The 28th Annual Meeting of the **Academy of Surgical Research**

October 4–6, 2012 Charlotte, North Caronlina – Charlotte Marriott City Center



The 28th 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)

Program



Committee to making a unerence.



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MPI Research 54943 North Main Street Mattawan, MI 49071

Annual Meeting Overview

Friday, October 5

Registration Hours

12 pm

Thursday, October 4 Friday, October 5	7am – 5pm 7am – 5pm	7 am – 8 am	Continental breakfast Poster set-up
Saturday, October 6	7am – 12pm	8 am – 8:15 am	Opening Remarks
Wednesday, Oct	ober 3	8:15 am – 9:15 am	Keynote Speaker
5 pm – 7 pm	ASR Board Meeting		
		9:15 am – 12 pm	Scientific Sessions
Thursday, October	• 4	9:15 am – 12 pm	Technical Sessions
7:30 am	Bus departs from hotel to Carolinas Medical Center	12 pm – 1 pm	Lunch
8 am – 12 pm	ASR Examinations	1 pm – 5 pm	Scientific Sessions
	Light continental breaklast served	1 pm – 5 pm	Technical Sessions
8 am – 12 pm	Wet Labs • Rodent Implants & Devices OR3	5 pm – 6 pm	Poster Judging
	Rodent Stereotaxic Lab OR2	6:30 pm – 7:30 pm	Wine & Cheese Reception with Exhibitors Silent Auction Concludes
8 am – 5pm	Wet Labs Advanced Anesthesia OR1 Epicardial Leads/Thoracotomy Lab 		Foyer & Exhibit Hall

Suture Lab
 OR1

Medical Center

Bus departs/returns to Carolinas

Saturday, October 6

1 pm – 5 pm	 Wet Labs Introduction to Microsurgery using Loupes (rat) OR3 Multi-Species Intubation lab OR2 	7 am – 8 am	Continental breakfast Poster viewing
		8 am – 8:15 am	Opening Remarks
		9:15 am – 11:30 am	Scientific Sessions
5 pm	Busses return to Marriott City Center	9:15 am – 11:30 am	Technical Sessions
		11:30 am –12:30 pm	Guest Speaker
5:30 pm – 7:30 pm	Welcome Reception with Exhibitors Education Foundation Silent Auction <i>Exhibit Hall</i>	11:30 am – 1:20 pm	Awards Luncheon
		1:30 pm – 4:50 pm	Scientific Sessions
		1:30 pm – 4:50 pm	Technical Sessions
		4:50 pm	Adjourn
		5 pm – 6 pm	Board of Directors Meeting

Welcome

Welcome to Charlotte!

I am so honored to greet our members, speakers, test takers, vendors, corporate sponsors, and new attendees to the 28th Annual meeting of the Academy of Surgical Research.

During the past year, our various committees have been working behind the scenes to enhance the benefits of your membership – new for ASR this year:

- Publication Committee has held two webinars in conjunction with Veterinary Bioscience Institute, "Aseptic and Precise Surgical Techniques in Rodents" and "ASR Review Session for Certification Exams" which had over 500 people in attendance. An additional webinar "Swine Anesthesia" will be scheduled for late 2012. Additionally, two very informative issues of the "Surgical Savvy" newslet ter were e-published.
- Nominating Committee Four candidates were nominated to run for our two open Director positions and voter participation was greater than ever.
- Education Foundation Committee new committee for our brand new program to support ongoing education for Academy members! Be sure to check out their fundraising events during the meeting.

Most of these accomplishments originated from ideas and suggestions from you - the membership of ASR. The Academy continues to grow and develop due to the contributions of its members and I encourage everyone to continue to share their knowledge and ideas and become involved.

Thank you for the opportunity and privilege to serve ASR as President this year and enjoy the program!

Teresa Gleason President, ASR



Teresa R. Gleason, BS, LVT, SRS, RLATG, graduated from Michigan State University with a BS in Physiology and as a licensed veterinary technician. Began working as an in-life technician at a contract research organization (WIL Research) in 1990 with an emphasis in surgery since 1993. Was promoted to a supervisory position in 1991, and currently serves as Manager of the Surgery and Experimental Medicine department. Joined ASR in 1998 and earned SRS certification in 1999; AALAS certified in 2002. Served on the ASR board of directors since 2005; Program Chair for 2007 annual meeting; and co-authored two ASR white papers in 2009. Professional achievements include the Barry Sauer Award, the Michael DeLeo Award, and the C.W. Hall Award from ASR.



Board of Directors & Committee Chairs

Board of Directors

President Teresa Gleason, BS, LVT, LATG, SRS

> **President-Elect** Steve Hachtman, MS

Liaison Officer John C. Resendez, SRS, MS, RLATG, CMAR

> Secretary / Treasurer Tracie Rindfield, SRS, RLAT

Immediate Past President Jan Bernal, DVM

Directors at Large Erlinda Kirkman, DVM, SRS Margi Baldwin, BS, SRS, LATg Marcel I. Perret-Gentil, DVM, MS Lisa Johnson, SRS, LATg, LAT, BA Tom Long, PhD David Moddrelle, SRS

Awards Committee Jan Bernal, DVM

By-Laws Committee Kuldip Mirakhur, DVM, MVSc, PhD

Certification Committee Lisa Johnson, SRS, LATg, LAT, BA

Communications Committee Nance Moran, SRS, RLATG, MS

Education Foundation Committee Tom Long, PhD

> Exhibitors Committee Ken MacLeod

Membership Committee Randy Pielemeier, SRS, LVT, LATG

> Nominating Committee Jan Bernal, DVM

Program Committee Margi Baldwin,SRS, RVT, RLATG, MS

Strategic Planning Committee Steve Hachtman, MS

Journal Editor Luis Toledo - Pereyra, MD, PhD



Program Committee

Progam Chair



Margi K Baldwin, RVT, RLATG, SRS, MS, Earned an associate's degree in veterinary technology from Truman State University, Missouri; earned subsequent bachelors and masters degrees in Human Resources, with a focus on training from Lindenwood University, also while still in Missouri. Joined AALAS and became certified in '89; joined ASR in '98 and earned the SRS certification in '99. Career from '89 through '02 was in the Pharma side of the field; began as a floor technician and moved up through supervisory and managerial positions to become surgical/model development specialist and training coordinator. In 2002, moved to Florida and the University of South Florida as their training coordinator; currently provides consultation to St. Petersburg College Veterinary Technician Program in the area of laboratory animal science instruction and wet labs and continues to serve USF as an Assistant Director overseeing model de-

velopment and expansion of the training program.

Progam Committee

Tim Edwards, BS, RLATG, SRS WIL Research Laboratories LLC

Teresa Gleason, BS, LVT, LATG, SRS WIL Research Laboratories LLC

> Melanie Graham, MPH, PhDc University of Minnesota

Christina Gross, BS, SRS American Preclinical Services, LLC

Steve Hachtman Science & Health Technologies

> Julia Joyce, SRA Johnson & Johnson

John Long, DVM, DACLAM St. Louis University School of Medicine

David Moddrelle, SRS Primate Products, Panther Tracks Learning Center

> Nance Moran, SRS, RLATG, MS Genzyme Corporation

John C. Resendez, MS, RLATG, SRS, CMAR MPI Research

> Luis Toledo - Pereyra, MD, PhD Michigan State University

Karen Brocklehurst, RLATG, SRA University of South Florida



Distinguished Speakers

Keynote Speaker

Autumn Fiester, PhD is the Director of Graduate Studies in the Department of Medical Ethics at the University of Pennsylvania School of Medicine. She is the co-editor of the Penn Center Guide to Bioethics (Springer 2009), which was given the PROSE Award from the American Association of Publishers and named the Outstanding Academic Title for 2009 by CHOICE Magazine from the American Library Association. She is the Director of the Penn Center Mediation Project, which promotes clinical ethics mediation as a conflict-resolution method in both formal clinical ethics consultations and ethics conflicts at the bedside (http://www.med.upenn.edu/bioethics/mediation.shtml). She is the author of over 50 publications in the areas of animal ethics, clinical ethics, and gender and sexuality.

Vince Mendenhall, DVM, Ph.D., joined Piedmont Triad Research Park as Director, Preclinical Surgical Services in August, 2008. He received his Doctor of Veterinary Medicine degree at Colorado State University (CSU) in 1968, and his Ph.D. in Experimental Surgery/Comparative Anatomy, also from CSU, in 1981. In 1975, he joined 3M Company where he developed their Department of Surgical Research as it related to Medical Device development. There, he worked in all areas of experimental surgical techniques, including neuro-, ophthalmic, cardiovascular, microvascular, orthopedic, wound healing, and abdominal surgery in all species of laboratory animals. He completed more than 500 research projects in these areas in the 17 years he was at 3M, and is co-holder of the patents on Tegaderm[®], the Microvascular Anastomotic Device[™], the Ligament Augmentation Device[®], DuraPrep[™], silicone malleable retractors, and a biconvex, reverse haptic, hydrogel intraocular lens. He continued these efforts at Charles River's Preclinical Services, Massachusetts, developing many new surgical models for Safety Sciences, Pharmacology, Pharmacokinetics and Experimental Medicine. He is known worldwide for his innovative surgical techniques in all surgical specialties. To date, he has presented the results of his development work at 165 national and international peer reviewed meetings, published 11 book chapters, and 26 referred publications. He has received many awards for his work in these areas from organizations such as the Academy of Surgical Research (of which he was President in 2005), the Society for Biomaterials, the European Intraocular Implantlens Commission, The European Society of Arthroscopy and Knee Surgery, and local AALAS organizations.

Professor John A. Rogers obtained BA and BS degrees in chemistry and in physics from the University of Texas, Austin, in 1989. From MIT, he received SM degrees in physics and in chemistry in 1992 and the PhD degree in physical chemistry in 1995. From 1995 to 1997, Rogers was a Junior Fellow in the Harvard University Society of Fellows. He joined Bell Laboratories as a Member of Technical Staff in the Condensed Matter Physics Research Department in 1997, and served as Director of this department from the end of 2000 to 2002. He is now the Lee J. Flory-Founder Chair in Engineering at University of Illinois at Urbana/Champaign with a primary appointment in the Department of Materials Science and Engineering.

Rogers' research includes fundamental and applied aspects of materials and patterning techniques for unusual electronic and photonic devices, with an emphasis on bio-integrated and bio-inspired systems. He has published more than 300 papers and is inventor on more than 80 patents, more than 50 of which are licensed or in active use. Rogers is a Fellow of the IEEE, APS, MRS and AAAS, and he is a member of the National Academy of Engineering. His research has been recognized with many awards, including a MacArthur Fellowship in 2009 and the Lemelson-MIT Prize in 2011.

Venue

Charlotte Marriott City Center

Situated in the heart of downtown, this Charlotte, NC hotel is located in the business district near Charlotte Douglas International Airport, Bank of America Stadium, Time Warner Cable Arena, museums and Charlotte's finest restaurants and bars. Enjoy fine dining at our Charlotte hotel's Savannah Red Restaurant and Wine Bar, relax at Cutter's Cigar Bar, or stop by Champion's Sports Bar & Restaurant to catch a game. It is a favorite convention and wedding location among downtown Charlotte hotels.











Lab Descriptions

Device Implantation & Intrathecal Catheterization Rodent Lab

Instructors: Dr. Megan Swaab, Heather Bogie, Kimberly White, Marla Wilwol, Dr. Cristina Weiner

Hands-on surgical training session will demonstrate and teach advanced rodent model implantation procedures. The student training session will include carotid and femoral catheter placement in the rat to demonstrate how to obtain Pulse Wave Velocity, as well as intrathecal cannulation techniques. Experienced instructors will share information on preoperative care, surgical tips and techniques, and on post operative recovery support. Students will learn skills and approaches to these more technically complicated procedures via placement of training devices. Each student will be provided with their own individual surgical station, a small animal instrument set, and appropriate surgical supplies for their session.

Principles of Stereotaxic Surgery

Instructors: Randy Reed and Eric Adams

The main goal of this hands-on laboratory experience will be to introduce those who are unfamiliar with stereotaxic procedures to the equipment, basic techniques and nuances of performing stereotaxic surgical approaches in the rat and mouse model as commonly used in an academic or research setting. This lab will also be an opportunity for those with only experience with one species to fine tune their stereotaxic training through exposure to new techniques in both animal models. The following is a basic overview of the laboratory experience. Familiarization with the stereotaxic frame, manipulators, attachments and ear bars (species specific). Short exercise in reading the scales on the manipulators correctly. Basic anatomy and anatomical landmarks used in rodent stereotaxic surgery. Commonly used equipment and hardware in rodent stereotaxic surgery. Correct placement of a rodent in the frame. ICV cannula placement.

Experimental Techniques in Swine

Instructors: Tina Gross and David Moddrelle

Advanced Anesthesia: This portion of the lab will focus on patient prep (anesthesia selection, induction and intubation), monitoring during complex procedures and adjusting/correcting for complications. Participants will intubate swine, prepare the patient for surgical monitoring, and learn appropriate ventilation techniques.

