2nd CCRC Open House 2018

Francis Loth, Ph.D.
CCRC Executive Director
Professor and Harrington Chair
Departments of Biomedical and Mechanical Engineering

CCRC was established in 2012
1st Open House was 2013
What is the CCRC?

Group of professors, postdocs, and students conducting research on CM

We do not treat CM patients. UA has no medical school
CCRC Funded Projects (11 UA faculty)

Philip Allen (Psychology)
  • Biomarkers of surgical success in females with Chiari Malformation Type I, 2015
  • Non-invasive therapies for the treatment of chronic pain in CM, 2016
  • Chiari 1000 Project Manager, 2015

Rouzbeh Amini (Biomedical Engineering)
  • Biomechanical Assessment of Brain Deformation in Relation to Chiari Malformation, 2016

Brian Davis (Biomedical Engineering)
  • Gait Assessment in Chiari Malformation, 2018

Malena Español (Math)
  • MRI Based Classification of Chiari Malformation, 2014

Kevin Kaut (Psychology)
  • The Developmental and Psychoeducational Impact of Chiari Malformation, 2014

Nic Leipzig (Chemical and Biomolecular Engineering)
  • Transcriptional Profiling and microCT Assessment of Experimental Syringomyelia, 2015
  • Targeting Syrinx Transporters for Syringomyelia Treatment Strategies, 2013, 2015

Francis Loth (Mechanical and Biomedical Engineering)
  • Automated Morphometric Analysis for Diagnosis and Research, 2015
  • MRI Morphometric Traits of Type 1 Chiari malformation Across Age and Gender, 2015
  • Brain Damage in Chiari I Malformation

Bryn Martin, Aintzane Urbizu (Mechanical Engineering, Genetics)
  • Genetic Traits of CM Across Age and Gender, 2015

Leah Shriver (Chemistry/Biology)
  • Metabolic and Inflammatory Alterations in Patients with Chiari Malformation, 2013

David Tokar (Psychology)
  • Career Development Experiences of Individuals with CM, 2017

Co-Investigators: Ronald Otterstetter, (Exercise Science), John Elisa (Biomedical Eng.) and
Dawn Johnson (Psychology)
Goals of the CCRC:

• Apply the latest engineering, biological and psychological techniques to improve diagnoses and treatment options for Chiari

• Foster collaborations with leading clinicians and scientists

• Act as a focal point for the Chiari research community and attract more researchers to the study of Chiari
Two binders are placed on the table with the Clivus bone models with all the CCRC journal papers for your review.

Link to NCBI listing of CCRC Journal Papers:
Training/Exposure to CM Research:

- Several high school students
- Dozens of undergraduate students
- 6 Master Students
- 15 Doctoral students
- 2 Post Doctoral Fellows
- 2 Research Faculty

Two former UG students went on to get a neuroscience degree after leaving the university.
Bryn Martin, Ph.D.
Assistant Professor
Biological Engineering
University of Idaho
Brain Measurements Beyond Tonsillar Descent

Maggie S. Eppelheimer, James R. Houston, Soroush H. Pahlavian, Audrey M. Braun, Natalie J. Allen, Dipankar Biswas, Dorothy M. Loth, Aintzane Urbizu, Richard Labuda, Philip A. Allen, Jayapalli Bapuraj (Rajiv), Francis Loth

Jayapalli Bapuraj, MBBS
Associate Professor, Radiology
Division of Neuroradiology

Michigan Medicine
University of Michigan
Chiari Type I Malformation (CMI)

- Midsagittal MRI identification of tonsillar position of 3-5mm below foramen magnum (tonsillar ectopia)
- Symptoms: occipital headaches, neck pain, and balance problems (Fischbein, Saling et al. 2015)
- 0.1% of general population has CMI
- 1-2% of individuals without symptoms have tonsillar ectopia (Smith, Strahle et al. 2013)
Morphological data:

- CM Subjects came from *Chiari1000* project:
  - demographic info
  - MRI Images before surgery (>600) and after surgery (>120)
  - CT Image sets (>100)

- Controls came from many sources:
  - Human Connectome Project
  - Cleveland Clinic Foundation
  - National Institute of Mental Health

