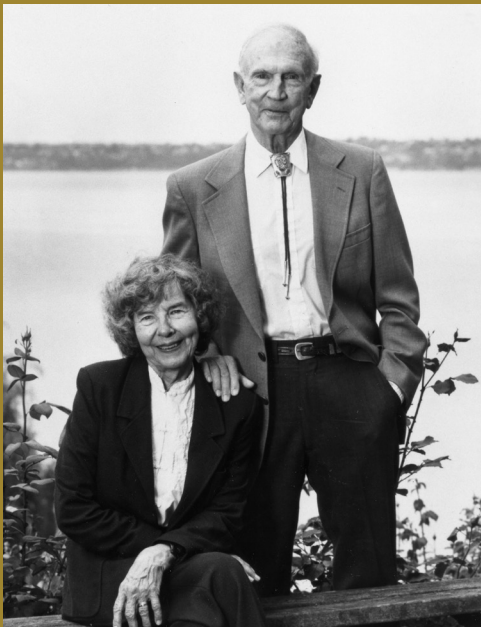


DEPARTMENT OF SURGERY
UNIVERSITY OF WASHINGTON

Presents



2014 RESEARCH DAY AND
20TH ANNUAL
HELEN & JOHN SCHILLING
LECTURE

UW TOWER AUDITORIUM
4333 BROOKLYN AVE. NE
SEATTLE, WA 98105

FRIDAY, JANUARY 31, 2014

Agenda

7:00 AM	Welcome	Carlos A. Pellegrini, MD, FACS, FRCSI (Hon.), <i>The Henry N. Harkins Professor & Chair</i> , Department of Surgery
7:05 AM	Introduction	David R. Flum, MD, MPH, Associate Chair for Research & Professor, Department of Surgery
7:15 AM	Galit Eliahoo	The Effect of P27Kip1 on Arterial Remodeling in Response to Hindlimb Ischemia
7:30 AM	Meghan Flanagan	Process-of-Care Utilization in Lung Cancer Surgery
7:45 AM	Meera Kotagal	Use and Accuracy of Diagnostic Imaging in the Evaluation of Pediatric Appendicitis: A Report from the SCOAP-CERTAIN Collaborative
8:00 AM	Nicholas Shubin	Epinephrine Induces Monocyte MKP-1 and NURR1 Counter-Inflammatory Molecule Expression
8:15 AM	Poster Session	
8:40 AM	Faculty Presentation: Thomas Hatsukami, MD, Professor, Division of Vascular Surgery	
8:55 AM	Stephanie Peng	Early Outcomes with Lymphaticovenular Anastomosis: A Single-Center Study
9:10 AM	Andrew Mesher	Routine Surveillance Blood Cultures During ECMO Detect Clinically Occult Bloodstream Infections
9:25 AM	Jonathan Sham	Novel Antibody-Targeted Zirconium-89 PET Imaging Of Hepatocellular Carcinoma
9:40 AM	Rebecca Plevin	Differences in the Genomic Signature of Inflammatory Cells in Severely Injured Trauma Patients
9:55 AM	Poster Session	
10:20 AM	Faculty Presentation: Leah Backhus, MD, Assistant Professor, Division of Cardiothoracic Surgery	
10:35 AM	Morgan Richards	ACGME Case Logs: Changing Rates of Minimally Invasive and Open Surgery Across Two Decades of Resident Training
10:50 AM	Bruce Swearingen	Achieving Tolerance in a Mismatched VCA Transplant While Reducing the Risk of GVHD: The Goal of Transient Chimerism
11:05 AM	Jarrod McAteer	Shifts Toward Pediatric Specialists in the Care of Common Childhood Surgical Conditions: Trends and Outcomes
11:20 AM	Lunch	
12:20 PM	Faculty Presentation: Jason Ko, MD, Assistant Professor, Division of Plastic Surgery	
12:35 PM	Sarasijhaa Desikan	Standardization of a Multidisciplinary Clinical Pathway Improves Outcomes in Ruptured Abdominal Aortic Aneurysms
12:50 PM	Ravi Sood	Dermal Fibroblasts from Duroc and Yorkshire Pigs Demonstrate Differences in Response to Injury
1:05 PM	Katherine Flynn-O'Brien	Craniectomy for Blunt Head Injury and Associated Morbidity and Mortality Trends in Washington State, 2000-2012
1:20 PM	Val Simianu	Appy-RADS: A Novel Appendicitis Reporting System to Improve Communication about Uncertainty in Appendicitis Imaging
1:35 PM	Closing	David R. Flum, MD, Associate Chair for Research

Please also join us in Hogness Auditorium (Room A402) in the UW Health Sciences Building at 4:00PM for the 20th Annual Helen & John Schilling Lecture:

Timothy R. Billiar, MD: Of Men and Mice - An Iterative Strategy to Dissect the Immune Response to Trauma

Introduction



Carlos A. Pellegrini, MD,
FACS, FRCSI (Hon.)
The Henry N. Harkins
Professor & Chair

Welcome to the Annual Department of Surgery Research Symposium! The purpose of this symposium is to bring together faculty, residents, fellows, students, and friends to share and discuss the exciting research taking place in our Department. This symposium serves as an important opportunity for residents and fellows to hone their presentation skills through oral and poster presentations, as well as through audience Q&A.

This year we celebrate the 20th anniversary of the symposium and Schilling Lecture, which was made possible by a generous gift from the late Helen Schilling in honor of her husband, Dr. John Schilling. The Schillings were deeply committed to teaching, scholarship, and research and we are honored to be able to continue this commitment through research-related event such as this.

Each year, the Department of Surgery invites a distinguished leader in surgical research to attend the symposium and give the annual Schilling Lecture. We are delighted to host this year's guest, Dr. Timothy R. Billiar, George Vance Foster Endowed Professor and Chair of the Department of Surgery, and Director of the Trauma Research Center at the University of Pittsburgh in Pittsburgh, PA. Dr. Billiar will help adjudicate the symposium, then at 4:00pm today in Hogness Auditorium he will give the Schilling Lecture, titled "Of Men and Mice: An Iterative Strategy to Dissect the Immune Response to Trauma." Dr. Billiar will discuss the recent findings in humans and experimental models on the mechanisms regulating immune dysfunction following trauma, and he will also present a framework around which to pursue a complex human disease through an iterative strategy between clinical data and mouse models.

We are also honored to be joined at this year's symposium by John Slattery, PhD, Vice Dean of Research and Graduate Education in the UW School of Medicine and Professor of Pharmacology and Medicine in the School of Medicine at the University of Washington. As Vice Dean, Dr. Slattery is responsible for the well-being of a \$575M research enterprise, including the development of the South Lake Union campus, a site projected to comprise two city blocks and which is home to many of our Department of Surgery research labs and a hub of intellectual activity.

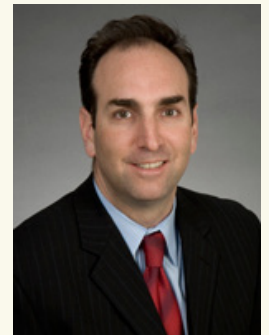
Finally, I am excited to announce this year's expanded symposium format. Having received a record number of abstract submissions this year, we have added two poster sessions, the first of which will be adjudicated by Dr. Billiar along with other research leadership, and the second consisting of posters meriting honorable mention. Additionally, we have assigned discussants to each abstract in the plenary session. Discussants will provide a framework for the presentation and ask each of our speakers a probing question in order to help them refine their skills as scientific presenters. This evening we will celebrate all participants and their co-authors, and present cash prizes to the top poster and oral presenters.

I am pleased that you are joining us today in recognizing the hard work of our residents, fellows, and their faculty mentors, and sharing in our celebration of research. I hope you find today's event both informative and engaging!

Sincerely,

Carlos A. Pellegrini, MD, FACS, FRCSI (Hon.)
The Henry N. Harkins Professor & Chair
Department of Surgery
University of Washington

David R. Flum, MD, MPH
Associate Chair for Research, Surgery
Professor, Surgery, Health Services, and Pharmacy
Department of Surgery
University of Washington



David R. Flum, MD, MPH
Associate Chair
for Research
Professor of Surgery

Timothy R. Billiar, MD



Timothy R. Billiar, MD
George Vance Foster Endowed Professor and
Chair of the Department of Surgery, and
Director of the Trauma Research Center at the
University of Pittsburgh

Timothy R. Billiar, MD is the George Vance Foster Endowed Professor and Chair of the Department of Surgery, and Director of the Trauma Research Center at the University of Pittsburgh in Pittsburgh, PA. He is also the Vice-President and Chief Academic Officer for University of Pittsburgh Physicians. Dr. Billiar graduated Summa Cum Laude 1979 from Doane College in Crete, NE with a BA in Natural Sciences. He then received his medical degree from the University of Chicago in 1983 followed by general surgery training and four years of surgical research training at the University of Minnesota and the University of Pittsburgh. In 1992, Dr. Billiar joined the University of Pittsburgh faculty as the Samuel P. Harbison Assistant Professor in the Department of Surgery and in 1999 was named Department Chair.

Dr. Billiar has a long standing interest in shock and sepsis and his laboratory studies the mechanisms leading to the initiation of the inflammatory response and organ injury after trauma. As a result of his research, Dr. Billiar has gained an international reputation for his contributions to discoveries on the role of nitric oxide in the shock and liver disease. Additionally, his laboratory is credited with initially cloning the human inducible nitric oxide synthase gene. He holds seven US patents associated with his research. Dr. Billiar is currently the Principal Investigator (PI) on a National Institutes of Health (NIH) trauma training grant, Director of a P50 Trauma Center Grant also from the NIH, and PI on an NIH RO1 grant.

Dr. Billiar is widely published, having edited 8 medical texts and authored over 600 peer-reviewed articles. He also sits on eight Editorial Boards, including the Journal of the American College of Surgeons, Molecular Medicine, and the Journal of Perioperative Medicine. Dr. Billiar is active in numerous professional societies and is past president of the Society of University Surgeons, the Nitric Oxide Society, and the Surgical Infection Society. He has previously served on the Surgery, Anesthesia, and Trauma Study Section at NIH and is currently a member of the Residency Review Committee of the Accreditation Council for Graduate Medical Education (ACGME). Dr. Billiar has given over 300 invited talks and is the recipient of numerous honors and awards. In 2006 Dr. Billiar was inducted into the Institute of Medicine of the National Academy Sciences, and in 2008 he received the Flance Karl Award for Scientific Achievement from the American Surgical Association. In 2011 he was named University of Pittsburgh Distinguished Professor, and he has been recognized by Best Doctors in America for each of the last 10 years.

About Helen & John Schilling



Helen & John Schilling

The Helen and John Schilling Endowed Lectureship was established by the late Helen Schilling to bring distinguished scholars to the Department of Surgery at the University of Washington, and to enhance the Department's commitment to the highest standards of patient care, teaching, research and scholarship. It was Mrs. Schilling's wish that the lectureship be in honor of her husband, John.

Dr. Schilling devoted his life to academic medicine in a career spanning 50 years. He was born and raised just outside Kansas City, Missouri, and at the age of 15 entered Dartmouth College. After graduating from Dartmouth in 1937, he attended Harvard Medical School as a member of the class of 1941, the last class to graduate before World War II. In the six months before the start of his internship and residency at the Roosevelt Hospital in New York City, he signed on as a ship's doctor on the schooner Effie M. Morrissey for a scientific expedition to the Arctic sponsored by the U.S. Bureau of Standards. After a number of perilous adventures along the Greenland coast and in the Hudson Straits, he returned to New York and started his training in general surgery. He joined the surgical staff at the University of Rochester in 1945 where he began his life long work on wound healing. His career at Rochester was interrupted for

several months by a stint in the central Pacific (Eniwetok) to participate in the study of flash burns as part of the atom bomb tests and the Manhattan Project. Subsequently he joined the Air Force as a volunteer and set up a surgical department at the new School of Aviation Medicine in San Antonio.

In 1956 Dr. Schilling was invited to be the chief of the first full-time department of surgery in the new medical school at the University of Oklahoma. He was successful in recruiting a number of outstanding junior faculty, many of whom have gone on to become chairmen. In addition to his administrative responsibilities, he maintained an extensive research program in wound healing in collaboration with Dr. Betty White. At the end of 18 years Dr. Schilling and his faculty had trained 75 surgeons from Oklahoma and adjoining states and had established a department known for its academic accomplishments.

Dr. Schilling came to the University of Washington in 1974 as a senior investigator and, upon the sudden resignation of the chairman, was asked to take over the management of the Department of Surgery. Thus began his third chairmanship which lasted eight years until his retirement. His first responsibility was to recruit faculty to fill the many vacancies, a task he achieved after several stormy years. Upon his retirement in 1983, he had recruited 41 new faculty members and graduated a total of 40 chief residents.

His career in academic surgery was marked by a devotion to patient care and teaching, as well as research. But, despite his commitment to the profession, Dr. Schilling still found time to engage in other activities. From his early childhood, he enjoyed the outdoors and had become an expert tennis player, skier, and fly fisherman; he always believed that one's life work should be punctuated by intervals of travel and recreation.

Helen Schilling shared with her husband both the non-academic as well as the academic side of his life. They first worked together in Rochester and continued their association through the years in Oklahoma and Washington. They were married in 1979. She had a career in newspaper work and administration after graduating from Oberlin College. This dual background enabled her to be his close associate and administrative assistant for 40 years.

