

Department of Surgery



27th Annual Research Symposium

KEYNOTE SPEAKER

Lloyd E. Ratner MD, MPH, FACS

Director, Renal and Pancreatic Transplantation

Department of Surgery, Columbia University Medical Center



Presenting at Grand Rounds at 7:30am in LH #2222

“How to Innovate and Bring New
Ideas to Clinical Reality”

**Research Symposium to follow in LH#1222

April 19, 2016 / 9:00 a.m. - 4:30 p.m.

Medical Education Bldg., Lecture Hall 1222

UCDAVIS

HEALTH SYSTEM

With appreciation,
we wish to
acknowledge
Shriners Hospitals for
Children Northern
California's
support of the
27th Annual
Department of Surgery
Research Symposium.

27th Annual Department of Surgery Research Symposium
 April 19, 2016
 Medical Education Bldg., Lecture Hall 1222

7:30am – WELCOME KEYNOTE SPEAKER – Lloyd E. Ratner MD, MPH, FACS Director, Renal and Pancreatic Transplantation Department of Surgery Columbia University Medical Center “How to Innovate and Bring New Ideas to Clinical Reality”		
8:30am – OPENING REMARKS <u>Medical Education Bldg., Lecture Hall 1222</u> Diana L. Farmer, MD, FACS, FRCS Tina L. Palmieri, MD, FACS, FCCM		
ORAL PRESENTATIONS – SESSION I: Moderators: David Greenhalgh, Rebecca Stark		
8:45am	Randomized comparison of packed red blood cell-to-fresh frozen plasma transfusion ratio of 4:1 versus 1:1 during massive burn excision	L. Galganski
9:00am	A nanoparticle based drug delivery system for the treatment of infantile hemangiomas	H. Orbay
9:15am	A single nucleotide polymorphism results in increased activity of human glucocorticoid receptor	T. Green
9:30am	Seeding mesenchymal stromal cells on extracellular matrix significantly reduces infarct development	M. Robinson
15 MINUTE BREAK: 9:45am – 10:00am		
ORAL PRESENTATIONS – SESSION II: Moderators: Soman Sen, Aijun Wang		
10:00am	Radiotherapy enhances natural killer cell homing and function in canine bone and soft tissue sarcoma	J. Park
10:15am	Engineering bioactive vascular grafts with a novel ligand against $\alpha\beta3$ integrin to improve <i>in situ</i> endothelialization	D. Hao
10:30am	Ex-vivo normothermic perfusion (EVNP) for assessment of high risk deceased donor kidneys for transplantation	S. Kabagambe
10:45am	A pilot study of the pharmacokinetics of tranexamic acid via intramuscular and intraosseous administration in two non-hemorrhage animal models	S. Ferencz

27th Annual Department of Surgery Research Symposium
 April 19, 2016
 Medical Education Bldg., Lecture Hall 1222

15 MINUTE BREAK: 11:00am – 11:15am

POSTER PRESENTATIONS: 11:15 AM – 12:15 PM

POSTER ROUNDS – GROUP I

Moderators: Kiho Cho, Michael Campbell

Creation of a small animal model of ex-vivo normothermic perfusion (EVNP) for treatment of kidney ischemia-reperfusion (I/R) injury	Y. Smolin
Isolation of canine placental mesenchymal stem cells to treat naturally occurring spina bifida in the dog	C. Long
Polymorphic stress responses of 64 endogenous mouse mammary tumor viruses isolated from 23 laboratory mouse strains	S. Leventhal
Predictors of residual disease after unplanned excision of unsuspected soft tissue sarcomas	A. Gingrich
Comparison of genetically identical placental and amniotic fluid mesenchymal stem cells in secreted proteins, exosome cargo, and neuroprotective functionality	S. Walker

POSTER ROUNDS – GROUP II

Moderators: Shinjiro Hirose, Linda Farkas

Presenting hypertension and mortality in combat casualties	A. Davidson
Design of a cost effective hemodynamically adjustable model for REBOA simulation	B. Keller
Pigtail catheters are not inferior to chest tubes for the drainage of ongoing hemothorax	R. Russo
A novel model of highly lethal uncontrolled torso hemorrhage in swine	A Davidson
Developing a murine model of injury-mediated immunothrombus	J. Becker

27th Annual Department of Surgery Research Symposium

April 19, 2016

Medical Education Bldg., Lecture Hall 1222

POSTER ROUNDS – GROUP III	
Moderators: Mohammed Ali, Gary Raff	
Pediatric surgical readmissions: Are they truly preventable?	E. Brown
Local anesthetic infusion via on-Q pump versus epidural for pain management following the nuss procedure	S. Kabagambe
Patency of the internal iliac artery after placement of common and external iliac artery stents	M. Vinogradova
Intercostal nerve cryoablation for pectus excavatum repair: preliminary outcomes in twenty-five patients	B. Keller
When is anticoagulation for traumatic vascular injury required?	M. Blume
LUNCH BREAK: 12:15 PM-1:00 PM	
POSTER PRESENTATIONS: 1:00 PM-2:00 PM	
POSTER ROUNDS – GROUP I	
Moderators: William Pevec, Junichiro Sageshima	
Ex-vivo normothermic perfusion (EVNP) and its attenuation of kidney ischemia-reperfusion injury (IRI): A proposed mechanism	I. Palma
Effect of stem cell seeding and extracellular matrix scaffolds on skeletal muscle regeneration	T. Sarrafian
Comparison of ex-vivo hypothermic (EVHP) versus normothermic perfusion (EVNP) of high-risk deceased donor kidneys	I. Palma
Refugee health: characterizing health conditions of asylum seekers in Dresden, Germany	L. Goodman
Global surgery activities and interest amongst general surgery trainees	G. Jensen
Proof of concept: Analysis of soft tissue changes in facial aging	P. Song

27th Annual Department of Surgery Research Symposium

April 19, 2016

Medical Education Bldg., Lecture Hall 1222

POSTER ROUNDS – GROUP II		
Moderators: David Sahar, Michael Wong		
	Surgical resident shift length does not impact types of errors made	J. Anderson
	Balanced transfusion in pediatric trauma patients	L. Goodman
	Young female vascular surgeons more likely to enter academia: A paradigm shift?	M. Kwong
	The morbidity and mortality conference should systematically address root causes of errors: Results of a departmental survey	J. Anderson
	The plastic surgeon as employee	N. Patel
	Assessing safety of negative pressure wound therapy over pedicle muscle flaps: A retrospective review of gastrocnemius muscle flap	M. Kaur
15 MINUTE BREAK: 2:00 PM – 2:15 PM		
ORAL PRESENTATIONS – SESSION III:		
Moderators: Robert Canter, Misty-Dawn Humphries		
2:15pm	Role of human placenta-derived mesenchymal stem cells in neuroprotection and neurogenesis	J. Becker
2:30pm	A novel glucocorticoid receptor isoform induced by LPS	A. Eley
2:45pm	In-vitro characterization of placenta derived mesenchymal stromal cells (PMSCs) on extracellular matrix (ECM)	Z. Saenz
3:00pm	In vitro and in vivo interaction of adipose-derived stem cells and breast cancer cells: Is fat grafting safe in post-mastectomy patients?	H. Charvet

27th Annual Department of Surgery Research Symposium

April 19, 2016

Medical Education Bldg., Lecture Hall 1222

15 MINUTE BREAK: 3:15pm – 3:30pm

ORAL PRESENTATIONS – SESSION IV:

Moderators: Garth Utter, James Holcroft

3:30pm	High tide raises all boats: Esophagectomy outcomes for low volume surgeons in high volume centers	H. Hashimi
3:45pm	Ultrasound guided anesthetic or botulinum toxin injection of the anterior and middle scalene muscles to assist with diagnosis and treatment of neurogenic thoracic outlet syndrome	N. Salhan
4:00pm	Variable aortic occlusion improves outcomes compared to complete occlusion	R. Russo
4:15pm	Lung resection is safe and feasible among stage IV cancer patients: An American College of Surgeons NSQIP analysis	S. Bateni

CONCLUDING REMARKS

Diana L. Farmer, MD, FACS, FRCS

Tina L. Palmieri, MD, FACS, FCCM

27th Annual Research Symposium Awards Banquet

6:00pm

Crocker Art Museum

216 'O' Street

Sacramento, CA

**ORAL
PRESENTATIONS
SESSION I**

Randomized comparison of packed red blood cell-to-fresh frozen plasma transfusion ratio of 4:1 versus 1:1 during massive burn excision

Laura Galganski MD, Tina Palmieri MD, David Greenhalgh MD, Soman Sen MD
UCDMC Division of Burn Surgery and Shriners Hospitals for Children Northern California

Introduction:

Major burn excision is associated with a 2% blood volume loss per percent excised; hence, massive blood loss (>50% blood volume) frequently occurs during major burn excisions. This prospective randomized controlled trial compared the impact of a 4:1 versus a 1:1 packed red blood cell-fresh frozen plasma (PRBC/FFP) transfusion strategy.

Methods:

Children with >20% TBSA burns were randomized to a 1:1 or 4:1 PRBC/FFP ratio during burn excision. Parameters measured on admission included demographics, burn size, and Pediatric Risk of Mortality (PRISM) scores. Laboratory values recorded preoperatively, at 1, 12, and 24 hours, and one week postoperatively included prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR), fibrinogen, protein C, and antithrombin C (AIII). Total number of blood products transfused during operative interventions and during hospitalization were recorded.

Results:

A total of 45 children were enrolled, 22 in the 1:1 and 23 in the 4:1 group. The groups were similar in age, TBSA, and PRISM at admission. Preoperative fibrinogen, AIII, protein C, hemoglobin, PT/PTT, INR, and platelets were similar between groups. In the first two major excisions, the 1:1 group received significantly more FFP per patient (3.43 ± 0.55 U vs. 1.39 ± 0.33 U, $p < 0.001$) and fewer PRBC (3.47 ± 0.53 U in 1:1 group vs. 4.13 ± 0.55 U in 4:1 group). The 1:1 group used 84 U FFP and 77 U PRBC compared to 34 U FFP and 90 U PRBC in the 4:1 group. At one hour postoperatively, PT and PTT were lower and Protein C and AIII were higher in the 1:1 group.

Conclusion:

A 1:1 PRBC/FFP transfusion strategy decreased intraoperative PRBC use, likely due to higher AIII and protein C and lower PT and PTT from the FFP transfusion.

A Nanoparticle Based Drug Delivery System for the Treatment of Infantile Hemangiomas

Hakan Orbay,¹ Yuanpei Li,² Wenwu Xiao,² Kit Lam,² Simon R Cherry,³ David E. Sahar¹

¹UCDMC, Division of Plastic Surgery. ²UCDMC, Department of Biochemistry and Molecular Biology.

³UCD Department of Biomedical Engineering

Introduction:

The current treatments for infantile hemangiomas (IHs) have unpredictable outcomes. The aim of this study is to develop a nanoporphyrin (NP) delivered, high-efficacy treatment for IHs using a mouse hemangioendothelioma (HT) model.

Methods:

We injected mouse hemangioendothelioma cells intradermally to axillary regions of five-week-old, female, nude mice (n=19) to induce HT growth. We documented NP accumulation in HTs using positron emission tomography (PET). For the treatment study, we randomized HT-bearing nude mice (n=9) into three groups (n=3, each). Animals in group I received only saline injections. Animals in group II received only laser treatment after saline injection, and animals in group III received laser treatment after NP injection (photodynamic therapy) via tail vein. We followed up the treatment response with digital caliper measurements.

Results:

HTs started to grow approximately one week after inoculation, and resembled IHs histologically. NP uptake in HTs was 19.7 ± 2.2 , 16.7 ± 2.02 , 8.4 ± 0.3 , and 4.9 ± 0.6 %ID/g at 3, 6, 24, 48 hours postinjection. NP uptake in HTs was significantly higher than blood at 24 and 48 hours postinjection ($p < 0.05$). Results of ex vivo biodistribution study were consistent with PET imaging. HTs in group III started to regress one day after the treatment and disappeared totally by day 21. The difference between tumor volumes in group III and other groups was significant on days 17, and 21 ($p < 0.05$).

