

# 26th Annual Department of Surgery Research Symposium



Keynote Speakers:

**“Best Way to Predict the Future...  
is to INVENT it.”**

**Thomas Krummel, MD, FACS, FAAP  
Professor and Chair  
Pediatric Surgery**



**“You’re going to do WHAT? A  
Vanguard’s View of Innovation in  
Academic Surgical Practice”**

**Walter Boyd, MD  
Professor  
Cardiothoracic Surgery**

**April 27, 2015 / 8:00 a.m.-5:00pm  
Research Presentations  
MIND Institute  
Auditorium 1115**

**UCDAVIS**  
**HEALTH SYSTEM**

With appreciation,  
we wish to acknowledge  
Ethicon, Inc.'s  
support of the  
26th Annual Department of Surgery  
Research Symposium.

**8:00am – WELCOME & OPENING REMARKS  
KEYNOTE SPEAKER – THOMAS KRUMMEL, MD  
Best Way To Predict The Future...Is To INVENT It.**

**ORAL PRESENTATIONS – SESSION I:**

**Moderators: Aijun Wang, PhD & K.C. Kent Lloyd, DVM, PhD**

<b>8:45am</b>	<i>A tri-nucleotide pattern in a 3' UTR segment affects the activity of a human glucocorticoid receptor isoform</i>	Debora Lim, BA
<b>9:00am</b>	<i>Chorionic Villus Derived Stem Cells for In Utero Treatment of Hemophilia A</i>	Maricel Miguelino, MD
<b>9:15am</b>	<i>Ex-vivo Normothermic Perfusion (EVNP) to Assess and Repair Kidney Ischemia-Reperfusion Injury</i>	Ivonne Palm, BS
<b>9:30am</b>	<i>Partial Resuscitative Endovascular Balloon Occlusion of the Aorta (P-REBOA) in a swine model (Sus scrofa)</i>	Rachel Russo, MD
<b>9:45am</b>	<i>Temporally “stressed” genomic landscapes of human white blood cells due to stressor-elicited activity of transposable repetitive elements</i>	Kang-Hoon Lee, PhD
<b>10:00am</b>	<i>Establishing an FDA Approved Placenta-Derived Mesenchymal Stromal Cell (PMSC) Delivery Vehicle for the Repair of Myelomeningocele in the Fetal Ovine Model</i>	Benjamin Keller, MD
<b>10:15am</b>	<i>Transplantation of Neonatal En-Bloc Kidneys: Do They Grow and Are They Subject to Hyperfiltration Injury?</i>	Jakub Woloszyn, MD

**10:30am – 15 MINUTE BREAK – 10:45am**

**ORAL PRESENTATIONS – SESSION II:**

**Moderators: Claus Sondergaard, MD & Kiho Cho, PhD**

<b>10:45am</b>	<i>A Novel Ex Vivo Peripheral Nerve Injury/Regeneration Model: Lab on a Chip</i>	Yalda Toofan, BA
<b>11:00am</b>	<i>Differential effects of sodium butyrate and lithium chloride on rhesus monkey trophoblast differentiation</i>	Priyadarsini Kumar, PhD
<b>11:15am</b>	<i>A Novel Noninvasive High-efficacy Technique using Nanoparticle-Conjugated Delivery System for Treatment of Infantile Hemangioma</i>	Lindsey Harrison, BS
<b>11:30am</b>	<i>Randomized Controlled Trial Comparing Dynamic Simulation to Static Simulation in Trauma</i>	Anthony Carden, MD
<b>11:45am</b>	<i>In Vitro Interaction of Adipose-Derived Stem Cells and Breast Cancer Cells Harvested from the Same Patient</i>	Heath Charvet, MD
<b>12:00pm</b>	<i>Neurological Function after Traumatic Brain Injury: Does Anemia Make It Worse?</i>	Tejveer Dhillon, MD
<b>12:15pm</b>	<i>Do Placental Mesenchymal Stem Cells Mediate Neuroprotection In Vitro?</i>	James Becker, MD
<b>12:30pm</b>	<i>Comparison of the Endothelial Cell Differentiation Capacity of Human Adipose-Derived Stem Cells and Rat Adipose-Derived Stem Cells</i>	Kamaljit Devi, BS

**12:45pm – LUNCH BREAK AND POSTER ROUNDS – 2:00pm**

<b>POSTER ROUNDS</b>	
<b>POSTER PRESENTATIONS:</b>	
<b>Moderators: Mohamed Ali, MD, David Greenhalgh, MD, Soman Sen, MD &amp; Richard Perez, M.D.</b>	
Isolation and enrichment of chorionic villus-derived myogenic cells from early gestation placentas	Lee Lankford, MA
Imported Kidney Grafts from Non-Conventional Adult Deceased Donors Can Successfully Increase Access to Transplantation for Elderly Patients	Jakub Woloszyn, MD
Prospective Observational Study of Point-of-care Creatinine in Trauma	Anthony Carden, MD
Predictors of Residual Disease after Unplanned Excision of Unsuspected Soft Tissue Sarcomas	Alexandra Elias, MD
Inability to Return Home and Hospital Readmissions are Frequent among Patients with Disseminated Malignancy Undergoing Surgical Intervention	Sarah Bateni, MD
Injury-related death disparity in children under age five in low-income countries: An analysis of World Health Organization data	Laura Goodman, MD
The Impact of Radiotherapy on Rates of Surgical Site Infection in Patients with Rectal Cancer: Benchmarks for Comparison	Noah Yuen, MD
The Adrenal Incidentaloma: Are Patients Managed According to the Guidelines?	James Becker, MD
Sustainable Humanitarian Surgical Care in a Warzone: Breast Disease Treatment in a US Military Hospital in Afghanistan	Jamie Anderson, MD, MPH
Clinical Outcomes Following Lower Extremity Soft-Tissue Reconstruction with Pedicle Flaps: A Review of 978 Cases	Katherine Hinchcliff, MD
Approaches to distal upper-extremity trauma: A comparison of plastic, orthopedic, and hand surgeons in academic practice	Chanukya Dasari, MD
Differing Rates of Severe Flame and Electrical Injury in Severely Burned Children from Mexico and the United States	Guy Jensen, MD
Burn Care in the 1800s	Eleanor Curtis, MD
Deep Inferior Epigastric Artery Perforator Flap Breast Reconstruction without Microsurgery Fellowship Training: A Comparison of our results with the Literature	Hakan Orbay, MD, PhD
Peri Operative Laser Scar Therapy Protocol: A National Survey	Michael Mirmanesh, MD
Endogenous Retrovirus and Their Effects on Hypertrophic Scar Formation	Sven Gunther, BS

<b>AFTERNOON SESSION</b>		
<b>ORAL PRESENTATIONS – SESSION III:</b>		
<b>Moderators: David Sahar, MD &amp; Garth Utter, MD</b>		
<b>2:00pm</b>	<i>Preventing Abdominal Adhesions with Decellularized Amniotic Membrane: A Pilot Study</i>	Benjamin Keller, MD
<b>2:15pm</b>	<i>Amnion extracellular matrix derived hydrogel - a novel stem cell delivery vehicle for regenerative medicine</i>	Volodymyr Ryzhuk, BS
<b>2:30pm</b>	<i>Body Image &amp; Quality of Life: Changes with Gastric Bypass Surgery &amp; Body Contouring</i>	Nirav Patel, MD, MS, JD
<b>2:45pm</b>	<i>Thirteen-year Review of Outcomes Relating to Pre-Hospital Traumatic Arrest in Children</i>	Huy Duc Hoang, BS
<b>3:00pm</b>	<i>The 4T score for heparin induced thrombocytopenia in burn patients: does HITting the target help select patients for testing?</i>	Peter Kwan, MD
<b>3:15pm</b>	<i>Older Patients Derive Greater Benefit from Adjuvant and Neoadjuvant Radiotherapy in Diverse Solid Malignancies</i>	Noah Yuen, MD
<b>3:30pm</b>	<i>Parathyroidectomy in dialysis patients: What is the risk?</i>	Jamie Anderson, MD, MPH
<b>3:45pm</b>	<i>Determinants of value in surgical care of common yet complex procedures</i>	Erin Brown, MD
<b>4:00pm – 15 MINUTE BREAK – 4:15pm</b>		
<b>4:15pm – SPECIAL GUEST SPEAKER – WALTER BOYD, MD You're going to do WHAT???</b>		
<b>A Vanguard's View of Innovation in Academic Surgical Practice</b>		
<b>CONCLUDING REMARKS</b> Diana L. Farmer, MD, FACS, FRCS K. C. Kent Lloyd, DVM, PhD Tina L. Palmieri, MD, FACS, FCCM		
<b>UCDMC Department of Surgery 26th Annual Research Symposium Awards Banquet 6:00pm Crocker Art Museum 216 'O' Street Sacramento, CA</b>		

## **Thomas M. Krummel, MD, FACS/FAAP**

**Emile Holman Professor and Chair**

Program Director, General Surgery Residency Program

Department of Surgery

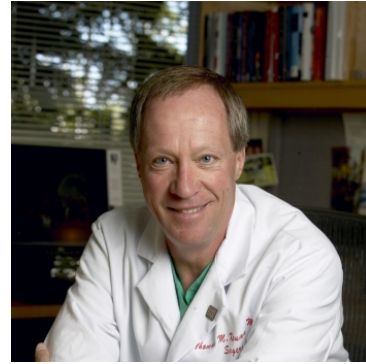
Stanford University School of Medicine

Susan B. Ford Surgeon-in-Chief

Lucile Packard Children's Hospital

Director, Goodman Simulation Center

**Co-Director, Biodesign Program**



Thomas M. Krummel, MD, completed his undergraduate degree at the University of Wisconsin with a medical degree at the Medical College of Wisconsin. His surgical residency was at the Medical College of Virginia with a Fellowship in Pediatric Surgery at the Children's Hospital of Pittsburgh followed by a Research Fellowship both at MCV and UCSF. Following five years on the faculty at MCV, he was named Professor of Surgery and Chief of Pediatric Surgery at the Pennsylvania State University College of Medicine and Surgeon-in-Chief at the Children's Hospital. In 1994, he was named John A. and Marian T. Waldhausen Professor and Chair of the Department of Surgery and Surgeon-in-Chief at University Hospitals. In 1998, he moved to Stanford to assume the position as Emile Holman Professor of Surgery and Chairman of the Department of Surgery at Stanford University.

Dr. Krummel has served in leadership positions in many of the important surgical societies including the American College of Surgeons, the American Pediatric Surgical Association, the American Surgical Association, the American Board of Surgery, the American Board of Pediatric Surgery, the American Board of Plastic Surgery and is currently President of the Halsted Society. He has mentored over 100 students, residents and post docs during their research training. Dr. Krummel has been a pioneer and a consistent innovator in the following important areas throughout his career:

While just a surgical resident, he formed what was then the world's second ECMO team. The success of that team served as a major impetus to more widespread adoption of this now well-established technique. He helped "jump start" the study of the cellular and biochemical mechanisms of scarless repair in the fetus; his work has been funded by the NIH for 15 years for over \$3M. Over the last 14 years he has been a pioneer in the application of information technology to simulation-based surgical training and surgical robotics. Dr. Krummel is the recipient of one of the first NIH Phased Innovation R21/R33 programs to develop a collaborative simulation-based surgical training system. For his work in this arena and in surgical robotics he has received two Smithsonian Information Technology innovation Awards.

Most recently he has founded the Surgical Innovation Program at Stanford. This program and its training program (a one or two year fellowship) are designed to teach the invention and implementation of new surgical technologies through interdisciplinary research and education at the emerging frontiers of engineering and the biomedical sciences. Dr. Krummel has lectured throughout the world and is author or co-author of over 300 publications, chapters, abstracts and books. He has served as a frequent consultant to the medical device industry, serving on the BOD or SAB of 11 start-ups. His concepts and thoughts are embodied in a number of laparoscopic, robotic and radiofrequency energy devices.

For his biomedical engineering contributions, he was recently elected to the American Institute for Medical and Biological Engineering, one of very few surgeons and the only pediatric surgeon to be elected to fellowship.