Participants (Alphabetical Order by Group)

Oral Presenters



Galit Eliahoo, PhD
Senior Research Fellow, Vascular Surgery

Hometown: Haifa, Israel
Medical School: Technion IIT,
Haifa, Israel
Research Interests: Angiogenesis after
hindlimb ischemia



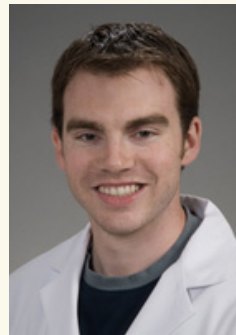
Meera Kotagal, MD
T32 Research Resident, PGY-5

Hometown: Cincinnati, OH
Medical School: Harvard
Medical School
Research Interests: Clinical outcomes,
pediatric surgery, global surgery



Meghan Flanagan, MD
T32 Research Resident, PGY-4

Hometown: Los Altos, CA
Medical School: Albert Einstein College
of Medicine
Research Interests: Clinical outcomes,
cancer epidemiology



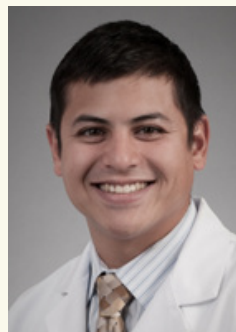
Jarod McAteer, MD, MPH
General Surgery Resident, R3

Hometown: Casper, WY
Medical School: University of
Washington School of Medicine
Research Interests: Pediatric surgical
outcomes research, practice
standardization



Katherine Flynn-O'Brien, MD
T32 Research Resident, PGY-3

Hometown: Albuquerque, NM
Medical School: University of
New Mexico
Research Interests: Pediatric trauma and
critical care, pediatric surgery, clinical
outcomes, healthcare quality



Andrew Mesher, MD
Research Resident, PGY-4

Hometown: Mercer Island, WA
Medical School: University of
Washington School of Medicine
Research Interests: Surgical innovation,
medical device design



Sarasijhaa Desikan, MD
Vascular Surgery Resident, R1

Hometown: Little Rock, AR
Medical School: University of Arkansas
for Medical Sciences
Research Interests: Natural history
and progression of aortic aneurysms,
popliteal entrapment syndrome



Stephanie Peng, MD
Plastic Surgery Chief Resident

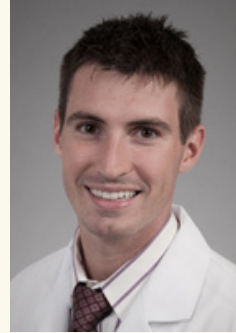
Hometown: Dallas, TX
Medical School: University of Chicago
Pritzker School of Medicine
Research Interests: Free flap outcomes,
lymphaticovenular anastomosis
outcomes

Participants — *Continued from page 5*



Rebecca Plevin, MD
T32 Research Resident, PGY-5

Hometown: Oakland, CA
Medical School: University of Southern California
Research Interests: Inflammation, sepsis



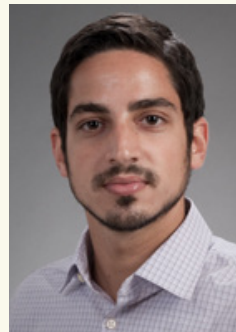
Vlad Simianu, MD
T32 Research Resident, PGY-4

Hometown: Carmel, IN
Medical School: Indiana University School of Medicine
Research Interests: Surgical outcomes, appropriateness, decision-making, surgical oncology



Morgan Richards, MD
Research Resident PGY-4

Hometown: Seattle, WA
Medical School: Case Western Reserve University School of Medicine
Research Interests: Outcomes research for pediatric diseases, medical education



Ravi Sood, MD
T32 Research Resident, PGY-3

Hometown: Chicago, IL
Medical School: University of Chicago Pritzker School of Medicine
Research Interests: Biology and epidemiology of hypertrophic scarring



Jonathan Sham, MD
T32 Research Resident, PGY-4

Hometown: Carrollton, TX
Medical School: University of Pennsylvania
Research Interests: Hepatobiliary oncology, antibody-targeted radiotheranostics, siRNA therapeutics



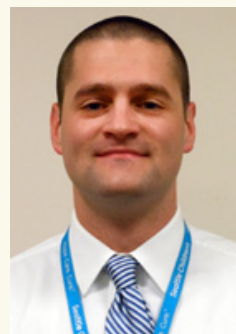
Bruce Swearingen, MD
Senior Research Fellow, Plastic Surgery

Hometown: San Antonio, TX
Medical School: New York Medical College
Research Interests: Vascularized composite tissue allograft (VCA) transplantation, hand and face transplantation



Nicholas Shubin, PhD
T32 Research Fellow

Hometown: Seattle, WA
Medical School: Brown University
Research Interests: Inflammation



Patrick Chesley, MD
Research Resident, PGY-3

Hometown: Cartersville, GA
Medical School: Medical College of Georgia
Research Interests: Short bowel syndrome, intestinal failure, necrotizing enterocolitis

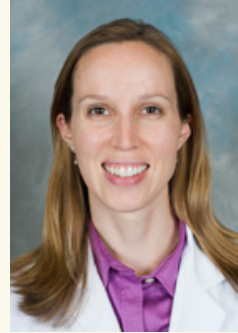
Posters

Participants — *Continued from page 6*



Matthew Delano, MD, PhD
Trauma and Critical Care Fellow

Hometown: East Brady, PA
Medical School: Temple University
School of Medicine
Research Interests: Immune system
dysfunction in trauma and sepsis



Ellen Morrow, MD
Minimally Invasive Surgery Fellow

Hometown: Baltimore, MD
Medical School: Stanford University
Research Interests: Outcomes in
foregut surgery



F. Thurston Drake, MD, MPH
General Surgery Resident, R4

Hometown: Ocean Springs, MS
Medical School: University of Utah
School of Medicine
Research Interests: Surgical outcomes,
patient decision-making, global surgery



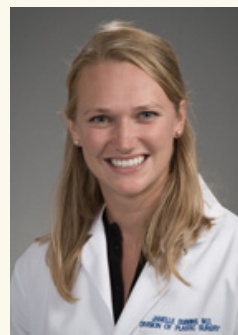
Brinkley Sandvall, MD
Plastic Surgery Resident, R3

Hometown: Arlington, TX
Medical School: Baylor College
of Medicine
Research Interests: General
reconstructive plastic surgery and hand
surgery



Timo Hakkarainen, MD, MS
General Surgery Resident, R3

Hometown: Olympia, WA
Medical School: Mount Sinai School
of Medicine
Research Interests: Comparative
effectiveness and long-term outcomes



Janelle Sousa, MD
Plastic Surgery Resident, R5

Hometown: Anchorage, AK
Medical School: University of
Washington School of Medicine
Research Interests: Clinical outcomes
in breast reconstruction and cleft lip/
palate repair



Martin I. Montenovo, MD
Transplant Fellow

Hometown: Casilda, Argentina
Medical School: National University of
Rosario, Argentina
Research Interests: Liver transplant
allocation



Barclay Stewart, MD, MscPH
General Surgery Resident, R3

Hometown: Savannah, GA
Medical School: Medical University of
South Carolina
Research Interests: Global health,
epidemiology, humanitarian aid



Callie Thompson, MD
General Surgery Resident, R4

Hometown: Dodgeville, WI
Medical School: Meharry
Medical College
Research Interests: Wound healing,
inflammatory responses to injury and
infection



Roberto Salas Fragomeni, MD
General Surgery Resident, R1

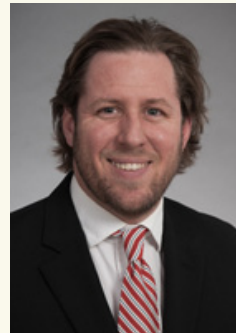
Hometown: Panama City, Republic
of Panama
Medical School: University of Panama,
Republic of Panama
Research Interests: Novel targets and
therapeutics

Posters—Honorable Mention



Nathan Airhart, MD, MPH
General Surgery Resident, R2

Hometown: Portland, OR
Medical School: Oregon Health and
Science University
Research Interests: Aortic disease,
vascular smooth muscle cell physiology



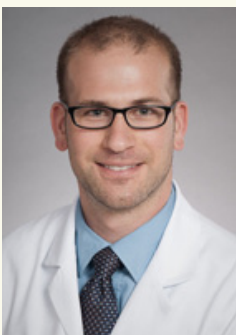
Joshua Hermsen, MD
Congenital Cardiac Surgery Fellow

Hometown: Tega Cay, SC
Medical School: Medical University of
South Carolina
Research Interests: Adult congenital
heart disease, organ donor
immunosuppression



Shinsuke Kikuchi, MD
Visiting Research Scholar

Hometown: Asahikawa, Japan
Medical School: Asahikawa Medical
University, Japan
Research Interests: Mechanism of
arterial graft healing



Matthew Bartek, MD, MPH
General Surgery Resident, R1

Hometown: Newton, MA
Medical School: University of
Massachusetts Medical School
Research Interests: Surgical outcomes in
resource poor settings, surgical culture



Catherine Kling, MD
SORCE Research Fellow, PGY-5

Hometown: Melbourne, Australia
Medical School: Vanderbilt University
Research Interests: Surgical outcomes,
preoperative health optimization



O. Maximiliano Crespin, MD
Senior Research Fellow, CVES

Hometown: Entre Rios, Argentina
Medical School: Universidad Adventista
del Plata, Argentina
Research Interests: Esophageal
physiology and gastroesophageal
surgery



Lacey LaGrone, MD
General Surgery Resident, R3

Hometown: Littleton, CO
Medical School: Washington University
in St. Louis School of Medicine
Research Interests: Trauma, global
health

Oral Presenters

THE EFFECT OF P27KIP1 ON ARTERIAL REMODELING IN RESPONSE TO HINDLIMB ISCHEMIA

Eliahoo G, Weitz K, Tang G

Background: Atherosclerosis is the leading cause of mortality and morbidity in the United States and leads to myocardial infarctions, stroke, and amputations from peripheral arterial disease. The molecular factors that control collateralization are not well understood. Recently, a genetic polymorphism was identified in the gene $p27^{Kip1}$ (p27), which affects human response to arterial injury. Additionally, previous studies showed that overexpression of p27 inhibits vascular endothelial and VSMC proliferation and angiogenesis. In order to test the hypothesis that p27 affects collateral artery development after ischemia, we tested p27 knockout mice against wild type mice for their response to hindlimb ischemia. We then performed in vitro experiments in vascular smooth muscle cells derived from either p27 knockout or wild type mice to better understand p27's effect on arterial remodeling.

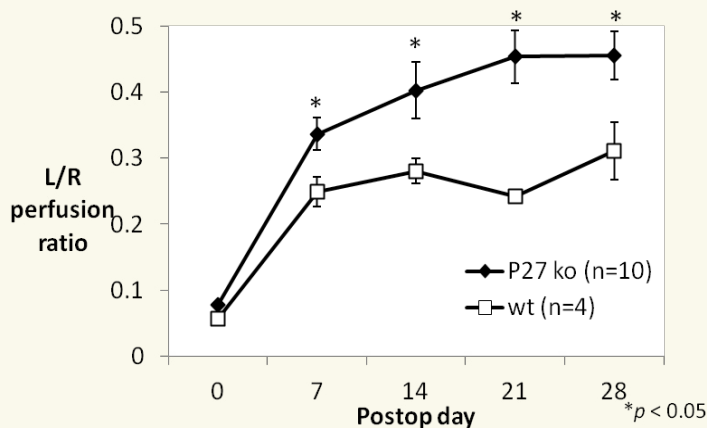
Methods: In all experiments p27^{-/-} (p27 ko) mice were served as experimental group and wild type (wt) mice (c57BL/6) as control. *In-vivo* studies were performed on p27^{-/-} and wt female mice. Hindlimb ischemia was induced by left femoral artery ligation. The mice were followed weekly by laser Doppler perfusion imaging of the foot pad until sacrifice at 28 days postoperatively. The perfusion ratio between the right and the left leg was compare for all the mice after each scan.

Aortic smooth muscle cells (aoSMC) were isolated from p27^{-/-} and wt mice. The scratch assays was performed under conditions of growth arrest, cell migration was tested for p27^{-/-} and wt at zero time and after 20 hours. A gel contraction assay was performed, and the area of the collagen structure was measured at zero time and after 18 hours.

Results: The in-vivo experiments showed that after 7 days the perfusion ratio between the right and the left leg for the p27 mice was 0.33 ± 0.02 which was better than the wt mice (and for the wt mice (0.24 ± 0.015). This continued up to the 28th day postoperatively (Figure 1). After 20 hours p27^{-/-} aoSMC show increased migration ($79.014 \pm 5.614\%$ vs. $55.92 \pm 6.21\%$ in wt) and gel contraction compared to wt aoSMC ($55 \pm 4\%$ of the initial area compare to $81 \pm 1.5\%$ for wt) (Figure1).

Conclusions: Mice deficient in p27 develop significantly greater collateralization of femoral arteries following ligation injury. P27 inhibits contraction in addition to inhibiting aoSMC migration. These in vitro assays will be used to identify key cells involved as well as molecular pathways needed for p27's effect on the arterial response to injury.

Figure 1:



PROCESS-OF-CARE UTILIZATION IN LUNG CANCER SURGERY

Flanagan M, Varghese TK, Backhus L, Wood DE, Mulligan MS, Cheng A, Flum DR, Farjah F

Background: Quality improvement in healthcare often focuses on reducing variation in care delivery with the aim of improving patient outcomes, and there has been increasing interest in measuring and implementing process-of-care metrics to achieve that goal. ProvenCare™ Lung Cancer is a quality improvement project that aims to improve care and outcomes for resectable lung cancer patients through strict all-or-none compliance with 38 process elements. The potential impact of ProvenCare™ is uncertain because existing patterns of care in lung cancer surgery are currently unknown.

Methods: A cohort study (2007-2011) was conducted using MarketScan—a nationally representative sample of persons with employer-provided health insurance and their inpatient and outpatient claims. Six processes identified by ProvenCare™, and measurable using claims data were evaluated for utilization—electrocardiogram (EKG) and pulmonary function testing (PFT) 180 days before resection, computed tomography (CT) and positron-emission tomography (PET) 60 days before resection, bronchoscopy and mediastinoscopy.

Results: Among 17,009 operated patients, process-of-care utilization for the 6 elements evaluated was as follows: EKG—77%, PFT—81%, CT—73%, PET—65%, bronchoscopy—59% and mediastinoscopy—19%. Only 6.3% of patients received all 6 processes-of-care in the recommended timeframe, and a significant proportion of patients underwent non-invasive tests more than once: EKG—32%; PFT—18%; CT—22%. There was no clear pattern of variation in utilization of processes-of-care observed across age, sex, and comorbidity, with the exception of health plan. Compared to other health plans, health maintenance organization plans were associated with less use of EKG, PFT, CT, PET, and bronchoscopy; more use of mediastinoscopy; and less repeat utilization (all $p < 0.001$).

Conclusions: Important processes-of-care relevant to lung cancer surgery are underutilized, and there is simultaneous evidence of potential overuse and untimely use. Widespread adoption of process-of-care measures such as ProvenCare™ Lung Cancer has the potential to dramatically change the delivery of lung cancer care, and hopefully improve patient outcomes.

USE AND ACCURACY OF DIAGNOSTIC IMAGING IN THE EVALUATION OF PEDIATRIC APPENDICITIS:
A REPORT FROM THE SCOAP-CERTAIN COLLABORATIVE

Kotagal M, Goldin A, Richards M, Acierno S, Weinsheimer R, Flum D

Background: There are concerns about the use of radiation-based imaging (computed tomography [CT]) in lieu of ultrasound (US) to diagnose appendicitis in children. Use of CT/US and factors associated with CT use remain to be determined and may be important in targeting quality improvement (QI) initiatives.

