Orthopaedic Research Center

2006-2007 Report

including the

Orthopaedic Bioengineering Research Laboratory

Colorado State University

This issue of achievement at the Orthopaedic Research Center and Orthopaedic Bioengineering Research Laboratory at Colorado State University is dedicated to Barbara Cox Anthony who passed away in 2007. Mrs. Anthony donated our first University endowed chair (as well as the first University endowed chair at the Animal Cancer Center in 2002) as well as supporting numerous other programs at the Orthopaedic Research Center.

Barbie was as unassuming and down to earth as she was generous. She is going to be greatly missed.

Preface

It is my pleasure to present our 2006-2007 Report from the Orthopaedic Research Center (ORC) and the Orthopaedic Bioengineering Research Laboratory (OBRL) 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 and also with Dr. Robert Sah of UC San Diego on another NIH Grant.

The past two years have seen a number of milestones. Based on a bequest from the estate of Kenneth and Virginia Atkinson together with some supplemental funding from Barbara Cox Anthony and Jon and Abby Winkelried, we were able to establish the Kenneth and Virginia Atkinson Chair in Musculoskeletal Imaging to support permanent funding of our MRI Faculty. Jon and Abby Winkelried's contribution was part of a $500,000 gift to the Orthopaedic Research Center (along with $500,000 to the Equine Reproduction Laboratory). Jon and Abby Winkelried and trainer, Tag Rice have made a rapid rise to prominence in cutting horses with Copaspepto, 2007 NCHA Horse of the Year and are equally enthusiastic and generous at ensuring the best care for these horses.

Another recent significant event has been the acquisition of a third $3,000,000 University Endowed Chair. This chair is the Abigail K. Kawananakoa Chair in Equine Integrative Therapies. We have added critical scientific evaluation of integrative therapies and rehabilitation techniques as adjunctive treatments in musculoskeletal disease as a research focus. The donor, Abigail Kawananakoa, has been a client and friend of mine for considerable time. Abigail has been a very successful owner and breeder of racing Quarter Horses including All American Futurity winner A Classic Dash and Los Alamitos Futurity winner Evening Snow. This chair completes one of our major goals of providing permanent funding for faculty positions within the ORC.

November 2007 was the 5 year anniversary of opening the Gail Holmes Equine Orthopaedic Research Center. Since then we have added the equine MRI center and completed renovation of the last laboratory in our Orthopedic Research Laboratory building, the latter involving acquisition of a new histopathology laboratory as well as Dr. Kisiday's cartilage biomechanics laboratory.

Accomplishments at the ORC over the past 2 years are detailed in this report. These accomplishments could not be achieved without the excellent support of our corporate and individual donors as well as funding from research agencies. I would also like to acknowledge the support of my Advisory Board as well as the support of Colorado State University and the College of Veterinary Medicine and Biomedical Sciences. We continue to achieve our goals but of course continue to make new ones to achieve the over-all mission.

Best wishes,

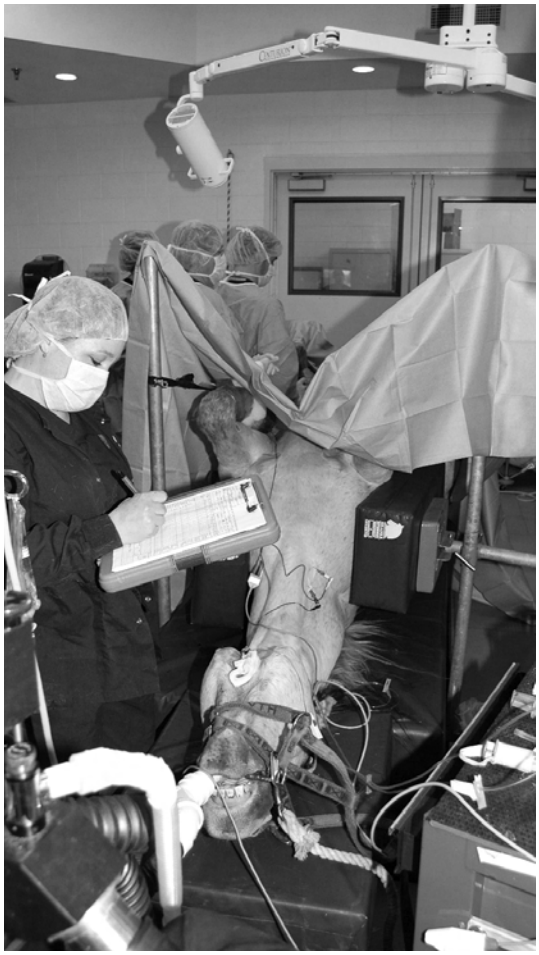
Wayne McIlwraith

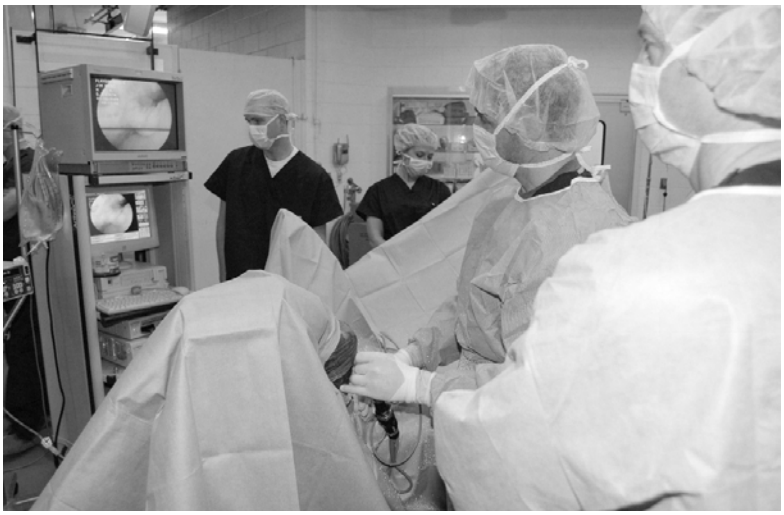
Table of Contents

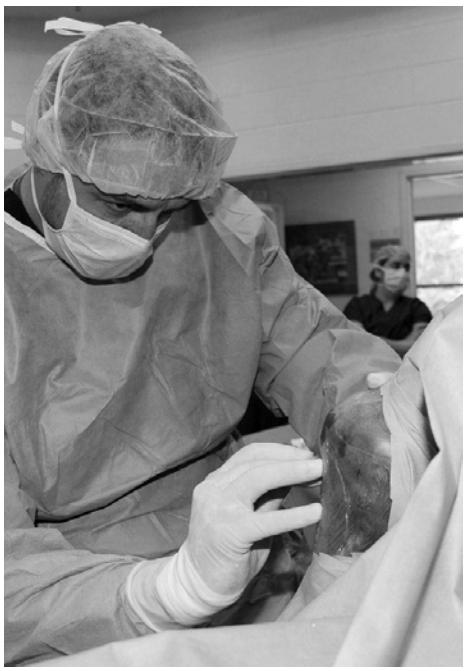
Table of Contents
Continued

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.







Joint Tissue Healing

Until recently, we have principally addressed articular cartilage healing and will continue to do so, but we are enlarging 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

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.

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, as well as biomechanical and modeling studies.

Investigation of Rehabilitation and Physical Rehabilitation 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.

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 Christian Puttlitz of the Orthopaedic Bioengineering Research Laboratory are co-coordinators of the program and Drs. Wayne McIlwraith, Chris Kawcak and John Kisiday of the Orthopaedic Research Center are core faculty members of the program 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.

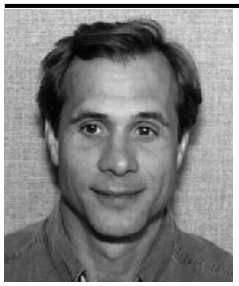
SBME now offers Masters of Engineering, Masters of Science and PhD degrees. The MS and PhD programs focus on three main research areas: biomechanics and biomaterials; molecular, cellular, and tissue engineering; and medical diagnostics, devices and imaging. Within these three areas, students participate 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 PhD students.

C. Wayne McIlwraith, BVSc (Dist.), MS, PhD, DSc (Purdue), Dr. med vet (honoris causa) (Vienna), DSc (honoris causa) (Massey), L.Dr. (honoris causa) (Turin), FRCVS, Diplomate ACVS, Diplomate ECVS, Barbara Cox Anthony University Chair, Professor of Surgery, Director of the Orthopaedic Research Center, Department of Clinical Sciences

Research Interests: Equine orthopaedic surgery and joint disease (arthritis) 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 and the American Association of Equine Practitioners, 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 250 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; Colorado State University Scholarship Impact Award 2007.



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

Research Interests: Initial research focused on the cause and treatment of equine laminitis. Dr. Baxter has more 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 and the 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 currently enrolled in The Medical Acupuncture for Veterinarians continuing education course and should become certified sometime in May.

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, DVM, MS, Diplomate ACVS, Associate Professor, Dept. 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 MD 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: 2003 Bloomberg International Sports Medicine Lecturer, 2007 International Musculoskeletal Transplant Foundation Speaker

David D. Frisbie, DVM, MS, PhD, Diplomate ACVS, Assistant 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 Bachelors Degree in Biochemistry and a Doctor of Veterinary Medicine (DVM) 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 Masters 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 PhD. During work on his PhD. 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.

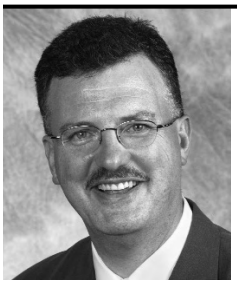
His current joint disease research is in two basic fields: 1) the evaluation of intra-articular therapeutics and their effects on joint disease (well known therapeutics he has evaluated include Legend, Adequan, Vetalog and Depo-Medrol, Orthokine (IRAP), stem-cells); 2) new methods of cartilage repair. 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, DVM, MS, PhD, 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 DVM 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 PhD 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 PhD 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.



Kevin K. Haussler, DVM, DC, PhD, 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 Bachelors 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, BS, MS, PhD, Professor and Director, Animal Reproduction and Biotechnology Laboratory

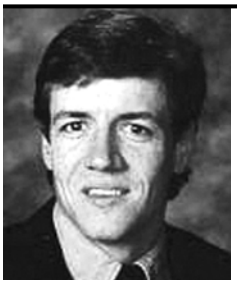
Collaborating on equine genomic research.

Ashley Hill, DVM, MPVM, PhD, 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 Bachelors 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 Masters in Preventive Veterinary Medicine (MPVM) at UC Davis in 1999, and a PhD 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.



Christopher E. Kawcak, DVM, PhD, 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 PhD. 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 to the Grayson-Jockey Club Research Foundation, 2007.

John Kisiday, PhD, Assistant Professor, Department of Clinical Sciences

Research Interests: Cartilage tissue engineering therapies and mechanobiology in order to build the bridge between basic laboratory studies and beneficial animal models.

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 PhD at MIT in Bioengineering and a collaborative post-doctorate 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.

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, DVM, PhD, 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.

Richard D. Park, DVM, PhD, 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.

Barbara E. Powers, DVM, PhD, Diplomate ACVP, Associate Professor, Department of Pathology

Research interests: Histology and histomorphometry of articular cartilage and bone, as well as effects of neoplasia and radiation on bone.

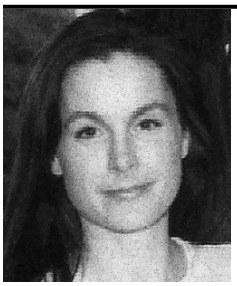
Dr. Powers is an Associate Professor in the Department of Pathology and Director of the Diagnostic Laboratory. She is author or co-author of over 150 abstracts, textbook chapters and monographs.

Honors include: The Academic Superiority Award for all years at Purdue Veterinary School and the Certificate of Merit for Outstanding Work in Veterinary Medicine in 1981; the Smith, Kline, Beecham Research Award in 1993; the Travel Award for the Radiation Research Society at the 10th International Conference, Wurzburg, Germany 1995.

Philip J. Steyn, BVSc, MRCVS, Associate Professor, Radiological Health Sciences

Research Interests: Nuclear imaging/scintigraphy

Dr. Steyn joined the faculty in 1993. He came with special training in nuclear imaging. His role in the orthopaedic research program is in the use of nuclear imaging (scintigraphy) in the diagnosis of orthopaedic entities that cannot be diagnosed by radiology, as well as the use of nuclear imaging as and orthopaedic research tool.



Natasha Werpy, DVM, Assistant Professor, Department of Clinical Sciences

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

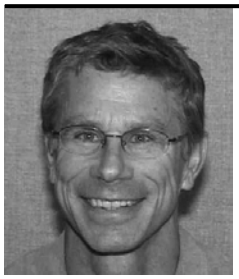
Dr. Werpy earned her DVM from CSU in 1999, followed by an internship at the San Luis Rey Equine Hospital in California which she completed in 2000. In 2003, she completed a residency directed by Dr. Norman Rantanen in collaboration with CSU, which focused on equine imaging. Dr. Werpy joined the CSU faculty 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, PhD, 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 PhD 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 in 1997, Semifinalist for Wallace H. Coulter Award for Medical Innovation and Entrepreneurship, Georgia Tech, Atlanta, Georgia in 2002. Women and Minorities in Engineering Appreciation Award at CSU in 2005, Jack E. Cermak Advising Award at CSU in 2006, and George T. Abell Outstanding Faculty Teaching and Service Award at CSU in 2006. Nominated for CSU Best Teacher Award, 2006.



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

Collaborating on proteomic studies

Christian Puttlitz, MS, PhD, Assistant 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 PhD 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.

Faculty
College of Applied Human Sciences

Raoul F. Reiser, II, PhD, Assistant Professor, Department of Health & Exercise Science

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

Dr. Reiser completed his BS in Mechanical Engineering at Cornell University, his MA in Kinesiology with a specialization in Biomechanics at the University of Texas at Austin and his PhD 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, PhD, Associate Professor, Department of Animal Science

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

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, BS, MS, PhD, Professor, Department of Statistics and Center for Bioinformatics, Colorado State University

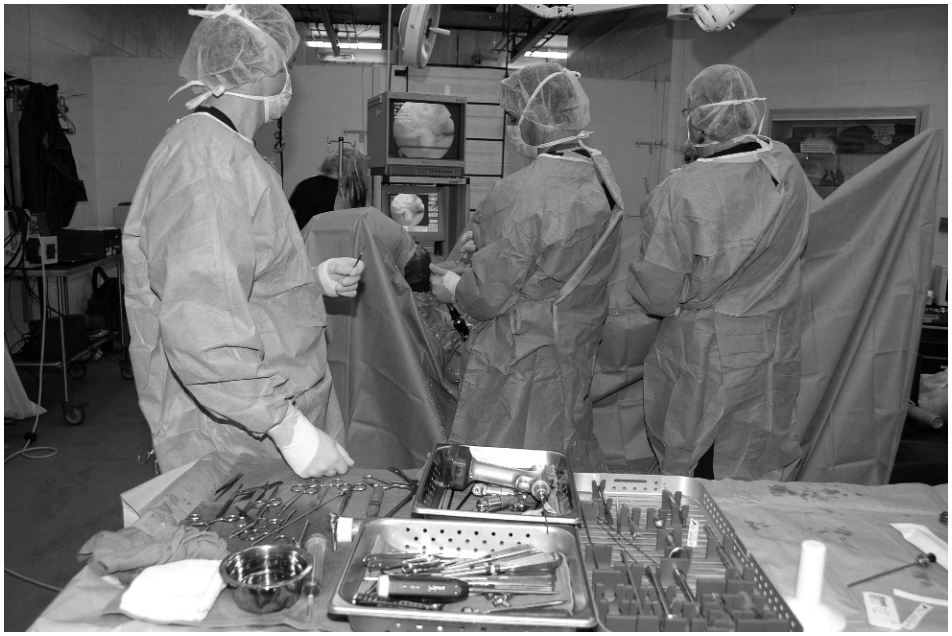
Research interest: Bioinformation–collaborating with Orthopaedic Research Center on multiple projects

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, PhD, Assistant Professor, Department of Statistics and Center for Bioinformatics, Colorado State University

Collaborating in Biostatistics with Orthopaedic Research Center

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

Chris Evans, PhD, 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 PhD 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. Dr. Evans has received many honors, including the 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.

Elwyn Firth, BVSc, PhD, 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.

Steven C. Ghivizzani, PhD, 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.

Clifford Michael Les, DVM, MS, PhD, Senior Staff Investigator, Bone and Joint Center Henry Ford Health System

Research Interests: Mechanical, histologic and material properties of bone

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 DVM at the University of California, Davis, his MS in Veterinary Biosciences at the University of Illinois, Urbana-Champaign and his PhD 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, BVSc, PhD, 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.

Marcus G. Pandy, PhD, 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.

Brigitte von Rechenberg, Dr. med. Vet., Diplomate ECVS, University of Zurich
Research Interests: The pathogenesis of subchondral cystic lesions in horses, studies of bone lysis in joint disease, nitric oxide production in horses with joint disease, biochemical changes at the bone-cement interface associated with implant loosening.

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

Collaborators

Alan Boyde, BDS, LDS, PhD, Professor, Department of Anatomy and Developmental Biology, University College London
Research interests: Changes in equine bone and articular calcified cartilage in response to training exercise, changes in human bone with aging, osteoporosis

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.

Collaborators

Neil David Broom, PhD, Associate Professor, Department of Chemical and Materials Engineering, University of Auckland

Research Interests: Heart valve biomechanics, joint tissue biomechanics/ biomaterials, intervertebral disc biomechanics

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, PhD, Assistant Professor, Department of Chemical and Bilogical Engineering, University of Colorado

Michael Buschmann, PhD, 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 PhD in Medical Engineering and Medical Physics from the Massachusetts Institute of Technology. He is well-known for his cartilage biomechanics research.

Bruce Caterson, BSc, PhD, Professor of Biochemistry, Connective Tissue Biology Group, School of Biosciences, Cardiff University, Wales, U.K.

He has degrees from Monash University, Clayton, Victoria, Australia, (B.Sc. and Ph.D. in Biochemistry, 1971 & 1976, respectively). From 1975-1995 he spent 20 years in academia in the USA; 1975-82, Postdoc - Assistant Professor, UAB, AL; 1982-89, Associate Professor - Professor, West Virginia University; 1989-95, Professor & Endowed Chair in Orthopaedic Research, University of North Carolina at Chapel Hill, NC. In 1995 he moved to Cardiff University into an Established Chair and from 1998 - 2003 was Head of Connective Tissue Biology in the School of Biosciences. He is currently an Executive Manager of the Cardiff Institute of Tissue Engineering & Repair (CITER) and Associate Director of Musculoskeletal Research in the School of Medicine.

He has served on several USA national research committees (N.I.H. Pathobiochemistry; Arthritis Foundation & Orthopaedic Research and Education Fund), been a member of Editorial Boards (J. Biol. Chem., Archives of Biochemistry and Biophysics, and Osteoarthritis & Cartilage). He was also the past-President

(1993) and Board of Directors member of the USA-based Orthopaedic Research Society (1988-1996). In the UK, he has served on the Wellcome Trust Cell & Molecular Grant Review Panel, been President of the Society for Back Research and is currently the Chairman of the British Society for Matrix Biology and President of the British Orthopaedic Research Society.

His primary research interests have centered around using monoclonal antibody technologies to study matrix proteoglycan structure, function and metabolism in health and disease with particular emphasis on musculoskeletal tissues. In the past 30 years he has published a total of 132 full papers and 26 chapters and reviews. In 1986 he was awarded the Benedum Distinguished Scholar Award in Biosciences and Medicine from West Virginia University and in 1998 the Kappa Delta Elizabeth Winston Lanier Award for Outstanding Orthopaedic Research from the American Academy of Orthopaedic Surgeons and Orthopaedic Research Society.

William Dernell, DVM, MS, Diplomate ACVS, Head Department of Clinical Sciences, Washington State University (previously core but leaving CSU - wants to continue to collaborate)

Alan J. Grodzinsky, ScD, 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.

Charles Ho, MD, PhD, Director, National Orthopedic Imaging Associates, California Advanced Imaging at Atherton.

Dr. Ho is experienced and active in musculoskeletal and sports medicine imaging and research, particularly in musculoskeletal Magnetic Resonance imaging, as a member of the Radiological Society of North America, the Society of Skeletal Radiology, 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 in radiologic and orthopedic conference proceedings. Dr. Ho is a member of the Scientific Advisory Board of the Steadman Hawkins Sports Medicine Foundation in Vail, Colorado. He is Radiologic Consultant for such teams as the San Francisco 49ers, San Francisco Giants, Cleveland Indians, Denver Broncos, Colorado Rockies, and the U.S. Ski Team.

Chris Little, BSc, BVMS, MSc, PhD, Diplomate ACVS, Asociate 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 MSc 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 PhD 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, PhD, 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 is collaborating 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.

Michael "Mick" Peterson, PhD, Associate Professor, University of Maine

Dr. Peterson is an Associate 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 PhD is in Theoretical and Applied Mechanics from Northwestern University in Illinois, and he also holds a BS in Mechanical Engineering from General Motors Institute (now Kettering University) and an MS 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, PhD, Professor, 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 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.

Christopher B Riley, BSc(Physics), BVSc(Hons), MSc, PhD, 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

Research interests: Joint disease (arthritis) and biomedical infrared spectroscopy. 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

MSc and PhD 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, PhD, 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.

William G. Rodkey, DVM, MS, Scientific Director for Regen Biologics and 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).

Collaborators

Robert Lie-Yuan Sah, MD, ScD, Professor and Vice-Chair of Bioengineering Affiliate in Orthopaedics, UCSD

Research Interests: Orthopaedic bioengineering
Dr. Sah received his ScD in Biomedical Engineering from the Massachusetts Institute of Technology and his MD 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.

Jude Samulski, PhD, Professor and Director, Gene Therapy Center, University of North Carolina, Chapel Hill, North Carolina

Kevin Shelburn, MS, PhD, Director of the Biomechanics Research Laboratory, Steadman-Hawkins Sports Medicine Foundation, Vail, Colorado

Roger K.W. Smith, MA VetMB PhD 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 PhD 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, MD, 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.

Michael R. Torrey, MS, PhD, 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.

René van Weeren, DVM, PhD, 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 PhD 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 PhD students, who have obtained their degree in the past years and currently supervises 5 PhD 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 PhD 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.

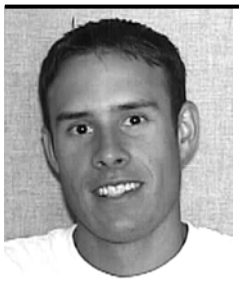
2006-2007 Post Doctoral Fellows

Christina Lee, PhD

Research interests: Investigate traumatic injury induced on and the molecular signaling mechanisms which contribute to the progression of the disease. In addition I am 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.

Dr. Lee received her BS 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. Dr. Lee 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 PhD dissertation studies, she 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 and the Professoriate Advantage Fellow, 2006, Funded by NSF
Eugene Cota-Robles Fellowship, 2003-2005 ($52,594)



Brandon Santoni BS, MS, PhD

Dr. Santoni earned his PhD in Mechanical Engineering in 2006 and worked as a post doctoral fellow at Orthopaedic Bioengineering Research Laboratory and is currently working in Washington State.

Caroline Adamson Adrian, MS, PT, CCRP

Caroline (Carrie) is a PhD 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 BS 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, BS

Ugur was born and raised in Adana, Turkey. He graduated from Bogazici University, Istanbul, Turkey with B.S. degree in Mechanical Engineering in 2005, prior to entering the graduate program of CSU Mechanical Engineering Department. His research project focuses on creating a FE model of the lumbar spine.

PhD Graduate Students

Katja Duesterdieck, Dr. med. vet., MS, DACVS

Katja is a PhD student at the Orthopedic Research Center and a part-time large animal emergency surgeon at the Veterinary Teaching Hospital of the College of Veterinary Medicine and Biomedical Sciences at Colorado State University. Her research interests are the pathophysiology of osteoarthritis, osteochondrosis dissecans and the influence of exercise on the musculoskeletal system.

She grew up on the island of Föhr in Germany and attended the Veterinary University Hanover, Germany and the University of Bern, Switzerland for her veterinary degree, which she obtained in 1996. Katja performed postgraduate studies at the Institute for Animal Nutrition, Veterinary University Hanover, Germany and obtained a Dr. med. vet. degree in 1999. She did a Large Animal Medicine and Surgery Internship and Residency/M.S. at the Virginia-Maryland Regional College of Veterinary Medicine. Her main clinical interests are minimally invasive surgery, equine lameness and osteoarthritis.

Melissa King, DVM

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 PhD 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.

Rachael Kurkowski, BS

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

Jason Marini, BS

Jason earned his MS 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 PhD in Mechanical Engineering, focusing his research on advanced polymers for use in spinal surgery. He expects to graduate in 2008.

Kirk McGilvray, BS, MS

Kirk has a BS in Engineering and a MS in Mechanical Engineering from CSU. He is currently working on a PhD in Mechanical Engineering at CSU, where he is studying the in vivo biomechanical parameters during fracture healing through the use of nanotechnology. He anticipates graduating in Spring 2010.

Valerie Perino, MS

Valerie Perino is currently a Ph.D. student with the Orthopaedic Research Center. She received her BS in Equine Sciences and her MS in Clinical Sciences from Colorado State University. While working toward her Masters degree, Valerie evaluated the Tekscan F-Mat system as an objective measure of lameness in the horse. Most recently, Valerie is continuing to test the Tekscan Equine In-shoe system as an objective measure of lameness in the horse, as well as comparing the F-Mat and Equine In-shoe systems to an equine force plate. She completed her PhD in November, 2007.

Wesley Womack, BS

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.

Susan Yonemura, BS

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 MS in the summer of 2006, after which she plans on continuing with her graduate studies in pursuit of a PhD.

2006-2007 DVM/PhD Graduate Students

Katrina Easton, BS

Katrina is currently in her first year of veterinary school. She received her BS 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.

Marti Shearin, BS

Marti received her BS in equine science from Colorado State University. Currently, she is working on her PhD in clinical sciences with an orthopaedic focus. She has completed three years of Veterinary school and is taking a leave to focus on her PhD work, and plans to return for her final clinical year of vet school. She worked on Dr. Chris Kawcak's PhD project, which involved examining exercise-related changes in the subchondral bone of the left fore third metacarpal condyle. Marti is continuing to examine age-related changes in the subchondral bone of the left fore third metacarpal condyle and more recently is examining bone and cartilage changes seen in racehorses' fetlocks. In her current research, Marti uses a special PC-based computer program called OsteoApp that reads CT scans and allows her to three-dimensionally measure features such as surface area and average surface density of the condyles. She is also looking at the difference in using OsteoApp and DEXA to measure bone density.

Myra Barrett, DVM

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.

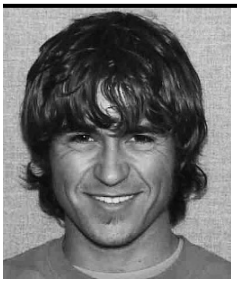
Myra's undergraduate degree was awarded by Stanford University. She went on to receive her DVM from Colorado State University. After a year internship at Oakridge Equine Hospital, a busy referral practice in Oklahoma, Myra returned to Colorado to pursue a specialty in equine orthopaedic imaging.

Peter Brookens, BS

Peter has a BS in Mechanical Engineering which focused on interdisciplinary studies in Biomedical Engineering. He anticipates completing his MS in Mechanical Engineering in Spring 2006.

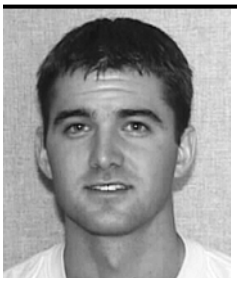
Erin Contino, BS

Originally from Concord, California, Erin moved to Fort Collins to attend CSU, graduating in 1999 with a bachelor's degree in Equine Sciences. She is currently pursuing a master's degree in Equine Radiology, researching abnormal radiographic findings in Quarter Horses and how these abnormalities affect cutting horse performance.



Cody Cranson, BS

Cody is a Mechanical Engineering graduate student at Colorado State University, where he also obtained his bachelor's of science degree in Mechanical Engineering. His research activities focus on hyaluronan derivatives for use in cell scaffold applications. He is also interested in alternative methods for increased healing response, such as lasers and acupuncture.



Brent Dietrich, BS, MS

Brent earned his MS in Mechanical Engineering in 2004. He is currently working in the engineering industry for Lockheed Martin.

2006-2007 MS Graduate Students

Ben Hale, BS

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. He is currently enrolled in the 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, BS

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

Joel Helgerson, BS, MS

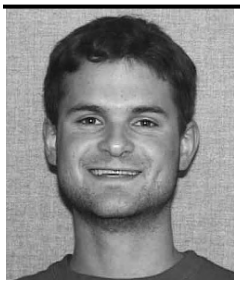
Joel earned his MS in Mechanical Engineering in 2004, and is currently working in the engineering industry in Utah.

Kindra Orr, BS

Kindra received her BA in molecular, cellular and developmental biology from the University of Colorado. Currently, she is working on her master's degree in clinical sciences under the guidance of Dr. David Frisbie. Kindra's research focuses on assessing extracorporeal shockwave therapy as a treatment for osteoarthritis. She is specifically looking at mRNA gene expression in cartilage and synovial membrane to evaluate extracorporeal shockwave therapy in an equine osteoarthritis model.

Adam Pelletier, BS

Adam was born in Lafayette, LA and after finishing high school joined the Louisiana Air National Guard as a member of the 159th Fighter Wing. He was activated in support of Operation Iraqi Freedom. During his term of service (9 years) he attended University of Louisiana at Lafayette and obtained a BS in Mechanical Engineering. Adam's MS thesis project deals with the design of a real time force/displacement measuring cervical distractor utilized in spinal surgeries.



Timothy Ruckh, BS

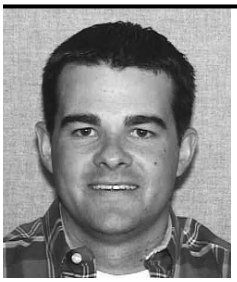
Tim was born Brookfield, WI and received a bachelors degree in mechanical engineering from University of Minnesota in May 2005. His main research interests include orthopaedic biomechanics, and his MS thesis project involves investigating fracture mechanisms of plated tibiae using the finite element method.

Colin Scruton, BVetMed MRCVS, Diplomate ACVS

Dr. Scruton received his BVetMed from the Royal Veterinary College in London, England. He then completed a large animal internship at Washington State University. He is currently an equine surgery resident at Colorado State University. Dr. Scruton's research focused on laser arthrodesis of the distal tarsal joints and examining the effects of intra-articular morphine on lameness resulting from carpal synovitis using an E. coli LPS model. He graduated from CSU with his MS in 2004, and became Board Certified in Large Animal Surgery in 2005. He is currently a Clinical Instructor at the University of Glasgow.

Scott Sulpizio, BS, MS

Scott earned his MS in Mechanical Engineering in 2004 and currently works in the bioengineering industry in Washington State.



Ty Wallis, DVM

Dr. Ty Wallis entered the combined masters program and equine surgery and lameness residency at CSU in July 2005. Prior to joining us, Dr. Wallis obtained his BS in biomedical sciences, as well as his DVM, 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 is currently working on a joint retrospective study with the ORC and CSU's Veterinary Teaching Hospital at evaluating the efficacy of injecting subchondral cystic lesions, mainly in the stifle, with corticosteroids. Soon he will begin 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.

Research Associates

Lynsey-Ann Bosch, BS

Lynsey graduated from Michigan Sate University with a Bachelors 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.

Jodi Callison, BS

Jodi earned her BS 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, MS

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.

Susan James, BA

Susan earned her BA 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

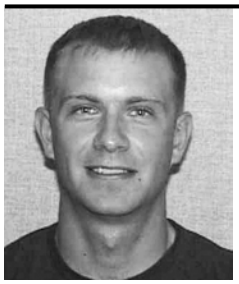
Jon is the Clinical Trial Research Coordinator for the Orthopaedic Research Center. Jon contributes to our research projects as a Surgical Assistant, is responsible for developing research protocols and coordinating activities with study sponsors. In addition, Jon's background includes three years with 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.

His formal training and education includes certifications as a Surgical Assistant with a focus on cardiac bypass and trauma surgery, a nationally registered Paramedic and medical photographer. Jon is an adjunct faculty member at Aims Community College's Department of Emergency Medicine and a trainer for the Union Colony Fire Rescue Department in emergency medicine and technical rescue.

Scott McCorvey, BS

Scott graduated in 2005 from the University of Georgia with a BS in Cell Biology. In the fall of 2007, he completed his MS 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.

Barn Manager



Jeff Ullmer, BA

Jeff earned his BA 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.

Program Coordinator

Paula Vanderlinden

Paula works full-time at the EORC 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.

