Welcome students, faculty and friends!

The Center for Biomechanical Engineering Research (CBER) is pleased to host the 15th annual Biomechanics Research Symposium. Since 2004, it has been a tradition for our biomechanics community to get together and celebrate the outstanding and various biomechanical research projects at the University of Delaware (UD). Throughout the day, poster and podium presentations will be led by UD student researchers with awards given to the best presentations.

We are also excited to have Dr. Jean Jiang, the Ashbel Smith Professor from UT Health Science Center at San Antonio, who will give a keynote lecture entitled "Hemichannels in mechanotransduction and cancer bone metastasis, a journey from basic research to potential therapeutic application". Dr. Jiang has a highly successful research portfolio spanning from eye, bone, to cancer with both basic and translational perspectives. Her research highlights the importance of interdisciplinary collaboration, which is also the goal of CBER and the motivation of this research symposium.

Thank each of you for contributing to this year’s research symposium. I would especially like to acknowledge the time and effort put in by the Organizing and Student Committees and the support from the Mechanical Engineering Department and Delaware Rehabilitation Institute.

Enjoy the symposium.

Liyun Wang
Professor, Center for Biomechanical Engineering Research Director

Resources for poster printing was provided by the Delaware Rehabilitation Institute/ DRI, Thomas Buchanan, Director.

2018 CBER RESEARCH SYMPOSIUM

ACKNOWLEDGEMENTS

ORGANIZING COMMITTEE

Liyun Wang
X. Lucas Lu
Elaine Nelson

STUDENT COMMITTEE MEMBERS

Jamie Benson
Elahe Ganji
Corey Koller
Connor Leek
Kelsey Neal
Luke Nigro
Nicole Ray
Shubo Wang
Jack Williams
Keynote Lecture

“Hemichannels in mechanotransduction and cancer bone metastasis, a journey from basic research to potential therapeutic application”

Jean X. Jiang, Ph.D.

The Ashbel Smith Professor, Department of Biochemistry and Structural Biology, University of Texas Health Science Center, San Antonio

Mechanosensitive osteocytes form hemichannels through transmembrane proteins such as the connexin 43 (Cx43). Integrins are also known mechanical sensors in many cell types, including osteocytes. We showed that the activation of hemichannels in osteocytes and functions of Cx43-hemichannels are regulated not only by mechanical stimulation, but also by α5 integrin. We further demonstrated that, upon mechanical activation, Cx43-hemichannels release anabolic factors that promote bone formation. Establishing the role(s) that α5 integrin plays in the regulation of hemichannel activities reveals a major mechanism for osteocyte signaling in response to mechanical stress. Moreover, we discovered that activation of Cx43 hemichannels by either mechanical stimulation or chemical reagents in osteocytes suppresses breast cancer migration, growth, and metastasis. The skeleton is the most preferred site for breast cancer metastasis and bone metastasis occurs in 70-80% of patients with advanced breast cancer. We recently developed a new biological reagent that can bind and activate the osteocytic Cx43 hemichannels both in vitro and in vivo. This reagent was shown to suppress human breast cancer bone metastasis, which could be further developed to as a potential new therapy in the treatment of cancer metastasis to bone.

BRIEF BIOGRAPHY

Dr. Jiang obtained her Ph.D. from the State University of New York at Stony Brook in 1991. Following her postdoctoral training at Harvard Medical School (1991-1995), Dr. Jiang became an instructor at Harvard Medical School (1995-1997) and joined the faculty at UT Health Science Center at San Antonio in 1997. Dr. Jiang is currently the Ashbel Smith Professor of Biochemistry and Structural Biology, and Associate Director of the Biomedical Engineering Joint Program. Dr. Jiang’s research focuses on connexin-forming gap junctions and hemichannels in lens, bone and cancer, mechanotransduction, and development of potential therapeutics for cancer and neurological diseases. Her lab has developed both cell-based and in vivo animal models and specific antibodies. Her research has been funded continuously by National Institutes of Health (NIH), Welch Foundation, and other funding agencies. She is the recipient of 2016 Cancer Therapeutic Research Center Discovery of the Year Award, 2017 Master Research Award for Distinguished Researcher and 2018 Presidential Distinguished Senior Research Award. Dr. Jiang has published 120 papers and 5 patents including publications in Proceedings in National Academy of Science, Developmental Cell, Oncogene, Journal of Biological Chemistry, Journal of Cell Science, Molecular Cell Biology, etc. Her studies are highly cited with an h-index of 44. Dr. Jiang has also served as an associate editor or board member for multiple journals including the Journal of Biological Chemistry, Matrix Biology and BMC Cell Biology. She has served in many research review and advisory panels, including NIH, NSF, NSFC, VA, American Heart Association, and American Foundation for Aging Research, UK Wellcome Trust, etc.
## Schedule of the Day

<table>
<thead>
<tr>
<th>TIME</th>
<th>WHAT</th>
<th>WHERE</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:30</td>
<td>BREAKFAST &amp; POSTER SET-UP</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>9:00</td>
<td>WELCOME &amp; INTRODUCTORY REMARKS</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>9:05</td>
<td>KEYNOTE LECTURE: DR. JEAN JIANG</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>10:20</td>
<td>BREAK</td>
<td></td>
</tr>
<tr>
<td>10:35</td>
<td>PODIUM SESSION 1</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>11:35</td>
<td>LUNCH</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>12:00</td>
<td>POSTER SESSION 1 (ODD #S)</td>
<td>STAR CAMPUS- MAIN CONCOURSE</td>
</tr>
<tr>
<td>1:00</td>
<td>POSTER SESSION 2 (EVEN #S)</td>
<td>STAR CAMPUS- MAIN CONCOURSE</td>
</tr>
<tr>
<td>2:00</td>
<td>BREAK</td>
<td></td>
</tr>
<tr>
<td>2:15</td>
<td>PODIUM SESSION 2</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>3:15</td>
<td>ANNOUNCING THE VINCE BARO UNDERGRADUATE RESEARCH Awardees</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>3:30</td>
<td>AWARDS SESSION</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>4:00</td>
<td>ADJOURN</td>
<td></td>
</tr>
</tbody>
</table>
# Podium Presentations

## Session 1:

<table>
<thead>
<tr>
<th>Podium #</th>
<th>Title</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>P10 DEFICIENCY OF PERICELLULAR PERLECAN AFFECTS LOADING-INDUCED INTRACELLULAR SIGNALING PATHWAYS</td>
<td>Shaopeng Pei</td>
</tr>
<tr>
<td>2</td>
<td>P10 FROM FRENCH PARADOX TO OSTEOARTHRITIS TREATMENT: HIERARCHICAL CHONDRO-PROTECTIVE ACTIONS OF RESVERATROL</td>
<td>Yilu Zhou</td>
</tr>
<tr>
<td>3</td>
<td>P11 DREADDS AS A NOVEL TOOL FOR SYNTHETIC CONTROL OF CALCIUM ACTIVATION IN CHONDROCYTES</td>
<td>Ryan McDonough</td>
</tr>
<tr>
<td>4</td>
<td>P11 IN VIVO HUMAN INTERVERTEBRAL DISC STRAIN AND ITS DEGENERATIVE CHANGE</td>
<td>John M. Peloquin</td>
</tr>
<tr>
<td>5</td>
<td>P12 ENGINEERING FUNCTIONAL VOCAL FOLD EPITHELIUM USING HYALURONIC ACID-BASED HYDROGELS</td>
<td>Anitha Ravikrishnan</td>
</tr>
</tbody>
</table>

## Session 2:

<table>
<thead>
<tr>
<th>Podium #</th>
<th>Title</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>P14 GENERATING FORWARD PROPULSION DURING USER-DRIVEN AND FIXED SPEED TREADMILL WALKING</td>
<td>Nicole Ray</td>
</tr>
<tr>
<td>2</td>
<td>P14 THE ASSOCIATION OF MODERATE-TO-VIGOROUS PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR WITH INCIDENT FUNCTIONAL LIMITATION IN KNEE OSTEOARTHRITIS</td>
<td>Hiral Master</td>
</tr>
<tr>
<td>3</td>
<td>P15 COMPARISON OF KNEE BIOCHEMICAL VARIABLES IN INVOLVED AND UNINVOLVED KNEES 6 MONTHS POST ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION (ACLR)</td>
<td>Kelsey Neal</td>
</tr>
<tr>
<td>4</td>
<td>P15 FREQUENCY OF PATHOLOGY ON DIAGNOSTIC ULTRASOUND AND IMPLICATIONS FOR TREATMENT IN INDIVIDUALS WITH INSERTIONAL ACHILLES TENDINOPATHY</td>
<td>Jennifer A. Zellers</td>
</tr>
<tr>
<td>5</td>
<td>P16 MODEL-BASED ESTIMATION OF INDIVIDUAL MUSCLE FORCE FROM INDIRECT MEASUREMENTS OF MUSCLE ACTIVITY</td>
<td>Andrea Zonnino</td>
</tr>
</tbody>
</table>

Denotes Podium #
POSTER PRESENTATIONS

Cell Tissue Biomechanics

**Bone**

P.18 FIBROBLAST GROWTH FACTOR 9 AND THE SIZE OF THE DELTOID TUBEROSITY (COI)

Connor Leek

P.18 EXPRESSION PATTERN OF THE MECHANORESPONSIVE ION CHANNEL PIEZO2 DURING SKELETAL GROWTH AND OSTEOARTHRITIS

Jerahme R. Martinez

P.19 NOVEL SYNTHETIC PEPTIDE, CK2.3, INCREASED LUMBAR SPINE BONE MINERAL DENSITY, ENHANCED FEMORAL SHAFT STIFFNESS, AND INHIBITED OSTEOCLASTOGENESIS IN VIVO

John Nguyen

P.19 HEPARIN TREATMENT RESCUED ALTERED OSTEOCLASTOGENESIS AND OSTEOBLASTOGENESIS IN PROGENITOR CELLS FROM PERLECAN DEFICIENT BONE MARROW

Ashutosh Parajuli

P.20 THE MICROSTRUCTURE OF OSTEOCYTIC LACUNAR-CANALICULAR SYSTEM VARIES WITH AGE AND BONE MINERAL DENSITY ON OSTEOPOROTIC AND OSTEOARTHRITIC PATIENTS

Victor Yuan Gao

P.20 EFFECTS OF PHYSICAL ACTIVITY ON BREAST CANCER BONE METASTASIS

S. Wang

P.21 DECREASED BMP2 MINERALIZATION IN PRIMARY HUMAN OSTEOBLASTS ISOLATED FROM OSTEOPOROTIC PATIENTS

Hilary Weidner

**Cartilage & OA**

P.23 THE EFFECTS OF CONTACT STRESS AND ARTICULATION AMPLITUDE ON FLUID LOAD SUPPORT IN ARTICULAR CARTILAGE

Jamie M. Benson

P.23 ZOLEDRONIC ACID DECREASES CHONDROCYTE VIABILITY, PROLIFERATION, MOTILITY, AND CYTOSKELETAL REMODELING IN VITRO

Michael David

P.24 MECHANICAL INJURY ALTERS TRIBOLOGICAL REHYDRATION AND LUBRICATION IN BOVINE OSTEOCHONDRAL EXPLANTS

Margot S. Farnham

P.24 HOW ACTIVITY FREQUENCY GOVERS CARTILAGE FUNCTION AND ITS IMPLICATIONS FOR JOINT HEALTH

Brian T. Graham

P.25 CHONDRO-PROTECTIVE MECHANISM OF STATIN

Mengxi Lv

P.25 THE ROLE OF TRANSIENT RECEPTOR POTENTIAL VANILLOID 4 IN OSTEOARTHRITIS

Nicholas Trompeter

P.26 QUANTIFYING SOLUTE DIFFUSIVITY IN HUMAN OSTEOARTHRITIC CARTILAGE VIA CORRELATION SPECTROSCOPY

Alison Wright

P.26 EXTRACELLULAR MATRIX SURFACE STIFFNESS REGULATES TRPV4 CHANNEL FUNCTION IN CHONDROCYTES

Mallory Griffin
CONTENTS

Spine & Others

P.28 MODELING BLOOD RHEOLOGY ACROSS SPECIES
Jeffrey S. Horner

P.28 IMMEDIATE EFFECTS OF PHOTOBIOMODULATION THERAPY ON ACHILLES TENDON STRUCTURAL AND VISCOELASTIC PROPERTIES
Patrick Corrigan

