Orthopaedic Research Center

including the
Orthopaedic Bioengineering Research Laboratory

2008-2009 Report

Colorado State University

Dedication

This issue of achievement at the Orthopaedic Research Center and Orthopaedic Bioengineering Research Laboratory at Colorado State University is dedicated to Alec Wildenstein who lost a long battle with prostate cancer and passed away in 2008. Alec was a well known racehorse owner and breeder and a member of the Orthopaedic Research Center's Advisory Board. Ecurie Wildenstein won the Prix de l'Arc de Triomphe four times with the most recent being won by Peintre Celebre who also gave the family their first French Derby victory. Their racing successes stretched into the United States, and Arcangues is best known for coming over and winning the Breeders' Cup Classic. Dr. McIlwraith has consulted and done surgery for the Wildenstein family for over 20 years. Alec supported research projects at the ORC particularly the global project on conformation in Thoroughbreds documenting the changes that occur in growth as well as the effect of different conformations on equine soundness.

Preface

It is my pleasure to present our 2008-2009 Report from the Orthopaedic Research Center and the Orthopaedic Bioengineering Research Laboratory at Colorado State University. Our principal focus continues to be solving the significant problems in equine musculoskeletal disease as can be seen in this report, but we will also continue to investigate questions relative to human joint disease and techniques and devices for human osteoarthritis and articular cartilage repair when the technique can also benefit the horse. We continue to partner with the laboratories of Dr. Alan Grodzinsky at MIT on an NIH Program Grant in cartilage repair (Dr. Frisbie PI of sub-contract) and also with Dr. Robert Sah of UC San Diego on another NIH Grant in joint lubrication and osteoarthritis (Dr. McIlwraith collaborator) and more recently with Dr. Jude Samulski at the University of North Carolina with Dr. Laurie Goodrich's NIH K08 grant on gene therapy (co-mentored by Drs. Samulski and McIlwraith).

It is probably safe to say that all research institutions at universities have had the same challenges we've had in 2008-2009 because of the economic recession. Our endowed corpuses which provide the salaries for our four endowed chairs within the Orthopaedic Research Center have certainly suffered greatly in the last 18 months. Fortunately we have had enough donated money uncommitted to endowments to make up for salary needs and we have continued to receive good external research funding which is based on the ability of our faculty and staff to compete for these dollars. We have received three "top-ups" from NIH with stimulus package grants. The program grant from MIT that Dave Frisbie is PI on the subcontract for cartilage healing received an additional infusion to increase the number of horses that we could evaluate; the K08 training grant of Dr. Laurie Goodrich received an additional grant of slightly over $100,000 to do a dose titration for gene therapy and a new grant involving stem cell therapy for cartilage healing headed up by Dr. Connie Chu at the University of Pittsburgh with Drs. Goodrich, McIlwraith and Kisiday involved in an equine subcontract was also recently funded.

We added a fourth building to our Orthopaedic Research Center complex, namely a Gait Center where gait analysis (kinetics and kinematics) for both horses and dogs has been set up. Much of the equipment for gait analysis came from courtesy of Dr. Robert Taylor and the Thaw Family Foundation and a 3 year scholarship for a Ph.D. student in canine rehabilitation was also provided by Jaynn and Walter Emery.

Accomplishments at the ORC over the past 2 years are detailed in this report. These accomplishments could not be achieved without our team of faculty and staff as well as the excellent support of our corporate and individual donors and funding from research agencies. With this help, we continue to achieve our goals and also make new ones as new clinical questions arise.

Best wishes,

Wayne McIlwraith

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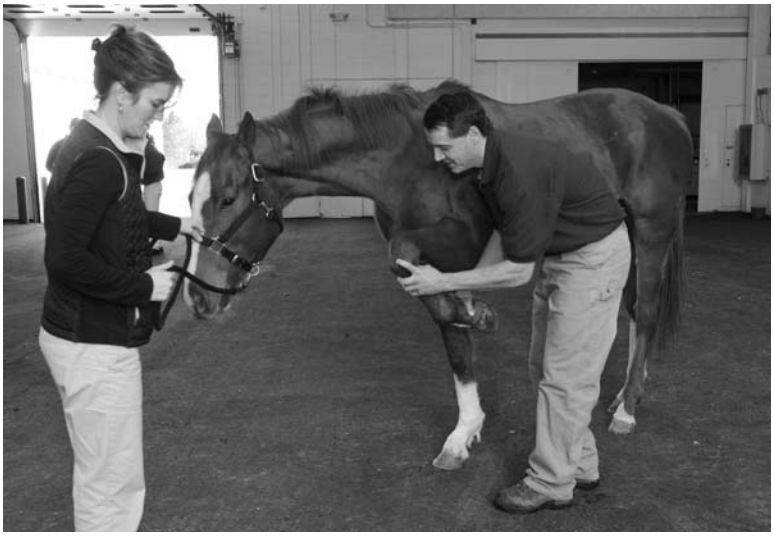
To investigate the pathogenesis, diagnosis, treatment and prevention of musculoskeletal disease and injury for the betterment of both animals and humans.

Orthopaedic Research Center faculty and staff.



Musculoskeletal Tissue Healing

Until now, we have principally addressed articular cartilage healing and will continue to do so, but we have enlarged the focus to include tendons, ligaments and menisci.

Early Diagnosis of Bone and Joint Disease

This includes the development of novel imaging techniques (present and future), body fluid markers and also molecular monitoring. The uses of these early diagnostic techniques include:

a. evaluation of the pathogenesis of bone and joint disease
b. early detection of disease processes
c. monitoring of therapy, with the long-term goal of preventing severe arthritis or failure

Improvement in the Understanding of the Pathogenesis of Exercise-Induced Traumatic Disease

These investigations use both molecular tools such as reverse transcriptase PCR for evaluation of tissues in various stages of the disease biomechanical and modeling studies, and computed tomography (CT) to monitor early events in bone disease.

Continued Development of Novel Therapies for Traumatic Synovitis, Capsulitis and Osteoarthritis in the Horse

These include evaluation of biologic inhibitors of critical mediators in joint disease, novel protein therapies, gene therapy techniques and mesenchymal stem cell therapies.

Validation of Rehabilitation and Physical Therapy Techniques for Musculoskeletal Disease

These include objective assessment of integrative therapies including manipulation and acupuncture for management of musculoskeletal disease and pain as well as rehabilitative techniques of swimming, underwater treadmilling and hyperbaric therapy.

Research Focuses at the Orthopaedic Bioengineering Research Laboratory

The Orthopaedic Bioengineering Research Laboratory (OBRL) is an interdisciplinary research and educational effort bringing together engineers, clinicians, biologists, and scientists all over campus. The goal of the laboratory is to provide an environment for undergraduate and graduate education in Biomedical Engineering while advancing treatment and/or prevention of muscular, neuromuscular or skeletal injury and/or disease. The primary research foci include:

Computational Simulation of Orthopaedic Conditions and Treatments

a. Finite element analysis
b. Cadaver and animal experiments to validate and augment the computational models

Biomaterials Development

a. Enhancing wear resistance of polymeric orthopaedic implant bearing materials
b. Biopolymer derivative synthesis and characterization
c. Bioactive and osteoinductive bone graft materials

Engineering and Growth Factor Therapy for Cartilage and Bone Repair

a. In vitro cell culture assessment
b. Animal models to evaluate repair
c. In vitro micro-assessment of mechanics of regenerated and normal tissue
d. Development and assessment of biomaterial carriers

Retrieval Analysis for Failure Assessment, Design Improvement and Tissue Interface

a. Orthopaedic implants
b. Allograft bone composites
c. Synthetic bone graft materials

Biocompatibility and Biomaterial/Tissue Interface

a. Interface biomechanics
b. Tissue response to biomaterials
c. Histomorphometry and image processing

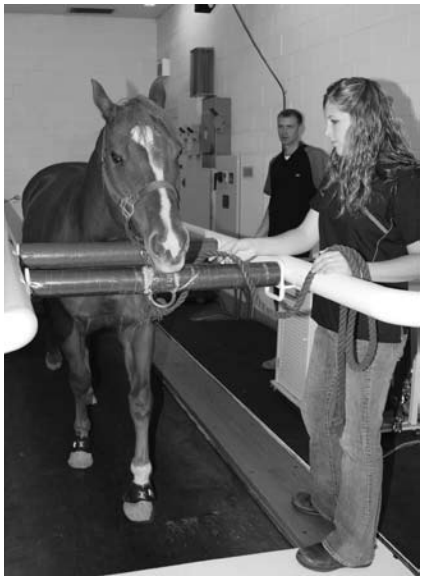
Comparative Orthopaedics and Animal Models

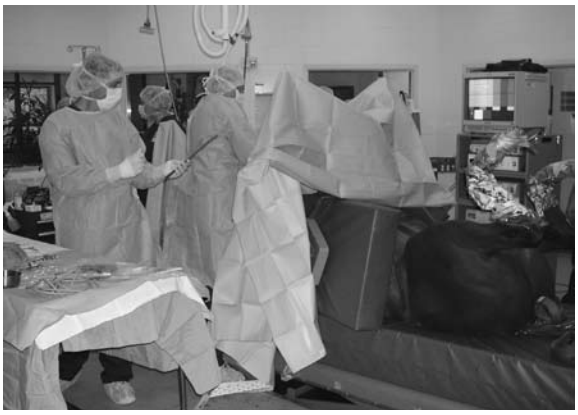
a. Animal model development and validation
b. Comparison of human and other animal disease mechanisms and treatment efficacy

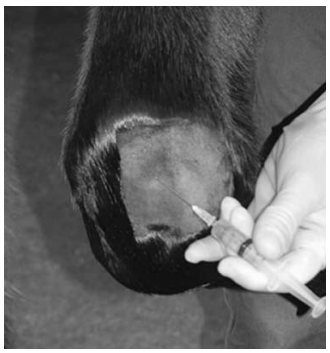
The **Musculoskeletal Research Program** has been designated as a Program of Research and Scholarly Excellence at Colorado State University (initially designated in 2004 and renewed in 2008 for four years).

The Musculoskeletal Research Program covers all orthopaedic research at Colorado State University and includes:

1. Orthopaedic Research Center
2. Orthopaedic Bioengineering Research Laboratory
3. Small Ruminant Orthopaedic Research
4. Orthopaedic Oncology







School of Biomedical Engineering

Colorado State University's School of Biomedical Engineering (SBME) was formed in March 2007 to address society's needs in bioengineering, one of the fastest emerging areas of scientific discovery. The SBME is an interdisciplinary program built on strong faculty and research programs in the Colleges of Applied Human Sciences, Engineering, Natural Sciences, and Veterinary Medicine and Biomedical Sciences. In particular, Drs. Sue James and Puttlitz of the Orthopaedic Bioengineering Research Laboratory are co-coordinators of the program and Drs. Wayne McIlwraith, Chris Kawcak, David Frisbie, Kevin Haussler, Laurie Goodrich and John Kisiday of the Orthopaedic Research Center are core faculty members of the program in Biomedical engineering research which is rapidly expanding to all areas of human health. New technologies being developed at CSU are enabling people to continue active and healthy lifestyles. SBME students have the opportunity to collaborate with faculty from these four colleges and eleven departments, including the highly ranked Professional Veterinary Medicine program.

SBME now offers Master of Engineering, Master of Science and Ph.D. degrees. The M.S. and Ph.D. programs focus on three main research areas: biomechanics and biomaterials; molecular, cellular, and tissue engineering; and medical diagnostics, devices and imaging. Within these three areas, students participate in cutting-edge research from therapies and imaging modalities for fighting cancer to improving equipment used in open heart surgery. In order to allow flexibility to explore the multiple research possibilities, fully funded (stipend and tuition) lab rotation fellowships are available for first-year Ph.D. students.

C. Wayne McIlwraith, B.V.Sc. (Dist.), M.S., Ph.D., D.Sc. (Purdue), Dr. med vet (hc) (Vienna), D.Sc. (hc) (Massey), L.Dr. (Turin), FRCVS, Diplomate ACVS, Diplomate ECVS, University Distinguished Professor, Director of the Orthopaedic Research Center, Barbara Cox Anthony University Chair in Orthopaedics; Department of Clinical Sciences

Research Interests: Equine orthopaedic surgery and joint disease (arthritis), biomarkers and cartilage repair research.

Dr. McIlwraith has been Director of the ORC since its inception, advancing the Orthopaedic Research Center's reputation through research and publications, scientific presentations at key meetings throughout the world, and fundraising efforts. He is a Past-President of the American College of Veterinary Surgeons, the American Association of Equine Practitioners and the Veterinary Orthopedic Society, and a recognized leader in the field of equine orthopaedic research and surgery. He consults worldwide as a specialist equine surgeon and has received national and international honors for his contributions to joint research and clinical orthopaedics. Dr. McIlwraith is the author of four textbooks: *Techniques in Large Animal Surgery* (two editions), *Equine Surgery: Advanced Techniques* (two editions), *Arthroscopic Surgery in the Horse* (three editions) and *Joint Disease in the Horse.* He has authored or co-authored over 300 refereed publications and textbook chapters, and has presented over 500 seminars both nationally and internationally to equine practitioners, veterinary specialty meetings and human orthopaedic meetings.

Honors include: Colorado State University AAEP Faculty Award for Excellence in Teaching Equine Medicine and Surgery, 1981-82; Colorado State University Alumni Outstanding Faculty Award, 1983; DLT Smith Visiting Scientist, University of Saskatchewan, 1992; Inducted into the George H. Glover Gallery of Distinguished Faculty and Alumni, CSU, 1993; Awarded the Tierklinik Hochmoor Prize at Equitana, 10th Equine Veterinary Conference, Essen, Germany, 1993, for international contributions to Equine Orthopaedics; the Schering-Plough Award from World Equine Veterinary Association for Equine Applied Research for outstanding research work in equine locomotor disorders in Yokohama, Japan, 1995; Jacques Jenny Lecturer, Veterinary Orthopaedic Society, 1997; John Hickman Award for Equine Orthopaedics for leading work in arthroscopic surgery and equine joint disease research, British Equine Veterinary Association and Equine Veterinary Journal, Harrogate, England, 1997; Dr. med vet (honoris causa), University of Vienna, 1995; D.Sc., Purdue University, 2002; D.Sc. (hc), Massey University, 2003, Laurea Dr. (hc), Turin University 2004; Inducted into UK Equine Research Hall of Fame 2005; Frank Milne Lecturer (Lifetime Contribution Award), AAEP 2005; Founders Award for Lifetime Achievement, ACVS, 2006; Elastikon Equine Research Award, Johnson & Johnson and Grayson-Jockey Club Research Foundation, 2008-2009; Colorado State University Scholarship Impact Award 2007, University Distinguished Professor, Colorado State University 2009; Distinguished Life Member, AAEP, 2009.

Gary M. Baxter, VMD, M.S., Diplomate ACVS, Professor, Assistant Department Head, Department of Clinical Sciences

Research Interests: Initial research focused on the cause and treatment of equine laminitis.

Dr. Baxter has most recently been involved with research evaluating the use of corticosteroids to treat horses with joint disease, the value of oral nutraceuticals as a preventative for osteoarthritis and the use of the diode laser for surgical arthrodesis of the distal hock joints in horses with osteoarthritis (bone spavin). He has recently obtained funding to evaluate the efficacy of urinary bladder matrix (UBM; ACell) in a model of superficial digital flexor tendonitis in young horses.

Dr. Baxter has a national reputation as an equine surgeon and is actively involved in the American College of Veterinary Surgeons and American Association of Equine Practitioners. He was chairman of the 2001/2002 ACVS examination committee and was on the ACVS Board of Regents from 2003-2005.He has spoken many times at the American Association of Equine Practitioners annual meeting and is currently chairman of the equine lameness wet lab that is given every year. Dr. Baxter came to CSU as an Assistant Professor in Clinical Sciences in 1990, became an Associate Professor in 1994 and a Full Professor in 2000. He is currently an equine clinician and surgeon at the Veterinary Teaching Hospital Large Animal Chief of Staff and Equine Section Chief as well as Assistant Department Head in the department of Clinical Sciences overseeing the veterinary residency and graduate program. He has been actively involved in research since coming to CSU and has authored or co-authored nearly 100 scientific publications, review articles and book chapters. He is certified in Medical Acupuncture for Veterinarians.

Honors include: Outstanding Research Publication in "Veterinary Surgery," 1989. Senior author of manuscript that received "Outstanding publication in Equine Veterinary Journal for 1992"

Nicole Ehrhart, D.V.M., M.S., Diplomate ACVS, Associate Professor, Department of Clinical Sciences

Research Interests: Guided Bone Regeneration, Allograft Healing, Distraction Osteogenesis, Limb Preservation, Bone Substitutes

Dr. Ehrhart is one of 20 fellowship-trained veterinary surgical oncologists in the world. She is an Associate Professor in surgical oncology at the highly acclaimed Animal Cancer Center and has been a member of the CSU faculty since 2002. She is the director of the Musculoskeletal Oncology Lab and has been actively involved in limb preservation research and sarcoma research for the last twelve years. She has been an invited speaker at various venues for M.D. researchers in translation medicine, both nationally and internationally. In addition to her research, she has held several prestigious positions in the American College of Veterinary Surgeons (Scientific Program Chair, Residents Forum Chair, Examination Committee) and Veterinary Orthopedic Society (Scientific Program Chair). She has authored numerous publications on limb preservation and translational cancer research. She is currently the co-director of the Musculoskeletal Oncology section of the University-wide Cancer Supercluster.

Honors include: Bloomberg International Sports Medicine Lecturer, 2003, International Musculoskeletal Transplant Foundation Speaker, 2007

David D. Frisbie, D.V.M., M.S., Ph.D., Diplomate ACVS, Associate Professor, Department of Clinical Sciences

Research Interests: Gene therapy, intra-articular therapeutics, new methods of cartilage repair.

Dr. Frisbie began his professional career after obtaining both a bachelor's degree in Biochemistry and a Doctor of Veterinary Medicine (D.V.M.) from the University of Wisconsin. He then went to New York, where he completed a Surgical Internship at Cornell University and began his research in joint disease. After completing his internship, Dr. Frisbie came to Colorado State University, where he continued his joint research, completed a Surgical Residency in Large Animal Surgery and obtained a master's degree in Joint Pathobiology. After completion of his residency, Dr. Frisbie began his work on a novel way to treat joint disease using gene therapy, which was the focus of his Ph.D. During work on his Ph.D. Dr. Frisbie became Board certified in Large Animal Surgery and is a Diplomate of the American College of Veterinary Surgeons. He joined the faculty as an Assistant Professor in 1999 and was promoted to Associate Professor (with tenure) in 2007.

His current joint disease research is in two basic fields: 1) the evaluation of intra-articular therapeutics and their effects on joint disease (well known therapeutics he has evaluated include Legend, Adequan, Vetalog and Depo-Medrol, Orthokine (IRAP), stem-cells); 2) new methods of cartilage repair. These methods include cutting edge technology aimed at arthroscopic repair of cartilage in the athletic horse. Dr. Frisbie is also exploring methods to augment fracture healing using gene transfer.

Honors include: Pfizer Animal Health Award for Research Excellence, 2001.

Laurie Goodrich, D.V.M., M.S., Ph.D., Assistant Professor, Department of Clinical Sciences

Dr. Laurie Goodrich joined the faculty at CSU College of Veterinary Medicine in April of 2005 as an assistant professor in Equine Surgery and Lameness. Prior to joining the faculty she obtained her D.V.M. from the University of Illinois, and completed an internship in Large Animal Surgery and Medicine at Virginia-Maryland Regional College of Veterinary Medicine. Following her internship, Dr. Goodrich joined the faculty at Virginia for one year as an equine ambulatory clinician before going on to complete her residency in Equine Surgery at the Equine Medical Center in Leesburg, Virginia. She also obtained a Master of Science in Pharmacology during her residency. Dr. Goodrich subsequently joined the large animal surgery faculty at Cornell University's College of Veterinary Medicine and became Board Certified in Large Animal Surgery in 1999. At Cornell she rotated as Chief-of-Service for the Orthopedic, Soft Tissue and Emergency Surgery Services. In 2000 she began a Ph.D. in Cartilage Repair and Gene Therapy. Her research included the transplantation of genetically modified chondrocytes (cells of cartilage) into the defects of cartilage to improve cartilage healing. She completed her Ph.D. in the fall of 2004. Dr. Goodrich's clinical interests are broad and include joint disease, lameness, arthroscopy, laparoscopy, upper airway disease, and wound healing, neoplasia and pain management. Dr. Goodrich's research interests are primarily focused on cartilage healing and cartilage repair currently using growth factor gene therapy modalities. Side interests include bone healing and pain management research.

Honors include: Orthopaedic Research Society, New Investigator Research Award, Semi-Finalist, 2006; Recipient 5-year NIH KO8 Training Grant, 2008.

Faculty

College of Veterinary Medicine and Biomedical Sciences

Kevin K. Haussler, D.V.M., D.C., Ph.D., Assistant Professor, Department of Clinical Sciences

Research Interests: Etiopathogenesis and objective assessment of musculoskeletal pain, spinal dysfunction and sacroiliac joint disorders. Spinal kinematics and conservative management of spinal-related disorders. Clinical research in the areas of veterinary chiropractic, acupuncture, physiotherapy modalities, and musculoskeletal rehabilitation.

Dr. Haussler obtained a Bachelor of Science in Agriculture from the University of Nebraska - Lincoln in 1984. He graduated in 1988 from The Ohio State University, College of Veterinary Medicine, followed by a small animal internship at the Sacramento Animal Medical Group in 1989. Dr. Haussler was a relief veterinarian for multiple small animal practices, emergency clinics and humane societies from 1989 to 1994, when he became interested in pursuing further specialized training in the diagnosis and management of pain and musculoskeletal disorders in animals. He enrolled in Palmer College of Chiropractic – West, a human chiropractic program, to learn how to apply human chiropractic techniques and principles to the treatment of animals with musculoskeletal-related disorders. Dr. Haussler started veterinary chiropractic practice with equine and small animal patients in 1992. After graduating with a Doctor of Chiropractic (D.C.) degree from Palmer College of Chiropractic - West in 1993, Dr. Haussler obtained a Ph.D. degree in Comparative Pathology from the University of California - Davis, School of Veterinary Medicine in 1997. The focus of his Ph.D. research was the evaluation of the anatomy, pathology and biomechanics of the lower back and pelvis of Thoroughbred racehorses. He then went on to complete a post-doctorate investigating in-vivo equine spinal kinematics in 1999 at the Department of Anatomy, College of Veterinary Medicine at Cornell University. As a Lecturer at Cornell University until 2005, he was responsible for teaching equine anatomy, biomechanical research and initiation of a clinical Integrative Medicine Service at the Cornell University Hospital for Animals in both the large and small animal clinics that provided chiropractic, acupuncture and physical therapy services. Dr. Haussler's research studies included evaluation of in vivo equine spinal kinematics, paraspinal muscle morphometry and histochemistry, and the initiation of equine chiropractic research assessing pain and spinal flexibility.

Currently, Dr. Haussler is an Assistant Professor at the Colorado State University at the Equine Orthopaedic Research Center with continued research interests in objective assessment of musculoskeletal pain and spinal dysfunction.

Honors include: James M. Wilson Award for Equine Research, School of Veterinary Medicine, University of California, Davis. 1997.

Thomas R. (Tod) Hansen, B.S., M.S., Ph.D., Professor and Director, Animal Reproduction and Biotechnology Laboratory

Collaborating on equine genomic research.

Ashley Hill, D.V.M., M.P.V.M., Ph.D., Assistant Professor, Department of Clinical Sciences

Research Interests: Epidemiology of equine athletic injuries, simulation modeling. Research topics have included the effect of mild/moderate injury on the subsequent development of catastrophic injury; the effects of exercise and horseshoe type on development of catastrophic injuries; and simulation modeling of the incidence of metacarpal condylar fractures in California.

Dr. Hill obtained a Bachelor of Arts in English literature at Haverford College. She graduated in 1998 from the University of California, Davis School of Veterinary Medicine, then completed a master's in Preventive Veterinary Medicine (M.P.V.M.) at UC Davis in 1999, and a Ph.D. in Epidemiology in 2003. Theses for both degrees focused on the epidemiology of forelimb injuries in Thoroughbred racehorses. Dr. Hill came to CSU as an Assistant Professor in the Department of Clinical Sciences in 2006. She is interested in the relationship between exercise, rest, pre-existing injury, and the development of severe or catastrophic injuries. She is also interested in return to function following severe injuries or surgery.

Honors include: Mark Gearhart Award for Best Graduate Student Manuscript, Association of Veterinary Epidemiology and Preventative Medicine, 2003.

Faculty

College of Veterinary Medicine and Biomedical Sciences

Christopher E. Kawcak, D.V.M., Ph.D., Diplomate ACVS, Associate Professor, Iron Rose College Chair in Musculoskeletal Research, Department of Clinical Sciences

Research Interests: Subchondral bone histomorphometry, biomechanical modeling of joint loading, and imaging of early subchondral disease in pathogenesis of joint disease.

Dr. Kawcak joined our faculty in 1998 as an Assistant Professor after completing his Ph.D. He is now an Associate Professor in the Iron Rose Ranch Chair in the ORC, and is expanding his duties to include clinical work in the VTH and veterinary student teaching. His collaborations with the Biomedical Engineering Program at CSU, the Mechanical Engineering Program at the University of Texas, the Department of Chemical and Materials Engineering, The University of Auckland, and other laboratories worldwide have allowed for more sophisticated assessment of joint disease and healing. Dr. Kawcak is currently involved with research projects evaluating a new type of horseshoe, the effects of exercise on the incidence of musculoskeletal injury, and the development of computerized models of joints. Specifically, he is collaborating with Dr. Reiser and Puttlitz to develop a functional model of the fetlock joint in horses. He has over 100 publications and has been an invited speaker in the U.S. and Europe and is involved with the American Association of Equine Practitioners and the American College of Veterinary Surgeons. He currently sits on the Research Committee for the Grayson Jockey Club Research Foundation.

Honors include: Ken Atkinson Scholar in the College of Veterinary Medicine and Biomedical Sciences, 1995-98; Pfizer Award for Research Excellence, 2003; Elastikon Equine Research Award, Johnson & Johnson Consumer Products Company and Grayson-Jockey Club Research Foundation, 2007.

John Kisiday, Ph.D., Assistant Professor, Department of Clinical Sciences

Research Interests: Mechanobiology of cartilage and repair tissue, tissue engineering.

Dr. John Kisiday was hired as an Assistant Professor in Clinical Sciences in a research and teaching appointment at the ORC in January 2005 after doing his Ph.D. at MIT in Bioengineering and a collaborative post-doctorate of fellowship with CSU and MIT. His doctorate work primarily focused on mechanobiology, the study of the impact of physical deformation on cells, and the use of a novel peptide-based material (discovered at MIT in the early 1990's), as a three-dimensional scaffold for cartilage tissue repair. Dr. Kisiday's post-doctorate work explored chondrogenesis of equine stem cells for potential applications to equine and human therapies. The research Dr. Kisiday will focus on at the ORC will involve cartilage tissue engineering therapies and mechanobiology in order to build the bridge between basic laboratory studies and beneficial animal models.

Honors include: Young investigator Award, Engineering Tissues Workshop, Hilton Head, 2003; NIH Biotechnology Pre-doctoral Training Grant, 2001-2003; MIT President Pre-doctoral Fellowship, 1999.

Robert W. Norrdin, D.V.M., Ph.D., Diplomate ACVP, Professor, Department of Pathology

Research Interests: Articular cartilage and bone histology and histomorphometry

Dr. Norrdin joined the faculty at Colorado State University, Department of Pathology, as an Assistant Professor in 1969. He became a full Professor in 1988. Dr. Norrdin has an international reputation in the areas of metabolic bone disease, orthopaedic pathology, and bone remodeling activity in metabolic bone diseases. Dr. Norrdin is an author or co-author on over 80 publications, most of which are in internationally recognized orthopaedic journals. Dr. Norrdin was critical in the acquisition of a National Science Foundation grant for biomechanical testing equipment and state of the art equipment to section nondecalcified bone sections. Dr. Norrdin retired in 2008.

Richard D. Park, D.V.M., Ph.D., Diplomate ACVR, Professor, Department of Radiological Health Sciences

Research Interests: Imaging in orthopaedic disease, including radiology, ultrasonography, computerized tomography (CT) and magnetic resonance imaging (MRI).

Dr. Park is internationally renowned in the field of imaging (previously called radiology). He has been actively involved in the Orthopaedic program, acquiring expertise in CT and CT osteoabsorptiometry (used for quantitative assessment of bone density), as well as the introduction of magnetic resonance imaging (MRI) for imaging in orthopaedic research.

Natasha Werpy, D.V.M., Diplomate ACVR, Assistant Professor, Department of Clinical Sciences

Research Interests: Imaging in orthopaedic disease, including radiology, ultrasonography, computerized tomography (CT) and magnetic resonance imaging (MRI).

Dr. Werpy earned her D.V.M. from CSU in 1999, followed by an internship at the San Luis Rey Equine Hospital in California which she completed in 2000. In 2003, she completed a residency directed by Dr. Norman Rantanen in collaboration with CSU, which focused on equine imaging. Dr. Werpy joined the CSU faculty in 2004, overseeing research imaging and directing MRI examination of clinical patients at the Orthopaedic Research Center. Her current research centers on MRI, ultrasound and histology correlation in order to develop imaging protocols for clinical patients.

Susan P. James, Ph.D., Associate Professor, Department of Mechanical Engineering

Research Interests: Biomaterials, wear of orthopaedic implants, tissue engineering of cartilage.

Dr. James joined the faculty at CSU in 1994 after receiving her Ph.D. in polymer science and technology from Massachusetts Institute of Technology in September 1993 and working for a year as an engineer at the Failure Analysis Associate in California. She initiated the Biomedical Engineering Program at CSU and served as the program's director from 1999 to 2003, and is currently the Director of BEP. CSU and the College of Engineering recently invested in and institutionalized BEP, which serves multiple colleges on campus. Dr. James is also the Associate Department Head of Mechanical Engineering. Her current research is focused on novel hyaluronan/polyethylene composites for use in joint replacements, cartilage repair and other biomedical applications. She teaches courses in biomaterials, biomedical engineering and materials science at both the undergraduate and graduate level.

Honors include: Outstanding Faculty Member, American Society of Mechanical Engineers, Engineering Faculty Award of Excellence at CSU,1997; Semifinalist for Wallace H. Coulter Award for Medical Innovation and Entrepreneurship, Georgia Tech, Atlanta, Georgia, 200;. Women and Minorities in Engineering Appreciation Award at CSU, 2005; Jack E. Cermak Advising Award at CSU, 2006; George T. Abell Outstanding Faculty Teaching and Service Award at CSU, 2006; Nominated for CSU Best Teacher Award, 2006.

Christian Puttlitz, M.S., Ph.D., Associate Professor, Department of Mechanical Engineering and School of Biomedical Engineering

Research Interests: Orthopaedic biomechanics, tissue and biomaterials interactions.

Dr. Puttlitz joined the CSU faculty in 2005 after spending 4 years as an Assistant Professor in the Department of Orthopaedic Surgery at the University of California, San Francisco. After receiving his Ph.D. in Biomedical Engineering at the University of Iowa in 1999, Dr. Puttlitz performed a 2 year Postdoctoral Fellowship in San Francisco. Dr. Puttlitz's research interests are mainly focused on using experimental and computation techniques to investigate orthopaedic conditions and their treatments. Examples of his current research include using the finite element method to study how loading changes in the spine following intervertebral disc replacement. Dr. Puttlitz teaches an undergraduate course in bioengineering and a graduate biomechanics class.

Honors include: Mark S. Bloomberg Memorial Award for Outstanding Research, Veterinary Orthopaedic Society, March 2008; Elastikon Equine Research Award, Grayson-Jockey Club Research Foundation, May 2007;Best Basic Science Award, Inman-Abbott Society, San Francisco, May 2005; Finalist, Basic Science Award at the Cervical Spine Research Society, Boston, December 2004; Finalist, Basic Science Award at the Cervical Spine Research Society, Scottsdale, December 2003; Best Poster Award at the International Society for the Study of the Lumbar Spine, Edinburgh, June 2001; Inducted into Sigma Xi, National Research Honorary Society, January 2001; Nordby-Smith Best Paper Award on Minimally Invasive Surgery at the North American Spine Society Meeting, New Orleans, October 2000; Finalist, Doctoral Student Paper Competition, American Society of Mechanical Engineers, Nov. 1999; Inducted into Tau Beta Pi, National Engineering Honor Society, Fall 1995; Inducted into Academic All-American Society, Spring 1993; Inducted into Alpha Sigma Mu, National Materials Science and Engineering Honor Society, Spring 1992.

Kenneth Reardon, Professor, Department of Chemical Engineering, College of Engineering, Colorado State University

Research Interests: Collaborating on proteomic studies.

Faculty
College of Applied Human Sciences

Raoul F. Reiser II, Ph.D., Associate Professor, Department of Health & Exercise Science

Research Interests: Musculoskeletal biomechanics, fabrication and implementation of custom equipment/instrumentation.

Dr. Reiser completed his B.S. in Mechanical Engineering at Cornell University, his M.A. in Kinesiology with a specialization in Biomechanics at the University of Texas at Austin and his Ph.D. in Mechanical Engineering at Colorado State University. The emphasis of his dissertation was the biomechanics of recumbent cycling and the power output capabilities, pedal force measuring and analysis system and inverse-dynamics analysis of recumbent versus standard cycling. After working as an Assistant Professor at the University of Wyoming in the Division of Kinesiology and Health, Dr. Reiser began work as an Assistant Professor at CSU in the Department of Health and Exercise Science in August of 2002.

Honors include: Elected Fellow, American College of Sports Medicine, 2007; Colorado State University College of Applied Human Sciences Tenure Track Faculty Scholarly Excellence Award, 2007; CSU College of Engineering's Outstanding Research Assistant, 2000; GAANN Three-Year Fellowship, 1997; CSU Graduate Fellowship, 1997; NSCA Challenge Scholarship, 1996.

Faculty
College of Agricultural Sciences

Jason Bruemmer, Ph.D., Associate Professor, Department of Animal Science

Research Interests: Maternal recognition, follicular cell differentiation, sperm physiology

Dr. Jason Bruemmer, Assistant Professor, was born and raised in El Paso, Texas. He received his B.S. degree in Animal Science and his M.S. degree in Physiology of Reproduction from Texas A&M University, and his Ph.D. in Reproductive Physiology from New Mexico State University.

While at Texas A&M, Dr. Bruemmer served as a lecturer and manager of the horse farm for more than three years. He bred 60 to 75 mares a year, in addition to teaching reproduction, reproductive short courses, all levels of equine science, and conducting research in nutrition and exercise physiology. During his stay at NMSU, Dr. Bruemmer again taught many equine classes and conducted research in a variety of species including horses, cattle, goats and sheep. Further studies were conducted at the University of Arizona Medical School.

Dr. Bruemmer joined Colorado State University in 1996. He teaches Equine Management, Equine Production and Industry, and other courses, and continue to conduct research in reproductive physiology with an emphasis in follicular dynamics of the mare, the area in which he did his dissertation work at New Mexico State University.

Hariharan K. Iyer, B.S., M.S., Ph.D., Professor, Department of Statistics and Center for Bioinformatics, Colorado State University

Honors include: Fellow of the American Statistical Association, the College of Natural Sciences Graduate Teaching Award, 1993; Fellow Cooperative Institute for Research in the Atmosphere (CIRA), 2004-present.

Ann Hess, Ph.D., Assistant Professor, Department of Statistics and Center for Bioinformatics, Colorado State University

Dr. Hess completed her M.S. and Ph.D. in Statistics at CSU. Her research interests are mainly focused on bioinformatics and experimental design.

She has been involved in a number of microarray studies as well as other bioinformatics projects.

Affiliate Faculty

Elwyn Firth, B.V.Sc., Ph.D., Diplomate ACVS, Professor and Director, Massey Equine Research, Massey University, Palmerston North, New Zealand

Dr. Firth is an internationally renowned equine orthopaedic researcher. He has worked closely with Dr. McIlwraith for many years, and, more recently, has become closely involved in a collaborative effort with Drs. McIlwraith and Kawcak, as well as other researchers at Massey University, the University of London, and Utrecht in the Global Equine Research Alliance.

Clifford Michael Les, D.V.M., M.S., Ph.D., Senior Staff Investigator, Bone and Joint Center Henry Ford Health System

Dr. Les is a Senior Staff Investigator at the Bone and Joint Center, Henry Ford Health System in Detroit, Michigan. He is also a member of the Michigan Bone Center at the University of Michigan's School of Medicine and an adjunct Assistant Professor in the Department of Anatomy and Cell Biology at the Wayne State University School of Medicine. Dr. Les received his D.V.M. at the University of California, Davis, his M.S. in Veterinary Biosciences at the University of Illinois, Urbana-Champaign and his Ph.D. in Comparative Pathology at the University of California, Davis. His dissertation work was on material heterogeneity in the equine metacarpus and biomechanical consequences.

Alan J. Nixon, B.V.Sc., Ph.D., Diplomate ACVS, Professor of Orthopaedic Surgery, Director of the Comparative Orthopaedic Laboratory, Cornell University

Dr. Nixon is a Professor of Orthopaedic Surgery and Director of the Comparative Orthopaedic Laboratory at Cornell University, Ithaca, New York. His research focus is in chondrocyte metabolism and cartilage repair methods using chondrocyte or pluripotent stem cell transplantation. Dr. Nixon's research group has focused on the cloning of growth factor molecules for use in gene therapy protocols, inserting the growth factor gene into cartilage cells at the time of transplantation of synovial cells by direct joint injection. The laboratory group also studies the molecular changes associated with OCD in horses and man, and investigates treatment methods for tendonitis in athletes.

Dr. Nixon's current interests include the use of combination gene therapy using stimulatory growth factors, and, in collaboration with the Orthopaedic Research Center at Colorado State University, the combined use of interleukin receptor antagonist gene therapy to diminish degradation in arthritic joints.

William G. Rodkey, D.V.M., M.S., Scientific Director for Regen Biologics and Chief Scientific Officer Steadman-Hawkins Research Foundation, Vail, Colorado

Dr. Rodkey was formerly Director of Orthopaedic Research at the Letterman Institute in San Francisco. He is currently Scientific Director for Regen Biologics and the Steadman-Hawkins Research Foundation. Dr. Rodkey is one of three veterinarians with a long-term reputation in human orthopaedic research and collaborated with the CSU Orthopaedic Research Center on articular cartilage resurfacing research.

Honors include: Excellence in Research in Basic Science Award (American Orthopaedic Society for Sports Medicine); H. Edward Cabaud Memorial Award for Ligament Research (American Orthopaedic Society for Sports Medicine; Co-recipient of Albert Trillat Award for Excellence in Knee Research (International Society of the Knee); U.S. Army Research and Development Achievement Award (Secretary of the Army); H. Edward Cabaud Memorial Award for Knee Research (2nd) (American Orthopaedic Society for Sports Medicine).

Jude Samulski, Ph.D., Professor, Department of Pharmacology, University of North Carolina, Chapel Hill, NC

Dr. Jude Samulski is an important collaborator to our group investigating gene therapy at the ORC. He is a Professor in the Department of Pharmacology and the Director of the Gene Therapy Center at the University of North Carolina at Chapel Hill. Dr Samulski earned his B.S. at Clemson University, a Ph.D. at the University of Florida in Molecular Biology. He did two post docs at SUNY in NY and Princeton University, respectively. He then was on faculty at University of Pittsburgh from 1986-1992 and recruited to UNC as Associate Professor in Pharmacology and Director of the Gene Therapy Center.

Honors include: Outstanding Young Men of America Award and the President's Distinguished Research Award; American Society of Gene Therapy Outstanding Achievement Award, 2009.

Collaborators

Alan Boyde, BDS, LDS, Ph.D., Professor, Department of Anatomy and Developmental Biology, University College London

Dr. Boyde is the author of many papers, chapters and abstracts on the development, structure and mineralization of bone, age changes in skeletal tissue and osteoporosis. He has developed enabling technologies for the microscopic investigation of mineralized tissues and cell biology.

Honors include: Wellcome Trust Biomedical Imaging Awards for Excellence, 1998 and 2002; President of the Anatomical Society of Great Britain and Ireland, 2002-2004; Elected Honorary Member of Bone and Tooth Society, 2002.

Neil David Broom, Ph.D., Associate Professor, Department of Chemical and Materials Engineering, University of Auckland

Dr. Broom's doctoral studies were concerned with mechanical and ultrastructural analysis of the high velocity deformation of metal single crystals. He was personally responsible for establishing the first transmission electron microscopy facility in New Zealand permitting quantitative crystallographic analysis of crystal dislocation structures. His postdoctoral research at University of Cambridge was concerned with fundamental structural (TEM) and mechanical studies of intermetallic single crystal fibers relevant to the development of high strength lightweight metal fiber-reinforced metal composites of interest to the UK aircraft industry. Since 1975, Dr. Broom has been funded continuously by the New Zealand Medical Research Council and Health Research Council to conduct biomechanical/biomaterials research in heart valve biomechanics, joint tissue biomechanics/biomaterials and intervertebral disc biomechanics.

Honors Include: University of Auckland Distinguished Teaching Medal, 1998; Engineering Faculty Award for Excellence in Undergraduate Teaching, 1999-2002.

Stephanie Bryant, Ph.D., Assistant Professor, Department of Chemical and Biological Engineering, University of Colorado

Michael Buschmann, Ph.D., Professor, Department of Chemical Engineering and Institute of Biomedical Engineering, Ecole Polytechnique, Montreal

Dr. Buschmann is an Assistant Professor in the Department of Chemical Engineering and Institute of Biomedical Engineering at the Ecole Polytechnique of Montreal. He is also an Affiliated Researcher with the Department of Pathology and Cell Biology, Faculty of Medicine, at the University of Montreal. Dr. Buschmann received his Ph.D. in Medical Engineering and Medical Physics from the Massachusetts Institute of Technology. He is well-known for his cartilage biomechanics research.

Bruce Caterson, Ph.D., Professor Connective Tissue Biology Laboratories, Cardiff School of Biosciences, Associate Director of Musculoskeletal Research, School of Medicine, Cardiff University, U.K.

