UNIVERSITY OF DELAWARE | College of Engineering

14th Annual

Biomechanics Research Symposium

May 12, 2017

Center for Biomechanical Engineering Research
201 Spencer Lab | Newark, Delaware 19716 | cber.udel.edu

Welcome students, faculty and friends!

Welcome to the 14th annual Biomechanics Research Symposium hosted by the Center for Biomechanical Engineering Research CBER. This is my fourth and final CBER day as director of the center and I would like to thank everyone for the cooperation and enthusiastic support you have shown me for the past several years. Let's all welcome Liyun Wang as the next center director starting this summer.

This year, we return to our traditional format of an all-day research symposium featuring podium presentations and posters covering the cutting-edge Biomechanics and Biomechanical Engineering related research being conducted by the students and post docs at the University of Delaware. We are also excited to have a keynote lecture by Dr. Johanna Temenoff from Georgia Tech/Emory University. The talk is entitled, "Characterizing Structural and Biochemical Changes to Joint Tissues During Rotator Cuff Injury." Also this year, the Stanley Family Foundation will present their generous gift in memory of Vincent Baro, a former CBER student and previous presentation award winner. The gift will be used to support student research in orthopedic biomechanics at UD.

I would like to thank the Department of Mechanical Engineering for providing support for this year's CBER day as well as the sponsorship for the keynote and poster printing provided by Delaware Rehabilitation Institute. I would also like to thank our students, faculty, and staff members for their participation and contribution, especially our Organizing Committee!

ACKNOWLEDGEMENTS

ORGANIZING COMMITTEE

Liyun Wang

Lucas Lu

Michael H. Santare

Jill Higginson

Elaine Nelson

Kate Campbell

Ashutosh Khandha

Jerahme Martinez

Axel Moore

Ashutosh Parajuli

Nicole Ray

Jennifer Zellers

Yilu Zhou

Event sponsored by the Center for Biomechanical Engineering Research , Department of Mechanical Engineering and Thomas Buchanan, Director of the Delaware Rehabilitation Institute

Keynote Lecture

"Characterizing Structural and Biochemical Changes to Joint Tissues During Rotator Cuff Injury"

Dr. Johnna Temenoff

Rotator cuff injuries represent a range of pathologies, from early tendon overuse to full thickness rotator cuff tendon tears. Increasingly, rotator cuff disease is viewed as a whole-joint pathology, but it is unclear how the various tissues involved respond at different disease stages. Our laboratory has recently identified and characterized cartilage degeneration as well as tendon injury in rodent models of both overuse (early stage) and full tear (late stage) rotator cuff disease. Moreover, degenerative changes to the supraspinatus muscle after tendon tear have been investigated. In particular, in this presentation, timing of changes in proteolytic activity after tendon injury will be outlined and our work developing biomaterials-based strategies to treat joint degeneration will be discussed.

BRIEF BIOGRAPHY

Dr. Johnna Temenoff completed her Ph.D. and post-doctoral fellowship at Rice University in tissue engineering and orthopaedic biomaterials. In 2005, she joined the faculty in Biomedical Engineering at Georgia Tech/Emory University. Dr. Temenoff has received funding from a range of sources, including federal agencies (NIH and NSF) and groups such as the Aircast Foundation and National Football League Charities, and currently serves at the Principle Investigator on a NIH T32 Predoctoral Training Grant in biomaterials. She also acts as the Co-Director for the Regenerative Engineering and Medicine Center, a statewide initiative encompassing three premier research universities in Georgia (Georgia Tech, Emory University, and the University of Georgia). Scientifically, Dr. Temenoff is interested in tailoring the molecular interactions between glycosaminoglycans and proteins for use in regenerative medicine applications. Her laboratory focuses primarily on promoting repair after injuries to the tissues of the shoulder, including cartilage, tendon, and muscle.

Dr. Temenoff has been honored with several prestigious awards, such as the NSF CAREER Award and the Arthritis Foundation Investigator Award, and was named to the College of Fellows of the American Institute for Medical and Biological Engineers (AIMBE). She recently was awarded the Education Award from TERMIS-NA, in part because she has demonstrated her commitment to undergraduate biomaterials education by co-authored a highly successful introductory textbook - *Biomaterials: The Intersection of Biology and Materials Science*, by J.S. Temenoff and A.G. Mikos, for which Dr. Temenoff and Dr. Mikos were awarded the American Society for Engineering Education's Meriam/Wiley Distinguished Author Award for best new engineering textbook.

Schedule of the Day

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8:30	BREAKFAST & POSTER SET-UP	STAR CAMPUS- GLASS ATRIUM
9:00	WELCOME & INTRODUCTORY REMARKS	STAR CAMPUS- GLASS ATRIUM
9:05	KEYNOTE LECTURE: DR. JOHNNA TEMENOFF	STAR CAMPUS- GLASS ATRIUM
10:20	BREAK	
10:35	PODIUM SESSION 1	STAR CAMPUS- GLASS ATRIUM
11:35	LUNCH	STAR CAMPUS- MAIN CONCOURSE
12:00	POSTER SESSION 1 (ODD #S)	STAR CAMPUS- MAIN CONCOURSE
1:00	POSTER SESSION 2 (EVEN #S)	STAR CAMPUS- MAIN CONCOURSE
2:00	BREAK	
2:15	PODIUM SESSION 2	STAR CAMPUS- GLASS ATRIUM
3:15	PRESENTING THE STANLEY FAMILY FOUNDATION GIFT IN MEMORY OF VINCENT BARO	STAR CAMPUS- GLASS ATRIUM
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Meredith Christiansen

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3
Ana Ebrahimi

P.15 ASSESSING THE VALIDITY OF THE G-WALK BTS ON INDIVIDUALS WITH UNILATERAL TRANSTIBIAL AMPUTATIONS
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Jerahme Martinez

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John Nguyen

P.19 4 EFFECTS OF PERLECAN/HSPG2 DEFICIENCY ON MRNA CHANGES IN MECHANICALLY LOADED B
Sucharitha Parthasarathy

P.20 5 METABOLIC LABELING OF OSTEOCYTE PERICELLULAR MATRIX IN VITRO AND IN VIVO
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Vrathasha Vrathasha

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Hilary Weidner

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Denotes Poster #

PODIUM PRESENTATIONS

Session 1

1 FAST AND RELIABLE MARKER-FREE CAPTURE OF CTCS BY 3D CARBON NANOTUBE SPONGE

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Carbon nanotube (CNT) materials have been widely used in engineering structures, energy storage devices and micro-electronics based on its outstanding electrical and mechanical properties. In biotechnology, CNT has been successfully adopted as biosensors in medical imaging for diagnostic purposes. Herein, for the first time, we have developed a 3D CNT-sponge-based platform to perform as the capture agent of rare CTCs from blood samples in half an hour. This platform can be massively fabricated at low cost and does not need specific immunochemical agent or biological cell adhesion enhancer to efficiently capture CTCs. The stability of CTC capture by this 3D CNT structure is proved by the strong binding affinity between CTCs and CNT sponge that limits the mobility of CTCs after capture. This 3D CNT sponge material can be directly used as the next generation of marker-free CTC capture devices for the fast diagnostic of early stage metastasis and give reliable evidence for the future TNM staging in cancer therapy.

2 CELLULAR MECHANISMS FOR THE OSTEOPOROTIC PHENOTYPE ASSOCIATED WITH PERLECAN-DEFICIENCY

Ashutosh Parajuli, Victor Gao, Catherine Kirn-Safran, Liyun Wang,

University of Delaware, Newark-Delaware

INTRODUCTION: Perlecan is a large multifunctional heparin sulfate proteoglycan present in basement membranes and tissue borders. Mutations of perlecan is associated with skeletal deformities in humans (Schwartz-Jampel syndrome (SJS) & Dyssegmental Dysplasia Silverman-Handmaker type (DDSH)). Using a perlecan-deficient mouse model (termed Hypo), we showed severe osteoporotic phenotype in these mice, suggesting impaired bone remodeling process. The purpose of this study was to investigate the cellular mechanisms underlying this severe osteoporotic phenotype. *METHODS:* Male C57BL/6J (WT) and Hypo mice were sacrificed at 8, 18 and 41 weeks. Femora were harvested and fixed in 4% PFA. Left femora were processed for paraffin embedding & sectioned at 5um to stain for tartrate-resistant acid phosphatase (TRAP) activity. Right femora were embedded in methyl methacrylate (MMA) and sectioned at 8 um for histo-morphometry. MSCs, harvested from femora, were plated in 25cm2 flasks for Colony forming unit-fibroblast (CFU-F) quantification and separate set of cells were cultured in osteogenic media (19 days) and stained with 2% Alizarin Red to access mineralization. *RESULTS:* TRAP staining showed higher osteoclastic activity in Hypo at 8 and 41 weeks. Mineral apposition rate (MAR) did not differ between WT and Hypo at 18 and 41 weeks, except higher MAR in WT at 8 weeks. The ability of MSCs forming colonies did not differ between WT and Hypo. However, MSCs from Hypo differentiated faster than WT. *DISCUSSION:* Our histo-morphometry and histology show impaired osteoblastic activity (MAR) in Hypo at 8 weeks and significantly higher osteoclastic activity at 8 and 41 weeks. MSC study suggests that perlecan-deficiency doesn't diminish the "stemness" of MSCs. The faster mineralizing rate in Hypo-MSC suggests that the pool of osteoblast progenitors might be spent faster in Hypos. These observations may partially explain the significantly lower trabecular bone volume in Hypos. *SIGNIFICANCE:* Perlecan deficiency is a risk factor of osteoporosis. This study attempted to elucidate the cellular mechanisms underlying the severe osteoporotic phenotype

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

3 MODELING PRESSURE-DRIVEN FLUID FLUX AND TRIBOLOGICAL REHYDRATION IN ARTICULAR CARTILAGE

Margot Farnham[1], Brian T. Graham[2], David Burris[1,2], Christopher Price[1,2]

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Osteoarthritis (OA) is the most common chronic joint condition and a leading cause of adult disability. Healthy articular cartilage maintains low friction under large applied loads, allowing for smooth joint motion and minimal wear. Such function is made possible in part through a recently discovered mechanism: tribological rehydration, where fluid lost to exudation is driven back into cartilage through sliding-induced hydrodynamic pressurization, restoring load and lubrication supported by interstitial fluid. Understanding the mechanisms responsible for this behavior is key, because when cartilage lubrication mechanisms breakdown, friction increases, causing wear which may contribute to the initiation/progression of OA. Currently, no computational models link the low-friction behavior of cartilage with sliding-induced fluid flow through the tissue. In this study, a finite element (FEBio) model was created to examine fluid transport within articular cartilage to understand how tissue is rehydrated during simulated sliding conditions. This model is validated against experimental data collected from large bovine osteochondral plugs. Cartilage is compressed to 7N and slid at physiologically relevant speeds against a rigid platen on a custom tribometer. Tribological rehydration is accounted for in the model through implementing a variety of pressure-driven fluid flux boundary conditions in the contact between a biphasic-modeled cartilage section and a rigid platen in the convergent-wedge stationary contact area configuration. This model predicts the strain responses of cartilage during compression and simulated sliding using inputs of sample-specific material properties, enabling comparison of healthy tissue to tissue affected by OA. The model allows for examination of fluid flow within the solid contact, providing another source of support for tribological rehydration. This model can be expanded further to elucidate fluid flow for other applications like drug delivery, providing a way to simulate preliminary studies for fluid flow involved in cartilage biomechanics.

