

32nd Annual Meeting of the

Academy of Surgical Research

32
YEARS

September 29 - October 1, 2016

New Orleans, Louisiana
Hotel Monteleone

“Surgical Models; Supporting the Research and Embracing the Three R’s”

The **32nd Annual Academy of Surgical Research 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:

- o Interventional Radiology
- o Imaging Modalities
- o Organ Transplantation
- o Round Table on Chronic Access for Biological Samples
- o Telemetry in Small & Large Animals
- o Surgical and Medical Devices
- o Tissue Bioengineering
- o Refinements to Routine Models
- o Surgical Writing
- o Pain Management
- o Various Surgical and Anesthetic Techniques and Models

Meeting attendees will have the opportunity to network with speakers and presenters, colleagues and friends. This meeting will offer diverse scientific content that will promote and encourage the advancement of the field of surgery.



Academy of Surgical Research

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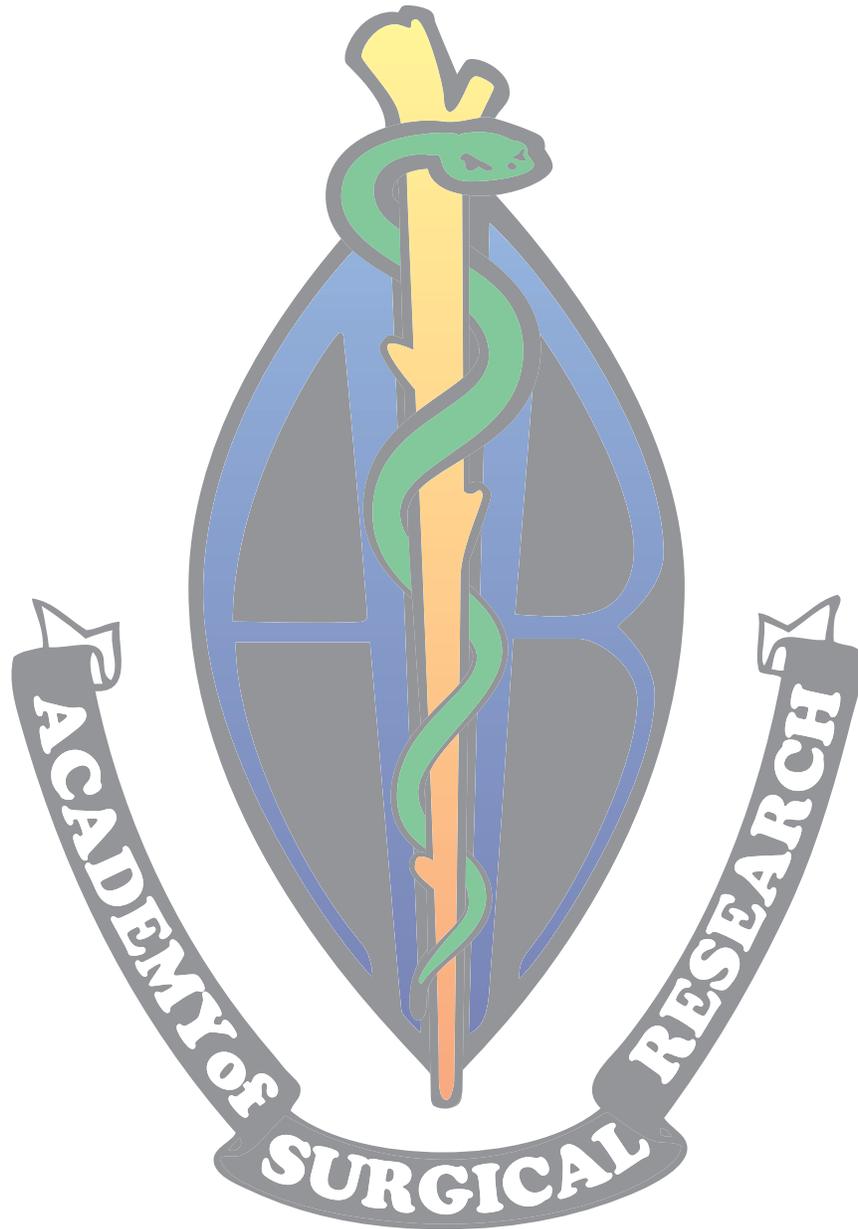
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Welcome

Welcome to NOLA! I am honored to welcome you to the French Quarter in New Orleans, Louisiana, one of my favorite locations in the United States, for the 32nd Annual Academy of Surgical Research Meeting. It seems like only yesterday I was awed by attending my first meeting, the 13th annual meeting, in San Antonio, Texas. The Academy has come a long way since then, as have I, and I am proud to be involved with this organization.

The Program Committee has done a tremendous job putting together a remarkable program for you this year. I would like to acknowledge and thank the Program Committee and especially the Program Chair, Jon Ehrmann. He has put in a lot of hard work to put this program together for all of us. I also want to thank all of the volunteer committee members for their continued efforts in making the Academy a success. I would encourage each of you to find a committee you would like to get involved with and sign up. We are always looking for new committee members. Your ideas do matter, and we use them to help form the basis of the next year's meeting, especially the wet labs.

The Academy is founded on sharing our ideas and experiences, not just our successes but our failures as well. It is in this way that we learn from each other. If this is your first meeting, please take advantage of the opportunity to network and brainstorm with your peers. You won't find a better opportunity to do this. I assure you we are all approachable and will be happy to chat with you. If we can't answer your question, we'll most likely know somebody who can. If you're a seasoned attendee, please introduce yourself to a new member and make them feel welcomed.

You may have had a chance to visit the exhibitor booths last night at the reception. Please be sure to visit them throughout the day today. We have a good line up of vendors this year, and you won't find a better opportunity to ask them questions about their products. I want to personally thank all of our Sponsors and Exhibitors for their support, without which we would not be able to put on such a successful meeting year after year.

This year the Board of Directors created a new scholarship, The Ken MacLeod Memorial Scholarship, as an off-shoot of the ASR Foundation. This scholarship is named for and honors a longtime supporter, and friend, of the Academy, who we lost a few years ago to esophageal cancer. Ken was a huge supporter of our certification program and this scholarship is directed towards applicants who need assistance with funding to take one of the certification exams.

I am honored to have served as your President this year and hope you enjoy the program we have put together for you.

Lisa Johnson





Lisa Johnson, BA, SRS, RLATg

Study Director

Lisa is currently a Study Director in the Efficacy and Surgical Research Services Department at Toxikon Corporation, a contract research organization outside of Boston, Massachusetts. Lisa has over twenty years of experience in preclinical and surgical research, having worked previously at Pfizer/Wyeth Pharmaceuticals and Primedica Research (which was purchased by Charles River). She is certified as a Surgical Research Specialist (obtained in 1997) by the Academy. Lisa has been active in the Academy since 2005 (member of the Certification Committee, served on the Board of Directors as a Director at Large, and Certification Committee Chair, prior to be elected as Liaison Officer in 2013) and was a recipient of the Michael DeLeo award in 2010. Lisa has presented at regional and national AALAS meetings as well as at annual ASR meetings.

Welcome

Welcome to the Big Easy for the 32nd Annual Meeting of the Academy of Surgical Research! It has been a pleasure to coordinate and develop all the moving parts that will make this meeting a great experience!

This year's theme, "**Surgical Models; Supporting the Research and Embracing the Three R's**", embodies what we do as research surgeons and anesthesiologists on an everyday basis. It also represents the mission of the Academy, to promote humane use and treatment of experimental animals and prevent the use of animals when other means can bring about the same scientific results and to encourage the advancement and refinement of the field of surgery in all aspects, including research, education, and critical promotion of research products for clinical applications.

In my eyes, a true surgeon will continuously innovate and challenge the status quo of any surgical procedure no matter how routine or trivial it has become to the individual. The animals we work with and care for on a daily basis rely on us to continuously Refine, Replace and Reduce all aspects of surgical research.

Over the next few days, you will have multiple opportunities to learn and apply innovative techniques to refine procedures at your institution through wet labs, dry labs, presentations, posters and networking.

We have four exceptional keynote speakers and 21 general session presenters. Combine this with 14 posters, 4 wet labs and 3 dry labs it adds up to a very exciting and eventful meeting!

The program content is exceptional this year covering a myriad of topics from anesthesia to new surgical models. In addition to all of the informative sessions, we also have numerous exhibitors. The exhibitors are a major component of our meeting and we would not be able to offer all that we do without their support. Be sure to stop by and visit each and every one of them and thank them for supporting the Academy.

I would also like to thank the vendors and our generous corporate sponsors for supporting this year's meeting and helping to make it a success. Your presence and generosity is greatly appreciated!

A meeting such as this is not planned alone. There are many people who have donated their time and energy to develop and implement this meeting. I would like to personally thank the members of the Program Committee, Tracy Ziegelhoffer, Heather Bogie, Jennifer Sheehan, Lisa Johnson, Susan Fleming, Leslie Stoll, Scott Stoll, Tim Edwards and Margi Baldwin for their time and effort in constructing this exceptional meeting!

I sincerely hope you enjoy your time invested in the conference, learn some cool tips, tricks and innovations and meet new friends to further advance your personal growth in surgical research. Once again, welcome!

Jon Ehrmann

2016 Program Chair





CHAIR

Jon Ehrmann BS, SRS, SRA, LATG

Technical Operations Manager, Bristol Myers Squibb
 Department of Veterinary Sciences
 Veterinary Care and Research Support

Jon Ehrmann is the Technical Operations manager for the Veterinary Care and Research Group at Bristol Myers Squibb (BMS). He manages a specialized group within BMS providing surgical models and advanced study support to multiple therapeutic areas across several BMS sites. Additionally, his group supports the clinical research programs for the central New Jersey BMS facilities.

Jon has over 17 years of experience in preclinical and surgical research with a focus on cardiovascular, neurological and vascular surgery.

He is certified by ASR as a Surgical Research Specialist and a Surgical Research Anesthetist, having received the Barry Sauer Award for each certification exam. Jon joined ASR in 2004 and has served on the certification committee for 6 years.

Jon has served on the Board of Directors since 2013 and is currently the Program Chair and President-Elect for 2016.

He has coauthored several peer reviewed publications and is a frequent presenter at national conferences.

Jon earned a Bachelor's of Science degree in Zoology from Michigan State University.

Program Committee

Heather Bogie, CVT, SRS, RLATG
 Data Sciences International (DSI)

Susan Fleming
 Colonial Medical Supply

Tracy Ziegelhoffer, BS, SRS, LATG
 Envigo

Margi Baldwin, MS, SRS, LATG, RVT
 University of South Florida

Leslie J. Stoll, SRS, LATG, LVT, AS
 Charles River Laboratories

Tim Edwards, BS, SRS, RLATG
 Charles River Laboratories

Jennifer Sheehan, BS, SRS, LATG
 Envigo

Scott Stoll, Pre-Press Technician
 Fort Dearborn Inc.

Lisa Johnson, BA, SRS, RLATG
 Toxikon

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ASSOCIATION
MANAGER

Jim Manke, CAE

Association Solutions, Inc. (ASI)

Jim Manke is owner and founder of Association Solutions, Inc. (ASI) since 1998. ASI is headquartered in Minneapolis and has a client portfolio of seven associations. Jim started in the association business in 1977. He served for 14 years as Executive Director of the Minnesota Association of REALTORS, a 12,000 member association.

In 1996 he was selected by the National Association of REALTOR, the largest trade association in the country, to serve as their Chairman of the Executive Officers Committee. That role led him to working with numerous REALTOR associations around the country on developing strategic plans to boost their value propositions to the membership. It eventually culminated in his working with the startup of the Russian REALTORS Guild to introduce free market thinking and processes into their members' business operations.

Back in 2002, Association Solutions Inc., became the management arm of the Academy of Surgical Research.

SENIOR ACCOUNT
MANAGER

Kathi Schlieff

Association Solutions, Inc. (ASI)

Kathi serves as senior account manager at ASI. She has supported ASR since 2004. She is responsible for all aspects of the Annual Meeting, the Certification Program and responding to membership questions.

Prior to that she worked 15 years with the Minnesota Independent Insurance Agents and Brokers Association as their Director of Education.

In that role, Kathi was responsible for all aspects of the CIC certification Program. During her tenure, the CIC program achieved an all time high in participation and profitability.

Jim and Kathi are married and have five daughters.



S P E A K E R

Dennis Burkett, VMD, PhD, DACVECC, DACVIM (Cardiology)

Hospital Executive Director,
Hope Veterinary Specialists

Dr. Dennis Burkett, a native of Philadelphia, Pennsylvania, is a 1984 graduate of the University of Pennsylvania School of Veterinary Medicine. He obtained both MS (1980) and PhD (1986) degrees in Physiology and Biophysics from Hahnemann University in Philadelphia and completed a residency in Internal Medicine (with a concentration in emergency and critical care medicine) at the University of Pennsylvania School of Veterinary Medicine in 1987. Dr. Burkett received professional certification as a Diplomate in the American College of Veterinary Emergency and Critical Care in September 1993.

In 2002, Dr. Burkett returned to academia and, in 2005, completed a residency in cardiology at both Red Bank Veterinary Hospital in New Jersey and the Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania. He received professional certification as a Diplomate in the American College of Veterinary Internal Medicine in the subspecialty of cardiology in 2007.

He is a past president of the Veterinary Emergency and Critical Care Society and a past president of the American College of Veterinary Emergency and Critical Care. He is a well-known lecturer and scientific reviewer for many professional publications including the Journal of Veterinary Emergency and Critical Care.

For many years, Dr. Burkett has worked in the pharmaceutical industry in cardiovascular research; he therefore has a special interest and knowledgeable background in cardiopulmonary emergencies. His special interests are cardiology, interventional cardiology, emergency medicine and surgery, and critical care medicine.

In founding the Animal Critical Care and Specialty Group, now Hope Veterinary Specialists, Dr. Burkett laid the foundation for exceptional emergency and critical care services for referring veterinarians in the greater Philadelphia region.



S P E A K E R

James Cook, DVM, PhD, OTSC

Diplomate, American College of Veterinary Surgeons / American College of Veterinary Sports Medicine & Rehabilitation / William & Kathryn Allen Distinguished Professor in Orthopaedic Surgery Director, Thompson Laboratory for Regenerative Orthopaedics, Orthopaedic Research Division & Mizzou BioJoint Center, University of Missouri, Missouri Orthopaedic Institute

Recipient of the 2016 Jacob Markowitz Award

After receiving his B.S. degree from Florida State University and competing for 5 years as a professional waterskier, Dr. James (Jimi) Cook completed his DVM in 1994 and PhD in 1998. In 1999, he founded the Comparative Orthopaedic Laboratory at the University of Missouri, a multi-disciplinary team of physicians, veterinarians, engineers, and basic scientists dedicated to translational orthopaedic research. He has over 180 peer-reviewed publications, over \$20 million in research funding, received numerous awards including America's Best Veterinarian (2007), holds 14 US Patents and has seen 3 biomedical devices through FDA approval to human clinical trials. He is currently Director of the Mizzou BioJoint Center, Director of The Comparative Orthopaedic Laboratory and the William and Kathryn Allen Distinguished Professor in Orthopaedic Surgery, and serves as Director of the Division of Research for the Department of Orthopaedics at the University Hospital's Missouri Orthopaedic Institute. He is also co-founder of Be The Change Volunteers a NGO dedicated to building schools in remote villages in the developing world whose teams have built 32 educational facilities in 15 countries, providing educational opportunities to more than 6,000 students.



Dr. David G. Baker, DVM, PhD, MPA, DAACLAM

Professor of Laboratory Animal Medicine
Director, Division of Laboratory Animal Medicine
School of Veterinary Medicine, Louisiana State University

Dr. David G. Baker is Professor of Laboratory Animal Medicine, Director of the Division of Laboratory Animal Medicine, Attending Veterinarian for LSU, and personal veterinarian for LSU's live tiger mascot, "Mike" the Tiger. He earned his B.S. (Zoology), M.S. (Comparative Pathology), Ph.D. (Comparative Pathology/Parasitology), and D.V.M. from the University of California, Davis. He joined the faculty at LSU in 1995. He earned the Master of Public Administration (M.P.A.) degree from LSU's E.J. Ourso College of Business. Dr. Baker teaches in 11 courses in the LSU School of Veterinary Medicine, covering topics such as laboratory animal medicine, parasitology, personal finance and business management, leadership, and veterinary medical ethics. He also teaches workshops at national meetings and consults with other universities regarding development of cost accounting and analysis systems for laboratory animal facilities. He has authored, coauthored, or edited 54 peer reviewed journal articles, 57 scientific presentations, 19 book chapters, and 5 books. Dr. Baker serves as faculty sponsor for three veterinary student organizations, including the LSU Student Chapter of the American Society of Laboratory Animal Practitioners, the School of Veterinary Medicine Student Bookstore, and the LSU Chapter of Christian Veterinary Fellowship.



