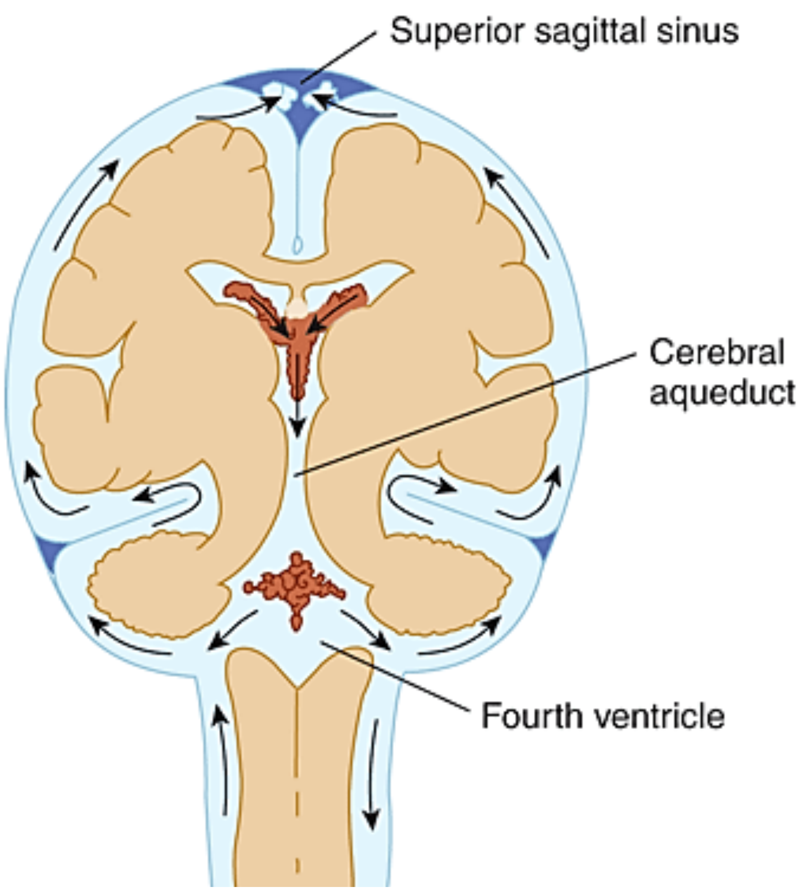
New Tools in NPH



3T
TOMORROW'S TECHNOLOGY TODAY FROM LOS GATOS MRI

Murray A. Solomon, MD
Los Gatos MRI and the Memory Evaluation Center of San Jose

Los Gatos MRI

Financial Disclosures

- Board of Directors with Stock Options: MR Instruments Inc.
- Speakers Bureau:

  Amgen
- In the Past: Paid Speaker for Philips Medical Systems

The Official Party Line……

- NPH is very rare.
- NPH is over-diagnosed.
- The benefits of shunting do not outweigh the risks.
- Shunting improves gait abnormalities but not cognitive deficits.
- Shunting has a high complication rate limiting its benefits.

Neurology®

Neurology 1992;42;54

Shunting normal-pressure hydrocephalus: Do the benefits outweigh the risks?

A multicenter study and literature review

J. Vanneste, MD; P. Augustijn, MD; C. Dirven, MD; W.F. Tan, MD; and Z.D. Goedhart, MD

Article abstract—We performed a multicenter retrospective study in 166 consecutive patients shunted for presumed normal-pressure hydrocephalus (NPH) in the four neurosurgical departments of Amsterdam. Overall improvement occurred in 36%, substantial improvement in 21%. In the subgroup of idiopathic NPH (N = 127), marked improvement was only 15%. The incidence of shunt-responsive NPH in our area was 2.2/million/year. The rate of severe and moderate shunt-related complications was 28%, leading to death or severe residual morbidity in 7%. The substantial benefit/serious harm ratio in the whole group was only three (21%/7%), decreasing to 1.7 in idiopathic NPH. By excluding patients at high surgical risk, this ratio might have risen to 10 in the whole group and to six in idiopathic NPH. Our experience is much less favorable than that encountered in the literature, reporting overall improvement in 74% and marked improvement in 55% of the shunted patients. We conclude that NPH is probably a very rare and still overdiagnosed syndrome and that the overall morbidity rate for each patient demonstrating meaningful improvement is high.

NEUROLOGY 1992;42:54-59

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Clinical outcome in NPH patients following ventricular shunt surgery

	Responders	Non-responders
Gait	15 (94%)	1
Cognitive	7 (54%)	6
Urinary Incont	9 (70%)	4

Serulle, Y.·Milch, H.·Kirov, I.·Golomb, J. B.·Rusinek, H.·Gonen, O.·George, A. E.

New York University School of Medicine
New York, NY

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Correlation of preoperative brain volumes with cognitive improvement following shunting

Cognitive Improvement	GM	WM	CSF	Vent
Yes	652 ± 71	390 ± 79	658 ± 88	187 ± 15
No	460 ± 51	385 ± 20	658 ± 96	132 ± 11

$P<0.05$

Serulle, Y.·Milch, H.·Kirov, I.·Golomb, J. B.·Rusinek, H.·Gonen, O.·George, A. E.
New York University School of Medicine

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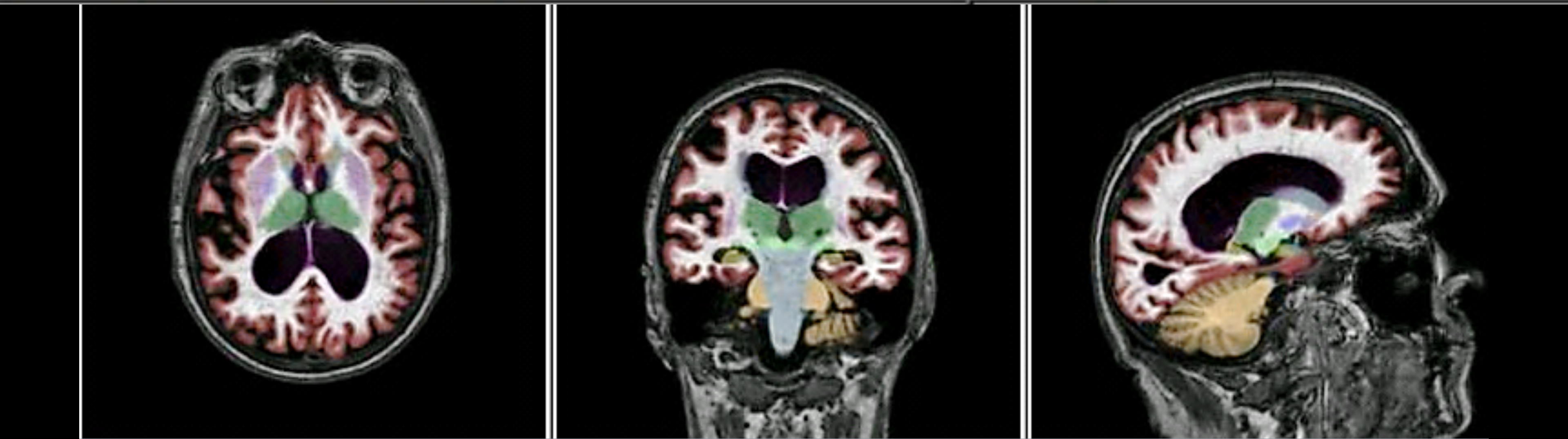
MORPHOMETRY RESULTS



Brain Structure	LH Volume (cm³)	LH Volume (% of ICV)	RH Volume (cm³)	RH Volume (% of ICV)	Asymmetry Index (%)*
Forebrain Parenchyma	471.59	27.93	480.28	28.44	-1.83
Cortical Gray Matter	244.34	14.47	244.81	14.50	-0.19
Lateral Ventricle	68.82	4.08	61.71	3.65	10.90
Inferior Lateral Ventricle	3.47	0.21	2.81	0.17	21.14
Hippocampus	4.16	0.25	4.38	0.26	-5.03
Amygdala	1.73	0.10	1.75	0.10	-1.21
Caudate	4.88	0.29	5.53	0.33	-12.46
Putamen	4.52	0.27	4.48	0.27	0.89
Pallidum	0.79	0.05	1.24	0.07	-44.61
Thalamus	10.29	0.61	8.92	0.53	14.28
Cerebellum	67.22	3.98	68.60	4.06	-2.02

*The Asymmetry Index is defined as the difference between left and right volumes divided by their mean (in percent)

Correlation of preoperative brain volumes with cognitive improvement following shunting

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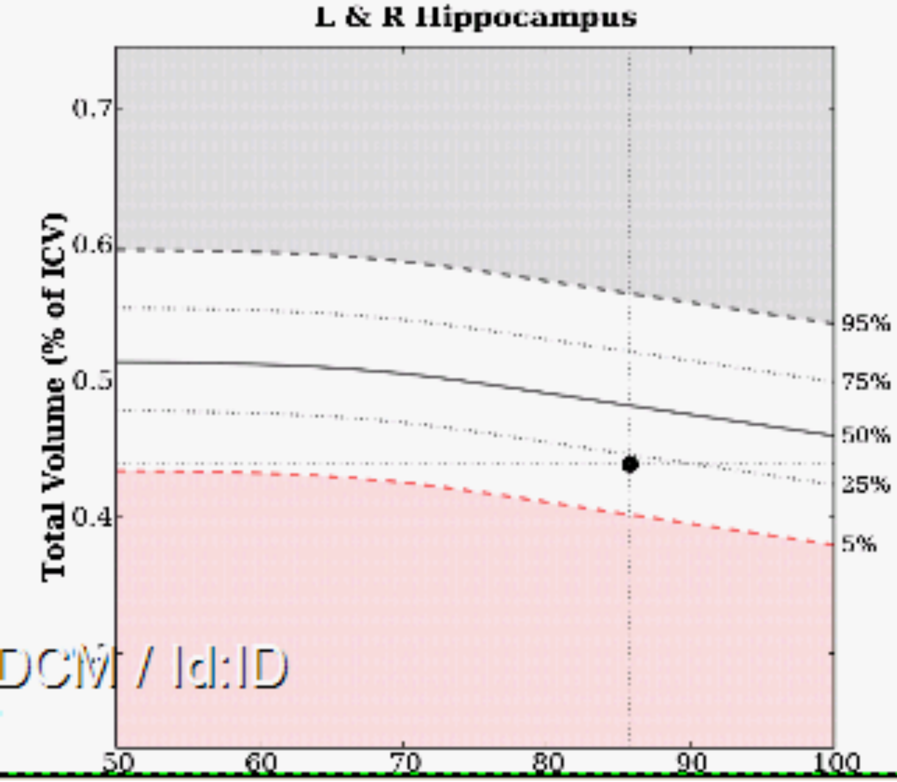
New York University School of Medicine
New York, NY

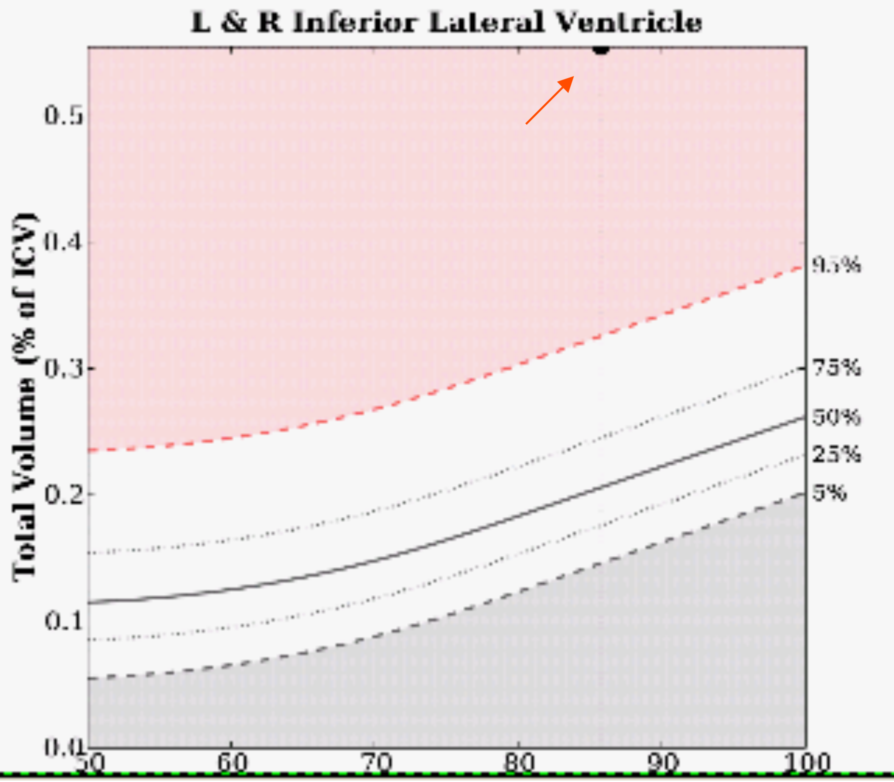
Measuring CSF Volume

Volumetric Brain Volume Measurement is now available clinically.

Brain Structure	Volume (cm³)	% of ICV (5%-95% Normative Percentile*)	Normative Percentile*
Hippocampi	6.34	0.44 (0.40-0.56)	20.43
Lateral Ventricles	118.41	8.20 (1.61-4.69)	**> 99**
Inferior Lateral Ventricles	8.01	0.55 (0.15-0.33)	**> 99**

AGE-MATCHED REFERENCE CHARTS*





Fiber Tracking

Fiber Trak®

FOV: 220

Voxel Size: 2.2 x 2.2 x 2

Slice Thickness: 2mm

Recon Matrix: 128

Sense: Yes

Slices: 60 Transverse

EPI Single Shot

Echoes: 1

Half Fourier: .692

Shortest TR: 7960ms

TE: 60ms

No. of b factors: 2

b factor order: ascend.

