

# 30th Annual Meeting of the Academy of Surgical Research

30  
YEARS

September 18–20, 2014

Minneapolis, Minnesota  
Hyatt Regency Hotel

## **"30 years of surgical collaboration-sharing the knowledge"**

The **30th Annual ASR Meeting** will include presentations on new and refined methods and materials used in preclinical and clinical surgical investigations, as well as new procedures that will enhance the attendees' fields of scientific and surgical research. Renowned academic and industry experts will share cutting-edge surgical concepts, research, and techniques, thereby fostering an interdisciplinary transfer of ideas and theories in experimental surgery.

**Learn about** surgical research and surgical challenges in areas including:

- Orthopedic surgical models
- Neurologic surgical models
- Advanced cardiac models
- Transplantation & Immunology
- Refinement, Replacement and Reduction Innovations
- Biomedical Ethics & Welfare
- Anesthesia and Pain Management
- General Surgery & Suturing
- Disease Specific Surgical Model Development
- Pre and Post-Operative Care
- Microsurgery
- Surgical Training/Management





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## So tell us about your global CRO needs.

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When you work with us, you're working with an organization of more than 1,200 professionals located throughout the world. But more than that, you're working with people who truly care about your results.

Congratulations to ASR  
on your 30th anniversary.

[www.wilresearch.com](http://www.wilresearch.com)



We have **listening** down to a **science**.

# Let's spend our anniversary together.



## Please join us for the **ASR 30th Anniversary Celebration.**

It promises to be a magical night with good food and even better camaraderie. The Teddy Holidays will provide live entertainment and the City of Minneapolis will supply magnificent views.

**TIME:** 6:00 p.m. – 9:00 p.m.

**DATE:** Friday, September 19

**PLACE:** Windows on Minnesota  
710 Marquette Avenue  
Minneapolis

**ROOM:** Stars Ballroom

**A sincere thank you to our generous sponsors.**



# Welcome

Welcome to the Twin Cities!

On behalf of the Officers and Board of Directors, welcome to the 30th annual meeting of The Academy of Surgical Research. To all of our devoted members, honored speakers, exam takers, exhibitors, corporate guests, veterinary students, and first-time attendees, I would like to personally extend a warm welcome to the wonderful city of Minneapolis. I am confident that this year's meeting will be an exciting and productive experience.

This year the Academy celebrates its 30th anniversary – “30 years of surgical collaboration-sharing the knowledge”. The Academy was founded to encourage, foster, promote, and advance professional and academic standards, education, research, and development in the arts and sciences of experimental surgery. Over the years, ASR has remained committed to this mission and continues to impart surgical knowledge to its members and supporters and has provided a venue for continued advancements in surgical research and techniques. It is this mission that will drive us toward another 30 years of surgical excellence.

Each year our volunteer members work tirelessly to put together a program that is educational, informative, and at the forefront of surgical research. This is possible because of ideas and suggestions we get from you – our membership. My sincere appreciation goes out to everyone that contributed time, ideas, and support to make this meeting possible. I encourage everyone to continue to share your ideas, opinions, knowledge, and experiences. This collaboration and idea exchange is what will foster new innovation and perspectives that are essential for advancements in surgery.

This year, the Board of Directors approved revisions and updates to the ASR Bylaws. Most notably, we amended the Bylaws to create a new standing committee: Veterinary Oversight Committee (VOC). The Veterinary Oversight Committee will review and comment on proposed letters and white papers on regulatory, veterinary medical and / or science or other pertinent issues brought before the Academy. I have asked Dr. Jan Bernal to serve as the first VOC chairperson. We are excited for the contribution that this new standing committee will bring to the Academy and wish it much success.

It has been an honor and privilege to serve ASR as President this year. The lasting friendships I have made over the years through the Academy and at past meetings will undoubtedly be cherished for years to come. ASR grows and evolves because of these types of friendships and collaborations and because of the contributions of its membership. I encourage everyone to continue to share their knowledge, ideas, and experiences – please become involved in YOUR Academy of Surgical Research.

Be sure to mark your calendars for the 31st Annual Meeting in Winston-Salem, North Carolina, October 8-10, 2015!

Sincerely,

John Cody Resendez  
President, ASR







PRESIDENT

## John Cody Resendez, SRS, MS, RLATg, CMAR

Director, Infusion Toxicology, Surgery and Experimental Medicine

**Cody** is Director of Infusion Toxicology, Surgery and Experimental Medicine at WIL Research, U.S. Prior to joining WIL Research, Cody was the Director of Infusion Toxicology and a Senior Study Director at MPI Research. He obtained a BS in biology from Texas A&M University and a MS in animal science from the University of Nevada. Cody is currently completing a Doctorate in Business Administration. He has over 17 years of experience in preclinical and surgical research, with a specific focus in infusion toxicology. Cody is very active in the infusion toxicology arena, delivering presentations and posters through various national and international venues, and has authored/co-authored many peer reviewed scientific abstracts and publications. Most recently, Cody was author/co-author of two book chapters; 'Canine Infusion' in the revised edition (2013) of the Handbook of Pre-Clinical Continuous Intravenous Infusion and 'Infusion Toxicology and Techniques' in A Comprehensive Guide to Toxicology in Preclinical Drug Development. His areas of expertise include cardiovascular physiology, infusion toxicology, and vascular surgery. Cody is also certified as a Surgical Research Specialist by the Academy of Surgical Research (ASR). He is a member of AALAS, the Academy of Surgical Research (2010 Annual Meeting Program Chair; 2010-2013 Board Member, 2014 President), the Society of Toxicology, the Infusion Technology Organisation (ITO), and the Safety Pharmacology Society (SPS).

# Welcome

## Welcome to Minneapolis!

I would personally like to welcome you to Minneapolis, MN for the 2014 Annual Meeting of the Academy of Surgical Research. This year's theme, '30 years of...' is an acknowledgement to the significance of the long history of our society.

Over the next few days, we will hear presentations on the most up to date methods and innovations in the surgical sciences. Of the 55 abstracts accepted, the program committee has crafted a unique and interesting program consisting of four keynote lectures, 30 concurrent general sessions, 6 wetlabs and 18 posters. It is the intent that the numerous discussions and interactions that will take place over the next several days will continue to inspire the innovative spirit of the attendees and will serve to invigorate and catalyze new and exciting surgical discoveries.

In addition to the abstracts and the attendees, the participation of exhibitors and support from our sponsors play an integral role for the success of this scientific meeting. For this, we greatly appreciate the support from our numerous sponsors and participating exhibitors who have helped make this 2014 meeting possible. Anyone who has ever been involved in planning an annual conference knows that it takes a team of amazing volunteers to plan and organize a successful event of this caliber. I would like to personally thank the members of the Program Committee (Renee Bodinizzo, Heather Bogie, Liisa Carter, Christina Gross, Nance Moran, Randy Pielemeier, Matthew Ruiter, Leslie Stoll, Luis Toledo-Pereyra, Marlo Volberg, Rasa Zhukauskas, and Tracy Ziegelhoffer) for their time and assistance with the organization and assembly of a very exciting 2014 program.

**Justin Prater,**  
2014 Program Chair





C H A I R

## **Justin Prater, BS, SRA, RLATg**

### **Program Chair**

**Justin Prater** is currently completing a Master's degree in Pharmacology through Michigan State University. Justin started his career in 2006 as a technician at MPI Research where he progressed through research levels to study coordinator in 2012. Currently, Justin is a Program Manager at an innovative start-up preclinical research organization within Wake Forest University in North Carolina, where he assists the Program Director; Vince Mendenhall Ph.D., DVM in development and execution of all preclinical surgical studies. Justin has worked with the Academy of Surgical Research for the last five years. During that time, he has obtained his Surgical Research Anesthetist certification, given several talks on topics ranging from GLP compliance to new technology in surgery, and volunteered with computer services and various wet-labs. He has enjoyed working with the ASR Board members and was approached by the President to chair the 2014 ASR program. Justin has embraced the unique opportunities and challenges of putting together this year's conference, and hopes you enjoy this 30th anniversary meeting in the lovely city of Minneapolis.

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## **Program Committee**

**Nance Moran, SRS, MS, BLA, RLATg**  
Genzyme

**Randy Pielemeier, LVT, SRS, BS, LATg**  
MPI Research

**Rasa Zhukauskas, MD, CTBS**  
RTI Surgical

**Leslie J. Stoll, SRS, LATg, RVT**  
Charles River Laboratories

**Tracy Ziegelhofer, SRS, BS, LATg**  
Huntingdon Life Sciences

**Renee Bodinizzo, SRS,**  
Sanofi US

**Marlo Volberg, SRS**  
Pfizer

**Liisa Carter, SRS, CVT, ALAT**  
American Preclinical Services, LLC

**Christina Gross, BA, SRS**  
American Preclinical Services, LLC

**Heather Bogie, CVT, SRS, RLATg**  
Data Sciences International (DSI)

**Luis H. Toledo-Pereyra, MD, PhD**  
Western Michigan University Homer  
Stryker School of Medicine

**Matthew Ruiter**  
SAI Infusion Technologies





# Board of Directors & Committee Chairs

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## Board of Directors

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Tracie Rindfield, SRS, RLAT

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David Moddrelle, SRS

### Directors at Large (2012-2015)

Margi Baldwin, RVT, LATg, SRS, CMAR, MS

Szczepan Baran, VMD, MS

### Directors at Large (2013-2016)

Heather Bogie, SRS, RLTA, CVT

Jon Ehrmann, SRS, SRA, LATV

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## Committee Chairs

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Szczepan Baran, VMD, MS

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Matt Ruiter

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Szczepan Baran, VMD, MS

### Nominating Committee

Steve Hachtman

### Program Committee

Justin Prater, SRA, BS, LATg

### Publications Committee

Cristina Weiner, VMD, MS

### Strategic Planning Committee

Nance Moran, SRS, RLATg

### Journal Editor

Luis Toledo-Pereyra, MD, PhD

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Teresa Gleason, SRS, BS, LVT, LATg

**Paul A. Iaizzo, PhD**

Director for Education of the Lillehei Heart Institute  
Director of the Malignant Hyperthermia Muscle Biopsy Center  
Medtronic Professor of Visible Heart Research

**Paul Iaizzo** is a Professor in the Departments of Surgery, Integrative Biology and Physiology, and the Carlson School of Management at the University of Minnesota. Additionally, he serves as the Director for Education for the Lillehei Heart Institute and Associate Program Director for Education and Outreach for the Institute for Engineering in Medicine, also at the University of Minnesota. Dr. Iaizzo earned his PhD degree from the University of Minnesota, with a focus on Physiology/Neurophysiology.

In 2002, Paul Iaizzo was recognized as a Distinguished University Teaching Professor. Since 1990, he has trained 125+ graduate students, postdoctoral fellows, and medical students in his laboratory. In 2012, he was elected to the College of Fellows in the American Institute for Medical and Biological Engineering.

His main research focus is translational systems physiology, and his research group has developed a unique isolated working large mammalian heart model. The Visible Heart Laboratory is well known for its novel imaging techniques of cardiac anatomy and physiology, and is an ideal place to perform translational systems physiology research. Other research interests include cardiac pacing, skeletal muscle pathophysiology, thermoregulation, black bear hibernation, wound healing, and spine biomechanics.

Dr. Iaizzo has authored more than 190 original articles, edited 4 books, and holds multiple patents (both US and European) related to cardiac anatomy, physiology, and devices.

**Rachel Lynne Tapp, BS, LATg**

Senior Study Director  
MPI Research

**Rachel Tapp** is a Senior Study Director in the neurobehavioral sciences department at MPI Research. She received her BS (2002) and is completing her MS (expected - 2014) from Michigan State University. During her 11 year tenure at MPI Research, Mrs. Tapp has been involved with a variety of non-clinical studies, including development of efficacy and safety studies to evaluate stem cell products, efficacy of antibacterial, antiviral, and anti-seizure drugs, and has also tested many compounds for safety pharmacology within cardiovascular, pulmonary, and neurobehavioral studies. She is responsible for ensuring high-level performance of these contracted studies for regulatory and non-regulatory submissions. Prior to her time at MPI, she spent many years developing an interest in research while working with National Audubon Society and also in the aquatic toxicology laboratory at Michigan State University.

For the past several years, Rachel has been the primary study director evaluating the ototoxicity of compounds at MPI Research. As these studies have many complicated endpoints she has developed and expanded the ototoxicity platform within her organization to allow MPI to be a leader in the CRO industry within this specialized study type. She has promoted the development of internal capabilities to assess standard measures of ototoxicity both functionally and physiologically. This focus to increase capabilities also spans various routes of delivery, including surgical administration of compounds, and expanding across multiple species (rodent and non-rodent). Most recently, she has been working to help develop guidance and study methods to support the vestibular impact of compounds to add to the repertoire that MPI can offer for its ototoxicity evaluations. Mrs. Tapp is also an active member of the Association for Research in Otolaryngology, the Safety Pharmacology Society, and the Society for Neuroscience.



S P E A K E R

## David Stoloff, DVM, MS, Diplomate ACVS

Distinguished Research Fellow Global Surgery Group  
Preclinical Research Center of Excellence– Ethicon, Inc.

**Recipient of the 2014 Jacob Markwitz Award**

**Education including specialty training:** B.S. (Agricultural Science) – University of Connecticut; DVM – Michigan State University; MS– (Veterinary Surgery) – Kansas State University ; Internship in Radiology– Kansas State University, Residency – Small Animal Veterinary Surgery (Kansas State University)

After receiving his DVM from Michigan State University, Dr. Stoloff went into private practice for several years before taking an Internship in Veterinary Radiology and later enrolling in a Residency in Veterinary Surgery and a Masters Program at Kansas State University's College of Veterinary Medicine. Following completion of his residency and Masters Program, he stayed on as a member of the faculty for an additional year before taking an Assistant Professor position in the Veterinary Clinical Sciences Department at Louisiana State University's School of Veterinary Medicine. Three years after joining LSU's faculty he relocated to the East Coast to take a clinical position at Rowley Memorial Animal Hospital (Springfield, MA).

In 1984, Dr. Stoloff joined Ethicon's R&D Organization (Somerville, NJ), and has worked for Ethicon for 27 of his 30 years with Johnson & Johnson. Three of his years with the corporation were spent at Ethicon Endo-Surgery (Blue Ash, OH). Dr. Stoloff was a member of the team that designed and built the Ethicon Endo-Surgery Institute in Blue Ash, Ohio. Currently, Dr. Stoloff is a Distinguished Research Fellow in the Preclinical Research Center of Excellence in Somerville, NJ. The Distinguished Research Fellow title is the highest level within Johnson & Johnson's Scientific Ladder. His specialty is developing preclinical models that support product development, and conducting performance (functionality) testing. He supports product development programs across multiple businesses and the assessment of new product opportunities. Some of the products Dr. Stoloff has collaborated on over the years include the following: STRATAFIX™ Knotless Tissue Control Devices, EVARREST™ Fibrin Sealant Patch, GYNECARE THERMACHOICE® III Uterine Balloon Therapy System, LIGACLIP® Multi-Clip Applier, GYNECARE VERSAPOINT™ Bipolar Electrosurgery System, PANALOK® Anchor, ETHICON Powerstar Bipolar Scissors, ABSOLOK Absorbable Ligating Clips, PROXIMATE® Mechanical Staplers, EMBRACE Heart Positioner, EMBRACE Sternal Retractor, EVICEL® Fibrin Sealant, PDS™ Flexible Plates, ETHICON DERMABOND® Topical Skin Adhesive, DERMABOND PRINEO® Skin Closure System, ETHICON SECURESTRAP® 5mm Absorbable Fixation Device, & SURGIFLO® Hemostatic Matrix Family of Products. Dr. Stoloff was co-chair of Ethicon's Innovations Seminar Series, and currently chairs the committee for Johnson & Johnson's 2014 Excellence in Science Symposium.

Dr. Stoloff is a member of Phi Kappa Phi, Alpha Zeta, Phi Zeta and Gamma Sigma Delta honor societies. He is a Diplomate of the American College of Veterinary Surgeons and is licensed to practice in six states (MI, CT, MA, KS, NJ, OH). He is a recipient of Johnson & Johnson's prestigious Philip B. Hofmann Research Scientist Award for his contributions to research. Dr. Stoloff is a mentor to scientists and engineers, and is passionate about developing innovative products that offer significant benefit to patients, healthcare professionals and providers, and advance the standard of care.

GUEST



SPEAKER

## Peggy Callahan

Co Founder, Executive Director Wildlife Science Center

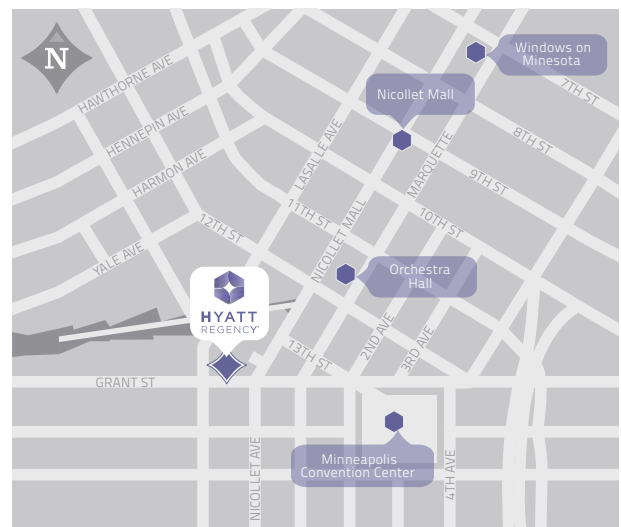
A native of Rochester, MN, Peggy first became interested in canines through her family dogs who were her constant companions. Inspired by a reply to a letter she had sent to a wolf biologist asking for a job at age eight, Peggy earned a degree in Biology from Carleton College and began working for the 'Wolf Project' in August 1985. For five years she managed the colony for research, focusing on refining chemical immobilization techniques for use in the field. In addition to her wolf time, Peggy also assisted with studies involving Black Bear, Red Fox, White-tailed Deer and Wolves in the field, including assisting with the Isle Royale wolf captures in 1989 and 1991. When federal funding for the Wolf Project ceased in 1991, the Wildlife Science Center was created by Peggy, her husband Mark Beckel, and wildlife Veterinarian Terry Kreeger, to keep the facility open. After three years of intensive building and program planning, the Wildlife Science Center opened its doors to the public as a non-profit education and research facility. Peggy is a co instructor for multiple wildlife handling courses each year in which she trains wildlife professionals from state, federal, and international government agencies. She is frequently called upon to assist State and Federal agencies in identifying wolves and wolf/dog hybrids. Peggy and the wolves at the center have been featured extensively on both Animal Planet and National Geographic programs.