Cathy Willis Spraez

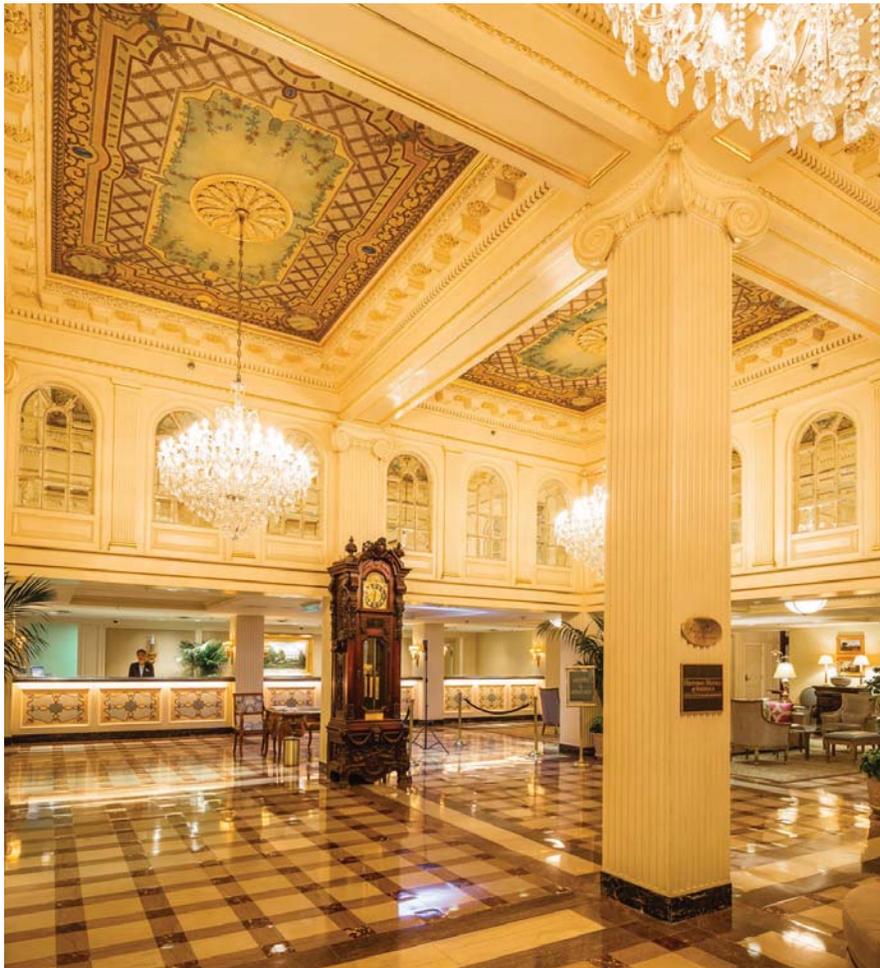
President and Chief Executive Officer CHIMP HAVEN

Prior to joining Chimp Haven in 2013, Cathy, an Atlanta native, served several nonprofit organizations in Georgia, focusing primarily in the area of disabilities and domestic violence. She has more than 30 years of experience as a chief executive and with that brings extensive expertise in administration, fiscal accountability, staff and program development, and fundraising.

Cathy serves on the NAPSA (North American Primate Sanctuary Alliance) Steering Committee and is an avid animal lover. She finds it a special privilege to be leading Chimp Haven and values the ongoing opportunity to learn more about our magnificent relative, the chimpanzee, while working to ensure they have a forever home in sanctuary. She has gained significant knowledge and insight into the overall management of chimpanzees and the history of these amazing animals in captivity and is often asked to speak on these topics.

She earned a bachelor's degree in Urban Studies with a concentration in Nonprofit Administration from Georgia State University. She is a scholarship recipient of the 2005 Harvard Business School's Strategic Initiatives in Nonprofit Management.

Venue



Floor Plan

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 FRENCH QUARTER, RIVERSIDE, VEUX CARRE ROOM, TERRACE OVERLOOKING 14TH FLOOR POOL, ELEVATOR

MEZZANINE
 SERVING AREA, PERMANENT STAGE, LA NOUVELLE ORLEANS EAST, CORRIDOR, LA NOUVELLE ORLEANS WEST, MEN, LADIES, BIRVILLE ROOM, BEVILLE ROOM, BUSINESS CENTER, FRENCH MARKET ROOM

MEZZANINE
 QUEEN ANNE BALLROOM, PANTRY, CORRIDOR, QUEEN ANNE PARLOR, MEN, REGISTRATION LOBBY, LADIES, BONNET CARRE ROOM, ORLEANS ROOM

MEZZANINE
 GALLIER SALON, BEAUREGARD SALON, PONTALBA SALON, URSULINES SALON, THE BOARD ROOM, PRESBYTERE SALON, CATHEDRAL SALON, CABLDO SALON, GABRIEL ROOM, GUEST ROOMS, GUEST ROOMS, GUEST ROOMS, GUEST ROOMS

GROUND FLOOR
 Parking Garage, LOBBY, CRIOLLO RESTAURANT, CAROUSEL BAR & LOUNGE, ROYALS SALON(S), E D C I S A, ELEVATORS, LOBBY GIFT SHOP, POWER, MEN, WOMEN, ELEVATOR

CONVENTION FACILITIES
 24,000 square feet of meeting space | 24 ballroom, meeting and reception rooms | Largest at 6,236 square feet accommodating up to 500

Meeting Overview

Registration Hours	
Thursday, September 29	07:00 am – 05:00 pm
Friday, September 30	07:00 am – 05:00 pm
Saturday, October 1	07:00 am – 12:00 pm
Wednesday, September 28	
02:00 – 05:00 PM	ASR Board Meeting
Thursday, September 29	
07:00 AM – 08:00 AM	Registration for test takers and wet lab attendees
07:00 AM – 08:00 AM	Light continental breakfast for test takers
07:30 AM	Vans depart from hotel to Wet Labs at LSU Health
08:00 AM - 12:00 PM	ASR Examinations – Royal Salon D
08:00 AM – 12:00 PM	Wet Labs DSI – Microsurgical Telemetry Implantation Techniques Rabbit Thoracotomy (Morning session)
08:00 AM – 04:00 PM	Wet Labs - Swine Kidney Autograft
08:00 AM - 12:00 PM	Web Labs - Rat Stroke Model
01:00 - 04:00 PM	Wet Labs - Rabbit Thoracotomy (Afternoon session)
12:15 PM	Vans depart from Hotel to LSU
01:00 PM	Vans depart from LSU to Hotel - Morning Labs
04:00 PM	Vans depart from Hotel to LSU - Afternoon Labs
04:00 PM – 07:00 PM	Welcome Reception with Exhibitors
Friday, September 30	
08:00 AM – 09:00 AM	Continental Breakfast w/ Exhibitors Poster Set up - Queen Anne Parlor / Bonnet Carre
09:00 AM	Opening Remarks
09:00 - 10:00 AM	Keynote Speaker
10:00 AM - 10:30 AM	Break with Exhibitors
10:30 AM - 12:00 PM	Track 1 and 2 Scientific Sessions
11:00 PM – 12:00 PM	Suture Dry Lab Morning Session - Royal Salon D
12:00 PM – 01:00 PM	Lunch With Exhibitors
01:00 PM - 02:00PM	Keynote Speaker
02:00 PM – 04:30 PM	Track 1 and 2 Scientific Sessions
02:00 PM – 03:00 PM	Catheter Use & Maintenance Dry Lab - Royal Salon D
03:00 PM – 03:30 PM	Break with Exhibitors
03:30 PM - 04:30 PM	Suture Dry Lab Afternoon Session - Royal Salon D
04:30 PM – 05:30 PM	Poster Judging
05:30 PM - 07:00 PM	Friday Night Reception & Foundation Auction
Saturday, October 1	
08:00 AM – 09:00 AM	Continental Breakfast w/ Exhibitors
09:00 AM – 09:15 AM	Opening Remarks
09:15 AM – 10:15 AM	Keynote Speaker
10:15 AM - 10:30 AM	Break
10:30 AM – 12:00 PM	Track 1 and 2 Scientific Sessions
10:30 PM – 12:00 PM	Surgical Writing Workshop - Royal Salon D
12:00 PM - 02:00 PM	Business Lunch/ASR Awards Presentations w/Keynote Speaker
02:00 PM – 03:00 PM	Track 1 and 2 Scientific Sessions
03:00 PM	Adjourn
03:00 PM - 05:00 PM	Board of Directors Meeting

Lab Descriptions

Wet Lab Instructors

Ludmila Belayev, MD

Larissa Khoutorova, BS

LSU Health Sciences Center

Heather Bogie, SRS, RLATG, CVT

Kathryn Nichols, MS, SRS

Data Sciences International (DSI)

Vince Mendenhall, PhD, DVM

Consultant in Preclinical Surgery

Wendy Johnson BS, SRS, LVT, RLATG

Jon Ehrmann BS, SRS, SRA, LATG

Bristol-Meyers Squibb

Dry Lab Volunteers

Candace Rhode-Johnson

SAI

Jan Bernal, DVM

Pfizer

Leslie Stoll, SRS, LATG, LVT, AS

Charles River Laboratories

Dr. Marc Basson, MD, PhD, MBA

University of North Dakota

Wet Lab Volunteers

Margi Baldwin, MS, SRS, LATG, RVT

Karen Brocklehurst, SRA, LATG, CMAR

Jane Perkins, SRT, SRA, BS, LATG

University of South Florida

Jan Bernal, DVM

Steven Kreuser, SRA

Pfizer

Thank you to LSU Health Sciences Center for hosting our wet labs and all of your support!



Wet Labs

Louisiana State University (LSU)

Thursday, September 29, 2016

8:00 a.m. - 12:00 p.m. (Lunch will be provided)

Microsurgical Telemetry Implantation Techniques: Recording Continuous Blood Glucose in Rodents

Heather Bogie, BS, SRS, RLATG, CVT, Kathryn Nichols, Data Sciences International (DSI)

Telemetry has become the gold standard of physiologic monitoring due to its ability to monitor numerous physiological 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 biological research including disease model development, drug discovery, and safety assessment. The telemetry device highlighted in this workshop creates exciting research opportunities by continuously monitoring blood glucose in rodents. 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.

8:00 a.m. - 4:00 p.m. (Lunch will be provided)

Anesthesia and Surgical Techniques for Kidney Autograft in Pig

Vince Mendenhall, PhD, DVM, Consultant in Preclinical Surgery

Participants will learn the anesthesia and surgical techniques necessary to study the effects of preservation solutions on kidneys for use in transplantation. The techniques involve nephrectomy, preservation and re-implantation as an autograft. There will be three students per animal to practice the nephrectomy and re-implantation.

8:00 a.m. - 12:00 p.m. (Lunch will be provided)

Experimental Stroke Model in Rats

Ludmila Belayev, MD, Larissa Khoutorova, BS, LSU Health Sciences Center

During your time in the lab, lab members will teach you basic protocols that you will need to know in order to run stroke experiments in rats. We will provide you a basic knowledge of general anesthesia, physiological monitoring of rats during and after surgery (body and cranial temperature, blood gases, glucose, hematocrit). We will demonstrate a surgical procedure for experimental stroke (middle cerebral artery occlusion), behavioral testing and perfusion of animals with brain removal for histopathology

08:00 a.m. - 12:00 p.m. (Morning Session, Lunch will be provided)

1:00 p.m. - 04:00 p.m. (Afternoon Session)

Thoracotomy in the Rabbit

Wendy Johnson BS, SRS, LVT, RLATG, Jon Ehrmann BS, SRS, SRA, LATG - Bristol-Meyers Squibb

This lab will demonstrate thoracic access in the rabbit via a lateral thoracotomy. A step by step procedure for performing the thoracotomy will be demonstrated by an experienced SRS surgeon. Attendees will then have the opportunity to work individually, under the guidance of experienced surgeons. Once thoracic access has been achieved the student will have the opportunity to learn common thoracic procedures such as proper handling and packing off of lung lobes, excising the pericardium, cardiovascular suturing techniques, placement of epicardial leads, placement of a left ventricular pressure transducer and/or other techniques specific to the student's interest. Additionally, anesthesia protocols and techniques will be taught including pre-operative sedation, endoscope guided intubation, ventilation, blood gas evaluations and intravenous access.

Dry Lab Opportunities



Proper Technique for Accessing, Flushing and Locking Catheters and Implanted Devices
Candace Rhode-Johnson, SAI
Friday, September 30th, Time 2:00 – 3:00 pm
Maximum # of participants: 10, Cost: Free

One of the most overlooked aspects of catheter success comes after the surgery is complete. Proper technique in accessing the implanted device, as well as appropriate routines for flushing and locking are essential to the ongoing success of any catheter. In this workshop, we will focus on the post-surgical care of your catheter including discussion on locking solutions, recommended frequency of flushing, aseptic technique for accessing the catheter, and troubleshooting. In addition to the discussion, participants will have the opportunity to practice proper cleaning, flushing and locking procedures for both the catheter and for the vascular access harness using realistic rodent models. Participants will be introduced to several types of access devices, including harnesses, buttons, and VAPs and will understand the benefits and limitations of each. This session is ideal for anybody who is new to catheter implantation and maintenance, but can also serve as a great refresher and forum for discussion on the best techniques and new products that aid in catheter care and longevity.



Still Suturing with the "Oldies"
Jan Bernal, Pfizer and Leslie Stoll, CRL
Friday, September 30th
Time 11:00 AM – 12:00 PM & 3:30 PM - 4:30 PM
Maximum # of Participants: 10, Cost: Free

The objective of this dry lab is to provide an opportunity to learn and improve one's suturing skills. Using a skin simulator, participants practice various suturing techniques, including simple and straight lacerations, deep-layer closure, skin closures, and tying knots using hand and instrument ties. The dry lab offers a variety of common procedures performed in the primary care setting. Didactic information as well as a hands-on component will be available. This dry lab is geared toward those wishing to refresh their suturing skill, as well as those interested in practicing advanced suturing techniques under professional direction and guidance.



Surgical Writing-From Protocol Development, Conception of the Research Hypothesis, Data Collection, Manuscript Preparation through Publication.
Dr. Marc Basson, University of North Dakota
Saturday, October 1st, Time 10:30 AM – 12:00 PM, Cost: Free

An interactive workshop on surgical writing with the new Editor-in-Chief of the Journal of Investigative Surgery. The session will include an overview of the process from hypothesis and experimental design through manuscript writing and submission and handling peer review and interaction with journals. The most common reasons for rejection of manuscripts will be discussed. In addition to a Q&A session, there will be an opportunity to participate in guided peer review of your own manuscript or someone else's manuscript.

