ORTHOPAEDIC RESEARCH CENTER

2015 REPORT

Colorado State University

MISSION

TO INVESTIGATE THE PATHOGENESIS, DIAGNOSIS, TREATMENT, AND PREVENTION OF MUSCULOSKELETAL DISEASE AND INJURY FOR THE BETTERMENT OF BOTH ANIMALS AND HUMANS.

PREFACE

"Our principal focus continues to be solving the significant problems in equine musculoskeletal disease"

It is my pleasure again to present our 2015 report from the Musculoskeletal Research Program which includes the Orthopaedic Research Center (including the Orthopaedic Bioengineering Research Laboratory), as well as, the Preclinical Surgical Research Laboratory and Orthopaedic Oncology 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 also continue to investigate questions relevant to human joint disease and techniques and devices for human osteoarthritis and articular cartilage repair when the technique can potentially benefit the horse. The increased number of translational projects and funding support from the National Institute of Health (NIH) and human orientated industry partners support our mission of helping both horses and humans.

As part of that evolution the big news for 2015 was answering the matching challenge from John and Leslie Malone to achieve full funding for the Institute of Biologic Translational Therapies (IBTT) building. As presented in the 2014 report, we received a matching challenge of half the cost of the IBTT building with a $10 million commitment from Colorado State University President Dr. Tony Frank and $20 million from another donor who, at the moment, wishes to remain anonymous but identity to be disclosed after some other estate planning issues are settled. The donor of the $20 million has been a long term client of mine and has already donated considerably to our Orthopaedic Research Program. With the last $5 million coming from other sources, we now have the $65 million to start building.

As mentioned in an earlier report, the vision of the IBTT is to investigate next generation remedies based on living cells and their products including patient-derived stem cells to treat musculoskeletal disease and other ailments and to literally be able to carry basic science discoveries in the Institute all the way to bedside with entrepreneurial and regulatory abilities within the IBTT. At the ORC we have developed expertise at analyzing and developing medical treatments for animal patients, then providing knowledge gained to boost human medical advancements. This progression is known as translational medicine and is successful because of similarities in animal and human physiology and disease. Our being able to raise the funding for the IBTT building in a two and one half year period is truly transformational for our Orthopaedic Research Program, will take us to a higher level but is also an endorsement of what we have achieved already.

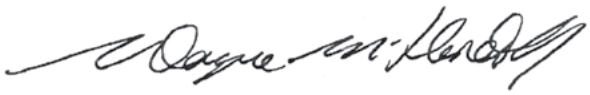
Another initiative that we hope to be a critical step forward for diagnosing early musculoskeletal disease and prevention of more severe injuries has been additional funding from the Louis L. Borick Foundation through Robert Borick. Last year we mentioned how their funding had allowed us to

purchase and house the first standing equine computed tomographic unit (CT) to be installed in the US and with a further gift we now have the funding required to partner with a private company and develop a CT that will image the standing limb (the earlier unit has a circular ring which will only allow standing imaging of the head and neck). The total gifts of the Louis L. Borick Foundation in the past three years ($750,000) has allowed us to independently pursue the evolution of this cutting edge technology.

We have continued to have new developments in the faculty and staff. Dr. Josh Donnell graduated from the residency program July 1, 2015 and passed the examination in January 2016 to become a Diplomate of the American College of Veterinary Sports Medicine and Rehabilitation. Dr. Donnell was our third graduate of our Equine Sports Medicine and Rehabilitation Program and each resident has successfully passed the examination. Josh's residency was funded by the Ranches of Cherry Creek in honor of Don Ulmer as well as a collaboration with Equine Sports Medicine, LLC in Pilot Point, Texas. Dr. Erin Contino is now an Assistant Professor in the Equine Sports Medicine and Rehabilitation Program. Jen Suddreth, our research trials coordinator/barn manager, as well as, Chrissy Battaglia, our research scientist/lab manager have continued to make critical contributions.

Other accomplishments at the ORC over the past year are detailed in this report. This is the second single year report because of the amount of information we have. As stated previously, our accomplishments in this report could not be achieved without our team of faculty and staff as well as the excellent support of equine funding agencies (Grayson-Jockey Club Research Foundation, American Quarter Horse Association and United States Equestrian Federation), corporation funding, NIH funding and individual donors. With this help we continue to achieve our goals and also the new ones of IBTT are particularly exciting.

Best wishes,



Wayne McIlwraith

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continued...

FOCUS 5
VALIDATION OF REHABILITATION AND PHYSICAL THERAPY TECHNIQUES FOR MUSCULOSKELETAL DISEASE

RESEARCH FOCUSES OF THE ORTHOPAEDIC RESEARCH CENTER

Including the Orthopaedic Bioengineering Research Laboratory

MUSCULOSKELETAL TISSUE HEALING

This focus addresses articular cartilage, tendon, ligament, and menisci healing.

EARLY DIAGNOSIS OF MUSCULOSKELETAL DISEASE

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

a. Evaluation of the pathogenesis of bone and joint disease

b. Early detection of disease processes

c. Monitoring of therapy, with the long-term goal of preventing severe arthritis or failure

IMPROVEMENT IN THE UNDERSTANDING OF THE PATHOGENESIS OF EXERCISE-INDUCED AND DEVELOPMENTAL MUSCULOSKELETAL DISEASE (INCLUDING NEW MODELS)

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

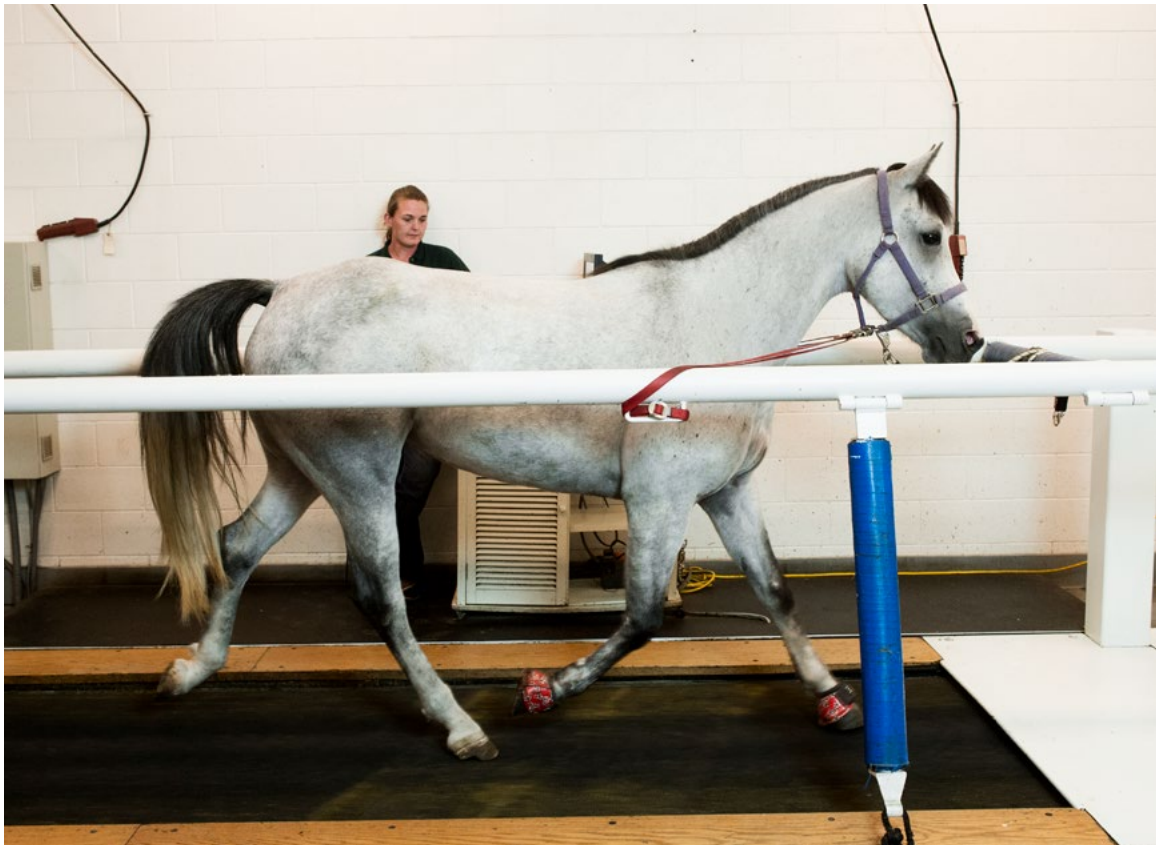
CONTINUED DEVELOPMENT OF NOVEL THERAPIES FOR TRAUMATIC SYNOVITIS, CAPSULITIS, AND OSTEOARTHRITIS

This focus includes evaluation of biologic inhibitors of critical mediators in joint disease, novel protein therapies, including platelet-rich plasma (PRP), gene therapy techniques, and mesenchymal stem cell therapies.

VALIDATION OF REHABILITATION AND PHYSICAL THERAPY TECHNIQUES FOR MUSCULOSKELETAL DISEASE

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

MUSCULOSKELETAL RESEARCH PROGRAM



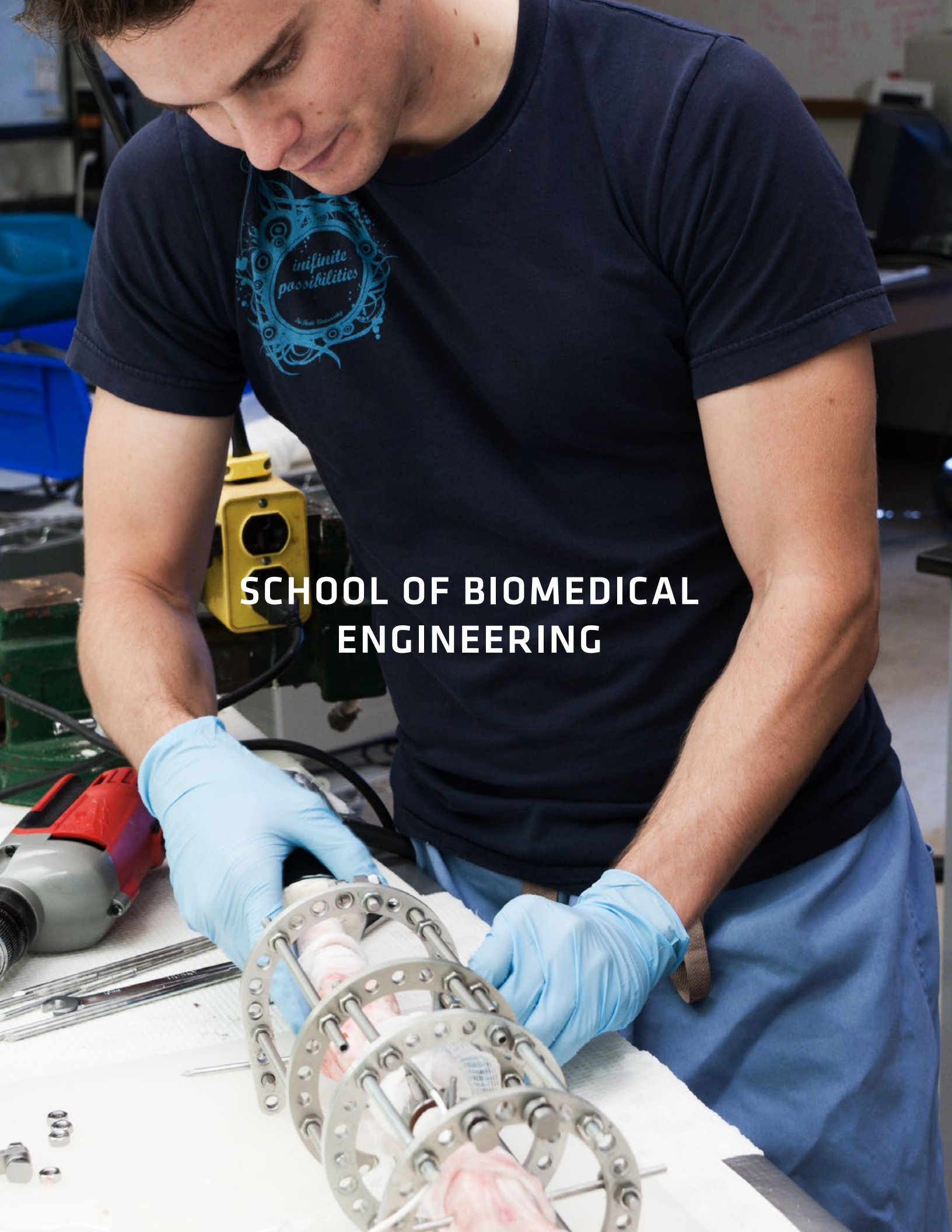
The Musculoskeletal Research Program has been designated as a Program of Research and Scholarly Excellence at Colorado State University (initially designated in 2004, renewed in 2008, 2012, and again in 2014).

THE MUSCULOSKELETAL RESEARCH PROGRAM COVERS ALL ORTHOPAEDIC RESEARCH AT COLORADO STATE UNIVERSITY AND INCLUDES:

1. Orthopaedic Research Center, including Orthopaedic Bioengineering Research Laboratory

2. Preclinical Surgical Research Laboratory

3. Orthopaedic Oncology



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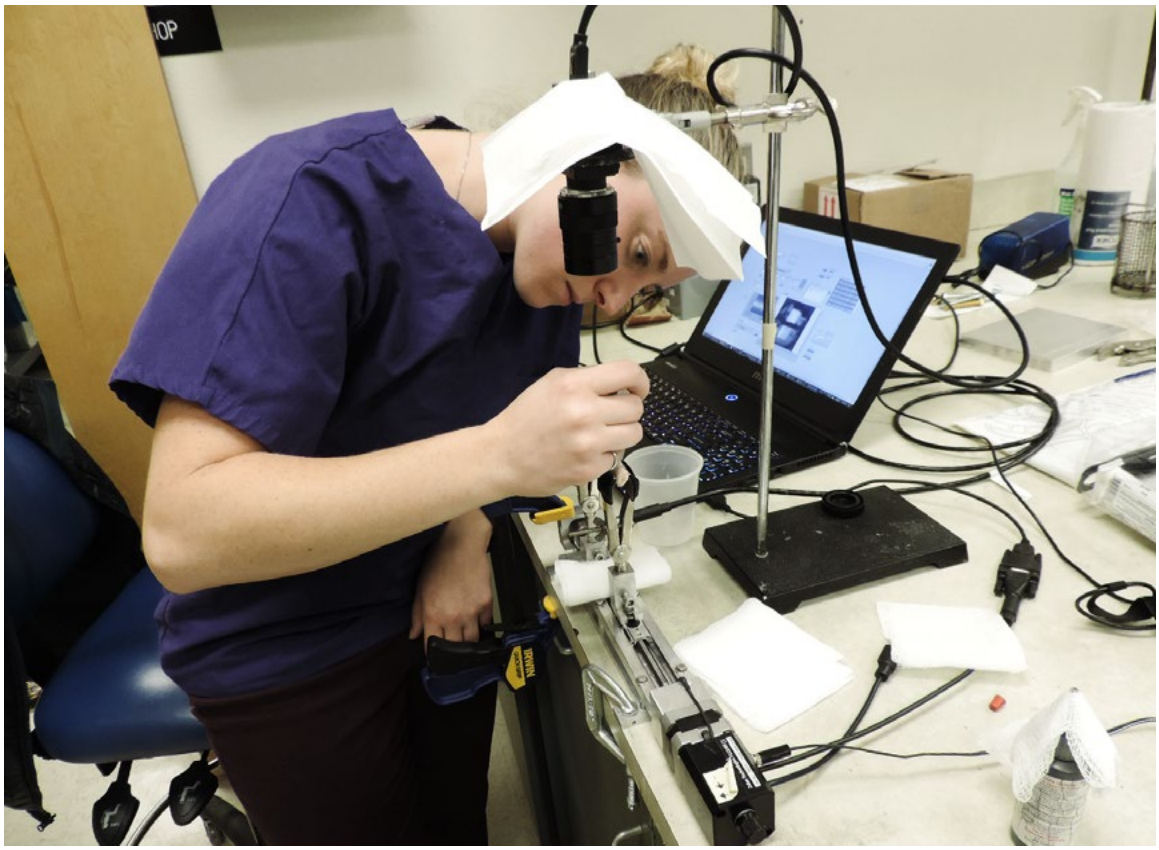

Most of the faculty within the Musculoskeletal Research Program are also faculty in the School of Biomedical Engineering. Colorado State University's School of Biomedical Engineering (SBME) was formed in March 2007 to address society's needs in bioengineering, one of the fastest emerging areas of scientific 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. Drs. Christian Puttlitz, Tammy Donahue, Wayne McIlwraith, David Frisbie, Chris Kawcak, Seth Donahue, Laurie Goodrich, Kevin Haussler and John Kisiday of the Orthopaedic Research Center are core faculty members of the program in biomedical engineering research, which is rapidly expanding to all areas of human health. New technologies being developed at CSU are enabling people to continue active and healthy lifestyles. SBME students have the opportunity to collaborate with faculty from these four colleges and eleven departments, including the highly ranked Professional Veterinary Medicine program.

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

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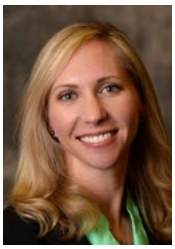
C. Wayne McIlwraith

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

Research Interests: Equine orthopaedic surgery and joint disease (arthritis), musculoskeletal biomarkers, cartilage repair and novel biologic treatments including stem cells

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 also through his fundraising efforts. He is a Diplomate of the American College of Veterinary Surgeons and the American College of Veterinary Sports Medicine & Rehabilitation; a Past-President of the American College of Veterinary Surgeons, the American Association of Equine Practitioners, and the Veterinary Orthopedic Society; and a recognized leader in the field of equine orthopaedic research and surgery. He consults worldwide as a specialist equine surgeon, and has received national and international honors for his contributions to joint research and clinical orthopaedics. Dr. McIlwraith is the co-author of five textbooks: Techniques in Large Animal Surgery (two editions): Equine Surgery: Advanced Techniques (two editions); Arthroscopic Surgery in the Horse (four editions); Joint Disease in the Horse (second edition just published); and Equine Welfare. He has authored or co-authored over 445 refereed publications and textbook chapters, and has presented more than 600 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, 2001; D.Sc. (hc), Massey University, 2003, Laurea Dr. (hc), Turin University 2004; Inducted into UK Equine Research Hall of Fame 2005; Frank Milne Lecturer (Lifetime Contribution Award), AAEP 2005; Founders Award for Lifetime Achievement, ACVS, 2006; Elastikon Equine Research Award, Johnson & Johnson and Grayson-Jockey Club Research Foundation, 2008-2009; Colorado State University Scholarship Impact Award 2007, University Distinguished Professor, Colorado State University 2009; Distinguished Life Member, AAEP, 2009; Dr. vet. med. (honoris causa), Royal Veterinary College, University of London, 2010; Life Member, New Zealand Equine Veterinary Association, 2011; Jacob Markowitz Award, Academy of Surgical Research, 2013; Marshall R. Urist M.D. Award for Excellence in Tissue Regeneration Research, Orthopaedic Research Society, 2014; American Association Equine Practitioners Distinguished Service Award, 2014.



Myra Barrett

D.V.M., M.S., Diplomate ACVR, Assistant Professor of Radiology,
Department of Environmental & Radiological Health Sciences

Research Interests: Equine musculoskeletal imaging and comparative imaging

Dr. Barrett earned her D.V.M. from Colorado State University. After graduating, she completed a year-long internship at Oakridge Equine Hospital in Edmond, Okla. Dr. Barrett underwent a non-conforming radiology residency in order to particularly focus on equine diagnostic imaging. The residency was based at CSU, but included training with multiple equine imaging experts in the U.S. and internationally. At the same time, Dr. Barrett obtained a master's degree through the ORC. She remained at CSU and is currently an assistant professor of radiology. Dr. Barrett works closely with the Equine Surgery and Sports Medicine services. She has spoken at multiple large national meetings and is regularly involved in continuing education courses. Dr. Barrett is dedicated to the advancement of the specialty of equine diagnostic imaging and is currently the president-elect of the Large Animal Diagnostic Imaging Society, a subgroup of the American College of Veterinary Radiology.

Erin Contino

D.V.M., M.S., Diplomate ACVSMR, Assistant Professor, Department of Clinical Sciences

Research Interests: Equine musculoskeletal imaging, diagnostic analgesia, lameness

Dr. Contino joined our faculty as an Equine Fellow in Imaging in 2014 and was promoted to Assistant Professor in the Equine Sports Medicine and Rehabilitation Program in 2015. Erin is a Colorado State University D.V.M. graduate, who after interning at Pioneer Equine Hospital, did a three year Sports Medicine and Rehabilitation Residency at CSU (completed June 30, 2014) and then passed the examination to become a Diplomate of the American College of Veterinary Sports Medicine and Rehabilitation in August 2014. Before and during her time as a D.V.M. student she also completed an M.S. degree at the Orthopaedic Research Center.

Nicole Ehrhart

D.V.M., M.S., Diplomate ACVS, Professor, Ross M. Wilkins, M.D. Limb Preservation University Chair in Musculoskeletal Oncology and Biology; Department of Clinical Sciences

Research Interests: Stem cell therapy, tissue engineering, guided bone regeneration, allograft healing, limb preservation, bone substitutes

Dr. Ehrhart is one of 30 fellowship-trained veterinary surgical oncologists in the world. She is a full 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 Laboratory of Comparative Musculoskeletal Oncology and Traumatology and has been actively involved in limb preservation research, regenerative medicine, tissue engineering, and sarcoma research for the last sixteen years. She has been an invited speaker at various venues for MD researchers in translational research, both nationally and internationally. She holds joint faculty positions in the School of Biomedical Engineering, the Cell and Molecular Biology program, the Gates Regenerative Medicine Center at the University of Colorado, and The University of Colorado Cancer Center. In addition to her research, she has held several prestigious positions in the American College of Veterinary Surgeons (Scientific Program Chair, Residents Forum Chair, and Examination Committee) and Veterinary Orthopedic Society (President). She has authored numerous publications on limb preservation and translational cancer research. She is currently the director of the Musculoskeletal Oncology section of the University-wide Cancer Supercluster.

David D. Frisbie

D.V.M., M.S., Ph.D., Diplomate ACVS, Diplomate ACVSMR, Professor, Department of Clinical Sciences

Research Interests: Treatment and diagnosis of joint disease, biologic treatment of musculoskeletal injuries, gene therapy

Dr. Frisbie began his professional career after obtaining both a B.S. in biochemistry and a D.V.M. from the University of Wisconsin. He then went to New York, where he completed a Surgical Internship at Cornell University and began his research in joint disease. After completing his internship, Dr. Frisbie came to CSU, where he continued his joint research, completed a surgical residency in Large Animal Surgery, and obtained a master's degree in joint pathobiology. After completion of his residency, Dr. Frisbie began his work on a novel way to treat joint disease using gene therapy, which was the focus of his Ph.D. During work on his Ph.D., Dr. Frisbie became board certified in Large Animal Surgery and is a Diplomate of the American College of Veterinary Surgeons. He joined the faculty as an assistant professor in Equine Surgery in the Department of Clinical Sciences in 1999, was promoted to associate professor (with tenure) in 2007, and then to professor in 2013. He is also a Diplomate of the American College of Veterinary Sports Medicine and Rehabilitation. His current joint disease research is in two basic fields: 1) treatment of joint disease (therapeutics he has evaluated include Adequan®; corticosteroids, such as Vetalog® and Depo-Medrol®; Orthokine® (IRAP®); and stem cells), and new methods of diagnosing joint disease, such as standing arthroscopy of the equine stifle; and 2) biologic methods for treating musculoskeletal injuries, including tendon and ligaments, as well as joints. This research focus has blossomed into the testing of multiple biologic agents, allowing for side-by-side comparisons, as well as pioneering novel techniques for treating joint, tendon, and ligamentous injuries.

Honors include: Pfizer Animal Health Award for Research Excellence, 2001; American Association Equine Practitioners Presidential Award, 2011.

Laurie Goodrich

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

Research Interests: Gene therapy, stem cell therapy

Dr. Laurie Goodrich joined the faculty at CSU College of Veterinary Medicine in April of 2005 as an assistant professor in Equine Surgery and Lameness. Prior to joining the faculty, she obtained her D.V.M. from the University of Illinois, and completed an internship in Large Animal Surgery and Medicine at Virginia-Maryland Regional College of Veterinary Medicine. Following her internship, Dr. Goodrich joined the faculty at Virginia for one year as an equine ambulatory clinician before going on to complete her residency in Equine Surgery at the Equine Medical Center in Leesburg, Va. She also obtained a Master of Science in Pharmacology during her residency. Dr. Goodrich subsequently joined the large animal surgery faculty at Cornell University's College of Veterinary Medicine and became Board Certified in Large Animal Surgery in 1999. At Cornell, she rotated as Chief-of-Service for the Orthopedic, Soft Tissue, and Emergency Surgery Services. In 2000, she began a Ph.D. in Cartilage Repair and Gene Therapy. Her research included the transplantation of genetically modified chondrocytes (cells of cartilage) into the defects of cartilage to improve cartilage healing. She completed her Ph.D. in the fall of 2004. Since commencing her position at CSU, Dr. Goodrich has focused on gene therapy and regenerative medicine for musculoskeletal disease in joint and bone repair. Specifically, her main focuses have included using IGF-I, IL-1ra, and BMP gene therapy to enhance cartilage repair, reduce inflammation in osteoarthritis, and improve bone repair, respectively. Further, she has investigated stem cell therapy applications for enhancement of cartilage repair. She is now an associate professor in equine surgery and lameness. Dr. Goodrich's clinical interests are broad and include joint disease, lameness, arthroscopy, fracture repair, laparoscopy, wound healing, neoplasia, and pain management.

Honors include: Orthopaedic Research Society, New Investigator Research Award, Semi-Finalist, 2006; Recipient five-year NIH KO8 Training Grant, 2008-2013; Clinician of the Year Award for Teaching Excellence, 2011; Elastikon Equine Research Award, 2011.

Kevin K. Haussler

D.V.M., D.C., Ph.D., Diplomate ACVSMR, Associate 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 B.S. 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. 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 associate professor with continued research interests in objective assessment of musculoskeletal pain and spinal dysfunction, and evaluation of rehabilitation approaches to both large and small animals.

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

Christopher E. Kawcak

D.V.M., Ph.D., Diplomate ACVS & ACVSMR, Professor, Iron Rose University Chair in Musculoskeletal Research, Department of Clinical Sciences

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

Dr. Kawcak joined our faculty in 1998 as an Assistant Professor after completing his Ph.D. He is now a Professor in the Iron Rose Ranch Chair in the ORC, and is Director of Equine Clinical Services in the James L. Voss Veterinary Teaching Hospital. His collaborations with the Biomedical Engineering Program at CSU, the Southwest Research Institute in San Antonio, Texas, The I-STAR Laboratory at Johns Hopkins University, 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 the effects of exercise on the incidence of musculoskeletal injury, the development of computerized models of joints and joint diseases, and development of a new standing computed tomography machine for 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, the American College of Veterinary Surgeons, and the American College of Veterinary Sports Medicine and Rehabilitation.

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

Dr. Melissa King

D.V.M., Ph.D., Diplomate ACVSMR, Assistant Professor, Department of Clinical Sciences; Lead Clinician, Equine Sports Medicine and Rehabilitation Service

Research Interests: Equine sports medicine and rehabilitation

Dr. Melissa King received her D.V.M. from CSU in 1997 and then completed an internship at Rood & Riddle Equine Hospital in Lexington, Ky. Upon completion of her internship, Dr. King returned to northern Colorado to begin her career as an equine ambulatory clinician focusing on equine sports medicine. In 2011, Dr. King completed a Ph.D. at the ORC assessing the efficacy of underwater treadmill exercise to diminish the progression of carpal osteoarthritis. Currently, Dr. King is an assistant professor and the lead clinician for the Equine Sports Medicine and Rehabilitation Service at CSU. Dr. King is actively involved in clinical research to advance the quality and effectiveness of rehabilitation for the equine athlete.

John Kisiday

Ph.D., Associate Professor, Department of Clinical Sciences

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

Dr. John Kisiday was hired as an assistant professor in Clinical Sciences in a research and teaching appointment at the ORC in January 2005 after doing his Ph.D. at MIT in bioengineering, and a collaborative post-doctorate of fellowship with CSU and MIT. He is now an associate professor in Clinical Sciences. Dr. Kisiday is currently involved with research projects evaluating the potential of bone marrow mesenchymal stem cells to heal orthopaedic injuries, with an emphasis on cartilage repair. He has collaborated with ORC faculty to bring autologous mesenchymal stem cell treatments to the clinic. In the laboratory, he is investigating factors that influence mesenchymal stem cell differentiation with the goal of increasing the effectiveness of clinical treatments.

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

Valerie Moorman

D.V.M., Ph.D., Diplomate ACVS, Assistant Professor, Equine Surgery and Lameness

Research Interests: Early detection of musculoskeletal injury and methods of quantitative lameness detection

Valerie Moorman graduated from North Carolina State University with a B.S. in Animal Science in 2000. She graduated from North Carolina State University College of Veterinary Medicine in 2004. She then completed an internship in large animal medicine and surgery at Auburn University in June 2005 and continued as a large animal ambulatory clinical instructor through June 2006. She then completed a combined equine surgery residency and master's program at Oklahoma State University in July 2009. She became a Diplomate of the American College of Veterinary Surgeons in March 2010, and in July 2009, she began a Ph.D. program at the Orthopaedic Research Center at CSU, where she worked to develop a hoof-mounted motion analysis system. From July 2009 until June 2012, she also provided after-hours surgical emergency coverage at the CSU James L. Voss Veterinary Teaching Hospital. From July 2012 until July 2013, she served as staff veterinarian at the ORC. In July 2013, she was named an Assistant Professor of Equine Surgery and Lameness in the Department of Clinical Sciences at Colorado State University.

Richard Slayden

Ph.D., Associate Professor of Microbiology, Executive Director and founding member of the Center for Environmental Medicine at CSU

Dr. Slayden has 14 years of drug discovery and genomics experience with bacterial pathogens (F. tularensis, Burkholderia pseudomallei, Y. pestis, M. tuberculosis) and mouse models of infection. In the last several years, Dr. Slayden has employed Next Generation Sequencing techniques and metagenomics strategies to perform systems-based transcriptional studies to investigate molecular marks and metabolic tendencies of complex biological systems, including animal models of infection. During this time, Dr. Slayden has formed multi-disciplinary collaborations in the areas of microbiology, infectious disease, mathematics, and computational modeling to study host-pathogen interactions. Using this approach, Dr. Slayden has successfully characterized the host response to different infections and the unique in vivo transcriptional patterns and metabolism of bacterial pathogens.

Dr. Melinda Story

DVM, Diplomate ACVS, Assistant Professor, Department of Clinical Sciences

Research Interests: Assessment and treatment of spinal dysfunction and pain; clinical research interest in the areas of acupuncture and chiropractic therapy

Dr. Melinda Story is a native of Colorado and joined CSU's Equine Sports Medicine team in 2013. She earned her B.S. in microbiology from CSU, and following a year at Texas A&M University in biomedical research, Dr. Story returned to CSU to obtain her D.V.M. in 1999. She completed an internship at Rood and Riddle Equine Hospital in Lexington, Ky., and then moved to Kansas and completed her residency training program in large animal surgery at Kansas State University. Following her residency, Dr. Story spent a year as a clinical instructor at the KSU veterinary teaching hospital. She became a diplomate of the American College of Veterinary Surgeons in 2004. She and her family returned to Colorado in July 2004 when she joined the staff at Littleton Equine Medical Center with interests in surgery and sport horse lameness. In 2006, Dr. Story became certified in Veterinary Medical Acupuncture, and in 2011 she became certified by the International Veterinary Chiropractic Association.

Seth W. Donahue

Ph.D., Associate Professor, Department of Mechanical Engineering

Research Interests: Naturally occurring models of bone metabolism and mechanical adaptation in extreme environments, and bone regeneration for metabolic diseases, fracture, and large bone defects

Dr. Donahue's research interest is the role of mechanical forces in bone cell metabolism, tissue engineering, bone adaptation, bone fracture, and osteoporosis. He has established hibernating bears as a model for preventing immobilization-induced osteoporosis. He has published 46 peer-reviewed journal manuscripts and conference abstracts on his hibernating bear research and its translational potential. He won the American Society of Biomechanic's Post-Doctoral Young Investigator Award for his research on bears. Dr. Donahue's laboratory cloned the gene for black bear parathyroid hormone, obtained a U.S. patent on it, and uses the recombinantly produced protein to reverse osteoporosis, improve fracture healing, and repair large bone defects in animal models.

Raoul F. Reiser, II

Ph.D., Associate Professor, Department of Health & Exercise Science

Research Interest: Musculoskeletal biomechanics

Dr. Reiser completed his B.S. in mechanical engineering at Cornell University, his M.A. in kinesiology with a specialization in biomechanics at the University of Texas at Austin, and his Ph.D. in mechanical engineering at CSU. The emphasis of his dissertation was the biomechanics of recumbent 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, and was promoted to associate professor with tenure in 2008. His current research is mainly in the area of fall prevention in the elderly, understanding how muscle and tendons change as we age. He also continues to explore bilateral asymmetries of the low extremities and how they may relate to performance and potential injury risk.

Honors include: Elected Fellow, American College of Sports Medicine, 2007; CSU College of Engineering's Outstanding Research Assistant, 2000; GAANN Three-Year Fellowship, 1997; CSU Graduate Fellowship, 1997; NSCA Challenge Scholarship, 1996.

Susan P. James

Ph.D., Professor and Head, Department of Mechanical Engineering; Professor, School of Biomedical Engineering

Research Interests: Biomaterials for orthopaedic, cardiovascular, and ocular applications, including permanent implants and tissue engineering

Dr. Susan James joined the CSU Mechanical Engineering faculty in 1994 as an assistant professor. She is now the Head of Mechanical Engineering Department at CSU, and was the founding director of the School of Biomedical Engineering. She received her Ph.D. in polymers from MIT and her B.S. in metallurgical engineering and materials science from Carnegie Mellon. Professor James' research focuses on characterization and development of biomaterial solutions to health care problems. These include orthopaedic, cardiovascular, and ocular applications, as well as regenerative medicine and tissue engineering. She and her students invented the BioPoly® materials, now in clinical use in partial resurfacing knee implants (http://www.biopolyortho.com/). Much of her current work is on hyaluronan-enhanced plastics, which do not cause blood clotting and platelet activation like most synthetic plastics. In collaboration with several faculty, students, and researchers, she is working on developing hyaluronan-enhanced flexible leaflets for heart valve prostheses. Her group is also researching new materials for small diameter vascular grafts, and contact and intraocular lenses. Dr. James is committed to giving back and has been involved with many organizations over the years, including Africa Higher Education Partnerships (AAHEP), Women and Minorities in Engineering Program (WMEP), and SWE. She has also performed countless outreach programs for young girls to get them interested in engineering careers. Dr. James was awarded the prestigious Margaret Hazaleus award this year for her strong commitment to mentoring and helping women

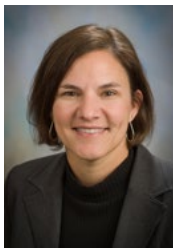
Christian Puttlitz

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

Research Interests: Orthopaedic biomechanics, tissue and biomaterials interactions

Dr. Puttlitz and his team have global interests in how engineering mechanics can be applied towards solving orthopaedic-related problems, including both experimental and computational modeling to better understand the underlying tissue-level mechanobiology. Dr. Puttlitz and his colleagues have leveraged well-known orthopaedic hardware systems to functionally isolate the ovine metatarsus to develop a Haversian bone model of microgravity. The model will be used to simulate the fracture healing cascade that is expected to occur during deep space flight. In addition, the model will be used as an evaluation platform for emerging technologies that seek to enhance fracture healing in microgravity environments. These experiments are complemented by a computational effort that merges musculoskeletal and finite element models of the ovine hindlimb in an attempt to span numerous length scales and relate the observed biological response to the localized (i.e., tissue-level) mechanics. Dr. Puttlitz received his B.S. in material science and engineering mechanics from Michigan State University, his M.S. in bioengineering from Clemson University, and his Ph.D. in biomedical engineering from the University of Iowa. Dr. Puttlitz became a Postdoctoral Fellow in the Orthopaedic Bioengineering Research Laboratory at the University of California, San Francisco. He joined the Department of Orthopaedic Surgery faculty at UCSF as an assistant professor in 2001, and directed the Orthopaedic Biomechanics Laboratory at the San Francisco General Hospital. In 2005, he accepted a faculty position at CSU in the Department of Mechanical Engineering and is currently appointed as an associate professor. He also holds secondary appointments in the School of Biomedical Engineering and the Department of Clinical Sciences.

Honors include: Monfort Professorship, May 2011; 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, November 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.



Tammy Haut Donahue

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

Research Interest: Orthopaedic biomechanics

Dr. Haut Donahue joined the faculty at CSU in December 2011 after spending 11 years in Mechanical Engineering at Michigan Technological University. She earned a Ph.D. from the University of California at Davis, where she received the Allen Marr Distinguished Dissertation Award in Biomedical Engineering in 2002 and the Microstrain Award for Innovative Instrumentation in Biomechanics for her master's work. Dr. Haut Donahue was a post-doctoral fellow in the Department of Orthopaedics at Pennsylvania State University before joining the faculty at Michigan Tech. She is a member of the School of Biomedical Engineering at CSU as well. She is an associate editor for the Journal of Biomechanical Engineering and an editorial consultant for the Journal of Biomechanics. She is currently the Program Chair for the 2016 Summer Biomechanics, Bioengineering and Biotransport meeting. She is currently the Chair of the Meniscus Section of the Orthopaedic Research Society. Dr. Haut Donahue's research includes analytical and experimental biomechanics of the musculoskeletal system with ongoing research in orthopaedic biomechanics and post-traumatic osteoarthritis. An emphasis is put on prevention, treatment, and repair of injuries to the soft tissue structures of the knee, focusing primarily on the meniscus. With funding from Whitaker Foundation, DOD, NIH, NSF, as well as industrial sponsorship her research program, she has had 15 Ph.D. students, 18 M.S. student, and more than 35 undergraduates. She has national collaborations with Michigan State and Mayo Clinic, as well as international collaborations with Trinity College Dublin and UMC Utrecht. Dr. Haut Donahue has brought in more than $12 million in funding as a PI and co-PI that has led to over 55 journal publications. She is now the Associate Department Head for Undergraduate Studies in the Department of Mechanical Engineering.

Honors include: The Ferdinand P. Beer and E. Russell Johnson Jr. Outstanding New Mechanics Educator Award, 2006, presented by the American Society of Engineering Education

Suzanne M. Tabbaa

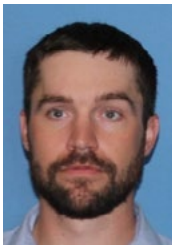
Ph.D., Clemson University

Dr. Suzy Tabbaa joined the ORC in the Fall of 2015 as a postdoctoral researcher working jointly between the ORC and the Cartilage Tissue Engineering (CTE) Laboratory at UCSD under the guidance of Dr. Dave Frisbie and Dr. Bob Sah. Suzy completed her Ph.D. in bioengineering from Clemson University and worked as a Senior Commercialization Technology Analyst at the Clemson University Research Foundation prior to joining the ORC team. Her two main projects are efforts to improve a cartilage repair strategy and contributions to correlating the equine induced osteoarthritis (OA) model to human OA. This work includes determining the commercial potential of her research projects and developing commercialization strategies for translation to the clinic.

Ellison Aldrich

D.V.M.

Dr. Ellison Aldrich received her B.A. in 2008 from Skidmore College in Saratoga Springs, N.Y., where she studied biology and studio art, and earned her VMD from the University of Pennsylvania in 2012. She then completed a one-year large-animal surgery internship at Tufts Cummings School of Veterinary Medicine and is now an equine surgery resident at CSU. She enjoys all aspects of equine surgery and lameness, with a primary research interest in regenerative medicine.



Ian Devick

D.V.M.

Dr. Ian Devick is originally from British Columbia, Canada. He received his DVM from the University of Saskatchewan, Canada in 2013. He then completed a one-year equine internship at Littleton Equine Medical Center and is now an equine surgery resident at CSU.

Lynn Pezzanite

D.V.M.

Dr. Lynn Pezzanite joined the CSU Equine Surgery Service residency program in July 2015 following completion of a one year rotating equine internship at Littleton Equine Medical Center. Dr. Pezzanite graduated from Cornell University College of Veterinary Medicine in 2014. She previously worked in the Comparative Orthopedics and Regenerative Medicine Laboratory of Dr. Lisa Fortier at Cornell University. Her research interests include regenerative medicine and diagnostic imaging.

Sherry Johnson

D.V.M.

Dr. Sherry Johnson joined the Equine Sports Medicine & Rehabilitation Service's residency program in July 2015 following completion of a one-year Equine Diagnostic Imaging Internship with Dr. Myra Barrett. Dr. Johnson graduated from Iowa State University's College of Veterinary Medicine, and then completed an equine internship in Ocala, Florida prior to continuing her Sports Medicine training at CSU.

Philippe Manchon

B.V.Sc

Dr. Philippe Manchon joined the Equine Sports Medicine and Rehabilitation Service's residency program in July 2013. Dr. Manchon is originally from Queensland, Australia. He received his veterinary degree at the University of Queensland, graduating in 2010, at which time he accepted a scholarship to continue his clinical training at the university's equine hospital. Dr. Manchon then pursued an internship in 2011 at Weatherford Equine Medical Center, Weatherford, Texas, and did an additional year in that practice before joining us at CSU.

Frances Peat

B.V.Sc

Dr. Peat joined the Equine Sports Medicine and Rehabilitation Services residency program in July 2013. She is the fifth resident in our program that remains unique as the only residency in Equine Sports Medicine and Rehabilitation. Dr. Peat is from New Zealand and received her veterinary degree (B.V.Sc.) from Massey University. She has also done a postgraduate clinical diploma at Massey and was in practice for five years at one of the leading equine practices in New Zealand, Matamata Veterinary Services.

Aimee Colbath

V.M.D. (University of Pennsylvania), M.S. (Colorado State University)

Dr. Aimee Colbath graduated from the University of Pennsylvania School of Veterinary Medicine in 2010 and became interested in stem cell research and biologic therapies during her general large animal internship at the University of Georgia, where she worked in Dr. Peroni's research laboratory. She then moved on to a surgical internship at the Tufts Cummings School of Veterinary Medicine, where she worked in the regenerative medicine laboratory studying the effects of shipping on stem cells. In 2015, Aimee earned her master's in clinical sciences and completed her surgical residency with CSU. In July of 2015, she began her Ph.D. in clinical sciences where she works closely with both the ORC and the Stem Cell and Regenerative Medicine Laboratory in the Animal Cancer Center. Since joining CSU, her research focus has been on the immunomodulatory effects of equine stem cells. In addition, Aimee has begun working with induced pluripotent stem cells (iPSC) and induced mesenchymal stem cells (iMSCs). In 2015, Dr. Colbath received the Grayson Jockey Club Career Development Award and an American Association of Equine Practitioners Research Fellowship Award.

Kristine Fischenich

M.S., The University of Mississippi

Kristine received her M.S. in mechanical engineering at CSU in 2013 and is now working toward a Ph.D in biomedical engineering. Her current work is a collaborative effort between mechanical and chemical and biological engineering under the advisement of Tammy Donahue and Travis Bailey. She is designing an artificial meniscal replacement using a block co-polymer specifically focusing on creating a construct with mechanical properties and load distribution mimetic of the native tissue.

Ben Gadomski

Ph.D., Colorado State University

Ben received his B.S. in mechanical engineering from Trine University in 2009 and earned his Ph.D. from Colorado State University studying under Dr. Christian Puttlitz in 2015. Ben is now an instructor in the Department of Mechanical Engineering at Colorado State University and continues to work with Dr. Puttlitz to investigate the risk of spinal cord injury during intubation procedures.

Livia Camargo Garbin

D.V.M., M.Sc., Minas Gerais Federal University

Livia graduated in Veterinary Medicine at Lavras Federal University in Brazil in 2010. She completed an equine internal medicine internship in 2011 at Minas Gerais Federal University in Brazil, where she also completed her master's degree in 2012. In her master's research, Livia compared the effects of two different protocols of mesenchymal stem cell isolation and its effects in equine-induced desmitis. Currently, Livia is engaged in a Ph.D. program at CSU with Dr. Frisbie as her advisor. Her project involves the study of the protective effects of allogeneic freeze-dried platelet-rich plasma (PRP) and conditioned serum (CS) in cartilage and synovium explants under inflammatory condition, in vitro.

Brad Nelson

D.V.M., M.S., Diplomate ACVS, Colorado State University

Dr. Brad Nelson started in a Ph.D. program at the ORC in 2013. Brad graduated from the University of Wisconsin- Madison with a D.V.M. in 2009, and then completed an equine internship in surgery and medicine at Washington State University, followed by a residency in large animal surgery at CSU. He also received a master's degree in clinical sciences as part of the residency program in 2013. Dr. Nelson's Ph.D. research focuses on articular cartilage imaging, specifically in the use of contrast enhanced computed tomography as a method to improve the diagnosis of articular cartilage injury. Brad also served as ORC veterinarian in 2015.

Hannah Pauly

B.S., Vanderbilt University

Hannah is currently working towards a Ph.D. in biomedical engineering under the mentorship of Dr. Tammy Donahue. Hannah's major area of research is fabricating a tissue engineered replacement for the anterior cruciate ligament using biocompatible and biodegradable polymers to replicate the complex hierarchical ligament structure. Additional projects include investigating the effects of knee injury on subchondral bones and assessing mechanical properties of hydrogels for use as a treatment for osteoarthritis.

Nicole Ramo

B.S., Kettering University

Nicole graduated in December of 2012 with a B.S. in mechanical engineering from Kettering University in Flint, Mich. and is currently a doctoral student in Dr. Christian Puttlitz's research group. Now in her third year of the School of Biomedical Engineering PhD program, Nicole's research is focused on characterizing and modeling the material properties of the soft tissues that make up the spinal cord-meningeal complex. These properties will be implemented into computational models of the spine to study spinal cord injury mechanisms and treatments.

Brett Steineman

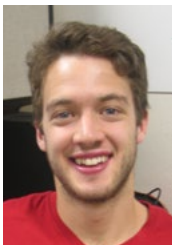
B.S., Trine University

Brett graduated in May of 2014 with a B.S. in mechanical engineering from Trine University in Angola, Indiana. Through Trine's co-operative education program, Brett worked for two years as a product development engineering intern at Zimmer-Biomet, Inc. in Warsaw, Indiana developing surgical instruments and implants for partial and total knee replacements. Brett is working toward his Ph.D. in bioengineering under Dr. Tammy Haut Donahue where he is currently developing a finite element model of the human knee to optimize the surgical technique for proper repair of meniscal root tears.

Suwimol Tangtrongsup

M.S., Mahidol University

Suwimol graduated and received her B.Sc. in biology and her M.Sc. in physiology from Mahidol University, Bangkok, Thailand. She spent the next four years as an instructor in the Department of Physiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. Suwimol joined the ORC under a scholarship from The Royal Thai Government and is currently working on a Ph.D. under Dr. John Kisiday. Her current research is the effect of reactive oxygen species on chondrogenic differentiation of equine bone marrow-derived mesenchymal stem cells in an agarose-gel culture system.



Benjamin Wheatley

B.S., Trinity College

Ben joined Dr. Haut Donahue's lab in fall 2012 as a Ph.D. student in engineering. His main research area is muscle mechanics. His current project is the development of a finite element model of skeletal muscle to predict intramuscular pressure. The goal of this project is cooperation with a clinical tool to determine muscle force. Ben has also developed nonlinear viscoelastic models of muscle and performed finite element analysis on other orthopaedic tissues such as the meniscus.

Gustavo Miranda Zanotto

D.V.M., M.Sc., Sao Paulo University

Dr. Gustavo Zanotto is originally from Curitiba, Brazil, where he received a D.V.M. from Parana Federal University in 2007. Gustavo then moved to Sao Paulo where he completed a residency in large animal internal medicine and surgery, and received a master's degree in veterinary surgery at Sao Paulo University. For his master's degree, Gustavo evaluated chitosan hydrogel as a scaffold for equine stem cells. The main objective of this study was to improve the tissue engineering techniques for repair of osteochondral defects. From 2010 to 2013, Gustavo was an assistant professor of large animal internal medicine and surgery at Anhanguera Educational School of Veterinary Medicine. Currently, Gustavo is a visiting researcher at the ORC working with Dr. David Frisbie on a project to compare the freeze-dried and fresh platelet-rich plasma in injured tendon explants. Additionally, Gustavo is doing an internship with CSU's Veterinary Diagnostic Imaging Service focusing on equine musculoskeletal imaging under the supervision of Dr. Myra Barrett-Frisbie.

Alyssa Ball

B.S., Colorado State University

Alyssa graduated from CSU in 2013 with a B.S. degree in biochemistry and started her M.S. graduate program in the fall of 2013 under the direction of Dr. Laurie Goodrich. In 2014, Dr. Goodrich and Alyssa received CRC funding to explore the use of genetically modified stem cells in equine fracture repair. In 2015, Alyssa received a NIH-T32 Fellowship allowing her to take a year off of veterinary school and complete the final year of her master's. She will return to veterinary school at CSU in the fall of 2016. After completing veterinary school, Alyssa plans to continue pursuing equine musculoskeletal research.

Kate Remley

B.S., University of Kansas

Kate graduated from the University of Kansas in 2011 with a B.S. in chemistry. In the fall of 2014, Kate started the M.S. program in biomedical engineering under the direction of Dr. Tammy Donahue and expects to graduate in the summer of 2016. Her current research is focused on determining the efficacy of P188 in mitigating meniscal damage.

John Schwartz

M.S., Colorado State University

John Schwartz joined the EORC under Dr. Laurie Goodrich as a Research Associate in June 2015. He received his B.S. in journalism from Boston University in 2010 and his M.S. in microbiology from CSU in May 2015. Before coming to CSU, he spent four years working in the Orthopaedic Research Laboratory at the Feinstein Institute for Medical Research under Dr. Daniel Grande researching cartilage regeneration, tendon repair, and 3D bioprinting.

Christine Battaglia

M.S., Virginia-Maryland Regional College of Veterinary Medicine

Christine (Chrissy) began her appointment at the Orthopaedic Research Center as a Research Scientist/Lab Manager in January 2014. Chrissy attended St. Michael's College in Colchester, VT and obtained a B.S. in environmental science. She obtained an M.S. in biochemical toxicology from Virginia-Maryland Regional College of Veterinary Medicine in Blacksburg, VA in 2001. Shortly after, Chrissy moved to Fort Collins and began working at Colorado State University in the Environmental and Radiological Health Sciences. She has worked in a variety of research areas since her arrival at CSU, including the Center for Environmental Toxicology, Neurobiology and Radiation Cancer Biology. She looks forward to participating in the exciting research advancements being made at the ORC.

Kirk McGilvray

Ph.D., Colorado State University

Dr. Kirk McGilvray is currently working as an Assistant Research Professor and severs as one of the Principal Investigators (PI) at the Orthopaedic Bioengineering Research Laboratory (OBRL). He is a Colorado native and received his B.S., M.S., Ph.D., and Post-doctoral education at CSU. His research efforts focus on comparative animal studies investigating pathways to enhance both soft tissue and bone healing following surgical intervention or trauma. He is also responsible for directing much of the day-to-day operations within the biomechanical testing center at the OBRL, which includes mentoring students in research techniques. Kirk's overreaching goals are to develop advance in vitro and in vivo measurement techniques that can be used to assess biological tissue in both its normal and diseased states.

Jennifer Suddreth

B.S., Colorado State University

Jen is originally from Altamont, Utah, and graduated from CSU in 2009 with a bachelor's degree in equine science and agricultural business. She started at the ORC on feed crew, and returned after graduation to work as an animal care technician. Jen joined the ORC full time as Research Trials Coordinator, Barn Manager and Volunteer Coordinator in June 2010. She was named the 2013 Technician of the Year, an award coordinated by the American Association for Laboratory Animal Science and the International Council for Laboratory Animal Science.

Britt Madsen

B.S., Colorado State University

Britt is a Colorado native and graduated from CSU in 2002 with a B.S. in equine science. She managed horses for several equine operations in the area, including Chatellen Farm and Double Dove Ranch. In addition, she worked as a technician for Pilchuck Animal Hospital in Snohomish, WA and CSU's Equine Sports Medicine Service, and was a representative in the HR department of Starbucks Coffee Co. before joining the team as the Equine Operations Manager. Britt brings a balance of customer service experience and extensive equine industry connections to her new position. In her downtime, Madsen spends time at home in the garden with her daughter, Riley, and attempts to find time to ride one of her three horses.

