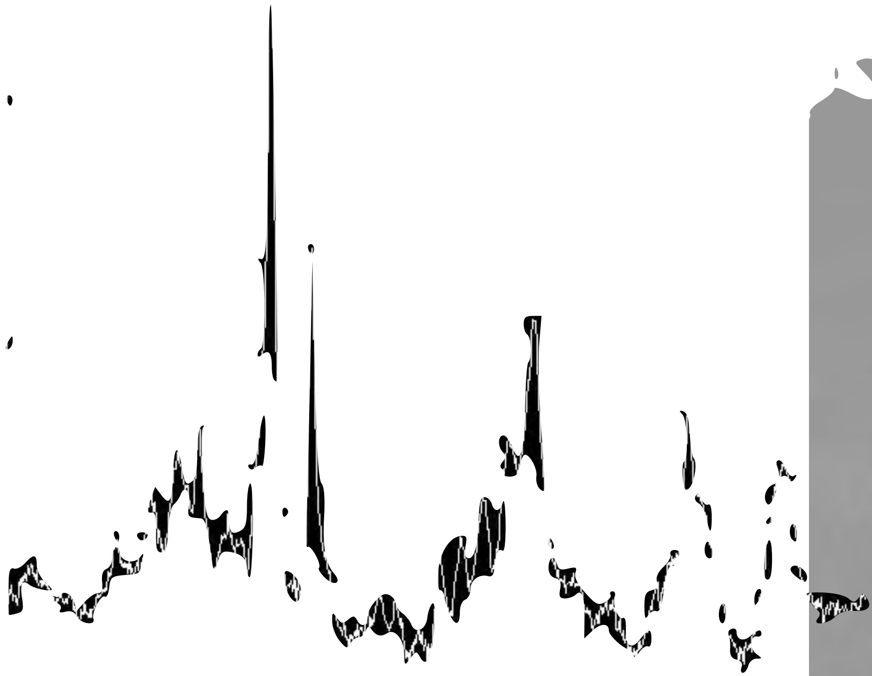
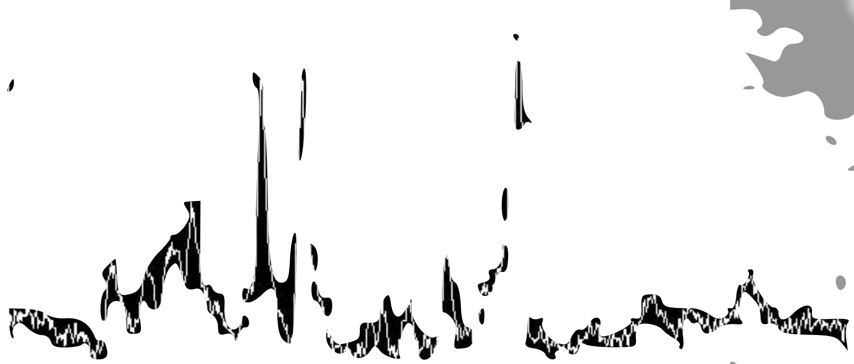
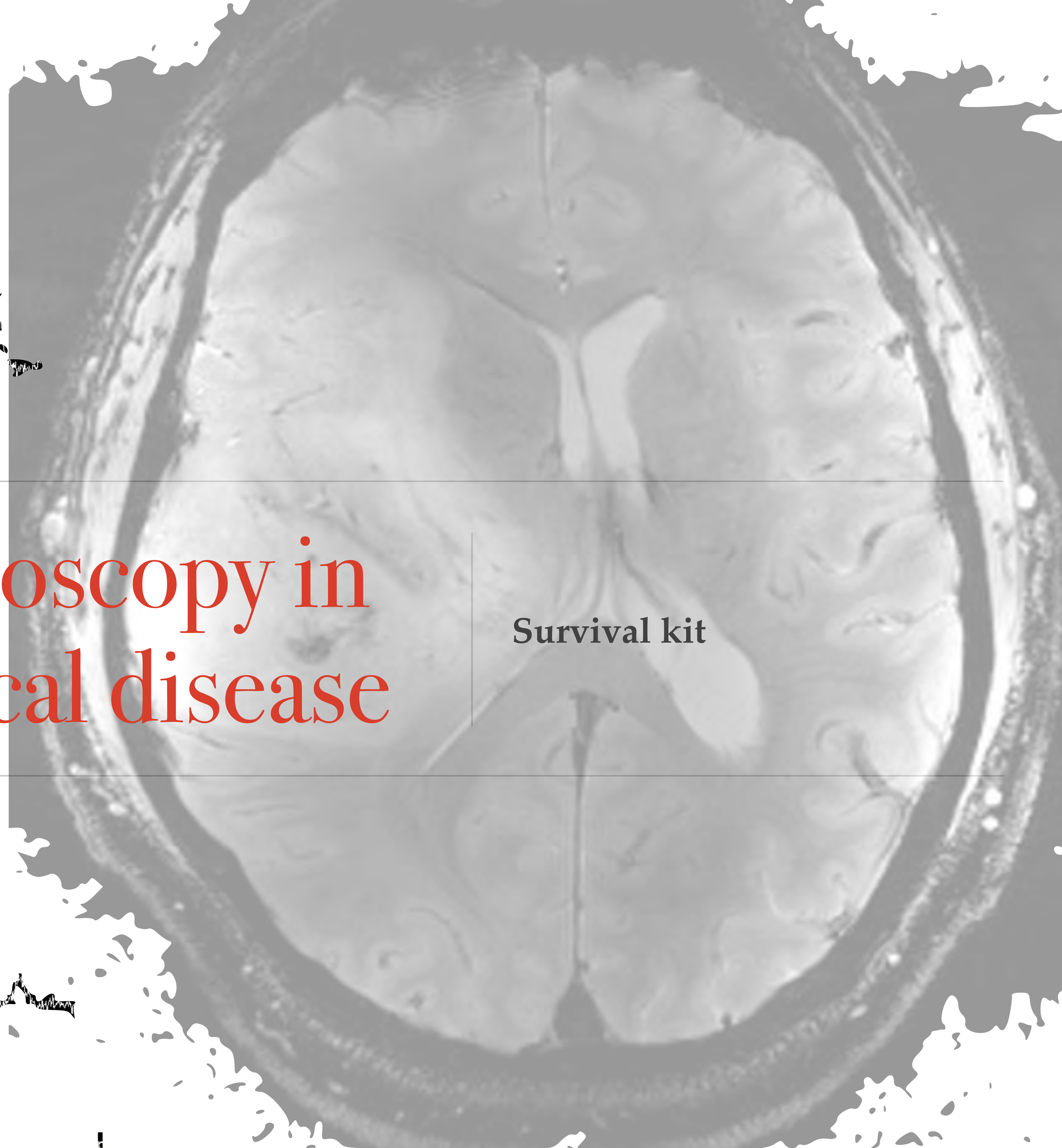


*Sotirios Bisdas*

# MR spectroscopy in neurological disease

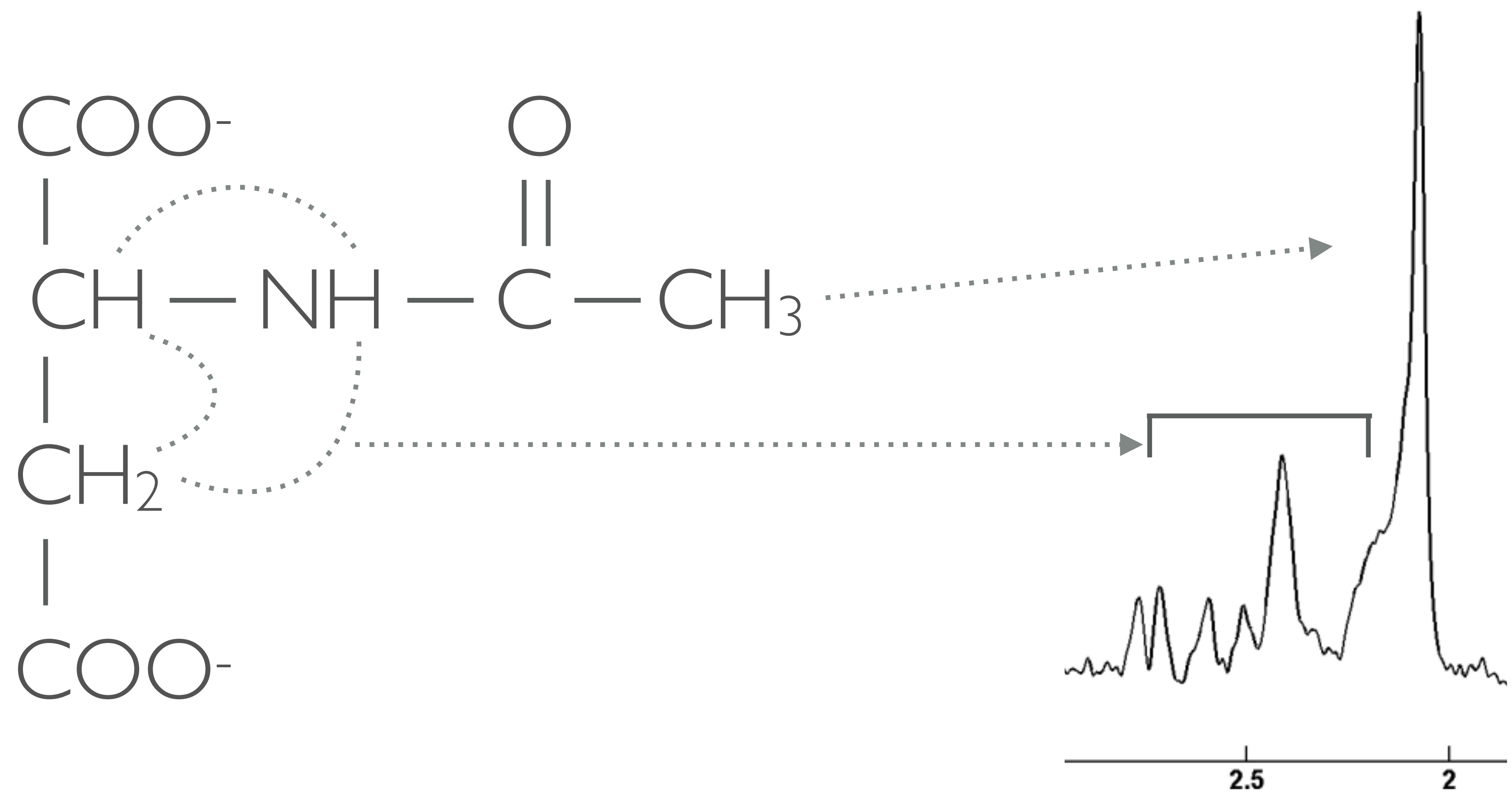
**Survival kit**





# Key physical principles of H-MRS

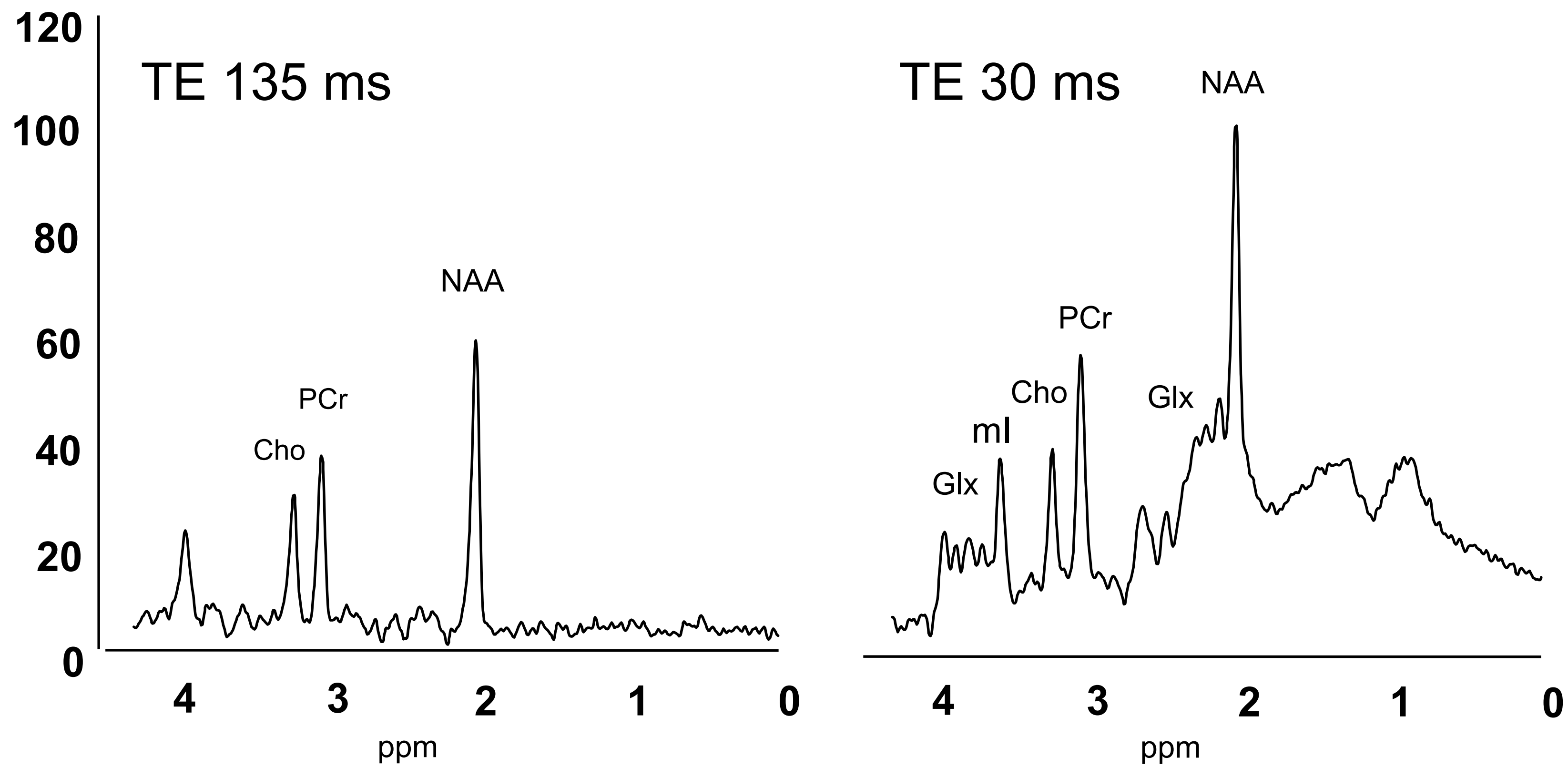
- Chemical shift
- **J-coupling**
- Echo time (TE)
- Editing

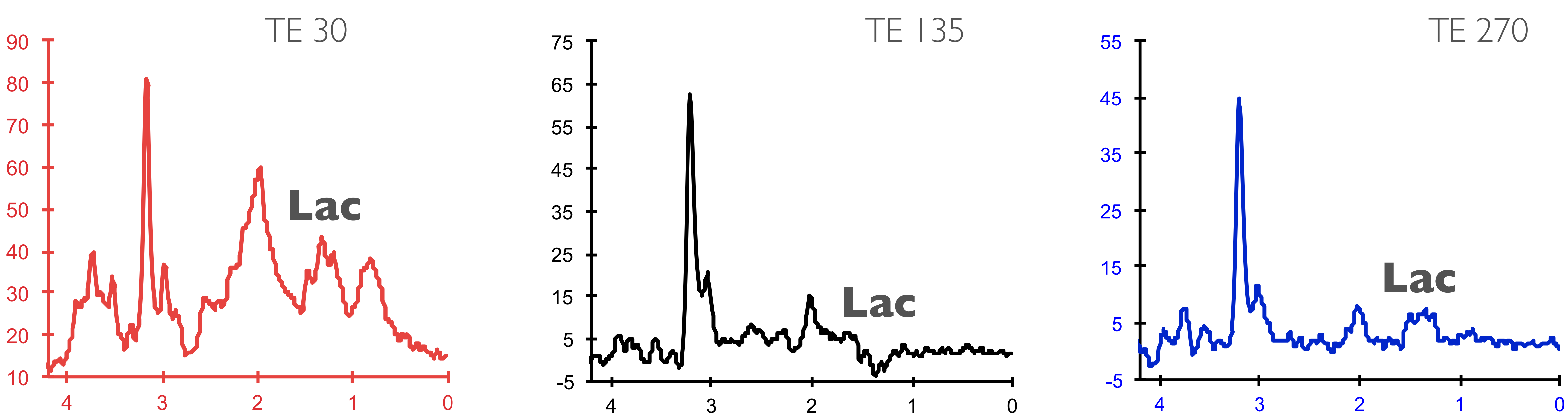


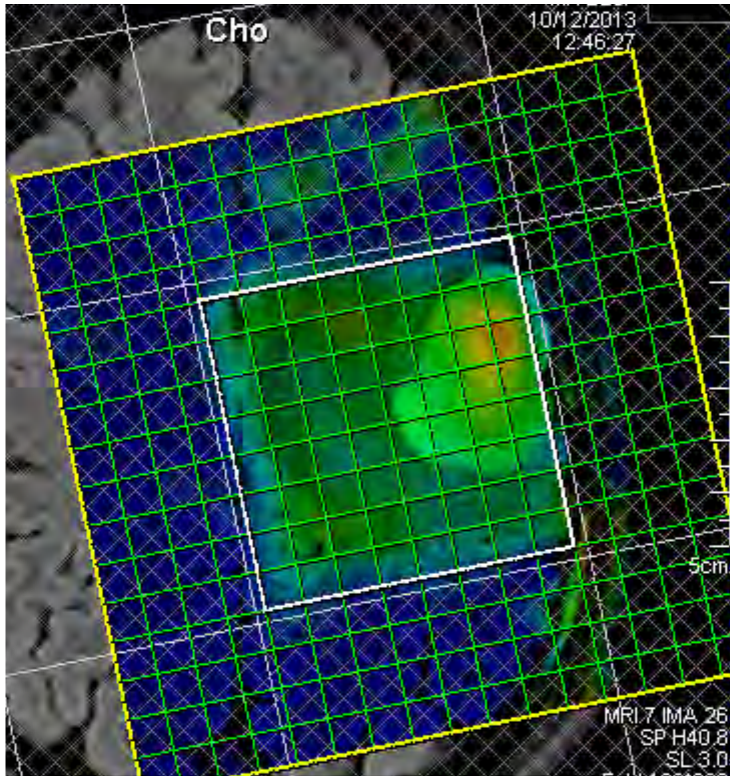

*N*-acetyl-aspartate

# Key physical principles of H-MRS

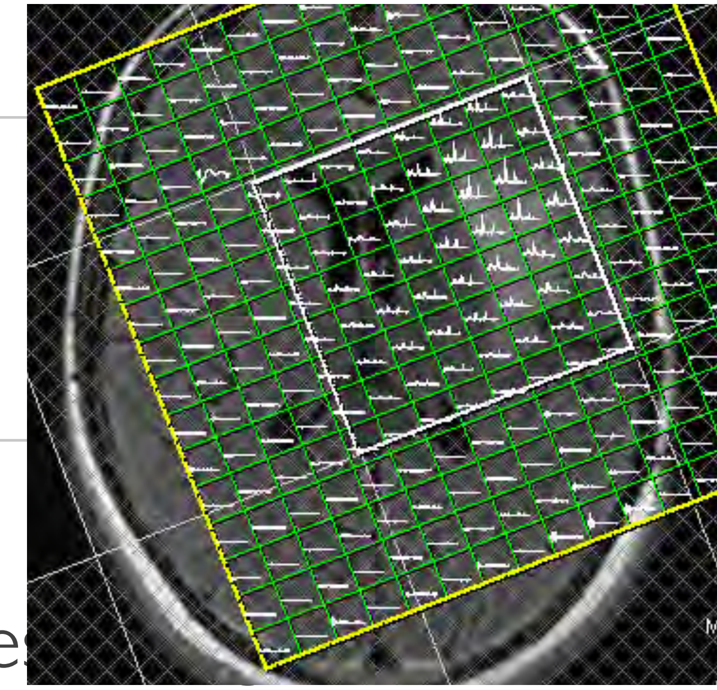
- Chemical shift
- J-coupling
- **Echo time (TE)**
- **Editing**






# Protocol design




troscopy: it requires slice selection pulse
limited coverage

- Multiple voxel (spectroscopic) techniques: extensive (rectangular) coverage; non-uniform metabolite excitation across (PRESS) box and some external signal may contaminate.
- Smallest possible FOV (R-L < A-P) may result into 20-30% scan time saving.
- Fast MRSI: turbo MRSI, PEPSI, spiral MRSI, SENSE-MRI
- Lipid suppression (saturation bands, inversion pulses, frequency selective saturation pulses)
- Higher $B_0$
- Water suppression

# Brain metabolites

**N-acetyl-Aspartate (NAA)**

Relatively high concentrations, dependent on brain site

Related to neurones density,

Never high peaks in brain tumours

**Creatine / Phosphocreatine (Cr/PCr)**

Short-term energy deposit

Spatially independent distribution; internal reference (?)