Dr. Caterson is a Professor in the Cardiff School of Biosciences and is currently Associate Director of Musculoskeletal Research in the School of Medicine. He was previously head of Connective Tissue Biology at Cardiff and prior to that was the Norfleet-Raney Professor of Research in Orthopaedics and Professor of Biochemistry and Biophysics at the University of North Carolina, Chapel Hill School of Medicine. He is world renowned in articular cartilage biochemistry and pioneered the use of monoclonal and polyclonal antibodies as biomarkers of joint disease. He has received the Kappa Delta Elizabeth Winston Lanier Award for Outstanding Orthopaedic Research from the American Academy of Orthopaedic Surgeons and Orthopaedic Research Society in 1998 and currently has large programme grant from the Arthritis Research Campaign on mechanisms of matrix proteoglycan catabolism in articular cartilage as well as EPSRC Platform Grant on bioresponsive polymer therapeutics: synthesis and characterization of novel nanomedicines.

Chris Evans, Ph.D., Professor, Brigham and Women's Hospital, Center for Molecular Orthopaedics, Harvard University, Boston, Massachusetts

Dr. Evans is world-renowned in the area of human joint disease research, particularly in the use of gene therapy to treat arthritis. He was an outside member on the Ph.D. Committee of Dr. Dave Frisbie when he worked on his gene therapy with interleukin-1 receptor antagonist to treat equine traumatic arthritis and osteoarthritis. He continues to collaborate with the scientists at the Orthopaedic Research Center at CSU.

Honors include: Kappa Delta Award, AAOS; the Cabaud Award, American Society for Sports Medicine; the Henry Kunkle Award, American College of Rheumatology; Osteoarthritis Research Award, OARSI; and the Synos Award for Orthopaedic Research (with Paul Robbins), Synos Foundation.

Steven C. Ghivizzani, Ph.D., Associate Professor, Research Division; Departments of Orthopaedics and Rehabilitation and Molecular Genetics & Microbiology, Gene Therapy Laboratory, University of Florida, Gainesville, Florida

Dr. Ghivizzani is an Associate Professor in the Gene Therapy Laboratory at the University of Florida. He has collaborated with the Orthopaedic Research Center on several projects. Currently, he is working with the CSU researchers on adeno-associate virus and lenti virus delivery of interleukin-1 receptor antagonist.

Alan J. Grodzinsky, Sc.D., Professor, Director of the MIT Center for Biomedical Engineering, Department of Mechanical Engineering and Biological Engineering Division, MIT

Dr. Grodzinsky is a Professor in the departments of Electrical, Mechanical, and Biological Engineering at the Massachusetts Institute of Technology. He is also the Director of the MIT Center for Biomedical Engineering. Dr. Grodzinsky research focuses on the mechanobiology of articular cartilage, including the response of native tissue to physiological and injurious loading as well as the mechanobiology of neo-tissue development for applications to cartilage resurfacing.

Collaborators

Charles Ho, M.D., Ph.D., Director Imaging Research, Scientific Advisory Board Steadman-Hawkins Research Institute

Dr. Ho is experienced and active in musculoskeletal and sports medicine imaging and research, particularly in musculoskeletal Magnetic Resonance Imaging. He is a member of the Radiological Society of North America, the American Roentgen Ray Society, the American Academy of Orthopaedic Surgeons, the American Orthopaedic Society for Sports Medicine, and the ACL Study Group, among other professional organizations. He has published numerous papers and book chapters in the radiologic and orthopedic literature, and presented numerous papers internationally in radiologic and orthopedic conference proceedings. Dr. Ho is Director of Imaging Research and a member of the Scientific Advisory Board of the Steadman Philippon Research Institute in Vail, Colorado. He has served as Radiologic Consultant for the San Francisco 49ers, the San Francisco Giants, Cleveland Indians, Denver Broncos, Colorado Rockies, the U.S. Ski Team, and the U.S. Decathlon Team.

Chris Little, B.Sc., B.V.M.S., M.Sc., Ph.D., Diplomate ACVS, Associate Professor and Director, Raymond Purves Bone & Joint Research Laboratories, University of Sydney Dept. of Orthopaedics & Traumatic Surgery, Royal North Shore Hospital

Dr. Little received his veterinary training at Murdoch University in Western Australia, where he also undertook an internship in equine medicine and surgery (1978-1984). He then completed a residency in large animal surgery and an M.Sc. studying arthritis in horses at the University of Minnesota. Chris was appointed to the faculty at the Ontario Veterinary College, University of Guelph and during this time passed his certifying examinations to become a Diplomate of the American College of Veterinary Surgeons (1990). He then moved to back to Australia and was awarded a Ph.D. degree from the Faculty of Medicine at the University of Sydney in 1996. Following a 5 year postdoctoral position at Cardiff University School of Biosciences in the UK, he was granted a two year Arthritis Foundation of Australia Ulysses Research Fellowship at the University of Melbourne. In 2004 he was appointed as Director of the Raymond Purves Bone & Joint Research Laboratories at the Royal North Shore Hospital, University of Sydney. Chris's research interests centre on the biochemical and molecular mechanisms of cartilage and more recently tendon breakdown in disease. In particular he has studied changes in aggrecan and small proteoglycan biosynthesis and degradation and the proteolytic pathways responsible in cartilage breakdown in arthritis and during tendon degeneration. Chris has been extensively involved in the development and use of neoepitope antibody methodologies, novel animal models and most recently genetically modified mice, to study disease pathways. He has received over $3 million in basic and industrial research grants and has authored/co-authored 53 papers and 6 book chapters.

Van Mow, Ph.D., Professor and Director of Orthopaedic Research, University of Columbia, New York

Dr. Mow is a renowned international authority in biomechanics in joint disease in humans. He has collaborated with Dr. Chris Kawcak on work with biomechanical forces on joint surfaces, assessment of these forces by MRI, and how it can contribute to osteoarthritis.

Marcus G. Pandy, Ph.D., Professor, Chair of Mechanical and Biomedical Engineering, Department of Mechanical and Manufacturing Engineering, University of Melbourne, Melbourne, Australia

Dr. Pandy is a Professor at the University of Melbourne and a leader in the study of musculoskeletal biomechanics. He is interested in applying the principles of mechanics and control theory to describe and explain the relationships between structure and function of the human body. By combining data obtained from biomechanical experiments with detailed computer models of the neuromusculoskeletal system, he is able to determine muscle, ligament, and joint loading during movement. Dr. Pandy is currently collaborating with CSU Orthopaedic researchers to develop a computer model of the entire equine forelimb to aid in the early detection of joint disease in horses.

Michael "Mick" Peterson, Ph.D., Associate Professor, University of Maine

Dr. Peterson is Libra Foundation Professor of Mechanical Engineering at the University of Maine. Prior to coming to the University of Maine, he was a faculty member at Colorado State University and was a Post-Doctoral Researcher at Northwestern University. He has also worked in industry at General Motors and General Dynamics Corp. His Ph.D. is in Theoretical and Applied Mechanics from Northwestern University in Illinois, and he also holds a B.S. in Mechanical Engineering from General Motors Institute (now Kettering University) and an M.S. in Theoretical and Applied Mechanics from Northwestern University. He has also done additional graduate work in Mechanics, Materials and Mathematics from Yale University, Cornell University and the University of Connecticut. His primary expertise is in the dynamic responsive materials and waves in solids.

A. Robin Poole, Ph.D., Professor Emeritus, Director of Joint Diseases Laboratory, McGill University, Montreal, Quebec

Dr. Poole is a pioneer in the use of markers in the early diagnosis of arthritis before other imaging techniques can reveal change. He is a world-renowned arthritis researcher, having previously led arguably the most prominent laboratory in the world in this area of research. He was the mentor of Dr. Billinghurst, and Dr. McIlwraith spent time with him on sabbatical leave. He is the co-author of two publications from the CSU Orthopaedic Laboratory. He is now retired but continues to be active and most recently was a keynote speaker at our 2009 Havemeyer Symposium on Biomarkers.

Honors include: Kappa Delta Award of the American Academy of Orthopaedic Surgeons, the Howard and Martha Holley Research Prize in Rheumatology, Carol Nachman International Prize for Rheumatology.

Christopher B. Riley, B.Sc. (Physics), B.V.Sc. (Hons), M.Sc., Ph.D., Diplomate ACVS Associate Professor and Service Chief of Large Animal Surgery Department of Health Management, Atlantic Veterinary College, University of Prince Edward Island, Charlottetown PE Canada

Following military service in the Royal Australian Air Force, Dr. Riley received degrees in physics and veterinary medicine from the University of Melbourne, Australia. After time spent in an internship and private practice in Australia, he completed a surgical residency at the University of Saskatchewan in Canada. Concurrently he completed M.Sc. and Ph.D. degrees in the fields of tendon in-vitro biology and biochemistry. Dr Riley then

worked at briefly at Iowa State University and in private practice during which time he became Board certified as a Diplomate in the American College of Veterinary Surgeons. He joined the faculty at the Atlantic Veterinary College, Canada in 1999 where he is currently an Associate Professor and Service Chief of Large Animal Surgery. Following the granting of tenure, Dr Riley has focused his research on the development of biomedical tests for animal diseases using the emerging technologies of infrared spectroscopy and bioinformatics. He established the first laboratory of its kind in Canada, developed to investigate the veterinary potential biomedical infrared spectroscopy. Dr Riley has a special interest in orthopedic disease, but is also interested exploring the full potential of infrared technology as it applies to veterinary and comparative medicine. Dr Riley has partnered with the workers from the Orthopedic Research Center at Colorado State University, and the Institute for Biodiagnostics, National Research Council of Canada, to develop the first infrared test for equine traumatic arthritis in the world. He looks further to continued collaboration and advances in this new field of research.

Paul D. Robbins, Ph.D., Professor of Molecular Genetics and Biochemistry and Orthopaedic Surgery, University of Pittsburgh School of Medicine, Director of the Vector Core Facility and Basic Research for the Molecular Medicine Institute

Dr. Robbins is currently a Professor of Molecular Genetics and Biochemistry and Orthopaedic Surgery at the University of Pittsburgh School Of Medicine. He is also Director of the Vector Core Facility and Director of Basic Research for the Molecular Medicine Institute. He received his Ph.D. from the University of California at Berkeley and worked as a post-doctoral fellow at the Whitehead Institute for Biomedical Research at the Massachusetts Institute of Technology. He is an Associate Editor for *Cancer Research* and *Gene Therapy* as well as on the Editorial Boards for *Cancer Gene Therapy, The Journal of Gene Medicine, Arthritis Research,* and *Genes & Immunity.* Dr. Robbins has co-authored over 180 peer-reviewed manuscripts, 110 book chapters and reviews and has edited two books on gene therapy. He is a member of the PathB study section, the Telethon Scientific Review Committee and the Scientific Review Board of National Gene Vector Laboratory.

Robert Lie-Yuan Sah, M.D., Sc.D., Professor and Vice-Chair of Bioengineering Affiliate in Orthopaedics, UCSD

Dr. Sah received his Sc.D. in Biomedical Engineering from the Massachusetts Institute of Technology and his M.D. from Harvard Medical School. He did postdoctoral work at Massachusetts General Hospital in Orthopaedic Bioengineering. He is currently a reviewer for Arthritis Foundation, NIH, NSF and Orthopaedic Research & Education Foundation and the 2004 Chair of Gordon Research Conference on Musculoskeletal Biology and Bioengineering.

Honors include: "Mechanical Blueprint for Cartilage" cited as one of the Great Advances in Scientific Discovery in Disease and Injury Treatment, The Science Coalition, 1998; Accelerated academic advancements, UCSD, 1999 and 2001; American Academy of Orthopaedic Surgeons Kappa Delta Young Investigator Award, 2001; American Academy of Orthopaedic Surgeons Best Poster Award, 2003.

Kevin Shelburne, M.S., Ph.D., Assistant Director of the Biomechanics Research Laboratory, Steadman-Hawkins Sports Medicine Foundation, Vail, Colorado; Faculty Colorado State University, Department of Biomedical Engineering and Veterinary Medicine; Associate Research Professor at the University of Denver

Kevin Shelburne received his bachelor's and master's degrees in Mechanical Engineering from Texas A&M University in 1985 and 1988, respectively. He then worked as a Systems Engineer at McDonnell Douglas Space Systems Company, Houston, Texas, where he designed and tested assembly and servicing tasks and robotics systems for the International Space Station. Kevin completed his Ph.D. in Mechanical Engineering at the University of Texas at Austin in May 1997. The focus of his dissertation was the computer modeling and analysis of the normal and reconstructed knee joint. Following his dissertation, Kevin worked for Lockheed Martin Space Systems in the design of new satellite launch vehicles.

In 2000, he joined the Biomechanics Research Laboratory at the Steadman Philippon Research Institute. Kevin is the author of numerous articles regarding the modeling and simulation of knee mechanics and is a current member of the American Society of Biomechanics and the American Society of Mechanical Engineers.

Honors include: Journal of Biomechanics Award from the World Congress of Biomechanics, 2002.

Roger K.W. Smith, M.A. VetMB Ph.D. DEO DipECVS MRCVS, Professor of Equine Orthopaedics, Royal Veterinary College, London, United Kingdom

Roger Smith qualified as a veterinary surgeon from Cambridge University in 1987 and, after 2 years in practice, returned to academia to undertake further clinical training as a Resident in Equine Studies at the Royal Veterinary College. Following his residency, he undertook a 3 year research project culminating in the award of a Ph.D. for his studies on the extracellular matrix of equine tendon. He remained at the Royal Veterinary College, first as a Lecturer in Equine Surgery, then as Senior Lecturer in Equine Surgery before his appointment to a Professorship in December 2003. He holds the Diploma of Equine Orthopaedics from the Royal College of Veterinary Surgeons, and is both a Diplomate of the European College of Veterinary Surgeons and a Royal College of Veterinary Surgeons Specialist in Equine Surgery. He currently divides his time equally between running a specialist orthopaedic service within the Royal Veterinary College and continuing to direct research into equine tendon disease. His main area of research is understanding the mechanisms of tendon ageing but also has projects investigating the epidemiology of tendon disease in the horse, the development of a serological assay for tendonitis, and stem cell therapy for tendons in conjunction with a commercial company, VetCell Bioscience Ltd.

J. Richard Steadman, M.D., Head of the Steadman-Hawkins Clinic and Steadman-Hawkins Sports Medicine Foundation, Vail, Colorado

Dr. Steadman graduated from the University of Texas Southwestern Medical School in Dallas. Following internship, two years in the army, and an orthopaedics residency at Charity Hospital in New Orleans, Louisiana, Dr. Steadman moved to Lake Tahoe, California, where practiced orthopaedics with increasing emphasis on the treatment of knee disorders. While living there, he was named Chief Physician for the United States Ski Team. During his time at Lake Tahoe, Dr. Steadman developed special surgical techniques which allowed several ski team

members to return to competition and win Olympic medals and championships. At Lake Tahoe, Dr. Steadman started a non-profit sports medicine foundation in order to conduct research in knee surgery and rehabilitation projects. That organization exists today as the Steadman Hawkins Sports Medicine Foundation in Vail, Colorado. In 1990, Dr. Steadman moved to Vail, Colorado and was joined in practice there by Dr. Richard Hawkins, a specialist in shoulder disorders. By this time, Dr. Steadman had limited his practice to the surgical and conservative treatment of knee disorders. Today, Dr. Steadman is regarded as a world-renowned human orthopaedic surgeon. He is a prominent knee surgeon and the inventor of two significant new techniques in orthopaedics. His Foundation has supported several research projects at CSU. Dr. Steadman serves as a consultant regarding clinical relevance of our research work, and the CSU orthopaedic research lab has done controlled studies investigating his techniques used in human orthopaedic surgery.

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Michael R. Torrey, M.S., Ph.D., Director of the Biomechanics Research Laboratory, Steadman-Hawkins Sports Medicine Foundation, Vail, Colorado

Dr. Torrey is the Director of the Biomechanics Research Laboratory at the Steadman-Hawkins Sports Medicine Foundation in Vail, Colorado. He is also an adjunct faculty member in the Department of Kinesiology at the University of Colorado, Boulder and in the Department of Clinical Sciences at Colorado State University. Dr. Torrey consults on the physical therapy and athletic training programs of the Denver Broncos (NFL), the Denver Rockies (MLB) and the Baltimore Ravens (NFL). He is currently collaborating with the Orthopaedic Research Center on the Charismatic Project, in which the researchers are working to develop a computer model of the entire equine forelimb, which will lead to the ability to determine joint surface forces in the fetlock joints of horses. This would aid in the early detection of subtle joint disease in horses.

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Brigitte von Rechenberg, Dr. med. Vet., Diplomate ECVS, University of Zurich

Honors include: SSRS Award 1996-1997 for the abstract, "Spontaneous production of nitric oxide and prostaglandin E2 in media of cartilage explants."

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René van Weeren, D.V.M., Ph.D., Diplomate European College of Veterinary Surgeons and Specialist in Equine Surgery, Royal Dutch Veterinary Association. Associate Professor, Department of Equine Sciences, Faculty of Veterinary Medicine, Utrecht University, The Netherlands.

Paul René van Weeren (1957) graduated in 1983 "cum laude" from the Utrecht University Veterinary Faculty (The Netherlands). He obtained his Ph.D. degree in 1989 and became a Diplomate of the European College of Veterinary Surgeons in 1994. Currently he is the coordinator of scientific research of the Department of Equine Sciences of the Faculty of Veterinary Medicine of Utrecht University and a member of the Management Board of the Department. His special interest is in equine orthopaedics. He has been a supervisor of 14 Ph.D. students, who have obtained their degree in the past years and currently supervises 5 Ph.D. students, who will be graduating within the next few years. He is a member of the board of reviewers of the *American Journal of Veterinary Research* and a member of the advisory board of *Equine Veterinary Journal.* He has been external examiner for Ph.D. students abroad at various occasions in the UK, France, Austria, Sweden and Finland. He is author or co-author of more than 150 peer-reviewed scientific publications or book chapters.

Christina Lee, Ph.D.

Research interests: Investigate traumatic injury induced OA and the molecular signaling mechanisms which contribute to the progression of the disease. In addition she is interested in the use of gene therapy as a means of therapeutic intervention to prevent the destruction of bone and cartilage in response to injury.

Christina Lee received her B.S. in animal science at UC Davis in December 2002, during which time she worked in Dr. Sue Stover's lab for Dr. Hill Collecting data to investigate correlations between equine suspensory apparatus injury with suspensory apparatus failure and metacarpal condylar fracture. Additionally, she examined equine hoof morphology and began graduate school at UC Davis in 2003 in the Molecular, Cellular and Integrative Physiology graduate group working in Dr. Clare Yellowley's laboratory. For her dissertation studies, Dr. Lee investigated the effects of oxygen tension on the expression of proteins associated with bone remodeling and hypoxic regulation of gene expression in osteoblastic cells.

Fellowhips and Financial support during graduate school: National Research Service Award, National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases, 1 F31 AR053467-01, 2006-2007 ($90,039); UC Davis Alliance for Graduate Education; Professoriate Advantage Fellow, 2006, Funded by NSF Eugene Cota-Robles Fellowship, 2003- 2005 ($52,594)

Kirk McGilvray, Ph.D.

Kirk is currently working as a Post-doc at the OBRL. He is a Colorado native and received his B.S., M.S. and Ph.D. from CSU. His research efforts included soft tissue biomechanics and computational simulations, focusing on heart valve replacements, spine instrumentation, and cardiovascular mechanics. Kirk's overreaching goals are to improve surgical techniques and cardiovascular health through solid research efforts in the field of biomedical engineering.

Brandon Santoni, Ph.D. (Research Scientist)

Brandon Santoni received his Ph.D. in Mechanical Engineering from Colorado State in 2006. After completing post doctoral training in both the Musculoskeletal Oncology Laboratory and the Orthopaedic Bioengineering Research Laboratory, Brandon now serves as a Research Scientist in the OBRL. Brandon currently has grants in review as a Principle Investigator at the Musculoskeletal Transplant Foundation (MTF), the Department of Defense (DOD), and the National Institutes of Health (NIH-NIBIB). Brandon assists in procuring and completing industry-supported projects within the lab and provides general oversight of ongoing biomechanics projects in the OBRL.

2008-2009 Ph.D. Graduate Students

Caroline Adamson Adrian, M.S., PT, CCRP

Caroline (Carrie) is a Ph.D. graduate student in canine biomechanics at Colorado State University. Her research interests include the application of physical therapy on animals, more specifically, compensatory gait analysis, biomechanics and neuromotor control of normal and pathological canine gait.

She received her B.S. in Biology in 1994 from Allegheny College in Meadville, PA and gained animal experience working in veterinary hospitals since 1990. She received her Master of Science in Physical Therapy degree from North Georgia College in 1999. Carrie has participated in a number of continuing education seminars on animal rehabilitation, both as a participant and lecturer since 1998. She has lectured nationally and internationally on the topic of animal physical therapy. She is a contributor to the book Canine Rehabilitation & Physical Therapy, Veterinary Clinics of North America and the upcoming edition of the Clinical Textbook for Veterinary Technicians. She presently serves as Vice President for the Animal Special Interest Group within the American Physical Therapy Association. Carrie is the Director of Physical Therapy Services for VCA Hospitals and manages the Physical Therapy and Sports Medicine Department at VCA Alameda East Veterinary Hospital in Denver. Her department serves as one of the few nationally approved clinical practicum sites for the first formal animal rehabilitation training program offered in the country. Carrie also teaches canine anatomy and pathology at the Boulder College of Massage Therapy.

Ugur Ayturk, B.S.

Ugur graduated with a B.S. degree in mechanical engineering from Bogazici University, Istanbul, Turkey in 2005. He has been with the OBRL lab since then, and is currently working towards his Ph.D. His dissertation work focuses on the biomechanical effects of degenerative disease on the human lumbar spine and intervertebral discs, and the utilization of computational and experimental methods to investigate this.

Zobaida Ben Musa, M.S.

Zobaida is from Libya, North Africa and obtained her B.S. from Veterinary Medicine faculty of El-Fatah University, Tripoli, Libya, in 1998. Zobaida received her M.S. from Czech Agriculture University, Prague, Czech Republic, in 2006. Zobaida is currently working in the Musculoskeletal Oncology Laboratory under the direction of Dr. Ehrhart and her work includes effects of MSC cells on bone allograft healing.

2008-2009 Ph.D. Graduate Students

Kaydence Cowley, B.S., M.S.

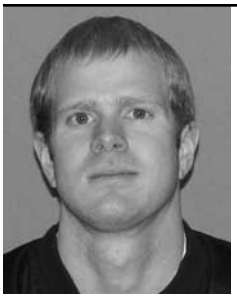
Kaydence completed an undergraduate degree in Mechanical Engineering from Lafayette College in Easton PA, and a master's degree in Bioengineering from the University of California Riverside. She did previous work in orthopaedic repair and injury at the Colorado Health Science Center and has presented work at the Orthopaedic Research Society, Biomedical Engineering Society, and Biophysical Society Conference. Kaydence joined the ORC in May 2009 as a Ph.D. student under Dr. Frisbie and Dr. Kisiday. Her dissertation project is to develop a clinically relevant in vitro model of tendon injury utilizing tissue explants in order to understand the biological mechanism of healing and repair.

Daniel Hemphill, B.S.

Daniel Hemphill graduated with a B.S. in chemical engineering in 2008 from CSU and started his Ph.D. in Bioengineering. He worked with Dr. Laurie Goodrich doing gene therapy research after completing lab rotations through the school of biomedical engineering.

Melissa King, D.V.M.

Melissa graduated from Colorado State Veterinary School in 1997. After graduating she did a one year internship at Rood and Riddle Equine Hospital in Lexington, KY. Upon completion of her internship Melissa returned to northern Colorado to begin her career as an equine ambulatory clinician focusing on equine lameness. After practicing for 10 years Melissa sold her ambulatory practice to pursue a Ph.D. in equine lameness and rehabilitation. Melissa's research interests are orthopedic rehabilitation and the affects of underwater treadmill exercise on the biomechanics of the equine limb.



Devin Leahy, B.S.

Devin received B.S. in Mechanical Engineering from The Ohio State University in 2004. He is now working towards a Ph.D. under Dr. Christian Puttlitz. He has experience in the areas of composite materials, ergonomics, and aerospace and motorsports. He is currently developing a finite element model for a human upper cervical spine.

2008-2009 Ph.D. Graduate Students

Jason Marini, M.S.

Jason earned his M.S. in Mechanical Engineering here at CSU in Spring 2006, where his research has given him experience in biomechanical testing, material testing, and scanning electron microspopy. He is continuing his graduate work at CSU in pursuit of a Ph.D. in Mechanical Engineering, focusing his research on advanced polymers for use in spinal surgery. He expects to graduate in 2008.

Valerie Moorman, D.V.M.

Valerie Moorman graduated from North Carolina State University in 2004 with a D.V.M. She completed a large animal medicine and surgery internship at Auburn University in 2004-2005, and then stayed on as a clinical instructor in Auburn's large animal ambulatory service. During this time, she worked with Dr. Robert Gillette and the sports medicine service on a research project using 2-D kinematic analysis. In 2006, she began an equine surgical residency and combined master's degree at Oklahoma State University, which she completed in 2009. In July 2009, she accepted a position at Colorado State University as an after-hours large animal emergency clinician and Ph.D. at the Orthopedic Research Center. She has an interest in equine sports medicine and surgery, as well as lameness and imaging. In her free time, Valerie enjoys sailing, hiking, and riding hunter-jumpers.

Trinette Ross, M.S.

Trinette is currently working on a Ph.D. through joint collaboration between the EORL and the Department of Animal Sciences. She received her B.S. in Animal Science from Montana State University and her M.S. in Animal Science from Texas A&M University. Her current research interests are in equine osteoarthritis and efficacy testing of oral nutraceuticals used in treating joint inflammation.

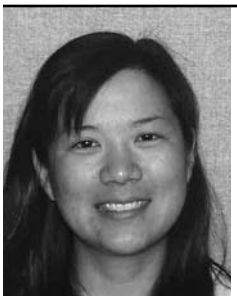
Snehal Shetye, M.S.

Snehal obtained his B.E. in Mechanical Engineering from the University of Pune in India. He moved to Fort Collins for higher studies and obtained his M.S. in Computer-Assisted Engineering under Dr. David Alciatore in the Mechanical Engineering department. Currently, he is working towards his Ph.D. in Biomechanical Engineering under Dr. Christian Puttlitz. His Ph.D. project involves the development of a finite element model of the canine antebrachium. This model will be instrumental in developing novel designs for limb-sparing endoprostheses for the treatment of canine distal radius osteosarcoma.

2008-2009 Ph.D. Graduate Students

Suwimol Tantrongsup, M.S.

Suwimol attended Mahidol University, Bangkok, Thailand and received her B.Sc. in 1999 and her M.Sc. in 2009. She spent the next four years as in instructor in the Department of Physiology, Faculty of Medicine, Chiang Mai University in Chiang Mai, Thailand. Suwimol is currently working on a Ph.D. and her current research interests are gene therapy; stem cells and biological repair; and embryology and embryo abnormality.



Susan Yonemura, M.S.

Susan joined the OBRL team after a stint in corporate America, where she worked on test and measurement systems for Hewlett-Packard and Agilent Technologies. A native of San Jose, CA, she earned her undergraduate degree in Electrical and Computer Engineering from the University of California at Santa Barbara. Her current research focus is spinal biomechanics; specifically, for her thesis she is evaluating the sensitivity of biomechanical tests to gradations in lumbar interbody fusion using a cadaveric ovine model. She plans on defending her M.S. in the summer of 2006, after which she plans on continuing with her graduate studies in pursuit of a Ph.D.

2008-2009 D.V.M./Ph.D. Graduate Students

Katrina Easton, B.S.

Katrina is currently in her first year of veterinary school. She received her B.S. in biology and minor in computer science from Stanford University. She is currently investigating methods of assessing contact area and correlating it to subchondral bone density patterns in the equine fetlock joint. The goal is to gain insight as to how certain changes in contact area under different loads can lead to unfavorable bone density adaptations which may predispose a horse to injury. Her main research interests are computer modeling and the application of engineering methods in clinical research and practice.

2008-2009 M.S. Graduate Students

Katie Amend, D.V.M.

Katie Seabaugh Amend received her D.V.M. degree from Washington State University. Following graduation she performed an internship at Pioneer Equine Hospital, a private equine referral practice, in Oakdale, California. During her time at WSU and Pioneer Equine Hospital she pursued her interests in equine lameness and surgery. It seemed only natural to pursue a residency in equine surgery and lameness upon completion of the internship. She began her residency at Colorado State University in July 2008.

Myra Barrett, D.V.M.

Myra is a Master's student at the CSU Orthopaedic Research Center as well as a resident in an equine-focused non-traditional diagnostic imaging residency. Myra's Master's research is focused on the clinical significance of various radiographic lesions in cutting horses.

Myra's undergraduate degree was awarded by Stanford University. She went on to receive her D.V.M. from Colorado State University. After a year internship at Oakridge Equine Hospital, a busy referral practice in Oklahoma, Myra returned to Colorado to pursue a specialty in equine orthopaedic imaging.

Peter Brookens, B.S.

Peter has a B.S. in Mechanical Engineering which focused on interdisciplinary studies in Biomedical Engineering. He anticipates completing his M.S. in Mechanical Engineering in Spring 2006.

Erin Contino, B.S.

Originally from Concord, California, Erin moved to Fort Collins to attend CSU, graduating in 1999 with a bachelor's degree in Equine Sciences. In 2009, she completed a master's degree in Equine Radiology, researching abnormal radiographic findings in yearling and 2 year old cutting horses.

2008-2009 M.S. Graduate Students

Ben Gadomski, B.S.

Ben is from Christiana, Tennessee. He graduated from Trine University in Angola, Indiana with a Bachelor of Science degree in Mechanical Engineering. He is currently a Master of Science student at Colorado State University performing research in the area of spinal implant design.

Ben Hale, B.S.

A native of Loveland, CO, Ben graduated from the University of Colorado at Boulder with a bachelor's degree in civil engineering in August 2007. In 2009, he completed a Master's of Science degree program in the newly formed School of Biomedical Engineering. His research interests include exploring the therapeutic applications mesenchymal stem cells for orthopedic injury, and mammalian cell culture techniques.

Jeff Harris, B.S.

Jeff will graduate in May 2006 with his B.S. in Mechanical Engineering and a certificate in Biomedical Engineering from CSU. He will continue his studies here at CSU, pursuing an M.S. in Mechanical Engineering with an emphasis in biomedical engineering, and plans on graduating in the summer of 2007.

Rachael Kurkowski, B.S.

Rachael received a B.S. in Biomedical Engineering from Michigan Technological University in 2004. She is currently working towards an M.S. in Mechanical Engineering with emphasis on bioengineering applications, and hopes to continue working towards a Ph.D. here at CSU. Her research interests are biomaterial science, bioengineering, tissue engineering and mechanical engineering, with emphasis on articular cartilage and joint replacement prosthesis.

2008-2009 M.S. Graduate Students

Ty Wallis, D.V.M.

Dr. Ty Wallis entered the combined master's program and equine surgery and lameness residency at CSU in July 2005. Prior to joining us, Dr. Wallis obtained his B.S. in biomedical sciences, as well as his D.V.M., from Texas A&M University. He then completed a one-year internship at Oakridge Equine Hospital in Edmond, Oklahoma. Although he enjoys all aspects of equine surgery, his primary clinical interests are in lameness, orthopedics, and sports medicine/surgery. Specifically, he is interested in arthroscopy, fracture repair, degenerative joint disease, joint arthrodesis, tendon healing, and upper airway surgery.

Dr. Wallis completed a joint retrospective study with the ORC and CSU's Veterinary Teaching Hospital in 2008 at evaluating the efficacy of injecting subchondral cystic lesions, mainly in the stifle, with corticosteroids. He also completed a project evaluating the effects of intra-lesional injection of an acellular matrix for horses with tendon injuries, as well as a project evaluating the efficacy of using thermography to detect osteoarthritis in the horse.

Dustin Williams M.E.

Dustin starting working on his Master of Biomedical Engineering at CSU in the fall of 2009. He received his bachelor's degree in Biology from Mesa State College in Grand Junction, Colorado. His past research experience has included autoimmune response to hantavirus, and mechanosensitive ion channel activity utilizing voltage clamp experiments. Dustin has been working with Drs. Haussler, Worley, and Reiser to understand the kinematics and kinetics of canine amputee gait compensation. Their goals are to better understand the bio-mechanics of gait compensation when a limb has been amputated. This better understanding will help in the diagnosis of canine osteosarcoma, as well as aid in the decision making process of treatment options.

Wesley Womack, B.S.

Wes grew up in Billings, Montana and received his B.S. in mechanical engineering from Montana State University in Bozeman in 2001. He is currently working on an M.S. in mechanical engineering with a focus on biomechanics. His research involves computer modeling of the cervical spine.

Lynsey-Ann Bosch, B.S.

Lynsey graduated from Michigan Sate University with a bachelor's degree in Veterinary Technology, and worked there as a technician throughout her education and for one year after graduation. At MSU, Lynsey helped with equine emergencies, daily treatments, and out-patient appointments. Lynsey moved with her husband to Colorado and worked at an equine private practice for one year, and taught at a veterinary technician training college for two years. Lynsey came to the lab in 2005 as an administrative assistant, and to implement an archiving computer program which will digitally document the research studies and associated data, and will make the wealth of information produced at the ORC easily searchable.

Cecily Broomfield, M.S.

Cecily received a B.S. in microbiology from California Polytechnic State University in 2000, and a Master of Science in agriculture from Colorado State University in 2006. She is currently working as the research coordinator for the OBRL.

Jodi Callison, B.S.

Jodi earned her B.S. in Biology from Colorado State University and then worked as a tech in equine ambulatory medicine. Jodi's interests include radiology and surgery. The EORC hired Jodi in July 2007 to assist as a surgery and clinical tech. Jodi lives in Wellington, CO with husband Adam, dogs, horses and barn cats.

Beth Carbone, M.S.

Beth earned her M.S. in Microbiology from Colorado State University in 2001, and then spent the next five years in Denver at National Jewish Medical and Research Center. There she worked on Chronic Obstructive Pulmonary Disease and Osteoarthritis projects where she purified RNA, performed quantitative PCR, tissue culture, and proteomics. She was hired by the Orthopaedic Research Laboratory in July 2004 as a research associate to assist in the ORL to conduct proteomics research. Currently she's working on adeno-associated viral cell culture, bone growth factor cloning, PCR, RNA purification & quantitative PCR projects.

Research Associates

Tom Hraha, B.S.

Tom earned his B.S. with a Double Major in Microbiology and Environmental Health in August 2008 from Colorado State University. He joined the ORC as a research associate to perform ELISA assays, immunohistochemistry, cell cultures and further his independent research projects.

Susan James, B.A.

Susan earned her B.A. in Biology from CU and worked as a Biologist at the National Institutes of Health in Bethesda, Maryland before returning to her native Colorado. Susan has worked for CSU in the histology field for the past two years. Previously she worked as a research associate at the CSU Arthropod-borne Infectious Diseases Laboratory where she assisted with research on ticks as vectors of West Nile Virus and Lyme disease. She also assisted with cancer treatment research at CSU's Vet Teaching Hospital. Susan joined the EORC team in June 2007 as a Research Associate and Histology Technician.

Jon Kushner

Jon is the Clinical Trial Research Coordinator for the Orthopaedic Research Center. Jon contributes to our research projects as a Surgical Assistant, is responsible for developing research protocols and coordinating activities with study sponsors. In addition, Jon's background includes three years with the College of Engineering at CSU as the Orthopaedic Biomechanical Laboratory Coordinator where his focus was biomechanical and bio material testing working with spine fusion, allograft, autograft, and tendon and ligament research.

Amy Lyons, M.S., Research Associate

B.S. in Mechanical Engineering from CSU in 2000. M.S. in Mechancial Engineering, Interdisciplinary studies in Biomedical Engineering from CSU, 2004. Have been a full time Research Associate in the OBRL since 2003 specializing in histopathology and histomorphometry. Currently she is an Associate Research Director of the OBRL (since 2006).

Scott McCorvey, B.S.

Scott graduated in 2005 from the University of Georgia with a B.S. in Cell Biology. In the fall of 2007, he completed his M.S. in Cell and Molecular Biology at Colorado State University, where he studied the interactions of the immune system and cancer. In November of 2007, he was hired by the Orthopaedic Research Laboratory as a research associate and is responsible for the collection and analysis of synovial fluid, serum, and cartilage from our research studies.

Nikki Phillips, B.S.

Nikki received her B.S. in Cell and Molecular Biology in May 1997 from Tulane University. She has been at Colorado State University since 2001 working in the Department of Pathology for a year before working for both Clinical Sciences and Biomedical Sciences. Nikki joined the ORC in January 2008 as a research associate to assist in the ORL.

Jeff Ullmer, B.A., Research Coordinator

Jeff earned his B.A. in Management from the University of Kentucky in 2003, and then spent the next four years in the Army. He served as a Scout Platoon Leader where he conducted surveillance and reconnaissance of the Iraq/Syrian border. In his last year in the military, Jeff commanded the Fort Carson Mounted Color Guard, an equine drill unit that travels the country promoting the goodwill of the Army. Jeff joined the EORC in August 2007 as the Barn Manager and Research Animal Care Technician and was recently accepted to Colorado State University's veterinary program.

Bob Zink, B.S.

Bob received his B.S. in Biological Sciences in 1969 from California Polytechnic State University. He has been at Colorado State University as a histotechnologist since 1990 and with the OBRL since 2007. His specialty is immunohistochemistry.

Staff Veterinarian

Dora Ferris, D.V.M.

Dr. Ferris joined the ORC in July 2008. She is fulfilling the role of attending veterinarian; responsible for the clinical management of research horses, overseeing treadmill training of the horses, assisting with clinical cases and aiding research associates. She received her D.V.M. from Washington State University's College of Veterinary Medicine in 2007. Last year she completed an internship focusing on equine lameness and surgery at Oakridge Equine Hospital in Edmond, OK. Her veterinary interests center on equine lameness and sports medicine, rehabilitation and complementary therapies.

Administrative Staff

Paula Vanderlinden, Program Coordinator

Paula joined the ORC in March 2007 as Program Coordinator and as Dr. McIlwraith's personal assistant. Paula manages the Annual Stallion Auction, publishing of the annual newsletter and bi-annual lab report. Prior to working at CSU, Paula worked in the pharmaceutical industry.

Joyce Reid, B.S., Business Manager

Joyce joined the EORC in May, 2005 as Accountant. Joyce handles all the financial reporting for the Center as well as monitors all the research projects. Previously, she was with the Office of Sponsored Programs at CSU. Joyce is beginning her sixth year at CSU. She has a Bachelor of Science in Business from Ohio Wesleyan University.

Orthopaedic Research Program

Areas of Expertise of Personnel

Core Faculty

College of Veterinary Medicine and Biomedical Sciences

C. Wayne McIlwraith, B.V.Sc., Ph.D., D.Sc., FRCVS, Diplomate ACVS, University Distinguished Professor
- Clinical Orthopaedics
- Joint Pathobiology
- Gene Therapy
- Medical and Surgical Treatment
- Rehabilitation
- Cartilage Healing

David D. Frisbie, D.V.M., Ph.D., Diplomate ACVS
- Cartilage Healing
- Biochemistry
- Molecular Biology
- Gene Therapy
- Clinical Orthopaedics

Laurie Goodrich, D.V.M./Ph.D., Diplomate ACVS
- Clinical Orthopedics
- Gene Therapy
- Vector Development
- Cartilage Healing

Kevin Haussler, D.V.M., D.C., Ph.D.
- Complementary (Integrative Medicine)
- Rehabilitation
- Spinal and Sacroiliac Disorders
- Anatomy
- Biomechanics

Christopher E. Kawcak, D.V.M., Ph.D., Diplomate ACVS
- Pathogenesis of Subchondral Bone Disease and Traumatic Joint Injury
- Histomorphometry
- Biomechanics
- Clinical Orthopaedics

John Kisiday M.S., Ph.D.
- Mechanobiology
- Cartilage Healing
- Biomechanical Characterization

Natasha Werpy D.V.M.
- Orthopaedic Imaging including Radiology, Computerized Tomography, MRI, and Ultrasonography

Collaborating Faculty

College of Veterinary Medicine and Biomedical Sciences

Gary M. Baxter, VMD, M.S., Diplomate ACVS
- Clinical Orthopaedics
- Medical and Surgical Treatment
- Vascular Physiology

Nicole Ehrhart, D.V.M., M.S., Diplomate ACVS
- Orthopedic Oncology
- Gene Delivery and Tissue Engineering

Thomas R. (Tod) Hansen, B.S., M.S., Ph.D.
- Gene Chip Technology

Ashley Hill, D.V.M./Ph.D.
- Epidemiology
- Experimental Design

Robert Norrdin, D.V.M., Ph.D., Diplomate ACVP
- Orthopaedic Pathology
- Bone Histomorphometry

Richard D. Park, D.V.M., Ph.D., Diplomate ACVR
- Orthopaedic Imaging including Radiology, Computerized Tomography and MRI

College of Engineering

Susan P. James, Ph.D.
- Biomechanics

Ketul Popat, Ph.D., Assistant Professor, Department of Mechanical Engineering, School of Biomedical Engineering

Christian Puttlitz, Ph.D.
- Orthopaedic Biomechanics

College of Agricultural Sciences

Jason Bruemmer, Ph.D.
- Gene Chip Technology

College of Natural Sciences

Hariharan K. Iyer, B.S., M.S., Ph.D.

Ann Hess, Ph.D.