Conclusions:

NP accumulated in HTs at high concentrations enabling a high-efficacy photodynamic therapy. NP based photodynamic therapy is a promising treatment for IHs.

A single nucleotide polymorphism results in increased activity of human glucocorticoid receptor

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

Introduction:

Glucocorticoids are one of the most widely used therapeutics in the treatment of inflammatory disorders, including sepsis. Their effectiveness, however, is known to be variable and unpredictable. Naturally occurring polymorphisms in the glucocorticoid receptor (GR) may be a fundamental factor in this variability.

Methods:

Ninety-seven healthy volunteers were surveyed for polymorphisms in the well-studied human GR-alpha (hGR α) isoform using reverse transcriptase-polymerase chain reaction followed by functional characterization of the resulting isoforms.

Results:

One isoform identified in the survey, named hGR DL-2, had four single nucleotide polymorphisms (SNPs), one synonymous and three non-synonymous, and a four base pair deletion resulting in a frame shift and early termination to produce a 743 amino acid putative protein. The hGR DL-2 isoform had a decrease in transactivation potential of more than 90% both with and without glucocorticoid stimulation. Interestingly, upon further analysis of the individual SNPs and deletion, an isoform with one SNP, hGR α -A829G (K277E), was found to have a transactivation potential greater than eight times the hGR α reference. Additionally, the hGR α -A829G isoform had a differential hyperactive response to three different exogenous glucocorticoids.

Conclusion:

Increasing our knowledge as to how various SNPs affect hGR activity may help us to understand the unpredictable patient response to both endogenous and exogenous glucocorticoids. This understanding is a vital step towards personalized care of patients with inflammatory conditions.

Seeding Mesenchymal Stromal Cells on Extracellular Matrix Significantly Reduces Infarct Development

Mikella Robinson, CS Sondergaard, WD Boyd
UCDMC Division of Cardiothoracic Surgery

Introduction:

Mesenchymal stromal cell (MSC) regenerative therapy for ischemic heart disease has had limited success clinically, ostensibly due to poor cell retention and viability post-implant. We used an innovative approach to address these limitations by topically seeding rodent MSCs on porcine small intestine submucosal extracellular matrix (ECM), thereby reducing infarct size and increasing angiogenesis, cardiac function and MSC retention.

Methods:

Rats with induced acute myocardial infarctions (AMI) were either injected intramyocardially with rat MSCs or epicardially administered a ECM patch with or without seeded MSCs over the infarct area (n=6) and evaluated for infarct size, vascular density and donor cell retention after 14 days. In a second AMI study, we compared functional recovery following implantation of MSC seeded ECM versus untreated control animals (n=6). Animals were scanned by CINE-MRI self-gated sequences at 0, 14, and 35 days, and left ventricle ejection volume (LVEF) was calculated. Cell retention was evaluated by chemiluminescence imaging in immune-deficient AMI rats transplanted with luciferase expressing human MSCs, intramyocardially or seeded on ECM (n=2).

Results:

We found that length and area of infarct were significantly smaller in animals treated with MSCs on ECM as compared to all groups (% infarct length for: control, +ECM, +MSC, +MSC on ECM: 27.2, 19.1, 18.3, 14.2). Endothelial percent change also favored MSCs on ECM over all groups, while donor cells were detected only in the MSCs on ECM group. LVEF at 14 and 35 days showed significant improvement in MSCs on ECM group compared to the control group (51.3% vs 37.0%; 52.1% vs 45.3%). By day 3 of the chemiluminescence study, ECM improved local MSC retention, as seen by a smaller trace signal with higher intensity.

Discussion:

MSCs seeded on ECM improve functional recovery with elevated LVEF and increased cellular retention. Notably, as seen by decreased scar burden and increased angiogenesis, this data indicates that MSCs when seeded on ECM show significant enhancement in disease modifying effects when compared to MSC or ECM alone.

ORAL

PRESENTATIONS

SESSION II

Radiotherapy Enhances Natural Killer Cell Homing and Function in Canine Bone and Soft Tissue Sarcoma

Jiwon S. Park, Steven Grossenbacher, Erik Ames, Stephanie Mac, Jaime Modiano, Jeffrey Miller, Arta Monjazebe, Michael Kent, William Culp, Mingyi Chen, William J. Murphy, Robert J. Canter
¹University of California Davis-Department of Surgery, ²University of California Davis-Laboratory of Immunology, ³University of Minnesota Department of Veterinary Clinical Sciences, ⁴University of Minnesota Department of Medicine, ⁵University of California Davis-Department of Interventional Radiology, ⁶University of California Davis-School of Veterinary Medicine, ⁷University of California Davis Department of Pathology

Introduction: Although effective in hematologic malignancies, natural killer (NK) cells have been less successful in solid cancers. We hypothesized that the cytotoxicity and homing of canine NK cells would be increased by combination therapy with radiation (RT). We used the canine model because sarcomas are common in dogs, and they are an excellent resource for immunotherapy protocols.

Methods: Canine NK cells were isolated from 10 mls of fresh whole blood using Ficoll separation and CD5 depletion. Isolated NK cells were then expanded in co-culture with irradiated K562c9IL21 for 2-3 weeks. Canine osteosarcoma tumor lines and fresh canine primary sarcomas were evaluated for NK killing before or after RT in vitro and in xenograft experiments. NK cytotoxicity was measured using 7AAD or chromium release killing assays.

Results: NK expansion was successful in 17/20 donors from baseline of $2-3 \times 10^6$ NK cells to $258.9 \pm 76.1 \times 10^6$ cells with mean fold increase of 46.2 ± 12.7 . NK cytotoxicity to dog sarcoma cancer lines in vitro and dog sarcoma PDX tumors ex-vivo was increased with increasing effector:target ratios ($P < 0.001$). NK killing was significantly increased after RT (1.3-3.4X increased killing, $P < 0.01$). Focal RT in vivo showed increased NK homing to the tumor following RT and IV NK transfer ($P < .001$)

Conclusion: Canine NK cells can be successfully expanded and activated ex-vivo, and canine NK cytotoxicity and homing is increased following RT. A canine clinical trial of palliative RT and autologous NK transfer for osteosarcoma is currently underway in collaboration with the UCD School of Veterinary Medicine.

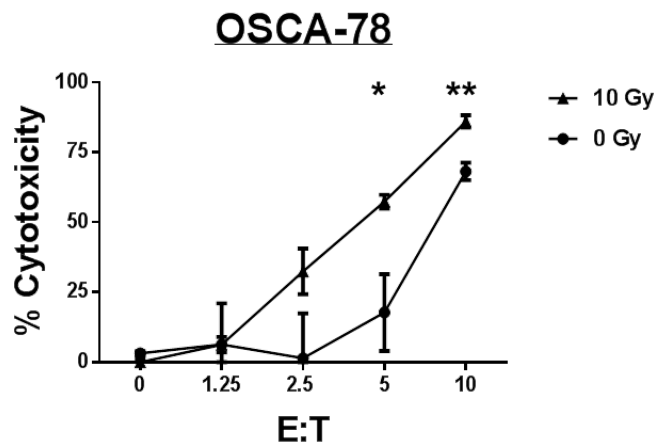


Figure 6. Irradiation Sensitizes Canine Sarcomas to NK Killing In Vitro. An osteosarcoma cell line was irradiated in vitro at a dose of 10 Gy and then co-cultured with allogeneic NK cells for 4 hours. Flow cytometry was used to assess the frequency of CD45-7AAD- target cells at indicated ratios compared to non-NK controls. * $P < 0.05$, ** $P < 0.01$ by two-way ANOVA with Bonferroni post-test.

Engineering bioactive vascular grafts with a novel ligand against $\alpha v \beta 3$ integrin to improve *in situ* endothelialization

Dake Hao¹, Yahan Fan¹, Yang Wu¹, Wenwu Xiao², Yuanpei Li², Ruiwu Liu², Christopher Pivetti¹, Diana Farmer¹, Kit Lam², Aijun Wang¹

¹Surgical Bioengineering Lab, Department of Surgery, UC Davis, ²Department of Biochemistry and Molecular Biology, UC Davis

Introduction:

Our purpose is to screen high-throughput one-bead-one-compound (OBOC) combinatorial libraries for peptides that bind to endothelial progenitor cells (EPCs) and endothelial cells (ECs) with high specificity and support EC functions to improve endothelialization of artificial vascular grafts.

Methods:

We screened LXW7, a ligand that has high-specific binding affinity against $\alpha v \beta 3$ integrin. Binding specificity and functions of LXW7 on active EPCs/ECs were examined *in vitro* via cell binding assay, flow cytometry, MTS assay and Western-blot. *In vivo* test, we functionalized small-diameter nanofibrous vascular grafts with LXW7 via CLICK chemistry and investigated its functions on endothelialization and graft patency in a rat carotid artery bypass model.

Results:

LXW7 showed strong binding affinity to various types of ECs and EPCs, but not to platelets and monocytes. LXW7 promoted the proliferation of ECs, and enhanced the phosphorylation of VEGF receptor 2 (VEGF-R2) and the activation of mitogen-activated protein kinase (MAPK) ERK1/2 in ECs. Immunohistological analyses showed that at 1 week after implantation, the LXW7 modified vascular grafts possess significantly more CD34⁺ EPCs in the middle segment of the luminal surface than the control grafts. At 6 week after implantation, mature endothelialization was present throughout the whole length of the LXW7 modified grafts while only a limited number of CD31⁺ ECs were seen in the middle of the control grafts. Patency testing results confirmed that at 6 week after implantation, 5 out of 6 LXW7-modified vascular grafts were patent versus in the control group only 1 out of 6 grafts was patent.

Conclusion:

Our results have demonstrated that LXW7 specifically supports EPC/EC attachment and functions, and can improve *in situ* endothelialization of vascular grafts. LXW7 and their derivatives hold great promise for endothelialization related tissue regeneration applications.

Ex-vivo Normothermic Perfusion (EVNP) for Assessment of High Risk Deceased Donor Kidneys for Transplantation

S Kabagambe, I Palma, Y Smolin, T Boyer, IP Palma, J Sageshima, C Santhanakrishnan, C Troppmann, J McVicar, R Perez
Transplant Surgery, University of California Davis

Introduction:

Despite the organ shortage, many procured deceased donor kidneys are deemed too high risk for failure and discarded. We have begun to utilize EVNP to assess and develop criteria by which high risk kidneys can be deemed transplantable.

Methods:

From June 2014 to October 2015, 9 deceased donor kidneys were imported to our center after being turned down by all local and regional centers. We conditionally accepted these organs but after further assessment considered them too high risk due to marginal hypothermic perfusion parameters or biopsy results. They were placed on EVNP for 3-12 hours, using oxygenated packed red blood cells and nutrition. Assessment was based on appearance, hemodynamic parameters, and urine output (UO).

Results:

Reasons for discard included marginal pump parameters (n=6) and biopsy results (n=3). On EVNP, 6 kidneys perfused well, made urine, and in retrospect were deemed transplantable with low risk for failure. Two kidneys appeared viable, had minimal UO, and in retrospect were possibly transplantable with moderate risk for failure. One perfused poorly, with no UO, and was considered non-transplantable. Unpaired t-test was used to compare donor factors and perfusion parameters between low and moderate risk kidneys, and only UO was significantly different (125.8 ± 43.14 and 2.25 ± 1.75 ml/hour respectively, $p=0.04$).

Conclusion:

Many discarded kidneys can be more completely assessed using EVNP and considered for transplantation. Further studies, possibly focusing on organ blood flow and function while on EVNP may be important to determine which organs can be transplanted with low risk for failure.