Epicardial Lead Placement/Thoracotomy: This portion of the lab will provide overview of device implantation including appropriate approach and exposure, and proper lead placement in the swine patient.

Suture Techniques: The aim of this workshop is to demonstrate and allow practice of more complex suturing techniques. A variety of suture techniques will be demonstrated during the closure of thoracotomy, sternotomy and laparotomy incisions, as well as closure appropriate following femoral or carotid cut down.

Introductory Microsurgical Techniques Using Loupes

Instructors: Dr. Robert Hoyt, Dr. Jennifer Smith, Marla Wilwol, Dr. Cristina Weiner

This introductory microsurgical training lab will cover basic aspects of microsurgical procedures such as instrumentation, use of a surgical loupes, and micro-suturing. Students will work hands-on utilizing surgical loupes (2.0-2.5x) to learn proper suturing techniques and basic dissections, vessel isolation and cannulation, and closure techniques in the rat. Please note on the registration form the check boxes for indicating the participant will need loupes supplied, or will bring their own.

Lab Descriptions

Multi-Species Intubation Lab Rabbits and Rodents

Instructors: Dr. George Vogler, Erlinda Kirkman, Jon Ehrmann

Rabbits are anatomically difficult to intubate due to their narrow oropharyngeal opening. Instructors will demonstrate use of the laryngeal mask airway (LMA) and the use of endoscope guided intubation, as well as the more traditional laryngoscope and blade approach to visualize. Rodents also pose a unique set of problems when intubating; students will be exposed to techniques that result in quick, efficient and minimally traumatic orotracheal intubation of both mice and rats. Instructors will demonstrate how to use specially designed positioning stands, intubation speculum and endotracheal tube guide wires to ensure successful intubaton.

Dry Labs

Laparoscopic Surgery in Rodents

10:15 am – 11:15 am

This dry lab demonstration will provide hands on experience with rodent laparoscopy/colonoscopy equipment, instruments and techniques using inanimate objects. Visual aids will be available to introduce participants to this technology. Further training will be required to perform these procedures in live rodents.

Electrocautery

11 am – 12 pm

Bovie Medical will be giving a demonstration on Electrosurgery from the perspective of the functional and safety aspects to be used with most electrosurgical generators (ESU). It will cover the range of general instruments/electrodes that can be used universally with most ESU's and concepts to always kept in mind when using any energy source. It will include a demonstration of generator outputs, power levels, and return electrode functional use. Bovie's new J-Plasma will also be featured with a product demonstration and safety precautions will be explained.

Suture Lab

1:30 pm - 2:30pm

A good suture pattern is only as good as the knots holding them in place. This hour long demonstration will cover the basics of suture selection, knot placement and tying techniques in a variety of suture boards and inanimate objects.

Anesthesia

3:30 pm – 5 pm

Inhalant anesthesia is a commonly used method to provide general anesthesia. The major component for this technique is an anesthetic machine. The three main functions of an anesthetic machine is to deliver oxygen and anesthetic gas, remove carbon dioxide and waste anesthetics, and provide a means for patient ventilation. A basic understanding of the anesthetic machine is essential for effective anesthetic troubleshooting. This dry lab will provide knowledge aimed at assisting the anesthetist with identifying and correcting various anesthetic-related problems. The workshop will focus on understanding the components of an anesthetic machine, anesthetic circuits, and ventilator settings.

Lab Sponsors



The 28th Annual Meeting of the

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> Program Maria

Program

Wednesday, October 3

5 pm – 7 pm ASR Board Meeting

Thursday, October 4

(Meeting registration hours, 7am – 5pm) 7:30 am Busses depart from Marriott City Center to Cannon Research Building

8 am – 12 pm	SRS, SRA, SRT Examinations	Meyers Park / Dilworth
8 am –12 pm	Swine Labs	
8 am – 10:30 a 11 am – 3 pm 3:30 pm – 5 pm	m Advanced Anesthesia Epicardial Leads/Thoracotomy Lab Suture Lab	OR 1 OR 1 OR 1
8 am –12 pm		
Wet Lab Wet Lab	Rodent Implants & Devices Rodent Stereotaxic Lab	OR 3 OR 2
12 pm Busses depart/	return to Marriott City Center	
1 pm–5 pm Wet Lab Wet Lab	Introduction to Microsurgery using Loupes (rat) Multi-Species Intubation lab	OR 3 OR 2
5 pm Busses return t	o Marriott City Center	
5:30 pm–7:30 Welcome Recp	om tion with Exhibitors	Exhibit Hall
Education Four	ndation Silent Auction begins	Salons ABCD



7 am – 8 am	Continental Breakfast with Exhibitors Sponsored by SAI Infusion Technologies
7 am – 8 am	Poster Viewing
8 am – 8:15 am 8:15 am – 9:15 am	Opening Remarks: ASR President, <i>Teresa Gleason</i> Keynote Speaker: Biotechnology, Casuistry, and the Moral Continuum <i>Dr.Autumn Fiester</i>
	Sponsored by Charles River

SCIENTIFIC TRACK

9:15 am – 9:40 am	Non-invasive ECG Monitoring in Animal Models of Human Disorders	Tom Hampton, PhD	Salons EFGH
9:40 am – 10 am	Design & Material Choice in Device Construction	John lannone	Salons EFGH
10 am – 10:15 am	Break with Exhibitors Sponsored by Access Technologies		
10:15 am – 10:45 am	Broadening Our Perspective on Refinement: Addressing Model Divergence to Target : A Net- Positive Animal Experience	Melanie Graham, MPH, PhD	Salons EFGH
10:45 am – 11:15 am	Animal Research Models and the Ethical Dilemma	Sylvia Gograffe, DVM, PhD, DCLAM	Salons EFGH
11:15 am – 11:45 am	Refinement Of Surgical Procedures And Methods In A Rodent Production Setting	Sera Murray, DVM, MS	Salons EFGH
11:45 am – 12pm	Effective Ways For Preventing Rodent Hypothermia During Surgery	Szczepan Baran, VMD, MS	Salons EFGH
12 pm – 1 pm	Lunch with Exhibitors Sponsored by VetEquip, Inc.		Salons ABCD
1 pm – 1:30 pm	Streamlining Surg ery and Increasing Surgical Efficiency	Szczepan Baran, VMD, MS	Salons EFGH
1:30 pm – 2 pm	The Development of a Reliable Control for Testing Gastro-Intestinal Sealants	Jenifer Sweet, BS, SRS, LATG	Salons EFGH
2 pm – 2:30 pm	Regulatory Xenotransplatation: GLPs and Surgical Research	Curtis Schondelmeyer	Salons EFGH
2:30 pm – 3 pm	Establishment and Maintenance of a Cesarean Derived Flock of SPF Sheep	Julie Hurley, DVM, MS, DACVPM	Salons EFGH
3 pm – 3:20 pm	Break with Exhibitors Sponsored by DRE, Inc.		
3:20 pm – 3:50 pm	The Relevance of Rabbit Models for investigating on Implants Designs, Chemistry, Surfaces Structuring and Related Effects on Bone Regeneration	Micheal Dard, DDS, PhD	Salons EFGH
3:50 pm – 4:20 pm	Critical Size Tibial Defect in Sheep: Notes on Improving Plating Techniques and Post-Operative Management	Randy Pielemeier, LVT, BS, SRS, LATG	Salons EFGH
4:20 pm – 5 pm	Patient-Specific Positioning Guides for Total Knee Arthoplasty: A Coronal Alignment and OperativeTime Study	Bill Pietrzak, PhD	Salons EFGH
5 pm	Poster Judging		
6:30 pm – 7:30 pm	Wine & Cheese Reception with Exhibitors & Conclusion Sponsored by Data Sciences International & Lomir I	on of Silent Auction Biomedical, Inc.	

7.000 0.000	Continental Deceléget with Euclidites
7 am – 8 am	Continental Breaklast with Exhibitors
	Sponsored by SAI Infusion Technologies
7 am – 8 am	Poster Viewing
8 am – 8:15 am	Opening Remarks: ASR President, Teresa Gleason
8:15 am – 9:15 am	Keynote Speaker: Biotechnology, Casuistry, and the Moral Continuum
	Dr.Autumn Fiester
	Sponsored by Charles River

TECHNICAL TRACK

9:15 am – 10 am	Anesthesia and Multimodal Analgesia in Rodent and Non-Rodent Models	Cholawat Pacharinsak, DVM, MS, PhD, DACVA Jen Smith, DVM, DCLAM	Myers Park/ Dilworth/ Eastover
10 am – 10:15 am	Break with Exhibit Sponsored by Access Tea	tors chnologies	
10:15 am – 11:15 am	Anesthesia and Multimodal Analgesia in Rodent and Non-Rodent Models(continued)	Cholawat Pacharinsak , DVM, MS, PhD, DACVA Jen Smith, DVM, DCLAM	Myers Park/ Dilworth/ Eastover
11:15 am – 12 pm	Anesthesia Platform : Panel & Roundtable (Case Presenta tions, Protocols & Troubleshooting)	Anne M. Kuszpit, LVT,BS, LATg, SRA	Myers Park/ Dilworth/ Eastover
12 pm – 1 pm	Lunch with Exhibitors Sponsored by VetEquip, Inc.		
1 pm – 2:30 pm	Basic Understanding of an Anesthetic Machine	Cholawat Pacharinsak , DVM, MS, PhD, DACVA	Myers Park/ Dilworth/ Eastover
2:30 pm – 3 om	"Hanna's Hope" Giant Axonal Neuropathy	Lori Sames, BS	Myers Park/ Dilworth/ Eastover
3 pm – 3:20 pm	Break with Exhibitors Sponsored by DRE, Inc.		
3:20 pm – 3:50 pm	Kidney Transplantation in a Large Animal Model	Gernot Kaiser, MD	Myers Park/ Dilworth/ Eastover
3:50 pm – 4:20 pm	Refinement of Gastro-Intestinal Procedure in Mouse Models for Obesity and Diabetes Studies	Szczepan Baran, VMD, MS	Myers Park/ Dilworth/ Eastover
4:20 pm – 4:50 pm	Peri-Operative Concerns In a Swine Face Transplant Model	Dawn Ruben, DVM	Myers Park/ Dilworth/ Eastover
5 pm	Poster Judging		
6:30 pm – 7:30 pm	Wine & Cheese Reception with Exhibitors & Sponsored by Data Sciences Internationa	Conclusion of Silent Auction al & Lomir Biomedical, Inc.	

7 am – 8 am	Continental Breakfast
	Sponsored by Instech Solomon
7 am – 8 am	Poster Viewing
8 am – 8:15 am 8:15 am – 9:15 am	Opening Remarks: ASR President, Teresa Gleason Guest Speaker: Nanotechnologies
	Dr. John Rogers

SCIENTIFIC TRACK

9:15 am – 9:45 am	Development and Management Of The Diabetic Nonhuman Primate Model	Melanie Graham, MPH, PhD	Salons EFGH
9:45 am – 10:15 am	Percutaneous Fine Needle Aspiration Biopsy of the Liver for RNA Extraction and Gene Expression Profiling	Lucas Mutch, AAS	Salons EFGH
10:15 am – 10:30 am	Break Sponsored by AVA Biomedic	al, Inc.	
10:30 am – 11 am	A Refined Model of Spinal Wear Debris in the Rabbit (Oryctolagus cuniculus)	Tyler Long, DVM, DCLAM	Salons EFGH
11 am – 11:30 am	Surgical Techniques for Improving Visualization and Reducing Dissection Required for Cervical Spinal Cord Injections in Gottingen Minipigs	Randy Pielemeier, LVT, SB, SRS, LATG	Salons EFGH
11:30 am – 1:20 pm	ASR Business Meeting & Awards Luncheon Guest Speaker: H. Vince Mendenhall, DVM, PhD Practicing the Art of Surgical Research in the Development of New Medical Devices and Pharmaceuticals Lunch Sponsored by Colonial Medical Supply Company		Salons ABCD
1:30 pm – 2 pm	A Refined Technique to Improve the Success of VAPs in Cynomolgus Macaques	Jen Sheehan, BS, SRS, LATG	Salons EFGH
2 pm – 2:30 pm	Translational Refinement Enabling Effective Transurethral Catheterization of Male Rhesus Macaques Permitting Minimally Invasive Diagnostic & Urodynamic Parameter Evaluation	Alexandra Wickham, BA, CVT, RLATG, SRS	Salons EFGH
2:30 pm – 3pm	Developing an Anaesthetised Neonatal Pig Model for a Safety Pharmacology Study	Helen Murphy, BVSc, BSc, PhD, MRCVS	Salons EFGH
3 pm – 3:20 pm	Break		
3:20 pm – 3:50 pm	Adhesives in Surgery	JM Llorisi, MD, PhD	Salons EFGH
3:50 pm – 4:20 pm	Advances in Transplantation Surgery	Alexander H. Toledo, MD	Salons EFGH
4:20 pm – 4:50 pm	Surgical Writing: Considerations for Successful Publication	Luis Toledo - Pereyra, MD, PhD Tracie Rindfield, SRS, LAT	Salons EFGH

