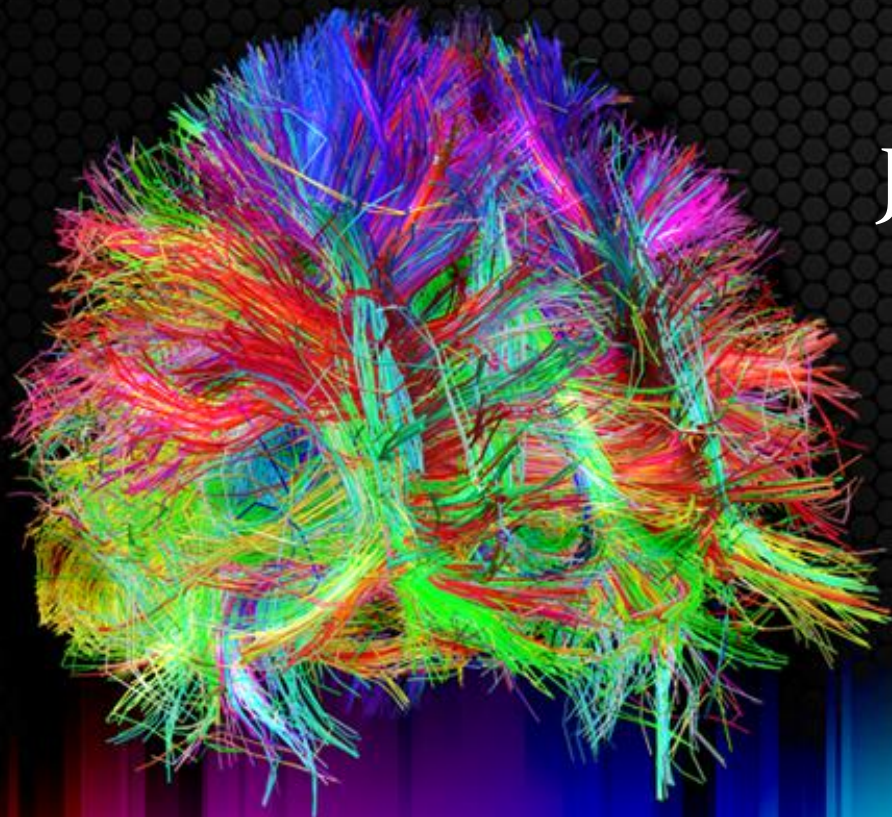


NA-MIC DBP: Traumatic Brain Injury (TBI)



John Darrell Van Horn, Ph.D.
UCLA

Driving Biological Project on TBI

- **UCLA**

- Jack Van Horn, PhD (PI of the NA-MIC Driving Biological Project)
- Andrei Irimia, PhD (Postdoctoral Scholar, DBP Engineer)
- Micah Chambers, MS (UCLA Biomedical Engineering Graduate Program)
- Paul Vespa, MD, FACN, FAAN (UCLA Neurology & Neurosurgery)
- David Hovda, MD (UCLA Brain Injury Research Center)
- Jeffrey Alger, PhD (UCLA Radiology)
- Arthur Toga, Ph.D. (UCLA Radiology)

- **University of Utah**

- Guido Gerig, Ph.D. (Scientific Imaging Institute)
- Marcel Prastawa, PhD
- Bo Wang, BS
- Sylvain Gouttard PhD

- **Harvard Medical School/BWH**

- Ron Kikinis, MD (PI of the NA-MIC Collaboration)
- Sonja Pujol, PhD

- **University of North Carolina, Chapel Hill**

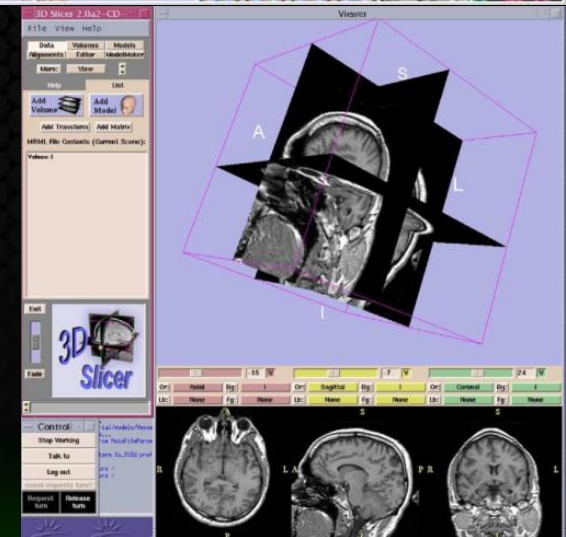
- Stephen Aylward, PhD

- **Georgia Tech, Atlanta, GA**

- Yifei Lou, Ph.D.
- Patricio Vela, Ph.D.

- **Boston University**

- Allen Tannenbaum, Ph.D.



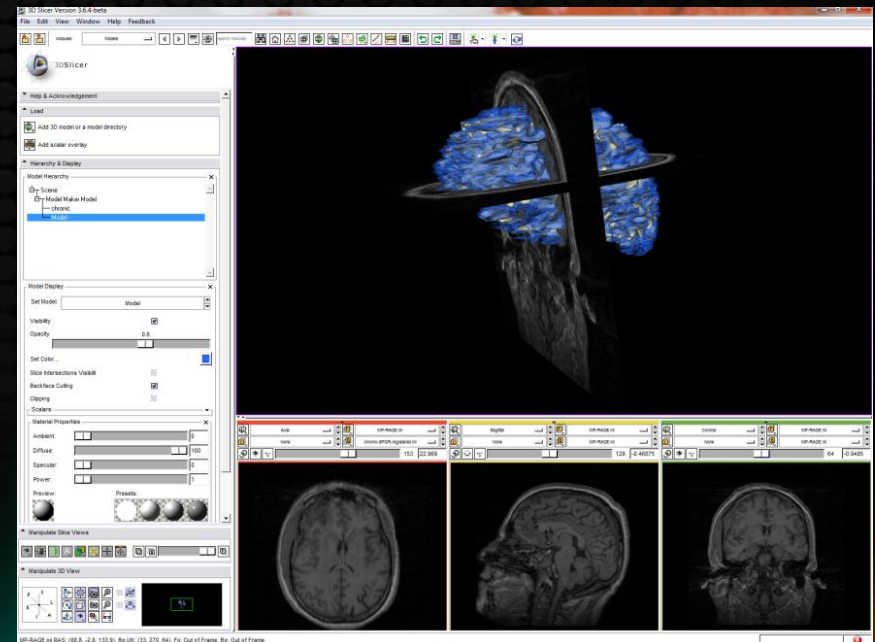
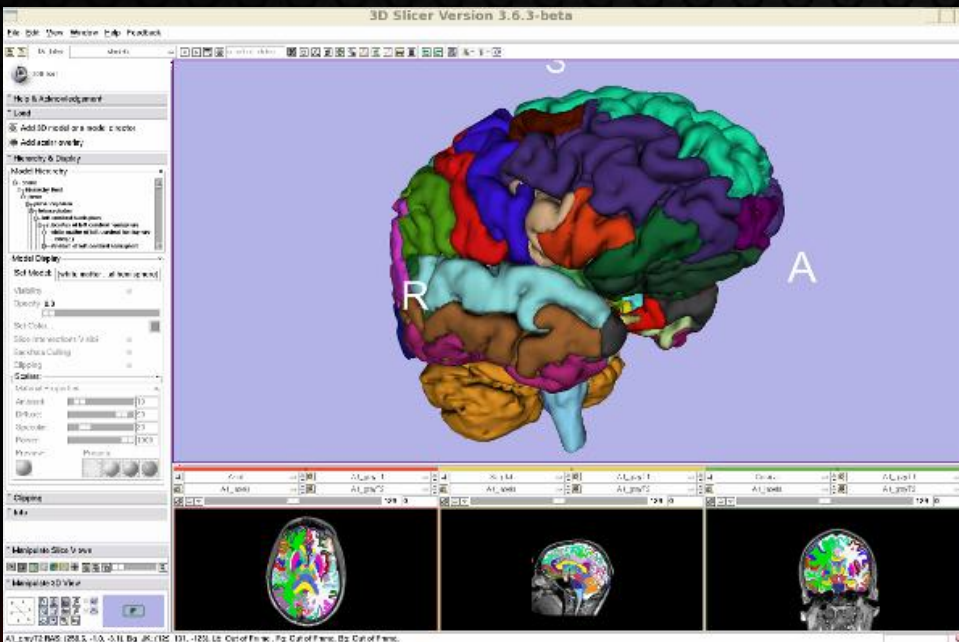
Motivation TBI Imaging Research

Traumatic Brain Injury is a Major Health Care and Research Challenge:

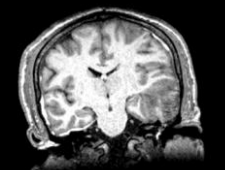
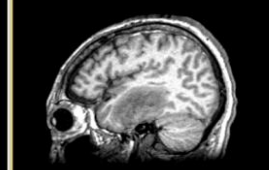
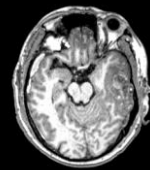
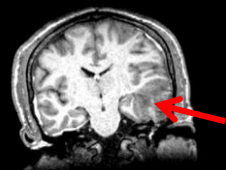
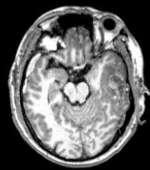
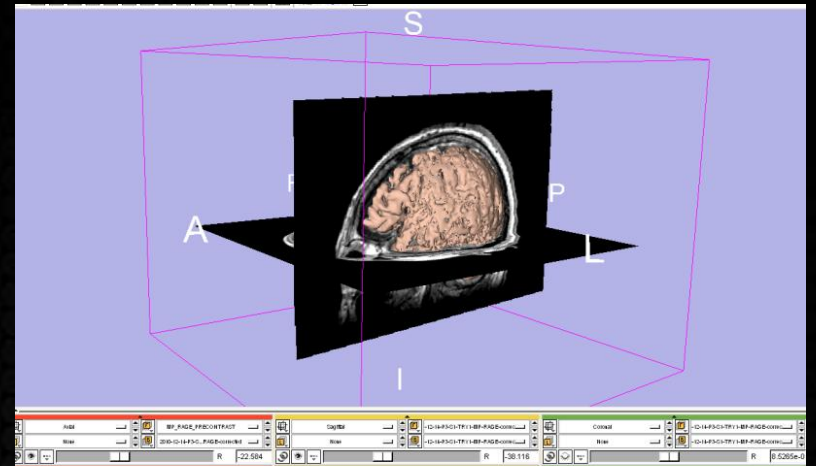
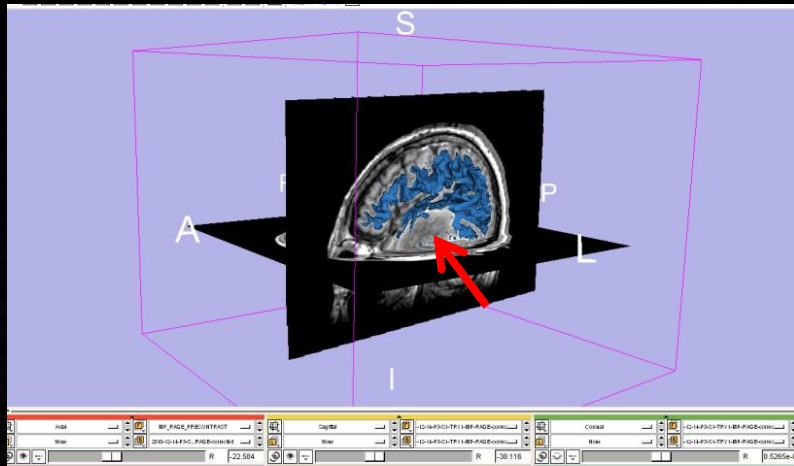
- 1.5 Million TBI cases per year, half are “mild” TBI
- 650,000 hospitalizations for long-term brain injury, known as the “silent death” (unresponsiveness; coma; brain death; eventual patient death)
- \$48 billion per year for management and loss to the US workforce
- **Many from automobile accidents and workplace incidents**
- Returning war veterans particularly affected; NFL/NCAA taking seriously
- Neurobiology of TBI is poorly understood
- Not uncommon for patients to suffer from TBI-related epilepsy, paralysis, memory loss, etc
- 85 clinical trials for therapy, all failed
- Few treatment options, no proven rehabilitation, but management
- Management: ~\$1 million per case
- See CDC web-site:
http://www.cdc.gov/TraumaticBrainInjury/tbi_concussion.html

Key Directions

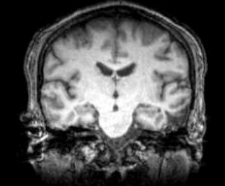
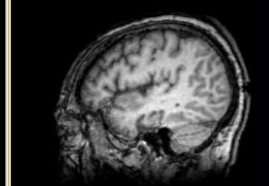
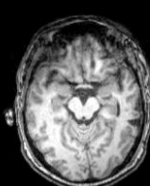
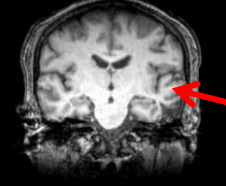
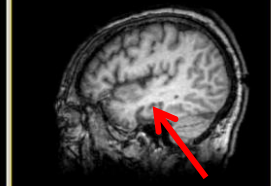
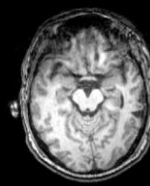
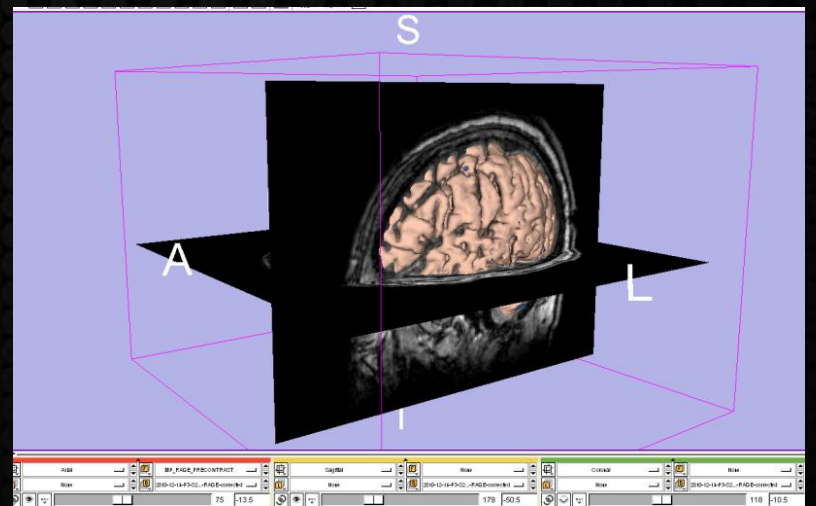
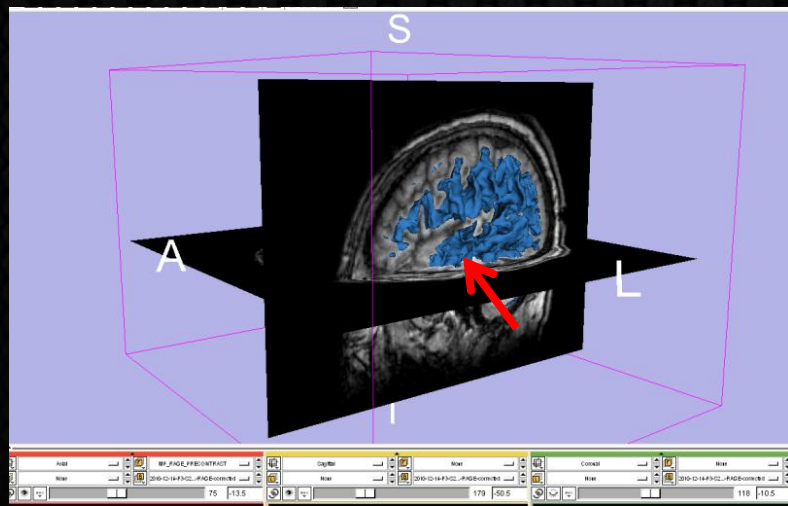
- Quantitative measurements of TBI using new research tools
 - multimodal data integration
 - longitudinal analysis: assess change and trajectories
 - Quantify the degree of atrophy and axonal damage
 - Study the relationship between rates of change and predictors of clinical outcome
- User-supervised, efficient, smart, flexible analysis, registration, parcellation
- Dynamic 3D imaging with multivariate information over time:
 - inform clinicians about damage extent and type
 - assess change over time and guide treatment options with reference to other published studies



