Magnetic Resonance Spectroscopy: Basic Principles and Selected Applications

Sridar Narayanan, PhD

Magnetic Resonance Spectroscopy Unit

McConnell Brain Imaging Centre

Dept. of Neurology and Neurosurgery

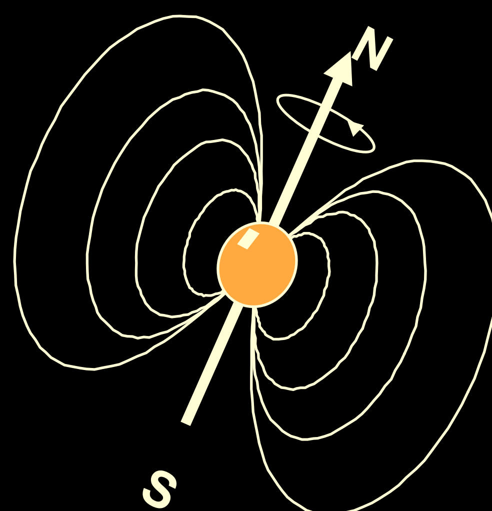
Montreal Neurological Institute

McGill University

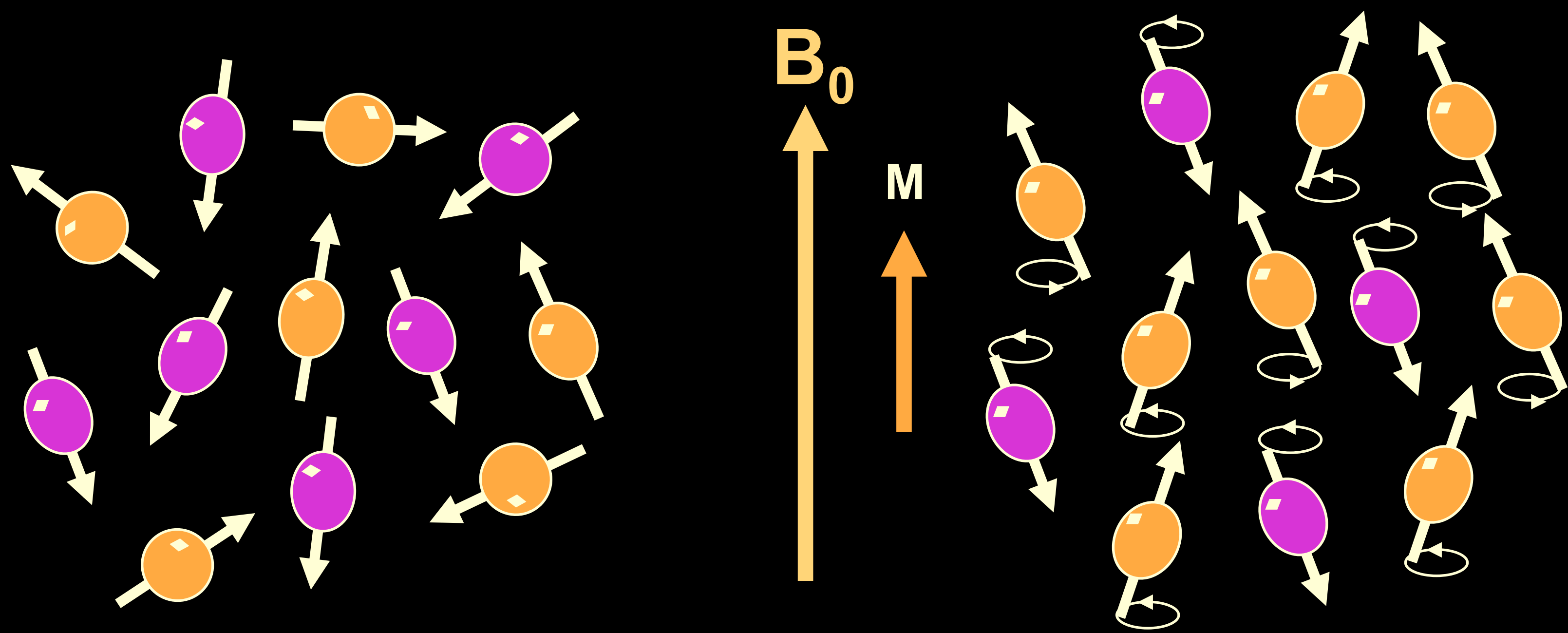
Montreal, Canada

NMR Basics

- Nuclei with odd number of protons and/or neutrons
  - nuclear spin angular momentum (“spin”)
  - nuclear magnetic moment
- Biological tissue rel. sens.
  - hydrogen (^{1}H) 100%
  - phosphorus (^{31}P) 6.6%
  - carbon (^{13}C) 1.6%



NMR Basics

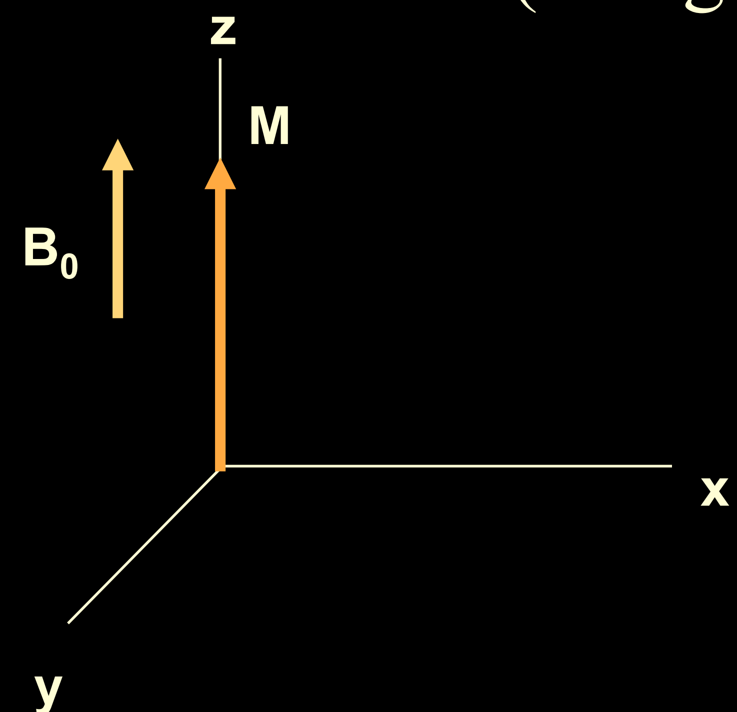


no external field

external field B_0
(spin 1/2)

Net Magnetization (M)

- static magnetic field B_0 produces a net magnetization vector M (along z-axis)



NMR Basics

- spins precess and exhibit resonance at the Larmor frequency

$$\omega = \gamma \mathbf{B}$$

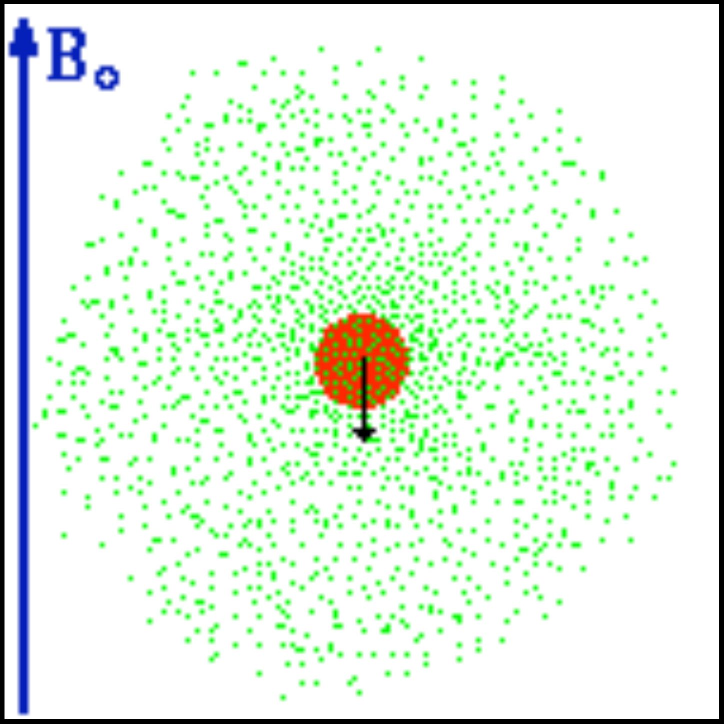
where γ = gyromagnetic ratio

$\gamma/2\pi$ = 42.58 MHz/T for hydrogen

^{1}H MRS Basic Principles

- ^{1}H nuclei resonate at a characteristic frequency dependent on the magnetic field strength B
- Within a given applied field B, ^{1}H nuclei in different chemical environments experience a slightly different effective field due to chemical shielding from surrounding electrons

