Multimodal Differentiation of Posterior Fossa Masses of Children

Rochelle M. Witt, HMS III
Radiology Core Clerkship
Gillian Lieberman, MD
August 23, 2010

Rochelle M. Witt, HMS III
Gillian Lieberman, MD

Outline

- Anatomy of the Posterior Fossa
- Menu of Tests
- Index Patient
    - Presentation
    - Differential Diagnosis
    - Multimodal Evaluation of Posterior Fossa Mass
- Companion Patients
- Future Directions

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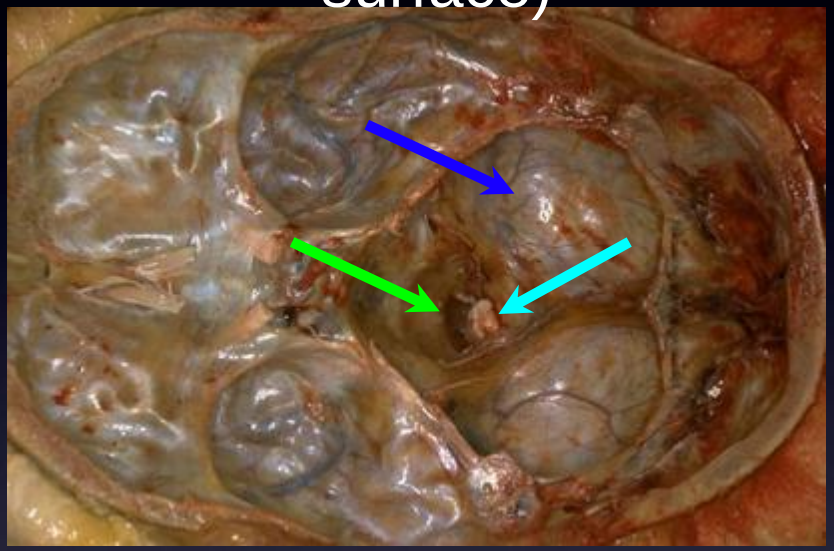
Posterior fossa anatomy

Transverse Section: Base of Skull (upper surface)

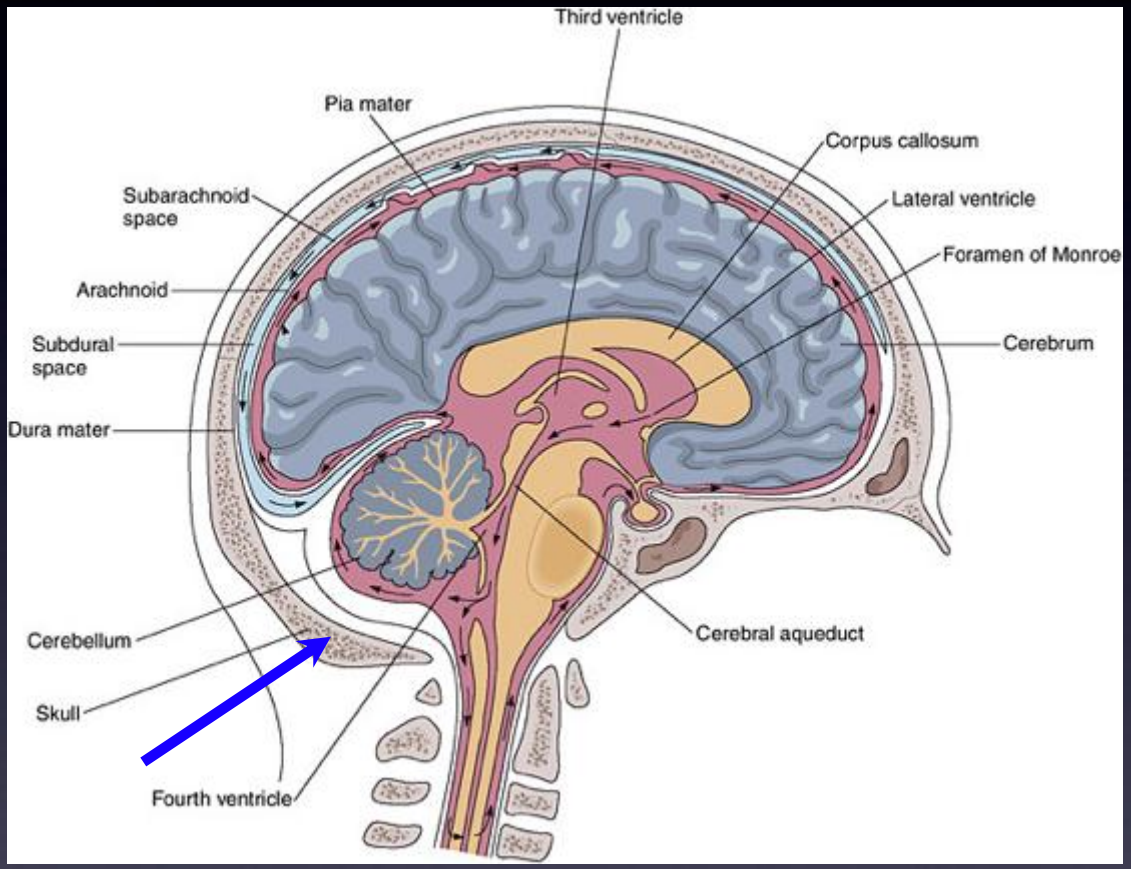


rostral caudal

posterior cranial fossa

cervical spinal cord

foramen magnum



sagittal section

"Neuroanatomy." *EHSL - Spencer S. Eccles Health Sciences Library Home Page*.

Rizzo, D.C. *Fundamentals of anatomy & physiology*

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Menu of tests for posterior fossa masses

- Magnetic Resonance Imaging (MRI): the clinical gold standard

- Plain Radiography
  - In general, poor choice for imaging posterior fossa structures
  - Sometimes used to examine foramina at skull base

- Computed Tomography (CT)
  - Speed of acquisition is an advantage
  - Initial test without contrast to consider subarachnoid bleeding
  - Does give superior detail regarding tumor histolo

Adam and Dixon, eds. (2008), sagittal view *Grangier and Allison's Diagnostic Radiology*

-Vascular Tests
  - Often used to examine proximity to blood supply

- Functional Tests:
  - Occasionally, PET used to consider tumor metabolism

Barkovich (2005) *Pediatric Neuroimaging*

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Menu of tests for posterior fossa masses

- Magnetic Resonance Imaging (MRI): the clinical gold standard

  - Multiplanar imaging capabilities

  - Compatible with computerized navigation techniques

  - CT imaging can have tissue artifacts, especially in the posterior fossa

  - Sensitivity: Can identify spread to subarachnoid spaces

Barkovich (2005) *Pediatric Neuroimaging*

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Menu of tests for posterior fossa masses

- Magnetic Resonance Imaging (MRI): the clinical gold standard
  - Multimodal approach using MR suite of tests
    - (Patient history and exam)
    - Conventional, structural MR imaging
    - MR perfusion - hemodynamic characterization
    - MR diffusion - restricted movement of nuclei
    - MR spectroscopy - biochemical environment of nuclei

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    - **MR spectroscopy - biochemical environment of nuclei**

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Patient Presentation

- 3 3/4 year old girl

- PMH: Asthma, RSV infection (1 yo)

- 3 weeks of headaches of increasing intensity
    - two weeks ago: one episode daily, lasting 1-2 minutes
        - debilitating (pt stops what she is doing, but she is responsive)
    - last week: several/day
    - this morning: 3 episodes
    - pain localized to the top of her head
    - frequently occurs in the morning, can awaken her from sleep
    - AM emesis

- Family Hx: noncontributory

- Physical Exam
    - active, alert, oriented; in no apparent distress
    - no seizures
    - no focal weakness
    - unsteady, with a wide-based gate; normal tone
    - no observed papilledema

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Patient Presentation

Indications for neuroimaging in pediatric headache

- Headaches of <6 months duration (no response to medical tx)

- Headache associated with abnormal neurologic findings

- Persistent headaches without family history of migraine

- Persistent headaches associated with substantial episodes of confusion, disorientation or emesis

- Headaches that awaken a child repeatedly from sleep or occur immediately on awakening

- Family/medical history predisposes to CNS lesions and clinical/lab findings suggestive of CNS involvement

Barkovich (2005) *Pediatric Neuroimaging*

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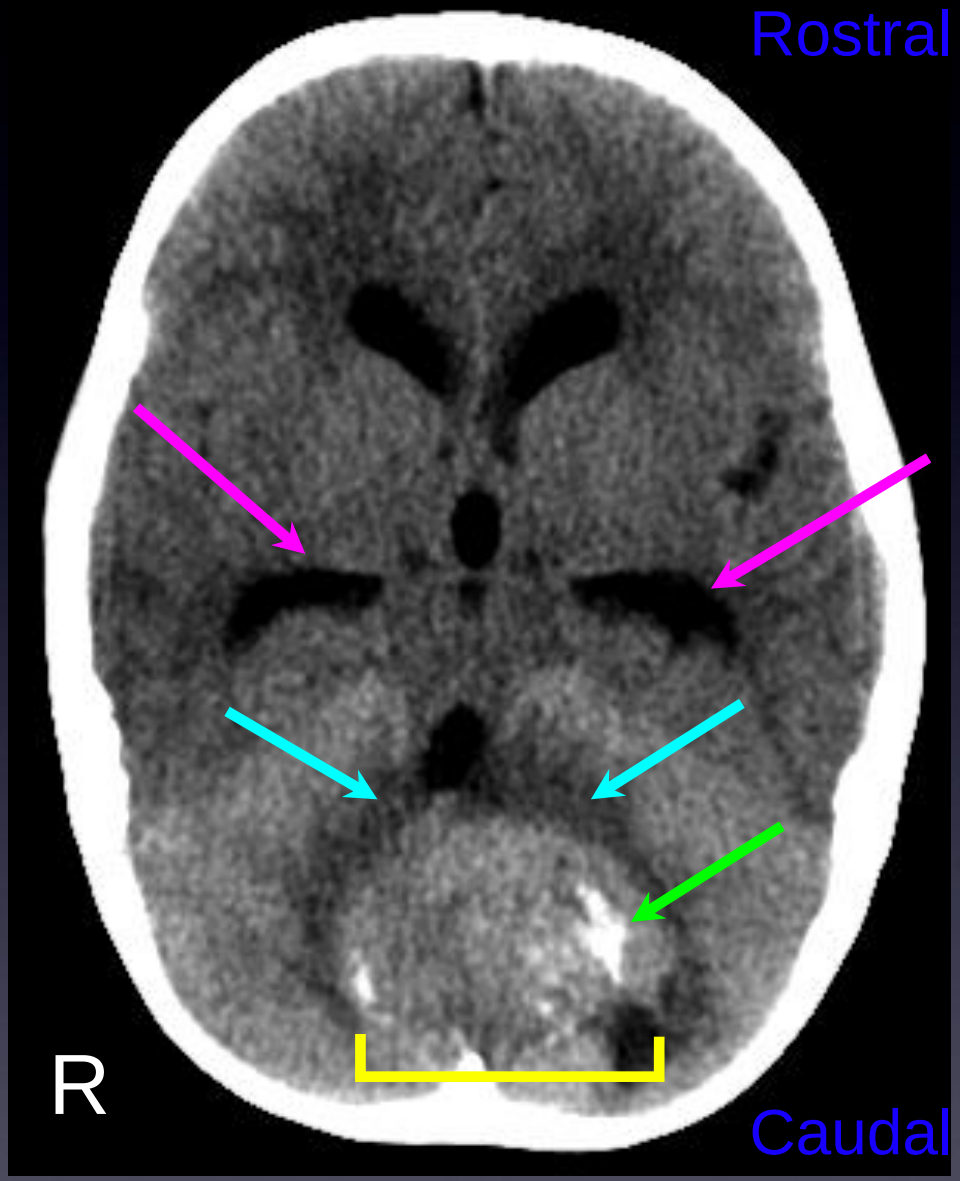
Index Patient: Initial Imaging



axial CT w/o contrast

large, dense, singular mass (infratentorial)

area adjacent to mass, poorly attenuating = surrounding edema

areas of high attenuation within = internal calcifications

dilated temporal horns = hydrocephalus

PACS, CHOB

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Index Patient: Differential Diagnosis

1) Patient Age and History of the Present Illness

2) Infratentorial area of focal, low attenuation with internal calcifications, surrounding edema and concomittant hydrocephalus

Nonneoplastic or Neoplastic

Could MR imaging techniques distinguish between these?

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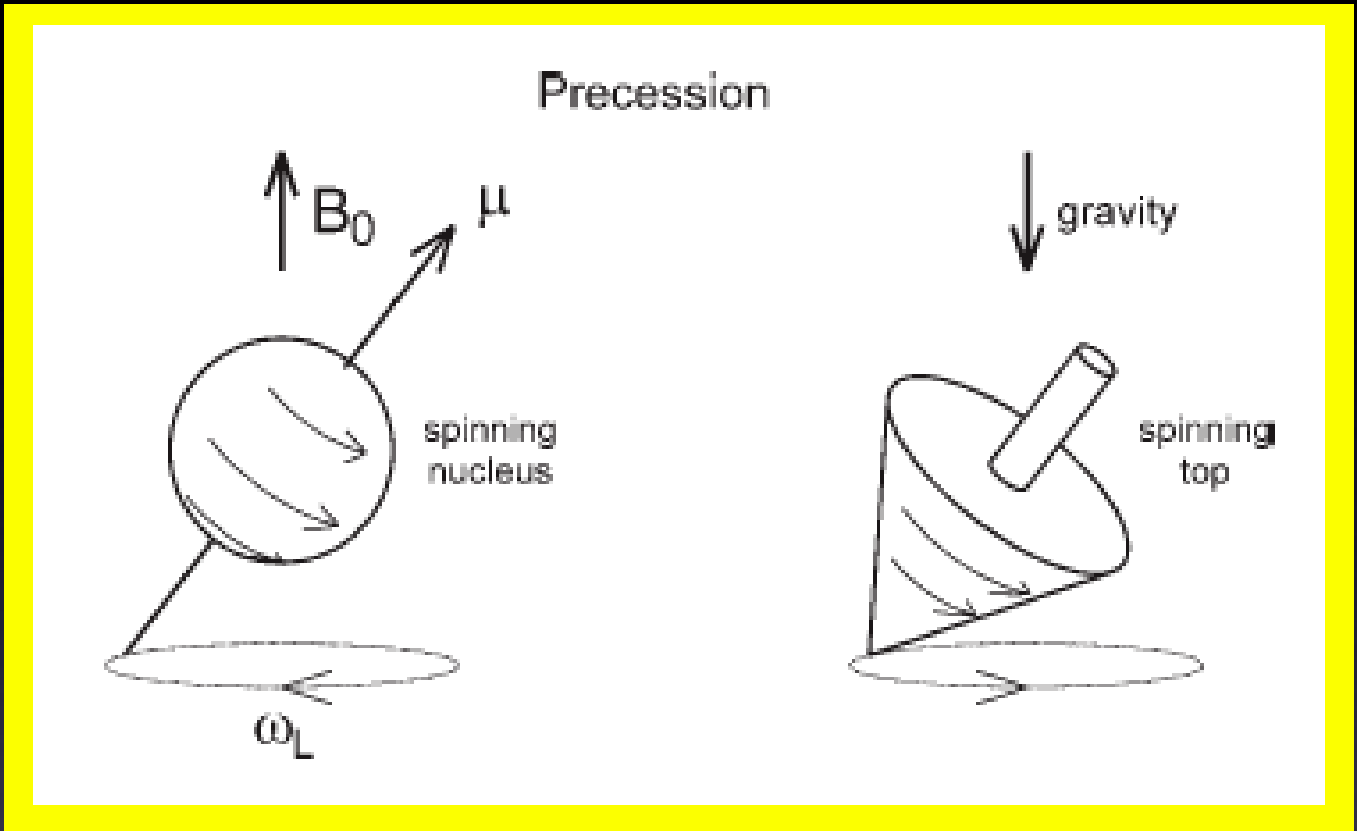
MRI: Basic Physics