A pilot study of the pharmacokinetics of tranexamic acid via intramuscular and intraosseous administration in two non-hemorrhage animal models

Ferencz, Sarah-Ashley E.¹; Davidson, Anders J.¹; Russo, Rachel M.¹; Neff, Lucas P.²; Hight, Rachel²; Brown, Ian E.¹; Grayson, J. Kevin²; Tran, Nam K.³; Galante, Joseph M.¹
UCDMC, Dept of Surgery¹ and Dept of Pharmacology and Lab Science³
²Clinical Investigation Facility, David Grant Medical Center

Introduction: Tranexamic acid (TXA) has been shown to reduce blood loss following surgery and may provide a mortality benefit in trauma patients. The addition of TXA to trauma transfusion protocols is now standard practice in many civilian and military sectors. TXA is routinely administered by the intravenous (IV) route and has been shown to be most effective when given within 3 hours of injury. However, in a field setting establishing IV access can be difficult and limited, so we examined the pharmacokinetics (PK) of TXA administered to pigs and sheep by intraosseous (IO) and intramuscular (IM) routes, compared to the IV route.

Methods: Two cohorts of three pigs and sheep were administered one gram TXA by the IV, IM or IO route, respectively. Twelve serum samples were obtained over a six-hour period, and TXA concentrations were determined by gas chromatography, time-of-flight, and mass spectrometry. Traditional compartmental PK modeling was performed to determine drug pharmacokinetics.

Results: Plots of TXA concentrations in serum from pigs are shown in figure 1, which demonstrates that the curves are similar for IV, IM and IO routes. There were differences in bioavailability depending on route and species, and the drug half-life was shorter in pigs compared to sheep.

Conclusion: Based on this pilot study, TXA delivered by IO and IM routes has potential to be a viable alternative to IV administration. Investigations should be expanded to human studies to further explore these alternative routes of administration of TXA. More data is needed to determine ideal dosages via these novel routes as well as the bioavailability profile during ongoing hemorrhage.

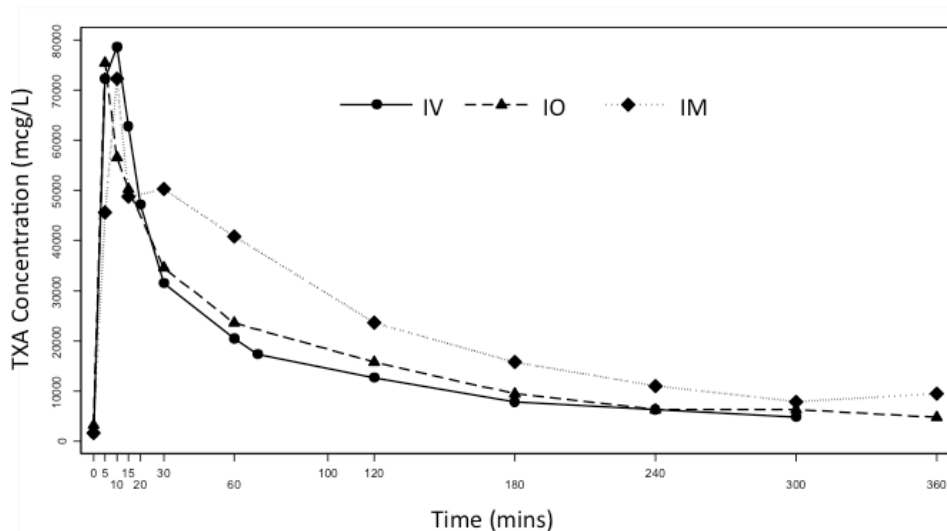


Figure 1. TXA concentrations in pig serum for IV, IM, and IO routes.

**ORAL
PRESENTATIONS
SESSION III**

Role of Human Placenta-derived Mesenchymal Stem Cells in Neuroprotection and Neurogenesis

J. Becker*, P. Kumar*, L. Lankford, B. Keller, D. Farmer, A. Wang (*equal contribution)
Surgical Bioengineering Lab, University of California Davis Medical Center

Introduction:

Our successful treatment of myelomeningocele (MMC) with early gestation chorionic villus-derived placental mesenchymal stem cells (PMSCs) consistently improves hind limb paralysis in the fetal lamb model of MMC. Additionally, our in vivo studies demonstrate neuronal preservation in the cords of PMSC treated animals. We hypothesized that PMSCs secrete numerous neuroprotective factors, angiogenic factors, and cytokines that can collectively improve neuronal survival after injury.

Methods:

We used staurosporine to induce apoptosis in the human neuroblastoma cell line SHSY5Y to characterize the neuroprotective function of PMSCs in indirect co-culture.

Results:

SHSY5Y cells treated for 4h with 1 μ M staurosporine showed increased caspase-3 activity, activation of caspase-3 on immunocytochemistry, and increased signal on TUNEL assay. Western blot analysis also showed decreased expression of pro-caspase-3, increased activated caspase-3 and increased cleavage of the caspase-3 substrate PARP1. Indirect co-culture with PMSCs was then performed to study neuroprotection. PMSCs cultured on hanging 24-well semi-permeable inserts for 24h in DMEM high glucose, 5% FBS plus 20 ng/ml FGF2 and 20 ng/ml EGF were transferred to a 24-well dish containing either injured SHSY5Y cells or DMSO treated controls grown in DMEM high glucose, 5% FBS. Short-term co-culture increased survival of staurosporine treated SHSY5Y cells compared to controls without PMSCs. Additionally, long term co-culture demonstrated increased numbers of DMSO treated SHSY5Y cells compared to wells without PMSCs, suggesting a potential neurogenesis effect.

Conclusions:

PMSCs may mediate both neuroprotection and neurogenesis via secreted factors. Future receptor blocking studies may identify relevant pathways for these effects.

A novel glucocorticoid receptor isoform induced by LPS

Anna Eley, Stacey Leventhal, Debora Lim, Tajia Green, Kiho Cho, and David Greenhalgh
UC Davis Division of Burn Surgery & Shriners Hospitals for Children, Northern California

Introduction:

A patient's ability to respond to injury depends on the appropriate response to glucocorticoids, which is highly influenced by the human glucocorticoid receptor (hGR). Polymorphisms and post translational modifications lead to variability in hGR function. Prior work has shown that different hGR isoforms can either inhibit or augment hGR activity and steroid response. Even more interesting, however, is the finding that the structure of hGR changes in response to injury-related stress and sepsis. The goal of this study was identify hGR post-translational modifications and determine how they responded to stress in vitro.

Methods:

Leukocytes were isolated from a healthy volunteer and treated with three different combinations of LPS and Hydrocortisone: 5µg/mL LPS without hydrocortisone, 5µg/mL LPS + Hydrocortisone, and 10µg/mL LPS + Hydrocortisone. To evaluate for hGR expression, cells were harvested at 1 hour, 3 hours and 13 hours. RNA was then isolated, cDNA prepared and PCR used to amplify different hGR exon-to-exon combinations.

Results:

A novel isoform with a 54 base pair addition in the region of the hGR transactivation domain was identified. The expression of this new exon appeared to be time dependent with increased expression as LPS exposure went from 1 hour to 3 hours. In the cells exposed to LPS plus hydrocortisone, expression decreased at 13 hours.

Conclusions:

These findings show a direct link between exposure to physiologic stress and post-transcriptional modification of the human glucocorticoid receptor. Simultaneous treatment with hydrocortisone also appeared to affect this process after 3 hours. We are currently working on testing the functional activity of this novel isoform.

In-Vitro Characterization of Placenta derived Mesenchymal Stromal Cells (PMSCs) on Extracellular Matrix (ECM)

Y. Julia Chen MD, Lee Lankford MA, Zoe Saenz BA, Sandra Kabagambe MD, James Becker MD, Benjamin Keller MD, Priyadarsini Kumar PhD, Aijun Wang PhD, Diana Farmer MD, Surgical Bioengineering Laboratory, Department of Surgery

Introduction:

The purpose of the study is to characterize the viability, proliferation, and neuroprotective secretory profile of PMSCs seeded at varying densities on ECM (Small Intestine Submucosa, Cook Medical) in order to determine the optimal matrix loading density of PMSCs for in-vivo cell delivery.

Methods:

PMSCs were isolated from preterm chorionic villus samples via explant culture and transduced with green fluorescent protein. 12mm ECM matrices soaked in culture media overnight were seeded with PMSCs in the following densities (cells/cm²): 0 (ECM only control), 4.2x10⁴, 1x10⁵, 3x10⁵, 5x10⁵, 1x10⁶. Conditioned media was collected after 24 hours of incubation and analyzed using ELISAs for human brain-derived neurotrophic factor (BDNF), hepatocyte growth factor (HGF), and vascular endothelial growth factor (VEGF). Cellular metabolic activity and viability were respectively assessed using a colorimetric MTS proliferation assay and fluorescent viability assay. All wells were prepared in triplicate, and experiments were performed using three donor cell lines.

Results:

There was no evidence of gross acute cytotoxicity. Cellular metabolic activity increased with seeding density and plateaued at 3x10⁵ cells/cm². When normalized to cell seeding density, BDNF and HGF secretion trended downwards with increasing cell density while VEGF secretion increased and peaked at 5x10⁵ cells/cm² prior to trending down.

Conclusion:

PMSCs seeded onto ECM are viable. The optimal loading density of PMSCs on ECM is 3x10⁵ cells/cm². Secretion of BDNF and HGF is inversely related to cell density while VEGF secretion peaks at 5x10⁵ cells/cm².

In Vitro and In vivo Interaction of Adipose-Derived Stem Cells and Breast Cancer Cells: Is fat grafting safe in post-mastectomy patients?

Heath Charvet,¹ Hakan Orbay,² Katharine Hinchcliff,² Tima Dehghani,² Mankushpreet Kaur,² David E. Sahar²

¹UCDMC Division of Plastic Surgery, ²UCDMC Department of Surgery.

Introduction:

We investigate the in vitro and in vivo interaction of breast cancer cells (BCCs) and adipose-derived stem cells (ASCs) in an attempt to better understand the clinical risks of fat grafting in post-mastectomy breast reconstruction.

Methods:

For in vitro study BCCs and ASCs were obtained from the same patient. A homogenous (CD 90-/CD 24+) BCC population was obtained with flowcytometric cell sorting. The effect of ASCs on migration of BCCs was examined using a cell migration assay. In vivo arm of the study was performed using MDA-MB-231 BCCs and patient derived ASCs/fat grafts. BCCs were injected to the 4th mammary gland of female nude mice (n=20) bilaterally as shown in **Figure 1A**. 1.65×10^5 BCCs, 1.45×10^5 ASCs, and 150 μ l of unprocessed fat graft were injected in corresponding groups. Tumors were followed with serial digital caliper measurements and examined histologically after 4 weeks.

Results:

The percentage of CD 90-/CD 24+ BCCs in initial cell population was 0.61 %. BCCs migrated approximately 10 folds more when co-cultured with ASCs compared to BCC only cultures ($p < 0.01$). Tumor growth rate in group III and group IV was significantly higher than group I ($p < 0.01$) (**Figure 1B**). Histologically, injected fat grafts were largely replaced by BCCs after 4 weeks.

Conclusion:

ASCs significantly increase the in vitro migration of BCCs in co-cultures and in vivo growth of breast cancer xenografts.

**ORAL
PRESENTATIONS
SESSION IV**

High Tide Raises all Boats: Esophagectomy Outcomes for Low Volume Surgeons in High Volume Centers

Habiba Hashimi, BS¹, David L. Chin, PhD², Lisa M. Brown, MD, MAS^{1,3}, Elizabeth A. David, MD^{1,3}, David T. Cooke, MD^{1,3}

¹Section of General Thoracic Surgery, University of California, Davis Medical Center, Sacramento, CA, USA., ²Center for Healthcare Policy and Research, University of California, Davis, Sacramento, CA, USA, ³Department of Surgery Outcomes Research Group, University of California, Davis, Sacramento, CA, USA.

Introduction:

Hospital procedure volume is often used as a proxy for healthcare quality for esophagectomy and other high risk procedures. Although hospital volume is associated with improved patient mortality outcomes, surgeon volume effects have yet to be clarified.