# Venue



HYATT REGENCY MINNEAPOLIS  
1300 Nicollet Mall  
Minneapolis, MN 55403  
USA

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[minneapolis.hyatt.com](http://minneapolis.hyatt.com)



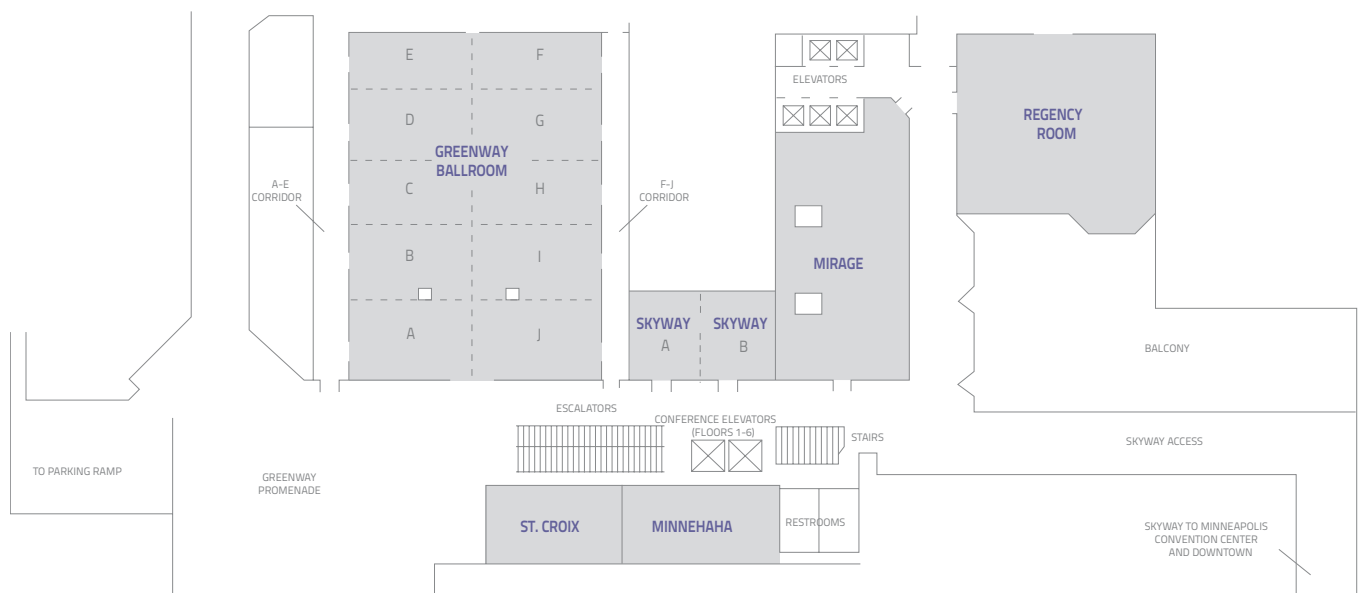
The contemporary Hyatt Regency Minneapolis is perfectly situated on Nicollet Mall. The recently redesigned hotel pays tribute to the unique culture of Minnesota, with sleek mid-century Scandinavian décor highlighted by a spacious lobby featuring an expansive stone fireplace framed by rustic wooden logs. The hotel's premiere downtown location provides convenient access to an incredible array of Twin Cities' attractions, from shopping to sports, the arts or the great outdoors.



# Floor Plan



## Second Level Meeting Rooms



# Meeting Overview

Registration Hours – Greenway Foyer	
Thursday, September 18	07:00 am – 05:00 pm
Friday, September 19	07:00 am – 05:00 pm
Saturday, September 20	07:00 am – 12:00 pm
Wednesday, September 17	
02:00 – 05:00 PM	ASR Board Meeting
Thursday, September 18	
07:00 AM – 08:00 AM	Registration for test takers and wet lab attendees – Greenway Foyer
07:00 AM – 08:00 AM	Light continental breakfast for test takers and wet lab attendees
07:30 AM	Bus departs from hotel to DSI and APS Wet Labs
08:00 AM – 12:00 PM	ASR Examinations
08:00 AM – 12:00 PM	Wet Labs APS – Rodent Femoral Critical Sized Defect DSI – Microsurgical Telemetry Implantation Techniques
08:00 AM – 05:00 PM	Wet Labs APS – Swine Valve Replacement APS – Echocardiography Laboratory
12:15 PM	Bus departs from Hotel to DSI and APS
12:30 PM	Bus departs from DSI to APS
01:00 PM	Bus departs from APS to Hotel
01:00 PM – 05:00 PM	Wet Labs APS – Rodent Post Lateral Fusion
05:00 PM	Busses return to hotel
04:00 PM – 07:30 PM	Welcome Reception with Exhibitors
Friday, September 19	
07:00 AM – 08:15 AM	Continental Breakfast Poster set-up
08:15 AM – 08:30 AM	Opening Remarks
08:30 AM – 09:30 AM	Keynote Speaker
09:30 AM – 10:00 AM	Break with Exhibitors
10:00 AM – 12:00 PM	Track 1 and 2 Scientific Sessions
12:00 PM – 01:00 PM	Lunch with Exhibitors
01:00 PM – 02:00 PM	Keynote Speaker
02:00 PM – 04:30 PM	Track 1 and 2 Scientific Sessions
02:00 PM – 03:00 PM	Suture Dry Lab (On-site registration required)
03:00 PM – 03:30 PM	Break with Exhibitors
04:30 PM – 05:30 PM	Poster Judging
06:00 PM – 09:00 PM	30th Anniversary Reception
Saturday, September 20	
07:00 AM – 08:15 AM	Continental Breakfast
08:15 AM – 08:30 AM	Opening Remarks
08:30 AM – 09:30 AM	Keynote Speaker
09:30 AM – 10:00 AM	Break
10:00 AM – 11:30 AM	Track 1 and 2 Scientific Sessions
11:45 AM – 1:45 PM	Business Lunch/ASR Awards Presentations Keynote Speaker
1:45 PM – 02:30 PM	Surgical Writing Workshop (Registration required)
02:00 PM – 03:00 PM	Track 1 and 2 Scientific Sessions
3:00 PM	Adjourn
03:00 PM – 05:00 PM	Board of Directors Meeting

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YEARS

# Lab Descriptions

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## Wet Lab Instructors

**Rasa Zhukauskas, MD, CTBS**  
RTI Surgical

**Liisa Carter, SRS, CVT, ALAT**  
American Preclinical Services, LLC

**Christina Gross, BA, SRS**  
American Preclinical Services, LLC

**Heather Bogie, CVT, SRS, RLATg**  
Data Sciences International (DSI)

**Vince Mendenhall, Ph.D, DVM**  
Wake Forest Innovations

**James Berry, RDCS**  
American Preclinical Services, LLC

**Megan Swaab Fine, DVM, MS**  
Data Sciences International (DSI)

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## Wet Lab Volunteers

**Kimberly Holliday-White**  
DSI

**Kathryn Lillegard**  
DSI

**David FitzMiller**  
Kent Scientific

**Mark Beckel, SRS, BS**  
APS

**Tyler LaMont**  
APS

**Melissa Carlson**  
APS

**Joe Vislisel**  
APS

Thank you to APS and DSI for hosting our wet labs and all of your dedication and support!



# Wet Labs

## Labs at American Preclinical Services

### All Day Lab (8:00 AM – 4:00 PM)

APS

#### Swine Valve Replacement

In this lab, participants will learn the techniques of bypass assisted valve replacement in the swine. Participants will learn anesthetic methods, bypass techniques and implantation styles to achieve successful outcomes in this difficult surgical model.

### All Day Lab (8:00 AM – 4:00 PM)

APS

#### Echocardiography Laboratory

This lab will present multiple approaches to echocardiography in research animal models including Transthoracic (TTE), Transesophageal (TEE), Epicardial and Intracardiac (ICE). The lab will describe some of the advantages and disadvantages of each approach in the animal models versus the human. Different key views will be taught and features to look for within those views to assist in ensuring the right imaging plane has been achieved. The lab is taught by a clinically practicing Registered Diagnostic Cardiac Sonographer with many years of experience in all areas preclinical research. The participants will learn about these different techniques and have the opportunity to obtain some images during the class. At the end of the session, the participants can join the Cardiopulmonary Bypass Lab to obtain Echocardiographic imaging of the implanted aortic valve.

### AM Lab (8:00 AM – 12:00 PM)

APS

#### Rodent Femoral Critical Sized Defect

In this lab, participants will learn the techniques of successful critical sized femoral defect creation rats. This method of orthopedic implantation allows for high throughput of new devices or drugs to assist with bone healing in non-healing defects. Prior surgical experience is strongly recommended, but not required.

### PM Lab (1:00 PM – 5:00 PM)

APS

#### Rodent Post Lateral Fusion

In this lab, participants will learn the techniques of post lateral fusions in rats. This method of orthopedic implantation allows for high throughput of new devices or drugs to assist with bridge formation in a repeatable fashion.



## Labs at Data Sciences International

**AM Lab (8:00 AM – 12:00 PM)**

DSI

### **Microsurgical Telemetry Implantation Techniques: Recording Continuous Intra-vascular Blood Glucose in Rats**

Telemetry has become the gold standard of physiologic monitoring due to its ability to monitor numerous physiologic traits without the need for anesthesia or restraint. This decreases stress to the animals, increases the accuracy of the data and allows for a reduction in numbers of animals used and refinement of study design. Telemetry is used in multiple fields of biomedical research such as basic science, discovery and safety pharmacology. The recently developed telemetry device highlighted in this workshop provides an exciting advancement as it allows for the continuous monitoring of blood glucose for the first time in rats. The steps for surgical implantation of this telemetry device will first be demonstrated by an expert small animal telemetry surgeon. Attendees will then have the opportunity to work individually, under the guidance of experienced surgeons to surgically implant devices in rats. Each attendee will have a surgical station, a microsurgical instrument set and an individual microscope for use during the workshop. Emphasis will be placed on proper microsurgical technique and appropriate handling of the telemetry device. Prior surgical experience is strongly recommended, but not required.

## Surgical Writing Workshop

**Saturday (10:30 AM – 11:45 AM, 1:45 PM – 2:30 PM)**

HYATT

### **Surgical Writing-From Protocol Development, Conception of the Research Hypothesis, Data Collection and Publication**

#### **2 Parts:**

**Part 1:** A one hour lecture open to all will be given during one of the full meeting sessions.

**Part 2:** Limitation of participants, must register in advance. A "hands-on" workshop will address the details associated with protocol development from the conception of the idea and characterization of the hypothesis to integration of the written scientific protocol. Possibility of success will be related to the individual interest and participation in the process. A final written abstract with a completed version of the whole workshop will be gathered at the end of this experience. (workshop participants must bring research idea (hypothetical or real) for workshop instruction).

## Suture Dry Lab

HYATT

**Friday (2:00 PM – 3:00 PM)**

A good suture pattern is only as good as the knots holding them in place. This hour long demonstration will cover the basics of suture selection, knot placement and tying techniques using a novel Multilayer Suture Pad.

# Lab Sponsors



Manthei Hogs





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# Program Schedule

Wednesday, September 17

2:00 – 5:00 PM

ASR Board of Directors Meeting – **St. Croix**

Thursday, September 18

8:00 AM – 5:00 PM

Wet Labs

8:00 AM – 12:00 PM

Certification Exams – **Minnehaha Room**

4:00 – 7:30 PM

Welcome Reception with Exhibitors – Sponsored by Instech Laboratories  
**Greenway Ballroom**



# Friday, September 19

7:00 – 8:15 AM	Continental Breakfast – Sponsored by Kent Scientific – <b>Greenway Ballroom</b>	
7:00 – 8:15 AM	Poster Setup – <b>Greenway Ballroom</b>	
8:15 – 8:30 AM	Opening Remarks – ASR President Cody Resendez – <b>Regency Room</b>	
8:30 – 9:30 AM	Keynote – Paul Iazzo – The Visible Heart Laboratory – <b>Regency Room</b>	
9:30 – 10:00 AM	Break with Exhibitors – Sponsored by DRE, Inc. – <b>Greenway Ballroom</b>	
TRACK 1 – Regency Room		
10:00 – 10:30 AM	Short-Acting and Long-Acting Buprenorphine Therapeutic Drug Levels Following Single Subcutaneous Administration in Diabetic Yucatan Miniswine	Brian Hanks, DVM
10:30 – 11:00 AM	Continuous Measurement of Renal Blood Flow and Blood Pressure Changes While Testing Antihypertensive Compounds in Freely Moving Rats	Xuening Hong
11:00 – 11:30 AM	Large Animal Model of a Critical Sized Defect that Allows Discrimination Among Grafting Materials	Liz Pluhar, PhD
11:30 – 12:00 PM	Trials and Tribulations of the Refinement of Femoral Critical Sized Defects in the Rat	Vince Mendenhall, DVM, PhD
12:00 – 1:00 PM	Lunch – Sponsored by SAI Infusion Technologies and VetEquip, Inc. – <b>Greenway Ballroom</b>	
1:00 – 2:00 PM	Keynote – Rachel Tapp, BS – Auditory Safety Evaluations and the Need for Surgical Support for Access to These Specialized Compartments for Compound Administration and Placement of Devices	
2:00 – 2:30 PM	Process Improvement for Surgically Implanted Bilateral Middle Ear Cannulae in Guinea Pigs	Jenifer A. Sweet, BA, LAT, SRS
2:30 – 3:00 PM	The Chinchilla Model of Acute Otitis Media: Two Pathogens, Three Treatment Administration Routes, and the Apparent Disconnect Between Clinical Signs and Bacteria Burden	James Justen
3:00 – 3:30 PM	Break with Exhibitors – Sponsored by Taconic – <b>Greenway Ballroom</b>	
3:30 – 4:00 PM	Using Pressure-Volume Loop Analysis to Understand Dystrophic Cardiomyopathy in Mouse and Dog	DeWayne Townsend, PhD
4:00 – 4:30 PM	ITS Cardiovascular Telemetry Implantation in the Canine	Jon Ehrmann BS, SRS, SRA, LATg
4:30 – 5:30 PM	Poster Judging – <b>Greenway Ballroom</b>	
6:00 – 9:00 PM	30th Anniversary Reception – Windows on Minnesota – IDS Tower – <b>Stars Ballroom</b>	

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7:00 – 8:15 AM	Continental Breakfast – Sponsored by Kent Scientific – <b>Greenway Ballroom</b>	
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9:30 – 10:00 AM	Break with Exhibitors – Sponsored by DRE, Inc. – <b>Greenway Ballroom</b>	
TRACK 2 – Mirage		
10:00 – 10:30 AM	Biliopancreatic Route for Islet Viral Transduction	Kate Banks, DVM, MSC
10:30 – 11:00 AM	Abrasion Assessment of Staple Line Reinforcement Materials in a Novel Canine Thorax Model	Ludovic Bouré, DVM, MSc, DES, DACVS, DECVS
11:00 – 11:30 AM	Development and Utilization of a Canine Model to Assess Staple Line Reinforcement Materials in the Abdomen	Ludovic Bouré, DVM, MSc, DES, DACVS, DECVS
11:30 – 12:00 PM	The Effect of Site of Surgical Implantation on Regulating the Prostate Function Using Adult Castrated Rats as a Model	Ham A. Benghuzzi, PhD, FAIMBE, FBSE
12:00 – 1:00 PM	Lunch – Sponsored by SAI Infusion Technologies and VetEquip, Inc. – <b>Greenway Ballroom</b>	
1:00 – 2:00 PM	Keynote – Rachel Tapp, BS – Auditory Safety Evaluations and the Need for Surgical Support for Access to These Specialized Compartments for Compound Administration and Placement of Devices – <b>Regency Ballroom</b>	
2:00 – 2:30 PM	Targeted Animal Safety: Development of a Radiotelemetry Implanted Surgical Model in the Adult and Juvenile Feline	Teresa R. Gleason, B.S., LVT, SRS, LATg
2:30 – 3:00 PM	Implantable Glucose Telemetry in Rodents	Megan Swaab Fine, DVM, MS, Veterinary Surgeon
3:00 – 3:30 PM	Break with Exhibitors – Sponsored by Taconic – <b>Greenway Ballroom</b>	
3:30 – 4:00 PM	Refining the Consistency of the Mouse Subtotal Nephrectomy Procedure	Marla A. Wilwol, LVT, CMAR, SRS, LATg
4:00 – 4:30 PM	A Midline Open-Chest Approach for Myocardial Infarction Induction in Rats	Pilar Ariza Guzman, PhD
5:00 – 5:30 PM	Poster Judging – <b>Greenway Ballroom</b>	
6:00 – 9:00 PM	30th Anniversary Reception – Windows on Minnesota – IDS Tower – <b>Stars Ballroom</b>	

# Saturday, September 20

7:00 – 8:15 AM	Continental Breakfast – Sponsored by Colonial Medical – <b>Greenway Promenade</b>	
8:15 – 8:30 AM	Opening Remarks – ASR President Cody Resendez – <b>Regency Room</b>	
8:30 – 9:30 AM	Peggy Callaghan – Captive Wolves in Research – <b>Regency Room</b>	
9:30 – 10:00 AM	Break – Sponsored by Access Technologies – <b>Greenway Promenade</b>	
Track 1 – Regency Room		
10:00 – 10:30 AM	Echo-Guided Procedures Training Using an Image Fusion System and a Biocompatible Synthetic Tumor Model	Michele Diana, MD
10:30 – 11:00 AM	Ultrasound in Preclinical Research: Four Decades of Experience with Ultrasound as a Diagnostic Tool for Evaluation and Guidance of Medical Device Research	James Berry, RDCS
11:00 – 11:30 AM	Refining Anesthesia Through High-Frequency Oscillatory Ventilation	Szczepan Baran, VMD, MS
11:45 AM – 1:45 PM	Business Lunch/ASR Awards Presentations "Innovation in Surgery..." Sponsored by Charles River Laboratories <b>Greenway Ballroom</b>	Keynote – David Stolloff, DVM, MS, Diplomate ACVS
2:00 – 2:30 PM	Rodent Physiological Monitoring According to the Guide	Szczepan Baran, VMD, MS
2:30 – 3:00 PM	Surgical Staff Selection, Training and Retention in a CRO Environment	Jennifer Sheehan BS, SRS, LATg
3:00 – 5:00 PM	Board of Directors Meeting – <b>Skyway Suite A-B</b>	

# Saturday, September 20

7:00 – 8:15 AM	Continental Breakfast – Sponsored by Colonial Medical – <b>Greenway Promenade</b>	
8:15 – 8:30 AM	Opening Remarks – ASR President Cody Resendez – <b>Regency Room</b>	
8:30 – 9:30 AM	Peggy Callaghan – Captive Wolves in Research – <b>Regency Room</b>	
9:30 – 10:00 AM	Break – Sponsored by Access Technologies – <b>Greenway Promenade</b>	
Track 2 – Mirage		
10:00 – 10:30 AM	Intrathecal Catheterisation in the Rat	Kate Read, MA, VetMB, MRCVS
10:30 – 11:00 AM	Vascular Access Ports – A Look At Recent Advancements and Refinements	Jon Ehrmann BS, SRS, SRA, LATg
11:00 – 11:45 AM	Surgical Writing – From Protocol Development, Conception of the Research Hypothesis, Data Collection and Publication – Part 1	Luis Toledo, MD, PhD Richard Bianco, PhD
11:45 AM – 1:45 PM	Business Lunch/ASR Awards Presentations "Innovation in Surgery..." Sponsored by Charles River Laboratories <b>Greenway Ballroom</b>	Keynote – David Stoloff, DVM, MS, Diplomate ACVS
1:45 – 2:30 PM	Surgical Writing – From Protocol Development, Conception of the Research Hypothesis, Data Collection and Publication – Part 2	Luis Toledo, MD, PhD Richard Bianco, PhD
2:30 – 3:00 PM	Chronic Lymph Collection in the Canine	Vince Mendenhall, DVM, PhD
3:00 – 5:00 PM	Board of Directors Meeting – <b>Skyway Suite A-B</b>	





