Update on MRI and Mild Traumatic Brain Injury

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Introduction

- Importance of magnetic resonance imaging (MRI) in patients with traumatic brain injury (TBI)

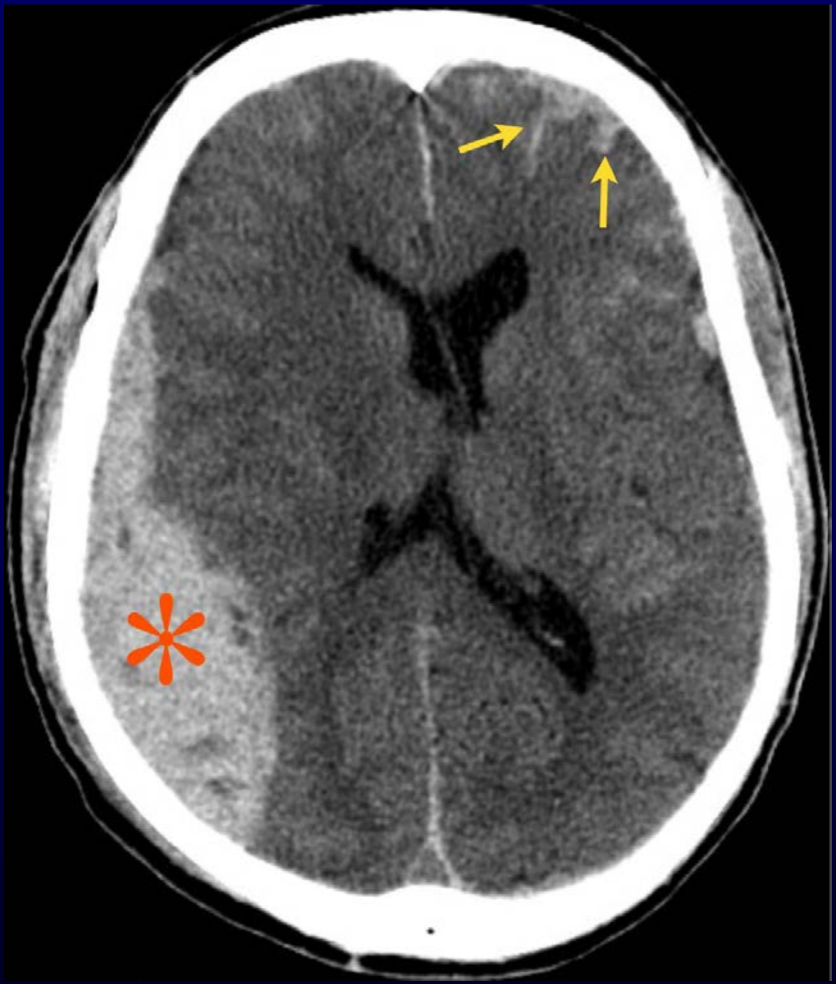
Overview

- History of structural brain imaging
- Modern techniques for measuring MRI brain volume

History of Structural Brain Imaging

- 1970s: Computerized tomography (CT) scans

CT scan: abnormal



CT scan in a patient who fell from a second-story window shows:
- large subdural hematoma (*)
- subarachnoid blood (yellow arrows) .

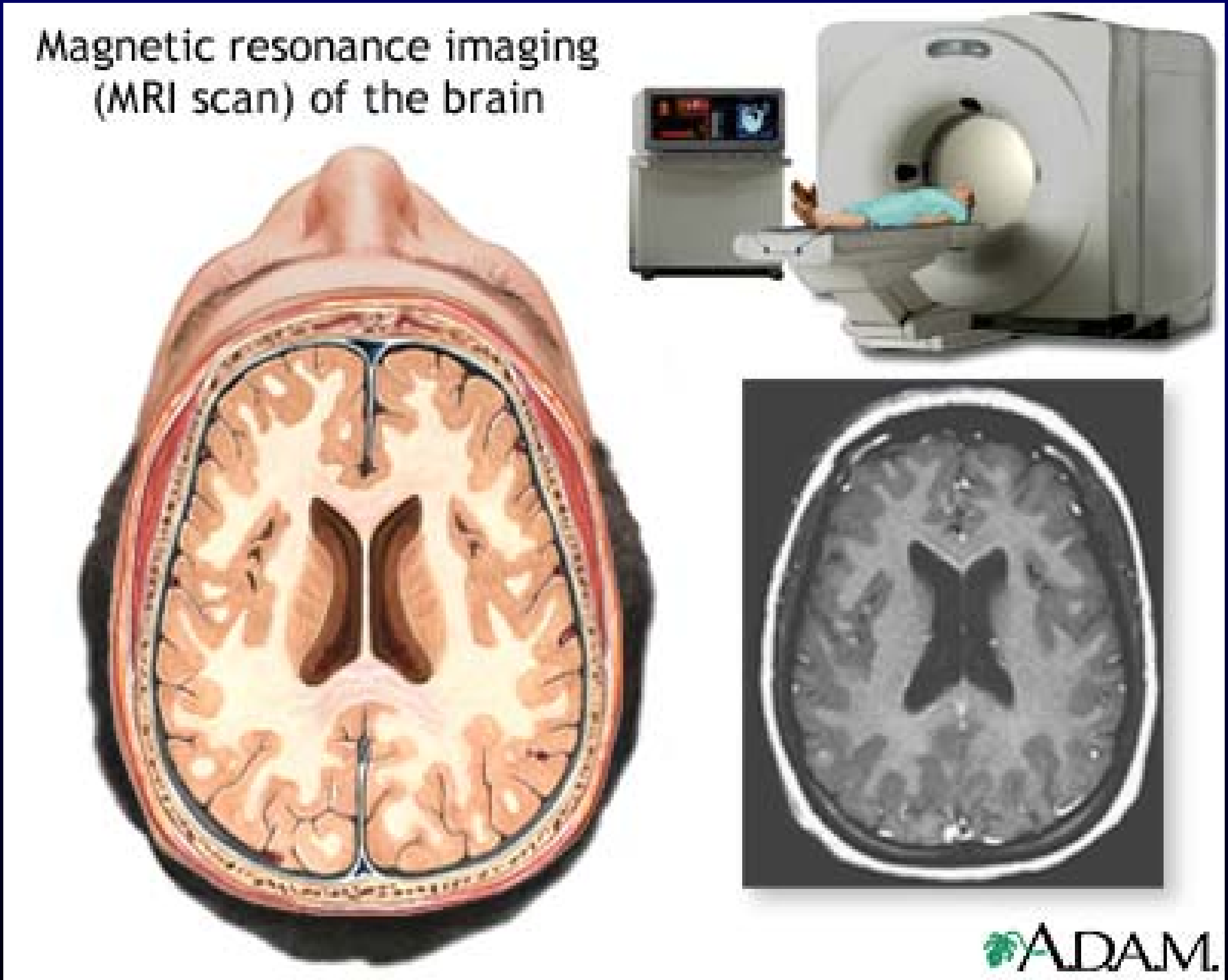
History of Structural Brain Imaging

- 1970s: CT scans
- 1980s: Magnetic resonance imaging (MRI) scans

MRI scan

A patient undergoing an MRI examination of the head.

MRI scanning



MRI in TBI

- Radiologists interpretations are based on simple visual inspection. They typically find:
  - Patients with <u>moderate to severe</u> traumatic brain injury usually have multiple abnormalities on MRI.
  - Patients with <u>mild</u> traumatic brain injury usually have on little to no abnormalities MRI

History of Structural Brain Imaging

- 1970s: CT scans
- 1980s: MRI scans
- 1990s: Brain volume measurement

MRI in TBI

- Summary of MRI brain volumetry through 2000
  - Traumatic brain injury causes brain atrophy.
  - Brain volumetry was performed by human operator with computer assistance.
  - Brain volumetry took about 15 hr per subject/MRI.
  - Brain volumetry was confined to research settings.

References

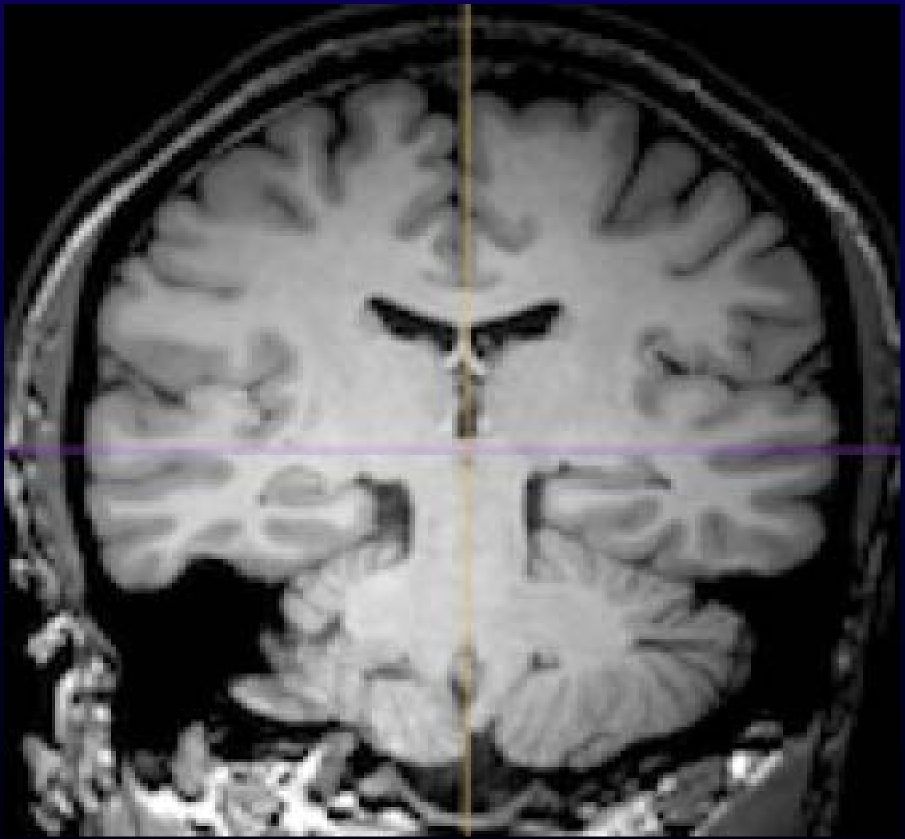
Bigler, E. D. (2005). Structural imaging. Textbook of traumatic brain injury. J. M. Silver, T. W. McAllister and S. C. Yudofsky. Washington, DC, American Psychiatric Publishing, Inc.**:** 79-105.

Bigler, E. D. (2011). Structural imaging. Textbook of Traumatic Brain Injury. J. M. Silver, T. W. McAllister and S. C. Yudofsky. Washington, DC, American Psychiatric Publishing, Inc.**:** 73-90.

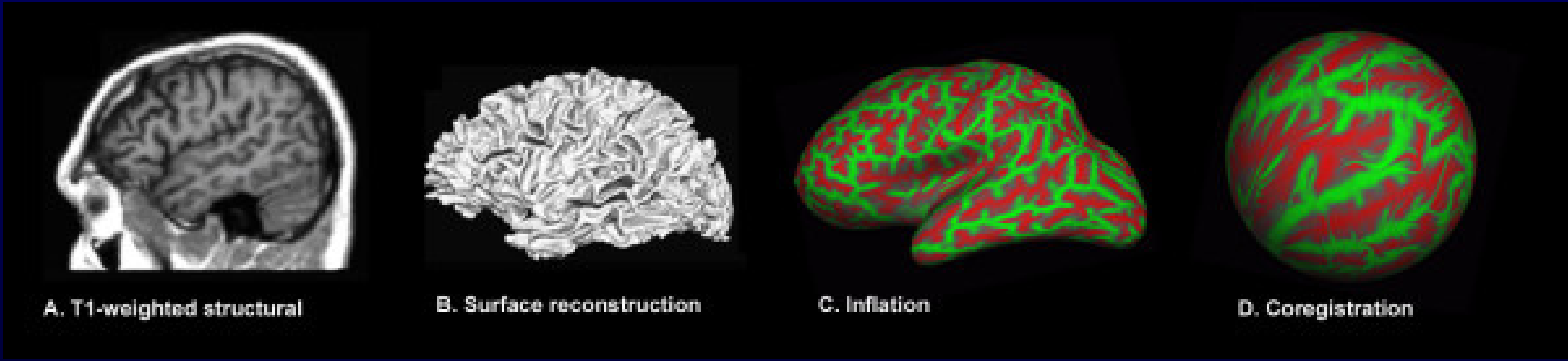
History of Structural Brain Imaging

- 1970s: CT scans
- 1980s: MRI scans
- 1990s: Brain volume measurement
- 2000s: Automated brain volume measurement
  - FreeSurfer

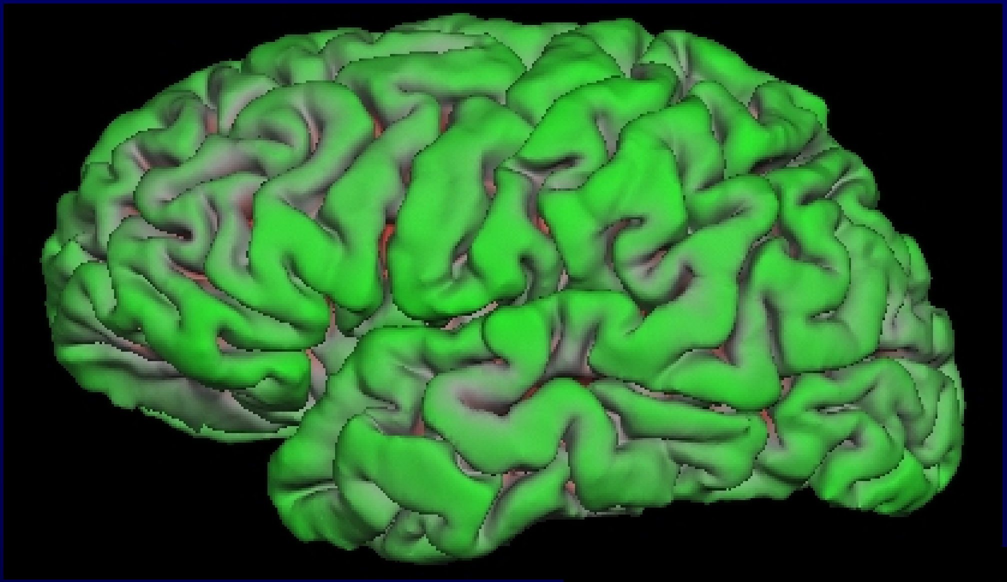
FreeSurfer Methods
Segmentation and Volumetry