- nucleus with nonzero spin → magnetic moment

- exogenous magnetic field, B_0

Storey (2006), Chp.1, *Methods in Molecular Medicine*

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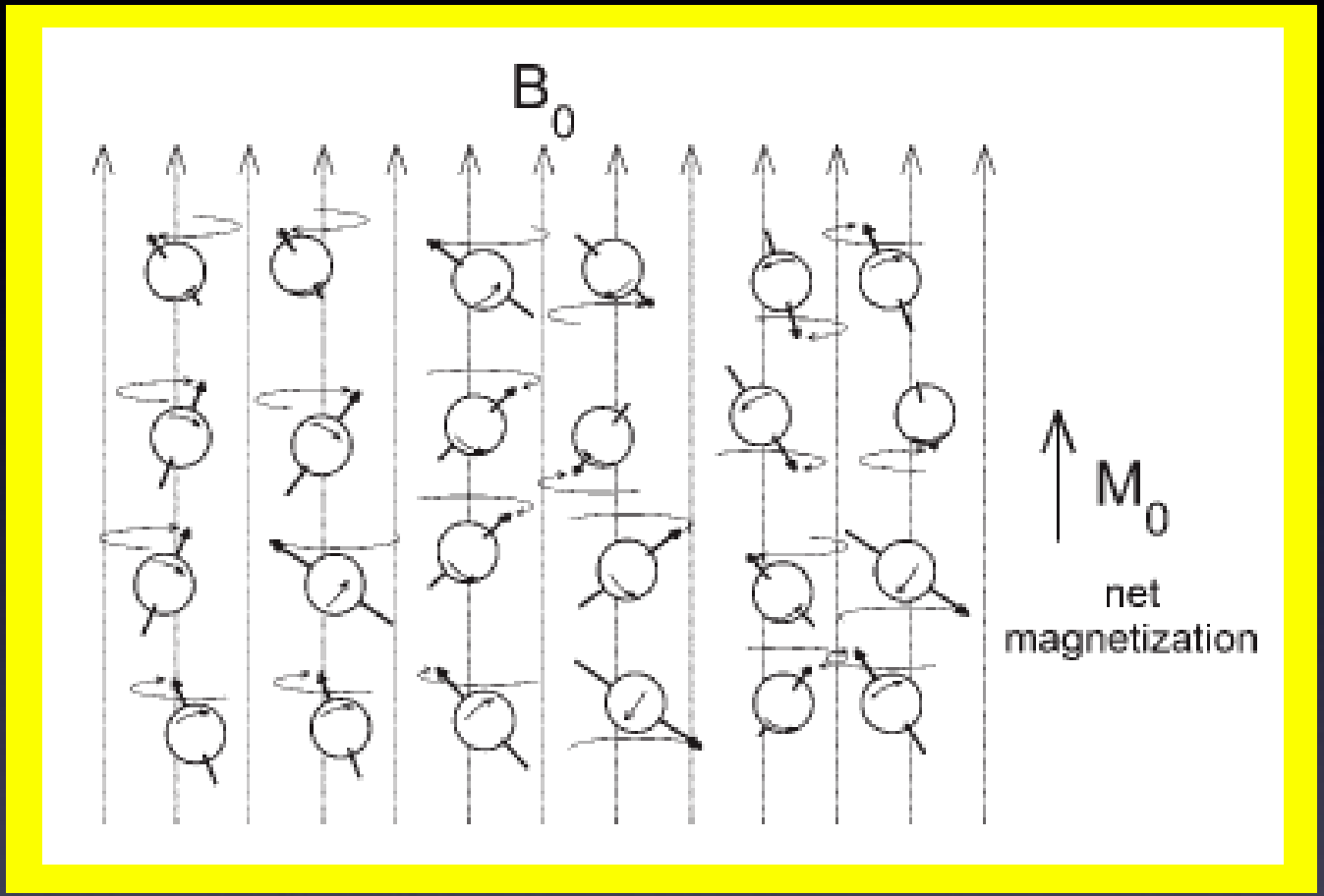
MRI: Basic Physics



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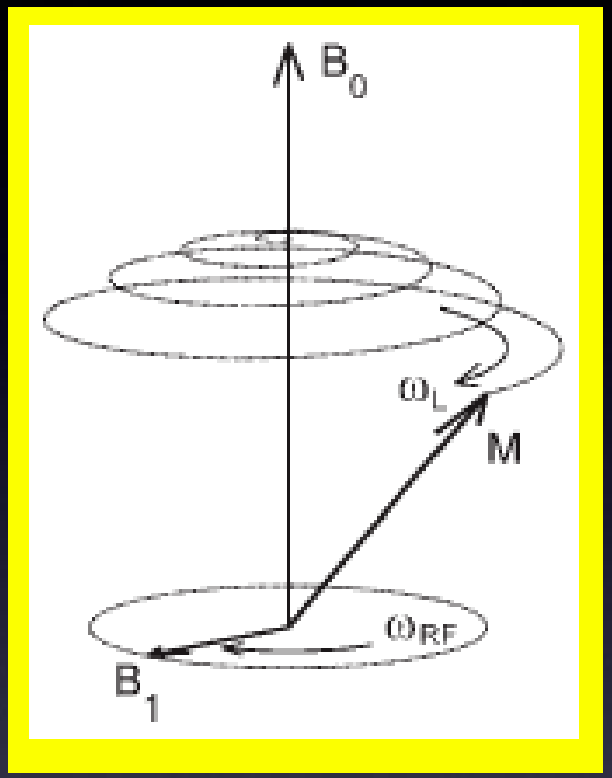
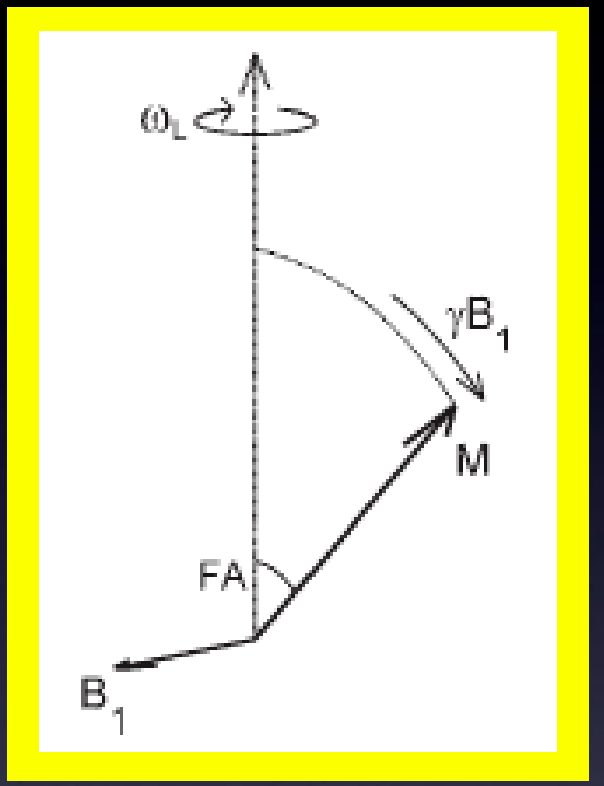


Resonance condition

$\omega_{RF} = \omega_L$



Longitudinal relaxation (E loss): T1
Transverse relaxation (Loss of phase coherence): T2 and T2*
MR Diffusion: phase-disrupting pulse sequence
MR Spectroscopy: chemical shift

Storey (2006), Chp.1, *Methods in Molecular Medicine*

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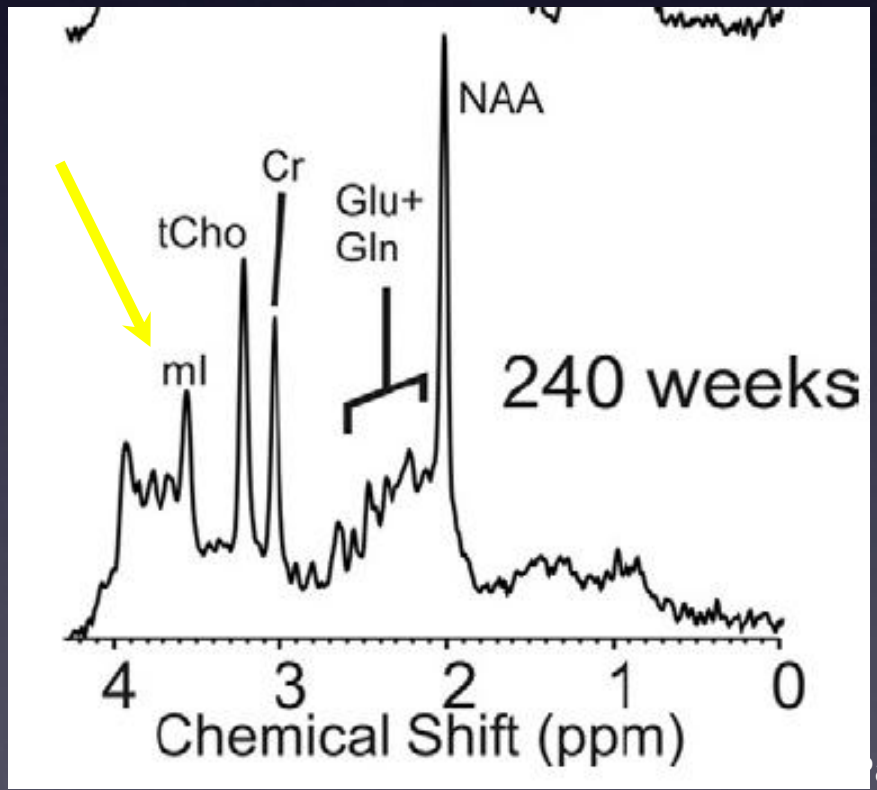
MR Spectroscopy

myo-inositol (mI):

- astrocytic marker
- osmolyte
- phosphatidyl inositol metabolism

4 yo child

T2-weighted, axial MRI ROIs (boxed)



anigrahy et al. (2010) *Seminars in Perinatology*

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Choline (tCho, complex):
- breakdown of phosphatidyl choline
- increased membrane turnover
- increased cell density

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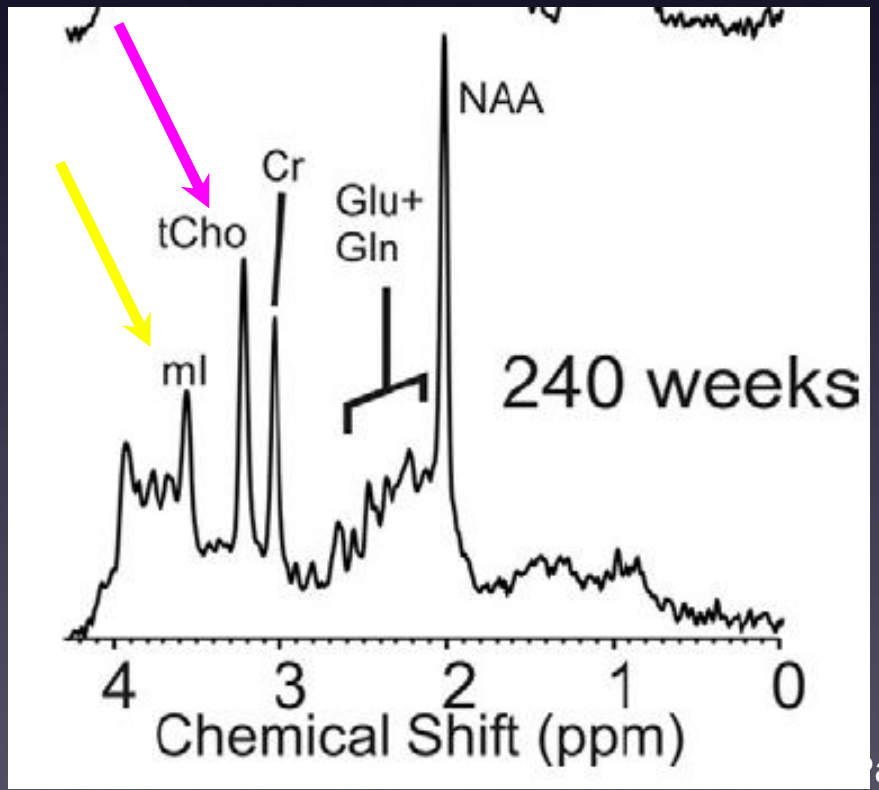

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- tissue energy metabolism
- used to replenish ATP levels

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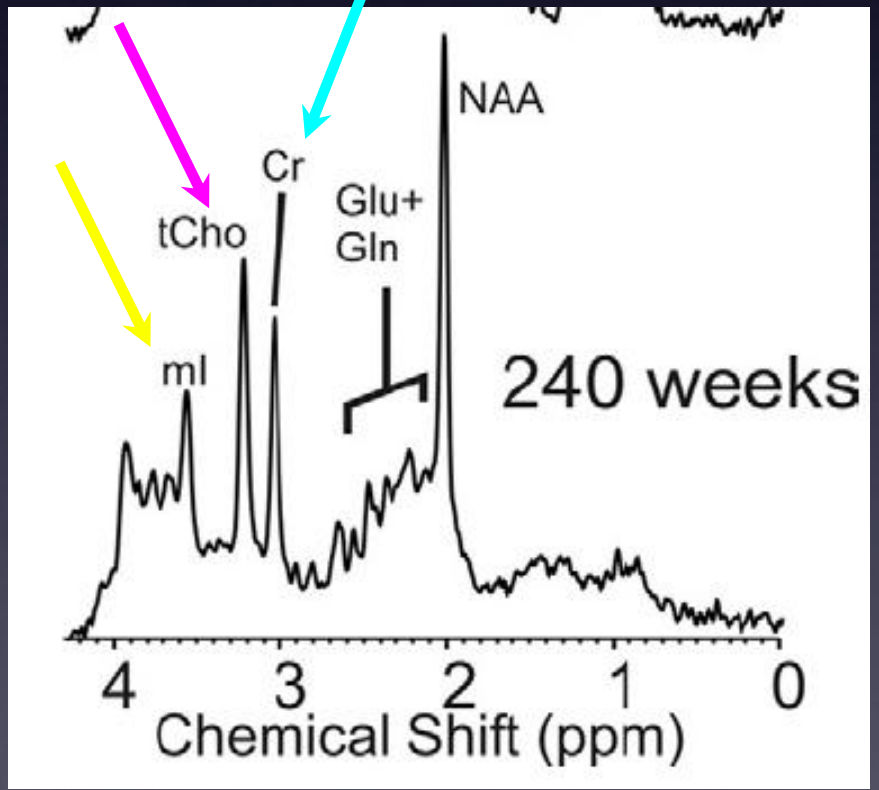