College of Applied Human Science

Raoul F. Reiser II, Ph.D.
- Musculoskeletal Biomechanics
- Custom Equipment/Instrumentation

Student Work Study/Student Hourly Assistants at ORC 2008-2009

Aimee Aaroe
Lauren Anderson
Jack Conner
Melissa Dicamillo
Lauren Farrington
Mary Huerter
Stephanie Lowe
Lauren Luedke
Meaghan Tumlinson
Wade Walker
Chelsea Zimmerman

Volunteers at ORC

2008

Aimee Aaroe
Mackenzie Adams
Claire Aitken
Jill Cadmus
Caroline Cervelli
Lauren Farrington
Eric Garcia
Kristin Height
Kelly Horgan
Rachel Motsinger
Jessica Nieset
Lauren Pastewka
Meaghan Tumlinson

2009

Karla Penman
Gretchen Lund
Kaitlin Williams
Becky Otten
Ashlee Shelly
Molly Johnson
Collins Lehman

Graduate Students – Placement Since Inception

Student	Degree	Date Graduated	Current Position
Gayle Trotter	M.S.	1981	Professor of Emeritus (Retired) from Colorado State University
Alan J. Nixon	M.S.	1983	Professor, Cornell University; Director of Orthopaedic Research Laboratory
Susan Yancik	M.S.	1983	Research Scientist, Synergen, Boulder, CO
Kenneth E. Sullins	M.S.	1984	Associate Professor, University of Virginia--Maryland
John V. Yovich	M.S./Ph.D.	1986/1988	Professor and Dean, University of Murdoch Veterinary School, Perth, Australia
Alicia L. Bertone	M.S./Ph.D.	1986/1988	Professor of Surgery, Ohio State University; Director, Equine Orthopaedic Research Program
Anne Vachon	Ph.D.	1989	Staff Surgeon, Chino Valley Equine Hospital, Chino, CA
Katherine Gibson	M.S.	1989	Senior Lecturer (equivalent to Associate Professor), Equine Surgery, University of Murdoch Veterinary School, Perth, Australia
Scott B. Gustafson	M.S.	1989	Staff Surgeon, Private Practice, Colorado Springs, CO
Matthew J. Reeves	M.S.	1989	Research Scientist, Center for Disease Control
Chris Pasquini	M.S.-Anatomy	1990	Assistant Professor, Anatomy, Ross University, St. Kitts
Jeffrey Foland	M.S.	1992	Equine Specialist Surgeon, Weatherford, TX
Rick Howard	M.S., Ph.D.	1993/1996	Associate Professor of Surgery, University of Missouri; Director of Orthopaedic Research
Christopher S. Ray	M.S.	1994	Specialist Equine Surgeon, Weatherford, TX
Dan Steinheimer	M.S.	1995	Consultant Radiologist, Private Practice, Denver, CO
Christopher E. Kawcak	M.S./Ph.D.	1995/1998	Associate Professor and Iron Rose Ranch Chair, Orthopaedic Research Center, Department of Clinical Sciences, Colorado State University
David D. Frisbie	M.S./Ph.D.	1996/1999	Associate Professor (Research), Orthopaedic Research Center, Department of Clinical Sciences, Colorado State University
Sreeram Santhanam	M.S.	1996	Engineer in private industry.
Mary O'Connell	M.S.	1997	Ph.D. candidate Stanford University
Joanne Ingle-Fehr	M.S.	1997	Specialist Surgeon, Snohomish, Washington
Fahd Al-Sobayil	M.S.	1997	Assistant Professor, King Saud University, Riyadh, Saudi Arabia
Abigail Dimock	M.S.	1997	Currently a Ph.D. student, Equine Nutrition (Orthopaedic Related), Rutgers University

Graduate Students – Placement Since Inception

Student	Degree	Date Graduated	Current Position
Becky Woodward	M.S.	1998	Graduate Researcher on S-V Dagon Research Vessel, University of British Columbia
Tina Anderson	Ph.D.	1998	Director of Marketing
Louise Southwood Perante	M.S.	1998/2002	Associate Professor, University of Pennsylvania School of Veterinary Medicine
Charles Hubbeling	Ph.D.	1999	Private consulting
Guy Beauregard	Ph.D.	1999	Senior scientist/researcher for private industry.
Andrew Green	M.S.	1999	Engineering Manager for private industry.
Elisha Rentfrow	M.S.	1999	Private consulting
Tara Ruttley	M.S.	2000	Engineer for NASA
Carson Shellenberger	M.S.	2000	Engineer for private industry
Al Kane	Post-Doc	2000	Analytic Epidemiologist, USDA; Affiliate Faculty for Colorado State University's Center of Veterinary Epidemiology and Animal Disease Surveillance Systems
Julie Dechant	M.S.	2000	Assistant Professor, University of California Davis
Troy Trumble	M.S.	2000, 2004	Associate Professor, University of Minnesota
Chengcheng Lui	M.S.	2001	Continuing in school
Jana Read	M.S.	2001	Employed in Quality Control
Erin Peterson	M.S.	2001	Faculty Member, Department of Animal Science, University of Maryland
Anne DePalma	M.S.	2002	
Joel Millets	M.S.	2002	Employed at Osteotech, Allograft Company
Carolyn Skurla	Ph.D.	2002	Assistant Professor, Baylor University
Louise Southwood Perante	Ph.D.	2002	Faculty Member, University of Pennsylvania School of Veterinary Medicine
Awad Al-Zaben	Ph.D.	2003	Faculty Member, Electronics Engineering Department, Yarmouk University, Irbid, Jordan
Sophie Morisset	Ph.D.	2003	Assistant Professor, Department of Clinical Sciences, Université de Montréal
Thomas Young	M.S.	2003	Currently job searching
Thomas Young	M.S.	2003	Currently job searching
Colin Scruten	M.S.	2004	Private Practice, Alberta, Canada

Graduate Students – Placement Since Inception

Student	Degree	Date Graduated	Current Position
Lea Rempel	Ph.D.	2004	Post-Doctoral Fellow, University of Kansas Medical School, Currently, Research Scientist, United States Meat Animal Research Center, Clay Center, NE
Chris Sorensen	Ph.D.	2004	Post-Doctoral, National Mass Spectrometry Facility, Environmental Molecular Sciences Laboratory and Biological Sciences Division, Pacific Northwest National Laboratory,Richland, WA
Brandon Santoni	Ph.D.	2006	Posdoctoral Research Fellow, ORBL, Colorado State University
Katja Duesterdieck	Ph.D.	2006	Assistant Professor, Oregon State University
M. Shearin	D.V.M./ Ph.D.	2006	Assistant Doctoral Fellow, University of Tennessee
Valerie Perino	M.S., Ph.D.	2007	Completed Ph.D., Equine Orthopaedic Research, Colorado State University
Sam Hendrix	M.S.	2008	Equine Practice, Utah
Ty Wallis	M.S.	2008	Equine Speciality Practice
Erin Contino	M.S.	2009	Final year D.V.M. student
Ryan Carpenter	M.S.	2009	Equine Practice, Southern California

Surgery Residents Supervised (and Outcome)

Resident	Years of Residency	Date Achieved Board Certification in the American College of Veterinary Surgery
G. W. Trotter	1979-1981	1983
A. J. Nixon	1980-1983	1985
G. S. Martin	1980-1983	1986
R. M. De Bowes	Phase III, 1983-1984	1985
K. Sullins	1981-1984	1986
J. V. Yovich	1983-1986	1987
A. L. Bertone	1983-1986	1988
C. Kobluk	1987-1988	1990
K. T. Gibson	1986-1989	1990
S. B. Gustafson	1986-1989	1990
M. J. Reeves	1986-1989	1990
D. French	1988-1990	1992
J. F. Foland	1989-1991	1994
R. D. Howard	1990-1992	1994
C. S. Ray	1991-1994	1998
C. E. Kawcak	1992-1995	1996
D. D. Frisbie	1993-1996	1999
J. Ingle-Fehr	1994-1997	1999
L. Southwood	1995-1998	2000
T. Trumble	1996-1999	2000
J. Dechant	1997-2000	2001
J. Alldredge	2000-2003	2004
C. Scruton	2001-2004	2004
E. Farstvedt	2002-2005	2005
S. Hendrix	2003-2006	2006
J. Joyce	2005-2007	2007
T. Wallace	2006-2008	2008
R. Carpenter	2007-2009	

History

The Orthopaedic Research Center (ORC) began as a multidisciplinary equine program dedicated to finding methods to treat and prevent equine musculoskeletal disease and injury. Prior to 1984, the program's research was primarily clinical. During this time, many of the techniques for arthroscopic surgery currently used to treat joint problems more effectively and to enable continued athletic function were developed at CSU. We also identified and defined a number of new clinical conditions and documented some of the best methods for diagnosis and treatment. A major goal of the program has always been to find solutions to musculoskeletal problems, especially joint injuries and arthritis. The researchers strive to offer the best possible treatment of clinical cases with continual and critical assessment of the results, which are then used to modify treatments and direct the research toward disease prevention. The program's goals are to use state-of-the-art research techniques to find new methods to rehabilitate damaged joints, to prevent or decrease the occurrence of joint disease and musculoskeletal injuries, find methods of early detection and develop better treatments to prevent permanent damage to injured joints and validate manual therapies and rehabilitation techniques. Significant collaboration with the College of Engineering, School of Bioengineering and the Orthopaedic Bioengineering Research Laboratory (OBRL) as well as the Department of Health and Exercise Sciences has added considerable to our research strengths. In recent years considerable human-based funding (Foundation, NIH and corporate) has been added to ORC and OBRL support.

Research Activities

The Orthopaedic Research Center focuses on the following areas:

1. *Joint tissue healing.* This principally focuses on repair of articular cartilage defects in horses and humans. More recently, treatments for tendonitis including, A-cell therapy, Shock Wave therapies and mesenchymal stem cell therapies have been assessed.

2. *The role of microdamage to subchondral bone in traumatic joint disease in the equine athlete.* Catastrophic injury is a major problem in the equine athletic industry, and we have demonstrated that these severe fractures and injuries start as microfractures in the subchondral bone. Our ongoing mission is to develop methods of detecting this damage in the clinical patient before it becomes severe, irreversible damage.

3. *Development of imaging and fluid biomarkers (in synovial fluid, serum, urine) to detect early articular cartilage and subchondral bone damage in joint disease (arthritis).* Early detection will allow early treatment intervention, as well as potentially prevent fractures and catastrophic injuries.

4. *Developing molecular biology techniques to document early molecular events in arthritis and establishing therapeutic techniques to treat them.* Using techniques such as gene therapy and protein administration to specifically inhibit disease processes sufficiently early would obviate the need for the palliative drugs currently used.

5. *Continued evaluation of new treatments for traumatic arthritis, including corticosteroids, hyaluronan (hyaluronic acid), polysulfated glycosaminoglycans, pentosan polysulfate, oral glycosaminoglycans, other oral nutraceuticals, shock wave therapy, gene therapy, IRAP™, mesenchymal stem cells and other biologic therapies.*

6. *Evaluation of other factors that contribute to traumatic joint injury, including conformation and racetrack surfaces.* The latter area involves collaboration with biomechanical engineers. Recent focuses include the use of joint modeling to look at the pathogenesis of condylar fractures and other disease processes, as well as mapping of pressure distribution and articular cartilage thickness in equine joints, objective therapy analysis of racetrack surfaces, and the effects of various conformations as contributors to musculoskeletal injury.

Program Synopsis

7. *Significance of radiographic lesions in terms of subsequent musculoskeletal problems.* Findings in Thoroughbreds have been published and a study in cutting horses is nearly complete.

8. *Integrative and Manual Therapies and Rehabilitation Techniques for Post-Operative Management and Spontaneous Musculoskeletal Disease.* This is a new area of research which includes study of pathogenesis of musculoskeletal problems biomechanically and using gait analysis (using kinetics and kinematics), methods of pain detection and methods of controlling pain, as well as manipulative therapies. More recently work has been initiated in evaluating the rehabilitation techniques of swimming, underwater treadmilling and hyperbaric oxygen therapy.

In recent years, the Orthopaedic Research Center has acquired the personnel and technical abilities to do more sophisticated orthopaedic research and to address critical questions at a more basic level. Development of this expertise has allowed us to use the horse as a model to resolve problems in human arthritis where conditions are comparable to those in horses. This has led to collaborations with human health researchers, foundations and industry. The construction of the new orthopaedic research facility and the remodeling of the laboratory, as well as acquisition of much state-of-the-art equipment have allowed the program's scientists to bring their research to an even higher level.

Impact

As a preeminent equine orthopaedic research program, both nationally and internationally, the Orthopaedic Research Center provides critical new findings of significant clinical impact and has been able to attract talented students who wish to pursue careers in orthopaedic research. Students choose this program because of its excellent reputation and because of the opportunities they have to be involved in research during their undergraduate and pre-veterinary programs. Many pre-veterinary students have served as volunteers in the equine orthopaedic research program over the past ten years; this allows students to develop a high level of research expertise during this undergraduate experience. This involvement encourages students to pursue advanced degrees and ultimately research careers rather than traditional private veterinary practice. Our program also impacts undergraduate and pre-veterinary education by applying findings from research studies to clinical veterinary medicine.

The breadth of dissemination of information from the Orthopaedic Research Center is extensive, with information distributed to graduate and undergraduate students in eight Departments within five Colleges at Colorado State University. Many faculty members from these eight Colleges who are participants in the Orthopaedic Research Program are internationally recognized; they are therefore able to share research findings worldwide to academia, the equine industry, the scientific community and private biomedical industry. The Orthopaedic Research Center's extensive collaboration with the Steadman-Hawkins Sports Medicine Foundation and biotechnology companies has significantly impacted the treatment of humans with orthopaedic injuries and osteoarthritis. Human medicine, as well as veterinary medicine, has been positively affected by the dissemination of the Orthopaedic Research Center's findings.

Program Trends

Over the last 10 years, funding for our orthopaedic research and specialized personnel availability has increased dramatically. Until 1994, orthopaedic research was being performed by faculty members within the Department of Clinical Sciences. Since that time, the Orthopaedic Research Center has acquired seven full-time faculty senior scientists and also have two Bioengineering Faculty in our Center. To support the work of the Faculty Researchers, we now have eight research associates. We have had seven Ph.D. students and twelve M.S. students in the program the past two years. Current funding is around $4 million annually. Thanks to generous private donors, the construction of a new Orthopaedic Research Center facility and the remodeling of the existing laboratory have been completed. In addition, a state-of-the-art

equine MRI facility has been in operation for five years, and this has also been funded by private donations. We have also received three $3 million University Endowed Chairs from Barbara Cox Anthony, Iron Rose Ranch and Abigail K. Kawananakoa. We have also acquired a $1.5 million Chair in Musculoskeletal Imaging from the estate of Kenneth and Virginia Atkinson. We continue to pursue endowed funding to make all of our positions permanent. In addition, the Orthopaedic Bioengineering Laboratory has had 2 full-time faculty senior scientists, 5 Ph.D. students and 12 M.S. students in the past two years.

Program Goals

Goals Accomplished 2008-2009

1. *Construction of Equine Gait Analysis Building.* A gait analysis building that has four force plates for assessing lameness objectively in the horse is completed. Due to a recent donation from the Thaw Foundation and Colorado's Helping Hands Foundation, an already established gait analysis laboratory for dogs has been relocated and become part of this gait analysis center.

2. *Construction and Opening of Equine Histology Laboratory.* A fully equipped equine histology laboratory has been established where all decalcified histology is being done and makes us independent from the Histopathology Lab and Histopathology. In recent years, we have had our own research associate working in pathology, but now Susan James will have her own equipped facility to provide our histology for both our research projects and assessment of biopsies of individual clinical cases. This was funded by donated monies.

3. *Cartilage Biomechanics Laboratory.* This is the second part of the recently built Equine Histology Laboratory. This houses Dr. John Kisiday and his biomechanical testing equipment for assessment of cartilage, as well as culturing of mesenchymal-derived stem cells. This was funded by Dr. Kisiday's start up funding from the University as well as donated monies.

4. *Achieve Extramural Research Funding to Continue Quality Orthopaedic Research.* Dr. Dave Frisbie is the PI for the CSU sub-contract on an NIH Program Grant with MIT and tissue engineering for cartilage healing has been assessed first in a rabbit model and the definitive preclinical study in the horse is now underway in our equine model. Most recently an additional $100,000 has been allocated by NIH to allow increased numbers for the equine study. Dr. Laurie Goodrich received a 5 year NIH K08 training grant (with Dr. Jude Samulski of the University of North Carolina and Dr. McIlwraith as Co-mentors). This is a 5-year grant which funds 75% of Dr. Goodrich's time for her ongoing research

5. *Unrestricted Funding from Donors and Foundations.* In 2008 we added our fourth endowed Chair, the Abigail Kawananakoa University Endowed Chair thanks to a $3,000,000 donation from Miss Kawananakoa. This allowed us to make a tenure track position for Dr. Kevin Haussler and we now have four of our seven faculty positions funded by endowed chairs. Unfortunately in the 2008-2009 period the corpuses decreased as they did with all foundation corpuses because of the recession. Fortunately thanks to the generosity of Herbert Allen and other donors we have been able to make up the payout necessary to fund salary and benefits for our four faculty positions. Marilyn Simpson Trust's five year commitment of $100,000 a year finished in 2008 as did the five year commitment (also $100,000 per year) from the Walton Family Foundation. Fortunately we have received sufficient donations which, along with our research grants, have enabled us to maintain all our positions.

Current Goals

1. Continue to achieve adequate funding from Federal Grant Agencies, industry and private funding.

2. Identify funding for construction of a building to house offices for faculty and graduate students for both the Orthopaedic Research Center and the Orthopaedic Research Bioengineering Laboratory.

Program Synopsis

3. Create endowed funding for two staff positions, one post-doctoral fellow and scholarships for graduate students.

4. Provide Quality Education to Undergraduate PVM and Graduate Students.

5. Continue to do State-of-the-Art Research within the Orthopaedic Research Center's Research Focuses.

Research Goals

Research Goals Achieved 2008-2009

1. *Focus 1 Musculoskeletal Tissue Healing*

We continued to explore the use of mesenchymal stem cells (MSCs) for repair of articular cartilage and other tissues in the joint. Fibrin, a hydrogel material widely used in medical and tissue engineering applications as a delivery vehicle for MSCs was further investigated to look at degree of migration if used as an implantation media. It was found that 25% concentration of fibrin hydrogels encouraged a fourfold increase in cell migration and this has led to changes in media in matrix that we use in implantation. This work was done by bioengineering grad student Ben Hale working under the supervision of Dr. Kisiday and this work has been accepted in the Journal of Tissue Engineering and Regenerative Medicine.

A clinical study was also completed involving the intralesional injection for the repair of tendon and ligamentous injuries and intra-articular injection for soft tissue injuries in joints. The use of MSCs improved what we had previously seen as healing with other techniques of repair and these results were recently presented by Dr. Dora Ferris at the American Association of Equine Practitioners annual meeting.

In other work Dr. Kisiday demonstrated that dynamic compression stimulated proteglycan synthesis by mesenchymal stem cells in the absence of chondrogenic cytokines and this paper has recently been published in Tissue Engineering.

A study of both adipose derived stromal vascular fraction cells in bone marrow derived MSCs for the treatment of osteoarthritis using our carpal osteoarthritis model demonstrated minimal positive effects questioning how much value MSCs will be in OA. This paper was published in the Journal of Orthopedic Research in 2009

Bone morphogenic proteins 2 and 7 (BMPs 2 and 7) there was assessed for their potential to stimulate bone repair. BMP-2 delivered with an adenoviral vector (AdBMP-2) elicited the greatest affect on alkaline phosphatase production indicating that this had the best potential for clinical use with bone healing. This work was done by Surgery Resident Ryan Carpenter working with Dr. Goodrich.

Evaluation of the potential of an adenoviral (AAV) vector to allow more effective gene therapy techniques for repair has continued in work headed up by Dr. Laurie Goodrich.

In this 18 month study both mushroom and cylindrical shaped equine osteochondral allografts provided durable cartilage repair even in the face of strenuous exercise.

2. *Focus 2 Early Diagnosis of Bone and Joint Disease*

A prospective study looking at fluid biomarkers to predict injury in racing Thoroughbreds that was done in Southern California was led by Dr. McIlwraith and Frisbie working with Drs. Jeff Blea, Rick Arthur, and Vince Baker and their practices. This work has been accepted by the Equine Veterinary Journal. The main goal was too able to assess the predictive value of serum biomarkers prior to an injury occurring. Injuries that were monitored included intra-articular fracture, tendonitis/ligamentous injuries, stress fractures and dorsal metacarpal disease. When longitudinal samples were compared leading up to injuries significant changes were seen with all injury types and these changes were typically three to six months prior to the time of injury. Using a newer statistical technique an accuracy of 73.9% in predicting injury was achieved showing promising results for the value

of serum biomarker levels to predict injury prior to its occurrence.

Work continues in the development of a wireless gait analysis system for horses and is headed by Drs. Chris Kawcak and Raoul Reiser. This easy-to-use system can be applied to the horse's legs in order to objectively detect lameness.

Biomechanical modeling work continues. In collaboration with Drs. Chris Whitton and Marcus Pandy at the University of Melbourne, Dr. Chris Kawcak continues to develop computer models of joint disease. The study includes data collection using the instrumented shoe of Dr. Sue Stover's group at UC Davis to provide validation of the models.Dr. Werpy evaluated a new technique for examination of the suspensory ligament using ultrasound. MRI is the gold standard for such examinations but because of the practicality of ultrasound examination enhancement of the ability of this modality to diagnose suspensory desmitis is getting done with the research.

Dr. Werpy also demonstrated a magic angle effect in the normal collateral ligament of the distal interphalangeal joints imaged with a high-field magnetic resonance imaging system. There have been previous considerations that this artifact did not occur with high-filed magnets and Dr. Werpy demonstrated that it could occur and this study has been accepted for publication by the Journal of Radiology and Ultrasound.

3. *Focus 3 Improvement in the Understanding of the Pathogenesis of Exercise-Induced Traumatic Disease*

One of the most notable studies is demonstration of the effects of joint surface geometry on the potential for condylar fracture. This was a collaborative study done between the ORC and Dr. Tim Parkin's group in the UK. The lateral condyle to medial condyle width ratio was significantly different between fractured condyles and control condyles in almost all locations and there was also a difference in curvature in the palmar lateral parasagittal groove in fracture cases. These findings are not only important from a pathogenesis point of view but also could be important in predicting horses prone to fracture. This work was headed up by Dr. Chris Kawcak working with graduate students Chelsea Zimmerman and Katrina Easton.

Dr. Christina Lee, working with Drs. Frisbie and McIlwraith, has been developing a reproducible model of cartilage injury that can be done in a dish in the laboratory. Mechanical load is applied to rapidly compressed cartilage explants to 60% of the total thickness and success was demonstrated at inducing histologic changes in cartilage that mimic injury induced OA that we see clinically. Using co-culture models of cartilage with synoviocytes under load we hope to be able to screen molecular based therapies including gene therapy to alter the progression of OA in response to injury and minimize the use of testing in live horses.

The collaborative research between Dr. Mick Peterson of the University of Maine and Dr. McIlwraith with track surface studies has continued. A laboratory has been set up to evaluate track materials supported by the racing industry and this has been used to provide recommendations on optimal maintenance of the racetracks. Papers have been demonstrated evaluating the effect of temperature on synthetic track surfaces as well as daily changes in the properties of dirt racetracks.

4. *Focus 4 Continued Development of Novel Therapies for Traumatic Synovitis, Capsulitis and Osteoarthritis in the Horse*

A number of key studies were completed and published in 2009. The most notable was a controlled study using our equine osteoarthritic model with the commonly used intra-articular medications polysulfated glycosaminoglycans (PSGAG) and or hyaluronan (hyaluronic acid) (HA)(published in the American Journal of Veterinary Research, 2009). These studies clearly indicate that both drugs are viable therapeutic options for horses with osteoarthritis. While PSGAG (Adequan™) and HA have long been used in horses and is only with this study that there has been clear documentation of value in a clinically relevant model. PSGAG was shown to have significant influence on parameters of inflammation

and there was also significantly less fibrillation (early OA change) in the articular cartilage seen with HA treatment compared with controls (and a trend for a decrease in cartilage fibrillation with PSGAG). These results indicate that PSGAG and HA have beneficial disease-modifying effects and were both viable options for osteoarthritis.

Another study with the topical NSAID diclofenac (Surpass™) showed considerable benefit in equine osteoarthritis and superior results to systemic phenylbutazone and was also published in the American Journal of Veterinary Research, 2009. Local treatment with of experimental equine OA (CSU made) with this product not only provides benefit to the carpus but reduces the risk of systemic toxicity.

The results of shockwave therapy in experimental osteoarthritis were reported in the American Journal of Veterinary Research, 2009. These showed positive results in our equine osteoarthritis model.

A project assessing the value of a combination of intra-articular hyaluronic acid, chondroitin sulfate, and N-acetyl-D-glucosamine (Polyglycan) in the treatment of osteoarthritis has been completed. Positive results for the intra-articular product were demonstrated and these were recently presented by Dr. David Frisbie at the 2009 AAEP Meeting. There were some anomalies with the intravenous product. A second study is about to be commenced looking at intravenous Polyglycan™ compared to an intravenous placebo in equine OA.

Considerable work also continues with adenoassociated viral vectors (AAV). Dr. Goodrich, working with Dr. Jude Samulski has shown certain aav serotypes to be superior and they plan to move on to in vivo studies.

5. *Focus 5 Validation of Rehabilitation and Physical Therapy Techniques for Musculoskeletal Disease*

Dr. Haussler headed up a significant study demonstrating deformation in the equine pelvis in response to *in vitro* 3D sacroiliac joint loading providing objective information on what physical manipulation might be able to achieve for clinical problems in this area. This work was published in the Equine Veterinary Journal in 2009.

Dr. Haussler also completed studies on the effects of chiropractic, massage and phenylbutozone on spinal mechanical nociceptive thresholds in horses as well as mechanical nociceptive thresholds with the pastern region of non-sored Tennessee Walking Horses.

Work has continued in evaluating underwater treadmilling in horses. This study in our equine osteoarthritis model is being done by Ph.D. Student Dr. Melissa King working with Drs. Kawcak and Haussler. A clinical study assessing underwater treadmilling after arthroscopic surgery in a study at Pegasus Training Center in Seattle by Dr. McIlwraith is also ongoing.

Details of these projects are in the Summaries.

Research Goals for the Future and Current Research

The 2008-2009 years have been challenging but still exciting times for the Orthopaedic Research Center. The scientists have continued to achieve considerable extramural funding in the last two years, including long-term funding to offset the economic difficulties associated with endowed funding.

The research projects continue to revolve around the programs five main focuses.

1. *Focus 1 Joint Tissue Healing*

A 12-month study evaluating the effect of intra-articular injection of bone marrow derived MSCs to enhance repair of treated with microfracture full thickness defects on the medial femoral condyle has been completed and final results are currently being analyzed. This project was funded by the Steadman-Hawkins Foundation and the hypothesis is that intra-articular MSCs can further enhance repair of these defects.

The NIH Program Grant with MIT (Dr. Frisbie is the PI on the sub-contract) continues. Preliminary work in rabbits showed one tissue engineering technique to be superior to others and a 12-month study in horses is ongoing.

Another study headed up by Dr. Frisbie is evaluating the effects of clinically relevant autologous conditioned blood products (IRAPII™, ACP™, and various other PRP products) on the anabolic properties equine digital flexor tenocytes and suspensory ligament fibroblasts to examine these products on tendon healing.

Another study has been done looking at gene and protein expression with autologous conditioned plasma (ACP™) and comparing the newer product IRAPII to the earlier product IRAPI. This study is looking at relative expression of desirable proteins with these products.

2. *Focus 2 Early Diagnosis of Bone and Joint Disease*

Dr. McIlwraith hosted a Dorothy Havemeyer Foundation funded International Symposium at Steamboat Springs to bring together the experts on fluid biomarkers. From this a strategic plan has been developed for research from which we hope to develop a clinically available biomarker platform for early diagnosis of musculoskeletal diseases. A number of projects are being developed and commenced as part of this initiative.

Research on improved methods for imaging bone and joint disease is being led by Dr. Kawcak. The long term aim of this work is development of clinically useful imaging biomarkers.

3. *Focus 3 Improvement in the Understanding of the Pathogenesis of Exercise-Induced Traumatic Disease*

Work continues with finite element modeling to understand the pathogenesis of traumatically induced osteochondral disease and fractures in the equine athlete. This work is headed by Dr. Kawcak.

Dr. Peterson and Dr. McIlwraith continue to work on performance parameters for engineering track management and further exploration of the role of maintenance and weather conditions on synthetic tracks in the pathogenesis of exercise induced musculoskeletal disease. Drs. Peterson and McIlwraith chair a Materials and Testing Laboratory to help with maintaining the ideal racetrack.

Dr. McIlwraith in collaboration with Drs. Jeff Blea, Rick Arthur in Southern California as well as Dr. Peterson of the University of Maine and Dr. Ashley Hill of Colorado State University are currently funded by Grayson-Jockey Club to explore the real rate of non-fatal injuries prospectively in Thoroughbred racehorses in Southern California. There is no baseline data on non-fatal injury and how it may be affected by weather conditions as well as track maintenance and this study is currently being done in horses on synthetic racetracks in Southern California. Data is being gathered by multiple practicing veterinarians in a prospective manner using a customized data sheet. It is hoped to extend these studies in the rest of the country. Drs. Blea and McIlwraith have developed a reporting that they hope to be used in other locations.

4. *Focus 4 Continued Development of Novel Therapies for Traumatic Synovitis, Capsulitis and Osteoarthritis in the Horse*

A second study with the combination of intra-articular hyaluronic acid, chondroitin sulfate and N-acetyl-D-glucosamine (Polyglycan®) in the treatment of osteoarthritis is about to commence. A group of horses receiving Polyglycan intravenously will be compared to a group of horses receiving intravenous placebo using our osteoarthritis chip fragment model.

Program Synopsis

Work continues with the evaluation of intra-articular PRP, IRAPII as well as MSCs as intra-articular therapies for equine traumatic arthritis and OA.

Dr. Laurie Goodrich is developing gene therapy vectors, specifically adenoassociated Virus (AAV) to deliver important genes to cells of joint tissues such as cartilage, synovium and mesenchymal stem cells. Collaborations with Dr. Jude Samulski at The Gene Therapy Center at UNC has already resulted in a paper submission to Gene Therapy Journal describing the ideal serotypes of these vectors in joint tissues. It appears that these vectors will safely and efficiently deliver important gene sequences to the cells of the normal or injured joint and result in long-term protein expression. The definitive study planned is to test AAV-IL-1ra in our equine osteoarthritis model. This work is supported by an NIH KO8 grant obtained by Dr. Goodrich (with Dr. Jude Samulski of the University of North Carolina and Dr. McIlwraith as Co-mentors).

In addition to assessment of these new therapies, our pursuit of better biological therapies continues. The use of bone marrow-derived mesenchymal stem cell therapies has been used in a clinical study of soft tissue healing in joints. This study has been coordinated by Drs John Kisiday and Dave Frisbie in collaboration with a number of private practitioners and clinicians at CSU. The basis for this study was the excellent results obtained after experimental meniscectomy in the goat. At the moment the results look very promising.

Dr. Kisiday is also assessing the influence of dynamic loading on mesenchymal stem cells and their activity.

5. *Focus 5 Validation of Rehabilitation and Physical Therapy Techniques for Musculoskeletal Disease*

With regard to our new fifth focus (integrative therapies and physical manipulation and rehabilitation therapies), a number of studies are being led by Dr. Kevin Haussler. These include, looking at mechanical nociceptive thresholds for pain detection in the axial skeleton of horses using pressure algometry, the use of pressure algometry for the detection of back pain in the horse, the effects of spinal mobilization and manipulation on kinematics of the thoracolumbar region in standing horses and the determination and use of mechanical nociceptive thresholds of the thoracic limb to assess pain associated with induced osteoarthritis of the middle carpal joints in horses.

Dr. Melissa King's project assessing underwater treadmilling on kinetic and kinematic parameters as well as pathologic change in our equine osteoarthritis model will be completed by mid 2010.

A second project assessing swimming, underwater treadmilling, and hyperbaric oxygen therapy following arthroscopic surgery for middle carpal joint chip fragments in clinical cases continues at Pegasus Training Center in Seattle, Washington. This project is led by Dr. McIlwraith working with Dr. Haussler and the owner of Pegasus, Dr. Mark Dedomenico.

Carrie Adrian, who has a master's in physical therapy and is pursuing a Ph.D., is working on kinetic, kinematic and EMG changes in dogs following cruciate ligament rupture.

Research Techniques Available at the Orthopaedic Research Center

The Orthopaedic Research Center at Colorado State University is a comprehensive research facility predominantly focusing on the prevention and repair of orthopedic disease in humans and animals. In addition to protein biomarker analysis and development, this program is additionally supported by several molecular biology applications such as gene expression analysis, antibody purification, real time PCR analysis, cell culture techniques, gene chip microarray, biomechanical testing and histological procedures. As the support structure for biomedical research continues to expand with modern medical discoveries and advances, the Orthopaedic Research Center will continue to provide ground-breaking research for the future.

Below is a brief list of the laboratory applications and services provided by the ORC.

Biomarker Analysis

Fully equipped to run any commercially available absorbance or fluorescence biomarker immunoassay in 96 or 384-well plate format. Using Molecular Devices SpecraMax 384 plus, microplate absorbance/transmittance reader, as well as a Gemini-XS Fluorometer.

Extensive experience with the following biomarker assays:

- **Detection of Cartilage Markers:**
  - **Alcian Blue:** Standardize measurement of 35S labeled proteoglycan complexes.
  - **C1,C2:** An assay to standardize the measurement of Types I and II collagen degradation.
  - **CPII:** An assay to measure type II collagen carboxy propeptide (C-propeptide).
  - **CS-846:** Measurement of Aggrecan Chondroitin Sulfate 846 Epitope.
  - **Eq. Col 2 ¾ (CEQ):** An assay to quantify equine specific Type II collagen, which has also been proven to work with canine fluid.
  - **GAG DMMB:** An assay for standardized measurement of glycosaminoglycans in biological fluids and/or tissues.
  - **Prolagen-C:** Measurement of C-Terminal propeptide Type-I collagen.
  - **Pyd Assay:** An assay to standardize measurement of pyridinoline crosslinks in serum and urine.
  - **Pyrilinks-D:** To standardize measurement of deoxypyridinoline crosslinks in urine.
  - **TCA:** Assay to measure 3H content in media or cartilage digested samples.
  - **YKL-40:** Assay for measurement of YKL-40, human cartilage glycoprotein 39, in serum.

- **Detection of Bone Markers:**
  - **C1,2C:** An assay to standardize measurement of Type I and II collagens (378 assay, MMP1 and MMP13).
  - **Metra™ BAP:** Quantification of bone-specific alkaline phosphatase in serum and synovial fluid samples.
  - **Metra™ Osteocalcin EIA:** An enzyme immunoassay for the quantification of intact (de novo) osteocalcin.
  - **Serum Cross Laps® (CTX):** Assay for the quantification of degradation products of C-terminal telopeptides of Type-I collagen in serum and plasma.

- **Cytokine Assays:**
  - **HIL-1ra:** To standardize the measurement of interleukin 1 receptor antagonist concentrations in cell culture supernatant, serum and plasma.
  - **IGF:** To standardize the measurement of Insulin-like Growth Factor in Serum, Cell culture and plasma.
  - **TGF-β:** An assay to quantify measurement of Transforming Growth Factor-beta in serum, cell culture supernatant, plasma and urine.
  - **TNF-alpha:** An assay to quantify levels of Tumor Necrosis Factor-alpha in serum, plasma, synovial fluid and cell culture supernatant
  - **IL-10:** An assay to quantify levels of Interleukin-10 in serum, plasma and cell culture supernatant.

  - **PDGF-BB:** An assay to quantify levels of Platelet-Derived Growth Factor-BB subunit in serum, plasma and cell culture supernatant.
  - **PGE2:** An assay to quantify levels of Prostaglandin E2 in serum, plasma, synovial fluid, cell culture supernatant and urine.

- **Pre-assay sample processing including: papain, hyaluronidase and collogenase digestion as well as chromatography extraction of synovial fluid and tissues.**

- **Western, Southern, and Northern Blotting**

- **Many other assays available. Please inquire.**

Biomechanical Testing

- **Displacement control testing for compressive, tension and shear material properties**

- **Tissue explants or cell-seeded scaffolds**

- **Displacement control testing for compressive, tensile, and shear material properties**

- **Light to moderate load cells are suitable for testing small tissue explants or cell-seeded scaffolds**

Molecular Biology

- **Evaluation of metabolic activity in living tissues**
  - Radiolabel protocols available

- **GeneChip® Microarray Analysis**
  - Complete Affymetrix GeneChip® 3000 scanner, fluidics 450 and hybridization system.

- **Real Time PCR Analysis**
  - ABI Prism® 7000 Sequence Detection System
  - Optimization of PCR Primers

- **RNA/DNA Extractions/Isolations**
  - cDNA synthesis from RNA
  - RNA from cells, tissue or whole blood
  - Gel extraction and purification
  - Purification of plasmid DNA
  - PCR amplification

- **Isolation of Synoviocytes, Chondrocytes, and Tenocytes**
  - Cell culture expansion of freshly collected cells

- **Culturing of Mesenchymal Stem Cells (bone-marrow derived or fat-derived)**
  - Cell culture expansion of bone-marrow derived or adipose-derived cells, including three-dimensional culturing for clinical use

- **Adenoviral**

Histology Services

- **Decalcification**

- **Non-decalcified histology service is provided by the ORBL (see next section).**

- **Immunohistochemistry**

- **Paraffin and frozen Sectioning and staining of paraffin embedded samples**

Tissue Imaging

- **Scanco µCT 80 Micro Computed Tomography System**

Research Techniques Available at the Orthopaedic Bioengineering Research Laboratory

The Orthopaedic Bioengineering Research Laboratory (OBRL) is part of a consortium for musculoskeletal related research developed at CSU. The consortium's research resources include cell culture, microarray and molecular biology facilities; bone and soft tissue histology; bone densitometry; veterinary surgical facilities, surgeons and animal care; gait/motion analysis and force plating; biomechanical testing and computer modeling; biomaterials development and testing; and a computer modeling/ finite element analysis facility. The musculoskeletal research laboratory is located adjacent to the Veterinary Teaching Hospital campus just south of the main CSU campus.

Biomechanics Laboratory: A 1400 ft2 laboratory is available for biomechanical testing. The laboratory contains a MTS 858 servohydraulic materials testing system. Two load cells are available for use, one with a 20,000 pound (tension/compression)/10,000 in-lb (torsion) capability and the other with a 500 pound axial capacity. A three camera, high resolution (4 megapixel) camera system is available to measure local tissue strains as well as kinematic/kinetic displacements and rotations is avialable. Ancillary items such as LVDTs, extensometers and non-contact optical measurement systems to measure sample displacement are also available. Environmetnal chambers and various test fixtures are also available. A pentium-based computer is interfaced with the MTS firmware for data acquisition and analysis.

Computational Mechanics: A dedicated computational facility for performing large scale finite element analyses has been established. A high performance workstation (4 Pentium 2.0 GHz processors, 8 Gb RAM, 1.3 Tb disc space) running on a dual Windows/LINUX platform is used to run non-linear finite sliding contact analyses in ABAQUS. Models of the spine are currently being developed to investigate the mechanical implications of spinal patholgy, surgery, and treatment.

Biomaterials and Histology Laboratory: A 1500 ft2 laboratory has been dedicated to the synthesis and characterization of biomaterials and to histology of orthopaedic tissues. The biomaterials laboratory includes fume hoods and equipment typical of a wet chemistry laboratory. Much of the characterization (SEM, FTIR, XPS, NMR, DSC and TGA) is performed at the Central Instrument Faciilty on CSU's main campus. The hard tissue aspects of thie histology include a wet dental grinder, Exakt bone saw and microgrinder, and fume hoods. Ancillary items necessary for bone histology are also available which include an explosion proof refrigerator, flammable storage cabinets, Metler balances, hotplates, stirring plates, Eberbach shaker tables, 1 isotemp ovens, and 3 large isotemp waterbaths.

Imaging/Microscopy Laboratory: A 200 ft2 laboratory is available for microscopy. The lab contains 2 Nikon research microscopes, and upright and an inverted scope, which both have fluorescence capabilities. One CCD camera and one SPOT high resolution digital camera are available for microscopic image capture. Two Pentium based computers and Image Pro Plus image analysis software are available for quantification of in vitro and in vivo assays.

Cell culture facility: A 200 ft2 laboratory has been dedicated to tissue culture work, both bone and cartilage. The equipment within this facility includes: Class IIA biological safety laminar flow hood, humidified incubator (5% CO2), centrifuge, -80oC freezer (storing samples until assayed), automated pipettor, microscope (especially for cell cultures), refrigerators, plate readers, pH meters, and all culture supplies (culture media and additives, cryotubes and culture plates).

Laboratory Animal Resources and Veterinary Teaching Hospital: CSU provides research animal services for faculty and staff. These services cover virtually all mammals used in research, including mice, rats, rabbits, cats, dogs, sheep, pigs and horses. These state-of-the-art facilities contain surgical suites, animal procedure rooms, housing, and veterinary care staff to facilitate the planned surgeries. The facility will provide anesthesia assistance, analgesic administration, housing and care for research animals. All animal research performed at CSU is conducted according to protocols approved by the CSU Animal Care and Use Committee (ACUC).

Scientific Publications and Presentations

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2008

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Patel V, Abjornson C, Turner S, Seim H, Lyons A, Puttlitz C. Failure analysis of absorbable cervical plates. 23rd Annual Meeting of the North American Spine Society, Toronto, October 14-18, 2008.

Patel V, Lyons A, Abjornson C, Turner AS, Puttlitz C. Histological evaluation of bioresorbable plates in a sheep model. European Cervical Spine Research Society, Geneva, May 26-31, 2008.

Paulus D, Reiser R, Troxell W. Interactive variable resistance exercise system: concept and preliminary results. Biomedical Sciences Instrumentation. 2008;44: 237-242.

Scientific Publications and Presentations

Peterson M, McIlwraith CW. In situ properties of racing surfaces. Proceedings 6th International Conference on Equine Locomotion. Cabourg, France June 16-18, 2008.

Puttlitz CM, McGilvray K, Lyons AS, Santoni BG, Patel V, Turner AS. Kinetic implications of replacement of a cervical intervertebral disc at adjacent levels and associated salvage procedure. 54th Annual Meeting of the Orthopaedic Research Society, San Francisco, CA, March 2-5, 2008.

Puttlitz C, Patel V, Santoni B. A biomechanical investigation of two-level cervical disc replacement and associated salvage procedure. European Cervical Spine Research Society, Geneva, May 26-31, 2008.

Puttlitz C, Woldtvedt D, Womack W. Cervical facet joint cartilage thickness distributions. European Cervical Spine Research Society, Geneva, May 26-31, 2008.

Reiser R, Dalton E, Pault J. Trial number and duration effects on standing weight- bearing asymmetry measures. Biomedical Sciences Instrumentation. 2008;44:262-267.

Reiser R, Tracy B, Endrizzi M, Keene A, Hitchcock L. Decoupled elliptical machine training: withdrawal and crossed-extensor reactions. In, Proceedings of the 6th International Conference on Strength Training. Colorado Springs, Colorado, October 30. 2008:113-114.

Riorden A, Fortier L, Mohammed H, McIlwraith CW, Cheetham J. Analysis of race performance data for all horses in North America for statistical comparisons and outcome assessment studies. Proceedings 2008 ACVS Veterinary Symposium.

Santoni BG, Gall TT, Egger EL, Puttlitz CM. In vitro biomechanical comparison of polypropylene mesh, a three-loop pulley suture pattern and a combination of these treatments for the reconstruction of ruptured canine Achilles tendons. 54th Annual Meeting of the Orthopaedic Research Society, San Francisco, CA, March 2-5, 2008.