# Exhibitor Directory

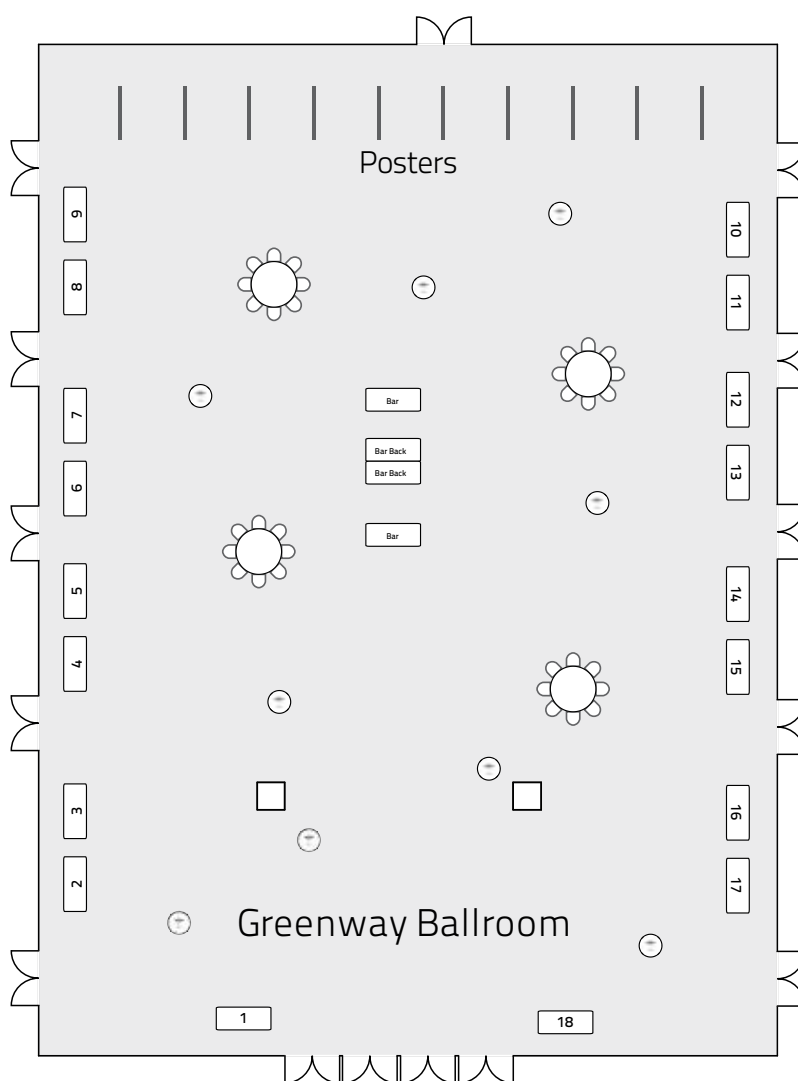
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### Access Technologies

[www.norfolkaccess.com](http://www.norfolkaccess.com)

BOOTH 6

For over 33 years Access Technologies has been the world leader in the design and manufacture of implanted access and infusion systems in support of Pre-Clinical research. The acquisition of Solomon Scientific will allow Access Technologies to offer a more complete line of infusion devices for all species to the research community. Access Technologies prides itself on offering high quality products and superior technical and customer support. Custom design and prototyping is our specialty. To learn more visit us at [www.norfolkaccess.com](http://www.norfolkaccess.com), email [pwolf@norfolkmedical.com](mailto:pwolf@norfolkmedical.com) or call us 847-674-7131.



### Advanced Anesthesia Specialists LLC

[www.darvallvet.com](http://www.darvallvet.com)

BOOTH 4

Advanced Anesthesia Specialists is a global leader in the design and manufacture of research anesthesia equipment. AAS is owned by veterinary anesthesia specialists who engineer equipment that is effective and easy to use. We offer 'zero dead space' rodent anesthesia mask systems in single or 5-patient modules; masks are heated and non-heated, MRI and fluorescence imaging-compatible. Our low flow heated smooth-wall rebreathing circuits reduce resistance and warm patients. AAS develops innovative anesthesia equipment that prevents hypothermia, reduces workplace contamination and lowers anesthesia costs by up to 80%. Let us design a complete anesthesia system to meet your research needs.



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BOOTH 10

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BOOTH 2

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## DRE Scientific, a division of DRE Veterinary

BOOTH 15

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Established in 1984, DRE, Inc. is a full service supplier of medical and operating room equipment. DRE's Scientific Division is on the leading edge of technologies for the rapidly growing field of animal research. We offer full lines of new and professionally refurbished animal specific equipment that include: Anesthesia Machines, Vital Signs Monitors, Specialty Surgical Tables, Electrosurgical Equipment, IV Pumps, Microscope, Ventilators, Vaporizers, Surgical Lighting Systems and more. Along with DRE's private label equipment lines, our 18,000 sq. ft. warehouse is stocked with new and certified refurbished equipment from all the major brands you know and trust.



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BOOTH 17

[www.finescience.com](http://www.finescience.com)

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## Hilltop Lab Animals, Inc.

BOOTH 8

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Hilltop Lab Animals, Inc. produces research animals including rats, mice and guinea pigs. Hilltop also provides: contract housing including aged animals, precisely time-mated animals, tissues, blood products, and wide variety surgical procedures including catheter (vascular, bile duct, intra-gastric, urinary bladder) implants. For more information call customer service at 724-887-8480.



## Instech Laboratories, Inc.

BOOTH 16

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Instech designs and manufactures products for rodent infusion, sampling and oral gavage, including: catheters, tethers, swivels, infusion pumps, automated blood sampling systems, and rodent feeding tubes. Products highlighted at ASR will include the PinPort, for quick aseptic access to externalized catheters, and new additions to our mouse and rat catheter lines.



## ISIS Services, LLC

BOOTH 12

[www.isisservices.com](http://www.isisservices.com)

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## Kent Scientific Corporation

BOOTH 11

[www.kentscientific.com](http://www.kentscientific.com)

With over 20 years experience, Kent Scientific Corporation continues to serve medical and research scientists as a worldwide provider of integrated solutions for pre-clinical research and drug discovery advancement. As the World Leader in non-invasive blood pressure, physiological monitoring and anesthesia systems for mice and rats, we enable our customers to achieve results that are fast, consistent and exceedingly accurate. Customers can rely on our informative web site to effortlessly purchase research products through our online shopping cart. You can choose from thousands of products in our online catalog. Enjoy the latest technological advances in research products at the best prices.



## Lomir Biomedical Inc.

BOOTH 1

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Lomir is the world's largest manufacturer of animal jackets, infusion products and restrainers. Currently celebrating our 25th Anniversary our mission has been to manufacture equipment that is reliable, durable and easy to use. In depth knowledge enables Lomir to design and manufacture equipment with the exact precision to meet your scientific requirements. New products made using innovative materials enable researchers to consider new applications, often reducing labor while improving comfort and well-being of the subjects. Visit our booth to find out how working with the manufacturer can help you achieve your objectives.



## Marshall BioResources

BOOTH 13

[www.marshallbio.com](http://www.marshallbio.com)

Marshall BioResources supplies Marshall Beagles, Gottingen Minipigs, ferrets, and mixed breed mongrels and hounds from our AAALAC accredited facilities. For 75 years our animals have been recognized as standard research models, known around the world for their good health, genetic consistency, gentle temperament and uniformity. We remain a family owned and operated company dedicated to the highest standards of animal care and customer satisfaction.



## Medline Industries, Inc.

BOOTH 9

[www.medline.com](http://www.medline.com)

Started in 1910, Medline is the largest privately-held manufacturer and distributor of healthcare products in the United States. We manufacture and distribute over 350,000 products to hospitals, surgery centers and researchers. We are an ASR corporate partner and continue to expand our support to the surgical research community, providing direct-from-manufacturer pricing and knowledge on items such as gloves, surgical supplies and safety supplies. With our established relationships as a manufacturer and distributor, we can provide surgical technicians and researchers with recognized brands including BD and ethicon. Let our experience in a variety of surgical environments and applications work for you.



## SAI Infusion Technologies

BOOTH 3

[www.sai-infusion.com](http://www.sai-infusion.com)

SAI Infusion Technologies designs and manufactures systems and components for preclinical infusion and sampling. SAI Surgeons and Scientists provide onsite comprehensive training for all of our systems including: Wireless infusion management software (Axios), pumps, harnesses, access ports, jackets, swivels, catheters, and virtually everything else used in research involving infusion or sampling.



## Stoelting

BOOTH 7

[www.stoeltingco.com](http://www.stoeltingco.com)

Stoelting has been a leader in research equipment design, development and sales since 1886. Our Stereotaxic Instrument line is world-renowned and now includes the New Standard and Just for Mice Stereotaxic Instruments. Visit [www.StoeltingCo.com](http://www.StoeltingCo.com) to see our complete line of Surgical Instruments and Surgical Accessories. Our surgical line includes Complete Mobile Anesthesia Systems. These systems are available with everything you need for small animal surgery including - an Active Gas Scavenger, Oxygen Generator, Wheeled Cart, Induction Chamber, Vaporizer, Anesthesia masks, Low Flow Meters for Rats and Mice, etc. We also carry an impressive line of Surgical Instruments at competitive prices.



## SurgiReal Products, Inc.

BOOTH 18

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SurgiReal offers "life-like" surgical training technology to students (veterinary, medical, PA, NP) and laboratory researchers. Surgical skills simulators are available for comprehensive training and improved surgical outcomes. The realism of the SurgiReal technology reduces the need for live animal procedures and improves the confidence level of learners. The SurgiReal simulated tissue simulators provide the most realistic training platform available.

SurgiReal's products incorporate proprietary technology (RealLayer Technology & RealFlow Technology) and include a variety of multilayer simulated tissue products, some available with artificial bleeding.





## Toxikon Corporation

[www.toxikon.com](http://www.toxikon.com)

BOOTH 5

Toxikon Corporation is a preclinical Contract Research Organization (CRO), with ISO/IEC 17025 accreditation that is registered with the US FDA and Japanese MHLW for drug and medical device testing. The Company provides in vivo, analytical, and in vitro testing services for the pharmaceutical, biotechnology, and medical device sectors. Toxikon's safety services include toxicology (acute, subchronic, and chronic toxicity, reproductive toxicity, genetic toxicology, carcinogenicity), pharmacokinetics, toxicokinetics, bioavailability, ADME, chemical characterization, impurities analysis and synthesis, bioanalytical, and microbiology.



## TSE Systems

[www.tse-systems.com](http://www.tse-systems.com)

BOOTH 14

TSE Systems develops, manufactures and markets sophisticated life science research instrumentation for preclinical cardiovascular, behavioral, metabolic, physiological and toxicological research since 1886. Featured product: Stellar Telemetry next generation implantable telemetry system (BP, Biopotentials (ECG/EEG/EMG/EOG), Activity, Temperature) for any laboratory animal.



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# Poster Abstracts

## Hyperuricemia in Injuries Due to Ischemia and Reperfusion

POSTER 1

Alicia Aliena-Valero

Universidad Católica de Valencia

### ABSTRACT

Ischemia and reperfusion syndrome is a pathophysiological process caused by a blockage of blood flow with tissue anoxia and blood re-circulation, resulting in permanent structural and functional injuries in the organs affected. In this process, due to the lack of oxygen, the metabolic pathway of the xanthines becomes impaired due to energy changes, thus contributing to the development of ischemic lesions. Furthermore, hyperuricemia is a metabolic disorder that occurs with a rise in uric acid in the blood, which may be caused by overproduction of uric acid or less excretion of it. In a previous clinical study by our university, we noted that untreated hyperuricemic patients ( $n = 93$ ) had more severe injuries and death from stroke, myocardial infarction and peripheral ischemia, when compared to the group of patients treated with allopurinol ( $p < 0.05$ ;  $n = 107$ ). 2.- For the experimental study of the effects of hyperuricemia in situations of ischemia-reperfusion, we used Wistar rats treated for 4 weeks with oxonic acid (750 mg/kg) orally, leading to increased levels of uric acid. Six experimental groups were created with a total of 130 animals divided into: Sham, groups with untreated ischemic injury (ischemia, hyperuricemia, and hyperuricemia together with ischemia) and treated groups (allopurinol after ischemia, and pre-treated with allopurinol (50 mg/kg)). The biochemical analyses carried out were: uric acid, creatinine, urea, blood urea nitrogen (BUN) and LDH, protein (cytokines and proinflammatory molecules) and the histologies to determine the physiopathological changes occurring during this process. 3.- The preliminary results indicate that the animals with a clear increase in uric acid expressed necrosis and inflammation lesions with more intensity in situations of ischemia-reperfusion (warm ischemia). The values for renal function, biochemistry of the cytokines and the immunohistological study of the anatomical specimens confirmed that allopurinol reduced damage due to ischemia in kidneys subjected to ischemia-reperfusion. Allopurinol reduced the uric acid levels and slowed the progression of renal ischemia injuries, emulating the situations observed in the initial clinical study situations. 4.- This work and the previous clinical studies allow us to indicate that the use of allopurinol for preventive reasons and monitoring of hyperuricemic patients with cardiovascular risk may reduce the impact of injury from ischemia, if these appear, thereby reducing morbidity and mortality for these vascular events.

## Advances in Rabbit Anesthesia at PRL

Cheryl Griesse, RLATg

Medtronic Physiological Research Laboratory

### ABSTRACT

Historically rabbits have been used extensively for biomaterials testing at Medtronic, PRL. Biomaterial studies typically involve subcutaneous implant of the test article utilizing relatively non-invasive techniques resulting in fast implant times. In the past couple of years, rabbits have been used for more complicated studies which have necessitated revising our anesthetic induction and post-operative pain management protocols. In addition, intra-operative monitoring procedures have evolved to allow for better survival rates for these complicated procedures. Literature searches of gold standard rabbit anesthesia and monitoring practices were performed to establish new protocols at PRL. In addition; multiple veterinary training events for our technical staff were conducted to become proficient at rabbit intubation, successful arterial access, and understanding normal physiologic parameters. Following this training, we compared surgical implant time, anesthetic induction/maintenance, intra-operative monitoring, and pain management protocols used in past biomaterial study implants to current practices. This was a comparison of methods used between the subcutaneous implants and double laminectomy implants therefore no statistical methods were used. Protocols from a 12 rabbit subcutaneous implant study were compared to current practices for a rabbit double laminectomy study. The subcutaneous implants were 12 male New Zealand White rabbits 4 months old at the time of implant. Anesthesia doses were Ketamine 55 mg/kg with Xylazine 10 mg/kg IM. Analgesia for the subcutaneous implants consisted of Buprenex 0.01 mg/kg SQ given in post-op after the rabbit recovered from anesthesia. The double laminectomy implants were 12 male New Zealand White rabbits 4 to 5 months of age at the time of implant. Anesthesia doses were Ketamine 40 mg/kg with Xylazine 4.4 mg/kg IM; Glycopyrrolate at 0.02 mg/kg IM. Analgesia for the double laminectomy implants consisted of Buprenex 0.01 mg/kg given in post-op after the rabbit recovered from anesthesia and given SID on Day 1 after surgery. Buprenex after Day 1 was given SID as needed based on a pain score. A Fentanyl Patch 12 mcg was placed on each rabbit in post-op after the surgery was completed. The Fentanyl Patch was removed on Day 3 post-op. At the completion of the study both the subcutaneous implants and the double laminectomy rabbits were given Heparin 300 u/kg IV and then five minutes later given Pentobarbital Sodium 390 mg IV. Differences in anesthetic induction, anesthetic maintenance, surgery length, and pain management were noticed. Due to the more invasive nature of the laminectomy procedures, different anesthetic procedures and monitoring practices were required. As rabbit studies have become more complex, involving longer surgery procedure times, PRL's anesthetic, monitoring, and pain management practices have changed significantly. Due to the current higher standard of care, our technical staff have learned new skills that were not considered core competencies in earlier biomaterials studies. These competencies include invasive blood pressure monitoring, intubation, and normal physiologic parameters for rabbits. These new standards and acquired skills have served to improve patient care and allow for data collection to demonstrate maintenance of normal physiologic parameters even during long and complicated surgical procedures.

## Dexmedetomidine As a Maintenance Anesthetic for Non-Human Primates Undergoing fMR and PET Imaging

POSTER 3

Shannon Mary Sleboda, BS, CVT, RLAT  
Massachusetts General Hospital

### ABSTRACT

General anesthesia choices for non-human primates (NHPs) are limited, especially in studies requiring stimulation of specific neuro-receptors. We performed a NHP imaging study involving evaluation of nicotinic and dopamine receptor activity, using Dexdomitor® in combination with ketamine as a total intravenous maintenance anesthetic (TIVA) for imaging sessions lasting 4-8 hours. Results of a literature review suggested that this regimen would have minimal impact on these receptors and provide adequate levels of anesthesia. Adult male rhesus NHPs (*Macaca mulatta*) (n= 5), were premedicated with ketamine hydrochloride (hcl) (7 mg/kg) and dexmedetomidine (0.02 mg/kg) intramuscularly, and maintained with ketamine hcl (4-6 mg/kg/hr) + dexmedetomidine (2-4 mcg/kg/hr) intravenously for each imaging session. Respiratory rate (RR), heart rate (HR), end tidal (Et) CO<sub>2</sub>, O<sub>2</sub> saturation (SPO<sub>2</sub>), and non-invasive blood pressure (NIBP) was recorded every 5 minutes. Saline 0.9% was administered intravenously (5-10 mg/kg/hr). Atipamezole hydrochloride (hcl) (0.2 mg/kg) was administered intramuscularly at the end of each session. Images were collected on a 3T Siemens Trio with a Brain PET insert. Dopamine receptor (D<sub>2</sub>) availability was assessed by measuring raclopride binding potential (BP) in the striatum (caudate and putamen). <sup>11</sup>C-raclopride was injected with 5-6 mCi activity as a bolus/infusion (50/50), followed by a nicotine challenge (0.3-0.5 mg/kg) 35 min later to assess changes in brain activity. This was repeated with a two hr interval, while imaging PET and pharmacMRI (phMRI) simultaneously. None of the animals in this study experienced adverse events under anesthesia or during recovery. Relevant fluctuations (during the first 30 min vs. the end of the scan session) in physiology showed only: EtCO<sub>2</sub> 41.2±1.7 vs. 39.9±2.6; systolic NIBP 86.5±4.3 vs. 93.3±4.3 (p<0.05 paired t-test); diastolic NIBP 53.7±4.5 vs. 52.9±4.7; and HR 89.4±2.5 vs. 86.6±2.7. Average recovery time to sternal recumbency was under 60 minutes after completion of imaging and atipamezole hcl injection. Average D<sub>2</sub> BP measured using PET and <sup>11</sup>C-raclopride was compared with previous study data using either isoflurane or the awake state. Using one-way ANOVA, measurements of BP in awake rhesus monkeys (2.56±0.23) were not significantly different from Dexdomitor® (3.18±0.14) whereas it was significantly different from isoflurane (2.18±.18 p<0.01). phMRI of nicotine stimulation showed consistent patterns of activation with nicotine across numerous brain regions as seen with prior studies in rodents and humans. Long term (>6 hours) TIVA with dexmedetomidine + ketamine allowed for the study of nicotinic and dopaminergic receptors with little or no interference. Further, this anesthetic regimen shows potential as an alternative option for long term non-invasive imaging studies in rhesus macaques. Additional evaluation is needed to establish efficacy and/or potential variability in additional animals, age groups and gender as well as other NHP species.