Clinical Biomechanics

Design & Innovation

P.30 SMARTBOOT 2.0
Sheridan Parker

P.30 PERSONALIZED PASSIVE-DYNAMIC ANKLE-FOOT ORTHOSES BENDING STIFFNESS IMPROVES PEAK PLANTAR FLEXION MOMENT FOR INDIVIDUALS POST-STROKE
Corey Koller

Gait & OA

P.32 ASSOCIATION OF CLINICAL AND FUNCTIONAL OUTCOMES WITH RISK OF FALL IN KNEE OSTEARTHRITIS PATIENTS
Moiyad Aljehani

P.32 PRELIMINARY FINDINGS OF A NOVEL PHYSICAL THERAPIST ADMINISTERED PHYSICAL ACTIVITY INTERVENTION AFTER TOTAL KNEE REPLACEMENT
Meredith Christiansen

P.33 COORDINATION OF BALANCE MECHANISMS DURING WALKING
Tyler Fettrow

P.33 SEX AND MECHANISM OF INJURY (MOI) INFLUENCE KNEE MECHANICS AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION (ACLR)
Naoaki Ito

P.34 CONTRIBUTION TO FORWARD PROPULSION WITH INDUCED ASYMMETRIC GAIT AND USER-DRIVEN TREADMILL CONTROL
Kelley M. Kempski

P.34 PROXIMAL SHANK KINEMATICS IN PROSTHETIC GAIT
Rosa Kolbeinsdottir

P.35 THE RELATION OF CUMULATIVE LOAD TO WORSENING KNEE CARTILAGE DAMAGE OVER TWO YEARS: THE MOST STUDY
Mathews D

P.35 BALANCE RESPONSES TO VISUAL PERTURBATIONS DURING LOCOMOTION
Hendrik Reimann

P.36 DYNAMIC STABILITY DURING WALKING IN CHILDREN WITH AND WITHOUT CEREBRAL PALSY: PILOT STUDY
James B. Tracy

P.36 MINIMUM-INTERLIMB DIFFERENCE OF TRICOMPARTMENT KNEE CARTILAGE T2 VALUES IN HEALTHY INDIVIDUALS
Jack R. Williams
Neuromuscular Modeling & Assessments

P.38 THE NEURAL CORRELATES OF MOTOR ADAPTATION TO DYNAMIC PERTURBATIONS
Andria J. Farrens

P.38 THE EFFECTS OF FALL-RECOVERY TRAINING ON SINGLE- AND MULTIPLE-STEPPING THRESHOLDS IN INDIVIDUALS WITH CHRONIC STROKE
Jamie Pigman

P.39 IMPAIRED QUADRICEPS FUNCTION MAY NOT BE CAPTURED BY STANDARD CLINICAL MEASURES IN PATELLAR TENDINOPATHY
Andrew L. Sprague

P.39 INCORPORATING HIERARCHAL STRUCTURE WITHIN HYDROGEL BIOMATERIALS USING MULTIFUNCTIONAL COLLAGEN MIMETIC PEPTIDES
Eden M. Ford
1 DEFICIENCY OF PERICELLULAR PERLECAN AFFECTS LOADING-INDUCED INTRACELLULAR SIGNALING PATHWAYS

Shaopeng Pei¹, Sucharitha Parthasarathy¹, Ashutosh Parajuli¹, Shuo Wei¹, X. Lucas Lu¹, M. Cindy Farach-Carson², Catherine B. Kim-Safran¹, Liyun Wang¹

¹University of Delaware, Newark, DE

Introduction: Perlecan, a large linear proteoglycan encoded by the HSPG2 gene, was discovered to be present in the pericellular matrix around osteocytes in the lacunar-canalicular pore system. It is hypothesized to serve as a critical component of the mechanosensing apparatus, which interact with fluid flow in the LCS and allow osteocytes to sense and respond to mechanical signals. Our previous work has shown that perlecan deficiency reduced in vivo bone formation in response to anabolic mechanical loading.

Methods: Adult male mice (19 weeks, n = 4-10 mice/group) with either normal (wild type, WT) or deficient (hypomorphic, Hypo) perlecan expression undergone 1 day or 7 days unilateral tibial loading (peak 8.5N), while the right tibia as non-loaded control. RNA was collected from both tibiae 24 hrs post loading for RNA sequencing and RT-qPCR. Differentially expressed (D.E.) genes, and KEGG enriched pathways were obtained by comparing the loaded vs. non-loaded tibiae, Hypo vs. WT, and 1-day vs. 7-day loading conditions. Pearson’s correlation coefficient was obtained for each D.E. gene by correlating its fold change pattern against that of HSPG2 as shown in all groups comparisons.

Results & discussion: (1) Mechanical loading activates “outside-in” signaling pathways in the whole bone samples. Our data demonstrated strong molecular effects of mechanical loading on ECM-receptor interaction pathway, focal adhesion pathway, and PI3K-Akt signaling pathway in both WT and Hypo animals, regardless of the status of perlecan. These pathways have been essential for the “outside-in” mechanotransduction process. (2) Diminished mechano-transduction sensitivity in perlecan-deficient Hypo mice. (3) The novel Pearson’s correlation analysis based on the fold changes helps us identify potential binding targets of perlecan such as col6, Cacna1c and wnt5A.

2 FROM FRENCH PARADOX TO OSTEOARTHRITIS TREATMENT: HIERARCHICAL CHONDRO-PROTECTIVE ACTIONS OF RESVERATROL

Yilu Zhou, Tiange Zhang, Mengxi Lv, Tong Li, Earl M. Bampo, Megan E. Hoerner, Mary P. Watson, X. Lucas Lu

University of Delaware, Newark, DE

Introduction: Resveratrol, a major anti-oxidant in red grapes, has been extensively studied due to its health benefits originated from the “French Paradox” phenomenon. Recent studies found that resveratrol can inhibit the OA progression in knee joints, while the mechanisms are barely understood. Here, resveratrol’s chondro-protective effects and its interactions with collagen molecules are investigated.

Methods: Cartilage explants were harvested from calf knee joints. Resveratrol was added together with inflammatory cytokine IL-1β. Loss of GAG and collagen contents, SEM images, expression of catabolic genes was evaluated. Resveratrol’s direct action on collagen was also quantified: resveratrol pretreated decellularized cartilage explants were used to track the collagen loss over degeneration period. Molecular dynamics simulation was performed to investigate the interaction between the collagen and resveratrol molecule. Results: Resveratrol effectively inhibited the IL-1β-induced GAG and collagen loss, and suppressed the IL-1β promoted expression of ADAMTS-4, -5, MMP-1, -3, -9 in chondrocytes. IL-1β+resveratrol treated explant has much thicker and more bundled collagen fibrils than the IL-1β alone group. Pre-treating decellularized explants with resveratrol significantly inhibited the collagenase induced collagen digestion, indicating the direct action of resveratrol on collagen. Molecular dynamics simulation demonstrated the resveratrol molecule acting as a linker among collagen fibrils. Discussion: Resveratrol can protect chondrocytes from the inflammatory attack. Molecular dynamics simulation demonstrated that the resveratrol molecule facilitates binding among collagen molecules. Therefore, resveratrol could directly protect collagen network, which is particularly critical to battle the chronic and middle stages of osteoarthritis, where sparse surviving chondrocytes are of the least help.
**DREADDS AS A NOVEL TOOL FOR SYNTHETIC CONTROL OF CALCIUM ACTIVATION IN CHONDROCYTES**

*Ryan McDonough¹, Janty Shoga², Christopher Price¹*

¹Biomedical Engineering, University of Delaware, ²Biomechanics and Movement Science, University of Delaware, Newark, DE

Calcium is a critical second messenger involved in chondrocyte mechanotransduction. Several distinct calcium signaling mechanisms implicated in chondrocyte mechanotransduction have been identified using interrogative techniques, such as mechanical perturbation or application of soluble factors. These approaches can lack specificity in the mechanisms by which they initiate calcium signaling; mechanical forces can target several mechanosensitive components and soluble factors can have off-target interactions. Synthetic tools allowing for the precise, well-controlled regulation of calcium-specific signaling may better assist in isolating the role of intracellular calcium ([Ca²⁺]i) in chondrocyte homeostasis and disease.

Recent developments in molecular biology have generated engineered G-protein-coupled receptors that are solely activated by clozapine n-oxide (CNO), a pharmacologically inert compound that only activates these receptors. These receptors, termed DREADDs (Designer Receptor Exclusively Activated by Designer Drugs), include one member, hM3Dq, that can regulate calcium activation through control of the PLCβ-IP3-ER pathway. Here, hM3Dq-transfected ATDC5 cells were exposed to increasing CNO concentrations (100nM-1µM), GSK101, or 50% hypo-osmotic shock, the latter two of which are known to cause upregulation of [Ca²⁺]i entry. A custom MATLAB program was developed to analyze the calcium response and temporal kinetics via Fluo-8 AM fluorescence. CNO administration results in a coordinated, dose-dependent, transient calcium response in hM3Dq-transfected cells that does not negatively impact cell health. CNO-mediated calcium signaling duration was similar hypo-osmotic shock, but significantly faster than GSK101 signaling. Following activation, hM3Dq becomes inactivated and requires a 4-hour refractory period to regain its coordinated signaling capability. hM3Dq inactivation does not inhibit alternative calcium activation mechanisms via GSK101 or hypo-osmotic shock. This study established the successful use of hM3Dq for safe, targeted, and well-controlled activation of calcium signaling in chondrocyte biology, cartilage pathology, and improving cartilage tissue engineering.

