NPH and Macrocephaly

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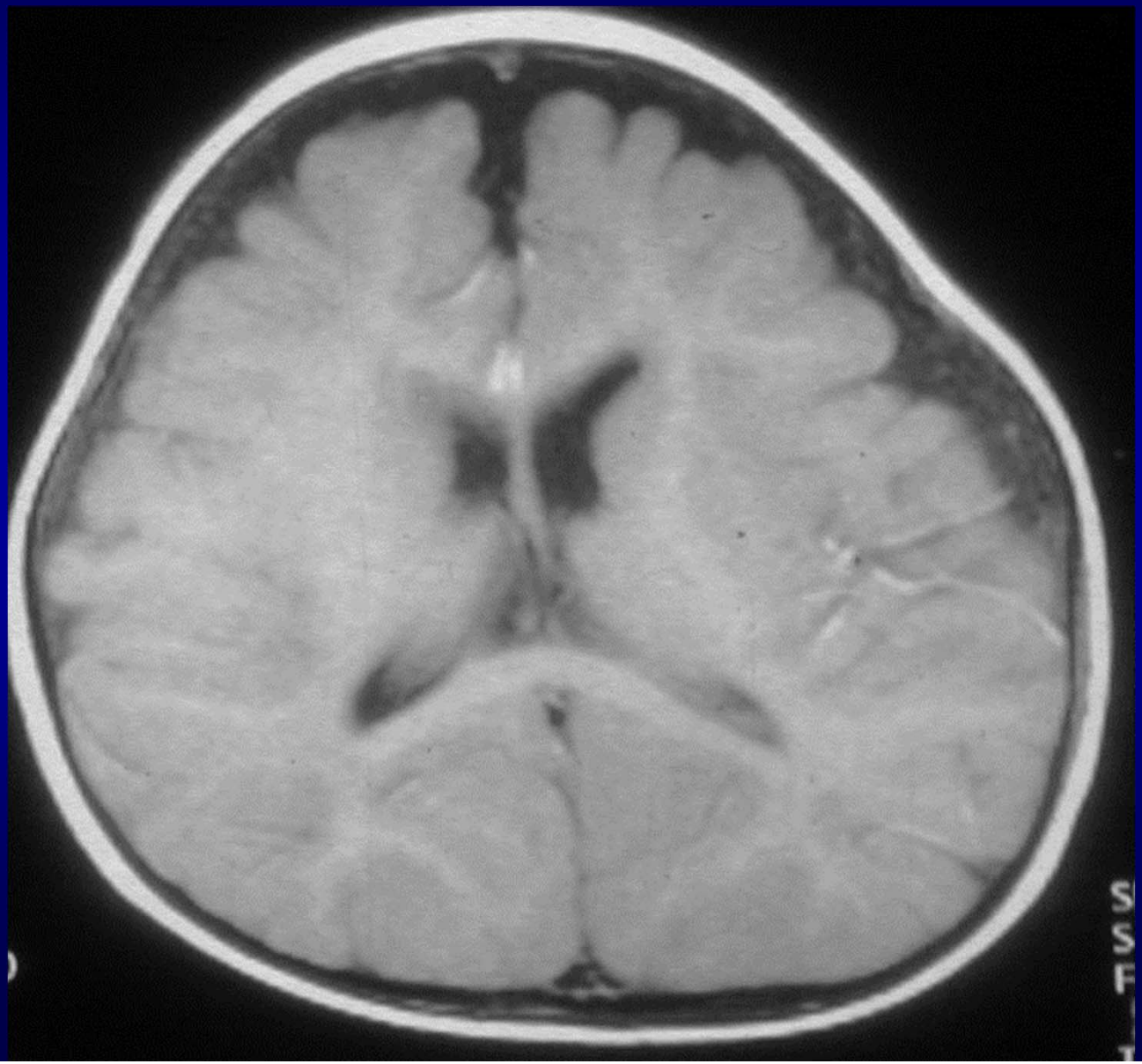
Benign External Hydrocephalus



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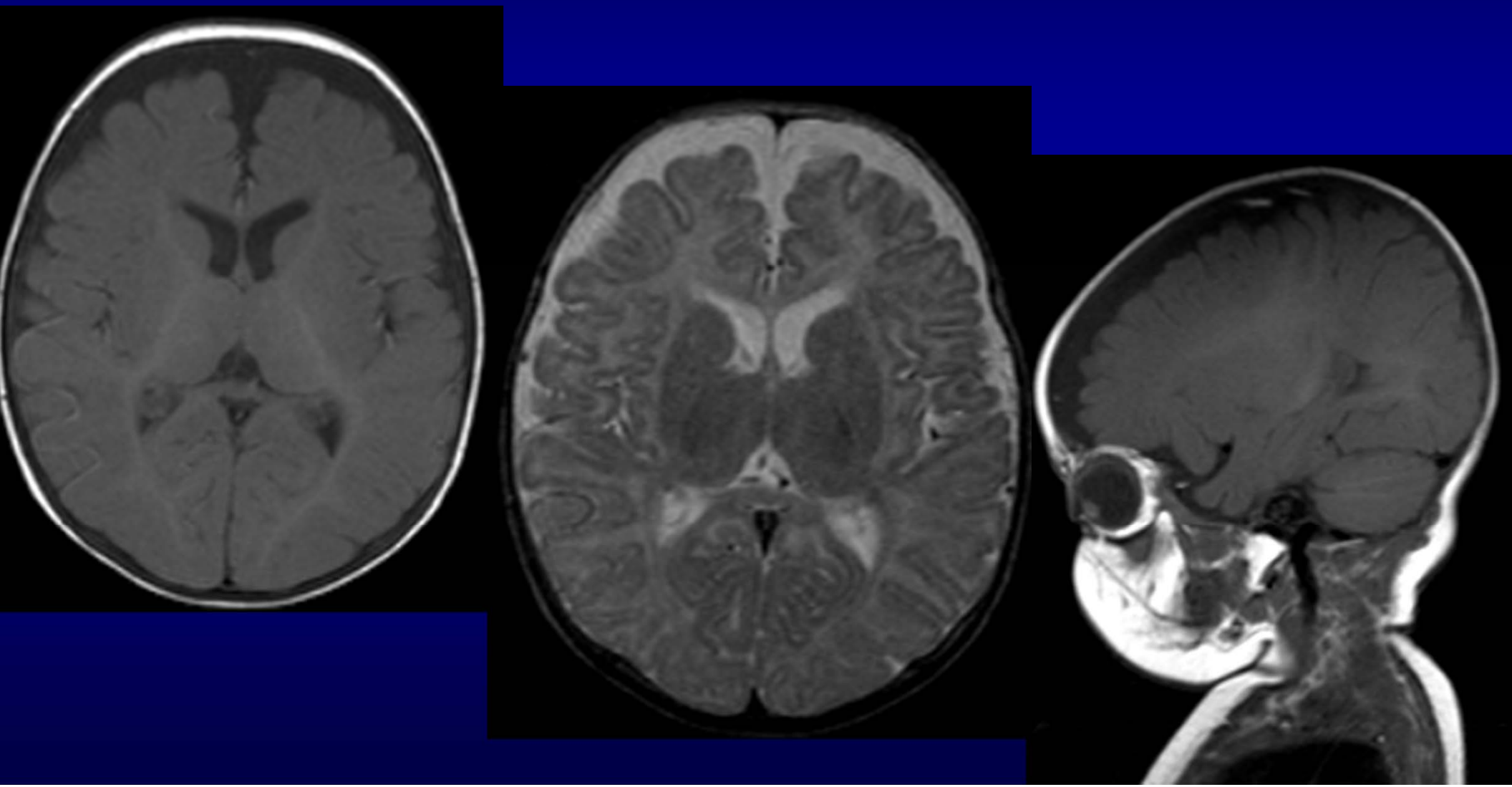
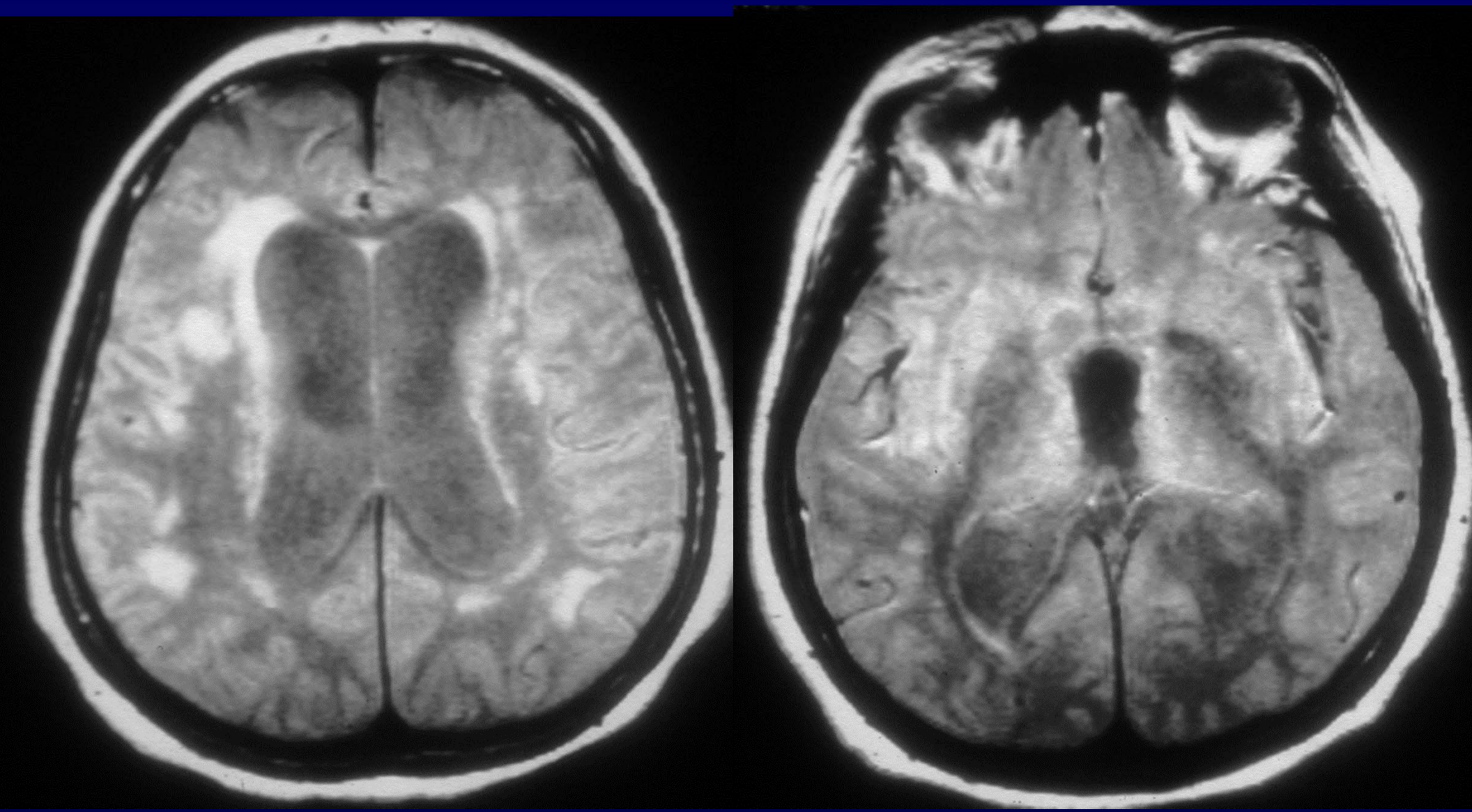
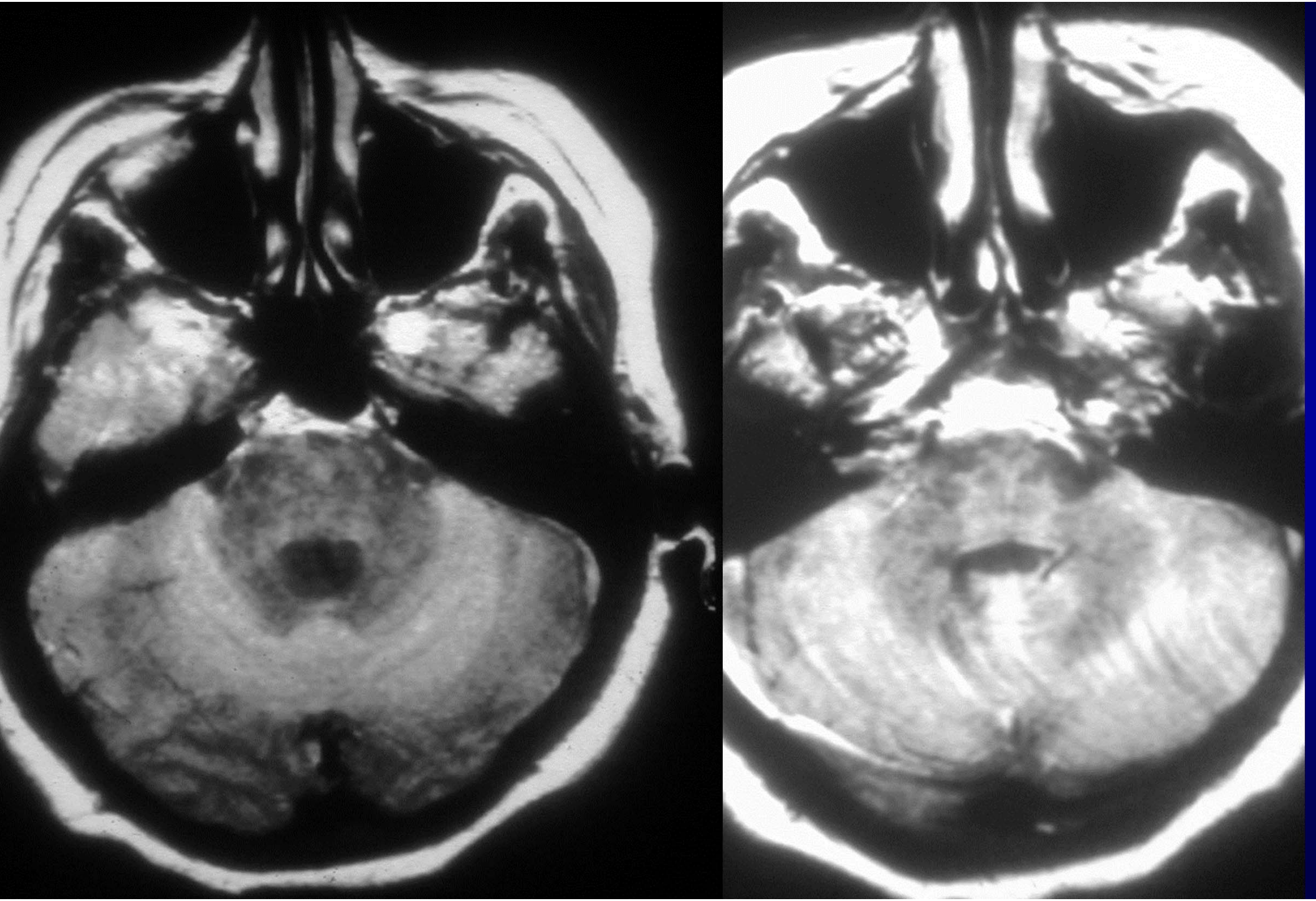


Tectal Glioma

How does the CSF get out??