Lynsey-Ann Bosch

B.S., Michigan State University

Lynsey graduated from Michigan State University (MSU) with a B.S. in Veterinary Technology, and worked at MSU's Large Animal Hospital as a veterinary technician throughout her education. After moving to Colorado she worked as a lead technician at an equine practice and as a teacher at Bel-Rea Institute of Animal Technology. Lynsey joined the ORC in 2005 as a Research Associate and currently assists the PI's at the ORC with multiple tasks such as editing and submission of research articles, grant submission, presentation creation and project management. Additionally, Lynsey coordinates 3- and 4-day continuing education courses hosted by the ORC at CSU.

Cecily Broomfield

M.S., Colorado State University

Cecily received a B.S. in microbiology from California Polytechnic State University in 2000, and an M.S. in agriculture from CSU in 2006. She is currently working as a research associate for the Orthopaedic Bioengineering Research Lab (OBRL).

Whitney McMillan

B.S., Colorado State University

Whitney joined the Equine Sports Medicine and Rehabilitation service at the end of 2014 as a technician. She is a Georgia native and has a bachelor degree in Equine Science from CSU. She has been working in equine orthopedic research since 2005 and now brings her extensive experience to the Equine Sports Medicine team.

Mindy Meyers

M.S., University of Minnesota-Duluth

Melinda Meyers is a Research Associate with ten years of experience in the biomedical and biotechnology field. She received a B.S. from the University of Minnesota-Duluth and an M.S. in a focus on equine biotechnology, flow cytometry, and genetic preservation. Mindy is a research associate (laboratory) for the Orthopaedic Research Center.

Meredith Park

B.S., Virginia Tech

Meredith Park joined the Equine Sports Medicine and Rehabilitation service as a veterinary technician in November of 2015. Although originally from Louisiana, Meredith considers Virginia to be "home." Growing up in Middleburg, she was heavily involved in the fox hunting and racing community (flat and steeplechase). Meredith left Middleburg to attend Virginia Tech, graduating with a B.S. in Animal and Poultry Sciences in 2010. Following graduation, she returned to Northern Virginia to work for Spring Hill Farm—a world-class thoroughbred breeding and racing operation—foaling out mares, prepping yearlings for sales, and rehabbing layups off the track. After the dispersal of the farm, Meredith made her way to Virginia Equine Imaging, where she worked as a veterinary assistant and managed the farm for Drs. Kent Allen and Rae Stone before making the move to Colorado.

Lindsay Richardson

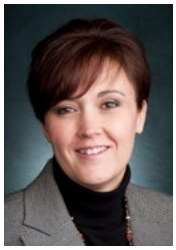
B.S., Colorado State University

Lindsay joined the Equine Sports Medicine and Rehabilitation team as a technician in December 2014. She is originally from Illinois and has a bachelor's degree in animal science from CSU. She has several years of experience working at the Orthopaedic Research Center and assisting in equine research projects. She is currently attending the Front Range Community College Veterinary Technician Program and will become a certified veterinary technician in 2016.

Nikki Phillips

B.S., Tulane University

Nikki received her B.S. in cell and molecular biology in May 1997 from Tulane University. She has been at CSU since 2001, working in the Department of Pathology for a year before working for both Clinical Sciences and Biomedical Sciences. Nikki joined the ORC in January 2008 as a research associate to assist in the laboratory.



Candice Hastings

Business Officer

Candice is the business officer for the Department of Clinical Sciences, and in May 2011, she began managing the accounting activity for the ORC.

Lindsie Talkington

Veterinary Transcriptionist

Lindsie came to work for the ORC in 2015 as a veterinary transcriptionist. Along with medical transcription, she has previously worked as a veterinary technician and also as a medical assistant.

Lindsey McCormick

Equine Sports Medicine
Administrative Assistant

Lindsey grew up in Littleton, Colorado. She attended Colorado State University and graduated with an Equine Science degree in 2012. Before working for the ORC, she organized horse shows for the National Western Stock Show, as well as local Colorado Hunter Jumper Association shows. She rides horses and spends time with her dogs for fun.

Paula Vanderlinden

Program Coordinator

Paula joined the ORC in March 2007 as program coordinator and Dr. McIlwraith's personal assistant. Paula manages the development and publication of the annual ORC lab report and newsletter, prepares the PRSE reports and reapplications, as well as, other reports.

ORC Student Hourlies in 2015

Katie Baber

Alyssa Ball

Bree Copeman

Matt Ford

Kenzie Keefer

Jadyn McCoy

Savanah Spears

Megan Steele

Cassi Uhart

Not pictured:

Kim Cerjan

Volunteers in 2015

Jayne Ellis
Amelia Haddad
Stephany Lunn
Kathryn Crone
Zach Sprague
Kim Cerjan
Elise Koszarek
Savannah Spears
Meghan Barrett
Westly Oberman
Mikayla Coddingtion
Nadia Postek
Kassidy Cadd
Billie Glenn
Brooke Davis
Lindsay Cooley
Paige Clements
Vanessa Schilling
Maddy Pielage
Shelby Stiles
Jenny VanDeventer
Colten White
Morgan Heinrichs
Matt Ford
Kim Cerjan

Elwyn Firth

B.V.Sc., Ph.D., D.Sc., Diplomate ACVS, Professor in the Department of Exercise Science and the Liggins Institute at the University of Auckland, New Zealand

Dr. Elwyn Firth is a Professor in the Department of Exercise Science and the Liggins Institute at the University of Auckland, New Zealand. He has worked in other universities as a specialist in equine surgery and a researcher in musculoskeletal sciences. His current research interests include the effect of exercise on bone and joint growth and function, the effect of nutritional and exercise interventions on early and later responses of various body systems, and how exercise during pregnancy and early postnatal life affects metabolic outcomes in later life.

Mark W. Grinstaff

Ph.D; Distinguished Professor, Boston University, Boston, MA

Dr. Mark W. Grinstaff is the Distinguished Professor of Translational Research and a Professor of Biomedical Engineering, Chemistry, and Materials Science and Engineering, and Medicine at Boston University. Mark received his Ph.D. from the University of Illinois under the mentorship of Professor Kenneth S. Suslick and was an NIH postdoctoral fellow at the California Institute of Technology with Professor Harry B. Gray. Mark's awards include the ACS Nobel Laureate Signature Award, NSF Career Award, Pew Scholar in the Biomedical Sciences, Camille Dreyfus Teacher-Scholar, Alfred P. Sloan Research Fellowship, the Edward M. Kennedy Award for Health Care Innovation, and a Fellow of the National Academy of Inventors. He is an author or co-author on more than 200 peer-reviewed manuscripts, given more than 275 oral presentations, and an inventor or co-inventor on more than 200 issued patents or pending applications. His students and fellows have given more than 125 oral presentations and 350 posters at national and international meetings. He is a co-founder of four companies that are commercializing his ideas, and he has three products being sold and used in the clinic. His current research activities involve the synthesis of new macromolecules and biomaterials, self-assembly chemistry, imaging contrast agents, drug delivery, and wound repair.

Charles Ho

Ph.D., M.D.

Dr. Ho is experienced and active in musculoskeletal and orthopaedic sports medicine imaging and research, particularly in musculoskeletal Magnetic Resonance Imaging. He has been a member of the Radiological Society of North America, the American Roentgen Ray Society, 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 radiologic and orthopaedic literature, and presented numerous papers internationally in radiologic and orthopaedic conference proceedings. Dr. Ho is Director of Imaging Research and a member of the Scientific Advisory Board of the Steadman Philippon Research Institute in Vail, Colo. He has served as Radiologic Consultant for the San Francisco 49ers, the San Francisco Giants, Cleveland Indians, Denver Broncos, Colorado Rockies, the U.S. Ski Team, and the U.S. Decathlon Team.

Johnny Huard

Ph.D.

Dr. Johnny Huard is a Professor in the Department of Orthopaedic Surgery at the University of Texas Health Science Center at Houston as well as being Chief Scientific Officer of the Steadman-Philippon Research Institute and Director of SPRI's Center for Regenerative Medicine. Prior to these two recent appointments, Dr. Huard was an endowed Professor and Vice Chair for the Department of Orthopaedic Surgery and Musculoskeletal Cellular Therapeutics at the University of Pittsburgh. He also served as the Director of the Stem Cell Research Center at the University of Pittsburgh School of Medicine.

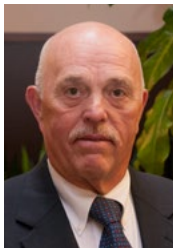
Dr. Huard completed his Ph.D. in neurobiology at Laval University in Quebec before earning two post-doctoral degrees in gene therapy, the first from McGill University in Quebec and the second from the University of Pittsburgh. Dr. Huard is internationally recognized in the areas of gene therapy, tissue engineering and regenerative medicine application based on the use of muscle-derived stem cells (MDSCs). His primary areas of interest are in basic stem cell biology and their translation to clinic to aid in the healing and the regeneration of a variety of tissues. Dr. Huard's research has received multiple honors and awards nationally and internationally and he and his team have published over 300 peer reviewed papers and 82 book chapters. In addition, of significant international recognition in the form of major awards received from organizations in the field of orthopaedic medicine, Dr. Huard has received funding from the National Institutes of Health, the Department of Defense, and the Muscular Dystrophy Association.

Robert F. LaPrade

M.D., Ph.D.; Chief Medical Officer, The Steadman Philippon Research Institute; Complex Knee and Sports Medicine Surgery, The Steadman Clinic, Vail, Colo.

Dr. Robert LaPrade is an internationally recognized orthopaedic surgeon who specializes in the treatment of complex knee injuries, in particular posterolateral knee injuries. He is currently the chief medical officer for the Steadman Philippon Research Institute, the co-director of the sports medicine fellowship, and the director of the international scholars program.

He has published over 300 peer-reviewed scientific manuscripts, over 80 invited articles, over 100 book chapters, and one textbook. He also is on the Editorial Board for the American Journal of Sports Medicine (AJSM) and Knee Surgery, Arthroscopy and Traumatology (KSSTA), and is a peer reviewer for over 10 journals. He has received numerous international awards, including the OREF Clinical Research Award, considered one of the Nobel prizes of orthopaedic surgery. Dr. LaPrade was recognized for his research which has led to the development of over a dozen anatomic-based surgical procedures to treat knee injuries. Dr. LaPrade is also the founder of the Vail International Complex Knee Course, recognized as one of the best international courses on complex knee injuries. Dr. LaPrade is a member of numerous professional associations, including AOSSM, ISAKOS, and ESSKA, and is a frequent contributor to orthopaedic surgery expert groups, instructional course lectures, and research committees.



William G. Rodkey

D.V.M., M.S.; Chief Scientific Officer and Senior Scientist, Director, Center for Translational and Regenerative Medicine; Research Chairman, Scientific Advisory Committee, Steadman Philippon Research Institute, Vail, Colo.

Dr. Rodkey has been chief scientific officer and director of the Center for Translational and Regenerative Medicine Research at the Steadman Philippon Research Institute in Vail, Colo., since 1990. He is also the chairman of the Scientific Advisory Committee. Dr. Rodkey's research is focused on tissue regeneration with scaffolds, and cellular therapy with an emphasis on articular cartilage, meniscus, and ligaments. Prior to joining Dr. Steadman in Vail, Dr. (Colonel, U.S. Army, retired) Rodkey was chairman of Military Trauma Research at Letterman Army Institute of Research in San Francisco and earned numerous awards and military decorations, including the United States of America Legion of Merit Medal, Meritorious Service Medal, U.S. Army Commendation Medal (with five oak leaf clusters), Humanitarian Services Medal, Order of Military Medical Merit, and the U.S. Secretary of the Army Research and Development Achievement Award. He has authored more than 200 published works and has made more than 450 presentations at national and international meetings. Dr. Rodkey has received numerous awards, including the Excellence in Research Award from AOSSM, the Cabaud Memorial Award from AOSSM twice, the Albert Trillat Award for Knee Research, and GOTS-Beiersdorf Research Award 2000. He received undergraduate and Doctor of Veterinary Medicine degrees from Purdue University and completed medical education and surgical and orthopaedic residency training at University of Florida. He is a member of AAOS, AOSSM, ISAKOS, ESSKA, ICRS, OARSI, EFORT.

Jude Samulski

Ph.D., Professor, Department of Pharmacology, University of North Carolina, Chapel Hill, N.C.

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

Honors include: Outstanding Young Men of America Award and the President's Distinguished Research Award; American Society of Gene Therapy Outstanding Achievement Award, 2009. President of American Society of Cell and Gene Therapy, 2012

Coen Wijdicks

Ph.D.; Director, Department of BioMedical Engineering; Senior Staff Scientist, Steadman Philippon Research Institute, Vail, Colo. In late 2014 became Director of Research, Arthrex GmbH, Munich, Germany

Dr. Wijdicks is an orthopaedic researcher who currently serves as the director of the Department of BioMedical Engineering and as a senior staff scientist at the Steadman Philippon Research Institute (SPRI). His focus is in utilizing biomedical engineering principles to advance healthcare treatments by combining the design and problem solving skills of engineering with medical and biological sciences. Specifically, Dr. Wijdicks is interested in bench-to-bedside translational research for the development, optimization, and validation of surgical procedures for common injuries.

Charles Archer, Ph.D., Professor of Regenerative Medicine, School of Medicine, Swansea University, Swansea SA2 8PP

Dr. Charles Archer took up his current position in 2012. Prior to that, from 2002–2012 he was professor of Reparative Biology and Tissue Engineering at Cardiff University, and head of the Connective Tissue Biology Laboratories within Biosciences until 2006, one of the-then 16 research groups within the school. Having graduated the University College of Swansea in zoology, he remained there to pursue a Ph.D. in the effects of pulse-magnetic fields and fracture healing. He then carried out post-doctoral work at the Middlesex Hospital Medical School on cartilage morphogenesis under Prof. Louis Wolpert before moving to the Institute of Orthopaedics, University College, London, as lecturer and then senior lecturer in cell biology before moving to Cardiff in 1990. Most of his work has been on articular cartilage, from initial mechanisms of joint formation through to its morphogenesis, aging and the onset of degenerative disease. More recently, he has focused on endogenous cartilage stem cells as a therapeutic option for repair of damaged cartilage.

Frank Barry, Ph.D., Professor of Cellular Therapy at the Regenerative Medicine Institute (REMEDI), National University of Ireland Galway.

Frank Barry directs a large group of researchers who focus on the development of new repair strategies in stem cell therapy and gene therapy in orthopaedics. Previously, he was Director of Arthritis Research at Osiris Therapeutics in Baltimore, Md., and a Research Fellow at Shriners Hospital for Children, Tampa, Fla. He has contributed to the fields of tissue engineering and regenerative medicine by developing innovative and successful cellular therapies for the treatment of acute joint injury and arthritic disease. This has included the generation of a large body of new data in ground-breaking preclinical studies, and has led to the first phase of clinical testing of mesenchymal stem cells in clinical trials for joint injury. In a career that has spanned both industry and academic research, he has been a driver in the development of cellular therapy as a biological repair strategy. It is his belief that the application of new technologies in regenerative medicine, including cellular therapy, gene therapy, growth factor augmentation, implantable scaffolds, and nanomaterials, will have a profound impact in Orthopaedics. Frank Barry was the recipient of the 2012 Marshall Urist Award for excellence in tissue regeneration research from the Orthopaedic Research Society.

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

Professor Neil Broom's initial training in metallurgy has been applied successfully to experimental tissue mechanics that has earned him an international reputation in this field. His earlier aortic valve research fundamentally altered processing procedures in the bio-prosthetic valve industry world-wide. Neil's key achievements in joint-tissue research include the development of new collagen-based physical models for cartilage to account for the structural weakening occurring in the cartilage matrix arising from both early degeneration and trauma. He has provided rigorous, experimentally-based analyses of both the role of the strain-limiting articular surface, and the biomechanically critical junction region between the compliant cartilage and bone in its physiological state. He and his team have produced evidence of primary bone formation beneath the still-intact cartilage adjacent to lesion sites thus clarifying the elusive pre-osteoarthritic state. His research has produced a structural gold standard for the international community of 'tissue engineering' researchers, challenging them to 'engineer' matrices that are biomechanically viable. Neil's most recent research has focused on the intervertebral disc (IVD). He and his team have developed new structural insights into the micro-anatomy of the disc wall to explain the mechanical basis of annular disruption and prolapse, these being linked to two of the most prevalent and debilitating clinical conditions of the modern world - low back and radicular pain. He has shown experimentally how nucleus material interacts with the disc wall and endplate, and how combinations of flexion, torsion, and rate of loading can cause nuclear fragments to migrate out through the wall and cause prolapse. This pioneering research is the first published integration of disc micro-architecture, functional posture, and loading rate, with susceptibility to failure. Neil is an elected Fellow of the Royal Society of NZ, and in 2013 was awarded the Society's MacDarmid Medal for his contributions to research that most benefits human health.

Constance R. Chu, M.D., Professor and Vice Chair Research, Department of Orthopedic Surgery, Stanford University; Director of Joint Preservation Center and Chief of Sports Medicine, VA, Palo Alto

Dr. Constance R. Chu was previously the Albert Ferguson Professor of Orthopaedic Surgery at the University of Pittsburgh. She is a clinician-scientist who is both principal investigator of several projects funded by the National Institutes of Health, and who has been recognized as a Castle-Connelly/US News and World Report "Top Doctor" in orthopedic surgery, as well as on Becker's list of 125 Top Knee Surgeons in the U.S. Her clinical practice focuses on knee reconstruction, arthroscopy, ACL and meniscus surgery, and cartilage repair. She graduated from the U.S. Military Academy at West Point and earned her medical degree from Harvard Medical School. As director of the multi-disciplinary Joint Preservation Center structured to seamlessly integrate basic, translational and clinical research with clinical practice, Dr. Chu developed the center to advance the concept of early diagnosis and treatment of cartilage injury and degeneration as a strategy to delay or prevent the onset of disabling osteoarthritis. Towards this end, she is leading innovative translational research from bench to bedside in three main areas: quantitative imaging and biomarker development for early diagnosis and staging of joint and cartilage injury and degeneration; cartilage tissue engineering and stem cell based cartilage repair; and molecular and biological therapies for joint restoration and rejuvenation. Her research efforts have led to more than 30 professional awards and honors to include a Kappa Delta Award, considered to be the highest research honor in Orthopedic Surgery. Dr. Chu also regularly holds leadership and committee positions in major professional organizations such as the American Association of Orthopedic Surgeons (AAOS) and the American Orthopedic Association (AOA). In her subspecialty of Orthopedic Sports Medicine, she is a past president of the Forum Sports Focus Group, a member of the prestigious Herodicus Society of leaders in sports medicine, and immediate past Chair of the American Orthopedic Society for Sports Medicine (AOSSM) Research Council. She is alumnus of the highly selective AOA American, British, Canadian (ABC) Traveling Fellowship and the AOSSM Traveling Fellowship, opportunities enacted to recognize and promote careers of emerging leaders in orthopedic surgery and orthopedic sports medicine, respectively.

Lisa Fortier, D.V.M., Ph.D., Diplomate ACVS
Lisa Fortier is a professor of surgery at Cornell University in Ithaca, N.Y.

She received her D.V.M. from Colorado State University and completed her Ph.D. and surgical residency training at Cornell University. She is boarded with the American College of Veterinary Surgeons and is an active equine orthopaedic surgeon at Cornell University and the Cornell Ruffian Equine Specialists Hospital at the Belmont race track in New York. Her laboratory studies the intracellular pathways involved in the pathogenesis of osteoarthritis, with particular emphasis on post-traumatic osteoarthritis. In addition, Lisa's research program investigates the clinical application of stem cells and biologics such as PRP for cartilage repair and tendonosis. She has received the Jaques Lemans Award from the International Cartilage Repair Society, the New Investigator Research Award from the Orthopaedic Research Society, and the Pfizer Research Award for Research Excellence from Cornell University. Lisa is the vice president of the International Veterinary Regenerative Medicine Society and past president of the International Cartilage Repair Society.

Alan J. Grodzinsky, Sc.D., Professor, Director of the Center for Biomedical Engineering, Departments of Biological Engineering, Mechanical Engineering, and Electrical Engineering and Computer Science, MIT

Dr. Grodzinsky is a professor in the departments of Biological, Electrical, and Mechanical Engineering at the Massachusetts Institute of Technology. He is also the director of the Center for Biomedical Engineering. Dr. Grodzinsky's 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.

Johnny Huard, Ph.D., former director of the Stem Cell Research Center at the University of Pittsburgh, has been named chief scientific officer of the Steadman Philippon Research Institute and director of SPRI's Center for Regenerative Sports Medicine.

At Pittsburgh, Dr. Huard also served as vice chair for Musculoskeletal Cellular Therapeutics in the Department of Orthopaedic Surgery, and deputy director of Cellular Therapeutics Research at the McGowan Institute for Regenerative Medicine.

Huard, 49, is internationally recognized for his leading edge research in the field of stem cells and regenerative medicine as it relates to the musculoskeletal system. In his new position at SPRI, Huard will be establishing a regenerative and translational medicine institute in Vail, Colorado.

Huard has spent the past 19 years at the University of Pittsburgh. As the Henry J. Mankin Professor in the Department of Orthopaedic Surgery, he has extensive knowledge in the areas of gene therapy, tissue engineering, and regenerative medicine applications based on the use of muscle-derived stem cells.

In addition to significant international recognition in the form of major awards received from organizations in the field of orthopaedic medicine, Huard has received generous grants and other forms of financial support, including funding from The National Institutes of Health, the Department of Defense, and the Muscular Dystrophy Association, as well as other private and public foundations.

"The opportunity to accelerate our pioneering advances in regenerative sports medicine and stem cell research with Dr. Huard as our chief scientific officer is enormous," said Dr. Marc Philippon, managing partner of The Steadman Clinic and co-chairman of SPRI. "In the future, our team of physicians and researchers envision every person having the opportunity to harvest his or her own stem cells and then re-inject them into the body to help delay various aging processes such as osteoporosis or osteoarthritis, or to speed up recovery from injury or illness."

"Dr. Huard's work in regenerative medicine has been recognized world-wide and his research and contributions in this area of study will represent another important milestone in our efforts to keep people active," said Dan Drawbaugh, CEO of The Steadman Clinic and SPRI.

"In his new role, Dr. Huard will focus on regenerative medicine and lead the conversion of his research into orthopaedic treatments at The Steadman Clinic. The ability to collaborate with The Steadman Clinic will mean that Dr. Huard can test his premise that transplanting autologous stem cells will help delay the degeneration of joints."

"Dr. Steadman, who was finding ways to treat sports injuries through regenerative methods 25 years ago, laid the groundwork for those that followed him – including Dr. Philippon, who has made tremendous advances in the field of hip surgery," said Huard. "We have the opportunity to discover ways to further delay joint replacements and help patients at The Steadman Clinic recover faster and stronger. I'm grateful for all of the work that Dr. Steadman, Dr. Philippon, and their team have done over the years and look forward to working with them."

If musculoskeletal disease is slowed or if injuries are successfully repaired and rehabilitated, people can remain active longer, reducing the risk of conditions associated with inactivity, including cardiovascular disease, high blood pressure, obesity, diabetes, osteoporosis, certain cancers, and depression. The efforts of SPRI and The Steadman Clinic to keep people active have already resulted – and will continue to result – in significant savings in healthcare costs over a person's lifetime.

Christopher Little, B.Sc., B.V.M.S., M.Sc., Ph.D.; Diplomate ACVS; Professor and Director, Raymond Purves Bone & Joint Research Laboratories, Kolling Institute, Institute of Bone and Joint Research, University of Sydney at Royal North Shore Hospital

Professor Christopher Little is director of the Raymond Purves Bone and Joint Research Labs at the Kolling Institute and the SubDean of Research for Sydney Medical School (Northern) at Royal North Shore Hospital, Australia. Dr. Little received his veterinary training at Murdoch University in Western Australia, where he also undertook an internship in equine medicine and surgery (1978-1984). He then completed a residency in large animal surgery and an M.Sc. studying arthritis in horses at the University of Minnesota. Chris was appointed to the faculty at the Ontario Veterinary College, University of Guelph, and during this time passed his certifying examinations to become a Diplomate of the American College of Veterinary Surgeons (1990). He then moved to back to Australia and was awarded a Ph.D. degree from the Faculty of Medicine at the University of Sydney in 1996. Following a 5-year postdoctoral position at Cardiff University (U.K.), he was awarded an Arthritis Foundation of Australia Fellowship at the University of Melbourne. In 2004, he moved to his current position in the University of Sydney Faculty of Medicine. Chris's research interests focus on defining the biochemical and molecular mechanisms of joint pathology in OA, and tendon and intervertebral disc degeneration, and are based on the belief that it is only through a better understanding of the mechanisms that drive the initiation and progression of these diseases that new therapies can be developed. 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 and disc degeneration. Chris is recognized internationally for his expertise in the development and use of animal models of bone and joint disease. He has served as an Associate Editor of Osteoarthritis and Cartilage, and as leader of the OARSI international initiative to establish standardized methods for evaluation of animal models of OA. Chris received the 2010 Barry Preston Award from the Matrix Biology Society of Australia and New Zealand, presented to an outstanding leader in the field. He has authored/co-authored 112 scientific papers and seven book chapters.

Helen McCarthy, Ph.D.

Dr. Helen McCarthy is a senior post-doctoral research scientist within the division of Pathophysiology and Repair at Cardiff School of Biosciences in the U.K. Her research interests focus on the development of translational technologies based on articular cartilage progenitor cell biology, primarily in the equine field. This work has resulted in the first large animal studies utilizing both equine (Colorado) and caprine (Davos, Switzerland) models. Her interests also lie in the biology of both the articular cartilage progenitor cell and a meniscus- specific stem/progenitor cell in human tissue and their role in tissue repair and osteoarthritis.

Alan J. Nixon, B.V.Sc., M.S., 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 osteochondritis dissecans (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 ORC at CSU, the combined use of interleukin receptor antagonist gene therapy to diminish degradation in arthritic joints.

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

Dr. Peterson is a professor of mechanical engineering at the University of Maine. Prior to coming to the University of Maine, he was a faculty member at CSU and was a post-doctoral researcher at Northwestern University. He has also worked in industry at General Motors and General Dynamics Corp. His Ph.D. is in theoretical and applied mechanics from Northwestern University in Illinois, and he also holds a B.S. in mechanical engineering from General Motors Institute (now Kettering University) and an M.S. in theoretical and applied mechanics from Northwestern University. He has also done additional graduate work in mechanics, materials, and mathematics from Yale University, Cornell University, and the University of Connecticut. His primary expertise is in the animal biomechanics, dynamic response of materials, and waves in solids.

Christopher B. Riley, B.Sc. (Physics), B.V.Sc. (Hons), M.Sc., Ph.D., Diplomate ACVS, PGCertInnovation Mgt, Professor, Chair and Service Chief, Equine Group, Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerton North, New Zealand

Following military service in the Air Force, Dr. Riley received degrees in physics and veterinary medicine from the University of Melbourne, Australia. After an internship and private practice in Australia, he completed a surgical residency at the University of Saskatchewan in Canada. Concurrently, he completed M.Sc. and Ph.D. degrees in the fields of tendon in-vitro biology and biochemistry. Dr. Riley then worked at briefly at Iowa State University and in private practice during which time he became a Diplomate in the American College of Veterinary Surgeons. He joined the faculty at the Atlantic Veterinary College, Canada, in 1999 rising to the rank of professor, and completed an MBA course in Innovation Management in 2007 at the University of Melbourne. In 2010 he accepted an appointment as the inaugural professor and chair of Equine Health the University of Adelaide, establishing the equine curriculum, teaching and veterinary hospital facilities. He commenced his current position at Massey University in 2013 during the veterinary program's 50th Anniversary year. Dr. Riley has focused his research on the development of biomedical tests for animal diseases using the emerging technologies of infrared spectroscopy (FTIR), optoacoustics, and bioinformatics. He established the first FTIR laboratory of its kind in Canada, developed to investigate the veterinary potential biomedical infrared spectroscopy. He has continued this work with ~US $6.7 million in funded projects to date. Dr. Riley has a special interest in biomarkers for orthopaedic disease, and humoral immunity, but is also interested exploring the full potential of emerging technologies as they apply to veterinary and comparative medicine. Dr. Riley partnered with the Orthopaedic Research Center and the Institute for Biodiagnostics, National Research Council of Canada, to develop the first FTIR test for equine traumatic arthritis and osteochondrosis. More recently, he has collaborated with Prof. Sheila Laverty at the University of Montreal and Prof. James Cook at the University of Missouri to examine and characterize this technology further in rabbit and canine models of orthopaedic disease. He looks further to continued collaboration and advances in this new field of research. Currently, he is continuing work with the carpal chip fracture model established at the ORS.

Robert Lie-Yuan Sah, M.D., Sc.D., Professor of Bioengineering & Adjunct Professor of Orthopaedic Surgery, UCSD; Professor, Howard Hughes Medical Institute

Dr. Sah received his Sc.D. in medical engineering from the Massachusetts Institute of Technology and his M.D. from Harvard Medical School. He did postdoctoral work at Massachusetts General Hospital in orthopaedic bioengineering. He is currently co-director of the Center for Musculoskeletal Research at UCSD, and also co-director of an NIH pre-doctoral training grant on Translational Musculoskeletal Research at UCSD. In addition, he is on the Editorial Board of Cartilage, Osteoarthritis and Cartilage, and Tissue Engineering, and a standing review panel member for the NIH.

Honors include: Arthritis Foundation, Hulda Irene Duggan Investigator, 1993; Young Investigator Award, National Science Foundation, 1994; "Mechanical Blueprint for Cartilage," cited as one of the Great Advances in Scientific Discovery in Disease and Injury Treatment, The Science Coalition, 1998; American Academy of Orthopaedic Surgeons Kappa Delta Award, 1993 and 2001; American Society of Mechanical Engineers Van C Mow Medal, 2006; Howard Hughes Medical Institute, Society of Professors, 2006; American Institute for Medical and Biological Engineering, 2007

Roger K.W. Smith, M.A., VetMB, Ph.D., FHEA DEO, AssocECVDI, Diplomate ECVS MRCVS; Professor of Equine Orthopaedics, Royal Veterinary College, London, U.K.; RCVS and European Specialist in Equine Surgery (Orthopaedics); President, International Veterinary Regenerative Medicine Society

Roger Smith qualified as a veterinary surgeon from Cambridge University in 1987 and, after two 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 three-year research project culminating in the award of a Ph.D. for his studies on the extracellular matrix of equine tendon. He remained at the Royal Veterinary College, first as a lecturer in equine surgery, then as senior lecturer in equine surgery before his appointment to a professorship in December 2003. He holds the Diploma of Equine Orthopaedics from the Royal College of Veterinary Surgeons, and is both a Diplomate of the European College of Veterinary Surgeons and a Royal College of Veterinary Surgeons Specialist in Equine Surgery. He is also an Associate member of the European College of Veterinary Diagnostic Imaging and Fellow of the Higher Education Academy. 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 pathogenesis of tendinopathy 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.

J. Richard Steadman, M.D.; Founder and Managing Partner, The Steadman Clinic; and Founder and Co-Chairman, Steadman Philippon Research Institute, Vail, Colo.

Dr. Steadman graduated from the University of Texas Southwestern Medical School in Dallas. Following internship, two years in the U.S. Army, and an orthopaedics residency at Charity Hospital in New Orleans, La., Dr. Steadman moved to Lake Tahoe, Calif., where he practiced orthopaedics with increasing emphasis on the treatment of knee disorders. While living there, he was named chief physician and medical chairman 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 Philippon Research Institute in Vail, Colo. In 1990, Dr. Steadman moved to Vail, Colo. 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 Research Institute has supported several research projects at CSU. Dr. Steadman serves as a consultant regarding clinical relevance of our research work, and the CSU Orthopaedic Bioengineering Research Laboratory has done controlled studies investigating his techniques used in human orthopaedic surgery.

Stephen B. Trippel, M.D., Orthopaedic Surgeon; Professor of Orthopaedic Surgery and Anatomy and Cell Biology, Indiana University School of Medicine

Dr. Stephen Trippel is an orthopaedic surgeon with a clinical focus on adult reconstructive surgery and a research focus on musculoskeletal repair. He is professor of Orthopaedic Surgery and of Anatomy and Cell Biology at Indiana University School of Medicine and is an advisory member of the graduate faculty at Purdue University. Dr. Trippel received his M.D. from Columbia University College of Physicians and Surgeons, and completed his orthopaedic residency in the Harvard Combined Orthopaedic Residency Program. He also completed a fellowship in orthopaedic research at Massachusetts General Hospital and a Pediatric Endocrinology research fellowship at the University of North Carolina, Chapel Hill. He served on the faculty of Harvard Medical School before joining the faculty of the Indiana University School of Medicine. Dr. Trippel's current research is focused on the development of new approaches to the treatment of articular cartilage damage, including tissue engineering and gene therapy. This includes an ongoing study with the ORC investigating a novel approach to articular cartilage repair in an equine stifle joint model.

René van Weeren, D.V.M., Ph.D., Diplomate ECVS, Royal Dutch Veterinary Association; Professor of Equine Musculoskeletal Biology, Department of Equine Sciences, Faculty of Veterinary Medicine, Utrecht University, The Netherlands

Paul Rene van Weeren (1957) graduated in 1983 from the Utrecht University Veterinary Faculty (The Netherlands). He became a staff member of the Department of General and Large Animal Surgery in that year and obtained his Ph.D. in 1989. From 1991-1993 he worked as a visiting professor at the Escuela de Medicina Veterinaria of the Universidad Nacional in Heredia, Costa Rica. He became a diplomate of the European College of Veterinary Surgeons in 1994. He was appointed as full professor to the chair of Equine Musculoskeletal Biology in 2007, and is now mainly involved in research with focus areas articular cartilage, tendons, and biomechanics. He became head of the Department of Equine Sciences of the Faculty of Veterinary Medicine of Utrecht University in 2012. Rene van Weeren has been a supervisor of 27 Ph.D. students, who have obtained their degree in the past years and currently supervises 10 Ph.D. students, who will be graduating within the next few years. He is an associate editor of Equine Veterinary Journal, member of the editorial board of The Veterinary Journal, and member of the scientific board of several others. He has been, or is, guest editor of various Special Issues or Supplements of a variety of scientific journals. He has been external examiner for Ph.D. students abroad at various occasions in Belgium, the U.K., France, Austria, Sweden, Norway, and Finland. He is author or co-author of more than 250 peer-reviewed scientific publications and has contributed various chapters to a variety of text books.

Student	Degree	Date Graduated	Current Position
Gayle W. Trotter	M.S.	1981	Formally Professor in equine surgery, Colorado State University now private practice Weatherford, TX
George Martin	M.S.	1983	Private practice, specialist equine surgeon
Alan Nixon	M.S.	1983	Professor in Equine Surgery, Cornell University
Kenneth Sullins	M.S.	1984	Professor, University of Virginia, Marion DuPont Scott Equine Center
Alicia Bertone	M.S., Ph.D.	1987	Professor and Truman Endowed Chair, Ohio State University
John Yovich	M.S., Ph.D.	1988	Vice Chancellor, Murdoch University (now retired)
Cathy Gibson	M.S.	1989	Regulatory veterinarian, Australia
Scott Gustafson	M.S.	1989	Associate Professor, University of Oregon, Corvallis, OR
Jeff Foland	M.S.	1992	Co-owner and specialist equine surgeon, Weatherford Equine Hospital, TX
Dan Steinheimer	M.S.	1995	Specialist radiologist, Veterinary Clinics of America, Loveland, CO
Rick Howard	M.S., Ph.D.	1996	Specialist surgeon private practice, Arizona Equine Medical, AZ
Fahd Al-Sobayil	Ph.D.	1997	Assistant Professor, King Saud University, Riyadh, Saudi Arabia
Abigail Dimock	M.S.	1997	Currently a Ph.D. student, Equine Nutrition (Orthopaedic Related), Rutgers University
JoAnne Engel-Fehr	M.S.	1997	Specialist equine surgeon, Pilchuck Veterinary Hospital, WA
Becky Woodward	M.S.	1998	Graduate Researcher on S-V Dagon Research Vessel, University of British Columbia
Tina Anderson	Ph.D.	1998	Director of Marketing, Purina
Chris Kawcak	M.S., Ph.D.	1998	Professor, Iron Rose Ranch University Endowed Chair in Musculoskeletal Research, Colorado State University
David Frisbie	M.S., Ph.D.	1999	Professor, Orthopaedic Research Center, Colorado State University
Brigitte von Rechenberg	Ph.D.	1999	Dean, College of Veterinary Medicine, University of Zurich
Charles Hubbeling	Ph.D.	1999	Private consulting
Guy Beauregard	Ph.D.	1999	Senior scientist/researcher for private industry.
Andrew Green	M.S.	1999	Engineering Manager for private industry.
Elisha Rentfrow	M.S.	1999	Private consulting
Louise Southwood	M.S., Ph.D.	1998/2002	Associate Professor, University of Pennsylvania School of Veterinary Medicine
Tara Ruttley	M.S.	2000	Engineer for NASA
Carson Shellenberger	M.S.	2000	Engineer for private industry

Student	Degree	Date Graduated	Current Position
Al Kane	Post-Doc	2000	Analytic Epidemiologist, USDA; Affiliate Faculty for Colorado State University's Center of Veterinary Epidemiology and Animal Disease Surveillance Systems
Julie Dechant	M.S.	2000	Assistant Professor, University of California Davis
Troy Trumble	M.S., Ph.D.	2000, 2004	Associate Professor, University of Minnesota
Chengcheng Lui	M.S.	2001	Continuing in school
Jana Read	M.S.	2001	Employed in Quality Control
Erin Peterson	M.S.	2001	Faculty Member, Department of Animal Science, University of Maryland
Anne DePalma	M.S.	2002	
Joel Millets	M.S.	2002	Employed at Osteotech, Allograft Company
Carolyn Skurla	Ph.D.	2002	Assistant Professor, Baylor University
Awad Al-Zaben	Ph.D.	2003	Faculty Member, Electronics Engineering Department, Yarmouk University, Irbid, Jordan
Sophie Morisset	Ph.D.	2003	Assistant Professor, Department of Clinical Sciences, Université de Montréal
Thomas Young	M.S.	2003	Currently job searching
Colin Scruten	M.S.	2004	Private Practice, Alberta, Canada
Lea Rempel	Ph.D.	2004	Post-Doctoral Fellow, University of Kansas Medical School, Currently, Research Scientist, United States Meat Animal Research Center, Clay Center, NE
Chris Sorensen	Ph.D.	2004	Post-Doctoral, National Mass Spectrometry Facility, Environmental Molecular Sciences Laboratory and Biological Sciences Division, Pacific Northwest National Laboratory, Richland, WA
Brandon Santoni	Ph.D.	2006	Postdoctoral Research Fellow, ORBL, Colorado State University
Katja Duesterdieck	Ph.D.	2006	Assistant Professor, Oregon State University
Marti Shearin (Drum)	D.V.M., Ph.D.	2006	Assistant Doctoral Fellow, University of Tennessee
Valerie Perino	M.S., Ph.D.	2007	Completed Ph.D., Equine Orthopaedic Research, Colorado State University
Sam Hendrix	M.S.	2008	Equine Practice, Utah
Ty Wallis	M.S.	2008	Equine Specialty Practice, Texas
Erin Contino	M.S.	2009	Assistant Professor, Equine Sports Medicine and Rehabilitation, Colorado State University
Ryan Carpenter	M.S.	2009	Equine Practice, Southern California
Jennifer Antonnici	Ph.D.	2010	University of California San Diego
Christina Lee	Post-Doc	2010	
Myra Barrett	M.S.	2010	Assistant Professor, ORC, CVMBS, Colorado State University
Melissa King	D.V.M. Ph.D.	1997 2011	Assistant Professor Equine Sports Medicine and Rehabilitation

Student	Degree	Date Graduated	Current Position
Katrina Easton	D.V.M., Ph.D.	2011	University of Sydney
Carrie Adrian	Ph.D.	2011	Director of Rehabilitation Services, VCA Animal Hospitals
Katie Seabaugh	M.S.	2011	Assistant Professor, Farm Practices/Field Services, University of Georgia Hospitals
Lacy Kamm	M.S.	2012	Equine Surgeon, Veterinary Associates, Auckland, New Zealand
Brad Nelson	M.S.	2013	Ph.D. student, ORC
Valerie Moorman	Ph.D.	2013	Assistant Professor, Equine Medicine & Surgery, Colorado State University
Ali Daniel	M.S.	2014	Private Referral Practice, Florida
Josh Donnell	M.S.	2015	Residency in Equine Sports Medicine, Colorado State University
Aimee Colbath	M.S.	2015	Ph.D. student, ORC

Resident	Years of Residency	Date Achieved Board Certification in the American College of Veterinary Surgery
G. W. Trotter	1979-1981	1983
A. J. Nixon	1980-1983	1985
G. S. Martin	1980-1983	1986
R. M. De Bowes	Phase III, 1983-1984	1985
K. Sullins	1981-1984	1986
J. V. Yovich	1983-1986	1987
A. L. Bertone	1983-1986	1988
K.J. Easley	Phase II 1986, Phase III 1986-87	
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. R. Ray	1991-1994	1998
C. E. Kawcak	1992-1995	1996
D. D. Frisbie	1993-1996	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	2010
A. McCoy	2008-2010	2011
K. Seabaugh	2009-2011	2013
L. Kamm	2010-2012	2013
B. Nelson	2010-2013	2014
A. Daniel	2010-2014	2015

Resident	Years of Residency	Date Achieved Board Certification in the American College of Veterinary Sports Medicine and Rehabilitation
D. Ferris	2012-2013	2015
E. Contino	2013-2014	2015
J. Donnell	J. Donnell	2016

PROGRAM SYNOPSIS

History

The Orthopaedic Research Center (ORC) began as a multidisciplinary equine program dedicated to finding methods to treat and prevent equine musculoskeletal disease and injury. Prior to 1984, the program's research was primarily clinical. During this time, many of the techniques for arthroscopic surgery currently used to treat joint problems more effectively and to enable continued athletic function were developed at CSU. We also identified and defined a number of new clinical conditions and documented some of the best methods for diagnosis and treatment. As we developed arthroscopic surgical techniques to treat these clinical conditions, we identified limitations in terms of secondary osteoarthritis (OA) and articular cartilage loss and this led into phase two of our program of finding solutions through scientific research.
A major goal of the program has always been to find solutions to musculoskeletal problems, especially joint injuries and arthritis. The researchers strive to offer the best possible treatment of clinical cases with continual and critical assessment of the results, which are then used to modify treatments and direct the research toward disease prevention. The program's goals are to use state-of-the-art research techniques to find new methods to rehabilitate damaged joints, to prevent or decrease the occurrence of joint disease and musculoskeletal injuries and methods of early detection, and develop better treatments to prevent permanent damage to injured joints and validate manual therapies and rehabilitation techniques. The ORC now includes the Orthopaedic Bioengineering Research Laboratory (OBRL), and we function as a single unit. The ORC and OBRL, together with the Preclinical Surgical Research Laboratory (previously Small Ruminant Orthopaedic Research), and Orthopaedic Oncology make up the Musculoskeletal Research Program, which is a Program of Research and Scholarly Excellence in the university. This designation was originally granted in 2004, renewed in 2008, and renewed again in

2012. The significant collaborations with the College of Engineering, School of Bioengineering, as well as the Department of Health and Exercise Sciences, has added considerably to our research strengths. In recent years, considerable human-based funding (Orthopaedic Foundations, NIH, and corporate grants) has added to our support. The most recent addition to our program has been the development of an equine ambulatory sports medicine service and an equine sports medicine and rehabilitation residency program. This followed the accreditation of the new American College of Veterinary Sports Medicine and Rehabilitation specialty and four of our faculty being Charter Diplomates. This has led to both considerable clinical and research advancements in the rapidly emerging field of equine sports medicine and rehabilitation as a specialty. Most recently, we have achieved funding of $65 million to build an Institute of Translational Biological Therapies.

Research Activities

The following are the research focuses of the ORC. Details of recent and current projects can be found on pages 108-219.

1. Musculoskeletal Tissue Healing

Until a few years ago, we have principally addressed articular cartilage healing and continue to do so, but we have enlarged the focus to include tendons, ligaments, and menisci. For instance, treatments of tendonitis including A-cell therapy, extracorporeal shock wave therapy (ESWT), and mesenchymal stem cell therapies have been assessed and a new traumatic model of tendonitis validated. Projects including a controlled study assessing meniscus repair with mesenchymal stem cells (MSCs) in fibrin, articular cartilage repair with MSCs in autologous platelet-enriched fibrin scaffolds, as well as a clinical study with meniscal injuries in the horse have most recently been published. Other projects include looking at synovial fluid lubricant properties and showing them to be transiently deficient after arthroscopic articular cartilage defect repair with platelet-enriched fibrin with and without MSCs, and the examination of the immunological activity of allogenic equine MSCs.

2. Early Diagnosis of Bone and Joint Disease

This area includes the development of novel imaging techniques (present and future), body fluid biomarkers, and also molecular monitoring. The uses of these early diagnostic techniques include a) Evaluation of the pathogenesis of musculoskeletal disease, b) Early detection of disease processes, and c) Monitoring of therapy, with the long term goal of preventing severe osteoarthritis or failure of joints, tendons, ligaments, and menisci. Work in biomarkers has progressed into imaging biomarkers with particular emphasis on the use of ultrasonography, MRI and computed tomography (CT) in diagnosing early disease change in the limb. Considerable work has also been accomplished using subject-specific finite element modeling of the equine metacarpal phalangeal joint which helps us better understand the stresses that play a role in injury of this critical joint. Other papers under the focus of Early Diagnosis of Bone and Joint Disease include a study on in vivo diffusion characteristics following perineural injection of the deep branch of the lateral plantar nerve with mepivacaine or iohexol in horses, the use of an inertial measurement unit to assess the effect of forelimb lameness on three-dimensional hoof orientation in horses at a walk and trot and also validate a human cervical spine finite element model for risk assessment of spinal cord injury. Other clinically relevant areas include diagnostic stifle joint arthroscopy using a needle arthroscope in the standing horse, a technique developed at the ORC led by Dr. Frisbie as well as hosting a Havemeyer Foundation funded workshop on equine musculoskeletal biomarkers to assess current knowledge and future needs. We have also made advances in contrast enhanced CT as well as development of a standing CT unit.

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

Catastrophic injury is a major problem in the equine athletic industry and we, as well as researchers elsewhere, have demonstrated that the 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. Exercising horses have been followed with imaging techniques including computed tomography (CT) and MRI, nuclear scintigraphy, defined sentinels of early damage, and fluid biomarkers as a means of identifying horses at risk studied with promising results. Recently, biomechanical and modeling studies have been done to monitor early events in bone disease.

Modeling has been used 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. Other factors that can potentially contribute to traumatic musculoskeletal injury including race track surface and conformation have also been part of this research focus. Examples of recent research projects summarized in this section include looking at the impact of race training on volumetric bone mineral density and its spatial distribution in the distal epiphysis of the third metatarsal bone of 2-year-old horses by comparing 2-year-old Thoroughbreds with training compared to untrained controls, a finite element investigation of fracture healing under simulated microgravity loading conditions, evaluation of meniscal mechanics and proteoglycan content in a model of anterior cruciate ligament rupture, and dynamic testing of horseshoe designs with regard to their impact on synthetic and dirt Thoroughbred racetrack materials. We also hosted a second Havemeyer sponsored workshop on equine tendon disease with an overall theme of advances in the understanding of tendinopathies in horses and in humans.

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

Objective evaluation of currently available pharmaceutical agents as well as new potential ones have been a significant focus of our work. These evaluations also include examination of specific biological inhibitors including gene therapy, novel protein therapies, and mesenchymal stem cells therapies. These newer therapies offer the potential of inhibiting the disease process sufficiently early so that the need forpalliative drugs currently used is decreased. Recent projects summarized in Summaries of Research Projects include evaluation of an intravenous combination of sodium pentosan polysulfate, N-acetyl glucosamine, and sodium hyaluronan, the use of genomics in drug discovery, a review of the use of firocoxib (Equioxx™) for the treatment of equine osteoarthritis, a comparison of subjective methods to identify mild forelimb lameness and its response to therapy as well as the evaluation of intravenous hyaluronan, sodium chondroitin sulfate and N-acetyl-D-glucosamine combination (Polyglycan®) versus saline for equine osteoarthritis, and development of a new technique for injection of the navicular bursa so that the bursa can be medicated with minimal risk of puncturing the deep digital flexor tendon (DDFT).

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

This is a newer focus that includes objective assessment of integrative therapies including physical manipulation and acupuncture for management of musculoskeletal disease and pain as well as rehabilitative techniques of swimming, under water treadmilling and hyperbaric therapy. This area also includes study of the pathogenesis of musculoskeletal problems biomechanically and using gait analysis (kinetics, kinematics) and electromyography (EMG), as well as novel methods of pain detection. 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. Summaries include a chapter reviewing problems of the back and pelvis in the horse and their treatment, the physiologic effects of long term immobilization of the equine distal limb, a review chapter on chiropractic treatment for athletic horses as an equine rehabilitation technique and a review chapter on aquatic rehabilitation.

Impact

As a preeminent equine orthopaedic research program, both nationally and internationally, the Orthopaedic Research Center provides critical new findings of significant clinical impact and has been able to attract talented students who wish to pursue careers in orthopaedic research. Students choose this program because of its excellent reputation and because of the opportunities they have to be involved in research during their under-graduate and pre-veterinary programs. Many pre-veterinary students have served as volunteers in the equine orthopaedic research program over the past 10 years; this allows students to develop a high level of research expertise during this undergraduate experience. This involvement encourages students to pursue advanced degrees and ultimately research careers rather than

traditional private veterinary practice. Our program also impacts undergraduate and pre-veterinary education by applying findings from research studies to clinical veterinary medicine. The breadth of dissemination of information from the Orthopaedic Research Center is extensive, with information distributed to graduate and undergraduate students in eight Departments within five Colleges at Colorado State University. Many faculty members from these five 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 ORC's extensive collaboration with the Steadman Philippon Research Institute and biotechnology companies, as well as collaboration in five NIH research grants, 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 ORC's findings.

Program Trends

1. Faculty and Staff. Over the last 10 years, funding for our orthopaedic research and specialized personnel availability has increased dramatically. Until 1994, orthopaedic research was being performed by faculty members within the Department of Clinical Sciences. Since that time, the ORC research involves fourteen full-time faculty members (including three Bioengineering Faculty) in our Center. To support the work of the Faculty Researchers, we now have eight research associates. We had eleven Ph.D. students and nine resident M.S. students in the program in 2014. Current funding is around $4 million annually.

2. Facilities. Thanks to generous private donors, the construction of the Gail Holmes Equine Orthopaedic Research Center and the remodeling of the orthopaedic research laboratories was completed 13 years ago. In addition, a state-of-the-art equine MRI facility has been in operation for eight years, and this was also funded by private donations. More recently, a state-of-the-art gait analysis facility has been added and, most recently, the roof of the ORC Laboratories has been replaced as a gabled roof, and further renovations to accommodate expansion of Bioengineering has been done. We have also received three $3 million University Endowed Chairs from Barbara Cox Anthony, Iron Rose Ranch, and Abigail K. Kawananakoa, a $1.5 million Chair in Musculoskeletal Imaging from the estate of Kenneth and Virginia Atkinson, and most recently, a $6 million Presidential Endowed Chair from John and Leslie Malone. We continue to pursue endowed funding to make all of our positions permanent.

3. Further development of an Equine Ambulatory Sports Medicine Service. An equine ambulatory sports medicine service was initiated in 2010, and has now grown to where Drs. Chris Kawcak and Melissa King have been joined by Dr. Mindy Story. There are now three research associates, Whitney McMillan, Lindsay Richardson, and Meredith Park assisting in this service offering state-of-the-art expertise in equine musculoskeletal problems in athletic horses. Britt Madsen joined the team as an administrative coordinator of the program. We have three equine sports medicine residents (one in each year) and are have graduated our second resident from her three-year program in 2014. The service commenced in 2011 and has continued to exceed our expectations in demand.

4. Establishment of Equine Sports Medicine and Rehabilitation Residencies. A new American veterinary specialty, the American College of Veterinary Sports Medicine and Rehabilitation has been developed and was accredited by the American Veterinary Medical Association in May 2009. There were 27 Charter Diplomates established by a nomination and Delphi election system. Four of our faculty, Drs. McIlwraith, Haussler, Kawcak, and Frisbie, were made Charter Diplomates of the new College. We then established an equine sports medicine and rehabilitation residency program to train future specialists in 2010. Our first resident, Dr. Dora Ferris commenced in July 2010 followed by our second resident, Dr. Erin Contino starting in July 2011, and our third resident Dr. Josh Donnell started in July 2012.

5. Unrestricted Funding from Donors and Foundations. The period 2015 has been one of continuing to function with good support and further increase in faculty and staff positions. Donor support is critical to our continued operation and growth.

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 orthopaedic disease in humans and animals. In addition to protein biomarker analysis and development, this program is supported by several molecular biology applications such as antibody purification, real time PCR assay development and gene expression analysis, cell and tissue culture techniques, adenoviral construction and cloning, gene chip microarray, biomechanical testing, and histological procedures. As the support structure for biomedical research continues to expand with modern medical discoveries and advances, the Orthopaedic Research Center will continue to provide groundbreaking research for the future.