Acute
Baseline



6 Month
Follow-up

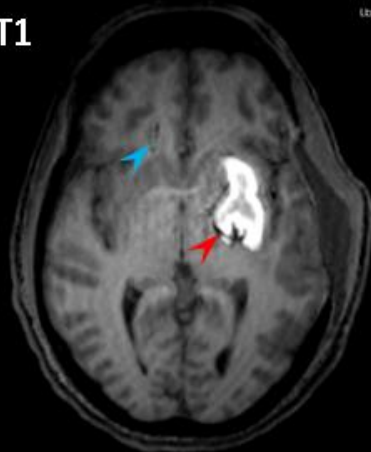
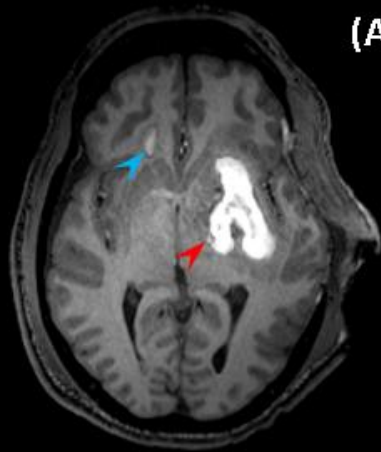


ACUTE

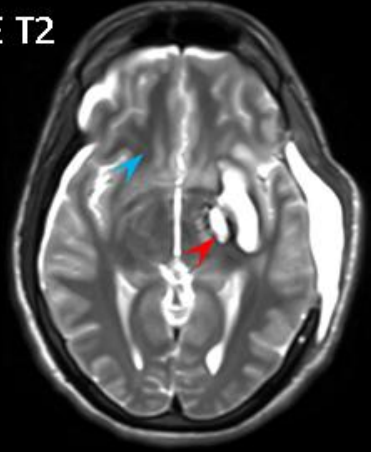
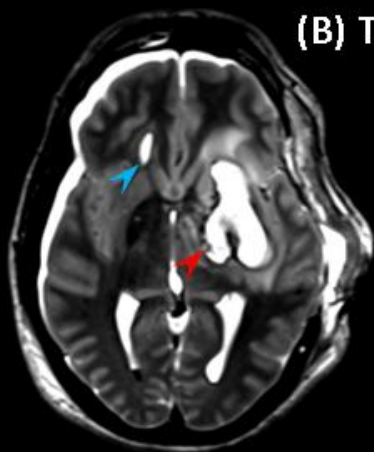
CHRONIC

Case 1

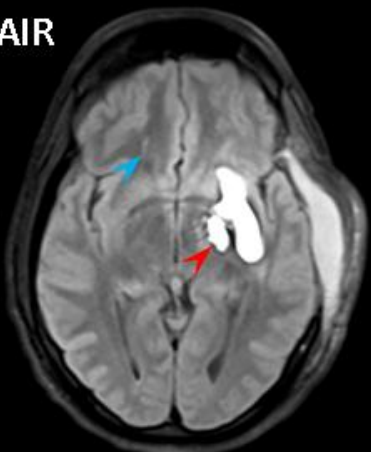
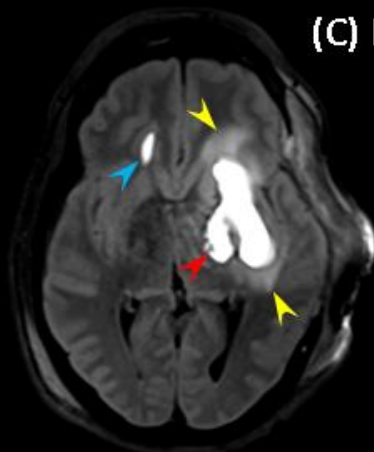
(A) T1



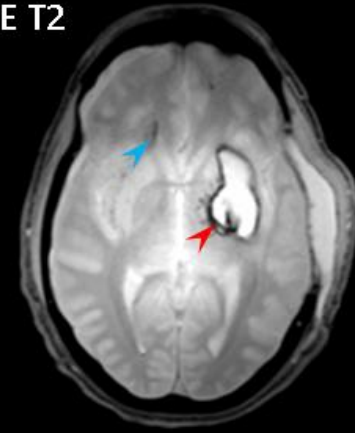
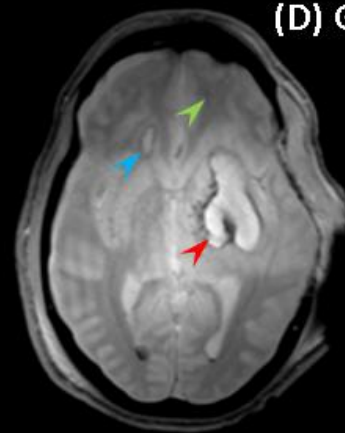
(B) TSE T2



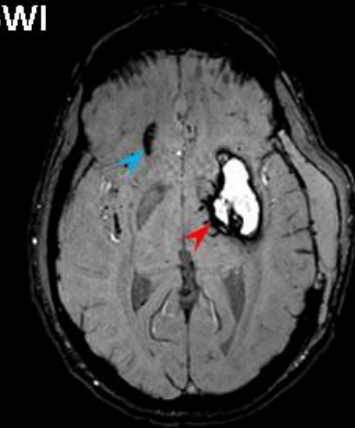
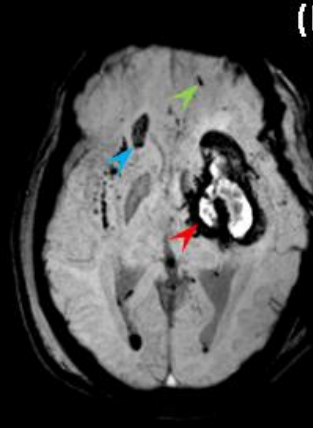
(C) FLAIR



