Quantitative MRI and MR spectroscopy of Multiple Sclerosis, Alzheimer's Disease, Epilepsy and Cancer Microimaging Techniques

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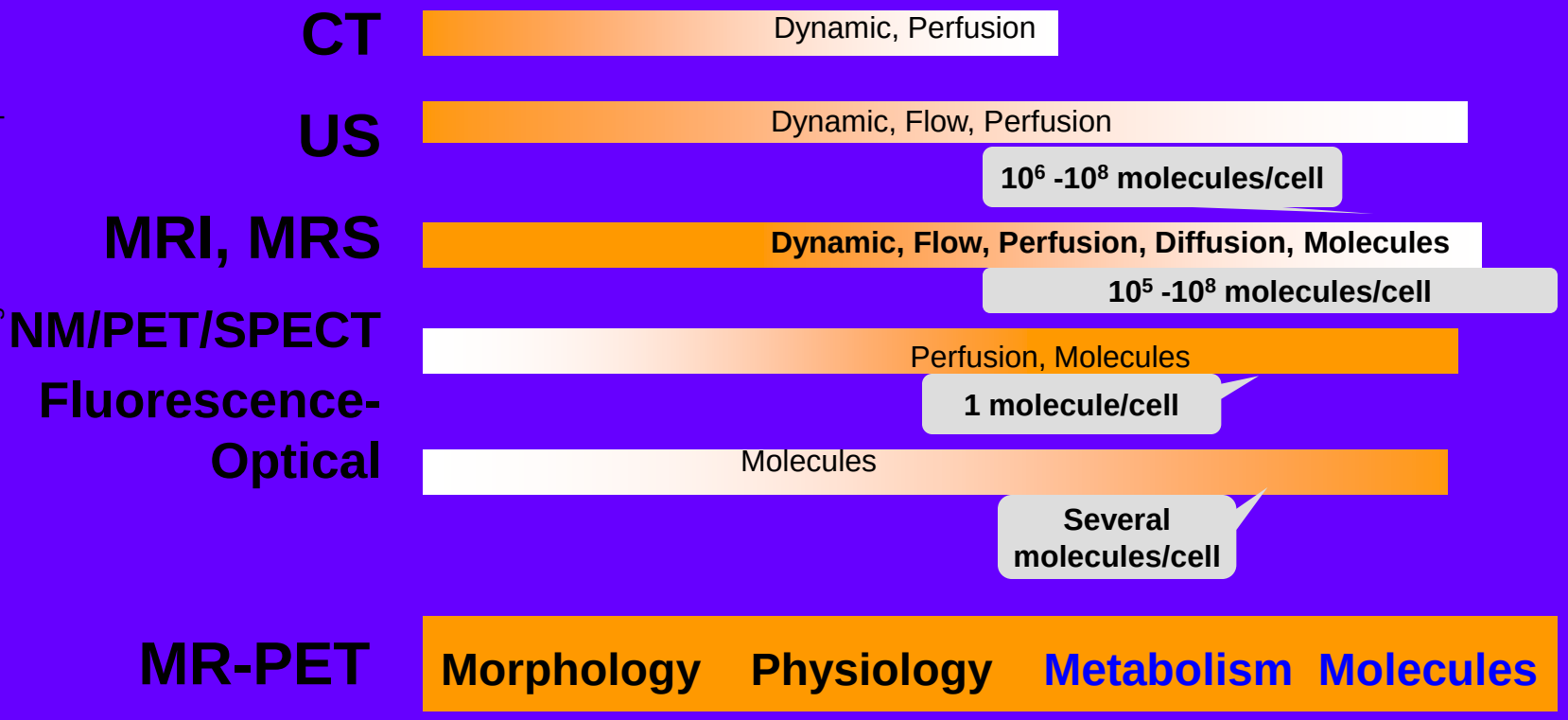
Imaging Combines Molecular Information with Anatomy

Visualization of Biological Processes In Vivo: Imaging Signal



MRI Imaging: Concepts

- **Proton spins resonate with RF pulse in high magnetic field gradients: Slice imaging**
- **High magnetic field α high MRI signal**
  (900 MHz is highest field 21 T MRI magnet at NHMFL)
  (171 MHz is highest field 4 T MRI approved by FDA)
  (64 – 128 MHz is routine 1.5 – 3 T MRI in hospitals)
- **T1, T2, proton density weighting by scan parameters of TE, TR, TI etc.**
- **Quantitative Analysis: Interactive co-analysis by MRI and MR Spectroscopic Imaging measure localized morphometry and metabolism**

Quantitative MRI

Optimized Scan parameters: TR, TE, FOV, NEX, ETL,

- 2D Slice imaging: MSME, DWI, EPI,
- 3DVolume imaging: FLASH, RARE; Factors: ST, SNR
- Dynamic imaging: SENSE, GRAPPA

Registration: Edge-detection, Morphometry-matching

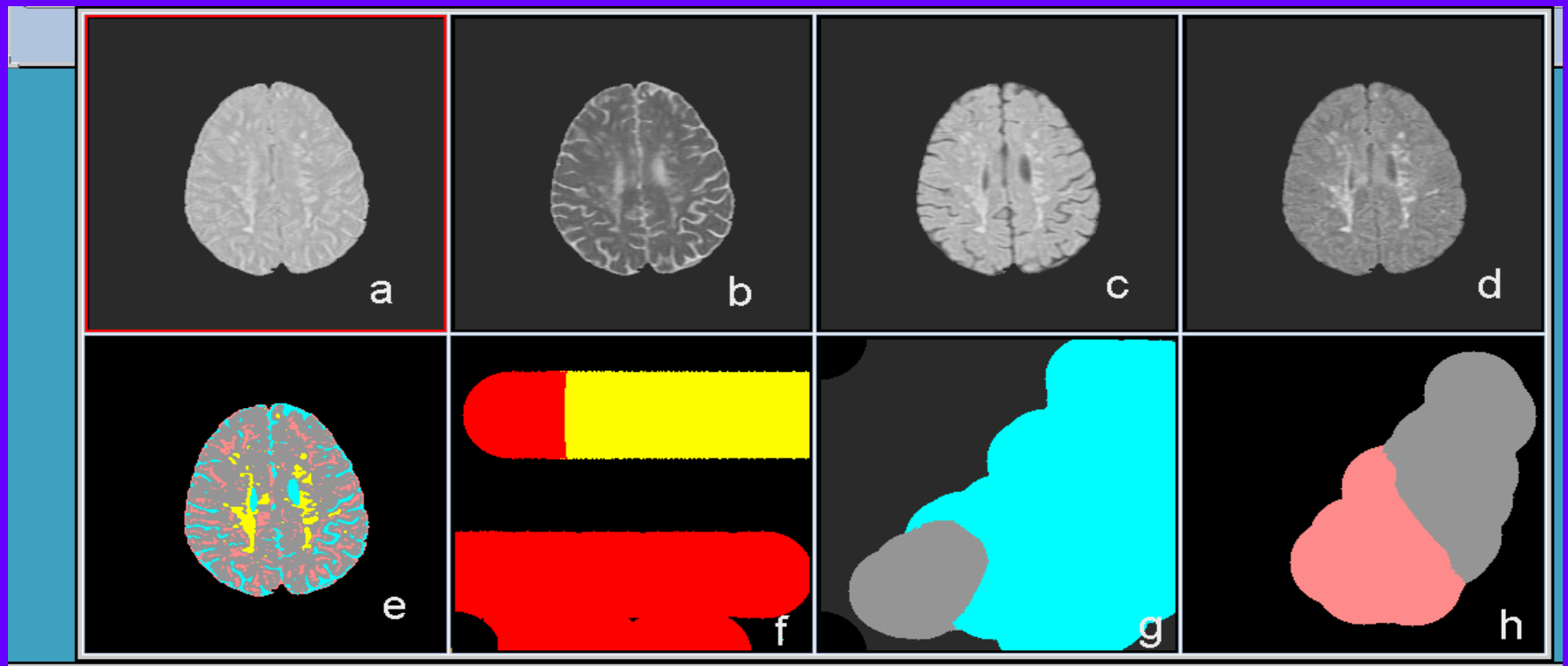
Segmentation: Classification of tissues

Boundary-based; Region-based: Thresholding, Feature plot

- Masking to highlight subtle points
- Manipulation and Analysis: Interactive
- Surface rendering: Surface Formation Contours, Patches, Surface Tracking; Rendering: Hidden-part removal, Shading
- Volume Rendering: Preprocessing Binary volumes, Gray Volumes
- Preprocessing: VOI selection
- Filtering
- Interpolation

Multidimensional display and multiparametric data

Magnetic Resonance Image Analysis Package



2D Feature Map Generation and Setup

	File Path	Display Window	Feature Window Axis #1	Feature Window Axis #2	Intensity Range Axis #1	Intensity Range Axis #2	
eature Map #1:	/opt/mr/lib/segmaps/lesion320.map	6 7 8	3	4	1024	1024	Load Sav
eature Map #2:	/opt/mr/lib/segmaps/csf.map	6 7 8	2	3	1024	1024	Load Sav
eature Map #3:	/opt/mr/lib/segmaps/tissue.map	6 7 8	1	3	1024	512	Load Sav

Image Segmentation Canvas Control

Window #1:	Display Echo #:	1 2 3 4
Window #2:	Display Echo #:	1 2 3 4
Window #3:	Display Echo #:	1 2 3 4
Window #4:	Display Echo #:	1 2 3 4

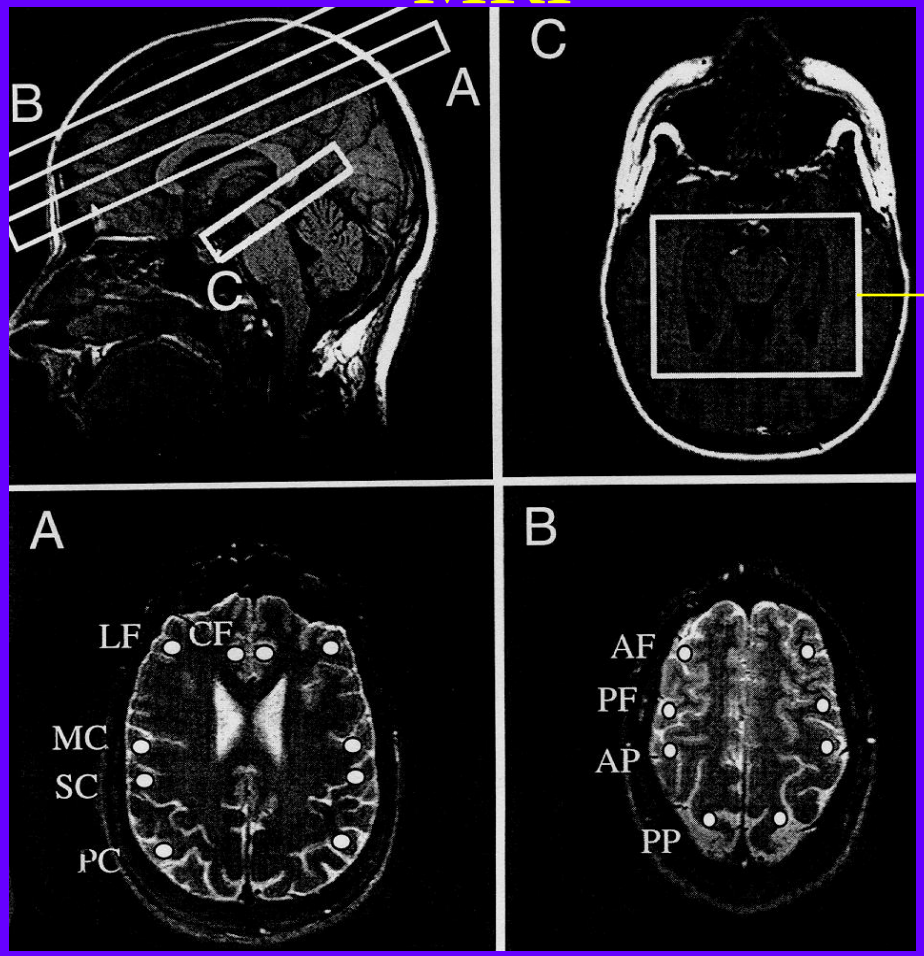
Image Segmentation Main Control

Segmentation Mode:
- Manual -- Paintbrush
- Manual -- Seed Growing
- Manual -- Editing
- Manual -- Erasing
- Supervised
- Automatic
- Contrast Enhancements

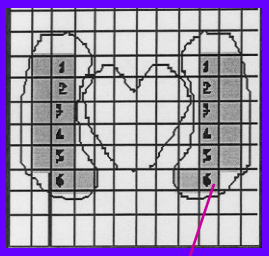
Nature Precedings : doi:10.1038/npre.2009.3485.1 : Posted 28 Jul 2009

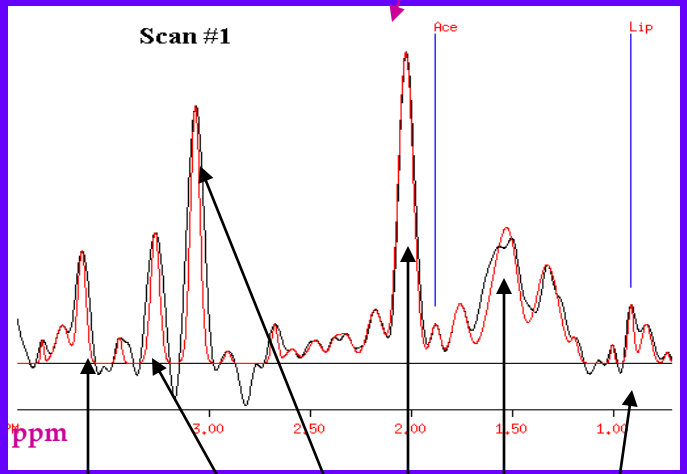
Quantitative MRS + MRI predict Hippocampal Volumes and measure the Neurometabolites

MRI



MRS

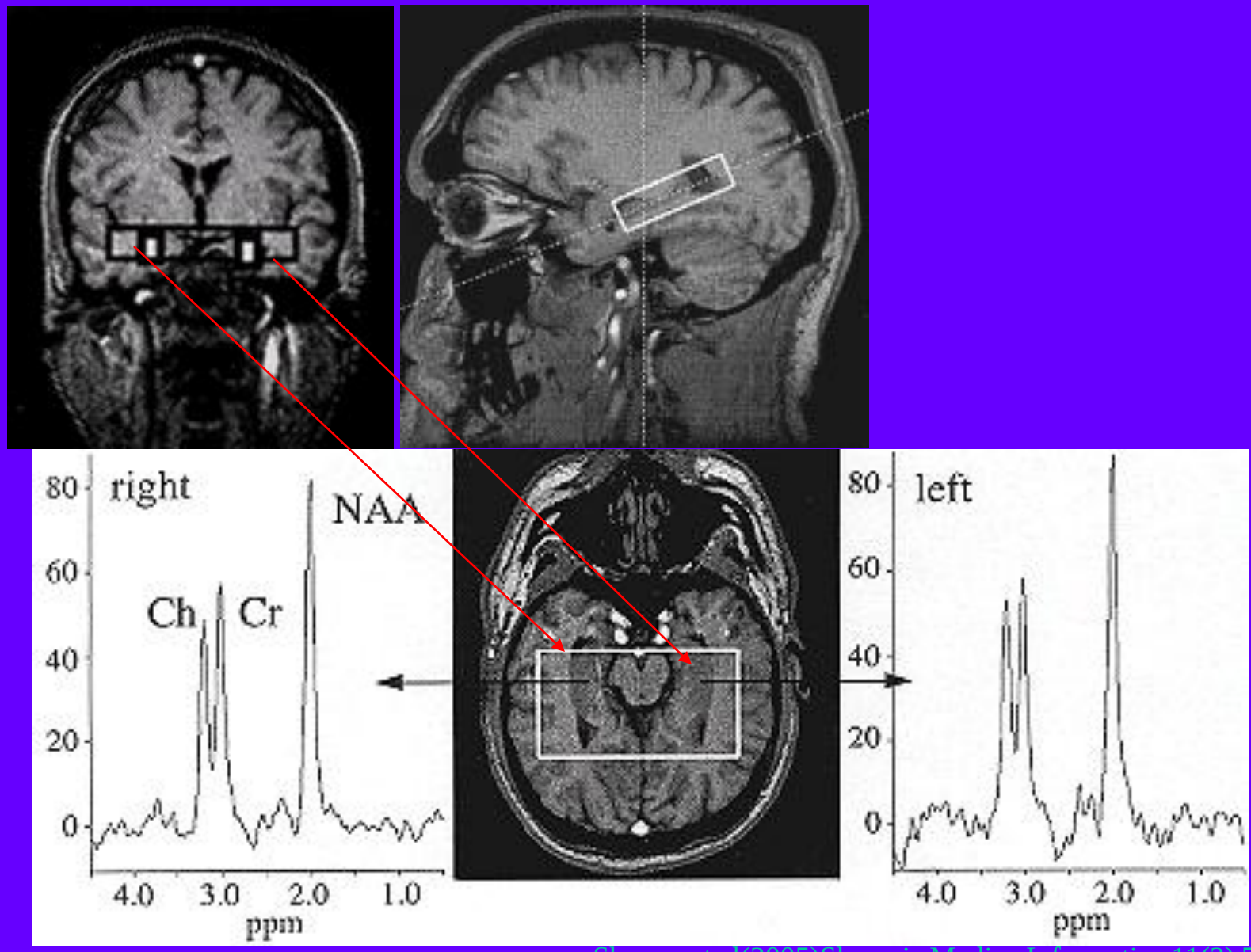




Myoinositol, Choline, Cr, NAA, Lactate, Lipid

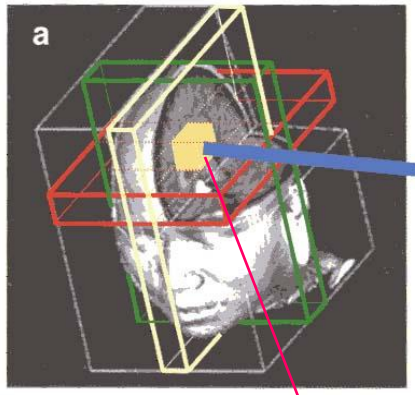
Sharma(2005) Medical Inform. 1(2) 55.

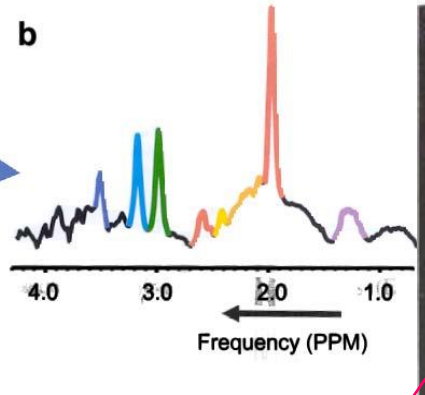
PRESS: H-1 MRS of Hippocampus



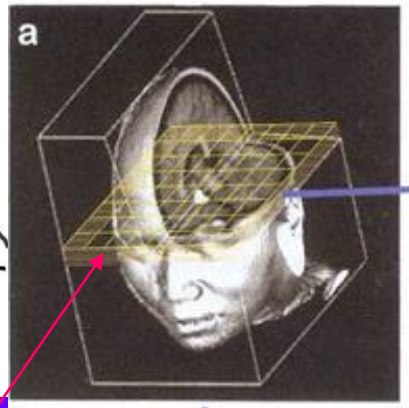
Sharma et al(2005)Slovenia Medica Informatica 11(2) 55-72.

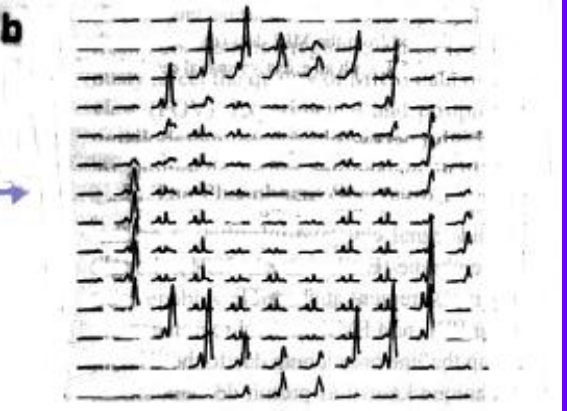
Quantitative MRSI: Slice Selection, Metabolite Maps and CSI imaging





- Selective Single Voxel Spectroscopy(left)
- Single Plane Chemical Shift Imaging

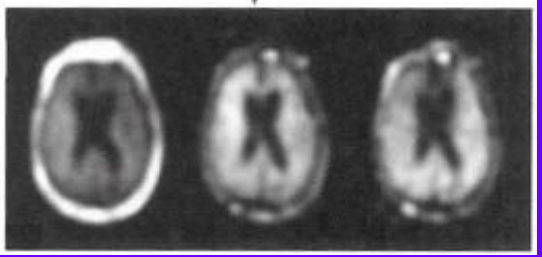




Co-registered MRI

CSI

Image formation

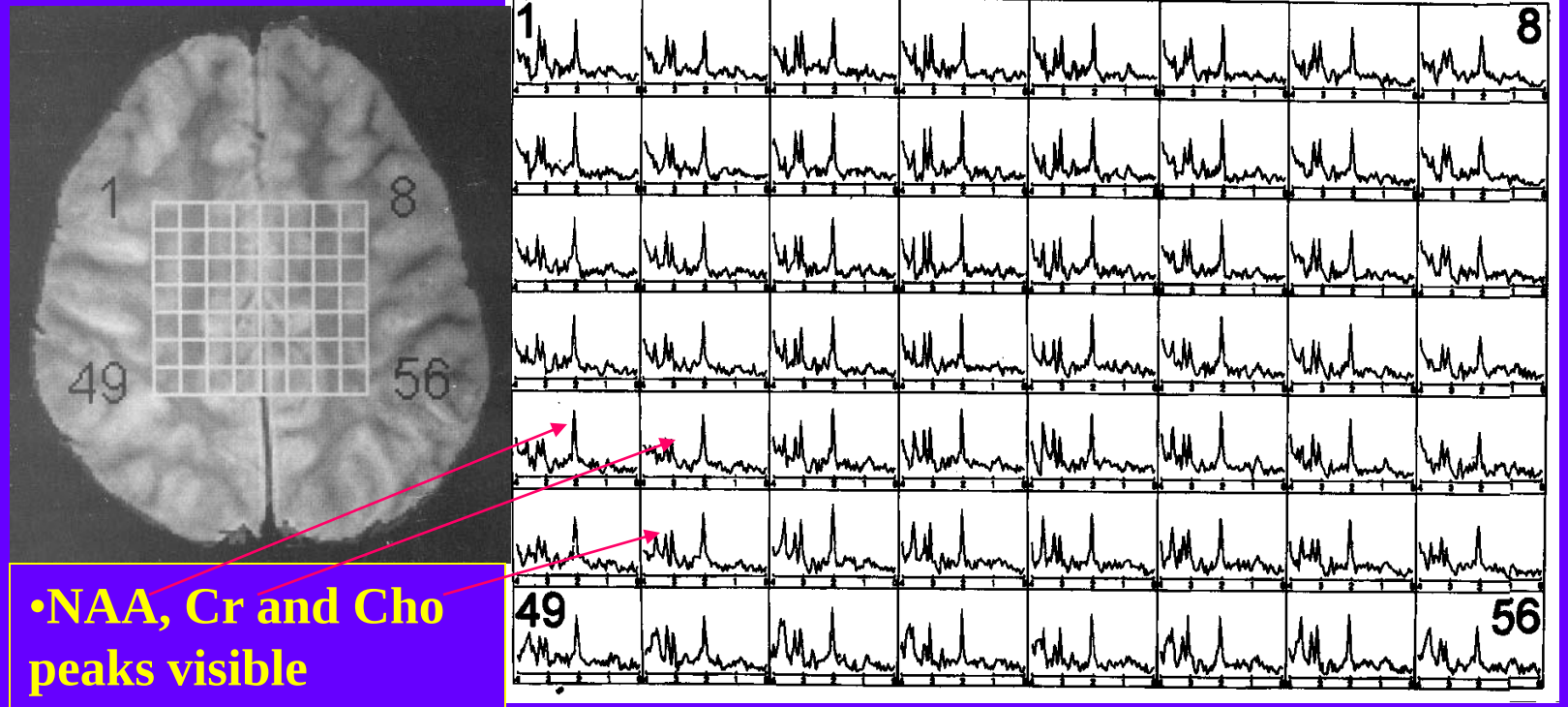


Proton MRI

NAA, Cho, Cr

MRSI

MRS metabolite peaks in Normal Volunteer



- NAA, Cr and Cho peaks visible

Quantitative Proton Magnetic Resonance Spectroscopic Imaging(MRSI) Technique

Data Acquisition:

-In-house developed MRSI sequence (AFFIRMATIVE)

-Prelocalization with stimulated sequence

-Volume-of-interest 90 x 90 x 15 mm^3 with centrum semiovale

-Field-of-view 240 mm^2

-32 x 32 phase encoding steps; TE/TR/NEX=30/1000/1;

-Bandwidth 1000 Hz; data points 256; voxel size 0.8 cc

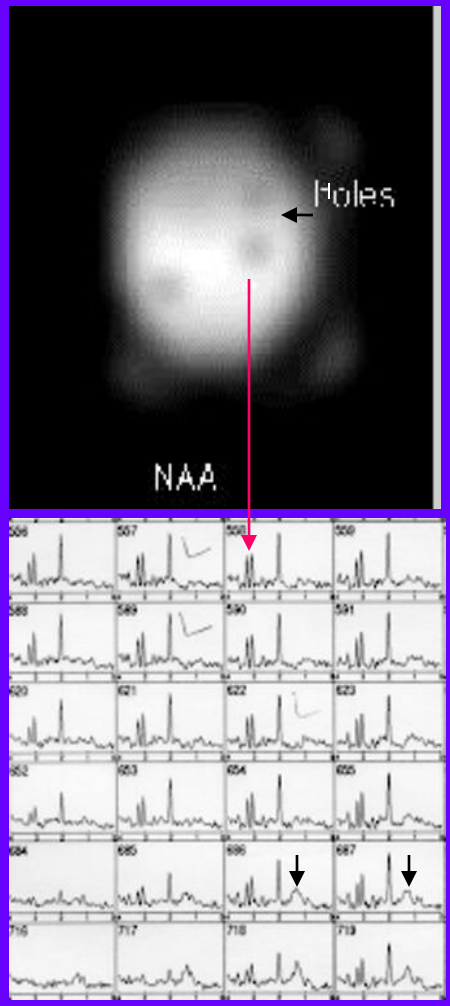


Image Postprocessing

-**O**uter volume suppression for minimizing extramengial lipids

-**V**ariable TR for reducing scan time

-**A**utomatic analysis software (APSIP)

-Spectral analysis

-Metabolic map generation, Segmentation, Co-registration

-**I**nterfacing MRS with MRI by software (MRIAP)

Outcome of Quantitative MRI-SI

•Transfer and storage of MRI scans from various MRI acquisition centers

-Preprocessing per scan, including:

- **-Image sorting**
- **-Inhomogeneity correction**
- **-Noise reduction**
- **-Conversion of image format**
- **-Coregistration**
- **-Database creation and export to SPSS or Excel file**

- **Calculation of number and volume of Gd-enhancing lesions**
- **Calculation of number and volume of T2 lesions**
- **Calculation of number and volume of T1 hypointense lesions**
- **Calculation of brain atrophy, gray and white matter atrophy**
- **Calculation of regional brain atrophy (26 regions)**
- **Calculation of third ventricular width and bicaudate ratio**
- **Calculation of lateral ventricular volume**
- **Calculation of magnetization transfer ratio (MTR) (including WB-MTR, NABT-MTR, NAGM-MTR and NAWM-MTR)**
- **Calculation of regional MTR (26 regions)**
- **Calculation of diffusion tensor imaging (DTI) measures (ADC, FA, entropy) and tractography**
- **MRI Spectroscopy analysis**
- **MRI Iron measures analysis**
- **FMRI analysis**
- **PET-MRI combined analysis**
- **Optic nerve analysis (including determination of lesions, calculation of optic nerve atropy, MTR, and DTI measures)**
- **Spinal cord analysis (including determination of lesions, calculation of spinal cord atrophy, MTR, and DTI measures)**
- **Development of MRI pulse and software programs, web-based programs and slide animations**

MS: Non-Inflammatory GM Lipid Disorder

- Multiple Sclerosis(MS) shows lesions due to demyelinating White Matter disorder
- Occasional presence of GM lesions on MRI
- Multiple Sclerosis is non-inflammatory with lipid-rich Normal Appearing White Matter or Gray Matter (NAWM or NAGM)

1st Example

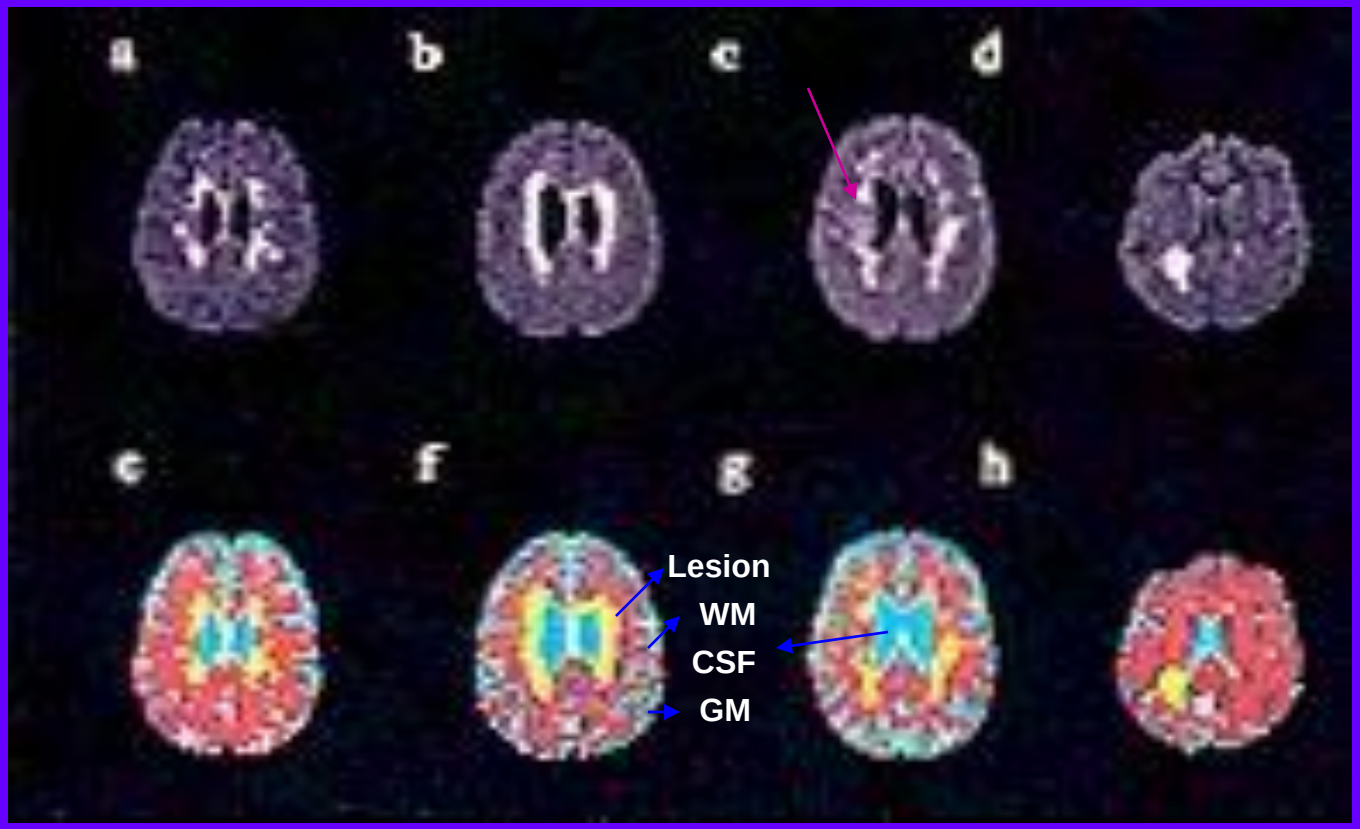
Can we measure MS load by MRI/MRS?

Hypothesis

Lipids accumulate and NAA lost initially followed by amino acid release at lesion sites.