NPH





Proposed Causes of CSF Motion

- Production by choroid plexus (500 ml/day)
- Cardiac pulsations
  - Choroid plexus (Bering, 1959)
  - Large arteries
  - Cerebral hemispheres (phase-contrast MRI)

CSF Flow Void vs. Surgical Response

- 20 patients shunted for presumed NPH (1984)
- All had gait disturbance and dementia
- 17/20 had incontinence

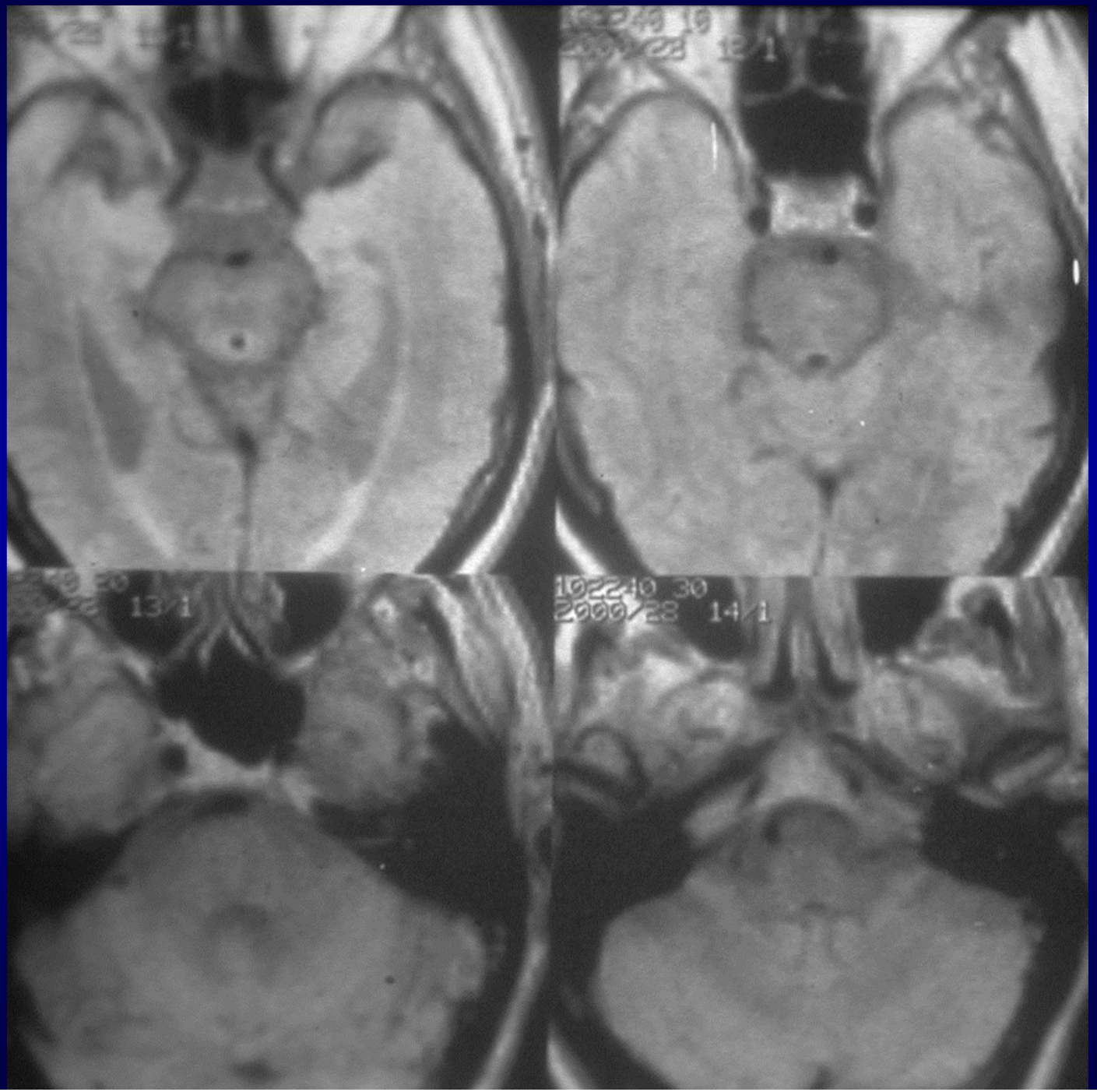
NPH vs CSF Flow Void

- Surgical Response graded (1984)
  - Excellent-good
  - Fair-poor
- CSF flow graded (1989)
  - Absent-mild
  - Moderate-severe

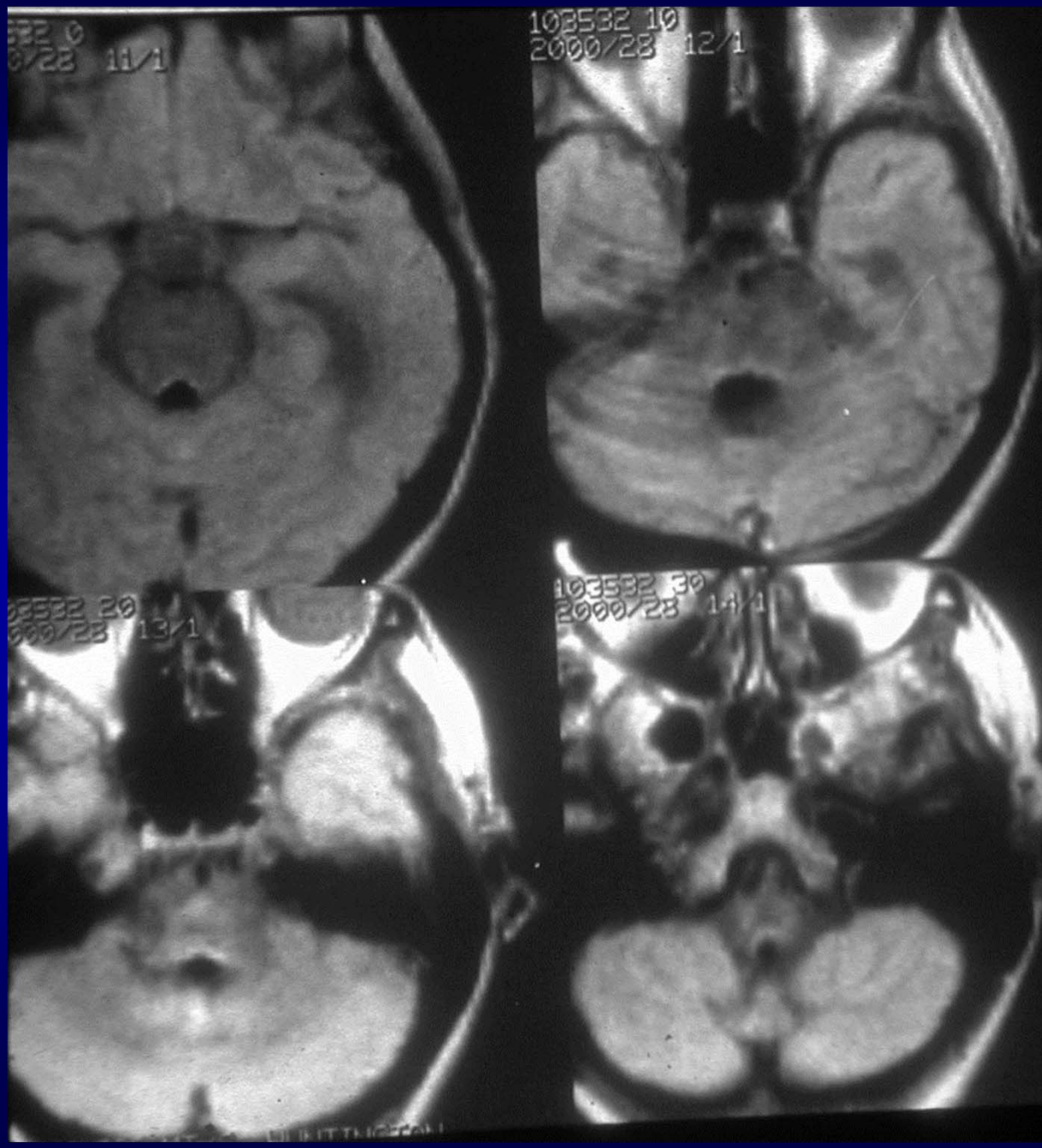
Materials and Methods

- Surgical Response Compared to:
- CSF Flow Void on Routine MRI
  - 1984
  - No flow compensation

Normal (1984)



Hyperdynamic flow (1984)

