Translational Research Scholars Program
Personal Statement

- **How will the Translational Research Scholars Program benefit your career development?**

My career objective is to conduct meaningful research that shapes clinical practice to improve patient outcomes and enhance their overall health. I believe I have many necessary components to meet this goal including excellent research training, solid publication history, superb laboratory infrastructure, and strong clinical support from on-site rehabilitation facilities as well as strong relationships with clinics in our surrounding community. The greatest shortcoming limiting my ability to meet my career objective at the University of Montana (UM) is a lack of on-site mentorship. In particular, my greatest unmet mentorship need is to work with scientists who have success conducting clinical trials of emerging treatment paradigms. I have developed strong preliminary data for an innovative treatment paradigm from some recent pilot funding grants, but I fear I my progress is constrained without focused mentorship in NIH grantsmanship. I have tried to problem solve this issue with my Chair, and my institution does not have mentors that are well aligned with my field of rehabilitation research. Therefore, I believe the Translational Research Scholars Program (TRSP) will the ideal solution to meet my desired career goal of NIH funding by providing the missing pieces of high quality mentoring and grant training that is otherwise unavailable to me in Montana.

- **How will the program facilitate submission of your grant proposal?**

Many of my faculty colleagues in my School of Physical Therapy are new investigators; more experienced scientists at UM are focus on different areas of study (e.g. chemical and drug science). Gaining dedicated time with an experienced grant writer and accomplished scientist in my field will provide an essential, but missing element, to allow my continued career development as a clinical researcher. My regular interactions with Dr. Stevens-Lapsley will allow for discussion of career development strategies and will provide mentorship in grantsmanship and research design to allow me to achieve my goal of R-level funding. She has an impressive history of success in mentoring others towards obtaining extramural funding. In addition, the TRSP program will provide funds to pilot an early intervention with our custom unweighting device to provide data that will shape and support the decisions made during our future clinical trial design. Further, the TRSP grant budget includes cartilage biomarker assays that typically exceed the budget of the small grant funding available for piloting at my University. Additionally, my acceptance into the TRSP represents a formal endorsement of my Chair's commitment to my scholarly agenda and laboratory development. This investigation will ensure I have the protected time and resources of mentorship and pilot data needed to complete my grant applications. Finally, I thrive in an environment of peer feedback and consistent writing activities that are aligned with the Core Program of the TRSP. The opportunity to learn and the shared feedback with a cohort of Scholars is an activity I relish.

- **What are your longer-term (next 5 years) translation and/or clinical research goals?**

I have spent 4 years developing a custom harness device needed for a new treatment paradigm that will catalyze the benefits of movement retraining and motor relearning in patients with knee disorders. Several foundation-based extramural grants produced some convincing evidence of our new treatment's safety and clinical worth for athletes who develop early post-traumatic knee osteoarthritis after ACL reconstruction. Our goal will be to continue this research to provide novel intervention strategies to thwart the costs and disability associated with knee ligament injury. Pilot data obtained with TRSP funding will progress the development of our treatment paradigm by confirming efficacy and safety when starting earlier during recovery. Once we have these new data from the TRSP funding, then I will apply for a 3 year R21 mechanism designed to bring emerging technology forward to provide baseline data for a larger treatment applications. The R21's design will answer key questions regarding optimal timing of the training and define the treatment effect with early intervention. Once the treatment timing is determined with the efficacy trial, then we will apply for R01 funding to support a 5-year multi-site clinical effectiveness trial with longitudinal tracking an array of patient outcomes such as self-report surveys, arthritis markers, and sports participation.

Translational Research Scholars Program – Research Proposal

Rupture of the anterior cruciate ligament (ACL) remains one of the most common knee injuries in young and physically active populations (Spindler et al. 2008). Most young patients undergo ACL reconstruction to resolve joint laxity and prevent knee joint instability with physical activities. While their prevailing belief is that ACL reconstruction is chondroprotective (Bennell et al. 2016), the majority of patients will display radiographic evidence of knee osteoarthritis (OA) within 15 years of surgery (von Porat et al. 2004)(Oiestad et al. 2010). The high prevalence of ACL injuries coupled with the disability and costs of early post-traumatic knee OA represents a ***significant*** threat to our nation's health.

