THE 29TH ANNUAL MEETING

of the

Academy of Surgical Research

September 26–28, 2013

Clearwater Beach, Florida – Sandpearl Resort

The 29th Annual ASR Meeting will include presentations on new and refined methods and materials used in preclinical and clinical surgical investigations, as well as new procedures that will enhance the attendees' fields of scientific and surgical research. Renowned academic and industry experts will share cutting-edge surgical concepts, research, and techniques, thereby fostering an interdisciplinary transfer of ideas and theories in experimental surgery.

Meeting attendees will have the opportunity to engage in dialogue 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.

Learn about surgical research and surgical challenges in areas including

- Organ transplant surgery
- Long-term vascular access/infusion
- Medical device implantation/surgical/orthopedic models
- Surgical techniques
- Surgical research
- Cardiovascular surgery
- Minimally invasive surgery (MIS)

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Registration Hours

Thursday September 26	7 am – 5 pm
Friday September 27	7 am – 5 pm
Saturday September 28	7 am – 12 pm

Wednesday , September 25

ASR Board Meeting	3 – 5 pm

Thursday, September 26

Light Grab and Go Breakfast for Wetlab Attendants and Exam Participants	6:30 am
Bus Departs for Wetlabs (front of hotel)	7 am
ASR Examinations	**8 am – 12 pm**
Wetlab #1-3	**8 am – 12 pm**
**Pizza will be served to am attendees*	
Buses Depart from Hotel to Wetlab #4-7	12 pm
Buses Depart from Wetlab #1-3 Return to Hotel	1 pm
Wetlab #4-7	**1 – 5 pm**
Buses Return to Sandpearl from Wetlabs	5 pm
Welcome Reception	**4:30 – 7 pm**

Friday September 27

Continental Breakfast and Poster Set-up	7 – 8 am
Opening Remarks	8 – 8:15 am
Poster Hanging	8:30 am
Keynote Speaker	**8:15 – 9:15 am**
Podium Sessions	9:15 am – 12 pm
Lunch	12 – 1 pm
Keynote Speaker	**1 – 2 pm**
Podium Sessions	1 – 5 pm
Poster Judging	5 pm
Wine and Cheese Reception with Exhibitors	**5 – 7 pm**
Posters Take-down	**7 – 8 pm (no later than 8 pm)**

Saturday September 28

Continental Breakfast	7 – 8 am
Opening Remarks	8 – 8:15 am
Keynote Speaker	**8:15 – 9:15 am**
Podium Sessions and Drylab (10:20-11:30AM)	9:15 – 11:30 am
Guest Speaker	11:30 am – 12:30 pm
Awards Luncheon	**11:30 am – 1:20 pm**
Podium Sessions and Surgical Writing Workshop	1:30 – 3 pm
Adjourn	3 pm
Board of Directors Meeting	**3 – 3:45 pm**

WELCOME

Welcome to Clearwater Beach!

It is a great pleasure to welcome our members, speakers, test takers, vendor sponsors, corporate guests, and new attendees to this wonderful waterside setting and to the 29th Annual meeting of the Academy of Surgical Research.

Each year a large team of volunteer members collects ideas and suggestions from the membership and laboriously crafts them into our annual meeting. They contribute personal support and countless hours toward making these meetings interesting, educational, and informative for each of us. My thanks go out to all of you for contributing your thoughts and support in so many ways that make this meeting possible. My special appreciation goes out to the members of the program committee and to our Program Chair, Nance Moran, who was a vital part of forming this year's meeting content.

The Academy has a long history of bringing surgical knowledge and new surgical methods to those who attend. While you are here at the meeting please do not hesitate to share your thoughts, opinions, and ideas with the board members and with other attendees. This live peer to peer cross fertilization of thoughts and perspectives is what has served to make this meeting uniquely valuable to it's attendees over the years. It has been my pleasure to make new contacts and wonderful lasting friends each time I have attended this meeting. I wish you the same success. I am personally confident that you will leave the meeting with new enthusiasm for your profession and with useful new ideas for advancing your skills.

It has been an honor for me over the years to serve the Academy on the board and in a number of different positions. It has been a special privilege this past year to participate as President. I invite each of you to join the group of member volunteers that contribute their time and effort to make this academy a functional reality. Their effort and your input are what makes this society relevant and valuable for all of us.

My best wishes for a wonderful and productive meeting.

Steven W. Hachtman

Steve Hachtman
President, ASR

Steve Hachtman, BA, MA is currently founder of Science Health and Technology where he is working part time as a medical device and life science technology marketing consultant. Previously he worked at Data Sciences International for 16 years. At DSI he served in several managerial roles: Director of Applications Development, Director of Education, Vice President of Business Development, and Vice President of Sales. In these roles he coordinated scientific meetings, managed trade shows, initiated educational events, coordinated world wide user groups, conducted staff trainings,established industry partnerships, and hired/trained the growing sales team.

He has a 25-year background in management of emerging technologies and new medical devices. He has held positions as President of Acculife International, an intra vascular stent company, at Schneider USA as Senior Product Manager for guide wires and stents, and as VP of Sales and Marketing at Everest Medical developing and marketing bipolar electrosurgery devices. He also worked at United States Surgical Corporation where he spent 10 years in sales, market research, sales training, surgical education, and product development of innovative mechanical wound closure devices.

Prior to his career in industry he worked as a college teacher and clinical psychologist. He studied electrical engineering at Ohio University and later earned his undergraduate psychology degree and his master's degree in experimental psychology at Adelphi University in New York. He is published in text books, trade journals, and scientific periodicals. Over the past 17 years he has presented on wireless physiological monitoring at numerous meetings and educational seminars around the world.

He is a member of a number of scientific societies, serves on the board of the MN AALAS, and participates on several IACUC's. He considers himself a contributing activist for advancing scientific methodology, improving animal welfare, and moving forward the life sciences in our world. For the past decade he has served on the board of the ASR in various roles and has enjoyed the close support of his peers in his current role as President for 2013.

He has served as a BSA Scoutmaster for over 25 years and is currently enjoying studying Spanish while working with an inner city Minneapolis Hispanic troop.

BOARD OF DIRECTORS

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PROGRAM COMMITTEE

Program Chair

Nance Moran, MS, BLA, SRS, RLATg, is a Staff Scientist at a successful biotechnology company where she has investigated therapies for degenerative orthopedic diseases of the joint and spine for over 11 years. Nance served in small animal practice for 7 years after achieving a degree in Veterinary Technology at Becker College in Leicester, and finally a Master's degree in Biology. Nance has further interests in teaching, leading a Science Kids program with over 120 students, ecology, and areas of companion animal behavioral psychology and training. For the past several years she has enjoyed chairing the Communications Committee along with some great team members and most recently serving as Liaison on the Board of Directors. She has had the opportunity to help within other great teams to develop and establish the Surgical Savvy Newsletter, as well as the all-new free webinars offered to our ASR members to help in achieving further education and standardization of good surgical practices. She has enjoyed working with all of the ASR board members as well as our individual members and was asked to chair the 2013 ASR program. She enjoys being approached with a challenge and invites constructive critique, as it will only strengthen our organization and validate the worth of all of our members. She believes in sharing information and peer education. As Liaison Officer, she hopes to emphasize these values and strengths while promoting collaboration and involvement by all. Nance endeavors to represent the qualities of the organization to the best of her abilities and to help our members understand the value of their contributions to research and one another. So please enjoy the meeting that so many volunteers have contributed to in bringing our members together!

Program Committee

Heather Bogie, *Wetlab Leader*
Christina Gross, *Wetlab Co-leader*
Margi Baldwin, *USF Liaison*
John C. Resendez, *Abstract Committee Leader*
Tracy Ziegelhofer, *Abstract Committee Co-leader and Session Facilitator Lead*
Tim Edwards, *Poster Committee Leader*
Stacy Porvasnik, *Poster Committee Co-leader*
Ken MacLeod, *Exhibitor Committee Leader*
Tom Long, *Exhibitor Committee Co-leader*
Matt Ruiter, *Exhibitor Committee Co-leader*
Luis Toledo-Pereyra, *JIS Editor*
Randy Pielemeier
Vince Mendenhall
Szczepan Baran
Michele Danielson
April Lindon
Karen Brocklehurst
Mary Jane Perkins
Steve Hachtman
Justin Prater
Lisa Yoder

Event Organizer and ASR Management

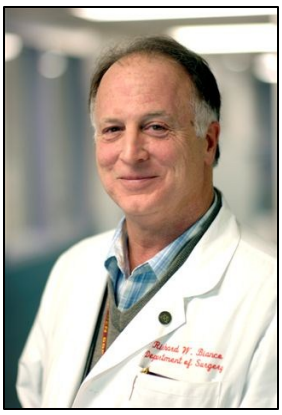
Kathi Schlieff, Association Solutions Inc
Jim Manke, Association Solutions Inc

Keynote Speaker

Gloria Matthews is a Senior Director and Head of Orthopaedic/Regenerative Medicine Research and Early Development at Genzyme, a Sanofi company. She received both her DVM (1993) and PhD (2001) from Cornell University and became board certified by the American College of Veterinary Surgeons (1999) following an equine surgery and sports medicine residency at Tufts University. During her 10 year tenure at Genzyme, Dr. Matthews has been involved in clinical and preclinical development and/or post-market support of cell, gene, growth factor and biomaterial based products for orthopaedic and rheumatologic indications, including Carticel®, MACI®, Synvisc®, and Synvisc One®. Areas of active research include cell and molecular biology of osteoarthritis and cartilage repair as well as orthopaedic imaging.

Most recently she has directed her research organization toward a focus on the role of bone in development and perpetuation of osteoarthritis pain as well as in the pathophysiology and natural progression of focal chondral defects. The group routinely leverages collaborations with internal and external partners while evaluating external business opportunities in an effort to solve the preclinical and clinical challenges of therapeutic development in this space. Dr. Matthews has received the American College of Veterinary Surgeons Research Publication Award, the Samuel F. Scheidy Memorial Award, administered by the American Veterinary Medical Foundation, a Phi Zeta Research Award, and best research/best poster awards at New England Baptist and Cornell University Research Symposia. Dr. Matthews sits on the Board of Directors for the Orthopaedic Research Society, for which she chairs the Executive Finance Committee as Treasurer. She also serves on the NIH SBIR Scientific Review Group/Grant Review Committee (study section), the Strategic Alliance Committee of the Osteoarthritis Research Society International, the Executive Committee of the fNIH Osteoarthritis Biomarkers Working Group, and the Musculoskeletal Committee of the American Society for Gene and Cell Therapy.

Keynote Speaker



Richard W. Bianco is Director of Experimental Surgery and Associate Professor of Surgery at the University of Minnesota. He has 30+ years of experience in the management of Experimental Surgical projects and has authored numerous refereed journal articles and book chapters on the topics of animal model development and the assessment of new or modified medical devices with a major emphasis in the area of cardiovascular prostheses. His particular research interest is in the development of accurate and humane animal models that predict safe clinical performance and efficacy Experimental Surgery at the University of Minnesota is the premier GLP facility in the world and is recognized both domestically and internationally as the leading facility conducting pre-clinical safety evaluations.

Professor Bianco has served on various committees of the International Standards Organization (ISO) and is currently is expert member of several working groups and sub-committees including Animal Welfare, Cardiac Valves, and Vascular Grafts (Co-Chair).

Finally , Professor Bianco has been a national leader in promoting the humane use of animals in medical research and has served on the Boards of both the National Organization for Biomedical Research (NABR, Americans for Medical Progress (AMP), and the National Marine Mammal Advisory Board).

Keynote Speaker

Dr. Wayne McIlwraith obtained his veterinary degree from Massey University, New Zealand, was in practice in New Zealand and the UK for 3 ½ years followed by an internship at the University of Guelph, Canada and a surgical residency at Purdue University. He also obtained MS and PhD degrees from Purdue University. Since 1979 he has been a faculty member at Colorado State University. Currently he is a University Distinguished Professor, holds the Barbara Cox Anthony University Endowed Chair in Orthopaedics and is Director of the Orthopaedic Research Center. He also directs the Musculoskeletal Research Program which is a CSU Program of Research and Scholarly Excellence. He also has a referral surgical practice in Southern California as well as Seattle and is a consultant and surgeon for clients in Ireland, England and France.

Dr. McIlwraith has published over 350 scientific papers and book chapters and five textbooks. Honors include doctoral degrees (honoris causa) from the University of Vienna, Purdue University, Massey University, the University of Turin and the University of London, the Tierklinik Clinic Hochmoor Award in Germany, the Founders Award for Lifetime Achievement from ACVS, the Frank Milne Lecturer from AAEP, and the Hickman Award in Orthopaedics from the British Equine Veterinary Association. He is also a Diplomate of the American College of Veterinary Surgeons, the American College of Sports Medicine and Rehabilitation and the European College of Veterinary Surgeons.

Guest Speaker

John Belluardo spent most of his business career with two companies, first with the NCR corporation where he worked many years in field engineering, sales and product development. A milestone at NCR was working with Paul Allen and Bill Gates at a then small computer company in Albuquerque, NM by the name of Altair Computer (Paul & Bill then started a new company called Microsoft). John then designed the communications extensions to the "Basic" programming language that were later adopted by both Microsoft and IBM. In 1981 he left NCR and formed his own company (BASS, INC.) were he designed and manufactured the first portable wireless bar code scanning system for the supermarket industry.

The company grew very rapidly and provided a comprehensive suite of applications to retailers large and small from regional retailers like King Kullen, in New York, to international retailers like Walmart. He was later plagued with heart related health issues and decided to sell the company and devote his time to researching heart disease and a complete life style change. John started to run and has completed many Marathons and half Marathons. He continues to run today, but now primarily on trails, and avoids pavement when possible. Barbara, his wife of 48 years enjoys accompanying me on long distance bike rides. When not running he trains on a daily basis at a number of local gyms. He serves on the advisory board of his local recreation center. He has had two open heart surgeries, the first in Dayton in 1993 where he had 5 bypass grafts installed on his heart and the second at the Cleveland Clinic were 2 more grafts were installed and his bicuspid aortic valve (congenital defect) was replaced with a human donor valve provided by a young man killed in a car wreck. It is an incredible story and he is willing to share, just ask him during this time in Clearwater… The valve was replaced three weeks following his completion of the New York City Marathon!

VENUE

Sandpearl Resort

Located on sun-kissed beachfront, the Sandpearl Resort, Clearwater Beach invites guests to get away from the ordinary and experience a resort unlike any other. Powder-white sand and clear blue water surround this Clearwater, Florida beach resort, offering plenty of relaxation under the year round Florida sunshine.

Thursday September 26

Light Grab and Go Breakfast for Wetlab Attendants and Exam Participants	6:30 am
Bus Departs for Wetlabs (front of hotel)	7 am
Wetlab #1-3	**8 am – 12 pm**
Buses Depart from Hotel to Wetlab #4-7	12 pm
**Pizza will be served to am attendees*	
Buses Depart from Wetlab #1-3 Return to Hotel	1 pm
Wetlab #4-7	**1 – 5 pm**
Buses Return to Sandpearl from Wetlabs	5 pm
Welcome Reception *Sponsored by ISIS Services*	**4:30 – 7 pm**

*Lunch will be provided for morning wetlab attendees.

Wetlab Volunteers and Instructors

Wetlab Co-chairs: Heather Bogie, DSI and Christina Gross, APS
Wetlab Liaison USF: Margi Baldwin, USF
Randy Pielemeier, MPI
Karen Brockelhurst, USF
Mary Jane Perkins, USF
Vince Mendenhall, PTS Wake Forest Innovations
Tina Weiner, Taconic
Bonnie Lyons, JAX
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Tom Hampton, Mouse Specifics
Michele Danielson, USF
Monica Torres, USF
April Lindon, USF
Jim Driver, Starr Life Sciences
Eric Ayers, Starr Life Sciences
Liisa Carter, APS
Tim Edwards, WIL Research
Szczepan Baran, VBI

Wet Labs 1-3 (8-12am) Labs 4-7 (1-5pm)

Workshop #1

Surgical Techniques in the Mouse: Kidney Capsule Implantation and Prostate Injection

The Jackson Laboratory will conduct a workshop on two surgical techniques in the mouse: Kidney Capsule Implantation and Prostate Injection. In support of the development of murine models to study human cancer, this workshop will provide the participants with the training to transplant tumors under the kidney capsule or inject cells in the prostate. This hands-on workshop will also cover regional mouse anatomy, surgical standards and postoperative care. Participants should have basic surgical knowledge and the ability to work under a dissecting microscope.

Workshop #2

Surgical Anatomy and Techniques For PLF, PLIF and Vertebral Body Plating and Pedicle Screw Implantation in Sheep

The surgical anatomy and techniques to study the safety and efficacy of osteoinductive and osteoconductive materials within vertebral body spacers [posterolateral intervertebral body fusion (PLIF)] or as a conventional posterolateral vertebral fusion (PLF) will be demonstrated in cadaver sheep and goat spines. Participants will be shown the necessity of essential instrumentation, as well as to how to avoid the numerous possible pitfalls and complications in this procedure.