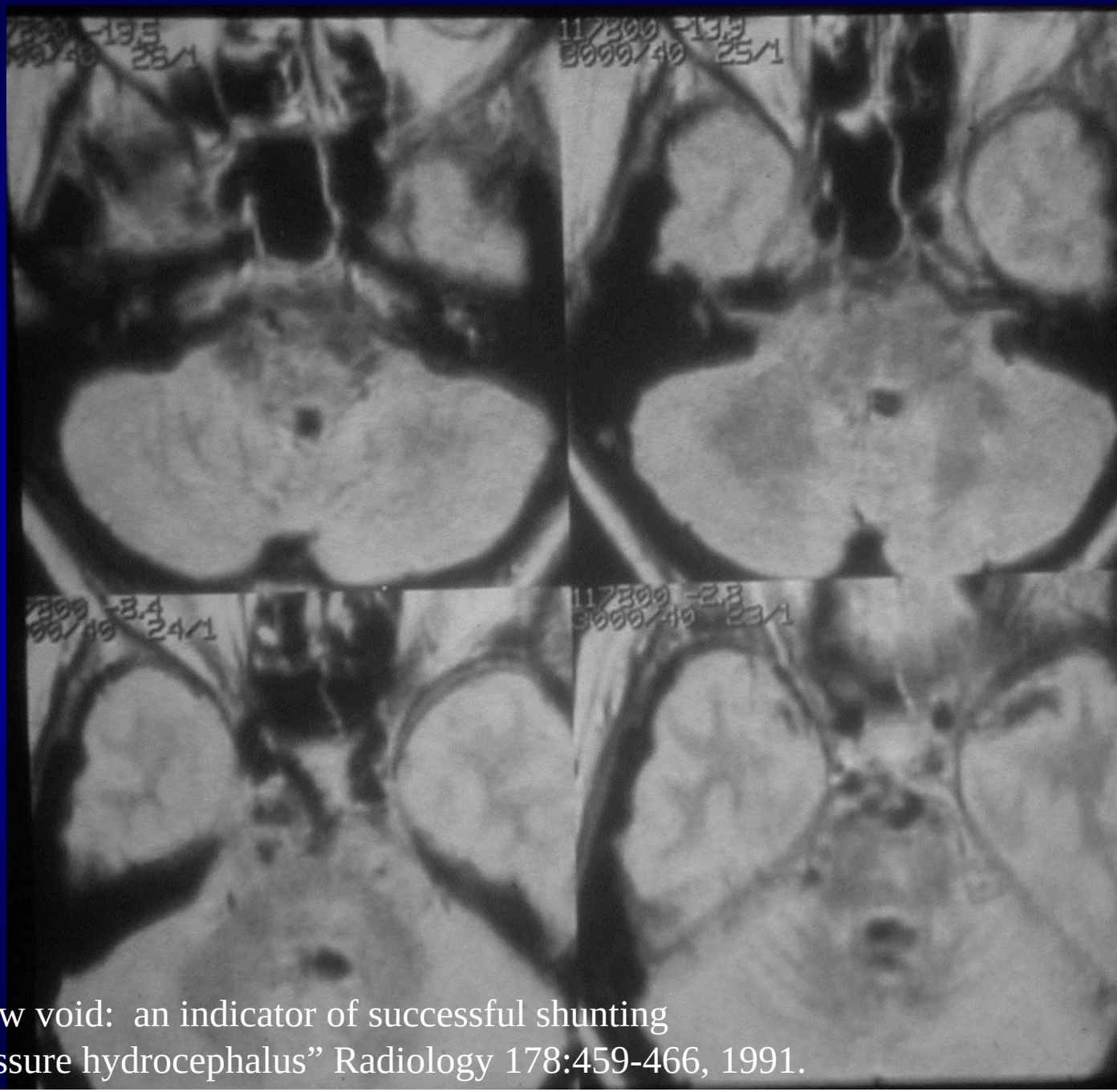


CSF Flow Void

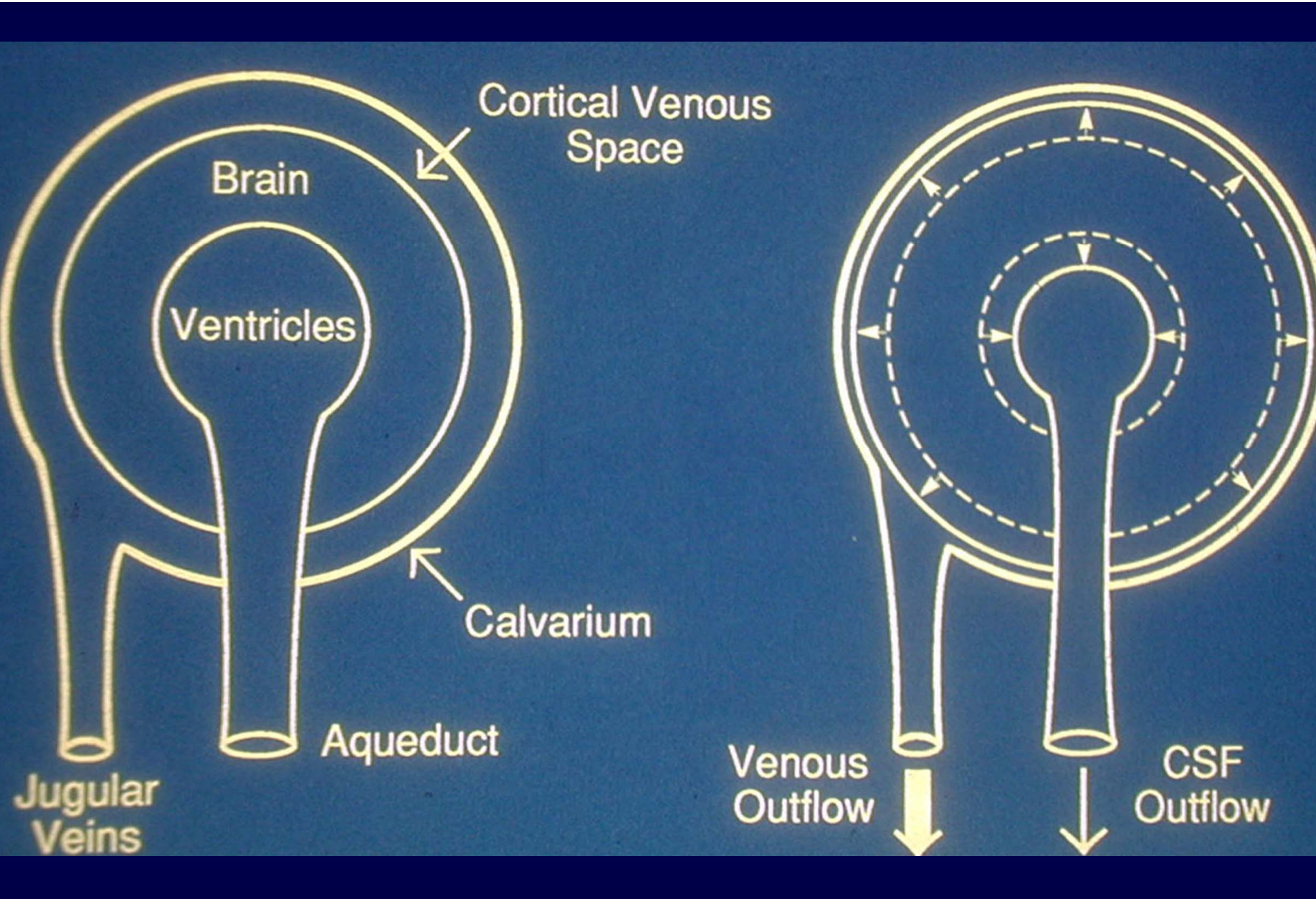
Surgical Response	Marked	Minimal
Good	8	1
Poor	2	9

Fisher's Exact Test
p< .003

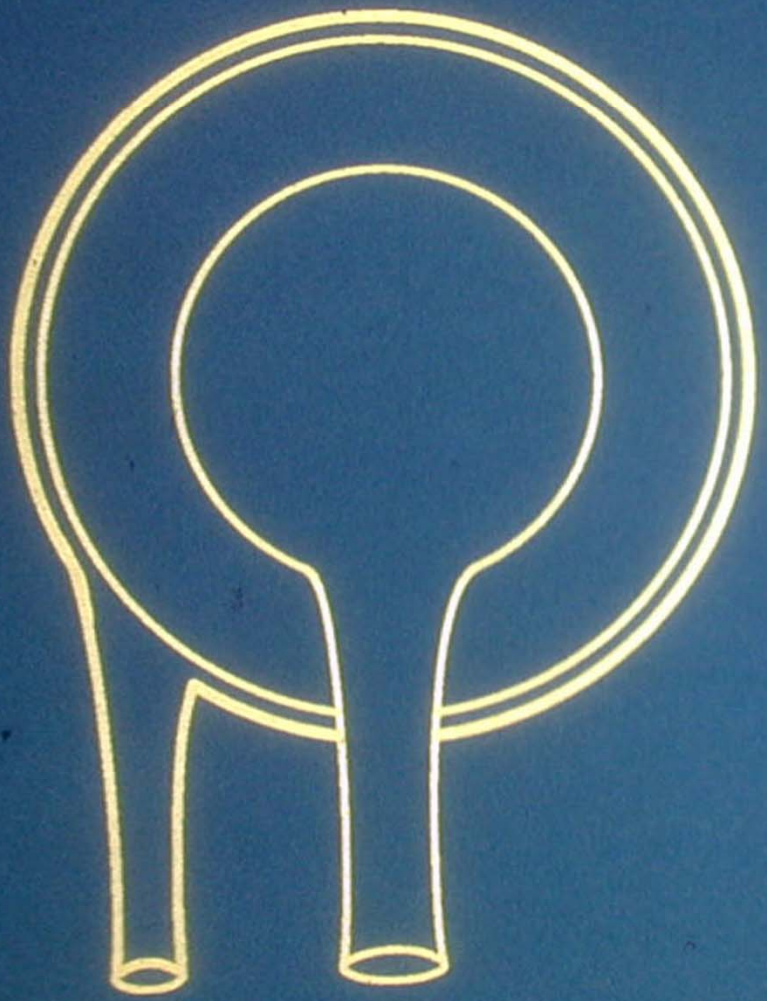
To shunt or not to shunt (1984)



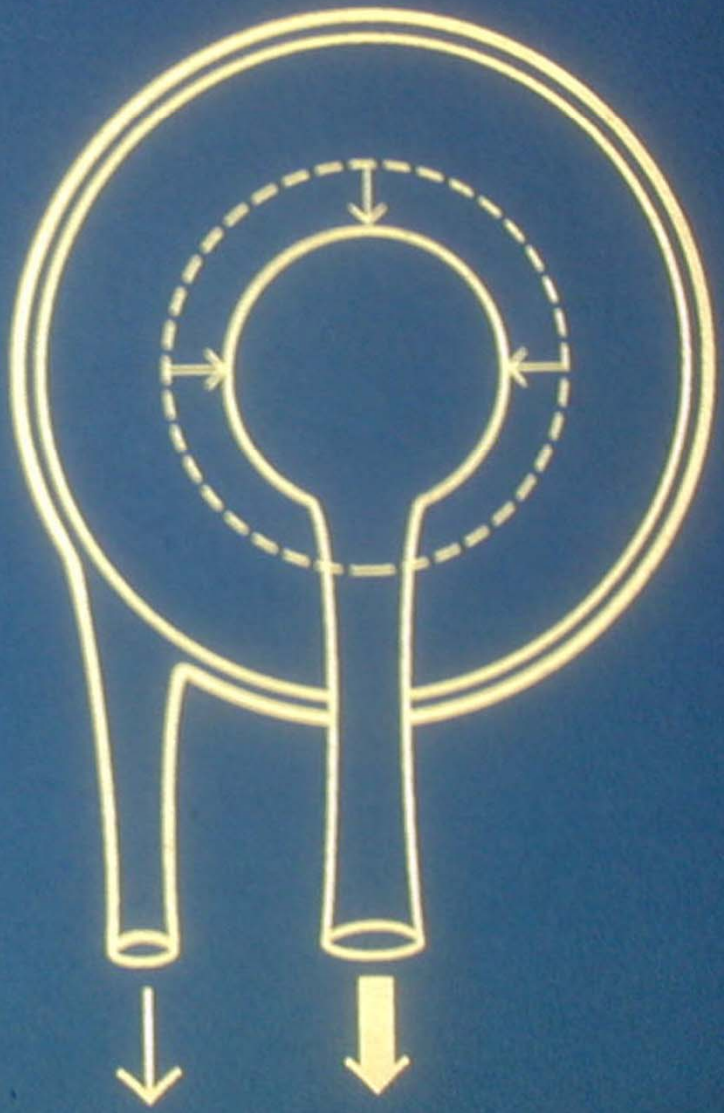
Bradley WG, et al, “Marked CSF flow void: an indicator of successful shunting in patients with suspected normal pressure hydrocephalus” Radiology 178:459-466, 1991.


Cortical Venous Space
Brain
Ventricles
Calvarium
Aqueduct
Jugular Veins
Venous Outflow
CSF Outflow

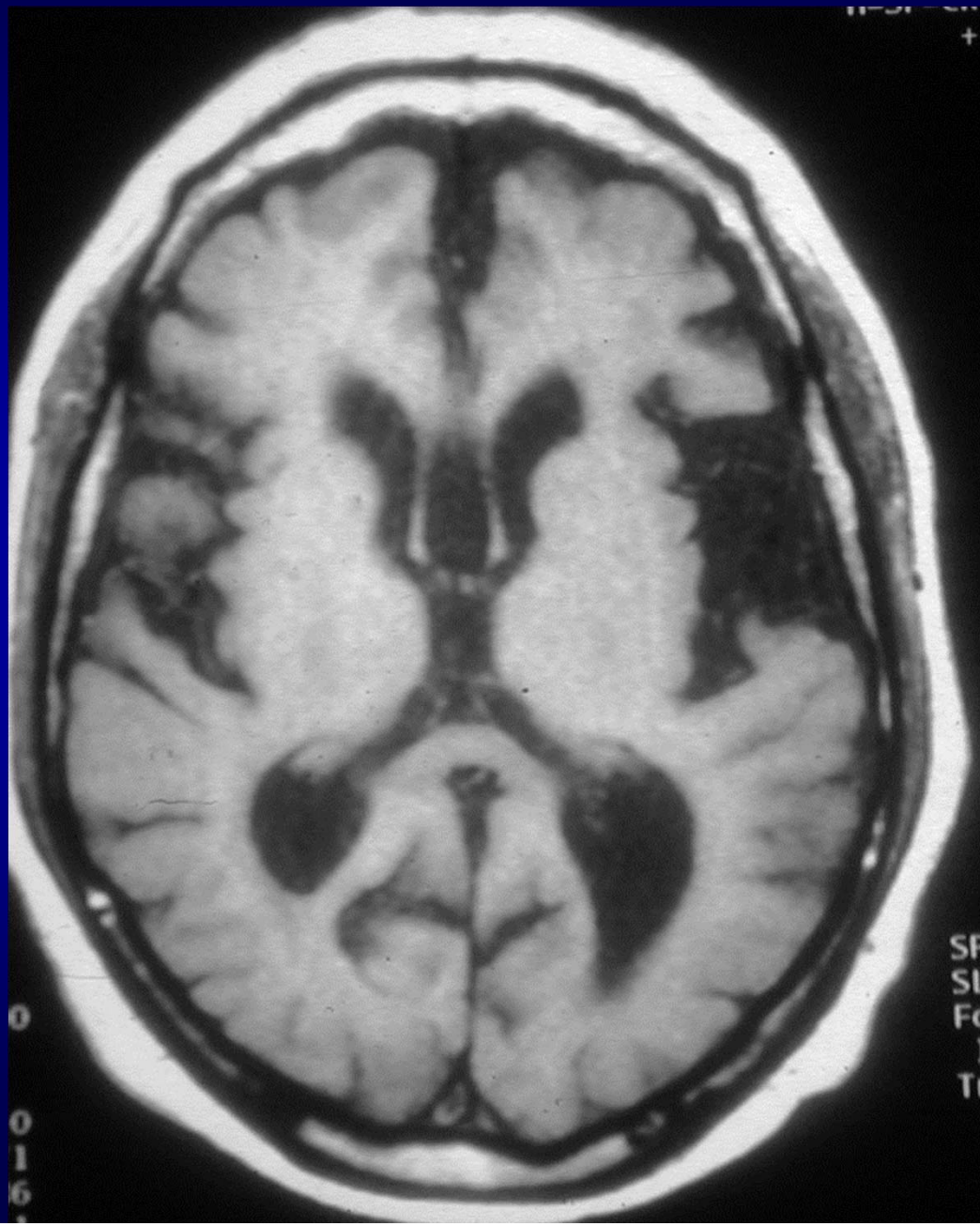
Communicating Hydrocephalus:
Diastole



Communicating Hydrocephalus:
Systole



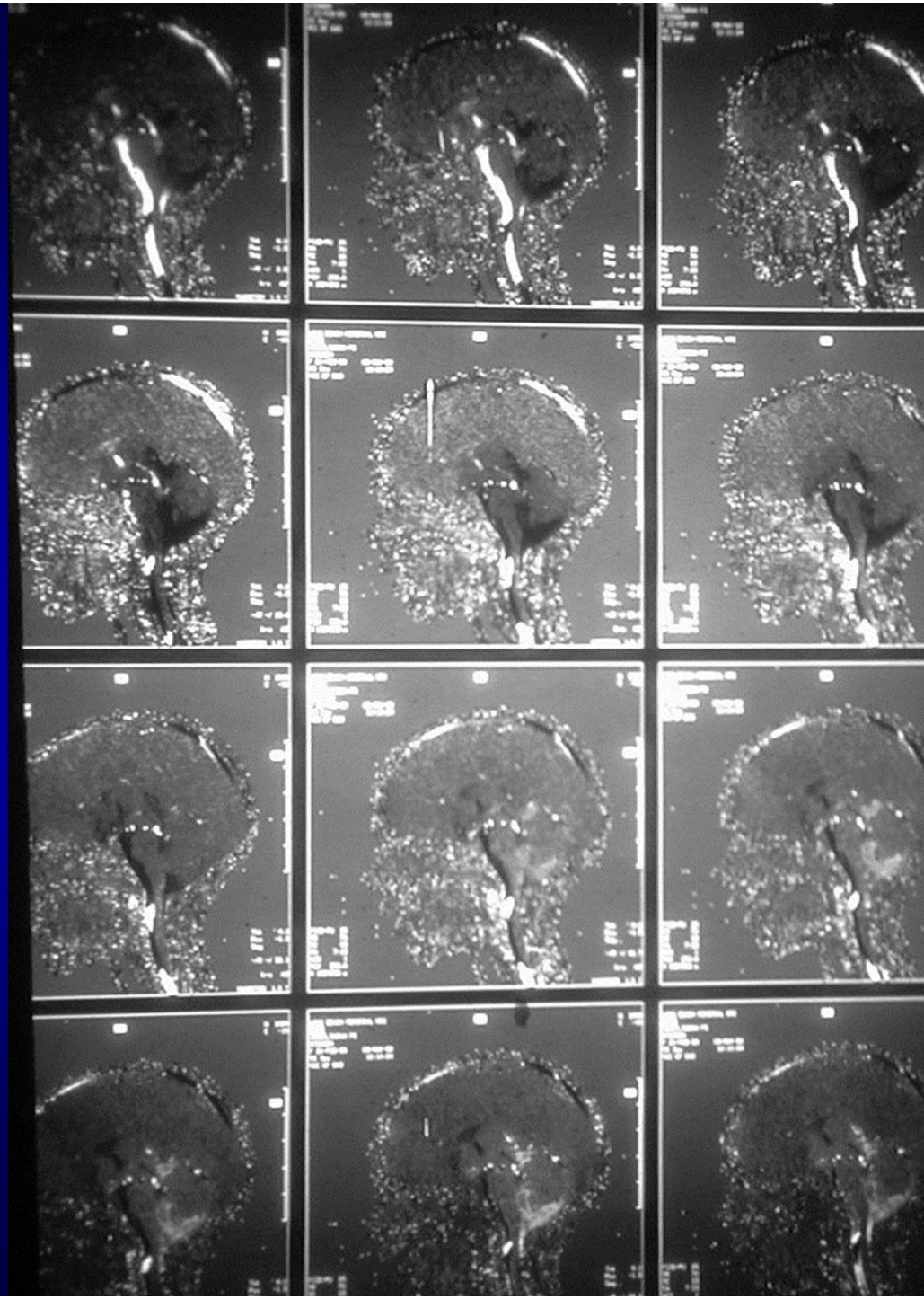
Enlarged Sylvian cisterns in NPH



Phase Contrast CSF Velocity Imaging

- “Velocity” is speed plus direction
- Flow sensitization along craniocaudal axis
  - Flow up: shades of black
  - Flow down: shades of white
  - No flow: gray
  - Set aliasing velocity
  - Quantification of velocity or flow