**IN VIVO HUMAN INTERVERTEBRAL DISC STRAIN AND ITS DEGENERATIVE CHANGES**

*John M. Peloquin, Kyle D. Meadows, Edward J. Vresilovic, Dawn M. Elliott*

University of Delaware, Newark DE

Disc mechanics have important roles in the pathogenesis and symptoms of disc degeneration, but measurement of disc mechanics in living humans is a challenge. To fill this critical knowledge gap, our group extended our previous work, which used MRI to measure strain between loading states in cadaver discs, to measure disc strain in vivo associated with three loading scenarios: AM–PM (cumulative loading over one work day), spinal flexion, and spinal extension. Our objective was to determine if strain in these loading states varied with disc health (degeneration). For each scenario, the reference image was acquired at ~ 9 AM with the subject supine in the MRI scanner. The deformed image was acquired supine at ~ 4 pm for AM–PM loading (7 subjects) or immediately after the reference, with postural change effected using pillows, for flexion (3 subjects) and extension (4 subjects). Reference-to-deformed strain was calculated using 3D image registration. The accuracy of the image registration results was confirmed against manual measurements. Axial strain varied significantly by region for flexion and extension, but not for AM–PM. Discs with healthy overall morphology trended (p = 0.07) to have greater AM–PM axial compression than degenerate discs. Discs with high central water content (measured by MRI T2, indicating disc health) had more axial compression in flexion and more axial tension in extension (p < 0.05), regardless of region. These results support the hypothesis that degeneration is associated with altered disc mechanics in living humans. This work is the first successful translation of 3D disc strain techniques to in vivo imaging. In vivo 3D disc strain measurement opens many possibilities for study of degenerative etiology and treatment outcomes.
ENGINEERING FUNCTIONAL VOCAL FOLD EPITHELIUM USING HYALURONIC ACID-BASED HYDROGELS

Anitha Ravikrishnan, Eric Fowler and Xinqiao Jia

Department of Materials Science and Engineering, University of Delaware, Newark, DE

The human vocal fold is a laminated structure, consisting of stratified squamous epithelium, lamina propria and vocalis muscle. Vocal fold is highly mechanically active, and can be easily damaged by mechanical factors and chemical irritants. Current treatment options for vocal fold disorders are limited, and the development of new procedures has been slow owing to the inaccessibility of the tissue, its susceptibility to damage, and the anatomical differences of animal models from the human tissue. Our long-term goal is to engineer a reliable, physiologically relevant in vitro tissue model that can be used to investigate vocal fold development, health, and disease. We have successfully isolated and characterized primary porcine vocal fold epithelial cells (PVFEs) and fibroblasts (PVFFs) as the vocal fold structure and the wound healing response of pigs are similar to that of humans. We have also synthesized hyaluronic acid (HA)-derived synthetic matrices of varying stiffness and displaying covalently conjugated peptide signals derived from the basement membrane and the connective tissue, the lamina propria. Our results show that the proliferation, stratification and differentiation of PVFEs are strongly dependent the matrix properties. PVFEs readily attach and proliferate on soft (35 Pa) or stiff (2000 Pa) gels in presence of RGD (from fibronectin) or AG73 (from laminin 111) peptides. However, these cells stratify only on the stiffer hydrogel in presence of both AG73 and RGD peptide signals, indicating both topographical and biomechanical cues serve as important regulator of epithelial cell fate. Incorporation of metalloproteinase degradable crosslinks in the bulk of the HA matrices promotes the spreading, migration and proliferation of cells of mesenchymal origin. Coculture of PVFEs and PVFFs in tissue-mimetic HA matrices under dynamic vibratory conditions will lead to the development of physiologically relevant vocal fold tissue models.
PODIUM PRESENTATIONS // SESSION 2

PODIUM PRESENTATIONS

Session 2
GENERATING FORWARD PROPULSION DURING USER-DRIVEN AND FIXED SPEED TREADMILL WALKING

Nicole Ray and Jill Higginson

University of Delaware, Newark, DE

Nearly 800,000 Americans have a stroke annually, and many do not improve their walking function after rehabilitation. Therefore, we designed a user-driven treadmill (UDTM) controller to match the user’s walking speed in real time. The objective of this study was to determine the contribution of sagittal plane joint moments to forward propulsion during UDTM and fixed speed treadmill (FSTM) walking at matched speeds.

Eleven healthy adults (23±5 years, 1.69±0.106 m, 66.2±10.7 kg, 3M-8F) walked for one-minute on an instrumented treadmill in its UDTM mode and another minute in its FSTM mode at the average speed from the UDTM trial. An induced acceleration analysis was performed to determine the contribution of each joint moment to the acceleration of the body’s center of mass (CoM), and the results were compared using a one-way ANOVA (α=0.05).

The contributions of trailing limb sagittal plane joint moments to the acceleration of the body’s CoM differed during the early (40-50%) and late (50-60%) 2nd double limb support (DLS) intervals of the gait cycle (p<0.05). The ankle plantarflexion moment contributed more to forward propulsion in early 2nd DLS during UDTM walking and more in late 2nd DLS during FSTM walking. This suggests UDTM control may enable more direct delivery of the ankle moment to forward propulsion.

The knee flexion moment slows the CoM in early 2nd DLS during UDTM walking and accelerates the CoM forward in late 2nd DLS during FSTM. Since the ankle moment contributes more to forward propulsion in early 2nd DLS for UDTM walking, the braking knee moment may be used to maintain a steady-state walking speed. These differences suggest UDTM control algorithms may be designed to manipulate the timing and magnitude of joint moments and optimize forward propulsion.

THE ASSOCIATION OF MODERATE-TO-VIGOROUS PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR WITH INCIDENTAL FUNCTIONAL LIMITATION IN KNEE OSTEOARTHRITIS

Hiral Master, Louise Thoma, Meredith Christensen, Dana Mathews, Daniel K. White

University of Delaware, Newark DE

Engaging in an adequate levels of moderate-to-vigorous physical activity (MVPA) reduces the risk of functional limitation in knee osteoarthritis (OA). Sedentary behavior (SED) is common in those with either high or low levels of MVPA and is linked to poor health outcomes in knee OA. However, it remains unclear whether being sedentary regardless of MVPA level increases one’s risk of developing functional limitation in knee OA. The purpose of this study was to examine the association of MVPA and SED with incident functional limitation four years later in knee OA. We used publically available data from the Osteoarthritis Initiative. Our primary exposures (time spent in MVPA and SED) were collected at the baseline using an accelerometer. We classified people as being 1) “Active-Exercisers” (≥1 MVPA bouts and lowest SED tertile, i.e., less sedentary), 2) “Sedentary-Exercisers” (≥1 MVPA bouts and top two SED tertiles, i.e., more sedentary), 3) “Light-Movers” (No MVPA bout and lowest SED tertile), and 4) “Non-Movers” (No MVPA bout and top two SED tertiles). Our outcome, incident functional limitation, was defined as >12 sec for the five repetition sit-to-stand test (STS) or <1.22 m/sec gait speed during a 20-meter walk four years later. To examine the association of MVPA and SED with incident functional limitation, we calculated risk ratios and 95% confidence intervals [RR (95%CI)] adjusted for potential confounders. We found, compared to “Active-Exercisers”, the risk of incident functional limitation over four years was similar in “Sedentary-Exercisers” but was significantly higher in “Light-Movers” and “Non-Movers.” Thus, being active may potentially offset the functional consequences of SED. Effective clinical interventions to improve MVPA are needed for knee OA.
COMPARISON OF KNEE BIOCHEMICAL VARIABLES IN INVOLVED AND UNINVOLVED KNEES 6 MONTHS POST ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION (ACLR)

Kelsey Neal, Jack Williams, Ashutosh Khandha, Thomas Buchanan

University of Delaware, Newark, DE

About 40% of individuals who undergo ACLR develop knee osteoarthritis (OA) within 8 years of surgery. Quantitative MRI (qMRI) can measure biochemical variables that can help identify early onset OA. Chemical exchange saturation transfer (CEST) is a technique that indirectly estimates glycosaminoglycan (GAG) content in knee cartilage. Low GAG-CEST values in cartilage is an indicator of GAG loss which is indicative of early onset OA. Transverse relaxation (T2) time of cartilage, another biochemical variable measured using qMRI, can also help detect OA post ACLR. High T2 values indicate collagen matrix degradation. As the first step in a longitudinal study, we sought to investigate both GAG-CEST and T2 values at 6 months post-ACLR, in the medial compartment of the involved and uninvolved knees.

16 subjects (8 women, mean age: 21 years) were studied at 6 months post unilateral ACLR. Each subject underwent supine bilateral knee MRI using a GAG-CEST and T2 mapping sequences. For GAG-CEST and T2 measurements, three slices corresponding to the center of the medial compartment were analyzed. Each slice was segmented into six regions of interest (ROIs) including anterior, central, and posterior regions of the femur and the tibia. The mean values GAG-CEST and T2 values for each ROI were compared for involved vs. uninvolved knee using students t-test.

For GAG-CEST, four out of the six ROIs showed lower gag values in the knee, with the central tibial ROI having a statistically significant difference (p = 0.029). T2 values were higher in four out of the six ROIs, none were statistically significant. These preliminary results warrant further investigation of these variables, with both a larger sample size and long-term follow-up.

FREQUENCY OF PATHOLOGY ON DIAGNOSTIC ULTRASOUND AND IMPLICATIONS FOR TREATMENT IN INDIVIDUALS WITH INSERTIONAL ACHILLES TENDINOPATHY

Jennifer A. Zellers, PT, PhD¹, Bradley C. Bley, DO², Ryan T. Pohlig, PhD², Nabeel Hamdan Alghamdi, PT, MSc¹, Karin Grävare Silbernagel, PT, PhD¹

¹University of Delaware, Newark, DE
²Delaware Orthopaedic Specialists, Wilmington, DE

**Background:** Insertional Achilles tendinopathy likely is caused by a variety of underlying conditions, which may partially account for the recalcitrant nature of this condition to treatment. Ultrasound imaging may assist in identifying underlying pathology to improve specificity of treatment. **Objectives:** The purpose of this study was to quantify the presence of underlying Achilles tendon insertional pathology using ultrasound imaging. Secondly, we sought to examine the alignment of treatment strategy to underlying pathology. **Methods:** Individuals with a primary clinical diagnosis of insertional Achilles tendinopathy were included in this study. B-mode ultrasound imaging was used to descriptively and quantitatively describe tendon pathology. Use of diagnostic imaging and treatment modalities in clinical management was measured via participant survey. **Results:** Of the 56 individuals included in this study, 51.8% had a bony defect, 35.7% had intratendinous calcifications, 51.8% had distal tendinosis, 28.6% had midportion tendinosis, 33.9% had bursitis, and none had isolated paratenonitis on their more symptomatic side. Participants reported previously having the following imaging for their Achilles tendon-related condition: 44.6% X-ray, 16.1% MRI, 14.3% ultrasound, and 1.8% CT scan. For treatment, 17.9% of participants reported having received shockwave treatment, 12.5% laser treatment, 10.7% injection, and 3.6% surgery. **Conclusion:** Patients with insertional symptoms present with multiple underlying pathologies which may respond differently to treatment. It may be helpful to differentiate insertional Achilles tendinopathy based on underlying pathology to better understand response to interventional strategies and tailor treatment accordingly.
MODEL-BASED ESTIMATION OF INDIVIDUAL MUSCLE FORCE FROM INDIRECT MEASUREMENTS OF MUSCLE ACTIVITY

Andrea Zonnino, Fabrizio Sergi

University of Delaware, Newark, DE

The estimate of individual muscle force during tasks requiring coordinated muscle co-activation would provide considerable insights on neuromuscular physiology, and enable accurate diagnosis and management of neuromotor disorders. However, direct measurement of individual muscle forces is often not possible in-vivo because it is not ethical to dissect musculo-tendon attachment points and place force sensing elements. Regrettably, this endeavor represents one of the biggest challenges in biomechanics.

A common muscle force estimation technique combines knowledge of the geometry of the limb under analysis, and the measurement of a quantity that is proportional to the muscle force, typically using surface electromyography (sEMG). This approach, however, has two main issues: 1) sEMG can only measure the activity of superficial muscles and 2) sEMG is affected by crosstalk of different muscles. Also, the effect of measurement error on the accuracy of the EMG-to-force estimate is currently unknown.

We have developed a computational framework based on a realistic musculoskeletal model to quantify the accuracy of an isometric calibration procedure used to estimate muscle force from indirect measurements of muscle activity. Our framework accounts for the correlation between measurements of the activity of multiple muscles, for the fact that activity is measured only for a partial set of muscles, and for variability in muscle force generation during a torque-controlled isometric task. Our computational framework is applied to the wrist joint, demonstrating the difficulty in estimating individual wrist muscle force from sEMG measurements because of the effect of multiple finger muscles that, if unmeasured, provide biased estimates for the force of wrist muscles. Our technique is sufficiently general that it can be applied to alternative methods for measuring activity of multiple muscles, such as force myography and elastography.
POSTER PRESENTATIONS // BONE

Cells Tissue Biomechanics

Bone

Denotes Poster #
1. **FIBROBLAST GROWTH FACTOR 9 AND THE SIZE OF THE DELTOID TUBEROSITY (COI)**

Connor Leek, Megan Killian

The deltoid tuberosity (DT) is a bone ridge where the deltoid tendon anchors. Bone ridges like the DT initiate and grow during embryonic development. Loss of protein encoding genes such as Scleraxis and Bmp4 during the embryonic stages of development lead to impaired initiation and decreased size of the DT. Conversely, the DT may be enlarged in fibroblast growth factor 9 (Fgf9) knockout mice. To date, the comparison of DT size has not been quantified. Therefore, this study developed a method to measure DT size in embryos.