7 am – 8 am	Continental Breakfast
	Sponsored by Instech Solomon
7 am – 8 am	Poster Viewing
8 am – 8:15 am 8:15 am – 9:15 am	Opening Remarks: ASR President, Teresa Gleason Guest Speaker: Nanotechnologies
	Dr. John Rogers

TECHNICAL TRACK

9:15 am – 9:45 am	Stapled Partial Gastrectomy in Athymic Nude Rats	Marisha Godek, PhD	Myers Park/ Dilworth/ Eastove ^r
9:45 am – 10:15 am	Targeting Brain Structures in the Growing Rat	Christina Nelson, BS, SRS, LAT	Myers Park/ Dilworth/ Eastover
10:15 am – 10:30 am	Break Sponsored by AVA Biomedica	l, Inc.	
10:30 am – 11:30 am	Bringing Surgical Savvy To Life	Nance Moran, SRS, RLATG, MS Jason Ogle, LVT, SRS, LATG Eric McCloud BS, LAT Marlo Volberg, BS, LVT, SRS, LATG Jane Perkins, LATG, SRA, BS	Myers Park/ Dilworth/ Eastover
11:30 am – 1:20 pm	ASR Business Meeting & Awards Luncheon Guest Speaker: H. Vince Mendenhall, DVM, PhD Practicing the Art of Surgical Research in the Development of New Medical Devices and Pharmaceuticals Lunch Sponsored by Colonial Medical Supply Company		Salons ABCD
1:30 pm – 3 pm	Bringing Surgical Savvy To Life	Renee Bodinizzo, BS, SRS Teresa Cunio, BS, SRT Matt Flegal, BS	Myers Park/ Dilworth/ Eastover
3 pm – 3:20 pm	Break		
3:20 pm – 3:50 pm	Development of a Surgical Wound Model of Staphylococcus aureus Infection	Heather Devantier, MS	Myers Park/ Dilworth/ Eastover
3:50 pm – 4:20 pm	Development and Optimization of Targeted Drug Delivery via the Hepatic Artery in the Mouse Model of Hepatocellular Carcinoma	Devra Batdorf, BA, SRS, LATG	Myers Park/ Dilworth/ Eastover
4:20 pm – 4:50 pm	Targeting the Intestinal Epithelium in a Murine Model through the Superior Mesenteric Artery using a Lateral Microsurgical Approach	Stacy Porvasnik, MS, LAT, SRS	Myers Park/ Dilworth/ Eastover



The 28th Annual Meeting of the

Academy of Surgical Research

2012 Poster Presentations						
Poster Title	Author(s)	Poster Number				
Rat Alveolar Bone Loss via Maxillary Molar Ligation	Sean Davis, SRS <i>Amgen</i>	1				
Wound Healing Model Development in SKH1 Hairless Mice	Connie Kliwinski, MLAS, RLATG, SRS <i>Janssen Pharmaceutical</i> <i>Companies of J&J</i>	2				
Development of a Porcine Model to Study the Metabolic Consequences of Bile Diversion	Michelle Lewis, AHT, BBA, SRS <i>Ethicon Endo-Surgery</i>	3				
Dual Intrathecal Catheterization Feasibility as Canine Colony Model	Justin Prater, BS, SRA, LATG <i>MPI Research</i>	4				
Effects Of Combined Small-Diameter Proximal Splenorenal Shunt And Partial Devascularization In Patients With Portal Hypertension	Weihua Qiu, MD, PhD; Weiping Yang MD; Zhiwei Xu MD, PhD Ruijin Hospital, Shanghai Jiao Tong University School of Medicine	5				
Unilateral vs. Bi-Lateral Middle-Ear Cannulation In Guinea Pigs	Jenifer Sweet, BA, SRS, LAT; Rachel L. Tapp, BS, LATG; Janelle Gesaman, AS, LATG,SRA, SRT; Lindsay Tawoda, BS, SRA, SRT, LAT; Claudia Almazan, DVM; Randall Pielemeier, LVT, BS, LATG, <i>SRS</i> <i>MPI Research</i>	6				
A Novel Approach To Identify Source Of Palpable Laryngeal Muscle Stimulation	Kristin Wise, BS, DVM Boston Scientific	7				
Comparative Analysis Between Acellularized And Immunologically Non-Treated Vascular Xenografts In Long-Term Survival Animals	<u>Kim Won-Gon, MD, PhD;</u> Ji-Min Chang, MD, PhD; Wook-Sung Kim, Md, PhD Seoul National University Hospital	8				

Alphabetically listed by Author. <u>Underline</u> indicates presenting Author.

Abstracts

Refinement of Gastro-Intestinal Procedures in Mouse Models for Obesity and Diabetes Studies

Szczepan W. Baran, VMD, MS Veterinary Bioscience Institute

We have previously described refinement of gastro-intestinal procedures in rat models. Recently many transgenic mouse models for diabetes and obesity studies have been developed which are useful for the discovery of surgical and therapeutic interventions applicable to these human diseases. Surgical interventions to study the mechanisms of gastrointestinal surgery as treatment for type 2 diabetes and obesity include procedures such as Roux-en-Y gastric bypass, ileal transposition, duodenal-jejunal bypass, gastric liners and vertical sleeve gastrectomy. We evaluated current surgical practices and identified areas of improvement of these surgical procedures in mouse models. Areas of improvement included specific pre- and post-surgical fasting periods, incision closure, specific suture materials, physiological peri-operative monitoring, anesthesia, pre- and post-surgical drugs and ancillary peri-operative enhancements. The pre-surgical fast period was decreased from 24 hours to 2-4 hours. The post-surgical fasting period was decreased from 24-72 hours to a maximum of 20 hours. The amount of suture material used was decreased by utilizing smaller diameter suture and a continuous suture patterns. The average dose of isoflurane was decreased from 2.5% to 1.0% and oxygen flow from 1 to 0.3 Liters/minute through utilization of physiological monitoring, which resulted in guicker recovery and a more stable respiratory rate. The use of a homoeothermic blanket, water heating pad, elevating ambient temperature, and the utilization of warmed saline to decrease tissue dehydration, normalized mouse's body temperature, and contributed to faster recovery and a survival rate of ~90%.



Streamlining Surgery and Increasing Surgical Efficiency

Szczepan W. Baran, VMD, MS Veterinary Bioscience Institute

Rodents are the most commonly utilized species in biomedical research and undergo a myriad of surgical procedures, ranging from simple to complex. Commonly many of the same procedures are performed in multiple patients by a single surgeon within one day. This provides an opportunity to streamline surgical processes to increase surgical efficiency. The research community has streamlined many processes such as cage changing and animal care, however the streamlining of surgical procedures has received less attention. Here, we will review data and demonstrate that streamlining of surgical procedures through global and specific checklists, surgical set up and adding or realigning surgical staff leads to shorter surgical times, more efficient use of personnel and decreases overall costs. This can all be accomplished while maintaining, and in some cases improving, surgical outcomes. The process of how to assess a surgical procedure and identify areas of potential refinement to streamline the entire process will be demonstrated. This will be an interactive session, which will require attendee participation.



Effective Ways For Preventing Rodent Hypothermia During Surgery

Szczepan W. Baran, VMD, MS Veterinary Bioscience Institute

Prevention and treatment of perioperative hypothermia during rodent surgery is challenging due to the rodents high surface to body weight ratio, their size and complexity of the procedures. Hypothermia is associated with disturbances of coagulation, raises oxygen consumption, inhibits the immune system, lowers respiratory rate, leads to a higher incidence of wound infection, and prolongs recovery. Furthermore, it lowers metabolic rate, which leads to with a reduction of heat production and slower clearance of anesthetics and analgesics. Severe hypothermia depresses the central nervous system and leads to peripheral vasodilation, resulting in continued core heat loss. Our data demonstrates that mice and rats' body temperature decreases between 1-3°C within first 10 minutes of of gas anesthesia and between 2.5-3.5°C within first 10 minutes of injectable anesthesia depending where animals are being anesthetized, how they are being prepared for surgery and where the surgery takes place. This heat loss is exacerbated with abdominal procedures and application of room temperature physiological fluids. This presentation will review currently available rodent temperature monitoring equipment, heating items and equipment, and provide recommendations for effective methods to prevent perioperative hypothermia for specific mouse and rat procedures. This lecture is design for IACUC personnel, investigators, veterinarians, surgical and veterinary technicians and research staff involved in performing or assisting in rodent surgery.

Development and Optimization of Targeted Drug Delivery via the Hepatic Artery in the Mouse Model of Hepatocellular Carcinoma

Devra Batdorf, BA, SRS, LATg PhaseRx, Inc.

A novel method of targeted drug delivery to the mouse liver through hepatic artery infusion was developed to reliably screen test compounds. Clinically, administration of drug via the hepatic artery is required for treating non-resectable Hepatocellular Carcinoma (HCC) lesions, which are primarily supplied by arterial blood. Numerous orthotopic and xenograft HCC models have been developed in the mouse; however, delivering test compounds has been largely limited to systemic (intravenous) and local (intratumoral) administration due to size and complexity of hepatic artery delivery. This presentation will describe the process of development and optimization of the surgical procedure for hepatic artery infusion in both naïve and tumor-bearing mice. First, rat and mouse cadavers were used to identify the critical structures and to refine the surgical approach. Trypan blue dye was injected in order to visualize and map the hepatic artery and gastroduodenal branch, which is ultimately catheterized for the infusion procedure. The pilot survival study included 20 adult athymic nu/nu mice and was intended to optimize the approach, closure, anesthesia, analgesia, volume and infusion rates, and to inform on post-surgery survival rates, body weight changes, liver enzyme elevations, and localization of drug in liver versus tumor tissue. The preliminary study revealed a 94% survival rate to 24 hours and a 74% needle placement success. Serum chemistry elevations, body weight loss, and mortalities were effectively minimized through practice, improving the analgesic regimen, and acquiring the appropriate instrumentation. Identification of variable anatomy, maintaining hemostasis and gentle retraction of tissues throughout the surgery were key elements to a successful and reproducible hepatic artery infusion procedure in mice.

The procedures described in this presentation were performed according to an approved IACUC protocol and is original work.

The Relevance of Rabbit Models for investigating on Implants Designs, Chemistry, Surfaces Structuring and Related Effects on Bone Regeneration

Michel Dard, DDS, PhD New York University, College of Dentistry

The general aim was to establish versatile experimental and animal models whose size can potentially allows for use of different implants dimensions and shapes. The specific aim intended to investigate on healthy and compromised rabbit models dedicated to different surgical approaches in the knee, mandible and calvaria.

Materials and Methods:

Female and male rabbits (Swedisch loop and New Sealand white) weighting about 3 kgs were included in the trials. At the end of the acclimatization period and if requested by the working hypothesis females were ovariectomized in order to induce a decrease of their bone trabecular mass over a period of 6 months.

The materials under investigations consisted on dental implants manufactured from titanium or titanium alloys (i.e. titanium-zirconium) or ceramic materials, with different designs, with or without hydrophilic surfaces, presence or not of nanostructures or new bone substitutes placed at their contact.

All surgical procedures were conducted in operations suites under aseptic conditions. Rabbits were anesthetized without intubation by injections of ketamin-medetomidin and routinely monitored.

Depending on study purposes and designs the animals were operated in the calvaria for investigations on bone substitutes or in tibia and femur where cylindrical implants made of titanium, titanium alloys or ceramic were inserted or disks positioned or operated at the mandible using a lateral surgical approach to test vertical bone augmentation under a specially shaped device covering the dental implant.

Acute defects creation and/or implantations were performed bilaterally and by help of guided surgery devices to assure accuracy.

The terminal procedures were conducted 3, 4 or 8 weeks after implantation.

The post-surgical analysis included observations and measurements based on regular radiology, computed tomography, micro-computed tomography, biomechanical tests (removal torque, pull out), histology-histomorphometry.

Results:

These models allowed to qualify: 1. a new dental implant design called bone level with non-matching abutment, 2. a hydrophilic metal surface with nanostructures, 3. a zirconium alloyed titanium comparatively to the existing titanium routinely used, 4. a ceramic material submitted to an aging preparation, 4. an absorbable scaffold based on polyethylene glycol hydrogel supplemented or not with growth factors (rhBMP2 and rhBMP7).

Conclusion:

Quantitative analysis concluded to the ability of these models to discriminate between different implant chemical compositions, designs, surface textures or surrounding materials.

These rabbit animal and experimental models demonstrated their usefulness, versatility and reliability in oral surgical research when tooth replacement and bone regeneration issues are addressed. They offer a broad range of possibilities spreading from pre-translational to more translational aspects.

