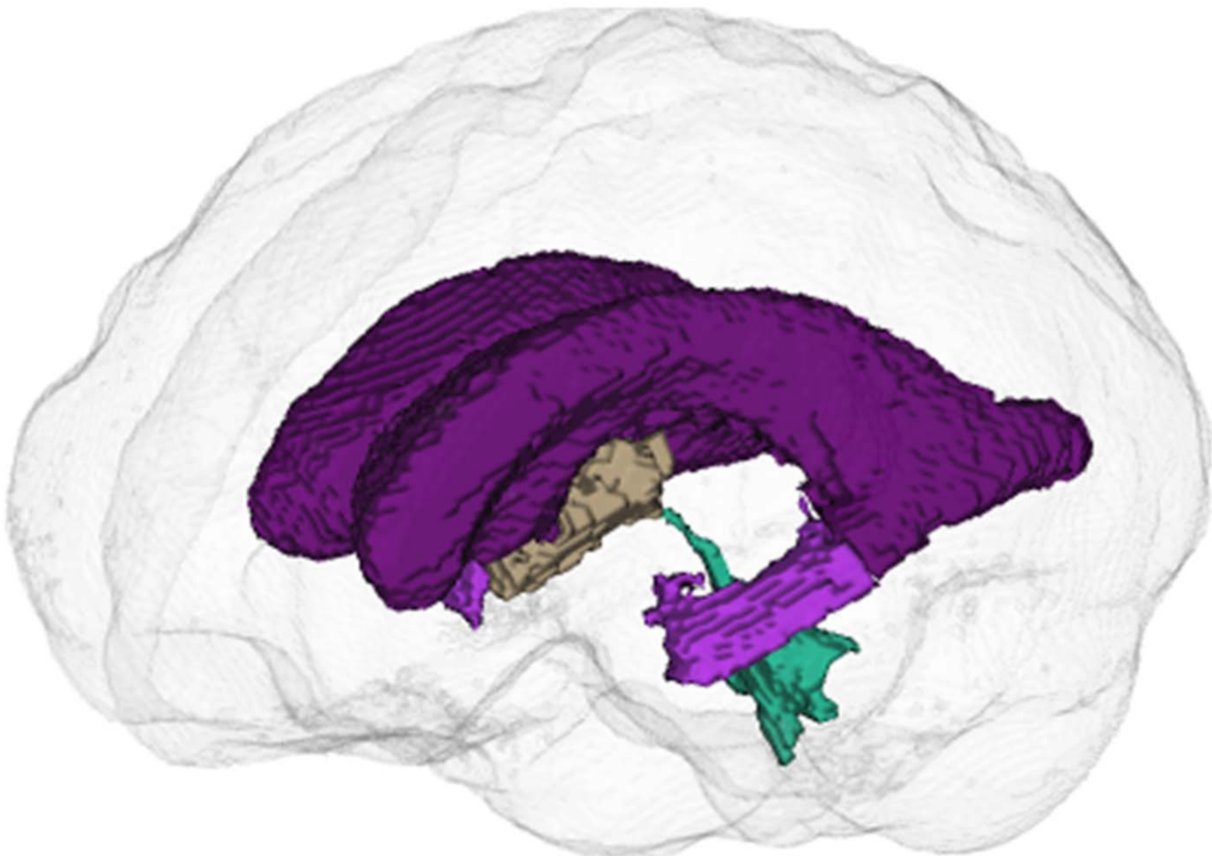
AAN 2012

Neuroimaging of Normal Pressure Hydrocephalus



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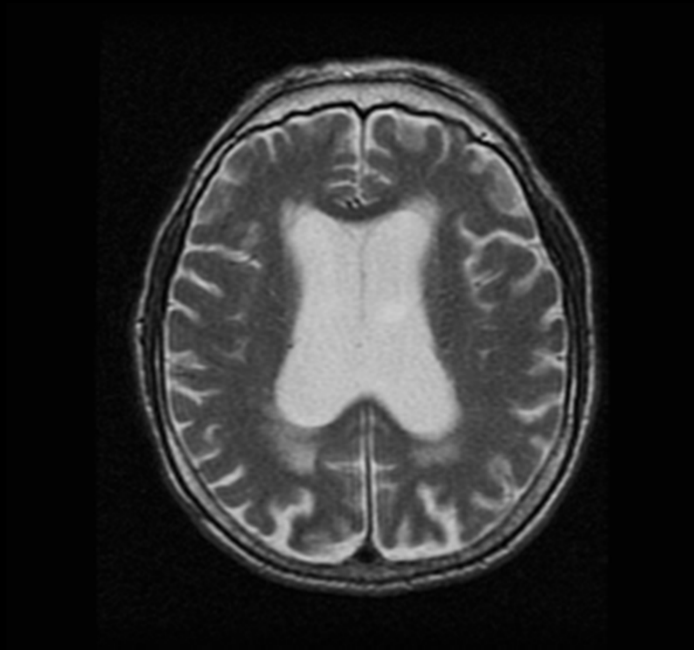
New York, NY

Objectives

- Recognize the structural changes in the brain associated with idiopathic Normal Pressure Hydrocephalus (iNPH)
- Identify the most appropriate imaging modalities for use in iNPH diagnosis and management
- Describe at least three advanced MRI techniques that have shown promise for improving iNPH evaluations

The Radiologist's Hedge



"The lateral ventricles are enlarged relative to age. This could be a consequence of central atrophy or an element of communicating hydrocephalus may be present…"

- MRI clinical report

Clinical Roles of Neuroimaging in NPH

- NPH Recognition and Differential Diagnosis
- Prognostication of Treatment Response
- Management post Treatment
- Outcome Assessment

Role of Imaging in NPH Diagnosis

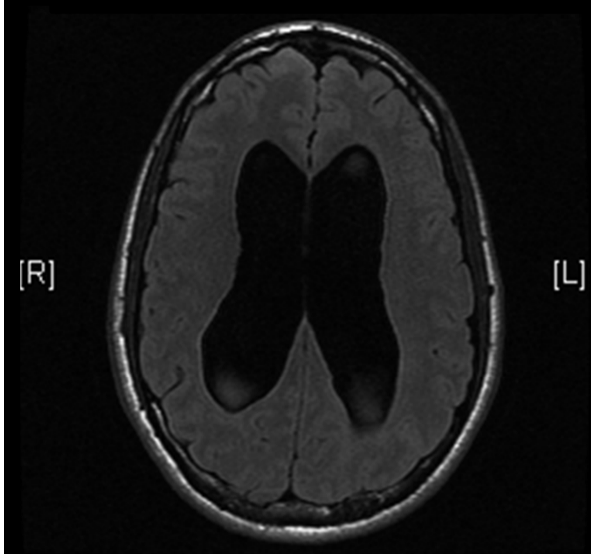
Use	Aim	Modality
Fulfill primary imaging criterion for iNPH	Document ventricular enlargement greater than brain atrophy	MRI, CT
Distinguish communicating from non-communicating hydrocephalus	Documents absence of macroscopic obstruction to cerebrospinal fluid	MRI, CT
Identifies other anatomic features associated with iNPH diagnosis	Document high convexity effacement, enlarged Sylvian fissue, callosal thinning, increased ventricular angle	MRI, CT
Provides indications of abnormal CSF flow	Document CSF flow void, ventricular reflux, hyperdynamic flow	Proton Density MRI Phase Contrast MRI Radionuclide cisternography

Uses of Imaging in NPH Therapeutics

Use	Modality
Guide LP or lumbar drain placement	X-ray, X-ray Fluoroscopy
Confirms correct shunt placement, setting and shunt integrity	X-ray, CT (MRI)
Monitors ventricular size (shunt failure, overdrainage syndromes)	CT (MRI)
Identify post-shunt complications (subdural effusions and hematomas)	CT (MRI)