## **Walter Douglas Boyd, M.D.**

**Professor, Department of Surgery**

Surgery - Cardiothoracic, Surgery – Robotic

Department of Surgery

Division Cardiothoracic Surgery

UC Davis Medical Center



Walter D. Boyd, M.D. is board certified by the Royal College of Physicians and Surgeons of Canada in general and cardiothoracic surgery. He specializes in minimally invasive cardiac surgery and robotic surgery. Dr. Boyd did his undergraduate work at Carleton University in Ottawa, graduating with a Bachelor of Science degree in biology. He pursued a Master's of Education from the University of Toronto and completed his medical degree at the University of Ottawa. He received his clinical training in comprehensive surgery at Ottawa Civic Hospital and completed a residency in cardiovascular and thoracic surgery at the University of Ottawa where he was Chief Resident in the departments of Surgery and of Cardiovascular and Thoracic Surgery. Dr. Boyd has received numerous fellowships, scholarships and awards including a fellowship in Medical Education

Dr. Boyd is recognized for his pioneering work in cardiothoracic surgery and for his use of robotic-assisted surgical systems. He specializes in minimally invasive cardiac and robotic-assisted heart surgery. He completed the world's first closed-chest, beating-heart coronary artery bypass surgery using a robotic system in 1999 and performed the first human extracellular matrix xenograft implant for cardiovascular repair several years later. Prior to his appointment as a professor of surgery at UC Davis Health System, Dr. Boyd served as chair of the Department of Cardiothoracic Surgery at the Cleveland Clinic in Florida. As the author of more than 50 peer-reviewed, journal articles, Dr. Boyd's research interests include cardiac tissue regeneration using extracellular matrix/stem cells, new techniques for robot-assisted minimally invasive coronary artery revascularization, valve surgery and telesurgery.

## PAST VISITING PROFESSORS

### **Haile T. Debas, MD**

Dean, School of Medicine  
Maurice Galante Distinguished  
Professor of Surgery  
University of California, San Francisco  
June 10, 1995

### **Basil A. Pruitt, Jr., MD**

Professor, Department of Surgery  
University of Texas Health Science Center  
June 6, 1996

### **Douglas Wilmore, MD**

Frank Sawyer Professor of Surgery  
Harvard Medical School  
June 10, 1997

### **Richard L. Simmons, MD**

George Vance Professor of Surgery  
Chairman, Department of Surgery  
University of Pittsburgh  
June 8, 1999

### **Clyde F. Barker, MD**

John Rhea Barton Professor of Surgery  
Chairman, Department of Surgery  
University of Pennsylvania  
June 1, 2000

### **John A. Mannick, MD**

Moseley Distinguished Professor of Surgery  
Harvard Medical School, Department of Surgery  
Brigham and Women's Hospital  
June 5, 2001

### **David N. Herndon, MD**

Chief of Staff  
Director of Research  
Shriners Burns Hospital, Galveston, Texas  
June 11, 2002

### **Alden Harken, MD**

Chair, Department of Surgery  
UCSF East Bay Surgical Program  
June 10, 2003

### **Carlos O. Esquivel, MD, PhD**

The Arnold and Barbara Silverman Professor of Pediatric  
Transplantation, Professor of Surgery and Chief, Division  
of Transplantation  
Stanford University  
June 1, 2004

### **Sarah Yuan, MD, PhD**

Pearl Stamps Stewart Professor  
Director of Research, Department of Surgery  
UC Davis Medical Center  
June 7, 2005

### **Henri R. Ford, MD**

Vice-President and Surgeon-in-Chief  
Childrens Hospital Los Angeles  
Department of Surgery, Keck School of Medicine  
May 16, 2006

### **Michael Longaker, MD**

Denae P. and Louise Mitchell Professor  
Director, Children's Surgical Research  
Stanford University School of Medicine  
May 15, 2007

### **Andrew M. Lowy, MD**

Professor of Surgery  
Director of Surgical Oncology,  
Moore's UCSD Cancer Center  
University of California, San Diego  
June 3, 2008

### **John D. Birkmeyer, MD**

George D. Zuidema Professor & Chair  
Surgical Outcomes Research  
University of Michigan Health Systems  
June 16, 2009

### **Dai Chung, MD**

Professor of Surgery  
Department of Pediatric Surgery  
Vanderbilt University  
June 15, 2010

### **Colleen Brophy, MD**

Professor, Vascular Surgery  
Vanderbilt University Medical Center  
June 14, 2011

### **Jeffrey R. Saffle, MD, FACS**

Professor of Surgery  
Department of Surgery  
University of Utah School of Medicine  
June 19, 2012

### **Frederick A. Moore, MD, FACS, MCCM**

Professor of Surgery and Anesthesia  
Chief, Division of Acute Care Surgery  
College of Medicine, University of Florida  
April 16, 2013

### **K.C. Kent Lloyd, DVM, PhD**

Professor and Director, Mouse Biology Program,  
Associate Dean, Research, Graduate Education, School of  
Veterinary Medicine, University of California Davis  
April 16, 2013

### **Alan Flake, MD, FACS, FAAP**

Professor of Surgery, Obstetrics and Gynecology  
Perelman School of Medicine, University of Pennsylvania  
April 22, 2014

26th Annual Department of Surgery  
Research Symposium

**Oral Presentations**

## **A tri-nucleotide pattern in a 3' UTR segment affects the activity of a human glucocorticoid receptor isoform**

Debora Lim, Stacey M. Leventhal, Tajia L. Green, Kiho Cho, and David G. Greenhalgh.  
Department of Burn Surgery, UC Davis, and Shriners Hospitals for Children

**Introduction:** Steroids are the standard recommended treatment for many inflammatory conditions, such as sepsis in burn patients; however, patient response can vary widely. In our laboratory, we examine natural variations in the human glucocorticoid receptor (hGR) as a contributor to the diversity in response to injury. We previously identified a truncated hGR isoform that demonstrated hyperactivity after glucocorticoid treatment. This isoform had a putative length of 118 amino acids (reference hGR $\alpha$ : 777 amino acids) and further experiments indicated the involvement of its newly formed extended 3' untranslated region (UTR) in its hyperactivity. A similar truncated isoform (-1199), whose 3' UTR region ended 1199 base pairs (bp) from the end of the standard hGR $\alpha$  termination site, had unusually high activity with or without glucocorticoid stimulation.

**Methods:** To dissect the underlying mechanisms for the hyperactivity, a series of hGR isoforms, with consecutive deletions in the 3' UTR (from 100 bp down to a single base pair), was created and tested for their transactivation potential in luciferase reporter assays.

**Results:** We found that hyperactivity peaked with a 3'UTR deletion of -1189 bp. Unexpectedly, a complete loss of activity at -1209 bp and -1239 bp was observed. Upon further analysis of the well-conserved 20 bp region neighboring the -1209 bp site, a pattern emerged. Termination at every third base pair resulted in a loss of transactivation potential while the other sites retained hyperactivity with or without glucocorticoid stimulation.

**Conclusion:** Variations in the activity of an hGR isoform, due to changes in the 3' UTR sequence configuration, may provide an important clue to explain the control of glucocorticoid receptor function and diversity in patient response to steroid treatment. Understanding the mechanisms underlying the cyclic hyperactivity/loss of activity phenomenon may be a step towards identifying a novel mechanism of gene regulation and ultimately creating personalized care regimens for burn injury patients.

## Chorionic Villus Derived Stem Cells for *In Utero* Treatment of Hemophilia A

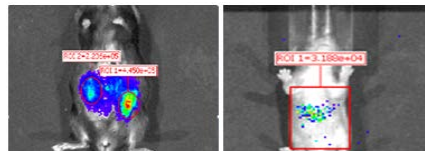
Maricel G. Miguelino, M.D.<sup>1</sup> Christopher Pivetti, M.S.<sup>2</sup> Lee Lankford, M.A.,<sup>2</sup>  
Priyadarsini Kumar, Ph.D.<sup>2</sup> Jerry S. Powell, M.D.<sup>1</sup> Aijun Wang, Ph. D.<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, Division of Hematology Oncology

<sup>2</sup>Department of Surgery, Surgical Bioengineering Laboratory

**Introduction:** Pregnancy is a paradox where fetal cells are able to enter the maternal circulation as early as six weeks of gestation, and persist for decades without graft rejection. Gestation presents ontogenic opportunities of an immune naïve fetal environment and continually dividing cells where introduction of donor cells may be recognized as self, therefore inducing tolerance permissive for long term engraftment. Chorionic villus sampling can be used to diagnose genetic disorders such as hemophilia A (HA), an X-linked recessive coagulation disorder, suggesting the potential for prenatal treatment. The aim of this study is to investigate the safety and survivability of *in utero* transplantation (IUT) of genetically modified human chorionic villus stem cells (PMSCs) that express Factor VIII (FVIII).

**Methods:** Characterization of mesenchymal stem cell (MSC) properties of PMSCs isolated from first trimester placenta was assessed via tri-lineage specific induction and flow cytometry. FVIII protein expression, after lentiviral vector transduction of PMSCs was examined via flow cytometry and quantified by enzyme-linked immunosorbent assay. Furthermore, biologically active FVIII (FVIII:C) was assessed in cell supernatant.



**Figure 1: Bioluminescence image (BLI) analysis.** BLI of gravid dam (A) showing focal density of PMSCs transplanted in the fetuses and in the 5-day-old pup (B) born 12 days after IUT.

**Results:** PMSCs expressed MSC markers CD105, CD90, CD73, CD44, and CD29, and did not express CD184, HLA-DR or hematopoietic and endothelial markers CD45, CD34 and CD31. Tri-lineage differentiation potential was observed under different conditions. Transduction of PMSCs showed FVIII protein expression and FVIII:C *in vitro*. Bioluminescence imaging analysis revealed focal density and transgene expression in the fetuses 1-3 days after IUT and persisted 5-7 days after birth (Figure 1).

**Conclusion:** Our data demonstrate that IUT of genetically modified human PMSCs may be a feasible approach for autologous stem cell-mediated gene therapy for hemophilia A.

## Ex-vivo Normothermic Perfusion (EVNP) to Assess and Repair Kidney Ischemia-Reperfusion Injury

I. Palma<sup>1</sup>, J. Woloszyn<sup>1</sup>, R. Abbott<sup>1</sup>, Y. Smolin<sup>1</sup>, R. Ramsamooj<sup>2</sup>, N. Tran<sup>2</sup>, C. Santhanakrishnan<sup>1</sup>, R. V. Perez<sup>1</sup>

<sup>1</sup>University Of California – Davis, Surgery-Transplant, Sacramento, CA, USA

<sup>2</sup>University Of California – Davis, Pathology and Laboratory Medicine, Sacramento, CA, USA

**Introduction:** Recent studies have shown that Ex-Vivo Normothermic Perfusion has the potential to both repair and assess viability of marginal organs prior to transplantation by restoring normal metabolism. The optimal perfusion solution for these functions has not been determined.

**Methods:** Paired high-risk human kidneys initially procured for transplantation but discarded were placed on 3 hours of pressure dependent EVNP at 37°C with either leukocyte depleted Packed Red Blood Cells (PRBC) or Whole Blood (WB). Blood and urine were collected both at the start and in increments of 30 minutes and analyzed for pH, oxygen, electrolytes, creatinine, lactate and Neutrophil Gelatinase-Associated Lipocalin (NGAL).

**Results:** The mean age of donors was 60 years while the mean static cold ischemia time was 52.5 hours. The Maryland Aggregate Pathology Index and Kidney Donor Prognostic Index were equal in both groups (5.25% and 87% respectively). Hemodynamic parameters evaluated were flow and resistance, and neither showed any statistical significance (p=0.19 and p=0.20). However, PRBC showed a better trend in both parameters. Functional parameters appeared more favorable in the PRBC group but only achieved statistical significance with urine NGAL as shown in the table below.

		<i>T0</i> (minutes)	<i>T1</i>	<i>T2</i>	<i>T3</i>	<i>T4</i>	<i>T5</i>	<i>T6</i>	<i>P value</i>
<b>Cr</b>	WB	10.83	9.05	8.81	8.45	8.67	8.17	8.28	0.17
	PRBC	11.12	8.23	7.56	6.91	6.89	6.65	6.26	
<b>Urine NGAL</b>	WB	0	287	319	369	368	404.5	367.5	0.02
	PRBC	0	33	29	38	36	26	30	
<b>Urine Volume</b>	WB	0	8.56	2.94	2.1	2.04	1.1	3.7	0.17
	PRBC	0	44.37	26	23.37	18.31	15.82	17.17	

**Conclusion:** EVNP of high-risk kidneys is possible and POC testing can be used to assess organs in real time; this potentially decreases the risk of post-transplant dysfunction. Perfusion with PRBC may have a beneficial effect on the kidney, but may not accurately assess the degree of ischemia-reperfusion injury when compared to the more physiologic WB perfusion.