Santoni B, Goh CS, Palmer RH, Puttlitz CM. Biomechanical evaluation of semi- contoured, locking plate/rod versus anatomically-contoured, conventional plate/rod fixation in a canine femoral defect model. British Veterinary Orthopaedic Association Spring Meeting, Birmingham, United Kingdom, April 2, 2008.

Santoni BG, Hynes R, Henson MAW, McGilvray K, Rodriguez-Cannessa G, Lyons A, Henson M, Womack WJ, Puttlitz CM. Lumbar pedicle screw design and trajectory affects bone quality available for purchase and fixation mechanics. 54th Annual Meeting of the Orthopaedic Research Society, San Francisco, CA, March 2-5, 2008.

Santoni BG, Hynes RA, McGilvray KC, Rodriguez-Canessa G, Lyons AS, Henson MA, Womack WJ, Puttlitz CM. Lumbar pedicle screw design and trajectory affects bone quality available for purchase and fixation mechanics. 54th Annual Meeting of the Orthopaedic Research Society, San Francisco, CA, March 2-5, 2008.

Shetye SS, Malholtra K, Rodriguez-Canessa G, Ryan S, Puttlitz CM. Mechanical behavior of canine antebrachial ligaments and its relation to collagen content. Veterinary Orthopaedic Society Conference, Big Sky, Montana, March 8 – 15, 2008.

Tranquille C, Swindlehurst J, Kawcak C, McIlwraith CW, Morgan KL, Murray R, Parkin TD. MRI and post mortem detected pathology is associated with subclinical lateral condylar fracture. In, Proceedings British Equine Veterinary Association, 2008.

Werpy NM, Charles B, Rantanen N. Should I throw away my ultrasound machine now that MRI is here? A review of ultrasound and MRI for the diagnosis of musculoskeletal injury in the equine patient. AAEP Proceedings, 2008;54:450- 451.

Werpy NM, Ho CP, Kawcak CE. Magic angle effect in normal collateral ligaments of the distal interphalangeal joint in horses imaged with a high-field magnetic resonance imaging system. ACVR Proceedings, 2008

Werpy NM, Ho CP, Pease A, Kawcak CE. Preliminary study on detection of osteochondral defects in the fetlock joint using low and high field strength magnetic resonance imaging. AAEP Proceedings, 2008;54:447-451.

Womack WJ, Woldtvedt D, Puttlitz CM. Diametral compression: computational and experimental investigation of a new bone strength test. 54th Annual Meeting of the Orthopaedic Research Society, San Francisco, CA, March 2-5, 2008.

Womack WJ, Woldtvedt D, Puttlitz CM. An analytical description of cartilage thickness mapping and shape of the cervical spine facet joints. 54th Annual Meeting of the Orthopaedic Research Society, San Francisco, CA, March 2-5, 2008.

Published Abstracts/Proceedings
2009

Ayturk UM, Puttlitz CM. Determination of the in situ properties of the annulus fibrosus using available in vitro experimentation data. 55th Annual Meeting of the Orthopaedic Research Society, Las Vegas, February 22-25, 2009.

Ayturk UM, Puttlitz CM. The effect of mesh refinement on the predictions of finite element models of the spine. 2009 ASME Summer Bioengineering Conference, Lake Tahoe, CA, June 17-21, 2009.

Ayturk UM, Santoni BG, Woldtvedt D, Puttlitz CM. Modeling of the Transverse Post- Yield Behavior of Bovine Cortical Bone. 4th International Conference on Computational Bioengineering, Bertinoro (Forli), Italy, September 16-18 2009.

Barrett ME, Frisbie DD, McIlwraith CW. Arthroscopic and ultrasonographic boundaries of the equine femorotibial joints. Proceedings 55th Annual Convention AAEP 2009:457.

Cabano NR, Santoni BG, Palmer RH, Troyer KT, Puttlitz CM. Mechanical comparison of two suture materials for extra-capsular stifle stabilization. Veterinary Orthopaedic Society Conference, Steamboat Springs, February 28- March 7, 2009.

Carpenter RS, Goodrich LR, Frisbie DD, Kisiday JD, Carbone B, McIlwraith CW, Hidaka C. Osteoblastic differentiation of human and equine bone marrow derived mesenchymal stem cells with combined bone morphogenetic protein 2 and 7 in the presence and absence of dexamethasone. Veterinary Orthopedic Society, 2009

Scientific Publications and Presentations

Coleman SH, Ehteshami JR, Kisiday J, Altchek DW, Warren RF, Turner AS. The effects of mesenchymal stem cells on rotator cuff muscle in a chronic injury model in sheep. Proc 55th Orthop Res Soc, Las Vegas, NV (Abstr.) 2009:167.

Contino EK, McIlwraith CW, Park RD. Prevalence of radiographic changes in yearling and 2-year-old Quarter Horses. Proceedings 55th Annual Convention AAEP 2009:470.

Culp WTN, Ehrhart NP, Withrow SJ, Burraco P, Boston S, Schallberger S, Brown DC. A retrospective evaluation of lingual neoplasia: results of surgical excision. Veterinary Cancer Society, Austin Oct 2009.

Culp WTN, Olea-Popelka F, Aldridge C, Withrow SJ, Lafferty MH, Ehrhart NP. Factors affecting survival in dogs living greater than one year with osteosarcoma. Veterinary Cancer Society, Austin Oct 2009.

Doan B, Amack A, Nelson J, Brothers M, Reiser R. Comparison of muscle activity during jumping on the ground versus the Pneubounder. Med. & Science in Sports & Exercise. 2009;41(5S): S396.

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Ehrhart N. Postoperative Considerations in Circular Fixator Patients. In, Proceedings for the Small Animal Circular External Skeletal Fixation Course, Imex Veterinary, 2009:168-175.

Ferris DJ, Frisbie DD, McIlwraith CW. Current Joint Therapies in Equine Practice: A Survey of Veterinarians. In, Proceedings American Association of Equine Practitioners Annual Convention, Las Vegas, Nevada, December 5-9, 2009:57-58.

Ferris DJ, Frisbie DD, Kisiday JD, McIlwraith CW, Hague BA, Major MD, Schneider RK, Zubrod CJ, Watkins JJ, Kawcak CE, Goodrich LR. Clinical follow-up of horses treated with bone marrow derived mesenchymal stem cells for musculoskeletal lesions. In, Proceedings American Association of Equine Practitioners Annual Convention, Las Vegas, Nevada, December 5-9, 2009:59-60.

Frisbie DD. Cutting Edge in Orthopaedics – Stem Cells. In, Proceedings ACVS Veterinary Symposium. The Surgical Summit, Washington, D.C, October 8-10, 2009.

Frisbie DD, Kawcak, CE, McIlwraith CW, Werpy NM. Intraarticular treatment of osteoarthritis with Polyglycan assessed using an equine experimental model. In, Proceedings Veterinary Orthopaedic Society, Steamboat Springs February-March 2009.

Frisbie DD, Kawcak CE, McIlwraith CW, Werpy NM. Assessment of Intravenous or intra-articular hyaluronic acid, chondroitin sulfate, and N-acetyl-D-glucosamine (Polyglycan) in treatment of osteoarthritis using an equine experimental model. In, Proceedings American Association of Equine Practitioners Annual Convention, Las Vegas, Nevada, December 5-9, 2009:61.

Garcia JJ, Puttlitz CM. A simplified strain energy function to represent the mechanical behavior of the annulus fibrosis. 2009 ASME Summer Bioengineering Conference, Lake Tahoe, CA, June 17-21, 2009.

Godek ML, Cranson CN, Prawel D, Oldinski R, James SP. Characterization of a Novel Hyaluronan-Polyethylene Graft Copolymer for the Delivery of Bioactive Materials. Society for Biomaterials, April 22-25, 2009 San Antonio, TX, no. 518.

Haussler KK. The effect of chiropractic treatment on back function and performance. In, Proceedings of the 48th British Equine Veterinary Association Congress, Birmingham, England. September 2009:197-198.

Haussler KK, McGilvray KC, Ayturk UM, Puttlitz CM, Hill AE, and McIlwraith CW. Sacroiliac joint loading and pelvic deformation: How rigid is the pelvis? In, Proceedings of the 48th British Equine Veterinary Association Congress, Birmingham, England. September 2009:193-194.

Jalota S, Jaasma MJ, Turner AS, Bauer TW, Kisiday JD, Delaney DC, Yetkinler DN. In vitro and in vivo study of Callos calcium phosphate cement containing autologous bone. Orthopaedic Research Society, Las Vegas, NV, 2009.

Kawcak DD. Use of Tildren in the Equine Athlete. In, Proceedings American College of Veterinary Surgeons Veterinary Symposium, Washington D.C., October 8-10, 2009.

Kawcak CE, Easton K, McIlwraith CW. Effects of third metacarpus geometry on the incidence of condylar fracture in Thoroughbred racehorses. Proceedings 55th Annual Convention AAEP 2009:197.

Kisiday JD, Lee CM, McIlwraith CW, Frisbie DD Induction of mesenchymal stel cell chondrogenesis during short-term suspension culture. Orthopaedic Research Society, Las Vegas, NV, 2009.

Kobayashi H, Turner AS, Seim HB III, Kawamoto T, Bauer TW. Evaluation of a Cement-Directing Vertebroplasty System in a Sheep Model Proc 55th Orthop Res Soc, Las Vegas, NV (Abstr.) 2009:1826.

Kopskey P, Vanderploeg E, Kisiday JD, Frisbie DD, Sandy J, Grodzinsky AJ. A single- dose of TGFβ induces chondrogenesis in MSC-seeded peptide and agarose hydrogels. Orthopaedic Research Society, Las Vegas, NV, 2009.

Lee H-Y, Kopesky P, Plaas A, Diaz M, Sandy J, Frisbie D, Kisiday J, Ortiz C, Grodzinsky A. Adult Equine MSCs synthesize aggrecan having nanomechanical compressibility and biochemical composition characteristic of young growth cartilage. Annual Meeting of the ORS, Las Vegas, Nevada, February 22-25, Paper No. 172, 2009

Lyons AS, Bonin H, Seim HB, Turner S, Puttlitz C. Intermediate term effects of HA- coated pedicle screws with and without BMP-2 used in conjunction with rigid instrumentation in an ovine model. 55th Annual Meeting of the Orthopaedic Research Society, Las Vegas, February 22-25, 2009.

Lyons AS, Seim HB, Turner S, Abjornson C, Lindley E, Patel VV, Puttlitz C. Evaluation of a bioresorbable anterior cervical plate: a pilot study in sheep. 55th Annual Meeting of the Orthopaedic Research Society, Las Vegas, February 22-25, 2009:1784.

Lyons AS, Seim HB III, Turner AS, Puttlitz CM. Intermediate Term Effects of HA- Coated Pedicle screws With and Without BMP-2 Used in Conjunction With rigid Instrumentation In an Ovine Model. Proc 55th Orthop Res Soc, Las Vegas, NV 2009:1760.

Scientific Publications and Presentations

Maher SA, Doty SB, Rosenthal L, Rodeo SA, Brophy R, Turner AS, Warren RW. Evaluation of a Meniscal Repair Scaffold in an Ovine Model. Proc 55th Orthop Res Soc, Las Vegas, NV (Abstr.) 2009:1292.

Martinelli MJ, Overly LR, McIlwraith CW. Observations related to catastrophic injuries in racing Quarter Horses from 2005-2008. Proceedings 55th Annual Convention AAEP 2009:187-189.

Martinelli MJ, Overly LR, McIlwraith CW. Survey of horseshoe characteristics and their relationship to catastrophic injuries in a population of racing Quarter Horses. Proceedings 55th Annual Convention AAEP 2009:226-228.

McGilvray KC, Puttlitz CM. Mechanical characterization of deep vein thrombosis in a murine model using nanoindentation. Eighth International Conference on Modeling in Medicine and Biology, Crete, Greece, May 26-29, 2009.

McGilvray K, Santoni B, Moynihan D, Getelman M, Puttlitz C. Acute Mechanical Evaluation of Three Shoulder Tendon Repair Suture Techniques. 55th Annual Meeting of the Orthopaedic Research Society, Las Vegas, February 22-25, 2009.

Michels E, Pechey CL, MacLea, JM, Mager M, Turner AS, Les CM. The Interaction of Estrogen Depletion and Dietary Induced Metabolic Acidosis on Bone Time- dependent Structural Properties: A Single Branch, Or A Bundle Of Sticks? Proc 55th Orthop Res Soc, Las Vegas, NV (Abstr.) 2009:697.

Oldinski RA, Godek ML, Staiger MP, James SP. Biostability,Biocompatibility and Mechanical Properties of a Hyaluronan-Polyethylene Copolymer. Society for Biomaterials, April 22-25, 2009 San Antonio, TX, no. 68.

Oldinski RA, Luers KA, Godek ML, Staiger MP, James SP. A Hyaluronan-Polyethylene Copolymer for Articular Cartilage Repair, 2009 Orthopedic Research Society.

Pechey CL, MacLeay JM, Turner AS, Les CM. Seasonal Variation in Ovine Compact Bone Time-dependent Material Properties. Proc 55th Orthop Res Soc, Las Vegas, NV (Abstr.) 2009:677.

Reiser R, Sisneros K, Tracy B, Feldman C, Jørgensen B, Hitchcock L. Center of pressure trends during 60 s standing balance tests. In, Proceedings of the 14th Annual Meeting of the Gait & Clinical Movement Analysis Society. Denver, Colorado, March 10-13. 2009;274-275.

Reiser R, Tracy B, Endrizzi M, Keene A, Hitchcock L. Decoupled elliptical machine training: withdrawal and crossed-extensor reactions during bipedal stance. Med. & Science in Sports & Exercise. 2009;41(5S): S462-3.

Ryan SD, Withrow SJ, Ehrhart NP, Custis J, Worley DR, Harmon JF, LaRue S. Stereotactic radiosurgery for treatment of extremity osteosarcoma. International Society of Limb Salvage/ Musculoskeletal Tumor Society Meeting, Boston, Sept 2009.

Santoni BG, Joslyn AG, Ronhodlt CJ, Bogdansky S, Klein RJ, Turner AS, Puttlitz CM. The Effects of a Novel Cleaning Process on the Structural Architecture and Biomechanical Properties of Ovine Patellar Tendon Grafts. 33rd Annual Meeting of the American Association of Tissue Banks, Las Vegas, September 13-16, 2009.

Santoni BG, Puttlitz CM. Development and biocompatibility characterization of a BioMEMS sensor for monitoring the progression of fracture healing. 2009 ASME Summer Bioengineering Conference, Lake Tahoe, CA, June 17-21, 2009.

Santoni BG, Ronholdt CJ, Bogdansky S, Turner AS, Puttlitz CM. A biomechanical, histological and TEM analysis on the effect of a novel cleaning process on ovine patellar tendon grafts. 55th Annual Meeting of the Orthopaedic Research Society, Las Vegas, February 22-25, 2009:1477.

Schallberger S, Farese J, Bacon N, Amsellem P, Cavanaugh R, Pozzi A, Coomer A, Milner R, Lurie D, Ehrhart NP, Worley DR, Ryan SD. Steriotactic radiosurgery and fracture fixation in 6 dogs with appendicular osteosarcoma. Veterinary Cancer Society, Austin, Oct 2009.

Staiger MP, Eilbracht S, Lengersdorf M, Tucker N, James S. Electrospinning of poly(vinylidene fluoride) nanofibre assemblies. The MacDiarmid Institute for Advanced Materials and Nanotechnology, 8-12, Feb. 2009, University of Otago, New Zealand.

Tichota R, Puttlitz C, Lyons A, Troyer K, Shetye S, Womack W, Arslanoglu R, Santoni B. A biomechanical study of a limited motion device for lumbar posterior stabilization in an ovine model. 55th Annual Meeting of the Orthopaedic Research Society, Las Vegas, February 22-25, 2009.

Tichota R, Puttlitz C, Patel V, Deviren V. The effect of upper end vertebra selection on adjecent segment stability in selective lumbar instrumentation. 55th Annual Meeting of the Orthopaedic Research Society, Las Vegas, February 22-25, 2009.

Womack WJ, Puttlitz CM. Nonlinear structural finite element modeling of the human annulus fibrosis. Eighth International Conference on Modelling in Medicine and Biology, Crete, Greece, May 26-29, 2009.

Oral Presentations
2008

Carter K and Reiser R. Don't cheat! A biomechanical analysis of the biceps curl exercise. Rocky Mountain American College of Sports Medicine Annual Meeting. Estes Park, Colorado, February 22-23, 2008.

Carter K and Reiser R. Don't cheat! A biomechanical analysis of the standing biceps curl exercise. 6th International Conference on Strength Training. Colorado Springs, Colorado, October 30, 2008.

Duesterdieck-Zellmer KF, Kisiday JD, Kawcak CE, Iyer HK, Hess AM, Norrdin RW, McIlwraith CW, Frisbie DD. Gene expression patterns in the tangential and radial layers of cartilage from equine osteoarthritic and control joints. Orthopaedic Research Society, San Francisco, CA, 2008.

Ehrhart N. Small Animal Surgery North American Veterinary Conference Invited Lecturer Orlando, FL 2008.

Scientific Publications and Presentations

Ehrhart N. Surgical Forum American College of Veterinary Surgeons Session Chair and Invited Lecturer San Diego, CA 2008.

Ehrhart N. Surgical Oncology New Jersey Veterinary Medical Association Invited Lecturer Red Bank, NJ 2008.

Endrizzi M, Keene A, Hitchcock L, Reiser R, Tracy B. Effects of decoupled elliptical training on interlimb coordination. Front Range Neuroscience Group Annual Meeting. Fort Collins, Colorado, December 8, 2008.

Frisbie DD. American Association of Equine Practitioners Annual Resort Symposium – Interactive lameness case presentations in the western performance horse (5 hours of lecture). Vail, Colorado January 28, 2008.

Frisbie DD. Hambletonian Society Annual Continuing Education Seminar for Veterinarians. August 1, 2008.

Frisbie DD. Current Surgical Treatment of Joint Disease Focusing on Cartilage Resurfacing and Subchondral Bone Cysts. Arkansas Veterinary Medical Association Equine Meeting, Hot Springs National Park, Arkansas, March 24-25, 2008.

Frisbie DD. Current Treatment of Equine Joint Disease: What We Know About the Mainstay Medications. Arkansas Veterinary Medical Association Equine Meeting, Hot Springs National Park, Arkansas, March 24-25, 2008.

Frisbie DD. Current and Future Treatments of Joint Disease. Ocala Equine Hospital Dinner Meeting, sponsored by Nutramax Laboratories, Inc. & Boehringer Ingelheim Vetmedica. Ocala, Florida, January 3, 2008.

Frisbie DD, Kawcak CE, Werpy NM, McIlwraith CW. Evaluation of intra-articular polysulfated glycosaminoglycan or sodium hyaluronan for treatment of osteoarthritis using an equine experimental model. In: Proceedings, American Association of Equine Practitioners Annual Convention, San Diego, CA, December 6-10, 2008;54:250-251.

Goodrich L. High Efficiency Gene Targeting to Mammalian Joint Tissue using Self- Complementary Adeno-Associated Viral Vector Serotypes. Orthopaedic Research Society 54th Annual Meeting, March 2008.

Goodrich L. How to harvest bone marrow derived mesenchymal stem cells for expansion and injection American Association of Equine Practitioners 54th Annual Convention, Denver, CO, December, 2008.

Goodrich L. How to prepare and inject Cisplatin for treating Sarcoids. Colorado State University, Annual Conference, Fort Collins, CO, 2008.

Goodrich L. Laparoscopy for ovariectomies, Colorado State University Continuing Education, Fort Collins, CO, 2008.

Griffin L, Hitchcock L, Chrastil C, Babayigit G, Reiser R, Tracy B. Dynamic control of postural steadiness: experimental protocol development. Rocky Mountain American College of Sports Medicine Annual Meeting. Estes Park, Colorado, February 22-23, 2008.

Haussler KK. Canine and equine rehabilitation. Pre-Vet Day, Colorado State University, Fort Collins, CO. October 2008.

Haussler KK. Canine rehabilitation and physical therapy. Medical Massage for Animals: Canine Course, Colorado Veterinary Medical Association and Colorado State University, Fort Collins, CO. November 2008.

Haussler KK. Chiropractic evaluation of the equine spine and sacroiliac joint. Current equine chiropractic research: Pain, stiffness and muscle hypertonicity. First Annual Holistic & Integrative Veterinary Medicine Symposium, College of Veterinary Medicine, Gainesville, FL, March 2008.

Haussler KK. Equine chiropractic spinal examination. Student Chapters of the American Association of Equine Practitioners and the American Holistic Veterinary Medical Association, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO. April 2008.

Haussler KK. Equine chiropractic examination. Student Chapters of the American Association of Equine Practitioners and the American Holistic Veterinary Medical Association, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO. November 2008.

Haussler KK. Focus on the Equine Spine: Advanced course (Part 1), Barneveld, Netherlands. 9 hours lecture; 14 hours laboratory. Sept-Oct 2008.

Haussler KK. Horse chiropractors – Is this for real? Pre-Vet Club, Colorado State University, Fort Collins, CO. February 2008.

Haussler KK. How to do a proper saddle fitting for your hourse. 29th Annual Veterinary Hospital Open House, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO. April 2008.

Haussler KK. Medical diagnosis and management of back pain in horses. Spinal nociceptive thresholds in asymptomatic horses: effects of chiropractic, massage and phenylbutazone. Fifth International Symposium on Rehabilitation and Physical Therapy in Veterinary Medicine, Minneapolis, MN. August 2008.

Haussler KK. Pelvic and sacroiliac joint pain and dysfunction: Review of injection techniques, pain provocation tests, and orthopaedic tests. Focus on the Equine Spine: 1st Annual Conference. Barneveld, Netherlands. Oct 2008.

Haussler KK. Sacroiliac joint motion and pelvic deformation in horses. 54th Annual Convention of the American Association of Equine Practitioners, San Diego, CA. December 2008.

Haussler KK. Technology for enforcement: Pressure algometry. Proposed research needed: Pressure algometry. Sound Horse Conference, College of Veterinary Medicine, The Ohio State University, Columbus, OH, April 2008.

Haussler KK. Three-dimensional pelvic deformation in horses. Sixth International Conference on Equine Locomotion, Cabourg, France. June 2008.

Kawcak CE. Advances in Equine Joint Therapy. Mid Coast California Equine Practitioners Meeting. September 2008.

Scientific Publications and Presentations

Kawcak CE. Diagnosis and Medical Management of Disorders of the Sacroiliac Joints and Pelvis. Physiotherapy Management of Chronic Sacroiliac Dysfunction in the Horse. 5th International Symposium on Rehabilitation and Physical Therapy in Veterinary Medicine. August 2008

Kawcak CE. Diagnosis & Treatment of Lameness in Horses – Conditions of the pelvis and back. Colorado State University CE Course. Fort Collins, CO. September 2008

Kawcak CE. Diagnosis & Treatment of Lameness in Horses – New treatment options for musculoskeletal injuries. Colorado State University CE Course. Fort Collins, CO. September 2008.

Kawcak CE. Diagnosis & Treatment of Lameness in Horses – Joint medications and intra-articular treatment. Colorado State University CE Course. Fort Collins, CO. September 2008

Kawcak CE. Diagnosis & Treatment of Lameness in Horses – Conditions of the carpus. Colorado State University CE Course. Fort Collins, CO. September 2008

Kawcak CE. The science, efficacy and protocols of IRAP therapy and stem cells – Countryside Large Animal Veterinary Service client dinner. Greeley, CO. April 2008

Kawcak CE. Joint Therapy for the practitioner – 69th Annual Conference for Veterinarians. Colorado State University, Fort Collins, CO. January 2008

Lee HY, Kopesky PW, Daher L, Mosquera Pelegrina A, Frisbie DD, Kisiday JD, Grodzinsky AJ, Ortiz C. Morphology of aggrecan produced by adult equine mesenchymal stem cells and chondrocytes in self-assembling peptide hydrogels. Orthopaedic Research Society, San Francisco, CA, 2008.

McIlwraith CW. Symposium on Welfare and Safety in Race Horses, Lexington, KY. Lecture and section leader for 2 day symposium. 2008.

McIlwraith CW. Glenwood Equine Veterinarians Meeting "Stem cells". January 5th, 2008.

McIlwraith CW. Racetrack Surface Seminar, University of California at Davis, Davis, California. "Objective methods for evaluating racetrack surface" (joint presentation with Dr. Mick Peterson). January 18th, 2008.

McIlwraith CW. World Equine Veterinary Association Meeting, Moscow, Russia. Keynote Lecture, "Managing osteoarthritic joints" and presentation of AAEP News Hour (2 hours) with Dr. Scott Palmer. January 28th – 31st, 2008.

McIlwraith CW. Christchurch Hospital Orthopaedic Group, Christchurch, New Zealand. "Use of equine cartilage healing models to validate and prove methods of cartilage repair". February 20th, 2008.

McIlwraith CW. Massey University, Palmerston North, New Zealand. 'Use of adult derived stem cells in equine orthopaedics'. February 27th, 2008

McIlwraith CW. AVEF Rossy Meeting on Whats New in Equine Imaging, Paris, France. 2 presentations, "Arthroscopy and tenoscopy in the diagnosis of lameness", "Nuclear scintigraphy and MRI in diagnosis of carpal, fetlock and stifle disease". March 15th, 2008.

McIlwraith CW. Colorado State University Celebrates, New York, New York. "Osteoarthritis and research at Colorado State University". March 26, 2008.

McIlwraith CW. Summit on Racetrack Surface and Injury, Woodbine Racetrack, Toronto, Canada. "The issues with racetrack surfaces. The Jockey Club Initiative". May 13, 2008

McIlwraith CW. AO North America Basic Equine Fixation Course. 4 lectures, "Lag screw fixation of carpal fractures using 3.5mm and 4.5mm screws", "A review of articular cartilage healing after joint trauma", "Non-surgical and surgical management of fractures of the third phalanx", "Lag screw arthrodesis of the pastern joint for degenerative arthritis and fracture treatment". May 15-18, 2008

McIlwraith CW. Cornell University, Ithaca, New York. 2 Lectures, "New strategies in arthritis control", "Use of synovial fluid and serum biomarkers for early diagnosis of musculoskeletal disease and injury". May 19, 2008

McIlwraith CW. Basic Arthroscopic Surgery Course, Telgte, Germany. 3 one hour lectures, Basic arthroscopic technique, Arthroscopy of the carpus and Arthroscopy of the tarsocrural joint and 3 two hour laboratories. May 23-24, 2008.

McIlwraith CW. Stockholm, Sweden – 3rd International Workshop on Equine Osteochondrosis. Lectures, "The use of serum biomarkers in early cases of OCD, indicating changes in metabolism and to predict severity" and "New thoughts on pathogenesis of subchondral cystic lesions in the medial femoral condyle based on experimental and clinical data" and discussion panels. May 29-30, 2008.

McIlwraith CW.Washington DC Congressional Subcommittee of Commerce, Trade and Consumer Protection Committee on Energy and Commerce Hearing on the State of Thoroughbred horse racing and the welfare of the Thoroughbred race horse. Testified before this committee on efforts of Thoroughbred safety (5 hours). June 19, 2008.

McIlwraith CW. The Northern Colorado Health Research Coalition Summer Series. (Poudre Valley Health System/Colorado State University/Colorado Bioscience Association). Translational research – Orthopaedics. "Recent research advances to replace lost articular cartilage in traumatically injured and osteoarthritic joints". June 23, 2008.

McIlwraith CW. European College of Veterinary Surgeons Annual Meeting, Basel, Switzerland, "Designing a research project" (1 hour symposium). July 10, 2008.

McIlwraith CW. Steadman-Hawkins Research Foundation Annual Symposium, "The use of stem-cells in orthopaedics." July 26, 2008.

McIlwraith CW. American Association of Equine Practitioners Focus Meeting, Austin TX, "Management of angular limb deformities, flexural deformities and osteochondritis dissecans in foals" (1 hour lecture with Dr. Allen Ruggles), and "Management of orthopaedic infection in foals" (1.5 hours with Dr. Allen Ruggles). July 28-29, 2008.

McIlwraith CW. 5th International Symposium on Rehabilitation and Physical Therapy in Veterinary Medicine, Minneapolis, MN, Keynote lecture: Arthroscopic surgery in the equine athlete – we need rehabilitation as well. August 14, 2008.

Scientific Publications and Presentations

McIlwraith CW. Irish Equine Centre 25th Anniversary Celebration, Kildare, Ireland. Guest lecture: "developmental and traumatic joint problems in equine athletes – significance and advances in management." September 5, 2008

McIlwraith CW. Cornell University, Ithaca, NY, First International Advanced Workshop in Arthroscopic Surgery of the Stifle Joint. 5 lectures and 2 laboratories. September 19-20, 2008.

McIlwraith CW. Muenster Germany – International Advanced Course in Arthroscopic Surgery. 6 lectures and 3 laboratories. September 26-27, 2008

McIlwraith CW. Beaulieu Convention Centre, Lausanne, Switzerland 2nd International symposium on biotechnology and musculoskeletal repair, AO "Use of equine models to evaluate articular cartilage repair". October 3-4, 2008,

McIlwraith CW. Pre-Vet Club Meeting, "The challenge of bringing equine athletes back from joint injury". October 8, 2008.

McIlwraith CW. Teramo, Italy Symposium on use of stem cells in Tissue Engineering. "Advanced strategies in joint resurfacing." November 13-14, 2008.

McIlwraith CW. American Association of Equine Practitioners Convention, San Diego, CA, "A review of the potential indications and contraindications for equine oral joint health supplements." "Subclinical lateral condylar fracture in Thoroughbreds: A potential target for screening to prevent catastrophic fracture". Also moderated table topic "Joint medications". December 6-10, 2008.

McIlwraith CW. Arizona Racing Symposium, Tucson, Arizona – Safety and Welfare Session "Racing Injuries – Reporting and Prevention" (1.5 hours). December 11, 2008.

Paulus D, Reiser R, Troxell W. Interactive variable resistance exercise system: concept and preliminary results. 45th Rocky Mountain Bioengineering Symposium & 45th International ISA Biomedical Sciences Instrumentation Symposium. Copper Mountain, Colorado, April 4-6, 2008.

Reiser R, Dalton E, Pault J. Trial number and duration effects on standing weight-bearing asymmetry measures. 45th Rocky Mountain Bioengineering Symposium & 45th International ISA Biomedical Sciences Instrumentation Symposium. Copper Mountain, Colorado, April 4-6, 2008.

Reiser R, and Tracy B. The neural mechanisms of ankle muscle steadiness and their relation with control of posture in elderly fallers and non-fallers. Colorado Injury Control Research Center Seminar Series. Colorado State University, November 3, 2008.

Reiser R, Tracy B, Endrizzi M, Keene A, Hitchcock L. Decoupled elliptical machine training: withdrawal and crossed-extensor reactions. 6th International Conference on Strength Training. Colorado Springs, Colorado, October 30, 2008.

Ryan S. The biology and biomechanics of limb salvage surgery. November 2008, CSU School of Biomedical Engineering seminar series.

Ryan S. Risk factors for bacterial contamination of osteoarticular allografts collected from cadaveric donors. Orthopedic Research Society Meeting, San Francisco, March 2008.

Oral Presentations
2009

Carter K, Dalton E, Pault J, Reiser R. Lean to the left, lean to the right: underlying cause of low back pain? Rocky Mountain American College of Sports Medicine Annual Meeting. Colorado Springs, Colorado, February 27-28, 2009.

Coleman S, Ehteshami J, Altchek D, Warren R, Turner S, Kisiday JD. The effects of mesenchymal stem cells on rotator cuff muscle in a chronic injury model in sheep. Orthopaedic Research Society, Las Vegas, NV, 2009.

Doan B, Amack A, Nelson J, Brothers M, Reiser R. Comparison of muscle activity during jumping on the ground versus the Pneubounder. ACSM 2009 Annual Meeting. Seattle, Washington, May 28, 2009.

Ehrhart N. Oncology Surgery for the Small Animal Practitioner. Unique Seminar Destinations Invited Lecturer Puerto Vallarta, Mexico, 2009.

Ehrhart N. Surgical Forum American College of Veterinary Surgeons **Session Chair** and Invited Lecturer Washington, DC, 2009.

Ehrhart N. Small Animal Circular External Skeletal Fixator Course IMEX, Inc Laboratory Faculty and Lecturer Dallas , TX, 2009.

Ehrhart N. University of Minnesota Cancer Research Seminar University of Minnesota

Invited Speaker Minneapolis, MN, 2009.

Frisbie DD. Cutting Edge in Orthopaedics – Stem Cells. In Proceedings, ACVS Veterinary Symposium. The Surgical Summit, Washington, DC, October 8-10, 2009.

Frisbie DD, Kawcak, CE, McIlwraith CW, Werpy NM. Intraarticular treatment of osteoarthritis with polyglycan assessed using an equine experimental model. Veterinary Orthopaedic Society, Steamboat Springs February-March 2009.

Frisbie DD. Clinical Evaluation of Bone Marrow-Derived Mesenchymal Stem Cells In Naturally Occurring Joint Disease. World Conference on Regenerative Medicine, International Meeting of the Veterinary Stem Cell Consortium, Leipzig, Germany, October 29-31, 2009.

Frisbie DD. Treating Performance Horses: The Horizon. Boehringer Ingelheim Vetmedica Presentation, June 18th, 2009.

Godek ML, Cranson CN, Prawel D, Oldinski R, James SP. Characterization of a Novel Hyaluronan-Polyethylene Graft Copolymer for the Delivery of Bioactive Materials, presented at the 2009 Society for Biomaterials, April 22-25, San Antonio, TX, no. 518. 2009.

Scientific Publications and Presentations

Hausler KK. Focus on the Equine Spine: Thoracolumbar Region, Colorado State University, Fort Collins, CO. 10 hours lecture; 3 hours laboratory. August 2009.

Haussler KK. Focus on the Equine Spine: Advanced course (Part 2). Barneveld, Netherlands. 6 hours lecture; 9 hours laboratory. March 2009.

Haussler KK. Focus on the Equine Spine: Instructor Training Course. Barneveld, Netherlands. 3 hours lecture; 3 hours laboratory. March 2009.

Haussler KK. Sacroiliac joint loading and pelvic deformation: How rigid is the pelvis?

The effect of chiropractic treatment on back function and performance. 48th British Equine Veterinary Association Congress, Birmingham, England. September 2009.

Haussler KK. Diagnosis and treatment of horses with chiropractic techniques.

Equine Back Days, Vienna, Austria. Demonstration–Case studies: Chiropractic evaluation and treatment of the equine spine Case presentation: Chiropractic evaluation and treatment of the equine spine. July 2009.

Haussler KK. Objective measures of somatic pain and the effects of manual therapies.

American Association of Equine Practitioners Focus Meeting: Pain Management, Columbus, OH. July 2009.

Haussler KK. Chiropractic evaluation and treatment of the equine spine.

Current equine chiropractic research. Thirty-First Lake Tahoe Equine Conference, Incline Village, NV. January 2009.

Haussler KK. Hearts & Horses Therapeutic Riding Center, Staff Education, Loveland, CO. Demonstration–Stretching techniques for horses used in therapeutic-riding programs. July 2009

Jalota S, Jaasma MJ, Turner AS, Bauer TW, Kisiday JD, Delaney DC, Yetkinler DN. In vitro and in vivo study of Callos calcium phosphate cement containing autologous bone. Orthopaedic Research Society, Las Vegas, NV, 2009.

Kawcak CE. Diagnosis and Medical Management of Disorders of the Sacroiliac Joints and Pelvis. Rehabilitation and Physical Therapy Symposium 2009.

Kawcak CE. Advances in Musculoskeletal Medications, Influence of Exercise on Growing Horses, Managing Equine Athletes Birth – Training, Managing Equine Athletes Training and Competition, Managing Older Horse Lameness, Surgical Advances for Musculoskeletal Diseases and Using Biological Based Therapies for Lameness. Central Veterinary Conference 2009.

Kisiday JD, Lee CM, McIlwraith CW, Frisbie DD Induction of mesenchymal stel cell chondrogenesis during short-term suspension culture. Orthopaedic Research Society, Las Vegas, NV, 2009.

Kopskey P, Vanderploeg E, Kisiday JD, Frisbie DD, Sandy J, Grodzinsky AJ. A single- dose of TGFβ induces chondrogenesis in MSC-seeded peptide and agarose hydrogels. Orthopaedic Research Society, Las Vegas, NV, 2009.

Lee HY, Kopesky P, Plass A, Diaz M, Sandy J, Frisbie DD, Kisiday J.D, Ortiz C, Grodzinsky AJ. Adult equine MSCs synthesize aggrecan having nanomechanical compressibility and biochemical composition characteristic of young growth cartilage. Orthopaedic Research Society, Las Vegas, NV, 2009.

Lucas M and Reiser R. A biomechanics primer: slow, fast, and ballistic movement. Rocky Mountain American College of Sports Medicine Annual Meeting. Colorado Springs, Colorado, February 27-28, 2009.

McIlwraith CW. California Horse Racing Board Track Safety Meeting, University of California, Davis. "Surfaces: standardized tests, engineering support and national laboratory". March 10, 2009.

McIlwraith CW. Finnish Equine Practitioners Conference, principal speaker (Four 1.5 hour presentations). "Targets for therapy", "Advances in diagnosis", "Stem cells – Where are we?", "New biological treatments and recent advances". March 13-15, 2009.

McIlwraith CW. Basic arthroscopic surgery course, Newmarket Equine Hospital, Newmarket, England (3 hours lecture and 6.5 hours of laboratory). May 8-9, 2009

McIlwraith CW. University of Brno, Czech Republic. "Advances in the diagnosis and treatment of equine joint disease" (Two 1 hour lectures). May 14, 2009

McIlwraith CW. University of Vienna, Vienna Austria – Post graduate course for equine veterinarians. "Equine joint disease – diagnosis and therapy". (4 hours of lecture and 5 hours of laboratory instruction). May 15-16, 2009.

McIlwraith CW. American Association for Laboratory Animal Science, Mile High Branch Spring Meeting. "Equine orthropaedic research" (1 hour) and showing of logistic video (45 min). May 19, 2009.

McIlwraith CW. International Cartilage Research Society Meeting, Miami Florida – Moderator and discussant, session 19.2 large animal studies (1.5 hours). May 25-26, 2009.

McIlwraith CW. Basic Arthroscopic Surgery course, Colorado State University, Fort Collins, CO (4 hours of lecture and 4 hours of laboratory). June 4, 2009.

McIlwraith CW. Advanced Arthroscopic Surgery course, Colorado State University, Fort Collins, CO (8 hours of lecture and 4 hours of laboratory). June 5-6, 2009.

McIlwraith CW. National Cutting Horse Association (NCHA) Convention, Denver, CO. "Radiographic changes in yearling cutting horses. What is really significant?", "Advances in medications and treatment of joint injury and disease for the athletic cutting horse" (2.5 hours). June 20, 2009.

McIlwraith CW. Goulburn Valley Equine Hospital Equine Practitioners Conferences, Shepparton, Vic., Australia. Keynote speaker (7 hours of lecture). July 1-3, 2009.

Scientific Publications and Presentations

McIlwraith CW. Steadman-Hawkins Research Foundation Annual Symposium. "Bone marrow derived mesenchymal stem cells to augment microfracture in a chondral defect model in horses". July 24-25, 2009.

McIlwraith CW. Equine Tenoscopy and Bursoscopy Speciality course, Cornell University, Ithaca, NY. "Carpal sheath tenoscopy – anatomy and approaches", "Tenoscopic proximal check desmotomy osteochondroma removal", "Tenosynovial conditions of the tarsal sheath" and 4 hours laboratory instruction. September 18-19, 2009.

McIlwraith CW. The 11th World Equine Veterinary Association Congress, Guaruja, Sao

Paulo, Brazil. Kester News Hour (with Dr. Nat White) (2 hours). "Update on osteoarthritis and new targeted therapies" (1.5 hours), "Advances in diagnosis of equine joint disease" (0.5 hours). September 24-26, 2009.

McIlwraith CW. Dorothy Russell Havemeyer Foundation Symposium on Equine Skeletal Biomarkers. "Where were we with equine biomarkers four years ago?" (opening lecture) and moderator and strategic planning leader for 4 day meeting. September 28-October 2, 2009.

McIlwraith CW. American College of Veterinary Surgeons Veterinary Symposium – Surgical Summit. "Interleukin-1 receptor antagonist (IRAP) therapy" (in cutting edge therapies in orthopaedics) and "Interleukin-1 receptor antagonist (IL-1Ra) – therapeutic avenues (in molecular therapies). Participant in panel on cutting edge therapies in orthopaedics. October 8-10, 2009.

Oldinski RA, Godek ML, Staiger MP, James SP. Biostability, Biocompatibility and Mechanical Properties of a Hyaluronan-Polyethylene Copolymer, to presented at the 2009 Society for Biomaterials, April 22-25, San Antonio, TX, no. 68. 2009.

Reiser R, Sisneros K, Tracy B, Feldman C, Jørgensen B, Hitchcock L. Center of pressure trends during 60 s standing balance tests. 14th Annual Meeting of the Gait & Clinical Movement Analysis Society. Denver, Colorado, March 10-13, 2009.

Reiser R, Tracy B, Endrizzi M, Keene A, Hitchcock L. Decoupled elliptical machine training: withdrawal and crossed-extensor reactions during bipedal stance. ACSM 2009 Annual Meeting. Seattle, Washington, May 29, 2009.

Ryan SD. Stereotactic Radiosurgery for treatment of extremity osteosarcoma in dogs. European College of Veterinary Surgeons Conference, July 2009.

Ryan SD. Stereotactic Radiosurgery for treatment of extremity osteosarcoma in dogs. Veterinary Orthopedic Society Conference, March 2009.

Staiger MP, Eilbracht S, Lengersdorf M, Tucker N, James S. Electrospinning of poly (vinylidene fluoride) nanofibre assemblies, presented at AMN4, The MacDiarmid Institute for Advanced Materials and Nanotechnology, University of Otago, New Zealand. 8-12, Feb. 2009.