Workshop #3

Intra-articular Injections and Orthotopic Abdominal Injections

In this workshop we will cover methods for test article administration in the IA space as well as the kidney, liver, and spleen of SD rats. Alternative routes for access and methods of closure will be explored. Finally, methods to support proper aseptic technique while allowing high throughput will be detailed.

Workshop #4

Renal Disease Model in the Rat and Mouse

The goal of this hands-on workshop will be to demonstrate and train participants on creating a surgically induced renal failure model in rodents. The workshop will include performing two different versions of a subtotal nephrectomy procedure. One will be done in mice and the other in rats. Participants will also gain knowledge about the background of the procedure, pre and post-operative care and surgical techniques.

Workshop #5

Non-invasive Monitoring Techniques for the Conscious and Unconscious Animal

How to Record ECG in [Conscious] Mice Non-invasively at Baseline, During Anesthesia, and During Recovery (2 hours)

The electrocardiogram can provide a wealth of information about a mouse, including its health status, depth of anesthesia, and extent of pain. This workshop will illustrate for researchers the speed and ease of recording the ECG, even from newborn mice. Attendees will learn how changes in heart rate and heart rate variability may be used as markers of depth of anesthesia, and how certain types of pain can be reflected via the ECG. Data from interesting developmental disorders, such as spinal muscular atrophy, will be presented. Participants will take with them data sets from ECGs they record non-invasively in conscious mice.

Non-invasive Monitoring of The Vital Signs of Mice And Rats Undergoing Anesthesia: Enhance Awareness of the Effects Of Anesthesia, Temperature And Oxygen in Order to Improve Mortality of Subjects and Accuracy of Research. (2hours)

This workshop will give you hands on experience to see why the Guide for the Care and Use of Laboratory Animals suggests monitoring anesthetized rodents as you would other animals. Utilizing pulse oximetry, you will have the opportunity to see how the vital signs of subjects are affected by different types of anesthesia (we will be utilizing Isoflurane and injectable anesthesia).

Specifically you will be able to see how different variables such as the amount of anesthesia, oxygen and temperature impact a subject's vital signs.

Lastly, we will discuss how non-invasive monitoring can help shed light on your research and how it relates to translational medicine.

Workshop #6

Principles of Long Bone Plating in Large Animals

Sheep Legs will be used to teach the principles of plate application in a critical length defect model. The techniques taught will be applicable to multiple species. Participants will be instructed in plate and screw size and type selection and application. Hands-on application of plates to a sheep femur and tibia will be performed by each participant, including muscle dissection of the surrounding tissues. Post-operative care of this model will also be discussed.

Workshop #7

Surgical Anatomy and Techniques for Postero-lumbar Fusion (PLF) in Rabbits

The surgical anatomy and techniques to study the safety and efficacy of osteoinductive and osteoconductive materials as a conventional postero-lumbar vertebral fusion (PLF) will be demonstrated in the rabbit. Participants will be shown the necessity of essential instrumentation, as well as to how to avoid the numerous possible pitfalls and complications in this procedure.

Accession of Exteriorized Catheters Drylab:
Friday 1:30-2:30PM
Sponsored by SAI Infusion Technologies
There is a rapidly increasing need for direct vascular access in pre-clinical research. Direct vascular access is crucial in models such as: acute, intermittent, and chronic infusions; rapid PK/TK sampling (especially with biologics); self-administration studies for addictive behavior; and a host of other disease models. Vascular access often means implantation of chronic catheters which are placed in animals under sterile surgical conditions. Successful catheter access to any internal body space requires not only aseptic technique to prevent contamination, but also proper maintenance in order to maintain patency. This dry lab will demonstrate the proper methods for accessing exteriorized catheters. We will also address optimal methods to initiate and maintain a sterile infusion system, such as in a study room. Additional focus will cover troubleshooting, along with volume and rates of infusion.

1) Proper Exteriorized Catheter Maintenance:
    a. Items needed for proper catheter maintenance
    b. Use of Aseptic Techniques to flush and lock an exteriorized catheter
    c. Use of Aseptic Techniques to remove a blood sample with an exteriorized catheter
    d. Use of Aseptic Techniques when using a catheter port.
2) Proper Catheter maintenance using a Harness or Jacket:
    a. Selection criteria for Harnesses/Jackets & Access Devices
    b. Exteriorized Catheter connection procedure with adaptations for the access device
3) How to assemble the Infusion system:
    a. How to use a Harness with a Tethered Access System for infusion or sampling
    b. How to use a Jacket with a Tethered Access System for infusion or sampling
    c. Complete Tethered Access System - Infusion Pump, Syringe, Extension Line, Swivel & Holder, Tether, Harness connection and Catheter
    d. How to properly prime the fluid system
    e. How to disconnect and re-connect an animal during procedures such as weighing
4) Infusion Volume and Rate Considerations:
    a. How to determine the total dead-volume of the system
    b. How to address high and low rate infusion situations
5) Troubleshooting Tethered Infusion Systems:
    a. Disconnection – ensuring air does not enter the animal's blood stream while maintaining aseptic techniques.
    b. Contamination - how to change the components if required

Surgical Microscope Use and Care Drylab: Friday 3:20-4:20 pm
Sponsored by Micro Optics of Florida

Electrocautery Drylab: Friday 3:20-4:20 pm
Sponsored by Bovie

Dry Labs and Workshop (FREE)

Surgical Writing-From Protocol Development, Conception of the Research Hypothesis, Data Collection and Publication.
2 parts:
Part 1: A one hour lecture open to all will be given during one of the full meeting sessions.
Part 2: Saturday 1 – 3 pm limitation of participants, must register in advance

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

Microsurgery Drylab: Friday 10:20 – 11:20 am
Instructor: Erlinda Kirkman
Most microsurgical procedures utilize a set of basic technique that must be mastered by the surgeon. These include blood vessel repair or vascular anastomosis, grafting & nerve repair.
The aims of this dry laboratory session are:
- Practice vascular anastomoses end-to-end (between two ends of blood vessel) or end-to-side (a connection of one cut ends of blood vessel to the wall of another vessel) with the commonly use surgical loupe as magnification aid.
- Comfortably repair vessels or grafts using 8.0-10.0 sutures.
- Practice intravascular insertion of small catheters.

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Thank you to our drylab sponsors who have offered free opportunities to learn at our meeting:
- Erlinda Kirkman, USC
- Micro-Optics
- SAI Infusion Technologies
- Bovie

Thank you to USF for hosting our wetlabs and all of your dedication and support!

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Academy of Surgical Research

September 26–28, 2013

Clearwater Beach, Florida – Sandpearl Resort

PROGRAM

THURSDAY, SEPTEMBER 26 / FRIDAY, SEPTEMBER 27

THURSDAY, SEPTEMBER 26		
4:30 – 7 pm	Welcome Reception *Sponsored by ISIS Services*	Hunter Ballroom
FRIDAY, SEPTEMBER 27		
7 – 8 am	Continental Breakfast with Exhibitors *Sponsored By SAI Infusion Technologies*	Hunter Ballroom
8:30 am	Poster Setup	Cove Room
8 – 8:15 am	**Opening Remarks** ASR President Steve Hachtman	Harbor Ballroom
8:15-9:15 am	Keynote-Gloria Matthews "Toward Translation of Animal Model Data Into Clinically Relevant Outcomes for Bringing Therapeutics to Market"	Harbor Ballroom

TRACK ONE

9:15 – 9:35 am	Modifications In Swine Anesthesia For Orthotopic Liver Transplantation	Mike Talcott, DVM, DACLAM	Harbor A & B
9:35 – 9:55 am	Twelve Week Bone Implantation Study In Sheep To Assess Local Tissue Reaction And Mechanical Strength	Jolee Bartrom, BS, LAT	Harbor A & B
9:55 – 10:15 am	Break with Exhibitors *Sponsored By Access Technologies*		Hunter Ballroom
10:20 – 10:40 am	Preclinical Evaluation Of A Two-stage Incisional Ventral Hernia Model In The Yucatan Miniature Pig	Pullen Shnoda, DVM	Harbor A & B
10:40 – 11 am	Biocompatibility Explained: A Simple Understanding To A Complex Topic	John Iannone, BS, BME	Harbor A & B
11 – 11:20 am	Reduction Of Animal Use In Microsurgical Training Through The Use Of Basic And Complex Inanimate Training Models	Szczepan Baran, DVM, MS	Harbor A & B
11:20 - 11:40 am	Post-surgical Occlusive Thrombosis, And Leg Disuse Syndrome In Telemeterized Cynomolgus Macaques	Leslie Stoll, BS, SRS	Harbor A & B
11:40 am -12:00 pm	Parabiosis: Pre-operative, Intraoperative, And Post-operative Considerations In Mice	James McCabe, BA, SRS, CMAR, RLATG	Harbor A & B
12 – 1 pm	Lunch Buffet *Sponsored by Colonial Medical Supply*		Hunter Ballroom
1 – 2 pm	Keynote-Richard Bianco "Four Decades of Using Large Animals to Assess Human Safety of Heart Valves and Other Class III Devices"		Harbor Ballroom
2 – 2:20 pm	Bad Bugs, No Drugs: Targeting The ESKAPE Pathogens For Antibacterial Drug Discovery	Lindsey Shaw, PhD	Harbor A & B
2:20 – 2:40 pm	Competency And Proficiency Assessment Of Microsurgical Skills Utilizing Mouse Animation Models And OSATS	Szczepan Baran, DVM, MS	Harbor A & B
2:40 – 3 pm	Creating Cost Efficient Tools And Devices For Teaching The Basic Principles Of Small Rodent Surgery	Wendy Williams, BA, HBSc, DVM, DACLAM	Harbor A & B
3 – 3 :20 pm	Break with Exhibitors *Sponsored by DRE*		Hunter Ballroom
3:20 – 5 pm	The Regulations and ASR's Role in Your Animal Care Program (A Roundtable Discussion)	Randy Pielemeier, Carol Clarke (USDA-APHIS), Christian E. Newcomer (AAALAC), Steven Niemi (ACLAM)	Harbor A & B
5 pm	Poster Judging (posters to be taken down by 8pm)		Cove Room
5 – 7 pm	Wine and Cheese Reception with Exhibitors *Sponsored by Lomir and Data Sciences International*		Gulf Lawn

FRIDAY, SEPTEMBER 27

THURSDAY, SEPTEMBER 26			
4:30 – 7 pm	Welcome Reception *Sponsored by ISIS Services*		Hunter Ballroom

TRACK TWO			
9:15 - 9:35 am	Implantation Of Left Ventricular Pressure Telemetry With Solid Tip ECG In The Cynomolgous Macaque: Surgical And Anesthetic Considerations	Kate Read, MA, VetMB, MRCVS	Harbor C
9:35 – 9:55 am	Comparison, Refinement, And Training Of Mouse Endotracheal Intubation Methods	Szczepan Baran, DVM, MS	Harbor C
9:55 – 10:15 am	Break With Exhibitors *Sponsored By Access Technologies*		Hunter Ballroom
10:20 am – 10:40 am	An Innovative Surgical Method For Simultaneous Measurements Of Pulmonary And Systemic Vascular Resistances In Conscious Freely Moving Rats	Xuening Hong, MD	Harbor C
10:40 - 11:00 am	Characterization Of Maternal Pathology, Fetal Viability, And Hypertension With Surgical And Non-surgical Models Of Preeclampsia In The Sprague Dawley Rat	Teresa Gleason, SRS, BS, LVT, LATg	Harbor C
11 – 11:20 am	A Modified Technique Of End-to-side Anastomosis	Sione Fanua, MSM	Harbor C
11:20 – 11:40 am	Parenteral Fluid Therapy Response During General Anesthesia In The Rat	Kimberly Wasko, CVT, VTS, RLATg, SRS	Harbor C
11:40 – 12 pm	A Common Animal Care And Use Program – Just Different	Sylvia I. Gografe, DVM, Ph.D., DACLAM	Harbor C
12 – 1 pm	Lunch Buffet *Sponsored by Colonial Medical Supply*		Hunter Ballroom
1 – 2 pm	Keynote-Richard Bianco "Four Decades of Using Large Animals to Assess Human Safety of Heart Valves and Other Class III Devices"		Harbor Ballroom
2 – 2:20 pm	In Vitro And In Vivo Studies For The U.S. Navy On Strategies For Predicting And Preventing CNS Oxygen Toxicity	Jay Dean, PhD	Harbor C
2:20 – 2:40 pm	Combined Alcohol Intoxication And Hemorrhagic Shock Affect The Microcirculation In The Gut	Travis Doggett, BS, BA	Harbor C
2:40 - 3 pm	Lumbar Intrathecal Catheterization In Canine And Primate	Jon Ehrmann, BS, SRS, SRA, LATG	Harbor C
3 – 3:20 pm	Break with Exhibitors *Sponsored by DRE*		Hunter Ballroom
3:25 – 3:45 pm	Development of retroperitoneal fibrosis in a cohort of feline renal allograft recipients: 1998-2012	Heidi Phillips, DVM	Harbor C
3:45 – 4:05 pm	An invivo hemostasis evaluation method for comparing surgical devices	Mary E. Mootoo, BBA, RVT, SRS	Harbor C
4:05 – 4:25 pm	Costochondral thoracotomy as a means to access the left ventricular apex for intramyocardial injection with survival in the rat	Christie Cunningham, BS, RVT	Harbor C
4:25 – 5 pm	Cell-Based Gene Therapy for the Central Nervous System	Dave Morgan, PhD	Harbor C
5 pm	Poster Judging (posters to be taken down by 8pm)		Cove Room
5 – 7 pm	Wine and Cheese Reception with Exhibitors *Sponsored by Lomir and Data Sciences International*		Gulf Lawn

SATURDAY, SEPTEMBER 28

7 -8 am	**Continental Breakfast *Sponsored By Instech Solomon***		**Hunter Ballroom**
8 – 8:15 am	Opening Remarks (Steve Hachtman)		Harbor Ballroom
8:15 - 9:15 am	**Keynote -Wayne McIlwraith "Evolution of Arthroscopic Surgery With the Management of Arthroscopic Surgery as a Clinical Tool in the Horse and the Development of Equine Models for Surgical Repair of Cartilage Defects"** *Sponsored By Charles River Laboratories*		**Harbor Ballroom**

TRACK ONE			
9:20 – 9:40 am	Assessment of Mandibular Nerve Block Using Bupivicaine In Yucutan Miniature Swine as a Model for Mandibular Condylectomy and Implant Surgery	Jonathan Bova, DVM	Harbor A & B
9:40 – 10 am	An Orofacial Thermal Pain Assay for Assessing Analgesic Doses Buprenorphine and Tramadol In Rodents: a Clinically Relevant, Non-invasive Approach	Harvey Ramirez, DVM	Harbor A & B
10 – 10:20 am	**Break *Sponsored By ClearH20, Inc.***		**Harbor Foyer**
10:20 – 11:20 am	Surgical Writing--from Protocol Development, Conception Of The Research Hypothesis, Data Collection and Publication (Part I Lecture Of Workshop)	Luis Toledo-Pereyra, MD, PhD	Harbor A & B
11:30 am – 1:20 pm	**ASR Business Meeting/Awards Lunch** ***Sponsored by Vet Equip, Inc.*** **Guest Speaker: John Belluardo "Reversing heart disease"**		Hunter B & C
1:30 – 1:50 pm	Decreased Nerve Conduction Velocity in Peripheral Nerves Following Exposure to Bone Morphogenic Protein-2	David Margolis, MD	Harbor A & B
1:50 – 2:10 pm	Microbiological Evaluation of An Alternative Surgical Draping Material	Gregory Voronin, DVM	Harbor A & B
2:10 – 2:30 pm	Experiences in Implanting Microelectrode Arrays for Chronice Neural Recording in Nonhuman Primates	Oscar A. Bermeo, DVM, RLATg, SRS	Harbor A & B
2:30 – 2:50 pm	Precise Complete Caudate Lobectomy for Hepatocellular Carcinoma Based on Computer-assisted Operative Program	Weihua Qiu, MD, PhD	Harbor A & B
3 pm	**Adjournment**		
3- 3:45 pm	**Board of Directors meeting**		

TRACK TWO			
9:20 – 9:40 am	Refining The Use Of Cautery To Perform Kidney Ablation	Marla Wilwol,LVT, RLATG, SRS	Harbor C
9:40 – 10 am	Technical Procedures Necessary To Achieve Successful Endothelial Cell Keratoplasty In The Cat	Vince Mendenhall, DVM, PhD	Harbor C
10 – 10:20 am	**Break *Sponsored By ClearH20, Inc.***		
10:20 – 10:40 am	Single Technician Sheep Intubation: Twenty Five Years Of Experience And Innovation	Jed Pugsley, RLAT	Harbor C
10:40 – 11 am	Technique And Methodology Of TAVI In Ovine Models	Selwan Abdullah, BS	Harbor C
11 – 11:20 am	Improvements In Microdialysis Method Result In Increased Experimental Success	Susan Champagne, BS, RLAT	Harbor C
11:30 am – 1:20 pm	**ASR Business Meeting/ Awards Lunch** *Sponsored by Vet Equip, Inc.* **Guest Speaker: John Belluardo "Reversing Heart Disease"**		**Hunter B & C**
1:30 – 1:50 pm	Surgical Preparation Of A Cat For Brainstem Respiratory And Swallow Control Of Breathing Research	Mary Jane Perkins, BS, LATG, SRA	Harbor C
1:50 – 2:10 pm	Hepatic Portal Vein Cannulation In The Dog	Kate Read, MA, VetMB, MRCVS	Harbor C
2:10 – 2:30 pm	Cardiovascular Ultrasound Screening For Rodent Surgical Studies: Why And How	Matt Flegal, BS, SRS	Harbor C
2:30 – 2:50 pm	ASR certification spotlight	Lisa Johnson, SRS, LATg, BA	Harbor C
3 pm	**Adjournment**		
3 – 3:45 pm	**Board of Directors meeting**		
1:30 – 3 pm	Surgical Writing--From protocol development, conception of the research hypothesis, data collection and publication (Part II Workshop)	Luis Toledo-Pereyra, MD, PhD	Channel Boardroom

THE 29TH ANNUAL MEETING
of the

Academy of Surgical Research

September 26–28, 2013

Clearwater Beach, Florida – Sandpearl Resort

ABSTRACTS

Modifications In Swine Anesthesia for Orthotopic Liver Transplantation

AUTHOR: Michael Talcott

ABSTRACT:
Chronic liver disease is one of the leading causes of death in the United States and liver transplantation is the definitive therapy for end stage liver disease. However, there is a critical shortage of organs available for transplantation due to the strict criterion for eligible donors. Thus, expansion of the donor pool by increasing the use of non-heart beating donors and marginally steatotic livers could help meet the demand for liver transplantation. A recent study has been undertaken to evaluate normothermic preservation vs. cold storage to maintain physiologic conditions and allow normal cellular metabolism prior to transplantation. The pig model was chosen to evaluate this technique and standard liver transplant surgical techniques were used. Venovenous bypass was avoided during this procedure due to complications associated with the technique including postoperative renal failure, cerebral edema and thromboembolism. However, this led to an anhepatic period in which the vena cava was occluded resulting in a significant reduction in vascular return and necessitating modifications in anesthesia and vascular support. This presentation will discuss the use of various drug combinations and other techniques used to support the veterinary patient during the anhepatic stage and will also discuss complications associated with this liver transplant model.