(D) GRE T2






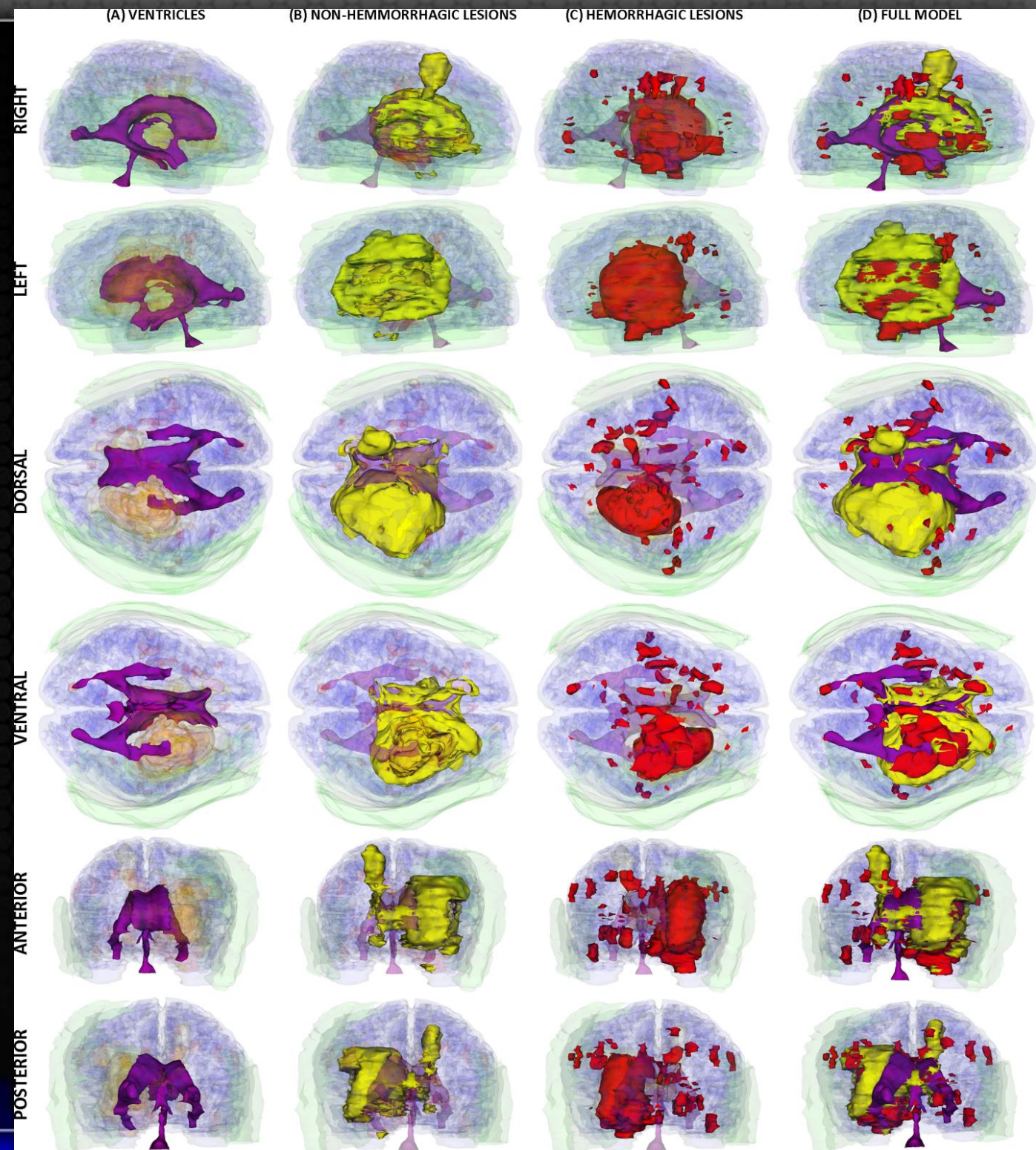
(E) SWI






Unknown origin

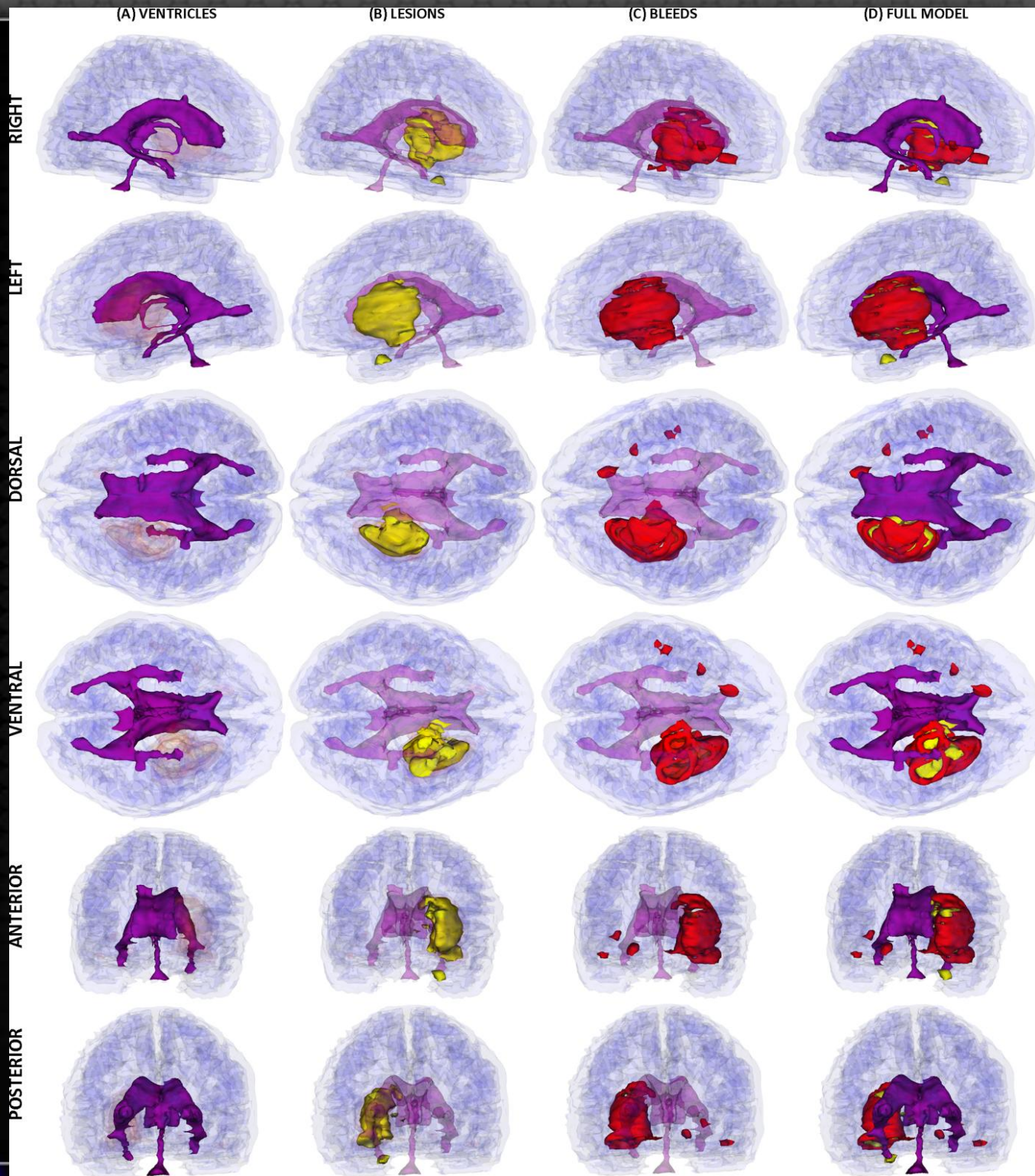
Case 1 acute

-  ventricular system
-  edema
-  hemorrhage



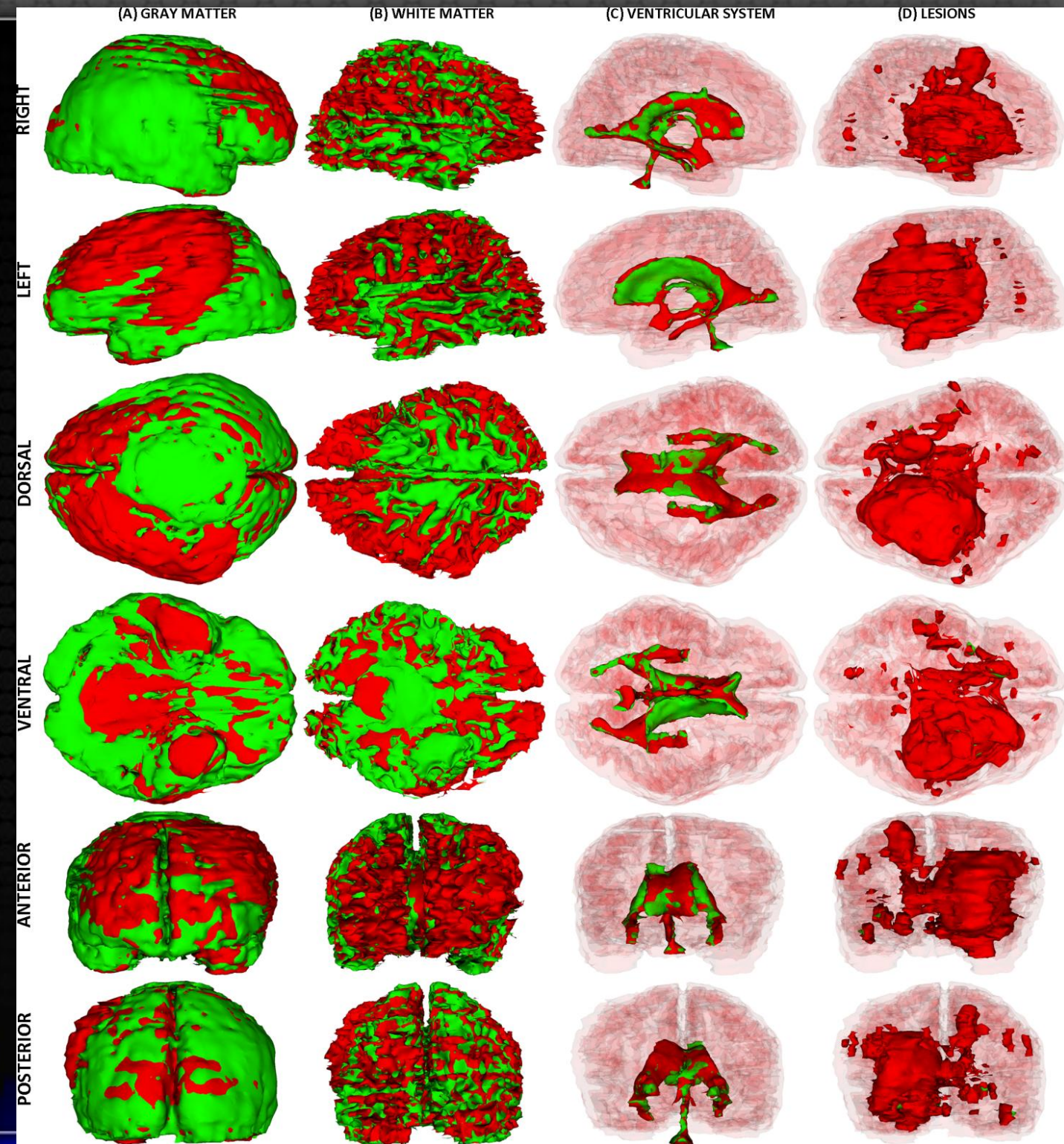
Case 1 chronic

-  ventricular system
-  lesion
-  bleed



Case 1 longitudinal comparison

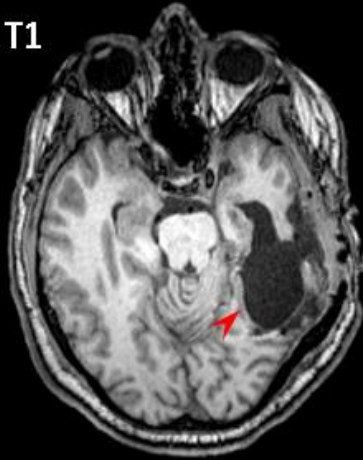
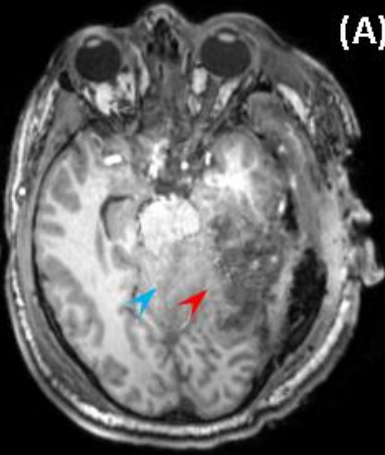
 acute
 chronic



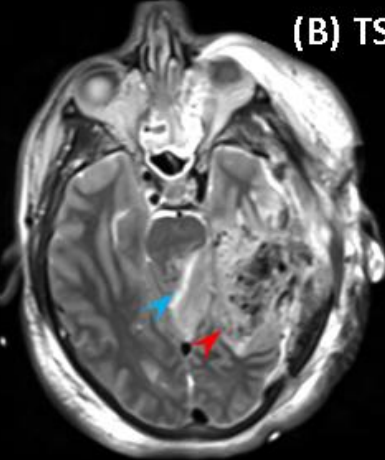
ACUTE

CHRONIC

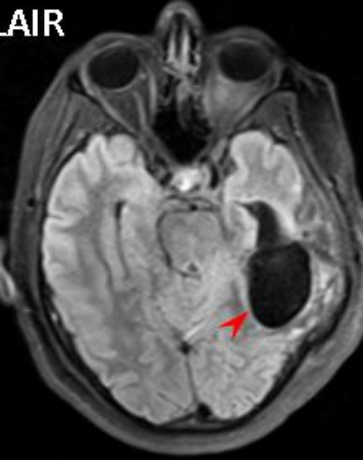
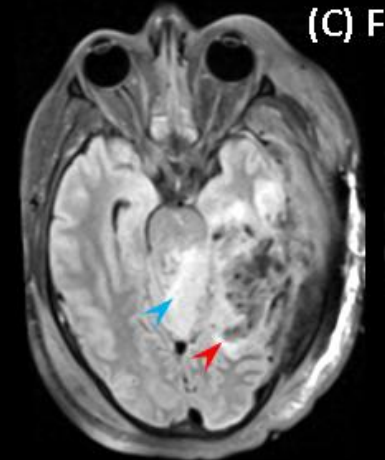
(A) T1



(B) TSE T2

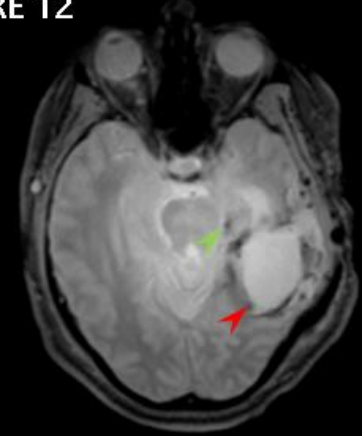
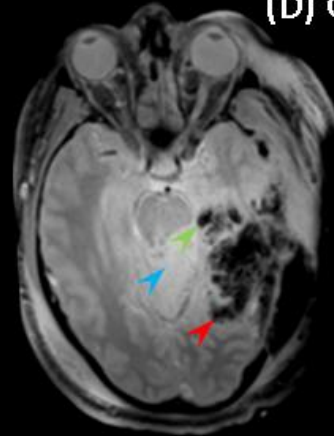


(C) FLAIR

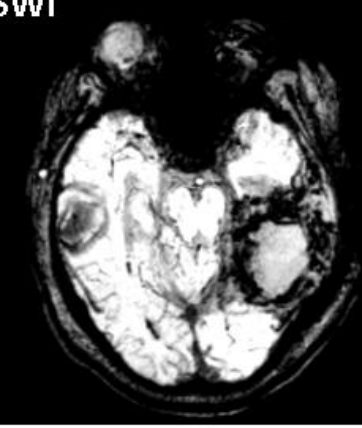
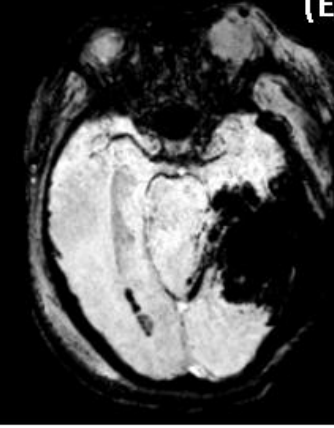


