, were more likely to be perforated, and had higher representation rates. Further research on the impact of the pandemic is necessary.

Aspects	Variables	2019 N = 182	2020 N =179	p-value
Presentation	Duration of symptoms (days), mean (SD)	2.7 (7.2)	2.2 (3.1)	0.36
	ED Severity Score (Emergent), N (%)	23 (13%)	112 (63%)	<0.001
	Ruptured diagnosis in ED, N (%)	29 (16%)	36 (20%)	0.02
Management	Admitted to hospital, N (%)	174 (96%)	173 (97%)	0.57
	Surgery Performed, N (%)	150 (82%)	156 (87%)	0.47
Outcomes	Readmission (within 30 days), N (%)	8 (4%)	23 (13%)	0.01
	Discharge on antibiotics, N (%)	35 (19%)	52 (29%)	0.04
	Length of stay (days), mean (SD)	3.2 (2.8)	3.2 (3.2)	0.89

Central Line Training Requires Deliberate Practice and Deliberate Training

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Introduction: Procedural training to minimize central line-associated infections and complications has been studied for many years. At a large academic institution, surgical residents undergo a comprehensive, simulation-based curriculum for central line placement which utilizes a 31-item binary checklist for assessment. This study aims to evaluate this institutional practice in the context of restricted in-person learning and abbreviated training time.

Methods: A retrospective review evaluated resident score reports (n=81) from 2018 to 2020. Statistical analyses, including descriptive statistics, independent t-test, and x2 tests, were performed to evaluate how learners' performance during Summer 2020 compared to "pre-COVID" years, 2018-2019.

Results: Comparison of 2020 trainees to pre-COVID trainees revealed no significant differences in average scores [28.14±4.07 v. 28.66±3.25 (p=.56)], respectively. Pass rates with established objective measures (cut-score and "critical fail" parameters) also showed no significant difference (71.4% vs 73.3%, p = 0.87). However, significant differences were observed in 4 specific checklist items: patient positioning, draping the patient, sterile ultrasound probe cover placement, and finder needle (FN) positioning before venous access (Table 1).

Conclusion: Ultimately, this study finds that modifications to procedural training within current in-person restrictions did not adversely affect residents' overall performance, but rather, it likely affected the trainers in their execution of demonstrating each step for learner acquisition. Differences in successful completion of certain steps may identify expert automaticity in performing these steps within the procedure.

Table 1. Rate of Successful First-Time Completion of Task

Task:	Pre-COVID (2018, 2019)	2020	p-value (Pearson Chi-Square)
Chart reviewed: INR, platelets checked	96.7%	100.0%	0.397
Consent verified	96.7%	100.0%	0.397
Allergies confirmed	88.3%	90.5%	0.788
EKG and SpO2 verified	96.7%	95.2%	0.765
Team introduction	88.3%	100.0%	0.102
Verify patient with 2 identifiers	98.3%	100.0%	0.552
Hands washed	90.0%	95.2%	0.462
Vein and artery identified with US (non-sterile)	95.0%	95.2%	0.965
Mask, eye protection, hair cover	100.0%	100.0%	-
Adequate sterile prep with chlorhexidine (wait 3 minutes)	100.0%	100.0%	-
Patient placed in Trendelenburg*	95.0%	71.4%	0.003
Gowned and gloved without breaking sterility	90.0%	95.2%	0.462
Wide drape placed correctly*	90.0%	71.4%	0.039
Ultrasound probe sheath applied correctly*	93.3%	76.2%	0.031
All equipment verified, prepared, and placed (CVC kit)	93.3%	95.2%	0.755
Catheter flushed and capped	88.3%	76.2%	0.178
Location of IJ confirmed with US (sterile)	98.3%	95.2%	0.431
Needle placed at proper location, aiming at the ipsilateral nipple*	98.3%	85.7%	0.022
Vein accessed: no more than 3 needle passes	96.7%	90.5%	0.260
Venous blood return verified	98.3%	95.2%	0.431
Wire advanced 12-17cm	86.7%	95.2%	0.282
Wire visualized with US in longitudinal view	80.0%	61.9%	0.098
Skin nick made with 11 blade	91.7%	95.2%	0.591
Dilator deployed and removed properly (2-3 cm, no kinking of wire)	91.7%	81.0%	0.179
Catheter advanced over wire, 12-17cm	93.3%	90.5%	0.667
Control of wire maintained at all times	85.0%	85.7%	0.937
Wire removed and stored without breaking sterility	93.3%	90.5%	0.667
Catheter checked for blood return and flushed (all ports)	85.0%	90.5%	0.528
Catheter secured in place with suture	85.0%	90.5%	0.528
Sterile dressing applied	86.7%	85.7%	0.913
Chest x-ray of correct placement confirmed	91.7%	95.2%	0.591