The Challenge

A



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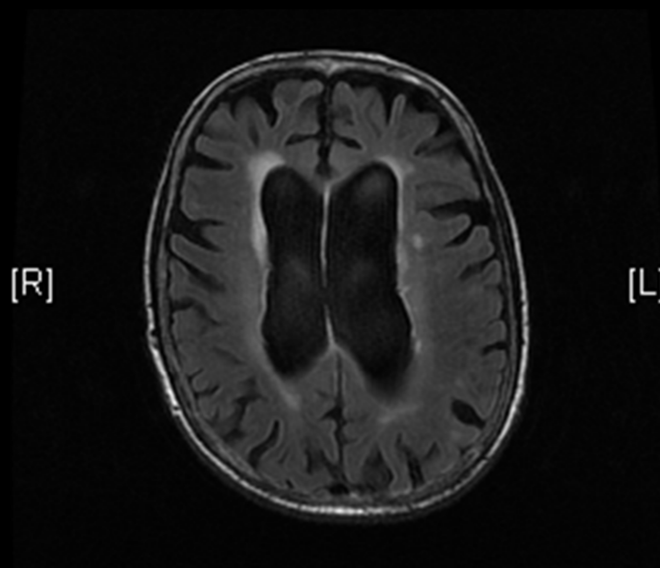

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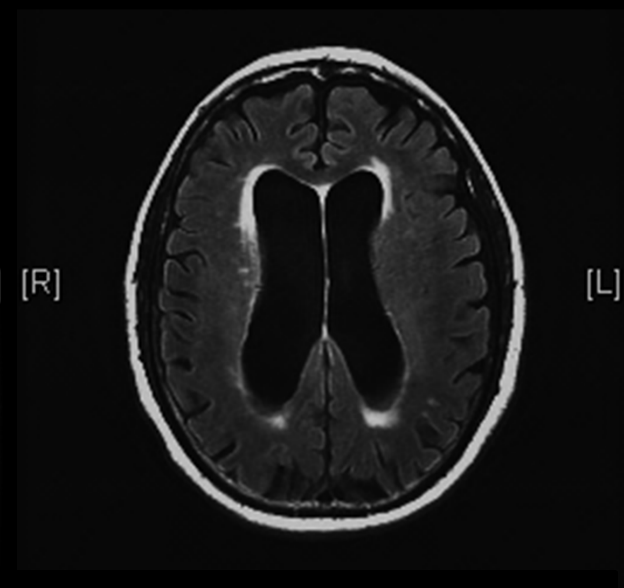


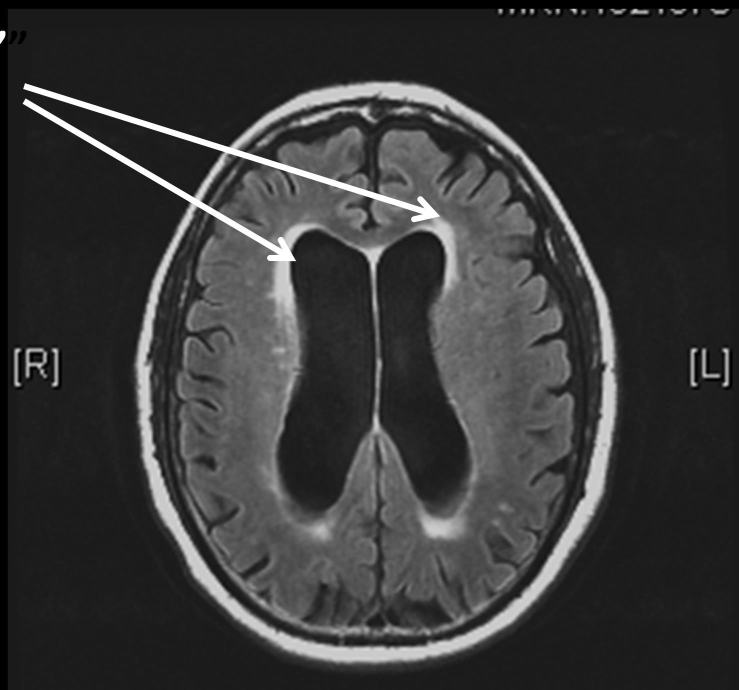
T2 FLAIR Images

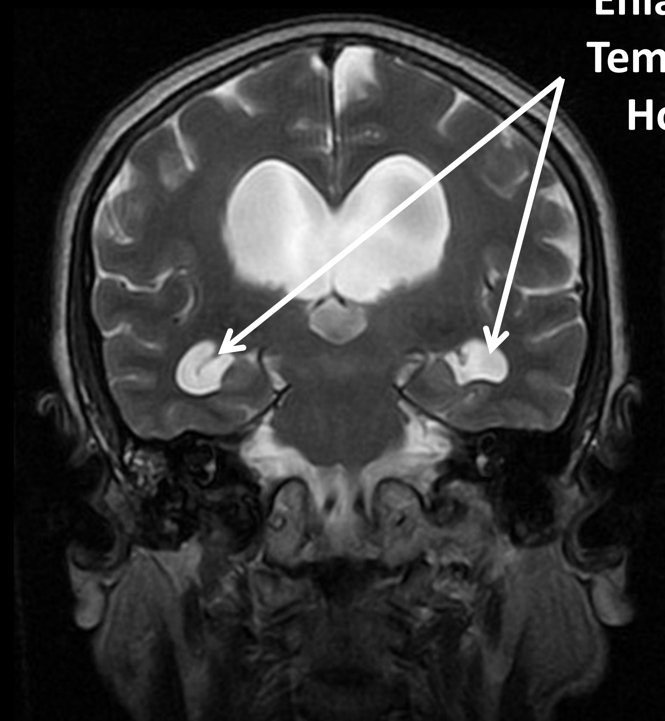
35 year old
with Aqueductal
Stenosis

79 year old
with Alzheimer's
Disease

87 year old
with Shunt responsive
Normal Pressure
Hydrocephalus

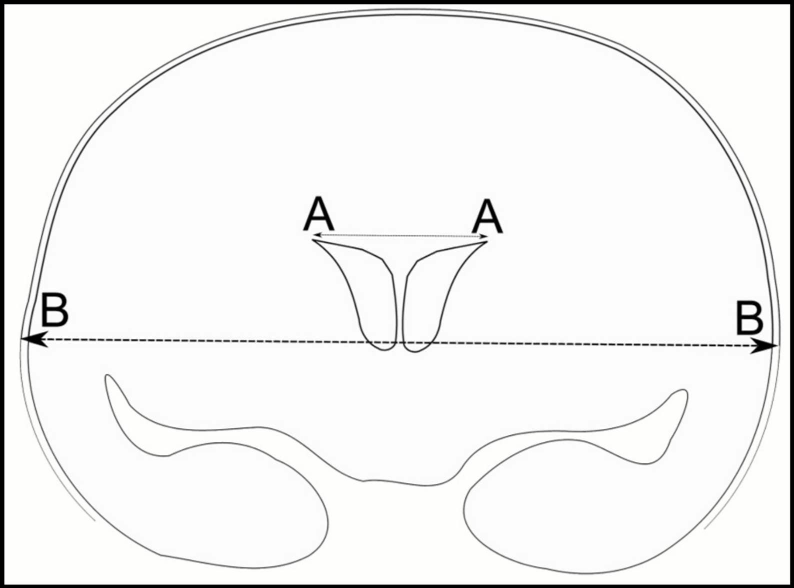
Ventricles are symmetrically enlarged in NPH