Method:

Discharge data for 6022 patients were extracted from the 2007-2013 New York and Florida State Inpatient Databases. The relationship between hospital- and surgeon- esophagectomy volume on mortality, length of stay ≥ 14 days and postoperative complications was studied using hierarchical generalized linear mixed effects models, adjusted for patient demographics, comorbid disease, and hospital characteristics. A Bonferroni correction was used to adjust for multiple comparisons.

Results:

High center volume resulted in reduced mortality odds (OR = 0.48, $p < 0.001$), reduced odds of incident length of stay ≥ 14 days (OR = 0.76, $p = 0.002$), and reduced odds of hematologic complications (OR = 0.67, $p < 0.001$). High surgeon volume was associated with reduced odds of pulmonary complications (OR = 0.76, $p = 0.006$) and gastrointestinal complications (OR = 0.64, $p = 0.004$).

Conclusion:

Hospital volume and surgeon volume are modifiable risk factors associated with reduced morbidity and mortality in patients undergoing elective esophagectomies. Our analysis shows that patients have reduced odds of mortality and adverse postsurgical events when treated at high volume hospitals and by high volume surgeons. Hospital volume served as a proxy for risk of mortality. Patient postoperative complication risk is attributable with surgeon esophagectomy volume.

Ultrasound Guided Anesthetic or Botulinum Toxin Injection of the Anterior and Middle Scalene Muscles to Assist with Diagnosis and Treatment of Neurogenic Thoracic Outlet Syndrome

Misty Humphries, MD¹, Navjeet Salhan, BS¹, Samir Sheth, MD², Charles De Mesa, DO, MPH², Julie A. Freischlag, MD¹

University of California, Davis, Sacramento, California, ¹Department of Vascular Surgery and

²Department of Anesthesia and Pain Medicine

Introduction:

Anesthetic scalene block predicts success for neurogenic thoracic outlet syndrome (nTOS) treatment. Ultrasound-guided injection technique advantages include low cost, absence of ionizing radiation and direct visualization of a needle's path. We describe the technique, outcomes and complication following ultrasound-guided anesthetic with corticosteroid scalene injection in subjects with suspected nTOS.

Methods:

Retrospective chart review identified patients suspected of nTOS referred for diagnostic anesthetic block of scalene muscles. Ultrasound injections technique involved identification of safety landmarks of the interscalene triangle. Outcomes, complication and demographic information including nTOS pain disability index were summarized.

Results:

23 procedures (3 patients bilateral; 61% women, median age 34; range 20-52 years; nTOS symptoms average 5.0± 7.2 years; nTOS Pain Disability Index -moderate to severe for work tolerance and recreation; 3 patients with prior rib resection; 1 botulinum toxin scalene injection) were identified. Technical success achieved in all procedures. Average pain intensity (Visual Analog Scale 1-10) was rated 6±2.06 before injection and 2±2.06 10 minutes after injection. Twenty-two patient encounters (95.7%) had positive outcome. Pain relief lasted average of 7.5 days for anesthetic injections and 6 weeks for botulinum toxin injection. One complication (4.3%) was sub-acute pain three weeks following injection. Post-procedure MRI of the brachial plexus was normal with no neurological or vascular sequela. In all cases, there was no nerve injury, vascular puncture, hematoma, infection, local hemodynamic consequences or pneumothorax.

Conclusion:

Our experience with ultrasound injection of these muscles demonstrated safe and well-tolerated procedure in the diagnosis of nTOS.

Variable aortic occlusion improves outcomes compared to complete occlusion

R Russo¹, T Williams², L Neff², S Ferencz¹, A Davidson¹, J Grayson²

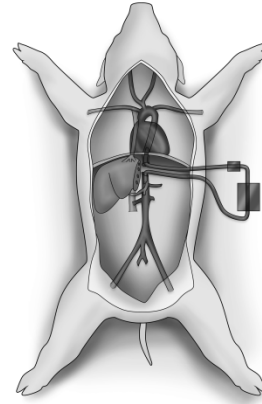
¹UC Davis, Division of Trauma; ²Clinical Investigation Facility, Travis AFB

Introduction:

Complete aortic occlusion is limited by the short duration of tolerable ischemia and the consequences of massive reperfusion injury. We have developed an automated extracorporeal circuit to overcome these limitations.

Methods:

Twenty-five swine underwent partial liver amputation with uncontrolled hemorrhage. Ten received rapid intervention with variable aortic occlusion, and ten with complete aortic occlusion using our device (figure). Five received no intervention. Definitive hemorrhage control (DHC) was achieved at 90 minutes. The effects of intervention were observed over 6 hours.



Results:

Variable aortic occlusion reduced hemodynamic extremes, ischemia-reperfusion injury, resuscitation requirements, and end organ damage and was associated with a trend toward improved survival compared to complete aortic occlusion in an otherwise rapidly fatal injury.

Conclusions:

We used a novel automated extracorporeal circuit to demonstrate that variable aortic flow regulation is capable of limiting exsanguination while providing improved homeostasis to vital organs compared to complete aortic occlusion during highly lethal injury.

Lung Resection is Safe and Feasible Among Stage IV Cancer Patients: An American College of Surgeons NSQIP Analysis

Sarah B. Bateni, MD, Elizabeth A David, MD, Richard J. Bold, MD, David T Cooke, MD, Frederick J. Meyers, MD, Robert J. Canter, MD.
UC Davis Division of Surgical Oncology

Introduction:

Although surgical intervention among patients with disseminated malignancy (DMa) carries high morbidity and mortality, retrospective studies have demonstrated improvements in survival following lung resection among advanced lung cancer patients and patients with lung metastases. We sought to evaluate the rates of acute morbidity and mortality following lung resection in DMa patients to further describe risks associated with such intervention.

Methods:

We identified 6,360 patients from the American College of Surgeons NSQIP undergoing lung resection (i.e. segmentectomy, wedge resection, lobectomy, or pneumonectomy) from 2011-2012, including 603 patients with DMa. Standard parametric/nonparametric statistics and logistic regression analyses were used compare 30-day morbidity and mortality among patients with and without DMa.

Results:

Among DMa patients, 183 (30.3%) were diagnosed with primary lung cancer and 348 (57.7%) had lung metastases. Most DMa patients had independent functional status (99.2%). Overall 30-day morbidity, serious morbidity and mortality for DMa patients were 12.1%, 7.6% and 1.8%, respectively, and 95.9% were discharged home. DMa patients with lung cancer had greater mortality compared to patients with lung metastases (3.5% vs. 0.6%, $p < 0.01$). Pneumonectomy had far worse overall and serious morbidity and mortality compared to other types of lung resections (28.6% vs 12.1%, 28.6% vs 7.6%, and 7.1% vs 1.8%, respectively, $p < 0.05$). When comparing outcomes for DMa versus non-DMa, there were no significant differences in overall morbidity (12.1% vs. 15.4%), serious morbidity (8.3% vs. 9.8%) or mortality (1.8% vs. 1.8%) for all lung resections ($p > 0.05$ for all). Subgroup analysis by type of lung resection also demonstrated no differences in rates of overall and serious morbidity and mortality for DMa versus non-DMa patients ($p > 0.05$ for all).

Conclusion:

With the exception of pneumonectomy, DMa patients undergoing lung resections experienced low rates of morbidity and mortality, with comparable rates for DMa and non-DMa patients. These data suggest that lung resections may be performed safely on select patients with DMa with both primary lung cancer and pulmonary metastatic disease, with important implications for both symptom palliation and multimodality care.

**MORNING
POSTER
ROUNDS**

GROUP I

Creation of a Small Animal Model of Ex-vivo Normothermic Perfusion (EVNP) for Treatment of Kidney Ischemia-Reperfusion (I/R) Injury

Y. Smolin, I. Palma, C. Pivetti, S. Kabagambe, J. Woloszyn, Y. J. Chen, T. Boyer, I. P. Palma, J. Sageshima, C. Santhanakrishnan, R. V. Perez
UCDMC Transplant Division

Purpose:

Recent studies have suggested that EVNP may be utilized to assess and repair marginal donor organs subjected to severe I/R injury. The purpose of our study is to develop a small animal EVNP system.

Methods:

Sprague Dawley rat kidneys were procured en-bloc, cannulated via the distal aorta, and perfused ex-vivo at 37 °C for 3 hours on a cardiopulmonary bypass circuit. The perfusate consisted of packed red blood cells, Plasma-Lyte, albumin, parenteral nutrition, exogenous creatinine, insulin, multi-vitamins, heparin and bicarbonate. The optimal perfusate composition was developed by testing varying concentrations of perfusate components on EVNP. The system is flow controlled and pressure regulated. Continuous assessment was via monitoring of hemodynamic parameters, urine output (UO), and blood collection for blood gas exchange and electrolytes.

Results:

During development of the optimal perfusate, kidneys placed on EVNP had inconsistent hemodynamics, varied urine output with frequent thrombosis. Kidneys placed on EVNP with optimal perfusate were consistently well-perfused with O₂ saturation >98% and normal urine output. Stable hemodynamic status was achieved after 30 minutes and blood creatinine and potassium levels decreased with time.

Conclusion:

EVNP in a small animal model is technically feasible and allows for assessment of graft viability and function. This system can be used for pre-clinical exploration of different interventional strategies to treat I/R injury prior to transplantation.

Isolation of canine placental mesenchymal stem cells to treat naturally occurring spina bifida in the dog

Connor Long, B.Sc.¹, Lee Lankford, M.A.¹, Priyadarsini Kumar, Ph.D.¹, Diana Farmer, M.D.¹, Aijun Wang, Ph.D.¹

¹UC Davis Department of Surgery, Surgical Bioengineering Laboratory

Introduction:

The surgically induced fetal lamb model is the current gold standard for spina bifida research, but induced models of disease have limitations. English bulldogs naturally develop spina bifida at high rates due to inbreeding, and can serve as a naturally occurring animal model for postnatal spina bifida treatment.

Methods:

Canine mesenchymal stem cells were isolated from term placenta and cultured on plastic. Cells were characterized for mesenchymal stem cell marker expression via flow cytometry and trilineage differentiation potential. The secretion of therapeutic growth factors was assessed by ELISA.

Results:

Canine stem cells were spindle shaped, plastic adherent, expressed typical mesenchymal stem cell markers CD44, CD90, and CD105 and did not express hematopoietic and endothelial markers CD34 or CD45. Canine stem cells were capable of trilineage differentiation into osteogenic, adipogenic, and chondrogenic lineages. Canine cells expressed angiogenic factor VEGF, which is expressed in mesenchymal stem cells used for wound healing applications.

Conclusion:

The phenotype of placental canine mesenchymal stem cells is consistent with human placenta mesenchymal stem cells that have been used to successfully treat induced spina bifida in the fetal lamb model. We hope to use these cells to develop a postnatal treatment of spina bifida in the bulldog model.

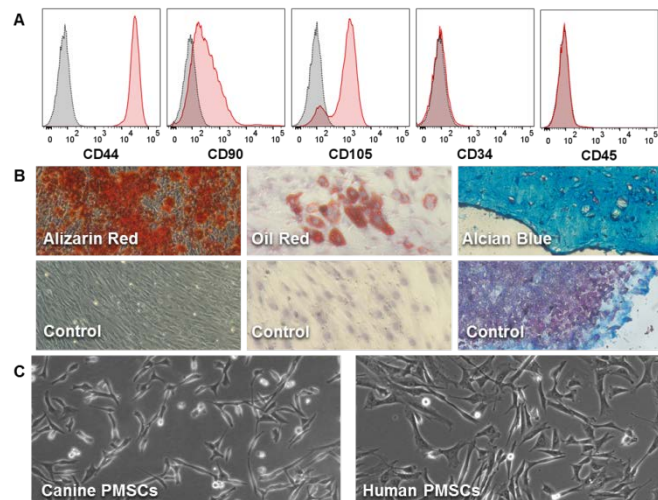


Figure: Canine placental cells express typical mesenchymal stem cell markers (A). Cells can differentiate into osteogenic, adipogenic and chondrogenic lineages (B), and express spindle morphology and plastic adherence consistent with therapeutic human mesenchymal stem cell lines (C).