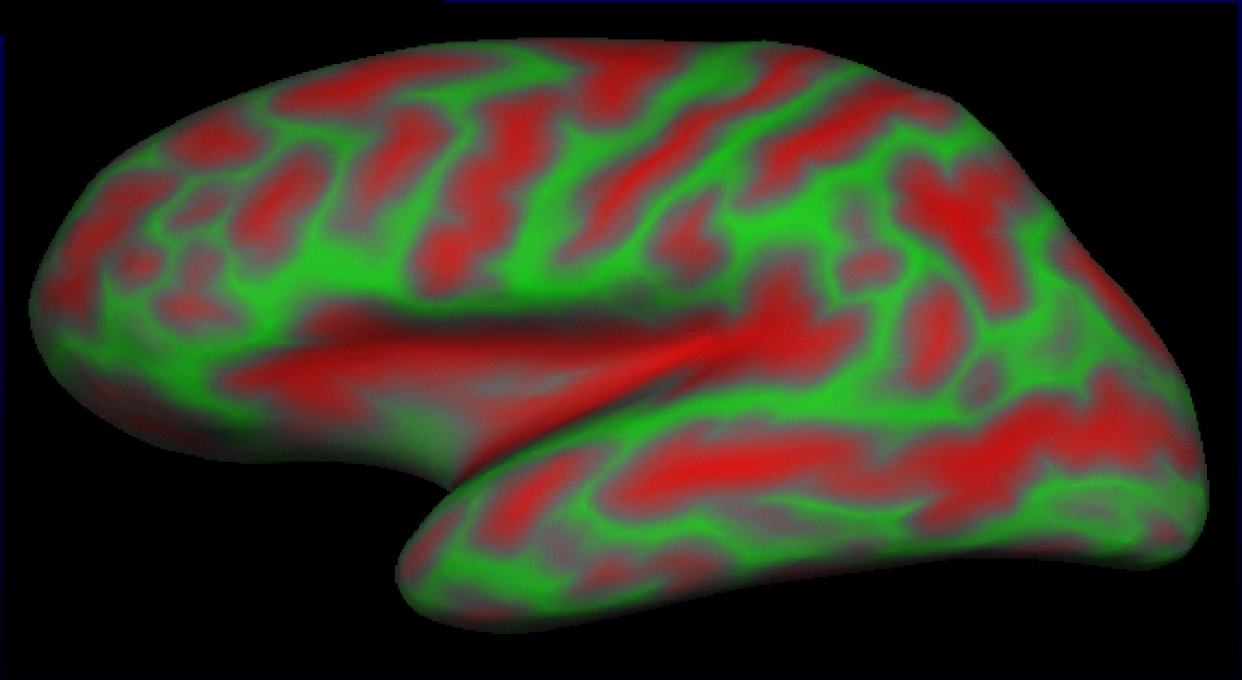


FreeSurfer Methods

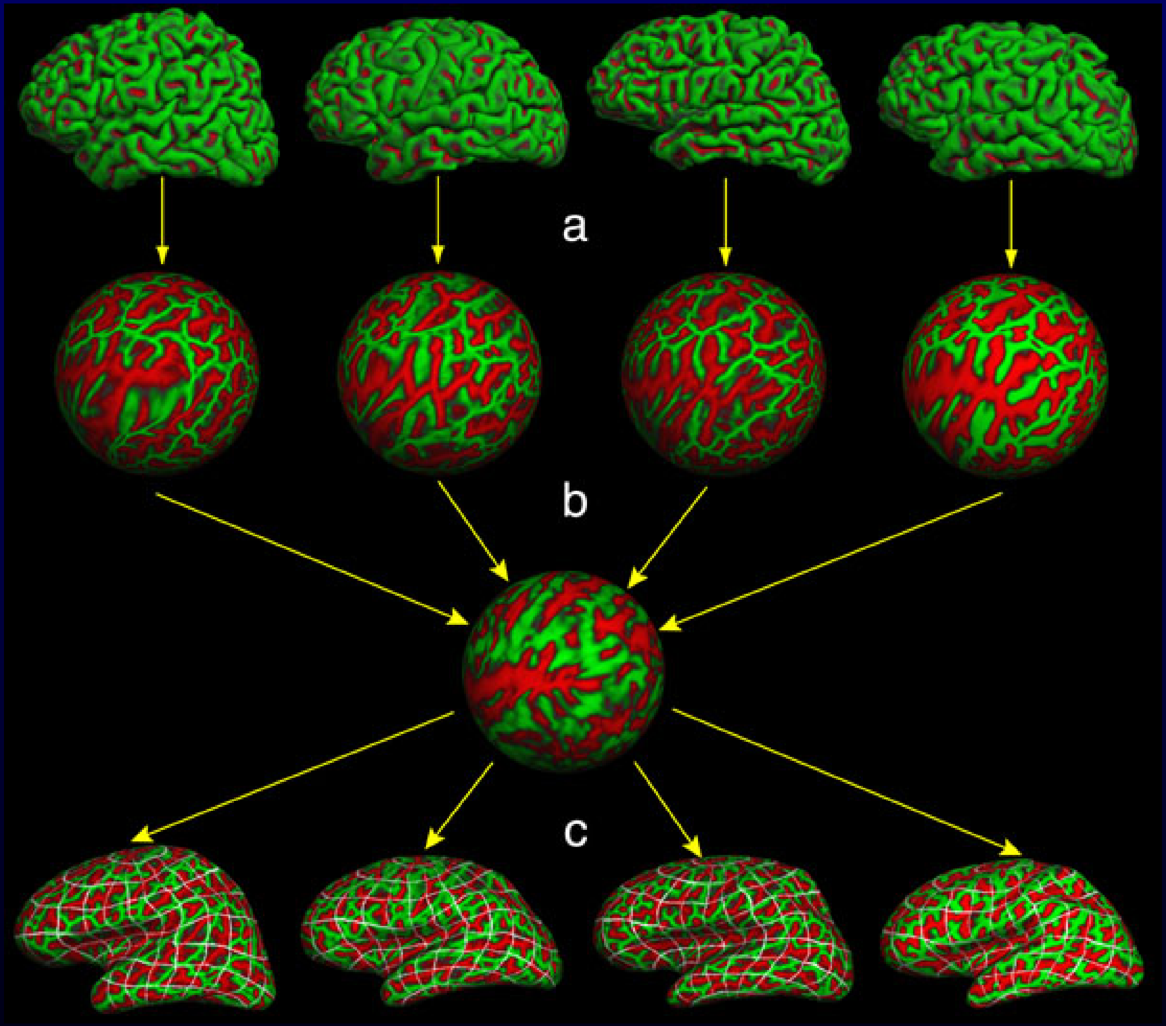


Inflation





FreeSurfer Methods

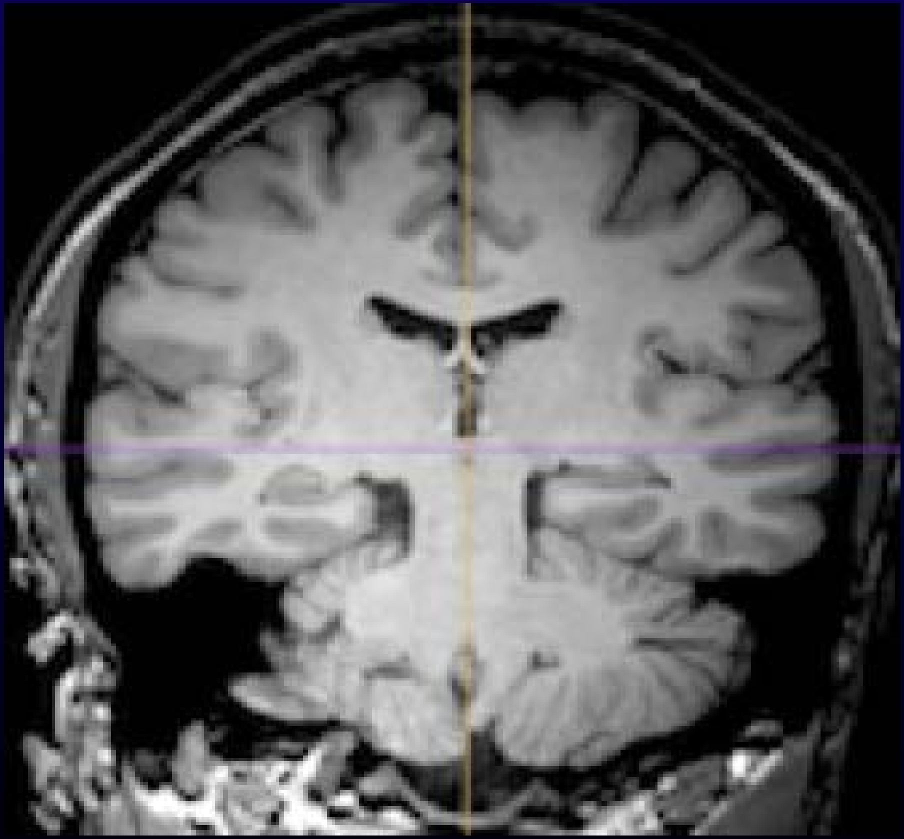


a) Inflation and spherification

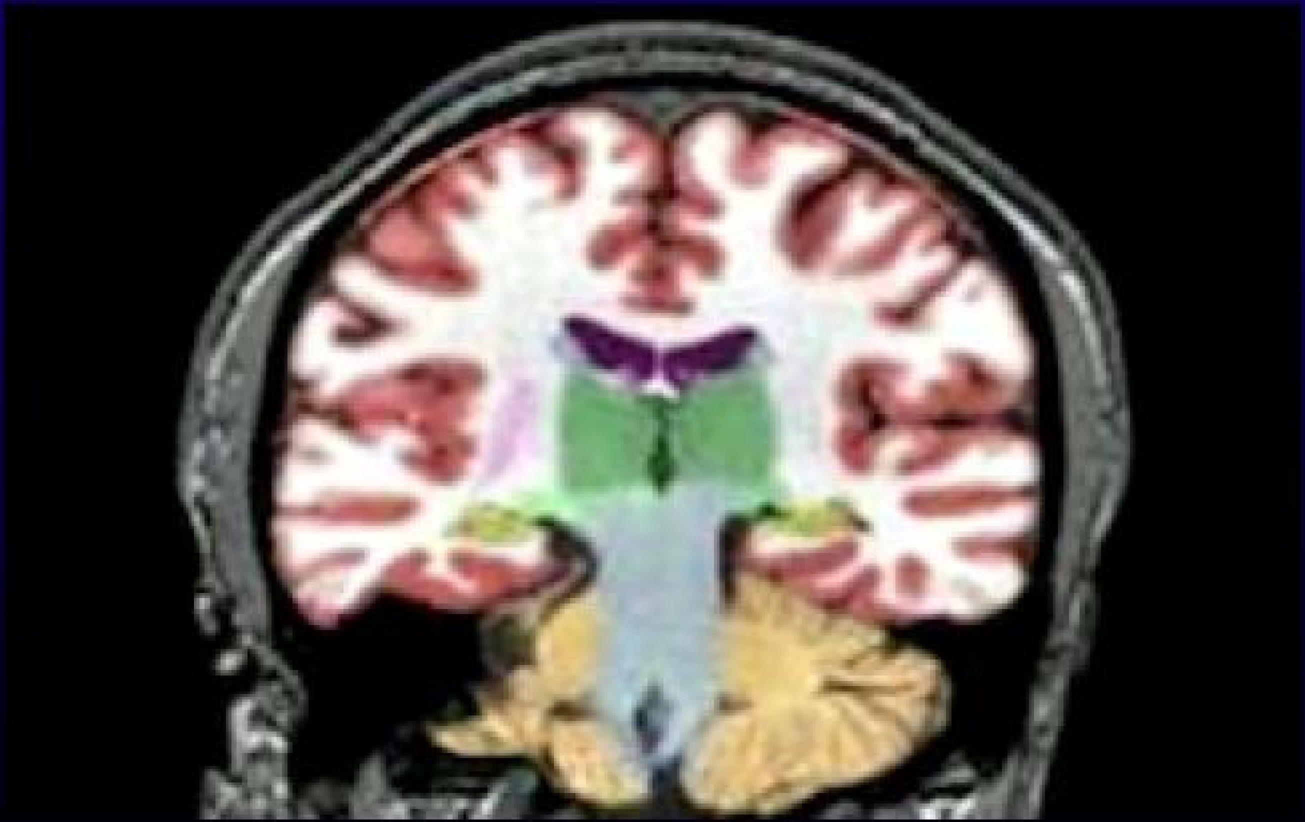
b) Mapping to common space and comparison to brain atlas

c) Return with brain regions mapped

Typical MRI Slice



Segments Differentiated



Automated Brain Volume Measurement

- 2000s: FreeSurfer
  - Limitations
    - Not available for commercial use
    - Restricted to research settings

History of Structural Brain Imaging

- 2000s: Alzheimer's Disease Neuroimaging Initiative
  - Standardized collection of MRI data
  - Online database with normal control MRI data

References
Jack Jr, C. R., M. A. Bernstein, et al. (2008). "The Alzheimer's Disease Neuroimaging Initiative (ADNI): MRI methods." J Magn Reson Imaging **27**(4): 685-691.

History of Structural Brain Imaging

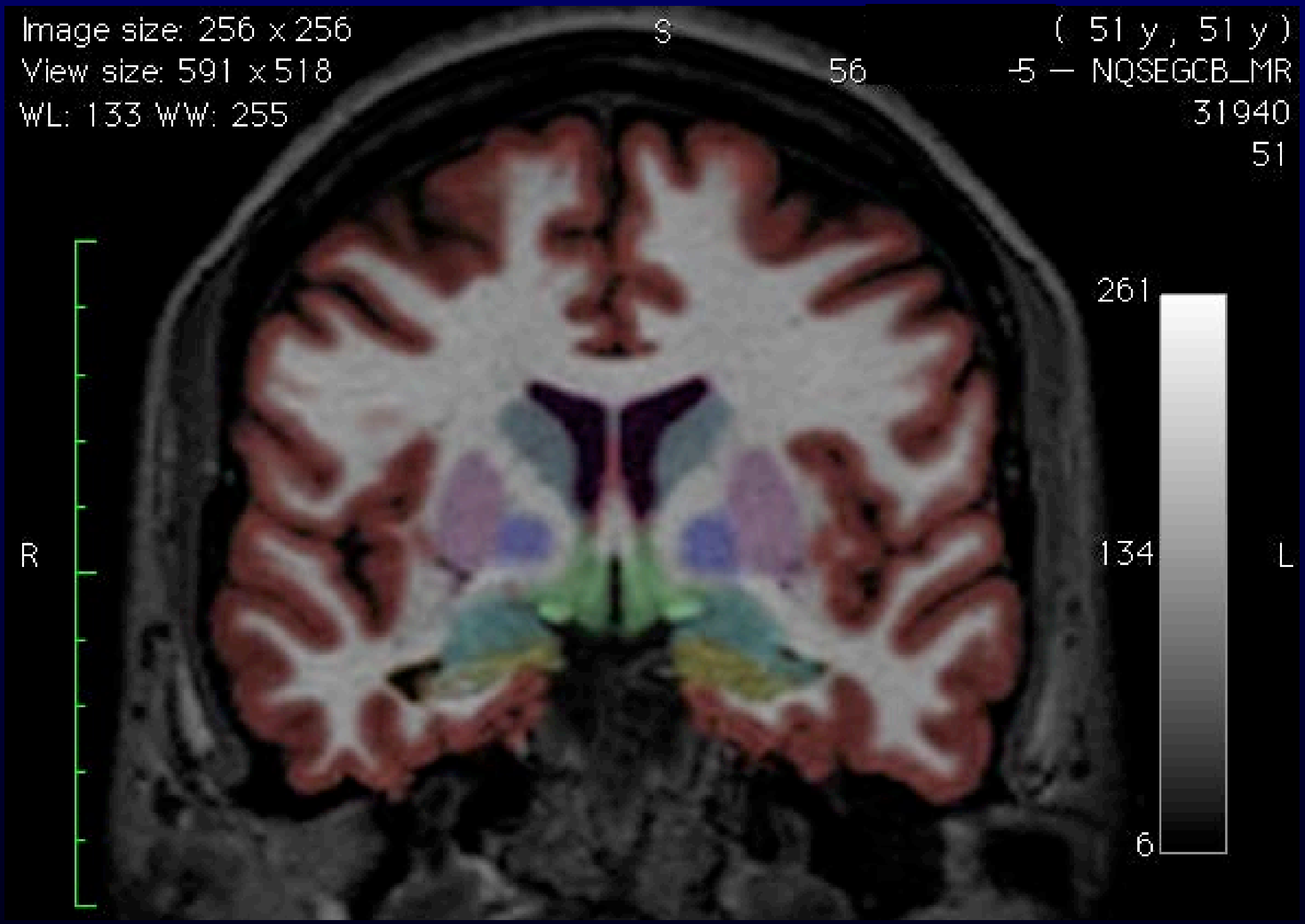
- 1970s: CT scans
- 1980s: MRI scans
- 1990s: Brain volume measurement
- 2000s: Automated brain volume measurement
  - FreeSurfer
  - ADNI
- 2007: NeuroQuant®

History of Structural Brain Imaging

- 2007: NeuroQuant®
  - Developed by CorTechs Labs
  - Based on FreeSurfer
    - Computer-automated analysis of brain MRI volume
  - Commercially available
  - FDA-approved method

References
Birk, S. (2009). "Hippocampal Atrophy: Biomarker for Early AD? : Hippocampal volume in patients with AD is typically two standard deviations below normal." Retrieved 02/25/12, 2012, from http://www.internalmedicinenews.com/index.php?id=2049&type=98&tx_ttnews%5Btt_news%5D=10034&cHash=da03e20e36.
Fischl, B. (2011). "[Freesurfer] general info about FS." Retrieved 02/25/12, 2012, from https://mail.nmr.mgh.harvard.edu/pipermail//freesurfer/2011-March/017501.html.

NeuroQuant® Segmented Brain Image

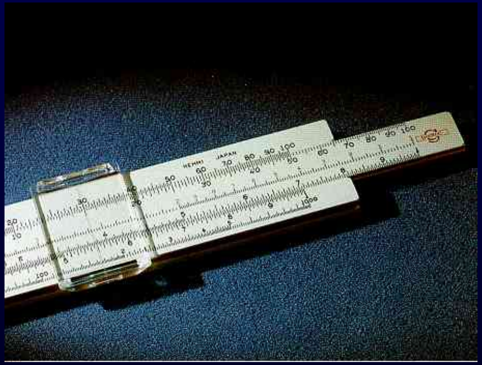


History of Structural Brain Imaging

- 2007: NeuroQuant®
  - FDA-approved method
    - Cleared for marketing by the US FDA [510(k) K061855] as a medical device to measure brain MRI volume in human subjects
    - Highly reliable with the earlier approach based on computer-assisted, manual identification of brain regions
    - “Brain ruler”

Reference
http://www.cortechs.net/products/neuroquant.php

History of Structural Brain Imaging



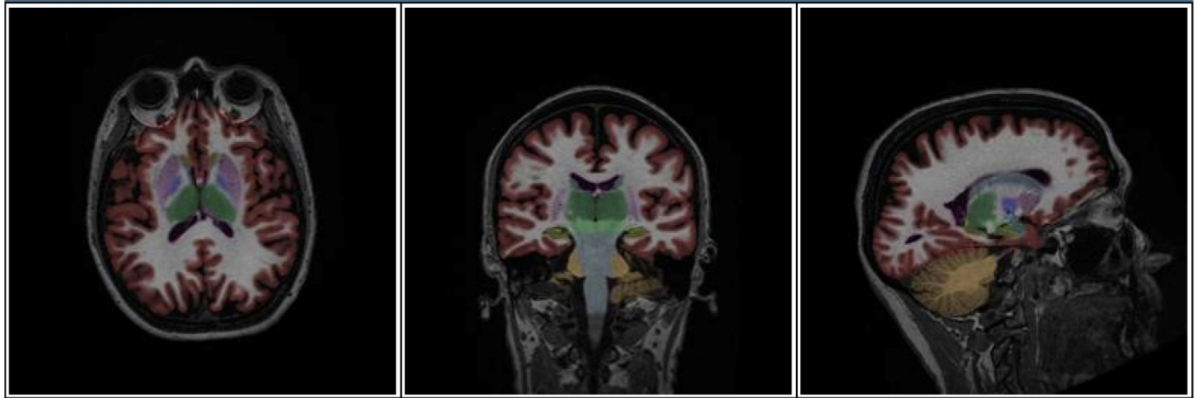
Reference

http://www.cortechs.net/products/neuroquant.php

NeuroQuant® Standard Report
Page 1

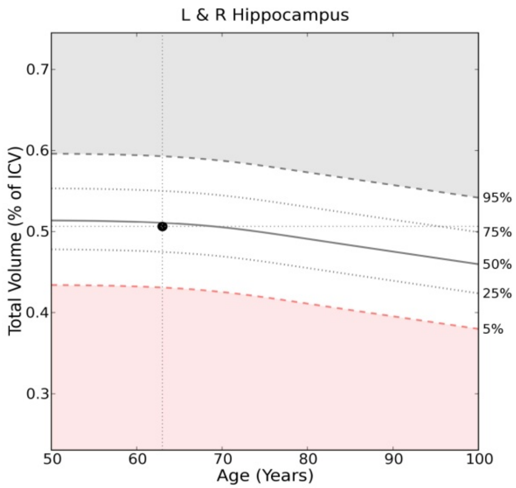
Accession Number:	Referring Physician:	Exam Date:
277625	ROSS, DAVID MD	2010/11/02 12:00:00 AM

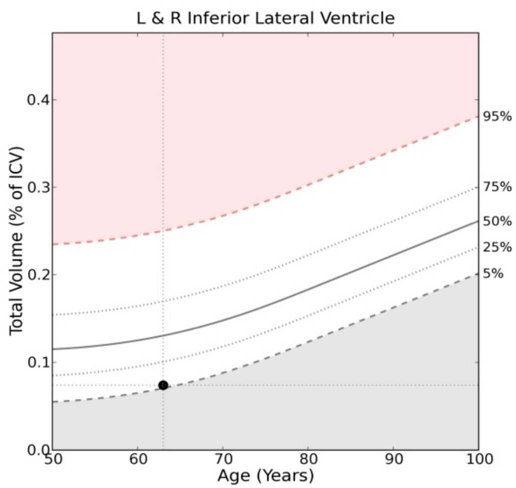
MORPHOMETRY RESULTS



Brain Structure	Volume (cm³)	% of ICV (5%-95% Normative Percentile*)	Normative Percentile*
Hippocampi	7.71	0.51 (0.43-0.59)	47
Lateral Ventricles	18.66	1.23 (0.28-3.36)	41
Inferior Lateral Ventricles	1.13	0.07 (0.07-0.25)	7

AGE-MATCHED REFERENCE CHARTS*





NeuroQuant® Standard Report
Page 2

MORPHOMETRY RESULTS

Brain Structure	LH Volume (cm^3)	LH Volume (% of ICV)	RH Volume (cm^3)	RH Volume (% of ICV)	Asymmetry Index (%)*
Forebrain Parenchyma	530.42	33.41	544.54	34.30	-2.63
Cortical Gray Matter	238.78	15.04	239.66	15.10	-0.37
Lateral Ventricle	11.93	0.75	10.80	0.68	9.91
Inferior Lateral Ventricle	0.75	0.05	0.55	0.03	30.02
Hippocampus	3.98	0.25	4.02	0.25	-0.97
Amygdala	1.98	0.12	1.95	0.12	1.32
Caudate	4.07	0.26	3.67	0.23	10.33
Putamen	5.23	0.33	4.30	0.27	19.55
Pallidum	1.31	0.08	1.32	0.08	-0.83
Thalamus	7.66	0.48	6.95	0.44	9.70
Cerebellum	65.25	4.11	66.08	4.16	-1.25

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

Reliability of NeuroQuant®

- NeuroQuant is reliable with FreeSurfer (Kovacevic, Rafii et al. 2009).
- NeuroQuant® is reliable with a computer-supported manual technique using NeuroMorphometric software (Brewer, Magda et al. 2009).
- The segmentation error rate of NeuroQuant® was found to be very low (9 out of 822) (Heister, Brewer et al. 2011).