## Refining a Porcine Thromboembolic Heterotopic Mechanical Aortic Valve Model to Reduce Surgical Complications and Provide Multi-Dose Continuous Infusion Anticoagulant Therapy

Patrick Lester, DVM, MS, DACLAM

Conrad Jobst Vascular Surgical Laboratory, University of Michigan

### ABSTRACT

**AIM:** To refine and minimize surgical complications, augment analgesia, and develop an economical jacket-tether catheter system for multi-dose continuous infusion in a porcine heterotopic mechanical aortic valve surgical model.

Venous thrombosis is a serious health care concern. We refined a published heterotopic aortic valve model for testing thromboprophylaxis of mechanical heart valves with the goal to minimize surgical complications, augment analgesia and minimize distress associated with frequent sample collection and administration of test articles.

For infection control, animals received a 4% chlorhexidine bath the day before surgery. Ceftiofur and cefazolin were administered sixty minutes prior to the first incision. Pre-emptive analgesia included a fentanyl transcutaneous patch 12 hours prior to surgery and intravenous carprofen during surgical prepping. A percutaneous saphenous arterial catheter was placed for direct blood pressure monitoring and arterial blood gas sampling. To maintain optimal blood pressure, balanced anesthesia consisted of tiletamine/zolazepam for sedation followed by mask induction and maintenance with isoflurane/100% oxygen and intravenous fentanyl via continuous rate infusion. A vascular access port was implanted in the left external jugular vein immediately prior to placement of the heterotopic mechanical aortic valve to provide additional venous access and facilitate post-surgical sampling. A separate indwelling catheter was implanted in the external jugular vein for continuous infusion of test article. To deflate the left lung and facilitate thoracic aorta surgical access, a Cohen endobronchial blocker was placed through a 9 Fr endotracheal tube using a pediatric fiberoptic scope into the left main stem bronchus and inflated prior to graft placement. The right cranial bronchiole, unique to swine, was utilized as a landmark to facilitate placement of the endobronchial blocker. With enhanced surgical access, average blood loss was reduced to < 100 ml. Surgical graft and anesthesia time were also reduced. A bupivacaine intercostal block was performed prior to surgical closure to enhance post-operative analgesia. To facilitate a post-operative 14 day multi-dose continuous infusion, swine were fitted with a jacket and tether system handcrafted from a construction safety vest and flexible electrical conduit (approximate cost \$40.00) connected to a swivel system which housed the infusion line. A programmable infusion pump with multi-step capability provided eight separate continuous infusion rates per day for a two week infusion period.

**CONCLUSION:** Our refinement techniques reduced surgical complications, surgical and anesthesia time, and augmented post-operative analgesia. An economical jacket-tether infusion system was developed and successfully utilized for long-term continuous multi-dose infusion therapy.



## Sodium Citrate Catheter Locking Solution As an Alternative to Heparin in Rats

POSTER 6

Yiying Luo

Charles River Laboratories

### ABSTRACT

Pharmacokinetic studies in rats are conducted using a chronically implanted catheter that allows for repeated blood sampling, however maintaining continuous patency sets practical limits on its uses. Catheter patency is affected by factors including flushing regimen, catheter material, and choice of locking solutions. In this study, a recently introduced non-heparin based locking solution containing 4% sodium citrate is compared with traditional heparinized locking solutions with respect to their ability to maintain patency of indwelling polyurethane vascular catheters in rats. Locking solutions of heparinized (500 IU/ml) 50% dextrose (LOCK 1) and heparinized (500 IU/ml) glycerol (LOCK 2) were obtained from SAI infusion technologies. Sodium citrate (4%) with 30% glycerol (LOCK 3) pH adjusted to 6.2 (range 6.0 to 6.5) with citric acid was provided by Cary Pharmaceuticals, Inc. Sixty adult male 200-225 gm CD rats (CrI:CD® (SD)IGSBR) were randomly allocated into 3 groups of 20 each for LOCK1, LOCK2 and LOCK3. Standard feed, bedding and water were provided ad libitum. The study was approved by the CRL IACUC. Rats were anesthetized and a polyurethane catheter was inserted into the femoral vein as previously described (Luo et al 2000). LOCK1, LOCK2, or LOCK3 was applied, the catheter was sealed with metal plug and the extravascular portion was extended subcutaneously, exiting at the interscapula region. Patency of the catheter was checked for five animals within each lock solution group at 7, 14, 21 and 28 days post-implantation. The plug was removed, and the catheter was aspirated to determine the ability to remove the lock solution and withdraw blood. If this aspiration failed, we attempted to flush with saline. If flush solution was infused, a second aspiration was made to check patency. Catheter was considered fully patent if withdraw of blood was successful with first or second attempt. LOCK1 and LOCK2 groups (heparinized) retained 100% patency to Day21. Patency rates decreased to 40% and 25% per group (respectively) at Day28, confirming earlier findings (Luo, et. al 2000). 80% of LOCK3 group retained patency to Day7, decreasing to 40% - 60% at Day14, 21 and 28. These findings support heparinized catheter locking solutions to maintain patency, however sodium citrate locking solution may be used as an alternative, at a lower patency rate, where heparin is contraindicated or unavailable.

**REFERENCE:** Y Luo et. al. AALAS 2000, Comparison of catheter lock solutions in rats.

## Monitoring and Maintenance of an Azotemic Environment in an Acute Renal Failure Model in Swine

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### ABSTRACT

**AIMS:** Uremia is a clinical syndrome in humans associated with chronic kidney disease or acute kidney injury if loss of renal function is severe. Progression of uremia is characterized by fluid, electrolyte, and hormone imbalances and metabolic abnormalities, resulting from retention in the bloodstream of waste products normally excreted in the urine. In an acute renal failure model in swine, we sought to establish and post-operatively maintain an azotemic environment, accumulation of abnormally large amounts of nitrogenous waste products in blood similar to that observed in uremia, for preclinical evaluation of novel therapeutic devices.

Yorkshire swine (female, 60-70 kg, n=7) underwent laparoscopic bilateral nephrectomy on Day 0. Venous blood collection was performed immediately prior to surgery, and at 8h and ~24h post-surgery for hematology and clinical chemistry analysis. Blood gases were concurrently performed for immediate analysis of physiological state, including blood urea nitrogen, creatinine, potassium, and glucose monitoring. To decrease the severity of post-operative electrolyte imbalances fluid therapies were restricted to 0.9% normal saline administration, which was ceased following ligation of the first kidney.

Increases in average baseline levels for blood urea nitrogen and serum creatinine were 82% ( $p = 1 \times 10^{-6}$ ) and 190% ( $p = 2 \times 10^{-5}$ ), respectively, at 8 hours post-nephrectomy, which further escalated to 239% ( $p = 4 \times 10^{-6}$ ) and 417% ( $p = 4 \times 10^{-9}$ ), respectively, at ~24 hours post-nephrectomy. Animals also became hyperkalemic the day after surgery. Serum potassium levels at 8 hours post-nephrectomy were similar to baseline levels; however, at ~24 hours post-nephrectomy potassium levels significantly increased on average 45% ( $p = 0.006$ ) from baseline. The most severe example of hyperkalemia occurred in the first animal to undergo bilateral nephrectomy. Sudden cardiac arrest occurred under anesthesia during therapeutic evaluation 24h post-nephrectomy. The animal was revived several times and treated with lidocaine, atropine, phenylephrine, calcium chloride/gluconate, and 50% dextrose. For subsequent animals, a successful plan utilizing insulin and 50% dextrose was devised to proactively combat hyperkalemia.

This acute renal failure model utilizing swine has been established with consistent and repeatable elevation of serum blood urea nitrogen and creatinine levels. Post-operative electrolyte imbalances can successfully be combated to allow for this model to be maintained in an azotemic environment for preclinical development and evaluation of novel therapeutic devices.

## Refinement of an Anesthesia Protocol for a Porcine Model for a Free-D Powered Ventricular Assist Device

POSTER 8

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### ABSTRACT

Congestive heart failure therapy can be revolutionized via a wirelessly powered ventricular assist device (VAD) that eliminates the transcutaneous drivelines and the associated morbidity. A free-range resonant electrical energy delivery (FREED-D) system can efficiently transfer energy across a room to power a VAD. Porcine models of VAD support are difficult to establish due to the high incidence of arrhythmia that is witnessed in this species. Objective: The goal of this presentation is to convey the key modifications to our standard swine anesthetic regimen that markedly improved outcomes and enabled in vivo testing of this VAD system. Methods: The animals include eight 50 kg Yorkshire pigs. The standard anesthesia protocol consisted of induction with ketamine 2.2 mg/kg + Telazol® 4.4 mg/kg + xylazine 2.2 mg/kg + atropine 0.05 mg/kg + buprenorphine 0.01 mg/kg IM followed by maintenance with isoflurane and a continuous rate infusion (CRI) of low dose lidocaine 0.25 mg/minute + ketamine 0.1 mg/minute IV. Bupivacaine 0.5% was used for nerve block prior to thoracotomy and lidocaine 2% IV bolus just prior to insertion of the inflow cannula was used to manage arrhythmias. Volume support was provided by IV fluids (LRS or 0.9% saline). The revised protocol consisted of ketamine 16 mg/kg + midazolam 1 mg/kg + atropine 0.05 mg/kg + buprenorphine 0.01 mg/kg IM followed by maintenance with isoflurane and a CRI of low dose lidocaine + ketamine IV. Oral amiodarone 400 mg once daily was given for eight days prior to the surgery. Cisatracurium besylate, a nondepolarizing skeletal muscle relaxant was given via CRI at 0.05-0.25 mg/minute IV to effect to facilitate the thoracotomy portion of the procedure. Dobutamine CRI was added at 0.05 – 0.2 mg/minute IV to effect when needed for blood pressure support and IV colloids (VetStarch™) and fluids (LRS or 0.9% saline) were used as needed for volume support. In a second refinement step IV Amiodarone 1.0 mg/minute CRI was started at induction. Results: With our standard anesthetic regimen loss of heart function was common on handling the cardiac structures resulting in ventricular fibrillation, despite epinephrine and defibrillation attempts (n = 2 of 2). With the refined anesthetic regimen the heart maintained good function throughout the entire three hour per animal study and required euthanasia with Euthasol® (n =2 of 3 for oral Amiodarone and n = 3 of 3 for oral + CRI IV Amiodarone) to stop the heart. Discussion or Conclusions: Inclusion of amiodarone and exclusion of the alpha-2 adrenergic receptor agonist (xylazine) are thought to be two key among other technical refinements that contributed to sustained heart function. This study is ongoing and by September we expect to have data from additional animals to include in this presentation.

## The Pharmacology of Ischemia-Reperfusion

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### ABSTRACT

Ischemia and reperfusion injury (IRI) is a pathophysiological situation that generates significant cellular damage, leading to injuries that impair the functionality and viability of the cells due to inflammation, necrosis and apoptosis. That is why it has been considered extremely important to conduct a thorough literature review as a basis for future experimental studies focused towards this disease. Assuming that done the hypoxia resulting from hypoxemia that is generated in such a vascular incident changes the metabolic dynamics characteristic of the cell, leading to a reduction in aerobic metabolism while increasing the energy generated from the anaerobic pathways. This leads, therefore, to a depletion of ATP available with a resulting increase in intracellular  $Ca^{++}$ , caused primarily by the release of intracellular deposits. This in turn activates the release of lysosomal enzymes, causing cell lysis due to autodigestion. In turn, the generation of free radicals in ischemia and in reperfusion contributes to the necrosis while activating the pathway for the caspases that induce apoptosis. There are, therefore, many processes involved in IRI, above all: A, B, C Activation of the anaerobic pathway for glucose catabolism, which brings with it the acidosis arising from the accumulation of lactic acid, lysosomal instability and mitochondrial alterations. Production of free oxygen radicals that are seriously harmful to cells during reperfusion. Increased intracellular  $Ca^{2+}$ , which leads to activation of phospholipase A and C in the cell membrane, altering its permeability and producing a series of biochemical reactions that lead to the formation of vasoactive substances. These transform the capillary dynamics and their permeability with the consequent loss in maintaining membrane potential, as well as the cellular excitability. This entails intracellular accumulation of  $Na^{+}$  in the cytoplasm and thus generates cellular edema. The actions designed to protect against ischemic damage range from generating short periods of ischemia (preconditioning) to administering different active principles that alter the pathophysiological mechanisms that cause damage due to I/R. Studying the pathophysiological mechanisms involved in IRI and the action of drugs or physical methods such as applying cold and pressure, may give us the key to progress and to evaluate therapeutic strategies to be developed: a) Treatment for the donor; b) Better extracorporeal preservation; c) Prevention of complications with treatments for the receiver; d) Monitoring of organ viability, identifying selective injury markers. Considering that antioxidant chemicals, calcium blockers or even decreased ATP catabolism have positive effects in mitigating damage due to ischemia-reperfusion, it is conceivable that drugs such as allopurinol, dantrolene, pentoxifylline, adenosine and others may provide us with an efficient therapeutic effect. There are many contributions to this review provides prospects for improvement in the field of pathophysiology by IRI, which could be used as a starting point for future experimental investigations and subsequent clinical trials.

## Development and Validation of a Chronic Portal Vein Catheterization Model in the Nonhuman Primate

POSTER 10

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### ABSTRACT

Nonhuman primates are used to evaluate the extent of oral absorption of test compounds by comparison of drug concentrations in portal vein and systemic blood with surgically-implanted portal vein catheters for blood collection. Portal vein and systemic sampling allows the estimation of dose absorbed from the GI (Fa), intestinal available (Fg) and hepatic availability (Fh). Eight animals were created in 2013-2014 for experimental use by the Pharmacokinetics, Dynamics & Metabolism (PDM) group. Surgery consisted of a routine laparotomy and selection of a mesenteric vein to introduce a custom-made 6-4 Fr tapered polyurethane catheter into the portal vein, and connected to a low profile titanium vascular access port. Optimal catheter tip placement was verified by digital palpation of the tip positioned in the portal vein between the liver hilus and the duodenum. The ease of blood withdrawal and the position of the catheter in postoperative radiographs were also used for verification. All animals completed a 14-day postoperative care plan with no complications. In 2013, one animal was patent at 10 months, but was euthanized due to clinical issue unrelated to the surgery; unfortunately, no data was gathered at euthanasia. The remaining three animals were patent for ~10 months, and were sent to necropsy to determine cause of patency loss. Postmortem findings found one catheter tip in the mesenteric vein and two were found in the region where they were originally placed, with one of the catheter tips occluded with fibrous tissue. Each of these necropsies provided additional information which led to potential refinements to increase the success of this model. In the 2014 production, 3 of 4 animals were immediately assigned to study; one animal had experienced an altercation with his partner, which may have contributed to loss of bidirectional patency. Radiographs confirmed the catheter was no longer in the vessel, and the inserted length was found adjacent to the gastrointestinal tract. Contrast enhancement ruled-out any association with the vascular system. Necropsy of instrumented animals in conjunction with study data, provides verification of desired (and ongoing) catheter placement, and the ability to predict migration of the catheters in comparison to surgical placement.

## Surgical And Non-Surgical Drug Delivery Methods in Miniswine Models

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### ABSTRACT

Miniswine models have evolved to become very important in the preclinical evaluation of drugs. Moreover, translational medicine programs are confirming that the minipig is the model of choice for pharmacokinetics assessment, in addition to its role in the evaluation of drug efficacy and safety. Miniswines provide numerous advantages when conducting pharmacokinetics (PK) studies: their body size allows numerous blood samples with large volumes, their smaller body size as compared to domestic pigs facilitates their handling, their anatomy and physiology size-proportional when compared to humans and biotransformation factors (e.g. CYP450 enzymes) are similar to humans. However, although most classical routes of exposure are possible in the miniswine, some do require the use of specialized drug delivery methods. Purpose: In the present report, we will illustrate selected surgical and nonsurgical drug delivery methods that can be applied to the minipig amongst the broad available array of delivery devices. Methods: For example, vascular access in minipigs includes surgical and non-surgically placed catheters or direct venipuncture. Subcutaneous vascular access ports (VAPs) are placed surgically into the external jugular vein and may be placed bilaterally to facilitate both dosing and sampling. Repeated access of the port through the skin is possible using a specially designed needle (Huber point). Port useful lifetime in minipigs can be quite long but good port maintenance is essential. Troubleshooting of port malfunction includes assessment for infection, complete occlusion or partial withdrawal occlusion (PWO or fibrin flap). Results: In addition, we will describe the feasibility and ease of use of the following devices: Surgical Delivery Methods: Intestinal Delivery Cannulas, Femoral Catheters, Cardiac or Pericardial Catheters, Drug-Eluting Devices. Non-Surgical Delivery Methods: Percutaneous Catheters, Infusion Catheters, Topical Delivery Pumps, Endoscopic Drug Delivery, Dermal Patches, Intrathecal and Intracisternal Catheters. In conclusion, the use of the miniswine has been validated for pharmacokinetic modeling over the years and most drug delivery methods are compatible if adapted to their anatomy and physiology.

# The Effects of Cyanoacrylates in Surgical Repair of Kidney Damage

POSTER 12

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## ABSTRACT

In abdominal trauma, renal lesions are relatively common (30.3%) and in approximately 4% of the cases of renal trauma, a complete nephrectomy is necessary. The search for a fast, effective hemostatic method has led us to evaluate a new elastic cyanoacrylate in renal penetrating trauma injuries. After a night without feeding, 80 male Wistar rats were weighed and anaesthetized with intraperitoneal Ketamine (80mg/kg) and Xilacine (10mg/Kg) to perform a midline laparotomy. The experiment was divided into four groups: the Control Group, Time 1 (after 48 hours of healing), Time 2 (after 6 days) and Time 3 (18 days after surgery). In the Control Group, a laparotomy was performed and closed in layers with conventional suture. In groups Time 1, 2 and 3, a laparotomy was carried out and a penetrating traumatic injury was carried out in the superior and inferior poles of each of the kidneys, making a total of four lesions per animal with a biopsy punch 0.8 cm in diameter at a depth of 3 mm. In each lesion, a different treatment was applied: One with a purified collagen sponge (Gelita-Spon®), another sponge with fibrinogen and thrombin (TachoSil®), one with the elastic cyanoacrylate adhesive, and one wound was left to heal by itself. The animals were euthanized with intraperitoneal sodium pentobarbital (80 mg / kg body weight) after the time chosen for all groups. After taking samples, a full histopathologic study was carried out, involving staining with hematoxylin-eosin, Masson's trichrome, Schiff (PAS) and the immunohistochemical markers CD31 (angiogenesis) and CD68 (macrophages). Measurements were also taken in microns ( $\mu\text{m}$ ) for the distance between the edges of the lesion. Proteomic determinations for the proinflammatory cytokines and metalloproteinases levels were also made by Array and ELISA tests. ANOVA was applied to the results and the differences found were described by the HSD of Tuckey and the Scheffe's contrast. The histopathology reveals that the inflammatory response observed is similar in all the treatments studied. There are no significant differences between the lesions where cyanoacrylate adhesive was applied and the other treatments as regards the distance between the edges of the lesion. The average areas marked by CD68 after 18 days of healing for each treatment were: Cyanoacrylate: 8447,6 pixels, GelitaSpon: 9745,8 pixels, Tachosil: 9356,6 pixels, without significant differences between them ( $p>0,05$ ). Cyanoacrylate has proven to be a fast, efficient method for achieving hemostasis in renal penetrating injury. Furthermore, the tests have not detected differences with the other treatments used. However, one should keep in mind that it was the treatment that caused the most abdominal adhesions. Despite this, it could be a new alternative technique.