Polymorphic stress responses of 64 endogenous mouse mammary tumor viruses isolated from 23 laboratory mouse strains

Karen Hsu, Young-Kwan Lee, Alex Chew, Sophia Chiu, David Greenhalgh, and Kiho Cho
Burn Division, Department of Surgery, University of California, Davis and Shriners Hospitals for Children Northern California

Introduction:

Our recent studies demonstrated that injury-elicited stress signals differentially alter the expression (both mRNA and protein) of murine endogenous retroviruses (MuERVs), both murine leukemia virus-type and mouse mammary tumor virus (MMTV)-type (MMTV-MuERV). We postulate that differential stress responses of MuERVs are linked to their promoter characteristics.

Method:

In this study, to identify putative MMTV-MuERVs, which can be activated by stress (*e.g.*, injury, infection)-elicited systemic elevation of glucocorticoid (GC) levels, we examined the GC-stress response of 64 MMTV-MuERV promoters isolated from the genomes of 23 laboratory mouse strains using a luciferase reporter system.

Results:

All 64 promoters responded to treatment with a synthetic GC, dexamethasone (DEX), at a wide range from a 0.6- to 85.7-fold increase in reporter activity compared to no treatment. An alignment analysis of the promoter sequences of the 10 lowest and 10 highest DEX responders revealed a number of promoter regions exclusively present in either the three lowest or the two highest responders. Each promoter had a unique profile of transcription regulatory elements and the glucocorticoid response element (GRE) was identified in all promoters with the number of GREs ranging from 2 to 7. The three lowest DEX responders were the only promoters with two GREs. Interestingly, there was a relatively high copy number of the TATA-binding protein element in the lowest compared to the highest DEX responders.

Conclusion:

The results from this study suggest that certain MMTV-MuERVs may be highly activated in response to stress-elicited systemic GC elevation. The unique genomic MMTV-MuERV profile of each mouse strain and the individual MMTV-MuERVs' differential responses to GC-stress might explain, at least in part, the variable responses to stress (*e.g.*, injury, infection) often observed among different mouse strains.

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

Alicia A. Gingrich^{1*}, Alexandra Elias^{1*}, Chia-Yuan Michael Lee², Yves-Paul Nakache¹, Chin-Shang Li³, Dhruvil Shah¹, Jeremy Katz⁴, Robert D. Boutin⁴, Robert Steffner⁵, Robert J. Canter¹

¹ Division of Surgical Oncology, UC Davis School of Medicine, ² Department, ³ Public Health Sciences, ⁴ Department of Radiology, UC Davis School of Medicine, ⁵ Department of Orthopedics, Division of Orthopedic Oncology, UC Davis School of Medicine, Sacramento, CA 95817

Background and Objectives:

Unplanned excision of soft tissue sarcomas (STS) is an important quality of care issue given the morbidity related to a tumor bed excision. Since not all patients harbor residual disease at the time of re-excision, we sought to determine predictors of residual STS following unplanned excision.

Methods:

We identified 76 patients from a prospectively maintained university database (1/2008 – 9/2014) who received a diagnosis of primary STS following unplanned excision. We used univariate and multivariate analyses to evaluate predictors of residual STS, accuracy of interval magnetic resonance imaging (MRI), and predictors of oncologic outcome.

Results:

Mean age was 52 years, and 63.2% were male. 50% had fragmented unplanned excision, and 82% underwent repeat excision. Among patients undergoing re-excision, 70% harbored residual STS. On univariate analysis, MRI showing gross disease and fragmented excision were significant predictors of residual STS (OR 10.588, 95% CI 2.136-52.490, P=0.0039 and OR 3.611, 95% CI 1.092-11.944, P=0.0354, respectively). Tumor size predicted distant recurrence and overall survival (HR 1.161, CI 1.023-1.316, P=0.0203 and HR 1.198, CI 1.015-1.413, P=0.0329). Combining equivocal and positive MRI for analysis, the sensitivity and specificity of MRI for predicting residual STS were 86.7% (95% CI 73.8-95.9%) and 57.8% (95% CI 32.9-81.6%), respectively, with an overall accuracy of 78.1% (95% CI 66.6-88.8%).

Conclusions:

70% of patients undergoing repeat excision after unplanned excision of STS harbor residual tumor. Although interval MRI and fragmented excision appear to be the most significant predictors of residual STS, the accuracy of MRI remains modest.

Comparison of genetically identical placental and amniotic fluid mesenchymal stem cells in secreted proteins, exosome cargo, and neuroprotective functionality

Scott Walker B.Sc.¹, Priyadarsini Kumar Ph.D.¹, Lee Lankford M.A.¹, James Becker M.D.¹, Diana Farmer M.D.¹, Aijun Wang Ph.D.¹

¹UC Davis Department of Surgery, Surgical Bioengineering Laboratory

Introduction:

Two main types of mesenchymal stem cells (MSCs) can be obtained during the first trimester of pregnancy: 1. Chorionic villus of the placenta (P-MSCs) and 2. Amniotic fluid (AF-MSCs). It is likely there are many inherent differences between the two types of cells that could be exploited for therapeutic use due to the highly secretory nature of MSCs. However true differences are convoluted due to the extremely high individual differences of donors, thus this study seeks to compare portions of the secretome of the two cells types on a genetically identical background by obtaining sets of both cell lines from the same donor.

Methods:

All lines were characterized as MSCs by flow cytometry. Cell lines were compared for free secreted proteins using BDNF, HGF, and VEGF ELISAs, as well as cytokine and angiogenesis proteome array kits. Proteins contained in exosomes secreted by the cells were analyzed by exosome isolation by ultracentrifugation and then underwent LC-MS/MS proteomics for full protein content. Cell lines were assessed functionally by a neuroprotective assay for their ability to rescue neuron-like cells from apoptosis.

Progress:

Significant differences have been noted in free protein secretion by ELISA and proteome arrays, particularly in a large fold increase in BDNF in AF-MSCs and lack of VEGF and HGF production by AF-MSCs.

Conclusion:

The results from the ELISAs and proteome arrays show that there are significant differences between the secretomes of the AF-MSC and P-MSC cell lines.

**MORNING
POSTER
ROUNDS**

GROUP II

Presenting Hypertension and Mortality in Combat Casualties

Davidson A, Ferencz S, Sosnov J, Chung K, Sen S, Stewart I
David Grant Medical Center, Division of Burn Surgery

Introduction:

The effect of presenting hypertension is poorly studied in combat casualties. We hypothesized that elevated mean arterial pressure (MAP) on presentation to combat hospitals would be associated with poor outcomes.

Methods:

Data was obtained from the Department of Defense Trauma Registry and the Armed Forces Medical Examiner System. Variables analyzed included presenting vital signs to Role I-III, demographic variables, injury severity score (ISS), location and mechanism of injury, presence of traumatic brain injury (TBI), acute kidney injury (AKI), and mortality. Patients were stratified by decile of MAP and logistic regression analysis was employed to adjust for confounders.

Results:

A total of 4026 subjects injured from 2002 to 2011 were identified. Compared to patients in the middle deciles of presenting MAP, patients in the highest and lowest MAP deciles were the only groups that demonstrated a higher mortality on univariate analysis (OR 2.06, 95%CI 1.16-2.31 and OR 2.86, 95%CI 1.76-4.67, respectively), this relationship persisted after adjustment for ISS, HR, temperature, presence of burn injury, TBI, and AKI. Further multivariate analysis limited to patients without burn injury, did not demonstrate an association between high MAP and mortality (OR 0.84, 95%CI 0.36-1.99; p=0.70). Conversely, when limited to patients with burn injury, high MAP was associated with mortality (OR 3.78, 95%CI 1.74-8.20; p=0.001).

Conclusion:

The relationship between mortality and presenting MAP appears to be U shaped, with increased mortality in the lowest and highest deciles. However, mortality in the highest MAP decile appears to be limited to casualties with associated burn injury, even after adjustment for TBI, AKI, and ISS. Military physicians should recognize that burn patients presenting with an elevated MAP are at an increased risk for poor outcomes.

Design of a Cost Effective Hemodynamically Adjustable Model for REBOA Simulation

Keller B¹, Williams T², Salcedo E¹, Neff L², Carden A¹, Li Y³, Gotlib O³, Tran N⁶, Galante J¹

¹Divisions of Trauma surgery, ²David Grant Medical Center, ³UCD Department of Biomedical,

⁴Engineering, Department of Pathology and Laboratory Medicine

Purpose:

Resuscitative endovascular balloon occlusion of the aorta (REBOA) is an adjunct technique to salvage patients with non-compressible torso hemorrhage. Current REBOA training paradigms require large animals or human cadavers for skill acquisition. This adds cost and logistic obstacles to training that may prevent widespread dissemination of REBOA. We propose the development of a low-cost, high fidelity, pulsatile REBOA simulator for physician training.

Methods:

A REBOA simulator was designed and assembled. Pulsatile perfusion was achieved using a Harvard Apparatus pump and the anatomic vascular circuit was constructed out of latex and PVC tubing. Retrograde balloon occlusion was achieved using a Cook CODA balloon catheter. Real time pressure sensors were placed in the proximal aorta and distal iliac artery for pressure monitoring and arterial tracings were obtained.

Results:

A pulsatile simulator capable of generating cardiac outputs ranging from 1.7-4.5 liters per minute with corresponding arterial pressures of 89-184/65-121 mm Hg was successfully created. Upon deployment of the REBOA catheter, the arterial waveform distal to the occlusion flattens and distal pulsation within the simulator is lost. Systolic pressures proximal to the inflated occlusion balloon increase by 62 mm Hg, simulating the ability to increase proximal perfusion when the catheter is deployed.

Conclusion:

We have designed a cost effective simulator capable of physiologic blood pressure and flow dynamics that respond in real time to balloon catheter manipulation. Further development and validation of this simulator will allow for refinement, reduction, and replacement of large animal models and cadavers for training purposes.

Pigtail catheters are not inferior to chest tubes for the drainage of ongoing hemothorax

Ferencz, Sarah-Ashley E.¹; Russo, Rachel M.¹; Davidson, Anders J.¹; Neff, Lucas P.²; Grayson, J. Kevin²; Galante, Joseph³
Univ of California Davis, Dept of Surgery¹ and Trauma^{3,2}Clinical Investigation Facility, David Grant Medical Center

Introduction:

In a previous pilot study, we demonstrated that pigtail catheters perform as well as large-bore chest tubes in draining static hemothorax (HTx) in a swine model. To simulate a more realistic clinical scenario, this follow-up study compared the ability of chest tubes and pigtail catheters to evacuate HTx in the setting of continued hemorrhage into the chest.

Methods:

Eight swine were anesthetized, instrumented and mechanically ventilated. A 32F chest tube was placed in a randomly assigned hemithorax and a 14F pigtail catheter was placed in the other. Over 60min, approximately 750mL of arterial blood was continuously instilled into each hemithorax. The chest drains were unclamped after 35min of infusion, and output from each drain was measured every 5min for 55mins. Following euthanasia, the quantity and quality of retained HTx was measured.

Results:

The median percentage (interquartile range [IQR]) of total HTx evacuated by the pigtail catheter (52.6%, IQR 29.2-65.8%), was not significantly different than that drained by the chest tube (65.0%, IQR 56.5-72.3%, $p=0.18$). There was no difference in amount of retained clot, as expressed as a percent of total volume of instilled HTx, in either the pigtail catheter (14.2%, IQR 12.2-16.7%,) or chest tube groups (13.4%, IQR 11.1-19.1%, $p=0.48$) (figure 1).

Conclusion:

In this preliminary study there was no difference in the performance of 14F pigtail catheters and 32F chest tubes in the drainage of persistent HTx or in the amount of residual clot in the chest. These results suggest that 14F pigtail catheters may be a viable alternative in the management of HTx.