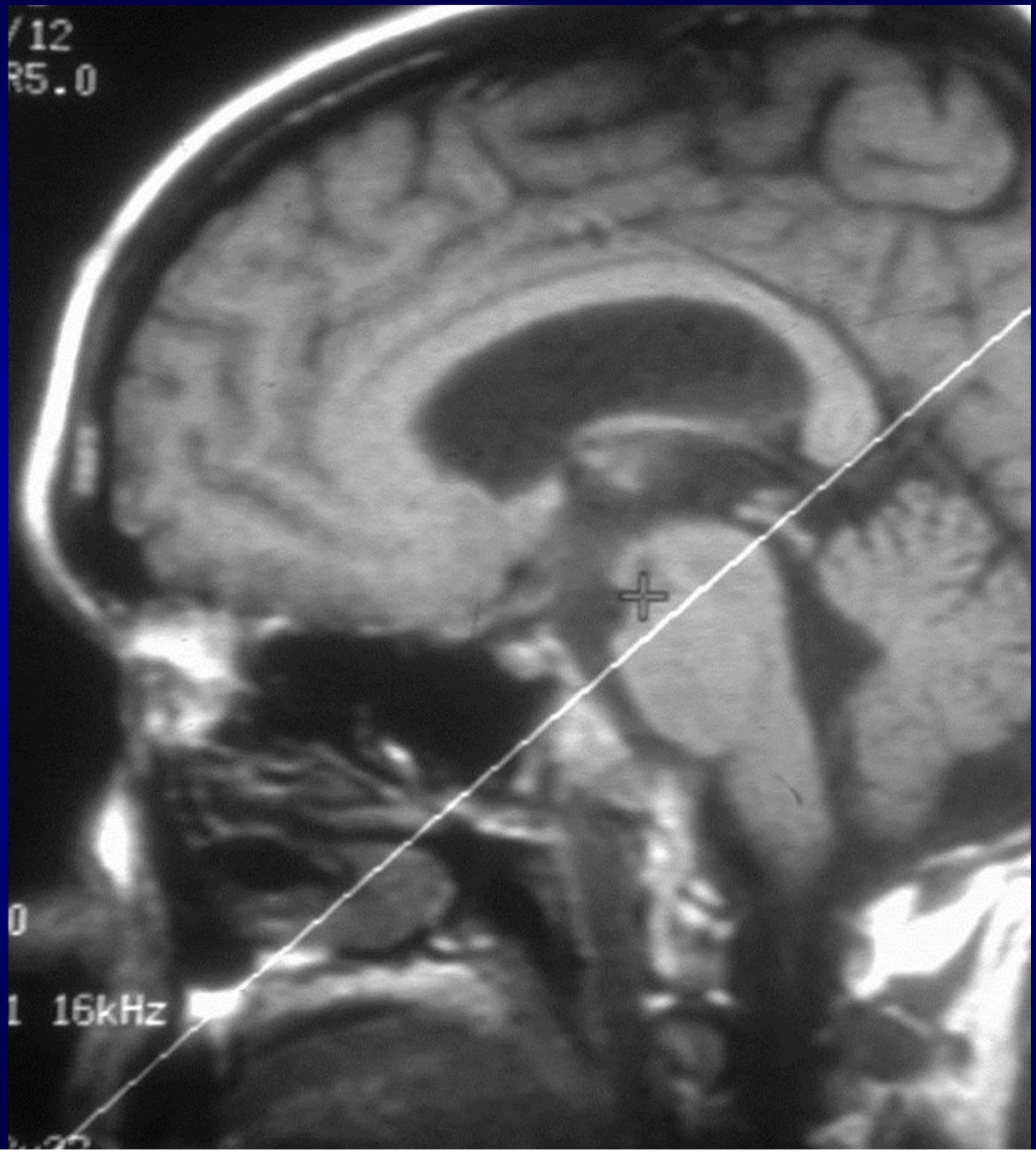
Qualitative CSF Velocity Imaging



Quantitative CSF Flow Study

- 512x512; 16 cm FOV
- .32 mm pixels
- 4mm slice angled perpendicular to aqueduct
- Velocity-encode in slice direction
- Retrospective cardiac-gating (not EKG triggering)

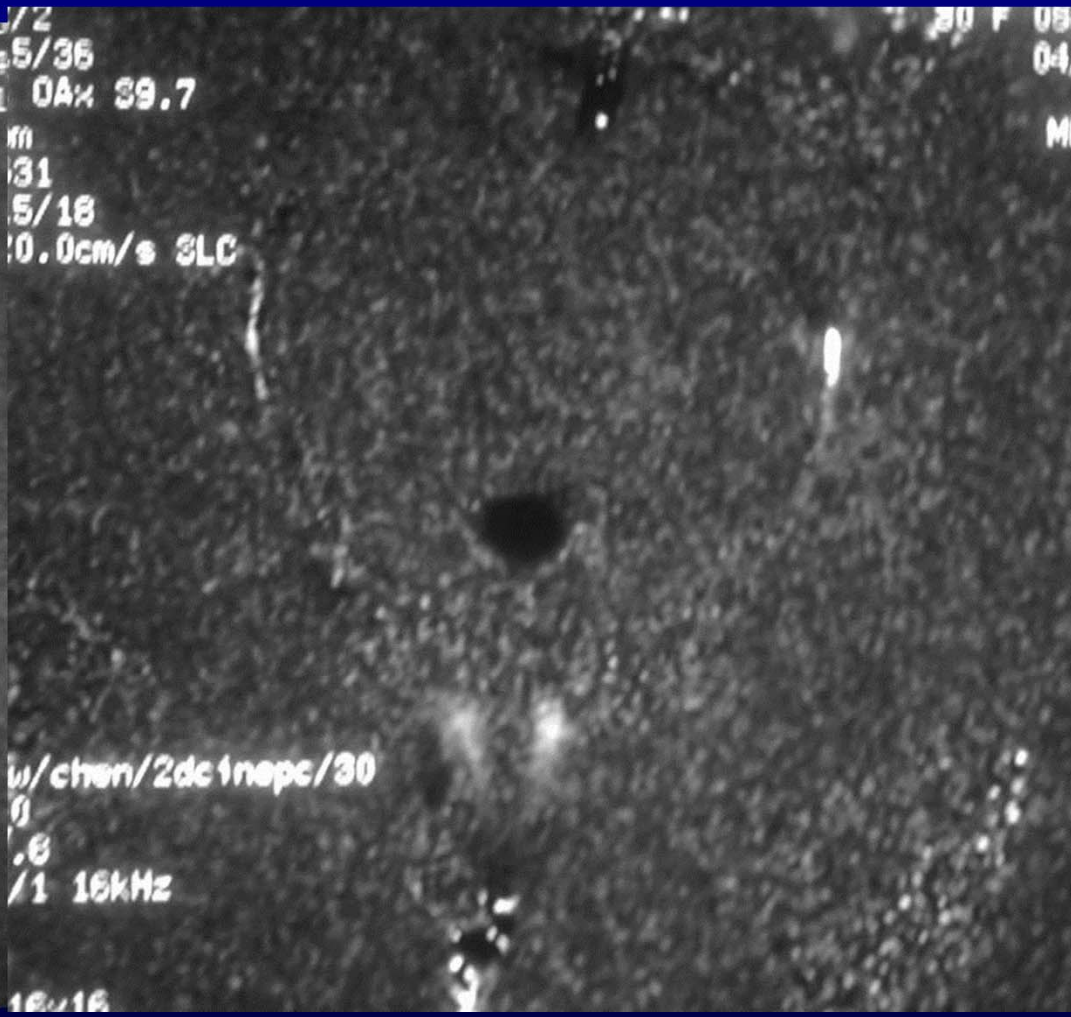
Quantitative CSF Velocity Imaging



Quantitative CSF Flow Study

- Through-plane flow-encoding
- Venc= 10, 20, 30 cm/sec (NPH)
- Venc= 5 mm/sec (shunt malfunction)

Communicating Hydrocephalus



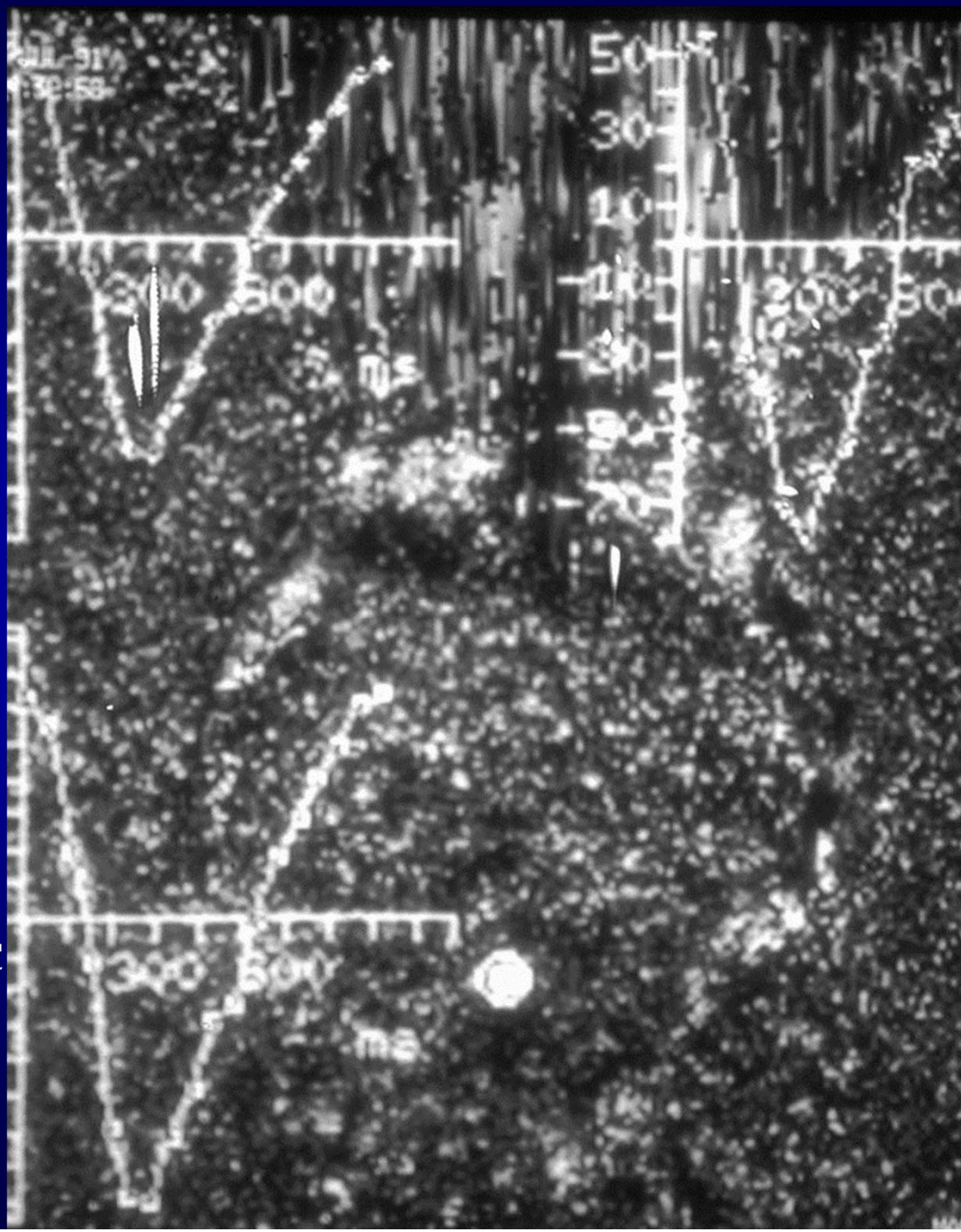
Quantitative CSF Flow

- GE: Cine PC 40/min/30 degrees
- Siemens: Retrospective Cardiac Gating
  - Flash 100/10/15 degrees
- Both: 18 Cine Frames

Quantitative CSF Velocity Imaging

cm/sec

ml/sec



Quantitative CSF Velocity Imaging

- Calculates “Aqueductal CSF stroke volume”
- Stroke volume: microliters of CSF flowing back or forth over cardiac cycle
- Verified by pulsatile flow phantom using ultrasound flow meter (Mullin, 1993)

NOVA 4D CSF FLOW

VasSol

NOVA®

Materials and Methods

- 20 Patients (age 54-85)
- Suspected NPH
- Routine MRI of Brain
- Quantitative CSF Velocity Imaging
- VP Shunt
- Follow up at 1 month

Bradley WG, et al, "Normal-pressure hydrocephalus: evaluation with cerebrospinal fluid flow measurements at MR imaging" Radiology 198:523-529, 1996.