Business Manager

Joyce Reid, BS

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

Core Faculty

C. Wayne McIlwraith, BVSc, PhD, DSc, FRCVS, Diplomate ACVS
- Clinical Orthopaedics
- Biomarkers
- Joint Pathobiology
- Medical and Surgical Treatment
- Cartilage Healing

David D. Frisbie, DVM, PhD, Diplomate ACVS
- Cartilage Healing
- Biochemistry
- Molecular Biology
- Gene Therapy
- Clinical Orthopaedics

Christopher E. Kawcak, DVM, PhD, Diplomate ACVS
- Pathogenesis of Subchondral Bone Disease andTraumatic Joint Injury
- Histomorphometry
- Biomechanics
- Clinical Orthopaedics

John Kisiday, MS, PhD
- Mechanobiology
- Cartilage Healing
- Biomechanical Characterization

Kevin Haussler, DVM, DC, PhD
- Complimentary and Alternative Medicine
- Rehabilitation
- Spinal and Sacroiliac Disorders
- Anatomy
- Biomechanics

Natasha Werpy, DVM
- Orthopaedic Imaging including Radiology, Computerized Tomography, MRI, and Ultrasonography

Collaborating Faculty

College of Veterinary Medicine

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

Nicole Ehrhart, DVM, MS, Diplomate ACVS
- Orthopedic Oncology
- Gene Delivery and Tissue Engineering

Laurie Goodrich, DVM/PhD, Diplomate ACVS
- Clinical Orthopedics
- Gene Therapy
- Vector Development
- Cartilage Healing

Thomas R. (Tod) Hansen, BS, MS, PhD
- Gene Chip Technology

Ashley Hill, DVM/PhD
- Epidemiology
- Experimental Design

Robert Norrdin, DVM, PhD, Diplomate ACVP
- Orthopaedic Pathology
- Bone Histomorphometry

Richard D. Park, DVM, PhD, Diplomate ACVR
- Orthopaedic Imaging including Radiology, Computerized Tomography and MRI

Barbara E. Powers, DVM, PhD, Diplomate ACVS
- Orthopaedic Pathology
- Histology and Histomorphometry

Philip Steyn, BVSc, MRCVS, Diplomate ACVR
- Orthopaedic Imaging including Radiology and Nuclear Imaging

College of Engineering

Susan P. James, PhD
- Biomechanics

Ketul Popat, PhD, Assistant Professor, Department of Mechanical Engineering, School of Biomedical Engineering

Christian Puttlitz, PhD
- Orthopaedic Biomechanics

College of Agricultural Sciences

Jason Bruemmer, PhD
- Gene Chip Technology

College of Natural Sciences

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

Student Employees and Volunteers

Student Work Study/ Student Hourly Assistants	Volunteers 2006	Volunteers 2007
Mike Maher	Kari Bevevino	Aimee Aaroe
Christine Martin	Anne Biedenstein	Mackenzie Adams
Meaghan Tumilson	Stephanie Butler	Claire Aitken
Wade Walker	Jillian Daniels	Jill Cadmus
Chelsea Zimmerman	Leslien Edmonds	Caronine Cervelli
	Kelly Fagerstone	Lauren Farrington
	Emery Hickman	Eric Garcia
	Laurel Lachowiez	Kristin Height
	Meredith Leary	Kelly Horgan
	Lauren Marchenitz	Rachel Motsinger
	Kate Richards	Jessica Nieset
	Anna Rothman	Lauren Pastewka
		Meghan Tumlinson
		Anna Wienen

Table 1

Graduate Students - Placement Since Inception

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

Table 1

Graduate Students - Placement Since Inception

Student	Degree	Date Graduated	Current Position
Abigail Dimock	MS	1997	Currently a PhD student, Equine Nutrition (Orthopaedic Related), Rutgers University
Becky Woodward	MS	1998	Graduate Researcher on S-V Dagon Research Vessel, University of British Columbia
Tina Anderson	PhD	1998	Director of Marketing
Louise Southwood Perante	MS	1998/2002	Associate Professor, University of Pennsylvania School of Veterinary Medicine
Charles Hubbeling	PhD	1999	Private consulting
Guy Beauregard	PhD	1999	Senior scientist/researcher for private industry.
Andrew Green	MS	1999	Engineering Manager for private industry.
Elisha Rentfrow	MS	1999	Private consulting
Tara Ruttley	MS	2000	Engineer for NASA
Carson Shellenberger	MS	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	MS	2000	Assistant Professor, University of California Davis
Troy Trumble	MS	2000, 2004	Associate Professor, University of Minnesota
Chengcheng Lui	MS	2001	Continuing in school
Jana Read	MS	2001	Employed in Quality Control
Erin Peterson	MS	2001	Faculty Member, Department of Animal Science, University of Maryland
Anne DePalma	MS	2002	
Joel Millets	MS	2002	Employed at Osteotech, Allograft Company
Carolyn Skurla	PhD	2002	Assistant Professor, Baylor University
Louise Southwood Perante	PhD	2002	Faculty Member, University of Pennsylvania School of Veterinary Medicine
Awad Al-Zaben	PhD	2003	Faculty Member, Electronics Engineering Department, Yarmouk University, Irbid, Jordan
Sophie Morisset	PhD	2003	Assistant Professor, Department of Clinical Sciences, Université de Montréal
Thomas Young	MS	2003	Currently job searching
Thomas Young	MS	2003	Currently job searching
Colin Scruten	MS	2004	Private Practice, Alberta, Canada

Table 1

Graduate Students - Placement Since Inception

Student	Degree	Date Graduated	Current Position
Lea Rempel	PhD	2004	Post-Doctoral Fellow, University of Kansas Medical School, Currently, Research Scientist, United States Meat Animal Research Center, Clay Center, NE
Chris Sorensen	PhD	2004	Post-Doctoral, National Mass Spectrometry Facility, Environmental Molecular Sciences Laboratory and Biological Sciences Division, Pacific Northwest National Laboratory, Richland, WA
Brandon Santoni	PhD	2006	Posdoctoral Research Fellow, ORBL, Colorado State University
Katja Duesterdieck	PhD	2006	Assistant Professor, Oregon State University
M. Shearin	DVM/PhD	2006	Assistant Doctoral Fellow, University of Tennessee
Valerie Perino	MS, PhD	2007	Completed PhD, Equine Orthopaedic Research, Colorado State University

Table 2
Surgery Residents Supervised (and Outcome)

Resident	Years of Residency	Date Achieved Board Certified 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 Program 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 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.

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 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, hyaluronic acid, polysulfated glycosaminoglycans, pentosan polysulfate, oral glycosaminoglycans, other oral nutraceuticals, shock wave therapy, gene therapy 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.

7. *Significance of radiographic lesions in terms of subsequent musculoskeletal problems.*

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 the preeminent equine orthopaedic research program, both nationally and internationally, the Orthopaedic Research Center 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 orhopaedic 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 Program 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

During the recent five years, funding for 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 six full-time faculty senior scientists. To support the work of the Faculty Researchers, we now have eight research associates. We have had seven PhD students and twelve MS students in the program the past two years. Current funding is around $3 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 three 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 PhD students and 16 MS students in the past two years.

Program Goals

Goals Accomplished 2006-2007

1. *Construction of Equine Gait Analysis Building:* A gait analysis building that will have four force plates for assessing lameness objectively in the horse is completed. Due to a recent donation from the Thaw Foundation, an already established gait analysis laboratory for dogs is also going to move 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 will be 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.

3. *Cartilage Biomechanics Laboratory:* This is the second part of the recently built Equine Histology Laboratory. This will house Dr. John Kisiday and his biomechanical testing equipment for assessment of cartilage, as well as culturing of mesenchymal-derived stem cells.

4. *Achieve Extramural Research Funding to Continue Quality Orthopaedic Research.* Dr. Dave Frisbie is the PI for the CSU sub-contract and tissue engineering for cartilage healing being assessed first in a rabbit model and later in our equine model.

5. *Unrestricted Funding from Donors and Foundations:* In addition to a second $3,000,000 endowed chair being acquired in 2004-2005, additional funding has provided continued support for salaries and building programs. Generous donations from the Walton Family Foundation and Allen & Company have helped support faculty salaries. A new donation of $500,000 from John and Abbey Winkelried has allowed us to partially support an endowed fund for a faculty position, as well as provide salary support. While most Research Associate salaries come from competitive research grants, funding from foundations also helps in this critical support. The Marilyn Simpson Trust provided $100,000 per year (this amount has been provided over the past five years, for a total of $500,000) and we have also had support from the Equus Foundation and the Thoroughbred Charities of America. The Steadman-Hawkins Research Foundation has continued to support investigations in cartilage healing.

6. *Abigail K. Kawananakoa University Endowed Chair in Equine Musculoskeletal Integrative Therapies:* A $3 million endowed chair was instituted thanks to the generosity of the Abigail K. Kawananakoa. The chair has not been awarded at this time. The $3 million corpus allows us to fund this chair in perpetuity for research in equine musculoskeletal integrative therapies.

7. *Kenneth and Virginia Atkinson University Endowed Chair in Equine Musculoskeletal Imaging.* A $1.5 million endowed Chair was instituted thanks to the generosity of Kenneth and Virginia Atkinson. This chair has not been awarded at this time. The $1.5 corpus will be able to fund in perpetuity a half-time position for equine musculoskeletal imaging, specifically MRI. Dr. Natasha Werpy currently occupies this position in a half-time role and this funding will continue to support her salary.

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 Bioengineering Laboratory.

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 Center's Research Focuses.

Research Goals for the Future

The 2006-2007 years have been exciting times for the Orthopaedic Research Center. The scientists have continued to achieve considerable stability in the last two years, and the program has also obtained the long-term funding that it needs to provide stability for the future.

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

In cartilage healing the previously reported in vitro assessment of gene therapy using a combination of insulin-like growth factor 1 (IGF-1) and interleukin-1 receptor antagonist (IL-1Ra) has continued into in vivo assessment. This work was done by Dr. Sophie Morrisset working with Dr.'s Frisbie and McIlwraith, as well as in collaboration with Dr.'s Chris Evans and Paul Robbins. The in vivo project showed that gene therapy could further augment the microfracture response by increasing the amounts of type II collagen and aggrecan production.

Another project was done assessing the ability of electrostimulation (Bionicare) to further stimulate cartilage repair over and above microfracture. This study was done in a controlled fashion with defects on the medial femoral condyle. Unfortunately, no benefit was demonstrated with augmentive electrostimulation therapy.

With previous projects, the evaluation of autologous chondrocyte implantation (cultured) is in press with Osteoarthritis and Cartilage. The second project using morselized cartilage fragments was presented at the International Cartilage Research Society meeting in Warsaw in 2007 by Dr. Frisbie and a paper has currently been submitted on this exciting technique. Based on the results in the horse, the FDA gave permission for a phase I study in humans and this study is approaching completion.

Other cartilage healing studies have included the assessment of autologous photo-oxidized osteochondral plugs. While this study has just been completed the arthroscopic results at 18 months post-implantation were exiting. This project funded by Zimmer Biologics.

In the area of subchondral microdamage, work has continued with the GERA material. Dr. Kawcak and McIlwraith, working in collaboration with Dr. Neil Broom in New Zealand have reported on changes in the mechanical properties of articular cartilage with exercise. Other work done by Drs. Kawcak and McIlwraith with Dr. Elwyn Firth at Massey University has demonstrated that there certainly is change in the third metacarpal bone with exercise and with a significant increase in bone formation in exercised horses midway through the study. However, there appeared to be a maturation effect later in the control horses, as the bone volume at the end was not different between both groups of horses (as assessed by CT).

In other work, Katrina Easton, a DVM PhD student working with Drs Kawcak, Puttlitz and McIlwraith has developed a finite element model of the equine fetlock joint. The main aim of this model development is to look at change in the distal metacarpal bone that could predispose to osteochondral disease and fractures. In addition, work is being done to look at areas of contact,

which appear to be associated with effects of joint congruency (or lack of joint congruency) are also being assessed.

In the area of diagnosis, work has continued to develop with Dr. Kawcak, Raoul Reiser, and McIlwraith working with Dr. Michael Davies of EQUUSYS to develop and validate wireless technology to track horse movement, as well as measure forces. The technology uses accelerometers, gyroscopes and magnetometers in a compact wireless device, which can be attached to the horse's limb and used at a high speed to monitor how the limbs are used and measure the stresses they undergo. This should provide excellent objective information for not only examining the pathogenesis of injury, but also of racetrack and arena surfaces, as well as providing objective diagnostic data.

In addition, both clinical and research assessment of magnetic resonance imaging (MRI) continues. Dr. Werpy has studied the effects of intrabursal injection on MRI assessment on the navicular bone, navicular bursa and digital tendon sheath. A second study has been done comparing the histopathology of changes in the foot compared to the MRI changes. Much commentary has been made, both in human and equine MRI on bone marrow signal changes (commonly referred to as bone marrow edema) and this study will depict more accurately what the actual changes are histologically as seen on MRI.

The Centers fourth focus of investigating novel therapies to treat joint diseases has continued. The previously presented work with unsaponified avocado and soy extract as an oral nutraceutical, as well as the evaluation of autologous-conditioned serum (Orthokine™ in UK, IRAP™ in the US) to treat equine osteoarthritis had been published in the *American Journal of Veterinary Research.* A third project evaluating the use of fat-derived regenerative cell therapy in the treatment of osteoarthritis showed decreased PGE2 levels in both carpal joints (and the same with bone-derived cultured cells), but otherwise not many significant changes. Projects have been completed (but await final analysis) on assessing a topical, non-steroidal, anti-inflammatory drug (Surpass™), intra-articular polysulfated glycosaminoglycan (Adequan™) (funded by IDEXX) compared to intramuscular Adequan in our osteoarthritis model, assessment of magnetic imaging therapy in our equine osteoarthritis model (funded by MBST Technologies), as well as assessment of both intravenous and intra-articular Polyglycan.

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.

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. Continued work will reveal efficacy in animal models.

With regard to our new fifth focus integrative therapies and physical manipulation and rehabilitation therapies, a number of studies have been 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. Work continues in these modalities and more recently we have initiated studies in both the dog and the horse looking at rehabilitative therapies. A project assessing swimming, underwater treadmilling and hyperbaric oxygen therapy will be done on horse in collaboration with Pegasus Training Center in Seattle, Washington and a second PhD student is working on objective assessment of rehabilitation in the dog.

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. While specializing in 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, 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 ^{35}S labeled proteoglycan complexes.
Col 2 ¾ Long: An assay to standardize the measurement of Type II Collagen.
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:
Col 2 ¾ Short: 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.

Western and Northern Blotting

Many other assays available. Please inquire.

Biomechanical Testing

Displacement control testing for compressive and shear material properties
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

Research Techniques Available at the Orthopaedic Research Center

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

Isolation of Synoviocytes and Chondrocytes
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

Histology Services
Decalcification
Decalcification and non-decalcification histology processing
Staining and sectioning
Immunohistochemistry
Ventana Nex-ES stain and scanner

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 ft^2 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 ft^2 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 ft^2 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 ft^2 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

Textbook Chapters
2006

McIlwraith CW. Healing of articular cartilage in Bojrab Mechanisms of Disease, 2006.

DiAngelo DJ, Puttlitz CM. "Biomechanical aspects associated with cervical disc arthroplasty." In Dynamic Reconstruction of the Spine, DH Kim, FP Cammisa, RG Fessler (eds.), Thieme Medical Publishers, 2006.

Textbook Chapters
2007

Santoni BG, Puttlitz CM. "Biomechanical aspects associated with cervical spine instrumentation and arthroplasty." Minerva Ortopedica e *Traumatologica 57:303-22, 2007.*

Dernell W, Ehrhart N. Tumors of the Skeletal System. In Small Animal Clinical Oncology Withrow and MacEwan eds. 4th edition, Saunders, 2007 pp 540-582.

Ehrhart N, Withrow SJ. Biopsy Principles. In Small Animal Clinical Oncology, Withrow and MacEwan eds. 4th edition, Saunders, 2007 pp 147-156.

McIlwraith CW, Rodkey WG. The Horse-Human Relationship: Research and the future. Chapter 15, JA Feagin & JR Steadman (eds) The Crucial Principles in the Care of the Knee, Lippincott, Williams & Wilkins, 2007.

McIlwraith CW. Nutraceuticals in Joints. Current Therapy in Equine Medicine, 2007.

McIlwraith CW. Bone, Joint and Muscle Disorders. The Merck/Merial Manual for Health. Home Edition. 2007:664-708.

Miclau T, Bozic K, Tay B, Kim H, Colnot C, Puttlitz CM, Gan J, Boyan B, Eames B, De La Fuente L, Helms J. "Bone injury, repair and regeneration." In Orthopaedic Basic Science: Foundations of Clinical Practice (3rd Edition), TA Einhorn, RJ O'Keefe, JA Buckwalter (eds), American Academy of Orthopaedic Surgeons, p. 331-48, 2007.

Refereed Publications
2006

Boston SE, Ehrhart NP, Dernell WS, Lafferty M, Withrow SJ. Evaluation of survival time in dogs with stage III osteosarcoma that undergo treatment: 90 cases (1985-2004). J Am Vet Med Assoc. 2006 Jun 15;228(12):1905-8.

Comerford L, Ma B, Wilson J, Puttlitz CM. "Biomechanical analysis of arthroscopic rotator cuff repairs - double vs. single row fixation." Journal of Bone and Joint Surgery 88:403-10, 2006.

Dennis MM, Ehrhart N, Duncan C, Barnes AB, Ehrhart EJ. Frequency of and risk factors associated with lingual lesions in dogs: 1,196 cases (1995-2004). J Am Vet Med Assoc. 2006 May 15; 228(10):1533-7.

Frisbie DD, Morisset S, Ho CP, Rodkey WG, Steadman JR, McIlwraith CW. Effects of calcified cartilage on healing of chondral defects treated with microfracture in horses. Am J Sports Med, 2006;11:1824-1831.

Fujita M, Diab M, Xu Z, Puttlitz CM. "A biomechanical analysis of sublaminar and subtransverse process fixation using metal wires and polyethylene cables." *Spine* 31:2202-8, 2006.

Goodrich LR, Choi VW, Carbone BC, McIlwraith CW, Samulski RJ. High efficiency gene targeting to mammalian joint tissue using self-complimentary adeno-associated viral vector serotypes. Molecular Therapy 2006;13:S191.

Joyce J, Baxter GM, Sarrafian TL, Stashak TS, Trotter G, Frisbie DD. Use of transfixation pin casts to treat adult horses with comminuted phalangeal fractures: 20 cases (1993-2003). *JAVMA* 229(5):725-30, 2006.

Lindsey C, Deviren V, Xu Z, Yeh RF, Puttlitz CM. "The effects of rod contouring on spinal construct fatigue strength." Spine 31:1680-7, 2006.

Liptak JM, Ehrhart N, Santoni BG, Wheeler DL. Cortical bone graft and endoprosthesis in the distal radius of dogs: a biomechanical comparison of two different limb-sparing techniques. Vet Surg, 2006, 35(2):150-60.

Liptak JM, Dernell WS, Ehrhart N, Lafferty M, Monteith GJ, Withrow SJ. Cortical allograft and endoprosthesis for limb-sparing surgery in dogs with distal radial osteosarcoma: a prospective clinical comparison of two different limb-sparing techniques. Vet Surg. 2006 Aug;35(6):518-33.

Vijarnsorn, M, Riley CB, Shaw RA, McIlwraith CW, Ryan DAJ, Rose, P, Spangler, E. Establishment of a method for the diagnosis of traumatic arthritis in the horse using infrared spectroscopy. Am J Vet Res 2006;67:1286-1292.

Werpy NM, Ho CP, Kawcak CE, Rantanen NW, McIlwraith CW. A review of principles and clinical applications of magnetic resonance imaging in the horse. Proceedings American Association of Equine Practitioners Annual Convention, December, 2006;Vol 52:427-440.

Refereed Publications
2007

Bacon NJ, Dernell WS, Ehrhart N, Powers BE, Withrow SJ. Evaluation of primary re-excision after recent inadequate resection of soft tissue sarcomas in dogs: 41 cases (1999-2004). J Am Vet Med Assoc. 2007 Feb 15;230(4):548-54.

Scientific Publications

Boyd B, Puttlitz CM, Noble-Hausslein LJ, John CM, Trivedi A, Topp KS. "Gait analysis using a pressure mapping system after traumatic injury to the central or peripheral nervous system in rat." Journal of Neuroscience Research 85:2272-83, 2007.

Drum MG, Les CM, Park RD, Norrdin RW, McIlwraith CW, Kawcak CE. Correlation of quantitative computed tomographic subchondral bone density and ash density in horses Journal of Orthop Res, In Press, 2007.

Drum MG, Kawcak CE, Norrdin RW, Park RD, Les CM, McIlwraith CW. Comparison of Gross and Histopathologic Findings with Quatitative Computed Tomographic Bone Density in the Distal Third Metacarpal Bone of Racehorses. Veterinary Radiology and Ultrasound, In Press, 2007.

Dykgraff S, Firth EC, Rogers CW, Kawcak CE. Effect of exercise on chondrocyte viability and subchondral bone sclerosis of the distal third metacarpal and metatarsal bones of young horses. Equine Vet J, In Press, 2007.

Easton KL, Kawcak CE. Evaluation of increased subchondral bone density in areas of contact in the metacarpophalangeal joint during joint loading in horses. Am J Vet Res 68(8):816-21, 2007.

Firth EC, Rogers CW, van Weeren PR, Barneveld A, Kawcak CE, McIlwraith CW, Goodship AE, Smith RKW. Changes in diaphyseal and epiphyseal bone parameters in thoroughbred horses after withdrawal from training. Musculoskelet Neuronal Interact 2007; 7: 74-76.

Frisbie DD, Kawcak CE, Werpy NM, Park RD, McIlwraith CW. Clinical, biochemical and histologic effects of intra-articular administration of autologous conditioned serum in horses with experimentally induced osteoarthritis. *Am J Vet Res* 2007; 462: 221-228.

Frisbie DD, Kawcak CE, Werpy NM, Park RD, McIlwraith CW. Clinical, biochemical and histological effects of intra-articular administration of autologous conditioned serum in horses with experimentally induced osteoarthritis. *Am J Vet Res* 68(3):290-296, 2007.

Gupta S, Carrillo F, Li C, Pruitt L, Puttlitz CM. "Adhesive forces significantly affect elastic modulus determination of soft polymeric materials in nanoindentation." *Materials Letters* 61:448-51, 2007.

Haussler KK. Equine anatomy and biomechanics: Comparative anatomy of the pelvic limb. Home Study Course, Basic Science for Animal Physical Therapists, Orthopaedic Section, APTA, Inc., 2007; 1-36.

Haussler KK. Equine anatomy and biomechanics: Comparative anatomy of the thoracic limb. Home Study Course, Basic Science for Animal Physical Therapists, Orthopaedic Section, APTA, Inc., 2007; 1-32.

Haussler KK. Equine anatomy and biomechanics: Comparative anatomy of the axial skeleton. Home Study Course, Basic Science for Animal Physical Therapists, Orthopaedic Section, APTA, Inc., 2007; 1-27.

Haussler KK, Hill AE, Frisbie DD, McIlwraith CW. Determination and use of mechanical nociceptive thresholds of the thoracic limb to assess pain associated with induced osteoarthritis of the middle carpal joint in horses. Am J Vet Res 2007; 68:1167-1175.

Haussler KK, Hill AE, Puttlitz CM, McIlwraith CW. "Effects of spinal mobilization and manipulation on kinematics of the thoracolumbar region in standing horses." *American Journal of Veterinary Research* 68: 508-16, 2007.

Jehn CT, Lewis DD, Farese JP, Ferrell E, Conley W, Ehrhart N. Transverse bone transport osteogenesis: A morphologic comparison of two techniques for limb salvage in dogs. Vet Surg 2007 36:324-334.

Kawcak CE, Frisbie DD, McIlwraith, Werpy NM, Park RD. Evaluation of avocado and soybean unsaponifiable extracts for treatment of horses with experimentally induced osteoarthritis using an equine model. Am J Vet Res 2007; 68: 598-604.

Kim T, Ayturk U, Haskell A, Miclau T, Puttlitz CM. "Fixation of osteoporotic distal fibula fractures: a biomechanical comparison of locking versus conventional plates." *Journal of Foot and Ankle Surgery* 46:2-6, 2007.

McIlwraith CW. Bone abscessation in the horse - how comparable to Brodie's abscess is it? Equine Vet Educ 2007; 19:298-299.

Morisset S, Frisbie DD, Robbins PD, Nixon AJ, McIlwraith CW. IL-1ra/IGF-1 gene therapy augments repair of microfractured chondral defects. *Clinical Orthopaedics and Related Research* 462:221-228, 2007.

Perino VV, Kawcak CE, Frisbie DD, Reiser RF, McIlwraith CW. The accuracy and precision of an equine in-shoe pressure measurement system as a tool for gait analysis. *Journal of Equine Vet Sci* 27(4):161-166, 2007.

Puttlitz CM, Harms J, Xu Z, Deviren V, Melcher RP. "Acute stability afforded by C2 replacement constructs." *Spine Journal* 7:210-215, 2007.

Puttlitz CM, Masaru F, Barkley A, Diab M, Acaroglu E. "A biomechanical assessment of thoracic spine stapling." *Spine* 32:766-771, 2007.

Wehling P, Moser C, Frisbie D, McIlwraith CW, Kawcak CE, Krauspe R, Reinecke JA. Autologous conditions serum in the treatment of orthopedic diseases. The Orthokine® Therapy. Biodrugs 2007; 21: 323-332.

Published Abstracts/Proceedings
2006

Diab M, Howlett J, Puttlitz CM. "Clinical and biomechanical effect of eyelet screws on Ender nails for fixation of femoral shaft fractures in children." Annual Meeting of the Orthopaedic Trauma Association, Phoenix, October 5-7, 2006.

Scientific Publications

Duesterdieck KF, Frisbie DD, Kisiday JD, Kawcak CE, McIlwraith CW. RNA Isolation from microscopic tissue samples. Proceedings Phi Zeta Research Day, Fort Collins, Colorado, 2006:29.

Easton KL, Kawcak CE. A Multiple dye staining technique to evaluate change in metacarpophalangeal joint contact area under load. Proceedings Phi Zeta Research Day, 2006:32.

Ehrhart N, Dernell WS, Withrow SJ, Ehrhart EJ, Steyn P, Anderson PM. Targeted Internal Radiotherapy for Osteosarcoma: Isolated Limb Perfusion using a Bone Seeking Radiopharmaceutical (^{153}Sm-EDTMP). Proceedings for the 97th American Association for Cancer Research Annual Meeting, Washington DC, 2006 p 978.

Ehrhart N, Dernell WS, Withrow SJ, Ehrhart EJ, Steyn P, Anderson PM. Targeted Internal Radiotherapy for Osteosarcoma: Isolated Limb Perfusion using a Bone Seeking Radiopharmaceutical (^{153}Sm-EDTMP). Proceedings for the Musculoskeletal Tumor Society Meeting, Key West, FL 2006 p 57.

Firth EC, Rogers CW, van Weeren PR, Barneveld A, Kawcak CE, McIlwraith CW, Goodship AE, Smith RWK. Change in bone parameters in Thoroughbred horses months after training has ceased. 7th Int Conference on Equine Exercise Physiology, ICEEP Proceedings, 2006. p.104.

Frisbie DD, Kawcak CE, McIlwraith CW. Evaluation of Oral Avocado/Soybean Unsaponifiables Using an Experimental Model of Equine Osteoarthritis. In: Proceedings, American Association of Equine Practitioners Annual Convention, San Antonio, Texas, 2006:570-571.

Frisbie DD, Kawcak CE, Werpy NM, McIlwraith CW. Evaluation of Bone Marrow Derived Stem Cells and Adipose Derived Stromal Vascular Fraction for Treatment of Osteoarthritis Using an Equine Experimental Model. In: Proceedings, American Association of Equine Practitioners Annual Convention, San Antonio, Texas, 2006:420-421.

Frisbie DD. Biological Therapy of Acute Joint Injuries. In: Proceedings, World Veterinary Orthopaedic Congress, Keystone, Colorado, 2006:53-55.

Frisbie DD, Kisiday JD, McIlwraith CW. Adipose Stem Cell Grafting. In: Proceedings, World Veterinary Orthopaedic Congress, Keystone, Colorado, 2006:142-144

Frisbie DD, Colhoun HA, Bowman S, Kawcak CE, McIlwraith CW. Autologous Chondrocyte Transplantation Via a Collagen Membrane: A Long-Term Study. In: Proceedings, Annual Meeting of the Orthopaedic Research Society, Chicago Illinois, 2006:1441.

Goodrich LR, Choi VN, Carbone BC, McIlwraith CW, Samulski RJ. High effieiency gene trargetting to mammalian joint tissue using self-complimentary adeno-associated viral vector serotypes. Transactions 9th Annual American Society of Gene Therapy 2006:12 (CD-Rom).

Haussler KK. Functional anatomy and pathology of the equine spine. Proceedings of the 4th International Symposium on Rehabilitation and Physical Therapy in Veterinary Medicine, Arnhem, Netherlands, October 2006.

Haussler KK. What is sacroiliac joint disease? Voorjaarsdagen European Veterinary Conference, Amsterdam, Netherlands. April 2006.

Haussler KK. Functional anatomy and pathology of the sacroiliac joint. Voorjaarsdagen European Veterinary Conference, Amsterdam, Netherlands. April 2006.

Haussler KK. Clinical features of sacroiliac disease: Palpation and manipulation. Voorjaarsdagen European Veterinary Conference, Amsterdam, Netherlands. April 2006.

Haussler KK, Engeli E. Sacroiliac joint injection techniques. Voorjaarsdagen European Veterinary Conference, Amsterdam, Netherlands. April 2006.

Haussler KK. How to perform objective assessment of mechanical nociceptive thresholds in the equine spine. Voorjaarsdagen European Veterinary Conference, Amsterdam, Netherlands. April 2006.

Haussler KK. Functional anatomy and pathology of the canine spine. Proceedings of the 78th Annual Western Veterinary Conference, Las Vegas, NV. February 2006.

Haussler KK. Scientific basis of chiropractic care in veterinary medicine. Proceedings of the 78th Annual Western Veterinary Conference, Las Vegas, NV. February 2006.

Haussler KK. Small animal chiropractic techniques. Proceedings of the 78th Annual Western Veterinary Conference, Las Vegas, NV. February 2006.

Haussler KK. Equine back pain, joint stiffness and muscles spasms. Proceedings of the 78th Annual Western Veterinary Conference, Las Vegas, NV. February 2006.

Haussler KK. Complementary medicine: Spinal evaluation, chiropractic and massage techniques. Proceedings of the 78th Annual Western Veterinary Conference, Las Vegas, NV. February 2006.

Haussler KK. Functional anatomy and pathology of the equine spine. Proceedings of the 78th Annual Western Veterinary Conference, Las Vegas, NV. February 2006.

Haussler KK. Clinical applications of equine chiropractic. Proceedings of the 78th Annual Western Veterinary Conference, Las Vegas, NV. February 2006.

Haussler KK. Assessment of back pain and spinal flexibility in horses. Proceedings of the 78th Annual Western Veterinary Conference, Las Vegas, NV. February 2006.

Haussler KK. Rehabilitation of the equine spine. Proceedings of the 78th Annual Western Veterinary Conference, Las Vegas, NV. February 2006.

Haussler KK. Chiropractic approaches to back pain in horses. Proceedings of the 67th Annual Conference for Veterinarians, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO. January 2006.

Scientific Publications

Kandemir U, Matityahu A, Desai R, Puttlitz CM. "Distal radius fixation using dorsal non-locking plate vs. volar locking plate." Annual Meeting of the Orthopaedic Trauma Association, Phoenix, October 5-7, 2006.

Kawcak, CE. Update on Diagnosis of Foot Disease. In Proceedings, Central Veterinary Conference, Kansas City, Missouri, 2006.

Kawcak, CE. Magnetic Resonance Imaging of the Hoof. In Proceedings, Central Veterinary Conference, Kansas City, Missouri, 2006.

Kawcak, CE. Management of Equine Hoof Pain. In Proceedings, Central Veterinary Conference, Kansas City, Missouri, 2006.

Kawcak, CE. Recent Advances in Intraarticular Medications. In Proceedings, Central Veterinary Conference, Kansas City, Missouri, 2006.

Kawcak, CE. Farm based approach to managementof developmental orthopedic diseases. In Proceedings, Central Veterinary Conference, Kansas City, Missouri, 2006.

Kisiday JD, Kopesky PW, Szafranski JD, Evans CH, Grodzinsky AJ, McIlwraith CW, Frisbie DD. Evaluation of TGF-beta 1 mediated chondrogenesis of bone marrow and adipose-derived stem cells encapsulated in agarose and self-assembling peptide hydorgels. ICRS Proceedings, 2006:134.

Kisiday JD, Dopesky PW, Szafranski JD, Evans CH, Grodzinsky AJ, McIlwraith CW, Frisbie DD. Evaluation of Chondrogenesis of Bone Marrow and Adipose-Derived Stem Cells Encapsulated in Agarose and Self-Assembling Peptide Hydrogels. ORS Proceedings, 2006:783.

Kisiday JD, Evans CH, Frisbie DD, Grodzinsky AJ. Effects of Dynamic Compression on Chondrogenesis of Adult Equine Mesenchymal Stem Cells Encapsulated in Agarose Hydrogel. In: Proceedings, Annual Meeting of the Orthopaedic Research Society, Chicago, Illinois, 2006:132.

Kisiday JD, Kopesky PW, Szafranski JD, Evans CH, Grodzinsky AJ, McIlwraith CW, Frisbie DD. Evaluation of TGF-beta 1 mediated chondrogenesis of bone marrow and adipose-derived stem cells encapsulated in agarose and self-assembling peptide hydrogels. In: Proceedings, 6th Annual Symposium of the International Cartilage Repair Society, San Diego, California, 2006:134.

Liptak JM, Ehrhart N, Santoni BG Wheeler D. Cortical bone graft and endoprosthesis in the distal radius of dogs: a biomechanical comparison of two different limb-sparing techniques. Proceedings for the15th Annual Scientific Meeting of the European College of Veterinary Surgeons, Seville, Spain, 2006 pp 454-455.

McIlwraith CW, Frisbie DD. Influence of Calcified Cartilage Layer Removal and Microfracture on Cartilage Repair Obtained Using a Single Step Autologous Cartilage Transplantation (CAIS). In: Proceedings, American Orthopaedic Society for Sports Medicine. Articular Cartilage Regeneration Repair and Repair Workshop: A grant workshop. (June 28, 2006).

McIlwraith CW, Frisbie DD, Lu Y, Colhoun HA, Kawcak CE, Binette F. In-Vivo Evaluation of A One-Step Autologous Cartilage Resurfacing Technique (CAIS) Compared To A Modified ACI Technique In A Long-Term Equine Model. In: Proceedings, 6th Symposium of the International Cartilage Repair Society, San Diego, California, 2006:16.

McIlwraith CW, Frisbie DD, Lu Y, Colhoun HA, Kawcak CE, Binette F. In-Vivo Evaluation Of A One-Step Autologous Cartilage Resurfacing Technique (CAIS)- Comparison Of Three Different Scaffolds. In: Proceedings, 6th Annual Symposium of the International Cartilage Repair Society, San Diego, California, 2006:93.

Orr KE, Frisbie DD, Kawcak CE, McIlwraith CW. Joint Tissue mRNA Expression in an Equine Osteoarthritis Model to Evaluate Extracorporeal Shockwave Therapy. Proceedings Phi Zeta Research Day, Fort Collins, Colorado, 2006:53.

Puttlitz CM, Johnson N, Hindman B, Weeks J, Maktabi M, Todd M. "Effects of manual in-line stabilization on the magnitude and distribution of pressures exerted by a laryngoscope blade during direct laryngoscopy and intubation." 34th Annual Meeting of the Cervical Spine Research Society, Palm Beach, FL, November 29-December 2, 2006.

Rogers CW, Firth EC, van Weeren PR, Barneveld A, Kawcak CE, McIlwraith CW, Goodship AE, Smith RWK. The Measurement of work load in a population of Thoroughbred foals. ICEEP Proceedings, 2006.

Shearin MG, Kawcak CE, Norrdin RW, Park RD, Les CM, McIlwraith CW. Comparison of gross pathologic, histologic, & subchondral density changes in racing horses. ORS Proceedings, 2006.

Southwood LL, Kawcak CE, McIlwraith CW, Frisbie DD. Evaluation of an Equine Metacarpal IV Fracture Defect Model. ACVS Proceedings, 2006:E25.

Shearin MG, Kawcak CE, Norrdin RW, Park RD, Les CM, McIlwraith CW. Comparison of Gross Pathologic, Histologic, and Subchondral Density Changes in Racing Horses. Proceedings Phi Zeta Research Day, 2006:43.

Wallis TW, Goodrich LR, McIlwraith CW, Hendrickson DA, Trotter GW, Frisbie DD, Baxter GM, Kawcak CE. Arthroscopic injection of corticosteroids into the lining of subchondral cystic lesions of the medial femoral condyle in horses: a retrospective study of 39 cases (2001-2005). ACVS Proceedings, 2006:E27.

Werpy NM, Ho CP, Kawcak CE, Rantanen NW, McIlwraith CW. A Review of Principles and Clinical Applications of Magnetic Resonance Imaging in the Horse. AAEP Proceedings, 2006.

Scientific Publications

Published Abstracts/Proceedings
2007

Duesterdieck KF, Frisbie DD, Kisiday JD, Kawcak CE, Norrdin RW, Iyer HK, McIlwraith CW. Laser Capture Microdissection of Articular Cartilage to Determine Chondrocyte Gene Expression Patterns. ORS Proceedings, 2007.