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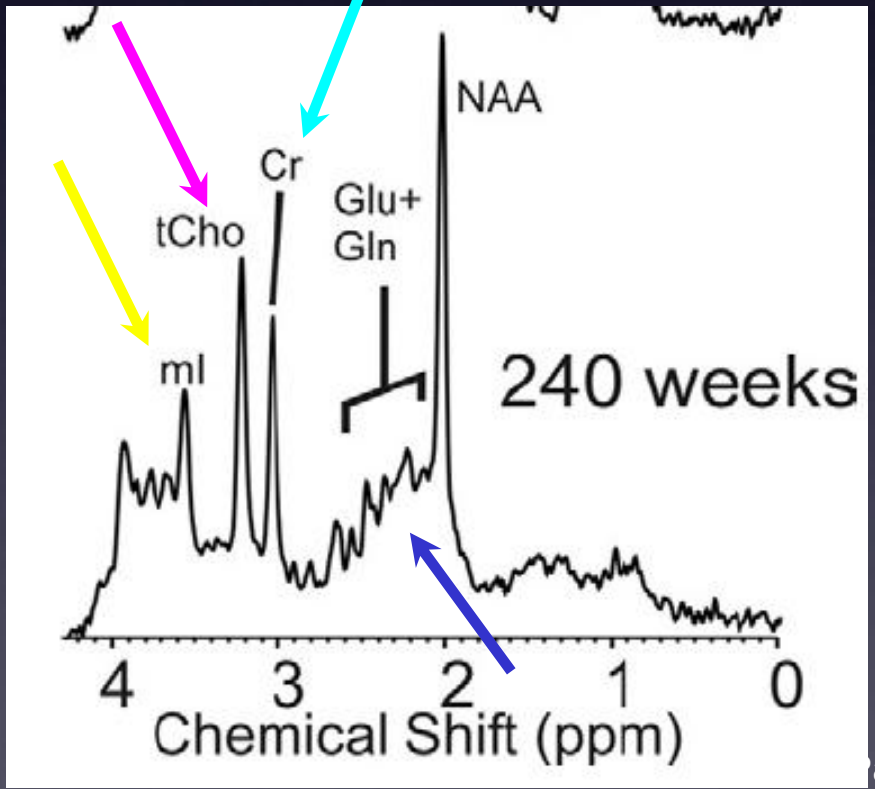
Glutamate+Glutamine (Glu+Gln):

- neurotransmitter
- energy consumption



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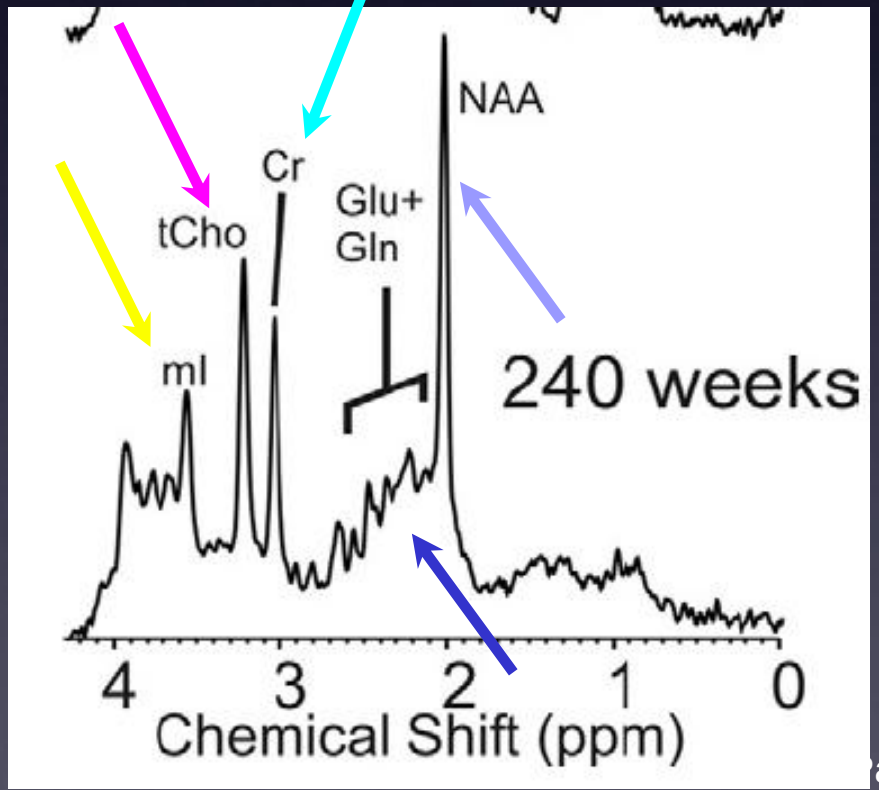

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N-acetyl aspartate (NAA):

- normally functioning neurons
- component of soma and neuronal processes

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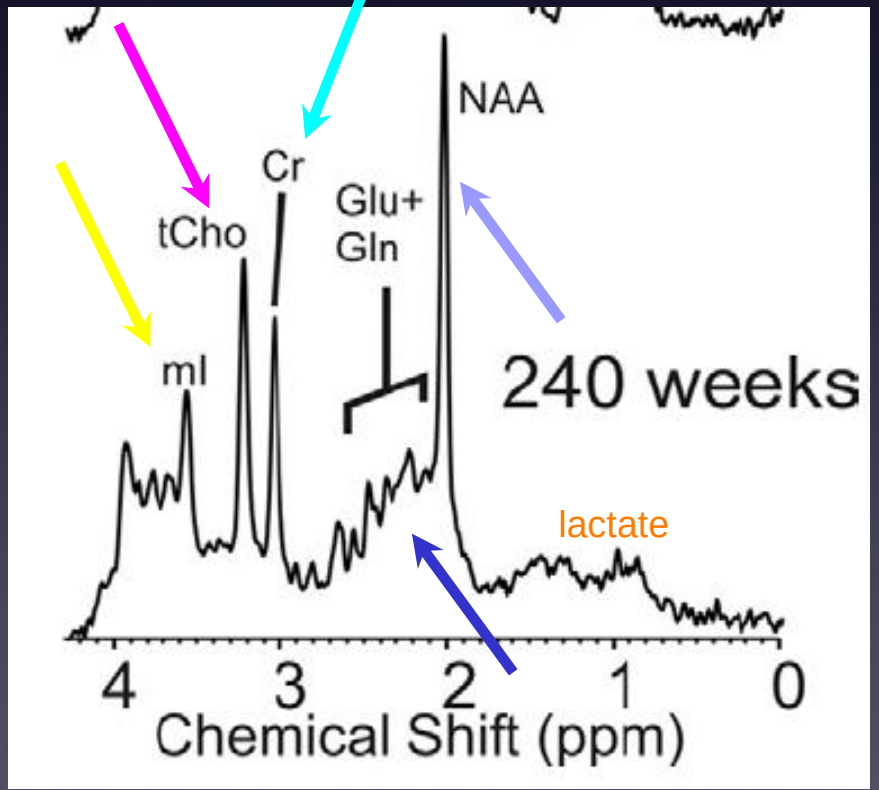

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N-acetyl aspartate (NAA):

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Lactate:

- anaerobic metabolism
- concentration low in healthy tissue

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Ordered Approach to reading MR Spectroscopy

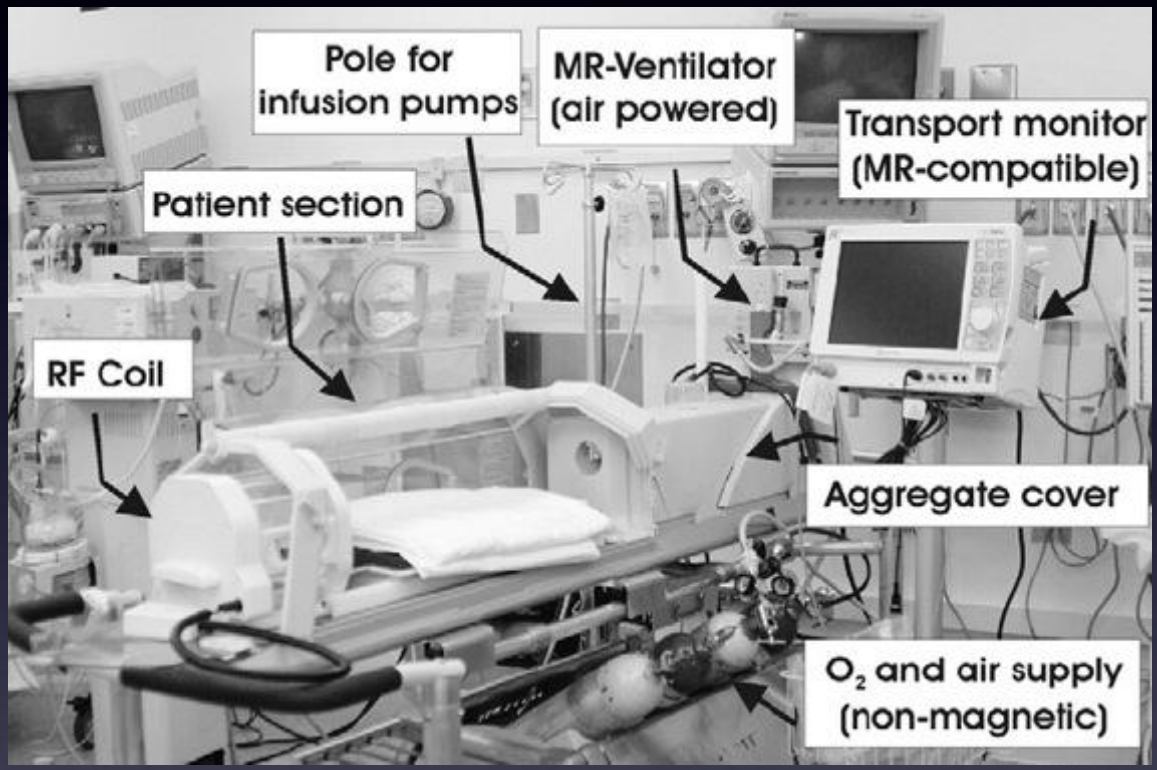
1) Quality Control

- Patient Information
- Clinical History and Study Rationale
- Procedural statements
- Basic utility of MR Spectroscopy
- ID scanner and echo times used
- Spectral Quality (“exposure”)
- Limitations ((“exposure”), eg. sampling, motion artifact)

2) Findings - repeat for each voxel

- Voxel Placement (“ROI”/location)
- Voxel Size (“ROI”/location)
- Echo time for region
- Detail metabolite levels
- Qualitative assessment

3) Impression (“Interpretation”)



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Index Patient: Differential Diagnosis

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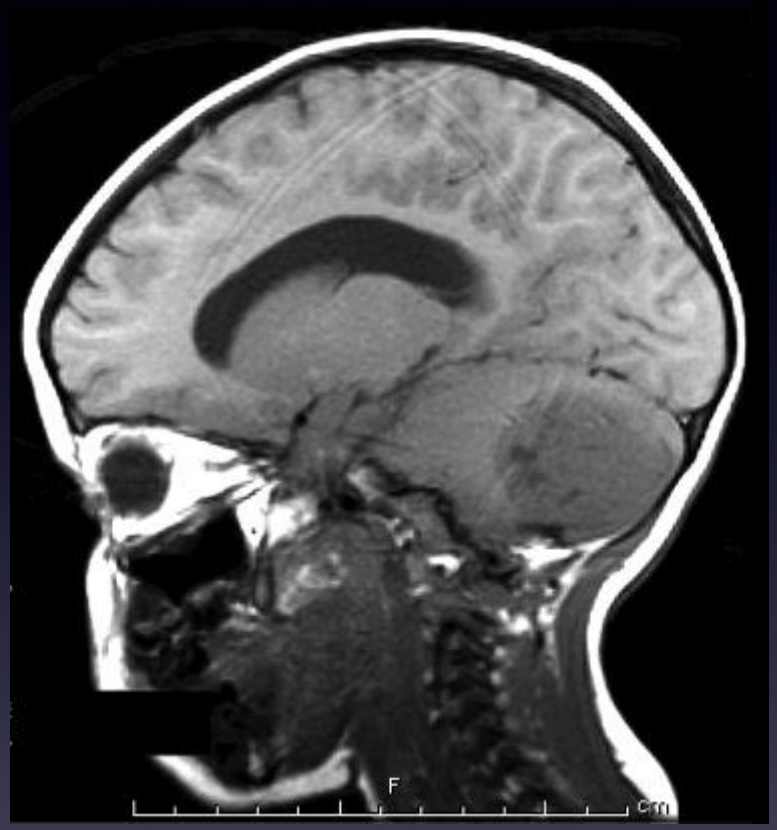
Proton MR Spectroscopy distinguishes between nonneoplastic and neoplastic lesions

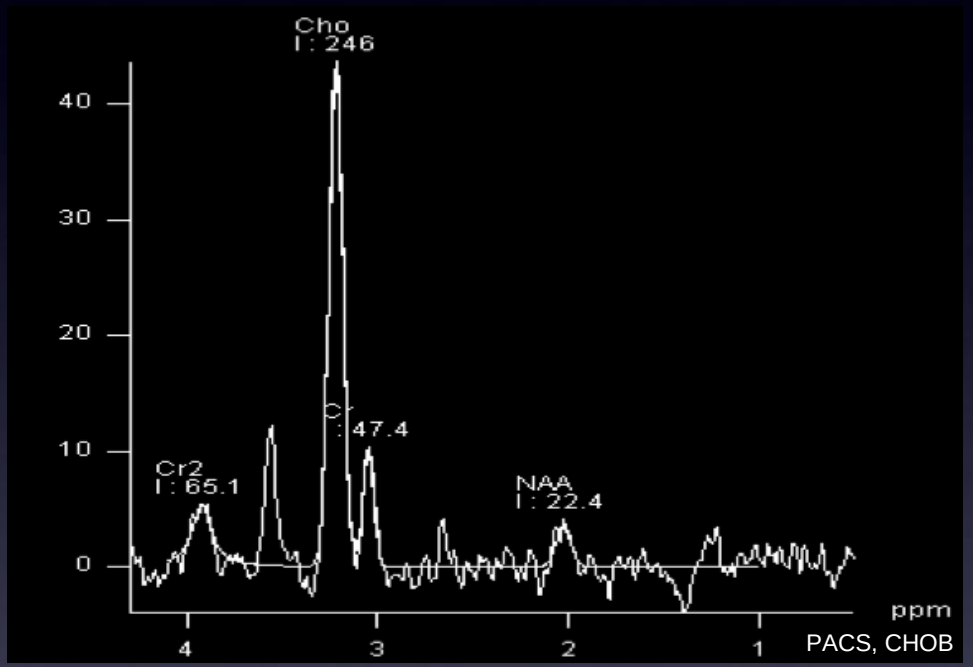
Index Patient



PACS, CHOB

T1-weighted image, sagittal

Companion Patient #1 (same dx)