## **Partial Resuscitative Endovascular Balloon Occlusion of the Aorta (P-REBOA) in a swine model (*Sus scrofa*).**

RM Russo MD, CM Lamb FRCS, JL Galante, JK Grayson PhD, LP Neff MD, TK Williams MD  
UCDMC Department of Surgery, Division of Trauma, and Division of Vascular Surgery; USAF

**Introduction:** Resuscitative endovascular balloon occlusion of the aorta (REBOA) is used to support patients dying from torso hemorrhage, but complete REBOA (c-REBOA) causes significant ischemia to distal tissues. p-REBOA, 80-90% aortic occlusion, may augment mean arterial pressure proximal to the balloon (pMAP) while preserving distal perfusion. We investigated the hemodynamic and physiologic effects of p-REBOA versus c-REBOA.

**Methods:** Fifteen Yorkshire-cross swine were anesthetized, instrumented, splenectomized, subjected to rapid 25% total blood volume loss, then randomized to 90 minutes of treatment with c-REBOA, p-REBOA, or no intervention. Aortic MAP (proximal and distal to the balloon), visceral arterial pressures, and serum markers of ischemia were recorded. At the end of 90 minutes, balloons were deflated and the experiment continued for 15-minutes to evaluate the immediate effects of reperfusion. Following euthanasia, end organs were histologically examined.

**Results:** Compared with no treatment, c-REBOA produced considerable increases in pMAP after hemorrhage ( $p<0.01$ ) and substantially higher levels of serum lactate ( $p<0.01$ ), followed by a precipitous drop in blood pressures on balloon deflation. p-REBOA produced pMAP increases higher than control ( $p<0.01$ ) while maintaining a lactate profile similar to control. Maintenance of aortic pressure gradient across the p-REBOA balloon was reliable and reproducible. Qualitative histological analysis revealed acute tubular necrosis in the c-REBOA group with no evidence of ischemia in control or p-REBOA groups. Necrosis of the duodenal mucosa was present in all individuals in the c-REBOA group, 4/5 in the control group, and 1/5 in the p-REBOA group.

**Conclusion:** This initial investigation indicates that p-REBOA is feasible and may minimize systemic physiologic insult and damage to tissues distal to the balloon. Further work is needed to determine if the hemodynamic improvements associated with p-REBOA will translate into a survival benefit in the face of persistent blood loss.

## **Temporally “stressed” genomic landscapes of human white blood cells due to stressor-elicited activity of transposable repetitive elements**

Kang-Hoon Lee, Debora Lim, Tajia Green, David Greenhalgh, and Kiho Cho  
Burn Division, Department of Surgery, University of California, Davis and Shriners Hospitals for Children Northern California

**Introduction:** Approximately 50% of the human genome is known to be composed of various types of transposable repetitive elements (TREs). Human endogenous retroviruses (HERVs), a TRE family, make up ~8% of the human genome. HERVs were considered to be nonfunctional remnants of ancient germline infections. We reported that burn-elicited stressors temporally alter the expression of certain HERVs in a patient-specific manner. In this study, we examined whether treatment of primary human white blood cells with stressors (lipopolysaccharide [LPS] or hydrocortisone) alters the activity of HERVs, leading to temporally “stressed” genomic landscapes.

**Methods:** Aliquots of white blood cells from a leukopak were treated with vehicle, LPS, and/or hydrocortisone and incubated for 1 hour, 3 hours, and 13 hours followed by genomic DNA isolation. Upon digestion of the genomic DNAs with Hind-III, inverse-PCR (I-PCR) analyses were performed using the HERV-K2 sequence as a probe for HERV position mapping in order to examine stressor-elicited changes in the genomic landscapes.

**Results:** Marked changes in the genomic landscapes, reflected in the I-PCR amplicon profiles, were observed at 1 hour and 3 hours after treatment with LPS or hydrocortisone, while there were no significant differences among all three groups at 13 hours.

**Conclusion:** The findings from this study indicate that stress signals, which are elicited by treatment with LPS or hydrocortisone, alter the activity of HERV-K2, leading to temporally “stressed” genomic landscapes. Further interrogation of the stress-elicited temporal alterations of genomic HERV landscapes may allow us to identify novel genomic loci for the study of a range of injury/stress-related disease processes.

## **Establishing an FDA Approved Placenta-Derived Mesenchymal Stromal Cell (PMSC) Delivery Vehicle for the Repair of Myelomeningocele in the Fetal Ovine Model**

BA Keller, JC Becker, L Lankford, CD Pivetti, A Wang, DL Farmer  
UCDMC Department of Surgery

**Introduction:** Myelomeningocele (MMC) is the most common cause of childhood paralysis. Research demonstrates the promising functional improvement following PMSC treatment during *in utero* MMC repair. We hypothesize that fetal lambs treated with PMSCs seeded on an FDA approved Dural Matrix will have similar motor function improvements compared to historic lambs treated with PMSCs seeded in a lab grade collagen hydrogel.

**Methods:** Fluorescent microscopy was used evaluate PMSC morphology when cells tagged with green fluorescent protein were seeded on both delivery vehicles. Two fetal lambs underwent surgical creation of a MMC defect at 75 days gestational age (GA) followed by *in utero* repair with human PMSCs seeded on Dural Matrix at 100 days GA. Lambs were born via vaginal delivery at term. Motor function was assessed at 24 hours of life and weekly thereafter after using a locomotor rating scale.

**Results:** PMSC morphology was similar between the two delivery vehicles. Lambs treated with PMSCs on Dural Matrix were capable of near normal ambulation at birth. One lamb had a decline in motor function over the first month and was euthanatized. Post-mortem MRI demonstrated scoliosis with spinal cord compression. The remaining lamb maintained near normal motor function at one month of age.

**Conclusion:** PMSC seeded Dural Matrix confers similar improvements in motor function compared to PMSCs seeded in a lab grade collagen hydrogel. The development of progressive lower extremity motor dysfunction raises concerns about the durability of PMSC repair and the musculoskeletal consequences of the MMC defect. Additional animal experiments are required to evaluate the Dural Matrix and the natural history of MMC lambs when survived long term.

## Transplantation of Neonatal En-Bloc Kidneys: Do They Grow and Are They Subject to Hyperfiltration Injury?

J. Woloszyn, C.Santhanakrishnan, C. Troppmann, A. DeMattos, J. McVicar, J. Sageshima, R. Perez  
Transplant Surgery

**Introduction:** Neonatal Intensive Care Unit (NICU) kidney donation is rare but a potentially significant kidney source. Concerns with these kidneys include the risk for early failure from thrombosis and for injury/failure from hyperfiltration (HF). We evaluated our transplants from NICU donors focusing on graft function, growth and HF injury.

**Methods:** Recipients of NICU donor en-bloc transplants from 2011-2014 were reviewed. Kidney growth was calculated by comparing graft length on post-operative ultrasound (US) to more recent US when available. Resolution of proteinuria (PU) was defined as 3 consecutive negative urinalyses.

**Results:** 27 transplants were performed without mortality and with 4 early graft failures (2 graft thromboses; 2 primary non-functions). 10 (37%) patients had delayed graft function. All experienced post-operative PU. Of those >6 mo. post-transplant, 4 (22%) had unresolved PU.

Donor ( <i>median, range</i> )		Recipient ( <i>mean±SD</i> )		Time to resolution of PU ( <i>d; mean±SEM</i> )	Recipient/Donor Wt ( <i>mean±SEM</i> )	
Age ( <i>d</i> )	Wt ( <i>kg</i> )	Age ( <i>yrs</i> )	Wt ( <i>kg</i> )		Persistent PU n=4	Resolved PU n=14
8, 1-155	3.4, 1.9-4.9	50.7±15.2	54.8±7.5	165±42	21.1±3.3	15.2±0.9

Kidney Length Increase ( <i>%; mean±SD</i> )			e-GFR ( <i>ml/min; mean±SD</i> )			
14-60 d n=5	60-180 d n=3	>180 d n=3	1 mo n=22	6 mo n=18	12 mo n=16	2 yr n=10
45±14	44±23	62±43	19±11	59±33	76±35	103±54

Table 1: Graft; donor characteristics; graft outcomes

**Conclusion:** Kidneys from NICU donors can be successfully transplanted and show significant growth and improving renal function. In the majority, early PU resolves within 6 mo. Those who experience persistent PU warrant longer follow up to determine if HF injury develops. Strategies to improve outcomes, including appropriate size matching of recipients and donors, will need to focus on prevention of early thrombosis and possible HF injury.

## A Novel *Ex Vivo* Peripheral Nerve Injury/Regeneration Model: Lab on a Chip

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### Introduction:

Peripheral nerve injury is very common in clinic and the most widely used model for evaluation of the regeneration process is the rodent sciatic nerve model. To establish an effective, high throughput and cost-effective *ex vivo* peripheral nerve injury/regeneration model, we designed a microfluidics model to study the process of nerve injury and effects of exogenous stimuli, such as electrical stimulus, on nerve regeneration.

### Methods:

The model consists of a micro-channel with six wells, two electrodes connected by salt bridge, and an inverted microscope (Figure 1). Dorsal root ganglia (DRGs) are cultured in the cell body-containing well and the bundle of neurites extend along the channel. Physical injury is then mechanically induced to the axon bundle, then an electric current is applied via the salt bridge and time-lapse video recording used to measure the process of axon injury/regeneration.

### Results:

Experimental results suggest a preference of nerve regeneration towards the cathode at 250mV over 6 hours, shown through time lapsed photography (Figure 2). Over time and higher voltage, axons regressed towards the DRG cell clump, further experiments showed death at 39°C. Our preliminary work shows promise and has helped us design our experimental model depicted (Figure 1).

### Conclusion:

The use of this model has significant implications for the study of peripheral nerves, and it could lead to novel therapies and a better understanding of nerve injury and regeneration. We have found that electric fields show promise in guiding nerve regeneration, but more work must be done to better understand the effect of ionization and heat caused by the electric current.

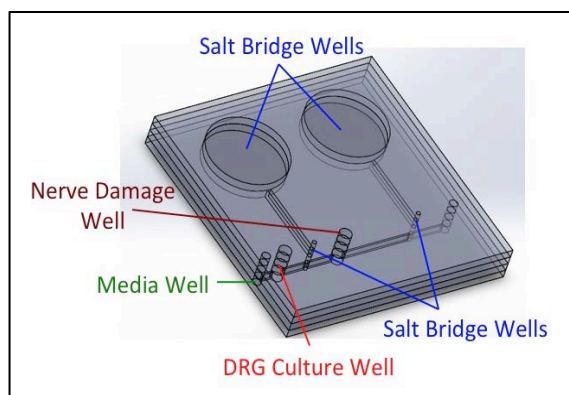


Figure 1: Peripheral Nerve Injury Model

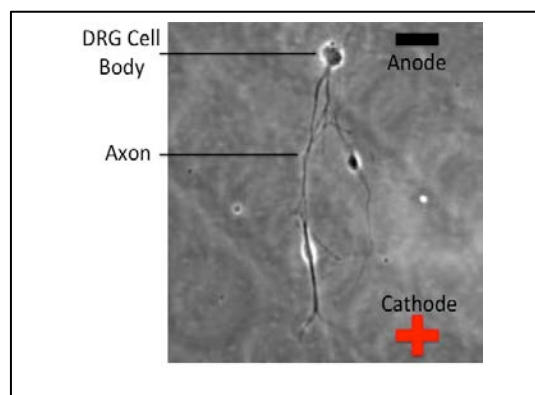


Figure 2: Axon growth in an electrical field

## **Differential effects of sodium butyrate and lithium chloride on rhesus monkey trophoblast differentiation**

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**Introduction:** Trophoblast differentiation during early placental development is critical for successful pregnancy and aberrant differentiation causes preeclampsia and early pregnancy loss. During the first trimester, cytotrophoblasts are exposed to low-oxygen tension and differentiate into syncytiotrophoblast, extravillous and endovascular trophoblasts. This study hypothesized that sodium butyrate (an epigenetic modulator) induces trophoblast differentiation through activation of the Wnt/ $\beta$ -catenin pathway.

**Methods:** Cytotrophoblast cells were isolated from first trimester placenta of rhesus monkey and treated with sodium butyrate for 7 days at 2% oxygen tension. Differentiation was analyzed by immunocytochemistry, gene and protein expression.

**Results:** The results show that butyrate treatment increased syncytiotrophoblast formation, nuclear accumulation of  $\beta$ -catenin, increased expression of EnvV2, galectin-1, and placental lactogen. Inhibition of GSK $\beta$  can mimic Wnt activation and cause nuclear accumulation of  $\beta$ -catenin. When trophoblasts were incubated with lithium chloride, an inhibitor of GSK3 $\beta$ , differentiation into syncytiotrophoblast was not observed. Instead the cells differentiated to mononucleated spindle-shaped cells and showed characteristics of endovascular trophoblasts. However, CHIR99021, a highly specific inhibitor of GSK3 $\beta$  failed to induce endovascular trophoblast characteristics. These observations suggest that activation of the Wnt/ $\beta$ -catenin pathway alone does not necessarily correlate with trophoblast differentiation. Other experiments suggested that the differential effects of sodium butyrate and lithium chloride could be explained by their effects on TNF- $\alpha$  production.