Frisbie DD, McIlwraith CW. What has been proven to work and what we need to do to be confident the others are effective? In Proceedings, American Association of Equine Practitioners Focus on Lameness, Fort Collins Colorado, 2007:28-50.

Frisbie DD, Kawcak CE, McIlwraith CW, Baxter GM. The use of intra-articular corticosteroids in combination with other intraarticular medications. American Association of Equine Practitioners Focus on Lameness and Imaging Blue Ribbon Lameness Panel, Fort Collins, Colorado, 2007:24-26.

Frisbie D, McIlwraith CW. Manipulation of endogenous healing beyond microfracture. Proceedings 7th World Congress International Cartilage Repair Society (ICRS), Warsaw, Poland, 2007:88-89.

Frisbie DD, Kawcak CE, Werpy NM, McIlwraith CW. Evaluation of topical diclofenac lipsomal cream for treatment of equine osteoarthritis using an equine experimental model. Proceedings AAEP 2007;53:256-257.

Goodrich LR, Choi VN, Carbone BC, McIlwraith CW, Samulski RJ. High effieiency gene trargetting to mammalian joint tissue using self-complimentary adeno-associated viral vector serotypes. Vet Surg 2007;34;E26.

Haussler KK. Examination and manipulation of the back, sacroiliac area and pelvis. Proceedings of the American Association of Equine Practitioners Focus on Lameness and Imaging, Fort Collins, CO., 158-182. July 2007.

Kawcak CE, McIlwraith CW. Lameness of the Distal Limb: Medical Therapies, Including Intraarticular, Intrabursal and Intrathecal Therapies, as Well as Tildren®. In Proceedings, American Association of Equine Practitioners Focus on Lameness, Fort Collins Colorado, 2007:86-7.

Kraft S, Ashton E, Ehrhart EJ , SestinaL, Arceneaux B, Thamm D, Dernell WS, Ehrhart N. Estimation of % Tumor Necrosis by 3D Compartmental Analysis of Dynamic Contrast-Enhanced MRI in Spontaneous Canine Osteosarcomas. Proceedings for ISMRM-ESMRMB Berlin Germany May 19-25 2007 p 564.

McGilvray K, Lyons A, Turner AS, MacGillivray J, Coleman S, Puttlitz CM. "Shoulder tendon repair biomechanics using a polyurethane patch in a chronic ovine defect model." 2007 ASME Summer Bioengineering Conference, Keystone, CO, June 20-24, 2007.

McGilvray J, Lyons A, Turner AS, Patel V, Puttlitz CM. "Kinetic and biomechanical testing of two-level cervical disc replacement." 2007 ASME Summer Bioengineering Conference, Keystone, CO, June 20-24, 2007.

McIlwraith CW, Kawcak CE. Surgical treatments of Problems of the Proximal Forelimb and Susupensory Area. In Proceedings, American Association of Equine Practitioners Focus on Lameness, Fort Collins Colorado, 2007:190-01.

McIlwraith CW. Subchondral cystic lesions of the medial femoral condyle-intra-lesional injection. Proceedings 16th Annual Scientific Meeting ECVS, Dublin, Ireland, 2007. pp.108-109.

McIlwraith CW. What is meant by bone (and joint) quality and how can we address it? Proceedings 2nd Waltham® Int Breeding Symposium, Newmarket, UK, 2007. pp.27-35.

McIlwraith CW. Nutraceuticals and Osteoarthritis - Myths and Realities. Proceedings 2nd Waltham® Int Breeding Symposium, Newmarket, UK, 2007. pp.57-59.

McIlwraith CW, Kawcak CE. Update on 'Global Equine Research Alliance' projects. Proceedings 2nd Waltham® Int Breeding Symposium, Newmarket, UK, 2007. pp.61-64.

McIlwraith CW. How to perform a check ligament desmotomy. Proceedings British Equine Veterinary Association Congress, Edinburugh, UK, 2007. p163.

McIlwraith CW . How to manage and infective joints. Proceedings British Equine Veterinary Association Congress, Edinburgh, UK, 2007. p167.

McIlwraith CW, Frisbie DD, Kawcak CE, Werpy NM, Haussler K, Kisiday JD. Addressing problems of equine joints. American Association of Equine Practitioners Focus on Lameness and Imaging Blue Ribbon Lameness Panel. Ft.Collins, CO 2007:17-18.

McIlwraith CW, Frisbie DD. Use of equine models to evaluate articular cartilage repair. Proceedings 7th World Congress International Cartilage Repair Society (ICRS), Warsaw, Poland, 2007:133-135.

McIlwraith CW, Kawcak CE. Surgical treatments of Problems of the Proximal Forelimb and Susupensory Area. In Proceedings, American Association of Equine Practitioners Focus on Lameness, Fort Collins Colorado, 2007:190-01.

Puttlitz CM, Womack W, Ames C. "A modified quasi-linear viscoelastic parametric study of the cervical disc." 7th Annual Meeting of the Spine Arthroplasty Society, Berlin, May 1-4, 2007.

Puttlitz CM, McGilvray K, Lyons A, AyturkU, Turner AS, Pate V. "Acute biomechanical implications of two-level cervical disc replacement and associated salvage procedure." 7th Annual Meeting of the Spine Arthroplasty Society, Berlin, May 1-4, 2007.

Puttlitz CM, McGilvray K, Lyons A, Ayturk U, Turner AS, Patel V. "Biomechanical implications of adjacent level cervical disc replacement and associated salvage procedures." 14th International Meeting on Advanced Spine Techniques (IMAST), Paradise Island, Bahamas, July 11-14, 2007.

Scientific Publications

Sah RL, McIlwraith WC, Bae KR, Gratz, BL, Wong, BL, Antonaci JM, Schmidt TA, Schumacher BL, Temple-Wong MM. Cartilage lubrication and diarthroidal joint MechanoBiology. Proceedings 7th World Congress of the ICRS, Warsaw, Poland, 2007:121-122.

B Santoni, W Womack, D Wheeler, Puttlitz CM. "A mechanical and computational investigation on the effects of conduit orientation on the strength of massive bone allografts" 2007 ASME Summer Bioengineering Conference, Keystone, CO, June 20-24, 2007.

Werpy NM, Ho CP, McIlwraith CW. Review on magnetic resonance imaging systems available for use in equine patients and the implications of field strength on clinical imaging: comparasion of high- and low-field systems. Proceedings AAEP 2007;53:22-29.

Womack W, Puttlitz CM. "Diametral compression of hollow non-circular bone sections." 2007 ASME Summer Bioengineering Conference, Keystone, CO, June 20-24, 2007.

Oral Presentations
2006

Frisbie DD. Evaluation of Oral Avocado/Soybean Unsaponifiables Using an Experimental Model of Equine Osteoarthritis. American Association of Equine Practitioners Annual Convention, San Antonio, Texas.

Frisbie DD. Evaluation of Bone Marrow Derived Stem Cells and Adipose Derived Stromal Vascular Fraction for Treatment of Osteoarthritis Using an Equine Experimental Model. In: Proceedings, American Association of Equine Practitioners Annual Convention, San Antonio, Texas.

Frisbie DD. Biological Therapy of Acute Joint Injuries. World Veterinary Orthopaedic Congress, Keystone, Colorado.

Frisbie DD. Adipose Stem Cell Grafting. World Veterinary Orthopaedic Congress, Keystone, Colorado.

Goodrich L. Catabolic cytokine profiles in cartilage surrounding chondral defects explain the biomechanically inferior tissue. International Cartilage Repair Society, San Diego, CA, January, 2006.

Goodrich L. Catabolic cytokine profiles in cartilage surrounding chondral defects explain the biomechanically inferior tissue. Orthopaedic Research Society 52nd Annual Meeting, Chicago, March, 2006.

Goodrich L. Catabolic cytokine profiles in cartilage surrounding chondral defects explain the biomechanically inferior tissue. American College of Veterinary Surgeons 41st Annual Conference, Washington DC, October, 2006.

Haussler KK. "Functional anatomy and pathology of the equine spine". Fourth International Symposium on Rehabilitation and Physical Therapy in Veterinary Medicine, Arnhem, Netherlands. October 2006.

Haussler KK. "What is sacroiliac joint disease?", "Functional anatomy and pathology of the sacroiliac joint","Clinical features of sacroiliac disease: Palpation and manipulation", "Sacroiliac joint injection techniques", "How to perform objective assessment of mechanical nociceptive thresholds in the equine spine". Voorjaarsdagen European Veterinary Conference, Amsterdam, Netherlands. April 2006.

Haussler KK. September 2006 - Colorado Veterinary Medical Association Annual Convention, Keystone, CO, "Chiropractic evaluation of the equine vertebral column", "Current equine chiropractic research".

Haussler KK. 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. December 2006. "Equine chiropractic spinal examination".

Haussler KK. First Annual Rocky Mountain Academic Spine Research Symposium, University of Colorado, School of Medicine, Denver, CO. October 2006. "Equine spinal research".

Haussler KK. Equine Medical Service, 4th Annual Client Education Seminar, Fort Collins, CO. February 2006. "What a pain in the back".

Haussler KK. Northern Colorado Dressage Association, Fort Collins, CO. January 2006
"Equine back problems".

Haussler KK. 67th Annual Conference for Veterinarians, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO. January 2006
"Chiropractic approaches to back pain in horses".

Kawcak CE. Update on Treatment of Equine Joint Disease. Northwestern Equine Practitioners Association. Portland, Oregon, November 2006.

Kawcak CE. Equine Lameness Short Course. College of Veterinary Medicine and Biological Sciences, Colorado State University, September 2006.

Kawcak CE. Update on Diagnosis of Foot Disease. Central Veterinary Conference. Kansas City, Missouri, September 2006.

Kawcak CE. Magnetic Resonance Imaging of the Hoof. Central Veterinary Conference. Kansas City, Missouri, September 2006.

Kawcak CE. Management of Equine Hoof Pain. Central Veterinary Conference. Kansas City, Missouri, September 2006.

Kawcak CE. Recent Advances in the Intraarticular Medications. Central Veterinary Conference. Kansas City, Missouri, September 2006.

Presentations

Kawcak CE. Farm based approach to management of developmental orthopedic diseases. Central Veterinary Conference. Kansas City, Missouri, September 2006.

Kawcak CE. Recent advances in diagnosis of equine joint disease. Arkansas Veterinary Medical Association. Hot Springs, Arkansas, March 2006.

Kawcak CE. Perspectives on choosing medications for equine joint disease. Arkansas Veterinary Medical Association. Hot Springs, Arkansas, March 2006.

Kawcak CE. Farm-based approach to managing developmental orthopedic diseases. Arkansas Veterinary Medical Association. Hot Springs, Arkansas, March 2006.

Kawcak CE. Management of orthopedic conditions in the equine athlete. Arkansas Veterinary Medical Association. Hot Springs, Arkansas, March 2006.

Kawcak CE. Pathogenesis of Early Acute Joint Injuries. WVOC, Keystone, Colorado. February 2006.

Kawcak CE. Advances in Diagnosis of Equine Joint Dieseases. Oklahoma Veterinary Conference. Tulsa, Oklahoma. January 2006.

Kawcak CE. Medical Treatment of Equine Joint Diseases. Oklahoma Veterinary Conference. Tulsa, Oklahoma. January 2006.

Kawcak CE. Surgical Treatment of Equine Joint Diseases. Oklahoma Veterinary Conference. Tulsa, Oklahoma. January 2006.

McIlwraith CW . January 10, 2006 - 6th Symposium of International Cartilage Repair Society. "Evaluation of A New One-Step Autologous Cartilage Transplantation (CAIS) Technique in An Equine Model."

McIlwraith CW . January 26, 2006 - Michigan State University. Wade O. Brinker Lecture "Unraveling the Mystery of Osteoarthritis: Lessons Learned from Horses and Humans" also three other lectures "Update on Diagnosis of Joint Disease," "Update on Treatments of Joint Disease," and "Effects of Conformation on Lameness."

McIlwraith CW . February 25, 2006- March 3, 2006 - 2nd World Veterinary Orthopaedic Congress, Keystone, Colorado. State-of-the-Art Lecture, "Other Methods of Cartilage Repair."

McIlwraith CW . March 5, 2006 - 3rd Annual Meeting of the Veterinary Endoscopy Society, Keystone, Colorado. Invited Lecture: "Equine Arthroscopy: Present and Future."

McIlwraith CW . March 7, 2006 - Colorado Biosciences Group, Fort Collins, Colorado. "Orthopaedic Research Capabilities at CSU."

McIlwraith CW . March 12, 2006 - Nature Vet Seminar, Dubai, United Arab Emirates. "Evaluation of Pentosan Polysulfate and Current Thinking on the Use of Glycosamine Glycans in the Management of Osteoarthritis."

McIlwraith CW . April 7-April 8, 2006 - Fairfield Equine Seminar on Imaging, Conditions and Therapeutics of the Fetlock and Distal Limb. "Update on Treatment of Joint Disease."

McIlwraith CW . May 4-May 7, 2006 - AO ASIF Equine Principles of Fracture Management, Columbus, Ohio. Three lectures "Nonsurgical and Surgical Management of Fractures of the Third Phalynx," "A Review of Articular Cartilage Healing After Joint Trauma," "Treatment of Small Metacarpal Stroke Tarsal Fractures," and three two-hour laboratories.

McIlwraith CW . May 18-May 19, 2006 - International Conference on Preclinical Models of Osteoarthritis, Hotel Omni Mont-Royal, Montreal, Quebec, Canada. Two papers, "Naturally Occurring Equine Models," and "Surgically Induced Horse Models."

McIlwraith CW . June 9-10, 2006 - Basic Arthroscopic Surgery Course, Muenster, Germany. 4 Lectures and 8 Hours of Laboratory.

McIlwraith CW . June 28, 2006 - American Orthopaedic Society for Sports Medicine. Articular Cartilage Regeneration Repair and Repair Workshop: A grant workshop. "Influence of Calcified Cartilage Layer Removal and Microfracture on Cartilage Repair Obtained Using a Single-Step Autologous Cartilage Transplantation (CAIS)."

McIlwraith CW . June 30-July 2, 2006 - 15th Annual Scientific Meeting European College of Veterinary Surgeons. Two invited presentations, "How Has 20 Years of Osteoarthritis Research Changed Clinical Practice?" and "Orthokine: A Revolution in Therapy of OA?" Also, Master class "Interarticular Medication."

McIlwraith CW . July 11, 2006 - Vail Valley Medical Center Foundation, Luncheon, Vail, Colorado. Collaborative research in answering the questions of equine and human cartilage healing.

McIlwraith CW . July 20-23, 2006 - Conference on Equine Sports Medicine and Science, Cambridge, UK. Seminar on condormation and effects on soundness, and Invited lecture "Management of osteoarthritis and traumatic joint disease".

McIlwraith CW . July 28, 2006 - Steadman Hawkins Advisory Committee, Vail Colorado, "New efforts in augmenting articular cartilage repair".

McIlwraith CW . August 26-27, 2006 - 4th Annual Peninsula Equine Summer Symposium in conjunction with The International Society of Equine Locomotor Pathology. "Therapy of problems of the upper forelimb".

McIlwraith CW . September 9-10, 2006 - Horse wellness - 2nd Meeting Internazionale di Medicina Veterinania, Congresso di Ortopedia Equina, padora, Italy. 7 hours of lecture on Equine Orthopaedics and Equine Joint Disease.

McIlwraith CW . September 14-16, 2006 - British Equine Veterinary Association Congress, Birmingham, UK. John Hickman Memorial Lecture, "Manipulating the intrasynovial environment: Past, present

and future" and 4 other lectures; "Intraarticular medication: Overview of products and uses", "The Future of Intraarticular medication", "Evaluating conformation for flat racing" and " Evaluating the benefits of sales radiography in the USA".

McIlwraith CW . September 29-30, 2006 - Advanced Arthroscopic Surgery course, Muenster, Germany, 6 hours of lecture and 6 hours of laboratory.

McIlwraith CW . October 5-7, 2006 - American College of Veterinary Surgeons Symposium, Washington DC, "Arthroscopic management of complicated femorotibial injuries" and "What is IRAP and autologous conditioned serum?"

McIlwraith CW . October 13-14, 2006 - Association Veterinaire Equine Francaise, Versailles, France, "Kester News Hour" (3 hours), and Frank Milne Lecture, "From Arthroscopy to Gene Therapy - 30 years of Looking in Joints" (3 hours).

McIlwraith CW . October 16-17, 2006 - Kentucky Equine Research Symposium.

McIlwraith CW . October 16, 2006 - The Welfare and Safety of the Racehorse Summit, Lexington KY, "Joint trauma and osteoarthritis (DJD) A major cause of attrition in Thoroughbred racehorses - what do we know and what can we do about it?"

McIlwraith CW . November 1, 2006 - The National Turf Writers Association 47th Annual Awards Dinner. Presentation and Introduction for the Joe Palmer Award to Dr. Dean Richardson and New Bolton Center.

McIlwraith CW . November 16, 2006 - Basic Arthroscopic Surgery Course, Colorado State University, Fort Collins, CO (4 hrs of lecture, 4 hrs of laboratory).

McIlwraith CW . November 17-18, 2006 - Advanced Arthroscopic Surgery Course, Colorado State University, Fort Collins, CO (9 hrs Lecture and 4 Hrs of Lab).

McIlwraith CW . December 3-6, 2006 - American Association of Equine Practitioners Annual Convention, San Antonio, TX. "Review of Glucosamine-Containing Oral Joint Supplements: Are They Effective in the Horse?" Spoke on behalf of the authors; Oke, SL, and Weese, JS.

Oral Presentations
2007

Goodrich L. High Efficiency Gene Targeting to Mammalian Joint Tissue using Self-Complementary Adeno-Associated Viral Vector Serotypes. American Society of Gene Therapy 9th Annual Convention, Baltimore, MD, June, 2006. American College of Veterinary Surgeons 42nd Annual Conference, Chicago, Illinois October, 2007.

Haussler KK. "Differential diagnosis of equine back problems". De Solleysel Veterinary and Physical Therapy Symposium, Department of Equine Sciences, Utrecht University, Netherlands. April 2007.

Haussler KK. "Alternative therapies: Acupuncture, Manual Therapy and Physical Therapy". American Association of Equine Practitioners Equine Lameness Research Meeting, Fort Collins, CO. July 2007.

Haussler KK. "Examination and manipulation of the back, sacroiliac area and pelvis". American Association of Equine Practitioners Focus on Lameness and Imaging, Fort Collins, CO. July 2007.

Haussler KK. "Equine aquatic therapy". Equine Rehabilitation Conference, Fort Collins, CO. June 2007.

Haussler KK. "Clinical evaluation of the canine vertebral column", "Integrating canine chiropractic techniques and rehabilitation into veterinary practice", "Chiropractic care in small animal veterinary medicine", "Small animal chiropractic techniques", "Canine rehabilitation: assessment and therapy", "Clinical assessment of equine chiropractic cases", "Performing spinal mobilization and equine chiropractic techniques", "Assessing equine back pain and spinal flexibility". CVC Central, Kansas City, MO, September 2007.

Haussler KK. 7th Annual Holistic Veterinary Medicine Symposium, School of Veterinary Medicine, University of California, Davis, May 2007, "Current equine chiropractic research".

Haussler KK Equine Medicine Club, School of Veterinary Medicine, University of California, Davis, May 2007. "Differential diagnosis of equine back problems and chiropractic spinal examination".

Kawcak CE. Advanced Imaging of Tendon Pathology. Havemeyer Meeting-New Advances in the Understanding of Tendinopathies. Reykjavik, Iceland, September 2007.

Kawcak CE. Advances in diagnostic imaging of orthopedic disease. Wild West Veterinary Conference. Reno, Nevada, October 2007.

Kawcak CE. Advances in medical and surgical therapy for joint disease. Wild West Veterinary Conference. Reno, Nevada, October 2007.

Kawcak CE. Farm-based management of developmental orthopedic disease. Wild West Veterinary Conference. Reno, Nevada, October 2007.

Kawcak CE. Management of the equine athlete. Wild West Veterinary Conference. Reno, Nevada, October 2007.

Kawcak CE. Equine Joint injections and diagnostic nerve blocks. Wild West Veterinary Conference. Reno, Nevada, October 2007.

Kawcak CE. When to use MRI for diagnosis of equine orthopedic disease. Central Veterinary Conference. Kansas City, Missouri, September 2007.

Kawcak CE. Diagnostic Analgesia. Central Veterinary Conference. Kansas City, Missouri, September 2007.

Kawcak CE. Managing musculoskeletal pain in older horses. Central Veterinary Conference. Kansas City, Missouri, September 2007.

Presentations

Kawcak CE. Treating equine orthopedic pain with bisphosphonates. Central Veterinary Conference. Kansas City, Missouri, September 2007.

Kawcak CE. Advances in medical therapy of joint disease. Central Veterinary Conference. Kansas City, Missouri, September 2007.

Kawcak CE. First aid for orthopedic trauma. Central Veterinary Conference. Kansas City, Missouri, September 2007.

Kawcak CE. Farm-based management of developmental orthopedic disease. Central Veterinary Conference. Kansas City, Missouri, September 2007.

McIlwraith CW . January 8-10, 2007 - IDEXX Symposium, Cancun, Mexico. "Evaluation of medications using the OA model".

McIlwraith CW. February 11, 2007 - Orthopaedic Research Society, San Francisco, CA. Invited Symposium, "Equine models for studying osteoarthritis, articular cartilage repair and tendinopathy".

McIlwraith CW . March 2, 2007 - Orthopaedic Research Society, San Francisco, CA. "Equine models for studying osteoarthritis, articular cartilage repair and tendinopathy".

McIlwraith CW . April 2, 2007 - Sanuwave Board of Directors Meeting, Atlanta, GA. "The use of shockwave therapy in horses."

McIlwraith CW . April 16, 2007 - University of Tennessee Equine Rehabilitation Short Course, 7 hours of lecture on bone and joint disease, diagnosis, therapies, surgical treatments, promotion of cartilage healing, developmental orthopedic disease (osteochondritis dessecans and subchondral bone cysts) and management of infection.

McIlwraith CW . April 19, 2007 - Nature Vet Symposium, Hong Kong. (2 lectures) "Principals of treatment of osteoarthritis including new developments" and "Evaluation of the effectiveness of sodium pentosan polysulfated in the osteochondral fragment model of osteoarthritis in horses."

McIlwraith CW . June 15-16, 2007 - Basic Arthroscopy Surgery Course, Muenster, Germany. (4 lectures and 8 hours of laboratory).

McIlwraith CW . June 29, 2007 - 16th Annual Scientific Meeting of European College of Veterinary Surgeons, Dublin, Ireland - Subchondral cystic lesions of the medial femoral condyle-intra-lesional injections.

McIlwraith CW . July 3, 2007 - 2nd Waltham® International Breeding Symposium, Newmarket, England. (3 lectures). "What is meant by bone (and joint) quality and how can we ascess it?", "Nutraceuticals and osteoarthritis - myths and realities" "Update on 'Global Equine Research Alliance' projects".

McIlwraith CW . July 29-31, 2007 - AAEP Focus Lameness and imaging, Ft. Collins, CO. Seminar "What has been proven to work and what we need to do to be confident the others are effective" and Participation on panel. "Surgical treatments of lameness of the proximal forelimb and suspensory area" (also Co-chair of meeting).

McIlwraith CW . August 1, 2007 - AAEP Foundation Equine Lameness Research Meeting and Panel. Participation in all day panel and presentation on "Joints".

McIlwraith CW . September 12-15, 2007 - British Equine Veterinary Association Congress 2007, Edinburgh, Scotland - Lectures "How to perform a check ligament desmotomy", "How to manage infected joints", Particiaption in Lameness Diagnosis panel (2 hours), Chair of Clinical Orthopedics Program on painful joints, and with Michal Schramme "State of the Art: What's new in clinical orthopedics?".

McIlwraith CW . September 24-26, 2007 - Havemeyer Meeting 2007. New advances in the understanding of tendinopathies, Reykjavik, Iceland. 2 ½ day symposium (Co-organizer with Roger Smith) including 2 presentations "Current best practices and methods of assessing outcome in equine tendinopathy" and "Rehabilitation protocols".

McIlwraith CW . October 2, 2007 - 7th World Congress of the the International Cartilage Repair Society, Warsaw, Poland. "Use of equine models to evaluate articular cartilage repair" (also Program Committee Member).

McIlwraith CW . October 5-6, 2007 - Advanced Arthroscopic Surgery Course, Muenster, Germany, 6 hours of lecture and 6 hours of laboratory.

McIlwraith CW . October 18-21, 2007 - American College of Veterinary Surgeons Symposium, Chicago, IL. Arthroscopic assisted equine fracture repair laboratory (4 hours), Joint preservation in veterinary practice: evidence-based medicine keynote symposium "When and how are joint preservation compounds used in equine medicine", "New minimally invasive techniques for management of cartilage engineering", moderator speaker Cutting Edge Panel "Surgical Management of Stifle Cysts" and participation in Year in Review Panel.

McIlwraith CW . October 25, 2007 - Breeders' Cup Veterinary Seminar, Monmouth Park, New Jersey. "New and Emerging Technologies for Managing Equine Joint Disease" (1.5 hour symposium).

McIlwraith CW . November 10, 2007 - Harvest of Hope Black Tie Gala to benefit Comparative Orthopaedic Laboratory, University of Missouri. Guest speaker "Mountaineering and osteoarthritis - there is a connection".

McIlwraith CW . November 15, 2007 - Basic Arthroscopic Surgery Course, Colorado State University, Fort Collins Colorado - 4 hours of lecture, 4 hours of laboratory.

McIlwraith CW . November 16-17, 2007 - Advanced Arthroscopic Surgery Course, Colorado State University, Fort Collins, Colorado - 8 hours lecture and 4 hours laboratory.

Presentations

McIlwraith CW . November 30, 2007 - Nutramax Laboratories and Veterinary Learning Systems Roundtable Symposium on Equine Joint Health Care. Orlando, FL. Moderator and discusant for 3 hour roundtable symposium.

McIlwraith CW . November 30, 2007- Sanuwave Dinner Symposium, Orlando, FL. "New Technologies in the Treatment of Equine Joint Disease".

McIlwraith CW . December 4, 2007 - 53rd Annual Convention American Association of Equine Practitioners. Prepared and moderated 2 hour panel on current controversial issues in ethics in equine practice.

Title	Investigators	Sponsor	Time Period	Amount
Evaluating Reduction in Lameness or Prevention of Pathological Bone Changes Following Application of Dynamix Shoes	Frisbie, DD, McIlwraith, CW, Kawcak, CE	Hippodynamix AG, Switzerland (5-38239)	November 1, 2001 - June 30, 2006	$432,174
Prevention of severe musculoskeletal injury in the equine athlete through optimization of musculoskeletal tissues to accommodate athletic performance and development of techniques to identify early change prior to clinical injury.	Kawcak, CE, McIlwraith, CW	Charitable Trust for the Will of Mrs. Marilyn M. Simpson (6-45601)	2001-2006	$600,000
Evaluating laser capture microdissection as a method to obtain mRNA and evaluation using an equine specific GeneChip	Frisbie DD, Duesterdieck K, Kawcak CE, McIlwraith CW	Dynamix	2001-2006	$145,215
Autologous Chondrocyte Transplantation via a Collagen Membrane - 7000.003	McIlwraith, CW, Frisbie, DD	Mitek (5-38272)	April 9, 2002 - December 31, 2006	$802,748
Implantation of Autologous Cartilage-Fragment- loaded Scaffolds - Mitek 7000.004	Frisbie, DD, McIlwraith, CW, Kawcak, CE	Mitek/DePuy Biologics (5-38292)	October 28, 2002 - December 31, 2006	$669,282
Growth factor gene mediated cartilage repair	Goodrich, LR	NIH (Individual National Research Service Award)	2002-present	$108,704
Growth factor gene mediated cartilage repair in horses	Goodrich, LR, Nixon, AJ, Hidaka, C	Institute for Sports Medicine Research	2002-present	$80,000
Efficacy of Rimadyl, Cosequin or a combination of both in a meniscectomy model of early osteoarthritis (OA) in beagles.	McIlwraith, CW, Frisbie, DD, Ricketts, AP, Toffoli, CA, Haven, ML	Pfizer (5-38212)	2002-2006	$262,873
Effects of Early Exercise on Osteochondral Tissues	Kawcak, CE, McIlwraith, CW, Firth, EC, Broom, ND	Grayson-Jockey Club Research Foundation	April 1, 2003 - March 31, 2006	$68,523
Effects of early exercise on osteochondral tissues.	Kawcak CE McIlwraith CW	Grayson Jockey Club Research Foundation	2003-2006	$68,523
Evaluation of Avocado And Soya Unsaponifiable (ASU) With Molasses Versus Molasses Alone For Osteoarthritis	Frisbie DD McIlwraith CW Kawcak CE	Vetoquinol	August 10, 2004 - February 1, 2006	$203,903
Evaluation of Bone Healing Using Functional in vivo MRI Imaging	Ehrhart, N	Musculoskeletal Transplant Foundation	2004-2006	$100,000
Evaluation of PHA-739521 and Phenylbutazone Administered Orally vs. Placebo Control using an Equine Model	Frisbie, DD, Kawcak, CE, McIlwraith, CW	Pfizer (5-38256)	March 11, 2005 - March 10, 2007	$298,001
Gene Transfer of BMP-2 for Enhancing Fracture Healing	Frisbie, DD, Southwood, L, Kawcak, CE	Grayson-Jockey Club Research Foundation	April 1, 2005 - March 31, 2006	$74,506
Equine Cartilage Repair	Frisbie, DD, McIlwraith, CW, Kawcak, CE	Isto Technologies (5-38397)	June 1, 2005 - May 31, 2006	$276,384

Funded Research Projects

Title	Investigators	Sponsor	Time Period	Amount
Evaluation of Equine Stem Cell Administration Intra-Articularly compared to Saline in Treatment of Osteoarthritis	Frisbie, DD, McIlwraith, CW, Kawcak, CE	Vet Stem®	June 1, 2005 - May 31, 2006	$206,043
In Vitro Chondrogenesis of Equine Mesenchymal Stem Cells in Response To Dynamic Compression	Kisiday J, Frisbie DD (Co-PI), Duesterdieck, K	CVMBS College Research Council	July 1, 2005- June 30,2006	$21,030
Pilot Study to Assess the Short Term Effects of Chondrofix in an Equine Model (18,000.01)	Frisbie, DD, McIlwraith, CW, Kawcak, CE	Zimmer Biologics	December 21, 2005- June 17, 2007	$151,032
In vitro chondrogenesis of equine mesenchymal stem cells in response to dynamic compression.	Frisbie, DD, Kisiday, J	CVMBS College Research Council	2005-2006	$16,500
The neural mechanisms of ankle muscle steadiness and their relation with control of posture in elderly fallers and non-fallers.	Reiser, RF, Tracy, BL	Colorado Injury Control Research Center Small Grant Program	2005-2006	$15,000
Evaluation of MRI sequences for characterization of lesions in the equine foot.	Werpy, NM, Kawcak, CE, Ho, CP, McIlwraith, CW	CVMBS College Research Council	2005-2006	$24,500
Bionicare electrical stimulation unit & potential enhancement of the quality and quantity of cartilage repair tissue after microfracture.	Frisbie, DD, Kawcak, CE, McIlwraith, CW	Steadman Hawkins Research Foundation/Bionicare (6-46601)	2005-2006	$135,000
The Neural Mechanisms of Ankle Muscle Steadiness and their Relation with Control of Posture in Elderly Fallers and Non-fallers	Reiser, RF Tracy, B	Colorado Injury Control Research Center Small Grant Program	2005-2006	$15,000
Viscoelastic Properties of Cortical Bone in an Ovine Model of Osteoporosis	MacLeay, J, Clifford, L	CVMBS College Research Council	2005-2006	$27,000
Growth of Trabecular Damage Due to Off Axis Loads	Neibur, G, MacLeay, J	NIH	2005-2007	$206,985
Comparison of 1% Diclofenac Sodium Topical Cream with Phenylbutazone and Placebo in the Equine Model used in treating Osteo-arthritis	Frisbie, DD, McIlwraith, CW, Kawcak, CE, Werpy, NM	IDEXX	January 1, 2006 - December 31, 2008	$298,000
The Effect of Upper End Selection on Adjacent Segment Stability in Selective Lumbar Instrumentation	Puttlitz, C	Medtronic Sofamor Danek, Inc.	January, 2006- December, 2007	$40,000
Shoulder Tendon Biomechanics in a Chronic Defect Model	Puttlitz, C	Biometrix Inc.	February 1, 2006- February 1, 2007	$26,530
A Finite Element Investigation of Cervical Intervertebral Disc Replacement Biomechanics	Puttlitz, C	Synthes Inc.	02/2006- 12/2007	$102,019

Title	Investigators	Sponsor	Time Period	Amount
Genetic Modification of joint tissues with Adeno-associated virus	Goodrich, L	CVMBS College Research Council	3/2006-2007	$28,000
Epidemiology of joint injuries in Thoroughbreds in training	McIlwraith, CW (consultant)	Horse Racing Levy Board, UK	April 1, 2006-March 31, 2007	no salary to CSU
Which geometric, structural, and pathological features of distal McIII may be detectable markers for lateral condylar fractures?	Parkin, T, Morgan, K, Murray, D, Bvurdin, A, Kawcak, CE, McIlwraith, CW	Horse Racing Levy Board, UK	April 1, 2006-June 30, 2008	92,478£ (CSU portion 30,000£ = $60,000)
Effect of a Novel Cleaning Process On Ovine Patellar Tendon Grafts: A Biomechanical and Histological Analysis	Puttlitz, C	Allosource Inc.	May 1, 2006-August 31, 2007	$50,998
Colorado Racehorse postmortem Evaluation project	Kawcak, CE, Norrdin, RW	CVMBS College Research Council	06/01/2006-05/30/2007	$12,000
Assessment of Wireless Kinematics in Horses- Development and Assessment of System	Kawcak, CE, McIlwraith, CW	Equisys Limited-Equine Orthopaedic Research Foundation	07/06/06- open	$20,000
Effect of Tiludronate on an Immobilization model of equine joint disease	Kawcak, CE, McIlwraith, CW, Werpy, N, Frisbie, DD	Ceva Sante Animale	7/2006-6-2008	$333,942
Microarray Analysis of Immune Responses Elicited by CERT + hGMCSF in Dogs with Advanced Cancer	Frisbie, DD	Sirius Medicine, LLC	Sep-06	$11,567
Determination of contact stresses in the equine metacarpophalangeal joint	McIlwraith, CW, Kawcak, CE, Reiser, RR	Lufkin Foundation	01/01/2006-08/30/2008	$100,000
Acute Rotator Cuff Repair with a Plasma Rich Scaffold: A Histological study in Sheep	Puttlitz, C	Musculoskeletal Transplant Foundation	November 1, 2006- November 1, 2007	$3,903
Orthopaedic Soft Tissue Fixation with Shape Memory Polymers	Puttlitz, C	Medshape Solutions Inc.	11/2006-11/2007	$7,399
Orthokine Protocol to Assess Serum Protein Factors	Frisbie, DD, McIlwraith, CW, Reardon, K, Carbone B	Arthrex	11/2006-10/2008	$49,307
Partial Joint Resurfacing with Biopoly® RS- A Hydrophilic Polymer	James, S, Puttlitz, C	Schwartz Biomedical and Indiana 21st Century Research & Technology Fund (part of a $2 million award to Schwartz to support commercialization of Dr. James technology)	December 1, 2006- December 31, 2008	$400,000
Histological Processing of HA Coated and Non-coated Titanium Pedicle Screws in Ovine Lumbar Vertebrae	Puttlitz, C	Medtronic Sofamor Danek	12/2006-11/2007	$18,474
Biological and Biomechanical Reaction to a Dynamic Stabilization Rod System in a Sheep Model	Puttlitz, C	Medtronic Sofamor Danek	12/2006-11/2007	$3,984