Max b factor: 800

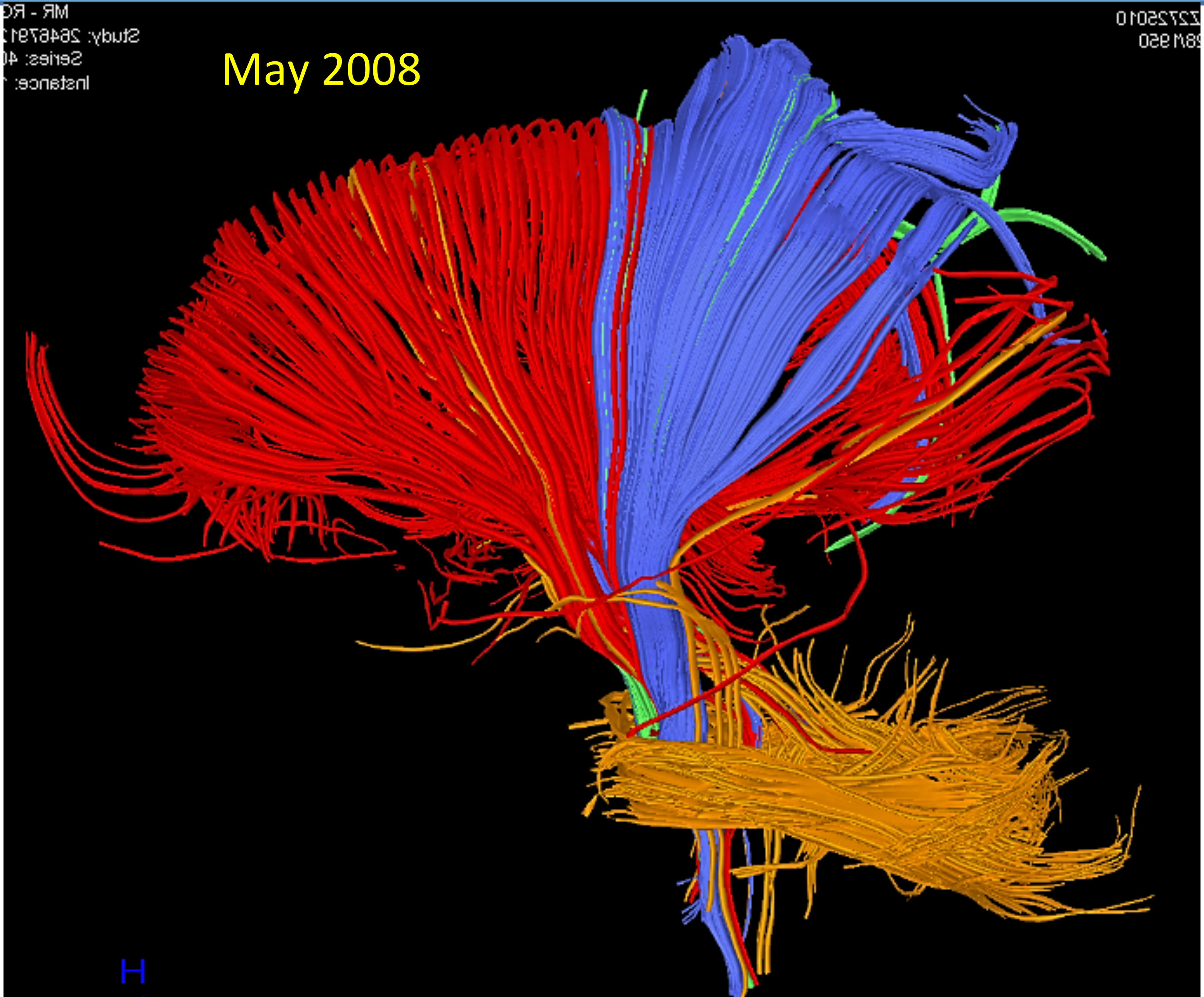
15 Directions

NSA: 1

Acquisition Time: 5:53

Processing Time: 7-10 min

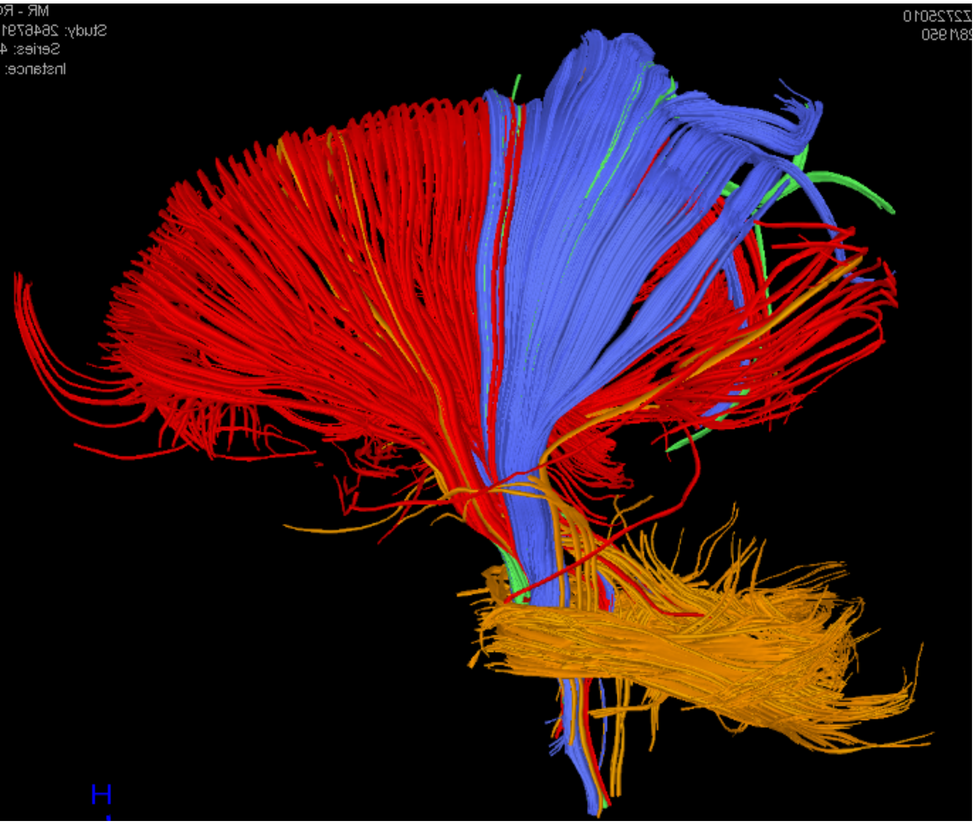
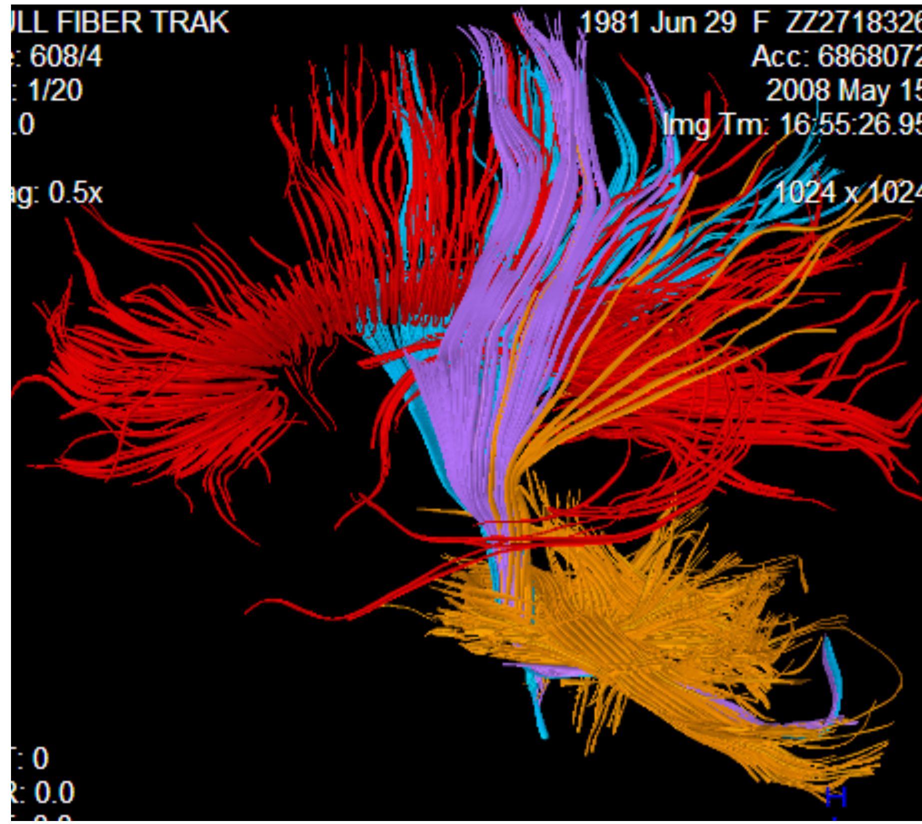
CSF Pressure and CSF Flow



CSF Pressure and CSF Flow

CSF Pressure and CSF Flow

CSF Pressure and CSF Flow

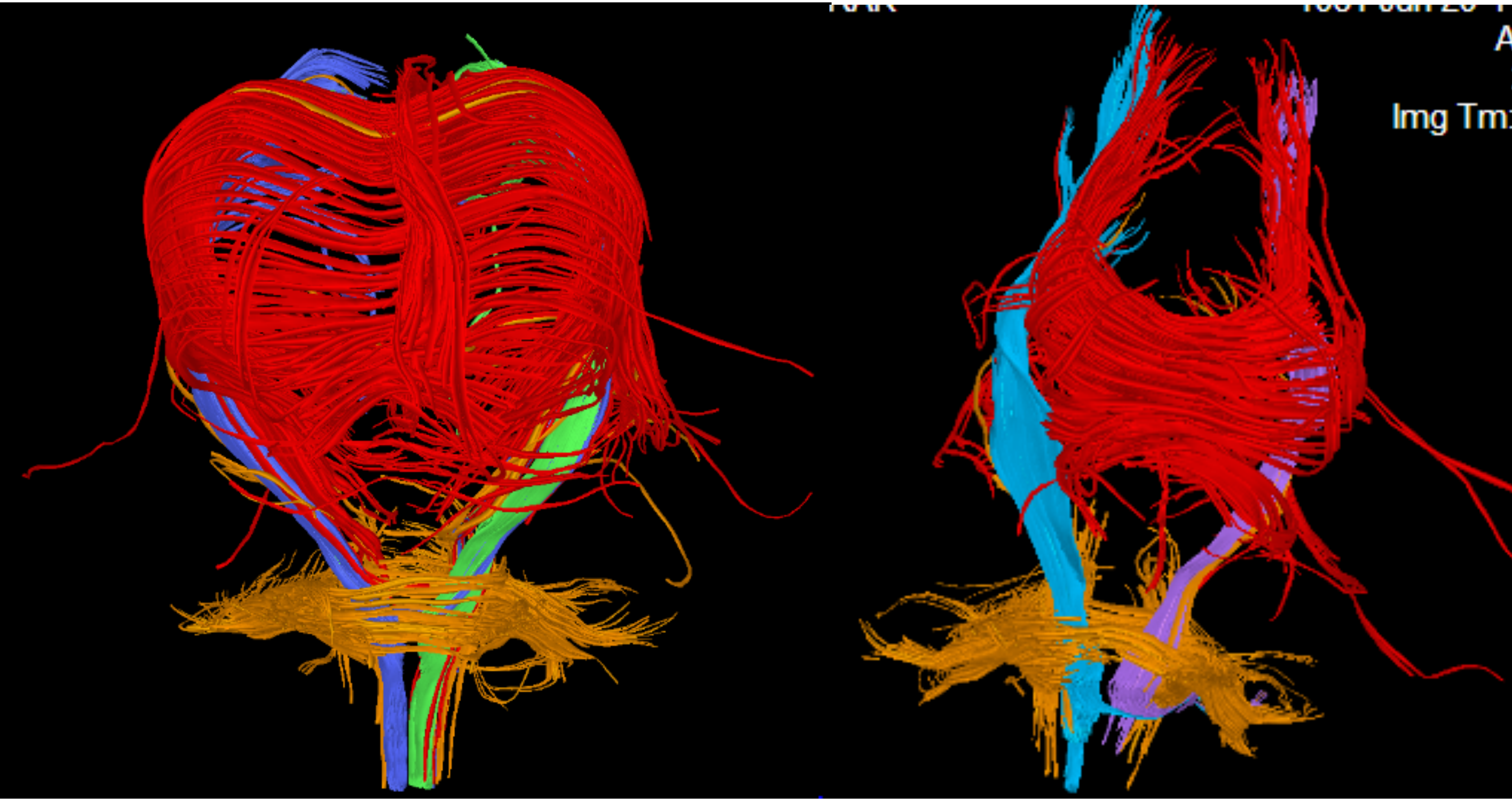
NPH	Normal
	

"I like light, color, luminosity. I like things full of color and vibrant"