Reference

Brewer, J. B., S. Magda, et al. (2009). "Fully-automated quantification of regional brain volumes for improved detection of focal atrophy in Alzheimer disease." Am J Neuroradiol **30**(3): 578-580.

Heister, D., J. B. Brewer, et al. (2011). "Predicting MCI outcome with clinically available MRI and CSF biomarkers." Neurology **77**(17): 1619-1628.

Kovacevic, S., M. S. Rafii, et al. (2009). "High-throughput, Fully Automated Volumetry for Prediction of MMSE and CDR Decline in Mild Cognitive Impairment." Alzheimer Dis Assoc Disord **23**(2): 139–145.

Validity of FreeSurfer

- FreeSurfer is valid in assessing traumatic brain injury
  - Merkley, Bigler et al. 2008
  - Bigler, Abildskov et al. 2010
  - McCauley, Wilde et al. 2010
  - Strangman, O'Neil Pirozzi et al. 2010
  - Warner, Youn et al. 2010
  - Hudak, Warner et al. 2011

References

Bigler, E. D., T. J. Abildskov, et al. (2010). "Diffuse damage in pediatric traumatic brain injury: a comparison of automated versus operator-controlled quantification methods." Neuroimage 50(3): 1017-1026.

Hudak, A., M. Warner, et al. (2011). "Brain morphometry changes and depressive symptoms after traumatic brain injury." Psychiatry Res **191**(3): 160-165.

McCauley, S. R., E. A. Wilde, et al. (2010). "Patterns of cortical thinning in relation to event-based prospective memory performance three months after moderate to severe traumatic brain injury in children." Dev Neuropsychol 35(3): 318-332.

Merkley, T. L., E. D. Bigler, et al. (2008). "Diffuse changes in cortical thickness in pediatric moderate-to-severe traumatic brain injury." J Neurotrauma 25(11): 1343-1345.

Strangman, G. E., T. M. O'Neil_Pirozzi, et al. (2010). "Regional brain morphometry predicts memory rehabilitation outcome after traumatic brain injury." Front Hum Neurosci **4**: 182.

Warner, M. A., T. S. Youn, et al. (2010). "Regionally selective atrophy after traumatic axonal injury." Arch Neurol **67**(11): 1336-1344.

Validity of NeuroQuant®

- NeuroQuant is valid in assessing traumatic brain injury
  - Ross, Ochs et al. 3 articles in press

References

Ross, D. E., A. L. Ochs, et al. (2012). "NeuroQuant® revealed hippocampal atrophy in a patient with traumatic brain injury." Journal of Neuropsychiatry and Clinical Neurosciences **24**: E33.

Ross, D. E., A. L. Ochs, et al. (in press). "Progressive brain atrophy in patients with chronic neuropsychiatric symptoms after mild traumatic brain injury: A preliminary study." Brain Injury.

Ross, D. E., A. L. Ochs, et al. (in press). "Man vs. Machine: Comparison of Radiologists' Interpretations and NeuroQuant® Volumetric Analyses of Brain MRIs in Patients with Traumatic Brain Injury." Journal of Neuropsychiatry and Clinical Neurosciences.

Case example: Patient LK

- History
  - 57 years old
  - MVA on 06/11/09

Ross, D. E., A. L. Ochs, et al. (2012). "NeuroQuant® revealed hippocampal atrophy in a patient with traumatic brain injury." Journal of Neuropsychiatry and Clinical Neurosciences **24**: E33.

Case example: Patient LK

- History
  - 57 years old
  - MVA on 06/11/09
  - Traumatic brain injury (TBI), mild
  - Headaches, neuropathic
  - Muskuloskeletal injuries

Ross, D. E., A. L. Ochs, et al. (2012). "NeuroQuant® revealed hippocampal atrophy in a patient with traumatic brain injury." Journal of Neuropsychiatry and Clinical Neurosciences **24**: E33.

Case example: Patient LK

- 08/01/09: 1.5 Tesla MRI of brain:
  - Radiologist's interpretation:
    - Normal

Ross, D. E., A. L. Ochs, et al. (2012). "NeuroQuant® revealed hippocampal atrophy in a patient with traumatic brain injury." Journal of Neuropsychiatry and Clinical Neurosciences **24**: E33.

Case example: Patient LK

- 08/01/09: 1.5 Tesla MRI of brain:
  - Radiologist's interpretation:
    - Normal
- 03/04/10: 3.0 Tesla MRI of brain:
  - Radiologist's interpretation:
    - Two linear white matter hyperintensities in left frontal lobe subcortically, nonspecific

Ross, D. E., A. L. Ochs, et al. (2012). "NeuroQuant® revealed hippocampal atrophy in a patient with traumatic brain injury." Journal of Neuropsychiatry and Clinical Neurosciences **24**: E33.

Case example: Patient LK

- 08/01/09: 1.5 Tesla MRI of brain:
  - Radiologist's interpretation:
    - Normal
- 03/04/10: 3.0 Tesla MRI of brain:
  - Radiologist's interpretation:
    - Two linear white matter hyperintensities in left frontal lobe subcortically, nonspecific
  - NeuroQuant Standard Analysis:
    - Hippocampal volume = 0.29 % of intracranial volume (less than 1st normative percentile)

Ross, D. E., A. L. Ochs, et al. (2012). "NeuroQuant® revealed hippocampal atrophy in a patient with traumatic brain injury." Journal of Neuropsychiatry and Clinical Neurosciences **24**: E33.

Patient LK: NeuroQuant Standard Analysis

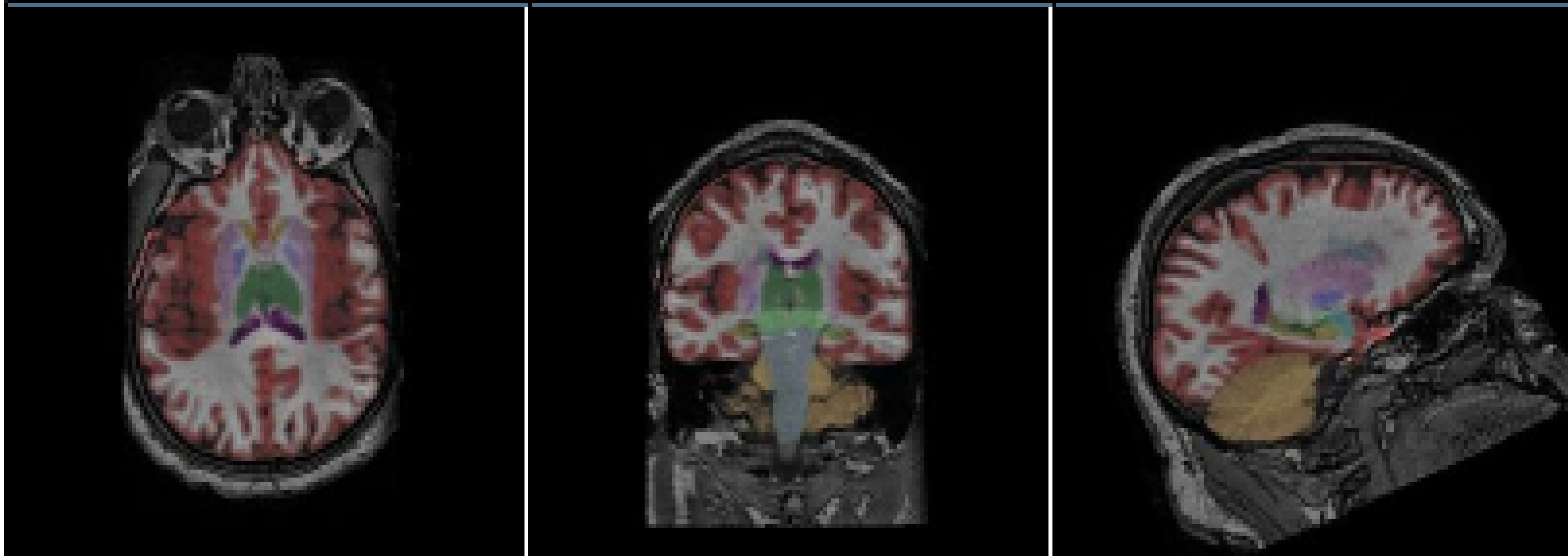
NeuroQuant®
Age-Related Atrophy Report

Virginia Institute of Neuropsychiatry
324 Branns Hill Ct
Midlothian, Va. 23114
Toni Hughes

PATIENT INFORMATION

Patient ID:	Patient Name:	Sex: M
Accession Number:	Referring Physician: ROSS DAVID MD	Exam Date: 2010/03/04 12:00:00 AM

MORPHOMETRY RESULTS



Brain Structure	Volume (cm^3)	% of ICV (5%-95% Normative Percentile*)	Normative Percentile*
Hippocampi	4.37	0.29 (0.43-0.60)	< 1
Lateral Ventricles	11.99	0.80 (0.03-3.11)	34
Inferior Lateral Ventricles	2.30	0.15 (0.06-0.24)	74

NeuroQuant® Extended Analysis

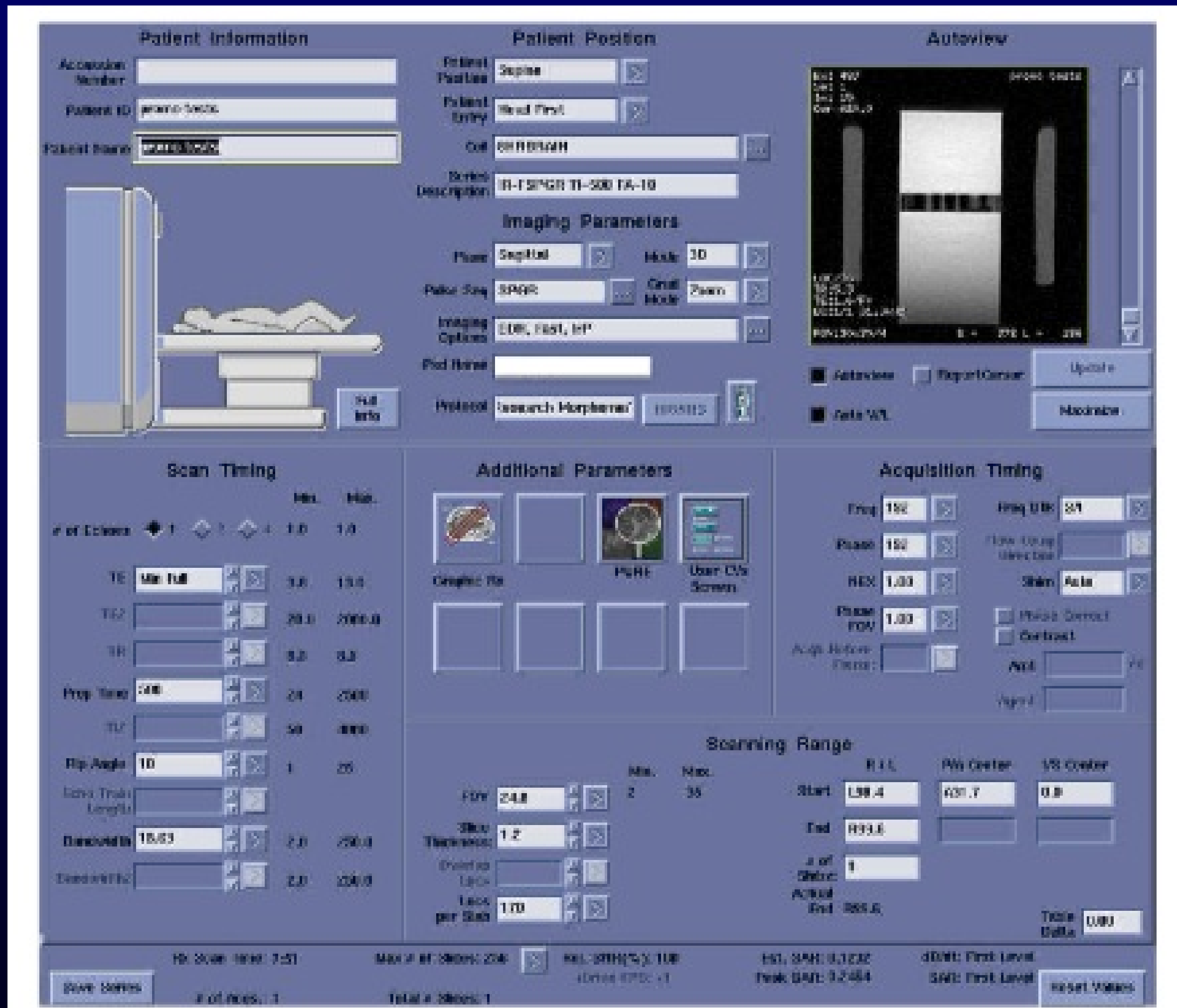
- Developed at VIN
- Compares data to normal controls
  - Alzheimer's Disease Neuroimaging Initiative (ADNI) database (Jack et al)
  - 20 normal control subjects (10 men, 10 women)
  - Age: 68.3 yr (mean), 60.0 -71.5 yr (range)
- 15 brain regions compared to normal controls
- All patients compared to normal controls, even patients less than 50 years old

Jack Jr CR, Bernstein MA, Fox NC, Thompson P, Alexander G, Harvey D, et al (2008): The Alzheimer's Disease Neuroimaging Initiative (ADNI): MRI methods. *J Magn Reson Imaging* 27:685-691.

Experience with NeuroQuant® at the Virginia Institute of Neuropsychiatry

- Over 100 NeuroQuant® analyses since 2010.
- Quality control
    - Prior to data collection, communicate with radiology center
        - NQ website: "NeuroQuant-Compatible MRI Scanners Setup"

Experience with NeuroQuant® at the Virginia Institute of Neuropsychiatry



Example of scanner setup from NQ website:
"NeuroQuant-Compatible MRI Scanners Setup"

Experience with NeuroQuant® at the Virginia Institute of Neuropsychiatry

- Quality control
  - Prior to data collection, communicate with radiology center
  - NeuroQuant® software automatically checks several parameters
  - Visual inspection of each set of segmented brain images
  - Inspection of the numerical and statistical results of the analyses

NeuroQuant® Extended Report:

Example of p. 1

Virginia Institute of Neuropsychiatry

Extended Volumetric Analysis based on NeuroQuant® data

Patient: Location of MRI

Date of MRI: Date of report:

Region	LH Volume (% of ICV)	%tile rank	RH Volume (% of ICV)	%tile rank	Asym-metry Index %	%tile rank
Whole Brain Parenchyma	35.732%	47.1%	35.450%	26.0%	0.791%	96.4% *
Forebrain Parenchyma	30.580%	37.4%	30.270%	17.1%	1.019%	97.4% *
Cortical Gray Matter	15.402%	72.9%	15.581%	71.6%	-1.158%	54.2%
Cerebral White Matter	13.473%	17.4%	12.955%	4.7% *	3.918%	100.0% *
Lateral Ventricle	1.514%	88.4%	1.680%	95.2% *	-10.370%	22.8%
Inferior Lateral Ventricle	0.225%	100.0% *	0.146%	99.9% *	42.688%	96.8% *
Total CSF	1.880%	93.3%	2.065%	96.8% *	-9.344%	35.1%
Caudate	0.270%	64.3%	0.262%	46.2%	3.052%	87.8%
Putamen	0.318%	47.1%	0.274%	15.6%	14.866%	91.4%
Pallidum	0.041%	10.5%	0.060%	37.2%	-37.405%	1.4% *
Thalamus	0.518%	36.0%	0.475%	5.0% *	8.622%	94.9%
Amygdala	0.105%	23.7%	0.113%	43.8%	-7.521%	25.0%
Hippocampus	0.191%	0.3% *	0.255%	36.6%	-28.811%	0.1% *
Cerebellum	4.488%	87.0%	4.397%	84.7%	2.061%	66.3%
Brain Stem	0.663%	6.0%	0.783%	12.8%	-16.573%	27.8%

	L+R Volume (% of ICV)	%tile rank
Whole Brain Parenchyma (L+R)	71.181%	35.5%

Virginia Institute of Neuropsychiatry

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(866) 586-8977 (fax)
www.VaNeuropsychiatry.org

Patient information

DOB :

NeuroQuant® Extended Report:

Example of p. 1: Zoom in

Virginia Institute of Neuropsychiatry

Extended Volumetric Analysis based on NeuroQuant® data

Patient:

Location of MRIs:

Date of MRI:

Date of report:

Region	LH Volume (% of ICV)	%tile rank	RH Volume (% of ICV)	%tile rank	Asym-metry Index %	%tile rank
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NeuroQuant® Extended Report:

Example of p. 1: Zoom in

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Whole Brain Parenchyma (L+R)	L+R Volume (% of ICV)	%tile rank
	71.181%	35.5%

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www.VaNeuropsychiatry.org

Patient information

DOB :

NeuroQuant®
Extended Report:

Example of p. 2

Virginia Institute of Neuropsychiatry

<u>Note</u>: LH = left hemisphere. RH = right hemisphere. %tile = normative percentile. AI = Asymmetry Index.