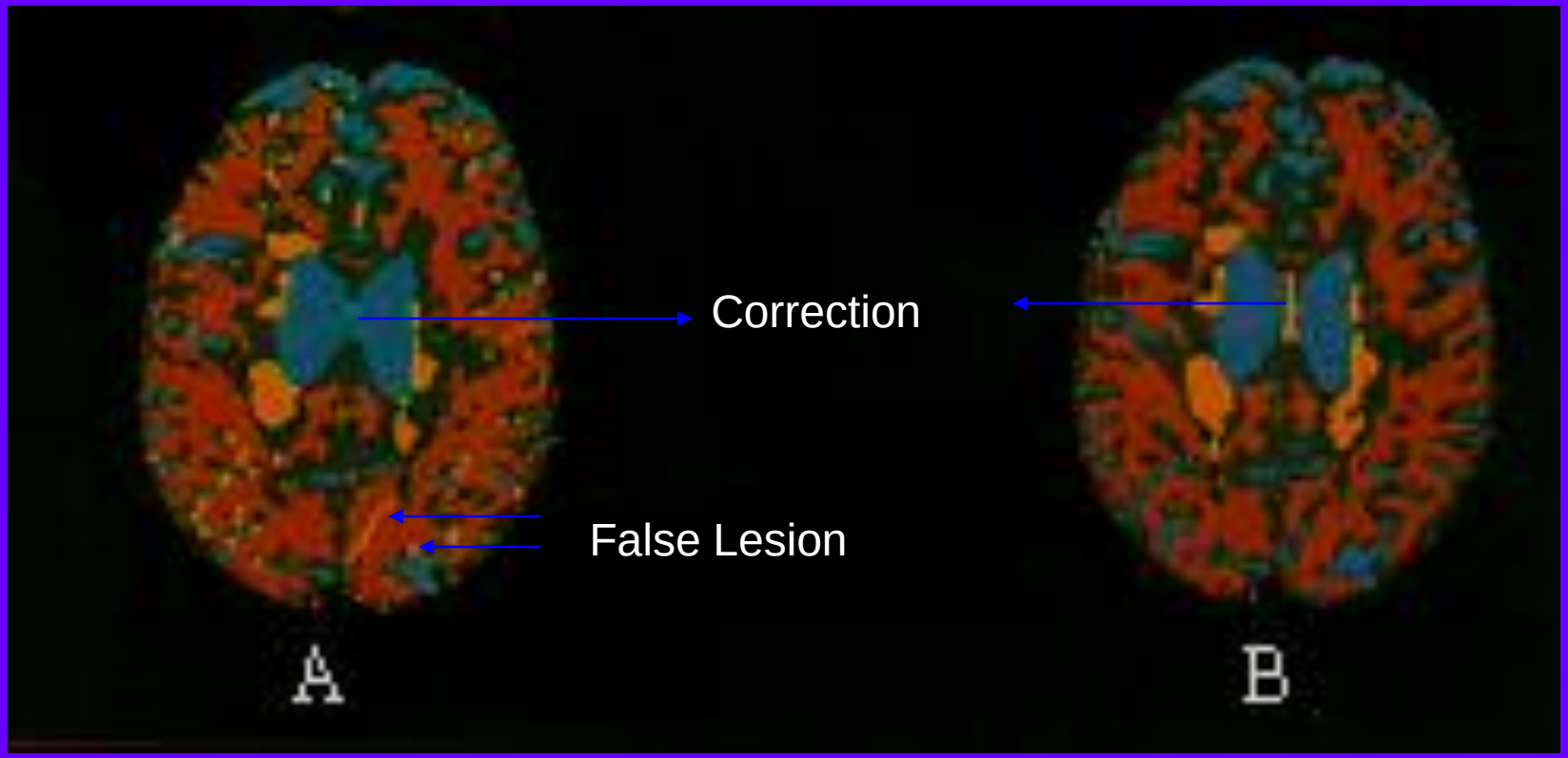
Lesion load: lesion volume and neurochemicals

Automated Tissue Segmentation
(Perzen Non-parametric Method)

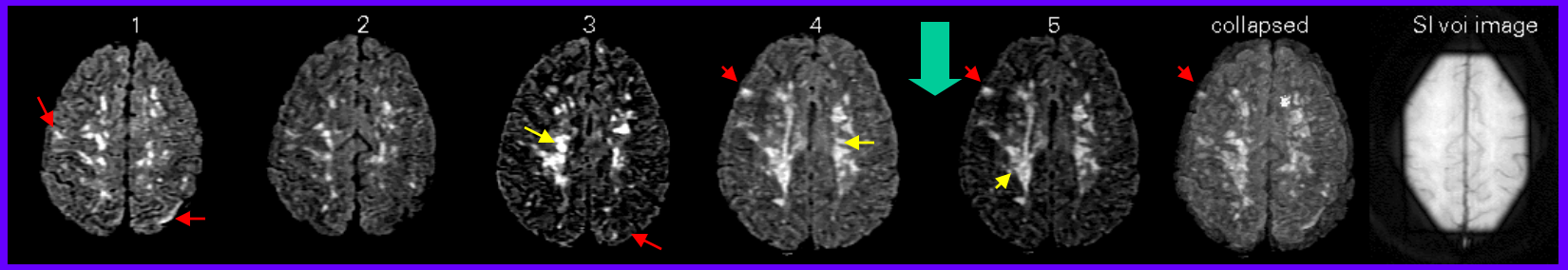


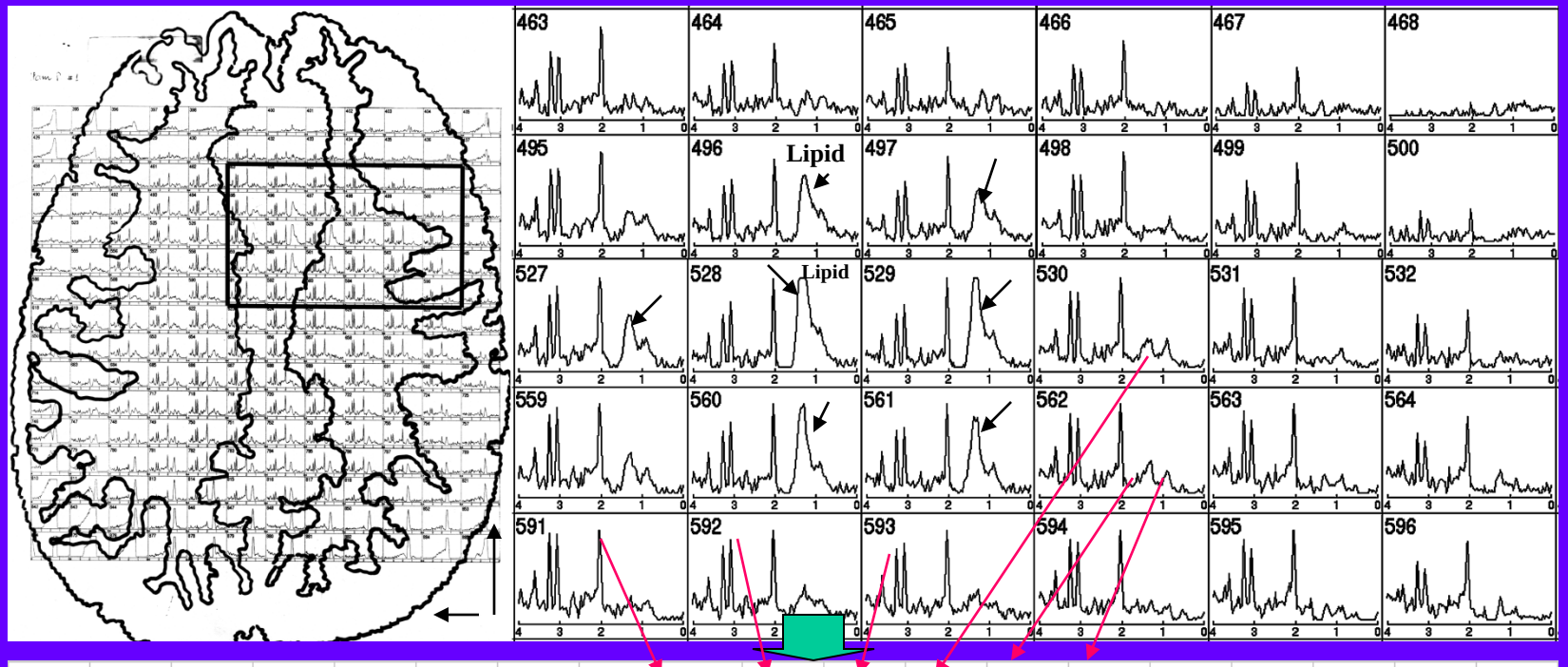
- MRI images at different level (top)
- Different color-coded tissues(GM,WM,CSF, lesion and non-lesion) by supervised training data-set

Feature maps of different regions in MS brain: Minimization of false lesion



PROMISCOL Trial: MS Lesions Showing Abnormal Tissue and Metabolites in WM/GM and NAWM/GM

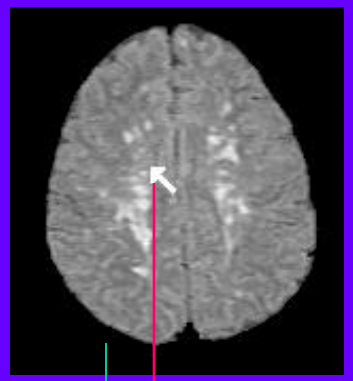




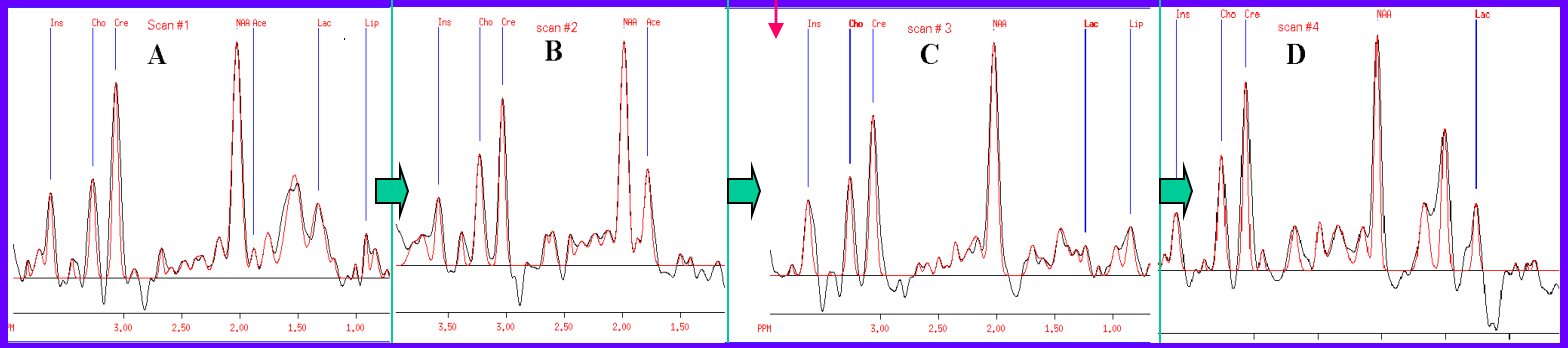
patient	age	sex	scan#	date	voxel	X	Y	NAA	Cr	Cho	Lac	Ace	Lipid	GM	WM	CSF	Lesion
16	35	F	1	101897	460	12	15	381	221	212	145	41	90	0.0025	0.0017	0	0
16	35	F	1	101897	461	13	15	380	249	260	181	34	93	0.0025	0.0017	0	0
16	35	F	1	101897	462	14	15	368	255	251	86	40	75	0.0034	0.0008	0	0.0026

Sharma et al.(2000) IEEE CBMS Proc. 12,87

PROMISCOL® Trial: Time dependent metabolite changes in MS brain

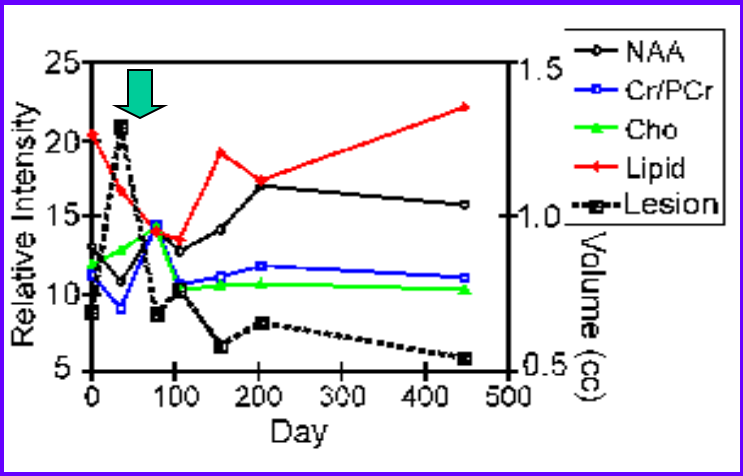


- Brain volume
- Lesion volume
- NAA, Choline, Cr/PCr concentrations



Promiscol:

Reduces lesion burden



Quantitative MRI + MRSI of Alzheimer's Disease

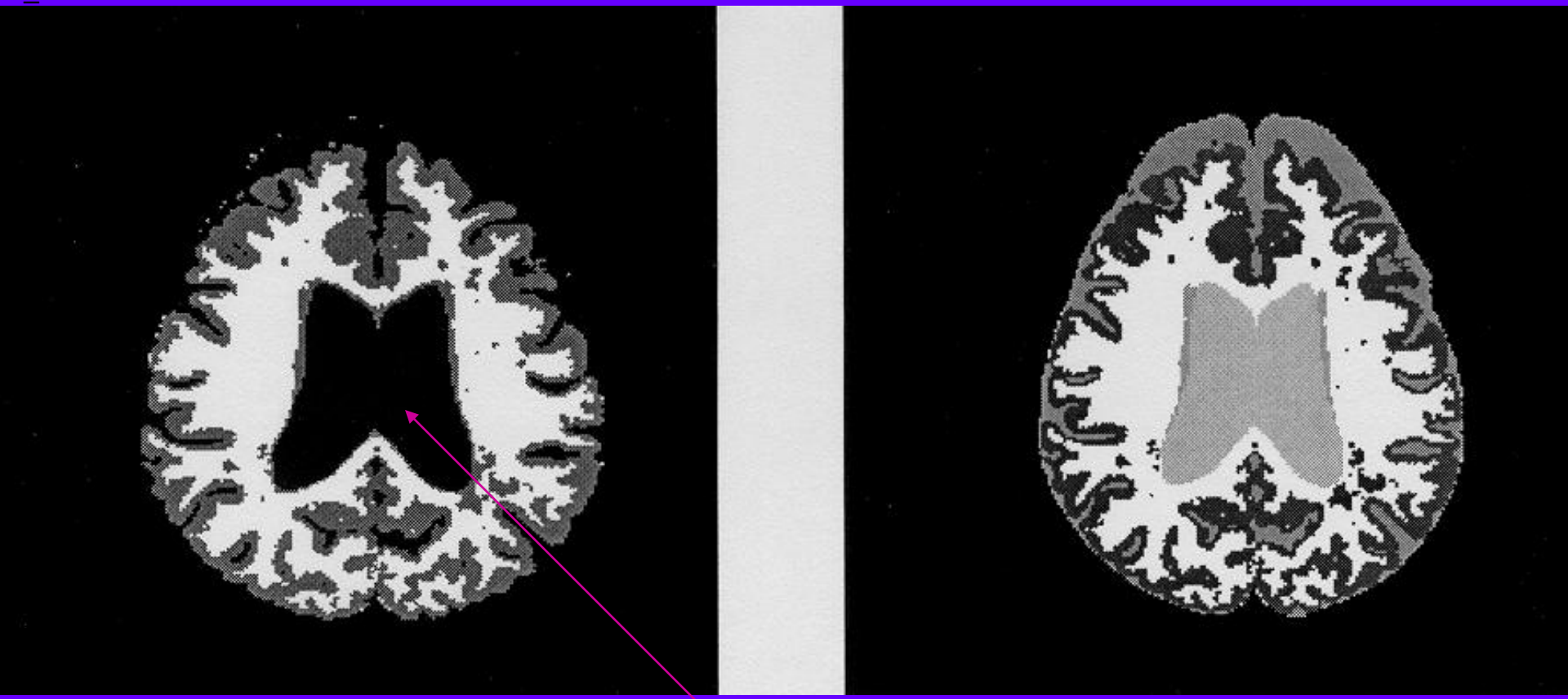
AD: Amyloid plaques, hippocampal atrophy change due to dementia

Hypothesis

MRI combined with MRSI characterize & measures the disease better

2nd Example

Tissue MRI segmentation
(supervised K-NN cluster method)



AD: Gray matter loss and viscous CSF

Sharma (2002) Adv. Segmentation Chapter 7,187

MRSI: Metabolite* distribution and tissue content in AD

Metabolite –	AD	Control	% Diff
NAA(mM)			
Right	7.55 ± 0.5	10.01±0.6	13.2
Left	7.61 ± 0.4	9.82 ±0.9	22.6
Cho(mM)			
Right	2.02 ± 0.7	2.08 ± 0.2	2.9
Left	2.04 ± 0.4	1.89 ± 0.5	7.4
Cr(mM)			
Right	7.02 ± 0.6	7.75 ± 0.5	9.4
Left	7.96 ± 0.6	7.49 ± 0.8	5.9

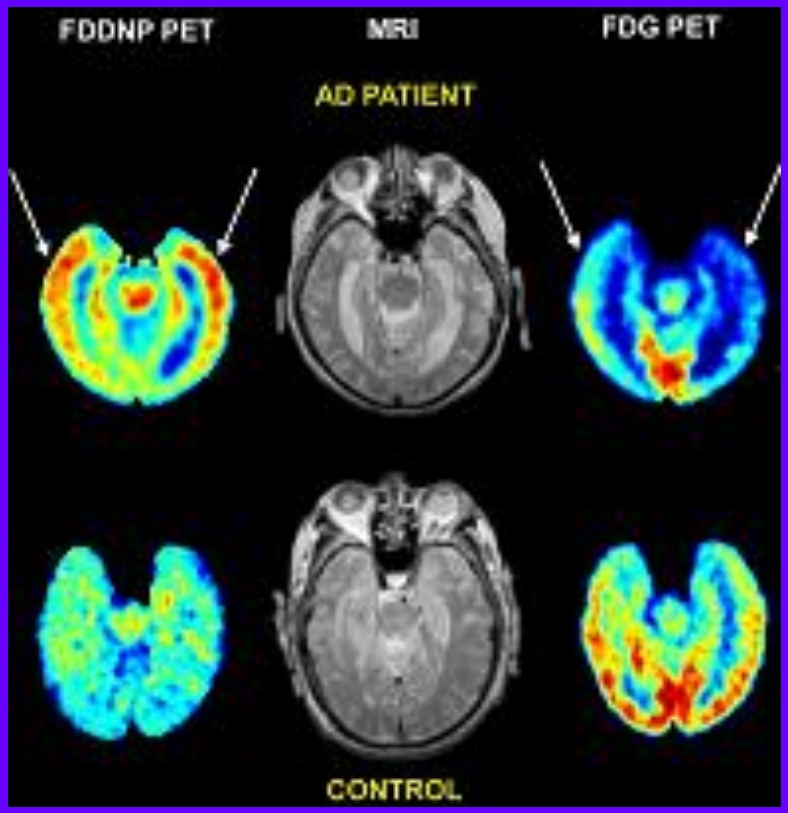
Metabolite ratio	AD	Control	% Diff
NAA/Cr			
Right	1.08 ±.06	1.39±.03	20.8
Left	0.96 ±.04	1.31±.02	26.7
NAA/Cho			
Right	3.74 ±.07	4.81±.09	22.2
Left	3.73 ±.03	5.1±.06	26.9
@ Tissue content ρ (%)			
Right	84 ± 3	98± 2	14.3
Left	87 ± 3	96 ± 3	0.93
Gray matter index (f)			
Right	0.45 ± 0.03	0.55 ± 0.05	18.2
Left	0.62 ± 0.02	0.62 ± 0.04	n.s.

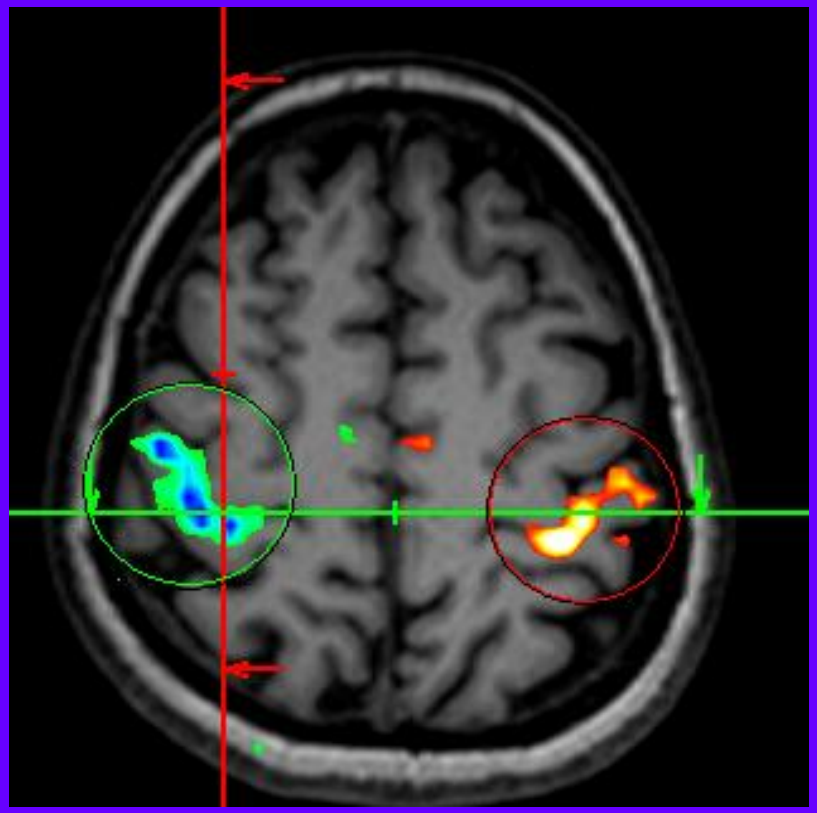
*Atrophy corrected metabolite concentrations of NAA, Cho, and Cr and NAA/Cr and NAA/Cho ratios from right and left hippocampus in AD patients and control subjects.

@Tissue content ρ (in percent of the MRSI voxel volume) and gray matter index (f) of the MRSI voxels positioned at right and left hippocampus, characterizing MRSI partial volume effects.

Sharma (2002) Adv. Segmentation Chapter 7.187

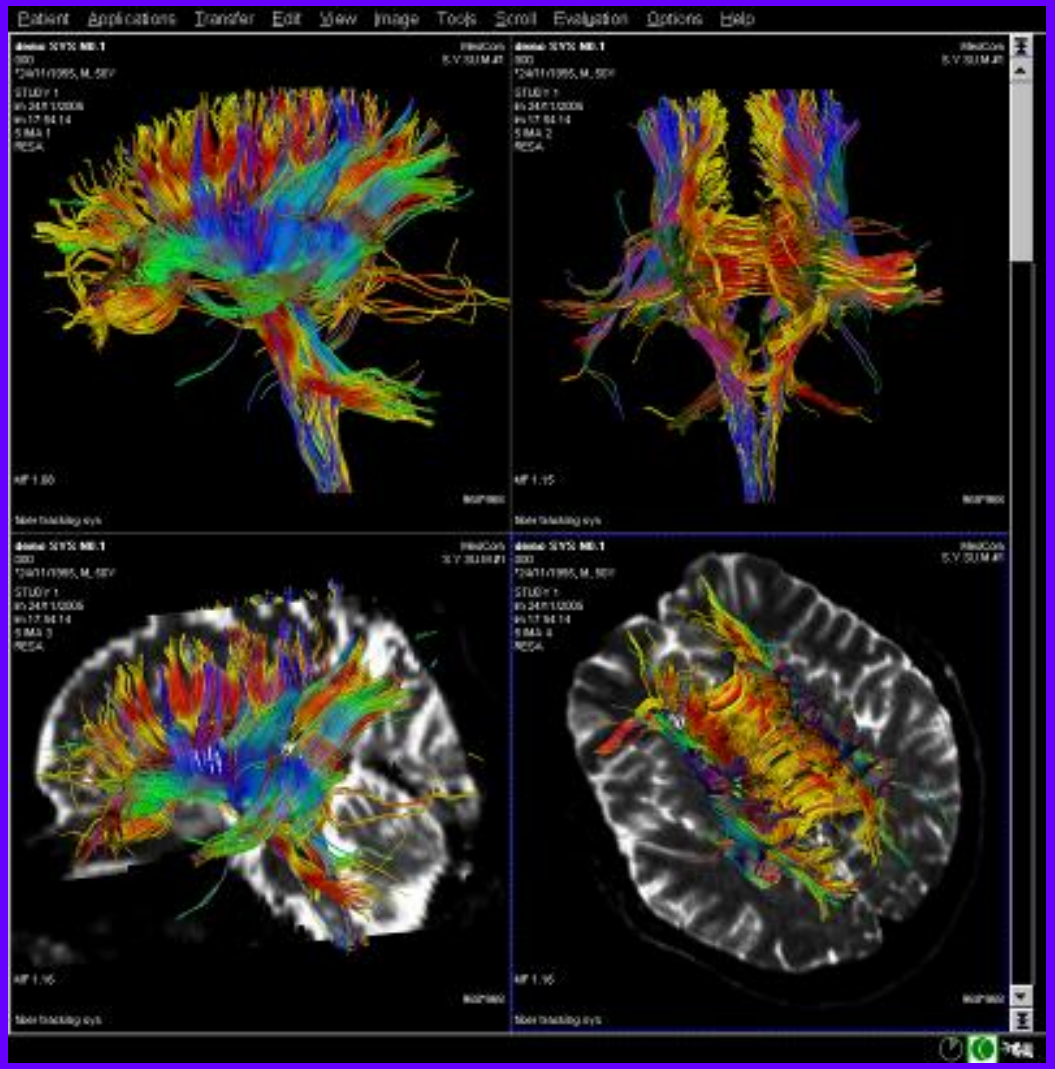
AD: Where are sites of poor glycolysis?





Poor Glucose metabolism in both Temporal sites due to amyloid plaques

Anisotropy for Fiber Tracking: Precursor of Alzheimer's disease ?



MRI+MRSI Predicts Better Tissue Composition and Volume in AD

	AD	Control	% diff.
HP-volume(mm^3)			
Right	1982 ± 134	2884 ±102	31.1
Left	1868 ± 88	2943 ± 86	36.5
Ventricular CSF(%)	4.2 ± 0.3	2.8 ± 0.3	33.3
Sulcus CSF (%)	23.4 ± 2	18.2 ± 0.5	22.2
White Matter(%)	35.2 ± 0.9	38.1 ± 0.8	7.6
Cortical GM(%)	38.8 ± 1.1	42.2 ± 0.6	8.0
Subcortical GM(%)	1.2 ± 0.08	1.4 ± 0.03	n.s
TIV(cm^3)	1342 ± 5	1402 ± 52	n.s.
FDG-PET+MRI			
Asymmetry Index > 3	12	0	
NAA/(Cho+Cr)	1.2	5.4	
AI > 12 %	7	1	

Sharma et al.(2003)Medica Inform. 3(4) 386

MRI + MRSI: Epilepsy

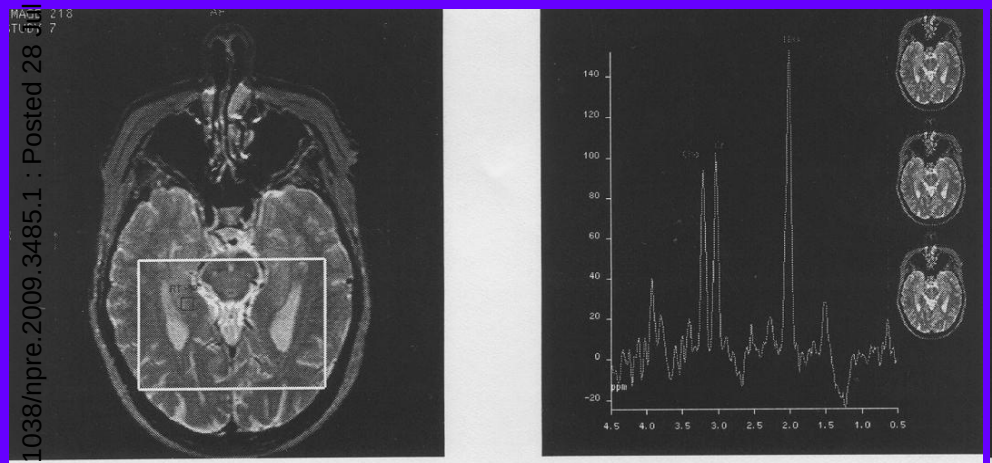
- Neocortical Epilepsy
- Mesial Lobe Epilepsy
- Post-operative Mesial Lobe Epilepsy

3rd Example

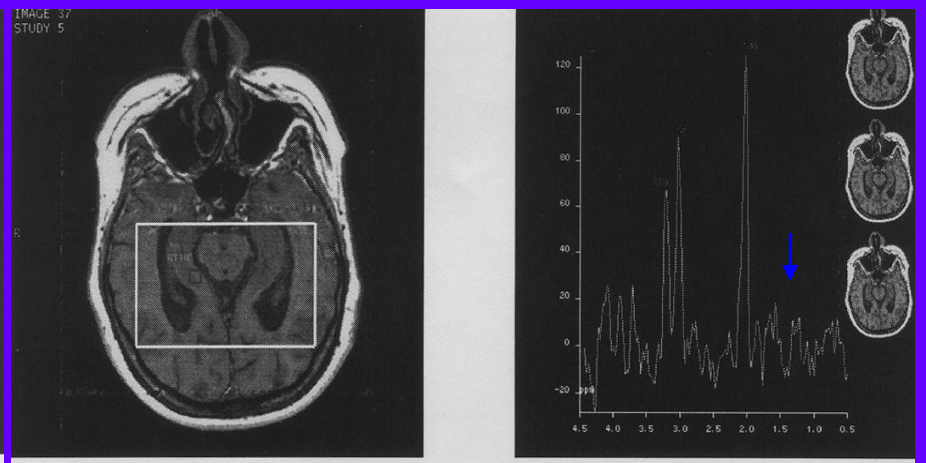
Combined (multislice MRI+ PRESS MRSI) in mLE

- Unilateral mTLE (ipsilateral side)
- PRESS volume pre-selection on hippocampus(TR/TE=1800/140 ms; voxel 9 x 9 x 15 mm^3); circular K-space encoding of 24 points
- Multislice (TR/TE=1800/140 ms; voxel 8 x 8 x 15 mm^3); circular K-space encoding of 36 points

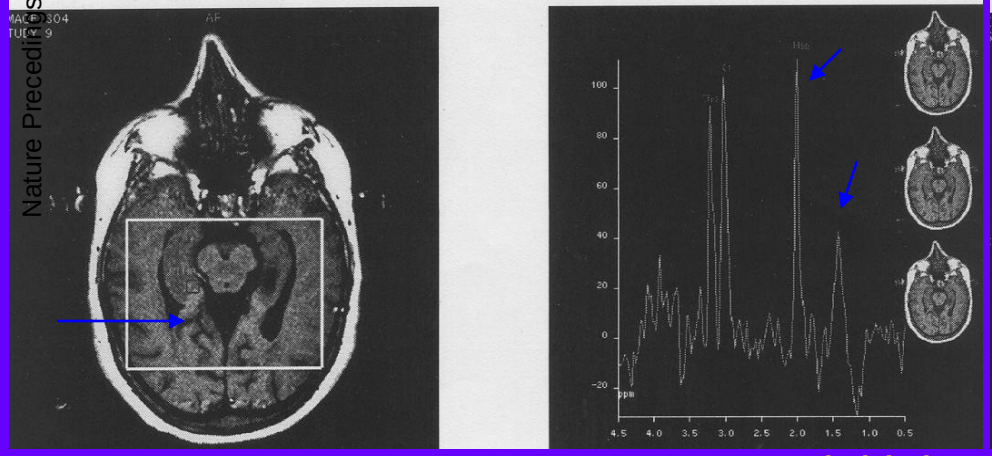
Hippocampus Volume Reduction and PRESS-MRS Lipids and Choline

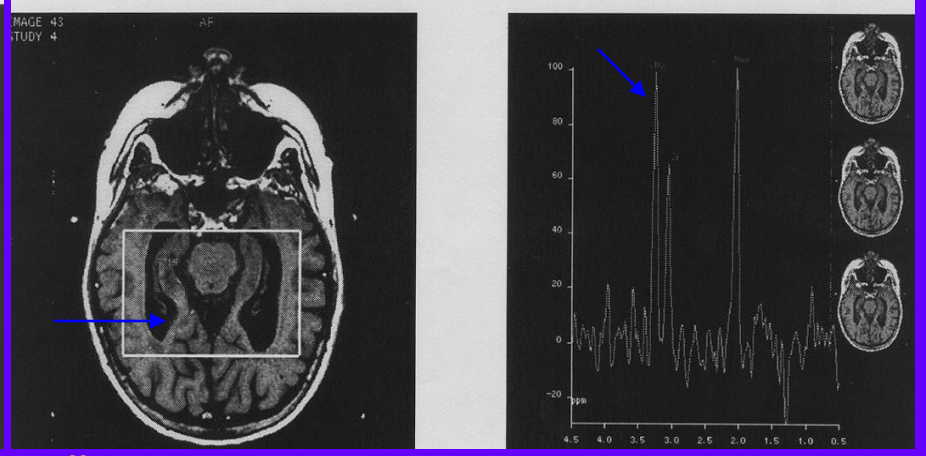


(A) Control (B)



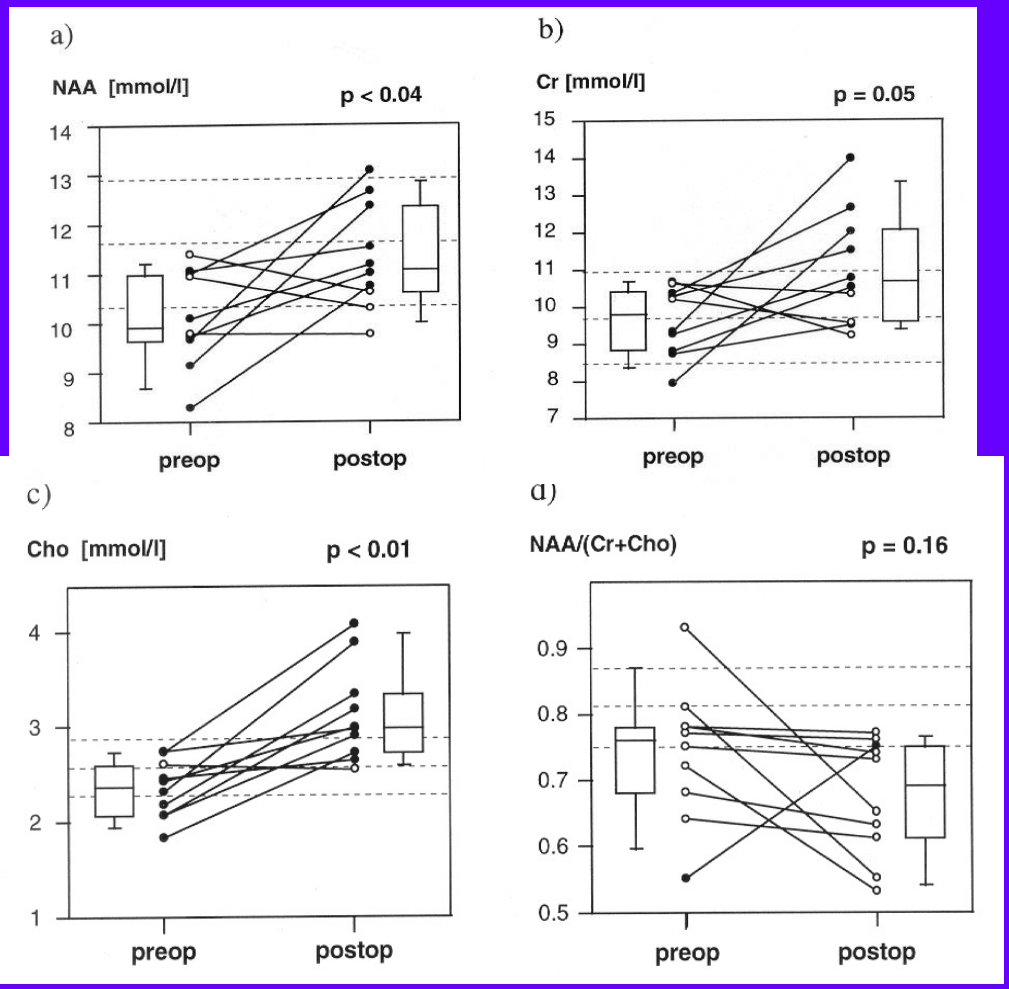
(A) Control (B)