**Conclusion:** The results provide us tools to manipulate trophoblast differentiation in vitro and to better understand the differentiation pathways that occur during early gestation in the rhesus monkey and in the human placenta.

## **A Novel Noninvasive High-efficacy Technique using Nanoparticle-Conjugated Delivery System for Treatment of Infantile Hemangioma**

Lindsey Harrison, BS<sup>1</sup>, Hakan Orbay, MD, PhD<sup>1</sup>, Kamaljit Devi, BS<sup>1</sup>, Yuanpei Li, PhD<sup>2</sup>, Wenwu XiaoPhD<sup>2</sup>, Kit Lam, MD, PhD<sup>2</sup>, David E. Sahar, MD<sup>1</sup>

<sup>1</sup>UC – Davis Medical Center, Department of Surgery, Division of Plastic Surgery, Sacramento, CA

<sup>2</sup>UC – Davis Medical Center, Department of Biochemistry and Molecular Biology

**Introduction:** Our purpose is to define a noninvasive treatment method for infantile hemangiomas by combining photodynamic therapy and pharmacotherapy delivered by a nanoparticle carrier.

**Methods:** Nude mice were injected with mouse hemangioendothelioma cells. Positron emission tomography (PET) imaging and in vivo near infrared fluorescence (NIRF) imaging and was performed when the tumors reached to 500 mm<sup>3</sup> volume. Biodistribution studies and ex vivo imaging was performed after in vivo imaging. Tumors were further examined with histologically.

**Results:** <sup>64</sup>Cu-NP accumulation was 18.1±5.4 percent injected dose per gram (%ID/g) in left tumor and 21.3±6.3 % ID/g in right tumor at 3 hours post-injection. At 6 hours post-injection accumulation was 15.6±5.04 %ID/g in left and 17.8±2.1 %ID/g in right tumor. The uptake declined gradually at 24 and 48 hours post-injection. The results of biodistribution study paralleled PET imaging. In vivo and ex vivo NIRF imaging revealed that most of the injected dose was taken up by the liver and lung, followed by the infantile hemangioma. Infantile hemangiomas were histologically highly vascular like human tumors.

**Conclusion:** Nanoporphyrin accumulated in infantile hemangiomas selectively after systemic injection. The next step will be the treatment of infantile hemangioma with a combination of photodynamic therapy and propranolol loaded nanoporphyrin. We have an ongoing pilot treatment study right now.

## **Randomized Controlled Trial Comparing Dynamic Simulation to Static Simulation in Trauma**

A Carden, MD; E Salcedo, MD; D Leshikar, MD; G Utter, MD; M Wilson, Ph.D.; J Galante, MD  
Division of Trauma and Acute Care Surgery

**Introduction:** Open simulation classically focuses on anatomically accurate, static models, but lacks practicality when hemorrhage control is the life-saving maneuver. The purpose of this study is to determine whether training on a dynamic simulator is more effective than training on an anatomically accurate, static cadaver for TVS placement.

**Methods:** We enrolled 54 general surgery residents a randomized controlled trial comparing training of TVS placement on a dynamic simulator of original design (n= 28) versus a cadaver arm (n= 26). Our research team developed an inexpensive, reusable simulator with hemorrhage to duplicate the steps of TVS placement. After standardized video didactics, trainees practiced on the simulator or cadaver arm. Once competent, they were recorded placing a TVS in a live swine femoral artery. Two blinded trauma surgeons evaluated the recorded performances using a validated modality, Objective Structured Assessment of Technical Skills (OSATS). Additional outcomes included times to hemorrhage control and procedure completion.

**Results:** The simulator was created from simple parts for \$40.00, compared to a cadaver arm (\$380.00) or a training swine (\$1250.00). After completing training, all residents in both groups successfully completed the task. Subjects trained on the simulator placed the TVS faster than those trained on a cadaver (584s vs. 751s,  $p=0.0096$ ), with a trend towards faster time to hemorrhage control (110s vs. 148s,  $p=0.086$ ). There was no significant difference in OSATs score (3.70 vs. 3.60,  $p=0.53$ ).

**Conclusion:** Skills acquisition is at least as effective on the simulator as a cadaver arm, at a fraction of the cost. The addition of dynamic hemorrhage control provides a critical training element required for trauma skills development. Observationally, residents trained on the dynamic simulator were more comfortable in the face of active hemorrhage than those trained on a cadaver. Use of dynamic simulation for hemorrhage control operations is an inexpensive and effective way to supplement low operative volume for training in critical open trauma skills.

## **In Vitro Interaction of Adipose-Derived Stem Cells and Breast Cancer Cells Harvested from the Same Patient**

Heath Charvet<sup>1</sup>, Hakan Orbay<sup>1</sup>, Lindsey Harrison<sup>1</sup>, Kamaljit Devi<sup>1</sup>, David E. Sahar<sup>1</sup>  
<sup>1</sup> UC – Davis Medical Center, Department of Surgery, Sacramento, CA

**Introduction:** Fat grafting for breast cancer reconstruction and breast augmentation is becoming increasingly popular. A major area of debate and controversy is the effect of adipose-derived stem cells (ASCs) on remnant or undetected breast cancer cells (BCCs). We investigate the in vitro response of BCCs to ASCs in a co-culture model with regards to cell migration.

**Methods:** The study was approved by the IRB. Breast cancer and adipose tissue specimens were obtained from the same patient. BCCs and ASCs were harvested with either explant culture or enzymatic digestion and grown to establish adequate cell libraries. ASCs from adipose specimens were characterized with flow cytometry. A homogenous CD 90-/CD 24+ BCC population was obtained with flow cytometric cell sorting. Immunofluorescence (IF) staining for CD 24 was also performed on BCCs. The in vitro migration of BCCs was examined in co-culture with and without ASCs using a Cytoselect™ cell migration assay (Cell Biolabs, Inc.).

**Results:** ASCs harvested from the adipose specimens were positive for mesenchymal stem cell markers CD 90 and CD 34 and negative for endothelial cell marker CD 31 and leucocyte marker CD 45. The percentage of the CD 90-/CD 24+ BCCs in the initial cell population harvested from breast cancer specimens was 0.61 %. The BCCs morphologically had large nuclei and small cytoplasm under the light microscope suggesting a cancer cell phenotype. CD 24 expression on the surface of BCCs was confirmed with IF staining. The number of BCCs migrated in ASCs co-culture was approximately 10 times higher than the BCCs migrated without ASCs ( $5.1 \times 10^6$  vs.  $5.6 \times 10^5$  respectively).

**Conclusion:** ASCs significantly increase the migration capacity of BCCs in in vitro co-cultures. Future studies include increasing the sample size and performing BCC vs BCC/ASC co-injections and monitoring tumor size/growth in a murine model.

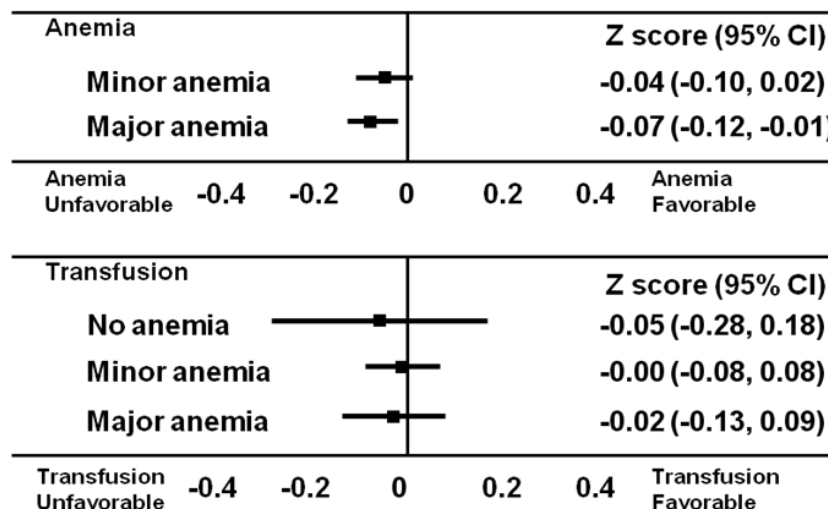
## Neurological Function after Traumatic Brain Injury: Does Anemia Make It Worse?

Tejveer Dhillon, MD, Yingjia Chen, MPH, Daniel Tancredi, PhD, Patrick Romano, MD MPH, Nancy Temkin, PhD, Sureyya Dikmen, PhD, J. Paul Muizelaar, MD PhD, Garth Utter, MD MSc  
 Division of Trauma and Acute Care Surgery

**Introduction:** Anemia in patients with acute traumatic brain injury (TBI) may cause a secondary insult to vulnerable brain tissue, but the optimal transfusion threshold remains unknown. We hypothesized that worse anemia would be associated with worse six-month functional neurological outcomes, but that in anemic subjects, blood transfusion would counteract this effect.

**Methods:** We conducted a secondary analysis of data from two previous randomized trials involving TBI. We determined each subject’s level of anemia during the first 96 hours after injury using an area under the curve (AUC) approach to capture both its duration and severity below a hematocrit of 30%. We categorized subjects into three groups based on the AUC: no anemia, minor anemia, and major anemia. We evaluated the relationship between anemia and neuropsychological test scores at six months (14 different tests, 5 common to both trials), normalized as “Z scores” (mean 0, SD=1). We further analyzed the relationship between transfusion and neuropsychological test scores.

**Results:** We started with 891 subjects and ultimately analyzed 753. Major anemia was associated with slightly worse combined six-month neuropsychological test scores (Z score difference -0.07, 95% CI -0.12 to -0.01), while minor anemia was not. Transfusion was not associated with changes in neuropsychological scores.



**Conclusion:** Major anemia is associated with subtly worse six-month neuropsychological outcome in patients with TBI. However, blood transfusion does not correct this phenomenon. TBI patients with hematocrit greater than 21% do not seem to warrant transfusion for the purposes of improving long term neurological function.

## **Do Placental Mesenchymal Stem Cells Mediate Neuroprotection *In Vitro*?**

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Department of Surgery, Surgical Bioengineering Lab, University of California Davis

**Introduction:** Placental mesenchymal stem cells (PMSCs) have cytoprotective and immunomodulatory effects. We have demonstrated that PMSC treatment confers improved motor function and preservation of spinal neurons in a fetal ovine model of spina bifida, but the mechanism is unclear. We hypothesize that PMSCs will improve neuron-like cell survival after injury *in vitro* via paracrine secretion.

**Methods:** PMSCs were immunophenotyped with flow cytometry for classic mesenchymal stem cell (MSC) markers and hematopoietic cell markers. Tri-lineage differentiation was induced. Hepatocyte growth factor (HGF) and brain-derived neurotrophic factor (BDNF) secretion was quantitatively compared to bone marrow MSCs with enzyme-linked immunosorbent assays (ELISAs). We used the neuroblastoma cell line SH-SY5Y treated with 6-hydroxydopamine (OHDA) to model apoptosis in neuronal precursors. A dose response curve was developed (1% Triton X-100 control) using an MTS assay. We similarly assessed the toxicity of amniotic fluid to SH-SY5Y cells. We incubated SH-SY5Y cells with 10  $\mu$ M retinoic acid (RA) for 4 days to differentiate them to a mature neuron phenotype.

**Results:** PMSCs were positive for CD29, CD 44, CD73, CD90, CD105, and negative for CD31, CD34, and CD45. Tri-lineage differentiation was observed in all PMSC lines. Mean PMSC secretion of HGF ( $p=.032$ ) and BDNF ( $p=.003$ ) was greater than bone marrow MSCs. SH-SY5Y cells demonstrated time-dependent survival after OHDA treatment for 2, 4, and 6 hours. 24 hour incubation with dilute and full strength amniotic demonstrated toxicity also. Differentiation was successful, with RA treated cells assuming a mature neuronal morphology.

**Conclusion:** Further investigation will confirm the anti-apoptotic effect of PMSCs in a transwell co-culture. We will investigate the roles of BDNF and HGF in neuroprotection. RA differentiation will be confirmed with immunohistochemistry for mature neuron markers.