Methods: Washington State's Surgical Care and Outcomes Assessment Program (SCOAP) is a quality improvement initiative with detailed information about patients undergoing appendectomy. For patients ≤ 18 years old, we evaluated type and order of diagnostic imaging performed, patient clinical characteristics, type of hospital, and concordance between imaging results and pathology (2008-2012).

Results: Among 2538 children (mean age 11.3 years, 57.6% male), 99.7% underwent some pre-operative imaging. Over half (52.7%) of children had a CT scan as their first imaging study. After adjustment, age (OR 1.6 (95% CI 1.4-1.8) for 5-10 years; OR 2.9 (95% CI 2.2-4.0) for >10 years), Hispanic ethnicity (OR 1.7, 95% CI 1.5-1.9), and being overweight (OR 1.1, 95% CI 1.1-1.2) or obese (OR 1.7, 95% CI 1.4-2.1) were associated with having a CT scan as the first imaging study. Evaluation at a free-standing pediatric hospital was associated with significantly lower odds of having a CT scan (OR 0.36, 95% CI 0.35-0.37). Ultrasound concordance between imaging and pathology was significantly higher for males (72.3 vs. 66.4%, $p=.03$), for patients with perforated appendicitis (75.9 vs. 67.5%, $p=.009$), and at free-standing pediatric hospitals compared to general adult hospitals (77.3 vs. 62.2%, $p<.001$). CT use has decreased yearly statewide.

Conclusions: Statewide, over 50% of children with appendicitis undergo radiation-based imaging. Understanding patient and provider factors associated with CT use allows for better targeting of QI interventions to reduce radiation exposure for children. Pediatric hospitals may use more US because of greater awareness of the risks of CT, standardization of protocols in pediatric hospitals, and availability of high quality US services.

EPINEPHRINE INDUCES MONOCYTE MKP-1 AND NURR1 COUNTER-INFLAMMATORY MOLECULE EXPRESSION

Shubin N, O'Keefe G

Background: Post-traumatic immune-suppression is considered a major contributor to nosocomial infection and is responsible for a considerable proportion of the 200,000 annual sepsis-related deaths in the US. Circulating monocytes and tissue macrophages are thought to lose innate inflammatory function following severe trauma; however, the reasons for why this occurs are many and are incompletely understood. Following severe head trauma, circulating catecholamines are chronically induced 5-10 fold, lasting at least 2 weeks. Previously, it was demonstrated that catecholamines exhibit an anti-inflammatory effect on monocytes by decreasing pro-inflammatory cytokine secretion (e.g., IL-1 beta, IL-6, and TNF alpha). The direct mechanisms for this, however, have not been fully elucidated. Therefore, we hypothesized that the trauma-induced catecholamine, epinephrine, stimulates monocyte counter-inflammatory molecule expression, thus leading to decreased monocyte pro-inflammatory cytokine secretion.

Methods: A pilot study evaluating human primary monocyte genome-wide expression changes (Affymetrix U133 plus 2.0 arrays) following 30 minutes of epinephrine and/or LPS exposure (n=3 for each group) was conducted to broadly determine which counter-inflammatory molecules were induced. Additionally, THP-1 human monocyte cells were stimulated for 1h with epinephrine (10uM) and/or LPS (10ng/mL) to validate the mRNA expression changes determined in the genome-wide arrays.

Results: Following monocyte epinephrine stimulation, we observed a marked increase in MAP kinase phosphatase-1 (MKP-1) and NURR1 expression (27.3 and 28.2 fold-increase compared with non-stimulated cells, respectively). Additionally, following epinephrine and LPS dual exposure, MKP-1 and NURR1 expression levels were further induced (53.0 and 51.9 fold-increase compared with non-stimulated cells, respectively). These results were validated in THP-1 cells, whereby MKP-1 and NURR1 levels were significantly elevated following epinephrine and/or LPS exposure. Moreover, these MKP-1 and NURR1 expression increases coincided with significantly diminished TNF alpha expression levels following epinephrine and LPS exposure, when compared with LPS exposure alone.

Conclusions: In monocytes, MKP-1 dephosphorylates the MAP kinases, p38 and JNK, leading to diminished pro-inflammatory cytokine levels (e.g., TNF α and IL-1 β). Additionally, NURR1 is an orphan nuclear receptor that binds to and causes dissociation of DNA bound NF κ B, thus inhibiting the ability for NF κ B to upregulate pro-inflammatory cytokine expression. Together, these data suggest that epinephrine-induced MKP-1 and NURR1 expression suppresses monocyte pro-inflammatory cytokine expression following LPS stimulation; therefore, further suggesting that MKP-1 and NURR1 play a novel mechanistic role in trauma-induced monocyte suppression.

EARLY OUTCOMES WITH LYMPHATICOVENULAR ANASTOMOSIS: A SINGLE-CENTER STUDY

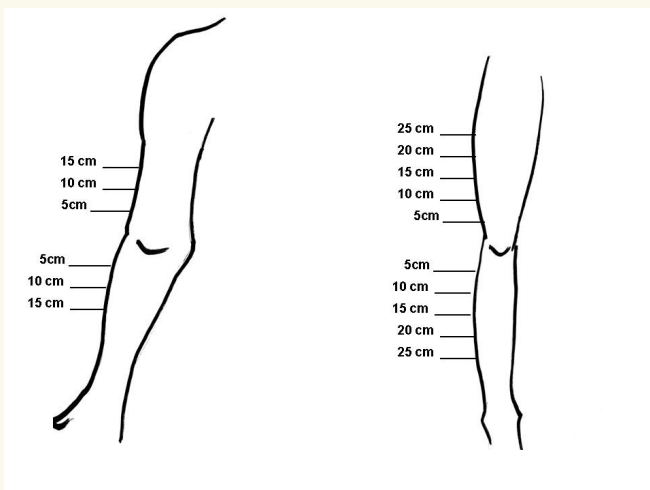
Peng S and Neligan PC

Background: Handley described the first reconstruction of lymphatic pathways in 1908. Sixty years later, the introduction of the operating microscope greatly advanced the surgical treatment of lymphedema. Now super-microsurgical lymphaticovenular anastomosis (LVA) is a common procedure in Asia. Here we present our early experience with LVA for both primary and secondary lymphedema.

Methods and Results: From April 2011 to May 2012, consecutive patient records were reviewed for etiology of lymphedema, pre- and postoperative compression, pre- and post-operative limb circumference, and patient satisfaction. Standardized limb measurements were obtained by a single observer (Figure 1). Intraoperative infrared lymphangiogram was used to identify lymphatic vessels in all patients. Lymphaticovenular anastomosis was performed end-to-end or end-to-side according to surgeon preference. Twenty-four patients (21 women, 3 men) were identified. One patient was lost to follow-up. Two patients were excluded from the outcomes analysis due to lack of adequate lymphatics. Therefore, data from 21 patients were analyzed, six of which had primary lymphedema. In total, 25 limbs received lymphaticovenular anastomoses, comprising nine upper extremities and 18 lower extremities. Follow-up period ranged from two weeks to 12 months. Eighteen of 26 patients reported satisfaction with their surgery, citing softer or lighter limbs. Average decrease in limb circumference was 2.0 cm. Nine of 19 (48%) patients decreased their need for compression, and three patients discarded compression completely. Subgroup analysis of primary lymphedema patients also revealed a net decrease of 2 cm. Within this subgroup, all patients required compression garments at follow-up.

Conclusions: Our experience suggests that lymphaticovenular anastomosis is a promising treatment modality for both primary and secondary lymphedema. One initial problem with primary lymphedema was inability to locate suitable lymphatics during surgery. As a result, patients who give a history of primary lymphedema are now referred for preoperative MR lymphangiogram to assess their likelihood of benefiting from LVA. This study is limited by small sample size, which will improve as patients are continuously enrolled. Another limitation is observer bias, since the operating surgeon performs all limb measurements. MRI volumetric assessments of the affected limbs will minimize this bias in the future. Finally, long-term outcomes data are needed. Other studies suggest that patients who respond early to LVA are likely to continue seeing improvement over the next several years. Although encouraging, this outcome remains to be seen in our patient population.

Figure 1. Limb measurements were obtained pre- and post-operatively at standardized locations.



ROUTINE SURVEILLANCE BLOOD CULTURES DURING ECMO DETECT CLINICALLY OCCULT BLOODSTREAM INFECTIONS

Meshher AL, Heath J, Smith J, Brogan TV, McMullan DM

Background: Primary bloodstream infections (BSI) within the critically ill pediatric and neonatal populations convey significantly increased morbidity, mortality, and associated healthcare costs. Patients requiring extracorporeal membrane oxygenation (ECMO) are at increased risk for primary bloodstream infection due to invasive vascular access. However artificial temperature regulation, inflammatory response to the circuit, and hematologic perturbations while on ECMO make traditional clinical indicators of sepsis difficult to interpret. The practice of surveillance blood cultures from the ECMO circuit has been employed, however this methodology is institutionally variable and anecdotal. At Seattle Children's Hospital our practice is to obtain routine surveillance blood cultures from the ECMO circuit every 48 hours.

Methods: A retrospective review was performed for all ECMO runs at Seattle Children's Hospital from 2007 to 2013 (n=251). Clinical microbiological records were queried to identify causal organisms and patients who had positive blood cultures a) remotely prior to initiation of ECMO, b) while on ECMO but also within 48h prior to initiation, c) *de novo* while on ECMO or within 48h of cessation of ECMO and d) while on ECMO but related to another infectious site. Infections were identified as EA-BSI if they met 2013 CDC/NHSN criteria. EA-BSI was classified as either unforeseen (therefore solely detected by routine blood culture) or suspected based on clinical scenario. Multivariate analysis was performed to identify clinical and patient specific risk factors to identify at-risk populations for ECMO-associated BSI.

Results: A total of 32/251 (12.7%) patients had at least one positive blood culture while on ECMO or within 48 after ECMO. Primary EA-BSI was identified in 46.8% (15/32) of patients with at least one positive blood culture, representing 6.0% (15/251) of all ECMO runs. 18.8% (6/32) of patients with a positive blood culture had only a single positive blood culture bottle with a commensal organism and were considered to represent a contaminant. 21.9% (7/32) of patients with a positive blood culture had a simultaneous infectious source. Antecedent infection prior to ECMO cannulation was identified in 12.5% (4/32). The most commonly identified organisms in primary EA-BSI were *S. marcescens* (3) and *E. faecalis* (3). Neither central chest cannulation nor historical bacteremia were associated with higher rate of BSI (p>.1) Review of the electronic medical record revealed *a priori* suspicion of infection in 7/15 cases of EA-BSI that resulted in a work-up that detected or confirmed bacteremia. However, 8/15 cases of EA-BSI appeared to be identified solely by routine surveillance blood cultures. Successful separation from ECMO occurred in 60% of patients with EA-BSI but overall survival to discharge was only 47%. 174 routine blood cultures (number needed to screen) were needed to identify one ECMO-BSI for which clinical suspicion did not exist at the time of diagnosis at a cost of \$44,000.

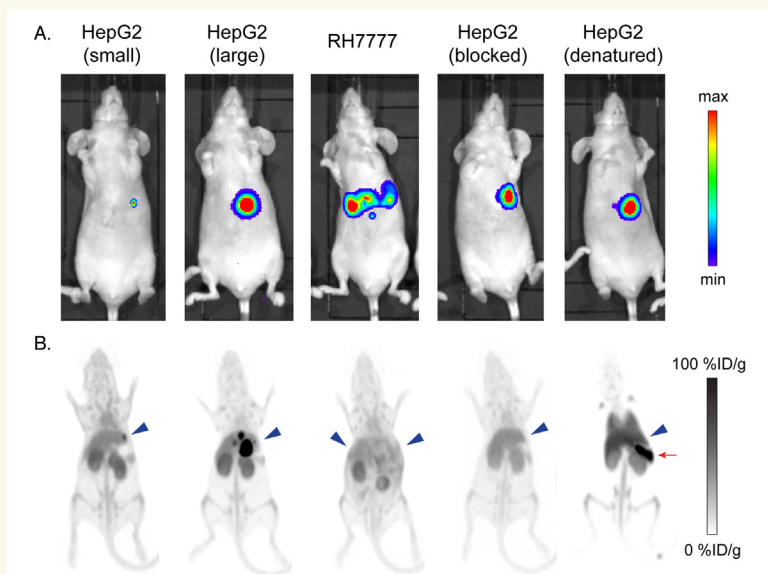
Conclusions: ECMO-associated bloodstream infection is a rare but significant complication of ECMO therapy with a rate of 6% at our institution from 2007-2013. Delay in appropriate antimicrobial therapy in sepsis is associated with worse mortality, underlying the importance of early diagnosis. Routine surveillance blood cultures identified 8 cases of EA-BSI (53%) in which treatment may have otherwise been delayed. Due to the unreliability of clinical markers inherent to the current state of ECMO therapy, surveillance blood cultures remain a viable tool in the early identification of blood stream infections but at a significant financial cost.

NOVEL ANTIBODY-TARGETED ZIRCONIUM-89 PET IMAGING OF HEPATOCELLULAR CARCINOMA

Sham J, Kievit F, Grierson J, Miyaoka R, Yeh M, Zhang M, Yeung R, Minoshima S, Park J

Background: Hepatocellular carcinoma (HCC) is a devastating malignancy in which imperfect imaging plays a primary role in diagnosis. Current limitations in CT/MRI technology hamper preoperative diagnostic accuracy and negatively impact patient outcomes. Glypican-3 (GPC3) is an HCC-specific cell surface proteoglycan over-expressed in the majority of HCCs. This study presents the first use of a Zirconium-89 (⁸⁹Zr) conjugated monoclonal antibody against GPC3 (α GPC3) for intrahepatic tumor localization using micro positron emission tomography (micro-PET).

Methods: Radioactive ⁸⁹Zr was conjugated to homegrown α GPC3 using the chelator p-isothiocyanatobenzyl-desferrioxamine. In vitro binding, in vivo biodistribution and micro-PET studies using this conjugate were performed in GPC3-expressing HepG2 and GPC3 non-expressing HLF cells and RH7777 orthotopic xenografts established in athymic nude mice. Tumor size was evaluated by histology.



(A) IVIS luminescent images prior to administration of ⁸⁹Zr- α GPC3. (B) Selected micro-PET images of the same animals showing tumor concordance. Blue arrowheads indicate tumor location, red arrow indicates spleen.