**Choline (Cho)**

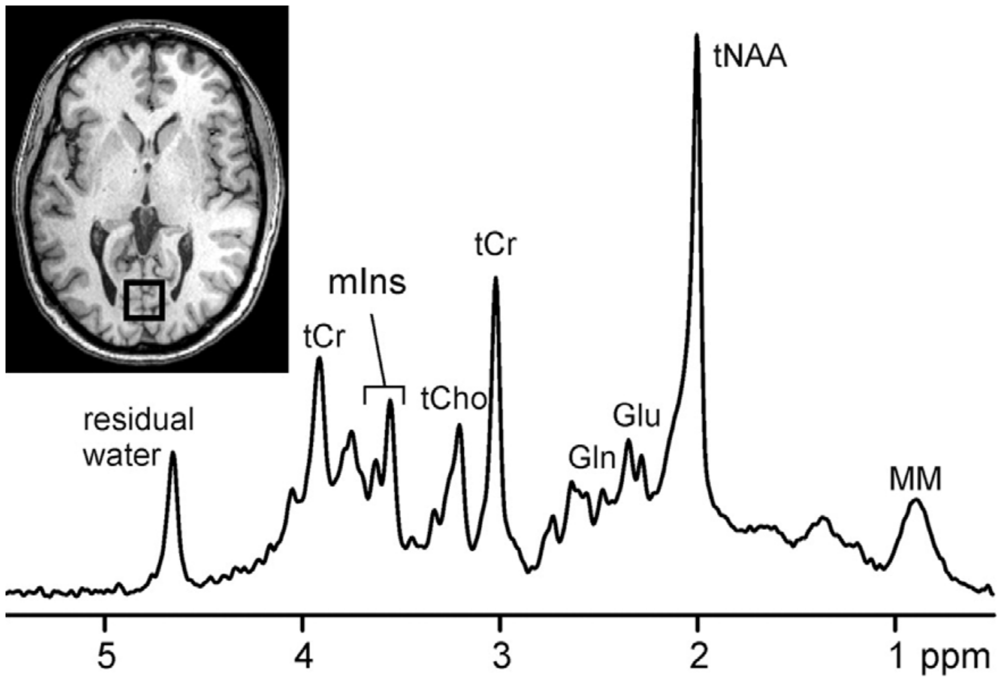
Synthesis of neurotransmitter AclCho, membrane component PCho

Cho-changes associated with high cell membrane activity and with immunohistological proliferation marker Ki-67

**Myo-Inositol (Ins or ml)**: Marker of gliosis

**Lactate**: Product of anaerobic glycolysis

hypoxia, stroke, infection, rapid growing tumors

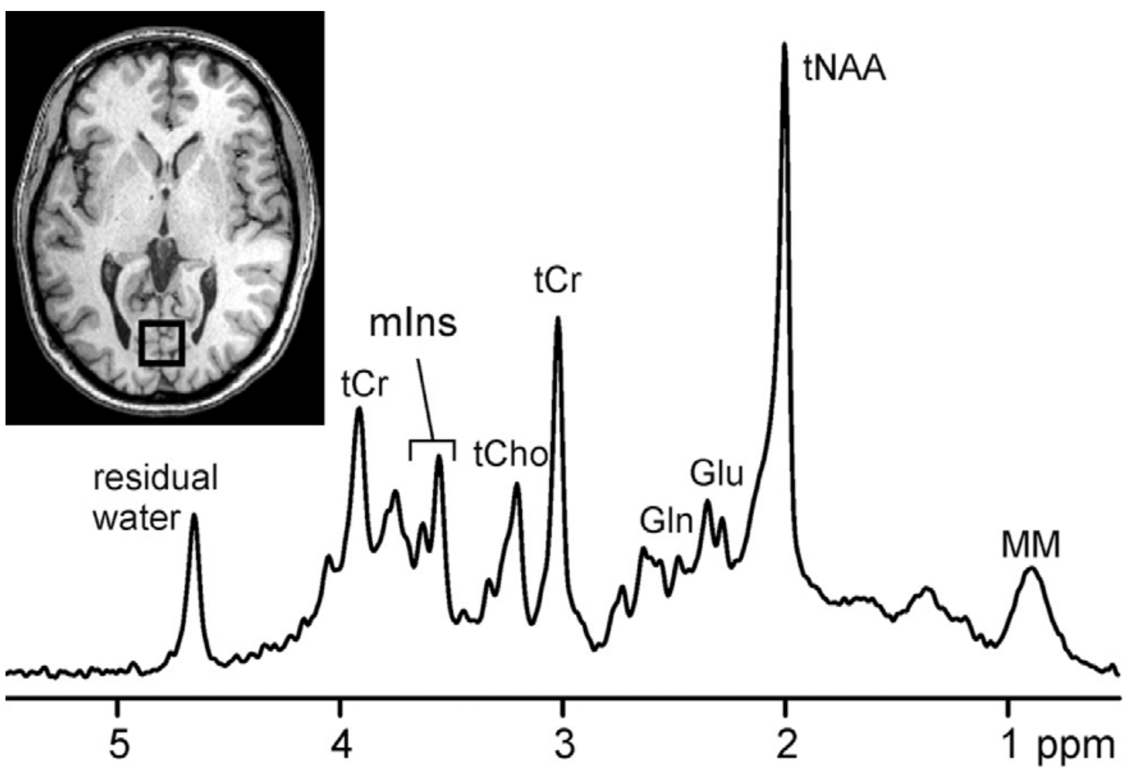


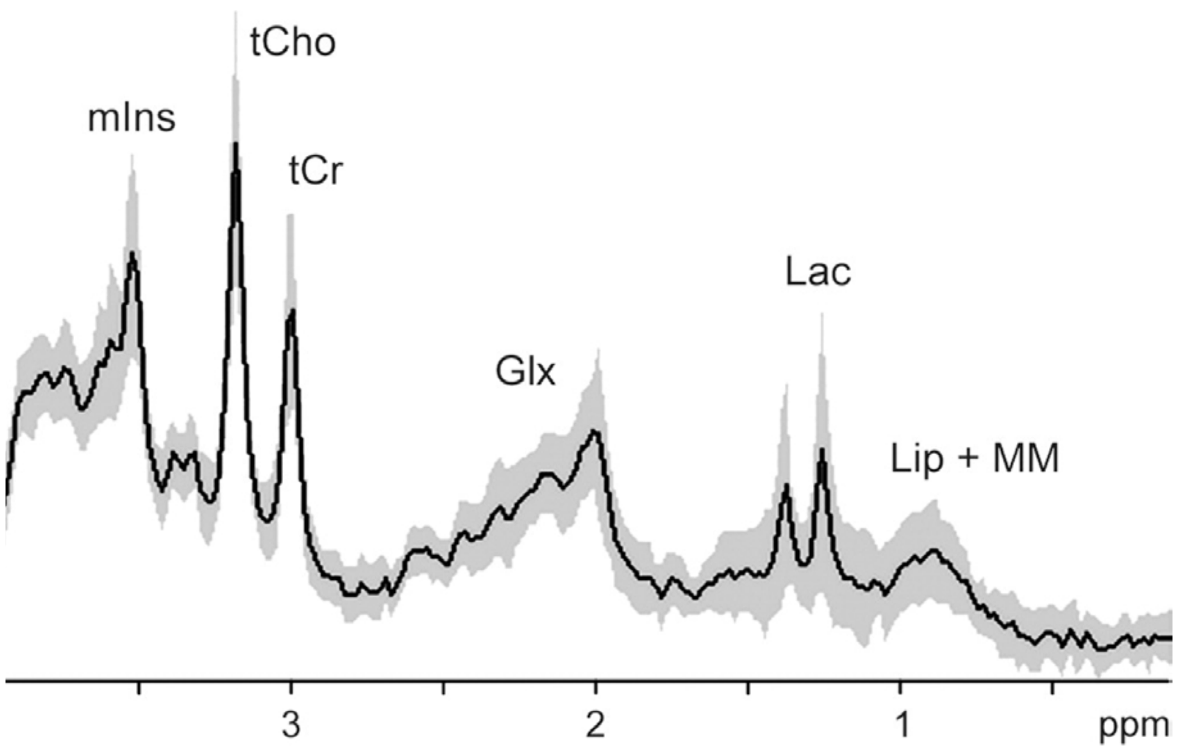

**Glutamate and glutamine (Glx)**

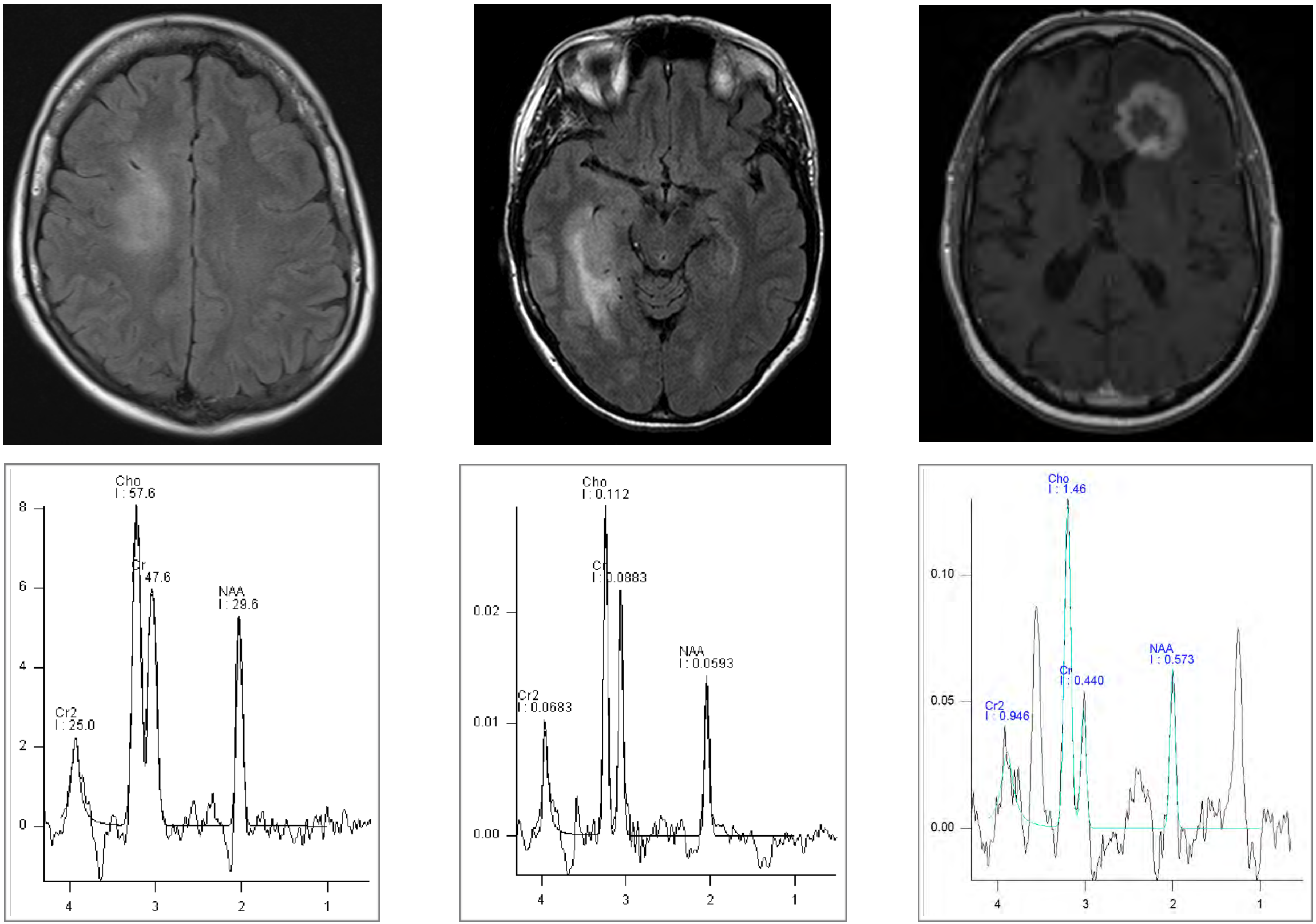
Glu is the most abundant amino acid in the brain. Astrocytes convert Glu to Gln. Glu-Gln cycle consumes 80-90% of the total cortical glucose usage.

**GABA, GSH, Glc**

# Neurooncology–baseline diagnostics

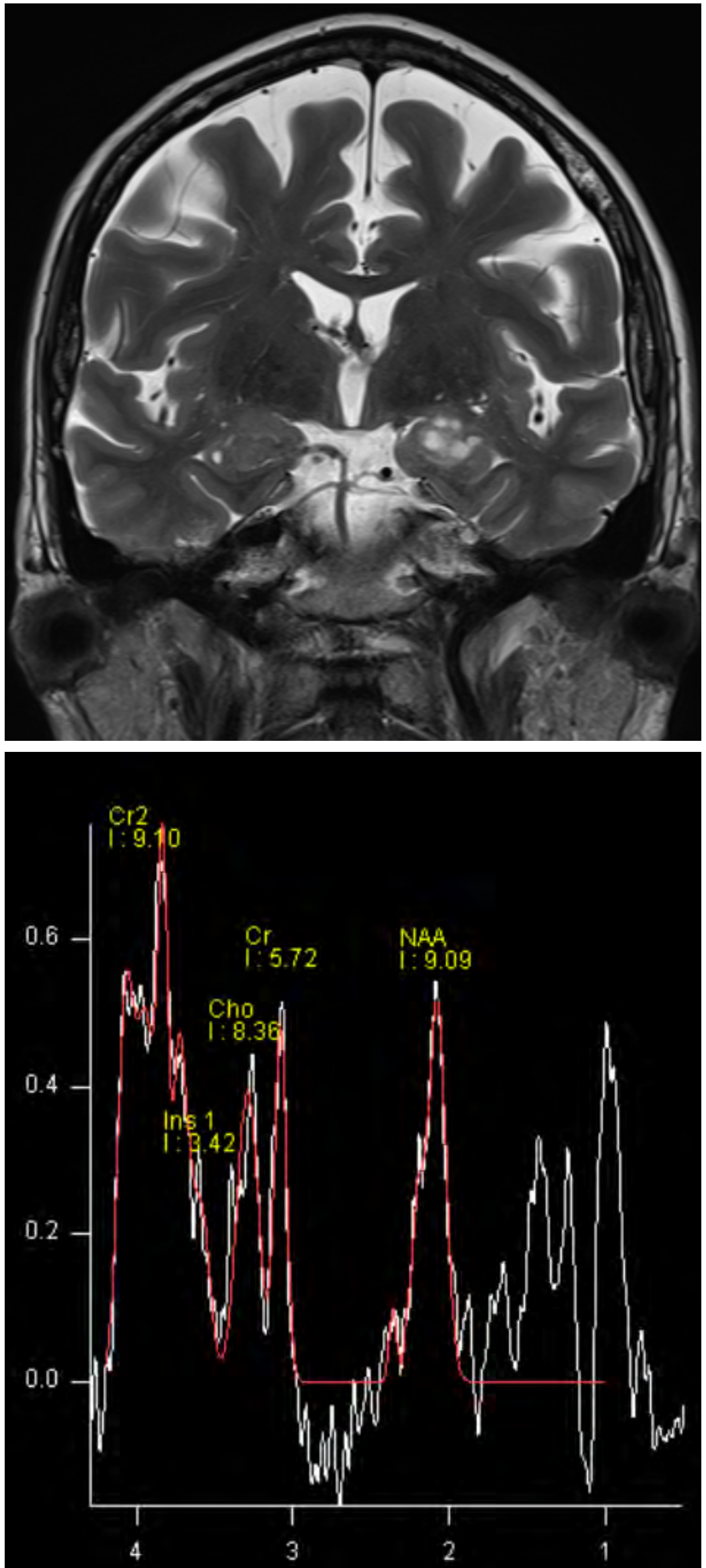


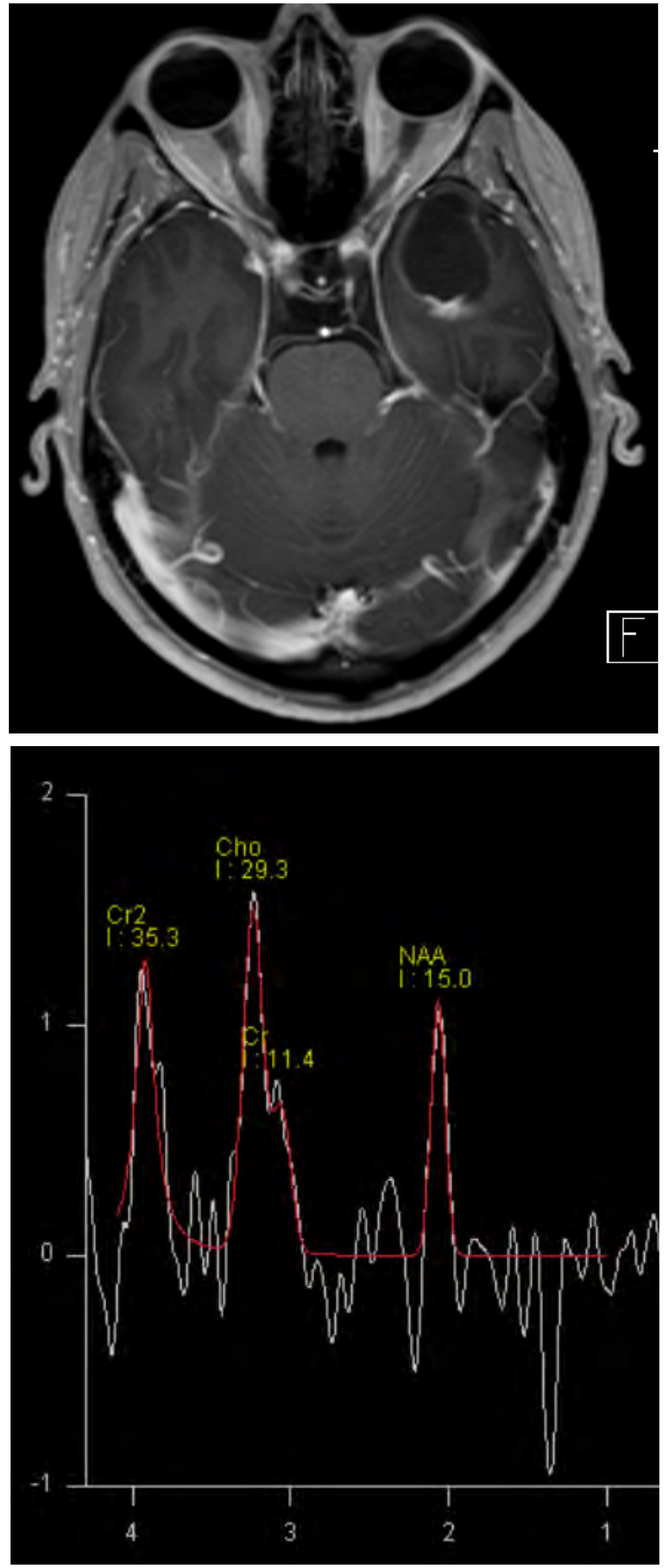


Cho
I : 57.6
Cr
47.6
NAA
I : 29.6
Cr2
I : 25.0
8
6
4
2
0
4
3
2
1
Cho
I : 0.112
Cr
I : 0.0883
NAA
I : 0.0593
Cr2
I : 0.0683
0.02
0.01
0.00
4
3
2
1
Cho
I : 1.46
Cr
I : 0.440
NAA
I : 0.573
Cr2
I : 0.946
0.10
0.05
0.00
4
3
2
1