12 Week Bone Implantation Study in Sheep to Assess Local Tissue Reaction and Mechanical Strength

AUTHOR(s): Jolee Bartrom and Lindsay Stevenson

ABSTRACT:
The objective of this study was to compare an experimental and marketed bone void filler by evaluating local tissue reaction and mechanical bone strength. Due to the size of the defects needed, sheep were used as the animal model because they have a bone structure of similar size to humans. Anesthesia was induced in sixteen young adult female sheep by intramuscular injection of ketamine (11 mg/kg), combined with xylazine (0.1 mg/kg). Each animal was also given an intramuscular injection of flunixin meglumine (1.1 mg/kg), atropine (0.05 mg/kg), enrofloxacin (5 mg/kg), a subcutaneous injection of buprenorphine (0.01 mg/kg), and fentanyl patches (2 ug/kg/hr). Each animal was intubated and maintained on isoflurane inhalant anesthetic. One metaphyseal defect was created in each femur by exposing the lateral aspect of the femur (over the lateral condyle). An initial pilot hole was created, using a drill with an approximate 4 mm bit. The hole was enlarged with an approximate 10 mm drill bit and had an approximate depth of 20 mm. The defect sites were implanted with either the experimental or marketed bone void filler. Immediately after implantation, one animal was euthanized (prior to recovery) with an intravenous injection of a sodium pentobarbital-based euthanasia solution to serve as a baseline for mechanical bone strength testing. Animals were given post-operative analgesics and antibiotics, observed twice daily for general health, and body weights were collected throughout the study (all animals gained body weight throughout the study and were considered healthy). Radiographic images were taken immediately after implantation and at termination to evaluate placement. At 12 weeks, the animals were anesthetized with ketamine (11 mg/kg) combined with xylazine (0.1 mg/kg) and euthanized with euthanasia solution. The femurs of ten animals were macroscopically observed, histologically processed, and microscopically evaluated. Mechanical bone strength testing was conducted on the femurs from the five remaining animals after macroscopic observation. Evaluation of the radiographs at 12 weeks showed that all defect sites had been sufficiently filled indicating no displacement or profound absorption had occurred. The mechanical bone strength data indicated that the defect sites were not statistically significantly different ($p > 0.05$) between the experimental and marketed bone void fillers when comparing average maximum push-out force, average maximum shear stress, and average energy to failure. At 12 weeks post implantation, the experimental bone void filler performed comparably to the marketed bone void filler when evaluating local tissue reaction and mechanical bone strength.

Preclinical Evaluation of a Two–stage Incisional Ventral Hernia Model in the Yucatan Miniature Pig

AUTHOR(s): Pullen Shnoda, Amy Poulin Braim, Timothy Muench, Stephanie Werrlein, and Larry Johnson

ABSTRACT:
The purpose of this study was to develop a two-stage hernia model for evaluation of a novel hernia repair mesh (HRM) in Yucatan miniature pigs. Four female Yucatan pigs were approved for use by the Institutional Animal Care and Use Committee in a facility licensed by the United States Department of Agriculture, which is accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care International. On the day of surgery, the animals received Buprenorphine SR® (0.12 – 0.30 mg/kg, IM) preoperatively as analgesic. Animals received midazolam, 250-500 µg/kg IM while in their animal room for sedation. Isoflurane was administered via facemask at 1-4% with 1-3 liters of oxygen per minute until animal could be intubated. After intubation, the animal was maintained by inhalation of isoflurane (approximately 1.0%–4%) and 100% oxygen at a flow rate of approximately 1-2 liters /minute. The surgical site was prepared aseptically for surgery. A final preparation of the ventral abdomen consisted of chlorhexidine scrub and 70% isopropyl alcohol (IPA), followed by alternating applications of chlorhexidine solution and IPA. The first stage surgically created a ventral midline abdominal wall defect. The animal was recovered and healing of the surgical site occurred over 35 days. The second stage surgically repaired the resulting hernia created in Stage One using an open approach with a novel Hernia Repair Mesh (HRM) followed by the endpoint evaluation of the repair site at 28 days. Stage One: Hernia Creation A 3.0 cm ventral midline incision was made cranial to the cranial extent of the proposed hernia site through the skin and subcutaneous tissue to the level of the linea alba. Using a combination of blunt and sharp dissection in a cranial to caudal direction, a tunnel between the subcutaneous tissue and the linea alba was created. The linea alba was incised within this tunnel for a length of 7.5cm. Penetration of the peritoneum was avoided. The incision site was closed with appropriately sized suture. The linea alba was not closed. Stage Two: Hernia Repair An approximately 7cm incision was made directly over the hernia defect site through the skin, subcutaneous tissue and peritoneum. An edge of the hernia defect was biopsied. The novel HRM was fixed intraperitoneally using an open Intra Peritoneal Onlay Mesh (IPOM) method. The subcutaneous tissue and skin closed routinely. The linea alba was not closed. At 28 days following repair each animal was sedated with an intramuscular injection of Telazol® (5 mg/kg), xylazine (5 mg/kg) and glycopyrrolate (0.011mg/kg). When a sufficient level of sedation was reached, the animal was euthanized with an intravenous injection of EUTHANASIA III at a dosage of 10-15 ml/45 kg of body weight. After confirmation of euthanasia, the hernia repair sites were macroscopically and microscopically evaluated. No surgical or unexpected post-surgical complications were noted during the course of this study. No animal pain or discomfort was observed. All animals developed a visible hernia after Stage One. One animal had spontaneous resolution of a visible hernia at day 21. The average size of resultant hernias was 4 cm wide and 8 cm long. The hernias were successfully repaired without complications. After repair, no hernias, or seromas were observed during the in-life phase or at necropsy. Biopsies taken before repair demonstrated a steady state of wound repair with limited chronic inflammation. No statistics analysis was conducted due to the pilot nature of this study. The Two-stage model demonstrated the feasibility to create a uniform shape and size ventral midline hernia defect, which could subsequently be repaired with a novel HRM. This allowed for evaluation of tissue response, integration, and mesh compression that more closely mimics the human clinical scenario of hernia repair.

Biocompatibility Explained: A Simple Understanding to a Complex Topic

AUTHOR: John Iannone

ABSTRACT:
Biocompatibility testing comprises the safety evaluation of medical devices and materials, often in accordance to the various regulatory guidelines such as ISO 10993, USP, MHLW, etc. Biocompatibility is typically performed on the final version of medical devices, although cases exist where specific tests are designed for the analysis of raw materials. The determination of which guideline to follow depends upon which countries the devices will be marketed, as well as the nature of what is being tested (medical device vs. raw material). The majority of the world accepts the ISO 10993 testing guidelines when assessing the safety of a medical device and/or material intended for medical applications. This presentation will provide an explanation on how to determine what tests are required to assess the safety of a device or material used for a particular application. This will be achieved by reviewing the structure outlined in ISO 10993-1, which provides guidance on the classification of a device/material based on the type (location and duration) of patient contact expected during its intended use. Following classification, the mechanisms of biocompatibility that must be assessed is defined and will be presented. Further, an introduction and explanation to common testing categories outlined in the ISO 10993 will be detailed. Finally, frequent concerns of proceeding with a testing program will be discussed to impart direction in navigating this complex landscape.

Reduction of Animal use in Microsurgical Training through the use of Basic and Complex Inanimate Training Models

AUTHOR(s): Szczepan W. Baran, Elizabeth Johnson, and James Kehler

ABSTRACT:
With the growth and expansion of mouse and rat transgenic models in recent years, the need for skilled microsurgeons is growing at an unprecedented pace. Historically, microsurgical training has relied on the utilization of animals. Due to the three R's, and more rigorous legislation in Europe and in the United States, many inanimate models have been introduced into microsurgical training and also described in the literature. This presentation will provide an overview of available inanimate models (home made and purchased) and discuss the advantages and disadvantages and provide recommendations for training of specific procedures. Incorporation of inanimate models as an alternative to live animals into microsurgical training provides an opportunity to reduce the number of animals required for this training. After this session, participants will be able to identify inanimate models to complement their microsurgical training and learn how to incorporate these models into their training program.

Post-surgical Occlusive Thrombosis and Leg Disuse Syndrome in Telemeterized Cynomolgus Macaques

AUTHOR: Leslie Stoll

ABSTRACT:
The bodyweight of a telemetry implant candidate may influence the occurrence of arterial thrombosis and acute clinical presentation of leg disuse post-surgically. 16 cynomolgus macaques, ages 2-4.5 years, 8 M/F, with bodyweights ranging from 2.8-6.3kg, were surgically implanted with femoral arterial telemetry or dual (telemetry and arterial access port) catheterization for collection of telemetry parameters and blood gases for various CV safety toxicology studies. Animals with both telemetry and arterial access ports were bilaterally implanted in each femoral artery. Of these 16 animals, 5 presented with varying degrees of leg disuse yndrome. These signs were occurring immediately following surgery(recovery) to 72 hours post-surgically. Clinical presentation included acute limb failure to mild disuse, loss of deep pain sensation, muscle atrophy and necrosis of distal extremities post-surgically. The animals were humanely euthanized, as approved in our NHP Surgical protocol, and had necropsy performed so we could better understand the pathogenesis of this process and prevent the further occurrence of this syndrome in our animals. At necropsy, vital organs and select tissues were collected for each animal. Portions of the lung, liver, kidney, heart, descending aorta, iliac bifurcation (just above, on the bifurcation, just below), distal iliac artery, femoral artery, and gastrocnemius muscle we trimmed for gross and histopathological evaluation Photo's and cross section slides of the aortic/iliac vessels and bifurcation were generated. The remaining 11 animals recovered from surgical implant and arterial catheterization well, with normal extremity health and mobility. Following release from study, these animals were humanely euthanized , as approved in our NHP Surgical protocol and the same tissues were collected for comparison of "normal" vessel/limb pathology following arterial catheterization with no leg disuse, atrophy or necrosis. Initial findings include occlusive thrombosis, intimal thickening , resulting in ischemic tissue damage and ungula detachment, distal right lower limb and digits and muscular necrosis. With the assistance of my colleague, an Anatomical Pathologist, the data collected from these 16 animals is in the process of being evaluated and reviewed. Our objective is to associate the occurrence of arterial thrombosis and leg disuse syndrome with the bodyweight (size) of the animals affected. With this information , we can justify procurement of larger animals for telemetry and arterial access port projects and through this investigation, further our understanding and provide insight for others.

Parabiosis: Preoperative, Intraoperative, and Postoperative Considerations in Mice

AUTHOR(s): James McCabe and Sandra Duarte Vogel

ABSTRACT:
Parabiosis is a technique in which two living animals are joined together surgically and develop a single, shared circulatory system. This technique has been well documented in the literature for over 100 years. It has regained popularity as a research model based on the number of recent publications. The purpose of this presentation is to present information on our experience with this model and to compare the two most common surgical approaches utilized to join mice (thoracic muscle attachment vs. knee and elbow joint). The success of this model has as much to do with preoperative planning and conditioning of the mice and postoperative care as it does with performing the actual surgery. Several surgical approaches have been published and we have found that the key to a successful surgery is in the selection of the proper anesthetic agent, appropriate points of muscle attachment as well as being expeditious when closing the incision. The muscles to be joined are determined by weather the surgery is heterochronic (mice of different ages /different size, i.e. obese joined non-obese) or isochronic (mice of similar size) in nature. For the purpose of this study we looked at isochronic pairings of full sibling C57BL/6 females. This is to avoid parabiotic disease (graft-versus-host disease) and focus on the stability of the muscle attachments, the pair's ability to ambulate (groom, feed, move, etc.). We performed this study as a pilot to insure we were able to attach the animals and that they were able to behave in a normal manner over the course of 14 days. The mice (surgically attached) were weighed post postoperative, 7 and 14 days. Shared circulation between the parabiotic animals was verified by using Evans blue dye (IV) injection into one mouse 24 hours prior to euthanasia (day 14). Blood was removed from both mice (cardiac puncture) to insure that the blood chemistry was within the normal limits of the strain, age and sex of the mice. Muscle and skin attachments were visually inspected to insure that they were intact and vascularized. Long term survival of the pair is directly affected by the stability and location of the attachments (serratus ventralis vs. knee and elbow joint) as well as the size and shape of the skin incision (skin flap vs. straight line incision). The surgeon's ability to maintain a sterile field in a confined space between two tiny bodies until the closure is complete also affects the outcome and weather antibiotics are required postoperatively.

2,4-diaminoquinazolines are Broad Spectrum Antimicrobial Agents Against Multi-drug Resistant Bacterial Pathogens

AUTHOR: Lindsey N. Shaw

ABSTRACT:
Over the last few decades, there has been an alarming increase in antibiotic resistance in bacterial pathogens that cause infection in both hospital and community settings. This rise in resistance, and the decline in discovery and development of novel antibiotics, means that the post-antibiotic era may be soon at hand. With the rapid emergence of pan-resistant organisms, it is vital that we uncover novel agents to treat infections caused by these organisms. To this end, our group has identified 2,4-Diaminoquinazolines that have potent antimicrobial activity. Specifically, they have MIC values ranging from 0.5 μg ml^{-1} to 10 μg ml^{-1} against two important nosocomial pathogens, *Staphylococcus aureus* and *Acinetobacter baumannii*. Interestingly, a number of these compounds also demonstrate anti-biofilm activity against *A. baumannii* strains. When screening for toxicity, we observed no hemolytic activity of lead agents towards human erythrocytes. In addition, an MTT assay using human epithelial cells revealed that these compounds have limited cytotoxic, particularly at lower concentrations. Analysis of spontaneous mutation frequencies revealed a very low incidence of innate resistance towards these drugs against MRSA. In an effort to identify how resistance is mediated, we present data from whole genome sequencing of resistant strains. Upon analysis we found mutations in several genes that are involved in translation, indicating that these compounds may be protein synthesis inhibitors. We also determined that these quinazoline based compounds are efficacious *in vivo* using a murine model of MRSA peritonitis. These findings support the use of 2,4-Diaminoquinazolines derivatives as novel, broad-spectrum antimicrobials agents.

Competency and Proficiency Assessment of Microsurgical Skills Utilizing Mouse Animal Models and OSATS

AUTHOR: Szczepan Baran

ABSTRACT:
Proficient microsurgical skills are considered essential in developing bariatric surgical rodent models. To evaluate microsurgical skills, an adaptation of a mouse model and the validated objective structured assessment of technical skills (OSATS) was used to determine competency and proficiency skills. 18 participants with novice level of surgery experience learned to perform intestinal side to side and side to end intestinal anastomosis, including six specific microsurgical tasks as part of a Roux-en-Y Gastric Bypass. Training included regimented expert instruction, peer instruction/observation, and experienced-based learning. Pre- and post-training video recordings of tasks were obtained. Two blinded microsurgical experts compared pre- and post-training performance using a checklist and global rating scale. Participant's post-training performance was significantly better than pre-training performance for each checklist item and the global rating scale (as calculated by paired t test) was $P < .001$. The mouse model provides an effective means of teaching and evaluating basic and advanced microsurgical skills for novice surgeons. With repeated practice, there was significant improvement in performance. Using OSATS for this mouse model suggests that we can effectively measure microsurgical competency with the potential to reliably determine proficiency. This model could potentially be translated for training clinical surgeons and assessing their competency outside of the surgical suite.