## Comparison of the Endothelial Cell Differentiation Capacity of Human Adipose-Derived Stem Cells and Rat Adipose-Derived Stem Cells

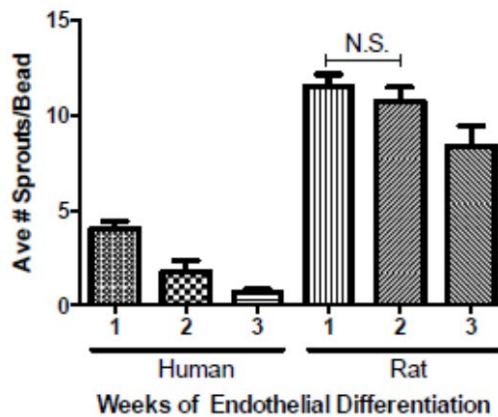
Kamaljit Devi, BS<sup>1</sup>, Priscilla Williams, BS<sup>2</sup>, Hakan Orbay, MD, PhD<sup>1</sup>, Lindsey Harrison, BS<sup>1</sup>, Eduardo Silva, PhD<sup>2</sup>, David E. Sahar, MD<sup>1</sup>

<sup>1</sup> University of California Davis Medical Center, Department of Surgery, Division of Plastic Surgery, Sacramento, CA. <sup>2</sup> University of California Davis, Department of Biomedical Engineering, Davis, CA.

**Introduction:** The aim of this study is to compare the endothelial cell differentiation capacities of rat and human adipose-derived stem cells using the same differentiation medium to determine if it is clinically applicable.

**Methods:** Adipose-derived stem cells were characterized with flow cytometry and multi-lineage differentiation. Cells from PIII-V were fed with endothelial cell differentiation medium (EGM-2 MV, Lonza Pharmaceuticals) and harvested after 1, 2 and 3 weeks of differentiation. Endothelial differentiation was evaluated with qRT-PCR, flow cytometry, and fibrin sprout test.

**Results:** Adipose-derived stem cells were CD90+, CD44+, CD31-, CD45- and successfully differentiated into osteogenic, chondrogenic and adipogenic lineages. The expression of CD31, VEGF receptor and Von Willebrand's Factor genes in rat adipose-derived stem cells made a peak at second week of differentiation. Surface expression of CD31 also made a peak at second week in both rat (from 2.8% at week 1 to 4.8% at week 2) and human (1.4 % at week 1 to 3.9 % at week 2) cells. The results of fibrin sprout assay were not correlating well with flow cytometry (**Fig. 1**) probably because CD31 is not the only determinant of endothelial cell function.



**Conclusion:** Rat and human adipose-derived stem cells showed similar endothelial cell differentiation characteristics. We are working on qRT-PCR experiments for human adipose-derived stem cells and also CD31 immunofluorescence staining for both groups.

## Preventing Abdominal Adhesions with Decellularized Amniotic Membrane: A Pilot Study

BA Keller, JC Becker, CD Pivetti, DL Farmer, A Wang  
UCDMC Department of Surgery, Surgical Bioengineering Laboratory

**Introduction:** Post operative abdominal adhesions are a costly and common problem. Amniotic membrane (AM) is a unique biologically active membrane with anti-inflammatory properties. Removal of cellular components (decellularization) is a common process utilized to reduce the immunogenicity of a tissue for regenerative medicine applications. We hypothesize that decellularized AM can be used to prevent postoperative abdominal adhesions in a rodent model.

**Methods:** AM was obtained, decellularized, and characterized microscopically. Biologic activity was evaluated using cytokine arrays. A total of six Sprague Dawley rats underwent abdominal laparotomy and peritoneal button creation to illicit adhesion formation. Four rats had decellularized AM placed over the abdominal viscera prior to closure. The remaining two did not. Animals were euthanized two weeks after their index procedure and adhesions were graded using a standardized scale.

**Results:** Microscopy confirmed near complete decellularization of the AM. Cytokine arrays demonstrated the presence of anti-inflammatory (IL-1RA) and immunomodulatory SERPIN E1, TIMP-1) cytokines in the decellularized product. Animals treated with decellularized AM demonstrated a decrease in the quantity and severity of peritoneal adhesions compared to control animals.

**Conclusion:** Successful decellularization of the AM is achieved using a simple protocol and AM appears to maintain some of its biologically active cytokines after decellularization. When applied in a rodent model of abdominal adhesions, decellularized AM holds promise in preventing adhesion formation. Further *in vivo* and *in vitro* studies comparing the effectiveness of decellularized AM to commercially available anti-adhesions products are currently underway.

# Amnion extracellular matrix derived hydrogel - a novel stem cell delivery vehicle for regenerative medicine

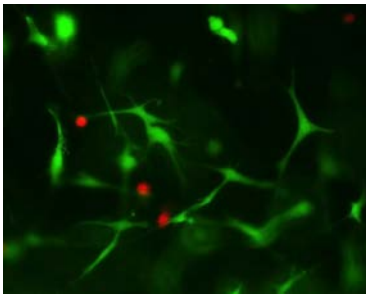
Volodymyr Ryzhuk, Xu-xin Zeng, Aijun Wang, Ph.D.

Surgical Bioengineering Laboratory, Department of Surgery, UC Davis Medical Center

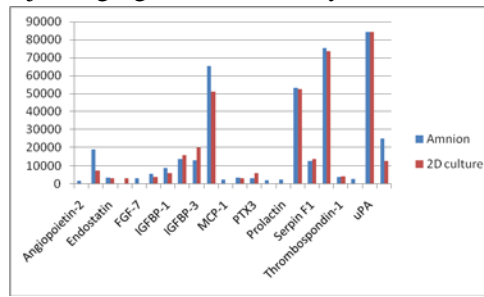
**Introduction:** Current regenerative strategies are limited by poor cellular survival, distribution and integration after transplantation in part due to the methods of stem cell delivery. Human amnion is easily accessible and its primitive, immunoregulatory and angiogenic nature indicates the potential applications in regenerative medicine. We developed a novel human-derived, decellularized, amnion extracellular matrix (ECM)-based stem cell delivery vehicle that supports stem cell survival and paracrine activity.

**Methods:** Amnion was dissected from term placenta and decellularized. Amnion-derived hydrogel was then produced and assessed for its biophysical properties (gelation kinetics, nanofiber structure and compressive modulus), and biochemical composition of ECM molecules (collagen, elastin, and GAGs). *In vitro* three-dimensional stem cell growth dynamics and angiogenesis related paracrine secretion were also characterized.

**Results:** Mechanical properties of amnion-derived hydrogel can be manipulated by changing its concentration. Preliminary results demonstrate that this scaffold supports stem cell growth and proliferation and may enhance secretion of major angiogenesis related cytokines.



**Figure 1.** Placenta derived mesenchymal stem cells viability in hydrogel was assessed using Molecular Probes Live/Dead fluorescent assay kit



**Figure 2. Stem cell cytokine secretion.** Paracrine activity of placenta derived mesenchymal stem cells grown in 3D hydrogel or 2D monolayer was detected via Human Angiogenesis Cytokine Array.

**Conclusion:** Human amnion-derived hydrogel holds great promise for stem cell delivery and other regenerative medicine applications.

## Body Image & Quality of Life: Changes with Gastric Bypass Surgery & Body Contouring

Patel NB, Gunther S, Song, P, Li C-S, Kludt NA, Lee CYG, Patel KB, Ali MR, Wong MS.  
Plastics, Bariatrics

### Introduction:

Bariatric surgery leads to massive weight loss changes that patients may not anticipate and can affect expectations; studies are lacking that evaluate body image and quality of life as patients undergo bariatric surgery and body contouring. We examined these effects and their durability.

### Method:

A prospective, 2 year experience followed patients who underwent bariatric surgery; questionnaires were given preop and at 6, 12, and 24 months postop. The MBSRQ is an inventory of body image, with sub-scores of Appearance Evaluation, Appearance Orientation, Body Area Satisfaction, Overweight Preoccupation, and Self-classified Weight. We used the SF-36 to assess quality of life; repeated ANOVA F-tests evaluated mean survey scores.

### Results:

Prior to bariatric surgery, 121 patients were surveyed; 8 patients surveyed 6 month follow up; 16 patients at 12 months; and 4 patients at 24 months. Pre-operative AE improved across all time-points ( $p = 0.007$ ). AO improvements approached statistical significance ( $p = 0.058$ ). BASS demonstrated significant improvements ( $p = 0.020$ ). There was no decrease in OP scores ( $p = 0.809$ ). SW scores decreased across all time points ( $p = 0.001$ ). SF-36 scores progressively increased ( $p = 0.002$ ).

Table 1. MBSRQ

	Pre-op	Postop 6 mo.	Postop 12 mo.	Postop 24 mo.
AE	2.12 [2.01, 2.23]	2.50 [1.87, 3.31]	2.90 [2.43, 3.38]	2.82 [1.59, 4.05]
AO	3.40 [3.29, 3.51]	3.30 [3.00, 3.61]	3.77 [3.47, 4.08]	4.04 [3.52, 4.56]
BASS	2.40 [2.32, 2.47]	2.85 [2.39, 3.30]	2.73 [2.35, 3.11]	2.75 [1.75, 3.75]
OP	3.26 [3.13, 3.39]	3.22 [2.72, 3.71]	3.16 [2.84, 3.47]	3.00 [2.00, 4.00]
SW	4.70 [4.57, 4.83]	3.69 [3.10, 4.27]	3.84 [3.60, 4.09]	3.63 [2.54, 4.71]

Table 2. SF-36

	Pre-op (%)	Postop 6 mo. (%)	Postop 12 mo. (%)	Postop 24 mo. (%)
QOL	54.5 [51.3, 57.7]	74.8 [66.5, 83.2]	75.3 [64.1, 86.5]	76.7 [61.7, 91.7]

### Conclusion:

The MBSRQ demonstrates body image improvements and reduced overweight perceptions; the SF-36 inventory demonstrates durable quality of life improvements. Understanding body satisfaction as patients proceed from bariatric to body contouring surgery will assist clinicians in facilitating stable weight loss and optimal aesthetics.

## **Thirteen-year Review of Outcomes Relating to Pre-Hospital Traumatic Arrest in Children**

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UCDMC Department of Surgery, Trauma

**Introduction:** Pediatric patients can compensate for severe traumatic shock however once those compensatory mechanisms are exhausted, children have little physiologic reserve to sustain life. The purpose of this study is to evaluate the outcomes of children with pre-hospital traumatic arrest at a level I pediatric trauma center.

**Methods:** A retrospective review of all patients 18 years and under presenting to a level I pediatric trauma center under cardiopulmonary resuscitation (CPR) from January 1, 2002 to December 31, 2014 was conducted. The primary outcome was survival to hospital discharge. Secondary outcomes included survival after resuscitative thoracotomy (RT), effect of the duration of CPR on survival, and the return of spontaneous circulation (ROSC) after arrival in the emergency department (ED).

**Results:** Out of 11,273 pediatric trauma activations over a 13-year period of time, 51 (0.4%) presented under CPR. Thirty-six patients (71%) suffered from blunt trauma and 15 sustained penetrating injuries. Eight children underwent resuscitative thoracotomy. Ninety-eight percent of patients died from their injuries, including all eight patients who underwent RT. There were 13 patients who had return of spontaneous circulation after arrival to the ED with only one patient surviving to hospital discharge. This patient died less than one year after injury, secondary to complications of anoxic brain injury. Duration of CPR did not affect the likelihood of survival.

**Conclusion:** This 13-year retrospective review demonstrates the dismal mortality rate of pediatric patients who present to a level I trauma center under CPR. Furthermore, RT provides no additional survival benefit. The inability to save these children warrants re-evaluation and development of pre-hospital traumatic arrest protocols specific for children.

## **The 4T score for heparin induced thrombocytopenia in burn patients: does HITting the target help select patients for testing?**

P Kwan, N Tran, R Gosselin, S Sen, D Greenhalgh, T Palmieri  
Division of Burn Surgery

**Introduction:** Burn patients often receive venous thromboembolism heparin chemoprophylaxis, which can result in heparin-induced thrombocytopenia (HIT). Burn patients also frequently have transient thrombocytopenia, making HIT diagnosis problematic. In critically ill patients the 4T score predicts the pretest probability of HIT, and an anti-PF4 antibody test is used as an initial screen. We hypothesized that the 4T score and anti-PF4 antibody tests would be of low utility in burn patients.

**Methods:** A retrospective chart review was conducted for all adult patients with burns admitted to a single burn center from 2009 to 2013. Study variables included demographics, injury characteristics, medical treatment, and test results. The 4T score was calculated, and anti-PF4 antibody tests were performed on a separate subset of burn patients.