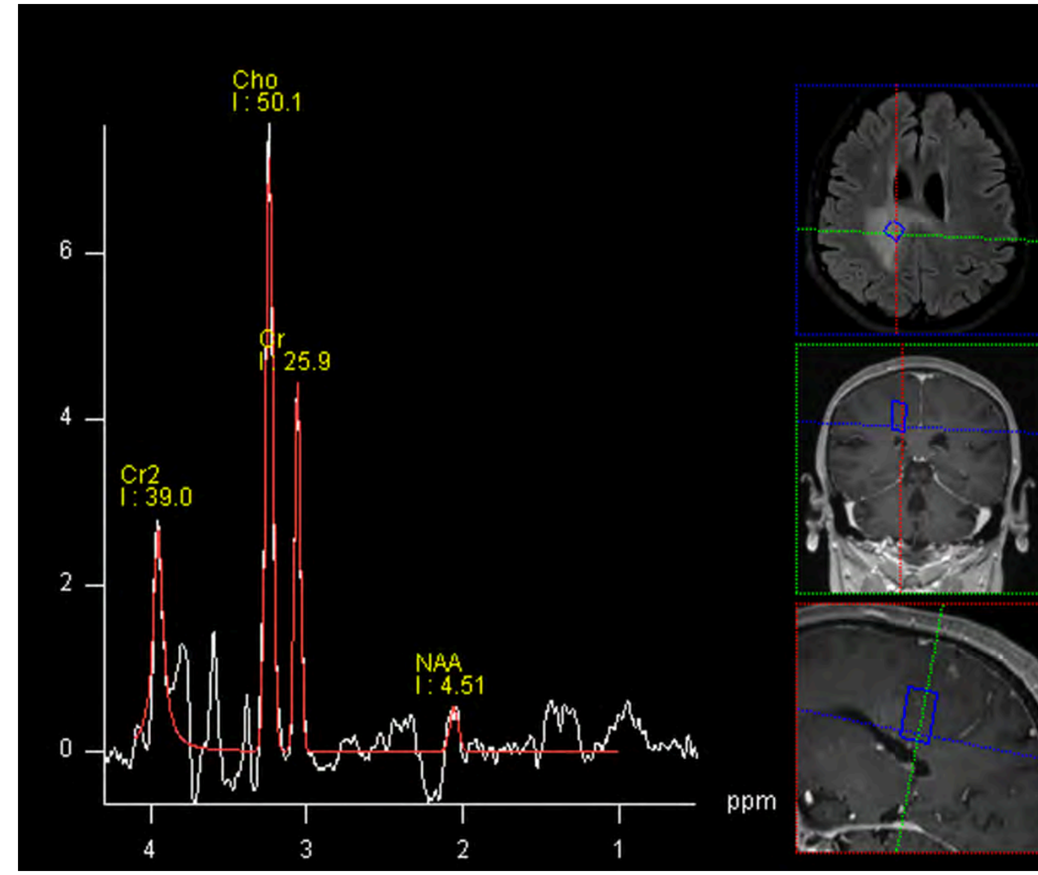
DNET



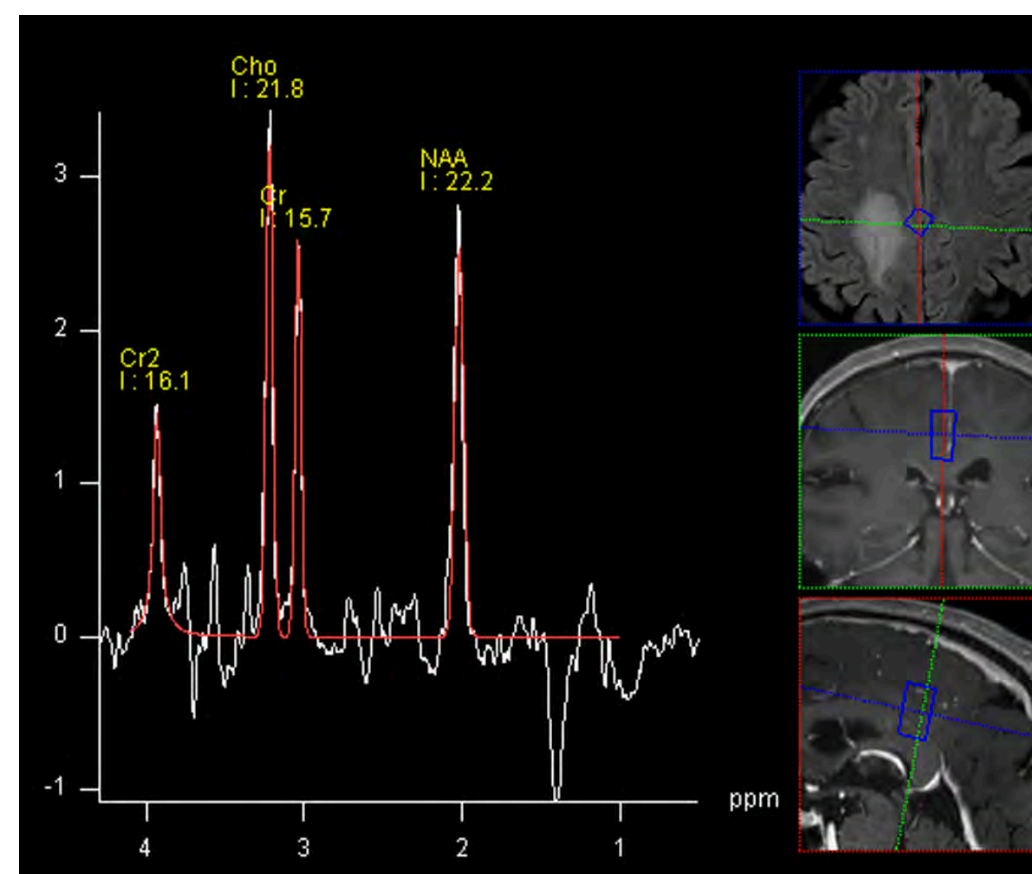

Pilocytic astrocytoma



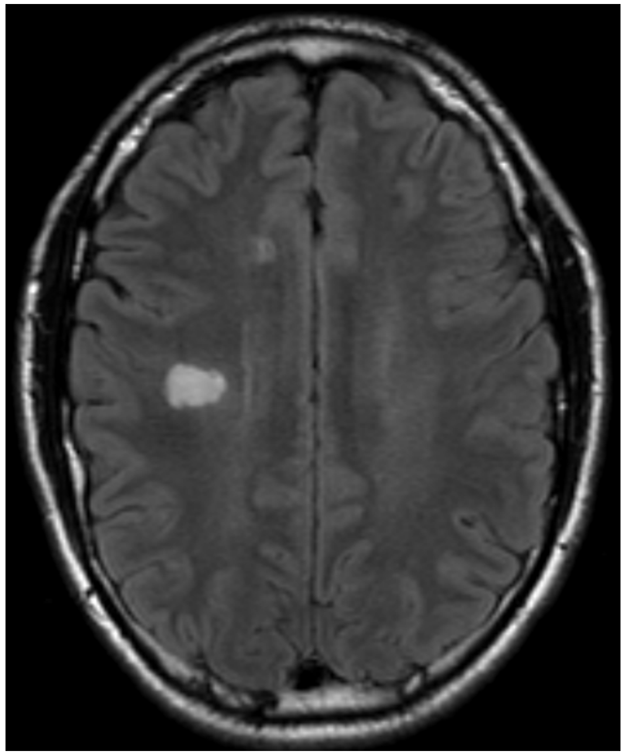

Tumour zone

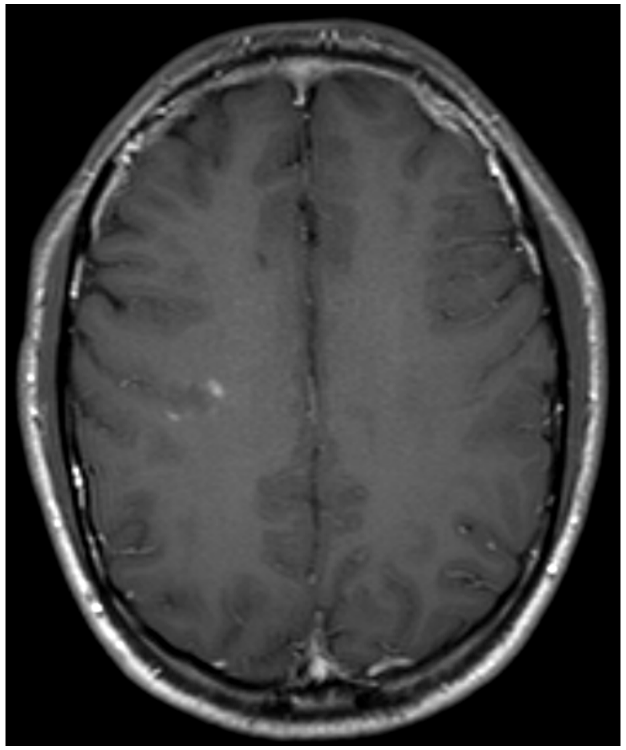


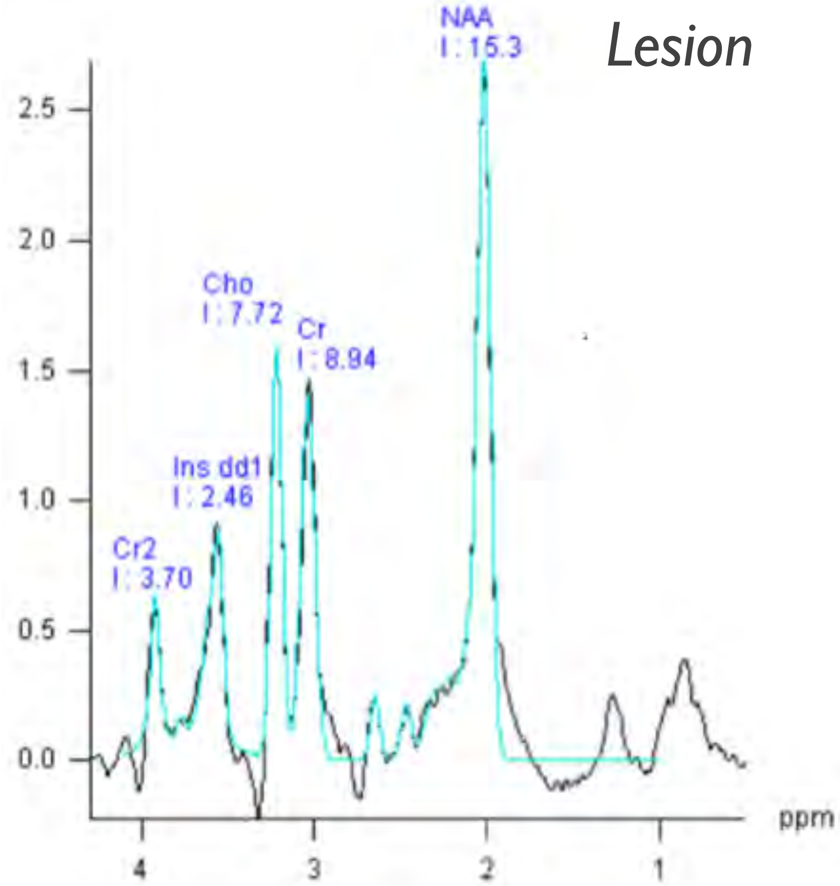

Infiltration zone

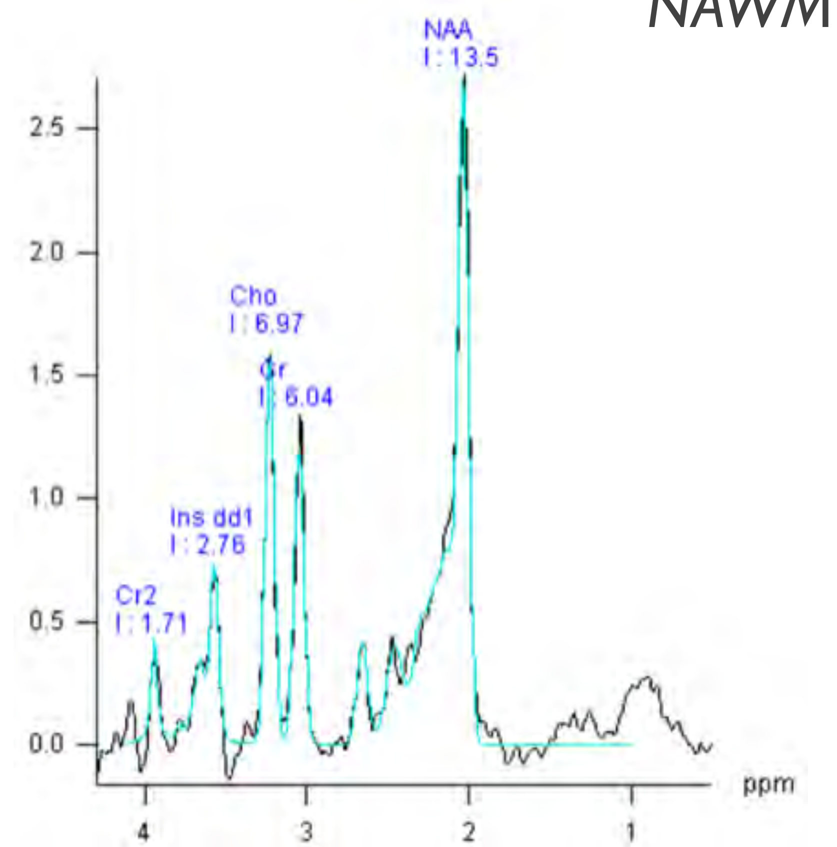


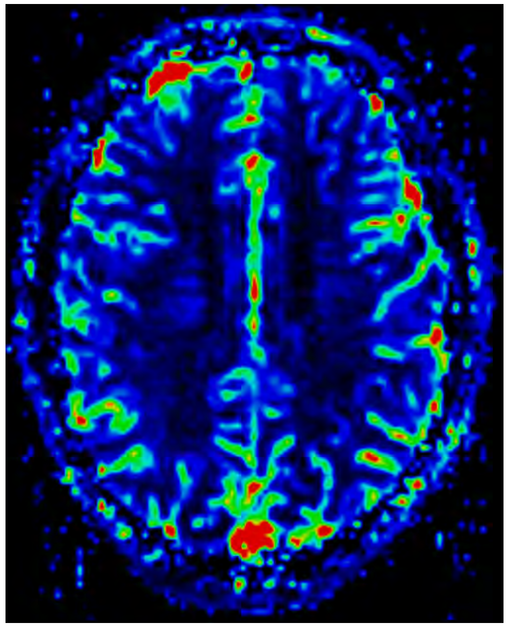
# Neurooncology – differential diagnosis





