Cranial Nerves II-VII As Neuromonitors: Pupillometry, Eye Tracking and Blink As Indicators of Injury and Disease

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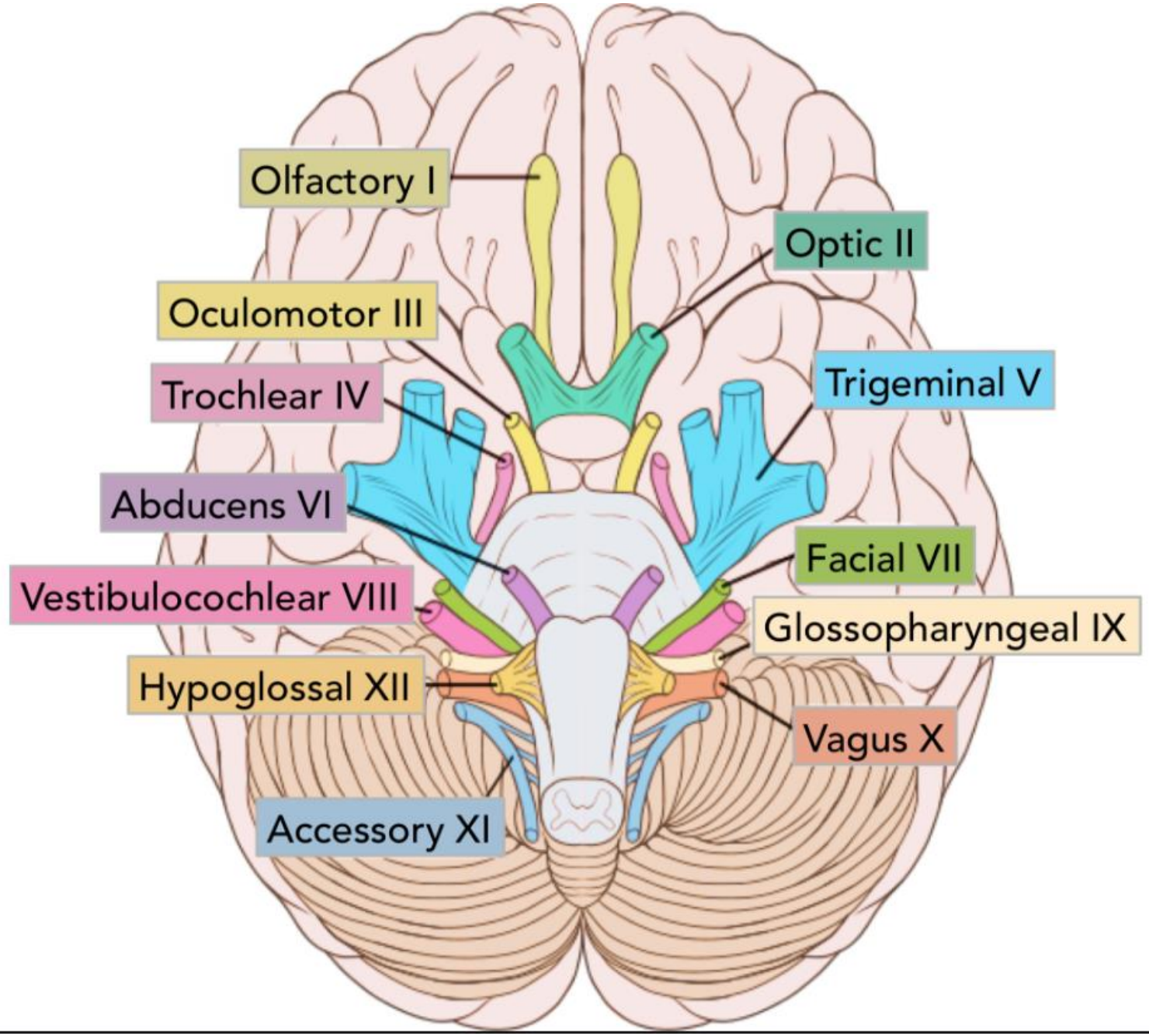
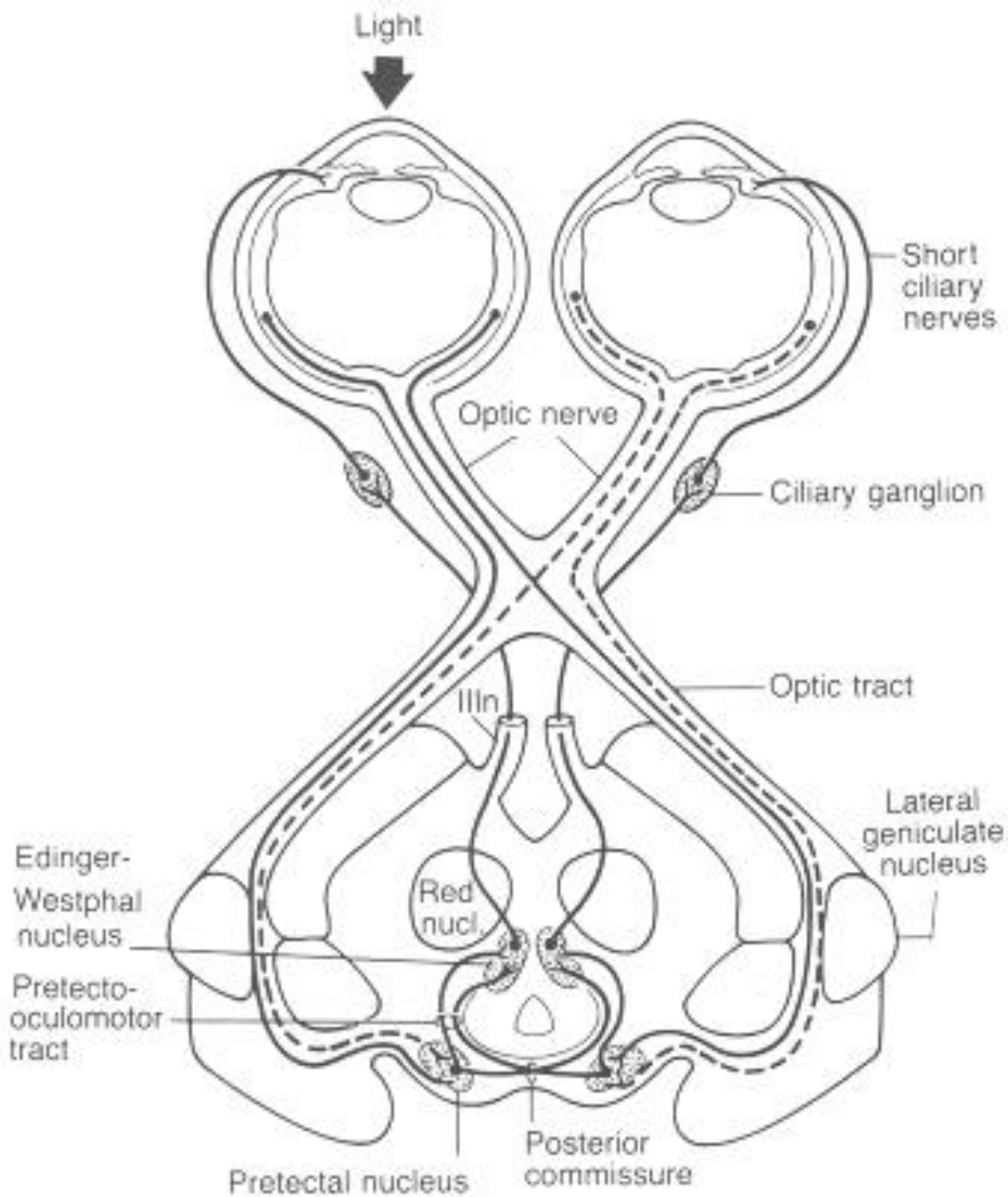


https://teachmeanatomy.info/head/cranial-nerves/summary/

Method:

The subject watches a 220 second video playing inside of an aperture moving around the perimetry of a video monitor while a camera records eye movements.

CN II and III (pupillometry)



http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=cm&part=A1745

frontiers in Neurology

PERSPECTIVE
published: 12 July 2021
doi: 10.3389/fneur.2021.685313

Check for updates

The Expanding Role of Quantitative Pupillometry in the Evaluation and Management of Traumatic Brain Injury

Jason H. Boulter[1], Margaret M. Shields[2], Melissa R. Meister[1], Gregory Murtha[2], Brian P. Curry[1] and Bradley A. Dengler[1]*

[1] Division of Neurosurgery, Walter Reed National Military Medical Center, Bethesda, MD, United States, [2] School of Medicine, Uniformed Services University, Bethesda, MD, United States

J Clin Neurosci. 2021 Sep;91:88-92. doi: 10.1016/j.jocn.2021.06.044. Epub 2021 Jul 2.

Quantitative pupillometry in patients with traumatic brain injury and loss of consciousness: A prospective pilot study

Jeffrey I Traylor [1], Tarek Y El Ahmadieh [1], Nicole M Bedros [2], Nadeem Al Adli [1], Sonja E Stutzman [3], Aardhra M Venkatachalam [3], Mark N Pernik [1], C Munro Collum [3], Peter M Douglas [4], Venkatesh Aiyagari [5], Carlos A Bagley [1], DaiWai M Olson [5], Salah G Aoun [6]

Affiliations + expand

PMID: 34373065 DOI: 10.1016/j.jocn.2021.06.044

Pupil dilation velocity correlates with loss of consciousness

BMJ Open

Outcome Prognostication of Acute Brain Injury using the Neurological Pupil Index (ORANGE) study: protocol for a prospective, observational, multicentre, international cohort study

Mauro Oddo,[1,2] Fabio Taccone,[3] Stefania Galimberti,[4,5] Paola Rebora,[4,6] Giuseppe Citerio ,[4,7] on behalf of the Orange Study Group

To cite: Oddo M, Taccone F, Galimberti S, *et al*. Outcome Prognostication of Acute Brain Injury using the Neurological Pupil Index (ORANGE) study: protocol for a prospective, observational, multicentre, international cohort study. *BMJ Open* 2021;**11**:e046948. doi:10.1136/bmjopen-2020-046948

► Prepublication history and supplemental material for this paper is available online. To view these files, please visit

ABSTRACT

Introduction The pupillary examination is an important part of the neurological assessment, especially in the setting of acutely brain-injured patients, and pupillary abnormalities are associated with poor outcomes. Currently, the pupillary examination is based on a visual, subjective and frequently inaccurate estimation. The use of automated infrared pupillometry to measure the pupillary light reflex can precisely quantify subtle changes in pupillary functions. The study aimed to evaluate the association between abnormal pupillary function, assessed by the Neurological Pupil Index (NPi), and long-term outcomes in patients with acute brain injury (ABI).

Methods and analysis The Outcome Prognostication

Strength and limitation of this study

- The study will cover the more common neurological emergencies and, in a large population of patients with acute brain injury, the relationship between pathological Neurological Pupil Index and outcome.
- The standard data acquisition in the centres, transferred from the device into the eCRF, and the granularity of data will guarantee high-quality data.
- Due to the observational nature of our study, we will report only associations and not causality relationship.

J Surg Res. 2021 Jun;262:27-37. doi: 10.1016/j.jss.2020.12.042. Epub 2021 Feb 1.

Efficacy of Noninvasive Technologies in Triaging Traumatic Brain Injury and Correlating With Intracranial Pressure: A Prospective Study

Kathleen E Singer [1], Taylor E Wallen [1], Timothy Jalbert [1], Devin Wakefield [1], Anthony Spuzzillo [1], Sameer Sharma [2], Ryan Earnest [1], Victor Heh [1], Brandon Foreman [2], Michael D Goodman [3]

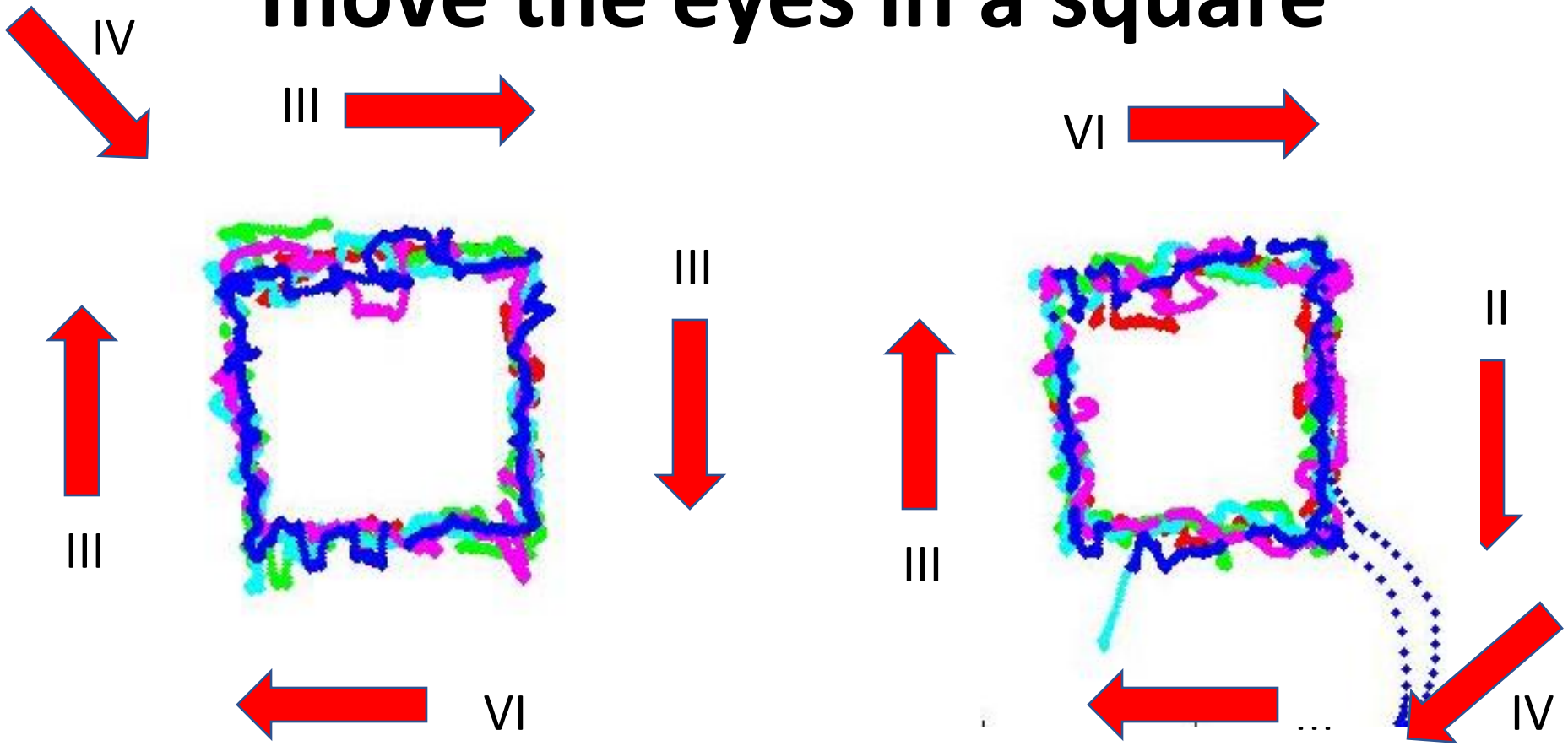
Affiliations + expand

PMID: 33540153 DOI: 10.1016/j.jss.2020.12.042

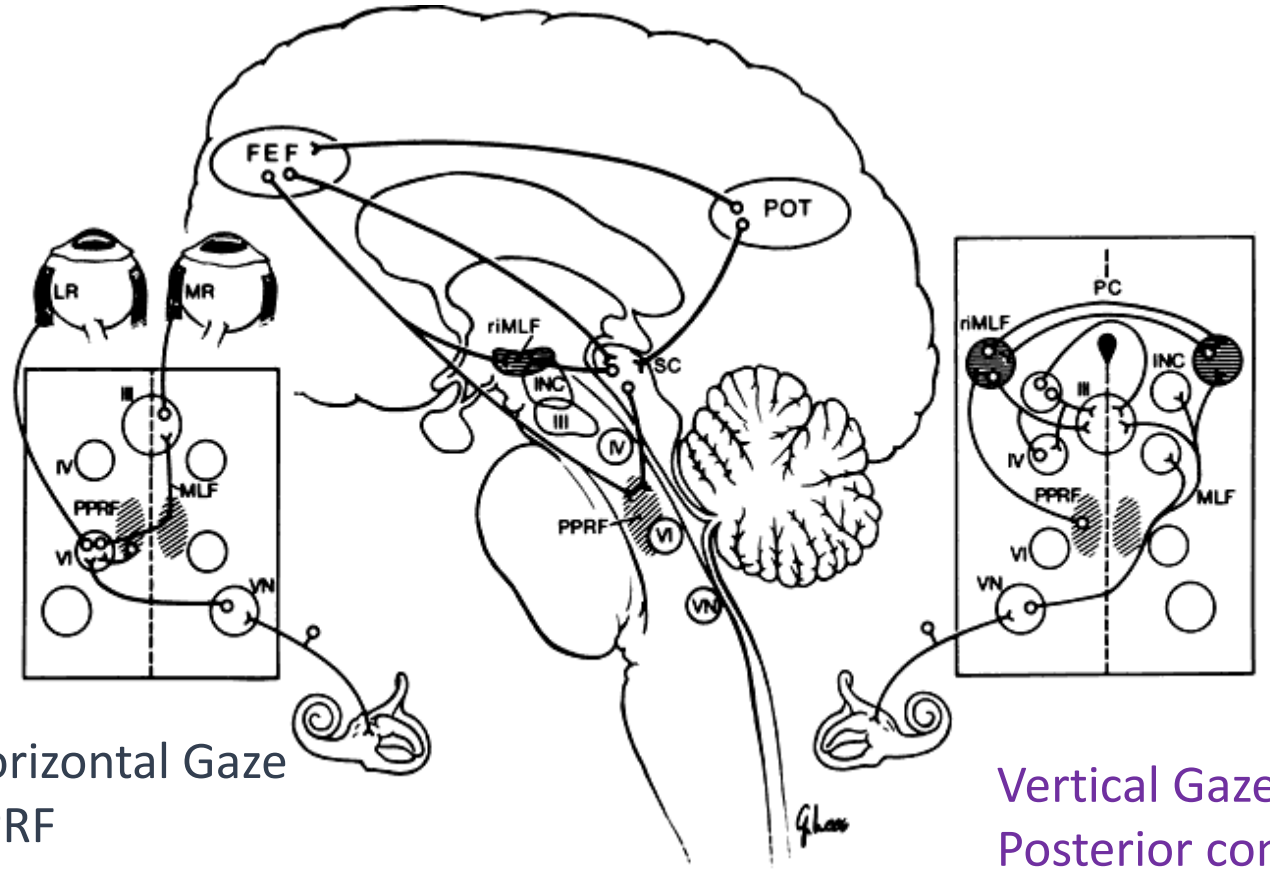
Results: ONSD differed significantly in patients with severe TBI compared with patients with mild and no TBI, but did not correlate with ICP. Pupillometric constriction velocity, dilation velocity, and percent change in pupil diameter were significantly different in patients with severe TBI, but also did not correlate with ICP. TCD did not differ among TBI severities, but middle cerebral artery peak systolic velocity, middle cerebral artery flow velocity, and carotid flow velocity correlated with ICP.