Strategies to mitigate the ubiquitous and costly accelerated knee joint degeneration after ACL reconstruction remain limited. The development of early knee OA is often linked with excessive joint compression and limb loading (Shakoor et al. 2002). Most patients with ACL reconstruction exhibit inadequate force absorptive strategies for the large limb loads present during sports tasks (Hart et al. 2010) that persist for years after finishing rehabilitation (Elias et al. 2015). Their typical load absorption strategy for physically demanding tasks such as jump landing is to restrict flexion motion and bending torque at their knee. The resultant stiff-kneed landings are associated with high co-contraction of the thigh musculature that worsens knee joint compression (Tsai et al. 2013).

Training interventions to teach patients with ACL reconstruction more compliant joint movement strategies during jump landings can have a catabolic influence on articular cartilage metabolism (Chmielewski et al. 2016). Clinicians understandably limit jump practice during training to avoid joint damage from the high loading inherent in even the lowest intensity jump tasks (Chmielewski et al. 2006). Unfortunately, limiting practice curtails potential motor learning from the training intervention. Novel strategies that mitigate excessive loading during jump training are needed to safely allow sufficient practice to obtain lasting correction of patients' inadequate force absorptive landing strategies.

Our long-term goal is to develop clinically effective treatments that quickly improve physical function while reducing the risk of early post-operative knee osteoarthritis. Our **central hypothesis** is that early post-operative knee OA develops due to abnormally high rates and magnitudes of compressive loading on knee cartilage during training and upon return to the demanding physical activities of their sport. To mitigate the aberrant joint compressive loads during training intervention, we have developed a custom body weight support (BWS) harness device. The harness device effectively creates a gravity-reduced environment (Elias et al. 2016) that allows practice of sports specific jumping and cutting tasks without restricting patients' movements. We recently finished an efficacy trial of jump retraining with and without BWS in patients with poor load absorption strategies who were 2 years post ACL reconstruction (Elias et al. 2017). Retraining with BWS induced large effects for better physical function with improved force absorption landing mechanics. Further, patients adopted favorable reduced muscle co-contraction to reduce joint compression and had a significantly lower prevalence of knee joint effusion compared to training without BWS. There was retention of training benefits for months after treatment, which is particularly important as patients' early load absorption strategies carry forward throughout their recovery (Sigward et al. 2016). The next step from the success of this efficacy trial is to incorporate our training intervention with BWS earlier into standard rehabilitation after ACL reconstruction.

A key deliverable of our TRSP grant application is a R21 NIH grant targeting FOA: PAR-17-293 Exploratory Clinical Trial Grants from NIAMS. The **Specific Aim of the future R21 application will be to determine if jump training with BWS early after ACL reconstruction makes lasting improvements in the force absorptive ability of the operated leg to enhance functional recovery and preserve knee cartilage health.** We posit that training benefits are realized though reduced joint compression forces from softening impact loads during landing with a concurrent reduction in thigh muscle co-contraction. Our secondary hypotheses are two-fold: A) training benefits will be retained over time; B) early training with BWS will have enhanced long-term benefits compared to a late start of training.

To test these R21 grant hypotheses, our **approach** will utilize a prospective, blinded clinical trial design with a sex-matched distribution of group allocation. Sixty patients with ACL reconstruction will be randomized to an 8 week BWS jump training group (Early Group) or attention-matched control starting 4 months after surgery. The control group will have a two month delayed entry to intervention (Late Group). Both groups will complete baseline tests at 4 months after surgery followed by testing again at 6, 8, and 12 months post ACL reconstruction. For each test point, we will collect both the rate and magnitude of knee joint compression forces during jump landing and sports tasks via a previously described (DeVita et al. 2001) and validated (Fregly et al. 2012) musculoskeletal model. The model utilizes leg joint kinematics and kinetics to estimate thigh and calf muscle forces, thus accounting for knee joint muscle co-contraction (Messier et al. 2011). We will complete standard measures of clinical safety (e.g. knee pain, muscle soreness, knee effusion) as well as patient reported and performance based outcomes taken as part of our laboratory's historical database of over 100 patients (Elias et al. 2015, Elias et al. 2017). We will supplement these data with a commercially available enzyme-linked immunosorbent assay (ELISA) of serum and urine based cartilage biomarkers that replicate prior work that tracked articular cartilage's response in ACL patients who completed jump training (Chmielewski et al. 2016). Collagen carboxy propeptide (CP II) is a serum marker of cartilage synthesis which will be coupled with C-telopeptide fragments of type II collagen (CTX-II) which is a urine cartilage marker of degradation to create a ratio of net cartilage metabolism throughout the clinical trial (Chmielewski et al. 2012). Independent and repeated ANCOVA's with concomitant meniscal repair as a covariate will be used to test differences in treatment benefits achieved between groups (Early vs Late training) and over time. Regression analyses will explore the relationship between compressive knee joint loads and articular response. The clinical exam data from testing will allow comparison with our historical database and work from published practice guidelines from recognized experts (Adams et al. 2012, Wilk et al. 2012, Wilk et al. 2017)

