CONQUER CHIARI®
RESEARCH CENTER

The University of Akron

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

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 Espańol (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

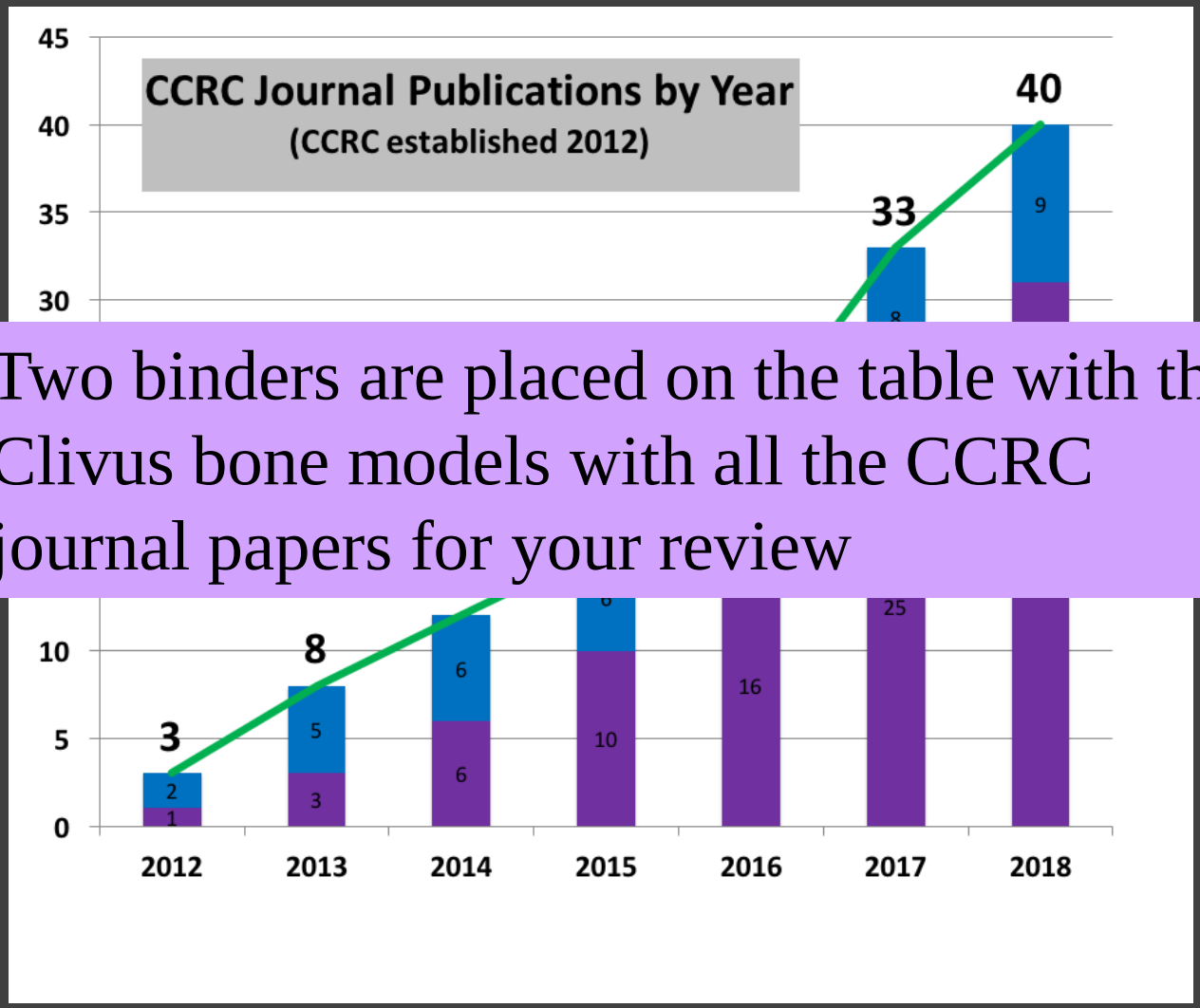
David Tokar (Psychology)
- Career Development Experiences of Individuals with CM, 2017

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

CCRC Journal Paper Report – Summer 2018



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:
https://www.ncbi.nlm.nih.gov/sites/myncbi/francis.loth.1/collections/54455604/public/

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 when on to get a neuroscience degree after leaving the university.