"—" indicates that the data were unreliable due to segmentation error.

"*" indicates a normative percentile which was statistically and clinically significant, defined as any of the following:

- A parenchymal region ≤ 5th normative percentile, consistent with atrophy
- A ventricular region ≥ 95th normative percentile, consistent with atrophy of the surrounding parenchyma
- Asymmetry index ≤ 2.5th or ≥ 97.5th normative percentile, consistent with atrophy of the smaller structure
- Asymmetry index ≤ 5th or ≥ 95th normative percentile for cases in which there were other unilateral, homodirectional signs of head or brain injury, including:
  - scalp contusions or lacerations
  - cranial fractures
  - unilateral brain abnormalities identified by the attending radiologist which are consistent with or associated with parenchymal atrophy
  - a second asymmetry index ≤ 5th or ≥ 95th normative percentile and homodirectional with the first asymmetry index

<u>Inspection for image segmentation quality</u>: NeuroQuant® segmented (color-coded) DICOM images were inspected visually by A.L.O. and D.E.R. The following segmentation errors were identified:

- None

Otherwise, the regions of interest were found to be accurately identified by the NeuroQuant® software.

<u>Summary of positive findings</u>: Abnormal volumes consistent with parenchymal atrophy were found in the following regions:

- The right whole brain parenchyma was significantly smaller than the left.
- The right forebrain parenchyma was significantly smaller than the left.
- The right cerebral white matter was significantly smaller than normal and was significantly smaller than the left.
- The right lateral ventricle was abnormally large.
- Both inferior lateral ventricles were abnormally large.
- The left inferior lateral ventricle was significantly larger than the right.
- The right total cerebral spinal fluid volume was abnormally large.
- The left pallidum was significantly smaller than the right.
- The right thalamus was abnormally small.
- The left hippocampus was abnormally small and significantly smaller than the right.

NeuroQuant® Extended Report: Example of p. 2: Zoom in

Virginia Institute of Neuropsychiatry

Note: LH = left hemisphere. RH = right hemisphere. %tile = normative percentile. AI = Asymmetry Index.

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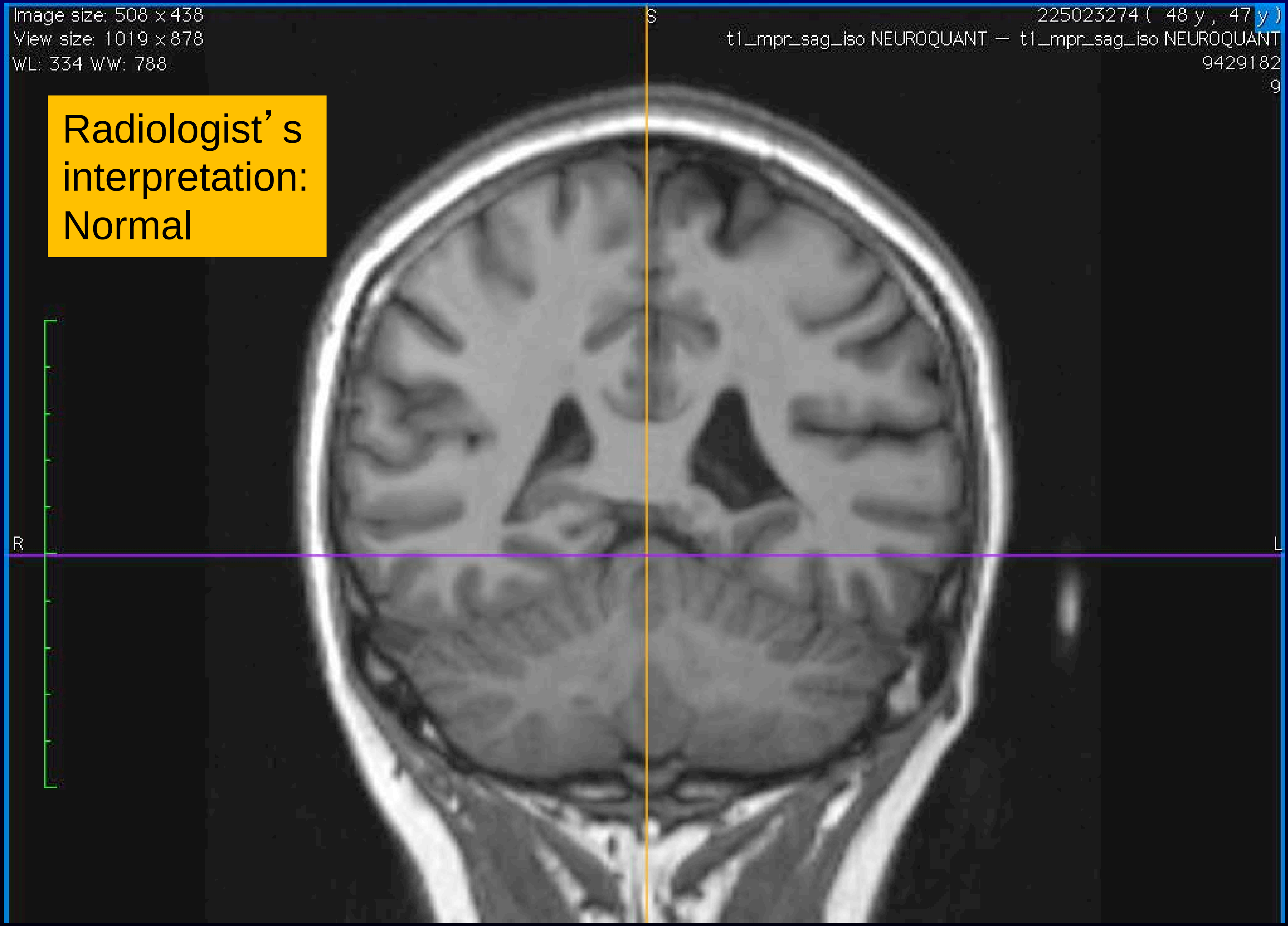
- The right cerebral white matter was significantly smaller than normal and was significantly smaller than the left.
- The right lateral ventricle was abnormally large.
- Both inferior lateral ventricles were abnormally large.
- The left inferior lateral ventricle was significantly larger than the right.
- The right total cerebral spinal fluid volume was abnormally large.
- The left pallidum was significantly smaller than the right.
- The right thalamus was abnormally small.
- The left hippocampus was abnormally small and significantly smaller than the right.

Case example: Patient KM

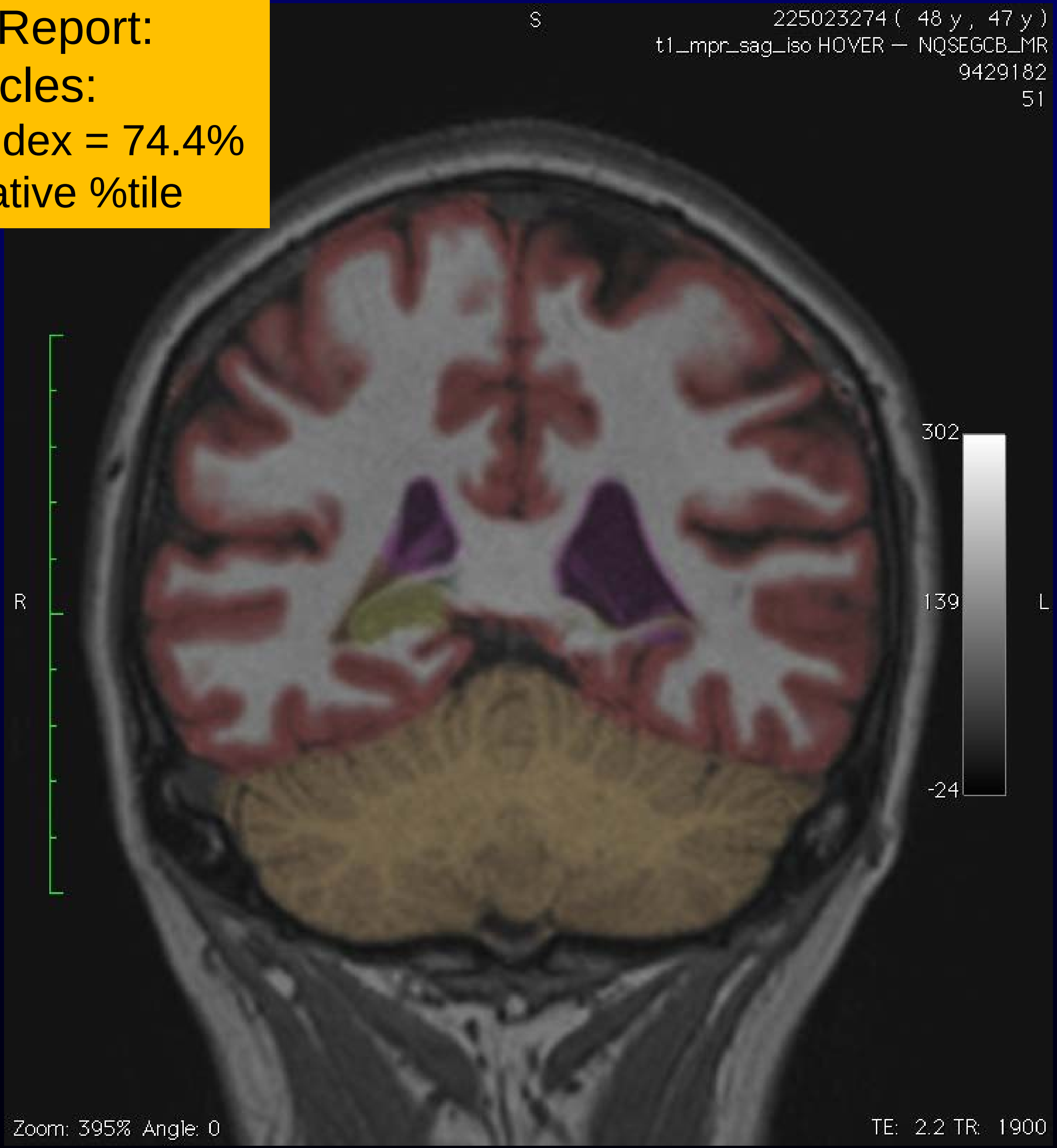
- History
  - 46 years old
  - Motor vehicle accident
- Diagnoses
  - Traumatic brain injury, mild
    - Cognitive impairment
    - Dysphoria
    - Impaired sleep and wakefulness

Case example: Patient KM



Case example: Patient KM

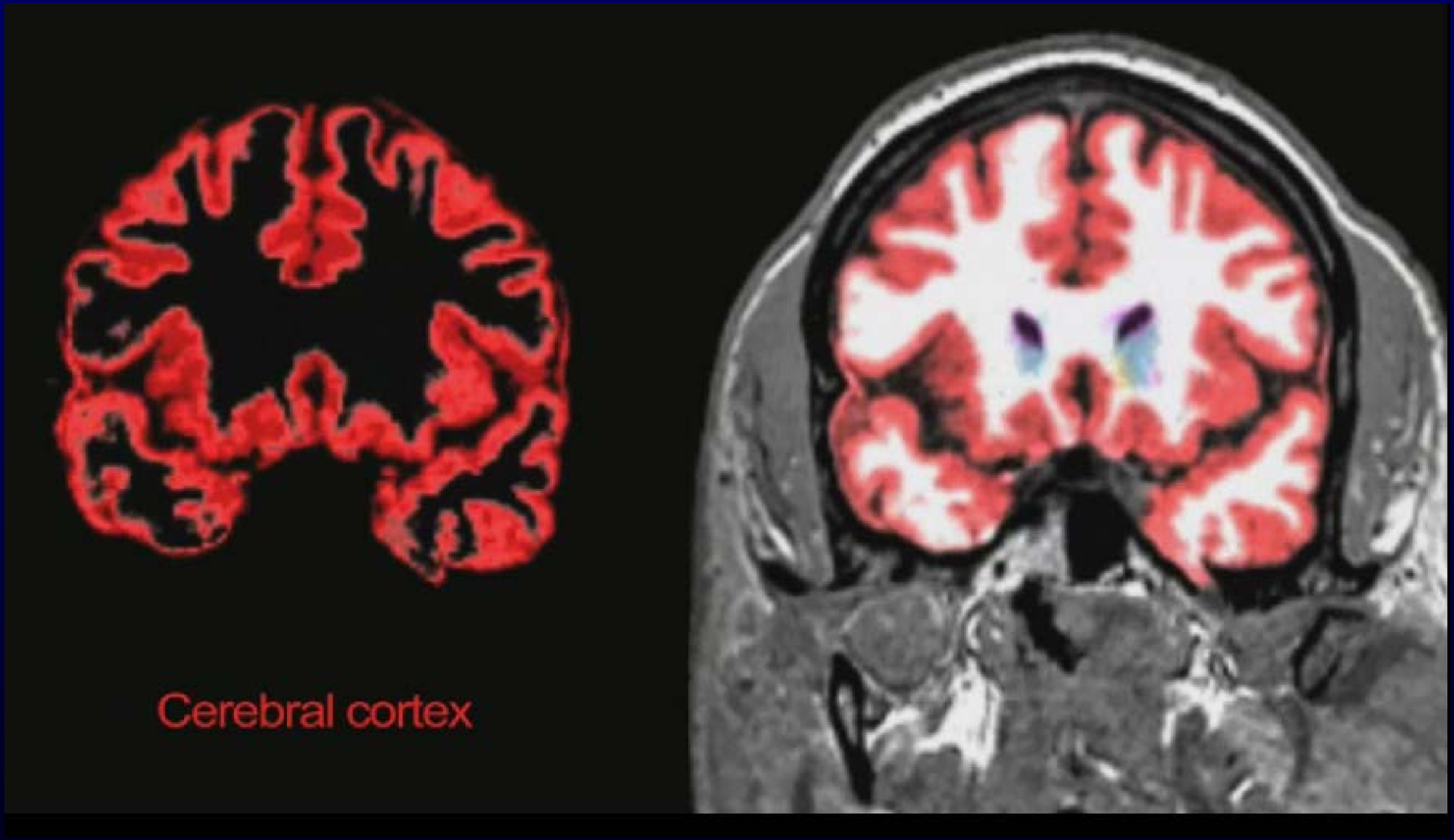
NQ Extended Report:
Lateral ventricles:
Asymmetry index = 74.4%
100.0 normative %tile



NeuroQuant Illustrations

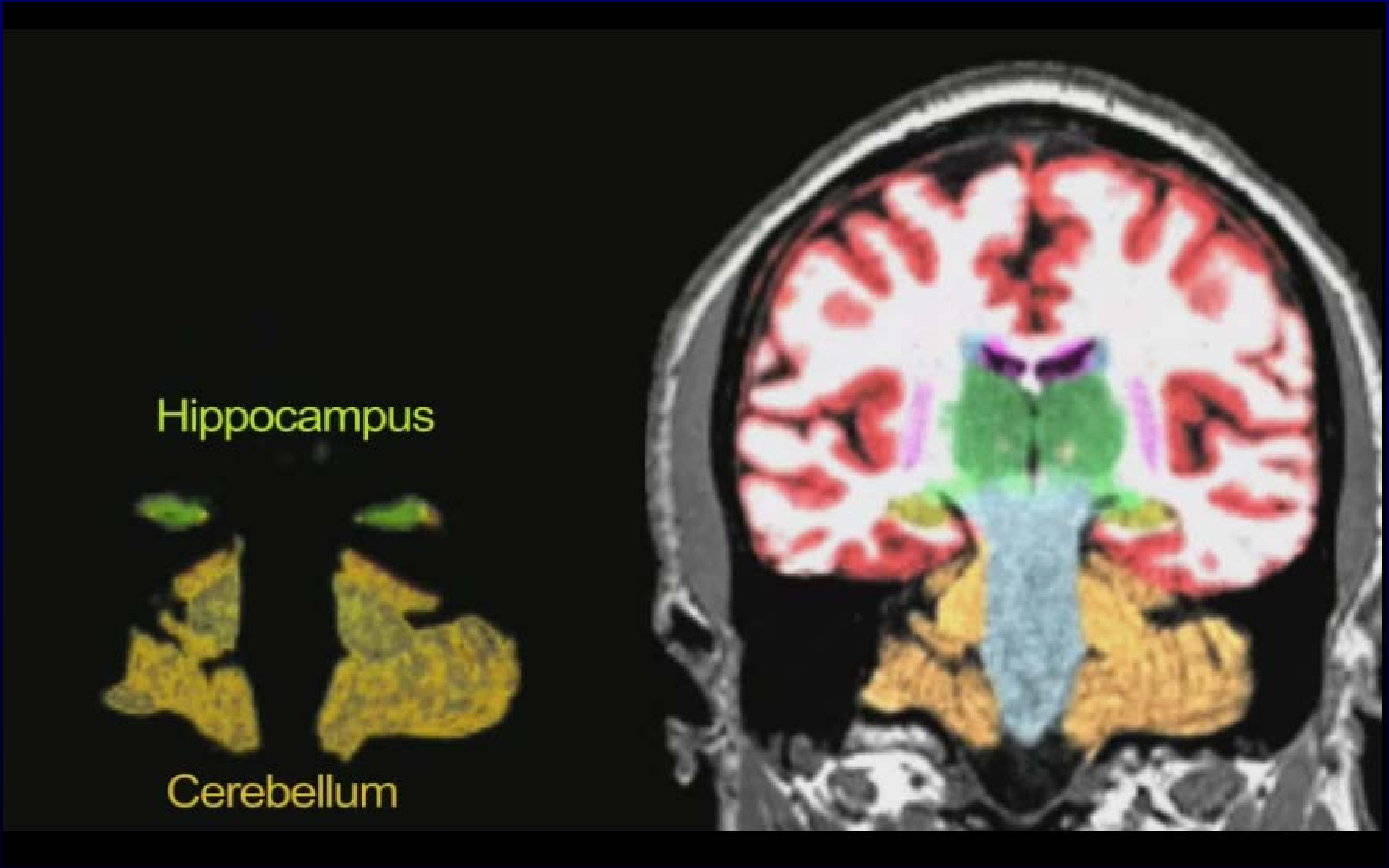
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