*significant statistical difference (p < 0.05)

Feasibility and Interest in Establishing a Longitudinal Surgical Skills Performance Database

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Introduction: Despite interest in artificial intelligence, big data, and video-based coaching for practicing surgeons, there is a paucity of research reporting feasibility and surgeon interest in performance databases. This project explored the feasibility and surgeons' perceptions of the utility of a skills performance database.

Methods: During the 2019 ACS meeting, attendees participated in a surgical skills assessment. A pre-survey, surgical procedure(~30min), and post-interview(~30min) were completed. The pre-survey and post-interview questions related to demographic data, opinions on skills evaluation of practicing surgeons, ethics, and interest longitudinal skills database. Descriptive and chi-square statistics, plus grounded theory were used to analyze responses.

Results: The results included survey participants (n=189) and interview participants (n=23). 96% of participants (n=181) indicated an interest in contributing their data to a longitudinal performance database and 96% demonstrated interest in tracking their individual performance against this database. 82% (n=149) believed there was an ethical obligation to have skills assessment to protect the public. While 16 of 23 interview participants expressed interest in formal standardized testing or peer evaluation, 5 participants indicated there is no role for formal evaluation of practicing surgeons without first creating a safe and supportive environment.

Conclusion: Large scale skills testing is feasible and national or regional scientific meetings may be the ideal location for this. While formal skills assessment for practicing surgeons has previously been reported to be of no interest to surgeons, this study identifies specific interests in safe and supportive environments as well as interest in performance databases that allow information sharing and peer/self-assessment.

Preoperative β-Lactam Antibiotic Prophylaxis is Superior to Bacteriostatic Agents: Analyzing Outcomes in Immediate Breast Reconstruction with Acellular Dermal Matrix

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Background: Staged implant-based breast reconstruction is the most common reconstructive modality following mastectomy. Postoperative implant infections can have significant impact on adjuvant oncologic care and reconstructive outcome. Here, we investigate the impact of β-lactam antibiotics (i.e. bactericidal) compared to alternative antibiotic agents on postoperative outcomes for implant-based breast reconstruction.

Methods: A retrospective analysis of patients who underwent immediate sub-pectoral tissue expander placement with an inferior acellular dermal matrix (ADM) sling at a single institution between May 2008 and July 2018 was performed. Patient demographics, comorbidities, and complication rates were retrieved. The impact of antibiotic regimen on postoperative outcomes, including infection rate and reconstructive failure, was investigated.

Results: A total of 320 patients with a mean age and BMI of 48.2 years and 25.0 kg/m2, respectively, who underwent 542 immediate breast reconstructions were included in the study. The use of a β-lactam antibiotic was protective against postoperative infection (odds ratio [OR] = 0.467, p = 0.046), infection requiring operative management (OR = 0.313, p = 0.022), and reconstructive failure (OR = 0.365, p = 0.028). Extended, i.e. post-discharge, prophylaxis was not associated with any clinical benefit.

Conclusion: The use of β-lactam antibiotics for pre-/peri-operative prophylaxis is superior to alternative antibiotics with a bacteriostatic mechanism of action in regard to rates of postoperative infection and reconstructive failure following immediate tissue expander-based breast reconstruction. Extended, i.e. post-discharge, prophylaxis is not indicated regardless of the antibiotic chosen.