Creating Cost-efficient Tools And Devices For Teaching The Basic Principles Of Small Rodent Surgery

AUTHOR: Wendy Williams and David Mooneyhan

ABSTRACT:
To ensure individuals acquire the appropriate skills to perform survival rodent surgery, we created a training module that utilizes several handmade simulation devices and dexterity tools. The *Principles of Aseptic Rodent Surgery* module is intended to be the first hands-on step in the process of learning to perform experimental surgery. The tools we have created can be used to teach proper selection and handling of surgical instruments, as well as gentle tissue handling, hand positioning and other skills essential to good surgical technique. These training tools serve to emphasize the importance of building the students' fine motor skills before they handle animal tissues. The students gain an appreciation for the dexterity required to perform surgery and the ergonomic issues that can arise with improper instrument handling. We use the tools at a macro level first then progress to finer and smaller tools to refine skills for microsurgery. When designing the course, we researched many of the commercially available training tools and simulation models as well as investigating ideas for creating our own homemade tools. We found innovative ways to use simple, inexpensive and readily available materials to create several useful dexterity tools as well as models for practicing thin-tissue incisions, stab incisions, multi-layer closures and hemostasis. In this session, we will review some of the materials we developed while highlighting the training goals of each exercise and the source of the materials used to create each device.

The Regulations and Asr's Role in Your Animal Care Program (a roundtable discussion)

AUTHOR: Randy Pielemeier, Carol Clarke, Christian E. Newcomer, and Steven Niemi

ABSTRACT:
This session will provide a rare opportunity to help understand the regulations that govern day to day surgical activities in our laboratories and how ASR fits into the ever shifting regulatory puzzle. Topics will include, Training of Surgeons and Anesthesia personnel, Perioperative Care and Pain Management, Classification of Procedures as Major or Minor. Other topics will be discuss based on audience questions.

Implantation of Left Ventricular Pressure Telemetry with Solid Tip ECG in the Cynomolgous Macaque: Surgical and Anaesthetic Considerations

AUTHOR: Kate Read

ABSTRACT:

Implantation of the D70-PCTP transmitter allows measurement of cardiovascular parameters for safety pharmacology studies. Historically, we have implanted the ECG electrodes subcutaneously over the thorax in the primate, resulting in a variable signal with occasionally large noise:signal ratio. Repair surgery to ammend ECG lead placement may be required. Recent implants were of the solid-tip negative ECG electrode configuration, aiming to eliminate muscle noise and movement artefact from the ECG waveform. This presentation will focus on the surgical techniques and anaesthetic considerations associated with implanting the D70-PCTP solid-tip device. A balanced anaesthetic technique was used, providing a surgical plane of anaesthesia; premedication with 8mg/kg ketamine, 0.2mg/kg methadone and 0.05mg/kg atropine intramuscularly, induction with propofol intravenously to effect and maintenance with continuous rate infusions of propofol (15mg/kg/hr titrated to 7mg/kg/hr) and remifentanyl (2.4µg/kg/hr titrated to 15µg/kg/hr). Multimodal analgesia was provided as necessary, including local anaesthetic blocks, 0.01mg/kg buprenorphine intramuscularly, 2mg/kg tramadol orally and 0.2mg/kg meloxicam orally. Antibiosis was administered in the form of amoxicillin clavulanic acid (25mg/kg intravenously at induction followed by 8.75mg/kg subcutaneously once daily). The dual pressure catheters were surgically implanted into the apex of the left ventricle via a midline laparotomy and incision in the diaphragm, and into the abdominal aorta via the left femoral artery. The device body was anchored in the abdominal cavity to measure core body temperature. The positive ECG electrode was positioned on the diaphragm close to the apex of the heart, and the negative electrode advanced into the superior vena cava via the right jugular vein. The exact position of the negative (solid-tip) electrode was ascertained at surgery by monitoring ECG morphology. Radiographs were taken post-operatively to confirm placement of the device, and to ensure no pneumothorax remains. Recovery was closely monitored, and post-operative pain was assessed, with analgesia being tailored to the individual animal. The solid-tip negative electrode configuration ensures the surgical procedure for implantation is reproducible and simplified compared to subcutaneous ECG lead placement. To date 23 telemetry devices with solid tip ECG configuration have been implanted into the cynomolgous macaque, 9 of which were the D70-PCTP device, and no surgical complications have been noted. ECG waveforms from these implants are considered good, and the animals recovered well without associated complications. Our peri-operative protocol provided stable anaesthesia and suitable analgesia for this surgical procedure. To date none of our D70-PCTP macaques implanted with a solid tip ECG configuration have required surgical repair, compared to four animals requiring ECG repair from a total of 17 animals with subcutaneous ECG lead placement in the previous 12 month period. The solid-tip ECG lead D70-PCTP device provides a potential improvement in ECG waveform quality in the primate, reducing noise associated with muscle contraction and movement. It also allows for improved animal welfare due to decreased surgical/anaesthesia time and should reduce the need for surgical repairs.

Comparison, Refinement and Training of Mouse Endotracheal Intubation Methods

AUTHOR: Szczepan Baran

ABSTRACT:

Safe and correct endotracheal intubation is used to mechanically ventilate rodents for various surgical and non-surgical studies. Endotracheal intubation training is challenging because of the small size of rodents upper airways, and the fact that repeat intubation attempts lead to a high incidence of injury of the upper airways including hemorrhage and swelling. Such injury may result in undesirable research outcomes and can have a deleterious effect on the mice usually resulting in euthanasia. The goal of this study was to determine the number of times a mouse can be intubated per training session without resulting in severe trauma to the airway. Mice were assessed endoscopically after intubation and graded using the Kircher scale; erythema (score 1), excoriation (score, 2), and frank hemorrhage (score, 3). All mice demonstrated some degree of injury during the initial phase of training resulting in a recommendation of no more than three intubation attempts per mouse per training session, and one attempt per mouse in a study. In this presentation the presenter will discuss the study findings, compare the advantages and disadvantages of five intubation techniques, list equipment required to perform each of these techniques and provide recommendations for intubation techniques for specific studies. Techniques will be presented with videos and images. After attending this session, attendees will be able to select reliable and expeditious methods for intubating rodents for specific studies.

An Innovative Surgical Method for Simultaneous Measurements of Pulmonary and Systemic Vascular Resistances in Conscious Freely Moving Rats

AUTHOR(s): Xuening Hong, Xiaolan Shen, Huawei Zhao, Kersten Small, Colena Johnson, and Bernard Doering

ABSTRACT:
Pulmonary arterial hypertension (PAH) is a progressive, usually fatal disease characterized by exacerbated vasoconstriction and abnormal vascular remodeling, resulting in an increase in pulmonary vascular resistance and an elevation of pulmonary artery pressure. We developed an innovative surgical method in the rodent to continuously monitor pulmonary and systemic arterial pressures and cardiac output to measure pulmonary and systemic vascular resistance. Briefly, a blood flow probe (Transonic Systems, Inc) was placed around the ascending aorta to measure cardiac output, and a dual channel telemetry device (HD-S21, DSI) was used in which we implanted one catheter into the pulmonary artery (PA) through the right ventricle for monitoring pulmonary artery pressure and the other catheter into the abdominal aorta through the femoral artery (FA) for systemic blood pressure. The success rate was greater than 90%. This surgical method allowed our pharmacologists to continuously monitor cardiac output, pulmonary arterial pressure and systemic blood pressure in the same conscious and freely moving rat and subsequently calculate pulmonary and systemic vascular resistances. In conclusion, we developed an innovative animal surgical method in rodents with a high survival rate that allows us to simultaneously monitor blood flow and arterial pressure and compare pulmonary and systemic hemodynamic activities in rodent models.

Characterization of Maternal Pathology, Fetal Viability, and Hypertension with Surgical and Non-surgical Models of Preeclampsia in the Sprague Dawley Rat

AUTHOR: Teresa Gleason

ABSTRACT:
Preeclampsia (PE) is a complex disease associated with pregnancy affecting an estimated 8% of women annually. Common maternal symptoms include hypertension, hyperuriceamia, proteinuria, and reduced placental perfusion. Ultimately, this often leads to an increased incidence for both maternal and neonatal complications during pregnancy. Although the etiology of this disease is not well understood, there are various rodent models used to study the maternal pathology, as well as the impact of PE on the developing fetus. Therefore, the objective of this study was to characterize and evaluate PE in the RUPP (reduced uteroplacental perfusion), adriamycin (doxorubicin hydrochloride), and L-NAME (N-Nitro-L-arginine methyl ester) models, as compared to SHAM and control groups in the female Sprague Dawley Crl:CD(SD) rat. The RUPP model (15 F) consisted of restricting blood flow through the abdominal and ovarian arteries beginning on gestation day (GD) 13 through GD 20. Adriamycin (5 mg/kg) treatment (17 F) consisted of a single IP dose approximately 14-days prior to mating. For the L-NAME treatment (13 F), an estimated 35 mg/kg/day was ingested via drinking water from GD 6 through 20. A comparator control group (7 F) and SHAM surgical group (7 F) (with surgery occurring on GD 13) were also used. Just prior to scheduled euthanasia on GD 20, the anesthetized mean systolic pressure was collected via carotid artery catheterization which confirmed hypertension in the PE models. The RUPP and adriamycin treated female GD 20 body weights were decreased by 18% and 12%, respectively, with the remaining treatment groups being generally similar to controls. Overall fetal viability consisted of <30% survival for RUPP, <55% for adriamycin and <85% for L-NAME treatment groups. This corresponded to RUPP females showing the lowest number of viable fetuses and greatest number of early resorptions and post-implantation loss. However, malformation findings of hemimelia and localized fetal edema along with variations of the rudimentary ribs and ossified cervical vertebrae were generally associated with L-NAME treated females. Maternal serum chemistry and urinalysis parameters were generally similar across all groups. Therefore, the results of this study successfully established, characterized, and compared various rodent models of PE. Additionally, improved post-operative care methods were developed and will be discussed.

A Modified Technique of End-to-side Vascular Anastomosis in the Rat Model

AUTHOR: Sione P. Fanua

ABSTRACT:
A Modified Arteriotomy Technique On A Rat Model Using End-to-side Vascular Anastomosis Is Presented. When Using The Traditional Technique Described By Ellertson (1974) And Linton (1955) For End-to-side Anastomosis In A Rat Model, It Is Difficult To Control The Size Of The Arteriotomy Because The Length And Width Of The Cut Is Variable Due To The Fact That It Is Made At A 45-60 Degree Angle. We Have Developed An Alternative Way Of Controlling The Arteriotomy In The Rat Model And Have Employed This Technique For The Past 14 Years As Part Of Microsurgery Training In Our Fellowship Program. Objective: To Provide A Method For Controlling The Size Of The Aperture When Performing End-to-size Anastomosis. The Modified Arteriotomy Technique In A Rat Model Is Performed As Follows: Using A #5 Jeweler's Forceps, Lightly Grasp The Adventitia Of A 0 – 2 Mm Vessel Diameter And Lift Upward At A 90 Degree Angle. Then, Using A 15 Or 11 Surgical Blade Or Sharp Scissors, Make The Cut In The Vessel At A 90 Degree Angle To The Longitudinal Axis Directly Behind The Jeweler's Forceps. The Size Of The Arteriotomy Will Depend On Vessel Size And Size Of The Donor Vessel. If Done Correctly, The Arteriotomy Will Look Like A Rhombus, I.E. Quadrilateral Having All 4 Sides Of Equal Length. Place A Suture At Each Lateral Edge And Apply Traction To Convert The Arteriotomy To A Transverse Suture Line For Attachment Of The Donor Vessel. The Modified Technique Gives Better Control Of The Arteriotomy Aperture Size, Achieves Better Blood Flow, And Decreases Vessel Spasm And Stenosis. The Technique Is A Modification Of The Technique Described By Ellertson Et Al (1974) And Linton In (1955).

Parenteral Fluid Therapy Response During General Anesthesia in the Rat

AUTHOR: Kimberly Wasko

ABSTRACT:
To determine the effects of parenteral fluid therapy response during general anesthesia in the rat model. When anesthetics reach the bloodstream, the drugs that affect the brain pass through the peripheral circulation and affect organ blood flow. The effects of volatile anesthetics include vasodilation of the coronary circulation affecting systemic vascular resistance – hemodynamics. These changes result in a fluctuation of preload and afterload which can affect blood pressure, thermoregulation, and hydration status. Improper or inadequate hemodynamic support during general anesthesia can result in tissue and/or organ injury due to inadequate tissue oxygenation and perfusion. Four groups comprised this animal study. The control group did not receive anesthesia or fluid therapy. The remaining three groups received gas anesthesia for equal amounts of time. Only two of the groups, however, received fluid therapy by different administration routes. Animals were monitored closely throughout the experiment. Upon completion of this study, the animals were transferred to Institutional Animal Care and Use Committee approved protocols to observe the 3R's – Reduce, Refine and Replace. Animals that received fluids recovered quickly, demonstrated less blood pressure drops (50
vs. 118 mm/Hg), had minimal to no weight loss (2% vs. 16%), normal appetite, normal biologic outputs and minimal to no dehydration (1% vs. 11% to positive control). Intravenous hydration was associated with the best hemodynamic parameters. The intravenous hydration group had shorter time of emergence from anesthesia and exhibited typical behaviors. The animals that received no fluid therapy stabilized 2-4 days post-anesthesia. All animals that undergo general anesthesia should receive fluid therapy thus improving recovery. SUPPORT:
Johns Hopkins Center to Alternatives to Animal Testing Grant Proposal #AWE-2009-50

A Common Animal Care and Use Program – Just Different

AUTHOR: Sylvia I. Gografe

ABSTRACT:
The Animal Care and Use Program at Florida Atlantic University is comparably small with about 45 Principal Investigators and approximately 100 active protocols. However, the species diversity sets it apart from programs with traditional laboratory animal species. More than half of the PIs are engaged in research utilizing wild birds, fish, amphibians, reptiles and nontraditional mammals. Research is conducted in the field with the majority taking place in the Everglades, while others involve in house FAU facilities requiring physical facility, program and training adaptations to accommodate the needs of the species and the safety of personnel. This presentation describes the program from the perspective of the Attending Veterinarian, Clinical Veterinarian and Research Collaborator all combined in one person. It will focus on marine species, emphasizing the challenges and rewards related to working with atypical laboratory animal species. Whereas small size is a common obstacle for rodent researchers, it is the large size in the Bottlenose Dolphin Health and Risk Assessment Project, the sea turtle study in which sex can only be evaluated via a surgical approach or the stingrays that are difficult to adapt to captivity while enrolled in research. All are unique projects and exciting situations can arise. How often does it happen that an IACUC requests that the veterinary staff establishes a stingray sentinel protocol? Although sounding simple it has proven to be a daunting task. Education and public outreach are important as well when working with marine wildlife in Florida, which can include being watched by school kids while conducting research. All together one can state, working at Florida Atlantic University has been a rewarding journey so far.

In Vitro and *In Vivo* Studies for The U.S. Navy on Strategies for Predicting and Delaying CNS Oxygen Toxicity (CNS-OT)

AUTHOR(s): Jay B. Dean and Dominic P. D'Agostino

ABSTRACT:
The risk of developing CNS-OT (grand mal seizures) is the limiting factor in the use of hyperbaric oxygen (HBO2) in hyperbaric, diving and submarine medicine. Currently, U.S. Navy SEALs using closed circuit rebreathers (100% O2) are limited to only 10 minutes of bottom time in 50 feet of seawater (2.5 atmospheres absolute) to avert seizures. Likewise, submariners that become pressurized in a disabled submarine, but who pre-breathe HBO2 to "denitrogenate", are threatened by an increased risk of CNS-OT; oxygen pre-breathing is required to reduce the risk of decompression sickness during a rapid buoyant ascent to the surface. Accordingly, the goal of the U.S. Navy's "Ox Tox" research program is to develop strategies for predicting and delaying onset of CNS-OT. We have used the combination of in vitro (rat brain tissue slices) and in vivo animal models (intact unanesthetized rats) in our studies of CNS-OT for the U.S. Navy. Using brain slices, we are gaining insight into how hyperoxia affects production of reactive oxygen species (ROS) that in turn stimulate electrical signaling in mammalian neurons. In vitro experiments also have revealed that putative central CO2-chemoreceptor neurons in the brainstem, which contribute to the control of ventilation, are highly sensitive to ROS produced during HBO2. This suggested that early changes in ventilation while breathing HBO2 may precede onset of CNS-OT seizures. If so, then changes in ventilation may be a "physiological marker" of an impending seizure. Subsequent studies using radio-telemetry adapted for use in HBO2 confirmed that "hyperoxic hyperpnea" precedes onset of seizure in unanesthetized rats by ~8-10 minutes. In addition, this same animal model has enabled us to identify therapeutic interventions that accelerate and, more importantly, delay onset of CNS-OT. For example, overdosing with the decongestant pseudoephedrine increases the risk for CNS-OT in male rats. Conversely, pretreatment with a synthesized ketone ester just 30 minutes prior to diving on HBO2 mimics the blood chemistry produced by the ketogenic diet; recall that the ketogenic diet has been used successfully to treat drug-resistant epilepsy. Likewise, oral ingestion of ketone ester delays onset of seizure in rats breathing HBO2 by ~580%. In summary, we've identified a means of predicting (hyperoxic hyperpnea), delaying (therapeutic ketosis), and accelerating (decongestant overdose) CNS-OT in a mammalian animal model. Future studies will exploit this model further to study improved mitigation strategies against oxygen toxicity of the brain, lungs & eyes (ONR N000141310405 Dean; N000141310062 D'Agostino).