Wet Lab Sponsors


charles river

DSITM



Program Schedule

Wednesday, September 28th

02:00 –5:00 PM	ASR Board of Directors Meeting – Vieux Carre Room
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Thursday, September 29th

07:00 AM - 08:00 AM	Registration for Test Takers - Main Lobby Lite Continental Breakfast for Test Takers - Royal Salon D
07:00 AM - 7:30 AM	Registration for Wet Lab Participants - Main Lobby
07:30 AM	Vans Depart from Hotel to LSU - Main Lobby
08:00 AM - 12:00 PM	Certification Exams - Royal Salon D
08:00 AM - 04:00 PM	Wet Labs - LSU Health Sciences - Lunch Sponsored by Dr. Vince Mendenhall
04:00 PM - 07:00 PM	Welcome Reception with Exhibitors - Sponsored by Colonial Medical Supply East and West La Nouvelle Orleans Ballrooms



Friday, September 30th

08:00 – 09:00 AM	Continental Breakfast – Sponsored by Kent Scientific Corporation East and West La Nouvelle Orleans Ballrooms	
08:00 – 09:00 AM	Poster Setup – Queen Anne Parlor/Bonnet Carre	
09:00 AM	Opening Remarks – ASR President Lisa Johnson - Queen Anne Ballroom	
09:00 - 10:00 AM	Keynote – Dr. Dennis Burkett - Interventional Radiology - Queen Anne Ballroom	
TRACK 1 – Queen Anne Ballroom		
10:00– 10:30 AM	Break with Exhibitors – Sponsored by DRE Scientific East and West La Nouvelle Orleans Ballrooms	
MODERATOR	Melanie Graham	
10:30 - 11:00 AM	Dorsal Laminectomy and Durotomy Sheep Model	Darcy Gagne
11:00 - 11:30 AM	Establishment and Utility of Antithrombotic Efficacy and Bleeding Liability De-Risking Models in Cynomolgus Macaques	Alexandra Wickham
11:30 - 12:00 PM	Development of a Swine Model of Behind Helmet Blunt Trauma	Michael Horsmon
12:00 – 01:00 PM	Lunch with Exhibitors – East and West La Nouvelle Orleans Ballrooms	
01:00 – 02:00 PM	Keynote – Ms. Cathy Willis Spraetz - Chimp Haven: The National Chimpanzee Sanctuary Queen Anne Ballroom	
MODERATOR	Steve Kreuser	
02:00 – 03:00 PM	Round Table - Chronic Access for Sampling Biological Samples - Vascular and Intrathecal Access	Dr. Vince Mendenhall, Jon Ehrmann, Eric Adams, Marlo Volberg
03:00 – 03:30 PM	Break with Exhibitors – Sponsored by Toxikon Corporation East and West La Nouvelle Orleans Ballrooms	
MODERATOR	Steve Kreuser	
03:30 – 04:30 PM	Round Table - Chronic Access for Sampling Biological Samples - Bile and Lymph Access	Dr. Vince Mendenhall, Jon Ehrmann, Eric Adams, Marlo Volberg
04:30 PM - 05:30 PM	Poster Judging – Queen Anne Parlor / Bonnet Carre	
05:30 PM - 07:00 PM	Reception / Foundation Auction – Sponsored by Data Sciences International (DSI) and Lomir Biomedical, Inc. - Riverview Room	

Friday, September 30th

08:00 – 09:00 AM	Continental Breakfast – Sponsored by Kent Scientific Corporation East and West La Nouvelle Orleans Ballrooms	
08:00 – 09:00 AM	Poster Setup – Queen Anne Parlor/Bonnet Carre	
09:00 AM	Opening Remarks – ASR President Lisa Johnson - Queen Anne Ballroom	
09:00 - 10:00 AM	Keynote – Dr. Dennis Burkett - Interventional Radiology - Queen Anne Ballroom	
TRACK 2 – Royal E		
10:00– 10:30 AM	Break with Exhibitors – Sponsored by DRE Scientific East and West La Nouvelle Orleans Ballrooms	
MODERATOR	Michele Danielson	
10:30 - 11:00 AM	Acquisition of Left Ventricular Pressure, Systemic Blood Pressure, Epicardial Electrocardiograms, Core Body Temperature and Activity Utilizing Stellar TSE's Type PPBTA-XL Telemetry Transmitter in the Vervet (Caribbean Green Monkey)	David Moddrelle
11:00 - 11:30 AM	Unique Challenges of Stereotaxic Surgery in Swine	Randy Pielemeier
11:30 - 12:00 PM	Maintenance of a Swine Model with Chronic and Indwelling Catheters for Total Parenteral Nutrition	Samantha Archer and Melissa Card
12:00 – 01:00 PM	Lunch with Exhibitors – East and West La Nouvelle Orleans Ballrooms	
01:00 – 02:00 PM	Keynote – Ms. Cathy Willis Spraetz - Chimp Haven: The National Chimpanzee Sanctuary Queen Anne Ballroom	
MODERATOR	Melanie Graham	
02:00 - 02:30 PM	Development of a Novel Ultrafiltrate Perfusion Device Bioengineered for High Density Islet Cell Transplantation without Immunosuppression	Jody Janecek
02:30 - 03:00 PM	Training Nonhuman Primates for Cooperation with Medical Device Management to Enhance Human Factor Prediction and Usability Evaluations	Lucas Mutch
03:00 – 03:30 PM	Break with Exhibitors – Sponsored by Toxikon Corporation East and West La Nouvelle Orleans Ballrooms	
MODERATOR	Jane Perkins	
03:30 - 04:00 PM	Refinement of a Bile Duct Catheterization Technique in Rabbits	Dr. Delphine Bouard
04:00 - 04:30 PM	Assesment of Murine Colorectal Cancer by Micro-Ultrasound using Three Dimensional (3D) Reconstruction and Non-Linear Contrast Imaging	Jessica Freeling
04:30 PM - 5:30 PM	Poster Judging – Queen Anne Parlor / Bonnet Carre	
05:30 PM - 07:00 PM	Reception / Foundation Auction - Sponsored by Data Sciences International (DSI) and Lomir Biomedical, Inc. - Riverview Room	

Saturday, October 1st

08:00 – 09:00 AM	Continental Breakfast - East La Nouvelle Orleans Ballroom	
09:00 – 09:15 AM	Opening Remarks – ASR President Lisa Johnson - Queen Anne Ballroom	
09:15 - 10:15 AM	Keynote - Dr. James Cook - Experimental Surgery - The Foundation for Improving Delivery of Care - 2016 Markowitz Award Winner - Queen Anne Ballroom	
Track 1 – Queen Anne Ballroom		
10:15 - 10:30 AM	Break – Sponsored by AVA Biomedical, Inc. - Queen Anne Parlor / Bonnet Carre and Pavillion Ballroom	
MODERATOR	Allison Parlapiano	
10:30 - 11:00 AM	Preclinical Evaluation of the Medtronic Hancock Bioprosthetic Valved Conduit for Right Ventricular Outflow Tract Reconstruction in the Pediatric Population	John Carney
11:00 - 11:30 AM	Validation of Heart Failure Model in Mice utilizing an Electrocautery method of Subtotal Nephrectomy	Jan Bernal
11:30 - 12:00 PM	Surgical Techniques for Cesarean Section in the Cynomolgus Macaque	Leslie Stoll
12:00 - 2:00 PM	Business Lunch/ASR Awards Presentations - Sponsored by Bristol-Myers Squibb Keynote - Dr. David Baker "Mike VI: The Tradition Lives On" - Queen Anne Ballroom	
MODERATOR	Allison Parlapiano	
02:00 – 02:30 PM	So What Else Can We Use This Fluoroscope For?	Randy Pielemeier
02:30 – 03:00 PM	Establishing and Maintaining Relationships with Vendors	Steven Kreuser
03:00 – 05:00 PM	Board of Directors Meeting – Royal Salon C	

Saturday, October 1st

08:00 – 09:00 AM	Continental Breakfast - East La Nouvelle Orleans Ballroom	
09:00 – 09:15 AM	Opening Remarks – ASR President Lisa Johnson - Queen Anne Ballroom	
09:15 - 10:15 AM	Keynote - Dr. James Cook - Experimental Surgery - The Foundation for Improving Delivery of Care - 2016 Markowitz Award Winner - Queen Anne Ballroom	
Track 2 – Royal E		
10:15 - 10:30 AM	Break – Sponsored by AVA Biomedical, Inc. - Queen Anne Parlor / Bonnet Carre and Pavillion Ballroom	
MODERATOR	Karen Brocklehurst	
10:30 - 11:00 AM	Development of a Novel Intratibial Implantation Model using Non-invasive In Vivo Imaging for the Evaluation of Antibody-Drug Conjugate Bystander Activity	Devra Olson
11:00 - 11:30 AM	Automated Arterial Blood Sampling in Rhesus Monkey PET Imaging Studies	Liza Gantert
11:30 - 12:00 PM	Evaluation of Rabbit Telemetry Drug Protocol	Evan Pagano
12:00 - 02:00 PM	Business Lunch/ASR Awards Presentations - Sponsored by Bristol-Myers Squibb Keynote - Dr. David Baker "Mike VI: The Tradition Lives On" - Queen Anne Ballroom	
MODERATOR	Karen Brocklehurst	
02:00 – 02:30 PM	A Model of Wound Healing in the presence of Cytotoxic Distending Toxins	Heidi Phillips
02:30 – 03:00 PM	Acute Compartment Syndrome in a Cynomolgus Macaque (<i>Macaca fascicularis</i>) After Surgical Cannulation of the Femoral Artery	Adam Murphy
03:00 – 05:00 PM	Board of Directors Meeting – Royal Salon C	

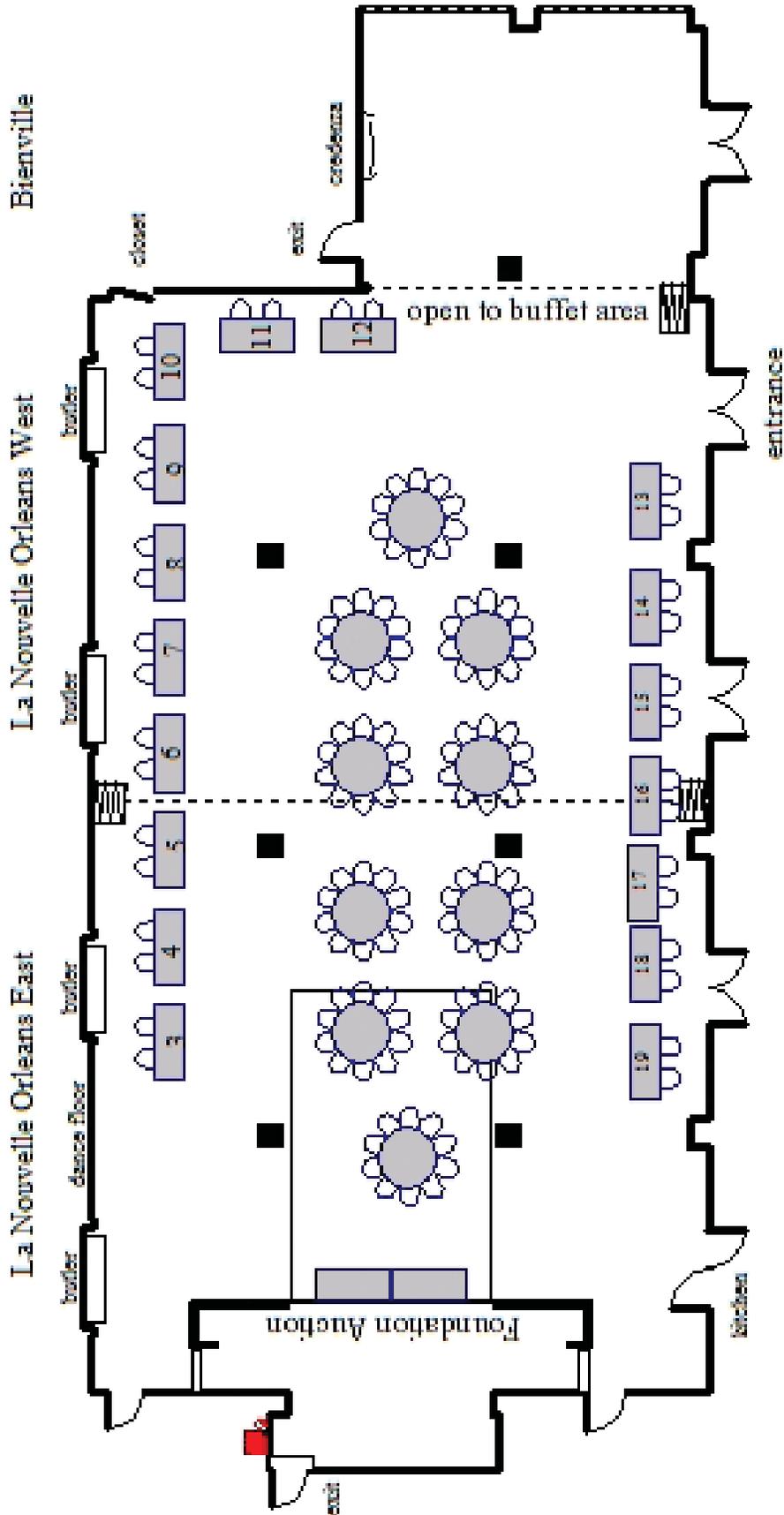
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Exhibitor Directory





Access Technologies

BOOTH 14

www.norfolkaccess.com

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ALZE T® Osmotic Pumps

BOOTH 11

www.alzet.com

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AVA Biomedical, Inc.

BOOTH 3

www.avabio.com

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Colonial Medical Supply

BOOTH 15

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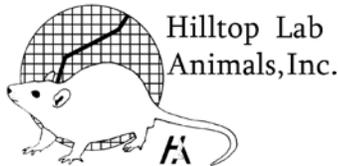


DRE Scientific, a division of DRE Veterinary

BOOTH 13

www.dreveterinary.com

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 10

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Instech Laboratories, Inc.

BOOTH 17

www.instechlabs.com

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Kent Scientific
CORPORATION

Kent Scientific Corporation

BOOTH 9

www.kentscientific.com

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Lomir Biomedical Inc.

BOOTH 16

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BIORESOURCES

Marshall BioResources

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BOOTH 18

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www.medline.com

BOOTH 19

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Patterson Scientific

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BOOTH 6

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SAI Infusion Technologies

www.sai-infusion.com

BOOTH 7

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Taylor & Francis
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BOOTH 8

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Toxikon Corporation

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BOOTH 12

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TSE Systems

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BOOTH 4

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UID Identification Solutions

www.uidevices.com

BOOTH 5

RFID provides a secure method for the identification of animal and other laboratory items using implantable and external RFID Transponders. The UID Identification system included RFID implantable transponders, readers, programmers and software for laboratory processes. Using RFID and the pi Suite by UID, researchers can track and verify procedures such as body weights, blood sampling, and cage sanitation as well as surgical data. The pi Suite Surgical application will allow surgeons to track critical surgical data and inventory items to make the data easy to access. Compatible with all LIMS Systems for easy integration.

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YEARS

Keynote Speakers



Interventional Radiology (IR)/Cardiology Abstract

Dennis E. Burkett VMD, PhD , DACVECC , DACVIM (Cardiology)
Hope Veterinary Specialists
Malvern, PA

Interventional radiology (IR), also known as vascular and interventional radiology (VIR) or surgical radiology, is an independent medical specialty (previously a sub-specialty of radiology) providing minimally invasive image-guided diagnosis and treatment of diseases in every organ system. Although the range of procedures performed by interventional radiologists is broad, the unifying concept behind these therapies is the use of the most modern, least invasive technique available in order to minimize risk to the patient and improve health outcomes.

As the inventors of angioplasty and the catheter-delivered stent, interventional radiologists pioneered modern minimally invasive medicine. Using X-rays, CT, ultrasound, MRI, and other imaging modalities, interventional radiologists obtain images which are then used to direct interventional instruments throughout the body. These procedures are usually performed using needles and catheters, rather than by making large incisions into the body as in traditional surgery. Many conditions that once required open surgery can now be treated non-surgically by interventional radiologists. By minimizing the physical trauma to the patient, non-surgical interventions can reduce infection rates and recovery time, as well as shorten hospital stays.

Interventional cardiology is a branch of cardiology that deals specifically with the catheter based treatment of structural heart diseases. Andreas Gruentzig is considered the father of interventional cardiology after the development of angioplasty by interventional radiologist Charles Dotter. A large number of procedures can be performed on the heart by catheterization. This most commonly involves the insertion of a sheath into the femoral artery (but, in practice, any large peripheral artery or vein) and cannulating the heart under X-ray visualization (most commonly fluoroscopy). The main advantages of using the interventional cardiology or radiology approach are the avoidance of the scars and pain, and long post-operative recovery.

NOTES

Experimental Surgery – The Foundation for Improving Delivery of Care

Dr. James Cook DVM, PhD, OTSC

As Dr. Markowitz so clearly demonstrated throughout his incredible and innovative career, experimental surgery is a foundational process for safely, ethically, and effectively improving delivery of care and outcomes for patients in every area of medicine. This is certainly true in orthopaedics and has served as the catalyst for my career. As a veterinary clinician-scientist, I have had the additional opportunity to use the process of experimental surgery to directly benefit animal health as well. This One Health – One Medicine approach has allowed for efficient progress towards optimizing treatments for the common joint disorders that affect millions of people, and animals, each year. This presentation will highlight the clinical solutions that we have guided to fruition because of experimental surgery, hopefully honoring the life and legacy of Dr. Markowitz and this award

NOTES

Dr. David G. Baker, DVM, PhD, MPA, DAACLAM

Professor of Laboratory Animal Medicine
Director, Division of Laboratory Animal Medicine
School of Veterinary Medicine, Louisiana State University

For more than 80 years LSU's live tiger mascot, 'Mike' the Tiger, has represented the enduring character of all people and things LSU. From Mike I through the current Mike VI, each tiger has been unique, with their own personalities, quirks, and challenges. In this presentation, Dr. Baker discusses the origin of the fighting tiger tradition, which dates back to the Civil War, how the first tiger came to LSU, and then talks about each 'Mike', concluding with Mike VI and his recent medical challenges.

NOTES

Chimp Haven: The National Chimpanzee Sanctuary

Cathy Willis-Spraetz

The use of electronic instrumentation to monitor physiological function in conscious research animals and humans has become routine. Beyond basic research, animal studies using these methods are required by government regulatory agencies worldwide before human testing of potential new drugs. Living, as we do, in an age of miniaturized high-tech electronic devices, we are accustomed to believing this technology is easy; however, this has not always been the case. While a broad supporting cast of engineers, physiologists, fellows, and technicians was involved, the true innovators were Dr. Robert Rushmer, Dr. Robert Van Citters, and Mr. Dean Franklin. Before Dean Franklin's death in 2007, the primary author recorded 5 h of interviews with him at his home in Columbia, MO. An additional approximate 1.5-h interview was recorded with Dr. Van Citters via telephone. The information contained herein is based on the recollections of these men as recorded in their interviews.