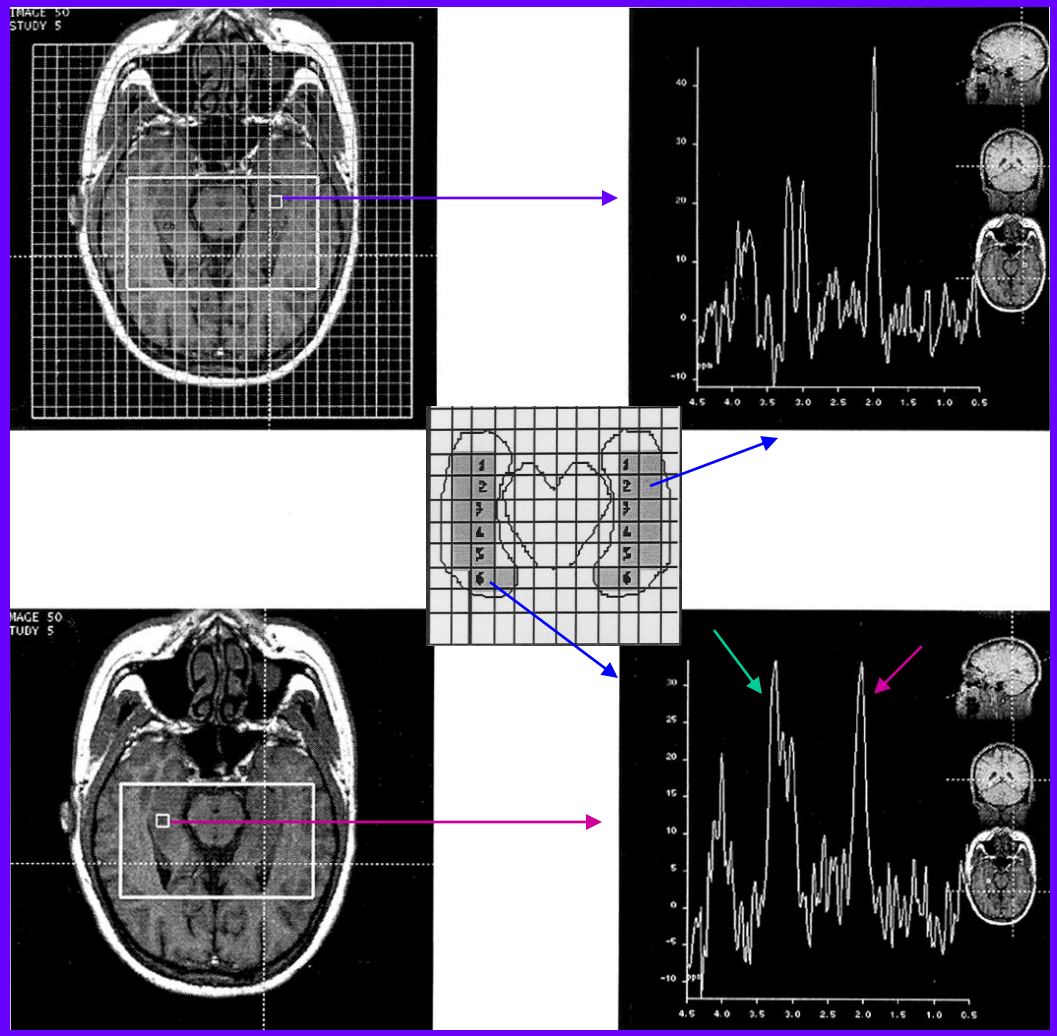
Mesial lobe Epilepsy

MRSI: Metabolites in Pre-op vs post-op Epilepsy

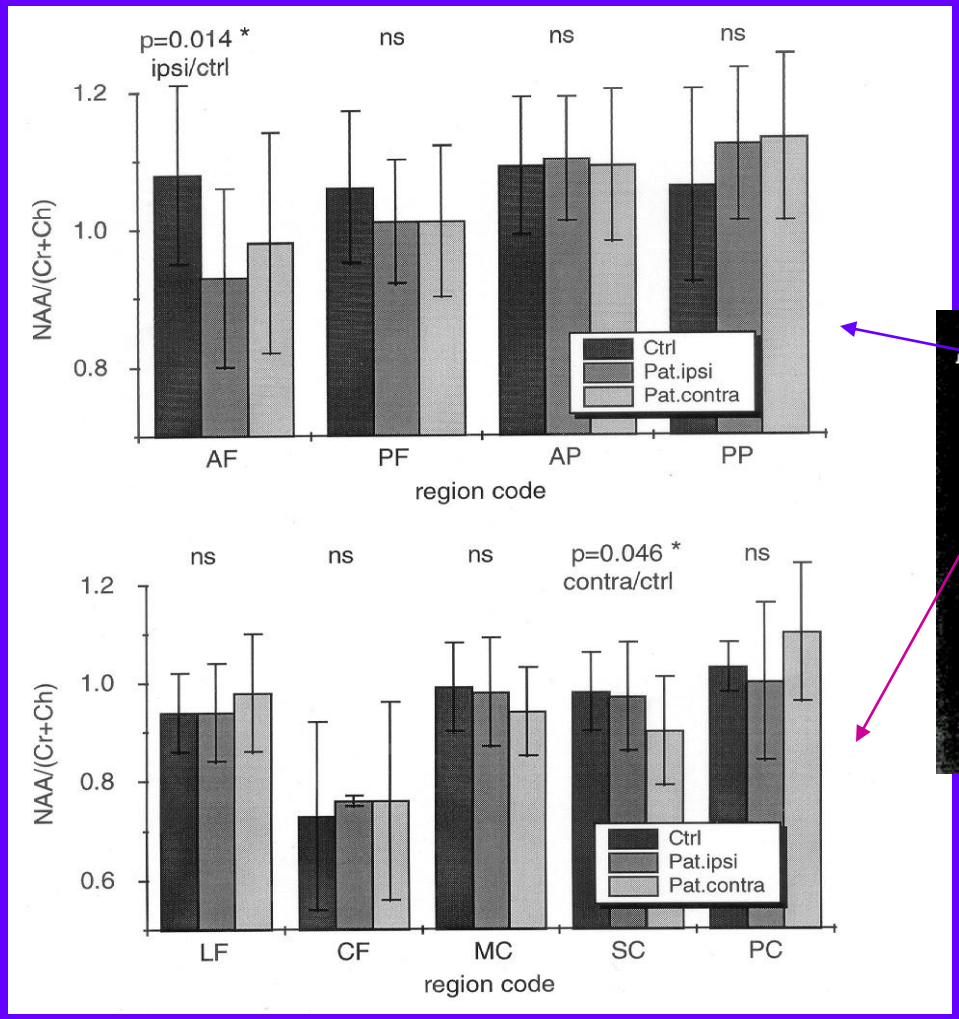


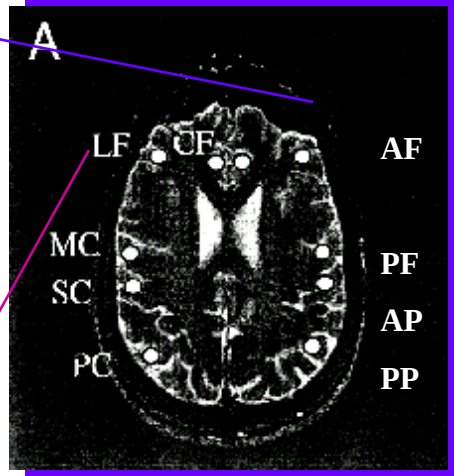
Sharma et al (2005) Slovenia Medical Informatica,3(4)686

Neurochemicals by MRS lateralize Hippocampus in Mesial Lobe Epilepsy



NAA/(Cr+Cho) in Control vs Epilepsy ipsi- and contra-lateral sides at different brain regions





Sharma et al (2003) Slovenia Medical Informatica 3(4) 686

CONCLUSION 1

- **Gray Matter and Normal Appearing Gray Matter and White Matter regions in MS are abnormal and measurable**
- **Neurochemicals in AD, Epilepsy suggest the utility of MRI and MRS → to confirm**

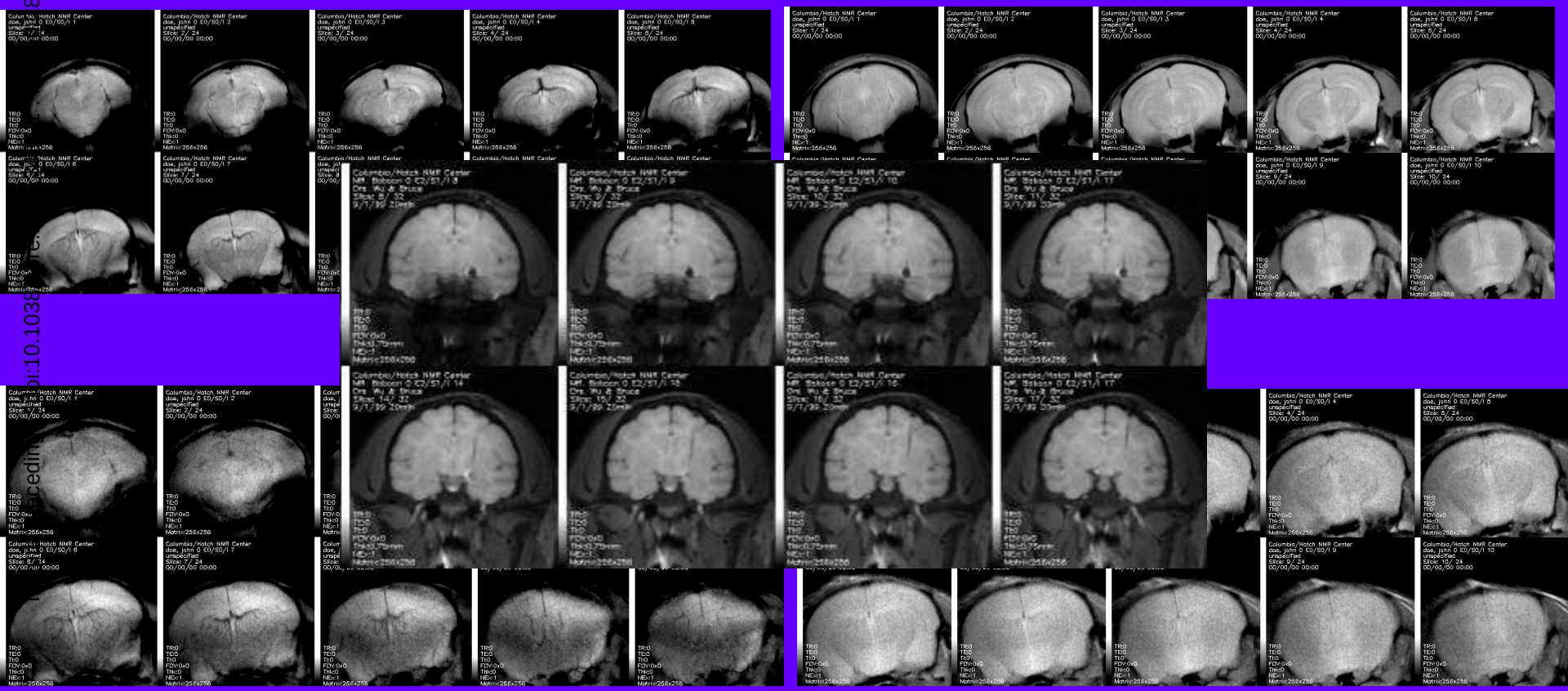
  hippocampus volume heterogeneity and regional (tissue composition and neurochemical) differences due to neuronal dysfunction in brain

Outcome of MRI +MRSI

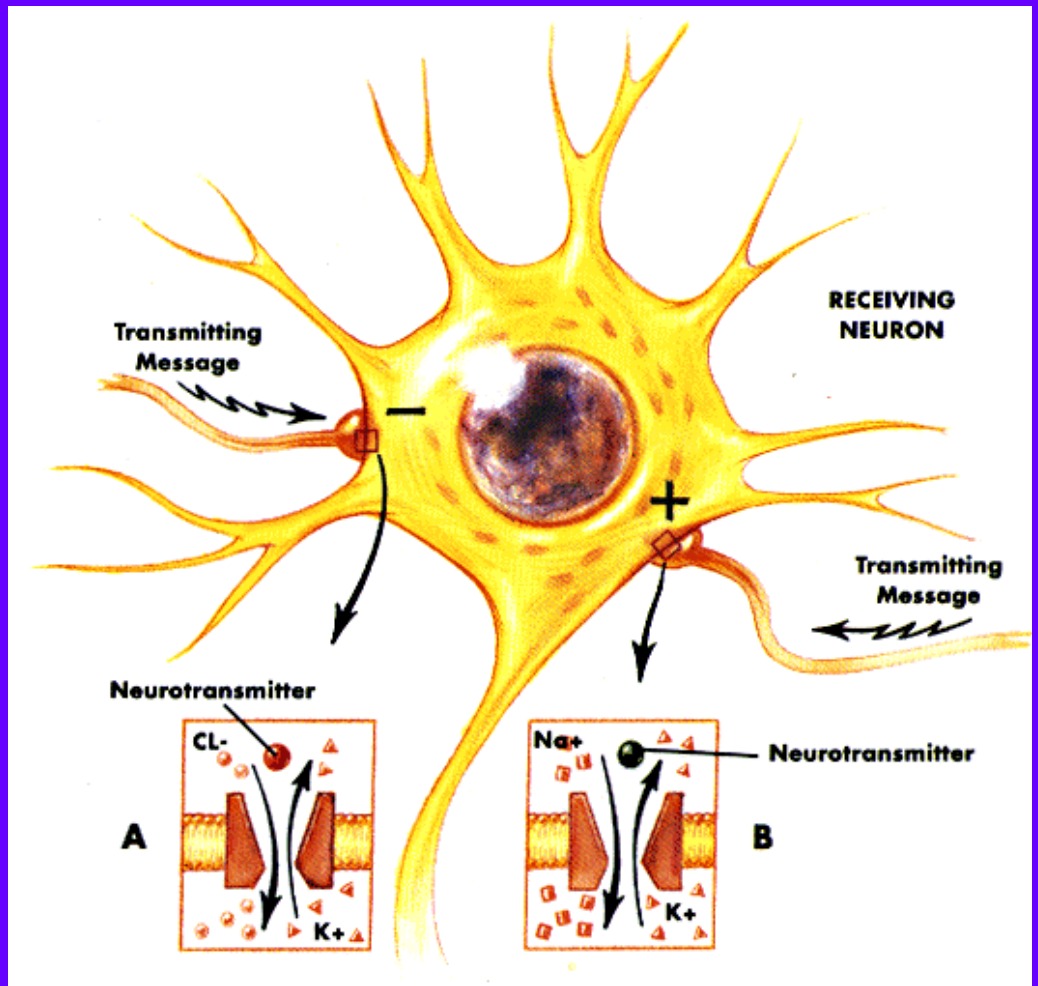
- Metabolites measure optimum lateralization
- Decreased NAA to hippocampus atrophy
- Bilateral abnormalities by asymmetry index
- Relationship of MRS peaks with post-op surgery seizure condition (bilateral abnormalities)
- Lateralization and discordance of lobes:

  Atrophy; HV;T2; NAA; NAA/(Cho+Cr)
- Multi-slice MRI approach for better Asymmetry Index

Maccaque Monkey Brain images by 5 Tesla Clinical Imager



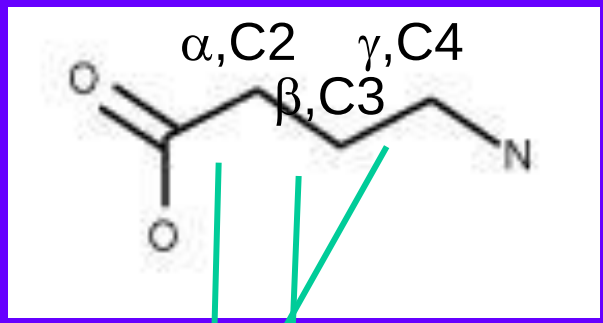
Detection of GABA, an inhibitory neurotransmitter

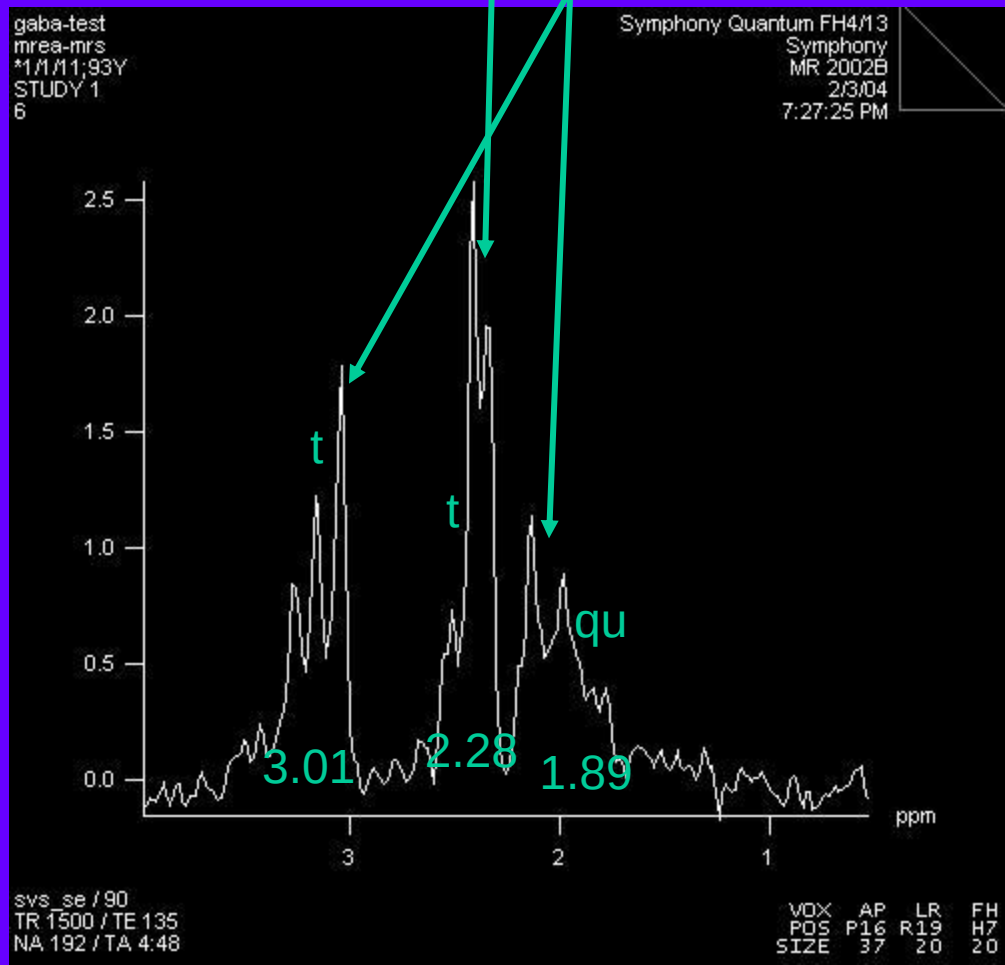


4th Example

The GABA molecule

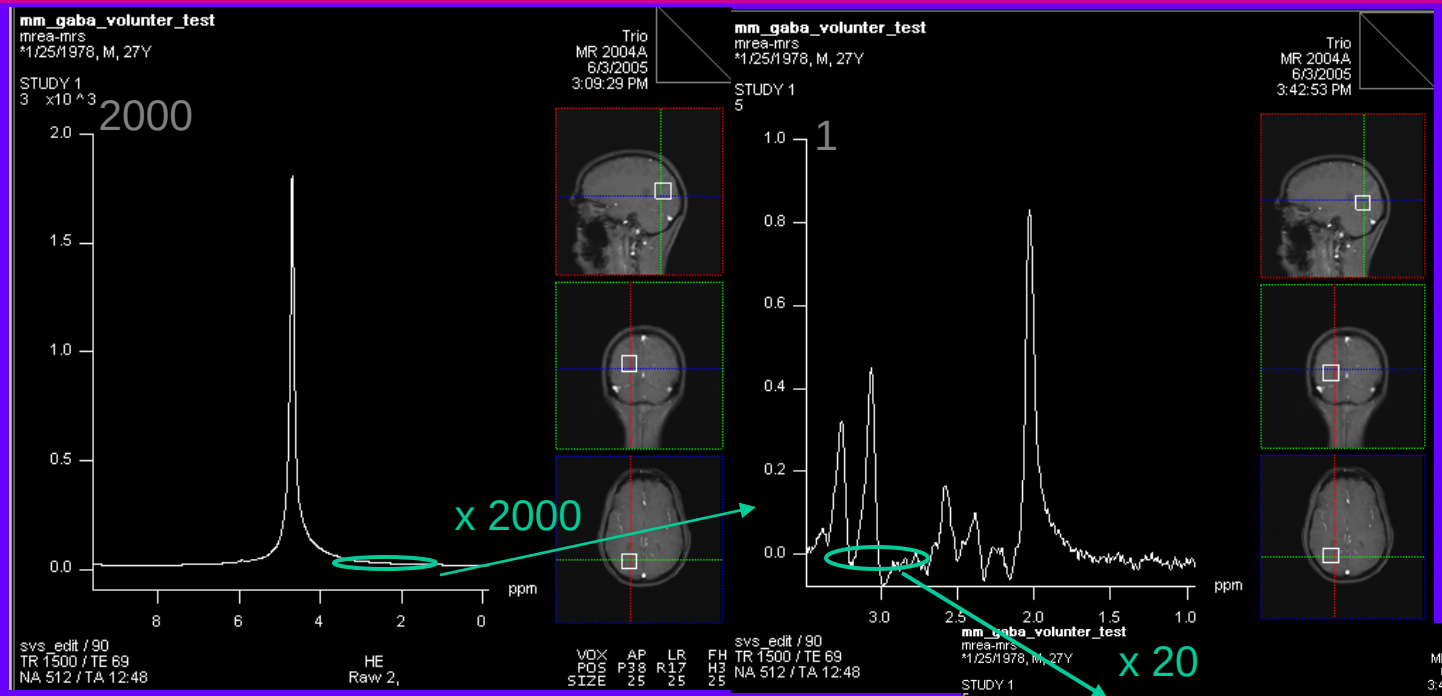
- **γ-Amino butyric acid: $C_4H_9NO_2$**
- **methylene groups form $A_2M_2X_2$ system**
- **γ and β protons are weakly coupled, A_2X_2**
- **J = 7.3 Hz**





The challenge of GABA detection

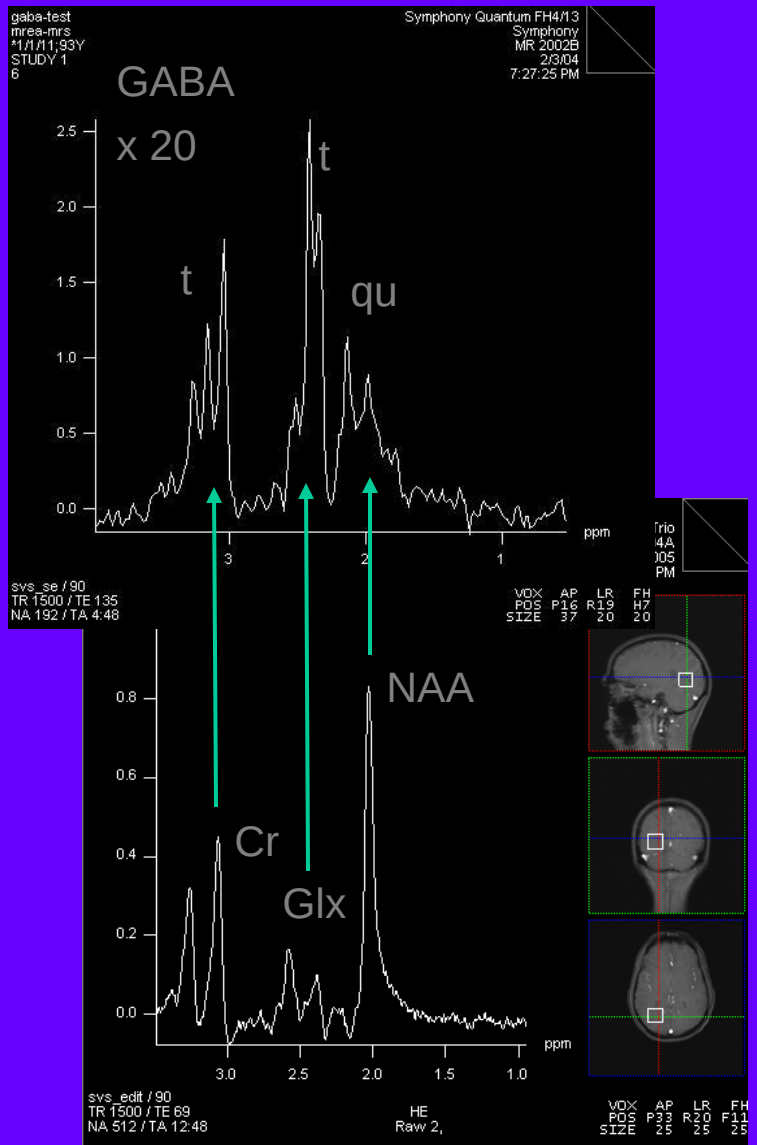
Nature Precedings : doi:10.1038/npre.2009.3485.1 : Posted 28 Jul 2009



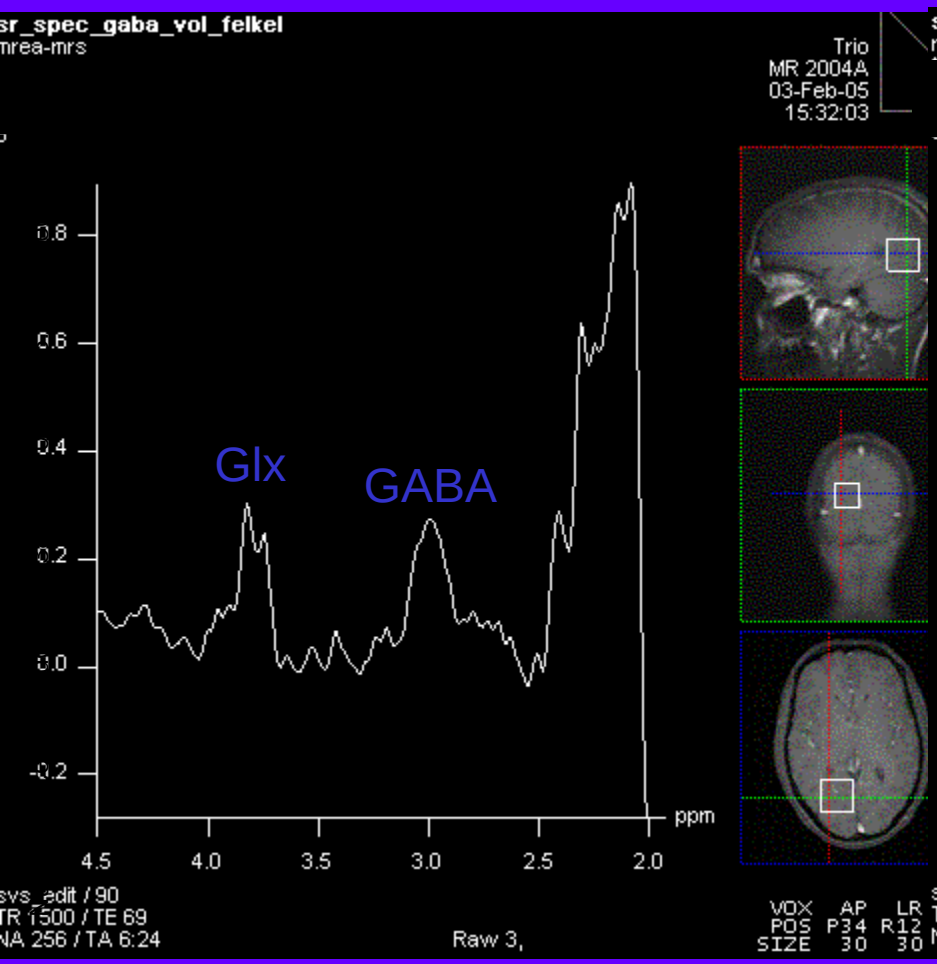
- GABA conc. in the healthy right occipital cortex: 1.0 mM
- Signal 40.000 times smaller than water proton signal

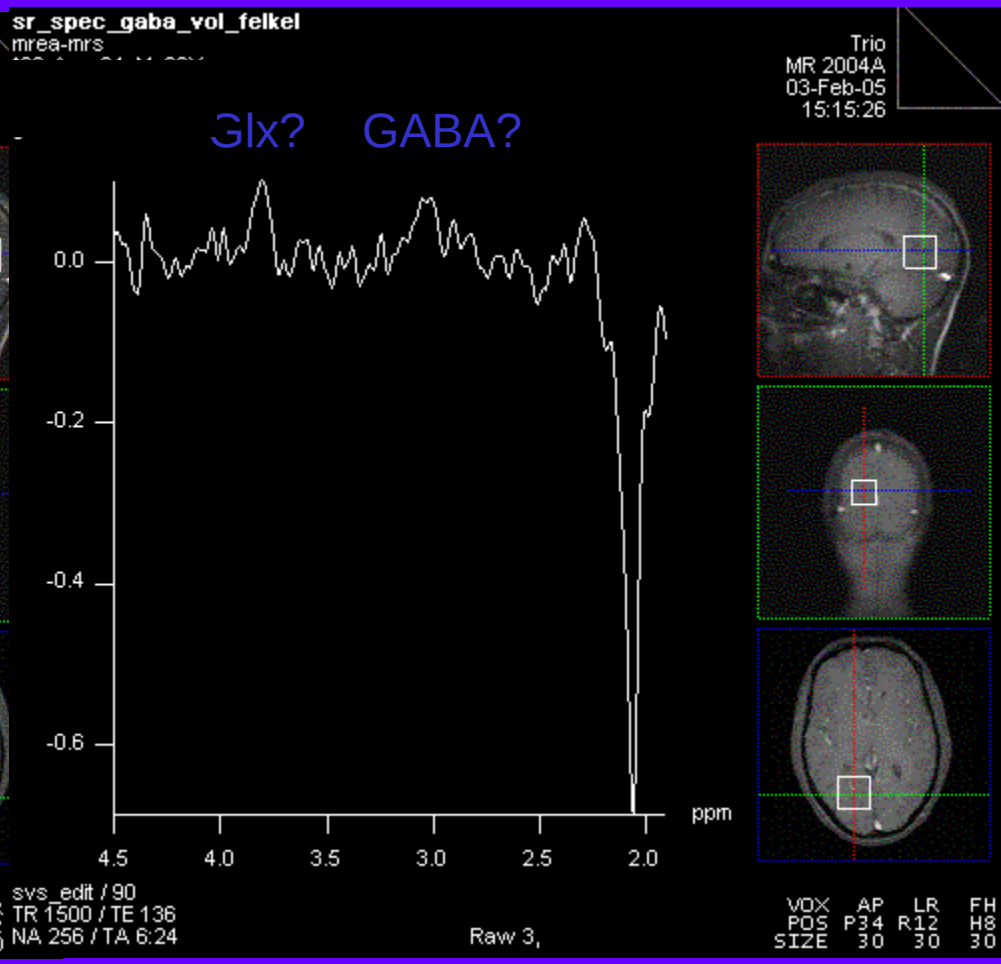
GABA detection = suppressing overlapping other signals

- singlet signals (Cr, NAA)
- coupled signals (Glu, Gln)
- macromolecules



GABA editing: experience at 3T



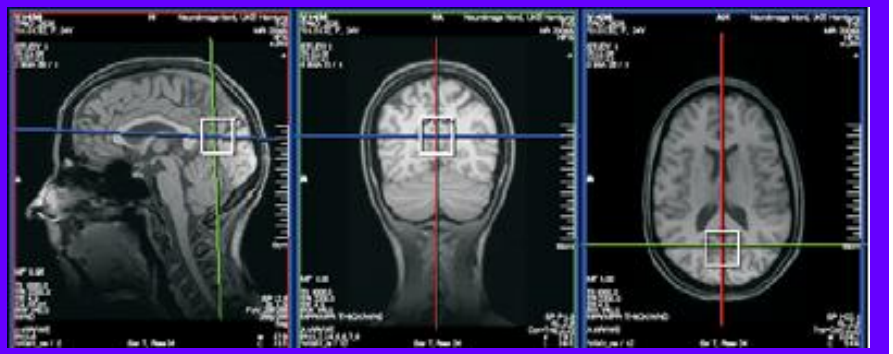


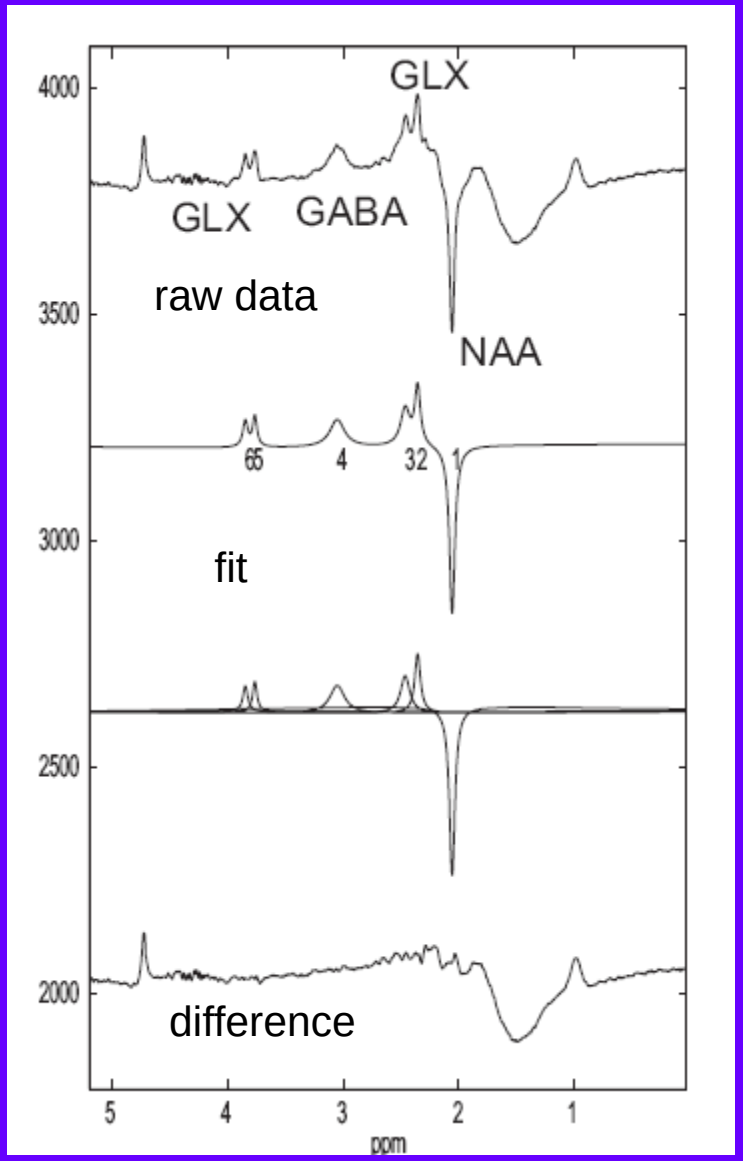
TE = 69 ms TE = 136 ms

Voxel size = 27 cc, TA = 6’24 min

MAGNETOM Trio: GABA Editing

- **svs_se_edit**
  In vivo spectral editing (MEGA, 2-shot)
- **TE 68 ms**
- **voxelsize = 27 cc**
- **TA = 6'24min**
- **8-Channel Array Coil and offline signal combination**
- **fitting with MRUI program**





CONCLUSION 2

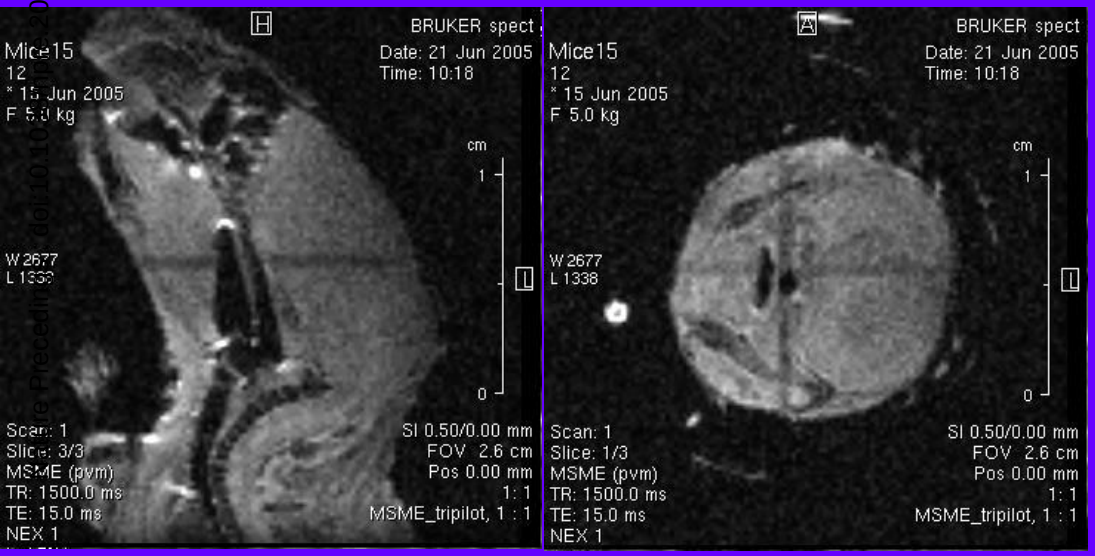
- GABA is inhibitory neurotransmitter
- GABA is predictive of seizure outcome
- GABA is MRS visible