Assessing the Impact of Alcohol Intoxication Combined with Hemorrhagic Shock on the Mesenteric Microcirculation Using Intravital Microscopy

AUTHOR(s): Travis M. Doggett and Jerome W. Breslin

ABSTRACT:
The microvascular endothelium of capillaries and post-capillary venules form a semi-permeable barrier that allows the selective transport of fluids and solutes. Endothelial barrier dysfunction resulting from hemorrhagic shock causes excessive fluid leakage and is a significant clinical problem in trauma medicine. Alcohol intoxication increases the risk for traumatic injury and more than 40% of trauma patients have intoxicating blood alcohol levels. We hypothesized that acute alcohol intoxication exacerbates hemorrhagic shock/resuscitation-induced endothelial hyperpermeability. Male Sprague-Dawley rats were anesthetized and catheters were implanted into the left carotid artery and right jugular vein. In some cases a gastric catheter was also implanted. Following 2-3 days of recovery, the animals received 2.5 g/kg ethanol (EtOH) or water as a control via oral gavage or the gastric catheter. Blood pressure was monitored continuously from the arterial catheter. A fixed-pressure hemorrhage was achieved by withdrawing blood through the carotid line to a pressure of 40 mm Hg for 1 h followed by resuscitation (i.v.) with Lactated Ringers (LR) (40% total blood removed (TBR) bolus and a 2x TBR infusion for 1 h). Next, the rats were anesthetized and a midline laparotomy was preformed. The mesentery was externalized for view on an upright fluorescent microscope. FITC-albumin, 100 mg/kg in LR i.v. bolus and 0.15 mg/kg/min infusion for 1 h served as a tracer. Arteriolar diameter, integrated optical intensity of extravasated FITC-albumin, rolling and adhesion of leukocytes, and lymphatic diameter were measured. This model allows for an integrated view of the microcirculation in response to inflammation caused by combined alcohol intoxication and hemorrhagic shock. Supported by NIH R01HL098215, R21AA020049, and the ABMRF/Foundation for Alcohol Research.

Lumbar Intrathecal Catheterization in the Canine and Primate

AUTHOR: Jon Ehrmann

ABSTRACT:
Alzheimer's Disease (AD) is a progressive neurodegenerative disorder characterized by an excessive production of extracellular amyloid plaques and intracellular neurofibrillary tangles in the brain. It is estimated to affect 5.3 million people and is the 6th leading cause of death in the Unites States. In an effort to support the investigation of specialized CSF biomarkers, a reliable and reproducible chronic system was developed to collect lumbar CSF from conscious dogs and primates. Several non-surgical and surgical procedures have been published for accessing lumbar CSF. We investigated the use of a lumbar catheter with a vascular access port to collect lumbar CSF. Although the surgical model is not novel, we evaluated various modifications to described surgical and maintenance procedures to increase patency of chronic indwelling lumbar CSF catheters. With our final modified surgical procedure and catheter maintenance program, our patency rate with several animals is approaching twenty eight months. Although our model is currently being used for collection of CSF, it can also be used for the infusion of compounds as well. Based on the results of the proof of concept studies, our model proved to be useful for single and multiple dose pharmacokinetic studies in a search for an effective Alzheimer's treatment.

Development of Retroperitoneal Fibrosis in a Cohort of Feline Renal Allograft Recipients: 1998-2012

AUTHOR: Heidi Phillips

ABSTRACT:

To report the prevalence of retroperitoneal fibrosis (RF) in feline renal allograft recipients, describe the condition, treatment, and prognosis, and identify possible risk factors for further evaluation. Retroperitoneal fibrosis is a rare condition marked by the formation of fibro-inflammatory tissue in the retroperitoneal space. Macroscopically the condition is characterized by a white, fibrous plaque that surrounds the abdominal aorta, caudal vena cava, iliac vessels, and ureters.[1] Microscopically, diffuse mononuclear cell inflammatory infiltrate and abundant collagen bundles comprise the tissue. Physiologically, progressive loss of ureteral peristalsis may lead to functional obstruction and renal disease. In feline and human patients, the pathogenesis of the condition and risk factors for its development have not been reported. Retrospective review of feline recipients undergoing renal allograft transplantation at the Veterinary Hospital of the University of Pennsylvania from 1998-2012. During the study period, 138 cats underwent renal allograft transplantation. Of these, 29 (21%) developed clinically significant RF confirmed by abdominal exploration. All cats were azotemic and anemic at the time of diagnosis, and all had received cyclosporine oral solution and prednisolone immunosuppressive therapy. The mean time from transplantation to diagnosis of RF was 125 days (range 4-730 days, median 62 days). Sixty-three percent of cases were neutered males, and 37% spayed females. Five of 29 cats (17 %) were diagnosed with diabetes mellitus prior to diagnosis of RF. Evaluation for the presence of concurrent disease, occurrence of trauma or iatrogenic injury, and the use of specific medications did not reveal significant risk factors for the development of RF. Treatment by surgical ureterolysis relieved clinical signs and resulted in improved clinicopathologic data in all patients. Retroperitoneal fibrosis is a possible complication of renal transplantation surgery in felines. Risk factors for its development were not identified; however, further prospective study is needed comparing data from cats that develop RF to data from a control group of feline renal allograft recipients that do not develop RF. Treatment by surgical ureterolysis appears to be effective in relieving clinical signs and improving renal clinicopathologic data.

An *In Vivo* Hemostasis Evaluation Method for Comparing Surgical Devices

AUTHOR(s): Mary Mootoo, Peter Shires, and Heather Rentschler

ABSTRACT:

The hypothesis was that hemoglobin (Hb) or protein concentrations could be used to quantify low levels of bleeding typically seen when dissecting through muscle or connective tissue with surgical devices. Four paired incision sets were performed in the longissimus dorsi muscle of one porcine model to compare cold steel scalpel, monopolar energy and 3 ultrasonic blades. A transverse linear incision was made dorsally across the muscle through the fascial sheath. The muscle itself was incised using the test or control devices – one device per incision. Suction was performed within the incision for 5 minutes. All fluid suctioned was contained in an isolated receptacle inserted into the suction line. The suction tubing and tip were rinsed with 200mls of distilled water which was captured in the same receptacle. One clean dry 2x2 sponge was inserted into the incision between the cut surfaces of the muscle and left in place for 15 minutes. The sponge was then removed and inserted into the saved receptacle of suction fluid and distilled water. A reference venous blood sample was drawn and mixed with 200mls of distilled water. Distilled water causes all the red blood cells to rupture and the Hb protein creates a red color intensity in the water. Analyzing a sample of the water determines both the Hb and protein concentrations. The color can then be calculated back to actual absolute amounts. There were clear differences in Hb concentrations between all incisions except two ultrasonic blade incisions which were equal. The Hb results were mirrored by subjective observations for all paired incisions. Protein values followed the same trend as Hb values, but seemed more erratic. This was especially true in the reference sample where a fibrin clot was obvious. This suggests that protein evaluation is less specific in these circumstances and should not be solely used. This is a viable hemostasis evaluation method that can be used to compare and contrast devices. Validation of the method will be the next step.

Costochondral Thoracotomy as a Means to Access the Left Ventricular Apex for Intramyocardial Injection with Survival in the Rat

AUTHOR(s): Christie Cunningham, Szczepan Baran, David Flynn, James McCloud, and Andrew Douglas

ABSTRACT:
To describe an optimal means to access the left ventricular apex for intramyocardial injection with survival in the rat. The rat heart is typically accessed via a 4th or 5th intercostal thoracotomy. This approach often results in visual interference from the lungs and poor access to the left ventricular apex. In this study we describe an alternative surgical and anesthetic approach to minimize both respiratory effects and manipulation of the heart. Seventy Sprague Dawley rats were premedicated with glycopyrrolate (0.01 mg/kg, SC) and ketoprofen (5 mg/kg, SC), anesthetized with dexmedetomidine (0.1 mg/kg, IP) and sevoflurane (1 - 4% in O2), intubated and ventilated using a dual mode [Intermittent Positive Pressure Ventilation (IPPV) or High Frequency Oscillatory Ventilation (HFOV)] ventilator. The rats were secured in dorsal recumbency and hair was shaved from the ventral thorax and cranial abdomen. The shaved area was disinfected with chlorhexidine and 70% isopropyl alcohol. DuraPrepTM was applied to the skin prior to aseptically draping with both paper and SteriDrape®. Cefotaxime (50 mg/kg, SC) and atipamezole (1 mg/kg, SC) were administered prior to incising the skin overlying the costochondral junctions from the 3rd rib to the xiphoid, approximately 5 mm left of the sternum. The underlying pectoral muscle was bluntly dissected and reflected laterally to create a muscle flap over the thoracotomy. The intercostal muscles surrounding the 4th - 6th or the 5th - 7th costochondral junctions were dissected and the cartilage transected. An Alm selfretaining retractor was used to maintain heart exposure. Lidocaine (2%) was applied topically to the heart after opening the pericardium. Each rat received a single 80 >L intramyocardial fluid injection into the left ventricular apex using a 28 gauge needle. During injection, the ventilator was converted to HFOV mode to minimize respiratory motion. Following injection, ventilation was returned to IPPV mode. Oxygen saturation was monitored throughout the procedure using a pulse-oximeter. Chest closure was accomplished in 3 layers. Prior to tightening the final rib suture, the chest was compressed to remove residual air. The pectoral muscle was secured over the apposed ribs and the skin closed. During recovery, rats were rehydrated with 0.9 % saline (5 mL, SC) and slow release buprenorphine (ZooPharm, 1.2 mg/kg, SC) was administered for postoperative analgesia. Rats were survived for 1, 3 or 6 months. A costochondral thoracotomy with ventricular apex injection was successfully performed in seventy rats. Two rats died due to respiratory distress during the immediate postoperative period. The remaining animals survived to their appointed necropsy date (68/70 = 97% survival). Rats were necropsied at 30 and 60 days (n=22 each). By 30 days, skin and muscle surrounding the costochondral thoracotomy were fully healed. Thirty and 60 day radiographs confirmed that the transected costochondral cartilage was typically not fused. The thoracic cavity was normal in all animals. None of the excised hearts showed evidence of bruising or enlargement. The pericardium adhered to the ventricular wall in two rats (2/44 = 4.5%) without clinical complication. A small blanched area (typically ≤ 3x3 mm) was observed near the left ventricular apex in the majority of rats (32/44 = 73%) corresponding to the site of fluid injection. Six month necropsy results are pending. A costochondral thoracotomy paired with well-controlled ventilation resulted in excellent visibility and access to the left ventricular apex for intramyocardial injection.

Cell-based Gene Therapy for the Central Nervous System

AUTHOR: Dave Morgan

ABSTRACT:
Alzheimer's disease is a challenging medical problem without meaningful treatments. One approach is to reduce amyloid in the brain, and gene therapy with proteases that degrade amyloid injected directly into the mouse brain have shown benefit. However, the human brain is large and the diffusion of viral gene therapy vectors so restricted that this approach will be hard to use in human patients. In this project we demonstrate the proof of principle of using transfected circulating monocytes to shuttle the therapeutic gene into the brains of amyloid depositing mice. This required the use of a subcutaneous chronically indwelling catheter in which cells were injected intravenously twice weekly for 2moths. This treatment with monocytes transfected ex vivo with the protease neprilysin arrested the development of brain amyloid in these mice.

An Orofacial Thermal Pain Assay for Assessing Analgesic Dose Buprenorphine and Tramadol in Rodents: a Clinically Relevant, Non-invasive Approach

AUTHOR(s): Harvey Ramirez and John Neubert

ABSTRACT:
Assessment and relief of post-surgical pain in rats and mice has been a major topic of discussion in during the past decade. However, there are few animal systems capable of efficiently testing analgesic medications. Here we present an innovative, automated operant behavioral approach for evaluating analgesic efficacy in rats and mice. Male and female rats (Crl:SD, N=10 per group) and hairless mice (Crl:SKR-*Hrhr,* N=12) were placed in boxes trained to reach a liquid reward while contacting the thermal elements with their cheeks. A solution of sweetened condensed milk was used as a reward. Thermal pain was experienced when the animals' cheeks, after they were sensitized with capsaicin cream, contacted the thermal element placed at 450C. We tested subcutaneous injection (SQ) of buprenorphine (0.005, 0.01, 0.03, 0.05 mg/kg, plus saline), voluntary ingestion (VI) of buprenorphine (0, 0.3, 0.4, 0.5, 0.6 mg/kg, VI of tramadol (0, 10, 20, 30, 40 mg/kg) in rats and SQ buprenorphine (0.01, 0.05, 0.1, 0.2 mg/kg, plus saline) in mice. All animals within each group received each dose plus vehicle only in a crossover fashion with a washout period of 4-5 days between testing. The total number of licking events was divided by the number of facial-contact events to generate a ratio of reward-licking events to facial-stimulus contact event per dose. Repeated measures ANOVA was used to analyze data from each group. Results indicate that 1) buprenorphine SQ at dosages of 0.03 ($p<0.05$) and 0.05 ($p<0.5$) mg/kg in male rats, while only 0.03 mg/kg ($p<0.05$) in female rats resulted in a statistically significant difference; 2) dosages of 0.05 ($p<0.05$) and 0.1 ($p<0.01$) mg/kg were effective in male mice but only 0.05 mg/kg ($p<0.05$) was effective in female mice. 3) VI buprenorphine at 0.5 mg/kg ($p<0.05$) and 0.6 mg/kg ($p<0.05$) resulted in a statistical significant difference male rats while none of the dosages tested in female rats were able to provide a statistical significant difference; and 4) VI of tramadol at 40 mg/kg ($p<0.05$) was effective in providing analgesia in male rats while dosages of 30 ($p<0.5$) and 40 ($p<0.5$) mg/kg were effective in female rats. This assay was effective at obtaining analgesic doses that fall within currently published doses of parenteral buprenorphine. The non-invasive, automated nature allows us to 1) perform studies while minimizing experimenter bias, 2) directly compare different drugs and routes of administration. Finally, its sensitivity allows us to optimize doses based on sex differences.

Surgical Writing-from Protocol Development, Conception of the Research Hypothesis, Data Collection and Publication

AUTHOR: Luis Toledo-Revera

ABSTRACT:
Part 1: A one hour lecture open to all will be given during one of the full meeting sessions.
Part 2: limitation of participants, must register in advance A "hands-on" workshop will address the details associated with protocol development from the conception of the idea and characterization of the hypothesis to integration of the written scientific protocol. Possibility of success will be related to the individual interest and participation in the process. A final written abstract with a completed version of the whole workshop will be gathered at the end of this experience. (workshop participants must bring research idea (hypothetical or real) for workshop instruction)

Decreased Nerve Conduction Velocity in Peripheral Nerves Following Exposure to Bone Morphogenetic Protein-2

AUTHOR(s): David Margolis, Gregory Powell, David Bennett, Ralph Fregosi, and Lisa Truchan

ABSTRACT:
To measure the effect of recombinant human bone morphogenetic protein-2 (rhBMP-2) on peripheral nerves. Due to its efficacy in treating open tibia fractures and promoting spinal fusion, there has been increasing off label use of rhBMP-2. Recent studies show that rhBMP-2 may cause axonal loss when used in the vicinity of peripheral nerves. The purpose of this study is to measure nerve conduction velocity (NCV) in rat peripheral nerves following exposure to rhBMP-2. Methods: Ten male adult Wistar rats were used in this study. The rats were anesthetized using 2% inhaled isoflurane. The isolfurane dose was adjusted between 1-2% throughout surgery as needed. A lateral incision was made through the thigh and the sciatic nerve was identified and exposed using blunt dissection. rhBMP-2 (Infuse) was implanted directly on the sciatic nerves. The contralateral control nerve underwent a sham surgery where a collagen carrier without rhBMP-2 was implanted. After surgery all rats received analgesia with 2mg/kg subcutaneous burpenorphine for two days. Three weeks following surgery NCV measurements were performed on anesthetized rats. Nerves were then harvested for histological analysis. Rats were euthanized by exanguination prior to recovering from anesthesia. rhBMP-2 induced ectopic bone formation in muscle tissue in all rats after three weeks. In one animal the ectopic bone was directly adherent to the sciatic nerve. In this rat the NCV was decreased by 80% in the rhBMP-2 exposed nerve (14m/s in experimental vs. 67.7m/s in control nerve). In another animal NCV was decreased by 50% following rhBMP-2 exposure (41.4m/s in control vs. 88.9m/s in the experimental nerve). NCV measurements were collected from 5 additional rats, but due to equipment malfunctions, data was not collected from both the experimental and control nerves within an individual animal. In addition to the axonal dropout, this study demonstrates that exposure to rhBMP-2 may result in decreased NCV in peripheral nerves. This effect is independent of nerve compression, which may additionally decrease NCV as was seen the case of the peripheral nerve that was adherent to ectopic bone. Additional data are needed to perform statistical analysis and to correlate changes in nerve function to histological changes. Support: Provided by the Orthopaedic Research and Education Foundation through a Resident Education Grant.