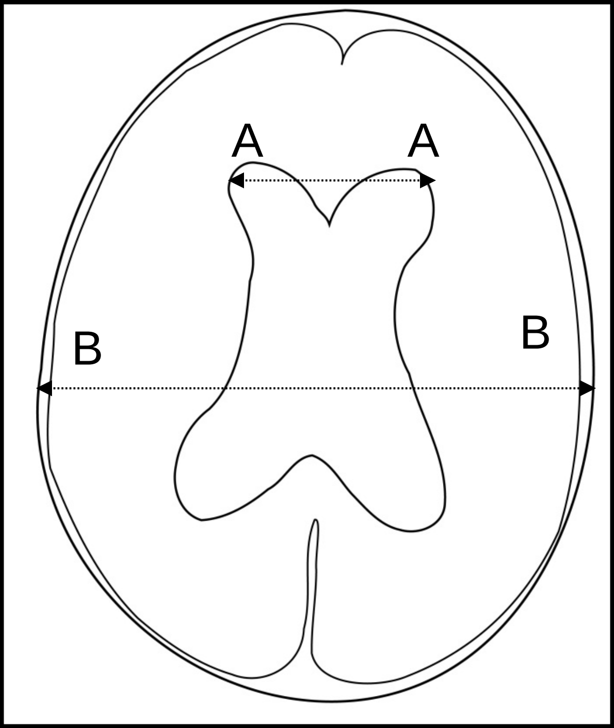




The Evan's Index = A÷B

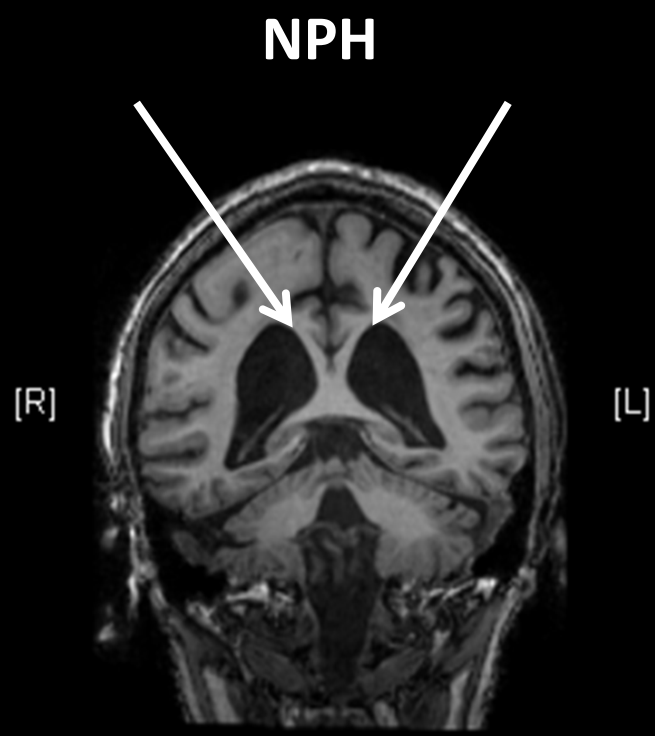
Ratio of diameter of anterior horns of lateral ventricle to intracranial diameter