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

1. Biomarker Analysis

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

Extensive experience with the following biomarker assays:

Detection of Cartilage Markers:

- **Alcian Blue:** Standardize measurement of 35S labeled proteoglycan complexes.
- **C1,C2:** An assay to standardize the measurement of Types I and II collagen degradation.
- **CPII:** An assay to measure type II collagen carboxy propeptide (C-propeptide).
- **CS-846:** Measurement of Aggrecan Chondroitin Sulfate 846 Epitope.
- **Eq. Col 2 ¾ (CEQ):** An assay to quantify equine specific Type II collagen, which has also been proven to work with canine fluid.
- **GAG DMMB:** An assay for standardized measurement of glycosaminoglycans in biological fluids and/or tissues.
- **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.
- **Sircol Assay:** Assay to assess the amount of newly synthesized collagen in cartilage, tendon or cell culture media.

Detection of Bone Markers:

- **C1,2C:** An assay to standardize measurement of Type I and II collagens (378 assay, MMP1 and MMP13).
- **Metra™ BAP:** Quantification of bone-specific alkaline phosphatase in serum and synovial fluid samples.

- **Metra™ Osteocalcin EIA:** An enzyme immunoassay for the quantification of intact (de novo) osteocalcin.
- **Serum Cross Laps® (CTX):** Assay for the quantification of degradation products of C-terminal telopeptides of Type-I collagen in serum and plasma.

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

Western, Southern, and Northern Blotting

Many other assays available. Please inquire.

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

2. Biomechanical Testing

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

Tissue explants or cell-seeded scaffolds

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

3. Molecular Biology

Evaluation of metabolic activity in living tissues
- Radiolabel protocols available

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

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

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

Culturing of Mesenchymal Stem Cells (bone-marrow derived or fat-derived)
- Cell culture expansion of bone-marrow derived or adipose-derived cells, including three-dimensional culturing for clinical use
- Flow cytometry analysis of MSC and other cellular cultures

Adenoviral Vector construction and cell transfection
- The development of adenoviral vectors for the delivery of genes into cells

4. Histology Services

Decalcified tissue histology

Immunohistochemistry

Paraffin and frozen Sectioning and staining of paraffin embedded samples

Live/Dead Cellular Tissue Staining and Fluorescent Imaging

Histomorphometric analysis

RESEARCH TECHNIQUES AVAILABLE 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, cardiovascular, neuronal or skeletal injury and/or disease. The primary research foci include:

1. Computational Simulation of Orthopaedic Conditions and Treatments

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

2. 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

3. Engineering and Growth Factor Therapy for Cartilage and Bone Repair

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

4. Retrieval Analysis for Failure Assessment, Design Improvement, and Tissue Interface

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

5. Biocompatibility and Biomaterial/ Tissue Interface

a. Interface biomechanics
b. Tissue response to biomaterials

6. Comparative Orthopaedics and Animal Models

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

7. Biomechanical Analysis Equipment available includes: minibionix MTS machine, standard MTS, spine tester, biaxial tester

a. Range of motion/kinematics
b. Materials testing for biomechanical strength
c. Dynamic and Quasi-static analyses
d. Fatigue and life-cycle analyses

8. Histological structural analyses

a. MicroComputedTomography (μCT) – High resolution imaging of bone and / or implants to determine bone growth and healing
b. Decalcified and non-decalcified tissue histology
c. Dynamic and Static Histomorphometric analysis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Lauryssen C., Fanton G.S., Ehrhart E.J., Ruehlman D., Seim H.B., Easley J.T . Comparison of a novel porous titanium-nickel intervertebral fusion device and a poly-ether-ether-ketone intervertebral fusion device in a sheep lumbar fusion study. In, Proc of Orthopaedic Research Society Symposium. Las Vegas, NV. March, 2015.

Luan T., Liu X., Easley J.T., Ravishankar B., Puttlitz C., Feeley B. Muscle atrophy and fatty infiltration after an acute rotator cuff repair in a sheep model. In, Proc of Orthopaedic Research Society Symposium. Las Vegas, NV. March, 2015.

Mama K., Frisbie D.D., Ullmer J.J. The effects of xylazine, dexmedetomidine and clonidine on normal and interleukin-1 conditioned equine articular cartilage explants. In, Proceedings World Congress of Veterinary Anesthesiology. Kyoto, Japan. September 1-4, 2015.

McIlwraith C.W., McCarthy H., Archer C., Barrett M., Frisbie D.D. Articular cartilage progenitor cells for the repair of articular defects: A long-term strenuous exercise model in horses. International Cartilage Repair Society 12th World Congress. Chicago, Illinois. May 8-11, 2015. Abstract 7029.

McIlwraith C.W. Stem cell treatment for cartilage injuries: Equine studies (extended abstract). International Cartilage Repair Society 12th World Congress. Chicago, Illinois. May 8-11, 2015. Abstract 7163.

McIlwraith C.W. Mesenchymal stem cells – evidence of usefulness in equine orthopaedics. American College of Veterinary Surgeons Surgical Summit. Nashville, Tennessee. October 22-24, 2015.

McIlwraith C.W. Stem cell treatments for cartilage injuries: In situ or intraarticular administration? American College of Veterinary Surgeons Surgical Summit. Nashville, Tennessee. October 22-24, 2015.

Moorman V.J., Frisbie D.D., Kawcak C.E., McIlwraith C.W. Effect of sensor position on kinematic output of an inertial sensor system. In, Proceedings American Association of Equine Practitioners Annual Convention. Las Vegas, Nevada. December 5-9, 2015;61:454.

Murray M., Fleming B.C., Easley J.T., Palmer R.H. Biologic treatments for sports injuries. Orlando, FL. American Orthopaedic Society for Sports Medicine Grant Development Workshop. July 2015.

Murray M., Fleming B.C., Easley J.T., Palmer R.H. Use of extracellular matrix scaffold and blood cells to augment rotator cuff healing. Proc 2015 Meeting of Am Ortho Soc Sports Med (AOSSM).

Pascual-Garrido C., Chahla J., Goodrich L., Mei-Dan O., Mardones R., Easley J.T. A novel transchondral microfracture technique for chondral bubble lesions in a goat animal model. American Orlando, FL. American Orthopaedic Society for Sports Medicine Grant Development Workshop. July 2015.

Palmer R.H. Canine lameness: Is the elbow or the shoulder? In, Proc 2015 Poland Small Animal Veterinary Assoc;pp. 89-98.

Palmer R.H. Canine Lameness: Is the hip or the stifle? In, Proc 2015 Poland Small Animal Veterinary Assoc:pp. 99-104.

Palmer R.H. Tell me where it hurts. The Art of the Canine Lameness Exam. In, Proc 2015 Poland Small Animal Veterinary Assoc:pp. 105-111.

Palmer R.H. Strategies for Effective Management of Canine Osteoarthritis. In, Proc 2015 Poland Small Animal Veterinary Assoc:pp. 113-120.

Palmer R.H. Concepts, Controversies & Errors to Avoid in Extracapsular Stifle Stabilization. In, Proc 2015 Poland Small Animal Veterinary Assoc:pp. 121-130.

Palmer R.H. Concepts, Controversies & Technique Tips for Patellar Luxation Correction in Small Breed Dogs. In, Proc 2015 Poland Small Animal Veterinary Assoc:pp. 131-142.

Palmer R.H. State of the Art Lecture – TPLO: Excellence vs. Error. Bangkok, Thailand; May 16, 2015. In, Proc 2015 World Small Animal Veterinary Association:89-98.

Palmer R.H. Principles of the CORA System. Rimini, Italy; May 29, 2015. In, Proc 2015 Meeting of SCIVAC.

Palmer R.H. Angular limb deformity correction. Rimini, Italy; May 29, 2015. In, Proc 2015 Meeting of SCIVAC.

Palmer R.H. Treatment of limb length discrepancies. Rimini, Italy; May 29, 2015. In, Proc 2015 Meeting of SCIVAC.

Palmer R.H. Medial coronoid process disease: pathophysiology and treatment options. Nashville, TN; October 22, 2015. In, Proc 2015 Meeting of Am Coll Vet Surgeons.

Pauly H. M., Popat K.C., Kelly D.J., Haut Donahue T. L., Flat and 3D Electrospun Scaffolds for Ligament Tissue Engineering: Mechanical Properties and Cellular Response. Annual Orthopaedic Research Society meeting. Las Vegas, NV. March 2015.

Pauly H. M., Popat K.C., Kelly D.J., Haut Donahue T. L., Influence of nano- and micro-scale structure of aligned electrospun scaffolds on mechanical properties and cellular response. SB3C2015 Summer Biomechanics, Bioengineering and Biotransport Conference. Snowbird Resort, Utah. June 17-20, 2015.

Pimentel R., Ketelhut N., Kindred J., Tracy B., Rudroff T., & Reiser R. Greater role for less affected limb in standing balance with MS. International Journal of MS Care. 2015;16(6): 301.

Rowland A.L., Goodrich L.R., Bass L.D., Aldrich E.D., Edmondson E.F., Mueller L.W. Bilateral keratomas in a draft horse mare. Equine Veterinary Education. 2015. Accepted and in press.

Steineman B. D., Barber T., Haut Donahue T. L., Development of Shoe Midsole Design Using Material Natural Frequencies. SB3C2015 Summer Biomechanics, Bioengineering and Biotransport Conference. Snowbird Resort, Utah. June 17-20, 2015.

Taylor B., Conway J., Porter E., Matyjaszek S., Easley J.T. Computed tomographic findings of a severely destructive mandibular osteosarcoma in a horse. Minneapolis, MN, October 2015. In, Proc of ACVP/ASVCP/STP Combined Annual Meeting. 2015.

Wheatley B.B., Morrow D.A., Odegard G.M., Kaufman K. R., Haut Donahue T.L., Predicting the Stress and Intramuscular Pressure Response of Whole Skeletal Muscle Through Optimized Finite Element Analysis. SB3C2015 Summer Biomechanics, Bioengineering and Biotransport Conference. Snowbird Resort, Utah. June 17-20, 2015.

Wheatley B. B., Pietsch R., Haut Donahue T. L., Williams L. N. Numerical Modeling of Skeletal Muscle Under High Strain and Stress Relaxation Compression Conditions. SB3C2015 Summer Biomechanics, Bioengineering and Biotransport Conference. Snowbird Resort, Utah. June 17-20, 2015.

Oral Presentations

Contino E.K. Making Sense of Diagnostic Analgesia. Texas Equine Veterinarian Associations Summer Symposium. Marble Falls, Texas. August, 2015.

Contino E.K. Physical Therapy–The Art and Science. Texas Equine Veterinarian Associations Summer Symposium. Marble Falls, Texas. August, 2015.

Contino E.K. Physical Therapy and Rehabilitation panel discussion. Texas Equine Veterinarian Associations Summer Symposium. Marble Falls, Texas. August, 2015.

Contino E.K. Equine Rehabilitation. American Association of Equine Practitioners 360° 'Foot to Fetlock' course. Fort Collins, Colorado. June, 2015.

Contino E.K. Equine Lameness. Colorado State University Junior practicum. Didactic lecture (1 hour) and lab (3 hours); 3rd year veterinary students. 2015.

Contino E.K. Lab instructor on anatomy (4 hours), joint injections (4 hours), ultrasound guided injections (4 hours) and lameness workup (8 hours). American Association of Equine Practitioners 360° Foot to Fetlock course. National and International Equine Veterinarians. Fort Collins, Colorado. June, 2015.

Contino E.K. Physical Therapy Modalities. Colorado State University Equine Sports Medicine practicum. Didactic lecture (2 hours) and lab (2 hours); 3rd year veterinary students. April, 2015.

Contino E.K. Pitfalls of Diagnostic Analgesia; Colorado State University's Annual Conference. Fort Collins, Colorado. Interactive lecture (1 hour); local veterinarians. April, 2015.

Contino E.K. From Diagnosis Through Rehabilitation; Colorado State University's 4th Annual Equine Symposium. Fort Collins, Colorado. Lecture (1 hour); local veterinarians and students. February, 2015.

Contino E.K. Equine joint injections and musculoskeletal ultrasound. Zoetis Equine Joint Injection and Musculoskeletal Ultrasound Course. Co-organizer of this 2-day CE course, didactic lecture (1 hour) and lab (8 hours); large animal practitioners. January, 2015.

Palmer R.H. Orthopedic Lecture Series. World Small Animal Veterinary Association. Invited Lecturer. Bangkok, Thailand. 6 hours. May, 2015.

Easley J.T. Animal Welfare in Orthopaedic Research: Focus on Refinement and Reduction Invited Lecturer and Panelist Las Vegas, NV. 3 hours. March, 2015.

Easley J.T. Equine Respiratory Update North American Veterinary Conference Invited Lecturer. Orlando, FL. 8 hours. 2015.

Easley J.T. Equine Local Anesthesia and Pain Management, North American Veterinary Conference, Invited Lecturer. Orlando, FL. 8 hours. 2015.

Ehrhart N.P. Dutch Oncology Conference. Soesterberg, Holland. Lecturer, 6 hours. 2015.

Ehrhart N.P. Invited Lecturer. University of Liege. Liege, Belgium. 2 hours. 2015.

Ehrhart N.P. New Jersey Veterinary Medical Association. Lecturer, 10 hours. Newark, NJ. 2015.

Frisbie D.D. Ultrasound and Standing Arthroscopy of the Equine Stifle Joint. Lecture, Stifle: Anesthesia, normal anatomy, standing arthroscopy, case examples and medical treatments, lab and demo. 2 hours of lecture, 4 hours of lab. Colorado State University. Fort Collins, CO. September 19, 2015.

Frisbie D.D. Advanced Arthroscopy Surgery Course. Lecture, Femoropatellar joint, lab, proximal forelimb, distal limb, proximal hindlimb and delegates choice. 30 minutes of lecture, 6.5 hours of lab. Colorado State University. Fort Collins, CO. September 17-18, 2015.

Frisbie D.D. Basic Arthroscopy Surgery Course. Arthroscopic surgery of the carpus and fetlock 4 hours of lab. Colorado State University. Fort Collins, CO. September 16, 2015.

Frisbie D.D. European Advanced Arthroscopy Course. Lecture, Elbow joint, Femoropatellar joint, Standing diagnostic arthroscopy, Lab, proximal forelimb, distal limb, proximal limb and delegates choice. 1.5 hours of lecture, 4 hours of lab. Newmarket, UK. April 17-18, 2015.

Haussler K.K. Focus on the Equine Spine: Advanced Course (Part 1). 9 hours lecture, 10 hours laboratory. Utrecht, Netherlands. October, 2015.

Haussler K.K. Equine Rehabilitation Certificate Program. 4 hours lecture, 15 hours laboratory. College of Veterinary Medicine, University of Tennessee. Knoxville, TN. November, 2015.

Haussler K.K. Equine Rehabilitation Certification Course, 8 hours lectures, 5 hours laboratory. Espaco Equus, Cotia, Sao Paulo, Brazil. June, 2015.

Haussler K.K. Medical Acupuncture for Veterinarians. 2 hours lecture. 4 hours laboratory. Fort Collins, CO. October, 2015.

Haussler K.K. ABRAVEQ, 4 invited lectures. Biomechanics of the equine pelvis and sacroiliac joints. Treatment options for sacroiliac joint disease. The effect of chiropractic treatment on back function and performance. Diagnosis and treatment of cervical spine issues. 14th Annual Conference. Aguas de Lindoia, Sao Paulo, Brazil. June, 2015.

Haussler Kevin K.K. 4 hours lecture. 8 hours laboratory. Diagnosis and treatment of sacroiliac joint disease. Medical and surgical management of back problems. Equine spinal rehabilitation. Veterinary technician program, Equine spinal rehabilitation, Laboratory, Clinical examination of the back, laboratory, saddle fitting. Northeast Association of Equine Practitioners, Pittsburgh, PA. September, 2015.

Haussler K.K. Conditions and treatment of the equine neck. Conditions and treatment of the equine back, Conditions and treatment of the equine pelvis. 2015.

Haussler K.K. Student Chapter of the American Association of Equine Practitioners, College of Veterinary Medicine and Biomedical Sciences, Demonstration and wet lab: Equine chiropractic evaluation. Colorado State University. Fort Collins, CO. October 2015.

Haussler K.K. Equine Research Seminar Series. Clinical presentation and pathogenesis of ill-defined neck problems. Dept. of Clinical Sciences, Colorado State University. Fort Collins, CO. April 2015.

Haussler K.K. Canine Rehabilitation Rounds. Fort Collins, CO. April 2015.

Haussler K.K. Departmental of Large Animal Clinical Sciences. The role of the neck in equine health and performance. Michigan State University, East Lansing, MI. March, 2015.

Haut Donahue T. L. The ORS and its Role in Encouraging Collaboration. Orthopaedic Research Society Annual Meeting. Las Vegas, NV. March, 2015.

Kawcak C.E. Treatment and rehab options Round Table, clinical workups (7 hours). International Society of Equine Locomotor Pathology. 3 Day Module-Hindlimb Prox. Susp. & Distal Hindlimb at Animal Imaging. Irving, TX. March, 2015.

Kawcak C.E. American Association of Equine Practitioners 360 meeting. Diagnosing, Imaging, and Treating from the Foot to the Fetlock: Everything You Need or Want to Know. .5 hours gross anatomy lab. 1 hour arthroscopic anatomy lab, 4 hours radiology lab, 1.5 case presentation lecture, 1.5 lameness lecture, 6 hours lameness lab. Fort Collins, CO. June 28–July 1, 2015.

Kawcak C.E. Ultrasound and Standing Arthroscopy of the Equine Stifle Joint Course. Colorado State University. Fort Collins, CO. 3 hours of laboratory. September 2015.

Kawcak C.E. Basic Arthroscopic Surgery Course. Colorado State University. Fort Collins, CO. 4 hours of laboratory. September 2015.

Kawcak C.E. Subchondral bone anatomy and microstructure. The response of subchondral bone to loading, Medical therapies and their role in managing subchondral bone pain, Imaging biomarkers and their role in injury prevention. Dorothy Russell Havemeyer Foundation Symposium: Subchondral Bone Problems in the Equine Athlete, Newmarket Equine Hospital, Newmarket, UK. May 2015.

King M.R. Diagnostic Analgesia of the Deep Branch of the Lateral Plantar Nerve: Where Does it Go? NAVC; American Association of Rehabilitation Veterinarians Section Invited Speaker. Gainesville, FL. 2015.

King M.R. Equine Therapeutic Exercise: Can We Make a Difference? NAVC; American Association of Rehabilitation Veterinarians Section Invited Speaker. Gainesville, FL. 2015.

King M.R. Equine Aquatic Therapy: Unchartered Waters NAVC; American Association of Rehabilitation Veterinarians Section Invited Speaker. Gainesville, FL. 2015

King M.R. Rehabilitation Modalities: Mobile Practice and Hospital Practice NAVC; American Association of Rehabilitation Veterinarians Section Invited Speaker. Gainesville, FL. 2015.

King M.R. Equine Regenerative Medicine Equine Rehabilitation Conference Invited Speaker. Gainesville, FL. 2015.

McIlwraith C.W. AAEP 17th Annual Resort Symposium. Hawaii. Joint therapies in the horse. 5 hours of lecture. January 28, 2015.

McIlwraith C.W. Commercial Consigners and Breeders 2015 Educational Symposium. Lexington, KY. Significance of radiographic changes of the sesamoid bone in later soundness in the Thoroughbred racehorse. February 3, 2015.

McIlwraith C.W. Ontario Racing Commission Annual Meeting. Guelph, Ontario, Canada. Guest speaker. Advances in the diagnosis and treatment of joint disease in the Thoroughbred racehorse. February 11, 2015.

McIlwraith C.W. Save the Cord Foundation webinar. Advances in the use of mesenchymal stem cells in the treatment of musculoskeletal disease in horses and humans. March 17, 2015.

McIlwraith C.W. Advanced arthroscopic surgery course. Newmarket Equine Hospital, Newmarket, UK. 4 hours lecture and four 2 hour laboratories. April 17-18, 2015.

McIlwraith C.W. 4th Annual Penn. Cartilage Repair Symposium. Invited lecture. Stem cell therapeutics and animal models for osteochondral repair and participation in laboratory involving hydrogel implantation into human articular cartilage defects. April 24-25, 2015.

McIlwraith C.W. Equine arthroscopic surgery course. Hong Kong. Principal speaker. 6 hours of lecture and 4 laboratories. May 5-6, 2015.

McIlwraith C.W. 12th World Congress of the International Cartilage Repair Society. Invited lecture. Stem cell treatment for cartilage injuries: equine studies and abstract podium. Articular cartilage progenitor cells for the repair of articular defects: a long-term strenuous exercise model in horses. May 8-11, 2015.

McIlwraith C.W. Dorothy Havemeyer Symposium on Subchondral Bone Problems. Can subchondral bone regenerate and can we influence this? Fluid biomarkers and their role in bone injury prevention. Organizer and moderator with 2 lectures. May 13-16, 2015.

McIlwraith C.W. TOBI the Orthobiologic Institute 5th annual conference. Invited speaker. Use of bone marrow-derived autologous MSCs and autologous conditioned serum in equine traumatic joint injury, osteoarthritis and articular cartilage repair, and panelist. White blood cells in PRP: friend or foe? June 12-13, 2015

McIlwraith C.W. AAEP360 Diagnosing, Imaging and Treating from the Foot to the Fetlock: Everything you need or want to know. Lecture, Arthroscopic pathology of joint/tendon sheath and bursa from foot to fetlock. June 28-July 1, 2015.

McIlwraith C.W. Goulburn Valley Equine Hospital. Referring veterinarian seminar. Five 1-hour presentations. Current conventional treatments for traumatic joint disease. New biologic therapies. Current surgical and conservative management in the treatment of osteochondritis dessicans. Treatment of subchondral cystic lesions of the stifle and Mesenchymal stem cells – appropriate use in equine joint disease. August 10, 2015.

McIlwraith C.W. 2-day clinic in arthroscopic surgery techniques. Scenic Rim Veterinary Services. Beaudesert, Queensland, Australia. August 11-12, 2015.

McIlwraith C.W. Basic Arthroscopic Surgery Course. Colorado State University. Fort Collins, CO. 4 hours lecture, 4 hours laboratory. September 16, 2015.

McIlwraith C.W. Advanced Arthroscopic Surgery Course. Colorado State University. Fort Collins, CO. 3 hours lecture, 8 hours laboratory. September 17-18, 2015.

McIlwraith C.W. American College of Veterinary Surgeons Surgical Summit. 2 presentations, Mesenchymal stem cells – evidence of usefulness in equine orthopaedics and Stem cell treatments for cartilage injuries: in situ or IA administration? October 24, 2015.

Palmer R.H. Lameness & Orthopedic Surgery Lecture Series. Poland SAVA. Invited Lecturer. Warsaw, Poland. 6 hours. November, 2015.

Palmer R.H. Orthopedic Lecture Series. Japan Veterinary Practitioners Group. Invited Lecturer. Osaka, Yokohama, Tokyo, Japan. 6 hours. October 2015.

Palmer R.H. Orthopedic Lecture Series. American College of Veterinary Surgeons. Lecturer & Session Director. Chicago, IL, 6 hours. October, 2015.

Palmer R.H. Orthopedic Course, 22nd Annual Complete Course on External Skeletal Fixation. Lecturer/Lab Instructor. Frisco, TX. 14 hours. September, 2015.

Palmer R.H. Orthopedic Lecture Series, Congreso Veterinario de Leon. Invited Lecturer. Leon, Mexico. 6 hours. August, 2015.

Palmer R.H. Joint Surgery & Lameness, Wyoming VMA. Lecturer. Sheridan, WY. 4 hours. June, 2015.

Palmer R.H. Limb Deformity, Traumatology, Joint Surgery Lecture Series. SCIVAC. Invited Lecturer. Rimini, Italy, 6 hours. May, 2015.

Palmer R.H. Orthopedic Lecture Series. World Small Animal Veterinary Association. Invited Lecturer. Bangkok, Thailand. 6 hours. May, 2015.

Palmer R.H. Orthopedic Lecture Series, North American Veterinary Conference Lecturer. Orlando, FL, 9 hours. January, 2015.

FUNDING, REVENUE AND EXPENSES

Investigators	Sponsor	Title	Period	Amount
Tammy Donahue (Primary PI)-1374; Ketul C. Popat (Co-PI)-1374	NSF - National Science Foundation	Development of a Novel Bioinspired Fiber Reinforced Hydrogel that Recapitulates Developmental Processes to ...	7/15/2013-6/30/2016	$77,500.00
Tammy Donahue (Primary PI)-1374	NSF - National Science Foundation	International Undergraduate Research Experiences Involving the Jaipur Foot	9/1/2014-8/31/2017	$82,659.00
Tammy Donahue (Primary PI)-1374	Technology Service Corporation	University Engineering Design Challenge - Development of Rapid Innovation Processes for RRMMS Requirements	8/15/2014-8/14/2015	$20,000.00
Tammy Donahue (Primary PI)-1374; Ketul C. Popat (Co-PI)-1374	NSF - National Science Foundation	Development of a Novel Bioinspired Fiber Reinforced Hydrogel that Recapitulates Developmental Processes to ...	7/15/2013-6/30/2016	$97,500.00
Nicole P. Ehrhart (Primary PI)-1678	AlloSource	Consulting Task Order #4	1/1/2009-12/31/2017	$88,000.00
David D. Frisbie (Primary PI)-1678; C. Wayne McIlwraith (Co-PI)-1678	Indiana University NIH ROI	Gene Transfer Treatment of Articular Cartilage Damage	3/1/2012-2/28/2015	$134,867.00
David D. Frisbie (Primary PI)-1678; C. Wayne McIlwraith (Co-PI)-1678	Indiana University NIH ROI	Gene Transfer Treatment of Articular Cartilage Damage	3/1/2012-2/28/2015	$12,999.00
David D. Frisbie (Primary PI)-1678; C. Wayne McIlwraith (Collaborator)-1678; Christopher E. Kawcak (Collaborator)-1678; Myra Frances Barrett Frisbie (Collaborator)-1681	LifeNet Health Foundation	Equine Osteochondral Defect Study	2/12/2014-2/11/2015	$4,812.00
David D. Frisbie (Primary PI)-1678	M.I.T. Massachusetts Institute of Tech.	Cartilage Repair Using Self Assembling Peptide Scaffolds	9/1/2013-8/31/2015	$44,585.00
Laurie R. Goodrich (Primary PI)-1678; Aimee Carol Colbath (Co-PI)-1678; Steven W. Dow (Collaborator)-1678	Grayson-Jockey Club Research Foundation	Comparing Immune Properties of Autogenous and Allogeneic Bone Marrow Derived Mesenchymal Stem Cells	4/1/2015-3/31/2016	$15,000.00
Laurie R. Goodrich (Primary PI)-1678; Steven W. Dow (Collaborator)-1678; C. Wayne McIlwraith (Collaborator)-1678	Grayson-Jockey Club Research Foundation	Immune Properties of Autogenous and Allogeneic Bone Marrow Derived Mesenchymal Stem Cells	4/1/2015-3/31/2017	$40,860.00
Christopher E. Kawcak (Primary PI)-1678; Bradley Bernard Nelson (Co-PI)-1678; Laurie R. Goodrich (Collaborator)-1678; Myra Frances Barrett Frisbie (Collaborator)-1681; C. Wayne McIlwraith (Collaborator)-1678	Grayson-Jockey Club Research Foundation	Contrast Enhanced CT for Detection of Cartilage Injury	4/1/2014-3/31/2016	$68,750.00
John D. Kisiday (Primary PI)-1678	Morris Animal Foundation	Chondrogenic Priming of Equine Bone Marrow-Derived Mesenchymal Stem Cells	3/1/2014-2/28/2016	$37,817.00
Christian M. Puttlitz (Primary PI)-1374; Stewart D. Ryan (Co-PI)-1678; Raymond Clifton Browning (Co-PI)-1582	NASA - Natl Aeronautics & Space Admin.	Fracture Healing in Haversian Bone Under Conditions of Simulated Microgravity	8/24/2011-8/23/2014	$66,801.00

Investigators	Sponsor	Title	Period	Amount
Christian M. Puttlitz (Primary PI)-1374; Stewart D. Ryan (Co-PI)-1678; Raymond Clifton Browning (Co-PI)-1582	NASA - Natl Aeronautics & Space Admin.	Fracture Healing in Haversian Bone Under Conditions of Simulated Microgravity	8/24/2011-8/23/2015	$117,154.00
Christian M. Puttlitz (Primary PI)-1374; Kirk McGilvray (Collaborator)-1374	Acuitas Medical Limited	Acuitas - Comparative Analysis of Human Lumbar and Thoracic Vertebra using Micro Computed Tomography and the fineSA algorithm	11/10/2014-3/31/2015	$23,871.00
Christian M. Puttlitz (Primary PI)-1374; Raymond Clifton Browning (Co-PI)-1582; Stewart D. Ryan (Co-PI)-1678	NASA - Natl Aeronautics & Space Admin.	Fracture Healing in Haversian Bone Under Conditions of Simulated Microgravity	8/24/2011-8/23/2015	$177,849.00
Christian M. Puttlitz (Primary PI)-1374; Raymond Clifton Browning (Co-PI)-1582; Stewart D. Ryan (Co-PI)-1678	NASA - Natl Aeronautics & Space Admin.	Fracture Healing in Haversian Bone Under Conditions of Simulated Microgravity	8/24/2011-8/23/2015	$100,000.00
Christian M. Puttlitz (Primary PI)-1374	Medtronic, Inc.	Biomechanical Analysis of the OLIF25 Plate Cage: A Cadaveric Study	10/21/2014-10/21/2015	$89,424.00
Richard A. Slayden (Primary PI)-1682	Anacor Pharmaceuticals, Inc.	Overcoming Resistance by the Application of Born to Ribosomal Inhibitors	10/16/2013-4/16/2017	$463,329.00
Richard A. Slayden (Primary PI)-1682	Stony Brook University	FtsZ Inhibitors for Anti-TB Chemotherapy Novel Antimicrobials Targeting Cell Division	12/1/2008-11/30/2014	$7,306.00
Richard A. Slayden (Primary PI)-1682	Stony Brook University	FtsZ Inhibitors for Anti-TB Chemotherapy Novel Antimicrobials Targeting Cell Division	12/1/08-11/30/14	$33,297.00
Richard A. Slayden (Primary PI)-1682	Anacor Pharmaceuticals, Inc.	Overcoming Resistance by the Application of Born to Ribosomal Inhibitors	10/16/13-4/16/17	$207,653.00

Funded Research not included on Award Dollars Received Report from Office of Vice President of Research report

Christopher Kawcak (PI)	CRC CVMBS CSU	Postmortem Racing Project	7/1/2014-6/30/2015	$16,017.00
David Frisbie (PI)	CRC CVMBS CSU	Evaluation of freeze-dried autologous conditioned serum (ACS) for the prevention of pathologic changes in joint tissue exposed to inflammatory conditions	7/1/2014-6/30/2015	$18,383.00
TOTAL				**$1,805,483.00**

Donations	Amount
The Louis L. Borick Foundation	$250,000.00
Allen and Company	$250,000.00
Steadman Philippon Research Institute	$110,000.00
Dea Family Foundation	$50,000.00
Winkelried, Jon & Abby	$50,000.00
Equine Sports Medicine, LLC	$45,500.00
Mr. Stephen D. Reynolds	$30,000.00
Gooding Family Foundation	$25,000.00
Stallion Auction FY14	$17,008.39
Anonymous Donors FY2015	$16,191.37
C. Wayne McIlwraith and Nancy L. Goodman McIlwraith, D.V.M.	$15,000.00
Verdad Foundation	$10,000.00
Raymond James Char. Endowment Fund	$10,000.00
Mr. Yaron P. Goldman	$8,332.00
Dellora A. & Lester J. Norris Foundation	$5,000.00
Platinum Performance, Inc.	$5,000.00
Biovision Veterinary Endoscopy	$2,000.00
C. George Dewell, D.V.M.	$2,000.00
Ms. Cathy L. Carpenter Dea	$568.00
Mr. Mike J. Long	$568.00
Rick A. Pederson, LLC	$568.00
Secretariat Foundation	$500.00
Ms. Julie L. Kahn	$500.00
Ms. Nancy G. Dickenson	$500.00
Mr. William T. O'Donnell, Jr.	$500.00
Ms. Pamela C. Jones	$300.00
Ms. Martha P. Baxter	$250.00
Mr. Timothy R. Sommerfeld	$250.00
Hendrix Trading B.V.	$200.00
Marc R. McCall, D.V.M.	$200.00
Mr. Jeremy Sparrow	$150.00
Mr. Steven J. McCarthy	$150.00
Dr. Ann E. Dwyer	$150.00
Mr. Ronald W. Williams	$142.00
Ms. Deborah Carter	$142.00
Ms. Brianna Davis	$142.00
Charles F. Scoggin, D.V.M.	$142.00
Mr. Patrick Vahey	$142.00
Robert D. Allen	$100.00

Donations	Amount
Cherry Creek Equine	$100.00
Colorado Equine Clinic PC	$100.00
Mr. Armand S. Kafesjian	$100.00
Ms. Taylor S. Cowles	$71.00
Sheryl Scolnick, D.V.M.	$71.00
Mrs. Nancy R. Tuor Moore	$71.00
Mr. Mark E. Gill	$71.00
Cross Country Veterinary Services	$60.00
Ms. Denise B. Zink	$50.00
Susan D. Birney, D.D.	$25.00
Total Donations	**$907,914.76**

Interest on Endowments	Amount
McIlwraith Scholarship	$7,340.00
Cox Anthony Chair	$179,247.00
Iron Rose Ranch Chair	$139,805.00
Atkinson Chair	$61,727.00
Kawananakoa Chair	$123,957.00
Malone Chair	$291,245.00
Total Interest	**$803,321.00**

Medical Center Clinical Services	Amount
Anesthesia	$20,758.00
Per Diem	$975.20
IRAP	$6,948.40
MRI	$80,883.60
PRP	$1,000.00
Shockwave	$3,088.80
Surgery	$50,577.40
Xray	$23.80
Client Services Total	**$164,255.20**

continued...

Research Projects	Amount
MIT	$44,585.00
NexVet	$149,414.00
Grayson	$124,610.00
Morris	$37,817.00
Research Accounts Total	**$356,426.00**
ORC ESM	**$15,086.00**
ORC CORE Lab Revenue	**$3,750.00**
Continuing Education Activities	**$43,500.00**
Stallion Auction	**$16,729.00**

State Funds	Amount
Kawcak CRC Grant	$16,017.00
Frisbie CRC Grant	$18,383.00
State Funds Total	**$34,400.00**
TOTAL REVENUE	**$2.357,913.84**

Expenses	Amount
Faculty Salaries	$653,279.22
Research Associate Salaries	$312,608.00
Administrative Salaries	$232,849.58
Residents	$156,595.50
Graduate Student Salaries	$8,237.57
Hourly EORC students	$85,563.13
Total Salaries	**$1,449,133.00**
Faculty Travel	$67,881.33
Building Repairs	$349,551.40
Materials & Supplies	$614,893.49
Other Direct	$18,423.00
Equipment	$570,660.66
Expense Subtotal	**$3,070,542.88**
Facility & Administrative Overhead Costs	$162,710.66
Expense Total	**$3,233,253.54**
ACCOUNT BALANCE	**$(875,339.70)**

HEADLINES

Chelsea Bahney

PhD, Assistant Professor, UCSF Department of Orthopaedic Surgery,
UC Berkeley Department of Bioengineering & Material Science

"A new model for endochondral ossification: basic and translational implications on bone regeneration" - February 16, 2015

Dr. Bahney's laboratory develops translational therapies for the treatment of musculoskeletal diseases and injuries. Specifically, the focus is on improved tissue regeneration by recapitulating the normal sequences of development and repair. Dr. Bahney's background is a degree in chemical engineering from the University of Colorado at Boulder, a Ph.D. in stem cell and developmental biology from Oregon Healthy and Science University and a postdoctoral fellowship in orthopaedic surgery at the University of California, San Francisco. Current aims are to utilize biologically modified polymers to promote a sequence of biological milestones that parallel native repair by endochondral ossification.

Phillippe Benoit

PhD

"My thoughts on diagnosing and treating the equine athlete" - March 25, 2015

Dr. Philippe Benoit is a French veterinarian who graduated from Alfort Veterinary School in Paris, France in 1989 and then obtained an M.S. in nutrition and exercise physiology in 1991. He established an equine clinic in Les Breviaires next to Versailles and now also has a part time presence in the US. His primary interests is in sport horses, especially jumpers. His practice focusing in ultrasound imaging, orthopaedics and sports medicine. He has team veterinarian for the French equestrian team between 1992 and 1999 and has been a consultant for other foreign teams since 2000. Recently Dr. Benoit became a Diplomate of the American College of Veterinary Sports Medicine and Rehabilitation (ACVSMR). Dr. Benoit's topic was "My thoughts on diagnosing and treating the equine athlete" and, in addition to his talk, gave a clinic on his techniques on diagnosing and treating the equine athlete.

Charles P. Ho

PhD, MD, Director, Imaging Research, Steadman Clinic and Steadman Philippon Research Institute

"Applications and directions of musculoskeletal MRI in human orthopaedic sports medicine" - July 17, 2015

Dr. Ho is the Director of Imaging Research for the Steadman Clinic and Steadman Philippon Research Institute. The title of his talk was "Applications and directions of musculoskeletal MRI in human orthopaedic sports medicine". His talk addressed the diagnosis and treatment of common injuries in human sports medicine. In addition to his duties in Vail, Dr. Ho is responsible for imaging interpretation at the NFL combine for both the Denver Broncos and the San Francisco 49ers. His talk was particularly illuminating on the comparisons in both imaging screening of athletes as well as the clinical problems that occur in them.

Mark Hurtig

DVM, MVSc, Diplomate ACVS, Professor, University of Guelph

"Slow release platforms for intra-articular medication" - October 26, 2015

Professor Mark Hurtig is the Director of the Comparative Orthopaedic Research Laboratory at the University of Guelph in Canada which was established by the Canadian Arthritis Network as a Strategic Research Resource Laboratory. The focus of the laboratory is translational studies to facilitate regulatory approval of new therapies for both the human and veterinary fields. His work includes industrial and academic collaborations on osteoarthritis mechanisms, disease modifying therapies and cartilage repair strategies. He was the primary investigator for two human knee injury research studies centered in Toronto that study factors driving knee OA progression after injury and patient-specific optimization of arthroscopic microfracture—a technique used for cartilage repair. His work includes collaborations in tissue engineering, computer-assisted surgery, nutraceuticals, intra-articular delivery of drug and biologics as well as imaging.

Mark Grinstaff

PhD, Departments of Biomedical Engineering and Chemistry,
Metcalf Center for Science and Engineering, Boston University

"Contrast Enhanced Computed Tomography (CECT) as a Quantitative Tool for Monitoring Cartilage Composition and Structure in Pre-clinical Models of Osteoarthritis" - August 24, 2015

Dr. Grinstaff is the Distinguished Professor of Translational Research and a Professor of Biomedical Engineering, Chemistry and Materials Science and Engineering and Medicine at Boston University. Mark received his Ph.D. from the University of Illinois and was an NIH post-doctoral fellow at the California Institute of Technology. He is currently collaborating with us at the ORC in contrast enhanced computed tomography to quantitate cartilage composition in the horse. Dr. Grinstaff is currently collaborating with us at the ORC in this technique as we investigate its applicability in the horse (also a major project for Dr. Brad Nelson's Ph.D.). Dr. Grinstaff has received a number of significant awards and is a fellow of the National Academy of Inventors including being the Co-Founder of four companies that are commercializing his ideas. He has three products being sold and used in the clinic.

Ashlee Watts

DVM, PhD, DACVS, Assistant Professor, Texas A&M University,
Department of Large Animal Clinical Sciences

"A randomized, double-blind, placebo-controlled, clinical trial in 45 performance horses with hock lameness" - November 23, 2015

Dr. Watts is an Assistant Professor in the Department of Large Animal Clinical Sciences at Texas A & M University where her research emphasis include techniques for improved stem cell isolation and expansion for autologous therapy, techniques for the optimization of stem cells for tendon, cartilage, bone and anti-osteoarthritis therapy, and investigation into the basic mechanisms of successful stem cell therapy. Dr. Watts received her D.V.M. degree from Colorado State University and worked at the ORC when she was a student. She did her surgical residency and Ph.D. at Cornell University before going to Texas A & M.

Richard A. Mansmann

VMD, PhD, hon ACVIM-LA

“The relationship between hind feet break over, gluteal area pain and performance? If you can measure it, you might be able to prove it” - December 11, 2015

Dr. Mansmann was a 1968 V.M.D. graduate of the University of Pennsylvania, School of Veterinary Medicine and received his Ph.D. in 1974 from UC Davis School of Veterinary Medicine. He has had a long standing interest in equine sports medicine. Dr. Mansmann retired from NC State University and reopened his private practice in 2010, the same year he was made an honorary Diplomate of the American College of Veterinary Internal Medicine.

Honors and Awards

Haut Donahue, T. Fellow – American Society of Mechanical Engineers, 2015

Reiser, R.F. Best Teacher Award, CSU Alumni Association, 2015

Reiser, R.F. Outstanding Teacher Award, College of Health and Human Sciences, 2015

Professional Associations

Barrett, M.F. American College of Veterinary Radiology, American Association of Equine Practitioners, American Veterinary Medical Association, Colorado Veterinary Medical Association, Texas Veterinary Medical Association

Donahue, S.W. American Society of Bone and Mineral Research, American Society of Biomechanics, International Bone and Mineral Society, Orthopaedic Research Society

Haut Donahue, T.L. American Society of Biomechanics, American Society of Mechanical Engineers, Biomedical Engineering Society, Orthopaedic Research Society, American Society for Engineering Education

Ehrhart, N. American Veterinary Medical Association, The American College of Veterinary Surgeons, Veterinary Cancer Society, Veterinary Orthopedic Society

Frisbie, D.D. 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, American College of Veterinary Sports Medicine and Rehabilitation

Goodrich, L.R. Veterinary AO Society, 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.K. American Veterinary Medical Association, American College of Veterinary Sports Medicine and Rehabilitation, American Association Equine Practitioners, Colorado Veterinary Medical Association, International Veterinary Academy of Pain Management, Phi Zeta National Honor Society

Kawcak, C.E. AOVET, American Veterinary Medical Association, American Association of Equine Practitioners, American College of Veterinary Surgeons, American College of Veterinary Sports Medicine and Rehabilitation, Osteoarthritis Research Society, International Orthopaedic Research Society, Veterinary Orthopaedic Society

Kisiday, J.D. Orthopedic Research Society

McIlwraith, C.W. Royal College of Veterinary Surgeons, American College of Veterinary Surgeons, 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, International Society of Arthroscopy and Knee Surgery, International Cartilage Research Society,American Academy of Orthopaedic Surgeons, American College of Veterinary Sports Medicine and Rehabilitation

Moorman, V.J. American College of Veterinary Surgeons, American Veterinary Medical Association, American Association Equine Practitioners

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

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

Slayden R.A. American Society of Microbiology, American Chemical Society

Story, M.R. American College of Veterinary Surgeons, American Association of Equine Practitioners, American Veterinary Medical Association, Colorado Veterinary Medical Association, International Veterinary Chiropractic Association Honors and Awards

PRCA Photo by Larry Smith. Photo courtesy of PRCA.

SUMMARIES OF RESEARCH PROJECTS

Microsphere-based gradient implants for osteochondral regeneration: a long term study in sheep

This is a summary of an article by N. Mohan, V. Gupta, B.P. Sridharan, A.J. Mellot, J.T. Easley, R.H. Palmer, R.A. Galbraity, V.H. Key, C.J. Berkland and M.S. Detamore published in Regenerative Medicine, 2015:10(6), 709-728. This work was done in the Preclinical Surgical Research Laboratory at Colorado State University.

Take Home Message

In this cartilage repair study the repair tissues in the microfracture group were mostly fibrous and had scattered fissures with degenerative changes. Defects repaired with the gradient plugs (PLGA-based scaffold with opposing gradients of chondroitin sulfate and β-tricalcium phosphate) had; 1) equal or superior mechanical properties, 2) had lacuntated cells and 3) stable matrix as in hyaline cartilage.

Introduction

Articular cartilage has limited healing capabilities, and may contribute to the development of osteoarthritis if left untreated after an impact injury. Abrasion

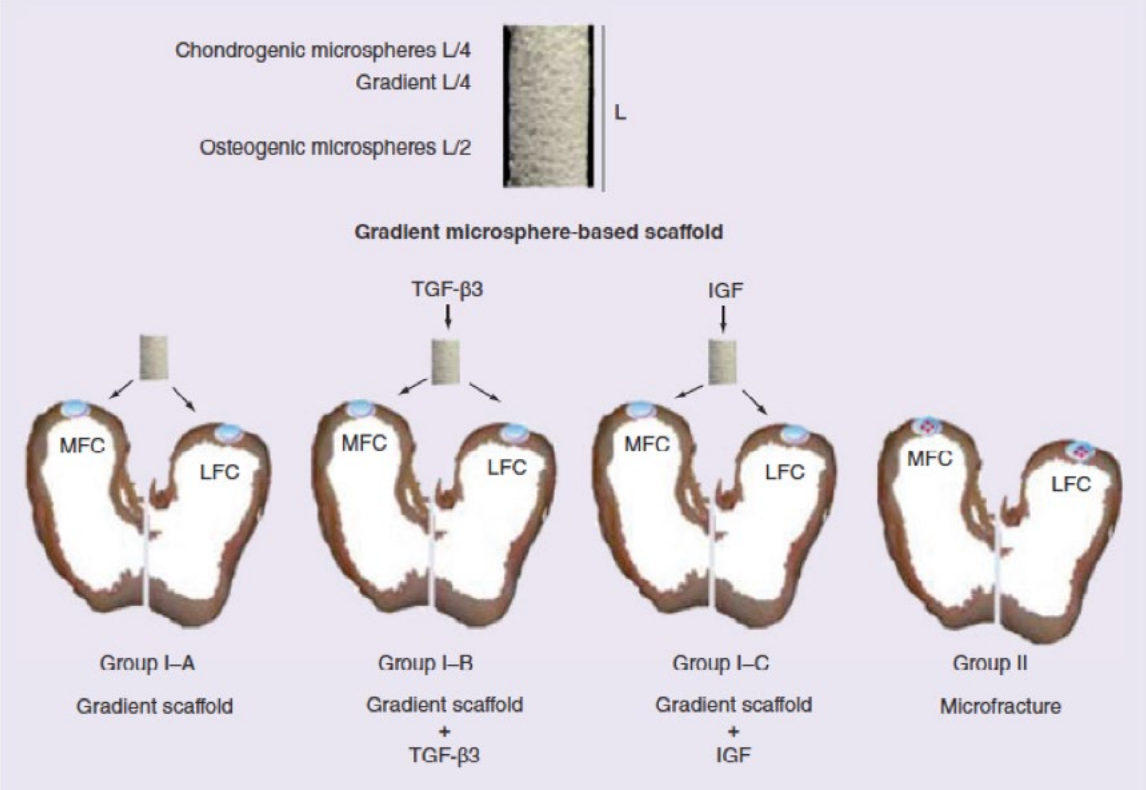

Figure 1. A schematic representation of microsphere-based gradient scaffold and the various groups for implantation. Gradient scaffolds were implanted into critical size osteochondral defects (D = 6 mm Å~ H = 6 mm) in the lateral and medial femoral condyles of knee joints of group I animals. Group I–A received only the gradient scaffold (n = 6), and was the primary test group. Group I–B was a pilot group, where 1 µg TGF-β3 was added to the scaffold in the operating room immediately prior to implantation (n = 3). Similarly, 0.5 µg IGF-1 was added to the scaffold immediately prior to implantation in pilot group I–C (n = 3). Microfracture procedure was performed in group II animals (n = 6) following induction of full-thickness, chondral-only defects (D = 6 mm). The cartilage regeneration was evaluated 1 year post-implantation. LFC: Lateral femoral condyle; MFC: Medial femoral condyle.

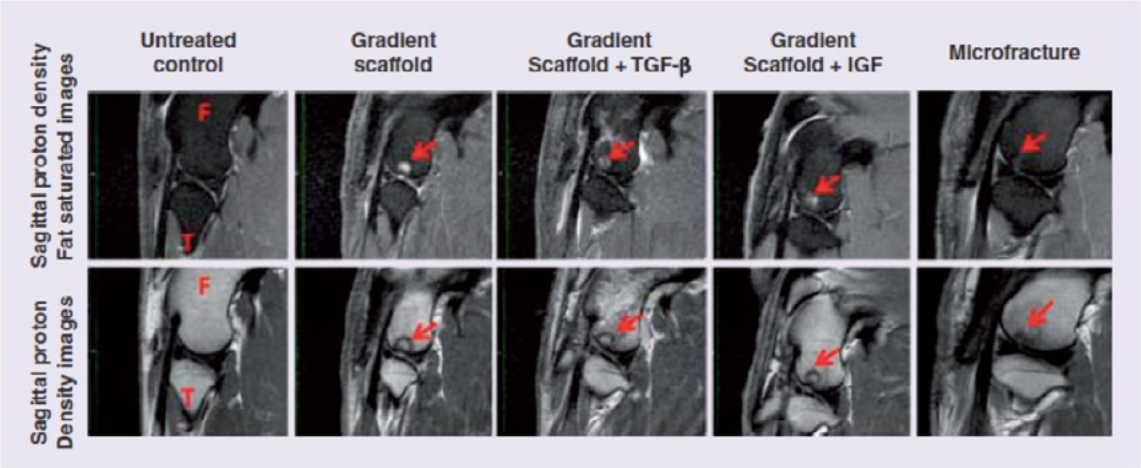

Figure 2. Representative 1.5 T MRI images of femoral condyles of sheep 4 months post implantation, showing progress of cartilage and bone regeneration. A total of three knees were imaged for each group. The arrows point to the defect site on the images. F and T denote femur and tibia respectively. Cartilage regeneration was observed in all of the samples at 4 months, and defect areas were generally well-contained. The microfracture group showed faster defect fill in the bone, due to the microfracture procedure being only a chondral defect with small holes made in the subchondral bone, in contrast to the gradient scaffolds, which filled osteochondral defects 6 mm in depth and likely had remnants of the polymer remaining at the time these MRIs were taken. From left to right, the representative samples are from the following animals: control, D02 lateral femoral condyle (LFC), D09 LFC, D10 LFC and D15 LFC.

arthroplasty, subchondral drilling and microfracture strategies induce the formation of fibrocartilage, which helps to alleviate painful symptoms and to restore the function of affected joints; however, fibrocartilage has a limited life span and poor mechanical performance in comparison to articular cartilage[1]. While there is a greater chance of producing articular cartilage in the injured area by ACI, the technique has several disadvantages, which include the need for two surgical procedures, generation of a large quantity of chondrocytes based on the defect size and issues with graft fixation, delamination and periosteal hypertrophy[2]. An advantageous strategy would be to implant a biodegradable material that promotes biochemical cues that stimulate osteochondral regeneration without the need to induce additional injuries, or implant autografts or allografts. The current study thus presents the first evaluation of the microsphere-based gradient plugs in a large animal model, with a long-term end point of 1 year. The hypothesis of the current study was that microsphere-based gradient plugs with opposing continuous gradients of chondroitin sulfate and β -tricalcium phosphate (β -TCP) in osteochondral defects would provide cartilage regeneration superior to that achieved by microfracture in chondral-only defects in a sheep model. The primary purpose of this study was to evaluate the aforementioned hypothesis, thereby evaluating microsphere-based gradient plugs for the first time in a large-animal cartilage repair study and in a translational context with a current standard-of-care control. The secondary purpose was to demonstrate the feasibility and proof of concept of adding a metered dose of growth factor to an osteochondral implant immediately preceding implantation in the operating room, which was evaluated in two pilot groups with the microsphere-based gradient plugs.

Methods

Gradient scaffolds were composed of poly(lactic-co-glycolic acid) microspheres with opposing continuous gradients of chondroitin sulfate and β-tricalcium phosphate. (Figure 1) describes the study design and implantation procedures.

Progression of cartilage regeneration was evaluated using MR imaging at 4-months for group I (n=3 knees) and group II (n=3 knees). Explanted knees also underwent morphological analysis, mechanical testing, finite element analyses, and histological analysis (Modified from O'Driscoll et al.)[3].