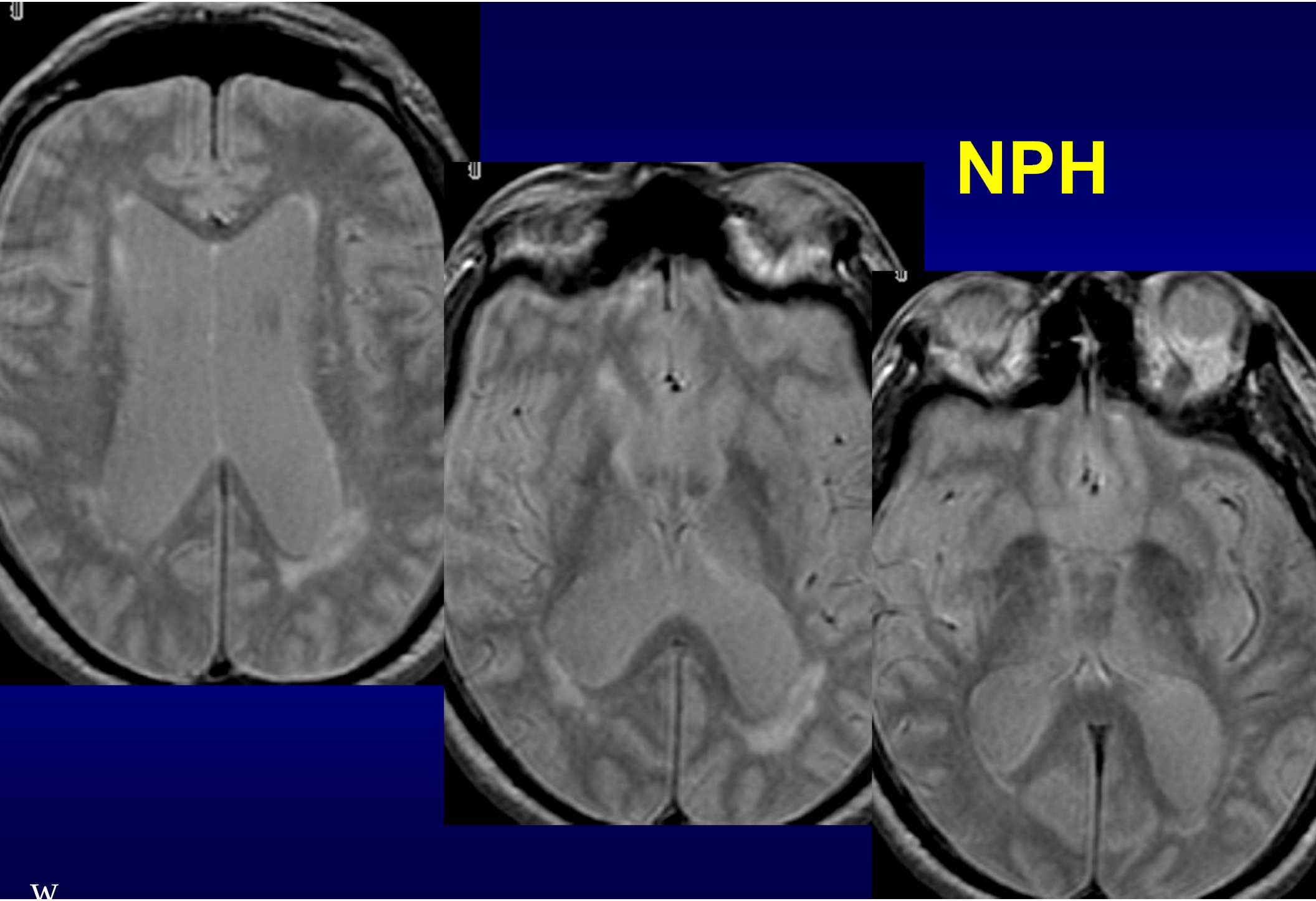
Results

- Of 20 shunted patients:
- 14 had hyperdynamic flow
  - (SV>42 microliters; NB: machine specific!)
  - 13 had a good surgical response
  - 1 did not (chronic MS)
- 6 had normal or decreased flow
  - (SV<42 microliters)
  - 3 had a good surgical response
  - 3 did not (concomitant atrophy)

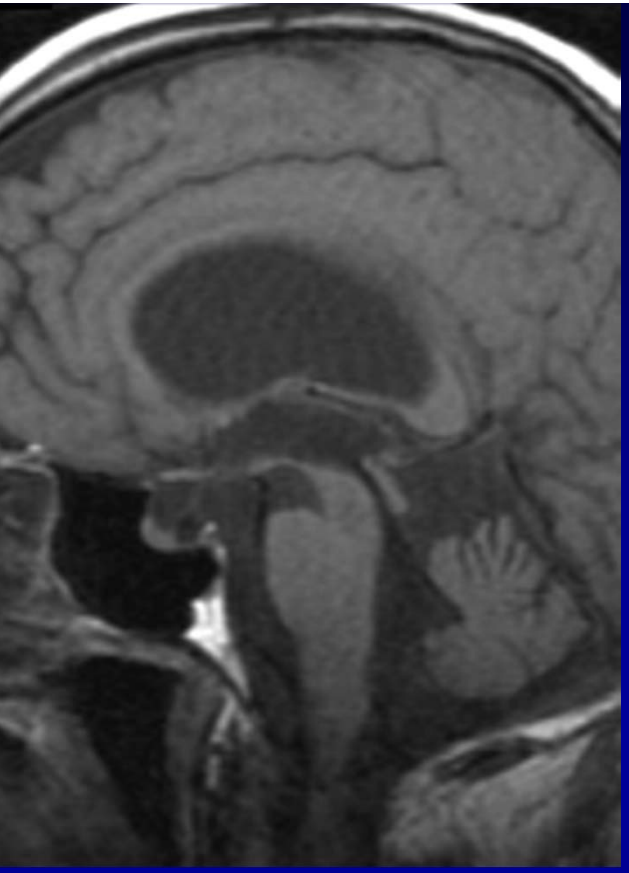
Bradley WG, et al, "Normal-pressure hydrocephalus: evaluation with cerebrospinal fluid flow measurements at MR imaging" Radiology 198:523-529, 1996.

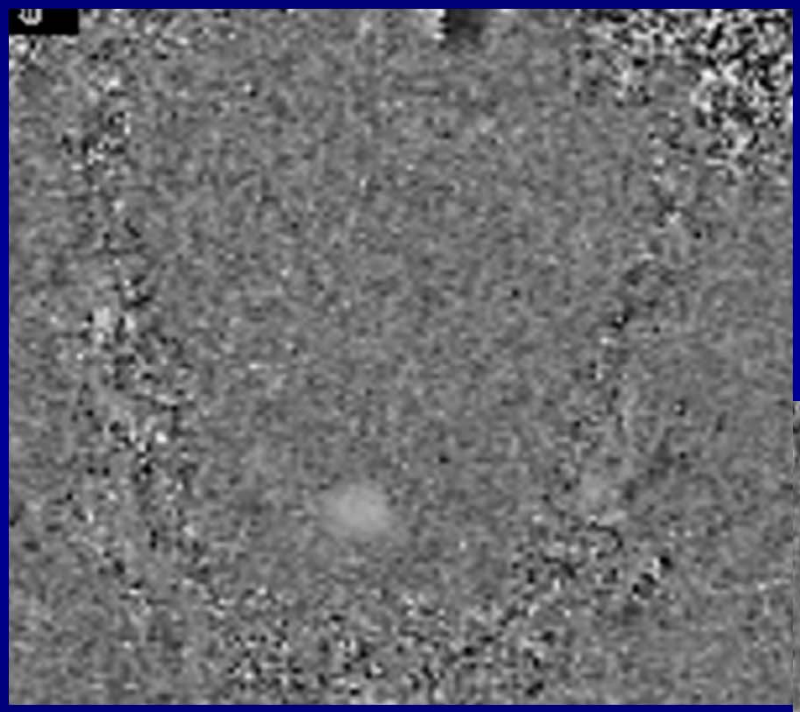
B

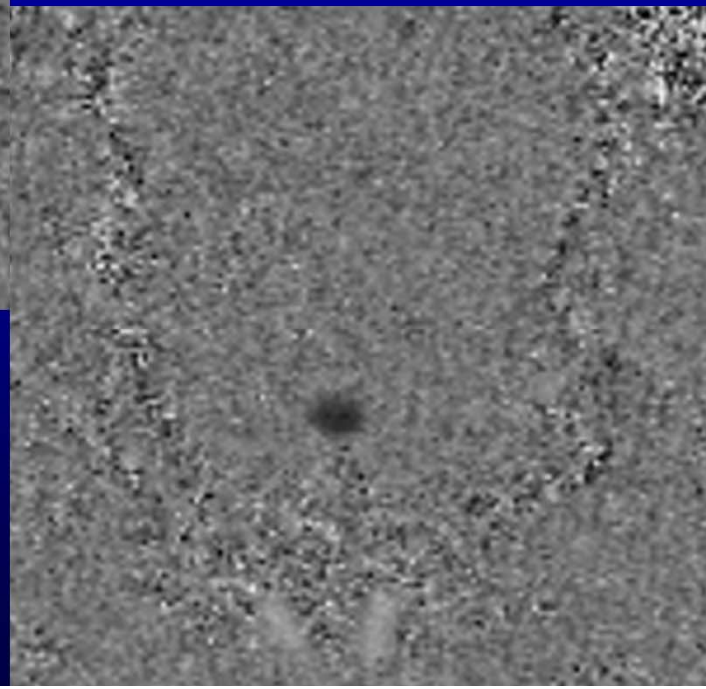
NPH



NPH (SV = 121 uL)







Results

- Only 7 of 14 (50%) patients with hyperdynamic flow had prominent aqueductal CSF flow void or routine MR images

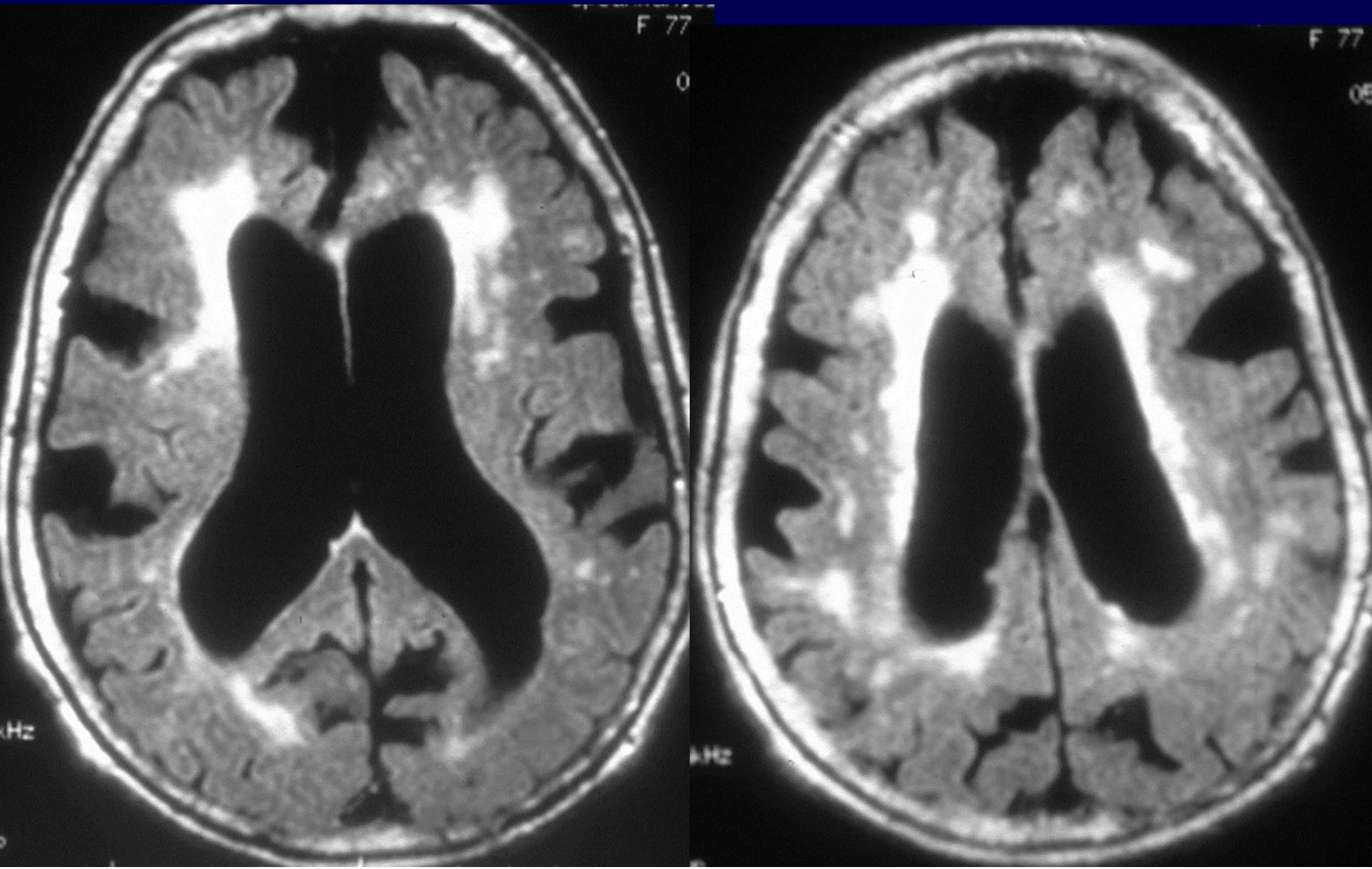
- Ubiquitous Flow Compensation; FSE

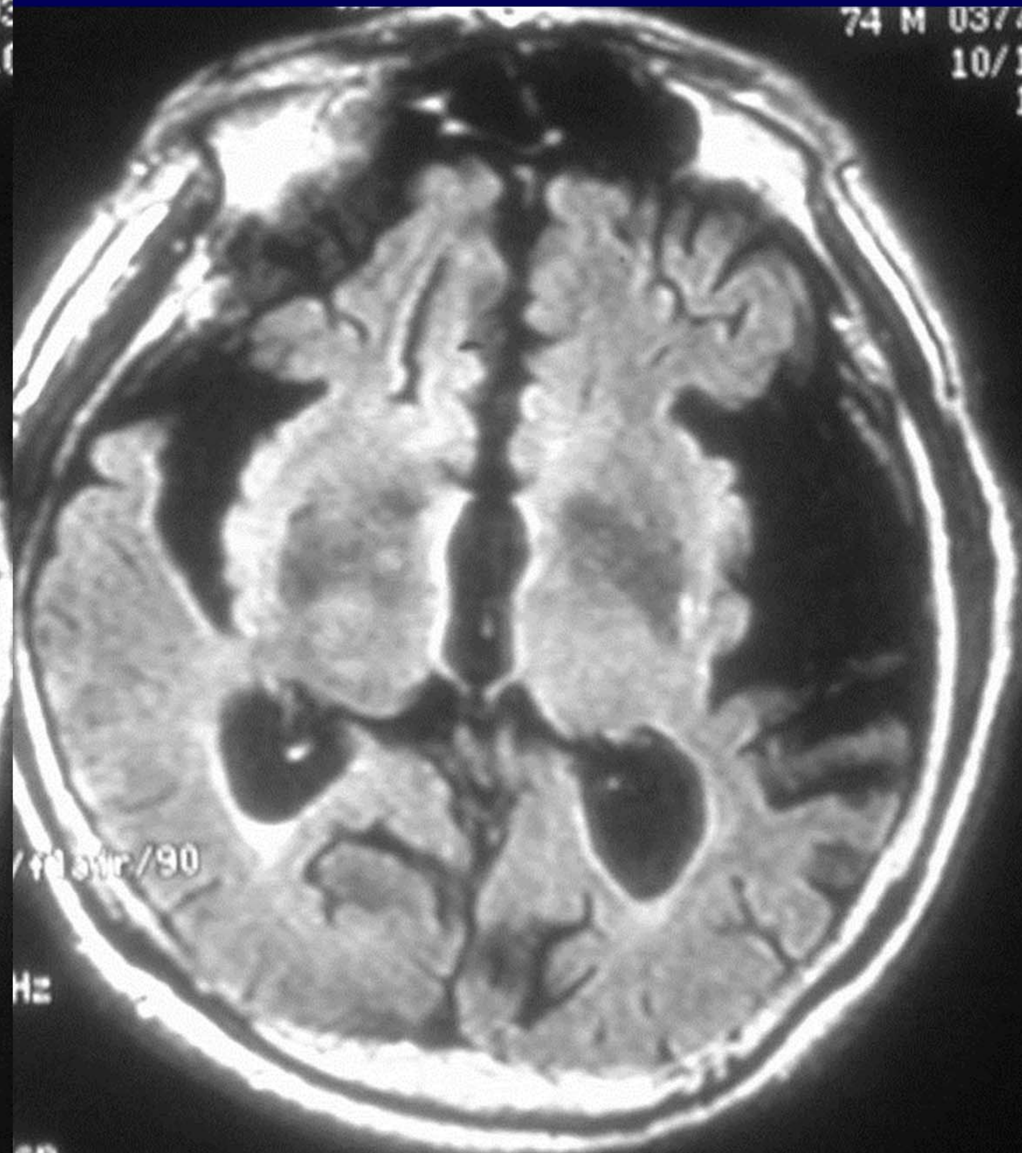
What Causes Idiopathic NPH?