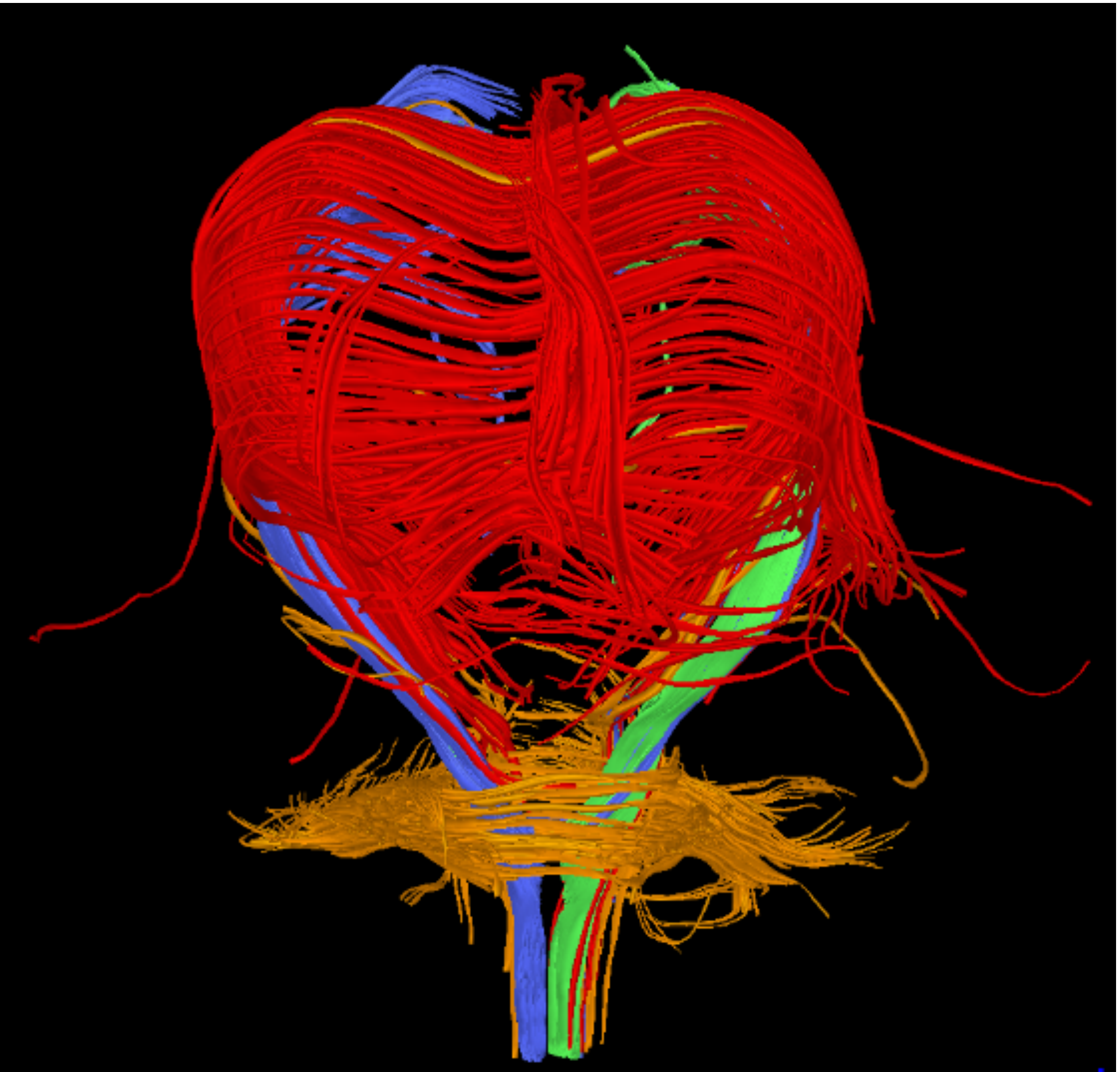
Oscar de la Renta

CSF Pressure and CSF Flow

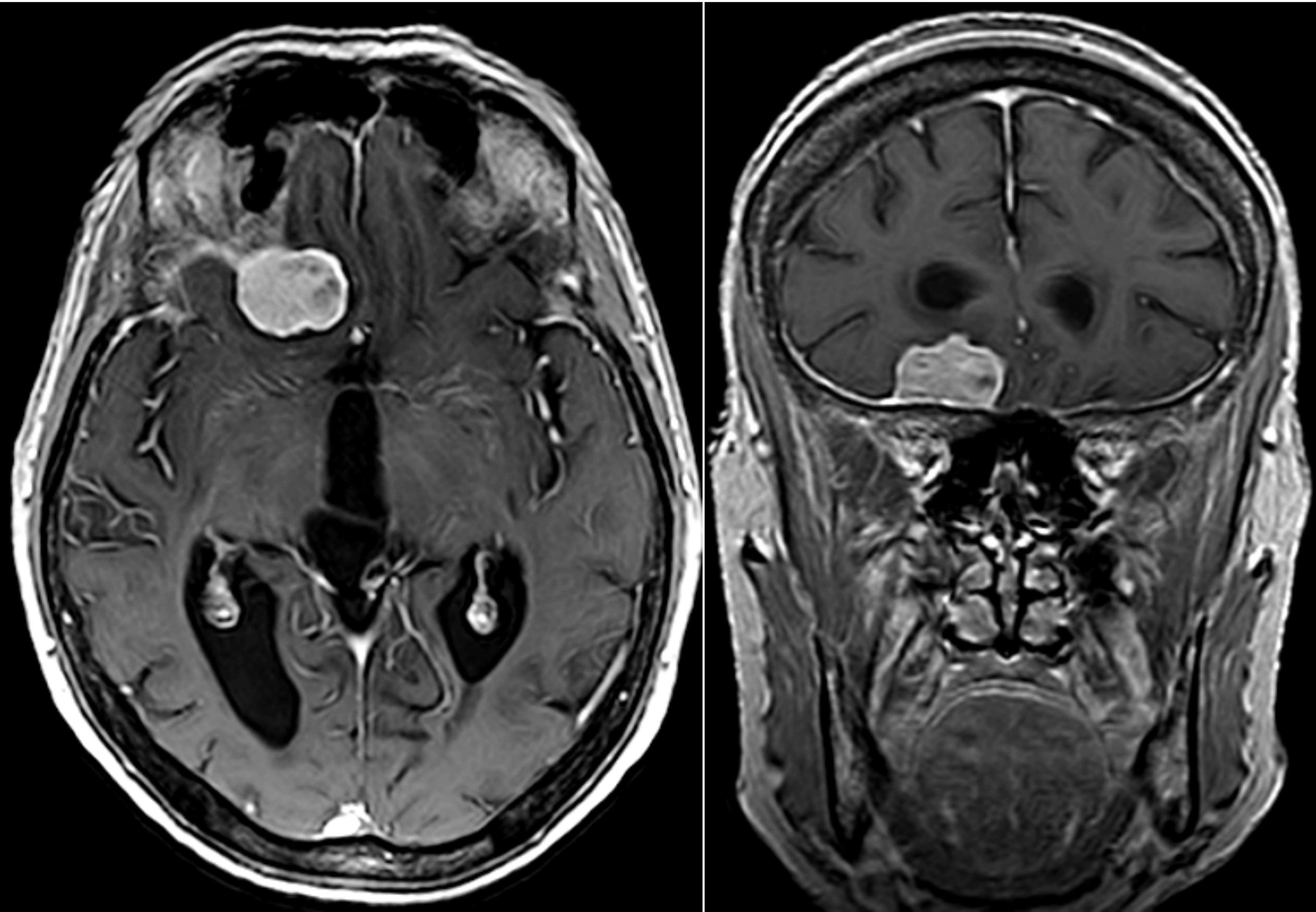
Normal

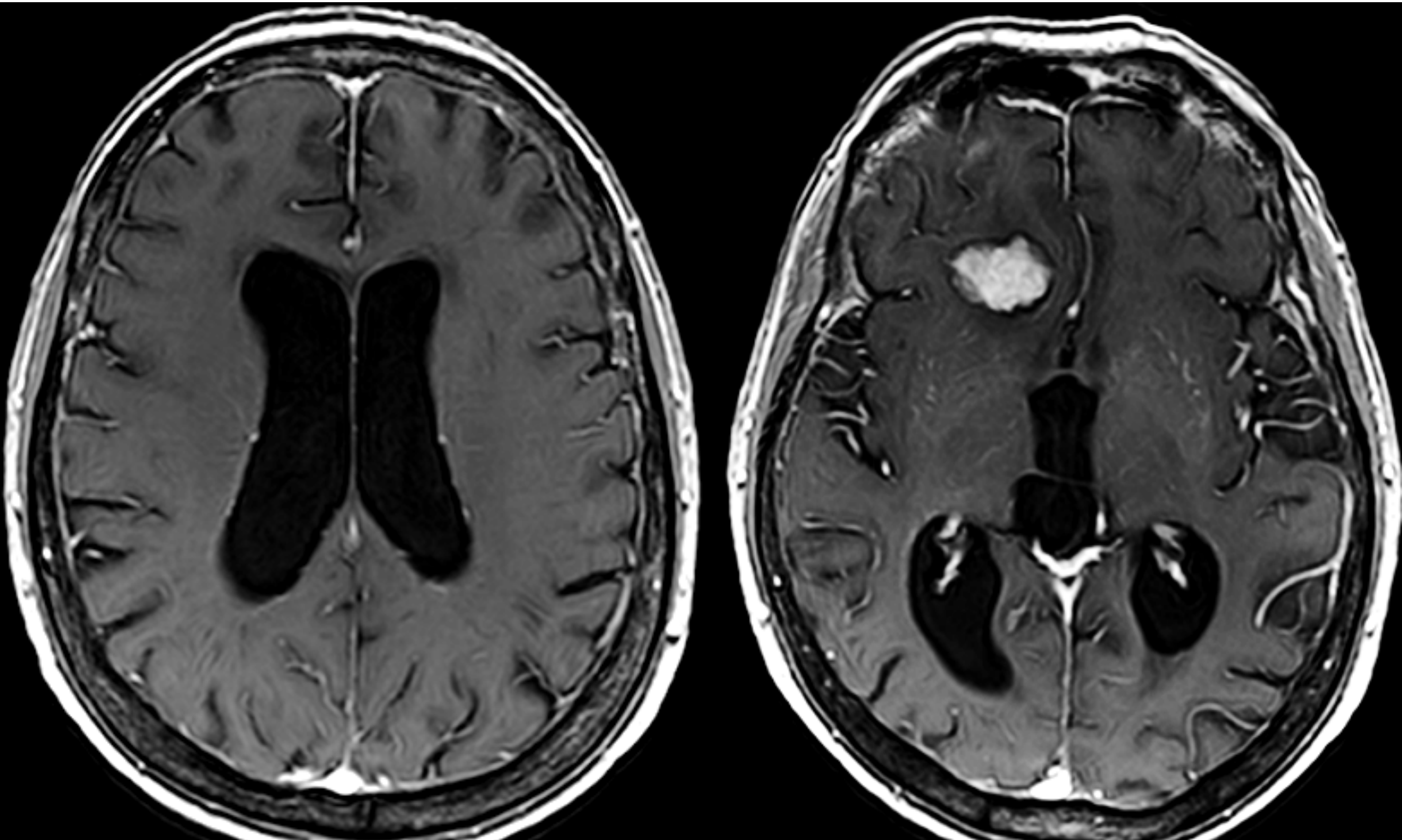


The "Heart" Sign

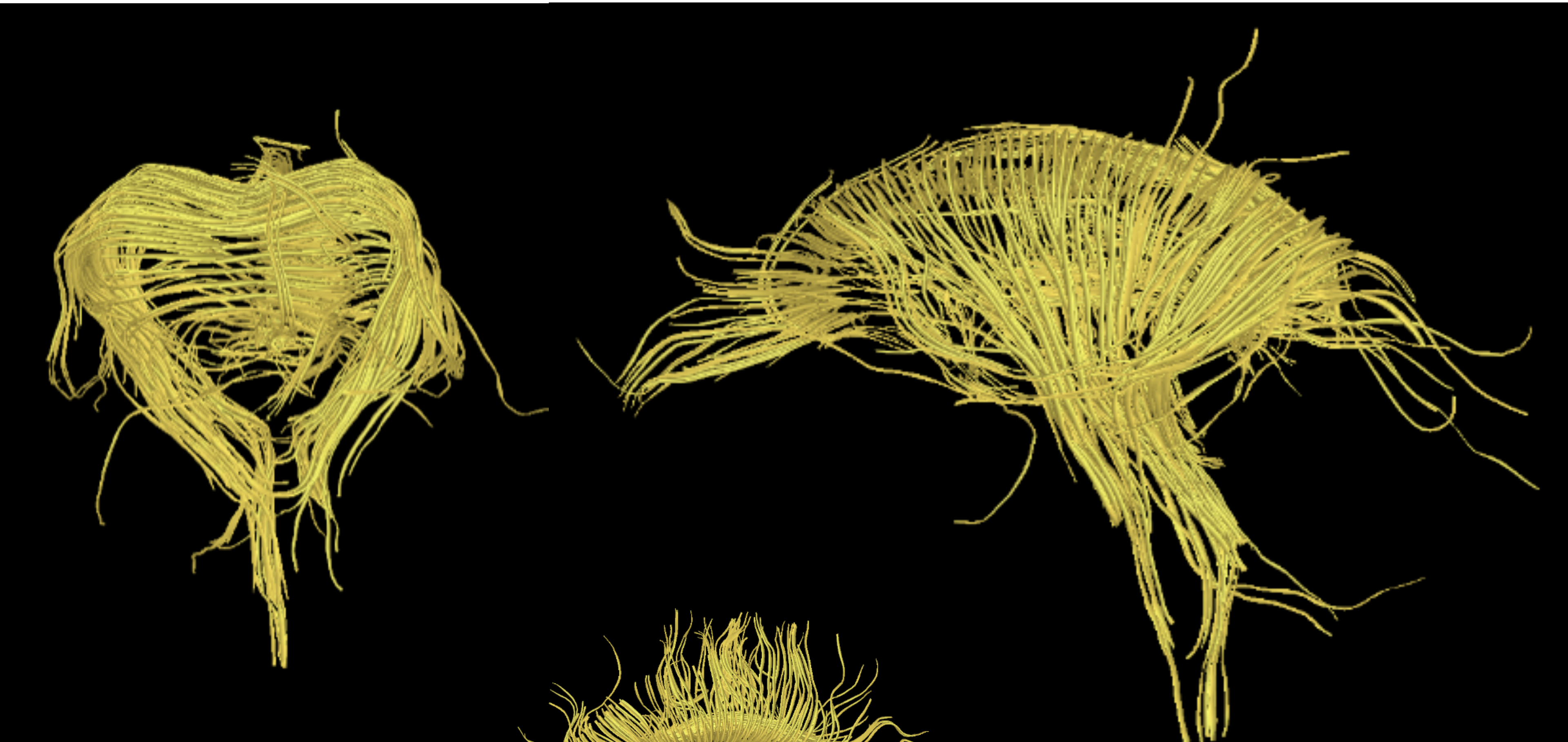


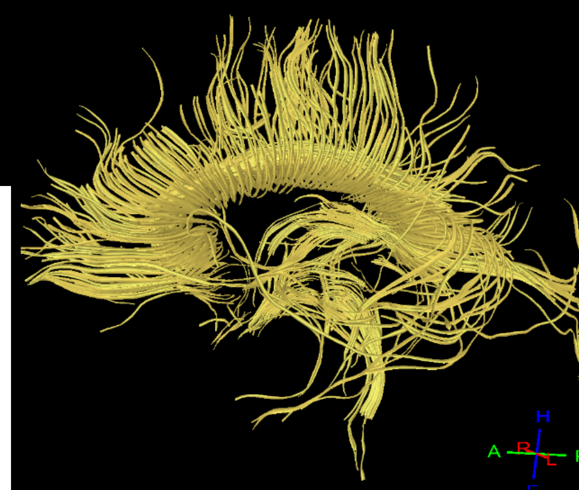
Patient with a Meningioma now presenting with gait disturbance





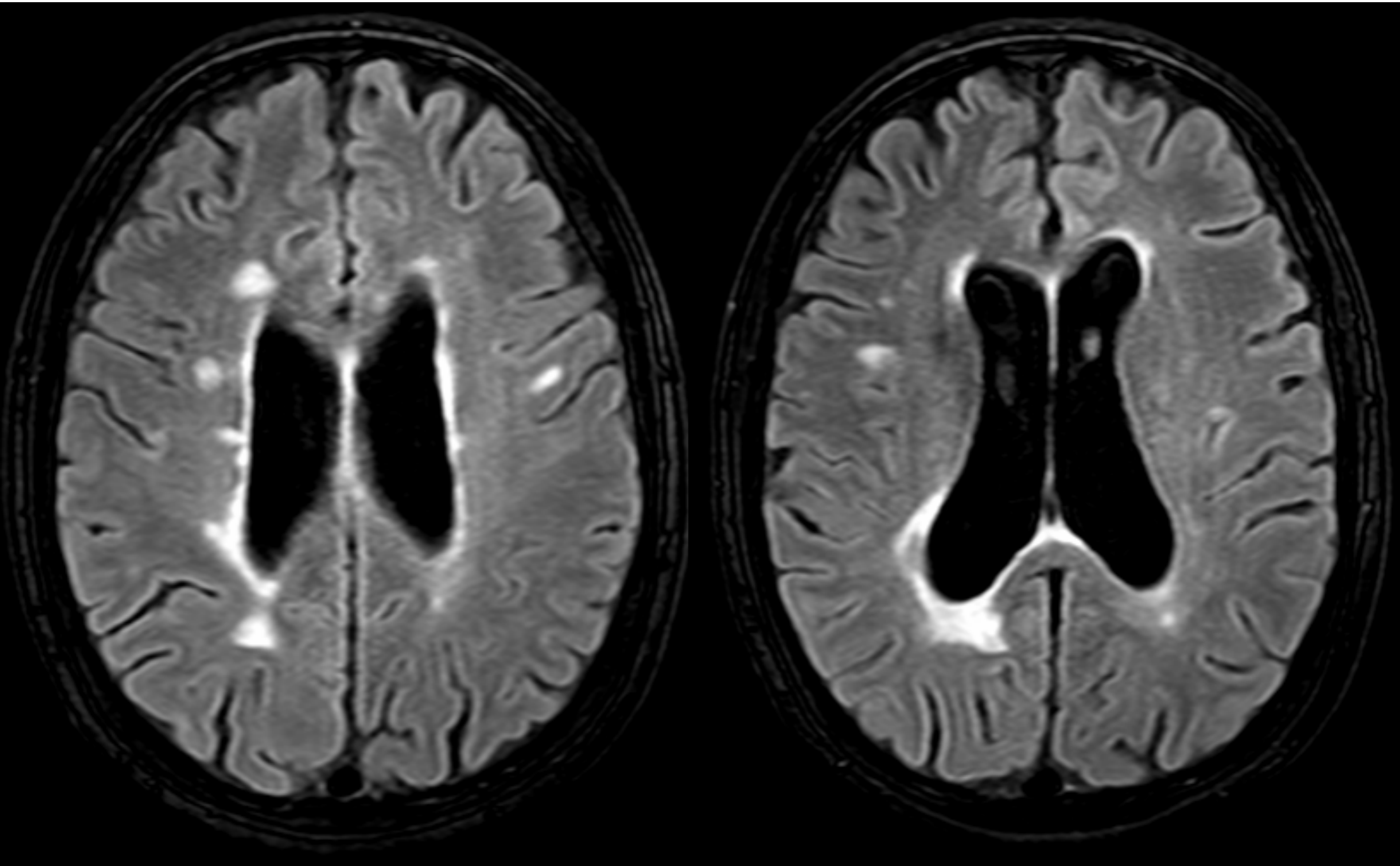
65 YF with a Meningioma



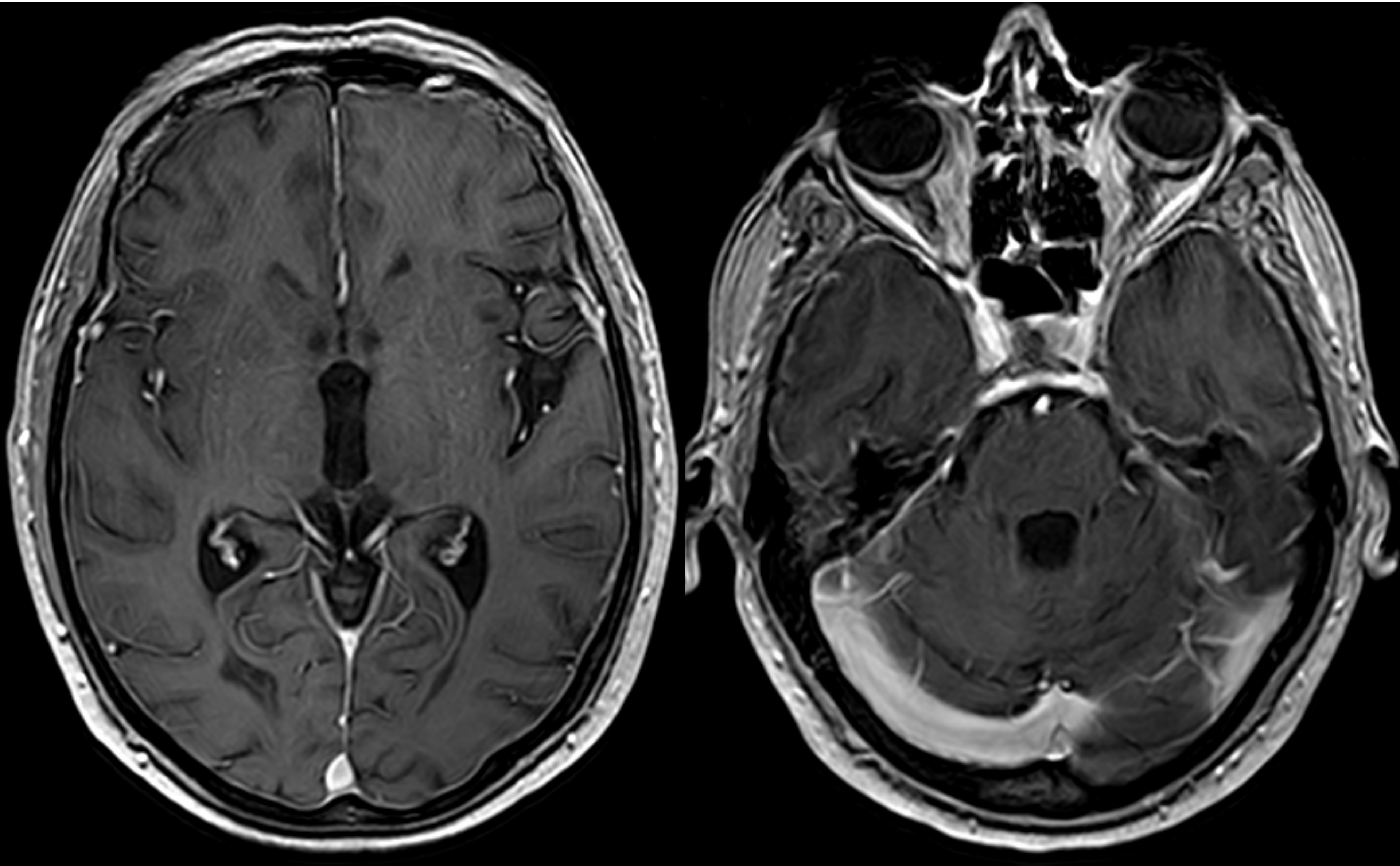


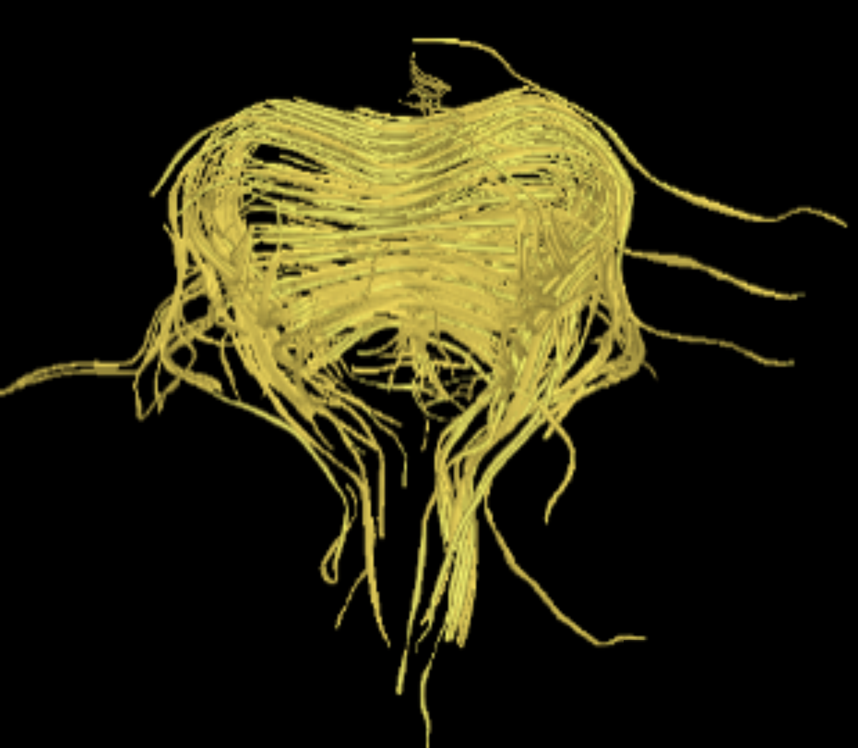
Normal for Comparison

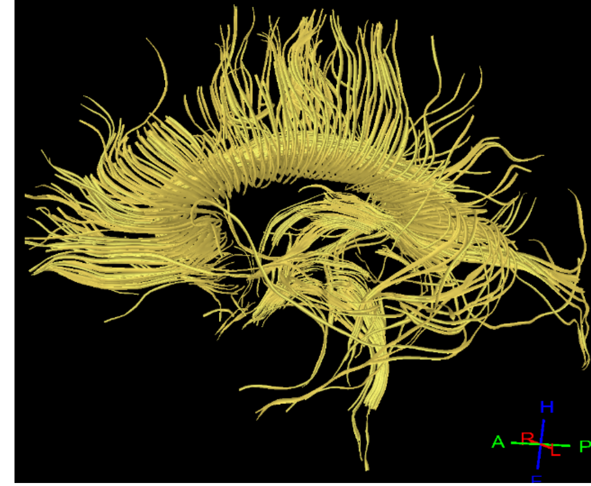
58YF with a 30Y History of Multiple Sclerosis