NeuroQuant® Illustrations



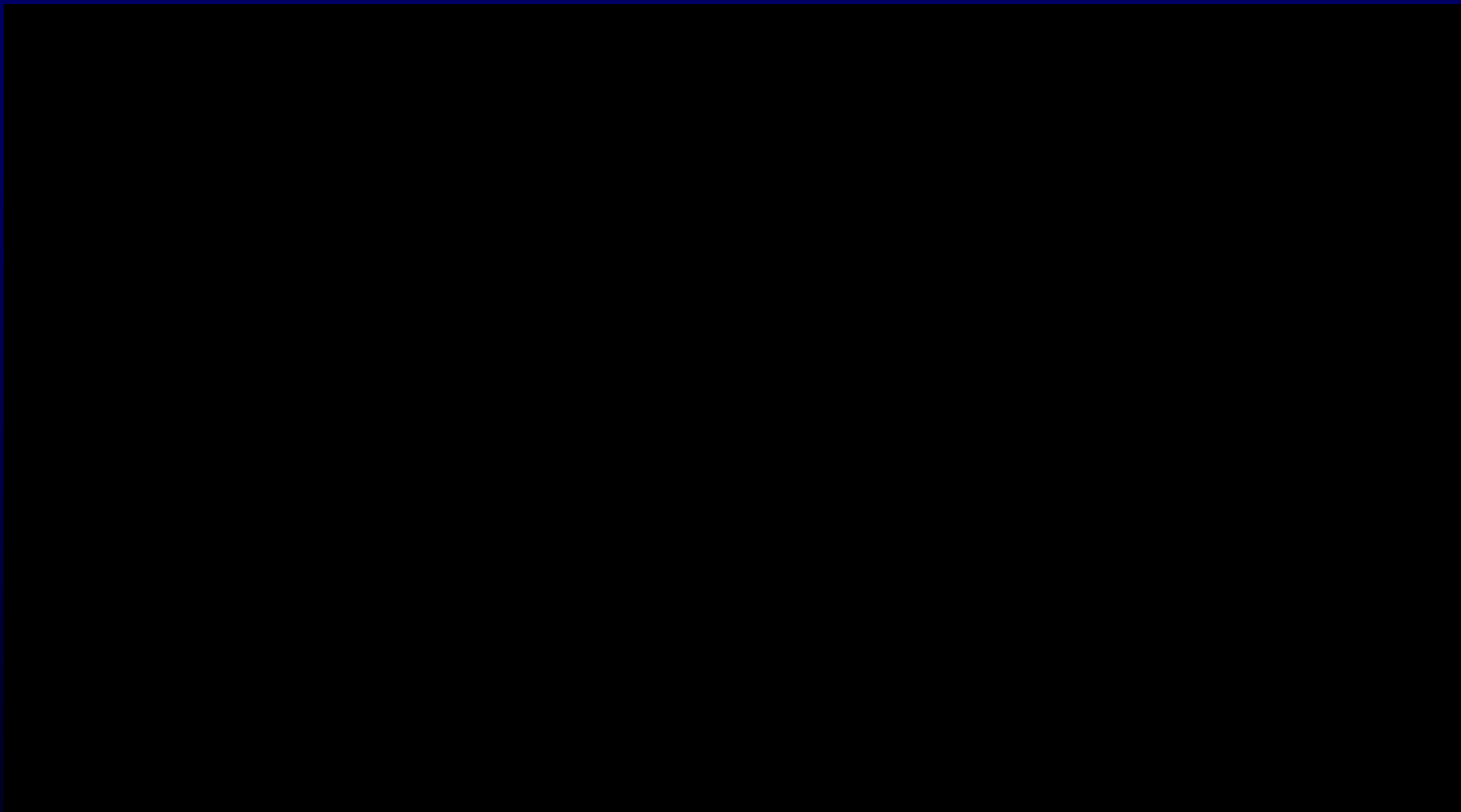
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

NeuroQuant® Illustrations



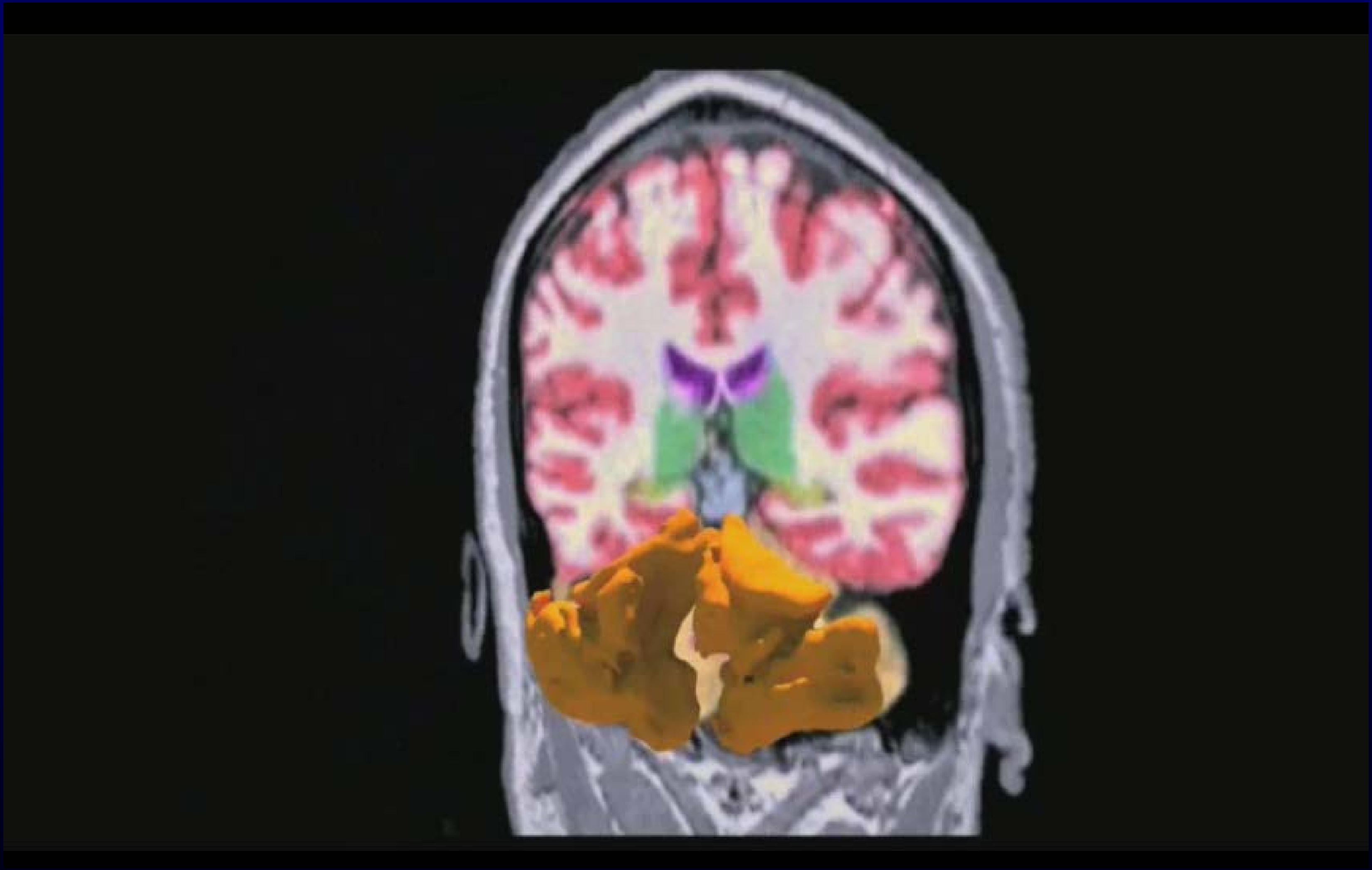
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

NeuroQuant Illustrations



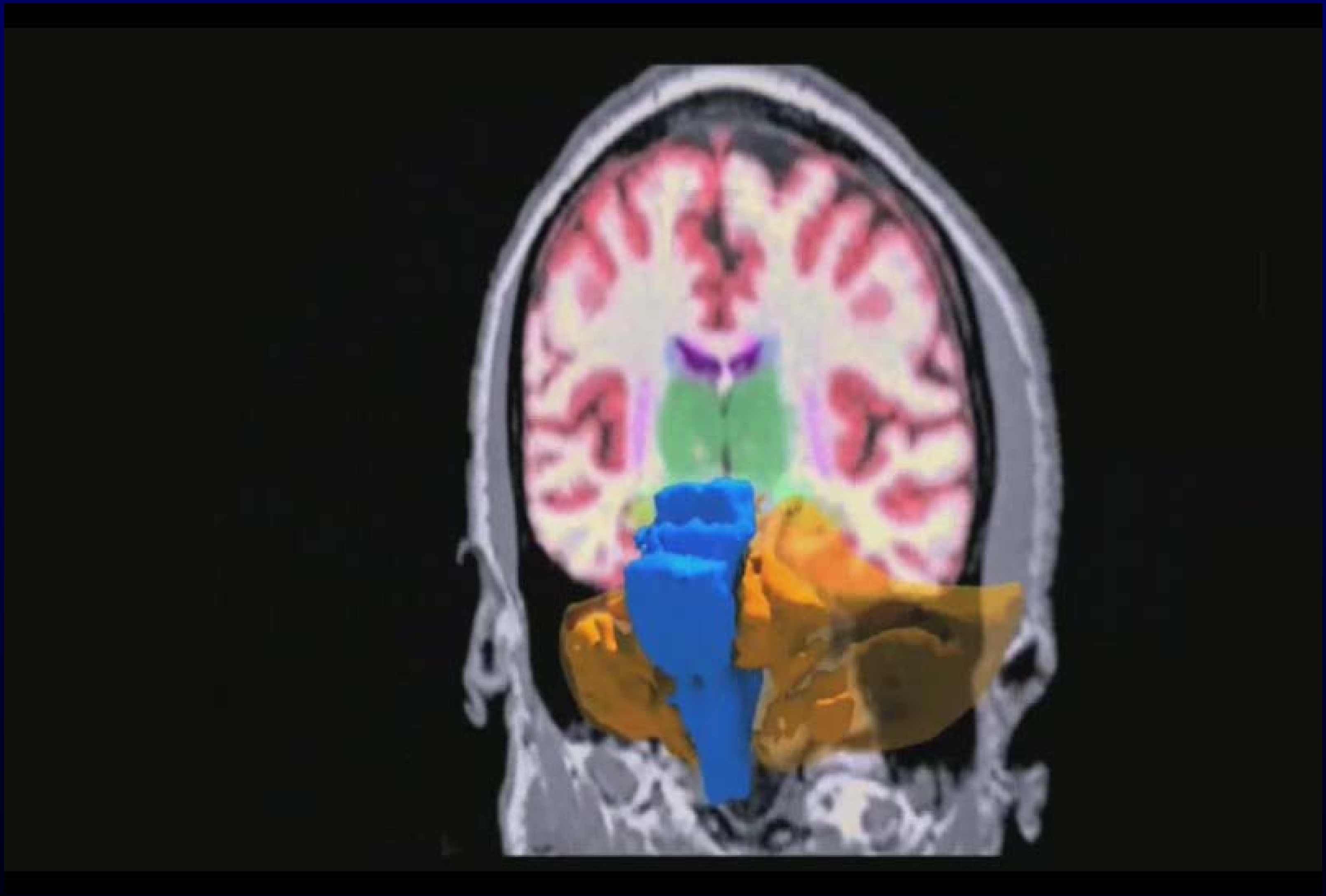
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

NeuroQuant® Illustrations



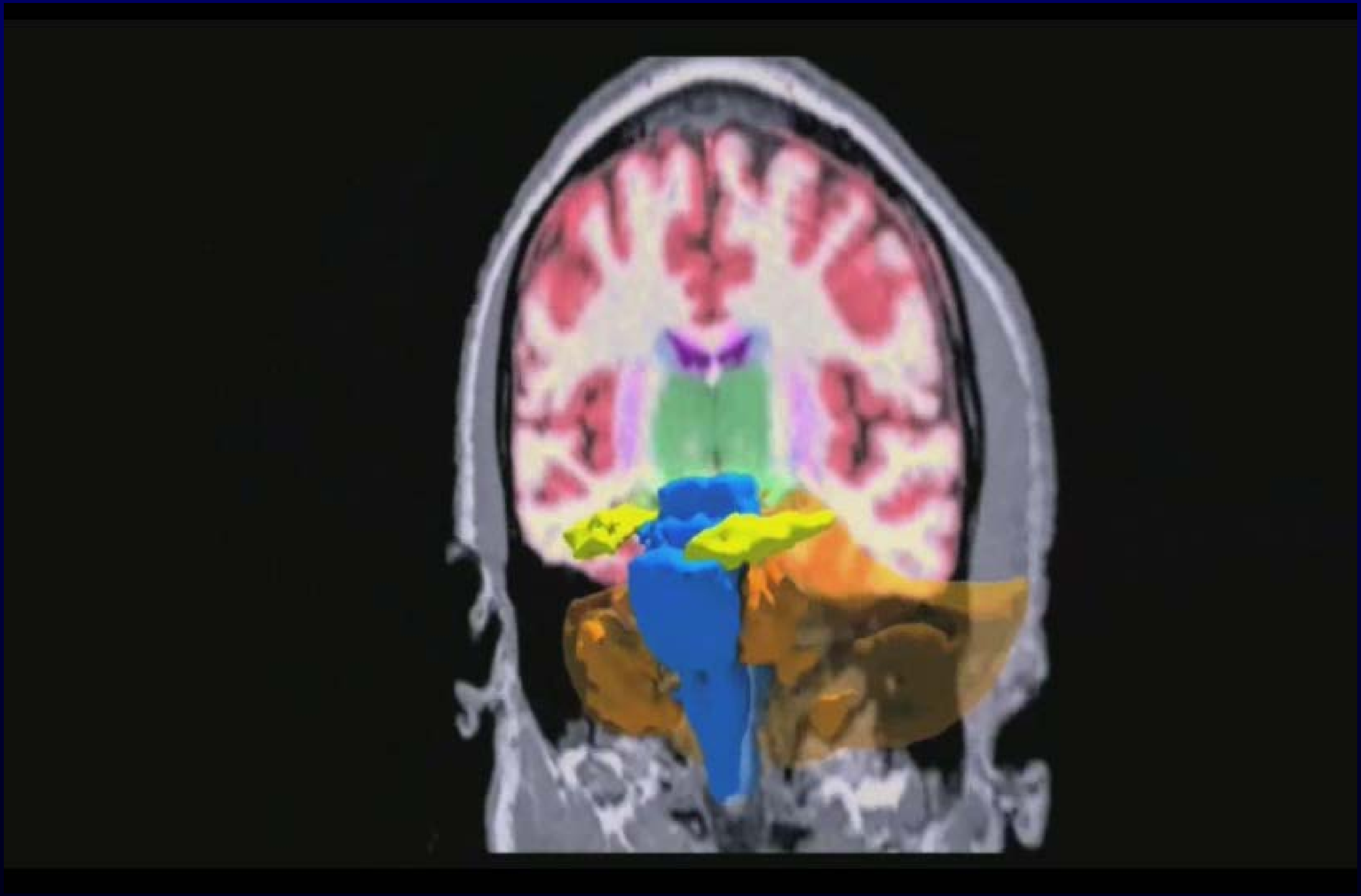
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

NeuroQuant® Illustrations



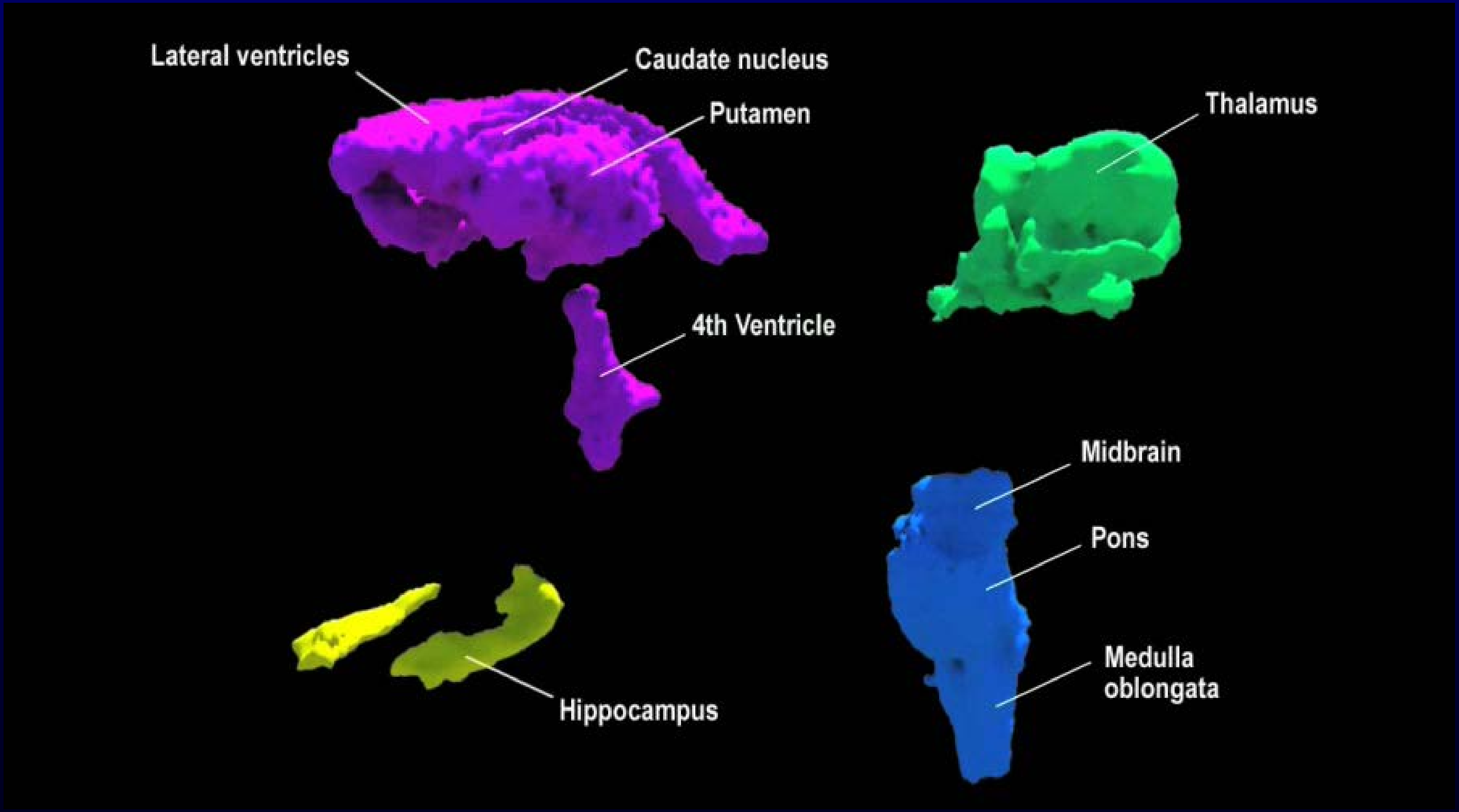
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