Results: ⁸⁹Zr- α GPC3 demonstrated highly sensitive antibody-dependent, antigen-specific tumor binding. HepG2 liver tumors exhibited high peak micro-PET signal (836.6 ± 86.5 %ID/g) compared with background liver (27.5 ± 1.6 %ID/g). Tumor-to-liver contrast ratio was high and peaked at 32.5 on day 3. Day 7 radioactivity was still substantial in HepG2 tumors (466.3 ± 87.5 %ID/g) compared with control RH7777 tumors (3.8 ± 1.2 %ID/g, $p < 0.01$) indicating antigen-specificity of ⁸⁹Zr- α GPC3. Animals treated with heat-denatured ⁸⁹Zr- α GPC3 or co-injected with an excess of unlabeled α GPC3 as a competition assay demonstrated markedly lower tumor uptake (3.9 ± 1.3 %ID/g, 29.0 ± 8.6 %ID/g, respectively) confirming antibody-dependency. The largest tumor measured 3.8 mm on histologic examination.

Conclusions: This study demonstrates the feasibility of utilizing a ⁸⁹Zr- α GPC3 PET imaging probe to visualize minute HCCs in the liver with high specificity. Clarifying the identity of indeterminate liver lesions found by conventional CT/MRI would enhance the accuracy of the surgeon's preoperative evaluation and therefore warrants further investigation for clinical translation.

DIFFERENCES IN THE GENOMIC SIGNATURE OF INFLAMMATORY CELLS IN SEVERELY INJURED TRAUMA PATIENTS

Plevin R, Delano MJ, Moldawer LL, Baker H, Lopez C, O'Keefe G, Maier RV, Cuschieri J

Background: An abnormal base deficit is an indicator of ongoing hypoperfusion, physiologic shock, and worse outcome in the trauma patient population. However, little is known about the genomic changes that result from periods of hypoperfusion. In this study, we sought to determine whether the degree of hypoperfusion, as identified by base deficit, correlates with different patterns of genomic alteration in the monocyte cell population of severely injured blunt trauma patients.

Methods: We performed a retrospective review of clinical and genomic data contained in the Inflammation and the Host Response to Injury multicenter trauma database. Inclusion criteria were blunt trauma patients with age ≥ 18 years who had a base deficit (BD) recorded within the first 12 hours of admission. Patients fitting these criteria were classified into 3 groups according to base deficit: 1) $BD \geq -6$; 2) $10 \leq BD < -6$; and 3) $BD < -10$, and a univariate analysis was performed to evaluate the effects of base deficit grouping on patient outcome measures. The genomic analysis was completed using Affymetrix Glue Grant Human Transcriptome (GG-H) Arrays™ obtained at 12 hours of admission and at 6 other standardized time points over the next 28 days in 244 trauma patients. The microarray data was normalized and a paired t-test was used to compare the probe set changes among base deficit groups at each time point. A pseudo-time ANOVA was incorporated by BRB Array™ tools to compare the genomic changes across all groups with time using a false discovery rate of 0.05%.

Results: Univariate analysis of severely injured blunt trauma patients revealed that worsening base deficit was associated with poor outcomes, including longer hospital and intensive care unit length of stay, higher rates of multisystem organ failure, and longer time to recovery from organ failure. Gene expression analysis identified 1173 probe sets that were differentially expressed between patients in the three base deficit groups at 12 hours post-injury. A time series analysis demonstrated 8190 probe sets whose expression significantly differed during the 28-day period. Of these, 477 probe sets differed significantly between the base deficit groups during this time period. Of these 477 probe sets, 177 fit into known pathways, including pathways related to cytokine & cell-cell signaling, metabolism, apoptosis, and cyclic adenosine monophosphate-mediated signaling.

Conclusions: It has previously been demonstrated that increasing base deficit is associated with worse outcomes in severely injured blunt trauma patients. In this study, we found that increasing base deficit is associated with an increased risk of organ failure and a longer time to recovery from organ dysfunction. The blood monocyte genomic expression signature also differs with the degree of hypoperfusion as measured by the initial base deficit value. These alterations in the genomic signature of cell mediators of inflammation may contribute to poor outcomes, although additional work will be necessary in order to identify potential causality.

ACGME CASE LOGS: CHANGING RATES OF MINIMALLY INVASIVE AND OPEN SURGERY ACROSS TWO DECADES OF RESIDENT TRAINING

Richards M, McAteer J, Drake M, Goldin A, Khandelwal S, Gow K

Background: Over the past two decades Minimally Invasive Surgery (MIS) has become increasingly common. Given this evolution in the skill set required of general surgeons, the rise of MIS has impacted resident training. Our objective was to evaluate changes in general surgery operative experience with regard to MIS.

Method: Review of Accreditation Council for Graduate Medical Education case logs from the time of the first MIS designation, academic year 1993-1994, through 2011-2012. Total MIS and associated open cases were analyzed over time. Data were combined into four blocks: Period I (AY1993-94 to AY1997-98), Period II (AY1998-1999 to AY2002-03) Period III (AY2003-04 to AY2007-08) and Period IV (AY2008-09 to AY2011-12).

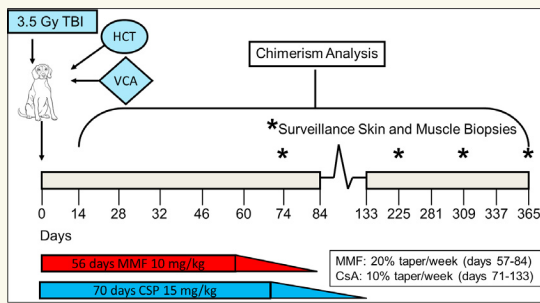
Results: The MIS approach has surpassed the open approach in multiple case categories including anti-reflux surgery, partial gastric resection, appendectomy and thoracic wedge resection (t -Test $p < 0.05$). Only for cholecystectomy was the MIS approach significantly more common than the open approach for the entire time period ($p < 0.05$). The open approach is still significantly more common for gastrostomy, vagotomy, enterolysis, enterectomy, ileostomy, abdominal exploration, common bile duct exploration, splenectomy, inguinal hernia repair and lobectomy/segmental resection of lung. Over the study period the percentage of MIS cases done by chief residents compared to junior residents decreased in nearly all case categories including adult and pediatric antireflux surgery, gastrostomy, partial gastric resection, enterectomy, ileostomy, appendectomy, abdominal exploration, cholecystectomy, common bile duct exploration, splenectomy, thoracic exploration, thoracoscopic wedge resection and lobectomy.

Conclusions: MIS has an important role in general surgery training; however, the open approach continues to be more common. Residents today must learn multiple approaches to the same procedures, which presents challenges to achieving competence in either approach.

ACHIEVING TOLERANCE IN A MISMATCHED VCA TRANSPLANT WHILE REDUCING THE RISK OF GVHD: THE GOAL OF TRANSIENT CHIMERISM

Swearingen B, Chang J, Butts T, Graves S, Storb R, and Mathes DW

Background: Transplantation of vascularized composite allografts (VCA) to reconstruct devastating facial injuries and lost extremities offer the opportunity to truly restore both form and function. Due to the necessity of life-long immunosuppression, the clinical application of these techniques is limited. One promising method of inducing tolerance to an organ allograft is the development of mixed chimerism. We have previously demonstrated that a non-myeloablative stem cell transplant can lead to tolerance in a mismatched dog model. However, the application of this protocol has been limited by graft-versus-host disease (GVHD). The hypothesis for this study was that our non-myeloablative hematopoietic stem cell transplant protocol could be used to induce tolerance to a recipient VCA without the need for persistent donor cell chimerism. To more closely mimic the clinical setting, our protocol was modified to an extended tapered cessation of immunosuppression.



Methods: Five haploidentical canine recipients (median weight and age were 12.1kg and 10.9 months) received a non-myeloablative conditioning regimen of 350 cGy TBI, mobilized donor stem cells (PBMC) and VCA transplantation followed by a short course of immunosuppression (MMF for 56 days and Cyclosporine for 70 days). Peripheral blood chimerism was evaluated by PCR techniques weekly. VCA rejection was followed clinically and confirmed histologically after routine biopsies. Three haploidentical canine recipients (median weight 13.3kg) were then transplanted following a modified immunosuppression protocol. Donor chimerism was evaluated as above.

Results: All 5 animals tolerated the conditioning regimen. One dog rejected the PBMC at 35 days post transplantation and went on to reject the VCA transplant following the cessation of immunosuppression (POD 84). One dog fully engrafted and converted to 100% donor chimerism and long-term tolerance to the VCA but developed GVHD. 3 dogs demonstrated a prolonged period of transient chimerism (7 to 10 weeks post-transplant) and went on to reject their donor stem cells after the cessation of immunosuppression without acute rejection of their donor VCAs. One of these dogs was euthanized for persistent fevers at post-operative day 147 with no sign of rejection. The remaining two had long-term acceptance of their VCA (>200 days) with no evidence of acute rejection. However, more recently both of these animals have demonstrated evidence of chronic rejection. No dog developed GVHD. In the modified protocol, all 3 animals tolerated the conditioning regimen. All dogs fully engrafted and converted to 100% donor chimerism and long-term tolerance to the VCA. One dog developed GVHD upon cessation of immunosuppression.

Conclusions: In this study we demonstrate that our non-myeloablative protocol allows for selective rejection of donor stem cells and elimination of GVHD risks without acute rejection of the VCA transplant and that persistent donor chimerism can lead to GVHD.

SHIFTS TOWARD PEDIATRIC SPECIALISTS IN THE CARE OF COMMON CHILDHOOD SURGICAL CONDITIONS: TRENDS AND OUTCOMES

McAteer J, LaRiviere C, Oldham K, Goldin A

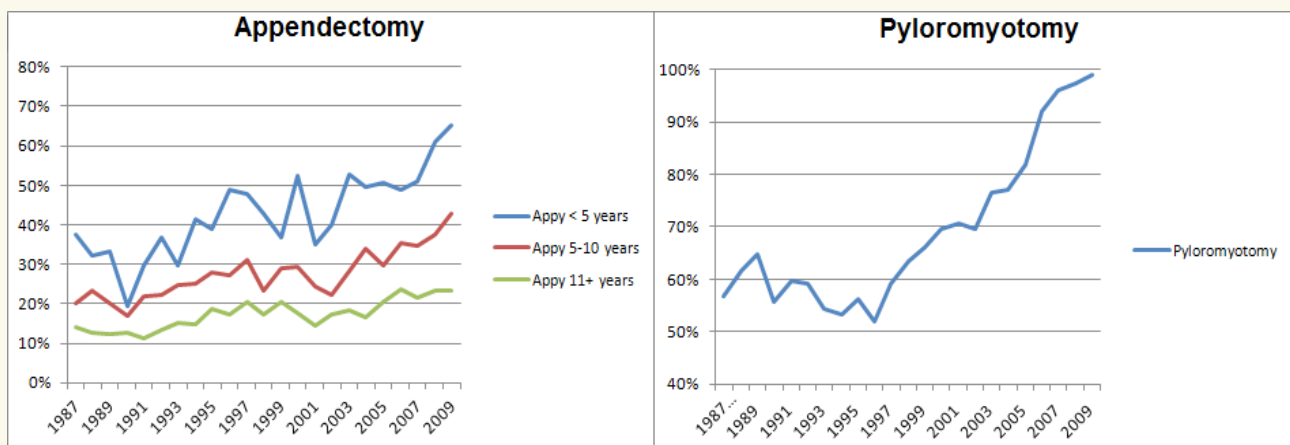
Background: Several position statements have urged referral of certain childhood surgical conditions to fellowship-trained pediatric surgeons, but it is unclear whether such changes have occurred. We hypothesized that an increasing proportion of common procedures are performed in pediatric hospitals over time, and that outcomes are superior at these centers.

Methods: We conducted a population-based retrospective cohort study using Washington State discharge records. All children ages 0-17 years undergoing non-incidental appendectomy (n=39,472) and pyloromyotomy (n=3,500) from 1987-2009 were included. Pediatric hospitals were defined as centers with full-time pediatric surgeons. Outcomes were examined for two time periods (1987-2000, 2001-2009). Logistic regression was used to adjust for confounding demographics, disease specifics, and comorbidities.

Results: Among appendectomy patients, children’s hospitals (compared to non-children’s) treated a greater proportion of patients under age 5 (8.9% vs. 3.3%), as well as children with perforation (31.6% vs. 25.4%) and comorbidities (6.5% vs. 3.6%). Children’s hospitals also treated a greater proportion of pyloromyotomy patients with comorbidities (6.5% vs. 1.8%). Over the study period, the percentage of procedures performed at children’s hospitals steadily increased. From 1987 to 2009, the percentage for appendectomies increased from 17% to 32%, and that for pyloromyotomies increased from 57% to 99% (Figure). For pyloromyotomy, care at a pediatric hospital was associated with a decreased risk of postoperative complications (OR=0.36, p<0.001) for both time periods. Appendectomy outcomes did not differ significantly in the early time period, but in the later time period specialist care was associated with a lower risk of complications in children <5 years of age (OR=0.54, p=0.03), and a lower risk of negative appendectomy in children <5 years (OR=0.51, p=0.02) and 5-10 years (OR=0.46, p=0.001).

Conclusions: There has been a shift towards pediatric hospitals for certain procedures, with a widening disparity in outcomes between pediatric and non-pediatric hospitals over time. These disparities are most pronounced in younger children. These results suggest that procedures in younger patients may best be performed by providers familiar with these patient populations.

Figure. Percentage of all procedures performed at children’s hospitals in Washington State, by year.



STANDARDIZATION OF A MULTIDISCIPLINARY CLINICAL PATHWAY IMPROVES OUTCOMES IN RUPTURED ABDOMINAL AORTIC ANEURYSMS

Garland BT, Desikan SK, Tran NT, Quiroga E, Singh N, Jacobs P,
Collier E, Roche A, Nandate K, Starnes BW

Objectives: While standardized protocols have been shown to improve safety in aviation and multidisciplinary care improves outcomes in oncologic surgery, a standardized multidisciplinary pathway for the treatment of ruptured abdominal aortic aneurysms (rAAA) has not yet been described. We aim to describe and evaluate a standardized clinical pathway for the care of rAAA.

Methods: Since 2002 our institution has managed an average of 30 rAAA per year. In 2007 we developed and initiated a multidisciplinary clinical pathway to aid in expediting care of patients with rAAA from initial presentation at the referring facility to definitive care. This pathway includes electronic publication of prehospital care protocols for referring providers as well as streamlined system for electronic transfer of outside imaging and records. We have initiated protocols for prehospital and transfer providers including guidelines for permissive hypotension as well as emergent patient registration, emergency department bypass and transfer directly to the operating room once the patient arrives at our institution. Circulating and scrub nurse protocols for education and OR preparation are in place, as well as anesthetic guidelines including delay of induction until proximal aortic control is achieved. Finally, the rEVAR procedure and post-operative transfer of care is outlined in detail to achieve optimal patient outcomes.