4 MODELING TENDON VISCOELASTICITY, PLASTIC DEFORMATION, AND DAMAGE USING REACTIVE INELASTICITY

Babak N. Safa [(1,2)], Michael H. Santare [(1)], Dawn M. Elliott [(2)]

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Tendon transmits load from muscle to bone and with large and/or frequent loading a loss in mechanical properties can lead to clinical disorders such as tendinopathy. This loss of mechanical properties is a form of inelastic behavior. The major inelastic behaviors of tendon are viscoelasticity, plastic deformation, and damage. Due to the overlapping effect of these behaviors, their direct experimental evaluation is a convoluted problem. Thus, a theoretical framework is needed to characterize these behaviors. Despite decades of studies on tendon mechanics a comprehensive theoretical treatment of inelasticity is missing. The objective of this study was to formulate a comprehensive modeling framework, reactive inelasticity, for modeling inelastic behaviors that is based on molecular bond kinetics.

In this study we utilize the kinetics of molecular bonds based on the irreversible thermodynamic process framework to model: viscoelasticity, plasticity, and damage. We define three types of bonds: (1) Formative (for viscoelasticity), (2) Permanent (for hyperelasticity), and (3) Sliding (for plastic deformation). These bonds result in three distinct mechanical behaviors at different ranges of kinetic rates of breakage and reformation of bonds, where the same sets of constitutive equations are used. Damage is modeled by reducing the number fraction for each type of bond that results in a softening behavior. Finally, we provide several numerical examples of the mechanical responses of individual bond types and their combinations, such as incremental stress relaxation softening, and creep rupture that have practical importance for characterization of mechanical behavior of tendon and other soft tissue. This study is significant in addressing inelastic behavior of tendon based on its molecular structure, which can be used to identify structural relationships between its mechanical behavior and external loading.

5 STATIN AND BISPHOSPHONATE PREVENT OA INITIATION BY INHIBITING RHO ACTIVITY

Yilu Zhou, Mengxi Lv, Liyun Wang, X. Lucas Lu

Department of Mechanical Engineering,
University of Delaware

Bisphosphonates are a class of drugs for the treatment of osteoporosis. A few animal studies have shown that administration of bisphosphonates immediately after joint injuries can prevent or delay the cartilage degeneration, i.e., post-traumatic OA. However, the mechanisms of the chondro-protective function of bisphosphonates is unknown. In this study, we will test the hypothesis that the chondro-protective function of bisphosphonate is related to the inhibition of mevalonate pathway in chondrocytes.

Cylindrical cartilage explants with no subchondral bone attached were harvested from calf knee joints. After one-week culture in serum medium to mimic the joint bleeding induced damage on cartilage, two downstream chemicals of mevalonate, FOH and GGOH, were added together with the ZA (1μM) to examine whether FOH and GGOH can abolish the protection effects of ZA. Two specific inhibitors of mevalonate pathway, GGTI and FTI, were added to examine whether they have similar chondro-protective effects with ZA. Outcome parameters in three cartilage explant studies included the mechanical properties of tissue, GAG and collagen content, histological analysis, gene expression by qRT-PCR, and chondrocyte calcium signaling.

After one week serum exposure, cartilage explants were cultured in ZA or ZA+FOH+GGOH supplemented medium. The beneficial effects of ZA was partially abolished by the presence of FOH and GGOH (n = 12), indicating the involvement of mevalonate pathway in the action of ZA. Moreover, co-treating the samples with FTI/GGTI revealed protection effects of GGTI on the tissue (n = 8).

In this study, we demonstrated the chondro-protective effects of bisphosphonates and this effect can be related to the inhibition of mevalonate pathway in chondrocytes.

PODIUM PRESENTATIONS

Session 2

1 INFLUENCE OF KNEE FLEXION ANGLE ON PATELLAR TENDON STRUCTURE AND MECHANICAL PROPERTIES

Andrew Sprague[1], Courtney Cox[1], Daniel Cortes[2], Karin Silbernagel[1]

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INTRODUCTION: Patellar tendinopathy is a chronic, degenerative condition of the patellar tendon. The structure and mechanical properties of the patellar tendon may assist in diagnosis and provide insight into tendon health. Patient positioning while performing these examinations varies and the effects of changing knee angles is unclear. Therefore, the purpose of this study was to determine the influence of knee angle on patellar tendon structure and mechanical properties.

METHODS: Ten healthy subjects (5 male) with a mean (SD) age of 24.1 (±5.6) years were recruited to assess patellar tendon structure via ultrasound imaging. Nine healthy subjects (2 male) with an mean (SD) age of 29.3 (±14.8) years were recruited to examine patellar tendon mechanical properties by continuous shear wave elastography (cSWE). Repeated ultrasound images were taken for tendon length, thickness, and cross-sectional area (CSA) at 30° and 90° of knee flexion. cSWE was also completed at 30º and 90º of knee flexion to obtain patellar tendon shear modulus and viscosity. Measures were performed by a single examiner. Average measures were used for comparison. Paired t-tests were used to compare differences in outcome measures between positions.

RESULTS: There were no statistical differences for patellar tendon length, thickness or CSA between 30° and 90° of knee flexion ($p>0.05$). Shear modulus and viscosity were significantly higher at 90° than 30° of knee flexion ($p<0.001$).

CONCLUSIONS: In research and clinical practice a standardized patient position should be used when assessing patellar tendon mechanical properties to allow for comparison between individuals and time points.

2 RECOVERY OF DAILY WALKING WITHIN THE FIRST MONTH AFTER TOTAL KNEE ARTHROPLASTY (TKA): A PRELIMINARY STUDY

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

University of Delaware Departments of Physical Therapy

Purpose: Patients are encouraged to walk immediately after TKA. Post-operative impairments such pain, and restricted range of motion initially limit the ability to take more steps/day, i.e., daily walking. However, as these impairments resolve, physical function and daily walking is thought to improve. Little is known about recovery of daily walking immediately after TKA and how this relates to recovery of physical function. Methods: We utilized data from 68 participants enrolled in a study at the University of Delaware. All participants received PT for a unilateral TKA. Daily walking was measured as steps/day using an accelerometer. Physical function was measured on the Knee Outcome Score (KOS). Participants were categorized into three post-TKA groups based on the number of days from surgery to the start of PT; Group 1 (≤ 7days), Group 2 (8-14 days), Group 3 (15-30 days). We compared change in daily walking and physical function across groups using linear regression (alpha level 0.05). Results: 58 participants were included ([mean (±sd)] age 65±8 years, 55% female, BMI 33±6.7 kg/m2). There was no difference in daily walking between groups. Group 2 walked 213 steps fewer than Group 1 (95% CI [-1435, 1008]) and Group 3 walked 677 more steps than Group 1 (95% CI [-530, 1884]). In contrast, physical function was statisically different, 22-points better for Group 3 compared to Group 1 (KOS difference 95% CI [10, 38]) but not different in Group 2 compared with Group 1, with a 7-point difference (KOS difference 95% CI [-6, 21]). Conclusion: While physical function improves, daily walking does not within the first month after TKA.

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

3 POWER IMBALANCE RESOLVED WITH NOVEL 6 DOF SEGMENTAL POWER ANALYSIS

Anahid Ebrahimi[1], John Collins[1,2], Jill Higginson[1] and Steven Stanhope[1]

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[2]Naval Medical Center, San Diego

Segmental powers are indicative of energy flow to and between segments and are traditionally calculated using segment endpoint dynamics (traditional kinetic method). A theoretically equivalent method is to measure changes in the segment's energy state (kinematic method). However, the traditional kinetic and kinematic methods do not provide experimentally equivalent results for segments proximal to the foot during stance phase of gait, resulting in a "power imbalance". The purpose of this study was to computationally equate the kinetic and kinematic methods by accounting for movement at segment ends in a 6 degree-of-freedom (DOF) segmental power analysis (6 DOF kinetic method). Our computational derivation determined a power correction term, equal to the dot product of the ground reaction force with the cross product of segment angular velocity and a vector from the distal end of the segment to the proximal end of the adjoining distal segment. A statistical equivalence test revealed that mean powers calculated with the 6 DOF kinetic method were experimentally equivalent to the kinematic method for the shank, thigh, and pelvis, while the traditional kinetic method was not. Power imbalance between the 6 DOF kinetic method and the kinematic method was reduced by an order of magnitude compared to the imbalance between the traditional kinetic method and the kinematic method. This novel 6 DOF kinetic segmental power method is computationally correct and supports the improved analysis of energetic flow between segments.

4 ASSESSING THE VALIDITY OF THE G-WALK BTS ON INDIVIDUALS WITH UNILATERAL TRANSTIBIAL AMPUTATIONS

[1]Daniel Courtney, [1]Corey Koller, BS, [1]Cory Cacciola, [2]John Horne, CPO, [1]J. Megan Sions, PhD, DPT, PT, [1]Elisa S. Arch, PhD

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Prosthetists lack an objective, cost effective, quick, and easy method to assess prosthesis prescription for an individual with a lower limb amputation. The G-Walk BTS is a small, portable device that uses tri-axial accelerometers, gyroscopes, and magnetometers to measure spatiotemporal parameters of gait, thus providing the potential to readily assess these parameters in a clinical setting. The aim of this study was to determine the concurrent validity of the G-Walk BTS with traditional Motion Capture Analysis. Nine unilaterial transtibial subjects (6 males, 60.9 ±11.4 years, 1.74 ±0.11 meters, 85.9 ±25.7 kilograms) consented to participate in this study. Subjects walked over a flat surface for a distance of 6 meters at their self-selected walking speed determined by a 10-meter walk test before the commencement of the trials. The G-Walk device rested on the fifth lumbar vertebra and connected to G-Studio software via bluetooth while the Motion Capture system used a six-camera set-up, reflective markers, and two ground-embedded force plates. Spatiotemporal parameters of cadence, speed, gait cycle duration on prosthetic and sound limbs, and step length on both prosthetic and sound limbs were obtained and analyzed from a minimum of 3 trials from each subject. Absolute average percentage error was less 8% for all of the parameters except speed and was less than 4% for gait cycle duration of the prosthetic limb and cadence. Levels of agreement between the two systems were all less than 15% difference, providing evidence that the G-Walk may be clinically acceptable for assessing gait pending further research.

5 MECHANICAL PROPERTIES OF THE ADOLESCENT BRAIN

GMcIlvain, CJohnson

University of Delaware

Introduction: The mechanical properties of the brain, imaged by magnetic resonance elastography (Manduca, 2001), have emerged as sensitive measures of tissue stiffness. Studies of the adult brain have revealed a strong structure-function relationship between hippocampal viscoelasticity and memory performance. However, there are currently no MRE studies that have characterized the stiffness of adolescent brains. This work aims to address this gap in the literature to provide in vivo measurements of the adolescent human brain. Ultimately, these MRE measurements can provide a sensitive approach to studying how the brain matures.