Chemical Shielding



σ = diamagnetic screening constant

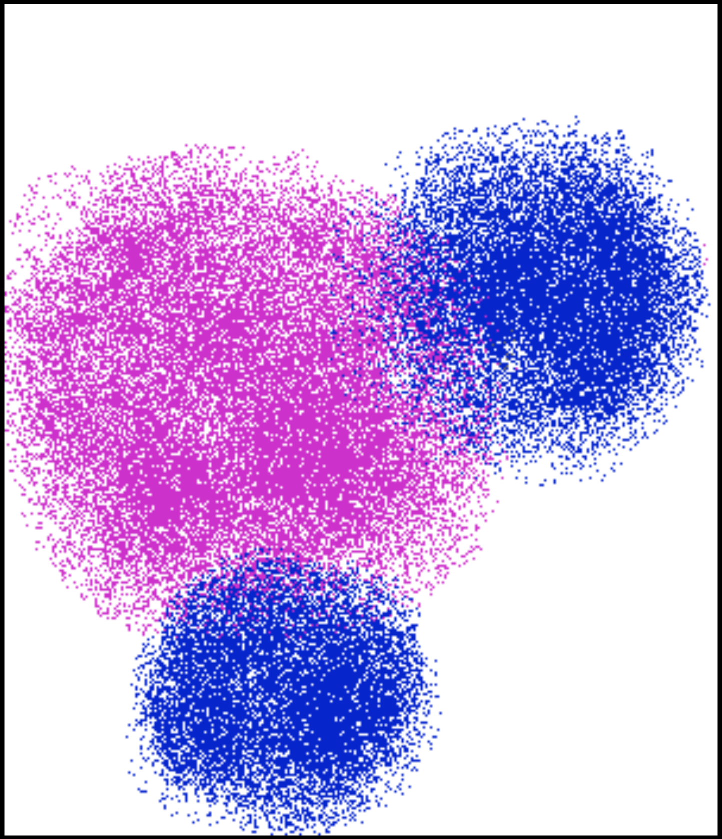
$$B = B_o\,(1\text{-}\sigma)$$

Joseph P. Hornak

Chemical Shielding

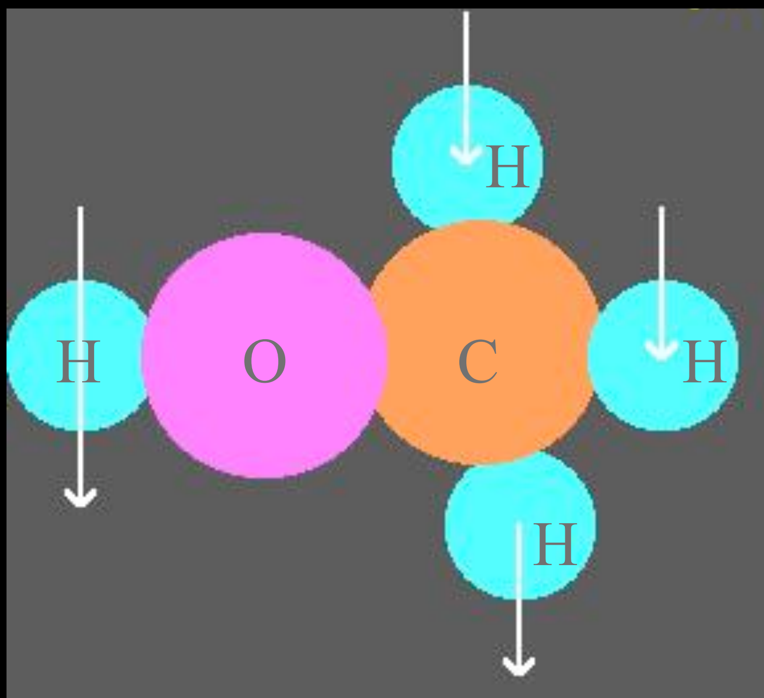
- Magnitude of σ depends on local electron density => chemical environment
  - Adjacent atoms
  - Bonds
- This causes the ^1H nuclei to resonate at slightly different frequencies => chemical shift

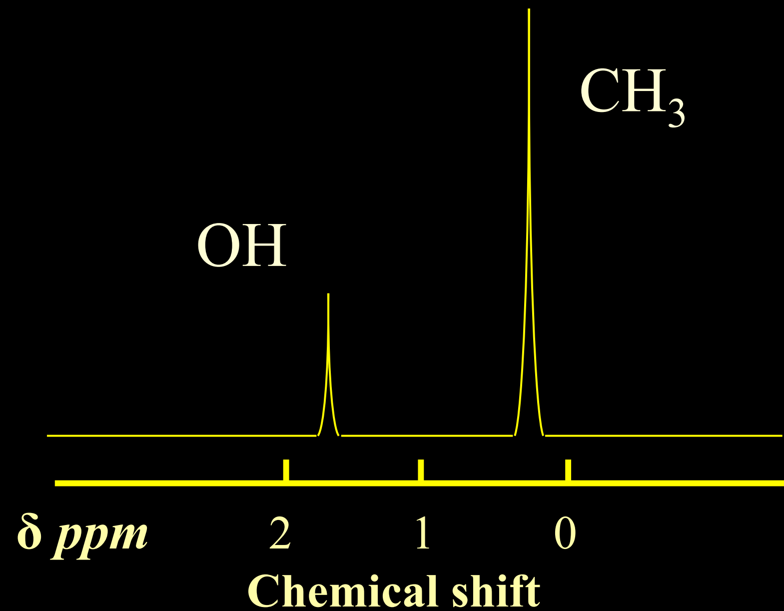
$$\nu = (\gamma/2\pi)\, B_o\, (1-\sigma)$$



Joseph P. Hornak

Chemical shift: Methanol





- Horizontal axis
  - Frequency (ppm)
- Vertical axis
  - Area proportional to concentration
    - T1 & T2 weighting

After Joseph P. Hornak

Hz vs. ppm

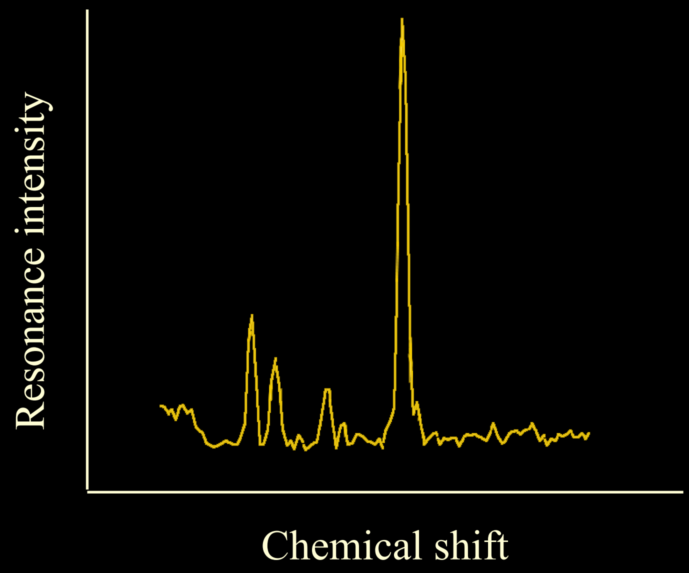
- The chemical shift when expressed in Hz is B_0 dependent
- Expressed in parts-per-million (ppm) the frequency shift is independent of B_0

$$\delta_{ppm} = (\nu - \nu_{ref})/\nu_{ref} \text{ x } 10^6$$

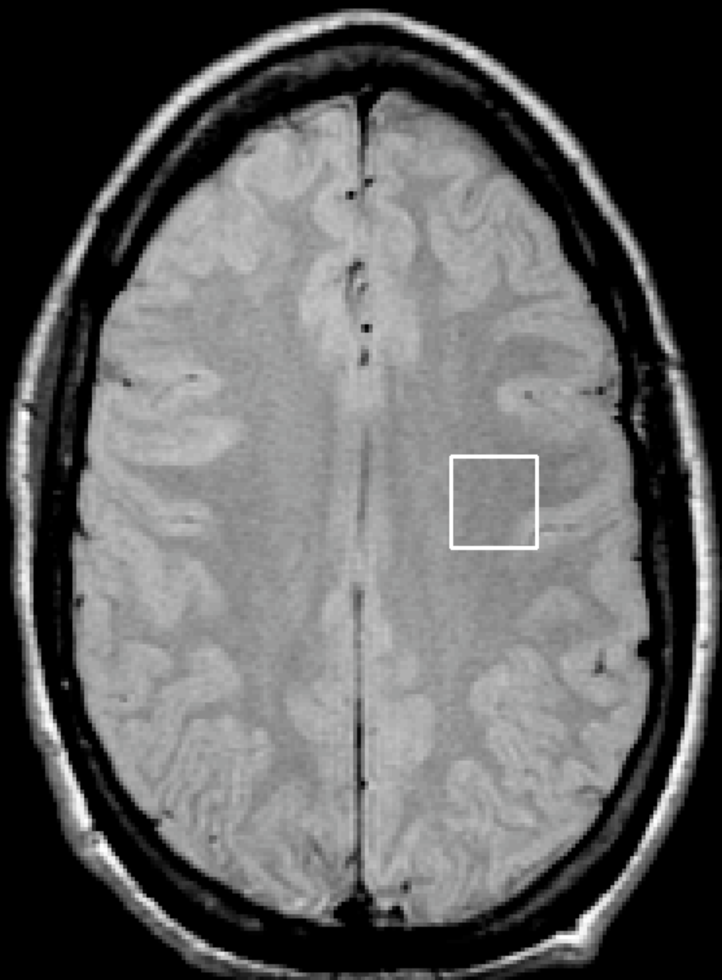
- where v_{ref} is typically the resonant frequency of tetra-methyl silane (TMS)

What is a spectrum?

- An NMR spectrum is a plot of signal intensity versus chemical shift
  - Hz - field dependent
  - Parts per million (ppm)
    - Field independent

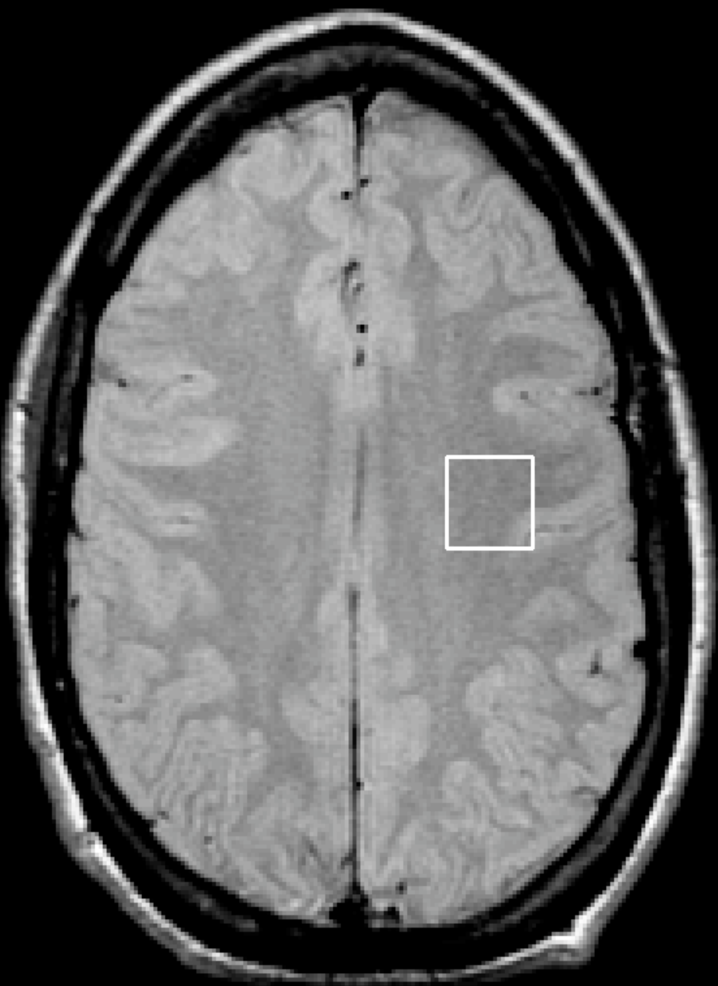


Spatial localization: Single Voxel



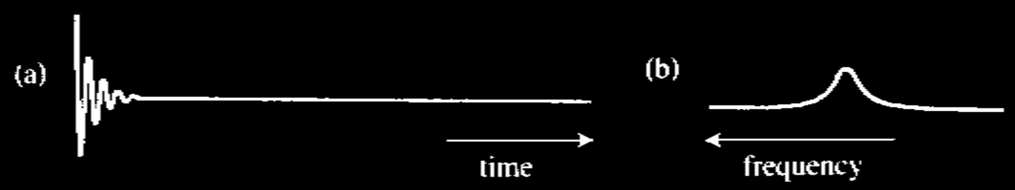
- PRESS
  - Point RESolved Spectroscopy
- 90˚-180˚-180˚
  - Slice selective in 3 planes
  - Acquire 2nd echo
- TE needs to be somewhat longer
  - 30ms on modern MRIs