Rat Alveolar Bone Loss via Maxillary Molar Ligation

Sean Davis, SRS Amgen

The goal of this animal model is to create a predictable, measurable, and reproducible rat model for alveolar bone loss. By placing non-absorbable braided ligatures on the maxillary molars, at the cervical neck of the tooth, periodontitis results from continual bacterial contact below the gingival margin. The onset of periodontitis induces an inflammatory cascade that leads to the destruction of the periodontium and subsequent alveolar bone loss. The placement of ligatures around the cervix of the maxillary molars also induces an acute physical irritation that helps to facilitate rapid alveolar bone loss. By establishing a reliable model for alveolar bone loss, novel treatment methods can be explored and monitored. Studies were required to validate the ligature model in rats. For ligature placement, animals were anesthetized with 42mg/kg Ketamine + 0.28mg/kg Dexmedetomidine cocktail, injected intraperitoneal. The ligature was placed on the M1/M2 maxillary molars using a figure 8 ligation. Instruments required for ligature placements are; 2 Castro-Viejo needle holders, rodent mouth retractors, 45° angled Bonn micro probe, serrated Adson forceps, and a periodontal pocket probe/pick combo.

The primary comparative study used a total of 8-10 animals to compare silk ligature vs. cotton ligature in the destruction of alveolar bone (3-5 animals w/silk, 3-5 animals w/cotton, 2 negative controls). Following ligation, anesthesia was reversed with 0.5mg/kg Antesedan intraperitoneal. Animals used for all studies were CD male rats (CRL), approximately 12 weeks of age. Ligatures were checked 1-3 times weekly to ensure ligature retention, and any lost ligatures were replaced during that time. A minimum of once weekly body weights were obtained to ensure weight gain and adequate animal health management during the course of the study. All animals received micro CT imaging of the maxilla once weekly to provide a dynamic overview of alveolar bone loss. Six weeks following ligature placement, all animals were euthanized and maxillas were submitted to histology for assessment of alveolar bone loss, and classification of bone degradation. *At termination of study, significant alveolar bone loss was observed in all animals that received molar ligation. The ligature model does appear to provide a predictable, measurable, and reproducible rat model for alveolar bone loss. *final study results pending as of 5/10/12.



Development of a Surgical Wound model of Staphylococcus aureus Infection

Heather Devantier, MS Pfizer

Staphylococcus Aureus is a gram-positive coccal bacteria that affects millions of people each year. In the U.S. alone 780,000 out of 30 million surgical procedures performed annually in the U.S. result in surgical site infections (SSI). Common causes include complications from surgical hypothermia, contamination of the incision area by skin flora and surgical instrument contamination. Historically, medical treatments have been limited to prophylactic antibiotics, but resistant bacterial strains (MRSA) are both limiting and decreasing the effectiveness of current therapies. We present a model of local surgical site infection currently supporting development and evaluation of potential vaccine candidates being developed as a pro-active preventative approach to this common infectious disease. CD1 Mice are anesthetized and a small incision is made into the quadricep muscle. The incision pocket is then inoculated with Staph aureus and the incision is closed with a purse-string suture. We present here the details of time course of infection, strains used, CFUs at time of infection and surgical refinements.



Keynote Speaker

Biotechnology, Casuistry, and the Moral Continuum

Autumn Fiester, PhD University of Pennsylvania School of Medicine

There is a large spectrum of ethical issues raised by advances in animal biotechnology. One way to sort through these difficult ethical issues is to compare projects within one area of this science. Making these comparisons can help each us define for oneself a "moral continuum," in which certain projects seem morally permissible and others more worrisome. This mode of ethical analysis is called "casuistry," and it particularly helpful in working through new ethical terrain. This presentation looks at two different types of transgenic projects (biopharming and xenotranplantation) and compares the ethical issues raised by each.

Stapled Partial Gastrectomy in Athymic Nude Rats

Marisha Godek, PhD, Michael Soltz, Elizabeth M. Contini and Dwight Bronson Covidien

Surgical staplers are frequently employed in a variety of gastrointestinal procedures to remove and join tissue. Although complications of gastrointestinal stapling procedures (e.g., anastomotic leaks) are rare, when they occur they are associated with high morbidity and mortality rates and represent a significant health care cost. Research aimed at reducing the incidence of leaks is challenging because scalable in vivo models are required for studying the time dependent cellular aspects of wound healing. Furthermore, the size of commercially available stapling devices requires large animal models which come at high financial and ethical costs. This work describes a stapled partial gastrectomy procedure in an athymic, nude rat model. The novel use of immunocompromised rats is advantageous because it allows investigation of the cellular components of gastrointestinal wound healing without the superimposition of T-cell mediated interactions that can otherwise influence healing outcomes. Six animals were subjected to the removal of approximately one third of their stomach using commercially available endoscopic linear staplers; anesthesia was induced with three percent isoflurane and then maintained between two and three percent to achieve a desirable anesthetic depth. Pain management was achieved by subcutaneous injection of 0.03 mg/kg buprenorphine for 48-72 hours

post-operatively. Animal weights were carefully tracked post-operatively and subjects were survived to ≥ 56 days. Necropsies were performed and tissues were harvested for histopathological evaluation using standard methods to evaluate healing at the staple line. Results of the pilot study indicate one hundred percent survivability for the surgical procedure, with few complications (e.g., adhesions), excellent long term (months) survivability and normal healing response. This model should allow assessment of novel stapling technologies in a small animal model where factors that affect wound.



Animal Research Models and the Ethical Dilemma

Sylvia Gografe, DVM, PhD, DACLAM Oklahoma Medical Research Foundation

"The decision to use animals in research requires critical thought, judgment and analysis" (Guide 2011), which is especially true for animal models involving surgically invasive experimental techniques. In addition, the new Guide, emphasizes the need for training of all interest groups involved in surgical manipulation of research animals. Graduate students in doctoral and postdoctoral training programs in the basic sciences rarely spend more than the minimum training in the performance of anesthesia and surgery involving their research models. The use of surgical experimental techniques requires a great deal of preparation and planning. Protocol preparation involves consideration of ethical questions like cost-benefit-ratio and assessment of the 3R's as well as the skills and experience of the research team regarding administration of anesthesia, assessment and monitoring parameters of the anesthetized patient, recognition of depth and complications associated with the choice of anesthesia and analgesia as well as the skills required to perform aseptic surgery with minimal tissue damage while monitoring for complications and recovery of the animal patient. One important aspect is how IACUC's evaluate surgical models during protocol review and planning and how the research team can be pro-active to expedite protocol approval. IACUCs must carefully weigh each protocol description involving surgery. There is no one correct answer to the right definition of multiple major survival surgeries or whether endoscopic surgeries are always minimally invasive. Many researchers, veterinarians and IACUC members have been struggling with concerns of humane care and animal welfare when it comes to rather controversial models such as chronic cranial implants in large animal species (e.g. nonhuman primates and cats), surgically induced ischemia, cecal ligation leading to sepsis and acute myocardial infarction via ligation of the left anterior descendent artery. Numerous questions arise when it comes to post-operative analgesia. Is the withholding of analgesics because of anti-inflammatory properties of the drugs always justified one might ask? These and other problem-laden examples will be used to provoke discussion and critical review of surgical animal models in vitally needed research of human and animal diseases.



Development and Management Of The Diabetic Nonhuman Primate Model

Melanie L Graham, MPH, PhD University Of Minnesota

Background: NHPs are widely used in models of Type 1 (T1) diabetes. The close similarity of their immune response to grafted organs, tissues or cells, has demonstrated value in translational research and extrapolation to patients. Instead of total pancretectomy, we studied induction of diabetes by streptozotocin (STZ) in NHPs in preparation for islet transplantation, with respect to the diabetic state and emergence of adverse events (AEs), their severity, and to identify risk factors.

Methods: STZ was given based on body surface area (1050-1250mg/m2, equivalent to 80-108mg/kg) or on body weight (100mg/kg) to 54 cynomolgus and 24 rhesus macaques. Follow-up was for clinical and laboratory AEs. Observation of AEs was analyzed by risk factors, i.e., obesity parameters, age, and STZ dose.

Results: Clinical AEs after infusion prompted euthanasia of 3 obese animals. Except for those 3 animals, diabetes was successfully induced as shown by circulating C-peptide levels, the intravenous glucose tolerance test, and/or arginine stimulation test. C-peptide after infusion weakly correlated (P=0.048) with STZ dose in mg/m2. Grade \geq 2 clinical AEs occurred in 7 of 78 animals, reversed in 4 cases with supportive care, and significantly correlated with obesity parameters. Taking girth-to-height ratio as an obesity indicator, with threshold value 0.92-0.95, the positive predictive value of obesity for AEs was 92% and the specificity 94%. Grade \geq 3 laboratory AE, nephro or hepato -toxicity (serum markers >3 x or >5 x baseline, respectively), occurred in about 10% of cases, generally without clinical manifestation and were reversible.

Conclusion: Diabetes is consistently and safely induced in fit animals using 100 mg/kg STZ. Obesity is a significant risk factor, obese animals should preferably receive a lower dose. The incidence of relevant AEs is low. Protocol refinements like dose adjustment, post STZ standard monitoring, and supportivemedical intervention can avoid or result in recovery of AEs, and reduce total number of animals neededby increasing eligibility for enrollment in experimental studies.

Broadening Our Perspective on Refinement: Addressing Model Divergence to Target : A Net-Positive Animal Experience

Melanie L Graham, MPH, PhD University Of Minnesota

Refinement strategies in animal models are essential when replacement techniques are unavailable and where experimental design has already been optimized to ensure a minimum number of animals are used. Likewise, often replacement and reduction are realized via stepwise refinement, illustrating the complex interplay between the 3Rs. Although it is generally assumed that refinement measures to improve animal well-being support scientific objectives, it should be acknowledged that this is not automatic, and refinement techniques should be evaluated with the same intensity as our research questions. Applications of progressive refinement methods that enhance the scientific value of the model present an opportunity to engage scientists in a meaningful way with the 3Rs. In this way refinement is of practical importance in the development and evaluation of animal models.

We describe pragmatic and proven refinement techniques in a complex animal model, namely islet transplantation in diabetic nonhuman primates, and their unified effect on animal well-being and model validity. These techniques include cooperative handling (training), enrichment, novel instrumentation, model characterization, and advanced clinical care strategies. The refinement methods implemented are of relevance to scientists, veterinarians, technicians, and husbandry staff. Their application could be adapted to NHP research models in the fields of transplantation, immunology, virology, CNS research, toxicology and pharmacokinetics.



Non-invasive ECG Monitoring in Animal Models of Human Disorders

Thomas G. Hampton, PhD Mouse Specifics, Inc.

Objectives: Heart rate (HR) monitoring of laboratory animals is useful pre-operatively, during surgery, and as a measure of post-surgical pain and recovery. Non-invasive methods can significantly improve outcomes and reduce costs. Here, we describe non-invasive recording of the electrocardiogram (ECG) in rodent models of human disease pre-operatively, during anesthesia, during surgery, and post-operatively.

Methods: The ECGenie is patented electrocardiography technology that detects the ECG passively through the paws of the animals as they actively explore an instrumented platform. The system has recently been expanded to include ECG recording in awake neonatal mice, rats, hamsters, and guinea pigs. Neither anesthetic nor surgery is required to obtain electrocardiographic signals from conscious animals.

Results: In pre-clinical surgical models of human diseases, for example cerebral artery occlusion to mimic ischemic stroke, monitoring sympathetic and parasympathetic activity adds important information to more precisely characterize the neurobehavioral consequence of the brain ischemia. Surgical pain itself, moreover, has been shown to result in alterations in HR and heart rate variability (HRV). Time domain indices of HRV and power spectral analysis of ECG intervals recorded non-invasively indicate the relative contribution of the low frequency (sympathetic) and high frequency (parasympathetic) components of HR regulation. Anesthesia induction reduces HR and HRV, threshold changes of which indicate that animals have reached an adequate plane of anesthesia prior to surgical incisions. Changes in the electrocardiogram post-surgically indicate the health status of the animals; changes in HRV can be used as surrogate markers of pain. Non-invasive ECG monitoring has described novel observations in animal models of muscular dystrophy, diabetes, and heart failure, to name a few.

Conclusions: Non-invasive ECG monitoring in pre-clinical surgical animal models has several advantages over telemetric implants for much of the same electrocardiographic data. These include advancement of the 3 R's of animals in research, improved anesthesia and pain management, and improved pre- and post-operative care.