Index Patient

Markedly depressed NAA

Elevated choline

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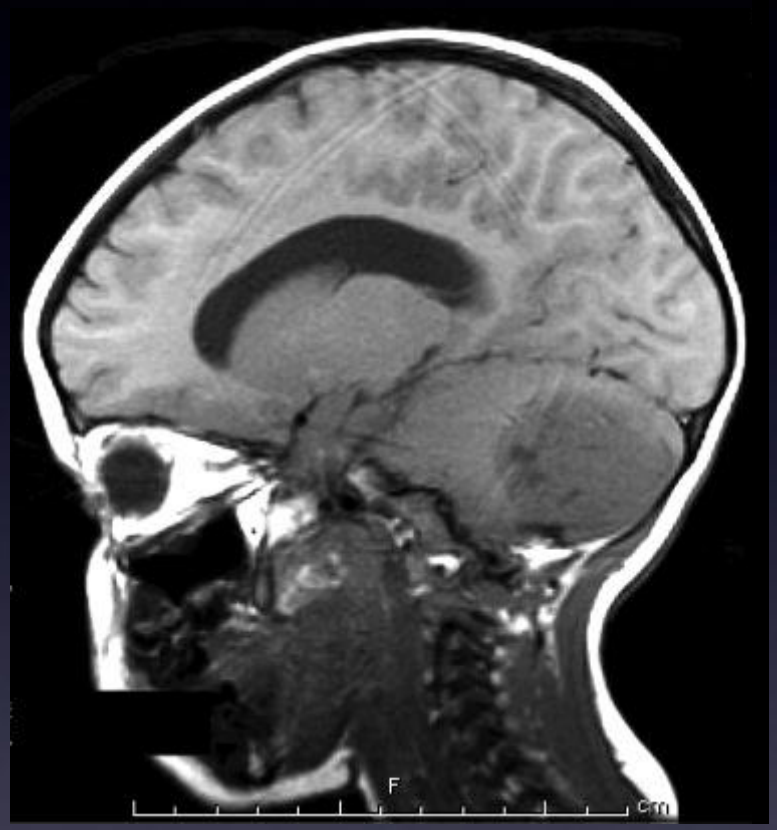
Proton MR Spectroscopy distinguishes between nonneoplastic and neoplastic lesions

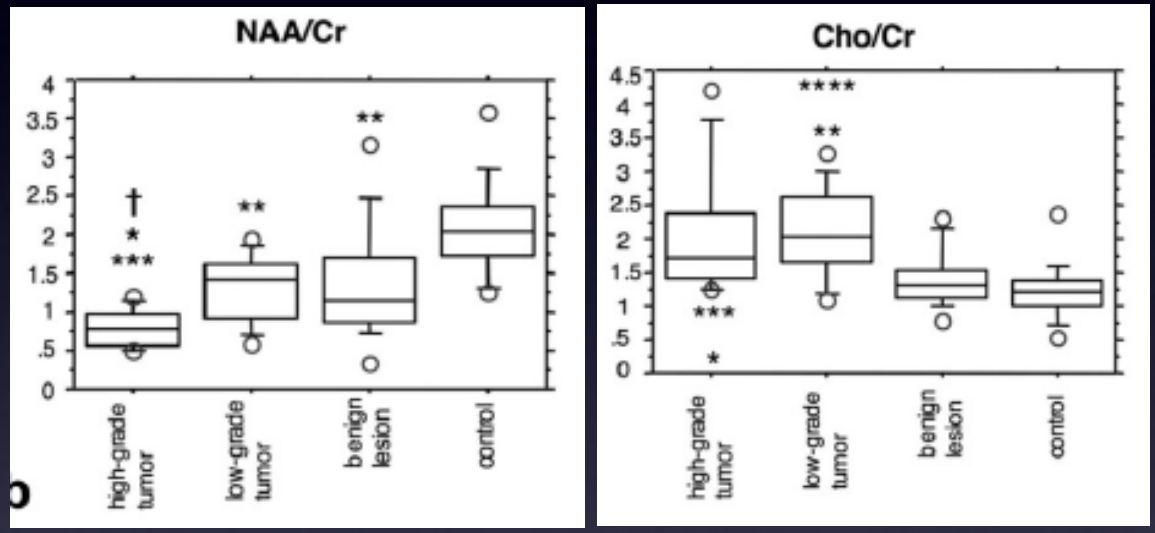
Index Patient



PACS, CHOB

T1-weighted image, sagittal

Cho/Cr ratio, 78.1% grouped cases correctly classified



Hourani et al (2006) *Journal of Magnetic Resonance Imaging*

Index Patient

Markedly depressed NAA
Elevated choline
= suspicious for tumor

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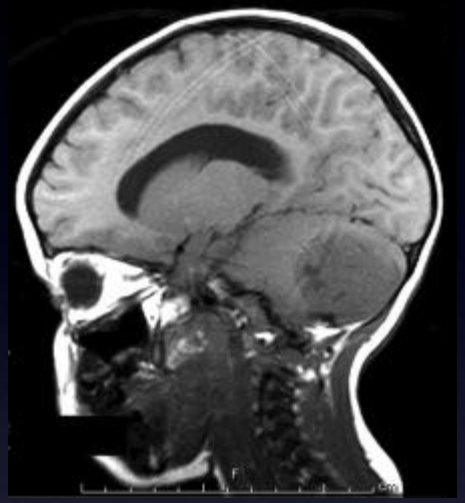
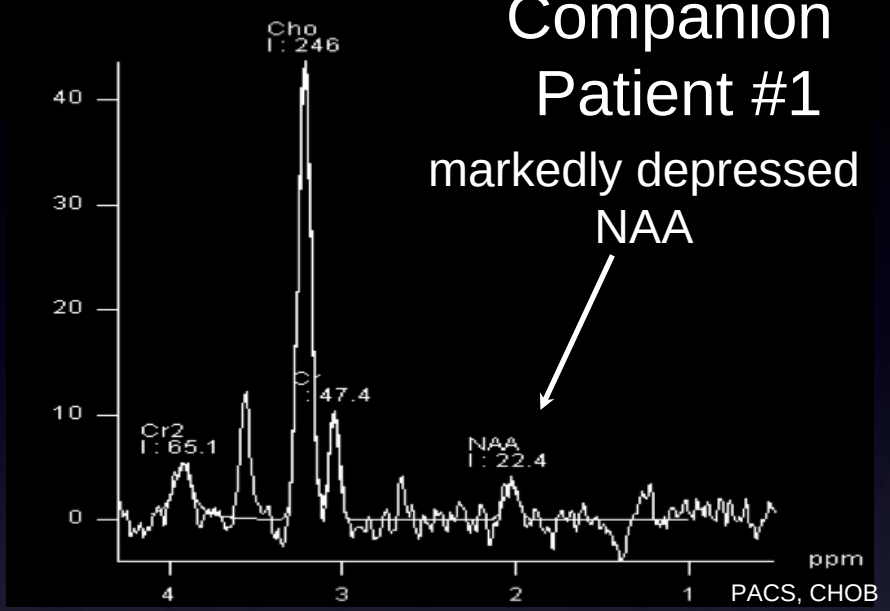
Index Patient



T1-weighted image, sagittal PACS, CHOB

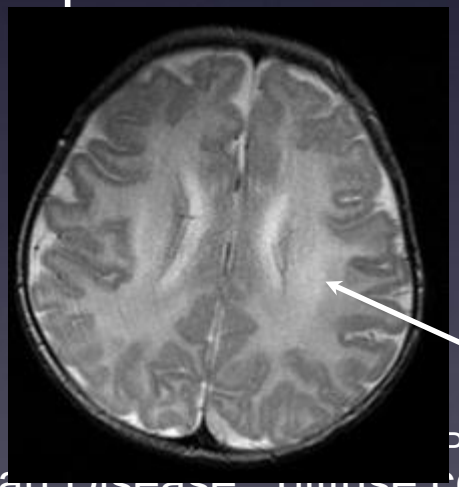
Companion Patient #1



markedly depressed NAA

PACS, CHOB

Companion Patient #2



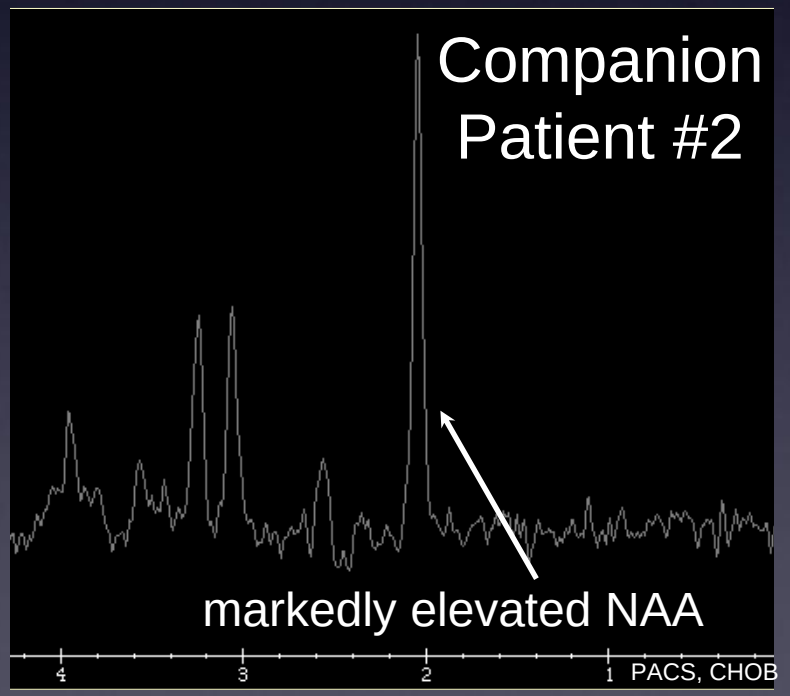
hyperintense

PACS, CHOB

Canavan Disease: diffuse confluent demyelination

axial T2-weighted image

Companion Patient #2



markedly elevated NAA

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Index Patient: Differential Diagnosis

1) Patient Age and History of the Present Illness

2) Infratentorial area of focal, low attenuation with internal calcifications, surrounding edema in posterior fossa and concomittant hydrocephalus

- Infratentorial Tumors (%)
  - Medulloblastoma (32.4)
  - Pilocytic Astrocytoma (28.3)
  - Ependymoma (12)

Could MR imaging techniques distinguish between these?

Menkes, Harvey and Maria (2006) *Child Neurology*

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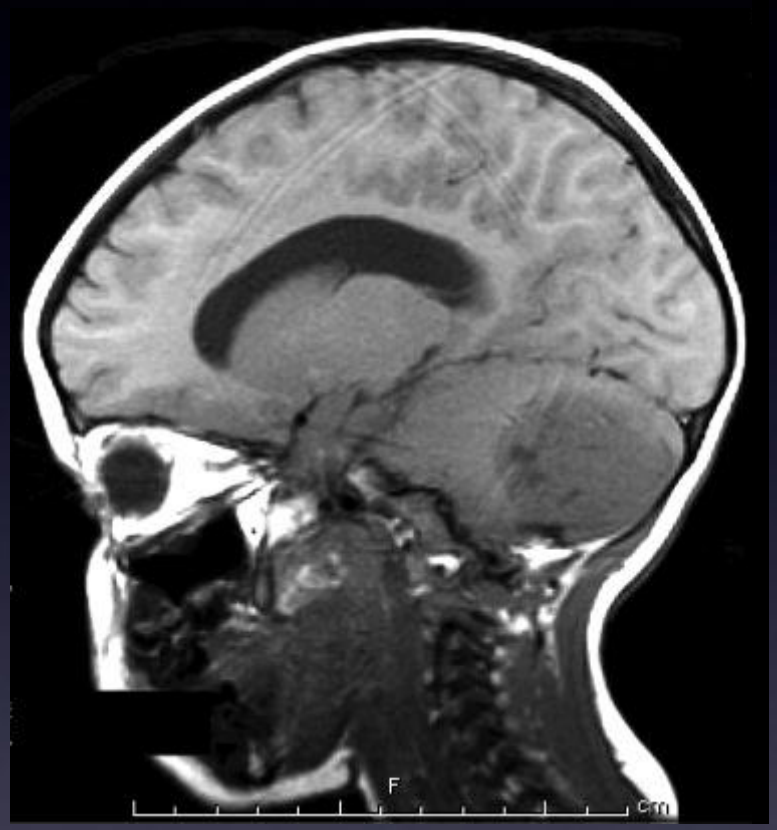
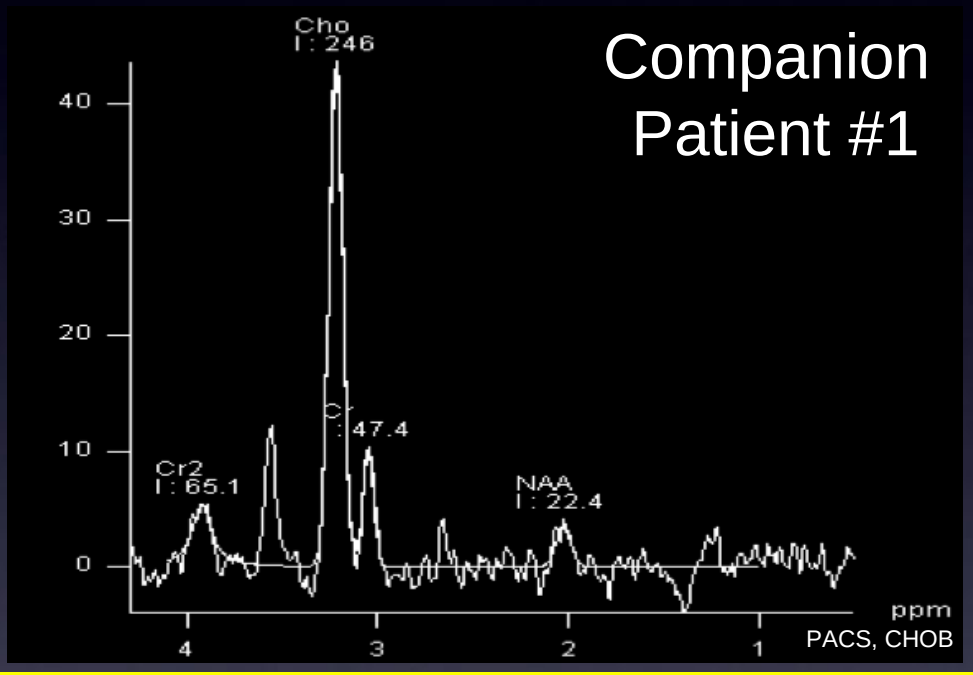
Do common neoplastic lesions of the posterior fossa have distinct MR spectra?