Microbiological Evaluation of an Alternative Surgical Draping Material

AUTHOR: Gregory O. Voronin

ABSTRACT:
Department of Safety Assessment and Laboratory Animal Resources, Merck & Co., Inc. Kenilworth, New Jersey USA. Proper aseptic technique is essential to the successful outcome of clinical and research surgeries. From the surgical facility, surgical equipment to the surgical team and the surgical site, attention must be given to all the elements involved in a surgical procedure to ensure asepsis. Surgical drapes used to isolate and protect the surgical site, are an essential component of proper aseptic surgical technique. Recently the use of a commercial wrapping product, Glad Press'n Seal, has been suggested by some as alternative to conventional surgical draping material for small animal research surgeries. Advocates of its use suggest that the ease of application, adherence, water proof nature and low cost of this material make it an excellent surgical draping material. In the interest of evaluating this material for routine use as a small animal surgical drape, a serial microbiological evaluation of the material was undertaken. After obtaining the material, equal portions were either sterilized with ethylene oxide or left in an unsterilized state. Weekly aerobic and anaerobic cultures were obtained from each sample over the course of a month. Encouragingly, only the external packaging of the unsterilized material yielded positive culture results over the course of sampling. The results of these cultures and the role of surgical drapes in the context of proper aseptic technique in surgery will be discussed in this presentation.

Experiences in Implanting Microelectrode Arrays for Chronic Neural Recording in Nonhuman Primates

AUTHOR: Oscar A Bermeo Blanco

ABSTRACT:
Two NHPs were implanted with a microelectrode arrays from Blackrock Microsystems in the motor cortex of the brain. We will discuss our experiences during the surgery procedures, pre-intra and post operative craniotomy and array implantation. We will show summarized data obtained in a 9 month period from the neurosignal activity recordings and histopathology results at the end of the study.

Precise Complete Caudate Lobectomy for Hepatocellular Carcinoma Based on Computer-assisted Operative Program

AUTHOR(s): Weihua Qiu, Jiajun Ren, Jiabin Jin, Baiyong Shen, Xiaxing Deng, Hongwei Li, and Chenghong Peng

ABSTRACT:
To investigate the significance of operative program using 3D image–processing software and virtual liver resection systems to improve the safety for complete caudate lobectomy (isolated or combined lobectomy). Total isolated caudate lobectomy is a technique-demanding procedure, and accurate knowledge of tumor-surrounding vascular anatomy is essential for operative program. 36 patients with HCC located in the caudate lobe underwent complete caudate lobectomy at a single tertiary referral center between May 2002 and Oct 2012. Based on IQQA-Liver 3D software and virtual liver resection systems, the tumor-bearing vessels were identified and virtually resected. The depending parenchymal volume was calculated for definition of an optimal liver division plane as well. Guided by intraoperative ultrasound, the actual lobe resections were then performed according to the simulations. The clinical data of these patients were compared with those from other 12 traditional caudate lobectomies (control group). Twenty-four of 36 patients underwent isolated total caudate lobectomy whereas twelve received a total caudate lobectomy combined with an additional partial hepatectomy. The median diameter of the tumor was 6.9±3.9cm (range, 2-16 cm). The average operative time was 239±101 min (range from 60-540min), and estimated blood loss was 450ml (50-2300). Median blood transfusion was 3.5u (range, 2-11u). There were no perioperative deaths. Postoperative complications included bile leak in four patient and ascites in two. Median length of hospitalization was 12 days (range, 9-21). Both resection margin and volume were significantly correlated with those predicted by preoperative simulations. After precise local resection, neither ischemia nor congestion was observed in the remnant livers. All patients obtained adequate resection margins without recurrences in the resection sites after a median follow-up time of 18 months. The amount of intraoperative bleeding and blood transfusion, as well as liver function, was more favorable in precise caudate lobectomy group than control group. Moreover, the incidence of complications and hospitalization length were decreased significantly in precise caudate lobectomy group. The 1-year, tumor-free survival rate was 88.89 % (32/36) in precise hepatectomy group, which is 66.67 % (8/12) in control group. Preoperative evaluation of tumor-surrounding vessels by 3D analysis is of great value for individual operative program. The precise complete caudate lobectomy could preserve functional liver tissue with complete venous return to a great extent, resulting in fewer incidences of postoperative complications. Precise caudate lobectomy also has the potential to achieve more adequate tumor-free resection margin, which may result in higher tumor-free survival rate. This study was supported by Nature Science Foundation of China (81172326), Shanghai Science and Technology Commission Grant (10ZR1419400) and Shanghai Charity Foundation for Cancer Research.

Refining the use of Cautery to Perform Kidney Ablation

AUTHOR(s): Marla A. Wilwol, Jennifer M. O'Hare, and Cristina M. Weiner

ABSTRACT:
One surgical method to perform a subtotal nephrectomy in a rodent is ablation of the kidney poles with a cautery device. This procedure can be used to remove both kidney poles to render only a fraction of the remaining kidney viable. In our experience, there are five factors that affect the condition/appearance of the kidney tissue after ablation: (1) temperature of cautery tip; (2) temperature adjustment on cautery unit; (3) battery vs. AC powered cautery unit; (4) size and shape of cautery tip; and (5) time needed to incise through the kidney. We theorized that refining the power, heat, and tip type would yield consistency with the surgical procedure. We trialed four different types of cautery units: (1) battery operated high temperature unit; (2) battery operated low temperature unit; (3) battery operated adjustable temperature unit and (4) AC powered adjustable temperature unit. Four different types of cautery tips were also tested on the AC powered unit: (1) loop tip; (2) flat fine tip; (3) angled loop tip and (4) vasectomy tip. Training animals were used and through the process of trial and error we found the ablation procedure to be most successful when using an AC powered adjustable temperature unit with the dial set at 9 (Thermal Cautery Unit, Stoelting Co., Wood Dale, IL). Success of the procedure was determined by the appearance of the tissue immediately following ablation. We also found that the flat fine cautery tip produced the best tissue separation and coagulation when delicately advanced through the tissue.

Technical Procedures Necessary to Achieve Successful Endothelial Cell Keratoplasty in the Cat

AUTHOR(s): Vince Mendenhall, Matt Giegengack, Belinda Wagner, Eric McCloud, Mickey Flynn, Christie Cunningham, and Andrew Douglas

ABSTRACT:

The corneal endothelium is essential for the maintenance of normal corneal hydration, thickness, and transparency. The corneal endothelium of humans and carnivores has little to no regenerative capacity when damaged, and its loss results in irreversible corneal edema. This condition is currently treated by either full or partial corneal transplantation, of which Descemet's Stripping Endothelial Keratoplasty (DSEK) is becoming the surgical treatment of choice in preference to full thickness corneal transplantation. This procedure does have limitations, however, and several methods of improving on it are being investigated – thus the need for animal studies to establish the safety and efficacy of new treatments. Corneal endothelial cells regenerate naturally in herbivores such as rabbits; thus they are not suitable for use as a Test System in developing new treatment regimens for endothelial cell loss. Cats are currently thought to be the most appropriate animal model to project the outcome of similar procedures when performed in humans. To develop an appropriate surgical regime in the cat for studies evaluating the safety and efficacy of candidate products designed to treat corneal endothelial dystrophy. Human corneal endothelial cells and the posterior stroma from cadaveric human eyes donated to eye banks were used as the test material, and were cut to a diameter of 7.5 mm. The animals were preanesthetized with buprenorphine, glycopyrrolate, and dexmedetomidine, intubated, and maintained in anesthesia with sevoflurane. The hair around the right eye was clipped, and the area prepared with chlorhexidine and 70% isopropyl alcohol. The animal was placed in dorsal recumbency and the head was immobilized so that the limbus of the eye to be operated was horizontal. The area around the eye was then wiped with DuraPrep™ and two drops of 5% ophthalmic Betadine® was applied to the eye itself. The site was draped for strict aseptic surgery including the use of Steri-Drape™. A lateral canthotomy was created to aid in the elevation and stabilization of the eye with three to four stay sutures placed through the sclera to provide for good visualization of the limbus and the entire cornea. A circle was marked on the corneal epithelium with an 8.0 mm trephine densely coated with gentian violet. One small limbal incision was made about 90° opposite to the proposed superior corneal incision in order to preemptively irrigate the anterior chamber with balanced salt solution (BSS PLUS®) containing 100 IU/mL heparin and 1.0 mL, 1:1,000 epinephrine/250 mL to prevent fibrin formation due to loss of intraocular pressure. A viscoelastic solution was then infused into the anterior chamber, and a small clear corneal incision was made superiorly. A reverse Sinsky hook was introduced through it to remove the endothelial cells and score Descemet's membrane on the posterior side of the cornea along the circle marked on the anterior cornea. The corneal incision was enlarged to about 4 mm and two drops of viscoelastic material applied to the endothelial surface of the transplant tissue. It was loaded into an EndoSerter® device and introduced into the anterior chamber through the corneal incision. The implant tissue was unfolded and centered under the previously stripped Descemet's membrane. The corneal incision was then closed with three to four interrupted sutures of 10-0 nylon suture material, and the anterior chamber hyper-inflated with air in order to hold the transplanted tissue against the posterior cornea. Three to four simple interrupted sutures of 10-0 nylon were then placed through-and-through the cornea and implant in order to secure it in position. The side port corneal incision was then closed with a single suture of 10-0 nylon, and the lateral canthotomy was closed with 4-0 Monocryl™. Finally, a subconjunctival injection of 10 mg of methylprednisolone (DepoMedrol®) was performed. Postoperatively, the eyes were treated with tobramycin and dexamethasone eye drops twice a day for the duration of the study. The animals were observed for periods of up to 8 weeks, at which time they were euthanized and the eyes submitted for histologic examination. The described surgical procedure differed from that used in humans in the following ways: (1) Addition of heparin and epinephrine to the BSS solution; (2) lateral canthotomy and placement of stay sutures; (3) clear corneal incision instead of a temporal conjunctival peritomy; (4) destruction of endothelial cells and Descemet's membrane instead of removing them; (5) stabilization of the implant with through-and-through corneal/implant sutures. These slight modifications to the procedure as done in humans proved necessary in cats to more closely resemble the procedure as done in humans. These allowed for an accurate evaluation of various treatments to the donor cornea with good prediction of the outcome as it would occur in humans.

Single Technician Sheep Intubation: Twenty Five Years of Experience and Innovation

AUTHOR(s): Jed Pugsley, Jake Bair, and Raymond Olsen

ABSTRACT:

To describe the means and methods for improved single technician endotracheal intubation. Through twenty-five years of experience and innovation, a system has been developed that easily allows a single technician to safely place an endotracheal tube (intubation) in a large animal laboratory setting. Anesthesia is induced by intravenous injection of either a Ketamine/Diazepam cocktail or Propofol, at a dose of 3.0-6.0 mg/kg BW, 0.05-0.5 mg/kg BW, or 3.0-6.0 mg/kg respectively. Animals are then placed on a floor level mechanical lift cart which allows the animal to be effortlessly moved onto the surgery gurney. With the swallowing reflex no longer present, a custom speculum is inserted into the mouth between the upper and lower jaw. Using one hand to open and manipulate the speculum, a laryngoscope is used to visualize the epiglottis and the opening of the trachea. An appropriately sized intubation tube is inserted and correct placement confirmed. A customized bite block is then inserted through the speculum and fastened. The speculum is then removed. The intubation tube is then secured through a central hole in the bite block. Care is taken to assure that the tongue does not get between the speculum or bite block and the teeth. The bite block allows a protected and unobstructed passage to both the esophageal opening and airway. The bite block provides open access for other implements such as a rumen tube, esophageal stethoscope, endoscope, or stomach pump. Data has been recorded from 2008 to current. In that time more than 1000 cases of sheep intubation has been carried out using this system. While employing this system no significant trauma caused by intubation and no animal deaths related to airway problems have occurred during surgical manipulations. Total anesthesia related deaths over the time period outlined above are less that 1%. Animals have recovered from anesthesia with minimal to no adverse reactions, which in turn, alleviates distress and discomfort to the animals. The time required to intubate and prepare an animal for surgery has been reduced and multiple cases per day are achieved. Additionally, no injuries to our technicians have occurred when working with sheep exceeding more than 100 kg in weight. Employment of these innovative tools, practices, and methods has proven to be beneficial. These intubation and handling methods are repeatable at other institutions. These methods are also applicable to other research animals such as pigs, goats, dogs, and other large animals.

Technique and Methodology of Transcatheter Aortic Valve Implantation (TAVI) in Ovine Models

AUTHOR(s): Selwan Abdullah, Matthew Lahti, and Richard Bianco

ABSTRACT:

To describe techniques used to overcome the challenges and successfully create ovine models for TAVI experimentation. Historically, Aortic stenosis (AS) has been treated with balloon valvuloplasty, Surgical Aortic Valve Replacement (SAVR), and, more recently, TAVI. Today, TAVI is increasingly utilized for AS patients who are not eligible to receive SAVR. TAVI is associated with higher risks of stroke and paravalvular regurgitation when compared to SAVR. Despite the complications, providers are now beginning to use TAVI in patients that may still be eligible to undergo SAVR. Little has been published about animal modeling for TAVI. Creating accurate animal models is challenging. Our objective was to address these challenges by using stepwise methodology and technique modification to successfully protocol animal models. First, the femoral artery approach is difficult in ovine models because the sheep arteries are too small for the transcatheter wire. Therefore, a transapical approach can be performed. Second, the prosthetic valves require a firm surface to push against when deployed in order to anchor properly. In humans, sclerotic lesions provide that surface. Animals do not develop sclerotic lesions. To address this, we created a hard surface by attaching a nitinol band around the aorta. The nitinol band is sewn at the distal edge of the right coronary artery. Lastly, another anatomic challenge is that the arch of the aorta in sheep turns at a narrower angle than in humans. There should be a 50mm distance between the annulus and aortic arch curve in order to deploy a tall-type valve in the proper vertical position. A novice operator may deploy the valve in an improper oblique position. Increased operator experience is necessary for successful valve deployment. The following is a summary of the surgical protocol for a TAVI ovine model. The animal is sedated with 0.04 mg/kg atropine, 10 mg/kg ketamine IM and 2-6 mg/kg propafol IV. 3mg/kg of ceftiofur is administered. The surgical procedure involves a thoracotomy for transapical access, and a separate thoracotomy for nitinol band placement. A pigtail catheter is advanced and aortic root is measured. An appropriate sized nitinol band is applied. The valve is then delivered and deployed in a vertical position. Lidocaine and bupivacaine are provided for analgesia. Prior to nitinol band implementation, 18 TAVI procedures were completed on ovine models via vascular access. Only 6 of 18 trials were without complication, with the most common complications being femoral artery hemorrhage and valve migration. After protocol modification, 25 transapical procedures with nitinol band placement were attempted. 20 of the 25 were without complication, with the most common complication being nonfatal arrhythmia. Valve migration was no longer an issue. An ovine model for TAVI in humans is possible. Transapical approach, and use of a nitinol band result in decreased rates of hemorrhage and valve migration. These models will help in optimizing device design and implementation. Designing animal model protocols for TAVI will open the future possibility of using similar models in assessing other operations such as aortic root replacement.

Improvements in Microdialysis Method Result in Increased Experimental Success

AUTHOR(s): Susan Champagne, Hong Cao, Jonathan Johnston, Robert Lew, and Maria Quinton

ABSTRACT:
For traditional microdialysis experiments, probes/guide cannulae are implanted into the brain of an anesthetized rat according to pre-defined stereotaxic coordinates. The probes/guide cannulae are secured to the skull with dental cement. After 24-48hr recovery, rats are placed in microdialysis bowls. Artificial cerebrospinal fluid is pumped through the probe(s) and the perfusate is collected at specific time intervals for analysis of various neurotransmitters. The dental cement mixture typically used produces heat and fumes, takes a long time to solidify, and therefore can be potentially detrimental to both rat and surgeon. We have found that machine-mixed dental cement capsules produce no heat or fumes, and dry within seconds, thus improving animal/surgeon safety and also greatly reducing the time that animals are anesthetized. Implanting probes directly into the brain using the stereotaxic apparatus instead of manual insertion into guide cannulae reduces the operator error and probe damage. Traditionally, rats are set up in microdialysis cages using a zip-tie around their midsection. Instead, we implant a metal loop into the cement on the skull, to which we attach the hook of the microdialysis setup. Another improvement is the use of rotating microdialysis chambers instead of multichannel swivels. Multichannel swivels are designed to prevent tangling of the tubing between infusion pumps, rat and fraction collectors by turning in a counter direction to the animal's movement. However, the swivels can spin erroneously and actually cause the tubing to tangle. They also clog easily and are prone to leaks, which ultimately leads to failure of the experiment. Microdialysis chambers on turntables rotate in a direction counter to the rat's movement, and preclude the need for swivels. Tangling, clogging, and leaks are avoided. Altogether, we have improved our methods to increase the percentage of success and decrease the number of animals needed per experiment.