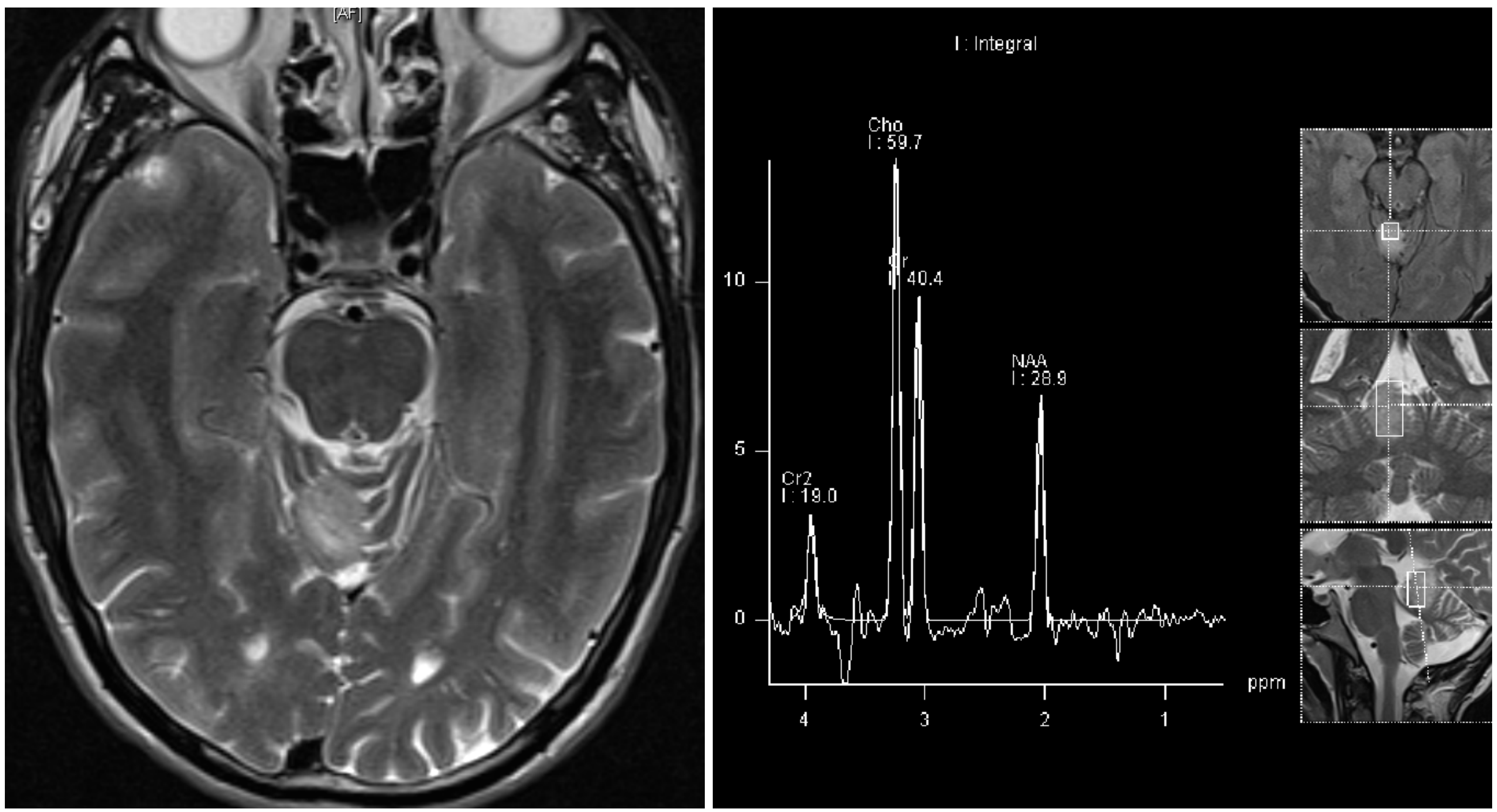


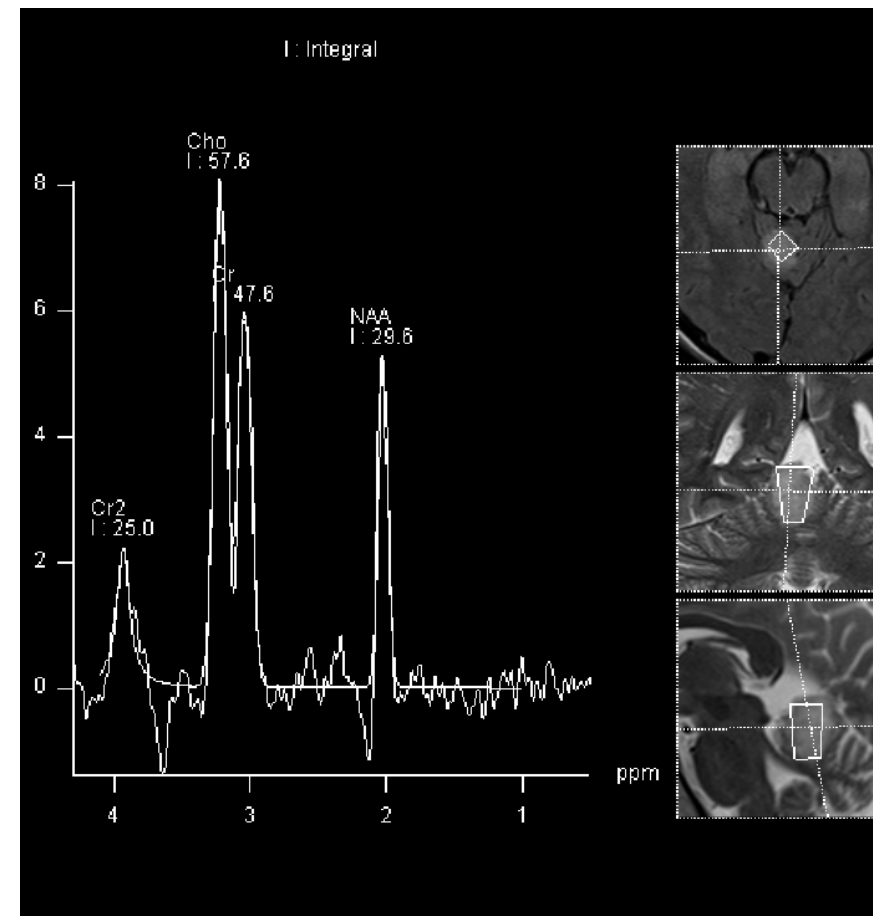



*rCBV*

# Neurooncology – surveillance diagnostics



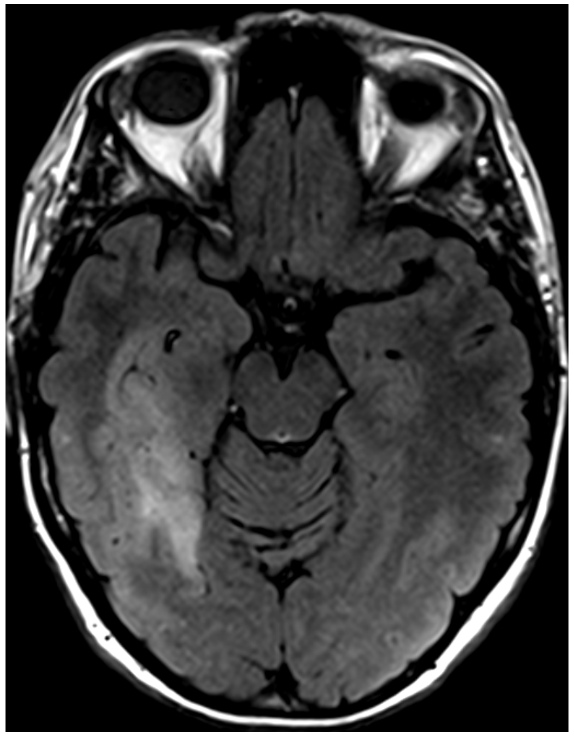

Baseline

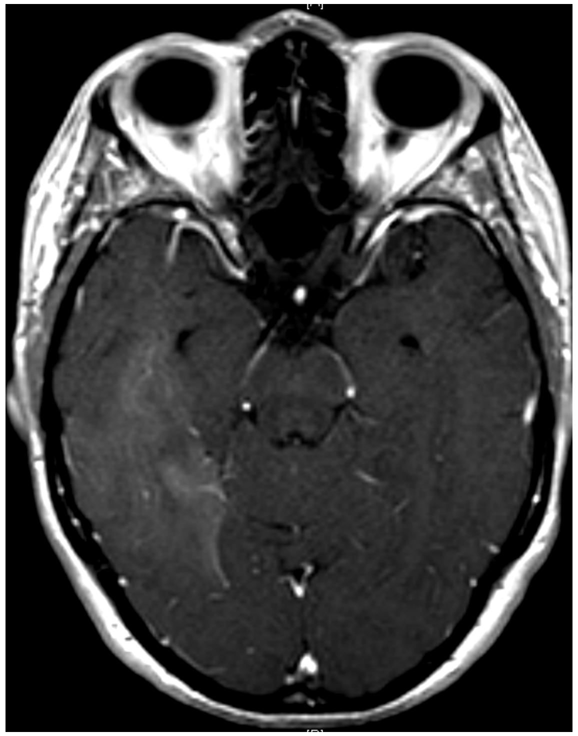


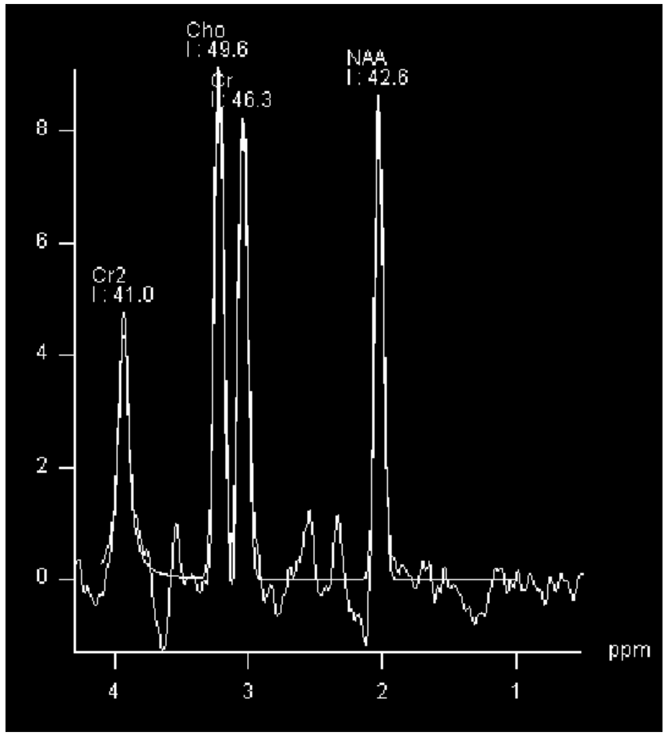

@ 6 months

# Neurooncology – surveillance diagnostics

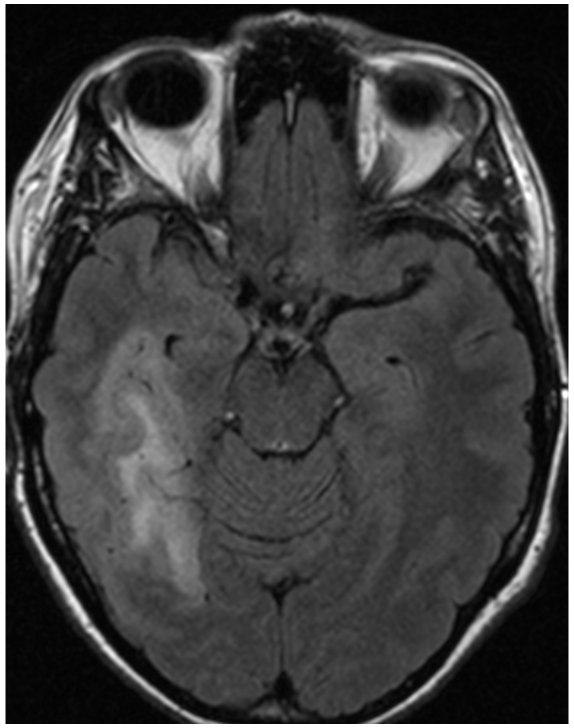
Baseline

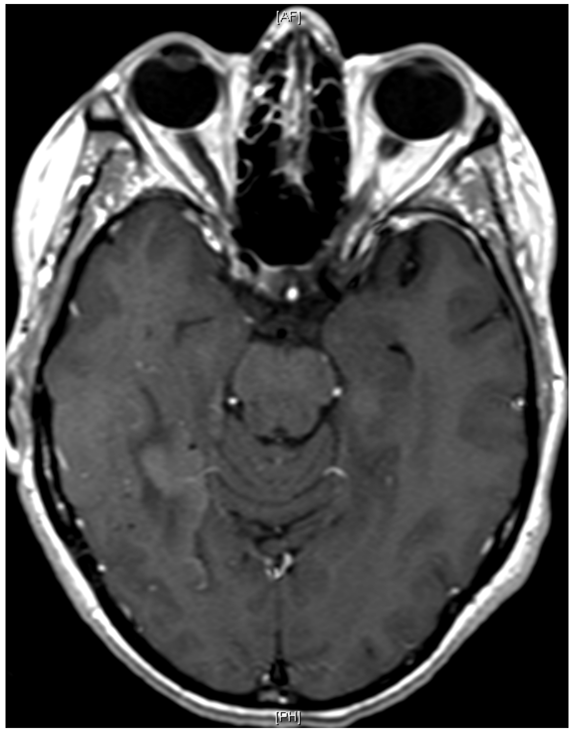


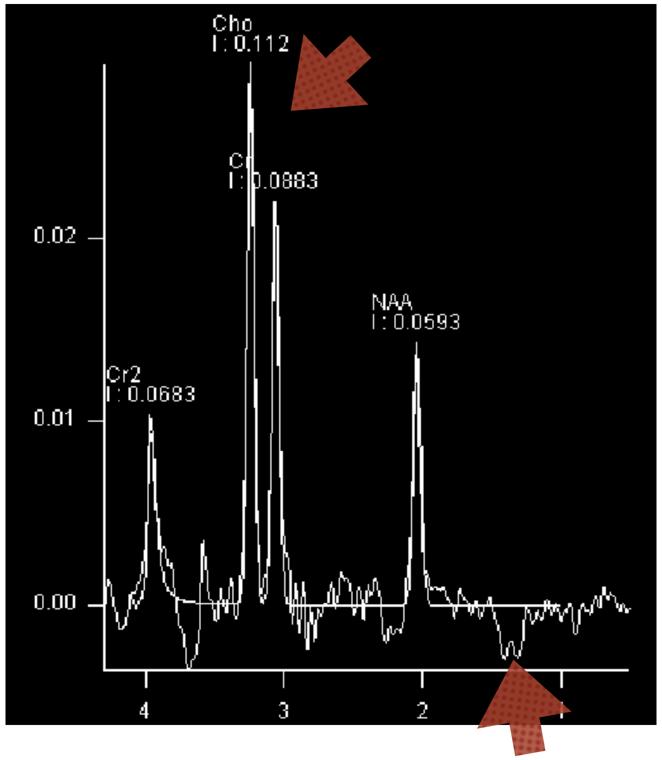




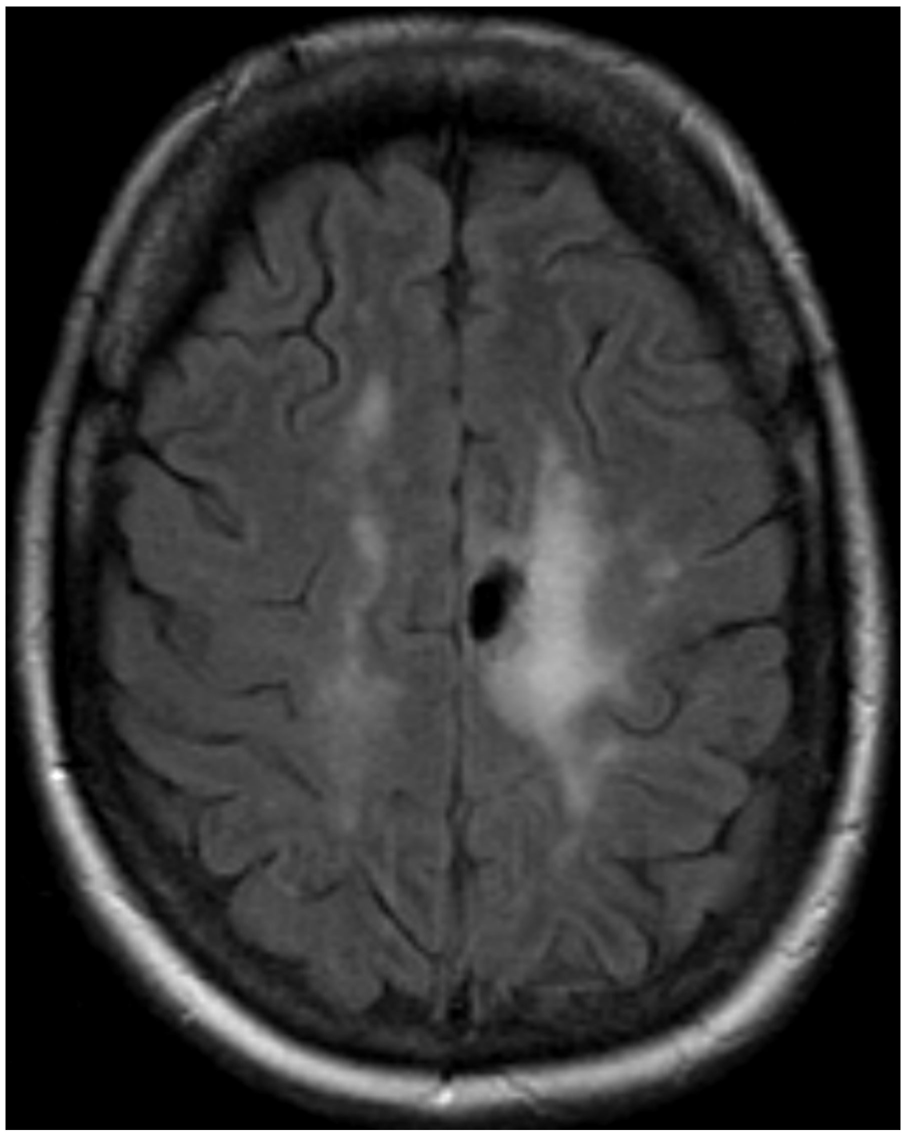

@ 3 months

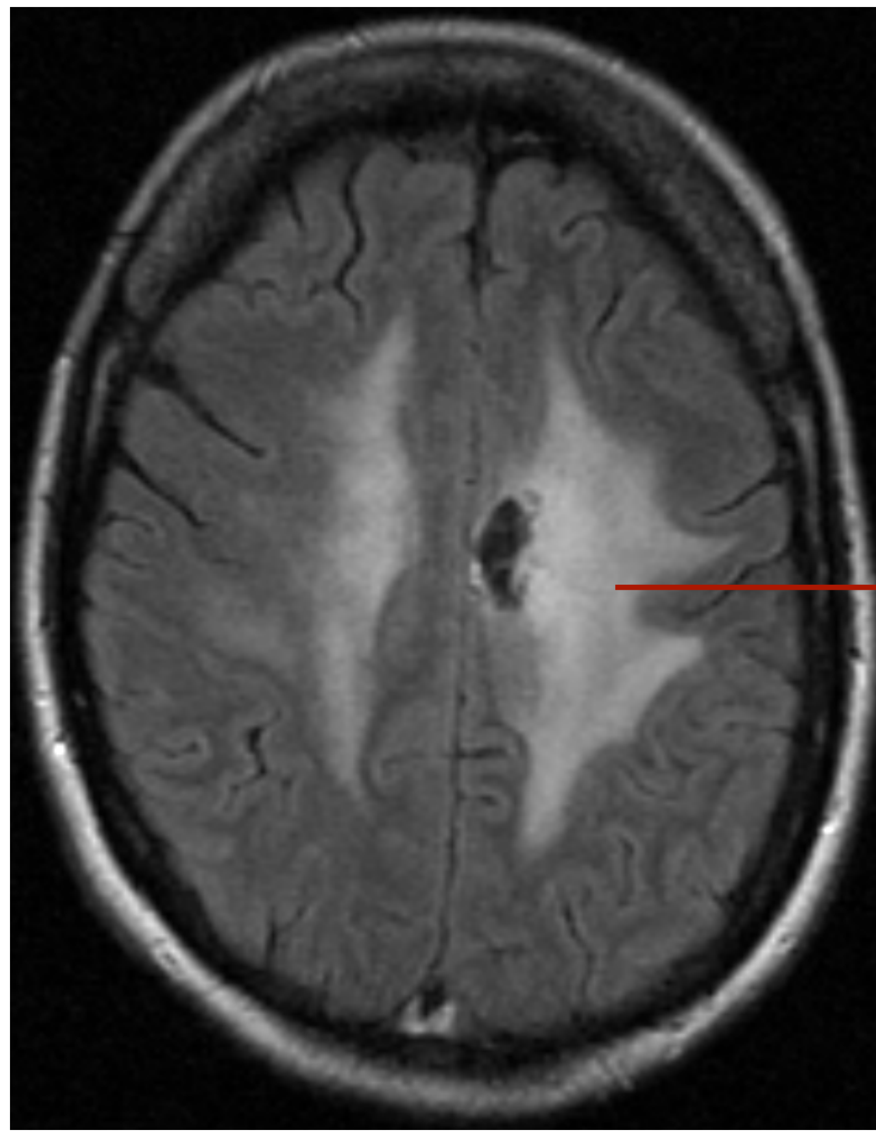


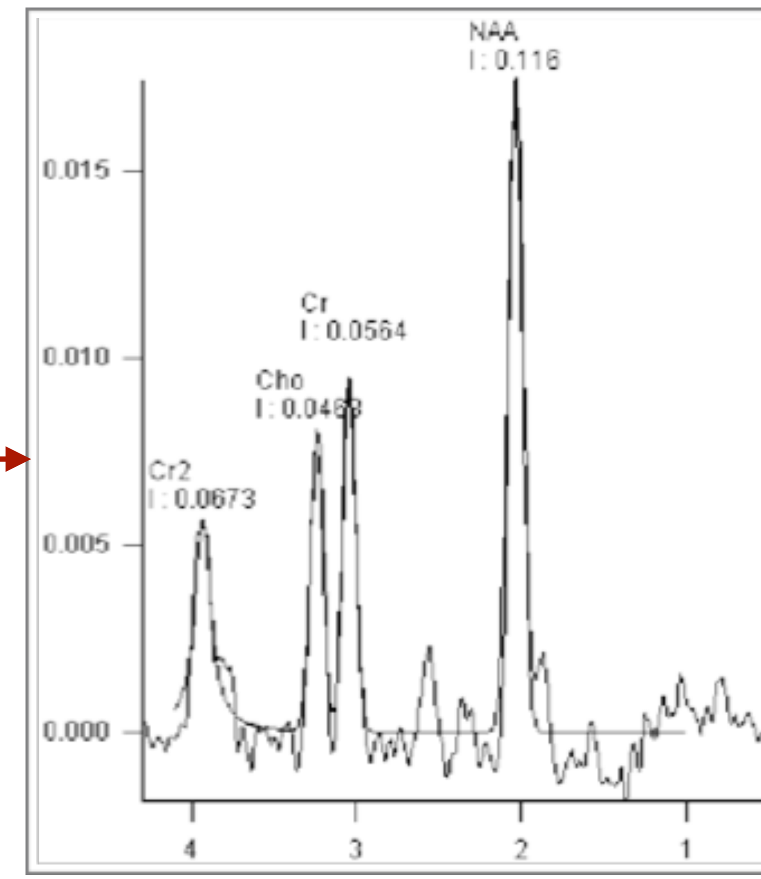




# Neurooncology – surveillance diagnostics
# pseudoprogression

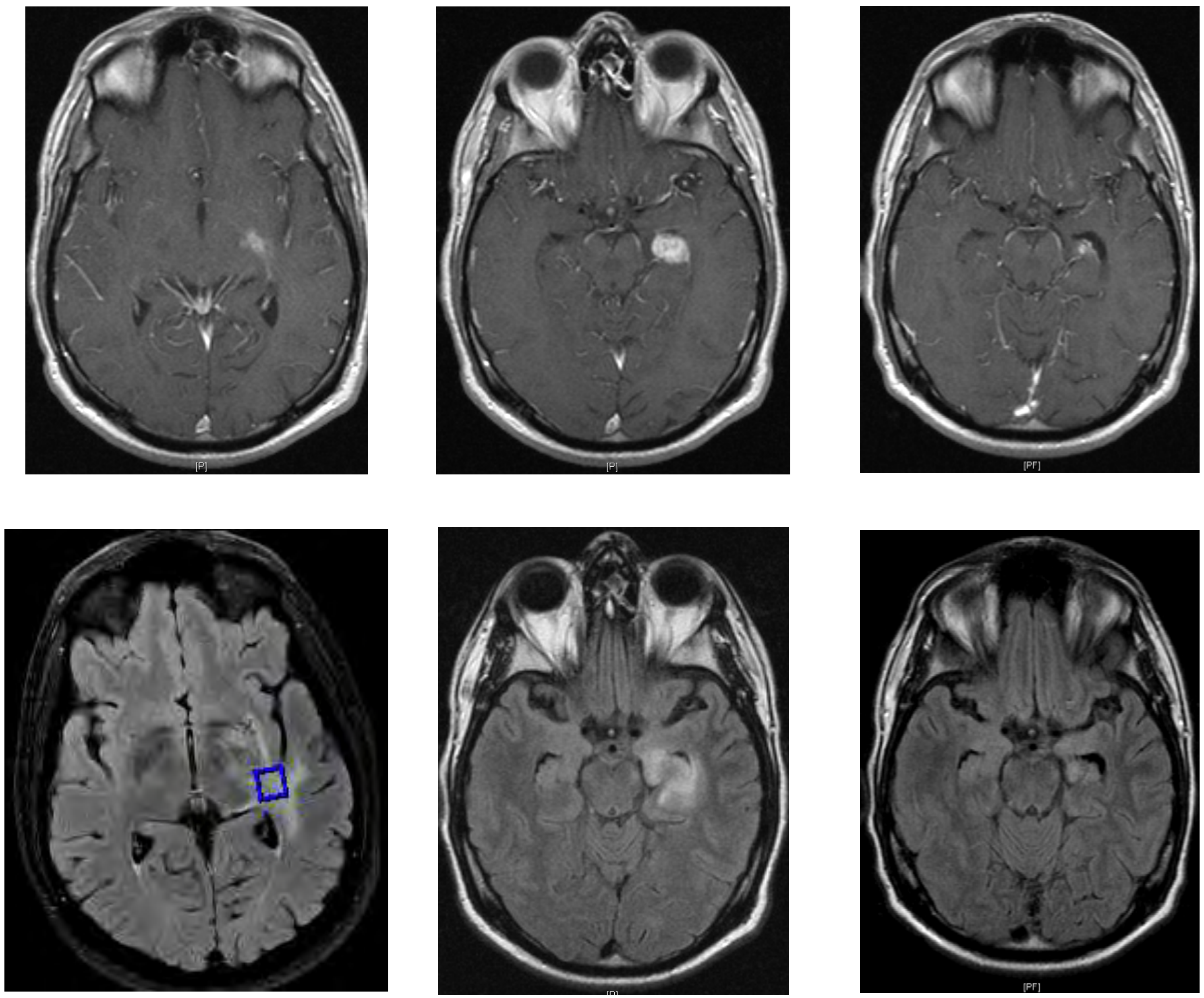