NOTES

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YEARS

Presentation Abstracts



Friday, Track 1

Dorsal Laminectomy and Durotomy Sheep Model

Darcy H. Gagne, ScM, SRS, CVT, RLATG
C.R. Bard, Inc. (Daval)

Background: According to the National Spinal Cord Injury Association, approximately 450,000 people in the U.S. are living with a spinal cord injury. When surgery is required for repair, biocompatible materials must be tested for spinal indication to demonstrate safety.

Purpose: Due to the size of the animal and historical data with spinal cord application, the Polypay sheep model (~40 kg) was chosen. A total of six animals in two time points with three groups were chosen including test, control and untreated groups for a total of 36 animals. The animals were survived to a sub-chronic (Day 3) and chronic (Day 90) time points to understand the response over time. On Day 0, all animals received a dorsal laminectomy and durotomy. The animals were monitored for clinical and incision site observations, neurological examination, body weight and condition scores for the duration of the study.

Methods: Dorsal laminectomy with durotomy in sheep was a very meticulous procedure. The planning, setup, anesthesia, and recovery were very complex. The hay and food was removed the evening prior to surgery. The animal was anesthetized, an orogastric tube placed and positioned in kyphotic ventral recumbency. The site was prepared for strict aseptic procedures and supportive intravenous fluids were administered. A midline skin incision was created over the L2/L3 vertebral segments. The muscles were retracted to expose the dorsal spinous processes of the L 1 to L4 vertebral bodies and fluoroscopic guidance was utilized to confirm the location of the laminectomy site. The dorsal spines of L2 and L3 were removed until the dura mater was exposed. During this time, the end tidal CO₂ was reduced to increase the intrathecal space in preparation for the durotomy. Once the dura mater was exposed, a 1cm durotomy was created and treated, as appropriate. The incision was closed in layers and the animals were weaned off ventilator support. The animals were recovered in group housing on rubber floor mats; which seemed to help with hoof traction post-operatively. The animals showed no neurological abnormalities throughout the duration of the study and gained weight, as expected.

Conclusions: The goal of this study was to demonstrate safety of a test device when applied to the dura mater and at least some of the spinal cord through the durotomy. Careful planning, meticulous surgical procedures and pre-, intra-, and post-operative monitoring were the keys to success with this animal model. Even with a very prepared and well trained surgical team, errors can still take place. Knowing how to resolve them and plan for them is invaluable. This procedure is a very clinically relevant animal model and data collected demonstrated safety with the device tested as the results were comparable to control and untreated.

Citations: In summary, we describe a model of dorsal laminectomy with durotomy in sheep for the evaluation of safety and efficacy of biomaterials. Our experience indicates that this represents a robust model and clinically relevant approach to evaluating dynamic devices that may come into contact with spinal tissue.

NOTES

Establishment and Utility of Antithrombotic Efficacy and Bleeding Liability De-Risking Models in Cynomolgus Macaques.

L. Alexandra Wickham, CVT, RLATG, SRS
Merck & Co., Inc.

Background: Thrombosis can lead to serious morbidity and mortality. Since antithrombotic drugs play a major role in the clinical management of thrombosis, vigilant evaluation of novel candidates is essential for comprehensive pre-clinical efficacy and risk characterization. The need for nonhuman primate (NHP) models for evaluating novel antithrombotics is high because NHPs possess target expression patterns similar to human, thus lending greater translational potential to the clinic. To this end, NHP models of mixed arterial and venous thrombosis (arteriovenous shunt (AV- shunt)) and arterial specific thrombosis (ferric chloride (FeCl₃)) and template bleeding time (BT) tests were developed for characterizing antithrombotic efficacy along with bleeding liability.

Purpose: Cynomolgus macaques were sedated with ketamine HCl (10-15 mg/kg,IM) and anesthetically maintained using Isoflurane (1.25 - 2.5%,IT) with subsequent instrumentation with femoral artery and vein catheters for AV-shunt studies or left and right carotid artery Transonic flow probes for FeCl₃ injury mediated arterial thrombosis studies. Thermotherapy was provided along with routine monitoring of vital parameters. AV-shunt study subjects underwent sequential dosing using a 4 shunt paradigm with test agent administration initiated 20 minutes prior to each shunt engagement and discontinued 60 minutes post-initiation with subsequent thrombus weight quantification. FeCl₃ study subjects underwent test agent administration followed by carotid artery injury with topical FeCl₃. Doppler ultrasound monitoring of blood flow was used to measure time to thrombotic occlusion of the injured artery. Template BT tests in the buccal mucosa, finger pad, tail were concurrently evaluated. All animal procedures were approved by the Merck Institutional Animal Care and Use Committee and in accordance with the Guide for the Care and Use of Laboratory Animals.

Methods: The AV-shunt model demonstrated consistency of shunt to shunt thrombus generation and stability over time in vehicle (0.9% Saline or 35% HP CD: 2 ml/kg/hr,IV) treated NHPs (n=3). Model utility was validated by demonstration of assay sensitivity using Apixaban, a direct Factor Xa inhibitor, wherein a reduction in thrombus weight was observed (n=3) compared to vehicle treatment following intravenous administration of Apixaban including Apixaban titration (0.0015-0.015 mg/kg/hr,IV) which resulted in a dose dependent reduction in thrombus weight. An arterial specific thrombosis model was developed by exposing the carotid artery to 50% FeCl₃ for 5 minutes, which produced consistent injury leading to complete sustained thrombus occlusion within 25 minutes (n=3). Utility of the model was validated by model benchmarking with antiplatelet P2Y₁₂ antagonist, clopidogrel (1.0mg/kg,PO:n=3), and protease-activated receptor antagonists PAR4 (1.0mg/kg,PO:n=6) and PAR1 (1.0mg/kg,PO:n=6). The template BT model that simultaneously evaluates BT in the buccal mucosa, finger pad and tail was established independently and then applied for concurrent use with the FeCl₃ thrombosis model.

Conclusions: No Discussion. Please see below for compete authorship list: Author List: L. Alexandra Wickham, Gary Sitko, Maria Michener, Brad Smith, Yuchen Zhou, Larry Handt, Lin Chu, Karen Owens, Xiaofang Li, Joe Metzger and Tian-Quan Cai

Citations: Effective approaches for evaluating antithrombotic efficacy using AV-shunt and FeCl₃ models of thrombosis were established in Cynomolgus macaques. In addition, a dual capability platform combining FeCl₃ and peripheral template BT models enabled simultaneous antithrombotic efficacy and bleeding liability de-risking in the same animal promoting a reduction in animal use whilst increasing efficiency and permitting observation of differential responses.

NOTES

Development of a Swine Model of Behind Helmet Blunt Trauma

Michael S Horsmon, MS

US Army Edgewood Chemical Biological Center

Background: Behind helmet blunt trauma (BHBT) is a unique form of traumatic brain injury (TBI) caused when the back-face of a helmet makes contact with the head following a ballistic impact to the helmet. Understanding the injury mechanisms of BHBT is critical in assisting materials development and generating a physiologically relevant testing standard. To that end, a miniature swine model was developed in which data regarding the mechanical inputs to the head can be measured. Thirty Gottingen swine were used in this pilot study to develop all aspects of this testing procedure. Here we focus on the surgical procedure and outcomes of a group of six that were recovered and survived for three days following a BHBT event.

Purpose: Skin and skull surface force, skull surface strain, and impact intracranial pressure (ICP); as well as physiological responses including ICP, blood pressure, electrocardiogram, electroencephalogram, body temperature, and animal activity. Two DSI M-11 telemetry implants were placed in each animal. The first was utilized to collect ICP and EEG. The second was used to collect systemic blood pressure and ECG. Additionally, one force and one three axis strain gauge were placed on the skull surface. Finally, a second pressure sensor was placed in the right lateral ventricle of the brain to measure the impact pressure. Swine were initially anesthetized with telazol/ketamine/xylazine cocktail (4.4, 2.2, 2.2mg/kg IM) supported by buprenorphine (0.05mg/kg IM), atropine (0.04mg/kg IM), and enrofloxacin (10mg/kg IM). Surgery was carried out under general anesthesia with isoflurane (1.5-2.5%). Post-operative pain was managed with buprenorphine, enrofloxacin was continued for five days post-surgery.

Methods: Typical results from a hand gun threat are strain values in excess of $\pm 3,000\mu\text{strain}$, and impact intracranial pressures of 120-140psi. Transient physiological responses to BHBT (under propofol anesthesia) include peak ICP of 41.0mmHg $\pm 7.2\text{mmHg}$, peak HR of 211.8bpm $\pm 9.4\text{bpm}$, peak MAP of 172.0mmHg $\pm 7.2\text{mmHg}$. One of six swine showed slight functional deficits in open field observations. Several animals showed increase plasma concentrations of ubiquitin carboxyl-terminal hydrolase isozyme L1 (UCH-L1).

Conclusions: When compared to the data from a range of other threats tested over the course of the pilot study, the physiologic responses are classified as mild to moderate. Most important is the transient nature of the physiologic responses, more severe outcomes are correlated with sustained changes in physiology. Strain and impact intracranial pressures are on the low end of the scale as well. These strain values are indicative of cases with no fracture and impact ICP has been recorded in excess of 1,000 PSI. At this time it is impossible to interpret these data as prognostic of outcome. Most interestingly, the animals in which UCH-L1 was elevated represent the cases with moderate effects. Elevation in plasma UCH-L1 is congruent with studies of human TBI.

Citations: The results of this study indicate that the miniature swine maybe a good large animal model for BHBT. Additional refinements to sensor preparation and the surgical method will improve this model in future studies.

NOTES

Round Table on Chronic Access for Biological Samples

Dr. Vince Mendenhall, DVM, Surgical Consultant

Jon Ehrmann, BS, SRS, SRA, LATG , Bristol Myers Squibb

Eric Adams, BS, SRS, Northern Biomedical

Marlo Volberg, BS, SRS, RVT, RLAT, Pfizer

This year's round table will be a two hour interactive session consisting of brief presentations by each panel member followed by a Q&A session with the audience. Topics will include Vascular, Intrathecal, Bile and Lymph chronic access focusing on surgical descriptions, aseptic technique and sample collection, locking solutions, trouble shooting, and species specific differences. Members are welcome to submit specific questions ahead of time for the panel to discuss during the Q&A session in addition to asking them during the presentation.

NOTES

Friday, Track 2

Acquisition of Left Ventricular Pressure, Systemic Blood Pressure, Epicardial Electrocardiograms, Core Body Temperature, and Activity Utilizing Stellar TSE's Type PPBTA-XL Telemetry Transmitter, in the Vervet (Caribbean Green Monkey).

David Moddrelle, SRS

RxGen/St Kitts Biomedical Research Foundation

The Caribbean vervet (*Chlorocebus Sabaeus*) has a unique place in the history of primate research. Their use in safety pharmacology is not as well documented as other primates, but has been expanding as researchers begin to understand the importance of a more genetically homogeneous primate species for use in biomedical research, particularly safety pharmacology. In this project we explored a novel telemetry device produced by Stellar TSE for acquiring left ventricular pressure (LVP), systemic blood pressure (BP), epicardial electrocardiography (ECG), core body temperature (BT), and activity. Several unique aspects of this cost competitive device include the use of solid state pressure tipped sensors, the capability of catheters to be designed to any length or diameter, and the relatively small profile of the transmitter body. Other aspects of the device and system will be explored during the presentation. Five (5) animals were implanted according to an IACUC approved protocol. Each animal was prepped accordingly for an off midline laparotomy and left thoracotomy (i.e. shaved, peripheral catheter placed, intubated and given pre-surgical ketamine HCL, atropine sulfate, cetiofur, buprenorphine and iron dextran) and then delivered to a surgical suite for final prep. A circulating warm water blanket was employed to assist in maintaining BT. The animal was placed on ventilated isoflurane, to effect, prepped with alternating chlorhexidine scrub and solution, and draped accordingly. A betadine impregnated adhesive barrier (Ioband) was placed and an off midline incision performed, the internal iliac isolated with 4-0 silk ligature. An arteriotomy was performed and systemic BP catheter (specifically designed to 3.5 fr) was inserted cranially approximately 15 cm and anchored into place with the 4-0 Excel ligature. BP confirmed and the transmitter body anchored to the abdominal wall with 2-0 Excel suture. A left thoracotomy was performed at the 5th intercostal space and the bio-potential leads and LVP catheter tunneled to the thoracic cavity via the 7th intercostal space. The heart was cradled in the pericardium and the LVP catheter inserted into the ventricle via the ventricular apex. The catheter was anchored into place with concentric 4-0 Prolene purse string sutures and LVP confirmed. The positive bio-potential lead was anchored to the epicardium near the LV apex and the negative lead anchored to the pericardium over the right atrium with 4-0 Prolene sutures. ECG was confirmed and a chest tube, connected to suction, was inserted into the thorax via the 7th intercostal space. The lungs were hyper-inflated to alleviate the effects of any atelectasis that may have occurred. The ribs were apposed with sterilized 2 mm cable ties. The abdominal cavity was irrigated with warm saline and closed with individual 2-0 PDS suture. All musculature and skin incisions were apposed appropriately with absorbable suture. The chest tube was removed after spontaneous breathing was established. The animal was allowed to recover normally and received meloxicam/5 days and buprenorphine/3days for pain management and cefazolin/5 days as an antibiotic prophylaxis. Implant data will be exhibited during the presentation for comment.

NOTES

Unique Challenges of Stereotaxic Surgery in Swine

Randy Pielemeier, LVT, BS, SRS, LATG
MPI Research

Performing stereotaxic based brain surgery on swine presents a variety unique of anatomical and equipment challenges that are not seen in the more commonly used large animal species of canines and primates for stereotaxic surgery. There are a variety of publications concerning stereotaxic surgery in swine which are helpful. The stereotaxic frames are typically custom built, using some commercially available components such as rails and manipulator arms. 1The mouth bar, ear bars or other alternatives to fixing the skull laterally are custom built by the individual laboratories involved. No complete commercial stereotaxic frames are available for swine. 2,3One author has an MRI compatible frame for use with MRI based targeting. It is necessary to use younger animals in swine for many stereotaxic surgeries due to the fact that the frontal sinus in swine grows caudally eventually covering the entire dorsal surface of the brain. Gottingen minipigs under 6 months of age are suitable for injections or catheter placements at or caudal to bregma. Younger animals may have to be used for work in the forebrain. There are no stereotaxic atlas's published for swine, likely due to the significant variation between breeds of swine as well as changes due to the age of the animals. This leaves us with anatomical targeting based on necropsies of the same breed, age and sex of animals to be used, or MRI based targeting using reconstruction software. MRI based targeting can be further facilitated with the surgical placement of fiducials (Civico) which are implanted into the animals skull prior to the MRI. Reaching deeper structures in the caudal brain, such as the cerebellum, can be most effectively targeted with an angled approach from the caudal surface of the skull. This targeting is best performed with MRI guidance.

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NOTES

Maintenance of a Swine Model with Chronic Indwelling Catheters for Total Parenteral Nutrition

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University of Colorado Hospital

Total parenteral nutrition (TPN) has been limited by toxicities including cholestasis, hepatic dysfunction, and systemic infection. Changes in formulations have done little to improve outcomes. If TPN associated complications could be limited, it would become more useful in patient care. Standard physiology has metabolites from the gastrointestinal tract passing through the liver through the portal venous circulation. Typical central venous delivery of TPN bypasses this route and may be the cause of many of the complications noted. Therefore, we hypothesize that providing TPN through the portal vein will address the problems of TPN-related toxicity.

Juvenile York Yorkshire-cross pigs, were used for model development. Under general anesthesia, control pigs had central venous catheters placed in the jugular vein, while experimental pigs had port portal vein catheters placed. Minimally invasive catheter placement occurred with the use of ultrasound and fluoroscopic guidance. Proper placement was confirmed with an injection of contrast and imaged with fluoroscopy. Animals received post-operative analgesics and continuous TPN was administered via an infusion tether system.

During this study we encountered complications related to long-term TPN administration including; loss of catheter sterility, development of gastric ulcers, and fluid-overload. In order to decrease the risks of infection, changes were made in catheter placement and aseptic technique during line manipulations and maintenance. These changes included the use of prophylactic antibiotics, change in dressing material at catheter insertion sites, and avoiding unnecessary disconnection from the infusion tether system. Moderate to severe gastric ulcers were present in the majority of the pigs. Swine are naturally predisposed to the development of GI ulcers and situations involving changes in diet and stress can further heighten the risk. Due to constraints of the TPN study, pigs could not receive anything orally that could be metabolized. To increase gastric emptying and aid in gastric acid dilution, we provided crushed ice and prophylactic treatment with GI protectants. Due to the amount of technical manipulations to maintain TPN and the catheters, stress was a significant concern. The use of stuffed animals provided companionship as well as a soft structure to lay on when performing clinical assessments and catheter maintenance. This appeared to decrease their stress levels and all allowed for minimal restraint during procedures. Due to the high volume of TPN required to meet the experimental needs of the study, the pigs were also at risk for fluid-overload. To assess this concern, TPN administration rates were gradually increased in the beginning of the experiment to allow cardiovascular adjustment. In addition, strict parameters on body weight and caloric needs were assessed daily to ensure the experimental needs were being met concurrently with clinical condition.