Results: Before initiation of the multidisciplinary pathway, 131 patients with rAAA presented between 2002 and 2007. 128 of these patients were treated with open surgical repair (OSR) with 30-day mortality rate of 57.8%. After initiation of our multidisciplinary clinical pathway, 118 patients presented with rAAA between July 2007 and February 2012. 100 were treated surgically, and 72 survived to discharge with an overall 30-day mortality of 28%. Subset analysis revealed 21 of 39 patients treated with OSR survived with 30-day mortality of 46% and 51 of 61 patients treated with EVAR survived with 30 day mortality of 16%.

Conclusions: RAAA remains a clinical challenge despite advances in pre, intra and postoperative care. While adherence to protocols across multiple sites and specialties can be difficult, standardization of a multidisciplinary clinical pathway from prehospital transfer through postoperative ICU care is associated with improved patient outcomes following open and endovascular repair of rAAA suggesting there is benefit beyond the “EVAR first protocol” to a standardized multidisciplinary pathway.

DERMAL FIBROBLASTS FROM DUROC AND YORKSHIRE PIGS DEMONSTRATE DIFFERENCES IN RESPONSE TO INJURY

Sood R, Muffley L, Ga M, Sirimahachaiyakul P, Hocking A, Gibran N

Background: Hypertrophic scarring occurs commonly after burns and is challenging to patients and physicians alike, as incomplete understanding of its pathogenesis has limited the development of effective therapies. Duroc pigs form thick, contracted scars after dermal wounding, in contrast to Yorkshire pigs, which heal normally. Dermal fibroblasts synthesize extracellular matrix and differentiate into contractile myofibroblasts and are thus key mediators of cutaneous wound healing. We tested the hypothesis that Duroc (DFs) and Yorkshire dermal fibroblasts (YFs) exhibit different fibroproliferative phenotypes in response to TGF- β 1.

Methods: DFs and YFs isolated from uninjured porcine skin were studied before passage 9. Contractility was assessed by collagen-gel contraction. Focal adhesions were measured via image analysis of vinculin and actin immunofluorescence. Gene expression was determined by real-time PCR.

Results: Untreated DFs contracted collagen more avidly than YFs at 48h (50% vs. 29%, $p = 0.003$). TGF- β 1 increased YF (39%, $p = 0.04$) but not DF (53%, $p = 0.31$) collagen contraction. DFs demonstrated a higher fraction of supermature ($\geq 6 \mu\text{m}$) focal adhesions compared to YFs (66% vs. 49%, $p = 0.01$), and TGF- β 1 increased YF (68%, $p = 0.01$) but not DF (66%, $p = 0.89$) supermature focal adhesions. DFs had higher baseline expression of myofibroblast markers alpha smooth muscle actin (α -SMA; $p = 1.6 \times 10^{-6}$) and type I collagen (COL1A1; $p = 7.4 \times 10^{-4}$) compared to YFs. TGF- β 1 induced α -SMA ($p = 0.003$) and COL1A1 ($p = 2.6 \times 10^{-6}$) expression in YFs but not in DFs ($p = 0.24$ and $p = 0.17$). Decorin expression was 25-fold lower in DFs compared to YFs ($p = 2.8 \times 10^{-6}$) and decreased in TGF- β 1-treated YFs ($p = 3.7 \times 10^{-4}$) but not DFs ($p = 0.42$). DFs had low expression of the anti-proliferative factor dickkopf 1 that did not respond to TGF- β 1 ($p = 0.26$); expression was higher in YFs ($p = 2.2 \times 10^{-4}$) and decreased with TGF- β 1 ($p = 1.3 \times 10^{-4}$).

Conclusions: Our data indicate that intrinsic differences in fibroblast responses to injury and TGF- β 1 responsiveness underlie the pathologic scarring in Duroc pigs. These findings parallel observations in human hypertrophic-scar fibroblasts and further validate the Duroc/Yorkshire model of fibroproliferative scarring.

CRANIECTOMY FOR BLUNT HEAD INJURY AND ASSOCIATED MORBIDITY AND MORTALITY TRENDS IN WASHINGTON STATE, 2000-2012

Flynn-O'Brien K, Shorter Z, Fawcett V, Rivara F, Davidson G,
Bulger E, Chestnut R, Vavilala M, Arbabi S

Background: In the United States, traumatic brain injury (TBI) is the leading cause of death due to injury and accounts for significant long term disability leading to lost productivity. In select cases of severe head injury, decompressive craniectomy is necessary to reduce morbidity and mortality. Recently, there has been a notable decline in neurosurgeons in Washington State. We undertook this study to determine if the changes in the provision of care in Washington State negatively affected morbidity and mortality in the injury-related TBI population.

Methods: All patients with a diagnosis of blunt head injury with intracranial pathology, who also met the Washington State Trauma Registry inclusion criteria between the years of 1995 and 2012, were evaluated as part of a state-based quality improvement (QI) project. Injury mechanism, operative and non-operative management, and morbidity and mortality trends were assessed.

Results: A total of 41,234 patients met inclusion criteria for this study, of which 12% underwent craniectomy. Over the study period, the incidence of craniectomy among blunt head injury patients declined from 36% to 9% per year in all patients, and from 38% to 11% in patients with head AIS 3-5. Overall, the relative risk of mortality decreased over the study period. The relative risk of mortality in patients with head AIS 3-5 decreased by 48% between 1995 and 2012 (adjusted MRR 0.52, 95% CI 0.43, 0.63). Modified functional independence measure (FIM) scores improved over the study period, as well. The relative risk of a discharge FIM score <12 in patients with head AIS 3-5 decreased by 9% between 1995 and 2012 (adjusted RR 0.91, 95% CI 0.85, 0.97).

Conclusions: Between 1995 and 2012, there has been a decline in the proportion of patients receiving craniectomies for blunt head injury in Washington State. Simultaneously, there has been a decline in mortality and improved functional outcome measures for both surgically and medically managed TBI patients. Therefore, the change in provision of care and neurosurgical capabilities has not negatively affected patient outcomes in Washington State. Further analyses must be completed to understand the relationship between management practices and improved mortality and morbidity in the injury-related TBI population.

APPY-RADS: A NOVEL APPENDICITIS REPORTING SYSTEM TO IMPROVE COMMUNICATION ABOUT UNCERTAINTY IN APPENDICITIS IMAGING

Simianu V, Drake F, Godwin B, Hippe D, Dighe M, Cuevas C, Bastawrous S, Bhargava P, Flum D

Background: Appendicitis remains a diagnostic challenge despite improvements in computed tomography. A standardized reporting system for appendicitis is needed to increase accuracy and improve communication about uncertainty in diagnosis.

Methods: We developed a standardized appendicitis reporting system including objective imaging findings common in appendicitis and certainty scale ranging from 1 (definitely not appendicitis) through 5 (definitely appendicitis). We identified 96 appendectomy patients between 2008 and 2012 with complete preoperative radiologic information and postoperative pathology. The imaging from these patients was reviewed using the new scoring system by four radiologists blinded to corresponding pathology. The presence of imaging findings and confidence scores were compared with final pathology.

Results: The appendix was visualized in 89 patients, of which 71 (80%) had pathology-positive appendicitis. Appendicitis was associated with appendiceal diameter (OR 14, >10mm vs. ≤6mm; p=0.002), periappendiceal fat stranding (OR 8.9; p<0.001), and appendiceal mucosal hyperenhancement (OR 8.7; p<0.001). In patients whose initial report was indeterminate (n=40), 30 (75%) had appendicitis. Radiologists assigned higher scores (4-5) in 22 (73%) patients and lower scores (1-2) in 4 (13%) patients with appendicitis whose initial report was indeterminate.

Conclusion: Both objective and subjective components of the new reporting scale performed well. Evaluation of the diagnostic performance characteristics of these metrics on a cohort of patients undergoing rule-out appendicitis imaging is currently underway.

Appy-RADS Objective Findings	N	Positive (N=71)	Negative (N=18)	OR (95% CI)	p*
Outer-outer wall diameter, mm	89				0.002
≤ 6 mm		8 (11)	6 (33)	(ref)	
6-10 mm		26 (37)	10 (56)	1.9 (0.5, 7.1)	
> 10 mm		37 (52)	2 (11)	14 (2.4, 82)	
Tip diameter, mm	89				0.007
≤ 6 mm		17 (24)	10 (56)	(ref)	
6-10 mm		37 (52)	8 (44)	2.7 (0.9, 8.1)	
> 10 mm		17 (24)	0 (0)	∞	
Muscoal hyper-enhancement†	82	51 (78)	5 (29)	8.7 (2.3, 36)	<0.001
Surrounding fat stranding	89	58 (82)	6 (33)	8.9 (2.5, 34)	<0.001
Periappendiceal air	89	5 (7)	0 (0)	∞	0.58
RLQ fluid/ /abscess	89	7 (10)	0 (0)	∞	0.34

NEUROCOGNITIVE OUTCOMES IN CHILDREN WITH INTESTINAL FAILURE

Chesley P, Sanchez S, Horslen S, Bennett F, Javid P

Background: Recent advances in medical and surgical management have led to improved survival in children with intestinal failure. Yet, these patients remain at high risk for long-term neurodevelopmental morbidity, and there are limited data on their cognitive outcomes. The aim of this study was to measure neurocognitive function in a cohort of children with intestinal failure.

Methods: Children actively enrolled in a regional intestinal failure program underwent prospective neurodevelopmental and psychometric evaluation using an objective scoring tool. Neurocognitive impairment was defined as a mental developmental index (MDI) < 70. Demographic, clinical, and nutritional variables were recorded after retrospective review of the medical record. Univariate analyses were performed using the Wilcoxon rank sum test. Data are presented as median (range).

Results: Twelve children with a remnant bowel length of 29 (10 - 85) cm were studied at 20 (12 - 67) months of age. This cohort had required intensive treatment including 12 (1 - 21) operations under general anesthesia and 118 (46 - 362) inpatient hospital days. Ten patients remained dependent on parenteral nutrition, and six subjects had received parenteral fish oil-based lipid emulsion. Nine (75%) subjects scored within the normal range on formal neurocognitive testing. Of the three children with cognitive impairment, one child with necrotizing enterocolitis was born at 26 weeks gestation and two children survived cardiac arrest secondary to sepsis and congenital heart disease. One additional subject with normal cognition was diagnosed with hearing impairment. On univariate analysis, neurocognitive impairment was associated with longer inpatient hospital duration and increased number of surgical procedures ($p < 0.05$).

Conclusions: Despite their inherent risk factors for neurodevelopmental morbidity, a majority of children with intestinal failure demonstrated normal cognitive outcomes using objective psychometric testing. Neurocognitive impairment was seen in three subjects with comorbidities separate from intestinal failure that are known to increase neurodevelopmental risk.

MONOCYTE GENOMIC SIGNATURE PERTUBATIONS IN SEVERELY INJURED TRAUMA PATIENTS CORRELATE WITH OUTPATIENT DISPOSITION AND INCREASED ONE YEAR MORTALITY

Delano MJ, Plevin R, Moldawer LL, Baker H, Lopez C,
Arbabi S, O'Keefe G, Maier RV, Cuschieri J

Background: Discharge disposition in severely injured trauma patients is associated with increased mortality up to a year after trauma injury and hospital discharge. Severely injured trauma patients able to return home immediately upon hospital discharge have an improved one year survival compared to those that require inpatient rehabilitation (Rehab) or skilled nursing facility (SNF) support. Patients that require SNF support carry an additional 13% mortality risk up to one year following hospital discharge due to sepsis. We sought to determine whether severely injured blunt trauma patient discharge disposition to home, Rehab, or SNF correlates with different patterns of genomic expression in peripheral blood monocytes prior to hospital discharge.

Methods: A review of the clinical and genomic data contained in the Inflammation and the Host Response to Injury multicenter trauma database was performed. Inclusion criteria were blunt trauma patients with age ≥ 18 years with disposition discharge data. Patients fitting the criteria were classified according to their discharge disposition as follows: 1) home; 2) Rehab; and 3) SNF. Univariate analysis was performed to evaluate the effects of discharge disposition on patient outcome measures. Peripheral blood genomic analysis was completed using Affymetrix Glue Grant Human Transcriptome (GG-H) Arrays™ obtained at 12 hours of admission and at 6 additional standardized time points over the next 28 days in 167 trauma patients. The microarray expression data was normalized across all subsets using Robust Multi-array Average™ (RMA) software. A paired t-test was used to compare probe set changes in each disposition group at each time point. A pseudo-time ANOVA was incorporated by BRB Array Tools™ version 4.2.1 to compare the genomic changes across all groups with time using a FDR of 0.05%.

Results: Univariate analysis of severely injured blunt trauma patients revealed that discharge disposition was associated with poor outcomes, including longer hospital and intensive care unit length of stay, higher rates of multisystem organ failure, longer time to recovery from organ failure, and increased one year mortality. Monocyte gene expression analysis 12 hours after trauma injury identified 76 probe sets that were significantly expressed between patients in the three discharge disposition groups. Many of the significant probe sets were related to histone function and protein transcription. A time series analysis demonstrated 9167 probe sets whose expression significantly differed with time during the 28-day period. Of these, 1058 probe sets differed significantly between the discharge disposition groups over time by the end of the 28 day period. Probe sets representing Th1 and Th2 cytokines, gene transcription, protein synthesis, histone compatibility, cell signaling and replication, interferon signaling, HLA recognition, and TLR signaling were among the various pathways identified.

Conclusions: We have demonstrated that blood monocyte genomic expression differs significantly at early and late time points in severely injured trauma patients and becomes more pronounced with time. Moreover, the genomic signature significantly varies between patients that are discharged home vs Rehab and SNF, and appears associated with an increased risk for infection. Thus, the early and late genomic signature patterns may serve as predictor and indicator of increased morbidity and mortality due to infection following discharge in severely injured trauma patients requiring discharge to SNF.

PATIENT DECISION-MAKING IN ACUTE APPENDICITIS: THE APPENDICITIS INTERVIEW PROJECT

Drake F, Castelli A, Kotagal M, Bilderback P, Jutric Z, Alfonso-Cristancho R, Evans, H, and Flum D

Background: Time from symptom onset to treatment affects prognosis in several acute conditions. Patient decision-making has been studied for MI and stroke, but there are no such studies for acute appendicitis. Clinical practice is based on the premise that timely presentation lowers perforation risk. Our objective was to identify themes in the pre-hospital decision-making of patients with appendicitis.