Surgical Preparation of a Cat for Brainstem Respiratory and Swallow Control of Breathing Research

AUTHOR: Mary Jane Perkins

ABSTRACT:
This surgical savvy talk will highlight two surgeons working in tandem to prepare a cat for a long term non-survival brain stem preparation to study swallow control and respiratory research. This will be a photographic journey through the surgical actions (and complications) to prepare a cat for neural recording from the brain stem, as well as stimulus recordings on a variety of other specific nerves. The post surgical goal is to study many single brainstem neurons which are acquired, amplified, recorded and tested for communications with other brainstem or spinal sites. CO_2, O_2 and a variety of other stimuli are tightly controlled for the development of neural recordings and chemoreceptor studies on asthma and other illnesses where some may develop difficulty in swallowing (as in cases of many strokes). However getting the animal properly prepared and long term stabilized in order for this research to occur can be a little taxing. Due to the extensive nature of the surgical preparation, euthanasia is the endpoint post surgical manipulations.

Surgical Writing-from Protocol Development, Conception of the Research Hypothesis, Data Collection and Publication

AUTHOR: Luis Toledo-Revera

ABSTRACT:
Part 1: A one hour lecture open to all will be given during one of the full meeting sessions.
Part 2: limitation of participants, must register in advance A "hands-on" workshop will address the details associated with protocol development from the conception of the idea and characterization of the hypothesis to integration of the written scientific protocol. Possibility of success will be related to the individual interest and participation in the process. A final written abstract with a completed version of the whole workshop will be gathered at the end of this experience. (workshop participants must bring research idea (hypothetical or real) for workshop instruction)

Hepatic Portal Vein Catheterisation in the Dog

AUTHOR: Kate Read

ABSTRACT:

Catheterisation of the hepatic portal vein in the dog has been described for both infusion and withdrawal, along with measurement of portal pressure. Historically a number of different techniques have been described, with no major refinements to the procedure in recent literature. An ADME study at our facility required investigation of the extent of first-pass metabolism of the test article when delivered orally. Four male beagle dogs (11.5-13kg) were implanted with a modified polyurethane catheter (tapering from 6F to 4F at the tip with a suture bead 100mm from tip). The catheter tip was advanced into the hepatic portal vein from either the caudal pancreatico-duodenal vein, or the cranial mesenteric vein (accessed via a jejunal vein). The catheter was connected to a subcutaneous vascular access port tunnelled to an accessible site over the right thorax. Multimodal anaesthesia was applied (premedication of 0.005mg/kg dexmedetomidine and 0.2mg/kg methadone intramuscularly, induction with propofol intravenously to effect and maintenance with continuous intravenous infusion of propofol 30 to 15mg/kg/hr and remifentanyl 2.4 to 15 µl/kg/hr). Peri-operative analgesia (bupivacaine hydrochloride provided as a local splash block, 4 mg/kg carprofen subcutaneously, buprenorphine 0.01mg/kg intramuscularly and tramadol 5mg/kg orally) and antibiosis (amoxicillin clavulanic acid administered 25mg/kg intravenously at induction followed by 12.5mg/kg orally twice daily) were provided. Patency was maintained by regular flushing with heparinised saline (50IU/ml), and the catheter locked with heparinised saline (500IU/ml) between access time-points. All four animals were successfully implanted, however a fragile caudal pancreatico-duodenal vein in one animal necessitated catheterisation of the superior mesenteric vein via a jejunal vein. No post-surgical complications were noted and all animals recovered from surgery as expected. Literature regarding this procedure describes difficulties with patency, in particular thrombophlebitis and clot formation over the catheter tip. However, the implants in this study remained patent for the postoperative period; all dogs were used successfully on study, with the collection of all required portal vein PK samples. Blood flow through the catheter was positional in one animal, and was assisted by gentle exercise. Correct catheter placement was confirmed on necropsy following completion of the study, and examination of the tip of the catheter indicated no macroscopic clot formation. Cannulation of the hepatic portal vein using this technique appears to provide reliable portal blood sampling over the time frame of 6 weeks. With only four animals as a pilot study no statistics have been carried out, more animals implanted in this manner are required to further assess this surgical model. With future implantations, refinements can be made to the peri-operative medication protocol, and the post-operative flushing regime.

Cardiovascular Ultrasound Screening For Rodent Surgical Studies: Why And How?

AUTHOR: Matthew Flegal

ABSTRACT:

Compound testing on cardiovascular disease models is routine in laboratory animal research. Unfortunately, rodents in particular are rarely screened for pre-existing cardiac abnormalities which introduces uncertainty into the results. This is typically due to the expense of the equipment and training as well as a lack of concern about their effects on study. Using cardiac ultrasound, we will examine some of these issues as well as describe a successful training methodology for technicians to perform these basic exams. By utilizing these techniques, researchers can increase data reliability and quality as well as lower the numbers of animals needed for study.

Four Decades of Using Large Animals to Assess Human Safety of Heart Valves and other Class III Devices

AUTHOR: Richard W. Bianco

ABSTRACT:

The use of animal models to assess pre-clinical safety is a required regulatory phase in the process of bringing a medical device to the clinical arena. Requirements are both ethical, and legal (ISO and FDA). Many improvements in technique, in vitro screening of potential devices, avoidance of financial interest in research outcomes, and investigator understanding of model selection are all major contributors to the enhanced ability to predict human safety and performance. The remarkable success of the development, approval, and application to human disease of cardiac valve substitutes is a case study of the process and progress in pre-clinical research. More effective use of in- vitro pre-screening of potential devices therefore advancing only technology that may have success to the animal phase, appropriate and limited animal assessment of safety in relevant animal models, and advancement of devices demonstrating safety to clinical trials and eventual approved clinical use has been remarkably successful as a regulatory process. This process has resulted in relatively few clinical complications and mortality as a result of poorly designed and manufactured heart valves. Countless lives have been positively improved as a result of cardiac valve technology developed via this regulatory model. The in vivo or animal phase, of the regulatory process is a required and effective technique to predict clinical safety. Over the past four decades, many improvements have been introduced and implemented relative to the use of animals in these types of studies. These improvements have effectively reduced the number of animals used while enhancing the effectiveness of the overall assessment of preclinical safety. The development of established and reproducible animal models to mimic the human condition, (in this case valve replacement), has resulted in the site specific implantation of devices in every appropriate anatomical position in which the device is projected to be used clinically. Improved understanding of these models, relative to animal vs. device interactions, has resulted in a more accurate assessment relative to the etiology of complications (model vs. device) This delineation of results directly contributes to the understanding of potential clinical performance. Resultant recommendations concerning the device performance in animal model may result in a re-engineering of the device or may state that the device is not implicated in the complication and therefore can proceed to clinical trials. Moreover, the application of risk analysis to pre clinical protocol development allows for a more rational study design as determined by the specific projected risk that each device could introduce. These refined protocols have resulted in effective assessment of new or modified devices which has reduced the need to repeat poorly designed investigations. Laboratories conducting pre-clinical investigations have established data banks containing pathologic and performance results obtained from the implantation of control devices (clinically approved devices) used in each investigation . The banking of control data dramatically reduces the number of control animals needed in each subsequent assessment since performance data can be compared to the banked historical control data. Finally, the complete avoidance of financial conflict of interest has resulted in an unbiased assessment of pre clinical safety of new or modified devices. It is important to note that not- for profit laboratories are more effective in avoiding these types of conflicts. Importantly, there is an increased sense of the ethical burden that using animals imposes on the investigators and the staff involved with the use of animals. This increased awareness has served to both improve animal care and has resulted in careful consideration of the justification of the numbers of animals used and the care and husbandry required to assure that each animal is treated with utmost care and respect. The prediction of clinical safety of new or modified heart valves (or other Class III) devices has been enhanced, refined and proven effective over the past four decades. This improvement is due in large part to the developmental enhancements discussed previously. The overall impact of this improvement has been a net reduction of the number of animals used while enhancing the quality and accuracy of the pre-clinical safety assessment of these devices. The result has been the approval and availability of important technology available to the clinician. Ultimately, the patients benefit.

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Hepatic Portal Vein Catheterisation in the Dog

AUTHOR: Kate Read

ABSTRACT:
Catheterisation of the hepatic portal vein in the dog has been described for both infusion and withdrawal, along with measurement of portal pressure. Historically a number of different techniques have been described, with no major refinements to the procedure in recent literature. An ADME study at our facility required investigation of the extent of first-pass metabolism of the test article when delivered orally. Four male beagle dogs (11.5-13kg) were implanted with a modified polyurethane catheter (tapering from 6F to 4F at the tip with a suture bead 100mm from tip). The catheter tip was advanced into the hepatic portal vein from either the caudal pancreatico-duodenal vein, or the cranial mesenteric vein (accessed via a jejunal vein). The catheter was connected to a subcutaneous vascular access port tunnelled to an accessible site over the right thorax. Multimodal anaesthesia was applied (premedication of 0.005mg/kg dexmedetomidine and 0.2mg/kg methadone intramuscularly, induction with propofol intravenously to effect and maintenance with continuous intravenous infusion of propofol 30 to 15mg/kg/hr and remifentanyl 2.4 to 15 µl/kg/hr). Peri-operative analgesia (bupivacaine hydrochloride provided as a local splash block, 4 mg/kg carprofen subcutaneously, buprenorphine 0.01mg/kg intramuscularly and tramadol 5mg/kg orally) and antibiosis (amoxicillin clavulanic acid administered 25mg/kg intravenously at induction followed by 12.5mg/kg orally twice daily) were provided. Patency was maintained by regular flushing with heparinised saline (50IU/ml), and the catheter locked with heparinised saline (500IU/ml) between access time-points. All four animals were successfully implanted, however a fragile caudal pancreatico-duodenal vein in one animal necessitated catheterisation of the superior mesenteric vein via a jejunal vein. No post-surgical complications were noted and all animals recovered from surgery as expected. Literature regarding this procedure describes difficulties with patency, in particular thrombophlebitis and clot formation over the catheter tip. However, the implants in this study remained patent for the postoperative period; all dogs were used successfully on study, with the collection of all required portal vein PK samples. Blood flow through the catheter was positional in one animal, and was assisted by gentle exercise. Correct catheter placement was confirmed on necropsy following completion of the study, and examination of the tip of the catheter indicated no macroscopic clot formation. Cannulation of the hepatic portal vein using this technique appears to provide reliable portal blood sampling over the time frame of 6 weeks. With only four animals as a pilot study no statistics have been carried out, more animals implanted in this manner are required to further assess this surgical model. With future implantations, refinements can be made to the peri-operative medication protocol, and the post-operative flushing regime.

Comparison of Gel and Injection Delivered Carprofen for Post-Operative Pain Management in Mice

AUTHOR(s): Denise Giuvelis, Jay H Palmer, Ivy Bergquist, Lisa Harding, Dan Brazeau, and Edward J Bilsky

ABSTRACT:
Post-operative pain management in laboratory animals can be a challenge from both a delivery and cost perspective. The purpose of this study was to determine if carprofen could be effectively delivered to mice using dietary gel technology. Efficacy was assessed by measurement of a reduction in pain behaviors following ovariectomy in mice. Control or carprofen-formulated gels were made available to animals ad libitum 24 hrs prior to surgery and throughout the recovery period. Subcutaneous carprofen injections were given 30 min prior to surgery and at 24, 48 and 72 hrs post-surgery. Groups receiving carprofen had quicker recoveries of bodyweight compared to vehicle injections. Behavioral pain assessment included open-field measurement of locomotor activity and tactile hypersensitivity (abdominal von Frey). The carprofen gel group had similar reductions in pain behaviors compared to animals treated with conventional injections of the analgesic. Pharmacokinetic measurements of carprofen plasma levels indicated that the gel and injection delivery methods yielded equivalent plasma levels of the analgesic. These studies suggest that the gel technology represents a convenient and cost effective alternative to traditional post-operative pain management in mice.

Endoscopic Placement of a Percutaneous Endoscopic Gastrostomy Feeding Tube in Juvenile Swine

AUTHOR: Justin Prater

ABSTRACT:
The purpose of this model was to determine the feasibility of the use and maintenance of a percutaneous endoscopic gastrostomy tube (PEG tube) to repeatedly administer substances directly into the stomach of preweaning juvenile swine without utilizing standard oral gavage techniques. Percutaneous endoscopic gastrostomy is an endoscopic procedure in which a soft plastic tube is placed into the stomach and through the abdominal wall to provide direct access to the stomach and the gastrointestinal tract in situations where oral administration is difficult or not practical. This study utilized a total of eight Yorkshire-crossbred piglets (Source: Baily Terra Nova) obtained on lactation day 16-19 and weighing between 1.7-2.6kg. An IACUC and veterinary approved protocol was used to conduct surgery. All animals were anesthetized with Acepromazine (0.1 mg/kg IM), Atropine sulfate (0.05 mg/kg IM), Buprenorphine (0.02 mg/kg IM), Ketoprofen (3 mg/kg IM), Cefazolin (25 mg/kg IV), and Excede (5 mg/kg IM). Animals were induced with Telazol (5-8 mg/kg IM) and maintained with Isoflurane delivered in O2 to effect. Animals were intubated and ventilated as needed. Hydration was maintained with Lactated Ringer's Solution at 10-15mL/kg/hour IV. Animals were implanted with a 20 French Bard PEG tube kit as follows: A flexible scope was threaded through the esophagus into the stomach for internal visualization of the procedure. A small incision was made in the skin and a catheter was inserted percutaneously into the stomach. A looped wire was threaded through the catheter, grasped with endoscopic graspers and exteriorized through the oral cavity. The looped wire was looped around the PEG tube and pulled out of the abdomen, exteriorizing the PEG tube. Medical tape and an external bumper was placed to further secure the device, and a clamp was placed on the distal end of the PEG tube. Triple antibiotic ointment was placed at the exteriorization site, the site was bandaged and the animals were jacketed for the remainder of the study. Necropsy occurred four days following the start of dosing. The stomach and area around implant site were grossly examined. All animals recovered from surgery. Two of the animals were noted to have slight hyperthermia which may have been due to a combination of the warm room, the jacket and the anesthetics used. All animals were successfully dosed through the PEG tube twice daily for the 3 days post- surgery with no failures of the implants noted during dosing or at time of necropsy. Only gross necropsies were conducted, no scoring or histology was required. Due to the small sample size and pilot nature of this experiment, no statistics were conducted for the surgical procedure. Endoscopic placement of the feeding tube in this model required a small amount of maintenance however proved excellent for delivery of a large amount of material directly into the stomach of preweaning piglets.

Improvements in Microdialysis Method Result in Increased Experimental Success

AUTHOR(s): Susan Champagne, Hong Cao, Jonathan Johnston, Robert Lew, and Maria Quinton

ABSTRACT:
For traditional microdialysis experiments, probes/guide cannulae are implanted into the brain of an anesthetized rat according to pre-defined stereotaxic coordinates. The probes/guide cannulae are secured to the skull with dental cement. After 24-48hr recovery, rats are placed in microdialysis bowls. Artificial cerebrospinal fluid is pumped through the probe(s) and the perfusate is collected at specific time intervals for analysis of various neurotransmitters. The dental cement mixture typically used produces heat and fumes, takes a long time to solidify, and therefore can be potentially detrimental to both rat and surgeon. We have found that machine-mixed dental cement capsules produce no heat or fumes, and dry within seconds, thus improving animal/surgeon safety and also greatly reducing the time that animals are anesthetized. Implanting probes directly into the brain using the stereotaxic apparatus instead of manual insertion into guide cannulae reduces the operator error and probe damage. Traditionally, rats are set up in microdialysis cages using a zip-tie around their midsection. Instead, we implant a metal loop into the cement on the skull, to which we attach the hook of the microdialysis setup. Another improvement is the use of rotating microdialysis chambers instead of multichannel swivels. Multichannel swivels are designed to prevent tangling of the tubing between infusion pumps, rat and fraction collectors by turning in a counter direction to the animal's movement. However, the swivels can spin erroneously and actually cause the tubing to tangle. They also clog easily and are prone to leaks, which ultimately leads to failure of the experiment. Microdialysis chambers on turntables rotate in a direction counter to the rat's movement, and preclude the need for swivels. Tangling, clogging, and leaks are avoided. Altogether, we have improved our methods to increase the percentage of success and decrease the number of animals needed per experiment.