## Experimental Splenic Trauma

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### ABSTRACT

The abdomen is one of the body's areas most often affected by trauma. According to statistics, the spleen is one of the most frequently injured organs (30.3%). Furthermore, approximately 10% of splenic trauma cases require a complete splenectomy. The search for a fast, effective hemostatic method has led us to evaluate cyanoacrylate in splenic trauma injuries.

After a night without feeding, 80 male Wistar rats were weighed and anaesthetized with intraperitoneal Ketamine (80mg/kg) and Xilacine (10mg/Kg) to perform a midline laparotomy.

The experiment was divided into four groups: the Control Group, Time 1 (after 48 hours of healing), Time 2 (after 6 days) and Time 3 (18 days after surgery). In the Control Group, a laparotomy was performed and closed in layers with conventional suture. For all animals, a laparotomy was carried out and four penetrating traumatic injuries were created in the spleen per animal with a biopsy punch of 0.8 cm in diameter at a depth of 3 mm. In each lesion, a different treatment was applied: One with a purified collagen sponge (GelitaSpon®), another sponge with fibrinogen and thrombin (Tachosil®), the elastic cyanoacrylate adhesive, and one wound was left to heal by itself. The animals were euthanized with intraperitoneal sodium pentobarbital (80 mg/kg body weight) after the time chosen for all groups. After taking samples, a full histopathologic study was carried out, involving staining with hematoxylin-eosin, Masson's trichrome, Schiff (PAS) and the immunohistochemical markers CD31 (angiogenesis) and CD68 (macrophages). Measurements were also taken in microns ( $\mu\text{m}$ ) for the width of the inflammatory layer. Proteomic determinations for the proinflammatory cytokines and metalloproteinases levels were also made by Array and ELISA tests. ANOVA was applied to the results and the differences found were described by the HSD of Tuckey and the Scheffe's contrast. The histopathology measurements indicate that the lesions treated with Cyanoacrylate had an increased distance between the lesion's healthy borders, as well as the width of the inflamed band. The average band width was 48 hours: 250  $\mu\text{m}$ , 6 days: 89,52  $\mu\text{m}$ , 18 days: 171,52  $\mu\text{m}$ , significantly wider than the other treatments ( $p < .05$ ). The presence of cyanoacrylate crystals is detected in the wound bed throughout the healing process. Although cyanoacrylate has proven to be an effective method in achieving hemostasis for splenic lesions, these tests show that it causes a granulomatous reaction to a foreign body that delays the healing process compared to the observations in the other treatments used.

## Healing of Hepatic Lesions with Different Repair Systems

POSTER 14

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### ABSTRACT

The large amount of violence and traffic accidents today has led to an increase in the incidence of abdominal trauma. Because of its large volume and position, the liver is the most commonly wounded organ (73%). The usual methods for solving traumatic hepatic lesions have been suture stitching and hemostatic protein sponges. The appearance of new cyanoacrylate adhesives could spell an alternative, due to their fast hemostatic action. After a night without feeding 80 male Wistar rats were weighed and anaesthetized with intraperitoneal Ketamine (80mg/kg) and Xilacine (10mg/Kg) to perform a midline laparotomy. The experiment was distributed into four groups: The Control Group, Time 1 (after 48 hours of healing), Time 2 (after 6 days) and Time 3 (18 days after surgery). A laparotomy was used in the Control Group and the wound was closed in layers with a conventional suture. For all animals, a laparotomy was carried out and four penetrating traumatic injuries were created in the liver per animal with a biopsy punch of 0.8 cm in diameter at a depth of 3 mm. In each lesion, a different treatment was applied: One with a purified collagen sponge (Gelita-Spon®), another sponge with fibrinogen and thrombin (Tachosil®), the elastic cyanoacrylate adhesive, and one wound was left to heal by itself. The animals were euthanized with intraperitoneal sodium pentobarbital (80 mg/kg body weight) after the time chosen for all groups. After taking samples, a full histopathologic study was carried out, involving staining with hematoxylin-eosin, Masson's trichrome, Schiff (PAS) and the immunohistochemical markers CD31 (angiogenesis) and CD68 (macrophages). Measurements were also taken in microns ( $\mu\text{m}$ ) for the distance between the edges of the lesion. Proteomic determinations for the proinflammatory cytokines and metalloproteinases levels were also made by Array and ELISA tests. ANOVA was applied to the results and the differences found were described by the HSD of Tuckey and the Scheffe's contrast. The histopathology results showed that the injuries treated with Cyanoacrylate had the longest distance between the edges ( $p < 0,05$ ) in every group. In addition, the average distance increased during the healing process 48 hours: 1920,69  $\mu\text{m}$ , 6 days: 2515,60  $\mu\text{m}$ , 18 days: 2857,10  $\mu\text{m}$ . Differences were not found for the cytokine levels attending to the treatment. However, the proteases MMP1-2-8-9-13 had significantly higher levels in the Cyanoacrylate samples and those concentrations reached the Time 3 (18 days of healing), which fits with a chronic inflammatory reaction. Although Cyanoacrylate glue was the quickest hemostatic agent, it resulted in a foreign body reaction which delays the wound healing.

## Comparative Analysis of Elastic Cyanoacrylates and Other Methods of Studying Tissue in Experimental Dermatological Lesions

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### ABSTRACT

Since the beginnings of surgery, the attempts at repairing skin lesions have been varied and ingenious. Applying cyanoacrylates has become a common practice in different surgical areas from simple, superficial lesions to major surgery. We have carried out a study comparing elastic cyanoacrylates with other rigid ones and conventional sutures in the healing process of dermatological lesions, determining the effectiveness of them in primary closure of the skin on Wistar rats. Based on the classification of the response of the injured skin's tissue and healing process, we studied its reabsorption, capacity for adhesion and the healing's inflammatory process. In Wistar rats weighing 250 g, we made a medial incision in the skin at the level of the abdomen of 4 cm in length and used the three materials under study to close the skin on each laparotomy. Three experimental groups were established (T1, T2 and T3 to 2 - 6 and 18 days after surgery, respectively). The anesthetic used was sodium pentobarbital intraperitoneally (30 mg/kg, - 0.5 ml per rat). Once the surgical field is prepared to proceed to a supra-half infraumbilical laparotomy, large enough to provide a good field of view (5-6 cm). The closure of the laparotomy incision was performed by dividing into three equal parts and use as sealants traditional nonabsorbable suture in the middle third, rigid cyanoacrylate (Loctite®) in the cranial third and elastic cyanoacrylate (EC) in the distal third. Finished the experimental study, animals were euthanized by cervical dislocation technique. We assessed the viability of the scar (tension tests and evaluation of the dehiscences seen), histology and histochemistry (specific inflammation markers, necrosis and apoptosis), a study of the biochemical markers for the healing process (inflammatory cytokines (Array008 R&D Systems)) and metalloproteinases (Mosaic ELISA Human MMP Panel, R&D Systems). As regards the wound's biomechanical behavior, with the data from the dehiscences and the tension test, the ethyl cyanoacrylate (Loctite®) showed the best behavior in closing up the wound, with no cases of dehiscence appearing on using the suture. Macroscopically we valued the number of dehiscences for n = 67 Total animals), (0) suture (S), (8) in elastic cyanoacrylate (EC) and (18) Loctite® (L®) (p < 0.05 EC vs. L®). The distances between the edges of the wound, were lower in the case of the suture (S) to those obtained with (L®) and (EC) (T1: 1.839 vs. 1.018 ± 0.12 ± 1.413 ± 0.22 & 0, 17 (p < 0.05) (T2: 0.48 ± 0.05 vs. 1.080 ± 0.13 & 0.25 ± 2.141 (p < 0.05)), (T3: 0.15 ± 1.153 vs. 2.691 ± 0.32 & 1.802 ± 0.21 (p < 0.05)). Inflammatory areas produced (mm<sup>2</sup>) T = 1 (L®) (4.264 ± 0.511) were greater than (EC) & (S) (2.048 ± 0.678 ± 0.245 & 0.081) (p < 0.05) (T = 2 in the (CD) (4.920 ± 0.59) vs. (1.253 ± 0.15) and (L®) (0.906 ± 0.108), and T = 3 (L®) (9.439 ± 0.113) vs. (EC) (7.537 ± 0.904) & (S) (1.411 ± 0.170) (p < 0.05). The inflammation marker values (ARRAY 008) indicated that most of the inflammatory cytokines showed higher concentrations in the early period of the study except Loctite®, whose highest levels appeared in the later stages of the study. This suggests chronicity in the healing process due to the presence of the encapsulated adhesive. In normal healing, the highest levels of MMP 1-8 and 9 are found in the inflammatory phase, since these metalloproteinases are expressed by neutrophils. In our study, we saw that the MMP1 serum levels stayed far above the normal values in the longest study time (18 days). This seems to confirm that the inflammatory reaction remains over time and the healing is altered due to the presence of foreign bodies. The immunohistochemistry showed a delay in healing for the specimens that were adhered with cyanoacrylate, whether elastic or rigid, with a significant a sub-epidermic inflammatory reaction and foreign bodies (remains of the adhesive) in most specimens over the 18 days during which the scar healed. Due to their ease of dissemination to deeper layers of the skin and their slow metabolism, cyanoacrylates in experiments delay the normal healing of skin wounds in rats, giving rise to reactions to foreign bodies not resolved in the study period (18 days of healing).

## Effects of Pentoxifylline in Renal Ischemia

POSTER 16

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### ABSTRACT

Renal ischemia and reperfusion injury syndrome (IRI) is a physiopathology due to the stoppage of blood flow in the organ, resulting in a period of tissue hypoxia, followed by a restoration of the flow known as reoxygenation. During this period of tissue anoxia, the cellular metabolism is altered by varying the xanthine pathway, producing an energy imbalance. All of this increases ischemic lesions, leading to a dysfunction in the organ. Pentoxifylline (PTX) is a methylxanthine known for its effects as a phosphodiesterase inhibitor and as a potent vasodilator. The vascular advantages of PTX have been known for some time. They are attributed to its effect on erythrocyte deformability and a reduction in blood viscosity because it is a drug with potent hemorrhaging properties. This promotes blood flow, playing an antithrombotic role in the ischemic region, and thus improving the injuries. Moreover, PTX is able to inhibit inflammatory cytokines such as TNF- $\alpha$ , thereby exerting an additional protective effect. After a night without feeding, the animals (130 male Wistar rats) were weighed and anaesthetized with Ketamine (80mg/kg) and Xilacine (10mg/Kg) to induce and maintain the anesthesia. The abdomen was explored via a midline laparotomy and the right kidney was dissected. Ischemia (I) of the right kidney was induced by clamping the renal pedicle for 90 minutes with a microvascular clamp. The kidney was carefully inspected to ensure that it was ischemic, as well as for adequate reperfusion after removing the microvascular clamp. The left kidney remained untouched during the reperfusion (RF) period (24 h). For the experimental study of the effects of PTX on IRI, we used Wistar rats randomly divided into 4 experimental groups (n = 5): sham, a group with untreated ischemic injury (I/R); an ischemic injury group pre-treated with PTX (pentoxifylline 24h before surgery), and an ischemic injury group post-treated with PTX (pentoxifylline after ischemia). Pentoxifylline was administered at 10mg/kg. Biochemical analyses were carried out (uric acid, creatinine, urea, blood urea nitrogen (BUN) and LDH), as were protein analyses (cytokines and proinflammatory molecules), flow cytometry (ROS) and the histologies to determine the renal morphology and the physiopathological changes occurring in the kidney during the period of damage due to IRI. The results show that PTX has a protective effect on the organ, since the treated groups showed improved renal function compared to the untreated groups and creatinine levels (I / R 1'22 mg / dl, Pre-PTX 1.04 mg / dl; Post-PTX 0.96 mg / dl). Survival was increased in the groups treated with PTX (I / R 40% 65% Pre-PTX, PTX Post 70%). We also observed the ability of PTX to reduce the inflammatory process that occurs during the ischemic injury. This is also seen in the immunohistological study of the anatomical specimens. Pentoxifylline reduced the damage in the kidneys subjected to ischemia and reperfusion processes. Neutrophil activity (MPO) was reduced with the administration of PTX at the time of reperfusion I / R (I / R 0'466 u / l, Pre-PTX 0'336 u / l; Post-PTX 0'242 u / l). With flow cytometry leukocytes found in ROS changes in the groups studied: peroxynitrite (I / R 381 UAF, UAF Pre-PTX 375; Post-PTX 349 UAF) and peroxides (I / R 1999 UAF, UAF Pre-PTX 1890; post-PTX 1539 UAF). The results of this study enable us to provide information additional to the information that already exists, to indicate that pentoxifylline has a protective role in the organ subjected to ischemia and reperfusion. This leads us to believe that this drug could be used as preventive treatment in clinical situations such as kidney transplants, increasing the organ's viability. As a conclusion treatment with PTX (pre & post) improve organ viability in this experimental model.

## Nonhuman Primate Hepatic Biopsy Collection Method

POSTER 17

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### ABSTRACT

**AIM:** To describe surgical procedure for obtaining liver samples. Developed to allow direct visualization of liver and excisional biopsy vs. core needle biopsy to increase sample size and improve safety for animals.

One hundred eleven biopsy samples were obtained over a four month period of time with multiple samples taken from some animals during the course of the assigned studies. A minimum of two weeks was required for healing. The procedure was conducted under general isoflurane gas anesthesia after induction with ketamine and propofol. Animals were given IV fluids (maintenance rate) and monitored for blood pressure, temperature, pulse oximetry. The animals were placed on the table in a dorsal recumbent position.<sup>1</sup> The cranial abdomen left of midline under the rib cage was prepped for surgery and a bupivacaine block was placed at surgical site. A stab incision approximately 1-2cm was made into the abdominal cavity.<sup>2</sup> Forceps and hemostats were used to isolate the edge of a liver lobe, the lobe was grasped and lifted to the abdominal incision where a scalpel blade was used to excise the tissue. Following excision the lobe was replaced into the abdomen and monitored for hemorrhage.<sup>3</sup> Once hemorrhage was controlled, the abdominal incision was closed in two layers with absorbable monofilament suture. Animals were then placed in anesthesia recovery until fully alert.

This technique is superior to a needle biopsy in that we can directly visualize the liver avoiding any accidental sampling of other organs, uncontrolled hemorrhage, perforation of gall bladder and obtain a larger sample that can then be used for histological and/or biochemical assay examination. There were no complications noted in this group of animals. When compared to laparoscopic surgery for hepatic biopsy, this technique is perhaps less invasive due to one incision only and advantageous due to the added expense of equipment and training required for laparoscopy.

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# Clinical Trial of a New Elastic Cyanoacrylate for General Surgery

POSTER 18

Jaime Ballester-Alvaro

Exterior

## ABSTRACT

**BACKGROUND:** Cyanoacrylate bioadhesives have been widely studied and used in recent decades as an alternative method to conventional sutures for closing wounds and surgical incisions. Adhflex® is the first tri-component adhesive which, due to its composition, allows tissues to be joined in bending areas subject to extreme tension and deformations, easily adapting to the anatomy of each zone and providing strong, fast, and flexible seams. Repair of inguinal hernia is one of the most common surgical procedures in the world. The method traditionally used for the closure is suture, which is why we have chosen this technique as the control group for our study.

After the experience of different preclinical studies, which demonstrated the efficacy and safety of this experimental technique for the closing wounds, a clinical trial has been performed transferring this experimental technique into the daily practice clinic in patients with hernioplasty required.

**METHODS:** A prospective, open-label, randomized, controlled, Phase III clinical trial was performed to evaluate the efficacy and safety of the flexible tissue adhesive (Adhflex®) in comparison to conventional suture techniques for the inguinal hernia closing wounds. Seventy-one patients were enrolled, 60 of them were randomized and divided into two groups (28 patients in the suture group and 32 patients in the flexible tissue adhesive group). The primary objective of the study was to evaluate the superiority of Adhflex® in terms of speed for closing wounds compared to the use of conventional sutures. Furthermore, wound healing and complications, scar appearance, ease of adhesive application, postoperative satisfaction and cosmetic outcomes were measured as secondary endpoints using different standard subjective scales (Hollander, VAS and POSAS scales) at Day 1 and 7, 30 and 90 days after surgery. Continuous variables were summarized with mean, standard deviation and median indicating number of data observed and missed. t-Student and/or Wilcoxon test were carried out. Absolute and relative frequencies were calculated for categorical variables. Statistical software used for the analysis was R.

Patients were operated on under general regulated anesthesia as per the standard procedure of the site at Visit 2 (Day 1) and evaluated at Day 1 and 7, 30 and 90 days after surgery. Surgery of hernia was performed according to the Lichtenstein's repair technique. Results: Results from the Per Protocol Population (PP) and the Intention-to-Treat Population (ITT) were obtained. In both cases the flexible tissue adhesive group had better results than the suture group. Mean speed for PP and ITT in the flexible tissue adhesive group was 62.94% and 84% faster than in the other group (p-value < 0.05), respectively. Overall wound appearance 90 days after the surgery, sensation felt by the patient 7 and 90 days after the surgery, subjective investigator assessment 90 days after the surgery or cosmetic outcomes 90 days after the surgery were significantly better (p-value < 0.05) for the flexible tissue adhesive group. Conclusions: Wound closure is faster with cyanoacrylate adhesive than with conventional sutures, and cosmetic outcomes are similar in both methods.



## Development of a Posterolateral Intertransverse Lumbar Arthrodesis Model in the New Zealand White Rabbit

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NAMSA (North American Science Associates)

### ABSTRACT

In order to be able to assess the safety and effectiveness of medical devices appropriately, testing facilities must establish proven test methods. The objective of this study was to develop the posterolateral intertransverse lumbar arthrodesis model in the rabbit at NAMSA with a fusion percentage of greater than 50%. The study was approved by the NAMSA Institutional Animal Care and Use Committee. The animal model chosen for this study was based on available peer-reviewed literature for lumbar arthrodesis. There were no available validated in vitro assays or computer simulated models that could mimic the complexity of arthrodesis in the lumbar vertebrae. Thirty-six female, New Zealand white rabbits, weighing 3.9 to 5.0 kg, were used in the study. Anesthesia was induced by an intramuscular injection of ketamine hydrochloride (34 mg/kg) and xylazine (5 mg/kg). The analgesics, buprenorphine (0.05 mg/kg) and fentanyl (25µg/hr patch), were given along with a prophylactic dose of an antibiotic, enrofloxacin (10.0 mg/kg). Each animal was placed on isoflurane inhalant anesthetic for the remainder of the surgical procedure. All surgical procedures utilized standard aseptic technique. The left and right transverse processes of L5 and L6, as well as the corresponding pars interarticularis, were decorticated in each rabbit. Autogenous corticocancellous bone (autograft) was harvested from the iliac crests of each rabbit. The autograft was minced and loaded into a syringe for application. The autograft was placed over the intertransverse ligament so that it extended the distance between L5 and L6 (approximately 2.5 mL of autograft was placed on each side). Animals were observed daily for general health; however, strict cage rest was maintained for the first 4 weeks after surgery (no removal from the cage occurred during this time). Six weeks following the surgical procedure, the animals were euthanized with an intravenous injection of 390 mg pentobarbital and 50 mg phenytoin (Euthasol®). The spines were harvested and fusion was evaluated by manual manipulation. Radiographic images were taken and then the sites were histologically processed for microscopic evaluation. Posterolateral intertransverse lumbar arthrodesis was achieved with a fusion percentage of 86%. Bone formation was observed in all sites, but there was not enough boney development to cause complete fusion in 14% of the animals. Radiographic images and histology results were supportive of manual palpation fusion scores. The results from this study will allow NAMSA to safely and effectively assess biomaterials intended to promote spinal fusion in a demonstrated model.