Methods: A sample of N=46 healthy, adolescent children (20/26 M/F; age 12-14) completed an MRE scan session on a Siemens 3T Trio scanner. MRE displacement data was used to create maps of viscoelastic shear stiffness (McGarry, 2012). The regional stiffness was quantified for comparison with literature values of adult stiffness by creating regions of interest of the brain lobes and subcortical regions and compared to (Murphy 2013) and (Johnson 2016) respectively.

Results: Both the cerebrum and cerebellum showed similar stiffness values as in the adult brain, with adolescent brain with differences of -0.3% and 1.7%, respectively. The four main lobes of the cerebrum are all softer in adolescents (differences -5% to -13%). For the subcortical regions, the caudate and thalamus were very similar in adults and adolescents (-0.8% and 0.5% difference); the pallidum and the putamen were much stiffer in adolescents (8.4% and 6.9%); the amygdala and the hippocampus were much softer (-18.3% and -10.8%).

Conclusions: MRE of the adolescent brain can be used to identify trends relating to the development of brain structure and eventually provide insight into behavior and social development through sensitive structure-function relationships.

POSTER PRESENTATIONS

Track 1

Cells Tissue Biomechanics

Bone

1 QUANTIFYING THE LACUNAR-CANALICULAR SYSTEM OF HUMAN BONE

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Departments of Biological Sciences and Mechanical Engineering

Osteocytes are embedded within an interconnecting pore network and play an important role in maintaning bone health.The extensive pore network (termed lacunar-canalicular system, LCS) houses the osteocytes' cell bodies and their numerous dendrite cell processes. LCS is the major transport conduit responsible for nutrient supply between osteocytes and vasculature and for cell-cell signaling among osteocytes and with surface cells. Recent evidence suggests that LCS parameters such as osteocyte lacunar density and the number density of canaliculi may function as indicator to bone health. While there have been studies providing information on the LCS of animals such as mice, quantified data concerning human LCS are currently lacking. In this study, we obtained human femur samples from 25 patients ranging from 51 to 95 years old (8 males and 17 females). Among the 25 patients, 19 were treated for osteoporosis (10 endured hip fracture) and 6 osteoarthritis. Transverse sections were cut from the femoral neck, grind down to 100-200 μm and bulk-stained with sodium fluorescein dye. Confocal laser scanning microscopy was used to image one section per patient and three locations per section and 3 imaging fields per location. Our results demonstrate that age has significant effects on the area, perimeter, major and minor axis length of the lacunae and the total number of canaliculi. However, the number density of canaliculi (per unit lacunar perimeter) did not differ with age in agreement with our previous results on mice. Significantly higher total canaliculi length per unit volume were observed in bones from male patients. Due to the small sample size, we did not detect significant effects of osteoporosis and osteoarthritis diagnostics on bone LCS parameters.

2 PROFILING THE COMPOSITION OF OSTEOCYTE PERICELLULAR MATRIX (PCM) IN VIVO AND IN VITRO

Jerahme Martinez, Shaopeng Pei, Shubo Wang, Ashutosh Parajuli, Liyun Wang

Department of Mechanical Engineering, University of Delaware

Osteocytes make up the overwhelming majority of the cells in bone and play a crucial role in maintaining bone homeostasis and orchestrating bone's responses to mechanical loading. Increasing evidence suggests the proteoglycan-rich osteocyte pericellular matrix (PCM) functions as a mechanical sensor for detecting external loading signals. Previously, we identified perlecan/HSPG2, a large heparan sulfate proteoglycan, as a key component of the osteocyte PCM and demonstrated its importance for in vivo loading and unloading. In those studies, we used a perlecan-deficient mouse that mimics the human skeletal disorder Schwartz-Jampel syndrome (SJS), which has symptoms of osteoarthritis and osteoporosis. We hypothesize that, in addition to perlecan, other molecules associated with cell membrane are present in the osteocyte PCM. We aimed to test this hypothesis in vivo and in vitro. We first characterized the in vivo PCM composition, using a mass spectrometry-based glycoproteomic approach on bone tissue extracts isolated from the wild-type and perlecan-deficient mice. We also investigated the PCM of commonly used osteocyte cell lines, MLO-Y4 and IDG-SW3. To enrich PCM constituents for mass spectroscopy analysis, we used a azide-modified sugar to metabolically label osteocyte-secreted sialyated glycoproteins, and then isolated labeled products via dibenzocyclooctyl (DBCO) copper-free click chemistry. Here, we provide a comprehensive expression profile of native osteocyte matrix molecules, which will aid future studies seeking to identify candidate targets that may be involved in osteocyte's mechanosensing complex. As demonstrated, our strategy serves as a powerful approach to quantitatively detect PCM alterations in vivo and in vitro.

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

3 ACTIVATION OF ERK BY A NOVEL PEPTIDE, CK2.3, INHIBITS OSTEOCLASTOGENESIS OF RAW264.7 CELLS

*John Nguyen, Anja Nohe**

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Osteoporosis is a bone disease characterized by the loss of bone mass in patients. Available treatments for osteoporosis, including bisphosphonates and parathyroid hormones, often limit their target to either inhibiting osteoclastogenesis or enhancing osteoblastogenesis. There has never been a treatment that can target both.

Bone morphogenetic protein 2 (BMP2) was demonstrated to have effect on enhancing both osteoclastogenesis and osteoblastogenesis. In addition, our laboratory previously showed casein kinase 2 (CK2) to have a regulatory function on BMP2-induced osteoblastogenesis and osteoclastogenesis. We designed a synthetic peptide, namely CK2.3, to inhibit the interaction of CK2 to BMP receptor Ia (BMPRIa) at amino acid 475-479. CK2.3-injected mice showed increase of osteoblastogenesis and decrease of osteoclastogenesis, however, the mechanism was unknown.

The focus of this project was on the suppressing effect of CK2.3 on osteoclastogenesis. Akt, Erk, and p38 were shown to act downstream of BMP2 and played critical roles in osteoclastogenesis. Interestingly, we previously showed CK2.3-injected mice had an increase in p-Erk expression. These mice also had an increase in bone mineral density. To elucidate the mechanism of CK2.3, we used monocyte/macrophage RAW264.7 cells as a model to study its effect on osteoclastogenesis. Using inhibitors to inhibit pathways that were known to involve in osteoclastogenesis, we showed that U0126, a Erk inhibitor, increased osteoclastogenesis at 10μM in the presence of 100nM CK2.3. Osteoclastogenesis was decreased in the presence of 100nM CK2.3 alone. Together, the result suggested CK2.3 suppressed osteoclastogenesis of RAW264.7 cells via activation of Erk. For the first time, we were able to show CK2.3 promoted osteoblastogenesis and inhibited osteoclastogenesis via activation Erk.

4 EFFECTS OF PERLECAN/HSPG2 DEFICIENCY ON MRNA CHANGES IN MECHANICALLY LOADED BONE

Sucharitha Parthasarathy[1], Ashutosh Parajuli[2], Jerahme Martinez[3], Catherine Kirn-Safran[1], Liyun Wang[1,2,3]

Department of Biological Sciences[1], Biomedical Engineering[2], Mechanical Engineering[3], UD

Introduction: Perlecan/HSPG2 (Pln), a large Heparan Sulfate Proteoglycan found residing in the osteocytic pericellular matrix (PCM) is a major component of the transverse tethering elements present in the lacunar-canalicular system that help relay mechanical signals. Pln's role in osteocytic mechanosensing was studied by using a transgenic mouse model with reduced Pln expression (termed Hypo) that mimics the conditions of human Schwartz-Jampel Syndrome. Previous studies have shown that Pln deficiency alters pericellular space and attenuates Hypo bone's anabolic response to loading. We hypothesize that the presence of Pln in the PCM is partly responsible for the bone anabolic response to load and that its absence in Hypo bone PCM alters their mRNA expression profile after loading when compared to loaded WT bones.

Method: 19-week-old WT (n=10) and Hypo (n=7) male mice were subjected to uniaxial-tibial compressive loading (8.5N peak load, 4 cycles/sec, 5 minutes/session) and euthanized 24 hrs post-load. RNA was extracted from the loaded and non-loaded tibiae of both WT and Hypo and the steady state mRNA levels of various bone cell marker genes and matrix proteins were compared using a real-time PCR approach.

Results: One bolus of loading resulted in 3-, 2.3- and 1.6-fold increases in transcript levels of osteoprotegerin (OPG), E11/gp38, and RANKL in WT tibiae whereas only 1.75-, 1.4- and 1.25-fold increases were observed in Hypo animal tibiae, respectively. Bone matrix proteins in WT animals showed an approximate 2.6-fold increase for ALP and Pln transcripts and 1.6-fold increase for Col1a1, OCN, DMP1 and OPN transcripts while Hypo animals showed less than 1.5-fold change with all the matrix proteins studied.

Conclusions: Our results support the postulate that Pln deficiency is a risk factor for osteoporosis via decreased bone mechanosensivity to load.

5 METABOLIC LABELLING OF OSTEOCYTE PERICELLULAR MATRIX IN VITRO AND IN VIVO

Shaopeng Pei, Jerahme Martinez, Shubo Wang, Shongshan Fan, Catherine Kirn-Safran, X. Lucas Lu, Liyun Wang

Introduction: In bone, the pericellular matrix(PCM) surrounding osteocytes is hypothesized to form a mechanosensing complex for bone mechanotransduction. Yet, there are very limited data on the dynamics of osteocyte PCM. We developed a novel metabolic labeling method using click chemistry to label the osteocyte PCM and track the fate of labeled PCM components in vitro as in a classic "Pulse-Chase" experiment. Our overall goal is to track and quantify the composition of the osteocyte PCM and the changes under various mechanical environments. Methods:MLO-Y4 cells were fed with a modified sugar (Ac4GalNAz) for 3 days before "click reaction" with fluorescent dye MB 488 DBCO on day 4. The labeled PCM was imaged at 1,2,3,4,5 days post click to track the PCM turnover. Male B6 mT/mG transgenic mice were intraperitoneally injected with Ac4GalNAz or vehicle (DMSO) for 7 consecutive days. MB 488 DBCO was injected on day 8. Tibiae from the mice were harvested and imaged under the confocal microscope. Results: For in vitro PCM visualization, we observed a nicely labeled fibrous matrix outside the cell body. For in vivo labeling studies, the labeled osteocyte PCM shows "halo" like structure surrounding the red stained membrane, with negligible green signal form the vehicle treated group. In vitro PCM tracking showed a rapid loss of the newly synthesized PCM with a half-life time of approximately 24 hrs. Conclusion: Rapid loss of PCM in vitro may result from faster diffusion in media compared to the confined environment in vivo. The successful labeling of osteocyte PCM in vivo will help us further study the turnover rate of osteocyte PCM in their native environment and the components of the PCM mechanosensing complex.

6 DEVELOP AN ACTIVE FLUORESCENTLY-TAGGED CK2.3 PEPTIDE TO ANALYZE ITS BONE INDUCING CAPABILITIES.

Vrathasha, Rebecca Noll, and Anja Nohe.