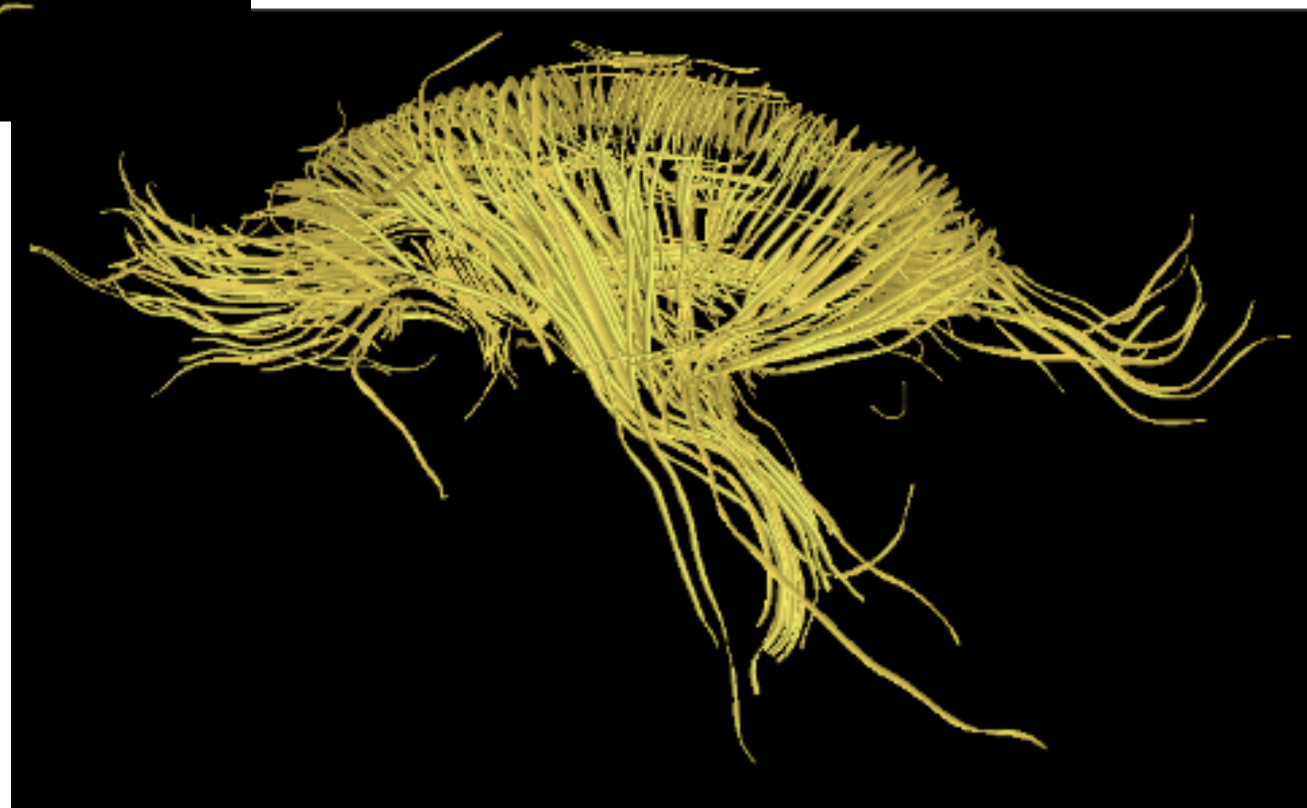
58YF with a 30Y History of Multiple Sclerosis