# Presentation Abstracts

30  
YEARS



# Presentation Abstracts

## Short-Acting and Long-Acting Buprenorphine Therapeutic Drug Levels Following Single Subcutaneous Administration in Diabetic Yucatan Miniswine

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### ABSTRACT

Sustained and controlled analgesia for animals involved in potentially painful procedures is required for animal welfare and ethical considerations. We designed a study to assess the PK for buprenorphine (BUP) analgesics in diabetic Yucatan miniswine. Four castrated male alloxan diabetic animals weighing approximately 30 kg were used in a complete cross-over design. For BUP, animals were dosed subcutaneously (left flank fold) with either 0.01 mg/kg (low-dose) or 0.02 mg/kg (high-dose), while for BUP SR (sustained release) the dose was either 0.12 mg/kg (low-dose) or 0.24 mg/kg (high-dose) s.c. in left flank-fold. Washout was set at 9d before animals were redosed with another formulation. For the BUP, blood samples were collected at pre-dose, 0, 15, 30, 60, 120, 240 and 480 minutes (8 timepoints targeted). For the BUP SR, samples were collected at pre-dose, 0, 30, 60, 90, 240 and 480 minutes, and 12h, 24h, 48h, 72h, and 96h (12 timepoints targeted). Buprenorphine was analyzed in K2EDTA plasma samples by liquid-liquid extraction and LC-MS/MS (quantitation range is 50 to 5000 pg/mL). Results were reported in picograms/mL of plasma. All data were quality controlled and outliers removed before summary statistics were calculated and plotted. Results for buprenorphine high- & low-dose plasma drug profile curves showed that BUP peaked at 2192 pg/mL for the high-dose and 842 pg/mL for the low dose. Following single s.c. administration, shorter-acting BUP drug was in plasma for 240-480 min (above 0.1 ng/mL efficacious threshold for 480 min or 8 hrs). Results for BUP SR plasma drug profile curves showed peaks at 1795.5 pg/mL at 240 min (high-dose) and at 1531.8 pg/mL (low dose) at 30 min. Sustained release drug was present in plasma for 96 hrs for both high- & low-dose (above 0.1 ng/mL). In conclusion, these data show that these dose levels provide sufficient plasma levels of drug for analgesia (>0.1 ng/mL) for at least 8 hr (short-acting BUP) or 96 hr (long-acting BUP SR).

### NOTES

## Continuous Measurement of Renal Blood Flow and Blood Pressure Changes While Testing Antihypertensive Compounds in Freely Moving Rats

Xuening Hong  
Merck

### ABSTRACT

Regional blood flow measurement is an essential tool to understand target organ effects of a therapy. We developed a surgical method to measure renal flow and pressure simultaneously in freely moving rats and applied it to cardiovascular drug discovery. In the present study, a BP radiotransmitter (model TA11PAC40; Data Sciences, St. Paul, MN) was inserted, via the femoral artery, into the abdominal aorta to measure systemic blood pressure. An ultrasonic transit time flow probe (1RB; Transonic Systems) was placed around the left renal artery for measurement of renal blood flow (RBF). Data acquisition system was modified; wireless (radiotransmitter) and wired (flow probe/meter) data acquisition systems were configured for simultaneous collection of pressure, heart rate, and flow measurements enabling calculation of renal vascular resistance. In addition, radiotelemetric technology for BP measurements and the measuring BP with fluid-filled catheters were compared in this study. The radiotransmitter implantation eliminates the needs of catheter maintenance and meticulous care of the catheters. The model was validated by using standard of care anti-hypertensive compounds. In summary, chronic implantation of the transonic flow probe and radiotransmitter in rats is a useful approach for long-term and continuous measurements of renal blood flow and BP. These continual renal measurements may provide valuable information about mechanism of action questions around a therapeutic response

### NOTES

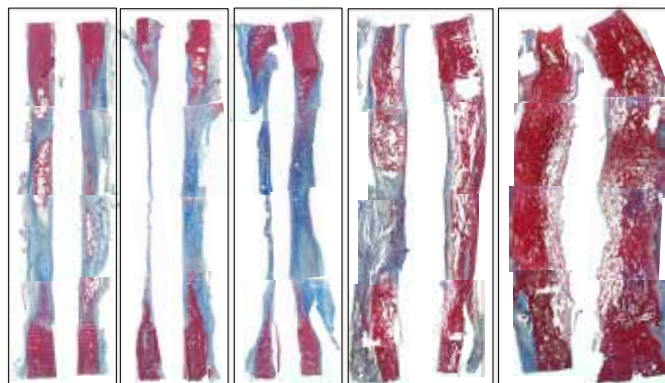
# Large Animal Model of a Critical Sized Defect that Allows Discrimination Among Grafting Materials

Liz Pluhar, PhD  
University of Minnesota

## ABSTRACT

When testing the efficacy of treatments for segmental bone defects, it is advantageous to use a model that accurately simulates the severity of injuries in human patients. All current published critical-sized defect models in large animals heal if grafted with fresh autogenous cancellous bone (ACB), which does not recapitulate the situation with large bone defects in people. We recently developed the caprine chronic tibial defect (CTD) model that incorporates loss of regional bone, periosteum and soft tissue, local tissue scarring, and creation of a fibrous membrane using a polymethylmethacrylate (PMMA) spacer. There was minimal regenerate bone within these defects three months after engraftment with fresh ACB when local muscle loss and a PMMA spacer with a smooth surface were included in the protocol. We used this model to compare healing three months after treatment with five commonly used grafting techniques.

Forty-five adult (5-7 yrs) female Spanish Boer goats, mean BW = 65 kg, were used. The defect is created by osteotomy of 5-cm of tibial diaphysis, stripping of 2-cm periosteum from each remaining bone segment, and debridement of 10-gm of cranial tibialis/gastrocnemius mm. Bone segments are stabilized with an interlocking nail and smooth PMMA spacer is placed in the defect. Four weeks later, the spacers are removed and replaced one of five grafting materials: ACB from the sternum, mineralized cancellous allograft [MCA], MCA + bone marrow aspirate from the sternum [BMA], MCA + rhBMP-2, MCA + BMA + rhBMP-2 (n=9 goats/treatment). Radiographs were taken after each surgery and then every 4 weeks for 3 months to assess healing. Tibias were harvested after euthanasia 3 months after grafting and regenerate tissue in the defect was evaluated by microCT and histology (Figure 1).



After 12 weeks, allograft alone resulted in least amount of new bone formation and defect grafted with ACB had slightly more bone formation relative to MCA, but none had bridging callus. The addition of BMA provided an incremental increase in new bone formation. Defects treated with rhBMP-2 had the greatest amount of new bone formation. The defects grafted with a source of osteoconduction (MCA), osteoinduction (BMP), and osteogenesis (ACB) had the greatest amount of bone healing with circumferential bridging bone callus in most cases.

Our model closely replicates non-union and open fractures of military extremity injuries, which are often recalcitrant to standard bone grafting procedures. We were able to distinguish differences in bone formation among the various grafting methods using our model in this study. The greatest degree of healing was seen when osteogenic, osteoinductive and osteoconductive materials were delivered to the defect, whereas osteoconductive material, with or without marrow aspirate, resulted in minimal new bone formation.

## Trials and Tribulations of the Refinement of Femoral Critical Sized Defects in the Rat

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Wake Forest Innovations

### ABSTRACT

This presentation is intended to discuss the model development and implementation of a successful femoral critical sized defect model in the rat. Rodent models are often preferred in the screening phase of new compounds in orthopedic studies due to cost and relatively uncomplicated recoveries. Nevertheless, the femoral critical size defect in the rat can carry a number of surgical complications included intraoperative and postoperative fracture/dislocation of the immobilizing plate and screws, as well as postoperative infections that can lead to mortality. Various methods used to help counteract these complications will be discussed. A recent IACUC approved study utilizing this model will be presented as a case example of some of the problems that can be associated with a femoral CSD in rats. At the start of the study; up to 30% of animals were euthanized due to issues regarding infection and surgical technique. Refinement of the surgical preparation and technique reduced mortality to 0% for the remaining animals. This discussion is a follow-up to the wet-lab being presented at APS where the refined techniques will be demonstrated.

### NOTES

## Process Improvement for Surgically Implanted Bilateral Middle Ear Cannulae in Guinea Pigs

Jenifer A. Sweet, BA, LAT, SRS

MPI Research

### ABSTRACT

Ototoxicity is a growing field in research. As such, varying methods have been developed to test pharmacological agents in pre-clinical practice for ototoxic effects. Methods include trans-tympanic dose administration, dosing through a myringotomy or tympanostomy tube, and direct dosing via the bulla. The surgical method in question consisted of one lengthened, exteriorized 24 gauge angiocatheter with injection cap permanently placed in the round window niche via the bulla. The procedure was adjusted in-house to include bilateral implantation, and repeatedly used for nearly a decade. Over time, a number of functional problems arose that were deemed possible to either improve upon or eliminate. 30 CRL:HA (Albino Hartley) guinea pigs underwent surgery. Process improvement involved modification of both materials and methods. The number of screws used for the procedure and the amount of methacrylate on the skull were both decreased by half. The methacrylate skull cap did not remain exposed, but was covered completely during closure. Skin sutures were replaced with subcuticular sutures, and the 24 gauge angiocatheter with injection cap was replaced with the much smaller customized PinPort™ from Instech Laboratories, Inc. All changes allowed for an improved general appearance post-operatively. The smaller incisions and decreased bulk increased animal welfare and technician comfort during handling. The change in dosing procedure reduced the threat of dislodging the methacrylate cap. Post-operative supply and labor costs were reduced due to the vanished need to remove suture, routinely change injection caps, and anesthetize animals to re-apply methacrylate. Data collection continues to take place with respect to positive control testing and auditory brainstem response; however, detailed collaboration and communication concerning this improvement process has thus far produced a superior outcome.

### NOTES



## The Chinchilla Model of Acute Otitis Media: Two Pathogens, Three Treatment Administration Routes, and the Apparent Disconnect Between Clinical Signs and Bacteria Burden

James Justen  
MPI Research

### ABSTRACT

**AIM:** To assess clinical responses of anti-infective agents in the chinchilla model of acute otitis media (AOM). A model of AOM was developed in chinchillas because middle ear anatomy including cochlear size, nervous system connections, and hearing range are similar to humans. **Methods:** AOM was induced in isoflurane anesthetized female chinchillas (n=6, 12 ears/group) by transbullar injection (0.2 mL) of either *Haemophilus influenzae* (~10E3 cfu/ear) or *Pseudomonas aeruginosa* (~10E6 cfu/ear). Chinchillas infected with *H. influenzae* were treated with either amoxicillin (30 mg/kg, BID, oral, Days 2-8), a combination of ciprofloxacin/dexamethasone (0.3% ciprofloxacin, 0.1% dexamethasone, 0.14 mL, BID, topical ear canal, Days 2-8) or ciprofloxacin alone (0.3%, 0.14 mL, once daily, transbullar injection, Day 2 or Days 2 and 5). Chinchillas infected with *P. aeruginosa* were treated with ciprofloxacin/dexamethasone (0.3% ciprofloxacin, 0.1% dexamethasone, 0.14 mL, BID, topical ear canal, Days 4-10). Middle ear fluid (MEF) was collected from both ears of all animals for bacterial enumeration at the conclusion of treatment administrations. Detailed clinical observations were performed daily. **Results:** Amoxicillin, ciprofloxacin/dexamethasone and ciprofloxacin effectively eliminated *H. influenzae* from MEF, although clinical signs of middle ear disease such as head tilt and circling remained. Ciprofloxacin/dexamethasone failed to eliminate *P. aeruginosa* from MEF, although the middle ear-related clinical signs were resolved. **Conclusion:** Chinchilla AOM models can be useful in determining the effectiveness of anti-infective agents, although clinical signs of the middle ear condition do not correlate with bacterial clearance.

**SUPPORT:** MPI Research

### NOTES

# Using Pressure-Volume Loop Analysis to Understand Dystrophic Cardiomyopathy in Mouse and Dog

DeWayne Townsend, PhD

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## ABSTRACT

Pressure-volume loop analysis offers a detailed assessment of cardiac function, providing both structural and hemodynamic information. Furthermore, the high temporal resolution of this method allows for the real-time assessment of changes in loading of the heart. This ability to measure load independent function of the heart is a significant strength of this approach. The objective of this presentation is to present a practical view of the use of pressure-volume loop analysis for the assessment of cardiac function in a wide variety of animal models. A general discussion of the information that can be obtained from this analysis and its advantages and disadvantages over other methods of cardiac assessments will be included. Examples of how this methodology has been used to better understand new therapeutic approaches for the heart disease associated with muscular dystrophy will be included to provide some experimental context.

## NOTES

## Its Cardiovascular Telemetry Implantation in the Canine

Jon Ehrmann, BS, SRS, SRA, LATg

### ABSTRACT

Implantable telemetry devices are commonly used for pre-clinical studies in safety assessment pharmacology and toxicology. The device allows for a hands off approach to the collection of cardiovascular, pulmonary and neurological data from animals on study. This presentation will discuss in detail the surgical procedure for the implantation of a cardiovascular telemetry device in the canine. There are several makes and models of telemetry devices currently being used in the research field. This presentation will focus on the surgical procedure to implant a device produced by Integrated Telemetry Solutions (ITS). The model being discussed includes solid state pressure transducers for the left ventricle and aorta, ECG electrodes, an abdominal temperature probe, transmit antenna, On/Off antenna and the electronics/ battery pack. Pre-, peri-, and post-operative anesthetic and analgesic protocols, as well as potential complications and learned best practices will be reviewed.

### NOTES

## Biliopancreatic Route for Islet Viral Transduction

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### ABSTRACT

Gene transduction with viruses has been notoriously difficult to achieve in pancreatic islets both in vivo and ex vivo. While some success has been achieved ex vivo, transduction has been limited to the superficial layers of the islet. Given the potential benefits of direct targeting of insulin producing  $\beta$  cells of the islet core, we explored surgical approaches to virus delivery in vivo to improve the efficiency of transduction.

Previous attempts at manipulation of gene expression in pancreatic islets have had limited success despite multiple approaches. Administration of virus into the blood circulation has been ineffective in achieving sufficient viral dosage into the pancreas.  $\beta$  cell targeting has also been attempted by incorporating specific  $\beta$  cell promoters into the virus. However this approach is associated with limitations in that some brain regions, particularly the hypothalamus which has profound effects on glucose homeostasis, are also affected by these insulin promoters.<sup>1</sup> A recent method described direct infusion into the pancreatic duct of bile acid to model acute pancreatitis.<sup>2</sup> We adapted this surgical technique to assess whether pancreatic islets could be reached as an efficient means of adenoviral gene transduction.

A technique was developed for retrograde surgical infusion into the rat biliopancreatic duct with a test adenovirus containing a construct co-expressing GFP for detection of infected cells. GFP expression was evaluated by confocal microscopy.

Pancreatic islets isolated after acute infusion and cultured for two days showed GFP expression in the entire islet and in almost all islets. When rats were recovered after infusion, and islets isolated at 1 and 8 weeks post-operatively, we continued to see extensive islet GFP expression, though at reduced levels by 8 weeks.

This strategy of surgical biliopancreatic ductal perfusion of viruses is an effective way to transduce gene expression in pancreatic islets for both acute and chronic study.

This work was supported by a grant from the Canadian Institutes for Health Research (Herbert Gaisano).

### REFERENCES:

<sup>1</sup>Gannon et al. Analysis of the Cre-mediated recombination driven by rat insulin promoter in embryonic and adult mouse pancreas. *Genesis*. 2000;26:139-42.

<sup>2</sup>Perides G et al. Experimental acute biliary pancreatitis induced by retrograde infusion of bile acids into the mouse pancreatic duct. *Nat Protoc*. 2010;5: 335-341.

## Abrasion Assessment of Staple Line Reinforcement Materials in a Novel Canine Thorax Model

Ludovic Bouré, DVM, MSc, DES, DACVS, DECVS

Covidien

### ABSTRACT

To develop and utilize a novel canine surgical model to assess the abrasiveness of buttressed and non-buttressed staple lines in the thorax.

Buttress materials are used in conjunction with surgical staples to transect thin or diseased thoracic tissue. Preclinical surgical models are required to assess abrasiveness of buttress materials to be placed in the thorax.

Pilot model development and pivotal trials were performed. For both, buttressed and non-buttressed staple lines were applied on the apex and surface of the lung lobes (Day 0) in canines. Five individual staple line sites, crossed and single lines, were created per hemi-thorax (a single material assigned to each hemi-thorax). Intraoperatively, staple lines were assessed for air leak. Two buttress materials were tested. In the pilot study, up to 30 staple line sites per buttress material were surgically placed in ten canines. Staple line contact with and movement against the pleura was verified by trans-parietal ultrasonography on Day 2, and thoracoscopic pleural abrasion assessment was conducted on all animals on Day 3 using an ordinal scale (0 to 5). Animals were euthanized on Day 7 (n=3), Day 10 (n=3), and Day 14 (n=4), and assessed for pleural abrasions, per the ordinal scale from the pilot study, at necropsy. In the pivotal study, n=50 staple line sites per buttress material were surgically placed in 12 canines (Day 0). All animals were observed for abnormal clinical signs, euthanized at Day 7 and assessed at necropsy for pleural abrasions. Statistical comparisons were done using Kruskal-Wallis ( $\alpha=0.05$ ).

The surgical procedure was well tolerated by all. No intraoperative air leaks from the staple lines, and no post-operative complications were observed. From the pilot, abrasion severity did not increase beyond Day 3 as evidenced by no difference being found between Day 3 thoracoscopy scores and Day 7, 10 and 14 necropsy scores ( $p=0.585$ ,  $p=0.326$  and  $p=0.508$  respectively). Likewise, abrasion scores from necropsy Day 7, 10 and 14 were no different ( $p=0.176$ ). For the pivotal study, a difference in abrasion scores was observed between buttress materials ( $p=0.0016$ ), but between buttress and non-buttress results were varied ( $p=0.0008$  and  $0.3446$ ).

The model was sufficiently sensitive to detect differences in the abrasiveness of two buttress materials in the thorax. Abrasion scores were mild for both buttress materials, and observed differences in abrasion scores between the two materials were not of clinical significance. SUPPORT: None

# Development and Utilization of a Canine Model to Assess Staple Line Reinforcement Materials in the Abdomen

Ludovic Bouré, DVM, DSc, DES, DACVS, DECVS

Covidien

## ABSTRACT

**AIM:** To develop a canine abdominal surgical model to assess buttressed and non-buttressed staple lines.

Surgical buttressed staple lines are used to transect thin or diseased gastro-intestinal tissue. Surgical models to assess buttress materials abrasiveness and abdominal adhesion genicity do not exist in the literature.

The surgical procedure for pilot and pivotal studies was similar to a Billroth II with a partial resection of the stomach along with a jeju-jejunostomy. In total, eight individual staple lines were created in each canine abdomen. Three groups of staple lines were assessed: staple lines without buttress material, staple lines with buttress material 1 (BM1) and staple lines with buttress material 2 (BM 2). In the pilot study, an omentectomy was performed to assess organ-to-organ abdominal adhesions; however, for the pivotal study the omentum was left intact to create a more clinically relevant model. Eight animals (n=16 staple lines per group) received surgery during the pilot study and 12 animals (n=40 staple lines per group) received surgery during the pivotal study. Intra-operatively, each anastomosis was qualitatively assessed for leak and patency. Post surgically, all animals were observed for abnormal clinical signs. Post mortem examination (Day 14) included a gross assessment of the abdomen, the characteristics of adhesions to each staple line, and characteristics of tissues abrasions surrounding the staple lines. Ordinal scales were used to score adhesions and abrasions. Statistical comparisons were conducted using a Kruskal-Wallis ( $\alpha=0.05$ ).