Grant funding from the TRSP will support testing and training of a pilot cohort of 5 patients who will complete the test procedures and methods described above. These pilot data are needed to accomplish 3 items for a future successful R21 grant application. 1) Confirm treatment safety and methodology of early use of BWS jump training starting just 4 months post-operatively instead of our prior work that averaged training two years post-surgery; 2) Provide proof of feasibility, refine methodology, and evidence of collaboration for the serum and urine data collection and ELISA testing which are new techniques in our lab; and 3) Develop data to improve estimates of the training effects and expected results for improved accuracy with a priori sample size estimations.

The ***innovation*** in our research proposals lies in the utilization of our unique body weight support system that affords a large volume of practice of sports specific training in a gravity-reduced environment. Most prior investigations utilize surrogates of mechanical articular cartilage load from ground reaction forces or muscle co-contraction levels and then speculate on the potential influence of change in surrogate compression data might have on cartilage health. In contrast, our proposal will use a validated musculoskeletal model to directly measure joint compressive load and as well as directly quantifying cartilage metabolic response with validated biomarkers shown to be responsive to training intervention early in recovery after surgery. Our proposal has a high ***translational impact*** as it builds off strong preliminary work to develop a promising new treatment approach to mitigate a source of considerable disability in a large population of patients. The custom BWS device represents a key advancement needed to catalyze the success of promising jump training treatment strategies. The proposed trial we suggest for R21 funding will provide the data needed to determine when to initiate acute training as well as the sample needed to power a large-scale effectiveness trial. The results of the current line of study have implications beyond just patients with ACL reconstruction. Utilizing BWS to allow early and high repetition of safe jump training is a promising treatment for other populations with compromise articular cartilage health such as knee meniscectomy or chondroplasty repairs

