Neuroimaging of Normal Pressure Hydrocephalus

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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 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

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

<table>
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<tr>
<th>Use</th>
<th>Modality</th>
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<tr>
<td>Guide LP or lumbar drain placement</td>
<td>X-ray, X-ray Fluoroscopy</td>
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<tr>
<td>Confirms correct shunt placement, setting and shunt integrity</td>
<td>X-ray, CT (MRI)</td>
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<tr>
<td>Monitors ventricular size (shunt failure, overdrainage syndromes)</td>
<td>CT (MRI)</td>
</tr>
<tr>
<td>Identify post-shunt complications (subdural effusions and hematomas)</td>
<td>CT (MRI)</td>
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The Challenge

Which of these images is from a patient who has iNPH and is likely to respond to shunt?

A. 35 year old with Aqueductal Stenosis
B. 79 year old with Alzheimer’s Disease
C. 87 year old with Shunt responsive Normal Pressure Hydrocephalus
Ventricles are symmetrically enlarged in NPH
The Evan’s Index = $A \div B$

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

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

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
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 (e.g., 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

Normal

NPH

Alzheimer’s

= Ventricular Volume Maps

= Cortical Thickness Maps
Neither ventricular volume nor cortical thickness measurements alone distinguish iNPH cases from Alzheimer’s disease

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

Weill Cornell Memory Disorders Program
Diffusion Tensor Imaging: MD Histogram Analysis

Brain diffusivity is altered in NPH

Ventricular peak evident in NPH but not normal
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

<table>
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<tr>
<th>Subject 1</th>
<th>Subject 2</th>
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<tbody>
<tr>
<td>WMH (mls)</td>
<td>Baseline 19.4</td>
</tr>
<tr>
<td></td>
<td>ACZ 125mg/d 14.6</td>
</tr>
<tr>
<td></td>
<td>ACZ 250mg/d 13.5</td>
</tr>
<tr>
<td>Cumulative WMH change</td>
<td>-23%</td>
</tr>
<tr>
<td>Boon Gait Score</td>
<td>12</td>
</tr>
<tr>
<td>Cumulative Boon change</td>
<td>-29%</td>
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</table>

- Table showing changes in WMH and Boon Gait Score for two subjects after ACZ treatment.
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.
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.