Case 2

(D) GRE T2






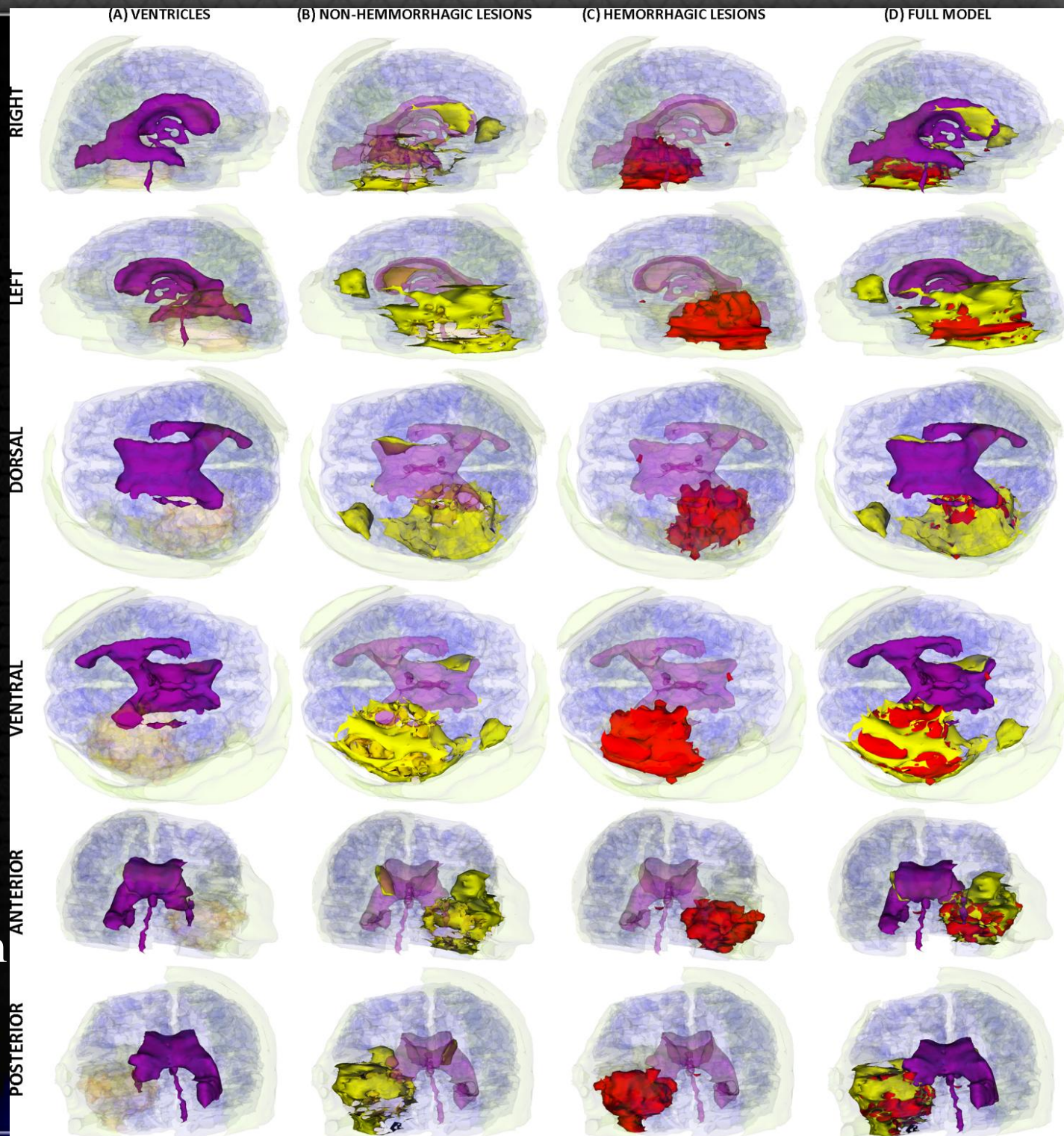
(E) SWI






Gunshot victim

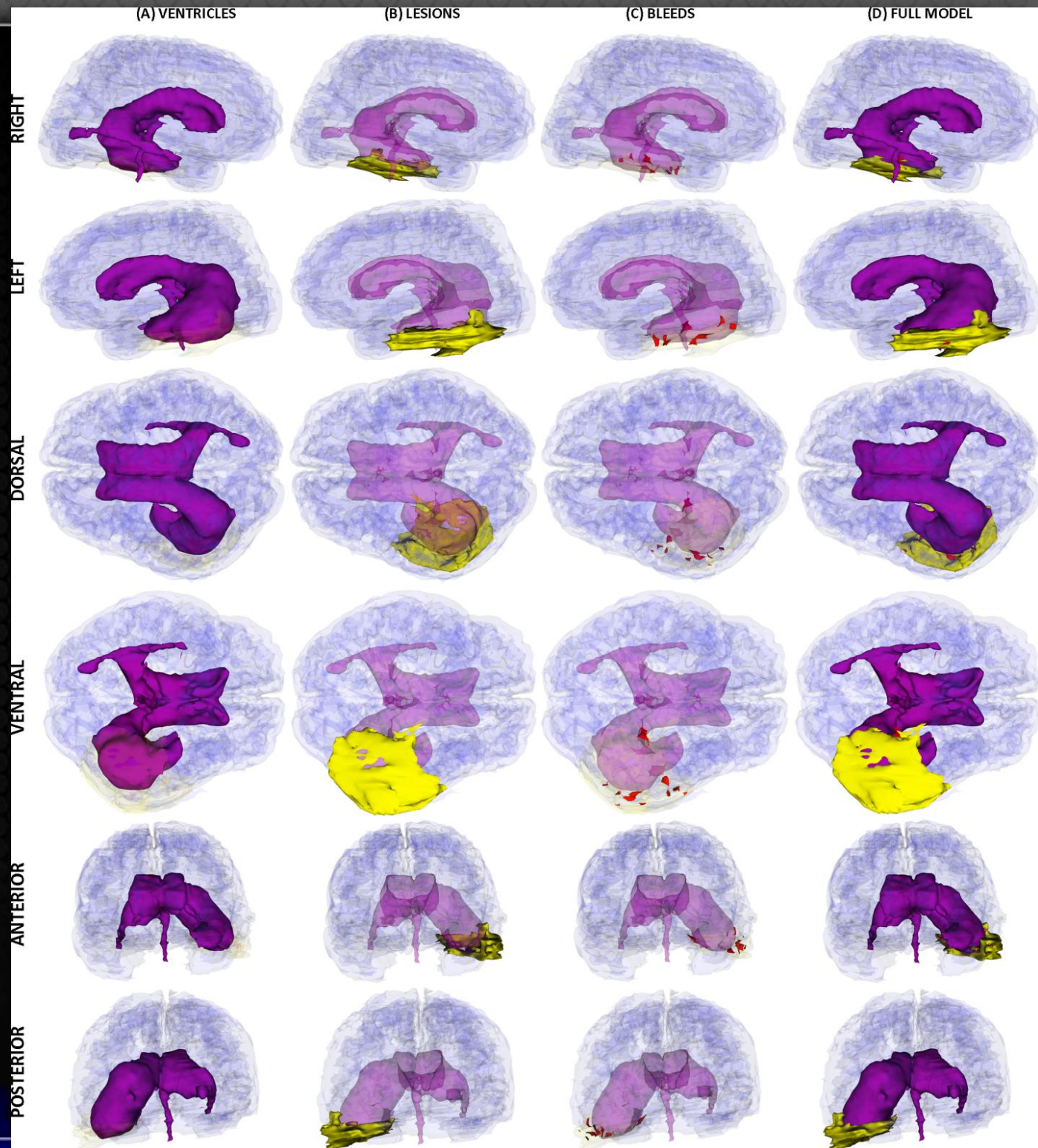
Case 2 acute

-  ventricular system
-  edema
-  hemorrhage



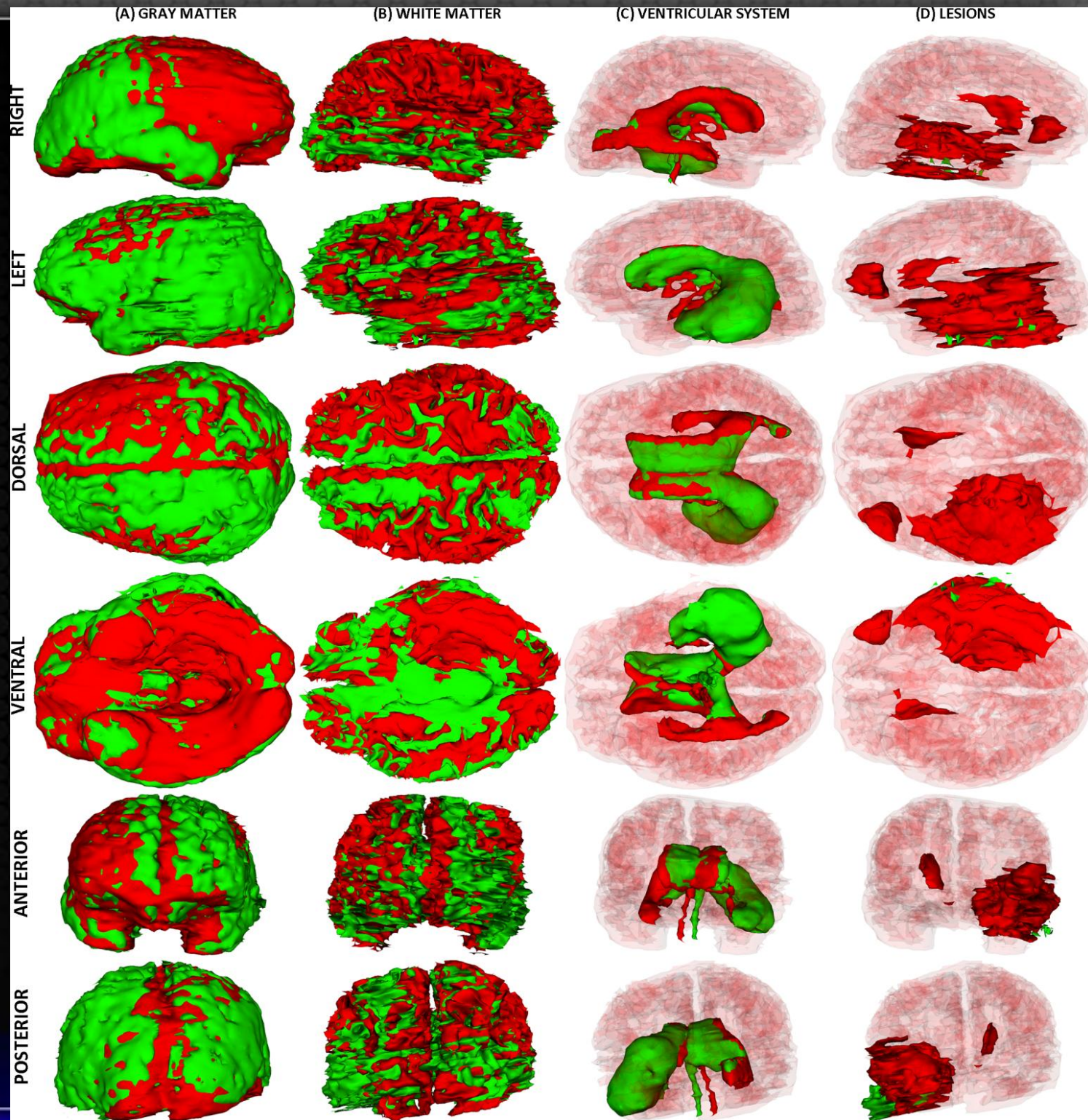
Case 2 chronic

-  ventricular system
-  lesion
-  bleed



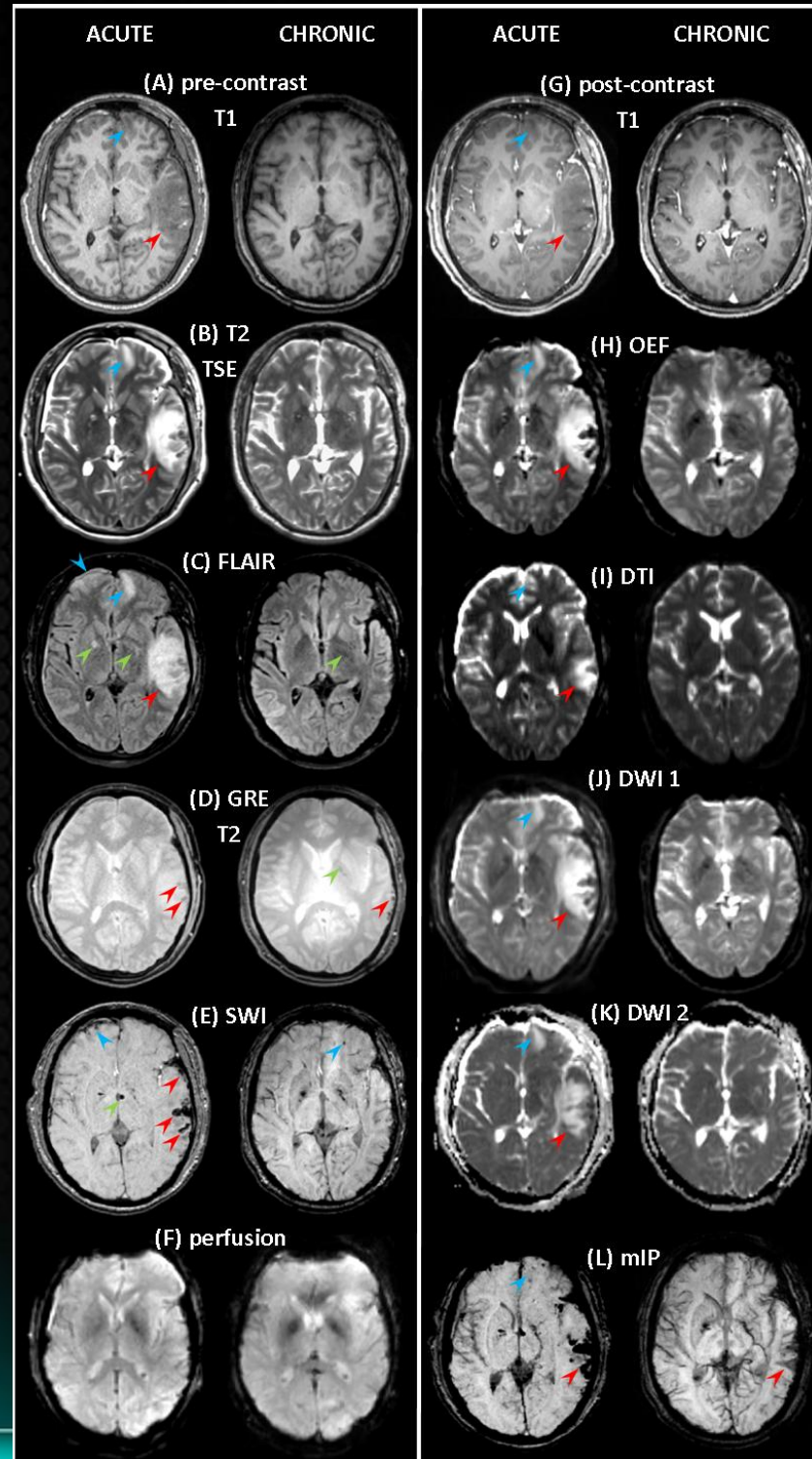
Case 2 longitudinal analysis

 acute
 chronic






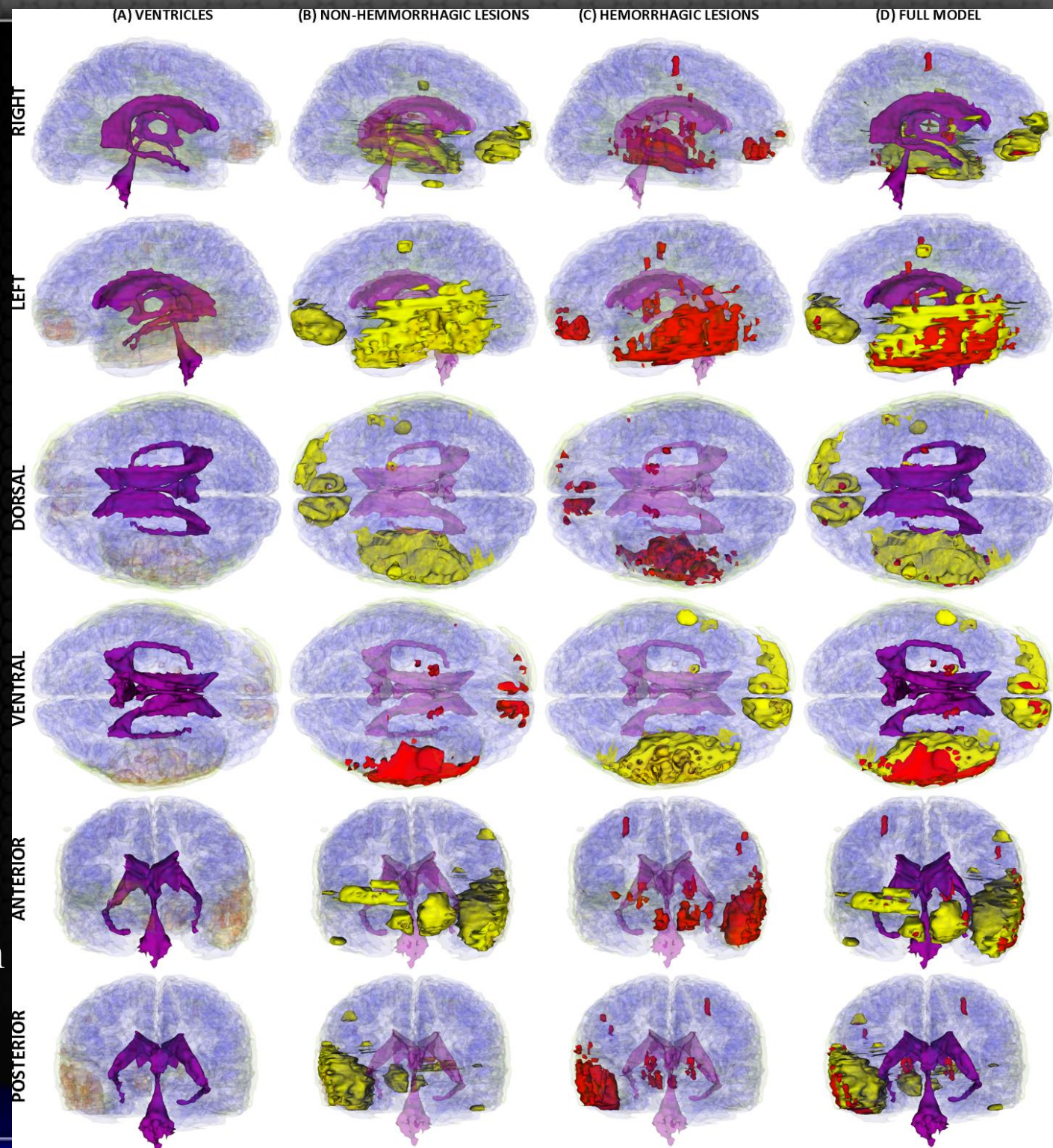
Case 3

Blunt force trauma






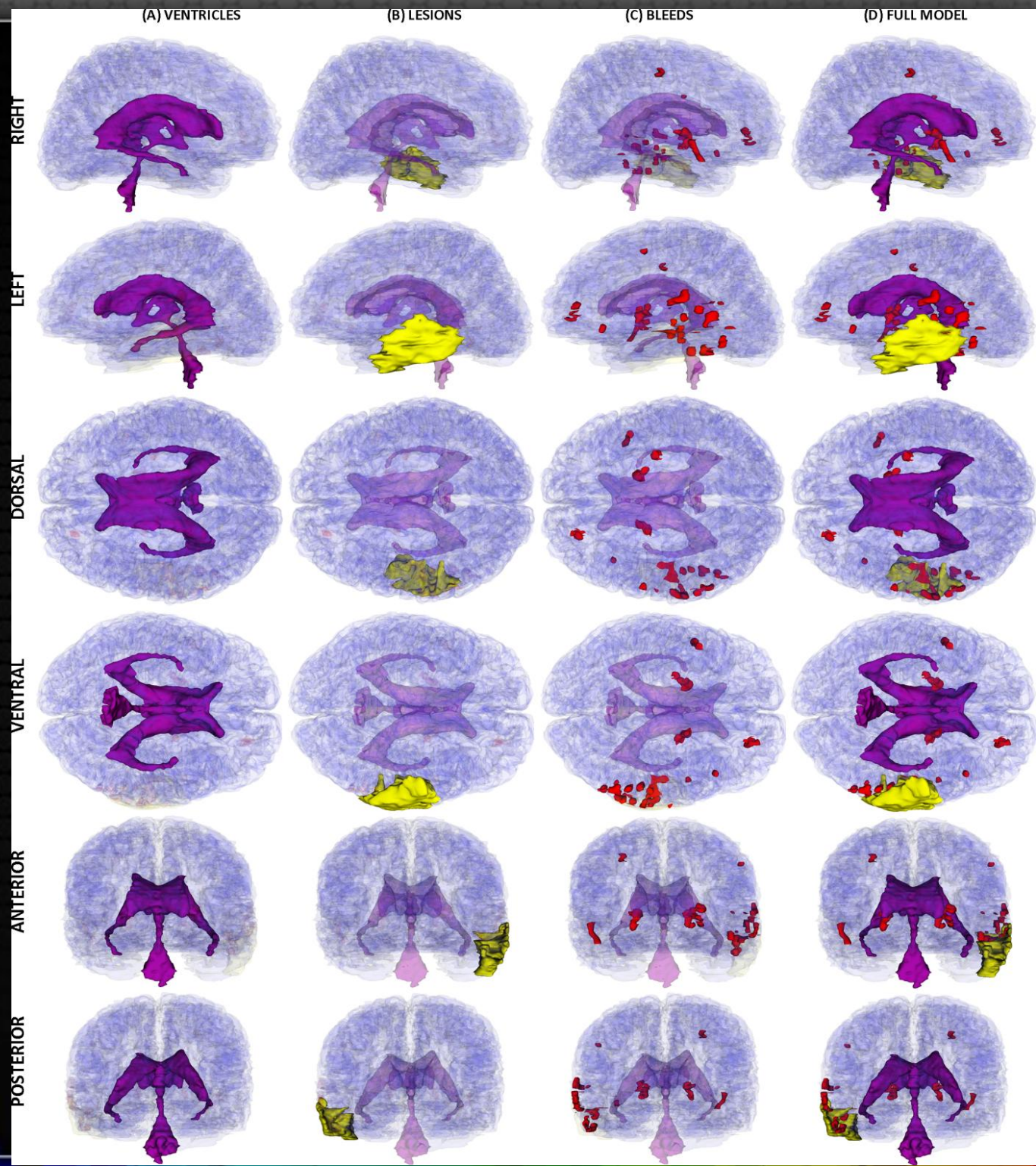