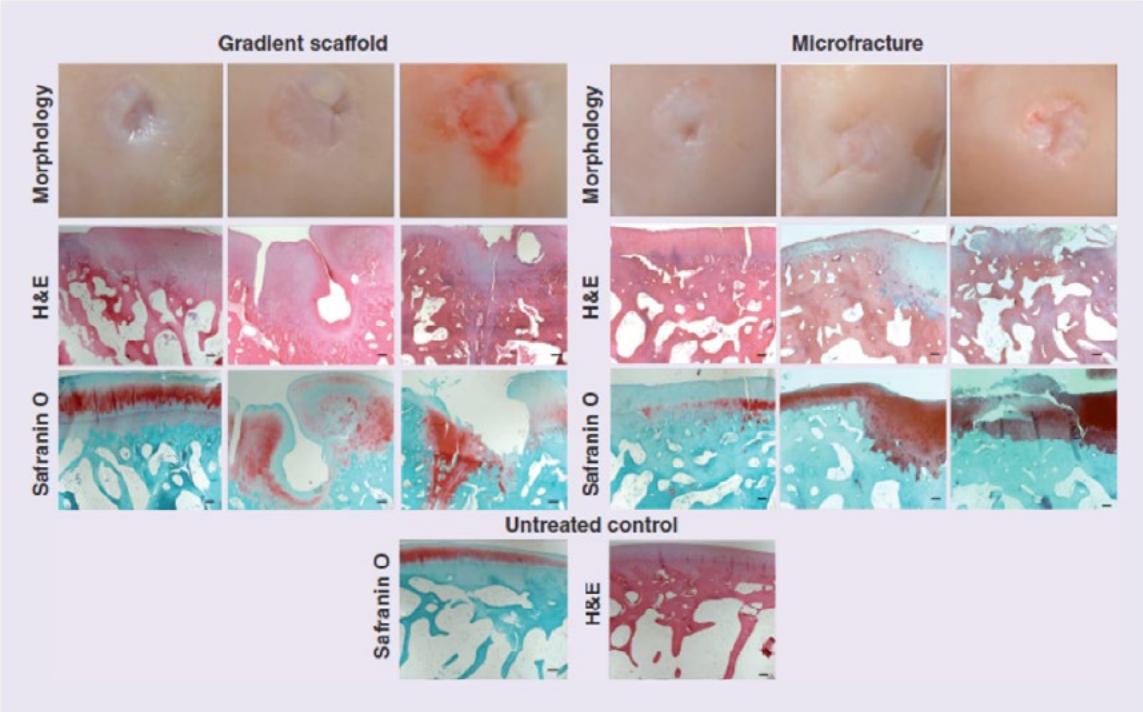

Figure 3. Representative images for gross morphology and histological analysis of the gradient scaffold only group and the microfracture group at 1 year post-implantation. Each column in the left panel represents a representative sample that received high (D01 medial femoral condyle [MFC]: score 24), medium (D02 MFC: score 20) and low (D04 MFC: score 13) histological scores of for the gradient scaffold-only group. Total scores for the gradient scaffold-only group were in the range of 13–26 (out of 28). Each column in the right panel represents a representative sample that received high (D15 lateral femoral condyle [LFC] score 25), medium (D16 LFC: score 21) and low (D17 LFC: score 18) histological scores in the microfracture group. Total scores for microfracture group were in the range of 15 to 25. The cells in gradient scaffold-only group had lacunated cells and resembled those normally seen in hyaline cartilage, and normal to moderate levels of Safranin-O staining and had no inflammatory reaction in the subchondral bone. The microfracture group had near to normal Safranin-O staining, had cells resemble those normally seen in hyaline cartilage or fibrous chondrocytes and chondrocyte clusters in the resting and proliferative zone, which indicated signs of degeneration. The bottom row represents images of untreated control. H&E and Safranin O staining shows the cellular morphology and glycosaminoglycan deposition respectively.

Results

The MR imaging data collected at 4-months after implantation indicated the bone regeneration was less in the gradient scaffold groups (that received osteochondral defects) compared with the microfracture group (that received shallower chondral defects) (Figure 2).

Sheep that received gradient regenerated cartilage that was more native-like (hyaline cartilage) in terms of structure, gross appearance and cell morphology (Figure 3). The repair tissues in the microfracture group were mostly fibrous and had scattered fissures with degenerative changes (Figure 3). No obvious advantage of the growth factors could be demonstrated due to the small sample number.

There were no statistically significant differences in the total histological scores among groups (Figure 4).

Conclusions

The current study made a direct comparison between two different approaches to cartilage repair: microfracture (standard of care control), and an osteochondral approach with microsphere-based gradient plugs. We engineered osteochondral scaffolds with continuous opposing gradients of 'raw materials', CS and β -TCP, to implant into critical size defects

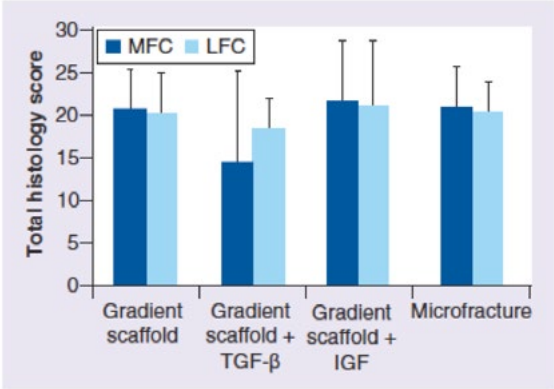

Figure 4. Total histology scores received for each groups. Joints retrieved 1 year post-implantation were stained with Hematoxylin & Eosin and Safranin-O and scored using a modified O'Driscoll score [3]. Histology scores were compiled by three co-authors based on parameters in Box 3. The maximum possible score is 28. Average scores are represented as means Å} standard deviation. Gradient scaffold only group (n = 6), gradient scaffold + TGF-β3 group (n = 3), gradient scaffold + IGF group (n = 3) and microfracture group (n = 6). There were no statistically significant differences among the groups (p > 0.05). LFC: Lateral femoral condyle; MFC: Medial femoral condyle.

of the right knee joint of sheep for the purpose of evaluating cartilage regeneration with gradient scaffolds against microfracture. Furthermore, we demonstrated that metered doses of either TGF-β 3 or IGF-1 could be added to the gradient scaffolds in the operating room immediately prior to implantation. The current study is the first to evaluate gradient scaffolds in a large animal model, and demonstrated that CS/β –TCP gradient scaffolds regenerated cartilage that was more native-like (hyaline cartilage) in terms of structure, gross appearance and cell morphology than the fibrous tissue that forms as a result of microfracture, even in spite of regenerating deeper osteochondral defects compared with the shallower chondral-only defects with microfracture. The current study has established proof of concept and feasibility with a large animal model. The microsphere-based gradient plugs in the clinic may hold the additional advantage of rapid return to weight-bearing activity.

References

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2. Marquass B., Schulz R., Hepp P. et al. Matrix-associated implantation of predifferentiated mesenchymal stem cells versus articular chondrocytes: in vivo results of cartilage repair after 1 year. Am. J. Sports Med. 39(7), 1401–1412 (2011).

3. O'driscoll S.W., Keeley F.W., Salter R.B. The chondrogenic potential of free autogenous periosteal grafts for biological resurfacing of major full-thickness defects in joint surfaces under the influence of continuous passive motion. An experimental investigation in the rabbit. J. Bone Joint Surg. Am. 68(7), 1017–1035 (1986).

Addition of Mesenchymal Stem Cells to Autologous Platelet-Enhanced Fibrin Scaffolds in Chondral Defects. Does It Enhance Repair?

This is a summary of a study published in 2016 by Drs. Goodrich, Chen, Werpy, Williams, Kisiday, Su, Cory, Morley, McIlwraith, Sah and Chu[1].

Take Home Message

The use of autologous platelet-enriched fibrin (APEF) scaffold enhanced chondral repair of critical-sized full-thickness chondral defects in horses, which was not improved by the addition of bone marrow-derived mesenchymal stem cells (BMDMSCs). This work supports further investigation to determine whether APEF enhances cartilage repair in humans.

Introduction

The chondrogenic potential of culture-expanded bone-marrow-derived mesenchymal stem cells (BMDMSCs) is well described. Numerous studies have also shown enhanced repair when BMDMSCs, scaffolds, and growth factors are placed into chondral defects. Platelets provide a rich milieu of growth factors and, along with fibrin, are readily available for clinical use. The objective of this study was to determine if the addition of BMDMSCs to an autologous platelet-enriched fibrin (APEF) scaffold enhances chondral repair compared with APEF alone.

Methods

A 15-mm-diameter full-thickness chondral defect was created on the lateral trochlear ridge of both stifle

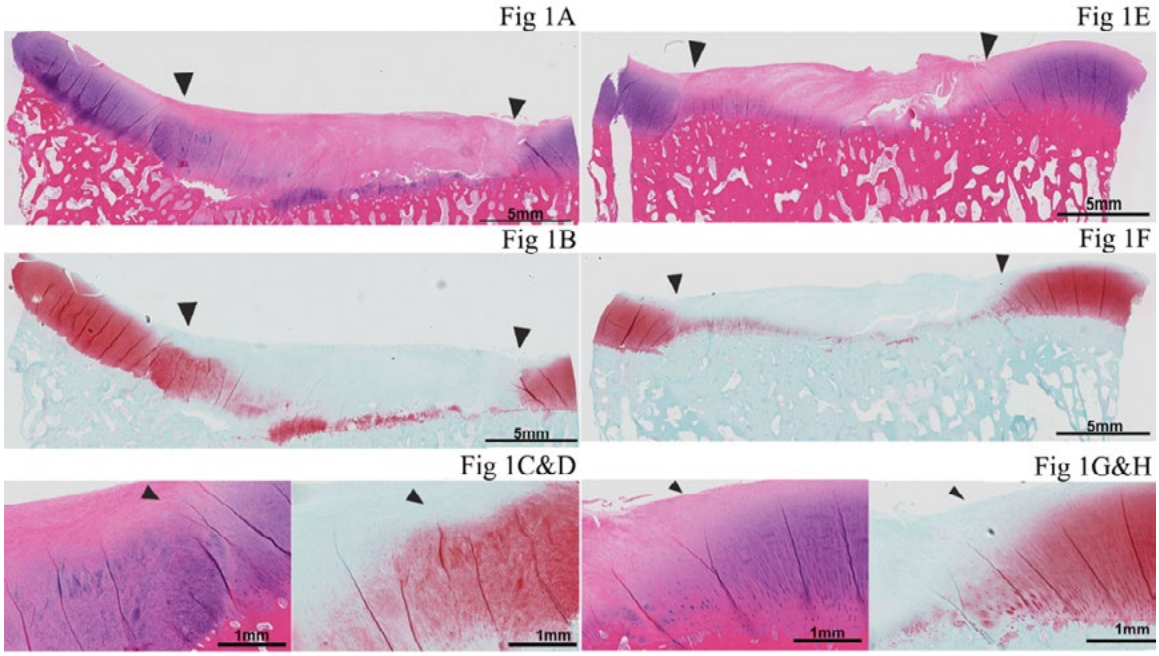

Figure 1. Histological appearance of repair tissue from the APEF (Figs. 1-A through 1-D) and APEF+BMDMSCs (Figs. 1-E through 1-H) groups. Figures 1-A, 1-C, 1-E, and 1-G are stained with hematoxylin and eosin, and Figures 1-B, 1-D, 1-F, and 1-H are stained with safranin O. The arrowheads point to the periphery of the defect, where the repair tissue borders the surrounding peripheral tissue. The images in the bottom row are close-up photomicrographs of the integration of the repair tissue with the surrounding peripheral cartilage in the APEF group (Figs. 1-C and 1-D) and the APEF+BMDMSCs group (Figs. 1-G and 1-H).

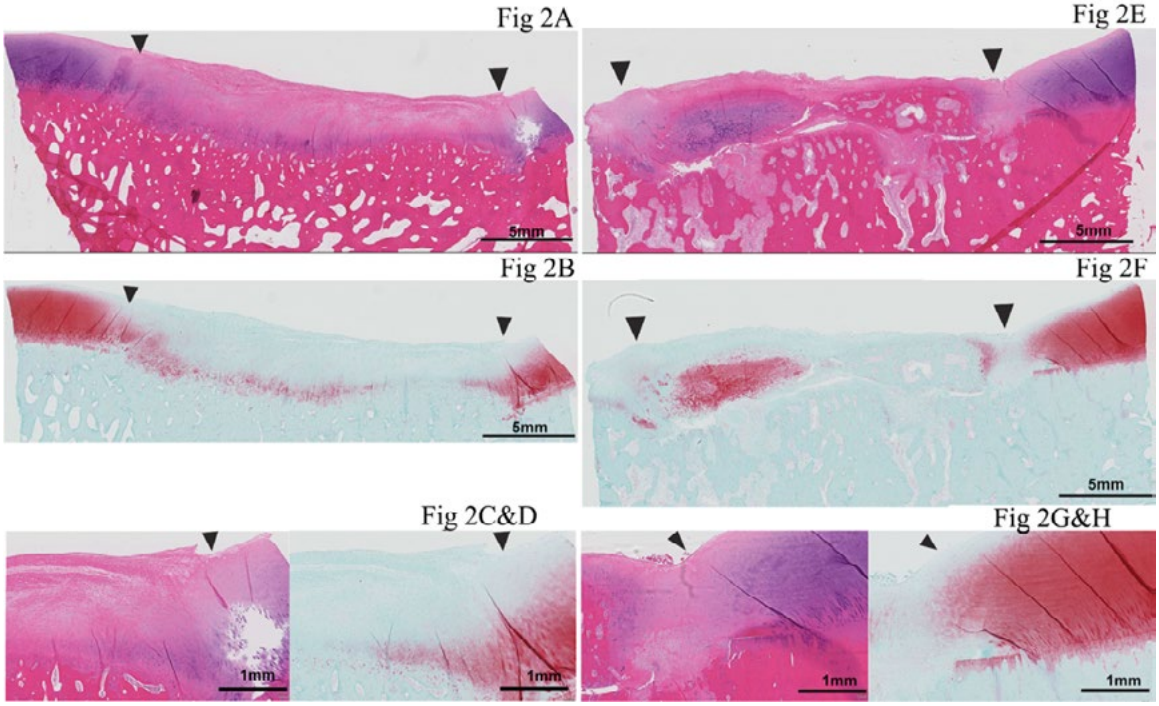

Figure 2. Histological appearance of the defects of a horse in which bone formed within the repair tissue in the limb treated with APEF+BMDMSCs. Figures 2-A, 2-C, 2-E, and 2-G are stained with hematoxylin and eosin, and Figures 2-B, 2D, 2-F, and 2-H are stained with safranin O. The defect repaired with APEF is shown on the left (Figs. 2-A through 2-D) and the defect repaired with APEF1BMDMSCs is shown on the right (Figs. 2-E through 2-H). The arrowheads point to the periphery of the defect, where the repair tissue borders the surrounding peripheral tissue. The images in the bottom row are close-up photomicrographs of the integration of the repair tissue with the surrounding peripheral cartilage in the APEF group (Figs. 2-C and 2-D) and the APEF+BMDMSCs group (Figs. 2-G and 2-H). The defect repaired with APEF+BMDMSCs (Figs. 2-E and 2-F) has bone (arrows) within the repair tissue.

joints of twelve adult horses. In each animal, one defect was randomly assigned to receive APEF and BMDMSCs and the contralateral defect received APEF alone. Repair tissues were evaluated one year later with arthroscopy, histological examination, magnetic resonance imaging (MRI), micro-computed tomography (micro-CT), and biomechanical testing.

Results

Twenty-three of the twenty-four chondral defects had fair-to good fill (with the APEF or APEF and BMDMSCs) and integration with the surrounding cartilage on histologic analysis (Figure 1).

Repairs in general had a cellular appearance at the base of the defect with positive staining for glycosaminoglycan (GAG). The middle-to-superficial part of the repair had a more fibrous, hypocellular appearance with an absence of GAG staining.

Bone formed within 4 of the 12 defects repaired with APEF and BMDMSCs (Figure 2) but in none of those repaired with APEF alone. Bone formation within the defects appeared to be separate from the underlying bone and did not seem to be advancement of the subchondral bone.

Defects repaired with APEF alone had less trabecular bone edema (as seen on MRI) compared with defects repaired with APEF plus BMDMSCs (Figure 3).

Micro-CT analysis showed thinner repair tissue in defects repaired with APEF and BMDMSCs than those treated with APEF alone ($P<0.05$).

Conclusions

APEF alone resulted in thicker repair tissue than was seen with APEFand BMDMSCs. The addition of BMDMSCs to APEF did not enhance cartilage repair and stimulated bone formation in some cartilage defects.

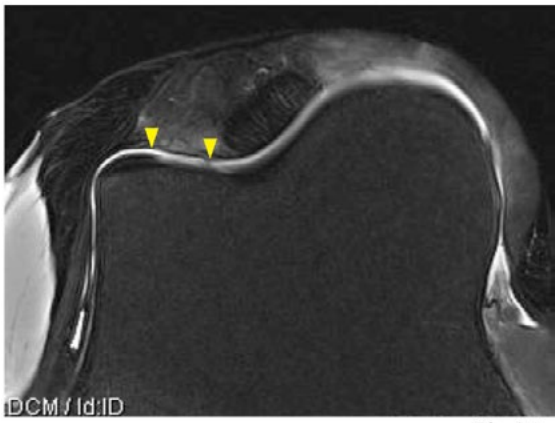

Fig 3A

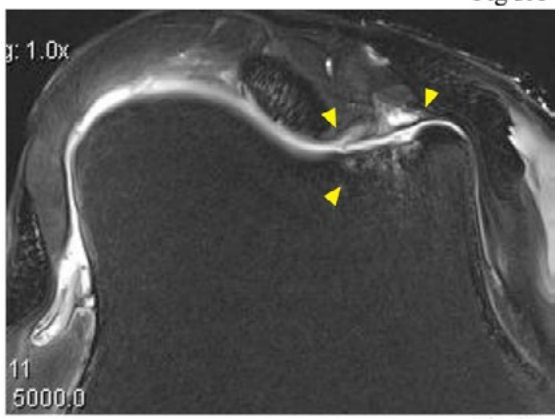

Fig 3B

Figure 3. Proton density of fat-saturated axial plane MRIs of lateral trochlear ridges treated with APEF (Fig. 3-A) or APEF+BMDMSCs (Fig. 3-B). The down pointing arrowheads indicate the periphery of the defects, and the arrowhead pointing up in Figure 3-B indicates decreased subchondral bone density as well as subchondral and trabecular bone fluid/edema.

Acknowledgments

This project was funded by the following National Institutes of Health (NIH) grants RC2 AR058929 (C.R.C., L.R.G., and R.L.S.), 1K08AR054903-01A2 (L.R.G. and C.W.M.), R01 AR051963 (C.R.C.), R01AR044058 and P01 AG007996 (R.L.S.).

References

1. Goodrich L.R., Chen A.C., Werpy N.M., Williams A.A., Kisiday J.D., Su A.W., Cory E., Morley P.S., McIlwraith C.W., Sah R.L., Chu C.R. Addition of mesenchymal stem cells to autologous platelet-enhanced fibrin scaffolds in chondral defects. Does it enhance repair? J Bone Joint Surg Am. 2016;98:23-34.

Evaluation of articular cartilage progenitor cells for the repair of articular defects in an equine model

This summary is from a paper by Drs. Dave Frisbie, Helen McCarthy, Charles Archer, Myra Barrett and Wayne McIlwraith and was published in Journal of Bone and Joint Surgery.[1]

Take Home Message

Autologous chondroprogenitor cells cultured from the superficial layer of articular cartilage and implanted in fibrin yielded a modest improvement in articular cartilage repair compared to fibrin alone and with a 128% decrease in central osteophyte formation compared to fibrin-only treatment. There was a measurable benefit and comparisons with other cartilage resurfacing techniques should be considered.

Introduction

Focal chondral defects are identified in more than one-half of the arthroscopy procedures performed in the human knee[2-4], and similar numbers are seen in clinical cases of equine stifle (knee joint arthroscopy5. Despite a vast amount of research, a rent systematic review of Level-I and II studies involving 421 human patients who had been treated with autologous chondrocyte implantation, osteochondral autograft transfer, matrix-induced autologous chondrocyte implantation, or microfracture and who had long-term follow-up indicated that no technique consistently yielded superior results[6], confirming that improved cartilage repair techniques are desired. Bone-marrow-derived mesenchymal stem cells (MSCs) implanted in a fibrin-based matrix have not shown long-term benefit[7]. Furthermore, it is our experience that MSCs implanted in a fibrin matrix or in a matrix with other increased growth factors lead to excessive mineralization of the repair tissue[8].

Our group has characterized a novel cell type, isolated from the superficial layer of both human[9] and equine articular cartilage that may have characteristics superior to those of bone-marrow-derived MSCs for matrix implantation. Equine articular cartilage progenitor cells demonstrate a multipotent differentiation capacity similar to that of bone-marrow-derived MSCs[10]. Specifically, these cells form colonies from an initial low seeding density and have been shown to express the putative stem cell markers STRO-1, CD90, and CD166. In vitro, chondrogenic induction reveals positive labeling for type-II collagen and aggrecan without detection of type-X collagen. The lack of type-X collagen or a hypertrophic cartilage (endochondral) phenotype is expected to limit repair tissue mineralization in vivo.

Unlike mature chondrocytes, these cartilage progenitor cells exhibit delayed senescence and retain their

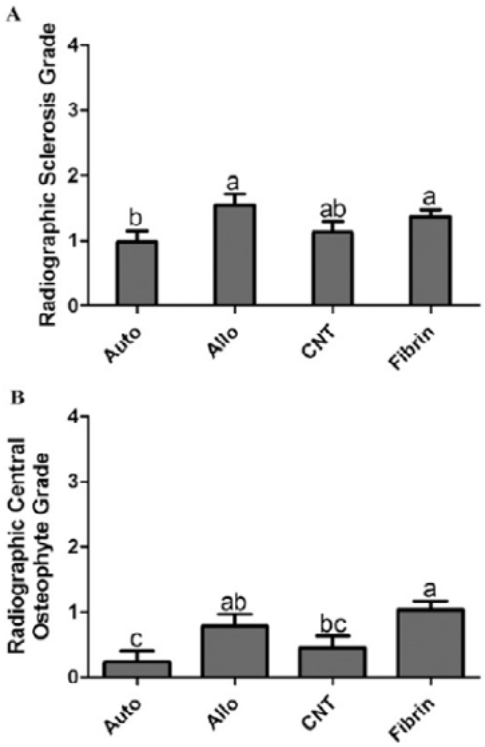

Figure 1. Mean radiographic grade (and standard error) of sclerosis (Fig.1-A) and central osteophytes (Fig.2-B) averaged over time. Groups labeled with the same letter did not differ significantly from each other.

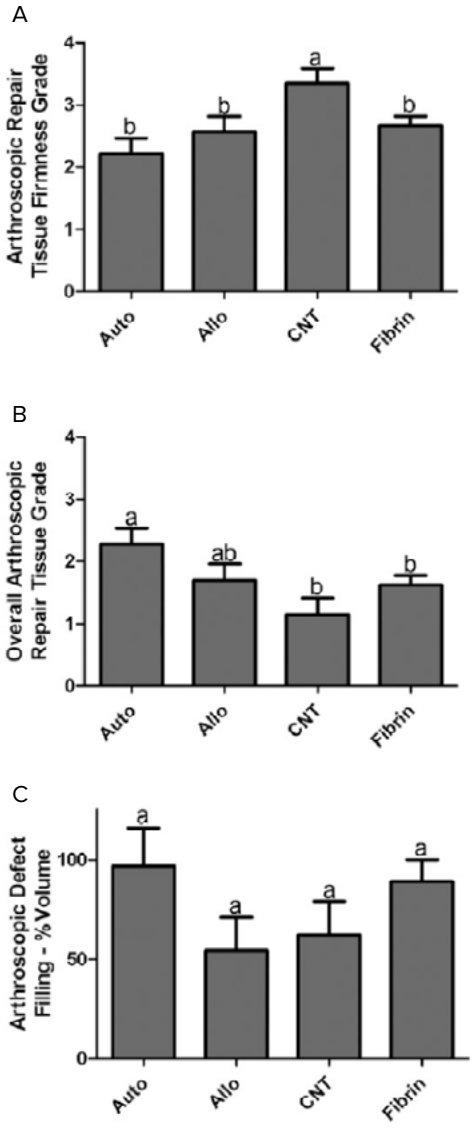

Figure 2. Mean arthroscopic grade (and standard error) of repair tissue firmness (Fig.2-A), overall repair tissue grade (Fig.2-B), and volume of defect filling (Fig.2-C) estimated at the time of the post mortem examination. Groups labeled with the same letter did not differ significantly from each other.

chondrogenic potential following extensive in vitro expansion[11]. The cells have been shown to demonstrate plasticity both in vitro and in vivo[9,10,12] and maintain Sox-9 gene expression in monolayer culture during up to fifty population doublings.[11,12] The purpose of this study was to evaluate autologous and allogenic cartilage progenitor cells implanted in a fibrin matrix to heal critical-sized articular defects over a twelve-month period in an equine model that included controlled strenuous exercise. Comparisons were made with empty defects and defects filled with fibrin only.

Materials and Methods

There were four treatment groups: (1) autologous chondroprogenitor cells transplanted in fibrin, (2) allogenic chondroprogenitor cells transplanted in fibrin, (3) fibrin alone, and (4) empty defects.

Twelve skeletally mature horses (age, two to six years) with normal musculoskeletal examination results were used. Under general anesthesia, superficial cartilage was harvested arthroscopically taking approximately 100 mgs of cartilage from the lateral trochlear ridge on each side. Cartilage from one randomly chosen side was utilized for autologous treatment, and cartilage from the other side was utilized for allogenic treatment of a different, randomly chosen horse. The superficial chondroprogenitor cells were cultured from the superficial zone cartilage by previously described method of Dowthwaite, et al[12]. After fourteen days of expansion, cells were cryopreserved in liquid nitrogen. Viability after thawing was assessed by a trypan blue assay and was found to be 88% or greater.

A defect 15mm in diameter and extending down to the level of the subchondral bone plate was made on the medial aspect of the trochlea at the distal aspect of each femur through a femoropatellar arthrotomy[13]. The dry defect was slightly overfilled with the autologous fibrin and thrombin solution (1:1 ratio by volume) with or without cells or was left empty. One defect in each animal was filled with fibrin alone (Fibrin group, n = 12). The defect in the contralateral limb received autologous cells in fibrin (Auto group, n = 4), received allogenic cells in fibrin (Allo group, n = 4), or remained empty (CNT[control] group, n = 4). Musculoskeletal exams at two month intervals, femoropatellar radiographs at two month intervals, gross assessment after twelve month arthroscopy and euthanasia at twelve months followed by histologic and immunoshistochemical analysis. Analysis of each outcome parameter was performed with the use of SAS software and involved descriptive statistics, nonparametric frequency tables, and/or mixed-model ANOVA (analysis of variance).

Results

The degree of sclerosis was less in the Auto group than in both the Allo and Fibrin groups when averaged over

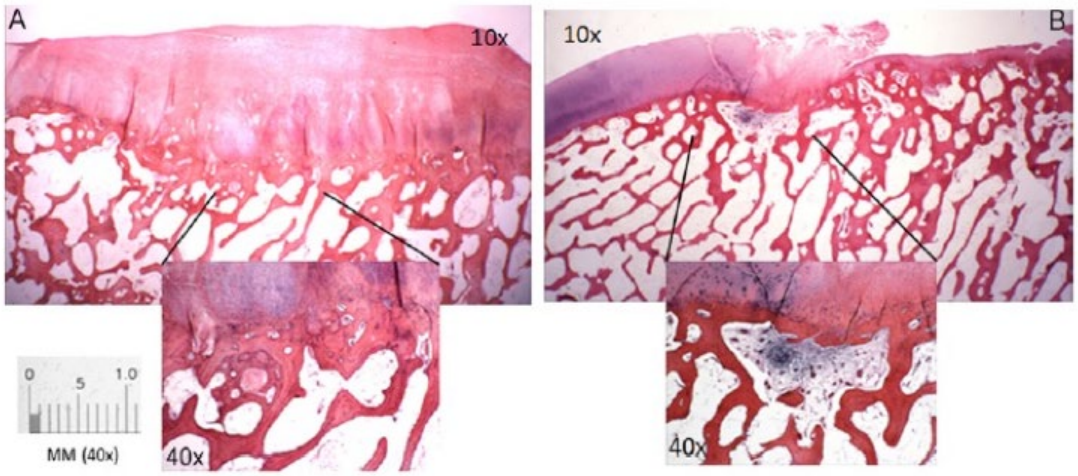

Figure 3. Representative photomicrographs from the control (Fig.3-A) and allograft (Fig 3-B) groups demonstrating increased inflammatory cells in the subchondral bone. The values on the rules are 0.0, 0.5, and 1.0 mm.

the study period and the degree of central osteophyte formation was least in the Auto group when averaged over the study period.

On second look arthroscopy cartilage and bone attachment as well as firmness of the repair tissue were inferior in the CNT group compared with the other treatment groups and the Auto group, with the Auto group having the best result when averaged over the study period (Figure 2A) repair tissue quality as evaluated by the arthroscopic examination showed that it was significantly better in the Auto group than in the CNT group (Figure 2B). On post-mortem examination parameters that were similar to those assessed by arthroscopy. The greatest defect filling by repair tissue was observed in the Auto group (Figure 2C).

On histologic examination the repair tissue at twelve months was predominantly fibrocartilage in the Auto group, whereas mostly nonchondrocytic cells with some fibrocartilage was seen in the other groups. Reconstitution of the subchondral bone in the Auto group was superior to that in the CNT group at 12 months the inflammatory response in the subchondral bone at 12 months was significantly greater in the Allo and CNT groups than in the Auto and Fibrin groups (Figure 3). The extent of safranin-O staining at twelve months was significantly superior in the repair tissue in the Auto group than in the other treatment groups and the total histology score at 12 months was significantly better than the Auto group than the other groups. The score in the fibrin group was also significantly better than in the control group; the difference between the Fibrin and Allo groups did not reach significance (Figure 4).

Discussion

The model utilized in this study allows comparison between defects in the same subject, which is an important consideration because a substantial amount of variation occurs between subjects of all species in such studies. Another unique aspect of the study design is the controlled and strenuous exercise that the subjects underwent, simulating athletic training for high-speed racing. In contrast, self-exercise in a pasture, which has been utilized in other models, is variable among individuals. Although loads or muscle forces are not definitively known, we have previously used pressure-sensitive intraarticular devices to show that the contact area increases as the femorotibial joint is flexed during maximal exercise. In our opinion, controlled treadmill exercise provides a loading pattern at defect locations that is more consistent and increased compared with animals that self-exercise. (Horse trochleae are not expected to see any loading in a stationary full weight-bearing position comparable to standing in humans.)

Radiographic outcomes were approved with autologous cell treatment compared with allogenic cell treatment or fibrin treatment alone; this improvement was

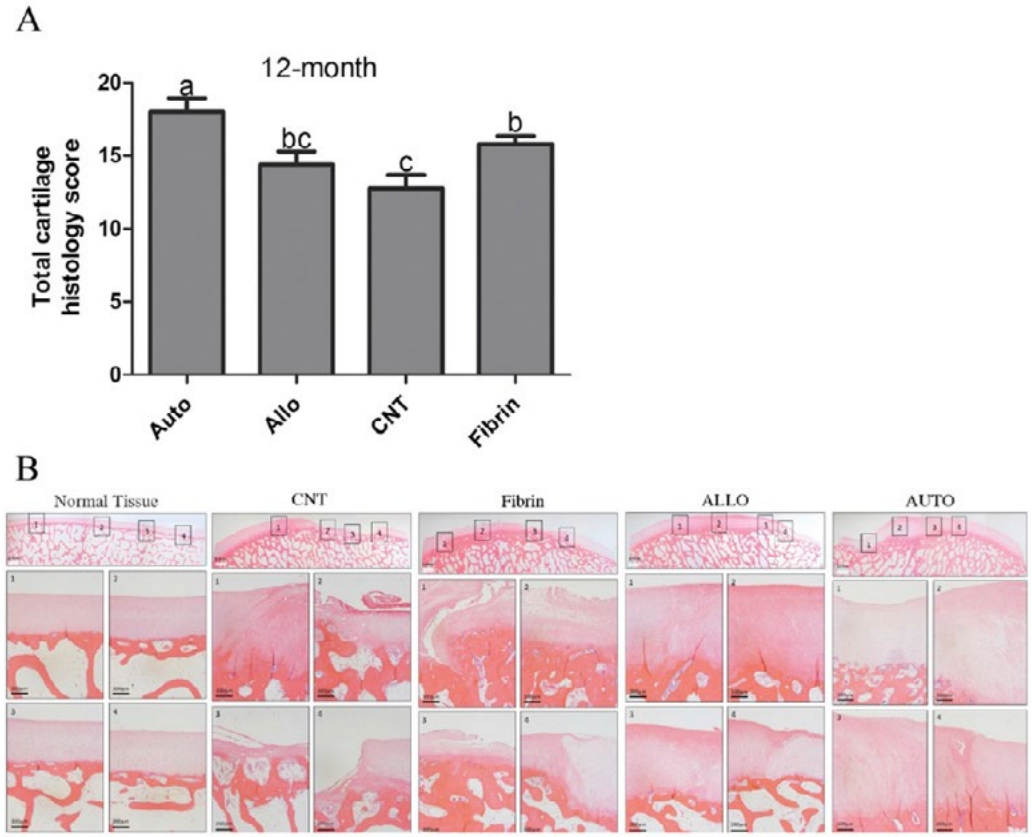

Figure 4A and 4B. Cartilage histology at twelve months. Figure 4-A Mean total histology score (and standard error). Groups labeled with the same letter did not differ significantly from each other. Figure 4-B Photomicrographs of a representative histologic section from each treatment group as well as a normal reference (hematoxylin and eosin).

seen both for sclerosis of the subchondral bone adjacent to the defect and repair tissue as well as for central osteophyte formation. In humans, central osteophytes are generally reported to occur in conjunction with peripheral osteophytes and other osteoarthritic changes. In horses, however, peripheral osteophyte formation on the trochlear ridges is very uncommon. Thus, the findings of sclerosis and proliferative new bone adjacent to the defect (central osteophytes) are the radiographic findings that would result from the creation of the articular cartilage defect. These changes were smaller in the group treated with autologous cells than in the groups treated with fibrin and allogenic cells. Furthermore, histologic evidence of less subchondral bone inflammation was noted, with a 55% difference when the autologous and allogenic treatments were compared. The immunogenicity of autologous compared with allogenic cells in horses has not been well studied in vitro, and even less in vivo information exists. The radiographic findings coupled with the subchondral bone inflammation findings would support preferential use of autologous cells rather than allogenic cells until further information is gained.

The firmness of the repair tissue, when it was probed arthroscopically, was improved in all three groups in which the treatment included fibrin, suggesting that much of this improvement resulted from the fibrin alone. However, the overall arthroscopic grade of the repair tissue was best in the Auto group (with a 33% difference compared with the Fibrin group). There was a 51% difference between the overall arthroscopic grade of the repair tissue in the Auto group and that with the historic treatment that utilized subchondral bone microfracture alone in a similar model (defect location, treatment period and rehabilitation protocol18) plus the Auto group appears to be better than microfracture alone; however the repair tissue quality is still only fair and an improvement is needed.

The results suggest that fibrin alone was mostly responsible for improvement in histology scores. Although the arthroscopic evaluation of the repair tissue treated with autologous cells was superior to that in a historic study of microfracture alone the histologic evaluation of the repair was inferior to that of microfracture alone in another study.

Immunohistochemistry demonstrated that the percentage of type-II collagen was greatest in the repair tissue from the horses receiving either of the cellular treatments (with a 90% difference in the Auto group compared with the Fibrin group) but it is to be recognized that this percentage remains significantly less than in normal cartilage (in which 100% staining is expected).

Acknowledgments

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Comparison of subjective lameness evaluation, force platforms and an inertial-sensor system to identify mild lameness in an equine osteoarthritis model

This is a summary of an article by Drs. J.R. Donnell, D.D. Frisbie, M.R. King, L.R. Goodrich and K.K. Haussler published in The Veterinary Journal, 2015;206:136-142. doi: 10.1016/j.tvjl.2015.08.004.

Take Home Message

Subjective lameness evaluation is more reliable in detection of mild forelimb lameness (caused by an OCF within the distal aspect of the radiocarpal bone) compared to force platforms and an inertial-sensor system. In mild forelimb lameness, agreement is higher between subjective evaluation and the inertial-sensor system than agreement between force platforms and an inertial-sensor system. Correlations between output parameters of all methods are moderate in horses with mild lameness, and leave room for needed improvement.

Introduction

When mild lameness exists, agreement between clinicians is often controversial due to its subjective nature. The goal of the study was to compare subjective and objective methods to identify the presence of mild lameness using an established model of osteoarthritis.

Methods

Osteoarthritis was induced by creating a unilateral carpal osteochondral fragment (OCF) in the radiocarpal joint of sixteen horses. Subjective lameness evaluations (blinded and unblinded), force platforms (FP), and an inertial-sensor system (ISS) were used to detect forelimb lameness at four time points (Figure 1). Limb identified as lame by each method were compared as well as compared to the OCF limb at each time point. Pearson correlations were calculated between all outcome parameters.

Results

Independent of time blinded subjective evaluation (54%) and an ISS (60%) identified a higher percentage of horses as lame in the OCF limb compared to FP (40%: Figure 2).

Blinded subjective evaluation and an ISS agreed on which forelimb was lame more often (50%) than blinded subjective evaluation with FP (38%) (Figure 3).

Induction of mild lameness within the OCF limb was supported by an increase in the frequency of horses considered lame by both subjective evaluations the ISS and a decrease (3.6%) in mean (among all horses) peak vertical force from baseline to post OCF induction (Figure 4).

Percentage of horse identified as lame in the OCF limb, independent of time, was highest by the ISS (60%) followed by blinded subjective evaluation (51%) and the FP (42%)(Figure 5).

Conclusions

Results of this study suggest the sole use of a force platform or inertial-sensor system for detection of mild lameness detection is not recommended and

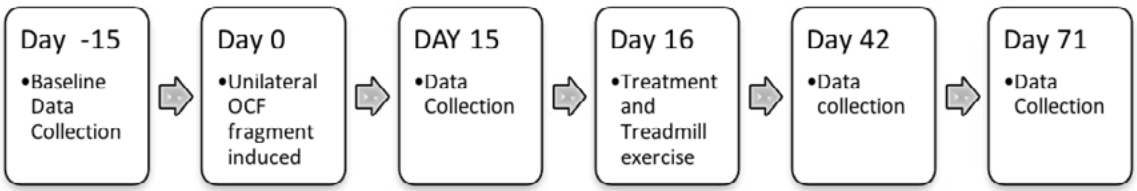

Figure 1. Schematic illustration of the study time line.

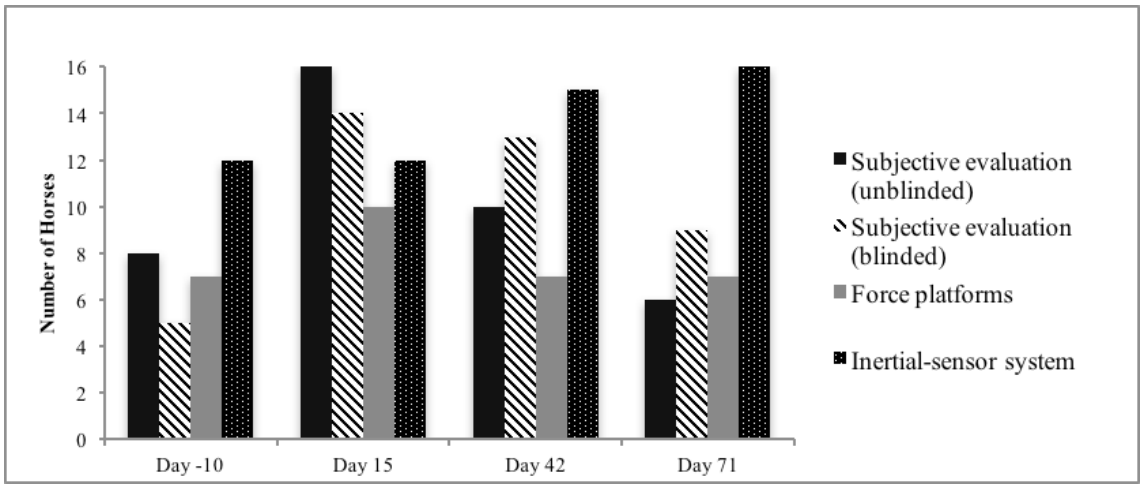

Figure 2. Number of horses (n =16) identified as having forelimb lameness (OCF or sham-operated limb) by each method plotted by study day.

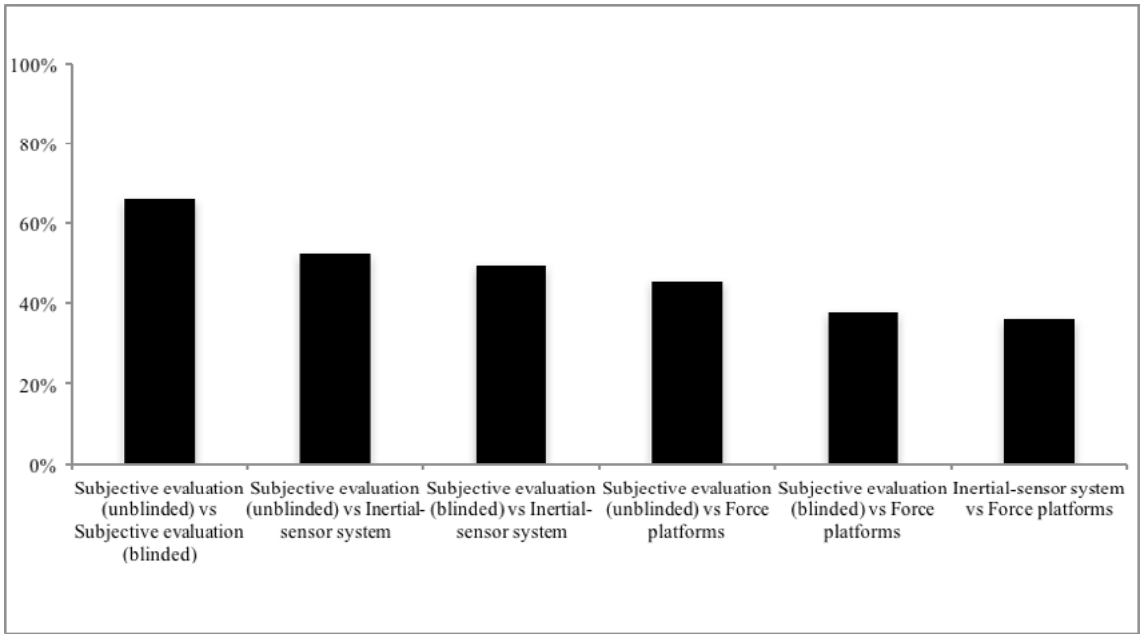

Figure 3. Overall percentage agreement between lameness detection methods for identifying the same forelimb as lame independent of time point.

the current assumption that force platform data is the gold standard for objective lameness detection should be reconsidered. Surgical induction of an osteochondral fragment within the middle carpal joint causes subtle to mild lameness and was more easily identified by subjective evaluation or an inertial-sensor system than by force platforms.

Acknowledgments

The Orthopaedic Research Center Foundation, Colorado State University, Fort Collins, CO funded study. Horses used in this project were shared with project funded by the Grayson-Jockey club and NIH grant # K08AR054903-01A2. Equinosis LLC, loaned the Equinosis Lameness Locator© (inertial-sensor

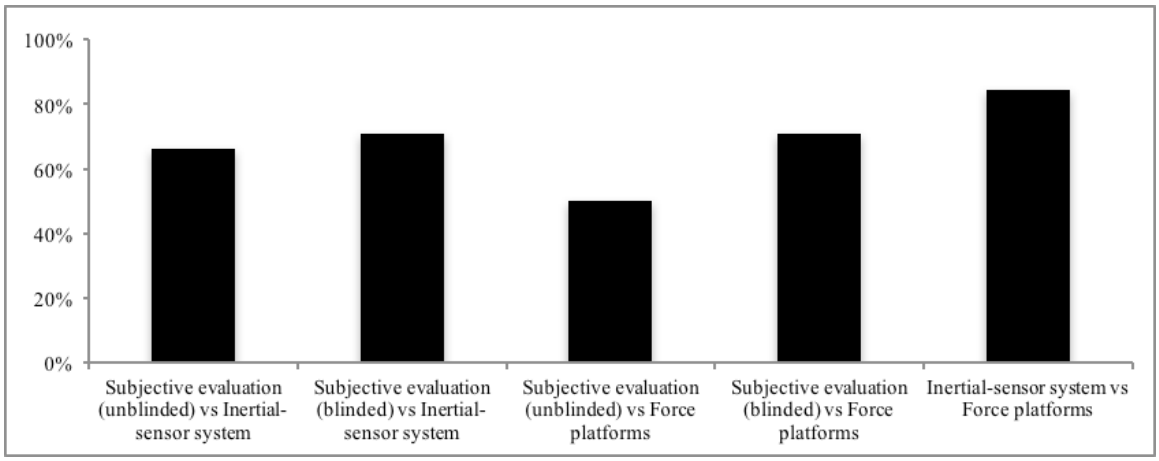

Figure 4. Overall percentage agreement between lameness detection methods for identifying asymmetry in the same direction, independent of time point. Comparison between force plate and inertial sensor system was made between all evaluations and comparisons with subjective evaluation were only performed when lameness was identified by subjective evaluation.

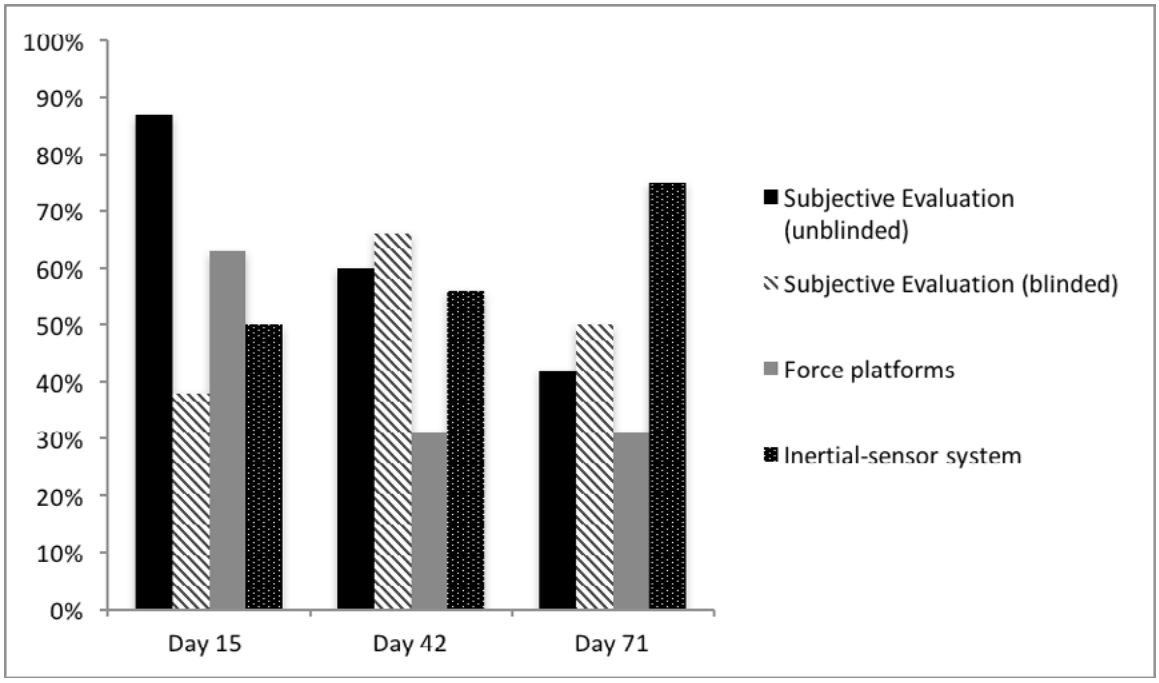

Figure 5. Percentage agreement of each method to identify the limb with an induced OCF as lame, plotted by study day post disease induction.

system) for use during the study, but did not participate in design study, data acquisition or data interpretation. The authors' would like to thank Dr. Ann Hess for her help with statistical analysis and review of results, Dr.'s Wayne McIlwraith and Chris Kawcak for their help with evaluation of the videoed lameness examinations, Ranches at Cherry Creek in honor of Don Ulmer and Equine Sports Medicine LLC, Pilot Point, TX for their continued financial support of the first author's residency in Equine

Sports Medicine and Rehabilitation, and staff at the Gail Holmes Equine Orthopaedic Research Center at Colorado State University for their help in data collection. Preliminary results were be presented at the American Association of Equine Practitioners 60th Annual Convention in Salt Lake City, 6th-10th December 2014.

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Implantable Microelectromechanical Sensors for Diagnostic Monitoring and Post-Surgical Prediction of Bone Fracture Healing

This is a summary of a paper that was written by Kirk C. McGilvray, Emre Unal, Kevin L. Troyer, Brandon G. Santoni, Ross H. Palmer, Jeremiah T. Easley, Hilmi Volkan Demir, Christian M. Puttlitz[1]

Take Home Message

A diagnostic tool that could quantitatively describe the biomechanical stability of the fracture site in order to predict the course of healing would represent a paradigm shift in the way fracture healing is evaluated. Our paper describes the development and evaluation of a wireless, biocompatible, implantable, microelectromechanical system (bioMEMS) sensor, and its implementation in a large animal (ovine) model. These data verify that the bioMEMS sensor can be used as a diagnostic tool for detecting the in vivo course of fracture healing in the acute post-treatment period.

Introduction

It has been shown, in clinical practice and via animal models, that bony healing is critically-related to the degree of implant stability and loading[2-4]. Animal studies, using wired strain gages, have consistently demonstrated that the healing callus and bone assume an increasing proportion of the applied external load as fracture healing proceeds, thus reducing the mechanical burden on the implanted hardware[5,6]. In abnormal healing (leading to pseudarthrosis or non-union), this gradual transfer of the loading from the implant to native tissue is significantly altered.

Unfortunately, the course of fracture healing is currently not easily diagnosed in the healing early period, when standard radiographic information regarding the fracture site is not capable of discriminating the healing pathway due to the relative paucity of mineralized tissue[7]. Salvage or revision procedures involving surgery is the most common treatment modality for failed primary operations, and the clinical outcome of these procedures have been negatively

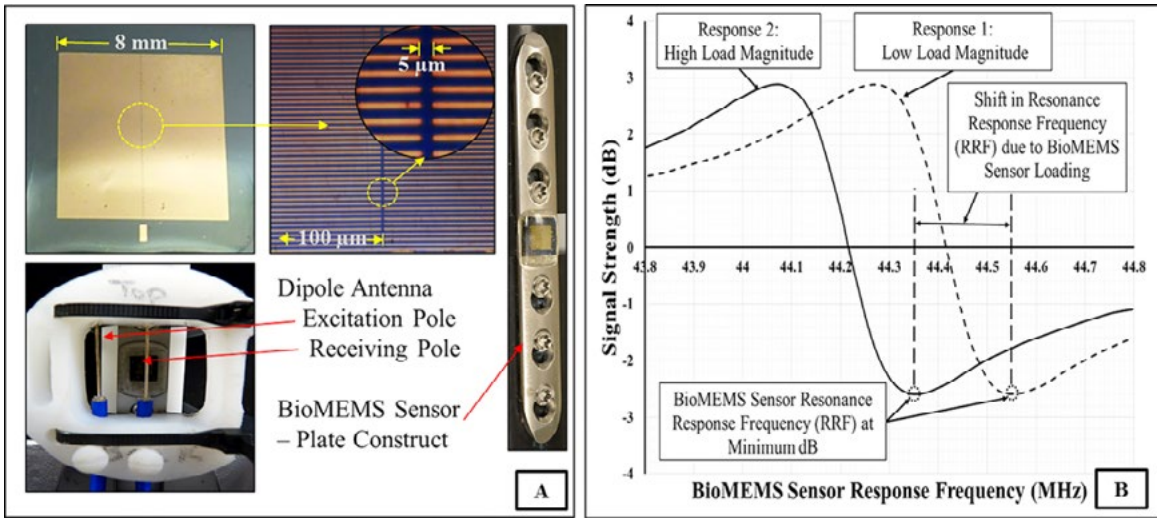

Figure 1. (A) Macro and micro digital images of the bioMEMS sensor, digital image of dipole antenna placed over the bioMEMS sensor; digital image of the BioMEMS sensor – locking plate construct. (B) Characteristic curves of measured signal strength (dB) versus the resonance response frequency (RRF) under applied loading demonstrating the shift in the RRF due to different load magnitudes imparted on the bioMEMS sensor.

correlated to the time between the initial and secondary surgeries due to the temporal course of fibrous tissue accumulation at the fracture site[9].

Therefore, there is a crucial clinical need to determine the course of bone healing (aberrant versus normal) in the vitally important early stages of fracture management when additional surgery or adjunctive therapies could be implemented with much greater efficacy and result in a much lower risk of clinical failure to the patient. Accordingly, we developed a biocompatible, microelectromechanical system (bioMEMS) sensor that telemetrically reports data regarding the in vivo mechanical environment of the implant-bone construct, providing a quantitative measurement of the relationship between implant mechanics, and ultimately, prediction of the fracture's healing cascade.