Spatial localization: Single Voxel

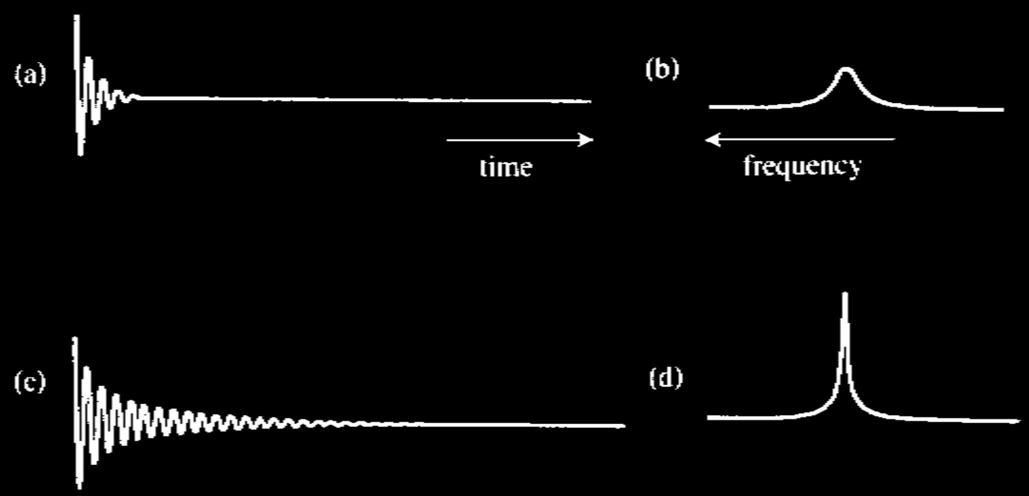


- STEAM
  - STimulated Echo Acquisition Mode
- 90˚-90˚-90˚
  - Slice selective in 3 planes
  - Trans=>long=>trans
- Shorter echo times than PRESS (~20ms)
- Half the signal
- Better localization