CN III, IV and VI

Cranial nerves III, IV and VI move the eyes in a square



Order: red, green, cyan, magenta, blue



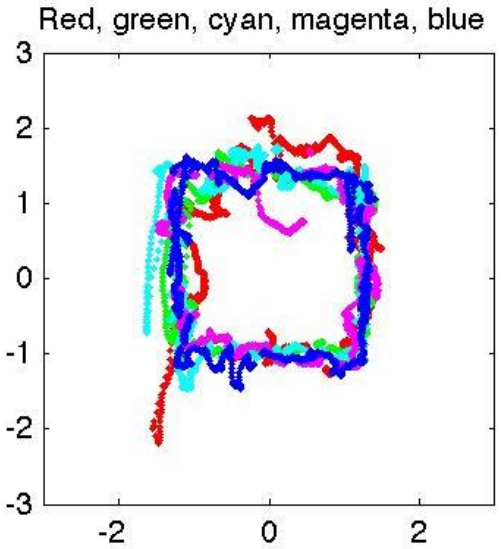
Horizontal Gaze
PPRF

Vertical Gaze
Posterior commisure
riMLF

Supranuclear control of eye movements
http://oculist.net/downaton502/prof/ebook/duanes/pages/v1/ch004/002f.html

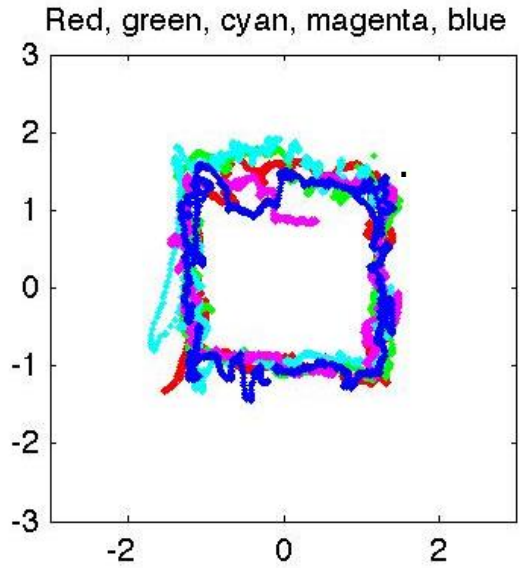
Binocular Tracking of A Normal Subject:

Left eye



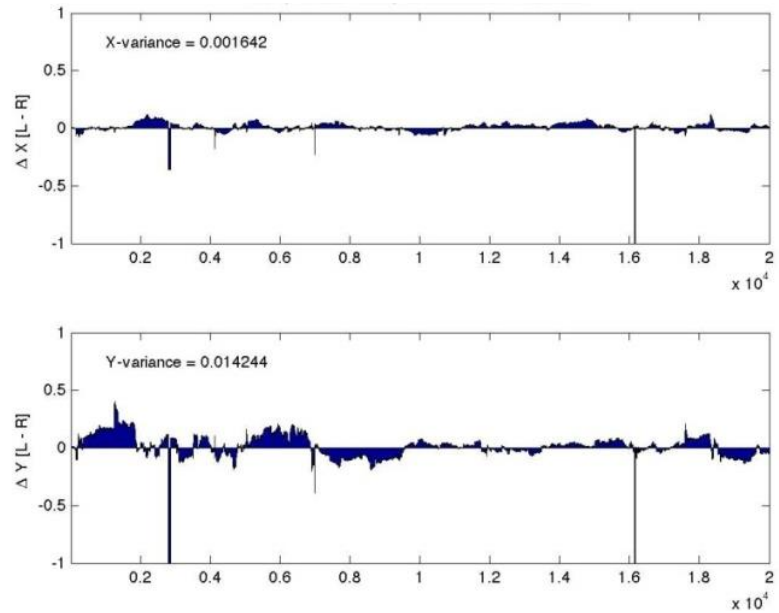
Aspect Ratio
0.97516

Right eye

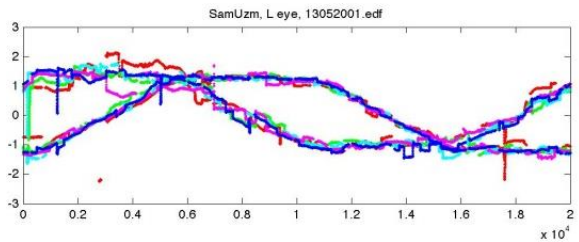


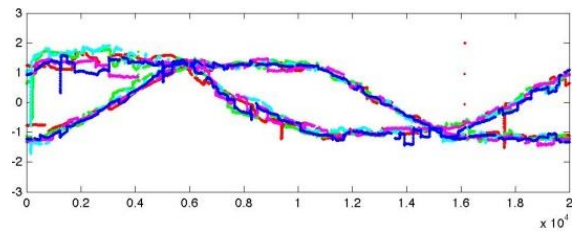
Aspect Ratio
0.99314

Conjugacy

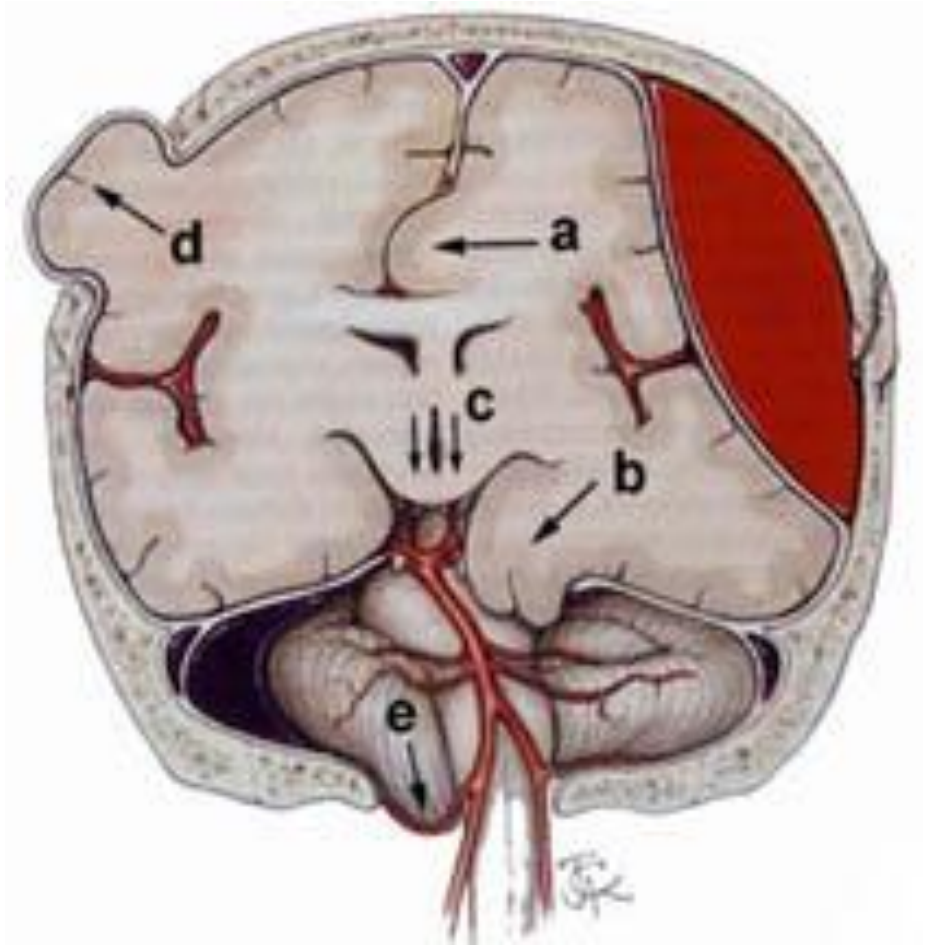


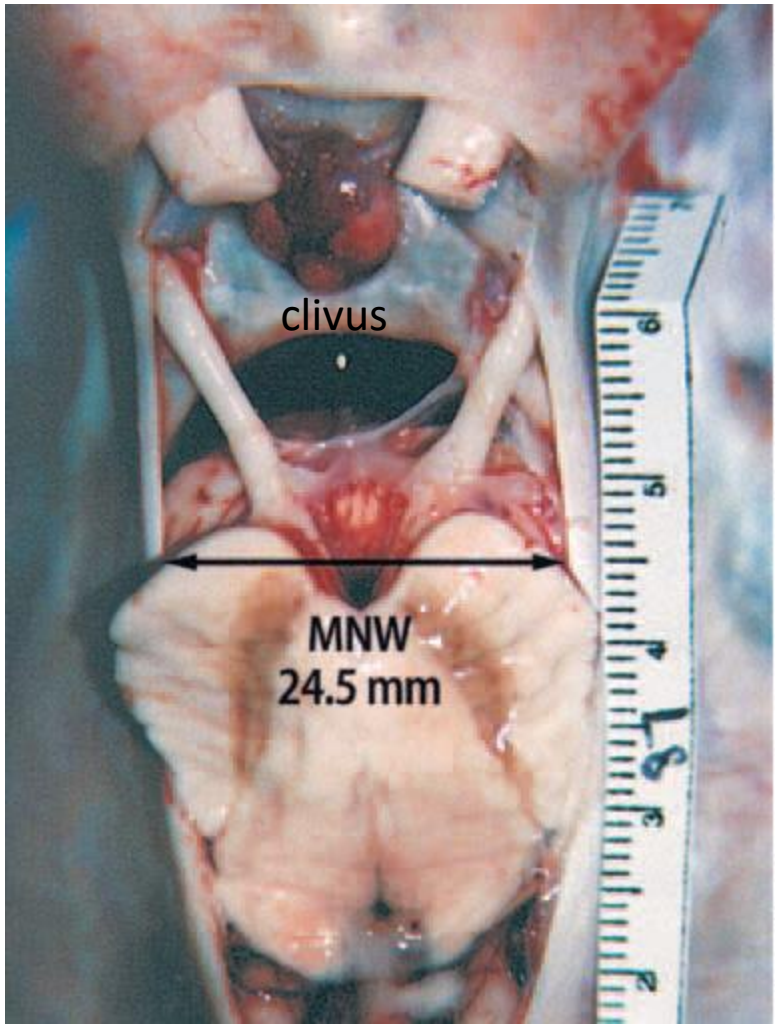
total var.015885





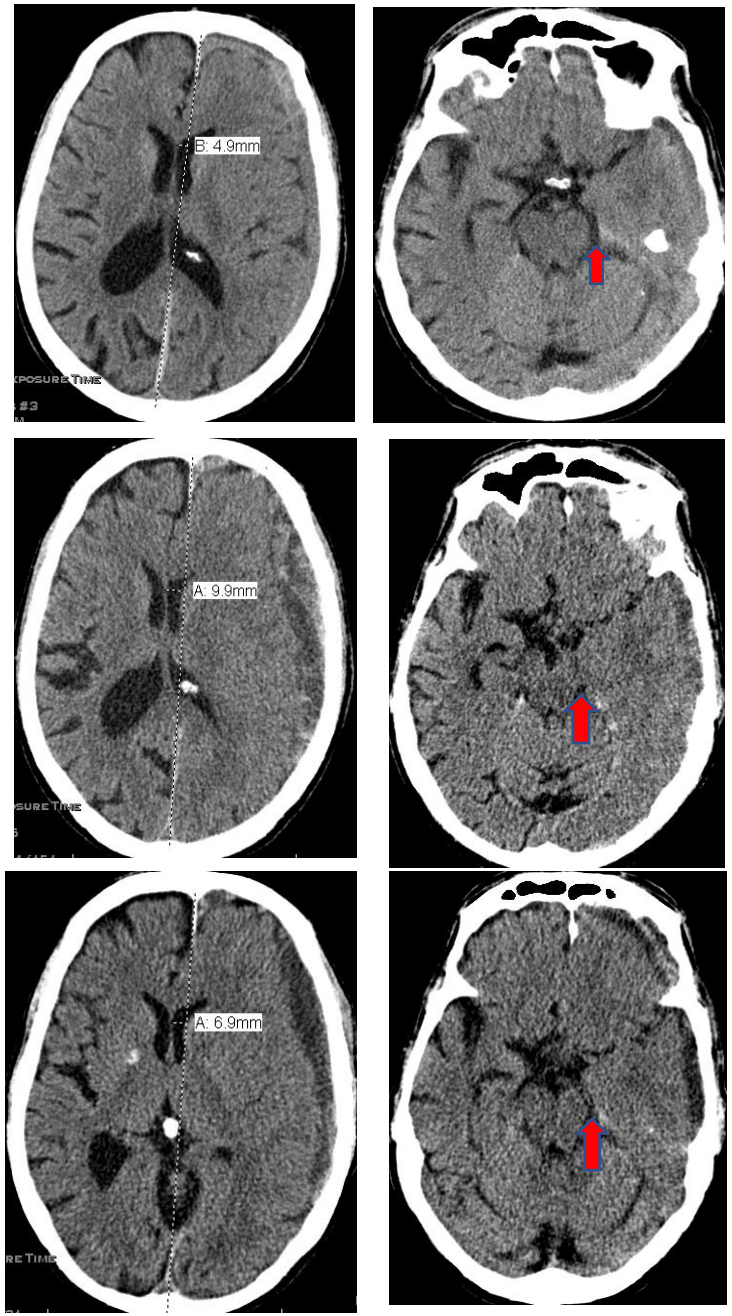
CN III





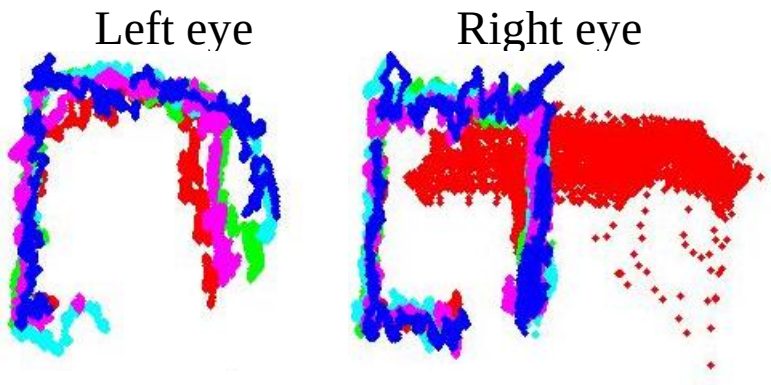
Mesencephalon section at the level of the tentorial edge to show maximal width of the notch in the axial plane

DAVID E. ADLER, M.D., AND THOMAS H. MILHORAT, M.D. J Neurosurg 96:1103–1112, 2002

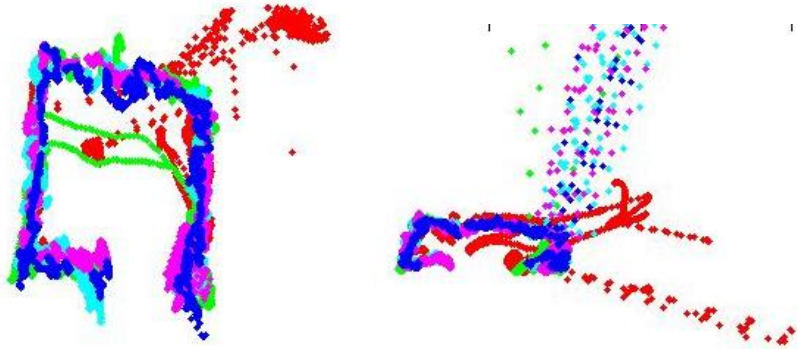


86 year old

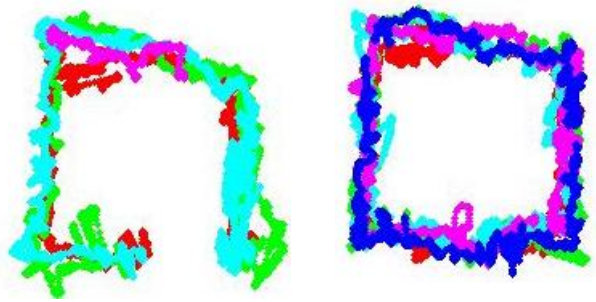
At presentation, complaining of a headache



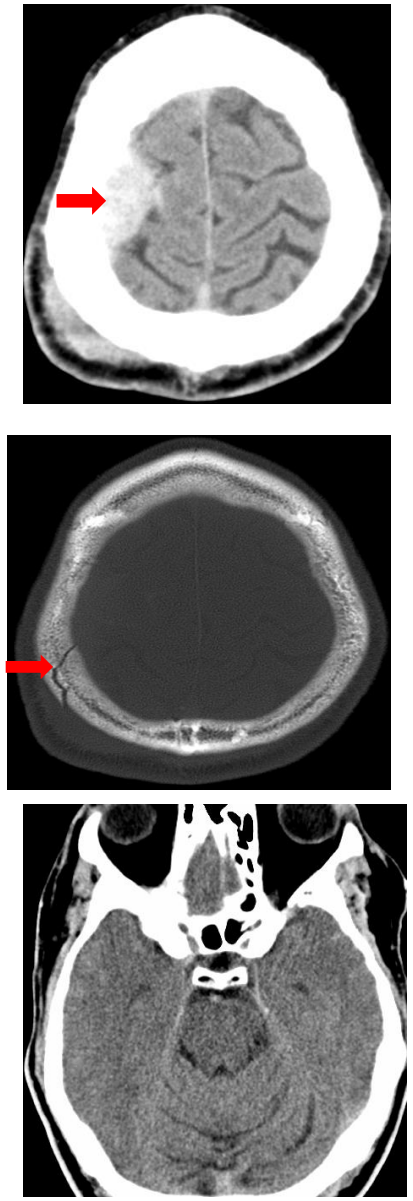
8 days later, the headache had resolved but then recurred



After 100 cc of subdural hematoma was evacuated

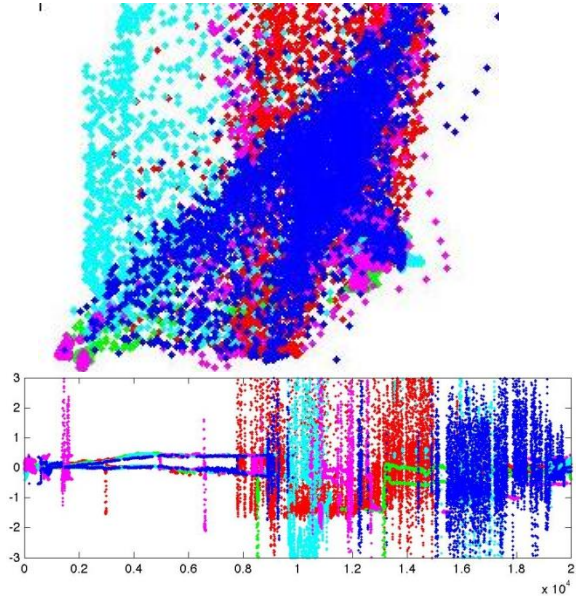


Hypertension, hyperlipidemia mild chronic renal insufficiency ophthalmologic history of bilateral cataract surgery (2 years and 8 years prior), pseudophakia and scleral buckling. He had a baseline visual acuity of 20/25 (right eye) and 20/30 (left eye)