1. Adams, D., D. S. Logerstedt, A. Hunter-Giordano, M. J. Axe and L. Snyder-Mackler (2012). "Current concepts for anterior cruciate ligament reconstruction: a criterion-based rehabilitation progression." J Orthop Sports Phys Ther 42(7): 601-614.
2. Bennell, K. L., A. van Ginckel, C. O. Kean, R. K. Nelligan, S. D. French, M. Stokes, B. Pietrosimone, T. Blackburn, M. Batt, D. J. Hunter, L. Spiers and R. S. Hinman (2016). "Patient Knowledge and Beliefs About Knee Osteoarthritis After Anterior Cruciate Ligament Injury and Reconstruction." Arthritis Care Res (Hoboken) 68(8): 1180-1185.
3. Chmielewski, T. L., S. Z. George, S. M. Tillman, M. W. Moser, T. A. Lentz, P. A. Indelicato, T. N. Trumble, J. J. Shuster, F. M. Cicuttini and C. Leeuwenburgh (2016). "Low- Versus High-Intensity Plyometric Exercise During Rehabilitation After Anterior Cruciate Ligament Reconstruction." Am J Sports Med 44(3): 609-617.
4. Chmielewski, T. L., G. D. Myer, D. Kauffman and S. M. Tillman (2006). "Plyometric exercise in the rehabilitation of athletes: physiological responses and clinical application." J Orthop Sports Phys Ther 36(5): 308-319.
5. Chmielewski, T. L., T. N. Trumble, A. M. Joseph, J. Shuster, P. A. Indelicato, M. W. Moser, F. M. Cicuttini and C. Leeuwenburgh (2012). "Urinary CTX-II concentrations are elevated and associated with knee pain and function in subjects with ACL reconstruction." Osteoarthritis Cartilage 20(11): 1294-1301.
6. DeVita, P. and T. Hortobagyi (2001). "Functional knee brace alters predicted knee muscle and joint forces in people with ACL reconstruction during walking. ." Journal of Applied Biomechanics 17: 297-311.
7. Elias, A. R., C. D. Hammill and R. L. Mizner (2015). "Changes in quadriceps and hamstring cocontraction following landing instruction in patients with anterior cruciate ligament reconstruction." J Orthop Sports Phys Ther 45(4): 273-280.
8. Elias, A. R., C. D. Hammill and R. L. Mizner (2016). "The Effect of Body Weight Support on Kinetics and Kinematics of a Repetitive Plyometric Task." J Appl Biomech 32(1): 69-77.
9. Elias, A. R., P. Lastayo, K. Harris and R. L. Mizner (2017). "Clinical Effectiveness of Jump Training Augmented with Body Weight Support Following ACL Reconstruction." Journal of Orthopaedic and Sports Physical Therapy 47(1 Conference proceedings): A40. In review with the American Journal of Sports Medicine.
10. Fregly, B. J., T. F. Besier, D. G. Lloyd, S. L. Delp, S. A. Banks, M. G. Pandy and D. D. D'Lima (2012). "Grand challenge competition to predict in vivo knee loads." J Orthop Res 30(4): 503-513.
11. Hart, J. M., J. W. Ko, T. Konold and B. Pietrosimone (2010). "Sagittal plane knee joint moments following anterior cruciate ligament injury and reconstruction: a systematic review." Clin Biomech (Bristol, Avon) 25(4): 277-283.
12. Messier, S. P., C. Legault, R. F. Loeser, S. J. Van Arsdale, C. Davis, W. H. Ettinger and P. DeVita (2011). "Does high weight loss in older adults with knee osteoarthritis affect bone-on-bone joint loads and muscle forces during walking?" Osteoarthritis Cartilage 19(3): 272-280.
13. Oiestad, B. E., I. Holm, A. K. Aune, R. Gunderson, G. Myklebust, L. Engebretsen, M. A. Fosdahl and M. A. Risberg (2010). "Knee function and prevalence of knee osteoarthritis after anterior cruciate ligament reconstruction: a prospective study with 10 to 15 years of follow-up." Am J Sports Med 38(11): 2201-2210.
14. Shakoor, N., J. A. Block, S. Shott and J. P. Case (2002). "Nonrandom evolution of end-stage osteoarthritis of the lower limbs." Arthritis Rheum 46(12): 3185-3189.
15. Sigward, S. M., P. Lin and K. Pratt (2016). "Knee loading asymmetries during gait and running in early rehabilitation following anterior cruciate ligament reconstruction: A longitudinal study." Clin Biomech (Bristol, Avon) 32: 249-254.

16. Spindler, K. P. and R. W. Wright (2008). "Clinical practice. Anterior cruciate ligament tear." N Engl J Med 359(20): 2135-2142.
17. Tsai, L. C., I. S. Scher and C. M. Powers (2013). "Quantification of tibiofemoral shear and compressive loads using a MRI-based EMG-driven knee model." J Appl Biomech 29(2): 229-234.
18. von Porat, A., E. M. Roos and H. Roos (2004). "High prevalence of osteoarthritis 14 years after an anterior cruciate ligament tear in male soccer players: a study of radiographic and patient relevant outcomes." Ann Rheum Dis 63(3): 269-273.
19. Wilk, K. E., L. C. Macrina, E. L. Cain, J. R. Dugas and J. R. Andrews (2012). "Recent advances in the rehabilitation of anterior cruciate ligament injuries." J Orthop Sports Phys Ther 42(3): 153-171.
20. Wilk, K. E., K. P. Spindler, E. McCarty, D. Grooms and K. G. Silbernagel (2017). "Improving ACL Reconstruction Outcomes." J Orthop Sports Phys Ther 47(3): 1-17.

Program Director/Principal Investigator (Last, First, Middle): Mizner, Ryan L.

ITHS Institute of Translational Health Sciences — Accelerating Research. Improving Health.