Methods: Twenty-five patients treated for appendicitis at 3 urban hospitals underwent open-ended ethnographic interviews structured into 3 segments: patient narrative, a series of open-ended questions, and specific questions regarding socio-economic and demographic characteristics. We employed content analysis methodologies to analyze interview transcripts (Atlas.ti software).

Results: 14 male and 11 female patients were interviewed. There was no pattern of delayed presentation among the 8 patients with perforation. Several themes emerged as factors in decision-making: an unusual experience of pain (location/character/severity), previous knowledge of appendicitis, information seeking, and confirmation seeking (especially in terms of advice or input from loved ones). Uninsured patients interviewed in this study did not report delaying decisions to seek care. For instance, one 30-year-old man with acquaintances who had died from perforated appendicitis stated:

“if you’re not treat[ed] right away on appendix...the appendix [is] going to burst, and...probably you’re going to die. ...I [was] afraid of money, billing, payment here. Finally, I compare money and life. Then I decide: I don’t care [if] they ask a million dollars.”

Conclusions: Content analysis identified several decision-making themes. Previous studies of socio-economic variables have attempted to *infer* decision-making behaviors from patient characteristics. Qualitative interviews allowed us to ask patients directly. A statewide quantitative survey of appendicitis patients is planned to follow-up this hypothesis-generating study.

OUTCOMES OF PATIENTS DISCHARGED TO SKILLED NURSING FACILITIES FOLLOWING ACUTE CARE HOSPITALIZATION

Hakkarainen T, Willis M, Arbabi S, Flum D

Background: Increasing numbers of older patients are being discharged to dedicated rehabilitation and skilled nursing facilities (SNFs) for post-acute care (PAC). Outcomes of patients discharged to SNFs may represent an opportunity for quality improvement. Little information is available to compare risk-adjusted outcomes between sites. The objective was to describe the features and outcomes of previously independent elderly patients discharged to a SNF, identify risk-factors associated with failure to discharge home and long-term mortality after discharge to a SNF.

Methods: Retrospective analysis of previously independent patients hospitalized for surgical, trauma, and non-trauma stroke diagnoses discharged to SNFs from 2007-2009 in the states of California, Florida, New York, Texas, and Washington. We assessed in-SNF and overall mortality using inpatient Medicare files and the National Death Index. Readmission and discharge to community were measured using a CMS-required Minimum Data Set. Logistic regression models were used to predict 1-year mortality, readmission, and successful discharge home.

Results: Of 416,997 patients admitted to a SNF after acute hospitalization, 3.8% died during the initial SNF stay, 28.6% were readmitted to the hospital, and 60.5% were discharged back the community. Among all patients discharged to SNF's 7.8% eventually died in a SNF and the overall 1-year mortality was 26.1%. The percentage of patients discharged back the community was 62% following surgery, 58.2% following trauma, and 49.6% following stroke. 50% of readmissions occurred in the first seven days. Of patients readmitted, the 1-year mortality was 48%. The most impactful risk factors associated with 1-year mortality were increasing age, male gender, increasing comorbidities, decreased cognitive function, decreased functional status, parental nutrition, and pressure ulcers. The same risk factors were found to be negatively predictive of discharge home from SNF.

Conclusion: Approximately 40% of patients discharged to SNF never return to the community with previously unknown risk factors increasing the risk of adverse outcomes. The predictive models developed in this analysis give care providers and families guidance about expected outcome after discharge to SNFs. It remains to be determined to what degree care delivery at the SNF contributes to these outcomes or the extent of outcome variability between SNFs. Further work to describe and assess care practices at SNFs and facility level variability in outcomes may be important in improving outcomes.

THE CLINICAL IMPACT OF HEPATITIS C-POSITIVE DONORS IN LIVER TRANSPLANTATION: PATIENT PROTECTION OR LOST OPPORTUNITIES?

Montenovo M, Hansen R, Reyes J, Dick A

Background: Liver disease caused by hepatitis C virus (HCV) is the main indication for orthotopic liver transplantation (OLT) in the United States. The high prevalence of HCV in the general population along with the significant shortage of organs, has resulted in an increased frequency of organ donors that are chronic carriers of the virus. The purpose of this study is to assess the clinical impact of HCV+ donors in patient and graft survival using the United Network for Organ Sharing (UNOS) database since the introduction of the MELD score.

Methods: We conducted a cohort study of LT recipients age 18 years or older from February 2002 through December 2012 utilizing UNOS data. We evaluated differences in patient characteristics between recipients of HCV+ vs. HCV- donor organs. We then compared patient and graft survival between these groups using the Kaplan-Meier estimator and multivariate stratified Cox regression models.

Results: We identified 59,899 LT recipients. Among those, 1,695 (2.8%) were HCV+ who received HCV+ grafts. HCV+ recipients of HCV- grafts were more likely to be hospitalized, in the ICU, on a ventilator, had higher MELD scores, and higher bilirubin. Patient and graft survival at 1, 5 and 10 years in HCV+ recipients was inferior to HCV- recipients, but HCV+ recipients who received HCV+ and HCV- grafts were equivalent (Figure 1). Multivariate regression revealed a number of variables associated with poor patient and graft survival (Table 1).

Figure 1. Graft and Patient Survival in HCV+ Recipients.

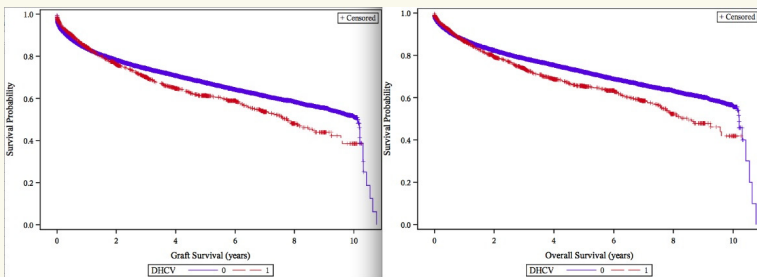


Table 1. Stratified Cox Proportional Hazards Regression Estimates for Graft and Overall Survival

Parameter	Overall Survival			Graft Survival		
	HR	95% CI	p-value	HR	95% CI	p-value
Recipient Characteristics						
HCV Serostatus	1.276	1.219 1.336	<0.0001	1.252	1.202 1.305	<0.0001
Age	1.015	1.013 1.017	<0.0001	1.006	1.004 1.008	<0.0001
Public insurance or uncompensated care	1.209	1.166 1.255	<0.0001	1.166	1.128 1.206	<0.0001
MELD score	1.007	1.002 1.012	0.0102	1.003	0.999 1.008	N.S.
On Dialysis at transplant	1.157	1.077 1.243	<0.0001	1.140	1.066 1.218	0.0001
In ICU prior to transplant	1.698	1.591 1.812	<0.0001	1.598	1.506 1.696	<0.0001
Inpatient prior to transplant	1.224	1.160 1.292	<0.0001	1.167	1.111 1.225	<0.0001
Donor Characteristics						
Cold ischemia time	1.010	1.006 1.015	<0.0001	1.012	1.008 1.016	<0.0001
Donor Risk Index	1.344	1.282 1.409	<0.0001	1.433	1.374 1.494	<0.0001

Conclusions: The use of HCV+ donors in HCV+ recipients does not have any impact in both overall patient and graft survival compared to HCV- donors. The sero-positivity status of the recipients is still an independent predictor of both patient and graft survival.

With the increase number of HCV+ recipients waiting for an organ in an era of significant organ shortage, more interest should be put of HCV+ donors who are very often disregarded due to concerns of long-term outcomes.

PULMONARY FUNCTION AFTER LAPAROSCOPIC ANTI-REFLUX SURGERY IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

Morrow E, Raghu G, Xiao K, Hinojosa M, Hayes J, Oelschlager B, Pellegrini C

Background: There is currently no effective medical therapy for Idiopathic Pulmonary Fibrosis (IPF). Increasing evidence associates IPF with Gastro-esophageal reflux disease (GERD). We hypothesized that patients with IPF would have decreased decline in pulmonary function after laparoscopic anti-reflux surgery (LARS), as measured by forced vital capacity (FVC).

Methods: We performed a retrospective review of surgical cases in a single institution. All patients who had a diagnosis of IPF (by CT or lung biopsy) and underwent LARS were included. Those who also underwent lung transplant without intervening PFTs were excluded. The study period was 09/1998 to 12/2012. Pulmonary function test, pH, and safety data were collected.

Results: 28 patients fit the inclusion criteria. There were no operative complications. There were two complications within 30 days: both dysphagia requiring readmission. There were no mortalities within 90 days of LARS. There were two reoperations: one patient was converted to a Dor at 3 months postoperative, and one redo Nissen was performed 12 years later. 23 patients had postoperative pH studies; all but two normalized. The mean DeMeester score dropped from 37 to 5 after LARS. The mean FVC increased from 2.69L to 2.79L from preop to postop. These tests were performed approximately 3 months preop and postop.

Conclusions: LARS can be performed safely in this high-risk patient population. Lung function stabilized after LARS in patients with IPF. LARS may be an effective treatment for IPF. Data from a randomized controlled clinical trial are needed to confirm these findings.

COMPARISON OF SYNTHETIC AND BIOLOGIC MESH IN VENTRAL HERNIA REPAIR USING COMPONENTS SEPARATION TECHNIQUE

Sandvall B, Suver D, Said H, Mathes D, Neligan P, Dellinger E, Louie O

Background: Ventral hernia repair (VHR) for large abdominal wall defects is challenging. Prior research established that the use of mesh is superior to suture closure alone and that components separation is an effective technique to combat loss of abdominal domain. Studies comparing components separation technique (CST) outcomes utilizing synthetic versus biologic mesh are limited.

Methods: A retrospective review was conducted of 72 consecutive patients who underwent VHR with CST between 2006 and 2010 at our institution. Surgeon preference and presence of contamination guided whether synthetic mesh (27 patients) or biologic mesh (45 patients) was used. Mean follow-up interval for all-comers was 13.9 months and similar in both groups ($p>0.05$).

Results: Degree of contamination and severity of pre-morbid medical conditions were significantly higher in the biologic mesh group, as reflected in the higher Ventral Hernia Working Group (VHWG) score (2.04 versus 2.86). Clinical outcomes, as measured by both minor and major complication rates and recurrence rates, were not significantly different ($p>0.05$). Minor complication rates were 26% in the synthetic group and 37% in the biologic group and major complication rates 15% in the synthetic group and 22% in the biologic group. There was one recurrence (4%) in the synthetic mesh group versus five (11%) in the biologic mesh group. Subset analysis of uncontaminated cases revealed recurrence rates of 4% in the synthetic mesh group and 6% in the biologic mesh group.

Conclusions: VHR using CST and either synthetic mesh or biologic mesh results in low recurrence rates with similar overall complication profiles, despite the higher average VHWG grading score in the biologic mesh group. Our results support the VHWG recommendation for biologic mesh utilization in higher VHWG grade patients. In VHWG grade 2 patients, our clinical outcomes were similar, supporting use of either type of mesh.

PREDICTORS OF COMPLICATIONS AND IMPLANT SALVAGE IN IMMEDIATE IMPLANT-BASED POST-MASTECTOMY BREAST RECONSTRUCTION

Sousa J, Prucz R, Neligan P, Said H, Louie O, Colohan S, Mathes D

Background: Immediate post-mastectomy implant-based breast reconstruction is an increasingly common and widely accepted method of breast reconstruction. Complication rates associated with this procedure have been reported in the literature, but few studies have examined salvage rates and predictors of implant loss or salvage. In addition, few studies have examined the therapeutic or prophylactic interventions that may allow for implant salvage.

Methods: A retrospective review of all consecutive immediate post-mastectomy tissue expander reconstructions between 2004 and 2012 was performed. We analyzed demographic data, breast cancer history and treatment, postoperative complications, and rates of implant salvage and explantation.

Results: Immediate post-mastectomy tissue expander reconstructions were performed for 407 breasts in 289 patients with a mean follow-up of 263 days. The overall complication rate was 27% (n=111) with epidermolysis of the mastectomy skin flaps and infection the most common complications (12.1% and 13.1% respectively). Smoking within 30 days of surgery, body mass index > 30, and nipple sparing mastectomy were predictors of a complication (p<0.05). The use of antibiotic irrigation, acellular dermal matrix, history of diabetes, or post-reconstruction radiation did not impact complication rates. Explantation occurred in 7% (n=29) of reconstructed breasts. For patients presenting with infection, seroma/hematoma, or delayed wound healing, 74% (n=82) of implants were salvaged. Infection requiring admission for intravenous (IV) antibiotics and mastectomy skin flap necrosis were the greatest predictors of failed salvage (p<0.04). Only 33% (n=7) of infections admitted for IV antibiotics were salvaged while 64% (n=14) of patients who did not warrant admission were salvaged with oral antibiotics (p=0.121). Patients who responded to IV antibiotics showed clinical improvement (i.e. recession of erythema) within 1.25 days of admission. Of the patients with implant exposure, 89% (n=8) were salvaged with delayed primary closure and antibiotics.

Conclusions: Smoking, obesity, and nipple sparing mastectomy continue to be predictors of higher complication rates in implant based breast reconstructions. When clinical judgment determines that a patient needs to be admitted for IV antibiotics, the rates of salvage are relatively low while outpatient treatment of less severe infections with oral antibiotics can be successful. Delayed primary closure of an exposed implant can be considered in the place of implant exchange or explantation.

THE GLOBAL BURDEN AND CHANGING EPIDEMIOLOGY OF EMERGENCY SURGERY

Stewart B, Khanduri P, McCord C, Ohene-Yeboah M, Uranues S, Vega Rivera F, Mock C

Background: Surgical disease is inadequately addressed globally. We reviewed the health burden from emergency surgical conditions.

Methods: Studies were included on the basis of their contribution to defining the burden of emergency surgical conditions (excluding trauma and obstetrics) and the status of capacity to address this burden.

Results: In 2010, there were 896,000 deaths, 20 million years of life lost, and 25 million disability adjusted life years from 11 emergency surgical conditions reported in the Global Burden of Disease Study. Mortality from these conditions was higher in high-income countries (HICs, 24 deaths per 100,000) than in low- and middle-income countries (LMICs, 11 deaths per 100,000); but because of their higher populations, 70% of deaths occur in LMICs. The higher rate in HICs was due primarily to higher rates of vascular-related disorders. However, deaths from vascular disease in LMICs rose from 15% of all surgical emergency-related deaths in LMICs in 1990 to 25% in 2010. Capacity to address this burden is sub-optimal, especially in LMICs. Some HICs have more than 14 operating theatres per 100,000, compared to less than 1 in many LMICs.