- Consider normal bulk flow of water in brain
- Consider association of deep white matter ischemia (DWMI) and NPH

Normal Bulk Flow of Extracellular Brain Water

- Water leaves upstream arterioles under pressure-osmotic gradients (eg, mannitol)
- Normal and excess water resorbed by downstream capillaries and venules
- Vasogenic edema flows centripetally to be absorbed by ventricles
- Interstitial edema flows centrifugally to subarachnoid space via extracellular space


F 77
F 77


74 M 03
kHz

74 M 0377
10/1
/90

Idiopathic NPH and DWMI

- Both diseases of elderly
- Significant association now shown by many
- CBF reduced in NPH and DWMI
- Acetazolamide challenge: no increase in CBF
  - Arterioles already maximally dilated (esp WM)
- DWMI more extensive than T2 abnormality
  - Magnetization transfer ratio decreased
  - Apparent diffusion coefficient increased
  - Increased lactate on proton spectroscopy

Possible Etiology of iNPH

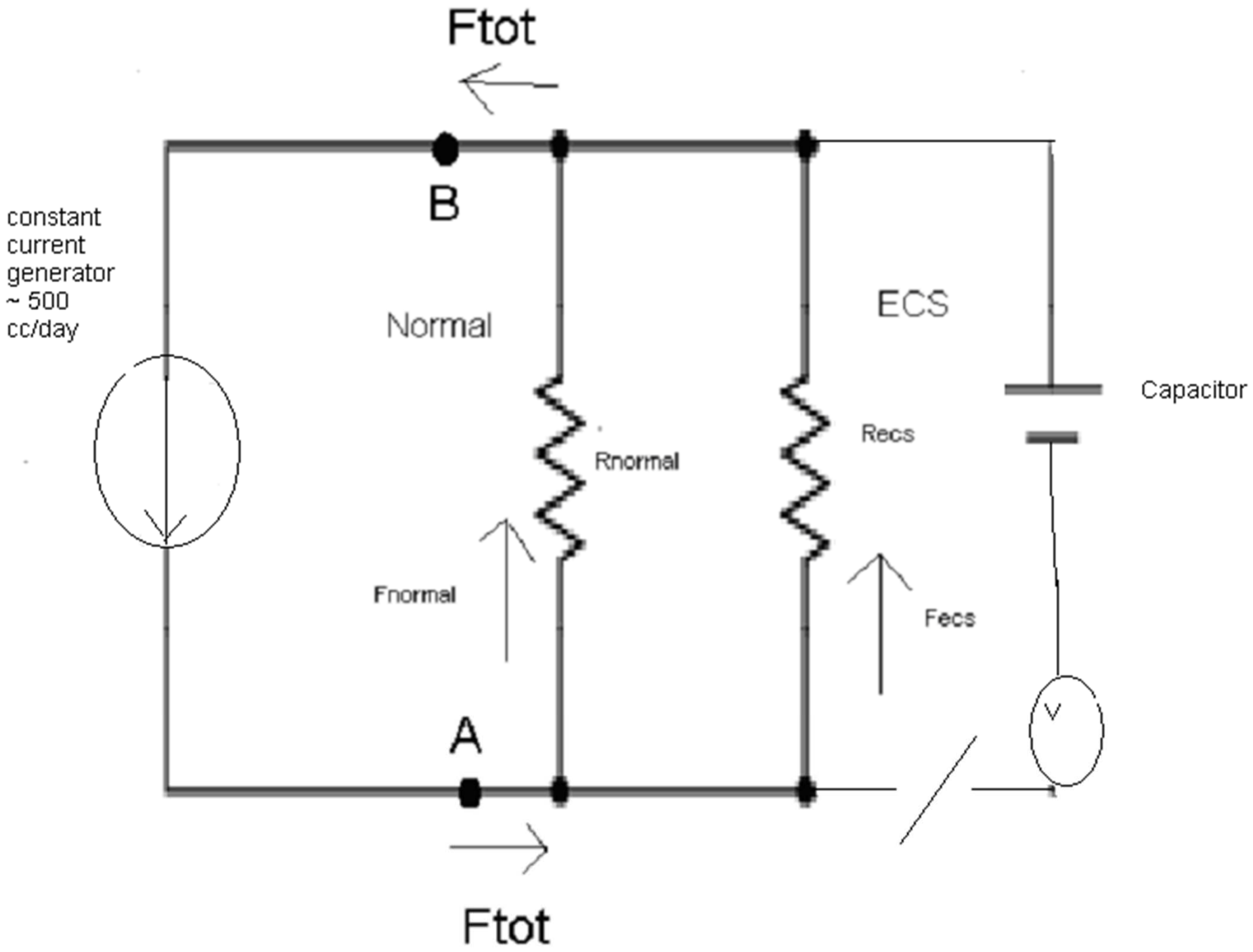
- Hypothesis: NPH patients have always had large ventricles (“slightly enlarged”)
  - Decreased CSF resorption (saline infusion test)
  - Unrecognized benign external hydrocephalus?
- No evidence for previous SAH or meningitis
- Significant CSF resorption pathway is via extracellular space of brain (like tectal gliomas)
- Everything fine until “second hit”: DWMI

- Bradley WG, Neurosurgical Clinics of North America 36:661-684;2001

DWMI is “Second Hit” in NPH

- No symptoms until DWMI occurs later in life
- Resistance to peripheral CSF flow through extracellular space increases slightly due to DWMI
  - loss of myelin lipid: more hydro*phili*c environment
  - Greater attraction of outflowing CSF to myelin protein
- CSF production continues unabated
  - Accumulates in ventricles -hydrocephalus worsens
  - Increased tangential shearing forces
  - NPH symptoms begin

- Bradley, WG Neurosurgical Clinics of North America 36:661-684;2001


Ftot
B
constant
current
generator
~ 500
cc/day
Normal
ECS
Capacitor
Recs
Rnormal
Fnormal
Fecs
V
A
Ftot

Normal 4th ventricular Outflow of CSF

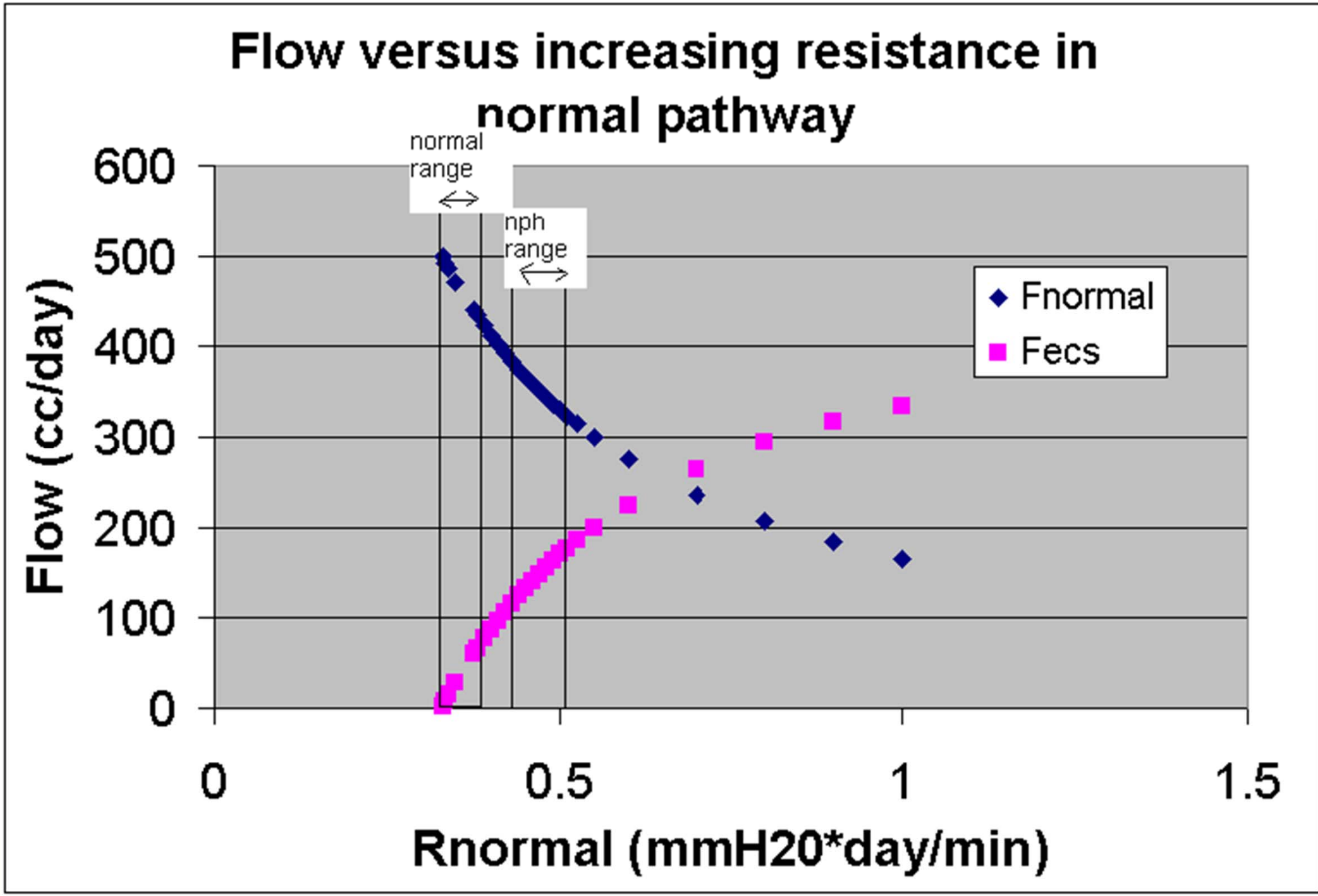
Reduced 4th ventricular Outflow of CSF

Increasesd CSF Outflow through 4th Ventricle and Extracellular Space

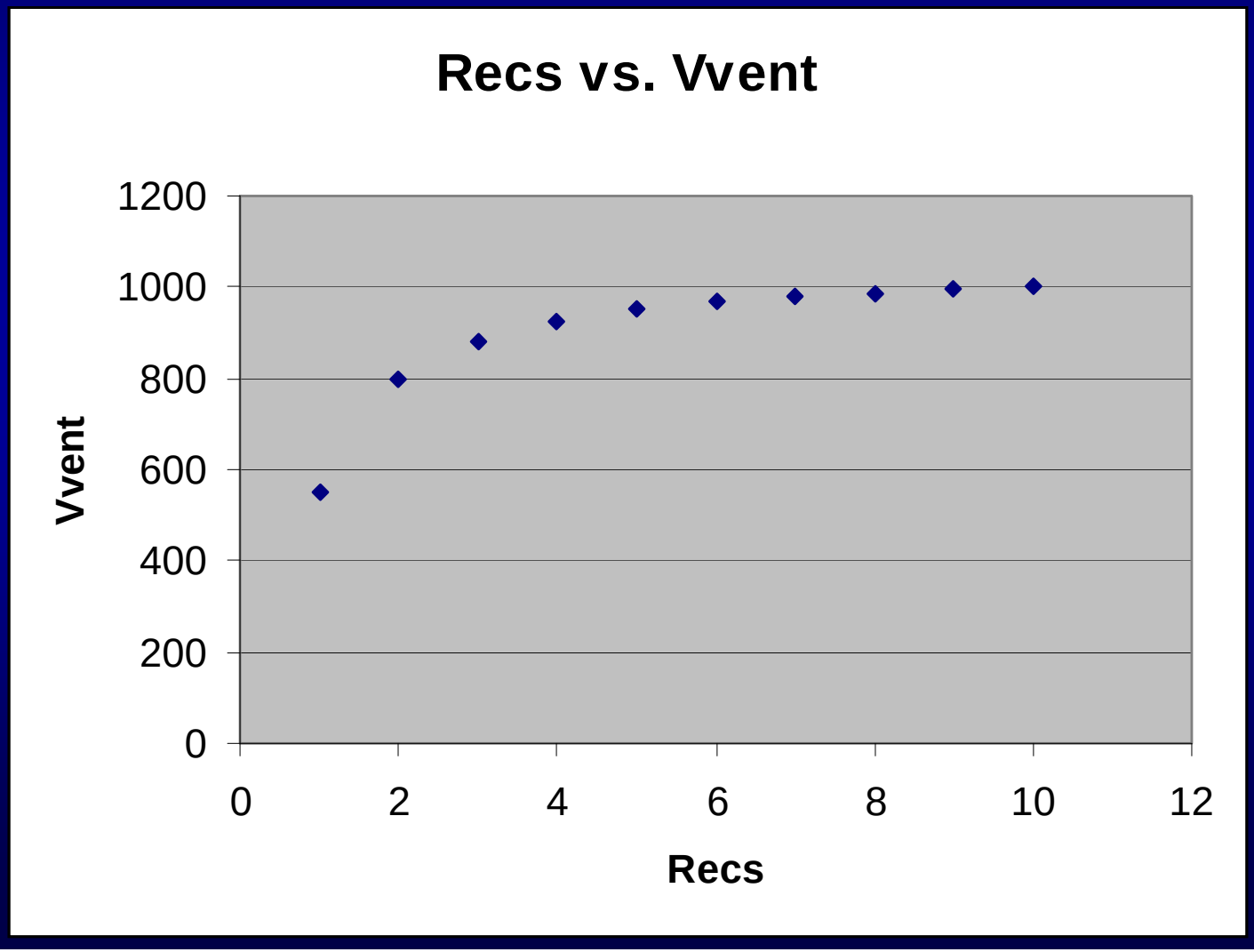
Normal Suction
Low Resistance
Good Flow

Normal Suction
High Resistance
Low Flow

Normal Suction
Lower Resistance
Better Flow


Flow versus increasing resistance in normal pathway
normal range
nph range
Fnormal
Fecs
600
500
400
300
200
100
0
Flow (cc/day)
0
0.5
1
1.5
Rnormal (mmH20*day/min)