Case 3 acute

-  ventricular system
-  edema
-  hemorrhage



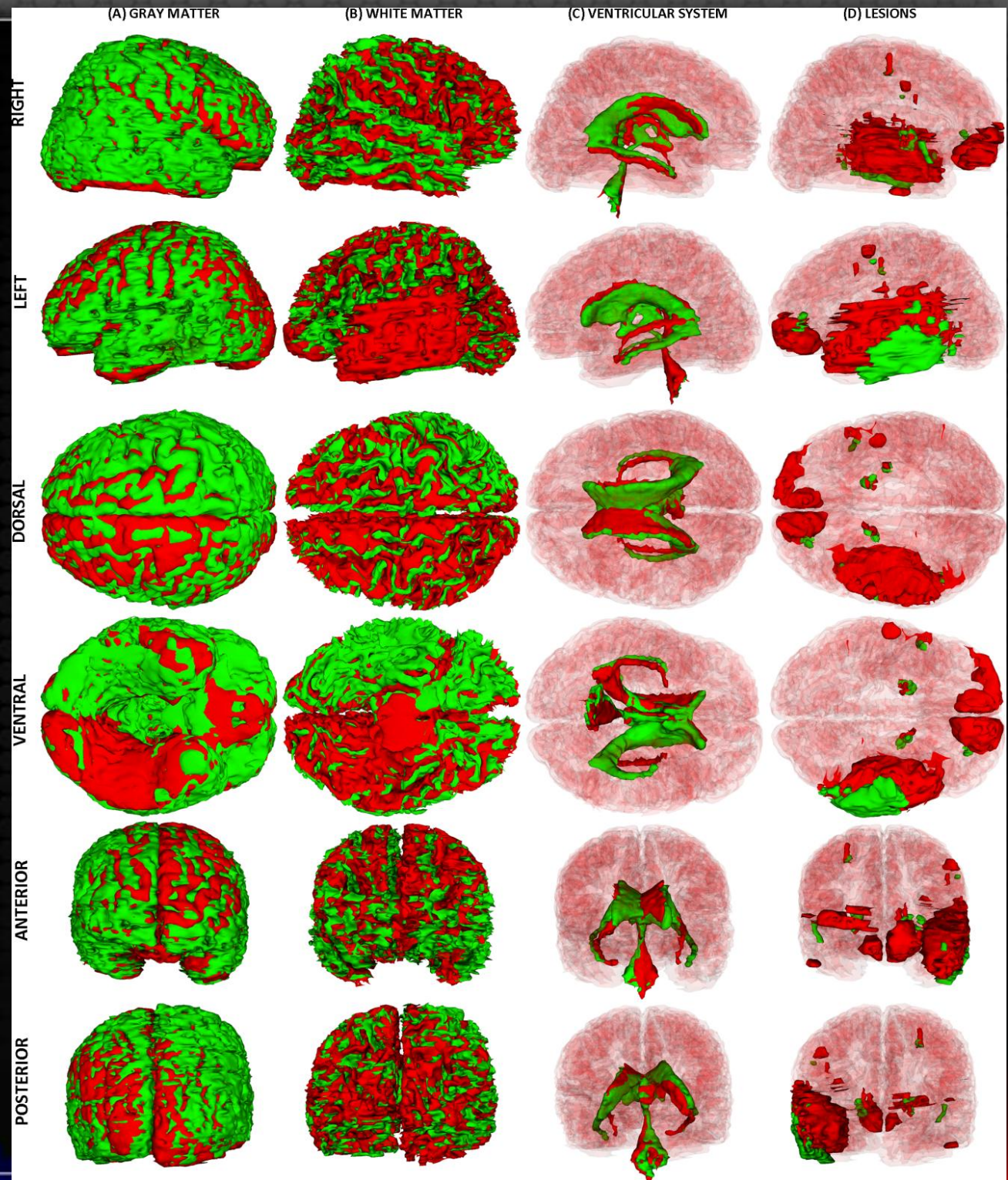
Case 3 chronic

-  ventricular system
-  lesion
-  bleed

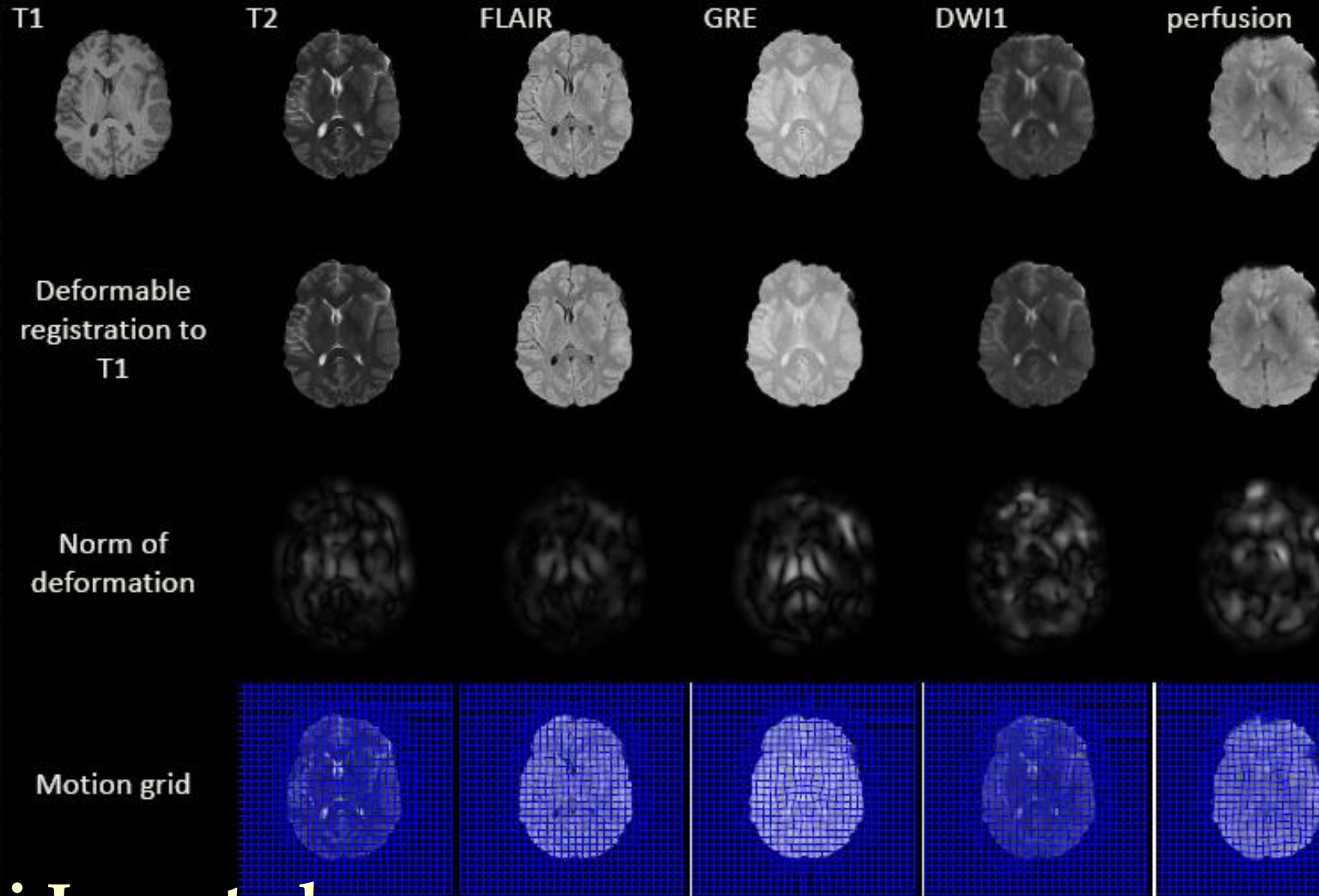


Case 3 longitudinal analysis

 acute
 chronic

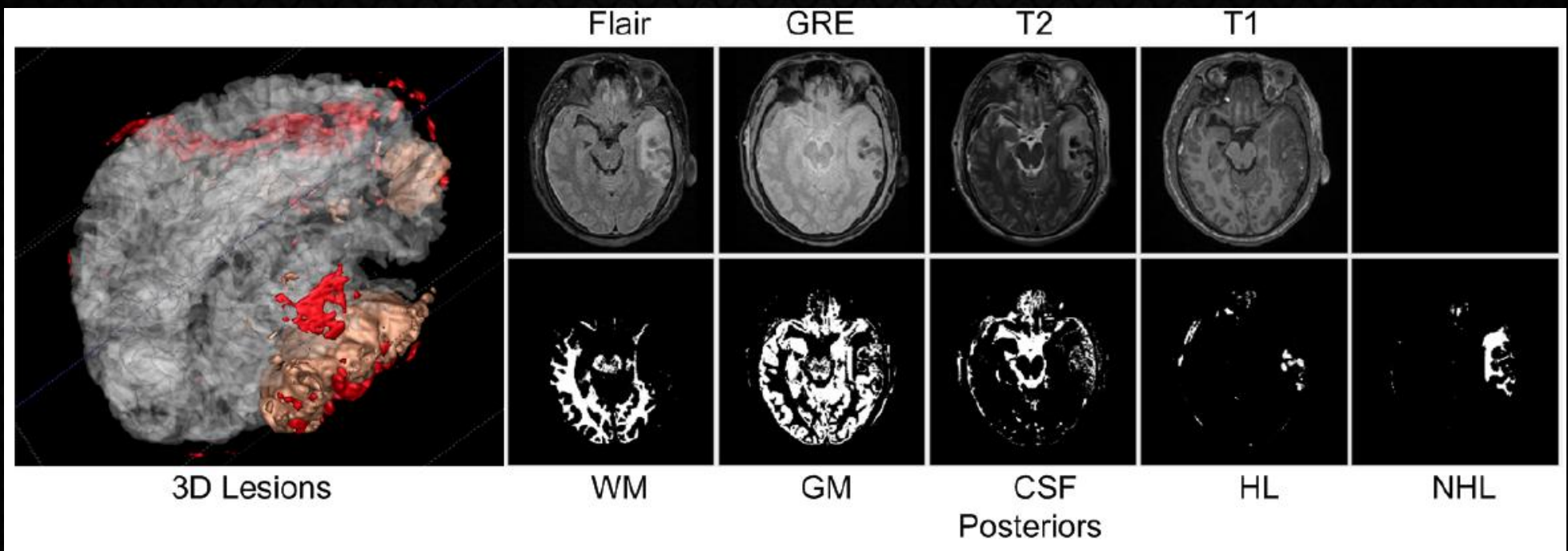


Acute/Chronic Multimodal Registration in TBI



Yifei Lou et al.

TBI Lesion Parcellation



HL = hemorrhagic lesions

NHL = non-hemorrhagic lesions

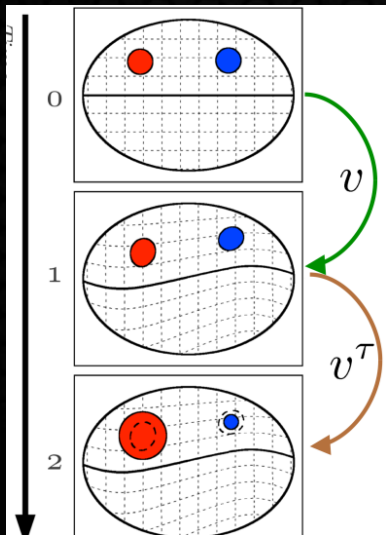
Bo Wang et al.