Conclusions: The above are bare minimum estimates, but indicate a tremendous health burden from conditions requiring emergency general surgery. Most of this burden is in LMICs, where the pattern of surgical disease is changing and capacity to deal with the problem is woefully inadequate. These data will be useful for both the surgical and public health communities to plan a more targeted response.

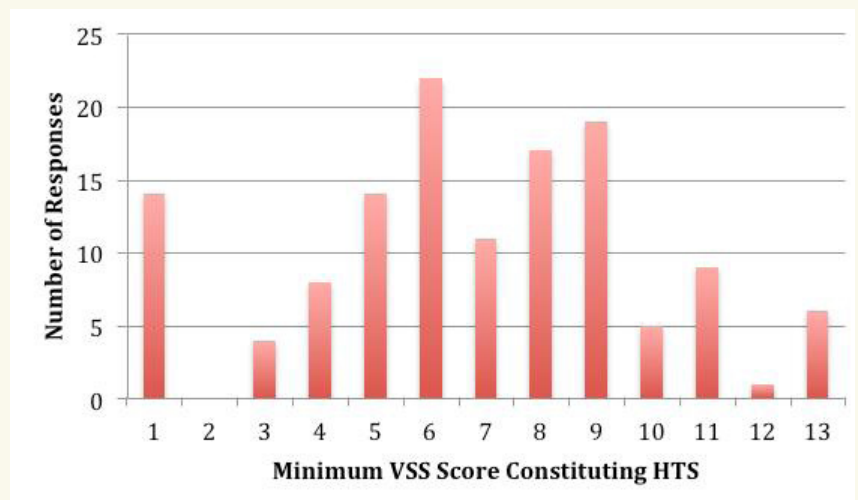
WHAT VANCOUVER SCAR SCALE SCORE CONSTITUTES A HYPERTROPHIC SCAR? RESULTS FROM A SURVEY OF AMERICAN BURN CARE PROVIDERS

Thompson CM, Sood RF, Honari S, Carrouger GJ, Gibran N

Background: What constitutes a hypertrophic scar (HTS) and how a scar evolves can challenge clinicians and researchers. The Vancouver Scar Scale (VSS) was introduced in 1990 and has been widely described in the literature. To date, no study has asked burn care providers to correlate a score on this scale with a clinical diagnosis of HTS.

Methods: An anonymous online survey was sent to one thousand burn care providers and researchers across North America. Among other questions, respondents were asked “What score on the VSS constitutes HTS?” They were also shown photos & asked if they believed the scar was hypertrophic; they were separately asked to give the scar a VSS score. Data were analyzed using Stata 13.

Results: We had 130 respondents (13%) several respondents felt that they were not able to adequately assess pliability by photographs and abstained from completing the survey. The low response rate is not unexpected since many recipients may be involved in early patient management and may not be comfortable with scar assessment. Most respondents were physicians (43.9%) and most had worked in burn care for over 10 years (63.1%). Most did not use the VSS in clinical practice (58.5%). The median response to the question of “What total score on the VSS constitutes HTS?” was 7; responses demonstrated significant variation (Figure). There was no statistical difference in median response when respondents were classified by job title, years in burn care, or use of VSS in practice ($p=0.36, 0.66, 0.31$). When asked specifically whether the each of the scar examples was hypertrophic, the response of “yes” correlated with median scores of 8, 8, & 10 for 3 photos and “no” corresponded scores with 3 & 4 for 2 photos (Table).



	Scar 1	Scar 2	Scar 3	Scar 4	Scar 5
Does this constitute a HTS? (% Yes)	97.7	98.5	3.8	82.3	16.2
Total VSS (mean±SD)	8.4±1.5	9.9±1.5	2.7±1.3	7.6±2	3.7±1.5
Pigmentation (mean±SD)	1.3±0.8	1.6±0.7	1±0.3	2±0.2	1.4±0.8
Pliability (mean±SD)	3.1±0.6	3.7±0.7	0.7±0.8	2.4±0.8	1±0.8
Height (mean±SD)	2.3±0.6	2.5±0.6	0.1±0.4	1.4±0.6	0.3±0.5
Vascularity (mean±SD)	1.5±0.6	2.1±0.5	0.8±0.5	1.8±1.4	1±0.4

Conclusions: Our survey suggests that the VSS is not widely used by burn clinicians and that even among those that use the scale there is wide variation in perceptions of what constitutes a HTS. This study illustrates the need for an objective tool to characterize scars to standardize HTS definition for clinical and research purposes, which could lead to a robust and descriptive multi-center database of burn scars.

Posters—Honorable Mention

SMOOTH MUSCLE CELLS FROM ABDOMINAL AORTIC ANEURYSMS ARE UNIQUE AND CAN INDEPENDENTLY AND SYNERGISTICALLY DEGRADE INSOLUBLE ELASTIN

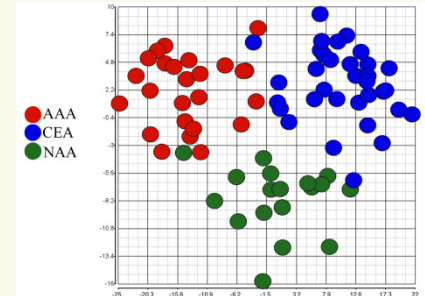
Airhart N, Brownstein B, Cobb P, Scheirding W, Arif B, Curci J

Background: The purpose of this study was to further elucidate the role of the vascular smooth muscle cell (SMC) in abdominal aortic aneurysm (AAA) disease. We hypothesized that AAA-SMC are unique and actively participate in the process of degrading the aortic matrix.

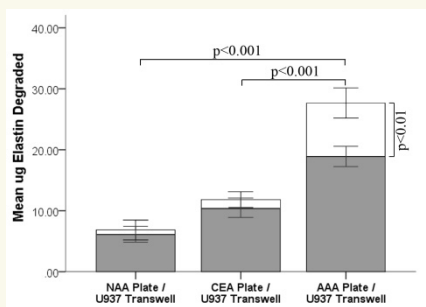
Methods and Results: Whole-genome expression profiles of SMC from AAA, normal abdominal aorta (NAA) and carotid endarterectomy (CEA) were compared. We quantified elastolytic activity by culturing SMC in [³H]elastin-coated plates and measuring solubilized tritium in the media after 7 days. MMP-2 and MMP-9 production was assessed using real-time PCR, zymography and western blotting. Each SMC type exhibited a unique gene expression pattern. AAA-SMC had greater elastolytic activity than NAA (+68%, $p < 0.001$) and CEA-SMC (+45%, $p < 0.001$). Zymography showed an increase of active-MMP-2 (62kD) in media from AAA-SMC. AAA-SMC demonstrated 2-fold greater expression of MMP-2 mRNA ($p < 0.05$) and 7.3-fold greater MMP-9 expression ($p < 0.01$) than NAA-SMC. Culture with U937 monocytes caused a synergistic increase of elastolysis by AAA-SMC (41%, $p < 0.001$) but not NAA or CEA ($p = 0.99$). Co-culture with U937 caused a large increase in MMP-9 mRNA in AAA and NAA-SMC ($p < 0.001$). MMP-2 mRNA expression was not affected. Western blots of culture media showed a 4-fold increase of MMP-9 (92kD) protein in AAA-SMC/U937 compared to NAA-SMC/U937 ($p < 0.001$) and a large increase in active-MMP2 (62kD) which was less apparent in NAA/U937 media ($p < 0.01$).

Conclusions: This study provides evidence that SMC play a direct role in the degradation of the aorta in AAA. AAA-SMC have a unique gene expression profile and a pro-elastolytic phenotype that is augmented by macrophages. This may occur via a failure of post-transcriptional control of MMP-9 synthesis.

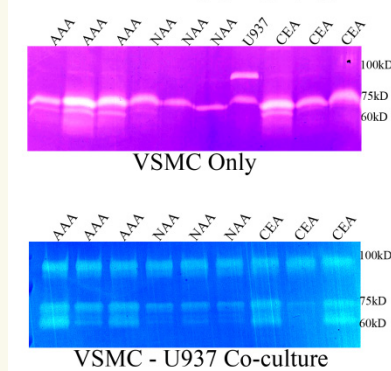
Principal component analysis of SMC Gene Expression



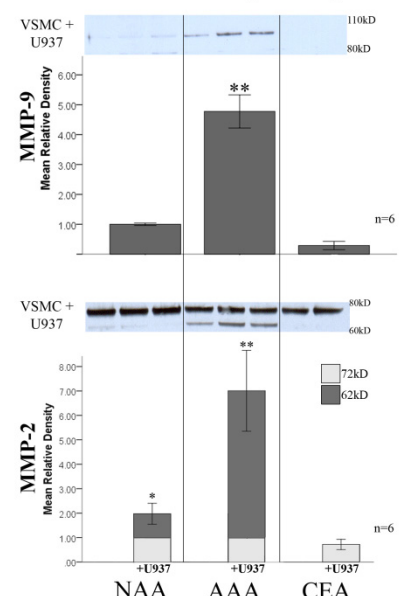
Elastolytic Assay



MMP Protein (Zymography)



MMP Protein (Western)



LECTURE HALLS IN THE 21ST CENTURY:
QUANTITATIVELY EXAMINING THE USE OF TECHNOLOGY IN THE MEDICAL SCHOOL CLASSROOM

Hansen J, Bartek M, Gagliardi S, Fischer M, Richards B

Background: Medical education faces the difficult decision of how to best utilize technology. The spectrum of educator and student response to technology in the classroom exemplifies the uncertain laptop culture within medical education. Medical schools are basing their technologic educational decisions on external perceptions, personal preference or anecdotal evidence. Despite this heterogeneity, there is a lack of research that addresses how medical students are using technology in the lecture hall. There is a need for evidence-based decisions regarding technology in medical education.

Objectives: This study examines 1) In a second year medical school lecture, what proportion of students are engaged in activities which enhance, rather than distract, from the achievement of classroom learning objectives? and 2) What lecture characteristics are associated with how the student or educator use technology in an educational environment and how can this resource be best utilized to achieve classroom learning objectives?

Methods: This study utilizes a prospective observational study design. Data was gathered from second year medical students at Columbia University for one month. Observations used a standardized, published medical educational observation tool (STROBE). The observational data captured use of student's electronic screens in a random snapshot manner at five specific time points during the lecture. Multiple lecture characteristics were also recorded.

Results: Observational data was categorized into "enhancing" or "distracting" from learning objectives. Frequencies of those who engage in "enhancing" versus "distracting" technologic use were calculated. Multi-Survey data will correlate with observational data on what factors shape student's technology behavior during lecture. Between 75 and 80% of the time, students were using technology for "enhancing" activities.

Conclusions: This study was the first to explore medical student's use of technology in a quantitative manner. It will inform future decisions on how to best utilize technology to enhance medical learning. Inferring that the screen is representative of a medical student's thoughts requires appropriate interpretation of study results.

SPASTIC MOTILITY DISORDERS OF THE ESOPHAGUS: CAUSE OR EFFECT?

Oscar M. Crespin, MD, Roger P. Tatum, MD, Mutlu Sahin, MD, Kagan Coskun, MD, Ana V. Martin MD,
Andrew Wright MD, Brant K. Oelschlager, MD, Carlos A. Pellegrini, MD

Background: Esophageal manometry, performed as part of the diagnostic work-up in patients with foregut symptoms, occasionally reveals abnormalities suggestive of a spastic motility disorder (Nutcracker esophagus (NE), distal esophageal spasm (DES), or hypertensive lower esophageal sphincter (HTLES)). Some of these patients have, in addition, abnormal esophageal acid exposure. To what extent the motility disorder or the acid reflux are responsible for the symptoms remains controversial. The aims of this study were to characterize the presenting symptoms, the presence of reflux, and the effect of Laparoscopic Nissen fundoplication (LNF) on symptoms, on reflux and on the motor function of the esophagus in this group of patients.

Methods: Analysis of 3400 high-resolution manometry studies performed between 2007 and 2013 in our laboratory yielded 221 patients with spastic esophageal motility disorders. The records of these patients were examined to define the manometric abnormality, to characterize symptoms and to measure esophageal acid exposure. A subset of these patients with spastic motility, reflux related symptoms and abnormal pH studies who underwent Nissen fundoplication and had postoperative physiologic testing were evaluated to determine changes in symptoms, esophageal acid exposure, and motility parameters.

Results: Seventy-nine of the 221 patients had NE, 30 patients had DES, and 112 patients had HTLES. The most frequent symptoms (both primary and secondary) among all patients were: heartburn and/or regurgitation, 69.2%; respiratory, 39.8%; dysphagia, 35.7%; and chest pain, 22.6%. Of the 221 patients, 192 had 24 hour pH monitoring and in 103 the esophageal acid exposure was abnormal. Sixty-two percent of those suffering from heartburn and regurgitation had abnormal 24-hour pH monitoring. By contrast, this was the case in 49% of patients with respiratory symptoms, 36.8% of patients with dysphagia, and 32.6% of patients with chest pain. Sixty-six of the 103 patients with abnormal 24 h pH results underwent a fundoplication. Thirty-eight (15 NE, 6 DES, and 17 HTLES) of these 66 patients had a minimum of 6 month follow up and postoperative evaluation of esophageal function. Symptoms resolved in 28 and improved in 10 of the 38 patients. Six patients (3 with NE and 3 with HTLES) had manometry post LNF. All showed improvement in motility parameters with normalization in 5 of them. All (38) patients had normal acid exposure postoperatively.

Conclusions: Typical reflux symptoms are common among patients with all 3 spastic motility disorders. The majority of patients with typical reflux symptoms and almost half of the patients with respiratory symptoms in all 3 disorders also have abnormal 24-hour pH monitoring, whereas the majority of patients with dysphagia or chest pain do not. It also appears that, in patients who have GERD, motility patterns improve after LNF. Fundoplication in those patients exhibiting abnormal acid exposure suggests that it is the abnormal acid exposure and not the spastic motility disorder itself that produces the symptoms.

CRM1 AND BRAF INHIBITION SYNERGIZE AND INDUCE TUMOR REGRESSION
IN BRAF-MUTANT MELANOMA

Salas Fragomeni RA, Chung HW, Landesman Y, Senapedis W, Saint-Martin JR,
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Background: Resistance to BRAF inhibitor therapy places priority on developing BRAF inhibitor-based combinations that will overcome *de novo* resistance and prevent the emergence of acquired mechanisms of resistance. The CRM1 receptor mediates the nuclear export of critical proteins required for melanoma proliferation, survival, and drug resistance. We hypothesize that by inhibiting CRM1-mediated nuclear export, we will alter the function of these proteins resulting in decreased melanoma viability and enhanced BRAF inhibitor antitumoral effects.