Establishment and Maintenance of a Cesarean Derived Flock of SPF Sheep

Julie J Hurley, DVM, MS, DACVPM New England Ovis, LLC

Russell and Burch first proposed the concept of the 3R's, Replacement, Reduction and Refinement, in their 1959 book on humane experimentation. Since then, great strides have been made in minimizing or eliminating the impact of non-experimental variables in research involving animals. A significant early refinement, the elimination of specific pathogenic organisms in rats and mice, resulted in an overall improvement in animal welfare and, in many cases, reduced the number of animals needed for obtaining statistically significant data. The advantages of specific pathogen free animals, however, have not been commercially available to investigators using sheep as animal models. We report here the successful establishment of a production flock of sheep free from over 30 pathogenic organisms. These include common enzootic pulmonary and upper respiratory pathogens, all parasites and zoonotic diseases. Full term lambs were surgically removed from the uterus, aseptically isolated, hand-raised and confirmed pathogen free after the establishment of rumen microflora. Ongoing surveillance using serology, PCR, microbial culture and pathology is performed to validate the unprecedented health status of this specific pathogen free sheep flock. The list of monitored and excluded agents include intestinal parasites (helminthes, cryptosporidium, giardia), lung worms, ringworm, ectoparasites, Bluetongue, BVD, Orf, OPPV, Toxoplasma, Brucella, Chlamydia, Campylobacter, Dichelobacter, Q-fever, Johne's, Leptospira, and all respiratory pathogens (culture negative). This single refinement eliminates the confounding impact that these diseases, as well as the host's response to these diseases, has on experimental data, improves the overall welfare of the animals by removing illness, both before and while on study, and has significantly reduced the number of animals needed in some studies. No less important has been the impact of the husbandry and housing criteria instituted to maintain the SPF health status of this production flock. These sheep have frequent, positive human interaction and are well acclimated to people. The outcome of this interaction is a more manageable and easy to restrain animal resulting in less stress and distress in the research setting.

Statement:

This novel accomplishment was the direct result of the efforts of the authors and was conducted as an agricultural project. There was no requirement for IACUC approval and New England Ovis, LLC is currently licensed as a Class A dealer by the USDA.

Kidney Transplantation in a Large Animal Model (Video)

Kaiser GM, MD, Gallinat A, Heuer M, Würzinger P, Paul A, Minor T University Hospital Essen

Objective

A model of orthotopic kidney transplantation in swine was developed to investigate advanced preservation methods. At all large animal models are of value for preclinical studies to simulate the clinical situation. Especially for organ procurement, preservation and transplantation procedures porcine models are suitable due to strong morphological and functional resemblance between human being and swine. Challenges for surgical technique, which occur during establishing an experimental model transplantation, will be focused in a video presentation.

Method

The presented animal model is well established and more than 100 cases were performed by our group. In the video the operation of an swine (BW 30kg) is shown. After operative introduction of a central venous line a midline laparotomie is performed. Then a left nephrectomy is done. In this case a cold storage of the kidney was established for 2 h. During preservation period of the left kidney the right kidney is resected. After cold storage the transplantation of the left kidney was performed as an autotransplantation to the right retroperitoneum. The venous and arterial revascularisation of the donor kidney was placed using an running suture in an end-to-end fashion of donor and recipient vena renalis and arteria renalis. An percutaneous ureterostoma was established for effective monitoring of the quality and volume of urine production after surgery.

Results

During the operative time of 4.5 hours no significant bleeding occurred and the procedure was carried out without complications. The animal was cardiopulmonary stable during the entire procedure of surgery and anaesthesia. Also reperfusion of the transplanted kidney was uneventful resulting in primary function of the organ. All steps of the operation are well documented by the video.

Conclusion

The presented method of kidney transplantation is safe and can be performed easily by an experienced surgeon for experimental studies. The experimental setting might be changed following the specific experimental requirements like prolonged ischemic time or otherwise challenging organ preservation methods. Many kinds of preclinical evaluation of new methods in kidney transplantation can be evaluated using modifications of this large animal model. Further swine are the ideal model to be used for training of residents and fellows in transplantation surgery under standardized conditions.



Wound Healing Model Development in SKH1 Hairless Mice

Connie Kliwinski, MLAS, RLATG, SRS Janssen Pharmaceutical Companies of J&J

Therapeutics being developed to treat various disease entities have the potential to affect the course of wound healing which is a complex multi-phase process. Any such interference, whether beneficial or detrimental, is important to determine prior to clinical trials. With this issue in mind we set out to design a model which could be used to easily and quickly assess the effects of new compounds on wound healing. Model development went through three iterations with various changes made to optimize the process. Variables evaluated were wound shape, size, and location, as well as dexamethasone dosing regimes. SKH1-E female mice were used for all studies and full thickness wounds were made with biopsy punches and/or scissor and forceps and ranged in size from 4 to 8 mm. Initially, wounds were made on the top of the head and were subsequently moved to the side over the area of the latissmus dorsi muscle. Dexamethasone 20 mg/kg and phosphate buffered saline were administered subcutaneously to positive and negative control groups, respectively. During the study, healing was assessed at various intervals based upon gross appearance and caliper measurements. At study end, representative specimens were collected for histopathology and collagen determination via Sircol assay. The first study involved 6-mm round and square wounds made over the skull which did not heal sufficiently by 18 days. Therefore, in the second study the wounds were moved to the back where they would not be over bone and were decreased in size to 4-mm round. These wounds healed very quickly making it difficult to determine a significant difference between the negative and positive control groups. The third study utilized slightly larger 6-mm wounds on the same area of the back which allowed us to distinguish a significant difference between the groups with regard to healing between 7 and 10 days. The Sircol assay for collagen did not prove to be particularly useful since healing occurred at different rates and samples could only be taken at study end. For our purposes, gross assessment and caliper measurements provided sufficient information. In the event that we would require additional parameters by which to assess the wound healing process, samples collected for histopathology could be examined for inflammation, granulation, apoptotic cells, etc., using various stains. Based upon our experimental results we successfully optimized a model for the assessment of test compound effects on wound healing using SKH1-E immunocompetent hairless mice.

Adhesives in Surgery

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Throughout history, different materials and interesting surgical methods give us an example of the genius and accomplishments of our ancestors. Just local fire, plant fibers, acacia tree thorns, animal gut strips even insect mandibles were used to treat tissue injuries and to improve wound healing (Kamer FM et al, 1989).

Among others, the initial use of biological adhesives and, specifically, the cyanoacrylates used in the Vietnam War, as an emergency treatment of wounds on the battlefield, marked an important step in surgical wound healing. Due to the ease of use, speed and economic advantages, its application has been widespread at the clinical level although its final characterization will depend on the effect exerted on the tissue biomechanical response.

The purpose of this project was to investigate the role of cyanoacrylates in wound healing by reviewing the literature through Pubmed/Medline with more than 600 scientific articles and by evaluating the recent advances encountered in a new clinical trial of adhesives sponsored by the Spanish Ministry of Health. Studies of wound healing behavior in Wistar rats, comparing the results with standard sutures and cyanoacrylates in commercial use, have been performed by determining the macroscopy response and evaluating the wound histology and histochemistry (metalloproteinases, collagen types III and IV, elastin, fibronectin and hyaluronic acid) (Loffek S et al, 2011; Masaru Y et al, 2010).

Molecular analysis of adherence, the pathophysiological mechanisms that occur on the injury with this biomaterial (Fink JK et al, 2005), the biomechanics of in vitro and in vivo adhesion and the development of the wound formation, not only dermal but also visceral, can help us to discern what happens with wound healing under these conditions (Park DH et al, 2003).

The evolution of standardized traumatic injuries in rat kidney, liver and spleen, using Punch Biopsy circulars of 8.0 and 3.0 mm. (Stiefel®) will help us to evaluate the behavior of the elastic cyanoacrylates in visceral injuries, comparing the results with standard sutures and fibrin sponges.

Finally, we analyzed the design and preliminary results in a clinical trial authorized by the Spanish Ministry of Health on the evolution of elastic cyanoacrylates and other suture methods with a total of 60 patients with bilateral surgical wounds, such as bilateral inguinal hernias or abdominal laparoscopic surgery. Parameters such as evolution of the injuries, reliability, execution time, possible postoperative complications, wound healing cosmetic outcome and comparative analysis of the total costs per groups allowed us to consider the appropriateness of this surgical procedure (Chambers A, Scarci M. 2010).

In conclusion, cyanoacrylates are important biological adhesives to consider in clinical surgery for the improvement of wound healing and for the better understanding of the molecular and pathophysiological events occurring after tissue injury.

Development of a Porcine Model to Study the Metabolic Consequences of Bile Diversion

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Background: Ileal transposition(IT) is a technically difficult bariatric procedure that involves relocation of a segment of ileum to the proximal jejunum. Clinically, the procedure promotes weight loss, early satiety, and improved glucose regulation. To explore the potential mechanisms responsible for the metabolic effects of IT, we wanted to study increased bile enterohepatic circulation by creating an intentional diversion of bile distally in the small intestine.

Objective: To develop a porcine model using a cholecystojejunostomy(CJ) as a bile diversion procedure and cholecystoduodenostomy (CD) as a sham procedure.

Methods: All studies were approved by institution IACUCs . Initial studies used 11 (2 CD, 9 CJ) cross bred production pigs survived up to 30 days to establish the methods. The target study included 20 (9CD, 11CJ) obese Ossabaw Miniature swine conditioned to obesity on a daily calorie dense high fructose diet (5KA6) for 7 months prior to the study. The Ossabaw pigs were survived up to 8 weeks after surgery. After laparotomy, the common bile duct was ligated. Animals received either a CJ bile diversion or a CD sham procedure. A 25-35 mm side-to-side anastomosis was created between the gallbladder and either the duodenum (CD) or jejunum (CJ). In the Ossabaw swine, pre and post-procedure diagnostics included body weight measurements (once/week), body fat (CT scan), fasting blood sample (obesity hormones, insulin, circulating bile acids assays) and oral glucose tolerance testing (OGTT).

Results: In the initial production animals 9 of 11 developed dark tarry feces and/or gastric ulcerations, therefore antacid therapy and antibiotic therapy were instituted. Four CJ animals developed ascending hepatic infections from retrograde movement of ingesta into the biliary tract. Therefore, antacids, antibiotics and a smaller size anastomosis were instituted for the Ossabaw swine.

Similar to the production pigs, the Ossabaw animals tended to develop ascending hepatic infection. A total of 14 animals survived to scheduled termination. At necropsy, the bile ducts were enlarged and impacted with yellowish/green material in 9/20 animals. Pre-existing hepatic fibrosis (i.e. stage 4) was observed in liver biopsies collected at surgery in all animals. In pre-surgical OGTT assessments most animals lacked strong glucose intolerance curves.

Conclusions: Adjustments made to prevent the procedure complications seen in productions pigs were insufficient in preventing the complications in the Ossabaw pigs. Additionally, the identified pre-existing conditions (hepatic fibrosis and lack of the desired impaired oral glucose response curves) complicated abilities to draw conclusions from this study. More model development (preconditioning and procedure optimization) is necessary to study bile diversion in swine.



A Refined Model of Spinal Wear Debris in the Rabbit (Oryctolagus cuniculus)

Tyler Long, DVM, DCLAM North American Science Associates (NAMSA)

Joint replacements are among the most successful surgical procedures and provide many benefits to patients; however, implant loosening due to wear debris formation and subsequent osteolysis can lead to significant patient discomfort and immobility in the long-term. This may force patients to undergo a revision surgery which generally has less success than the primary procedure or cause them to delay an elective primary joint replacement until years later. Thus, wear debris formation and its associated physiologic reactions warrant further research and the goal of this experiment was to refine the spinal wear debris model in rabbits. To simulate particulate wear debris generated from various spinal implants used for joint replacement and vertebral stabilization procedures, a dorsal laminectomy was traditionally performed at the author's institution to deposit wear debris around the lumbar spinal cord of rabbits. In an effort to reduce surgery and recovery times as well as decrease patient discomfort postoperatively, an alternative method was devised where particulate wear debris was percutaneously injected into the epidural space around the spinal cord under fluoroscopic guidance. After sufficient training, this refined method produced similar study results, required less analgesia, substantially decreased surgery and recovery times, and resulted in less postoperative patient complications such as inappetance, gastrointestinal stasis, and immobility. This study provides an alternative method for the spinal wear debris model in rabbits that reduces surgery and recovery times and enhances animal welfare.



Practicing the Art of Surgical Research in the Development of New Medical Devices and Pharmaceuticals Vince Mendenhall, DVM, PhD Preclinical Surgical Services

The definition of surgery is that branch of medicine that is concerned with the treatment of a disease or condition that has created pathologic anatomy and physiology, by manual and instrumental interventional procedures. In other words, it is the act of incising living tissue, which in and of itself creates an anatomic and physiological cellular event, involving damage, disruption and invasion of that tissue to accomplish a procedure that will result in more normal anatomy and physiology.

The definition of surgical research is that area of basic and applied research that is concerned with creating a minimal degree of pathologic anatomy and physiology by manual and instrumental interventional procedures. In other words, it is also the act of incising living tissue, which also in and of itself creates an anatomic and physiological cellular event, that involves creating controlled damage and disruption of living tissue to accomplish a procedure that will result in a minimal change in the normal anatomy and physiology in order to study the effect of a new medical device or pharmaceutical on the tissue so disrupted. Thus, the research operation is one that is intended to discover the cellular and tissue reactivity to a medical device or pharmaceutical, as well as its efficacy and safety while in use.