NeuroQuant® Illustrations



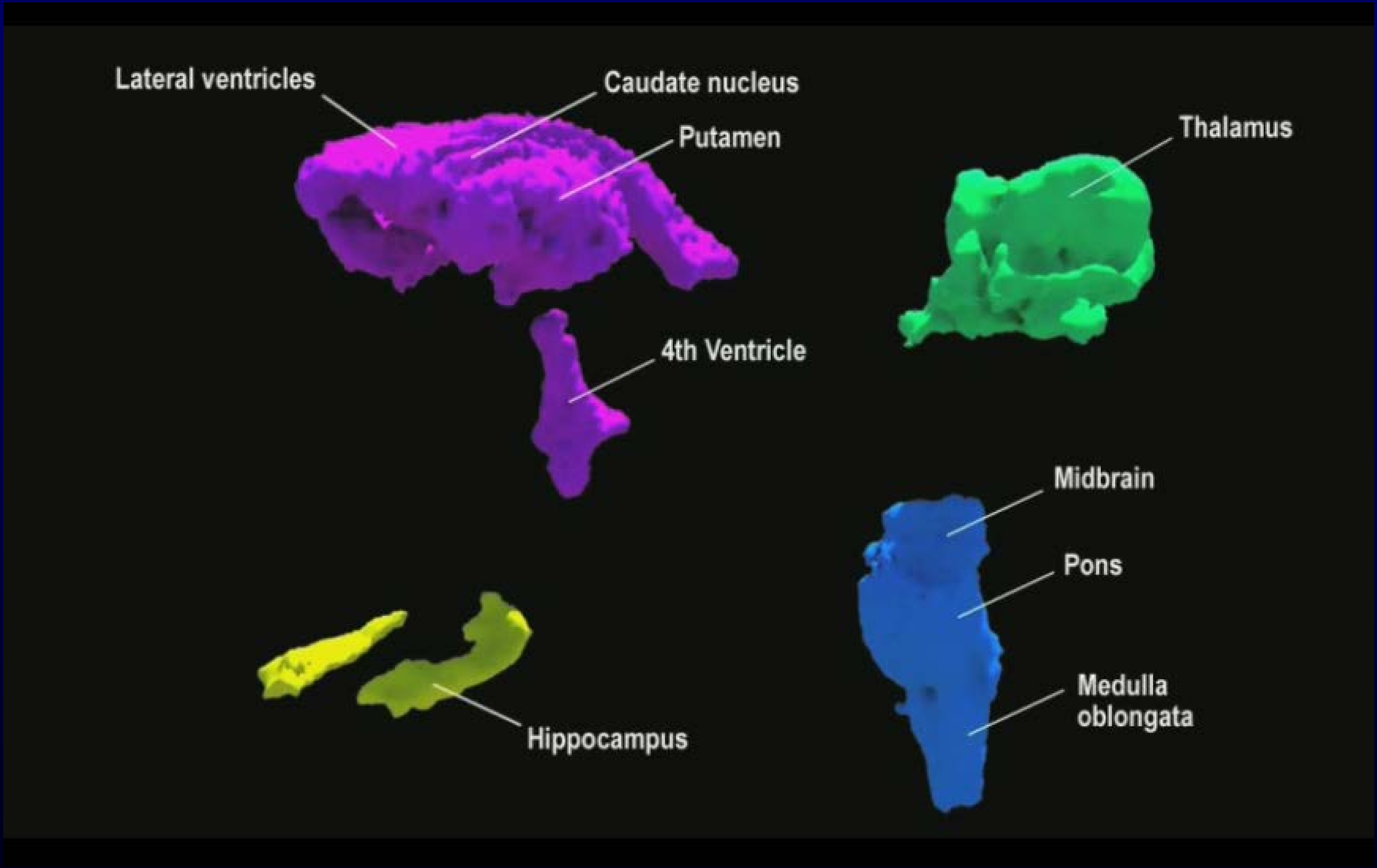
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

NeuroQuant® Illustrations



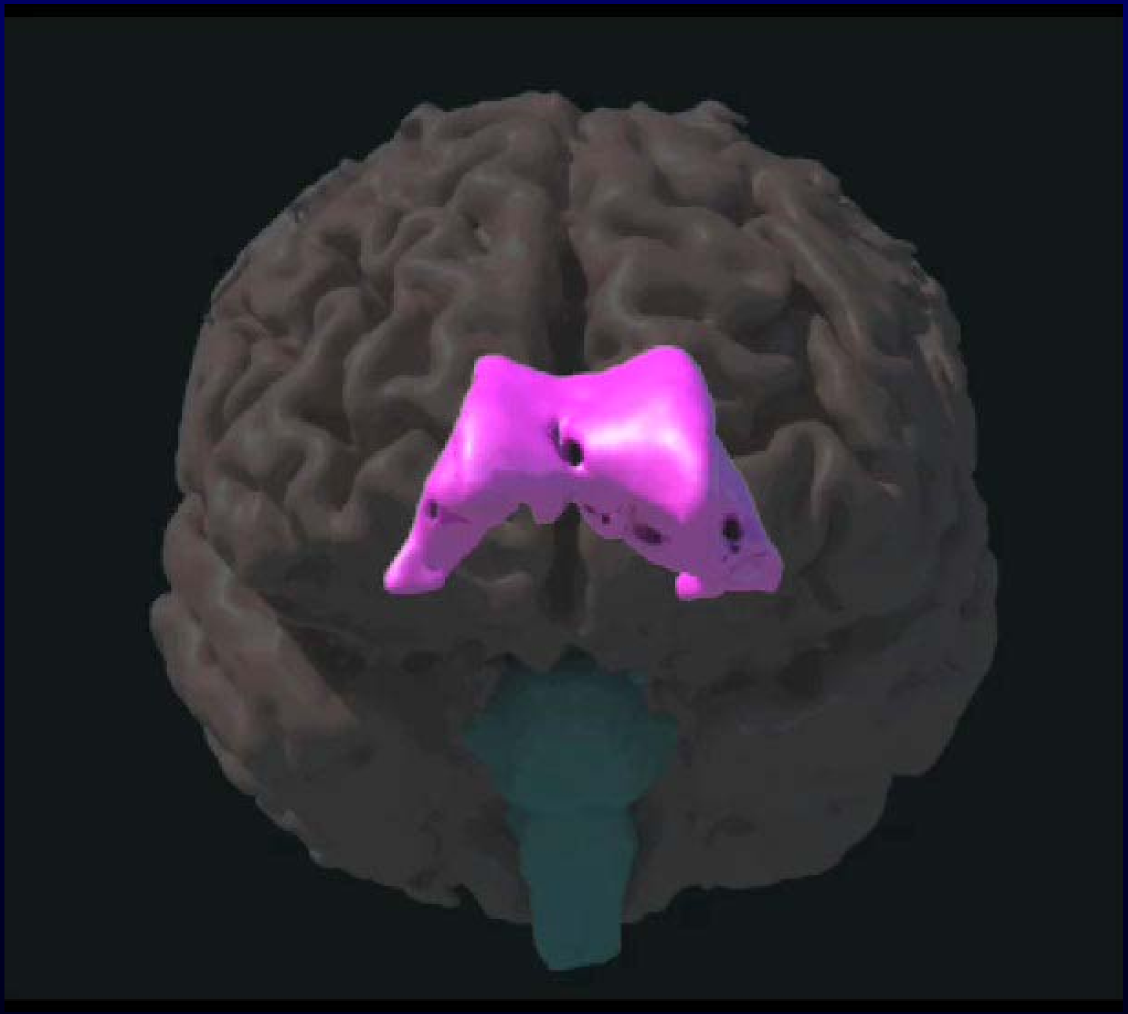
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

NeuroQuant® Illustrations



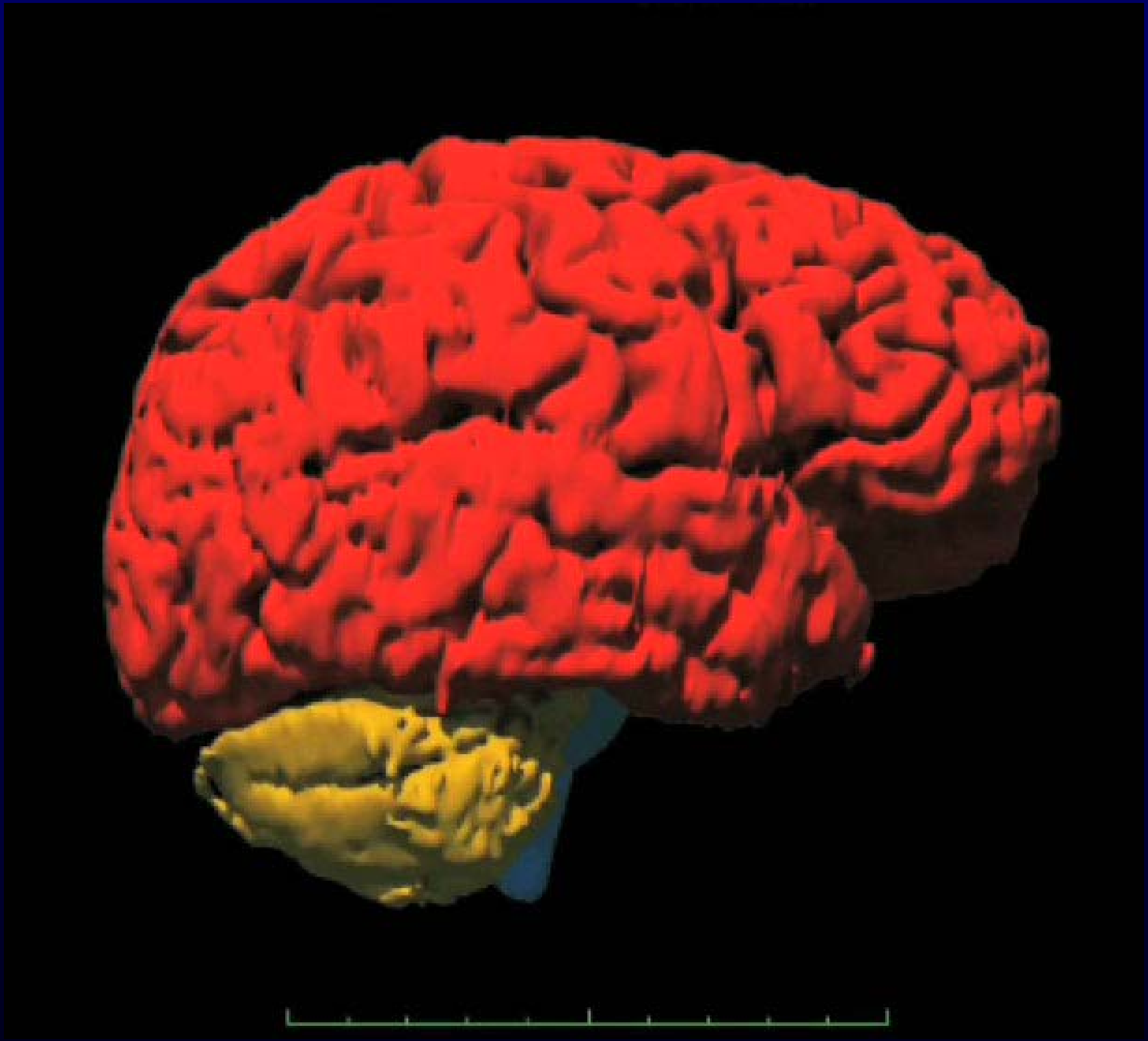
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

Case example: Patient KM



Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

NeuroQuant® Illustrations



Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

Radiologist vs. NeuroQuant®

	N positive/ Total N	% positive for atrophy
Radiologist atrophy	2/20	10%
NQ Extended atrophy	10/20	50%

Paired sign test, test statistic M =-4.00, P=0.02

<u>Reference</u>

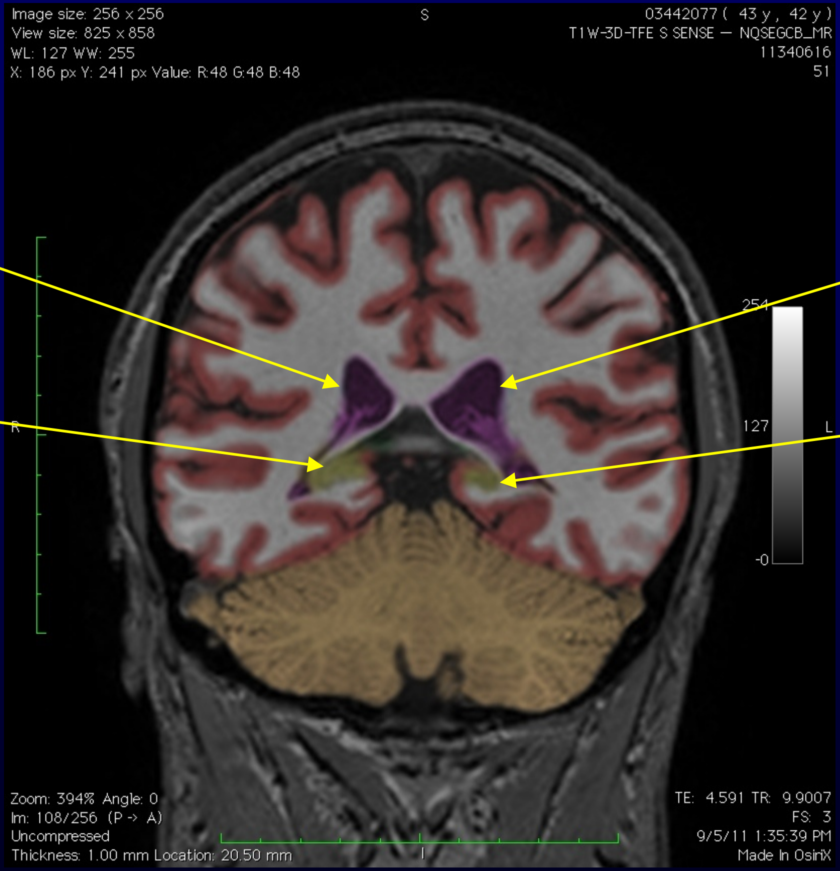
Ross DE, Ochs AL, Seabaugh JM, Shrader CR (submitted): Man vs. Machine: Comparison of Radiologists' Interpretations and NeuroQuant® Volumetric Analyses of Brain MRIs in Patients with Traumatic Brain Injury . *Journal of Neuropsychiatry and Clinical Neurosciences.*