MICROIMAGING
In
Mouse Brain

21 T MRI of Mice Brain

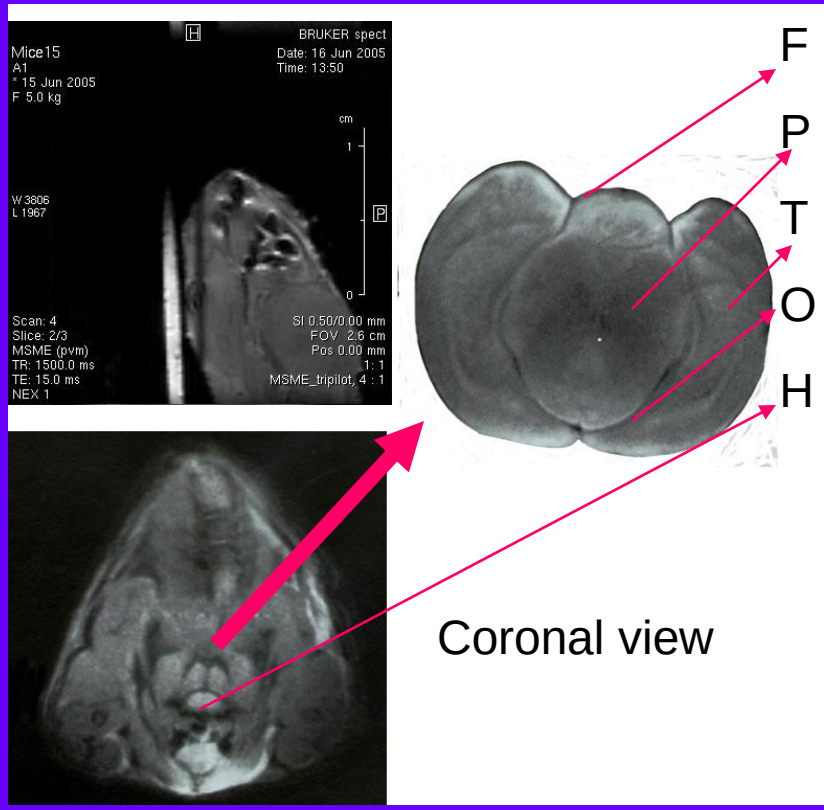
Aim: MRI imaging of mice brain anatomy

Outcome: Frontal(F), Parietal(P),Temporal(T), Occipital(O) lobes and Hippocampus(H) visible



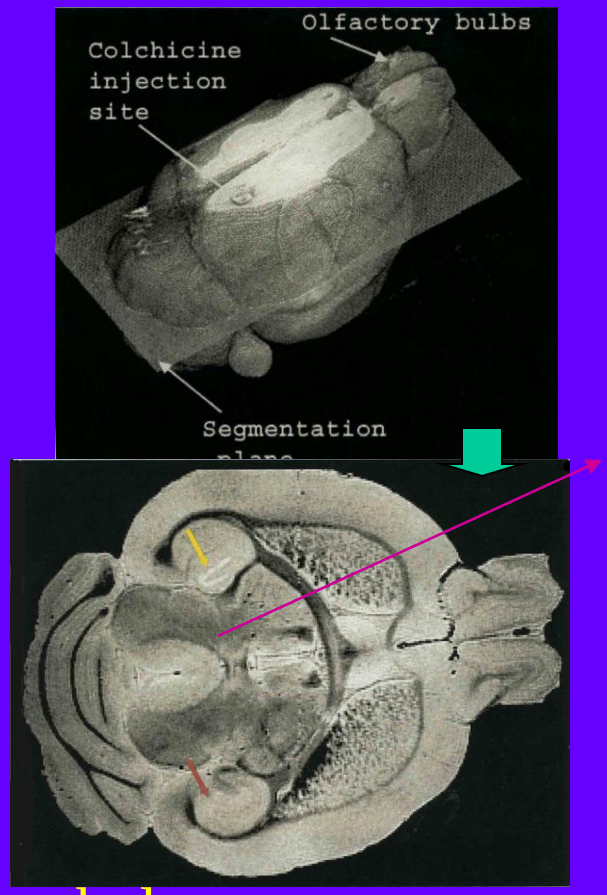
Sagittal View

Axial view

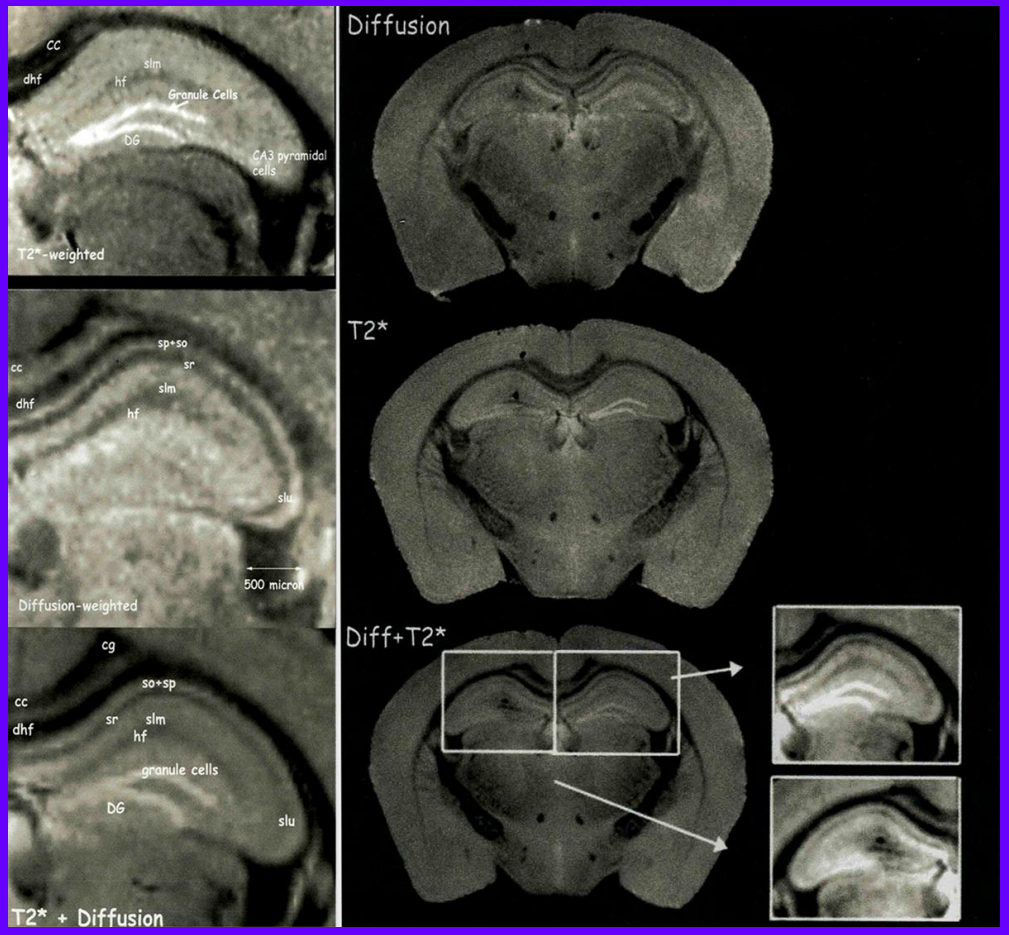


Coronal view

First time 21 Tesla MRI processed images of Mice Brain Reveal Details



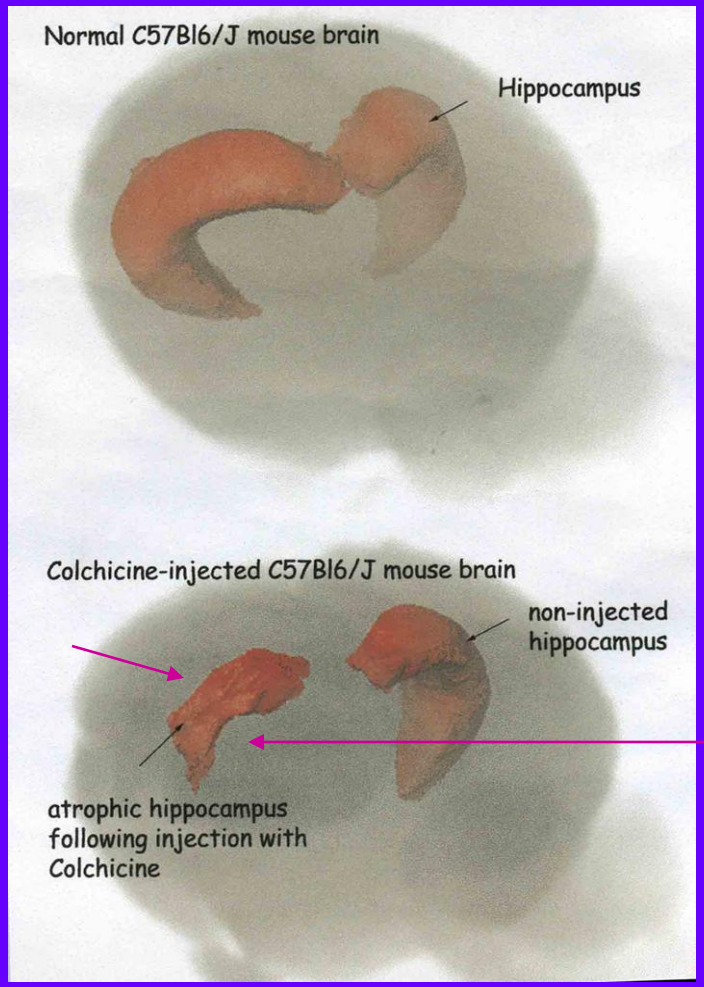
Morphology

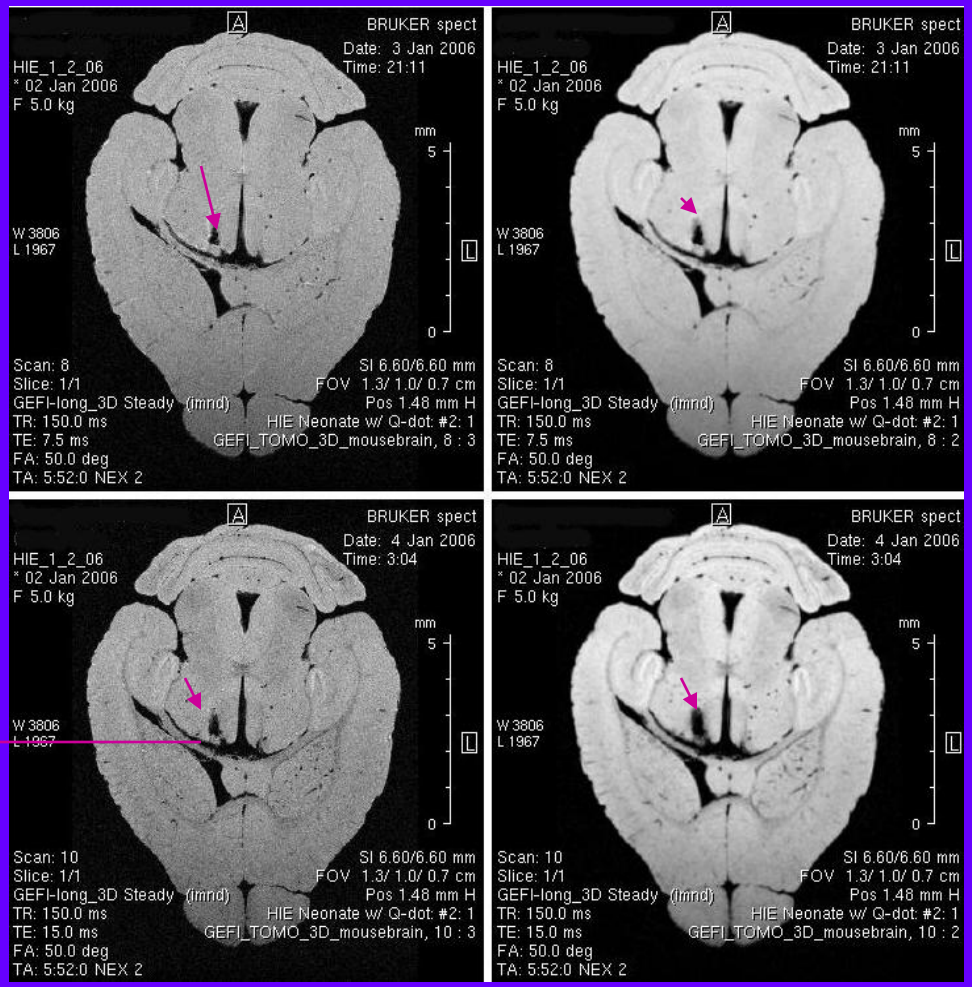


Hippocampus DG and other regions

21 T MRI: Colchicine Injection in Mice Reduced the Brain Hippocampus Volume

Nature Precedings : doi:10.1038/npre.2009.3485.1 : Posted 28 Jul 2009





CONCLUSION 3

- Mouse brain hippocampus is MRI visible in different regions
- Drug effect on hippocampus is MRI measurable

21 Tesla MRI Microimaging

Possibility of imaging cells and measurement up to 20 micron resolution with high MRI signal

Some examples

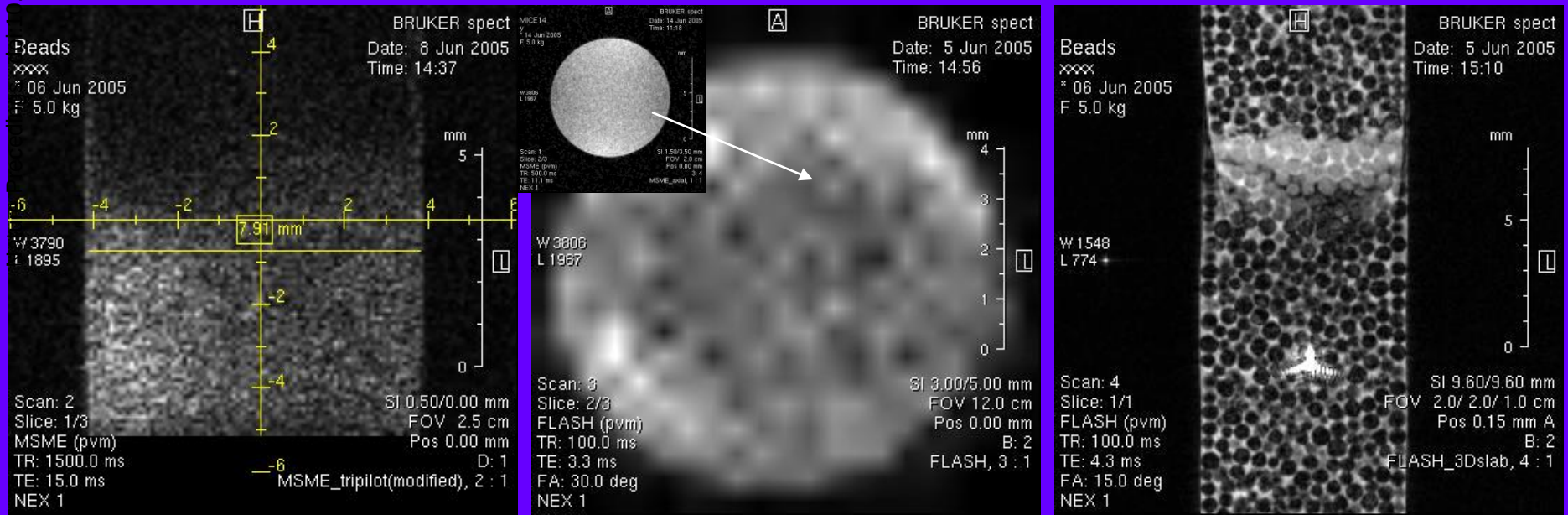
Micro-scale resolution by MRI

Aim: MRI of 50 µm, 90 µm, 500 µm polymer beads in tube with FeO-Gadolinium

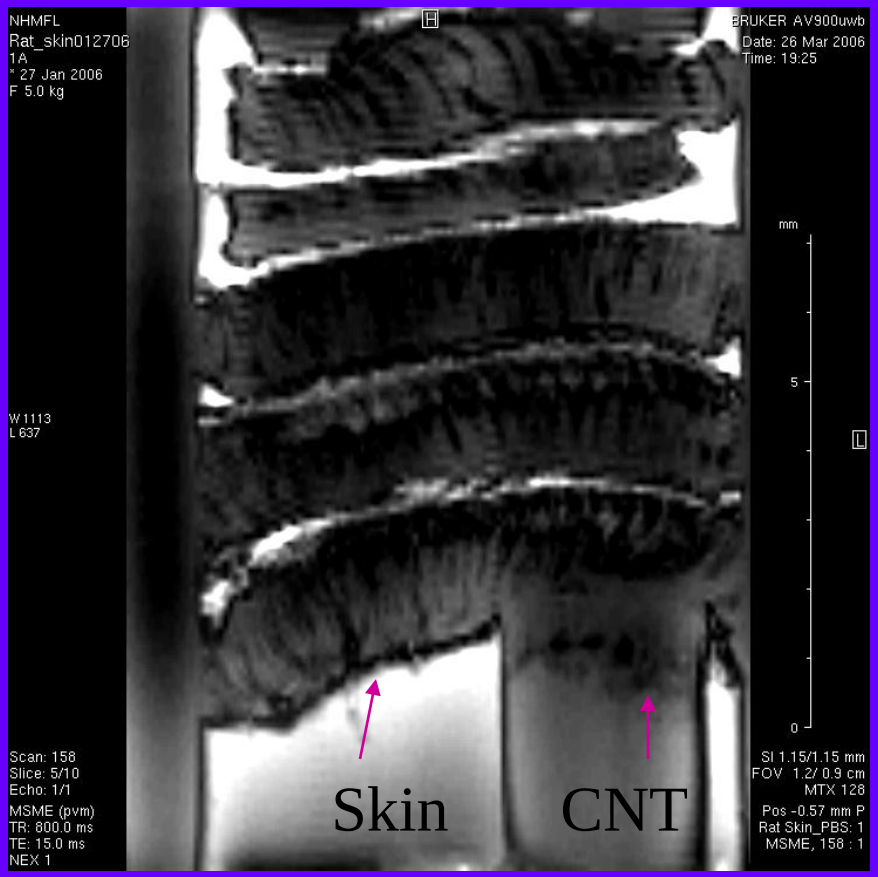
Outcome: MRI visualizes 50 µm beads(left) and ½ mm beads(rightmost)

Experiment: Polymer 50 µm beads(left) and 500 µm beads(right) were pushed in device at physiologic conditions & imaged by SE using T1 and proton density weight

Spatial resolution = 1mm /128 x 128, in-plane resolution = 0.1 mm



Nanotechnology: First time Carbon Nanotube Transport Across The Skin by 21 Tesla MRI



- Carbon Nanotubes (CNT) as future drug delivery system
- CNT are 1.8 million times lighter than iron.
- CNT can penetrate anywhere across the membrane channels (200 nm) in body tissues

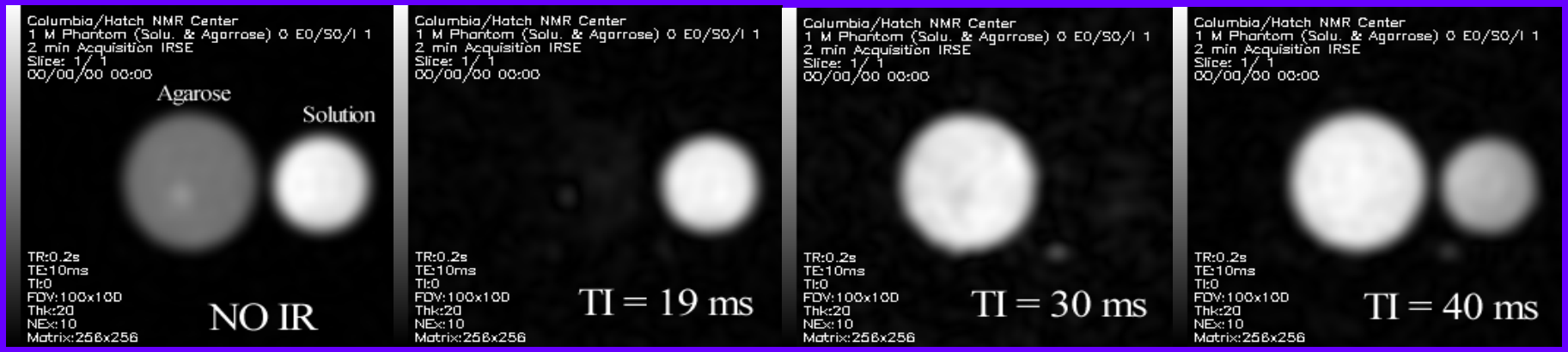
Conclusion 4

- Microimaging provide high sensitivity and resolution upto micron level
- Microimaging can be useful in micro-Anatomy, subcellular transport physiology

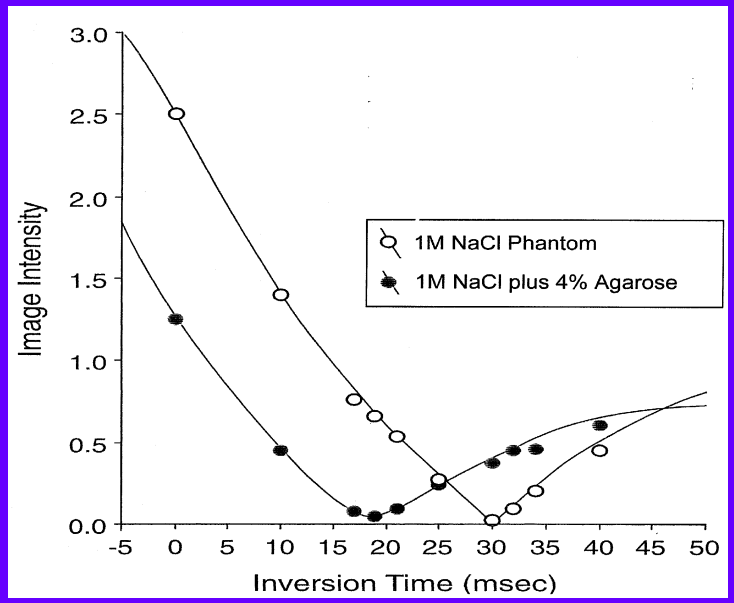
- **Final Take-home Message:**
  Quantitative MRI/MRS with PET is future molecular imaging choice, while Quantitative Microimaging is future dynamic monitoring/imaging choice.

MRI-PET in Brain Assessment

Sodium $[Na]_{ex}$ and $[Na]_i$ are MRI visible by IR pulse sequence at different null points

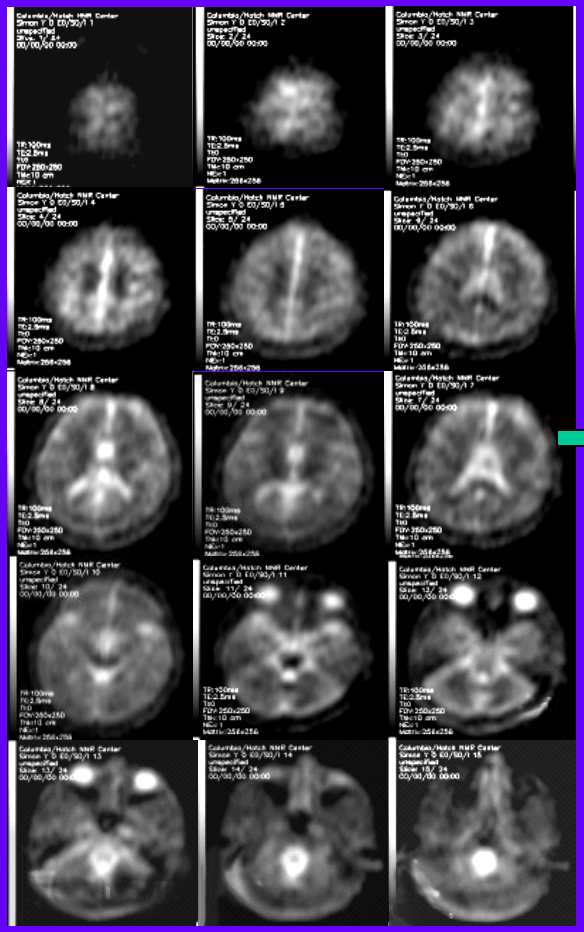


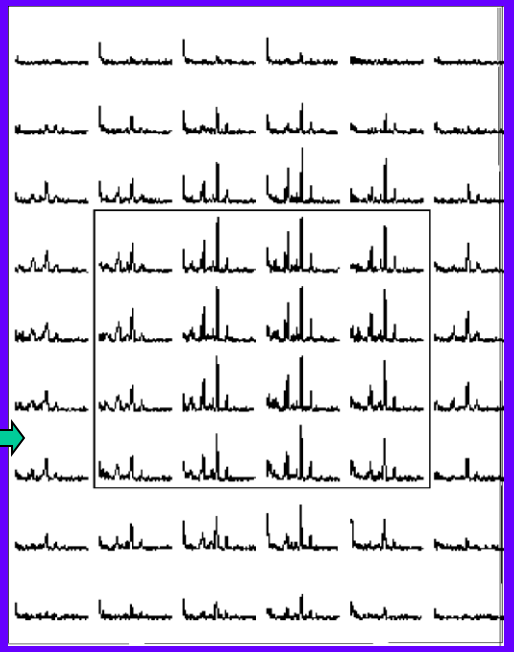
- Null points of $[Na]_{ex}$ and $[Na]_i$ are different
- Null point is inversion Time(TI) specific
- Distinct null points are tools for contrast



Sharma et al.(2001) ISMRM workshop11,126

4.25 T Sodium-MRI in human



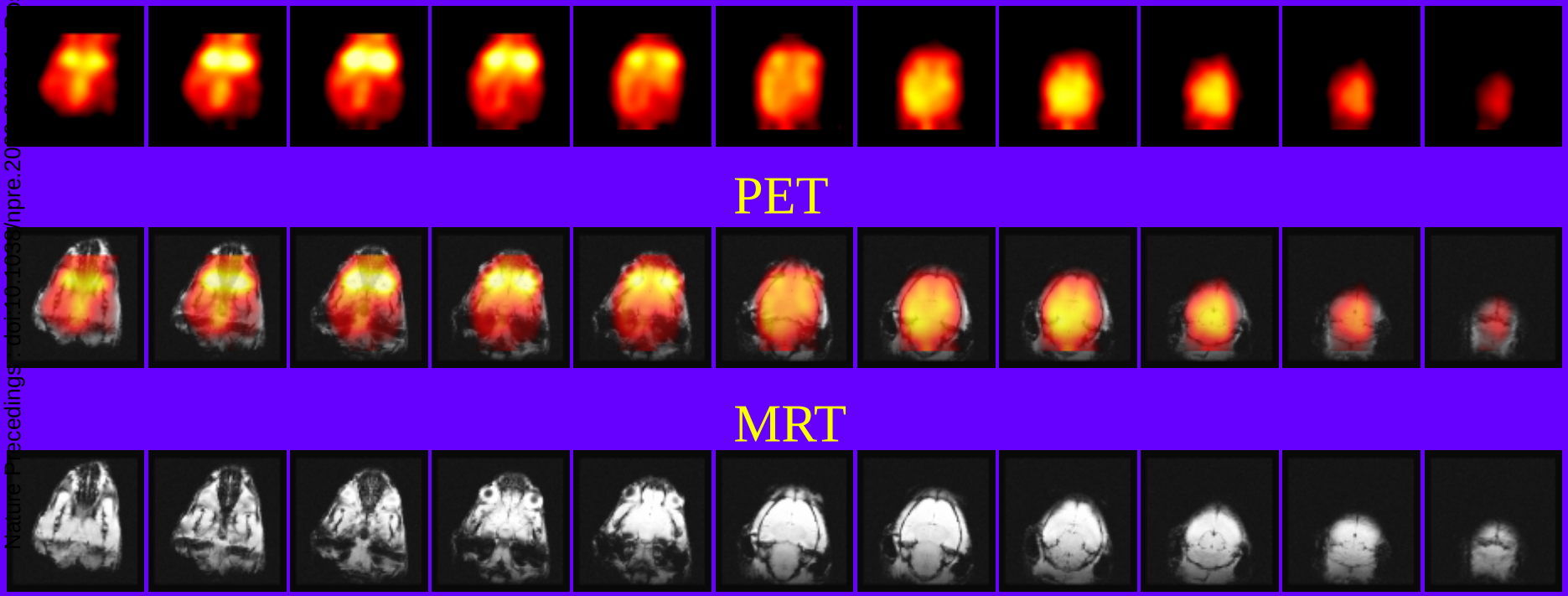


Raw Sodium images

Sharma(2005) Inform.Med.1(2)55.

Simultaneous Imaging of a [F-18]-FDG Mouse Head with Two Coincident APD Based LSO Block-Detectors and a 7 Tesla Small Animal MRT System

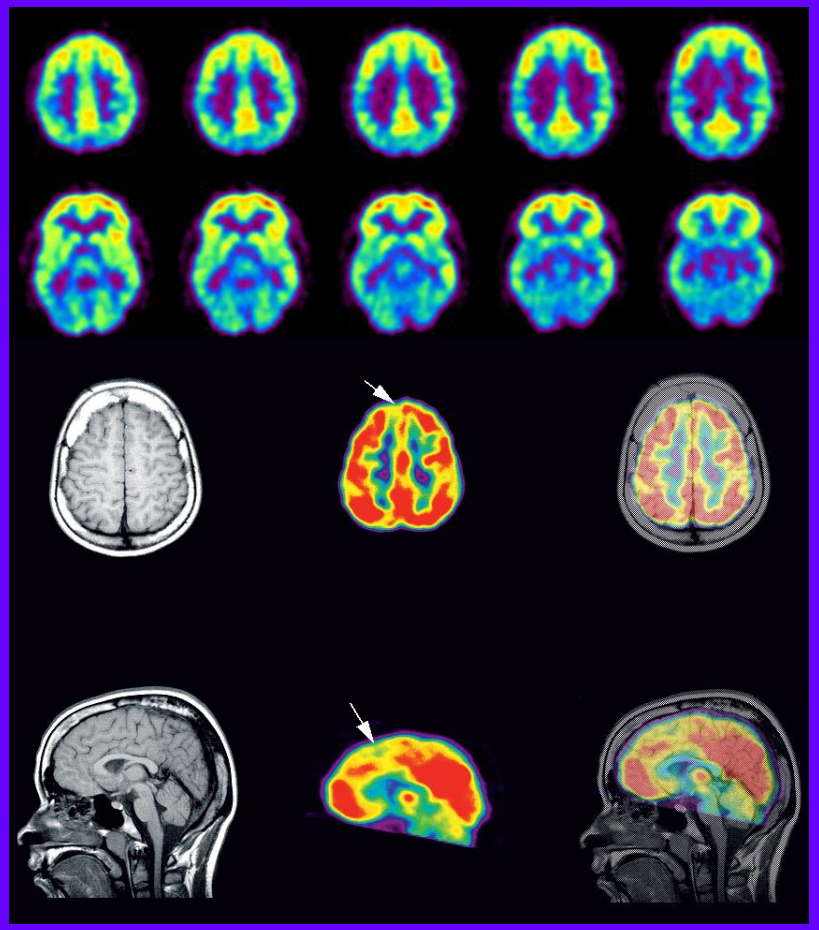
- Step and shoot PET acquisition (12 angles, each 6 min) while MRT images were taken.
- Filtered Back Projection (2.5 mm Gaussian image filtering post reconstruction)



70/30 Bruker Biospec system. B-GA20 gradient set. Micro Imaging Coil. FLASH MRT sequence. 1mm slice thickness.

MR-PET Applications

- Neurology
  - **Surgery and RT:** delineation of functionally significant brain sections and tumor mass
  - **Movement disorders:** Delineation of gray matter with receptor density
  - **Dementia:** Structure volumetry and metabolism (FDG) or even Plaque Imaging (FDDNP)
  - **Stroke:** improve MR perfusion by functional PET
  - **Epileptic foci:** accurate localization



Compatibility Challenges
What does it mean to really combine:

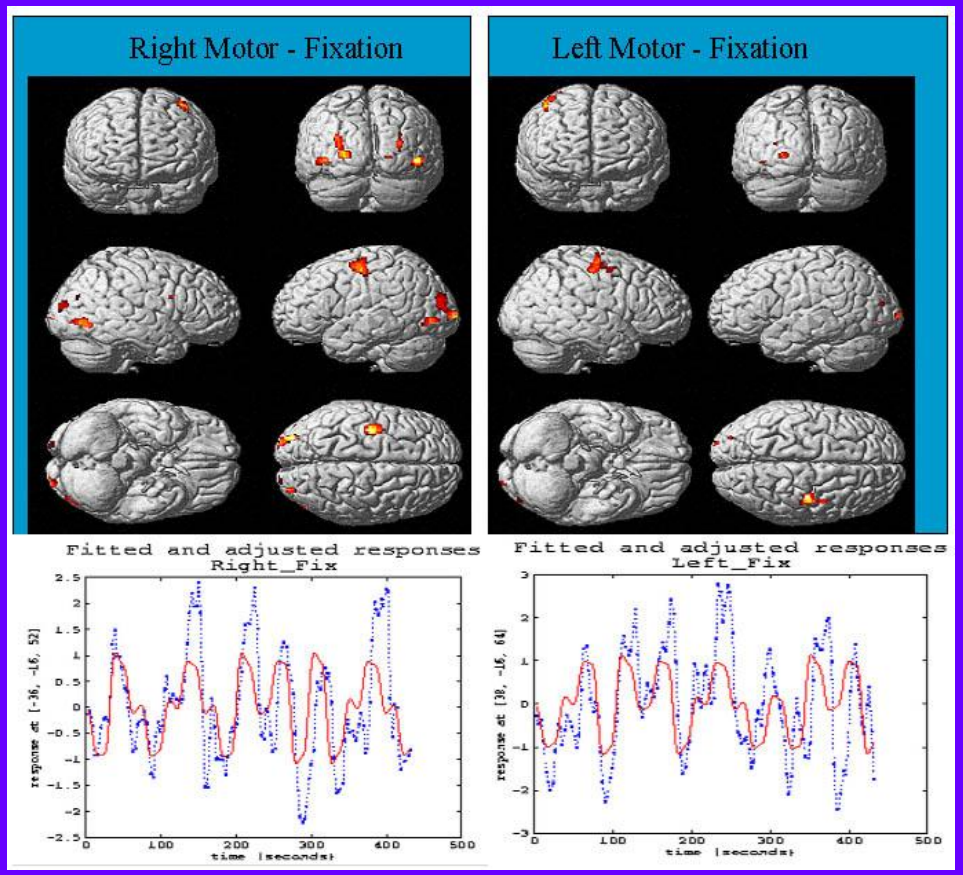
MR	MR-PET Challenge	PET
Cost	Space	Resolution
Homogeneity	Magnetic Field	Material restriction
No eddy currents	Gradient Field	Design restrictions, Heating, Signal interference
??	RF Field TX	Signal interference
Signal interference	RF Field RX	Shielding
Design restrictions	Attenuation	Signal loss

CONCLUSION 5

- MRI-PET predicts both morphology and oxygen metabolism

Functional MRI Measures the Blood Oxygen Stimulated Neuroactivation

Right and left finger tipping involves different brain regions & shows specific brain BOLD fMRI signal.