*Examination of these data has led to 6 journal papers ideas (2 published, 1 submitted, 3 in preparation)*
Research based software: **MorphPro**

**Commercial MRI software:**
- Manual drawing and calculations
- Manual recording and storage of morphometric data

**MorphPro:**
- Semi-automatic interface: automatic calculations
- Automatic recording and storage of morphometric measurements

**Measurement time:**
- 2-3 hrs
- 10-15 min
Results: Morphological markers:

1. Lowering of bone and soft tissue structures
   - 3mm reduction

2. Horizontally angled clivus bone
   - Wider basal and Boogard angle
   - Narrower Wackenheim angle

3. Odontoid process measurements
   - Extension into the spinal canal (Retrograde angulation)
Original Article

A morphometric assessment of type I Chiari malformation above the McRae line: A retrospective case-control study in 302 adult female subjects

James R. Houston, Maggie S. Eppelheimer, Soroush Heidari Pahlavian, Dipankar Biswas, Aintzane Urbizu, Bryn A. Martin, Jayapalli Rajiv Bapuraj, Mark Luciano, Philip A. Allen, Francis Loth

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6. Department of Radiology, Division of Neuroradiology, University of Michigan Health System, Ann Arbor, MI, 48103, USA
7. Department of Neurosurgery, Johns Hopkins University, Baltimore, MD, 21218, USA
Syringomyelia – smaller McRae Line for CM with SM compared to w/o EDS – smaller tonsillar position for those with EDS compare to those w/o EDS. Scoliosis – Basion to posterior axial line longer in CM with scoliosis compared to w/o
A Retrospective 2D Morphometric Analysis of Adult Female Chiari Type I Patients with Commonly Reported and Related Conditions

Maggie S. Eppelheimer¹, James R. Houston², Jayapalli R. Bapuraj³, Richard Labuda⁴, Dorothy M. Loth², Audrey M. Braun⁵, Natalie J. Allen⁵, Soroush Heidari Pahlavian⁵, Dipankar Biswas⁵, Aintzane Urbizu⁵,⁶, Bryn A. Martin⁷, Cormac O. Maher⁸, Philip A. Allen² and Francis Loth¹,⁵

¹ Department of Biomedical Engineering, Conquer Chiari Research Center, University of Akron, Akron, OH, United States, ² Department of Psychology, Conquer Chiari Research Center, University of Akron, Akron, OH, United States, ³ Department of Radiology, University of Michigan Health System, Ann Arbor, MI, United States, ⁴ Conquer Chiari, Wexford, PA, United States, ⁵ Department of Mechanical Engineering, Conquer Chiari Research Center, University of Akron, Akron, OH, United States, ⁶ Duke University Medical Center, Duke Molecular Physiology Institute, Durham, NC, United States, ⁷ Department of Biological Engineering, University of Idaho, Moscow, ID, United States, ⁸ Department of Neurosurgery, University of Michigan Health System, Ann Arbor, MI, United States
18 of these parameters to be different between CM and controls.

Notable Results:
- Cerebellum area was 15% larger than that of controls (8.4% even when excluding the tonsillar area below the FM)
- Much smaller CSF spaces in CM vs controls (as expected)
Quantification of Cerebellar Crowding in Type I Chiari Malformation

Dipankar Biswas¹, Maggie S. Eppelheimer², James R. Houston³, Alaaddin Ibrahimi¹, J. Rajiv Bapuraj⁴, Richard Labuda⁵, Philip A. Allen³, David Frim⁶, Francis Loth¹, ²

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Three Additional CM Morphometric Studies are in progress that also examine midsagittal MRI images

1. Changes after Decompression Surgery
2. Adult Males
3. Pediatric Subjects
Conclusions

• Developed software tools that help rapidly evaluate brain morphometrics in effort to discover new and important parameters that will help in diagnosis and evaluation of people with CM
  *(software demonstration this afternoon in the CCRC Lab)*

• Discovered many new parameters that are significantly different in CM compared to controls. Must determine the relationship of these parameters with symptomology to understand the pathophysiology of CM. This could help determine who are the best candidates for surgery or in evaluating different surgical procedures.
Acknowledgements

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