Funded Research Projects

Title	Investigators	Sponsor	Time Period	Amount
In Vitro Mechanical and Radiographic Evaluation of Lumbar Spine Screw Trajectories Using a Human Cadavar Model	Puttlitz, C	Medtronic Sofamor Danek	12/2006-11/2007	$44,432
Is Radiographic Measurement of Canine Femoral Varus Accurate and Repeatable	Palmer, RH, Park, RD, Egger, EE	College Research Council	2006	$6,829
In Vitro Sacroiliac Joint Kinematics: Effects of Sacroiliac Ligament Disruption	Haussler, KK, Puttlitz, D, James S	CVMBS College Research Council	2006-2007	$22,500
Self Assembling Peptides for Tissue Engineering	Frisbie DD (PI CSU Portion)	NIH Program Grant (PI AI Grodinsky)	8/01/2007-7/31/2010	$520,874
A Development Proposal of an Instrumental Cervical Intervertebral Disc Space Distracter	Puttlitz, C	Colorado Bioscience Development Grant/ Synthes	January 1, 2007 - March 31, 2008	$214,570
Evaluation of Intra-Articular Polysulfated Glycosaminoglycan (Adequan) Versus Intra-Articular Hyaluronate Sodium (Hyvisc) or Saline (0.9% NaCl) for Osteoarthritis	Frisbie DD, Kawcak, CE, McIlwraith, CW	Luitpold Pharmaceuticals	January 1, 2007 - December 31, 2008	$357,601
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, L	CVMBS College Research Council	3/2007-2008	$30,000
Mechanical Stimulation of Cells in Photopolymerized Gels	Bryant, S, McIlwraith, CW (Advisor)	NIH ROI (NIDCR) K22 Faculty Trasition grant	2006-2008	no funding to CSU
Mechanism of articular cartilage lubrication	Sah, R, McIlwraith, CW (Consultant)	NIH ROI (AR0515165-0A2)	6/01/2006-06/01/2111	no direct funding to CSU
Equipment Grant for Histologic Processing and Sectioning Equipment New Laboratory at Orthopaedic Research Center	McIlwraith, CW	Stavros Niarchos Foundation	Apr-07	$100,000
Effect of Disc Degeneration, Nucleus Replacement, and Disc Replacement of Facet Force Transmission- A Finite Element Investigation	Puttlitz, C	Synthes, Inc.	5/2007-4/2008	$33,278
A Biological and Histological Assessment of Tissue Ingrowth for a Dynamic Stabilization Micromotion System: An Ovine Model	Puttlitz, C	Innovative Spinal Technologies	6/2007-12/2008	$33,131
A Biological and Histological Assessment of Tissue Ingrowth for a Dynamic Stabilization Micromotion System: An Ovine Model	Puttlitz, C	Innovative Spinal Technologies	6/2007-12/2008	$33,131

Title	Investigators	Sponsor	Time Period	Amount
Effects of Joint Geometry on Fetlock Joint Disease	Kawcak, CE, McIlwraith, CW, Frisbie DD, Puttlitz, C	Grayson-Jockey Club Research Foundation (received 2007 Elastikon Award for Best Grant)	06/2007-05/2008	$80,480
Evaluation of Nuclear Magnetic Resonance (MBST) Therapy for Osteoarthritis Using an Equine Model	Kawcak, C, McIlwraith, CW, Werpy, N, Frisbie, DD	MBST Medical Devices, Inc.	06/2007-05/2008	$230,270
Colorado Racehorse Post-mortem Evaluation Project	Kawcak, CE, Les, C	CVMBS College Research Council	07/01/2007-06/30/2008	$15,760
Evaluation of Intra-Articular Polyglycan Versus Intravenous Polyglycan or Saline (0.9%NaCl) for Osteoarthritis Using...	McIlwraith CW, Frisbie DD, Kawcak C	ArthroDynamic Technologies	10/2007-9/2009	$357,602
Biomimetic Coatings for Improved Osseo-Integrative Capability in Spinal Disc Replacements	James, SP, Puttlitz, C, Godek, ML	2007 Research Grants and Fellowship Program	2007	$49,215
Mechaniobiology of Fracture Callus	Puttlitz, C	National Science Foundation	6/2008-5/2013	$401,101
Total Funded Research Grants				**$9,034,256**

Funded Research Projects

Other projects funded by private donations

Title of Proposal	Investigators	Sponsor	Time Period	Amount
Funding for MRI Coordinator and Technician for MRI Center	McIlwraith, CW, Werpy, N	Walton Family Trust	2003-2007	$500,000
Iron Rose Ranch Chair in Musculoskeletal Imaging	McIlwraith, CW, Kawcak, CE	Iron Rose Ranch	Sept 1, 2007	$3,000,000
Kenneth Atkinson Chair in Musculoskeletal Imaging	McIlwraith, CW	Kenneth Atkinson Estate	August 31, 2007	$980,000
Barbara Cox Anthony (prior donation)	McIlwraith, CW	Barbara Cox Anthony	2007	$270,000
		John and Abby Winkelried	April, 2006	$250,000
Abigail K. Kawananakoa Endowed Chair in Orthopaedic Integrative Therapies	McIlwraith, CW	Abigail K.Kawananakoa	August 30, 2007	$3,000,000
Gait Analysis Center	McIlwraith, CW, Kawcak, CE	Private donations- (33.33% Private donations: 33.33% CSU Provost, 33.33% VPRIT at CSU)	2007	$304,272 $295,577
Renovation of Room in Orthopaedic Research Laboratory	McIlwraith, CW, Kisiday, J	Private donations		
Salary Funding for Dr. K Haussler	McIlwraith, CW, Haussler, K	Herbert & Gail Holmes Allen	May 1, 2005 - April 31, 2008	$305,000
Total Funded Private Donations				**$8,904,849**
Grand Total				**$17,939,105**

Kawcak CE, Puttlitz CM, McIlwraith CW, Parkin TM, Morgan K. Elastikon Equine Research Award, Johnson & Johnson Consumer Products Company to the Grayson-Jockey Club Research Foundation, 2007.

McIlwraith CW. Wade O. Brinker Lecturer, Michigan State University, January 2006.

McIlwraith CW. John Hickman Memorial Lecturer British Equine Veterinary Association Congress, Birmingham, United Kingdom, September, 2006

McIlwraith CW. Founders Award for Lifetime Achievement, American College of Veterinary Surgeons, October 2006.

McIlwraith CW. President Veterinary Orthopaedic Society, 2006-2007.

McIlwraith CW. Scholarship Impact Award, Colorado State University. "In recognition of the impact of your research on the University, the Nation and the World", 2007.

Editorial and Scientific Advisory Boards 2006-2007

Baxter, G
- American Journal of Veterinary Research
- The Compendium for Continuing Education, Practicing Veterinarian

Frisbie, D
- Veterinary Therapeutics
- Equine Veterinary Journal
- Gene Therapy
- American College of Veterinary Research
- American Journal of Veterinary Research

McIlwraith, CW
- Ippologia
- J Equine Vet Sci
- The Horse
- Equine Veterinary Journal Advisory Board
- Grayson-Jockey Club Scientific Advisory Board
- Sanuwane Advising Board
- Steadman-Hawkins Foundation Scientific Advisory Board
- Vet Stem Advisory Board

Reiser, R
- Strength and Conditioning Journal Review Board

Siciliano, P
- Journal of Animal Science Editorial Review Board
- Compendium on Continuing Education for Veterinary Practitioners

Baxter, G
- American College of Veterinary Surgeons
- American Veterinary Medical Association
- American Association of Equine Practitioners
- Veterinary Orthopaedic Society
- American Association of Veterinary Clinicians
- Colorado Veterinary Medical Association
- Phi Zeta
- Phi Kappa Phi

Frisbie, D
- ICRS International Cartilage Research Society
- Orthopaedic Research Society
- American College of Veterinary Surgeons
- American Association of Equine Practitioners
- Osteoarthritis Research Society International
- American Veterinary Medical Association
- Veterinary Orthopaedic Society

Goodrich, L
- International Cartilage Repair Society
- American Society of Gene Therapy
- Orthopaedic Research Society
- American College of Veterinary Surgeons
- Veterinary Orthopedic Society
- California Veterinary Medical Association
- American Veterinary Medical Association

Haussler, K
- American Veterinary Medical Association
- American Association Equine Practitioners
- Colorado Veterinary Medical Association
- International Veterinary Academy of Pain Management
- Phi Zeta National Honor Society

James, S
- Society of Women Engineers (SWE)
- American Society of Mechanical Engineers (ASME)
- Society for Biomaterials

Kawcak, C
- American Veterinary Medical Association
- American Association of Equine Practitioners
- American College of Veterinary Surgeons
- Veterinary Orthopaedic Society

Kisiday, J
- Orthopedic Research Society

McIlwraith, CW
- Royal College of Veterinary Surgeons (Fellow)
- American College of Veterinary Surgeons (Diplomate)
- American Association of Equine Practitioners
- American Veterinary Medical Association
- Phi Zeta Veterinary Honor Society
- Gamma Sigma Delta Honor Society of Agriculture
- Colorado Veterinary Medical Association
- Orthopaedic Research Society
- Veterinary Orthopaedic Society
- American Association of Veterinary Clinicians
- European College of Veterinary Surgeons (Diplomate)
- International Society of Arthroscopy and Knee Surgery
- International Cartilage Research Society (ICRS)

Puttlitz, C
- Orthopaedic Research Society
- Cervical Spine Research Society
- American Society of Biomechanics
- American Society of Mechanical Engineers
- International Society of Biomechanics
- Spine Arthroplasty Association

Reiser, R
- National Strength and Conditioning Association (NSCA)
- International Society of Biomechanics in Sports (ISBS)
- American College of Sports Medicine (ACSM)
- International Sport Engineering Association (ISEA)

Professional Associations 2006-2007

Siciliano, P

American Society of Animal Science
Equine Science Society (formerly Equine Nutrition and Physiology Society)

Werpy, N

American Veterinary Medical Association
American Association of Equine Practitioners
American College of Veterinary Radiology

Advisory Board

John Adger
Racing and Bloodstock Manager

John Andreini
Racing Quarter Horse owner and breeder

Rick Arthur, DVM
Racetrack veterinarian, California; Past-president, American Association of Equine Practitioners

Larry Bramlage, DVM
Specialist Equine Surgeon, Rood & Riddle Equine Hospital, Lexington, Kentucky

Ms. Lindy Burch
Hall of Fame/Cutting Horse Trainer and Breeder

Mark Dedomenico, MD
Thoroughbred owner and breeder, Seattle

Ronald W. Ellis
Thoroughbred racehorse trainer

Joe Kirk Fulton
Racing Quarter Horse owner and breeder

John Halley, DVM
Veterinarian for Coolmore and Ballydoyle, Ireland

Gail Holmes
Quarter Horse owner and breeder, Longmont, Colorado

Robert Lewis
Thoroughbred owner, Southern California

Richard Mandella
Racing Thoroughbred trainer, Southern California; Racing Hall of Fame - inducted 2001

Wayne McIlwraith, DVM
Director, Equine Orthopaedic Research Laboratory, Colorado State University

Maria Niarchos-Gouazé
Thoroughbred owner, Europe

Dan Rosenberg
Manager, Three Chimneys Farm, Lexington, Kentucky; Vice President, Thoroughbred Charities of America

Bob Rosenthal
Racing Quarter Horse owner and breeder

Barry Simon, DVM
Manager, Ashford Stud (American Division of Coolmore Stud), Versailles, Kentucky

Ms. Melanie (Smith) Taylor
1984 Olympic Gold Medalist Show Jumping. Currently TV commentator and assistant to National Show Jumping teams.

Alec Wildenstein
Thoroughbred owner and breeder, New York and Paris

Mr. Martin Wygod
Thoroughbred Owner

Acknowledgements

Donors to Our Program 2006-2007

*Deceased

Platinum Level
$1,000,000 +

Barbara Cox Anthony
James M. Cox, Jr. Foundation

Tomas Bailey
Iron Rose Ranch

Abigail Kawananakoa
Kawananakoa Foundation

*Ken & Virginia Atkinson
Ken & Virginia Atkinson Estate

Herbert A. Allen
Allen & Company

Alice Walton
Walton Family Foundation, Inc.

Gold Level
$1,000,000-$999,999

Stadman-Hawkins
Sports Medicine Foundation

Niarchos Foundation

Marilyn M. Simpson Trust

Jon & Abby Winkerlried

Mark P. Dedomenico
Pro Sports Club

Wayne McIlwraith, DVM, PhD
& Nancy Goodman McIlwraith,
DVM

AAEP Foundation, Inc.

Lufkin Family Foundation

American Cuttin Horsie
Association Auction

Coolmore Stud

IDEXX Laboratories, Inc.

*Robert B. & Beverly J. Lewis

*Prince Ahmed Salman

Prince Sultan bin Muhammed

Luitpold Pharmaceuticals, Inc.

Pfizer Animal Health

Silver Level
$25,000-$99,999

Thoroughbred Charities of
America

Pavillard Scholarship

American Quarter Horse Assoc.

Bayer, Inc.

John Andreini
Andreini & Company

Bob Taylor

Rosenthal Ranch Trust

Martin J. & Pamela S. Wygod

Gooding Family Foundation

Oak Tree Charitable Foundation

S. California Equine Foundation,
Inc.

John M. & Karen Sparks III,
DVM

Bronze Level
$10,000-$24,999

Rod Richards
High Medical Technologies

Equus Foundation

Zory Kuzyk
Oak Creek Ranch

The Pidgeon Company

Nutramax Laboratories

Sue Allen

Vincent A. Baker

Bob Rosenthal
Calmark Corporation

California Authority of Racing
Fairs

Del mar Thoroughbred Charities

Hollywood Park Racetrack

Los Angeles Turf Club, Inc.

Barry W. Simon, DVM &
Kari H. Simon
Simon Trust

The EQQUS Foundation, Inc.

Thor BioScience

Thoroughbred Owners of
California

Blue Level
$1,000-$9,999

New Zealand Equestrian Foundation

Gayle & Judith Trotter

American Live Stock Insurance

William J. Keller

Britt Land & Cattle Company

Arthro Dynamic Technologies, Inc.

California Thoroughbred Breeders Association

Joelle Rogers
Essar Charitable Foundation

Volodar Kuzyk Britt
Land & Cattle

R&P Medical

Manfred Menzi
SanuWave Services, LLC

Sulzer Biologies

Robert L. & Melanie Taylor II

Auer, Joerg A.

Dorothy Russell Havemeyer Foundation Inc.

Animal Health Options–
ProMotion Studies

David F. Frisbie

Jenkins Veterinary Services

Tommy Manion, Inc.

C. George & Ruth Dewell

Equine Trust Foundation

Maggi McHugh
Pacific Coast Horse Shows Assoc.

Neil J. Mulholland

Rando Petersen

Trefethen Vineyard Winery, Inc.

Tom Bohanon
Glenwood Vet Clinic

Fossil Creek Veterinary

Dr. James P. & Michelle Morehead

Worldwide Medical, Inc.

R.A. & Farall Canning

Drs. James M. & Patricia D. Latham
Mill Creek Veterinary Service

J. mark Beverly, DVM

Dr. Edward & Darci Blach

Brokaw Family Foundation

Valley Oak Ranch

Fahd Al-Sobayil

Midge Leitch, VMD
Londonderry Equine Clinic

North american Specialty Insurance Company

Denise Opdahl

Bartlett & Ann Baker

Ron Crockett

Maynard M. Brittan
Fair Hills Farms

Brad R. Jackman & A. Lindsay Croom

Land 'O Lakes Farmland Feed

Dr. Terry Swanson
Littleton Large Animal Clinic

Susan & John Magnier

George S. Martin

Bonnie O'Neil

Dan & Linda Sauders

Round Mountain Ranch

Transoceanic Marine, Inc.

Green Level
$100-$999

Falcon Seaboard, LP/Snaffle Bit Ranch

Traub-Brittan Family Founation

David C. Davis

J Diamond 3

Joseph M. Singer

Joe & Terri Carter

Vaughn Cook

Acknowledgements

Donors to Our Program 2006-2007

Ashford Stud

Canning Family Trust

Fernando Canonici

Contract Veterinary Sales

Denali Stud

Melissa Lyons Gardner

Lezlie Rehagen

Summer Hills Veterinary Hospital

Three Chimneys Farm

Marshal & Anne Younglund

James A. & Juanita B. Winn

Atlantic Mutual Companies

Hagyard Equine Medical Institute

Napa Valley Veterinary Hospital

Rauscher (Dain) Foundation

Pamela Silverman

Von Hemel Racing Stable

Robert L. Rosenthal

Dr. James P. & Amy J. Foley

George W. Platt

Studio & TV Hire

Joe Petalino

John D. Roven

Double JK Ranch

Richard E. Mandella

LesterPedicord

Dennis A. Luedke, DVM

Gary L. Praytor

Jean Pierre
Dupuis Stable

Dr. Mark & Lori McCall

Dennis Bogott

Cecil & Hattie Davis

Ron Ellis Racing Stable

Fenton International

United Way of Kits

Cherry Creek Animal Clinic

Kenneth & Elizabeth Thomazin

Dr. Chip Beckett

Sharmin E. Bock

Charles Boles
Specifically Equine Vet Service

James J. Corbett

Claire Cox

Dearborn Stables, LLC

Joy Dreier

Lorna and Shannon Dueck

Employee's Community Fund

Heidi Gordon on behalf of Denise Steensland

Kate A. Gaughan

Cynthia Hampton

Harris Veterinary Clinic

John M. Harris, Jr.

Alex Harthill

James K. Irving

Jane M. Jenniings

James F. Kelly

Jens L. List

Steve R. Rael

Edgar R. Sander

Robert K. Shideler, DVM

Donald N. & Judith M. Family Stone

Patrick H. Young

Edward Murray
(Spur Veterinary Clinic)

Stillwater Veterinary Clinic

Placer County 4-H

John R. Steele & Associates

Dorothy L. Thielen

Bryan K. Hobson

Acknowledgements

Donors to Our Program 2006-2007

Hong Kong Jockey Club

Richard Mosier Del Oeste Equine Hospital

Alamo Pintado Equine Clinic

Alamogordo Animal Hospital

Dennis & Kerrie Allen

Bend Equine Medical Center

Bishben Cutting Horses

Blue Castle Racing, LLC

Brit & Sharon McLin

Columbia Equine Hospital

Barrie & Brenda Gerolamy

Goff (Lon) Custom Homes

Steven & Cynthia Gregory

Paul L. Grimm Law Offices

Ed Halpern

Heidi J. Hamlen

Harrington Equine Hospital

Robert A. Jackson

Gerard Kelly

Jessica A. Kidd

LaSalle Equine Clinic

Paul R. Loomis

Virginia L. Pabst

Robert & Anita Edmondson Pexton

Robert K. Shideler, DVM

The Ruffian Stables

Gary & Yvette Croteau Striker

Treve Williams

Ute Vaske

Simon Development & Construction Company

Equine Sports Medicine & Surgery Inc.

Loni D. Gattinger

John W. Kaufman

Susan Locke

London Equine Hospital Prof. Corp.

Gretchen Mathes
Powder Brook Farm

Mike & May Edwards Quarter Horses

Rosewood Hanoverians

Tiffany Farms & Stables

Wisconsin Equine Clinic

Clover Valley Veterinary Hospital

G.W. Ranch

Carolyn J. Hannaford

Jud E. & Catherine Miller

Okotoks Animal Clinic

Connie Inglish

Mary B. Lint

James C. Shircliff

Dr. William & Sandra Sutter

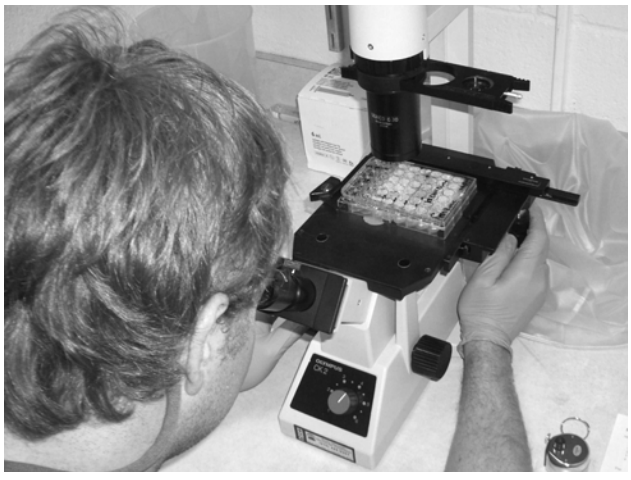
John V. & Neola J. Martz

Myron Yoknis

Heidi Gordon

ORTHOPAEDIC
RESEARCH CENTER

Summary of Research Projects 2006-2007



Effects of dynamic compression on chondrogenesis of adult equine mesenchymal stem cells encapsulated in agarose hydrogel

Take Home Message
Present strategies for treatment cartilage defects with mesenchymal stem cells involve transplantation while the cells are in an undifferentiated state. Given that the joint environment must support chondrocyte-like differentiation and subsequent neo-cartilage synthesis for effective repair, it is important to understand how joint factors can influence stem cell chondrogenesis. In this study, we show that compressive loading in the absence of chondrogenic growth factors is sufficient to generate evidence of chondrogenesis. However, this physical effect is modest compared to cytokine-induced differentiation, suggesting that additional stimuli would be necessary to maximize repair in vivo.

Introduction
Bone marrow-derived mesenchymal stem cells (MSCs) have emerged as a promising cell source for cartilage resurfacing due to the ease of tissue harvest and capacity to proliferate in vitro while maintaining progenitor capabilities (1). Induction of chondrogenesis has been well-characterized in response to TGF- exposure (2). However, recent studies have suggested that mechanical loading may also influence chondrogenesis (3, 4), a potentially critical factor in the development of MSC-based repair strategies in vivo. In this study, the effect of dynamic compression on chondrogenesis is explored for MSCs obtained from the bone marrow of skeletally mature horses. This work was performed by Dr. Kisiday in collaboration with Dr. Alan Grodzinsky at MIT.

Methods
Tissue harvest, cell preparation, and encapsulation in agarose - Bone marrow was harvested from the iliac crest of 2-5 year old horses. The marrow was spun at 1000g for 10 minutes, washed in PBS, and then resuspended in 0.8% ammonium chloride solution for 1-2 minutes to lyse the majority of the red blood cells. The remaining cells were washed, resuspended in low glucose DMEM plus 10% FBS, and seeded in tissue culture flasks at a concentration of 0.66x106 nucleated cells/cm^2 to allow for attachment of MSCs. Adherent MSC colonies were allowed to grow for 10-12 days, at which time the near-confluent colonies were trypsinized and cryopreserved in 5% DMSO, 95% FBS. For each experiment, cells were thawed and seeded in monolayer at a concentration of 12x103 cells/cm2. After reaching confluence, the cells were split 1:3 and grown to confluence prior to seeding in agarose hydrogels. MSCs were seeded in 2% agarose at a concentration of 10x106 cells/ml in a flat slab geometry 1.6 mm thick.
Hydrogel encapsulation and loading - 12 mm diameter agarose plus were transferred to an incubator-housed loading apparatus (5) immediately after MSC encapsulation. Experiments used a dynamic compression protocol of 2.5% sinusoidal strain amplitude superimposed on a 7.5% static offset. Two loading protocols were investigated: (1) Dynamic strain frequency of 0.3 Hz applied in cycles of 4 repetitions of 45 min of loading/5 hr 15 min of free-swell culture followed by 24 hours without loading. This protocol was previously found to stimulate extracellular matrix synthesis in primary chondrocyte cultures (6). (2) Dynamic strain frequency of 0.3 Hz applied in continuous cycles of 45 min of loading/45 min of free-swell culture. All samples were maintained in high glucose DMEM supplemented with ITS+, 0.1 M dexamethasone, and 37.5 g/ml ascorbate-2-phosphate. Unloaded control cultures were maintained in positive (10 ng/ml TGFβ) and negative (no TGFβ) control conditions for chondrogenesis (2). Dynamic compression was applied in the absence of TGFβ.
Analysis - Total GAG accumulation in the scaffold was quantified using the DMMB dye binding assay. Over the final 24 hours of the 21 day timecourse, samples were evaluated for protein and proteoglycan synthesis (^{3}H-proline and ^{35}S-sulfate radiolabel incorporation) in free-swelling condi-

tions. Histological analysis was used to identify the location of proteoglycan and type II collagen accumulation in the hydrogels.

Results

Alternate day loading did not stimulate chondrogenesis as ECM synthesis and accumulation (^{35}S-sulfate and 3H-proline incorporation on day 21, total GAG content) were similar to unloaded cultures maintained in parallel without TGF for MSCs derived from two animals (data not shown). The second loading protocol was designed to impart more frequent loading in an attempt to stimulate a chondrogenic response while maintaining similar static offset, dynamic amplitude, and dynamic strain frequency parameters. For four experiments using cells from different animals, extracellular matrix synthesis in response to loading protocol #2 was significantly higher (2-13 fold) than TGFβ -free negative control cultures, but at most 20-30% of positive control cultures containing 10 ng/ml TGFβ (representative data for a single experiment in Fig. 1). These data demonstrated that frequent loading was necessary to stimulate MSC chondrogenesis, although the overall effect was less than that seen in unloaded, TGFβ cultures.

Histological analysis was performed to explore potential heterogeneous cellular responses to the applied dynamic compression protocol. In unloaded control cultures, toluidine blue staining showed positive staining for proteoglycans in TGFβ but not TGFβ-free cultures (Fig. 2). Cross-sectional analysis of the dynamically-compressed sample showed positive toluidine blue staining in the dynamic compression sample, with little staining at the hydrogel surface in contact with the porous compression platen and the greatest amount of staining approaching the bottom of the sample that was in contact with the solid base (Fig. 2). Likewise, we have observed a similar pattern of type II collagen accumulation over a 21 day loading period (Fig. 3). Based on the assumption that loading approximates a confined geometry, these data suggest that the chondrogenic response due to loading was greatest in deeper zones that would experience largely hydrostatic pressure and little physical deformation, and that in select areas mechano-induction of chondrogenesis may have been as prevalent as that seen in TGFβ culture.

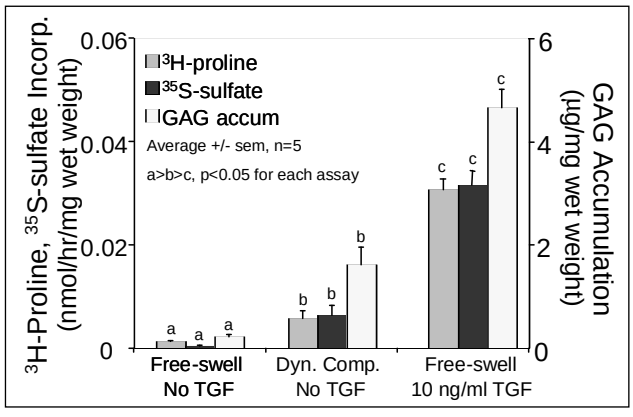


Figure 1. Biosynthesis in MSC-seeded agarose subjected to dynamic compression.

Discussion

In this study, dynamic compressive loading in the absence of TGF, chondrogenesis was observed only when loading was applied in continuous 50% duty cycles. Therefore, adult equine MSCs may require more frequent stimulation to increase chondrogenesis than was previously found to be effective in stimulating biosynthesis of primary chondrocytes. Furthermore, histological analysis suggested that loading may have stimulated chondrogenesis in a similar manner as TGF in a small population of cells within areas of high hydrostatic pressure at the base of the hydrogels.

1. Caplan AI: Mesenchymal stem cells. *J Orthop* Res 9:641-50, 1991
2. Johnstone B, Hering TM, Caplan AI, Goldberg VM, Yoo JU: In vitro chondrogenesis of bone marrow-derived mesenchymal progenitor cells. *Exp Cell Res* 238:265-72, 1998
3. Huang CY, Hagar KL, Frost LE, Sun Y, Cheung HS: Effects of cyclic compressive loading on chondrogenesis of rabbit bone-marrow derived mesenchymal stem cells. *Stem Cells* 22:313-23, 2004

4. Mauck RL, Byers BA, Yuan X, Tuan RS: Regulation of cartilaginous ECM gene transcription by chondrocytes and MSCs in 3D culture in response to dynamic loading. *Biomech Model Mechanobiol* 6:113-25, 2007
5. Frank EH, Jin M, Loening AM, Levenston ME, Grodzinsky AJ: A versatile shear and compression apparatus for mechanical stimulation of tissue culture explants. *J Biomech* 33:1523-7, 2000
6. Kisiday JD, Jin M, DiMicco MA, Kurz B, Grodzinsky AJ: Effects of dynamic compressive loading on chondrocyte biosynthesis in self-assembling peptide scaffolds. *J Biomech* 37:595-604, 2004

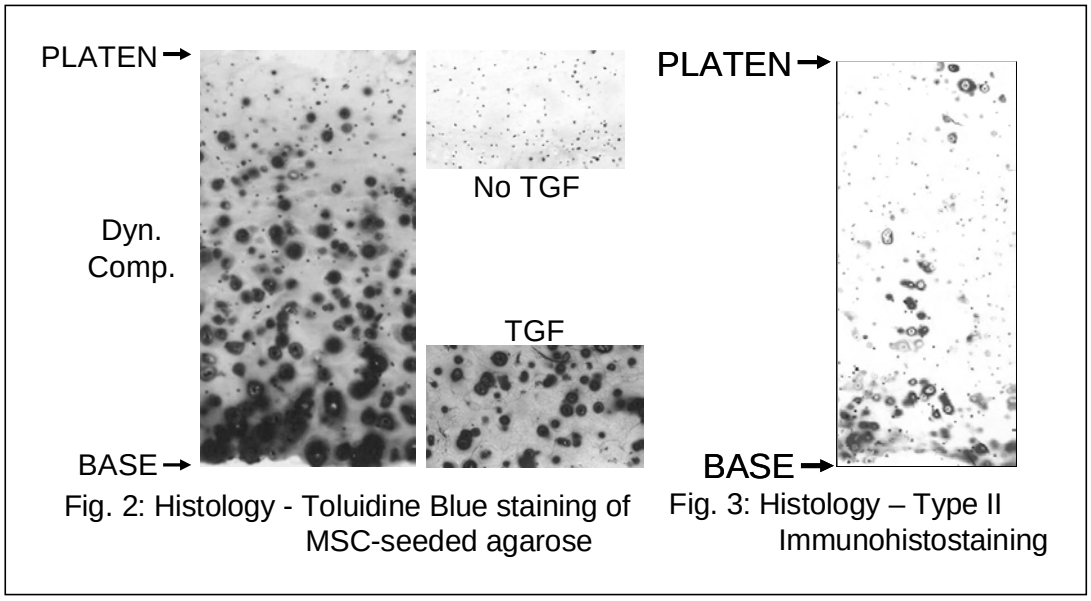


Fig. 2: Histology - Toluidine Blue staining of MSC-seeded agarose

Fig. 3: Histology – Type II Immunohistostaining

Figure 2. Histology - Toluidine Blue staining of MSC-seeded agarose

Figure 3. Histology - Type II Immunohistostaining

Stem cells: What are they and what do we do with them? A Review and Equine Studies

Stem cells are receiving a great deal scientific attention as well as coverage in the lay press. One of the many reasons for the attention stems from these cells having the potential to regenerate tissues without the production of scar tissue that is generally associated with healing processes. With any new technology comes a myriad of various terms many of which are poorly defined. One of the most difficult distinctions when discussing stem cells is defining what is a "stem cell". The first distinction to be made is between embryonic and adult stem cells. Adult stem cells are those which arise or are obtained from any post-natal source. Embryonic cells arise from an embryo, often in an 8 cell or fewer stage, and if they are capable of generating an entire organism they are referred to as "totipotent". A more restricted subset of cells that is capable of forming tissues from each of the germ layers is referred to as "pluripotent" cells or, when generating an even more restricted subset of cells, called "multipotent". It has long been thought that each tissue type had a resident population of adult stem cells present to maintain the tissue. The recent idea of plasticity suggests that adult stem cells can de-differentiate then re-differentiate down another cell lineage or transdifferentiate to another lineage. An example would be a hematopoietic stem cell (mesodermal in origin) that becomes neuron (ectomdermal origin).

Many of the early reports used bone marrow as a source of stem cells, but other sources of mesenchymal stem cells (MSC's) have been recently demonstrated. For example muscle, cartilage and adipose tissue all have been shown to contain multipotent MSC's.

Isolation of MSC's from the marrow or digested tissue extracts is most commonly achieved by simple adhesion and proliferation of MSC's to tissue culture surfaces. This crude technique does not ensure a homogenous population of MSC's as cell such as fibroblasts may likewise readily adhere and proliferate. While non-progenitor cell contamination may be an expected outcome of the adhesion sorting technique, the extensive volume of literature detailing bulk multipotent behavior of adherent MSC populations demonstrate the presence of a significant, if not homogenous, MSC population. In fact near-homogenous MSC populations have been reported from adhesion sorting 1. Researchers are currently working on more rigorous methods of identifying stem sells through the use of cell surface antigens such as cluster differentiation (CD) factor 34 and 44. Current research suggests that stem cells process the antigen for CD44 and lack the CD34 antigen, but there is still significant research to be done in this field.

Most of the research aimed at clinical treatments has been carried out using autologous MSC's, mainly from bone marrow [2]. Specifically, bone marrow derived stem cells have been used to generate bone, cartilage, tendon, ligament, meniscus, intervertebral disc, fat, muscle, and nerve [2]. Because of the availability of adipose tissue, it too has received a fair amount of recent research as a source of MSC's [3]. A clear delineation of the pros and cons of fat derived verses bone marrow derived MSC's is lacking. Ease of collection procedure, number of stem cells recovered, capacity and efficiency to differentiate in to various mesenchymal tissues, as well as morbidity associated with the collection procedure are all important points to consider when discussing bone-marrow versus adipose derived stem cells. Because MSC treatments are being used from both fat and bone, it is important to point out that few direct comparisons have been published, and at this point a definitive answer is lacking on which population of cells is better. The following section will detail some of the applications for stem cells and explore areas where adipose tissue has been used, as well as comparing bone versus adipose derived stems cells.