**Results:** There were 573 study patients. Admission platelet counts were similar between all 4T score groups, but those with high scores had significantly larger burns than intermediate/low scores ( $43.6 \pm 2.8\%$  versus  $14.7 \pm 0.6\%$ ) ( $p < 0.001$ ), and a significantly higher incidence of inhalation injury than intermediate/low scores ( $40.3 \pm 5.8\%$  versus  $8.0 \pm 1.3\%$ ) ( $p < 0.001$ ). Using the 4T pretest 1.6% had low scores, 84.5% had intermediate scores, and 14.0% had high scores. Maximum 4T scores occurred on day 5. Of those with a high 4T score, significantly more were on heparin (60%) than dalteparin (20%) ( $p < 0.001$ ), 8% had a diagnosis of HIT based on positive anti-PF4 antibody tests, and 89.1% had a return of platelets to admission levels  $8.7 \pm 0.3$  days post nadir without a change in therapy.

**Conclusion:** Platelet variability following burn injury leads to intermediate and high 4T scores for most burn patients in the absence of HIT, limiting the utility of this tool in this subpopulation. Anti-PF4 antibody HIT testing can often be falsely positive in burn patients.

## Older Patients Derive Greater Benefit from Adjuvant and Neoadjuvant Radiotherapy in Diverse Solid Malignancies

NK Yuen<sup>1</sup>, CS Li<sup>2</sup>, AM Monjazeb<sup>3</sup>, D Borys<sup>4</sup>, RJ Bold<sup>1</sup>, RJ Canter<sup>1</sup>

<sup>1</sup>UC Davis, Department of Surgery, Surgical Oncology

<sup>2</sup>UC Davis, Department of Public Health Sciences, Biostatistics

<sup>3</sup>UC Davis, Department of Radiology

<sup>4</sup>UC Davis, Department of Pathology

**Introduction:** Radiation therapy (RT) is a standard component in the multimodality management of numerous solid malignancies, although increasing studies are focusing on subpopulations that selectively benefit from this modality. We hypothesized that the effects of RT would be influenced by patient age across various cancer types, including sarcoma, breast, rectal, esophageal, and lung cancers.

**Methods:** Using SEER (1990-2011), we identified 959,731 adult patients (>18) with selected non-metastatic solid malignancies undergoing surgery with or without RT. Multivariable analyses and Cox PH were used to examine the effect of multiple variables on overall (OS) and disease-specific survival (DSS).

**Results:** Cancer type was 70.0% breast, 11.9% rectal, 1.2% esophageal, 13.5% lung, and 3.4% sarcoma. 43.2% of patients received either adjuvant (39.0%) or neoadjuvant (4.2%) radiotherapy in addition to surgery. With the exception of lung cancer (OS HR 1.12; 1.19-1.23), radiation was associated with improved survival in patients of all ages with breast cancer (OS HR 0.72; 0.71-0.73), rectal cancer (OS HR 0.81; 0.79-0.83), esophageal cancer (OS HR 0.83; 0.75-0.91), and sarcoma (OS HR 0.63; 0.56-0.70). These positive effects were amplified in elderly patients ( $\geq 65$  years old) with breast cancer (OS HR 0.66; 0.65-0.66) and rectal cancer (OS HR 0.74; 0.72-0.76).

**Conclusion:** RT was broadly associated with superior oncologic outcome compared to surgery alone among patients undergoing surgical resection for multiple solid malignancies. The positive effect of RT was exaggerated in older patients with breast and rectal cancer, suggesting an age-related selectivity of RT. Further investigation into the etiology of these associations is indicated.

## **Parathyroidectomy in dialysis patients: What is the risk?**

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Division of Surgical Oncology

**Introduction:** Patients with chronic kidney disease on dialysis commonly develop secondary and tertiary hyperparathyroidism, but are often not referred for surgical evaluation because of the belief that the risks of a parathyroidectomy are prohibitively high. This study uses the American College of Surgeons National Surgical Quality Improvement Project (ACS NSQIP) database to better quantify the risk of parathyroidectomy in patients on dialysis.

**Methods:** This is a retrospective study of patients undergoing parathyroidectomy in the ACS NSQIP database from 2005-2011. Complications for dialysis vs. non-dialysis patients were compared using univariate and multivariate logistic regression. Outcomes were also compared between patients undergoing parathyroidectomy and arteriovenous fistula creation among dialysis patients to understand the relative risk between the two procedures.

**Results:** 20,089 patients underwent parathyroidectomy. Of these, 1,330 (6.6%) were on dialysis. The incidence of death was higher for patients on dialysis (1.2% vs 0.1%,  $p<0.001$ ). On adjusted analysis, dialysis was associated with increased odds ratio of death (OR 13.12,  $p=0.002$ ). However, patients on dialysis did not have increased risk of death when undergoing parathyroidectomy compared to patients undergoing arteriovenous fistula creation ( $p=0.917$ ). Dialysis patients had an increased incidence of complications (7.1% vs. 1.4%,  $p<0.001$ ), but on multivariate logistic regression, dialysis did not increase the odds of adjusted morbidity ( $p=0.291$ ).

**Conclusion:** Patients on dialysis who undergo parathyroidectomy have a similar risk of complications, but are at an increased risk of death compared to patients not on dialysis. However, the risk is not increased in patients undergoing parathyroidectomy versus arteriovenous fistula creation.

## Determinants of value in surgical care of common yet complex procedures

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Department of Surgical Oncology

**Introduction:** Efforts to improve value in medicine include optimizing quality of care (QOC) or reducing hospital costs. We identified determinants of value across four complex procedures to further improve value of surgery.

**Methods:** Data from the University HealthSystem Consortium for patients hospitalized after elective pancreaticoduodenectomy, colectomy, AAA repair, and esophagectomy from 10/2010-6/2014 was obtained. A quality index score (QIS) was developed by totaling rank score (by quintiles) of five variables associated with optimal outcomes: incidence of postoperative complications, length of stay, 30-day readmission rate, mortality rate, and hospital volume. Value for each surgical procedure was defined as hospital-based QIS (5-25 points) divided by mean hospital charges.

**Results:** The majority of high value centers for each procedure were top performers in only 1-2 of 5 QOC indicators (Table), though rarely a low performer in any category. Low value centers consistently ranked as a low performer in multiple categories, though occasionally were high performers in 1 category (Table). Across all procedures, high-value centers had statistically lower charges than low-value centers ( $p < 0.0001$ ). Lastly, 75% of high value centers were identified as high value in only 1 out of 4 procedures.

**Conclusion:** While superior outcomes are a predictor of value, even low-value centers occasionally achieved high QIS for isolated QOC variables, reflecting the independent importance of charges in value. Furthermore, achieving excellence in one procedure does not necessarily transfer to high performance in other procedures.

High QOC#	High Value Centers				Low Value Centers			
	Whipple	Esophagectomy	Colectomy	AAA	Whipple	Esophagectomy	Colectomy	AAA
0	47%	31%	64%	57%	10%	0%	0%	6%
1	40%	38%	27%	29%	20%	8%	8%	20%
2	13%	27%	7%	14%	37%	62%	62%	26%
3	0%	4%	2%	0%	27%	19%	19%	
4	0%	0%	0%	0%	6%	12%	12%	11%
5	0%	0%	0%	0%	0%	0%	0%	0%

**Table.** Number of top performances out of 5 quality of care indicators for high and low-value centers for each of the four surgical procedures analyzed.

26th Annual Department of Surgery  
Research Symposium

**Poster Presentations**

## Isolation and enrichment of chorionic villus-derived myogenic cells from early gestation placentas

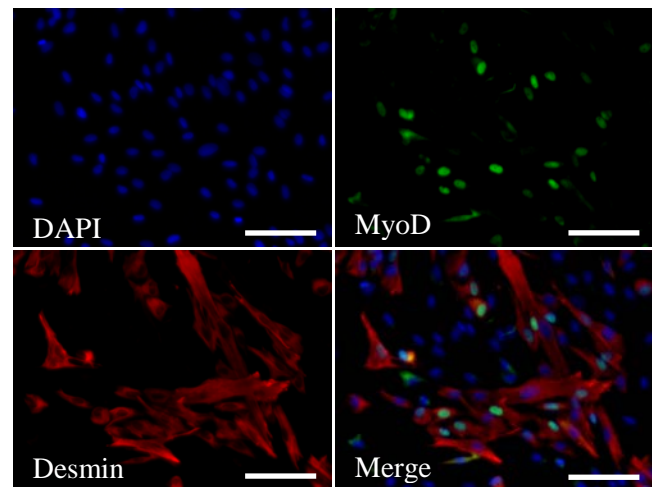
Lee Lankford, M.A.<sup>1</sup>, Priya Kumar, Ph.D.<sup>1</sup>, Connor Long<sup>1</sup>, Aijun Wang, Ph.D.<sup>1</sup>, Diana Farmer, M.D.<sup>1</sup>  
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**Introduction:** The chorionic villi of the human placenta are a promising source of fetal stem cells for regenerative medicine. A distinct subpopulation of cells displaying myogenic characteristics can be isolated from early gestation chorionic villus tissue. When enriched, these cells can be seeded onto aligned polymer nanofiber scaffolds to create a bioengineered muscle patch for in vivo tissue engineering.

**Methods:** Myogenic placental stem cells (MPSCs) were isolated from second trimester chorionic villi (GA 12-24 weeks). Cells were characterized for myogenic protein expression via immunocytochemistry, and enriched via magnetic micro-bead sorting. Myogenic-enriched cultures were then seeded onto aligned nanofiber scaffolds and assessed for mature muscle protein expression and cell alignment via immunocytochemical staining.

**Results:** Immunocytochemical staining of cells revealed that cultures contain a subpopulation of myogenic cells that are positive for transcription factor MyoD, and intermediate filament protein Desmin (Figure 1). Using CD56 micro-bead sorting it was possible to enrich the culture for MPSCs and increase the overall percentage of Desmin-positive cells when compared to the CD56-depleted population. Seeding experiments show that MPSCs cultured on aligned scaffolds were capable of adhering and aligning with the polymer fibers.

**Conclusion:** These results are very promising, and indicate that MPSCs integrate with the scaffold in the manner hypothesized. Before the completion of this study, we hope to generate myogenic cell-seeded scaffolds that closely mimic skeletal muscle in tissue structure and phenotype.



**Figure 1:** Myogenic placental cells are positive for transcription factor MyoD and intermediate filament protein Desmin. Scale bars = 100µm.

## Imported Kidney Grafts from Non-Conventional Adult Deceased Donors Can Successfully Increase Access to Transplantation for Elderly Patients

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Transplant Surgery

**Introduction:** The new kidney allocation policy assigns highest priority to patients with longest expected post-transplant survival. Elderly patients with end stage renal disease will be most disadvantaged. Innovative strategies to expand access to kidney transplantation for this candidate group are needed.

**Methods:** Objective was to assess whether imported grafts from non-conventional adult deceased donors (NCDDs) can increase access to renal transplantation for patients  $\geq 60$  years old transplanted 1/2008-12/2013. We defined the following as NCDD: expanded criteria (ECD), donation after cardiac death (DCD), acute kidney injury (AKI), Hep-C or Hep-B core antibody positive or cold ischemia time (CIT)  $>40$  hours. Outcomes of grafts from all adult donors recovered by our local organ procurement organization (OPO) were compared to those of NCDD grafts imported from outside our OPO's service area.

### Results:

	DCD (%)	ECD (%)	AKI (%)	CIT $>40$ (%)	HepB (%)	HepC (%)
Local (n=132)	8	17	11	4	5	1
Import (n=180)	22	41	28	20	9	4
P-value	0.005	0.0001	0.0004	0.0001	0.14	0.20

*Table 1: Graft; donor characteristics*

	Graft Survival (%)		Patient Survival (%)		DGF (%)	LOS (d, mean $\pm$ SD)	Wait List (d, mean $\pm$ SD)
	1 yr	5 yr	1 yr	5 yr			
Local (n=132)	97	89	98	91	8	6.9 $\pm$ 3.7	858 $\pm$ 48
Import (n=180)	89	81	97	89	32	8.2 $\pm$ 10.4	619 $\pm$ 36
P-value	0.03		0.55		0.0001	0.07	0.0001

*Table 2: Graft; recipient outcomes (DGF, delayed graft function; LOS, length of stay)*

**Conclusion:** Despite a significantly more challenging donor profile imported NCDD grafts afforded recipients the same patient survival benefit as local kidneys. Imported kidneys can be an important organ source for elderly recipients. Broader implementation of this organ acceptance strategy would reduce wait time for elderly patient and may help decrease national kidney graft discard rates.