Index Patient



PACS, CHOB

T1-weighted image, sagittal



PACS, CHOB

Companion Patient #1

Markedly depressed NAA

Elevated choline

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Medulloblastoma

Highly malignant tumor composed of very primitive, undifferentiated small, round cells; often situated within inferior vermis

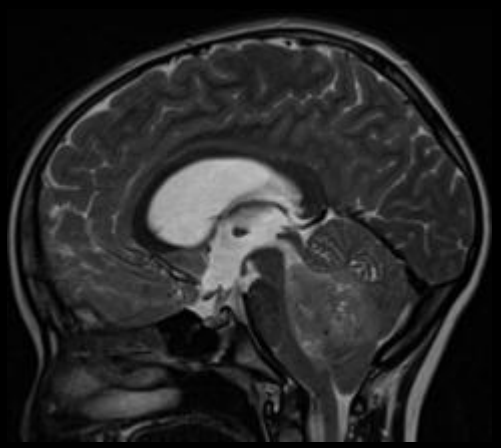
CT(-): hyperdense

Variable appearance on MR

T1: hypo/isointense to grey matter

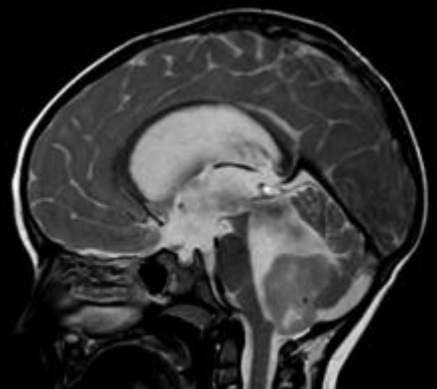
T2: hypo/isointense to grey (solid component),
decreased diffusion

MRS: markedly elevated choline, markedly depressed NAA, lactate usually present



sagittal T2-weighted image

sagittal T1-weighted image



sagittal T2-weighted image

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Barkovich (2005) *Pediatric Neuroimaging*

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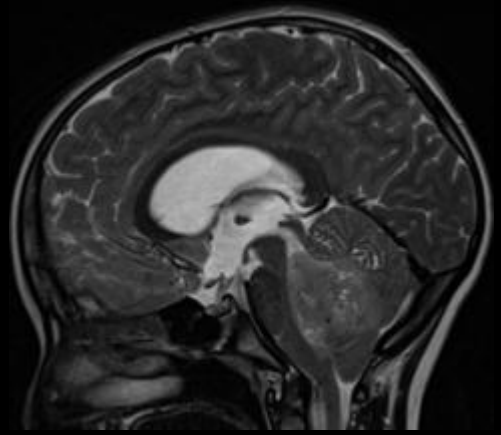
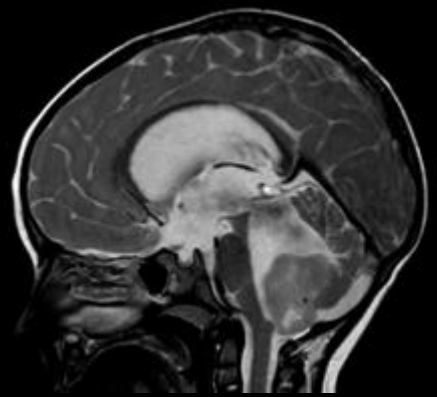
Medulloblastoma



sagittal T2-weighted image

sagittal T1-weighted image



sagittal T2-weighted image

Pilocytic Astrocytoma

Mixed cystic/solid mass with variable surrounding edema; endothelial cells within tumor have open tight junctions and fenestrations

CT(-): iso/hypodense to grey

Variable appearance on MR

T1 (solid portion) iso/hypointense to grey

T2 (solid portion) iso/hyperintense to grey

MRS: high choline, modestly low NAA

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Barkovich (2005) *Pediatric Neuroimaging*

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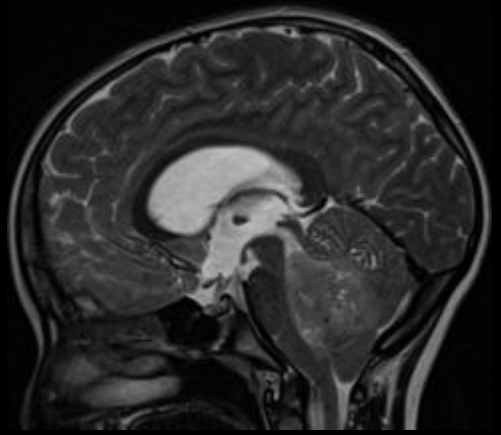
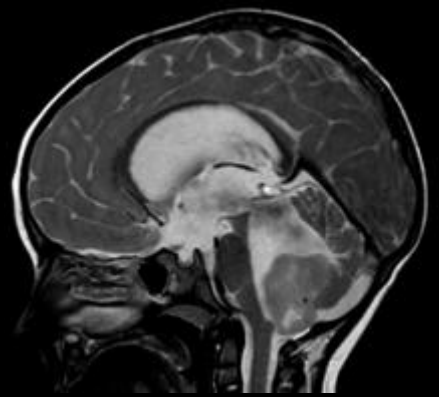


sagittal T2-weighted image

Medulloblastoma

sagittal T1-weighted image

Pilocytic Astrocytoma



sagittal T2-weighted image

PACS, CHOB

Ependymoma

Slow growing tumor of differentiated ependymal cells of the floor and roof of the 4th ventricle; often solid with calcifications (50%)

CT(-): iso/hyperdense to grey with punctate calcifications and small cysts

Homo- or heterogeneous on MR
T1: heterogeneous, usually slightly hypo- to isointense

T2: heterogeneous, usually isointense with hypo- and/or hyperintense components

Barkovich (2005) *Pediatric Neuroimaging*

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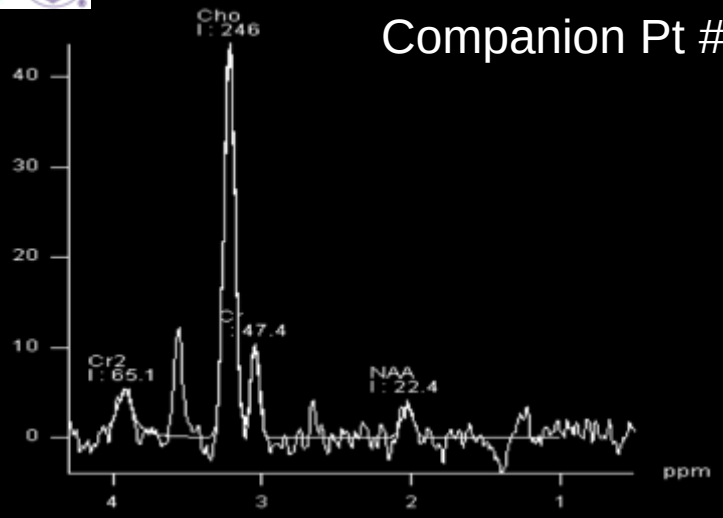
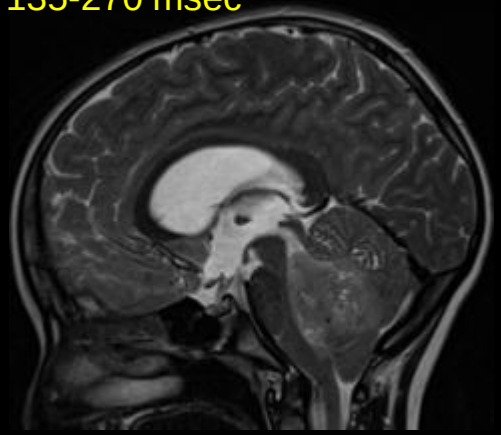
long-echo-time ^{1}H-MRS: 135-270 msec