Osteoporosis is a debilitating bone disorder where patients are characterized with low bone density. Per NOF, one in two women and one in four men age 50 and older will break a bone due to osteoporosis. Osteoporosis is caused by: a) excessive bone resorption by osteoclasts and/or b)failure of osteoblasts to produce and replace the resorbed bone leading to weak and porous bone. Majority of the existing treatments target osteoclast activity, but osteoclasts are essential for maintaining body homeostasis. Thus, there is a need for a novel treatment that specifically drives osteoblastogenesis.

One of the well understood BMP2 induced signaling occurs via BMPR-IA and BMPRII. Our lab has reported an interaction between BMPR-IA and Casein Kinase 2(CK2). CK2 is a ubiquitously expressed enzyme that plays a key role in various cellular activities. Using the interaction site(2.3), a peptide was synthesized that would bind to CK2, preventing it from interacting with BMPR-IA at the respective site. Treatment of primary osteoblast cultures with CK2.3 enhanced bone formation without the increase in osteoclast activity; and increased overall BMD and mineral apposition rate in 8-week-old mice. We have established that CK2.3 mediates MSCs to take on osteoblastic lineage.

To determine the effects of peptide CK2.3 within the cell and in-vivo, quantum dots(QDots) will be used as a probe. QDots are semiconductor nanoparticles that are fluorescent under UV light and ideal for live-cell imaging. Peptide will be conjugated to QDots by forming an amide bond. FTIR spectroscopy will be used to confirm the conjugation, while confocal imaging will show its uptake into C2C12 cells(murine myoblasts) and its interaction with CK2. This technique will provide insight into the workings of the peptide within a cell and eventually in-vivo.

Denotes Poster #

All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

7 A NOVEL BMP RECEPTOR PEPTIDE INCREASES BONE FORMATION IN ISOLATED PRIMARY CELLS

Hilary Weidner, Marks Eskander, Debbie Dibert, and Anja Nohe

Osteoporosis is a bone disease that is characterized by low bone density. This leads to deterioration of the bones, which ultimately increases the occurrences of bone fractures or breaks. The treatments are very expensive (both emotionally and fiscally), and the costs will only steadily rise as the population of elderly increases, which is why it is necessary to find novel treatments. On a cellular level, normal bone has a balance between bone forming cells (osteoblasts) and bone remodeling cells (osteoclasts). Primary osteoporosis is characterized by having more osteoclast activity, less osteoblast activity, and an increased amount of adipocytes (fat cells). However the majority of treatments on the market focus on decreasing osteoclast activity and not increasing osteoblast activity or decreasing adipocyte population. Our lab has designed a novel peptide known as CK2.3 that binds to an interacting protein called CK2 thus inhibiting it from binding to a specific portion of it's receptor, BMPRIa. Primary cells from patients undergoing osteoporosis or osteoarthritis were extracted and grown. The cells were from human femoral heads, which were removed via hip arthroplasty surgery from Christiana Care Hospital in Newark, Delaware. The cells were treated with our novel peptide, CK2.3 and a mineralization (osteoblast activity) and lipid droplet assay (fat cell formation) were conducted in order to measure cellular activity. Our lab has shown that treatment of CK2.3 increases the mineralization (osteoblast activity) and reduces lipid droplet formation (fat cells) in extracted primary cells from human femoral heads. The novel peptide CK2.3 could be utilized as a potential treatment for primary osteoporosis as it focuses on increasing osteoblast activity.

POSTER PRESENTATIONS

Track 1

Cells Tissue Biomechanics

Cartilage/ IVD/ Ligament/ Tendon

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

8 VALIDITY AND RELIABILITY OF ULTRASOUND IMAGING FOR EVALUATING ACHILLES TENDON INSERTION

Nabeel Hamdan Alghamdi, Bhavana Aitha, Megan Killian, and Karin Gravare Silbernagel

Introduction: Ultrasound (US) imaging for evaluating Achilles tendon (AT) structure is common, however its reliability and validity for measuring the insertion to the calcaneus has not been investigated. The purpose of this study was therefore to evaluate the reliability and validity of using US for measuring AT insertion area on the calcaneus.

Methods: Seven cadavers (12 tendons) were used to compare AT insertion length (distance from proximal attachment to distal attachment) and width (distance from medial to lateral tendon edge) measurements from ultrasound images with actual measurements after dissection. B-mode ultrasound imaging was used to obtain the images. Two testers measured the US images independently and inter-tester reliability of the measurements was analyzed with intra-class correlation coefficient ($ICC_{2,3}$).

Results: Inter-rater reliability for measuring insertion area on US imaging was good to excellent for insertion length, width at proximal attachment, distal attachment and before calcaneal level, (ICC=0.797, 0855, 0.806, and 0.622) respectively. There were no significant ($p>0.05$) differences between US measurements with cadaveric measurements for insertion length, tendon width at distal attachment and before calcaneal bone, $p>0.05$. There were moderate correlations between US measurements and cadaveric measurements for insertion length ($r=0.647$, $p=0.023$) and tendon width at the level before calcaneal bone ($r=497$, $p=0.12$). Although the correlation between US measurements with cadaveric measurements tendon width at the level of proximal attachment was good ($r=0.751$ $p=0.005$), there was a significant difference between the measurements ($p<0.01$).

Conclusions: US imaging was found to be reliable and valid to determine AT insertion length and tendon width. Having such methodologies to quantify changes at AT insertional area may be beneficial for understanding enthesopathy progression and the efficacy of treatment in the clinic.

9 REPEATED INTRA-ARTICULAR INJECTION OF ZOLEDRONIC ACID SUPPRESSES CARTILAGE EROSIONS FOLLOWING DESTABILIZATION OF THE MEDIAL MENISCUS IN MICE

Michael David, Melanie Smith, Rachael Pilachowski, John Lowman, Christopher Price

University of Delaware, Newark, DE

Post-traumatic osteoarthritis (PTOA), the accelerated degeneration of cartilage due to traumatic joint injury, is incurable and poses significant socioeconomic burden. In searching for PTOA modifying therapeutics, studies have explored the use of bisphosphonates (BPs), including the potent 3rd generation BPs (e.g. zoledronic acid [ZA]). Systemically delivered, high-dose ZA has demonstrable anti-osteoarthritic and anti-inflammatory efficacy pre-clinically. Nonetheless, risk of significant skeletal side-effects due to continuous, high-dose, systemic ZA treatment represents a barrier to systemic ZA administration as a clinical therapeutic. However, recent work has shown that ZA has direct, beneficial effects on chondrocyte metabolism and health in situ. Furthermore, ZA has macrophage depleting activities, which can reduce inflammation in a variety of diseases. These results suggest that local joint delivery of BPs, via intra-articular (i.a.) injection, represents an alternative strategy for utilizing ZA in preventing PTOA; yet, application of ZA in this manner is nascent. Specifically, we hypothesize that i.a. injection of ZA, through its direct chondroprotective and anti-inflammatory activities, will suppress cartilage damage and degenerative joint changes post-injury. Therefore, the objective of this study was to determine the efficacy of locally injected (single vs repeated injection) ZA into the knee as an anti-osteoarthritic and anti-inflammatory therapeutic in a mouse model of PTOA, the destabilization of the medial meniscus (DMM). In this study, we demonstrated that repeated, i.a. injection of ZA can suppress joint changes and cartilage erosions, but not inflammation, post-DMM. This research establishes a framework to investigate the in vivo mechanisms underlying the efficacy of i.a. ZA in treating PTOA, and for exploring the translation of i.a. ZA as an alternative strategy for PTOA therapy.

10 LASERS AND LUBRICATION: SHEDDING LIGHT ON HOW CARTILAGE REALLY WORKS.

Brian T. Graham[1], Axel C. Moore[2], David L. Burris[1,2], Christopher Price[1,2]

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Cartilage covers the ends of the bones in our joints, facilitating joint movement by providing low friction and absorbing the high impact loads experienced during activities. Furthermore, it appears to wear very slowly, with the 1-2 mm of cartilage observed in young adults lasting well into old age.

As a highly porous material, the majority of its mass consists of water residing within this pore space. Water plays two important roles in cartilage. First, since cartilage is avascular, the movement of the water facilitates nutrient, waste, and molecular exchange. Second, when a joint is loaded, the water in cartilage is pressurized and supports the applied force, shielding the solid matrix and cells from stress. This fluid load support is also necessary to maintain low friction.

However, over time, pressure gradients from constant loading cause water to flow out of the cartilage. This reduces the transport of molecules to the cells, puts more stress on the solid matrix and cells, and increases friction. Our collaborators have theorized that the relative sliding motion of cartilage in our joints creates hydrodynamic pressures that can pump the water back into the cartilage, preserving its function, a process called "Tribological Rehydration". Our interdisciplinary approach combines their mechanical test setups with state of the art biomedical imaging techniques to test this theory. Using a laser scanning confocal microscope and fluorescent tracer molecules, we tracked the movement of fluid in loaded and slid cartilage

11 VARIABLES MEASURED FROM MR IMAGES ACCURATELY CLASSIFIES PFIRRMANN DEGENERATION

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Discogenic low back pain (LBP), a disabling condition that affects over 20 million people, is associated to lumbar disc degeneration (LDD). In vivo assessments of LDD from magnetic resonance (MR) images do little to detect painful discs, as there is no physical reference standard for LBP3. The Pfirrmann grading scheme, the standard to assess LDD, subjectively classifies discs according to disc structure and hydration but does not classify discs relative to an age-normal population or to the normal patient anatomy itself. An LDD classification system that is based upon measurements from MR images and normalized to an inter- and intra-subject reference standard may provide a valid LDD diagnostic test. Identification of proper measurement variables ensures adequate objectivity of this classification system. The objective of the study is to 1) determine how well objective measurement variables can predict Pfirrmann grade and 2) identify variables that drive accurate Pfirrmann grade prediction. A set of measures including anterior-posterior (AP) width, mid sagittal area, a series of disc heights, and T2 relaxation time were acquired from T2-weighted MR scans of 222 cadaveric discs, which were scored according to Pfirrmann. Canonical discriminant analysis and multinomial logistic regression were applied to the data set to identify variables that drive accurate classification of Pfirrmann score. The set of MR measures accurately predicted Pfirrmann grade for ~75% of discs, and within ± 1 grade for ~98% of discs. The primary predictors of Pfirrmann score are AP width, area, T2 score, and central disc height. This study demonstrated that objective MR measures accurately predicts Pfirrmann grade. Identifying the key predictors of Pfirrmann-scored LDD is the first step in developing an objective classification system for LDD.

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

12 INVESTIGATING MECHANISMS OF TENDON DAMAGE OF RAT PLANTARIS TENDON AT MULTISCALE

Andrea H. Lee (1), Dawn M. Elliott (1).