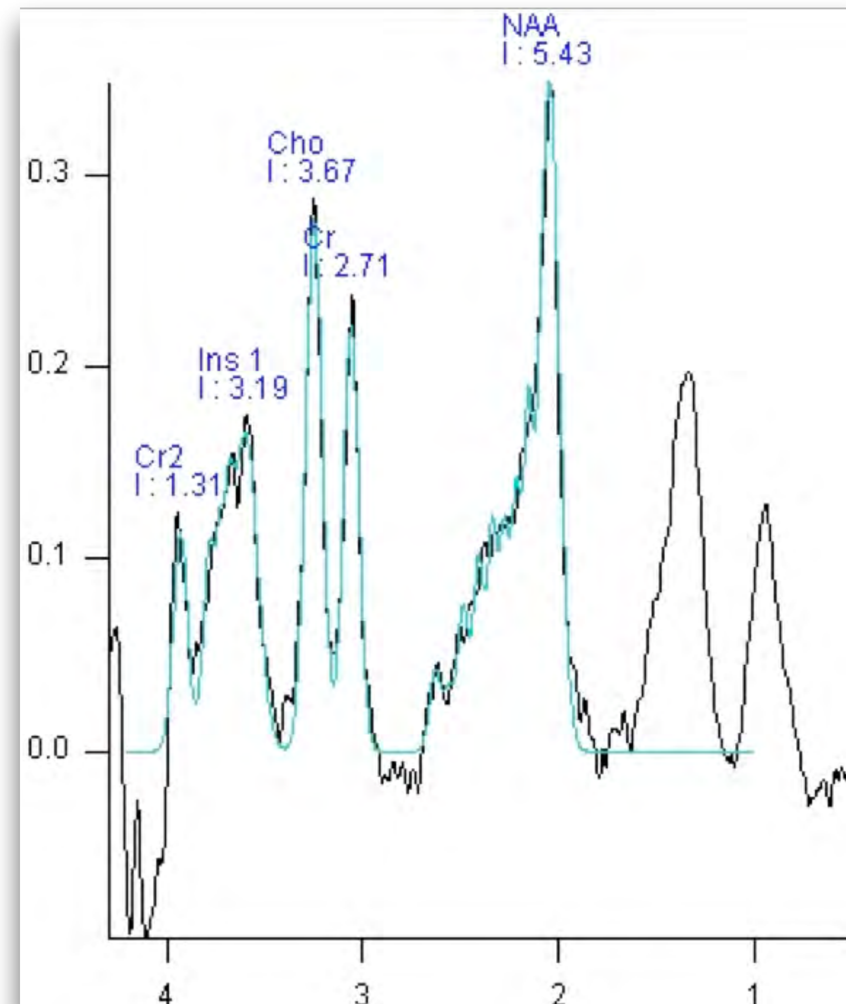





6 months after combined chemoradiation

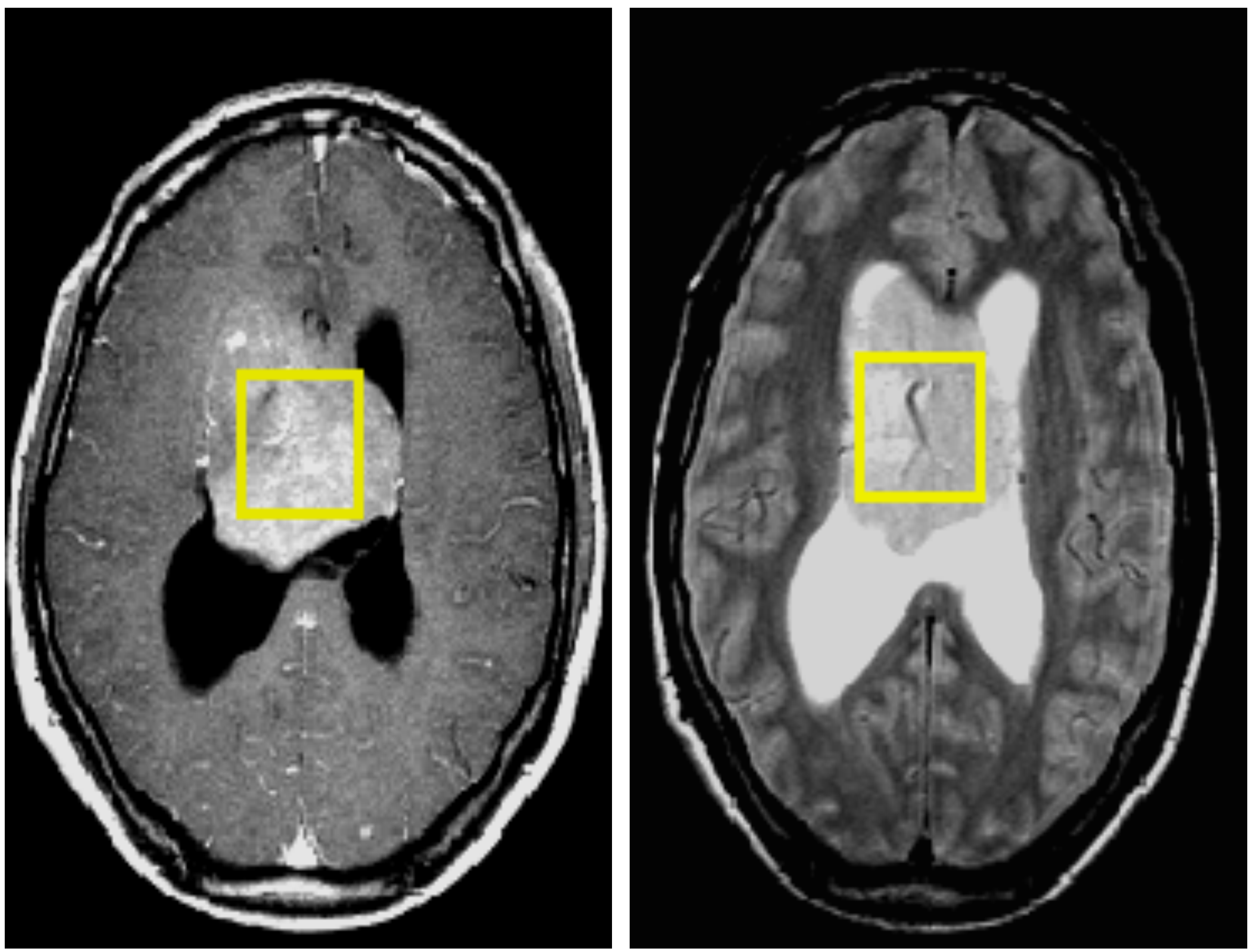
# Neurooncology – surveillance diagnostics radionecrosis

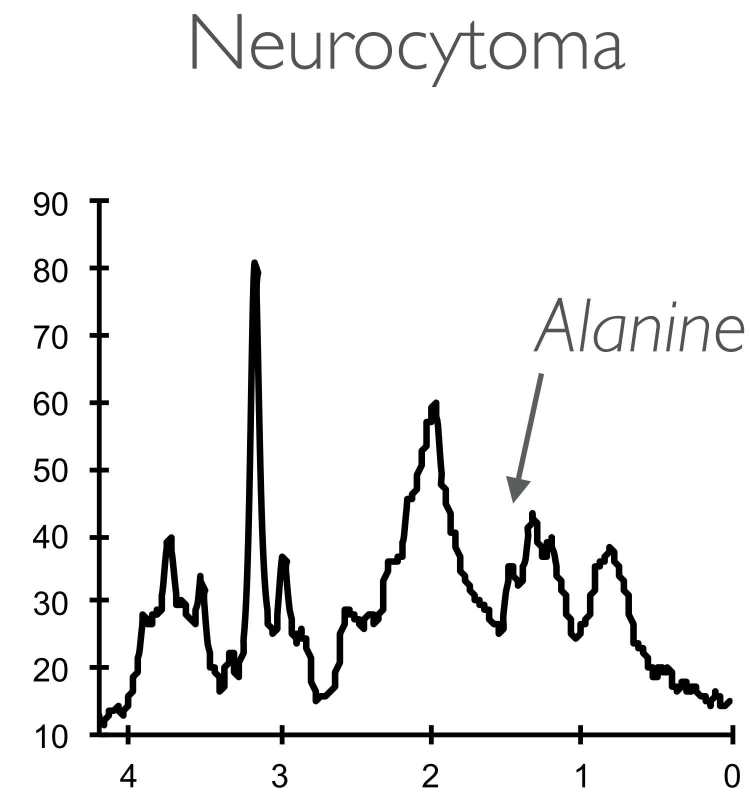




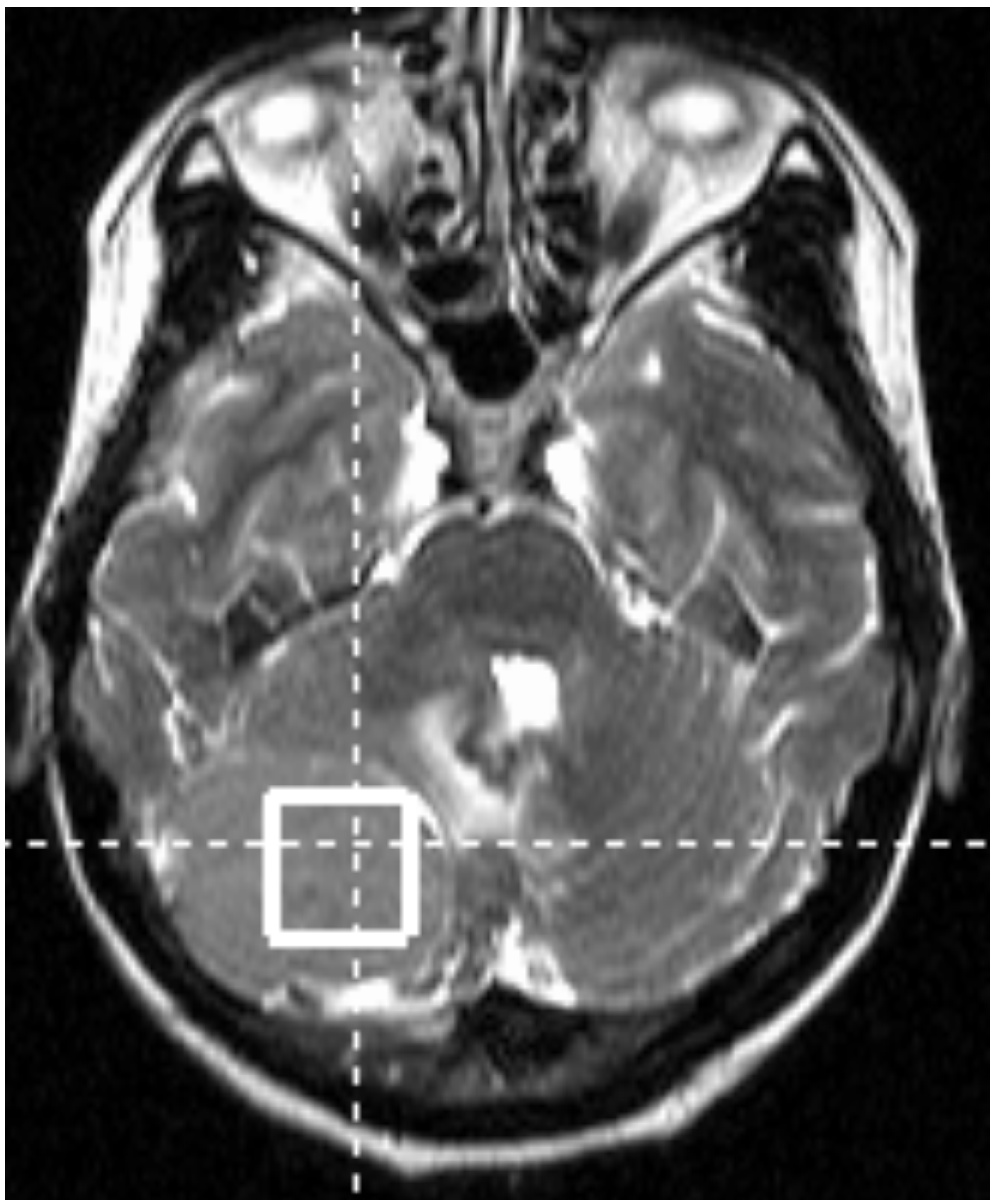

Baseline | @ 6 months | @ 18 months

# Oncometabolites

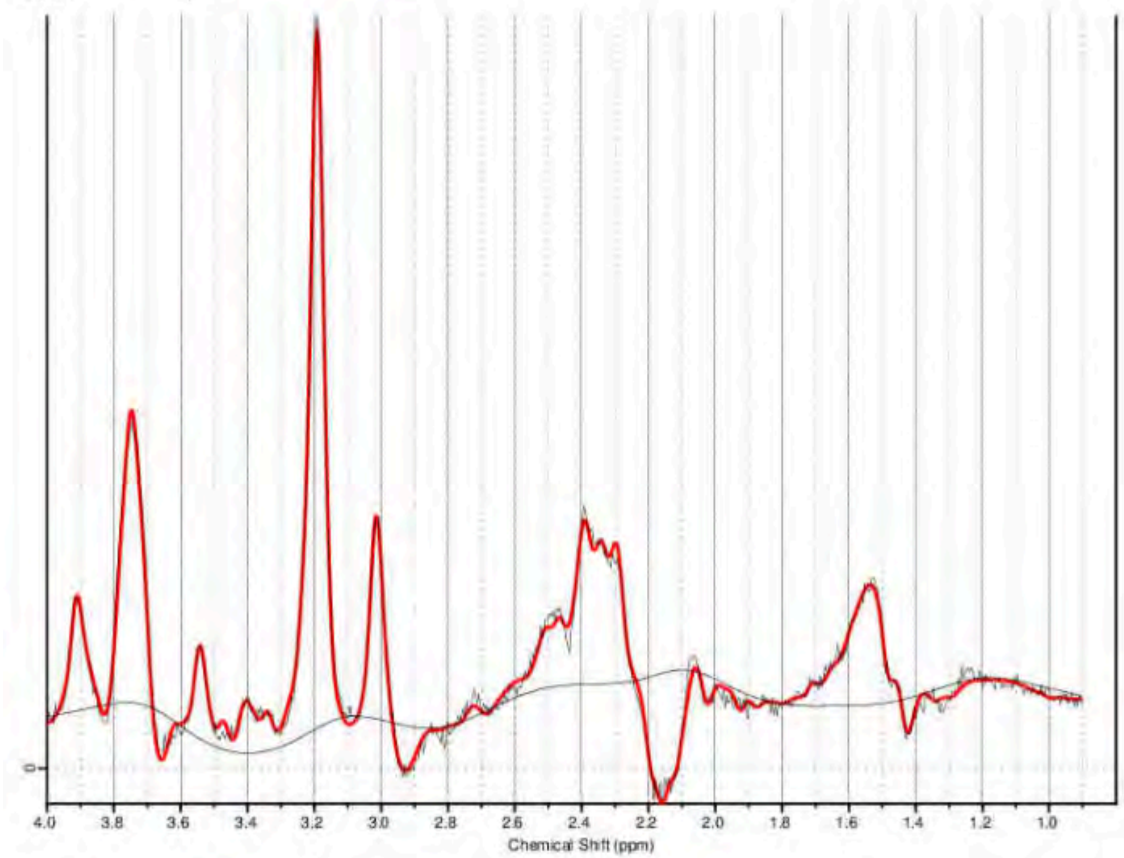




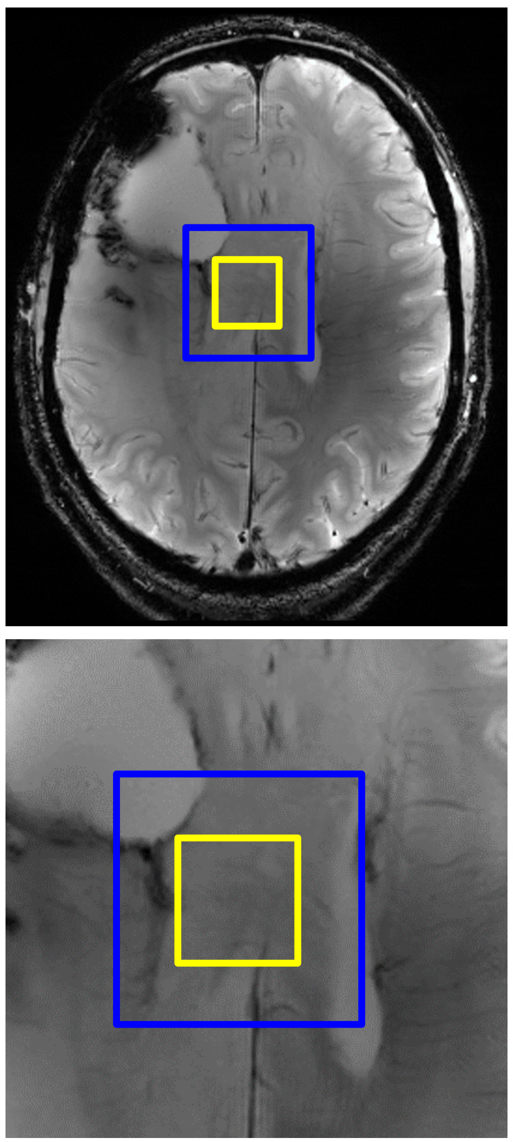
# Oncometabolites

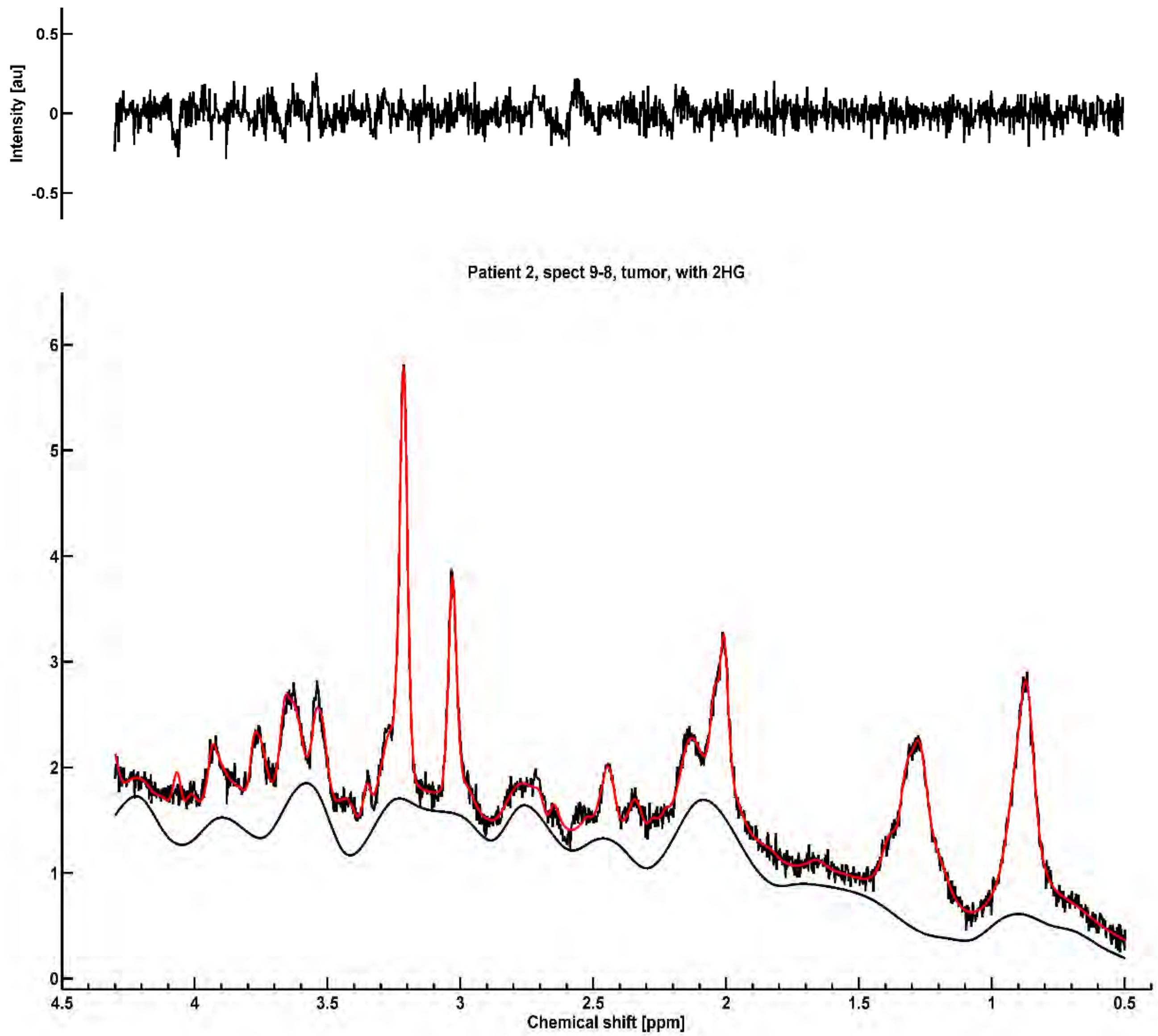


| | %CR |
|---|---|
| Ala | 10 (→ "Hauptsignal": Negatives Doublet bei 1,46 ppm) |
| Gln | 5 |
| Glu | 3 |
| GSH | 6 |
| Lac | 38 |
| Total NAA | 24 |
| Total Cr | 3 |
| Total Cho | 2 |
| Lip15 | 4 |