Companion Pt #1

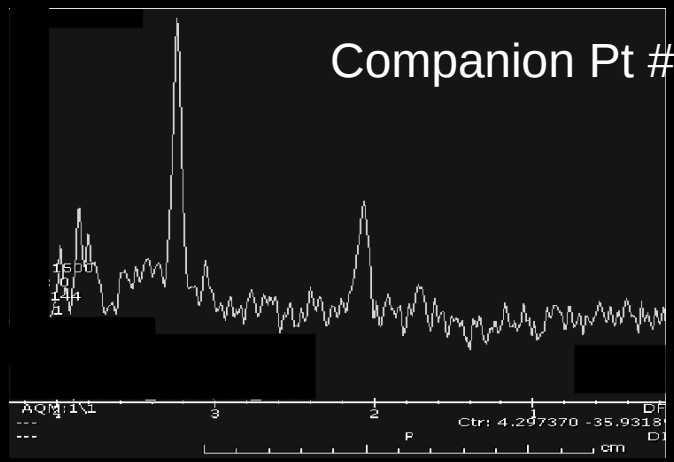




sagittal T2-weighted image

Medulloblastoma

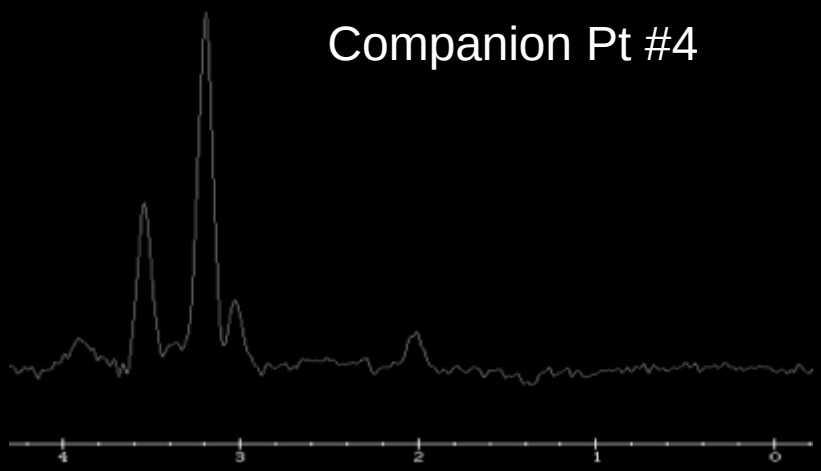
Companion Pt #3

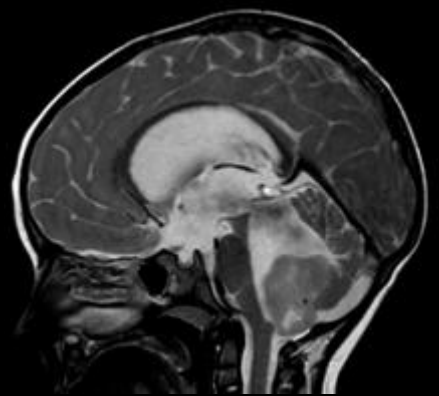


sagittal T1-weighted image

Pilocytic Astrocytoma

Companion Pt #4





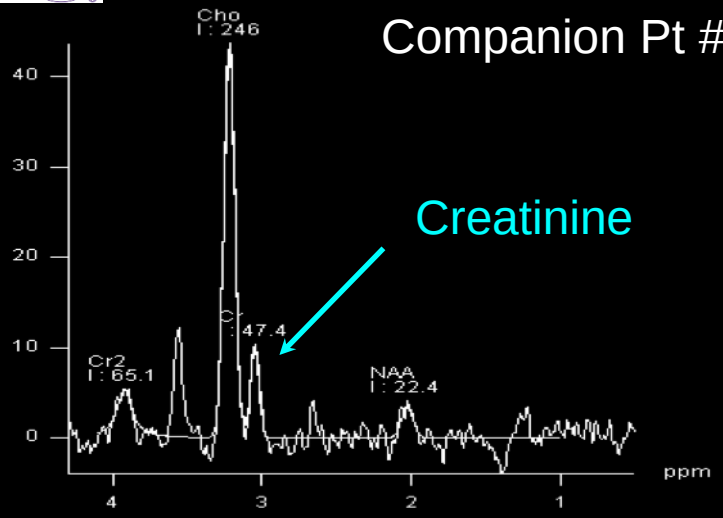
sagittal T2-weighted image

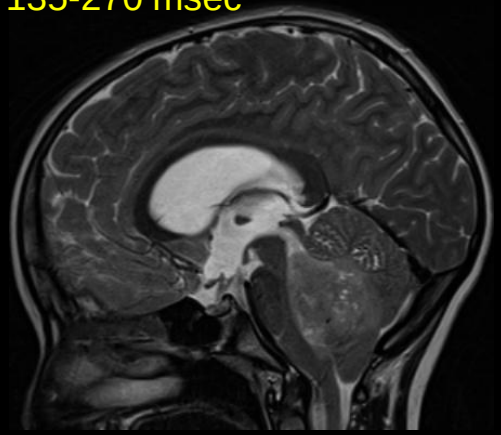
Ependymoma

Rochelle M. Witt, HMS III
Gillian Lieberman, MD

long-echo-time ^{1}H-MRS: 135-270 msec

Companion Pt #1

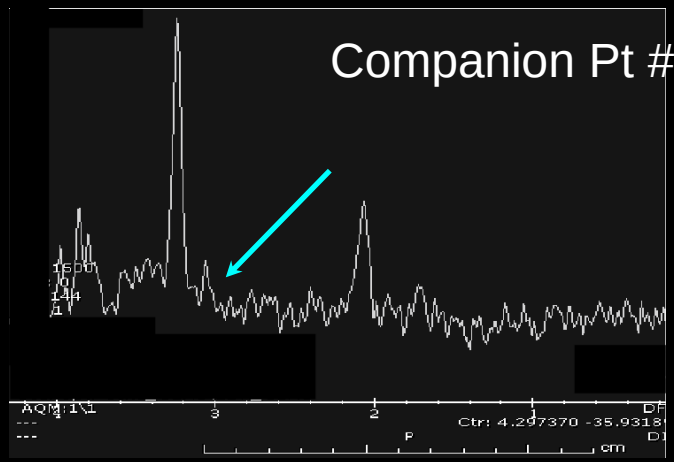




sagittal T2-weighted image

Medulloblastoma

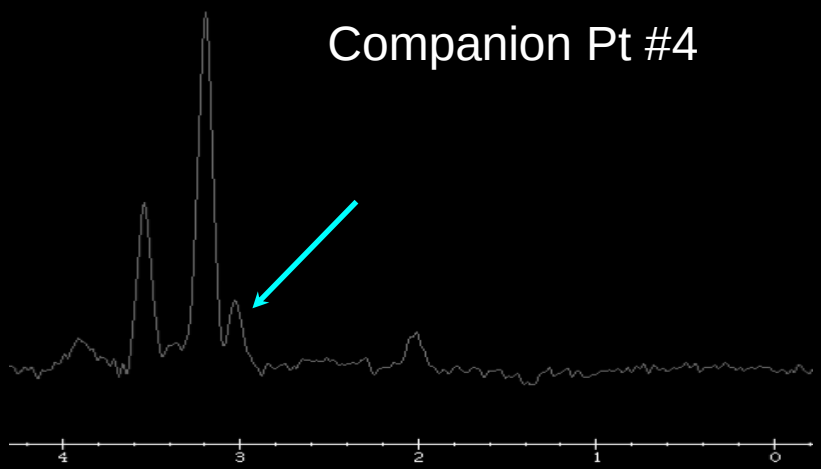
Companion Pt #3

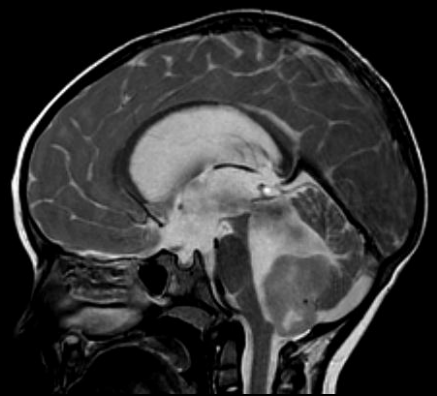


sagittal T1-weighted image

Pilocytic Astrocytoma

Companion Pt #4





sagittal T2-weighted image

Ependymoma

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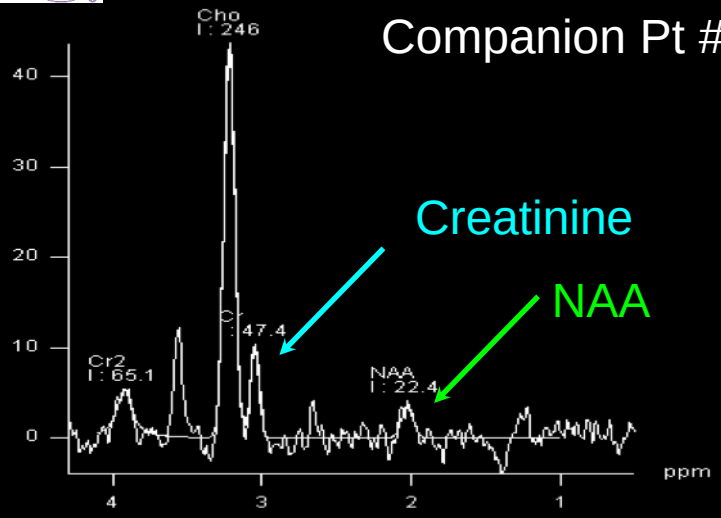
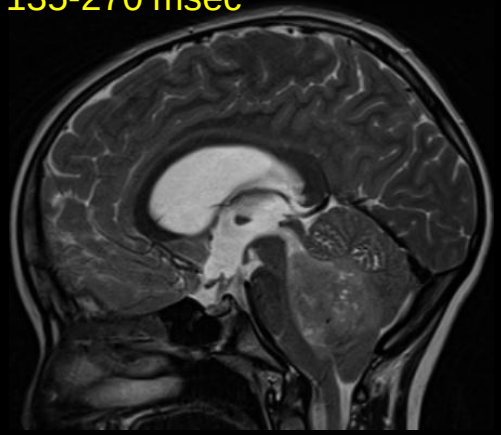
long-echo-time ^{1}H-MRS: 135-270 msec

Companion Pt #1

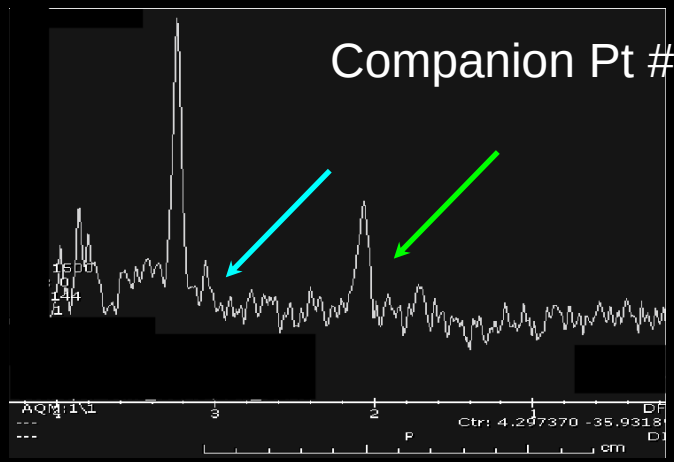




sagittal T2-weighted image

Medulloblastoma

Companion Pt #3

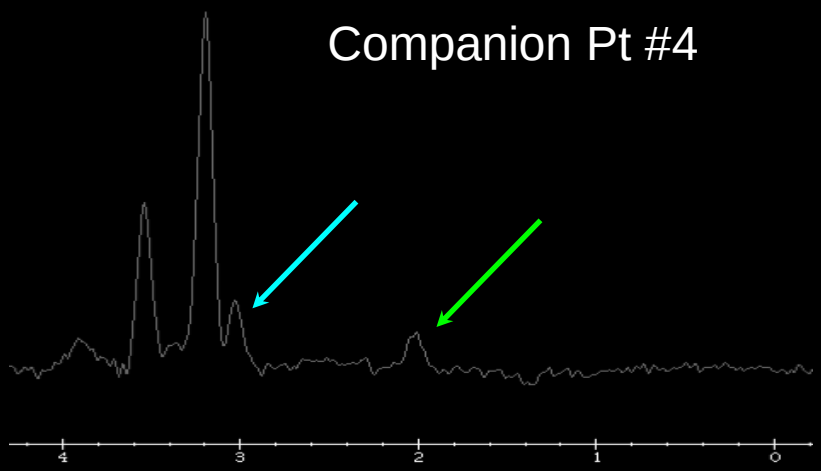


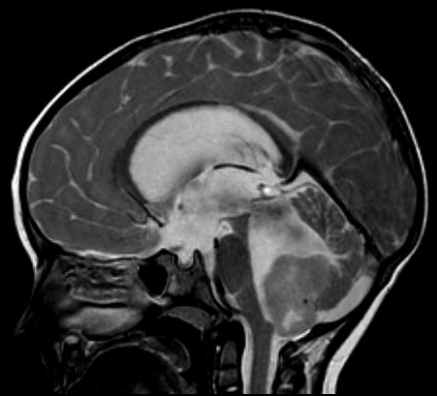
sagittal T1-weighted image

Pilocytic Astrocytoma

NAA/Cr = ?

Companion Pt #4





sagittal T2-weighted image

Ependymoma

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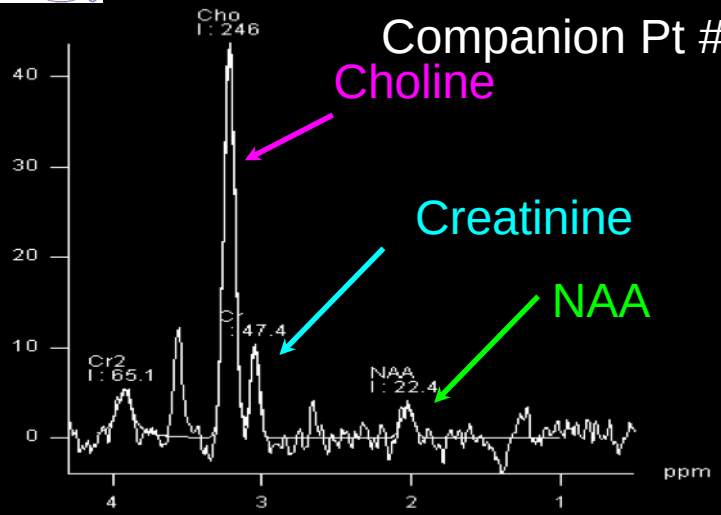
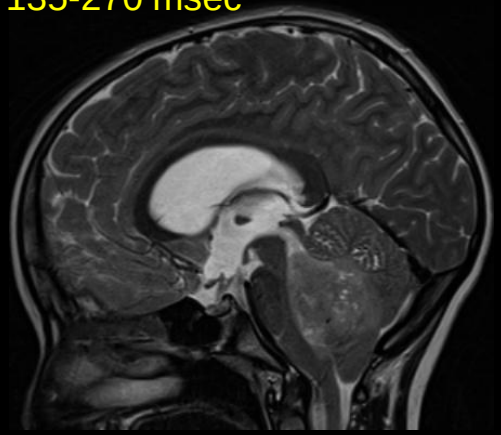
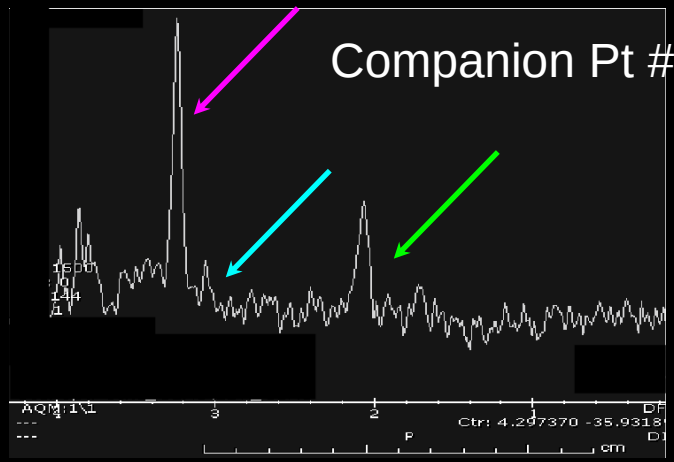
long-echo-time ^{1}H-MRS: 135-270 msec





sagittal T2-weighted image

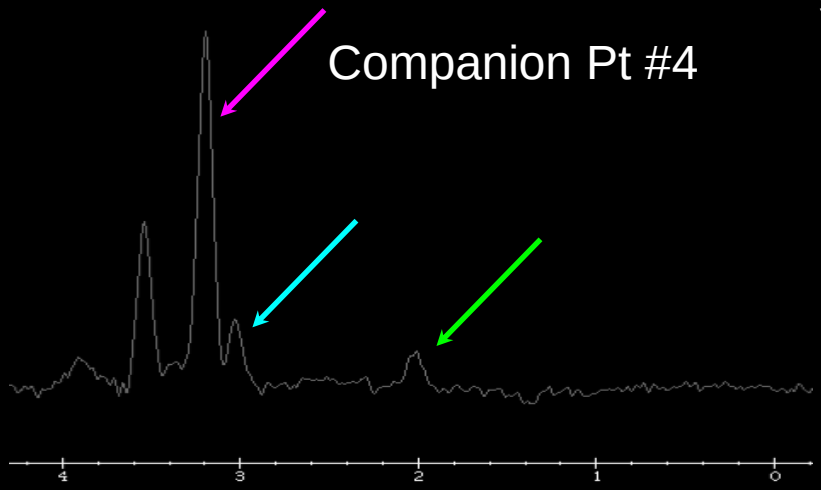
Medulloblastoma

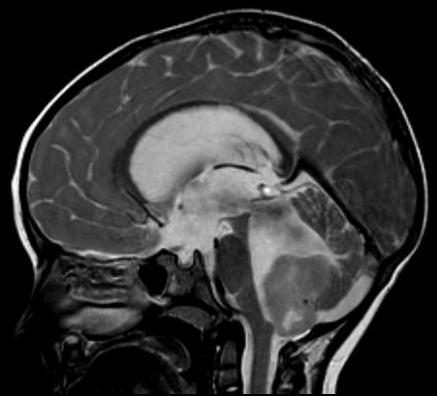


sagittal T1-weighted image

Pilocytic Astrocytoma

Cr/Cho = ?





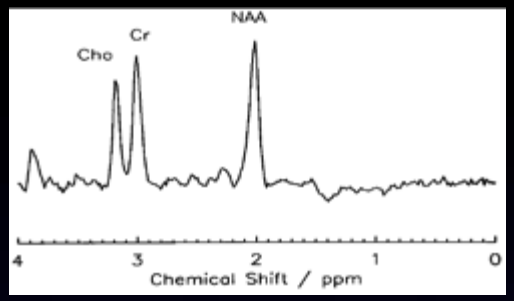
sagittal T2-weighted image

Ependymoma

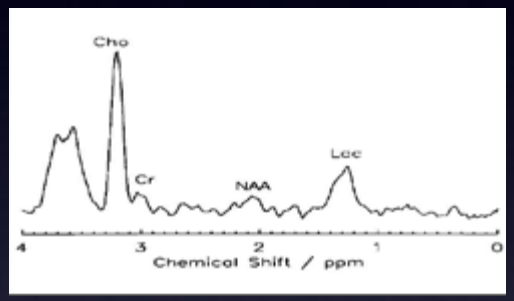
Rochelle M. Witt, HMS III
Gillian Lieberman, MD

Common neoplastic lesions of the posterior fossa have distinct MR spectra?