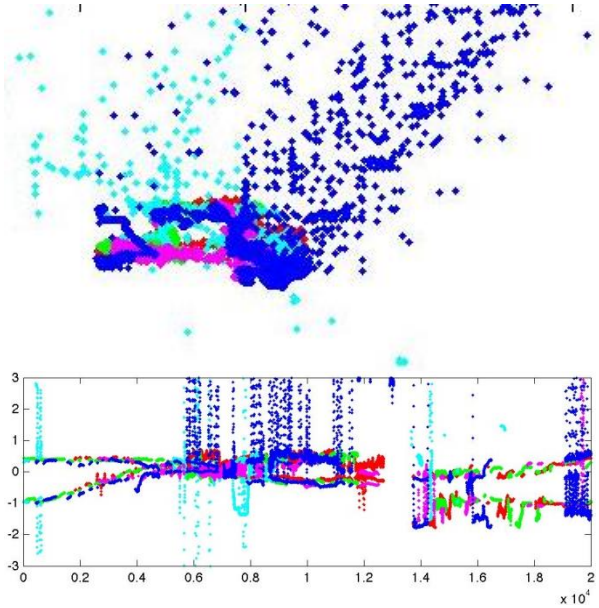


Preoperative CT images

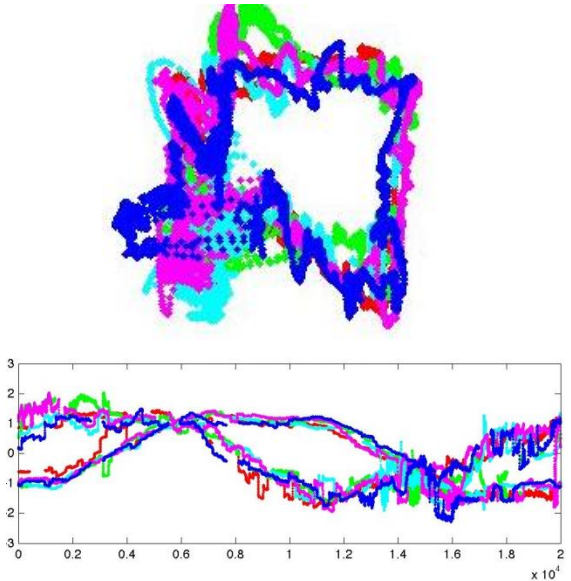
Preop Left Eye



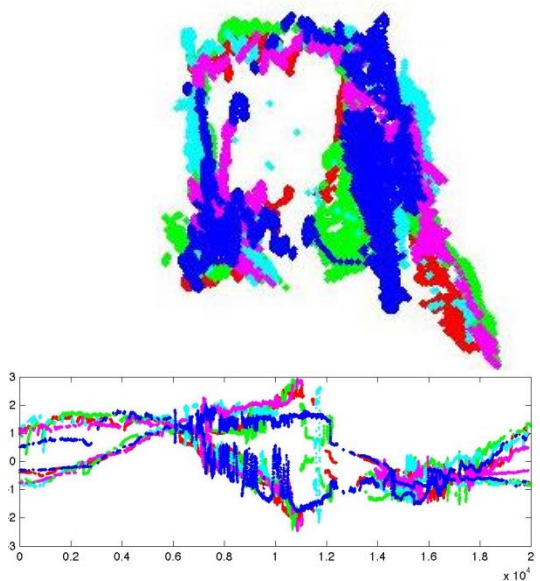
Preop Right Eye



7 Days Postop Left Eye

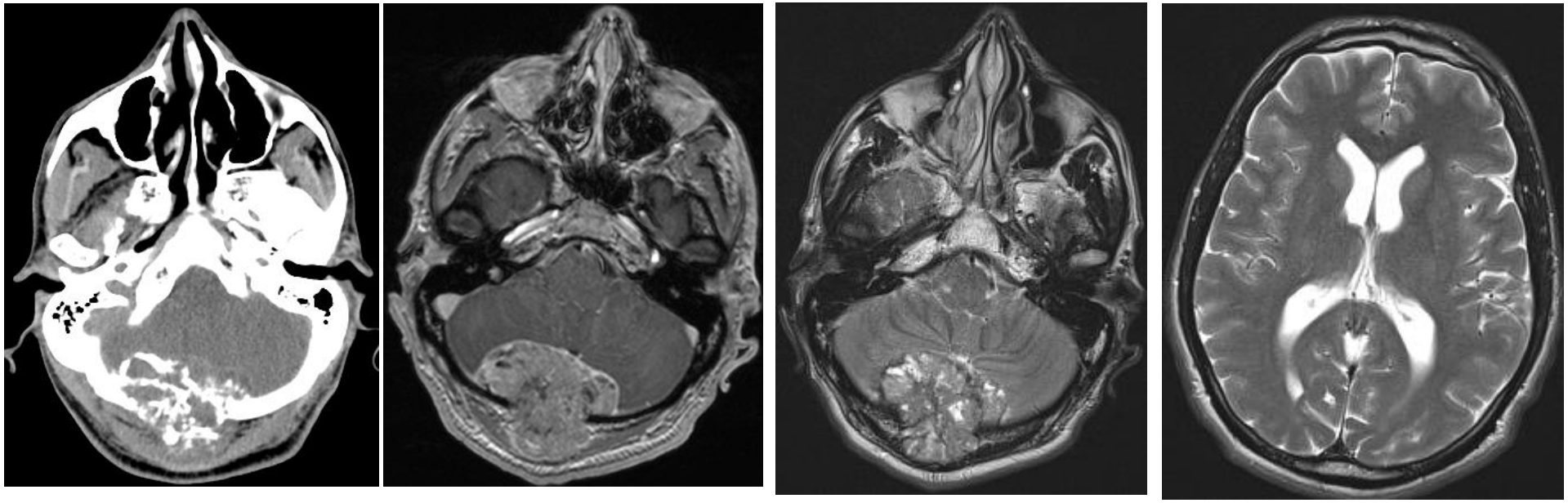


7 Days Postop Right Eye

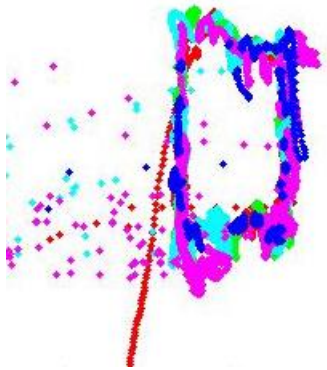


CN VI

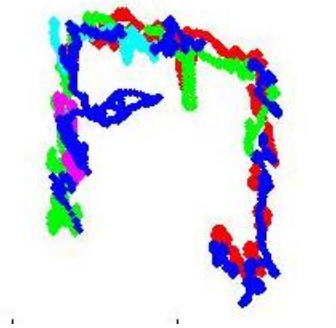
54 yo male with poorly differentiated papillary carcinoma, presented with a tender mass on the back of his head and a progressive headache



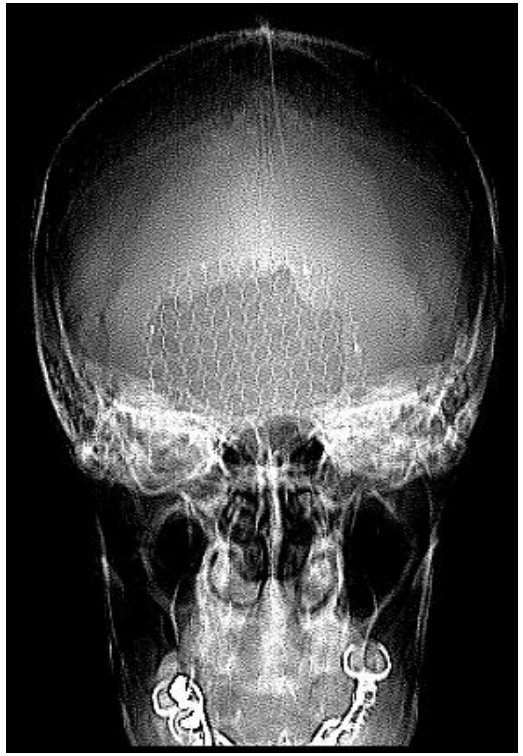
Ophthalmology: “no signs of papilledema”

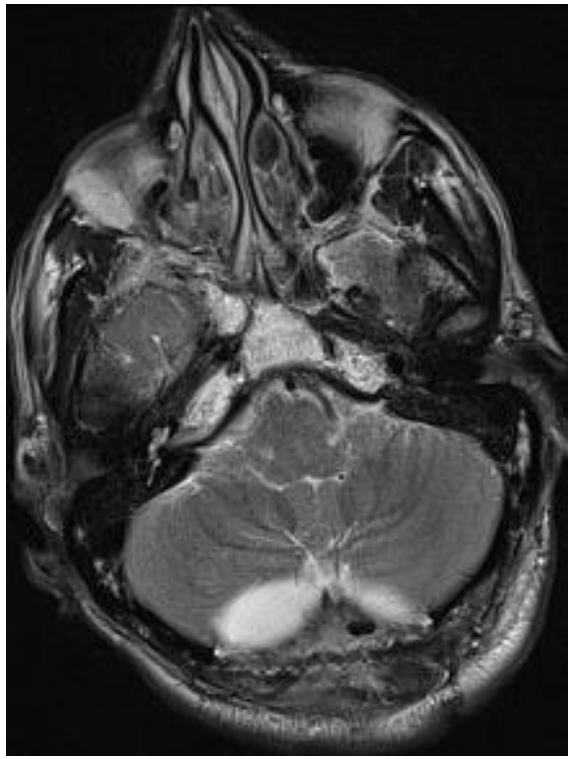


Left eye

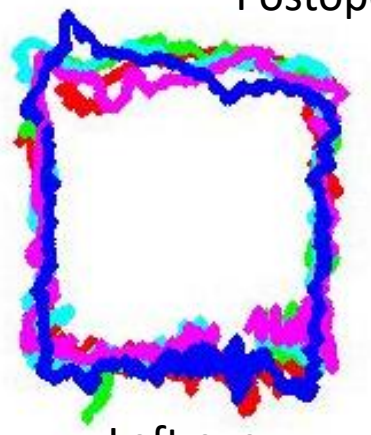


Right eye

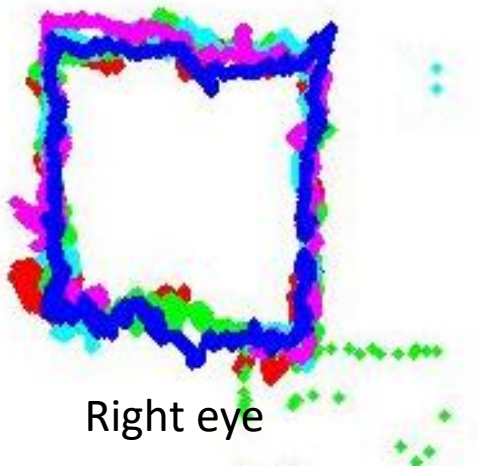




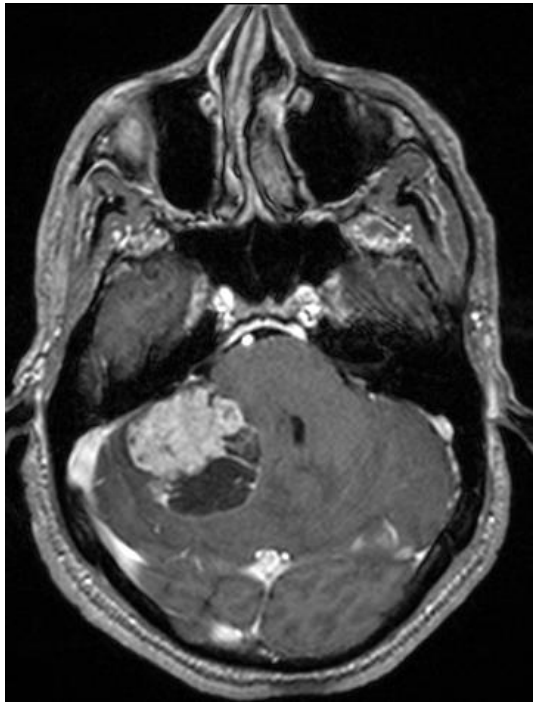
Postoperative day 1

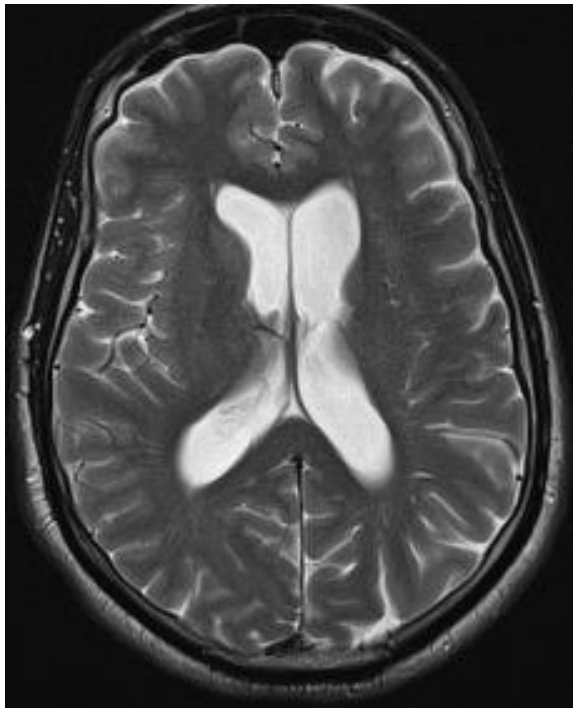


Left eye

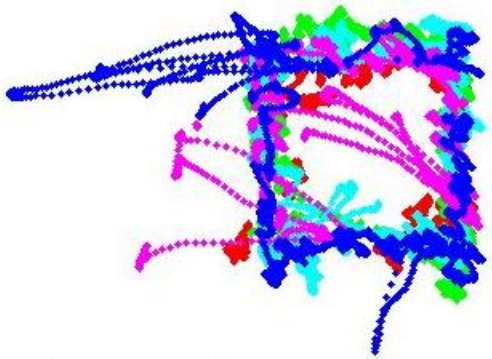


Right eye

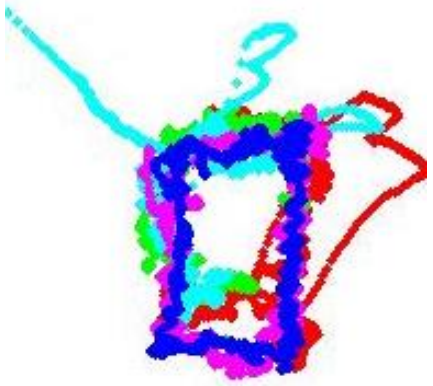




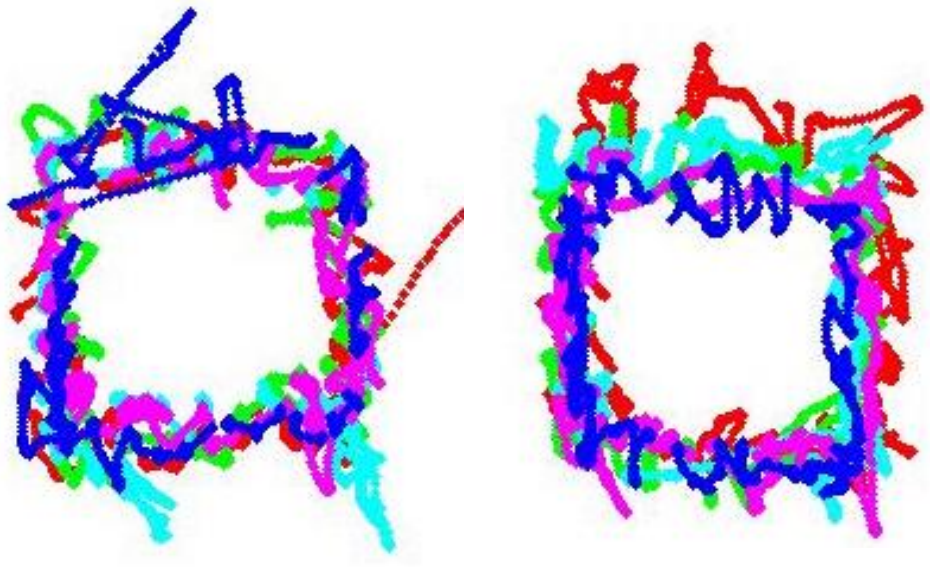
56 yo male with lung mass, headaches; Ophthalmology: no evidence of papilledema



Left eye



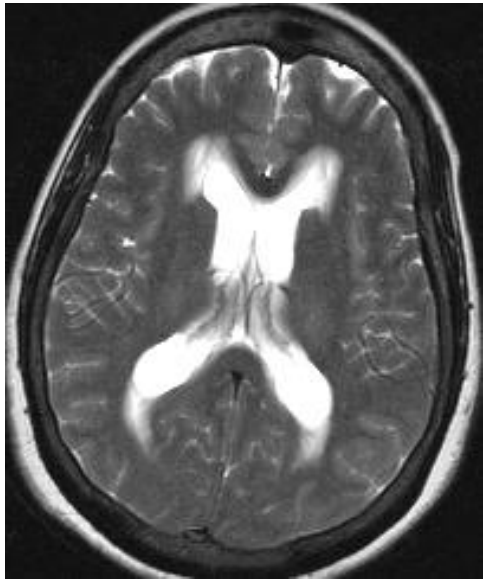
Right eye

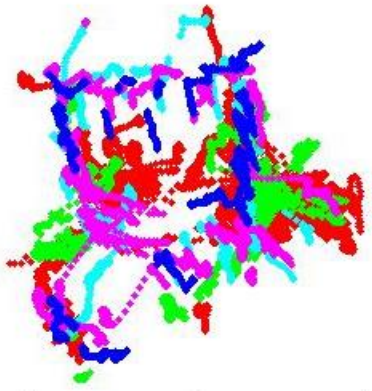


Left eye Right eye

Postoperative Day 1

59 yo woman presenting with dizziness and HA

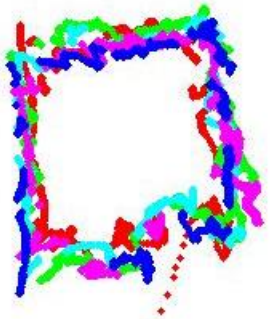




preop

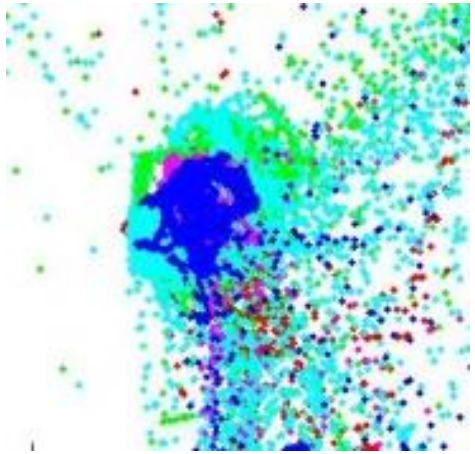
Left eye

Right eye



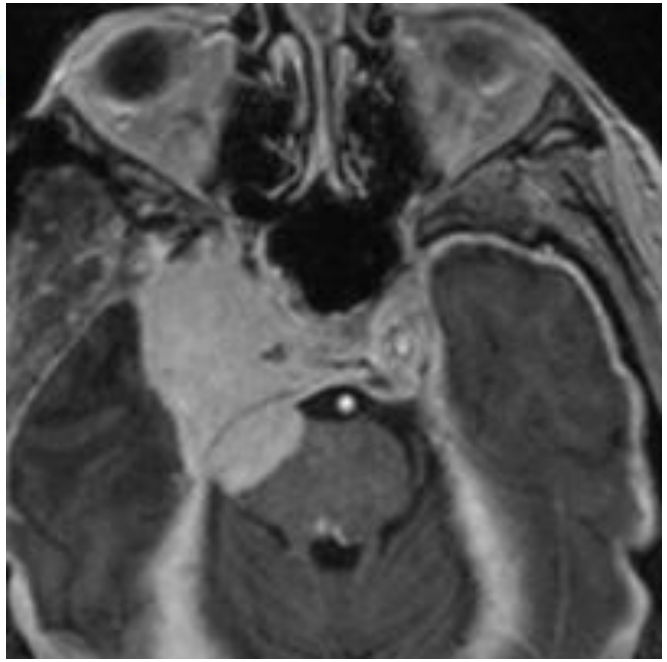
Post op
Day 2

63 yo male with right ophthalmoplegia from tumor

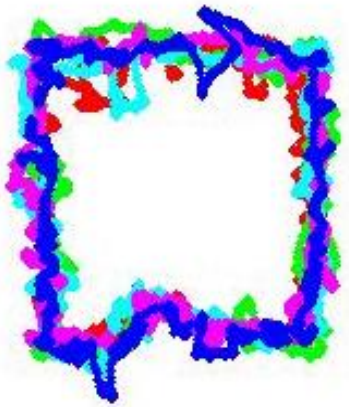


Left eye

Right eye



Left eye
No light perception

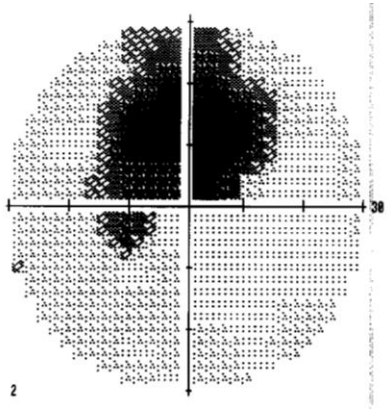


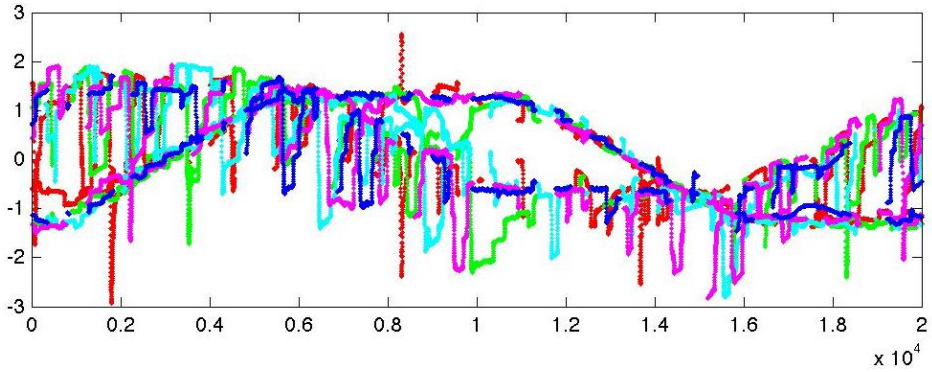
Right eye
Intact vision

65 yo male with a tumor compressing the left optic nerve resulting in no light perception in that eye