Sharma et al.2004 Biomed Engg 1(2) 29.

World's Largest MRI microimaging system

Acknowledgements

NHMFL, Tallahassee:

Ching J Chen, Bruce Locke, Kiran Shetty, William Brey

Columbia University,New York
Richard Kline

University of Texas Medical School, Houston
Ponnada A.Narayana
Jerry Wolinsky

Thank You

- Breast Spectroscopy
- Liver Spectroscopy
- IMAPS: An International Multi-Center Assessment of Prostate Spectroscopy
- Prostate Spectroscopy using Array Coils
- Spectroscopy of the Spinal Cord
- Detection of GABA
- Fast CSI I: EPSI
- Fast CSI II: SSFP
- 31P Spectroscopy of the Heart: Improvements
- DEPT 1H → 13C
- Metabolite Report

Breast Spectroscopy

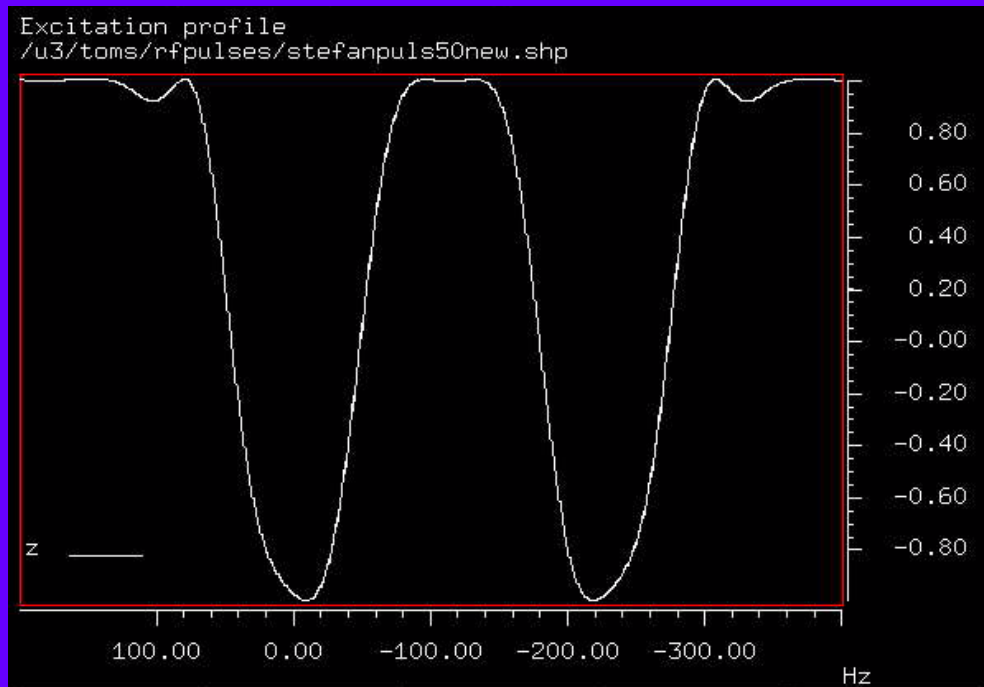
Breast Cancer - Clinical ^{1}H MRS Studies

- **(ce)MRI provides high sensitivity for differential diagnosis**
- **Will Cho-detection by ^{1}H MRS improve specificity?**
  - **overall cancer types true positive detection rate: 74 %**
  - **sensitivity low for non-infiltrating & high for infiltrating carcinoma**
  - **axillary node metastasis: sens. = 82%, spec. = 100%, acc. = 90 %**
  - **all results with respect to FNAB as gold standard**
  - **benign vs. malignant breast lesions: sens. = 82%, spec. = 85 %**

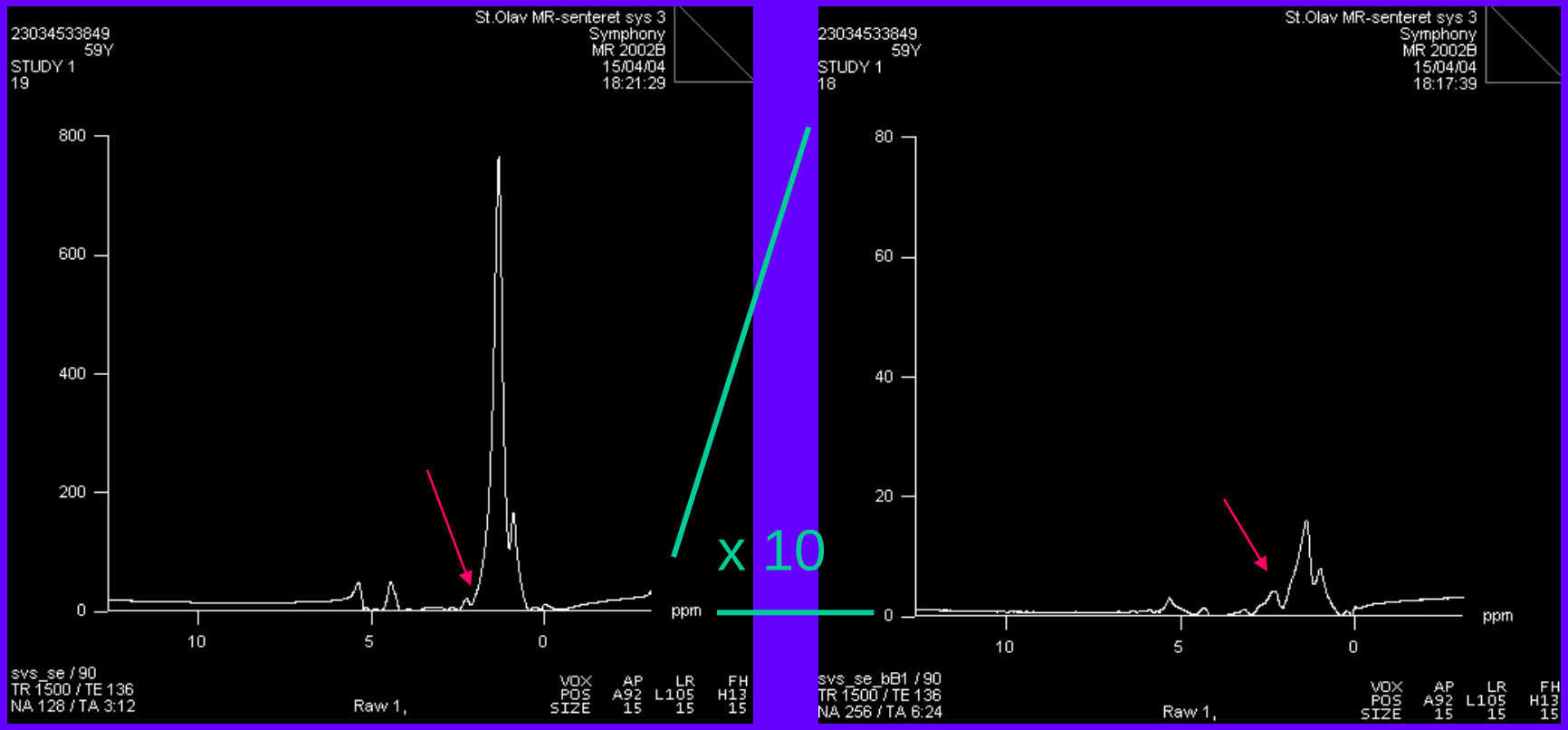
Lipid-Water Suppressed SE Sequence

svs_se_bB1 = svs_se + Spectral Suppression

- optimized spectrally selective pulses
- applied twice during TE; TE_{min} = 100 ms
- lipid and water suppression
- Acquisition using the Siemens Breast Coil