Long-term catheters paired with TPN pose many challenges. We intend to highlight how we strategically implemented minimal interventions to drastically reduce the number of complications in this model and how similar techniques could be performed for other difficult studies.

NOTES

Development of a Novel Ultrafiltrate Perfusion Device Bioengineered for High Density Islet Cell Transplantation without Immunosuppression

Jody L. Janecek

Department of Surgery, University of Minnesota

Background: Pancreatic islet allotransplantation is a valuable treatment modality for Type 1 diabetes that provides a physiologic source of insulin, prevents severe recurrent hypoglycemia, and reduces morbidity as well as secondary complications. Widespread clinical application of this therapy is hampered by the limited availability of islets, immunosuppressive risk, and moderate numbers of patients experiencing graft functional decline over time. Conventional intraportal islet infusion immediately subjects islets to intense inflammation and hypoxia. Both of these factors critically affect engraftment and influence long-term graft performance. We are developing a subcutaneous component-based macroencapsulation device designed to address these barriers, eliminate the need for immunosuppression, advantage a xenogeneic cell source, plus permit non-invasive access for loading, reloading, biopsy and graft recovery. The Cell-Safe™ (C-S) device is designed to generate autologous ultrafiltrate for perfusion to an immunoisolation chamber containing a three-dimensional hydrogel, Islet-Mate™ (I-M), high-density islet construct.

Purpose: Using the C-S device proof-of-concept studies were performed to evaluate the suitability of ultrafiltrate as a perfusion medium to sustain immunoisolated islet viability and function using Lewis rats. Under general anesthesia a dorsal midline incision was made and bluntly dissected to create a subcutaneous pocket to accommodate the device. Base characteristics including hematologic, chemistry, electrolyte, and oxygen content of ultrafiltrate generated by the accumulation disc were evaluated at 1, 3, and 6 weeks post-implant in 2 healthy rats. In a second group, porcine islets were loaded at a high density (>15,000IEQ) I-M embedded in the C-S in 3 non-immunosuppressed diabetic rats to evaluate immune protection and graft survival. Needle biopsies of the ultrafiltrate and I-M islet cell construct were performed at 0, 4, 10, and 20 days post-transplant (window ±3 days).

Methods: Interstitial fluid accumulated within the disc and had properties similar to serum with a neutral pH, normal electrolyte composition, but slightly lower protein profile. The average PO₂ level was 46±7mmHg at 1 week, increasing to an average PO₂ of 97±19mmHg at follow-up timepoints. The tissue surrounding the fluid accumulation disc was highly vascularized with only sparse inflammatory cells observed on histologic evaluation at 8 weeks post-implant. In transplanted animals, porcine c-peptide levels in ultrafiltrate were >50ng/ml at 4, 10, and 20 days post-transplant. Histologic analysis of the I-M islet cell construct at biopsy showed numerous islets throughout the hydrogel that were both viable and functional with no detectable inflammatory cell infiltrates.

Conclusions: The C-S device can be used to derive autologous blood ultrafiltrate for use as a perfusion medium to support I-M embedded islets in the cell immunoisolation chamber. The complete absence of infiltration and strong insulin staining of porcine islets recovered from the C-S device is compelling evidence of immunoprotective capability. Ultrafiltrate and graft samples were successfully obtained at biopsy timepoints, demonstrating the feasibility of non-invasive access to the graft.

Citations: The C-S is a fundamentally new device platform engineered to support islet cell replacement in the absence of immunosuppression with potential to dramatically increase the longevity of therapeutic benefit and accessibility to a larger population of diabetic patients.

NOTES

Training Nonhuman Primates for Cooperation with Medical Device Management to Enhance Human factor Prediction and Usability Evaluations

Lucas A Mutch

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Background: Medical devices play a critical role in prevention, diagnosis, and treatment of disease and quality of life improvement. Implantable device technologies are employing more sophisticated and dynamic designs, with some requiring continuous user management. In certain circumstances, especially combination devices containing a biological component, it is necessary to test devices in nonhuman primates (NHPs) to properly evaluate inflammatory and immunological responses. The biological complexity of the NHP and similar anatomical, physiological and behavioral characteristics with humans can improve prediction in studies that cannot be performed in vitro or in less sentient animal models. We have previously demonstrated that NHPs be trained to cooperate with clinical care necessary in disease modeling, and aim to expand training to manage medical devices with the perspective of most accurately modeling interactions with the user for clinically relevance. Optimization of device manipulations and user interactions, termed human factors, is a critical factor in maximizing the likelihood that the device will be safe and effective for use.

Purpose: Five adolescent male cynomolgus macaques (CM) and six adolescent male rhesus macaques (RM), all socially housed, were trained for cooperation with diabetic clinical care and management of a totally implantable bioartificial pancreas device (BPD) utilizing positive reinforcement. The training program included physical examination, presentation for blood collection and drug administration, hold for BPD charge events, and shifting. Specific training for BPD management included desensitization to a charging wand, positioning for wand placement, allowing the wand to be placed on the body, and holding for at least a five minute charge. The success of behavior acquisition and ongoing cooperation was evaluated. Since animals were trained to perform multiple behaviors, cooperation with device management was assessed with the perspective of usability. Three (CM) and one (RM) were implanted with a BPD, with behavior acquisition success as one criteria for enrollment and followed for the duration of implant.

Methods: All 11 animals completed the training program successfully, demonstrating competence with each of the behaviors. BPD training identified that wand design provoked apprehension in certain animals, which was resolved by covering the wand with a cloth sleeve. In all four animals implanted with a BPD, initial activation of the pump provoked a behavioral response to touch the device, which rapidly extinguished when trainers redirected them. Testing inductive charging in cooperating animals allowed us to observe animals would prematurely end the planned charge session to withdraw from thermal stimulus generated by energy transfer while still remaining willing to interact with the trainer. Thermal withdrawal was not consistent with expected tolerance device temperatures. No behavioral regression was observed during followup.

Conclusions: Devices moving to the clinic must have a strong safety and efficacy profile, but success also hinges on patient adoption, which is largely based on usability and willingness to interact with the device.

Citations: NHPs can be trained to closely approximate clinical usability and identify factors that may affect device acceptance prior to clinical testing and enhance acceptance. Alongside the scientific benefit, cooperative handling improves animal wellbeing.

NOTES

Refinement of a Bile Duct Catheterization Technique in Rabbits

Dr Delphine Bouard, DVM, Dip Vet LAS
Vetsalius

Background: Catheterization techniques for chronic bile sampling in rabbits have been described in the literature. However, only two articles are precisely describing a surgical protocol and the reported outcomes are suboptimal. Imavita and Vetsalius tried to refine the previously described techniques.

Purpose: Three batches (2 , 12 and 18 animals) of New-Zealand SPF male rabbits were operated . Animals were anesthetized with a mixture of ketamine and xylazine and have been previously injected with buprenorphine. Local anesthetics were also used. Surgeries were performed under strict aseptic conditions. A pilot study involving two animals was initially performed. Its goal was to check whether the chosen instruments and consumables were optimal. After a first refinement step, 12 animals were operated during a second surgery session. Regular bile sampling were performed after the surgeries. A third session in 18 animals was organized to allow further refinement of the model.

Methods: Pilot study : one animal had to be euthanatized during the surgery, because the bile duct was damaged during the procedure. Changes in instruments and in the technique (direct catheterization of the duodenum instead of double catheterization of the bile duct) were implemented to reduce the risks of bile duct damage. The other animal was operated according to the new method. The second animal recovered properly and its catheter remained patent for 2 weeks
Second phase : Out of the 12 operated animals, one animal had to be euthanatized during the surgery (bile duct damage), An animal died because of anesthesia problems and 2 animals were operated but didn't recover properly. Nine animals recovered properly and had patent catheters for 3 to 15 days. However, long term catheter patency performances were still suboptimal. During the third phase, 1 animal out of the 18 had to be killed during the surgery because of bile duct damages. Seventeen animals recovered from the surgery. Catheter were patent for at least 15 days post surgery in 11 animals. In the other 6 animals, catheter patency losses were reported between 5 and 15 days after the surgery.

Conclusions: The suboptimal results of the second step study were considered to be mostly due to bile leakages problems, related to the use of inappropriate suture material. A change of suture material allowed to significantly reduce bile leakages during the third phase. Peri-operative care improvement (use of more efficient heating pads, improved fluid therapy, administration of post-operative gels) also helped improving recovery and catheter patency between the second and the third session. Results of the third batch were globally good but can still be improved, several additional refinement options have been identified.

Citations: Catheterizing bile ducts in rabbits is, as in many other species, a challenge. High success rates for short term sampling are relatively easy to achieve but chronic sampling is much more difficult. Step by step improvement of technical details such as catheter design, suturing techniques and catheter protection is requested to reach optimal results.

NOTES

Assessment of Murine Colorectal Cancer by Micro-Ultrasound using Three Dimensional (3D) Reconstruction and Non-Linear Contrast Imaging

Jessica L Freeling MS, VT, LATG

The University of South Dakota, Department of Basic Biomedical Sciences, Sanford School of Medicine

Background: To examine the effectiveness of new anti-cancer drugs in animal models of tumorigenic cancer, it is essential to have an accurate assessment of therapy efficacy. Quantitative and longitudinal measurement of changes in tumor volume and their vascularization over the course of disease, with and without treatments, can provide valuable data for clinical pharmacology of anti-cancer drugs. Current methods for the longitudinal evaluation of colorectal cancer (CRC) in mice rely on sacrifice of animals at multiple time-points or invasive techniques with high mortality rates. This lack of in vivo and non-invasive longitudinal data limits the quantification to two-dimensional photographs evaluated for tumor areas and traditional histological analysis. These endpoint evaluations ignore the complexity of tumor morphology and adhesion during development, and more importantly, tumor vascularization during progression.

Purpose: In this study, we utilized a well-established murine model for the induction of CRC. The mice predominantly generated tumors in the mid and distal colon, recapitulating the adenoma-carcinoma sequence that occurs in human CRC. 3D micro-ultrasounds acquired over the course of cancer progression allowed us to monitor the tumor load in live animals. An anti-cancer compound was utilized to evaluate the impact on the size of the colon tumors and was quantitated before and after treatment. At endpoint, traditional photographic images of colons were compared to ultrasounds. In addition, enhancement of contrast using microbubbles enabled detection and quantification of relative colon vascularity.

Methods: Animals with disparate CRC tumor loads were accurately evaluated using non-invasive 3D ultrasound. Longitudinal evaluation of animals produced high quality quantitative volume data enabling the evaluation of treatment paradigms which would be impossible with traditional endpoint-only measures. Additionally, with the use of microbubbles, quantification of relative colon vascularity (Percent Agent) including relative blood volume (Peak Enhancement) and relative blood flow (Wash-In-Rate) was accomplished. It is noteworthy that this optimized method requires minimal training and is supported by a user-friendly software.

Conclusions: High resolution micro-ultrasound systems are commonly available and employed for pre-clinical imaging. 3D ultrasound techniques have been employed in mice for many other types of cancer such as liver metastasis and prostate cancer. While the 3D ultrasound reconstruction of xenograft tumors in mice has become mainstream, a simple and reproducible method for CRC is absent from the literature. This technique is not only applicable to inducible CRC models, but also CRC orthotopic models such as surgical transplantation, enema models, microinjection models, and transanal low dose electrocoagulation models. Additionally, given the clarity of the colon wall images obtained, this technique can be effectively utilized in mouse models of colitis and inflammatory bowel disease.

Citations: Our optimized non-invasive ultrasonography method provides meaningful longitudinal data further enhancing results provided by traditional endpoint analysis. There is a crucial demand for new targeted therapies for CRC which can improve the poor effectiveness of current treatments and increase patient survival rates. Monitoring and measurement of CRC tumors using 3D ultrasound is ideal for discovery of novel targeted therapies.

NOTES

Saturday, Track 1

Preclinical Evaluation of the Medtronic Hancock® Bioprosthetic Valved Conduit for Right Ventricular Outflow Tract Reconstruction in the Pediatric Population

John Carney, MBA

Experimental Surgical Services, University of Minnesota

Background: Xenograft conduits used to repair congenital heart defects are prone to failure over time. Development of new, superior xenografts is required to improve patient outcomes. To evaluate the safety of these new devices, they must first be compared against a clinically available control article, in a large animal model. Our goal was to characterize and evaluate the performance of a clinically available xenograft conduit used in RVOT reconstruction in the sheep model.

Purpose: Right ventricular outflow tract reconstruction was performed in thirteen adult and juvenile domestic sheep. Animals were implanted with a 22mm Medtronic Hancock® Bioprosthetic Valved Conduit, (MHBVC) utilizing cardiopulmonary bypass, using both clinically described methods, as well as the 'RVOT Extraction' technique developed by our laboratory. Animals were then recovered and monitored for predetermined term durations ranging from 70 to 140 days. Serial transthoracic echocardiography and blood sampling was performed throughout the postoperative period. At the end of the study term, animals were placed under general anesthesia for the collection of intracardiac pressures and angiograms. Animals were euthanized and gross necropsies were performed by a board certified veterinary pathologist. Animals used in this study were selected via an experimental protocol approved by our Institutional Animal Care and Use Committee.

Methods: Two out of thirteen animals died prior to their designated study terms, as a result of severe valvular stenosis and distal conduit narrowing. Eleven animals survived to the end of their designated study terms with little complication. Generally, maximal and mean transvalvular pressure gradients across the implanted conduits were observed to increase throughout the course of the post-operative term, as measured by spectral Doppler ultrasound. Of the eleven full term animals, seven of the implanted conduits were patent with mild to absent pseudointimal proliferation, and with flexible leaflets maintaining the hemodynamic integrity of the valve. Incidence of these successful outcomes was generally associated with our 'RVOT Extraction' technique, as verified by descriptive statistics.

Conclusions: Modes of failure observed in our study, i.e., valvular stenosis and distal narrowing, mimic those observed in clinical patients implanted with xenografts. Animals surviving to their designated study terms were free of postoperative complications and clinical symptoms of cardiac dysfunction. Explanted conduits free of grossly observable modes of failure demonstrate the MHBVC's validity as a control and standard of measure to which to compare new xenograft conduits in preclinical evaluation. Use of our 'RVOT Extraction' technique for RVOT reconstruction in the sheep model seemed to improve both surgical access as well as performance of the MHBVC. Animals implanted with the MHBVC using the 'RVOT Extraction' technique were generally associated with better gross pathological outcomes at study termination.

Citations: We have demonstrated that RVOT reconstruction using the Medtronic Hancock® Bioprosthetic Valved Conduit (MHBVC) can be successfully and reliably performed in the sheep model. With its extensive clinical history along with the ability to be used in long-term sheep models, the MHBVC is an ideal control device to compare new xenografts against in future preclinical studies.

NOTES

Validation of Heart Failure Model in Mice utilizing an Electrocautery method of Subtotal Nephrectomy

Jan Bernal, DVM
Pfizer

Background: The intimate and linked association between cardiovascular pathology and renal dysfunction is well documented. Animal models provide insight into the association and interactions of cardiorenal syndrome. Historically the rat has been the most utilized surgical model for cardiovascular and renal diseases, however focus is increasing on the development of mouse surgical models to intensify the understanding of the pathophysiology involved in a chronic kidney disease model to induce cardiovascular disease. The aim of this study was to induce chronic kidney disease in a mouse to facilitate the development of a heart failure model.

Purpose: The study design and protocol was approved by the Institutional Animal Care and Use Committee and included 32 male mice (C57BL/6) in two age groups (6-8 weeks and 12-14 month). The 12-14 month old male mice had previously been implanted with a carotid telemetry unit for continuous blood pressure collection. The mice were randomized and assigned to 4 study groups: sham surgery and blood pressure; sham surgery only; subtotal nephrectomy and blood pressure and subtotal nephrectomy only. A subtotal nephrectomy was performed using electrocoagulation of the renal cortex to induce a thermal injury with removal of the contralateral kidney 7 days after the thermal injury surgery. The thermal injury was created by a pointed cautery tip applied to the fully exteriorized left kidney via retroperitoneal approach in a 2 mm pattern; preserving the vascular hilum. Analgesia was initiated 24 hours prior to each surgery via Carprofen (5mg/gel) diet. Buprenorphine 0.03 mg/kg was administered subcutaneously pre-emptively and the mice were anesthetized utilizing 2-3% isoflurane. Post operatively, meloxicam SR (4 mg/kg) was administered subcutaneously. The mice had twice daily post-operative observations and pain assessment for 7 days after each surgery with additional pain medication prescribed by the veterinary staff based upon the observations and pain assessments

Methods: The evaluation of the model included imaging, biochemistry, and blood pressure collected prior to surgery (baseline), 4, 8, and 12 weeks post subtotal nephrectomy. Images collected for analysis were parasternal long axis in B-mode, parasternal short axis in B-mode & M-mode, tissue Doppler and PW Doppler of mitral annulus and renal blood flow and images of kidney remnant. Blood pressure data was collected from telemetered cohort at baseline and 4, 8, and 12 weeks post subtotal nephrectomy surgery. Blood and urine were collected for biomarkers and biochemistry at the same time points with the urine collection overnight in metabolism cages.