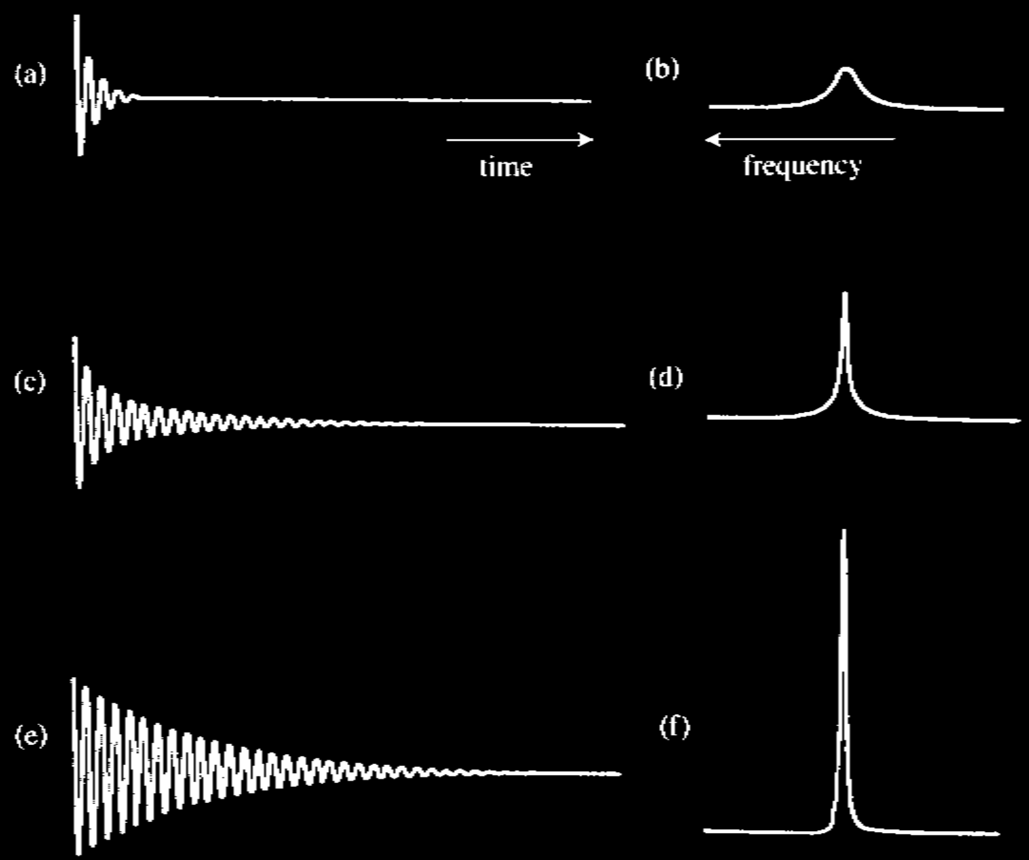
B_0 *homogeneity: Shimming*



B_0 homogeneity: Shimming

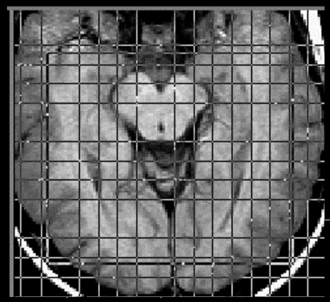


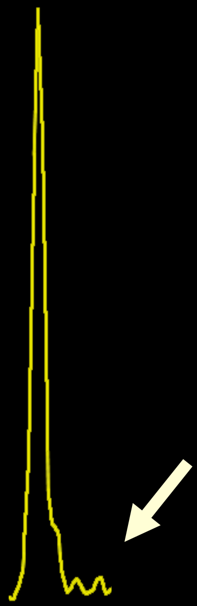
B_0 homogeneity: Shimming



MR *Imaging* 1H-MR *Spectroscopy*

H_2O: 70 M Metabolites: ~ 7 mM



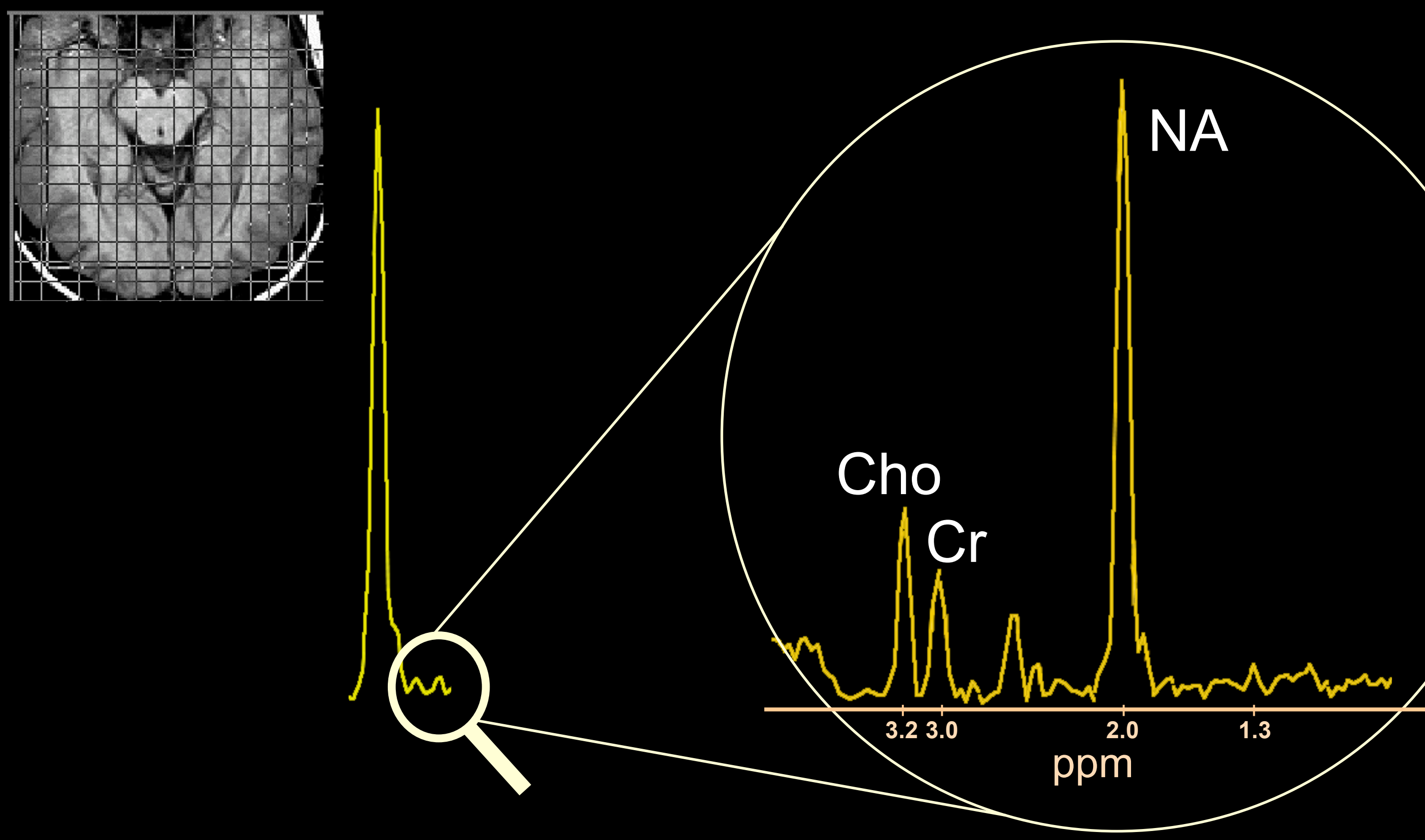


MR *Imaging*

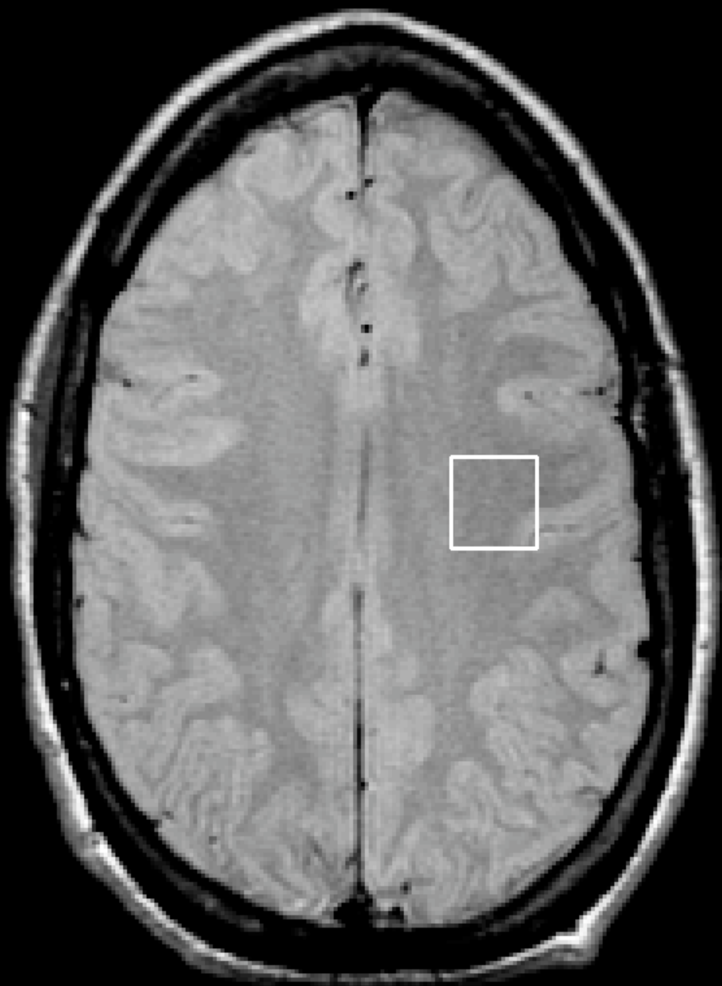
H_2O: 70 M

1H-MR *Spectroscopy*

Metabolites: ~ 7 mM

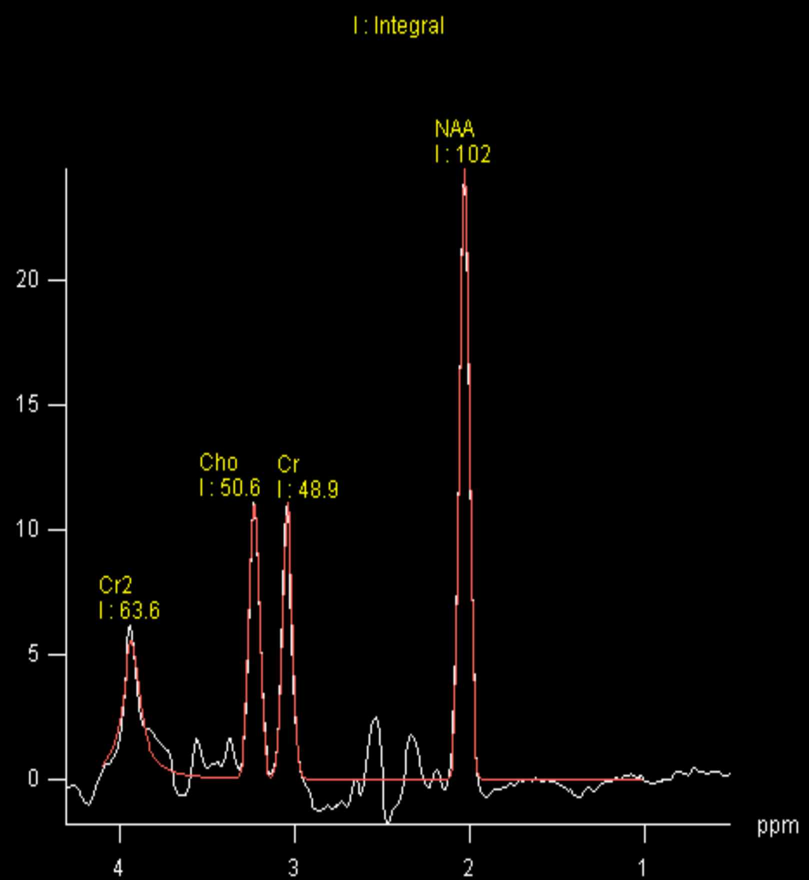


Water suppression



- CHESS
  - CHEmically-Selective Saturation
- 90˚ pulse frequency-selective for water, followed by spoiler gradient
- Destroy the net magnetization of water protons

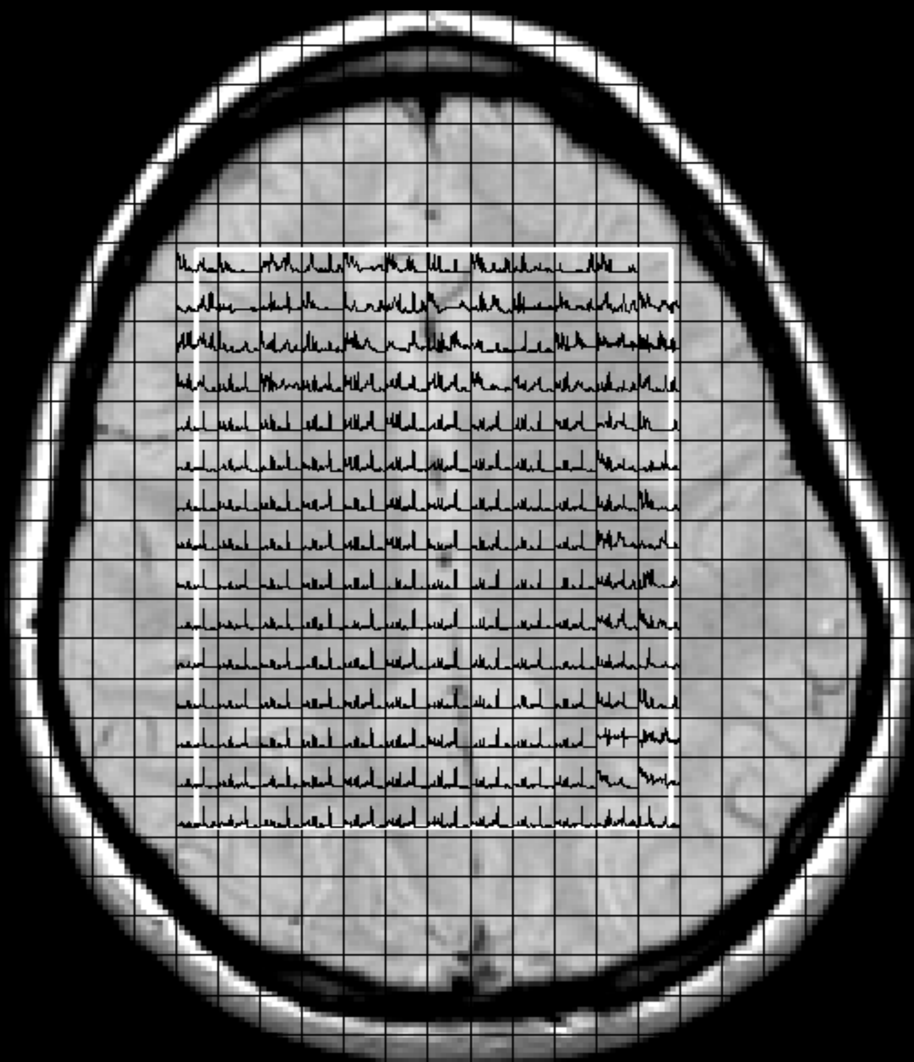
Example (Siemens Sonata)



PRESS, TR = 1500, TE = 135

- Eddy current compensation
- Filtering
- Zero filling
- Fourier transformation
- Frequency shift correction
- Phase correction
- Baseline correction
- Curve fitting