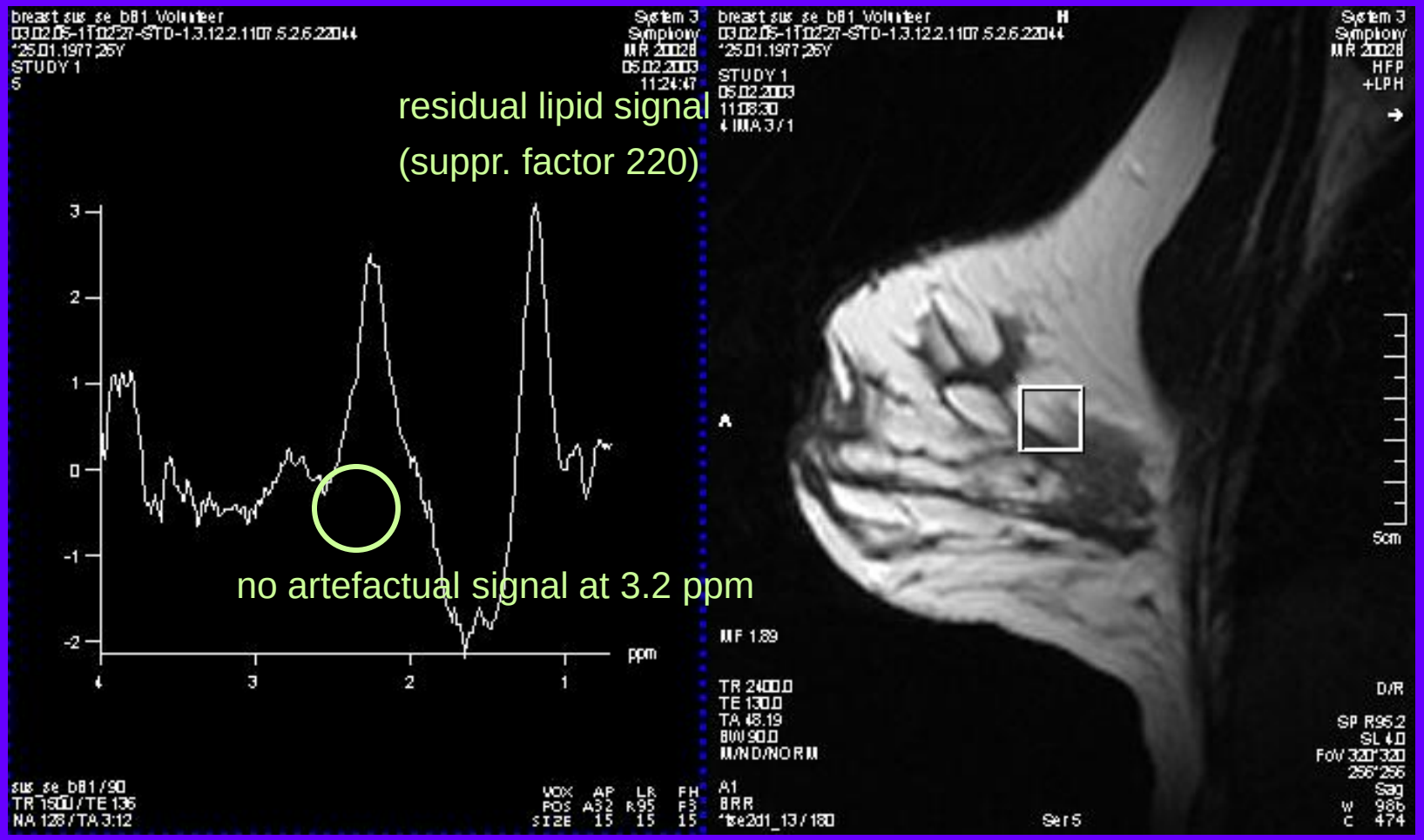


Breast Cancer

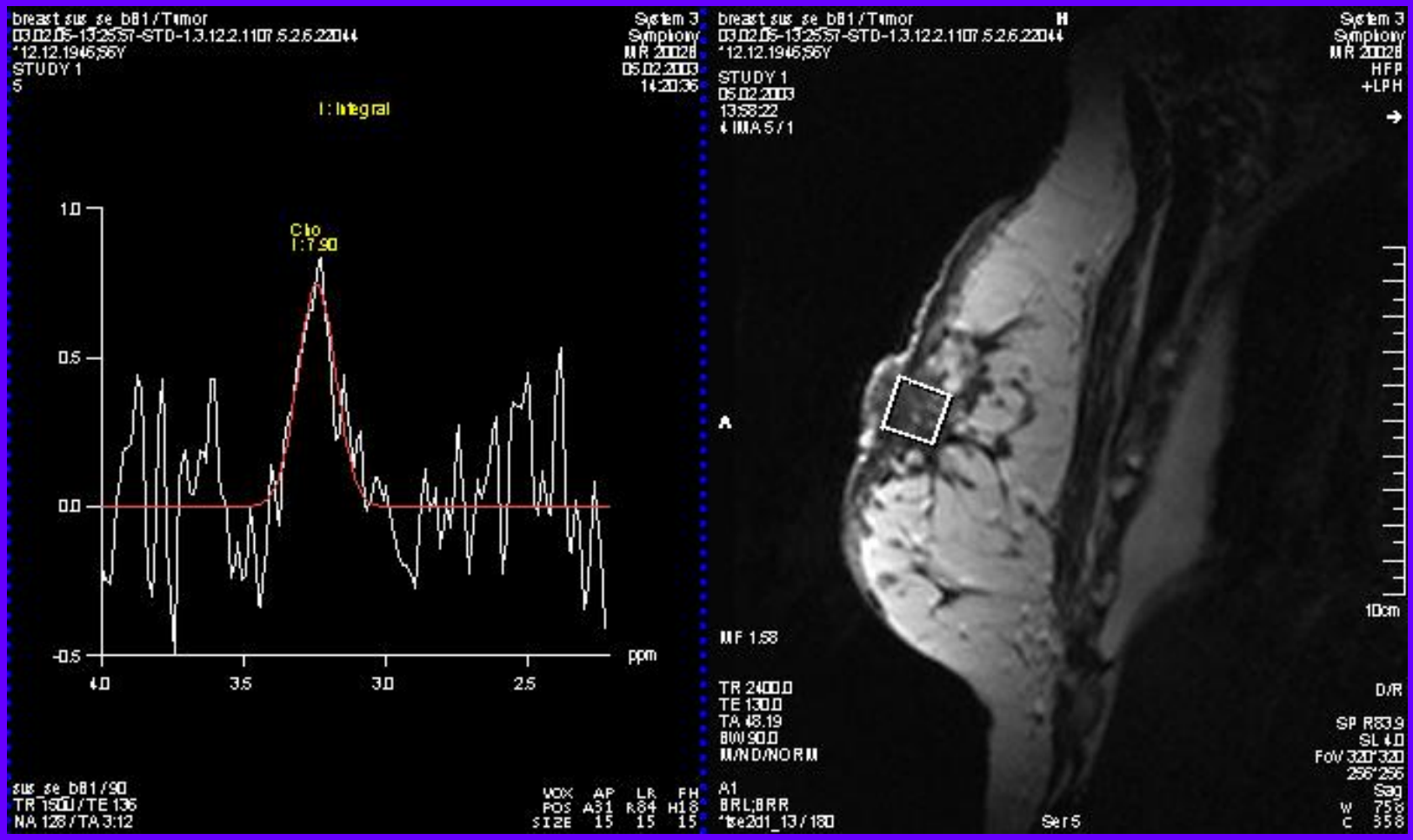


the effect of lipid suppression

Breast Cancer

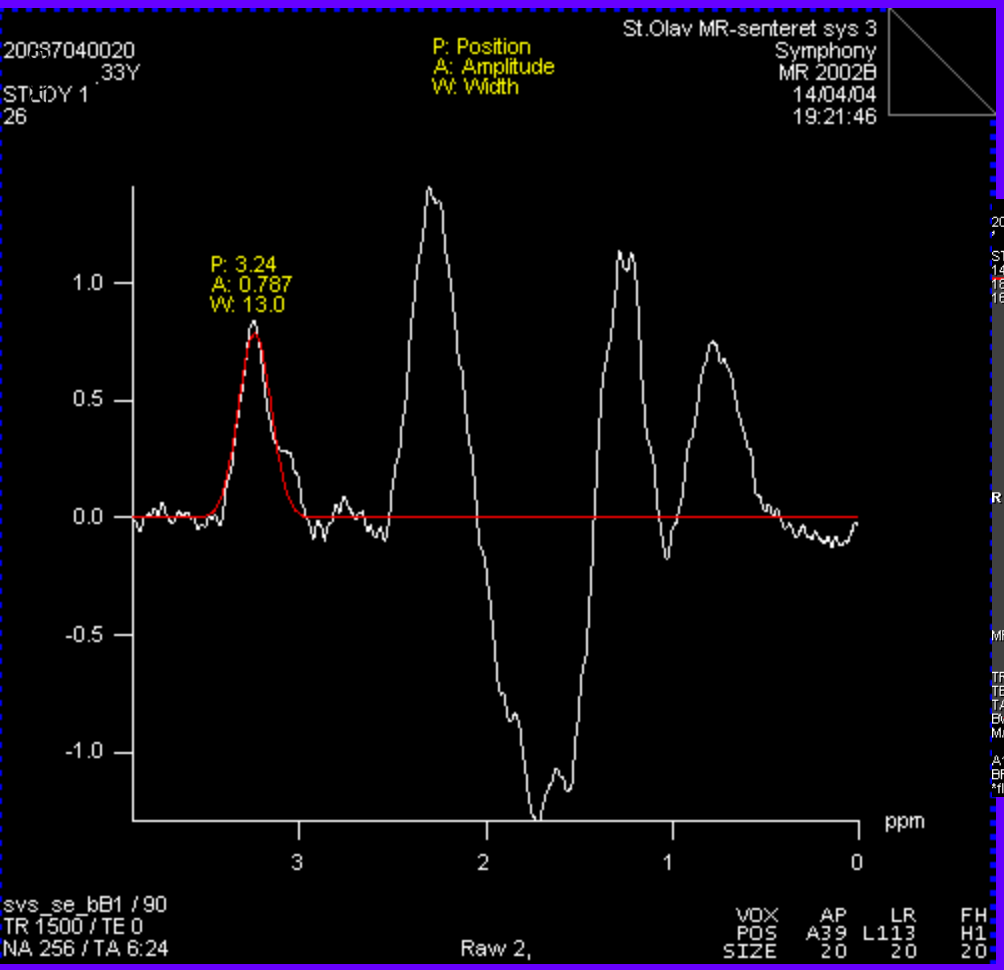


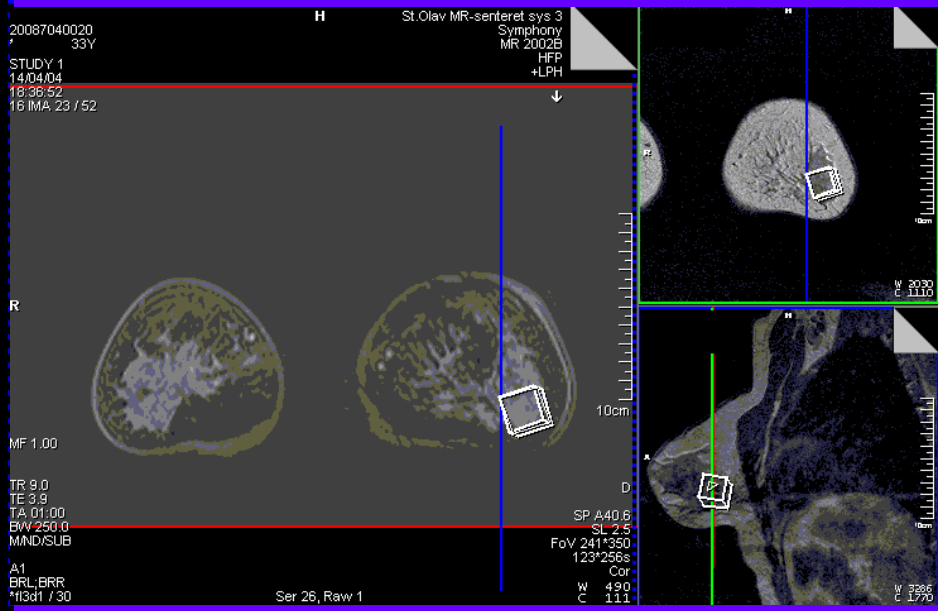
Breast Cancer



Voxel size = 3.4 cc, TA = 3 mins. 12 s

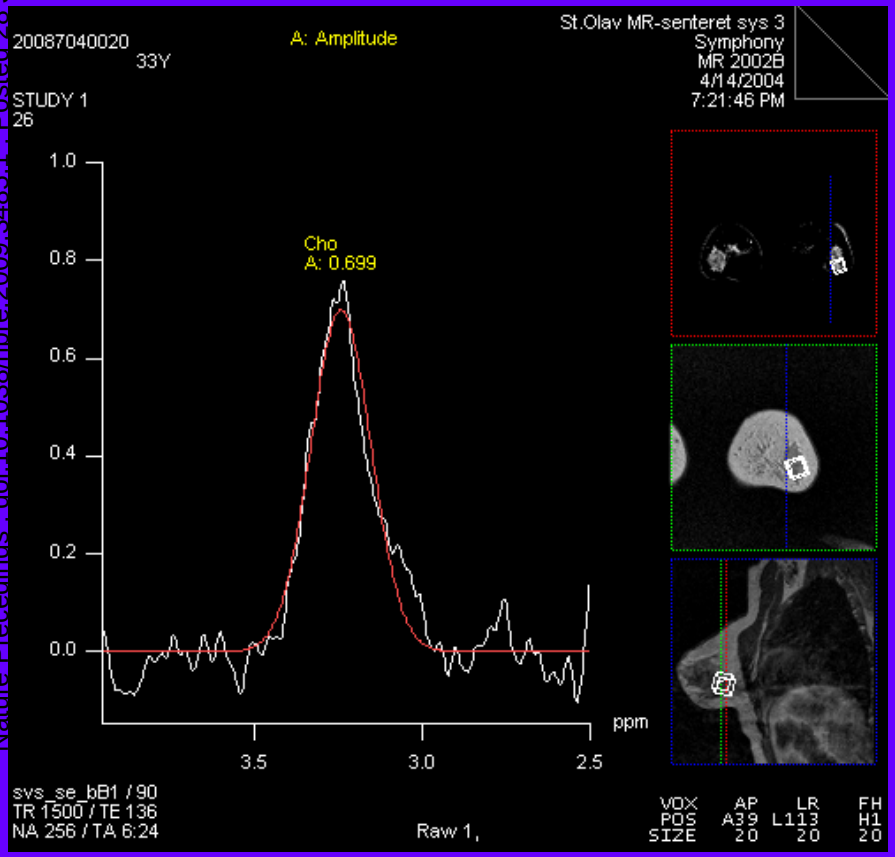
Breast Cancer



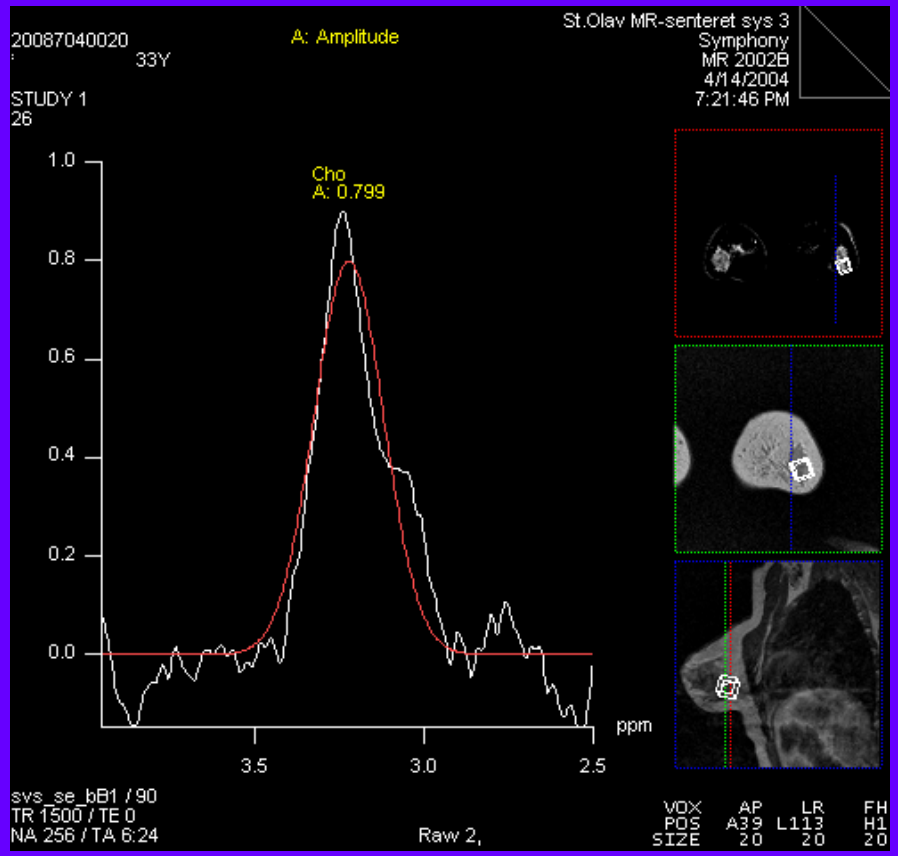


- voxelsize = 6 cc, TA = 6 mins. 24 s
- patient undergoing CT-MRI

Breast Cancer: Coherent Accumulation

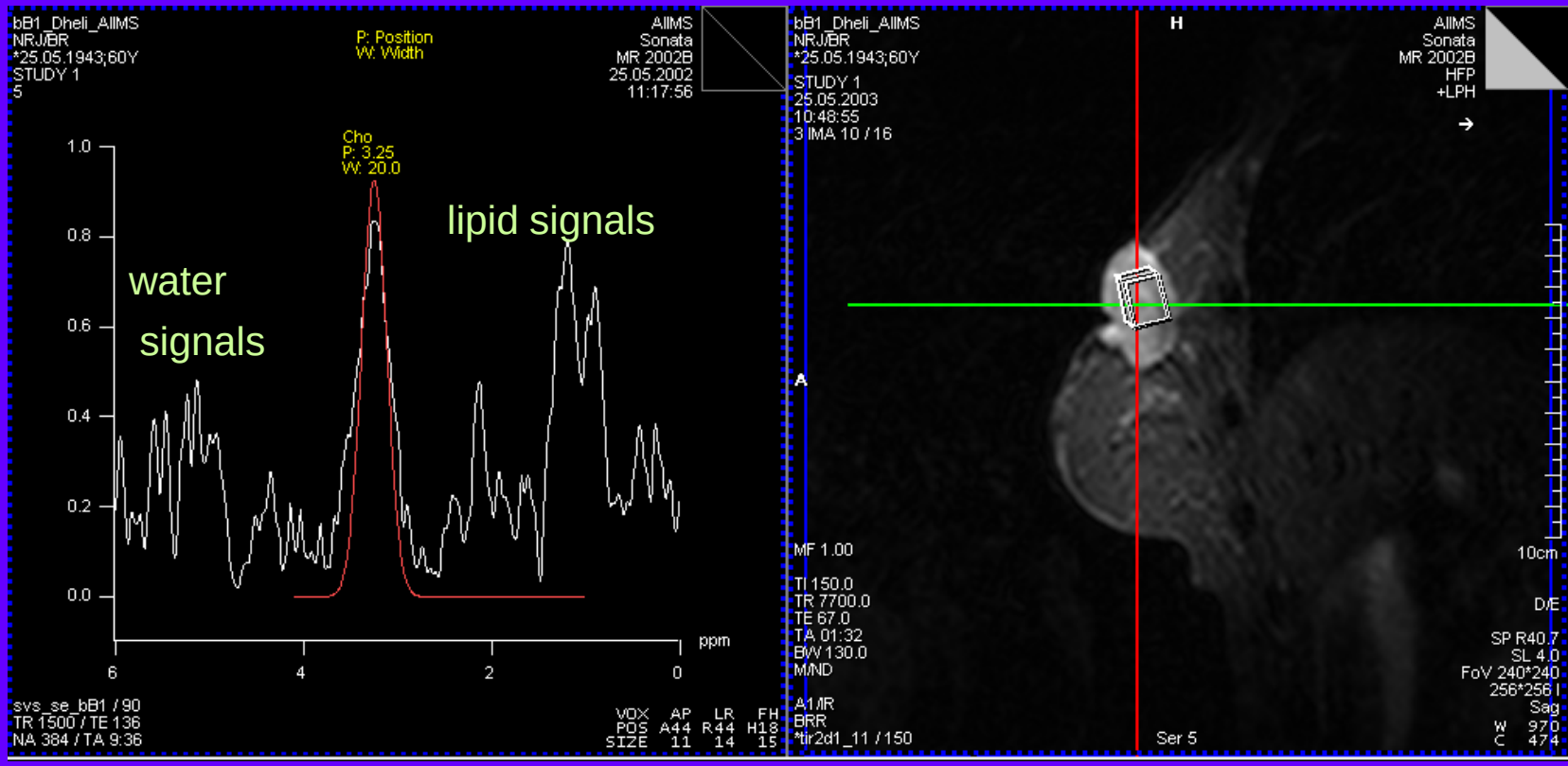


uncoherent accumulation



coherent accumulation

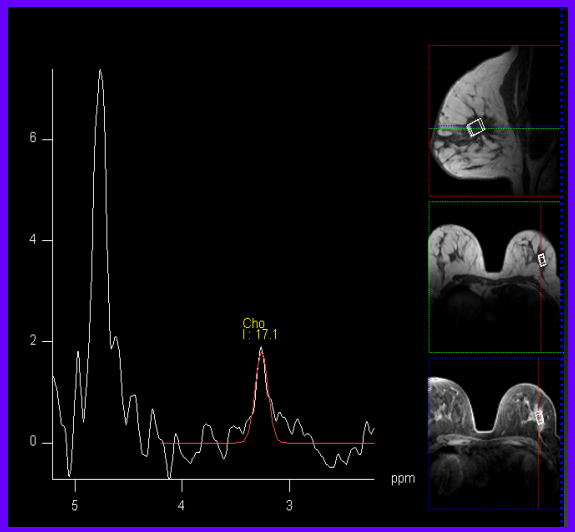
Pre-Clinical Results: Breast Cancer



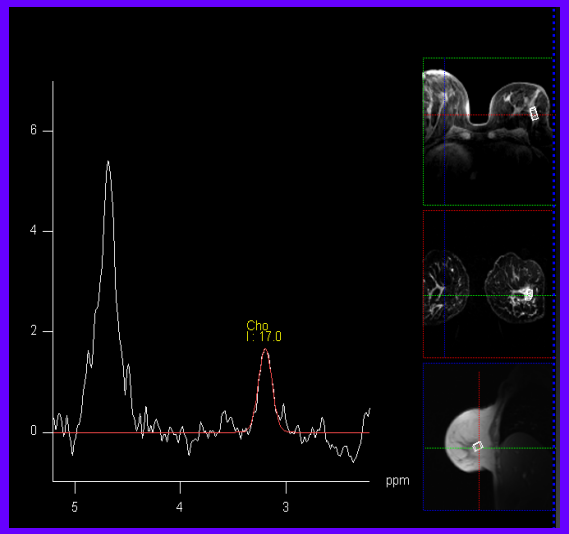
Voxel size = 2.3 cc, TA = 9 mins. 36 s

Breast cancer: MRSI monitoring

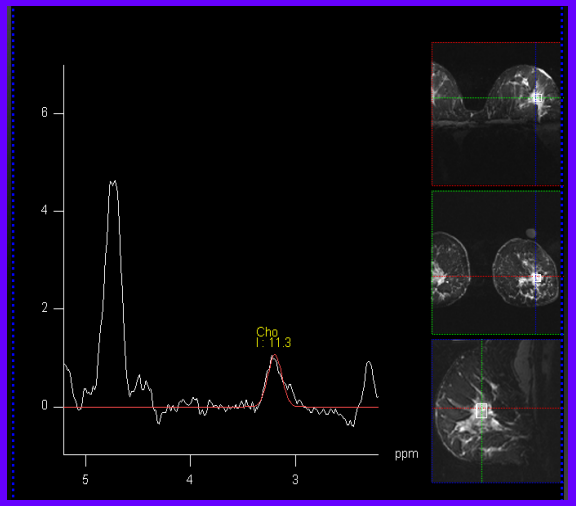
Before Chemo-therapy



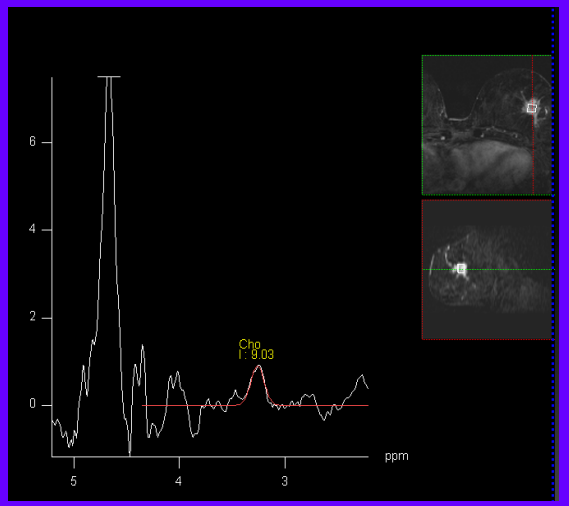
1st cycle



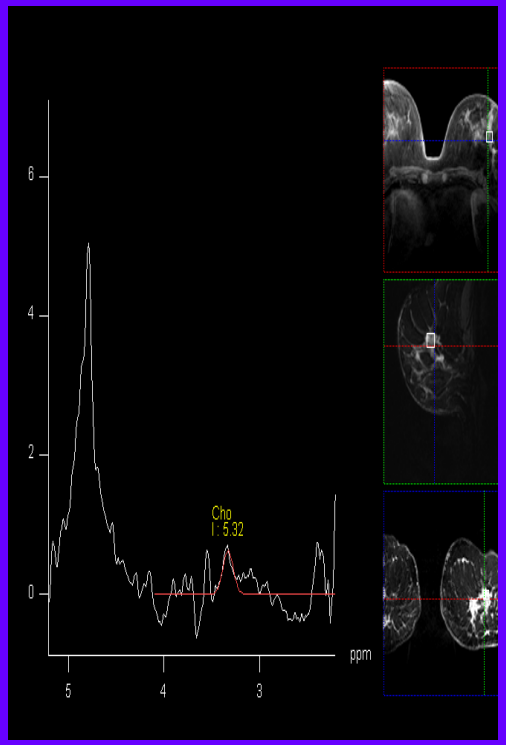
2nd cycle



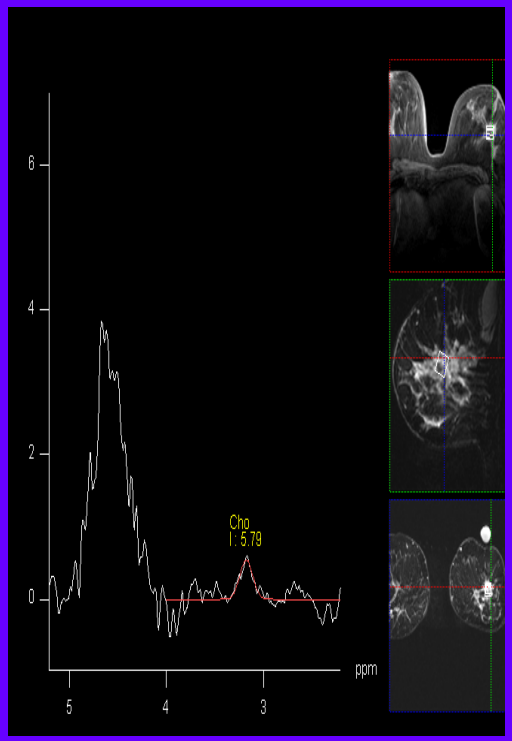
3rd cycle



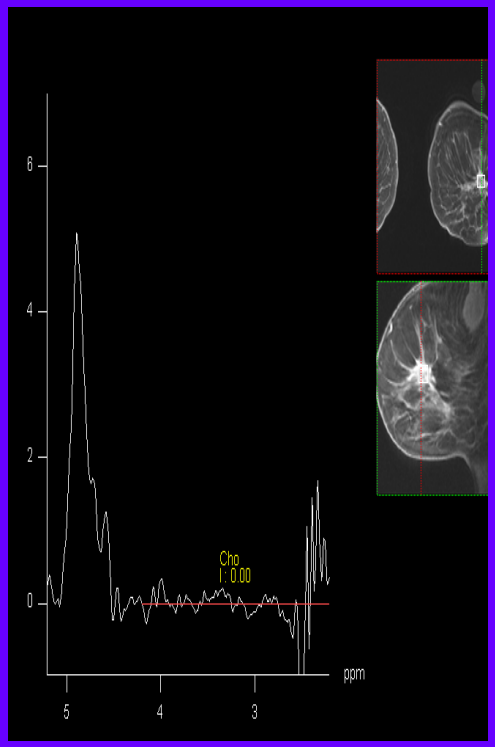
MRS monitoring of CT



4th cycle

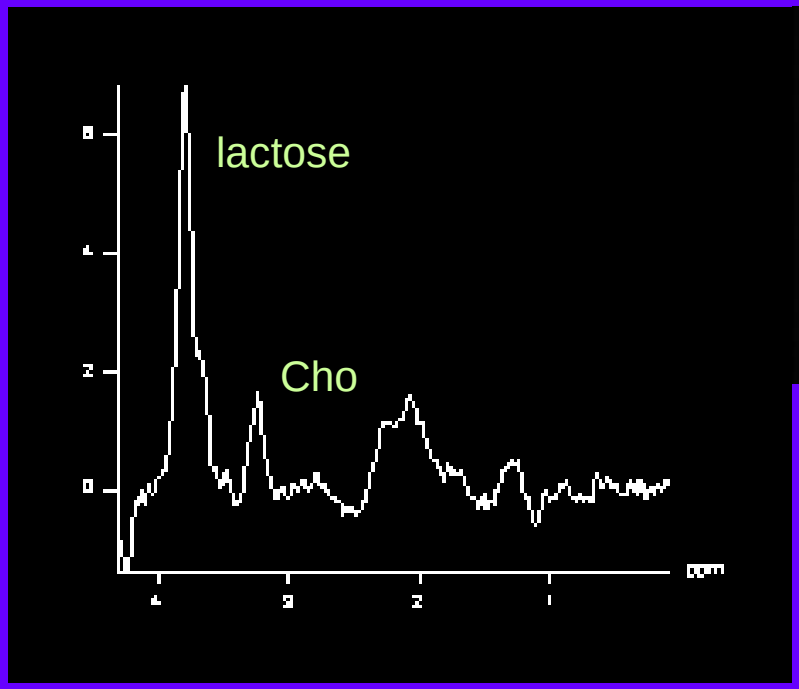


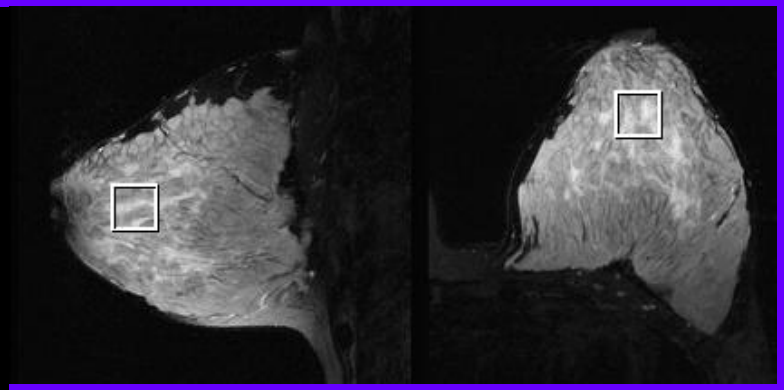
5th cycle



6th cycle

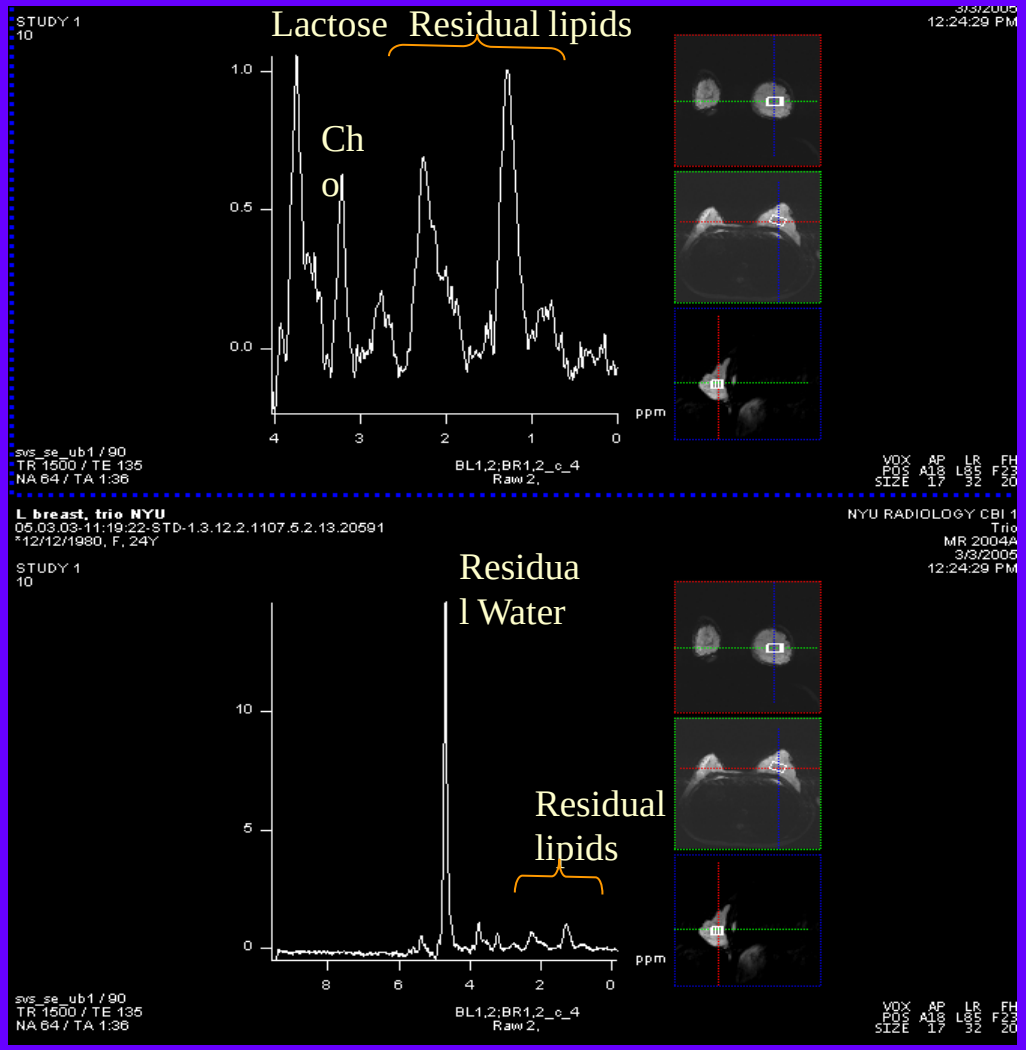
Lactating Breast





Voxel size = 8 cc, TA = 3 mins. 12 s TR/TE = 1500/135 ms

MAGNETOM Trio: Lactating Breast

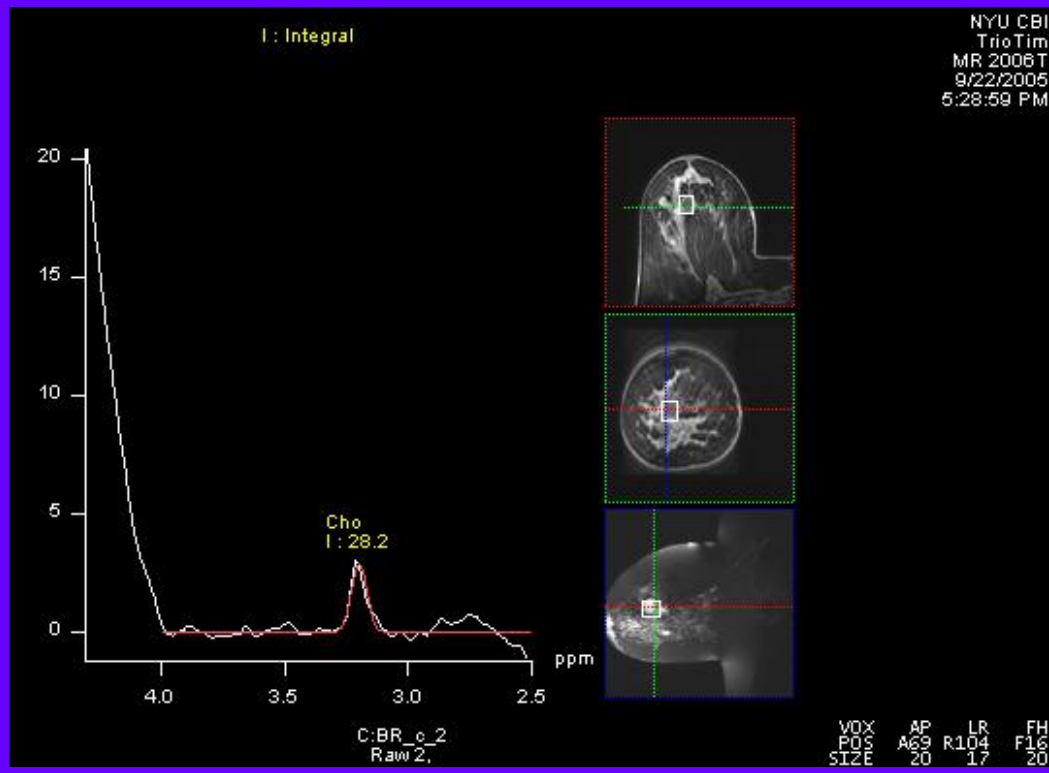


MAGNETOM Tim Trio: Breast MRS

- **svs_se body WIP**
- **spectral lipid suppression**
- **multi-array signal combination**
- **frequ. correction before accumulation**

- **TA = 2:08 min**

Detection of choline by MRS in pathologically proven adenocarcinoma

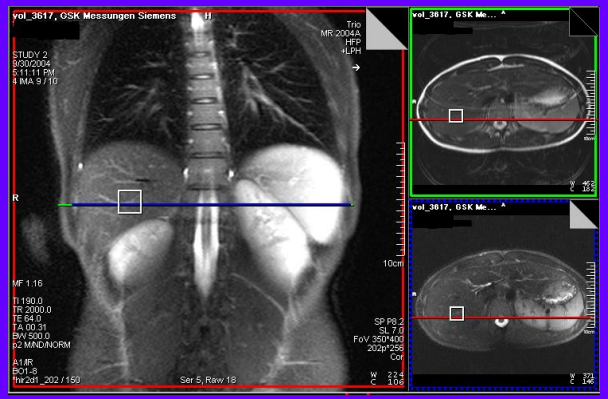


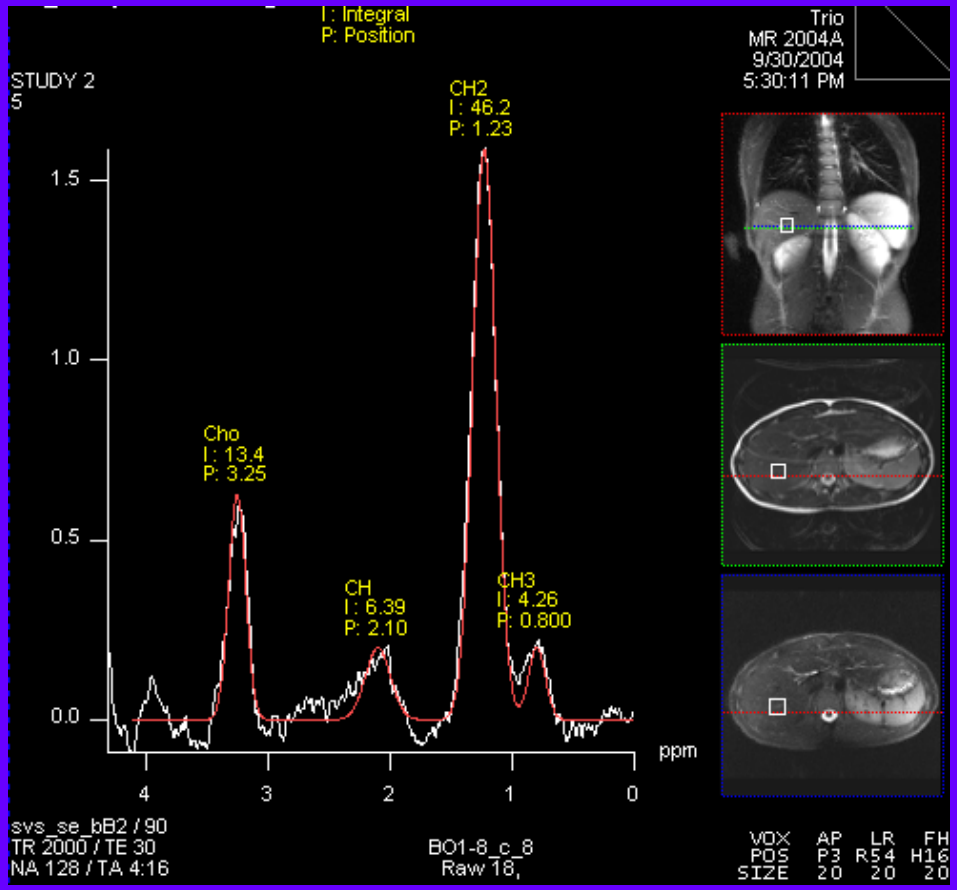
Liver Spectroscopy

Magnetom Trio: ^{1}H spectrum of liver

- free breathing SVS data acquisition
- frequency/phase lock for each acquisition
- combining spectra of 8 coil elements

TE = 30 ms
TR = 2000ms
TA = 4:16 min
Voxel = 8 cm^3





Magnetom Avanto: ^{1}H spectrum of liver

universal body WIP svs_se

free breathing

frequ. / phase lock

coil element combination

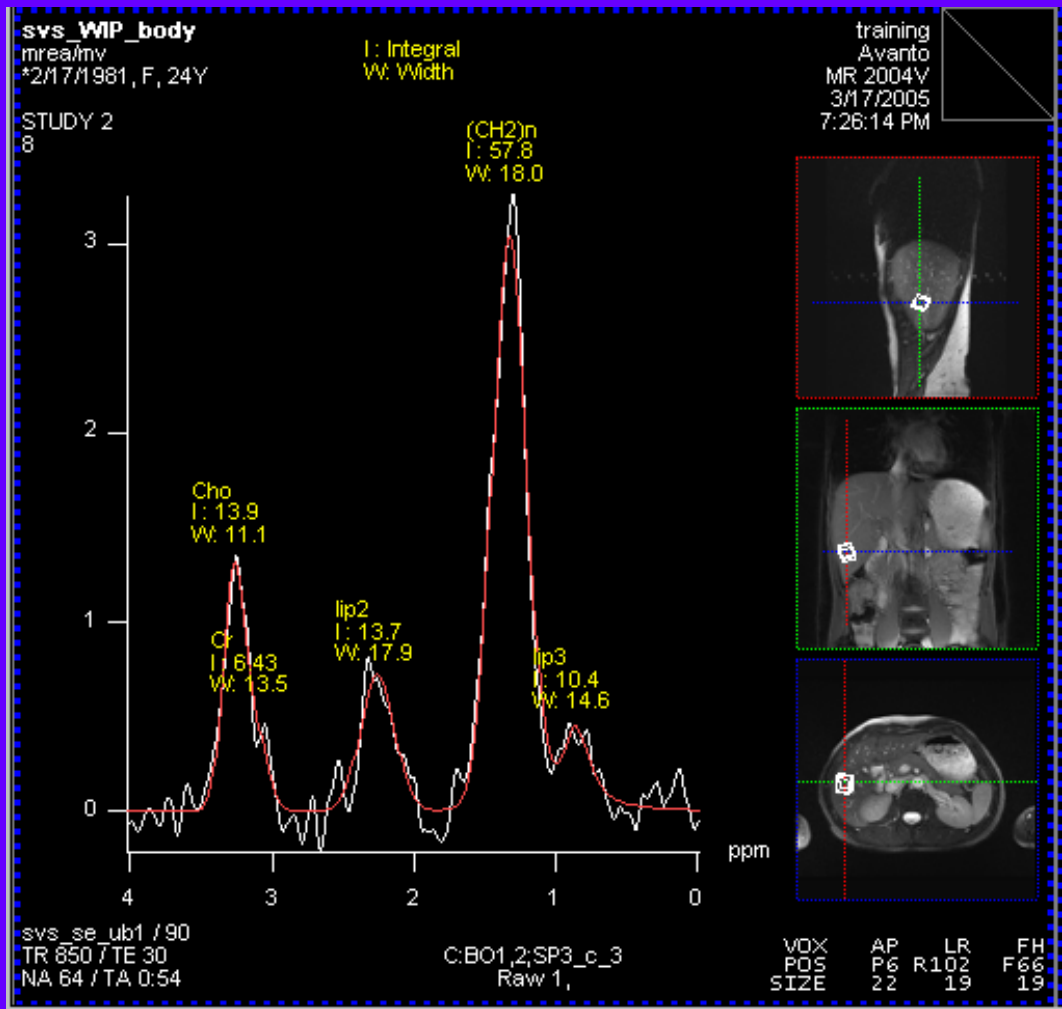
TR / TE =
650 / 30 ms

Voxel size = 8 cc

TA = 0:54 min

→feasibility

→the 3 major lipid signals and choline compounds detected

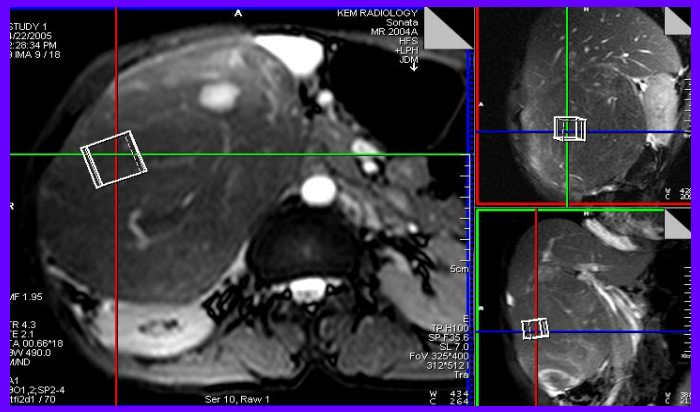


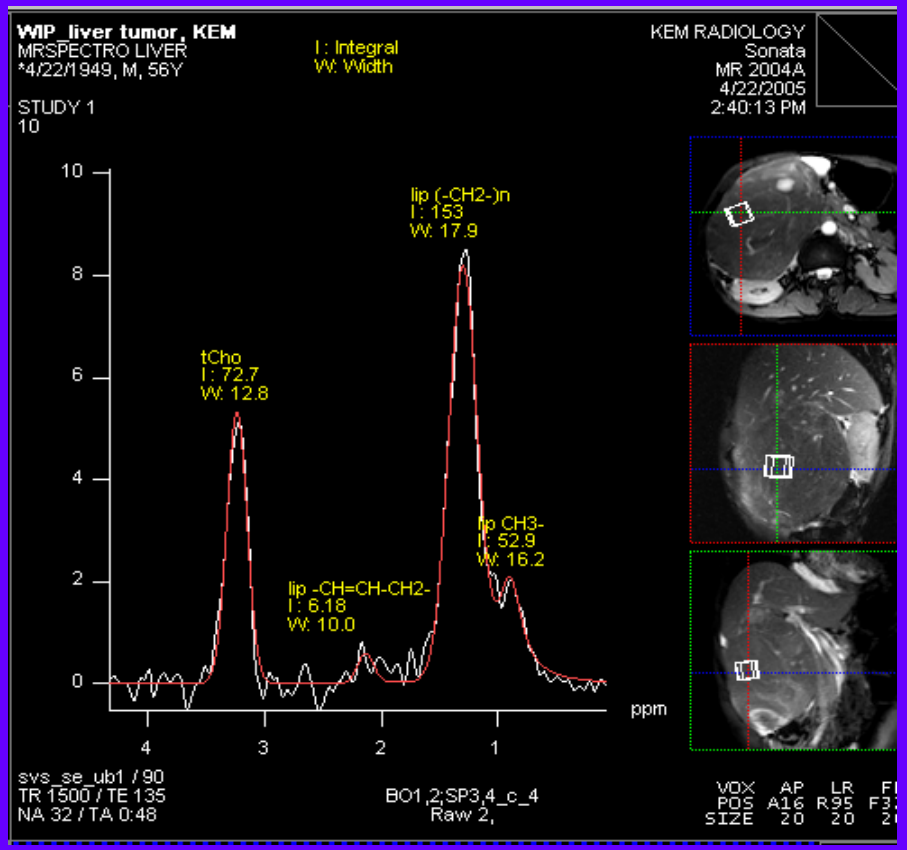
Single Voxel Spectroscopy in liver tumor

- free breathing SVS data acquisition
- frequency/phase lock for each acquisition
- combining spectra of 8 coil elements

Magnetom Sonata:
Spectrum shows lipid signals and increased Choline signal

TE = 135 ms
TR = 1500ms
TA = 0:48 min
Voxel = 8 cm^3

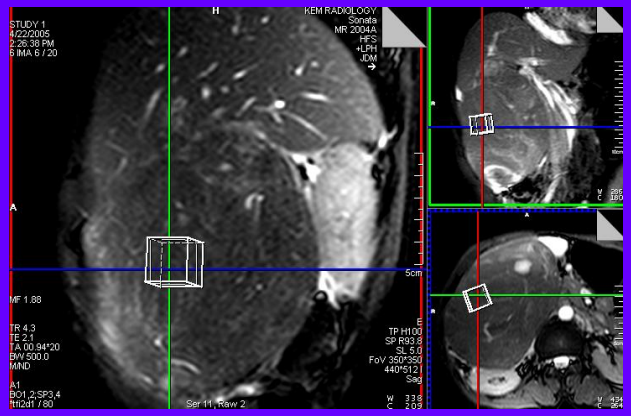


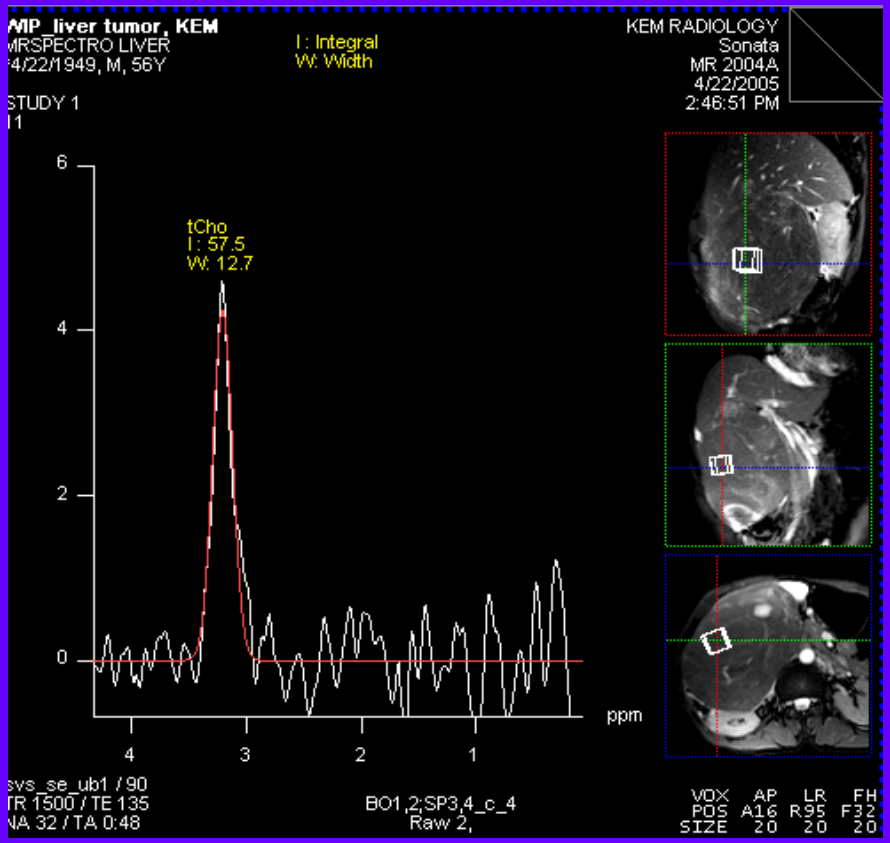


SVS in liver tumor

- free breathing SVS data acquisition
- frequency/phase lock for each acquisition
- combining spectra of 8 coil elements
- Spectral lipid suprression

Magnetom Sonata:
Spectrum shows highly increased Choline signal
TE = 135 ms
TR = 1500ms
TA = 0:48 min
Voxel = 8 cm^3

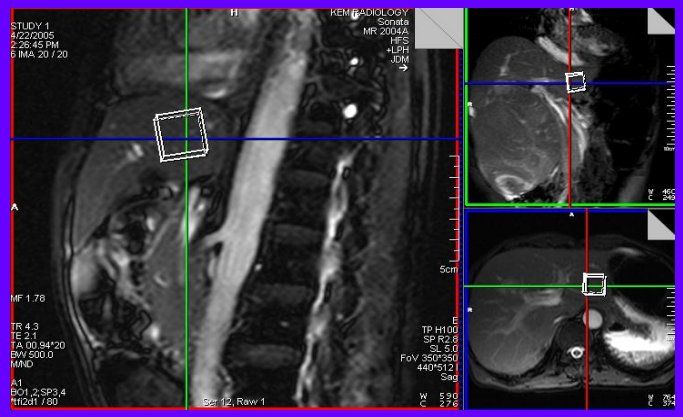


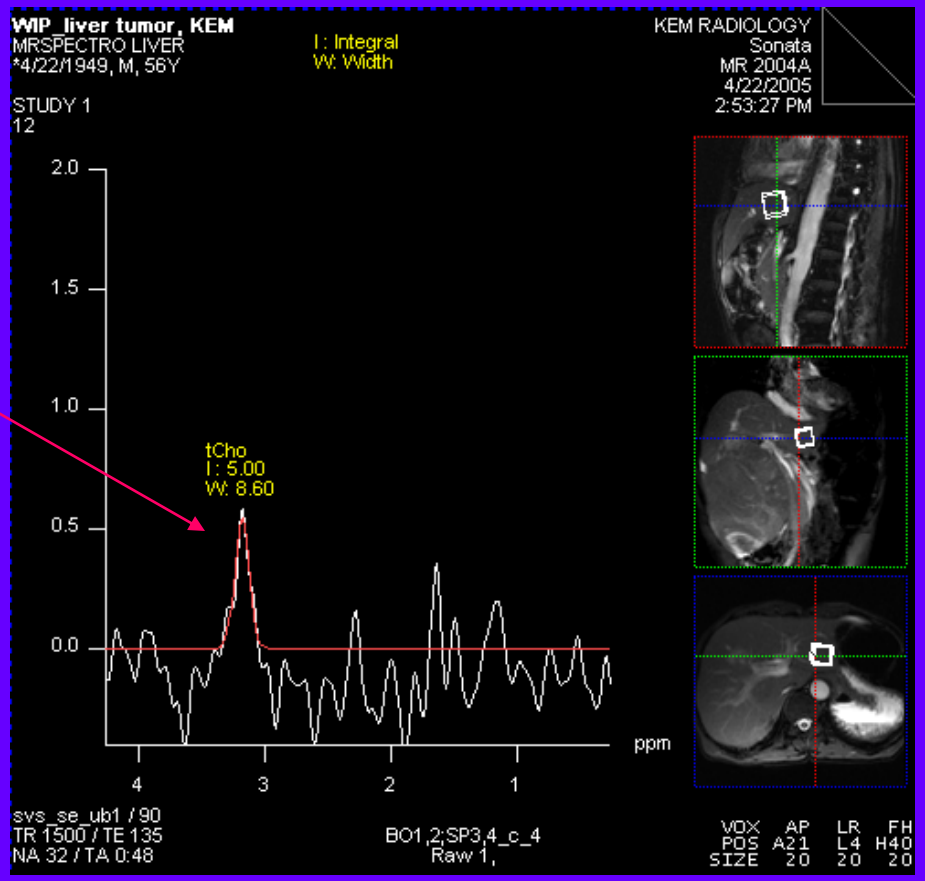


SVS in liver tumor

Reference spectrum:

Choline peak

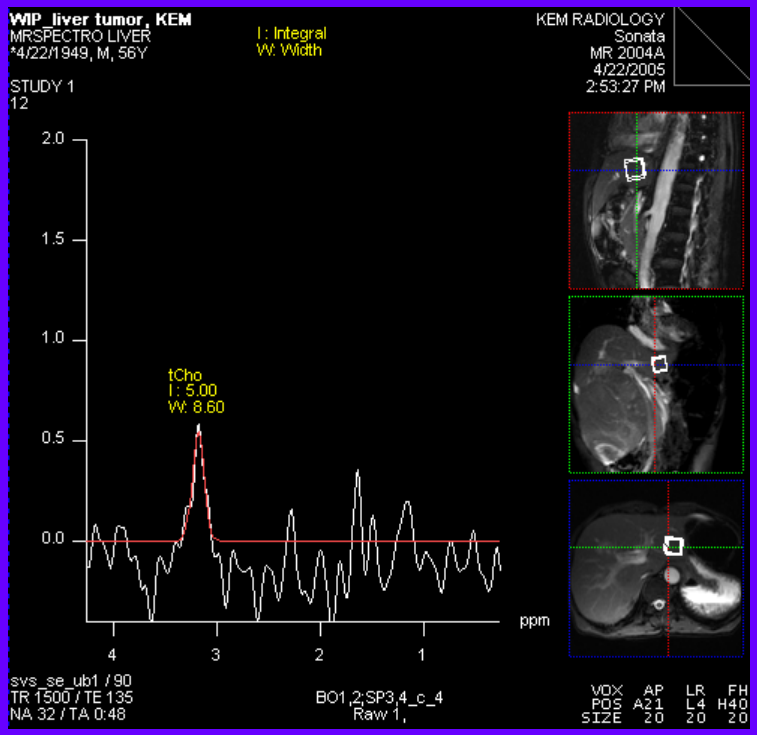




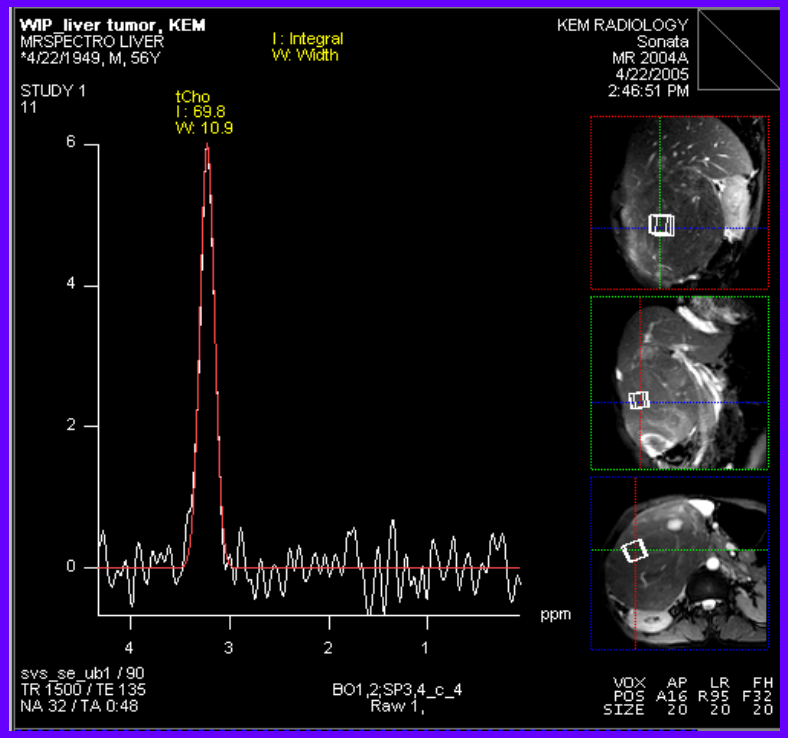
SVS in liver tumor

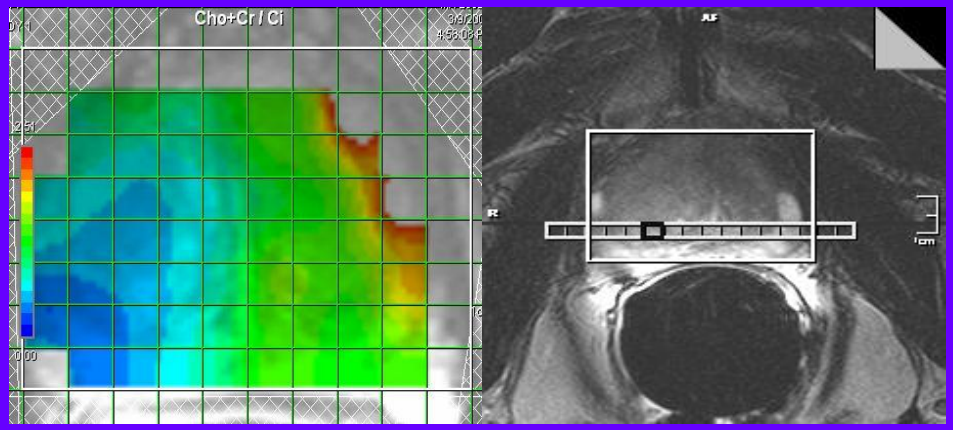
Comparison:

reference spectrum



tumor spectrum





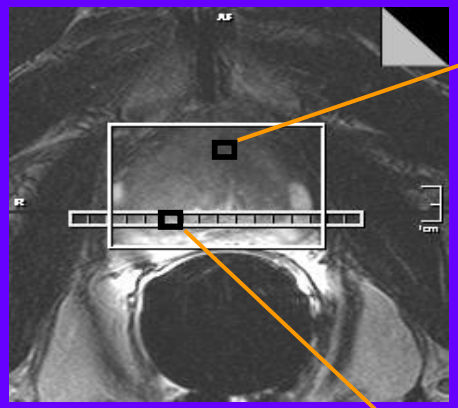
Prostate MR Spectroscopy

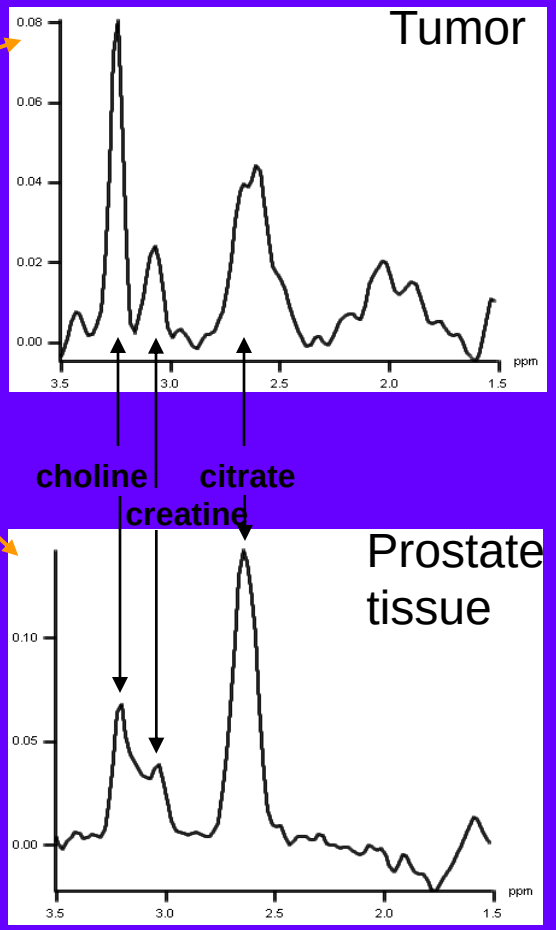
Prostate Cancer Trial

- MR spectroscopy of the prostate
- Outline of the trial
- Data
- PRISMA: Automatic post-processing
- status report
- Participating clinical institutions & partners

