Doctoral Dissertation Defense Announcement

Seung-Yi Lee

“From Characterization to Treatment of Cervical Spinal Cord Injury in Rat Models Using Multimodal Magnetic Resonance Imaging”

Candidate for Doctor of Philosophy in Biophysics
Graduate School of Biomedical Sciences
Medical College of Wisconsin

Committee in Charge:
Matthew Budde, PhD (Advisor and Chair)
Shekar Kurpad, MD, PhD
L. Tugan Muftuler, PhD
Andrew Nencka, PhD
Antje Kroner-Milsch, MD, PhD
Brian Schmit, PhD

Thursday, April 7th, 2022 at 2:00 PM (CST)

Live Public Viewing: https://mcw.edu.zoom.us/j/98964917748?pwd=VTI3UjFna1RMRHFGWXo3N2pCS0lpZz09
Meeting ID: 989 6491 7748
Passcode: LxvC84im
**Graduate Studies:**

Biochemistry of the Cell
Molecular and Cellular Biology
Mechanism of Cellular Signaling
Fundamentals of Neuroscience
Graduate Neuroanatomy
Neuroscience Journal Club
Introduction to MRI
Biostatistics I
Research Ethics Discussion
Functional MRI Contrast
Career Development in Biomedical Sciences
Journal Club MRI
Seminar
Reading and Research
Doctoral Dissertation
Abstract

Traumatic spinal cord injury (SCI) is a devastating event that can lead to permanent neurological impairment and dramatically affects quality of life. Diagnosis of SCI is based on neurological examination, but the acute neurological status is a poor predictor of long-term functional outcomes since some patients may have substantial recovery while others may not. Magnetic resonance imaging (MRI) is routinely used to aid diagnosis, but MRI measurements of anatomic features such as the lesion size are also poor predictors of outcome. Importantly, axonal injury is the pathology most related to long-term functional outcomes. A diffusion MRI technique optimized for the spinal cord, filtered diffusion weighted imaging (fDWI), was previously shown to enhance detection of axonal injury and improve prognostic accuracy of SCI in a rat thoracic SCI model. However, the cervical cord is the most common level of injury in patients with SCI. The utility of fDWI on a cervical SCI rodent model has not been investigated, despite the greater clinical relevance and clear anatomic and functional differences between the cervical and thoracic spinal cord.

To address these knowledge gaps, this dissertation investigates cervical contusion SCI using advanced MRI in the rat. Additionally, it examines the utility of a surgical intervention, myelotomy, as a possible therapy in the same rat model with MRI and functional assessments. First, acute MRI biomarkers in a rat model of cervical SCI was compared with long-term functional assessments and tissue-sparing. A strong association between early edema volume and chronic motor function was revealed. Further, analytic tools were developed to create a custom rat spinal cord template and perform spatial alignment of images across all animals. These methods enabled detection of damage to individual white matter tracts that were more correlated with function compared to values measured from the whole cord. Subsequently, an MRI method was developed and optimized to enhance diffusion imaging in the spinal cord. Motion of the spinal cord and anatomy-induced inhomogeneities in the MRI magnetic field cause significant artifacts that produce image ghosting and distortions in echo planar imaging, the most common acquisition strategy for spinal cord diffusion. We implemented a diffusion prepared fast spin-echo technique in combination with motion compensated diffusion gradients, respiratory, cardiac gating, and spinal cord-specific diffusion weighting schemes to achieve high-quality sagittal spinal cord diffusion imaging in the healthy and injured rat. Lastly, a surgical myelotomy was examined in the rat cervical SCI model. Myelotomy has been shown to improve outcomes in thoracic SCI by reducing the pressure in the swollen cord. Here, we evaluated myelotomy for the first time in cervical SCI utilizing the established contusion cervical SCI model and multimodal MRI including resolution-matched sagittal diffusion and perfusion weighted imaging. The results demonstrated immediate beneficial changes after myelotomy, such as restored perfusion.
and reduced edema. However, these biological changes did not translate into significant recovery of long-term motor function.

In summary, this dissertation thoroughly characterized rat cervical contusion SCI models and demonstrated important roles of MRI in assessing traumatic SCI and treatment effects. The results collectively reveal that while gains in monitoring the spinal cord with MRI enhanced visualization and quantification of salient features, the biological consequences of injury and those alleviated myelotomy have complex relationships with the ultimate functional recovery. Both MRI acquisition and analytic enhancements shown in this work may have potential for clinical translation.
Seung-Yi Lee, MS
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EDUCATION

Medical College of Wisconsin
Milwaukee, WI
Ph.D. Candidate in Biophysics
Expected gradation: May 2022
- Advisor: Matthew D. Budde, Ph.D.
- Dissertation: From Characterization to Treatment of Cervical Spinal Cord Injury in Rat Models Using Multimodal Magnetic Resonance Imaging

Pennsylvania State University
University Park, PA
Master of Science in Chemistry
May 2015
- Advisor: Paul S. Cremer, Ph.D.