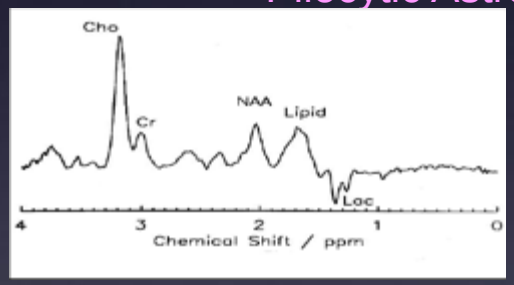
Control



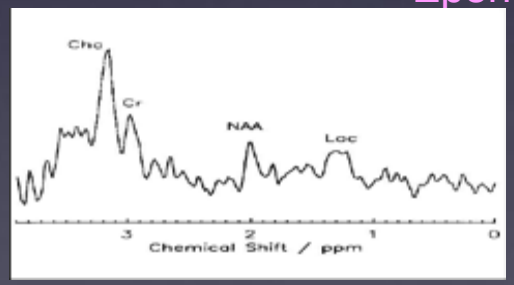
Medulloblastoma/PNET



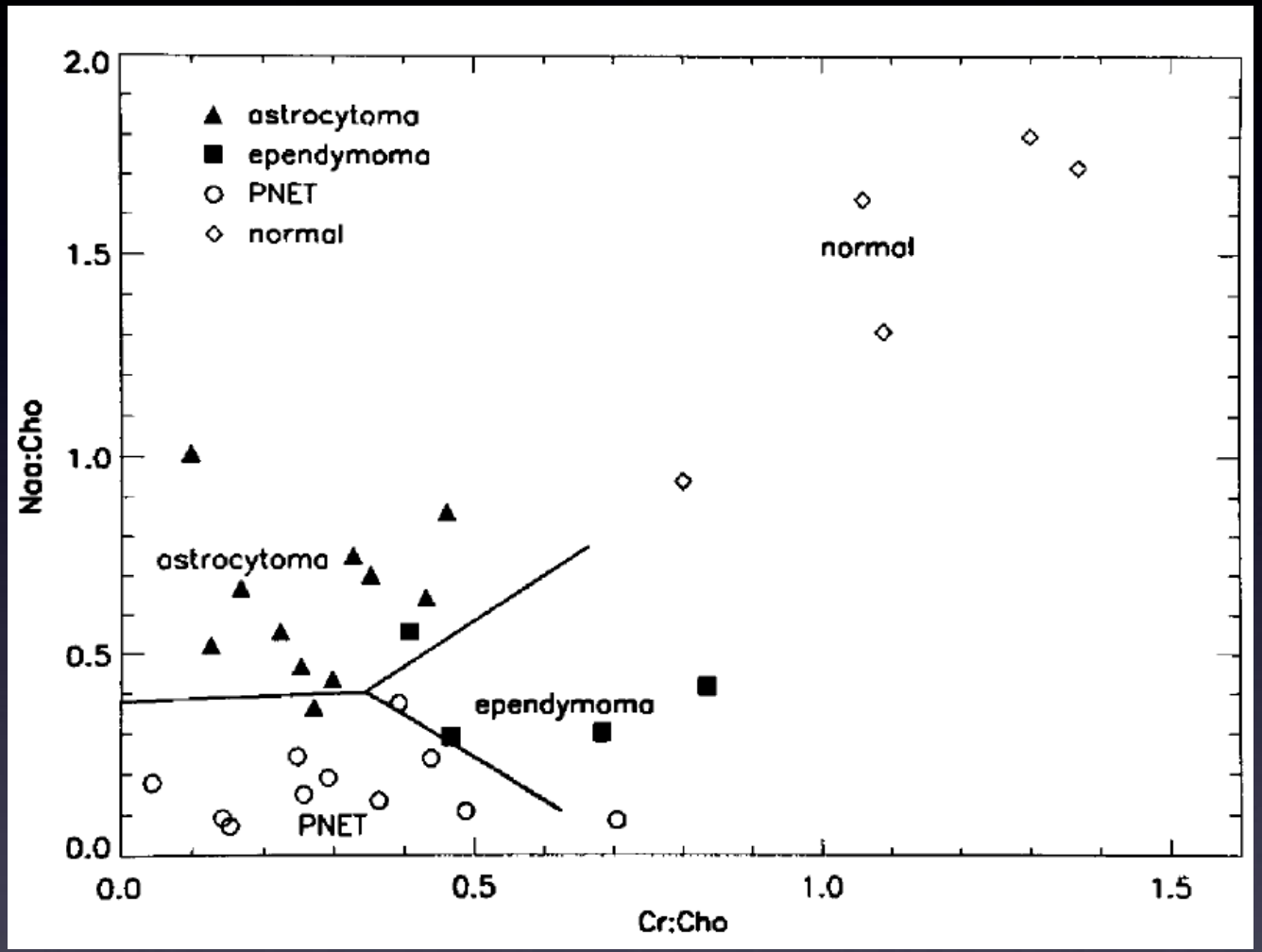
Pilocytic Astrocytoma



Ependymoma



Long-echo-time ^{1}H-MRS



Wang et al (1995) *AJNR Am J Neuroradiology*

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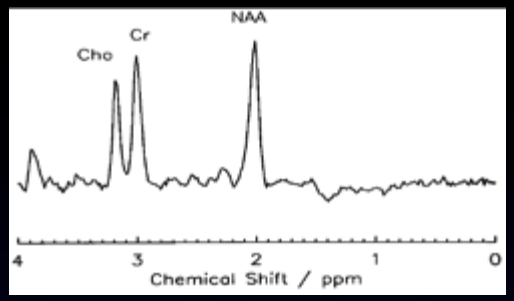
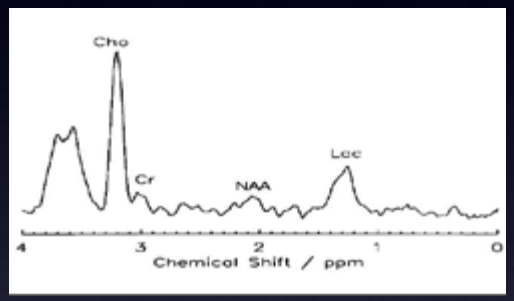
Common neoplastic lesions of the posterior fossa have distinct MR spectra?

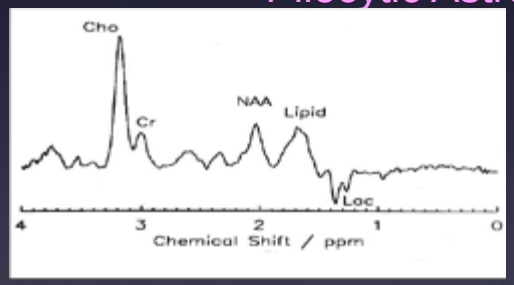
Control



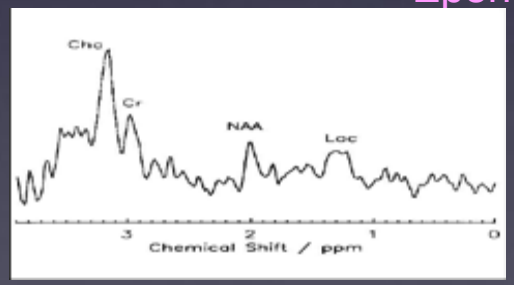
Medulloblastoma/PNET



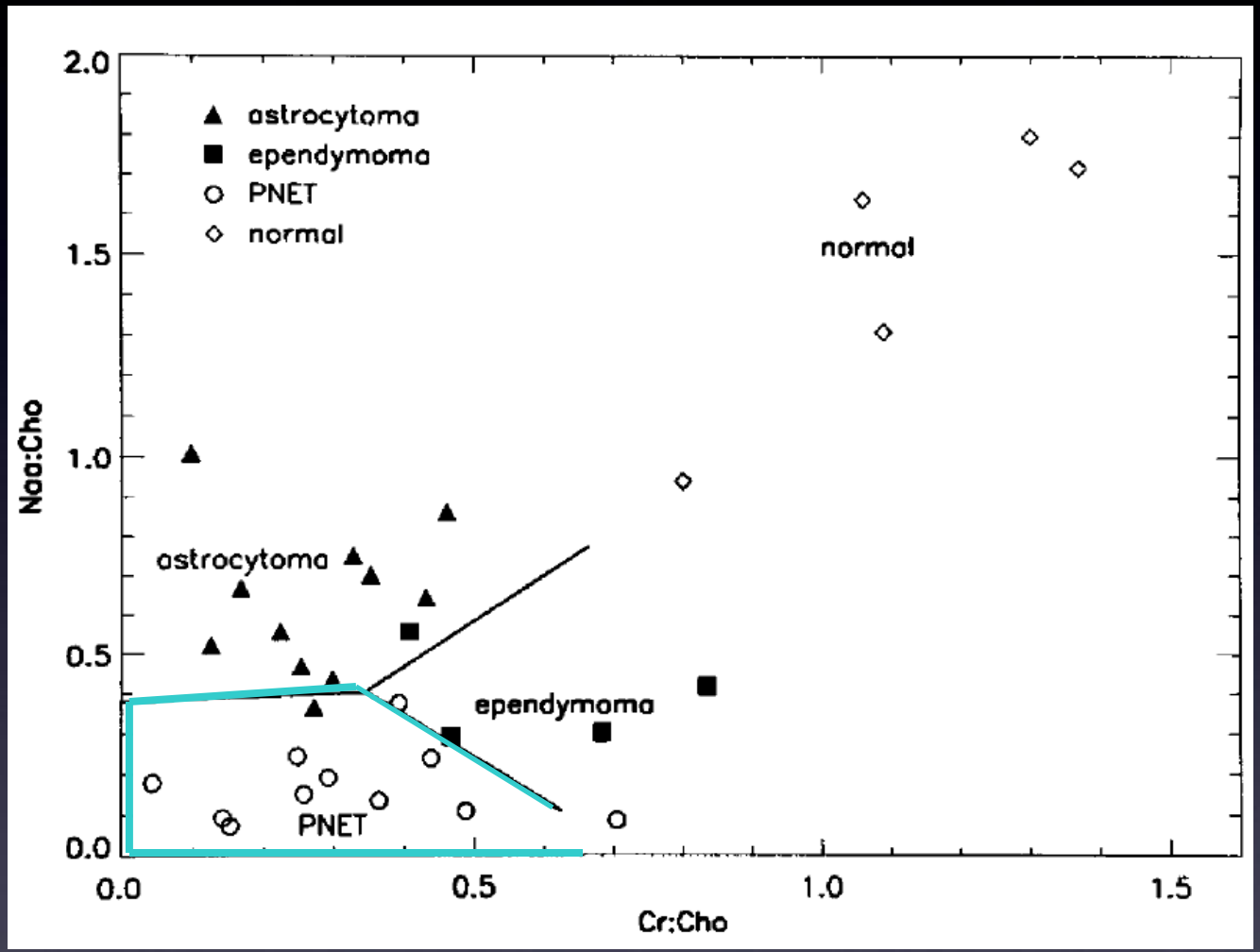
Pilocytic Astrocytoma



Ependymoma



Long-echo-time ^{1}H-MRS



Our patient's Naa:Cho and Cr:Cho ratios suggest a diagnosis of PNET.

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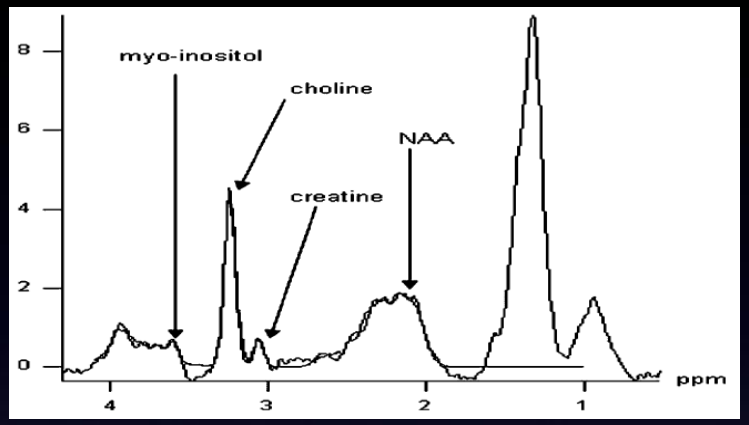
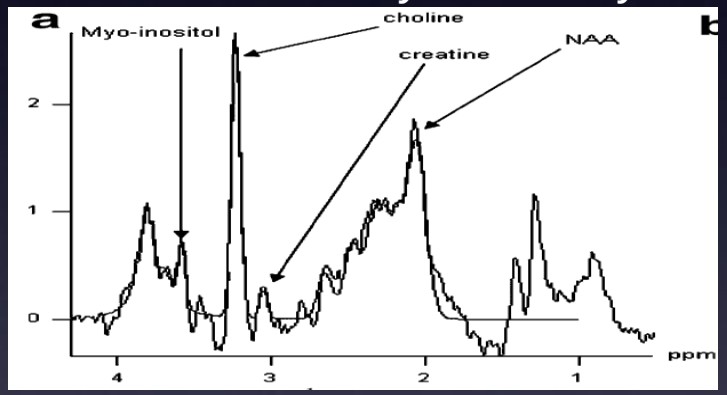
Medulloblastoma



Pilocytic Astrocytoma



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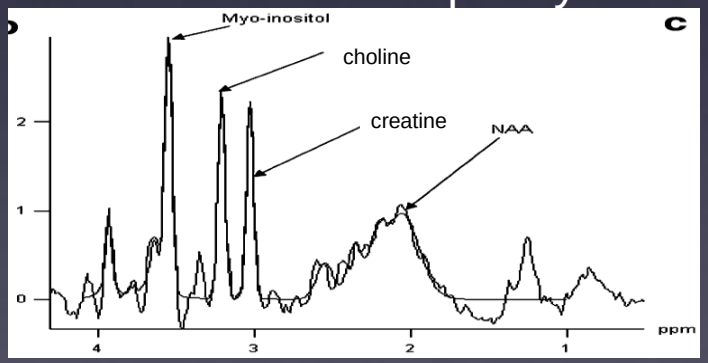
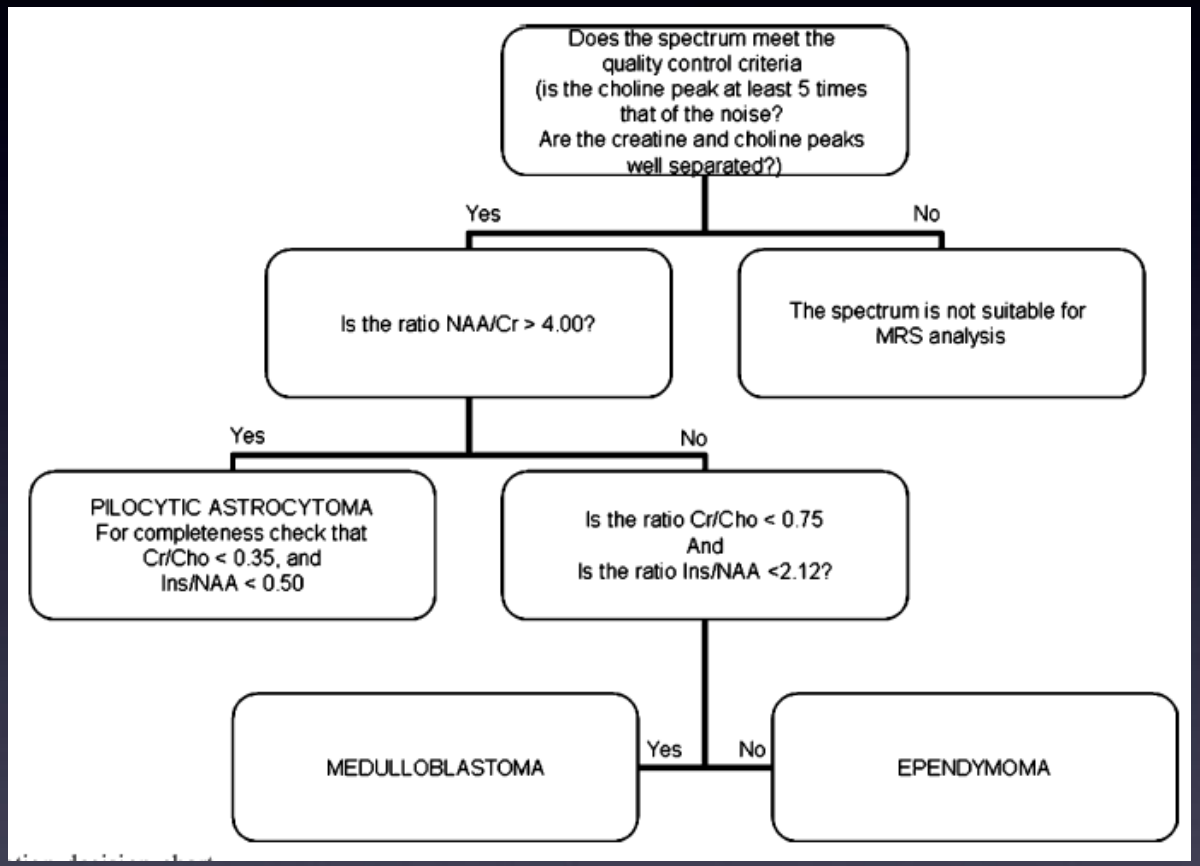


Short-echo-time ^{1}H-MRS

Short-echo-time ^{1}H-MRS algorithm



NB: Additional metabolic information may be obtained by short-echo-time ^{1}H-MRS, which offers increased diagnostic value.