MRSI: Spectroscopic Imaging



Size: 1-2 cc

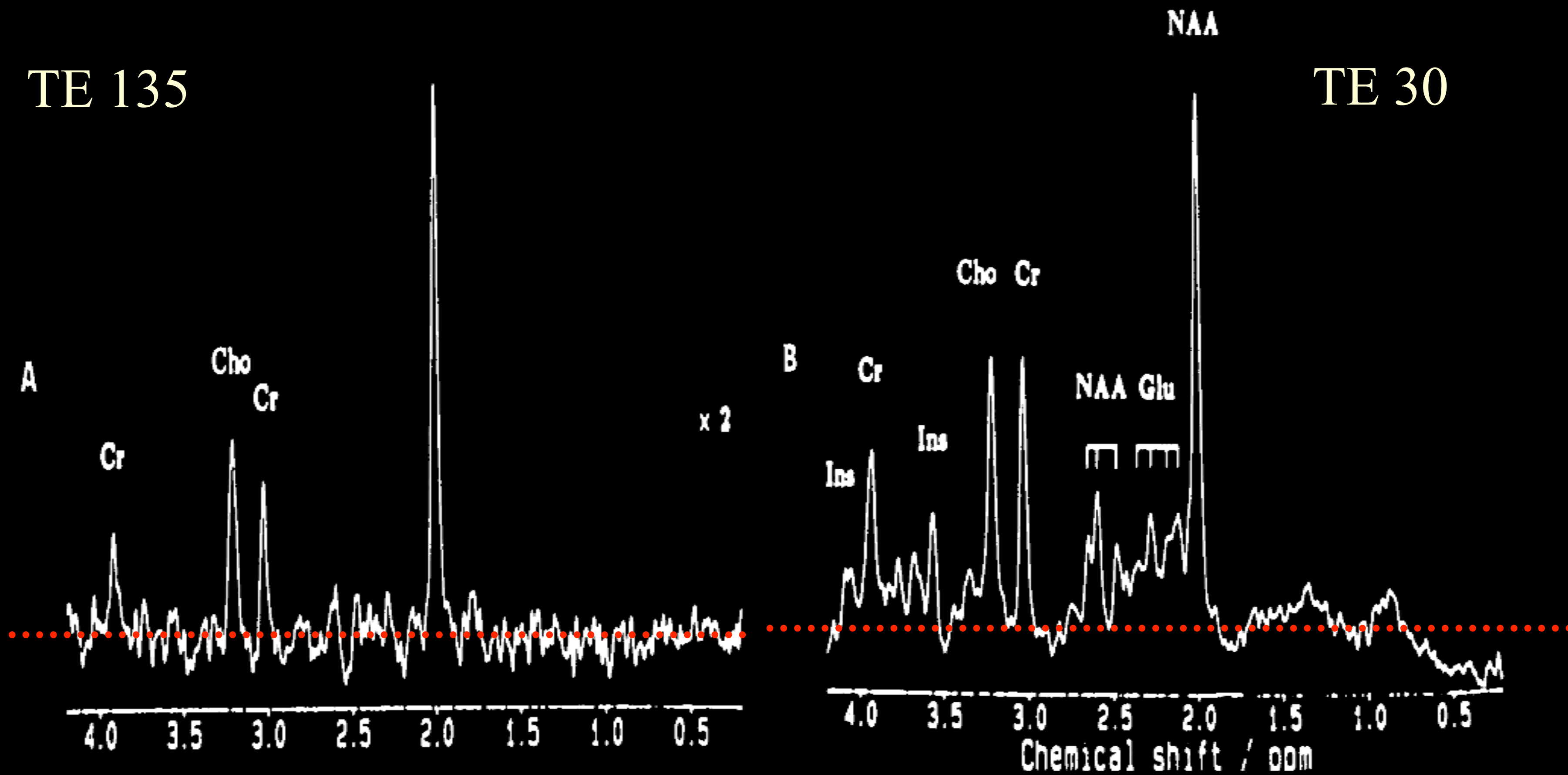
Scan times: 10-30 min

Quantitation: harder

MRSI

- 2D (single or multislice)
- 3D
- EPI

Long vs. short TE



Fewer metabolites, simpler baseline

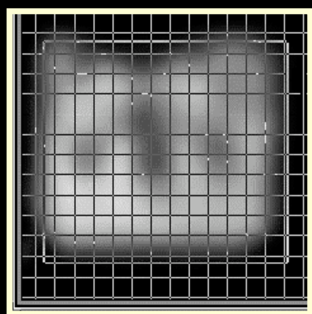
More metabolites, more complicated baseline

Research and Clinical Applications

Observable ^{1}H Metabolites

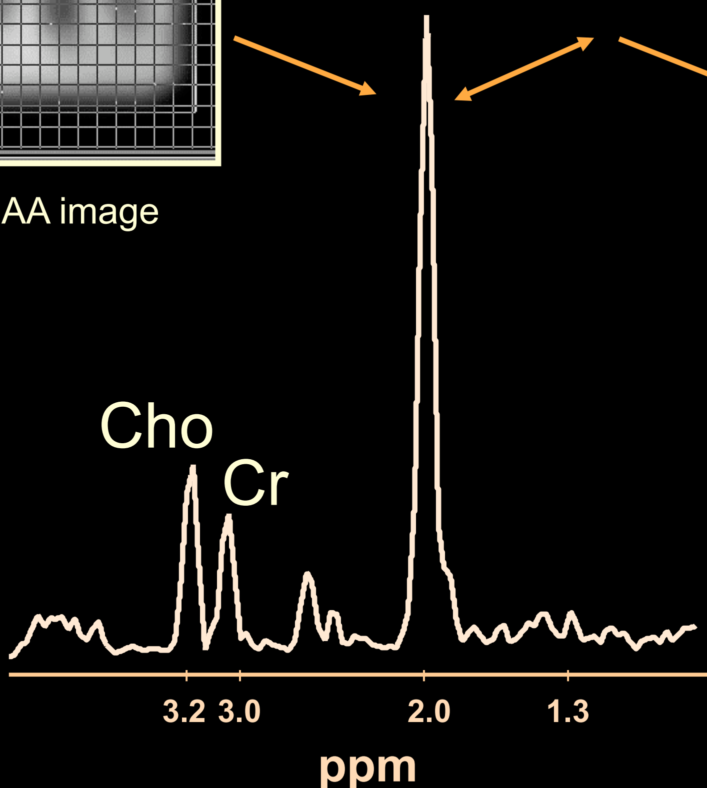
ppm	Metabolite	Properties
0.9-1.4	Lipids	Products of brain destruction
1.3	Lactate	Product of anaerobic glycolysis
2.0	NAA	Neuronal marker
2.2-2.4	Glutamine/GABA	Neurotransmitters
3.0	Creatine	Energy metabolism
3.2	Choline	Cell membrane marker
3.5	*myo*-inositol	Glial cell marker, osmolyte hormone receptor mechanisms
1.2	Ethanol	Triplet
1.48	Alanine	Present in meningiomas
3.4&3.8	Glucose	Increased in diabetes
3.8	Mannitol	Rx for increased ICP

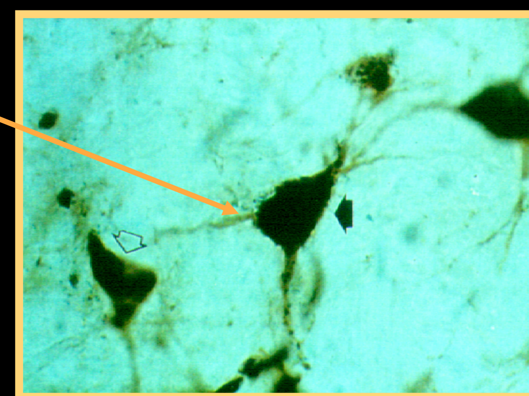
MR Spectroscopy: monitoring neuronal and axonal integrity in vivo



NAA image

NA





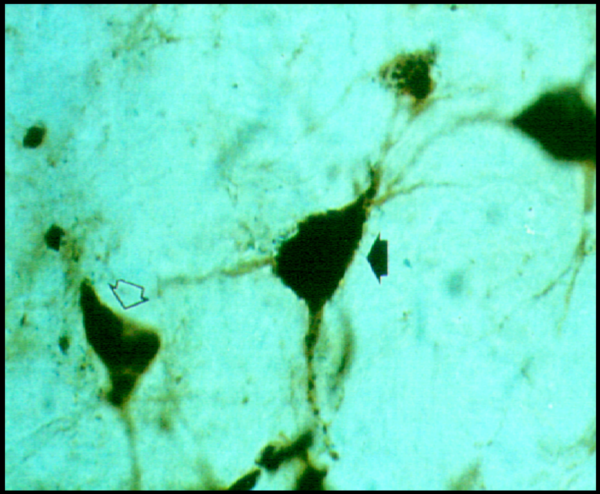
From Coyle, JT. (1989)

Simmons,M.L (1991)
Moffett, J.R. (1991)
Bjartmar, (2002)

Mechanisms of NAA decrease

Decreased density of NA

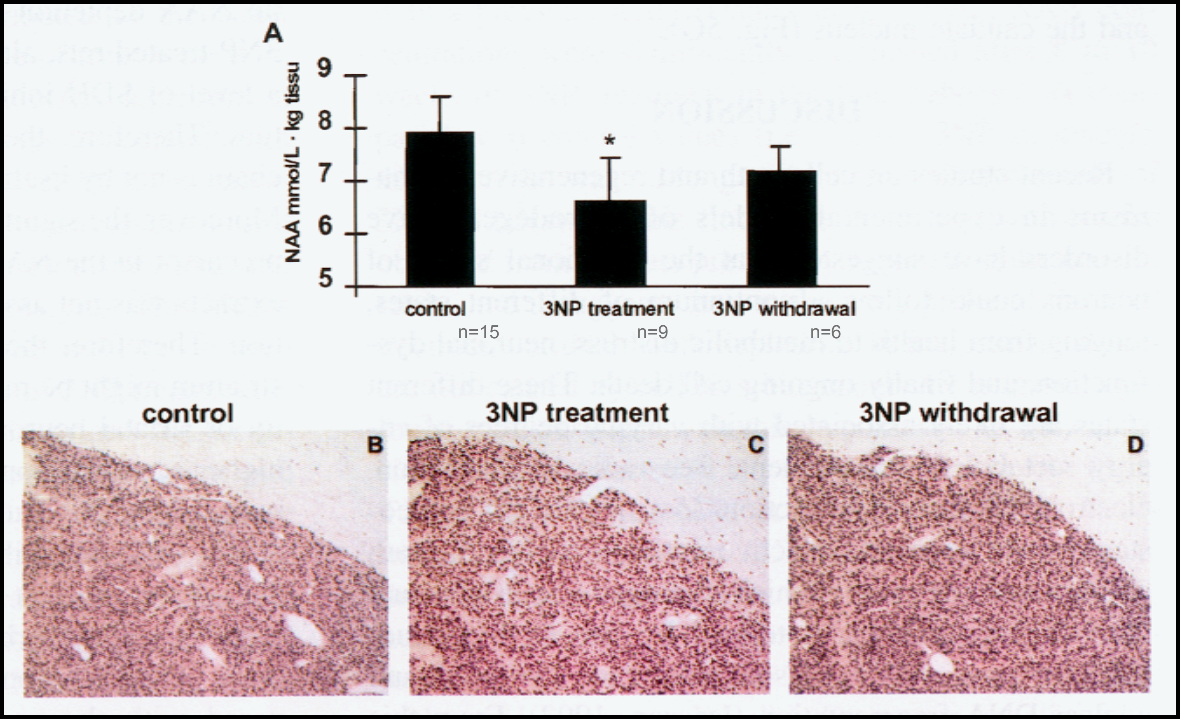
- axonal loss
- axonal shrinkage
- edema



Axonal metabolic dysfunction

(Demougeot, 2001; Dautry, 2000; Watson, 1998; Kalra, 1998; Cendes, 1997; Vermathen, 1996; Hugg, 1996; De Stefano, 1995)