Typically, aspirated bone marrow is described to contain 40 million nucleated cells, of which 2,000 are stem cells per milliliter (or 1 stem cell per 20,000 cells). In contrast, fat is far less cellular (approximately six million cells per cubic centimeter of tissue compared to 40 million in bone marrow aspirates), but the prevalence of stem cells in fat has been described as high as one per 4000 cells, which is higher than that in bone marrow.[2] Corrected for tissue volume, a bone marrow aspirate would contain 2,000 versus 1,500 stem cells in a fat aspirate per cubic centimeter. Most studies agree that if bone or fat derived stem cells are expanded, the fat derived cells appear to have a faster doubling by about 4 days.[4]

Some studies have suggested that fat-derived and bone-marrow-derived cells are similar.[5,6] Others have shown a decreased osteogenic and chondrogenic potential in fat when compared directly to bone derived stem cells.[2,7,8] Work in the author's laboratory also suggested a decreased chondrogenic potential of fat versus bone derived stem cells, even when harvested from the same animal.[9] The author has also recently completed a study using an in vivo equine model of OA in which fat or bone marrow derived stem cells were injected directly into the joint to assess an anti-arthritic potential. A summary of the results will be presented during the conference, and an abstract of the results can be found in the proceeding of the American Association of Equine Practitioners annual meeting December 2006. Currently the bone marrow techniques utilize bone marrow aspirates which are cultured to expand the MSC's prior to injection. This is in contrast to the fat based technique commercially available from Vet-Stem which utilizes total nucleated cells digested from fat, which is believed to have a low number of MSC's.

Preliminary work has also been completed assessing both adipose and bone marrow derived MSC's for the treatment of tendonitis [10,11.] Very little controlled work has been published in the peer-reviewed literature on either technique for treating tendonitis. Dahlgren et al completed a controlled pilot project were they experimentally induced tendonitis and saw decreased inflammation and better morphology of the repair tissue in adipose treated tendons. Thus some promising preliminary data exists. Both techniques have numerous anecdotal reports of acceptable clinical outcomes but lack any controlled studies.

Early work using labeled MSC'S has shown they do have a affinity for damaged joint tissue and more recently in vivo studies have confirmed their ability to localize and participate in repair of damaged joint structures, including cruciate ligaments, menisci, and cartilage lesions.[12] Most of the in vivo studies utilizing MSC'S has focused on meniscal repair, in some cases using MSC'S in a carrier or scaffold while in others utilizing direct injection into the joint.[13-15] These studies have shown good support for use of bone marrow derived cells for treatment of meniscal damage. The degree of damage has ranged from experimental meniscal lacerations treated with bone marrow aspirates, separating and utilizing only the nucleated cells,[16] to total medial meniscectomy treated with injection of bone marrow derived culture expanded MSC'S.[15] With respect to cartilage healing, early work indicted that the use of MSC'S deposited in a fibrin matrix would be useful in improving cartilage healing. Although a recent equine study demonstrated early benefit, no significant differences were noted when MSC'S plus fibrin was compared to fibrin alone at eight months.17 Based on this work, it appears likely that modulation of the matrix or cells will need to be accomplished to observe long term benefit of MSC'S for cartilage repair.

The previously mentioned goat study, while showing regeneration of the meniscus, was aimed at evaluating the in vivo effects of intraarticular stem cell injection on decreasing the progression of OA.[15] This study used a medial meniscectomy and cranial cruciate transection model to induce OA. The investigators concluded that the decrease in OA seen in the study appeared to be secondary to

the regeneration of the medial meniscal tissues, which was dramatic in 7 of 9 cases. However, the design of the study did not lend itself to determining if the stem cells had a direct effect on the articular cartilage and progression of OA.

An equine study was then done by Drs. Frisbie, Kawcak, McIlwraith and Kisiday using the osteochondral fragment model to induce OA, unlike the study by Murphy et al., which relied on joint instability (medial meniscal model) to create secondary OA. The results of this study indicated nominal improvement in symptom or disease modifying effects with bone or adipose derived cells.18 The results of this study and Murphy et al. combined suggest that the regeneration of the medial meniscus in Murphy et al.'s study may have in fact been the reason for less OA progression. Furthermore, these studies also suggest that MSC's by themselves do little to counteract the progression of acute OA mediated by enzymatic degradation and joint debris. It would appear that modification of the MSC's is needed if they are to be useful in treating the OA. Treatment timing in relation to the degree of pathology could also be a factor contributing to the insignificant results of the equine study. Specifically, because MSC's appear to have a tropism for damaged cells, including fibrillated articular cartilage, it may be that at day 14 (day of treatment) the degree of fibrillation was not great enough for an effect of MSC'S treatment to be realized. Evaluation in cases with more advanced fibrillation would need to be conducted to answer this question. Because significant improvement in acute OA could not be demonstrated following intraarticular treatment using either bone marrow derived culture expanded stem cells or adipose derived stromal vascular fraction, these treatments cannot be recommended at this time for use in clinical cases of acute OA. However based on the study in goats it was felt that cases with loss of soft tissue structures leading to instability, such as with meniscal damage and it seemed logical to pursue this treatment modality clinically specifically in a multicenter trial. This study was initiated by Drs. Frisbie and Kawcak in collaboration with Drs. McIlwraith, Kawcak and Goodrich at Colorado State University; Drs. Bob Schneider at Washington State University, Jeff Watkins at Texas A & M and Drs. Brent Hague and Mike Major at Oakridge Equine Hospital in Oklahoma City. Cases were selected to receive intra-articular MSC as a treatment when the condition was considered to have a poor prognosis with other conventional treatment modalities and concurrent intra articular soft tissue involvement. There were 15 horses that had at least 6 months post treatment follow up ranging from 6-18 months. Joints treated included 12 stifles, 2 coffin joints, 1 hip, and 1 fetlock. The range of ages for the horses treated was 1-16 years of age with a mean of 5 years. Follow up information was obtained by one of the authors either by examining the horses or by telephone conversation with owners and trainers. In horses that became sound, the average days post treatment with stem cells before they became sound was 78 days with a range from 30-240 days. There were 10 of 15 horses that became sound and returned to their previous level of work in the discipline they were used for prior to treatment. Given the fact that all horses in the treatment group had a poor prognosis prior to treatment, MSC therapy has yielded favorable results. Cases that did not respond favorably had joint surfaces devoid of cartilage with evidence of gross damage to subchondral bone at arthroscopy with radiographic signs consistent with moderate OA. Significant cartilage loss in full weight bearing areas such as distal MCIII and the medial femoral chondyle remain a difficult challenge. Earlier treatment with MSC before complete cartilage loss and partial joint collapse may be the key to preventing failure.

In summary, the use of MSC's in experimental and clinical practice is a burgeoning field that should be approach with cautious optimism while work to differentiate the appropriate tissue source and treatment applications are carried out.

References

1. Pittenger M, Mackay A, Beck S, et al. Multilineage potential of adult human mesenchymal

stem cells. *Science* 1999;284:143-147.
2. Muschler GF, Nakamoto C, Griffith LG. Engineering principles of clinical cell-based tissue engineering. *J Bone Joint Surg Am* 2004;86-A:1541-1558.
3. Zuk PA, Zhu M, Mizuno H, et al. Multilineage cells from human adipose tissue: implications for cell-based therapies. *Tissue Eng* 2001;7:211-228.
4. Nathan S, Das De S, Thambyah A, et al. Cell-based therapy in the repair of osteochondral defects: a novel use for adipose tissue. *Tissue Eng* 2003;9:733-744.
5. De Ugarte DA, Morizono K, Elbarbary A, et al. Comparison of multi-lineage cells from human adipose tissue and bone marrow. *Cells Tissues Organs* 2003;174:101-109.
6. Hattori H, Sato M, Masuoka K, et al. Osteogenic potential of human adipose tissue-derived stromal cells as an alternative stem cell source. *Cells Tissues Organs* 2004;178:2-12.
7. Im GI, Shin YW, Lee KB. Do adipose tissue-derived mesenchymal stem cells have the same osteogenic and chondrogenic potential as bone marrow-derived cells? *Osteoarthritis Cartilage* 2005;13:845-853.
8. Winter A, Breit S, Parsch D, et al. Cartilage-like gene expression in differentiated human stem cell spheroids: a comparison of bone marrow-derived and adipose tissue-derived stromal cells. *Arthritis Rheum* 2003;48:418-429.
9. Kisiday JD, Kopesky PW, Evans CH, et al. Evaluation of adult equine bone marrow- and adipose-derived progenitor cell chondrogenesis in hydrogel cultures. *J Orthop Res* 2007;26:322-331.
10. Dahlgren LA. Review of Treatment Options for Equine Tendon and Ligament Injuries: What's New and How Do They Work. 51st annual convention of the AAAEP 2005;376-382.
11. Smith RK, Korda M, Blunn GW, et al. Isolation and implantation of autologous equine mesenchymal stem cells from bone marrow into the superficial digital flexor tendon as a potential novel treatment. *Equine Vet J* 2003;35:99-102.
12. Agung M, Ochi M, Yanada S, et al. Mobilization of bone marrow-derived mesenchymal stem cells into the injured tissues after intraarticular injection and their contribution to tissue regeneration. *Knee Surg Sports Traumatol Arthrosc* 2006;14:1307-1314.
13. Izuta Y, Ochi M, Adachi N, et al. Meniscal repair using bone marrow-derived mesenchymal stem cells: experimental study using green fluorescent protein transgenic rats. *Knee* 2005;12:217-223.
14. Yamasaki T, Deie M, Shinomiya R, et al. Meniscal regeneration using tissue engineering with a scaffold derived from a rat meniscus and mesenchymal stromal cells derived from rat bone marrow. *J Biomed Mater Res A* 2005;75:23-30.
15. Murphy JM, Fink DJ, Hunziker EB, et al. Stem cell therapy in a caprine model of osteoarthritis. *Arthritis Rheum* 2003;48:3464-3474.
16. Abdel-Hamid M, Hussein MR, Ahmad AF, et al. Enhancement of the repair of meniscal wounds in the red-white zone (middle third) by the injection of bone marrow cells in canine animal model. *Int J Exp Pathol* 2005;86:117-123.
17. Wilke MM, Nydam DV, Nixon AJ. Enhanced early chondrogenesis in articular defects following arthroscopic mesenchymal stem cell implantation in an equine model. *J Orthop Res* 2007.
18. Frisbie DD, Kawcak CE, Werpy NM, et al. Evaluation of bone marrow derived stem cells and adipose derived stromal vascular fraction for treatment of osteoarthritis using an equine experimental model. American Association of Equine Practitioners 2006;420.

Acknowledgements
The authors would like to acknowledge Drs. Hague, Watkins, McIlwraith, Goodrich, Major and Zubrod for contribution to included clinical cases.

Acellular Urinary Bladder Matrix (ACell Vet®) in a Collagenase Model of Superficial Digital Flexor Tendonitis in Horses

Take Home Message
There were no significant differences in clinical, ultrasonographic, and histologic data between tendons treated with UBM and a saline control over an 84 day treatment period. Additional biochemical and molecular studies are needed to further determine the efficacy of intralesional UBM in treating superficial digital flexor (SDF) tendonitis.

Introduction
Tendonitis or "bowed tendon" usually results from a severe strain to the superficial digital flexor (SDF) tendon due to excessive loading and overstretching of the tendon.[1,2] This is a very common cause of lameness in performance horses, especially racing thoroughbreds and quarter horses due to the speed in which they travel, the small cross-sectional area (CSA) of the SDF tendon, and the excessive load placed on the tendon during the early and mid-stance phase of the stride (hyperextension of the fetlock).[3] Additional predisposing factors for SDF tendonitis in other types of performance horses include inadequate training, muscle fatigue, uneven and slippery ground, sudden turning, excessive pastern slope, improper shoeing, and the long toe-low heel hoof conformation.[3]

Appropriate treatment of tendonitis after resolving the initial inflammatory stage is one of the most debatable topics in equine medicine and surgery. Most treatment protocols focus on promoting faster healing or increased quality of healing, or a combination of both in an attempt to return horses to performance faster with less chance for re-injury. Treatments that have been used include intralesional hyaluronan and β-aminoproprionitrile fumurate (Bapten), intramuscular polysulfated glycosaminoglycans (Adequan®), tendon splitting with or without superior check ligament desmotomy, NSAIDs and rest with controlled exercise alone, and various physical therapy modalities such as ultrasound, laser and magnetic therapies.[1-5] More recent treatment options include extracorporeal shockwave therapy, and intralesional bone marrow, insulin-like growth factor 1, autogenous mesenchymal stem cells, and urinary bladder matrix (UBM; ACell Vet ®).[2,3,6,7] All of the more recent intralesional therapies focus on either directly providing or indirectly recruiting the needed growth factors and cells required for optimal tendon healing. However, little is known about these therapies, including their clinical efficacy in promoting a better quality tendon repair in a shorter period of time.

Clinically, progression of healing is measured using improvements in lameness, decreases in pain on palpation, decreases in the circumference of the limb, and improvements in fiber pattern and echogenicity on ultrasound.[8] Histologically, lesions progress from an amorphous, acellular lesion soon after injury to scar tissue filled with collagen fibers and fibroblasts arranged along tension-lines.[9]

ACell Vet® UBM powder is a lyophilized powder derived from the extracellular matrix of swine urinary bladder that is thought to recruit cells and needed growth factors for tissue differentiation from the circulatory system and local tissues.[7,10,11] In other species, UBM has been found to produce a profound angiogenic response in the first 5 -7 days after treatment.[10,11] It is thought to promote healing of tendonitis, provide a scaffold for collagen deposition within the damaged tendon, and minimize excessive fibrous tissue formation. Little definitive information is known about the benefit of intralesional UBM therapy for tendon injuries in horses. Anecdotally, it has shown promise with both tendonitis and desmitis in clinical cases. In a recent report of 53 horses treated with intralesional UBM, 81% of the horses that were 6 months or greater post-treatment were sound and in work.[7] Tendon and ligament healing was

thought to occur more rapidly and with better quality of repair tissue visible ultrasonographically compared with more conventional treatments. However, no controlled studies evaluating the efficacy of intralesional UBM for treating soft tissue injuries in horses have been performed.

It is the purpose of this study to determine the efficacy of intralesional UBM in horses with collagenase-induced tendonitis using clinical, ultrasonographic, and histologic data. The collagenase-induced tendonitis model has been used in several previous tendon healing studies and appears to be a repeatable method to induce tendonitis in horses.[4,6,12]

This study was carried out by Drs. Ty Wallis (a resident in surgery) with Drs. Gary Baxter, Natasha Werpy, Gary Mason and David Frisbie.

Materials and Methods
SDF tendonitis was created bilaterally in 8 horses using a collagenase model. One randomly selected limb of each horse was treated with UBM and the opposite limb was treated with an equal volume of saline as a control. Horses were evaluated clinically and ultrasonographically during the study, and were euthanized after 84 days to evaluate the tendons grossly and histologically.

Results
When the treated tendons were compared to the control tendons grossly and histologically, there were no significant differences found between the two groups for any of the response variables evaluated. Lesions tended to be smaller on gross measurements in the treated tendons, but the gross pathology scores were higher. Scores for all histologic variables except epitenon thickness were greater for the treated tendons than the control tendons, meaning they were more abnormal. There were no significant differences between any clinical parameters measured in the treated versus control limbs. There was a weak trend toward a significant difference in lameness between days for treated and control tendons (p=0.1), with the control tendons having higher lameness scores (Figure 1). The p-values for palpation, circumference, and tendon width were 0.97, 0.99, and 0.12 respectively. There was a trend toward a significant difference in CSA of the lesion (p=0.06) between days for treated and control tendons, with the control lesions having larger CSA's (Figure 2). However, when the lesion size was taken as a percent of tendon CSA, the difference was not significant (p=0.69). There was a trend toward a significant difference in estimated volume of the lesion using the lesion CSA multiplied by the lesion length for treated and control tendons between days (p=.11), again with the control tendons having a larger calculated volume (Figure 3). There were no other significant associations between ultrasound response variables between days for treated and control tendons. The p-values for fiber score, echo score, and lesion length were 0.43, 0.83, and 0.79, respectively.

Figure 1

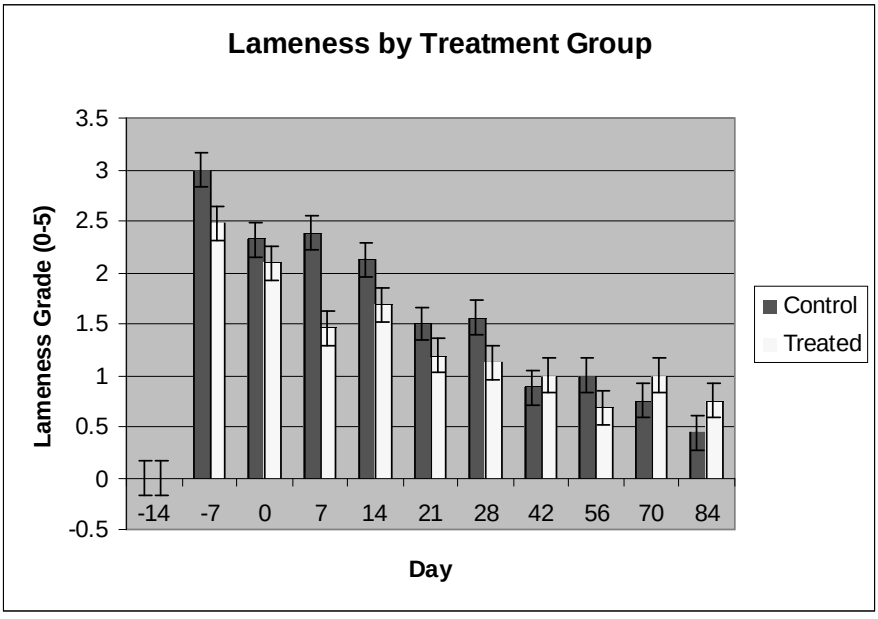


Figure 2

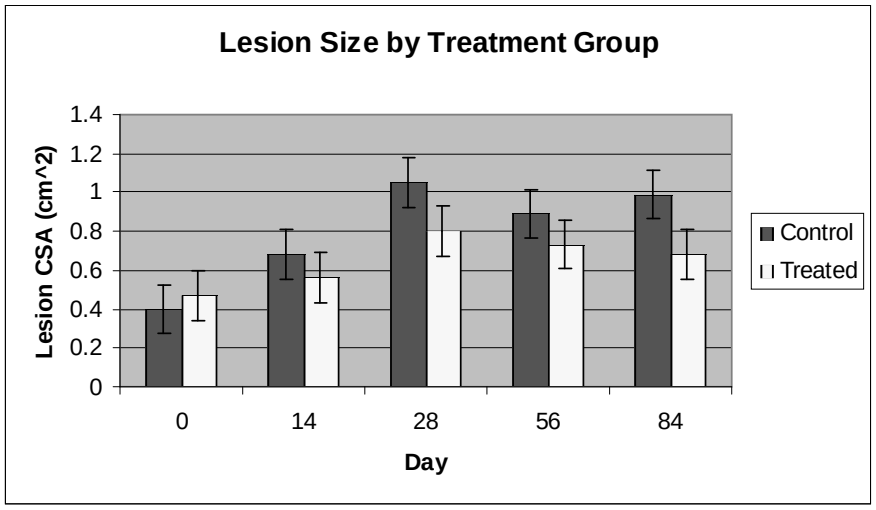
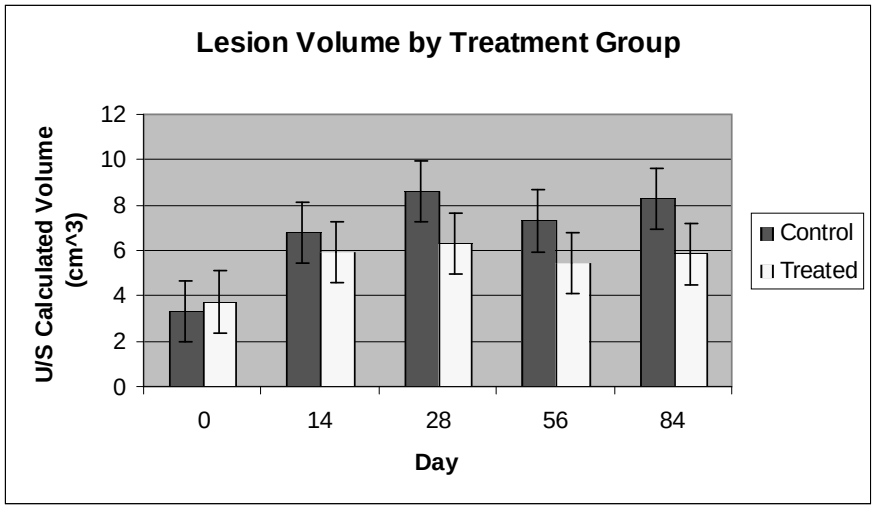


Figure 3



Discussion

SDF tendonitis often requires a long period of convalescence and has a high rate of recurrence.[2] Many different therapies have been or are currently being investigated to treat this condition.[1-7] UBM, if effective, would be advantageous because it is a commercially available product that requires no special preparation or ex vivo expansion.

Although UBM has been suggested as an effective treatment for tendonitis in horses in a clinical study, no controlled clinical trial with histologic evaluation has been performed previously. Based on the results of the present study, UBM does not appear to be an effective treatment for SDF tendonitis. Neither a significant advantage nor a significant detriment were seen in the tendons treated with the product. However, both the tendon lesion CSA and volume as seen on ultrasound appeared to be less in the treated tendons compared to the control tendons, and control limbs had higher lameness scores than the treated limbs, but these differences were not statistically significant.

There were some limitations in this study which should be considered. This collagenase model may not mimic clinical disease, as most of the tendon

lesions created in this study were more severe than many lesions seen clinically. Furthermore, while any treatment for tendonitis is aimed at reducing the healing time, the 84 day study period may have been too short to have detected a significant difference between the treatments Additionally, further studies are needed to evaluate differences in biochemical and molecular parameters between treated and control tendons.

References

1. Dyson SJ: Superficial flexor tendonitis in event horses, show jumpers, and dressage horses, in Ross MW, Dyson SJ (eds): Diagnosis and Management of Lameness in the Horse. Philadelphia, WB Saunders, 2003, pp 639-643
2. Ross MW: Management of superficial digital flexor tendonitis, in Ross MW, Dyson SJ (eds): Diagnosis and Management of Lameness in the Horse. Philadelphia, WB Saunders, 2003, pp 625-639
3. McIlwraith CW: Diseases and problems of tendons, ligaments, and tendon sheaths, in Stashak TS (ed): Adams' Lameness in Horses. Philadelphia, Lippincott Williams & Wilkins, 2002, pp 594-690
4. Foland JW, Trotter GW, Powers BE, et al: Effect of sodium hyaluronate in collagenase-induced superficial digital flexor tendinitis in horses. Am J Vet Res 53:2371-2376, 1992
5. Henninger R: Treatment of superficial digital flexor tendinitis. Vet Clin North Am Equine Pract 10:409-424, 1994
6. Dahlgren LA, van der Muelen MC, Bertram JE, et al: Insulin-like growth factor-1 improves cellular and molecular aspects of healing in a collagenase-induced model of flexor tendinitis. J Orthop Res 20:910-920, 2002
7. Mitchell RD: Treatment of tendon and ligament injuries with UBM powder (ACELL-Vet), in ACVS Syposium, pp 190-193
8. Jorgensen JS, Genovese RL: Superficial digital flexor tendonitis in racehorses, in Ross MW, Dyson SJ (eds): Diagnosis and Management of Lameness in the Horse. Philadelphia, WB Saunders, 2003, pp 628-635
9. Dahlgren LA, Mohammad HO, Nixon AJ: Temporal expression of growth factors and matrix molecules in healing tendon lesions. J Orthop Res 23:84-92, 2005
10. Badylak SF: The extracellular matrix as a scaffold for tissue reconstruction. Semin Cell Dev Biol 13:377-383, 2002
11. Badylak SF, Park K, Peppas N, et al: Marrow-derived cells populate scaffolds composed of xenogenetic extracellular matrix. Exp Hematol 11:1310-1318, 2001
12. Dowling BA, Dart AJ, Hodgson DR, et al: The effect of recombinant equine growth hormone on the biomechanical properties of healing superficial digital flexor tendons in horses. Vet Surg 31:320-324, 2002
13. Ross MW: Movement, in Ross MW, Dyson SJ (eds): Diagnosis and Management of Lameness in the Horse. St. Louis, Saunders, 2003, pp 60-73

Acknowledgement
This study was supported by ACell Europe.

Development of a gene therapy vector to accelerate bone healing in the horse

Take Home Message
Bone healing in horses is a challenge based on the need for horses to bear weight continuously. This greatly enhances the need to heal a fractured bone quickly before the devastating effects of support-limb laminitis results in a reduced return to athleticism or, worse yet, a reduced prognosis for survival.

Introduction
Bone marrow-derived mesenchymal stem cells (BMDMSC) have been targeted for use in enhancement of bone healing. Their osteogenic capacity can be further augmented by delivery of genes encoding bone morphogenic proteins (BMP's). BMP's are growth factors important for skeletal development and bone growth. The benefits of BMP's appear to occur early in healing, with more rapid bone formation and maturation and an early increase in mechanical strength compared to controls. In bone two or more BMP genes are often co-expressed. The goal of this project is to compare the effects of genetic modification of BMDMSC with gene sequences of various BMP's to determine if bone healing can be accelerated.

Materials and Methods
BMDMSC were harvested from the tuber coxae of different horses and cultured in tissue culture flasks. Different gene therapy vectors were placed on BMDMSCs and the amount of BMP and bone production was measured.

Results
BMP protein elution rates appeared to reach their maximal concentration by day 8 and then demonstrated a decline. Protein elution rates were higher for cells cultured in media that did not contain dexamethasone; whereas, protein elution rates rapidly declined towards baseline for cells cultured in media containing dexamethasone (Figure 1).

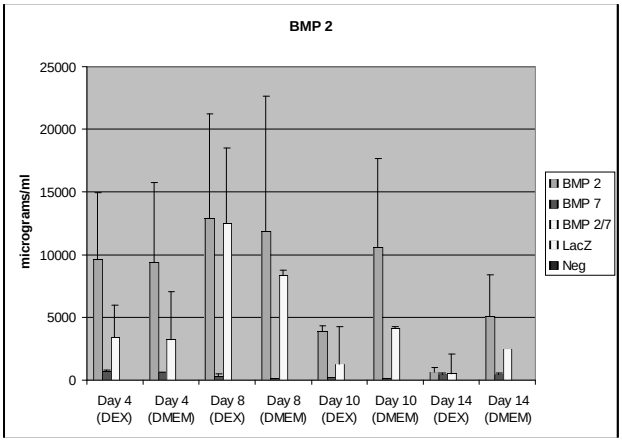


Figure 1. BMP-2 activity measured at days 4, 8, 10, and 14.

On day 7, genetically modified BMDMSC cultured in media supplemented with dexamethasone higher levels of BMP production over LacZ genetically modified or naïve cells (also cultured in media supplemented with dexamethasone), respectively. Genetically modified BMDMSC not supplemented with dexamethasone had a 4 fold (BMP-2), 7 fold (BMP-7) and 3.2 fold (BMP-2/7) increase over nongenetically modified cells or naïve cells respectively, however overall alkaline

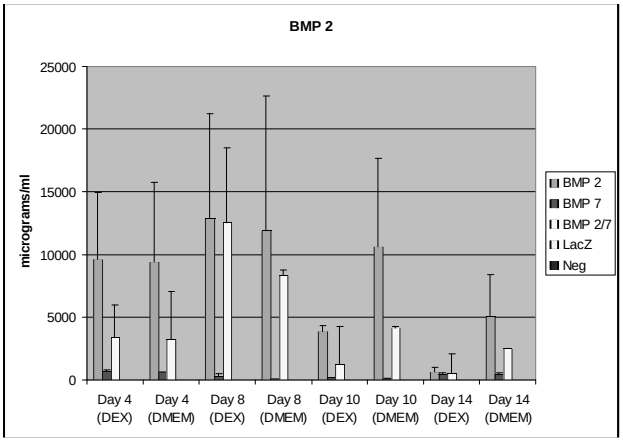


Figure 2. Alkaline phosphatase activity measured at day 7 and 14 for cells cultured in media that did not contain dexamethasone. BMP-2 activity measured at days 4, 8, 10, and 14.

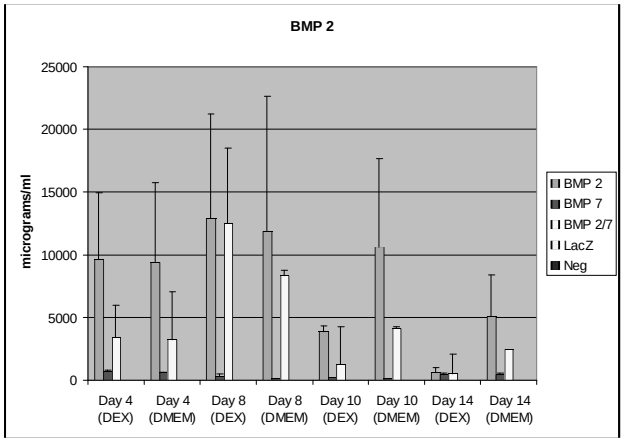


Figure 3. Alkaline phosphatase activity measured at day 7 and 14 for cells cultured in media that contained dexamethasone.

phospatase levels in BMDMSC cultured in media supplemented with dexamethasone was 15 to 120 fold higher than BMDMSC not supplemented with dexamethasone (Figure 2 and 3).

Summary

In conclusion, genetic modification of BMDMSCs with AdBMP-2, 7 or 2 and 7 had a beneficial effect on osteoblastic differentiation of BMDMSCs and dexamethasone supplementation appears to be important in this process. The ideal time of transfer of these cells to healing defects may be between day 5-7 of culture when they are eluting the highest amount of BMP protein and producing extremely high levels of alkaline phosphatase. The goal of this project is to enhance fracture healing in horses through genetically modifying stem cells that are easily harvested from bone marrow.

Acknowledgement

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

Summaries: Focus 1

Joint Tissue Healing

Development of gene therapy approach to cartilage healing

Take Home Message

Gene therapy based therapies in treating joint disease hold much promise for long-term cartilage healing. A gene therapy vector based on Adenoassociated Virus has shown excellent initial preliminary results of delivering long-term protein production to the tissues of joints. Researchers at the ORC, in collaboration with researchers at the University of North Carolina, to develop a safe and efficient gene therapy approach to healing cartilage and preventing progression of osteoarthritis.

Introduction

Gene therapy for joint diseases relies on a non-immunogenic gene delivery vector that can efficiently and persistently transduce joint specific tissues (eg. chondrocytes and synoviocytes). Recombinant adeno-associated virus (rAAV) is an emerging and 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. We hypothesized that optimal serotypes of scAAV existed in joint tissues.

Materials and Methods

Chondrocytes and synoviocytes were grown in monolayer. Two days after seeding, scAAV vector serotypes 1-6, and 8, carrying a GFP expression cassette were used to transduce cells. Fluorescence intensity was measured. Following initial testing, 4 optimal serotypes were tested at various doses and fluorescence intensity was measured. Cell viability was determined and vector toxicity was tested by relative gene expression of equine MMP-1, MMP-3, MMP-13 and Aggrecanase-1.

Results

The AAV vector appears to have excellent ability to deliver the genetic sequence of interest to cells of joints (Figure 1). Continued testing will reveal optimal "types (serotypes)" of AAV that will result in long-term and safe delivery of gene sequences to cells.

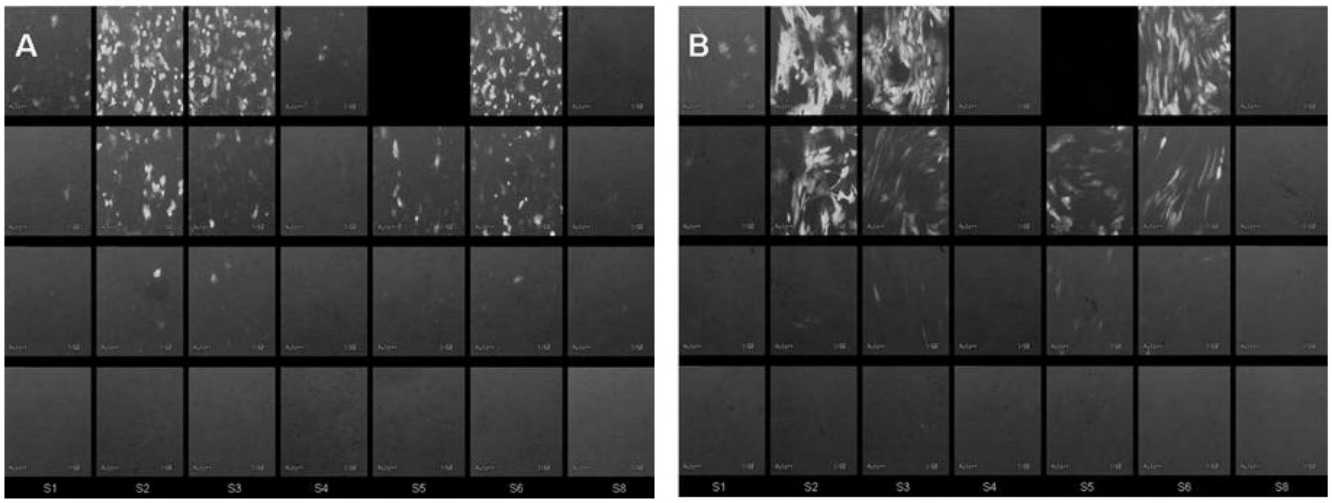


Figure 1: Fluorescence microscopy of chondrocytes (A) and synoviocytes (B) at Day 7 following transduction of AAVGFP serotypes 1, 2, 3, 4, 5, 6, and 8 (left to right) at 10,000, 1000, 100 and 10 (top to bottom) viral particles per cell.

Summary
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. The goal of this work is to develop the ideal gene therapy vector that safely and efficiently produces proteins that heal injured joints and prevents osteoarthritis. Further investigation on animal models and clinical applications of our system will be developed for therapeutic uses.

Acknowledgement
This study was funded by the College Research Council at Colorado State University.

Summaries: Focus 2

Early Diagnosis of Bone and Joint Disease

Development of a wireless gait analysis system for horses

Take Home Message

Objective measurement of limb use in horses has for years been met with frustration, since most of the techniques used to characterize gait are complex and not very practical to use. Researchers in the Orthopaedic Research Center at CSU have been working with a company to validate a system that is accurate and user friendly. There are early indications that this system will be practical to use in a clinical setting.

Introduction

It is common in human medicine to use objective assessment of limb movement to diagnose and monitor orthopedic and neuromuscular diseases. In horses, although techniques have been developed, they are complex and impractical to use in a clinical setting. A wireless gait analysis system has been developed and is currently being tested by Drs. Kawcak, McIlwraith, and Reiser in the ORC.

Methods

Researchers in the Orthopaedic Research Center at CSU are working with Equusys® Inc. to develop and refine a wireless sensor that can track movement of horse's limbs (http://www.equusys.com). In this system, miniaturized accelerometers, gyroscopes and magnetometers are incorporated into the unit (Figures 1 & 2). This 4 oz. sensor has both automatic calibration and drift compensation. This system provides highly repeatable 3-dimensional measurements of linear acceleration, angular rotation, relative positioning of the hoof, foot flight path, stride length and timing. The goal of this collaboration is to determine the accuracy of the sensors and to develop a protocol for its practical use in the clinic.