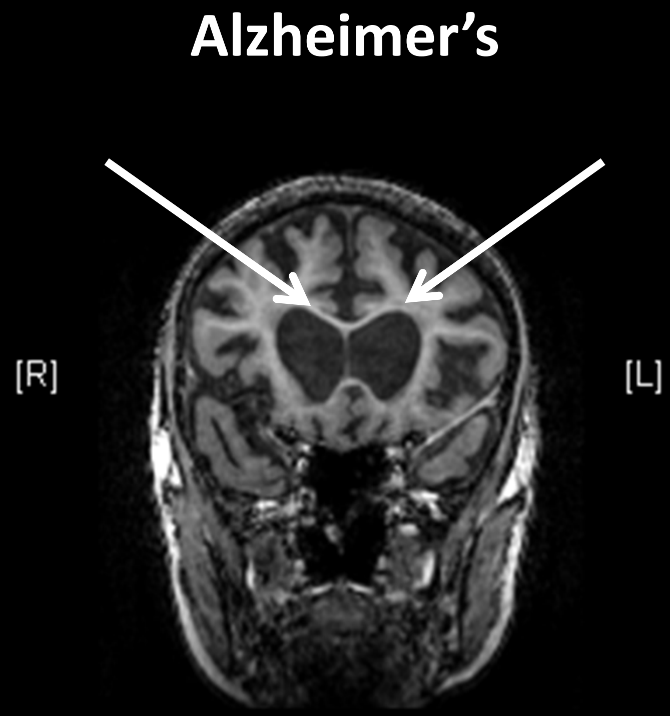




Diagnostic criteria for Idiopathic NPH require an Evan's Index of 0.3 or greater

Callosal Angle is steeper in NPH than in degenerative disorders

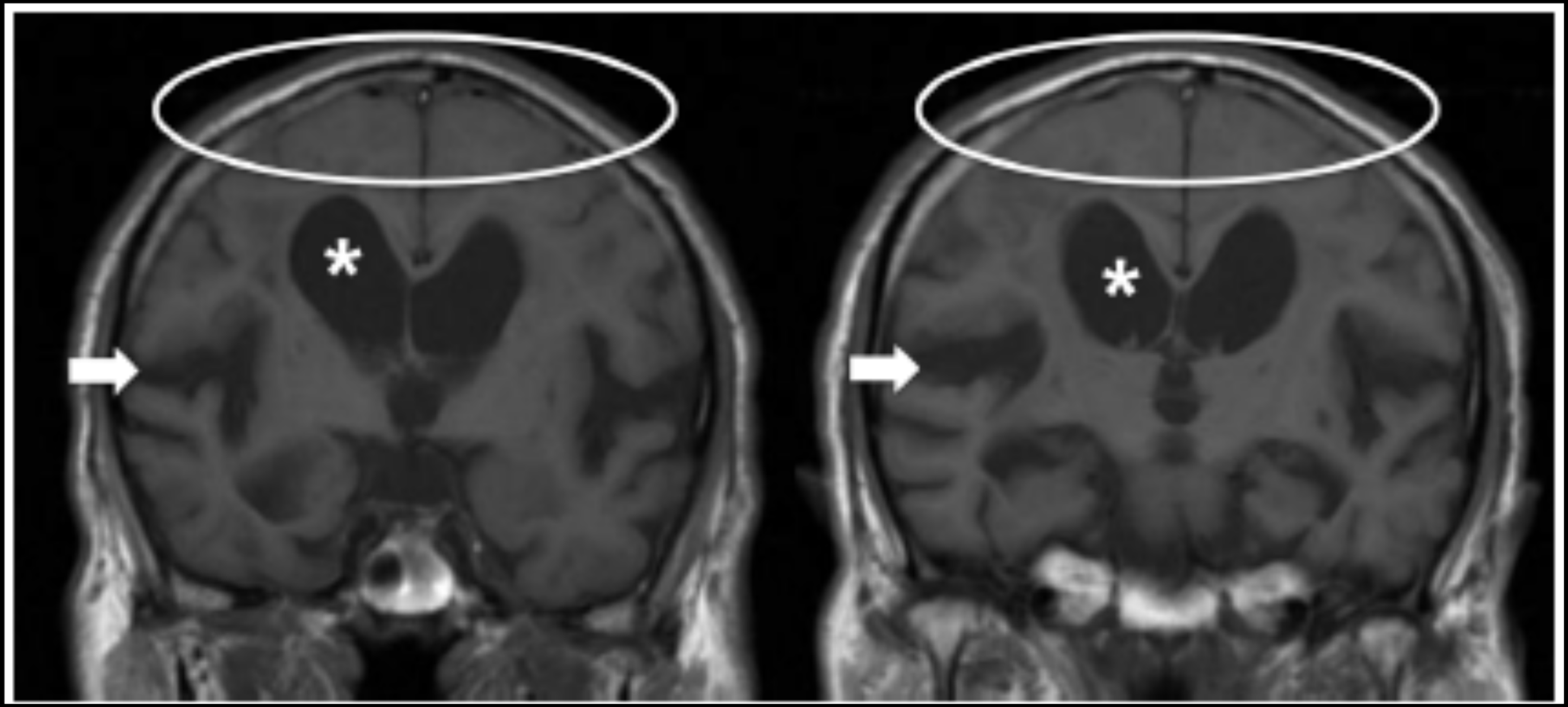




Coronal Reformatted T1-weighted images

DESH: Disproportionately Enlarged Subarachnoid Space Hydrocephalus

A useful radiologic finding in the diagnosis of iNPH

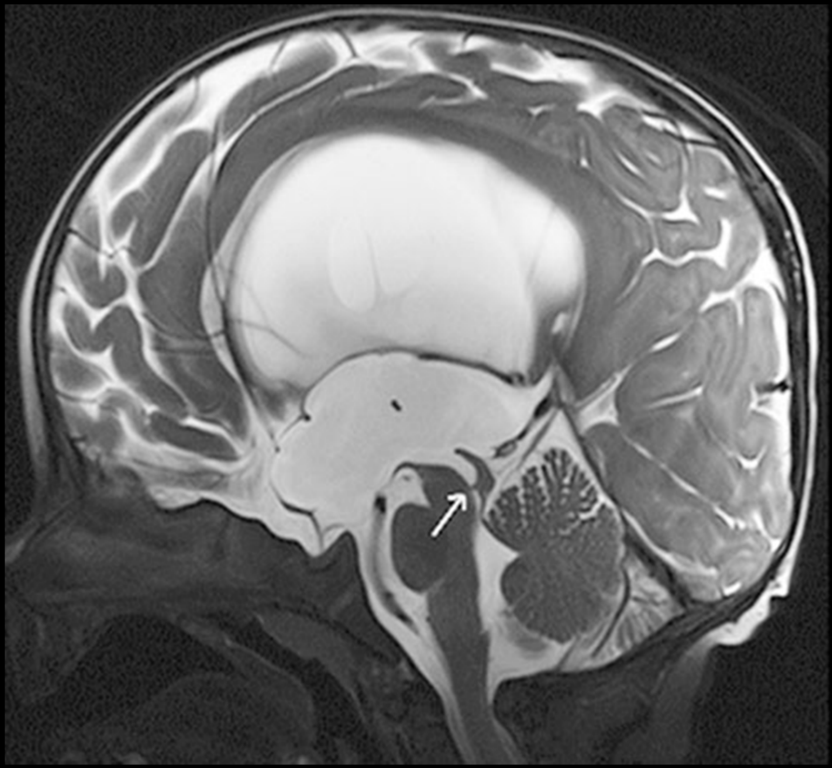


Circles: fronto-parietal convexity sulcal effacement and sagittal sinus abutment
Arrows: Enlargement and upward displacement of roof of Sylvian fissure

Image from Hashimoto M, et al (2010) Cerebrospinal Fluid Research 7:18

Steady State Free Procession MRI techniques (e.g.: FIESTA, 3D-CISS) reveals anatomic obstructions in Aqueductal Stenosis

FIESTA = fast imaging employing steady state acquisition (GE)
3D-CISS = constructive interference in steady state (Siemens)



- Aqueductal web (arrow) visualized by high resolution FIESTA MRI

Image from Parekh & Prabhu (2010) Pediatric Radiology S154)

Advanced MRI Imaging Protocol for NPH

Various Advanced MRI measurements can be performed as adjuncts to conventional clinical sequences in patients suspected of having NPH:

Volumetric MRI
Cortical Shrinkage
Ventricular Enlargement

Phase Contrast Imaging
Pulsatile CSF Flow
CSF Production
MR-ICP

Diffusion Tensor Imaging
Fractional Anisotropy
Quantitative Diffusion Tensor

Arterial Spin Label
Cerebral Blood Flow

Shunt responsive NPH associated with increased Aqueductal CSF flow

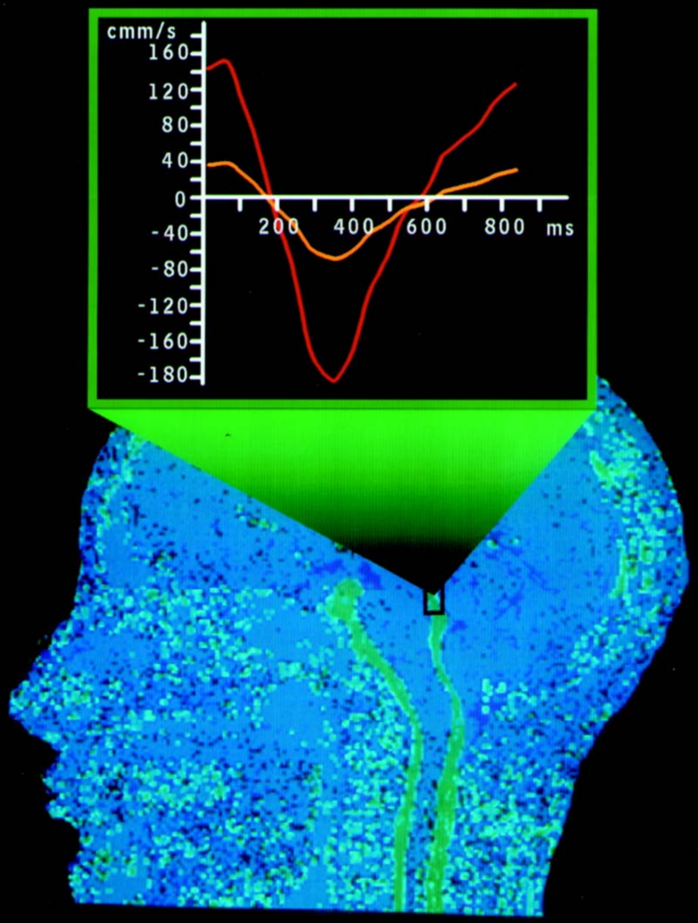


Image from Bradley, W (1999) J Neuropsychiatry

CLINICAL STUDIES

Measurement of Cerebrospinal Fluid Flow at the Cerebral Aqueduct by Use of Phase-contrast Magnetic Resonance Imaging: Technique Validation and Utility in Diagnosing Idiopathic Normal Pressure Hydrocephalus

Neurosurgery, Vol. 50, No. 3, March 2002

Patrick Luetmer, et al, Mayo Clinic, Rochester, Minnesota

236 patients studied,

- **47 normal elderly patients**
- **115 patients with cognitive impairment including 46 with Alzheimer's disease**
- **31 patients in whom NPH was suspected but ultimately excluded,**
- **43 patients with a final clinical diagnosis of NPH.**

- **The average flow rate in NPH was 27.4 +/- 15.3 ml/min**
- **The average flow rate in normals / non-NPH was 8.47 +/- 4.23 ml/min**

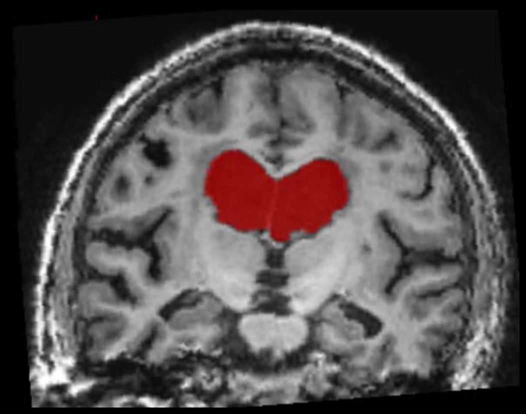
CONCLUSION: CSF flow measurements of less than 18 ml/min with a sinusoidal flow pattern are normal. CSF flow of greater than 18 ml/min suggests idiopathic NPH.