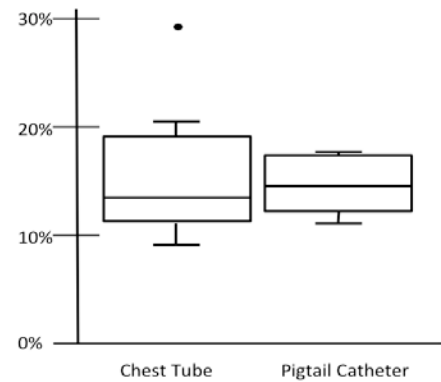


Fig 1: Percent of total HTx retained as clot

A Novel Model of Highly Lethal Uncontrolled Torso Hemorrhage in Swine

Davidson, A; Russo, R; Ferencz, S; Galante, J; Grayson, J; Williams, T; Neff, L
David Grant Medical Center

Introduction:

A reproducible, lethal uncontrolled torso hemorrhage model is of importance to civilian and military trauma research. Current porcine torso hemorrhage models are difficult to standardize as the duration and volume of blood loss is difficult to regulate. As such, lethality has not been uniform in the literature, limiting comparisons.

Methods:

Seven Yorkshire-cross swine were anesthetized, instrumented, splenectomized, and then subjected to traumatic amputation of 30% of the liver. A simple liver tourniquet was applied prior to injury to prevent unregulated hemorrhage during amputation. The tourniquet was released following the injury, allowing standardization of the onset and duration of uncontrolled hemorrhage. The tourniquet was then reapplied to end hemorrhage when mean arterial pressure was consistently less than 35mmHg for 5 minutes. Intra-abdominal blood loss was quantified. Weight, volume, and cut surface area of the resected and residual liver were measured. Hemodynamic parameters were recorded throughout the experiment.

Results:

This injury was rapidly and universally lethal (13.3 ± 5.7 min). Use of the tourniquet effectively halted pre- and post procedure blood loss, and facilitated creation of a consistent injury, reducing injury variability ($27\% \pm 2\%$ liver volume was removed).

Intra-abdominal blood loss was successfully standardized at $37\% \pm 7\%$ of total blood volume.

Conclusion:

Our novel swine uncontrolled torso hemorrhage model using an inexpensive liver tourniquet created a standardized, reproducible, highly lethal injury. It allowed for consistent liver resection volume, precise control over the time, duration, and volume of hemorrhage, and ensured survival can be reliably used as an endpoint when studying the efficacy of resuscitative interventions.

Developing a Murine Model of Injury-Mediated Immunothrombus

J. Becker, C. Pivetti, K. Chung, Z. Saenz, J. Galante, I. Brown
University of California at Davis Department of Surgery, Division of Trauma

Introduction:

Timing of death after injury is trimodal, with the late peak characterized by systemic inflammation, microvascular thrombus and organ failure. We hypothesize that monocyte expression of tissue factor is associated with injury and, in combination with vascular endothelial expression of adhesion molecules, is central to this cascade.

Methods:

Pulmonary contusion was induced under anesthesia with a 50g mass dropped from 0.35 meters, with or without 15% blood volume hemorrhage via retro-orbital (RO) puncture to simulate traumatic shock. Mice were sacrificed at 6 hours post-injury, undergoing terminal phlebotomy and transcardial fixation. Organs were harvested, cryosectioned, and tissue was processed with hematoxylin-eosin (H&E) or fibrin immunohistochemistry (IHC).

Results:

Our model reliably generates a survivable injury, and has features consistent with shock. H&E staining of the kidneys of mice undergoing weight-drop and hemorrhage consistently demonstrated microvascular thrombosis; a finding not seen in our sham controls. These microvascular clots were confirmed on IHC. Interestingly, we did not find thrombosis in those mice which underwent weight-drop injury without RO puncture.

Conclusions:

The absence of clot in the mice injured without RO hemorrhage suggests that microvascular clot deposition in trauma may be multifactorial. We plan quantify IL-6 in plasma of mice with and without injury and hemorrhage, assess the generation of monocyte-tissue factor-platelet complexes by flow cytometry, and ascertain the impact of resuscitation in these groups. We will also assess the presence of adhesion molecule on vascular luminal surfaces, via IHC.

**MORNING
POSTER
ROUNDS**

GROUP III

Pediatric Surgical Readmissions: Are They Truly Preventable?

Erin Brown, Debra Burgess¹, Richard Bold¹, Diana Farmer²

1. Division of Surgical Oncology, 2. Division of Pediatric Surgery

Introduction:

Reimbursement penalties for hospital readmissions in the adult population are driving health care systems to identify risk factors in order to reduce readmissions. These penalties may extend to the pediatric population; therefore, research to determine incidence and predictors is critical.

Methods:

Retrospective review of University HealthSystem Consortium database (N=258 hospitals; 2,723,621 patients) for pediatric patients (age 0-17 years) hospitalized from 9/2011 to 3/2015. Outcome measures were 7-, 14-, and 30-day all-cause readmission rates. Hospital, service, and patient characteristics were evaluated to identify predictors of readmission.

Results:

Readmission rates at 7, 14, and 30 days were 2.1%, 3.1%, and 4.4%, respectively. There were no significant differences in readmission rates for medical versus surgical services. Furthermore, an emergency index admission was not associated with higher readmission rates. For pediatric surgery patients (N = 260,042), neither length of stay (LOS) from the index hospitalization nor complication rate predicted higher readmissions. Evaluating institutional data (N=5,785), pediatric patients admitted for spine surgery, neurosurgery, transplant, or surgical oncology had higher readmission rates. The most common readmission diagnoses for surgical patients were infectious causes (35.6%) and nausea/vomiting/dehydration (48.9%); the most common procedure leading to readmission was appendectomy (28.9%). Patients with chronic medical conditions comprised 57.8% of surgery patients readmitted within 7 days of discharge, and 96.2% required multiple rehospitalizations.

Conclusion:

Readmission rates for pediatric patients are significantly lower than for adults. Furthermore, typical risk factors for readmission among adult patients (i.e. medical service, emergent admissions, LOS, or complication rates) do not predict readmission for pediatric patients. Readmission may be a misnomer for the pediatric surgical population as most are related to chronic medical conditions with only a minority for potentially preventable reasons (nausea, vomiting, dehydration).

Local Anesthetic Infusion via On-Q Pump versus Epidural for Pain Management following the Nuss Procedure

S Kabagambe, L Goodman, YJ Chen, B Keller, J Becker, R Stark, J Stephenson, G Raff, S Hirose;
University of California Davis Division of Pediatric Surgery

Introduction:

Pain is the primary factor limiting discharge after the Nuss procedure for pectus excavatum. Studies have compared epidural analgesia with IV narcotics. This study compares the effects of local anesthetic infusion via On-Q pump versus epidural analgesia on post-operative pain management, operating room (OR) time, and hospital length of stay (LOS) after the Nuss procedure.

Methods:

Retrospective chart review at two tertiary care centers comparing patients with epidural analgesia (n=19) and those with On-Q pump (n=12) after the Nuss procedure in 2013 and 2014. Mann-Whitney test was used to compare total intravenous (IV) narcotic requirement, average pain scores, operation time, total OR time, and hospital LOS.

Results:

The results are summarized in the table below.

Measured Outcomes	Epidural (mean±SD, n=19)	On-Q (mean±SD, n=12)	p-value
Hospital LOS (days)	5.78±0.81	5.13±0.84	0.13
OR time (minutes)	147±28	121±22	0.01
Operation time (minutes)	90±19	91±18	0.64
IV Morphine (mg)	88±59	149±76	0.02
Pain scores (0-10)	2.34±0.95	3.72±1.63	0.02

Conclusion:

Epidural analgesia is associated with better pain scores and lower use of IV narcotics than On-Q pump, but it is associated with longer OR time. There is no difference in hospital LOS.

Patency of the Internal Iliac Artery After Placement of Common and External Iliac Artery Stents

Margarita Vinogradova, BA, Hye Joon Lee, BS, Ehrin J. Armstrong, MD, MAS,
John Laird, MD, Misty Humphries, MD
UC Davis Medical Center, Division of Vascular Surgery

Introduction:

Treatment of severe Aortoiliac Occlusive Disease (AIOD) frequently requires long segment stenting of the common and external iliac arteries. This study evaluated IIA patency after placement of stents extending from the common iliac artery (CIA) into the external iliac artery (EIA).

Methods:

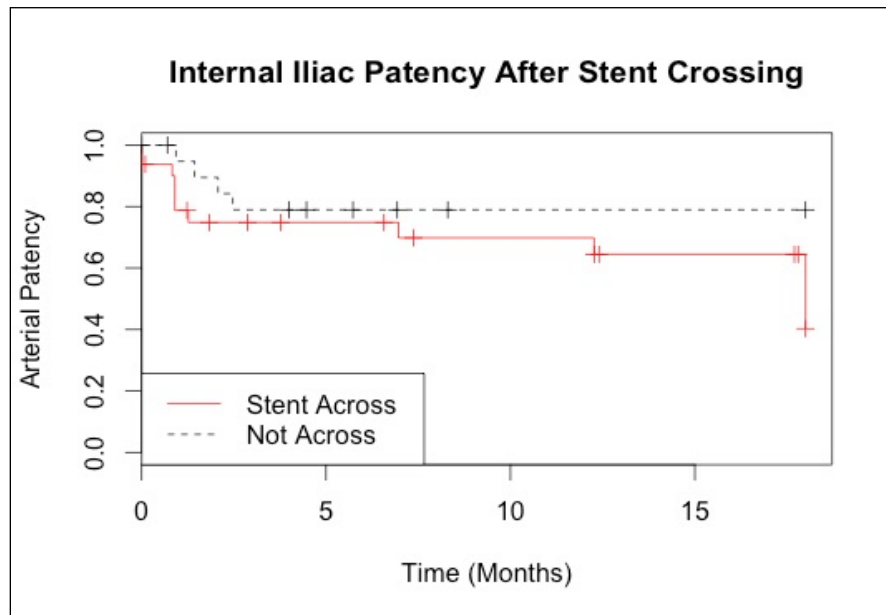
A retrospective analysis of all patients that underwent de novo ipsilateral stent placement in the CIA and EIAs between 2006 and 2014 was performed. Kaplan-Meier analysis was used to analyze patency of the IIA.

Results:

We identified 77 patients with ipsilateral common and external iliac artery stent placement in 93 limbs. Review of all pre-intervention angiograms revealed 41 (53%) patent ipsilateral IIAs. Angiography showed three IIA with stents across the origin (9%) occluded at the completion of the procedure. Patency was assessed by duplex surveillance at six-month. Kaplan-Meier analysis demonstrated a 37% patency in covered IIAs compared to 78% patency in uncovered arteries at 18 months, which was found to be statistically significant ($p=0.04$) (Figure). Two (15%) of patients with non-patent IIA developed buttock claudication, as compared to two (7%) of those with a patent IIA, one of which resolved at 6 months.

Conclusion:

Placement of stents across the origin of the IIA may not result in immediate occlusion, but long-term patency of covered IIAs is decreased compared to uncovered IIAs. This study is limited by a small sample size, but when treating AIOD coverage of the internal iliac origin should be avoided to maintain patency of pelvic circulation.



Intercostal Nerve Cryoablation for Pectus Excavatum Repair: Preliminary Outcomes in Twenty-Five Patients

Keller B, Becker J, Chen Y, Wronski J², Furukawa K², Rahm A³, Hirose S¹, Raff GW³
Divisions of: ¹Pediatric Surgery, ²Pediatric Anesthesia, ³Pediatric Cardiothoracic Surgery

Purpose:

Multimodal pain management strategies have been developed to improve postoperative pain control in patients undergoing pectus excavatum repair. However the optimal pain management regimen has not yet been identified. The purpose of this study is to describe our early experience with intercostal cryoablation as a novel technique for pain management in children undergoing the Nuss Procedure.