Reversible NAA decreases with mitochondrial dysfunction



NAA

NeuN

Early N-Acetylaspartate Depletion Is a Marker of Neuronal Dysfunction in Rats and Primates Chronically Treated with the mitochondrial Toxin 3-Nitropropionic Acid.
Dautry C., et al, *J Cereb Blood Flow Metab* 2000;20:789-99

CHOLINE overview

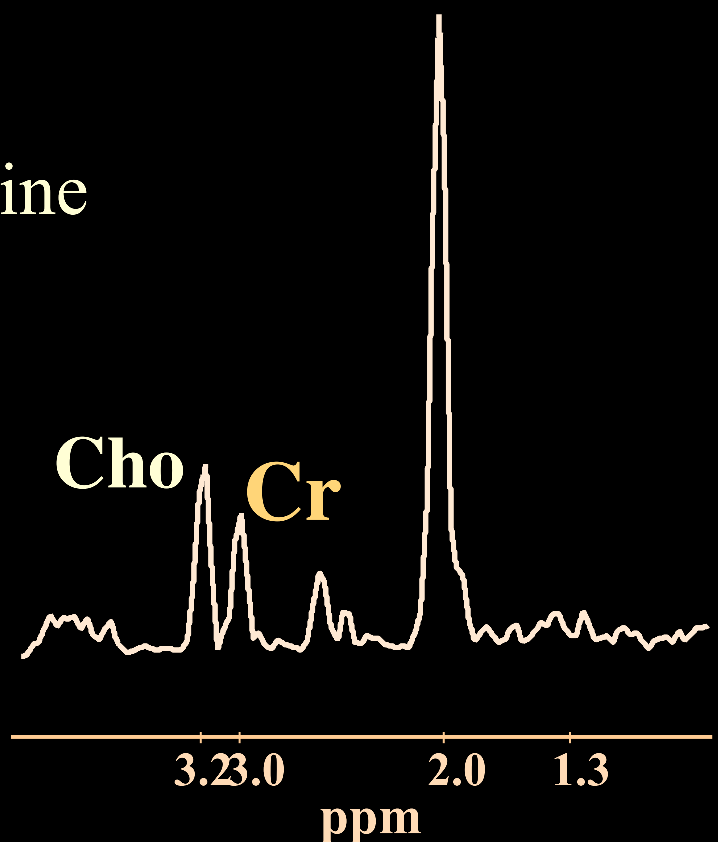
- Cho, PCho and GPCho
    - precursors of membrane components
- Cho and GPCho
    - products of membrane degradation

Increased Cho

membrane turnover   cellular density   Inflammation

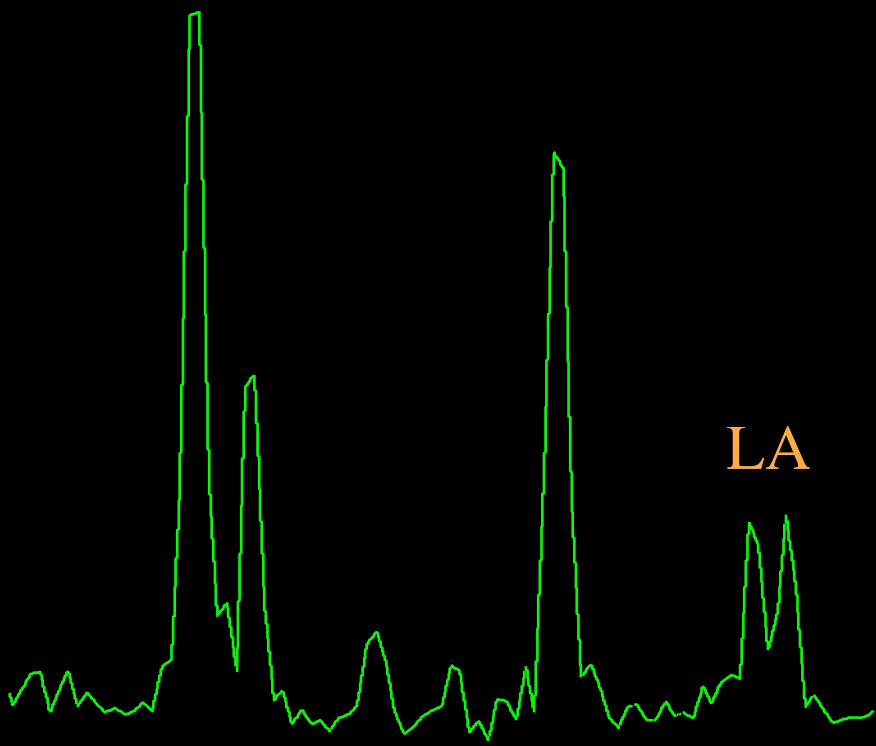
MRS: Creatine

- Creatine
  - Phosphocreatine + Creatine
- Internal standard
  - (if unaffected)