Increasing Resistance to Extracellular CSF Flow vs Ventricular Volume



Hypotheses

- If NPH patients had benign external hydrocephalus before 1 year of age, their intracranial volumes should still be larger than sex-matched controls
- If they rely on drainage of CSF through the extracellular space of the brain, the ADC should be elevated for a given degree of DWMI

Materials and Methods

- Intracranial volumes measured from T2WIs using workstation (Vital Images)
- 22 men with clinical NPH vs 55 controls
  - Ave stroke volume: 159 uL (normal: 42 uL)
- 29 women with NPH vs 55 controls
  - Ave stroke volume: 127 uL

- Bradley WG, et al, “Increased Intracranial Volume: A Clue to the Etiology of
- Idiopathic Normal-Pressure Hydrocephalus?” AJNR 25:1479-1484, 2004

Results: Intracranial Volumes

- NPH men (n= 22): 1682 cc
- Control men (n=55): 1565 cc
- NPH volumes significantly larger (p<.003)
  - 117 cc (7.5%)
- NPH women (n=29): 1493 cc
- Control women (n=55): 1405 cc
- NPH volumes significantly larger (p<.002)
  - 88 cc (6.5%)

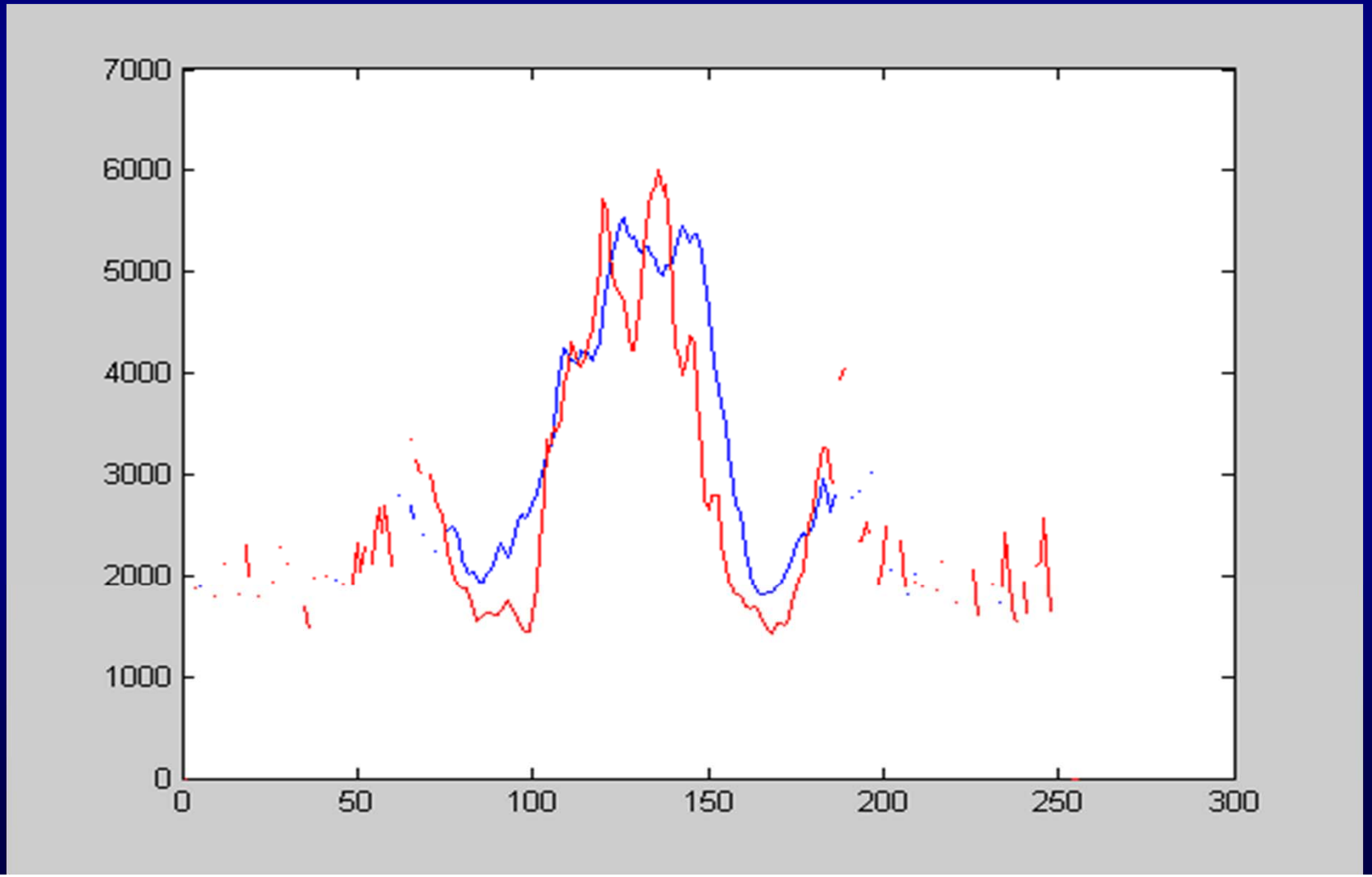
Implication

- Patients with “slightly enlarged ventricles” for no apparent reason should be observed carefully for onset of gait disturbance in later years
- Probable window of opportunity to treat

ADC: NPH vs Controls

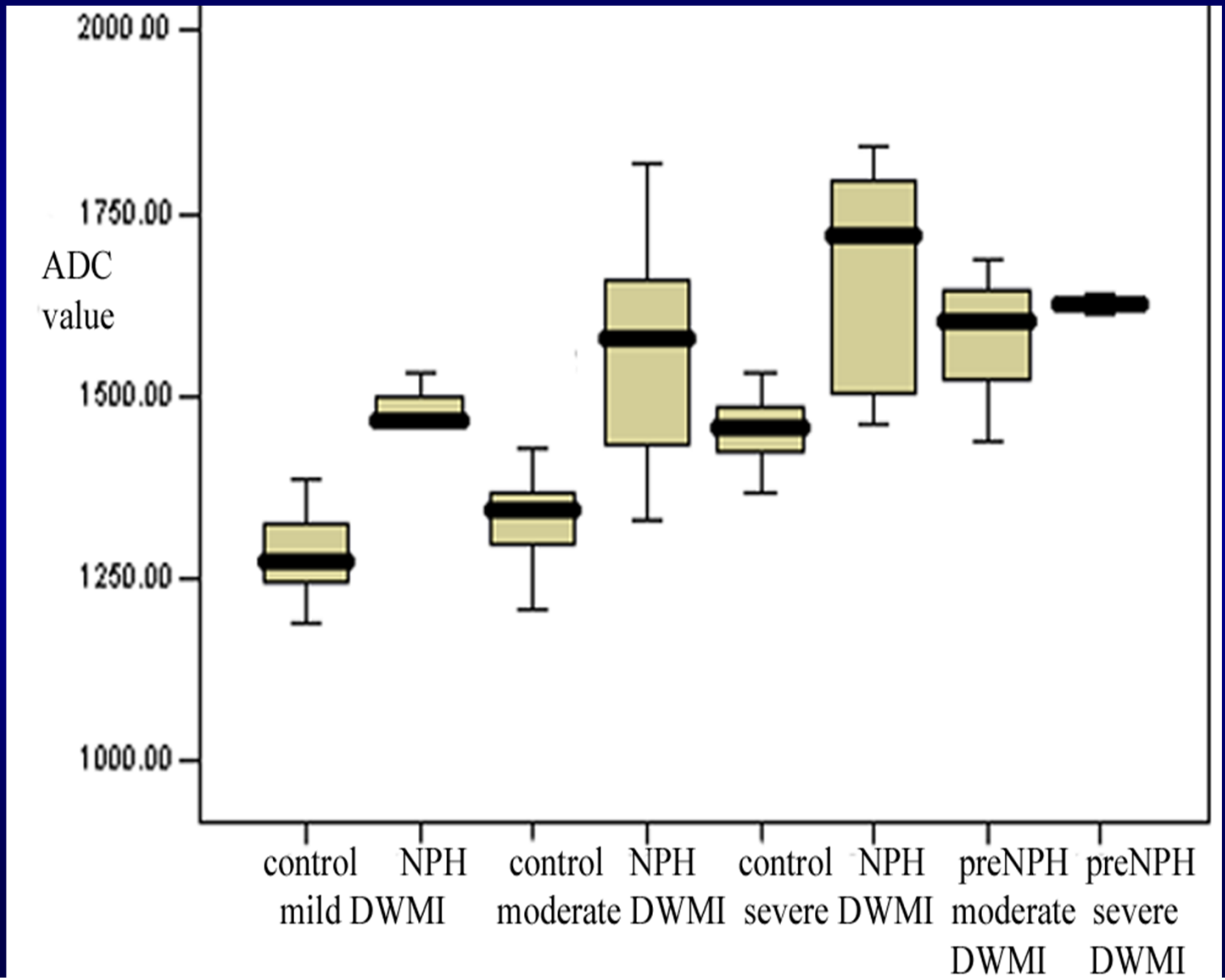
- Apparent Diffusion Coefficient (ADC) profile in 10 pixel wide coronal sections through axial slices through upper lateral ventricles
- ADC measurements in centrum semiovale controlled for a given degree of DWMI

ADC Profile: NPH vs Control
Anterior Coronal Location



Blue: NPH
Red: Control

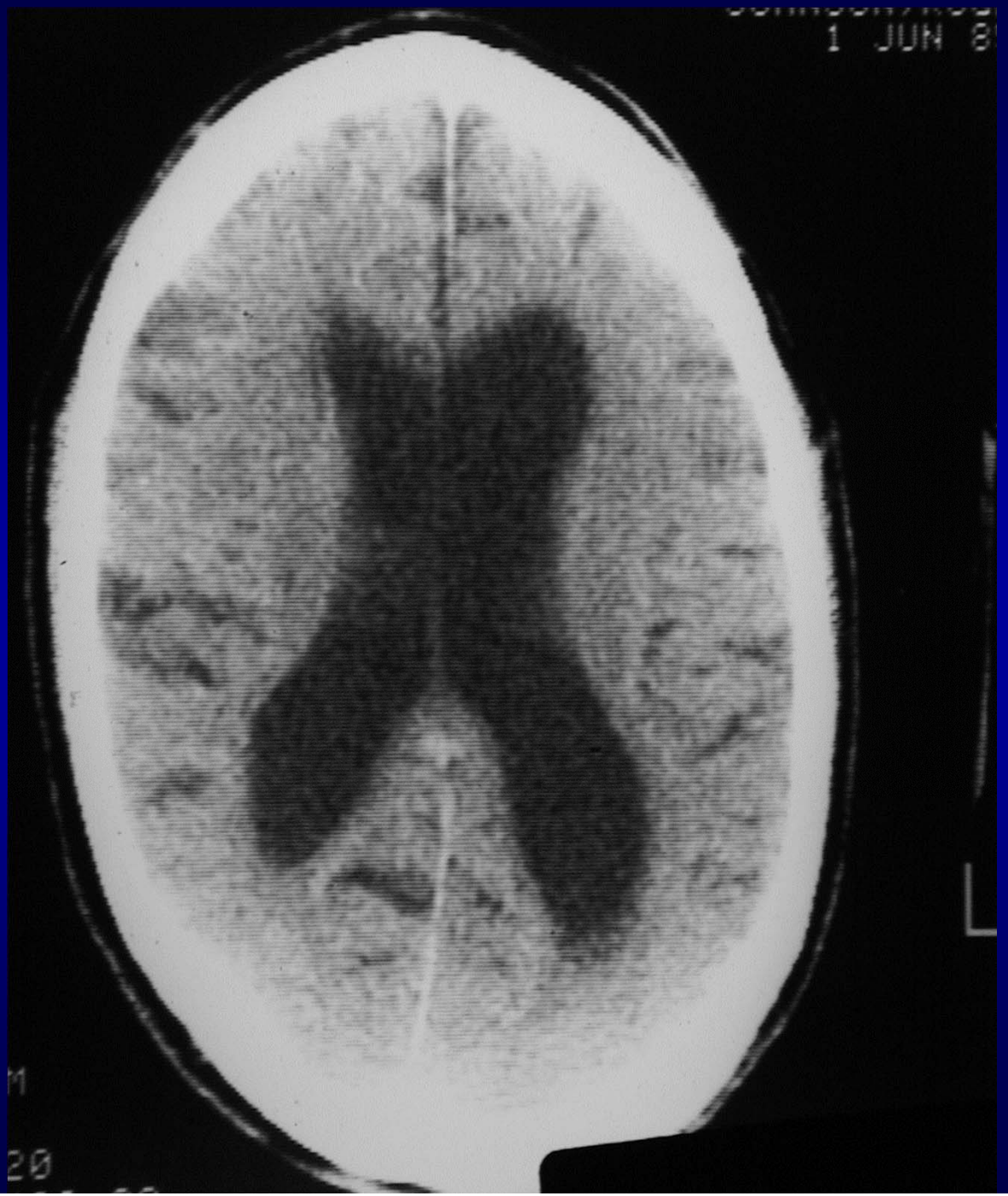
ADC vs NPH vs Control



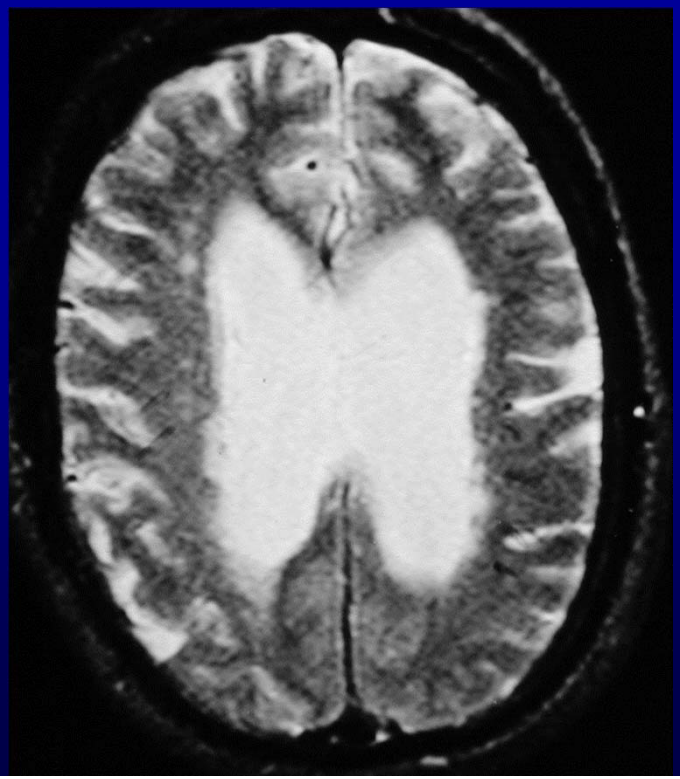
67 yo man will be shunted for NPH in 19 years; currently walking 20 miles a day