Methods:

A multi-institutional retrospective review of patients undergoing Nuss bar placement with bilateral intercostal cryoablation was conducted. The primary outcome was hospital length of stay. Secondary outcomes included operative time, length of ICU stay, duration of intravenous narcotic use, and complications related to cryoablation.

Results:

Twenty-five patients were identified. Nineteen were male (76%). Average age at repair was 15.6 years. Average Haller index was 4.3. All patients were managed with on-demand intravenous narcotics and 23 patients had local infusion catheters in addition to cryoablation. No epidurals catheters were used. Average operative time was 110 minutes (54–166 minutes). Average hospital LOS was 3.4 days (2.0-4.4 days). Median ICU LOS was 1.5 days. The majority of patients (88%) were weaned from intravenous narcotics by POD#2. No complications related to cryoablation were identified and limited three-month follow up demonstrates return to normal chest wall sensation.

Conclusion:

Intercostal cryoablation is a promising technique to manage postoperative pain in children undergoing pectus excavatum repair. Its use results in reduced time to hospital discharge, shorter ICU stays, decreased intravenous narcotic utilization, and has eliminated thoracic epidurals from our practice.

When is Anticoagulation for Traumatic Vascular Injury Required?

Mandy K. Blume,¹ Misty Humphries, MD¹, Maria Ceja-Rodriguez,¹ Joseph J. DuBose, MD¹, Joseph M. Galante, MD²

¹Division of Vascular Surgery, ²Division of Trauma Surgery

Introduction:

Limited data exist regarding the effects of systemic anticoagulation on outcomes after repair of traumatic vascular injuries. Guidelines for heparin use in trauma surgery have not been established.

Method:

Adult patients with open surgical repair for extremity traumatic vascular injuries, from 2006 to 2015 were identified. Retrospective review of vascular repairs prospectively entered in an institutional trauma registry. Presentation, mechanism of injury, technique of surgical repair, intraoperative and postoperative anticoagulation, as well as outcomes and complications were examined.

Results:

123 patients were treated for extremity traumatic vascular injuries. Penetrating trauma (n = 75) was the primary mechanism. Systemic intraoperative anticoagulation was administered in 69 patients. Patients with multilevel trauma (n=10) were less likely to receive intraoperative heparin (p= 0.29) Intraoperative heparin use did not affect complication risk. (42% with vs. 45% without, p= 0.95) Postoperative anticoagulation was used in 24 patients. These patients were more likely to have complex injuries (14% vs. 46%, p=0.001) and to require re-operation (7.5% vs. 25%, p=0.03).

Conclusion:

Despite the hypercoagulability of trauma, arterial repair may be safely accomplished without systemic anticoagulation in trauma patients. Intraoperative anticoagulation may only be needed for complex arterial injuries and postoperative anticoagulation was associated with an increased risk of complications.

**AFTERNOON
POSTER
ROUNDS**

GROUP I

Ex-Vivo Normothermic Perfusion (EVNP) and its Attenuation of Kidney Ischemia-Reperfusion Injury (IRI): A Proposed Mechanism

I. Palma¹, S. Kabagambe¹, Y. Smolin¹, T. Boyer¹, I.P Palma¹, O. Fiehn², J. Sageshima¹, C. Santhanakrishnan¹, C. Troppmann¹, R.V. Perez¹

Department of Surgery: Transplant Division, ²Department of Molecular and Cellular Biology & Genome Center, University of California, Davis

Background:

Ex-vivo normothermic perfusion has the potential to repair deceased donor renal ischemia-reperfusion injury. We hypothesize that ex-vivo normothermic perfusion may attenuate renal ischemia-reperfusion injury via alteration of lipid metabolism.

Methods:

Eight paired human kidneys deemed unsuitable for transplantation were placed on EVNP at 37°C for 3 hours. Kidneys were perfused with packed red blood cells (PRBC) as an optimal repair solution or whole blood (WB) to simulate early allograft IRI. Blood and urine were collected to analyze for pH, oxygen, electrolytes, creatinine, lactate, and the marker of kidney injury neutrophil gelatinase-associated lipocalin (NGAL). Renal biopsies were collected and lipid metabolomic profiles are being generated using gas chromatography-mass spectrometry. Results were measured with repeated measures ANOVA.

Results:

Based on preliminary data, kidneys perfused with PRBC showed more favorable hemodynamic and functional parameters. Higher flows and lower resistances were observed, however neither showed any statistical significance ($p=0.19$ and $p=0.20$). Functional parameters appeared more favorable in the PRBC group but only achieved statistical significance with urine NGAL ($p=0.02$).

Conclusion:

Based on preliminary data we hope to determine whether EVNP induces an alteration of lipid metabolism as a protective mechanism in renal IRI.

Effect of stem cell seeding and extracellular matrix scaffolds on skeletal muscle regeneration

Tiffany Sarrafian¹, Sue Bodine¹, Sue Stover¹, Kevin Grayson², Hakan Orbay¹, David Sahar¹

1. University of California, Davis, Surgical Bioengineering Laboratory and School of Veterinary Medicine 2. Clinical Investigation Facility, David Grant USAF Medical Center, Travis Air Force Base

Introduction:

There is clinical need for enhanced repair of volumetric muscle loss associated with severe injury. We hypothesize that extracellular matrix (porcine small intestinal submucosa (SIS) or peritoneum) will stimulate a muscle regenerative response in a rat gastrocnemius model, and healing will be augmented with adipose derived stem cells (ASCs).

Methods:

A 7mm full thickness lesion was surgically created utilizing custom instrumentation. Study groups included SIS or mesothelium, with or without seeded ASCs. Rats were sacrificed at 3 months for histologic evaluation and immunohistochemical assays to evaluate muscle healing.

Results:

ECM was successfully seeded with eGFP transduced ASCs. All groups were operated with no acute complication subsequent to initial implantation. Some animals with mesothelial ECM displayed fistula formation and increased inflammation. No group demonstrated remarkable muscle formation bridging the gap, however, seeded groups showed increased neovascularization and reduced inflammation.

Conclusion:

This model of VML and is useful for the study of skeletal muscle regeneration, however such a large muscle lesion eliminates continuity of the proximal portion of the gastrocnemius with its distal tendon. While the full thickness defect recapitulates the nature of severe injury, the regenerative strategies explored in this study were insufficient to regenerate substantial muscle across the large remnant gap. Additional strategies, in addition to those tested here, will be necessary to serve as a conduit and further enhance healing across the gap.

Comparison of ex-vivo hypothermic (EVHP) versus normothermic perfusion (EVNP) of high-risk deceased donor kidneys

I. Palma, S. Kabagambe, J. Woloszyn, Y. Smolin, R. Yoshikawa, J. Sageshima, C. Santhanakrishnan, R.V. Perez
Department of Surgery: Transplant Division

Background:

Current hypothermic preservation is inadequate to assess high-risk kidneys pre-transplant resulting in many discarded kidneys. This study was designed to evaluate ex-vivo normothermic perfusion as a better method for assessment and repair of organs in comparison to current hypothermic preservation pre-transplant

Methods:

Paired discarded high risk kidneys from 4 deceased donors were placed on an ex-vivo cardiopulmonary bypass circuit at 4°C with standard kidney preservation solution (EVHP). After one hour, one kidney from each pair continued on EVHP while the paired kidney was placed on EVNP at 37°C with oxygenated packed red blood cells and nutrition. After a 3-hour perfusion, both groups were perfused at 37°C with whole blood (WB). Kidneys were assessed by hemodynamic parameters, urine output, blood gases, creatinine, lactate, and the marker of kidney injury neutrophil gelatinase-associated lipocalin (NGAL). Results were compared with repeated measures ANOVA.

Results:

During perfusion with whole blood, kidneys preserved with EVHOP had higher blood NGAL levels, higher blood flow, lower resistance, and higher urine output when compared to those preserved with EVNP, but these values were not statistically significant. Blood gas, lactate, or creatinine levels were not different between the two groups.

Conclusion:

EVNP can be used as a tool for additional assessment of high-risk deceased donor kidneys. Further studies will be necessary to demonstrate whether EVNP provides additional benefit by improving function prior to transplantation.

Refugee health: characterizing health conditions of asylum seekers in Dresden, Germany

Laura Goodman MD, Stephanie Taché MD MPH, Diana Farmer, MD
Division of Pediatric Surgery

Introduction:

Over one million asylum seekers registered in Germany in 2015, the majority from Syria and Afghanistan. Healthcare is guaranteed by the Refugee Convention, but the delivery mechanisms and degree to which care is provided remain heterogeneous. Dresden, in the eastern German state of Sachsen, has one of three dedicated Refugee Clinics (Flüchtlingsambulanz) in the country, and serves as a critical point of access to medical care for both newly arrived and settled refugees. There is an urgent need for more data describing the health needs to guide best practices for healthcare for asylum seekers. The Refugee Clinic affords the unique opportunity to assess the health needs of the asylum seeking population in Dresden and the activities of the clinic itself.

Methods:

Medical diagnoses, referral information, and demographic data are extracted from the electronic medical records of patients seen at the ambulatory Refugee Clinic in Dresden between September 2015 and January 2016, in coordination with an effectiveness evaluation underway by the Evangelische Hochschule and the Kassenaerztliche Vereinigung Sachsen (Saxony state physician's union). Data analysis will be completed using Stata version 14.0.

Progress:

Approximately 4000 patients were seen in the Refugee Clinic for medical (non-psychiatric) complaints between September 1, 2015 and January 31, 2016. Data extraction is ongoing.

Future work:

Data extraction is expected to be completed by February 19, 2016. The data will then be assembled into a database and analyzed. Data for patients seen for primary psychiatric complaints will also be extracted and compiled prior to analysis. Disease incidence and prevalence will be compared to other refugee populations, and demographics will be compared with refugee statistics available through the UN and German government.

Global Surgery Activities and Interest Amongst General Surgery Trainees

Jensen G, Goodman L, Galante J, Farmer D.L.
Division of Pediatric Surgery

Background:

Global surgery is an emerging field of research and practice focused on increasing access to quality surgical care in underserved areas. There remains a very high unmet need for additional surgical training and infrastructure development, with an estimated 70 percent of the world's population lacking access to basic surgical care. Surgical trainees in the US and Canada have demonstrated interest and commitment to improving access to surgical care around the world. Previous surveys have found that between 60 and 80 percent of surgical trainees are interested in participating in global surgery. Around 30 percent of surgical training programs offer overseas experiences for trainees, but fewer have a dedicated training program for those trainees interested in building careers in global surgery. This survey of general surgery trainees (including subspecialties of general surgery) will determine the current level of interest and participation among trainees, while describing the global surgery programs that are currently available.

Methods:

A 28-question survey was administered to general surgery trainees via the Association of Program Directors in Surgery (APDS) mailing list. The survey has been deemed exempt by the UC Davis IRB.

Results/Progress:

The survey is currently awaiting dispersal via the APDS mailing list.

Conclusion/Next Steps:

The need has never been higher for global surgery training to prepare trainees to make meaningful contributions that are of value to host nations. This work will provide an overview of the current progress of global surgery training in meeting these goals.

Proof of Concept: Analysis of Soft Tissue Changes in Facial Aging

Ping Song MD, Shaili Gal MD, Paul Lee MD, Pirko Maguina MD.
Division of Plastic Surgery, Department of Neuroradiology

Introduction:

Many of the anatomical changes of the aging face are still poorly understood. Studies are lacking that study the deeper soft tissue structures of the aging face. We hope to objectively quantify these changes in the aging face over time.

Method:

This is a single-center, retrospective cohort observational study. Inclusion criteria include patients who undergo serial imaging for surveillance of intracranial pathology. Objective measurements of soft tissue structures are obtained through the radiologist's review. We hope to describe at this stage, as a proof of concept, specific soft tissue landmarks and how they change through aging.