Using a whole mount staining technique, we stained cartilage and mineralized bone. We took images of the stained arms using a dissection microscope. From these images, we acquired measurements of the area of the DT and length of humerus mineralization from the most proximal to most distal point. From these measurements we have shown that Fgf9 knockout mice have larger DTs and shorter mineralized humeri when compared to wild type mice. The humeri length proximal and distal to the DT were both smaller. Additionally, cartilage staining was observed along the edge of the DT in Fgf9 knockout mice. Fgf9 knockout mice had less mineralized bone and more cartilage at the DT, which suggests that Fgf9 may play a role in maturation of DT. This study develops a technique to measure the size of the DT and uses this technique to establishes that Fgf9 is necessary to limit the size of the DT.

2. **EXPRESSION PATTERN OF THE MECHANORESPONSIVE ION CHANNEL PIEZO2 DURING SKELETAL GROWTH AND OSTEOARTHRITIS**

¹Jerahme R. Martinez, ¹Ashutosh Parajuli, ²Sucharitha Parthasarathy, ¹Padma P. Srinivasan, ²Catherine B. Safran, ¹Liyun Wang

¹Department of Mechanical Engineering, University of Delaware; ²Department of Biological Sciences, University of Delaware

Piezo2, a recently discovered stretch-activated cation channel, plays an important role in mediating mechano-sensation and proprioception. The widespread expression of piezo2 in mechanosensitive tissues, such as cartilage, suggests a distinct physiological role in mechanotransduction. Mutations to the piezo2 gene have been associated with the human musculoskeletal disorder Gordon syndrome (GS; MIM #1143000), characterized by contractures of the limbs and short stature. The importance of piezo2 for musculoskeletal development and its ability sense mechanical stimuli prompted us to explore piezo2 bone tissue. We hypothesize piezo2 acts a mechanosensor in bone, and plays an important role in maintaining overall skeletal health and bone adaptation. To gain insight into its function we examined piezo2 transcript levels in bone under in vivo mechanical loading, and characterized the protein spatial and temporal expression patterns in healthy and osteoarthritic (OA) bone tissue, via quantitative real-time PCR (QPCR) and immunohistochemistry (IHC), respectively. Peizo2 mRNA levels were elevated in bone tissue in mice subjected to 7 days of axial tibia loading relative to the non-loaded control limbs. We demonstrated piezo2 protein expression coincided with endochondral bone formation in early development, and was found in bone cells (e.g. osteoblasts and osteocytes) of adult bone tissue. In human OA patient samples, IHC analysis revealed abundant piezo2 staining in damaged tissue of the femoral neck. These studies implicate piezo2 as a mechanically responsive gene, whose protein product is distributed in bone tissue in regions where high levels of mechanical load occur, and possible therapeutic target for load-induced damage in musculoskeletal tissues.
NOVEL SYNTHETIC PEPTIDE, CK2.3, INCREASED LUMBAR SPINE BONE MINERAL DENSITY, ENHANCED FEMORAL SHAFT STIFFNESS, AND INHIBITED OSTEOCLASTOGENESIS IN VIVO

John Nguyen, Lora M. Schell, Linda Sequeira, Saurabh Dharmadhikari, Anja Nohe

Osteoporosis is a bone loss disease that would put patients at risk of developing bone fractures especially at the hip and vertebrae. Osteoporosis can alter normal daily activities and reduces quality of life. Osteoporotic patients often live a sedentary lifestyle, thus, further reducing their life quality. Current treatments of osteoporosis can only target either osteoclasts (bone resorption) or osteoblasts (bone formation) to increase bone mass. The study of our laboratory led us to discover a peptide, namely CK2.3, that could enhance bone formation while inhibiting bone resorption. We reported that CK2.3 promoted osteoblast differentiation in vitro and in vivo via ERK activation and inhibited osteoclast differentiation in vitro. However, the underlying mechanism of CK2.3 inhibits osteoclast differentiation remains unclear. The result of this project, for the first time, showed that CK2.3 inhibited osteoclast differentiation in vivo. Furthermore, CK2.3 increased bone mineral density of lumbar spine and increased stiffness of femoral shaft in female 6-month-old mice. In addition, CK2.3 increased activation of ERK and AKT, and the inhibition of ERK and AKT activation reversed the inhibitory effect of CK2.3 on osteoclast differentiation of RAW264.7 cells. These results demonstrated CK2.3 as a promising treatment for osteoporosis and reveal for the first time the inhibition of osteoclastogenesis via activation of ERK and AKT by CK2.3.

HEPARIN TREATMENT RESCUED ALTERED OSTEOCLASTOGENESIS AND OSTEOBLASTOGENESIS IN PROGENITOR CELLS FROM PERLECAN DEFICIENT BONE MARROW

Ashutosh Parajuli, Ping Li, Catherine Kirn-Safran, Liyun Wang,
University of Delaware, Newark, DE

Introduction: Perlecan is a large multifunctional heparin sulfate proteoglycan present in basement membranes and tissue borders. Perlecan deficiency is a risk factor of osteoporosis. Previously, we found i) severe trabecular osteopenia and cortical hypermineralization in perlecan deficient (hypo) mice and ii) upregulated osteoclastogenesis and accelerated mineralization in progenitor cells from the hypo bone-marrow. The purpose of this study was to examine if exogenous treatment with Heparin, a hyper-sulfated glycosaminoglycan (GAG), can rescue the impaired differentiation associated with perlecan deficiency.

Methods: Osteoclastogenesis (OCs): Freshly harvested marrow from long bones was cultured in media supplemented with 25 ng/ml of M-CSF for 2 days. The non-adherent cells were cultured further for 9 days in media containing 25ng/ml of M-CSF and 20ng/ml of RANKL on dentin bone slices. Osteoblastogenesis (OBs): The adherent MSCs were cultured in osteogenic media for 19 days and stained with 2% Alizarin red to quantify mineralization. Treatments and Outcomes: Both OCs and OBs were carried out in 3 different concentration of Heparin: 0 µg/ml, 20 µg/ml and 200 µg/ml. Outcome measures included # of matured (TRAP-positive) OCs and area of resorbed pits and Alizarin red staining intensity.

Results: Significant decreases in both the # of multinucleated-osteoclast and amount of TRAP staining were found in Heparin treated Hypo cultures relative to no-treatment controls, while no effects seen in WT cultures; Similar decline in Alizarin red intensity (calcium deposition) with Heparin treatments was found in both Hypo and WT cultures. Discussion: Our results indicate that addition of Heparin can rescue the adverse effects of perlecan-deficiency on bone progenitor cells, by slowing down mineralization and decreasing osteoclastogenesis. Significance: This result, if translated in vivo, could help develop therapeutics to treat bone impairment/osteoporosis associated with perlecan (HSPG2) deficiency.
**THE MICROSTRUCTURE OF OSTEOCYTIC LACunar-CANALICULAR SYSTEM VARIES WITH AGE AND BONE MINERAL DENSITY ON OSTeoporotic AND OSTeoARTHritic PATIENTS**

_Victor Yuan Gao, Shaopeng Pei, Hilary E. Weidner, Mark Eskander, Anja Nohe, Liyun Wang_

University of Delaware, Newark, DE

Osteocytes play an important role in maintaining bone health, and the osteocytic lacunar-canalicular system (LCS) is the primary site for osteocytes to detect mechanical stimulation and the main conduit for them to obtain nutrients and signal with other cells. The objective of this study was to examine how LCS varies with age and bone material property in osteoarthritic and osteoporotic patients.

Femoral heads from 25 patients undergoing hip hemiarthroplasty were used, including 19 osteoporotic (14 females / 5 males) and 6 osteoarthritic patients (3 females / 3 males) from 51 to 95 years old (mean 73.8±13.1 years). The superolateral cortices were bulk-stained with sodium fluorescein, followed by confocal imaging (to obtain LCS structure) and microCT scanning (to obtain bone mineral density, BMD).

Large variations were found for the cortical bone morphometry and most LCS measures (coefficient of variation: 20%-36%), except for the canalicular number density, which was found to be highly consistent (1 canalculus per 3 μm lacunar perimeter or 8 μm² lacunar surface) regardless of age, sex, and diagnosis of osteoarthritis or osteoporosis.

Consistent with previous finding in murine LCS, this study showed that, despite the dynamic nature of the LCS network, the topological connectivity immediately around osteocytes appeared to be largely stable in adult and aged skeletons, and this connectivity was moderately and positively related to the surrounding matrix mineralization level ($R^2 = 0.30$, $p = 0.005$).

Our data demonstrated close relations and possible interactions between osteocytes and their matrix environment during their long life span in the adult skeleton.

---

**EFFECTS OF PHYSICAL ACTIVITY ON BREAST CANCER BONE METASTASIS**


Bone metastasis is a lethal end-stage of malignancy influencing 60-80% breast cancer patients. Mounting evidence in preclinical and clinical studies shows that physical activity can reduce the risks of breast cancer incidence, metastasis, and recurrence while it can increase the rates of survival, alleviate cancer associated symptoms, and improve quality of life. Recent animal studies showed that mechanical loading of bone suppressed breast cancer growth in murine bone marrow, suggesting that bone could potentially possess a self-defense mechanism activated by physical activities. We studied the effects of bone secretions on breast cancer cell by culturing mouse tibia explant and tibia marrow after administration of 1-day and 7-day tibial compression or 2-week treadmill running. Our results show that loaded-bone conditioned medium inhibit the migration of breast cancer cells in wound healing assay and this antitumoral effects are attributed to small molecules with molecular weights below 3000da. Further investigation shows that the antitumoral factors are likely to be lipid molecules. Our findings are in harmony with recent discoveries that the lipid signaling axis LysoPC/ Autotaxin/LysoPA plays a vital role in bone biology and breast cancer bone metastases.
DECREASED BMP2 MINERALIZATION IN PRIMARY HUMAN OSTEOBLASTS ISOLATED FROM OSTEOPOROTIC PATIENTS

Hilary Weidner, Victor Yuan Gao, Debbie Dibert, Dr. Mark Eskander, Dr. Liyun Wang, and Dr. Anja Nohe

Signaling pathways that are impaired in patients with osteoporosis must be identified in order to develop new treatments for osteoporosis. Osteoporosis is a bone disease that is characterized by low bone density, which ultimately increases the occurrences of fractures or breaks. On a cellular level, there is a balance between bone forming cells (osteoblasts) and bone remodeling cells (osteoclasts). The majority of treatments on the market focus on decreasing osteoclast activity or increasing osteoblast activity. BMP2 is a crucial growth factor in bone development and is known to induce osteoblast differentiation. BMP2 has also been approved for spinal infusion for anterior lumbar interbody fusion in order to promote bone growth and healing. BMP2 has been studied clinically for the treatment of osteoporosis, however long term use of BMP2 was actually shown to increase the risk of fracture, or increase osteoclast activity. Taking this prior knowledge into account human femoral heads were collected from Christiana Care Hospital in Newark, Delaware from patients undergoing hip arthroplasty surgery. The patients were diagnosed with either osteoporosis or osteoarthritis. Cells were extracted from the collected femoral heads and grown. The grown cells were treated with BMP2, and a mineralization assays (Von Kossa) were conducted in order to measure cellular mineralization activity. Our lab has shown that treatment of BMP2 within the osteoporotic population had no effect. This would be the first time, to our knowledge, that extracted human osteoporotic cells had no mineralization response upon BMP2 stimulation. This could indicate that BMP pathway is disrupted in some way in patients diagnosed with osteoporosis.
POSTER PRESENTATIONS

Cells Tissue Biomechanics

Cartilage & OA
THE EFFECTS OF CONTACT STRESS AND ARTICULATION AMPLITUDE ON FLUID LOAD SUPPORT IN ARTICULAR CARTILAGE

Jamie M. Benson¹, Jordyn L. Schrader¹, David L. Burris¹,²

¹Biomedical Engineering, ²Mechanical Engineering, University of Delaware, Newark, DE

Introduction: During mechanical loading of the joint interstitial pressure gradients develop in the cartilage as fluid is forced through the matrix. While the matrix carries a fraction of the load, the fluid pressurization carries a bulk of it. Using the migrating contact (MCA) setup we can induce this fluid load support, which leverages the intermittent bath exposure recovery theory. In this study, we used the MCA to elucidate the fluid load support in relation to varying applied contact stresses and articulation lengths.