Catholic University of Korea
Seoul, South Korea
Bachelor of Science in Chemistry, Graduated with Honors
August 2012

RESEARCH & TEACHING EXPERIENCE

Medical College of Wisconsin
Milwaukee, WI
Department of Biophysics & Neurosurgery
Graduate Research Assistant in Dr. Matthew D. Budde’s Lab
May 2017-present
- Established and characterized cervical spinal cord injury rat model and evaluated the effects of surgical treatment using multimodal MRI.
- Developed spinal cord tailored MRI scan protocols utilizing spin-echo diffusion imaging coupled with motion compensation gradient, respiratory and cardiac gating systems, which led to improved quality of diffusion imaging.

Pennsylvania State University
University Park, PA
Department of Chemistry
Research Assistant in Dr. Paul S. Cremer’s Lab
June 2013-April 2016
- Studied salting-out effects of osmolytes on hydrophobic bio-model polymers by differential scanning calorimetry.

Teaching Assistant
January 2013-May 2016
- Courses: Chemical Principles I (Chem 110): led problem-solving sessions and discussion.
- Experimental Chemistry I (Chem111): lectured and assisted students in performing introductory chemistry experiments.
Chr. Hansen Inc.  
Milwaukee, WI  
Food Technologist Intern  
January 2011-August 2011

- Designed and conducted pigment-stability studies using colorimetry.
- Generated spectrophotometric data to analyze color samples and created product samples based on data analysis.
- Documented customer reports for the products' studies.

AWARDS

- Graduate Student Travel Award for international conference  
  2022
- ISMRM Educational Stipend  
  2022
- Biohealth Communications Competition Top 10 Finalist  
  2021
- CTSI Biostatistical Consulting mini-grant  
  2021
- ISMRM Educational Stipend  
  2021
- Graduate Student Travel Award for domestic conference  
  2019

ACADEMIC SERVICE & MEMBERSHIP

- National Neurotrauma Society, Student Member  
  2018-present
- International Society for MRM, Student Member  
  2018-present
- Society for Neuroscience, Student Member  
  2019
- American Association for the Advancement of Science, Member  
  2018 - 2019

PUBLICATIONS


SUNMITTED MANUSCRIPT

- Seung-Yi Lee, Brian D Schmit, Shekar N Kurpad, Matthew D Budde. “Acute MRI Predictors of Chronic Motor Function and Tissue Sparing in Rat Cervical Spinal Cord Injury.”, *Under revision*


**Seung-Yi Lee**, Natasha Wilkins, Brian D. Schmit, Shekar N. Kurpad, Matthew D. Budde, “Comparison of diffusion tensor imaging and double diffusion encoding in a rat model of persistent spinal cord compression” *Neuro Trauma2018*, Toronto, ON Canada, August 2018 **Poster Presenter**


**Seung-Yi Lee**, Carol Everson, Matthew D. Budde, “Development of a Rat Brain Multimodal MRI Protocol for Applications to Mild TBI” *IDP/NDP welcome poster session*, Medical College of Wisconsin, Milwaukee, WI, August 2017 **Poster Presenter**

**Seung-Yi Lee**, Halil I. Okur, Kelvin B. Rembert, Paul S. Cremer, “Isotope effects of water on hydrophobic hydration” *The Biophysical Society Pennsylvania Network Meeting*, University Park, PA, October 2013 **Poster Presenter**
MENTORING & VOLUNTEERING

- Catalyst BioConsulting  
  *Business Consultant & Communications Lead*  
  Milwaukee, WI  
  *March 2020-February 2022*

- GE Girls GEHC Day  
  *Volunteer*  
  Waukesha, WI  
  *June 2021*

- Summer Programs Symposium for Undergraduate  
  *Judge*  
  Milwaukee, WI  
  *August 2019*

- GE Girls GEHC Day  
  *Volunteer*  
  Waukesha, WI  
  *June 2019*

- Research Experience for Teachers Program  
  *Mentor*  
  University Park, PA  
  *July 2015*

- Penn State Korean Catholic Church Graduate Chapter  
  *President*  
  University Park, PA  
  *2013-2014*

- International Circle K at Alverno College  
  *Volunteer Member*  
  Milwaukee, WI  
  *2010-2011*