Title	Investigators	Sponsor	Time Period	Amount
Evaluation of intra-articular polyglycan versus intravenous polyglycan or saline (0.9% NaCl) for osteoarthritis using an equine model	McIlwraith CW, Kawcak CE, Frisbie DD	ArthroDynamic Technologies, Inc	10/1/2007-1/30/2011	$644,832
The evaluation of mesenchymal stem cells to augment healing of chondral lesions treated using subchondral bone microfracture	McIlwraith CW, Frisbie DD, Kawcak CE	Steadman Hawkins Research Foundation	7/1/2008-6/30/2009	$211,561
Performance Parameters for Engineering Track Management	McIlwraith CW, Peterson M	Grayson-Jockey Club Research Foundation	4/01/08-03/31/2009	43,838
Incidence of nonfatal injuries in racing	McIlwraith CW, Peterson M	Grayson-Jockey Club Research Foundation	4/01/09-03/31/09/10	$44,397
Incidence of Nonfatal Injuries in Racing Thoroughbreds.	McIlwraith CW, Blea J, Arthur R, Hill A, Peterson M	Grayson-Jockey Club Research Foundation	4/1/2009-3/31/2010	$44,397.00
Patterns of Muscle Activation during Subclinical, Acute and Chronic Cruciate Ligament Disease	McIlwraith CW, Kawcak CE, Frisbie DD	Jaynn Emery Foundation	11/1/2008-10/31/2009	$45,937.00
Effect of Underwater Treadmill Exercise on Preventing the Developmnet of Carpal Osteoarthritis in an Equine Osteochondral Fragment Model	McIlwraith CW, Kawcak CE, Frisbie DD	EORC Foundation	10/27/2008-10/21/2009	$150,000.00
The Evaluation of Mesenchymal Stem Cell to Augment Healing of Chondral Lesions Treated Using Subcnondral Bone Microfracture	McIlwraith CW, Kawcak CE, Frisbie DD	Steadman Hawkins	10/27/2008-10/21/2009	$211,561.00
Refurbishment of Present Gait Analysis Building with Installation of Donated Equipment	McIlwraith CW, Kawcak CE, Haussler K	Thaw Charitable Trust	1/1/2008-12/31/2008	$95,000.00
Effect of rehabilitation on carpal osteoarthritis	McIlwraith CW, King M, Haussler KK, Kawcak CE, Reiser RF	Storm Cat Research Career Advancement Award, Grayson-Jockey Club Research Foundation	6/1/2009-6/30/2010	$15,000
Self Assembling Peptides for Tissue Engineering	Frisbie DD	M.I.T. Massachusetts Institute of Tech.	8/1/2007-7/31/2010	$282,708.00
Evaluation of PHA-739521 and Phenylbutazone Administered Orally vs Placebo Control using an Equine Model	Frisbie DD, McIlwraith CW, Kawcak CE	Pfizer Inc - Animal Health	3/11/2005-3/8/2009	$298,001.00
Gene Expression in Mechanically Injured Osteochondral Plugs	Frisbie DD	CRC Funding	7/1/2008-6/30/2009	$21,000.00
Orthokine Protocol to Assess Serum Protein Factors	Frisbie DD, McIlwraith CW, Reardon KF, Carbone BA	Arthrex	11/1/2006-10/31/2008	$49,307.00

Funded Research Projects

Title	Investigators	Sponsor	Time Period	Amount
Evaluating Reduction in Lameness or Prevention of Pathological Bone Changes Following Application of Dynamix Shoes	Frisbie DD, Kawcak CE	Dynamix	1/1/2001-6/30/2009	$432,174.00
Evaluation of Intra-Articular Polysulfated Glycosminoglycan (Adequan) Versus Intra-Articular Hyaluronate Sodium	Frisbie DD, McIlwraith CW, Kawcak CE	Luitpold Pharmaceuticals	1/8/2007-4/7/2010	$357,602.00
Evaluation of MRNA in Periphal White Blood Cells Count--Research Plan #1 Under MRA	Frisbie DD, McIlwraith CW, Hess AM	Pfizer Inc - Animal Health	12/10/2007-12/10/2009	$197,652.00
Pilot Study to Assess the Short Term Effects of Chondrofix in Equine Model #18,000.01	Frisbie DD, McIlwraith CW	Zimmer, Inc.	12/19/2005-6/30/2009	$296,061.20
Horse Gait Trials at CSU	Kawcak CE, Frisbie DD, Werpy NM, McIlwraith CW	Sharp Foundation	11/1/2008-10/31/2009	$28,500.00
Evaluation of Nuclear Magnetic Resonance (MBST) Therapy for Osteoarthritis Using an Equine Model	Kawcak CE, Frisbie DD, McIlwraith CW	MBST Medical Devices, Inc.	6/1/2007-5/31/2008	$230,270.00
An experimental model for tendon strain injury and mesenchymal stem cell interactions	Kisiday JD, Frisbie DD	CRC Funding	7/1/2008-6/30/2009	$10,500.00
Colorado Racehorse Postmortem Evaluation Project	Kawcak CE, Werpy NM	CRC Funding	7/1/2008-6/30/2009	$15,000.00
Mesenchymal stem cell proliferation and migration out of fibrin scaffolds in response to shockwave treatment	Kisiday JD, Frisbie DD, McIlwraith CW	Pulse Veterinary Technologies LLC	7/15/2009 – 7/31/2010	$20,420
Gene and protein expression in autologous conditioned plasma: A comparison of IRAP I and IRAP II	Frisbie DD, McIlwraith CW	Arthrex	2/10/2009 – 8/31/2009	$9,876
Effects of clinically relevant autologous conditioned blood products (ACBP) on the anabolic properties of equine digital flexor tencytes and suspensory ligament fibroblasts	Frisbie DD, McIlwraith CW, Hraha T	American Quarter Horse Foundation	10/1/2009-9/30/2010	$19,560
Evaluation of intrarticular polysulfated glycosaminoglycan (Adequan) and amikacin, versus intrarticular polysulfated glycosaminoglycan (Adequan) and triamcinolone acetonide with amikacin or saline (0.9% NaCl) with amikacin for osteoarthritis using an equine model	Frisbie DD, McIlwraith CW, Kawcak CE	Luitpold Pharmaceuticals	4/8/2009-4/7/2010	$357,601
Evaluation of polyglycan (at a single dose level and three time dose level) versus saline(0.9% NaCl) after intraarticular injection	Kawcak CE, McIlwraith CW, Frisbie DD	ArthoDynamic Technologies, Inc	6/1/2008 – 5/31/2009	$75,990

Title	Investigators	Sponsor	Time Period	Amount
Self Assembling Peptide for Tissue Engineering	Frisbie DD (Subcontract PI), Grodzinsky, AJ (Program PI)	HHS-HIH/MIT (NIH-Program grant) Grant # RO1-003805-01A1	4/1/2007-3/31/2010	$479,876
Gene therapeutic approaches to cartilage repair	Goodrich LR, McIlwraith CW	NIH Mentored Clinical Scientist Research Career Development Award (K08)	6/01/2008-5/01/2013	$677,875
A gene therapy approach to cartilage healing utilizing Adenoassociated viral vectors in bone marrow-derived mesenchymal stem cells	Goodrich LR, McIlwraith CW	College Research Council, Colorado State Universtiy	3/01/2008-3/01/2009	$26,000
The Effect of Adenovirus Mediated Co-expression of Combined Bone Morphogenetic Protein-2 and 7 on Osteoblastic Differentiation of Equine and Human Bone Marrow-Derived Mesenchymal Stem Cells	Goodrich LR, McIlwraith CW	College Research Council, Colorado State Universtiy	3/01/2007-3/01/2008	$30,000
Effect of Rehabilitation on Carpal Osteoarthritis	King MR, McIlwraith CW	Grayson-Jockey Club Research Foundation	4/1/2009-3/31/2010	$15,000.00
Investigation of osteochondral disease through finite element modeling	Easton, Katrina	HHS-NIH-National Institutes of Health	4/1/2008-5/13/2011	$29,777.00
Collaborative Research: Nanostructured Titania for Orthopedic Biomaterials	Popat KC	NSF - National Science Foundation	9/1/2008-8/31/2011	$180,000.00
Fibrotic Effects and Regulation of MMP Proteins in Thrombus Resolution	Puttlitz CM	N. CA Inst. for Research and Education	5/12/2006-4/30/2009	$126,298.00
The Annual Symposium on Computational Methods in Orthopaedic Biomechanics	Puttlitz CM	HHS-NIH-Arthritis, Musculoskel, & Skin	2/20/2009-8/31/2009	$15,000.00
A Development Proposal for an Instrumented Cervical Intervertebral Disc Space Distractor	Puttlitz CM	CSURF-CSU Research Foundation	7/12/2007-12/31/2008	$107,285.00
Performance Parameters for Engineering Track Management	McIlwraith CW, Peterson M	Grayson-Jockey Club Research Foundation	4/1/2008-3/31/2009	$43,838.00
Partial Joint Resurfacing with Biopoly™ RS – A Hydrophilic Polymer	James SP, Puttlitz CM, Kisiday JD	Schwartz Biomedical, LLC	12/1/2006-12/31/2008	$400,000.00
Augmentation of a Bone Tendon Reattachment with a PDGF Soaked Collagen Matrix in a Sheep Model	Puttlitz CM	Biomimetic Therapeutics, Inc.	11/1/2008-7/1/2009	$66,371.00
In vivo and In vitro Measurements of Human Cervical Stress Relaxation during ACD	Puttlitz CM	Synthes	1/1/2007-3/31/2009	$39,000.00
Acute Rotator Cuff with Biosynthesize Cellulose Repair Device: A Histological Study in Sheep: Phase 3	Puttlitz CM	Xylos Corporation	8/15/2008-4/30/2009	$27,615.00

Funded Research Projects

Title	Investigators	Sponsor	Time Period	Amount
Evaluation of the Magellan Intervertebral Body Fusion Device in a Sheep Spine Model	Puttlitz CM	Magellan Spine Technologies, Inc.	10/20/2008-7/1/2009	$10,393.00
Effect of Disc Degeneration, Nucleus Replacement, and Disc Replacement On Facet Force Transmission – A Finite Element...	Puttlitz CM	Synthes	4/3/2007-10/31/2010	$33,172.00
STS/GCD Ovine Histology	Puttlitz CM	NuVasive, Inc.	7/1/2007-7/1/2008	$53,071.00
A Finite Element Investigation of Cervical Intervertebral Disc Replacement Biomechanics	Puttlitz CM	Synthes	4/1/2006-3/31/2009	$102,015.00
Prevention of Epidural Fibrosis in a Sheep Laminectomy Model Phase II	Puttlitz CM	Kuros Biosurgery AG	10/1/2007-2/1/2009	$18,861.00
Prevention of Dural Leakage in a Sheep Craniotomy Model	Puttlitz CM	Kuros Biosurgery AG	11/15/2007-11/14/2008	$44,232.00
Prevention of Epidural Fibrosis in a Sheep Laminectomy Model Phase III	Puttlitz CM	Kuros Biosurgery AG	3/1/2008-2/28/2009	$32,677.00
Prevention of Epidural Fibrosis in a Sheep Laminectomy Model Phase IV	Puttlitz CM	Kuros Biosurgery AG	3/1/2008-2/28/2009	$10,650.00
Comparison of Bone Cements in Sheep	Puttlitz CM	Medtronic Spine LLC	3/17/2008-8/30/2008	$8,842.00
A Biomechanical and Histological Assessment of Tissue Ingrowth for a Dynamic Stabilization Micromotion System (DSF...	Puttlitz CM	IST-Innovative Spinal Technologies, Inc.	10/1/2007-4/30/2009	$58,503.00
Triple Damper System Chronic Sheep Study: Biomechanical and Histomorphometric Evaluation of Sheep Lumbar Region	Puttlitz CM	Blackstone Medical, Inc.	5/2/2008-11/30/2008	$134,180.00
Evaluation of Bone Void Filler Resistance to Bleeding and Irrigation and Correlation with New Bone Formation in ...	Puttlitz CM	Kuros Biosurgery AG	5/1/2008-5/1/2009	$73,961.00
Evaluation of the Anti-adhesion Properties of Human Amnion Tissue Patch Following Laminectomy in a Sheep Model	Puttlitz CM	AlloSource	6/17/2008-12/1/2008	$44,898.00
Evaluation of Polyglycan (At a Single Does Level and Three Times Dose Level) Versus Saline (0.9% NaCl) After ...	Kawcak CE, Frisbie DD, McIlwraith CW	ArthroDynamic Technologies, Inc.	6/1/2008-5/31/2009	$75,990.00
Failed Spinal Fusion Analysis	Puttlitz CM	NuVasive, Inc.	6/17/2008-7/31/2008	$784.00
Effect of Locally Delivered, Modified PTH in an Anterior Lumbar Interbody Fusion Model in Sheep	Puttlitz CM	Kuros Biosurgery AG	3/1/2009-4/1/2010	$183,615.00
Long Term Implantation Effects of Flexion Limiting Device in an Ovine Model	Puttlitz CM	Simpirica Spine	12/1/2008-12/1/2009	$130,784.00

Title	Investigators	Sponsor	Time Period	Amount
Evaluation of an Allograft Anchor for Pedicle Screw Augmentation in an Ovine Model	Puttlitz CM	Synthes	1/15/2009-12/1/2009	$83,353.00
Screw Insertion Device Torque Assessment	Puttlitz CM	High Plains Technology Group LLC	6/15/2008-1/15/2009	$744.00
Acute Rotator Cuff with Biosynthesize Cellulose Repair Device: A Histological Study in Sheep: Phase 4	Puttlitz CM	Xylos Corporation	10/1/2008-11/30/2009	$27,048.00
The Evaluation of Dermagraft® to Accelerate the Healing of Acute Rotator Cuff Injuries in a Sheep Model – Phase I: ...	Puttlitz CM	ABH-Advanced BioHealing	5/15/2009-11/15/2009	$33,451.00
Biodistribution Study of Single Dose Intravenous Radium223 in Normal Dogs	N Ehrhart, Ryan S, Steyn P, Dornish M	Algeta Inc, Norway	6/1/2007-6/30/2009	$367,000
			TOTAL	**$8,125,573**

Revenue and Expense, FY08 to FY09

	FY09 07/01/08 to 06/30/09		FY08 07/01/07 to 06/30/08
REVENUE			
Donations - 64 Accounts			
American Livestock	2,050.00	Allen & Company Inc	250,000.00
American Quarter Horse Assoc	4,010.00	Allen & Company Inc	25,000.00
ArthroDynamics	6,000.00	Allen, Susan	3,000.00
Bailey, Tom	80,000.00	American Livestock Insurance	2,000.00
Dedomenico	100,000.00	American Quarter Horse Assoc	9,484.97
Equus Foundation	5,000.00	Emery, Jaynn	50,000.00
Jayne Emery	50,000.00	Emery, Jaynn	50,000.00
Marylynn Fischer	5,000.00	Equus Foundation	5,000.00
McIlwraith	20,000.00	IDEXX Laboratories, Inc.	40,000.00
Moorehead	1,000.00	Kawananakoa Foundation (Abigail)	3,000,000.00
Rocky Mountain LAE	10,000.00	Luitpold Pharmaceuticals	15,000.00
Rosenthal Trust	10,000.00	Morehead, Dr. James P	1,000.00
Steadman Hawkins	110,000.00	Morehead/James P Dr. and Michelle	1,000.00
Walton Family Foundation (Alice Walton)	10,000.00	Rosenthal Ranch Trust	10,000.00
		Sparks III, John M. & Karen DVM	10,000.00
		Steadman-Hawkins Sports Medicine Foundation	110,000.00
		Taylor II,Robert L. & Melanie	5,000.00
		Walton Family Foundation (Alice Walton)	10,000.00
Total Donations	*413,060.00*		*3,596,484.97*
Interest on Endowments			
McIlwraith Scholarship	5,925.24	McIlwraith Scholarship	6,104.32
Cox Anthony Chair	159,514.00	Cox Anthony Chair	177,929.72
Iron Rose Ranch Chair	141,305.68	Iron Rose Ranch Chair	157,619.28
Atkinson Chair	60,915.32	Atkinson Chair	65,652.00
Kawananakoa Chair	123,623.48	Kawananakoa Chair	101,250.00
Total Interest	*491,283.72*		*508,555.32*
Medical Center Clinical Services			
Digital Xrays	9,312.00	Digital Xrays	-
Outpatient	33,658.27	Outpatient	14,383.42
MRI	34,694.87	MRI	26,450.37
Shockwave	23,451.80	Shockwave	11,993.45
Surgery	9,037.18	Surgery	19,245.49
Client Services Total	*110,154.12*		*72,072.73*

Revenue and Expense, FY08 to FY09

	FY09 07/01/08 to 06/30/09		FY08 07/01/07 to 06/30/08
ORC Ambulatory	34,224.00		13,761.00
ORC CORE Lab Revenue – 22 Account	13,990.80		25,489.10
Research Projects – 53 Accounts			
ArthroDynamics	75,990.00	ArthroDynamics	357,602.00
Dynamix - Dr. Lee	14,000.00	Grayson Jockey	48,383.00
Grayson - Incidence of Non-Fatal Injuries	44,397.00	Grayson Jockey	31,283.00
Grayson Storm Cat	15,000.00	HHS-NIH	29,213.00
Luitpold	357,602.00	MIT-NIH	100,000.00
MIT - NIH	182,698.00	Pfizer	197,652.00
NIH Fellowship - Katrina Easton	29,272.00	Thaw Charitable Trust	95,000.00
Pulse Veterinary	20,420.00	Zimmer	59,346.00
Solar Physics	18,181.00		
Steadman Hawkins	220,000.00		
Underwater Treadmill Project	150,000.00		
Whitton Pandy Modeling	29,645.00		
Research Accounts Total	*1,157,205.00*		*918,479.00*
Stallion Auction	62,710.00		61,239.80
State Funds – Various 14 and 16 Accounts			
CWM Salary Savings	167,949.87		167,850.00
Frisbie Salary Savings	5,029.95		32,785.00
Kawcak Salary Savings	5,298.74		14,513.09
Haussler/Kisiday Start up	33,333.00		37,500.00
ICR Return	27,518.26		44,864.00
Frisbie CRC Grant	21,000.00		14,000.00
Kawcak CRC Grant	29,000.00		
Kisiday CRC Grant	10,500.00		
PRSE Grant	22,500.00		
Werpy CRC Grant	17,000.00		15,000.00
State Funds Total	*339,129.82*		*326,512.09*
Total Revenue	***2,621,757.46***		***5,522,594.01***

Revenue and Expense, FY08 to FY09

	FY09 07/01/08 to 06/30/09	FY08 07/01/07 to 06/30/08
EXPENSE		
Salaries		
Faculty Salaries	653,037.00	647,155.60
Research Associate Salaries	219,295.00	255,919.00
Administrative Salaries	131,863.00	124,030.49
Graduate Student Salaries	184,562.00	161,551.68
Hourly EORC students	119,376.00	87,482.90
Total Salaries	*1,308,133.00*	*1,276,139.67*
Faculty Travel	26,114.00	41,380.56
Materials and Supplies	414,570.05	176,842.82
Other Direct	943,995.65	581,550.90
Equipment	—	211,231.94
Expense Subtotal	*2,692,812.70*	*2,287,145.89*
Facility and Administrative Overhead Costs	205,325.72	182,395.09
Total Expense	***2,898,138.42***	***2,469,540.98***
ACCOUNT BALANCE	**(276,380.96)**	**3,053,053.03**

McIlwraith CW, Peterson ML. Elastikon Equine Research Award, Johnson & Johnson Consumer Products Company to the Grayson-Jockey Club Research Foundation, 2008.

McIlwraith CW. University Distinguished Professor, Colorado State University, 2009

McIlwraith CW. Telly Award 2009 for documentary "Majestic" (featuring Dr. CW McIlwraith and LR Bramlage), produced by Foundation for Biomedical Engineering.

McIlwraith CW, Distinguished Life Membership, AAEP, 2009.

Goodrich LR, NIH Mentored Clinical Scientist Research Career Development Award (K08), 2008.

Goodrich LR, Orthopaedic Research Society, New Investigator Research Award, Semi-Finalist, 2008.

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- Phi Kappa Phi

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- Colorado Veterinary Medical Association
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- Society for Biomaterials

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- American Academy of Orthopaedic Surgeons (AAOS) (Associate Member)

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Summary of Research Projects 2008-2009

Induction of bone marrow mesenchymal stem cell chondrogenesis following short-term suspension culture

Take Home Message
Cartilage resurfacing using bone marrow-derived mesenchymal stem cells (MSCs) has been explored using undifferentiated cells taken directly from expansion culture. This strategy has not proven capable of long-term regeneration of neo-cartilage, and it is thought that pre-implantation induction of MSC chondrogenesis may be necessary to stimulate lasting repair. To address this challenge, we developed a scaffold-free culture strategy that resulted in chondrogenic differentiation in a subset of MSCs in a laboratory setting. This method may be applied to future animal studies to determine if partially committed MSCs are sufficient to stimulate lasting cartilage repair.

Introduction
In recent years, MSCs have received extensive consideration for applications to cartilage regenerative medicine (1, 2). The ability to undergo chondrogenesis is a hallmark of MSCs (3), and numerous *in vitro* models demonstrating MSC accumulation of a cartilage-like extracellular matrix (4) have generated enthusiasm that MSC-seeded scaffolds are capable of cartilage resurfacing. The extent to which chondrogenic commitment of MSCs *in vitro* is necessary to improve cartilage regeneration *in vivo* has yet to be defined, and the report of improved cartilage repair with implants conditioned in chondrogenic medium for seven days (5) suggests that pre-implantation conditioning may not require extensive *ex vivo* culture. Therefore, we hypothesized that three days of chondrogenic suspension culture enhances chondrogenesis relative to MSCs taken directly from monolayer expansion. To test this hypothesis, chondrogenesis of MSCs from suspension culture were compared to undifferentiated MSCs in agarose hydrogel. This work was done by Ben Hale under the supervision of Dr. John Kisiday.

Methods
Tissue harvest, cell preparation, and encapsulation in agarose: MSCs were expanded from bone marrow was harvested from 10 2-5 yr old horses (6). Suspension cultures consisted of polyHEME-coated T75 flasks into which 1.8x106 MSCs were seeded in defined medium (ITS+, 0.1 μM dexamethasone, and 37.5 μg/ml ascorbate-2-phosphate) plus 10 ng/ml TGFβ-3 (7). After 3 days, the MSCs in the suspension cultures were trypsinized to create an individual cell suspension. The first experiment in this study compared the effect of 3 days of suspension culture to control MSCs that were maintained in monolayer expansion culture only. In a second experiment, 3 days of suspension conditioning was followed by a return to monolayer cultures for 2 days prior to testing for chondrogenesis in agarose. Control cultures were created using MSCs from expansion culture. In both experiments, suspension and monolayer control preparations were tested for chondrogenesis in agarose hydrogels in the presence (TGFβ+) or absence (TGFβ-) of 10 ng/ml TGFβ. These four groups were abbreviated as 'Susp-TGFβ+', 'Susp-TGFβ–', 'Control-TGFβ+', 'Control-TGFβ–' in the text. Total GAG accumulation in the scaffold was quantified using the DMMB dye binding assay on day 15. Over the final 24 hours of culture, samples were evaluated for protein and proteoglycan synthesis via ^{3}H-proline and ^{35}S-sulfate radiolabel incorporation, respectively. On day 15, proteoglycan staining was colocalized with the viable cell population by incubating calcein-labeled samples in a 0.0005% Toluidine blue solution. Also, immunohistochemical staining was conducted for selected suspension conditions.

Statistics: Mixed model analysis of variance with individual comparisons using least square means procedure. p-values< 0.05 were considered significant.

Results
Experiment #1– Suspension conditioning: MSCs began to aggregate within hours after seeding in suspension cultures. From the 2.4 x 10^6 cells seeded for each of the 10 suspension culture, 1.14 +/- 0.06 x 10^6 MSCs were recovered. ***ECM synthesis:*** In monolayer control samples, 3H-proline and 35S-sulfate incorporation and GAG accumulation in TGFβ+ medium were 12-, 33-, and 16-fold higher than TGFβ–, respectively ($p < 0.01$). ECM synthesis in Susp-TGFβ– cultures was similar to Control-TGFβ–

(p = 0.12-0.82), and no greater than 15% of that in Control-TGFβ+ samples (p < 0.001). In TGFβ+, ^{3}H-proline incorporation and GAG accumulation in suspension cultures were 78% and 67% of monolayer controls, respectively, although these difference were not significant (p = 0.31, 0.14). ^{35}S-sulfate incorporation in suspension samples was 44% of monolayer control cultures (p < 0.01).

Experiment #2 – Suspension/expansion conditioning: From the 2.4 x 10^{6} cells seeded for 5 suspension culture in this experiment, 0.93 +/- 0.07 x 10^{6} MSCs were recovered. Over two days of monolayer culture in expansion medium, the suspension-recovered MSCs proliferated to 3.23 +/- 0.45 x 10^{6} MSCs, a 3.5-fold increase in cell number. ***ECM synthesis:*** In monolayer control samples, ^{3}H-proline and ^{35}S-sulfate incorporation and GAG accumulation in TGFβ+ were 31-, 52-, and 10-fold higher than TGFβ–, respectively (p < 0.005, Fig. 1). ECM synthesis in Susp-TGFβ– cultures was also higher than Control-TGFβ– (^{3}H-proline: 5.5-fold, ^{35}S-sulfate: 9.6-fold, GAG accumulation: 3.7-fold; p < 0.005). However, ECM synthesis in Susp-TGFβ– was 18-37% of Control-TGFβ+ (p < 0.005). ECM synthesis in Susp-TGFβ+ and Control-TGFβ+ were not significantly different (p = 0.67-0.82). ***ECM Staining – Toluidine Blue:*** In Control-TGFβ– samples, toluidine blue

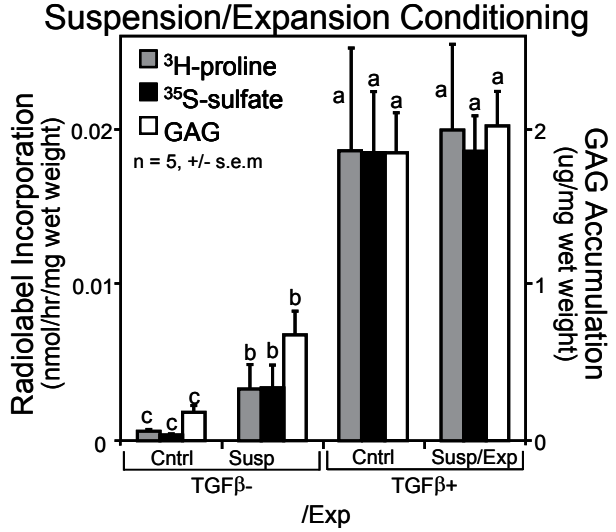

Figure 1.

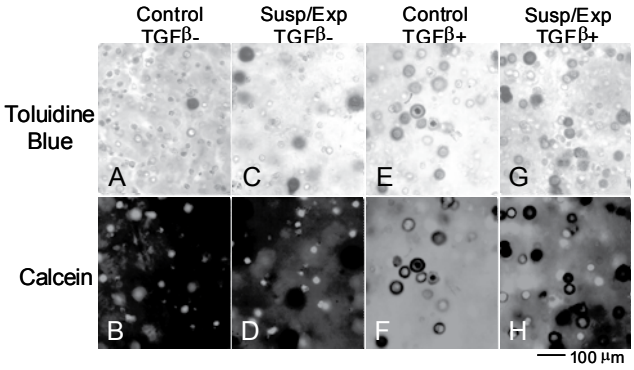

Figure 2.

staining was nearly absent (Fig. 2A). In Susp-TGFβ–, toluidine blue-positive MSCs were more numerous than in Control-TGFβ– cultures (Fig. 2C). However, many viable cells had not accumulated a proteoglycan-rich ECM (Fig. 2D). For both TGFβ– cultures, toluidine blue-positive MSCs were surrounded by an abundant ECM halo. In Control-TGFβ+ and Susp-TGFβ+ cultures, the majority of the viable cell population was surrounded by an abundant proteoglycan matrix (Fig. 2E, G). ***Immunohistochemical staining:*** Susp-TGFβ– samples were evaluated for type II collagen accumulation to confirm that the increases in ECM synthesis and accumulation over Control-TGFβ– coincided with the secretion of a cartilage-like neo-tissue. Staining for type II collagen was found in pericellular regions of ECM accumulation, as was observed for toluidine blue staining.

Discussion

In this study, suspension conditioning alone had little effect on MSC chondrogenesis. Instead, monolayer expansion following suspension conditioning was necessary to induce a moderate level of chondrogenesis without additional TGFβ exposure. Toluidine blue staining suggested that stimulation of chondrogenesis with suspension/expansion condition resulted from an increased frequency of MSC chondrogenesis. The potential impact of this chondrogenic conditioning technique on cartilage repair will require future in vivo testing. However, based on animal studies conducted with undifferentiated MSCs that have demonstrated early signs of cartilage-like repair tissue (8-13), the joint appears to provide at least a limited chondrogenic environment. Therefore, while suspen-

sion/expansion conditioning induced only partial chondrogenesis in the absence of a chondrogenic cytokine *in vitro*, it is possible that the joint environment may provide chondrogenic cues that enhance the cartilage repair response beyond that which was observed in TGFβ-free medium here.

Acknowledgements
Funding through a grant from the Colorado State University College Research Council

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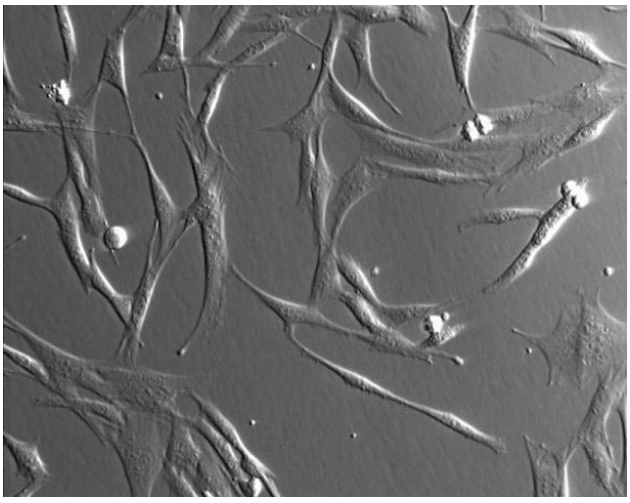
Clinical follow-up of horses treated with bone marrow derived mesenchymal stem cells for musculoskeletal lesions

Take Home Message
In 72% of intra-articularly treated (joint/collateral ligament) and 86% of soft tissue cases (suspensory ligament, collateral ligament, superficial digital flexor tendon, and deep digital flexor tendon) treatment with bone marrow derived mesenchymal stem cells (BMSCs) resulted in return to function when followed-up an average of 21 months post BMSC treatment. Cases with severe meniscal injuries and chronic suspensory lesions showed some of the more encouraging responses to treatment.

Introduction
BMSCs have gathered increasing attention as a viable therapy for musculoskeletal lesions in humans, horses, and other animal species. Work in humans supports the use of bone derived vs fat derived stem cells. BMSCs have been shown to result in marked meniscal regeneration in the goat. Clinical follow-up of a large number of horses treated for tendon injuries in the UK show promising results, with a high number of horses returning to work and most impressively, a decreased rate of injury.



Clinical follow-up of horses treated with BMSCs has been limited mainly to case reports with low numbers. This is especially true with horses treated for intra-articular lesions. The goal of this study was to follow-up a modest number of horses suffering from tendon, ligament, or intra-articular lesions treated with BMSCs.

Materials and Methods
Cases and bone marrow aspirates were obtained from six hospitals from different areas. All BMSC expansion occurred at CSU's Orthopaedic Research Laboratory (ORC) or Advanced Regenerative Therapies (ART). Attending veterinarians were encouraged to only treat severe cases or cases that had otherwise failed routine treatment methodologies, to use NSAID's prior to BMSC administration, and not to include antibiotics locally. In cases of intra-articular administrations, attending veterinarians were also encouraged to use a single dose of intra-articular hyaluronan at the time of BMSC treatment. During the time period chosen for the study (November 2005 to August 2007), 121 horses from the 6 centers were treated. Medical records were obtained from participating centers and reviewed. Information pertaining to the treated injury was collected from the medical records. Horses treated for both soft tissue and orthopaedic lesions (N=4) were analyzed with both groups. Follow-up with the attending veterinarian or current owner was obtained. Horses were considered "returned to work" if they were back in regular work and doing well. Horses were considered returned to work at a lesser level if they could not perform to previous standards or expectations, required more maintenance for their lameness, or were sound but still in rehabilitation.

Results
Follow-up was obtained on 39 horses treated intra-articularly, 58 treated by direct injection of a tendon or ligament, and 1 treated in the navicular bursa. The time period for follow-up ranged between 7 and 39 months post injection, with a mean time of 21 months.

Tendon and Ligament cases
Overall, 37 of the horses treated by direct injection of a tendon or ligament were able to return to or exceed their previous level of function, 13 returned at a lesser level (4 of these re-injured their tendon or ligament). Eight horses were unable to return to work. Interestingly, when looking at cases with chronic suspensory lesions (greater than 6 months), 7 of the 9 horses were able to return to some level of work post-stem cell treatment, despite failing previous surgical or medical management. Superficial digital flexor tendon cases also had encouraging results, with 10/11 race horses returning to race training and 6/6 sport horses returning to function.

Intra-articular cases
Twenty nine of the 39 intra-articularly treated cases involved treatment of the femorotibial joint, and 21 of these horses had medial meniscal damage. Six of 8 horses with an AAEP lameness score of 4/5 were able to return to work following stem cell treatment of their injury. Horses with severe meniscal injuries showed an increased percent return to function compared to horses in other studies with surgical intervention alone.

Adverse Events
An adverse event was reported by the owners of 3 horses treated intra-articularly and one horse treated in a suspensory ligament. None of these horses received NSAIDs prior to the injection of their cells. The intra-articular cases required only mild treatment and were able to return to work at a similar rate compared to horses in the study that did not have an adverse event.

Discussion
It was initially hypothesized that there would be an association between severity of lameness and the chance that a horse would return to their previous level. However, this was not statistically evidenced in this study. The percent return to function vs. AAEP lameness score was fairly evenly distributed between groups. However, it was encouraging that even horses with severe grade 4 lamenesses, chronic injuries, and severe injuries were able to return to work post treatment.

As evidenced in this prospective clinical study, treatment with bone marrow derived mesenchymal stem cells can result in increased soundness and return to function in horses afflicted with musculoskeletal injuries. This was achieved even when lesions were categorized as severe. Results found in this study were comparable to other clinical studies of horses treated with stem cells for soft tissue injuries. Likewise horses treated for joint related problems were improved to a similar degree (72%) as the authors had reported in a preliminary follow up of 15 cases where 67% when back to full work. Much more information regarding treatment with stem cells needs to be gathered; however, clinically, it shows promise for returning even severely injured horses to performance.

This study was headed up by Drs. Frisbie and Kisiday with data collection documentation by Dr. Dora Ferris.

Reference
Ferris DJ, Frisbie DD, Kisiday JD, McIlwraith CW, Hague BA, Major MD, Schneider RK, Zubrod CJ, Watkins JJ, Kawcak CE, Goodrich LR. Clinical follow-up of horses treated with bone marrow derived mesenchymal stem cells for musculoskeletal lesions. In, Proceedings AAEP Annual Convention 2009:59-60.

Osteochondral allografts for use in equine cartilage resurfacing

Purpose
One restriction on the clinical use of equine osteochondral (OC) grafts is the limited supply autogenic donor tissue. This study assessed two geometric shaped off-the-shelf allografts compared to fresh cylindrical allografts or empty defects. This work was done by Drs. Frisbie, Gao, Werpy, Kawcak, Yao and McIlwraith.

Material and Methods
OC plugs harvested from equine femoral condyles were machined into either mushroom (MOC) or cylindrical (COC) shape and then processed before implantation[1].

With IACUC approval, four defects (≈5.4mm wide by 8mm deep) were created in the medial femoral trochlea in 6 horses and were repaired by using OC grafts with either shape, or fresh OC allograft (FOC) or left untreated. Three animals were euthanized at 9 months after surgery and the remaining 3 at 18 months. Arthroscopic examinations were performed at 3, 6 and 9 months for all animals and at 12, 18 months for those 3 animals sacrificed at 18 months.

The horses underwent controlled strenuous exercise on a high-speed treadmill starting 4 months after surgery. Repair tissue was evaluated by follow-up arthroscopy, MRI, histology, and immunohistochemistry.

Results
Arthroscopically, significantly better subjective repair tissue was seen with the MOC compared to the other groups based on filling of defect, surface regularity, firmness of repair tissue and bonding to surrounding tissues (Figure 1). No significant differences were detected based on the endpoint MRI evaluations. Histologically throughout the study MOC performed significantly better than either the FOC or empty defects based on the nature of the predominate tissue (Figure 2). Type II collagen and aggrecan was labeled in cartilage tissue all tissues although significant improvement was seen with COC compared to empty defects.

Conclusions
A durable cartilage repair was achieved by implantation of both MOC and COC grafts after 18 months even in the face of strenuous exercise.

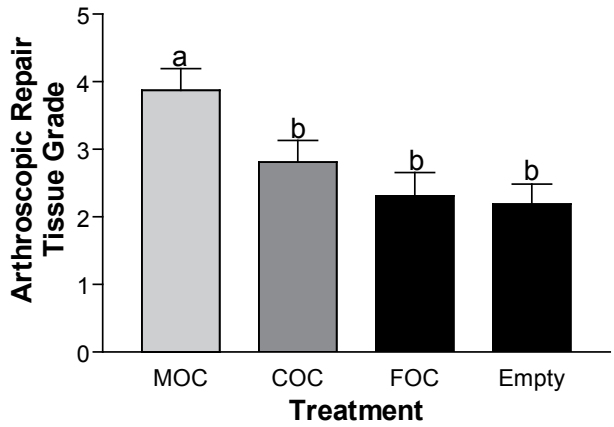


Figure 1. Plot of mean ± standard error of the mean (SEM) subjective arthroscopic repair tissue grade by treatment throughout the entire study based on a 0-4 scale (no tissue present, poor, fair, good & excellent respectively).

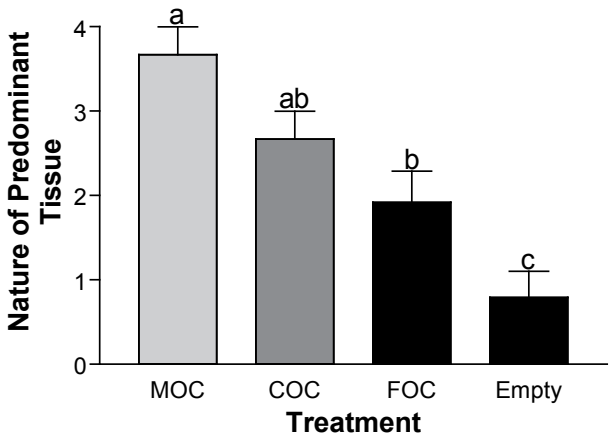


Figure 2. Plot of Mean score ± SEM for the histologic grading of the predominant repair tissue by treatment using a 0-4 scale (0 representing no hyaline to 4 representing hyaline tissue).

Autologous and commercially derived fibrin glues as a delivery vehicle for mesenchymal stem cells

Take Home Message
The potential of mesenchymal stem cells (MSCs) to heal orthopaedic tissues is still poorly understood. While the majority of MSC-based repair strategies employ a tissue engineering approach of containing repair tissue within a scaffold, recent work with intra-articular injections of MSCs suggest that a benefit may be realized by seeding MSCs on the surface of damaged tissue. In this study, we demonstrated that fibrin glues possess favorable properties as a delivery vehicle for seeding MSCs on tissues.

Introduction
Although it is well established that bone marrow-derived MSCs have the potential to regenerate damaged orthopaedic tissues [1], a consistently successful therapeutic strategy utilizing MSCs has yet to be implemented. Based on early experimental [2] and clinical [3] success of injectable stem cell therapies, it is postulated that a system allowing MSCs to populate the surface of a tissue defect may stimulate tissue repair. Here, we explored the ability of autologous and commercial fibrin hydrogels – a widely used scaffold for tissue-engineering [4] – to serve as a delivery vehicle for MSCs. MSC migration out of fibrin hydrogels was quantified for a range of protein concentrations to determine the effect of fibrinogen dilutions on the ability of MSCs to escape the hydrogel. This work was done by Ben Hale under the supervision of Dr. John Kisiday.

Methods
MSC isolation: MSCs were expanded from the bone marrow was aspirated from the iliac crests and sterna of four 2-4 year-old horses. MSCs were isolated and culture-expanded by seeding at a density of 12 x 103 cells/cm2. Each MSC population was expanded through 2-3 passages prior to seeding into fibrin hydrogels.

Autologous fibrinogen precipitation: 0.88 mL of 100% ethanol was added to 5 mL of plasma obtained from citrated whole blood. After sitting for 30 minutes on ice, the sample was centrifuged at 1500g for 15 minutes, the supernatant was aspirated, and the pellet was resuspended in 200 μL of fresh plasma.

Fibrin gel encapsulation: Both the autologous fibrinogen, and the fibrinogen component of the commercially available sealant Tisseel (lyophilized purified human fibrinogen reconstituted in fibinolysis inhibitor apoprotin at 75-115 mg/mL; Baxter US, Deerfield, IL), were diluted with PBS to concentrations of 75%, 50%, and 25% of the undiluted solutions. MSCs were suspended in a bovine thrombin solution (110 NIHU/mL, reconstituted in 40 mM CaCl2; MP Biomedicals, Solon, OH) at a concentration of 15×10^6 cells/mL. 10 μL of the appropriate fibrinogen solution was mixed with 10 μL of the cell/thrombin solution on the surface of a 12-well tissue culture plate for a final concentration of 7.5×10^6 cells/mL. Two beads were created per well, with three wells per fibrinogen concentration for each of the four horses. The beads were covered in 2 mL α-MEM + 10% FBS, and incubated at 37°C and 5% CO2 for 24 hours.

MSC migration: Cell Titer Blue viable cell assay (Promega, Madison, WI) was used to quantify the cell migration out of the fibrin hydrogels. MSCs that had migrated onto the tissue culture surface were trypsinized and plated in a 96-well plate with Cell Titer Blue reagent. A standard curve was established by seeding MSCs from the same animal in known concentrations and analyzing in parallel. After 12-18 hours of incubation, the plate was read in a fluorescent plate reader at 570/600nm abs/emit.

Protein analysis: Samples of both the autologous fibrinogen solution and plasma used were saved for total protein analysis with BCA Protein Assay.

Statistics: Post-hoc comparisons were made using a two-factor repeated measure mixed model on the log-transformed data, with Kenwood-Rogers method for estimating the denominator degrees of freedom. The significance level was chosen to be $p < 0.05$.