Methods: 19 mm diameter full thickness osteochondral plugs were extracted from the femoral condyles of adult bovine stifles, and were tested in the MCA. Explants were tested in static equilibrium and sliding equilibrium with probes of diameter sizes 6.35mm, 4.763mm, 3.969mm, 3.175mm and 2.381mm—across increasing track lengths and constant loads.

Results: The fluid load fraction of the plugs were calculated in response to the increasing probe size and track lengths. Under low contact stresses and high articulation lengths, represented by the fluid load support of the cartilage nears 100%. As the contact stresses increase, there is a reduction in the maximal fluid load support. But when articulation lengths remained low, regardless of contact stresses, the fluid load support diminished.

Conclusions: This study demonstrates that the fluid load support of cartilage is dependent on contact forces and articulation length. Fluid load support decreases with decreased track length and increased contact stresses—impeding its cartilages’ ability to recover fluid passively.


ZOLEDRONIC ACID DECREASES CHONDROCYTE VIABILITY, PROLIFERATION, MOTILITY, AND CYTOSKELETAL REMODELING IN VITRO

Michael David, Brianna Hulbert, Melanie Smith, Sejal Shah, Alexis Merritt, Christopher Price

University of Delaware, Newark, DE

Post-traumatic osteoarthritis (PTOA) is a degenerative joint disease that leads to a rapid loss of articular cartilage and joint function. With limited curative therapies, our team has been investigating Zoledronic Acid (ZA), an FDA-approved bisphosphonate, as a preventative therapeutic. We recently demonstrated that repeated intra-articular ZA preventions cartilage from erosions in a mouse model of PTOA. This prevention appears to be related to ZA’s ability to modulate chondrocyte death and proliferation; processes believed to drive PTOA progression. However, this study was unable to: i) directly demonstrate ZA’s ability to modulate chondrocyte’s death and proliferation independent of other joint processes; ii) directly show ZA’s effect on other chondrocyte processes such as motility, morphology, and cytoskeleton remodeling, which are associated with cell death and proliferation; and iii) uncover dose-dependent effects of ZA. To understand the dose-dependent effect of ZA on chondrocytes, we applied various concentrations of ZA (1 to 1000uM) to chondrocyte-like cells (ATDC5) for 72 hours. We hypothesized that increasing the concentration of ZA would enhance the biphasic effects of ZA on ATDC5 proliferation, death, motility, and morphology in vitro. In this present study, we found that as ZA concentration increases, there was: i) a decrease in ATDC5 proliferation and viability; ii) a drastic change in ATDC5 morphology (more rounded cells) and cytoskeleton remodeling (less F-Actin organization); and iii) less cell migration/motility. Overall, this study confirmed ZA’s ability to directly influence chondrocyte health, proliferation, and morphology. Our future in vitro and in situ (cartilage explant) work aim to investigate ZA’s effect on ATDC5 cell cycle stage and mode of death, and when ZA is dosed differently and in controlled delivery vehicles.
MECHANICAL INJURY ALTERS TRIBOLOGICAL REHYDRATION AND LUBRICATION IN BOVINE OSTEOCHONDRAL EXPLANTS
Margot S Farnham, Riley Larson, Christopher Price

In vivo, healthy articular cartilage maintains extremely low coefficients of friction (~0.02) near ‘indefinitely’; such conditions have only recently been replicated ex vivo using our convergent stationary contact area (cSCA) explant configuration. However, with injury, articular cartilage tribomechanics may breakdown, causing increased friction leading to more wear which may contribute to joint disease, e.g. osteoarthritis.

Using our custom tribometer, we can replicate in vivo frictional behaviors by sliding large, convex cSCA osteochondral explants against glass. The observed frictional response can be explained by a recently discovered mechanism, tribological rehydration, made possible by the biphasic nature of cartilage: hydrodynamic pressurization of bathing fluid is pumped back into cartilage during sliding. This allows applied loads to be primarily supported by the replenishment of cartilage’s fluid phase, as opposed to the solid matrix, thus decreasing friction through interstitial lubrication. This process has been observed in healthy explants but has not yet been explored in compromised (injured or diseased) cartilage.

19mm diameter bovine osteochondral explants were tested in the uninjured state, then again following subsequent injuries of increasing severity (surface vs. full-thickness fissures, 3mm vs. 6mm chondral defects). The testing protocol (30 minutes static compression at 7N + 30 minutes reciprocal sliding at 80 mm/s) was used to induce tribological rehydration.

As expected, injury caused decreased the degree of strain (and hydration) recovered by sliding because mechanical injury interrupts the natural paths of fluid flow within cartilage. Friction at the end of sliding also increased with injury, as a result of hindered lubrication. Other parameters including contact area and shear stress were also investigated. This study will establish how mechanical injury affects the tribomechanical properties of cartilage, providing us with a model to investigate how joint injury may lead to chondrocyte dysregulation, and cartilage degeneration and disease.

HOW ACTIVITY FREQUENCY GOVERNS CARTILAGE FUNCTION AND ITS IMPLICATIONS FOR JOINT HEALTH
Brian T. Graham¹, Axel C. Moore², David L. Burris¹,², Christopher Price²,¹

¹Mechanical Engineering, ²Biomedical Engineering, University of Delaware

Cartilage represents our body’s bearing surface, aiding joint movement by providing low friction articulation and load support. Conventional wisdom suggest that bearings wear with use, and thus for decades the prevailing thought was that higher activity levels could increase an individual’s risk of developing osteoarthritis (OA). However, epidemiological studies have found that more active individuals may have reduced risk of developing OA compared to their sedentary peers. Our recent advancements in cartilage explant testing methodologies have provided mechanistic evidence that more frequent activity could actually benefit cartilage health over the long-term.

As a porous biphasic biomaterial, cartilage must remain hydrated to function properly. Static loading, which occurs while individuals are sedentary, expells water out of the cartilage, causing it to lose lubricity and its ability to support load. It’s believed that movement causes fluid to be pumped back into the cartilage, restoring its thickness, lubricity, and load support. We can now replicate these processes in an explant test configuration called the convergent Stationary Contact Area (cSCA). The cSCA is a variation of more conventional explant tests, but is unique in that explants will rehydrate when slid against glass at physiological speeds, a process termed tribological rehydration (TR).

In this study, we have leveraged the ability of the cSCA explant configuration to replicate static exudation (sedentary) and sliding-induced TR (active) observed in vivo. We found that for a given volume of active time, shorter but more frequent bouts of activity significantly reduce the shear stresses and compressive strains experienced by cartilage; which could be beneficial to long-term cartilage health and explain the ‘paradoxical’ relationship between moderate activity and reduced OA risk.
**12 CHONDRO-PROTECTIVE MECHANISM OF STATIN**

*Mengxi Lv, Yilu Zhou, Tiange Zhang, Liyun Wang, X. Lucas Lu*

Department of Biomedical Engineering, University of Delaware

**Introduction:** Statins are a class of drugs prescribed to more than 25 million U.S. people to control blood cholesterol. Recent clinical trials found that use of statin is associated with lower occurrence of osteoarthritis (OA)1. However, clinical application of statin in OA treatment is hindered due to the lack of knowledge about its chondro-protective mechanisms. Statin is known to inhibit the mevalonate pathway in cells to reduce the cholesterol synthesis. In this study, we hypothesized that inhibition of the mevalonate pathway in chondrocytes by statins intervenes the downstream small GTPases (Rho, Ras, Rac etc.) activities, which prevents chondrocytes from entering the aberrant phenotypic shift under inflammatory attack, which protects the integrity of cartilage ECM.

**Results:** Cartilage explants (diameter=3 mm) from calf knee joints were cultured in vitro for 24 days. Statin significantly inhibited the GAG loss and completely abolished the collagen loss induced by IL-1β during in vitro culture. Expression of most catabolic genes in chondrocytes was suppressed in statin-treated samples when compared to the IL-1β alone group. Significant cell swelling and proliferation were observed in the IL-1β-treated samples, while both were completely inhibited by the statin co-treatment. Statin also suppressed the expression of cell-cycle-related genes, including CDC and CCN families, reflecting a retarded cell cycle transition.

Similar to statin, another mevalonate inhibitor, zoledronate, also demonstrated chondro-protective effects on IL-1β-treated cartilage explants. Moreover, systemic injection of zoledronate significantly suppressed the OA development in DMM mice.

**Discussion:** Repurposing of two classes of FDA-approved drugs, statin and bisphosphonate, could be a new pharmaceutical solution for PTOA prevention. Statin and bisphosphonate inhibit the mevalonate pathway in chondrocytes, which further induces the dormancy of small GTPases activities and prevents chondrocytes from entering the aberrant phenotypic shift under catabolic stimuli.

---

**13 THE ROLE OF TRANSIENT RECEPTOR POTENTIAL VANILLOID 4 IN OSTEOARTHRITIS**

*Nicholas Trompeter¹, Joseph Gardinier, PhD², Victor DeBarros³, Lauren Hurd, PhD³, Mary Boggs, PhD³, Randall Duncan, PhD³,²,³*

¹Department of Biomedical Engineering, ²Biomechanics and Movement Science Program, ³Department of Biological Sciences, University of Delaware, Newark, DE

The progressive loss of articular cartilage in osteoarthritis (OA) reflects the failure of the normally refined balance between anabolic and catabolic activities of chondrocytes. Three membrane proteins are important to this balance. Insulin-like Growth Hormone 1 (IGF-1) is a key mediator of cartilage homeostasis and the anabolic responses of chondrocytes while the Protease Activated Receptor 2 (PAR2) has been linked to synovitis and release of pro-inflammatory chemokines and proteases that drive OA onset and progression. Transient Receptor Potential Vanilloid 4 (TRPV4) channels are also important in cartilage development and homeostasis, however, we postulate that PAR2 and IGF-1 can modulate TRPV4 channel function to induce a catabolic or an anabolic response in chondrocytes, respectively. We show that treatment of chondrocytes with 300 ng/ml IGF-1 for 3hrs reduces TRPV4-mediated Ca2+ influx induced by mechanical forces or PAR-2 activation by increasing polymerization of actin stress fibers. This treatment significantly increased the stiffness of chondrocytes in vitro that correlated with the increase in actin stress fiber formation. This reduction in Ca2+ influx to hypotonic swelling was abrogated when the actin cytoskeleton was disrupted with Cytochalasin D. Pre-treating chondrocytes with IGF-1 also significantly reduced PAR2-mediated [Ca2+]i when these cells were challenged with the PAR-2 activator, trypsin. Our results demonstrate that IGF-1 tonically suppresses TRPV4 and the loss of IGF-1 during aging may initiate the progression of OA. By determining how IGF-1 and PAR2 regulate TRPV4 mediated Ca2+ signaling may lead to therapeutic targets for treating synovial inflammation and reduce the onset and progression of OA.
QUANTIFYING SOLUTE DIFFUSIVITY IN HUMAN OSTEOARTHRITIC CARTILAGE VIA CORRELATION SPECTROSCOPY