Volumetric MRI

- Quantitative analysis using semi- or fully-automated computer techniques can extract more information from MRIs than can be obtained by visual inspection alone
- Quantitative studies can be obtained on conventional MRI scanners but require 3D isotropic pulse sequences (e.g: 3D-BRAVO, MP-RAGE) and more acquisition stringency than is the case for standard clinical imaging protocols

MRI Volumetrics:
Ventricular Volume Determination

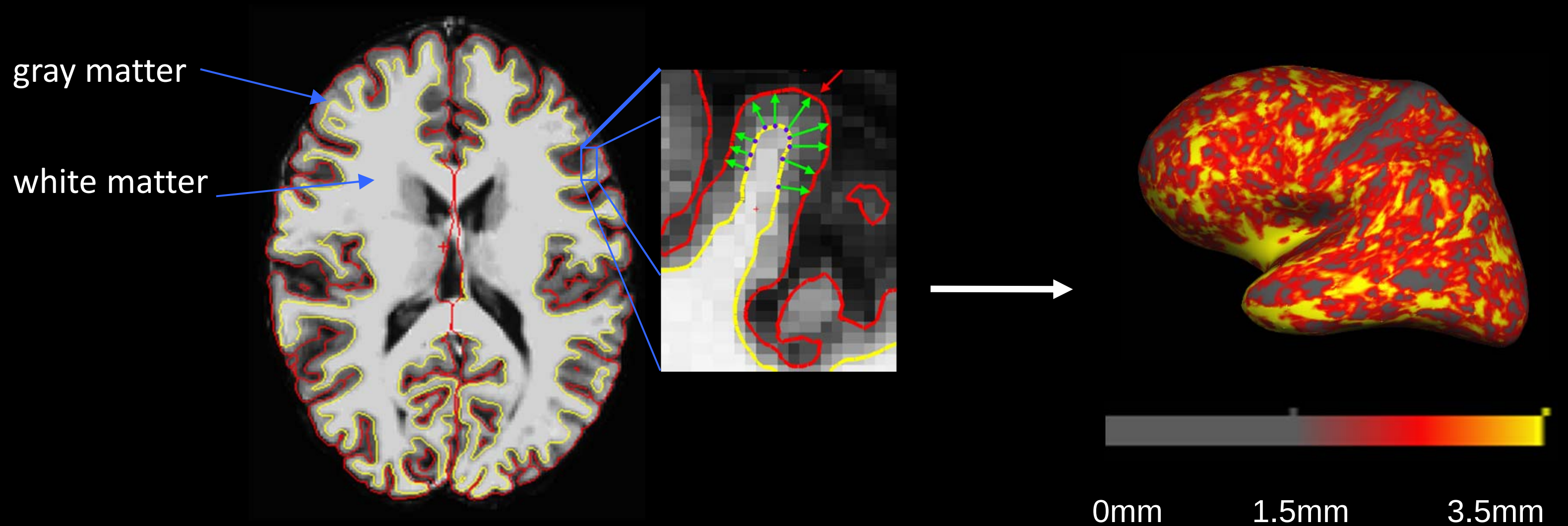
- **Automated segmentation software may fail to correctly segment enlarged ventricles as occurs in association with NPH**



- **At the present time, semi-automated programs such as Brain Ventricular Quantification ("BVQ") that use a region-growing method based on operator-selected seed points have provided the best performance with enlarged ventricles.**

MRI Volumetrics: Cortical Thickness Measurements

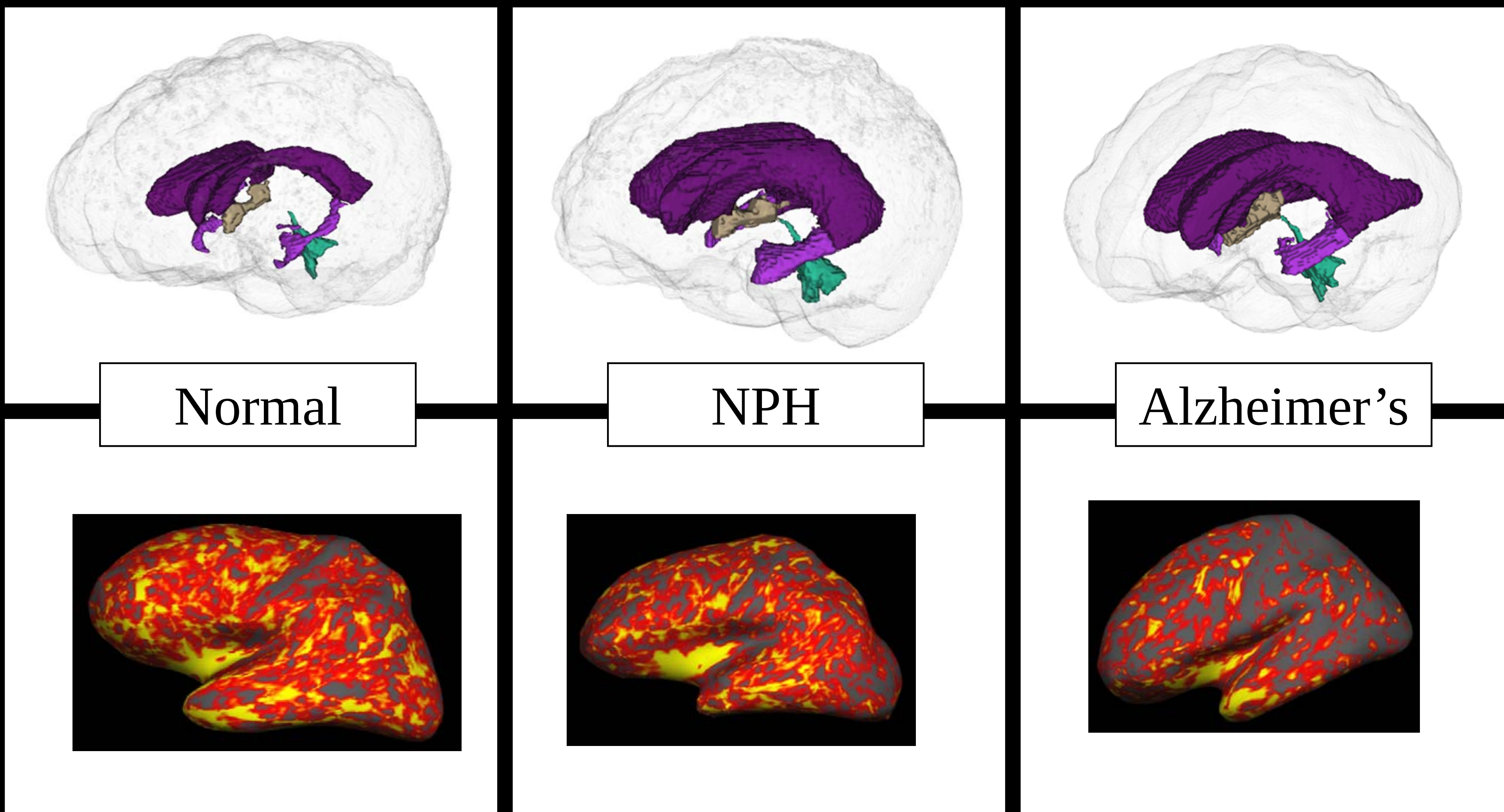
- Cortical thickness measurements provide an index of cortical atrophy and may be more refractory to artifactual distortion in the context of ventriculomegaly than regional brain volume measurements (eg hippocampal volume)



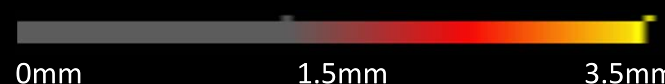
Programs such as FreeSurfer measures the thickness of the outer layer of the brain (the cortex) by measuring the distance between the gray and white matter boundaries.

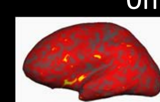
Thickness can be mapped across the entire surface of the brain.