Results
Quantitative analysis showed levels of migration that ranged from 0 to 3250 cells/gel. Although increased MSC migration was generally observed with decreased fibrin concentration in both the sources of fibrin, the response was significantly different

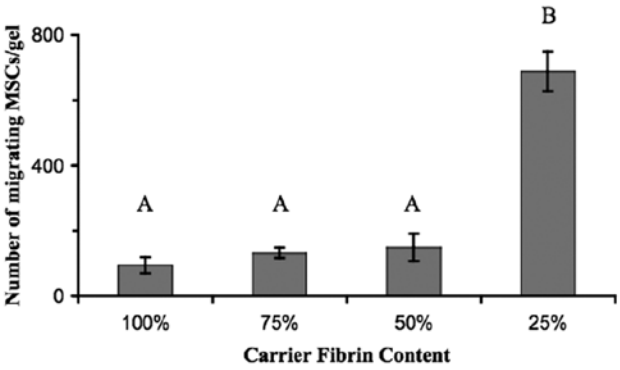


Figure 1. Autologous Fibrin.

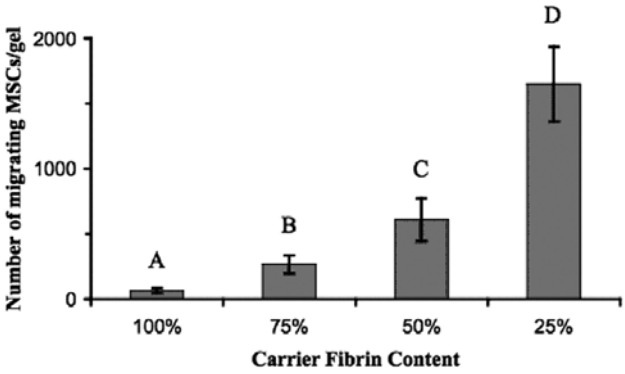


Figure 2. Tisseal.

between the autologous and commercial fibrin dilutions (significant fibrin type-by-percent interaction term). In the autologous suspensions, only the 25% dilution produced a significantly different level of cell migration than the undiluted concentration (100% v. 75% p= 0.0823; 100% v. 50% p = 0.1197. Fig. 1), whereas all of the commercial dilutions produced a significantly different level of migration from the full-strength suspension (Fig. 2). Moreover, each dilution of the commercial product was significantly different from adjacent dilutions. The magnitude of the migration from the 25% fibrin condition was significantly higher in the Tisseel than the autologous beads. Although there was not a statistical difference between the migration from the undiluted commercial and autologous hydrogels (p=0.1895), it was observed that cell spreading within the hydrogel was much more limited in the Tisseel beads, of which only one of twelve wells showed measurable outgrowth. In the autologous fibrinogen, analysis of the protein concentration for each horse showed an apparent migration threshold, with a spike in MSC migration below protein concentrations of ~20-30 mg/mL.

Discussion

The results we obtained for both products suggest that diluting the fibrinogen component of a fibrin scaffold will promote increased cell migration. Interestingly, the sensitivity of migration to dilution was different between the precipitated fibrinogen, and the purified fibrinogen Tisseel. Observations on the consistency of the solutions support this result: the undiluted commercial fibrinogen was much more viscous than its autologous counterpart, yet the highly diluted solutions did not handle or appear differently. Although further studies would be needed to determine the reason for this effect, it is possible that diluting the purified fibrinogen may alter the cross-linking of fibrin molecules differently than diluting the autologous fibrinogen solution, which contains additional proteins and clotting factors [5]. In practice, clinicians have a choice between using autologous derived fibrinogen or an off-the-shelf commercial product such as Tisseel. Autologous products are sometimes preferred to avoid complications with implanting allogeneic or xenogeneic materials, including adverse immune response and disease transmission. Although protein concentration of the autologous precipitate was variable, all 25% dilutions produced concentrations below the apparent threshold in Fig. 3. The minimal spreading and migration of MSCs in the undiluted commercial beads suggests that dilution is important to achieve MSC escape from this particular product. Durability of the dilute fibrin scaffolds may also be a primary concern. It has previously been shown that the fibrinogen concentration correlates with the shear strength [6], degradation rate in culture conditions [7] of fibrin beads. With the goal of populating a defect site with MSCs, however, it may not be necessary for the scaffold to endure a long implantation time, as escape was noted in the first 24 hours.

References

[1] Caplan AI, 1991. [2] Murphy JM, et al, 2003. [3] Pacini S, et al, 2007 [4] Tamer AE, et al, 2008. [5] Yoshida H, et al, 1999. [6] Glidden PF, et al, 2000. [7] Bensaïd W, et al, 2003.

Self-complementary adeno-associated viral vectors exhibit high efficiency in joint tissues depending on serotype selection

Take Home Message
Cell transplantation for the treatment of defects in cartilage, tendons and ligaments is a potentially important clinical tool. Genetic modification of cells prior to transplantation has shown to enhance healing. *Ex vivo* genetic modification of cells of joint tissue with various AAV serotypes has not been investigated. The transduction efficiencies of self-complementary AAV serotypes (1-6, 8) were determined in joint tissue containing chondrocytes and synoviocytes isolated from equine models. When comparing scAAV serotypes for efficient transduction ex vivo, in chondrocytes versus synoviocytes, serotypes 6 and 2, and serotypes 3 and 2, respectively, appeared superior for gene expression. Unlike adenoviral vectors, no up-regulation of inflammatory markers, such as matrix metalloproteinases and aggrecanase was seen upon treatment of joint tissue with AAV vectors ex vivo. Our findings also corroborate that ex vivo transduction of joint tissue can result in high transgene protein levels over time, and transplantation modalities might be feasible using AAV vectors in the treatment of joint-related diseases.

Introduction
Gene therapy for joint diseases relies on a non-immunogenic gene delivery vector that can efficiently and persistently transduce joint specific tissues (e.g. chondrocytes and synoviocytes). Recombinant adeno-associated virus (rAAV) is an emerging and

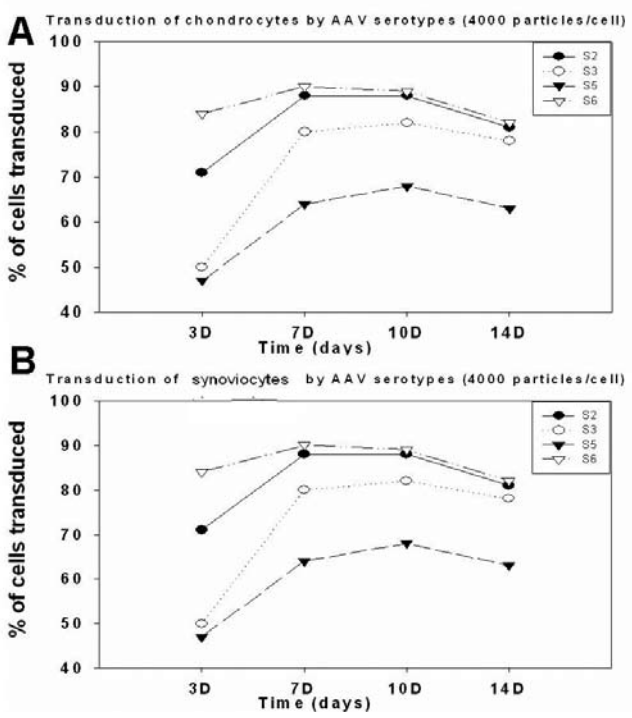


Figure 1. A&B Transduction efficiencies for chondrocytes (A) and synoviocytes (B) up to Day 14. Transduction efficiencies for 4 serotypes of AAV (2, 3, 5, and 6) in chondrocytes ranged from 48% to 90% on Day 3 (A) and 48% to 85% on Day 3 in synoviocytes (B). Transduction efficiencies rose at Day 7 and remained high at Day 14.

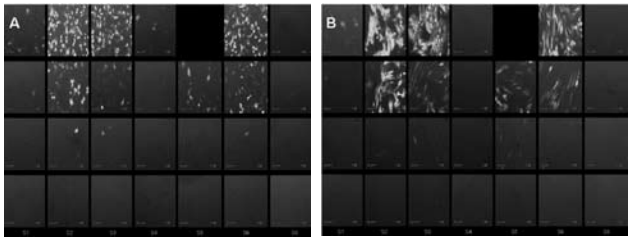


Figure 2. Fluorescence microscopy of chondrocytes (A) and synoviocytes (B) at Day 7 following transduction of AAVGFP serotypes 1, 2, 3, 4, 5, 6, and 8 (left to right) at 10,000, 1000, 100 and 10 (top to bottom) viral particles per cell.

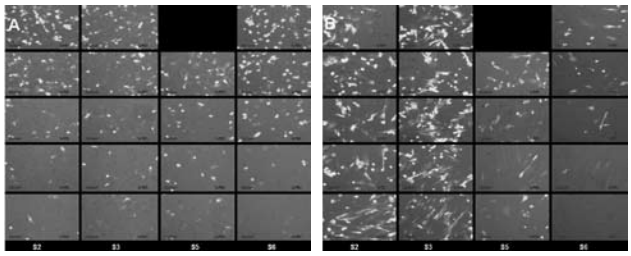


Figure 3. Fluorescence microscopy of chondrocytes (A) and synoviocytes (B) at Day 7 following transduction of AAVGFP serotypes 2, 3, 5 and 6 (from left to right) at 8,000, 4,000, 2,000, 1,000 and 500 (top to bottom). Both cell types transduced with AAV serotype 2 had slightly more rounded and crenated cells at Day 7 compared with the others. In chondrocytes, serotype 6 (A) and in synoviocytes, serotype 3 (B) appeared to have the best transduction with little to no variation of morphology of the cells. Furthermore, little variability existed between 8,000 and 4,000 viral particles per cell.

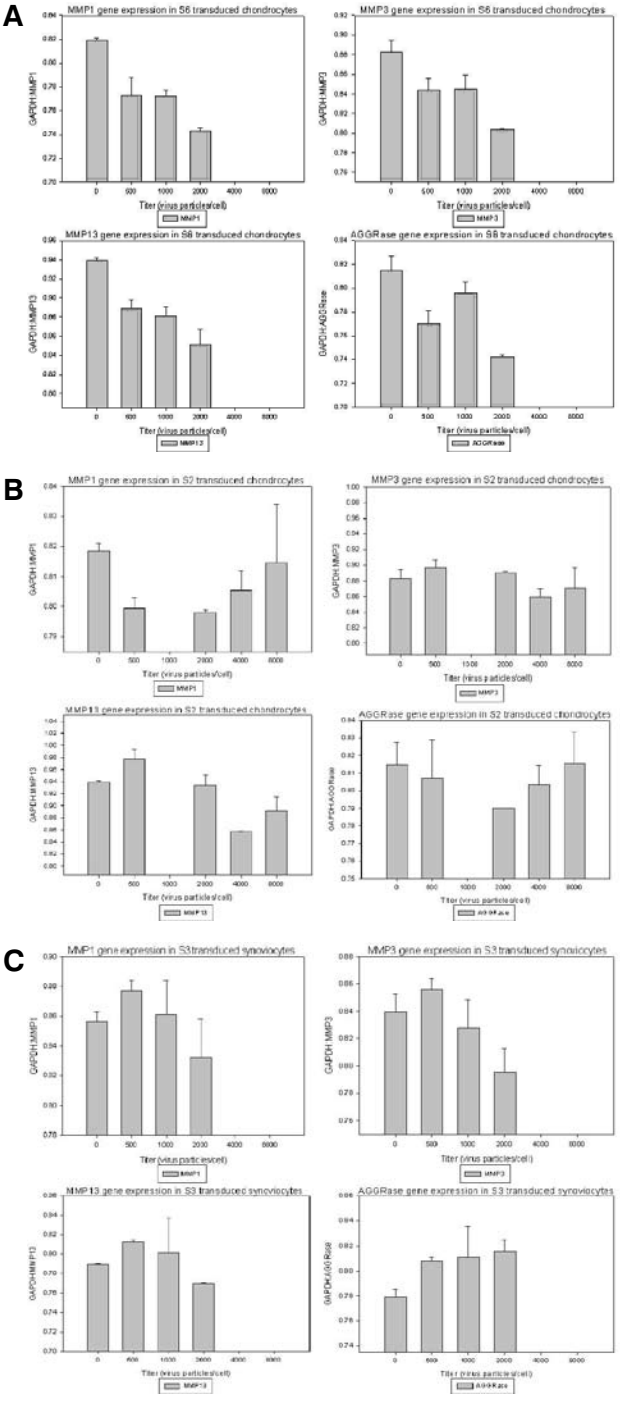


Figure 4. MMP-1, MMP-3, MMP-13, and Aggrecanase-1 expression in chondrocytes (A, B) and synoviocytes (C) transduced with AAVGFP serotypes 6 (A), 2 (B) and 3 (C) at increasing titers. No inflammatory effect was observed in serotypes 3 and 6 of increasing titer on either cell type. However, MMP-1 appeared to increase in expression with increasing titers while MMP-3, MMP-13 and Aggrecansase-1 did not with S2 (B).

promising vector for joint diseases due to its potential to efficiently express therapeutic genes for long periods of time and its purported low incidence of immune reactions and cell toxicity. With the increasing availability of different AAV-serotype vectors for tissue targeting, we investigated the best AAV serotype to deliver a self-complementary AAV (scAAV) genome to chondrocytes and synoviocytes for future gene therapy applications in joint diseases.

Materials and Methods

Chondrocytes and synoviocytes were harvested from joints of immature horses. Cell monolayers were cultured in a chondrogenic media. Two days after seeding, scAAV vector serotypes 1-6, and 8, carrying a GFP expression cassette were used to transduce cells in a dose-response manner. Fluorescence intensity was measured using a fluorometer and the number of transduced cells was measured by fluorescent microscope daily for a total of 10 weeks. Cell viability was determined using Trypan blue and vector toxicity was measured by quantitative PCR and relative gene expression of equine MMP-1, MMP-3, MMP-13 and Aggrecanase-1.

Results

Our results demonstrated that chondrocytes had a transduction efficiency of 48-90% at day 3 post-infection with scAAV serotypes 2, 3, 5, and 6 (Figure 1), as compared to <20% for scAAVserotypes 1, 4, and 8, respectively. In addition, prolonged gene expression was achieved with over 50% of chondrocytes remaining GFP-positive 6 weeks post-infection, which has not been previously demonstrated by other vectors used for this purpose. Similar results were obtained for synoviocytes as over 80% of cells remained successfully transduced by scAAV serotypes 2, 3, 5 and 6 two weeks post infection and 40-50% of cells continued to express transgene 6 weeks later. Cell viability of both chondrocytes and synoviocytes was determined to be over 80% throughout the course of the experiment and only S2 exhibited any elevations in expression of inflammatory molecules detected for the optimal serotypes determined.

Discussion
We established the use of specific scAAV serotypes for efficient tissue targeting with persistent transgene expression on mammalian chondrocytes and synoviocytes, which enhances the likelihood of successful gene therapy for joint diseases such as osteoarthritis and rheumatoid arthritis. Further investigation on animal models and clinical applications of our system will be developed for therapeutic uses.

This work was performed by Drs. Goodrich and McIlwraith, and Beth Carbone at the CSU ORC and Drs. Jude Samulski and Vivian Choi at the University of North Carolina. It has recently been published in Human Gene Therapy (December 2009).

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Funding
This study was funded by NIH 1K08AR054903-01A2 and the Colorado State University College Research Council Grant.

Osteoblastic differentiation of human and equine bone marrow-derived mesenchymal stem cells with combined bone morphogenetic protein 2 and 7 genetic modification in the presence and absence of dexamethasone

Take Home Message
Bone marrow-derived mesenchymal stem cells can be genetically modified to produce high amounts of BMP 2 and BMP 7 and potentially could be a novel method to aid bone healing. The genetic modification of these cells with both AdBMP2 and AdBMP7 (heterodimer) does not improve the osteogenic capacity of these cells over either homodimer (AdBMP2 or AdBMP7) alone and AdBMP2 seems to be the most effective homodimer to result in osteogenesis of these cells. Furthermore, dexamethasone supplementation appears to be important in furthering osteogenesis of BMP 2 or 7 equine stem cells and less important in human stem cells.

Introduction
Bone marrow-derived mesenchymal stem cells (BMDMSC) have been targeted for use in enhancement of bone healing.(1-4) Their osteogenic capacity can be further augmented by delivery of genes encoding bone morphogenic proteins (BMP's), growth factors important for skeletal development and bone growth, that has been shown to accelerate fracture healing clinically and in experimental models.(5-6) Previously, we have shown that BMP heterodimers, secreted when two BMPs are co-expressed, are more potent than their respective homodimer in a rodent spine fusion model.(7-8) For MSCs, on the other hand, dexamethasone is a known osteogenic supplement and has been demonstrated to induce early osteoblastic differentiation. Therefore, the specific aims of this project were to compare the effect of BMP-2, 7 and 2/7 genetic modification in the presence or absence of dexamethasone on the osteoblastogenic differentiation of human and equine BMDMSC.

Materials and Methods
The BMDMSC were harvested from the tuber coxae of three different human and horse patients and seeded in monolayer at 50% confluence. Two days after seeding, cells were transduced with 1.) AdBMP-2 (200,000 viral particles per cell (vpc)), 2.) AdBMP-7 (200,000 vpc), 3.) AdBMP-2 and -7 (100,000 vpc of each AdBMP-2 and -7), 4.) AdLacZ (a control vector encoding the marker gene β-galactosidease, at 200,000 vpc), or 5.) transduction media alone. Cells from each individual were then cultured in 1.) DMEM alone, 2.) DMEM with ascorbic acid phosphate (170 μM) and β-glycerol phosphate (5mM) or 3.) DMEM with dexamethasone (10-9 M). The assigned media was changed and the cells were evaluated for changes in cell morphology and viability every other day for a total of 14 days. Protein expression was directly measured with an ELISA for BMP-2 and BMP-7 on days 0, 4, 8, 10, and 14. Cells were stained for alkaline phosphatase and X-gal and evaluated for alkaline phosphatase activity using a *p*-nitrophenyl phosphate substrate on days 0, 8, 14. For statistical analysis, continuous data were analyzed using an ANOVA following log transformation of the raw data with a level of significance of $p < 0.05$.

Results
BMDMSC treated with AdBMPs exhibited BMP protein levels that were significantly higher than controls. The fold increase represents log data and the averages represent raw data. Human BMDMSC treated with AdBMP-2 and AdBMP-2/7 demonstrated a 4.5 (ave 1.7x106pg/ml) and 4.3 (ave 8.5x105pg/ml) fold increase in BMP-2 protein compared to controls, respectively. Human BMDMSC treated with AdBMP-7 and AdBMP-2/7 demonstrated a 4.5 (ave 3.0x106pg/ml) and 4.2 (ave 8.4 x105pg/ml) fold increase in BMP-7 protein compared to controls, respectively (Figure 1). Equine BMDMSC treated with AdBMP-2 and AdBMP-2/7 demonstrated a 4.1 (ave 9.9 x105pg/ml) and 3.8 (ave 5.0 x105pg/ml) fold increase in BMP-2 protein compared to controls, respectively (data not shown). Equine BMDMSC treated with AdBMP-7 and AdBMP-2/7 demonstrated a 7.1 (ave 1.1 x106pg/ml) and 6.7 (ave 4.2 x105pg/ml) fold increase in BMP-7 protein compared to controls, respectively.

Protein elution rates reached their maximal concentration between day 4 and 8 and declined thereafter (Figure 2).

Human BMDMSC treated with AdBMP-2 demonstrated significantly higher (14 fold increase) alkaline phosphatase levels compared to other treatment groups (Figure 3). Whereas equine BMDMSC treated with AdBMP-2 demonstrated significantly higher (1.7 fold increase) alkaline phosphatase levels compared to other treatment groups (Figure 3).

Additionally, equine BMDMSC cultured in media supplemented with dexamethasone demonstrated a 1.95 fold increase in alkaline phosphatase activity compared to media that did not contain dexamethasone, regardless of genetic modification. Alkaline phosphatase activity was significantly higher on day 14 compared to day 8. Alkaline phosphatase activity continued to increase in cells cultured in dexamethasone and remained relatively constant or showed a decline in the cells cultured in the media not supplemented with dexamethasone (Figure 4). Alkaline phosphatase activity was not affected in human BMDMSCs cultured in the presence of dexamethasone.

Discussion

In this in vitro cell culture study, genetic modification of BMDMSC enhanced osteogenic differentiation; however, AdBMP-2 appears to have the greatest effect in both human and equine BMDMSC. Furthermore, dexamethasone supplementation appeared to be important for the osteoblastic differentiation of both genetically modified and naive equine BMDMSC but not human BMDMSC. BMP protein expression data suggest that the ideal time to transfer these cells to a healing defect may be between day 4 and 8 of after transfection when they are secreting the highest amount of BMP protein. In the equine cells, the alkaline phosphatase activity continues to increase

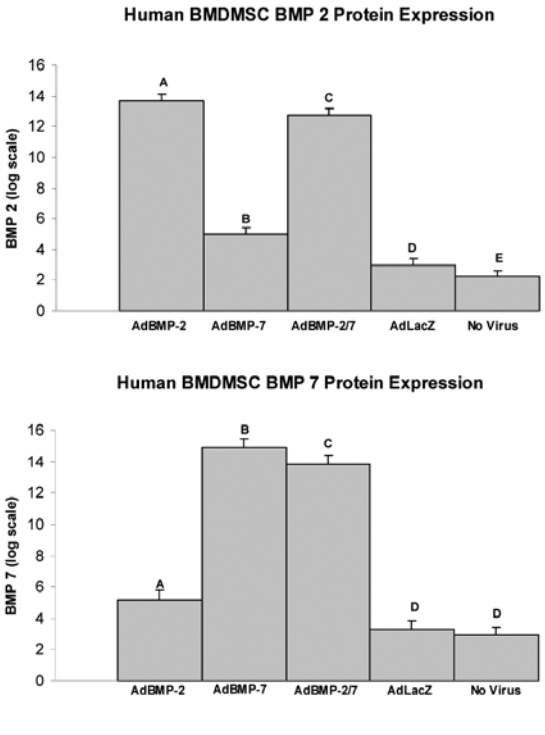

Figure 1. Protein elution rates measured with an ELISA for BMP-2 (top) and BMP-7 (above) for each of the 5 different human BMDMSC treatment groups. Different letters indicate significant differences ($P<0.05$) among groups.

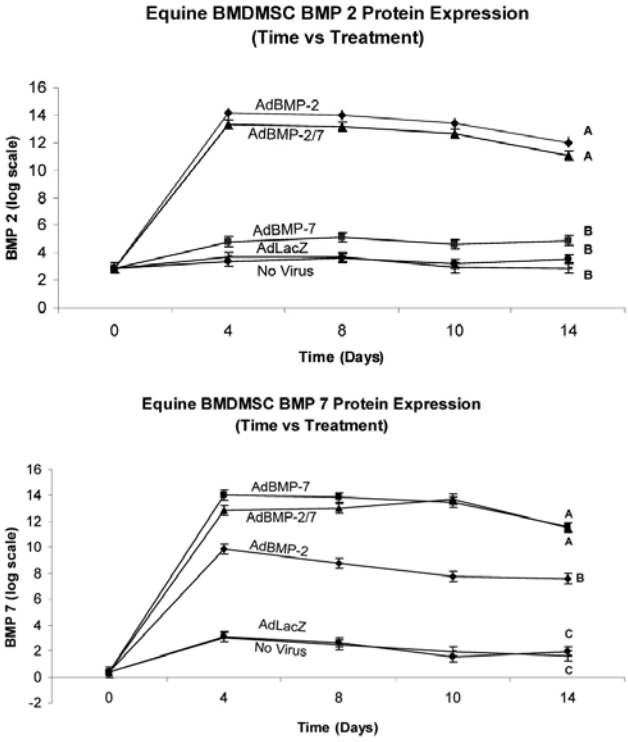

Figure 2. Protein elution rates for equine BMDMSC measured with an ELISA for BMP-2 (top) and BMP-7 (above) as a function of time for each of the 5 different treatment groups. The same letters are not significantly different.

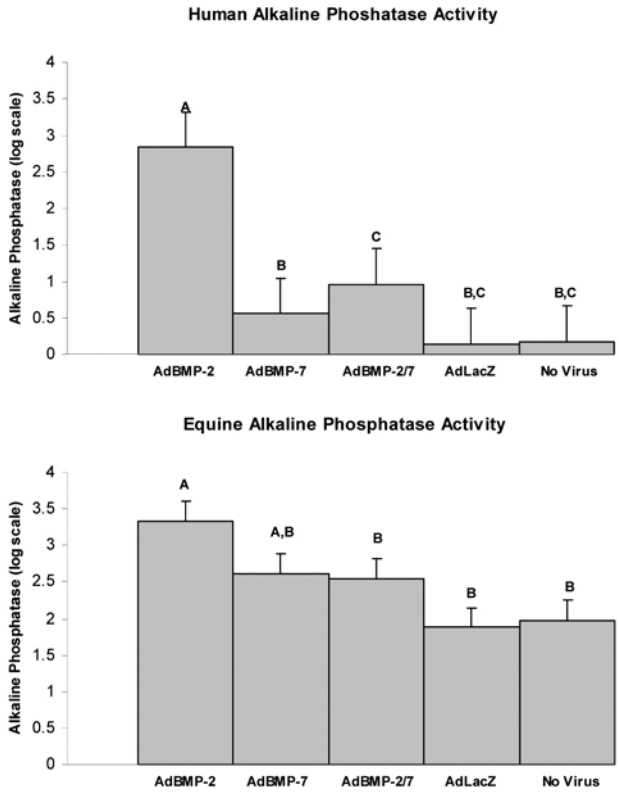

Figure 3. Alkaline phosphatase activity for genetically modified human (top) and Equine (above) BMDMSC for each of the 5 different treatment groups. Different letters indicate significant differences ($P<0.05$) among groups.

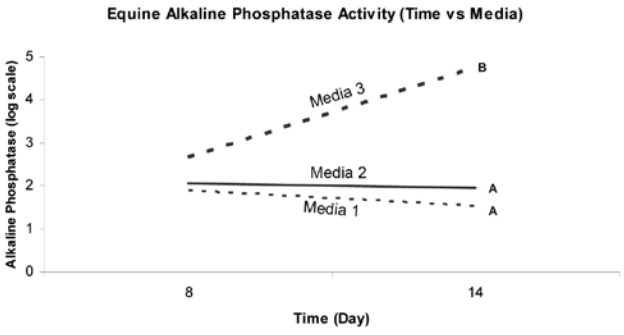

Figure 4. Alkaline phosphatase activity for equine BMDMSC for the different cell culture media as a function of time. Different letters indicate significant differences ($P<0.05$) among groups.

through day 14 in the presence of dexamethasone supplementation, therefore the addition of dexamethasone in the matrix surrounding these cells may be important when delivering them to a healing bone defect.

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Acknowledgements

Funding: Colorado State University CRC grant.

Lag screw fixation of dorsal cortical stress fractures in 116 racehorses

Take Home Message

Reasons for performing study: The effectiveness and best method to manage dorsal cortical stress fractures is not clear. This study was performed to evaluate the success of lag screw fixation of such fractures in a predominantly Thoroughbred population of racehorses.

Methods: One hundred and sixteen racehorses (103 Thoroughbreds) admitted to Equine Medical Centre, California between 1986 and 2008 were assessed. Information obtained from medical records included signalment, age, gender, limb(s) affected, fracture configuration, length of screw used in repair and presence of concurrent surgical procedures performed. Racing performance was evaluated relative to these factors using Fisher's exact test and non-parametric methods with a level of significance of $P<0.05$.

Results: Eighty three per cent of horses raced preoperatively. Eighty three per cent raced post operatively, with 62% having five or more starts. There was no statistically significant association between age, gender, limb affected, fracture configuration or presence of concurrent surgery, and likelihood of racing post operatively or of having 5 or more starts. The mean earnings per start and the performance index for the three races following surgery was lower compared to the three races prior to surgery; however 31% and 43% of horses either improved or did not change their earnings per start and performance index respectively.

Conclusions and potential relevance: Data show that lag screw fixation is successful at restoring ability to race in horses suffering from dorsal cortical stress fractures. Ninety five per cent of horses were able to race for at least 12 months without re-fracture.

Introduction

Dorsal metacarpal disease (DMD) is the accepted term for the range of pathologic change clinically manifested as pain over the dorsal aspect of the metacarpal diaphysis. The dorsal cortex of the third metacarpal bone (MCIII) experiences high strain loads in the young racehorse, with resultant modelling and remodelling. Pain and inflammation of this dorsal cortex ("bucked shins") is a frequent condition seen in young Thoroughbred racehorses (Boston and Nunamaker 2000; Verheyen *et al.* 2005). This pain and inflammation arises from the formation of new periosteal bone in response to the decreased bone stiffness that arises from high-strain cyclic fatigue. Dorsal cortical stress fractures are typically seen months after an initial episode of DMD in horses experiencing high-strain cyclic loading on inadequately remodelled bone. Failure of this bone occurs, usually manifested as an incomplete stress fracture, or less commonly as catastrophic midshaft fractures (Nunamaker 1996).

Several techniques have been described to manage dorsal cortical stress fractures including osteostixis (Cervantes *et al.* 1992; Dallap *et al.* 1999; Nunamaker 1996; Richardson 1984; Specht and Colahan 1990; Sullins 1989) Unicortical lag screw fixation of such fractures does not appear to be the accepted method of treatment. In one of the author's experience (C.W.M.), horses treated with lag screw fixation continue to race at a similar or higher level than previously. The objective of this study was to determine the racing success of racehorses with dorsal cortical stress fractures treated with lag screw fixation. Our hypothesis was that the majority of horses would successfully return to racing following lag screw fixation.

This study evaluated retrospectively the effectiveness of the lag screw fixation of such fractures in a predominately Thoroughbred population of horses. One hundred and sixteen racehorses (103 Thoroughbreds) operated by Dr. McIlwraith and admitted to Equine Medical Center, California between the years 1986-2008 were accessed.

Materials and methods

Medical records

The medical records of racehorses undergoing lag screw fixation for treatment of one or more dorsal cortical stress fractures between 1986 and 2008 were reviewed. A dorsal cortical stress fracture was defined as one or more oblique fracture lines radiographically evident in the dorsal cortex of the third metacarpus.

Information obtained from medical records included subject details (breed, age, gender), limb(s) affected, fracture configuration, number and length of screw used in the repair and concurrent surgery performed.

Surgery
Horses were placed under general anaesthesia, positioned in dorsal recumbency, and the limb prepared for aseptic surgery. Needle placement under radiographic guidance was used to ascertain the ideal positioning of the screw. A 1-2cm incision was made, retracting the extensor tendons as necessary, and a 4.5 mm hole drilled until the fracture line was crossed, usually for a distance of approximately 8mm. A 3.2mm hole was drilled beyond this, and the hole countersunk and tapped. A 4.5mm diameter screw was placed to the depth determined with the depth gauge, usually around 20mm in length, compressing the fracture. The incision was closed with skin sutures of size 3 nylon (Ethilon1), and a sterile bandage placed on the limb.

Results
One hundred and sixteen horses had a dorsal cortical fracture repaired by lag screw fixation. Of these, 103 were Thoroughbreds, 9 were racing Quarter horses, 3 were racing Arabians and 1 a racing Appaloosa. Fifty one horses (44%) were colts, 46 (40%) were fillies and 19 (16%) were geldings. The left forelimb (LF) was most commonly affected in 77/114 of horses (68%), the right forelimb (RF) was affected in 31/114 horses (27%), both forelimbs were affected in 6 horses (5%); the affected limb was unrecorded in 2 horses. Ninety two horses (79%) were considered to have fractures consistent with that of a "typical" dorsal cortical stress fracture (i.e. extending in a proximopalmar direction from the dorsolateral cortex of MCIII, and occurring in the middle one third of the bone or at the junction of the distal one third and proximal two-thirds of the bone). Ninety- six horses (83%) had lag screw fixation of the fracture as the only surgical procedure performed; sixteen horses (14%) had concurrent arthroscopic surgery of one or more joints performed, one horse was castrated, one horse concurrently received surgical treatment of proximal suspensory desmitis, two horses had osteostixis performed on stress fractures of the opposite forelimb. Ninety five fractures (82%) were repaired with a single lag screw of a length between 18-24mm.

All fractures appeared to have healed radiographically when examined at 60 days.

Of the 103 Thoroughbreds, 11 horses suffered re-fracture at the original site and underwent a second surgery. The remaining 92 Thoroughbreds that suffered from one fracture only were followed for a minimum of 12 months. Within this population 43 horses (47%) were colts, 37 (40%) were fillies and 12(13%) were geldings. Median age was 3 years (range 2-7 years). The LF was again most commonly affected (70%). Seventy three Thoroughbreds (79%) had typical fracture configuration.

Of the 11 horses that suffered re-fracture the median time between surgeries was 336 days (range 107-678). Eight horses re-fractured the same limb (5 LF, 3 RF), one horse fractured the opposite limb, and two horses suffered bilateral fractures after originally fracturing the right forelimb.

Of the 92 Thoroughbreds that had only one fracture operated on, 76 (83%) had raced pre-surgery and 76 (83%) raced post operatively, with 57 (62%) having 5 or more starts. There was no significant association between racing post-operatively and age group, gender, affected limb, concurrent surgical procedures performed or fracture configuration. There was no significant association between having 5 or more starts post-operatively and age group, gender, affected limb, concurrent surgical procedures performed or fracture configuration.

Forty-two horses had at least 3 races before and after surgery. The mean earnings per start for those 3 races pre-surgery was $9857, median $6320 (range $287-45,427) and for the 3 races post-surgery was $5688, median $2553 (range $0-52,647)(P=0.015). Thirteen of 42 (31%) horses improved, or did not change, their earnings in the three races post surgery compared with pre-surgery. The mean performance index for the 3 races pre- and post surgery were 1.25 points, median 1.33 points (range 0-3) and 0.75 points, median 0.5 points (range 0-3) respectively (P=0.008).

Eighteen of 42 (43%) either improved (n=11) or did not change (n=7) their performance index post-surgery compared with pre-surgery.

The mean number of starts pre-operatively was 4.68, median 3 (range 0-20). The mean number of months from surgery to first start for all horses that raced post-operatively was 11.3, median 10 months (range 3-36 months). There was no significant association between age and months to first start (P=0.17). Females and males had statistically similar numbers of months to first starts; additionally, the limb affected, presence of concurrent surgery and fracture configuration did not affect time to starting. The mean number of starts after surgery was 10.4, median 7.5 (range 0-50). Older horses and female horses had a lower number of total starts post-operatively; however the difference was not statistically significant. Limb affected, presence of concurrent surgery and fracture configuration had no statistically significant affect on total number of post-operative starts. The mean earnings for the post-operative period were $58,231, median $17,803 (range $0-1,247,744). Older horses, females, horses having concurrent surgery and horses with a fracture of the right forelimb had lower post-operative total earnings; the difference was not statistically significant.

Seventy six horses started after surgery. Within this group the mean number of starts after surgery was 12.5, median 9.5 (range 1-50) and the mean earning after surgery was $70,490, median $34,810 (range $153-1,247,744). Only gender was significantly associated with total starts (P=0.026).

All eleven horses that underwent a second surgery due to re-fracture raced again after the second surgery. Seven (64%) had five or more starts. The mean number of months from surgery to racing was 11, median 11.5 months (range 5-16 months). The mean total number of starts post-operatively was 11, median 9 (range 4-29). The mean total earning post-operatively was $92,443, median $28,735 (range $4,033-266,366). There was no significant difference in time to race and post-operative number of starts or earnings between these horses and those in which no re-fracture had occurred.

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Summaries: Focus 2

Early Diagnosis of Bone and Joint Disease

A new technique for examination of the suspensory ligament using ultrasound

Take Home Message

Ultrasound of the suspensory ligament with the carpus flexed and using an oblique angle of incidence allow differentiation of the fat and muscle within the normal suspensory ligament. This technique will aid in the accurate diagnosis of suspensory ligament injury with ultrasound sound.

Background

Injury to the suspensory ligament is a common condition affecting horses of different ages and disciplines.[1-2] Lameness is often localized to the suspensory ligament region using local infiltration of analgesia around the ligament or perineural analgesia.[3] Once injury of the suspensory ligament is suspected based on the clinical examination and response to analgesia, diagnostic imaging of this region is often performed. Radiography can be used to evaluate the bone fof sclerosis, lysis, proliferation or avulsion fracture at the attachment of the suspensory ligament.[4-5] Ultrasound has traditionally been the imaging modality of choice for diagnosis of suspensory ligament injury. The technique has been described and places the ultrasound probe of the palmar surface of the limb with the beam oriented perpendicular to the longitudinal axis of the fibers.[6] This ligament contains areas of muscle and adipose tissue as a result of the normal anatomy.[7] Variation in the echogenicity of the ligament is present due to the acoustic properties (how much a tissue reflects or absorbs the sound beam from the ultrasound machine) of the different tissues. No evidence of ligament damage on ultrasound images or overlap in the appearance of the normal anatomy and areas of pathologic change makes definitive diagnosis of the suspensory ligament injury difficult.

Magnetic resonance imaging provides excellent soft tissue detail. This modality is the most sensitive for detecting changes in the fluid content of tissue and is the gold standard for imaging of musculoskeletal injury. This modality is expensive, and accurate imaging of the suspensory ligament due to the complex anatomy requires the MR study be performed under general anesthesia. Improvement in the current ultrasound technique could allow additional diagnoses of suspensory ligament injury to be made without the additional expense and risk of anesthetic related complications.

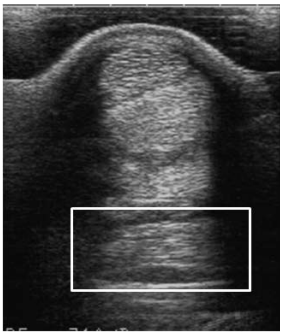

Figure 1. Transverse ultrasound image made using the current technique with ultrasound probe perpendicular to the ligament fibers in a weight-bearing limb. Palmar or the back of the leg is at the top of the image. The suspensory ligament is demarcated by a white rectangle. This ligament appears as a echogenic rectangular shaped structure with hypoechoic areas. The margin of the cannon bone is the white line just inside the bottom line of the rectangle.

The current technique for ultrasound of the suspensory ligament creates an image which causes to the suspensory ligament to appear as a rectangular shaped echogenic structure (Fig. 1).

This new ultrasound technique is performed with the limb mildly flexed at the carpus. This allows digital manipulation of the flexor tendons and the probe can be place directly over the suspensory ligament allowing visualization of the entire ligament. The decreased distance between the probe and ligament allows use of a higher frequency resulting in increased detail. The suspensory ligament is first imaged with the beam perpendicular to the long axis of the ligament creating an echogenic appearance (Fig. 2). The ultrasound beam is then angled obliquely relative to the long axis of the suspensory ligament (Fig. 2). This causes the margins of the suspensory ligament to become evident. The surround connective tissue remains bright. The ligament fibers become dark. The adipose tissue remains bright. The muscle becomes dark, but not as dark as the ligament fibers.

The ease and practicality of ultrasound compared to MRI makes the clinical use of ultrasound much more common. Current techniques of ultrasound appear to have poor correlation with tissue character based on preliminary MRI and histologic analyses. Our goal was to validate this improved technique for accurate ultrasonographic identification of suspensory ligament anatomy taking the first step in facilitating the accurate use of ultrasound for diagnosis of suspensory ligament injury. This work was done by Drs. Dave Frisbie and Natasha Werpy.

Methods and Materials
Ultrasound exams were performed on 12 horses using both the traditional technique and an oblique angle of incidence. Following examination with ultrasound, MRI was performed. The distribution of fat and muscle as well as the size, shape and margins of the suspensory ligament was analyzed on both modalities. Histology was performed to identify the fat and muscle distribution on the suspensory ligament at various levels and was compared to what was identified with imaging.

Results
Ultrasound using an oblique angle of incidence more accurately identified the anatomy of the normal suspensory ligament compared to the traditional technique. The images with ultrasound using an oblique angle of incidence more closely represented the anatomic detailed obtained with MR images when compared to the traditionally technique. Ultrasound examination of the suspensory ligament using an oblique angle of incidence with the carpus flexed will facilitate the diagnosis of suspensory ligament injury by allowing identification of the normal anatomy which can be differentiated from injury.

Acknowledgements
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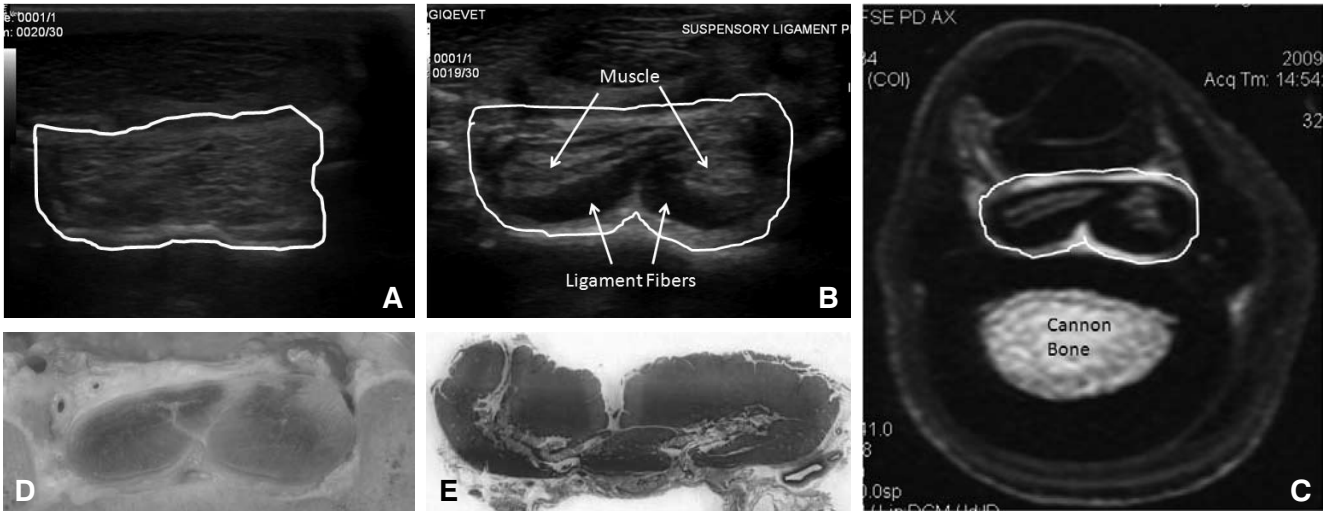

Figure 2. Transverse ultrasound (A,B), MRI (C), gross (D) and histologic (E) images of the suspensory ligament. A-D are images of the same ligament which is demarcated by the circumferential white line, E is from a different horse. Image A is made with the limbs in non-weight bearing position with the probe perpendicular to the ligament. Image B is a made at the same level as image A, but the probe is now oriented obliquely to the suspensory ligament. The ligament fibers are hypoechoic (dark gray). This horse has primarily muscle in the lobes of the ligament and is echogenic compared to the ligament fibers. The ultrasound image made with an oblique beam angle appears similar to the MR image, with a clear delineation of the ligament margins as well as the ligament fibers compared to Figure 1. These two images (B,C) correlate well with the gross image (D) and provide an accurate representation of the anatomy. The histology slide (E) shows how the Masson's trichrome stain allows visualization of the tissues, with the ligament fibers in blue, the muscle in red and the adipose tissue is clear. The histology slide show a different distribution of fibers, muscle and adipose tissue compared to the images A-D.