Surgical research of necessity must involve as few animals as possible. Thus, the importance of surgical knowledge and the effects of the surgical procedure itself upon the animal with regards to anatomy, clinical response, normal behavior of the animal, the tissue and cellular response to injury and infection, the signs of complications with regards to altered physiology and inflammatory processes, basic wound healing, anesthetic methods, microbiology, and the basic surgical principles and practices regarding aseptic technique for infection control and prevention, the effects of tissue handling, and finally, even the choice of instruments, suture and suture patterns must all be considered and are of utmost importance. The goal is to evaluate the new device or drug, not the skill of the surgeon or the environment in which the surgery was performed.

The effects of all these variables will be presented and discussed and recommendations made to help prevent the occurrence of both false positives and negatives in the area of surgical research.



Developing an Anaesthetised Neonatal Pig Model for a Safety Pharmacology Study

Helen Murphy, BVSc, BSc, PhD, MRCVS Huntingdon Life Sciences, UK

A terminal anaesthetic protocol for neonatal pigs was developed to enable 6 hour inhalation dosing with a test compound for a safety pharmacology study. Inhalation dose route and age of the animals (2-3 days) were chosen to reflect the intended use in a clinical setting. Effect of the test compound on cardiovascular parameters was to be investigated, alongside pharmacokinetic and pharmacodynamic parameters. As such, any variation due to anaesthesia needed to be minimised. The study included a 1 hour pre-dose monitoring period and 6 hours of continual inhalation dosing during which 13 blood samples of 0.5-1ml were obtained. All pigs were euthanased without recovery. Following literature review, pilot phase work was conducted in 2 pigs in order to establish optimum dose rates and routes of anaesthetic agents and establish the feasibility of the intended dosing method. A protocol was developed utilising a combination of injectable and inhalational anaesthetic agents during the set up phase, and total intravenous anaesthesia during the dosing phase, thereby allowing continual inhalation dosing via a nebuliser. Heart rate, blood pressure and SpO2 were monitored continually throughout and kept within acceptable limits for a 7 hour period enabling all 8 pigs used on study to be dosed successfully. The presentation will focus on the practical anaesthetic techniques used, considerations for neonatal patients and how refinements were applied.



Refinement of Surgical Procedures and Methods in a Rodent Production Setting

Sera Murray, DVM, MS Charles River Laboratories

The rodent production setting offers some challenges as it pertains to surgery. Balancing work load, efficiency, and sterility, all while maintaining animal welfare has proven to be a large task. Over the past year we have been able to refine some of our techniques and standard operation procedures to meet all these requirements. This talk will highlight these changes along with support from the literature and some data we have collected.



Percutaneous Fine Needle Aspiration Biopsy of the Liver for RNA Extraction and Gene Expression Profiling Luke Mutch University Of Minnesota

Background: Gene expression profiling is often utilized to increase understanding of biological regulatory systems both in the normal situation and during the development of disease or treatment. Specific organs, like the liver, can be biopsied to obtain sample for tissue-specific gene expression.

Methods: We evaluated a percutaneous fine needle aspiration technique in livers of macaques in our transplantation program for RNA yield, purity, and integrity. Animals were sedated and local anesthesia was administered at the anticipated needle insertion site. Percussion and palpation was used to establish the position of the liver. A regular bevel fine gauge needle (20-22g) attached to a syringe was advanced to enter the liver. Aspiration was used during advancement to extract tissue and cells into the needle. Post collection gentle pressure was applied to the insertion site. Tissue was immediately placed in buffer RLT (guanidine thiocyanate buffer) and β -ME (2-Mercaptoethanol). RNA extraction was performed using the animal tissue protocol from the RNeasy mini kit.

Results: 44 fine needle liver biopsies were performed in 30 macaques at different timepoints relative to transplant. The total RNA yield in those samples ranged between 0.8 to 19.20 μ g (mean = 4.3 μ g and stdev =3.6 μ g). The RNA purity based on the 260/280 ratio ranged between 1.8 to 2.3 (mean = 2.0). The RNA quality ranged between 2.0 and 10.0 (mean 8.1 and stdev 1.9) based on electropherograms and gel-like images were evaluated and a RIN (RNA integrity number). All but 4 had suitable quality contained at least 1.0 μ g for rt-PCR assays. The mRNA transcript levels for 47 unique primers were determined in over 90% of samples. No procedural complications were observed.

Conclusion: Gene expression profiling for tissue specific characterization, i.e. in this situation the transplant graft environment, can be performed with samples from a fine needle aspiration biopsy of the liver. Likewise, there are opportunities for expanded application, e.g. in pharmacokinetic models where tissue specific mRNA expression could be used as a surrogate for protein abundance and activity. This provides an opportunity for refinement by eliminating the need for more invasive approaches like large core biopsy or surgical wedge resection.

Targeting Brain Structures in the Growing Rat

Christina Nelson, BS, SRS, LAT University of Texas Medical Branch

Inaccurate surgical targeting of brain structures results in waste of animal life, invalidation of results, and a loss of time and resources. Surgical procedures in neuroscience research frequently rely upon reference to a Rat Brain Atlas for accurate targeting of brain structures. The most commonly used and referenced atlas, The Rat Brain in Stereotaxic Coordinates, details the exact stereotaxic coordinates to target various structures in the brain of a 270-290 gram rat. Laboratory rats (along with mice) make up about 90% of the animals used worldwide in animal research today, and frequently grow to almost double this size at maturity – especially when fed the standard ad libitum diet. Currently there are no alternative atlases or references to enable a researcher to determine the location of brain structures in a subject of increased size.

Rodents of varying sizes (275-560 grams), were used through the course of a study using 200 Long-Evans models for acute dorsal hippocampus infusions. A set of coordinates was determined for the growing rat so that the hippocampi were accurately and consistently targeted. Rats were anesthetized with isoflurane (5% induction, 2-3% maintenance), stereotaxically mounted, aseptically prepped, and infused with Bupivacaine 0.25% along incision line. After scalp incision, coordinates were stereotaxically drilled through the skull and hippocampi were acutely infused with an experimental substance using 27G blunt needles. The animal was euthanized by decapitation one hour after infusion. The brain was carefully removed, hippocampi were extracted from both hemispheres of the brain, and accuracy of placement was visually confirmed with examination of structures. A positive hit showed a needle track in the center of the dorsal hippocampus that did not pass through the structure and was approximately centered in the structure body.

An analysis of the data discovered direct linear correlations between subject size and hippocampal coordinates. The initial location of the dorsal hippocampus in a standard 270 gram rat is 3.2 mm anteroposterior from the bregma, 2.0 mm mediolaterally from the midline on both left and right sides, and at a depth of 3.5 mm from the dura. Starting from a 270 gram rat, the dorsal hippocampus coordinate showed a linear increase caudally to 4.2 mm in the largest specimen. As the subjects reached 390 grams, the mediolateral coordinate began linearly increasing on both the left and right sides to 2.8 mm in the largest specimen. Once the subjects reached 460 grams, depth began increasing linearly to 3.6 mm in the largest specimen. Linear fits to coordinate data had R-squared values of 0.97, 0.86, and 0.95, respectively.

Basic Understanding an Anesthetic Machine

Cholawat Pacharinsak DVM, MS, PhD, DACVA Stanford University School of Medicine, Department of Comparative Medicine

Inhalant anesthesia is a commonly used method to provide general anesthesia. The major component of this technique is an anesthetic machine functioning to deliver oxygen and anesthetic gas, remove carbon dioxide and waste anesthetics, and provide a means for patient ventilation. A basic understanding of the anesthetic machine is essential for effective anesthetic troubleshooting. This basic knowledge will assist the anesthetist to identify and correct various anesthetic-related complications.

Critical Size Tibial Defect in Sheep: Notes on Improving Plating Techniques and Post-Operative Management

<u>Randall T Pielemeier, LVT, BS, SRS, LATG</u>, Jennifer Sweet BA, SRS, LAT, Vince Mendenhall DVM, PhD, Betsy Geddings ALAT, Scott Adrian DVM; Claudia Almazan DVM; Heather Ramsay PhD MPI Research

Orthopedic models in sheep can be challenging from a number of fronts. Forty skeletally mature ewes received a tibial plate to immobilize a critical size defect. All animals underwent the necessary aseptic surgical procedures under a veterinary reviewed IACUC approved protocol with an anesthetic and postoperative plan including, ketamine 15mg/kg, xylazine 0.22mg/kg, glycopyrolate 0.01mg/kg, sevoflurane, bupivicaine 2mg/kg, buprenorphine 0.05mg/kg, ceftiofur 1.1mg/kg, ketoprofen 1mg/kg, Probios® 10g, and LRS 10-15mg/kg/hr. One difficulty arises as sheep bone is denser than human or dog bone. Commercially available screws and plates are designed for use with human or dog bone which is of lower density. As a result, self-tapping screws designed for less dense bone may cause significant far side cortical fractures, thus reducing the holding power of the screw/bone interface. This problem can be reduced by power tapping prior to screw placement, and with the use of cancellous bone screws superiorly. Post- operatively these animals require special care to prevent loosening and/or dislodgement of the screws. This begins in the preoperative period with good acclimation to human handling as these animals startle easily, thus placing tremendous force on the internal fixation devices used to immobilize the defected tibia. In the facility's standard sheep size pens (4ft x 8ft) the animals had difficulty rising to ambulate postoperatively. Increasing the pen size to 8ft x 8ft made standing easier for the animals as well as simplifying cleaning. Pain management and long term postoperative management is complicated as the return to weight bearing on the limb is extremely variable in this model, similar to humans. Slight loosening of the plates postoperatively can cause significant pain and swelling but is difficult to detect radiographically and can only be accurately diagnosed by palpation. Good palpation requires sedation of the animal in order to diagnose. Catastrophic failures are easily detected by radiographs or fluoroscopy. Identification of problems requires consistent careful monitoring to detect changes in ambulation. As many animals have some permanent changes in ambulation, subtle changes can be more difficult to detect than simply normal vs abnormal ambulation.

Surgical Techniques for Improving Visualization and Reducing Dissection Required for Cervical Spinal Cord Injections in Gottingen Minipigs Randall T Pielemeier, LVT, BS, SRS, LATG, Brian MacDougall BS, SRA, SRT; Jillian Horvath BS, SRA, Justin Prater BS, SRA; Rachel Tapp BS, LATG MPI Research

Gaining access to the cervical spinal cord of a Gottingen Minipig involves a midline dorsal dissection through 10-14 cm of soft tissue. Injecting test materials into the spinal cord at specific depths requires visualization of the injection needle touching the pia mater, this requires addition muscle dissections with conventional techniques.

Fifteen male Gottingen Minipigs 13-14 months of age were used. The animals received surgery under a veterinary reviewed and IACUC approved protocol. Anesthetic and pre-surgical medication protocol included Acepromazine 1mg/kg IM, Atropine 0.05mg/kg IM, Ketoprofen 3mg/kg IM SID, Cefazolin 25mg/kg IV, Methylprednisolone 10mg/kg IM and Buprenorphine 0.02mg/kg IM. Following injectable anesthesia, animals were intubated and ventilated. General anesthesia was induced with N02 and Isoflurane delivered in O2. Hydration was maintained with LRS delivered at 15ml/kg/hr for the duration of the procedure. A dorsal cervical approach was made by exposing C6. The dorsal bone and intervertebral connective tissue were dissected away, and the ligamentum flavum was removed. To reduce CSF pressure when incising the dura, the animal was hyperventilated to an expired CO2 below 20mmHg. After dura incision, 6-0 Prolene sutures were placed to elevate and retract the dura.

A standard Kopff stereotax manipulator arm and Hamilton syringe with 32 gauge needle was used for the injections. A 45-degree, 5mm rigid telescope attached to a laparoscopic tower with recording capabilities was lowered into the incision to provide visualization. The needle was targeted to avoid vasculature on the dorsal spinal cord. Once the intended injection site was visualized, a Pia Knife was used to incise the pia mater. Ventilation was stopped; the needle was lowered to the surface of the pia and then advanced 2mm into the spinal cord using the stereotax manipulator arm. The test article was injected and the needle was slowly withdrawn. The dura was closed with the 6-0 Prolene retraction sutures, and the remaining incision was closed in layers. Bupivicaine 2mg/kg was administered directly to the surgical site. Post-operatively, Ceftiofur 2.2mg/kg IM SID x 3 days, Ketoprofen 3mg/kg IM SID x 3 days and Buprenorphine 0.02mg/kg IM TID x 3 days were administered. All animals recovered well from surgery with no detectable neurologic abnormities. The use of the 45-degree rigid telescope allowed for excellent visualization of the spinal cord which facilitated an appropriate incision into the pia mater with the Pia Knife. This also allowed accurate visualization of the tip of the needle to assure accurate depth of injections as well as evaluation of any leakage of test material from the injection site.