TBI Image Registration

Goal: TBI longitudinal change detection and monitoring.

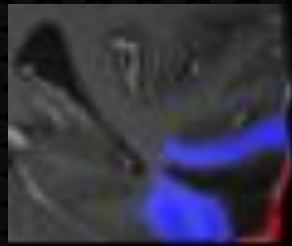
Geometric metamorphosis

- Jointly estimate global background deformation and pathology deformation.



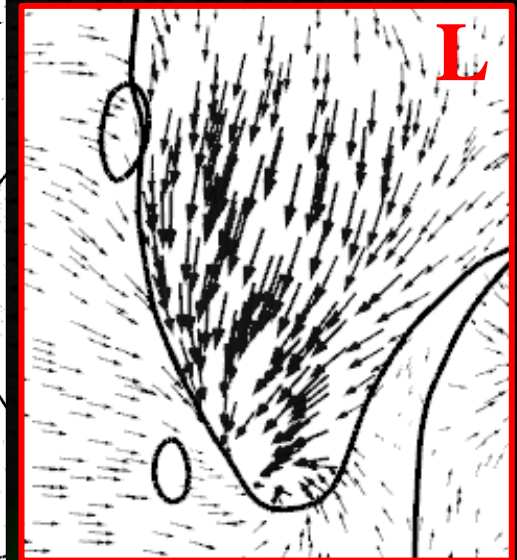
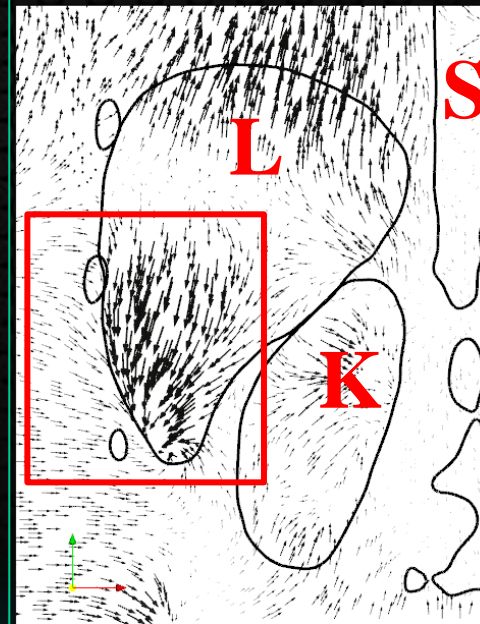
global
background
motion

pathology
grows or
contracts

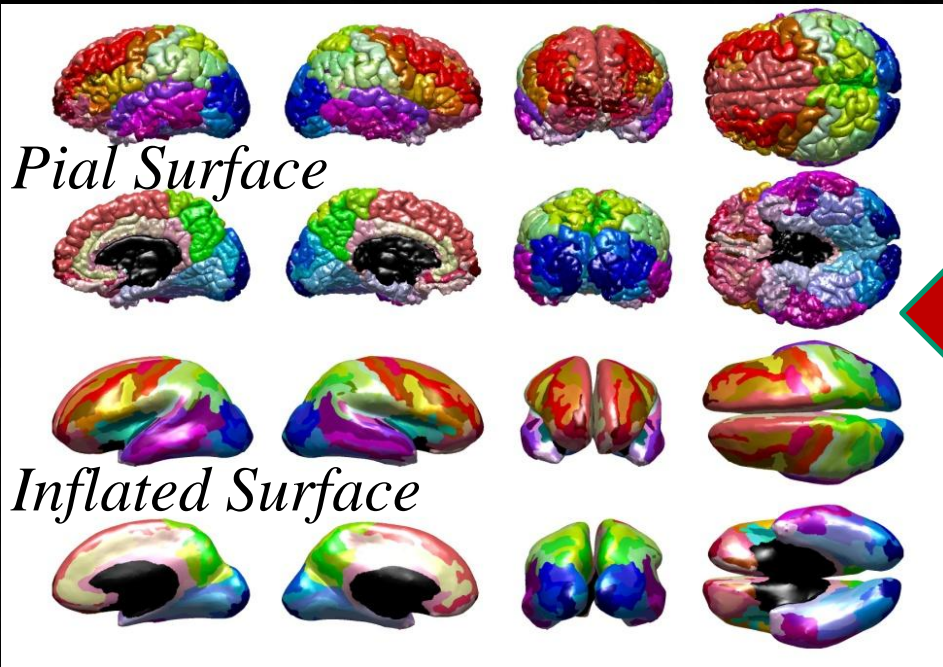


Sliding organ registration

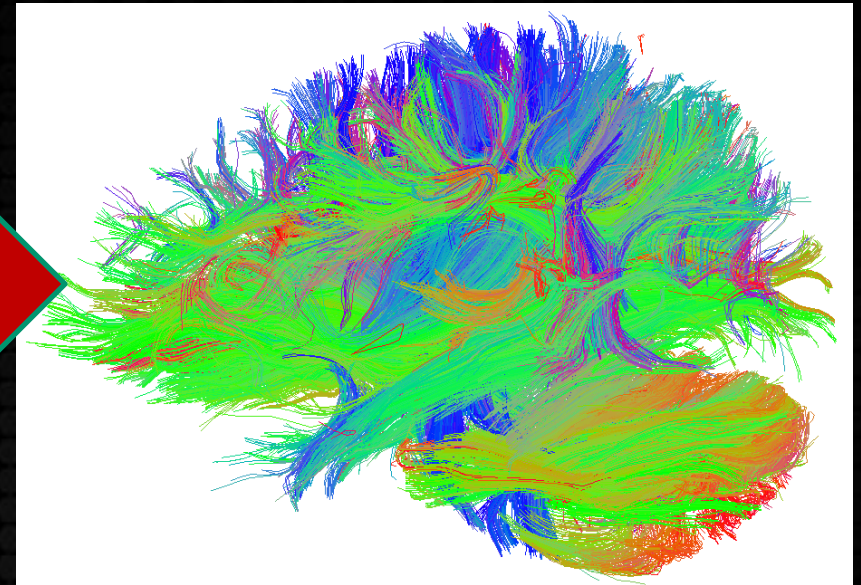
- Handle sliding motion (ex. between brain and skull).
- Validation evaluated in abdomen:



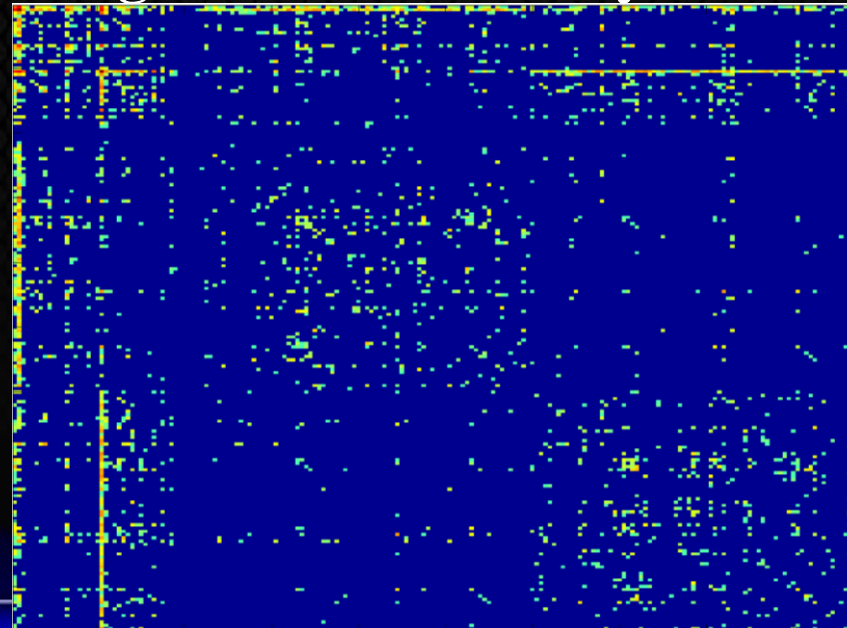
Cortical Parcellation Map



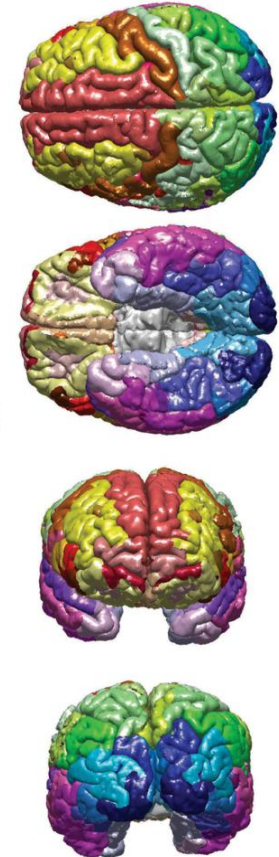
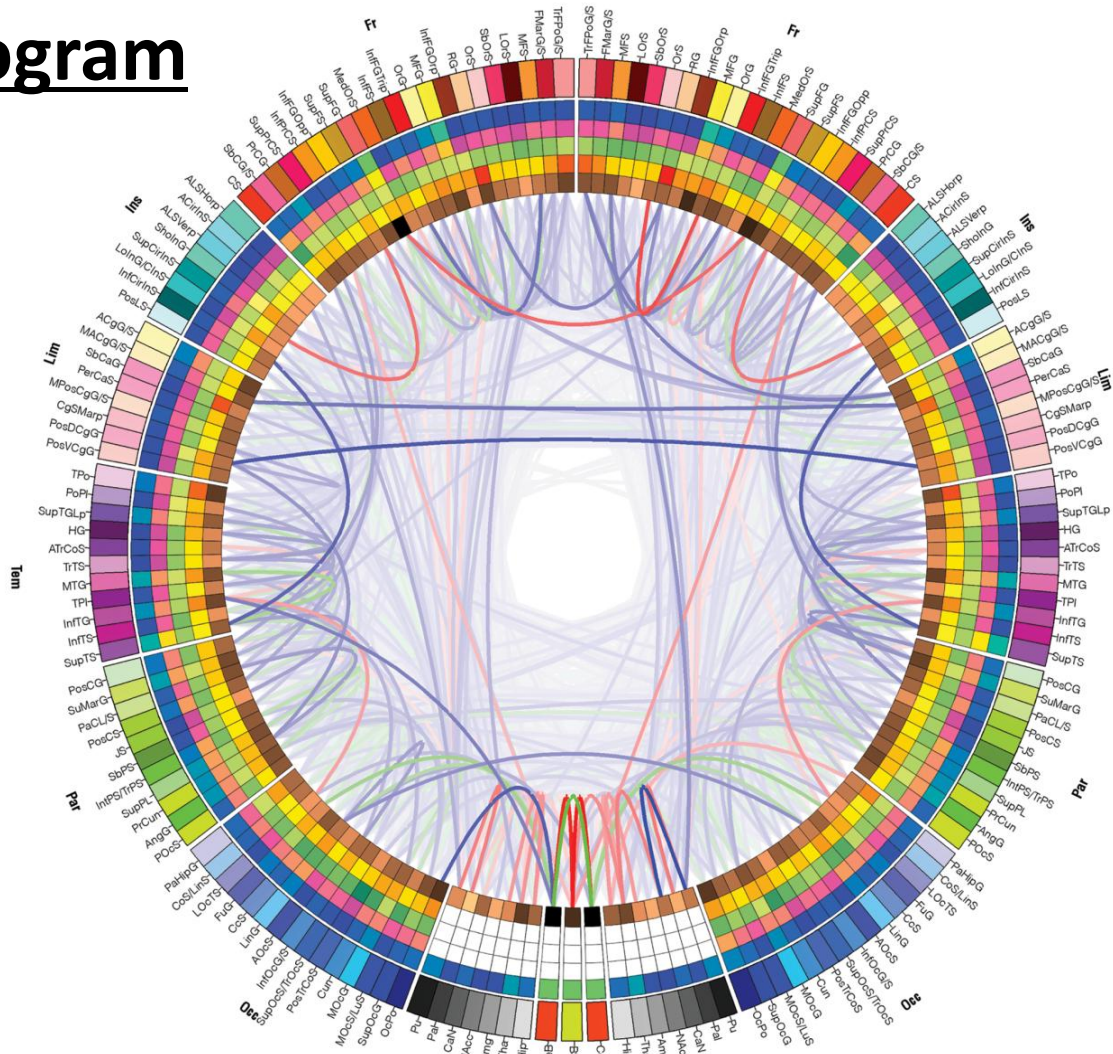
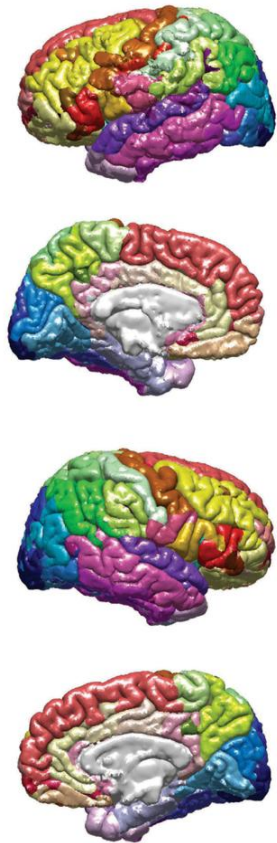
Diffusion Tractography