Result:

We identified a 74 year old male with head CTs performed over the span of 10 years. We measured soft tissue landmarks in relation to the infraorbital foramen, malar eminence, temporal fossa, and orbit position in relation to the orbital rim. At the infraorbital foramen, soft tissue height decreased from 12.4mm to 11.8mm on the right, and 14.2mm to 14.0mm on the left. At the malar eminence, soft tissue height decreased from 12.8mm to 9.4mm on the right, and 12.7mm to 5.0mm on the left. The temporalis muscle and its overlying soft tissue, measured in transverse, decreased from 14.2mm to 13.8mm and 24.4mm to 23.2mm, respectively, on the right side. While on the left, the temporalis muscle belly and overlying soft tissue increased from 15.2mm to 15.5mm and 26.6mm to 28.0mm, respectively. The globe projection increased as measured from the orbital rim, from 11.1mm to 12.9mm on the right, and 10.0mm to 10.2mm on the left.

Conclusion:

Our current proof of concept demonstrates objective changes in facial soft tissue over one decade. There has yet to be a study that follows the same patient through the aging process and objectively measures the soft tissue changes. We have since identified 6 new patients as part of this novel descriptive study to better characterize the aging face.

**AFTERNOON
POSTER
ROUNDS**

GROUP II

Surgical Resident Shift Length Does Not Impact Types of Errors Made

Jamie Anderson, MD; Laura Goodman, MD; Guy Jensen, MD; Joseph Galante, MD;
Trauma and Acute Care Surgery

Introduction:

In 2010, resident duty hours were restricted in an attempt to improve patient safety and resident education. The restrictions have increased hand-offs and created a “shift mentality,” increasing concerns about adverse effects on patient safety.

Methods:

All surgical mortality and morbidity submissions at a university hospital surgery department from July 1, 2013-June 30, 2015 were reviewed. During 2013-14, standard 2010 duty hours were in place. In 2014-15, duty hour restrictions at this institution were relaxed with no restrictions on length of shift. Root causes of adverse events were compared between academic years. 16 root causes were categorized as technical, judgment, cognitive, or team failure (including miscommunication, fatigue).

Results:

383 adverse events, including 54 deaths, were analyzed. There was no difference in errors resulting in mortality between years ($p=0.479$). There were no differences in categories of errors between years ($p=0.196-0.808$). The fewest number of errors were due to team failure (127, 17.0%). By subset, technical errors resulted in the highest number of errors (169, 22.6%), whereas fatigue resulted in the fewest (7, 0.9%). There were no differences between types of errors for adverse events involving urgent cases.

Conclusion:

There were no differences in types of errors when resident duty hours were less restrictive. Policies determining duty hours should thus be guided by optimizing resident education.

Balanced transfusion in pediatric trauma patients

Laura Goodman, MD, Joseph Galante, MD, Jacob Stephenson, MD
Division of Pediatric Surgery

Introduction:

Balanced transfusion, utilizing multiple separated blood products to approximate the ratios found in whole blood, is accepted practice in adult trauma patients but has not been clarified in pediatric patients. The purpose of this study is to examine outcomes of red blood cell (PRBC) transfusion and balanced blood transfusion (1:1-2:1 ratio of PRBC to plasma) at a pediatric level 1 trauma center.

Methods:

1,582 trauma patients ≤ 14 years of age in a prospective institutional database were divided into transfused (n=44) and non-transfused groups (n=1538), and further balanced transfused (n=14) and non-balanced transfused (n=30). Patient characteristics were compared using summary statistics and logistic regression was used to control for confounders.

Results:

Among transfused patients compared to non-transfused, significant differences were found in higher injury severity scores (ISS), lower GCS, lower initial hematocrit, longer length of stay, and higher rate of death (all $p < 0.0001$). Transfused patients were non-significantly younger than non-transfused (median 4 vs 6 years, $p = 0.183$). Controlling for GCS and ISS, the mortality rate was not significantly different between transfused versus non-transfused ($p = 0.901$). Balanced transfused patients were non-significantly older ($p = 0.165$) and heavier than non-balanced transfused patients ($p = 0.087$). Otherwise the two groups were not significantly different. Controlling for GCS and ISS, the mortality rate was not significantly different between balanced versus non-balanced transfused ($p = 0.877$).

Conclusion:

Balanced blood product transfusion did not affect mortality in this small study, but transfusion was rare. Further study is needed to determine if balanced blood transfusion improves pediatric trauma survival and outcomes.

Young female vascular surgeons more likely to enter academia: A paradigm shift?

Mimmie Kwong, MD, Ashley E Allen, BS, John G Carson, MD, Julie A Freischlag, MD, Nasim Hedayati, MD

Division of Vascular Surgery, U.C. Davis Medical Center

Introduction:

In the last decade, there has been a dramatic increase in the number of female trainees in vascular surgery programs. Our goal was to evaluate the differences in career paths based on gender and the factors influencing career decisions among young vascular surgeons.

Methods:

A 17-item web-based survey focusing on current employment status, reasons for choosing academic versus non-academic positions, and career satisfaction was distributed to 900 members of the Society for Vascular Surgery who completed vascular surgery training in the past ten years.

Results:

A total of 196 individuals responded to the survey (21.7%). The cohort included 148 (75.5%) men and 48 (24.5%) women. The majority of the respondents were non-Hispanic white (65.31%). 62% of all respondents were younger than 40 years of age. Overall, 72.9% of women applied to academic positions following their training, compared to 58.8% of men. Women were more likely to be in academic practice (54.1% vs. 37.1%, $p=0.038$) and cited mentorship more frequently (54.1% vs. 32.4%) as the reason for choosing an academic practice. Table 1 represents other major factors for choosing academics. Over 85% of all respondents were very *satisfied* or *somewhat satisfied* with their careers. Although men were more likely to be *very satisfied* (53% vs. 37.5%), this did not reach statistical significance ($p=0.055$).

Conclusions:

Career satisfaction remains high among young vascular surgeons. In this cohort of vascular surgery graduates, we found that women were more likely to pursue academic positions than men, with mentorship, ability to teach, and complexity of cases commonly cited as reasons for this choice. However, whether these women stay in academia and what directions they take in their later careers needs further evaluation.

TABLE 1.

Factors Cited for Choosing Academic Practice	Women (%)	Men (%)
Research opportunities	47.9	32.4
Mentorship	54.2	32.4
Teaching opportunities	58.3	39.2
Diversity/complexity of case load	52.1	36.5
Ability to subspecialize	4.2	8.8
Larger call pool	8.3	16.9
Other	2.1	2

The Morbidity and Mortality Conference Should Systematically Address Root Causes of Errors: Results of a Departmental Survey

Jamie E. Anderson, MD; Laura F. Goodman, MD; Diana L. Farmer, MD; Joseph M. Galante, MD; General Surgery

Introduction:

We surveyed residents and attending surgeons of the UC Davis Department of Surgery to identify current opinions about the morbidity and mortality (M&M) process.

Methods:

A 12-question survey was created and distributed to residents and attending physicians who attended an M&M conference in November 2015.

Results:

71 participants responded (32 attending surgeons, 33 residents, and 3 nurse practitioners or physician assistants). "Improving quality of patient care" was identified as the primary purpose, followed by "education" and "accountability." A majority agreed that the M&M conference is educational (n=62, 87.3%) and improves patient care (n=52, 73.2%). Respondents felt presenters are typically supported and encouraged (n=37, 53.6%), although 23 respondents (33.3%) were neutral on this issue. Complications are classified as needing "room for improvement (RFI)", no RFI, or possible RFI. When asked if this classification is adequate to characterize complications, 23 (32.4%) disagreed, while 33 (46.5%) agreed and 15 (21.1%) were neutral. Additional free text responses included suggestions on how to improve the M&M process.

Conclusions:

Most respondents felt the M&M process improves patient care and provides an adequate educational experience. This survey elucidated ways the M&M process can improve, such as by identifying and tracking root causes of errors.

The Plastic Surgeon as Employee

Patel NB, Arsalai M, Stevenson TR, Parento E, Pu LLQ
Division of Plastic Surgery

Introduction:

Plastic surgeons endure years of training yet remain poorly equipped to negotiate their first employment contracts. We sought to evaluate areas of concern in the typical plastic surgeon contract and identify standard elements that should be included to better preserve surgeons' interests.

Methods:

A brief survey was emailed to California Society of Plastic Surgeons members. Responses were anonymous. We collected demographic information and asked whether members sought legal counsel in their contract negotiations. A similar survey was sent to American Society of Plastic Surgeons members.

Results:

Over two-month periods, our CSPA survey generated 113 and our ASPS survey generated 324 responses. The in-state and national distributions of members were representative for both CSPA and ASPS.

41.4% and 32.6% of members reported having worked in a group practice consisting of 3 or more surgeons, 27.9% and 22.1% in partnership, and 23.4% and 24.8% in solo practice.

74.5% and 61.9% of members did not seek legal assistance.

For the CSPA, malpractice coverage varied from 51.6% with claims-made, to 21.7% with tail, to 33.0% with none at all. For the ASPS, 43.5% indicated claims-made, 17.3% with tail, 24.7% having unspecified type; 0.93% indicated having none.

63.9% of CSPA members had no disability policy offered by their employers. 23.6% of ASPS members reported employer purchased policies, whereas 66.8% purchased their own. For the ASPS, 73.0% indicated having "own occupation" coverage.

26.4% of CSPA and 22.7% of ASPS members reported annual income of < \$100,000; 49.1% and 54.3% reported \$101,000 - \$200,000; 17.9% and 13.4% reported \$201,000 - \$300,000; 6.60% and 9.58% reported > \$300,000.

Using a five-point scale, 7.69% of CSPA and 9.90% of ASPS members reported being "extremely dissatisfied" with their first contracts, while 24.0% and 25.6% were "perfectly happy."

82 CSPA and 252 ASPS members offered advice. Themes included seeking legal counsel; avoiding non-compete clauses; and going into solo practice.

Conclusion:

As U.S. health care evolves, more plastic surgeons may find themselves employed by institutions. Seeking an attorney may help protect financial and legal interests such as malpractice options and disability coverage.

Assessing Safety of Negative Pressure Wound Therapy over Pedicle Muscle Flaps: A Retrospective Review of Gastrocnemius Muscle Flap

Hakan Orbay,¹ Samuel Lance,¹ Mankushpreet Kaur,¹ Tima Dehghani,¹ David Boudreault,¹ Gavin Pereira,² David Sahar MD¹

¹UCDMC, Division of Plastic Surgery. ²UCDMC, Department of Orthopedic Surgery

Introduction:

The use of negative pressure wound therapy (NPWT) on muscle flaps is controversial due to the concerns about circulatory compromise. In this study, we evaluated the safety of NPWT as a method to secure the split thickness skin grafts (STSGs) over pedicle gastrocnemius muscle flaps.

Methods:

We applied NPWT to the STSGs covering gastrocnemius muscle flaps in eight patients between January 2011 and October 2013. The STSGs were 12/1000 inch thick and meshed 1:1. A continuous negative pressure of -75 mmHg was applied on the STSGs for 5 days post-operative using a Vacuum Assisted Closure (V.A.C) therapy unit. Outcomes were evaluated based on graft adherence and flap failure.

Results:

Mean grafted area was 57 ± 32.6 cm². Seven patients had medial and one patient had a lateral gastrocnemius flap. Four of the patients had multiple co-morbidities and one patient was a smoker. Post-operative follow-up period ranged from 6 weeks to 8 months. Average graft adherence was 97.5 ± 5.5 %. Reduction in flap edema was observed in all cases, with no evidence of STSG detachment or flap compromise in the form of congestion or necrosis.

Conclusion:

In our series, the use of NPWT for fixation of STSGs over pedicle gastrocnemius muscle flap was effective and had no negative impact on flap viability.

You are cordially invited to attend
the UCDCMC Department of Surgery

**27TH ANNUAL
RESEARCH
SYMPOSIUM**

**AWARDS
BANQUET**

4. 19. 2016
6:00 p.m.

Crocker Art Museum
216 'O' Street
Sacramento, California

RSVP: ricstevens@ucdavis.edu