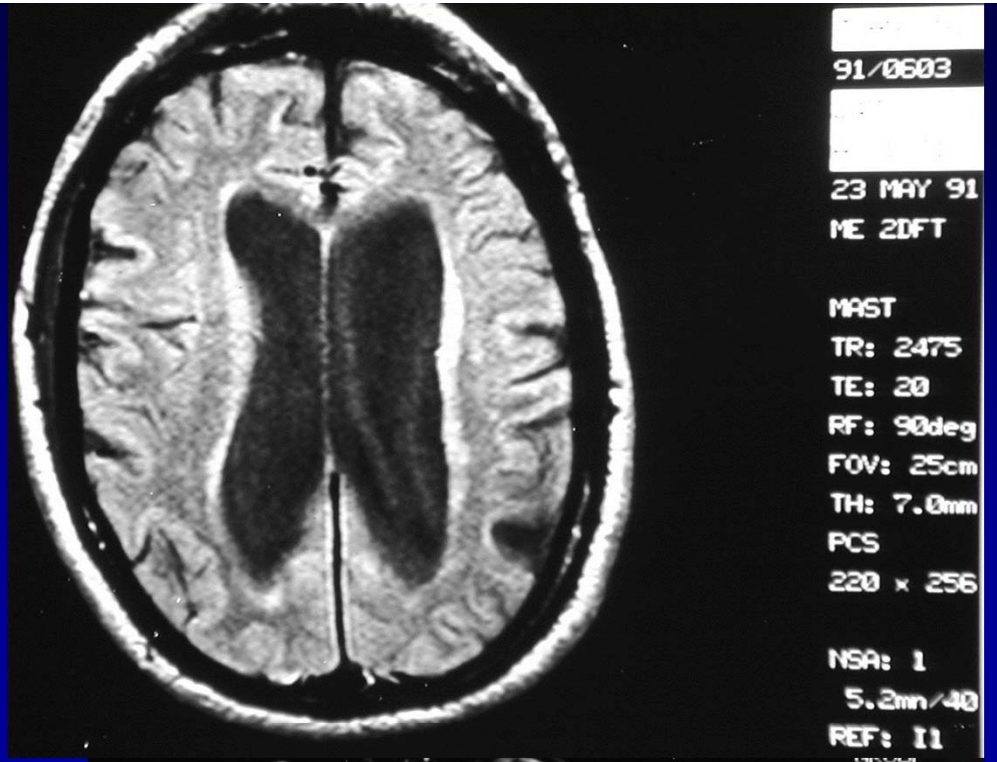
1982 CT for giant cell arteritis

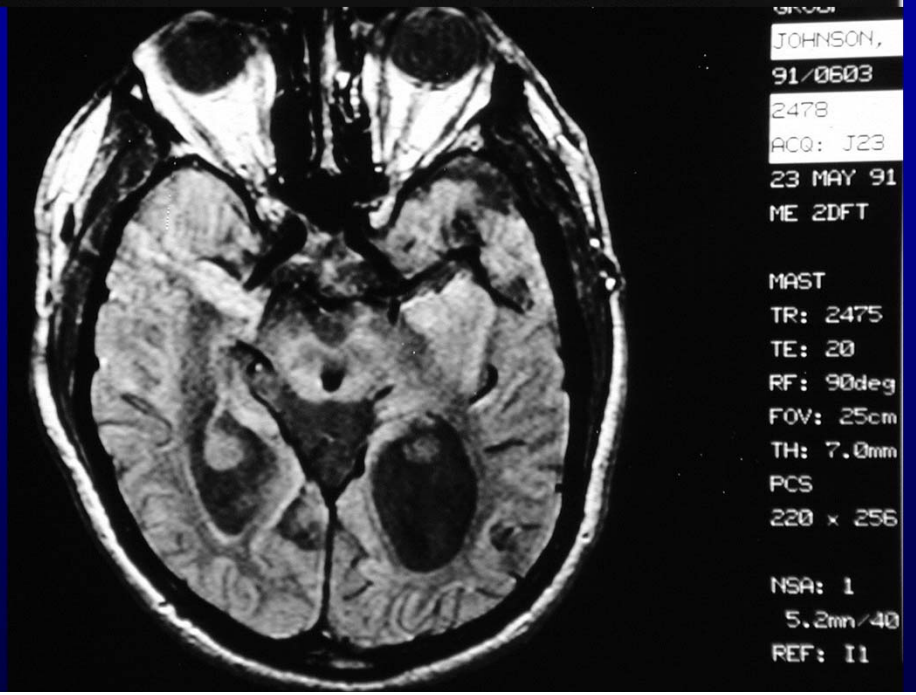
1985: Still no NPH symptoms (now age 70)



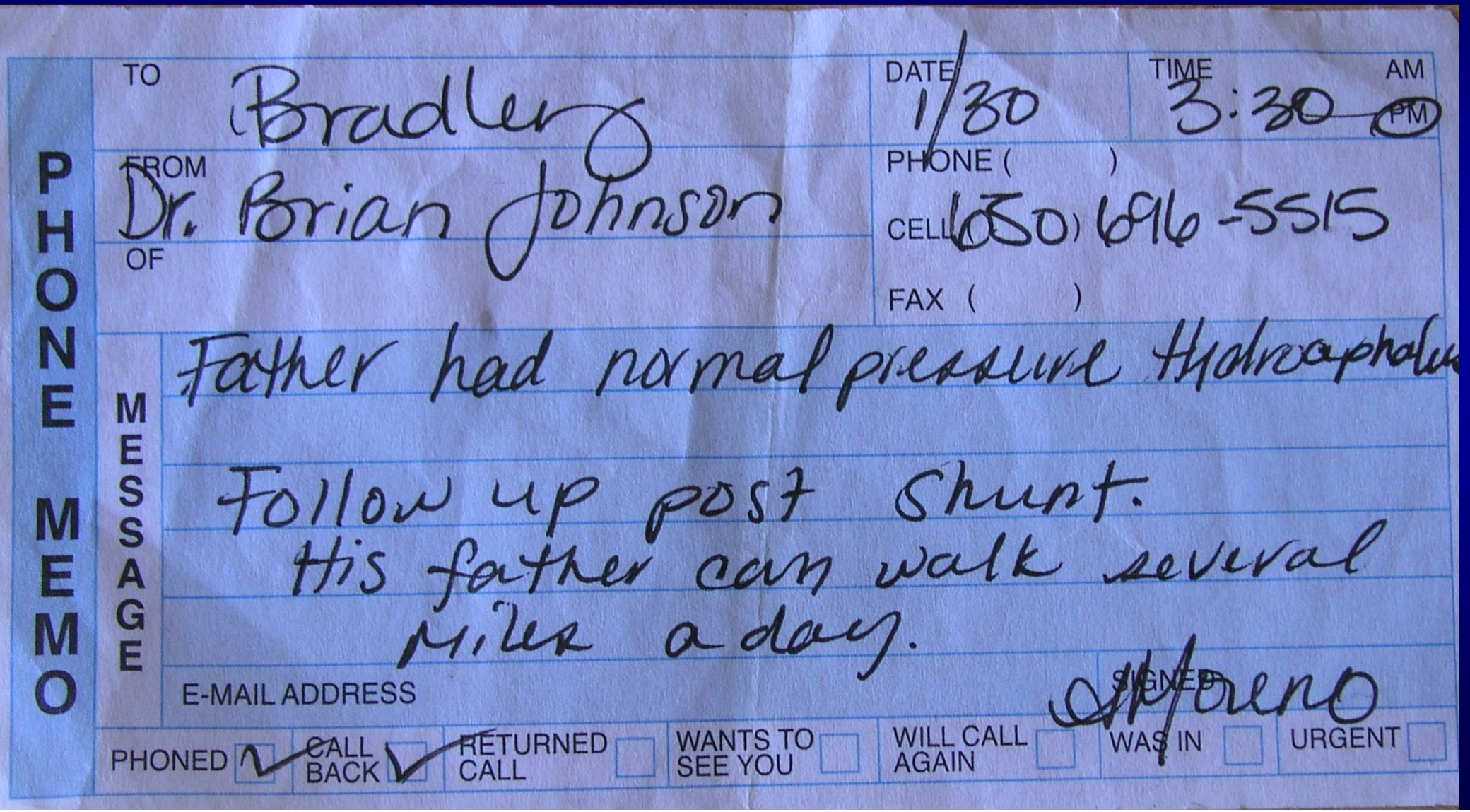
1991: Pt (now 76) will development NPH in 10 years







Follow up



PHONE MEMO

TO Bradley

FROM Dr. Brian Johnson

OF

DATE 1/30

TIME 3:30 AM (PM)

PHONE ( )

CELL (650) 696-5515

FAX ( )

MESSAGE

Father had normal pressure Hydrocephalus

Follow up post Shunt.
His father can walk several miles a day.

E-MAIL ADDRESS

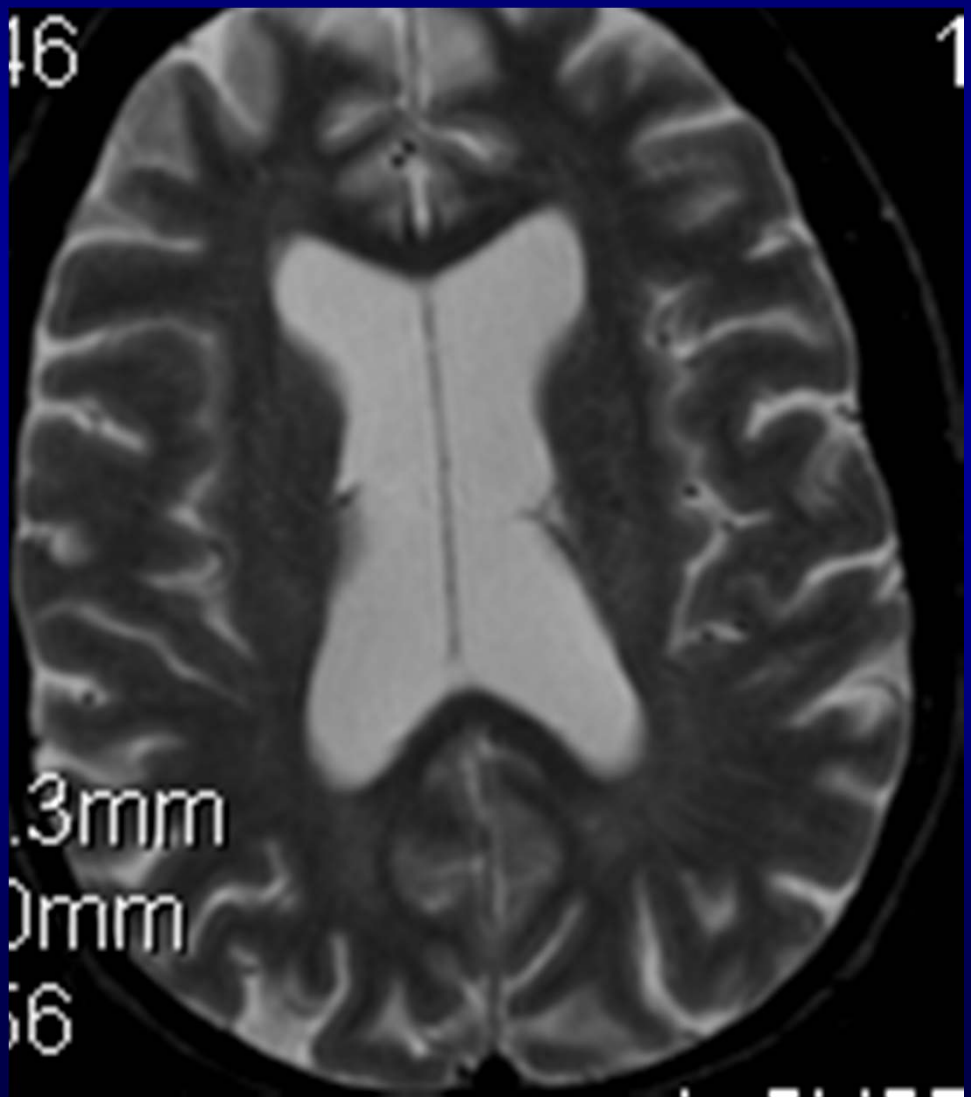
SIGNED Moreno

PHONED ✓ CALL BACK ✓ RETURNED CALL ☐ WANTS TO SEE YOU ☐ WILL CALL AGAIN ☐ WAS IN ☐ URGENT ☐

Testimonial from 86 yo physician with NPH

- Dr Bradley,
- Your optomistic verbal report to me re: the result of my CSF flow study proved accurate. Ventriculo-peritoneal shunt resulted in substantial improvement. Would it be possible for me to receive a written report for my records.
- Thank you.

55 yo r/o Metastatic Melanoma: Future NPH Patient?



Conclusions

- NPH diagnosed by symptoms, not MRI
- MRI used to confirm diagnosis of **shunt-responsive** NPH
- Asymptomatic patients may have dilated ventricles and elevated CSF flow: Pre NPH?
- Not everyone with benign external hydrocephalus gets NPH
- Keep your extracellular space open