Methods: To test our hypothesis, selective inhibitors of nuclear export (SINE) analogs KPT-185, KPT-251, KPT-276, and KPT-330 were used to induce CRM1 inhibition. Analogs PLX-4720 and PLX-4032 were used as BRAF inhibitors. Compounds were tested in xenograft and *in vitro* melanoma models.

Results: *In vitro*, we found CRM1 inhibition decreases melanoma cell proliferation independent of BRAF mutation status and synergistically enhances the effects of BRAF inhibition on BRAF-mutant melanoma by promoting cell-cycle arrest and apoptosis. In melanoma xenograft models, CRM1 inhibition reduces tumor growth independent of BRAF or NRAS status and induces complete regression of BRAF V600E tumors when combined with BRAF inhibition. Mechanistic studies show that CRM1 inhibition was associated with p53 stabilization and retinoblastoma protein (pRb) and survivin modulation. Furthermore, we found that BRAF inhibition abrogates extracellular signal-regulated kinase phosphorylation associated with CRM1 inhibition, which may contribute to the synergy of the combination.

Conclusions: CRM1 inhibition impairs melanoma survival in both BRAF-mutant and wild-type melanoma. The combination of CRM1 and BRAF inhibition synergizes and induces melanoma regression in BRAF-mutant melanoma.

OUTCOMES OF PEDIATRIC MITRAL VALVE REPLACEMENT WITH EXTREMELY SMALL PROSTHESES

Hermesen J, Permut C, Chen J, Mesher A, McMullan D

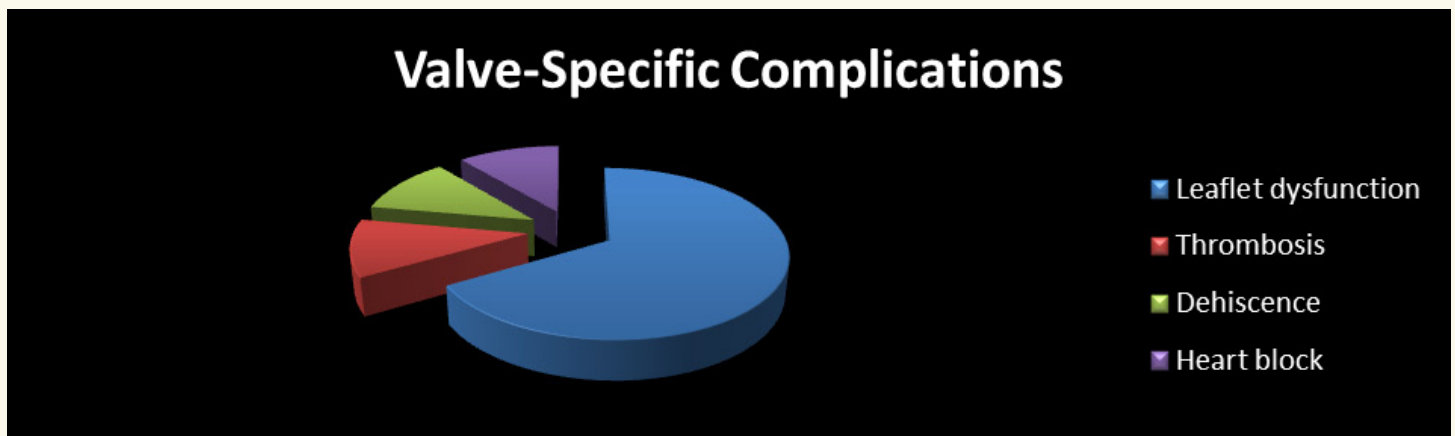
Background: Pediatric mitral valve replacement (MVR) is rare and usually demands a mechanical prosthesis to optimize hemodynamics and prevent left ventricular outflow tract obstruction. Little is published about outcomes following MVR with extremely small (<20mm) valves.

Methods: Patients were identified by Seattle Children's hospital implant records from 1993-2013. Clinical variables were gathered via review of charts and the Society of Thoracic Surgeons congenital database. All valves were inserted using cardiopulmonary bypass and cardioplegic arrest. Post-operatively patients were started on a heparin infusion within 24 hours and transitioned to warfarin with INR goal 2.5-3.5.

Results: Twenty prosthetic valves (17 mechanical, 3 bioprosthetic) were inserted into thirteen patients. Average age and weight at operation were 1.2 years and 7.6 kg, respectively. Six patients had undergone mitral valve repair prior to replacement.

There was 14% mortality, 60% morbidity with a valve specific complication rate of 45%. The most common complication was valve thrombosis causing impaired leaflet motion and requiring emergent re-replacement. Two patients required post-operative extracorporeal membrane oxygenation support. Both suffered impaired leaflet motion and did not survive to hospital discharge.

Other complications included bioprosthetic valve thrombosis requiring thrombolysis, valve dehiscence, complete heart block, re-operation for bleeding (2) and intracranial hemorrhage.



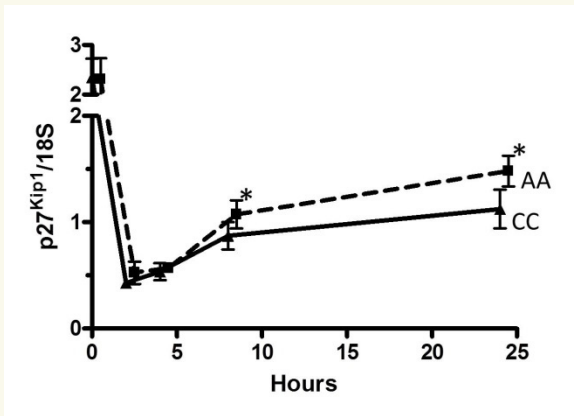
Conclusions: Infant mitral valve replacement is high risk and valve-specific complications are frequent. Anticoagulation regimens based on adult patients may be inadequate for valve sizes less than 20mm. Patients requiring extracorporeal membrane oxygenation support following mechanical mitral valve replacement appear to have an especially poor prognosis.

THE P27^{Kip1} -838 C>A SINGLE NUCLEOTIDE POLYMORPHISM ASSOCIATED WITH VEIN GRAFT STENOSIS: EFFECT ON P27^{Kip1} TRANSCRIPTION IN SAPHENOUS VEIN ADVENTITIAL FIBROBLASTS

Kikuchi S, Kenagy R, Chen L, Sobel M, Clowes A

Background: We have previously demonstrated that a single nucleotide polymorphism (SNP) in the promoter of the p27^{Kip1} gene, a cell cycle cyclin-dependent kinase inhibitor, is associated with vein graft performance. The primary patency of leg bypass grafts in patients with the p27^{Kip1} -838AA genotype is much better than in patients with the -838AC or CC genotype. In addition, a 1000 base pair p27^{Kip1} promoter-luciferase construct with -838A shows two fold higher promoter activity in saphenous vein fibroblasts compared to one with -838C. Therefore, we hypothesized that the AA genotype maintains graft patency by increasing p27^{Kip1} expression and inhibiting cell proliferation. The purpose of this study was to determine whether the p27^{Kip1} -838 genotype affects the transcription of p27^{Kip1} in vein wall fibroblasts from patients undergoing infrainguinal vein bypass grafting. Further, we tested the effect of knocking down p27^{Kip1} mRNA using siRNA to determine the effect on proliferation of these cells.

Methods: Passage 5 saphenous vein adventitial fibroblasts with the p27^{Kip1}-838AA genotype (AA) and with the -838CC (CC) genotype (4 AA lines and 5 CC lines) were made quiescent in serum-free medium for 48hrs. Cells were then stimulated with PDGF-BB (10ng/ml) for 2, 4, 8, and 24 hours and the level of p27^{Kip1} mRNA was measured using real-time PCR. Gene knockdown was accomplished using electroporation with either p27^{Kip1} specific siRNA or a scrambled control. Cells recovered overnight in 5% serum, and then were placed in 2% serum ± 10 ng/ml PDGF-BB. Cells were counted at day 1 and 4.



Results: Levels of p27^{Kip1} mRNA were the same in the growth arrested AA and CC cell lines and decreased about 80% in both cell types 2 hours after PDGF-BB treatment (Figure). However, p27^{Kip1} mRNA was re-expressed faster in the AA cells compared to CC cells such that by 8 and 24 hours there was ~30% and ~40% (P<.05) higher levels of p27 mRNA, respectively, in the AA cells. Treatment of fibroblasts with p27 siRNA decreased mRNA levels by 68±20%, which led to the stimulation of cell proliferation by 84±21% at day 4 (3 experiments; P<.05).

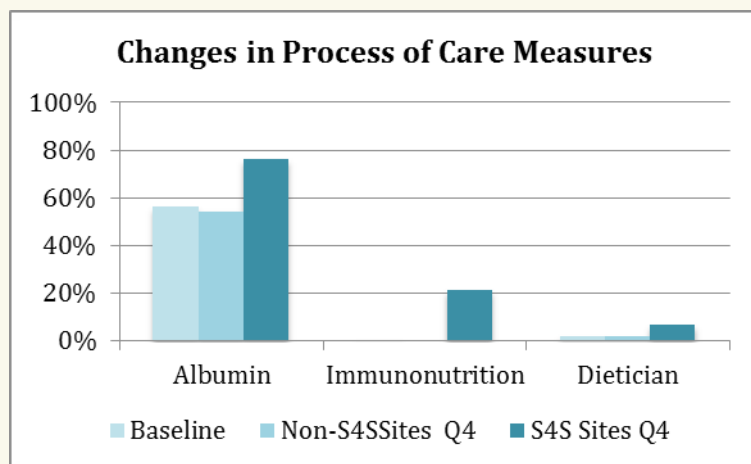
Conclusions: The p27^{Kip1}-838C>A SNP modulated the re-expression of p27^{Kip1} mRNA after down-regulation mediated by PDGF-BB. These results indicate that the p27^{Kip1}-838AA genotype maintains higher levels of p27^{Kip1} mRNA after growth stimulation than the CC genotype, and thus, may inhibit proliferation of saphenous vein adventitial fibroblasts after vascular injury. Knockdown of p27 verified the role of p27 as a growth inhibitor in these fibroblasts. Future experiments will determine rates of cell proliferation as a function of p27^{Kip1} -838C>A genotype.

THE STRONG FOR SURGERY INITIATIVE: IMPLEMENTATION OF THE NUTRITION CHECKLIST

Kling C, Varghese T, Fichera A, Thirlby R, Horton M, Johnson M, O’Keefe G, Farrokhi E, Javelli D, Kirk B, Devlin A, Klamp W, Flum D for the Strong for Surgery – CERTAIN Collaborative

Background: Interventions to address malnutrition and use of immunonutrition has been associated with lower surgical complication rates. CERTAIN, Washington State’s learning healthcare system, has launched a novel statewide surgical public health campaign – Strong for Surgery (S4S) – that brings checklists to clinics utilizing evidence-based practices aimed at optimizing a patient’s health prior to elective surgery. We aim to describe the baseline levels of nutrition process of care measures and determine if implementation of the S4S nutrition checklist can change practice patterns.

Methods: The Surgical Care and Outcomes Assessment Program (SCOAP), a benchmarking and QI program in 55 hospitals in Washington State, provided baseline data on albumin screening, dietician referral and immunosupplement use in patients undergoing elective colorectal resections. The S4S program was implemented in a convenience sample of colorectal surgery clinics over a 12-month period. The S4S nutrition checklist directs clinicians to 1) screen for malnutrition and make appropriate dietician referrals, 2) prescribe immunonutrition, 3) measure serum albumin levels. SCOAP data was used to collect process of care measures at 3-month intervals. Categorical variables were compared using chi-square tests and logistic regression was used to examine the association between S4S site status and process of care measures.



Results: In 12 months, S4S grew from 1 clinic, 1 surgeon to 6 clinics, 8 surgeons. Washington State elective colectomy patients enrolled at S4S hospitals increased from 56 (7.3%) of a total 772 in Q1, to 207 (31.1%) of a total 666 in Q4. The prevalence of albumin screening, immunonutrition use and dietician referrals all increased significantly from baseline to Q4 at S4S sites (56.3% to 76.3% for albumin, 0.2% to 21.3% for immunonutrition and 1.9% to 6.8% for dietician referral, all $p < 0.0001$) but remained unchanged at non-S4S sites (54.5%, 0% and 2% respectively, all $p > 0.05$). Being a S4S site was significantly associated with a patient receiving immunonutrition (OR 36.7, 95% CI 19.8, 68.0), seeing a dietitian (OR 4.73, 95% CI 3.0, 7.5) and measuring albumin (OR 2.6, 95% CI 2.0, 3.3). Q4 checklist compliance varied widely by site, from 18.8% to 66.7%.

Conclusions: Introduction of S4S checklist in preoperative clinics led to rapid uptake of evidence-based nutritional interventions within a 12-month period. Wide deployment of the S4S nutritional checklist is expected to reduce risk and improve outcomes.

DISSEMINATION OF TRAUMA QUALITY IMPROVEMENT PROGRAMS IN LATIN AMERICA

LaGrone L, Mock C

Background: Latin America experiences an annual trauma incidence of 163/100,000; over 60% higher than the world average. Trauma outcomes in this region are consistently worse than global averages.

A portion of the excess mortality attributable to trauma in Latin America may be secondary to particularly low implementation of QI programs. The Panamerican Trauma Society (PTS) has responded to the relatively high prevalence and mortality of trauma in the region by translating the WHO *pamphlet Guidelines for Trauma Quality Improvement Programmes* and calling for universal implementation.

Methods: The proposed project will evaluate the feasibility and effectiveness of a strategy to disseminate trauma QI programs in Latin American countries. A baseline assessment of existing QI methods, including morbidity and mortality conferences, use of trauma registries, and established institutional mode of addressing QI issues will be conducted.

Urban, rural, and academic hospitals will be randomized to intervention and control groups. A two day interactive, interdisciplinary course will train hospital leaders in the intervention group in trauma QI. This implementation strategy will be conducted in partnership with the multi-national professional trauma society network (PTS).

A follow-up assessment will be conducted to assess interval change in QI implementation in intervention and control hospitals. In addition, a qualitative assessment including focus groups and surveys, and a cost-analysis, will be performed.

Significance: The proposed project will improve scientific knowledge on effective methods to disseminate trauma QI programs. This knowledge will lead to improved morbidity and mortality in trauma.

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The Helen and John Schilling Lecture is an annual lecture established by the late Helen Schilling to bring distinguished scholars to the Department of Surgery at the University of Washington, and to enhance the Department's commitment to the highest standards of patient care, teaching, research and scholarship. It was Mrs. Schilling's wish that the lectureship be in honor of her husband, John.

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