Bryn Martin, Ph.D.
Assistant Professor
Biological Engineering
University of Idaho

Jim Houston, Ph.D.
Assistant Professor
Developmental Psychology
Middle Tennessee State University

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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

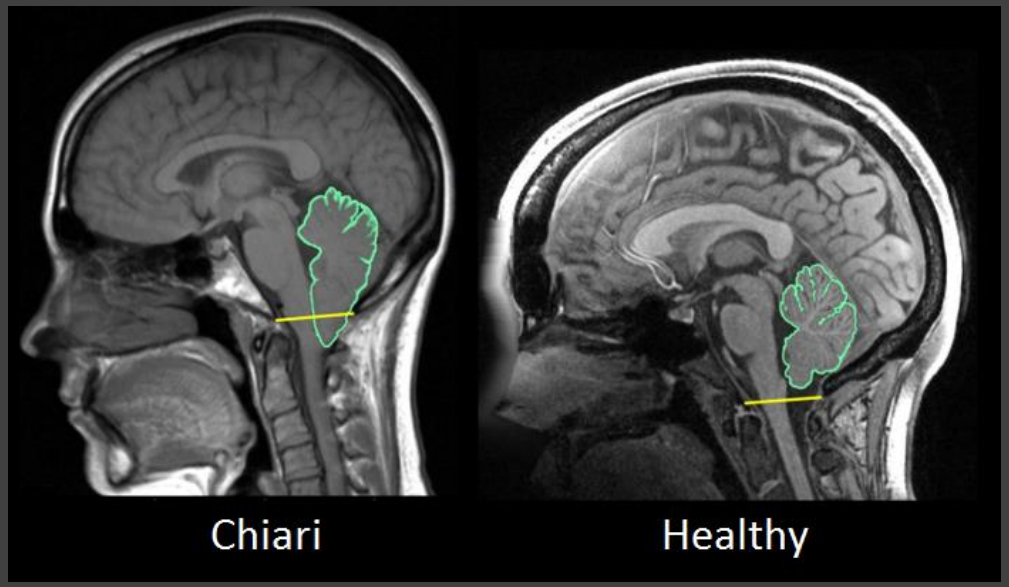
Jayapalli Bapuraj, MBBS

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)