DETAILED BUDGET

FROM 03/01/18 THROUGH 02/28/19

List PERSONNEL (Applicant Organization Only) — Use Cal, Acad, or Summer to Enter Months
Devoted to Project — Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe
Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Ryan Mizner, PT, PhD	PI		1.50			$0 (15% effort release time)	0	0
Undergrad assist - TBD	RA	1.50			20,000	2,500	125	2,625
SUBTOTALS →						2,500	125	2,625

CONSULTANT COSTS None	
EQUIPMENT *(Itemize)* None	
SUPPLIES *(Itemize by category)* Expendible supplies for motion analysis assessment of treatment effect: tape, wraps, etc. $117 Lab Supplies for ELISA assay (pipettes, syringe, needles, specimen containers) $2215 CTX-II cartilage biomarker ELISA $1,180 for 1 plate 96 wells = $1,180 C2C cartilage BIOMARKER Assay $850/plate for 1 plate and 96 wells = $850 Chemical Creatine Assay kit $81/plate = $81 CPII Procollagen Type II C-propeptide Assay $650 for 1 plate = $650 Hyaluronic Acid Samples $982 per plate = 1 plate = $982	4,075
TRAVEL Site visit direct flight to Colorado with mentor Jennifer Stevens-Laplsey (ticket = $ 550) = $550 Dr. Stevens-Lapsley will providing housing and M&I accomodations during my trip	550
OTHER EXPENSES (Itemize by category) Laboratory Testing for new assay procedures = $2000 Participants Payment for Testing (5 patients , 3 testing times, $50/test visit for travel and time spent) =$50 * 15 = $750	2,750

CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS		10,000
SUBTOTAL DIRECT COSTS FOR BUDGET PERIOD		$	10,000
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATION COSTS	0%	-
TOTAL DIRECT COSTS FOR BUDGET PERIOD		$	10,000
TOTAL INDIRECT COSTS FOR BUDGET PERIOD		$	0
TOTAL COSTS FOR BUDGET PERIOD		**$**	**10,000**

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Mizner, Ryan Loy

eRA COMMONS USER NAME (credential, e.g., agency login): RMIZNER

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Montana State University – Bozeman	BS	05/1998	Biomechanics
University of Delaware	MPT	08/2000	Physical Therapy
University of Delaware	PhD	01/2005	Biomechanics and Movement Science

A. Personal Statement

The proposed project for submission as part of the ITHS Scholars program describes a prospective clinical trial design to test the efficacy of a novel and newly invented rehabilitation treatment technique to improve successful and safe return to preinjury levels of physical participation. I am uniquely qualified to serve as the Principal Investigator for this work given its emphasis on clinical science, knee osteoarthritis, and interventions focused on adapting exposure to physical stress. After I completed my clinical degree, I chose to stay at the University of Delaware to complete my doctoral training as they housed a Center of Biomedical Research Excellence (COBRE) for Osteoarthritis Research. In addition, I benefited from the unique and required training experiences and mentorship required from my research assistantship support from UD's T32 training grant from the NIH. My RA role was to coordinate a randomized controlled trial in outpatient physical therapy for patients with total knee replacement. I completed hundreds of clinical research examinations that utilized a combined biomechanical and clinical methodology similar to our proposed pilot project. Since completing my doctoral training, I've successfully completed applied research projects that focus on measuring the impact of mechanical exposure as it relates to patient outcomes. At one extreme, I worked to lessen overexposure to physical stress in order to reduce the chance of injury in bricklaying masons. Conversely, I have quantified underexposure to physical stress on skeletal muscle hampering recovery of strength after total knee replacement. The results of my scientific efforts have had broad and meaningful impact with a purposeful mix of publications in well-respected medical, rehabilitation, and science journals. Over 3000 citations of my collective manuscripts provide evidence for the impact of our scientific works. I have established that I can continue my scholarly productivity with excellent institutional support at the University of Montana for the last seven years.

Publications below corroborate my scientific contributions to clinical practice and experience in clinical trials:

1. Petterson SC, **Mizner RL**, Stevens JE, Raisis L, Bodenstab A, Newcomb W, Snyder-Mackler L. Improved Function From Progressive Strengthening Interventions After Total Knee Arthroplasty: A Randomized Clinical Trial With an Imbedded Prospective Cohort. *Arthritis Rheum.* 2009 Feb:61(2):174-183. PMID: 19177542.
2. LaStayo PC, Meier WA, Marcus RL, **Mizner RL**, Dibble LE, Peters C. Reversing Muscle and Mobility Deficits 1 to 4 Years after TKA: A Pilot Study. Symposium: Advanced Techniques for Rehabilitation after Total Hip and Knee Arthroplasty. Clin Orthop Relat Res. 2009 June; 467:1493–1500.
3. **Mizner RL**, Petterson SC, Clements KE, Zeni JA, Irrgang JJ, Snyder-Mackler L. Measuring Functional Improvement after Total Knee Arthroplasty Requires both Performance-based and Self-Report Assessments: A Longitudinal Analysis of Outcomes. *J Arthroplasty*. 2011 Aug;26(5):728-37. PMID: 20851566. PMCID: PMC3008304.
4. **Mizner RL**. Emerging Perspectives Related to Quadriceps Central Activation Deficits in Patients with Total Knee Arthroplasty. Exerc Sport Sci Rev. 2012 Apr;40(2):61-62. PMID:22441557.