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Plantaris tendon is one of the superficial tendons and is involved with plantar flexion. Our previous study addressed damage mechanisms of tendon by relating the altered macroscopic mechanical parameters to the microstructural changes using rat tail tendon. Yet, it is still unclear if the damage mechanisms investigated in rat tail tendon can be applied in more stress bearing tendons. Thus, we choose plantaris tendon to investigate the damage mechanisms. Rat plantaris tendon was tested on a uniaxial tensile device mounted on a confocal microscope to simultaneous quantify both macro- and microscale responses. Investigation of damage mechanisms of plantaris tendon showed consistent result with our previous observations at both macro and microscale. The mechanical response at the macroscale showed elongated toe-region, decreased linear region modulus, and increased damage threshold. In addition, we observed localized damage at the interfibrillar structure at the microscale. Thus, our study suggests that the damage mechanisms we have established in rat tail tendon can apply to other higher stress bearing tendon such as plantaris tendon. Establishing the mechanism of damage at multiple length scales can improve prevention and rehabilitation strategies for tendon pathology.

13 A CHEMOGENETIC TOOL TO CONTROL CHONDROCYTE ACTIVITY IN VITRO

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[1]Biomedical Engineering
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Calcium is a critical second messenger involved in chondrocyte mechanosensing and mechanotransduction signaling cascades. Several distinct calcium signaling mechanisms implicated in chondrocyte mechanotransduction have been identified through non-specific interrogative techniques, such as mechanical perturbation or exogenous application of endogenous soluble factors. These approaches 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. Both approaches can converge on multiple signaling pathways that regulate calcium signaling through a variety of mechanisms. Thus, there is a need for a precise and well-controlled calcium-specific signaling tool to assist in dissecting the role of intracellular calcium ([Ca2+]i) in chondrocyte mechanobiology and homeostasis. Recent developments in molecular biology have generated an engineered G-protein-coupled receptor (GPCR) via directed molecular evolution that has been selected to be solely activated by clozapine n-oxide (CNO), a pharmacologically inert compound that only exhibits activity on this receptor. This GPCR, termed a DREADD (Designer Receptor Exclusively Activated by Designer Drugs), regulates calcium activation through the PLC-IP3-DAG pathway. Here, DREADD-transfected chondrogenic ATDC5 cells were exposed to a range of CNO concentrations (100nM-1uM), GSK101, or 50% hypotonic shock, the latter two of which have been shown to cause upregulation of [Ca2+]i entry. A custom MATLAB program was used to analyze the calcium response and temporal kinetics via Fluo-8 AM fluorescence. CNO administration resulted in a rapid, coordinated, dose-dependent transient calcium response in DREADD-transfected cells and the temporal kinetics of [Ca2+]i regulation were similar to hypotonic-shock-activated cells. This study demonstrates the potential use of a novel tool for exploring the role of controlled calcium signaling in chondrocyte biology, cartilage pathology, and the improvement of cartilage tissue engineering.

14 THE ROLE OF INTERFACIAL SLIDING IN MEDIATING THE FUNCTIONAL PERFORMANCE OF ARTICULAR CARTILAGE

A.C. Moore[1], B.T. Graham[2], C. Price[1], and D.L. Burris[2]

[1]Biomedical and [2]Mechanical Engineering

Cartilage loses interstitial fluid and, consequently, compresses over time in inactive joints. Conversely, cartilage recovers interstitial fluid and thickens in active joints. The balance between loss and recovery of interstitial fluid is critical to joint health since the tribological, mechanical, and cellular functions of cartilage depend on the presence of interstitial fluid. Whereas fluid exudation is the natural consequence of internal load-carrying pressure, recovery in the presence of load-carrying has only been explained on the basis that cartilage imbibes fluid when articulation intermittently exposes the contact to the bath. Here we demonstrate the same fluid recovery process found in-vivo without ever exposing the contact to the bath thereby eliminating the only existing explanation for the recovery phenomenon. We present evidence that fluid drawn into the contact by sliding is pressurized hydrodynamically and subsequently forced into the porous articular surfaces. The mechanism, which we call tribological rehydration, suggests that activity is the driving force behind long-term function and health of cartilage.

15 THE ORIGIN OF ADHESION IN ARTICULAR CARTILAGE AND HOW TO CONTROL IT

J. Schrader[1], G. Driscoll[2], A.C. Moore[1], and D.L. Burris[2]

[1]Biomedical and [2]Mechanical Engineering

Articular cartilage is the load bearing and lubricating material of human joints. Contact with articular cartilage creates a deformation induced pressure gradient that lends cartilage its superior load bearing and lubrication functions. However, this same pressure gradient drives fluid from the tissue, similar to the motion of wringing out a sponge, and leads to increased tissue strains and friction. While a lot is known about the fluid exudation response following contact, little is known about the mechanics of cartilage recovery.

In our early attempts to study cartilage recovery following contact we noticed large forces were required to separate the contact interface. While contact separation is traditionally thought of in terms of adhesion we hypothesize that for the same reasons contacting cartilage drives fluid from the tissue, unloading cartilage should draw fluid back into the tissue via a sub-ambient pressure condition.

Sub-ambient pressures may develop during contact separation if the stored elastic stress in cartilage cannot recover as fast as the separation rate. In other words, if the indenter is retracted faster than the rate of fluid recovery, then a negative pressure will develop at the interface and manifest as an adhesive force. Here a host of experimental and theoretical techniques are used to demonstrate and model suction in cartilage contacts. The results of this research will help to identify the most appropriate contact mechanics models for articular cartilage and will shed light on the principles that govern physiological lubrication.

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

POSTER PRESENTATIONS

Track 1

Cells Tissue Biomechanics

Cells/ Biomaterials/ Others

16 THE EFFECTS OF TURMERIC EXTRACT ON PC12 CELL ATTACHMENT

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Department of Biological Sciences, University of Delaware.

Previous research has shown that turmeric and its constituents have many benefits in neurological health. However, few studies focus on extracts of the raw root. PC12 cells experience rapid neurite outgrowth and increased adherence to growing surfaces after exposure to stimulants such as nerve growth factor, which activates the receptor tyrosine kinase (TrkA). The effects of turmeric extract on adherence to the growing surface of PC12 cells was studied and quantified to determine if a similar effect to NGF could be achieved.

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

Amber M. Hilderbrand[1], Chen Guo[1], Eden Ford[1], April M. Kloxin[1,2]

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Collagen is one of the most prevalent proteins within the body and is present in a wide range of tissues. The interactions between collagen and cells are important in a variety of diseases, namely fibrosis. In order to mimic these 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 different variants 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. In order to study 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. By incorporating these mfCMPs that capture the fibrillar structure of collagen on the nano- and microscale, we can impart a hierarchal structure within the hydrogel materials to better recapitulate 'soft', collagenous tissues. Fibrils were imaged using transmission electron microscopy to study fibril morphology in solution, and rheology was used to characterize mechanical properties of hydrogels with incorporated mfCMPs. Initial studies to observe cell behavior within these hydrogel materials indicate they are suitable for the culture of human mesenchymal stem cells (hMSCs), and further characterization of specific cell response (cell area, elongation, etc.) is ongoing.

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

18 CONNECTING HUMAN BLOOD RHEOLOGY TO PHYSIOLOGY

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Human blood is a complex suspension primarily composed of red blood cells, white blood cells, and platelets which are suspended in plasma containing various proteins. When subjected to flow, blood has been shown to exhibit interesting rheological phenomena including a shear thinning behavior under steady shear with a nonzero yield stress, both viscous and elastic effects, and thixotropy – a time dependent change in the viscosity. These phenomena are primarily due to the reversible aggregation and breakup of the red blood cells into rouleau structures. Despite nearly a century of research into the rheological behavior of human blood, the understanding of the full flow behavior of human blood is still limited to only a basic understanding of the steady shear flow behavior with limited relation to the physiological properties of the blood sample. These limitations are largely due to inaccuracies and inconsistencies in previous measurement techniques which result in unreliable data as well as a failure of previous works to provide thorough documentation on the physiological properties of the blood samples used. Due to the fact that several previous studies have found significant correlations between the rheological properties of blood and various cardiovascular diseases, fully understanding the rheology of human blood is critical for both the detection and prevention of these diseases. This work aims to standardize measurement procedures for human blood rheology while exploring possible correlations between the rheological and physiological properties of the blood samples.

19 EFFECTS OF AGING ON THE ENDOTHELIAL GLYCOCALYX OF RAT AORTAS

Shubo Wang, Liyun Wang

Department of Mechanical Engineering, University of Delaware

Endothelial cells lining all blood vessels' internal surface are constantly in contact with blood, experiencing both biochemical signals and mechanical forces resulted from the blood flow. In normal conditions, there exists a thin interfacial layer (termed endothelial glycocalyx) between the blood and endothelial cells. Endothelial glycocalyx plays a vital role in the regulation of vascular functions such as mechanotransduction, cross-wall permeability, and ligand-receptor interactions. Intact endothelial glycocalyx is believed to serve as the first-line defense for vascular health and its impairment has been found under various pathological conditions such as acute septic shock, chronic inflammation, and diabetes. Since aging is associated with many changes in vasculature cardiovascular functions, we examined the thickness and surface coverage of endothelial glycocalyx in thoracic aortas of rats from young to old ages (1-, 6, 12,18, and 24-month-old) using wheat germ agglutinin (WGA) staining and confocal microscopy. The results revealed that the thickness of EG increased from young rats (1-month-old) to mature rats (12-month-old), peaking at 12-month-old of age and then showing a trend of decrease afterwards. The percentage coverage of endothelial glycocalyz on the lumen surface also peaked at 12-month old and then significantly declined in 18-month-old rats. The decreased thickness and coverage rate associated with aging suggest a loss of functionality (transport barrier) and responsiveness of the endothelium to blood flow.

POSTER PRESENTATIONS

Track 2

Clinical Biomechanics

Cartilage/ IVD/ Ligament/ Tendon

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

20 BARRIERS FOR REMAINING PHYSICAL ACTIVE IN PATIENTS WITH MIDPORTION ACHILLES TENDINOPATHY

Patrick Corrigan[1], Laura Pontiggia[2], Karin Grävare Silbernagel[1], Daniel H. Cortes[3]

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INTRODUCTION: Midportion Achilles tendinopathy commonly leads to reduced physical activity even though it has been shown that remaining active does not negatively impact recovery. The purpose of this study was to explore differences between patients who are active at the time of evaluation and those who are not. METHODS: 29 patients with midportion Achilles tendinopathy were dichotomized into active (n=12, 9 Male) and inactive (n=17, 11 Male) groups. Demographics and clinical severity were obtained. Continuous Shear Wave Elastography and ultrasound obtained structural properties. Leg function was quantified with a single heel-rise test. Each tendon was defined as more or less symptomatic. Descriptives are presented as median (IQR). Wilcoxon Rank Sum tests analyzed between group differences, Wilcoxon signed-rank tests analyzed between limb differences, and analysis of covariance (ANCOVA) with age and BMI as covariates analyzed between group differences in mechanical properties and lower limb function. RESULTS: The active group (23.8 (21.6-25.8)) had a significantly ($p<0.01$) lower BMI (kg/m2) compared to the inactive group (29.4 (23.4-31.2)). VISA-A was significantly ($p=0.01$) higher in the active group (51 (43-57)) compared to the inactive group (40 (34-44)). No significant differences in mechanical properties ($p=0.15$-0.82) or lower limb function ($p=0.14$-1.00) between groups or limbs were found. Tendon thickening of the more symptomatic side was significantly ($p=0.002$) smaller in the active group compared to the inactive group. DISCUSSION: Findings show mechanical properties and function are not different between those who are physically active and those who are inactive. However, greater clinical severity and structural change may explain why some patients are able to remain active and others are not.