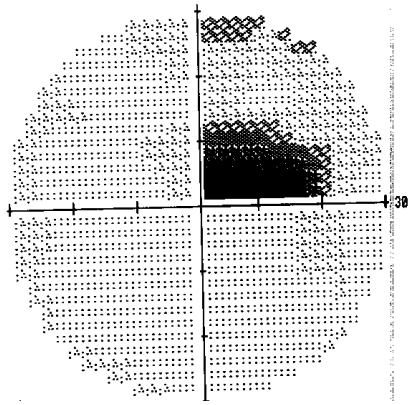
CN II

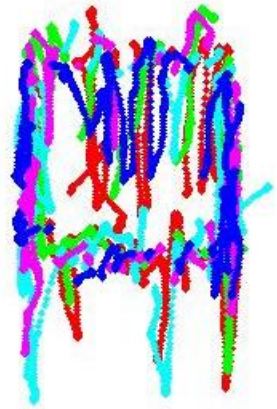
80 year old male with a history of ocular histoplasmosis

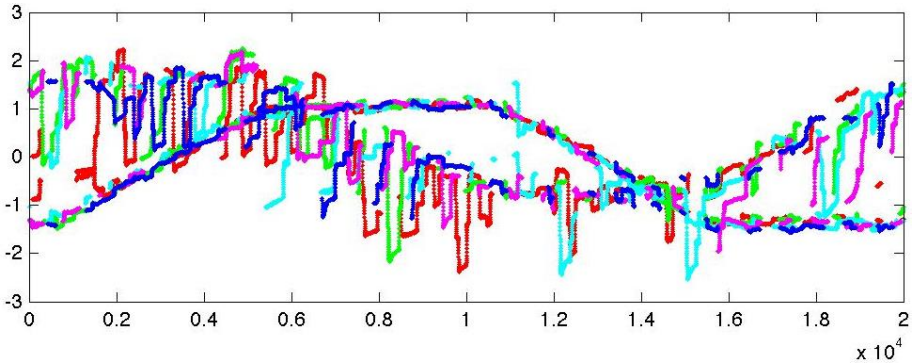




Left Eye
Counts fingers



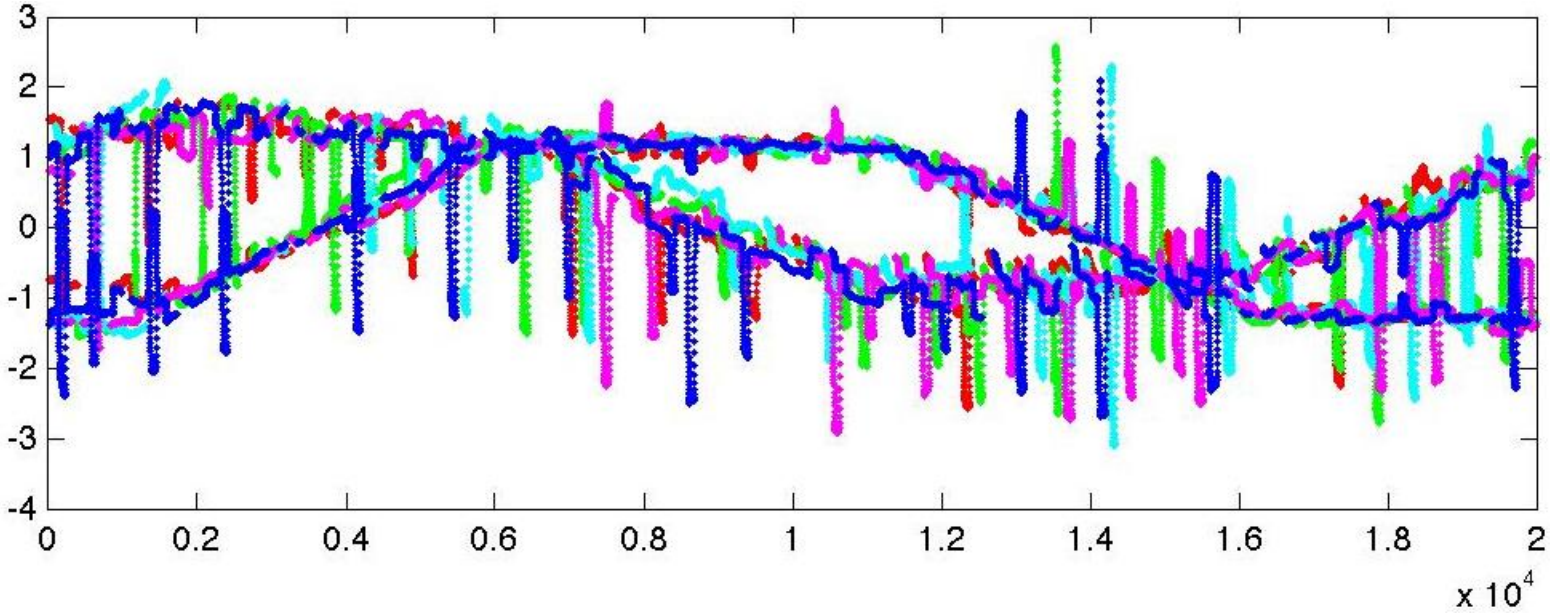


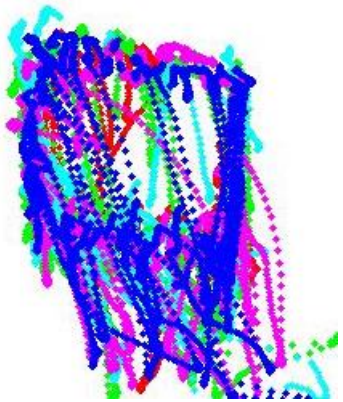


Right Eye
20/200

Central optic nerve atrophy = streaking vertical lines

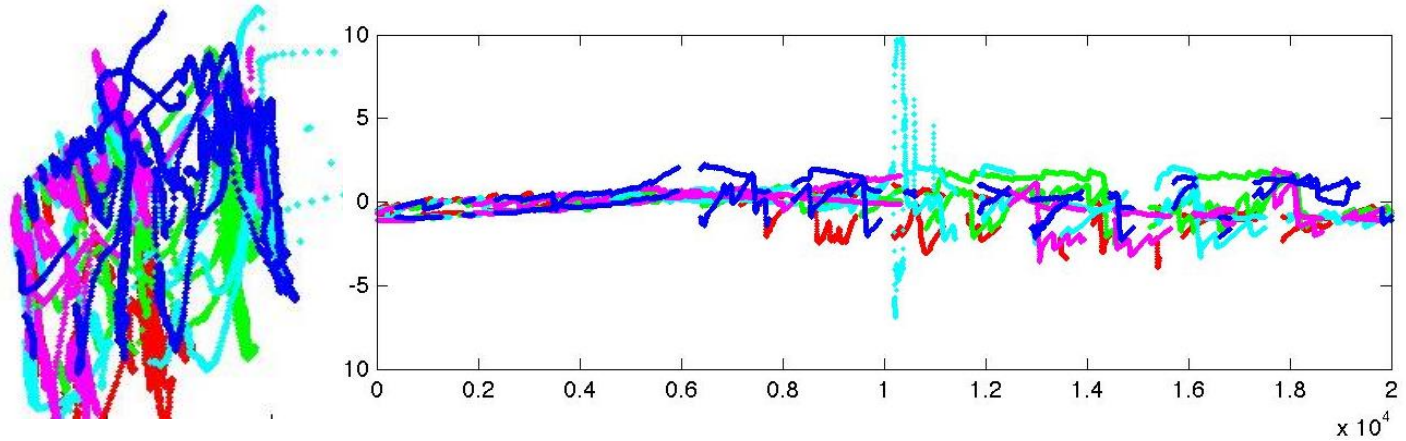
25 year old female presented with blurry vision – optic neuritis



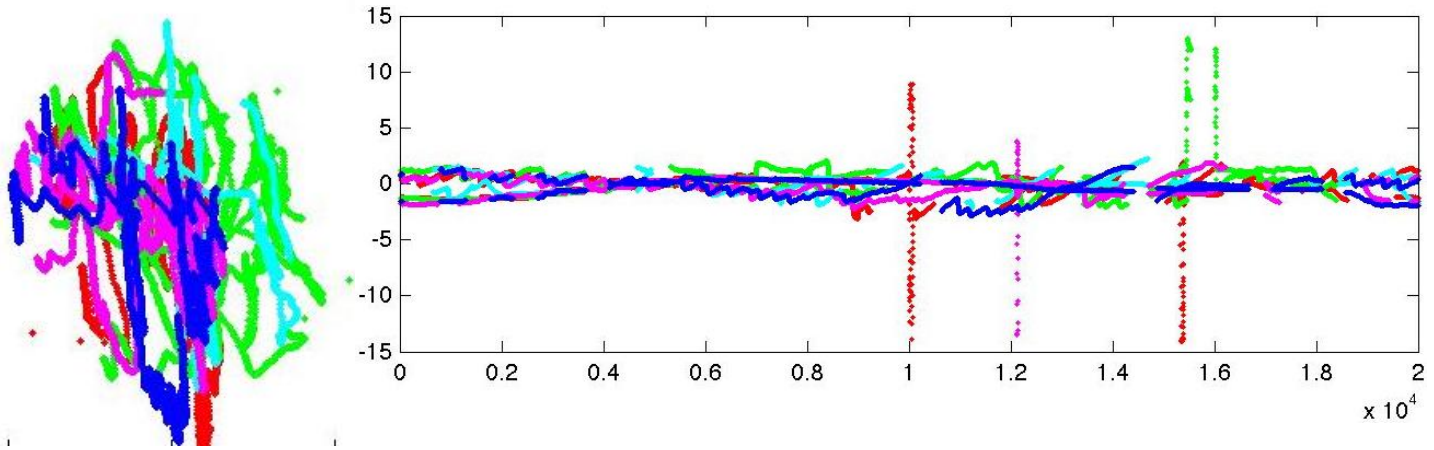


Advanced optic neuritis due to multiple sclerosis, with a disconjugate gaze

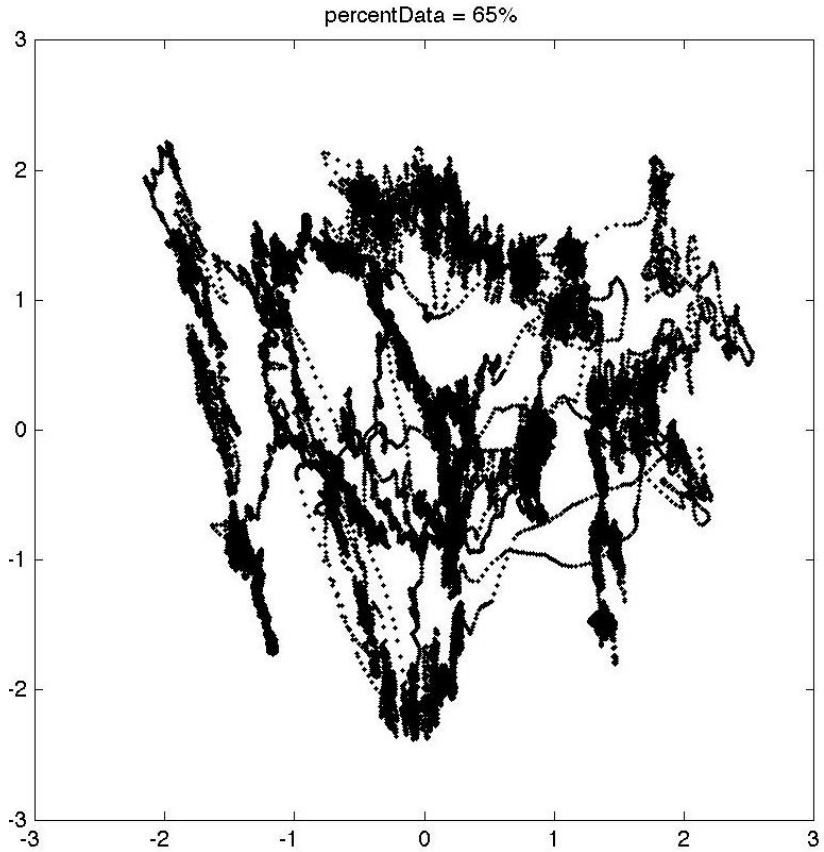
Left eye
20/100



Right eye
20/200

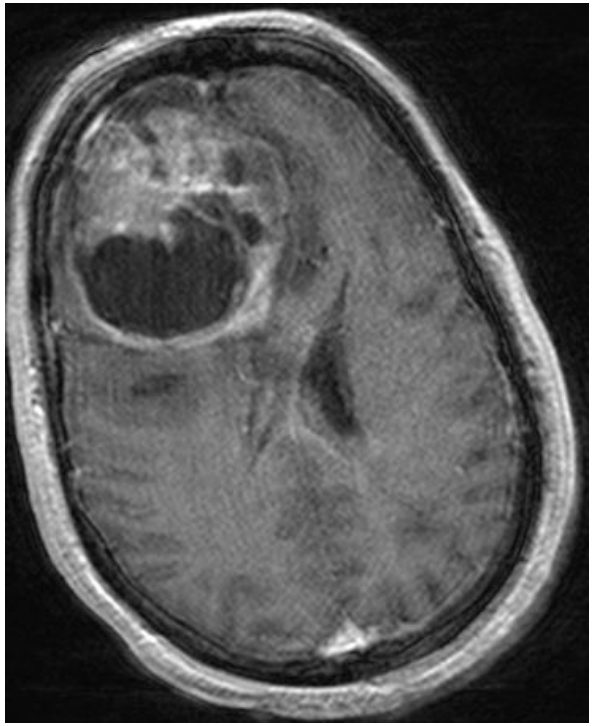


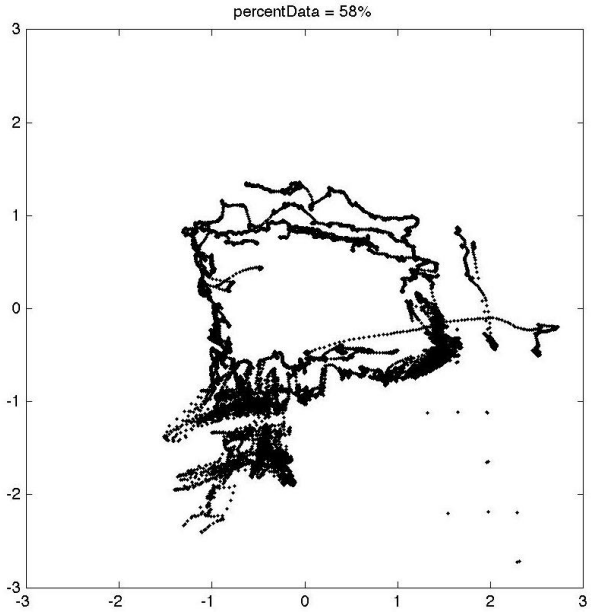
Elevated Intracranial Pressure Case: 63 yo male 2 ppd smoker, no medical care >40 years; presented with slow speech and gait; mild confusion 2 weeks after a flu-like illness. L pronator drift and neglect, Ox1, extra-ocular movements appeared grossly intact



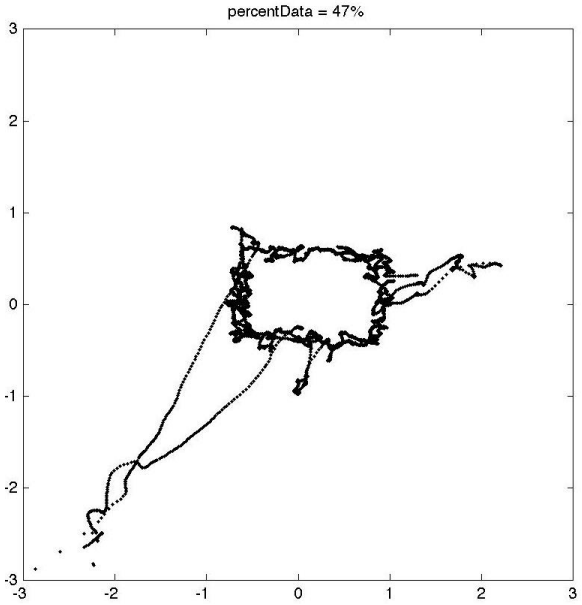
Left eye

CN II palsy (papilledema) ?





Left eye



Right eye

Papilledema gone -

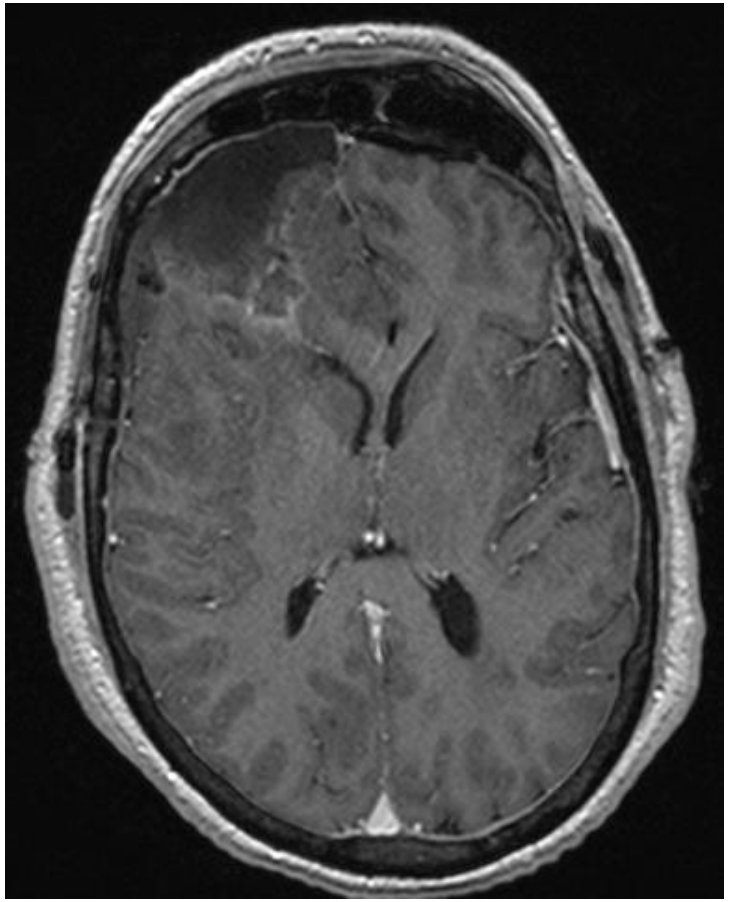
Immediately before the OR; after 10 mg decadron

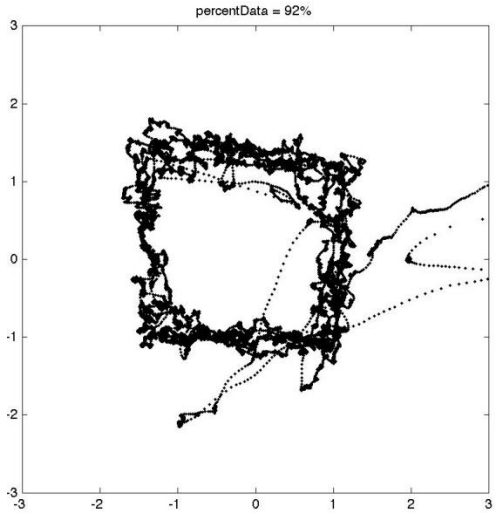
Every six hours x 4doses;

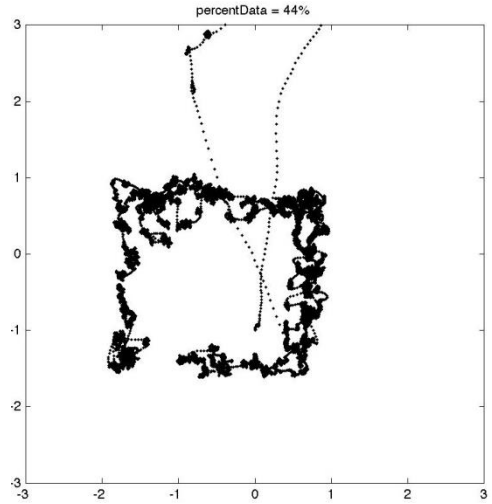
No left drift, neglect, oriented to person, place

Eye movements seemed grossly intact

One week postop:

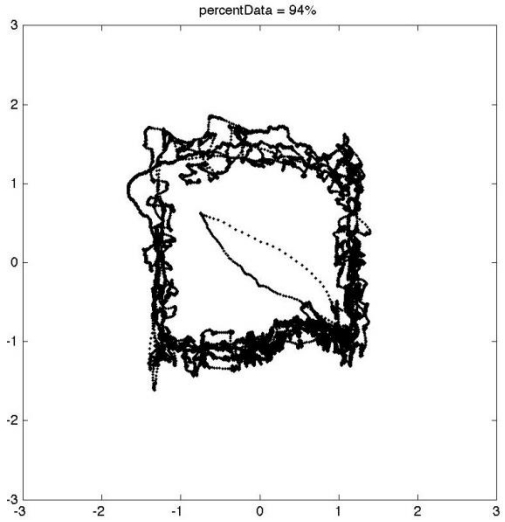


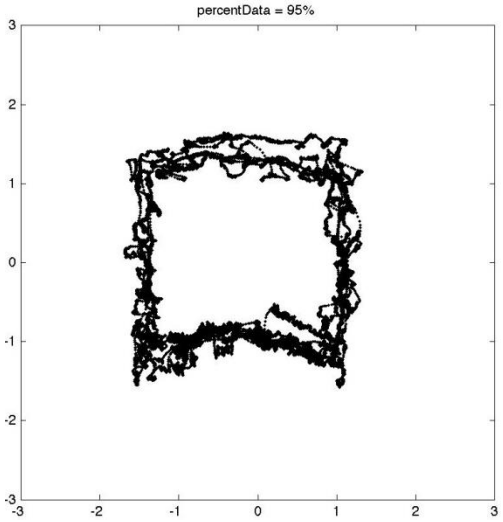




Left eye

Right Eye



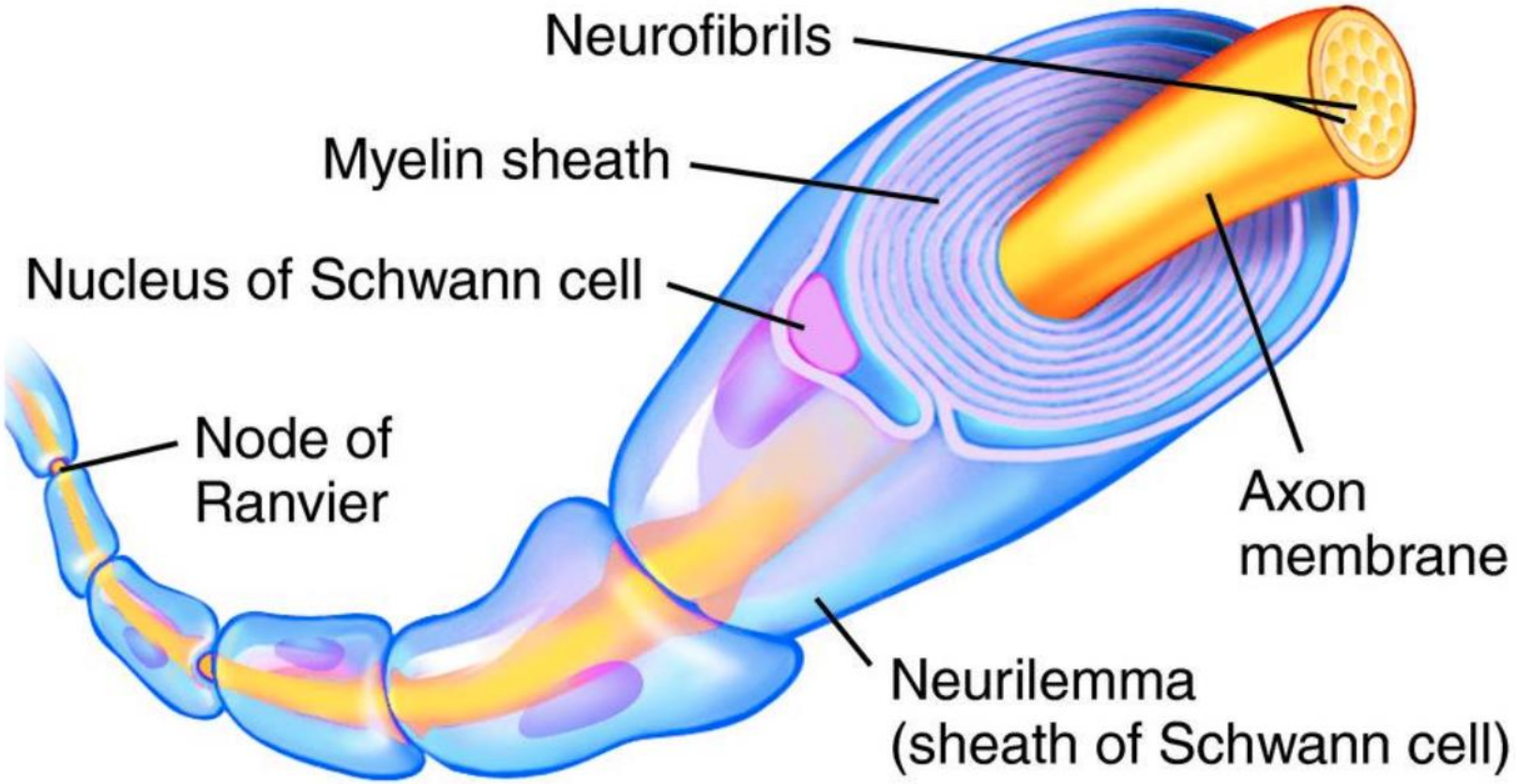


Two weeks postoperatively

No drift or neglect

Oriented x 3.

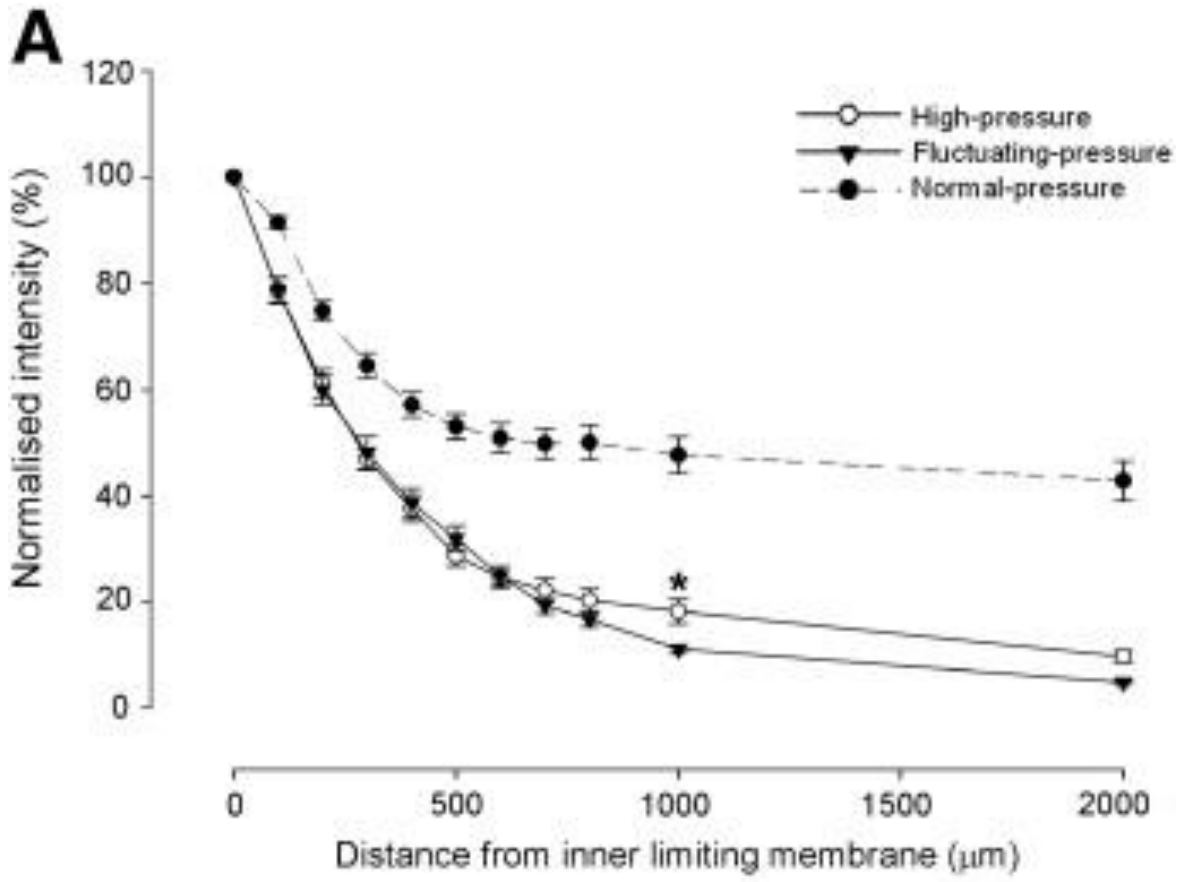
Am I getting on your nerves??? You'd be "myelin" if you said I was!



CNI and II are part of CNS (myelinated by oligodendrocytes)
III-XII are PNS (myelinated by Schwann cells)

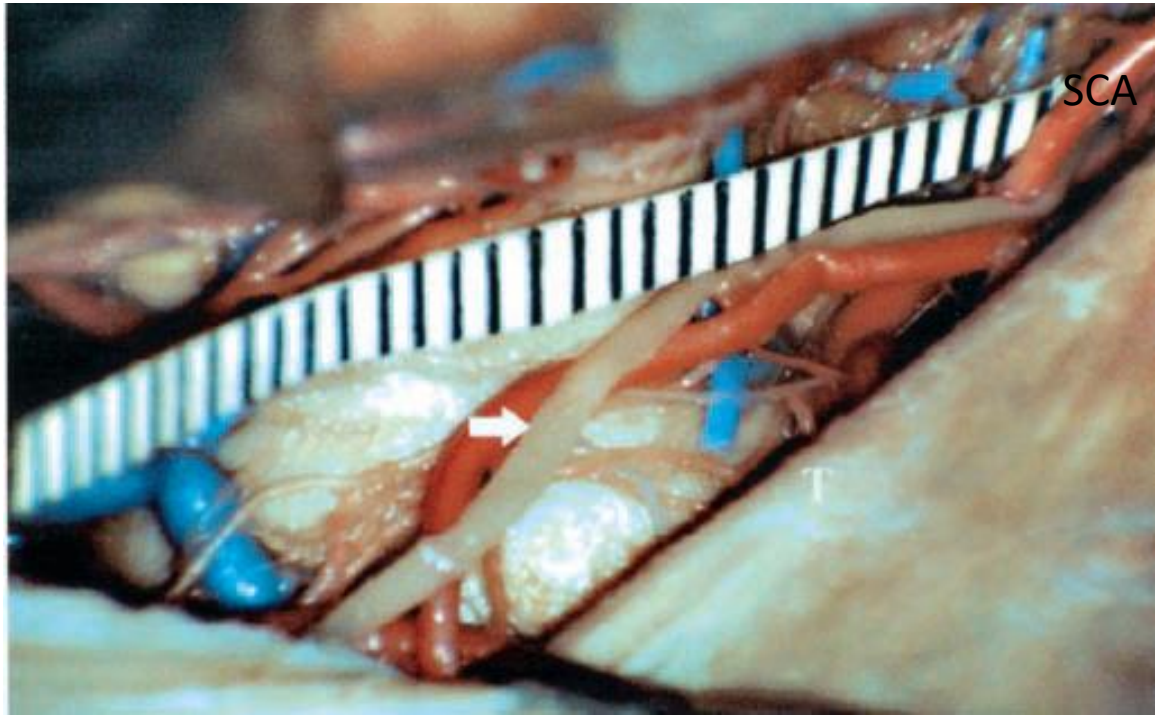
https://beyondthedish.wordpress.com/tag/myelin-sheath/

What happens to cranial nerves exposed to elevated pressure?



Comparison of fluctuating and sustained neural pressure perturbations on axonal transport processes in the optic nerve Balaratnasingam[aa] et al
Brain research Volume 1417, 12 October 2011, Pages 67–76

Which nerve is the most vulnerable to elevated ICP?



Hanson et al
Neurology - Volume 62, Issue 1 (January 2004)

Length of exposure to subarachnoid space:

IV – 33 mm

III – 26 mm

II – 5 to 16 mm

VI – 11 mm

Elevated intracranial pressure and reversible eye-tracking changes detected while viewing a film clip

Radek Kolecki, MS,[1] Vikalpa Dammavalam, BS,[2] Abdullah Bin Zahid, MD,[2] Molly Hubbard, MD,[2] Osamah Choudhry, MD,[1] Marleen Reyes, BA,[1] ByoungJun Han, BS,[1] Tom Wang, BA,[1] Paraskevi Vivian Papas, BS,[1] Aylin Adem, BS,[1] Emily North, BSE,[1] David T. Gilbertson, PhD,[2] Douglas Kondziolka, MD,[1] Jason H. Huang, MD,[3] Paul P. Huang, MD,[1] and Uzma Samadani, MD, PhD[2]

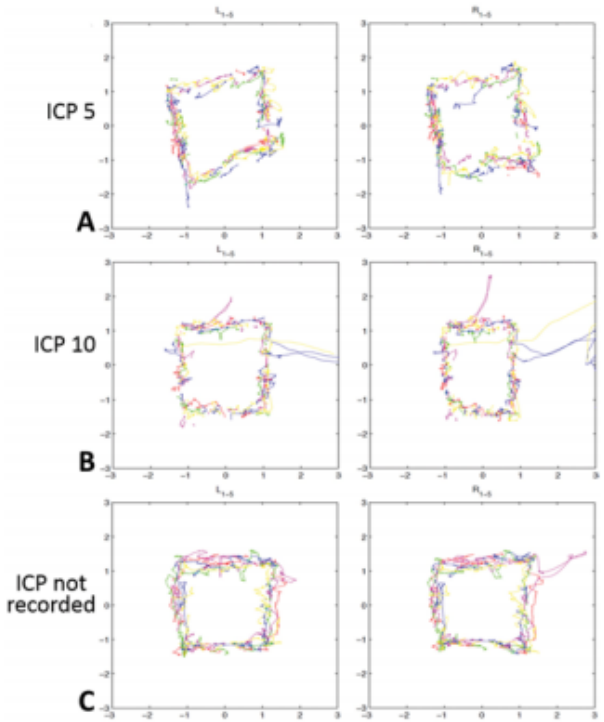


FIG. 2. Case 1. Eye tracking is impaired at elevated ICP and recovers as the patient recovers clinically. Serial eye tracking was performed in a 45-year-old woman who sustained an SAH. **A:** The first eye-tracking session was at an ICP of 5 mm Hg and demonstrated normal metrics. **B:** The second session was at an ICP of 10 mm Hg and tracking was impaired. **C:** The third trial was after clinical and radiographic recovery from hydrocephalus and removal of ventriculostomy. It demonstrated normal metrics. Figure is available in color online only.

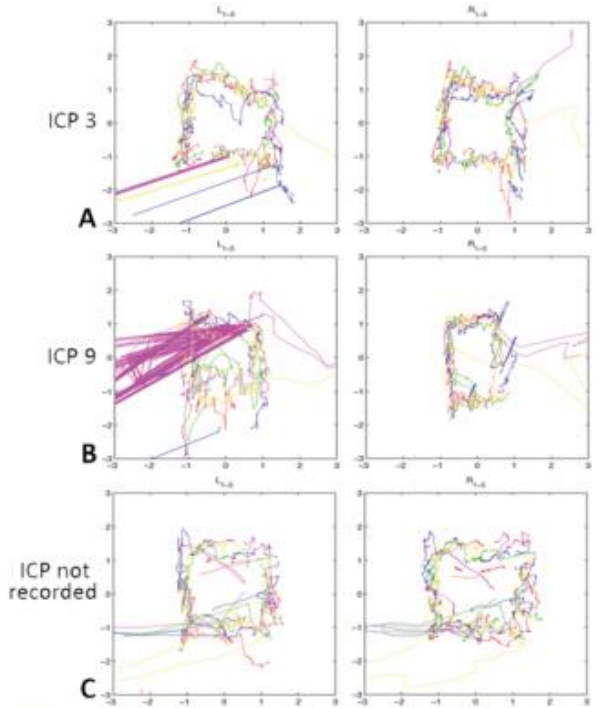
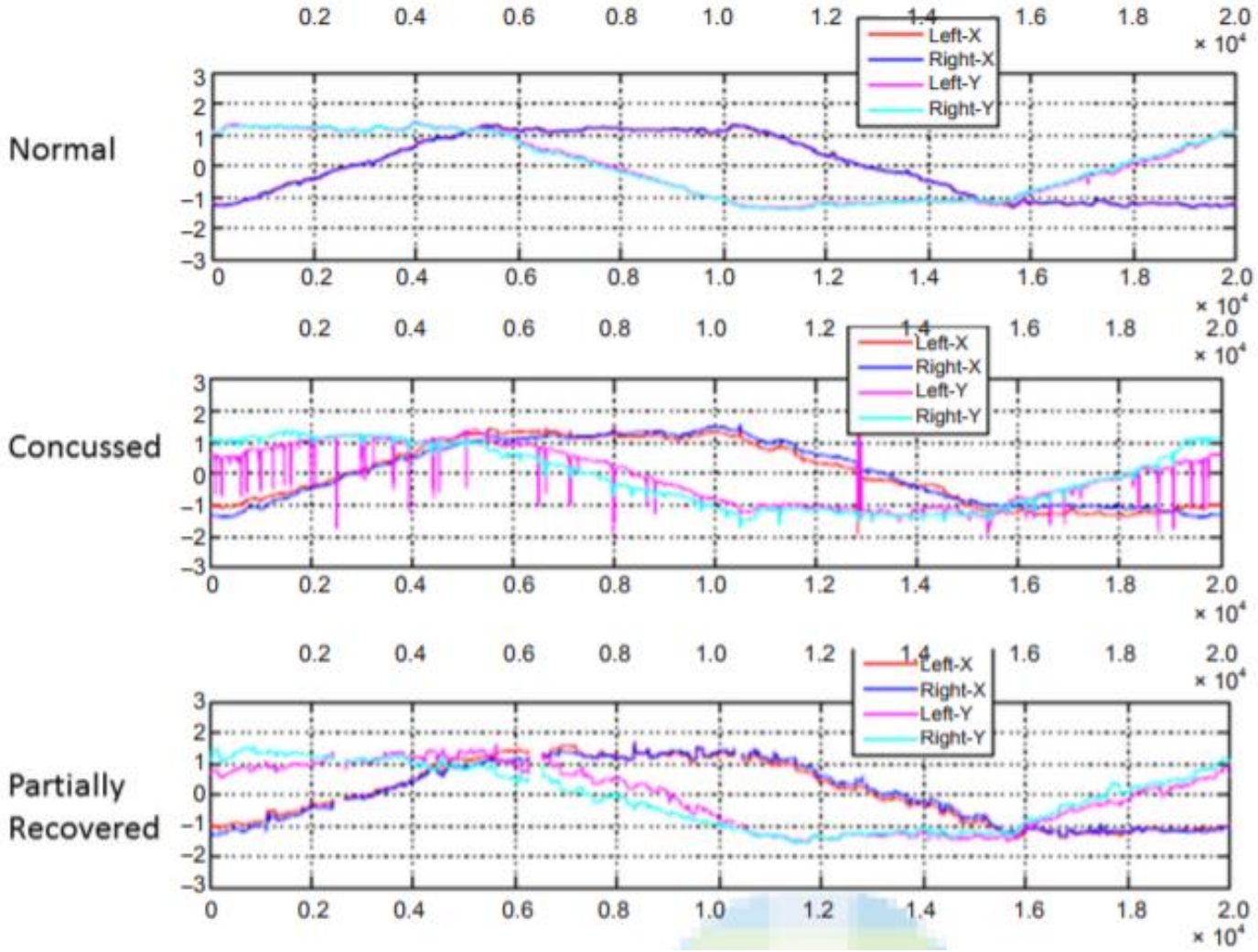


FIG. 3. Case 2. Eye tracking is impaired at elevated ICP and recovers as the patient recovers clinically. Serial eye tracking was performed in a 46-year-old woman who sustained an SAH. **A:** The first eye-tracking session was performed at an ICP of 3 mm Hg and demonstrated normal metrics. **B:** The second trial was at an ICP of 9 mm Hg and tracking was impaired. **C:** The third trial was performed after placement of a shunt to treat hydrocephalus and resolution of clinical symptoms. It demonstrated normal metrics. Figure is available in color online only.