Lasting improvements of a surgical infection prevention program: the sustainability of Clean Cut

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Introduction: Surgical infections are a major cause of perioperative morbidity and mortality, particularly in low resource settings. Clean Cut is a six-month quality improvement program proven to reduce surgical infections through improved adherence to perioperative infection prevention standards in several Ethiopian hospitals. Long term sustainability of the program had not been assessed,

Methods: Eight Ethiopian hospitals implemented Clean Cut between 2015-2019. Between 6-18 months after completion of the program, a two-week sustainability evaluation was undertaken at seven hospitals using the same direct observation of infection prevention practices. Compliance to standards was assessed, meaning 100% of expected behaviors within a particular standard were performed correctly. Data were entered into DHIS2 and analyzed using Stata v16.1.

Results: A total of 3385 patient encounters were included, 738 from pre-implementation, 2178 post-implementation and 469 from the sustainability audit period. Between the pre- and post-implementation period, compliance with each infection prevention area improved significantly. The sustainability audit period showed further improvement in use of the Surgical Safety Checklist use (50% to 58%), skin antisepsis (58% to 75%), antibiotic prophylaxis (59% to 66%), and gauze counting (94% to 95%). There was some attrition in compliance with surgical linen integrity and sterility (46% to 39%) and instrument sterility (55% to 42%) but performance in these areas remained far above baseline.

Conclusion: This sustainability evaluation demonstrates that behavior changes made as a part of Clean Cut are persistent and, in some cases, continue to improve. Wider implementation and evaluation in different contexts is valuable for improving patient safety and infection prevention behaviors over the long term.

Table 1:

Factor	Baseline	Clean Cut Implementation	Sustainability Audit	p-value*
N	738	2178	469	
Patient Characteristics				
Age (median, IQR)	26 (1, 35)	28 (22, 37)	26 (16, 32)	0.64
Female gender	493 (66.8%)	1539 (70.7%)	352 (75.1%)	0.002
Diabetes	14 (1.9%)	46 (2.1%)	2 (0.4%)	<0.001
Hypertension	25 (3.4%)	54 (2.5%)	12 (2.6%)	<0.001
Infection Prevention Process Measures				
Surgical Safety Checklist	194 (26.3%)	1089 (50.0%)	274 (58.4%)	<0.001
Hand & skin preparation	339 (45.9%)	1254 (57.6%)	351 (74.8%)	<0.001
Antibiotic prophylaxis	388 (52.6%)	1279 (58.7%)	308 (65.7%)	<0.001
Surgical linen sterility & integrity	46 (6.2%)	1002 (46.0%)	183 (39.0%)	<0.001
Instrument sterility	57 (7.7%)	1192 (54.7%)	196 (41.8%)	<0.001
Gauze counting	630 (85.4%)	2046 (93.9%)	444 (94.7%)	<0.001

*p-value indicates baseline vs. sustainability audit

Pilot testing of a fit-for-purpose surgical headlight in Ethiopia

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Introduction: Adequate lighting is a precondition for surgery, however quality surgical lighting is often lacking in operating rooms in low-resource countries. Commercial surgical headlights are not widely available in these settings, as they are expensive and lack suppliers and maintenance mechanisms. We aimed to understand user needs of a fit-for-purpose surgical headlight for use in low-resource settings by evaluating a preselected headlight and the local surgical lighting conditions.

Methods: We undertook observations of 10 surgeons using a single headlight model over two weeks in three hospitals in Addis Ababa, Ethiopia, with fieldnotes, questionnaires and photos. All surgeons completed a baseline survey and qualitative interview. Nine logbooks were completed by surgeons after every headlight use.

Results: The lighting quality in three large urban hospitals was poor: five surgeons ranked light quality as poor or very poor and seven have delayed or cancelled operations due to poor lighting within the last year. Five surgeons described intraoperative complications due to poor lighting. The headlight was considered useful (4.6/5, with 5 being "extremely useful"). The surgeons recommended nine specific improvements to meet their needs, including increased brightness, comfort, battery run-time, and an additional rechargeable battery. They also encouraged affordability.