Results

The system has been useful so far to track limb movement (figure 3). Now the accuracy of the

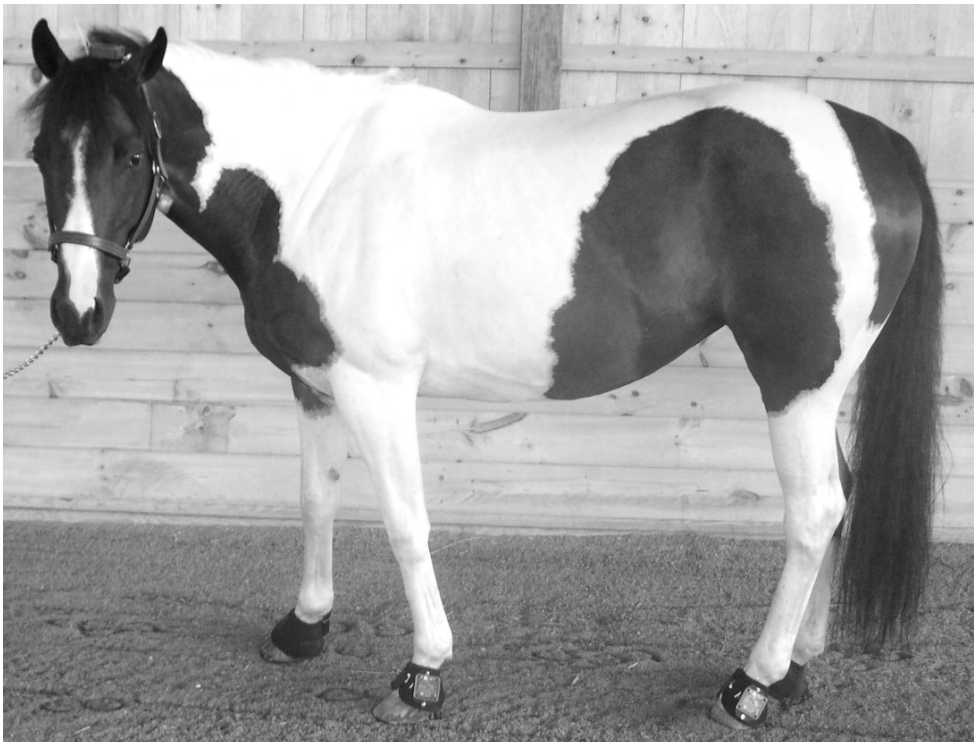


Figure 1: Wireless kinematic sensors placed on a horse demonstrate that they are well tolerated.

Figure 2: A close up view of the wireless kinematic system.

force measurements is being validated against data from a force plate.

Summary

In summary, this system is being modified for ease of use by the practitioner in the field. The goal of this collaboration is to not only provide data on limb movement for experimental studies but also to provide an easy to use and easy to apply system to objectively measure lameness in horses. The ultimate goal is to be able to use this in practice to not only better diagnose lameness, especially those that are subtle in nature, but to also monitor limb use over time

Acknowledgement

Sensors and modifications supplied by Equusys® Inc.

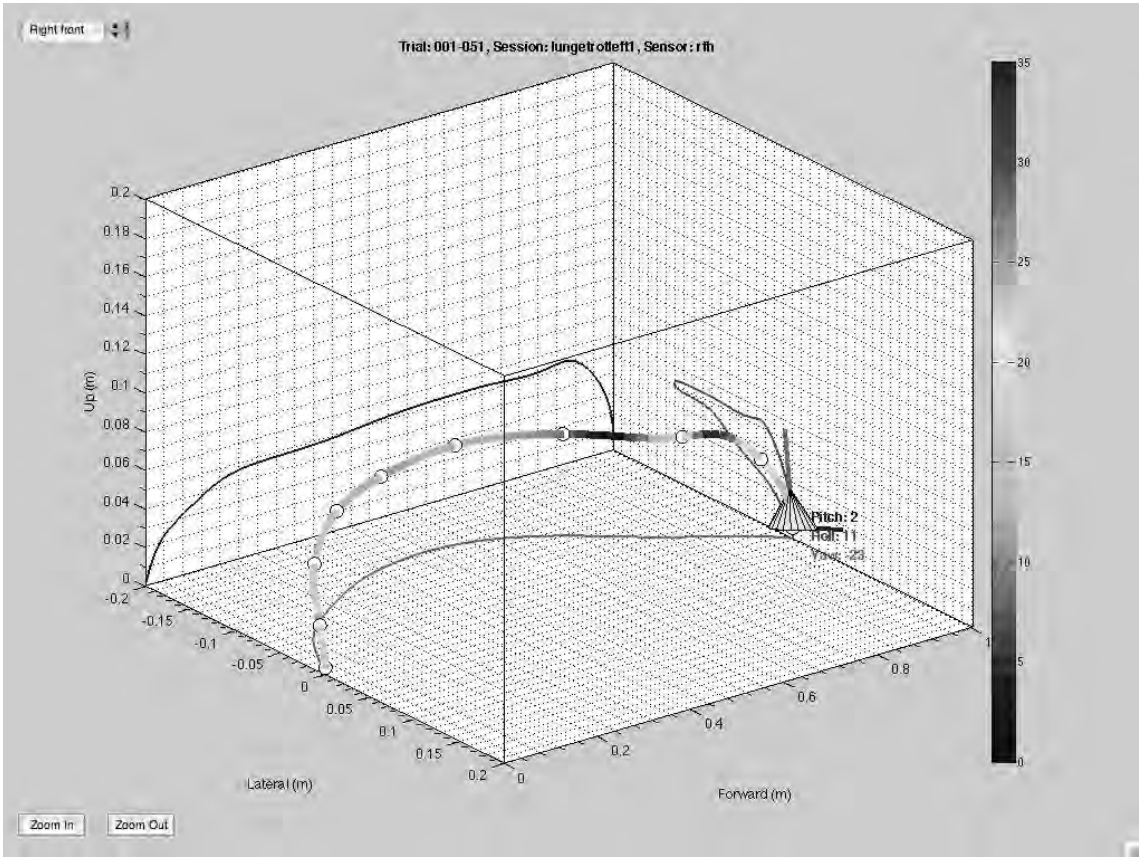


Figure 2: A 3-dimensional plot of hoof movement at a trot. This figure shows not only the hoof placement in space but also rotation and angular velocity during movement.

Imaging methods to determine the severity of disease in the heels of the equine limb

Take Home Message
MRI examination is commonly used to determine the source of pain in a horse's foot. If adhesions are present, the prognosis for return to an athlete is reduced. A technique was developed to determine the presence or absence of adhesions of important structures in the horse's digit. This in turn will allow clinicians the ability to determine an accurate prognosis, treatment and rehabilitation plan.

Introduction
Magnetic Resonance Imaging (MRI) is often performed to determine the cause of palmar heel pain. The presence of adhesions within the navicular bursa to surrounding soft tissue structures carries a poor to grave prognosis. The purpose of this study was to evaluate how injection/distension of the navicular bursa affects the MR appearance of the navicular bursa and associated structures.

Materials and Methods
An MR evaluation was performed on six normal cadaver limbs and two cadaver limbs with lameness localized to the foot. The normal navicular bursae were injected with 2, 4, or 6 mL of solution. The bursae of the feet with lameness were injected with 4 or 6 mL, and MRI was repeated. All the bursae were dissected out to verify the presence (or lack of) adhesions.

This procedure was also used in 2 clinical cases. Both Case 1 and 2 had abnormalities on the initial MRI, suggesting adhesions. The navicular bursa was injected with 6 and 4 mL, respectively.

Results
Distension of the proximal recess of the normal navicular bursa, proximal to the collateral sesamoidean ligament (CSL) was achieved with 2 mL. Separation of the CSL from the deep digital flexor tendon (DDFT) was achieved with 4 mL. The separation of the navicular bone (NB) from the DDFT and DSIL required 6 mL. Adhesions were more clearly defined in the bursa of the 2 pathologic cadaver limbs following distension.

Bursal distension of Case 1 separated the DDFT from the CSL, demonstrating the absence of adhesions between those structures. Bursal distension of Case 2 failed to separate the DDFT from the CSL, suggesting extensive adhesions between the DDFT, navicular bursa and CSL.

Summary
This study demonstrated the usefulness of distension of the navicular bursa in cases where the presence of adhesions cannot be clearly defined by MR imaging. The volume required to more clearly evaluate the bursa and surrounding structures depends on the area of interest and the severity of the abnormalities.

The Effects of Exercise versus Osteoarthritis on Imaging Outcomes

Introduction
Osteoarthritis is a common cause of lameness in athletic horses and unfortunately methods of early diagnosis are often difficult, making clinical signs often the first indication of a problem. The goal of this study was to determine the effectiveness of various imaging parameters on early diagnosis of osteoarthritis.

Materials & Methods
16 horses, 2 years of age and free of any joint problems were included in the study. Eight of those horses were exercise controls and eight of them had an osteochondral fragment placed in one middle carpal joint and represented the osteoarthritis group. All horses were exercised on a high speed treadmill daily up until day 21 when both middle carpal joints of each horse were evaluated arthroscopically and one middle carpal joint of the osteoarthritis group had an osteochondral fragment induced. This created 3 groups of joints: EXC which were the exercise control joints from the exercise control horses, OAF which were the joints from the OA horses that had the osteochondral fragment, and OAC which were the normal joints from the OA horses that did not have an osteochondral fragment. All horses began treadmill exercise on day 35 and the study ended on day 91. During that time horses had lameness, radiographic, computed tomographic, nuclear scintigraphic and magnetic resonance imaging examinations performed. Severity of lameness was graded as was severity of radiographic, nuclear scintigraphic, and MRI changes. In addition, objective measures of nuclear scintigraphy, and computed tomography were assessed.

Results
Lameness, response to carpal flexion and synovial effusion where significantly worse in the OAF group compared to the others. Radiographic changes of OA, including bone lysis, bone proliferation, and osteophytes were worse in the OAF group compared to the others. Nuclear scintigraphic changes were also worse in the OAF group compared to the others. The computed tomography results showed that trabecular bone volume was higher in the OAF group compared to the OAC group in the radiocarpal bone. However in the third carpal bone the subchondral bone volume was highest in the OAF compared to the OAC group. The grade for sclerosis in the radiocarpal bone was significantly higher in the OAC group compared to the OAF. Magnetic resonance imaging showed that synovial fluid volume was worse in the OAF group compared to the others as was synovial membrane proliferation, joint capsule thickening, joint capsule edema, radiocarpal bone sclerosis, and third carpal bone sclerosis.

Discussion
Osteochondral fragmentation consistently showed increased lameness and changes on imaging parameters consistent with osteoarthritis. In OAF joints, there were striking differences on radiographic and MR images and trends towards increase bone volume in those joints. However, the results of this study demonstrate the fact that disease changes often need to be present prior to being detectable when using any of these modalities. This suggests that more refined imaging parameters need to be developed in order to further detect early changes.

Acknowledgements
This study was done by Drs. Kawcak, Frisbie, Werpy, Park and McIlwraith and funded by The Thoroughbred Corp.

The Accuracy and Precision of an Equine in-Shoe Pressure Measurement System as Tool for Gait Analysis

Published in *Journal of Equine Veterinary Science, April 2007, Volume 27, 161-166.*

Take Home Message
In an effort to more objectively characterize lameness in horses, a study was undertaken to evaluate a pressure sensor that attaches to the hoof bottom. Horses were instrumented with this device, and vertical force measurements were compared to those obtained from a force plate. Results showed considerable variability in the sensor, and lack of agreement with results obtained from the force plate. The system cannot be recommended at this time for objective characterization of lameness.

Introduction
The goal of this study was to evaluate a new in-shoe pressure sensor as a means of detecting lameness in horses. Researchers and clinicians have for years attempted to objectively characterize lameness with simple to use devices. TekScan sensors have been used to measure pressure distribution in the feet of people, and investigators attempted to use it here for horses. The system displays a 2-dimensional image of the pressures across the bottom of the hoof (Figure 1). This work was spearheaded by Val Perino, a recently-graduated PhD student in the ORC. She worked with Drs. Kawcak, Frisbie, McIlwraith and Reiser on this project.

Materials & Methods
Vertical force measurements were recorded from both the pressure measurement system and a force plate, with the force plate acting as the gold standard. Six horses were trotted across each and data were compared between the pressure sensor and the force plate.

Results
The variability of the pressure system was significantly higher than for the force plate. In addition, when data were statistically analyzed there was a complete lack of agreement between the two systems.

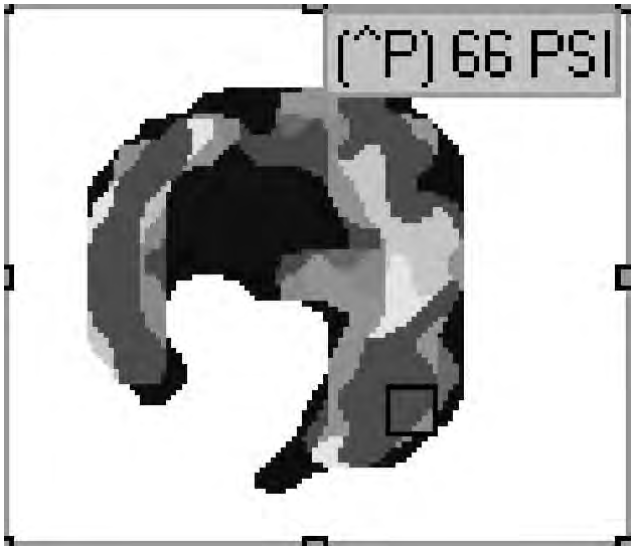


Figure 1. A 2-dimensional image of the pressure distribution across the sole of a horse's hoof using the TekScan system.

Discussion
It was concluded that the equine pressure sensor, in its current form cannot provide precise measurements of vertical ground reaction force and that this system at this time should not be used for objective measurement of lameness in horses.

Acknowledgement
Perino VV, Kawcak CE, Frisbie DD, Reiser RF, McIlwraith CW. The accuracy and precision of an equine in-shoe pressure measurement system as a tool for gait analysis. Journal of Equine Vet Sci 27(4):161-66, 2007.

Use of MRI in Clinicial Patients

This has been a busy 2 years at the Magnetic Resonance Center in the Gail Holmes Equine Orthopaedic Research Center with imaging of clinical patients. Dr. Natasha Werpy has supervised the imaging of both clinical patients and research horses.

Magnetic resonance imaging continues to be invaluable in the diagnosis of injury in equine patients. Diagnosis of soft tissue and osseous injury, not only in the foot but in all areas that can be imaged using MRI, has been greatly improved. These are just two examples of the many patients that have benefited from MRI.

Anna was a 10 year Quarter Horse mare with lameness localized to the foot and pastern. Although abnormalities had been detected in the deep digital flexor tendon at the level of the pastern, Anna's owners wanted to know the full extent of the injury. The MRI showed that the deep digital flexor tendon lesion that started in the pastern continued to the level of the insertion of the tendon on the third phalanx (Figure 1). Magnetic resonance imaging better characterized the lesion in the pastern and demonstrated the extensive nature of the lesion. This case showed that stages of injury can be well demonstrated with ultrasound and other stages that cannot, improving our knowledge of ultrasound. In this case a more precise diagnosis had an impact on both the prognosis and treatment.

Cat was a 14 year old Arabian mare. Her lameness was localized to the fetlock joint but there were no radiographic or ultrasonographic abnormalities. Cat has a focal area of bone loss in the distal aspect of the third metacarpus surrounded by fluid (Figure 2). She also has injury to the articular cartilage corresponding to the area of damaged bone. Her primary lesion was osseous, yet not visible on radiographs because of its size and location. A diagnosis in this case would not have been possible without advanced imaging. Although computed tomography would have been an appropriate choice to image the bone defect, it would not have readily shown the fluid in the adjacent bone or the articular cartilage injury. Magnetic resonance image demonstrated these abnormalities and allowed evaluation of the soft tissue structures of the joint.

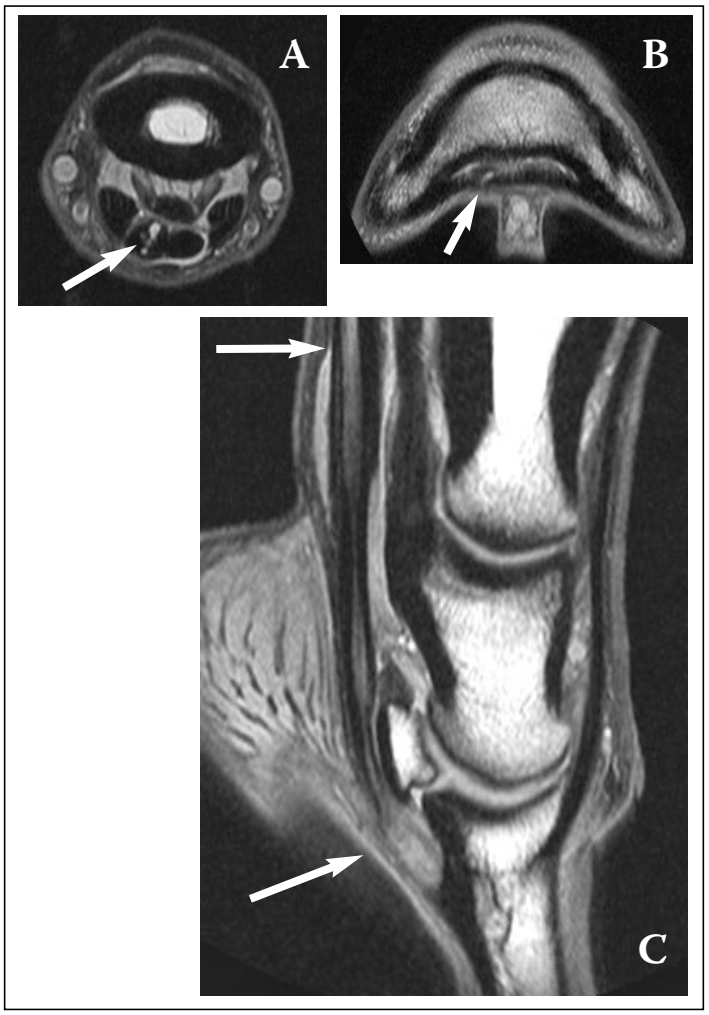


Figure 1: Transverse images (A&B) show the lesion in the deep digital flexor tendon. The sagittal image (C) shows the length of the lesion. The lesion in the pastern area was diagnosed with ultrasound. However, the full extent of the lesion could only be demonstrated with the use of MRI.

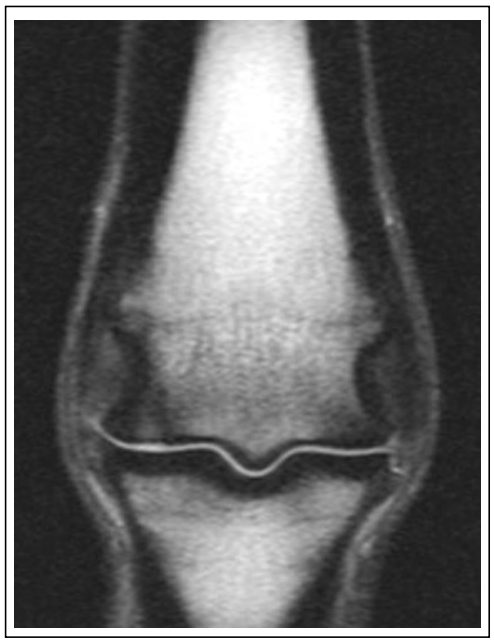


Figure 2: A frontal image of Cat's fetlock joint. A defect can be identified in the distal margin of the third metacarpus. On additional images joint fluid could be identified in the space that should be occupied by the articular cartilage. Cat has bone injury and cartilage loss. This injury could not be identified on radiographs.

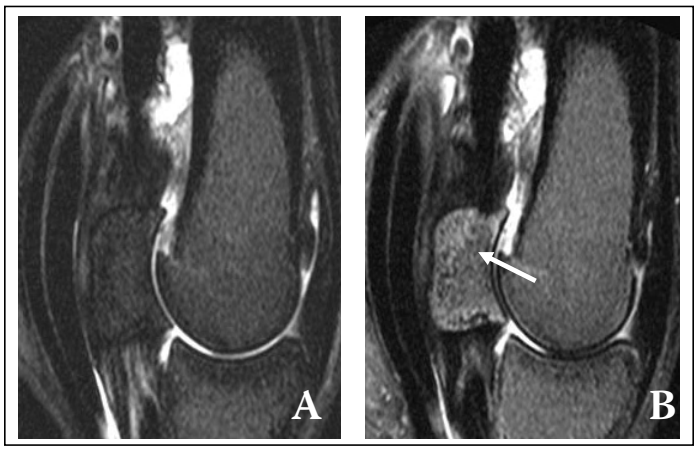


Figure 3: STIR sagittal images of a fetlock joint at two time points. At the initial time point (A) the bones have normal signal intensity. At the second time point, following cast immobilization, (B) the third metacarpus, first phalanx and sesamoid bone have increased signal intensity indicating the presence of fluid. The periphery of the sesamoid bone is most affected (arrow).

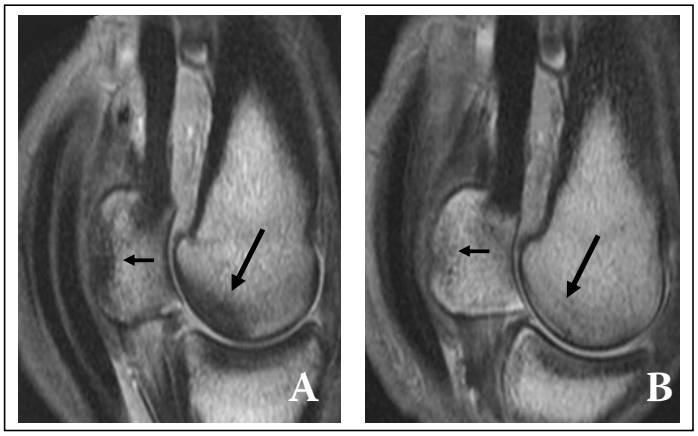


Figure 4: Proton density sagittal images of a fetlock joint at two time points. At the initial time point there was sclerosis in the distal aspect of the third metacarpus and in the palmar aspect of the sesamoid bone (A). This finding was not visible on radiographs on the initial time point. At the second time point, following cast immobilization, the sclerosis was no longer present and the cortices of all the bones were thinned indicative of generalized bone loss (B).

Use of MRI to Evaluate Changes in Bone and Soft Tissues of Fetlock Joint with Cast Immobilization

Magnetic resonance imaging was used to evaluation soft tissue and osseous structures in the fetlock joint for a project utilizing a cast immobilization model. Several findings were observed over the course of the study and evaluated. Changes in the presence of fluid and bone density could be observed and evaluated on the MR images (Figure 3 and 4). Signal abnormalities were also identified in soft tissue structures. These findings were then analyzed to determine the effect of the drug over the course of the study.

Acknowledgment
Financial support from the Walton Family Foundation.

Comparison of Low Field and High Field Magnets for Evaluation of Distal Limbs

Take Home Message
Examination of equine limbs using a musculoskeletal protocol demonstrated large and high contrast lesions are well demonstrated by high and low field MR systems. However, certain smaller and low contract lesions require a high field system to be accurately characterized (Figure 1).

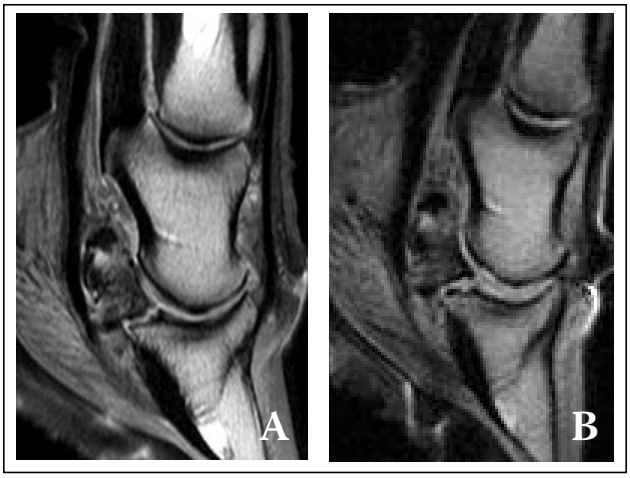


Figure 1: Cadaver limbs were imaged on a 1.0T high field system (A) followed by a 0.25T low field system (B). There is an erosion on the navicular bone flexor surface that is well demonstrated on both images. However, the adhesions between the deep digital flexor tendon and impar ligament as well as the enthesophytes on the proximal margin of the navicular bone require high field imaging to be accurately characterized.

Introduction
Magnetic resonance (MR) imaging provides excellent visualization of soft tissue and osseous injuries. Several MR systems, both high- and low-field, are available for imaging equine patients. High-field systems designed for use in human medicine have been modified to allow imaging of equine patients. Currently, there are low-field MR systems specifically designed for equine patients. There are fundamental differences between high- and low-field MR imaging systems including examination time, image quality and the implications on diagnostic accuracy.

Background
High-field systems
High-field MR imaging systems are defined as having a field strength of 1.0 tesla or greater. One tesla (T) is approximately 20,000 times the earth's magnetic field[1]. Many research centers use high-field, small-bore magnets ranging from 7.0 - 12 T for imaging tissue samples. These systems can characterize the articular cartilage layers and provide extremely detailed imaging of tissue samples. Clinical imaging systems with a field strength of 3.0 T have been introduced into the human market relatively recently, however 1.5 T is still most commonly used. The high-field MR systems currently in use in veterinary medicine are human systems that have been modified to allow imaging of equine patients. High-field, small-bore systems allow extremity imaging from the carpus and tarsus distally. High-field, large-bore magnets are available that allow imaging of the head and cranial cervical spine in addition to the extremities. High-field systems range in price from approximately $495,000 to millions of dollars and are cost prohibitive for many practices.

Low-Field systems
Low-field MR systems are defined as having a field strength of up to 0.3 T.[2] Both of the currently available equine specific MR imaging systems utilize low-field permanent magnets ranging in field strength from 0.20 to 0.27T. Permanent magnets create a magnetic field using the ferromagnetic properties of certain metal alloys[1]. The magnetic field is induced into the materials at the time of manufacturing. The cost of low field systems have made MR imaging accessible to many practices in the United States and Europe and allowed imaging of horses that may not have otherwise had access to this modality.

Examination Time
Direct comparison of the time required to complete a sequence or an examination using high-

and low-field systems is difficult[3,4]. Sequences have approximately 20 different interrelated parameters that affect the image produced. Optimization of images requires that these parameters are set differently on a high-field system compared with a low-field system. Therefore, it is impossible to produce images created with identical sequence parameters from both systems. Similar sequences take 2 - 5 minutes longer to acquire on a low-field system than a high-field system. Low-field systems have a smaller field of view and a higher incidence of artifacts at the periphery of the field of view compared with high-field systems. Therefore, additional sequences are often required to visualize the same area imaged with one acquisition by a high field, large bore system further increasing examination time. An average protocol using 6-8 sequences will take between 12 and 40 minutes longer on a low-field system when compared to a high-field system.

The Relationship Between Image Quality and Diagnostic Accuracy

The next step is to examine the relationship between image quality and diagnostic accuracy. Does the improved image quality achieved with high field systems translate into increased diagnostic accuracy or does it just produce nicer looking images? This has been a long and controversial debate in human medicine. Several papers concluded there is no statistically significant difference between the diagnostic accuracy of low-field and high-field MR systems[4,5.] Barret et al. focused on derangements of the human knee, such as meniscal or cruciate ligament tears, and found no significant difference in specificity or sensitivity for lesion diagnosis between low- and high-field systems[3]. In this paper, many of the cruciate injuries were full thickness tears and the mensical lesions were substantial in size and severity. Kladny et al. compared high- and low-field images of human knee lesions which included full thickness articular cartilage defects. Of 6 defects detected with a high-field system, only 1 was detected with a low-field system5. Currently, there is no publication that compares high- and low-field systems for identification of partial-thickness cartilage lesions in either people or horses. Taouli et al. compared detection of bone erosion in the hands and wrists of patients with a proven diagnosis of rheumatoid arthritis, and suggested that there was no significant difference in the diagnostic accuracy between low- and high-field systems4. However, patients with rheumatoid arthritis of < 6 months' duration were excluded from the study and the images presented in the article had areas of severe bone erosion with > 50 % of the affected bones destroyed as a result of the disease process. Critical analysis of the papers comparing high- and low-field MR images revealed that the lesion size and severity are neither specifically selected for, nor discussed. In reality, these are the most important intrinsic factors determining the conspicuity of lesions.

A review of the literature and evaluation of images from patients examined with both systems demonstrate that the diagnostic accuracy of high- and low-field systems is dependent on the lesion size and type. High-field systems allow detection of small and low contrast lesions that cannot be identified with low-field systems. Examples of structures which are more clearly delineated with a high-field system include: articular cartilage, the flexor surface of the navicular bone, and the distal sesamoidean impar ligament. Certain lesions, such as articular cartilage defects, will have clinical significance in most cases and probably cannot be consistently and definitively identified with a low-field system. Many injuries in the horse can be accurately diagnosed using both high-field and low-field MR systems. However, a high-field system is required to identify certain structures and lesions.

Level of confidence in diagnosis of images from high- and low-field systems has been evaluated in human medicine. Rand et al. reported a significantly superior level of confidence from the investigators in their diagnoses from high field images due to the higher conspicuity of lesions[6]. The in-

creased resolution of high-field images yields greater confidence in the diagnosis of lesions.

Low-field images undergo additional post-processing such as filtering or smoothing in comparison to high field systems. This process is used to prevent individual pixels from being visualized in the image. The filtering or smoothing process blends information in pixels together preventing visualization of individual pixels. The end result of this process creates images that appear as an accurate representation of the anatomy, however several important details are missing. This difference is apparent with comparing the trabecular bone pattern between high- and low-field systems. In most cases the pattern overlying the trabecular bone in an image from a low field system actually represents the noise pattern in the image. A comparison of the pattern in the bone to the image noise present in the background out side the anatomy following adjustment of the window and level will reveal that they are similar. The trabecular bone cannot be accurately represented on most low field images due the resolution limitations. Therefore differentiating diffuse fluid with intact trabecular bone from cystic fluid accumulation with loss or destruction of the trabecular often cannot be achieved. On a low field images the degree to injury to the trabecular bone can be presumed based on other abnormalities present. Assumptions about the trabecular bone can be made based on the severity of the signal intensity and the presence of a sclerotic rim surrounding the affected area however, it cannot be confirmed. These two situations have different implications for the patient. In certain cases diffuse fluid can resolve, however trabecular bone loss is a permanent change. Repair processes can take place, but the injured bone will never return to normal. Abnormalities accompanied by fluid infiltration are commonly encountered in frequently imaged regions such as the foot and fetlock. Accurately characterizing the lesion in these cases is important for treatment and prognosis. The difference in the trabecular bone pattern is just one example demonstrating that although on peripheral overview the images can appear similar, there are important differences.

Methods
Feet, fetlocks, carpi, suspensory ligaments and tarsi were imaged using a 1.0 Tesla magnet and a 0.25 Tesla magnet. Proton density, T2-weighted FSE and STIR sequences were used. The sequences were optimized for each system. Therefore sequence parameters and imaging times were not uniform. Abnormalities on the MR studies were graded for severity on the studies and level of confidence in lesion diagnosis was graded.

Results
Large and high contrast lesions were demonstrated on both systems. Small and low contrast lesions required a high field system for visualization.

Conclusions
Magnetic resonance imaging is an excellent diagnostic tool, but it is important to understand the uses, strengths, and limitations of this imaging modality. High and low-field MR systems have provided diagnostically valuable information to thousands of horses and will continue to do so. However, like all modalities proper use and understanding of the limitations is essential for accurate interpretation and diagnosis. Understanding the limitations of these different systems and accurately communicating it to in-house and referring veterinarians as well as clients reduces the chance of misconceptions and unmet expectations. High field systems have faster acquisition times and superior resolution, however the substantial investment required for purchase and maintenance make them prohibitive for many practices. Many injuries can be accurately characterized and diagnosed using a low-field MR system. However, certain structures and lesions are better characterized with a high-field system and certain lesions will require a high field system for visualization. It is necessary to determine a critical lesion size for each system and validate a protocol that is most effective for demonstrating lesions. In addition, studies are needed to determine the clinical signif-

icance of lesions based on size and type. As we continue to image horses and correlate findings with the results of clinical examination and other imaging modalities, we may be better able to determine which patients should be imaged which a high-field versus a low-field system.

References

1. Bushberg JT. Nuclear Magnetic Resonance. In: Bushberg JT, Seibert JA, eds. *The essential physics of medical imaging, vol 1. 2nd ed.* Philadelphia: Lippincott, 2002;373-467.
2. Tucker RL. Computed tomography and magnetic resonance imaging in equine musculoskeletal conditions. *Vet Clin North Am Equine Pract* 2001;17:145-157.
3. Barnett, M J. MR Diagnosis of Internal Derangements of the Knee: Effect of Field Strength on Efficacy. *American Journal of Radiology* 1993;161:115-118.
4. Taouli B, Zaim S, Peterfy C, et al. Rheumatoid Arthritis of the Hand and Wrist: Comparison of Three Imaging Techniques. *American Journal of Radiology* 2003;182: 937-943.
5. Kladny B, Gluckert K, Swoboda B, et al. Comparison of low-field (0.2 Tesla) and high-field (1.5 Tesla) magnetic resonance imaging of the knee joint. *Arch Orthop Trauma Surg* 1995;114: 281-286.
6. Rand T, Imhof H, Turetschek K, et al. Comparison of low field (0.2T) and high field (1.5T) MR imaging in the differentiation of torned from intact menisci. *Eur J Radiol* 1999;30: 22-27.
7. Denoix, JM. The Equine Distal Limb: *An Atlas of Clinical Anatomy and Comparative Imaging.* London: Manson Publishing, 2000;1-373.

Acknowledgement
Financial support from the Walton Family Foundation.

System Development for In-Situ Characterization of Horse Racing Track Surfaces

Take Home Message
The testing system has been developed and makes it possible to measure key biomechanical performance parameters for a horse racing track, including vertical stiffness and horizontal shear strength. Research has shown that this is a useful tool for monitoring the maintenance of horse racing tracks and work is continuing to determine differences in surfaces, with the ultimate aim of reducing musculoskeletal injury.

Background
A significant challenge in the operation of a horse racing venue is the maintenance of a consistent, safe and fair race track surface. The trainers, jockeys, owners and betting public expect a properly maintained track for racing and training. More importantly, the equine welfare issue is huge in terms of safety for horses and minimization of catastrophic injury. Currently the track conditions are evaluated in vague qualitative terms such as "fast and hard" or "wet". Maintenance of the surface depends on the experience and judgment of the track superintendent. Improved methods to test the track by measuring functional parameters would enhance safety for horses and jockeys while maintaining industry openness to innovative track designs. A study being carried out by Dr. Mick Peterson, Affiliated Faculty member at CSU and Professor of Mechanical Engineering at the University of Maine, together with Dr. McIlwraith and Dr. Raoul Reiser of Health and Exercise Science at Colorado State University has defined a system that approximates the initial impact and loading phase of the horse at a gallop.