Regional Connectivity Matrix

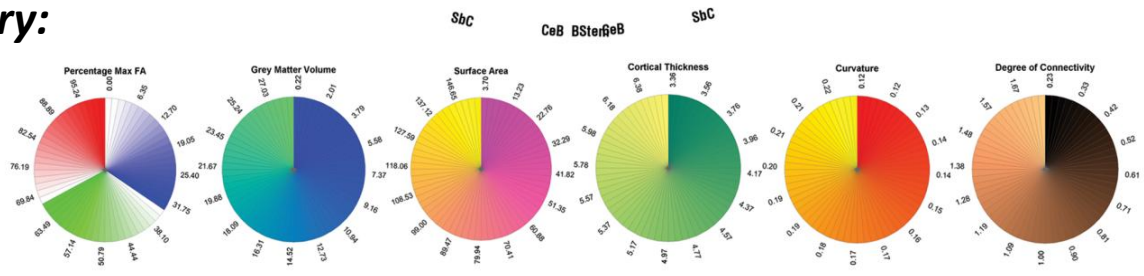


Connectogram

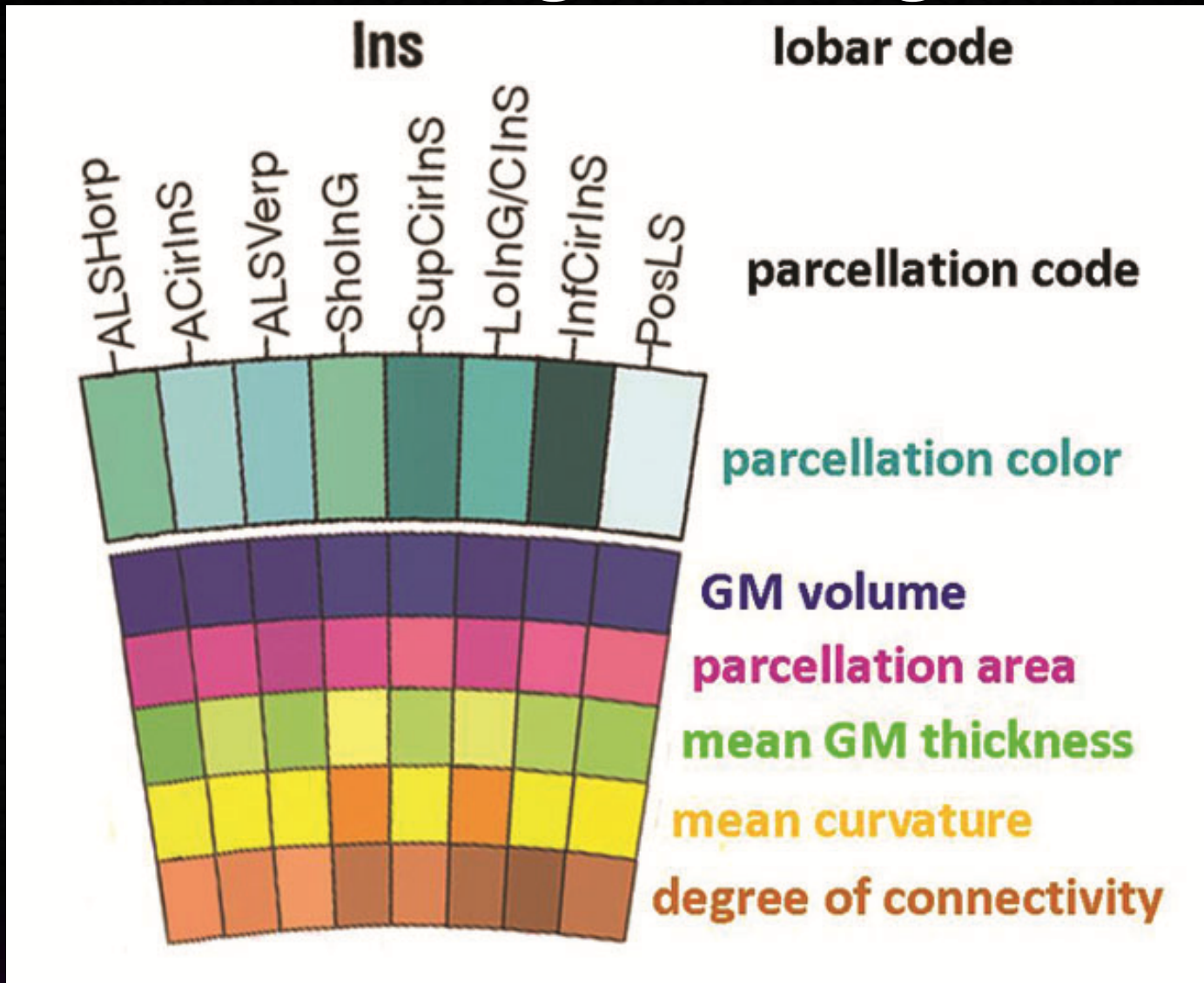


Sample Summary:

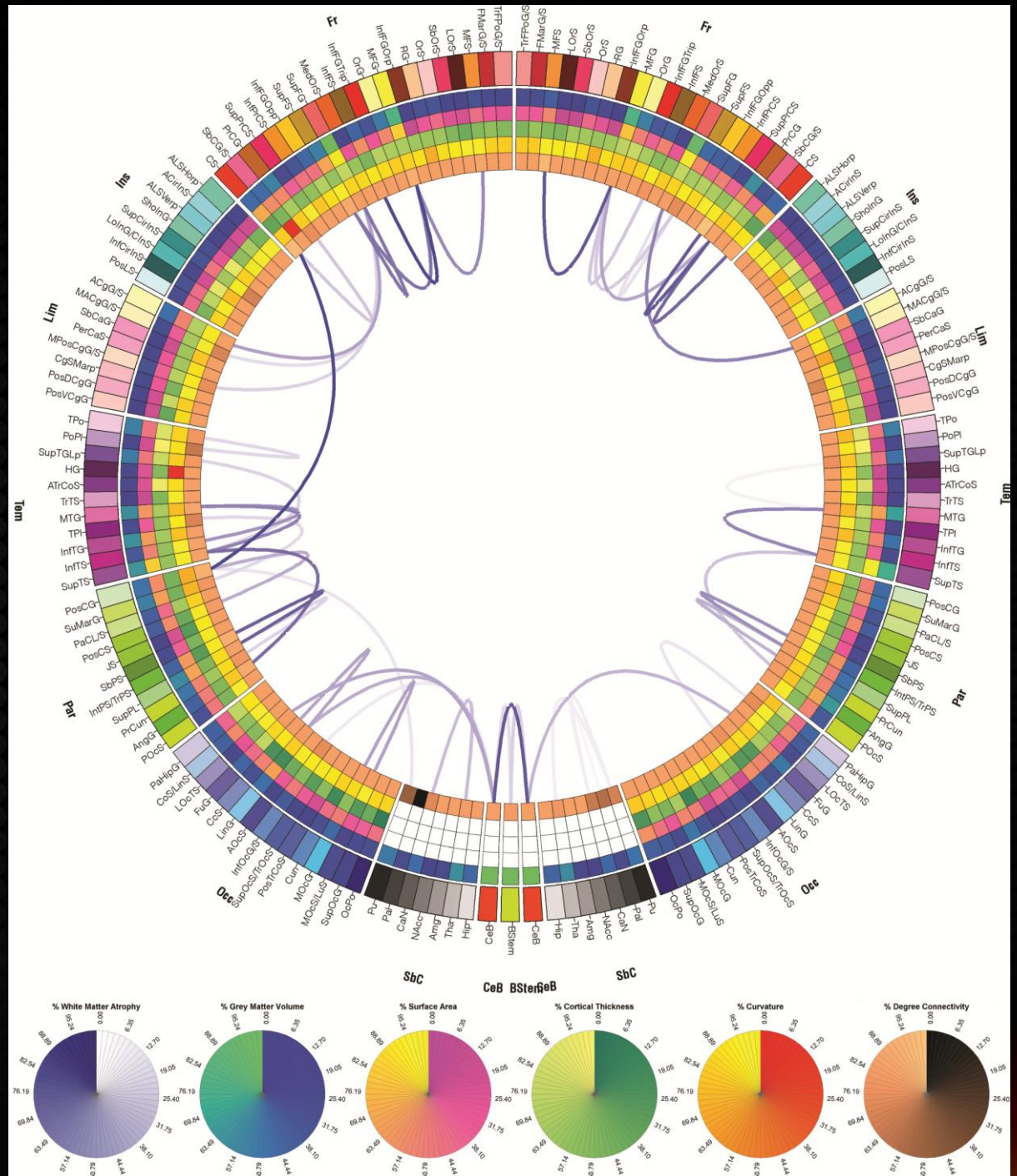
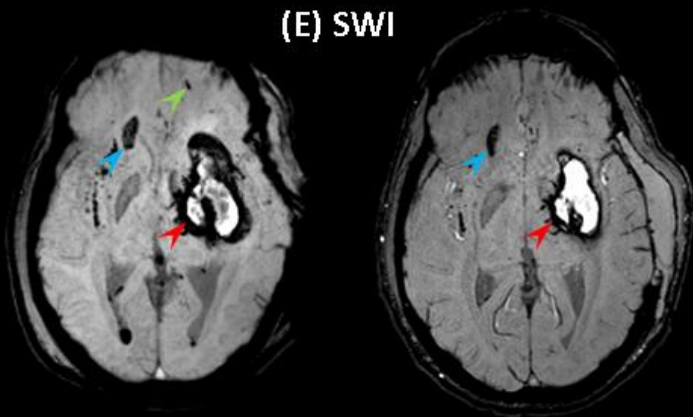
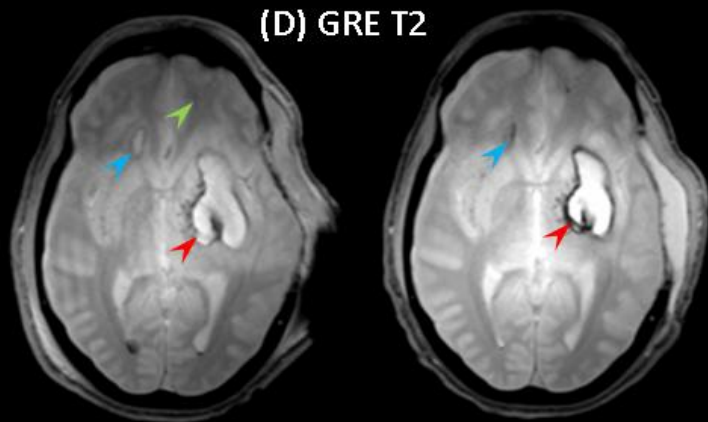
N=100
 Right handed
 Males
 25-36 years old



Connectogram Legend

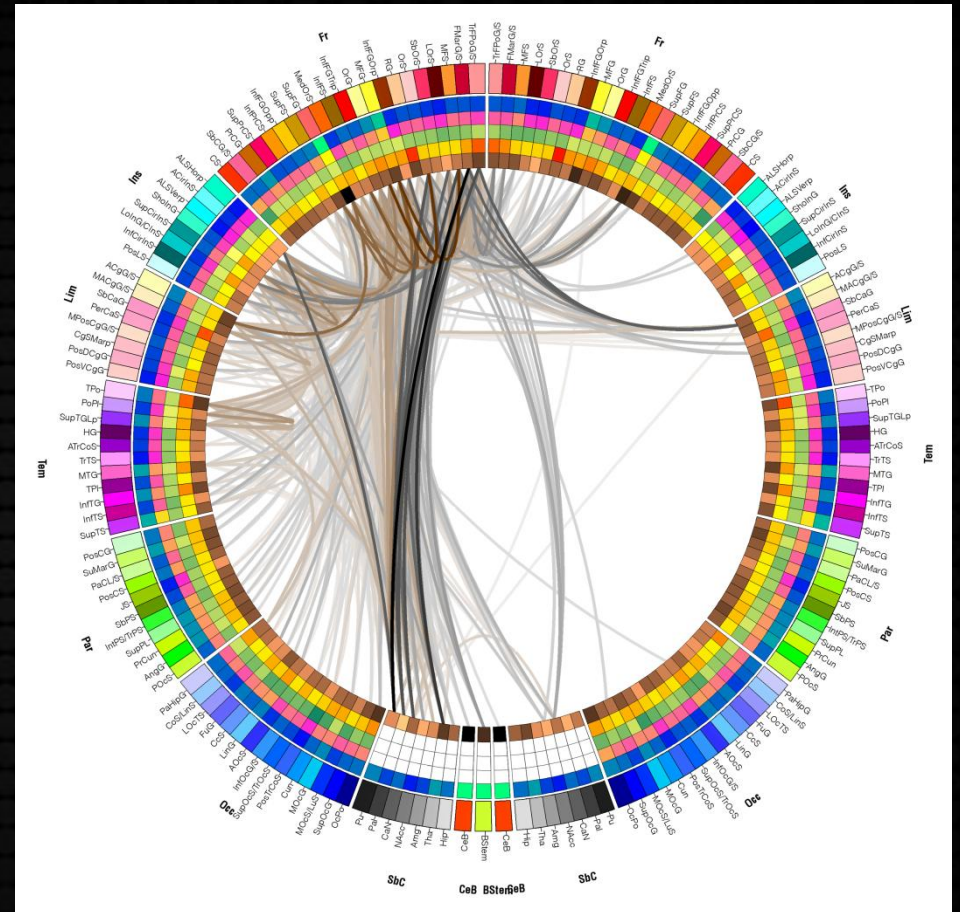


Characterizing Fiber Pathway Damage in TBI



Andrei Irimia et al.

A Famous Case of TBI



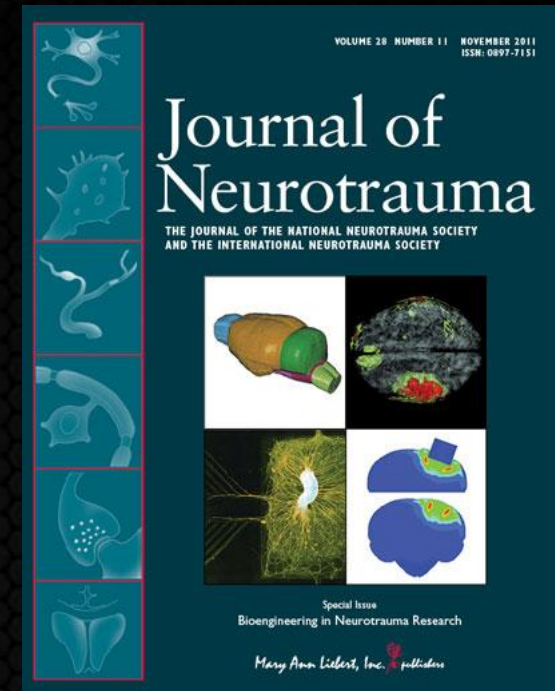
Sample; 110 healthy RH males
25-36 years old
4% grey matter volume loss
11% white matter affected

Van Horn et al.