Eye Tracking as an Algorithmic Diagnostic

NEURAL REGENERATION RESEARCH
August 2015, Volume 10, Issue 8
www.nrronline.org

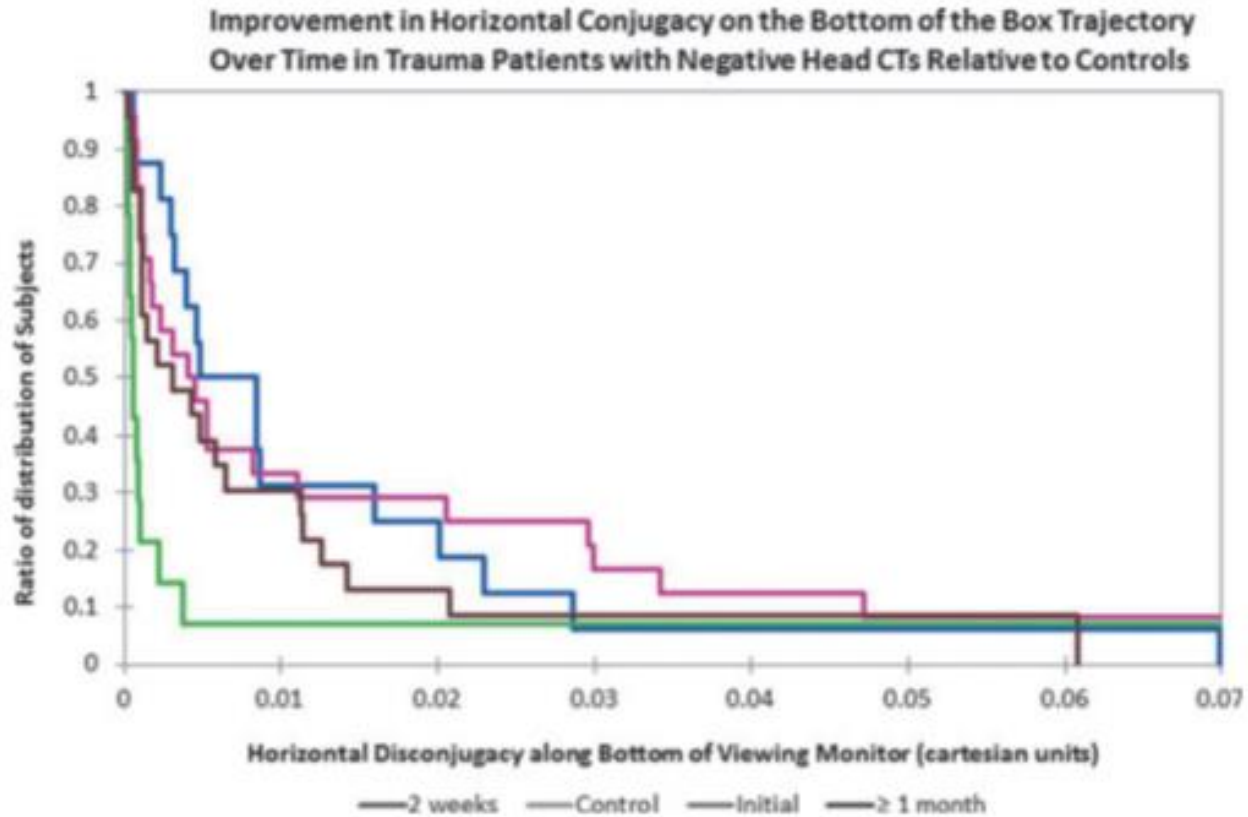


JOURNAL OF NEUROTRAUMA 32:548–556 (April 15, 2015)

DOI: 10.1089/neu.2014.3687

Eye Tracking Detects Disconjugate Eye Movements Associated with Structural Traumatic Brain Injury and Concussion

Uzma Samadani,[1–3] Robert Ritlop M. Eng,[3] Marleen Reyes,[2,3] Elena Nehrbass,[2,3] Meng Li,[1] Elizabeth Lamm,[3] Julia Schneider,[3] David Shimunov,[3] Maria Sava,[3] Radek Kolecki,[3] Paige Burris,[3] Lindsey Altomare,[3] Talha Mehmood,[3] Theodore Smith,[4] Jason H. Huang,[5] Christopher McStay,[6] S. Rob Todd,[7] Meng Qian,[1] Douglas Kondziolka,[3] Stephen Wall,[6] and Paul Huang[3]



Journal of Child Neurology
1-7

DOI: 10.1177/0883073818789320
journals.sagepub.com/home/jcn
SAGE

Objective Eye Tracking Deficits Following Concussion for Youth Seen in a Sports Medicine Setting

David R. Howell, PhD, ATC[1,2,3], Anna N. Brilliant, BS[3,4], Eileen P. Storey, AB[5], Olivia E. Podolak, MD[5], William P. Meehan III, MD[3,4,6], and Christina L. Master, MD, CAQSM[5,7]

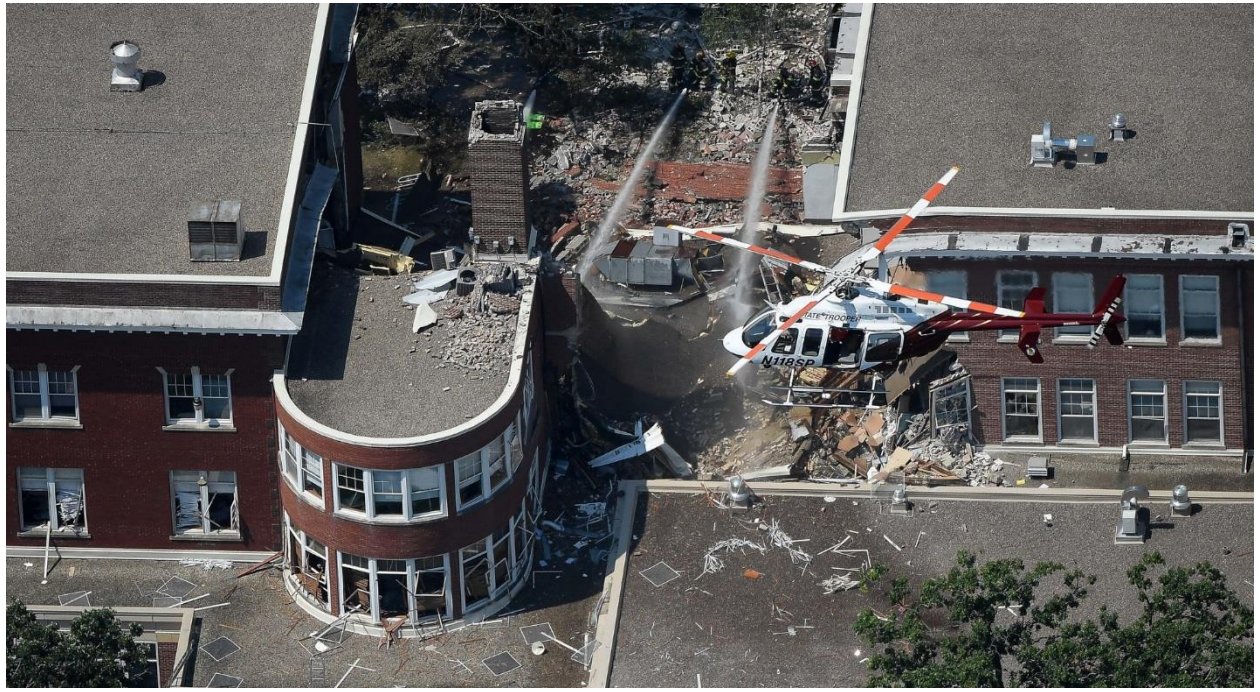
Abstract

Quantification of visual deficits may help to identify dysfunction following concussion. We evaluated eye-tracking measurements among adolescents within 10 days of concussion and healthy control participants. Patients who reported to 2 tertiary care sport concussion clinics within 10 days of concussion completed an objective eye tracking assessment. Seventy-nine participants completed the study, 44 with concussion (mean age = 14.1 ± 2.2 years, 39% female) and 35 controls (mean age = 14.3 ± 2.4 years, 57% female). Right eye skew along the bottom of the screen was significantly higher for the concussion group compared to controls (median = 0.022 [interquartile range = –0.263, 0.482] vs 0.377 [interquartile range = –0.574, –0.031]; $P = .002$), but not the left eye. Among the variables investigated, right eye skew was altered for adolescents with a concussion. Visual function is an important component in the postconcussion evaluation, and identifying deficits soon after injury may allow for earlier specialist referral and intervention.

Keywords

pediatric, adolescent, mild traumatic brain injury, eye tracking, vision

Received May 22, 2018. Accepted for publication June 25, 2018.



2 fatalities

7 patients admitted to the hospital

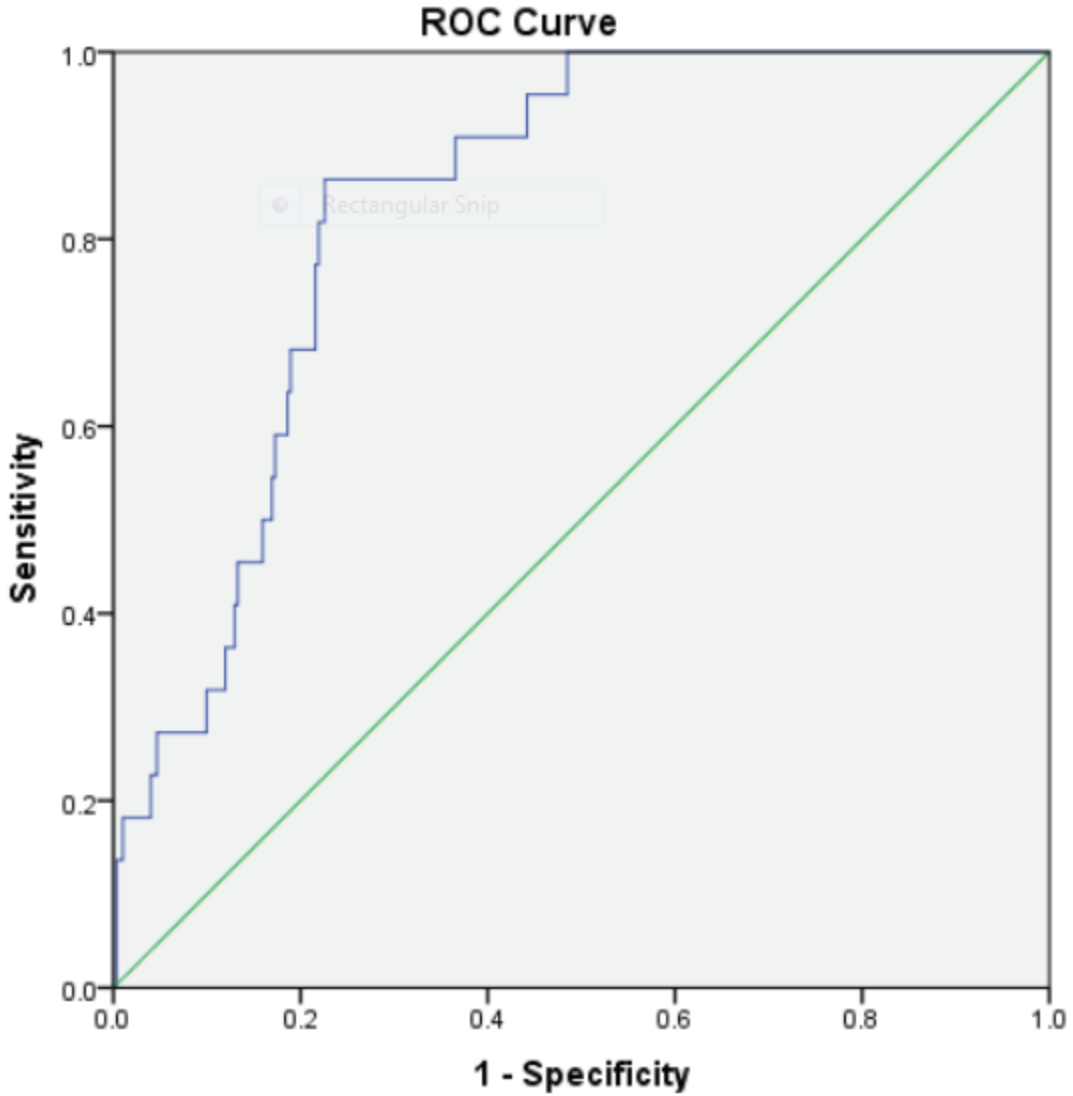
36 exposed survivors evaluated in the lab (tracking and SCAT3)

age (mean±sd)=35.6±17.5

range 13-70 years

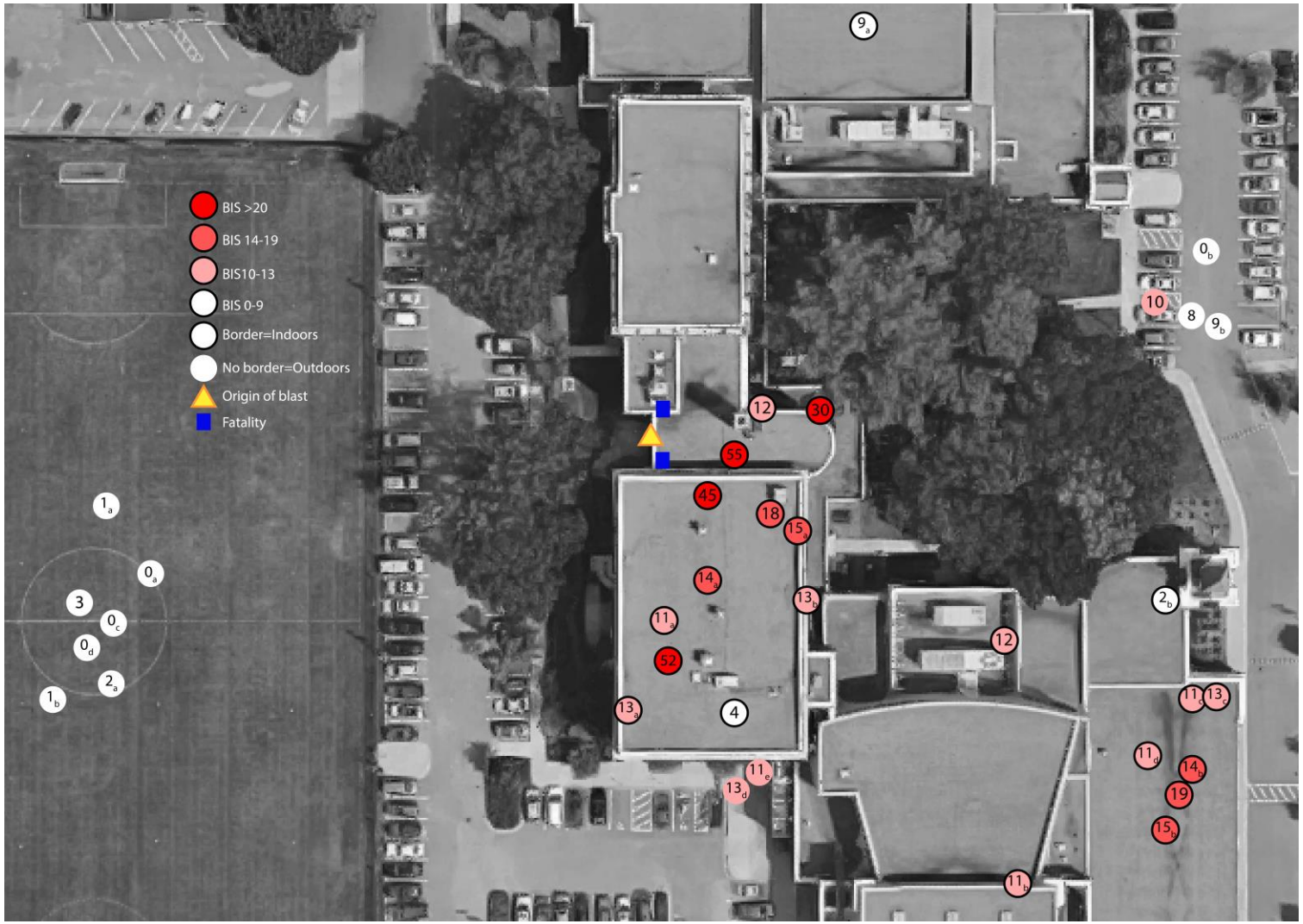
23 females

Eye tracking distinguishes between individuals exposed to blast and age matched controls



5 metrics significantly different between survivors and age/gender matched controls

AUC of 0.835 (95% C.I. = 0.773 to 0.897; FIG. 1), sensitivity of 86.4% and specificity of 77.4% to discriminate between blast patients and controls.



BIS also correlated with distance from the epicenter of the blast
spearman correlation=0.731; pvalue<.001

Concussion the obvious first indication

Included Group-wise demographic

	Concussion	Control	*p*-value
Sample size	135	665	-
Age	32.73 (18.30)	25.48 (12.86)	< 0.001
Sex	73% male	63% male	0.020
Symptom score (sss)	34.77 (31.56)	5.27 (8.81)	< 0.001

left.widthmean. 6th nerve palsy; elevated intracranial pressure and/or infratentorial mass effect

left.skewRit. 3rd nerve palsy; elevated intracranial pressure and/or supratentorial mass effect

left.varYbot

right.meanYlefall

right.varXritall

right.distmedianRit

right.blinklengthmedian 7th nerve palsy; elevated intracranial pressure and/or infratentorial mass effect

left.meanPathDeparture

left.saccadetravelXmean

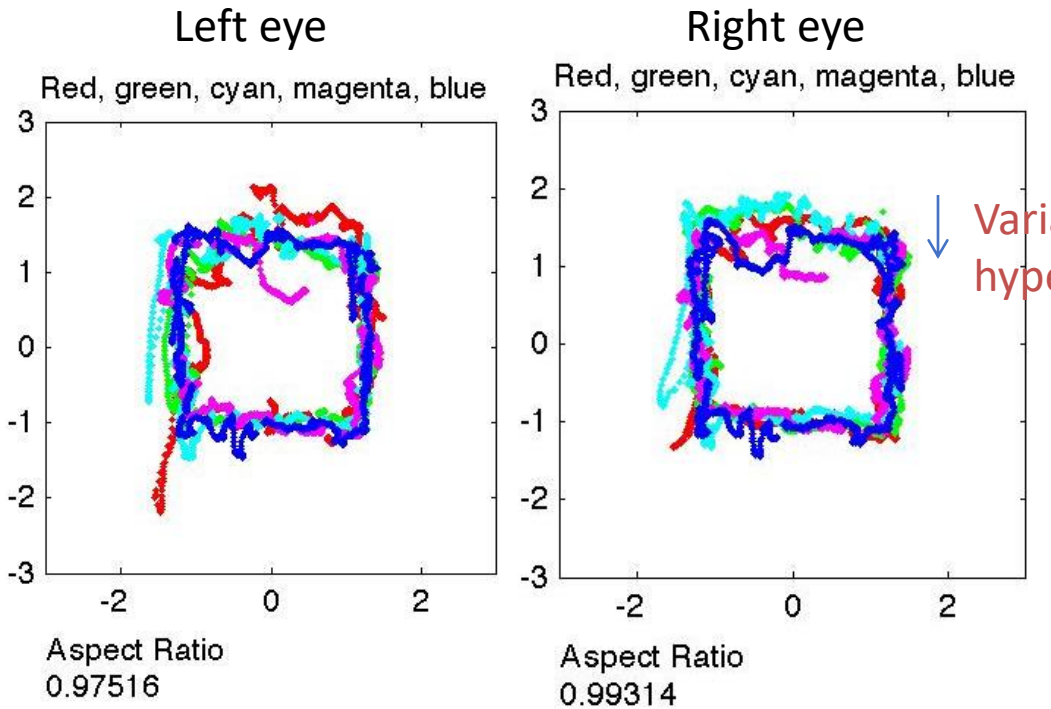
right.saccadesperminute

left.pupilsizemean. 3rd nerve palsy; elevated intracranial pressure and/or supratentorial mass effect

conj.varAspect. informs regarding asymmetric supra or infratentorial mass effect between the right and left brain

conj.blinkorphanratio 5th and 7th nerve palsies (opposite eyes); elevated intracranial pressure and/or infratentorial mass effect