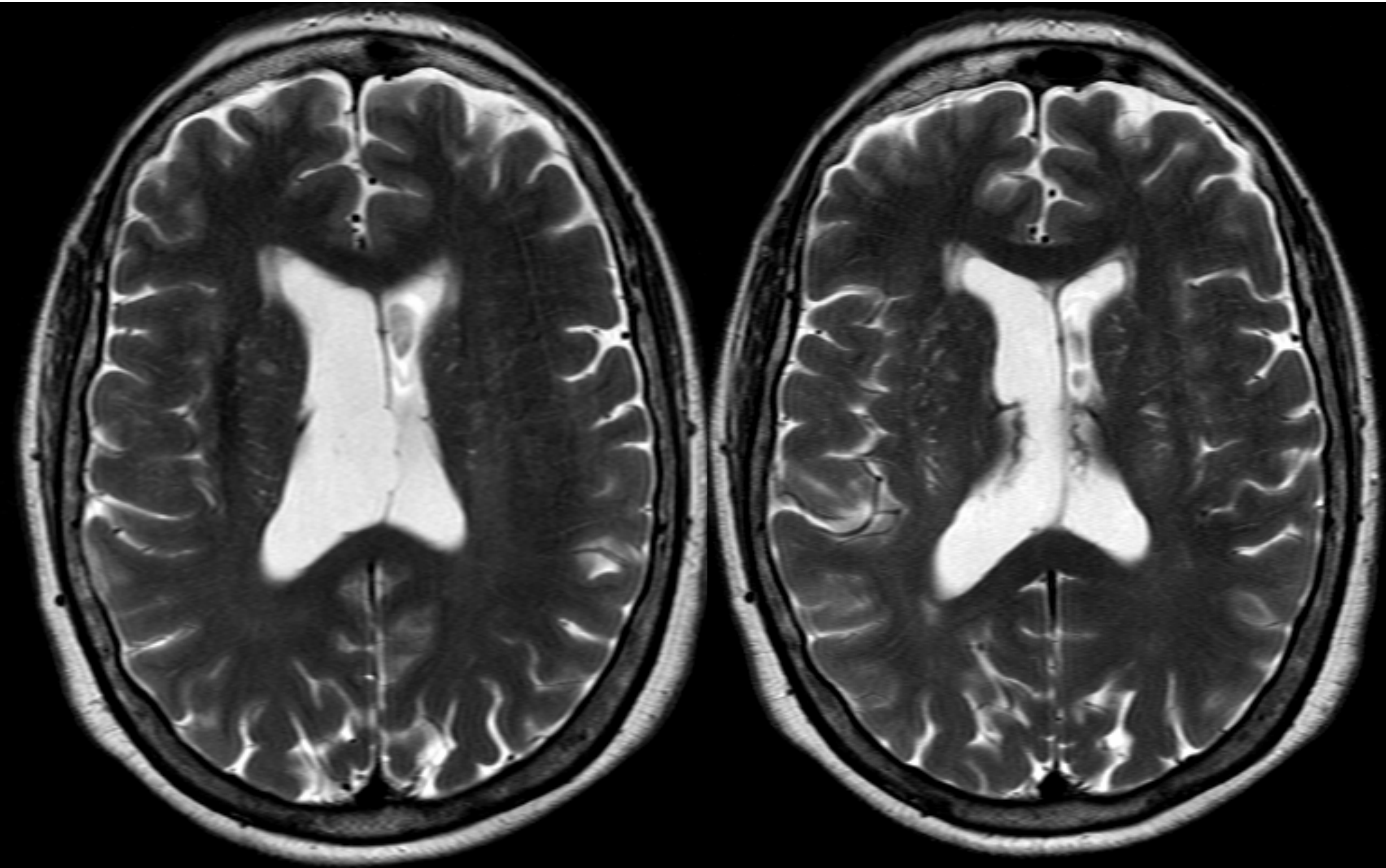


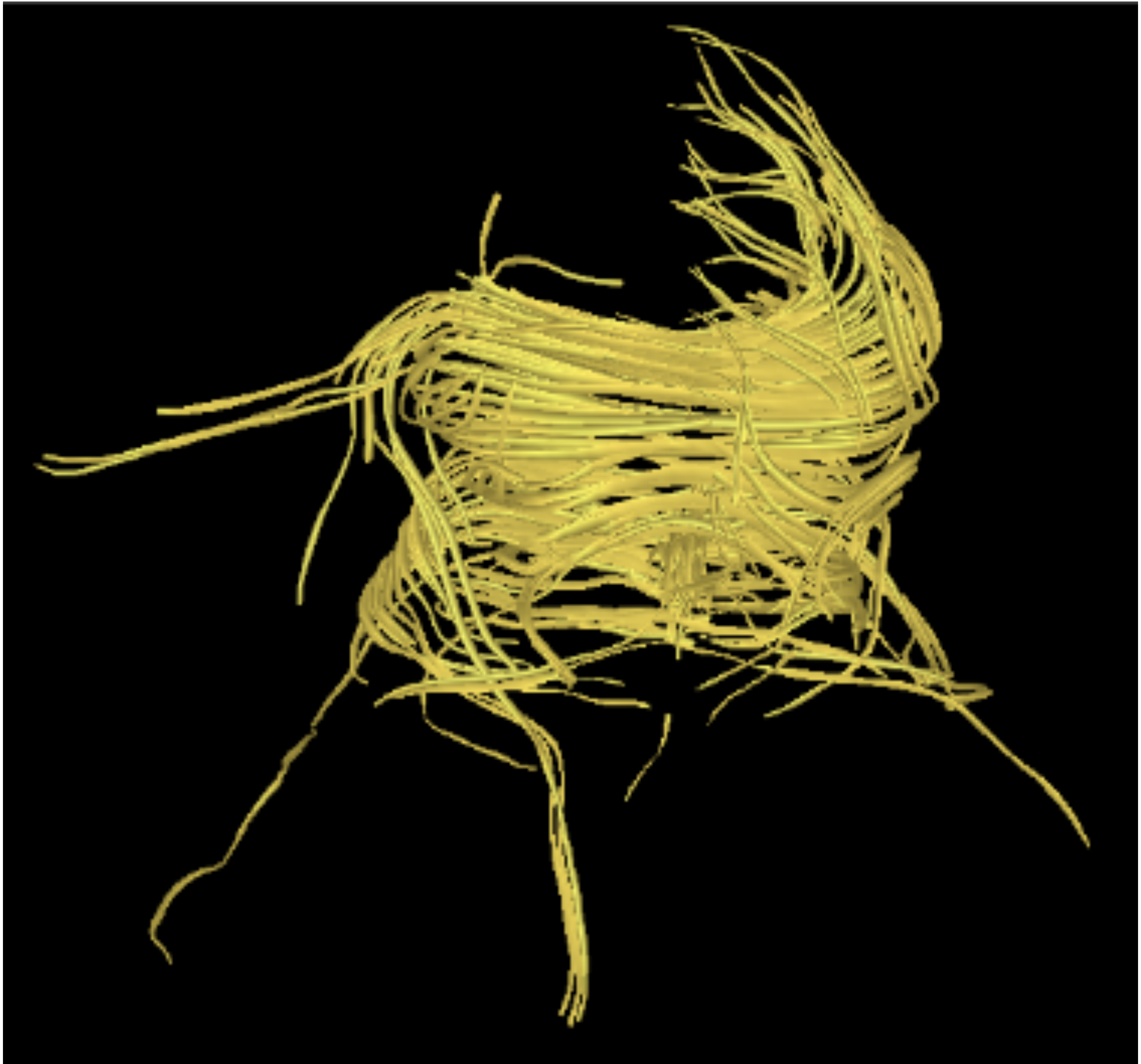


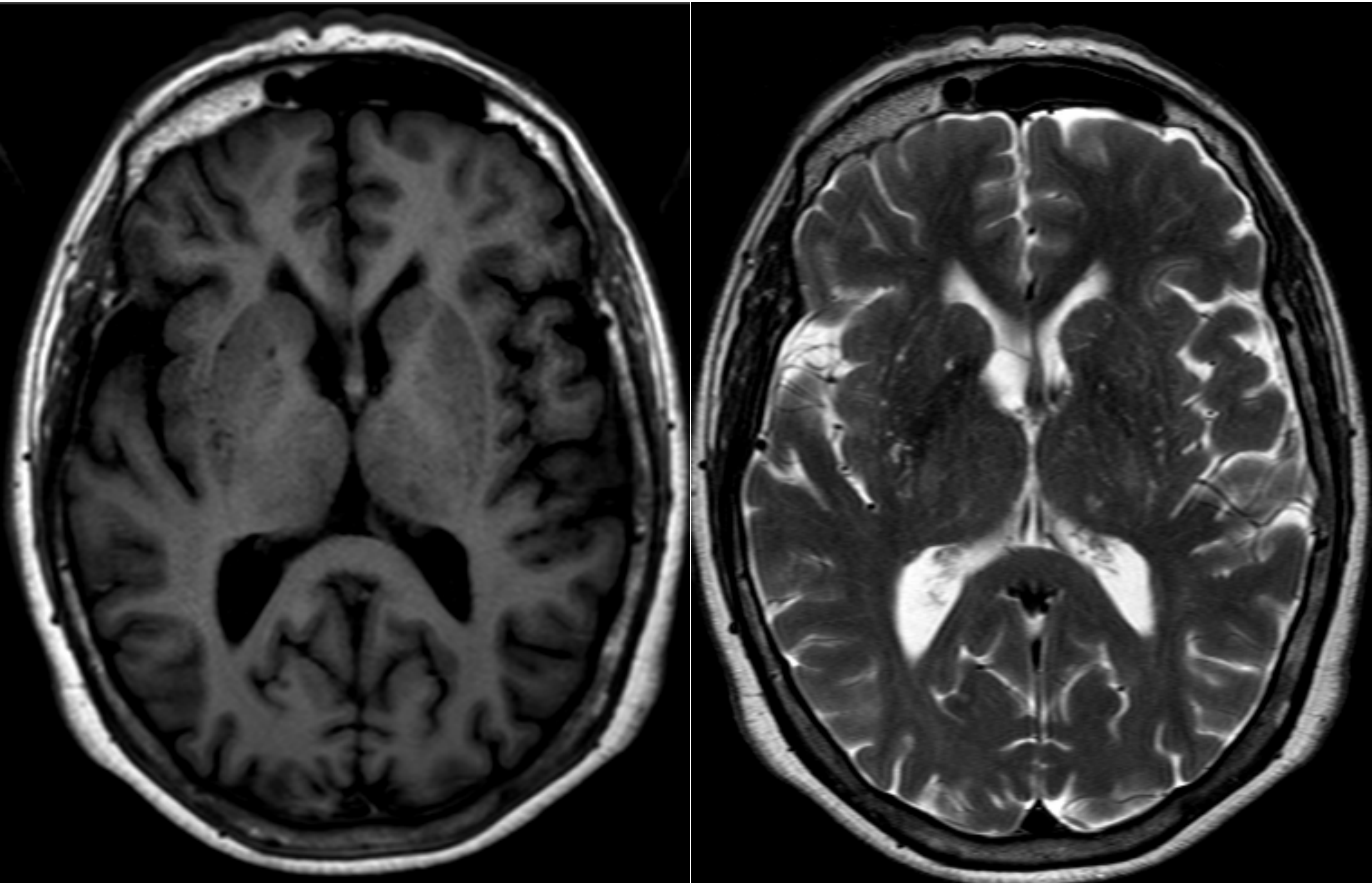
Normal for Comparison

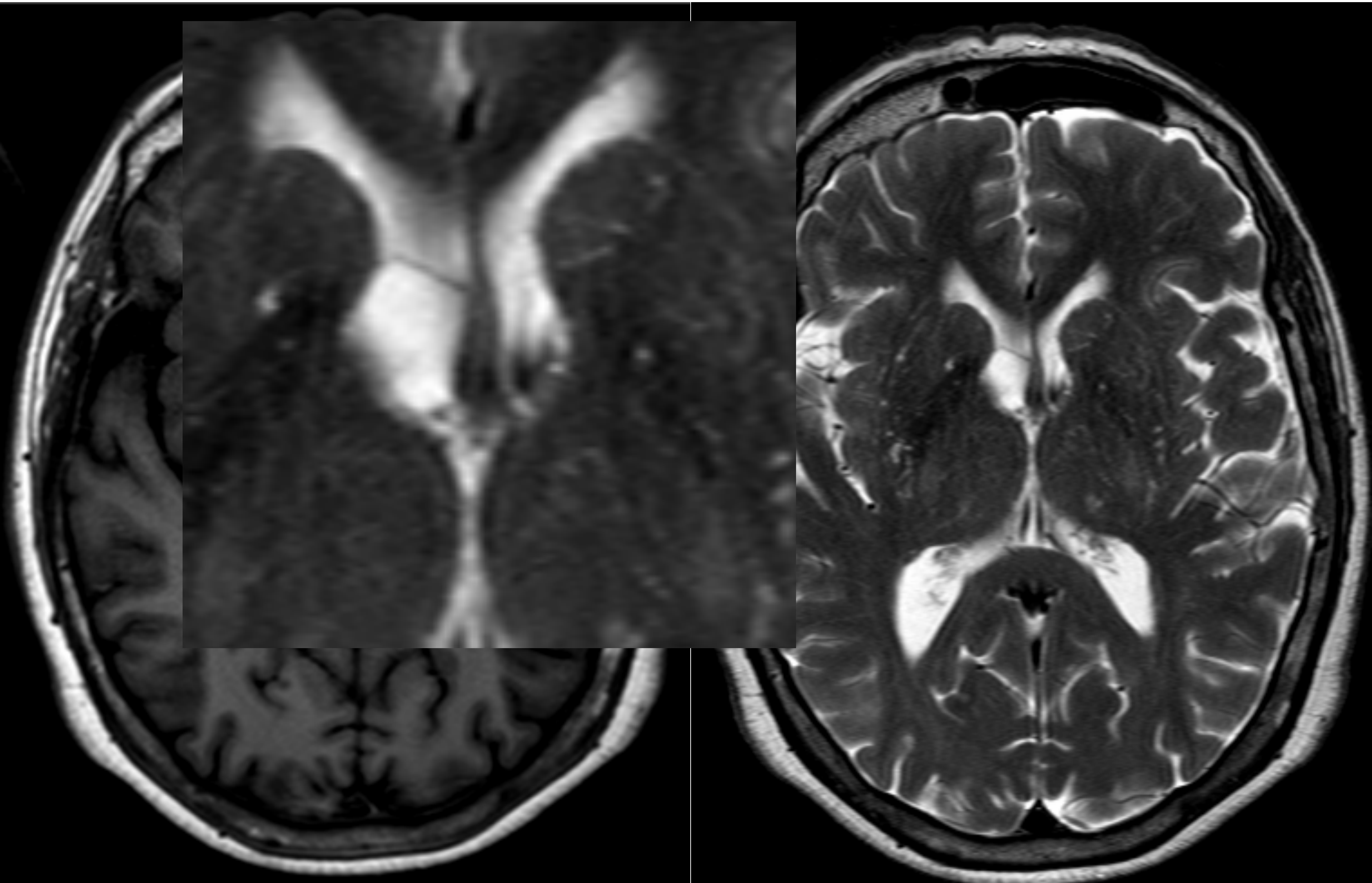


78YF with Headaches

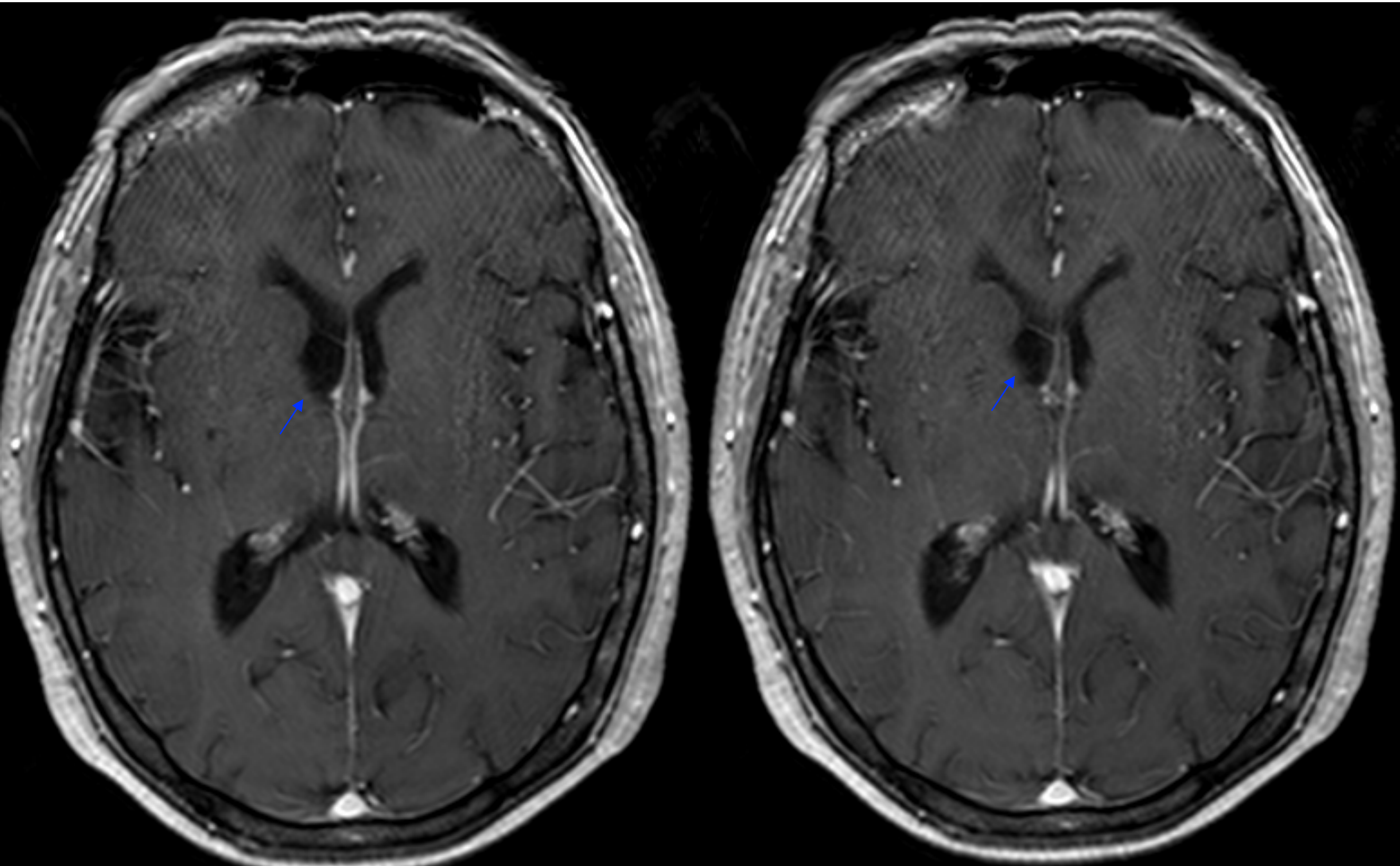








Post Gd 1.3mm T1W Images



Neurosurgery 66:917-924, 2010

Diffusion Tensor Imaging in Patients With Adult Chronic Idiopathic Hydrocephalus

Elke Hattingen, MD
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Institute of Neuroradiology, Goethe University, and Center for Research on Individual Development and Adaptive Education,

Julia Melber
Department of Neurology, Goethe University, Frankfurt am Main, Germany

Stella Blasel, MD
Institute of Neuroradiology, Goethe University, Frankfurt am Main, Germany

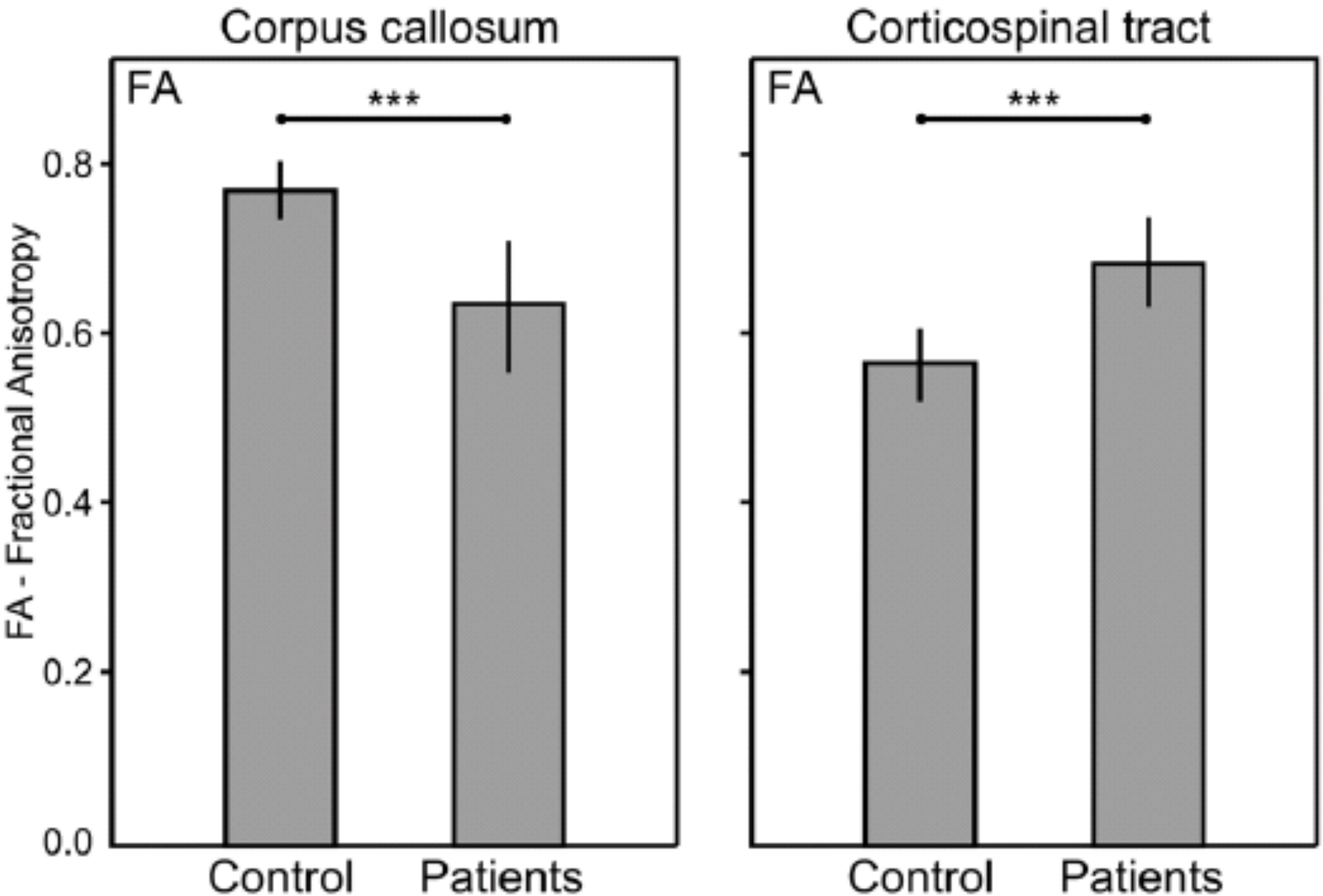
Friedhelm E. Zanella, MD, PhD
Institute of Neuroradiology, Goethe University, Frankfurt am Main, Germany

OBJECTIVE: Diffusion tensor imaging (DTI) parameters were investigated in patients with chronic idiopathic hydrocephalus to evaluate microstructural changes of brain tissue caused by chronic ventricular dilatation.

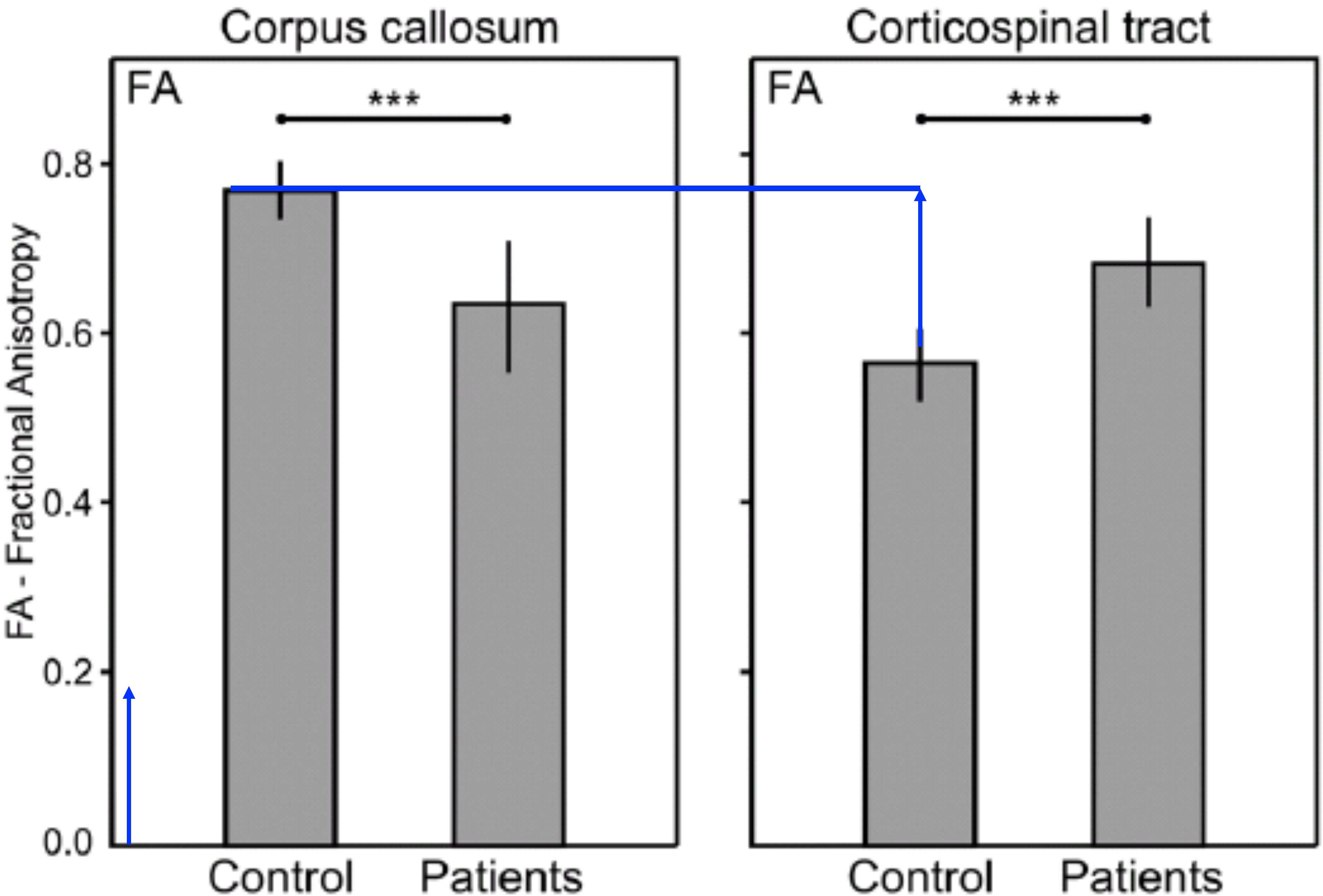
METHODS: Eleven patients fulfilling the criteria for possible or probable idiopathic normal pressure hydrocephalus and 10 healthy control subjects underwent MRI at 3 Tesla, including DTI with 12 gradient directions. Patients were scanned before lumbar cerebrospinal fluid (CSF) withdrawal tests. Differences in fractional anisotropy (FA) and mean diffusivity (MD) between patients and controls were assessed using 2 different methods: manual definition of regions of interest and a fully automated method, TBSS (Tract-Based Spatial Statistics). DTI parameters were correlated with clinical findings.

RESULTS: Compared with the control group, patients with chronic idiopathic hydrocephalus had significantly higher MD values in both the periventricular corticospinal tract (CST) and the corpus callosum (CC), whereas FA values were significantly higher in the CST but lower in the CC. DTI parameters of the CST correlated with the severity of gait disturbances.

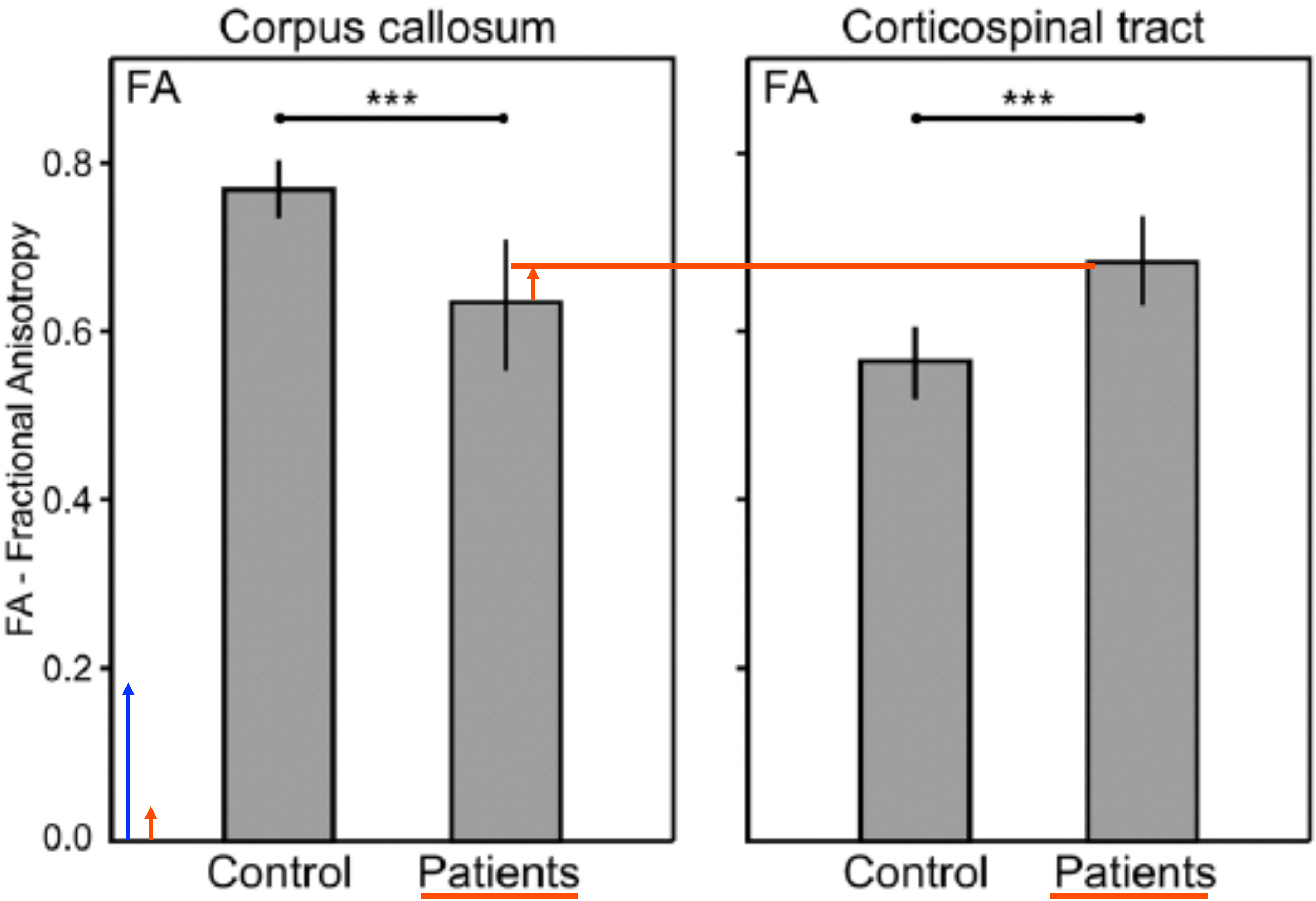
CONCLUSION: Microstructural changes in periventricular functionally relevant white matter structures (CSF, CC) in chronic idiopathic hydrocephalus can be visualized using DTI. Further studies should investigate the change of DTI parameters after CSF shunting and its relation to neurologic outcome.