Patient-Specific Positioning Guides for Total Knee Arthoplasty: A Coronal Alignment and Operative Time Study

William S. Pietrzak, PhD Biomet, Inc.,

Hypothesis: The restoration of a neutral overall mechanical axis for the lower extremity is an important goal for total knee replacement procedures. However, it is estimated that approximately 28% of cases performed with traditional manual instrumentation (MI) fall outside of the acceptable range of femoral/tibial alignment. The Signature[™] System (a Biomet and Materialise N.V. collaborative partnership) produces patient-specific positioning guides that can help the surgeon establish alignment. This study compared the coronal alignment and the operative time in cases where MI or the Signature™ system was utilized. The hypothesis was that the Signature™ system group would have a lower rate of coronal alignment outliers and shorter operative times than the MI group. Methods: All patients received the Vanguard® Complete Knee System (Biomet, Inc., Warsaw, IN) prosthesis. First, a meta-analysis was performed on published studies that included 626 Signature™ system-assisted cases and 212 cases that utilized MI to compare alignment between the groups, including the Hip-Knee-Ankle (HKA) axis and the Zone of Mechanical Axis (ZMA is the position of the intersection of a line connecting the centers of the femoral head and the ankle with the tibial base plate). Second, a prospective, controlled clinical study was performed to compare operative room time (prep, procedure, and post times) between the two groups that included 270 Signature™ system-assisted cases and 598 MI cases, respectively. Categorical data was compared using a Chi square test and interval data was compared using a two-tailed Student t-test (differences statistically significant if p <0.05). Results: Among the Signature™ system and MI groups, the percentage of HKA outliers (defined as >3° varus or valgus) was 14.8% and 19.6%, respectively (p=0.375). Among these groups, the percentage of ZMA outliers (defined as the intersecting line falling outside the center of the tibial base plate) was 14.2% and 26.9%, respectively (p<0.001). The mean prep, procedure, and post times for the Signature[™] system and MI groups were 28.4 and 30.9 minutes, 62.3 and 74.7 minutes, and 6.9 and 9.8 minutes, respectively (all p<0.001). Hence, on the average, the total operative room time was 19.9 minutes less for the Signature[™] system group compared to the MI group. Conclusions: Total knee replacement cases utilizing the Signature™ system required significantly less operating room time and had fewer coronal alignment outliers (significant and trend) than those utilizing MI, confirming the study hypothesis. Future studies will be required to determine the full potential of this system.

Targeting the Intestinal Epithelium in a Murine Model through the Superior Mesenteric Artery using a Lateral Microsurgical Approach

<u>Stacy L. Porvasnik, BS, MS, LAT, SRS</u>, Cathryn Mah, PhD, Steven Polyak, MD, University of Florida

Objective: Administration of molecular, pharmacologic, or cellular constructs to the intestinal epithelium is limited by oral, intraperitoneal, and systemic delivery techniques due to physical and biochemical barriers of the intestine and possible affects to other organ systems. Superior mesenteric artery (SMA) injections are used clinically in interventional radiology procedures. Injections into the SMA have been performed in rat, cat and mouse models. Our aim was to improve efficiency and elevate any postoperative complications; such as ileus. This study also verified biodistribution and anatomical distribution using the modified SMA injection to access the intestinal epithelium.

Methods: Ten male mice were anesthetized and placed in a right lateral recumbent position. Bupivacaine was injected into the last intracostal space and subcostal region along the left axillary line for localized analgesia. A 1-2 cm incision was made through the skin and abdominal muscle over the plenic area to expose the SMA. The SMA was gently dissected from the retroperitoneum. A tie was placed around the SMA and a microvascular clamp was used to clamp off the blood supply. A 33-gauge needle was inserted into the SMA with the tie being cinched around the vessel and needle to prevent leakage. The mice were divided into three groups and injected with methylene blue dye to grossly assess vascular distribution, fluorescent microspheres to assess biodistribution and recombinant adeno-associated virus pseudotype 8 to determine biological applicability. After injection the SMA was closed with a stitch and the clamp was removed. The abdominal muscle and skin were closed.

Results: There was only one complication and that was during surgery where the back wall of the SMA had been punctured and the bleeding could not be stopped even with suturing. Otherwise all mice recovered with no complications and minimal adhesions were found during biodistrubution dissections. Tissue analysis revealed good uptake in the small intestine and colon. Biodistribution analysis demonstrated some escape from the intestine with accumulation mainly in the liver.

Conclusions: The use of the lateral approach does not require removal the intestines from the abdominal cavity with less risk of heat and fluid loss. This microsurgical procedure provides an effective and efficient method for direct delivery of agents, including biological agents, to the small intestine and colon.



Dual Intrathecal Catheterization Feasibility as Canine Colony Model

Justin Prater, BS, SRA, LATG MPI Research

Intrathecal catheterization is a surgical technique used to determine if certain drugs are unable to pass the blood-brain barrier (BBB). The objective of this model was threefold; 1) To successfully place dual intrathecal catheters for dosing test article, 2) Collect CSF over time to determine test article concentration and 3) For repeat use as a colony of implanted animals.

Nine beagles (Source: Covance Research Products) at least 5 months old and between 5.0- 12.0kg were used. An IACUC and veterinary approved protocol was used to conduct surgery. The anesthetic protocol included: Acepromazine 0.1mg/kg SC, Atropine Sulfate 0.05mg/kg SC, Cefazolin 25mg/kg IV pre and post-surgery, Dexamethasone 2.0mg/kg IV pre-surgery and 0.5mg/kg post-surgery, Famotadine 0.5mg/kg SC pre-surgery prior to dexamethasone administration, Buprenorphine 0.02mg/kg SC TID on day of surgery, and a 50µg/hour Fentanyl Patch was applied transdermally and left in place two days following surgery. General anesthesia was induced with Propofol 6mg/kg IV and maintained with Isoflurane delivered in O2 to effect. Animals were intubated and ventilated. Hydration was maintained with Lactated Ringer's Solution 10-15mL/kg/hour IV.

Each animal was implanted with two 3.5 French ClearPort® VAPs. A dorsal L4 vertebral laminectomy was conducted to implant the catheters. The dura was incised and one catheter was placed at L1 vertebra and the other catheter was placed at L2 vertebra. The catheter tips were separated by one lumbar space to allow adequate circulation of test article prior to CSF sample collections.

Bupivacaine 2mg/kg was administered into the incision site. Post-operatively Famotadine 0.5mg/kg SC SID x 3 days, Dexamethasone (0.5mg/kg SC BID day 1 post surgery and 0.2mg/kg SC BID days 2 and 3 post surgery), and Cephelexin 250mg PO BID x 2 days. All animals recovered well from the surgical procedure with no noticeable neurological difficulties.

Bi-directional port patency was maintained by being flushed with 0.9% saline at least once prior to test article administration. Port patency was assessed bi-weekly until bi-directional patency failed. Port patency was maintained bi-directionally for 7.03±4.17 weeks post-implantation.

Conclusion: This model proved excellent for dosing and sampling the intrathecal space however, was not a reliable model for a catheter based CSF collection colony.

Guest Speaker

Nanotechnologies

John Rogers, PhD Department of Materials Science and Engineering University of Illinois at Urbana/Champaign

Biology is curved, soft and elastic; silicon wafers are not. Semiconductor technologies that can bridge this gap in form and mechanics will create new opportunities in devices that adopt biologically inspired designs or require intimate integration with the human body. This talk describes the development of ideas for electronics that offer the performance of state-of-the-art, wafer-based systems but with the mechanical properties of a rubber band. We explain the underlying materials science and mechanics of these approaches, and illustrate their use in bio-integrated, 'tissue-like' electronics with unique capabilities for mapping cardiac electrophysiology, in both endocardial and epicardial modes, and for performing electrocorticography. Demonstrations in live animal models illustrate the functionality offered by these technologies, and suggest several clinically relevant surgical applications.



Peri-Operative Concerns In a Swine Face Transplant Model

Dawn Ruben, DVM Johns Hopkins University

The first reported face transplant was performed in 2005. This transplant used cadaveric skin to replace severely damaged skin of the recipient. Subsequently several other partial to full skin face transplants have been performed. The most recent face transplant has involved bone, nerves and vessels. This is referred to as a composite tissue allograft. This type of procedure is quite complicated and no research has been done. Surgeons just performed the procedures and have recently realized that research is desperately needed to increase the knowledge and therefore success of face transplants.

In developing a model there are many concerns. Swine have been chosen because there is a breeding colony of pigs with genetics (SLA) known. This is similar to HLA typing in people. Although the shape of the pig's face is significantly different, after overcoming the challenges of this species as a model, more extensive face transplant research can begin. Our current task is to first determine what the challenges are and then come up with some solutions. Animal preparation and postoperative care are crucial to the success of the surgery. Concerns about eating, vascular access, breathing and analgesia must all be addressed. Additional issues such as infection, tracheal tube problems and general animal care will be discussed.



A Refined Technique to Improve the Success of VAPs in Cynomolgus Macaques

Jennifer Sheehan, BS, SRS, LATg Huntingdon Life Sciences

Vascular Access Ports (VAPs) have been used in monkeys for approximately 30 years. While they offer many advantages, there are some common issues associated with the long term use of VAPs.

This presentation is designed to outline issues reported to be associated with the common technique, including skin adhesions/ulcerations, tip positioning, patency, and infections. This will be supported through case studies and a literature survey, as well as our own observations.

In accordance with the 3Rs, this presentation will detail a holistic approach to refine the surgical technique, access procedures and long term maintenance and reduce the amount of animals lost to issues commonly associated with VAPs.



Anesthesia and Multimodal Analgesia in Rodent and Non-Rodent Models

Jennifer Smith DVM, DACLAM, Anne Kuszpit BS, LVT, LATg, SRA, Cholawat Pacharinsak DVM, MS, PhD, DACVA

Appropriate anesthetic and analgesic selection is an important part of the research refinement process. Different classes of anesthetics and analgesics provide both advantages and disadvantages. Because there is no ideal anesthetic and analgesic agent for all procedures, it is important to understand an agent's effects, including the pharmacology and physiology of anesthetic and analgesic agents before selecting an anesthetic and analgesic regimen. This presentation will focus on the concept of choosing anesthetic regimens and multimodal analgesic techniques in both rodent and non-rodent research models. The audience will participate in anesthetic and analgesic protocols focusing on anesthesia and multimodal analgesia regimens providing good anesthesia and analgesia while minimizing undesirable side effects in animals and research studies.

Unilateral Vs. Bi-Lateral Middle-Ear Cannulation In Guinea Pigs

Jenifer Sweet, BA, SRS, LAT, Rachel L. Tapp, BS, LATG; Janelle Gesaman, AS, LATG, SRA, SRT; Lindsay Tawoda, BS, SRA, SRT, LAT; Claudia Almazan, DVM; Randall Pielemeier, LVT, BS, LATG, SRS

MPI Research

Middle ear catheters are commonly placed unilaterally to allow for repeat administration of test compounds with the potential for ototoxicity. Placing bilateral catheters not only satisfies the client, but greatly reduces the number of animals on study. Concerns of bilateral cannulation include the ability of the animals to recover post-operatively as well as dose contamination or inflammation of the contralateral ear. The purpose of this study was to determine whether or not bilateral middle ear cannulation is an appropriate methodology for testing two compounds simultaneously in guinea pigs. All procedures were approved by MPI Research IACUC and veterinary staff. Two groups of CRL-HA Albino Hartley guinea pigs, males and females, weighing approximately 300-400g were placed on study. Animals were pre-medicated with 30mg/kg of Cefazolin SC and induced with 40mg/kg Ketamine/ 5-10mg/kg Xylazine IP. Analgesia consisted of 2% Lidocaine and 0.05mg/kg Buprenorphine SC. Incision sites were shaved and prepared with alternating iodine and alcohol. A midline skin incision was made on the dorsum of the head, continuing post-auricularly to the base of the ear. Bregma was identified and holes were drilled at predetermined locations for vertex and anchor screws. Muscle was bluntly dissected free from the surface of the tympanic bulla and a small hole was made slightly lower than midpoint of bulla. A pre-prepared catheter was placed in the defect and secured with Vet Bond adhesive and dental cement. It was then secured to the anchoring screws with fine gauge surgical steel and Methyl methacrylate. The procedure was repeated in the contralateral ear for Group 2 animals. Post-auricular incisions were closed, and the animals were allowed to recover. Group 2 animals were dosed with 10% neomycin in one ear and saline control contra-laterally BID for 14 days. Recovery time proved longer for Group 2 animals than Group 1 animals, though by post-op day 3, no significant difference in behavior or disposition was noted. Positive control administration to one ear did not negatively affect the contralateral saline control ears1; however, it is suggested to dose both ears of an animal with the same compound, equally reducing the number of animals for study assessments. Data indicates that bilateral middle ear cannulation in guinea pigs allows for assessment of both ears, providing cytocochleogram from one ear, and evaluation of relevant otic tissues from the contralateral ear.