Alison Wright¹, Brian Graham², Christopher Price¹,²

¹Biomedical Engineering, ²Mechanical Engineering, University of Delaware, Newark DE 19716

Osteoarthritis (OA) is a chronic disease characterized by articular cartilage degeneration. Cartilage provides cushioning and low friction during movement, and loss of these properties with OA results in stiffness, inflammation, and disability. As an avascular tissue, the transport of nutrients via diffusion is critical to cartilage health. Changes in cartilage microstructure during early OA should lead to changes in molecular diffusivity. A technique sensitive enough to detect changes in the diffusivity of molecules within cartilage may allow for the earlier identification of OA, thus facilitating intervention strategies. In this study, fluorescence correlation spectroscopy (FCS) and raster image correlation spectroscopy (RICS) were used to quantify solute diffusion in human osteoarthritic articular cartilage explants to determine if they are sensitive enough to detect changes in diffusivity associated with OA progression. Human cartilage explants were scored using International Cartilage Repair Society guidelines and soaked in solutions of a small (fluorescein 332Da) and mid-size (Texas Red-conjugated 3kDa dextran) solute. After determining diffusion coefficients for each solute via both FCS and RICS, a creep indentation test was used to determine sample permeability. Our data show significant increases in solute diffusivity and permeability with increasing ICRS score, and a significant increase in diffusion coefficient with increasing permeability. Compositional assaying of GAG and collagen content will determine if these changes are correlated with tissue composition. While further study is needed to elucidate the precise relationship between osteoarthritis progression and diffusivity measurements, these correlation spectroscopy techniques may prove to be a useful tool in the evaluation of cartilage health. Given recent advances in arthroscopic microscopy, diffusivity measurements via correlation spectroscopy may be applied as a diagnostic tool in the clinical setting.

EXTRACELLULAR MATRIX SURFACE STIFFNESS REGULATES TRPV4 CHANNEL FUNCTION IN CHONDROCYTES

Mallory Griffin¹, Nick Trompeter¹, Omar Banda¹, Mary Boggs, Ph.D², John Slater, Ph.D¹, Randall Duncan¹,²

Departments of ¹Biomedical Engineering and ²Biological Sciences, University of Delaware, Newark, DE

Osteoarthritis (OA) is the most common joint disorder in the U.S., currently affecting 27 million adults. It is characterized by joint pain and stiffness caused by degradation of articular cartilage, most commonly in the knee, hip or spine. Degradation is caused by a loss of anabolic factors, and a subsequent increase in catabolic factors that lead to long-term degeneration of the extracellular matrix (ECM). The loss of collagen type 2 and proteoglycans in the ECM leads to a 10-fold decrease in cartilage stiffness that we postulate alters the chondrocyte phenotype. The TRPV4 channel is a mechanosensitive non-selective cation channel with a strong affinity for calcium that has been linked to cartilage health and development. Thus, we focused on how ECM stiffness could alter TRPV4-mediated Ca2+ influx. We have been able to produce synthetic ECM surfaces that represent either intact or OA cartilage using various weight percent’s of PEG-DA with a PEG-SVA RGDS conjugation for cell attachment. To determine if changes in surface stiffness modulates TRPV4 channel activity that alters Ca2+ influx into the cell, we used Fluo-4 as a fluorescent calcium chelator to measure intracellular Ca2+. We found that decreased surface stiffness produced a more sustained influx of Ca2+ that may be important in the catabolic phenotype of chondrocytes. By altering the TRPV4 channel response to a less stiff ECM, we may be able to develop a therapeutic intervention to reduce the catabolic responses associated with OA.
POSTER PRESENTATIONS // SPINE & OTHERS

POSTER PRESENTATIONS

Cells Tissue Biomechanics

Spine & Others
MODELING BLOOD RHEOLOGY ACROSS SPECIES
Jeffrey S. Horner, Antony N. Beris, and Norman J. Wagner

Department of Chemical & Biomolecular Engineering, University of Delaware, Newark, DE

Blood is a complex suspension primarily composed of deformable red blood cells in an aqueous plasma phase. As a fluid, blood exhibits a unique viscoelastic and shear thinning behavior when subjected to flow. Additionally, blood from certain species also exhibits thixotropy, a time dependent viscosity. This arises as a result of microstructure coin stack aggregates called rouleaux which the red blood cells can form under low stresses. Understanding and modeling the rheology of human blood is important due to the fact that a number of cardiovascular diseases have been linked to changes in the rheology of blood. Additionally, by having more accurate models for human blood rheology, we can improve flow simulations which have a wide range of applications. Despite almost always containing the same constituents, blood from other species may demonstrate drastically different rheological characteristics. Understanding these changes and having a universal model for blood from all species is critical as one of the biggest barriers in drug scaleup is moving across species. In this work, we present our constitutive, microstructure based model for steady and transient blood rheology [1]. Additionally, we present rheological data for human and various animal blood samples and demonstrate the universality of the model while identifying the key components that change across species.

IMMEDIATE EFFECTS OF PHOTOBIOMODULATION THERAPY ON ACHILLES TENDON STRUCTURAL AND VISCOELASTIC PROPERTIES
Patrick Corrigan¹, Daniel H. Cortes², Karin Grävare Silbernagel³

¹Department of Physical Therapy, University of Delaware
²Department of Mechanical and Nuclear Engineering, Penn State University

Introduction: Clinical outcomes for Achilles tendinopathy are improved by supplementing a loading program with photobiomodulation (PBM) therapy. The mechanism and time course of these effects remain unclear. Therefore, we evaluated the immediate effects of PBM therapy on tendon morphology and viscoelastic properties in people with Achilles tendinosis. Methods: 12 subjects with Achilles tendinosis received PBM treatment to one Achilles tendon and sham treatment to the other. Subjects were blinded and order of treatment was randomized. PBM treatment was administered to the side of greatest tendinosis. Tendon thickness, cross-sectional area (CSA), shear modulus, and viscosity were quantified with ultrasound imaging and continuous shear wave elastography. Experimental procedures were performed on both sides at baseline and immediately, 2-hours, and 4-hours after treatment. Results: There was a significant main effect of treatment side (p=0.001-0.01; \( \eta^2 \text{Partial}=0.45-0.63 \)) for thickness and CSA, but not for viscoelastic properties (p=0.70-0.72; \( \eta^2 \text{Partial}=0.01 \)). There was no significant main effect of time (p=0.13-0.97; \( \eta^2 \text{Partial}=0.01-0.16 \)) or treatment by time interaction (p=0.32-0.73; \( \eta^2 \text{Partial}=0.04-0.10 \)) for all variables. On the treated side, reductions in shear modulus (4-hours) and CSA (immediately, 2-hours, and 4-hours) were greater than MDC95%. On the sham side, viscoelastic properties did not change, but there were reductions in CSA (4-hours) and thickness (2- and 4-hours) greater than the MDC95%. Conclusion: PBM treatment appears to effect tendon viscoelastic properties after four hours, but not effect morphology. Since PBM treatment does not alter viscoelastic properties until four hours after treatment, PBM may be administered at any time during a treatment session.
POSTER PRESENTATIONS // DESIGN & INNOVATION

Clinical Biomechanics

Design & Innovation
SMARTBOOT 2.0

Sheridan Parker¹, Katie Solon², Stephen Faulkenberry¹, Ian Goldie², Sagar Doshi², Kurt Manal², Erik Thostenson², Karin Gravare Silbernagel³, and Jill Higginson²

¹Biomedical Engineering, ²Mechanical Engineering, ³Physical Therapy, University of Delaware

Early weight bearing loading has been shown to have beneficial effects on Achilles tendon rupture (ATR) healing, however the optimal loading pattern and amount of loading is not known. Therefore, the objective of this study is to develop a device that measures, and records, real-time and long-term force and step count data from the sole of a walking boot to a computer which would allow clinicians to monitor and improve post injury rehabilitation protocols.

The main component of the SmartBoot 2.0 are two Carbon Nanotube piezoresistive sensors, split into Forefoot and Rearfoot sensors, that actively measures the resistive changes in response to ground reaction forces during a walking gait. The resistive data is read by an Arduino and saved to an SD card at a rate of 22Hz. The resistive values are converted to units of force and displayed with a custome user interface.

Testing of the SmartBoot 2.0 was performed with three healthy participants. Participants wore the SmartBoot 2.0 on their right foot and asked to walk at a comfortable pace on an instrumented treadmill for 1 minute per trial for three trials. SmartBoot 2.0 outputs were compared to the intrumented treadmill force data for validation. Even with a low sampling rate the sensors were sensitive enough to capture most heel strike and toe-off peaks during walking. It was determined that the SmartBoot 2.0 was within 21.03 Newtons of the instrumented treadmill within a 95% CI. Initial testing of the SmartBoot 2.0 was limited by a small sample size. Future implementations are to be used in ATRs research.

PERSONALIZED PASSIVE-DYNAMIC ANKLE-FOOT ORTHOSES BENDING STIFFNESS IMPROVES PEAK PLANTAR FLEXION MOMENT FOR INDIVIDUALS POST-STROKE

Corey Koller, M.S., BIOMS Program; Darcy Reisman, Ph.D., PT Department; Elisa Arch, Ph.D.

KAAP Departments

The plantar flexors (PFs) play a critical role in moving the body forward. Insufficient control of shank rotation due to PF weakness, a common post-stroke impairment, may result in gait dysfunctions. PF function during gait, or lack thereof, can be quantified by the peak PF moment. Passive-dynamic ankle-foot orthoses (PD-AFOs) can be prescribed to improve post-stroke gait. In particular, PD-AFO bending stiffness is a key orthosis characteristic that can replicate many functions of the PFs. However, outcomes with PD-AFOs are variable, likely because of improper personalization. We have developed a novel design and prescription process that objectively personalizes PD-AFOs based on each individual’s level of PF weakness. This study evaluated if objectively-personalized PD-AFOs improved gait biomechanics (peak PF moment) better than originally-prescribed AFOs (Original AFO) for individuals post-stroke. We hypothesized the peak PF moment would be significantly greater while wearing the objectively-personalized PD-AFO. Eleven individuals with chronic stroke participated in this study. PD-AFO bending stiffness was personalized as the difference between the individual’s peak PF moment and a healthy, speed-matched, peak PF moment obtained from the lab’s normative database, divided by a typical dorsiflexion range of motion. Simulation modeling analysis (SMA) was performed to determine which participants achieved a significant difference between the two conditions. Results showed that 9 out of 11 individuals had a significant increase in peak PF moment from the Original AFO to PD-AFO. Future research will investigate if these immediate benefits translate into improved outcomes longer-term.
Clinical Biomechanics

Gait & OA
ASSOCIATION OF CLINICAL AND FUNCTIONAL OUTCOMES WITH RISK OF FALL IN KNEE OSTEOARTHRITIS PATIENTS

Moiyad Aljehani, DPT; Kathleen Madara, PhD; Joseph Zeni, Jr. PhD

University of Delaware, Newark, DE

Introduction: Older adults with end-stage knee osteoarthritis (OA) have poor balance and high risk of falling. Therefore, the purposes of this study were to 1) determine differences in clinical and functional outcomes based on patients' history of falls and 2) determine if clinical and functional outcomes represent risk factors for falls.

Methods: 259 subjects with end-stage knee OA participated in this study. Subjects were divided into two groups (fallers and non-fallers) based on falling history in the past six months (at least reported one fall). We evaluated clinical outcomes (pain, range of motion, and quadriceps strength), and functional measures (six-minute walk test (6MWT), timed up and go, and Knee Injury and Osteoarthritis Outcome Score (KOOS)). Multiple independent t-tests were used to examine differences between groups (fallers and non-fallers). Odds ratio and p-values were calculated to examine the association of the clinical and functional measures with the chance of falling.