Corpus callosum
FA
***
0.8
0.6
0.4
0.2
0.0
FA - Fractional Anisotropy
Control
Patients
Corticospinal tract
FA
***
Control
Patients

Neurosurgery 66:917-924, 2010

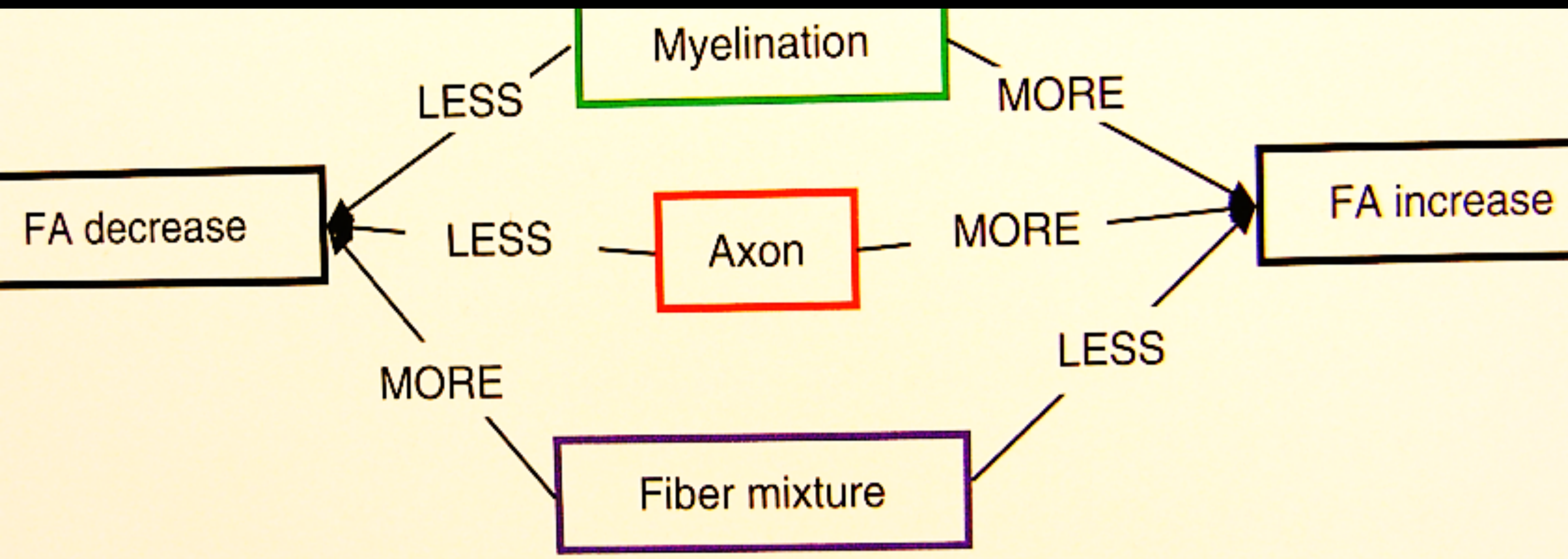


Neurosurgery 66:917-924, 2010



Diffusion through white matter probes:

- density of axons
- degree of myelination
- average fiber diameter
- c directional similarity of axons



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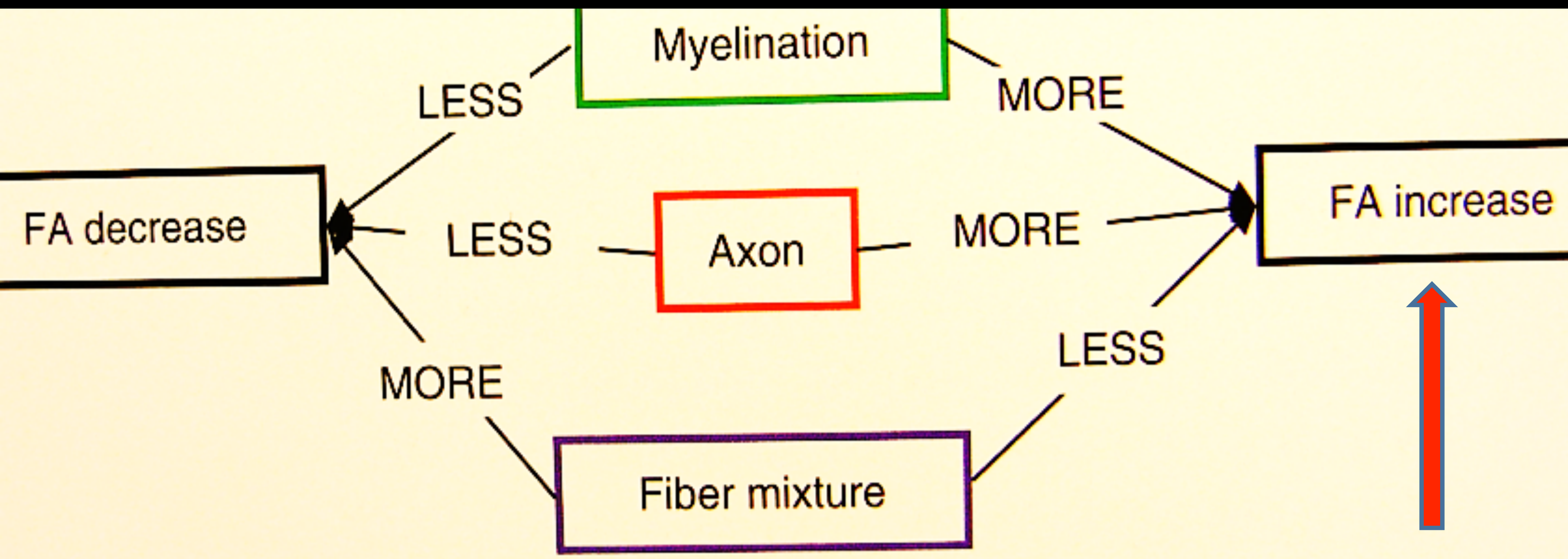


ORIGINAL RESEARCH

Altered Microstructure in Corticospinal Tract in Idiopathic Normal Pressure Hydrocephalus: Comparison with Alzheimer Disease and Parkinson Disease with Dementia

T. Hattori
T. Yuasa
S. Aoki
R. Sato
H. Sawaura
T. Mori
H. Mizusawa

BACKGROUND AND PURPOSE: Previous neuropathologic studies in chronic hydrocephalus have suggested the presence of white matter damage, presumably from mechanical pressure due to ventricular enlargement and metabolic derangement. This study aimed to investigate the diffusional properties of the CST in patients with iNPH by using DTI and to determine whether this method could be used as a new diagnostic tool to differentiate patients with iNPH from those with AD and PDD and control subjects.

MATERIALS AND METHODS: We enrolled 18 patients with iNPH, 11 patients with AD, 11 patients with PDD, and 19 healthy control subjects. Diffusion tensor metrics of the segmented CST, including FA values, axial eigenvalues, and radial eigenvalues, were evaluated by using tract-specific analysis. The anisotropy color-coding tractography of the CST was visually evaluated. The DTI findings were compared among groups.

RESULTS: Tract-specific analysis of the CST showed that FA values and axial eigenvalues were significantly increased ($P < .001$), whereas radial eigenvalues were not significantly altered, in patients with iNPH compared with other subjects. The CST tractographic images in patients with iNPH was visually different from those in other subjects ($P < .001$). In discriminating patients with iNPH from other subjects, the CST FA values had a sensitivity of 94% and specificity of 80% at a cutoff value of 0.59.

CONCLUSIONS: Our results suggest that patients with iNPH have altered microstructures in the CST. Quantitative and visual CST evaluation by using DTI may be useful for differentiating patients with iNPH from patients with AD or PDD or healthy subjects.

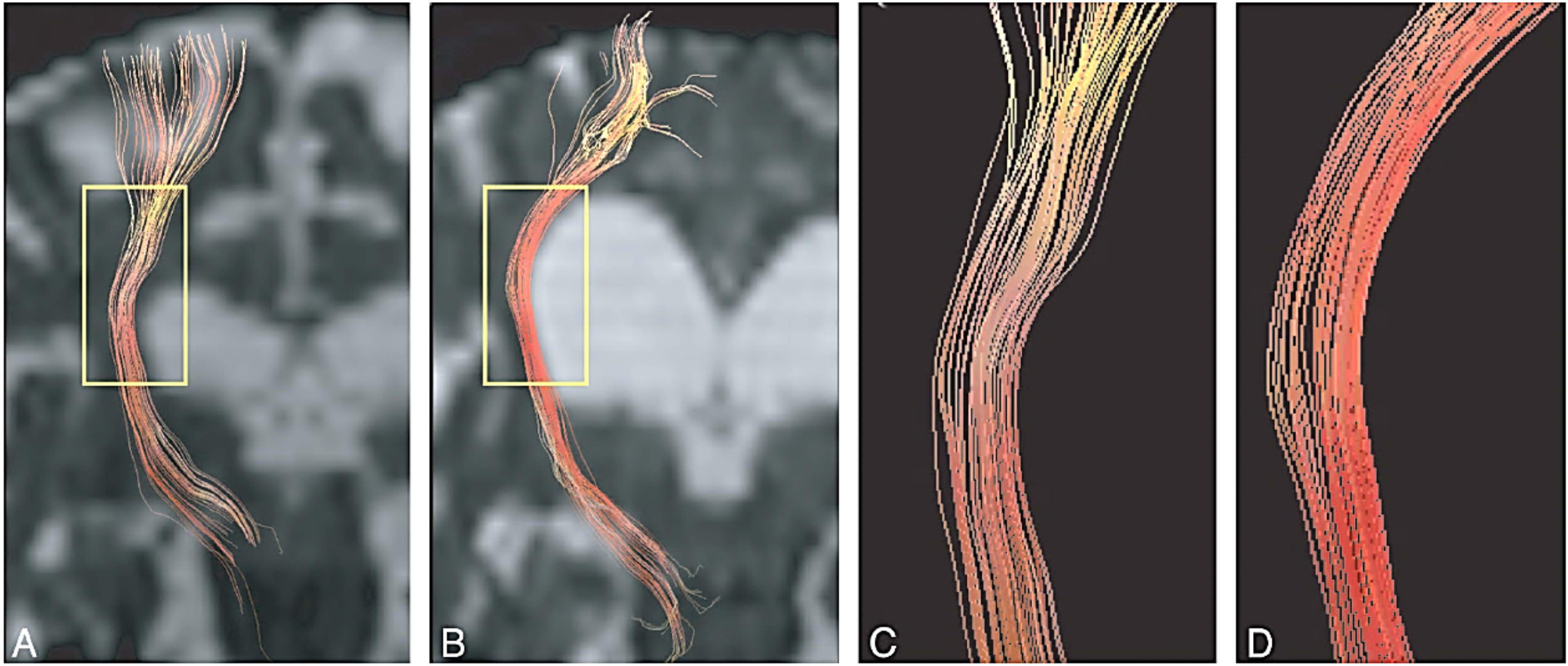


Fig 2. Visual evaluation of anisotropy color-coding tractography of the CST. Anisotropy color-coding tractography of the CST in a control subject (*A*) and a patient with iNPH (*B*) is shown, with $b = 0$ images. The areas defined by the yellow squares in *A* and *B* were used for visual evaluation in *C* and *D*. *C*, Type A (low anisotropy and rough). *D*, Type B (high anisotropy and straight).