B. Positions and Honors

Positions and Employment

2000-04: Research Assistant, Department of Physical Therapy, University of Delaware, Newark, DE
2000-04: Staff Physical Therapist, University of Delaware Physical Therapy Clinic, Newark, DE
2004-09: Assistant Professor, Depart of Physical Therapy, Eastern Washington Univ, Spokane, WA
2007-09: Per Diem Physical Therapist, Providence Rehabilitation Services, Spokane WA
2009-2013: Assistant Professor, School of Phys Ther & Rehab Sci, Univ of Montana, Missoula, MT
2009-present: Per Diem Physical Therapist, UMPT Sports & Orthopaedic Clinic, Missoula, MT
2010-present: Staff Physical Therapist, Deer Lodge Medical Center, Deer Lodge, MT.
2014-2015: Interim Chair, School of Physical Therapy & Rehab Sci, Univ of Montana
2014-present: Associate Professor, School of Physical Therapy & Rehab Sci, Univ of Montana

Professional Memberships

American Physical Therapy Association – Section member in Orthopaedics, Sports, and Research
American College of Sports Medicine -Northwest regional chapter

Manuscript Reviewer

Clinical Biomechanics (Clin Biomech)
Journal of Biomechanics (J Biomech)
Journal of Orthopaedic Research (J Ortho Res)
Journal of Orthopaedic and Sports Physical Therapy (J Orthop Sports Phys Ther)
Physical Therapy (Phys Ther)
Medicine and Science in Sport and Exercise (Med Sci Sports Exerc)
Arthritis and Rheumatism (Arthritis Rheum)

Honors

2005 New Investigator Recognition Award Finalist - Orthopaedic Research Society
2009 Outstanding Faculty Merit Award for Scholarship Eastern Washington University
2009 Margaret Moore Outstanding New Academic Faculty Award - APTA
2013 & 2017 Faculty Merit Awards – University of Montana, Missoula
2016 Best Annual Presentation Award - American Academy of Orthopaedic Manual Physical Therapists
2017 Best Poster Award from Gait and Clinical Movement Analysis Society Annual Conference

C. Contribution to Science

1. I serve as principal investigator in a series of studies that have examined the movement patterns of athletes who participate in cutting and pivoting sports such as basketball. I am particularly interested in the neuromuscular factors of the lower extremity joints as they relate to anterior cruciate ligament (ACL) injury risk and post-operative knee osteoarthritis. While many studies have shown improved patient reported outcomes with modern rehab

trials, reinjury rates are 15 times as high in athletes who have had an ACL reconstruction compared to their uninjured peers. Most biomechanical examinations of patients with ACL reconstruction focus on walking mechanics and relatively few examine jump landing. Even less utilize electromyography techniques to gauge muscle coordination patterns. Jump landing is the most common mode of non-contact ACL injury. We have found increased co-contraction between the quadriceps and hamstring muscles during jump landing in athletes with ACL reconstruction which has been previously associated with poor dynamic control of the knee joint and contributes to increased knee joint compressive loads. Our lab findings suggest that undesirable movement patterns are adaptable with instruction and are ripe for a training intervention. As jump landing is inherently a high intensity activity, it is generally performed at low training volumes. Limiting practice is understandable when patients are fearful and is prudent for safety reasons. Yet, restricting practice repetitions starkly contrasts with principles of motor learning, which emphasize high repetition to reestablish normal movement patterns. To address this shortcoming, we have devised a mechanical device that reduces the influence of gravity to attenuate physical loads and allow safe increase in the repetitions for jump landing. Our recent manuscript in IJSPT confirms we can use our custom unweighting device to substantially reduce the joint loads during jump training to safely allow high repetition of training while still managing to maintain task specificity of joint coordination and timing. We have a patent submitted (Serial No. 14/532,949) through our research office to protect this intellectual property and we currently have two competitive pilot grant awards to begin to test this intervention strategy in clinical trial. I will use similar methodology to examine the muscle recruitment of the ankle plantar flexor musculature during walking for our patients with PAD as I use to examine recruitment patterns of the thigh muscles in our athletes.