Results: 47 (18%) patients reported falls. There were no significant differences between groups for age, BMI, and sex. Compared to non-fallers, fallers group had greater low back pain (0.9 points; 30%, p=0.025) on VAS and walked shorter distances (44 meters; 12%, p=0.010) during the 6MWT. For every 1-point increase in low back pain, there is 14% (1.14 times, p=0.028) greater chance of falling. For every 10-meters increase on 6MWT, there is 3.8% (0.96 times, p=0.011) lesser chance of falling.

Conclusions: The findings suggest that low back pain and walking ability may contribute to the fall risk for end-stage OA patients. The higher low back pain was associated with higher chance of falling, while higher performance on 6MWT was associated with the lower falling chance.

PRELIMINARY FINDINGS OF A NOVEL PHYSICAL THERAPIST ADMINISTERED PHYSICAL ACTIVITY INTERVENTION AFTER TOTAL KNEE REPLACEMENT

Meredith Christiansen; Louise Thoma; Hiral Master; Laura Schmitt; Dana Mathews; Daniel K. White

University of Delaware, Newark, DE

Purpose: Physical inactivity is common after total knee replacement (TKR). Physical therapists are experts in exercise and routinely treat people after TKR in outpatient physical therapy (PT). However, it is not known whether a physical therapist administered physical activity (PA) intervention increases PA in people after TKR. Methods: Participants with a unilateral TKR were randomized into the control or intervention group. Both groups received outpatient standardized PT. The intervention group additionally received a Fitbit Zip, weekly personalized step goals provided by a physical therapist, and monthly phone calls after discharge from PT for 6 months. Objectively measured steps/day and minutes in MVPA/day were measured using an accelerometer (ActigraphGT3X) worn at the right hip for one week at initial PT evaluation (baseline), discharge from PT (DC) and 6 months after DC from PT (6m). Results: Of the 43 participants enrolled in the study, to date, 17 people in the control group and 15 in the intervention group completed the 6-month follow-up. The intervention group took 2,559 and 1,875 more steps/day than the control group at DC (p=0.003) and 6m (p=0.03), respectively. The intervention group spent 109.2 more minutes/week in MVPA than the control group at DC (p=0.01). Conclusion: Findings warrant a full scale study to confirm the effectiveness of at physical therapist-administered PA intervention after TKR.
COORDINATION OF BALANCE MECHANISMS DURING WALKING

Tyler Fettrow, Hendrik Reimann, John Jeka

Department of Kinesiology and Applied Physiology, University of Delaware, Newark, DE, USA

Currently there is not a well-defined, comprehensive theory for how the healthy human nervous system maintains balance during walking. Unlike quiet standing balance, the gait cycle creates a system that requires different strategies to achieve the task of balance. We have discovered multiple mechanisms of balance control during walking, in a young healthy cohort (n=20), that are temporally coordinated to explain the maintenance of upright balance in the medial-lateral direction.

The three mechanisms are:

Foot placement shift: Active control of swing foot placement in direction of perceived fall. In the event of a sensory perturbation and a perceived shift in the CoM, a correction must be made, and the most obvious way to do this is take a step.

Lateral ankle roll: Active control of center of pressure under the stance foot in the direction of the perceived fall. The active control of ankle inversion/eversion angle can be used to modulate the CoP under the stance foot during sustained locomotion.

Push-off modulation: Active shift of weight between two legs in double stance. During double stance, the feet are not directly in front of one another, but are offset laterally, so a weight shift between legs would have effects on the lateral balance. We are currently unaware of any reports of a push-off mechanism being used to aid in the maintenance of balance in the medial-lateral direction.

Ultimately, we strive to understand the coordination of the main mechanisms. Future work includes the investigation of the balance mechanisms in populations such as older adults and people with Parkinson’s Disease and children with Cerebral Palsy.

SEX AND MECHANISM OF INJURY (MOI) INFLUENCE KNEE MECHANICS AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION (ACLR)

Naoaki Ito, Jacob J. Capin, Ashutosh Khandha, Kurt Manal, Thomas S. Buchanan, Lynn Snyder-Mackler

University of Delaware, Newark, DE, USA

INTRODUCTION: ACLR is linked to altered knee gait mechanics such as medial compartment tibiofemoral underloading, which is associated with early joint degeneration and radiographic OA five years after ACLR. Women are especially at risk for sustaining ACL injury in a non-contact manner. The purpose of this study was to quantify gait mechanics after ACLR in male and female athletes who sustained contact versus non-contact ACL injury.

METHODS: 67 participants (28contact [18male/10female], 39non-contact [19male/20female]) were recruited. Joint kinematics, ground reaction forces, and electromyography data from 7 lower extremity muscles were collected during overground walking. Muscle and joint contact forces were calculated using a previously validated musculoskeletal model, and kinematic and kinetic variables using Visual3D. Peak knee flexion angle (pKFA), knee flexion moment (pKFM), knee adduction moment, medial compartment contact force (pMCCF), total contact forces (pTCF), knee flexor and extensor muscle force (ExtpKFM) at pKFM were measured. A 2x2x2 (sex by MOI by limb) ANOVA (α=0.05) was used for analysis.

RESULTS: A 3-way interaction effect was observed among limb, sex, and MOI for pMCCF (p=0.001). The male non-contact group underloaded their involved knee, while the female group overloading. The female contact group underloaded their involved knee. Main effects of limb were observed in pKFA (p<0.001), pKFM (p<0.001), pTCF (p=0.027), and ExtpKFM (p<0.001). All values were lower in the involved versus uninvolved limb.

DISCUSSION: Our findings suggest sex and MOI may influence medial tibiofemoral joint loading, a risk factor for early OA development after ACLR. It may be important to further investigate the influence of MOI on gait in athletes after ACLR, as targeted rehabilitation interventions may need to differ based on sex and MOI.
CONTRIBUTION TO FORWARD PROPULSION WITH INDUCED ASYMMETRIC GAIT AND USER-DRIVEN TREADMILL CONTROL

Kelley M. Kempski, Brian A. Knarr, Jill S. Higginson

Biomedical Engineering, University of Delaware
Mechanical Engineering, University of Nebraska at Omaha
Mechanical Engineering, University of Delaware

Fixed-speed treadmills do not perfectly simulate an individual’s typical overground locomotor patterns when being used for training interventions in affected populations, resulting in statistically significant differences in some kinematic parameters [1,2]. The objective of this study was to determine how healthy subjects’ contributions to forward propulsion change with an induced asymmetric gait and on a treadmill in user-driven mode. Nine healthy adults walked on a fixed-speed instrumented split-belt treadmill with one belt at the subject’s self-selected speed and the other at half of that speed. After four minutes, the treadmill transitioned to user-driven control which updated the speed of each treadmill belt in real-time based on how fast the subject was trying to walk. The slow leg on the fixed-speed treadmill, which mimics the paretic leg of an individual with post-stroke hemiparesis, contributes 43.3 ± 11.1% to forward propulsion. This demonstrates that the induced asymmetric gait on healthy individuals is representative of mild-to-moderate severity hemiparesis of individuals post-stroke [5]. There was no significant difference in percent contribution to propulsion between limbs for baseline or on the user-driven treadmill (p > 0.05). Healthy individuals returned to symmetric contribution to forward propulsion on the user-driven treadmill after an induced asymmetry. Being able to mimic hemiparetic gait in healthy individuals before implementing the user-driven treadmill may indicate how individuals post-stroke may respond to this novel rehabilitation paradigm.

PROXIMAL SHANK KINEMATICS IN PROSTHETIC GAIT

Rosa Kolbeinsdottir, Mechanical Engineering, and Elisa Arch

Introduction: Shank segmental kinematics have been analyzed recently in typical gait [1,2] yet are not well understood in prosthetic gait. The recent work on the kinematics of typical shank progression showed the proximal end of the shank stayed fairly horizontal due to an interplay of foot and ankle kinematics and only lowered about 3 cm throughout stance [2]. This analysis also used a kinematic model to predict the proximal shank kinematics in prosthetic gait and predicted the proximal shank would lower 13 cm in prosthetic users without the ability to plantarflex [2]. This study aimed to verify the model prediction by analyzing sagittal plane shank progression during stance in prosthetic gait.

Methods: Four males with unilateral transtibial amputation (height 1.76 ± 0.07 m, body mass 91.4 ± 24.8 kg) all wearing the Vari-Flex® energy-storing-and-returning prosthesis underwent an instrumented gait analysis. Shank kinematics (sagittal plane rotation and vertical and horizontal translation of the shank’s proximal end), were analyzed for each participant.

Results & Discussion: In the experimental data of prosthesis users, the shank rotated 70.6 ± 8.23°, horizontally translated 0.669 ± 0.109 m, vertically translated -0.043 ± 0.081 m, and there was no plantar flexion past neutral. These results indicated that, contrary to the model prediction, the proximal shank stayed fairly horizontal in prosthetic gait throughout stance and more closely resembled typical gait [2]. This unexpected finding is theorized to be a factor causing the spatiotemporal asymmetries often seen in prosthetic gait [3], as prosthetic users might end the stance phase early in order to avoid further drop of the proximal shank.

Worsening cartilage damage is a feature of knee osteoarthritis that is linked to obesity. Cumulative load can estimate the cumulative effect of obesity during daily walking, and may provide additional insight into changes in knee cartilage over time. Therefore, our study examined the relation of cumulative load to worsening cartilage damage over two years in the tibiofemoral and patellofemoral joints. We hypothesized that sex (male/female) and frontal knee alignment (normal/varus/valgus) would also modify this relationship (based on previous literature).

Data from the Multicenter Osteoarthritis Study were used. Participants had their BMI and average steps/day measured at baseline. Worsening cartilage damage was defined by changes on MRI between baseline and 2 years. Our exposure, cumulative load, was defined as BMI*steps/day. Tertiles of cumulative load (low, middle, high) were created, with the middle tertile as our reference group. Risk ratios were calculated using logistic regression. We performed separate stratified analyses by sex and frontal knee alignment.

We included 957 MOST participants. There were no effects of cumulative load on cartilage damage in men, or people with normal or varus alignment. Women with low and high cumulative load had greater risk of worsening damage in the lateral PF joint, with RR (95% CI) of 2.0 (1.1-3.6) and 1.9 (1.1-3.3), respectively. People with valgus malalignment and high cumulative load had 2.9 (1.2-7.0) times greater risk for worsening damage in the lateral TF joint.

For most people, daily walking should continue to be encouraged. However, women or people with valgus malalignment who are obese and perform high amounts of daily walking would benefit from weight reduction, as they seem to have higher risk of worsening cartilage damage in their knees.

For most people, daily walking should continue to be encouraged. However, women or people with valgus malalignment who are obese and perform high amounts of daily walking would benefit from weight reduction, as they seem to have higher risk of worsening cartilage damage in their knees.
DYNAMIC STABILITY DURING WALKING IN CHILDREN WITH AND WITHOUT CEREBRAL PALSY: A PILOT STUDY


Introduction: Cerebral palsy (CP) is associated with a high risk and rate of falling, especially during walking. This study compared the anterior and lateral dynamic stability, as quantified by the margin of stability (MOS), of children with and without CP during gait. We hypothesized that (1) children with CP would be less stable than typically developing (TD) children, (2) group differences would be greater when bearing weight with the non-dominant limb, and (3) group differences would be greater at fast versus preferred speeds. Methods: Five children with CP (3 boys, 2 girls, age mean (SD)=8.4 (2.2) years, GMFCS I or II) were age-matched with 5 TD children (3 boys, 2 girls, 8.4 (2.2) years). Gait was recorded at preferred and fast speeds using motion capture technology, and the MOS results were interpreted using main effect and interaction effect sizes (large: f=0.40, medium: f=0.25, small: f=0.10). Results: With faster speed, the anterior MOS at footstrike was more unstable (f=3.44, p<0.001), and participants allowed themselves to become more unstable when pushing off of their dominant limb (f=0.35, p=0.357). From the minimum lateral MOS, it was evident that children with CP were more stable at fast speeds and while bearing weight with the non-dominant limb at preferred speeds (Cohen’s d=0.78-2.00, p=0.015-0.17). Conclusion: Our hypotheses were not supported. This high-functioning group of children with CP exhibited no group differences in anterior stability during walking, but used a more conservative lateral stability strategy (i.e. larger MOS), especially on the non-dominant limb and at fast speeds.