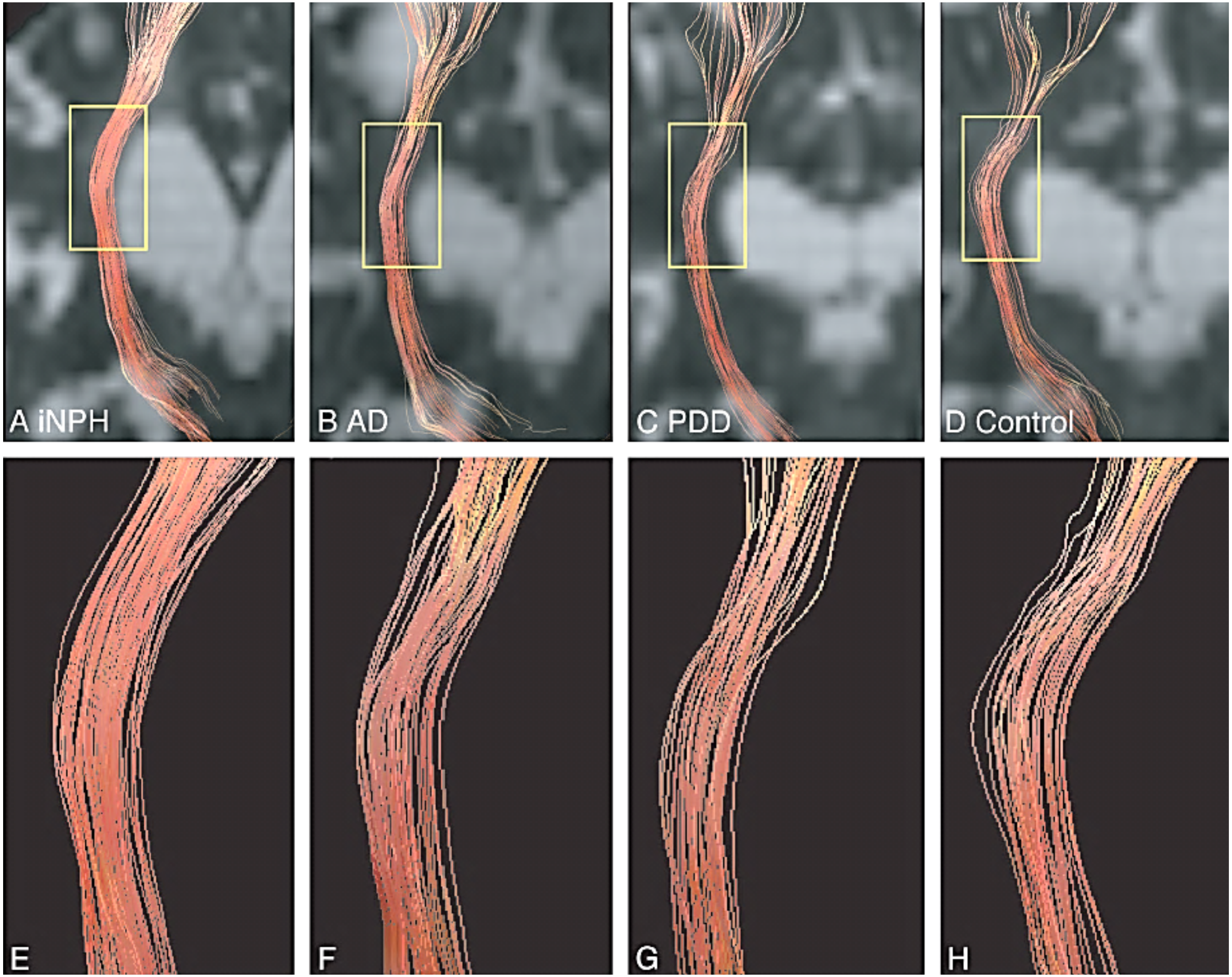
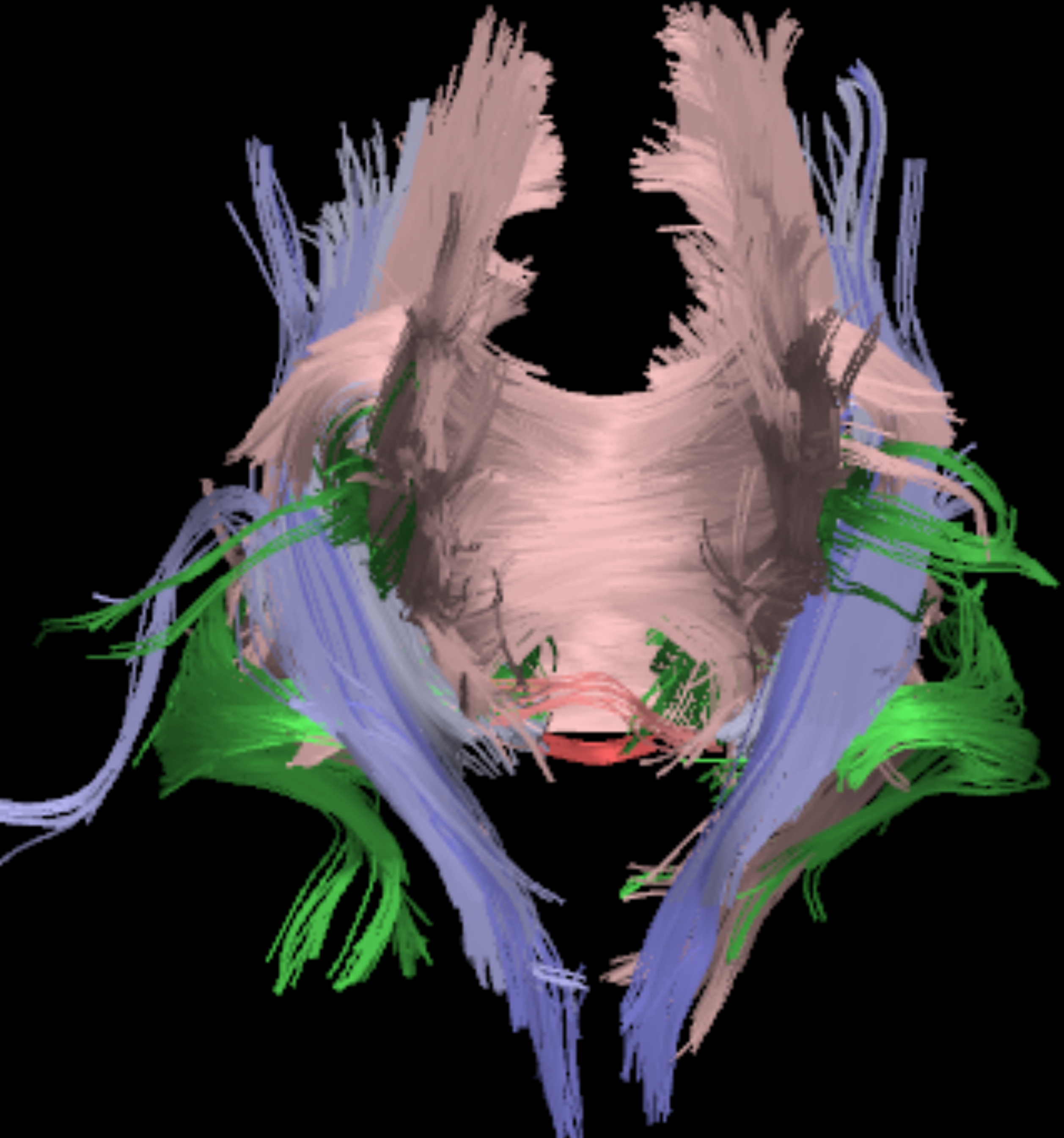
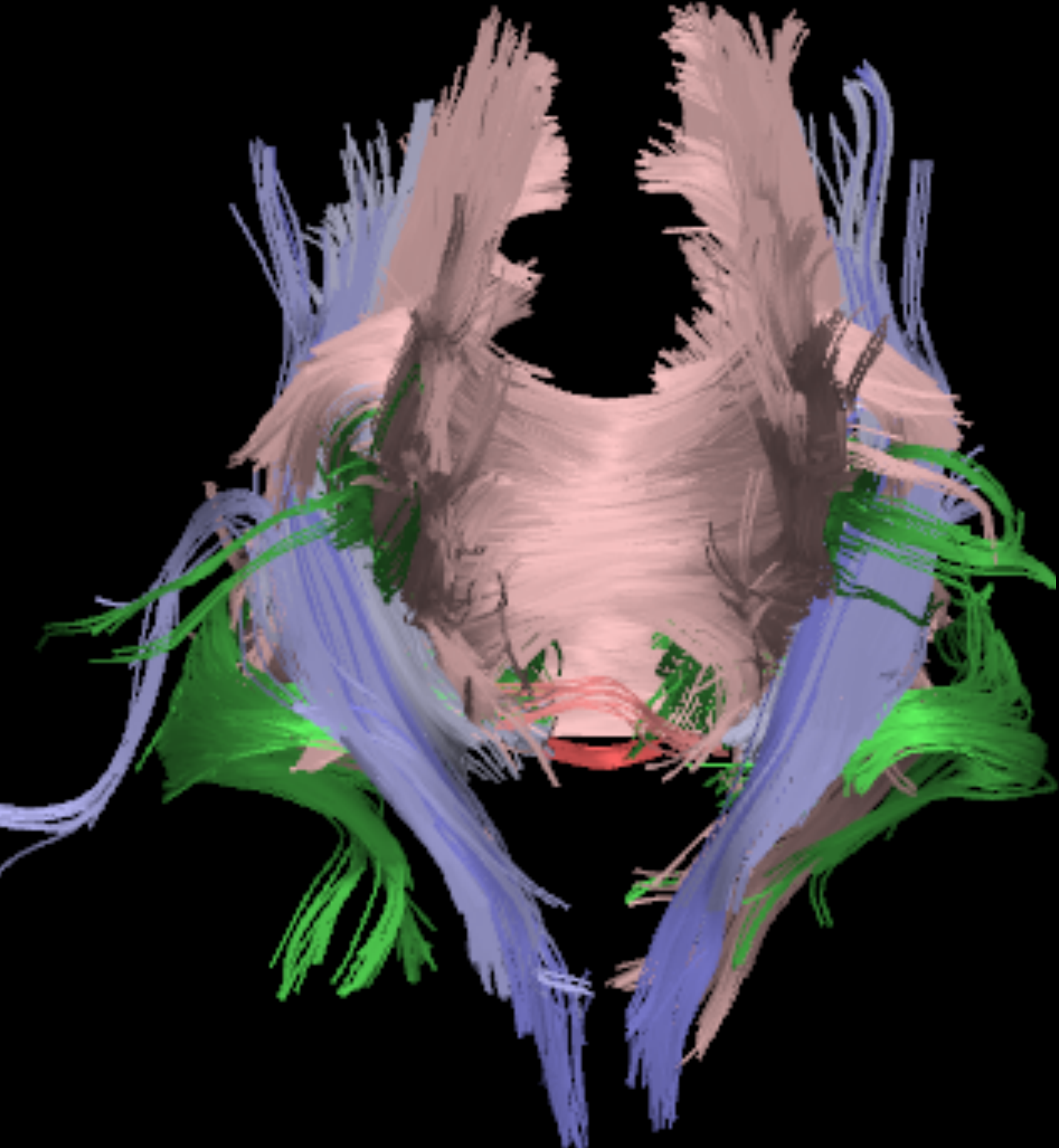
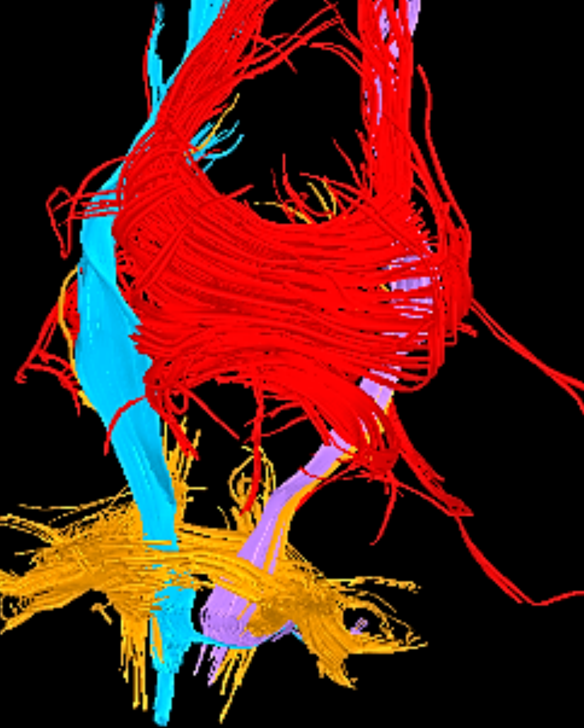
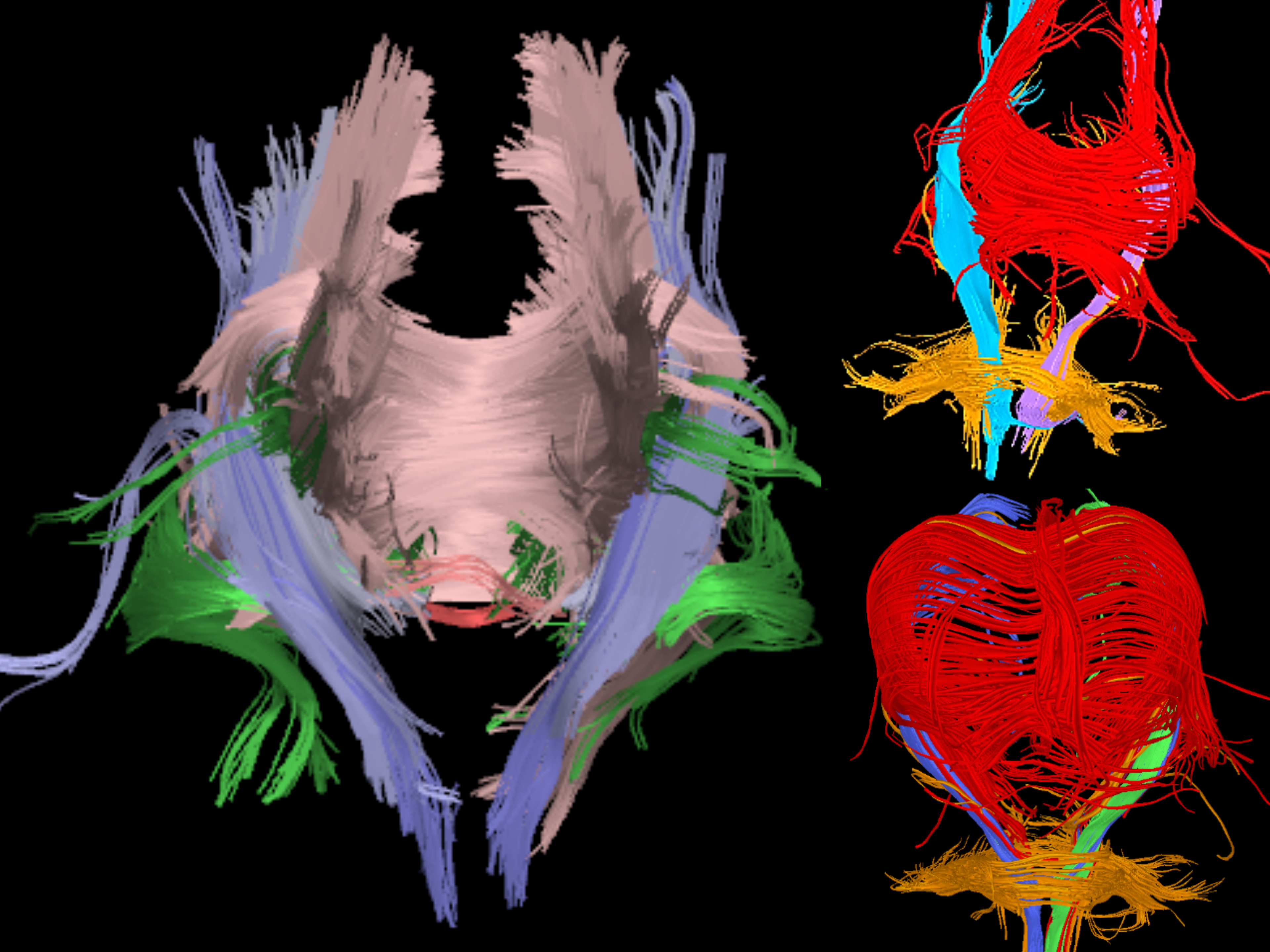


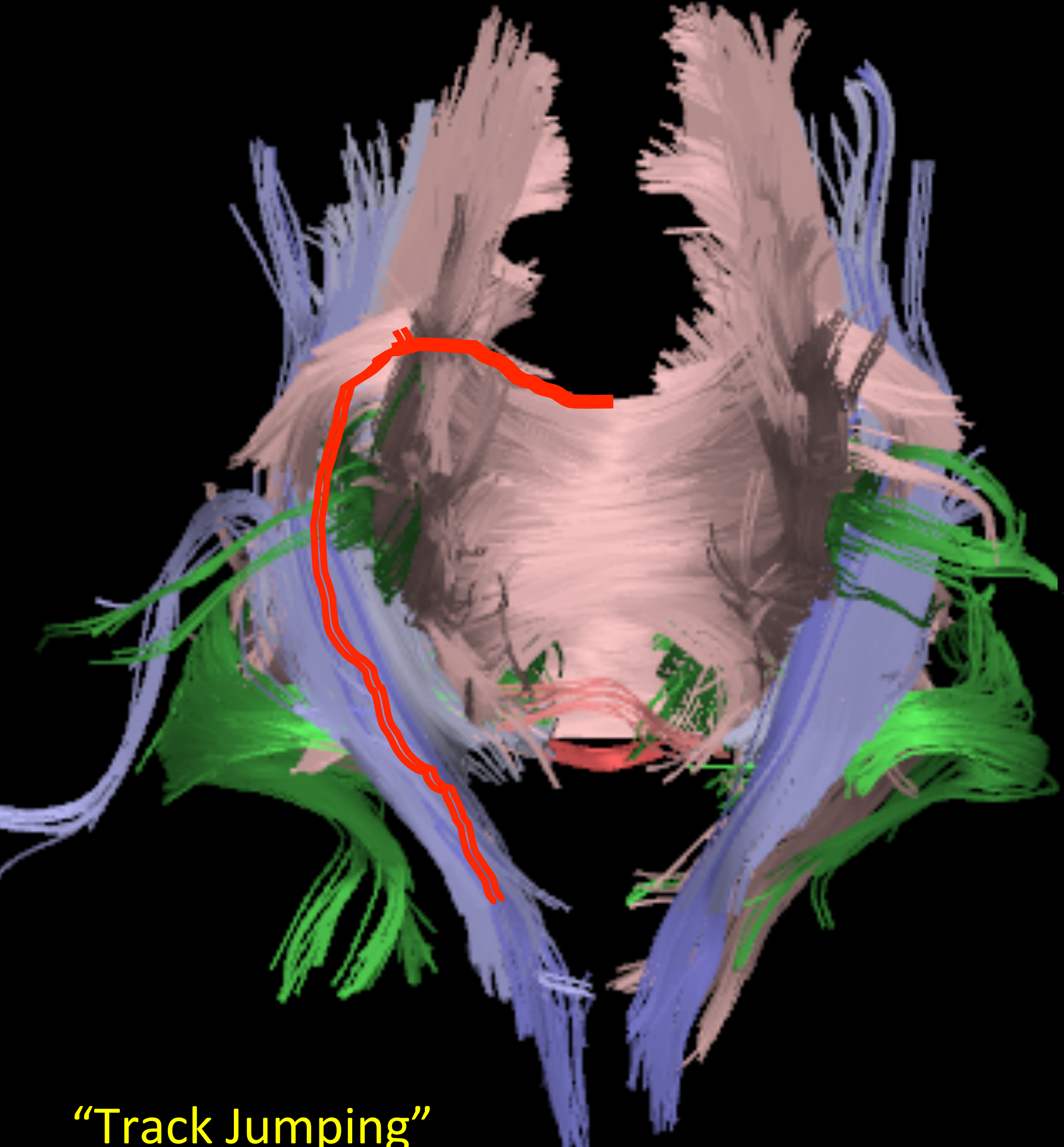
Fig 3. Examples of anisotropy color-coding tractography of the CST. Anisotropy color-coding tractography of the CST in patients with iNPH (Evans index: 0.31; *A*), AD (0.33; *B*), PDD (0.33; *C*), and a control subject (0.31; *D*) are shown, with $b = 0$ images. The areas defined by the yellow squares in *A*, *B*, *C*, and *D* are shown in *E*, *F*, *G*, and *H*, respectively.





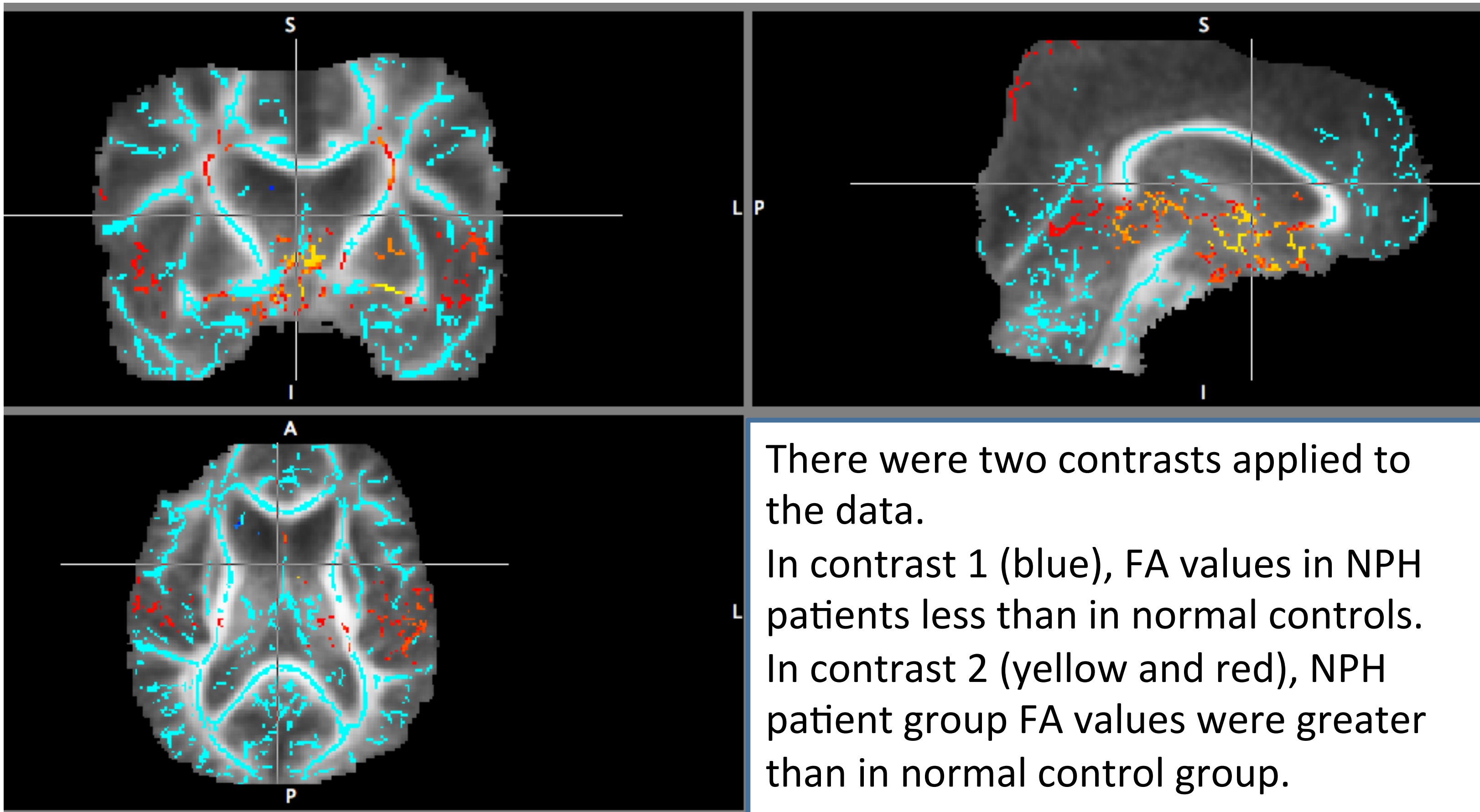






“Track Jumping”

Results



There were two contrasts applied to the data.
In contrast 1 (blue), FA values in NPH patients less than in normal controls.
In contrast 2 (yellow and red), NPH patient group FA values were greater than in normal control group.