An *In Vivo* Hemostasis Evaluation Method for Comparing Surgical Devices

AUTHOR(s): Mary Mootoo, Peter Shires, and Heather Rentschler

ABSTRACT:
The hypothesis was that hemoglobin (Hb) or protein concentrations could be used to quantify low levels of bleeding typically seen when dissecting through muscle or connective tissue with surgical devices. Four paired incision sets were performed in the longissimus dorsi muscle of one porcine model to compare cold steel scalpel, monopolar energy and 3 ultrasonic blades. A transverse linear incision was made dorsally across the muscle through the fascial sheath. The muscle itself was incised using the test or control devices – one device per incision. Suction was performed within the incision for 5 minutes. All fluid suctioned was contained in an isolated receptacle inserted into the suction line. The suction tubing and tip were rinsed with 200mls of distilled water which was captured in the same receptacle. One clean dry 2x2 sponge was inserted into the incision between the cut surfaces of the muscle and left in place for 15 minutes. The sponge was then removed and inserted into the saved receptacle of suction fluid and distilled water. A reference venous blood sample was drawn and mixed with 200mls of distilled water. Distilled water causes all the red blood cells to rupture and the Hb protein creates a red color intensity in the water. Analyzing a sample of the water determines both the Hb and protein concentrations. The color can then be calculated back to actual absolute amounts. There were clear differences in Hb concentrations between all incisions except two ultrasonic blade incisions which were equal. The Hb results were mirrored by subjective observations for all paired incisions. Protein values followed the same trend as Hb values, but seemed more erratic. This was especially true in the reference sample where a fibrin clot was obvious. This suggests that protein evaluation is less specific in these circumstances and should not be solely used. This is a viable hemostasis evaluation method that can be used to compare and contrast devices. Validation of the method will be the next step.

Single Technician Sheep Intubation: Twenty Five Years of Experience and Innovation

AUTHOR(s): Jed Pugsley, Jake Bair, and Raymond Olsen

ABSTRACT:
To describe the means and methods for improved single technician endotracheal intubation. Through twenty-five years of experience and innovation, a system has been developed that easily allows a single technician to safely place an endotracheal tube (intubation) in a large animal laboratory setting. Anesthesia is induced by intravenous injection of either a Ketamine/Diazepam cocktail or Propofol, at a dose of 3.0-6.0 mg/kg BW, 0.05-0.5 mg/kg BW, or 3.0-6.0 mg/kg respectively. Animals are then placed on a floor level mechanical lift cart which allows the animal to be effortlessly moved onto the surgery gurney. With the swallowing reflex no longer present, a custom speculum is inserted into the mouth between the upper and lower jaw. Using one hand to open and manipulate the speculum, a laryngoscope is used to visualize the epiglottis and the opening of the trachea. An appropriately sized intubation tube is inserted and correct placement confirmed. A customized bite block is then inserted through the speculum and fastened. The speculum is then removed. The intubation tube is then secured through a central hole in the bite block. Care is taken to assure that the tongue does not get between the speculum or bite block and the teeth. The bite block allows a protected and unobstructed passage to both the esophageal opening and airway. The bite block provides open access for other implements such as a rumen tube, esophageal stethoscope, endoscope, or stomach pump. Data has been recorded from 2008 to current. In that time more than 1000 cases of sheep intubation has been carried out using this system. While employing this system no significant trauma caused by intubation and no animal deaths related to airway problems have occurred during surgical manipulations. Total anesthesia related deaths over the time period outlined above are less that 1%. Animals have recovered from anesthesia with minimal to no adverse reactions, which in turn, alleviates distress and discomfort to the animals. The time required to intubate and prepare an animal for surgery has been reduced and multiple cases per day are achieved. Additionally, no injuries to our technicians have occurred when working with sheep exceeding more than 100 kg in weight. Employment of these innovative tools, practices, and methods has proven to be beneficial. These intubation and handling methods are repeatable at other institutions. These methods are also applicable to other research animals such as pigs, goats, dogs, and other large animals.

Clinical Management and Complications Associated with Intestinal Access Methods in Göttingen Minipigs®

AUTHOR(s): Tricia M Galassi, Elizabeth A Nunamaker, Amanda S Wilsey, and Kuldip K Mirakhur

ABSTRACT:
Intestinal access catheters in Gottingen Minipigs at Abbvie have been used for infusion and pharmacokinetic studies in association with vascular access ports. The intestinal access catheters (modified PEG J tubes) were placed in the jejunum via duodenostomy and then either externalized outside the abdominal wall or attached to a subcutaneous port to be accessed with a Huber needle. The two approaches have their advantages and disadvantages associated with clinical maintenance and study use. The time and details involved in maintaining the catheters varies greatly between the two methods. Complications included catheter infection and infusion failure depending on the access method. Things to consider when deciding which access method is better suited to a particular model include: (1) study duration and longevity of the model; (2) time involved in the maintenance of the catheter/port; (3) growth curves of the Gottingen Minipigs; and (4) viscosity of the test compound.

Parenteral Fluid Therapy Response During General Anesthesia In The Rat

AUTHOR(s): Kimberly Wasko

ABSTRACT:
Drexel University College of Medicine, Philadelphia, PA, USA
To determine the effects of parenteral fluid therapy response during general anesthesia in the rat model. When anesthetics reach the bloodstream, the drugs that affect the brain pass through the peripheral circulation and affect organ blood flow. The effects of volatile anesthetics include vasodilation of the coronary circulation affecting systemic vascular resistance – hemodynamics. These changes result in a fluctuation of preload and afterload which can affect blood pressure, thermoregulation, and hydration status. Improper or inadequate hemodynamic support during general anesthesia can result in tissue and/or organ injury due to inadequate tissue oxygenation and perfusion. Four groups comprised this animal study. The control group did not receive anesthesia or fluid therapy. The remaining three groups received gas anesthesia for equal amounts of time. Only two of the groups, however, received fluid therapy by different administration routes. Animals were monitored closely throughout the experiment. Upon completion of this study, the animals were transferred to Institutional Animal Care and Use Committee approved protocols to observe the 3R's – Reduce, Refine and Replace. Animals that received fluids recovered quickly, demonstrated less blood pressure drops (50 vs. 118 mm/Hg), had minimal to no weight loss (2% vs. 16%), normal appetite, normal biologic outputs and minimal to no dehydration (1% vs. 11% to positive control). Intravenous hydration was associated with the best hemodynamic parameters. The intravenous hydration group had shorter time of emergence from anesthesia and exhibited typical behaviors. The animals that received no fluid therapy stabilized 2-4 days post-anesthesia. All animals that undergo general anesthesia should receive fluid therapy thus improving recovery.
SUPPORT: Johns Hopkins Center to Alternatives to Animal Testing Grant Proposal #AWE-2009-50

Cerebrospinal Fluid (Csf) Sampling in Conscious Rats Using a Cisterna Magna (Cm) Cannula System and a Syringe Pump or Collection Port

AUTHOR(s): Eric L. Adams and Matthew Ruiter

ABSTRACT:

To investigate continuous or repeated sampling of CSF in freely moving rats using a CM cannula system and a programmable syringe pump or collection port. Major challenges previously faced by investigators with CSF collection in rats include the disadvantage of sample collection under anesthesia, contamination of the CSF sample by blood during a CM or lumbar puncture and the inefficiency or inability to collect serial CSF samples. A permanent cannula[2] was placed into the rat's CM and fixed to the skull by anchoring screws and dental cement or cyanoacrylate. The cannula connected to polyurethane tubing, was tunneled subcutaneously and externalized for CSF collection. For continuous collection, a standard tether system was utilized and either gravity flow or a pump driven system was implemented for more precise collection. Serial (intermittent) samples were collected using a PinPort[3] access device. Three animals were utilized during continuous CSF collection. These animals tolerated sample collection rates between 5 and 100 µl/hr for 16 hours. Actual collection volumes varied slightly between animals but were relatively consistent. Nine animals were utilized during serial collection periods. Serial (intermittent) samples, ranging from 25-100 µl, were collected using a PinPort[3] via gravity flow or an attached microliter syringe. Up to ten samples were collected over a 24 hour period. This method provided rapid, aseptic access to the externalized catheter, which is crucial for sequential CSF collection. Sampling patency varied between animals and lasted from 1 to 14 weeks. A highly practical method has been developed to provide continuous or serial CSF collection in freely moving rats using a novel cannula system. This method has several advantages, including sample collection with minimal manipulations to physiological conditions, improving compliance with the 3Rs, allowing for longitudinal sampling in individual animals, and dramatically reducing the possibility of CSF sample contamination. Further investigations will be conducted to characterize CSF chemistry and total protein changes following continuous and serial collection periods.

Surgical Model Of Induced Preeclampsia in Rats Using the RUPP Model

AUTHOR(s): Tim Edwards, Teresa Gleason, Jonathan Toot, Rebecca Moehle, Sara Loris and Eddie Sloter

ABSTRACT:

Hypertensive disease during pregnancy has risen 40% over the past 8 years affecting 8-10% of all pregnancies. The Reduced Uterine Perfusion Pressure (RUPP) was evaluated as an appropriate surgical model of preeclampsia in rats. On GD 13, 15 animals were pretreated with ampicillin (62.5 mg/kg) and buprenorphine (0.1 mg/kg) prior to induction of isoflurane anesthesia. The animal was aseptically prepared and wrapped in a sterile adhesive drape. A midline incision was made and the abdominal aorta was cleared below the renal arteries and above the iliac arteries. A silver clip (0.2 mm ID) was placed around the abdominal aorta. Similarly the left and right uterine-ovarian arteries were cleared and a silver clip (0.1 mm ID) was placed between the ovary and the first segmental artery. The incisions were closed and 5 ml of warmed lactated Ringers solution was administered subcutaneously. Animals were recovered in a warmed litter box and monitored twice daily for signs of pain and distress. A similar group of 7 animals underwent sham surgeries in which all procedures were carried out except the placement of the silver clips. Additionally, two non-surgical models were evaluated. One group was administered a single intraperitoneal dose of Adriamycin (5 mg/kg) two weeks prior to mating. Adriamycin is known to cause heart damage, cardiomyopathy, decreased mitochondrial oxidative phosphorylation, arrhythmia, and neutropenia. The other group was administered Nitro-L-Arginine Methyl Ester (L-NAME) in their drinking water on GD 6-20 providing a dose level of approximately 50 mg/kg/day. Animals were euthanized on GD 20 of pregnancy at which time a terminal blood pressure (BP) was taken using a telemetry device. The RUPP animals showed an average BP of 124 mmHg compared to 140 mmHG in the Adriamycin group and 103 mmHg in the L-NAME group. The non-surgical control and the sham surgery animals showed a mean BP of 90 mmHg and 94 mmHg respectively. Overall fetal viability consisted of <30% survival for RUPP, <55% for adriamycin and <85% for L-NAME treatment groups. This corresponded to RUPP females showing the lowest number of viable fetuses and greatest number of early resorptions and post-implantation loss. These results showed that the RUPP model is a viable model of preeclampsia in rats.

Experiences in Implanting Microelectrode Arrays for Chronic Neural Recording in Nonhuman Primates

AUTHOR: Oscar A Bermeo Blanco

ABSTRACT:
Two NHPs were implanted with a microelectrode arrays from Blackrock Microsystems in the motor cortex of the brain. We will discuss our experiences during the surgery procedures, pre-intra and post operative craniotomy and array implantation. We will show summarized data obtained in a 9 month period from the neurosignal activity recordings and histopathology results at the end of the study.

Considerations for the Canine Thrombogenicity Test (ISO 10993-4)

AUTHOR(s): Christopher Parker and Curtis W. Schondelmeyer

ABSTRACT:
Previous studies have demonstrated that ketamine induced apoptosis and degeneration in developing monkey brains. Dexmedetomidine (Dex) is a general anesthetic with a different mechanism of action from ketamine. The present study compared the neurotoxic effects of the two drugs in prenatal Cynomolgus monkeys.
Twenty pregnant monkeys at approximate gestation day 120 (±7days) were divided into 4 groups. Group 1 animals were cage controls and did not receive any treatment. Group 2 animals were dosed with ketamine at 20 mg/kg IM followed by a 12-hour infusion at 20-50 mg/kg/hr. Group 3 animals received Dex at 3µg/kg IV over 10 minutes followed by a 12-hour infusion at 3 µg/kg/hr (HED). Group 4 animals received Dex at 30µg/kg IV over 10 minutes followed by a 12-hour infusion at 30 µg/kg/hr (10X HED). Six hours following end of infusion, all animals were anesthetized with ketamine (20 mg/kg IM) and each fetus was removed by C-section. The entire duration of the C-section was no longer than 1 hour to minimize the exposure of ketamine to the fetus (especially the control and Dex-treated animals). Blood samples from both the dams and fetuses were measured for the concentration of Dex. Each fetus was perfusion-fixed with 10% NBF and the brains were then removed from all fetuses, stored in 10% NBF and processed for paraffin sections. Serial sections were cut through the frontal cortex and were stained to detect for apoptosis (Caspase 3 and TUNEL) and neurodegeneration (silver stain). The slides were evaluated by a board-certified veterinary pathologist and the incidences of neuroapoptotic and neurodegenerative cells were quantified. There were no significant neuroapoptotic lesions present in untreated fetal brains. *In-Utero* treatment with ketamine resulted in marked apoptosis and degeneration primarily in Layers I and II of the frontal cortex, thus reproducing previous findings reported by Slikker and Zou. In contrast, fetal brains from animals treated with Dex showed none to minimal neuroapoptotic or neurodegenerative lesions at both the low- and high-dose levels; lesion incidence for both groups were similar to untreated controls. PK samples confirmed systemic exposure of Dex in both dams and fetuses. The current study showed that unlike ketamine, Dexmedetomidine at both the low-dose (HED) and at 10X HED; did not induce apoptosis in the developing brain of Cynomolgus monkeys.

Comparative Neurotoxic Effects of Dexmedetomidine and Ketamine in Prenatal Monkey Brains

AUTHOR(s): Edward Koo and Timi Oshodi

ABSTRACT:
In the late 1980's, the 4-hour dog thrombogenicity test was developed as a way to evaluate the thrombogenic potential of the material components (not the geometry) of medical devices that come in direct contact with circulating blood. Each preclinical biocompatibility contract research organization (CRO) developed its own version of the test. While generally similar, each method varied in the specie of canine used (e.g., beagle vs. hound), the evaluation criteria, and the acceptability of the use of anticoagulants. There is a general push in the industry for a universal method of this test. There are a large number of factors that can contribute to thrombus formation during the test as well as to the final comparison analysis of test and control implants. Some of the primary factors affecting thrombus formation are device geometry, implanted vessel selection, individual animal blood properties (coagulation profile, blood pressure, etc.), and the use of anticoagulants during the test, sample preparation per device IFU, and implant length. In the evaluation of the test results, having an appropriate predicate control as a comparator is important for assessing intra-animal factors. This poster proposes a test method that addresses FDA expectations, practical considerations, and inherent limitations of the canine thrombogenicity test. It discusses:
• A brief history of the test
• Considerations when initiating the test
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Clearwater Beach, Florida – Sandpearl Resort

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Thursday, September 26

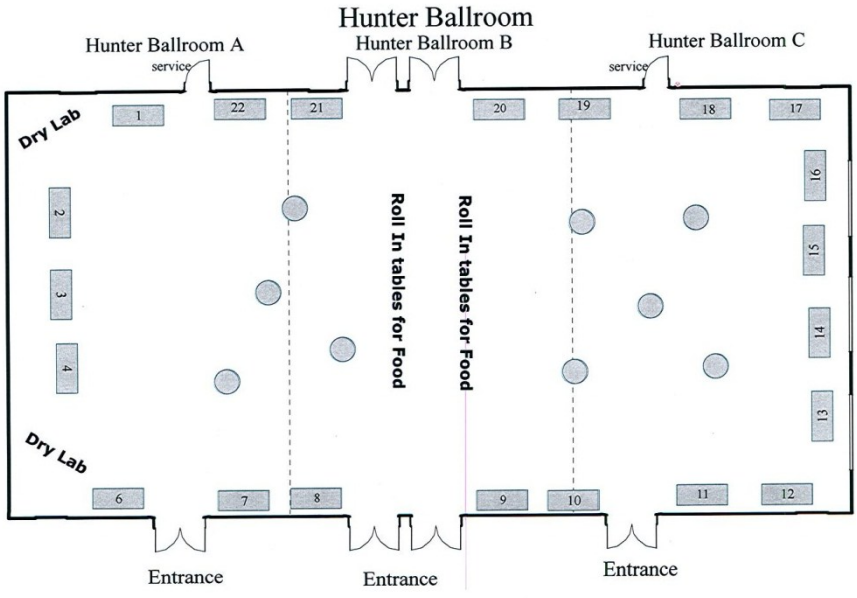
Set-up
8 am – 4 pm

Exhibit Hall Hours
4:30 – 7 pm

Friday, September 27

Exhibit Hall Hours
7 am – 8 am
9:55 am – 10:15 am
12 – 1 pm
3 – 3:20 pm

Teardown
4 pm



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Eric Ayres, STARR Life Sciences
Aries Baker, MPI Research
Margi Baldwin, University of South Florida
Szczepan Baran, Veterinary Bioscience Institute
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