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Magic angle effect in normal collateral ligaments of the distal interphalangeal joint in horses imaged with a high-field magnetic resonance imaging system

Take Home Message
The magic angle effect can be identified in the collateral ligaments of the distal interphalangeal joint when imaged in a high field magnetic resonance imaging system with a horizontally oriented main magnetic field. Magic angle effect should be considered as a possible cause of an asymmetrical signal pattern, depending on the positioning of the limb and the sequences used for imaging, when evaluating the collateral ligaments of the distal interphalangeal joint on images acquired with a high field magnetic resonance imaging system that has a horizontally oriented main magnetic field.

Background
The magic angle effect has been described in the distal aspect of the deep digital flexor tendon in high-field systems and in the collateral ligaments of the distal interphalangeal joint in low field systems.[1,2] This effect results in fibers of tendon and ligaments oriented at 55 degrees ±10 degrees, or any interval of this such as 125 degrees, 235 degrees, 305 degrees, from the main magnetic field to exhibit increased signal because dipole interactions have been minimized allowing signal to be produced from the tissue.[3,4] The increased tendon and/or ligament signal can be confused with disease. The magic angle effect occurs circumferentially around the central axis of the magnet, creating 2 cones in opposite directions. Any fibers which align along the cone margins are susceptible to the magic angle effect. The purpose of this study was to evaluate the signal intensity of normal collateral ligaments of the distal interphalangeal joint when imaged in high field system with a horizontally oriented main magnetic field. This work was done by Drs. Chris Kawcak and Natasha Werpy.

Methods and Materials
Distal forelimb specimens of eight skeletally mature horses with no history of lameness were imaged in high field MR using short and long TE sequences with the limbs at different angles relative to main magnetic field to demonstrate the influence of magic angle effect on the signal intensity of these ligaments. The asymmetry of the signal intensity between the medial and lateral the collateral ligaments of each foot was graded subjectively as none, slight, mild, moderate and severe (0-4). All data were analyzed using SAS 9.2 (SAS, Cary, NC). The linearity of the averaged angle-by-score relationship was evaluated for each sequence to determine appropriate statistical models. A mixed models analysis for repeated measures was used for analysis of the asymmetry scores and mean signal intensity. Sequence, angle and the interaction between the two were included in the model. $P<0.05$ was considered to be significant. Subjective analysis comparing the collateral ligaments of the limbs imaged on both the 1.0 and 1.5 Tesla systems was performed. The purpose of this analysis was to determine if the difference in field strength affected the degree or distribution of the altered signal intensity that was present following angulation of the limb in the dorsal plane relative to the central axis of the main magnetic field.

Following imaging, the limbs were sectioned (5mm) with one collateral ligament cut in the transverse plane and the other in the dorsal plane relative to the long axis of the ligament and evaluated for gross abnormalities. Fiber orientation and ligament margins were measured on the dorsal plane sections. These measurements were correlated with the signal pattern on the various sequences to determine the possibility of magic angle effect based on fiber orientation. One collateral ligament was stained with hematoxylin and eosin for descriptive histologic assessment.

Results
In a neutral position the long axis of the limb was parallel to the main magnetic field and the medial and lateral aspects of the limb were equidistant from the interior surface of the magnet bore. In the neutral position the collateral ligaments were symmetrical in size, shape and signal intensity. The signal pattern was variable when comparing limbs

Following a change in position of the limb relative to the main magnetic field, the signal intensity pattern of the collateral ligaments was no longer symmetric (Fig. 1). When compared to the appearance in the neutral position, increased signal intensity was identified in one of the collateral ligaments on proton density, T1-weighted SPGR, T2*-weighted GRE and to a lesser extent on STIR images. The degree of asymmetry was dependent on the angle of the limb relative to the main magnetic field. This pattern was present at both 1.0T and 1.5T. Subjective evaluation of the degree of alteration in the signal pattern based on the angle to the limb was similar when comparing the two field strengths.

The scores of asymmetry obtained at 4, 8, 12, 16 and 20 degrees on the proton density TSE, T1-weighted SPGR, and STIR sequences are significantly different than the asymmetry score obtained at 0 degrees with the difference between ligaments being greatest at 8, 12, and 16 degrees. The scores of asymmetry obtained at 8, 12, 16 and 20 degrees on the T2*-weighted GRE sequence are significantly different than the asymmetry score obtained at 0 degrees with the difference between ligaments being greatest at 8, 12, and 16 degrees (Table 1). The scores of asymmetry obtained at 12, 16, and 20 degrees on the T2 FSE sequences are significantly different than the asymmetry score obtained at 0 degrees (Table 1).

The mean signal intensity at angles 4, 8, 12, 16, 20 on the proton density TSE, T1-weighted SPGR, T2*-weighted GRE and STIR sequences is significantly different from the signal intensity at 0 degrees (Fig. 4). In certain limbs the effect of angle began to reverse at 20 degrees and with others the signal intensity continued to increase. There was no statistically significant difference in the mean signal intensity of the ligaments on the T2-weighted FSE images.

Evaluation of the gross specimens confirmed that the fibers in the collateral ligaments of the distal interphalangeal joint can align with the magic angle at the level of the middle phalanx. There were variable fiber patterns in the collateral ligaments at the level of the middle phalanx with variations in the fiber patterns among the different specimens. The range of the fiber orientation at the level of the middle phalanx measured between 24 and 82 degrees relative to the long axis of the limb. At this level the ligament margins measured between approximately 40 and 70 degrees.

Discussion

Based on this study, the magic angle effect can be present with the limb in a neutral position, parallel to the central axis of the main magnetic field, as well as with angulation of the limb. The medial and lateral collateral ligaments in this study had symmetric signal intensity with the limb a neutral position. The signal pattern of the ligaments was variable between limbs, as we have observed clinically. The effect can be seen in the collateral ligaments at the level of the middle phalanx when imaged using short TE sequences and depends on both the gross ligament alignment and the major fiber bundle orientation pattern and alignment relative to the main magnetic field. An asymmetric signal pattern will result in the collateral ligaments if the limb is not parallel to the main magnetic field. The magic angle effect may compromises the ability to detect certain types of disease in these structures. Further investigation is required to evaluate fiber bundle patterns and orientation in normal collateral ligaments as well as disease in the collateral ligaments so these findings can be correlated with magnetic resonance and histologic imaging. Awareness of magic angle effect in the collateral ligaments of the distal interphalangeal joint is important when assessing images of equine feet for diagnosis of injury.

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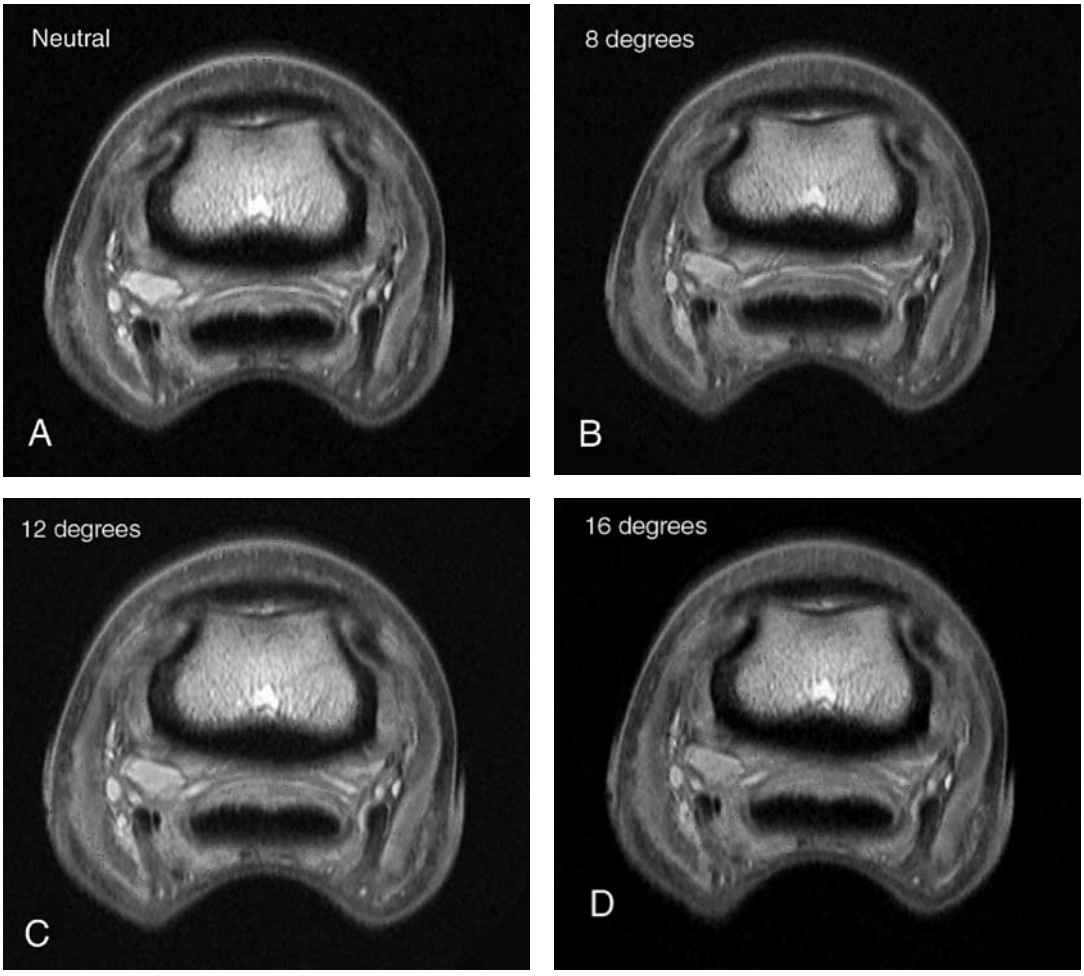

Figure 1. Transverse proton density images (1.0 T) of a limb in a neutral position (A) and then angled 8 (B), 12 (C) and 16 (D) degrees in the dorsal plane relative to the central axis of the magnet. The signal intensity in the medial collateral ligament (left side of image) gradually increases with increasing angle. The area of low signal intensity in the lateral collateral ligament (right side of the image) increases in size. The change in angle places more fibers in the medial collateral ligament closer to 55 degrees increasing the magic angle effect while moving the lateral collateral ligament further away and decreasing the magic angle effect that is present with the limb in a neutral position. The signal intensity of the collateral ligaments is asymmetric on the corresponding T2-weighted FSE image angled 12 degrees in the dorsal plane relative to the central axis of the magnet (E). The medial collateral ligament (left side of image) did not increase in signal intensity compared to the neutral position on the T2-weighted FSE image. However, the lateral collateral ligament (right side of the image) has a larger area of low signal intensity (arrow) compared to neutral. This signal intensity pattern in the lateral collateral ligament is similar to what is present on the proton density image (C) and creates an asymmetric appearance between the ligaments without any signal increase in the ligament at the magic angle.

Summaries: Focus 2

Early Diagnosis of Bone and Joint Disease

Serum biomarkers and prediction of injury in racing Thoroughbreds – where we are so far

The following manuscript will describe the history of serum biomarker analysis (for estimations and predictions of injury at the Orthopaedic Research Center (ORC) at Colorado State University (CSU). Investigators at the ORC first started their research work in biomarkers in the early 1990's with a study that assessed clinical cases of osteochondral fragmentation in the knee compared to a controlled population of horses that were found to be free of lameness and osteochondral fragmentation. In this study the retrospective use of serum biomarkers to discriminate these two populations part of the design. Eight horses were used as control and 26 clinical cases were considered the injured population. Serum markers 846, CPII, keratin sulfate as well as the degree of arthroscopic articular cartilage damage were recorded for each horse. The results of the study showed that serum levels of 846 and CPII were significantly elevated in horses that had osteochondral fragmentation. Serum CPII and 846 levels were also found to have a quadratic relationship to cartilage damage assessed arthroscopically. Finally, through the use of step-wise model selection it was found that serum CPII and 846 provided the best overall prediction of which group, injured or uninjured, the horse fell into. Using discriminate analysis the overall error rate was 20.6% which was felt to be an acceptable level for this pilot study.

From here the investigators undertook a randomized blinded experimental study where non-exercising horses underwent controlled exercise and then they either had a sham surgery or induction of OA. The goal of this study was to evaluate the synovial fluid and serum markers induced by exercise as well as the increases induced from experimental osteoarthritis (OA). The hope of this study was that biomarkers that increased with exercise could be differentiated from those that increased with pathology (OA). Outcome parameters that were measured were glycosaminoglycan (GAG), 846, CPII, 2-3/4CEQ, C1- 2C, osteocalcin and CTX1. The results of this study indicated that many of the biomarkers were significantly increased with exercise alone as well as a continued elevation with superimposition of experimental osteoarthritis that could be differentiated from the increase seen with exercise. The specifics of these results will be presented in the oral presentation.

Next the investigators undertook a longitudinal clinical prospective study in racing Thoroughbred horses to determine the mean biomarker levels prior to and after injury. Levels were compared to those horses that were in the study and did not incur an injury. The main goal was to be able to assess the predictive value of serum biomarkers prior to an injury occurring. The design of this study included 238 Thoroughbred racehorses that began their 2- or 3-year old race season. The exit criteria were defined as a horse that was out of training for > 30 days or had completed 10 months of the study and had not sustained an injury. All horses had to complete at least two months in the study to be considered. The injury criteria that were analyzed were only horses with a solitary musculoskeletal injury. More specifically a musculoskeletal injury was defined as intraarticular fragmentation, tendinis or ligamentous injury, stress fractures or dorsal metacarpal disease. All horses entering the study had a monthly lameness examination as well as serum collected for analysis of the seven biomarkers as previously mentioned in the experimental OA study. The analyses that were performed looked at the mean values both at entry into the study as well as after injury and the longitudinal data throughout the study. A specific study to look at the prediction of injury using pre-injury longitudinal data was also undertaken. The results of this study yielded 59 injured horses and 71 uninjured control horses that meet the previously define criteria. Sixteen horses were diagnosed with a solitary intraarticular fragmentation, 17 tendinis/ligamentous injuries, 7 stress fractures and 19 with dorsal metacarpal disease. The baseline marker levels, where uninjured or control horses were compared to the injured group, only yielded a significant difference in one biomarker.

When endpoint samples, or post injury and/or the final sample of control horses were compared no significant differences were seen. When longitudinal samples were compared leading up to injury significant changes were seen for all of the injury types. These changes were typically 3-6 months prior to the time of injury or exit from the study. Using these data standard discriminate analysis was undertaken as well as logistic regression. These techniques were found to be only 50-60% accurate in predicting which group, injured or uninjured, that the horse was in. This level of accuracy was felt by the investigators to be unacceptable and more sophisticated statistical methods were applied.

Kallie Meek, a master's graduate student in the Department of Statistics at CSU, was enlisted to help assess novel methods for analyzing these types of data. As part of her Master's thesis she was able to describe a local alignment kernel that improved the ability to analyze the data. This data was then analyzed using discriminate analysis, logistic regression and support vector machines. The results of her work using the local alignment kernel, which is a methodology analogous to provide alignment of disparate DNA sequences, also allows the degree of alignment to be quantified. Specifically, each horse, the number of months each horse was in the study, the specific results of each biomarker per month were analyzed for each horse. There were 130 horses, every horse was then compared to every other horse to create a 130 X 130 matrix of comparisons. The results showed that the alignment scores were significantly higher for uninjured horses when compared to other uninjured horses. While an uninjured horses compared to an injured horses had a lower alignment scores. Using the local alignment kernel, discriminate analysis was now repeated on the data and found to be 73.1% accurate with an average apparent error rate (APER) of 26.9%. Logistic regression had a 72.9% accuracy rate with a 27.1% APER. Finally support vector machines had the best accuracy at 73.9% and lowest APER at 26.2%.

The conclusion of this statistical exercise showed that a local alignment kernel was a very useful tool in dealing with this type of data. Discriminate analysis and logistic regression require step-wise selection of variables that are significant to model prediction and are very sensitive to multi-dimensional comparisons. Therefore, they do not yield themselves to this type of data analysis when large numbers are present. Support data machines provided the best accuracy in this data set and the lowest error rate, with no multi-dimensional sensitivity and thus appeared to be the best method for prediction models.

With this information in hand the investigators launched another longitudinal clinical prospective musculoskeletal disease study, this time using a population of reining horses. This population was selected, because unlike the Thoroughbreds, a varied exercise protocol would be implemented by different trainers. Although similar to the Thoroughbred racehorses they would have set target or show dates when the horses would be performing and thus defined endpoints that could be used for monitoring. In this particular study the addition of molecular markers was undertaken based on previous work at the ORC. The design of this study and the preliminary outcome will be presented in another manuscript.

In conclusion, work completed thus far at the ORC has shown promising results for serum biomarker levels and their ability to predict injury prior to its occurrence. This work has been advanced by more sophisticated statistical modeling that takes into consideration specific issues and challenges that are encountered with this type of data. The commercial application of these data are currently being undertaken.

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Effects of joint surface geometry on fetlock joint disease

Background
Catastrophic injury continues to plague horse racing and has now stimulated congressional oversight of the industry. Musculoskeletal injuries are the most common reason for euthanasia in racehorses. In the United Kingdom, distal limb fractures of the lateral condyle of the third metacarpal bone are the most common. In the U.S. only sesamoid fractures are more frequent than condylar fractures.[1-3] (Figure 1) Pathologic studies have shown that condylar fractures can be chronic in nature due to chronic repetitive loading and inappropriate bone remodeling.[4-7] Consequently methods to diagnose fatigue fractures prior to a complete catastrophic event is necessary. However, most imaging techniques today fail to identify preclinical injuries.

One form of imaging analysis that may be useful is that which assess the geometrical properties of the joint. In human studies, small geometric changes in the knees, such as lateral condyles with distal and posterior flattening, have been correlated directly with osteoarthritis.[8] Based on this information, the goal of this study was to determine differences in geometric properties between fractured and non-fractured joints of the same horse and compare those results to horses that were euthanized for non-musculoskeletal problems. The hypothesis was that horses that had sustained condylar fractures will have significant changes in the lateral-to-medial dimensions and curvature of the third metacarpal condyles compared to horses that did not fracture.

Methods and Results
Computed tomographic scans were obtained from a large epidemiologic study in the United Kingdom. A total of 192 condyles underwent computed tomographic imaging. Fifty one condyles were from the fractured limb of the horse (FX), 61 condyles were from the contralateral non-fractured limb from the fractured horse (NFX), and 80 condyles were from horses that were euthanized for non-musculoskeletal reasons (CTL). A custom-designed software package was used to reconstruct the condyle images into a three dimensional model. Using this model condylar width, condylar curvature, and surface area of each condyle were determined.

The lateral-to-medial width ratio was significantly different between FX and CTL condyles in almost all locations (Figure 2). In particular, the magnitude of difference was greatest in the palmar aspect of the joint. In addition, the lateral-to-medial ratio was significantly lower in NFX condyles compared to CTL condyles in two of the dorsal sites only. In addition there was significantly smaller lateral-to-medial ratio in the FX condyles compared to the NFX condyles over the entire palmar aspect of the condyles. Curvature in fractured cases was significantly higher in the palmar lateral parasagittal groove compared to NFX and CTL samples. For surface area ratio, the ratio of lateral to medial surface area was significantly lower in FX condyles compared to NFX and CTL.

The results of this study show that condylar width varies significantly between fractured condyles and non-fractured condyles. In particular, the lateral condylar width is significantly smaller in fractured condyles compared to non-fractured and control condyles in the palmar aspect of the joint. This difference in geometry may lead to excessive stress and fatigue in the lateral condyle of fractured horses. In addition, the ratio of curvature was higher, particularly in the

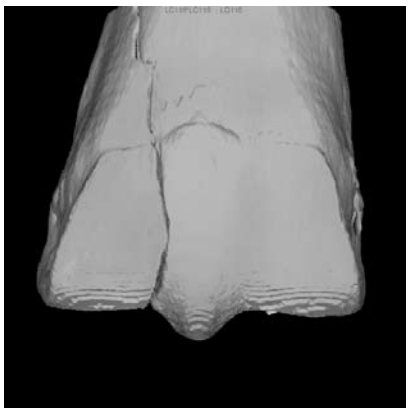

Figure 1. A CT image of the distal cannon bone within the fetlock of a horse that suffered from a condylar fracture.

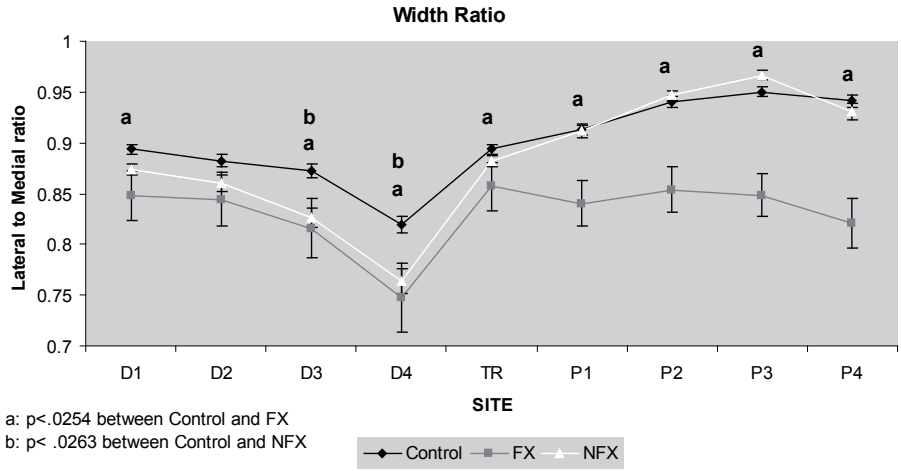

Figure 2 – Means and standard errors for lateral to medial ratio in the third metacarpal condyle of CTL, FX, and NFX condyles.
D1 – D4 represents measurements taken in the dorsal aspect of the condyle, TR represents the transverse ridge, and P1 – P4 represents measurements made in the palmar aspect of the condyle.

parasagittal groove of the lateral condyle. This indicates that the condyle was rounder in FX horses compared to NFX and CTL horses. The areas surrounding the parasagittal groove had significantly less curvature in the palmar aspect compared to the dorsal aspect of the condyle in fractured cases compared to controls. Therefore this may possibly increase the stress that may lead to fracture. The difference in surface area measurement also leads to the conclusion that the lateral condyles are relatively smaller in fracture cases compared to controls and non-fractured cases.

In the future these data will be placed into a finite element model that is currently being developed in order to demonstrate the amount of stress that the joint is truly undergoing. In addition, there is a concern that some of these geometrical abnormalities may be developmental in nature and future efforts will be made to determine the influence of limb conformation and shoeing on condylar geometry. The goal of this future work will be to identify factors that may lead to condylar fractures.

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Thermal transitions in wax blends used in horse racing track surfaces

Take Home Message
Techniques have been developed which allow variation in the waxes used in synthetic race track surfaces to be evaluated over time. Pilot epidemiological data and popular perceptions all suggest that the synthetic racing surfaces degrade over time. The most likely cause of the changes over time is the wax coatings. These techniques will allow changes in the surface to be quantitatively monitored. Understanding these waxes is likely to be a factor in the maintenance of synthetic horse racing tracks and work is continuing to determine differences in surfaces, with the ultimate aim of reducing musculoskeletal injury.

Background
While synthetic racing surfaces were expected to provide a more consistent and fairer racing surface than dirt, concerns also exist with the synthetic tracks. These surfaces have been noted for being slow in several cases and fast in others. One synthetic track in 2007 had an average 6 furlong race time that was 1.9 seconds slower than the average 6 furlong race time on the dirt track in 2006. There is a clear perception that the speed of the synthetic tracks also tend to vary with temperature. The temperature range experienced by these surfaces in operation is quite large. Figure 1 shows the temperatures measured on one synthetic track surface (Del Mar, California) over a 4-day period in 2007. Track temperature fluctuations of over 30°C (85°F) are seen in the course of a single day.

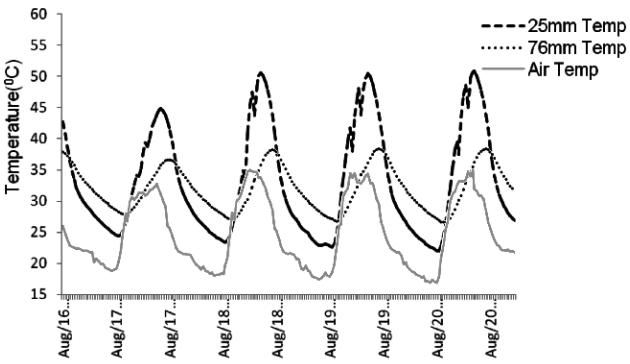

Figure 1. The track temperature profile for a California synthetic racetrack plotted over a 4-day period (Aug 16-20, 2007).

The question explored in this work is if these temperatures correspond to any significant changes in the track materials. The composition of these tracks makes a likely source of the variation clear. The synthetic tracks are made of relatively thermally stable components including polypropylene fibers, rubber, and silica sand. However all of these components are given a wax coating. The wax used in most of these surfaces is a slack wax which is sometimes mixed with more highly refined paraffin and microcrystalline waxes. The oil content can range from 3 to 50% depending on the crude oil from which it is derived and to the extent to which the oils present are separated.

Previous literature on the type of wax used in these tracks is limited. In most other applications oil is usually removed (to less than a few percent) prior to use. Therefore the properties of waxes with high oil contents are less well understood. In order to determine the effects of wax on the track performance, it is necessary to both measure the properties of the waxes and to better characterize the waxes used in this application. Five representative synthetic horseracing surfaces were considered. Material was used from Hollywood Park in Inglewood California, Golden Gate Fields in Albany California, Del Mar in Del Mar California, Santa Anita in Arcadia California and Keeneland in Lexington Kentucky. Keeneland was included to represent a surface used in a more variable climate and because it uses a wax-coated recycled material as one of the components. These five racetracks represent typical operating conditions for North American racing. The more arid and higher temperatures experienced by tracks in Southern California are in contrast to the greater rainfall and cooler climate of Golden Gate Park. The track at Keeneland is used year around and includes usage during cold winter and hot summer periods. All tracks with the exception of Del Mar are used for training year around.

Table 1. Wax Properties

Wax	n-Paraffin (%)	Isomers (%)	Density (g/cc)	Mw n-paraffin (g/mol)	Mw Isomers (g/mol)	Drop Melt (C)	Primary/Secondary Melting Range (C)			Tertiary Melting Range (C)		Total Avg Melting ΔH (J/g)
							Onset	Final	ΔT	Initial	Final	
SA	31.4	68.6	0.86	633	674	77.3	4	71	67	–	–	48
KL	32.0	68.0	0.81	521	536	>84*	2	67	65	–	–	36
DM	35.1	64.9	0.77	616	670	75.9	-2	73	75	77	85	54
HW	36.8	63.2	0.76	597	633	77.3	4	70	66	82	84	31
GG	37.9	62.1	0.79	584	642	67.1	7	68	61	–	–	49
n-octadecane (control)	99.8	0.2	0.76	254	257	28-30**	27	36	9	–	–	225

Methods and Results

In order to understand the composition and thermal response of the wax, density measurements, drop melt temperature tests, differential scanning calorimetry and gas chromatography were used. An n-octadecane paraffin wax was utilized as a control sample. Synthetic track samples were taken from five tracks after they had been in use for at least three months. Sampling of the track material was performed using a soil-sampling probe to remove a cylindrical section of the track surface to a depth of approximately 3 inches.

Gas chromatography and differential scanning calorimetry as well as drop melt tests provide useful information in the characterization of wax-oil blends extracted from horse tracks as shown in Table 1. All waxes in this study are believed to have originated as the wax-oil remnants from de-oiled slack waxes and have high oil content and n-paraffins beginning at 25 to 35 carbons in the chain and peaking at 40-44 carbon atoms. In particular the Keeneland wax sample showed a double peak distribution with an initial n-paraffin peak at 27 carbons and the second at 43 carbons indicating that it is a blend of two waxes. The solid to liquid transition regions for all waxes are very wide due to the different mass fractions in each of the blends with the thermal response correlating overall to the carbon distributions. No two tracks are identical in either carbon number distributions, oil content, or range/size of melting transition regions; though onset and end thermal transition temperatures are similar and carbon peak regions are fairly close. For a typical range of operating temperatures experienced by the Del Mar track, it is readily apparent that the wax is undergoing various degrees of melting. This general response is shared by all the tracks in this study. Future work will involve track material tests at various temperatures to determine if observed differences in thermal wax response are associated with changes in the mechanical properties of the track. This information can either lead to changes in the types of wax used in the track or the development of cooling procedures such as watering of the track to maintain the track within a target temperature range.

This work was done by Dr. Mick Peterson's research group as part of a long-standing collaboration between Dr. McIlwraith at CSU and R. Mick Peterson at the University of Maine.

Reference

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Acknowledgment

Partial funding for this research was provided by a grant to Drs. McIlwraith and Peterson from the Grayson-Jockey Club Research Foundation.

The effect of temperature on 6-furlong times on a synthetic racing surface

Take Home Message
The perception that the speed of synthetic tracks depends on the temperature is supported by data in this study. The synthetic track which was studied did not add water to the surface to control the temperature over the period of the study. The result was that 6 furlong race and work times had a significant correlation to track temperature. This suggests that control of the temperature of synthetic tracks is important for maintaining consistent performance.

Background
In 2006 the California Horse Racing Board declared that all major tracks in the state must install a synthetic track surface by the end of 2007. The board reasoned that the synthetic track would show improved consistency and safety. In general, this has been borne out with a significant reduction in catastrophic injury at some tracks and a more modest improvement at other tracks. However, the synthetic tracks have been noted for being slow in several cases and fast in others. For example, Student Council won the Pacific Classic race, at 1¼ miles in 2:07.29, more than 5 seconds slower than the previous worst time for the event. The new synthetic track at Del Mar in 2007 had an average 6 furlong race time that was 1.9 seconds slower than the average on the dirt track in 2006. In contrast, Arlington Park showed an increase in the 6-furlong race time on the synthetic surface compared to the dirt track of only 0.23 seconds. However, just as importantly, there is a clear perception that the speed of the synthetic tracks tend to vary with temperature.

The primary purposes of this study were: 1) to investigate the surface temperatures of a synthetic racing surface and 2) compare these temperatures to racing and training times to provide an objective measure of the impact of surface temperature on racing speed. The measured temperatures were also compared to thermal properties of wax that was separated from the racing surface. The results can provide insight into the role of wax on changes in track material performance. This information is critical to understanding if particular properties of the track contribute to musculoskeletal injuries.

Methods and Results
This study was undertaken at the Del Mar Racetrack in Del Mar, CA, USA. This track was chosen because it has a relatively constant horse population with a majority of the horses stabled and training at the track and consistently full barns for the race meet. Using this horse population allows training times in the morning to be compared to race times in the afternoon with an expectation that the overwhelming majority of the horses that race in the afternoon have worked in the morning over the same track. This approach increases the effective size of the population considered over the 42-day race meet. Times from the morning work sessions and afternoon racing were compiled for this analysis. A 6-furlong distance was used for analysis of the track since this is both the most common work distance as well as the most common race distance at the Del Mar racetrack. The standard daily morning workouts log for the Del Mar track included the distance trained, the number of horses, the fastest time, the slowest time, and the average time for each day of training held at the track. In addition to the work times, race data from the TRAKUS system (TKS, Inc., USA) was obtained for the Del Mar racetrack for the same period of time and the 6-furlong race data was compiled. Information on track and air temperature was measured on the track on a regular schedule during the entire racing meet.

Temperature (air, surface, and the four subsurface depths) data were examined across the time of day (7:30 AM, 10:00 AM, 2:30 PM, and 6:00 PM) with a 6x4 repeated measures analysis of variance (ANOVA). The morning workout times were reported as an aggregate value for the workout session and winning race times in the afternoon. In general, the temperature fluctuations of air and the synthetic race surfaces were nearly sinusoidal in time with a time lag between the depths of the surface caused by limited thermal conductivity. The air, surface, and top

Summaries: Focus 3

Improvement in the Understanding of the Pathogenesis of Excercise-Induced Traumatic Disease

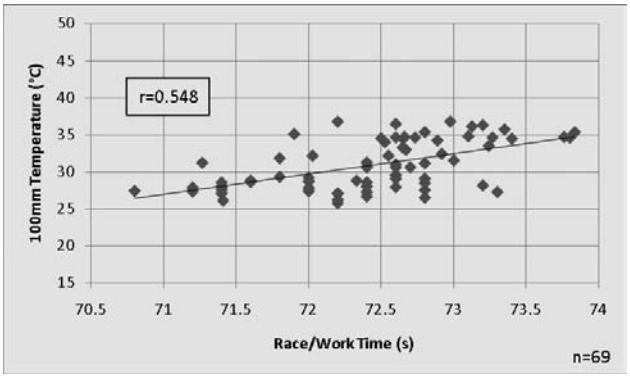

Figure 1. The correlation between track temperature and race/work time is evident in a plot of the data (shown here for a depth of 100mm).

Table 1. Pooled Morning and Afternoon Temperatures

	Morning		Afternoon	
	Mean	**SD**	**Mean**	**SD**
Air	22.6	1.6	28.0	1.5
Surface	25.3	2.4	37.9	5.0
25mm	24.9	0.8	41.5	2.8
50mm	26.1	1.3	41.5	2.5
75mm	26.8	1.0	36.3	2.0
100mm	28.5	1.6	34.2	2.0

All temperatures in °C.
P < 0.001 all morning to afternoon comparisons

two depths (25 & 50 mm) reached peak temperature mid afternoon before cooling at 6:00PM while the bottom two depths (75 & 100 mm) reached their peak temperature later in the day with the temperature at 6:00PM being the greatest. Furthermore, the temperature fluctuations are less extreme deeper in the track surface. In particular, the shallower locations (surface temperature and the subsurface temperatures at 25 and 50 mm) demonstrated high frequency changes when solar heating of the surface begins in the late morning. When combined into a single morning and afternoon temperature, all afternoon track temperatures were significantly greater than those in the morning ($p<0.001$; Table 1).

A significant difference also existed between the morning work and the afternoon race times (72.2 ± 0.6s versus 72.8 ± 0.6s, respectively; $p<0.001$). While on average this difference was less than one second, the 6-furlong work times were significantly faster than the afternoon race times of the same distance. Pooled race/work times were significantly correlated with temperature ($p<0.001$; Figure 1). The correlations were positive, indicating as temperature increased the work/race time also increased (i.e., the horses were slower). The correlations of work/race time with temperature were similar for the air, surface, and subsurface. The wax separated from the track was shown to have thermal transitions which begin with lower molecular weight components at -10°C and continue to occur until the higher molecular weight components melt at temperatures as high as 80°C. Therefore the range of temperatures in which these transitions occur is also the operational range for the track.

The results showed that there were direct correlations between temperature and work/race time, indicating the horses will have higher times (i.e., run slower) when the subsurface temperatures are the highest. This implies that the effects of temperature changes at depths up to 100 mm in the track and potentially even deeper were indicators of the ability of the track to support propulsion of the horse which then affects the work/race speed of the track. The fact that similar correlations were found below the surface as well as in air suggests that both biomechanical and physiological effects are likely to be responsible for the observed differences in speed. If air temperature produced a much stronger correlation then the effect would be expected to be primarily physiological.

The temperatures that were measured in the track were also comparable to temperatures for which the large thermal transitions occurred in the wax. The range of temperatures observed in the track includes the range at which melting of paraffin occurs, 43°C to 46°C. The more complex mixture of waxes used in the track included paraffin and other waxes with molecular weights which are liquids at the lowest temperature measured during the test period in the track (less than 20°C) and other waxes which remain solid at the

highest temperature measured in the track (50°C). The wax mixture will therefore not be completely solid even at the coldest temperature considered, with additional softening (melting of the lower molecular weight components) occurring at the surface down to the maximum depth considered, 100 mm.

The results of this study demonstrate the importance of thermal effects on synthetic race surfaces. This work was performed by Dr. Mick Peterson's research group at the University of Maine as part of the collaboration between Dr. McIlwraith and Peterson and their ongoing racetrack surface studies.

Reference

J.W. Bridge, M.L. Peterson, D.W. Radford, C.W. McIlwraith, "The Effect of Temperature on 6-furlong Times on a Synthetic Racing Surface", In Press, Equine Veterinary Journal.

Development of an in-vitro model of injury induced osteoarthritis using adult equine tissue

Take Home Message
In-vitro models of injury induced osteoarthritis (OA) provide a platform for high throughput investigations of the progression of OA after injury as well as for the development of therapeutic interventions. To develop an *in-vitro* model using adult equine tissue, we injured full thickness cartilage explants to various strains to determine which induced an OA histology that resembles *in vivo* cases of injured induced OA. With these data we demonstrate our ability to induce OA in cartilage explants including promoting articular surface fissures, chondrocyte cell death, and cluster formation after injury by at least 60% strain, or 14.68 (±1.31) MPa. This model is unique from other *in-vitro* models in that it utilizes a clinically relevant tissue type and provides a platform for *in-vitro* then *in vivo* testing of therapeutics to prevent and treat the progression of OA after injury.

Introduction
Articular cartilage has a low capacity for intrinsic repair. As such, traumatic joint injury often leads to the progression of osteoarthritis (OA) in both humans and horses. *In-vitro* models of cartilage injury are needed to understand the pathophysiology of OA progression and are excellent for high throughput inexpensive testing of therapeutic interventions. While there are *in-vitro* cartilage injury models currently in use, many injure skeletally immature animals or partial thickness cartilage and thus lack clinical relevance. The adult horse is an animal that naturally develops OA in response to injury. Additionally, the equine stifle has the greatest morphological similarities to the human knee. The development of an *in-vitro* model of cartilage injury using adult equine tissue creates a unique model system that is capable of *in-vitro* followed by *in vivo* testing that will have a direct clinical impact on horses and potentially humans as well. In this study, we developed a cartilage injury model that induced the hallmarks of OA including chondrocyte cell death, chondrocyte cluster formation, and damage to the extracellular matrix (ECM). This work was done by Dr. Christina Lee working with Drs. Frisbie, Kisiday, and McIlwraith and Alan Grodzinsky at MIT.

Methods
4.5 mm diameter full thickness cartilage samples were obtained from normal cadaveric stifle joints from 6 horses. Samples were assigned to either a free-swell control group or one of 4 injury groups. To injure, unconfined compressive load was applied at 100% strain rate until 50, 60, 70 or 80% compression of the cartilage was achieved followed by culture in normal growth media for 28 days. Samples were then processed for histologic evaluation by staining sections with Hematoxylin and Eosin (H&E) to visualize the presence of fissures, chondrocyte cluster formation and the incidence of cell death, or stained with Safranin O Fast Green (SOFG) to assess total proteoglycan (PG) content in the ECM. Immunohistocemistry was also conducted to visualize differences in ECM molecules including type I and II collagen. A grading scale detailing the degree of OA characteristics for each location (superficial, middle and deep zones and the regions adjacent to fissures) was used to evaluate all slides. Scores for each region were summed together for each slide to provide a cumulative slide score. Statistical differences between injury groups were determined using the GLIMMIX procedure, and individual comparisons were made using a least square means procedure, a $p < 0.05$ was considered significant.

Results
Samples had an average height of 1.7 mm ± 0.4. Stresses generated by each group differed significantly by strain ($p<0.0001$), ranging from 11.39 ± 4.62 MPa for the 50% group to 21.62 ± 4.59 MPa for the 80% group. All samples injured by 70% strain developed articular surface fissures. 78% of the samples fissured when injured by 60 and 80% strain, and only 50% of the samples fissured when injured by 50% strain, Figure 1. Injury had a significant effect on total proteoglycan content ($p<0.0001$), type II collagen ($p<0.05$), chondrocyte cell death ($p<0.0001$), focal cell

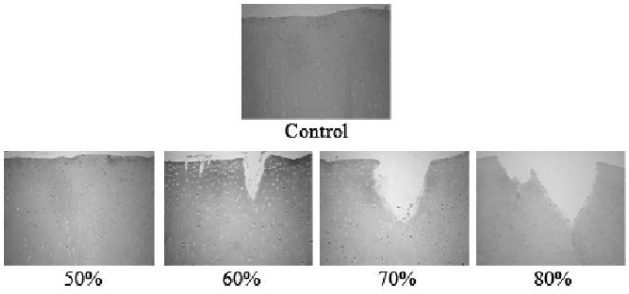

Figure 1. Sections of cartilage from the control and each injury group stained with H&E showing articular surface fissures.

loss ($p<0.0001$) and chondrocyte cluster formation ($p<0.0001$). Injury by 60, 70 and 80% consistently induced pathologies that were significantly more severe than uninjured controls, Table 1.

Discussion

The data from these experiments demonstrate our ability to consistently recreate *in-vitro* OA pathologies that mimic *in vivo* conditions using adult equine tissue. Specifically we were effective at inducing the hallmarks of OA, such as chondrocyte cell death, cluster formation, loss of ECM molecules and damage to the articular surface by fissure formation.

It is often thought that in the early stages after injury patients show few symptoms, if any, even though a cascade of naturally occurring irreversible events has begun. As a result, diagnosis typically occurs only after the disease has progressed to an irreversible state. With this highly controlled and reproducible *in-vitro* model, we now have the opportunity to investigate the progression of OA in response to injury to begin developing therapeutics to prevent or treat injury induced OA. This *in-vitro* model is unique from other models in that it utilizes full thickness cartilage samples from a mature animal source that naturally develops OA in response to traumatic injury. Because our equine model is capable of *in-vitro* then *in vivo* testing of therapeutics, our aim is to use it to develop and screen molecular based therapies prior to testing in live animals.

Acknowledgements

This work was funded by the College Research Council Colorado State University.