Methods

Prior work by our group has undertaken an extensive series of experimental and analytical analyses that included resonance response frequency (RRF) computational models, prototype fabrication, and ex vivo simulations which clearly demonstrated the feasibility of using MEMS technology to telemetrically report on the mechanical environment of the plate-sensor construct by monitoring shifts in the sensor's RRF[10-17].

There are two separate components to the bioMEMS system: (1) the bioMEMS sensor-implant construct (Figure 1); and (2) the external excitation/receiving apparatus consisting of an antenna (Figure 1) attached to a spectrum analyzer. The excitation/receiving antenna emits an electromagnetic wave that induces a current in the bioMEMS sensor. The sensor continuously resonates according to its architectural features. Physical loading of the composite and layered metamaterial sensor results in a change in the sensor's capacitance via physical deformation of the split ring resonator's architecture (Figure 1).

The bioMEMS sensors are fabricated using standard MEMS fabrication processes. For biocompatibility, silicon is used as the substrate material of the sensor, gold as the metal layer, and Si3N4 as the dielectric layer[10,17]. The sensor's MEMS architecture has been optimized to generate a high electric field density, which yields amplification of the signal strength and high signal-to-noise ratio (Q-factor ≈76)[11]. For this study, BioMEMS sensors were rigidly adhered to implants (i.e. modified six-hole locking fracture fixation plates; Synthes, West Chester, PA) using a two-part high tensile strength epoxy (2 Ton Clear Epoxy, Devcon, Danvers, MA) (Figure 1).

Following rigorous in vitro analyses and a comprehensive biocompatibility study, an in vivo large animal (ovine) study was initiated. We hypothesized that the healing cascade in the critically important early period (7 - 35 days post-surgery) could be determined by temporally monitoring the bioMEMS sensor's RRF, and that these quantitative changes in the sensor's response would be predictive of normal and aberrant bone fracture healing.

Fourteen skeletally mature sheep (Columbia x Rambuillet cross breed, ~3.5 yrs. old) were utilized in this study (IACUC approval # 09-1471A). The surgery site was aseptically prepared using standard practices. The metatarsal was exposed through an insertion in the lateral part of the left hind limb. The bioMEMS sensor – locking plate construct (Synthes, West Chester, PA) was placed on the metatarsal and the required holes were drilled under saline irrigation. Self-tapping locking screws (DLS System, Synthes, West Chester, PA) were used attach the hardware to the metatarsal. An oscillating bone saw was used to create the planned ostectomy with saline irrigation to reduce the possibility of thermal necrosis. Two osteotomy models were utilized (union and non-union). Pilot work (n=2) by our group showed that an in vivo ovine metatarsal osteotomy larger than 10.27 ± 1.25 mm would not form a mechanically stable callus after 6 weeks of healing, and thus this fracture gap dimension was used as a lower bound to create a non-union sized defect. Defects were classified as an expected union (n=7; 4.8 ± 1.2 mm osteotomy) when calcified tissue was expected to bridge the osteotomy after approximately 6 weeks of healing. Non-union sized defects (n=7; 13.8 ± 1.0 mm osteotomy) were classified as constructs wherein it was expected that calcified tissue would not bridge the osteotomy after 6 weeks of healing. These ovine osteotomy fracture models were deemed analogous to union and non-union human long bone fracture conditions.

Bi-weekly RRF data were recorded from the implanted sensor while the treated limb was serially load-

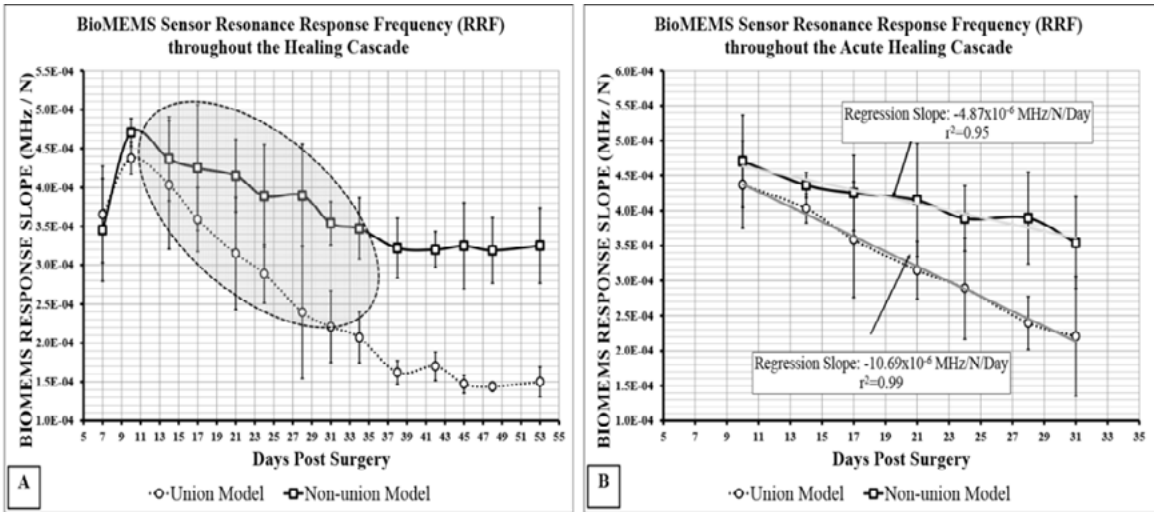

Figure 2. (A) BioMEMS sensor's mean (w/ one standard deviation error bars) temporal RRF response observed under loading during the healing cascade in an ovine metatarsal model. (B) The response during the acute healing phase (7-30 days post-surgery) demonstrated a statistically significant difference (p = 0.01) between the union (-10.69 ± 1.79 [Hz/N]/Day) and non-union (-4.87 ± 0.59 [Hz/N]/Day) models, indicating a substantial temporal reduction in hardware strain in the union model.

ed in compression (50 - 450 N) using a custom-designed fixture. Six loading cycles were performed per testing day; daily RRF means and standard deviations per treatment group were calculated.

Following euthanasia, the metatarsi were carefully collected and the bioMEMS plate constructs were removed from the underlying bone. Micro-computed tomography (µCT) analyses were performed at the mid-diaphyseal fracture (voltage: 70 kVp, current: 114 µA, integration time: 500 ms; Scanco µCT 80, Sanco Medical AG, Bruttisellen, Switzerland). µCT data was rendered into three-dimensional images and mid-sagittal slices were examined for continuous bone bridging between osteotomy cuts. Following µCT analyses, the treated metatarsi were processed for decalcified histological analysis. Histological sections were taken in the transverse (mediolateral) plane to include the fracture site and associated callus of the diaphyseal region of the metatarsus. High-resolution digital images were acquired for histomorphometric analysis using a Spot Imaging System (Diagnostic Instruments, Sterling Heights, MI), a microscope (E800, Nikon, AG Heinze, Lake Forest, CA), and analyzed with commercially available histomorphometry software (Image Pro, Media Cybernetics, Silver Spring, MD). Histomorphometric images (at 10x magnification) were acquired and area fractions of mineralized and fibrous tissue were calculated in the periosteal callus, diaphyseal cortices, and intramedullary canal. Total periosteal callus bone and fibrous tissue areas (mm2) were determined by selecting and segmenting callus material contralateral to the orthopaedic plate on the periosteal surface of the bone within the original osteotomy boundaries. Bone and fibrous tissue area percentages (%) were calculated within the periosteal callus, diaphyseal cortex, and intramedullary canal by normalizing the ratio of segmented tissue area to the total ROI.

Since all data passed normality and equal variance testing, statistical differences were detected between the treatment groups using a standard Student's t-test (SigmaPlot, San Jose, CA), where a p-value less than 0.05 was considered statistically significant. Statistical correlations were quantified using Pearson product moments (SigmaPlot, San Jose, CA).

Results

The in vivo data indicated a reduction in the measured RRF with respect to the applied load (RRF/N) as healing time increased ([RRF/N]/day) (Figure 2). These gradual decreases in the RRF over time reflect reductions in hardware strain due to fracture stabilization and healing, and closely mirror previously

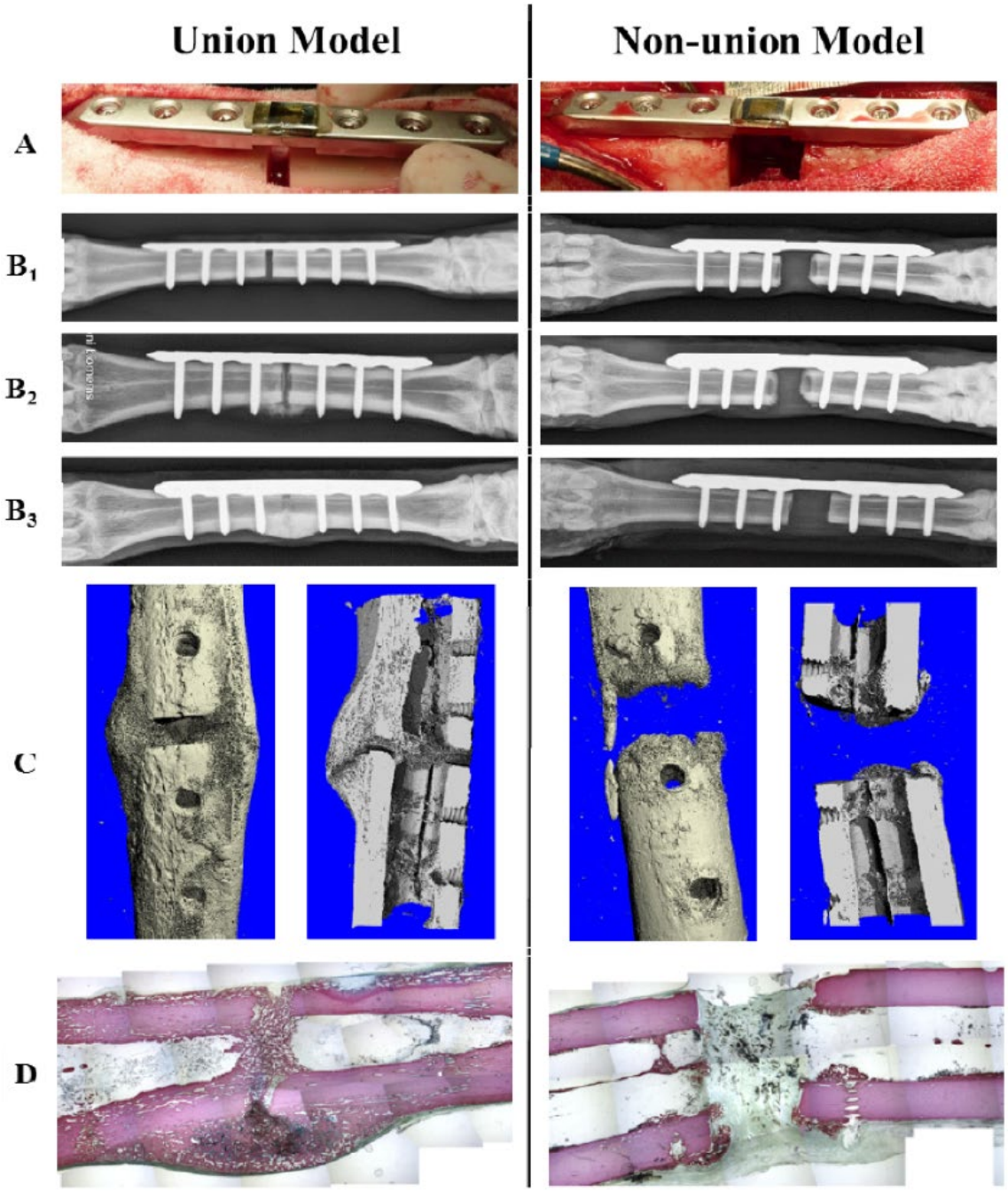

Figure 2.(A) Digital images obtained at the time of surgery that demonstrate the different osteotomy gaps used to model the union (4.8 ± 1.2 mm) and non-union (13.8 ± 1.0 mm) healing conditions. (B) Radiographs demonstrating the different model variants at (B1) 7 days, (B2) 24 day, and (B3) 45 days. Calcified tissue within the non-union osteotomy ranged from 2.1 ± 4.0% at 7 days post-surgery to 10.4 ± 20.1% at the time of sacrifice. Calcified tissue within the union osteotomy ranged from 2.8 ± 4.5% at 7 days post-surgery and 44.7 ± 27.7% at the time of sacrifice (C) μCT reconstructions demonstrated complete continuous calcified tissue bridging the entire osteotomy site for all (n=7/7) of the union samples and none (n=0/7) of the non-union surgical fractures (day 45 post surgery). (D) Histology sections stained with H&E to highlight the fibrous (gray stain) and calcified (red stain) tissue constituents model.

reported wired strain gage studies[4,5,18]. The RRF/N data (calculated between days 7 and 30 post-surgery) was used to compare the sensor's differential response between the two treatment groups during the acute healing period (Figure 2). The in vivo data indicated that the bioMEMS sensor was capable of detecting statistically significant differences (p-value < 0.04) between the two fracture healing groups as early as 21 days post-fracture. These RRF data also indicated a statistically significant difference (p = 0.01) between the union (-10.69 ± 1.79 [Hz/N]/day) and non-union (-4.87 ± 0.59 [Hz/N]/day) models during the initial 30 day healing period (Figure 2). This 220% difference in the rate of change in hardware strain within the acute fracture healing period for the union sized osteotomy group indicated the fracture callus in this group had a greater capacity to support limb loading and stabilize the fracture. Thresholding and segmentation analyses of weekly radiographic images of the fracture confirmed the differential healing response between the two groups (Figure 3). The non-union osteotomy group had little or no visible calcified tissue accumulation across the fracture site; the percentage of calcified tissue within the region of interest (i.e. osteotomy plus callus area) ranged from 2.1 ± 4.0% at 7 days post-surgery to 10.4 ± 20.1% at the time of sacrifice (day 45 ± 8). Conversely, the union osteotomy group demonstrated complete calcified tissue bridging of the osteotomy, with the calcified tissue component representing 2.8 ± 4.5% at 7 days post-surgery and 44.7 ± 27.7% at the time of sacrifice (day 45 ± 8). Correlation between the radiographic analyses and the RRF response was not observed during the acute healing phase for either group (p-value = 0.99), providing further confirmation that standard radiography cannot predict the course of fracture healing in the acute healing phase.

Post sacrifice (45 ± 8 days post-surgery) µCT reconstructions visually demonstrated complete continuous calcified tissue bridging the entire osteotomy site for all (n=7/7) of the union samples and none (n=0/7) of the non-union surgical fractures (Figure 3). Bone histopathology measurements within the area encompassing the osteotomy and the callus region (i.e. the region of interest, ROI) corroborated these µCT data (Figure 3. The non-union group had statistically less (p < 0.01) bone (11.4 ± 23.3% area of bone within the ROI) at the fracture site, a 73% decrease in mineralized tissue as compared to the union model (53.0 ± 28.5% area of bone within the ROI) group. A statistically significant correlation between the bioMEMS sensor response and percent bone at the fracture site for both the union (Pearson's correlation coefficient: -0.97; p-value < 0.01) and non-union groups (Pearson's correlation coefficient: -0.96; p-value < 0.01) was determined. These correlations indicated that the sensor has the ability to inform on the amount of bone present within the fracture gap, which is indicative of the relative biomechanical stability associated with the healing callus.

Conclusions

There is a critical need to discern the mechanical stability of the fracture site prior to callus calcification[25]. As healing progresses it is advantageous to quantify implant load, because not only does the plate load reflect the size of the callus, but also the degree of mineralization within the fracture site[5]. Our measurements showed that stability follows a continuous function, with biomechanical changes beginning well before they can be detected by radiographic imaging. If clinically available, these data could allow practitioners to optimize postoperative treatment regimens and avoid pseudarthrosis. Specifically, sequential bioMEMS RRF data could be used to indicate when a wide spectrum of minimally invasive (i.e. non-surgical) adjunctive therapies, including injections of osseous "biological" therapeutics, bone morphogenetic proteins (BMPs)[26,27] or other growth factors that potentiate the osteoinductive activities of BMPs[28-31], should be administered.

The RRF bioMEMS sensor data quantitatively described mechanical load sharing changes between the implant and the native tissue during the critically-important, acute, post-operative period of the healing cascade by demonstrating statistically significant differences in the sensor's response between the union and non-union groups.

Although a variety of methods are available to directly or indirectly determine the biomechanical characteristics of a healing fracture, most of these methods come with considerable limitations[25], which yields their routine implementation in the clinical milieu challenging. However, the specific MEMS structure, metamaterial architecture, and ra-

dio frequency technology used in the current study are advantageous for in vivo medical applications because: (1) the sensor can be inductively-powered obviating the need for an implantable power source; (2) the sensor can sense and transmit the in vivo biological data wirelessly, eliminating the internal-external physical connection; and (3) the sensor's size can be miniaturized allowing for its use in applications that require small dimension. We anticipate that with further experience with this device, it will be possible to predict complete fracture healing or eventual non-union based on the temporal mechanics of the fracture site.

Implantable MEMS devices for in vivo monitoring are a rapidly evolving field, with a constant stream of technologies being developed. MEMS devices including conventional pacemakers, implantable defibrillators, heart pressure monitors, and drug delivery devices have shown a great potential in the application of individualized medicine. Therefore, we envision that the developed device described herein has the potential to be translated for clinical applications.

Acknowledgments

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The Fifth Welfare and Safety of the Racehorse Summit

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The fifth Welfare and Safety of the Racehorse Summit was held 8–9 July 2014 in Lexington, Kentucky. Like previous summits, it was underwritten by the Jockey Club and Grayson-Jockey Club Research Foundation and hosted by the Keeneland Association. This summit has evolved from an identification of problems to being a good example of what the combination of data collection and analysis can accomplish with Thoroughbred horse racing. The programme was divided into various themes with several presentations and discussion following the presentations. The Chairman of the Summit was Mr Ed Bowen, President of the Grayson-Jockey Club Research Foundation.

Using data to keep horses safe

Three veterinarians, Dr Lisa Henelt, Dr Mary Scollay and Dr Jennifer Durenberger explained how the information, coupled with transparency and adjunctive examinations, had helped decrease injury. Dr Henelt used 'at risk alerts' identified by Dr Tim Parkin's preliminary analysis of the Equine Injury Database (EID) including horses remaining as nonwinners after 9 months of racing (especially a 3-year-old or older), having relatively few starts, recently changing trainers and also recent intra-articular injection with corticosteroids. After Dr Henelt at Finger Lakes Racetrack in upstate New York, Dr Scollay, the Equine Medical Director of the Kentucky Horse Racing Commission, confirmed that implementation of the data had led to a belief among regulatory veterinarians that fatal injuries can no longer be considered an inherent aspect of the sport and stated 'We must dispel the myth of inevitability'. Her other message was that acceptance without objectivity leads to complacency. Dr Durenberger, the Director of Racing for the Massachusetts Gaming Commission, explained that they had focused on changing the culture of racing by implementing new rules and holding trainers accountable and stated 'It's not just changing the rules, it's changing the culture' and used the example of rules requiring horses with overages for anti-inflammatory medication, such as phenylbutazone, to work off the vets list to continue racing. Steve Koch, Vice President of Thoroughbred Racing at Woodbine Entertainment, also expressed the importance of record keeping enabling management to make better decisions related to horse health and safety, licensing, safety and track maintenance. With regards to track maintenance, the variability of weather at Woodbine directly affects the tracks condition and keeping logs enables historical reference points to discuss track conditions and make management decisions. He felt that the combination of data collected including weather, maintenance logs, irrigation, going stick measurement and EID reports had 'tremendous implications for future understanding of track conditions, injury conditions and value-added opportunities for the wagering customer'. As a comment, these presentations gave examples of positively achieving a culture change but to achieve this overall the racing population in the US remains a challenge.

Today's Thoroughbred – what animals are we dealing with?

This panel addressed the question of why the average start per starter has dropped from 11 in 1960 to 6.3 in recent years. Mr Bowen addressed several generalisations including:

1. Fifty-seven per cent of the foal crop of 1958 raced at 2 compared with 30% of the 2008 foal crop racing (refuting the idea that we rush 2-year-olds more).

2. Although there are some 'mega' stables, 31 trainers each started at least 150 individual horses in 2013 but those stables accounted for only 7.5% of all starts (refuting the idea that huge stables race less frequently to avoid pitting one owner against another).

3. Refuting that American breeders' breed more for speed now, in 1888 the richest race was a 2-year-old sprint but the key targets are still the longer races now.

None of the panelists in this section bought into the connection commonly made between decline and starts being related directly to increased medication. A leading trainer, Todd Pletcher, had never observed medication to affect recovery time after racing. Dr Scollay cited advances in prerace veterinary screening as a possible factor as horses being excluded from racing based on better veterinary inspection today and Dr Larry Bramlage noted that he felt it was a pattern of using therapeutic medications indiscriminately that led to problems. Dr Rick Arthur also pointed out that in reviewing old racing form workouts considered 'bullet' work in earlier days would barely be seen as a breeze by today's standards and that 'some horses are working as fast as they are running in a race'.

National Uniform Medication Program update

Dr Dionne Benson, Executive Director and COO of the Racing Medication and Testing Consortium (RMTC), discussed the adoption of the National Uniform Medication Program. There are currently 26 therapeutic medications that have thresholds largely representing medication residues. There is a positive trend towards adoption of the National Uniform Medication Program in that she predicted by the end of 2014 that uniformity will carry across 78% of the USA. There is increasing adoption of third-party administration of furosemide or supervised furosemide administration which keeps practising veterinarians out of the stall on race day and avoids even the appearance of impropriety.

Grayson-Jockey Club Research Foundation update

Mr Bowen quoted Dr Sue Stover's work reporting 50% of fatalities being due to fetlock breakdowns (the majority being proximal sesamoid fractures) and that improved knowledge of mechanical properties affecting the interaction of the hoof with the race surface (work led by Dr Mick Peterson) was helping to understand the association with catastrophic injury and prevention that also enhanced jockey welfare. Dr Bramlage noted that equine herpesvirus-1 had the potential to derail any racing event, Dr Jim Belknap reported on advances in laminitis treatment and Dr Steve Reed noted that projects that had great impact include the evaluation of intra-articular medications by the Colorado State University group. Dr Bramlage also gave an excellent presentation on the complicated process of how bone responds to stress by strengthening and how bones are best strengthened through short, high-intensity loads followed by brief periods of little or no stress to allow the bone to 're-model' emphasising that the use of 2 mile, relatively strenuous gallops to build muscle and stamina might be counterproductive because it results in too much stress on bone. The benefits of regular exercise for 2-year-olds based on the physiology of bone growth was emphasised and studies showing that horses running at 2 suffer from fewer catastrophic injuries than other horses was noted.

Making safety a priority in your racing company

This panel was led by Dr Scott Palmer, Equine Medical Director for the New York State Gaming Commission. The overwhelming emphasis from all panel members was the importance of communication and transparency. In addition to monitoring catastrophic injury, there was discussion on the desirability of tracking nonfatal injuries and making medical records of horses more available so that a trainer taking over a horse from another trainer could make better and safer decisions about handling his/her new horse. Dr Foster Northrup noted that despite greatly improved recognition of early change that could predispose to an injury, this was not always heeded by the trainer. In addition, he noted that some veterinarians also exacerbated the problem by treating these horses rather than supporting recommendations by other veterinarians to give the horse a rest. Mr Gary Contessa, a successful trainer based in New York, described an emotional experience of having a very good prospect suffer a fatal injury and then months later, as a result of enquiry into a series of catastrophic injuries in New York, learning from the jockey's testimony that the filly warmed-up poorly but he was afraid to have her scratched. There was agreement that an improved culture was needed where the rider felt free to tell the trainer or the track veterinarian that they suspected a problem when the horse was warming-up.

Intra-articular joint therapies

There was strong emphasis on what is currently known about intra-articular corticosteroids in this panel. Dr Heather Knych of UC Davis described research work that had led to new corticosteroid regulation under the National Uniform Medication Program and how it was changing the behaviour and attitudes of trainers and veterinarians toward corticosteroid use. Dr Jamie Macleod reported on a recent project showing that all corticosteroids had some detrimental effects on the chondrocytes in cartilage at high concentrations and that doses should be reconsidered to ensure optimisation of safety and efficacy. Dr Knych's work had also demonstrated the potency of what have been previously considered relatively low doses of corticosteroids when gene expression changes are looked at after administration. Dr Wayne McIlwraith highlighted the changes that occur long-term associated with corticosteroid use and lauded the decreased use of corticosteroids generally and methylprednisolone acetate in particular. Alternative options for intra-articular medication were discussed as well as the potential for different medication combinations to enable testing below the new threshold levels and enhance safety were also presented.

Jockey injury database

Dr Carl Mattacola, an Assistant Professor of Athletic Training at the University of Kentucky, is overseeing data collection and analysis of the Jockey Injury Database and gave a report. He believes that the vast majority of injuries suffered by jockeys in races are not being reported despite potential to improve safety. He suggested more tracks need to be involved for consistent data collection. The goal of the database is to collect uniformly all the relative information when a rider injury occurs in an effort similar to the industry's EID.

Surfaces and technology integrations

Dr Mick Peterson's Racing Surfaces Testing Laboratory was an idea that grew from previous summits and has been made possible by the Jockey Club support. Dr Peterson's laboratory has tested more than 80 surfaces. During the summit, he emphasised that the track is only one of the many factors related to racehorse safety but it is a critical one. He said ongoing research on dirt surfaces still supports the long-held belief that water content is key to maintaining consistency both from the standpoints of trying to have the entire oval offer the same footing at race time as well as being the same from day-to-day. 'Consistency is perfection and that's what we are looking for' Dr Peterson said. Related to the recent trend away from synthetic surfaces, Dr Peterson said that a well-managed dirt surface can almost be as safe as the best synthetic surface and that better record keeping is making tracks safer. Glen Kozak, Vice President of Facilities and Racing Surfaces for the New York Racing Association, gave a presentation on the task of maintaining the total of 9 dirt tracks and training tracks as well as the turf courses at Belmont, Aqueduct and Saratoga. He reported the various tools he uses to record the maintenance procedures his crew undertakes, including combination with real-time weather data and GPS locations of routes of his tractors and water trucks. He works in close relationship with Dr Peterson and the Racing Surfaces Testing Laboratory. 'I never knew how much we were missing' Mr Kozak stated when talking about techniques based on data for bringing a scientific standard to what was formerly a subjective system used to call a track good, wet or muddy, for example. This comment seems to summarise the recurring underlying message from all sessions in the summit that, as a result of all of the initiatives described above, steps are being taken towards providing the evidence base which is needed to incrementally improve racehorse and jockey safety and secure the future of the sport.

Evaluation of articular cartilage matrix using contrast-enhanced computed tomography in the horse

Osteoarthritis (OA) is the degeneration of articular cartilage and is a significant problem in the horse, leading to decreased athleticism, early retirement and potentially necessitating euthanasia. OA results in significant costs both monetary and in the loss of use of the horse (>$700 million per year based upon an estimate from the USDA in 2000). OA also largely affects humans with estimates of 50% of adults over 65 years developing OA and costs hundreds of billions of dollars per year. The diagnosis of early OA and articular cartilage injury is challenging. Although magnetic resonance imaging is widely considered the best imaging modality to detect cartilage injury, routine MRI does not have the capacity to detect the early degenerative changes in cartilage that occur in OA. On a molecular level, one of the earliest markers of OA is the depletion of glycosaminoglycans (GAGs) from within the cartilage tissue.

The main objectives of this work is to improve the early detection of osteoarthritis and articular cartilage injury and thus develop strategies to slow or stop the progression of OA. We aim to use new diagnostic imaging techniques to detect this loss of GAGs from articular cartilage. Through collaboration with ORC researchers and

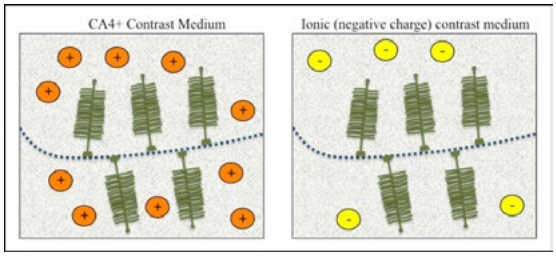

Figure 1. Pictorial description of how CA4+ (cationic) and anionic (negatively charged) contrast media interact with negatively charged glycosaminoglycans (GAGs, green) in articular cartilage. Note that with CA4+ more contrast media can penetrate the tissue and surround the GAGs when compared to the negatively charged contrast media.

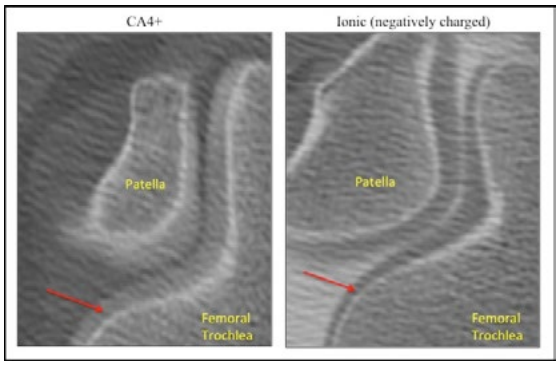

Figure 2. Computed tomography scans of the equine stifle using two different contrast media. The left image shows the femoropatellar joint compartment injected with CA4+ and the right image following injection of an anionic, negatively charged contrast media. The red arrow points to the articular cartilage in both images. In the left image, note how the cartilage has more of a light grey hue reflecting penetration of the CA4+ contrast media. In comparison, the right image shows most of the negatively charged contrast media being retained in the joint space not entering the cartilage; although the anionic media outlines the cartilage, it does not penetrate cartilage and limits evaluation on computed tomography.

Dr. Mark Grinstaff at Boston University (CSU affiliate faculty) we have evaluated a cationic (or positively charged) contrast medium (CA4+) developed by Dr. Grinstaff. Once injected into the joint, this novel contrast medium is attracted to the negatively charged GAGs in cartilage. Conversely, all commercially available contrast media are anionic (negatively charged) and thus do not penetrate cartilage as well as CA4+ (Figure 1). Once the injected contrast equilibrates within the cartilage, the amount of CA4+ in cartilage can be quantified using computed tomography (cationic CT)(Figure 2).

To evaluate the potential of cationic CT imaging in a joint with degenerative articular cartilage, cartilage defects were created in one stifle of one horse while

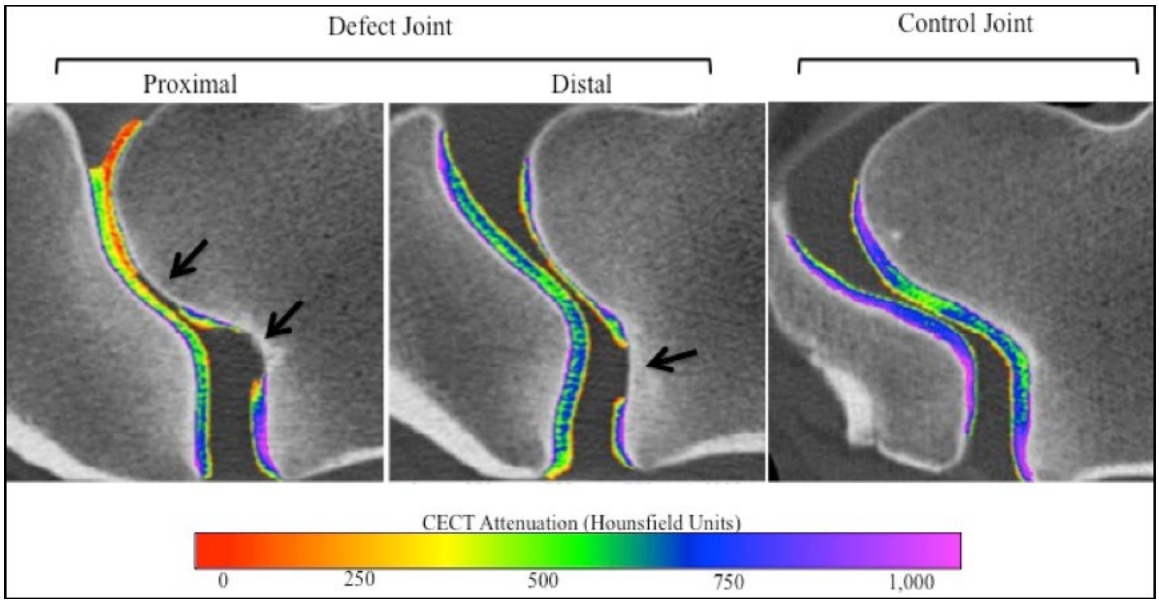

Figure 3. Cationic computed tomography scans of the equine stifle seven weeks following the creation of articular cartilage defects on the femoral trochlea of one horse while the opposite limb was maintained as a control. The articular cartilage in these three images has been segmented from the surrounding tissues and quantified on the Hounsfield unit scale. This is shown as a range of color values with blue/purple reflecting more penetration and higher amounts of CA4+ while yellow/orange hues demonstrate less CA4+. The black arrows point to the full thickness defects easily detected and comparison of the color values in the defect joint demonstrates less CA4+ in cartilage and therefore fewer GAGs present than in the control joint.

the opposite stifle remained as a control. Cationic CT imaging seven weeks later revealed that full thickness cartilage defects were readily detectable with this technique (Figure 3). Articular cartilage/bone plugs were collected postmortem. The GAG content and equilibrium compressive modulus (E, mechanical property) of cartilage was directly determined from each of these plugs. These values were then compared to the measurements made on the cationic CT images (recorded on the Hounsfield unit scale). Low quality cartilage tissue (low GAG or E) could be successfully predicted from the values measured on cationic CT images. Excitingly, some of the cartilage on visual inspection appeared normal and thus supports the potential of cationic CT to detect early microscopic changes in articular cartilage before macroscopic changes have occurred.

To expand upon this preliminary work, we have obtained funding through the Grayson-Jockey Club and the College Research Council at CSU to further investigate the cationic CT technique. The next study being performed is in the use of an impact device to simulate post-traumatic osteoarthritis in the equine stifle and to evaluate the subsequent degeneration of articular cartilage with cationic CT imaging.

The plan is to follow the progression of OA with cationic CT imaging. Multiple cationic CT imaging examinations will be performed biweekly after OA has been initiated. This study will help determine how early the degeneration of articular cartilage can be detected with cationic CT as well as determine any alterations in how OA progresses over time. Future directions are to evaluate cationic CT as a potential monitoring technique and to compare cationic CT to other quantitative MRI techniques available in research settings. The impact of this work will benefit the early detection of OA in horses, but there is also a translational application to humans with OA. If the long-term objectives of the cationic CT technique are achieved, then this technique may be explored in the evaluation of humans with OA. Potentially, by using a technique for in vivo preclinical research studies, cationic CT also has the potential to decrease the number of research horses needed in longitudinal studies that would normally require the sacrifice of the horse.

Chronic changes in the articular cartilage and meniscus following traumatic impact to the lapine knee

This is a summary of a study done by Dr. Tammy Donahue's group and recently published in the Journal of Biomechanics.[1]

Take Home Message

Traditional models for post traumatic osteoarthritis (PTOA) do not mimic the natural closed joint injury and thus may limit the conclusions that can be made from these studies. Using a novel closed joint impact model, this is the first study to document changes to both the menisci and articular cartilage following a concomitant ACL and meniscal acute injury. It is clear from the current study that unattended meniscal and ACL damage results in significant changes to the menisci, which possibly correlate with articular cartilage damage.

Introduction

High compressive tibiofemoral loading, often experienced during jump landings is one potential non-contact mode of ACL rupture[2] and has have been shown to cause acute damage to articular cartilage, bone, and the menisci[3,4]. Current models of knee PTOA have primarily been ACL transections models that do not account for occult and acute damages to the surrounding structures which are often present in ACL injuries[5,6]. The current study investigates mechanical and histological changes to the menisci and articular cartilage following a closed joint tibiofemoral impact lapine model.

Methods

Six skeletally mature Flemish Giant rabbits were used in this study. Rabbits were anesthetized and placed in a supine position with the right tibiofemoral joint at 90^0 flexion. A 1.75 kg mass was dropped from a height of 70 cm, striking the distal femur rupturing the ACL and creating acute damage to surrounding tissues. The left limb served as a control and rabbits were sacrificed 12 weeks post-surgery. Morphology, elastic moduli, and glycosaminoglycan (GAG) content of the menisci were determined. Articular cartilage was assessed for morphological changes, thickness, modulus, permeability, and histological changes.

Results

The articular cartilage had significantly higher degrees of surface damage on the impacted tibias and femurs compared to controls (Figure 1). Chronic meniscal damage was most prevalent in the medial central and medial posterior regions (Figure 2). Mechanical tests revealed significant changes to the articular cartilage including a 19.4% increase in tibial plateau cartilage thickness, a 34.8% increase in tibial plateau permeability, a 40.8% increase in femoral condyle permeability, and a 20.1% decrease in femoral condyle matrix modulus

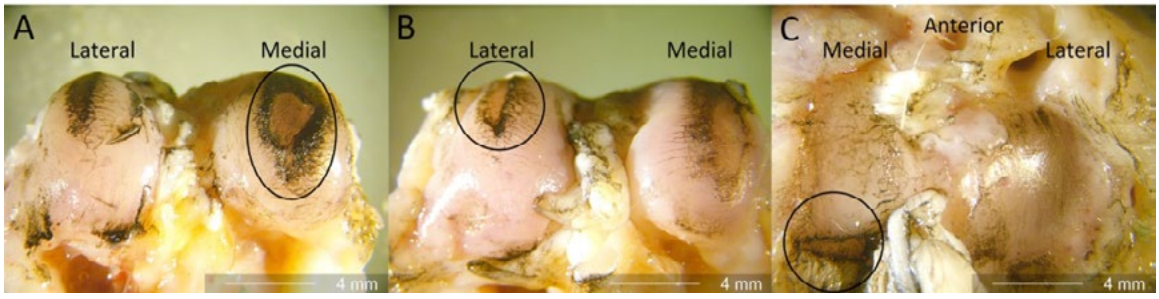

Figure 1. Full thickness cartilage erosion was noted on the medial femoral condyles (a), on the lateral femoral condyle (b), and full thickness erosion was noted in the medial-posterior aspect of the tibia (c).

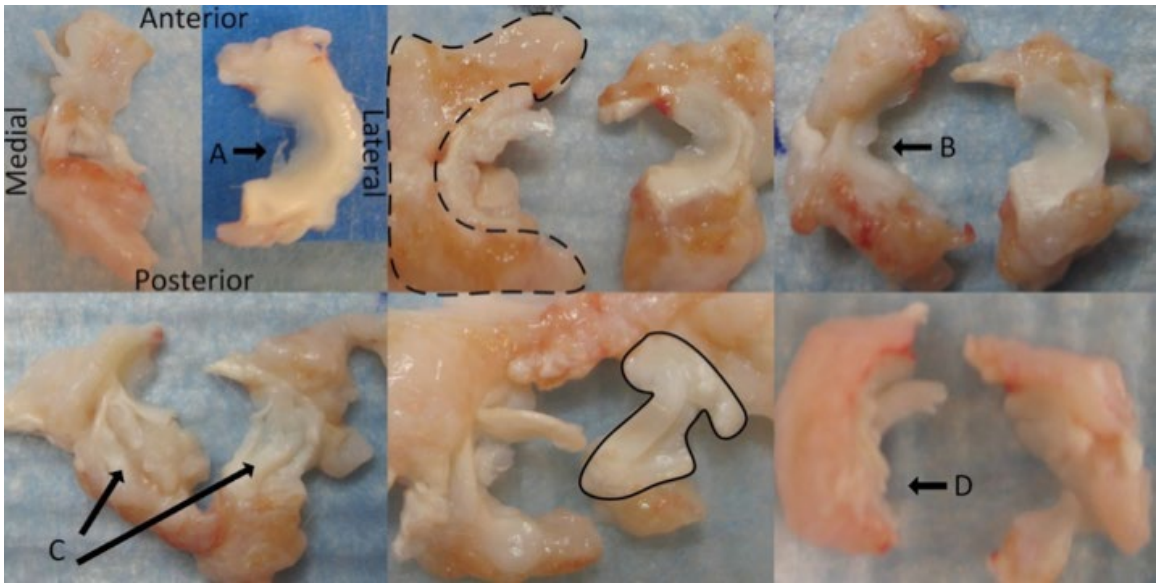

Figure 2. ACLF Menisci 12 weeks post-impact (animals 1-6 left to right and top to bottom, all specimens are oriented identical to the first image). Dashed line outlines example synovium, Solid line outlines example of meniscal tissue, displaced parrot beak tear (a), tissue maceration to central region (b), complex tearing of both the medial and lateral menisci (c), and tissue maceration of the posterior horn (d).

in impacted joints compared to controls. Both instantaneous and equilibrium moduli of the lateral and medial menisci were significantly decreased compared to control (Figure 3). Histological analyses revealed significantly increased presence of fissures in the medial femur, and in both meniscus and cartilage there was a significant decrease in GAG coverage for the impacted limbs.

Conclusions

Based on these results it is clear that an unattended combined meniscal and ACL injury results in significant changes to the soft tissues in this experimental joint 12 weeks post- injury.

Acknowledgments

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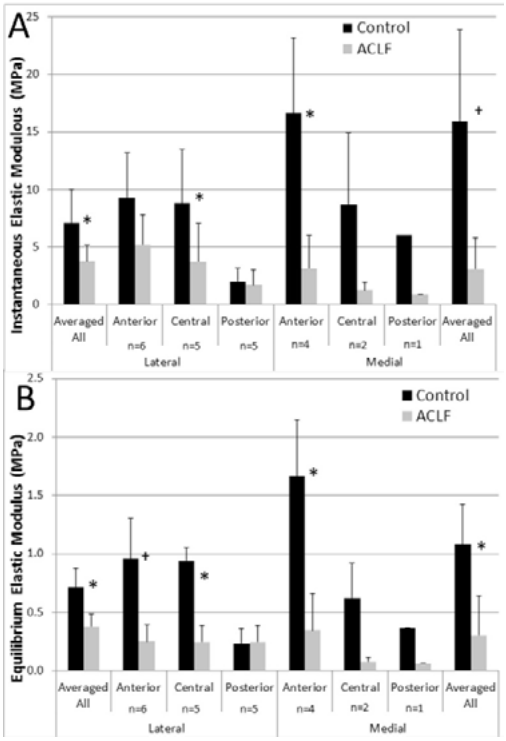

*Figure 3. A) Instantaneous elastic modulus of the menisci B) equilibrium elastic modulus of the menisci (mean with standard deviation) * denotes p<0.05 and + denotes p<0.1 between control and ACLF.*

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Non-fatal injury occurrence in Southern California Thoroughbred racehorses 2009-2010

This is a reproduction of an article on a study carried out by Drs. Ashley Hill (epidemiologist previously at CSU and now at UC Davis), Jeff Blea (racetrack veterinarian, Southern California), Rick Arthur (Equine Medical Center Director, California), and Wayne McIlwraith recently published in The Veterinary Journal, 2015;205:98-100.

Non-fatal injuries are common in Thoroughbred racehorses and are the primary reason that horses exit training (Perkins et al., 2005). Non-fatal injury incidence reports have focused on specific injuries, specific activities (racing or race-training), a particular age or stage of training, or are based on trainer reports of injury and do not report anatomical location (Peloso et al., 1994; Cogger et al., 2008; Dyson et al., 2008; Ramzan and Palmer, 2011; Reed et al., 2012). To our knowledge, no reported data describe the incidence of the full spectrum of veterinary-diagnosed non-fatal injuries incurred both during racing and race training in a population of Thoroughbred racehorses. The objectives of this study were to describe the incidence and anatomical distribution of non-fatal injuries in Thoroughbred racehorses in Southern California, to compare frequency of non-fatal and fatal injuries, and to compare a private practitioner non-fatal injury-reporting system to an existing racetrack regulatory non-fatal injury reporting system.

Data were collected through the not-for-profit Southern California Equine Foundation (SCEF), which operates equine hospitals utilized by all racetrack veterinary practices. All veterinarians using SCEF hospitals were invited to participate. Participating veterinarians recorded non-fatal injuries (definitive diagnosis of a musculoskeletal condition resulting in lameness, injury or loss of training >5 days) in Thoroughbred racehorses from 1 May 2009 to 30 April 2010. Diagnosis date, veterinarian, horse name, racetrack, racetrack surface, circumstances (racing, training, nonexercise), American Association of Equine Practitioners (AAEP) lameness score at diagnosis, injured limb(s), time course ('acute' for first diagnosis vs. 'chronic' for recurrence), and anatomical location were recorded. An injury was defined as damage to one structure (e.g. superficial digital flexor tendon) in one or more limbs. An injury event was one or more injuries diagnosed on the same date. Jockey Club records provided birth year and sex.

Participating horses were racing or in race training at four racetracks in Southern California. Nearly all training occurred on synthetic main track surfaces with all racing/training counterclockwise except for slow trotting allowed clockwise on the outside. Stable census records (monthly records of number of horses stabled per trainer) were used as denominator data for injury incidence. Horses stabled by trainers whose veterinary practice was participating in the study represented the population from which case horses were drawn.

Non-fatal injury rate was calculated as (number of injury events per month/number of participating stabled horses). Fatality data for the same time period, racetracks, and trainers were obtained from the California Horse Racing Board's (CHRB) Postmortem Program. Post-race injury or unsoundness (post-race AAEP lameness grade >3 identified by racetrack regulatory veterinarian) data from the same time period, racetracks, and trainers whose veterinarians were participating in the study were obtained from the Jockey Club's Equine Injury Database (EID).1

From 1 May 2009 to 30 April 2010, 477 non-fatal injuries were recorded by seven veterinarians in three veterinary practices. Participating veterinarians served 35.8% (11,764 of 32,872 horse-months) of the racehorse population at participating tracks. Injury reports covered 458 injury events in 425 horses (one to three events/horse; one to two injuries/event): 194 (45.7%) females, 130 (30.6%) geldings, 100 (23.5%) intact males, and 1 (0.2%) cryptorchid, with median age 3 years (range: 2–9).

Injury events occurred at Tracks A (192; 41.9%), B (187; 40.9%), C (77; 16.8%), and D (2; 0.4%) during training (375; 81.9%), racing(74; 16.1%), and unrelated to exercise (9; 2.0%). Cumulative non-fatal injury incidence was 2.29 (95% CI: 2.10–2.51) injury events per 100 horse-months. Track surface for 449 exercise-related injury events included synthetic (417; 92.9%), turf (22; 4.9%), and dirt (10; 2.2%).

Table 1
Descriptors of 344 non-fatal acute injuries in 316 Thoroughbred racehorses and 133 non-fatal chronic injuries in 123 Thoroughbred racehorses over a 1-year period (2009–2010) at four racetracks in Southern California.

			Acute		Chronic		Total	
Variable	Value	Sub-category	Frequency	Percent	Frequency	Percent	Frequency	Percent
Limb			344	100.0	133	100.0	477	100.0
	LF		155	45.1	64	48.1	219	45.9
	RF		121	35.2	39	29.3	160	33.5
	LF, RF		18	5.2	13	9.8	31	6.5
	LH		17	4.9	11	8.3	28	5.9
	RH		23	6.7	5	3.8	28	5.9
	LH, RH		9	2.6	0	0	9	1.9
	LF, RF, LH, RH		1	0.3	1	0.8	2	4.2
Lameness score	0		29	8.4	11	8.3	40	8.4
	1		45	13.1	33	24.8	78	16.3
	2		81	23.6	40	30.1	121	25.4
	3		103	29.9	40	30.1	143	30.0
	4		75	21.8	7	5.2	82	17.2
	5		9	2.6	2	1.5	11	2.3
	Unknown		2	0.6	0	0	2	0.4
Injury type				100.0				
	Fracture		171	49.7	56	42.1	227	47.6
		Carpal chip fracture(s)	22	6.4	19	14.3	41	8.6
		Tibial stress fracture	29	8.4	10	7.5	39	8.2
		Proximal sesamoid bone fracture	30	8.7	2	1.5	32	6.7
		Proximal phalanx (P1) chip fracture	23	7.3	9	6.8	32	6.7
		MCIII cortical stress fracture	14	4.1	6	4.5	20	4.2
		Condylar MCIII fracture	15	4.4	2	1.5	17	3.6
		Splint fracture/osteitis	12	3.5	5	3.7	17	3.6
		Third carpal (C3) slab fracture (complete or partial)	12	3.5	1	0.7	13	2.7
		Pelvic fracture/pelvic stress fracture	3	0.9	1	0.7	4	0.8
		Humeral stress fracture	3	0.9	0	0	3	0.6
		Condylar MTIII fracture	1	0.3	1	0.7	2	0.4
		Third phalanx (P3) fracture	2	0.6	0	0	2	0.4
		Proximal-palmar MCIII avulsion fracture	2	0.6	0	0	2	0.4
		Cortical stress fracture, radius/ulna	1	0.3	0	0	1	0.2
		2nd phalanx (P2) fracture	1	0.3	0	0	1	0.2
		Patella fracture	1	0.3	0	0	1	0.2
		Tarsal slab fracture	1	0.3	0	0	1	0.2
	Bony non-fracture		40	11.6	23	17.3	63	13.2
		Dorsal MCIII periostitis	13	3.8	8	6.0	21	4.4
		C3 sclerosis	9	2.6	5	3.8	14	2.9
		Subchondral bone disease (MCIII/MTIII)	6	1.7	7	5.3	13	2.7
		Carpal osteitis/periostitis	4	1.2	0	0	4	0.8
		Osteochondrosis dissecans stifle/femur	3	0.9	1	0.7	4	0.8
		Proximal sesamoid bone osteitis	2	0.6	1	0.7	3	0.6
		Splint fracture/osteitis	1	0.3	1		2	0.4
		Myositis	1	0.3	0	0	1	0.2
		P3 increased radioisotope uptake	1	0.3	0	0	1	0.2
	Soft tissue		107	31.1	28	21.1	135	28.3
		Superficial digital flexor tendonitis	58	16.9	15	11.3	73	15.3
		Suspensory ligament desmitis	44	12.8	11	8.3	55	11.5
		Deep digital flexor tendonitis	2	0.6	0	0	2	0.4
		Distal sesmoidean ligament desmitis	2	0.6	0	0	2	0.4
		Superficial digital flexor rupture	1	0.3	1	0.7	2	0.4
		Carpal sheath synovitis	0	0	1	0.7	1	0.2
	Joint		17	4.9	25	18.8	42	8.8
		Fetlock DJD/OA	11	3.2	15	11.3	26	5.4
		Carpal DJD/OA	3	0.9	8	6.0	11	2.3
		Stifle DJD/OA	2	0.6	0	0	2	0.4
		Tarsal DJD/OA	1	0.3	1	0.7	2	0.4
		Pastern sub-luxation (proximal interphalangeal)	0	0	1	0.7	1	0.2
	Other		9	2.6	1	0.8	10	2.1
		Foot bruise	3	0.9	1	0.7	4	0.8
		Cellulitis	2	0.6	0	0	2	0.4
		Foot abscess	2	0.6	0	0	2	0.4
		Laceration	2	0.6	0	0	2	0.4

LF, left fore; LH, left hind; RF, right fore; RH, right hind; MC/MTIII, third metacarpal/metatarsal bones; DJD/OA, degenerative joint disease/osteoarthritis.

Of the 477 injuries, 344 (72.1%) were acute and 133 (27.9%) were chronic. Fractures and soft tissue injury were the most common categories (47.6% and 28.3%, respectively; Table 1). The most frequent specific injuries were superficial digital flexor tendonitis (73; 15.3% of all injuries reported) and suspensory ligament desmitis (55; 11.5%). Injuries affecting the fetlock joint and carpus comprised 26.2% (125/477) and 17.4% (83/477), respectively, of all injuries reported. Stress fractures comprised 14% (67/477) of all injuries reported.

During the study, 27 racehorses among the study population died with fatal musculoskeletal injuries either racing or training. The ratio of non-fatal to fatal injury events was 458:27 or 17:1. The study recorded 74 racing-related injury events, whereas the EID recorded 57 racing-related injury events, with eight events recorded in both systems, indicating poor agreement between recording systems.

This study reported veterinarian-diagnosed injuries, whereas studies reporting higher rates used trainer-reported injuries (Perkins et al., 2005; Cogger et al., 2008). Perkins et al. (2005) found that 54% of musculoskeletal injuries causing training loss >7 days received veterinary examinations, with no examinations for 30–40% of nonfracture, ligament, and tendon injuries; 50% of back injuries; and >90% of cases of shin soreness. Shin soreness and foot problems may not be presented to a veterinarian or may not result in the loss of >5 days of training but are common lameness-associated injuries in racehorses in training, that were rare in the current study (Cogger et al., 2008; Dyson et al., 2008).