The Development Of A Reliable Control For Testing Gastro-Intestinal Sealants Jenifer Sweet, BA, SRS, LAT, Mark Johnson, MS; Scott Adrian, DVM; Claudia Almazan, DVM; Randall Pielemeier, LVT, BS, L.ATG, SRS MPI Research

Currently, up to 75% of gastrointestinalcontrol defects heal on their own (Tsereteli et. al.), proving no reliable control for leak testing GI sealants. The purpose of this study was to develop an acceptable and repeatable control for the prevention of post-surgical leakage at a gastrointestinal(GI) anastomosis site. All procedures conducted were IACUC and veterinary approved. Fourteen beagles, both male and female, at least 5 months of age and weighing approximately 8-12kg were placed on study. Animals underwent a GI cleansing regime of low residue diet, GoLytely gavage and warm water enemas beginning 3 days pre-operatively. Multiple variations of surgical methodology were performed, including staple defects, removal of mesenteric blood supply, and injections of the following: Formalin, Tween 80, and 50/50 Elastase/Formalin. Surgery was conducted in phases and methodology was changed based on the results of each phase. Final model methodology consisted of the following: A midline laparotomy was performed and a portion of the descending colon was isolated. An endoscopic circular stapling device was inserted and deployed. Following deployment, a 50/50 mixture of Elastase/Formalin was injected around a portion of the GI staple line. The abdomen was lavaged and closed. Animals were fed low residue diet BID post-operatively and were closely monitored by staff for signs of deteriorating health due to peritonitis and/or sepsis. Animals were euthanized prior to term if appropriate. All surviving animals were euthanized either 3 or 14 days post-surgery and peritoneal cavities were examined for any evidence of leakage. The presence and severity of adhesions to the descending colon at the site of anastomosis was recorded. Leak tests were performed to a maximum pressure of 25mm Hg postmortem. Tissue was collected for histological assessment of inflammation, fibrosis, and general wound healing. The removal of 3 staples prior to staple anastomosis resulted in 50% leakage for control animals. Formalin injections in combination with staple defect revealed no significant variation from control, and injection of Tween 80 resulted in excessive post-operative allergic reactions. Formalin injection without staple defect produced no discernibledefect upon examination, nor did it decrease leak pressure at necropsy. 100% of anastomoses with 50/50 Formalin/Elastase injected around the staple line displayed open defects at necropsy. Results indicate that a 0.5-1.0mL injection of 50/50 Elastase/Formalin is ideal for creating the appropriate sized defect for testing sealants in a GI staple anastomosis model.



Novel Placement of a Vascular Access Port in Nonhuman Primates for Bioimaging Marlo Volberg, BS, LVT, SRS, RLATG, Nancy Poy, DVM, Anne Kuzspit, BSM, LVT, SRA, LVT Pfizer Worldwide Research & Development

Imaging modalities such as MRI (Magnetic Resonance Imaging) and PET (Positron Emission Tomography) have become prevalent within the research community. Pfizer uses PET scanning to target specific areas of the body to measure occupancy of radioactive tracers for translatable human disease models and ultimately drug development. The Bioimaging center requested a small cohort of their nonhuman primates have arterial catheters placed with vascular access ports so that during the imaging process, serial blood samples could be collected and measured for radiotracer amounts in the blood. During the imaging process, the animal is placed in dorsal recumbency and the head immobilized for scanning. The location of the port has to be accessible for aseptic blood collection without moving or repositioning the animal. The surgery consisted of a routine approach to the femoral artery and connection to a vascular access port. Historically, we were placing the port subcutaneously above the iliac crest. However, this area was not completely optimal as it was easily accessible by the animal to manipulate access in one animal, the port perforated through the skin. We have refined the location and type of port by placing it along the lateral thigh between the Satorius and femoral biceps muscles. So far, we have instrumented two animals with the ports in this location with no postoperative complications. The port site is easily accessed for aseptic serial blood sampling with no special positioning of the nonhuman primate while undergoing the imaging scan.

Effects Of Combined Small-Diameter Proximal Splenorenal Shunt And Partial Devascularization In Patients With Portal Hypertension

Weihua Qiu, MD, PhD, Weiping Yang MD, Zhiwei Xu MD, PhD Ruijin Hospital, Shanghai Jiao Tong University School of Medicine

AIM: Shunt and devascularization are two widely used surgical interventions for patients with variceal hemorrhage and portal hypertension. Now combined shunt and devascularization is recognized as another acceptable surgical modality. This study aimed to evaluate the effects of combined small-diameter proximal splenorenal venous shunt and partial devascularization in the treatment of portal hypertension.

METHOSD: 39 patients who had received combined small-diameter proximal splenorenal venous shunt and partial devascularization and 42 only having received small-diameter proximal splenorenal venous shunt from 2003 to 2011 were included in this study. Hemodynamic parameters of the portal venous system were studied by Duplex Doppler ultrasonography pre- and post-operation. Rehemorrhage, encephalopathy and mortality were followed up during peri-operative and long-term period.

RESULTS: Compared to the preoperative data, a decreased free portal preasure (FPP) and a decreased flow of the portal vein (PVF) were found in the both group after operation. In the combined procedure group, during peri-operative period, the rate of rebleeding and mortality were 10.26% (4 cases) and 5.13% (2 cases), respectively. 36 patients were followed up ranging from 3.5 to 108 months, and long-term rate of rehemorrhage and encephalopathy were 0 and 5.56% (2 cases), respectively. One patient died due to the canceration of the liver. While in the shunt group, during peri-operative period, the rate of rebleeding and mortality were 9.52% (4 cases) and 2.38% (1 cases), respectively, 40 patients were followed up ranging from 35 to 103 months. The long-term rate of rehemorrhage and encephalopathy were 5% (2 cases) and 7.5% (3 cases), respectively. One patient died due to the pancreatitis.

CONCLUSION: The combined procedures could integrate advantages of shunt with those of the devascularization, maintaining the normal anatomy structure of the hepatic portal vein. It could be one of the best choices for patient with portal hypertension when surgical interventions are considered. However, because of the high requirements of the liver function and the vascular conditions within the operation area, the procedure extensively carried out has been limited. Personalized treatment program should be developed according to the etiology of each patient, the potential for liver function reserve and portal venous system hemodynamic factors to obtain best prognosis.

Translational Refinement Enabling Effective Transurethral Catheterization of Male Rhesus Macaques Permitting Minimally Invasive Diagnostic & Urodynamic Parameter Evaluation. L. Alexandra Wickham, Alison A. Kulick, Cesaire L. Gai, Loise Gichuru, Marcie Donnelly, & Hiroshi Nagabukuro

Merck Research Laboratories (MRL)

Objective: Transurethral bladder catheterization of male nonhuman primates can be very difficult to accomplish and repeated unsuccessful attempts can result in iatrogenic complications leading to serious morbidity. Thus, to satisfy unmet clinical and research needs for minimally invasive, atraumatic and reproducible catheterization outcomes, several approaches facilitating successful transurethral catheterization in challenging male human cases were identified and translated for optimal use in male macagues. This refinement of approach is defined along with the development of a translational urodynamic model platform enabling functional evaluation of lower urinary tract in conscious male rhesus macagues. Methods: All animal care and procedures were performed in compliance with the Merck Institutional Animal Care and Use Committee and the Guide for the Care and Use of Laboratory Animals at a facility accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International. Peri-operative analgesia was not routinely provided given the minimally invasive nature of this procedure. When indicated, animals were sedated with either ketamine HCI (15-20 mg/kg, IM; Wyeth) or Telazol (5 mg/kg, IM; Wyeth) or a constant rate infusion of propofol (6.5-12.5 mg/kg/hour, IV; Abbott Laboratories). Transurethral catheterization was performed on male rhesus of varying ages and body weights over time. A refined approach comprising optimal lubrication of the urethral canal, appropriate urinary catheters and operator dedication to gentle and non-forceful technique was utilized. An initial cohort consisting of sedated naïve (n = 9) and non-naive (n = 5) animals were catheterized while dorsally recumbent and selected animals then re-catheterized to test reproducibility using various catheter types. Technique translatability was subsequently confirmed by additional operators during urodynamic model development and validation utilizing cohorts that were either sedated (n = 8) or fully conscious (n = 11) and sitting during catheterization. These cohorts specifically consisted of animals highly conditioned to chair restraint and to catheterization and urodynamic procedures via positive reinforcement training. Urodynamic parameters were measured via cystometry using a pressure transducer connected to the urodynamic catheter during transurethral intravesicular filling with sterile saline. Results: Overall, sixty-five catheterization sessions were conducted on animals during method refinement and urodynamic model development phases realizing a success rate of 100% along with a low incidence of catheter (10%) and post-catheterization (2%) complications. A translational urodynamic model utilizing cystometric evaluation of the urinary bladder was also successfully developed and validated as a consequence. Conclusions: The urinary bladder of male rhesus can be safely and reproducibly catheterized using this approach supporting both clinical and research arenas. Importantly, utilization of this refinement facilitated an overall reduction in animal stress by minimizing iatrogenic and catheter associated tissue trauma and complications affording improved health and welfare for animals undergoing transurethral catheterization. Also, a reduction in the number of animals required for urodynamic research purposes was achieved since an animal could be effectively reused and serve as its own control thus improving data guality and sensitivity of study end points.



A Novel Approach To Identify Source Of Palpable Laryngeal Muscle Stimulation

Kristin Wise, BS, DVM Boston Scientific

During vagal nerve (VN) stimulation, certain levels of current controlled stimulation amplitudes may cause unintended movement of the muscles surrounding the larynx, complicating interpretation of the stimulation effects. The elucidation of the source of this stimulation was imperative to the outcome of the study. In order to achieve this, complete paralysis of the critical muscles of the larynx was required. Theoretically, this could be accomplished by transection of the recurrent laryngeal nerve (RLN), or local injection of a paralytic drug into specific laryngeal muscles. Multiple canines exhibited moderate laryngeal movement during conscious VN stimulation after chronic implantation of a VN cuff. The surgery was performed as an acute surgery, during terminal data collection. Two canines were sedated with Butorphanol IM (~0.44mg/kg), induced with Propofol IV (~5 mg/kg), and maintained on Isoflurane (1-2.5%) and mechanically ventilated. A second dose of Butorphanol IM (~0.44mg/kg) was administered for additional analgesia. An incision was made over the larvnx. Tissue dissection was performed to locate the cricoarytenoidieus lateralis and dorsalis muscle which are innervated by the (RLN). These muscles were exposed unilaterally, and fascia was removed. Succinvlcholine chloride (SCC) IM (0.07-0.22mg/kg) was injected evenly into these muscles. One canine received 1.6 mg SCC, and the second received 3 mg SCC. Duration of paralytic effects of SCC appeared dose dependent. For both canines, onset of paralysis was 2 minutes. However, duration of paralysis lasted ~16 minutes and 30 minutes respectively. VN stimulation continued after SCC administration, and cause of stimulation (either extraneous muscle or strong nerve stimulation) was readily identified. Due to known systemic effects of depolarizing neuromuscular blocking agents, such as malignant hyperthermia, arrhythmias, hyperkalemia, myoglobinemia and myoglobinuria, the animal was monitored via respiration rate, heart rate, end-tidal C02, inspiratory C02, SP02, arterial blood gases, blood glucose, continuous ECG, invasive blood pressure, pre and post -operative urinalysis, CBC and chemical analysis. No adverse effects were noted. Minor changes in parameters monitored were noted, but determined to be clinically insignificant, and within expected changes during a surgical procedure under anesthesia. Therefore, the use of local succinylcholine in specific laryngeal muscles is an effective method of differentiating whether VN stimulation is caused by the stimulation electrodes contacting nearby muscle or muscle movement is caused by extraneous RLN stimulation.

Comparative Analysis Between Acellularized And Immunologically Non-Treated Vascular Xenografts In Long-Term Survival Animals

Won-Gon, Kim, MD, PhD, Ji-Min Chang, MD, PhD, Wook-Sung Kim Md, PhD Seoul National University Hospital

We implanted acellularized and immunologically non-treated porcine xenografts as an arterial graft in goats and comparatively analyzed the explanted grafts with gross observation, as well as light microscopy and immunohistochemistry, following the predetermined periods. For immunologically nontreated xenografts, bilateral porcine carotid arteries were harvested, and after short-term freezing at -70°C, were implanted into goats. The preparation of acellularized xenograft vessels has been performed with Nacl-SDS solution and stored at the freezer until use. The goats were randomly assigned for three periods of observation (3, 6, and 12 months after implantation), four animals were observed at each of these times. Periodic ultrasonographic examinations were performed during observation period. Following the predetermined periods, the explanted grafts were analyzed. Among 12 animals, one goats died prematurely, and a total of 22 grafts were evaluated. Gross observations revealed nonthrombotic patent smooth lumens. Microscopic examinations of the explanted grafts showed satisfactory cellular reconstruction up to the 12-month observation period. The proportions of CD3 positive T lymphocytes among inflammatory cells infiltrations were very low. In conclusion, these findings, as a whole, suggest that porcine vessel xenografts can be clinically acceptably implanted in the goats as a form of small-diameter vascular graft, regardless of the acellularized xenograft or immunologically non-treated xenograft.

The 28th Annual Meeting of the **Academy of Surgical Research**

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Exhibitor Hours:

Thursday, October 4 8 am – 5 pm Set-up 5:30 – 7:30 pm Exhibits open during Welcome Reception

Friday, October 5 7:00 am – 3:20 pm 3 pm – 5 pm Teardown



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