Area =
Height x width
III x VI – informs regarding ICP, mass effect



Height =
Cranial nerve III
Supratentorial
Mass effect

Variability =
hypermetric saccades

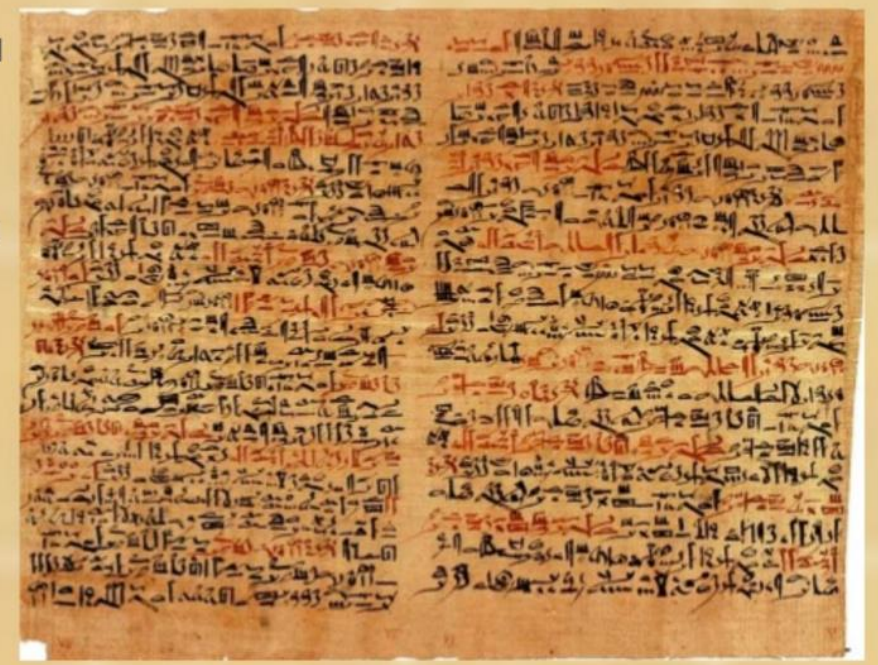
BIS = blast injury

Width =
Cranial nerve VI
Infratentorial
Mass effect – (ICP)

Velocity
(right eye alone or right vs left) =
Convergence Insufficiency

Edwin Smith

- Edwin Smith kept the ancient treatise
- In 1905, Mr Smith's daughter donated the artefact to New York Historical Society
- The medical treatise was written around 1700 B.C., but most of the information based on texts written around .3000B.C



An update on diagnostic and prognostic biomarkers for traumatic brain injury

Kevin K. Wang[1], Zhihui Yang[1], Tian Zhu[1], Yuan Shi[2], Richard Rubenstein[3], J. Adrian Tyndall[4], and Geoff T. Manley[5,6]

Journal
Expert Review of Molecular Diagnostics
Volume 18, 2018 - Issue 2

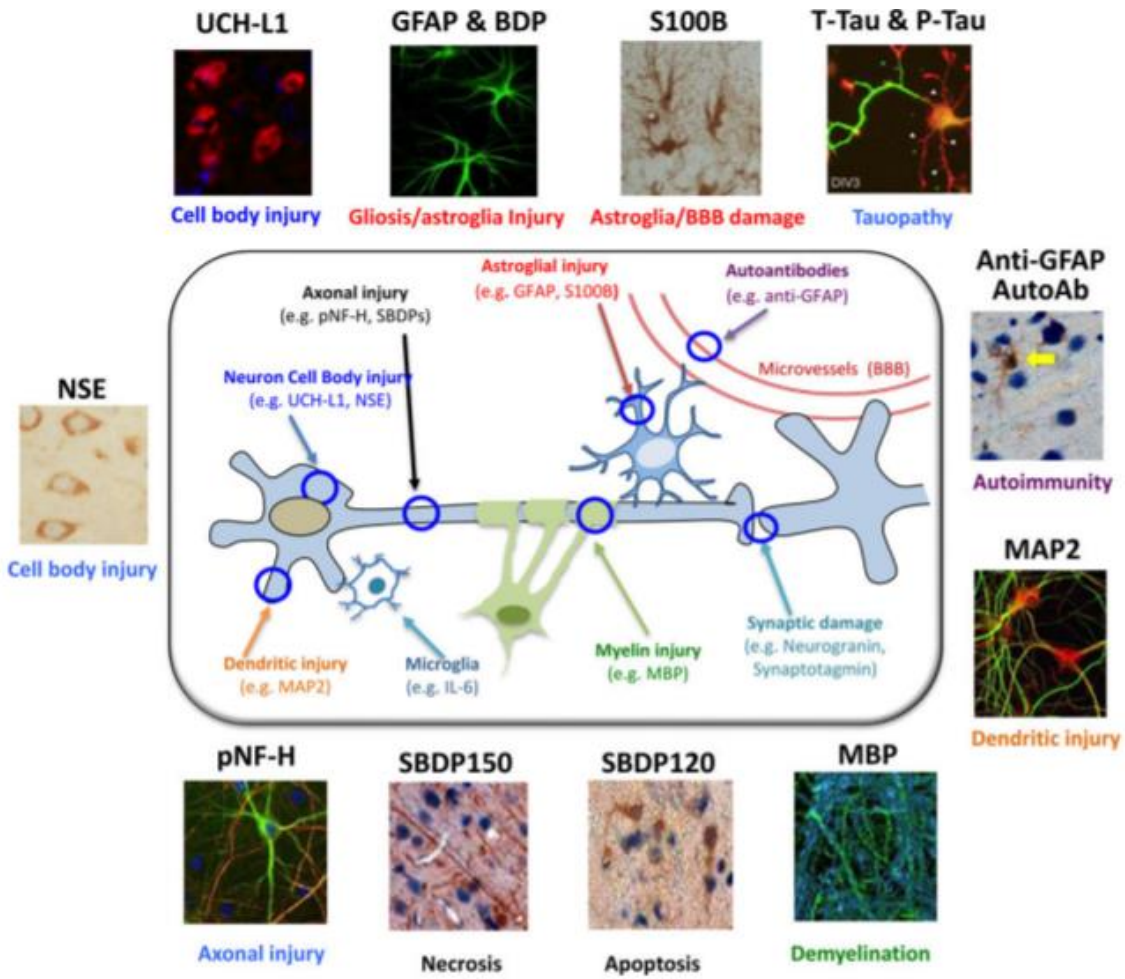


Figure 1. Graphic representation of major TBI protein biomarkers linked to different pathophysiologic processes in TBI.
These processes thus far include axonal injury, dendritic injury, neuronal cell body injury, demyelination, synaptic injury and astroglia injury and microglia responses. Cellular and subcellular localization of representative TBI biomarkers are also shown with immunocytochemical staining images (based on mouse brain data).

An update on diagnostic and prognostic biomarkers for traumatic brain injury

Kevin K. Wang[1], Zhihui Yang[1], Tian Zhu[1], Yuan Shi[2], Richard Rubenstein[3], J. Adrian Tyndall[4], and Geoff T. Manley[5,6]

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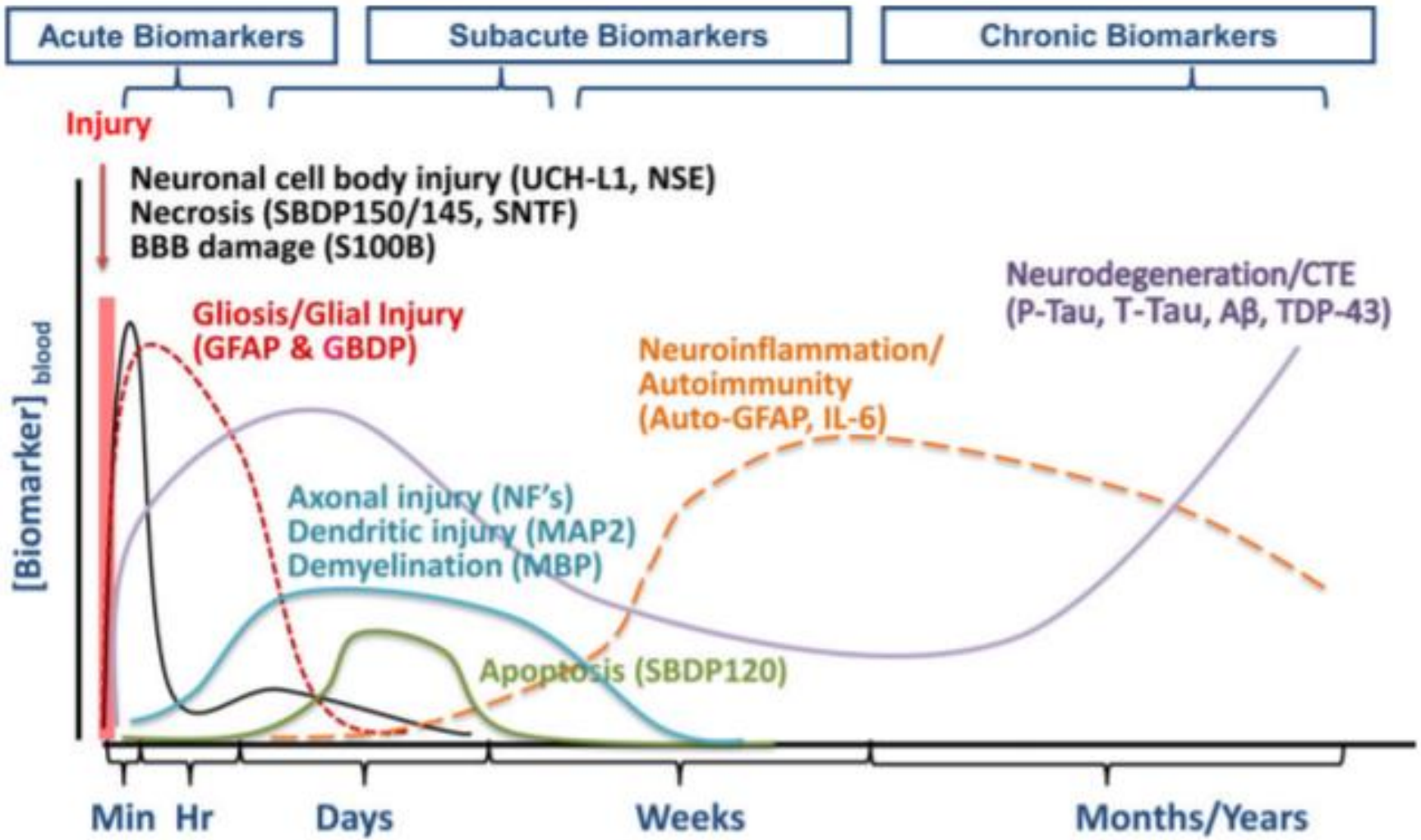
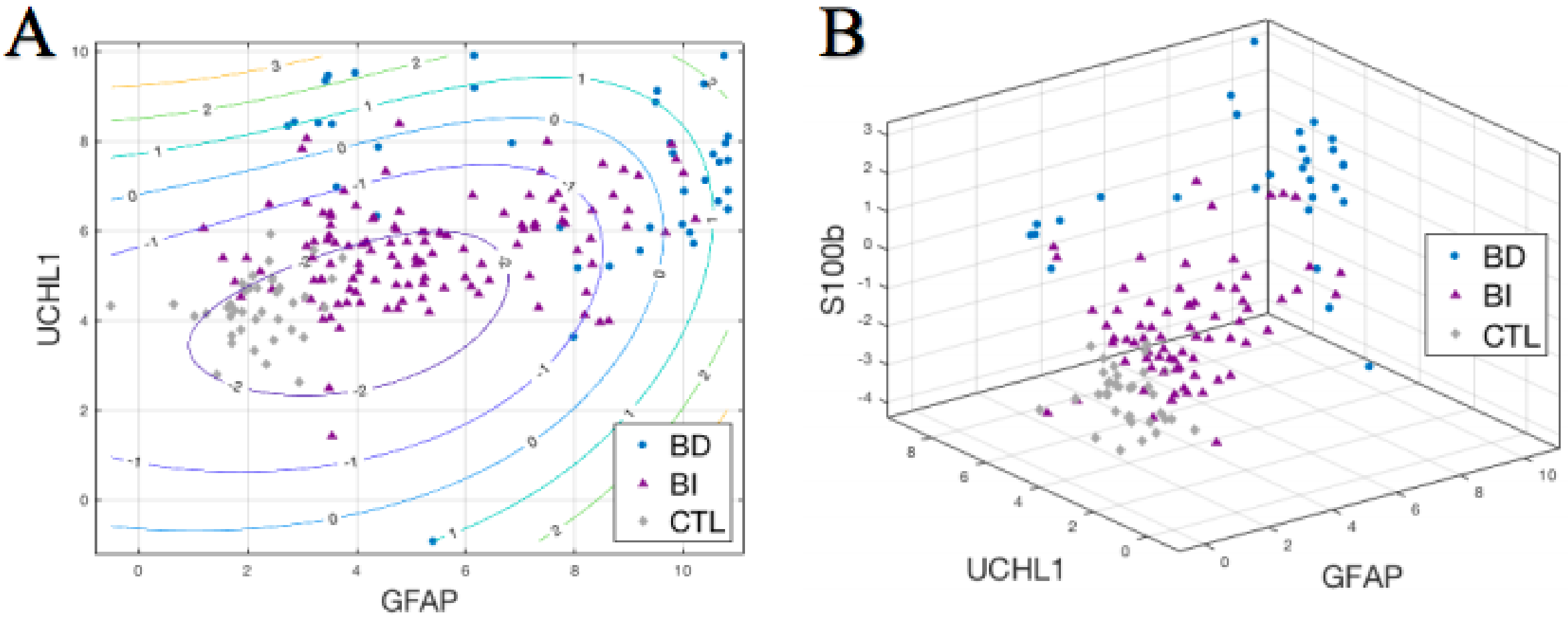
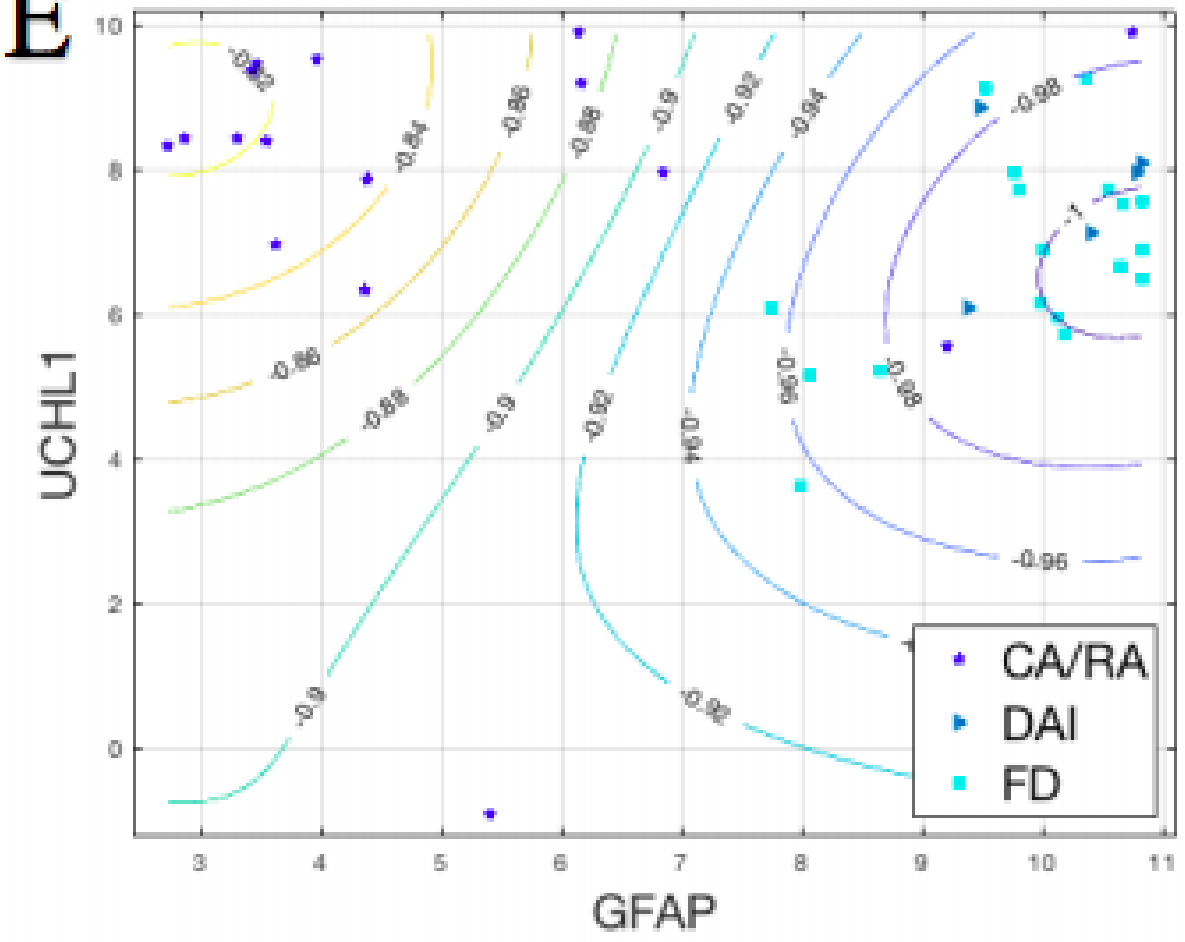


Serum markers differentiate between brain dead, brain injured, and control subjects