Volumetric Imaging of NPH and Alzheimer's

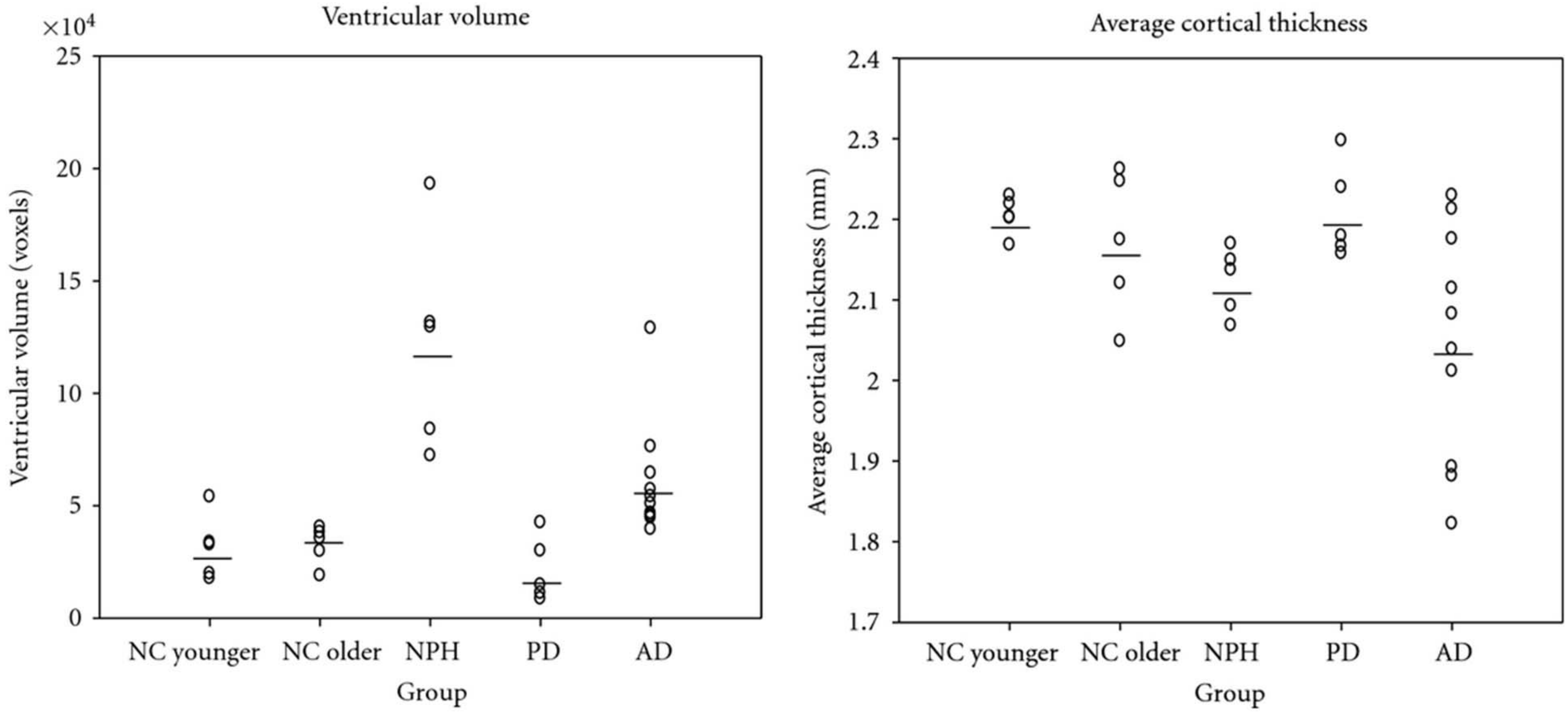


 = Ventricular Volume Maps



 = Cortical Thickness Maps

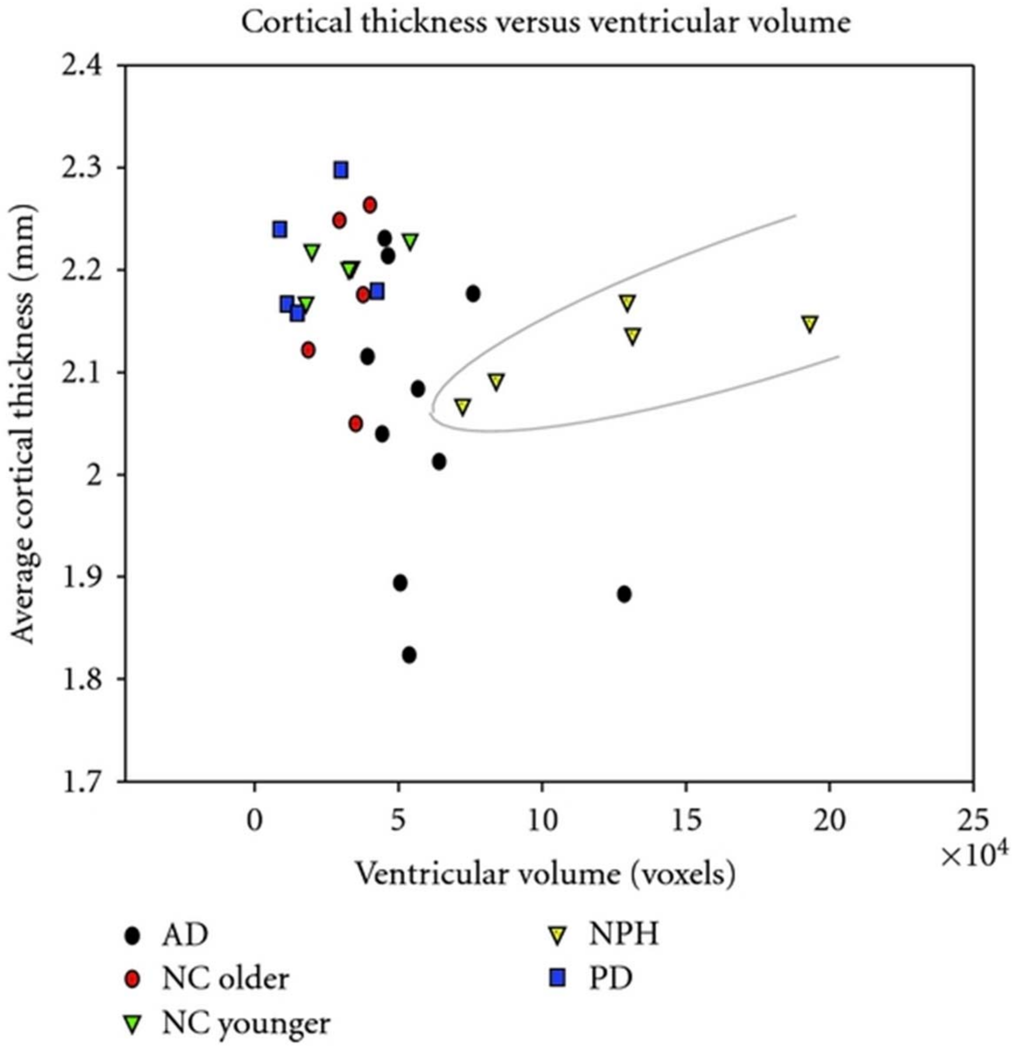
Ventricular Volume and Cortical Thickness in iNPH



Neither ventricular volume nor cortical thickness measurements alone distinguish iNPH cases from Alzheimer's disease