Conclusions: Biomarkers and biochemistry data collected from this study support the development of a chronic kidney disease model; however no corresponding changes in echocardiography parameters to indicate the development of a heart failure model in mice in 12 weeks

Citations: The subtotal nephrectomy via electrocautery (thermal injury) can induce chronic kidney disease in mice however it did not reproduce a heart failure model previously published in a 12 week timeframe.

NOTES

Surgical Technique for Cesarean Section in the Cynomolgus Macaque

Leslie J. Stoll, S.R.S., LATg, RVT
Charles River Laboratories

Background: To describe the Cesarean section procedure in a NHP and educate on key reproductive facts and the science driving the need for this procedure in research

Purpose: To support Developmental and Reproductive Toxicology Studies (DART) Pre/Postnatal Developmental Toxicology Embryo-Fetal Developmental Toxicology Placental Transfer Anesthesia The dam is pre-medicated with Buprenorphine (0.03mg/kg) IM and Rimadyl (4mg/kg) SQ, prior to surgery (calculated at current pregnant bodyweight) Ketamine HCl (10- 15mg/kg) is administered IM for initial sedation. An additional dose of Ketamine is calculated at (10mg/kg) but only given to effect IV to aid in intubation. Once intubated, the dam is placed on isoflurane inhalant anesthetic (1.0-1.5%) and 1 Liter of oxygen/min. Monitoring Procedures Parameters are carefully monitored throughout the procedure including HR, RR, temperature, indirect blood pressure, ECG, ETCO₂ and SPO₂. Surgical Preparation The dam is placed on a circulating warm water blanket and/or forced warm air blanket. An incisional line block with Bupivacaine 2% up to 2mg/kg is administered for local analgesia. The surgical site area is cleansed with 2% Chlorhexadine surgical scrub and warm water. Anesthesia is maintained with isoflurane inhalant anesthetic. The surgical area is prepared by applying ChlorPrep and allowed to dry. The area is appropriately draped for strict aseptic surgery. Cesarean Section A mid-line abdominal incision is placed. The uterus is gently externalized with from the abdomen. A low-transverse uterine incision is placed at the lower uterine segment, proximal to the cervix. The muscular and mucosal layers are dissected with a blunt ended surgical instrument or finger for entry. The placenta is located and blunt dissected away from the uterine wall digitally. The fetus and amniotic sac are carefully expelled manually from the uterus and the uterus inverted. Using a moist gauze sponge, the remaining attachments of the placenta are carefully dissected away from the uterine wall. The uterus is then returned to normal presentation and inspected for excessive hemorrhaging. Oxytocin 0.50ml is administered I.V. to stimulate contraction of the uterine body. The uterus is closed in 3 layers with a monofilament suture and tapered needle. The first being the internal myometrium with a continuous suture. The external myometrium musculature including the serosa is then closed in with an inverted mattress suture. A Cushing's over sew suture is placed in the serosal layer to cover any exposed suture material. The abdomen is closed with a standard 3 layer technique with a monofilament suture and tissue adhesive. Post-Operative Analgesia Buprenorphine (0.03mg/kg) IM is administered BID on the day of surgery approximately 8-12 hours apart. The Buprenorphine dose is then reduced to (0.01mg/kg) IM and administered BID for 2 subsequent days. Rimadyl (4mg/kg) SQ SID x 5 days is also administered.

Conclusion: Cesarean section as a means of collecting vital developmental toxicology data is a growing request among researchers and drug development companies. The Cynomolgus macaque continues to be, as a species, critically important to the evaluation of potential reproductive/developmental effects in biological drug products

NOTES

So What Else Can We Use This Fluoroscope For?

Randy Pielemeier, LVT, BS, SRS, LATG
MPI Research

The surgical services department at MPI Research purchased its first fluoroscope over 18 years ago. It has proven one of those technologies with more uses than ever imagined. The purchase was initially based on increased demand for drug-coated stent work in interventional cardiology. Since, we have used fluoroscopy for training and performing CSF collection, as well as intrathecal and epidural administration of compounds. Exact placement of intrathecal catheters is critical for long term collection and administration. Fluoroscopy is useful for confirming placement of ventricular dosing catheters during large animal stereotaxic procedures, reducing the number of animals needed for study. The longevity of our portal vein cannulations improved because of our ability to navigate the curved vasculature as it bifurcates into the liver lobes and avoid venous valves, allowing appropriate tip placement. Dosing of compounds to specific organ systems (liver, kidney, pancreas, spleen) in various species can be achieved without need for more traumatic open surgical procedures. Diagnosis of patency problems in any catheter system is facilitated by fluoroscopic imaging with contrast, helping ascertain the appropriate repair or replacement procedures needed. During a variety of orthopedic surgeries, fluoroscopy aids determining appropriate screw length and accuracy of drill target and implant placement. We have documented injection sites in intervertebral discs of rabbits by placing a screw into the vertebral body. This presentation is intended to stimulate discussion about the many potential uses of the fluoroscope as an imaging technology in the operating room.

NOTES

Establishing and Maintaining Relationships with Vendors

Steven Kreuser, AS, RLATg, SRA
Pfizer, Worldwide Comparative Medicine

Surgery and Anesthesia is a group within Pfizer's Comparative Medicine's (CM) Global Science and Technology (GST) organization. We provide expertise in laboratory animal surgical models and anesthesia support to research partners. Our mission is to provide investigative partners with the best possible model to meet study needs. This allows us to guide investigative staff to the best outcome to meet their study requirements, whether this involves in-house development and production, or evaluating suppliers that can provide surgical models to complete study work. We represent both the interests of CM and the customer by presenting the need, intended use of the model, performance expectations, and animal welfare considerations. Although surgical models and method development are available in-house, there are times when outsourcing surgical models is dictated by business needs to increase efficiencies and meet research timelines and goals. To ensure that outsourced Pfizer models meet quality standards for animal welfare and scientific endpoints, we have created collaborative partnerships with our suppliers. These established partnerships facilitate open, transparent and collegial conversations to share techniques and procedural improvements, and communicate feedback concerning the models; both positive and negative outcomes. In the past, suppliers were not aware of how their models were being utilized or performed once they arrived at Pfizer. Frequently used models such as rodent vascular catheterizations and telemetry implantations represent two examples. This process provides an opportunity for the supplier to become better educated, and refine the models they are producing for Pfizer to maintain consistency with each order. Suppliers also have the ability to develop their own surgical refinements when feedback is provided concerning the intended use of the model and expectations. This contributes to the overall performance of the model, and the ultimate reduction in animal usage. In situations where complications arise with surgical models, the GST team is called in to evaluate the model. This may involve post-surgical complications that affect health, or performance that is not meeting study standards. We investigate and report our findings to the supplier. In one example, we worked with the supplier through several validation studies, where we modified the surgical technique and post-operative clinical care. Because of the relationship we have created, we were able to move forward and improve the model that was being provided. In CM our number one priority is the health and welfare of the animals and the 3Rs. The health and well-being of the animal has a direct impact on the success of the model and the validity of the studies in which they are utilized. Partnerships can help prevent model failure, alterations in data, provide increased consistency of the research and benefit the well-being of the animals. All animal use was approved by the local Institutional Animal Care and Use Committee.

NOTES

Saturday, Track 2

Development of a Novel Intratibial Implantation Model using Non-invasive in vivo Imaging for the Evaluation of Antibody-Drug Conjugate Bystander Activity

Devra J Olson, BA, SRS, LATg
Seattle Genetics, Inc.

Background: Multiple myeloma (MM) is a non-clonal hematologic malignancy where tumor antigen expression is not necessarily uniform. Generating bystander effect models is important for the evaluation of antibody-drug conjugates (ADCs) to measure killing of antigen-negative tumor cells. The goal of this project is to create an orthotopic xenograft mouse model where antigen-positive and negative tumor cells are restricted to the tibial medullary space. We developed and optimized an in vivo bystander effect model to evaluate targeted ADCs under development for the treatment of MM.

Purpose: Thirty-six NOD scid gamma immunodeficient mice received surgery under an IACUC approved protocol. The mice were given Bupivacaine (0.5 mg/kg local SC) and Buprenorphine (0.05 mg/kg SC) and maintained under 2% isoflurane anesthesia. Antigen-positive NCI-H929 cells and luciferase-expressing, antigen-negative NCI-H929 cells were mixed at 1:1 and 3:1 ratios and implanted into the right tibia through a small skin incision. A 27-gauge pilot needle was used to enter the intramedullary space through the tibial plateau. The pilot needle was removed and replaced with a Hamilton syringe to administer the cells in a 10 µl volume. The incision was closed with suture and a skin staple. The mice recovered without issue and received an additional dose of Buprenorphine the following day to maintain analgesia.

Methods: Non-invasive bioluminescence imaging revealed significant signal from the luciferase-expressing NCI-H929 cells by 7 days post-implant, which steadily increased until the termination of the study. Three-dimensional MicroCT imaging and immunohistochemistry (IHC) staining confirmed that the cells remained within the intramedullary space of the tibia and did not metastasize into adjacent bones (e.g. femur). Three mice from each implant condition were removed at 2, 3, 4 and 5 weeks post-implant for ex vivo analysis. Flow cytometry staining of the bone marrow showed that the cell populations implanted at equal concentrations had remained about 50% antigen-positive and 50% negative. When implanted at a higher ratio of antigen-positive cells, approximately 75% were positive and 25% were negative as predicted. Additionally, IHC staining specific to the antigen-positive and negative cells revealed even distribution of engraftment within the tumor microenvironment.

Conclusions: The luciferase-expressing, antigen-negative NCI-H929 cells produced a progressively increasing bioluminescence signal, which will diminish in the presence of bystander cell killing in heterogeneous tumor populations. Imaging and IHC confirmed that the cells did not migrate to other bone marrow compartments ensuring that the tumor cells are restricted to the tibia region through late-stage disease. Analysis of bone marrow aspirates verified that the implant ratios are maintained over time, suggesting that the two cell populations grow at similar rates.

Citations: In conclusion, the intratibial implantation model provides a predictable, measurable and reproducible model system for testing MM ADC bystander activity.

NOTES

Automated Arterial Blood Sampling in Rhesus Monkey PET Imaging Studies

Liza T. Gantert, BS
Merck

Positron emission tomography (PET) is a non-invasive molecular imaging modality that allows the detection of radiolabeled molecules in living subjects. PET imaging of rhesus monkeys is used to perform target engagement (TE) studies by quantitatively characterizing the binding of therapeutic candidate molecules in the central nervous system. TE studies often require an arterial input function. Rapid arterial sampling is required for accurate arterial input function and kinetic modeling and analysis. In collaboration with Instechn, an automated blood system method (ABS) was developed. Repeated dual arterial studies were performed for testing timing, volumes and accuracy of the two methods. Kinetic modeling parameters determined from ABS input functions were in agreement with those obtained from manual measurements. The ABS technique is fully validated to collect rapid samples to measure PET input functions. Compared to manual technique, the ABS allows for a higher rate of sampling per study, reduces animal blood volume due to less waste, reduces personnel's radioactive and biological exposure from blood handling, and significantly reduces manpower demands.

NOTES

Evaluation of Rabbit Telemetry Drug Protocol

Evan Pagano, BS, LVT
Pfizer

A recent literature search revealed a lack of current information concerning anesthesia and analgesia protocols in rabbits. Based on experience with canine and primate anesthesia and analgesia protocols the following combination of medications was selected and evaluated for rabbits undergoing a minor telemetry procedure (n=8). The drugs utilized in the anesthetic plan consisted of Buprenorphine, Acepromazine, and Glycopyrrolate as preanesthetic medications. Preanesthetic medications were administered 30 minutes prior to induction and were assessed on characteristics including muscle relaxation, level of sedation, and ability to maintain body temperature. The rabbits were monitored utilizing manual techniques to check palpebral reflex, pupil dilation, eye position, toe pinch and jaw tone. Mucous membrane color and capillary refill time were also monitored. Initial body temperatures prior to premedication administration were taken rectally and compared to body temperatures prior to induction. During this time the rabbits were provided supplemental heat support. Heart rates and respiratory rates were also recorded prior and post premedication administration to assist in gauging level of sedation. Intravenous catheters were subsequently placed and secured in the right marginal ear vein. The NSAID Meloxicam SR (suspended release) was administered at this time. Induction medications of Ketamine combined with Midazolam were administered to facilitate intubation. Induction agents were assessed on depth of sedation, tranquilization, immobilization, and ability to maintain a safe plane of anesthesia during intubation. Supplemental isoflurane via a facial mask was made available as an additional induction anesthetic if needed to aide in intubation when laryngospasms were present. An endoscope was utilized for endotracheal intubation. Rabbits were intubated with size 3.0mm endotracheal tubes which were secured in place via cuff inflation and tied gauze. Once intubated, maintenance levels of gas anesthesia were adjusted based on continuous monitoring of vital signs with the use of a Cardell patient monitoring machine. The Cardell presented information on pulse oximetry, temperature, ECG, ETCO₂, oscillometric blood pressure, respiratory rate and inspired/expired isoflurane levels. These vitals were monitored and documented every 10- 15 minutes. Intra-operatively, maintenance levels of gas anesthesia continued to be adjusted based on continuous monitoring of vital signs. Post-operatively, observations such as presence or lack of thrashing, muscle relaxation and pain were assessed. The goal of a smooth post-operative recovery period was extremely crucial in these rabbits due to the increased risk of thrashing related injuries that could lead to euthanasia. Buprenorphine was administered intramuscularly post operatively the afternoon of surgery and the following morning. Pain assessments were conducted and additional buprenorphine was administered as needed. Recovery properties and immediate post-operative pain were assessed via palpation of surgical site and utilization a rabbit pain assessment scale documenting attitude, posture, gait movement, appetite and eliminations. Presentation will discuss the beneficial and adverse effects of the drug combination. All work involving animals was approved by the IACUC.

NOTES

A Model of Wound Healing in the Presence of Cytolethal Distending Toxins

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Wound healing is a complex process of inflammation, cellular proliferation and migration, angiogenesis, and wound contraction and epithelialization. Cytolethal distending toxins (CDTs) are produced by gram-negative pathogenic bacteria and have been suggested to impair wound healing.

A sterile biopsy punch was used to create standardized circular wounds in the skin of 4 mice. Surgical glue was applied to a silicone O-ring splint centered over each wound and anchored with simple interrupted sutures. Two gel foam plugs saturated with PBS or 500nM CDT in PBS were placed in the wounds which were covered with occlusive dressing. Mice were anesthetized daily, the diameter of each wound measured with surgical calipers, and a photomicrograph taken. 100µl PBS or CDT in PBS gel foam treatments were reapplied. Mice were euthanized when both wounds fully closed.

Treated tissues were collected at necropsy for evaluation. Initial results of the pilot study indicated delayed healing in the CDT treated wound compared to the PBS treated wounds. It was also observed that cessation of toxin application lead to recovery in the rate of healing suggesting the presence of active toxin was responsible for the delayed wound healing response.

Discussion and Conclusion: Although pathogens that produce CDTs cause mucosal damage directly, it was not known whether CDTs prevented healing of wounded tissue. We hypothesized that CDTs would delay wound healing in a murine model. Based on results of this pilot study and other studies, CDTs may affect cell proliferation and survival of many cell types involved in granulation tissue formation and epithelialization, such as polymorphonuclear cells, lymphocytes, fibroblasts, and epithelial cells. CDTs may also interfere with angiogenesis by inhibiting proliferation of normal microvascular endothelial cells and new blood vessel formation.

Further studies are needed to more completely characterize the exact effects of CDTs on wound healing in murine and other animal models.