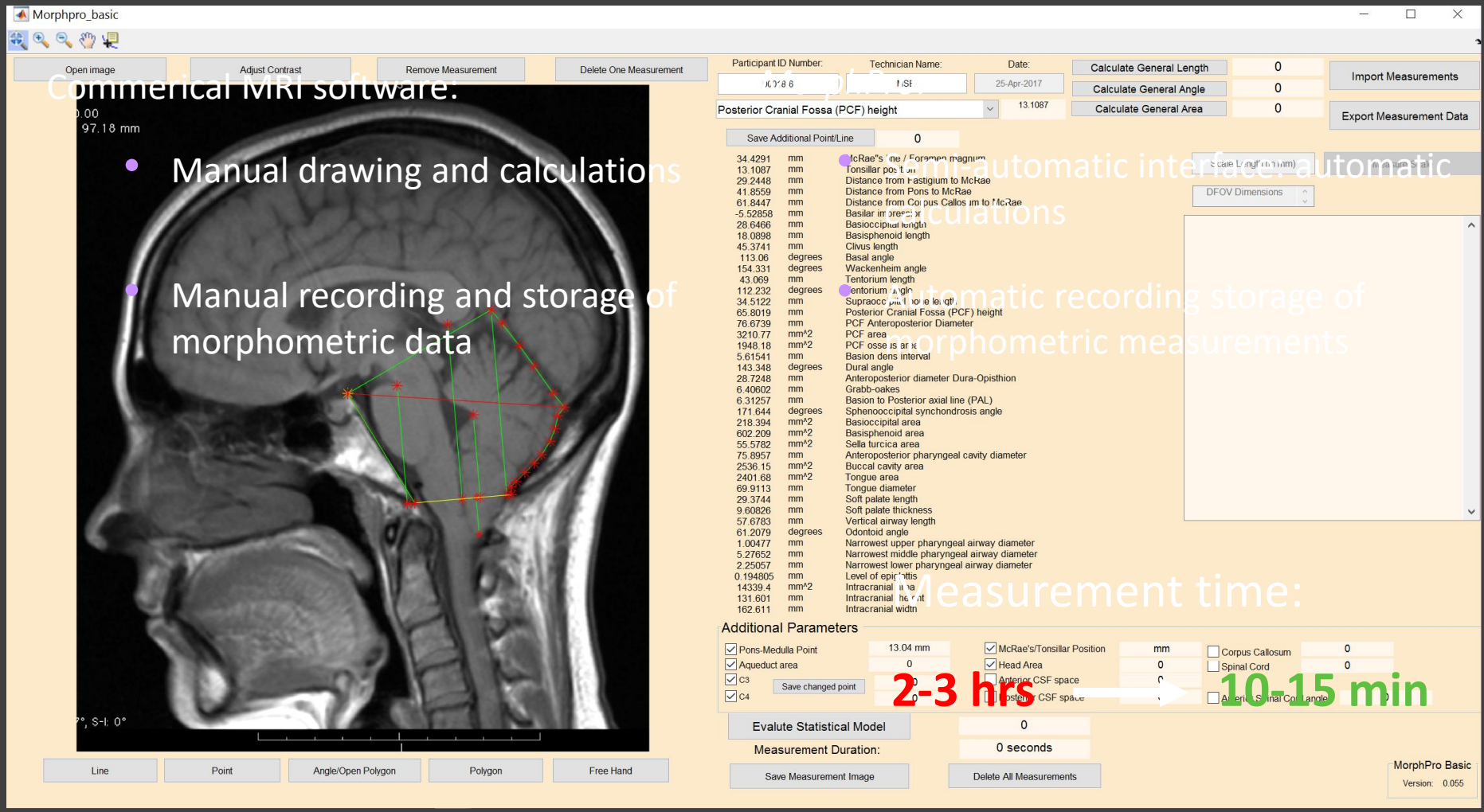
Morphological data:

- 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

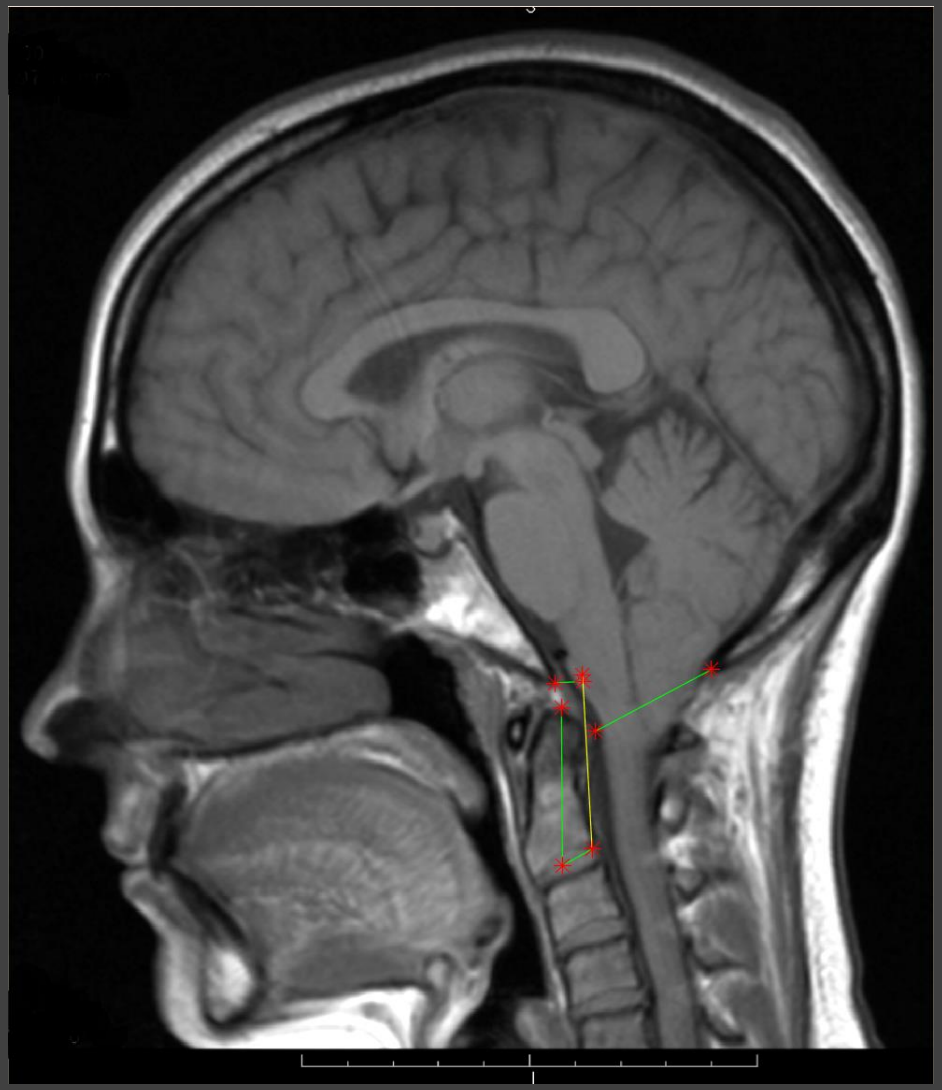
*Examination of these data has led to **6 journal papers ideas**