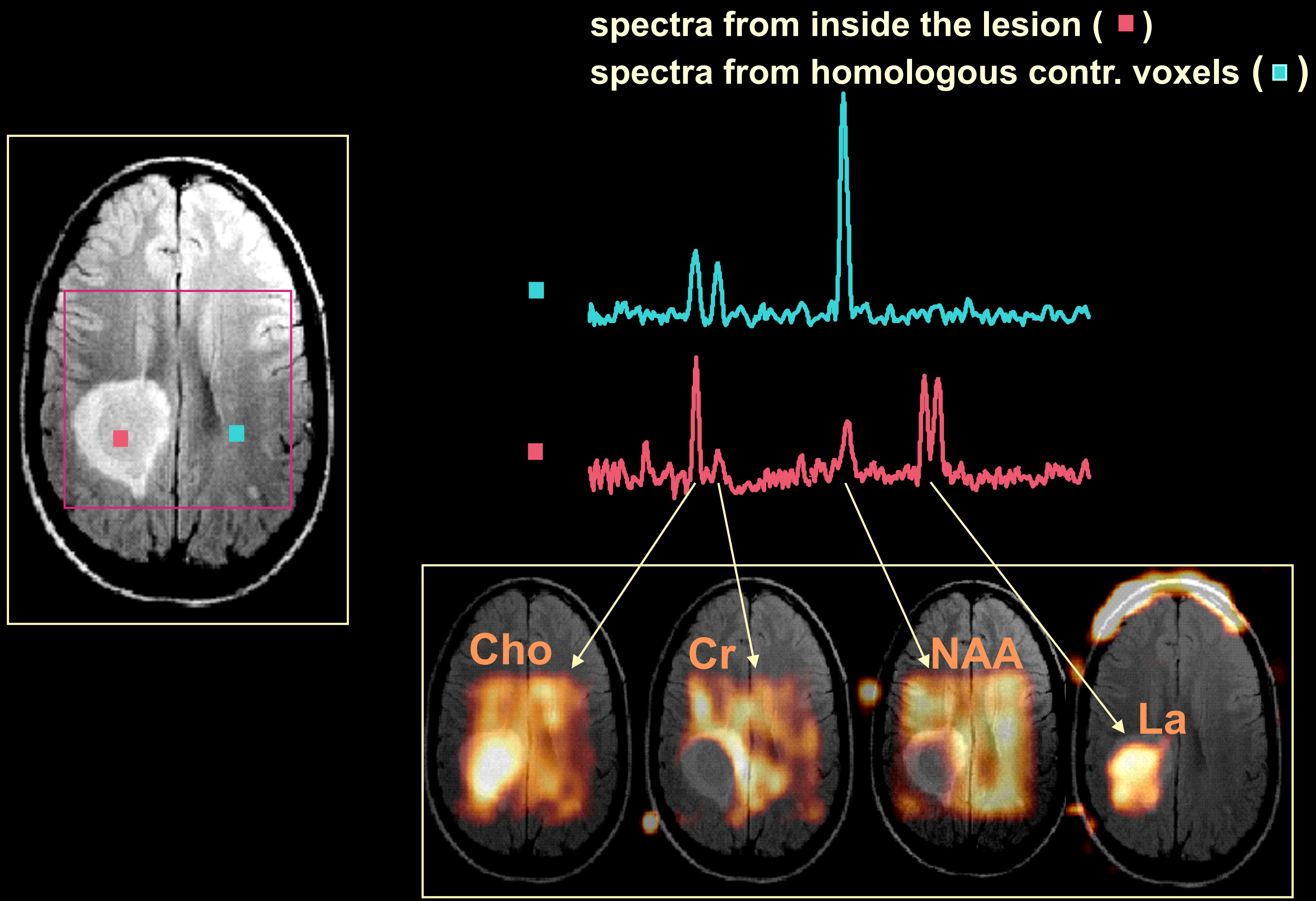


MRS: Lactate

- Lactate
  - Anaerobic metabolism
    - ischemia
    - inflammation
    - cysts

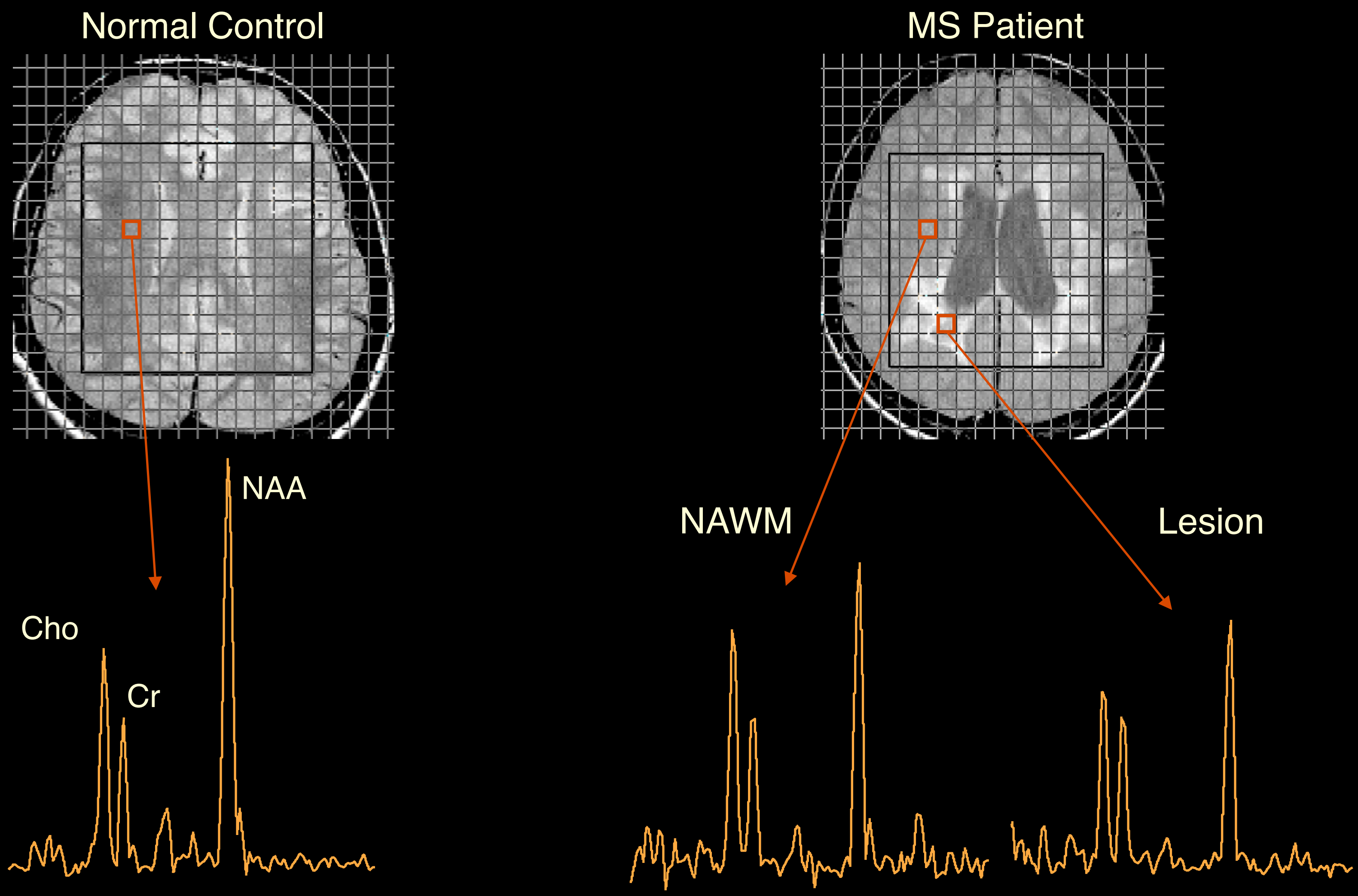


Multiple Sclerosis

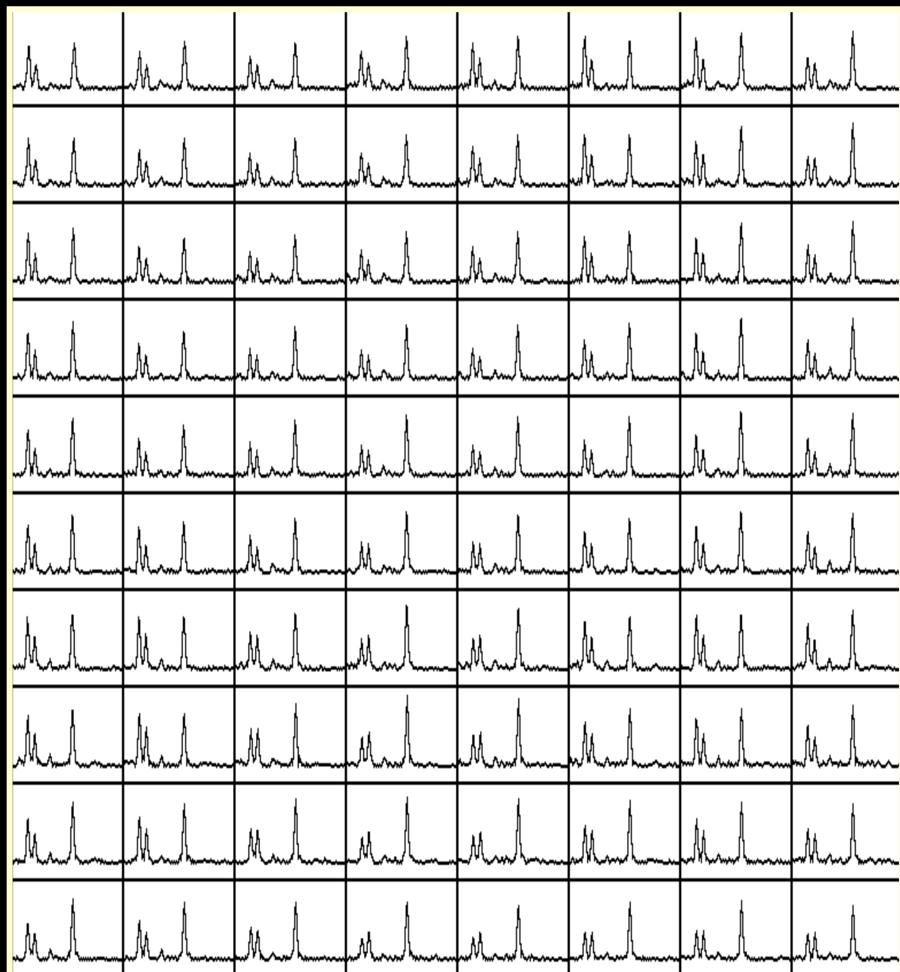


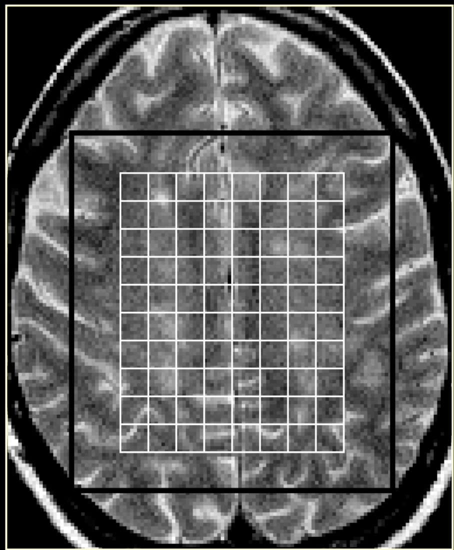
N. De Stefano

Chronic MS: Axonal damage in plaques and NAWM

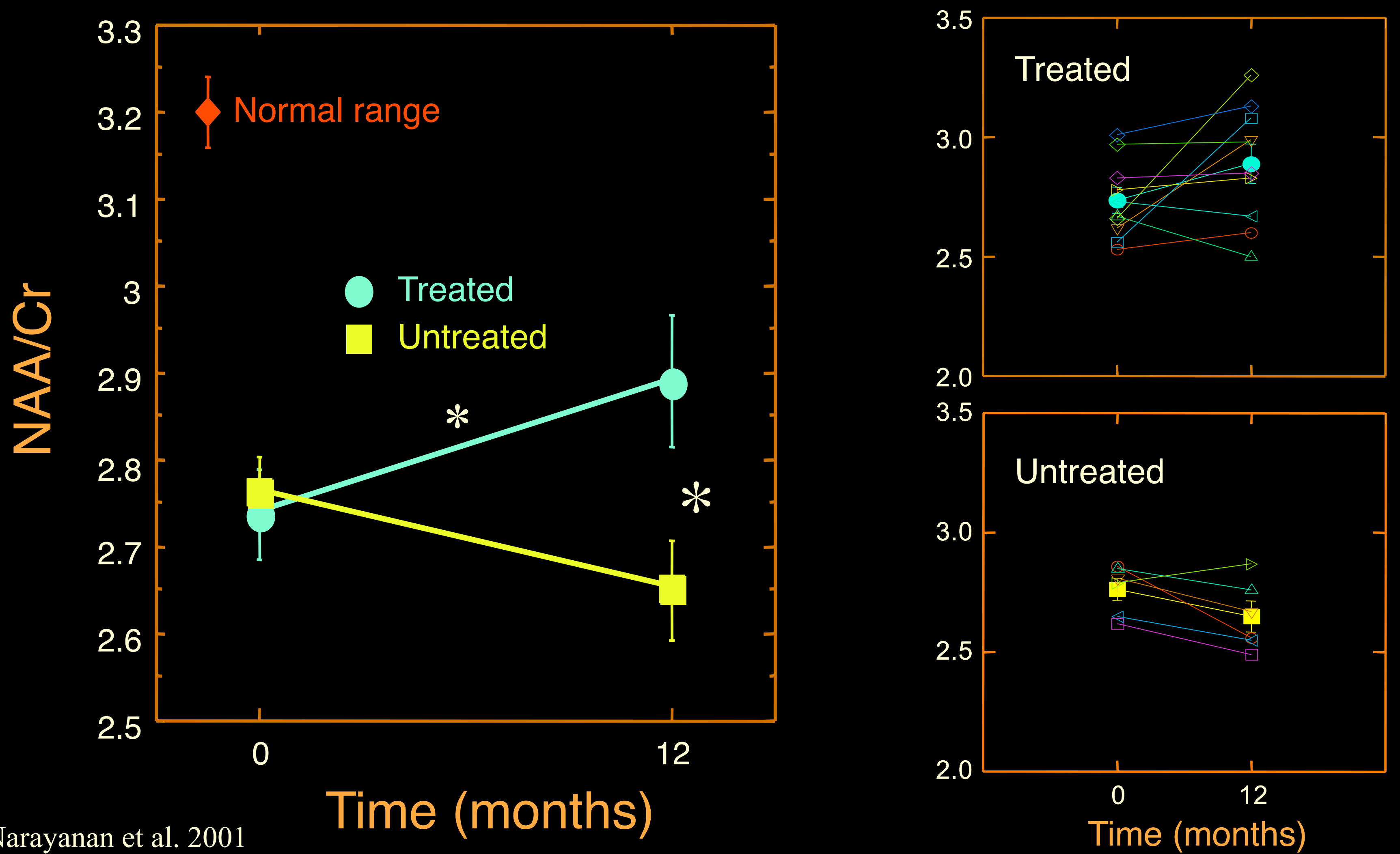


Monitoring therapy with MRS



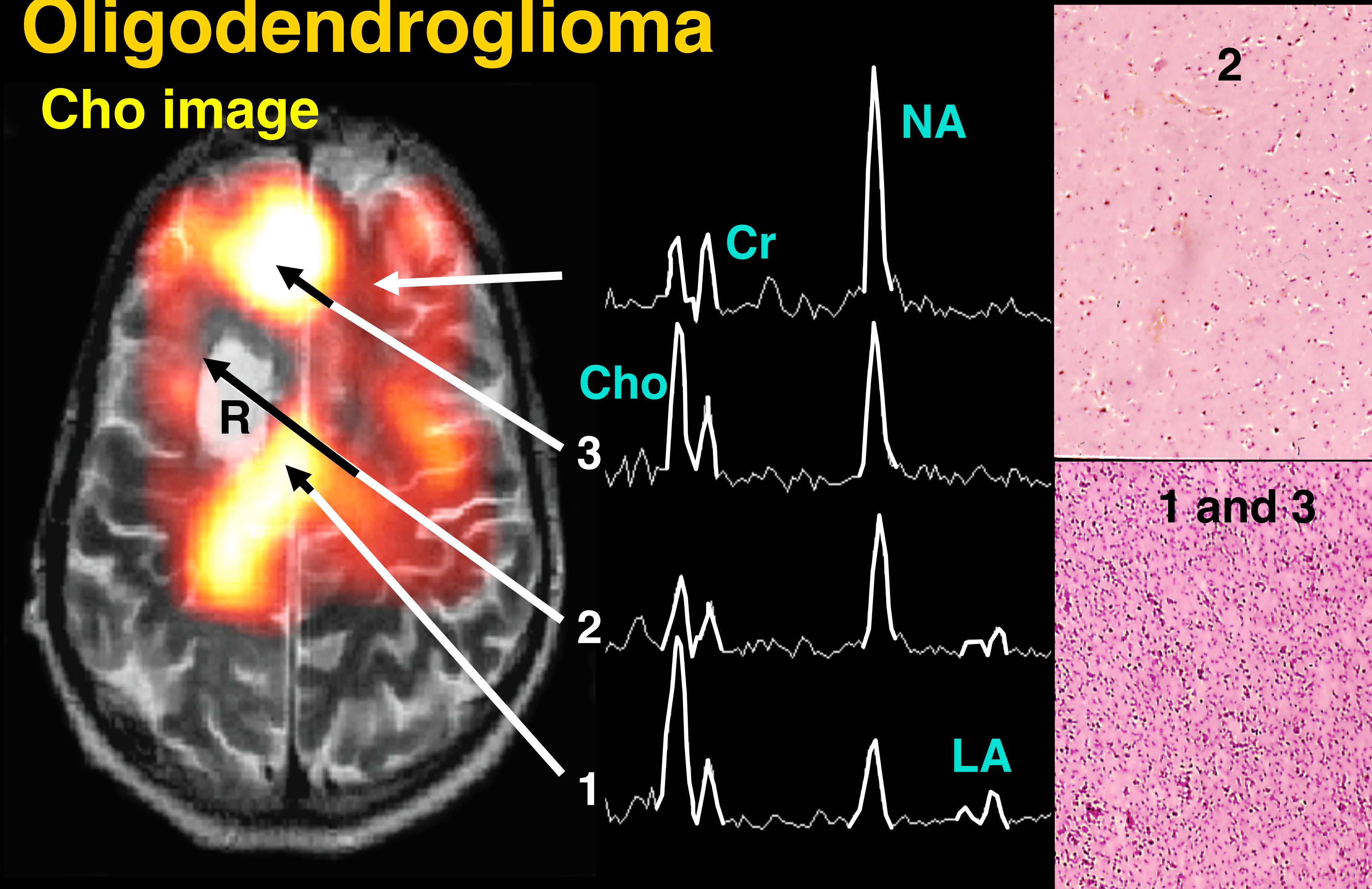


MS: ↑ NAA/Cr with IFNB



Narayanan et al. 2001

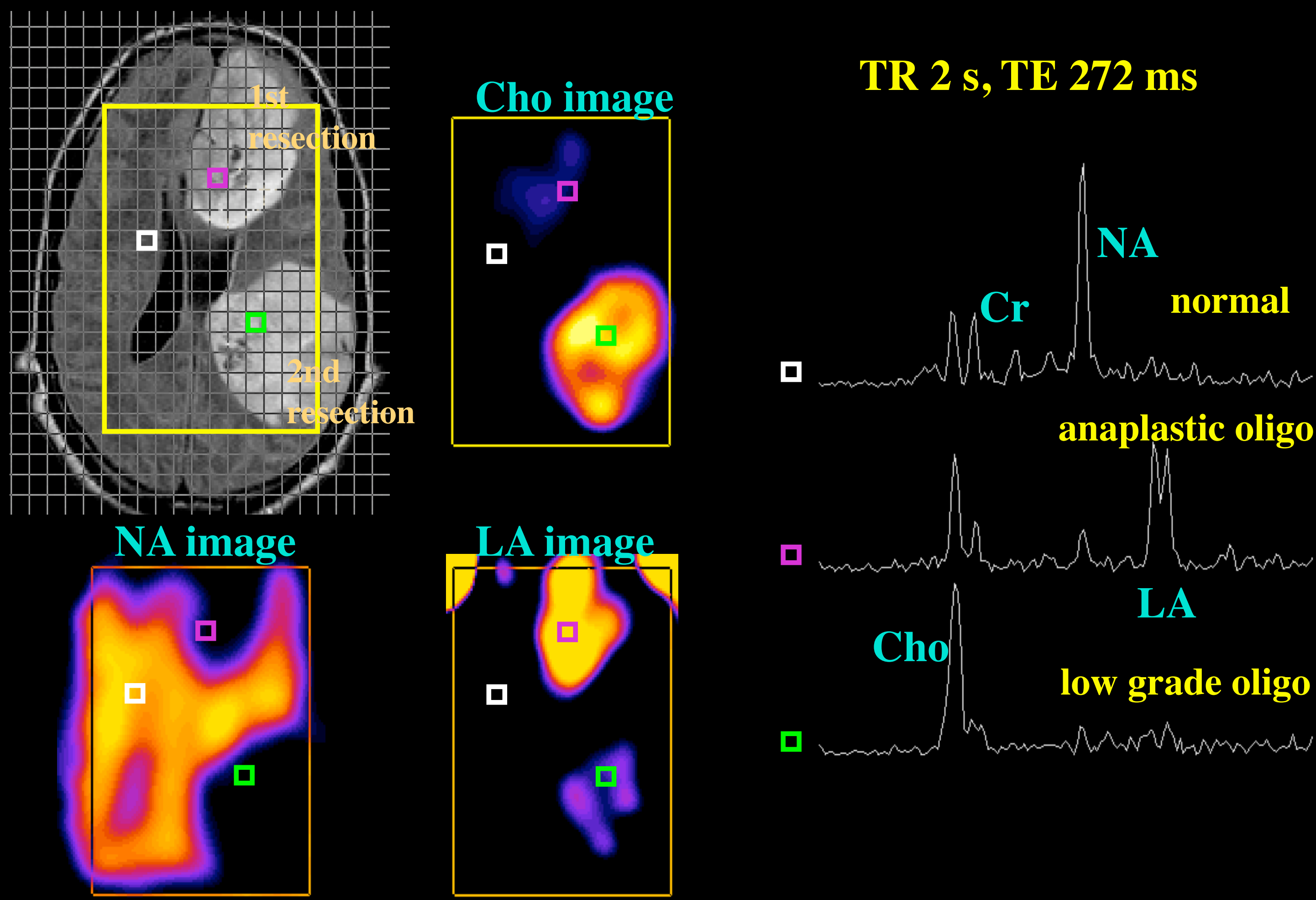
Recurrent Oligodendroglioma



M. Preul

Oligo, Anaplastic Oligo

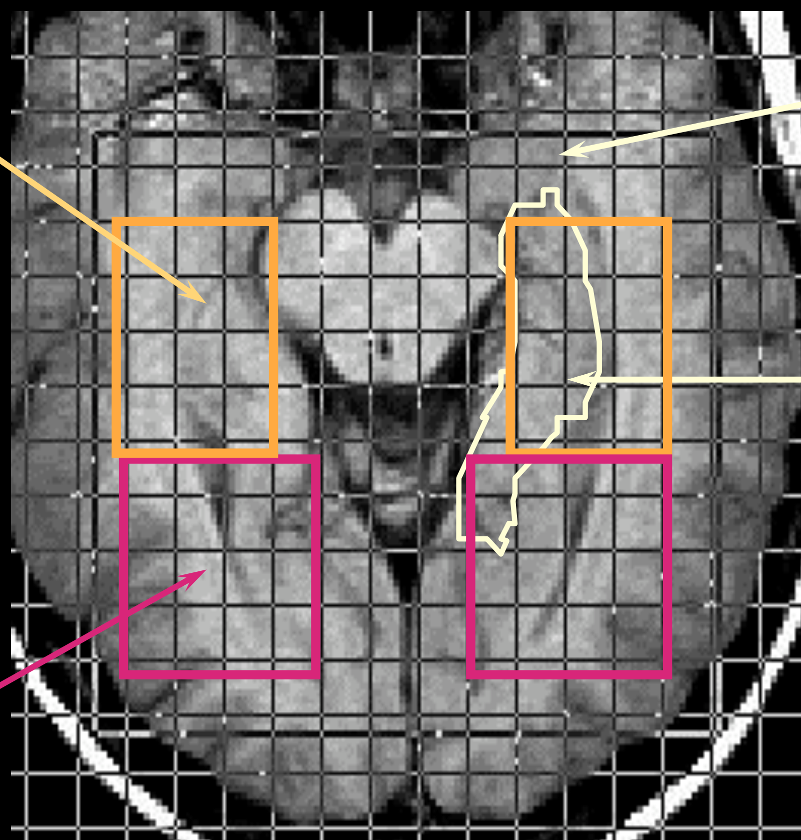
22 yo male



M. Preul

TLE: Regions of Interest

Intermediate Medial Temporal Lobe (Mid):
head and body of hippocampus



Posterior Medial Temporal Lobe (Post):
tail of hippocampus & axonal projections

Lateralization of TLE in 100 patients: Concordance with EEG-clinical findings

Neuroimaging	Abnormal	Lateralizing
AM+HF volumes:	88%	83%
Mid + Post-TL NAA/Cr:	99%	86%
MRSI + MRIVol :	**100%**	**90%**

L. M. Li

Conclusion

- MRS is a valuable tool to probe the chemical composition of the brain
- Provides metabolic information complementary to the structural information provided by MRI
- Powerful tool for research
- Can be diagnostically helpful in specific situations

Acknowledgments

- Douglas L. Arnold, MD
- G. Bruce Pike, PhD
- Nicola De Stefano
- Mark Preul, MD
- Li Li Min, MD
- Joseph P. Hornak, PhD

Questions?