Trainer decisions regarding veterinary attention may partly explain the poor agreement between the EID and the current study. Injuries only recorded in the EID may not have been presented for veterinary attention, or may not have been reported by the veterinarian if the injury was not considered to interfere with training.

Many injuries only recorded in the study had AAEP lameness grade ≤3 at diagnosis and may not have met EID criteria. Others may not have been as severely lame immediately post-race when observed by the regulatory veterinarian.

The anatomical distribution of non-fatal injuries differs from the distribution of fatal Thoroughbred racehorse injuries during the same time period (California Animal Health and Food Safety Laboratory System, 2011). Fatal injuries commonly affected the proximal sesamoid bones (35.7%) and third metacarpal/metatarsal bones (18.5%); tendon injuries (2.2%) and carpal fractures (3.5%) were less frequent. The frequency of these fractures was lower for non-fatal vs. fatal injuries, whereas tendon injuries and carpal fractures were more common.

The ratio of 17:1 non-fatal:fatal injuries is likely an underestimate. If a combination of the EID and the current study better represents the true incidence of non-fatal injury, then the current study captured 60% (74/[74 + 49]) of non-fatal racing injuries. Assuming similar under-reporting for training injuries, the number of non-fatal injuries may have been closer to 795 (477/0.6), with a 795:27 or 29:1 non-fatal:fatal injury ratio.

Most exercise-associated injuries in the current study occurred on a synthetic track, the same surface as the main track at the three largest tracks, where the bulk of racing and training occurred. The proportion of racing injuries on the synthetic surface (75.7%; 56/74) is higher than expected given that 66.9% (11,575/17,291) of race starts were on a synthetic surface during the study period (California Horse Racing Board, 2009, 2010).

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

Acknowledgments

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Musculoskeletal Pathology in Equine Pathology and Laboratory Diagnostics, Veterinary Clinics of North America: Equine Practice

This is a reproduction of a chapter by Drs. Frances Peat and Chris Kawcak on Musculoskeletal Pathology in the horse published in Veterinary Clinics of North America: Equine Practice, 2015;31:407-424, an issue devoted to equine pathology and laboratory diagnostics.

The current understanding of pathology as it relates to common diseases of the equine musculoskeletal system is reviewed in this article. Diseases have been organized according to the fundamental classifications of developmental, exercise-induced, infectious, and miscellaneous pathology.

DEVELOPMENTAL MUSCULOSKELETAL PATHOLOGY

A variety of specific growth-related musculoskeletal conditions occur in young horses, namely, osteochondral fragmentation, subchondral cystic lesions, physitis, incomplete cuboidal bone ossification, angular limb deformities, and flexural limb deformities. Traditionally, the term developmental orthopedic disease (DOD) has been used to encompasses all these conditions.[1] A new classification of equine JOCC has recently been proposed.[2] This classification encompasses lesions that occur as a direct result of osteochondrosis and also includes avulsion fractures of ossifying bones and physitis (Fig. 1).

Epidemiology

Juvenile osteochondral conditions

The age range for JOCC is considered to be the first 2 years of life.[2] However, lesions that have developed within this time frame may not become clinically apparent until after a horse commences athletic training. Subchondral bone cysts that manifest clinically within the first 2 years of life are considered to be a result of osteochondrosis.[3] However, subchondral cystic lesions can also develop in older horses as a result of exercise-induced trauma.[4] A large-scale study following up Irish thoroughbred foals up to the age of 18 months found that 11% had some form of DOD that required treatment. In 73% of these foals, the specific condition requiring treatment was either angular limb deformity or physitis.[5] The incidence of physitis peaks between 4 and 8 months of age, but it can occur at any time before closure of the growth plate. In a separate study investigating radiographically evident lesions of osteochondrosis in over 9000 warmblood horses, the overall prevalence of such lesions was 14%.[6]

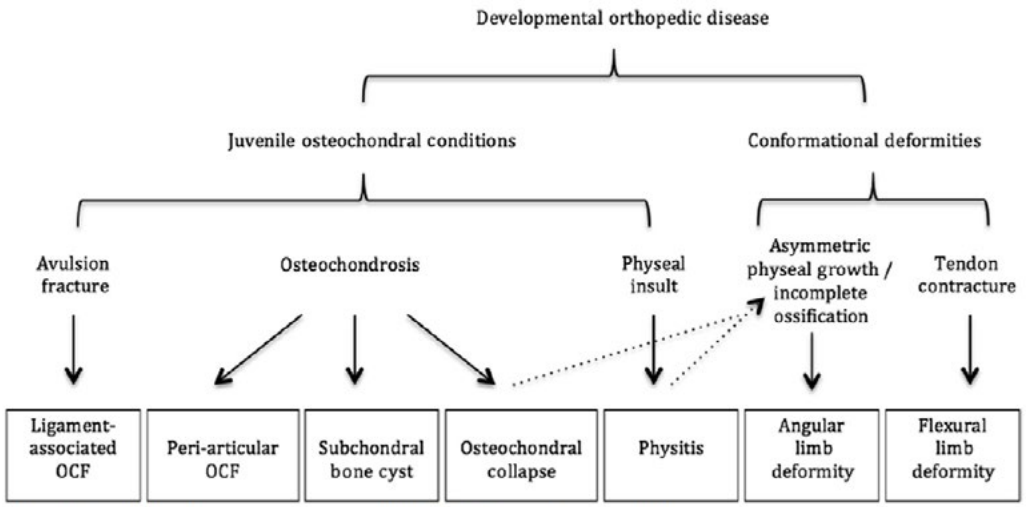

Fig. 1. Classification of developmental musculoskeletal pathology in the horse.

Conformational deformities

Angular and flexural limb deformities can be present congenitally or can be acquired postnatally. Their prevalence has been shown to decrease from birth to weaning in multiple breeds.[7] Prematurity or dysmaturity often results in angular deformities within the first 2 weeks of life, because of incomplete ossification of the cuboidal bones of the carpus or tarsus, or ligamentous laxity of the supporting periarticular soft tissues. Most angular deformities originate at the level of a distal growth plate, and the deviation is described with reference to the adjacent joint. Rarely, angular deviation can occur as a result of a bend within the metaphysis or diaphysis itself.[8] The most common angular limb deformities in neonates are carpal valgus, tarsal valgus, and fetlock valgus or varus.

Pathophysiology

Osteochondrosis

Osteochondrosis is a multifactorial disease process that involves focal failure of endochondral ossification within the articular epiphyseal growth cartilage or metaphyseal growth cartilage.[9] There is compelling evidence across multiple species of a polygenetic heritable component to the disease.[10] It is often assumed that the hereditary influence is linked to certain anatomic characteristics and a predisposition for higher growth rates. Current scientific evidence does not support a direct correlation with rapid growth rates or overnutrition, or mineral imbalances that have at times been implicated.[11,12]

Endochondral ossification occurs through a sequence of chondrocyte proliferation, extracellular matrix synthesis, cellular hypertrophy, vascular invasion, and matrix mineralization.[10] At the ossification front, there is an abrupt change in biomechanical strength, and the arterioles that traverse this zone are particularly vulnerable to insult.[13,14] In osteochondrosis, biomechanical loading is thought to result in focal microvascular changes that lead to ischemia, retention of cartilage cores, and subsequent chondronecrosis. Mechanical dissection of the lesion results in an osteochondral flap, which may detach and become a free-floating fragment within the joint.[3] Alternatively, continued biomechanical loading on retained chondronecrotic lesions can lead to the development of a juvenile subchondral bone cyst. Variations in biomechanical loading and pressure distribution at different anatomic sites could explain the occurrence of common distinct lesions of osteochondrosis.[2,3] These lesions are identified in Table 1.

Physitis

The clinical significance of asymptomatic growth plate enlargement is controversial, and recent research has suggested that there may be physiologic swelling associated with normal bone remodeling.[15] True pathology within an active physis is thought to result from persistent asymmetric loading that disrupts normal endochondral ossification. This condition can lead to asymmetric growth and subsequent angular deformity if not corrected. Common causes of unequally distributed, high-strain loading of physes in foals include excessive exercise combined with laxity of periarticular soft tissue structures, incomplete cuboidal bone ossification, incorrect foot trimming, contralateral limb lameness, and heavy body weight. The most commonly affected physes are those of the distal radius and distal third metacarpus or metatarsus.

Clinical Presentation

JOCC may remain clinically silent. Lesions that do become clinically apparent usually present with sudden-onset joint effusion and varying degrees of lameness because of debris or loose fragments causing synovitis within the joint.[3] Most commonly affected are the femoropatellar, tarsocrural, and metacarpophalangeal joints. Bilateral joint involvement was present in 26% of tarsocrural and 25% of femoropatellar cases in the study of over 9000 Hanoverian warmblood foals.[6] The scapulohumeral joint is less frequently involved. Overt lameness attributable to osteochondritis dissecans (OCD) is most common in the femoropatellar and scapulohumeral joints. Effusion without lameness is more common in OCD of the tarsocrural and metacarpophalangeal joints.[16] The introduction of presale yearling radiograph systems has resulted in a significant increase in the diagnosis of clinically silent, but radiographically apparent lesions.[17] Prospective data relating to their potential clinical significance in future athletic careers are still needed for many of these minor lesions.

Diagnosis

Lesions of osteochondrosis are most frequently diagnosed via radiography. Ultrasonography can be

Table 1
Juvenile osteochondral conditions

Type of JOCC	Lesion	Anatomic Region	Common Sites	Type of Biomechanical Overload
Osteochondrosis	Articular surface osteochondral fragment	Prominent articular ridge	Lateral trochlear ridge of the femur Sagittal ridge of metacarpal/tarsal condyle	Compression/ shear
Osteochondrosis	Periarticular osteochondral fragment	Articular margin	Distal intermediate ridge of the tibial cochlea Dorsoproximal margin of proximal phalanx	Compression at end ranges of joint motion
Osteochondrosis	Subchondral bone cyst	Heavily loaded (convex) articular surface	Medial femoral condyle Distal aspect of proximal phalanx Metacarpal/tarsal condyle	Compression/ shear
Avulsion Fracture	Extra-articular avulsed osteochondral fragment	Epiphyseal entheses	Palmar/plantar eminence of proximal phalanx at attachment of distal and oblique sesamoidean ligaments	Tension
Osteochondral Collapse	Physitis	Physeal cartilage	Distal radius, distal third metacarpus/ tarsus	Pressure
Osteochondral Collapse	Deformation	Articular surface	Cuboidal bones of tarsus and carpus, proximal interphalangeal joint of hind limbs, scapulohumeral joint	Pressure

useful in detecting lesions that only affect cartilage, although arthroscopy is often necessary for definitive diagnosis in such cases. Radiographic findings include the presence of an osteochondral flap or discrete fragment, articular surface irregularity or flattening, or lucencies within the subchondral bone and surrounding sclerosis.[18] Lesions that are not apparent radiographically are most common in the hock.[19] Radiographic changes of pathologic physitis are variable. The most common finding is paraphyseal bone production, often termed physeal lipping or metaphyseal flaring. Physeal radiolucency or widening is less commonly observed and can be difficult to interpret.

When the clinical presentation involves joint effusion accompanied by lameness, intra-articular anesthesia can be used to confirm the lameness that originates from the effused joint. Acute-onset joint effusion in foals also requires cytologic analysis of synovial fluid to rule out septic arthritis or hemarthrosis as the cause of lameness, which is important irrespective of radiographic findings, because radiographically evident osteochondrotic lesions can be clinically silent. OCD lesions are usually associated with synovial fluid total nucleated cell counts (TNCCs) of less than 1.0 109 cells/L.

Treatment

Osteochondrosis

Osteochondrosis is a dynamic process in horses younger than 12 months, and some lesions heal naturally.[20] For example, some tarsocrural lesions have been shown to resolve radiographically in foals aged up to 5 months. In the same study, resolution occurred with some femoropatellar lesions up to the age of 8 months, after which lesions tended to persist.[21] Lesions causing lameness or significant effusion are unlikely to heal without intervention, and in these cases, arthroscopic debridement is indicated.[22] Arthroscopy can be used simultaneously as a method of diagnosis and treatment when radiographic findings are inconclusive. A recent review of surgical versus conservative management of osteochondrosis discusses the topic in full detail.[23]

Surgical removal of palmar or plantar avulsion fragments of the proximal phalanx has been described,[24] but is of questionable necessity. Although previously associated with low-grade, high-speed lameness in racehorses,[25] a recent study showed no effect on the racing performance of standardbred trotters.[26]

Angular limb deformities

Management of angular deformities varies depending on the joint involved and the direction and severity of the deviation. Normal growth-related changes dictate that correct conformation for a skeletally mature horse does not equate to ideal conformation for a foal. A 2<?> to 5<?> carpal valgus deviation is normal through to weaning age and self-corrects during a period of rapid growth and chest widening at around 8 to 10 months of age. Conversely, fetlock varus deformities tend to worsen with age up to the age of 6 months.[27] Foals with incomplete cuboidal bone ossification require immediate restriction and splinting to facilitate even loading and increase the likelihood of normal ossification and long-term soundness.

Minor angular deviations are managed conservatively, and correct conformation is achieved via the Hueter-Volkmann law of mechanical modulation of epiphyseal growth.[28] Conservative treatment involves exercise restriction, modification of hoof conformation to minimize compressive forces on the affected physis, and weekly evaluation. Surgical intervention is indicated for deviations in excess of 10<?> to 15<?>, under which modeling does not result in self-correction.[29] The most reliable current surgical techniques are aimed at temporary unilateral physeal growth retardation, via transphyseal bridging in the form of staples, screws and wires, plating, or lag or positional screws across one side of physis.[30] Hemicircumfe ential transection and stripping of the periosteum was commonly used to accelerate growth on the concave aspect of the affected metaphysis but has been shown to be not more effective than stall confinement and hoof trimming alone.[31] With cessation of active physeal growth, the window for correction using the above methods closes. Subsequent correction is difficult and requires a surgical wedge ostectomy or step osteotomy.[32]

Prognosis

Osteochondrosis

The prognosis accompanying lesions of osteochondrosis depends on the extent of cartilage erosion and

presence of degenerative changes identified within the joint at the time of arthroscopy.[19] Of the joints affected by OCD, the prognosis is typically least favorable in the shoulder. Subchondral bone cysts are associated with a poorer prognosis because they occur on central weight-bearing areas and surgical treatment is limited.[3]

Angular limb deformities

The prognosis for angular limb deformities depends on the severity of the deviation and subsequent degenerative change because of abnormal loading. Mild carpal valgus deformities have been shown to be protective for carpal injuries in racing thoroughbreds.[33] Conversely, fetlock varus deformities are more problematic and can predispose to lameness if uncorrected before physeal closure. Angular deviation resulting from physeal fracture or cuboidal bone collapse carries a poor prognosis.

EXERCISE-INDUCED MUSCULOSKELETAL PATHOLOGY

Exercise-induced injury to tissues of the musculoskeletal system is one of the most significant causes of pathology in the horse and is responsible for the shortened careers of many horses used in athletic disciplines. It is now recognized that most exercise-related injuries are a consequence of cumulative microdamage caused by repetitive cyclic loading, rather than a single episode of high-energy trauma.

Epidemiology

Bone injuries are common in horses exposed to high-intensity exercise, especially racehorses.[34] Horses working out long distances at high speeds, or that rapidly work out at a high speed within a short period of training, are more likely to develop fatal skeletal injuries than horses exercising at lower intensities.[35]

Soft tissue musculoskeletal injuries also occur most frequently in horses with a high level of cumulative biomechanical loading. The soft tissues of the palmar metacarpus and digits are those most commonly plagued by tendinous and ligamentous injury in the horse. Injury to a forelimb superficial digital flexor tendon reportedly accounts for 6% to 13% of all racing-related injuries.[36] The risk of tendon injury also increases with age.[37]

Muscular pathology that is exercise induced occasionally involves acute high energy biomechanical trauma, but exertional rhabdomyolysis is more common. The 2 most-studied causes are recurrent exertional rhabdomyolysis (RER), which affects 5% to 10% of thoroughbreds in training, and polysaccharide storage myopathy (PSSM) in quarter horses.[38]

Pathophysiology

Bone

Exercise-induced bone injury occurs when biomechanical loading overwhelms the normal adaptive processes that function to replace pockets of weakened bone and strengthen areas subject to high strain, in accordance with Wolff law.[39] Repetitive cyclic overloading of bone results in focal microdamage, such as trabecular microfractures and focal breaks in the calcified cartilage layer identified in the metacarpal condyle of racehorses.[40] When cellular remodeling is activated to repair areas of weakened bone, osteoclasts exert their effect more rapidly than osteoblasts, resulting in a transient decrease in bone density. The potential exists for fracture propagation within the area of weakened bone if high cyclic losing continues.[41] Studies have identified the presence of such microdamage in sites of spontaneous fracture in racehorses, supporting the hypothesis that these are fatigue failure injuries.[42,43]

Adaptive cortical modeling is commonly seen in the third metacarpus of racehorses as increased dorsal cortical thickness and increased distal subchondral bone density.[44] Trabecular bone adaptation is evidenced by sclerosis within the radial facet of the third carpal bone and the palmar aspect of the metacarpal condyle.[45] Although this adaptive modeling affords increased strength to the areas sustaining high loads, excessive sclerosis alters the elastic deformation properties of the subchondral bone and is thought to result in stiffer, brittle bone that is predisposed to fracture.[46] When horses are rested from training, bone density in areas previously under high strain decreases, predisposing them to fracture on return to work if training is not resumed gradually.[47]

Joints

Osteoarthritis is a disorder of moveable joints characterized by degeneration and loss of articular cartilage.[48] Although previously believed to be the

result of cartilage wear and tear, the pathophysiology is likely to involve complex mechanical and biochemical interactions between the synovium, cartilage, subchondral bone, periarticular bone, fibrous joint capsule, and periarticular soft tissue joint stabilizers.[49] Damage to one or more of these joint tissues may have the potential to initiate a perpetuating cycle of degenerative change within the joint as a whole, through release of inflammatory mediators, direct trauma, loss of joint stability, or loss of shock absorption.[48,50]

Synovitis, in particular, is now recognized as a critical feature in the development and progression of osteoarthritis.[49,50] The inflammatory nature of osteoarthritis and the role of soluble inflammatory mediators, such as cytokines and prostaglandins, has increasingly been the subject of osteoarthritis research. The activity of cytokines, such as interleukin-1 and tumor necrosis factor, and synovial macrophages in the presence of synovitis may play an important role in the activation of chondrocyte matrix-metalloproteinase–mediated cartilage degradation and osteophyte formation.[51]

Tendons

Exercise-induced tendon injuries are believed to be preceded by subclinical degeneration, which progressively weakens the resistive strength of the tendon. Repetitive loading during high-speed exercise induces isolated fibrillar microdamage and matrix degeneration. During loading, a greater strain is placed on the central tendon fibers and strain-induced lesions most frequently occur within the tendon core.[52] Proteolytic enzyme activity to remove necrotic collagen results in an increase in size of the lesion within the first 2 weeks postinjury.[53] Fibroblasts then synthesize scar tissue in the form of randomly arranged type III collagen that lacks elasticity. Subsequent remodeling causes conversion to type I collagen over a period of months. Controlled exercise is important during this period to align fibrils with the predominant loading forces, thereby improving the eventual strength of the tendon.

There is evidence to suggest that low- to moderate-intensity exercise induces adaptive hypertrophy within the superficial digital flexor tendon of foals, which may increase its ability to withstand biomechanical loading later in life.[54] In older horses, studies have shown a reduced crimp morphology of central tendon fibers, decreased sliding of tendon fascicles, and altered levels of proteins involved in matrix organization, which may be the result of age-related deterioration or an accumulation of exercise related damage.

Muscle

Traumatic myopathy results from acute tearing of muscle fibers, often during extreme athletic maneuvers such as sliding stops, or when attempting to rise after a long period of recumbency. Specific reports include rupture of the gastrocnemius and gracilis muscles. Fibrotic myopathy is a separately recognized condition in which fibrosis tends to be chronic and progressive, with low-grade inflammation, muscle fiber atrophy, and replacement with fibrous tissue.[55] The semitendinosus muscle is usually involved, resulting in a characteristic gait with slapping of the foot at the end of a shortened cranial phase of stride.

RER in thoroughbreds is caused by an autosomal dominantly inherited abnormality in myocyte intracellular calcium regulation. PSSMs involve a deficiency of energy within muscle cells because of abnormal glycogen storage. A heritable defect in the glycogen synthase gene (GSY1) is responsible for a substantial proportion of PSSM in some breeds, including quarter horses. RER and PSSM both involve impaired myofilament relaxation, persistent painful contractures, and segmental myonecrosis.[56]

Regardless of the cause, macrophage infiltration occurs within 72 hours of muscle injury and regenerative myotubes form within 3 to 4 days. Within a month of injury, myofilaments are produced and aligned, forming new mature muscle fibers. If myofibers are damaged beyond their regenerative capacity by extensive trauma, prolonged compression, or ischemia, then fibrosis ensues.[56]

Clinical Presentation

The clinical presentation of exercise-induced pathology can range from acute, debilitating injury to insidious low-grade lameness that manifests as poor athletic performance. Pathology involving joints usually presents with effusion and pain on flexion.

Injury involving the diaphsyses of long bones or the palmar metacarpal soft tissues presents with pain on palpation and varying degrees of surrounding edema. Muscular pathology manifests with focal, painful swelling, which in the case of exertional rhabdomyolysis may become extremely firm and is accompanied by a stiff gait, shifting lameness, or reluctance to move entirely. Severe myolysis causes sweating, tachypnea, elevated heart rate, colic-like signs, and variable myoglobinuria.

Diagnosis

Exercise-induced pathology is diagnosed by incorporating clinical and historical findings with variable use of diagnostic anesthesia, imaging, and arthroscopy. Increasing use of MRI and computed tomography, in addition to radiography, ultrasonography, and scintigraphy, has enhanced the diagnosis of some injuries, particularly those within the distal part of the limb. Current research into the identification of serum biomarkers suggests that these may become valuable indicators of pathology in the future and allow for detection of subclinical disease.[57–59]

In RER, suggestive clinical signs are associated with significantly elevated serum creatinine kinase (CK) enzyme activity 4 to 6 hours post exercise, indicating cell membrane damage because of myonecrosis.[56] Serum muscle enzyme activity does not always reflect the severity of clinical signs, but serial measurements can be used to determine the progression of injury.[56] Serum aspartate aminotransferase (AST) activity is not specific for myonecrosis and increases more slowly than CK activity. Serum AST activity peaks 12 to 24 hours after a muscle insult and has a half-life of approximately 7 to 8 days, in contrast to the 2-hour half-life of CK.60 Therefore, elevated AST activity in the presence of normal or reducing CK activity indicates that muscle damage is no longer occurring. The gold standard for diagnosis of PSSMs involves genetic testing of a blood sample for the GYS1 mutation (Type 1 PSSM), followed by a semimembranosus muscle biopsy for histologic evidence of abnormal polysaccharide storage in horses that test negative for the mutation (Type 2 PSSM).

Prognosis

The prognosis for full return to athletic function depends on the severity of tissue damage and the extent to which it disrupts normal function. The presence of pathology is not always associated with a negative outcome.[61] However, the prognosis suffers greatly once disease is advanced, which can be because tissue repair is inherently not possible, as is currently thought to be the case with degradation of articular cartilage; it can also be because exercise conditions were not conducive to repair, as evidenced by the progression of bone stress-related injury to catastrophic fractures, or because the mechanical properties of the repaired tissue are inferior to those of the original. The latter is currently the case with many tendon injuries. Rates of return to racing after injury to the superficial digital flexor tendon currently range from 20% to 60%, with an injury recurrence rate of up to 80%.[62]

Improved prevention and management of exercise-related pathology requires early detection, which can be extremely difficult. Advances in diagnostic imaging and the development of biomarkers show promise in addressing this difficulty. Further research is required to better understand when certain normal adaptive change becomes pathologic.

INFECTIOUS MUSCULOSKELETAL PATHOLOGY

Musculoskeletal tissue can be infected by bacteria, fungi, viruses, and parasites. However, bacteria are by far the most common infectious agents. Bacterial infection of synovial structures, bone, and soft tissue can have devastating long-term consequences for soundness in the horse and may be life threatening.

Epidemiology

Musculoskeletal infection is estimated to cause death in approximately 5% of foals.[63] Neonatal foals with failure of passive transfer of immunity are at high risk of developing synovial and osseous infection. The most common cause of infectious arthritis in this age group is hematogenous spread of bacteria. Rhodococcus equi infection may also cause a reactive polysynovitis and does so in approximately 25% of affected foals.[64] In mature horses, traumatic wounds are reportedly responsible for 37% of joint infections and 55% of tendon sheath infections.[65] In the same study, intra-articular injection was responsible for 34% of joint infections and 22% of tendon sheath infections.

Pathophysiology

Synovial structures

Infection of joints, tendon sheaths, and bursae may result from wounds, intrasynovial injections, postoperative complications, hematogenous spread, or idiopathic causes. The most common pathogens in synovial sepsis of mature horses are coagulasenegative staphylococci and Streptococcus equi subsp zooepidemicus. Specifically, Staphylococcus aureus is the most common agent in postoperative and post injection sepsis and Escherichia coli is the most common agent in septic arthritis of foals.[66]

Bone

Osteomyelitis is a process in which an infecting microorganism causes inflammation and destruction of bone.[67] Infection that does not involve bone marrow, such as in the distal phalanx, is termed osteitis. In foals, as with septic arthritis, the bacteria most commonly isolated from hematogenous osteomyelitis and physitis are enteric gram-negative organisms. Osteomyelitis in adult horses can be caused by a mixed infection involving staphylococci, Enterobacteriaceae, and streptococcal species[68]

Muscle

Infection of skeletal muscles with clostridial species, most often Clostridium perfringens or Clostridium septicum, causes life-threatening clostridial myonecrosis or gas gangrene. Dormant spores have been detected in normal skeletal muscle, and the inciting cause of their germination may be a change in the muscle milieu via puncture wounds or intramuscular injection.[69] Irritating intramuscular solutions, especially those that have an alkaline pH or lower redox potential within muscle, are implicated.[55] The most commonly associated intramuscular injection is that of flunixin meglumine.[70] Clostridial toxins produce severe tissue necrosis, and animals may be found recumbent with painful muscle swellings or dead. Focal suppurative myositis can be caused by a range of bacteria including Streptococcus and Staphylococcus sp and, in some geographic regions of the United States, Corynebacterium pseudotuberculosis.[55]

Subcutaneous tissue

Cellulitis is an infection of the subcutaneous tissues, which in severe cases involves a deep suppurative process that dissects through soft tissue planes and causes extensive damage. Commonly identified exotoxin-producing cellulitis pathogens are coagulase-positive Staphylococcus sp, most commonly S aureus and Staphylococcus intermedius.[71]

Establishment of infection

Regardless of the tissue involved, bacterial colonization requires adhesion and subsequent permanent attachment of the bacteria to the substrata. Conditions that prevent effective elimination of transient bacterial contamination by host defense mechanisms include an overwhelming level of inoculum relative to the cellularity of the tissue, impaired host defense, trauma to tissue surfaces, or presence of a foreign body.[72] After bacterial colonization, leukocytes and various inflammatory factors contribute to necrosis of the infected tissue. In osteomyelitis, ischemic bone can become separated to form a sequestrum.67 This isolated fragment of bone can continue to harbor bacteria and act as a persistent focus of infection. The smooth articular surfaces of cartilage and cortical bone are predisposed to bacterial colonization because they have low cellularity and lack a protective layer. Furthermore, the ability of pathogenic bacteria to form a biofilm slime layer from their extracapsular polysaccharides enhances adhesion, promotes survival of microcolonies on the surface of infected tissues, and affords resistance to antimicrobials.[73]

Clinical Presentation

Clinical signs of musculoskeletal infection vary according to the location, duration, and severity of infection. Synovial infection usually results in rapid development of a severe, minimally weight-bearing lameness.[66] Common differentials include subsolar abscessation and fracture. Lameness, focal swelling, effusion, pain, heat, and pyrexia are all variably associated with tissue infection, and rapid progression of disease is a key characteristic.

Diagnosis

Musculoskeletal infection is diagnosed on the basis of clinical and historical findings, combined with the results of hematology, serum biochemistry, and synovial fluid analysis and culture. Imaging may provide useful information in the later stages of disease. Radiographic findings are often unremarkable in the early stages bone and joint infection.[18] Infection must

cause 50% to 70% demineralization of bone before lysis is detectable radiographically, and this can take up to 21 days.[74] Scintigraphy can identify areas of infection involving bone but lacks specificity, particularly in skeletally immature horses with active physes. Ultrasonography of septic synovial structures may reveal effusion with anechoic or echogenic fluid, synovial thickening, and fibrinous loculations; however, these findings vary depending on the time that has lapsed between the onset of clinical signs and veterinary examination.[75]

Hematology and serum biochemistry in the presence of bacterial musculoskeletal infection typically reveals leukocytosis, elevated serum amyloid A (SAA) levels, and later, hyperfibrinogenemia. Synovial fluid analysis is of prime importance in the diagnosis of synovial infections, unless compromised overlying tissue prevents an aseptic approach to the joint, sheath, or bursa. Increases in synovial fluid TNCC are seen within 8 hours of joint inoculation and reach significant levels within 12 to 24 hours. Diagnostic criteria for sepsis usually include a synovial fluid protein concentration greater than 40 g/L; TNCC greater than 30 109 cells/L, with a differential count of at least 80% neutrophils; or a positive result of bacterial culture. However, some cases of septic arthritis have lower values.[76] The total protein concentration and TNCC may vary depending on the duration of sepsis and the virulence of the bacteria. Transient increases have also been demonstrated in response to repeated synoviocentesis and injection with amikacin.[77] SAA concentrations in serum and synovial fluid have been shown to be greater than 1000 mg/L in the presence of septic arthritis.[78] This acute-phase inflammatory protein may be synthesized locally by chondrocytes, in addition to its systemic production by the liver, and evidence suggests that synovial fluid SAA concentration is a useful marker of local infection.[79]

Bacteria may sequester in the synovial membrane, and conventional methods of bacterial culture from synovial fluid are often unrewarding. However, the use of blood culture medium enrichment has shown a culture rate of up to 79% of infected joints and allows for fast isolation of bacteria and susceptibility testing.[80] Polymerase chain reaction analysis of bacterial DNA in synovial fluid may also become clinically available in the future.[76]

Prognosis

The factor considered by most to have the greatest influence on outcome of a septic synovial structure is the time between the onset of clinical signs and presentation for treatment.[81] A delay of greater than 24 hours has been shown to reduce the likelihood of survival to discharge.[82] Separate research has shown only evidence of bone or tendon involvement to negatively affect survival and athletic function.[83] Both these studies reported a rate of return to athletic function of approximately 50% after synovial sepsis.[82,83] Synovial total protein concentrations greater than 55 to 60 g/L preoperatively, and moderate to severe synovial inflammation at surgery, have been negatively associated with odds of survival to hospital discharge.[84] Synovial fluid analysis at 4 to 6 days after initiation of treatment has useful prognostic value.[83] Culture identification of antimicrobial-resistant bacteria carries a grave prognosis.[85]

MISCELLANEOUS MUSCULOSKELETAL PATHOLOGY

Laminitis

Laminitis is a debilitating disease of the equine foot that involves separation of the dermal and epidermal laminae. Progressive failure of the lamellar interdigitations can result in rotation of the distal phalanx away from the dorsal hoof wall or complete distal displacement away from the middle phalanx.

Epidemiology

Estimated rates of naturally occurring laminitis range from 1.5% to 34%, and a recent large-scale study in Great Britain indicates that active laminitis is the reason for 1 in every 200 cases seen by equine veterinarians.[86] In a hospital setting, laminitic subsets of particular concern include supporting limb laminitis and sepsis-related laminitis. Clinical signs of endotoxemia have been shown to be significantly associated with the development of acute laminitis during hospitalization.[87] Supporting limb laminitis develops after an average of 2 weeks post injury and reportedly occurs in 0.02% of hospitalized horses.[88]

Pathophysiology

Current knowledge indicates that laminitis should be regarded as a clinical syndrome in which there are several distinct possible mechanisms of structural failure. Inflammatory, metabolic, traumatic, and vas-

cular causes have been proposed.[89] A comprehensive review of the following models used to produce and study laminitis was recently published.[90]

Systemic inflammatory response syndrome laminitis

Laminitis that occurs in association with carbohydrate overload, exposure to black walnut extract, intestinal compromise, endometritis, or other causes of sepsis is thought to have a common link via initiation of a systemic inflammatory response syndrome (SIRS) that triggers lamellar dermal inflammation. A similar inflammatory response is seen in both forelimb and hind limb laminae, suggesting that mechanical factors are important in the progression to clinical laminitis in the forelimbs.[91]

Endocrinopathic laminitis

Endocrinopathic laminitis is most commonly seen in horses and ponies affected by equine metabolic syndrome or pituitary pars intermedia dysfunction and may be associated with hyperinsulinemia. Lamellar failure is thought to be triggered by insulinmediated changes in the metabolism and structure of the basal epidermal cells, rather than being a primary inflammatory condition.[92] Contrary to historical and widely held beliefs, there is no strong scientific evidence that intra-articular administration of normal doses of exogenous corticosteroids increases the risk of laminitis in systemically healthy horses.[93–95]

Supporting limb laminitis

Supporting limb laminitis occurs in the contralateral limb because of a separate musculoskeletal condition that has resulted in persistent, unilateral lameness with minimal weight bearing. Loss of a normal cyclic pattern of loading, rather than merely an increase in load, is thought to cause hypoperfusion, hypoxia, and energy failure within the lamellar dermis of the weight-bearing foot.[96] Inflammatory events seem to be secondary in this form of laminitis as well.[97]

Traumatic laminitis

A distinct presentation of laminitis is hypothesized to occur because of repetitive hoof trauma or concussion and appears with some frequency in feral horse populations. The description is similar to that of road founder, a long-accepted cause of foot pain in heavy working horses.[89] This form of laminitis seems to be unrelated to body condition or carbohydrate overload, but the contribution of pony breeds to the genetic makeup of some feral horses diagnosed with chronic traumatic laminitis has been noted.[98]

Regardless of the primary cause that triggers laminitis, a threshold is reached at which there is sufficient loss of adhesion between the epidermal and dermal laminae that the remaining intact interdigitations fail to withstand the forces of weight bearing. Thus, tearing of the remaining laminae and rotation or distal displacement of the distal phalanx results. A temporary radiolucent area is seen adjacent to the dorsal margin of the distal phalanx on radiographs when this occurs. Proliferation of epithelial germinal cells leads to filling of this space by a wedge of disorganized epithelial tissue, which can make realignment of the distal phalanx within the hoof capsule difficult.

Clinical Presentation

The 3 recognized stages of laminitis are the prodromal stage before the onset of clinical signs, the acute stage in which there are clinical signs but no radiographic change, followed by the chronic stage, which is defined by the presence of radiographic change. The most common clinical signs associated with acute laminitis are increased digital pulses, difficulty turning, and a short, stilted gait at walk.[86] A typical rocking horse stance is often adopted to shift weight off the front feet. Sensitivity is detected on application of hoof testers over the region of sole underlying the toe of the distal phalanx. Radiographic change can begin within days of onset of clinical signs, while there is still active displacement because of unstable laminae, and persists until alterations to the hoof are made and the inciting cause is resolved.

Diagnosis

The diagnosis of laminitis is currently made via a combination of clinical findings and radiographic evidence of rotation or displacement of the distal phalanx within the hoof capsule. Modeling of the dorsodistal aspect of the distal phalanx develops in chronic cases.

There is no widely accepted set of evidence-based guidelines for the management of laminitis.[89] Continuous digital hypothermia, or cryotherapy, is the sole intervention that has been proven effective in

preventing and treating early stages of SIRS-induced laminitis both experimentally and clinically.[99,100] In addition to shoe modifications designed to minimize the biomechanical strain on compromised digital laminae, management strategies for both the treatment and prevention of laminitis should be directed at mitigating the likely inciting cause.

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Computational characterization of fracture healing under reduced gravity loading conditions

This is a summary of a study done by Benjamin Gadomski, Zachary Lerner, Raymond Browning, Jeremiah Easley, Ross Palmer and Christian Puttlitz and accepted in the Journal of Orthopaedic Research December 21, 2015 and published online in Wiley Online Library. DOI 10.1002/jor.23143.

Take Home Message

Results of the study suggest that reductions in hydrostatic pressure and strain of the healing fracture for animals exposed to reduced gravitational loading conditions contributed to an inhibited healing process, with animals exposed to the simulated hypogravity environment subsequently initiating an intramembranous bone formation process rather than the typical endochondral ossification healing process experienced by animals healing in a 1g gravitational environment.

Introduction

The literature is deficient with regard to the specific alterations in the localized mechanical environment of skeletal tissue during the reduced gravitational loading characteristic of spaceflight and how these alterations affect fracture healing in Haversian systems. Additionally, investigations that have attempted to link the direct role of these reduced gravitational forces to fracture healing have been limited primarily to rodent studies[1-4]. Alterations in the localized mechanical environment within mineralized tissues due to hypogravity loading remain inadequately described due to the experimental limitations associated with such tasks. However, the use of computational techniques may aid in elucidating the mechanical underpinnings of skeletal adaptation and healing in mechanically unloaded environments. Thus, the purpose of this study was to develop a FE model to characterize the local mechanical environment responsible for the inhibited fracture healing observed under experimentally simulated hypogravity conditions.

Methods

A single high fidelity FE model of the ovine hindlimb extending from the tibia to proximal phalanges was constructed in order to quantify the localized stresses and strains experienced under simulated hypogravity unloading (Figure 1). An external fixation device was created in the FE model (ExFix model) to shield the metatarsal bone from mechanical loading. Additionally, a Control FE model was utilized in which the external fixation components were omitted. In order to investigate the effects of mechanical unloading on the local mechanical environment of a healing bone fracture, a 3mm mid-diaphyseal ostectomy was created in the ExFix and Control models. Hindlimb muscles were created in both ExFix and Control FE models using a constraint between a single reference node and a node set on the surface

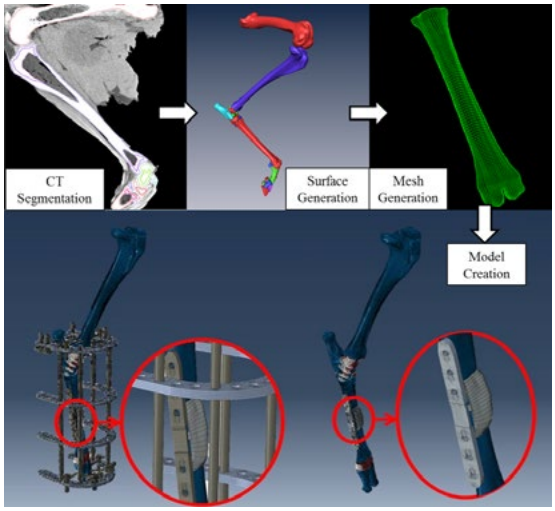

Figure 1. The FE model generation process. Surface geometry was segmented from a CT scan of a mature ewe before being meshed with 8-node hexahedral elements and imported into the finite element software. (Bottom) The (left) ExFix and (right) Control FE fracture models were generated by creating a 3mm ostectomy and callus (red insets) at the mid-diaphysis of the metatarsus and stabilized with a 6-hole orthopaedic plate. Components of the external fixation were explicitly modeled in order to replicate the experimental configuration, and the fracture callus geometry for each model was derived from experimental histological samples at the 4-week sacrifice timepoint[12].

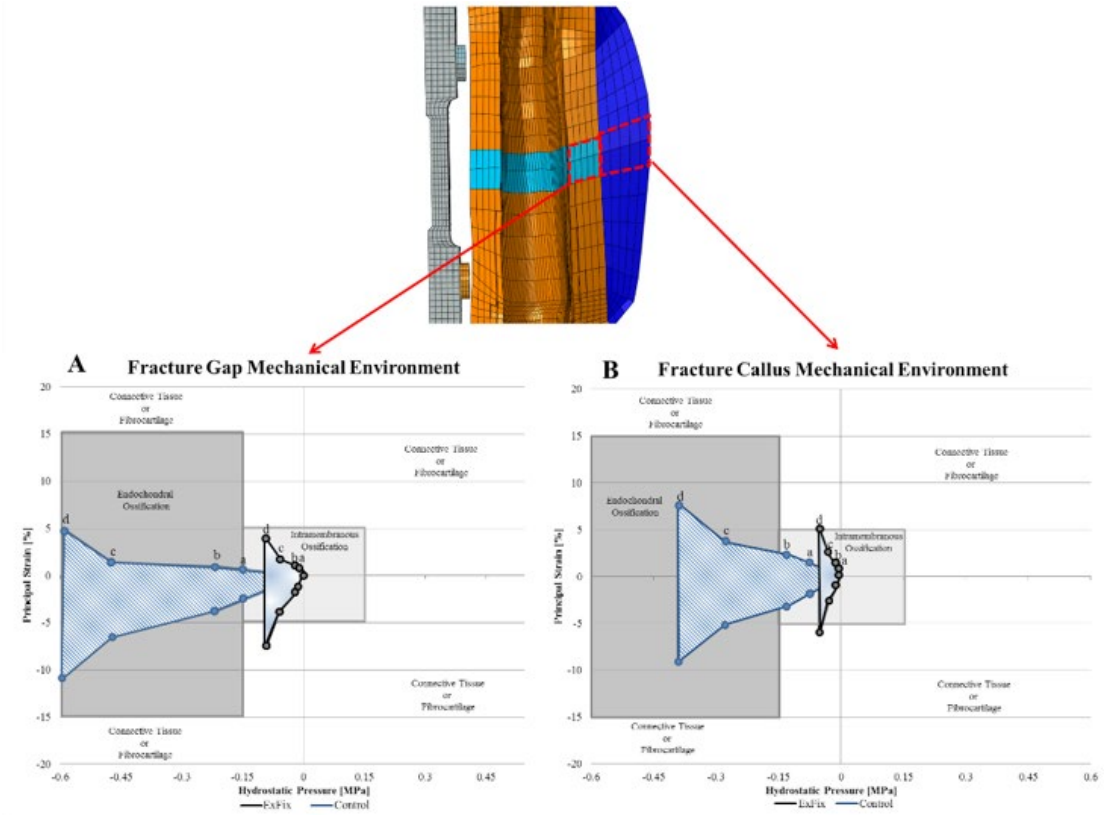

Figure 2. Specific hydrostatic and principal strain envelopes have been previously reported to initiate intramembranous ossification, connective tissue/fibrocartilage formation, and endochondral ossification by Claes and Heigele [7]. Plotting the data of the current study for GRFs of 100N, 200N, 300N, and 600N (points a, b, c, and d, respectively) over these previous results demonstrate the hypothesized course of healing for each model (The lower bound of each curve corresponds to the hydrostatic pressure and respective minimum principal strain while the upper bound corresponds to the hydrostatic pressure and respective maximum principal strain for GRFs from 0N to 600N). (A) Both models predicted the greatest levels of hydrostatic pressure and principal strain in the fracture gap contralateral to the fixation plate. The Control model predicted peak hydrostatic pressure and principal strains within the endochondral ossification envelope for GRFs greater than 100N while all hydrostatic pressure and strain predictions fell within the intramembranous ossification zone for the ExFix model. (B) Hydrostatic pressure and strain predictions were decreased within the fracture callus.

on the bone corresponding to the known muscle cross-sectional area. Each model was loaded with muscle and stifle joint contact forces predicted by a previously-developed musculoskeletal model of the ovine hindlimb[34] corresponding to 100N, 200N, and 300N GRF standing loads as well as a gait speed of 0.75m/s (corresponding to the maximum speed of the housed animals, or 600N). The local maximum and minimum strain components and hydrostatic pressure within the fracture gap and periosteal callus predicted by the model were then compared with histological results obtained from a corresponding in vivo animal study[12].

Results

Hydrostatic pressure and strain predictions were greatest when a GRF of 600N (corresponding to a 0.75m/s gait speed) was imposed on both FE models and decreased as a function of GRF. Both models predicted peak hydrostatic pressures and principal strains within the cortices of the fracture gap contralateral to the orthopaedic fixation plate, with both parameters decreasing radially toward the callus periphery (Figure 2). The Control model predicted a peak hydrostatic pressure of -0.59MPa (compressive) within the fracture gap and maximum

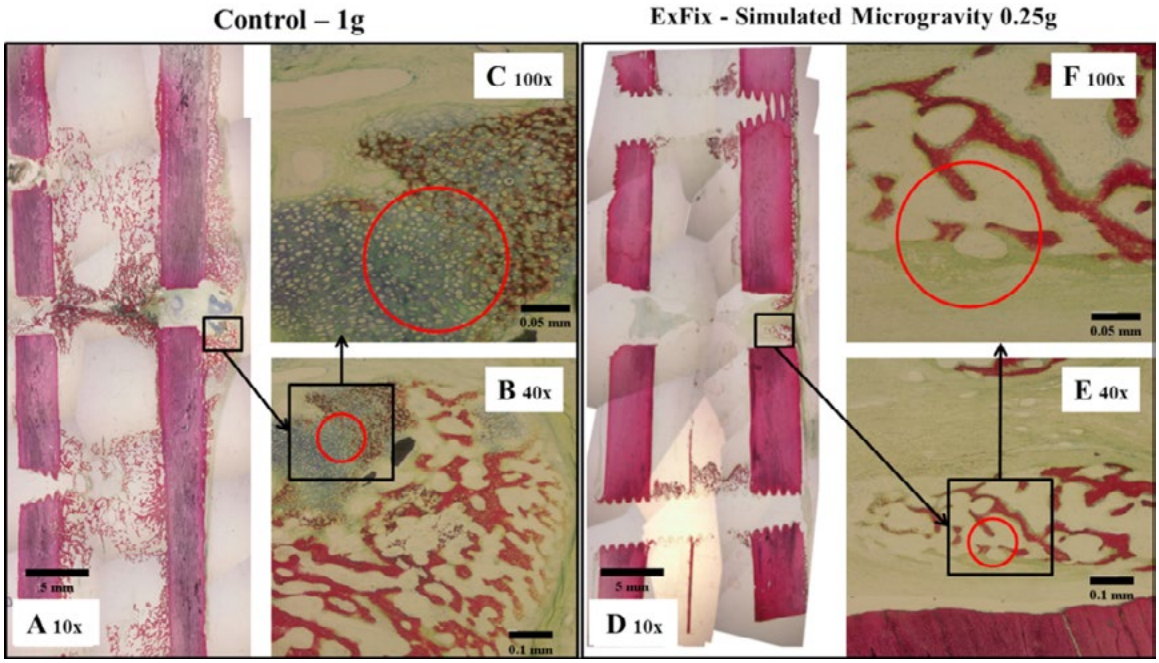

Figure 3. (Images A, B, and C) Experimental 1g control specimens routinely displayed endochondral ossification bone formation in the periosteal callus as well as reduced intramembranous bone formation around the callus perimeter. A combination of mineralized callus and hypertrophied chondrocytes (circled) can be seen within the healing callus. (Images D, E, and F) The mechanically unloaded specimens displayed significantly less mineralized callus than control specimens and demonstrated no evidence of chondrocyte activity at the sacrifice timepoint. Histology slides were stained with Sanderson's Rapid Bone Stain and counter-stained with Van Gieson.

and minimum principal strains of 5.0% and -10.9%, respectively. The ExFix model predicted a peak hydrostatic pressure of -0.1MPa within the fracture gap and peak maximum and minimum principal strains of 3.7% and -7.6%, respectively. The results of our complementary animal studies further support these findings. MicroCT and histomorphometric analyses demonstrated statistically significant reductions in total callus volume and its constituent components (bone and fibrocartilage) in Control animals as compared to ExFix specimens, resulting in diminished fracture mechanical strength (Figure 3).

Conclusions

The mechanical unloading experienced during simulated hypogravity is predicted to yield decreased magnitudes of hydrostatic pressure and, to a lesser extent, principal strain at the fracture site, leading to subsequent reductions in overall fracture healing rate and quality. The latter includes decreased stiffness due to an overall decrease in callus volume and limited amounts of intramembranous ossification rather than the traditional endochondral ossification healing pathway, which is characteristic of 1g Earth loading. The FE model predictions suggest that reduced hydrostatic pressure and strain of the healing fracture contributed to alterations in the healing process, with animals exposed to a simulated hypogravity environment inadequately healing, and only then, via limited amounts of via intramembranous bone formation rather than the more robust endochondral ossification process typically experienced by animals healing in an Earth gravitational environment. Further work should concentrate on candidate countermeasures that may be able to restore the natural loading milieu to fractures healing in hypogravity environments.

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Hemiepiphysiodesis for the Correction of Proximal Tibial Valgus in Growing Dogs

This is a summary of an article published in the Journal of Veterinary and Comparative Orthopaedics and Traumatology (VCOT) by Drs. Olsen, L. Vezzoni, Ferretti, Palmer, A. Vezzoni and Duerr. Vet Comp Orthop Traumatol 2016;29: http://dx.doi.org/10.3415/VCOT-15-12-0204.

Take Home Message

Hemiepiphysiodesis is a simple, effective technique for the treatment of proximal tibial deformities in immature dogs. This technique should be considered when presented with an immature patient with tibial deformities since it is less invasive than osteotomy techniques. Serial post-operative monitoring is imperative to avoid overcorrection. If overcorrection is observed, removal of the staple should be considered.

Introduction

Angular limb deformities (ALD) of the appendicular bones can lead to severe gait abnormalities, lameness, pain and degenerative joint disease.[1] The majority of ALD involve the paired bone system of the radius and ulna and result from altered physeal development due to an inherited condition or secondary to traumatic events and other physeal disturbances.[2,3] While growth plate defects affecting the proximal tibia have a historically low rate of occurrence[4], sequelae including cranial cruciate ligament disease[5,6] and/or patella luxation[7] have been described. Corrective osteotomy procedures have been developed to correct tibial deformities;[8] however, these osteotomies are invasive and technically demanding.

Tibial hemiepiphysiodesis using a transphyseal stapling technique has been widely used since 1949 in children for the progressive correction of genu varum and valgum deformities.[9-11] Temporary or permanent closure of the medial or lateral aspect of the proximal growth plate of the tibia allows for continued growth of the untreated portion of the physis. As such, it results in progressive correction of the deformity, as the staple resists growth of the operated portion of the physis.[12] Compared to corrective osteotomies, the advantages of temporary hemiepiphysiodesis include a much less invasive surgery with a lower risk of perioperative complications, the possibility of continued longitudinal growth upon staple extraction, and faster return to function postoperatively.[13,14]

Transphyseal stapling has been documented for the correction of ALD in foals with distal tibial, radial, metacarpal, or metatarsal valgus or varus deformities with varying results.[15,16] While this technique has been used in people, it is rarely used to treat dogs. Therefore, the goal of this research was to describe the surgical technique and the outcome of hemiepiphysiodesis for the treatment of proximal tibial deformities in immature dogs.

Methods

Skeletally immature dogs with proximal tibial deformities treated with hemiepiphysiodesis between March 2006 and January 2015 were included in this study. To be included, dogs were required to have radiographs or computed tomography performed preoperatively and at least eight weeks postoperatively. Radiographs were positioned to allow for measurement of mechanical medial proximal tibial angle (mMPTA) and tibial plateau angle (TPA). Preoperative and recheck mMPTA and TPA were measured on digital images. All dogs were required to have an excessive mMPTA pre-operatively, based on the previously described reference range of 93.3 ± 1.78°.[17] Medical record data gathered for each dog included signalment, age (months), weight (kilograms), limb affected, description of the deformity based on physical examination, the type of implant used, the number and position of each implant, concurrent surgical procedures performed, preoperative and recheck subjective lameness scores, and complications. Complications were considered major if there was a requirement for additional surgery or medical treatment, as previously described.[18] Minor complications included those not requiring additional surgery or medical treatment.