## Prospective Observational Study of Point-of-care Creatinine in Trauma

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Division of Trauma and Acute Care Surgery

**Introduction:** Renal function evaluation with creatinine is vital in trauma as baseline renal function can guide resuscitation. Trauma patients are at risk for renal dysfunction from hypovolemia or urologic injury. Laboratory creatinine levels are often available only after contrast has been administered for imaging. Contrast-induced nephropathy risk is increased in those with preexisting renal dysfunction. A portable, quick point-of-care device may be beneficial to guide initial resuscitation and workup of stable patients with low energy mechanisms. The Stat Sensor Point-of-Care Whole Blood Creatinine Tester by Nova Biomedical has been shown to be accurate in vitro and in limited clinical use. The purpose of this study is to determine if the StatSensor can be used in the trauma setting.

**Methods:** Forty major trauma patients will be enrolled in a prospective observational study over 10 weeks. Upon arrival at the Emergency Department, a drop of blood will be taken with the standard diagnostic lab draw, and used for point-of-care creatinine determination. The point-of-care creatinine value and lab value will be obtained for comparison. Elapsed time to point-of-care value and lab value availability will be recorded as well as time of arrival at the CT scanner if applicable.

**Results:** Twenty of a planned 40 patients have been enrolled to date. Mean creatinine values were similar, at  $0.93 \pm 0.24$  on the StatSensor compared to  $0.99 \pm 0.33$  from the laboratory, for a mean bias of 0.055 ( $p=0.27$ ). The point-of-care value was available in  $7 \pm 4$  minutes compared to  $72 \pm 23$  minutes for the laboratory value, for a difference of 65 minutes ( $p<0.0001$ ).

**Conclusion:** The StatSensor device reports similar creatinine values to the hospital laboratory and works significantly faster. During this study it has been successfully implemented into the standard trauma workflow. If the final results show the device to be accurate and efficient, it should be implemented into the trauma algorithm to guide resuscitation and workup prior to contrast injection of stable patients with low energy trauma and increased risk for underlying renal dysfunction.

## **Predictors of Residual Disease after Unplanned Excision of Unsuspected Soft Tissue Sarcomas**

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<sup>1,2,3,5,10</sup> Surgical Oncology; <sup>4</sup> Biostatistics; <sup>6,7</sup> Radiology; <sup>8</sup> Orthopedic Surgery

**Introduction:** Unplanned excision of soft tissue sarcomas is a quality of care issue, because re-excision exposes patients to potential morbidity. Since not all patients harbor residual disease, we sought to determine predictors of residual disease.

**Methods:** We identified 76 patients from a prospectively-maintained academic database (1/2008 – 1/2014) diagnosed with primary STS after unplanned excision. We used univariable and multivariable analysis to evaluate predictors of residual STS, sensitivity/specificity of interval magnetic resonance imaging (MRI), and predictors of oncologic outcome.

**Results:** Mean age was 52 years. 63.2% were male. 50% had fragmented excision. 81.6% underwent repeat excision. 70.3% harbored residual disease. MRI and fragmented excision were significant predictors of residual disease (Odds ratio 10.588, 95% Confidence Interval 2.136-52.490, P=0.0039 and Odds Ratio 3.611, 95% Confidence Interval 1.092-11.944, P=0.0354, respectively). Tumor size predicted distant recurrence and overall survival (Hazards Ratio 1.161, Confidence Interval 1.023-1.316, P=0.0203 and Hazards Ratio 1.198, Confidence Interval 1.015-1.413, P=0.0329, respectively). Sensitivity and specificity of MRI for predicting residual disease were 55.5% (95% Confidence Interval 42.1%-73.7%) and 88.2% (Confidence Interval 63.5%-98.5%), respectively.

**Conclusions:** 70.3% of patients referred to academic centers after unplanned excision harbor residual soft tissue sarcoma. Although interval MRI and fragmented excision appear to be the most significant predictors of residual disease, accuracy and negative predictive value of MRI remain low.

## **Inability to Return Home and Hospital Readmissions are Frequent among Patients with Disseminated Malignancy Undergoing Surgical Intervention**

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**Introduction:** Although surgical intervention for patients with disseminated malignancy (DMA) is high risk, few studies have examined the impact of surgery on discharge disposition and readmission rates for these patients. We sought to evaluate the rates of prolonged hospitalization (prLOS), hospital readmission, and discharge to nursing/rehabilitation (N/R) facilities, hypothesizing that these endpoints would be high.

**Methods:** We queried the American College of Surgeons National Surgical Quality Improvement Program from 2011-2012. Excluding patients undergoing a primary hepatic operation, we identified 18,111 patients with DMA. Data were analyzed using descriptive statistics, logistic and linear regression.

**Results:** Patients with DMA represented 2.1% of all NSQIP procedures during the study period. Among DMA patients, the most frequent operations were non-general surgery (combined ENT, CT, and GYN: 29.6%), bowel resections (25.1%), and other gastrointestinal operations (18.3%). Overall 30-day morbidity and mortality was 24.5% and 7.7% respectively, including 6.0% return to OR. Mean LOS was 9 days (median 6, range 0-380). 72.4% experienced prLOS. Overall, 78.8% of patients were discharged to home, 16.3% were transferred to N/R facility, and 14.3% of patients were readmitted within 30 days. 64.7% of those discharged to N/R facility had no recorded complication. On multivariate analysis, increasing age, poor functional status, elevated WBC, decreased albumin, emergency operation, postoperative morbidity, reoperation, and longer LOS predicted discharge to N/R facility ( $p < 0.01$ ).

**Conclusion:** Among patients with DMA, rates of discharge to N/R facility, prLOS, and hospital readmission are high, especially among patients undergoing bowel resection. These results highlight the impact of surgery on quality of life among patients with incurable cancer.

## **Injury-related death disparity in children under age five in low-income countries: An analysis of World Health Organization data**

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Division of Burn Surgery

**Introduction:** In the last 10 years there has been increasing attention given to injury as cause of childhood death, as the relative contribution of injury to mortality has increased. We hypothesize that childhood mortality due to injury is highest in the poorest countries and that the rate of injury related mortality has not changed since the year 2000.

**Methods:** We used World Bank country income groups (quartiles) and the WHO dataset for injury deaths in newborns (0-27 days old), and children (1-59 months old) from 2000-2012. Data was analyzed by analysis of variance (ANOVA) and linear regression modeling using R-statistical package. All death rates are deaths per 1000 live births. All mean values are mean  $\pm$  standard deviation. Statistical significance was set at  $p < 0.05$ .

**Results:** From 2000 to 2012 there was only a small but non-significant world-wide decrease in injury related death rates (2.3 vs. 1.7,  $p=0.99$ ). High-income countries (HIC) had a significantly lower death rate ( $0.46 \pm 0.3$ ) than low income (LIC) ( $3.4 \pm 2.2$ ,  $p=0.0000000$ ), low-middle income countries (LMIC) ( $2.3 \pm 1.4$ ,  $p=0.0000002$ ) and upper-middle income countries (UMIC) ( $1.6 \pm 1$ ,  $p=0.0036$ ). On analysis by linear regression of injury death rates by region, LIC ( $B=2.9$ ,  $p < 2 \times 10^{-16}$ ), LMIC ( $B=1.8$ ,  $p=1.8 \times 10^{-8}$ ) and UMIC ( $B=1.1$ ,  $p=0.0004$ ) are significantly associated with higher injury related death rates. Additionally, while injury related death rates decreased, from 2000 to 2012, by 42% in HIC ( $0.6 \pm 0.5$  to  $0.35 \pm 0.3$ ), death rates only decreased by 16% in LIC ( $3.7 \pm 2.8$  to  $3.1 \pm 2.4$ ). By age groups, newborns and children in LIC suffered significantly higher death rates ( $0.4 \pm 0.1$ ,  $p=0.0000000$ , and  $4.7 \pm 0.3$ ,  $p=0.0000000$  respectively) than their counterparts in HIC ( $0.04 \pm 0.01$  and  $0.42 \pm 0.3$  respectively).

**Conclusion:** There was no significant change in worldwide childhood annual mortality due to injury from 2000-2012. Low-income countries continue to bear the burden of world injury-related deaths in children under five. Efforts should be targeted at identifying the injury mechanisms causing these deaths in order to develop country and region specific preventative measures.

## **The Impact of Radiotherapy on Rates of Surgical Site Infection in Patients with Rectal Cancer: Benchmarks for Comparison**

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**Introduction:** Radiation therapy (RT) is a standard component in the multimodality management of rectal cancer. Although prior RT is widely considered a risk factor for poor wound healing and surgical site infection (SSI), limited multi-center data are available, particularly for patients with rectal cancer. We sought to evaluate the effect of RT on the incidence of SSI in a national database of patients with rectal cancer.

**Methods:** Using the NSQIP database (2005-2011) we identified 15,487 adult patients (>18) with a diagnosis of rectal cancer (ICD-09 154.0-154.1) undergoing surgery with or without RT. We evaluated patient demographics, comorbidities, and treatment-related variables on the rates of superficial and deep SSI. Logistic regression was used to calculate odds ratios (OR) using multivariable logistic regression analysis.

**Results:** Mean age was 62.1, 59.5% of patients were male, and 75.0% of patients were white. 27.2% of patients received preoperative RT, 9.3% chemotherapy, and 6.8% received both. Overall, the incidence of SSI was 15.1%, with 8.7% superficial, and 7.2% deep/organ space. On multivariable logistic regression analysis, gender, BMI, diabetes, smoking status, ASA, return to OR within 30 days, and RT predicted higher risk of both superficial and deep SSI. The Odds Ratio (OR) for radiotherapy was 1.37 ( $p<0.01$ ) for all SSI, 1.34 ( $p<0.01$ ) for superficial SSI, and 1.38 ( $p<0.01$ ) for deep SSI. Conversely, chemotherapy was associated with an OR 0.8 ( $p=0.036$ ) for superficial SSI.

**Conclusion:** Preoperative RT is associated with a higher risk of SSI (superficial and deep) in patients undergoing definitive surgery for rectal cancer. These nationwide data serve as current benchmarks for comparison as novel surgical techniques, tailored approaches to patient selection, and quality improvement projects are implemented in the multimodality management of patients with rectal cancer.

## The Adrenal Incidentaloma: Are Patients Managed According to the Guidelines?

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**Introduction:** Adrenal incidentalomas (AIs) are masses discovered on imaging done for unrelated reasons, and are found on 4% of computed tomography (CT) scans. Because 15% of AIs are hormonally active or malignant, the American Association of Clinical Endocrinologists (AACE) and American Association of Endocrine Surgeons (AAES) have published guidelines recommending that patients with AIs have further evaluation. We hypothesize that patients with AIs are rarely evaluated according to these guidelines, thus the purpose of this study was to quantify adherence to the recommendations.

**Methods:** 5063 consecutive abdominal CT scans ordered by PCPs in our health system from 01/2011 to 01/2014 were surveyed. We reviewed charts of patients with AIs for assessment of hypercortisolism, hyperaldosteronism, catecholamine excess by hormonal evaluation, and cancer by further imaging.

**Results:** 87 (1.7%) patients had AIs. 5 (5.7%) patients underwent an initial hormonal and radiologic evaluation that met the AACE/AAES guidelines. 3 (3.4%) patients had annual re-evaluation of hormonal status, and 35 (40.2%) patients had further imaging to assess for malignancy. 20 (23%) patients had either serum or urine metanephrines, 9 (10.3%) had a dexamethasone suppression test, and 8 (18.2%) hypertensive patients had a plasma aldosterone concentration:renin activity ratio.

Table 1: Components of Evaluation

	F/U Imaging n=87	PAC:PRA		Dex-suppression		Metanephrine		Complete (n=87)
		Initial n=44	F/U n=44	Initial n=87	F/U n=87	Initial n=87	F/U n=87	
% Complete	40.2	18.2	4.5	10.3	3.4	23	3.4	3.4

*F/U, follow-up; PAC:PRA, plasma aldosterone to renin activity ratio; Dex, dexamethasone*

**Conclusion:** Few patients with AIs found on abdominal CTs ordered by PCPs undergo an appropriate evaluation. This may lead to underdiagnosis of potentially treatable subclinical hypercortisolism, hyperaldosteronism, pheochromocytomas and adrenocortical cancer. Improved education and outreach efforts for PCPs are needed to improve the care of patients with AIs.