The surgical procedure was well tolerated by all animals, with no post-operative complications. No intraoperative leaks from the staple lines were observed. Gross observation of the abdomen at necropsy showed no indication of leak. For the pilot study, abdominal adhesions with involvement of more than one organ were observed for buttressed staple lines which was significantly different from non-buttress staple lines ( $p=0.0294$  BM1 1 and  $p=0.00003$  BM 2) but was not different between BM1 and BM2 ( $p: 1.000$ ). Blunt dissection was required for complete staple line isolation. For the pivotal study, in which the omentum was left intact, the adhesion extent for the buttressed lines was found to be no different from non-buttressed staple lines ( $p=1.000$ ). No abrasions were observed with either buttress material or non-buttressed staple lines in either study.

This surgical model allowed to assess and compare the induction of abdominal adhesions between buttress materials.

**SUPPORT:** None

## The Effect of Site of Surgical Implantation on Regulating the Prostate Function Using Adult Castrated Rats As a Model

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### ABSTRACT

This study was designed to investigate the effect of intraperitoneal (IP) and subcutaneous (SC) implantation of HA delivery system loaded with dihydrotestosterone (DHT) on prostate regulation of adult male castrated rats.

Traditional routes of administration allow drugs to be either injected or ingested, whereas, sustained release drug delivery systems can virtually be placed within any body cavity without inducing any traumatic side effects.<sup>1-2</sup>

A total of 120 adult rats (250-270 gm) were equally divided into five groups (n=24). Groups 1 and 2 were castrated and implanted with DHT loaded (40mg) HA capsules at IP or SC, respectively. Groups 3 and 4 animals were castrated and implanted (IP and SC) with empty capsules and served as sham groups. Group 5 animals were not castrated and served as intact animals. Aseptic surgical techniques were performed throughout the study approved institutional protocol (IACUC). At the end of 4, 8, and 12 weeks post-surgery, 8 animals from each group were sacrificed and HA capsules, prostate, vital organs and blood samples were collected for further analysis. RESULTS: The results indicated that, regardless of the site of surgical implantation, there is a fibrous capsule which encompasses the implanted HA delivery system, and the presence of inflammatory cells were evident after the first week of implantation. Regardless of the site of surgical implantation, the wet weights of vital organs showed no significant differences between the groups; however, the prostate wet weights collected from DHT treated animals were significantly higher ( $p < 0.05$ ) than those collected from castrated sham groups. Histopathological evaluations of the ventral prostate tissue revealed that sustained delivery of DHT from IP implanted group (not SC) induced tubular growth comparable to the intact control animals.

The results clearly showed that the surgical implantation site is an instrumental factor in the prognosis of major metabolic condition.

### REFERENCES:

<sup>1</sup>Benghuzzi HA, and Bajpai PK. Sustained Delivery of Difluoromethylornithine (DFMO) by means of Implantable Ceramic Devices. *Journal of Investigative Surgery*, 1988;1: 63-170. PMID: 3154094.

<sup>2</sup>Benghuzzi HA, and Bajpai PK. CRC Handbook of Bioactive Ceramics, Vol. II: Calcium Phosphate Hydroxyapatite Ceramics. (Invited Paper). Comparison of Polycaprolactone and Polylactic Acid Impregnation of ALCAP Ceramics and its Effects on the Delivery of Steroids. Yamamuro T, Hench LL, and Wilson-Hench, J (Editors), 1990.



## Targeted Animal Safety: Development of a Radiotelemetry Implanted Surgical Model in the Adult and Juvenile Feline

Teresa R. Gleason, B.S., LVT, SRS, LATg

WIL Research, USA

### ABSTRACT

The Target Animal Safety section of 21 CFR 514.1(b)(8)(i) recommends that studies must demonstrate whether or not a new animal drug is safe for the targeted species. In order to measure direct blood pressure in the non-anesthetized feline twice daily for a minimum of 18 consecutive days, a telemetry model was determined most appropriate. Four adult male cats (12 – 15 months) were pre-treated with subcutaneously administered ampicillin (6.6 mg/kg), atropine (0.05 mg/kg), acepromazine (0.1 mg/kg), and ketoprofen (2mg/kg), prior to induction of anesthesia with intravenous propofol (4mg/kg administered to effect). Anesthesia was maintained using inhalant isoflurane anesthesia. The animals were prepared for aseptic surgery and a telemetry device (DSI – D70-PCT) was placed via laparotomy. The pressure catheter was placed into the abdominal aorta via the left femoral artery and the electrocardiogram leads were placed in a lead II configuration. Incisions were closed and the animals were placed in a warmed cage and returned to their home cage when ambulatory. After surgical recovery, animals were subcutaneously dosed with 5 mL/kg of 0.9% saline or dipyridamole (2.5 mg/kg, 10 mg/kg, 40 mg/kg) in a latin square cross over design with approximately 3 days wash-out between doses. Telemetry data (HR, BP, ECG) was collected for one hour prior to, and continuously for 24 hours following each dose. These data effectively demonstrated the use of telemetry implanted cats for the purpose of evaluating cardiovascular liability for pharmaceuticals administered in felines. Additional model refinement required that the animals be less than 4 months of age at initiation of dosing. Due to the size of the animal at this age, the telemetry device used in the adults was determined to be inappropriate. Procedures for the juvenile animals were developed. Four juvenile female cats (12 weeks) underwent surgery as described above with the following exceptions: xylazine (2.2 mg/kg) was administered rather than acepromazine and a smaller telemetry device was implanted (DSI-C50-PXT). After recovery, the animals were subcutaneously dosed once with 0.1 ml/kg 0.9% saline. The positive control article was not administered as its effects were previously demonstrated. Telemetry data was collected twice daily at 10 am and 4 pm for one hour for three days following dosing to closely mimic the procedures to be used on the main study. Collecting cardiovascular data from adult and juvenile cats using appropriately sized, surgically implanted telemetry equipment was successful and could be implemented for target animal safety studies.

### NOTES

## Implantable Glucose Telemetry in Rodents

Megan Swaab Fine, DVM, MS  
Data Sciences International (DSI)

### ABSTRACT

Our objective was to develop a surgical approach for a novel telemetry implant using a chemical sensor to provide continuous intravascular glucose measurements. Our goals included a technique that was accessible by trained rodent surgeons, and caused minimal complications. While developing the surgical model, gross findings and all complications were recorded, and success rates were compared to determine the best implant configuration and surgical approach. This protocol was approved by DSI's Institutional Animal Care and Use Committee.

Initial work in the rat was performed using the abdominal aorta approach commonly used with our blood pressure catheters. Adjustments that were required in the rat model to prevent post-operative migration included the use of an additional fiber patch, and the addition of suture ribs to allow the connector piece to be secured to the lumbar muscles. In addition, the sensor design was modified to increase its robustness. In total, the developed surgical approach resulted in over 90% surgical success across >150 rats and has become our current surgical recommendation. Experimentation is currently underway to develop a surgical approach and optimize the device for the use in the mouse and latest developments will be reported. In conclusion, we have developed an effective surgical approach and directed required implant modifications to allow for the continuous measurement of blood glucose in rats. In both healthy and diabetic rats, we have achieved stable continuous blood glucose signals for 28 days or longer in over 80% of subjects.

### NOTES

## Refining the Consistency of the Mouse Subtotal Nephrectomy Procedure

Marla A Wilwol, LVT, CMAR, SRS, LATg

Taconic

### ABSTRACT

Renal ablation is one surgical approach used to perform a subtotal nephrectomy in rodents. Consistent removal of tissue volume can be critical for inducing reliable and reproducible disease. The desired outcome of the surgery is an animal that exhibits measurable indicators of renal disease, such as an albumin-creatinine ratio (ACR) value greater than 2500. With the aid of collaborators, we aimed to identify a weight range of kidney tissue to be removed that would induce a targeted ACR value but maintain an acceptable morbidity rate. For this study 168, 8-9 week old male 129S6/SvEvTac mice were modified according to Taconic's standard surgical procedure. All animals were modified by removing the entire right kidney and ablating the poles of the left kidney. The kidney and removed poles were weighed. The weight of the removed poles ranged from 35-70mg. Two weeks later, urine was collected and ACR values were determined by a collaborating laboratory. We and our collaborators concluded that removing between 35-45mg of kidney tissue induced ACR values >2500 while maintaining morbidity rates within predictable ranges. Repeated evaluations are needed to ensure reproducibility of these refinements.

### NOTES

## A Midline Open-Chest Approach for Myocardial Infarction Induction in Rats

Pilar Ariza Guzman, PhD  
University of Minnesota

### ABSTRACT

The majority of approaches to open-chest surgery in rats are performed on the left side and involve opening the ribs and cutting muscle tissue. Surgical recovery with this approach is therefore slower and normal circadian rhythm in the rat takes longer to re-establish. Because of these complications, I developed a midline approach for open-chest surgery in rats. With this approach, surgical recovery time and re-establishment of normal circadian rhythms are improved compared to the standard left-side approach. I have used this approach in three different major studies to date: 1) this approach was successfully used to remove the stellate ganglion (SGx) to assess the contribution of cardiac sympathetic nerves to neurogenic hypertension 'Role of cardiac sympathetic nerves in blood pressure regulation'. Wehrwein EA, Yoshimoto M, Guzman P, Shah A, Kreulen DL, Osborn JW. *Auton Neurosci*. 2014 Jul;183:30-5. doi: 10.1016/j.autneu.2014.02.005. Epub 2014 Mar 1.). 2) I have employed this approach to create a hemodynamic profile to study whole body autoregulation. In this particular study, a ultrasonic transit-time flows probe was implanted around the ascending aorta (model SB2.5, Transonic Systems; Ithaca, NY) 'Does whole body autoregulation mediate the hemodynamic responses to increased dietary salt in rats with clamped ANG II?' Fine DM, Ariza-Nieto P, Osborn JW. *Am J Physiol Heart Circ Physiol*. 2003 Dec;285(6):H2670-8. Epub 2003 Aug 7.). 3) Most recently, this approach was utilized to create a myocardial infarct by ligating the left anterior descending artery (LAD) of the heart and a week later treating the rats with denervation of several nerve beds in the rat. The data in these studies is proprietary and will not be presented, however the surgical method described here provides a novel midline approach to open-chest surgery in rats with many advantages over standard left-side approach.

### NOTES

# Echo-Guided Procedures Training Using an Image Fusion System and a Biocompatible Synthetic Tumor Model

Michele Diana, MD

IHU-Strasbourg, Institute for Minimally Invasive Image-Guided Surgery

## ABSTRACT

Intraoperative ultrasound (US) navigation is an important adjunct during liver surgery to identify lesions and resection margins. US-CT/MRI image fusion can increase operator accuracy in targeting lesions, particularly when those are undetectable with US alone. It can also increase technical success of ablation procedures. Surgeons are used to CT-scan imaging but receive no formal training with intraoperative US. We have developed a reproducible and modular gel to simulate contrast-enhanced solid lesions in the porcine liver for educational purposes in imaging and minimally-invasive ablation techniques (radiofrequency, cryoablation). The aim of this non-survival study was to assess the impact of image-fusion in targeting artificial hepatic lesions during the hands-on part of two courses on hepatobiliary surgery. Materials and methods Two pigs were premedicated by intramuscular injection of ketamine (20mg/kg) and azaperone (2mg/kg), induction was achieved by intravenous propofol (3mg/kg) combined with pancuronium (0.2mg/kg). Anesthesia was maintained with 2% isoflurane.

Under US guidance, 10 fake tumors of various sizes were created in the liver of two pigs (6 lesions in one and 4 in the second pig) at different locations, by percutaneous injection of a biocompatible gel made of alginate, gelatin, barium sulfate (Micropaque 98%), and calcium. The gel was specifically engineered to be hyperdense at CT-scanning and barely detectable at US, by eliminating air bubbles through repeated centrifugations. A CT-scan was obtained to verify the visibility on synthetic lesions and an expert radiologist performed CT/US image fusion using the ACUSON S3000™ ultrasound system (Siemens Healthcare). Participants to the first course included 3 surgical residents, and 3 hepatobiliary surgeons. Second course was attended by 6 residents. Reported experience with intraoperative liver US ranged from 0 to 150 hours. All were blinded to the locations of the lesions. In turn, participants performed a 10-minute liver scan with US alone followed by a 10-minute scan using image-fusion. At the end of the sessions, animals were sacrificed with an intravenous injection of a lethal dose of potassium chloride. Results Using US alone, the expert managed to identify all lesions successfully. The true positive rate of surgeons with US alone was 14/36 and 2/24 in the first and second group of participants, respectively. The total number of false positives identified by the surgeons was 26. Vessels and biliary structures were the most frequently misleading elements. With image-fusion, the rate of true positives significantly increased to 31/36 (Fisher's test:  $p=0.0001$ ) in the first and 16/24 in the second group (Fisher's test:  $p=0.0001$ ). The total number of false positives, considering all participants, decreased to 4 (Fisher's test:  $p=0.000234$ ). Conclusions The modular synthetic biocompatible tumor model allowed for a good simulation of cases in which US cannot find hepatic lesions that are visible on CT-scan. Image fusion significantly increases accuracy in targeting lesions by non-experts, and allows for an operator-independent evaluation. In the upcoming courses, a variety of gel combinations will be tested to confirm these findings.

## NOTES

## Ultrasound in Preclinical Research: Four Decades of Experience with Ultrasound as a Diagnostic Tool for Evaluation and Guidance of Medical Device Research.

James Berry, RDCS

American Preclinical Services, LLC

### ABSTRACT

This talk will discuss the use of ultrasound during surgical and hybrid surgical medical device implants. One example is the evolutionary change in valve implantation from fully surgical to partial or even fully interventional implantation with one diagnostic tool remaining constant, ultrasound. In the human, transesophageal echocardiography (TEE) is performed prior to or during the implant of the new valve. This eliminates the need for the sonographer's hands to be in the fluoroscopic or surgical field or the need for additional vascular access sites. In the animal model, a slight rotation of the heart due to the animal being a quadruped reduces the ability to achieve optimal views typically obtained in the human. As such multiple modalities may be required to obtain all images physicians are accustomed. In the animal, Transthoracic (TTE), Epicardial, Intracardiac (ICE) and Transesophageal approaches are routinely used with advantages and disadvantages to each approach. This registered diagnostic cardiac sonographer has had extensive experience in each of these modalities in all commonly used animal models while concurrently remaining active in the clinic. This provides excellent translation of the preclinical testing to the human.

# Refining Rodent Anesthesia and Surgery Through the Use of High-Frequency Oscillatory Ventilation

Szczepan Baran, VMD, MS

## ABSTRACT

One common and frequent challenge in performing rodent surgery is the constant movement of thoracic viscera (and to some extent abdominal viscera) when performing thoracic surgical procedures. Each inspiration and expiration movement makes precise surgery challenging, more risky and complicated, and in the case of cardiac procedures, access to the heart is hampered. High frequency oscillatory ventilation (HFOV) is mechanical ventilation, which uses a constant distending pressure with pressure variations oscillating around the mean airway pressure at very high rates, thus creating small tidal volumes, often smaller than the actual dead space. In conventional ventilation, large pressure changes create physiological tidal volumes and gas exchange that are dependent on expired gas exchanged for inspired gas. HFOV relies on molecular diffusion for gas exchange of gasses at the alveolar level. This type of ventilation eliminates large pressure changes and volumes associated with conventional ventilation, which make organ and tissue manipulation challenging during surgery due to continual expansion and collapse of the lungs.

This presentation will describe surgical set up and equipment required for HFOV. Advantages and disadvantages of HFOV will be addressed and selection of when HFOV should be utilized will be described.

## NOTES



## Rodent Physiological Monitoring According to the Guide

Szczepan Baran, VMD, MS

### ABSTRACT

With the growth and expansion of mouse and rat transgenic models in recent years, the demand for surgically altered models mimicking human diseases is growing at an amazing rate. Surgical procedures are performed under anesthesia, and this has a profound effect on physiological systems and makes many protective mechanisms ineffective. Therefore it is critical to manage anesthetic depth so as to minimize adverse effects such as depression of respiration, and disruption of the cardiovascular system and thermoregulation. Physiological monitoring is an integral part of overall peri-operative care to ensure animal safety, and allow for control of physiological functions through the use of drugs, instrumentation, and the anesthetist's own senses. Additionally, the 8th Edition of the Guide for the Care and Use of Laboratory Animals incorporated a new subsection on intraoperative monitoring, which underlines the importance of physiological monitoring and stresses its importance during anesthesia. During this session, veterinary technicians, veterinarians, scientists, trainers and IACUC personnel will learn about the hazards of not performing physiological monitoring, understand how anesthesia can be refined with the use of physiological monitoring. Attendees will also be able to select appropriate, adequate and reliable equipment for physiological monitoring of rodents and learn how it can significantly increase the efficiency of anesthesia and prevent the over-anesthetizing of rodents.

### NOTES

# Surgical Staff Selection, Training and Retention in a Cro Environment

Jennifer Sheehan BS, SRS, LATg  
Huntingdon Life Sciences

## ABSTRACT

Performing surgery in any environment requires a significant level of knowledge, skill and dedication. Maintaining a highly skilled surgical team in a contract research organization (CRO) can be very challenging due to the variety of projects that are often undertaken and potential distractions in this environment. The surgical team at Huntingdon Life Sciences (HLS) is a specialized group of individuals responsible for everything from basic anesthesia and study procedures to developing and managing complex surgical models and projects. Having a team that can turn their hand to any challenge requires that the individuals are carefully selected based on defined criteria, well trained and continually driven to refine and develop their skills. This, in turn, allows for the retention of specialized skills, lowers attrition rates and maintains a highly motivated and dynamic team that finds job satisfaction through constant challenge.

This presentation will describe a policy developed to address the selection, training and retention of surgical staff. It has been in place since 2006 and has proven to be quite effective in achieving the results it was developed to attain.

## NOTES

## Intrathecal Catheterisation in the Rat

Kate Read, MA, VetMB, MRCVS  
Huntingdon Life Sciences, UK

### ABSTRACT

Intrathecal administration in the rat may be required for the assessment of both local and systemic toxicity or pharmacokinetics. For specific therapeutic indications intrathecal administration, in particular in the lumbar region, will mimic clinical application. The catheter may be used to administer a single bolus, repeated boluses or to facilitate continuous infusion.

In total 127 Sprague-Dawley rats (aged 5-10 weeks and weighing 155-265g) underwent surgery to implant an intrathecal catheter. Anaesthesia was induced and maintained with inhaled isoflurane (2-3%) and multimodal analgesia administered (meloxicam 1mg/kg subcutaneously and buprenorphine 0.05mg/kg subcutaneously), including local anaesthetic blocks (bupivacaine 0.05mg/kg and lidocaine 0.5mg/kg administered at surgery). A dorsal midline incision was made in the lumbar region and the epaxial musculature blunt dissected away from the dorsal spinous processes in the region of L5-L6. A polyurethane catheter was inserted into the intrathecal space with the assistance of a short guide inserted between L5 and L6, then advanced cranially before being secured to epaxial musculature. Correct catheter placement was confirmed by identification of cerebro-spinal fluid flow. Investigations: In 47 animals on an ADME study a single bolus of volume 100µl was administered followed by heat sealing of the catheter which remained in the subcutaneous space. A pilot study of 8 animals were implanted to investigate continuous infusion into the intrathecal space. 72 animals underwent continuous intrathecal infusion for toxicity assessment. An iPrecio SMP-200 micro infusion pump<sup>(4)</sup> was programmed and filled before being inserted into a subcutaneous pocket and secured. The pump catheter was connected to the intrathecal catheter as advised by the manufacturer<sup>(4)</sup> and the loop secured to underlying musculature.