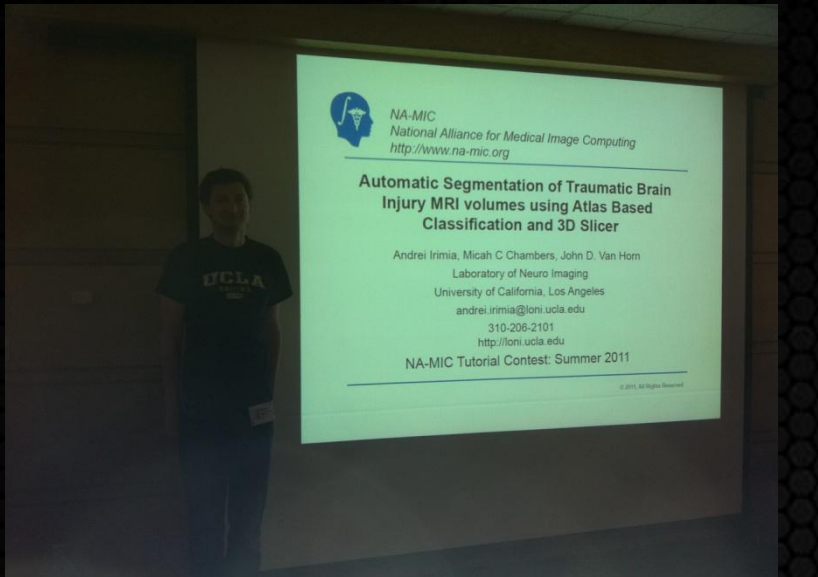
TBI DBP Publications


- **Journal Papers**

- A. Irimia, et al. (2011) “Comparison of acute and chronic traumatic brain injury using semi-automatic multimodal segmentation of MR volumes”. ***Journal of Neurotrauma***
- A. Irimia. Et al. (in press) “Patient-tailored connectomics visualization for the assessment of white matter atrophy in traumatic brain injury”, ***Frontiers in Neurotrauma***.
- B. Wang, et al. (accepted) “A Patient-Specific Segmentation Framework for Longitudinal MR Images of Traumatic Brain Injury” ***ISBI***.
- B. Wang, et al. (submitted) “A Segmentation Framework for Longitudinal MR Images with Traumatic Brain Injury” ***SPIE Medical Imaging***.
- M. Niethammer, et al.(2011) *Geometric metamorphosis*. ***Med Image Comput Comput Assist Interv***.
- D. F. Pace, et al., “Deformable image registration of sliding organs using anisotropic diffusive regularization,” **Proc. IEEE International Symposium on Biomedical Imaging**



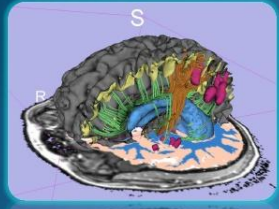
Conference Presentations




NA-MIC
 National Alliance for Medical Image Computing
<http://www.na-mic.org>


Automatic Segmentation of Traumatic Brain Injury MRI volumes using Atlas Based Classification and 3D Slicer

Andrei Irimia, Micah C Chambers, John D. Van Horn
 Laboratory of Neuro Imaging
 University of California, Los Angeles
andrei.irimia@loni.ucla.edu
 310-206-2101
<http://loni.ucla.edu>
 NA-MIC Tutorial Contest: Summer 2011



NAMIC DBP
Traumatic Brain Injury
UCLA

Jack Van Horn, A. Irimia, M. Chambers, A. Toga, J. Alger, P. Vespa,
 D. Hovda UCLA LONI, Neurology, Neurosurgery
 Guido Gerig, M. Prastawa, S. Gouttard
 University of Utah and SCI Institute
 Stephen Aylward, Kitware



Clinically-Driven Multimodal Imaging of Traumatic Brain Injury Using Semi-Automatic Segmentation in 3D Slicer

Andrei Irimia PhD¹, Jack Van Horn PhD², Micah Chambers³, Marcel Prastawa PhD⁴, Bo Wang⁵, Sylvain Gouttard⁶, Paul Vespa MD⁷, David Hovda PhD⁸, Jeffrey Alger PhD^{9,10}, Sonja Pujol PhD¹¹, Guido Gerig PhD¹², Stephen Aylward PhD¹³, Arthur Toga PhD¹⁴, Ben Kilbina MD¹⁵

¹Laboratory of Neuro Imaging (LONI), Department of Neurology, Geffen School of Medicine, UCLA; ²Scientific Computing and Imaging Institute, University of Utah, Salt Lake City, Utah; ³Brain Injury Research Center (BIRC), Department of Neurology, Geffen School of Medicine, UCLA; ⁴Brain Research Institute, Department of Neurology, Geffen School of Medicine, UCLA; ⁵Department of Radiological Sciences, Geffen School of Medicine, UCLA; ⁶Harvard Medical School, Boston, MA; ⁷Kitware, Inc., Clifton Park, NY

INTRODUCTION
 An estimated 1.7 million Americans sustain a traumatic brain injury (TBI) every year [1]. The use of automatic segmentation for the clinical investigation of TBI remains an elusive goal because such methods are insufficiently robust to accurately capture TBI-related changes in brain anatomy, despite recent progress in image analysis. It remains difficult to quantify traumatic brain injury multi-modally, especially for imaging clinical outcomes. To address the urgent need for clinically-oriented TBI analysis tools, we have used multimodal automatic TBI analysis methods with a view toward assisting clinical triage.

METHODS
 We employ the NA-MIC kit and 3D Slicer platform [2, 8, 9] to obtain medical images and derive data to therapy and/or recovery. We employ flexible segmentation of lesions, hemorrhage, edema and other pathology using Atlas Based Classification (ABC). ABC is a robust automatic segmentation framework which includes multi-modal image registration, model-based bias field correction, tissue classification and outlier detection [2, 6-7]. The ABC pipeline is considerably more suitable for TBI volume segmentation compared to standard methods. Longitudinal changes are assessed by registration and joint segmentation of baseline and follow-up data for the ultimate purpose of performing longitudinal analysis. Our tools allow cross-correlation of multimodal medical data: structural imaging (cortical thickness, volume, lesion) and DTI with clinical outcome variables (time since injury, age, gender, etc.).

RESULTS
 3D Slicer and the NA-MIC kit are applicable to the analysis of TBI neuroimaging to investigate alterations in cortical thickness and white matter changes. Software tools being developed allow us to obtain multimodal results for the analysis of neurobiological concentrations associated with TBI. Metrics can be extracted for uni- and multi-scale modeling to provide additional insights about neuro-anatomical changes and clinical outcome variables. Multimodal data processing solutions are to be made openly available, with accompanying training materials via the NA-MIC web site, and compliant with the NA-MIC open-source policies.

CONCLUSIONS
 We envision NA-MIC kit workflows to be suitable for TBI clinical practice and patient monitoring, particularly for assessing TBI damage and measuring changes over time. Longitudinal changes and degree of change, metrics can be assessed with clinical measures and subsequently used to suggest viable treatment options for individual subjects against patterns that are typical TBI populations.

REFERENCES
 [1] M. Faul, L. Xu, M. Wald, C. Lusa, "Traumatic Brain Injury in the United States: Estimates of Burden and Costs," *Journal of Neurotrauma*, vol. 27, pp. 15-28, 2010.
 [2] A. Irimia, M. Prastawa, S. Gouttard, G. Gerig, "Robust Tissue Classification and Outlier Detection in Brain MRI," *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2009*, pp. 103-112, 2009.
 [3] A. Irimia, M. Prastawa, S. Gouttard, G. Gerig, "Robust Tissue Classification and Outlier Detection in Brain MRI," *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2009*, pp. 103-112, 2009.
 [4] A. Irimia, M. Prastawa, S. Gouttard, G. Gerig, "Robust Tissue Classification and Outlier Detection in Brain MRI," *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2009*, pp. 103-112, 2009.
 [5] A. Irimia, M. Prastawa, S. Gouttard, G. Gerig, "Robust Tissue Classification and Outlier Detection in Brain MRI," *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2009*, pp. 103-112, 2009.
 [6] A. Irimia, M. Prastawa, S. Gouttard, G. Gerig, "Robust Tissue Classification and Outlier Detection in Brain MRI," *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2009*, pp. 103-112, 2009.
 [7] A. Irimia, M. Prastawa, S. Gouttard, G. Gerig, "Robust Tissue Classification and Outlier Detection in Brain MRI," *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2009*, pp. 103-112, 2009.
 [8] A. Irimia, M. Prastawa, S. Gouttard, G. Gerig, "Robust Tissue Classification and Outlier Detection in Brain MRI," *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2009*, pp. 103-112, 2009.
 [9] A. Irimia, M. Prastawa, S. Gouttard, G. Gerig, "Robust Tissue Classification and Outlier Detection in Brain MRI," *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2009*, pp. 103-112, 2009.



TBI DBP Presentations

- **Conference Proceedings**

- M Niethammer, G Hart, A Irimia, PM Vespa, JD Van Horn, SR Aylward (2011) Geometric metamorphosis *Proceedings of MICCAI 2011*
- Y. Lou, A. Irimia, P. Vela, M.C. Chambers, J.D. Van Horn, P.M. Vespa, and Al. Tannenbaum (submitted) “Multimodal Deformable Registration of Traumatic Brain Injury MR Volumes using Graphics Processing Units” *Workshop on Biomedical Image Registration 2012, Lecture Notes in Computer Science.*

- **Conference Abstracts & Posters**

- A Irimia, MC Chambers, PM Vespa, AW Toga, JD Van Horn (2011) Cortical network visualization and analysis in traumatic brain injury using multimodal neuroimaging *Proceedings of the Seventeenth Joint Symposium on Neural Computation, June 4, 2011, Institute of Neural Computation, University of California, San Diego*
- A Irimia, MC Chambers, M Filippou, JR Alger, MW Prastawa, B Wang, S Gouttard, SMA Pujol, SR Aylward, DA Hovda, G Gerig, AW Toga, R Kikinis, PM Vespa, JD Van Horn (2011) Three-dimensional calculation and quantification of morphometric and volumetric cortical atrophy indices of widespread clinical use from MRI volumes of traumatic brain injury using 3D Slicer *Proceedings of the Forty-First Annual Meeting of the Society for Neuroscience (SfN 2011), Washington, DC (this work received the First Prize in the Fine Science Tools Contest, UCLA Brain Research Institute)*
- A Irimia, JD Van Horn, MC Chambers, MW Prastawa, S Gouttard, PM Vespa, DA Hovda, JR Algers, SMA Pujol, G Gerig, SR Aylward, AW Toga, R Kikinis (2011) Automatic multimodal MR image segmentation for the clinical assessment of traumatic brain injury in 3D Slicer *Proceedings of the Seventeenth Annual Meeting of the Organization on Human Brain Mapping (OHBM 2011), Quebec City, Canada*

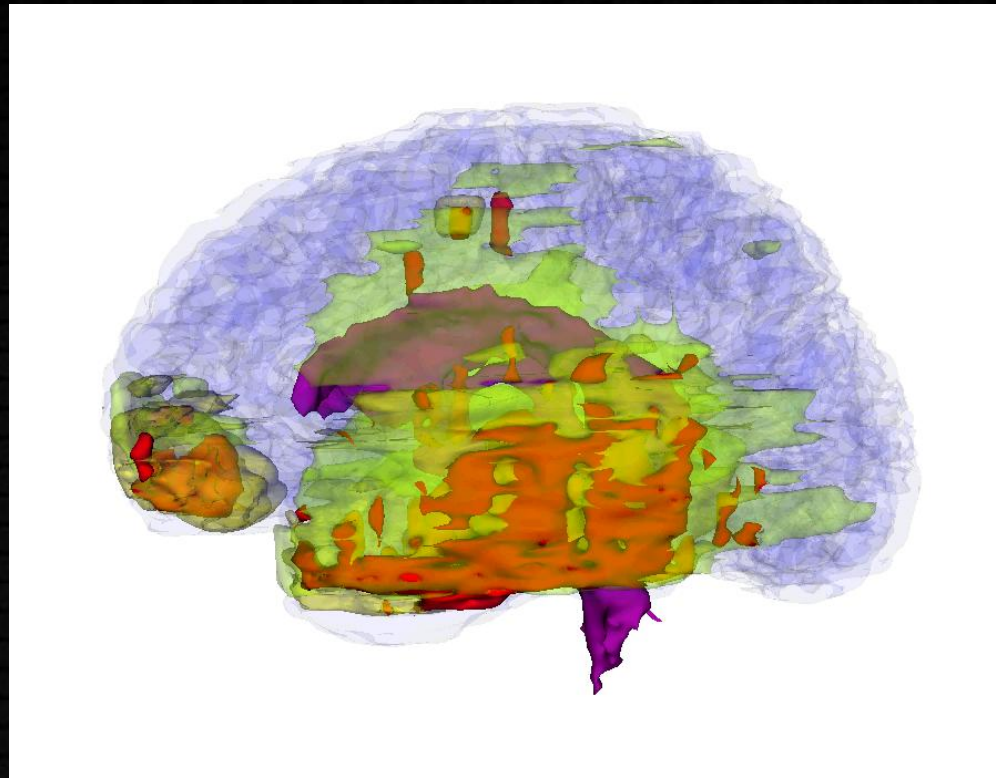
NA-MIC Winter Project

Week 2012 TBI Activities

- ***Segmentation of Serial MRI of TBI patients using Personalized Atlas Construction*** (Bo Wang, Marcel Prastawa, Andrei Irimia, Micah Chambers, Jack Van Horn, Guido Gerig, Danielle Pace, Stephen Aylward)
- ***Registration and analysis of white matter tract changes in TBI*** (Clement Vachet, Anuja Sharma, Marcel Prastawa, Andrei Irimia, Jack Van Horn, Guido Gerig, Martin Styner, Danielle Pace, Stephen Aylward)
- ***Validation, visualization and analysis of segmentation for TBI*** (Bo Wang, Marcel Prastawa, Andrei Irimia, Micah Chambers, Jack Van Horn, Guido Gerig, Danielle Pace, Stephen Aylward)
- ***Geometric Metamorphosis for TBI*** (Danielle Pace, Marc Niethammer, Marcel Prastawa, Andrei Irimia, Jack van Horn, Danielle Pace, Stephen Aylward)
- ***Multimodal Deformable Registration of Traumatic Brain Injury MR Volumes using Graphics Processing Units*** (Yifei Lou, Andrei Irimia, Patricio Vela, Allen Tannenbaum, Micah C. Chambers, Jack Van Horn and Paul M. Vespa, Danielle Pace, Stephen Aylward)
- ***Integration of unscented Kalman filter (UKF) based multi-tensor tractography in Slicer*** (Christian Baumgartner, Yogesh Rathi, Carl-Fredrik Westin)

Discussion and Directions

- Work Accomplished
 - Multi-modal fusion (linear co-registration, ABC)
 - Segmentation of lesions, bleedings, shunt etc.
 - Tissue classification with normal atlas prior, deformable (fluid) atlas to subject registration
 - Several peer-reviewed publications and conference presentations
- In progress and future directions:
 - Get more TBI imaging data and details on case history/outcome
 - White matter damage characterization in acute vs. chronic TBI
 - Robust tissue segmentation with outlier detection and more categories (wm, gm ,csf, hemorrhage, lesions, etc.)
 - Advanced registration via joint surface/volume deformable registration
 - “metamorphosis”-based methods for TBI lesion classification
 - User-guidance to “seed” categories of tissue within Slicer
 - TBI-related informatics wrt the current TBI literature



Thank you