1. **Mizner RL**, Kawaguchi JK, Chmielewski TL. Lower Kinetic Chain Muscle Strength Does Not Predict Post-Instruction Landing Pattern Improvement in Female Athletes. *Journal of Orthopaedic and Sports Physical Therapy.* 2008 June; 38(6): 265-271. PMID: 18515963.
2. Elias AR, Kinney AE, **Mizner RL**. High Repetition Jump Training Coupled with Body Weight Support in a Patient with Anterior Cruciate Ligament Reconstruction: A Case Report. International Journal of Sport Physical Therapy (IJSPT). 2015 Dec;10(7):1035-49. PMID:26672476.
3. Elias AR, Hammill CD, **Mizner RL.** Changes in Quadriceps and Hamstring Co-contraction Following Landing Instruction in Patients with ACL Reconstruction. *J Orthop Sports Phys Ther*. 2015 Apr;45(4):273-80. PMID: 25679342.
4. Elias AR, Hammill CD, **Mizner RL**. The Effect of Body Weight Support on Kinetics and Kinematics of a Repetitive Plyometric Task. *J Applied Biomech*. 2016 Feb;32(1):69-77. PMID: 26398961

2. My first series of publications were focused on the extent, source, and clinical impact of quadriceps muscle weakness on the perioperative care of patients with total knee arthroplasty (TKA) for knee osteoarthritis. Our understanding of how TKA surgery could change the muscle strength of limbs weakened by advance knee osteoarthritis was understudied especially in the acute recovery stages after surgery. We discovered that a patient's quadriceps muscle lost over half of its preoperative strength in the early recovery stages from surgery. Strength recovery was prolonged despite progressive rehabilitation efforts and the recalcitrant muscle weakness was a dominant physical impairment that limited patients walking ability and functional performance. Our findings have considerable impact as there are over half a million TKA procedures performed each year in the United States to treat disability from knee osteoarthritis. Our findings from these 4 early publications in my career have been well-cited and have spurred multiple intervention based trials to address quadriceps weakness to enhance functional

performance for patients with TKA. I served as a principal or co-investigator in these investigations. These early experiences provided critical foundational expertise to make important design and methodology decision to conduct a clinically focused research agenda. I continue to use these skills and outcomes style when designing clinical interventions as I work additional patient populations with knee disorders such as athletes with ACL reconstruction.

1. **Mizner RL**, Petterson SC, Stevens JE, Vandenborne K, Snyder-Mackler L. Early Quadriceps Strength Loss After Total Knee Arthroplasty: The Contributions of Muscle Atrophy and Failure of Voluntary Muscle Activation. *J Bone Joint Surg Am*. 2005 May; 87(5):1047-53. PMID: 15866968. PMCID: PMC1167681.
2. **Mizner RL**, Petterson SC, Stevens JE, Axe MJ, Snyder-Mackler L. Preoperative Quadriceps Strength Predicts Functional Ability One Year after Total Knee Arthroplasty. *J Rheumatol*. 2005 Aug; 32 (8): 1533-9. PMID: 16078331.
3. **Mizner RL**, Petterson SC, Snyder-Mackler L. Quadriceps Strength and the Time Course of Functional Recovery after Total Knee Arthroplasty. *J Orthop Sports Phys Ther*. 2005; 35(7):424-436. PMID: 16108583.
4. **Mizner RL**, Snyder-Mackler L. Altered Loading During Walking and Sit-to-stand is Affected by Quadriceps Weakness after Total Knee Arthroplasty. *J Orthop Res*. 2005; 23(5):1083-90. PMID: 16140191.