## **Sustainable Humanitarian Surgical Care in a Warzone: Breast Disease Treatment in a US Military Hospital in Afghanistan**

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Lucas P. Neff, MD; Division of General Surgery, UCDMC; US Air Force  
Daniel X. Choi, MD; US Air Force

**Introduction:** This prospective study evaluates pathology, treatment, and survival for patients undergoing breast surgery at a single US military hospital in Afghanistan to determine the feasibility of achieving US National Comprehensive Cancer Network (NCCN) guideline therapy in a warzone.

**Methods:** All Afghan civilians undergoing breast surgery during 21 months at a US military hospital were included. Two US military surgeons evaluated and treated all patients. Data on gender, age, presentation, menopausal status, family history, pathology, surgery, adjuvant treatment, outcomes, and 10-year-overall survival estimates were calculated.

**Results:** From January 2013-September 2014, 12 women underwent breast surgery. Seven (58%) patients had carcinoma and underwent modified radical mastectomy (n=5), lumpectomy (n=1), or excisional biopsy (n=1). Six patients (86%) received all necessary surgery. Four patients (57%) were estrogen receptor-positive, 3 (43%) were progesterone-receptor positive, and 3 (43%) were HER2/NEU positive. One patient (14%) was triple-negative. The 4 candidates for adjuvant endocrine therapy were given tamoxifen. Patients with cancer were followed a median of 241 days (range 112-298). At time of follow-up, five (71%) had no evidence of disease. Surgical excision offered a median estimated 10-year-overall survival of 25.6%; adjuvant endocrine therapy with tamoxifen further increased survival by 6.7%. One patient with DCIS was the only patient who received all care recommended by NCCN guidelines.

**Conclusion:** The majority of patients in this series did not receive treatment as recommended by NCCN guidelines. However, treatment offered survival benefits for all patients. Understanding local resources and performing definitive pathologic diagnoses are necessary to provide effective humanitarian oncologic care in austere environments.

## **Clinical Outcomes Following Lower Extremity Soft-Tissue Reconstruction with Pedicle Flaps: A Review of 978 Cases**

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**Introduction:** This study uses the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) database to review clinical outcomes of such a soft-tissue reconstruction based on generated multi-center outcome data.

**Methods:** The 2005-2013 ACS-NSQIP databases over an eight-year period were reviewed, identifying encounters by the CPT code for lower extremity soft-tissue reconstruction with pedicled flaps. Complications were characterized into three categories: thrombotic complications, wound complications, and complications requiring reoperation. Reoperation data were only available in the 2012 and 2013 datasets. Pre-operative risk factors were also analyzed for an association with increased rates of thrombotic complications, wound complications, and reoperation using Fischer's Exact Test.

**Results:** During the study period from 2005-2013, 978 lower extremity pedicled flaps were performed. The incidence of thrombotic complications was 1.9%. The incidence of wound complications was 11.3% (5.6% superficial infections, 2.6% deep wound infections, and 3.1% wound dehiscence). During the study period from 2012-2013, 423 lower extremity pedicled flaps were performed. The reason for reoperation was identified by CPT code. The incidence of reoperation for a complication was 5.6%. Complications requiring reoperation included hematoma, seroma, infection, dehiscence, and graft failure. With respect to risk factor analysis, the only association to achieve significance was between quadriplegia or paraplegia and increased reoperation rates. However, as only three patients in the collection period had this risk factor, the generalizability of this result may be limited.

**Conclusion:** This study characterizes clinical outcomes following lower extremity soft-tissue reconstruction with pedicled flaps using a large multicenter dataset. The overall complication rates after pedicled flap reconstruction in the lower extremity remain relatively low and the incidence of reoperation for a complication is also relatively low. Data derived from this study can be used to augment preoperative decision-making and as a benchmark to measure institutional outcomes

## **Approaches to distal upper-extremity trauma: A comparison of plastic, orthopedic, and hand surgeons in academic practice**

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**Introduction:** Hand trauma call duties at academic centers are split among plastic, orthopedic, and hand surgeons. Our aim was to characterize and compare the clinical experience of these three groups in addressing traumatic distal upper extremity injuries (utilizing the Faculty Practice Solutions Center dataset).

**Methods:** Annual data for CPT defined procedures related to traumatic injuries of the nail-bed, finger, hand, wrist, and forearm performed by plastic, orthopedic, and hand surgeons during calendar years 2010 to 2013 were included in the study.

**Results:** From 2010 to 2013, the experience of hand surgeons was consistently greater than that of plastic surgeons and general orthopedic surgeons across all categories. Injuries of the nailbed, were repaired more frequently by plastic surgeons than orthopedic surgeons. Fractures and dislocations involving the phalanx, and metacarpal were repaired equally by both groups; however, plastic surgeons employed mostly percutaneous and open methods (83% of repairs), while orthopedic surgeons utilizing mostly closed reduction (59% of repairs), splinting, and casting. Fractures and dislocations involving the carpal bones, radius and ulna were more frequently repaired by orthopedic surgeons, while tendon repairs in all segments were performed more frequently by plastic surgeons.

**Conclusion:** A large degree of variation exists in the treatment of distal upper extremity injuries, based on the specialty service. Hand surgeons, not surprisingly, have the most robust clinical experience, while plastic surgeons and orthopedic surgeons each display varying strengths and weaknesses, perhaps a consequence of their respective training.

## **Differing Rates of Severe Flame and Electrical Injury in Severely Burned Children from Mexico and the United States**

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UC Davis Department of Burn Surgery

**Introduction:** While scald burns are the most common burn in children in the United States (US), we hypothesized that flame and electrical injuries were more common in children from Mexico and result in increased morbidity. Shriners Hospital for Northern California provides an opportunity to assess the etiology and clinical course of burns in children from separate countries in a common environment.

**Methods:** Retrospective data was reviewed on children 0-21 years with burns involving total body surface area (TBSA) of 20% or greater, admitted to SHNC from 2006-2014. Outcomes included mortality, TBSA, type of burn, length of hospital stay (LOS), ventilator dependent time (VDT), number of operations, and need for blood components. Analysis was completed using R-statistical package ([www.r-project.org](http://www.r-project.org)). The study was approved by the institutional review board of the SHNC.

**Results:** Of 382 patients 66% were from Mexico and 34% from the U.S. TBSA ( $36\pm 19\%$  vs.  $34\pm 23\%$ ,  $p=0.4$ ) and inhalation injury (21% vs. 16%,  $p=0.29$ ) did not differ. There was no difference in LOS ( $p=0.33$ ), VDT ( $p=0.78$ ), operations ( $p=0.18$ ), or the amount of blood ( $p=0.9$ ) or FFP ( $p=0.4$ ) transfused. Mexican children had a higher incidence of flame burns (62% vs 49%,  $p=0.001$ ) and a higher incidence of electrical injuries (6.7% vs. 0%,  $p=0.0001$ ). Patients with flame or electrical burns had higher TBSA ( $p<0.0001$ ), longer LOS ( $p=0.0008$ ), and required more operations, and blood product resuscitation.

**Conclusion:** Electrical and flame burns are a significant source of injury among children in Mexico, and carry increased morbidity. Future efforts should address these mechanisms, and assess specifically in what regions these burns are most evident and whether specific interventions could be targeted to these environments and populations.

## **Burn Care in the 1800s**

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**Introduction:** A history of burn care with the objective of describing key advancements in the study and treatment of burns in the 1800s.

**Methods:** Review of primary and secondary sources and their translations of ancient to present burn care manuscripts.

**Results:** Prior to the 1800s burn care consisted of alterations of poultices and oils placed over acute burns in the hope the patient would survive. The 1800s showed the discoveries of the Curling and Marjolin's ulcers as well as the first understanding of inhalation injury and advancements in skin grafting leading to further understanding of the disease process.

**Conclusions:** The 1800s show a wide range of both understanding and misinterpretation of the pathophysiology and treatment of burns.

# Deep Inferior Epigastric Artery Perforator Flap Breast Reconstruction without Microsurgery Fellowship Training: A Comparison of our results with the Literature

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**Introduction:** The purpose of this study is to examine whether deep inferior epigastric artery perforator flap breast reconstruction can be performed safely without formal microsurgical fellowship training.

**Methods:** A total of 34 flaps in 28 patients were performed between August 2010 and August 2013. The occurrence total flap necrosis, partial flap necrosis, infection, hematoma/seroma, donor site complications, venous occlusion, arterial occlusion, and fat necrosis were recorded. A meta-analysis of the literature was performed using search terms ‘DIEP’, and ‘deep inferior epigastric artery perforator’. The results in our series and meta-analysis were compared.

**Results:** Complications in our series are shown in **Table 1**. Among the published studies, 18 met our inclusion criteria. Rates of partial flap necrosis were significantly higher in our series compared to previous studies (14.7% vs. 1.6%)(P = 0.003). Rates of venous complications were marginally higher in our series than in previous studies, with an observed rate of 11.7% in our series and an estimated aggregate rate of 3.3% elsewhere (P = 0.057).

**Conclusion:** With proper training during plastic surgery residency deep inferior epigastric artery flap can be performed with acceptable morbidity and failure rates.

**Table 1.** Complications in our series

Total Flap Loss	1 (2.9%)
Partial Flap Loss	5 (14.7%)
Infection	1 (2.9%)
Hematoma/Seroma	3 (8.8%)
Donor Site	5 (18.5%)
Venous	4 (11.7%)
Arterial	1 (2.9%)
Fat Necrosis	0 (0%)
<b>Total (flaps)</b>	<b>11 (32.3%)</b>

## Peri Operative Laser Scar Therapy Protocol: A National Survey

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**Introduction:** Despite widespread use of lasers, there is no consensus regarding optimal pre and post procedure patient management. To gain insight into best practices, we polled colleagues to identify current practice trends.

**Methods:** An IRB approved online survey was distributed to 3,394 members of the American Society of Plastic Surgeons (ASPS). Each was emailed a brief message and a link to the survey. The survey consisted of 34 questions about peri-operative protocols for laser scar therapy. Results were analyzed using Excel (Microsoft Corporation, Redmond, WA, USA).

**Results:** 3,394 surveys were sent, 210 emails were returned as undeliverable, and 2 replied declining participation. Thirty-seven plastic surgeons responded. Eighty-seven percent filled out the survey in its entirety while thirteen percent were incomplete. The most commonly used laser types are Fractional CO<sup>2</sup> (42%), Pulsed Dye (42%), and Fractional Er:Yag (39%). Pre-procedure the majority of providers favored using oral antivirals (72%) and sunblock (67%), as well as oral analgesics (60%), topical analgesics (58%), moisturizers (54%) and hydroquinone (54%). Less commonly reported adjuvants included oral steroids (10%), oral antifungals (10%), and topical antifungals (7%). Post-procedure treatments included oral analgesics (96%), moisturizers (88%), oral antivirals (70%), and hydroquinone (54%). Less frequently oral antifungals (10%) and topical antifungals (7%). Additional comments included 1 report of silicone and 1 report of sun block use post operatively.

**Conclusion:** A survey of plastic surgeons revealed that the majority is using Fractional CO<sub>2</sub> (42%) and Pulsed Dye lasers (42%) to treat scars. The study verified that there is no consensus regarding peri operative therapy regimens. This suggests the need for experts in the field to propose consensus protocols to be used as guidelines. This survey offers plastic surgeons access to data about the most common peri operative laser scar therapy approaches. We will expand our study by polling dermatologists next.

## **Endogenous Retrovirus and Their Effects on Hypertrophic Scar Formation**

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**Introduction:** A hypertrophic scar is a raised, disfiguring, painful, itchy skin lesion that forms commonly after thermal injury. We hypothesize that persistent stress from burn wounds lasting more than 2-3 weeks leads to significant variability in human endogenous retrovirus activity, which is linked to post-burn inflammatory processes and modifies the wound-remodeling pathway involved in hypertrophic scar formation.

**Methods:** Skin will be collected from burn patients via punch biopsy during burn excision and grafting procedures, focusing on time periods of 8-12 days and 16-20 days post injury. RNA and DNA will be isolated and changes in genomic copy number and expression of a set of human endogenous retroviruses (HERV) will be characterized, sequenced and mapped to the reference human genome. Protein coding regions of selected HERVs will be cloned and evaluated for their effects on the inflammatory process.

**Results:** Currently we have enrolled 7 patients (5 males, 2 females) at UC Davis Medical Center and Shriners Hospitals for Children into the study, ranging from 13 to 52 years old. All have sustained more than 20% total body surface area thermal burns requiring excision and grafting. We will begin sample processing and evaluating HERV profiles once all time points have been collected.

**Conclusion:** Burn wounds that develop hypertrophic scars are expected to have similar genomic HERV patterns (type, copy number and position) when compared to the well-healed wound. These results may lead to a better understanding of the healing process and to personalized care of excessive scar formation.



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