21 KNEE BIOMECHANICAL AND QUANTITATIVE MAGNETIC RESONANCE IMAGING VARIABLES THREE MONTHS AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

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

PURPOSE: ~ 32 % of subjects with anterior cruciate ligament (ACL) injuries have radiographic knee osteoarthritis (OA) 5 years after ACL reconstruction (ACLR). Those with OA also show inter-limb differences in knee mechanics and joint under-loading during gait early after ACLR (~ 6 months). Also, elevated cartilage T2 relaxation times indicate early OA related changes. In this first step of a longitudinal study, we aimed to investigate the relationship between gait variables and T2 values for the involved vs. uninvolved knee early after ACLR. METHODS: 8 subjects (sex = 6 men, 2 women; mean: age = 28 years, mass = 83.1 kg, height = 1.7 m) were enrolled ~ 3 months after ACLR. Subjects walked at self-selected speeds. We used a validated electromyography-informed musculoskeletal model to estimate the following variables: peak knee flexion angle (pKFA), peak knee flexion moment (pKFM), peak knee adduction moment (pKAM), peak medial compartment force (pMCF) and peak lateral compartment force (pLCF), during the first half of stance. Each subject also underwent supine bilateral knee magnetic resonance imaging using a sagittal T2 mapping sequence with 6 echoes. RESULTS: Subjects walked using smaller pKFA, pKFM, pMCF, and pLCF in their involved vs. uninvolved limb, and these inter-limb differences met or exceeded minimal detectable change (MDC) values. While not significant, subjects had higher cartilage T2 values in their involved vs. uninvolved knee for both the superficial layers of the medial compartment and the deep layers of the lateral compartment. CONCLUSIONS: Although joint over-loading is a hallmark sign of late-stage knee OA, early-stage OA may be related to under-loading and weakening collagen matrix, indicated by higher T2 values.

22 MRI QUANTIFICATION OF IN VIVO HUMAN DISC DIURNAL COMPRESSION AND INDUCED FLEXION/EXTENSION

Kyle D. Meadows[1], John M. Peloquin[1], Edward J. Vresilovic (2), Dawn M. Elliott (1)

(1) Department of Biomedical Engineering, University of Delaware, (2) Department of Orthopaedics and Rehabilitation, Pennsylvania State University

In vivo measures of intervertebral disc mechanical function are important for identifying abnormal discs. Disc degeneration is currently classified using qualitative integer scales based on the appearance of static T2 weighted MR images and is insufficient to identify symptomatic discs. In this study, we investigated mechanical changes in the disc caused by diurnal compression and induced flexion/extension using MRI sequences. Changes in disc geometry from morning to afternoon (diurnal change) or from supine to flexed/extended can elucidate how healthy and degenerate discs respond to loading. Measurements were made for disc height, disc volume, wedge angle, and T2 relaxation time. Because subject-specific classification requires data that is consistent from day to day, quantitative measurements were qualitatively evaluated for consistency at the AM starting point and between loading conditions. AM disc height, volume, wedge angle, and nucleus pulposus T2 were consistent between subjects. AM disc height and volume increased from L1 to L5, while degenerate and damaged discs showed lower disc heights, volumes, and T2 values as expected. Height and volume decreased from AM to PM, but the changes were not consistent. T2 changes were inconsistent. Extension caused an increase in wedge angle while flexion caused a decrease in wedge angle, as expected, with decent repeatability. Additionally, strain maps were made via registration of high-contrast disc boundaries and produced the expected anterior compression and posterior tension during in vivo flexion for a pilot disc. This work provides the foundation for future degeneration studies by quantitatively measuring the disc's change in geometry as opposed to static appearance.

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

POSTER PRESENTATIONS

Track 2

Clinical Biomechanics

Gait

23 THE NON-OPERATED LIMB MAY NOT BE A CONTROL COMPARATOR AFTER UNILATERAL TOTAL KNEE ARTHROPLASTY

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University of Delaware

Introduction: Despite unilateral symptoms and unilateral total knee arthroplasty (TKA), many patients have bilateral radiographic osteoarthritis (OA). This begs the question whether the contralateral limb can be used as a control limb for biomechanical studies. The purpose of this study was to determine if biomechanics in the non-operated limb differed between those with and without radiographic OA in the non-operated limb after unilateral TKA.

Methods: 36 subjects who underwent unilateral TKA participated in this study 6, 12, or 24 months after surgery. In order to identify a unilaterally symptomatic cohort, subjects were excluded if they had greater than 4 out of 10 pain in the contralateral limb or had plans to replace the contralateral knee. Subjects were grouped according to pre-operative Kellgren-Lawrence (KL) grades in the non-operated limb. The "No-OA Group" was defined as those with KL grade 0 or 1, while the "OA Group" had KL grades 2-4 in the non-operated limb. Sagittal plane biomechanical variables and knee pain in the non-operated limb were compared between groups using independent t-tests.

Results: The OA Group had 4 more knee flexion degrees at heel strike ($p=0.033$) and 5.5 degrees less peak knee flexion in mid-stance ($p=0.042$). Also, they had less knee extension excursion ($p=0.030$). No significant difference found between groups for knee flexion excursion ($p=0.063$) and pain ($p=0.544$).

Conclusion: Subjects with OA in the contralateral limb have abnormal gait biomechanics, even though there was no greater pain. The non-operated limb may not be a valid control limb for biomechanical outcome studies and researchers should consider the radiographic disease severity in the contralateral limb when identifying appropriate subject samples.

24 INTER-JOINT COMPENSATIONS WHILE WALKING WITH ANKLE RESTRICTION

Michael Christensen, Anahid Ebrahimi, Teresa Ferrara, Jill Higginson, and Steven Stanhope

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Individuals walking with ankle impairment have restricted ankle function, as quantified by a reduction in ankle mechanical power. Current literature reports an unilateral ankle restriction leads to an increase in mechanical power at the hip, while bilateral restriction leads to an increase in mechanical power at the knee. Furthermore, joint mechanical power produced more proximally may lead to an increase in net metabolic expenditure (NME) due to a shift from the highly efficient ankle to the less efficient knee and/or hip. The purpose of this study was to quantify the inter-joint mechanical power compensations when walking with the same level of ankle restriction unilaterally and bilaterally and determine the effect of these compensations on NME. Nine healthy individuals were fitted for ankle foot orthotics (AFOs) that restricted dorsiflexion and plantarflexion. Subjects walked for 10-minutes in each of three different conditions (with Shoes, with an AFO on the dominant limb, and with AFOs on both limbs) while motion and metabolic data were collected. NME was calculated by subtracting the metabolic expenditure at a seated baseline from steady-state walking. Average positive joint mechanical power per stride and corresponding joint metabolic cost were then calculated at the ankle, knee, and the hip using previous literature. While NME did not significantly change across all conditions ($p > 0.05$), joint mechanical power and estimated joint metabolic cost were found to significantly decrease at the ankle joint and increase at the knee joint with both unilateral and bilateral restriction ($p < 0.05$). Interestingly, the mechanical power deficit in the ankle was approximately equivalent to the increase in mechanical power at the ipsilateral knee for both unilateral and bilateral ankle restriction.

25 EVALUATION OF THE RELATIONSHIP BETWEEN GAIT AND CLINICAL MEASURES OF PLANTAR FLEXOR FUNCITON AND STRENGTH IN HEALTHY, OLDER INDIVIDUALS

Sarah Colón, BIOMS Interdisciplinary Program; Karin Silbernagel, Ph.D., PT Department; Elisa Arch, Ph.D., KAAP and BME Departments

The plantar flexors play a critical role in gait. The function of the plantar flexors, like many other muscle groups, decreases with age resulting in plantar flexor weakness and contributes to decreased mobility, thus increasing one's risk of fall or injury. During phyical therapy after a fall or injury to the plantar flexors, clinicians can conduct a single-leg heel rise test to determine if the individual has regained "normal" plantar flexor strength. However, regaining "normal" plantar flexor strength may not necessarily mean the individual has regained his/her typical plantar flexor function during gait. Currently, the relationship between plantar flexor strength and function during gait is unknown. Thus, the purpose of this study was to evaluate the relationship between measures obtained form the single-leg heel rise test and the peak plantar flexion moment during gait for healthy, older individuals. Eight consenting healthy, older individuals participated in this study (72.5±4.3yrs, 83.6±7.9kg, 0.83±0.12statures/sec). Half of the participants had less than a 10% difference in peak plantar flexion moment values from the single-leg heel rise test and during gait, which is often considered an acceptable threshold. Furthermore, there was a significant linear relationship between these two plantar flexion moment measures that may be further strengthened if outliers can be excluded. Ultimately, determining the relationship between measures of plantar flexor strength and function during gait may help clinicians determine if an older individual has regained typical plantar flexor function after a fall or injury without having to conduct a gait analysis.

26 MALE ATHLETES WHO WALK WITH GAIT ASYMMETRIES REPORT SIMILAR FUNCTION TO THOSE WHO WALK SYMMETRICALLY 1 YEAR AFTER ACL RECONSTRUCTION

Jessica L Johnson, Jacob J. Capin, and Lynn Snyder-Mackler, The University of Delaware

Patients demonstrate altered gait patterns up to 2 years after ACL reconstruction (ACLR), with knee excursion asymmetries in both weight acceptance and mid-stance. Previous research has identified a relationship between gait asymmetries and functional exams, and functional exams and self-report outcomes. We investigated gait asymmetries and self-report outcomes, and hypothesized that participants with gait asymmetries at the knee would have lower self-reported outcomes.

Thirty-eight male athletes completed gait assessment 1 year after ACLR. We defined asymmetry as a difference in sagittal plane knee excursion between the surgical limb and non-surgical limb that met or exceeded the minimal clinically important difference (MCID) of 3 degrees. We dichotomized groups during weight acceptance (WA) and mid-stance (MS) and compared each excursion group separately. Participants completed two self-reported function surveys, the International Knee Documentation Committee Subjective Knee Evaluation Form (IKDC) and Knee Injury and Osteoarthritis Outcome Score (KOOS). We used independent t-tests to compare outcome measures between groups.

We found no statistically significant or clinically meaningful difference between male athletes who walked with knee excursion asymmetry and those who did not on any self-reported outcomes measure 1 year after ACLR. The mean difference between limbs (involved – uninvolved) for knee excursion was -3.6±3.5° at WA and -4.6±4.5° at MS. Most participants had full participation in ADLs (KOOS ADL score 99.0±2.8) and high level activities (KOOS Sport/Rec 93.7±9.5). Within a high functioning group, these measures did not detect a difference in self-reported function between men who walked symmetrically versus asymmetrically. This may indicate relatively small gait asymmetries do not affect function in well-rehabilitated men.