Conclusion: Lighting in the surveyed operating rooms was poor and headlights were useful for addressing this issue. Specific key needs in a low-resource setting noted that headlights should be comfortable, durable, affordable and should have two rechargeable batteries. Refinement of a fit-for-purpose light for these environments is ongoing.

Qualitative Interviews (N = 10)

Data Element	Result
Factors influencing headlight use and utility	"So we had to do hepaticojejunostomy [..] I used it [the headlight] the whole time because the ceiling light in the theatre was not good. And on top of that there was power interruptions for about five minutes about twice during this surgery, so I did not stop operating because of the headlight,"
Existing hospital infrastructure	"every time there is any electrical shortage, we have to call the generator people to manipulate [the generator]. That takes lots of time to restart our surgeries."
Device improvement and considerations	"maintenance is most important thing now… the spare parts that might be inadequate. I don't think they will be available in our country that's my fear."
Device and specification feedback	"I can see deep into the pelvis, the cul-de-sac, the deepest place, I tried, I could see. So, there's no shadow."

Clean & Confident: Impact of Sterile Instrument Processing Workshops on Knowledge and Confidence in Five Countries

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Introduction: Proper sterilization of surgical instruments is essential for safe surgery, yet reprocessing methods in low-resource settings can fall short of standards. "Training of trainers" (TOT) workshops in Ethiopia and El Salvador instructed participants in sterile processing (SP) concepts and prepared participants to teach. Participant trainers subsequently taught SP workshops at their home institutions.

Methods: Five TOT workshops were conducted between 2018-2020 in Ethiopia and Central American (CA). Participant trainers then led nine non-TOT workshops in El Salvador, Guatemala, Honduras, and Nicaragua. Interactive sessions with SP nurses and technicians covered instrument cleaning, packaging, disinfection, sterilization, and transportation. Participants completed multiple-choice pre- and post-tests, demonstrated skill competencies, and shared feedback by survey. In Ethiopia, in-hospital observations of four SP metrics were also observed pre- and post-workshops.

Results: Ninety-five trainees participated in TOT workshops, while 179 participated in non-TOT workshops. Knowledge on a 10-point scale equally increased in Ethiopian TOT (+2.3±2.8), CA TOT (+2.9±1.7), and non-TOT (2.7±2.5) workshops (p>0.05). Scores on tests of SP theory also increased (Ethiopian TOT: +68±92%, CA TOT: +26±20%, non-TOT +36±10%, p<0.01). Most respondents felt "very confident" about teaching (Ethiopian TOT: 72%, CA TOT: 83%, non-TOT: 70%, p>0.05). Fewer participants felt "very confident" in realizing change (Ethiopian TOT: 36%, CA TOT: 58%, non-TOT: 38%, p>0.05). Reasons included lack of resources and inadequate support. However, in-hospital observations showed 7% improvement in sterility confirmation and 5% increase in instrument compliance (both p<0.01).

Conclusion: SP training workshops improve knowledge, confidence, and metric compliance. Future work will address both long-term efficacy and local sustainability.

Table 1. Knowledge and Confidence regarding Sterile Instrument Processing Technique after Training-of-Trainers and non-Training-of-Trainers Workshops in Five Low-and-Middle-Income Countries

	Ethiopia TOT	Central America TOT	Central America Non-TOT	p-value
Total: Percent (n)*	31% (82)	5% (13)	64% (169)	
Perceived Knowledge (n=169) *Mean Increase of 10 pt ± SD*	2.3 ± 2.8	2.9 ± 1.7	2.7 ± 2.5	0.555
Tested Knowledge (n=83) *Mean Percent Increase ± SD*	68 ± 92%	26 ± 20%	36 ± 10%	0.001
Helpfulness of Training (n=178) *Mean Increase of 10 pt ± SD*	9.1 ± 1.6	10 ± 0	9.8 ± 0.5	<0.001
Teaching Confidence *Percent Very Confident (n=168)*	72% (38)	83% (10)	70% (72)	0.690
Teaching Likelihood *Percent Very Likely (n=157)*	40% (17)	67% (8)	35% (36)	0.091
Confidence in Change *Percent Very Confident (n=165)*	36% (18)	58% (7)	38% (39)	0.356

*Total n per variable is noted in the first column and varies due to missing responses for some questions.