# Oncometabolites

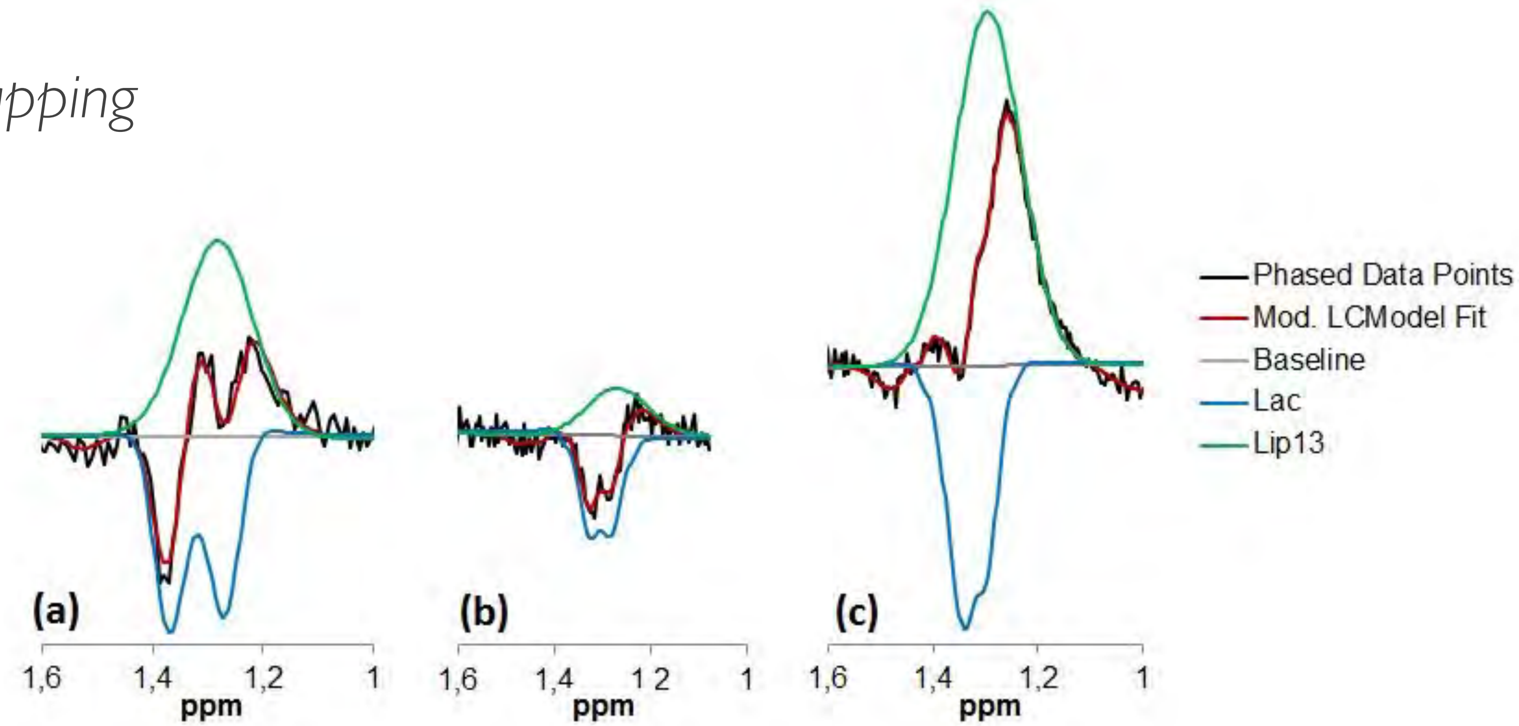


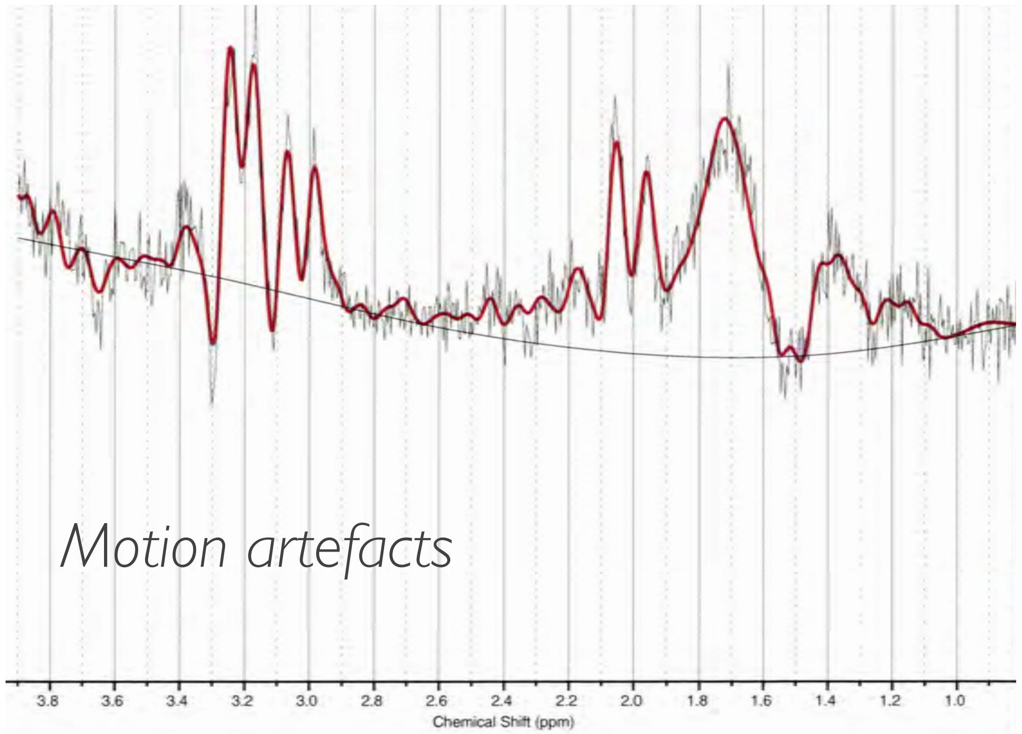



| | Conc [au] | CRLB [%] |
|---|---|---|
| **2HG** | 0.357↑ | 14% |
| **Asp** | — | — |
| **GABA** | 0.149↑ | 21% |
| **Gln** | 0.420↑ | 7% |
| **Glu** | 0.198↓ | 20% |
| **GPC** | 0.268↑ | 2% |
| **GSH** | 0.177↑ | 11% |
| **Ins** | 0.508↑ | 5% |
| **Lac** | 0.247↑ | 15% |
| **NAA** | 0.402↓ | 5% |
| **NAAG** | 0.209↓ | 9% |
| **PCr** | 0.611↑ | 11% |
| **Scyllo** | 0.054↑ | 13% |
| **Tau** | 0.251↑ | 12% |

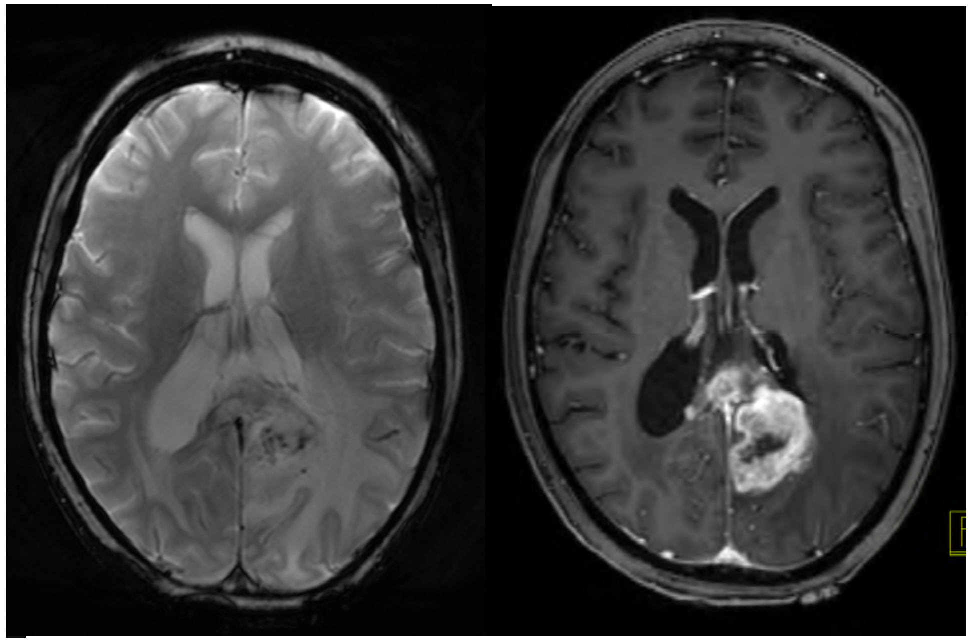
# Caveats

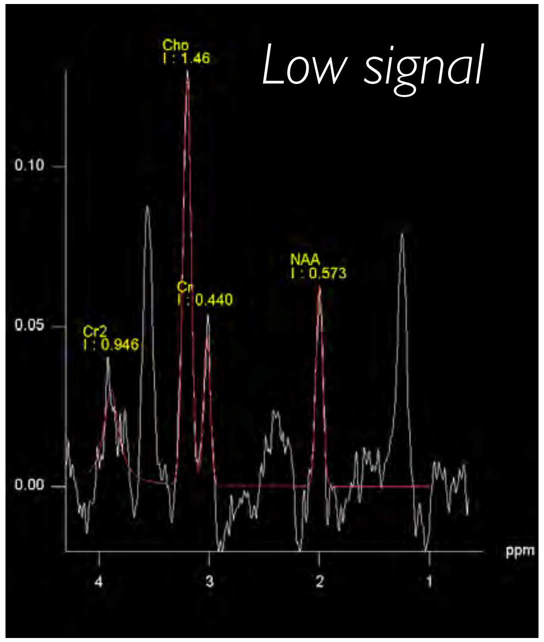
*Lactate lipids overlapping*




*Motion artefacts*






*Low signal*

Baseline brain tumour (meningiomas, low-grade glioma, GBM, metastases) staging accuracy: 90%
GBM versus metastasis accuracy: 78%
Combining short and long TE MRS diagnostic accuracy: 98% for the main childhood brain tumour types (pilocytic astrocytoma, medulloblastoma, and ependymoma)

Öz et al. Radiology 2014

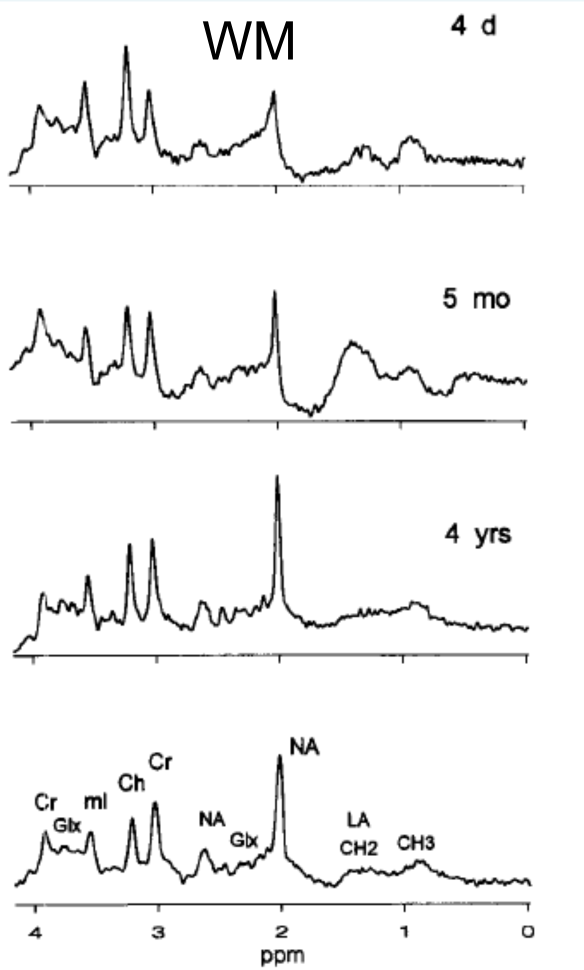
MRS accuracy for differentiation of tumour relapse from unspecific changes: 63%
Combined with perfusion MRI accuracy increases to 90%

Seeger, …Bisdas. Acad Radiol 2014

**CAVEAT**

Pilocytic astrocytomas often present with spectra similar to those of high-grade tumours.
Be sure for the spectrum quality before utilising it for diagnosis.

# MRS in paediatric neuroimaging




Kreis R et al. Magn Reson Med, 1993

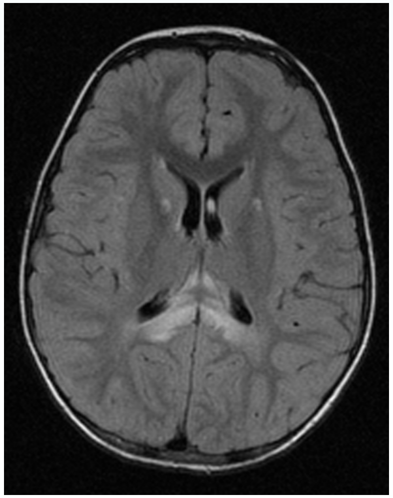
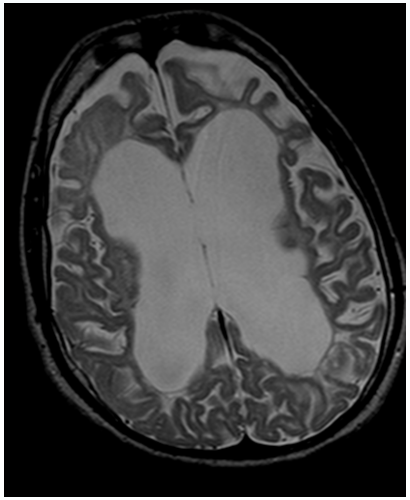
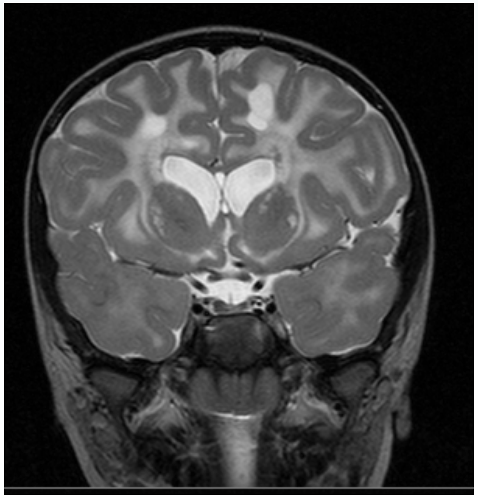
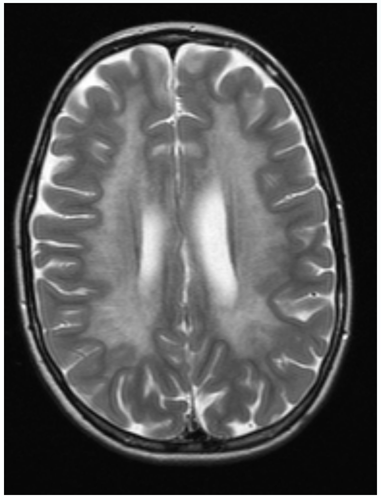
- Metabolite levels are age dependent.
- Normal levels reached around:
  - Choline – 4-5 y
  - NAA – 3-5 y
  - Myo-In – 1.5-2 y
  - Creatine – 1-1.5 y
- Most noteable changes within 1st y

# Leucoencephalopathies

For the age of the child not appropriate myelination seen as T2 hyperintense white matter changes.

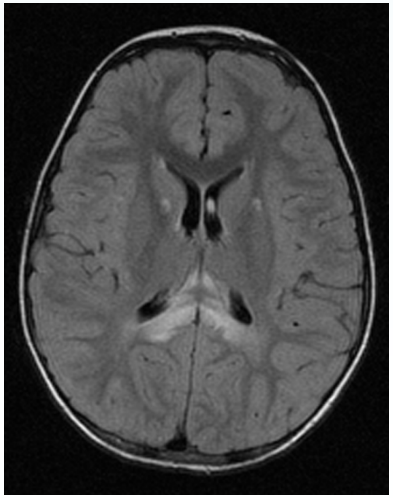
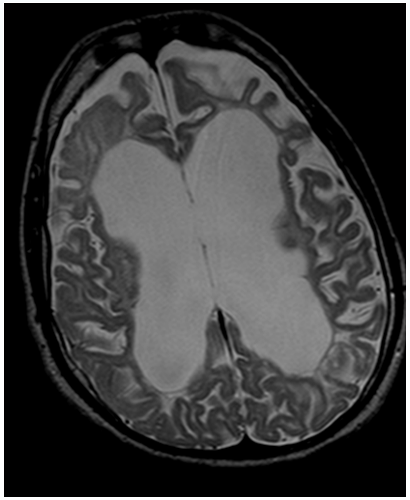
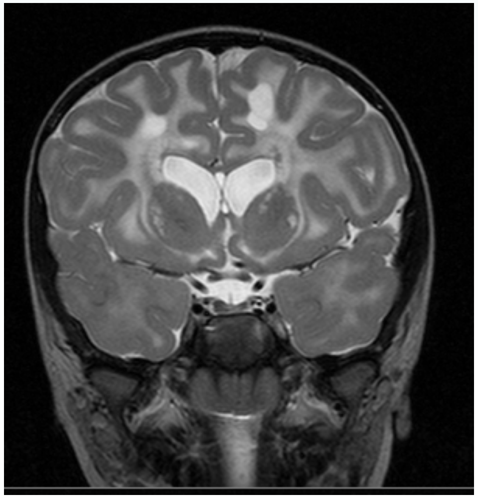
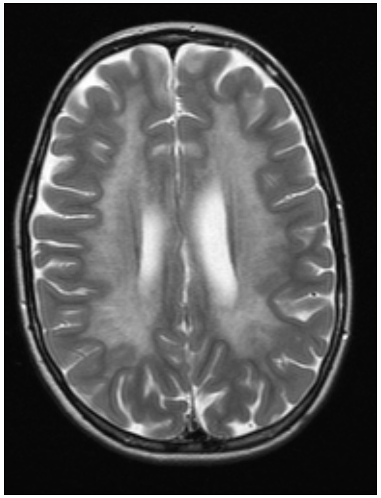
In some diseases the leucoencephalopathy distribution pattern is almost pathognomonic

**Different causes:** Hypomyelination, demyelination, tissue rarefication

# Leucoencephalopathies

- Hypomyelination
  - Relatively normal metabolite levels, usually no Lac and normal NAA
- Demyelination
  - **Cho increase, Lac increase**, *NAA decrease*
- Tissue rarefication
  - *Decrease of Cho, Cr, NAA*; **Lac increase**