27 ADAPTATIONS TO SPLIT-BELT USER-DRIVEN TREADMILL AFTER INDUCED ASYMMETRIC GAIT

Kelley Kempski[1] Nicole Ray[1] Brian Knarr[2] Jill Higginson[1]

[1]University of Delaware
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Nearly 7 million people in the United States are stroke survivors. A common consequence of stroke is hemiparesis, which is characterized by weakness and impaired control of one side of the body. Post-stroke hemiparesis affects gait and impairs nearly 80% of stroke survivors. To mimic hemiparetic gait, asymmetric gait can be induced on healthy individuals for treadmill gait training . Regular-controlled treadmills do not perfectly simulate an individual's typical overground locomotor patterns. To mitigate the differences between treadmill locomotion and overground locomotion, user-driven treadmill systems are being developed that adjust the speed of the treadmill belts in real-time based on how fast the subject is trying to walk. The objective of this study is to determine if healthy subjects converge to symmetry on a split-belt user-driven treadmill after an induced asymmetric gait. Six healthy, young adults walked on a split-belt treadmill for four minutes with one leg at self-selected speed and the other leg at half of that speed. After four minutes, the treadmill transitioned to a user-driven mode where each leg adjusted in real-time independent of one another. Walking speed (WS), anterior ground reaction force (AGRF), and trailing limb angle (TLA) were evaluated for each limb on each of these two treadmill modes. After an adjustment period on the user-driven treadmill, there was no statistically significant difference in WS, AGRF, or TLA between subjects' "paretic" and "non-paretic" limbs indicating that healthy individuals converge to symmetry on the user-driven split-belt treadmill after induced asymmetric gait. This suggests that individuals post-stroke may be able to converge to a more symmetric gait after gait-training interventions on the split-belt user-driven treadmill.

28 RHEOLOGICAL APPLICATIONS OF SHEAR THICKENING FLUIDS(STF) FOR TRANSTIBIAL PROSTHESES

Jehnae J Linkins, BIOMS, University of Delaware [1], Norman Wagner, Chemical Engineering, University of Delaware [2], Keyi Xu, Chemical Engineering, University of Delaware[3]

Shear Thickening Fluids are non-Newtonian colloidal dispersions that show increases in viscosity with increases in shear stress. They typically consist of some type of nanoparticle (ex. silica) dispersed at high concentration in a solvent (ex. polyethylene glycol). The unique flow properties of STFs can be utilized in a variety of applications [1]. Previous work in the literature has demonstrated that STFs are suitable for usage in hydraulic dampers. Zhang et al. have shown that dampers containing STF that operates under conditions where the STF exhibits shear thickening are able to dissipate four times more energy as compared to the low viscosity state [2]. There continues to be a lack of passive prosthetic devices with variable ankle stiffness on the market today. As a result, The Stage Gate Product Development process (SGPDP) was used to develop designs for a Shear Thickening Fluid(STF) ankle damper for a Transtibial prosthesis. Based on previous work done by Keyi Xu, a prototype device was built, human trials and mechanical testing was done to characterize the response of the prototype. The results from these experiments indicated that the STF damper device better mimics non-pathological ankle motion than the next best alternative on the market. The second design for the ankle damper was built in order to characterize the response of the Shear Thickening Fluid Tethers in comparison to the previous prototype device that was built.

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

29 NOVEL REHABILITATION PROTOCOL TO RETURN PATIENTS TO HIGH-LEVEL ACTIVITIES, SPORTS, AND OCCUPATIONS AFTER TOTAL HIP ARTHROPLASTY

Kathleen Madara, DPT1, Adam Marmon PhD2, Moiyad Aljehani, MPT1, Jason Brandl, SPT1, Leo Raisis, MD3, Joseph Zeni Jr. PT PhD1

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Background: There has been an increase in the number and age range of individuals undergoing total hip arthroplasty (THA). Although the surgical techniques and biomaterials have improved, rehabilitation has not kept pace with the needs of patients. The purpose of this study was to evaluate the feasibility and effectiveness of an progressive strengthening intervention that included high-level activity retraining after THA.

Methods: Ten subjects (5 Experimental/ 5 Control) completed this study. The experimental group was treated once every 2 weeks for 12 weeks, then 3 times a week for 4 weeks. Training was individualized to patient goals, including progressive home exercise and clinical components. Testing included three-dimensional gait analysis, clinical assessment and self-reported questionnaires. Statistical analysis included repeated measure ANOVA and post hoc t-tests.

Results: There was a group-by-time effect for the second peak vGRF; the Experimental group had greater peak vGRF at follow-up. Mean satisfaction was greater in the experimental group than the control (p=0.04). Although not significant, the experimental group showed greater hip strength at follow-up.

Conclusion: This novel treatment protocol is feasible in a clinical setting and had a positive impact on biomechanics and satisfaction. The intervention group exhibited biomechanical changes that are in the direction of healthy gait, with more normal loading on the involved side after surgery.

30 A CLINICALLY FEASIBLE ASSESSMENT OF PHYSICAL FUNCTION AS A "STRESS TEST" TO IDENTIFY PEOPLE WITH KNEE OSTEOARTHRITIS WHO ARE UNABLE TO BE PHYSICALLY ACTIVE

Authors: Hiral Master, Louise Thoma, Meredith Christensen, Emily Polakowski, Laura Schmitt, Daniel K. White.

Adopting a physically active lifestyle provides major health benefits to people with knee osteoarthritis (OA). Yet, most people with knee OA are sedentary. Difficulty with physical function, such as slow walking, may be one barrier to physical activity (PA) participation for people with knee OA. Little is known about what minimum level of physical function is necessary to engage in PA. Establishing minimum thresholds will help clinicians prioritize prescribing intervention for PA or physical function in knee OA. The purpose of the study was to identify minimum thresholds of performance on clinical tests of physical function required to target a goal of 6000 steps/day, an important benchmark of PA in knee OA. We used publically available data from the Osteoarthritis Initiative (OAI) whose purpose was to monitor the progression of knee OA. PA was measured with an accelerometer (Actigraph GT1M) worn during waking hours during the 48-month follow-up visit, and quantified as steps/day. Physical function was quantified with three clinical tests: timed 5 repetition sit-to-stand test (STS), timed 400-meter walk, and walking speed (calculated from a 20-meter walk). To identify a minimum threshold for each, we calculated cut-points at 80% to 95% specificity for walking 6,000 steps/day, i.e., the proportion classified with good physical function and > 6000 steps/day divided by all with > 6000 steps/day. Thresholds of high specificity (80-95%) of physical performance for walking > 6000 steps/day ranged from 11 to 14 seconds for STS, 315 to 350 seconds for the 400-meter walk, and 1.10 to 1.25 meters/sec for walking speed. Physical function at or worse than stated thresholds may represent insufficient physical function for attaining an important benchmark of physical activity.

31 FACTORS AFFECTING WALKING SPEEDS DURING NORMAL AND USER-DRIVEN TREADMILL WALKING

Nicole T. Ray[1], Brian A. Knarr[2], Jill S. Higginson[1]

[1]University of Delaware, Mechanical Engineering,
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Stroke affects nearly 795,000 people annually in the US. After stroke, hemiparesis changes muscle activation and movement patterns and decreases walking speeds. Since decreased walking speeds correspond to diminished quality of life, many poststroke motor rehabilitation programs aim to increase walking speeds. To incorporate active training principles in gait training, we developed an adaptive, user-driven treadmill controller that adjusts the treadmill's speed to match the user's walking speed in real time. The objective of this study is to determine the relative contribution of anterior ground reaction force (AGRF), trailing limb angle (TLA), and cadence to increased walking speed during fixed and user-driven treadmill walking. Previous studies show increased AGRF, TLA, and cadence are correlated with increased walking speed. Therefore, we hypothesize that similar linear relationships exist among walking speed and AGRF, TLA, and cadence for both treadmill types. 22 healthy adults walked on an instrumented split-belt treadmill in a motion capture lab in normal and user-driven modes. Walking speed, AGRF, TLA, cadence and were compared using linear models. These comparisons indicated strong relationships between walking speed and AGRF, TLA, and cadence at slow walking speeds. However, at faster walking speeds, the relationships weakened and changed slope for on both treadmill modes. These relationships may change because there are multiple strategies that may be used to increase walking speed. For example, one may increase their step length, cadence, or both. In this case, the relationships among walking speed, AGRF, TLA, and cadence changed in response to faster walking speeds no matter which treadmill mode was used.

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POSTER PRESENTATIONS

Track 2

Clinical Biomechanics

Neuromuscular Modeling & Training

32 PLAYSKIN AIR: A BUILDING BLOCK TO BETTER MOBILITY

Melissa Landman and Cory Cacciola

Move to Learn Innovation Lab

The scope of this project was to design a user-controlled, pneumatic garment to assist a child with movement impairments to lift his arms against gravity. The participant has a diagnosis of arthrogryposis that limits his arm mobility and ability to perform day-to-day tasks. It is important for children to be able to lift their arms to play, as well as to engage in necessary fine and gross motor skills. Through talking with a focus group of parents of children with arthrogryposis, it became apparent that every child with arthrogryposis had different constraints in their range of motion, elbow flexion, and finger dexterity. The initial iteration of the design involved using air-mattress pumps controlled by an Arduino to blow up heat-sealed nylon bladders. Testing showed that lightweight pumps and electronic components were too bulky and did not create the necessary amount of pressure to blow up a bladder. The final prototype involved three pieces of tubing: one that the user blows into to inflate the bladder, one that is inside the bladder to prevent creasing under the user's armpit, and one running from the bladder to a button that serves as a release valve. The prototype integrated these components into a garment made of fabric selected by the participant. Initial field testing was showed positive results that met most of the target metrics. Moving forward, the garment design will be improved to increase lifting action, the design will be tested on other users, a DIY will be fabricated to enhance accessibility, and utilization of the design by users should be analyzed. Further research is needed to determine if there is a pneumatic system that can increase the range of motion even more than the current prototype.

33 DERIVATION OF JOINT TORQUE PULSE PATTERNS FOR GOAL-ORIENTED ROBOTIC GAIT RETRAINING

Robert L. McGrath[1], Jill S. Higginson[2], Fabrizio Sergi[1]

[1]Biomedical Engineering Department, University of Delaware
[2]Mechanical Engineering Department, University of Delaware

Robot-assisted gait training is a therapeutic approach to support recovery of walking function after neurological injury. However, it is unknown how to target robotic assistance to obtain a desired effect in certain gait parameters, i.e. goals. We are investigating a method to control gait-training robots based on the analysis of the joint torques applied by healthy subjects to modulate such goals.

The main objective of this study is to understand how sagittal plane joint torques are affected by two important gait parameters, gait speed (GS) and stride length (SL). We used inverse dynamics to estimate joint torques of healthy subjects walking on a treadmill at different GS values, and asked to modulate SL via visual feedback. We used optimization to estimate the optimal timing and amplitude for sets of torque pulses to approximate the difference between joint torques measured at self-selected and modulated SL, at various GS values.

Our results show a strong effect of GS on the torque profiles in all joints considered, i.e. hip, knee, and ankle. In contrast, SL mostly affects the knee torque profile at early and late stance, with smaller effects on the hip and ankle joints. This analysis yielded a distinct SL-dependent pulse torque pattern for the knee across the various GS values. We found a strong correlation between SL and trailing limb angle (TLA), suggesting that the modulation of SL could be utilized to indirectly target TLA. In summary, our analysis generated a set of torque pulse assistance patterns that can be experimentally implemented on a gait training robot to induce desired dynamics of TLA during robot-assisted gait training.