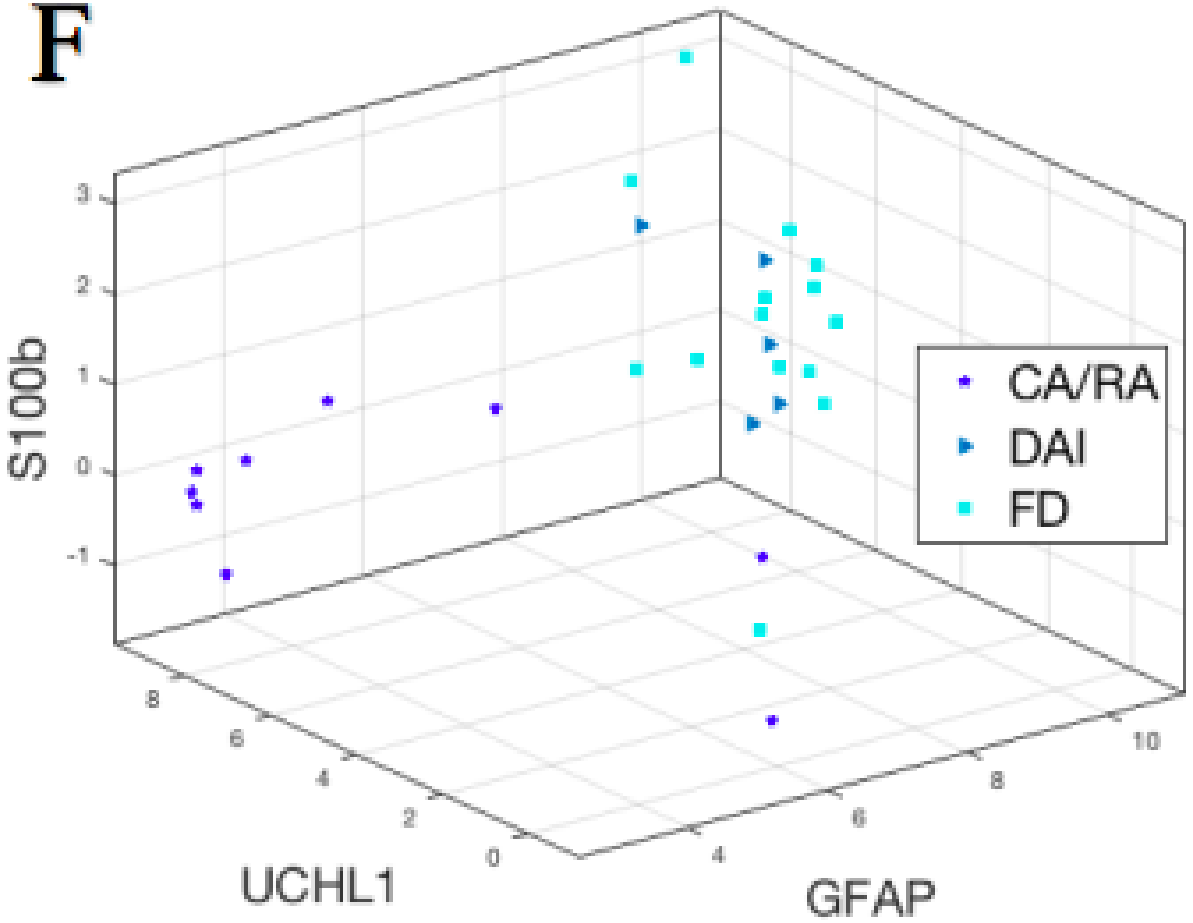


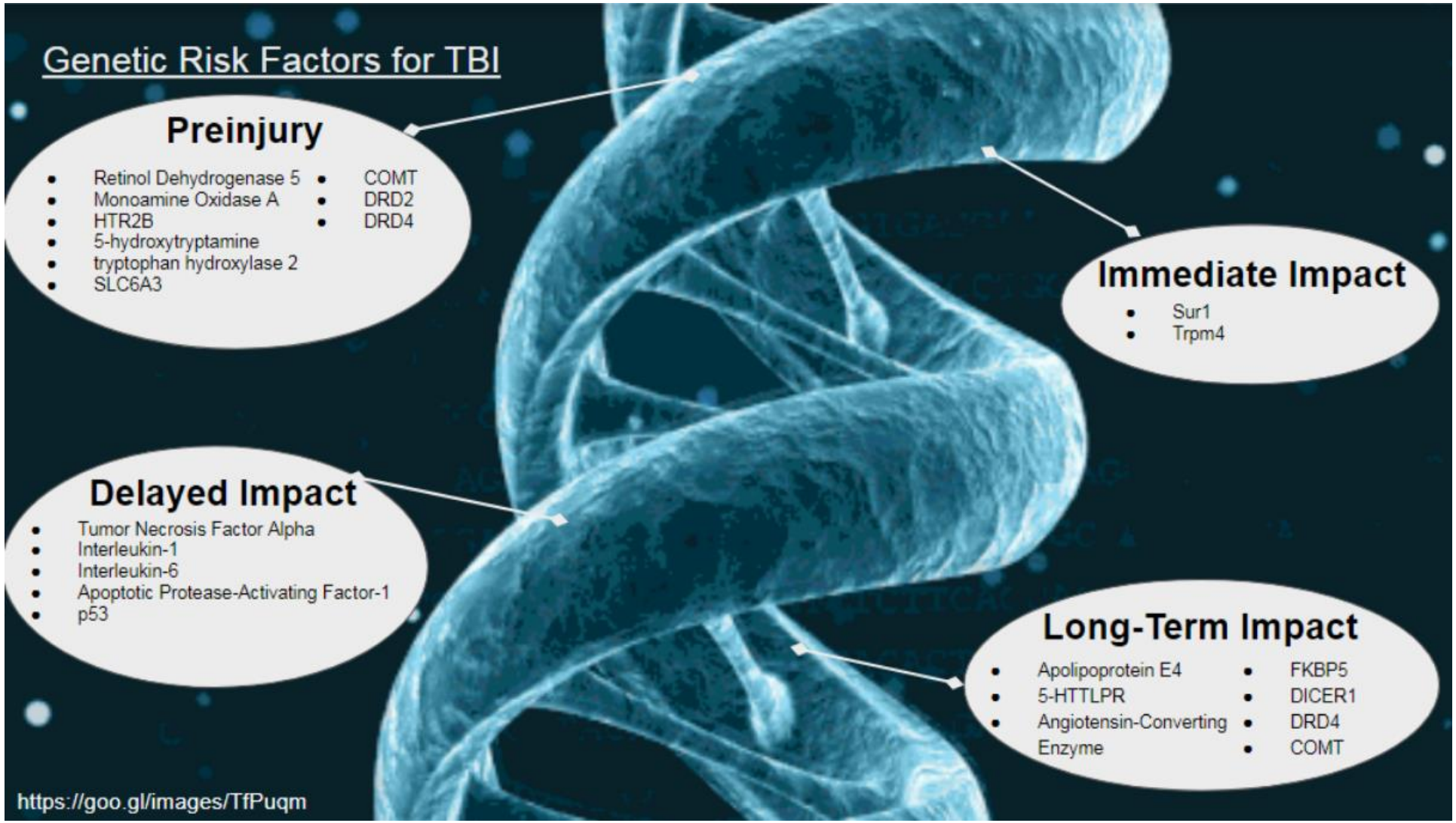
Serum markers differentiate between anoxic/hypoxic brain death and high velocity/blunt impact trauma brain death

E



F




Genetic Risk Factors for TBI
Preinjury
Retinol Dehydrogenase 5
Monoamine Oxidase A
HTR2B
5-hydroxytryptamine
tryptophan hydroxylase 2
SLC6A3
COMT
DRD2
DRD4
Immediate Impact
Sur1
Trpm4
Delayed Impact
Tumor Necrosis Factor Alpha
Interleukin-1
Interleukin-6
Apoptotic Protease-Activating Factor-1
p53
Long-Term Impact
Apolipoprotein E4
5-HTTLPR
Angiotensin-Converting Enzyme
FKBP5
DICER1
DRD4
COMT
https://goo.gl/images/TfPuqm

BLAST-CT

DOI 10.5281/zenodo.3746088

Brain **L**esion **A**nalysis and **S**egmentation **T**ool for **C**omputed **T**omography

This repository provides our deep learning image segmentation tool for traumatic brain injuries in 3D CT scans.

Please consider citing our article when using our software:

> Monteiro M, Newcombe VFJ, Mathieu F, Adatia K, Kamnitsas K, Ferrante E, Das T, Whitehouse D, Rueckert D, Menon DK, Glocker B. **Multi-class semantic segmentation and quantification of traumatic brain injury lesions on head CT using deep learning – an algorithm development and multi-centre validation study**. *The Lancet Digital Health* (2020). Monteiro and Newcombe are equal first authors. Menon and Glocker are equal senior authors.

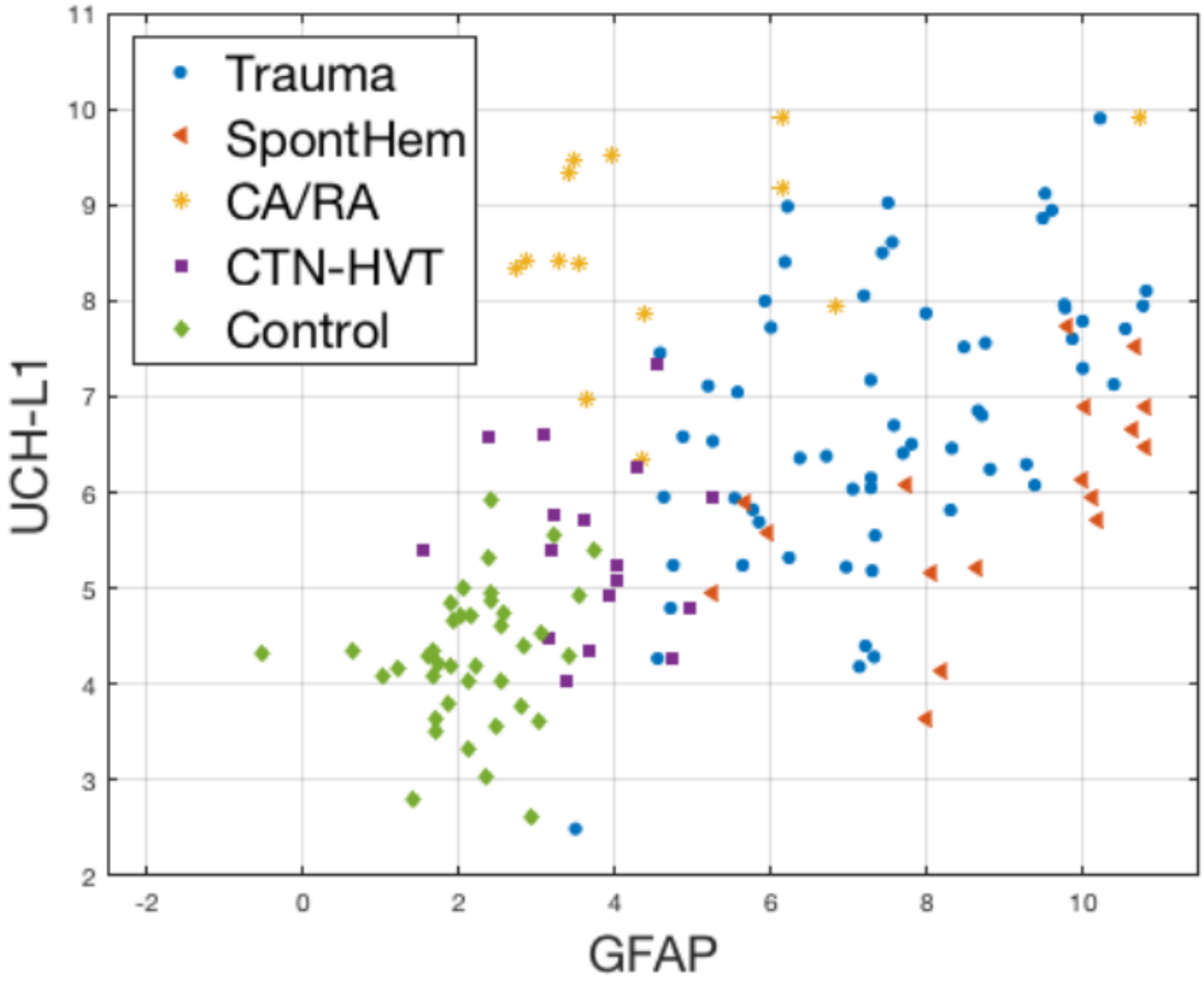

Trauma
SpontHem
CA/RA
CTN-HVT
Control
UCH-L1
GFAP
11
10
9
8
7
6
5
4
3
2
-2
0
2
4
6
8
10

Table 4 – SVM prediction accuracy from two serum biomarkers (GFAP and UCH-L1) and inclusion of multimodal prediction with Blast-CT output.

Comparison Groups	**GFAP, UCH-L1**		**GFAP, UCH-L1, Blast-CT**	
n = 203 samples	AUC	AP	AUC	AP
BD vs. CTL, NT, CTn, CTp	0·95	0·85	0·95	0·86
BD vs. NT, CTn, CTp	0·94	0·85	0·95	0·88
BD vs. NT, CTp	0·91	0·88	0·93	0·90
CA vs. FD, DAI	0·96	0·96	0·99	0·98

Table 4 footnotes: Support vector matrix (SVM), Control (CTL), Non trauma (NT), Computed tomography positive (CTp), Computed tomography negative (CTn), Found down (FD), and diffuse axonal injury (DAI), Area under the receiver operator curve (AUC), Average Precision (AP). The right columns of the table includes automated CT analysis using Blast-CT along with SVM serum biomarker determination of prediction accuracy.

Table 5. Classification with SVM based on the combinations of serum biomarkers and CT images [AUC]

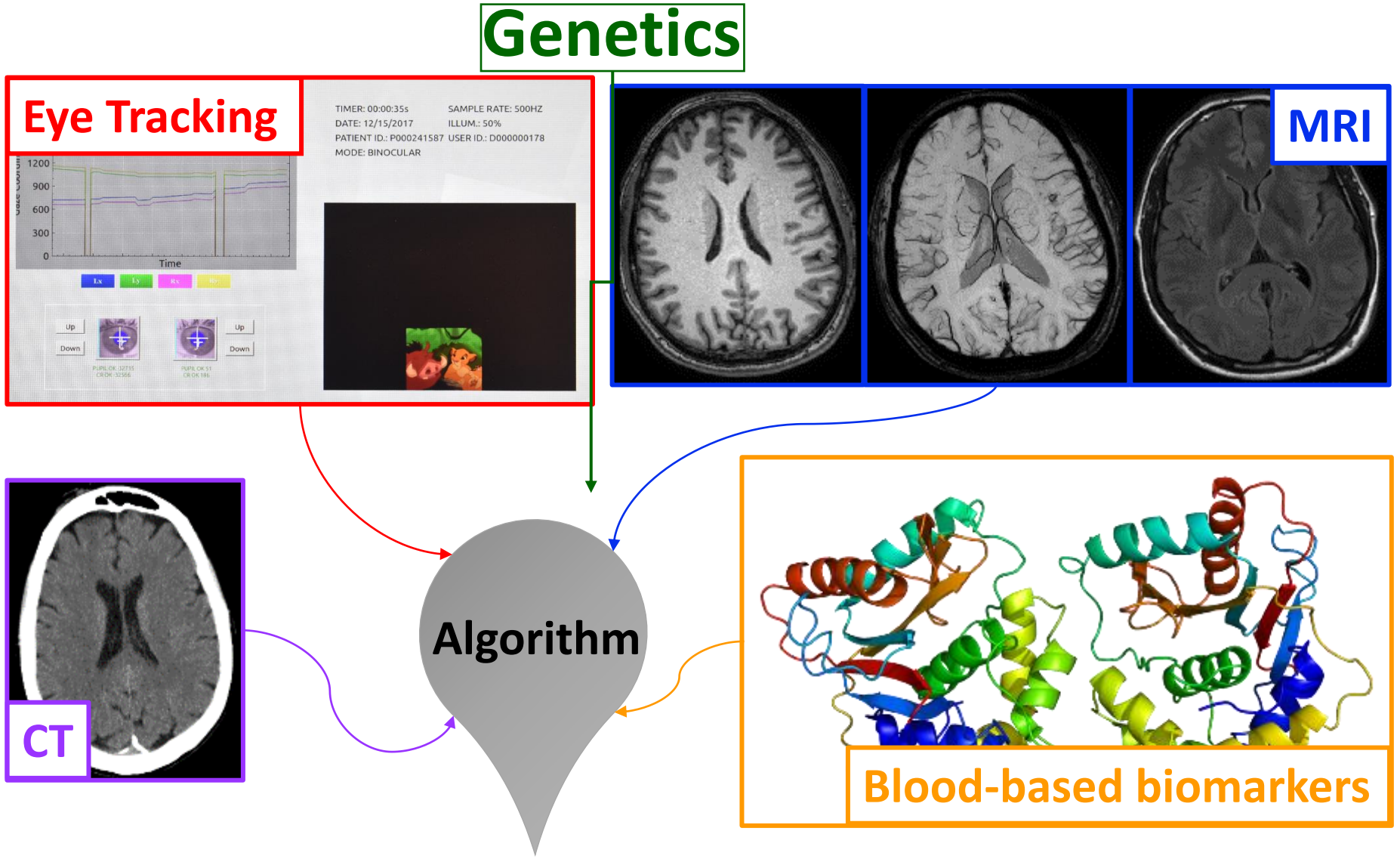
	SpontHem	CA/RA	CTN-HVT	Control
Trauma	0-96	0-99	0-98	1-00
SpontHem	-	1-00	1-00	1-00
CA/RA	-	-	0-98	1-00
CTN-HVT	-	-	-	1-00

Mechanisms for Assessing the Central Nervous System

Physical and psych examination – physiology	fxl heterogeneity, skilled examiner, time, bias
Plain films (xray) – what it looks like	radiation, not much information
EEG – electrical activity	technician, interpreter, time,
Angiography – what it looks like	radiation, not full information, $
EMG/NCS/SSEPS – assesses integrity	painful, technician, time,
CT scan – what it looks like	radiation, technician, time, $
TCDs, orbital, transcutaneous flow – blood flow.	technician, arbitrary #
MRI scan - what it looks like, some fx	time, technician, claustrophobia/instability, $$
ICP /licox monitoring – pressure, brain O_2	risk of devastating hemorrhage, arbitrary #, $$
Serum markers – molecular biology	time dep't requires blood, lab
Uncalibrated eye movement tracking	patient needs to be able to open eyes
Pupillometry	less conscious patient

- **fully automatable, objective, agnostic to language/culture/education, non-risky, non-radiation exposing, non-invasive, potentially remote**
- **The only method (other than examination) that is physiologic.**

Hierarchical Approach to Classification of Problem (is an examination cost-effective?!)



Molecule: https://commons.wikimedia.org/wiki/File:Protein_UCHL1_PDB_2etl.png

Students, Residents, LabFolk and Post Docs:

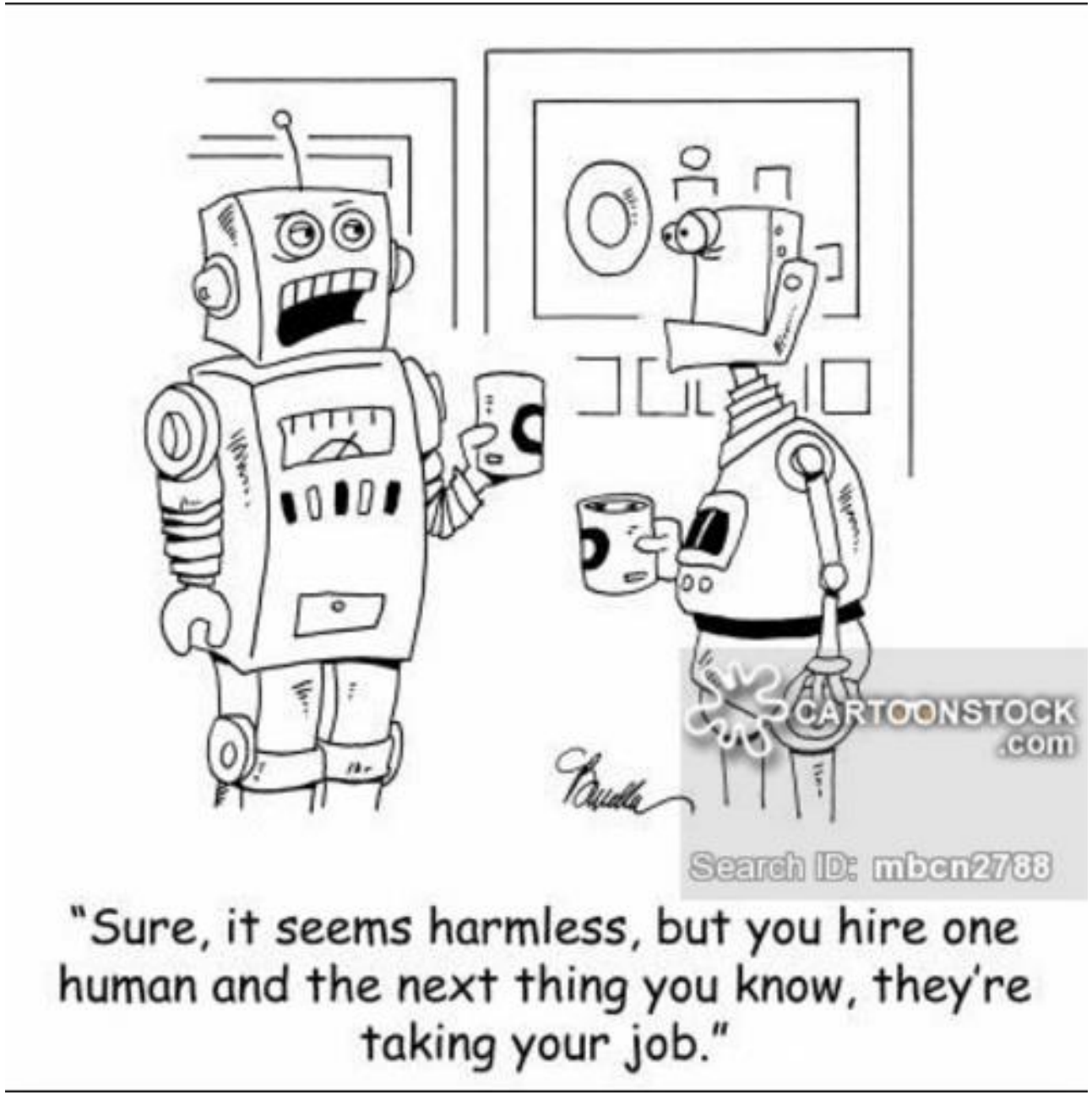
Abdullah BinZahid	David Balser
Maggie Mahan	Mohit Uppal
Caleb Hoover	Shivani Venkatesh
Dan Rafter	Christina Smith
Molly Hubbard	Tabitha Chettupally
David Darrow	Kriti Prasad
Aliya Ali	Tessneem Abdallah
Joe Toninato	Marcella Bravo

Collaborators:
Radiology:
Mark Oswood
Chip Truwit

Computer Science:
Rui Kuang
Zhuliu Li

Path/Lab:
Fred Apple

Trauma:
Chad Richardson



That's All Folks!

Wile E. Coyote created 1948-1963
(note anisocoric and disconjugate gaze)