MRS of the Prostate

3D MRSI in prostate cancer



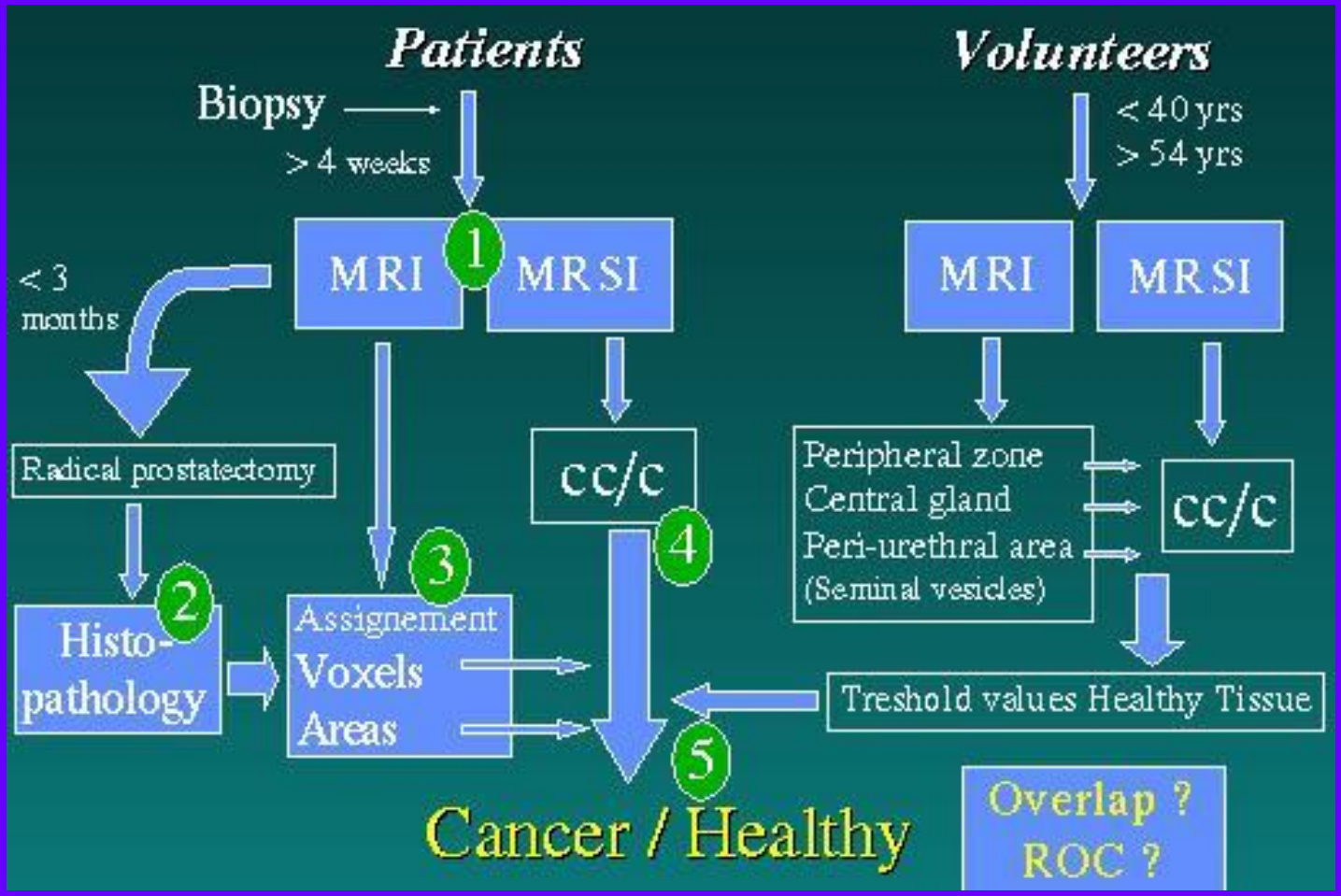


- **Functional prostate tissue shows a marked citrate signal.**
- **In tumors the choline signal is elevated while the citrate signal is decreased**

Objectives of the trial

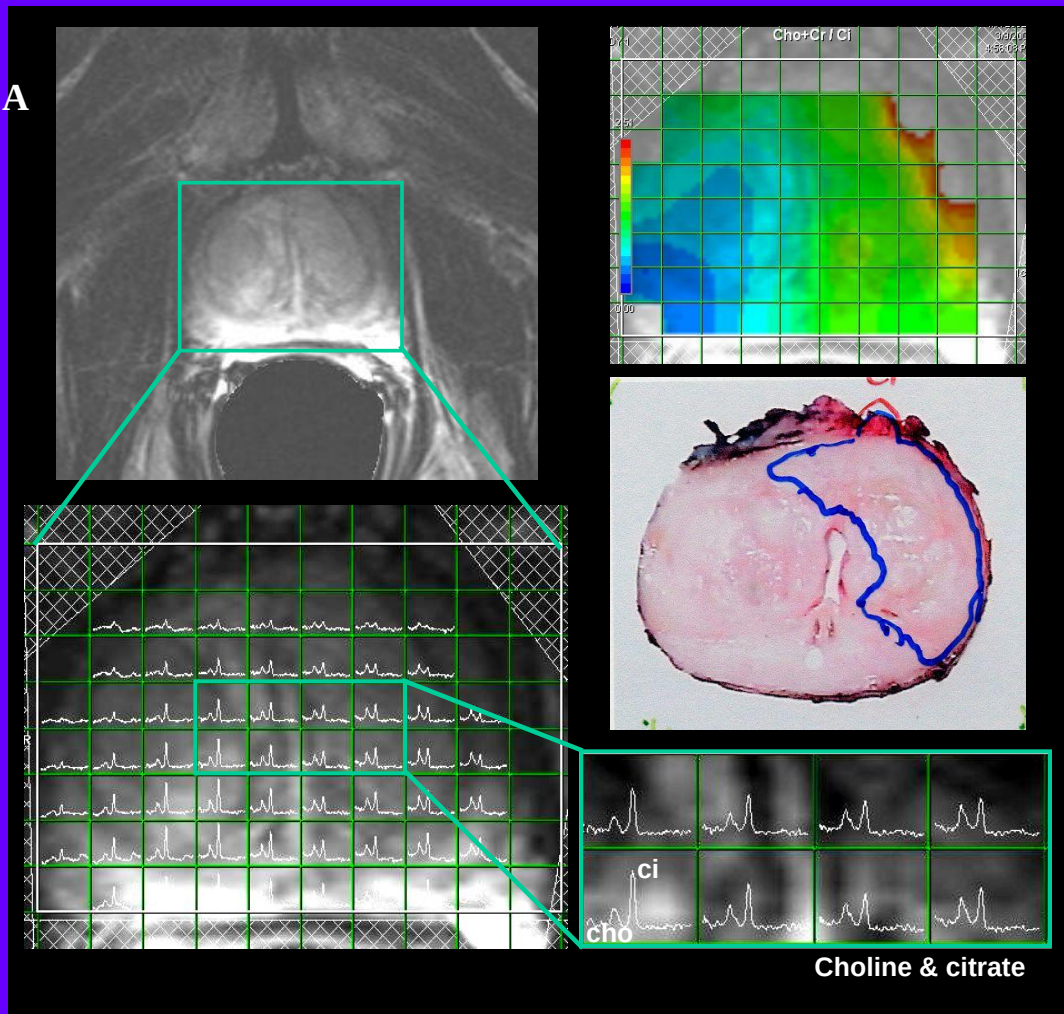
- **Primary objectives**
  - **3D ^{1}H CSI detects prostate carcinoma**
  - **3D ^{1}H CSI localizes prostate carcinoma**
- **Secondary objectives**
  - **documenting inter-patient reproducibility of method**
  - **documenting intra-patient reproducibility of method**
  - **documenting variation due to patient age**
  - **documenting the robustness of the method**
- **Hypothesis**
  - **Cho/Citrate or (Cho+Cr)/Citrate is significantly higher in tumor compared to healthy prostate tissue.**

Trial



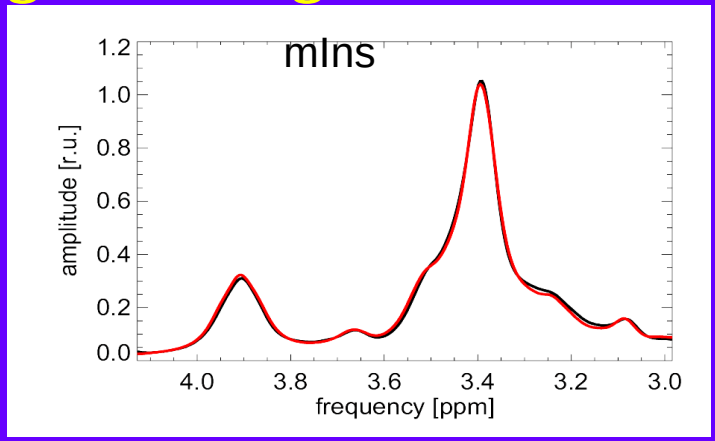
Patient's Prostate Cancer MRI-Histology

- The axial T2-weighted image is used for matching voxel locations to histopathological specimens.
- One of the spectral maps, partially expanded, shows the quality of the MRSI data throughout the slice.
- Deviations in the (Cho + Cr) / Ci metabolite ratio map largely correspond to the tumor location indicated with the blue line.



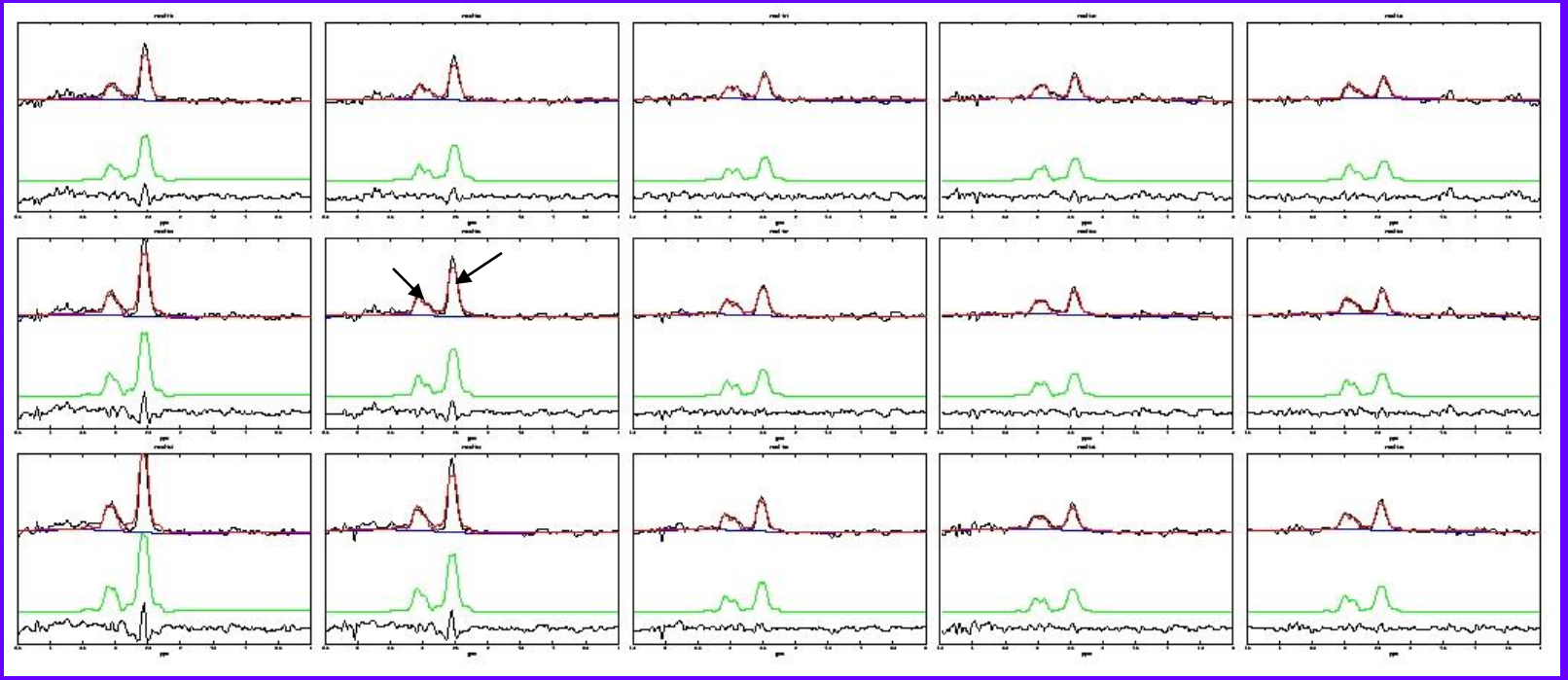
Automatic Post-Processing with PRISMA*

- **Complex time domain fit**
- **Metabolite model**
  - **Prior knowledge based model signals using complete spectral shapes**
- **Baseline model**
  - **Finite time model**
- **Automatic processing of 3D CSI data**



* prior knowledge based modeling of spectroscopic magnetic resonance applications

PRISMA: Quantification of Prostate Cancer Metabolites



Methodology

- **Patients with prostate cancer who underwent a radical prostatectomy without prior treatment**
  - **Anatomical imaging**
  - **3D MRSI**
  - **Histopathology**
  - **Case report forms**
- **Young (<40 years) and age-matched (>55 years) healthy volunteers**

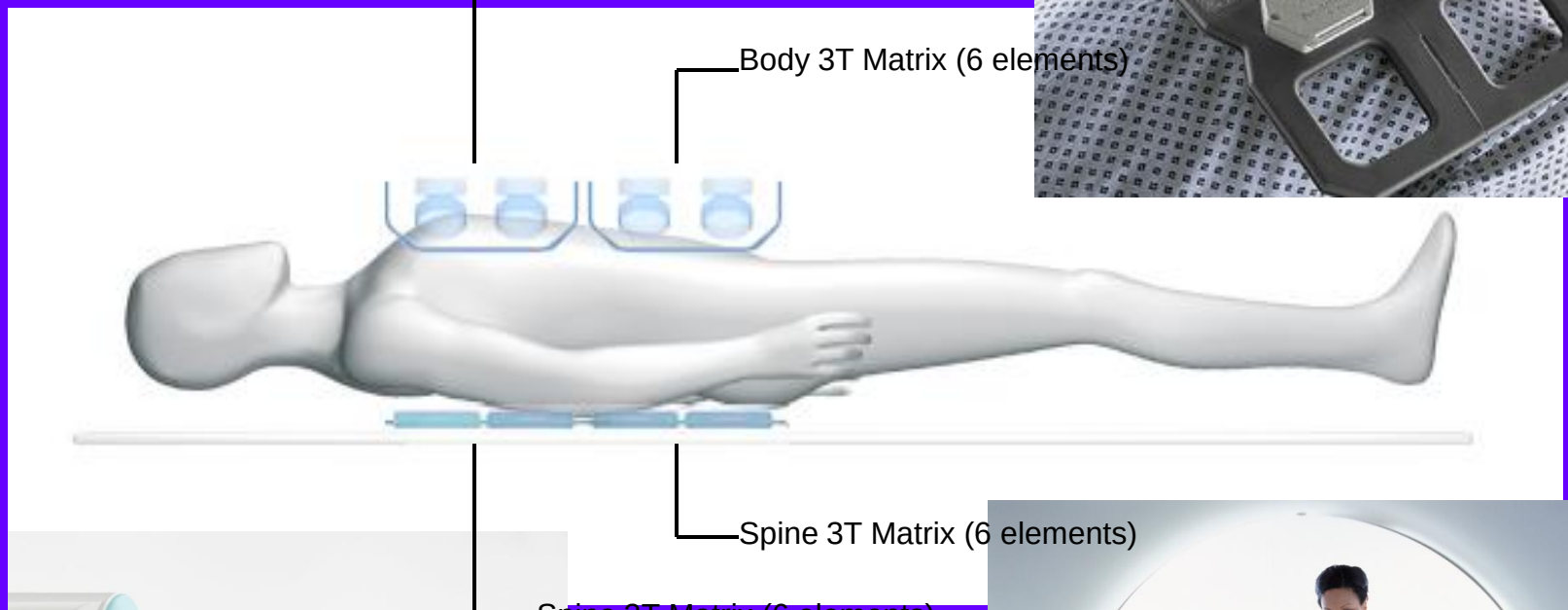
- Current work
  - **Matching and classification of the data by experienced radiologists and physicists**
  - **Data processing at two independent evaluation sites with PRISMA**

Surface Coils

clinical scanner

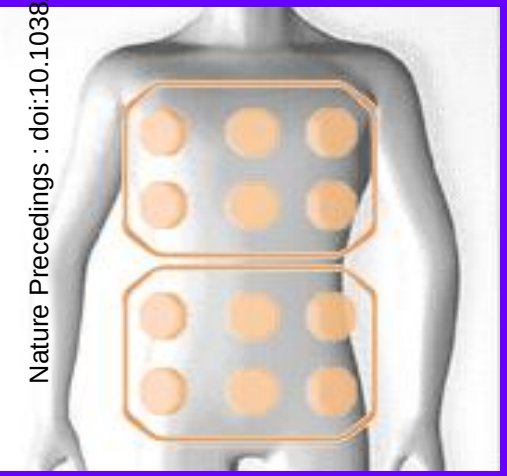
Surface coils consisting of many small elements

Nature Precedings : doi:10.1038/npre.2009.3485.1 : Posted 28 Jul 2009



routine clinical imaging

- Utilization of 24 i m elements



50 cm

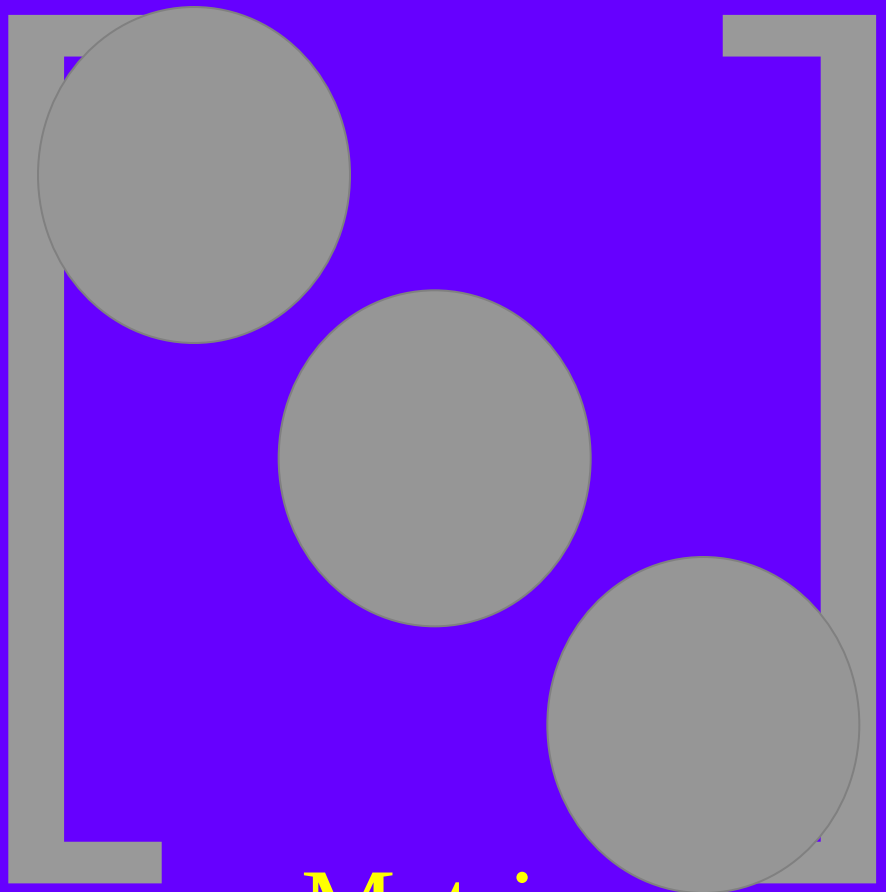
2D HASTE with PAT 2

1.3x1.7x6 mm^3, 20 slices, TA

9 sec

Signal Combination

$$\lambda \Sigma_i W_i^* S_i$$

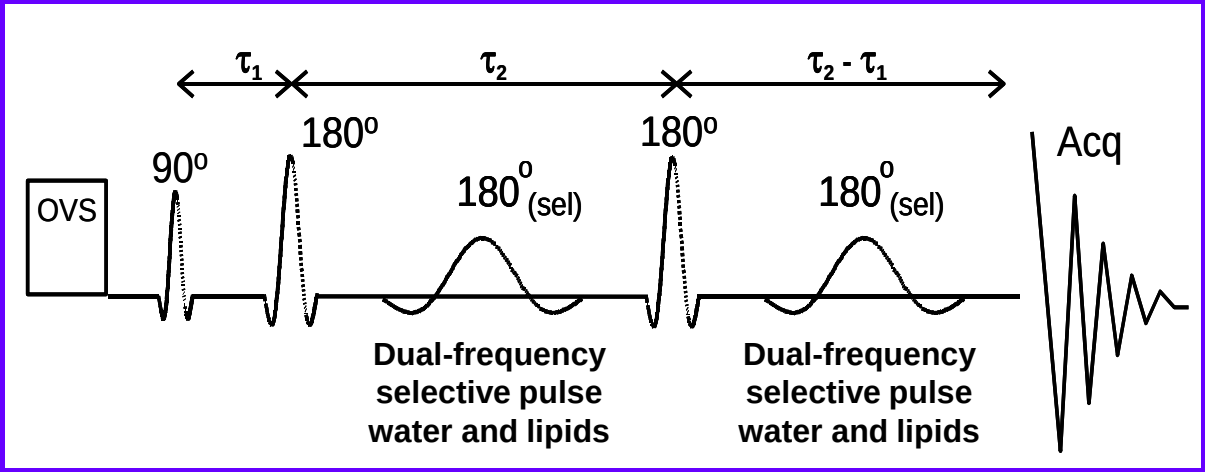


Matrix

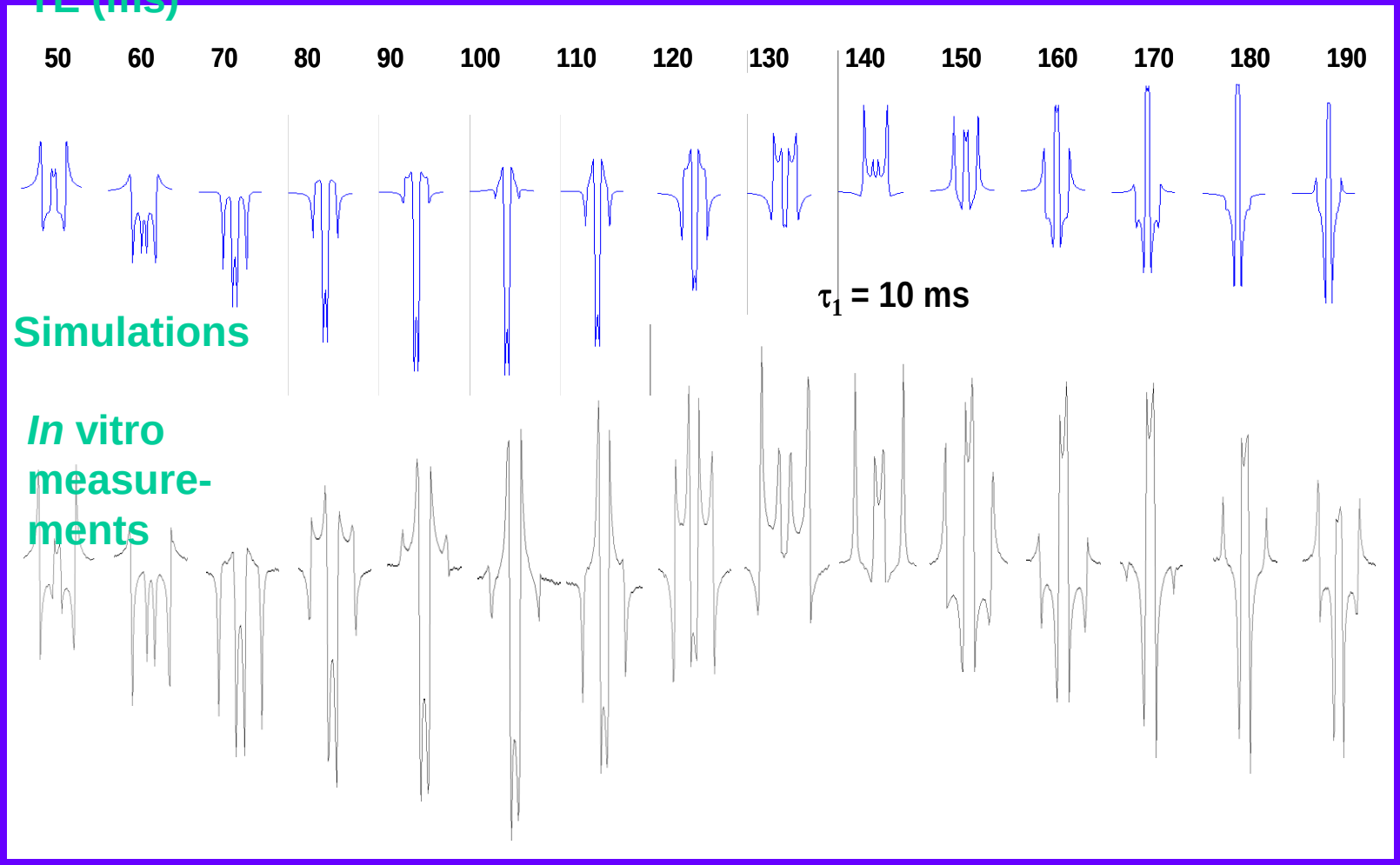
Spectroscopy

Pulse sequence

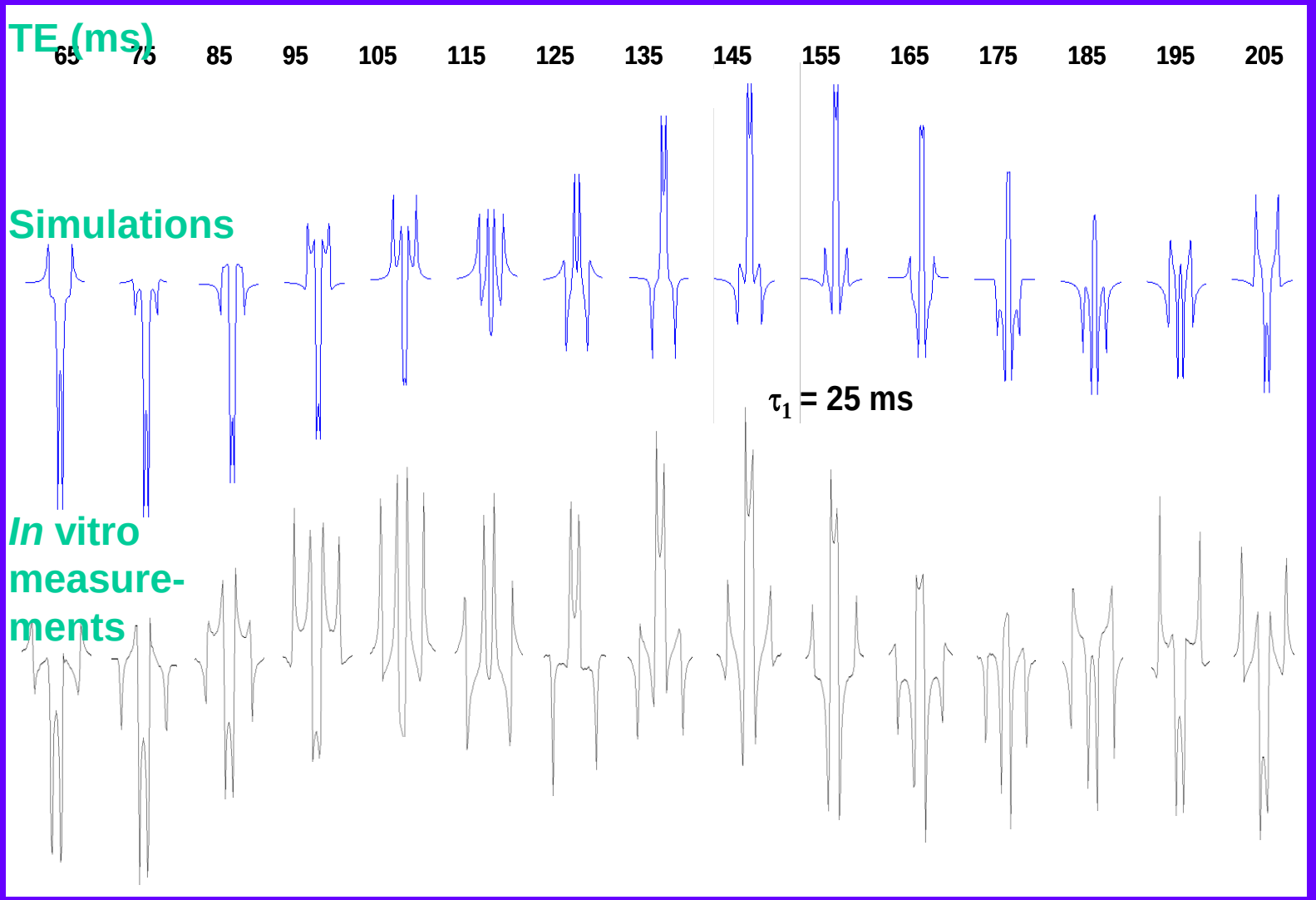
Pulse spacing in sequence defines spectral shape of citrate,
while choline and creatine as singlet signals remain unaffected by pulse timing



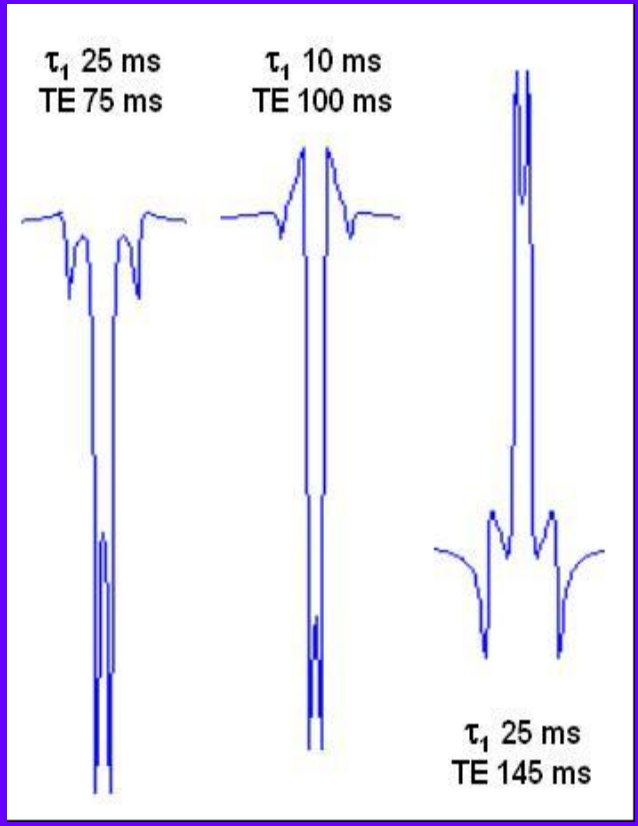
Spectral shape of citrate at 3T



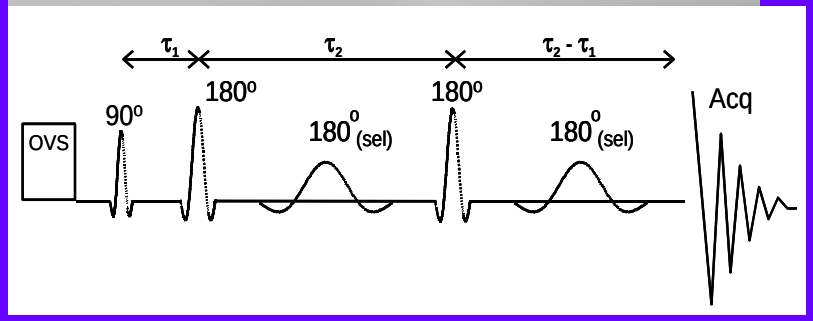
Spectral shape of citrate at 3T

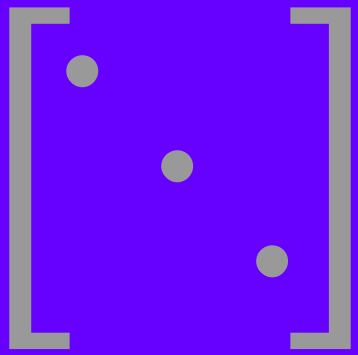


Selected spectral shapes for quantification



Sensitivity $A_{(TE)}$	0.901	0.869	0.831

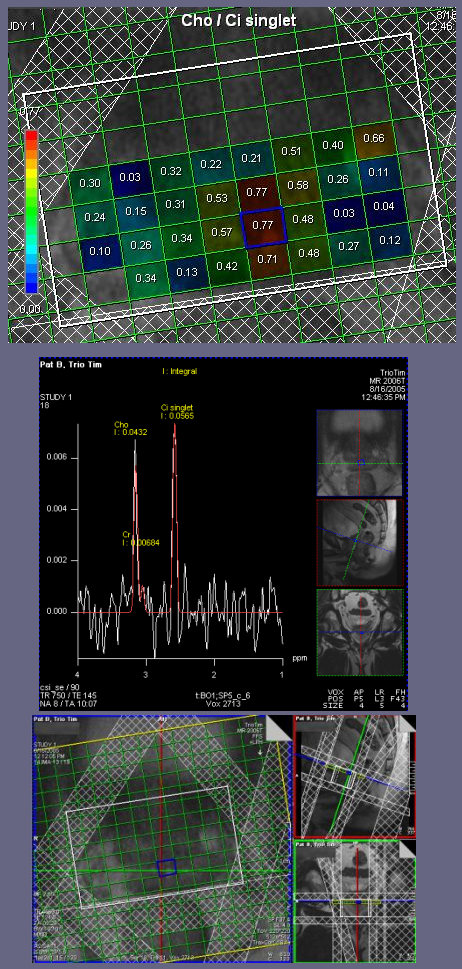




No need of guided wires

^{1}H-Prostate Spectroscopy at 3T MAGNETOM Trio a Tim System

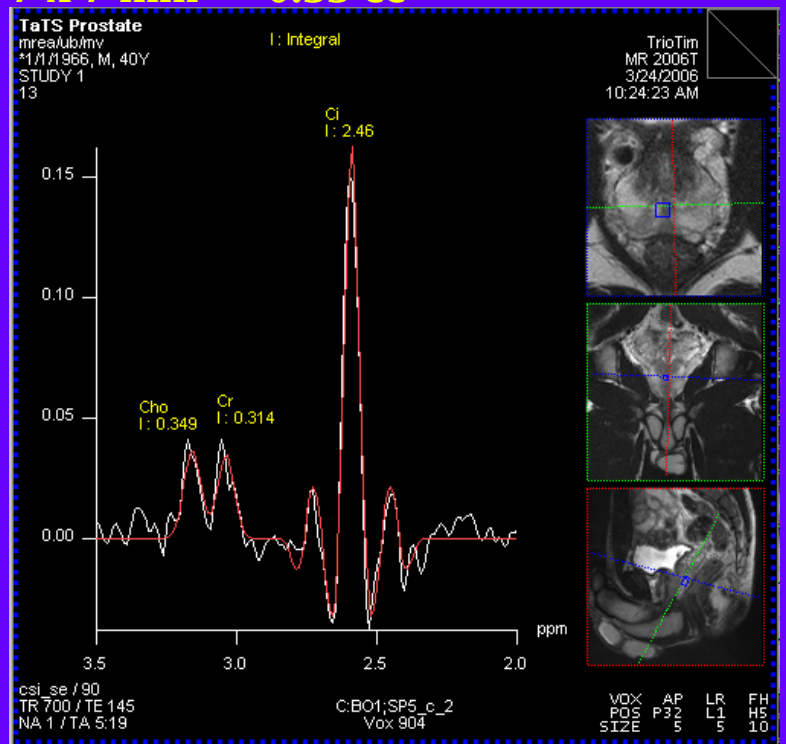
- **3D-CSI-SE scan for complete coverage of the prostate**
- **Measurement without an Endorectal Coil by using only Array Coils**
- **Optimized sequence timing for 3T**
  - **TE 145 ms**
  - **TR 750 ms**
- **7x7x7 mm^3 voxel**
- **Spectral and spatial saturation pulses**
- **Scan time: 10 min**