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

34 MOTOR UNIT RATE CODING AND RECRUITMENT IN ELBOW FLEXION AGONISTS

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1 University of Delaware
2 Nemours-A.I. DuPont Hospital for Children

Muscle redundancy is one of the greatest questions in the neuromuscular system. Understanding timing and recruitment information of agonist pairs would provide better predictive power and control characteristics in motor control. Fifteen subjects participated in an isometric elbow flexion force tracking task. Surface electrodes measured muscle activity on the right biceps and brachioradialis. The task was repeated for 20, 30 and 40 percent of the maximal trials. Surface electromyography was decomposed into motor unit action potential trains. Motor unit recruitment and rate coding for each muscle were compared across each of the contraction levels. All subjects demonstrated an increase in biceps firing rates with increase in torque. Distributions of these firing rates were more normal for biceps motor units while brachioradialis motor units had a more low-skewed distribution. Biceps motor units tended to be recruited earlier than brachioradialis motor units while brachioradialis motor units recruited at the same time across all contractions. This demonstrates that while biceps motor units tend to increase in firing behavior with similar increases in resultant torque brachioradialis motor units show no significant change in recruitment or rate coding across multiple low level contractions. Brachioradialis had high correlation between the peak firing rate of the contraction and initial firing rate of the contraction not observed in the biceps. These data present a brachioradialis that is more regulated and controlled across torque generation than the biceps. In conclusion biceps and brachioradialis motor units recruited and were regulated through different mechanisms across various low level contractions.

35 MODULATION OF WRIST JOINT STIFFNESS BY ACTIVE MUSCULAR CO-CONTRACTION: A MODEL-BASED ANALYSIS

Andrea Zonnino, Fabrizio Sergi

University of Delaware

Joint stiffness is actively modulated by healty humans during tasks requiring interaction with an external environment; however, subjects with neuromuscular disorders can fail to implement such a mechanism. Analysis of the joint stiffness is then valuable for both basic research in neuroscience and clinical assesment of neuromuscular diseases.

The stiffness of a joint is related to the stiffness of surrounding muscles, and can be described by two components: passive and active. The passive component is an intrinsic mechanical property of the muscle that depends on its passive elastic behavior. The active component instead relates to the capabilities of the muscle's contractile elements to modulate the applied force; it is well known that the muscle stiffness is related to the force applied by the muscle by a linear relationship (i.e. Short Range Stiffness (SRS)).

Previous studies measured the SRS on either a joint or a muscular level—however, the number of conditions analyzed, in terms of both joint posture and the levels of muscular co-contraction, were limited by the complexity and length of the experiments.

In this work we present a framework based on a realistic musculoskeletal model, implemented in OpenSim, to estimate the stiffness of the wrist joint, including both passive and active components. The model is a simplified version of the wrist including 2 degrees of freedom (Flexion-Extension and Radio-Ulnar Deviation) and 5 muscles. Our framework is capable to estimate the entire set of admissible joint stiffness values for an exhaustive set of joint posture and applied torques.

With proper experimental validation, this framework may allow to use current musculoskeletal model to study joint stiffness to optimize human-robot interaction and to quantify the evolution of neuromuscular disorders.

POSTER PRESENTATIONS

Track 2

Clinical Biomechanics

Stroke & Brain

Denotes Poster #

All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

36 USING FNIRS TO INVESTIGATE MOTOR PLANNING AND EXECUTIVE FUNCTION IN CHILDREN WITH AUTISM SPECTRUM DISORDER

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Introduction: Despite years of research, underlying mechanisms of Autism Spectrum Disorder (ASD) are still unclear. Children with ASD exhibit deficits in motor skills that may be due to Executive function (EF) and motor planning impairments. Functional Near Infrared Spectroscopy (fNIRS) is an emerging, cost-effective neuroimaging tool that provides cortical activation patterns and can be used to deferential EF and motor planning dysfunction. Identifying the main contributing factor to these impairments can have huge clinical implications for treating ASD. Methods: The experiment was designed to compare oxygenation of the prefrontal cortex in children with and without ASD during conditions with similar motor planning and different executive function requirements. These included tapping (low EF) and completing a Tower of Hanoi (TOH) puzzle (high EF). 12 young children (M= 9.8 years) with and without ASD performed the tasks for two minutes per condition on an iPad. fnirSoft (Version 4.3) was used to analyze the data and determine blood oxygenation values. Results: Preliminary results indicate children with and without ASD do not differ in their oxygenation patterns during the tapping task. However, children with ASD had significantly higher oxygenation than typically developing children during TOH task. Conclusion: Our results suggest that, in simple motor tasks with low EF, children with and without ASD show similar activation patterns in the PFC. The higher levels of oxygenation used in the TOH task by children with ASD suggests an increasing difficulty with tasks that include both executive function and motor planning

37 EFFECT OF A REAL-TIME BIOFEEDBACK TOOL ON ACCLIMATING INDIVIDUALS POST-STROKE TO WEARING A PERSONALIZED PASSIVE-DYNAMIC ANKLE-FOOT ORTHOSES

Cory Cacciola, ME Department; Corey Koller BIOMS Program; Darcy Reisman Ph.D., PT Department; Elisa Arch Ph.D., KAAP, BME, ME Departments

Ankle-foot orthoses (AFOs) are rehabilitative devices that are prescribed to individuals post-stroke who have ankle muscle weakness, with the goal of improving gait function. We have developed a novel AFO design and prescription process that personalizes the passive-dynamic ankle-foot orthoses (PD-AFO) bending stiffness to each individual to assist with their weakness. To use the personalized bending stiffness, the individual must be acclimated to properly loading the PD-AFO into dorsiflexion while walking. Therefore, the purpose of this study was to develop and evaluate efficacy of a real-time biofeedback tool that aims to help individuals post-stroke more effectively walk in their PD-AFO. A custom real-time biofeedback program was developed with LabView software (National Instruments, Austin, Texas). The biofeedback tool showed how the subject's shank and foot moved in real-time with the goal of helping the subjects load the PD-AFO by bending into (dorsiflexing) the brace. To test the biofeedback system, individuals post-stroke visited the lab for three real-time biofeedback acclimation visits. At the first visit, gait analysis was performed while walking with their originally prescribed AFO, and the subjects were fit with their new PD-AFO. During the second and third visits, subjects walked with their PD-AFO for four minutes, received training for ten minutes, and finally walked four more minutes without the biofeedback. Results indicated subjects could load the PD_AFO and accommodate to walking with their PD_AFO, as indicated by the subjects obtaining the desired dorsiflexion angle while training. Therefore, future research should examine the data collected during training to analyze how the subject was interacting with the biofeedback to potentially advance the tool.

38 THE EFFECT OF SPLIT-BELT TREADMILL TRAINING ON RESTING STATE FUNCTIONAL CONNECTIVITY WITHIN THE CORTICO-CEREBELLAR PATHWAY

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Stroke is a leading cause of disability in the United States that frequently results in impared walking function. Split-belt treadmill training is a rehabilitation strategy that seeks to reduce gait asymmetry and increase walking speed through motor adaptation. Motor adaptation refers to the process that subjects undergo when they are forced to adjust their motor control strategy to respond to modified environment dynamics. Previous studies have measured how adaptation induces short-term changes in gait asymmetry, which may be a powerful therapeutic tool for post-stroke rehabilitation. In this study, we seek to further investigate this process by identifying the neural correlates of split-belt locomotor adaptation using resting state fMRI.

We conducted a pilot study that involved two age-matched healthy subjects and three individuals with chronic stroke. Participants walked on a split-belt treadmill that drove the non-dominant (or non-paretic) leg at twice the speed of the other leg, which required subjects to adapt their gait to maintain inter- and intra-limb cordination. To measure changes in functional connectivity, we performed resting state fMRI scans of subjects immediately prior and post treadmill training. Because locomotor adaptation involves learning via error correction and control processes, we hypothesized that locomotor adaptation would affect the resting-state functional connectivity of the cortico-cerebellar network. Our preliminary anaylsis shows a significant increase in functional connectivity within the cerebellum after training, in agreement with previous studies that show the cerebellum is critical in the formation of short-term and long-term motor memories. Additionally, we found a decrease in M1 interhemispheric connectivity, which is unexpectedly in agreement with prior studies of unilateral motor learning tasks.

39 EFFECTS OF PERSONALIZED PASSIVE-DYNAMIC ANKLE-FOOT ORTHOSES BENDING STIFFNESS ON GAIT OF INDIVIDUALS POST-STROKE

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The plantar flexors play a critical role in controlling shank rotation. Insufficient control of the shank's rotation due to plantar flexor weakness, an impairment seen in individuals post-stroke, may result in gait dysfunctions. Ankle-foot orthoses (AFOs) are rehabilitative devices that can be prescribed to individuals post-stroke who have plantar flexor weakness. Individuals' post-stroke often experience variable outcomes with currently-prescribed AFOs, likely because these AFOs are not properly customized for each individual. We have developed a novel AFO design and prescription process that personalizes the passive-dynamic ankle-foot orthoses (PD-AFO) bending stiffness to each individual to assist their weakened plantar flexors. The bending stiffness can potentially replicate function of the plantar flexors, quantified by the peak plantar flexion moment, by adding to the resistance needed to control shank rotation. We hypothesized that PD-AFO bending stiffness can be customized to add to an individual post-stroke's peak plantar flexion moment, enabling the net (individual + PD-AFO) moment to reach a typical level. The purpose of this study was to evaluate if personalized PD-AFOs bending stiffness improved the gait of individuals post-stroke. Three individuals, two females and one male, with chronic stroke participated in this study. The PD-AFO improved the peak plantar flexion moment and gait symmetry in comparison to each subject's originally-prescribed AFO. Future research should investigate training the individuals how to use the PD-AFOs to determine if even greater benefits can be gained from the personalized bending stiffness.

 All researchers are from the University of Delaware, Newark, DE, USA unless otherwise noted.

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Schedule of the Day

TIME	WHAT	WHERE
8:30	BREAKFAST & POSTER SET-UP	STAR CAMPUS- GLASS ATRIUM
9:00	WELCOME & INTRODUCTORY REMARKS	STAR CAMPUS- GLASS ATRIUM
9:05	KEYNOTE LECTURE: DR. JOHNNA TEMENOFF	STAR CAMPUS- GLASS ATRIUM
10:20	BREAK	
10:35	PODIUM SESSION 1	STAR CAMPUS- GLASS ATRIUM
11:35	LUNCH	STAR CAMPUS- MAIN CONCOURSE
12:00	POSTER SESSION 1 (ODD #S)	STAR CAMPUS- MAIN CONCOURSE
1:00	POSTER SESSION 2 (EVEN #S)	STAR CAMPUS- MAIN CONCOURSE
2:00	BREAK	
2:15	PODIUM SESSION 2	STAR CAMPUS- GLASS ATRIUM
3:15	PRESENTING THE STANLEY FAMILY FOUNDATION GIFT IN MEMORY OF VINCENT BARO	STAR CAMPUS- GLASS ATRIUM
3:30	AWARDS SESSION	STAR CAMPUS- GLASS ATRIUM
4:00	ADJOURN	

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