Methods and Results
This system approximates the impact, velocity and loads applied to the track while acquiring five data channels. Data from the load cell is monitored and the vertical and horizontal accelerations are obtained from the device measurement. Initial baseline data from tracks around the country shows a large coefficient of variation for the two simple measured parameters that are considered in the paper, the peak load and the ratio of the horizontal to the vertical acceleration. The device is illustrated in Figure 1.

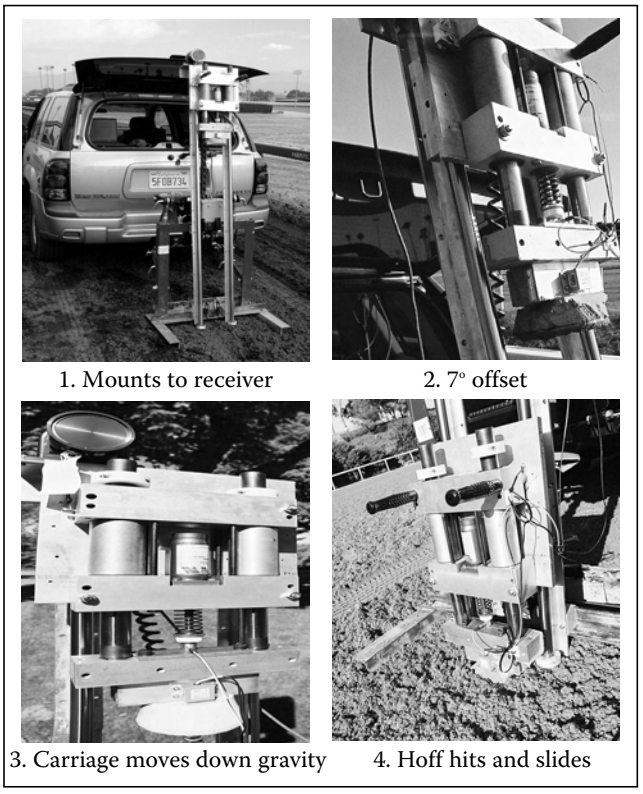


Figure 1: Photos of the apparatus mounted to the test vehicle (top left) with the offset for the two slides (top right), gravity propulsion and the strike and slide which allows two both shear and vertical properties to be measured in a single test.

Tests using the apparatus described were performed at five race tracks over a period of six months. The tracks were of similar construction with generally a sand construction with typical composition of 12% silt and clay, 85% sand with the balance organic material and a small amount of gravel. Additives in the form of fibers or waxes were added at two of the tracks to reduce moistures sensitivity and increase the shear strength. Data is shown for a comparison of the peak force

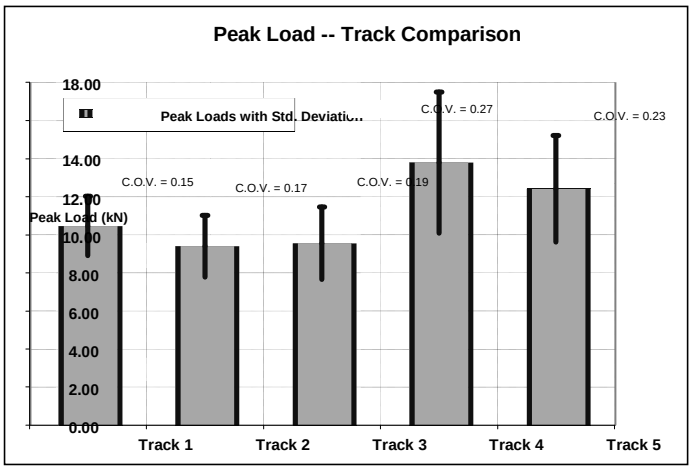


Figure 2: Peak load test results for tests performed at five racetracks with an error bar shown which represents the estimated standard deviation.

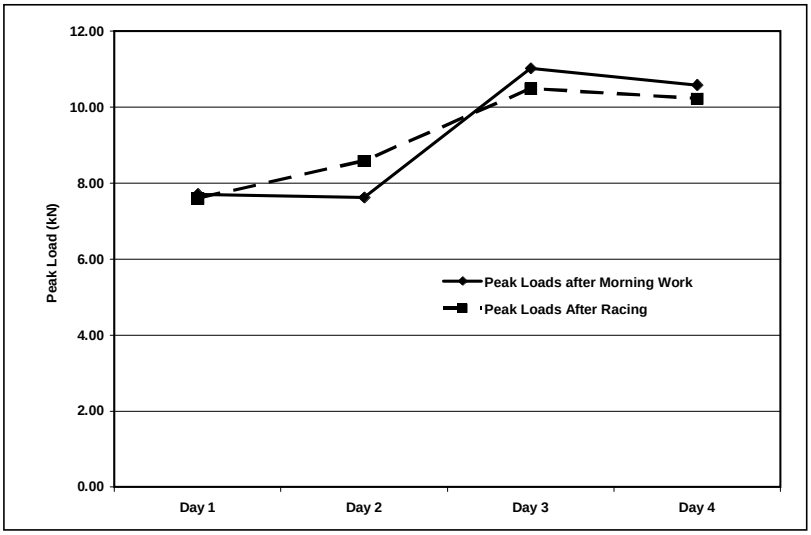


Figure 3: The average peak load measured at one track during a four day period. Lines show tests taken after morning work (dashed) and after racing (solid).

measured at five tracks in Figure 2.
The shear properties of the track were also measured. In Figure 3, the temporal variation over a period of four days at one track is shown. These data was taken both after the morning work and after racing was completed for the day. This example shows how temporal variation can be used to diagnose problems in track maintenance. Each data point represents 24 measurements with only the average value shown on the graph.

In conclusion, a system has been described that makes it possible to measure the key biomechanical performance parameters for a horse racing track, the vertical stiffness and the horizontal shear strength. The ability to detect a change in the track which was determined to be caused by malfunctioning equipment suggested that this can be a really useful tool for monitoring the maintenance of horse racing tracks. Future work will include determining the differences in surfaces some of which have recently been developed which are intended to reduce maintenance of the track while providing a safer racings surface.

Reference
Peterson ML, McIlwraith CW, Reiser RF. System development for in-situ characterization of horse racing track surfaces. Biosystems Engineering 2007, submitted.

Acknowledgment
Grant from American Quarter Horse Association.

Effect of Track Maintenance on Mechanical Properties of a Dirt Racetrack

Background
Racing and training Thoroughbreds often die or are euthanized because of catastrophic injuries. This wastage was first recognized in the literature 25 years ago (Jeffcott *et al.* 1982; Rossdale et al. 1985). Severe physical demands are placed on the musculoskeletal system of Thoroughbred race horses during the high speeds reached during racing and training (Evans *et al.* 1992). Because of the importance of musculoskeletal injuries in the race horse there has been considerable interest in studying factors that predispose to such injuries (Estberg *et al.* 1996; Peloso et al. 1994; Mohammed *et al.* 1991). Musculoskeletal injuries in Thoroughbred race horses have been associated with sex, age, age at first race, horseshoe characteristics, racing frequency, duration of racing career, number of starts per year, weather, season, pre-existing osseous lesions, experience of the trainer, class of race, physical interactions among horses during racing, racetrack, results of pre-race physical inspection and intensity of racing and training schedules. While anecdotal associations have been made between race track characteristics and the incidence of musculoskeletal injury, there have been few scientific studies performed. However, in a study in Minnesota associations were made between the vertical impact characteristics of the dirt racetrack and injury (Clanton *et al.* 1991; Robinson *et al.* 1988).

This is another study done by Dr. Peterson and McIlwraith. The study compared the properties of the track before and after periodic track was performed. Typically the track is harrowed races and after training with a light harrow. At many tracks the entire track surface is periodically tilled and re-compacted to create a partially compacted intermediate layer of soil between the top, lightly harrowed cushion and the firm, flat base.

This study showed that significant changes in a track occurred during routine maintenance. Proper investigation of tracks requires quantitative information describing the surface. Previous tracks measurements have used some type of drop test apparatus (Clanton *et. al.*, 1991; Oikawa *et. al.*, 2000; Ratzlaff *et. al.*, 1997; Pratt, 1985). The vertical component of the surface is the primary force transferred through the forelimb of the horse during a gallop (Clayton 2004). In most previous studies a smaller load was applied which does not properly account for the effect of the deeper layers of the track. The second essential element of loading during motion of a legged animal is horizontal which, in turn, depends on the shear strength of the track surface (Biewener 2003; Wong 2001). Clanton et al. (1991) measured the horizontal shear strength of the track using a load cell placed in the hitch of a harrow and by dragging cadaver hooves across the track. These tests only partially account for the complexity of soil since these are done at low speed and the soil response depends on the rate of loading. A specialized system was thus needed to reproduce the loads and speeds of a horse's hoof at a gallop and to measure the effects of the deeper layers on the impact loads on the small hoof area.

Methods
This study was done by Drs. Peterson and McIlwraith and describes tests which were used to evaluate the effect of maintenance on the mechanical properties of a racetrack. The composition of the track and style of maintenance is similar to that used over a large portion of the western and southern United States.

This study compared the properties of the track before and after periodic track maintenance was performed. Typically, the track is harrowed between races and after training with a light harrow. At many tracks the entire track surface is

periodically tilled and re-compacted to create a partially compacted intermediate layer of soil between the top lightly harrowed cushion and the firm flat base.

The testing system developed for this study used two axes of motion to reproduce the loads and speeds of the forelimb of a horse at a gallop (Peterson *et. al*. 2004). The slide with a synthetic hoof attached moves down a pair of steel rails a distance of 1.6m and impacts with an energy of 540 Joules (Figure 1).

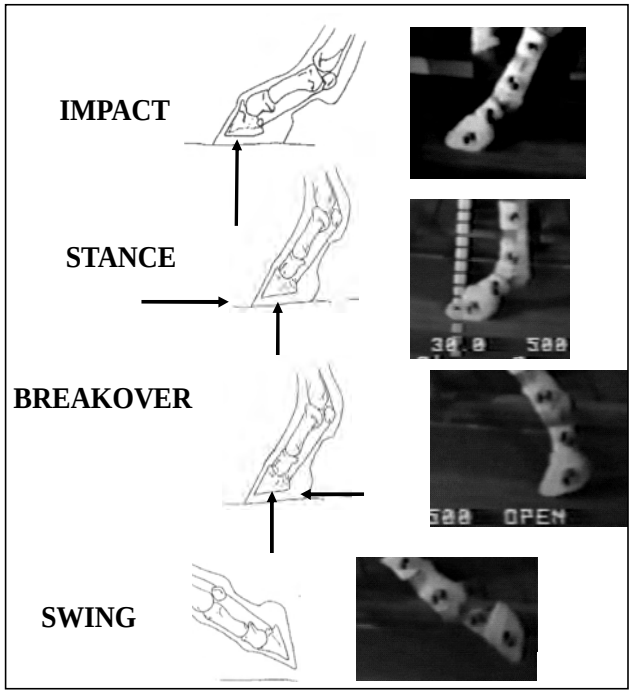


Figure 1: Drawings associated with video frames showing the phases of the gait with load direction on the soil shown with arrows.

A second set of linear rails are attached to the slide and held in position by a gas spring. When the hoof impacts the ground the second set of rails with the spring is compressed. Due to a difference in angle between the two set of rails, the hoof impacts the surface and must slide forward. This replicates the impact and deceleration of the hoof on the forelimb. Loads and accelerations are measured in the vertical and horizontal axes. These quantities are used to characterize the surface.

The loads and speed of contact of this system approximate the loads and speeds generated by a horse at a gallop. The impact velocity of the test machine is based on the vertical velocity of a hoof for a horse trotting at 10m/s (Johnston *et al.* 1991; Hjerten and Drevemo 1994). The system impacts the ground at a speed higher than has been recorded in a horse at a trot, since no comparable data exists for the vertical hoof impact velocity at the gallop (Reiser *et. al.* 2000).

The track considered was a 1 mile dirt oval used by Thoroughbred race horses in an area of minimal rainfall. The test procedures were tailored for testing during a racing meet. The schedule at most race tracks is highly regimented. Given training and racing requirements, two opportunities were available when the track was prepared for use but the horses were no longer on the track: after training in the morning and after racing in the afternoon. Data had to be taken quickly because the moisture content of the track would change and the track was soon occupied for maintenance, racing or training. Data in this study was taken during a 40 minute period after training and represents a longer time than normal without adding water.

The track measurements were taken after morning training on two days when a normal afternoon racing card was scheduled. The tests for the first of the two days was taken after one week of racing on a track where a lightweight roller harrow had been used on the track between races and during training breaks. The roller harrow was set with the teeth at a depth of 2 5/8" below the reference plane of the harrow rollers. A deeper cutting harrow was also used once a day which cuts 2 3/8" below a reference plane which is based on a lightly compacted top layer of the track. The result was a layered compaction profile of the two of the track which results in a partially compacted layer underneath the upper loose layer of material. The data for the second day was taken after a pavement ripper or road rake attachment on a grader was used to make a deeper cut into the track to a depth of

6" below a compacted top layer of the track. After ripping the surface a rototiller was used to break up the material and then the loose material using a roller. The track was then harrowed as normally done on all other days.

Results
Biomechanical hoof data taken on the track described the performance of the surface. The 24 data points taken prior to the heavy maintenance had an average peak load of 13,800 kN with a standard deviation of 578 kN. After maintenance was performed the average peak load was 9110 kN with a standard deviation of 1,320 kN. By loosening and re-compacting the lower levels of the track the average peak load on the track was reduced by 34 %. This result is statistically significant (student t-test at $P<0.05$). However, also notable is that the standard deviation of the peak load increased from 578 kN to 1320 kN. At two standard deviations the peak load on the hoof could vary as much as 57% in a single circuit around the track. The ratio of the peak acceleration in the vertical direction to the horizontal direction was used as a measure of the sliding of the hoof on the ground or the shear strength of the surface. Prior to maintenance the acceleration ratio had an average 0.021 and standard deviation of 0.007 while after maintenance the value was 0.016 with a standard deviation of 0.009.

The reduction in the peak load on the hoof as a result of this maintenance was shown to be significant. However, in addition to reducing the peak load on the hoof, the standard deviation of the peak load shows an increase. This change in variability may be a risk to the horse since it may be possible for a horse to adapt to a surface, but it is unlikely to be able to adapt each stride to an inconsistent surface. Track hardness and variability would then be competing factors for the health of the horse. A harder track may be associated with greater incidence of catastrophic injury. However, maintenance to reduce hardness increases variability. A possible scenario is that if the hardness exceeds a particular threshold maintenance must be performed since the increase in variability in the track is less deleterious than a hard track.

In contrast to hardness, the shear strength measurement was less significantly affected by the maintenance of the track. This suggests that shear strength was less sensitive to maintenance and may be more sensitive to composition. This is likely to be due to the primary role that the cohesive properties of the track material components such as clay play in maintaining the shear strength (Al-Shayea 2001).

The track composition and moisture content were typical of many of the tracks in the western and central United States. The wide particle size distribution may have made it more susceptible to compaction requiring more maintenance to reduce the hardness (Larson et al. 1980; Imhoff et al. 2004). The distribution could be narrowed by adding sand at a size corresponding to the peak of the existing particle size distribution. The tendency toward compaction was reduced by the organic material which also buffered the moisture content (Shainberg 2000). The silt and clay content from the sieve analysis appeared to be high until the clay mineralogy revealed that most of the material was silt which does not have the same cohesive properties as the clay (Mitchell 1993; Al-Shayea 2001).

Reference
Peterson ML. McIlwraith CW. The effect of major track maintenance on the mechanical properties of a dirt racetrack. *Equine Vet J*, submitted.

Three papers from this work have been submitted this year including one on development of the testing systems, the Evaluation of Racetracks before and after their maintenance conditioning and Changes in the nature of the synthetic racing surface polytrack at Delmar associated with change in temperature between morning and afternoon. Drs. McIlwraith and Peterson have just received a grant titled *Performance Parameters for Engineering Track Management* from the

Grayson-Jockey Club Research Foundation to objectively access differences between dirt and synthetic racetracks.

Acknowledgements
This work was initially funded by the American Quarter Horse Association and subsequently financial support came from various participating racetrack authorities. As indicated above a grant has just been allocated from the Grayson-Jockey Club Research Foundation.

Gene Expression of Phenotypically Homogeneous Chondrocytes from different Articular Cartilage Layers of Equine Osteoarthritic and Control Joints: Method Validation and Gene Array Analysis

Introduction
Osteoarthritis remains a common and debilitating disease in humans, horses and other mammalian species, despite advances in diagnosis and treatment. Hyaline cartilage is considered to play a central role in the pathophysiology of osteoarthritis. The investigation of differences in gene expression in cells from osteoarthritic and control cartilage is expected to yield genes that may play a role in the pathophysiology of osteoarthritis, representing possible new targets for the treatment of the disease.

The goals of this investigation done by Dr. Katja Duesterdeck-Zellmer working with Drs. Frisbie, McIlwraith, Iyer and Norrdin were (1) to develop of a methodology to isolate RNA from phenotypically homogeneous cells of various cartilage layers for gene array analysis and (2) to determine differentially expressed genes in these cells in osteoarthritic and control cartilage.

Materials and Methods
Laser capture microdissection was used to isolate phenotypically homogeneous chondrocytes from frozen sections of adult equine articular cartilage. Total RNA was isolated and its quality was estimated employing capillary electrophoresis. The RNA was amplified by 2 rounds of in-vitro transcription and the expression levels of aggrecan, collagen type II, transforming growth factor β (TGF-β) and matrix metalloproteinase 3 (MMP-3) were compared to those from paired cartilage samples, from which RNA had been isolated by an established conventional methodology.

Results
An average of 75µg RNA was obtained from laser captured, amplified samples. Expression levels in these samples were lower for aggrecan, collagen type II, and TGF-β, but not for MMP-3, compared to those from macroscopic samples. This was a consistent phenomenon, as indicated by similar variances for expression levels obtained with either RNA isolation method. It was concluded that the developed methodology was adequate to produce a sufficient amount of RNA to be used for gene array analysis, given that gene expression levels would be compared among samples that had been processed identically.

Six adult horses, enrolled in another study employing the carpal osteochondral fragment model for osteoarthritis were used to collect cartilage samples from the dorsal aspect of the radial facet of the 3rd carpal bones. The validated methodology, followed by gene array analysis was used to determine differentially expressed genes from the tangential and the radial layer of articular cartilage from osteoarthritic and control joints.

154 genes were found to be differentially expressed between tangential and radial cartilage layers ($q<0.05$). Tangential and radial layers of cartilage showed 2 different gene expression patterns. The gene expression pattern of chondrocytes from the tangential layer reflected support of cell proliferation, suppression of apoptosis and upregulation of several genes involved in cellmatrix interactions or inflammatory processes. In contrast, the gene expression pattern of chondrocytes from the radial layer was dominated by genes supporting the synthesis of proteins and proteoglycans, suggesting a higher synthetic activity in these chondrocytes compared to those from the tangential layer. Further, chondrocytes in the radiate showed gene expression suggestive of anticalcification mechanisms.

Only 17 genes were found to be differentially expressed between osteoarthritic and control cartilage ($p<0.01$, fold change>1.5). Similar to the comparisons between cartilage layers, different expression patterns were found for osteoarthritic and control cartilage. The expression pattern for osteoarthritic cartilage was similar for the 2 cartilage

layers, but changes in expression were more pronounced in the radial than the tangential layer. The gene expression pattern in osteoarthritic chondrocytes indicated the activation of the proinflammatory, catabolic NF-κB pathway. It further suggested a response to oxidative stress, but decreased ability to resent apoptosis, as well as downregulation of genes involved in proteoglycan synthesis and energy production.

Conclusions
This study was the first to determine gene expression patterns between 2 different layers of osteoarthritic and control articular cartilage. The present results improve our knowledge of zonal dependence of chondrocyte metabolism and its alterations under the influence of osteoarthritis. They provide the basis for future research into the pathophysiology of osteoarthritis, to identify new therapeutic targets for the treatment of this debilitating disease.

Acknowledgment
Funded by the Equine Orthopaedic Research Center's Discretionary Funds, Colorado State University.

Skeletal Adaptations During Growth and Development: The Results of Changes in the Fetlock Joint In Horses from the GERA Study

Introduction
It is known that tissue will adapt to the stresses that it sees and that these stresses, if seen within a physiologic range, can help strengthen tissues. In order to use this to our advantage, Drs. Kawcak and McIlwraith developed a study with Dr. Firth from Massey University in New Zealand to test the hypothesis that tissues can be conditioned at an early age in order to reduce injury later in life. The specific aims of this study were to evaluate the effects of exercise at an early age on articular cartilage and bone in the fetlock joints, a common site of injury in horses.

Materials & Methods
In this study 12 Thoroughbred foals were evaluated. Both sets of foals were reared in pasture however 6 of the foals also had 1030 meters per day of galloping exercise in addition to pasture turn out. At the end of this study the fetlock joints from these horses were analyzed. This included gross evaluation and histologic evaluation of both articular cartilage and subchondral bone.

Results
All foals went through the 18 months of training without injury. In 6 of the control horses and only 1 of the exercise horses there was visible evidence of joint damage. In work reported by Dygraff et al (Dykgraff S, Firth EC, Rogers CW, Kawcak CE. Effect of exercise on chondrocyte viability and subchondral bone sclerosis of the distal third metacarpal and metatarsal bones of young horses. Equine Vet J, In Press, 2007), there was shown to be 14% greater chondrocyte viability in exercise horses compared to control horses. In addition, there was a trend towards increased glycosaminoglycan (GAG) content in articular cartilage in exercised horses compared to control horses and a rebound effect in GAG synthesis which was higher in control horses compared to exercised horses. However in the work by Nugent et al (Nugent GM, Law AW, Wong EG, Temple MM, Bae WC, Chen AC, Kawcak CE, Sah RL. Site- and exercise-related variation in structure and function of cartilage from equine distal metacarpal condyle. Osteoarthritis and Cartilage 12(10):826-33, 2004), there was no significant difference in the amount of microscopic damage nor in cartilage material properties between control and exercised horses.

The joints of these horses were also evaluated using a 3-dimensional model of bone density. It was interesting to note that there was no significant difference in density between the two groups or in the density pattern within those joints. However, it was clearly evident that in both groups there were some foals that showed a tendency for a high density gradient in third metacarpal bones of the fetlock joints. In other words, there was a large density gradient with a significant reduction in bone density in the areas that commonly fracture in the third metacarpal bones of Thoroughbreds.

Histologic examination of the third metacarpal bone was also undertaken. Although there was no significant difference in the volume of bone between control and exercised horses, there was a significant increase in bone formation in the exercised horse's midway through the study. There appeared to be a maturation effect later in the control horses as the bone volume was not different between the two groups of horses. In addition, the exercised horses showed a trend toward increasing micro-damage in their bone compared to control horses. The differences were not significant however this trend may be indicative of the remodeling response that could be seen in the exercised horses.

Discussion
It appears that early exercise improved chondrocyte viability, cartilage matrix biochemical properties and increased bone formation in high areas

of stress early in the study. However there was no change in synovial membrane or material properties of articular cartilage. Early exercise appeared to stimulate an anabolic effect at the cellular level which may have resulted in a significant reduction of gross lesions in that group. The biggest concern from this study is the fact that the tendency to have a bone density pattern that may pre-dispose to fracture was not significantly different between control and exercised horses. This has led to further studies into this pattern in the fact that whether this pattern is produced by geometrical properties of particular horses.

Acknowledgment
Funded by the Marilyn M. Simpson Trust.

Development and Validation of a Musculoskeletal Model of the Equine Fetlock Joint

Take Home Message
The pattern of bone density in the fetlock joint of horses may have an influence on fracture occurrence. It is known that bone density pattern is determined from the stresses seen within the joint, and the best way to determine those stresses is through the development of computer models that simulate movement and stress in the joint. This article describes the methods being developed to use computer models to monitor joint loads.

Introduction
The metacarpophalangeal joint (MCP) of racehorses is especially susceptible to a wide variety of injuries. Previous studies have found patterns of subchondral bone (SCB) sclerosis in commonly fractured areas (Riggs et al., 1999) and marked site-associated variations in the structure, biochemical, and biomechanical properties of articular cartilage in the equine distal third metacarpal (MC III) condyle. In another study based on the GERA study it was concluded that variations in loading within different regions of an articular surface as well as the biomechanical environment can initiate degenerative changes (Nugent et al. 2004). These studies suggest that the type of injury that occurs may be related to how the joint surfaces articulate and how contact area changes with increasing load. The following studies are being done by Katrina Easton, a graduate student in the ORC, working with Drs. Kawcak, Puttlitz and McIlwraith.

Methods
In order to investigate the latter, computed tomographic (CT) scans of 6 intact MCPs were rendered into 3D reconstructions using OsteoApp. The limbs were loaded on the materials testing system (MTS) to an angle 150° and 120° between the MC III and the proximal phalanx and injected intra-articularly with a 1:1000 safranin-O solution and a 1:1000 toluidine blue solution respectively. This study is being done by DVM/PhD student Katrina Easton together with Drs. Kawcak, Puttlitz and McIlwraith.

Results
The total articular surface area of the distal condyle of the MCIII as well as the areas of articular contact were digitized and rendered. A significant increase in contact area on the condyle of MCIII, the proximal sesamoid bones, and the proximal phalanx was found. A subjective comparison of the computer model showing areas of contact with the CT model suggested that areas of contact may be associated with increased density (Figure 1). This supports the idea that the SCB adapts to the load applied to it. As load increased, contact area also increased suggesting that areas not normally loaded may experience a high degree of stress during impact loading (Easton and Kawcak, 2007).

Discussion
With all of the possible variations in loading parameters such as magnitude, rate, and repetitiveness, combined with patient conformation, gait patterns, loading history, and neuromuscular variations, the study of causative factors of osteochondral disease is difficult at best. Current studies are focusing on the use of finite element (FE) analysis which provides a computational method of investigating individual variables separately and in conjunction by allowing the user to change parameters such as bone geometry, joint laxity, and material properties in a computer model of the MCP.

A 3D finite element model of the MCP is currently being developed. The bone (trabecular and cortical), ligament, and tendon geometries have been manually segmented (Figure 2) from CT and magnetic resonance image (MRI) data. The segmented geometry will be subsequently meshed and material properties from CT data and biomechanical and biomaterial data from the lab will be applied. The model will be validated through dynamic me-

chanical loading experiments on cadaver limbs investigating strain in the bones, ligaments, and tendons of the MCP as well as the contact area and its associated pressure distribution.

The validated FE model will be used to examine how bone geometry including the width of the lateral condyle, the degree of palmar flattening, and the depth of the parasagittal groove, cartilage thickness, both surface articular cartilage and calcified cartilage, and joint laxity (defined here as ligament and tendon laxity) affect the contact stress and strains within the bones, ligaments, and tendons within the MCP. Specifically those parameters which lead to stresses and strains close to or in excess of the yield strength of the bones and soft tissue structures will be determined. The results will be compared to the normal joint as well as the ultimate strength of the bones and soft tissue structures. Based on these comparisons, the probability for and location of failure will be determined.

If this work demonstrates that certain patient specific parameters predispose an individual to osteochondral disease, the same models can then be used to determine how to alter these parameters through gait training, strengthening exercises, use of orthotics, or even surgery in order to slow the progression of disease. In a broader context, the methods to be developed will provide a valuable technique for investigating joint disease and can lead to insight into the pathogenesis of OA and other osteochondral diseases as well as possible methods of ultimately preventing the disease from ever initiating.

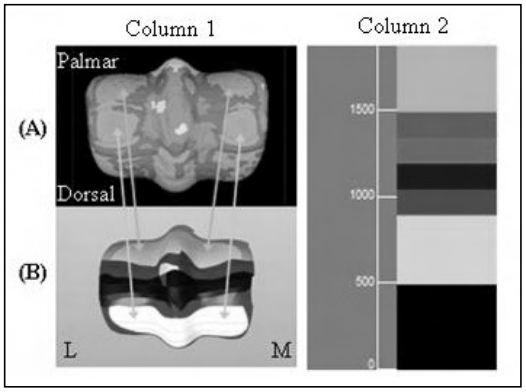


Figure 1: Comparison of CT scans and models of MC III. Column 1=Distal surface of the distal condyle of MC III. Column 2=Reference color scale for CT data. umbers are in Hounsfield units. ncreasing numbers correspond to increasing density. Row A=Three-dimensional rendering of CT scan of the distal condyle of MC III, revealing the SCB density pattern. Row B=Three-dimensional computer model revealing contact area (white=contact at both 150° and 120°; blue=contact at 150°, but not 120°; red=contact at 120°, but not 150°; purple=no contact at either angle; pink=diffuse staining). The blue arrows show where the proximal sesamoid bones are in contact with the distal condyle of MC III. This corresponds to a higher density, as indicated by the pink and green areas on the CT scan. The yellow arrows show where the proximal phalanx is in contact with the distal condyle of MC III. Again, the corresponding density gradient is increased in this area.

References

1. Riggs CM, Whitehouse GH, Boyde A. Pathology of the distal condyles of the third metacarpal and third metatarsal bones of the horse. Equine Vet J 1999;31:140-148.
2. Easton KL, Kawcak CE. Evaluation of increased subchondral bone density in areas of contact in the metacarpophalangeal joint during loading in horses. Am J Vet Res 2007;68:816-821.
3. Nugent GE, Law AW, Wong EG, Temple MM, Bae WC, Chen AC, Kawcak CE, Sah RL. Site- and exercise-related variation in structure and function of cartilage from equine distal metacarpal condyle. Osteoarthritis Cartilage 2004;12:826-833.

Acknowledgements

This study was funded by the College Research Council at Colorado State University, and the Lufkin Foundation.

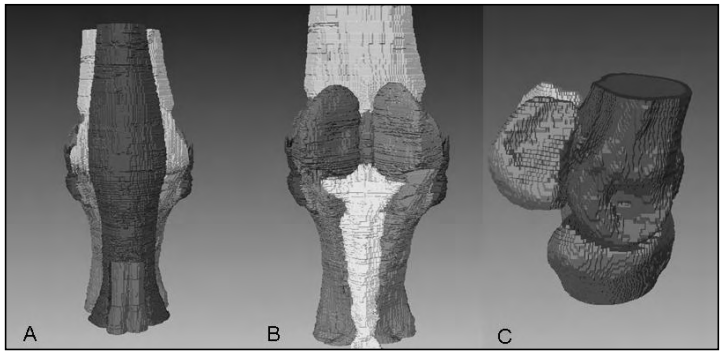


Figure 2: Example of the segmentation of the bones, ligaments, and tendons of the MCP from CT and MR data. A) Palmar view of the MCP showing the digital sheath and SDFT. B) Palmar view of MCP showing the proximal sesamoid bones and straight and oblique sesamoidean ligaments (DDFT, SDFT, and intersesamoidean ligaments removed). C) MC III, proximal phalanx, and lateral sesamoid bone.

Influence of Early Exercise on Lesion Development and Cartilage Matrix Changes in the Equine Metacarpophalangeal Joint

Take Home Message
The effect of early exercise on articular cartilage material properties was studied. Results showed that early exercise was beneficial in reducing the incidence of gross damage to the carpal joints, although there was not significant effect of exercise on material properties. Results did show though that articular cartilage in different locations within the joint has different properties, and that strength of tissues vary throughout their depth.

Introduction
Osteoarthritis is a common disease that affects horses and once the disease process starts most owners are faced with managing the problem. Ideally it would be good to prevent the problem however methods to do so are lacking. In a collaborative study between Dr.'s Kawcak and McIlwraith at Colorado State University, Dr. Elwyn Firth at Massey University in New Zealand, and Dr. Neil Broom at the University of Auckland in New Zealand, a study was developed to measure the effects of early exercise on preventing joint disease. Woong Kim, a graduate student in Neil Broom's laboratory spearheaded this study. The goal of the study was to determine the effects of early exercise on gross pathologic changes and articular cartilage mechanics in the middle carpal joints of horses.

Materials & Methods
Twelve Thoroughbred foals were divided into two groups. Six of those foals were in a control group and 6 were in the early conditioned group. Both groups were raised on pasture except the early conditioned group was exercised over 1030 meters daily until the end of the study at 18 months. At the end of the study the middle carpal joints from each group were analyzed. In addition, four sites on the radiocarpal and third carpal bones were obtained and processed to determine mechanical properties of the articular cartilage (Figures 1 and 2).

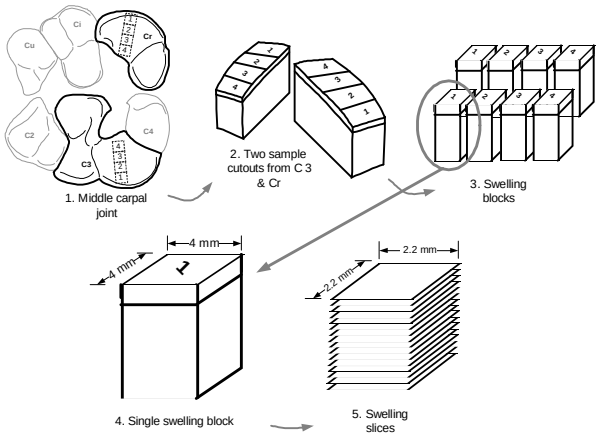


Figure 1. Diagram showing sampling sites from the middle carpal joint. This allowed for analysis of mechanical properties between different sites within the joint and within different layers of the articular cartilage.

Results
Horses in the control group had a significant increase of gross lesions in the dorsal aspect of the third carpal bone compared to the exercise group. However there was no influence of exercise on swelling strain in any of the articular cartilage samples. It was interesting to note that the swelling strain was affected by the location on the third and radiocarpal bones. In particular, sites 3 and 4, which were located on the palmar aspect of the joint surfaces had significantly reduced swelling strain compared to those on the cranial aspect of the joint surface. In addition, swelling strains were minimal in the superficial layers of cartilage depth then gradually increased to a maximum at the mid-level of the matrix, and decreased again as it approached the osteochondral junction. In addition, the overall magnitude of swelling strain was higher in the third carpal bone compared to the radiocarpal bone.