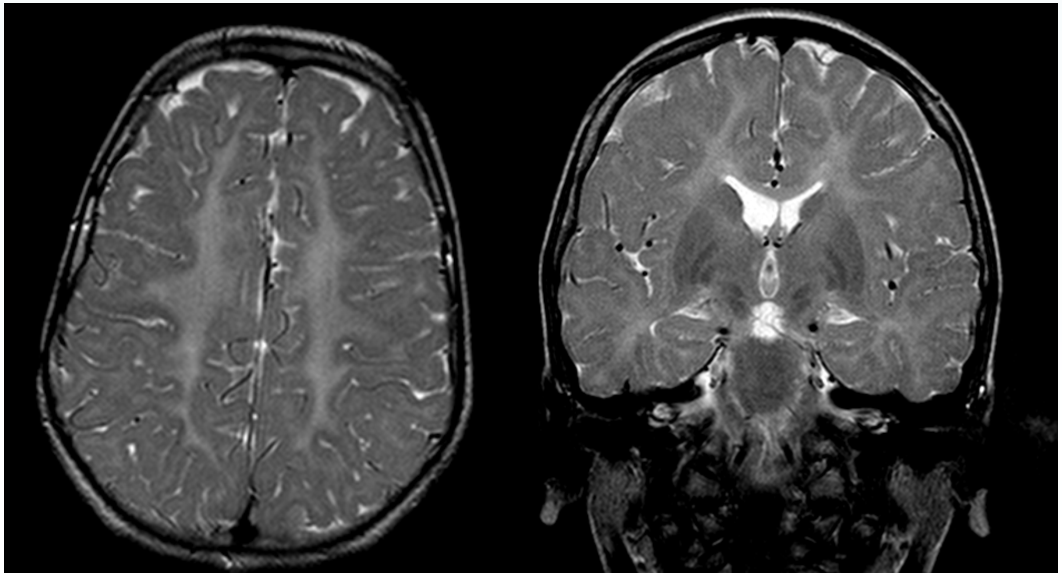





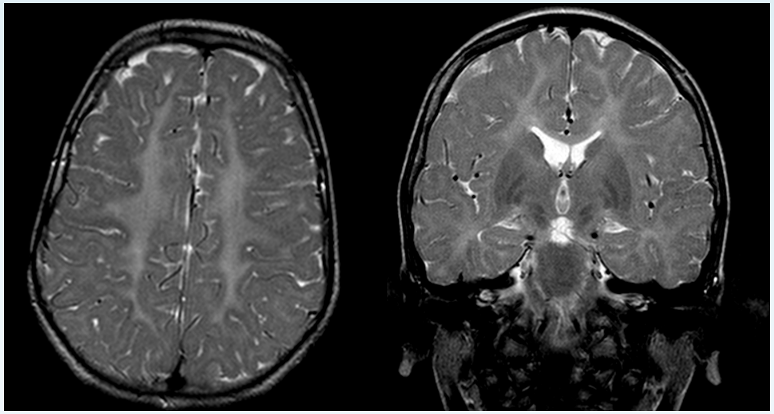
# Hypomyelination

Oligodendrocytes fail to build myelin sheaths

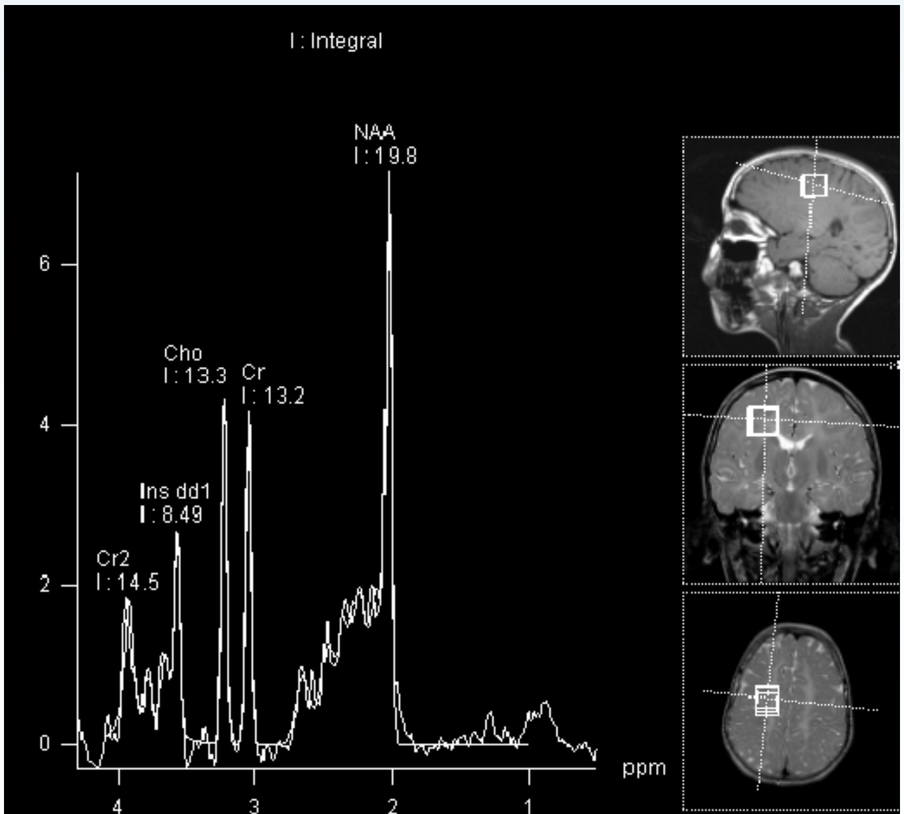
- Delayed myelination
- Pelizaeus-Merzbacher disease and Pelizaeus-Merzbacher like disease
- Jacobsen snydrome (11q-)
- 18q- deletion (18q22.3 q23)

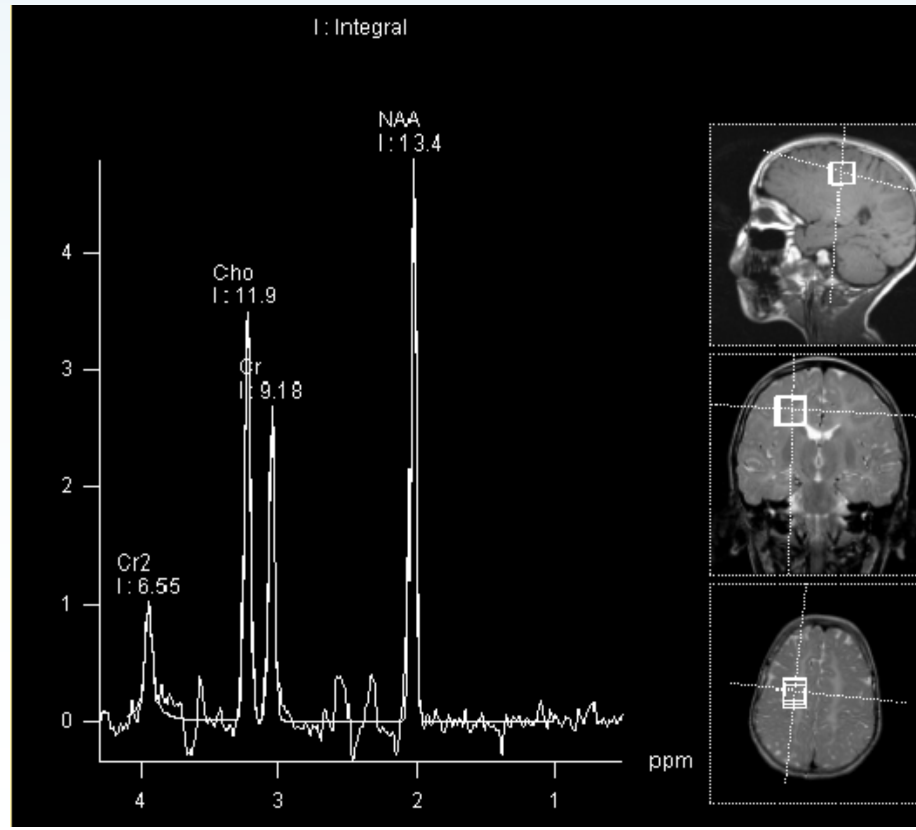
Pelizaeus-Merzbacher disease





Cho: (↑),(↓),↔, NAA: ↔,  Cr: ↔, Ins: (↑)

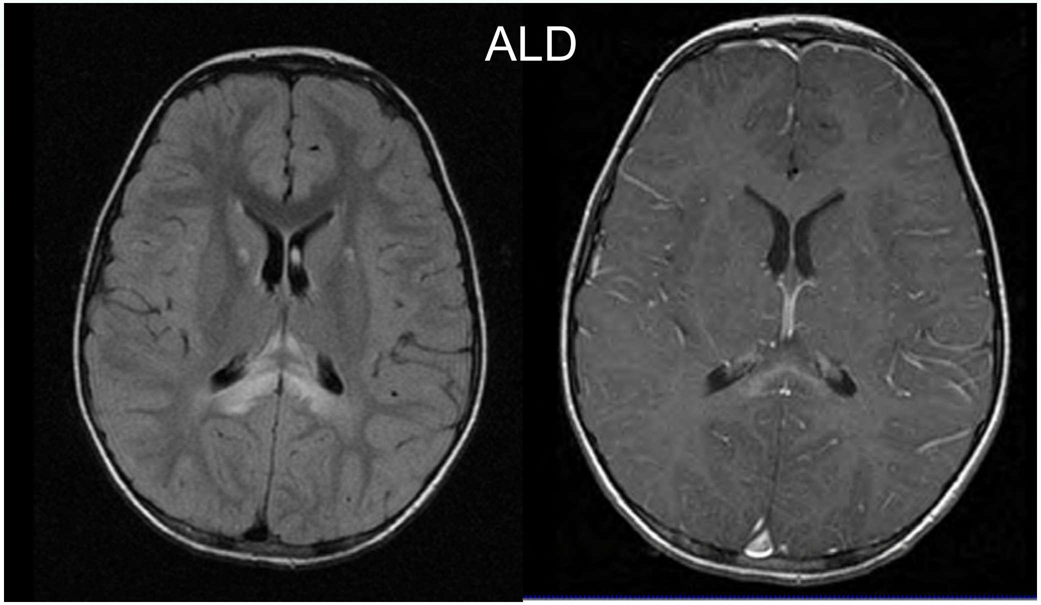


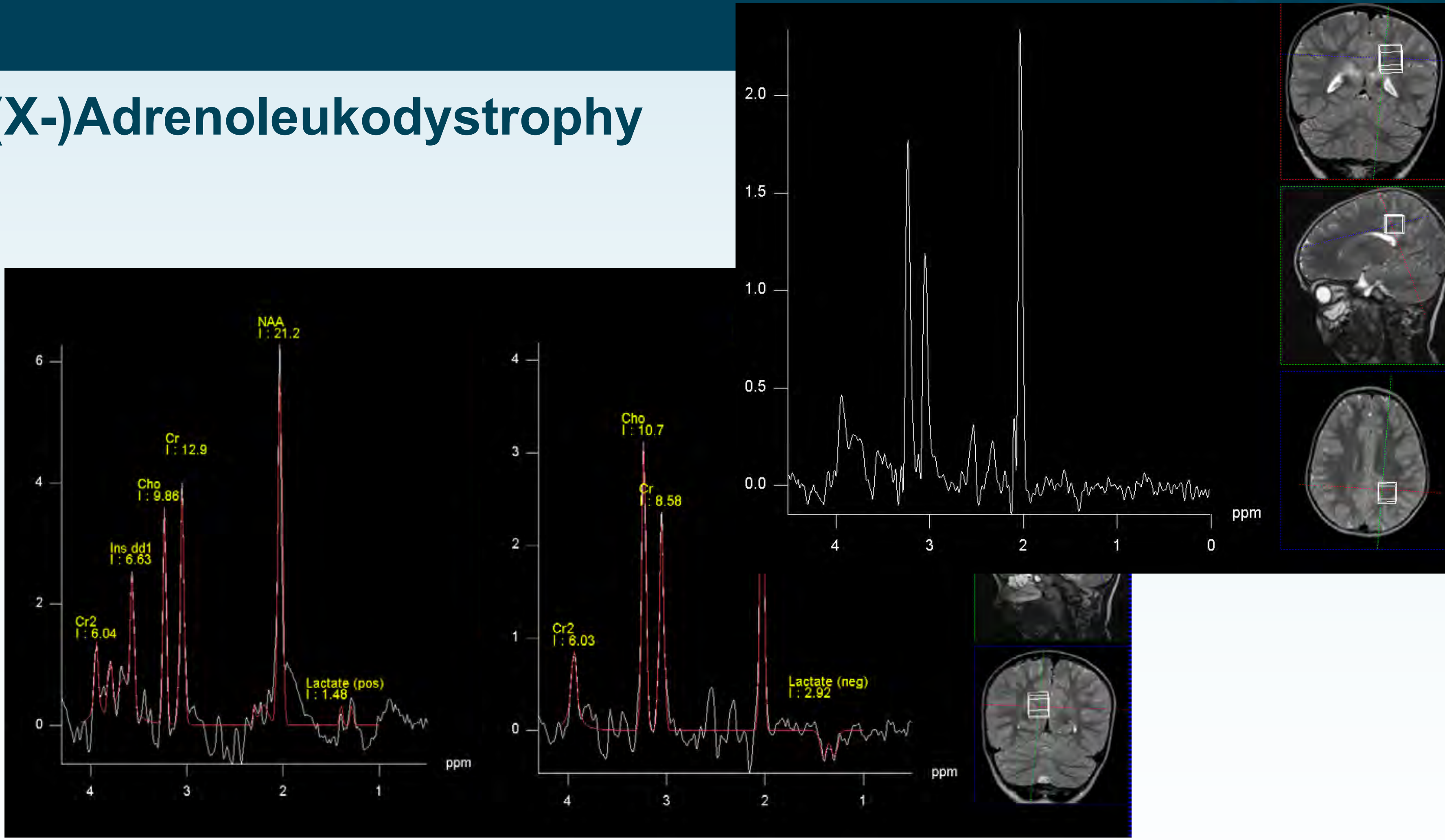
# Demyelination

Active destruction / loss of myelin sheaths → increase in Cho

- Adrenoleukodystrophy (ALD)
- Metachromatic leukodystrophy (MLD)
- Globoid cell leukodystrophy (GLD) - Krabbe disease



# (X-)Adrenoleukodystrophy




**Cho: ↑, NAA: (↓), Cr: ↔, Ins: ↑, Lac ↑**

Lactate → Disease activity, active demyelination

NAA ↓ → Disease progression, neuronal loss

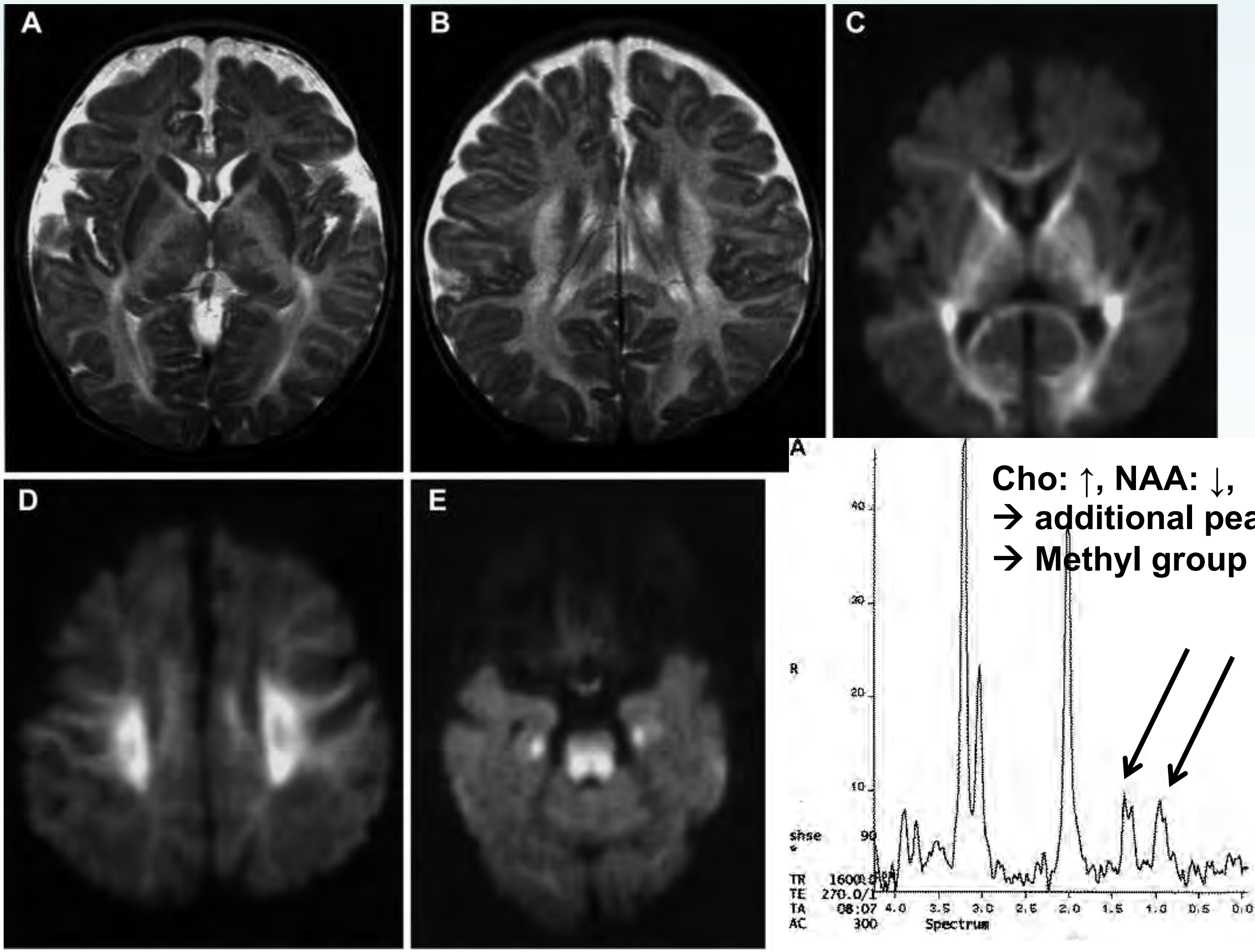
# Leucoencephalopathy: MRS specific patterns

– Maple syrup urine disease (MSUD)