NOTES

Acute Compartment Syndrome in a Cynomolgus Macaque (*Macaca fascicularis*) After Surgical Cannulation of the Femoral Artery

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Pfizer

Acute compartment syndrome (ACS) can occur post operatively or after localized trauma. Preexisting trauma, compromised vasculature or swelling caused by surgery can increase the complication rate post-surgery and may result in hind limb lameness. ACS is caused by increased pressure within a closed fascial space that compresses vasculature and results in decreased venous outflow followed by decreased arterial inflow. Increased intra compartmental pressure reduces the capillary perfusion below a level necessary for tissue viability. If this occurs, nerves, muscles, and vessels become ischemic and begin to degenerate. A male cynomolgus macaque was scheduled for telemetry implantation that involved surgical placement of a blood pressure catheter into the left femoral artery. A combination of bupivacaine (0.5%) and lidocaine (2%) was administered to the surgical site as a local block. A 2-4 cm skin incision distal to vascular lacuna was made in order to access the femoral artery. Intermuscular fascia was bluntly dissected to isolate the femoral artery. Three ligatures were pre-placed and temporary occlusion of the artery achieved with tension on the proximal and distal ligature. The distal ligature was tied to occlude back flow. A blood pressure catheter was tunneled subcutaneously from the inguinal incision site to the intermuscular pocket with a hollow trocar. The blood pressure catheter was inserted 10 cm into the femoral artery, caudal aorta or proximal left iliac artery using a catheter introducer and debakey forceps. The catheter was tied in place with two surgical ligatures (proximal and distal) and one Millar ligature. Acute compartment syndrome of the hind limb can occur postoperatively after placement of a femoral artery telemetry device. Hind limb lameness can occur immediately post-surgery or develop over the course of several days. In this surgical case, the primate exhibited prolonged non weight bearing behavior in the post-surgery phase. In contrast, the remaining cohort returned to normal weight bearing in the immediate post-surgery phase. Pain assessment parameters supported veterinary assessment that this primate needed additional supportive care consisting of extended analgesia using NSAID administration and increased food enrichment. As other primates continued to recover and heal within normal limits, this primate became an outlier in the cohort. The animal was assessed consciously cage side and in a conscious restraint chair by facility veterinary staff. A temperature difference and increased rigidity of the left hind limb in the gastrocnemius muscle region was noted. Compromised vascular perfusion was thought to have contributed to this presentation. The decision was made by facility veterinarian in consultation with the study director to euthanize the primate and remove from study. Upon necropsy, it was noted that the gastrocnemius muscles were firm, enlarged and pale. In addition, an old and fully remodeled fibular fracture was observed that likely further contributed to compromised circulation due to scarring and thickening of the fascia around the muscles. Microscopically, diffuse necrosis of the gastrocnemius muscles from the affected left limb with congestion, hemorrhage, mixed inflammation and nerve fiber degeneration was observed that was consistent with ischemic injury due to ACS

NOTES

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Repeated Blood Sampling by the Saphenous Vein in Rodents

POSTER 1

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DRDC Suffield Research Centre

Introduction: Blood collection from rodents for research purposes is a common practice. Repeated blood sampling from the same animal is not a routine procedure but in certain studies is desirable as it allows for significantly less animals being used as well as decreasing variability in the results of the experiments. The blood collection procedure may cause stress due to handling, restraint or the use of anaesthesia. In this study, we used a minimally invasive procedure for taking multiple blood samples from the saphenous vein in rats over a 24h period.

Methods: Twenty male Sprague Dawley rats weighing 230-300g were used for this study. All were housed under controlled environmental conditions of light and temperature with food and water available ad libitum. The photoperiod was a 12 hour light:dark cycle. All procedures conducted during the dark period were done under a dim red light (<2 lux) and with the animals' eyes covered. The light intensity was measured using a light meter. Animals were handled at least 5 days prior to the start of the study to condition them to human contact and to reduce stress. All blood collection procedures were carried out by the same two highly trained laboratory technicians. Blood was obtained from the lateral saphenous vein and each animal given 2.5ml of saline subcutaneously following sampling as fluid replacement. The total blood volume collected did not exceed 15% of the animal's body weight. Blood samples were taken from each animal over a 24-hr period every 4 hrs during the day and night, alternating hind legs at each collection time. The day after the 24hr blood collection period, the hind legs of each animal were inspected for lacerations, swelling, and/or bruising and at this time the animal's mobility was assessed for any signs of pain or discomfort. The 24hr blood samplings were conducted 3 times with a 6-7d interval between collection periods. **Results:** None of the animals showed any adverse health effects from the multiple blood samplings from the saphenous veins. Several animals had faint red marks on one or both legs 24hr post -blood collections but after several days these marks were no longer visible. No deleterious effects were observed in mobility of any of the animals. Animal weights were taken throughout the study and found to be comparable to a standard of growth chart for this strain of rat.

Conclusion: This method of blood collection from the saphenous vein can be used for studies where repeated blood samples are required from the same animal at multiple time points. Advantages of this method of blood sampling include no use of anaesthesia or an invasive catheter or cannula; only gentle restraint of the animal is needed. Although the technique is fairly simple, the individuals performing the blood collection must be adequately trained to minimize stress to the animals.

Improving Efficiency of Small Animal Telemetry by Implanting Multiple Devices into One Subject

James Destefano
Merck & Co Inc

Radiotelemetry is routinely used to remotely monitor and collect data from conscious freely moving animal subjects while reducing confounding stress artifacts produced by manipulation and direct observation. Currently, in-house rodent telemetry models are implanted with one device designed to capture data specific to the research they support. We have designed a dual implanted rat model with the ability to collect all data currently captured using two separate models, thereby reducing animal, compound and space requirements. This model was used to investigate surgical feasibility and postsurgery complications caused by simultaneous implantation of HD-S10 and 4ET units from Data Sciences International (DSI). Our prototype enabled validation of two different platforms that have combined electroencephalographic (EEG) with cardiovascular (CV) parameters in rats and demonstrated proof of concept to enable future fit for purpose combined studies. Animals were subjected to seven separate studies using compounds and a control that have historical data in both CV HD- S10 rats and EEG 4 ET rats. RPC-3 receivers were employed to allow data to be captured from both devices and data binning was synchronized to 15 minutes. Data was analyzed independently and compared to historical data. Dual implanted animals demonstrated similar and expected dose response for all studies across CV and EEG platforms. These results indicate that this dual implant rat model is a viable design for independent studies as well as comprehensive risk assessment for programs where central and peripheral liabilities may exist.

Characterization of Multiple Ovarian Carcinoma Orthotopic and Metastatic Models and Response to Chemotherapy using Bioluminescent Imaging

POSTER 3

Debra Ferguson, BS, SRS
AbbVie Inc

Background: The cell lines ES-2 LMC, IGROV-1 LMC, and OVCAR-5 OT LMC were inoculated into mouse subcutaneously (s.c.), intraperitoneally (i.p.), or orthotopically. Subcutaneous models were followed by tumor volume measurement while i.p. and orthotopic models were followed using bioluminescent imaging.

Purpose: All animal studies were conducted in accordance with the guidelines established by internal Institutional Animal Care and Use Committees at AbbVie, Inc. (North Chicago, IL). Subcutaneous tumors were followed by tumor volume measurements, intraperitoneal and orthotopic models were followed by bioluminescence imaging. The standard of care docetaxel (60 mg/kg/day, i.v., once) was provided at time of group allocation. Pharmacokinetic levels at 1 and 24 hour timepoints were determined for both plasma and tumor levels in the subcutaneous model. The effect of treatment on tumor growth inhibition and tumor growth delay were determined as %TGI and %TGD. Significance for %TGI was performed by two-tailed Student's t-test. Significance for %TGD was performed by Kaplan Meier log-rank analysis. $P < 0.05$ was considered significant.

Methods: The standard of care (docetaxel @ 60 mg/kg/day, i.v., once) provided highly statistically significant efficacy across all engraftment sites, in all three ovarian carcinoma cell lines. Subcutaneous tumors were allowed to grow to approximately 200 mm³, while intraperitoneal and orthotopic models were allowed to surpass a mean flux of 1×10^8 absolute photon fluxes (photons/s/steradian/cm²), at which time mice were allocated by tumor volume or flux into study groups (n=8 mice/group) so that the mean tumor volumes, or mean flux, of the groups were statistically similar. Histological H&E, %pH3, and % Caspase-3 were run of the three flank tumor models at 1 and 24 hour post docetaxel treatment. Significant increase in pH3 positive cells was observed in all three cell lines at 24 hours, however, of the three cell lines, only ES-2 LMC showed a mild increase in caspase-3 at 24 hours. The most significant increase in %pH3 at 24 hours occurred in the cell line with the slowest growth rate (IGROV-1 LMC), while the least significant occurred in the fastest cell line (ES-2 LMC).

Conclusions: Over the past 10 years, bioluminescent imaging techniques have facilitated non-invasive imaging of many disease systems, including oncology. One aspect that has required further optimization is the use of such systems for more high-throughput evaluation of anti-tumor efficacy of therapeutic agents. Surgical and randomization techniques outlined within utilizing multiple ovarian carcinoma cell lines expand upon initial efforts in the field and characterize approaches enabling highly reproducible preclinical models for the evaluation of therapeutic candidates in clinically relevant tissues.

Citations: In conclusion, bioluminescence has enabled establishment of multiple orthotopic and metastatic preclinical models of ovarian carcinoma. Importantly, these well-characterized models demonstrate reproducible engraftment rates, metastatic dissemination patterns, and histological features consistent with clinical disease. In the future, such model systems will build off this initial characterization of docetaxel sensitivity to assess novel therapeutic agents, alone or in combination, with clinically approved agents.

Comparison of the Mechanical Properties of Two Fully-Absorbable Meshes

Darcy H. Gagne, ScM, SRS, CVT, RLATG

C. R. Bard, Inc. (Davol), Warwick, RI

Background: The objective was to evaluate mechanical properties of two fully-absorbable meshes: one comprised of poly-4-hydroxybutyrate (Phasix™ Mesh), and the other polyglycolic acid: trimethylene carbonate (Gore® Bio-A® Tissue Reinforcement) in a porcine model of open ventral hernia repair.

Purpose: Meshes (3.25 inch diameter circular patches) were bilaterally implanted in the retromuscular plane and fixated over suture repaired muscular defects (1 inch diameter) in n=12 female, Yucatan swine (n=3 animals/mesh type/time point; n=6 repairs/mesh type/time point). A single mesh type was implanted per animal, with meshes placed on either side of the midline. Mechanical burst testing was performed on non-implanted (T0) meshes and mesh/repair sites and native abdominal wall (NAW) tissue lateral to these sites at 12 weeks and 24 weeks post-implantation. Data were statistically analyzed using individual unpaired, two-tailed t-tests with Welch's Correction to compare repair strengths relative to T0, NAW, and between mesh types. Data are presented as mean ± standard deviation (p<0.05 was considered to be statistically significant).

Methods: The initial, non-implanted (T0) burst strength of Phasix™ was significantly greater than Bio-A® (Phasix™-T0: 200.6 ± 25.2N vs. Bio-A®-T0 119.8 ± 10.6N, p<0.0005), as was burst strength of mesh/repair sites at 12 weeks post-implantation (Phasix™-12wk: 271.4 ± 52.7N vs. Bio-A®-12wk 197.5 ± 56.8N, p<0.05) and 24 weeks post-implantation (Phasix™-24wk: 317.1 ± 85.6N vs. Bio-A®-24wk 135.1 ± 88.7N, p<0.005). Both meshes exhibited significantly greater mesh/repair strength at 12 weeks compared to the NAW (Phasix™-12wk: 271.4 ± 52.7N vs. Phasix™-NAW (12wk): 70.5 ± 11.5N, p<0.0005 and Bio-A®-12wk 197.5 ± 56.8N vs. Bio-A®-NAW (12wk) 72.1 ± 21.0N, p<0.005). Only defects repaired with Phasix™ were significantly greater than NAW at 24 weeks (Phasix™-24wk: 317.1 ± 85.6N vs. Phasix™-NAW(24wk): 86.4 ± 33.0N, p<0.005). Defects repaired with Bio-A® were not significantly different than NAW at 24 weeks post-implantation (Bio-A®-24wk 135.1 ± 88.7N vs. Bio-A®-NAW (24wk) 92.9 ± 18.7N, p>0.05).

Conclusions: Phasix™ Mesh demonstrated significantly greater T0 mechanical strength and significantly greater mesh/repair strength at 12 and 24 weeks post-implantation, compared to Bio-A® in a porcine model of open ventral hernia repair. At 12 and 24 weeks, defects repaired with Phasix™ were 3.8x and 3.7x stronger, respectively, than NAW. By 24 weeks post-implantation, defects repaired using Bio-A® were not significantly greater than NAW.

Citations: At 12 and 24 weeks, defects repaired with Phasix™ were 3.8x and 3.7x stronger, respectively, than NAW. By 24 weeks post-implantation, defects repaired using Bio-A® were not significantly greater than NAW.

A Novel Vascular Access Button Connection Using Combined Technologies While Allowing for Social Enrichment by Pair Housing

POSTER 5

Amy Hehman, LAT
Incyte Corporation

Traditional practice has been to single-house vessel-cannulated rodents post-surgically to protect exposed exteriorized catheters. A port /protective cap model is currently available that allows for pair and group housing of cannulated animals and is compatible with a harness/swivel automated blood sampling system. Our goal was to develop a vessel cannulated surgical model that could be socially housed and would be compatible with response movement caging. To do this, we modified the automated blood sample connection to be compatible with the available port/protective cap system. A sterile custom connector was designed in collaboration with an industry vendor. Animals were dual jugular cannulated using the available port/protective metal cap to allow for pair or group housing. The newly designed custom connector was primed and attached to the port after removal of the protective metal cap. The modified connector allows the standard extension line from the response movement caging system to easily connect for blood sample withdraws. Studies were conducted using our standard in-house study design for pharmacokinetic studies with multiple blood sample collections out to 24 hours post dose. All dosing and blood sample collections were performed in accordance with an IACUC approved animal use protocol. The end result is a connector that allows for dosing and timed collections of high quality blood samples using a response movement caging automated blood sampling system. The modified connector further allows for enhancement to the welfare of the animals by providing social enrichment through pair and group housing without compromising the integrity of the surgical model.

A Utilitarian Model of Transplant Rejection

POSTER 6

Connie Kliwinski, MLAS, LATg, SRS
Janssen Pharma. Co. of J&J

Animal models provide an important means to investigate transplant rejection and immune responses affecting graft tolerance. While many transplant models exist utilizing a variety of species and organs, they can be time-consuming, invasive, technically challenging, and cost-prohibitive. In contrast, tail skin transplantation in the mouse may be the most efficient allograft rejection model available in terms of preparation, clinical assessment, and immune cell phenotyping. As many as three grafts can be transplanted per mouse tail allowing for a test graft, as well as positive (syngeneic) and negative (allogeneic) controls. Grafts are positioned with hair growth in the opposite direction of the recipient for ease of identification as healing occurs, which is particularly helpful when donor and recipient skin are of similar color. Grafts are protected by a glass tube during initial healing (4-6 days), thereby eliminating the problematic process of bandaging typically necessary with skin transplants. Rejection is tracked by visual monitoring and scoring (- or +) to indicate rejection. At study end, spleens and draining lymph nodes (dLNs) can be evaluated by fluorescent activated cell sorting (FACS) to determine T-cell activation protein percentages. Allografts typically reject within two weeks; syngeneic grafts may survive indefinitely; and test graft survival will depend upon the treatment protocol. Cells detectable in spleen and dLNs will be study dependent. By making adjustments to existing methods we established an efficient, reproducible model of transplant rejection which may be useful for studies dealing with immune-modulatory questions.

Surgical Approach to Creating an Adjustable Fractional Flow Reserve (FFR) in a Pig for MRI Perfusion Studies

POSTER 7

Shawn Kozlov, LATG

NHLBI/ASR

Fractional flow reserve (FFR) is defined as the ratio of blood pressure distal to a coronary artery stenosis divided by the pressure proximal to the stenosis during maximum coronary blood flow as typically induced by adenosine. In order to validate quantitative cardiac perfusion measurements using cardiac MRI (magnetic resonance imaging) in the presence of experimentally controlled coronary artery stenosis and different severities of FFR, an approach was needed that would allow for the monitoring of the pressure both distal and proximal to a stenosis along with a way to create and adjust the stenosis. The proximal arterial pressure was measured through a left carotid catheter placed either percutaneously or by performing a cut down. To obtain the distal pressure and stenosis, the pig was placed in dorsal recumbency and a midline sternotomy was performed to gain access to the ventral portion of the heart. The ideal location for the stenosis was determined to be below the first diagonal branch off the Left Anterior Descending (LAD) coronary. The tissue around the LAD was bluntly dissected and a 4mm balloon occluder was placed around the vessel. After placement of the balloon occluder, a site distal to the occluder was identified using the distance from the occlusion as the reference point. This was critical in order to prevent the occlusion of the distal pressure catheter. It also allowed for secure placement of the catheter via the hub with suture to the right ventricle to minimize the ischemia to the distal left ventricle. With a suitable site for catheter placement identified, the connective tissue and fat superior to the vessel were dissected away and a 24G angiocath was inserted into the vessel. Several drops of tissue adhesive were then used to hold the catheter in place while it was sutured to the right ventricle. The catheter hub was connected to the male end of pressure tubing that was tunneled through the chest wall to prevent pulling on the catheter. The chest was then loosely closed with suture and the animal transported to MRI. The balloon occluder was inflated to decrease the flow through the LAD until a decrease in the distal pressure measurement through the 24g angiocath decreased to the desired pressure for the experimental perturbation. This approach was successfully used in over twenty simultaneous MRI and FFR experiments lasting six to eight hours. All animals were euthanized while under general anesthesia at the end of the experiments and hearts were removed for histology.