The surgical procedure was carried out without major complications, with all animals catheterised successfully. Animals recovered well and anaesthesia and analgesia were suitable for this procedure. A single bolus dose of 100µl was tolerated well with no associated clinical signs. During pilot investigations into continuous infusion it was confirmed that flow up to 30µl/hr into the intrathecal space was tolerated well. This is considerably higher than infusion rates reported previously, but was important to achieve to satisfy regulatory demand.<sup>(1, 2, 3)</sup> During infusion over 72 hours 4 of 72 animals showed varying degrees of hindlimb paresis.

This method of catheterisation provides a model for administration into the intrathecal space of the rat. The surgical procedure is reproducible and considered to be less invasive than access via the cisterna magna. Cisterna magna access is not routinely performed and so no direct comparison between the two techniques is available. The use of the programmable iPrecio pump allows for an ambulatory infusion model without the need to tether the animals. This permits behavioural assessment and is an improvement in animal welfare; animals are able to display normal behaviours post-operatively and may be group housed. The iPrecio pump also allows for higher flow rates to be administered in comparison to the osmotic minipump.<sup>(5)</sup>

### REFERENCES:

- 1: Veening JG and Barendregt HP (2010) The regulation of brain states by neuroactive substances distributed via the cerebrospinal fluid: a review. *Cerebrospinal Fluid Research*. 2010, 7:1
- 2: Pardridge WM (1991) Transnasal and intraventricular delivery. Peptide drug delivery to the brain. Table 4.2. Raven Press 1991. Page 112.
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- 4: iPrecio: Micro infusion pump SMP-200. Available online at: <http://www.iprecio.com/products/tabid/128/Default.aspx>
- 5: Alzet Osmotic Pumps: Product specifications. Available at: [http://www.alzet.com/products/ALZET\\_Pumps/specifications.html](http://www.alzet.com/products/ALZET_Pumps/specifications.html)

This project was approved by the Ethical Review Committee under the Animals (Scientific Procedures) Act 1986. The author reports no conflicts of interest.

## Vascular Access Ports – A Look at Recent Advancements and Refinements

Jon Ehrmann BS, SRS, SRA, LATg  
Bristol-Myers Squibb Company

### ABSTRACT

Vascular Access Ports (VAP) were first developed in 1980 to provide a safe and chronic means to infuse chemotherapy drugs to cancer patients. A vascular access port is an implanted device located entirely under the skin. It consists of a catheter that is inserted into the desired vessel, duct, or organ system and a subcutaneously placed body that can be accessed repeatedly through the skin via a special needle. A VAP gives the investigator a totally implantable system to deliver experimental compounds, sample blood or other body fluid and measure direct blood pressure. Vascular access ports have seen many advancements and refinements over the past thirty years. These advancements include refinements to the device, to the surgical procedure, and to the maintenance procedures. Some refinements include changes to the structural components of the VAP body, the interior design of the septum and changes to the catheter properties. Additionally, researchers have adapted VAPs for use in non vascular applications such as the common bile duct, gastrointestinal, and the intrathecal space. The presentation will discuss the refinements noted above as well as a detailed review of the surgical procedure for implanting vascular access ports via the femoral artery and vein.

### NOTES

## A New Method of Chronic Lymph Collection in the Canine

H. Vince Mendenhall, DVM, Ph.D.

Wake Forest Innovations

### ABSTRACT

This presentation is intended to discuss the development of a chronic lymph collection model in the canine. Eighteen (18) male beagles (5-10kg) were used under an approved IACUC protocol for implantation of lymphatic and jugular catheters for chronic collection of lymph and blood for up to 72 hours post dose. Briefly, under general anesthesia a thoracic duct-to-external jugular vein shunt was created in which a 3 Fr CBAS catheter was placed via a neck incision into the thoracic duct at the junction of the left external jugular and axillary vein. A second catheter (5 Fr CBAS) was placed within the external jugular vein. The catheters were connected to a three-way stopcock to create a 'T-tube' port to allow for collection of both lymph and blood, but when not in use, allowed for continued flow of lymph into the external jugular vein. The catheters were routed subcutaneously to an area over the ribs which was close to the location of a pocket within an infusion jacket. The three-way stopcock was placed within that pocket. Additionally, the animals were bandaged over the jacket and pocket to help prevent removal of the catheter system. Collections occurred at 0.5, 1, 4, 6, 8, 24, 48 and 72 hours post dose. The catheters were flushed with heparinized saline following collections to help maintain catheter patency. Contrary to belief from previous research, the majority of lymph catheters remained patent for out to 72 hours. However the anatomy of the lymphatic system in this area is highly variable in the canine; not all animals were able to be utilized for lymphatic collections because many of the lymph vessels were too small to catheterize. Refinements to the collection system and surgical procedure will be presented along with thoughts for a longer term chronic implantation method.

### NOTES



# Keynote Speakers

30  
YEARS





## The Visible Heart Laboratory

Paul Iaizzo, PhD  
University of Minnesota

### ABSTRACT

Over the past seventeen years, the University of Minnesota has partnered with Medtronic to develop the Visible Heart® methodologies: which is a large mammalian isolated heart model, which can function in a four chamber working mode. Recently, the model has been expanded to include the whole heart/lung blocks. These specimens are extracted using standard cardioplegia procedures, allowing this model to also be used to investigate ways to enhance these procedures. Once isolated the heart is reanimated and eventually allowed to function within a four chamber working mode. Pressures and outputs are monitored and preloads and afterloads are controlled and can be adjusted. We have employed multimodal imaging techniques so to compare videoscopic images with clinically available modalities (e.g., fluoro and 2D and 3D echo). This has provided us with very unique footage of normal and abnormal functional anatomies of both reanimated human and animal hearts. We have also created a unique library of preserved perfusion-fixed specimens that have been MRI and CT scanned, allowing for computational modeling. Our group has most recently been performing research with the TranMedics Inc., Organ Care System, so to enhance mean for organ preservation.

### NOTES



## Auditory Safety Evaluations and the Need for Surgical Support for Access to These Specialized Compartments for Compound Administration and Placement of Devices

Rachel Lynne Tapp, BS, LATg  
MPI Research

### ABSTRACT

To describe the background for auditory safety evaluations and the support of surgical intervention to administer materials and place devices for testing. Evaluation of auditory tissues following directed administrations of materials to the ear has been recommended by FDA guidance issued in 2008. This discussion will detail the basic requirements for these assays, and how surgical access to the dosing compartment is required for the best exposure to the auditory tissues. A review of guidance documents and of procedures required for access to the auditory tissues was conducted. Auditory safety evaluations have been recommended by FDA guidance for drugs that are administered directly to auditory tissues. Access to the middle and inner ear via the ear canal is limited by the tympanic membrane as a barrier. As an intact tympanic membrane is important to reduce the variable in determining if the effect on the sound exposure is drug-related, alternate routes of administration have been developed. To allow directed access of these materials to the middle ear space, surgical access can be utilized. Surgical procedures including transtympanic dosing, myringotomy of the tympanic membrane, placement of middle ear catheters, and access to the semicircular canal are just a few methods that have been developed to support these study types.

### NOTES

## Surgical Innovation

David Stolloff, DVM, MS, DACVS  
Ethicon, Inc.

### ABSTRACT

Medical device companies, pharmaceutical corporations, research facilities, university hospitals, venture capitalists and others are looking for innovators and next great innovations. Innovations have changed our lives personally and professionally. We often think of the innovator as someone who has a spark of genius and seamlessly delivers a new product or procedure to the world with little help from others. In reality the great surgical innovations we enjoy are the result of the dedication and hard work of a large diverse team focused on developing a new product and/or a new procedure. The innovative idea is extremely important but is only the start of the lengthy process required to deliver the innovation to the healthcare provider (surgeon) and patient. When you are in the operating room using a new instrument with advanced capabilities, do you think about the hundreds of people and years of work that was required to develop that product?

We will discuss the behaviors that distinguish the innovator from others. The innovator looks at conventional treatments and surgical procedures that are familiar to all of us, and sees opportunities for improvement. People with different training and experiences outside of the medical field can often provide fresh perspectives on addressing a problem and offer solutions that may have been used to resolve similar problems in other fields. Innovations can be incremental (small) or transformational ("leap frog"). New and novel ideas come from a wide spectrum of sources. Don't dismiss an idea proposal because it comes from an unlikely source. It is often easy to dismiss an idea because the individual presenting the idea doesn't have the credentials you would expect.

Gaining support to pursue the innovative idea from a university, Industrial Corporation, venture capital group, or other resource can be challenging. The idea must have a champion. The surgical innovation must generate a compelling "value proposition" that clearly presents the benefits of the innovation to patients, healthcare providers and the healthcare payers. The value proposition may include a wide spectrum of advantages such as reduction of time in the operating room, reduction in postoperative pain, decreased postoperative infections, improved surgical outcome, reduced treatment cost, etc. There are risks associated with pursuing an innovative idea (financial, professional, patient, other). In general, the greater the innovation diverges from conventional thinking, the greater the risk. Risks need to be understood and managed properly to provide a path for innovation.

Preclinical data must be generated to document the safety and effectiveness of the product and support regulatory submissions. Clinical studies may be required. For the medical/surgical community to adopt the new product and/or procedure compelling evidence is needed supporting the benefits of the product and/or procedure (Evidence Based Medicine). Publications in peer reviewed journals, podium presentations, poster presentations, white papers, and more are needed to disseminate information about the product or procedure to the medical/surgical community. The greater the gap between the new product and conventional treatment, the greater the adoption challenge.

Training is required to ensure the new procedure is properly performed and the new product is correctly used. Depending on the product and procedure, the training requirements will differ significantly. If proper training is not provided, good clinical outcomes will be reduced, and a great procedure or product may fall into disfavor.

Finally, a system must be in place to monitor the clinical outcomes of the new product and/or procedure. The data collected must be used to continuously improve the product, procedure and advance the standard of care.



## Captive Wolves in Research

Peggy Callahan

### ABSTRACT

Dr. Dave Mech got his Ph.D. studying wolves of MN and Isle Royale, and made the world aware of the wolf in a new way through his publication of his book in 1970. What became clear to he and his colleagues is that there were questions that were unanswerable through free-ranging settings. Biology and politics allowed for the establishment of a captive colony of depredating wolves which lead to decades of controlled studies. These studies were initially to learn the basics about wolves-behavior, physiology, endocrinology, reproductive cycles etc. The studies transitioned to using captive wolves as test animals for questions ranging from BMP's for anesthesia to examining solutions for lowered reproductive success in Mexican gray wolves as a result of suffering a population bottleneck of 7 wolves in 1979. Within this context, abdominal heart rate/body temperature transmitters were inserted with sub-cutaneous leads that bracket the heart, in an attempt to pin point ovulation in wolves. Also different types of reversible forms of contraception have been tested both on female and males. In addition, captive wolves have been used to test a series of non lethal deterrents in hopes of 'teaching' wild wolves to avoid livestock, pets and other food sources. A complex apex predator like the wolf is highly adaptable, and provides a context for constant learning as they respond to a changing natural system in the western Great Lakes.



# Certifications & Attendees

30  
YEARS



# Certifications

## SRA

Jon Ehrmann  
Eric Flounders  
Tricia Galassi  
Janelle E. Gesaman  
Benjamin Gesaman  
Mary Ellen Goldberg  
Antoinette JG Guerra  
Rena D. Hall  
Jillian M. Horvath  
Erin Jeannotte  
Sarah A. Johnson  
Andrea Knipe  
Anne Kuszpit  
Mark LaBar  
Maureen Lamkin  
Angela Lewis  
April Lindon  
Terri L. Lucas  
Brian S. MacDougall  
Julie Maurer  
Colleen McGilton  
Michele M. Nichols

Porsha Osborne  
Stephanie Pacheco  
Mary Jane Perkins  
Justin L. Prater  
Kristin Reibling  
Karen Richmond-Mato  
Holly Sekellick  
Julie Sentz  
Lateya Smith  
Danielle Stephens  
Lindsay L. Tawoda  
Stephanie L. Werrlein  
Nathaniel Wheat  
Amy Jo Williams  
Amanda Wilsey

## SRT

Sheila M. Alonzo  
Holly Barber  
Carole Blaser  
Amanda L. Botta  
Leeta Brott  
Andrew Carlson  
Nikki Gattuccio  
Loise Gichuru  
Hannah Grothues  
Janet L. Herrada  
Eric Herrmann  
Kerry D. Hoffman  
Joanne C. Kuziw  
Mark LaBar  
Maureen Lamkin  
Brianna Marie LaViolette  
Patricia C. Mead  
Porsha Osborne  
Jed Pugsley  
Vicki Sekiguchi  
Michael D. Sheets  
Jay Simmons  
Nichole L. Stewart  
Lindsay L. Tawoda  
Tom Tlusty  
Monica Torres



## SRS

Eric L. Adams  
Antoinette K. Alderfer  
Daniel S. Allen  
Margi K. Baldwin  
Scott Barnhill  
Kimberly Bayer  
Corinna Beale  
Mark Beckel  
Stephen Bell  
Oscar A. Bermeo Blanco  
Renee Bodinizzo  
Heather Bogie  
Ashleigh Bone  
Deborah Braatz  
Mike Bravo  
Carol L. Burns  
John D. Carey  
Elizabeth Carter  
Jefferson K. Childs  
Holly Coleman  
Teresa Cunio  
Grace M. Daly  
Amy Davidson  
Sean Davis  
James A. Destefano  
Jennifer J. DeVries  
Deborah Dimke  
Stacey A. Drinen  
William P. Dyckman  
Timothy R. Edwards  
Jon Ehrmann  
Amy J. Evans  
Debra C. Ferguson  
Zoran Filipovic  
Darcy Gagne  
Nikki Gattuccio  
Janelle E. Gesaman  
Laura Gigliello  
Teresa Gleason

Christina Gross  
Hyking Haley  
Whitney Hartz  
James C. Hausamann  
Darla L. Jacob  
Dana Jansen  
Nina Jochnowitz  
Lisa Johnson  
Wendy Sue Johnson  
Yayoi Kimura  
Ken Kirk  
Erlinda L. Kirkman  
Lindsey Kist  
Connie M. Kliwinski  
George E. Kopchok  
Angela Kruse  
Nina Krutrök  
Alison Kulick  
Mark LaBar  
Andree Lapierre  
Michelle Lewis  
Marsha Loll  
Stacy J. Ly  
Morag Mackay  
James McCabe  
Julia L. McLane  
Elda Mendoza  
Benigno Benjamin Mills  
David Moddrelle  
Tamara Montgomery  
Gail Moore  
Mary E. Mootoo  
Nance Moran  
Jose Negron-Garcia  
Mary Jo Numerick  
Jason S. Ogle  
Devra J. Olson  
Maria L. Pedersen  
Ioan Petrescu

Randy Pielemeier  
Liane Pinkos  
Stacy L. Porvasnik  
Diane J. Posavec  
Cordelia G. Rasa  
Samir Reda  
Randall P. Reed  
Heather Rentschler  
John Resendez  
Tracie Rindfield  
Robert F. Roache  
Sheila J. Russell  
Mandy N. Sexton  
Jennifer Sheehan  
Allan Shuros  
Julianne Siegel  
Nichole L. Stewart  
Leslie Stoll  
Kathleen Stollberg  
Kimberly M. Swearingen  
Jenifer Sweet  
Lindsay L. Tawoda  
Joseph Terrazzano  
John P. Tessmer  
Amy S. Townsend  
Tu Trinh  
Marlo Volberg  
Carol S. Wally  
Makki Jo Walton  
Kimberly A. Wasko  
Alissa Welling  
Dennis Werner  
Kathy White  
L. Alexandra Wickham  
Amy Jo Williams  
Amanda Wilsey  
Marla Wilwol  
Angela Zeoli  
Tracy Ziegelhofer

# Attendees

Eric L. Adams, Northern Biomedical Research  
Pilar Ariza Guzman, University of Minnesota  
Neil Bailey, SNBL USA Ltd  
Wendy L. Baker, WIL Research  
Margi K. Baldwin, University of South Florida  
Kate Banks, University of Toronto  
Szczezan Baran, Veterinary Bioscience Institute  
Jessica N. Barnhart, American Preclinical Services  
Jolee Bartrom, NAMSA  
Bernhard Baumgartner, Baxter Healthcare Corp  
Kim Bayer, DaVinci Biomedical Research Products  
Ham Benghuzzi, University of MS Medical Center  
Jim Berry, University of MN Medical Center  
Tina Blair, RTI Surgical  
Heather Bogie, Data Sciences International  
Amanda L. Botta, CBSET, Inc.  
Ludovic Boure, Covidien  
Jay Budrewicz, CBSET  
Norleen Caddy, DRDC Suffield Canada  
Christina Callanta, Fine Science Tools  
Andrew Carlson, Northern Biomedical Research  
Heath Carter, St. Jude Medical - AFD  
Dolores Cejalvo, Universidad Catolica de Valencia  
Richard Craven, ISIS Services, LLC  
Mike Dalton, Access Technologies  
Grace M. Daly, W.L. Gore & Associates Inc.  
Sean Davis, Amgen, Inc.  
Arlene de Castro, Bristol Myers Squibb  
Heather B. DeLoid, Wake Forest Innovations  
Steve Denault, SAI Infusion Technologies  
Jennifer J. DeVries, MPI Research  
Michele Diana, IHU-Strasbourg  
Stacey A. Drinen, Washington University - St Louis  
Heidi Dulac, Bristol-Myers Squibb  
Kevin Dunwoody, Medline Industries, Inc.  
Edward Dy, Fine Science Tools  
Tim R. Edwards, WIL Research  
Jon Ehrmann, Bristol-Myers Squibb Company  
Megan E. Fine, Data Sciences International  
Penny Fitzmiller, Kent Scientific Corporation  
David FitzMiller, Kent Scientific Corporation  
Susan Fleming, Colonial Medical Supply Company

Laraine Fleming, RTI Surgical  
Darcy Gagne, Davol (C.R. Bard, Inc)  
Tricia Galassi, MED Institute, Inc  
Jorge L. Garcia, ISIS Services LLC  
Jeremy Gatesman, University of Virginia  
Janelle E. Gesaman, MPI Research  
Teresa Gleason, WIL Research  
James Goodrich, Yale University  
Melanie Graham, University of Minnesota  
Cheryl Griesse, Medtronic, Inc  
Tina Gross, American Preclinical Services  
Brian Hanks, Sinclair Research Center  
Jacob Hartman-Kenzler, ISIS Services LLC  
Janet L. Herrada, WIL Research  
Kimberly Holliday-White, Data Sciences International  
Xuening Hong, Merck  
Jennifer Hovland, Lovelace Respiratory Research Inst  
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The Academy of Surgical Research Educational Foundation is a 501 (c) (3) nonprofit organization supporting the education of preclinical experimental surgical candidates.

## What is the mission of the ASR Educational Foundation?

The mission is to provide opportunity through financial support in order to encourage the education and certification of individuals within the preclinical research community.

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