Table 1. Cumulative pathology scores by injury type. Average cumulative score for each pathology evaluated by injury. Score of 0 corresponds to normal cartilage, 12 corresponds to severe pathology. Scores with the same letter for each pathology are not significantly different from each other, significance set at alpha = 0.05. Data evaluate with a predictive F-value (Pr>F) which is used to predict the p-value.

	Injury type					
Pathology	Control	50%	60%	70%	80%	Pr > F
Total Proteoglycan	8.5 (0.46) [b]	9.3 (0.46) [b]	**10.9 (0.45)[a]**	**11 (0.49)[a]**	**11 (0.49)[a]**	<0.0001
Col II	1.0 (0.95) [b]	2.9 (0.95) [a,b]	**4.6 (0.9)[a]**	3.3 (1.0) [a,b]	2.7 (1.3) [a,b]	0.05
Col I	0 (0.14) [b,a]	0 (0.14) [b]	0 (0.13) [b]	0.2 (0.15) [b,a]	**0.4 (0.18)[a]**	0.24
Cell death	3.3 (0.57) [b]	4.7 (0.57) [b]	**7.3 (0.56)[a]**	**7.8 (0.63)[a]**	**8.5 (0.81)[a]**	<0.0001
Focal cell loss	0.79 (0.58) [c]	1.9 (0.58) [c]	**4.4 (0.57)[b]**	**5.6 (0.63)[b]**	**8.6 (0.81)[a]**	<0.0001
Cluster formation	0.6 (0.52) [c]	2.0 (0.52) [b,c]	**3.9 (0.50)[a]**	**4.4 (0.57)[a]**	**2.8 (0.74)[a,b]**	<0.0001

Summaries: Focus 4

Continued Development of Novel Therapies for Traumatic Synovitis, Capsulitis and Osteoarthritis in the Horse

Evaluation of intraarticular polysulfated glycosaminoglycan or sodium hyaluronan for treatment of osteoarthritis using an equine experimental model

Take Home Message

The use of intraarticular polysulfated glycosaminoglycan or sodium hyaluronan showed disease modifying effects and performed significantly better than placebo treatment in experimental OA. The results of this study support use of both these products of equine osteoarthritis.

Introduction

Lameness due to joint disease remains one of the most prevalent causes of loss of use in athletic horses. While numerous therapeutic options for the treatment of equine joint disease have been tested critical evaluation and publication in peer reviewed publications of polysulfated glycosaminoglycan (PSGAG) and sodium hyaluronan (HA) in a randomized placebo controlled study are limited. The purpose of the current study was to evaluate the symptom and disease modifying effects of PSGAG and HA compared to placebo treatments in experimental OA.

Materials and Methods

This study was a double blinded experimentally controlled randomized block design that utilized 24 horses (n=8 each treatment group) in an established model of osteoarthritis.[1] The investigators were Drs. Frisbie, Kawcak, Werpy and McIlwraith. On day 0 of the study, bilateral mid-carpal arthroscopic surgery was performed, and OA was induced unilaterally in one mid-carpal joint of all horses. On days 14, 21 & 28 horses received one of 3 intraarticular treatments: 1) 250 mg PSGAG + 125 mg amikacin, 2) 22 mg sodium hyaluronan + 125 mg amikacin, and 3) 2ml 0.9% NaCl + 125mg Amikacin (PCB), Also on day 14 the horses began a strenuous exercise regimen 5 days per week for the remaining 8 weeks of the study. Clinical, biochemical, gross and histologic outcome parameters were objectively measured.[1] Data were statistically evaluated using a generalized linear mixed model with PROC GLIMMIX of SAS (SAS Institute, 2006) with the appropriate fixed variables (Treatment, OA and Time when appropriate) and the horse acting as a random effect. p-values ≤ 0.05 were considered statistically significant.

Results

All horses completed the study and no adverse events were recorded.

Clinical Outcomes

Musculoskeletal: All horses showed a significant increase ($p<0.0001$) in lameness in the OA-affected (2.25 ±0.13 [mean ± standard error]) limb when compared to the sham operated limb (0.38 ±0.13) for Days 7 and 14. Change in lameness was calculated using Day 14 (the last pre-treatment evaluation) as the post-osteoarthritis pre-treatment baseline (a positive change score indicates improvement). There was no significant improvement in lameness score with respect to treatment.

Flexion: All horses showed a significant increase ($p<0.0001$) in flexion score in the osteoarthritis-affected (1.80 ±0.11) limb when compared to the sham operated limb (0.29 ±0.11) for Days 7 and 14. Change in flexion was calculated using Day 14 as the post-osteoarthritis pre-treatment baseline but there were no significant treatment effects observed.

Joint Effusion: All horses showed a significant increase ($p<0.0001$) in effusion score in the osteoarthritis-affected (2.42 ±0.13) joints when compared to the sham operated joints (1.13 ±0.13) for Day 14. Change in joint effusion was calculated using Day 14 as the post-osteoarthritis pre-treatment baseline. There was a significant ($p=0.0009$) improvement in joint effusion for osteoarthritis-affected joints by treatment. Specifically, joints treated with HA were significantly improved when compared to either Placebo or PGAGA treatment (Figure 1).

Radiographic Evaluation: A significant increase in radiographic joint pathology was induced for each radiographic outcome parameter post-surgery. Total radiographic scores pre-treatment for sham operated (0.40 ±0.35) compared to OA affected joints (4.08 ±0.26) were significantly different prior to treatment ($p<0.0001$). No significant treatment effects were detectable.

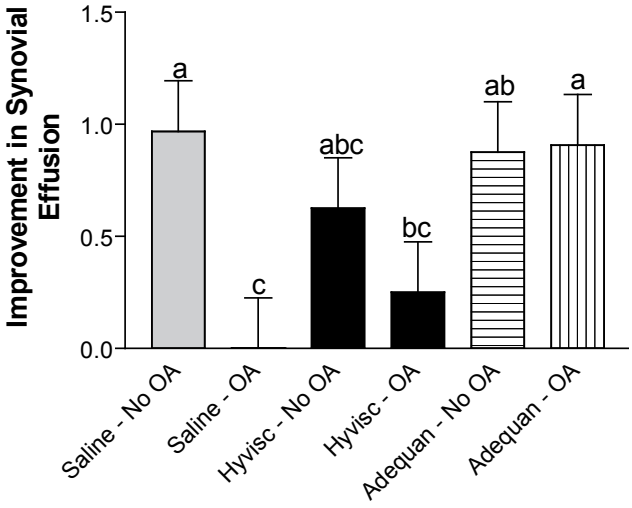

Figure 1. Plot of improvement in synovial fluid effusion after initiation of treatment. Different letters indicate a statistical difference between bars.

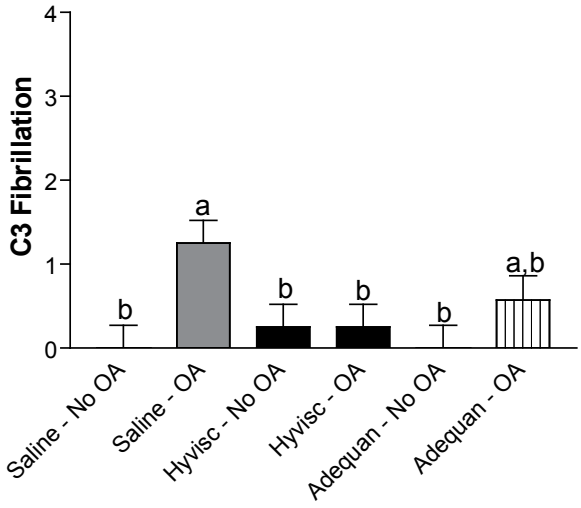

Figure 2. Plot of fibrillation score on the third carpal bone by treatment group. Different letters indicate a statistical difference between bars.

Synovial Fluid

Routine Analysis: Results of routine synovial fluid analysis indicated that, as expected, the total protein concentration increased significantly ($p<0.0001$) with induction of osteoarthritis throughout the study period when sham operated joints (2.04 ±0.08) were compared to OA-affected joints (2.37 ±0.08). Synovial fluid WBC counts were significantly increased ($p<0.0001$) by the induction of osteoarthritis with OA-affected joints having a higher WBC count compared to sham operated joints (437 ± 30 versus 308 ± 30 cell/dL, respectively). There were no significant treatment effects seen in synovial total protein or WBC counts.

Biochemical Analysis: The GAG concentrations in synovial fluid were significantly ($p<0.0001$) increased with induction of osteoarthritis, where OA-affected joints (3.36 ± 0.05 Ln ug GAG/ml) had an increase GAG concentration when compared to sham operated pre-treatment (3.85 ± 0.05 Ln ug GAG/ml). There were no significant treatment effects seen in synovial fluid GAG concentration. Synovial fluid PGE2 concentrations were significantly ($p<0.0001$) increased with induction of osteoarthritis (5.19 ± 0.10 Ln pg/ml), compared with findings in the sham operated joints (4.22 ± 0.10 Ln pg/ml). There was no significant treatment effects demonstrated.

Gross Pathologic Observations of Joints

At necropsy, hemorrhage within the synovial membrane was significantly ($p<0.0001$) increased in osteoarthritis-affected joints (1.83 ±0.15), compared with sham-operated joints (0.63 ±0.15). Similarly, the articular cartilage total erosion score was significantly ($p<0.0001$) increased in osteoarthritis-affected joints (1.67 ± 0.16) compared with sham-operated joints (0.42 ± 0.16). No significant treatment effects were seen for any of the gross pathologic observations.

Histologic Examinations

Synovial Membrane H&E: No significant effects of osteoarthritis induction was demonstrated in degree of synovial membrane cellular infiltration, subintimal edema or intimal hyperplasia, nor were significant treatment effects observed. There was a trend ($p=0.0850$) for a significant interaction between treatment and induction of osteoarthritis in synovial vascularity. Specifically, less vascularity was observed in OA-affected joints treated with HA ($p=0.0607$) or PSGAG ($p=0.0187$) when compared to OA-affected joints receiving placebo treatment. Similarly, a trend ($p=0.0571$) for a significant beneficial treatment effects was observed in synovial membrane fibrosis. Osteoarthritis-affected joints treated with HA ($p=0.0773$) and PSGAG ($p=0.0218$) had less subin-

timal fibrosis when compared to OA-affected joints receiving placebo treatment.

Articular Cartilage H & E: The histologic evaluation of the articular cartilage by H & E staining showed a significant ($p<0.0001$) increase in the modified Mankin score when osteoarthritis-affected joints (3.12 ±0.32) are compared with sham-operated joints (1.04 ±0.32) when all locations were considered. There were no significant treatment effects observed based on the total modified Mankin score, however, fibrillation was significantly ($p=0.0177$) better with treatment based on location of the sample when compared to placebo in OA-affected joints. Specifically, treatment with HA in OA affected joints significantly improved ($p=0.0074$) and treatment with PSGAG in OA-affected joints demonstrated a trend ($p=0.0831$) for improvement when compared to placebo treated OA affected joints on the third carpal bone (Figure 2).

Articular Cartilage SOFG: Evaluation of articular cartilage for SOFG staining demonstrated a significant ($p=0.0118$) decrease in osteoarthritis-affected joints (4.89 ± 0.47) as compared to sham-operated joints (6.33 ± 0.46) for the cumulative score on C3. No other comparisons were significantly different including treatment effects.

Discussion

The model of OA preformed as expected and provides a uniform comparison of PSGAG and HA to other commonly used clinical therapeutic agents for the treatment of joint disease. In this study treatment with PSGAG and HA both significantly improved parameters considered relevant for disease modifying osteoarthritis drugs (DMOAD) when compared to placebo treatment. Although surprising to the authors the results of this study did not demonstrate effects of symptom modifying osteoarthritic drugs (SMOAD) for either PSGAG or HA when compared to placebo treatment. In light of the DMOAD and SMOAD effects of PSGAG and HA they both appear less potent when compared to triamcinolone acetonide {Frisbie, 1997 #2546} and interleukin-1 receptor antagonist delivered using gene therapy {Frisbie, 2002 #2920} for the treatment of OA induced in this model. To the same extent, both PSGAG and HA showed relatively similar DMOAD activity as compared to autologous serum (ACS) although a significant SMOAD activity was also seen with ACS {Frisbie, 2007 #3193}. The use of IV HA also appeared superior, especial since it was able to demonstrate SMOAD activity {Kawcak, 1997 #2445} as did the use of. While a similar model used to test both HA's the IV study was conducted during the model genesis so subtle differences could not be ruled out. Different commercial products were used in the IV (Legend) versus the current study (Hyvisc). The use of diclofenac cream also showed both SMOAD and DMOAD activities using a similar model of OA (lynsey put in last year's surpass aaep article). Avocado and soybean unsaponifiable (ASU) extracts showed a similar level of DMOAD compared to both PSGAG and HA and like PGAG and HA demonstrated no SMOAD activity {Kawcak, 2007 #3233}. Similar improvement in articular cartilage fibrillation was noted with IM pentosan polysulfated when compared to the current study with PSGAG and HA (Lynsey need aaep abstract ref). Both PSGAG and HA performed better than oral HA and IM PSGAG which were both tested in a similar model of OA. Clinically anecdotal reports suggest that HA may work better in acute synovitis and PSGAG in OA but these findings were not supported by the current study {Caron, 1996 #2884}. It was difficult to ascertain which of the two medications worked better even with the side-by-side comparison made in this study. Both medications showed similar improvements in various outcome parameters with differences in p-values being observed. The authors will continue to use a combination of HA and triamcinolone based on this and other research looking at a combination therapy (lynsey put blue ribbon panel reference in) in many first line cases of joint disease. Likewise because of the effect on synovial effusion, synovial membrane parameters use IA PSGAG in the post-arthroscopic period and in cases of joint disease that appear refractory to Triamcinolone and HA that economics preclude the use of ACS.

In summary both PSGAG and HA administered IA with Amikacin showed DMOAD activity and as such are certainly indicated in the treatment of equine OA. This work has been published recently.

Acknowledgment
This study was funded in part by Luitpold Pharmaceuticals, Inc.

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Summaries: Focus 4

Continued Development of Novel Therapies for Traumatic Synovitis, Capsulitis and Osteoarthritis in the Horse

Evaluation of topical 1% diclofenac for treatment of equine osteoarthritis using an equine experimental model

Take Home Message

The use of topical 1% diclofenac (Surpass) showed disease modifying effects and performed significantly better than oral phenylbutazone. The results of this study support use of Surpass over systemic NSAID's for solitary joint OA.

Introduction

Lameness due to joint disease remains one of the most prevalent cause of loss of use in athletic horses. Non-steroidal anti-inflammatory drugs (NSAID's) remain one of the front line treatments for lameness' despite the well know detrimental side effects which can occur following prolonged use. The Food and Drug Administration has recently approved a novel liposome formulation of 1% diclofenac (Surpass) for use on horses. This formulation obviates much of the systemic absorption thus reducing the potential of negative side effects associated with common NSAID's. A blinded control clinical study was conducted using this formulation and demonstrated positive results. Specifically the most compelling data showing decrease in lameness as evaluated by the attending veterinarian.[1] The purpose of the current study was to evaluate the symptom and disease modifying effects of Surpass compared to both placebo and positive control (oral phenylbutazone) treatments in experimental OA.

Materials and Methods

This study was a double blinded experimentally controlled randomized block design that utilized 24 horses in an established model of osteoarthritis.[2] This investigators were Drs. Frisbie, Kawcak, McIlwraith and Werpy. On day 0 of the study, bilateral mid-carpal arthroscopic surgery was performed, and OA was induced unilaterally in one mid-carpal joint of all horses. On day 14 horses (continuing throughout the study period unless noted) received placebo (application of a moisturizing cream was only performed prior to clinical examination to blind the evaluators of treatment assignments), 7.2g of 1% sodium diclofenac cream (Surpass) topically (BID) over the OA joint or 2g phenlybutazone orally (SID). Also on day 14 the horses began a strenuous exercise regimen 5 days per week for the remaining 8 weeks of the study. Clinical, biochemical, gross and histologic outcome parameters were objectively measured.2 Data for categorical variables were statistically evaluated using a generalized linear mixed model in a multinomial repeated measures analysis of covariance framework with PROC GLIMMIX of SAS (SAS Institute, 2006) while continuous variables measured were evaluated using an analysis of variance (ANOVA) framework with PROC GLM of SAS. P-values < 0.05 were considered statistically significant.

Results

All horses completed the study and no adverse events were recorded. All horses showed a significant increase in lameness following induction of OA. The percent change in lameness score indicated a significantly ($p=0.037$) better response with Surpass treatment when compared to phenylbutazone (mean $\pm$ standard deviation 0.09 ± 0.25 versus 0.04 ± 0.35, respectively). While the percent change in lameness was greater when Surpass (0.09 ± 0.25) was compared to placebo (-0.14 ± 0.57) due to the standard deviation of the placebo group the comparison was not statistically different. ($p=0.23$). Similar results were noted with the degree of radial carpal bone sclerosis measured using magnetic resonance. Specifically, the Surpass (2.13 ± 0.35) treated horses demonstrated significantly ($p=0.04$) less sclerosis when compared to phenylbutazone (2.63 ± 0.52) treated horses and while the numeric value of Surpass was improved compared to placebo (2.25 ± 0.46) treatment the comparison was not statistically different ($p=0.58$). Articular cartilage demonstrated a significantly ($p=0.01$) better gylcosaminoglycan content in the Surpass (423 ± 30ug/ml) treated joints when compared to placebo (381 ± 28ug/ml). This was supported by a trend ($p=0.06$) for Surpass (1.57 ± 1.72) to decrease the histologic progression of OA measure by modified Mankin score when compared to placebo (3.56 ± 2.46) treatment.

Discussion

The results of this study indicate that Surpass cream applied to a joint with experimental OA responds significantly better than a horse having a similar lesion treated with systemic phenylbutazone. Furthermore, modest improvements in horses treated with Surpass compared to placebo were seen in almost all parameters. While not presented in this abstract accepted statistical models were assembled to simulate study results with a larger population of horses, N=32 vs n=8 (current study).[3] Results of these simulations suggest that statistical significance would have been reached in many of the Surpass compared to placebo outcome parameters if the number of horses had been greater. Never the less as completed (8 horses per treatment group) significant disease modifying effects were seen, specifically improved cartilage GAG concentrations in Surpass compared to placebo treated joints. Significant symptom modifying effects have been previously reported.1 Interestingly, phenylbutazone was associated with negative effects and had less symptom modifying effects than expected by the authors. In conclusion the results of this study support an improved response from the use of surpass over systemic NSAID's for solitary joint OA. This work has been published.[4]

Acknowledgment

This study was funded in part by Idexx.

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Summaries: Focus 4

Continued Development of Novel Therapies for Traumatic Synovitis, Capsulitis and Osteoarthritis in the Horse

Evaluation of extracorporeal shock wave therapy for osteoarthritis

Take Home Message

Extracorporeal shock wave therapy (ESWT) is an effective method of decreasing clinical signs of lameness associated with osteoarthritis; in this model ESWT performed better than intramuscular polysulfated glycosaminoglycans.

Introduction

Lameness, and more specifically joint disease, causes significant loss of use of athletic horses and has a large economic impact on the horse industry. Despite numerous medical treatments, novel treatments are needed. Recent experimental evidence and anecdotal clinical impressions of extracorporeal shockwave therapy (ESWT) for the treatment of osteoarthritis (OA) have been reported.[1-3] Unpublished clinical studies in the dog have shown promising results, as have anecdotal reports of treating shoulder, pastern and coffin joint OA in horses. This information led to the completion of the current study comparing ESWT to Adequan®[a] and sham treatments in horses. Investigators were Drs. Frisbie, Kawcak and McIlwraith.

Materials and Methods

This study was a blinded experimentally controlled randomized block design that utilized 24 horses in an established model of osteoarthritis (OA).[4] On day 0 of the study, arthroscopic surgery was performed on both mid-carpal joints of all horses, and OA was induced in one of the mid-carpal joints. On day 14 horses were divided into 3 treatment groups: sham control, positive control or shockwave treated (Figure 1). The sham control group had bubble wrap applied to the probe end which absorbed all of the energy but were treated similar to the shockwave treated group in all other respects. The positive control group received intramuscular Adequan®[a] administered every 4 days for 28 days. The shockwave treated horses received ESWT on days 14 and 28 using VersaTron®[b] 12mm probe. Specifically, the ESWT protocol was 2000 shock waves at the E4 energy level on study day 14 and 1500 shock waves at the E6 level on study day 28. The energy was delivered mainly to the intercarpal joint capsule attachment, but some energy was delivered to the area of fragmentation (≈20% of the shocks).

On day 14 the horses began a strenuous exercise regimen 5 days per week for the remaining 8 weeks of the study. Synovial fluid and serum were assessed every other week for total protein concentration, white blood cell count (WBC) and levels of the inflammatory marker, prostaglandin E_2 (PGE_2). Additionally, biomarkers for aggrecan synthesis (CS-846), proteoglycan release (sGAG), type II collagen synthesis (CPII) and type I and II collagen degradation ($COL2\text{-}3/4C_{short}$), and bone synthesis (osteocalcin) were also estimated. Horses were assessed for lameness using the AAEP grading scale every 2 weeks. At the termination of the study, operated joints were evaluated grossly, and tissues were harvested for biochemical and routine histologic examinations.

Statistical analysis utilized both a Mixed model analysis of variance and discriminate analysis, with p values <0.05 considered significant.

Results

Induction of OA resulted in a significant increase in lameness in the corresponding limbs. Significant improvement in clinical lameness (1.7 fold) was noted at the first evaluation time point post treatment (14 days) in the ESWT treated horses when compared to both the sham and positive control horses. This significant improvement was also noted for all subsequent evaluation periods (days 42, 56 & 70). No significant difference was noted between the sham and positive control horses when compared at similar time points. However, the positive control horses had significantly improved in lameness by day 70 compared to day 14, while the sham control horses had not.

Both the positive control and ESWT horses had significant improvement in synovial fluid total protein levels (up to 1.3 fold) within 14 days of treatment, indicating less synovitis as compared to the sham

control horses. Improvement with Adequan[a®] and ESWT treatment was also noted in the amount of glycosaminoglycan release into the bloodstream 14 days post treatment.

No significant differences were noted in gross or histologic examination of the tissue comparing any of the treatment groups.

Discussion

The study presented utilized an established model of osteoarthritis that has been used to test various medical treatments for arthritis, such as intra-articular corticosteroids, intravenous hyaluronan, and intramuscular pentosan polysulfate. Furthermore, the induction of arthritis has been shown to result in clinical lameness, histologic and biochemical alterations. These changes are noted in both the soft tissue and in the articular cartilage. Treatment with ESWT reduced the clinical signs of pain measured by lameness evaluations even 42 days after the last treatment, the longest time point measured. There was however, no significant improvement in response to flexion of the carpus. This suggests that the improvement in lameness was not due to local desensitization of the region or more specifically the joint capsule. Concurrently a parameter of synovitis, synovial fluid total protein, was significantly reduced suggesting a possible mechanism for the treatment effect of ESWT. At the gross or histologic level improvement was not seen with either ESWT or Adequan[a®] treatment and thus would not be considered chondroprotective in this model. These findings would suggest more of an effect on the soft tissues surrounding the joints as compared to the articular cartilage. Computer tomography and bone rate formation studies are being analyzed on these horses and may yield more information on mechanism by which ESWT improved the treated horses.

The results of this study suggest that ESWT is an effective method of reducing clinical lameness and synovitis but does not significantly improve gross or histologic progression of arthritis and therefore would be best considered in combination with a chondroprotective agent. This work has been published.[5] Also further work evaluating ESWT in clinical case of joint disease is definitively warranted.

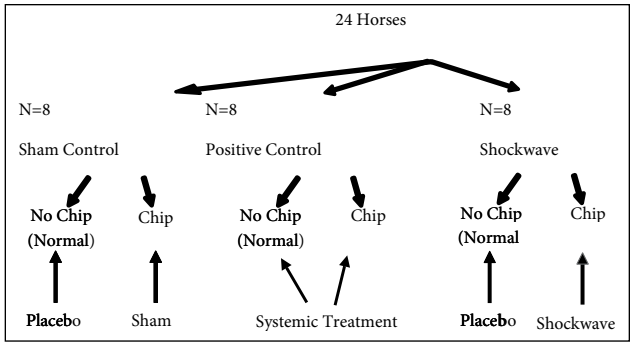

Figure 1. Experimental design of the study. Overall horse numbers, treatment groups, and treatment applied to specific carpal joints are indicated.

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Footnotes

[a] Adequan®, Luitpold Pharmaceuticals, Inc.,Shirley, NY 11967

[b] VersaTron®, High Medical Technologies, Kennesaw, GA 30144

Summaries: Focus 4

Continued Development of Novel Therapies for Traumatic Synovitis, Capsulitis and Osteoarthritis in the Horse

Survey of joint therapeutics use by veterinarians

Take Home Message

Medications are frequently employed by veterinarians to treat intra-articular pathologies in the performance horse. A fairly wide variety of medications are available on the market today. To determine the most commonly used medications in the profession today, a survey of American Association of Equine Practitioners members focused on the use of intra-articular joint treatment therapies was collected. Methylprednisolone acetate, triamcinolone acetonide, polysulfated glycosaminoglycan (PSGAG), and hyaluronate sodium were the most frequently used products by the respondents to this survey.

Introduction

Lameness issues continue to plague performance horses and result in financial loss for owners. Acute or chronic joint inflammation is commonly treated with intra-articular (IA) medications. A limited but expanding arsenal of intra-articular medications and treatments are available on the market today, with therapy focused on providing symptom modifying and disease modifying effects. Research supports the use of many different medications administered via specific routes, but others are only supported anecdotally or by extrapolation from use in other species. Direct knowledge regarding what is actually in use in clinical practice is scarce. The goal of this study was to establish the current clinical usage of a range of medications used for joint therapy in the horse.

Materials and Methods

A cross-sectional survey of American Association of Equine Practitioners members was performed. Contact of 6,305 members was attempted electronically, sending them a link for a web-based survey via email. International members were included, recognizing that drug names would differ in other countries. There was no filtration for area of specialty, major practice focus, or location of practice within the AAEP membership. Responses were uniquely identified to eliminate duplicates, but were not directly linked to the individual respondent to ensure all survey answers were confidential.

Results

In total, 830 completed responses were received. When asked about corticosteroid use, 73% indicated that they use methylprednisolone acetate (MPA) most frequently in low motion joints and77% indicated they use Triamcinolone acetate (TA) most frequently in high motion joints. When compared to the demographics of the respondents, respondents who had been in practice greater than 10 years were significantly more likely to use MPA in high motion joints; however there was no difference in usage in low motion joints compared to years in practice. Racehorse practitioners were more likely to use MPA in high motion joints than practitioners focusing on other disciplines. Practitioners who treated mainly western and English performance horses were more likely to use TA in low motion joints than other practitioners.

Fifty four percent of respondents indicated that they had used interleukin-1 receptor antagonist protein (IRAP) products. IRAP was used in joints non-responsive to steroids 38% or when it is available as a first choice joint treatment financially, 26%. Practitioners who focus on English performance were significantly more likely to use IRAP products than race horse practitioners or show horse practitioners.

Polysulfated glycosaminoglycan was most commonly administered intra-muscularly. Sodium hyaluronate in the form of Legend was most commonly administered intra-venously. Other sodium hyaluronate products were administered most commonly intra-articularly by 83.1% respondents. The product Map-5 (unlicensed in the US) was used intra-articularly by 19.6%, the product Polyglycan™ was used intra-venously by 24.9%.

When asked about including antimicrobials in intra-articular injections, 46.2% indicated that they always use antimicrobials. Twenty-one percent indicated that they never use antimicrobials in joint injections. Respondents practicing <10 years were significantly more likely to use antimicrobials. The majority of respondents (70.0%) indicated that they would not feel comfortable using compounded medications in intra-articular routes.

Summary
The results of this survey help delineate the current usages of common injectable joint therapy products among equine practitioners. This data can be used to aid in determining a current standard of practice for the profession, directing further development of therapeutics, and focusing future areas of research.

Acknowledgement
This study received financial contributions from Arthrodynamic Technologies.

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The effects of chiropractic, massage and phenylbutazone on spinal mechanical nociceptive thresholds in horses without clinical signs

Take Home Message
Changes in spinal mechanical nociceptive thresholds (MNTs) were measured in asymptomatic horses before and after chiropractic treatment, massage therapy and phenylbutazone and compared with active and inactive control groups. Single treatments of either chiropractic or therapeutic massage significantly increased MNTs within the caudal vertebral column at 7 days post-treatment.

Introduction
Back problems are a common cause of poor performance and reduced jumping ability in athletic horses.[1] Unfortunately, identification and localization of pain is often subjective. Pressure algometry has been used to objectively measure mechanical nociceptive thresholds (MNTs) within the axial skeleton and to localize and quantify bony and soft tissue pain.[2,3] Commonly prescribed treatments for chronic thoracolumbar pain in horses include stall rest, anti-inflammatories (i.e., phenylbutazone) and complementary therapies, such as chiropractic and massage therapy. Unfortunately, most back pain treatments have not been evaluated in controlled, clinical trials for efficacy in reducing pain or musculoskeletal dysfunction. The objective of this study was to compare the effects of three common treatment methods on spinal MNTs in asymptomatic horses.

This project was completed by Kayleigh A. Sullivan at Valley Central High School in Montgomery, New York and Drs. Kevin K Haussler and Ashley E. Hill at Colorado State University and was published in the Equine Veterinary Journal.[4]

Methods
Baseline MNTs at seven sites within the thoracolumbar and sacral regions were measured in 38 healthy adult horses. Horses were assigned to one of three treatment groups, which consisted of instrument-assisted chiropractic treatment, therapeutic massage and phenylbutazone or two control groups consisting of either ridden exercise (i.e., active control) or routine paddock turnout with no ridden exercise (i.e., inactive control). On Day 0, the chiropractic group (N=8) received high-velocity, low amplitude thrusts provided by a spring-loaded, mechanical-force instrument (Activator II Adjusting Instrument). The hand-held instrument produces a very short duration (< 5 msec) impulsive-type force that was applied to the articular processes of the cervical vertebrae, dorsal spinous processes of the thoracolumbar and sacral vertebrae, and the tubera sacrale based on the presence of vertebral stiffness, muscle hypertonicity or a localized pain response. On Day 0, the massage group (N=8) had manually-applied treatment (i.e., effleurage and petrissage) to all bilateral epaxial musculature of the cervical, thoracolumbar and sacral regions and the proximal thoracic and pelvic limb musculature. The phenylbutazone group (N=7) was given phenylbutazone paste (1 gram/500 pounds) orally, twice daily for seven days. MNTs were repeated one day after initiation of treatments (i.e., Day 1) and at three and seven days post-treatment. The percentage change from baseline MNT values was calculated within each group over time. Treatment group differences were assessed by ANOVA using Tukey's HSD (alpha = 0.05) for post-hoc comparison of means.

Results
On Day 7, the median MNT had increased 27% in the chiropractic, 12% in the massage, and 8% in the phenylbutazone groups. MNT changes of < 1% were seen within the active and inactive control groups. In treated horses, the caudal-most vertebral sites had the largest MNT increases.

Discussion
Instrument-assisted chiropractic treatment and therapeutic massage were effective at producing significant antinociceptive changes within the caudal vertebral column from baseline to Day 7. Whether the MNT changes are clinically important is not known; however, the ability and time-course of different treatment modalities to significantly change, or not change, MNT values was judged clinically relevant. Decreased MNTs on Day 1 within the chiropractic group are presumably due to mechanical irritation

of soft tissues or articular structures. In contrast, an immediate though non-significant increase in MNTs occurred in the massage group at Day 1 with gradually increasing MNTs noted at Days 3 and 7. These findings suggest that mechanisms of action other than endorphin release are responsible for MNT increases. In humans, the beneficial effects of massage are reported to be more psychological than physiological.[5] The single massage treatment produced progressive increases in the overall median MNT, which could have been due a reduction in anxiety. A limitation of the current study was that asymptomatic horses were used; therefore, we could not directly evaluate the effects of treatment or paddock confinement on back pain. The physiologic effects of chiropractic treatment and therapeutic massage on nociceptive modulation needs further research to evaluate combined treatment effects and longer-term MNT changes in horses with documented back pain.

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Summaries: Focus 5

Validation of Rehabilitation and Physical Therapy Techniques for Musculoskeletal Disease

Mechanical nociceptive thresholds within the pastern region of non-sored Tennessee Walking horses

Take Home Message

Soring is defined as the practice of inflicting pain with irritating chemicals or mechanical devices on the distal limbs of a horse with the purpose of accentuating gait. Current soring examinations are highly subjective and often use digital pressures < 0.5 kg/cm^2, which is substantial lower than reported normal mechanical thresholds within the distal limb. Using pressure algometry, non-sored Tennessee Walking horses readily tolerated mechanical pressures up to 19.5 ± 3.6 kg/cm^2 within the pastern region of the thoracic limbs. Pressure algometry has the potential to provide more objective assessment of pain thresholds in an effort detect pain-inducing procedures used for performance enhancement.

Introduction

Soring is the application of an irritant to the distal forelimbs of gaited horses with the sole intent of inflicting pain and inducing altered gait. Soring was banned by the Horse Protection Act in 1970 because of concerns about the non-humane treatment of sored horses.[1] One perceived limitation of the current soring examination is the inconsistent application of thumb pressure during digital palpation. Objective methods for the detection of limb pain due to soring are lacking. Pressure algometry applies quantifiable pressure and has been used to assess mechanical nociceptive thresholds (MNTs) within the axial skeleton and thoracic limb of normal horses.[2,3] The purpose of this study was to assess whether non-sored Tennessee Walking horses respond to manual pressures ≤ 10 kg/cm^2 and to establish reference MNTs within the pastern region in non-sored horses.

This project was completed by Drs. Kevin K Haussler and Ashley E. Hill at Colorado State University and by Dr. Todd H. Behre at the United States Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care, Horse Protection Program and was published in the Equine Veterinary Journal.[4]

Methods

In 25 adult non-sored, non-lame Tennessee Walking horses, MNTs were evoked by a pressure algometer at four pastern sites commonly found to be painful in sored horses within each thoracic limb by six different examiners. Prior to MNT measurements, two randomly selected examiners observed the horses walking in a figure-eight pattern and digitally palpated the unweighted thoracic limbs from carpus to hoof, with particular emphasis on the pastern region. Any pain response or skin lesions and scarring were subjectively graded as mild, moderate or severe. The effects of age, sex, weight, wither height, exercise, and hand dominance of the examiners on MNTs were assessed. Correlations between the horse's perceived mental status, tolerance to the procedure and MNT values were also evaluated. Calmer horses were hypothesized to have higher nociceptive thresholds than anxious horses.

Results

MNTs > 10 kg/cm^2 were reported in an average of 80% of the measurements recorded per limb. Within the four pastern sites, the palmar region had the lowest reference MNT value of 19.5 ± 3.6 kg/cm^2. Signalment, exercise, hand dominance, horse mental status, and horse procedure tolerance did not significantly affect MNT values. Horses with high initial mental status scores tended to have lower scores after repeat MNT examinations (i.e., they calmed down during the repeated examinations).

Discussion

Sored horses react strongly to the application of minimal pastern pressure, which is the primary mechanism for inducing the desired altered gait associated with most Tennessee Walking horses. Historically, examination methods have included applying only enough manual pressure to partially blanch the thumbnail in order to elicit a pain response in sored tissue within the pastern region. Given that an applied force of approximately 5 pounds (2.3 kg) is required to blanch the thumbnail and a typical thumbprint surface area is 4 to 6 cm^2, the resulting

applied pressure is 0.4 to 0.6 kg/cm^2. We do not know the typical MNT values or possible variation in nociceptive levels in sored horses, since we measured only non-sored horses in this study. The current project demonstrated that in non-sored horses examined by experienced examiners, none of the horses responded to pressures less than 6.4 kg/cm^2 and that the majority of MNT measurements were > 10 kg/cm^2. The single lowest MNT measurement recorded in these non-sored horses (i.e., 6.4 kg/cm^2) is between 11 and 16 times greater than the suggested pressure application defined within the current Horse Protection Act training manual.[1] When the lowest reference MNT at the palmar pastern region was considered (i.e., 19.5 kg/cm^2), the threshold difference was 33 to 49 times greater than the Horse Protection guidelines. The current study suggests that a more stringent pressure threshold of 5 kg/cm^2 or even 10 kg/cm^2 could be used to detect soring in Tennessee Walking horses, with a low risk of false positive tests for examiners inexperienced in using pressure algometry. Pressure algometry, in lieu of digital pressure, can quantify mechanical pressure applied during soring inspections and provide consistency between examiners. Pressure algometry has the potential to be used as an enforcement tool in Horse Protection as an objective measure of applied manual pressure and nociception within the pastern region of sored and non-sored Tennessee Walking horses. The Federation Equestre Internationale (FEI) Veterinary Regulations prohibit temporary or permanent limb desensitization or hypersensitization by any means. Future studies need to establish baseline MNT values within the distal limbs of other breeds, as pressure algometry may prove to be an objective enforcement tool in other disciplines as well.

Acknowledgement
This study was funded by the United States Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care, Horse Protection Program.

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Deformation of the equine pelvis in response to in-vitro 3D sacroiliac joint loading

Take Home Message
Sacroiliac joint injuries can cause poor performance; however, the interaction between pelvic mechanics and the sacroiliac joint is poorly understood. Pelvic deformation induced by three-dimensional sacroiliac joint motion produces complex patterns of pelvic deformation, depending on the loads applied. The equine pelvis is not a rigid structure and asymmetric pelvic deformation occurs during most sacroiliac joint movements. Asymmetric deformation of the pelvis may be a contributing factor to localized increased tissue strain and performance-limiting injuries.

Introduction
Sacroiliac joint injuries are a significant cause of poor performance in equine athletes but are often difficult to diagnosis and treat because of deep and inaccessible structures.[1] Motion at the sacroiliac joints is complex and direct measures of equine sacroiliac joint motion are limited. To better understand the pathophysiology of bony pelvic asymmetry, evaluation of normal pelvic mechanics associated with three-dimensional sacroiliac joint movements is needed. The objective of the current study is to determine the pattern and magnitudes of pelvic deformation induced during three-dimensional sacroiliac joint loading using quantified forces and moments. It was hypothesized that left and right pelvic bony markers will be displaced in equal magnitudes and directions during three-dimensional symmetric loading of the equine pelvis.

This project was completed by Drs. Kevin K Haussler, Kirk C. McGilvray, Ugur M. Ayturk, Christian M. Puttlitz, Ashley E Hill, C. Wayne McIlwraith at Colorado State University and was published in the Equine Veterinary Journal.[4]

Methods
Nine reflective triads were rigidly attached to bony prominences in sacropelvic specimens harvested from 14 horses for stereophotogrammetric analysis of triad displacements and joint kinematics. The sacrum was coupled to a multi-axis load cell and mounted vertically within a material testing system (MTS). A pneumatic actuator coupled to a wire rope and pulley system was used to apply 90 N-m moments to the ischial arch to simulate nutation-counternutation and left and right lateral bending of the sacroiliac joints. Axial rotation of the sacrum was induced by torsion of the upper MTS fixture. Vectors of marker displacement within orthogonal planes of motion were measured during loading of the sacropelvic specimens. Comparisons in the magnitude and direction of triad displacements were made between paired left-right markers and paired loading conditions.

Results
Nutation-counternutation of the sacroiliac joint caused vertical displacement of the ischial tuberosities and cranial-caudal displacement of the wings of the ilium. During both nutation and counternutation, the magnitudes of displacement were largest at the ischial tuberosities (up to 6.1 ± 2.7 mm) due to their location relative to the sacroiliac joint. Lateral bending induced rotational displacement within the horizontal plane of all pelvic landmarks, relative to the sacrum. The ischial tuberosities again had the largest magnitudes of displacement in both left and right lateral bending. Axial rotation of the sacrum caused elevation of the wing of the ilium ipsilateral to the direction of sacral rotation and depression of the contralateral ilial wing. Axial rotation of the sacrum under load control produced angular displacements of 3.9 ± 1.1° during left axial rotation and -4.0 ± 1.4° during right axial rotation. Significant paired left-right differences occurred during most sacroiliac joint loading conditions. Comparable magnitudes of pelvic displacement were measured during nutation-counternutation, left and right lateral bending, and left and right axial rotation.

Discussion

Bony pelvic deformation should be considered a normal response to any sacroiliac joint movement. The magnitudes and directions of displacement reported in the current study may not be directly applicable to in vivo sacroiliac joint motion during normal locomotion; however, basic modes of sacral and pelvic interaction and similar patterns of pelvic displacement and asymmetry are likely to occur in vivo. Translation of the ilial wings relative to sacral articular surfaces was clearly evident during lateral bending movements. In all three loading conditions, the axis of rotation of the pelvis relative to the sacrum appeared to be located near the sacroiliac joints. However, during nutation and counternutation, the ilial wing moved cranial and caudal, whereas the acetabula and ischial tuberosities tended to move dorsal and ventral. If the pelvis is a rigid structure, then the ilial wings should have been displaced dorsoventrally instead of craniocaudally. The directions of displacement measured during left and right lateral bending also demonstrate discordance between the cranial and caudal landmarks of the pelvis, indicating that the equine pelvis is not a rigid structure and that significant pelvic deformation occurs during most sacroiliac joint movements. Bilateral asymmetry in the magnitudes and directions of pelvic deformation occurred during all loading conditions, disproving our hypothesis of equal left and right pelvic marker displacement. Likely contributing factors include anisotropic mechanical properties of the bony pelvis and asymmetric recruitment and unequal deformation of paired sacroiliac ligaments.

The results of this study may provide insights into the pathogenesis of bony pelvic deformation that contributes to unilateral tuber sacrale height asymmetries and bilateral prominence (i.e., hunter's bumps). Differences in the magnitudes and directions of displacement of bony prominences within each ossa coxarum suggests that intermittent application of asymmetric forces or moments on the pelvis, potentially induced in vivo by chronic pelvic limb lameness or compensatory gait patterns, may be able to produce pelvic asymmetry and subsequent remodeling of the bony pelvis without obvious sacroiliac ligament disruption. This scenario could provide one explanation for the pathogenesis of pelvic asymmetry or tubera sacralia prominence in asymptomatic horses that lack a known history of pelvic trauma. The clinical significance of unilateral and bilateral tuber sacrale prominence or other pelvic asymmetries warrants future investigations with regard to their effect on sacroiliac joint function and athletic performance.

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Colorado State University

College of Veterinary Medicine and Biomedical Sciences

Orthopaedic Research Center
1678 Campus Delivery
Fort Collins, CO 80523-1678