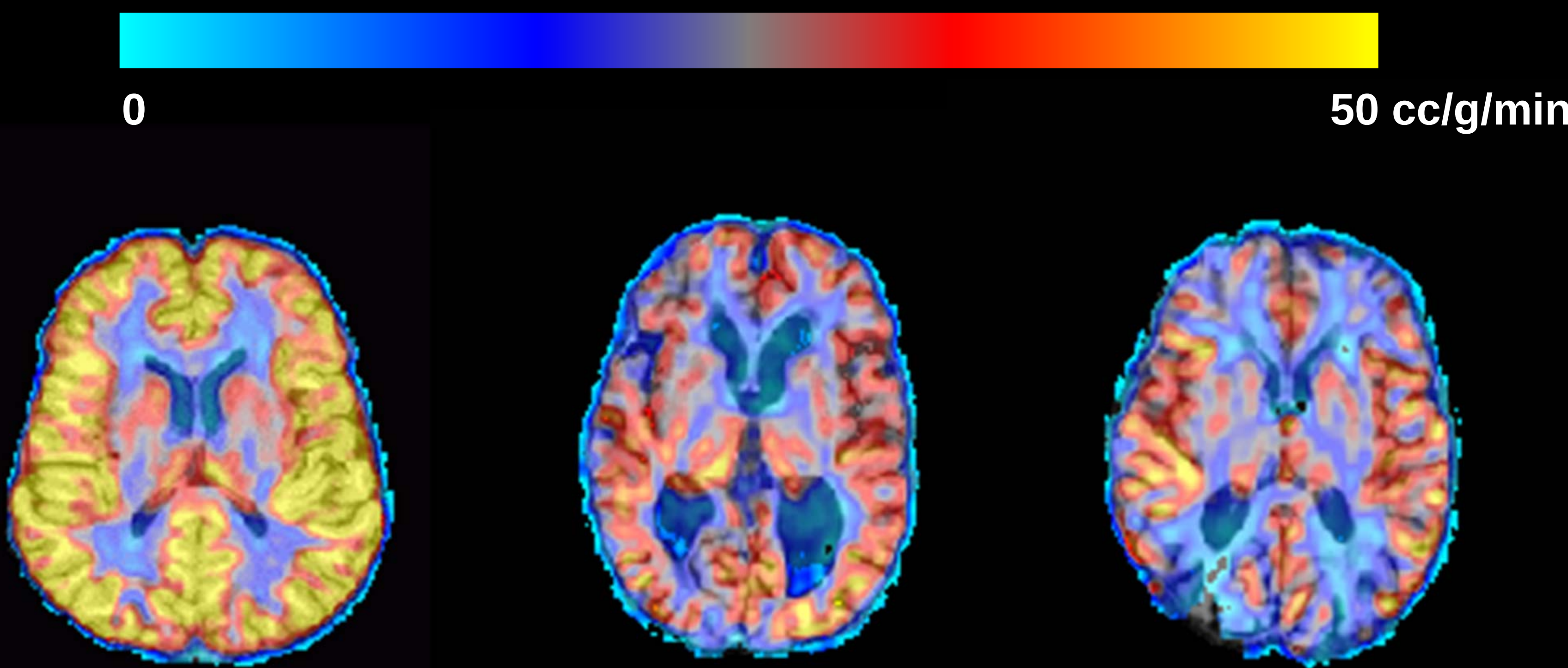
From Moore D, et al (2012) *Neurol Res Int.*

Combined Ventricular Volume and Cortical Thickness Measurements may better distinguish iNPH from other disorders