Harris et al (2007) *Pediatric Radiology*

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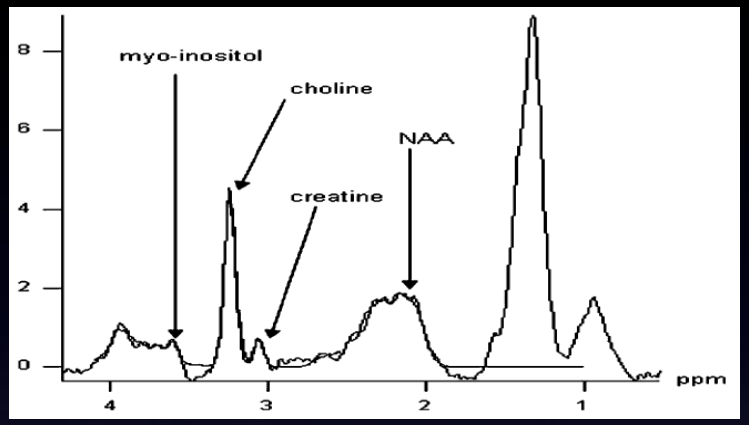
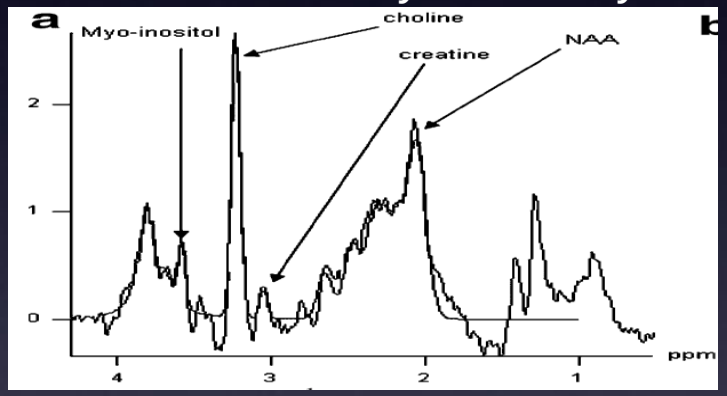
common neoplastic lesions of the posterior fossa have distinct MR spectra?

Medulloblastoma



Pilocytic Astrocytoma



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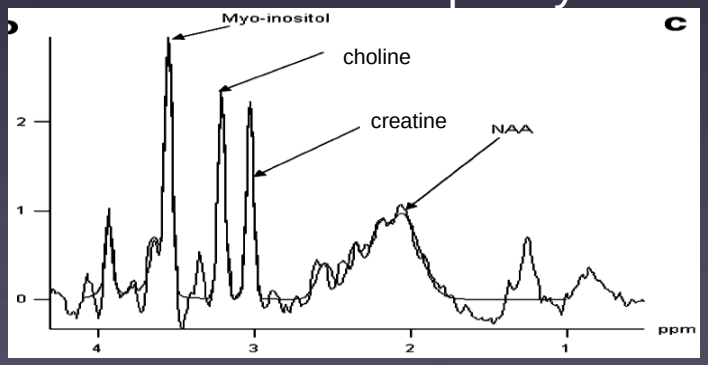
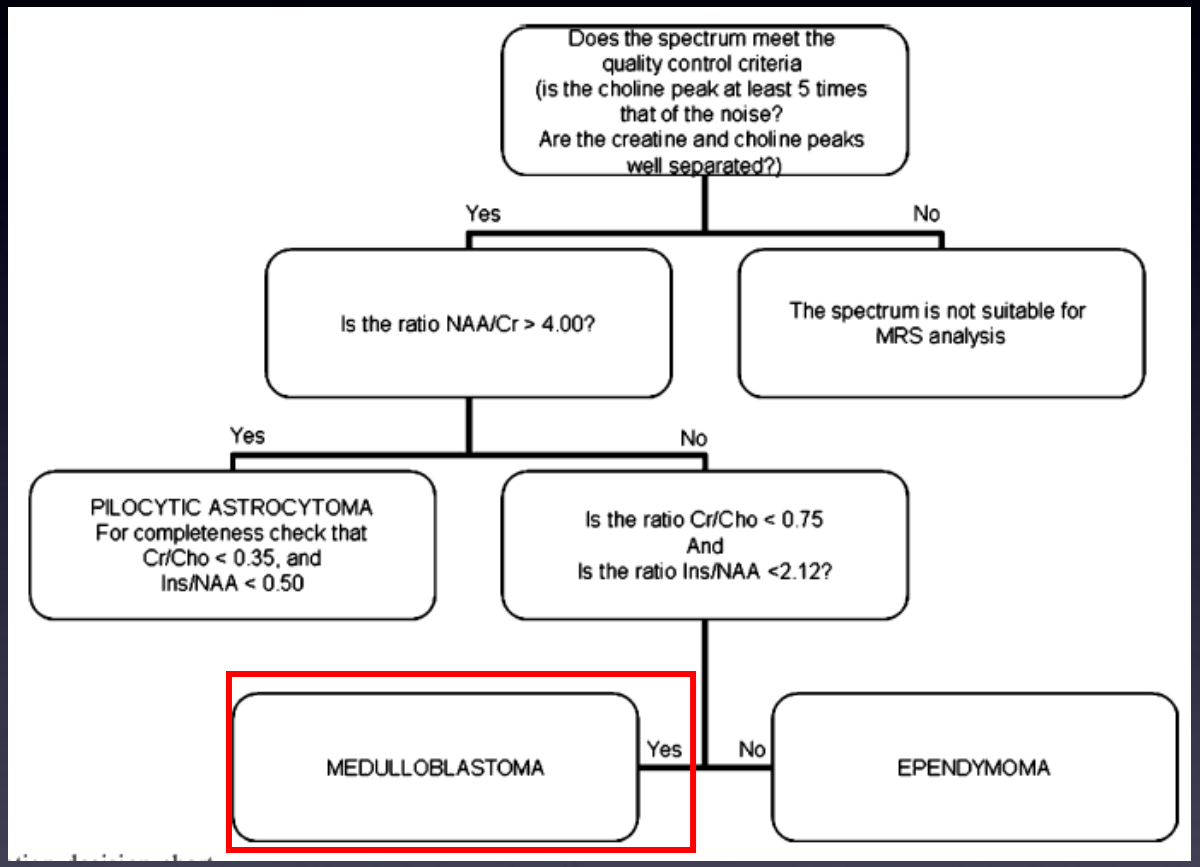


short-echo-time ^{1}H-MRS

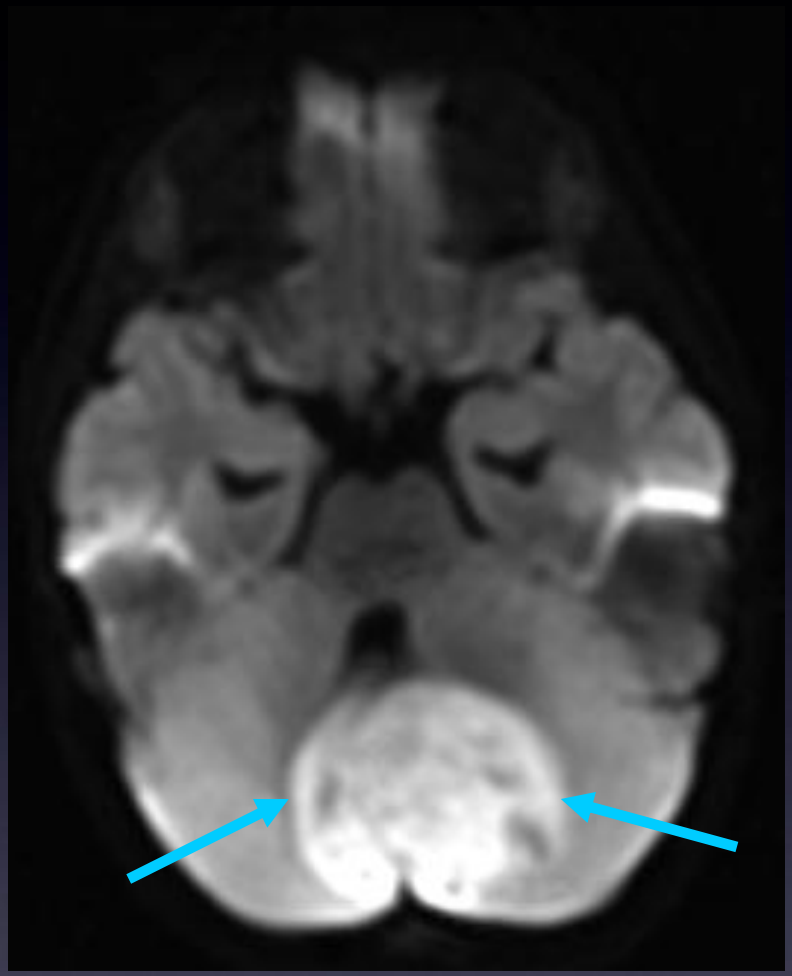
Short-echo-time ^{1}H-MRS algorithm



NB: Additional metabolic information may be obtained by short-echo-time ^{1}H-MRS, which offers increased diagnostic value.

Harris et al (2007) *Pediatric Radiology*

MR Diffusion: Index Patient



PACS, CHOB

DWI, axial image
Index Patient

Bright lesion = decreased diffusion within the medulloblastoma tumor

- In Diffusion-Weighted Imaging (DWI), the rate of microscopic water diffusion within tissues can be evaluated

- Restriction of motion can been seen in normal white matter tracts (anisotropy)

- Restriction of motion can also be seen in hypercellular/solid tumors

- DWI can be used to distinguish between:

  - epidermoid and arachnoid cysts

  - ring-enhancing brain abscesses and ring-enhancing cystic/necrotic high-grade gliomas

  -Different tumor grades: greater restricted diffusion correlates to hypercellularity, and subsequently, higher tumor grade

  -Different tumor types: restricted diffusion is less for low-grade gliomas as compared to embryonal tumors (PNET, medulloblastoma and malignant teratoid-rhabdoid tumor)

Poussaint and Rodriguez (2006)

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Patient follow-up: s/p Suboccipital Craniotomy

PACS, CHOB

T1-weighted image, sagittal view

- No evidence of residual medulloblastoma

- No evidence of leptomeningeal spread or drop metastases

- Radiation course

- Chemotherapy course

- 4 yrs s/p GTR, no evidence of recurrent medulloblastoma

- Bone age by plain radiography (AP view): 6 y, 10 mo
(chronological age: 7 y, 11 mo)

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Future Directions

- MR Spectroscopy could be used as part of a suite of diagnostic tests for the noninvasive, comprehensive diagnosis of posterior fossa masses. This might include MR Diffusion (and MR Perfusion).
- MR Spectroscopy could be used to consider:
  - Tumor Grading (including tumor heterogeneity)
  - Planning of Treatment/Monitoring of Treatment Response
    - Tumor therapy: chemotherapy/radiotherapy, surgical planning/need for complete resection
- MR Spectroscopy provides a novel, noninvasive way to ask more basic questions about tumor biology.
  - Privileged patient population
  - Intervention, even biopsy, carries risks.
  - Masses are often inaccessible.
  - As imaging resolution improves, we can ask about heterogenous environments within the tumor that may be important in oncogenesis. In addition, one could possibly monitor metabolic responses to therapy *in situ*.

Acknowledgements

- Radiology resident pediatric team: Ammar Sarwar, MD, Johannes Roedl, MD and David Li, MD
- Members of Children's Neuroradiology, especially Alvin Camacho, MD and Diana Rodriguez, MD
- Gillian Lieberman, MD
- Emily Hanson and Claire Odom, HMS Education Coordinators
- Graham Frankel

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Gillian Lieberman, MD

References

- Adam, A., Dixon, A.K., Grainger, R.G. & Allison, D.J. *Grainger & Allison's diagnostic radiology : a textbook of medical imaging* (Elsevier Churchill Livingstone, [Edinburgh], 2008).
- Barkovich, A.J. *Pediatric neuroimaging* (Lippincott Williams & Wilkins, Philadelphia, 2005).
- Harris, L.M.*, et al.* The use of short-echo-time 1H MRS for childhood cerebellar tumours prior to histopathological diagnosis. *Pediatric radiology* **37**, 1101-1109 (2007).
- Hourani, R.*, et al.* Proton magnetic resonance spectroscopic imaging to differentiate between nonneoplastic lesions and brain tumors in children. *J Magn Reson Imaging* **23**, 99-107 (2006).
- Menkes, J.H., Sarnat, H.B. & Maria, B.L. *Child neurology* (Lippincott Williams & Wilkins, Philadelphia, Pa. ; London, 2006).
- "Neuroanatomy." *EHSL - Spencer S. Eccles Health Sciences Library Home Page*. Web. 27 Aug. 2010. <http://library.med.utah.edu/WebPath/HISTHTML/NEURANAT/CNS243A.html>.
- Panigrahy, A., Borzage, M. & Bluml, S. Basic principles and concepts underlying recent advances in magnetic resonance imaging of the developing brain. *Seminars in perinatology* **34**, 3-19.
- Poussaint, T.Y., & Diana Rodriguez. Advanced Neuroimaging of Pediatric Brain Tumors: MR Diffusion, MR Perfusion and MR Spectroscopy. *Neuroimag Clin N Am* **16,** 169-192 (2006).
- Rizzo, D.C. *Fundamentals of anatomy & physiology*. (Thomson Delmar Learning; Clifton Park, 2006).
- Storey, P. Introduction to magnetic resonance imaging and spectroscopy. *Methods in molecular medicine* **124**, 3-57 (2006).
- Wang, Z., *et al.* Proton MR spectroscopy of pediatric cerebellar tumors. *AJNR Am J Neuroradiol.* **16**, 1821-33 (1995).