Surgical Lighting In Liberian ORs: Using Human-Centered Design To Close A Critical Patient Safety Gap

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Introduction: Operating room (OR) lighting is often inadequate in Liberia, and poses a safety risk for surgical patients. After assessing lighting challenges in Liberian ORs and conducting a pilot study of a fit-for-purpose surgical headlight for this environment, we conducted a ten-month follow-up of the previously distributed headlights using human-centered design principles.

Methods: Lifebox distributed 47 headlights to 44 surgeons in five public hospitals. A follow up was performed ten month following distribution with a sample of headlight recipients in four of the hospitals to assess headlight performance and perceived impact on safety in the OR.

Results: We were able to contact nine surgeons who had received headlights; the rest did not respond to repeated requests for information. Six surgeons reported an increase in confidence during surgery, two reported a reduction in delayed or cancelled cases and one reported an increase in speed and accuracy of surgery. Four rated the best features of the headlight as its comfort; two preferred the non-rechargeable battery to the rechargeable one. Recommendations for improvement included extending battery life span (4/9) and headband comfort (2/9). Eight of the nine respondents would recommend the headlight to colleagues.

Conclusion: In Liberia, where OR lighting is often poor, a robust but low-cost headlight was well-accepted by surgeons who also reported increases in perceived safety and reductions in cancellations. Optimizing some headlight features may increase utilization and are being integrated into a subsequent version. The low response rate is indicative of the challenges of working in this environment and reaching providers where they practice.

Keywords - human-centered design, surgical lighting, surgical safety, patient safety

Table: Results of Use of headlight after ten month observations and device feedback

Use of Lifebox surgical Headlight after a year		# Response (n=9)
Headlight impact on patient safety:	Increase confidence	6
	Reduce cancellation or delay	2
	Increase speed and accuracy of surgery	1
Headlight features appreciated	Comfort	4
	Non rechargeable Battery	2
	Rechargeable Battery	1
Headlight features to be improved	Battery life span	4
	Headband discomfort	2
Headlight utility	Recommend to other surgeons	8

Lymphatic Microsurgical Preventive Healing Approach (LYMPHA) for Lymphedema Prevention After Axillary Lymph Node Dissection – A Single Institution Experience and Feasibility of Technique

Kelsey Lipman MD, Mardi Karin MD, Irene Wapnir MD, Kimberly Stone MD, Dung Nguyen MD

Introduction: Lymphatic microsurgical preventive healing approach (LYMPHA) has emerged as a method for prevention of lymphedema for patients undergoing axillary lymph node dissection (ALND) for breast cancer. This study highlights details of our operative technique and postoperative experience.

Methods: Patients undergoing ALND were offered LYMPHA prior to surgery. Limb measurements, L-Dex, and body composition analysis (InBody, Biospace Co.) were performed pre and postoperatively. Intraoperatively, axillary reverse lymphatic mapping with indocyanine green (ICG) and lymphazurin was performed. SPY-PHI imaging (Stryker, MI, USA) was used to visualize ICG uptake into axillary lymphatics. Cut lymphatics from excised nodes were preserved for lymphaticovenous anastomosis (LVA). At completion of microanastomosis, ICG was visualized draining from the lymphatic through the recipient vein. Patient data including demographics, complications, and long-term outcomes were recorded.

Results: Retrospective review identified eleven patients who underwent ALND and LYMPHA over 16 months. Average age and BMI were 54 years and 24 kg/m2, respectively. Number of LVAs performed ranged from one to four per axilla. Operating time ranged 32-95 minutes. There were no complications, and no patients have developed lymphedema, with average follow up of 7 months. At follow up, ICG and SPY angiography confirmed intact lymphatic conduits with uptake of ICG across the axilla.

Conclusion: This study supports LYMPHA as a feasible and effective method for lymphedema prevention, specifically highlighting our use of ICG and SPY to confirm adequate lymphatic flow through the anastomoses. Long-term data will further determine its utility as an adjunct procedure to axillary dissection for breast cancer patients.

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