– Canavan disease

– Nonketotic hyperglycinaemia

# Maple Syrup Urine Syndrome



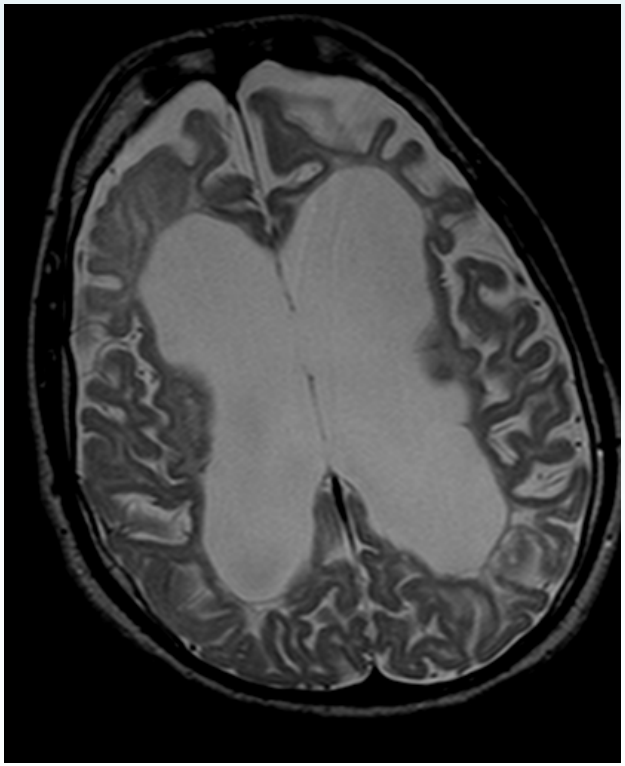

**Cho: ↑, NAA: ↓, Cr: ↔, Ins ↑, Lac ↑**

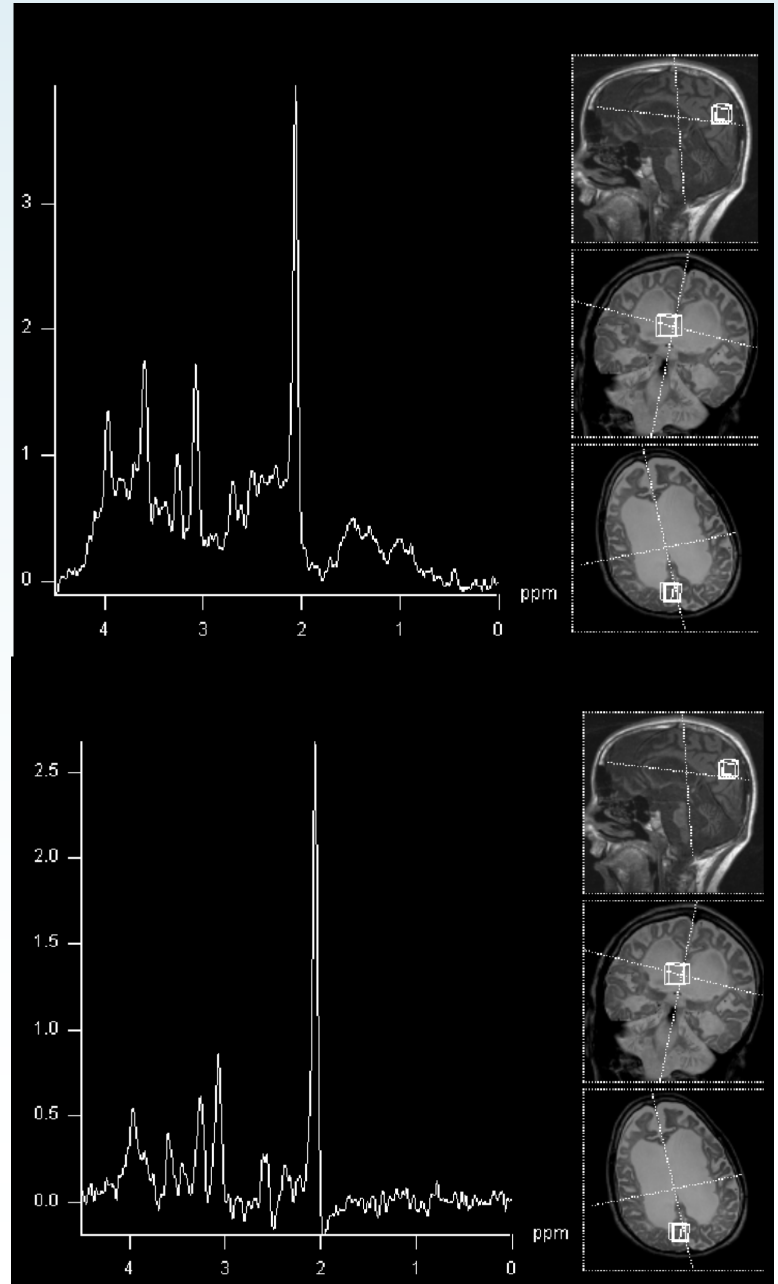
**→ additional peaks at 0.9 ppm**

**→ Methyl group of branched aminoacids**

Jan W. et al., Neuroradiology, 2003

# Canavan disease



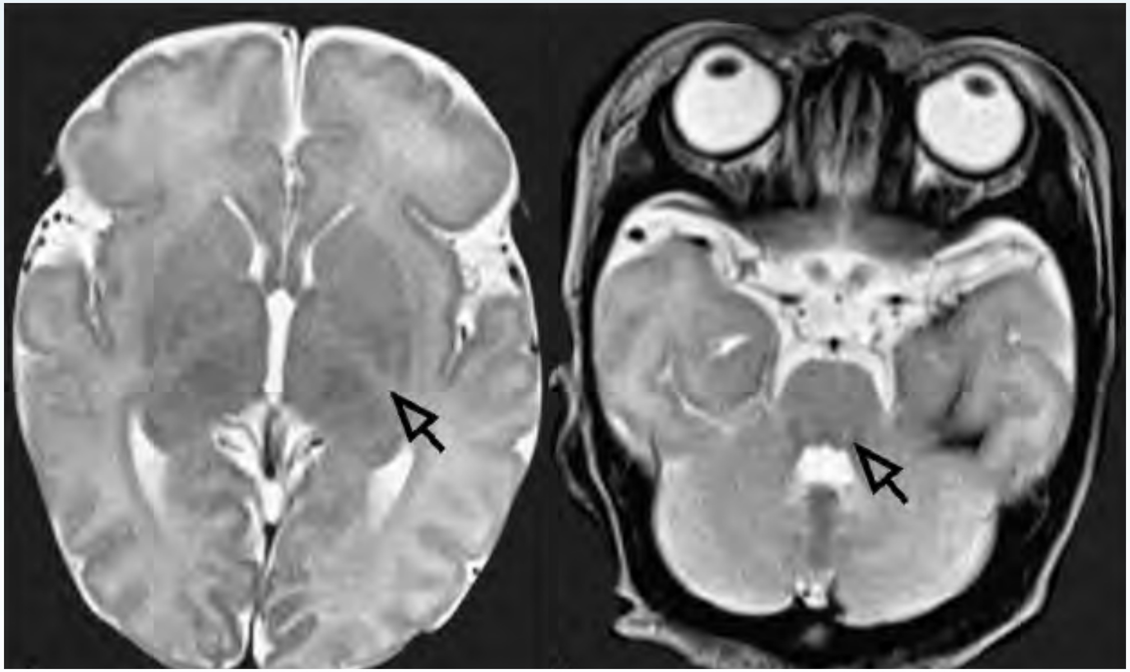


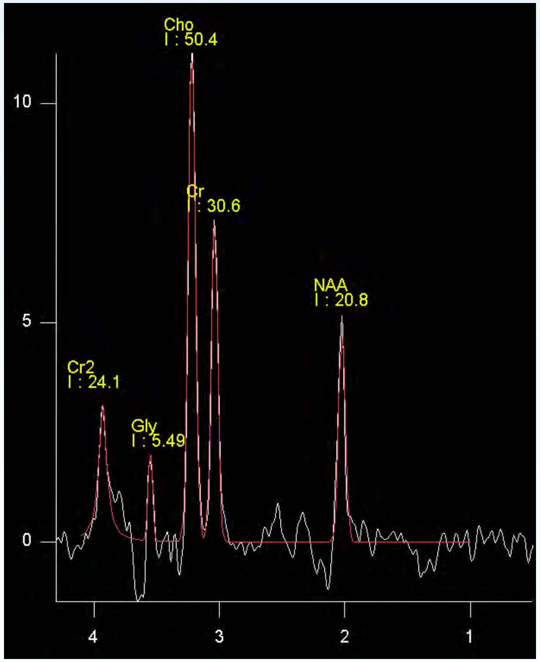

TE 35

TE 144

**Cho: ↔,(↓), <u>NAA: ↑</u>, Cr: ↔, Ins: ↑**

# Nonketotic hyperglycinemia



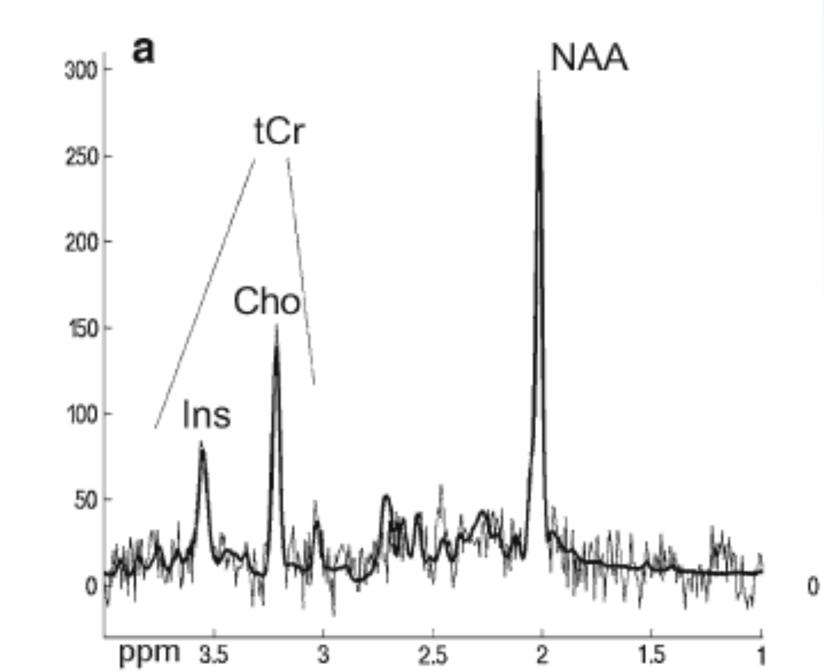



Culjat M et al., J Comput Assist Tomogr, 2010

# Other metabolic diseases: MRS patterns

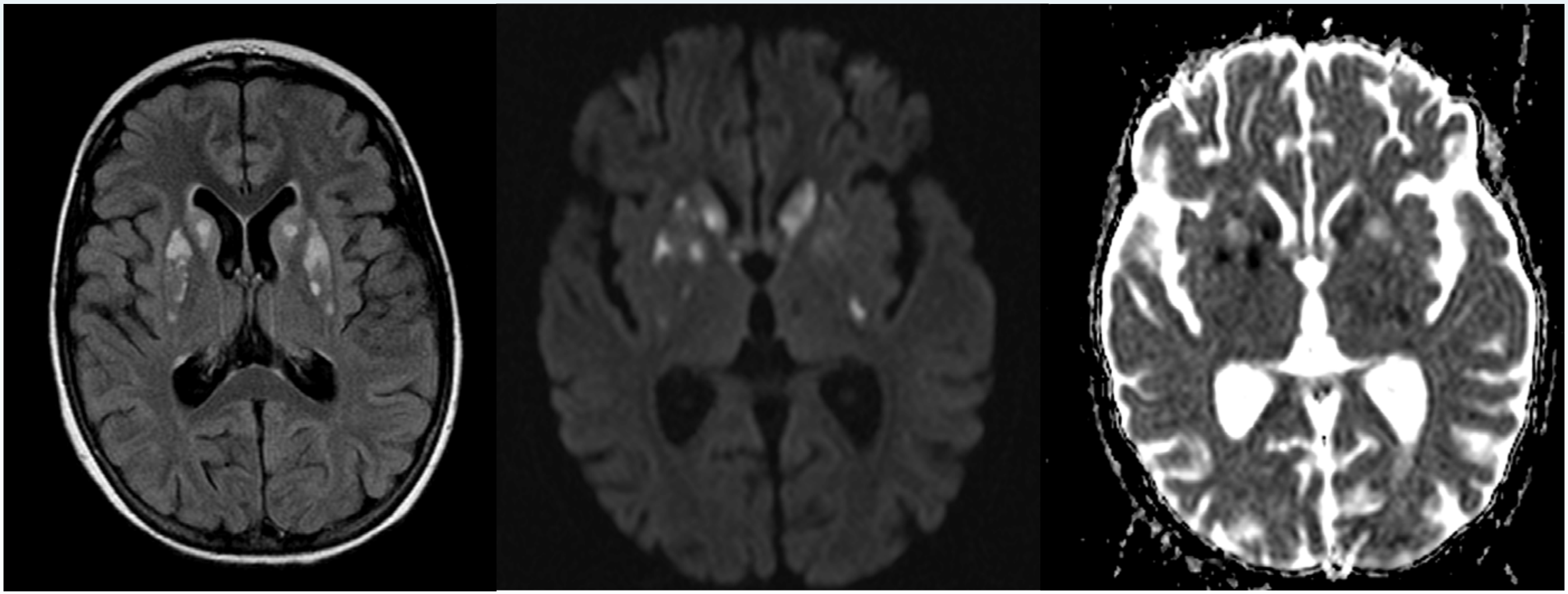
MRS patterns in metabolic disease without typical WM pattern:

- Phenylketonuria (PKU) – peak at 7.37 ppm
- Creatine deficiency syndrome – **missing creatine peak**

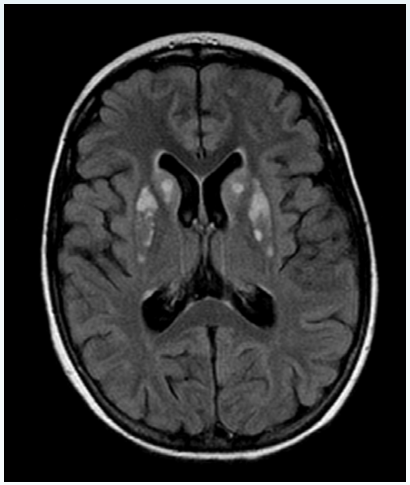


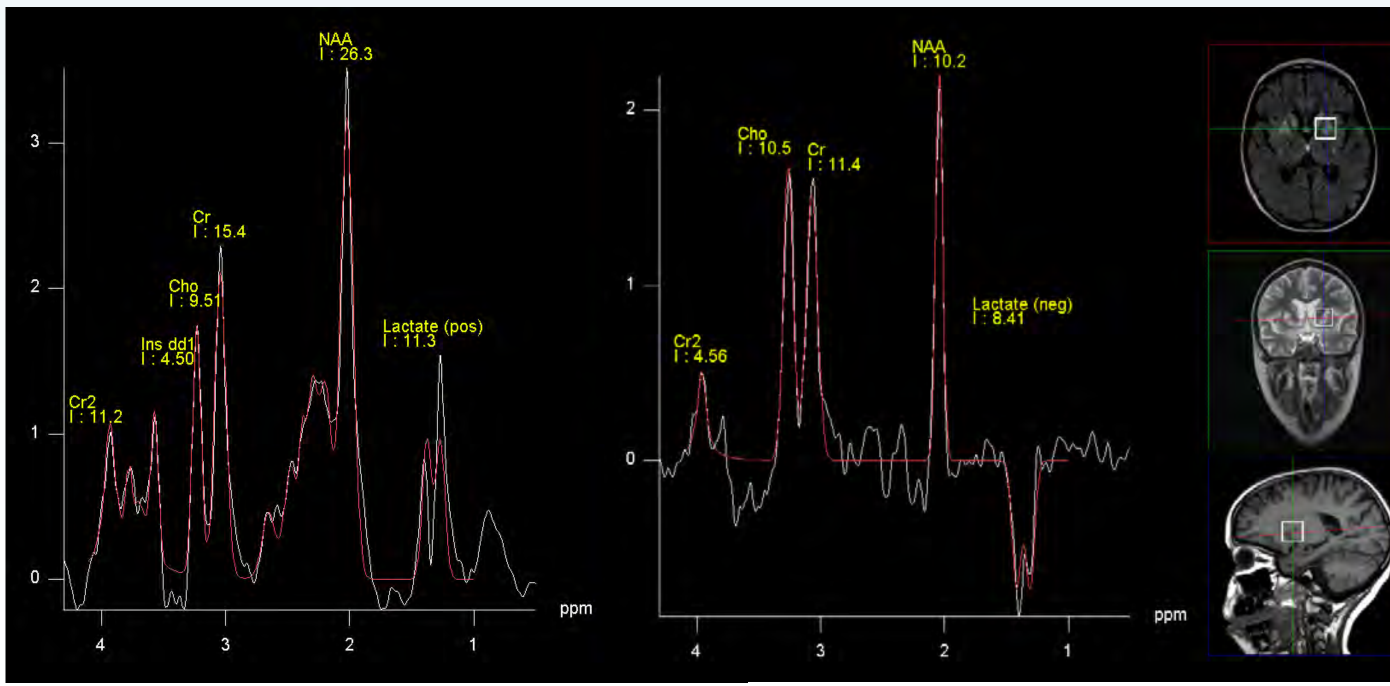

Dezortova M et al., 2008, Magn Reson Mater Phy

# Mitochondrial encephalopathies

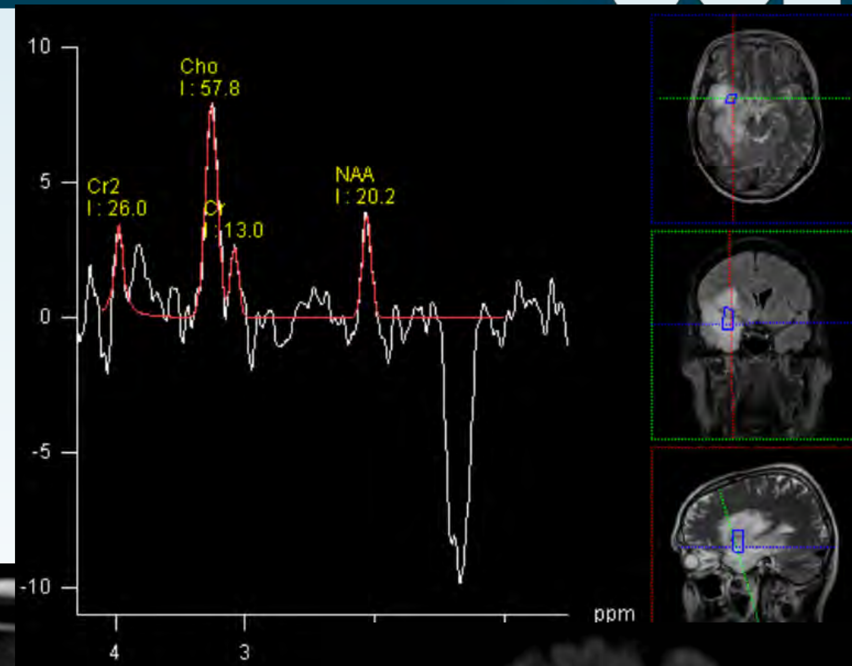


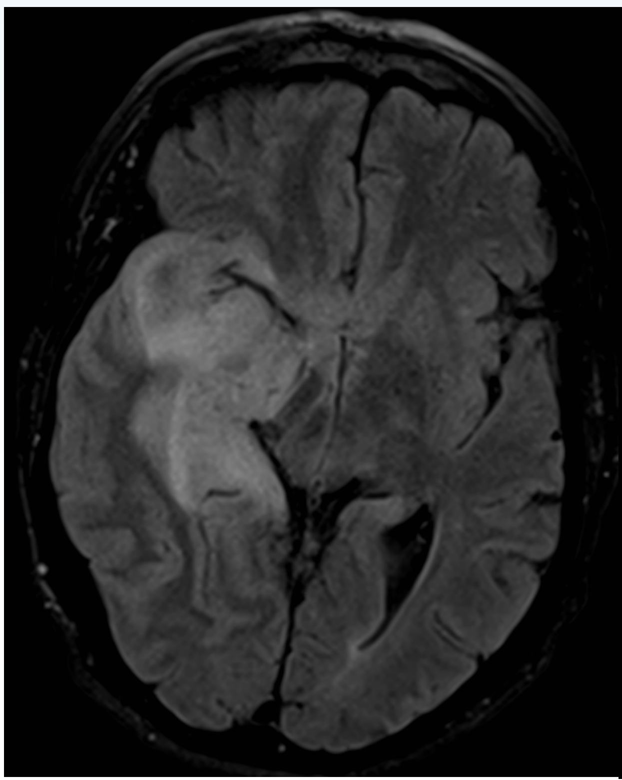
# Mitochondrial encephalopathies

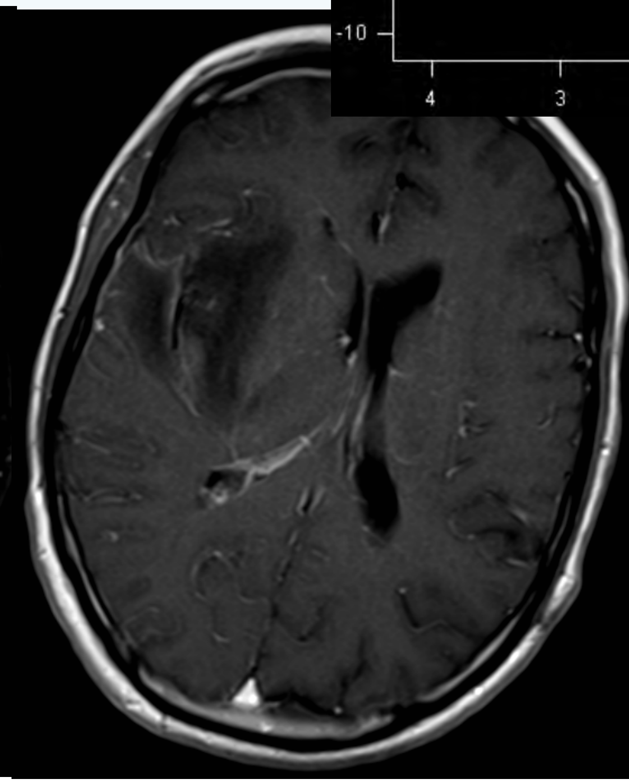


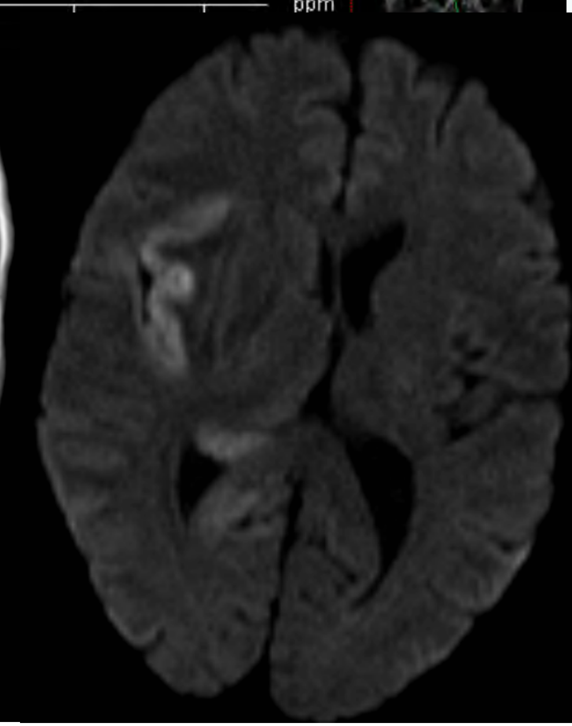


# Encephalitis







# MRS: pearls and pitfalls

- $^1$H-MRS does not require additional hardware
- Collection of peaks of different metabolites
- Single-voxel, 2D- and 3D-acquisitions
- New techniques enable detection of oncometabolites (eg 2-HG)
- Metabolic tumour profiling, staging, differentiation between tumour necrosis and recurrence
- Excellent clinical applications in neuro-paediatrics

- $^1$H-MRS is susceptible to field inhomogeneities (manual field shimming often needed)
- Acquisitions near skull and ventricles may be contaminated with lipids
- Partial volume averaging and noisy spectra may underestimate the pathology
- Overlapping resonances (eg glutamine, glutamate) need advanced post-processing
- Limited clinical applications in neuro-degeneration