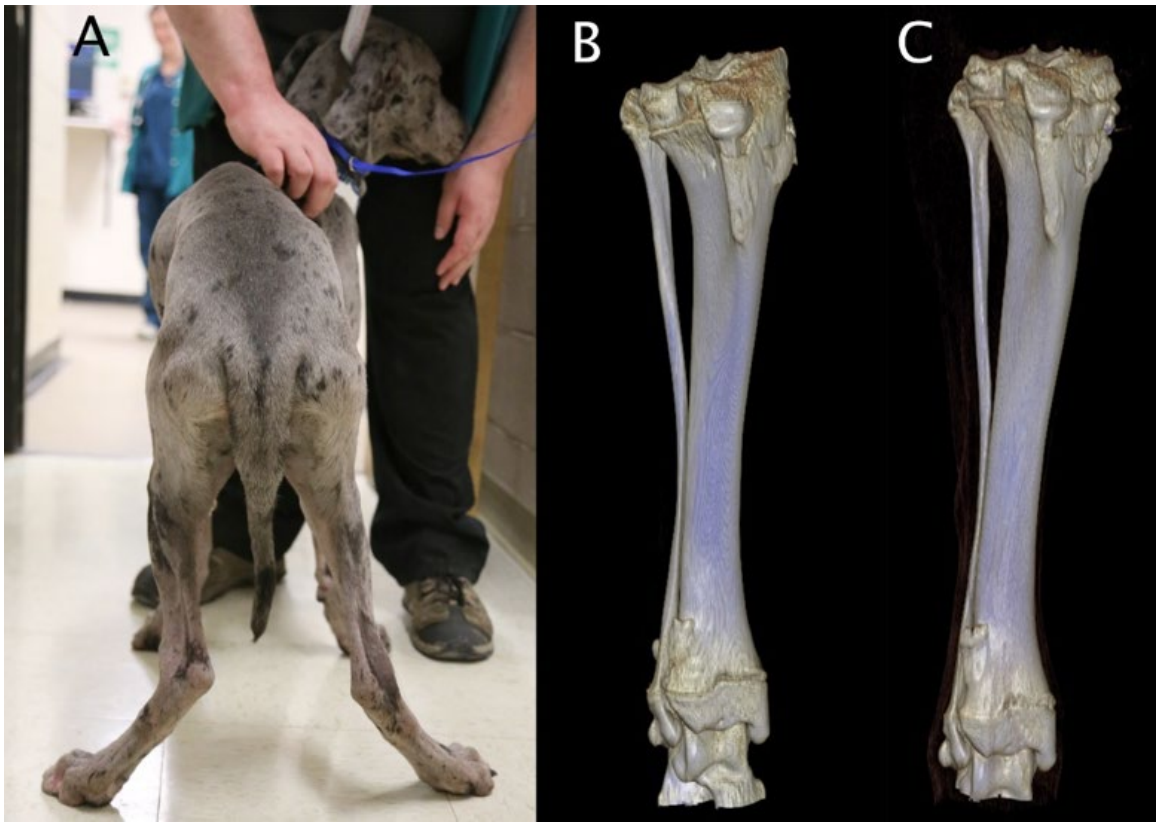

Figure 1. The image above depicts a dog with bilateral tibial valgus that underwent hemiepiphysiodesis of the medial proximal tibial physis. A) Preoperative image of the patient showing bilateral tibial valgus deformity. B) Preoperative computed tomography (CT) of the right tibia of the dog pictured in A. C) Recheck CT image demonstrating resolution of the proximal tibial valgus.

Surgery was performed via a limited approach to the proximomedial tibia. The tibial physis and femorotibial joint were identified by use of a small gauge needle and/or by fluoroscopic guidance. Fluoroscopy and/or needle placement were used to guide placement of the implant parallel to the physis. The width of the staple was chosen by estimating the proximal to distal length of the epiphysis and matching this size. An epiphyseal pilot hole was drilled approximately halfway between the physis and proximal articular surface using a drill bit approximately 0.2 mm smaller than the outer diameter of the fixation arm of the staple. This hole was placed cranial to the medial collateral ligament approximately at the level of the intercondylar eminence. The same drill bit was then used to drill a second hole in the metaphyseal region. This hole was aimed to place the staple in a perpendicular orientation to the physis and allowed to match the length of the staple's spanning arm. To allow parallel placement to the first hole, a K-wire was inserted into the first hole for judgment of alignment as needed. The depth of the drill holes was limited to the depth of the staple's fixation arms. The staple was then inserted by gently tapping into the holes. Variations of this technique were used for placement of custom-made staples, Kyon staples or plates.

Paired t-test was used to compare preoperative and recheck mMPTA and TPA measurements. For statistical comparison of TPA, animals that received procedures aimed at reducing TPA (cranial tibial epiphysiodesis) were excluded. Statistical significance was set at $p \leq 0.05$.

Results

A total of 19 dogs fulfilled the inclusion criteria. All dogs were sexually intact at the time of surgery.

14/19 (74%) dogs were male and 5/19 (26%) were female. At the time of surgery, the dogs had a mean weight of 28.5 ± 12.4 kilograms (range, 3.5 to 48 kg) and were a mean age of 5.4 ± 0.9 months (range, 4 to 7 months). Of the 19 dogs included, all were diagnosed with proximal tibial valgus based on radiographic evaluation. None of the dogs had concurrent patella luxation preoperatively. 12/19 (63%) dogs underwent bilateral, simultaneous hemiepiphysiodesis allowing for a total of 31 limbs being evaluated. Concurrent diagnoses included osteochondritis dessicans (OCD) of the lateral femoral condyle in 11/31 (35%) limbs, calcinosis cutis circumscripta (n=1), hip dysplasia (n=1), and a malunion Type II Salter-Harris fracture of the proximal tibia with resultant excessive TPA and valgus (n=1).

Of the 31 hemiepiphysiodesis procedures performed, 16 (52%) were performed on the left tibia and 15 (48%) were performed on the right. One implant was used for each procedure and all implants were placed across the medial aspect of the proximal tibial physis. The implants used for hemiepiphysiodesis included Kyon 12 mm staple (n=6), 2.7 mm DCP (n=5), 1.6 mm K-wire (n=5), 2.0 mm K-wire (n=5), 1.4 mm K-wire (n=3), Kyon 18 mm staple (n=2), Kyon 16 mm staple (n=2), Kyon 10 mm staple (n=1), 2.7 mm reconstruction plate (n=1) and 2.0 mm DCP (n=1). 14/19 (74%) dogs had an additional procedure performed at the time of surgery. Concurrent procedures at the time of hemiepiphysiodesis included fibular osteotomy (n=11), osteochondral autograft transfer system for treatment of the femoral OCD lesions (n=7), unilateral double pelvic osteotomy (n=1), and cranial tibial epiphysiodesis with a 2.4 mm screw (n=1). The mean time to final follow-up was 25 weeks (range, 8 to 67 weeks). No intraoperative complications were noted.

Preoperatively, the mean mMPTA was 102.5 ± 5.3o (range, 96 to 114o). The mean mMPTA at the time of the final recheck radiographs was 92.4 ± 7.2o (range, 81 to 109o). The mean difference in mMPTA was -10 ± 5.1o (range, -1 to -19o). The decrease in mean mMPTA was statistically significant ($p < 0.001$). At the time of the final analysis, nine limbs continued to have an increased mMPTA above the normal range, despite improvement in individual measurements. Sixteen limbs were below the mMPTA reference range and six were within normal limits.

Of the 31 implants placed, 15 (48%) were removed at a later date when mMPTA was within or below the normal range, or if clinical examination suggested satisfactory correction. The mean time of implant removal was 50.8 days (range, 21 to 84 days) after the initial surgery. Mean age at implant removal was 6.7 months (range, 5 to 8.5 months). Of the 15 limbs with implants removed, nine had repeat radiographs performed at a mean of 5.1 ± 3 months (range, 1.5 to 10.5 months) after implant removal. For these cases, the mMPTA had increased by a mean of 7 ± 4.4o (range, 0 to 13o) compared to mMPTA at time of implant removal.

Conclusions

Hemiepiphysiodesis for the treatment of proximal tibial valgus is a technique that can be safely performed in dogs. The technique allows for a statistically significant reduction in mMPTA and should be considered as an early treatment for immature animals presenting with proximal tibial deformities.

Temporary hemiepiphysiodesis relies on the principle that once the tethering device placed across a physis is removed, normal linear growth continues. The finding of deformed implants in 29 of 31 cases may suggest that the elasticity of the implants caused a delay in physeal growth rather than a complete arrest that could happen with stiffer implants. Based on the experience in this study, implant deformation does not necessarily correlate to correction failure. However, physeal closure may occur after removal of a transphyseal implant or alternatively rebound growth and recurrence of the deformity has also been described. In people, growth after implant removal is unpredictable and highly variable in instance and intensity. Hence, serial radiographs are recommended to determine the best time for removal of staples. In human patients, implant removal is usually performed once overcorrection of 5° has occurred. Based on the significant rebound growth observed in almost all cases where radiographic follow-up was available in our study, implant removal after slight overcorrection has occurred may be an appropriate guideline in dogs until further data is available. Serial monitoring and removal of the implant when mMPTA of 88 degrees is accomplished should be considered.

Further research into utilization of this technique for other physes should be considered as this technique offers a less invasive alternative associated with low risk and a quick recovery.

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High energy focused shock wave therapy accelerates bone healing. A blinded, prospective, randomized canine clinical trial

This is a summary of an article published in the Journal of Veterinary and Comparative Orthopaedics and Traumatology (VCOT) by Drs. Kieves, MacKay, Rao, Goh, and Duerr. Vet Comp Orthop Traumatol 2015;28:425-432. http://www.ncbi.nlm.nih.gov/pubmed/26449666

Take Home Message

Two sessions of high-energy shock wave therapy (SWT) applied immediately and two weeks after tibial plateau leveling osteotomy (TPLO) accelerate bone healing in patients undergoing TPLO.

Introduction

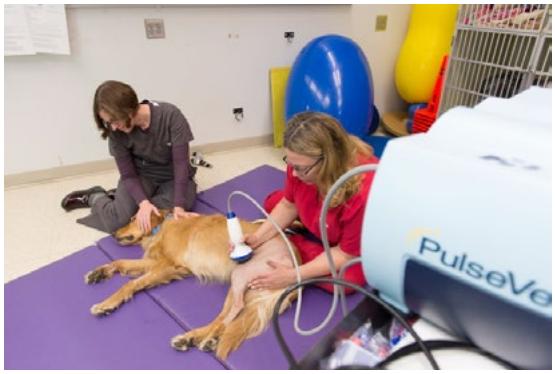
Delayed bone healing of naturally occurring fractures and osteotomies can lead to patient morbidity, revision procedures, and decreased patient function.[1,2] Cranial cruciate ligament disease (CCLD), one of the most common causes of hind limb lameness in canine patients, is frequently treated by tibial plateau leveling osteotomy (TPLO).[3-8] TPLO requires creation of an osteotomy (for more info about the procedure please refer to http://csu-cvmbs.colostate.edu/vth/small-animal/sports-medicine-rehabilitation/Pages/canine-cruciate-ligament-injury.aspx#treatmentsurgical) Complications associated with the creation of an osteotomy include delayed unions, malunions, and implant failure.[8-10] Strategies to avoid such complications related to bone healing are continually being evaluated. The TPLO provides a relatively standardized procedure allowing the study of the efficacy of therapies intended to promote bone healing in a clinical setting.

Shock wave therapy (SWT) has been utilized for many indications in dogs including tendinopathies, pain control, arthritis management and bone healing.[11-16] SWT has been shown to stimulate bone healing in dogs, horses, and humans.[11,12,17-23] Canine specific literature includes only four studies showing limited support for the use of SWT for bone healing in dogs.[11,12,22] Hastening of bone healing after TPLO would be beneficial to the individual patient to potentially decrease osteotomy complications and to shorten the convalescent period allowing earlier return to optimal function. Furthermore, TPLO can be viewed as a model to answer the broader question of whether SWT has a positive effect on bone healing. To the authors' knowledge, no study has objectively evaluated the effect of SWT on acute bone healing in canine clinical patients.

The aim of this study was to evaluate if SWT promotes acute bone healing in dogs undergoing TPLO for naturally occurring CCLD. We hypothesized that SWT would result in greater radiographic healing scores at 8 weeks post-operatively when compared to SHAM treatment.

Methods

This study was designed as a randomized, blinded (for radiographic evaluation), prospective clinical study of client-owned dogs presenting for surgical treatment of naturally occurring CCLD. If owners elected to pursue TPLO, they were offered the option to enroll in this study. Healthy dogs between 2-9 years of age who were randomly assigned to receive either SWT or sham treatment (SHAM).



SWT was applied with a VersaTron 4Paws device (PulseVet Technologies, Alpharetta, GA) immediately post-operatively and at the time of suture removal (approximately 2 weeks post-operatively). The first SWT treatment was applied under general anesthesia and the second SWT treatment was applied under sedation. A total of 1,000 shocks at

(setting: E6; pulse/min: 360) were applied at each treatment along the osteotomy site identified by palpation of the plate and review of the radiographs. Care was taken to avoid application of shocks over the bone plate; 500 shocks were applied from the caudomedial aspect using the 5mm trode and, then, 500 shocks were applied from craniolateral aspect using the 20mm focal spot trode, both at the E6 setting. The incision site was covered with an adhesive dressing to maintain sterility and acoustic transmission gel was applied directly to the treatment head. The treatment heads were slowly moved while applying the treatment (approximate treatment area 5-8cm). Sham treatment was performed as described above, but the SWT device was not activated.

Three blinded radiologists evaluated orthogonal radiographs performed at 8 weeks post-operatively with both a 5-point and a 10-point bone healing scale. Linear regression analysis was used to compare median healing scores between groups.

Results

Forty-two dogs (50 stifles) were included in the statistical analysis. No major complications were observed and all osteotomies healed uneventfully. The median healing scores were significantly higher 8 weeks post-operatively for the SWT group compared to the SHAM group for the 10-point ($P < 0.0002$) and 5-point scoring systems ($P < 0.0001$).

Conclusions

This is the first study evaluating the effect of SWT on acute bone healing in a larger population of clinical canine patients after routine TPLO. In the described study population, two sessions of electro-hydraulic SWT significantly increased radiographic bone healing scores at 8 weeks post-operatively. These results strengthen the available literature and support the use of SWT for promotion of acute bone healing in dogs. Additional studies are needed to evaluate its use for acceleration of bone healing following fracture, or with delayed union.

The ideal dosing frequency and optimal energy density to enhance fracture healing with SWT, however, remains unknown and a wide variety of protocols have been used in the literature.[11,12,17-23] We selected our treatment protocol based upon the available literature, cost associated with treatment, and client convenience. It is unknown which of the 2 treatments produced the beneficial effects in our study. We selected a fairly low number of shocks compared to previous reports, as clients are charged per shock and hence treatment cost rises with the number of shocks applied, and we wanted to mimic a true clinical application of SWT. The amount of shocks applied in this study is likely on the low end of the beneficial spectrum, especially given that we used a non-coupled device.

Acknowledgments

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Influence of Adipose-Derived Mesenchymal Stromal Cell Demineralized Bone Composite on New Bone Formation in Critical Sized Cortical Bone Defects.

This is a summary of a study done in Dr. Nicole Ehrhart's laboratory (orthopaedic oncology) and published in 2015: Ehrhart N., Chubb L., Flaumenthaft E., Barret C., Shi Y. Influence of Adipose-Derived Mesenchymal Stromal Cell Demineralized Bone Composite on New Bone Formation in Critical Sized Cortical Bone Defects. 2015 J Med Res Arch Jan 1; 1(1):3-10.

Take Home Message

Adipose derived MSCs delivered on a demineralized bone matrix scaffold are potent bone formers. The combination of cells, signal and scaffold optimize bone formation and provide an excellent substitution for bone graft in challenging bone healing environments.

Introduction

The relatively recent discovery that MSCs derived from various tissues will differentiate into osteoblasts in the presence of osteopromotive medium has allowed for new therapeutic opportunities in bone tissue engineering. We recently described the in vitro characteristics of a demineralized bone scaffold containing adipose-derived mesenchymal stromal cells (DBM/hMSC) harvested from human adipose tissue and demonstrated that this combination contains the three components that are considered optimal for bone repair: an osteoconductive scaffold, osteoinductive signaling proteins and osteogenic cells. The objective of this study was to compare and characterize the in vivo bone- forming activity of DBM/hMSC to that of DBM alone, hMSCs alone, cortico-cancellous isograft and human cortico-cancellous xenograft in an athymic rat model.

Methods

A series of animal experiments were performed comparing new bone formation in critical-sized bone defects implanted with DBM/hMSC, DBM, hMSC, corticocancellous isograft, human cortico-cancellous bone graft or no treatment (empty defect).

Results

New bone formation was greatest in bone defects implanted with DBM/hMSC when compared with DBM alone, hMSCs alone, corticocancellous bone isograft, or human corticocancellous bone graft.

Conclusions

Together, these data support preclinical proof-of-concept that DBM/hMSC will enhance bone formation in challenging healing environments.

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Do mesenchymal stromal cells influence residual or metastatic osteosarcoma in a murine model?

This is a summary of a study done in Dr. Nicole Ehrhart's laboratory (orthopaedic oncology) and published in 2015: Aanstoos ME, Regan DP, Rose RJ, Chubb LS, Ehrhart NP. Do Mesenchymal stromal cells influence residual or metastatic osteosarcoma in a murine model? Clin Orth Rel Res 2015 epub 28 May DOI 10.1007/s1999-015-4362-2.

Take Home Message

When delivered intravenously, exogenous MSC therapy may promote metastatic pulmonary osteosarcoma growth. However, local administration into a surgical wound, even in the presence of known residual microscopic tumor, appears not to promote local recurrence or to hasten onset of metastatic disease.

Introduction

Mesenchymal stromal cells (MSCs) have been shown in rodent models to promote primary and pulmonary metastatic sarcoma growth when injected in the presence of gross tumor. In theory, this would limit their use in a clinical setting after limb salvage treatment for osteosarcoma. Although concerning, these models do not translate to the clinical setting wherein MSCs could be used after primary tumor resection to aid in bone healing and incorporation of tumor endoprostheses. If we can determine whether the use of MSCs in this setting is safe, it might improve our ability to augment bone healing in patients undergoing limb salvage.

Methods

An orthotopic model of luciferase-expressing osteosarcoma was developed. At 10 days, resection of the primary tumor was performed. One hundred fourteen female C3H mice were inoculated with DLM8-luc osteosarcoma in the proximal tibia. Ninety-four mice developed orthotopic osteosarcoma with luciferase expression. Mice with bioluminescent evidence of a primary tumor received either a microscopically "clean" amputation at a time when residual microscopic metastatic disease was present in the lungs (pulmonary metastasis group; n = 65) or a "dirty" amputation (local recurrence group; n = 29). Mice were randomized to receive intravenous MSCs, MSCs at the surgical site, or no MSCs. Mice were monitored for development and progression of pulmonary metastasis and local recurrence by bioluminescence imaging and daily measurements at the surgical site. The number of pulmonary nodules, time to first evidence of metastasis, and size of recurrent tumor were compared using Kruskal-Wallis, analysis of variance, Welch's, t-tests, or Mann-Whitney tests as appropriate for the specific data sets with $p < 0.05$ considered significant.

Results

Mice receiving intravenous MSCs had a faster time to first detection of pulmonary metastasis (2.93 ± 1.90 days) compared with mice with local injection of MSCs (6.94 ± 6.78 days) or no MSCs (5.93 ± 4.55 days) ($p = 0.022$). MSC treatment did not influence whether mice developed local recurrence ($p = 0.749$) or size of recurrent tumors ($p = 0.221$).

Conclusions

MSCs delivered to the surgical site did not promote local recurrence or size of recurrent tumors, but intravenous injection of MSCs hastened onset of detection of pulmonary metastatic disease. If MSCs are to be used to augment bone healing in the post limb salvage setting in patients with osteosarcoma, it will be important to understand their influence, if any, on pulmonary micrometastsis or residual microscopic local disease. Although murine models do not completely recapitulate the clinical scenario, these results suggest that intravenous delivery of MSCs may promote micrometastatic pulmonary disease. Local administration into a surgical wound, even in the presence of residual microscopic disease, may be safe, at least in this murine model, but further investigation is warranted before considering the use of MSCs for clinical use in patients with osteosarcoma.

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Increased Duration of Heating Boosts Local Drug Deposition during Radiofrequency Ablation in Combination with Thermally Sensitive Liposomes (ThermoDox) in a Porcine Model

This is a summary of a study done in Dr. Nicole Ehrhart's laboratory (orthopaedic oncology) and published in 2015: Swenson CE, Haemmerich D, Maul DH, Knox B, Ehrhart N, Reed RA. Increased Duration of Heating Boosts Local Drug Deposition during Radiofrequency Ablation in Combination with Thermally Sensitive Liposomes (ThermoDox) in a Porcine Model. PLoS One. 2015 Oct 2;10(10):e0139752.

Take Home Message

Radiofrequency ablation (RFA) is a locoregional thermal therapy, and is clinically used to treat unresectable tumors of the liver, as well as in other organs such as the kidney, lung and bone. For larger liver tumors (>3 cm diameter), the local failure rate for RFA can be greater than 40%, because often tumor microsatellites exist distant from the macroscopic tumor. The use of thermally sensitive liposomal carriers of doxorubicin were evaluated in combination with RFA to determine if the deposition of doxorubicin could be enhanced and distributed in a manner expected to have therapeutic benefit against microsatellite tumor cells. The study design was to optimize the RFA procedure used in combination with LTLD to maximize the local deposition of doxorubicin in a swine liver model. Results demonstrated that increasing ablation duration by a factor of 3–6 increased the local concentration as well as the tissue volume exposed to drug. Further, doxorubicin delivery extended further from the ablation zone margin, beyond 1 cm, when multiple ablations were used. Both results are considered to increase the potential therapeutic benefit of the clinical combination of RFA and LTLD.

Introduction

Radiofrequency ablation (RFA) is used for the local treatment of liver cancer. RFA is effective for small (<3cm) tumors, but for tumors > 3 cm, there is a tendency to leave viable tumor cells in the margins or clefts of overlapping ablation zones. This increases the possibility of incomplete ablation or local recurrence. Lyso-Thermosensitive Liposomal Doxorubicin (LTLD), is a thermally sensitive liposomal doxorubicin formulation for intravenous administration, that rapidly releases its drug content when exposed to temperatures >40°C. When used with RFA, LTLD releases its doxorubicin in the vasculature around the zone of ablation-induced tumor cell necrosis, killing micrometastases in the ablation margin. This may reduce recurrence and be more effective than thermal ablation alone.

Methods

The purpose of this study was to optimize the RFA procedure used in combination with LTLD to maximize the local deposition of doxorubicin in a swine liver model. Pigs were anaesthetized and the liver was surgically exposed. Each pig received a single, 50 mg/dose of the clinical LTLD formulation (ThermoDox®). Subsequently, ablations were performed with either 1, 3 or 6 sequential, overlapping needle insertions in the left medial lobe with total ablation time of 15, 45 or 90 minutes respectively. Two different RFA generators and probes were evaluated. After the final ablation, the ablation zone (plus 3 cm margin) was dissected out and examined for doxorubicin concentration by LC/MS and fluorescence.

Results

The mean Cmax of plasma total doxorubicin was 26.5 µg/ml at the end of the infusion. Overall, increased heat time from 15 to 45 to 90 minutes shows an increase in both the amount of doxorubicin deposited (up to ~100 µg/g) and the width of the ablation target margin to which doxorubicin is delivered as determined by tissue homogenization and LC/MS detection of doxorubicin and by fluorescent imaging of tissues.

Conclusions

LTLD in combination with RFA was effectively optimized with increasing deposition of doxorubicin and width of the target margin as time increased.

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Deletion of ADAMTS5 does not affect aggrecan or versican degradation but promotes glucose uptake and proteoglycan synthesis in murine adipose derived stromal cells.

This is a summary of a paper that was written by D.J. Gorski, W. Xiao, J. Li, W. Luo, M. Lauer, J. Kisiday, A. Plaas and J. Sandy[1]. This was a collaborative research project between Dr. Kisiday at the ORC, Drs. Gorski, Plaas and Sandy from the Department of Biochemistry, Rush University Medical Center, Chicago (Dr. Plaas is also in the Department of Internal Medicine (Rheumatology) and Drs. Xiao and Luo of the Department of Internal Medicine (Rheumatology) at Rush University Medical Center and also the Department of Orthopaedics Xiangya Hospital, Changsha, China and Dr. Lauer of the Lerner Research Institute of the Cleveland Clinic, Cleveland, Ohio.

Take Home Message

The aggrecan-cleaving enzyme ADAMTS-5 is thought to contribute to joint disease by degrading aggrecan in cartilage. This study challenges this assumption by demonstrating that deletion of ADAMTS-5 does not alter proteoglycan degradation in adipose-derived stromal cells in vitro. Instead, the results suggest that ADAMTS-5 functions to reduce glucose uptake, which in turn suppresses intracellular degradation of aggrecan by an enzyme other than ADAMTS-5.

Introduction

The healing properties of connective tissue mesenchymal stem cells (MSCs) are influenced by the extracellular matrix that they secrete, including the large proteoglycan aggrecan[2,3]. Previous work has demonstrated an inverse relationship between aggrecan accumulation and the aggrecan-cleaving enzyme ADAMTS-5[4,5], but the extent to which proteoglycan accumulation is influenced by ADAMTS-5-mediated degradation is not known. This unknown is addressed in the current study using a cell culture model.

Methods

Adipose-derived MSCs and chondrocytes were obtained from wild-type (WT) mice, or mice in which the gene for ADAMTS-5 was deleted (knock out (KO)). Each cell type was maintained in monolayer culture. Proteoglycan turnover was evaluated using western blots for protein fragments. Low density lipoprotein receptor-related protein 1 (LRP-1) was detected using western blot. Cellular glucose uptake was quantified using the Amplex commercial kit.

Results

Aggrecan turnover was not affected by ADAMTS-5 KO in MSCs or chondrocytes. Similar results were found for the proteoglycan versican. These data do not indicate a role of ADAMTS-5 in proteoglycan degradation. In MSCs, ADAMTS-5 KO results in significantly higher glucose uptake. These data coincided with lower degradation of LRP-1, a protein that plays a critical role in glucose uptake.

Conclusions

These data indicate a new and apparently non-proteolytic role of ADAMTS-5 in proteoglycan degradation. It is postulated that increases in aggrecan synthesis with ADAMTS-5 KO is due to an increase in glucose uptake, which in turn potentiates the synthesis of aggrecan.

Acknowledgments

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Influence of an n-3 long-chain polyunsaturated fatty acid-enriched diet on experimentally induced synovitis in horses

This summary is from a paper published in 2015 by Drs. Trinette Ross-Jones, Wayne McIlwraith, John Kisiday, Tanya Hess, Karen Hansen and Jerry Black[1]

Take Home Message

Dietary treatment of 40 grams of n-3 long-chain polyunsaturated fatty acid (LCPUFA) altered serum phospholipid and synovial fluid lipid concentrations of EPA and DHA. Twelve mares were randomly assigned to either a control diet (CONT) or an n-3 long-chain fatty acid-enriched treatment diet (N3FA). Synovial tissue collected from N3FA supplemented horses exhibited lower expression of ADAMTS-4 (aggrecanase-1) compared to control horses and this decrease in expression warrants further investigation of n-3 LCPUFA as a joint therapy.

Introduction

Osteoarthritis (OA) is a debilitating condition characterized by degenerative changes in joint articular cartilage that results in chronic pain and decreased mobility. It is well recognized that an inflammatory stage of OA exists[2], with synovitis and joint effusion commonly preceding cartilage degeneration[3]. Proliferation of synoviocytes and lymphocytic infiltration of the synovium are active processes involved in synovitis[4] and result in clinical signs such as lameness, pain, and palpable swelling and heat around the joint. The synoviocytes produce pro-inflammatory proteins, such as cytokines [primarily interleukin-1beta (IL-1b)], and eicosanoids (including prostaglandin E2 [PGE2]). Interleukin-1beta also upregulates the release of eicosanoids (including PGE2) and catabolic proteases [including matrix metalloproteinases (MMP)] which have been identified in human osteoarthritic tissues[5], naturally occurring equine OA[6] and equine OA models[7,8]. PGE2 activates pain neuroreceptors and stimulates vasoconstriction and platelet aggregation in tissue[9] resulting in joint effusion, heat, lameness and decreased mobility. Such chronic inflammation can lead to articular changes that are common in advanced OA such as synovial tissue thickening and articular cartilage fibrillation[10] and erosion of the articular surfaces of cartilage by MMP and a disintegrin and metalloprotease with thrombospondin motifs (ADAMTS) enzymes[11].

Eicosanoids are potent biomolecules, most recognized in immune response, that originate via oxidative pathways from dietary long-chain polyunsaturated fatty acids (LCPUFAs) (20 carbons or greater in length) housed in the phospholipid bilayer of cellular membranes[12]. Arachidonic acid (ARA), derived from the 18-carbon LCPUFA linoleic acid (LA) and classified as an n-6 (first double bond on sixth carbon from terminal methyl end carbon) longchain fatty acid, is an abundant LCPUFA in cellular membranes and is the primary bioactive compound oxidized to PGE2 via COX pathways[13]. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are LCPUFA of the n-3 class (first double bond on third carbon from terminal methyl end carbon) and also incorporate into cellular membranes; however, they are metabolized into a less inflammatory class of eicosanoids than PGE2[14]. Eicosapentaenoic acid-derived eicosanoids, such as prostaglandin E3 (PGE3), have similar stereochemistry to ARA-derived molecules but function as weaker modulators of inflammation[15]. Docosapentaenoic acid (DPA) is another n-3 LCPUFA, intermediary to EPA and DHA; however, little is known of its anti-inflammatory properties[16]. Higher concentration of tissue ARA can lead to an increase in the formation of PGE2, exacerbating inflammatory responses in a variety of tissues[17]. Elevated plasma concentrations of ARA and decreased plasma concentrations of DHA have been positively correlated with knee synovitis and cartilage loss, respectively, in humans[18]. Endogenous formation of the 20-carbon fatty acid EPA and the 22-carbon fatty acid DHA through elongation of

the 18-carbon fatty acid, alpha-linolenic acid (ALA) is limited in mammals due the inefficient activity of desaturase enzymes[19].

Direct supplementation of these fatty acids is recommended in mammalian diets to increase tissue EPA and DHA. Dietary EPA and DHA compete with ARA for incorporation into the cellular phospholipid bilayer, reducing the amount of ARA released into the cytosol during immune responses. With less cytosolic ARA available, production of reduced. With the potential of EPA and DHA to alter eicosanoid production and thereby suppress inflammation, dietary treatment may have a role in managing symptoms or preventing the development of OA. The anti-inflammatory potential of oral n-3 LCPUFA supplementation has been demonstrated by reducing proinflammatory cytokine production in both arthritic[20] and healthy human subjects[21], decreasing MMP activity in canine OA cases[22] and in a guinea pig OA model[23] and lowering synovial white blood cells and plasma PGE2 in arthritic horses[24]. The recent report of elevated EPA and DHA in the synovial fluid of horses receiving dietary n-3 LCPUFA supplementation[25] justifies further enquiry into the potential of these LCPUFAs to modify the inflammatory response in the joint. Therefore, the objective of this study was to investigate the response to experimentally induced synovitis using the previously described method[25] in horses receiving an oral n-3 LCPUFA supplement.

Methods

Twelve skeletally mature (age 10± 1.2 years), healthy mares free of lameness and radiographic evidence of carpal joint disease were selected and blocked by age, body condition score and serum total lipid concentrations. They were then randomly assigned to one of two treatment groups: CONT (n=6) or N3FA (n=6).

After 90 days of feeding, temporary synovitis was induced in a random carpal joint of each horse by intra-articular injection of rIL-1 Beta as previously described at the ORC26. As a control, the contralateral joint was injected with an equivalent volume of physiologic buffered saline (PBS). Vital signs were monitored every two hours, lameness evaluation and joint circumference measurements taken at post-injection hour (PIH) 0, 4, 8, 24 and 240. Blood samples and synovial fluid samples from all joints were taken at hour 0, 4, 8, and 24 post-injection and synovium and cartilage samples were collected arthroscopically from both middle carpal joints in each horse via arthroscopic biopsy as previously described[26]. Horses remained on their respective diets during the 24 hour collection period.

Results and Conclusions

A 90 day- feeding period of n-3 LCPUFA increased serum phospholipids and synovial fluid lipid compositions of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) compared to CONT horses. The reIL-I Beta injection caused an inflammatory response; however, there was no effect of dietary treatment on synovial fluid PGE2 content and MMP activity. Synovial tissue collected from N3FA horses exhibited lower expression of ADAMTS-4 compared to CONT horses. Despite the presence of EPA and DHA in the synovial fluid of N3FA horses, dietary n-3 LCPUFA supplementation did not modify synovial fluid biomarkers compared to CONT horses; however, the lower ADAMTS-4 mRNA expression in N3FA synovium warrants further investigation of n-3 LCPUFA as a joint therapy.

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Management of joint diseases in horses: Current and future prospects

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Take Home Message

Surveys estimate that approximately 60% of lameness in horses is related to osteoarthritis (OA) (National Animal Health Monitoring Systems: Lameness in Laminitis in US Horses 2000; Caron and Genovese 2003). Rapid resolution of synovitis and capsulitis is critical in the management of OA because synovitis induces cartilage matrix degradation (McIlwraith 2005, 2011) and inhibition of catabolic processes can also aid in the enhancement of articular cartilage repair (Morisset et al. 2007). Two main properties are recognised with medications for equine traumatic arthritis and OA: 1) symptom modifying OA drugs (SMOADs); and 2) disease modifying OA drugs (DMOADs) and this is based on improvement of clinical signs in the first category and proof that progressive OA disease has been modified in the second category. Ideally we want a treatment that positively affects both symptom modifying and disease modifying effects, but the second is critical to long-term joint health.

Of the current 'conventional' treatments for traumatic joint disease, only SMOAD effects have been seen with systemic nonsteroidal anti-inflammatory drugs but there is some evidence that locally applied diclofenac ointment has some DMOAD effects, intra-articular (i.a.) hyaluronan (HA) has been shown to have DMOAD effects, and i.a. polysulfated glycosaminoglycan (PSGAG; Adequan)[1] has been shown to have potent SMOAD effects and a trend for DMOAD effects. The positive effects of triamcinolone acetonide with both SMOAD and DMOAD effects contrasts with methylprednisolone acetate (MPA), which has only shown SMOAD effects and negative degradative effects on the articular cartilage; its use is not recommended (McIlwraith 2010). Use of the latter product has virtually disappeared outside the USA but in the USA it was shown in a survey that 73% of equine veterinarians still use MPA to treat low motion joints (in the peculiar rationalisation that it will not be as harmful to the articular cartilage of low motion joints or that we might want to promote fusion) (Ferris et al. 2011). Veterinarians treating western performance and sport horses were significantly more likely to use triamcinolone acetonide in high motion joints than MPA. In the same survey, PSGAG and hyaluronate sodium (Legend)[2] were the most commonly used disease modifying product (63% and 57% of respondents, respectively). Also, sport horse practitioners were significantly more likely than race or show horse veterinarians to utilise IRAP products (discussed later). There has been minimal progress on systemic, conventional therapies since i.v. HA was shown to have SMOAD but not DMOAD effects. However, using the Colorado State University (CSU) OA chip fragment model no significant effects were seen with i.m. PSGAG (McIlwraith et al. 2012) but i.m. administration of sodium pentosan polysulfate has been shown to have DMOAD effects at a dose of 3 mg/kg bwt. There continues to be a paucity of good scientific data for in vivo effectiveness with oral joint supplements but randomised clinical studies have shown positive effects for oral HA and a proprietary mixture of bioactive lipids including New Zealand Green Lipped Mussel and abalone (McIlwraith 2013).

Recent work in the OA chip fragment model has shown that underwater treadmill exercise can possibly affect some outcome parameters with experimentally induced carpal joint OA and also positively affect postural sway as an indicator of improved proprioception (King et al. 2013). Again, in the equine carpal OA model, extracorporeal shockwave therapy decreased lameness and synovial parameters of inflammation supporting a pain and inflammation method of action but there is little evidence at this stage of a DMOAD effect (Frisbie et al. 2009a). The improved understanding of critical mediators in equine traumatic arthritis and OA has led to the identification of multiple pos-

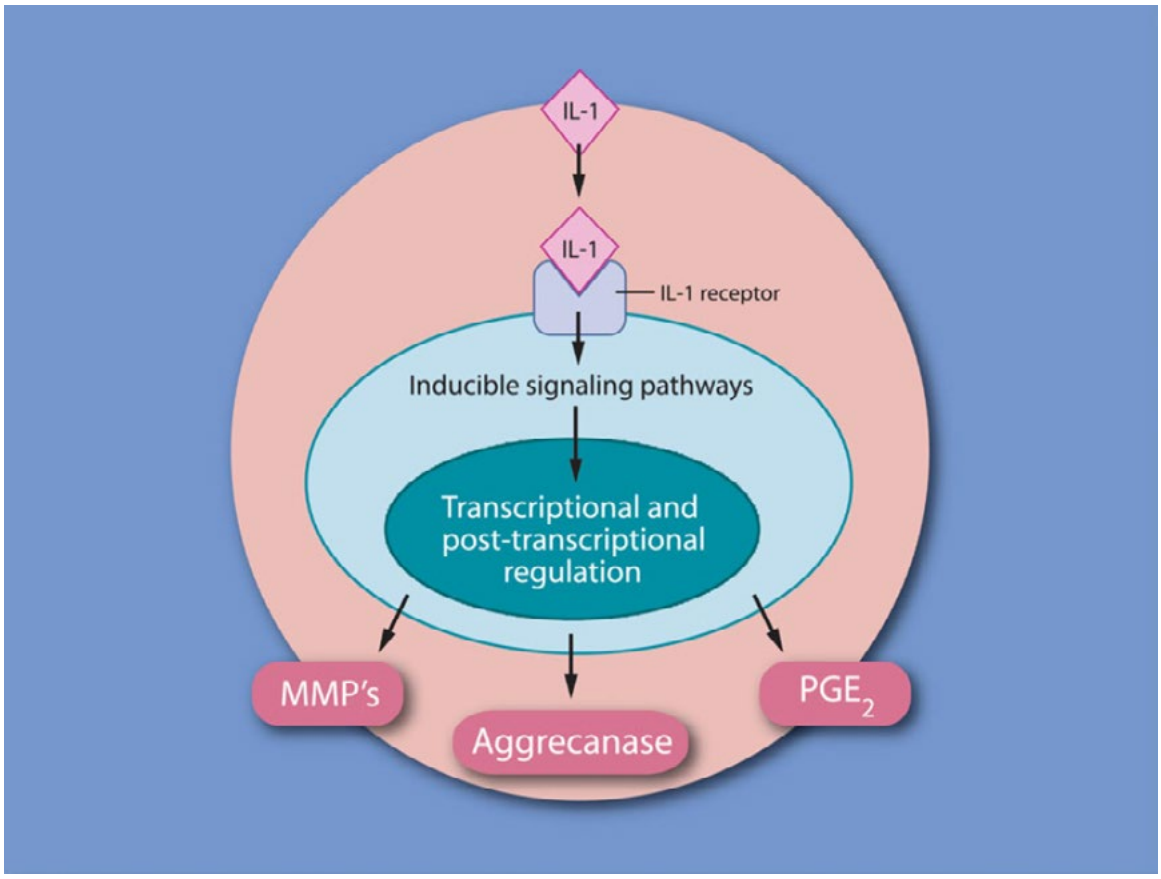

Figure 1. Diagram of interleukin (IL)-1 activation of matrix metalloproteinases (MMPs), aggrecanase and prostaglandin (PGE)2 release acting through IL-1 receptors on the cell memb

sible targets for therapy (McIlwraith 2005). Although there are multiple possible targets for inhibiting catabolism, most attention has been paid to interleukin-1 (IL-1) with some attention to metalloproteinases and aggrecanase (but no good in vivo evidence of use in the horse yet). It has been demonstrated using i.a. gene therapy with IL-1 receptor antagonist (IL-1ra) and an adenoviral vector that OA can be prevented, proving the importance of IL-1 in the equine OA cascade (Frisbie et al. 2002) (Fig 1). Because of problems with reactivity to the adenoviral vector in that study, gene therapy is still not a reality but considerable progress has been made recently (Goodrich et al. 2013a). There is no specific IL-1ra protein therapy available but a product developed in Germany called autologous conditioned serum (ACS; Orthokine)[3] has a significant increase in IL-1ra as one effect of the process (Wehling et al. 2007). This product was initially tested in horses in Europe by Dr Thomas Weinberg with positive results in OA of the distal interphalangeal joint not responding to triamcinolone and HA and more recently the product[4] was evaluated with the CSU experimental model of equine OA (Frisbie et al. 2007). Horses treated with ACS (3 treatments at weekly intervals) were observed to have significantly reduced lameness in OA limbs, even 5 weeks after the last treatment compared with placebo treated horses and also had a significant reduction in synovial membrane inflammation in treated compared with placebo-OA joints. There was also a trend for improvement of cartilage gross score and proteoglycan staining in ACS treated OA joints compared with placebo treated joints. When Orthogen discontinued their relationship with Arthrex in the USA, they developed a new product (IRAP II)[5]. Comparative cytokine profiles of IRAP and IRAP II using equine blood were then performed in the author's laboratory and have

been reported (Hraha et al. 2011). Both products had significant increases in IL-1ra concentrations with IRAP II being superior to IRAP. Of greater importance, it was noted that the IL-1ra: IL-1 ratio was significantly better with IRAP II. The production of the growth factors insulin-like growth factor-1 and transforming growth factor-b were both increased to about double the levels of serum with no difference between the products. It was noted, however, that IRAP produced significantly more tumour necrosis factor-a than IRAP II and this was considered to be a significant issue because of the known deleterious effects of tumour necrosis factor-a. In the 2009 survey of equine veterinarians in the USA, sport horse practitioners were significantly more likely than race or show horse veterinarians to use IRAP products. Outside the USA, IRAP products are being increasingly used by racehorse and show horse veterinarians in lieu of i.a. corticosteroids and this is somewhat associated with more restrictive corticosteroid thresholds.

The use of platelet rich plasma (PRP) has become a buzz word in the mainstream media – especially in the treatment of high-profile human athletes. There is a challenge for veterinarians to interpret the science and determine the appropriate indications to give advice to their clients about what PRP can and cannot accomplish. PRP has been advocated as a way to introduce increased concentrations of growth factors and other bioactive molecules to injured tissues in an attempt to optimise the local healing environment. There have been various definitions of PRP but the common one now is that the product should have an increase in platelet content over the level in blood. The initial enthusiasm for PRP was based on growth factors within the a-granules, but there are a number of other bioactive factors in PRP contained in dense granules of platelets and there is an emerging paradigm that more than just platelets are playing a role in PRP (Boswell et al. 2012). The use of PRP to treat joint disease in the horse is increasing. At CSU's Orthopaedic Research Center we have tended to recommend IRAP and IRAP II for joints and PRP (or autologous conditioned plasma) for treatment of tendon and ligamentous injuries. However, good clinical results with OA in man have been reported (Kon et al. 2011) and a recent in vitro study in our laboratory has shown beneficial effects on cartilage metabolism (Kisiday et al. 2012).

The effects of inflammatory and anti-inflammatory molecules from leucocytes in PRP have not been defined. A study from Cornell University using human blood evaluated 2 PRP systems designated as PRP-1 (autologous conditioned plasma; Double Syringe System)[5], which has a modest increase in platelets and minimises leucocytes and PRP-2 (GPS III Mini Platelet Concentration System)[6], which has high platelet and white cell concentrations (Sundman et al. 2011). PRP-1 had 1.99 times the platelet levels and 0.13 times the leucocytes whereas PRP-2 had a 4.69 times platelet and a 4.26 times leucocytes compared with blood. The growth factors were significantly increased with PRP-2 compared to PRP-1 but catabolic cytokines were also significantly increased in PRP-2 compared with PRP-1.

Mesenchymal stem cells (MSCs) have probably received the most attention of the newer therapies. Multipotent cells, which are present in mature bone marrow and can replicate as undifferentiated cells, have been used most commonly. While there are anecdotal reports of success with adipose-derived stromal vascular fraction cell preparations, cultured bone marrow-derived stem cells have been superior in controlled, comparative studies (Kisiday et al. 2008; Frisbie et al. 2009a,b). Both clinical and experimental studies support the i.a. route of administration as providing benefit in both articular cartilage repair (McIlwraith et al. 2011), soft tissue healing in clinical cases in the equine femorotibial joints (Ferris et al. 2014) and osteoarthritis (Frisbie et al. 2009b), which supports the concept that MSCs act as trophic mediators (Caplan and Dennis 2006). By contrast, implantation of bone marrow derived MSCs in fibrin has failed to show benefit in repair of articular cartilage defects (Wilke et al. 2007). We explored why this failure of MSCs to have a positive effect with in situ implantation and determined that the migration of MSCs increased as fibrin hydrogels were diluted (Hale et al. 2012). A more recent study where bone marrow-derived MSCs were implanted in a fibrin/PRP mixture for articular repair also demonstrated negative effects with bone formation in articular defects (Goodrich et al. 2013b). However, some positive results have been demonstrated recently with chondroprogenitor cells derived from the superficial layer of articular cartilage in promotion of articular cartilage repair (Frisbie et al. 2015).

Authors' declaration of interests

No conflicts of interest have been declared.

Manufacturers' addresses

[1]Luitpold Animal Health, Shirley, New York, USA.
[2]Bayer Animal Health, Shawnee Mission, Kansas, USA.
[3]Orthogen Veterinary GmbH, Dusseldorf, Germany.
[4]Dechra Veterinary Products, Overland Park, Kansas, USA.
[5]Arthrex Inc., Naples, Florida, USA.
[6]Biomet Biologics, Warsaw, Indiana, USA.

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Radiofrequency probe and sharp transection for tenoscopic-guided desmotomy of the accessory ligament of the superficial digital flexor tendon

This was a study done by Drs. Brad Nelson, Chris Kawcak, E.J. Ehrhart (pathology faculty) and Laurie Goodrich and has been published in Veterinary Surgery[1] as well as being presented at the 4th World Veterinary Orthopaedic Congress in Breckenridge, CO 2014, ACVS Surgical Summit in San Diego, CA in 2014 and at the Orthopaedic Research Society in Las Vegas, NV in 2015.

Take Home Message

Tenoscopic-guided desmotomy of the accessory ligament of the superficial digital flexor tendon using the radiofrequency probe showed no difference in measured clinical or histologic outcome parameters when compared with sharp transection using a tenotomy knife. However, the authors preferred the maneuverability of the radiofrequency probe and there was also a slight decrease in hemorrhage.

Introduction

Desmotomy of the accessory ligament of the superficial digital flexor tendon (ALSDFT; superior check ligament) has been performed for metacarpophalangeal joint flexural deformity and superficial digital flexor tendonitis.[2-6] Radiofrequency probes are electrosurgical devices that are used for debridement and desmotomy procedures due to their precision and apparent lack of collateral damage to nearby tissues.[7,8]

We chose the SaberRF probe (Saber30, ArthroCare Corp., Austin, TX)(Figure 1), due to the small size and configuration of the tip, which was anticipated to improve accuracy during desmotomy and help avoid the nutrient artery, that occasionally perforates the proximal portion of the ALSDFT.[5,9] The use of the SaberRF probe has the potential to precisely and safely perform ALSDFT desmotomy; however, the safety and performance of this method as it compares to sharp transection has not been investigated.

With tenoscopic ALSDFT desmotomy, there are adjacent structures within the carpal sheath that could potentially be damaged including the flexor carpi radialis (FCR) tendon, the radial head of the deep digital flexor tendon (RHDDFT) and the DDFT.[10] We hypothesized that tenoscopic-guided ALSDFT desmotomy using the SaberRF probe would cause minimal damage to adjacent carpal sheath structures, have decreased intraoperative hemorrhage, and shorter operative times compared to sharp transection.

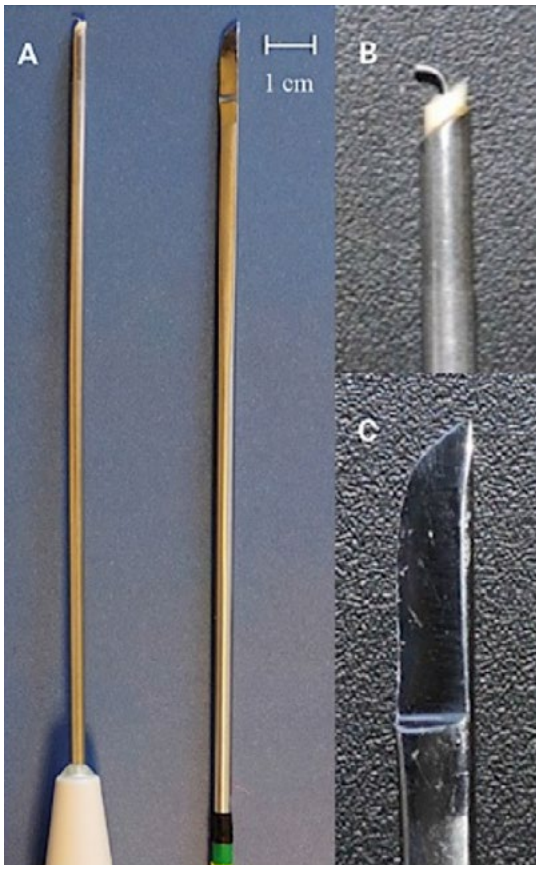

Figure 1. (A) Left: The Saber30 radiofrequency probe and Right: tenotomy knife. (B) Close-up of the Saber30. (C) Close-up of the tenotomy knife.

Methods

Six horses, 2-5 years of age, were included in the study and all procedures were approved by the Institutional Animal Care and Use Committee at Col-

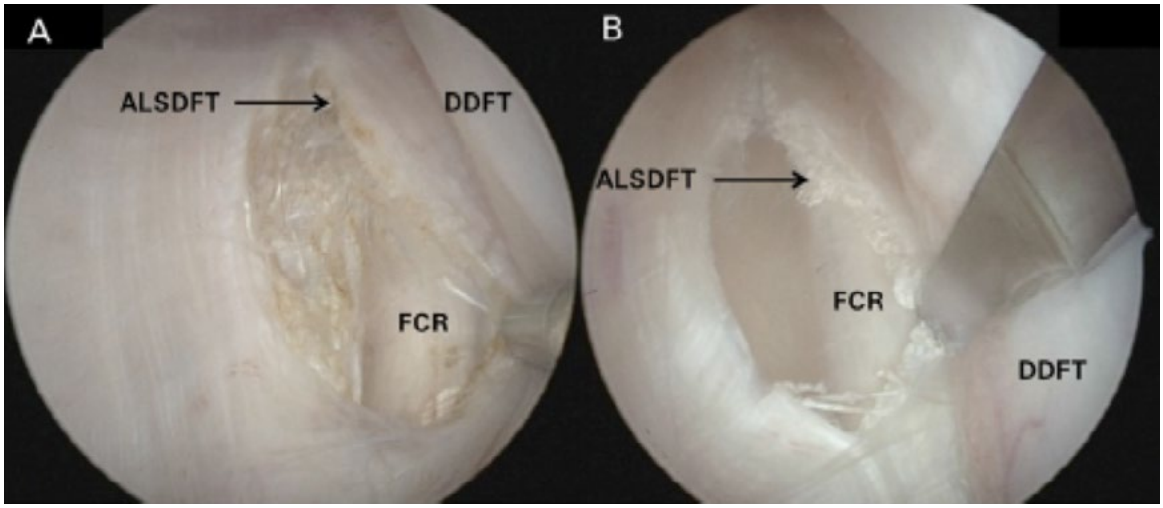

Figure 2. (A) Use of the Saber30 during desmotomy of the accessory ligament of the superficial digital flexor tendon (ALSDFT). (B) Use of the tenotomy knife for ALSDFT transection. Distal is to the top and cranial is to the left in both images. FCR, Flexor carpi radialis tendon; DDFT, deep digital flexor tendon.

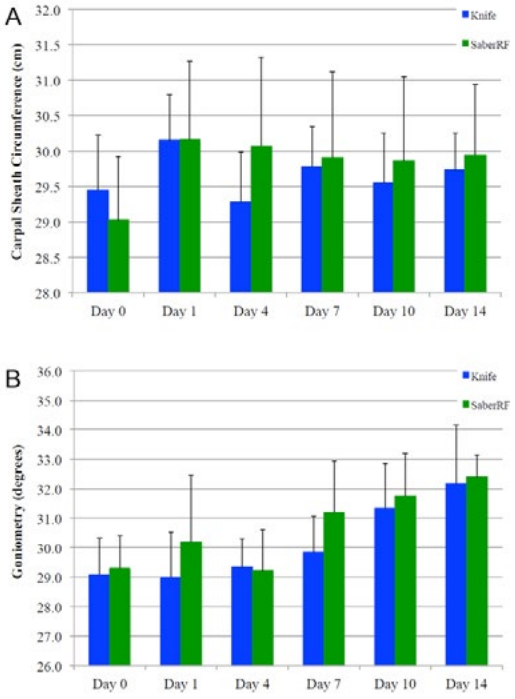

Figure 3. Mean +/- standard error carpal sheath circumference measurements (A) and carpal goniometry measurements (B) over time following desmotomy of the accessory ligament of the superficial digital flexor tendon using the tenotomy knife (Knife) or Saber30 radiofrequency probe (SaberRF). Day 0 represents pre-surgical measurements. There was no significant difference in these measurements between methods.

orado State University. Tenoscopic-guided ALSDFT desmotomy was performed bilaterally in all horses with one forelimb randomly assigned to the SaberRF and the other to the tenotomy knife (Figure 2).

Intraoperative assessments included hemorrhage during desmotomy, time required for desmotomy and the difficulty of ALSDFT transection. Carpal sheath effusion and circumference measurements, carpal goniometry measurements, and carpal flexion pain were performed before surgery (day 0) and on days 1, 4, 7, 10, and 14 postoperatively. Lameness examinations (with carpal flexion tests) were performed every 7 days.