Modeling Endovascular Therapeutic Hypothermia in Rats

POSTER 8

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Background: Hypothermia is the most potent protective therapy available for cerebral ischemia with endovascular approaches showing the most promise. Available animal models incorporate surface cooling methods that are slow, and do not allow for precise control of the target temperature. To address this need, we developed a rapid, simple, inexpensive model for inducing hypothermia using a perivascular implanted closed-loop cooling circuit for precise control of the target temperature.

Purpose: All the procedures were performed as per the IACUC guidelines. Briefly, adult male Sprague Dawley rats (n=14) weighing 290-310g were anesthetized with 4% isoflurane in 70% N₂O and 30% O₂. After surgical prep of the abdomen and a 0.4mg/kg carprofen subcutaneous injection, a midline incision was made and a previously prepared, sterile perivascular cooling circuit was positioned under the abdominal contents so that it was in close proximity to the large abdominal vessels (aorta and vena cava). The abdominal incision was closed after the long sections of the tubing were tunneled around to the nape of the neck. Buprenorphine at a dose of 0.05mg/kg was administered during recovery. One week later, the rats were subjected to a 4 hour middle cerebral artery occlusion followed by either 4 hours of cooling to 32°C (n=7) or 4 hours of 37°C (n=6) as measured by an implanted probe in the temporalis muscle.

Methods: All animals had returned to within 99.52±2.99% (Mean ± SD) of their pre-surgical weight at the time of hypothermia. One rat aggressively chewed at his abdomen and required euthanization 24hrs after implant surgery. Temporalis temperatures ranged from 35.4-37.4°C for all animals at the start of reperfusion and hypothermia. It took 13±1.07 minutes (Mean ± SE) to reach target temperature which equates to a rate of about 0.3°C/minute. For the first 15-20 minutes of the cooling period, the animal's innate thermoregulation resisted lowering the body temperature and tried to maintain homeostasis. Tweaking of pump speed was sufficient to achieve and maintain the desired temperature. After the target temperature was achieved, we were able to tightly regulate this temperature to within ±0.09°C.

Conclusions: The advantage of the perivascular approach for cooling animals is that the technique is powerful and cools the animal to target temperature much more quickly than surface cooling. Perivascular cooling allows more precise control of core body temperature than surface cooling and eliminates the stress response elicited by surface cooling.

Citations: A simpler cooling approach potentially could open the research field to more labs that don't have the time or money to invest in the complex telemetry and cage system required for servo-controlled surface cooling with computer controlled fans and misters. A perivascular cooling model would allow more rapid translational studies of the optimal depth, delay and duration for therapeutic hypothermia because the model simulates both the rapid cooling and the anesthetic treatment typical of human endovascular cooling techniques. More rapid and precise cooling may allow for more detailed studies of the optimal approach to designing therapeutic hypothermia.

Evaluation of Bone Healing, Biocompatibility, and Safety with a Photodynamic Bone Stabilization System in Rabbits

POSTER 9

Amanda L. McSweeney, BS, RLATG, SRS
CBSET, Inc.

Bone healing, biocompatibility, and safety employing a photodynamic bone stabilization system (PBSS), comprised of an inflatable balloon filled with photopolymerizable liquid monomer, was evaluated. Radiologic and histopathologic assessment showed abundant bone healing and progressive callus remodeling over 6 months with PBSS implants in fenestrated femoral cortices of New Zealand white rabbits. In additional rabbits, PBSS implants in brushed and saline-aspirated femoral intramedullary spaces elicited no adverse, local or systemic responses and displayed similar biocompatibility to K-wires in contralateral femurs up to 1 year post-implant. Simulated clinical failures up to 1 year were performed in other rabbits with intramedullary space exposure to PBSS components: liquid monomer or light hardened polymer. PBSS monomer leaked into intramedullary spaces were remediated or negated by light polymerization, resulting in histopathology indistinguishable from sham procedures. PBSS polymerized material displayed cortical bone and vasculature effects comparable to mechanical disruption of the endosteum. In a clinically unlikely scenario with no remediation or polymerization, a high dose monomer injection resulted in marked necrosis of cortical bone, as well as associated vasculature, endosteum, and bone marrow. Overall, when polymerized and hardened within bone intramedullary spaces, this light curable monomer system may provide a safe and effective method for fracture stabilization.

AN IN VIVO EVALUATION METHOD FOR COMPARING DISTAL TIP SEALING ABILITY OF SURGICAL DEVICES

POSTER 10

Mary Mootoo, BBA, AS, SRS

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Background: The hypothesis was that the base of the mesentery in larger pigs could be used to compare distal tip sealing ability with surgical devices as bleeding is typically seen from this area when sealing and transecting through thick tissues.

Purpose: All aspects of this acute study were performed in accordance with an IACUC approved animal research protocol. The procedure was performed with the pigs under general anesthesia. The pigs were anesthetized with an injection of a Telazol/Xylazine mixture (100mg/ml each drug, dose of 5mg/kg) and Glycopyrrolate (dose 0.01mg/kg) intramuscularly. After anesthetic induction, the pigs were intubated and maintained on inhalation anesthesia (Isoflurane in oxygen). Lactated Ringers Solution was delivered intravenously for the duration of the procedures. Blocks of four and then paired transections were performed in five porcine models to compare a currently marketed bipolar device to an advanced bipolar device in development. The transections were performed in the base of the small bowel mesentery, adjacent to the lymph nodes, in animals weighing 150 +/- 20 pounds. The applications were started near the cecum and were performed marching cranially along the base of the mesentery until the tissue was exhausted. Two devices were used in each group over the course of the study. Tissue thickness was measured prior to each transection. Upon completion of the transection, hemostasis at the distal tip was evaluated as Yes or No. The density of the vessels in the thick base of the mesentery tissues does not allow the operator to visibly place individual vessels completely within the jaws of the device. Therefore, lack of distal tip sealing with the device will result in bleeding.

Methods: No differences in performance (Test of Proportions, $p = 0.311$) were seen between the two advanced bipolar devices in development that were used in the study. A statistical hemostatic difference (Test of Proportions, $p = 0.000$) was demonstrated between the advanced bipolar device in development and the currently marketed bipolar device. For the currently marketed bipolar device, hemostatic failure (distal tip bleeding) increased linearly as tissue thickness increased. This was not true for the advanced bipolar device in development.

Citations: This is a viable evaluation method for distal tip sealing that can be used to compare and contrast devices.

chewed at his abdomen and required euthanization 24hrs after implant surgery. Temporalis temperatures ranged from 35.4-37.4C° for all animals at the start of reperfusion and hypothermia. It took 13±1.07 minutes (Mean ± SE) to reach target temperature which equates to a rate of about 0.3C°/minute. For the first 15-20 minutes of the cooling period, the animal's innate thermoregulation resisted lowering the body temperature and tried to maintain homeostasis. Tweaking of pump speed was sufficient to achieve and maintain the desired temperature. After the target temperature was achieved, we were able to tightly regulate this temperature to within ±0.09C°.

Conclusions: The advantage of the perivascular approach for cooling animals is that the technique is powerful and cools the animal to target temperature much more quickly than surface cooling. Perivascular cooling allows more precise control of core body temperature than surface cooling and eliminates the stress response elicited by surface cooling.

Citations: A simpler cooling approach potentially could open the research field to more labs that don't have the time or money to invest in the complex telemetry and cage system required for servo-controlled surface cooling with computer controlled fans and misters. A perivascular cooling model would allow more rapid translational studies of the optimal depth, delay and duration for therapeutic hypothermia because the model simulates both the rapid cooling and the anesthetic treatment typical of human endovascular cooling techniques. More rapid and precise cooling may allow for more detailed studies of the optimal approach to designing therapeutic hypothermia.

A METHOD OF MAGNETIC RESONANCE IMAGING TO CHARACTERIZE CARDIAC PERFORMANCE IN A YUCATAN HEART FAILURE MODEL

POSTER 11

Laura Pook, SRS
North American Science Associates

Background: Myocardial Infarction (MI) preceded by Coronary Artery Disease (CAD) is the most common contributing factor to heart failure. The development of therapies to treat heart failure rely upon an adequate animal model that translates to the human condition. **Purpose:** The objective of this study was to develop a method of magnetic resonance imaging to assess cardiac performance in a Yucatan heart failure model, with the goal of refining imaging techniques and to characterize the infarct and remodeling associated with balloon occlusion.

Methods: In this study, a total of 6 Yucatan pigs underwent surgical induction of a MI. Cardiac MRI was performed for morphology and function prior to surgical MI procedure (n=6) and approximately 130 ±7 days post-MI on a 1.5T mobile system (Siemens Med Systems, Erlangen, Germany). On the day of the imaging procedures, the pigs were sedated/anesthetized with an intramuscular injection of Telazol (2-7 mg/kg) and maintained using isoflurane (0.5-3% mixed in oxygen). Imaging was performed without (baseline) and with (terminal) contrast. For measurement of LV function and mass, free breathing gradient echo images were obtained in short axis orientation using prospective ECG gating (n=5) and prospective peripheral gating (n=1) with the following scan parameters: slice thickness 7mm, no gap, field of view 250X360X70, matrix 111x256, flip angle 30degrees, TR 33 and TE 4.0. Phases were 18 per slice with 3 averages. Post infarct imaging for morphology and function study were repeated with these same parameters. Infarct imaging was performed 10 minutes post gadolinium injection (0.2mmol/kg) with the available DE sequence. Analysis of images was performed for LV function, mass and % infarct size. Scanner limitations prevented retrospective gating for image acquisition. Analysis was performed using basic descriptive statistics (ex: mean, standard deviation, change from baseline).

Conclusions: Pre and post-infarct MRI procedures were successfully performed in the Yucatan model. Multiple adjustments to the typical clinical scan parameters were performed with the methods outlined above being adequate to translate to the animal model. Overall, this study successfully defined MRI methods in a Yucatan heart failure model for future development studies to evaluate therapies that translate to the human condition.

Effects of Fentanyl on Pain and Motor Behaviors Following an Induced-Intracerebral Hemorrhage in Rats

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Background: Traumatic brain injury (TBI) is one of the major causes of invalidity in our society and its most common sequela is an intracerebral hemorrhage (IH). In this condition there is a paucity of treatments to support an appropriate analgesia. The current study aims to assess pain and motor behaviours following different doses of fentanyl on an IH rat model, and to evaluate the associated histopathology. Fentanyl was chosen for this study, because it is the most widely used analgesic to relieve pain associated with TBI. The optimal goal would be to maximize analgesic use to relieve pain for IH patients without causing any motor or cognitive deficits.

Purpose: Twenty-one male Sprague-Dawley rats underwent a stereotaxic surgery to produce a collagenase-induced IH. The control group (n=6) received saline SC, and the experimental groups received 5 (n=6), 10 (n=6), and 20 (n=3) $\mu\text{g}/\text{kg}$ of fentanyl SC, 2h following surgery and on the 2 subsequent days. Only 3 animals received 20 $\mu\text{g}/\text{kg}$ because this dose caused catalepsy for 15-20min following the injection. The rat grimace scale was used to evaluate pain behaviour prior to and following the injection starting 24h following the surgery. A neurological exam, balance beam test and rotarod test were performed for 5 days postoperatively, starting 48h following the surgery. At the end of the experimentation, brain tissues were evaluated to determine the hematoma volume, number of reactive astrocytes and necrotic neurons.

Methods: When compared to controls, the grimace scale showed that 5 $\mu\text{g}/\text{kg}$ of fentanyl significantly alleviated pain on day 2 only ($p<0.01$) and that 10 $\mu\text{g}/\text{kg}$ of fentanyl alleviated pain on days 1 ($p<0.01$), 2 ($p<0.001$), and 3 ($p<0.01$). For the rotarod test, only the 10 $\mu\text{g}/\text{kg}$ group showed significant decreases in performance on days 5 ($p<0.05$) and 6 ($p<0.02$). The neurologic exam was not significantly different between groups, but the hopping test showed a poor recuperation for the 10 $\mu\text{g}/\text{kg}$ fentanyl group when compared to controls ($p<0.01$) that was not present for the fentanyl groups. No differences were found between groups for the balance beam test and the histopathological results. The results for the 20 $\mu\text{g}/\text{kg}$ animals are similar to the animals receiving 10 $\mu\text{g}/\text{kg}$ fentanyl group.

Conclusions: Fentanyl administered subcutaneously at 10 $\mu\text{g}/\text{kg}$ provides a substantial and safe analgesia in the IH rat model on the first days following the insult. However the lesser amelioration on the rotarod and the hopping test both indicate that 10 $\mu\text{g}/\text{kg}$ fentanyl affected motor performance on subsequent days. No cellular differences suggest a functional change of synaptic efficacy.

Citations: This study shows that fentanyl, at a sufficient dose, can provide substantial analgesia to relieve IH pain in rats on the first days following the insult, however motor performance may be affected for a longer period of time.

Comparison of Buprenorphine Post-Operative Pain Medication Delivery by Injection and Self-Medicating Gel

POSTER 13

Chang Zou, BS, RLATg

Pfizer

Oral self-administration of post-operative buprenorphine analgesic is a potential refinement that minimizes the negative effect of frequent handling and provides a more stable level of analgesia over time. In addition, self-administration of analgesia minimized the labor resources associated with post-operative care management. The purpose of this study was to compare the buprenorphine's analgesic effect of oral self-administration of buprenorphine in sucralose gel versus the traditional twice daily subcutaneous (SC) injection in mice after a transverse aortic constriction (TAC) procedure. Thirty C57BL/6J female mice between the ages of 8 to 10 weeks old had undergone TAC procedures. Just after Isoflurane induction, all 30 animals received Meloxicam SR injection SC (4 mg/kg) as well as one injection (0.1 mg/kg) of buprenorphine SC. Animals were then divided in 2 groups. Fifteen animals (14 TAC + 1 Sham) received SC twice daily (BID) injections of buprenorphine (0.1 mg/kg) and a daily portion (15 mL per cage) of fresh, non-medicated, sucralose gel for 4 days post-surgery. The other 15 animals (14 TAC+1 Sham) received a daily portion of fresh sucralose gel mixed with buprenorphine (15 mL per cage, 0.005 mg/mL) ad lib as a 'self-medicating' administration for 4 days post-surgery. The animals were monitored daily for the first week post-surgery. Every morning, gel consumption, body weights and Grimace Scale pain scores were captured to assess animal's recovery. There were no significant differences in pain scoring, body weight loss and daily gel consumption between animals that received the SC injection of buprenorphine and the animals that received the self-administered buprenorphine gel. There were tradeoffs for both methods of buprenorphine delivery. The injection delivery provided a precise, known and controllable dose of buprenorphine. However, it required twice a day injections which were more labor intensive and stressful for the animals. Also, Buprenorphine SC duration of action in mice last about 3 to 5 hours, so more frequent injections should be consider but labor resource necessary to perform injection 3-4 times a day was a limiting factor to implement such analgesia regiment. The medicated sucralose gel alleviated the stress related to restraining, minimized the disturbance of mice and offered a continuous pain medication regiment. However, the amount of pain medication each animal consumed had high variability and was difficult to accurately assess as mice were housed socially, and gel weights data were affected by environmental factors such as evaporation and cage debris. This method also drastically increased the amount of buprenorphine required for analgesia purposes. In conclusion, oral self-administration of post-operative buprenorphine analgesic was able to provide a similar level of analgesic to buprenorphine SC BID and was an adequate method of pain medication administration for mice that underwent TAC procedures.

Evaluation of Large Biodegradable Stents in Porcine Model of Aortic Coarctation

POSTER 14

Matthew Riegel

Background: Biodegradable stents (BDS) could impact management of congenital heart disease (CHD). Novel double opposing helical (DH) BDS made of Poly-L-Lactic Acid have the potential for use in CHD. Study aims were: 1. Create a model of coarctation of aorta (CoA) in a growing minipig. 2. Evaluate feasibility of large DH BDS implantation to treat CoA and 3. Assess short term vessel/stent patency and vessel inflammation.

Methods: Five newborn Yucutan minipigs (5-7kgs) underwent surgical CoA creation with a pledgeted suture technique via lateral thoracotomy. After 2 months, 10 and 12 mm diameter DH BDS were implanted to treat CoA. BDS were evaluated with angiography, intravascular ultrasound (IVUS) and histopathology at 2 months follow up.

Results: All 5 animals had CoA successfully created (angiography and IVUS) and survived the thoracotomy. Three DH BDS implantations were successful via femoral (2) and carotid (1) arterial access. Two animals died from vascular/bleeding complications at the stent implantation procedure. Unfortunately 1 survivor died within 24 hours from femoral access site bleeding complications. The 2 survivors at 2 months post BDS implantation showed good stent apposition on IVUS and angiography with luminal patency and mild neointimal proliferation. Histopathology showed complete endothelialization of stent material.

Conclusion: A technique of CoA creation is described in growing minipigs. Intervention with DH BDS with diameters up to 10-12mm is feasible but procedural risks need to be reduced. Further studies are needed to evaluate long-term stent performance and vessel appearance during/with degradation.

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