3. I was a co-investigator in project that investigated ergonomic controls to reduce work-related injury risk factors to the spine and shoulder for workers in the construction trades. We examined the use of and barriers to using several methods to reduce exposure to mechanical stresses from lifting concrete masonry blocks in the bricklaying trade. My role was to develop methodologies to accurately examine spine and shoulder motions by incorporating 3 dimensional motion analysis techniques into field working environments. Standard methods to determine movement induced stress in the construction trade industry consisted mainly of observational screening by experts or conduct movement coding by reviewing video tapes of worker performance. The novel nature of these investigations prompted publications in lay journals in the fields of work related injury and motion capture. We found considerable advantages in reducing mechanical over-exposure to peak and cumulative joint motions using ergonomically derived controls. We also quantified important adoption barriers such as cost and stakeholder perceptions. The study provides information from several perspectives about ergonomic controls for a high-risk bricklaying task, which will benefit occupational safety experts, health professionals, and ergonomists. These experiences provided me with robust problem-solving strategies in using the motion analysis techniques in our current grant application. We are using video-based motion analysis with force plates for the performance evaluation of movement behavior in patients with ACL reconstruction. These methods will be part of the primary outcome tools used in our upcoming grant proposal.
    1. Hess JA, **Mizner RL**, Kincl L, Anton D. Alternatives to lifting concrete masonry block over rebar: Biomechanical and perceptual evaluations. Ergonomics (Ergonomics). 2012 Oct;55(10):1229-42. PMID: 22849706.
    2. Anton D, **Mizner RL**, Hess JA. The Effect of Lift Teams on Kinematics and Muscle Activity of the Upper Extremity and Trunk. J Orthop Sports Phys Ther. 2013 Apr;43(4):232-241. PMID: 23321695.

Complete list of published work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1DyqsthNtLDku/bibliography/48820633/public/?sort=date&direction=descending

D. Research Support

Recent Past Research Support

Mini-Grant for the CTR-IN parent award: 1U54GM104944-01 Award Dates: 12/31/15 - 6/30/16
Role: Co-Principal Investigator (Co-PI: Mays RJ)
Awarding Institution: Sub-award from the University of New Mexico
National Institutes of Health (NIGMS) (PI: Langer R with UNM)
Title: Community-based walking exercise enhanced by orthoses to improve walking ability.
Aim: This project extends the Pilot Award funded previously to expand upon our pilot award for an open-label, interventional trial with a historical comparison group of carbon fiber ankle foot orthosis (AFO) to improve walking performance of patients with claudication from peripheral artery disease.

Miami-Marquette Challenge Research Grant
Role: Principle Investigator (15% effort) Award Dates: 1/1/2014 – 12/31/2016
Awarding Institution: Foundation for Physical Therapy
Title: A Novel Unweighting Technology to Address Psychological Impairments Limiting Outcomes after ACL Reconstruction
Aim: To determine if training with the Bodyweight Reduction Instrument to Deliver Graded Exercise (BRIDGE) will reduce psychological impairments and restore knee loading performance in the anterior cruciate ligament reconstructed (ACLR) knee more than standard jump training. Our long-term goal is to develop an effective treatment paradigm that will address the psychological factors that limit retraining efforts to restore the force absorption capacity of the ACLR knee.

New Investigator Grant
Role: Co-PI (10% effort) (Co-PI: Elias AR) Award Dates: 5/15/2014 – 1/15/2016
Awarding Institution: Orthopaedic Section of the American Physical Therapy Association
Title: A clinical trial to improve motor learning in plyometric training post-ACLR via a novel body-weight support system
Aim: To determine if high volume jump training with reduced loading intensity will preferentially enhance motor learning for improved load attenuation compared to standard jump training.

Pilot Project Grant (parent award: 1U54GM104944-01) Award Dates: 07/01/2014 - 6/30/2015
Role: Co-Principal Investigator (10% effort) (Co-PI: Mays RJ)
Awarding Institution: National Institutes of Health (NIGMS) (PI: Langer R with UNM)
Title: Community-based walking exercise enhanced by orthoses to improve walking ability in patients with peripheral artery disease
Aim: We will test the hypotheses that using carbon fiber ankle foot orthosis (AFO) with patients who have intermittent claudication from peripheral artery disease (PAD) will reduce barriers and improve the efficacy of community walking exercise.

OH008307 Agreement # 1030-53 Award Dates: 07/2006 - 06/2010
Awarding Institution: DHHS/NIOSH – The Center for Construction Research and Training (CPWR)
Title: Ergonomic Controls for the Masonry Industry
Role: Co-Investigator (PI: Anton, D)
Aim: The long-term goal of the work is to reduce the incidence of work-related MSDs among masonry workers by implementing effective ergonomic controls. The purpose of the investigation was to identify the current use of ergonomic controls (e.g. Lifting over Rebar, Use of Lift Teams with Large Concrete Block), evaluate promising controls for effectiveness, and disseminate knowledge of these controls throughout the industry.