Two weeks after surgery, all horses were humanely euthanized. Synovial fluid was collected and evaluated for total protein concentrations and total white blood cell counts (including neutrophil, lymphocyte, and monocyte proportions). The ALSDFT was evaluated to determine if the ligament was completely transected, and to determine if any macroscopic damage to nearby structures (FCR, RHDDFT and DDFT) had occurred. Three sections of each tissue (ALSDFT, FCR, RHDDFT and DDFT) were evaluated for cell viability and peripheral inflammation and architecture changes using histologic methods.

Results

Tenoscopic surgery was completed successfully

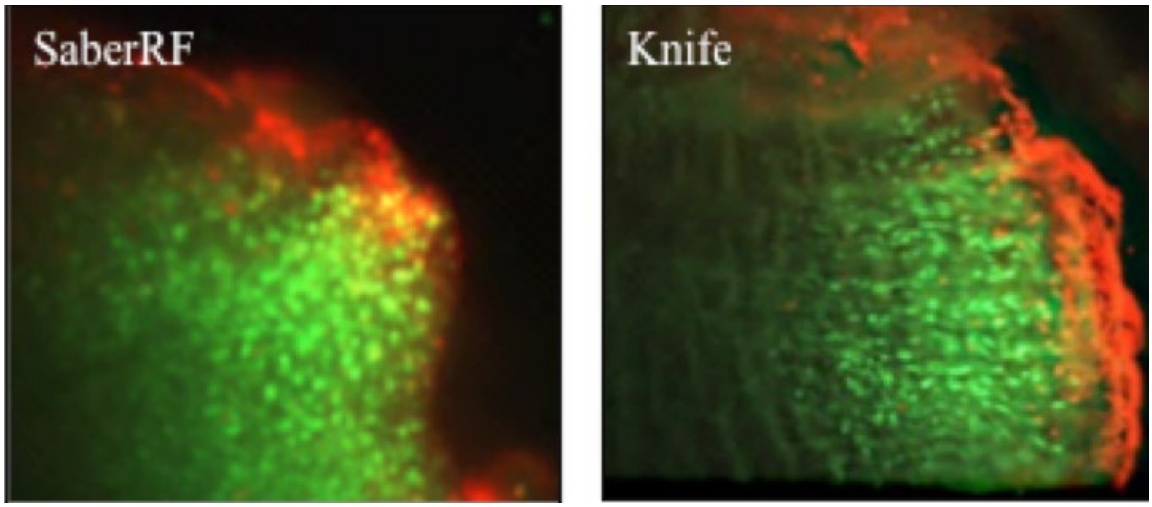

Figure 4. Representative images of cell viability staining of the accessory ligament of the superficial digital flexor tendon 14 days after transection with the Saber30 radiofrequency probe (left) and tenotomy knife (right). Green cells are alive and red cells are dead. There was no significant difference in cell death between methods.FCR, Flexor carpi radialis tendon; DDFT, deep digital flexor tendon.

in all limbs. Mean surgical time and the difficulty of ALSDFT transection was not significantly different between methods. Mild bleeding was observed during ALSDFT transection in 83% limbs where desmotomy was performed with the knife while in 40% limbs with the SaberRF probe and this difference approached significance (P=.078).

There was no significant effect of desmotomy method on carpal sheath effusion scores, carpal sheath circumference, carpal goniometry measurements, or carpal flexion pain (Figure 3).

There was no significant difference in lameness grades between methods. Postmortem evaluation confirmed complete transection of the ALSDFT in all limbs and there was no discernible macroscopic damage to the RHDDFT or DDFT in any limb in either group.

There was no significant difference in synovial fluid parameters between methods at day 14. There was no significant difference in cell death, tissue architecture, or peripheral inflammation grades for the ALSDFT, FCR, RHDDFT, or DDFT between desmotomy methods (Figure 4).

Conclusions

This study demonstrated the safety of using the SaberRF probe for ALSDFT desmotomy and revealed no significant adverse effects when compared to sharp transection. Less intraoperative hemorrhage was observed when using the SaberRF probe. There was no significant difference in surgical times with the SaberRF probe compared to the tenotomy knife.

Acknowledgments

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Integrative veterinary medical education and consensus guidelines for an integrative veterinary medicine curriculum within veterinary colleges

This is a summary of a paper published in the Open Veterinary Journal by M.A. Memon, J. Shmalberg, H.S. Adair III, S. Allweiler, J.N. Bryan, S. Cantwell, E. Carr, C. Chrisman, C.M. Egger, S. Greene, K.K. Haussler, B. Hershey, G.R. Holyoak, M. Johnson, S. Le Jeune, A. Looney, R.S. McConnico, C. Medina, A.J. Morton, A. Munsterman, G.J. Nie, N. Park, M. Parsons-Doherty, J.A. Perdrizet, J.L. Peyton, D. Raditic, H.P. Ramirez, J. Saik, S. Robertson, M. Sleeper, J. Van Dyke and J. Wakshlag. Open Veterinary Journal, (2016), Vol. 6(1): 44-56. Dr. Haussler was a contributing author.

Take Home Message

The authors of this consensus guideline agree that the veterinary profession should position graduates of AVMA-accredited colleges to be able to respond to the growing interest in integrative veterinary medicine (IVM) using an evidence-based approach. Veterinary curricula that do not educate students in the definitions, potential clinical applications, mechanisms of action and adverse effects of these modalities are hindering the education and clinical competency of new graduates in their daily interactions with clients and colleagues and the ability to provide effective treatment options to their patients.

Introduction

In 2001, the National Center for Complementary and Alternative Medicine awarded grants to medical and nursing schools for the development of a Complementary and Alternative Medicine (CAM) curriculum, which was based on developing foundational skills, evidence-based approaches and self-learning. Foundational skills were taught as an introduction to the principles of CAM before individual modalities were taught. Introductory concepts were designed to impart an understanding of the terminology of CAM, integrative medicine, and the basic principles of non-conventional medical philosophies, such as traditional Chinese medicine. Evidence-based analysis was encouraged with the following questions: 1. Is there significant scientific evidence for a therapy's efficacy or harm? 2. Is there evidence that a therapy is being widely used by patients? and 3. Does a therapy have the potential to treat a medical condition for which conventional medical approaches are lacking? These questions were also the basis for determining what modalities were discussed. For example, at least one criterion had to be satisfied for inclusion in the proposed CAM curriculum, and considerable deference was given to the presentation of evidence and safety of the included CAM modalities. The curriculum guidelines recommended Tools for the Future, or the stated goal that students develop long-lasting tools for self-learning about CAM.

There is a need for clear consensus guidelines as reported in a 2011 survey of AVMA-accredited colleges on the status of complementary and alternative veterinary medicine (CAVM) training programs for veterinary students (Memon and Sprunger, 2011). The survey respondents indicated that students should be aware of CAVM modalities because of the strong public interest in CAVM and because practitioners should be able to address client questions from a position of knowledge. Acupuncture, chiropractic, physical rehabilitation, integrative nutrition, herbal therapy, and homeopathy were the most common topics included in existing veterinary curricula. The most common barriers cited by respondents were related to limited teaching budgets, the lack of time in the current curriculum, the unavailability of qualified CAVM faculty or instructors whom would follow an EBM approach, or insufficient support from a college's administration.

The fundamental goal of an IVM course should be to provide unbiased exposure to CAVM modalities and to discuss their integration into the broader conventional veterinary medical framework. The course should strongly emphasize both positive and negative viewpoints and evidence surrounding the particular modalities, and it should be structured in such a way that students are challenged to make their own assessments of the suitability of tech-

niques to different patient populations. The primary areas of instruction are those that the students are most likely to encounter in clinical practice. A recent retrospective study of an academic IVM service found that acupuncture, physical rehabilitation, and hydrotherapy were the modalities most frequently administered to a patient population that suffered primarily from orthopedic and neurologic diseases (Shmalberg and Memon, 2015). The established IVM curriculum at many veterinary colleges provides instruction in acupuncture, veterinary manipulative therapy, physical rehabilitation, botanical or herbal medicine, and integrative nutrition (Memon and Sprunger, 2011). Divergent medical theories of TCVM and homeopathy should be presented for reference information.

Development of a sample veterinary course curriculum

Justification for proposed course topics

Students should be aware at the outset of the course of the fundamental debates surrounding integrative education in a biomedical context. The meanings assigned to integrative, complementary, holistic, alternative, conventional, and allopathic medicine by both the general public and veterinary professionals will help to inform the context of many of the modalities to be discussed. The evidence-based medicine evaluation system and grades of evidence provide students with an evaluation tool for all facets of medicine. The unique challenges of evidence-based medicine across the veterinary profession should be discussed, and the current understanding of human and animal placebo reviewed. The latter raises broader questions about the response of a disease to a treatment and why interventions may work when they in fact exerted no measurable or known effect. These reasons have been explored extensively elsewhere but include temporal changes in a disease, a regression to the mean, the effect of non-treatment influences, confirmation bias, cognitive dissonance, and owner outlook. The controversial aspects of homeopathy and Traditional Chinese Veterinary Medicine can be discussed in such a context, given that some authors suggest such interventions are “implausible on a priori grounds” lack scientifically acceptable rationale, have insufficient supporting evidence, have failed in clinical trials, and seem improbably on common sense grounds. The course faculty should be respectful, regardless of personal opinions or assessments, in understanding that this proposed course exists within the confines of conventional allopathic training. Personal bias, positive or negative, should not influence the nature of instruction. Finally, case scenarios should be used to demonstrate the possible interactions of therapies and the complicated nature of integrative medicine, which by definition may include the effects of accepted treatments and other modalities.

Course goals

1. Recognize the different complementary treatment modalities that are available to veterinary patients and the reasons why owners are increasingly interested in such therapies.

2. Understand the evidence-based application of IVM techniques in combination with conventional care.

3. Understand the benefits and limitations of complementary medical systems including acupuncture, veterinary manipulative therapy, physical rehabilitation, integrative nutrition, and botanical medicine.

4. Describe the common orthopedic and neurologic injuries in pets and performance animals and understand the benefits and limitations of complementary techniques for these conditions.

5. Evaluate novel trends in animal diets using evidence-based clinical nutrition.

6. Understand the approaches of alternative medical systems such as TCVM and homeopathy.

7. Research and communicate the advantages, disadvantages, and evidence for a CAVM modality as opposed to, or in combination with, a conventional approach (course project).

A course catalog description could include the following proposed language: “This course introduces critical concepts and modalities of IVM, with an emphasis on the integration of evidence-based complementary medical techniques. Students will learn to evaluate integrative medical interventions in the context of conventional care and to determine if such modalities could improve patient outcomes for manage-

ment of disease processes. Students should also expect to develop an improved ability to discuss such therapies with peers and clients". This course may be offered as an elective, but the authors view the course as an emerging part of a refined core veterinary curriculum. It is a necessary introduction to concepts that are required when graduates pursue future study in IVM and when practicing clinicians are confronted with clients' questions about these techniques.

The authors propose a model IVM course to serve as a minimal standard for veterinary student training in this area (Table 1).

Consumer demand has accelerated the incorporation of many CAVM modalities into conventional practice. Consequently, students should receive adequate exposure to the principles, theories, and current knowledge supporting or refuting such techniques. These proposed curriculum guidelines would broadly introduce students to the objective evaluation of new veterinary treatments while increasing their preparation for responding to clinical questions about IVM in practice. Such a course should be evidence-based, unbiased, and unaffiliated with any particular CAVM advocacy or training group. Each institution should ensure compliance and consistency with their college's educational standards by performing periodic

Table 1. Outline of a model integrative veterinary medicine course for veterinary students.

Course topic	*Lecture hours*	*Lab hours*	*Main sub-topics*
Basic concepts	3	0	(1) Integrative veterinary medicine: History, definitions, and context (2) Applications of evidence-based medicine to IVM and current controversies (TCVM, homeopathy, placebo) (3) Multi-modality treatments and integration of complementary therapies with conventional therapy
Acupuncture	3	2	(1) Anatomy and physiology of acupuncture with relation to soft tissue and neurologic concepts (2) Traditional theories of acupuncture: An assessment of the validity and current controversies (3) Integrative acupuncture: clinical approaches and current scientific literature Laboratory: Proposed location of acupuncture points in the canine/or equine with a discussion of the controversies in point placement and naming
Manual therapies	2	1	(1) Veterinary manipulative therapy: Neurology, biomechanics, and available evidence (2) Massage therapy and myofascial principles Laboratory: Palpation laboratory and demonstration of techniques
Botanical medicine	2	0	(1) Origins and major systems of herbal therapy with selected evidence-based interventions (2) Adverse events, herb-drug interactions, supplement evaluation and regulation
Integrative nutrition	2	0	(1) Novel trends in nutrition: Raw diets, home-prepared diets, grain-free diets, owner perceptions and current marketing (2) Nutrition in select conditions: Obesity, performance, physical rehabilitation, and integrative medical approaches
Physical rehabilitation	3	2	(1) Functional anatomy in physical rehabilitation and sports medicine with an emphasis on relevant orthopedic and neurologic pathology (2) Rehabilitative assessment and interventions (3) Photobiomodulation (laser), shockwave, ultrasound, hyperbaric oxygen, and other rehabilitative modalities Laboratory: Demonstration of canine/equine physical rehabilitation techniques and use of selected therapeutic modalities
Total hours	15	5	

Conclusions

IVM by definition requires constant refinement and should be guided by available scientific evidence. evaluation of integrative medicine courses. Student and graduate surveys provide one possible metric, but other authors recommend an objective faculty

panel evaluation. IVM courses will likely need routine updating as new information becomes available, and institutions without faculty trained in these areas should consider recruitment of outside speakers to provide education in this area when it is not logistically and financially feasible to recruit permanent faculty in these areas. Controversies regarding IVM and CAVM should be addressed within the course and throughout the entire curriculum. Instructional honesty regarding the uncertainties in this emerging field is critical. Skeptics of integrative medicine in human health professions understand the need for training in this area, and one prominent skeptic related that "without additional education about alternative medicine, physicians cannot obtain accurate information from patients about their use of alternative modalities, or provide information and guidance. The authors hope that increased training of our future colleagues will demonstrate the openness to new ideas that characterizes the scientific method and a willingness to pursue and incorporate evidence-based medicine in clinical practice with all therapies, including those presently regarded as integrative, complementary, or alternative.

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PT Evaluation of the Animal Rehab Patient; Physical Therapy Examination of the Equine Patient

This is a monograph that was written by Arlene White, an animal physiotherapist and Dr. Melissa King of the Orthopaedic Research Center and published by the American Physical Therapy Association.[1]

Take Home Message

The purpose of this monograph is to provide the equine therapist with guidelines for conducting a comprehensive functional assessment of the horse.

Introduction

Functional assessment of the horse should be divided into 2 categories; static and dynamic evaluation. Dynamic evaluation involves functional motion both passive and active range of motion as well as gait analysis.

Equine static assessment involves evaluating for structural correctness, symmetry and muscling. A horse's conformation should be assessed with a thorough understanding of the individual's discipline and the demands placed on the musculoskeletal system. Examination should include assessing the horse in a static balanced position and while moving. A well-balanced or symmetrically built horse that is structurally correct is more likely to remain sound upon being subjected to the repetitive cyclic loading naturally incurred with training and performance. Poor conformation leads to a greater risk of injury as well as limited function. The horse's body should be proportional with the neck, shoulder, back and hip approximately equal lengths. The dorsal aspect of the neck should be twice as long as the ventral side (2:1 ratio). An imbalance in the neck ratio often results in a neck that ties in low, which will limit cervical flexibility and the horse may travel more on the forehand. For every 10 cm increase in length of ventral (underline) aspect of the neck the odds of developing fetlock effusion increases by a factor of 5.1.1 While the dorsal aspect of the thoracolumbar region of the back should be half as long as the ventral abdominal side (1:2 ratio). A horse that has a longer thoracolumbar region will have limited ability to get his pelvic limbs underneath the body limiting power and impulsion, often distributing more weight onto the thoracic limbs.

Thoracic limb conformation

When looking at the horse from the side or the "lateral view" the slope of the shoulder should be approximately a 40° to 55° angle. A steeper shoulder angle results in a shorter, jarring stride. A study evaluating race horses demonstrated that horses with a steeper shoulder angle were at an increased risk of developing carpal osteochondral chip fragments.[1] Horses that are described as back at the knee (concave appearance to the dorsal aspect of carpus) are often predisposed to carpal injuries, especially race horses that have a tendency to hyperextend the carpus during fatigue.[2] Over at the knee or "buckling" describes a convex dorsal surface of the carpus. Over at the knee conformation may be sign of lameness as a way to relieve pain - for example proximal suspensory injuries often present with some form of carpal flexion or buckling during stance.[2]

Pelvic limb conformation

The balance of the pelvic limbs is critical to a horse's athletic ability. The length and slope of the croup should be similar to the thoracolumbar length and slope of the shoulder. A horse with a steep croup will have a decreased cranial phase of stride in the pelvic limbs and reduced range of motion, which combines to limit the horse's ability to produce power. The steeper croup angle shifts the center of gravity in a caudal direction increasing the risk of developing hindlimb lameness issues. A lateral hock angle of less than 150° is often referred to as having a sickle hock appearance.3 Sickle hock conformation concentrates load in the distal, plantar aspect of the hock predisposing horses to desmopathy of the long plantar ligament of the tarsus (curb) and to distal hock joint pain.[3] Horses that are straight behind are also more prone to hindlimb lameness issues, as the hock and stifle angles are in a more extended position.[2] Horses with a tarsal angle greater than 170° often develop upward fixation of the patella, suspensory desmitis and distal hock joint osteoarthritis.[3]

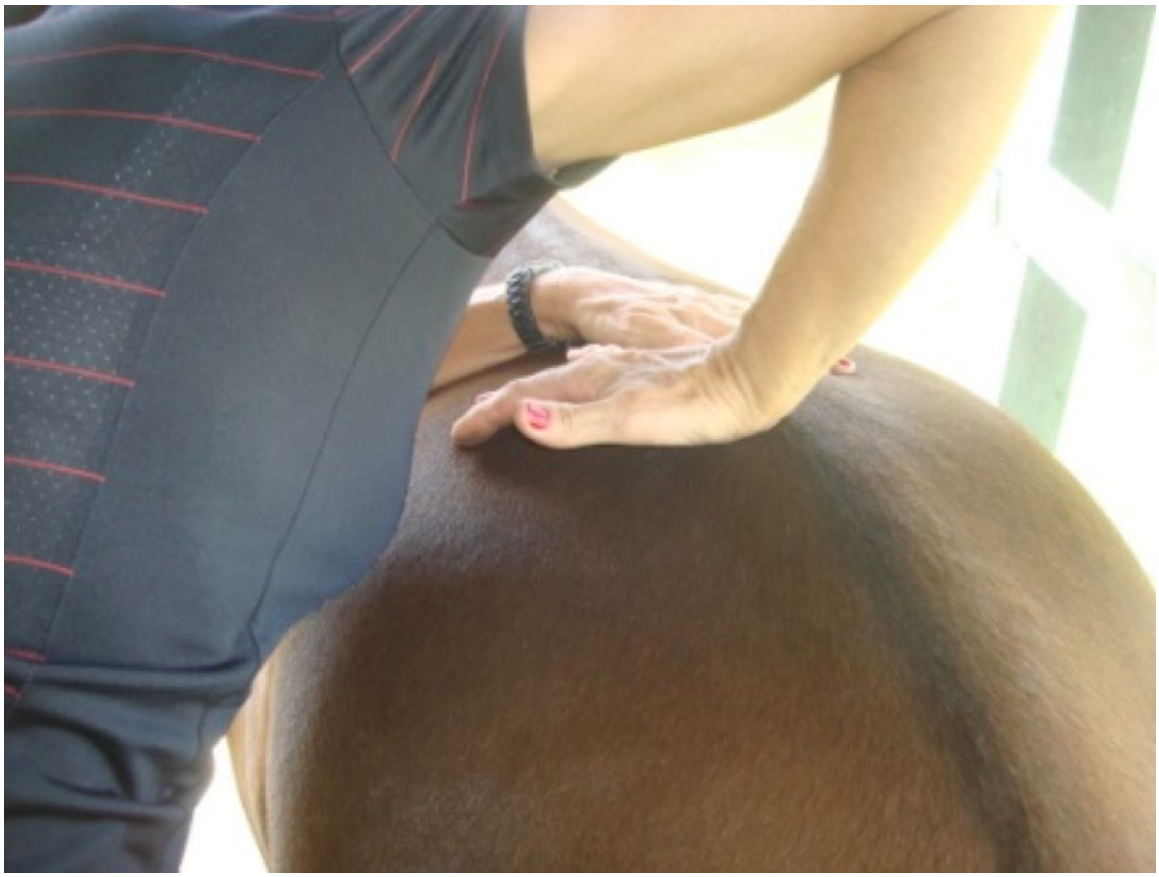

Figure 1. Assessing left sacroiliac joint motion (the pisiform process of the right hand is placed over the tuber sacrale as you take up tissue slack apply a ventrolateral force.

Understanding conformation allows the clinician to interpret the impact the conformation faults may have on future performance and where the limitations may occur. For example, a horse that toes in will asymmetrically load the lateral aspect of the distal limb, increasing strain on the lateral branch of the suspensory ligament. Furthermore, assessment of conformation in light of the injury can provide a realistic prognosis. Horses with straight hock conformation that have suffered a proximal suspensory injury are at an increased likelihood of developing chronic suspensory ligament desmitis. A thorough conformational assessment provides the client with a reliable prediction of athletic potential and soundness.

Methods

Starting at the skull and moving through the axial and appendicular skeleton a step-by-step description of palpation and range of motion techniques and assessments are described (Figure 1 as an example).

Conclusions

In the monograph, the authors stress the importance of obtaining a veterinary referral and diagnosis prior to assessing and treating the equine patient. They also advocate the importance of the team approach to rehabilitation of the equine patient. An understanding of musculoskeletal abnormalities, restrictions, pain, and range of motion abnormalities are described using a systematic approach. Upon completion of the monograph the participant will be able to formulate a thorough plan of assessing the equine patient, convey a problem list and initiate a rehabilitative plan based on clinical reasoning skills.

Acknowledgments

American Physical Therapy Association

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Modulating Tibiofemoral Contact Force in the Sheep Hind Limb via Treadmill Walking: Predictions from an OpenSim Musculoskeletal Model

This study was done by Zachary Lerner, Benjamin Gadomski, Allison Ipson, Kevin Haussler and Christian Puttlitz and accepted to the Journal of Orthopaedic Research January 15, 2015 and published online in Wiley Online Library. DOI 10.1002/jor.22829.

Take Home Message

The purpose of this study was to develop a musculoskeletal model of an adult sheep hindlimb and investigate the effects of treadmill walking speed on muscle and joint contact forces. Adjusting treadmill speed appears to be a viable method to modulate compressive and anterior-posterior tibiofemoral contact forces in the sheep hind limb. The musculoskeletal model is freely-available at www.SimTK.org.

Introduction

The hind limbs of sheep are used to study a variety of musculoskeletal and orthopaedic conditions in-vivo, including anterior cruciate ligament reconstruction[1], tendon-bone healing[2], tissue-engineered bone reconstruction[3] fracture healing[4], and fracture healing during simulated microgravity[5]. Since mechanical stimuli affect the biosynthesis, remodeling, and degradation of biological tissues, proper investigation of many such orthopaedic conditions requires knowledge and standardization of the loading environment in the sheep hindlimb[6-9]. The combination of treadmill locomotion and musculoskeletal modeling may allow researchers to modulate and quantify muscle and joint contact forces in-vivo. Musculoskeletal models and analysis software offer a method to non-invasively estimate the mechanical loads (i.e. muscle and joint contact forces) in weight-bearing limbs during locomotor activites[14-16]. However, while there are many open-source musculoskeletal models available to estimate muscle and joint contact forces in humans[17], we are not aware of a freely available model of the sheep hind limb. The first aim was to develop a freely-available musculoskeletal model of the sheep hind limb for use in OpenSim[16]. The second aim was to determine how treadmill walking speed alters estimates of in-vivo joint loading in the sheep hind limb.

Methods

The bony geometry of the musculoskeletal model was developed from computed tomography (CT) image data of a fully-mature Rambouillet Columbian ewe with no known diseases or abnormalities and segmented with AMIRA visualization software (ver. 5.0, VSG, Burlington, MA) (Figure 1). Anthropometric properties (segment mass (SM), center of mass (COM), and moment of inertia about the COM (Icom)) were quantified from dual x-ray absorptiometry (DXA) scans using the previously described procedure by Ganley et al[21]. All major lower-extremity muscles, represented by 31 muscle-tendon units, were incorporated into the model (Figure 1). Maximum isometric forces were based on previously reported values[22]. Muscle origins, insertion points, and lines of actions were established from the literature[23] and laboratory dissection of the hind limb. We refined the muscle moment arms in our musculoskeletal model by comparing to the moment arms measured experimentally using the tendon excursion method detailed previously by Carr et al.[23] for the gastrocnemius, deep digital flexor, extensor digitorum longus, and cranial tibial muscles. We used OpenSim's joint reaction analysis 15 to calculate the resultant forces and moments acting on each joint from all muscle forces as well as external and inertial loads applied to the model. Gait cycles corresponding to 0.25m•s-1 and 0.75m•s-1 walking speeds were simulated in the model, and the resultant muscle forces and tibiofemoral joint contact forces were predicted and compared.

Results

In general, muscle (Figure 2) and tibiofemoral contact forces (Figure 3) increased with walking speed. From 0.25m•s-1 to 0.75m•s-1, peak medial and lateral gastrocnemius muscle forces increased by 32% (0.15BW) (p=0.003) and 39% (0.11BW) (p=0.003), respectively. Peak cranial tibial muscle forces were not significant-

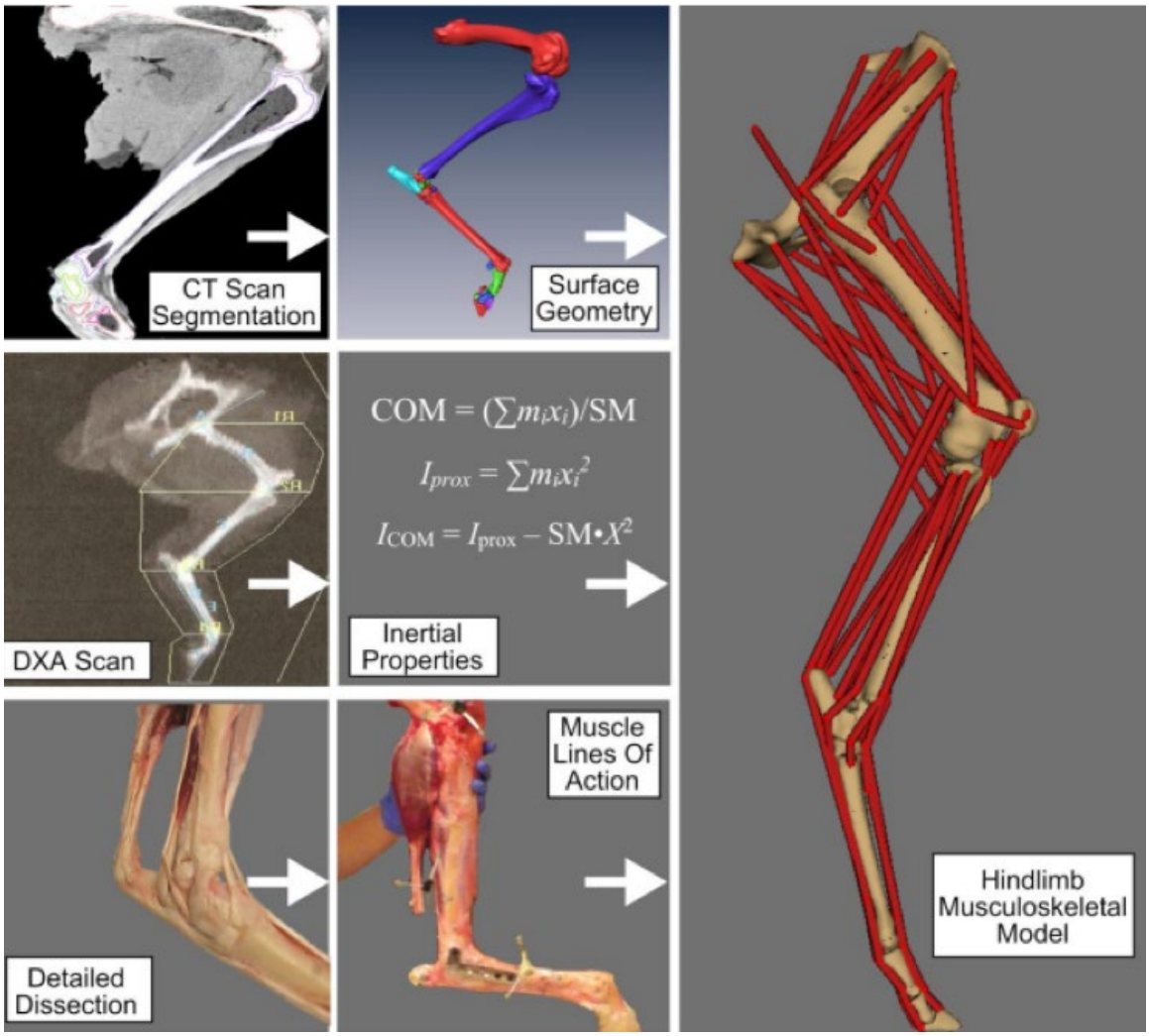

Figure 1. CT data was used to create the geometric reconstruction of the sheep skeleton (Small Top Panels). Inertial properties (center of mass (COM), moment of inertia about the proximal end (Iprox), and moment of inertia about the center of mass (ICOM)) of each segment were quantified using DXA, where SM is the segment mass, mi is the mass of the ith section, xi is the distance from the proximal segment boundary to the center of the ith section, and X is the distance from the proximal segment boundary to the COM (Small Middle Panels). Muscle origin and insertion points for the musculoskeletal model were determined in part through hind limb dissection (Small Bottom Panels). The skeletal geometry, inertial properties, and muscle lines of actions were incorporated into the full, lower-extremity model. A total of 31 muscle-tendon units represented all of the primary muscles of the sheep hind limb (Large Right Panel).

ly different (p=0.77) between speeds. Peak Medial and lateral gastrocnemius EMG activity increased by 48% (p=0.021) and 59% (p=0.013), respectively, at the faster versus the slower speed. Peak cranial tibial EMG activity was not significantly different (p=0.328) between speeds. Walking at the faster versus the slower speed increased the compressive tibiofemoral contact forces by 20% (0.38BW) (p=0.008) and the anterior-posterior tibiofemoral contact force by 37% (0.17BW) (p=0.040). The tibiofemoral contact force in the medial-lateral direction was not significantly different (p=0.64) between speeds. Peak vertical, anterior-posterior, and medial-lateral ground reaction forces increased with walking speed. The knee flexion-extension angle between walking speeds were generally similar across the gait cycle.

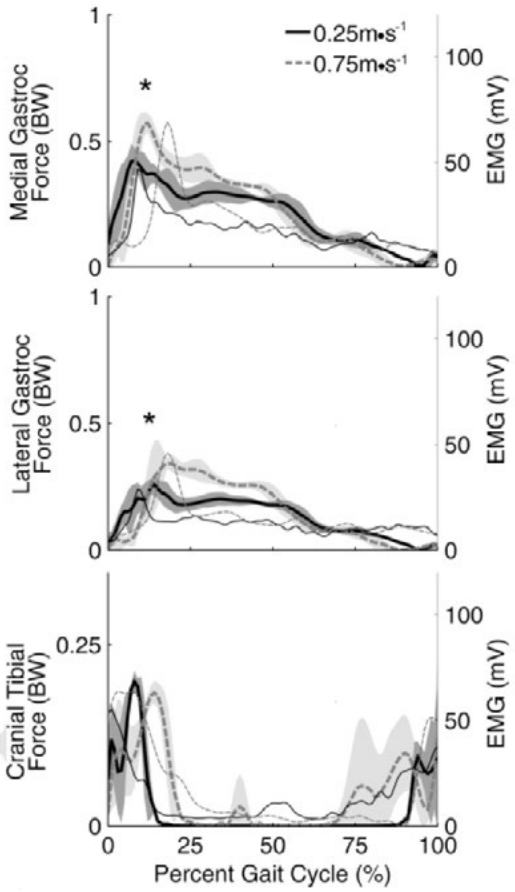

Figure 2. Medial gastrocnemius (top), lateral gastrocnemius (middle), and cranial tibial (bottom) muscle forces predicted from the sheep hind limb musculoskeletal model during treadmill walking at 0.25m•s-1 (thick black-solid line) and 0.75m•s-1 (thick gray-dashed line). The shaded regions represent ±SD. The EMG data for each muscle during treadmill walking at 0.25m•s-1 (thin black-solid line) and 0.75m•s-1 (thin gray-dashed line) are also plotted. The asterisk depicts a significant difference in peak muscle forces and EMG activity between the slower and faster speeds.

Conclusions

This study developed a sheep hind limb musculoskeletal model and determined whether treadmill walking was a viable approach to regulate muscle and joint contact forces in-vivo. Our results indicate that treadmill walking at slow to moderate speeds may be a viable method to control the compressive and anterior-posterior tibiofemoral contact forces in the sheep hind limb with low intra-specimen variability. This work provides an experimental and computational foundation for further orthopaedic research conducted in-vivo in the sheep hind limb. The musculoskeletal model is freely-available at www.SimTK.org and interested biomechanists are encouraged to build upon this initial modeling framework.

Acknowledgments

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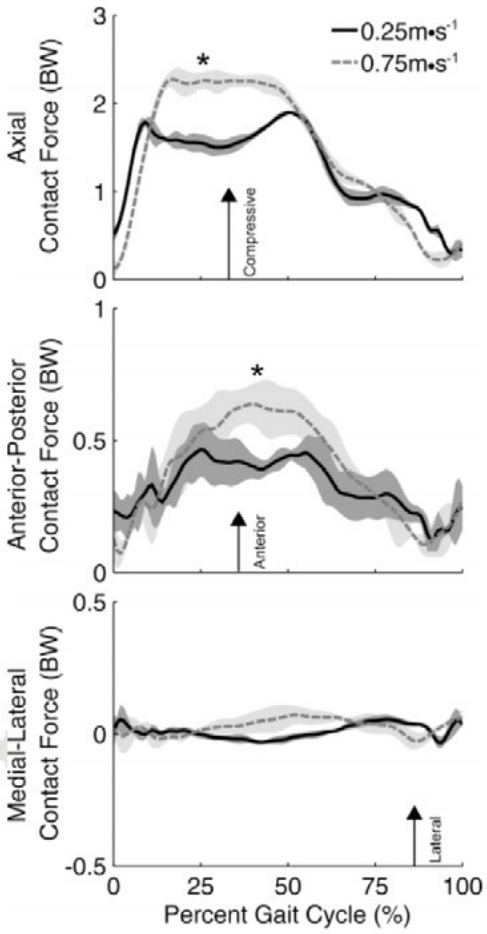

Figure 3. Compressive (top), anterior-posterior (middle), and medial-lateral (bottom) tibiofemoral contact forces predicted from the sheep hind limb musculoskeletal model during treadmill walking at 0.25m•s-1 (black-solid line) and 0.75m•s-1 (gray-dashed line). The shaded regions represent ±SD. The asterisk depicts a significant difference in peak forces between the slower and faster speeds.

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Lower extremity muscle activity during recumbent and upright cycling at low levels of effort

This is a summary of an article published in 2015 by Drs. McMurtrey, DeVoe and Reiser (Department of Health and Exercise Science, Colorado State University).[1]

Take Home Message

While lower extremity joint angles and ranges of motion were unchanged between the Upright Cycling Position (UCP) and Recumbent Cycling Position (RCP) at low levels of effort, many attributes relative to muscle activity were. Most notable were the increased use of the Soleus (SOL) and Gastrocnemius (GAS) in the RCP and the increased use of the Gluteus Maximus (GMX) in the UCP (especially at higher levels of effort). Also associated with effort level was differential change in the Tibialis Anterior (TA) and GAS compared to the more uniform increases of the other muscles examined. Subtle differences exist between sexes, with the greatest effect within the Rectus Femoris (RF) where men have increased activity in the RCP. These differences should be considered when choosing between the two cycling positions for rehabilitation and/or training and may explain some of the early differences in performance/comfort when switching from one position to the other. However, due to the limited magnitude of the differences, adapting to one or the other cycling position should occur relatively rapidly.

Introduction

Stationary cycle ergometry is a popular rehabilitation and fitness modality, incorporating a relatively large amount of lower extremity musculature without the impacts incurred during activities such as running and jumping. While the UCP is still the most common, the RCP is not the oddity it once was. The RCP has gained popularity as a low intensity exercise substitute to the UCP for a variety of reasons, to include reduced neck, low back and wrist strain, increased seat contact area beyond the perineal region, and increased stability from the backrest.

Assuming all other variables are equal (hip-to-pedal distance, crank arm length, body configuration, cadence, shoe-pedal interface, and workload), the altered orientation of the limbs relative to gravity and the altered saddle design constitute two mechanical reasons why muscle activity/recruitment may be altered between the RCP and UCP. Orientation relative to gravity will also affect sensory input from vestibular as well as foot pressure receptors, possibly altering task mechanics[1,2]. Altering the muscular contributions to the cycling task may make one position more suitable than another when targeting specific muscles. Altered muscular contributions may also place limits on how long a person can train or the intensity of training from one position to the other. At present, the details necessary to make appropriate decisions regarding cycling position are not available.

The goal of this investigation was to assess the muscle activation differences of the lower extremities between the standard UCP and RCP in both men and women at relatively low levels of power output that are more suitable for rehabilitation as well as extended cycling of the non-competitive cycling population as a means to increase daily physical activity. The general hypotheses to be tested relative to muscle activity were: 1) there would be differences between the RCP and UCP, 2) there would be differences with power level, and 3) there would be differences between men and women. The findings of this research may then be utilized by health care professionals to make more appropriate recommendations for use of the RCP and UCP in fitness programming and serve as a starting point for those interested in using cycling for rehabilitation of injuries to the lower extremities.

Methods

Fifteen healthy men and 15 women with RCP and UCP experience pedaled at 60 rpm and 60, 90 and 120 W in both positions while surface electromyography of the TA, GAS, SOL, vastus medialis obliquus, vastus lateralis, RF, hamstrings, and GMX were sampled simultaneous-

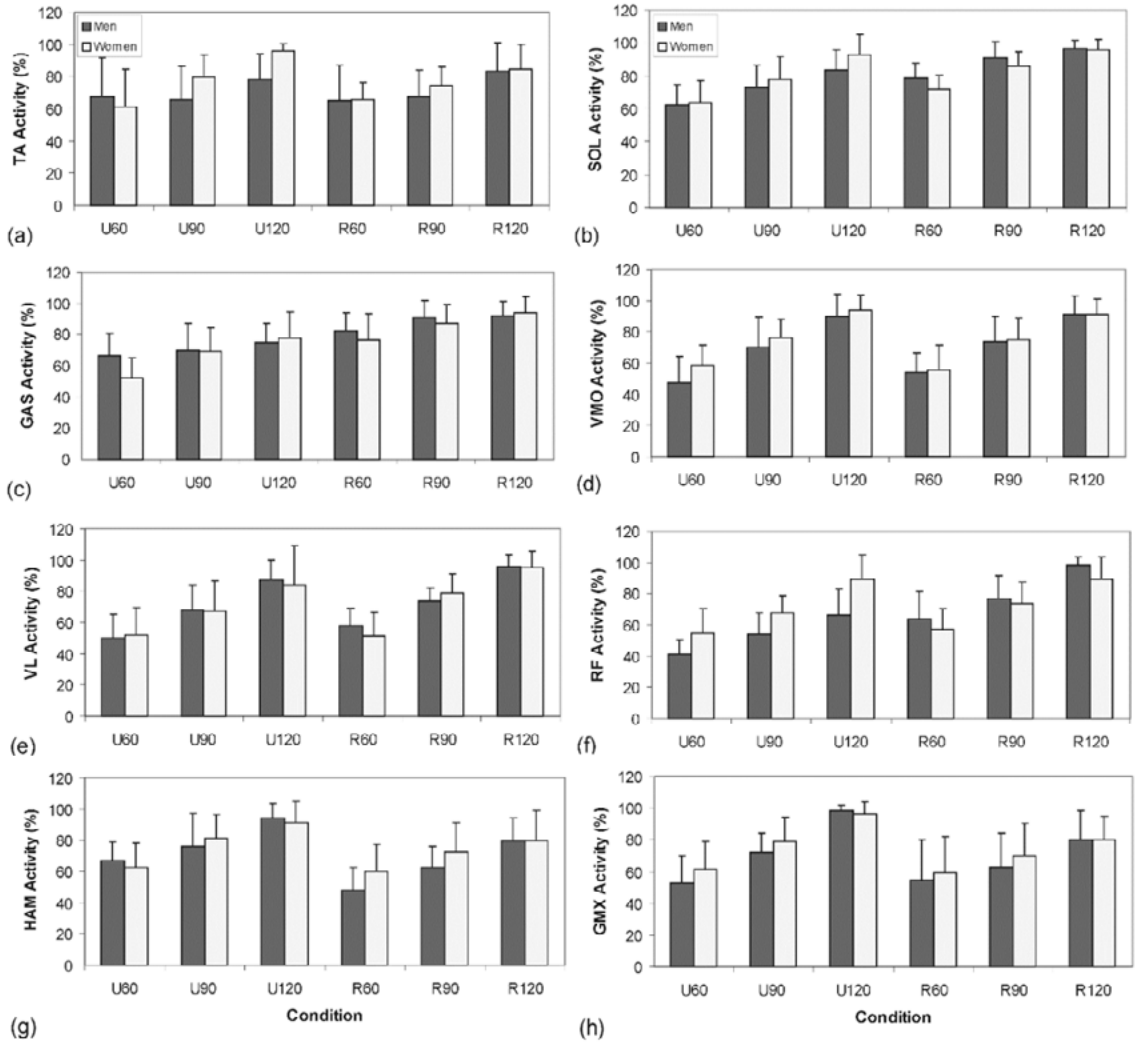

Figure 1. Average normalized muscle activation of the men and women separately for the tibialis anterior (a), soleus (b), gastrocnemius (c), vastus medialis obliquus (d), vastus lateralis (e), rectus femoris (f), hamstrings (g), and gluteus maximus (h) over the entire pedal revolution at each of the power levels 60, 90, and 120 W for the upright (U) and recumbent (R) cycling positions, respectively. Error bars represent the standard deviation.

ly with lower extremity kinematics. Lower extremity kinematics (joint angular positions) were measured via a video based optical capture system with retroreflective markers attached to the skin/clothing of boney landmarks. Statistical significance was assessed at $P < 0.05$ with Bonferroni adjustment for multiple comparisons.

Results

No differences existed in kinematics between sexes or with cycling position and power level. Subtle, qualitative differences were observed in all muscle activations between cycling positions within the pedal revolution. Average muscle activity across a whole pedal revolution is presented in Figure 1.

Activity was significantly increased in the SOL at 60 and 90 W and the GAS at all power levels and decreased in the GMX at 120 W in the RCP compared to the UCP. Non-linear increases existed in TA and GAS activity compared to more uniform increases of the other muscles as power increased regardless of position. Between sexes, the only significant difference was increased RF activity in the RCP of the men.

Conclusions

The goal of this investigation was to examine lower extremity muscle activity in a non-competitive, but recreationally familiar cycling population of men and women at low levels of effort while pedaling in both the UCP and Recumbent Cycling Position (RCP). General hypotheses expecting differences in muscle activity between position, power level, and sex were confirmed though similarities were more common than differences in all comparisons. Furthermore, it was confirmed that differences were due to the altered Hip Orientation Angle (HOA, angle of hip joint to ergometer bottom bracket and the horizontal) and saddle design between positions, not hip-to-pedal distance, Body Configuration Angle (BCA, included angle between rib cage, hip joint, and bottom bracket), or cadence. Also as hypothesized, there were no differences in joint angular kinematics between sexes or conditions.

Acknowledgments

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Relationships between lower-extremity flexibility, asymmetries and the Y-Balance Test

This is a summary of a paper published in 2015 by Drs. Overmoyer and Reiser.[1]

Take Home Message

In a young, healthy population with no specific reasons to be highly asymmetric, the Y-Balance Test may be useful as a screening tool in exposing some lower extremity flexibility asymmetries or bilateral deficits in flexibility. Ankle Dorsiflexion and Hip Flexion are the primary active range of motion measures contributing to overall Y-Balance Test scores. Additionally, side-to-side differences in Y-Balance Test scores may indicate asymmetries in Ankle Plantarflexion. How groups/individuals with higher levels of asymmetries as well as specific differences between men and women need further exploration.

Introduction

Flexibility (aka, range of motion (ROM)) is typically considered a necessary component of sport and fitness[4]. Lower-extremity flexibility, specifically, has been shown to be important for successful performance of sport movements[2] and activities of daily life[3]. Beyond flexibility for function, flexibility is an essential factor for reducing injury risk[6]. Side-to-side symmetry in flexibility is also likely to be an important aspect of performance and injury prevention[5].

The goniometer is arguably the most common and validated tool for measuring joint ROM[6]. Howev-

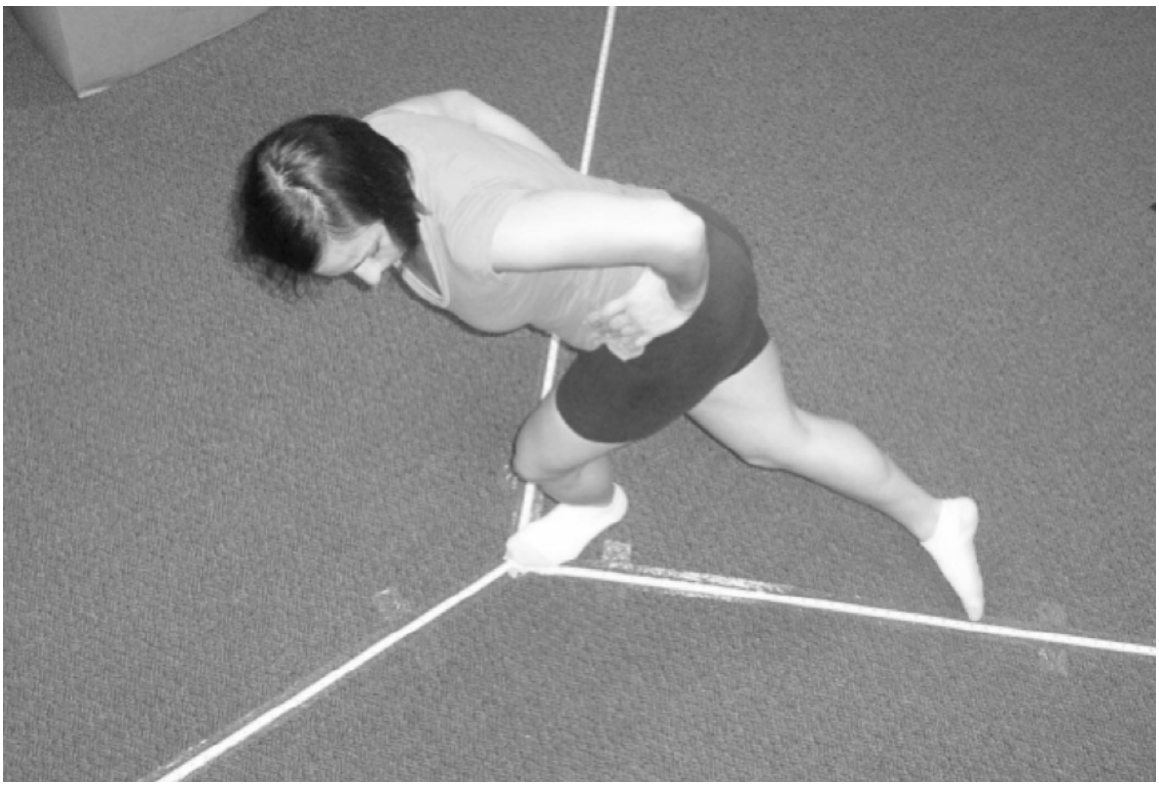

Figure 1. Demonstration of the Y-Balance Test. Right limb PostMed excursion shown here.

er, goniometry can be difficult to master, and time consuming to complete on multiple joints and multiple axes within a joint. This makes comprehensive ROM assessment difficult when screening large groups of athletes. Furthermore, goniometers only measure ROM without simultaneously capturing other potential factors affecting injury or performance. Considering this, alternative screening methods could prove useful under many circumstances. One possible test that fits these criteria is the Y-Balance Test (Figure 1).

The Y-Balance Test is a dynamic balance test requiring multiple reaches (aka, excursions) with one foot in a Y pattern of directions while maintaining balance on the stance leg (Anterior, Posterolateral and Posteromedial). The Y-Test is relatively inexpensive, portable and easy to administer and does not require much specialized training, but still shows good repeatability[3].

The goals of this investigation were to identify the correlations between bilateral flexibility in lower-extremity AROM measurements with bilateral performance in the Y-Test, in absolute terms (i.e., regardless of side to side asymmetry), and explore the relationship between lower-extremity asymmetries in active ROM in comparison to asymmetries in Y-Test performance in a healthy young adult population. It was hypothesized that larger values of bilateral active ROM would relate to larger excursion scores bilaterally on the Y-Test, and higher levels of side-to-side asymmetry in AROM measures would relate to higher asymmetry in Y-Test scores.

Methods

To accomplish the goals of this investigation, a cross-sectional research design was utilized. Healthy, active, pain free subjects with limited previous injury were recruited. A population of healthy adults was used because it has previously been demonstrated that measurable asymmetry exists even in healthy people with no known reasons for being asymmetric[5,8]. During a single visit lasting approximately 2 hours, subjects performed in order the Y-Balance Test (as described by Plisky et al.[8]), a battery of nine active ROM measures, to include hip flexion, extension, abduction, adduction, internal rotation, external rotation, and ankle plantarflexion, dorsiflexion with knee extended (0°), and dorsiflexion with knee flexed (90°) (as described by Norkin & White[8]), and four functional movements after adequate warm-up and practice. The relationships between ground reaction force asymmetries during the functional movements (standing, bodyweight squats, counter-movement jumps, and single-leg drop landings) and the Y-Balance Test are presented elsewhere[7]. Approximately half of the subjects returned for a second visit to repeat the measures.

To test the proposed hypotheses, relationships between measures were assessed through correlations. Specifically, average bilateral active ROM measurements were correlated to average bilateral Y-Balance Test scores and Y-Balance Test excursion direction asymmetries were correlated to active ROM asymmetries. Intra-class correlations were used to assess the repeatability of measures within those that returned for the repeat visit.

Results

Twenty (9 men, 11 women) healthy, active young adults (mean ± SD: age=21.9 ± 2.6 years; height=171 ± 8.8 cm; mass=67.2 ± 1.9 kg) voluntarily participated. Significant correlations ($p<0.05$) existed between bilateral average active ROM measures and bilateral average Y-Balance Test scores at the ankle and hip. Specifically, Ankle Dorsiflexion active ROM at 0° knee flexion significantly correlated with Anterior, Posterolateral, and Composite directional scores of the Y-Balance test (r=0.497-0.736). Significant correlations in Ankle Dorsiflexion active ROM at 90° knee flexion also existed with Anterior, Posterolateral, Posteromedial, and Composite directional scores (r=0.472-0.795). Hip Flexion active ROM was significantly correlated with Posterolateral, Posteromedial, and Composite directional scores (r=0.457-0.583). Significant correlations between asymmetries in active ROM and asymmetries in the Y-Balance Test existed only in Ankle Plantarflexion with Anterior, Posterolateral, and Composite directional scores of the Y-Balance Test (r=0.520-0.636).

Conclusions

Overall, our Y-Balance Test scores were highly comparable to other studies as previously discussed in Overmoyer & Reiser[7] with Y-Balance Test asymmetries demonstrating good day-to-day repeatability as was expected[8]. Bilateral averages for AROM measures were within expected ranges of healthy active adults [5,6]. Small

levels of asymmetries existed within this population during active ROM measurements, which is consistent with other studies[4] as well as when performing the Y-Balance Test[8]. The expression of active ROM also showed good repeatability from day-to-day in most cases as expected[6]. However, although active ROM asymmetries were frequently highly repeatable they exhibited low repeatability in some measures of some individuals. This day-to-day variability does not preclude the possibility that on any given day, active ROM asymmetries could still be a risk factor or associated with other measures. Furthermore, the observed small differences in anatomical leg length do not appear to play an important role in any of the observed asymmetries. Therefore, the results are appropriate for addressing the proposed goals which sought to explore how bilateral average active ROM measures in these joint motions related to bilateral average Y-Balance Test excursions as well as the relationships between asymmetries within lower extremity active ROM and asymmetries in Y-Balance Test performance in a healthy, active population.

Acknowledgments

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