(2 published, 1 submitted, 3 in preparation)

Research based software: *MorphPro*



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)

Journal of Neuroradiology 45 (2018) 23–31

Available online at ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

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[a], Maggie S. Eppelheimer[b], Soroush Heidari Pahlavian[c], Dipankar Biswas[c], Aintzane Urbizu[c,d], Bryn A. Martin[e], Jayapalli Rajiv Bapuraj[f], Mark Luciano[g], Philip A. Allen[a], Francis Loth[b,c,*]

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[d] Duke Molecular Physiology Institute, Duke University Medical Center, Durham, NC, 27703, USA
[e] Department of Biological Engineering, University of Idaho, Moscow, ID, 83844, USA
[f] Department of Radiology, Division of Neuroradiology, University of Michigan Health System, Ann Arbor, MI, 48103, USA
[g] Department of Neurosurgery, Johns Hopkins University, Baltimore, MD, 21218, USA

TABLE 2 | Prevalence of conditions in CMI sample with demographics.

Prevalent condition	*N*	Condition prevalence (%)	Mean age in years (*stdev*)	Percent caucasian (%)
Migraine headaches	147	62	36 *(10)*	91.2
Scoliosis	45	19	35 *(10)*	95.5
Syringomyelia	38	16	32 *(10)*	92.1
Fibromyalgia	33	14	37 *(10)*	93.9
Chronic fatigue syndrome	31	13	38 *(11)*	87.1
Spinal dysraphism	29	12	35 *(10)*	93.1
Ehlers Danlos syndrome	21	9	36 *(10)*	100.0
Other Endocrine Diseases	20	8	37 *(11)*	95.0
Pseudotumor cerebri	20	8	36 *(12)*	85.0
Raynaud phenomenon	18	8	38 *(10)*	94.4
Craniocervical instability	17	7	38 *(10)*	88.2
Sleep Apnea	16	7	41 *(12)*	93.8

Total CMI participants in study: 236. Conditions in bold are labeled as RC. Overall racial and ethnic prevalence in our sample: 2% Native American/Alaska Native, 2% Asian, and 6% Black/African American. PCs include some conditions that were diagnosed as a child.

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
Scoliosis – Basion to posterior axial line longer in CM with scoliosis compared to w/o

frontiers in Neuroanatomy

ORIGINAL RESEARCH
published: 19 January 2018
doi: 10.3389/fnana.2018.00002

Check for updates

A Retrospective 2D Morphometric Analysis of Adult Female Chiari Type I Patients with Commonly Reported and Related Conditions

*Maggie S. Eppelheimer[1], James R. Houston[2], Jayapalli R. Bapuraj[3], Richard Labuda[4], Dorothy M. Loth[2], Audrey M. Braun[5], Natalie J. Allen[5], Soroush Heidari Pahlavian[5], Dipankar Biswas[5], Aintzane Urbizu[5,6], Bryn A. Martin[7], Cormac O. Maher[8], Philip A. Allen[2] and Francis Loth[1,5]**