MINIMUM-INTERLIMB DIFFERENCE OF TRICOMPARTMENT KNEE CARTILAGE T2 VALUES IN HEALTHY INDIVIDUALS

Jack R. Williams, Ashutosh Khandha, Lynn Snyder-Mackler, Thomas S. Buchanan

T2 time of cartilage is a biochemical marker used in magnetic resonance imaging (MRI) to evaluate articular cartilage degradation. Individuals with knee osteoarthritis (OA) have significantly higher T2 values than those without. T2, therefore, has the potential to detect OA earlier than radiographs. The purpose of this study was to determine the minimum inter-limb difference (MILD) in knee cartilage T2 values in young healthy individuals. MILD is the smallest measured change that can be interpreted as a true difference. These values can be used as thresholds to determine OA related inter-limb differences in knee cartilage. MRI was performed for 9 subjects using a sagittal T2 mapping sequence. T2 maps were calculated in the medial and lateral tibiofemoral compartments as well as the patellofemoral compartment. Regions of interest were segmented in the anterior, central, and posterior regions of the femoral and tibial cartilage and medial, central, and lateral regions of the patellofemoral cartilage. MILDs were determined for each region.

MILDs of the medial tibiofemoral, lateral tibiofemoral, and patellofemoral compartments varied from 2.5 milliseconds (ms) to 9.5 ms. The maximum MILD occurred in the anterior femoral region of the lateral tibiofemoral cartilage; the minimum occurred in the lateral component of the patellofemoral cartilage. MILDs varied from compartment to compartment and from region to region. This study has provided a set of minimum inter-limb differences for T2 values between knees of healthy individuals. Values beyond the MILDs reported here can be interpreted as outside the normal range for healthy individuals. These differences were calculated to provide a baseline for further assessments of inter-limb difference in T2 values between uninjured knees and those that have undergone ACLR (anterior cruciate ligament reconstruction).
POSTER PRESENTATIONS // NEUROMUSCULAR MODELING & ASSESSMENTS

Clinical Biomechanics

Neuromuscular Modeling & Assessments
30 THE NEURAL CORRELATES OF MOTOR ADAPTATION TO DYNAMIC PERTURBATIONS
Andria J. Farrens, Andrea Zonnino, Fabrizio Sergi

Neuro-motor adaptation, the process of changing one’s motor output in response to error, plays a role in motor learning and is a useful paradigm in neuro-rehabilitation and robot-assisted training. While the behavioral effects of motor adaptation have been studied extensively, its neural correlates are much less understood. The neural correlates of motor adaptation can be studied using whole-brain imaging techniques such as functional magnetic resonance imaging (fMRI). Task-based fMRI, acquired during adaptation, can localize neural activity associated with adaptation processes occurring on different timescales. Resting state fMRI, acquired before and after adaptation, measures statistical associations between neural activity measured in different brain areas (i.e. functional connectivity). Changes in functional connectivity induced by motor adaptation can identify neural processes responsible for offline learning immediately following adaptation. Our group has recently developed a novel fMRI-compatible wrist robot, the MR-SoftWrist, to study the neural correlates of force-field adaptation using fMRI.

Here we present the results of our first fMRI pilot study on four healthy subjects. Our protocol had subjects perform visually-guided wrist pointing under three separate force conditions: no force, resistive force, and curl force. The first two conditions were used to assess neural activation during baseline and in a force-matched condition in the absence of adaptation, while the curl force condition was used to study adaptation to a learnable perturbation. Our behavioral results confirm the MR-SoftWrist is a valid tool for investigating motor adaptation of wrist pointing executed in the MRI environment. Our task-based neuroimaging results show increased activation in the posterior parietal cortex in the curl force perturbation mode. Finally, our resting-state analysis identified that connectivity scores within the cortico-thalamic-cerebellar network are significantly modulated by adaptation and not by motor execution.

31 THE EFFECTS OF FALL-RECOVERY TRAINING ON SINGLE- AND MULTIPLE-STEPPING THRESHOLDS IN INDIVIDUALS WITH CHRONIC STROKE.
Jamie Pigman, Darcy S. Reisman, Ryan T. Pohlig, Jeremy R. Crenshaw

University of Delaware, Newark, DE

The purpose of this study was to determine if clinical measures of balance and novel measures of reactive balance improved with fall-recovery training in individuals with chronic stroke. Clinical measures included the Berg Balance Scale (BBS) and Functional Gait Assessment (FGA). Reactive balance measures included single-stepping (SST) and multiple-stepping (MST) thresholds, defined as the anterior and posterior disturbance magnitudes that consistently elicited one or more than one step, respectively. We recruited six participants with chronic stroke (mean (SD) age: 60 (7) years, BMI: 29.5 (4.6) kg/m², Fugl-Meyer LE 23 (9)), each of which completed six sessions of fall-recovery training. Each session consisted of progressively difficult simulated trips and slips delivered by a computer-controlled treadmill. Training was accompanied by moderate effects in the BBS (Cohen’s d = 0.5, p = 0.3) and the FGA (d = 0.6, p = 0.2). Larger effects were observed for the anterior (d = 1.4, p = 0.03) and posterior SST (d = 1.3, p = 0.02). Motion capture analysis suggested that, with training, participants recovered from more dynamic instability during their feet-in-place reaction (d = 1.6, p = 0.3). Large training effects were observed for the posterior (d = 0.90, p = 0.06), but not anterior MST (d = 0.13, p = 0.77). For the posterior stepping response of the MST assessment, recovery steps became slightly longer and narrower (d = 0.41-0.43, p = 0.34-0.36). The results of this pilot study suggest that fall-recovery training can have beneficial transfer to some, but not all assessments of balance. The benefits of training coincided with moderate improvements in fall-recovery biomechanics.
**32 IMPAIRED QUADRICIPS FUNCTION MAY NOT BE CAPTURED BY STANDARD CLINICAL MEASURES IN PATELLAR TENDINOPATHY**

Andrew L. Sprague; Angela Hutchinson Smith; Karin Grävare Silbernagel

Department of Physical Therapy, University of Delaware

**Introduction:** Patellar tendinopathy is a clinical diagnosis of a painful patellar tendon, resulting in decreased sports performance. Arthrogenic muscle inhibition (AMI) is an inability to activate a muscle fully, in the absence of muscle or neural tissue damage. The purpose of this study was to determine if AMI is present in patients with unilateral patellar tendinopathy and its implications for jumping performance.

**Methods:** 3 (1F) subjects with a mean (SD) age of 28 (9) years, height of 1.8 (0.2) meters, weight of 86 (12) kilograms and a diagnosis of unilateral patellar tendinopathy were recruited. Isometric knee extension strength and quadriceps muscle activation testing was completed using the burst superimposition method. The peak maximal voluntary isometric contraction (MVIC) torque and the torque attributable to electrical stimulation were used to calculate quadriceps indexes (QI) and central activation ratios (CAR). Jumping performance was assessed using the single-leg counter movement jump (CMJ). Limb symmetry indexes (LSI) were calculated for height.

**Results:** All subjects had a normal QI (≥ 90%) but bilateral CAR deficits (< 90%). CARs (involved:uninvolved) for subjects 1, 2 and 3 were 69.0%:62.9%, 87.9%:88.8%, and 88.0%:88.8%, respectively. During CMJ testing, subject 1 had decreased performance on the involved limb, subject 2 had greater performance, and subject 3's performance was equivalent bilaterally (LSI = 75.1%; 114.8%; 99.5%).

**Conclusions:** Quadriceps AMI is present bilaterally in unilateral patellar tendinopathy. These subjects demonstrated a normal QI and lacked a clear relationship between AMI and jump performance. Therefore, impaired quadriceps function in patellar tendinopathy may not be detected with standard clinical measures of knee extension strength or lower extremity function.

**33 INCORPORATING HIERARCHAL STRUCTURE WITHIN HYDROGEL BIOMATERIALS USING MULTIFUNCTIONAL COLLAGEN MIMETIC PEPTIDES.**

Eden M. Ford², Amber M. Hilderbrand¹, Chen Guo¹, April M. Kloxin¹,²

¹Chemical & Biomolecular Engineering, University of Delaware, ²Material Science & Engineering University of Delaware

Extracellular matrix (ECM) properties are important regulators of cell function, particularly at early timepoints during bone healing. Physical and chemical properties enable regulation of cell behavior, and controlling these extracellular cues provides opportunities to direct bone regeneration. Collagen is one of the most prevalent proteins in the ECM and presents a variety of physical and chemical cues that control the bone healing process. In order to mimic these cell-collagen interactions in vitro we have designed multifunctional collagen mimetic peptides (mfCMPs) that are variants of the Proline-Hydroxyproline-Glycine repeat unit of native collagen. Two variants of this peptide were synthesized, one that promoted fibrillar assembly through ionic interactions using charged groups, and the other using hydrophobic interactions of aromatic groups on the C- and N-termini to promote end-to-end assembly. Toward studying cell response in vitro, these mfCMPs were covalently crosslinked within water-swollen polymer networks called hydrogels, which offer a tunable platform that can mimic a variety of soft tissues within the body. Through mfCMP incorporation, we are able to capture the fibrillar structure of collagen on both the nano- and microscale, providing a hierarchal structure within the hydrogel materials to better recapitulate ‘soft’ collagenous tissues (such as the collagen-rich hematoma in the first stage of bone repair). Fibrils were imaged with transmission electron microscopy to study fibril morphology in solution, and rheology was used to characterize mechanical properties of hydrogels with incorporated mfCMPs. Studies to observe cell behavior within these hydrogel materials indicate they are suitable for the culture of human mesenchymal stem cells (hMSCs), and suggest that the presence of mfCMPs may influence cell-matrix interactions.
## Schedule of the Day

<table>
<thead>
<tr>
<th>TIME</th>
<th>WHAT</th>
<th>WHERE</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:30</td>
<td>BREAKFAST &amp; POSTER SET-UP</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>9:00</td>
<td>WELCOME &amp; INTRODUCTORY REMARKS</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>9:05</td>
<td>KEYNOTE LECTURE: DR. JEAN JIANG</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>10:20</td>
<td>BREAK</td>
<td></td>
</tr>
<tr>
<td>10:35</td>
<td>PODIUM SESSION 1</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>11:35</td>
<td>LUNCH</td>
<td></td>
</tr>
<tr>
<td>12:00</td>
<td>POSTER SESSION 1 (ODD #S)</td>
<td>STAR CAMPUS- MAIN CONCOURSE</td>
</tr>
<tr>
<td>1:00</td>
<td>POSTER SESSION 2 (EVEN #S)</td>
<td>STAR CAMPUS- MAIN CONCOURSE</td>
</tr>
<tr>
<td>2:00</td>
<td>BREAK</td>
<td></td>
</tr>
<tr>
<td>2:15</td>
<td>PODIUM SESSION 2</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>3:15</td>
<td>ANNOUNCING THE VINCE BARO UNDERGRADUATE RESEARCH AWARDEES</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>3:30</td>
<td>AWARDS SESSION</td>
<td>STAR CAMPUS- GLASS ATRIUM</td>
</tr>
<tr>
<td>4:00</td>
<td>ADJOURN</td>
<td></td>
</tr>
</tbody>
</table>