The Threshold-Free Cluster Enhancement images were image corrected to display differences only in regions with statistical difference of p is less than or equal to 0.05

Propensity to Develop NPH

Developing NPH
Early NPH

Normal — **Mismatch between Ventricular Pressure and Brain Viscoelasticity with reduced CSF Clearance** — NPH

Ventricular Enlargment with Gait and Cognitive Changes

Congenital Hydrocephalus, SAH,RA,WM Lesion Load (Vascular Lesions, MS), Parkinson’s Disease, AD

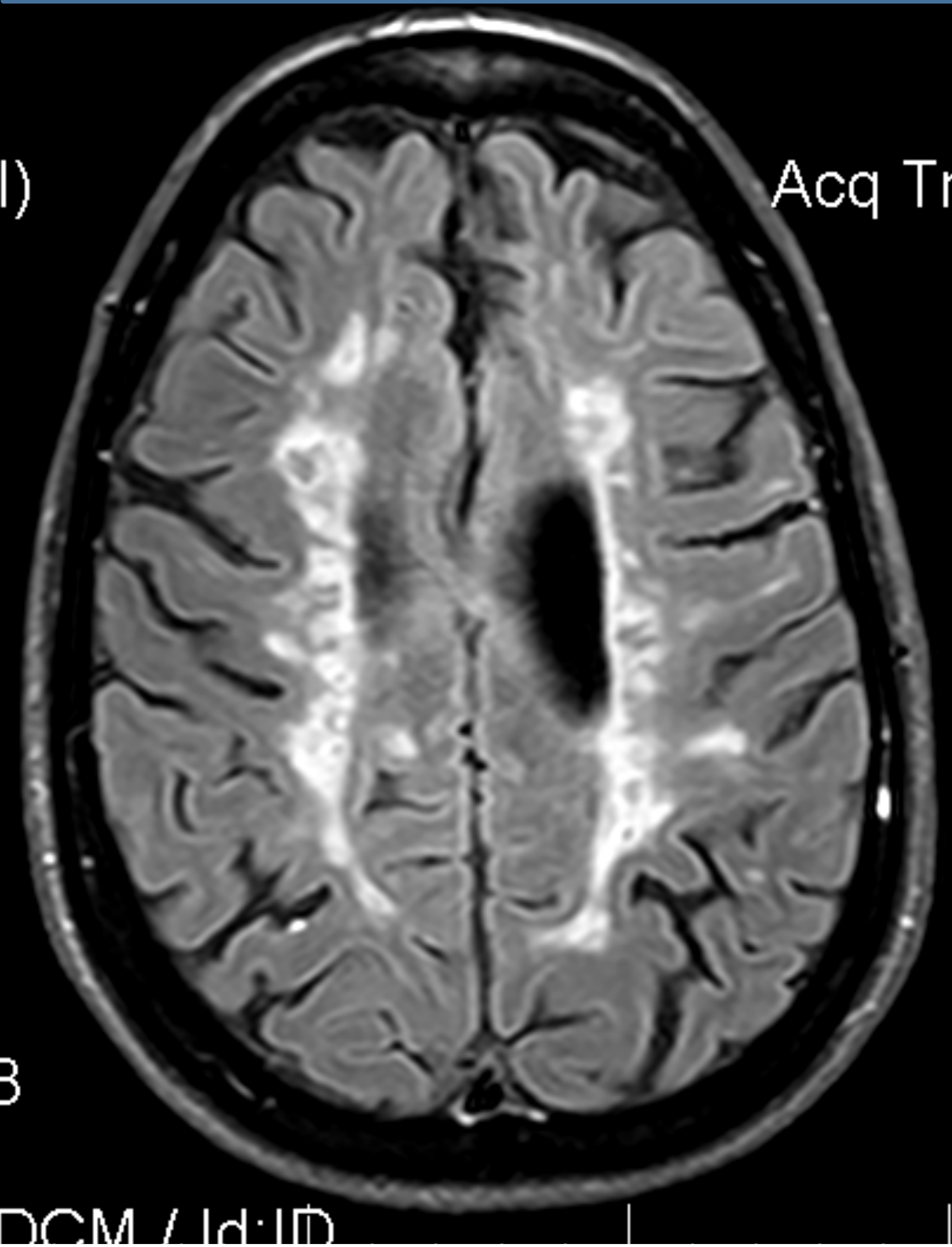
May take decades to develop the full syndrome

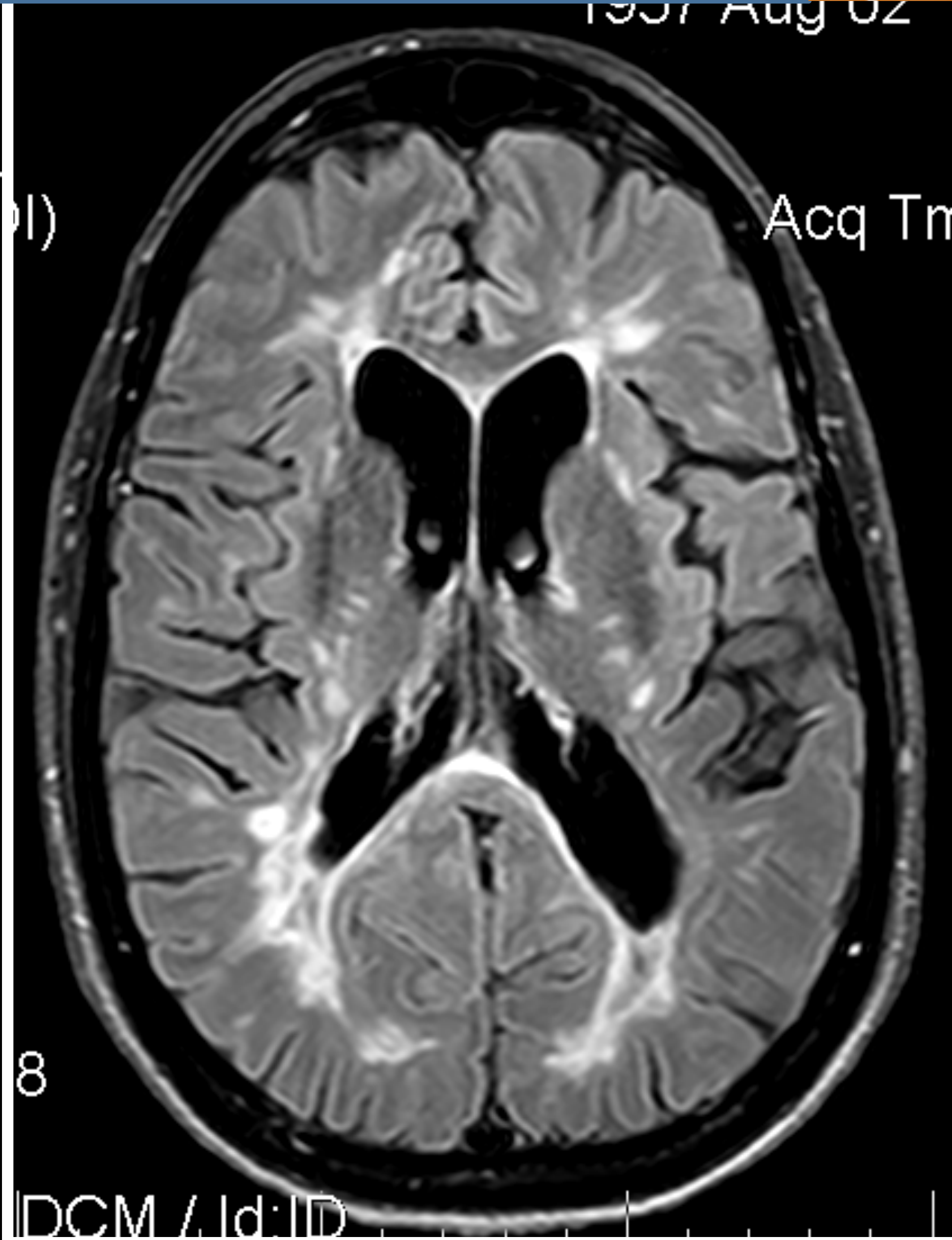
53YF with a 20Y Hx of Untreated MS

DH

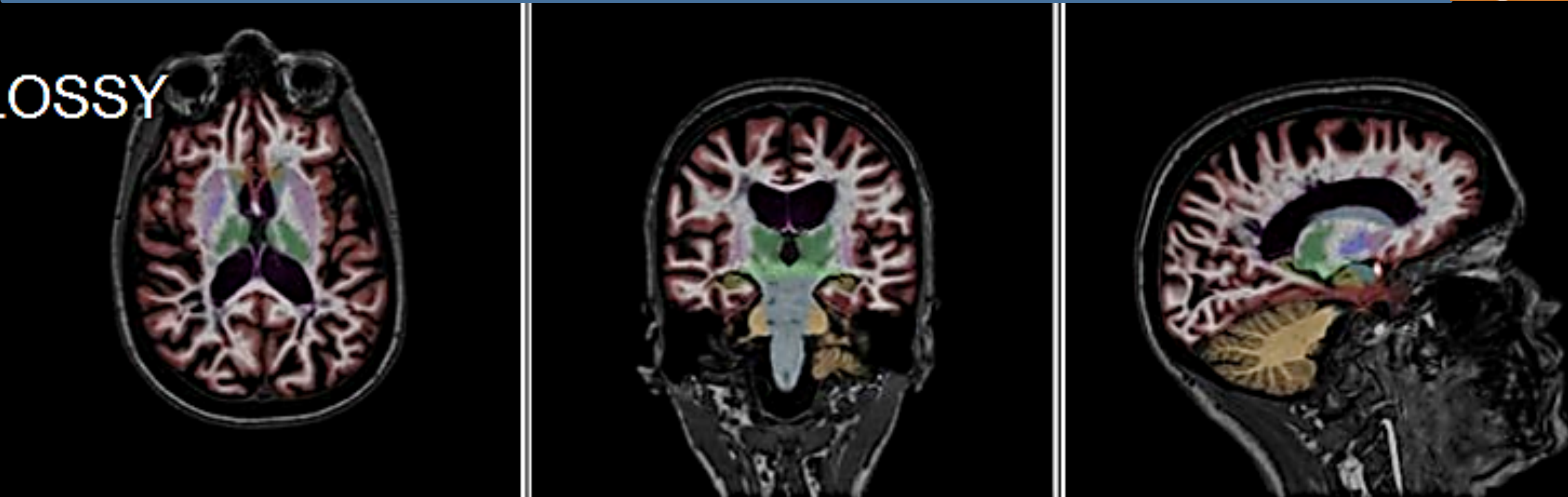
3T MRI 8/26/2010

CSF Pressure and CSF Flow

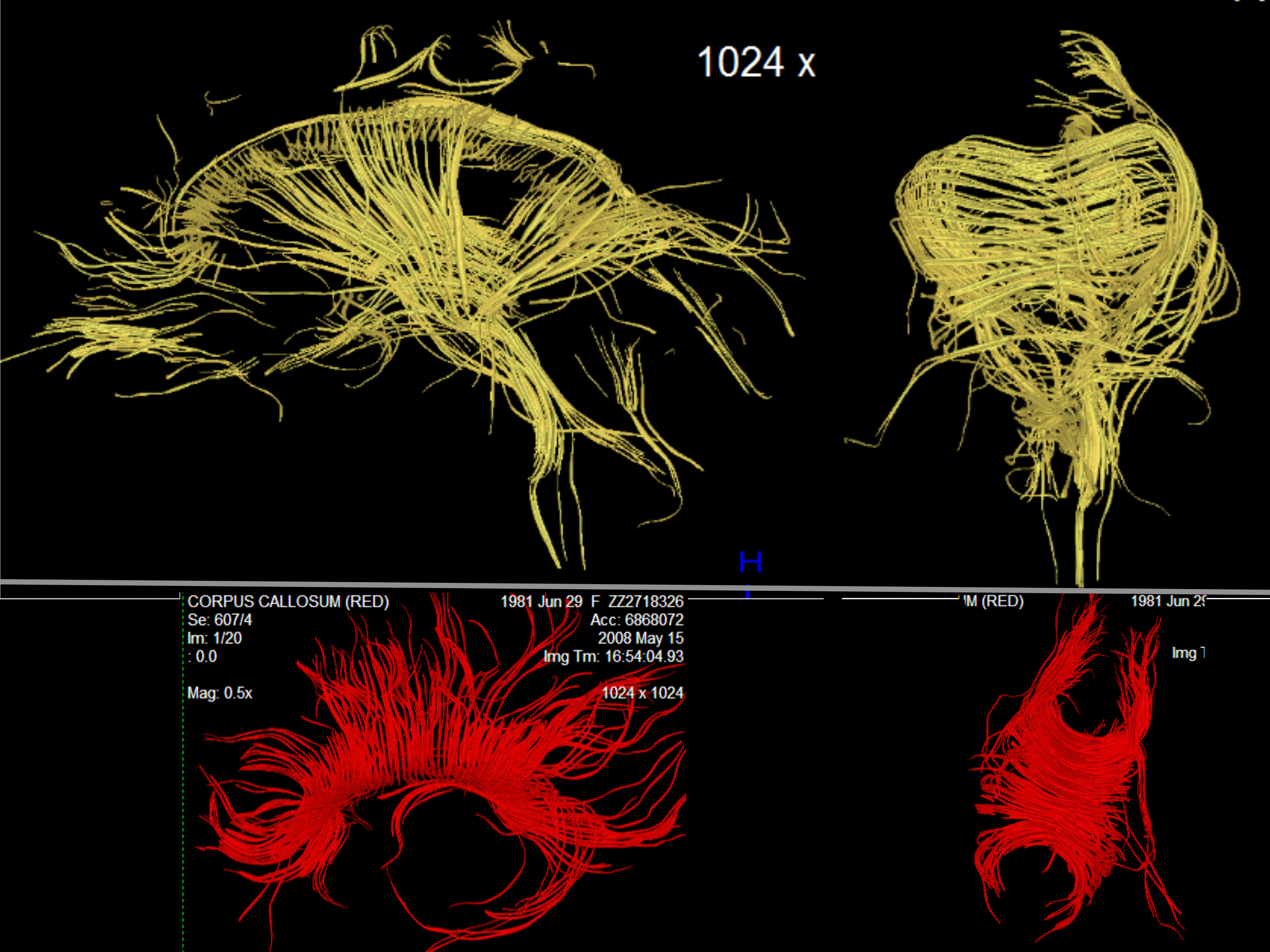




CSF Pressure and CSF Flow



Brain Structure	Volume (cm^3)	% of ICV (5%-95% Normative Percentile*)	Normative Percentile*
Hippocampi	8.00	0.51 (0.43-0.60)	47.46
Lateral Ventricles	70.86	4.52 (-0.02-3.06)	**> 99**
Inferior Lateral Ventricles	4.06	0.26 (0.06-0.24)	**97.08**


1024 x
H
CORPUS CALLOSUM (RED)
Se: 607/4
Im: 1/20
: 0.0
Mag: 0.5x
1981 Jun 29 F ZZ2718326
Acc: 6868072
2008 May 15
Img Tm: 16:54:04.93
1024 x 1024
M (RED)
1981 Jun 2
Img T

Prospective Fiber Tracking Study

- August 2008 to December 2010
- 47 Cases of "Heart Sign"
- 21/47 Patient Surveys returned
- 25 Normal Controls over 55Y with no Hx. Of Gait Instability, Dementia, or Urinary Incontinence. None had a "Heart Sign"

21 Cases with the "Heart Sign" and Returned Patient Survey

• Definite/Probable NPH	7/21	33.3%
• Possible NPH	10/21	47.6%
• No Clinical Evidence for NPH	4/21	19 %

Clinical Presentation of 21 Patients with "Heart Sign"

• Gait Instability + Dementia	8 cases
• Gait Instability + Urinary Incontinence	2 cases
• Gait Instability + Other*	2 cases
• Gait Instability Only	2 cases
• Dementia Only	1 case
• Encephalopathy	1 case
• No Clinical Evidence for NPH**	4 cases

* 1. Mild Decreased Memory and 2. Dizziness

** 1. Multiple Brain Mets s/p Radiosurgery, 2. Parkinsonism, 3. Ataxia post CVA

CSF Pressure and CSF Flow

CSF Pressure and CSF Flow

May the Force Be With You!