Case Example: Patient DG

MRI scan 2 years after injury

Right
lateral ventricle

Right
hippocampus



Left
lateral ventricle

Left
hippocampus

- NeuroQuant® results:
- Lateral ventricle: L > R
- Hippocampus: L small; L < R

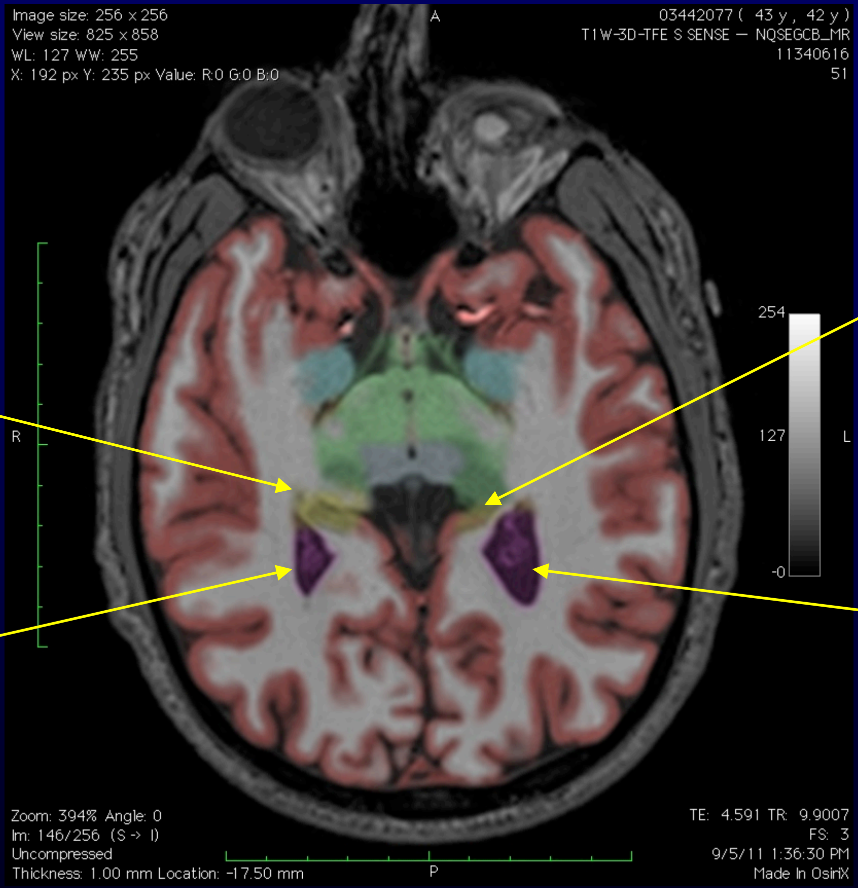
Case Example: Patient DG

MRI scan 2 years after injury

Higher level in brain

Right hippocampus

Right lateral ventricle



Left hippocampus

Left lateral ventricle

- NeuroQuant® results:
- Lateral ventricle: L > R
- Hippocampus: L small; L < R

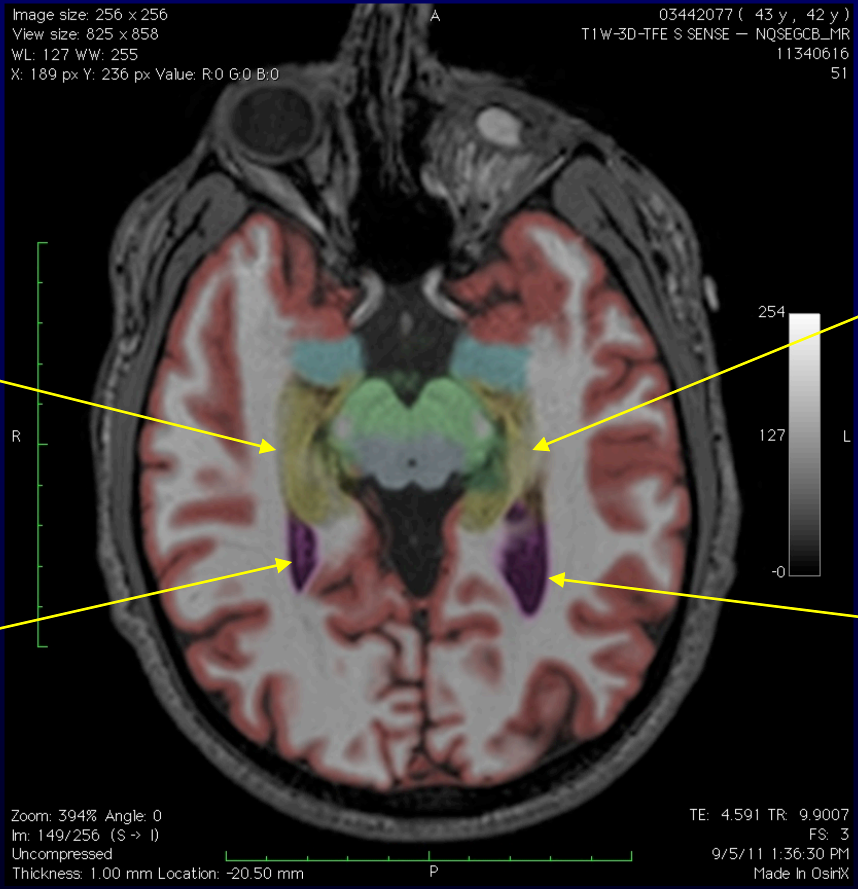
Case Example: Patient DG

MRI scan 2 years after injury

Lower level in brain

Right hippocampus

Right lateral ventricle



Left hippocampus

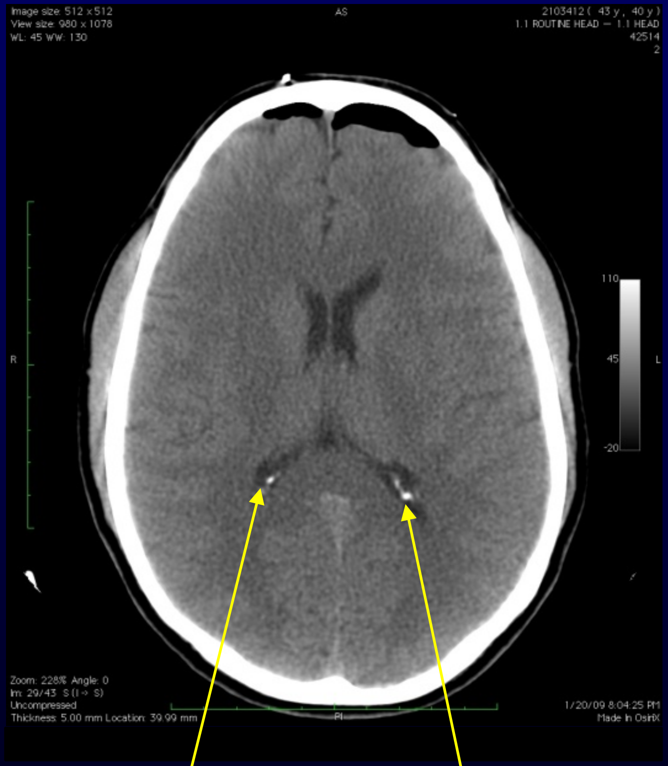
Left lateral ventricle

- NeuroQuant® results:
- Lateral ventricle: L > R
- Hippocampus: L small; L < R

Progressive enlargement of left lateral ventricle:
Patient DG

Higher level in brain

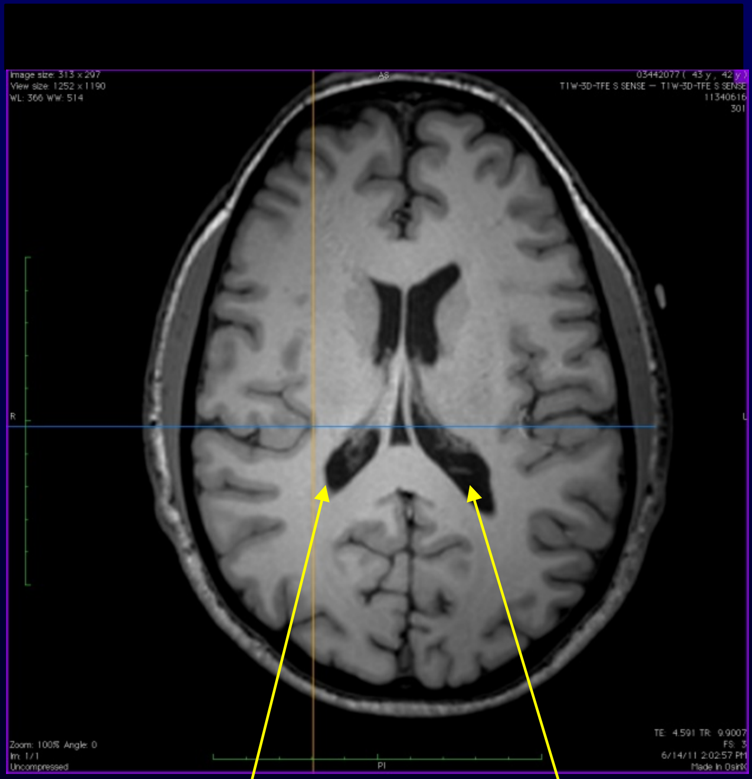
CT scan
Date of accident



Right occipital horn of LV

Left occipital horn of LV

MRI scan
2 years later



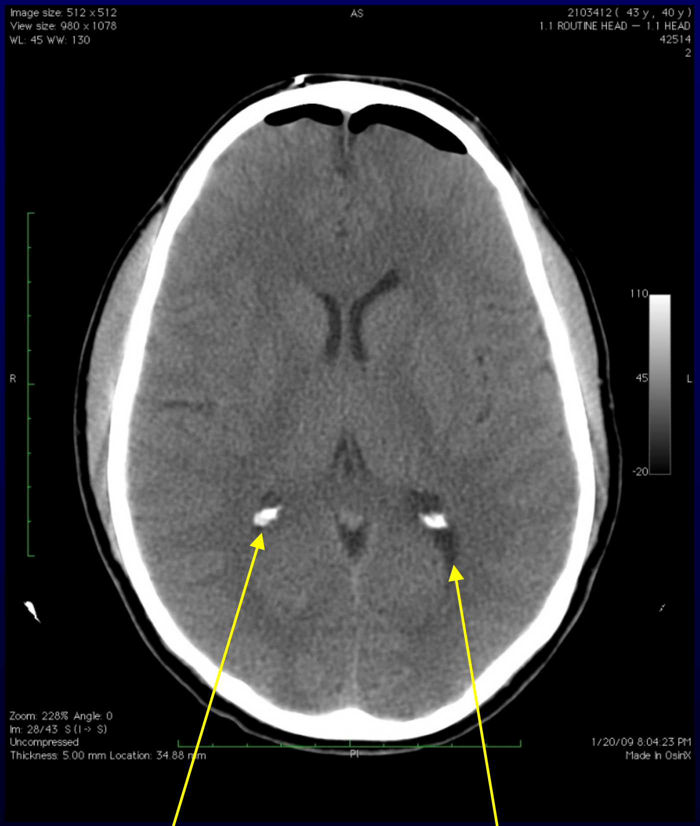
Right occipital horn of LV

Left occipital horn of LV

Progressive enlargement of left lateral ventricle:
Patient DG

Lower level in brain

CT scan
Date of accident



MRI scan 2
years later

Right occipital horn of LV

Left occipital horn of LV

Right occipital horn of LV

Left occipital horn of LV

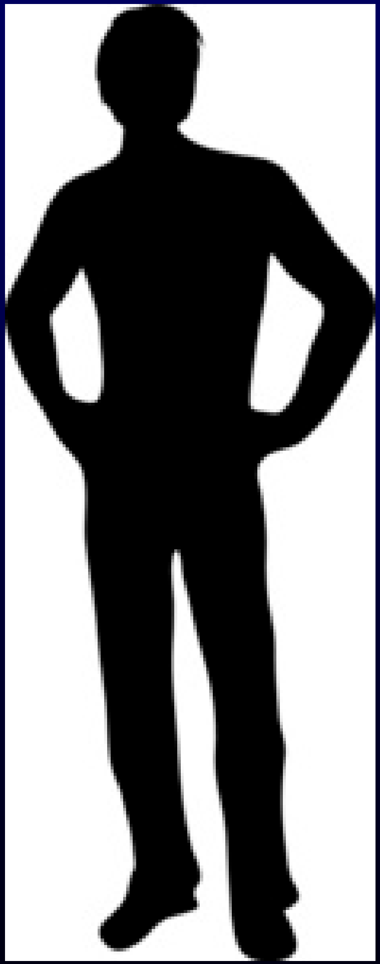
Longitudinal Analysis

- Literature review of longitudinal studies of brain volumetry in patients with TBI
  - Definitions
    - Longitudinal design: 2 points in time
    - Cross sectional design: 1 point in time

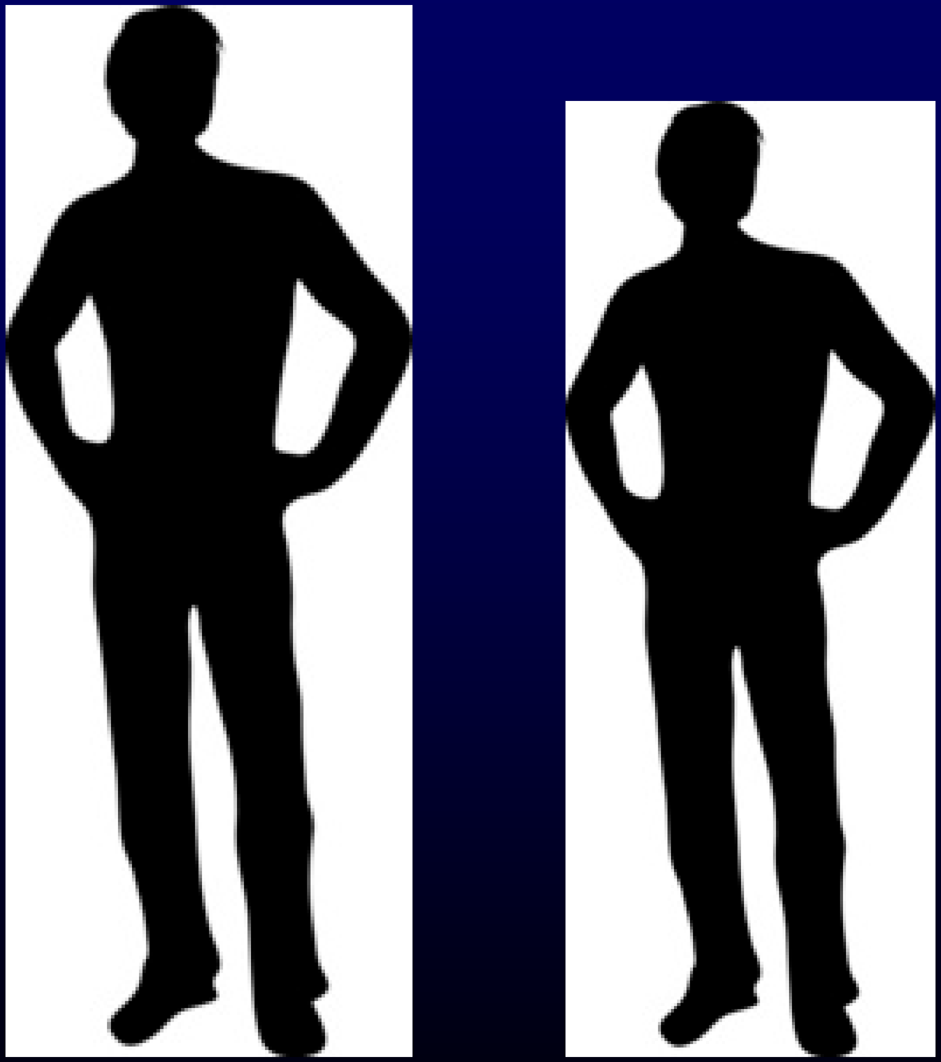
Reference:

Ross, D. E. (2011). "Review of longitudinal studies of MRI brain volumetry in patients with traumatic brain injury." Brain Injury **25**(13-14): 1271-1278.

Longitudinal Analysis



Longitudinal Analysis



Literature review of longitudinal studies of brain volumetry in patients with TBI

- Literature review of longitudinal studies of brain volumetry in patients with TBI*
  - 10 studies
    - Mild to severe TBI
    - Mean time between injury and first MRI: 2.5 mos
    - Mean time between 1st and 2d MRI: 13.2 mos

Reference:
Ross, D. E. (2011). "Review of longitudinal studies of MRI brain volumetry in patients with traumatic brain injury." Brain Injury **25**(13-14): 1271-1278.

Literature review of longitudinal studies of brain volumetry in patients with TBI

- Literature review of longitudinal studies of brain volumetry in patients with TBI*
  - Consistent pattern of brain atrophy
    - Total brain parenchyma
    - Gray matter and white matter
    - Hippocampi

Reference:
Ross, D. E. (2011). "Review of longitudinal studies of MRI brain volumetry in patients with traumatic brain injury." Brain Injury **25**(13-14): 1271-1278.

Literature review of longitudinal studies of brain volumetry in patients with TBI

- Literature review of longitudinal studies of brain volumetry in patients with TBI*
  - Atrophy correlated with important clinical variables
    - Duration of loss of consciousness
    - Duration of coma
    - Posttrauamtic amnesia
    - Hypoperfusion seen on SPECT scanning
    - Functional status measured by FSE and GOS-E

Reference:

Ross, D. E. (2011). "Review of longitudinal studies of MRI brain volumetry in patients with traumatic brain injury." Brain Injury **25**(13-14): 1271-1278.

Literature review of longitudinal studies of brain volumetry in patients with TBI

- Literature review of longitudinal studies of brain volumetry in patients with TBI*
  - Effect sizes much larger for longitudinal design vs. cross-sectional design

Reference:

Ross, D. E. (2011). "Review of longitudinal studies of MRI brain volumetry in patients with traumatic brain injury." Brain Injury **25**(13-14): 1271-1278.

Review of Longitudinal Studies

Measure	Number of studies	Effect size for cross-sectional analysis (mean)	Effect size for longitudinal analysis
Whole brain parenchymal volume	6	0.6	1.8
Hippocampal volume	2	0.6	1.9

- Effect sizes between patients with TBI and normal controls.
  - For effect size d:
    - small = 0.3
    - medium = 0.5
    - large = 0.7 or greater

Reference:

Ross, D. E. (2011). "Review of longitudinal studies of MRI brain volumetry in patients with traumatic brain injury." Brain Injury **25**(13-14): 1271-1278.

Literature review of longitudinal studies of brain volumetry in patients with TBI

- Literature review of longitudinal studies of brain volumetry in patients with TBI
  - Conclusions
    - All studies found progressive brain atrophy in patients with TBI.
    - Greater rates of atrophy correlated with worse vocational outcome.
    - The longitudinal design was more powerful than the cross sectional design for detecting differences between patient and controls.

Reference:

Ross, D. E. (2011). "Review of longitudinal studies of MRI brain volumetry in patients with traumatic brain injury." Brain Injury **25**(13-14): 1271-1278.

VIN Longitudinal Study

- Design
  - 16 patients with mild TBI vs. normal controls
  - Longitudinal design
    - Each subject had 2 MRI scans, about 1 year apart

Reference:

Ross, D. E., A. L. Ochs, et al. (submitted). "NeuroQuant® Reveals Progressive Brain Atrophy in Patients with Mild Traumatic Brain Injury." Brain Injury.

VIN Research: Test-retest Reliability

Brain region	Intraclass correlation coefficients
Total intracranial volume, Brain parenchyma, Cerebrospinal fluid, Forebrain parenchyma, Cortical gray matter, Cerebral white matter, Lateral ventricle, Inferior lateral ventricle, Caudate, Hippocampus, Cerebellum, Brainstem, Fourth ventricle	0.95 – 1.00
Thalamus, Amygdala, Exterior cerebrospinal fluid	>.90
Putamen	>.85
Third ventricle	>.80
Pallidum	>.75
Ventral diencephalon	>.35

Test-retest reliability for NeuroQuant® volumetric measures were mostly excellent.

Reference:

Ross, D. E., A. L. Ochs, et al. (submitted). "NeuroQuant® Reveals Progressive Brain Atrophy in Patients with Mild Traumatic Brain Injury." Brain Injury.

VIN Longitudinal Study

Brain regions	Sig. (2-tailed)	Effect size d
Whole brain parenchyma	0.003*	1.5
Forebrain parenchyma	0.003*	1.4
Cortical gray matter	0.579	0.2
Cerebral white matter	<0.001*	1.4
Cerebrospinal fluid	0.805	-0.1
Cerebellum	0.004*	1.5
Brainstem	0.074	0.8

Comparisons of progressive brain atrophy between patients with mild TBI and normal controls.