Discussion
It appears that early exercise may have had a protective effect on the middle carpal joints of these horses. The fact that there was a reduction in

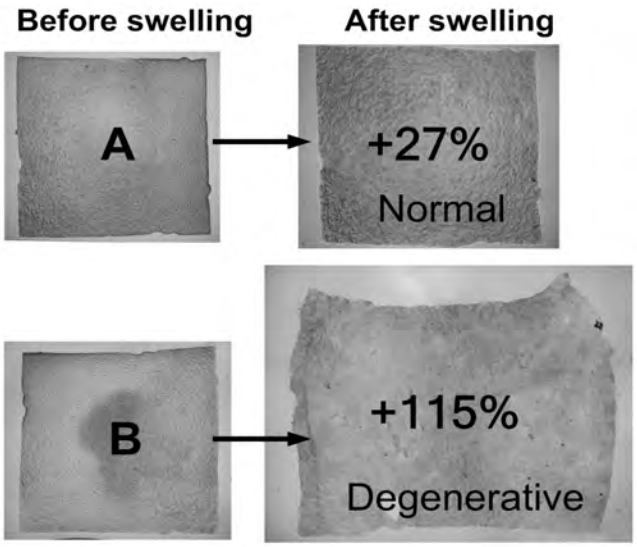


Figure 2. Method for determining swelling pressure of the articular cartilage slices. When normal slices are hydrated, they typically enlarge about 30% (A). However, if they are damage, they will swell significantly more (B). This indicates that the articular cartilage matrix is loosened due to degeneration.

gross lesions in exercised horses may mean that early exercise could increase material properties of the joints and protect them from lesions that normally occur in young horses. It was interesting to note that certain lesions did not affect the swelling behavior of cartilage in specific areas. Although there was a higher incidence of lesions in the control group, there was no significant difference in swelling strain between exercise and control groups. Therefore the lesions did not appear to weaken the articular cartilage at these sites. However, the swelling strain did correlate closely with the amount of load seen in different areas. In particular, the higher swelling strains correlated well with areas that had more intense loading and those with less loading such as in the back of the joint had lower swelling strain. Therefore even in the face of an apparent protective tendency of exercise on the development of gross lesions, the microscopic tendency of articular cartilage is to compensate for those changes in order to protect the joint. Therefore it can be concluded from this study that early exercise appears to protect the joint from articular cartilage damage but that, at least prior to 18 months of age, the articular cartilage molecular properties tend to compensate well. It is unknown however what this would mean later in life and one would have to be concerned that development of early lesions in the control horses may lead to joint disease later on.

Acknowledgement
Supported by a grant from the Grayson Jockey Club Research Foundation.

Mechanical Nociceptive Thresholds in the Axial Skeleton of Horses

Take Home Message
Mechanical nociceptive thresholds (MNTs) were repeatable and increased in a cranial-to-caudal gradient within the axial skeleton. Higher MNTs were measured in young, heavy, non-Thoroughbred, castrated males, and in horses that were ridden and actively exercised. Pressure algometry provides an objective, non-invasive, and repeatable tool to measure mechanical nociception in horses.

Introduction
Objectively interpreting the presence of pain is difficult, but essential, in the diagnosis and management of musculoskeletal injuries. Hoof testers, flexion tests and gait analysis have been the primary mechanical means of assessing lower limb lameness, but their interpretation is highly subjective. Pressure algometry is a repeatable clinical technique for quantifying and monitoring musculoskeletal nociception in humans.[1] Pressure algometry uses a calibrated pressure gauge attached to a rubber-tipped plunger that is pressed against a predetermined landmark until a perceived noxious reaction is produced (Figure 1). The MNT is defined as the minimum pressure that induces a pain response. In humans, nociception varies according to age, sex, weight, race, and exercise activity. Our purpose was to establish reference MNT values within the axial skeleton of normal horses and to evaluate the effects of signalment and ridden exercise on MNTs.

This project was completed by Drs. Kevin K. Haussler and Hollis N. Erb at Cornell University and was published in the Equine Veterinary Journal.[2]

Methods
Horses - Two groups of horses were assessed, which included ten horses that were stall-confined, had no turnout and were not ridden and 26 actively ridden horses. A pressure algometer with a 1-cm^2 rubber plunger tip and a calibrated range from 0 to 20 kg/cm^2 was used to determine MNTs.[3] Pressure was applied perpendicularly to 62 midline and bilaterally symmetric sites along the axial skeleton until a local avoidance reaction (skin twitching, local muscular contractions, induced lordosis or stepping away) was noted. The median of the three consecutive measurements at each site was used as the site-specific MNTs for that horse. The effects of age (< 13 years; ≥ 13 years), sex, weight (< 470 kg; ≥ 470 kg), breed (Thoroughbreds versus non-Thoroughbreds), and non-ridden versus ridden exercise on MNTs were assessed separately for each site.

Results
The three consecutive measurements at each site sequentially increased in 24%, decreased in 8%, and had no change or consistent pattern in 68% of measurements. The median range of three consecutive measurements across all sites and all horses was 1 kg/cm^2. There was a distinct cranial-to-caudal increase in the MNTs (Figure 2). The regional median MNTs were: cervical 9 kg/cm^2; thoracic 12 kg/cm^2; lumbar 13 kg/cm^2; and pelvic 16 kg/cm^2. Ridden versus non-ridden exercise comparisons had the only median differences larger than ± 1 kg/cm^2. MNTs were higher at all sites in the ridden horses.

Discussion
The pressure algometry was easy to use and well tolerated at all musculoskeletal landmarks. Consistent and predictable responses to the applied pressure were identified readily. Adaptation occurred in 24% of measurements and should be considered a contributing factor to poor repeatability. The 8% prevalence of sensitization is consistent with reports in humans. Nociceptors in the skin, subcutis, fascia, muscle and periosteum all contribute to detection of a noxious stimulus. Differences in bone, muscle and nerve MNTs within certain regions may be due to variations in

the concentration or depth of nerve fibers. Similar to humans, we found gradually increasing MNTs from the cervical to lumbar spine.[4] These regional differences might be due to a higher nociceptor density in the cervical spine to protect vital neurovascular structures or to increasing lengths in the regional pain pathways. There were trends for higher MNTs in young, heavy, non-Thoroughbred, castrated males. There was a consistent and substantial increase in the MNT for actively ridden horses compared to the non-ridden horses.

Clinical application
Reference MNTs of normal horses provide a standard to which horses with suspected or known axial skeleton pain can be compared. In horses with documented musculoskeletal injuries, MNTs in the affected areas are often $\leq$ 5 kg/cm^2.[2,3] In humans, MNTs of $\leq$ 3-4 kg/cm^2 are considered indicative of tenderness. Pressure algometry also provides an objective measure of a typically vague and poorly quantified clinical entity: muscle pain. Horses with myofascial pain often present with non-specific pain that is not related to any known trauma or documented pathology (i.e., abnormal muscle enzymes or muscle biopsies). In humans, pressure algometry has been used to quantify myofascial and osteoarthritis-related pain. Similar applications need to be explored in veterinary medicine.

Acknowledgement
This study was funded by the American Association of Equine Practitioners.

References
1. Fischer AA. Algometry in diagnosis of musculoskeletal pain and evaluation of treatment outcome: An update. J Musculoskeletal Pain 1998; 6(1): 5-32.
2. Haussler KK, Erb HN. Mechanical nociceptive thresholds in the axial skeleton of horses. Equine Vet J 2006; 38(1): 70-75.
3. Haussler KK, Erb HN. Pressure algometry: Objective assessment of back pain and effects of chiropractic treatment. Proc Amer Assoc Equine Practitioners 2003; 49: 66-70.
4. Hogeweg JA, Langereis MJ, Bernards AT, et al. Algometry. Measuring pain threshold, method and characteristics in healthy subjects. Scand J Rehabil Med 1992; 24(2): 99-103.

Pressure Algometry for the Detection of Induced Back Pain in Horses: A Preliminary Study

Take Home Message
Pressure algometry provides a quantitative and repeatable method for assessing the presence of musculoskeletal pain. The precise surgical sites could be recognized due to substantial and localized decreases in the MNTs, compared to surrounding landmarks. Further studies are needed to evaluate pressure algometry clinically for assessing musculoskeletal injuries and pain management strategies in horses.

Introduction
The ability to quantify and localize musculoskeletal pain is critical to both injury diagnosis and treatment assessment. Large discrepancies often exist between practitioners, especially in the clinical interpretation of mild-to-moderate back pain. Pressure algometry is a mechanical instrument used to quantify mechanical nociceptive thresholds (MNTs) within musculoskeletal structures and has the potential to provide an objective assessment of nociception and aid in localizing pain to affected structures. The ability of pressure algometry to identify and localize induced musculoskeletal pain in horses is unknown and the presence of peripheral or central sensitization has not been assessed objectively in horses with known back pain. The purposes of this study were to assess the ability of pressure algometry to identify and localize induced musculoskeletal pain and to evaluate the presence of peripheral or central sensitization after repeated noxious stimuli within the thoracolumbar spine of horses.

This project was completed by Drs. Kevin K. Haussler and Hollis N. Erb at Cornell University and was published in the Equine Veterinary Journal.[1]

Methods
Two groups of ten horses were assessed in 2 consecutive years. A pressure algometer with a 1-cm^2 rubber plunger tip and a calibrated range from 0 to 10 kg/cm2 or 0 to 20 kg/cm^2 was used to determine MNTs using previously described techniques. A pressure algometer with a higher upper limit (20 kg/cm^2) was used in the subsequent year to reduce the ceiling effect of the instrument. Pressure algometry was used to assess MNTs at midline and bilaterally symmetric anatomic sites along the axial skeleton. Experimentally induced pain was used to assess the ability of pressure algometry to detect a known musculoskeletal injury. All horses were instrumented with two fixation half-pins implanted in the dorsal spinous processes of two adjacent vertebrae as part of a concurrent project.[2] At all sites, the percent change in MNTs from before pin insertion to 1 day after pin insertion and removal was calculated (Pre1-Post1). The MNTs of landmarks not associated with the pin-placement sites (non-pain sites) were pooled for comparison to the surgical sites. All horses were re-instrumented with fixation half-pins at 7 to 15 days for repeat spinal kinematic assessment at the same locations (Post2-Post2). To assess longer-term adaptation or sensitization to the induced pain, the percent change in baseline MNTs from the beginning of the study were compared to MNTs measured at the end of the study (Pre1-End).

Results
At most non-pain sites, the median percent change in MNTs pre- versus post-pin placement was near zero (“10%). The precise site of the implanted fixation-half-pins could be recognized based on dramatic and localized decreases in the MNTs at and adjacent to the pin-placement sites (Figure 1). At the non-pain sites, the median percent change in MNTs from baseline to the end of the study was 4% in the first group of horses and 13% in the second group of horses (Table 1). At the surgical sites the distributions of the median percent change was positive (24%) in the first group of horses, but negative (-12%) in the second group of horses.

Discussion

This was a pilot study to investigate the ability of pressure algometry to identify induced pain and to assess alterations in nociception with repeated noxious stimuli. Establishing upper and lower limits (and ranges) of MNTs at both non-pain and surgical sites over time begins to provide a foundation for better understanding of back pain in horses. Pressure algometry provides a more quantitative evaluation of musculoskeletal pain than does manual palpation.[3,4] The presence of pain can be identified and also differentiated from adjacent non-painful landmarks. With no intervention, the expected distribution of the median MNTs is 0% change, with minima and maxima distributed symmetrically about the median. This distribution was readily apparent at the non-pain sites in both groups of horses, which indicates good repeatability, across years. In contrast, the surgical sites had noticeably lower MNTs, which indicated hyperalgesia at the pin-placement sites. Pin placement into the dorsal spinous processes was an adequate method of inducing bone pain in the thoracolumbar region and reproduced the lower MNTs that are seen in clinically affected horses with documented back pain. Large left-right differences are expected in horses with lateralized musculoskeletal pain, which was not investigated in this study. In humans with lateralized pain, MNT differences > 2 kg/cm^2 are considered clinically significant; the painful side of the body has the lower MNTs.[5] Pressure algometry might provide unique information about segmental dysfunction that is not readily available with current diagnostic techniques that attempt to assess peripheral or central sensitization. In our study, a regional reduction in MNTs was measured in the adjacent paraspinal muscles, which suggests peripheral sensitization to the induced pain. Further studies are needed to clinically evaluate pressure algometry for assessing musculoskeletal injuries and pain management strategies in horses.

Acknowledgements

Funding was provided by the American Association of Equine Practitioners and the New York Thoroughbred Horsemen's Association, Inc.

References

1. Haussler KK, Erb HN. Pressure algometry for the detection of induced back pain in horses: a preliminary study. Equine Vet J 2006; 38(1): 76-81.
2. Haussler KK, Bertram JEA, Gellman K, et al. Segmental in vivo vertebral kinematics at the walk, trot and canter: a preliminary study. Equine Vet J 2001; 33: 160-164.
3. Chambers JP, Waterman AE, Livingston A. Further development of equipment to measure nociceptive thresholds in large animals. J Vet Anaesthesia 1994; 21(2): 66-72.
4. Kosek E, Ekholm J, Nordemar R. A comparison of pressure pain thresholds in different tissues and body regions. Long-term reliability of pressure algometry in healthy volunteers. Scand J Rehabil Med 1993; 25(3): 117-124.
5. Vanderweeën L, Oostendorp RA, Vaes P, et al. Pressure algometry in manual therapy. Man Ther 1996; 1(5): 258-265.

Effects of Vertebral Mobilization and Manipulation on Kinematics of the Thoracolumbar Region

Take Home Message
The amplitudes of passive vertical displacement increased from cranial to caudal within the thoracolumbar portion of the vertebral column in standing horses. Spinal manipulative therapy (SMT) induced a 15% increase in displacement and a 20% increase in applied force, compared with control measurements, which indicated increased spinal flexibility and increased tolerance to pressure.

Introduction
Back problems in horses are often characterized by signs of pain, stiffness, and reduced performance. Unfortunately, the clinical assessment of back pain and stiffness is mostly subjective. Kinematic tools that quantify spinal mobility or stiffness have the potential to improve the diagnosis and management of spinal injuries. SMT involves the application of manually applied forces with the intent of reducing pain and promoting joint mobility and is being used with increased frequency for the conservative management of back pain in horses.1 Biomechanical assessment and quantification of manipulative techniques are critical to understanding the mechanical events that occur during a manipulative thrust. The objectives of the present study were to determine regional differences in vertical mobility and stiffness at five intervertebral sites within the thoracolumbar portion of the vertebral column in standing horses and assess the effects of SMT in a randomized crossover study. We hypothesized that SMT would increase spinal flexibility in horses with induced back pain.

This project was completed by Drs. Kevin K. Haussler, Ashley E. Hill, Christian M. Puttlitz, and C. Wayne McIlwraith and was published in the American Journal of Veterinary Research.[2]

Methods
Ten horses were used in this study. Baseline values of vertical displacement, applied force, stiffness, and frequency of the oscillations were measured during dorsoventral spinal mobilization at five thoracolumbar intervertebral sites. A concurrent study required attachment of a spinal kinematic transducer via fixation pins temporarily implanted into the dorsal spinous processes of adjacent vertebrae at two of the intervertebral sites. For this study, the fixation pins were used as a model for the induction of acute back pain. In the randomized crossover study, horses were allocated to control and treatment interventions, separated by a 7-day wash out period. Treatment consisted of high-velocity, low-amplitude thrusts applied to the three non-pin placement sites. Control horses received no treatment. The amplitude and frequency of vertical vertebral displacements were measured with a calibrated cable extensometer attached to a mobile overhead rail in the stocks (Figure 1). The distal end of the cable extensometer was attached to the examiner's hand, which was placed on the horse's back and used to manually induce cyclic loading and unloading of the vertebral column (i.e., passive spinal mobilization).[3] The force applied during each cyclic displacement was simultaneously measured with a calibrated pressure mat. The slope of the linear region of a single loading cycle randomly chosen in the last 10% of each data collection period was used to calculate stiffness at each intervertebral site.

Results
At baseline, vertical displacement progressively increased in a cranial-to-caudal direction among intervertebral sites (Table 1). No significant differences in stiffness or the frequency of oscillations were found among intervertebral sites. Compared with baseline values, pin implantation did not significantly affect most spinal variables. The exceptions were significant reductions in stiffness at L1-2 (-30%) and L5-6 (-24%) in the control portion of

the crossover study. SMT induced significant increases in displacement and applied force at the T14-15 and L1-2 intervertebral sites. Mean increase in displacement was 15% (range 7% to 25%) after SMT, compared with 0% (range -4% to 7%) after the control intervention in the control sessions. Mean increase in force was 18% (range 10% to 27%) after SMT, compared with -2% (range -7% to 5%) after the control intervention in the control session.

Discussion
The increasing cranial-to-caudal gradient in displacement in standing horses is most likely related to alterations in articular facet orientation and the increased amplitudes of flexion and extension at the lumbosacral joint.[4] Rotation of the pelvis about the coxofemoral joint is an underappreciated but major contributor to dorsoventral spinal mobility. Incorporating the potential contributions of the highly mobile lumbosacral and coxofemoral joints provides a more realistic and useful static and dynamic model of the equine thoracolumbar vertebral column. Results of the present study indicated some of the immediate beneficial effects of SMT on spinal mobility in horses. Objective evaluation of back flexibility or stiffness and the response to untested treatment modalities can provide a basis for the development of appropriate management strategies of horses with acute signs of back pain.

Acknowledgement
Supported by the Harry M. Zweig Memorial Fund for Equine Research, Cornell University, College of Veterinary Medicine.

References
1. Haussler KK. Chiropractic evaluation and management of musculoskeletal disorders. In: Ross MW, Dyson S, eds. Diagnosis and Management of Lameness in the Horse,. Philadelphia, PA: W.B. Saunders, 2003; 803-811.
2. Haussler KK, Hill AE, Puttlitz CM, et al. Effects of vertebral mobilization and manipulation on kinematics of the thoracolumbar region. Amer J Vet Res 2007; 68(5): 508-516.
3. Peterson DH, Bergmann TF. Principles of adjustive technique. In: Peterson DH, Bergmann TF, eds. Chiropractic technique, 2nd ed. St. Louis, MO: Mosby, 2002.
4. Townsend HG, Leach DH, Fretz PB. Kinematics of the equine thoracolumbar spine. Equine Vet J 1983; 15(2): 117-122.

Determination and Use of Mechanical Nociceptive Thresholds of the Thoracic Limb to Assess Pain Associated with Induced Osteoarthritis of the Middle Carpal Joint in Horses

Take Home Message
At baseline, a gradual increase in mechanical nociceptive thresholds (MNTs) was observed from proximal-to-distal sites within the thoracic limbs. From 2 to 6 weeks after surgery, the osteoarthritic limb had significantly reduced MNTs within the carpal region. Pressure algometry provides objective assessment of nociception of the thoracic limb; however, MNT values were poorly correlated with clinical variables used to assess osteoarthritis.

Introduction
Recognizing and managing musculoskeletal pain are important ethical and medical pursuits within the field of veterinary medicine. Unfortunately, the objective assessment of pain is difficult and often requires expensive and time-consuming kinematic and force plate analysis. Pressure algometry is a mechanical form of pain assessment that has been used in the diagnosis of musculoskeletal injuries and in the objective monitoring of the effectiveness of various pain management strategies in dogs, sheep, and horses.[1] Exercised research horses with surgically created osteochondral fragments (OCFs) of the middle carpal joint provide a means of inducing osteoarthritis.[2] In humans, MNT values are lower in patients with osteoarthritis of the knee joint, compared with age-matched controls. The purpose of the current study was to establish reference MNT values of the thoracic limb of clinically normal horses and to assess the ability of pressure algometry to detect pain associated with known articular disease produced in surgically induced osteoarthritis.

This project was completed by Drs. Kevin K. Haussler, Ashley E. Hill, David D. Frisbie, and C. Wayne McIlwraith and was published in the American Journal of Veterinary Research.[3]

Methods
Twenty-four horses were used to establish reference MNT values of the thoracic limbs. A pressure algometer with a 1-cm^2 rubber plunger tip and a calibrated range from 0 to 30 kg/cm^2 was used to establish reference MNT values at 17 anatomic locations within each thoracic limb (Figure 1). A separate non-blinded examiner subjectively graded (on a 0 to 5 scale) the overall willingness or tolerance of horses to stand quietly during the MNT measurements. As part of a concurrent study, all horses underwent bilateral arthroscopic surgery of the middle carpal joint to ensure no preexisting abnormalities. In 1 randomly selected middle carpal joint of each horse, an OCF was created on the distal aspect of the radial carpal bone to induce osteoarthritis. Beginning on day 3 and continuing weekly, MNT values were recorded for the control and osteoarthritic limbs and compared to determine whether pressure algometry was able to differentiate sites of pain (ie, osteoarthritic sites) from proximal or distal sites within the same or opposite limb. Lameness, carpal joint flexion, and joint effusion were also assessed weekly. Radiographs and gross pathology were evaluated at the end of the study. Correlations between MNT values and the clinical, radiographic, and necropsy scores were determined.

Results
A mean grade of 4.1 (out of 5) for tolerance to the procedure in both thoracic limbs was found for the initial baseline. At baseline, a gradual increase in mechanical nociceptive thresholds (MNTs) was observed from proximal-to-distal sites within the thoracic limbs (Figure 2). The mean range of 3 consecutive measurements across baselines was 2.0 ± 1.4 kg/cm^2. At baseline, no significant differences in MNT values were found between control and osteoarthritic limbs. On day 3, 2 of 10 (20%) sites had significantly higher MNT values within the osteoarthritic limb, compared with the control limb (Table 1). During weeks 1 to 4, 18% (3/17) to 42% (5/12) of sites had significantly lower MNT values within the osteoarthritic limbs, compared with the control limb. Sites within the carpal and distal por-

tion of the limb regions (ie, from the intermediate carpal bone to the suspensory ligament) had significantly lower MNT values within the osteoarthritic limb that persisted from weeks 2 to 5; indicating increased pain at the carpal and distal portion of the limb landmarks. From weeks 6 to 9, few significant differences in MNT values were found between control versus osteoarthritic limbs. Lameness, flexion test, and joint effusion scores all had significant increases within the osteoarthritic limb from week 2 to the end of the study. Radiographic and gross necropsy variables were also significantly increased within osteoarthritic joints, compared with control joints. In general, MNT values were poorly correlated with lameness, flexion tests, joint effusion, radiographic and necropsy scores.

Discussion

Tolerance to procedure scores were positively correlated with most overall pooled MNT values for each thoracic limb, which suggests a clinical relationship between observed pain behavior (as defined by the tolerance scores) and MNT values. Mechanical nociceptive thresholds were decreased significantly in the carpal region of limbs with osteoarthritis, compared with control limbs; however, MNT values were poorly correlated with clinical examination, radiographic findings, and necropsy scores. Poor correlation may have been caused by differences amongst the diagnostic methods being compared. The characterization and differentiation of joint pain is difficult and often requires a multimodal approach to diagnose and manage affected patients.4 Pressure algometry may prove to be an important adjunct to the traditional orthopedic or lameness examination. Further studies are needed to measure MNT values in naturally occurring osteoarthritis and in the treatment of other chronic musculoskeletal conditions.

References

1. Chambers JP, Waterman AE, Livingston A. Further development of equipment to measure nociceptive thresholds in large animals. J Vet Anaesthesia 1994; 21(2): 66-72.
2. Frisbie DD, Kawcak CE, Trotter GW, et al. Effects of triamcinolone acetonide on an in vivo equine osteochondral fragment exercise model. Equine Vet J 1997; 29(5): 349-359.
3. Haussler KK, Hill AE, Frisbie DD, et al. Determination and use of mechanical nociceptive thresholds of the thoracic limb to assess pain associated with induced osteoarthritis of the middle carpal joint in horses. Amer J Vet Res 2007; 68(11): 1167-1176.
4. Kidd BL, Photiou A, Inglis JJ. The role of inflammatory mediators on nociception and pain in arthritis. Novartis Found Symp 2004; 260: 122-133; discussion 133-128, 277-129.

Acknowledgement

Partial funding provided by the Equine Orthopaedic Research Center's Discretionary Funds, Colorado State University Foundation.

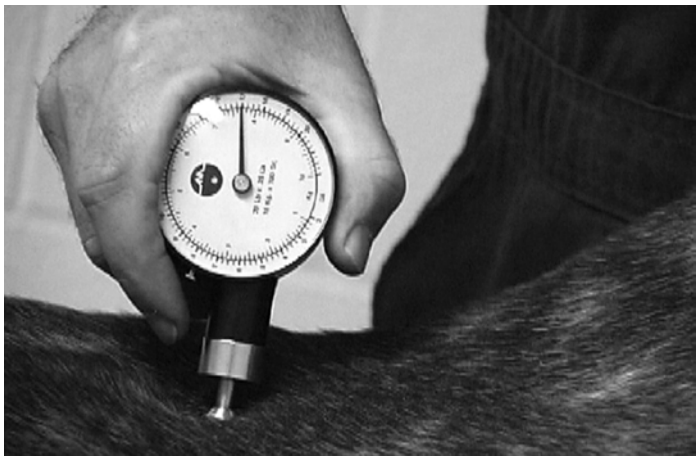


Figure 1. Photograph of a pressure algometer applied over the dorsal aspect of the right longissimus muscle at the base of the withers (i.e., T13 vertebral level).

Evaluation of Therapeutic MRI in our Equine Osteoarthritis model

A technique of therapeutic MRI has been developed in Germany and used in human osteoarthritis. This project took 16 horses with experimental OA and tested therapeutic MRI in 8 horses and with a sham therapy in the other 8 horses. This project is being funded by MBST. The goal of this study is to determine if there are any symptom- or disease-modifying effects of this treatment.

The Evaluation of Intra-articular Adequan and Intra-articular Hyaluronan (HA) in Experimental OA

We have previously evaluated intramuscular Adequan and also intravenous HA but never evaluated either intra-articular Adequan or intra-articular HA in our experimental chip fragment model. This project has 3 groups of horses comparing intra-articular Adequan to a second group of intra-articular HA to placebo control (intra-articular saline). This project is being funded by Luitpold Pharmaceuticals.

Evaluation of Polyglycan™ in Experimental Osteoarthritis

Polyglycan is a novel product consisting of HA, chondroitin sulfate and glucosamine produced by ArthoDynamics, inc. who funded this study. While this product is registered as a post-operative intraarticular device it has realized clinical use for the treatment of joint disease both through intraarticular and intravenous routes. There is little to no research to support either safety or efficacy via these routes. This project address the efficacy of this product through both intraarticular and intravenous routes, a safety study is planned for 2008.

Evaluation of tiludronate (Tildren™) in a model of equine osteoporosis

The goal of this study is to evaluate a bisphosphonate compound for treatment of bone and joint diseases in horses. Bisphosphonates are commonly used in humans to treat osteoporosis (bone loss), and the hope here is that it can do the same for horses. 16 horses each had a single forelimb placed into a cast (which significantly reduces bone density) and 8 of the horses were treated. Both symptom-and disease-modifying affects will be evaluated. This project is funded by CEVA.

Evaluation of the ability of ultrasonic examination compared to arthroscopy for evaluation of femorotibial joints

Ultrasonographers and surgeons are often frustrated by the disparity in the ultrasonographic findings of meniscal changes in the equine stifle compared to what is seen arthroscopically. The goal of this study is to delineate the boundaries of the meniscus that can be seen arthroscopically and translate these boundaries to the ultrasonographic image. This will allow the ultrasonographer and surgeon to better determine whether a lesion visualized ultrasonographically will be able to be seen and treated arthroscopically.

Current Research

Evaluation of contents of IRAP™

The ORC has performed a controlled study assessing the symptom and disease modifying effects of autologous conditioned serum (ACS) or IRAP (interleukin-1 receptor antagonist protein) as it is some times called. This work was published in American Journal of Veterinary Research in 2007 and did in fact show both symptom and disease modifying effects of this preparation. An important unanswered question with this product is the make up of the product i.e. what proteins are responsible for the beneficial effects. To date the preparation has been correctly referred to as a "soup". A current project at the ORC is analyzing this product using mass spectroscopy. This technique will enable researchers to identify the proteins that are up or down regulated.

Clinical Study with Bone Marrow Derived Stem Cells

This study being done by Drs. Kisiday and Frisbie in collaboration with clinicians at the ORC and VTH as well as outside veterinarians continues in evaluating the effects of intra-articular bone marrow derived stem cells in clinical cases of joint disease diagnosed arthroscopically.

Further Validation of the Equusys Sensor System

This is a continuing project involving Drs. Kawcak and Reiser working with Dr. Michael Davies of Equusys. The goal of this project is to validate the wireless system and to develop a user-friendly interface so that this can be used in the clinic to aid in lameness diagnosis and monitoring. The hope is to also use it to monitor racehorses during training.

Abnormal Joint Congruency and Potential Role in Fractures

This is DVM/PhD student Katrina Easton's project working with Drs. Kawcak, Puttlitz and McIlwraith and funded by the Grayson-Jockey Club Reasearch Foundation. The goal of this project is to determine the influence of joint geometry on the incidence of condylar fracture in the fetlock joints of racehorses. The data from this project will then be inputted into a computer modeling program to calculate how differences in shape of the joint may influence the forces across the joint surface.

Evaluation of the Physiologic and Biomechanical Effects of Underwater Treadmill Exercise on Experimental Osteoarthritis in Horses

The goal of this study is to evaluate the physiologic and biomechanical effects of underwater treadmill exercise on reducing the development of carpal osteoarthritis. Following aquatic rehabilitation, human patients have demonstrated improvements in joint stability, joint range of motion, and lower extremity strength. Underwater treadmill exercise has the potential to provide similar beneficial effects in horses. Sixteen horses will have an osteochondral fragment created in one randomly-selected radial carpal bone and then be assigned to a treatment or control group. Biomechanical and neurological measures of musculoskeletal dysfunction will be evaluated. This project is not yet funded; however grants have been submitted.

Evaluation of Muscle Activation and Compensatory Gait Patterns Associated with Cranial Cruciate Ligament Rupture in Dogs

The goal of this study is to evaluate patterns of muscle activation and compensatory gait associated with cranial cruciate injuries in dogs. Cranial cruciate ligament rupture is the most common orthopedic condition producing lameness in dogs. Numerous surgical techniques have been developed to attempt dynamic stabilization of the stifle, despite a poor understanding of adjacent muscle activation timing or duration and compensatory gait patterns. Eight dogs will be evaluated before and after induced cranial cruciate ligament rupture to assess changes in muscle function. This project is not yet funded; however, grants have been submitted to Morris Animal Foundation, American College of Veterinary Surgeons' Diplomate Clinical Research Program and American Physical Therapy Association, Orthopaedic Section, Clinical Research Grant Program.

Global Equine Research Alliance Study - Effect of Early Exercise on Osteochondral Tissue

Drs. Chris Kawcak and Wayne McIlwraith continue to investigate the material from the Global Equine Research Alliance Study. Serum and synovial fluid biomarkers have been taken over the entire three years of the study. The first 18 months of samples has been analyzed in the Orthopaedic Research Laboratory. Problems with shipping samples have delayed the last analysis but it will hopefully be done before the end of 2006. This overall GERA project has been funded by the Marilyn Simpson Trust.

Also in collaboration with Dr. Neil Broom in New Zealand and with funding support from Grayson-Jockey Club Research Foundation and the Marilyn Simpson Trust, biomechanical changes are being evaluated in samples from conditioned versus non-conditioned horses.

Evaluation of Cellular Changes at Different Levels of Non-Calcified and Calcified Cartilage with Exercise

This project is nearing completion. It is Dr. Katja Duesterdieck's PhD project. Using a new technique, laser capture microscopy, Katja has looked at the cells of cartilage and of non-calcified and calcified cartilage. The last part of the project is doing microarray analysis of the RNA extracted from individual cells. It is hoped that early expression changes can be detected in this tissue. Using these novel techniques, we will be looking at differential gene expression with both aging and exercise.

Evaluation of the effect of BioniCare® electrical stimulation unit in enhancing the quality and quantity of cartilage repair after microfracture.

We have previously shown that subchondral microfracture in full thickness articular cartilage defects significantly enhances the amount of repair tissue in defects on the medial femoral condyle. This project addresses whether adjunctive electrostimulation can further improve the quality of repair in full thickness defects on the medial femoral condyle. Defects are made in the same position and microfractured in the same fashion as previously. After creation of defects, electrostimulation units are being applied to the stifle joint. The results of this treatment will be assessed at four months. This project is funded by BioniCare through the Steadman-Hawkins Sports Medicine Foundation.

Current Research

Equine Articular Cartilage Repair Using Composite Chondrocyte Wafers and Allogeneic Cartilage Transplants

This project is led by Dr. David Frisbie and is assessing two different potential methods of articular cartilage repair. The first project uses multilayers of chondrocytes on a wafer fixed into defects with three different fixation techniques. The second project involves pieces of allogeneic cartilage (cartilage taken from another animal) repairing full thickness defects and assessing if good integration without immune reactions can be obtained. This project is funded by Isto Technologies.

Racetrack Surface Management

This is a continuation of the on-going work by Dr. Mick Peterson, of the University of Maine, working with Drs. Raoul Reiser and Wayne McIlwraith. As already outlined previously, technologies have been developed by Dr. Peterson to both assess the shear and compressive properties of the surface of the racetracks, as well as the angle and potential irregularities in the base (the latter using Doppler radar). Work is now being done to "validate" racetracks and assess problems within racetracks. The technology is now being used at the request of racetracks to assess the surface quality, find solutions if epidemiologic data suggest an unacceptable rate of injury, as well as assess the new synthetic racetracks that are available and are being placed in various locations. It is hoped that within the next year, these objective assessment techniques can be extended to evaluating indoor arenas such as used for cutting. This project is funded by various participating racetrack authorities and we have just received funding from the Grayson-Jockey Club Research Foundation.

Comparison of a 1% Diclofenac Sodium Topical Cream (Surpass®) With Phenylbutazone and Placebo in Our Equine Osteoarthritis Model

Surpass is a licensed topical NSAID product. The potential value of a topical NSAID is that it obviates the potential side effects of systemic administration and focuses on the problem area. In this study by Drs. David Frisbie, Wayne McIlwraith, Chris Kawcak and Natasha Werpy, the use of topical cream will be assessed in carpal osteoarthritis compared to phenylbutazone and placebo. In addition to previously used outcome parameters such as lameness examinations and other clinical parameters, as well as synovial fluid and synovial membrane and articular cartilage assessment, this project is utilizing MRI to assess the state of the fibrous joint capsule and synovial membrane and detect subtle changes in inflammation in these tissues that the topical cream is getting access to. This project is being funded by IDEXX.

Self-Assembling Peptides for Tissue Engineering Approach to Cartilage Repair

This project is part of a program grant being done by Drs. David Frisbie, John Kisiday and Wayne McIlwraith in collaboration with Dr. Alan Grodzinsky of MIT. Tissue engineered cartilage has been developed and tested in vitro to evaluate its biomechanical capabilities. Work is now ongoing testing this in vivo in rabbits and after this studies are planned in the horse. Funded by NIH Program Grant HHS-HIH.

Evaluation of Presale Radiographs in Cutting Horses

This study is being done by graduate student, Erin Contino, working with Drs. Wayne McIlwraith, Richard Park and Chris Kawcak. In 2005, the National Cutting Horse Association (NCHA) started a radiograph repository at the NCHA Futurity Sales similar to what has been done for a number of years for Thoroughbreds at Keeneland. The first part of the study involves assessing the incidence of radiographic changes and the second part assesses the significance of these changes with subsequent performance and soundness. Ms. Erin Contino has completed radiographic reading and follow-up for these horses (we need to go out 3 years) with Dr. Myra Barrett who is doing an MS as part of this project. Supported with proceeds from the Equine Orthopaedic Research Center's Annual Stallion Auction.

Colorado State University

College of Veterinary Medicine and Biomedical Sciences

College of Veterinary Medicine
and Biomedical Sciences

Orthopaedic Research Center
Fort Collins, CO 80523-1678