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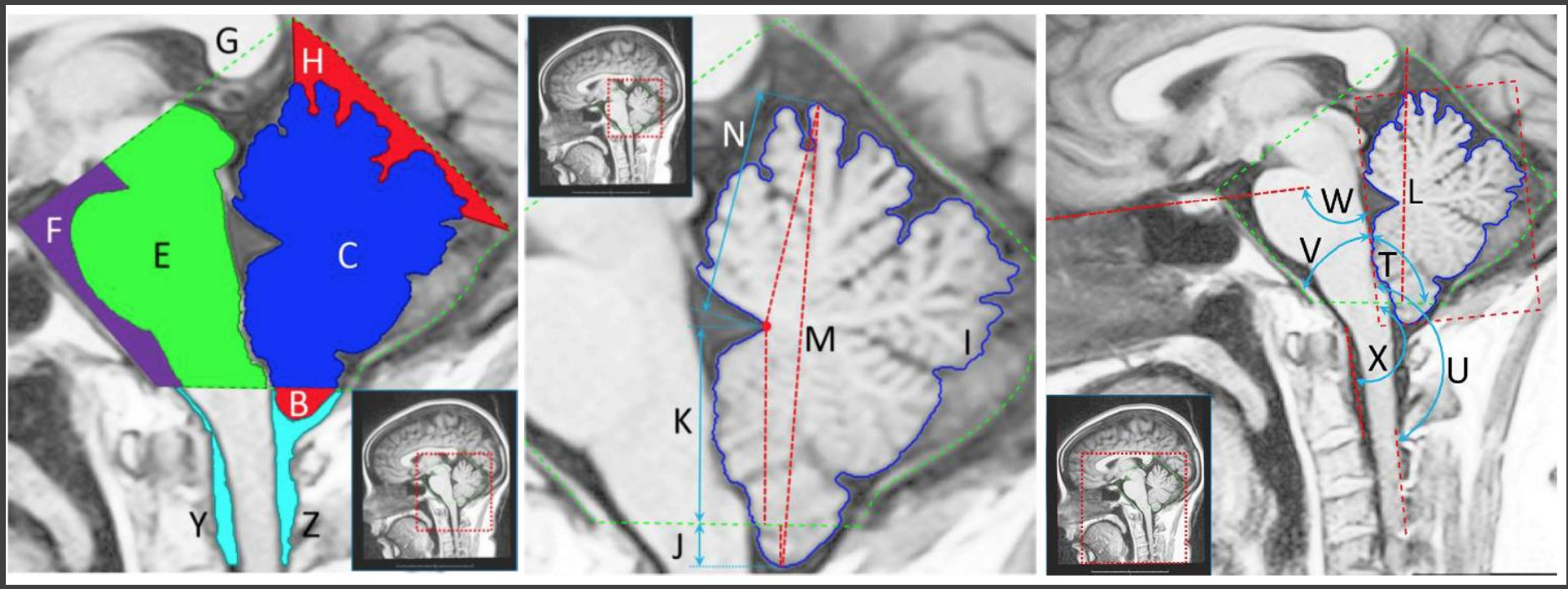
26 Additional Parameter for Morphometrics



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)

In review: *Annals of Biomedical Engineering*

Manuscript

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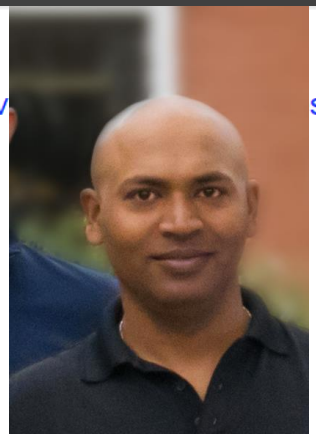

Quantification of Cerebellar Crowding in Type I Chiari Malformation

Dipankar Biswas[1], Maggie S. Eppelheimer[2], James R. Houston[3], Alaaddin Ibrahimy[1], J. Rajiv Bapuraj[4] , Richard Labuda[5], Philip A. Allen[3], David Frim[6], Francis Loth[1, 2]

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[5]Conquer Chiari, Wexford, Pennsylvania, USA
[6]Department of Neurology, The University of Chicago Medicine, Chicago, IL, USA

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

Grant support from Conquer Chiari