Arterial Spin Label (ASL) MRI

Quantitative brain perfusion measurements without contrast injection

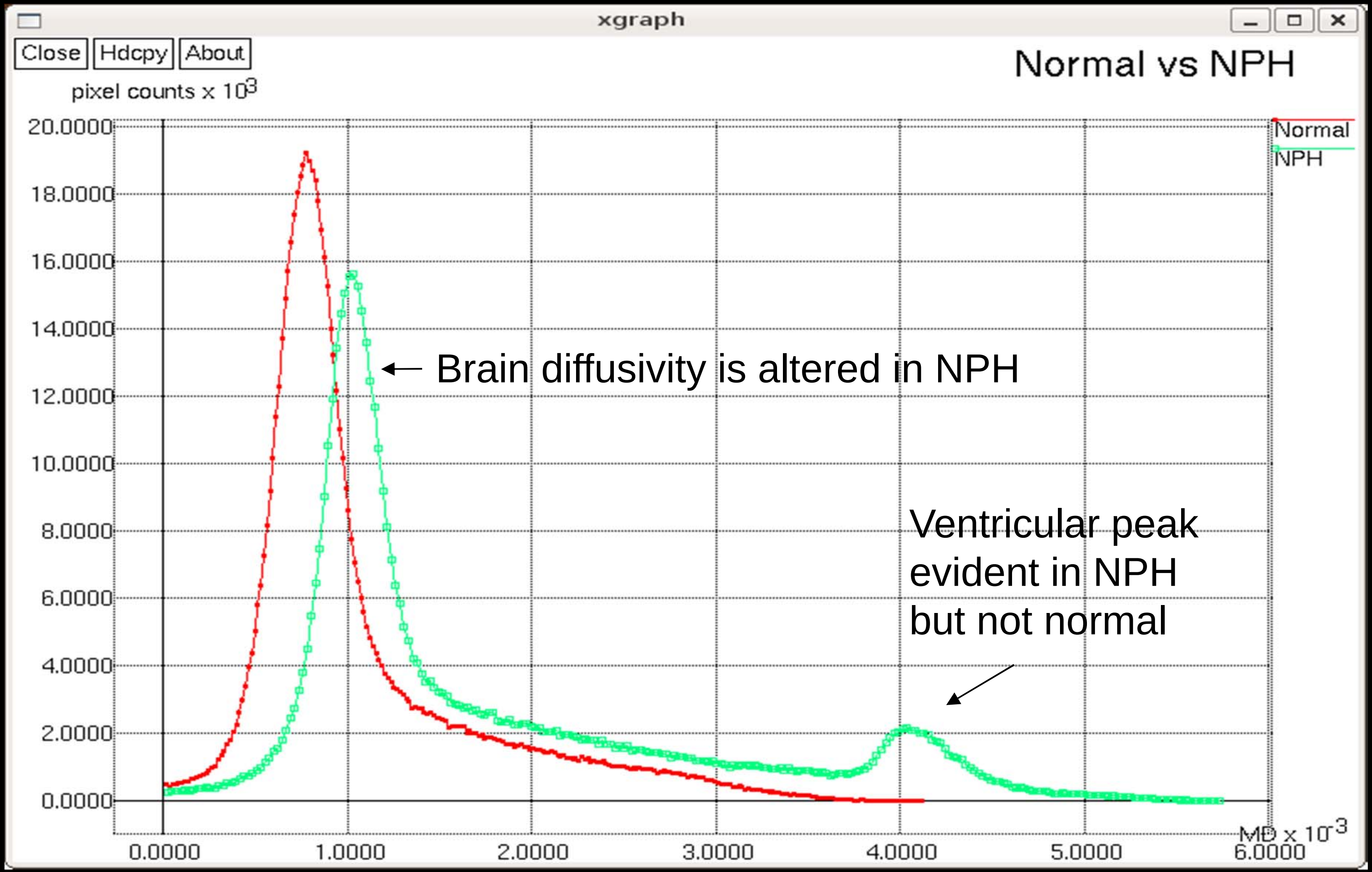


Young Normal Control

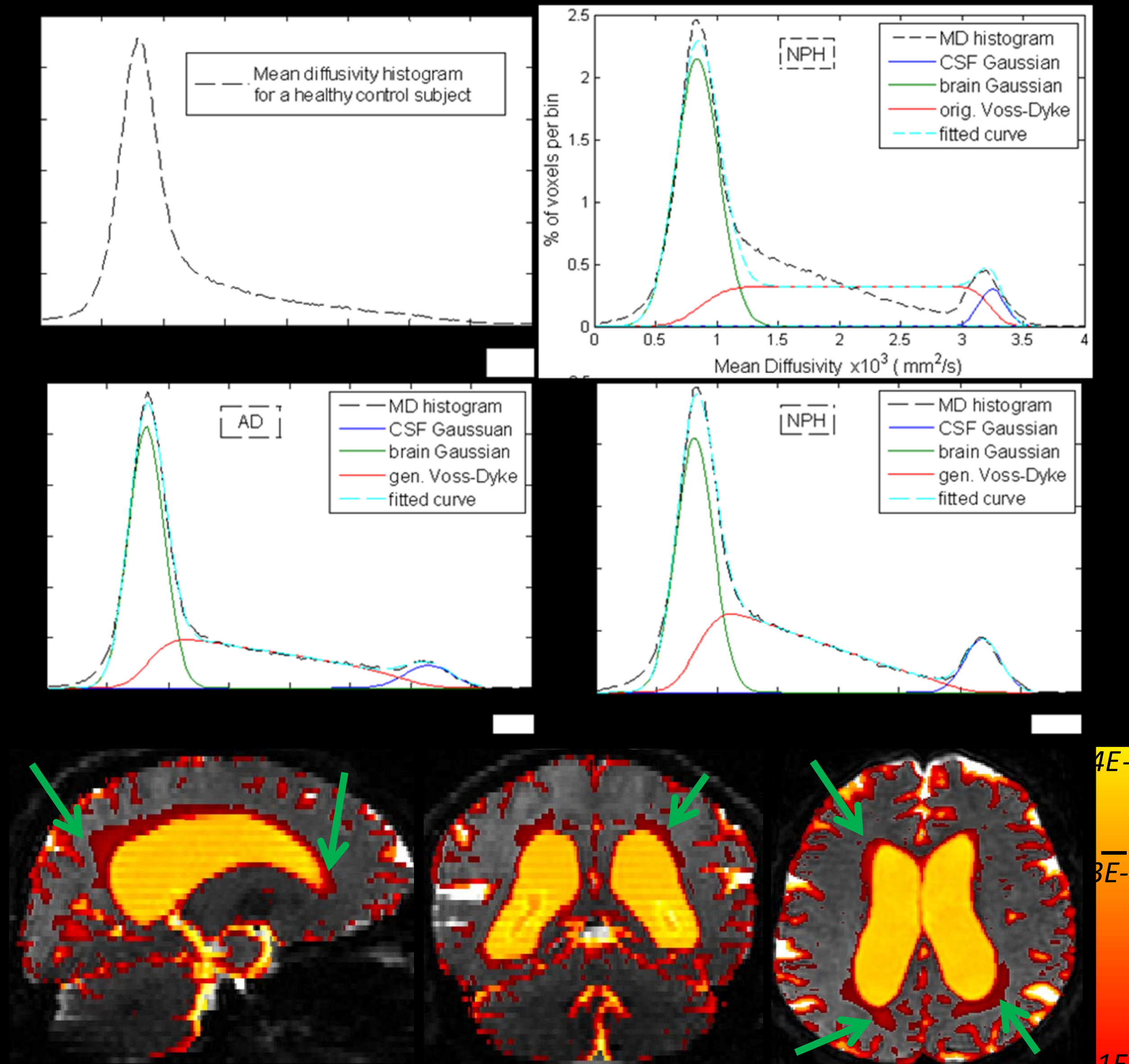
Normal Pressure Hydrocephalus

Alzheimer's disease

Diffusion Tensor Imaging: MD Histogram Analysis



Partial Volume pixels contribute to distinctive DTI signature of NPH

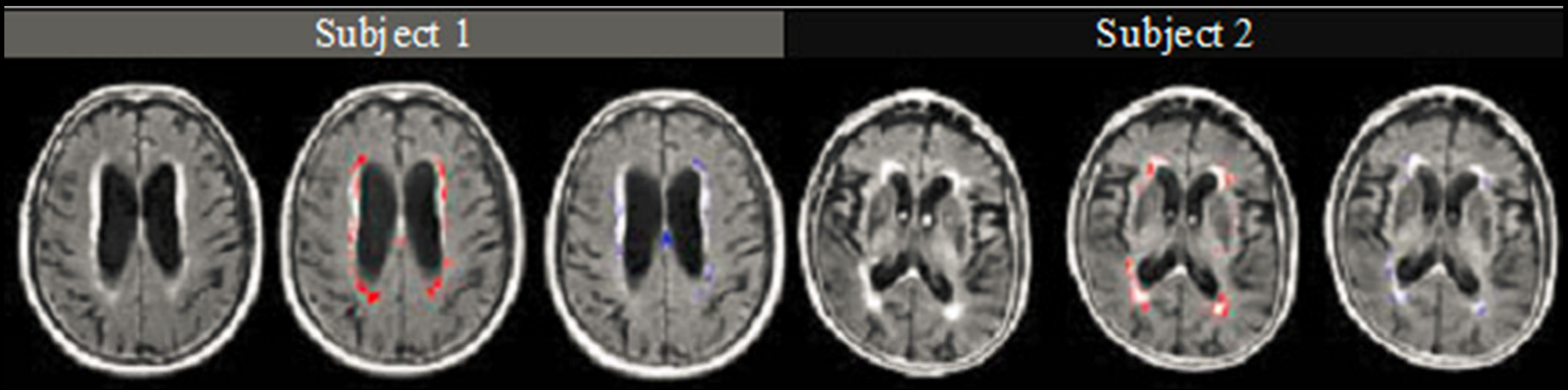


A pilot study of MRI Guided Pharmacotherapy for NPH

Relkin et al (2012) AAN Platform #992

- Recent advances in MRI methodology have created a powerful new platform for exploring the structural and hydrodynamic changes in the brain associated with NPH and its treatment
- We initiated a pilot study to examine the feasibility of using clinical and quantitative MRI measures to evaluate a potential drug treatment for iNPH
- An initial open label experience involved administering acetazolamide (ACZ) to 5 iNPH patients who consented to serial quantitative MRIs

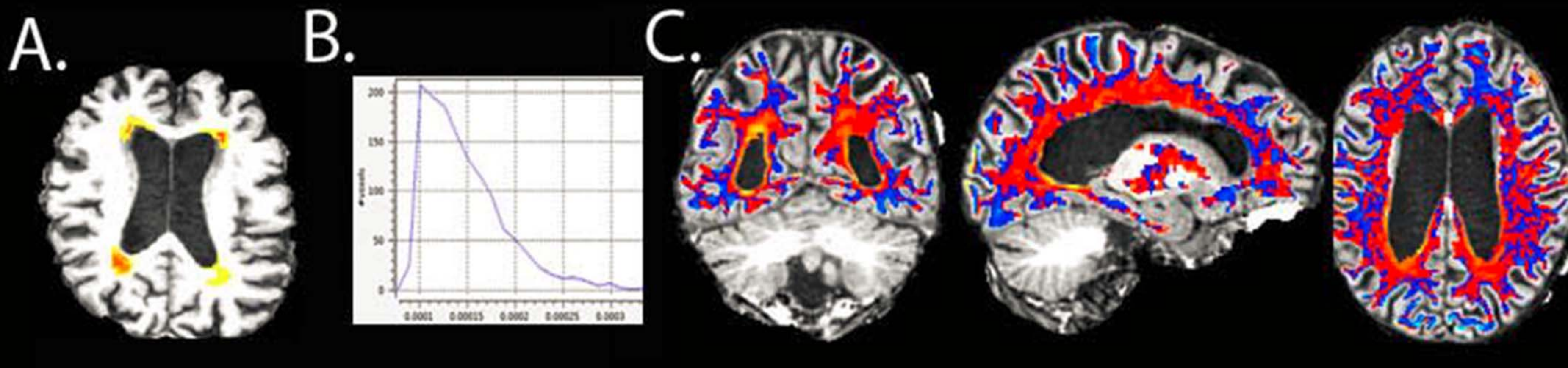
NPH Pharmacotherapy Feasibility Study
Volume of White Matter Hyperintensities decreases and Boon Gait Score Improves after ACZ treatment



	Subject 1			Subject 2		
	Baseline	ACZ 125mg/d	ACZ 250mg/d	Baseline	ACZ 125mg/d	ACZ 250mg/d
WMH (mls)	24.5	18.8	16.7	19.4	14.6	13.5
Cumulative WMH change		**-23%**	**-34%**		**-25%**	**-32.5%**
Boon Gait Score	17	12	12	8	6	4
Cumulative Boon change		**-29%**	**-29%**		**-25%**	**-50%**

MRI Feasibility Study Results

Diffusion Tensor Outcomes



A) T1 hyperintensities from NPH patient treated with 125mg/d ACZ for 1 month. Within these regions, MD decreased a maximum of 8.7% and the isotropic (free water) fraction decreased by maximum of 5.7% after ACZ

B) Histogram showing number of voxel (y-axis) with decreased Mean Diffusivity (x axis) after ACZ.

C) Free water fraction after ACZ. Red zones: pixels with decrease free water after ACZ treatment blue zones have increased free water fraction


Pre-Treatment

Conclusions

- Neuroimaging is essential to the diagnosis of NPH and plays an increasingly important role in guiding treatment
- Visual inspection of conventional clinical images can assist in distinguishing NPH from other conditions but is a subjective process
- Quantitative MRI techniques are advancing our understanding of the pathophysiology of NPH and are likely to transform clinical diagnosis and prognostication in the future.