Reference:

Ross, D. E., A. L. Ochs, et al. (submitted). "NeuroQuant® Reveals Progressive Brain Atrophy in Patients with Mild Traumatic Brain Injury." Brain Injury.

VIN Longitudinal Study

Brain region	Sig. (2-tailed)	Effect size d
Whole brain parenchyma	0.018*	-1.4
Forebrain parenchyma	0.016*	-1.4
Cortical gray matter	0.045*	-1.3
Cerebral white matter	0.817	-0.1
Cerebrospinal fluid	0.018*	1.6
Cerebellum	0.04*	-1.3
Brainstem	0.201	0.8

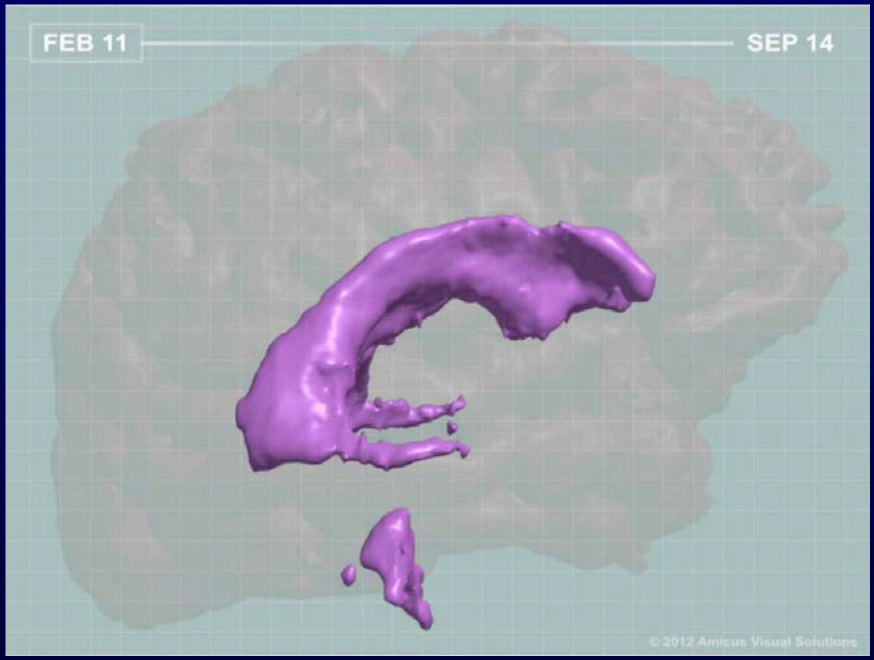
Comparisons of progressive brain atrophy between patient GOSE subgroups based on functional outcome.

References:

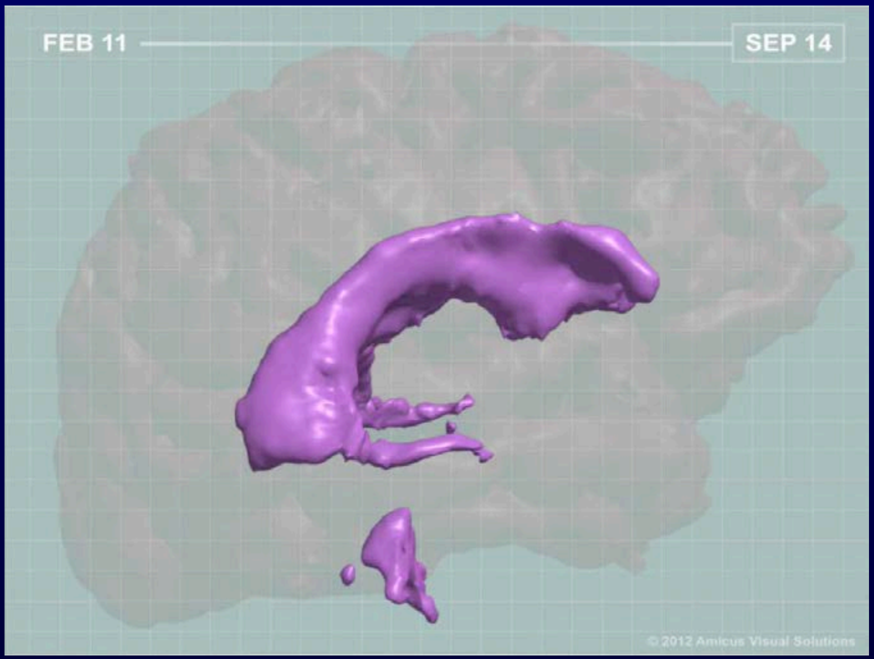
Ross, D. E., A. L. Ochs, et al. (submitted). "NeuroQuant® Reveals Progressive Brain Atrophy in Patients with Mild Traumatic Brain Injury." Brain Injury.

Wilson, J. T., L. E. Pettigrew, et al. (1998). "Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use." J Neurotrauma **15**(8): 573-585.

Example of Progressive Ventricular Enlargement



Time 1

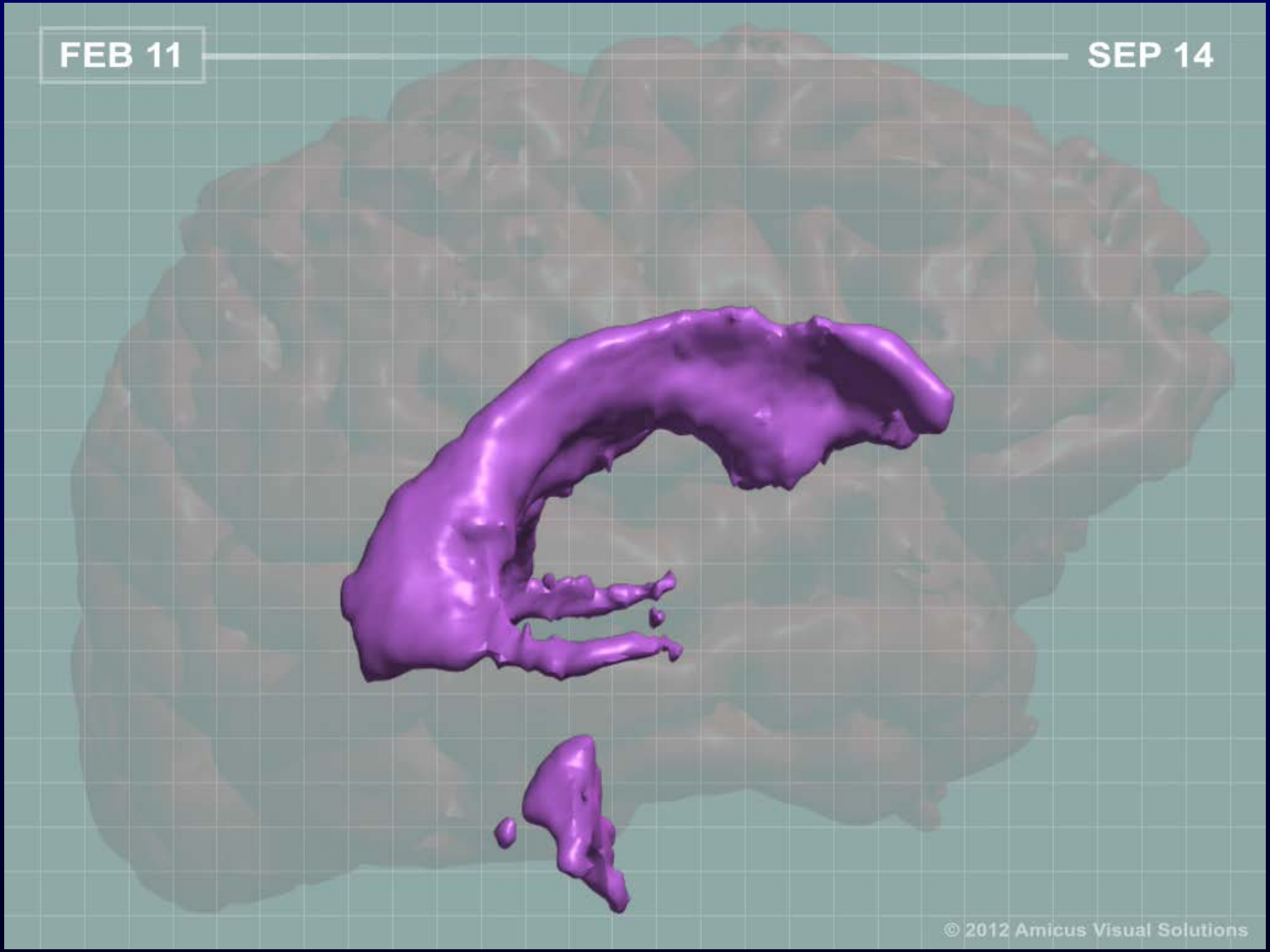


Time 2

3D reconstruction of NQ segmented images

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

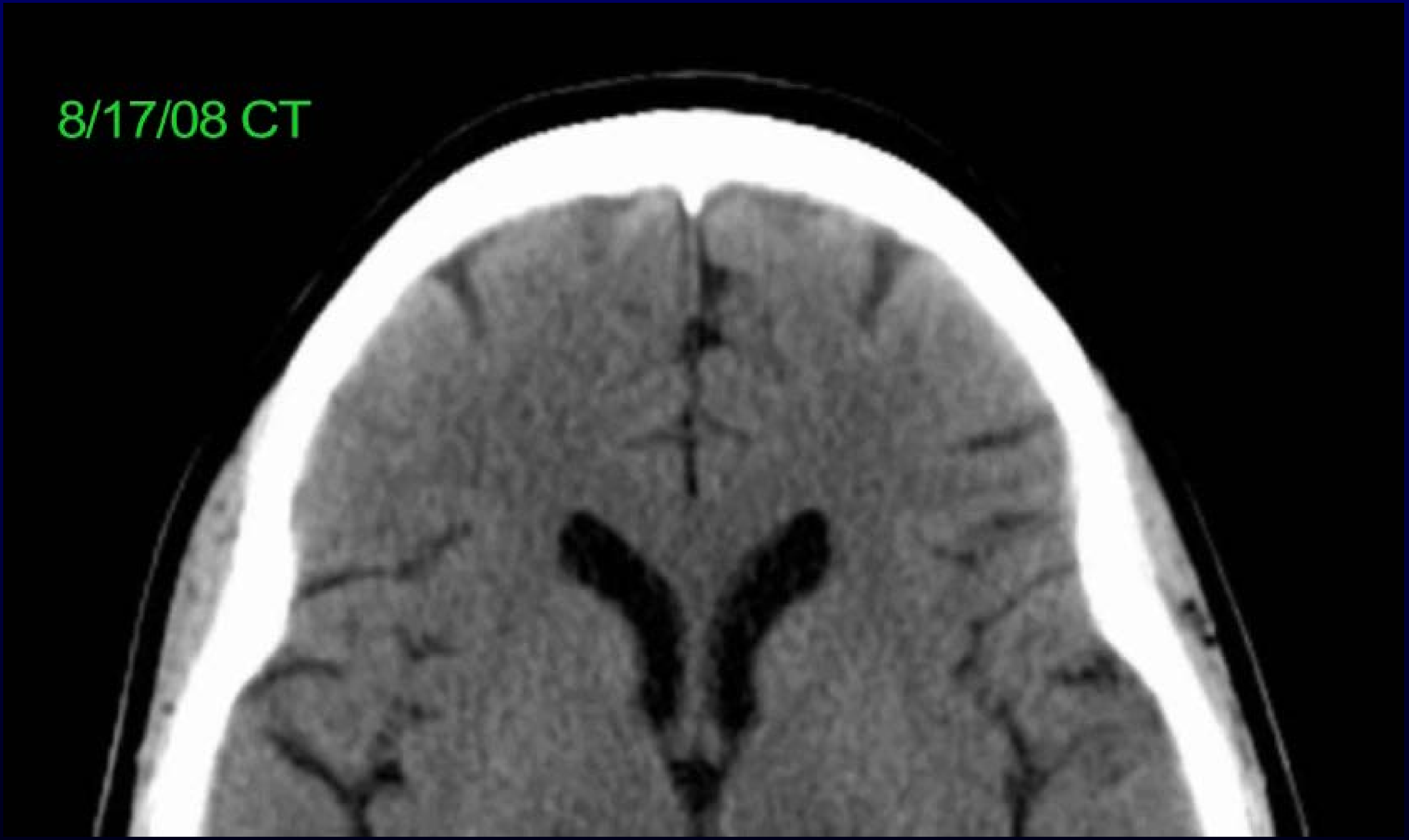
Example of Progressive Ventricular Enlargement



3D reconstruction of NQ segmented images

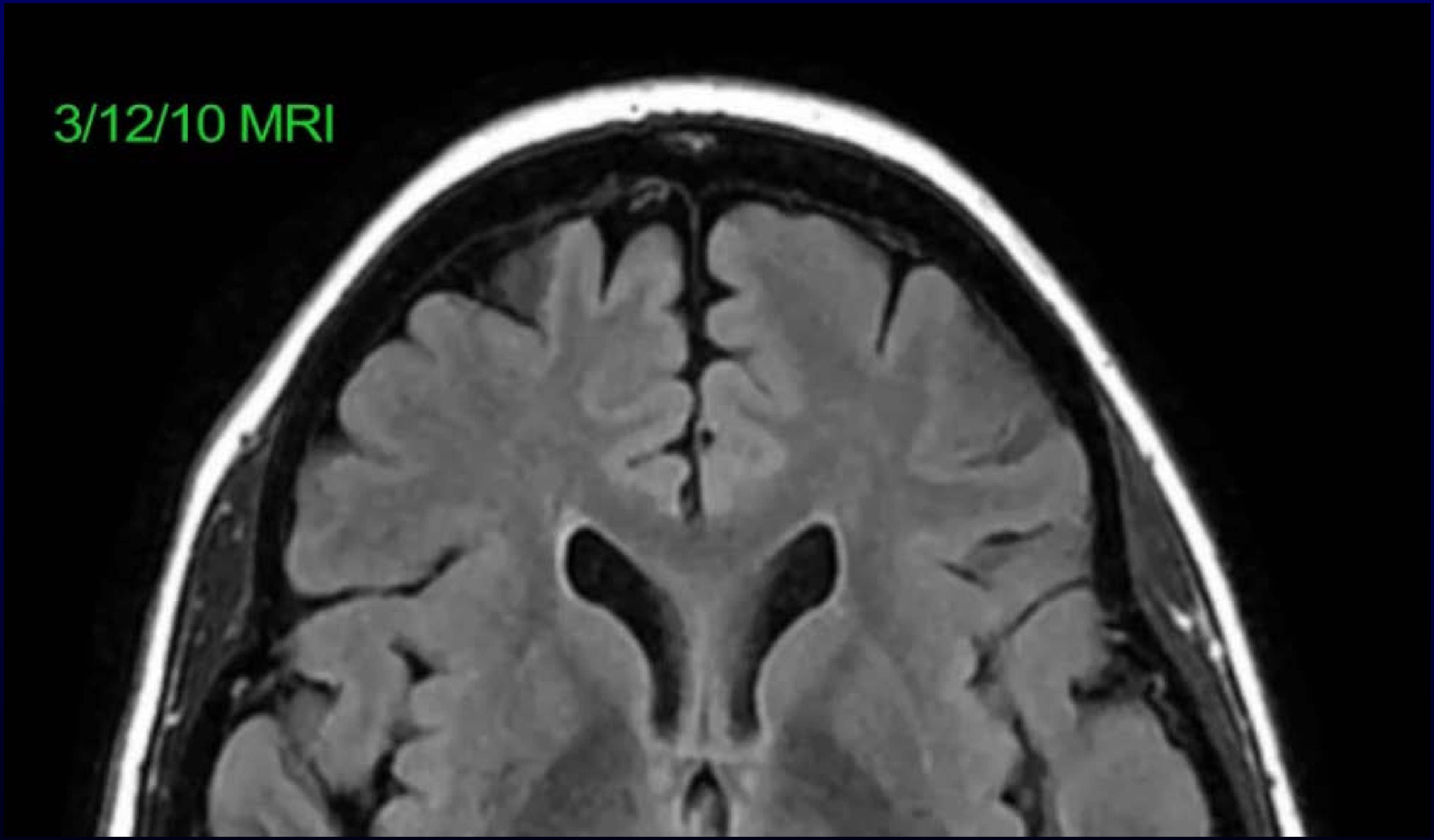
Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

Visualizing Progressive Atrophy



Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

Visualizing Progressive Atrophy



Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

Visualizing Progressive Atrophy

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions

Community Acceptance of NeuroQuant®

- NeuroQuant® is currently used in at least a dozen clinics and radiology centers across the USA:

West

Santa Rosa Imaging Center
3536 Mendocino Ave., Suite 280
Santa Rosa, CA 95403

Dr. James Brewer
University of California, San Diego, CA

San Joaquin Community Hospital
2615 Chester Avenue, Bakersfield, CA 93301

Liberty Pacific Advanced Imaging
16130 Ventura Blvd., Suite 100, Encino, CA 91436

Radnet, www.radnet.com
Sites in California

East

Lenox Hill Radiology & Medical Imaging Associates
61 East 77th Street, New York, NY 10075

East River Medical Imaging, PC
519/523 East 72nd Street, New York, NY 10021

Advanced Radiology
888 Bestgate Rd, Ste 101, Annapolis 21401

Washington Radiology Associates
2141 K St. NW, Washington, DC 20037

South

Virginia Institute of Neuropsychiatry
364 Browns Hill Court, Midlothian, VA 23114

Center for Neurorehabilitation Services
10710 Midlothian Turnpike, Suite 125, Richmond, VA 23235

MRI CT Diagnostics
4668 Pembroke Blvd, Virginia Beach, VA 23455

MRI in Individual Patients

- Clinical implications
  - Objective signs of brain injury provide vindication for patients
  - Continuing brain atrophy can be a motivating factor for patients
- Forensic implications
  - Defense specialists often argue that a patient does not have any objective signs of brain injury
  - MRI may provide the best chance for objective findings of brain injury for many patients, especially patients with mild TBI

Recommendations

- Obtain NeuroQuantable MRI as soon as possible.
- Obtain follow up MRIs about 6 and 12 months later.
- In addition to NQ standard analysis, perform:
  - NQ Extended analysis
    - 15 brain regions (vs. 3 regions for NQ Standard)
  - Longitudinal analysis
    - % volume change per year

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www.VaNeuropsychiatry.org

Virginia Institute of Neuropsychiatry

Acknowledgements

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