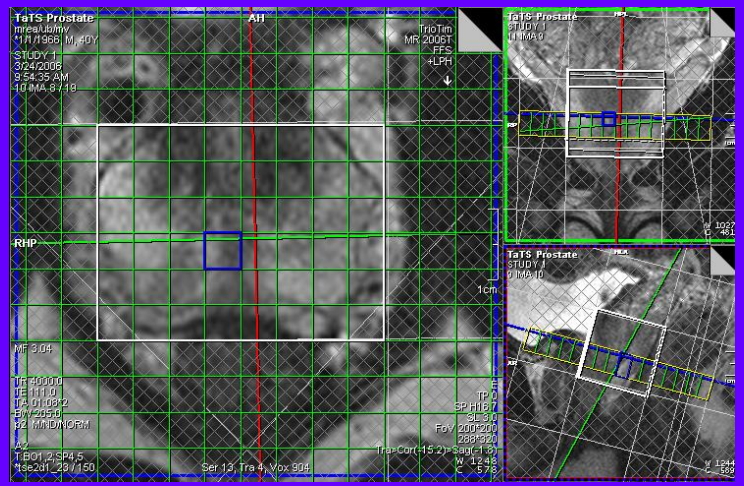


TIM Trio: Matrix Spectroscopy of the Prostate

- **3D Spin-Echo CSI**
- **sequence timing optimization → TE = 145 ms; TR = 700 ms**
- **TA = 5:19 min !!**
- **scan matrix 14 x 14 x 8**
- **nominal voxel size**
  7 x 7 x 7 mm^3 = 0.33 cc

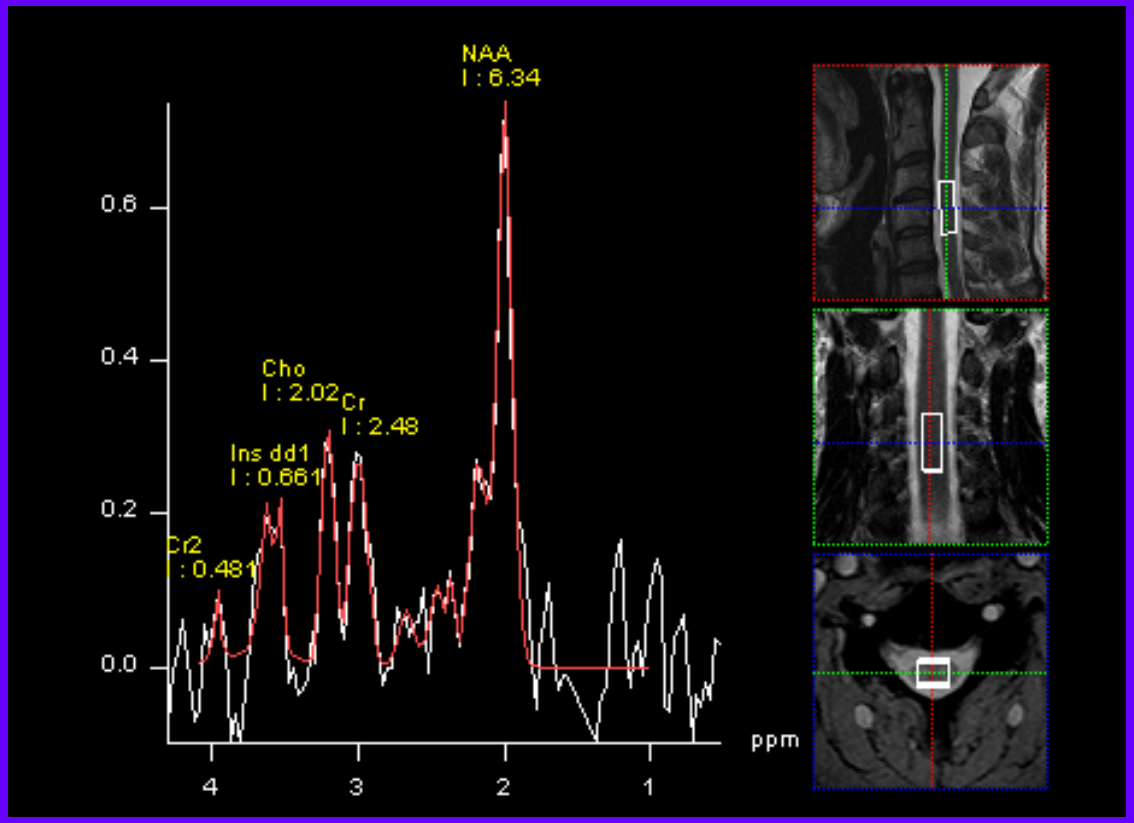
- **combined Spine and Body Matrix coil reception, no usage of ER coil**
- **truly non-invasive determination of the metabolic state of the entire prostate**





Spinal Cord Spectroscopy

Magnetom Avanto:
Single Voxel Spectroscopy in the Spinal Cord

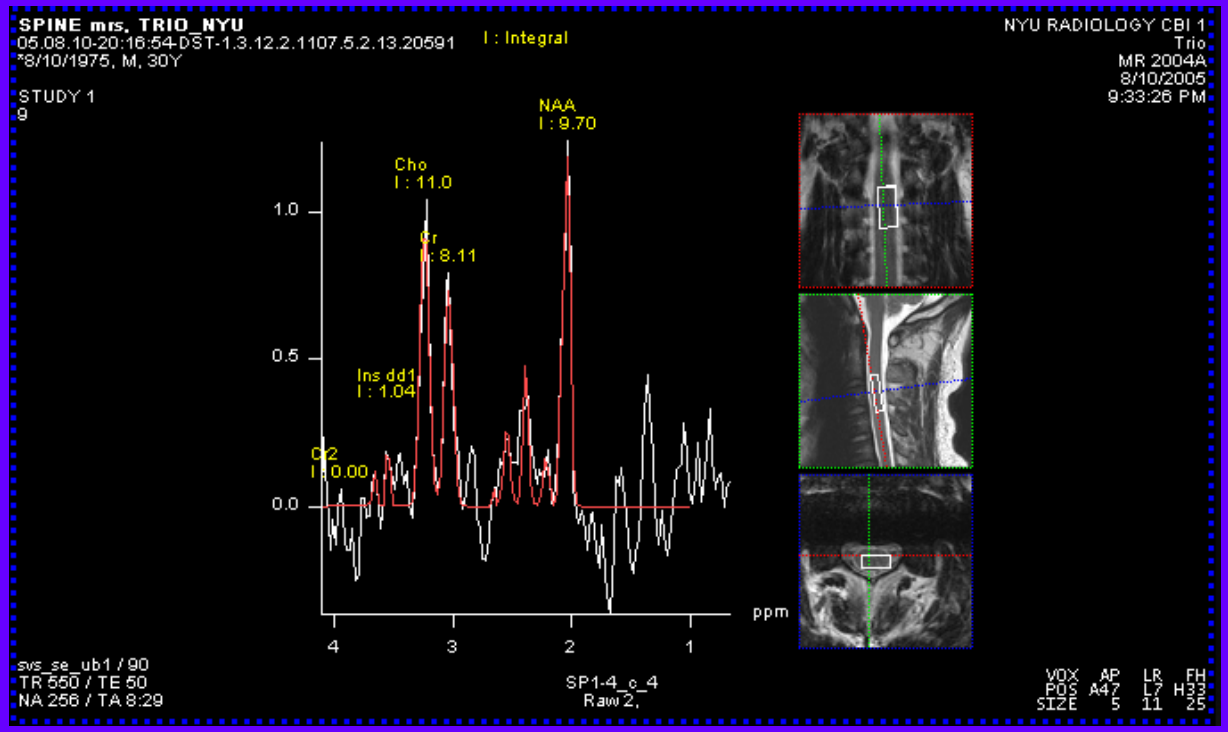


svs_se in the spinal cord, benefits from

- **Combined signal of body matrix**
- **ECG triggering**
- **Small voxel size: 7 x 9 x 25 mm^3**

Magnetom Trio:

Single Voxel Spectroscopy in the Spinal Cord

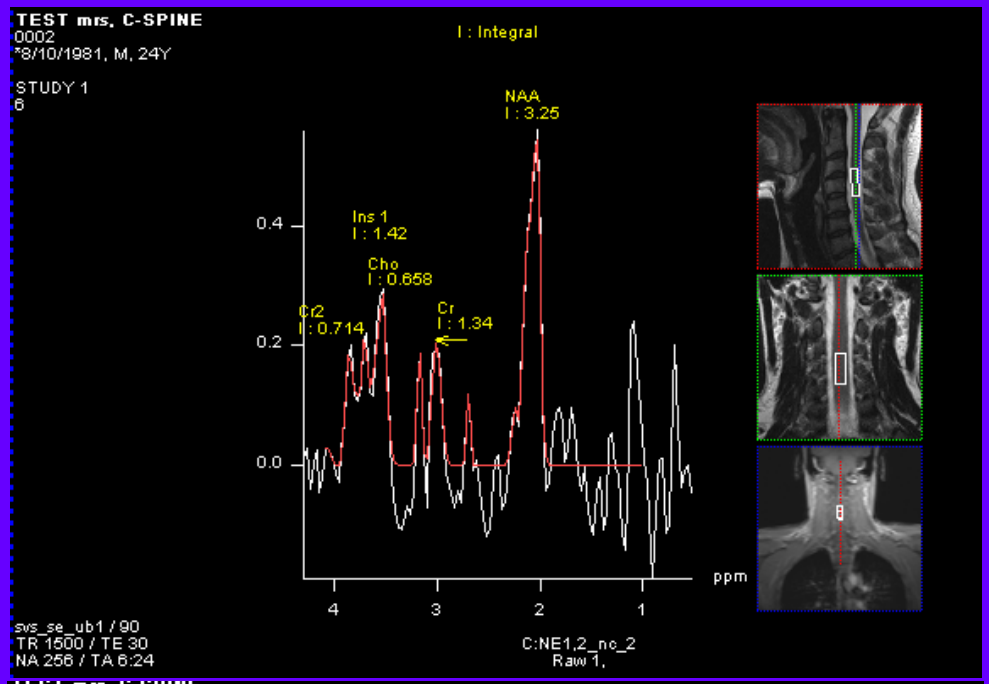


svs_se in the spinal cord, benefits from

- Combined signal of body matrix
- ECG triggering
- Small voxel size: 5 x 11 x 25 mm^3

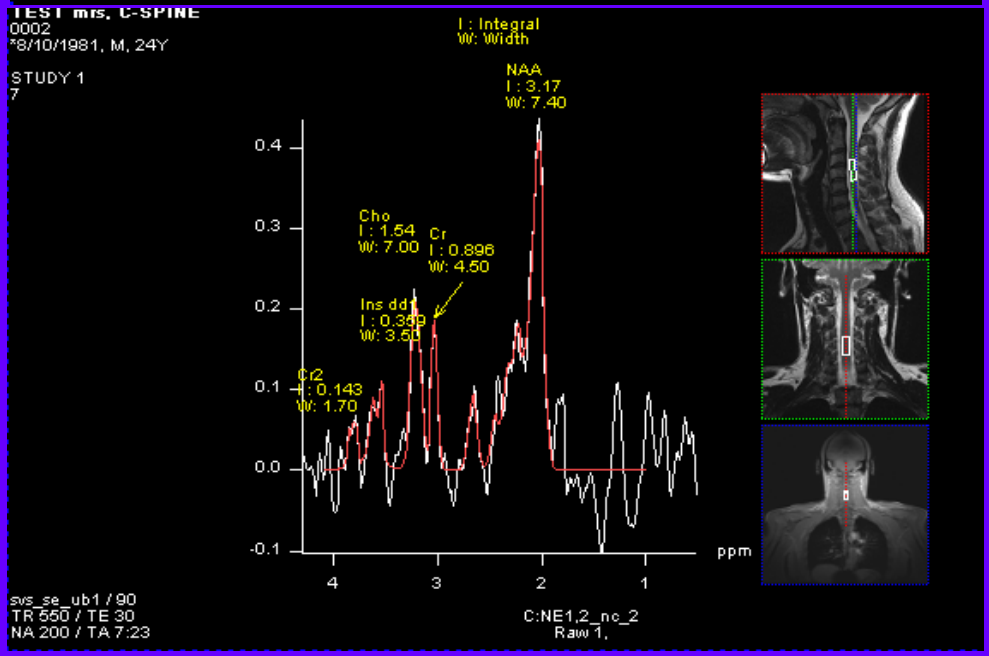
Avanto

Not triggered

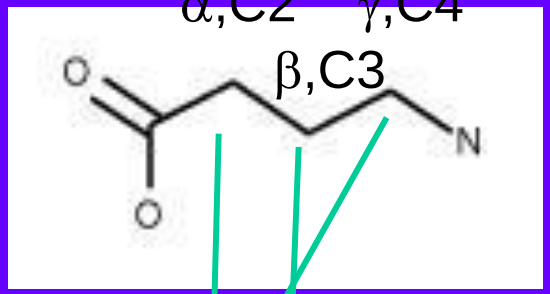


Triggered:
Same voxel

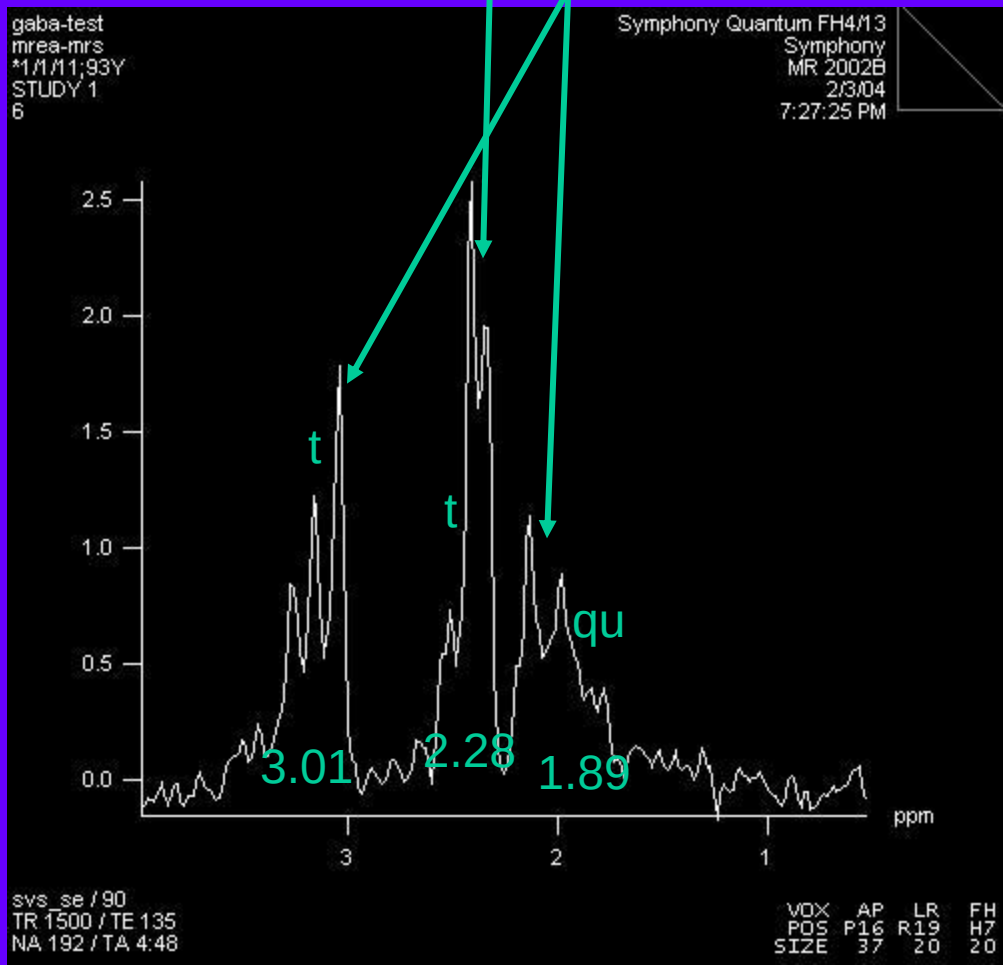
Lines are narrower than on non triggered scan



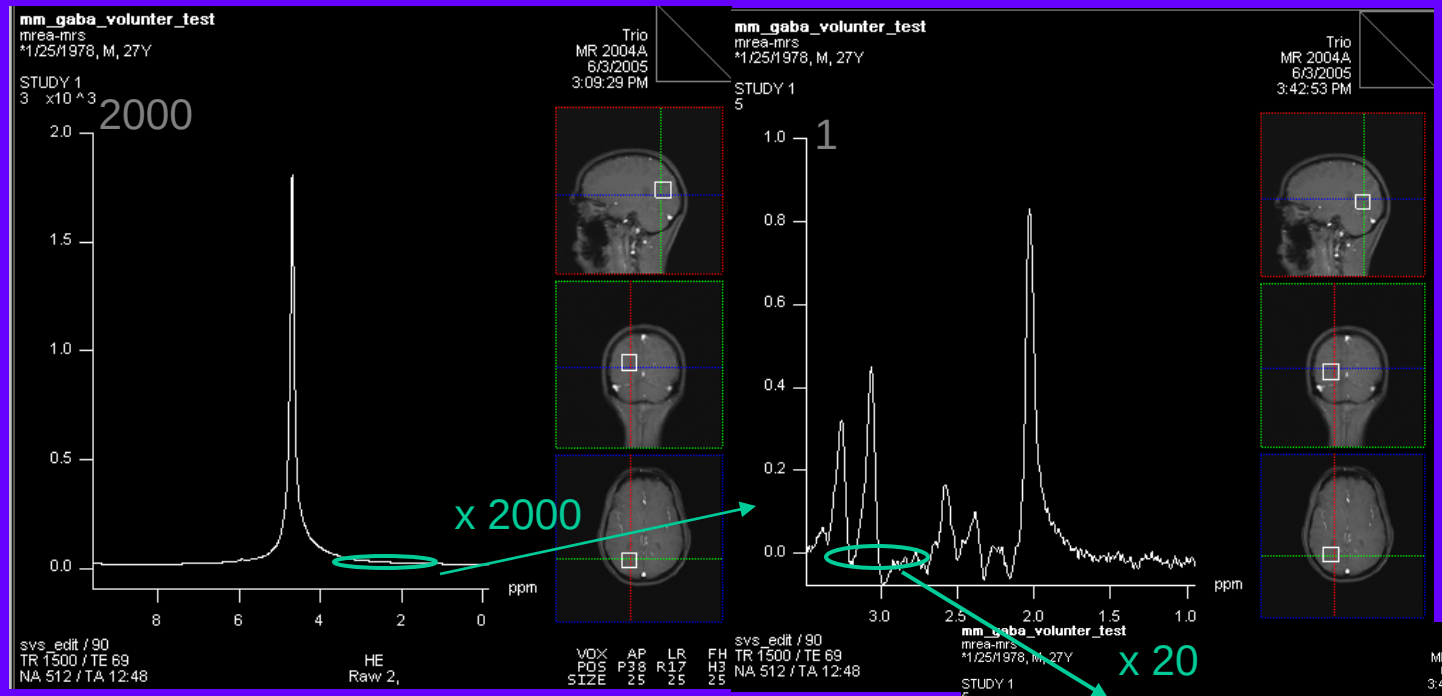
The GABA molecule



- **γ-Amino butyric acid: $C_4H_9NO_2$**
- **methylene groups form $A_2M_2X_2$ system**
- **γ and β protons are weakly coupled, A_2X_2**
- **J = 7.3 Hz**



The challenge of GABA detection

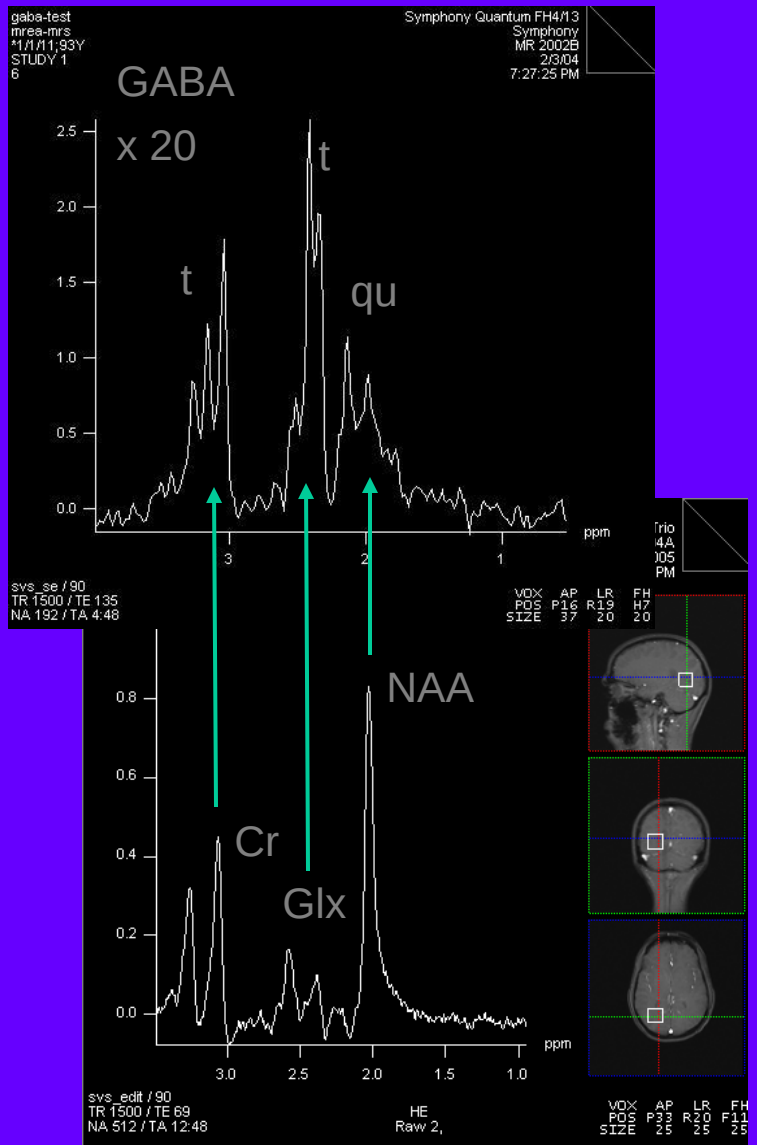


- GABA conc. in the healthy occipital cortex: 1.0 mM
- Signal 40.000 times smaller than water

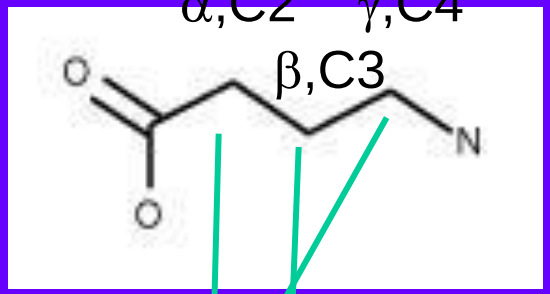
Nature Precedings : doi:10.1038/npre.2009.3485.1 : Posted 28 Jul 2009

GABA detection = suppressing overlapping signals

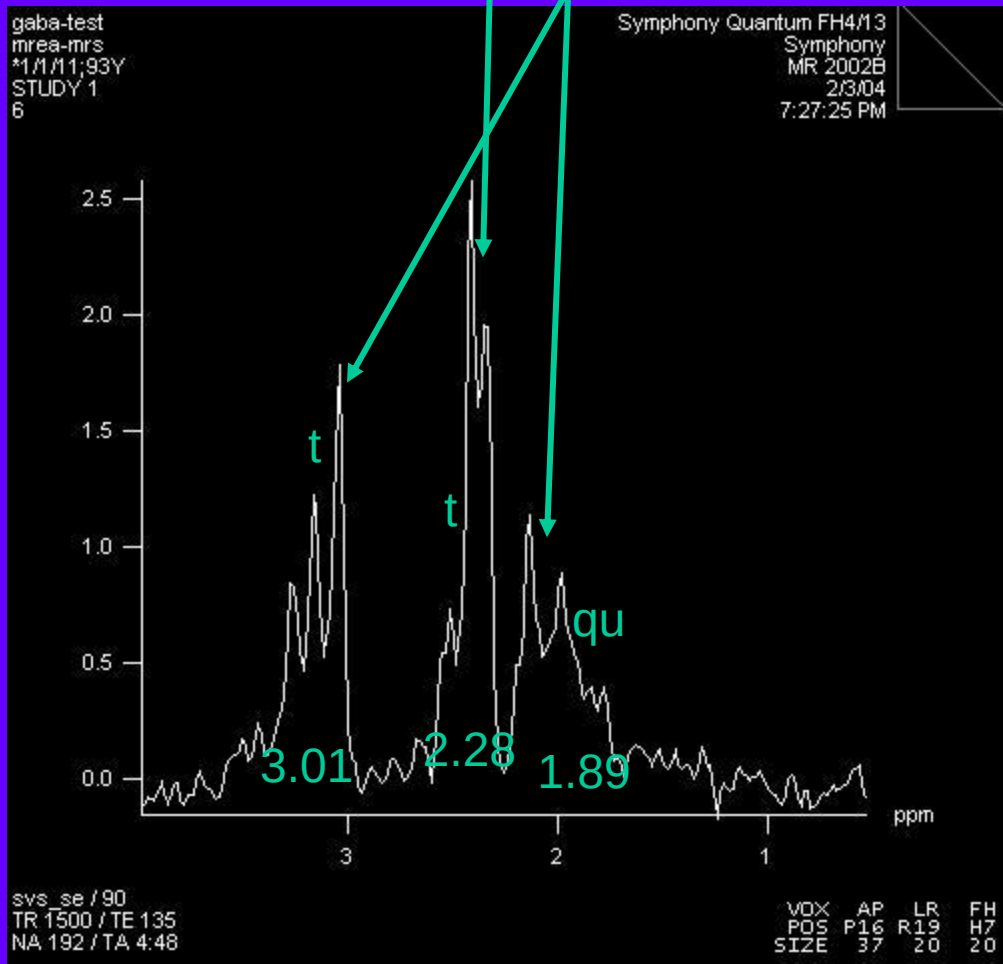
- singlet signals (Cr, NAA)
- coupled signals (Glu, Gln)
- macromolecules



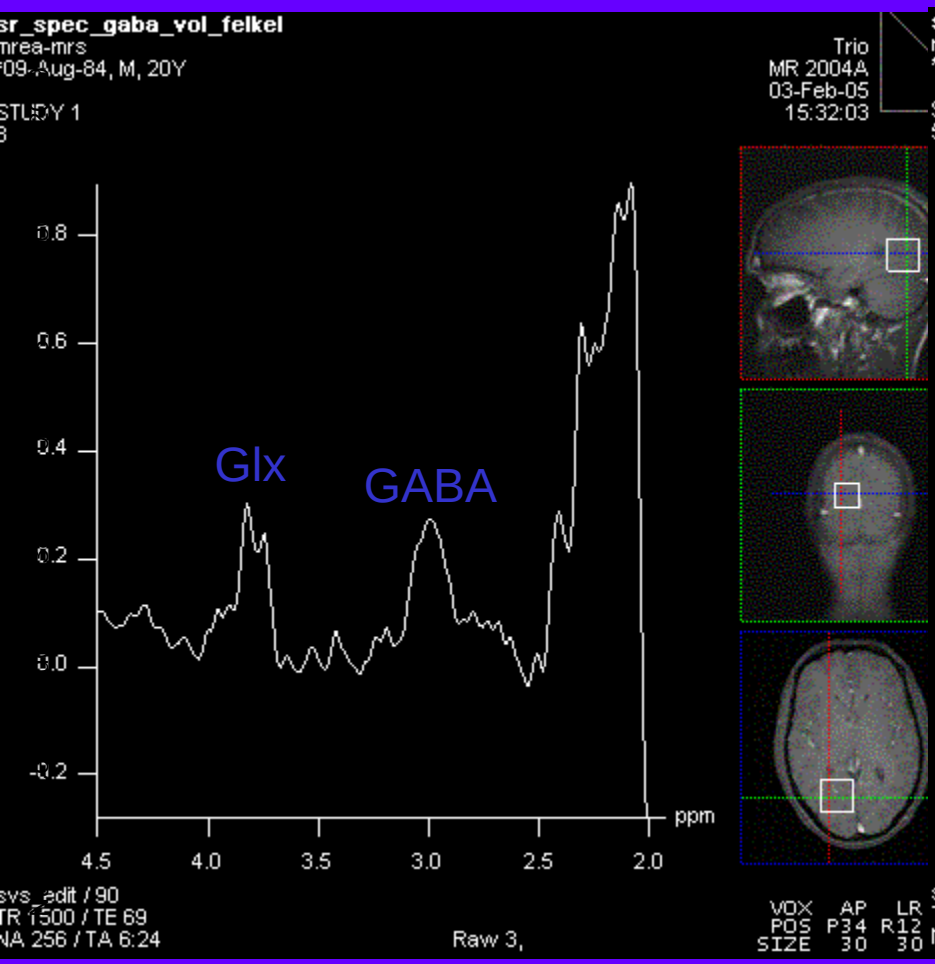
The GABA molecule

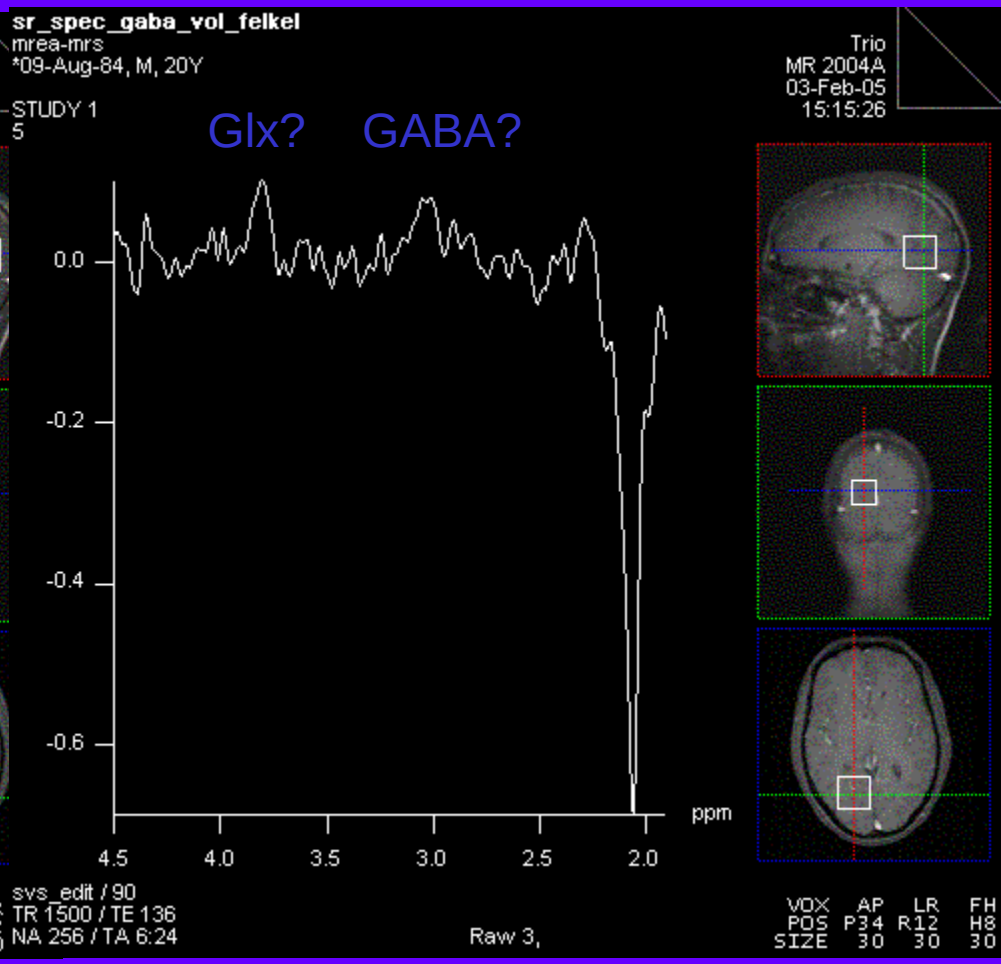


1. γ-Amino butyric acid: $C_4H_9NO_2$
2. methylene groups form $A_2M_2X_2$ system
3. γ and β protons are weakly coupled, A_2X_2 J = 7.3 Hz



GABA editing: first experience at 3T



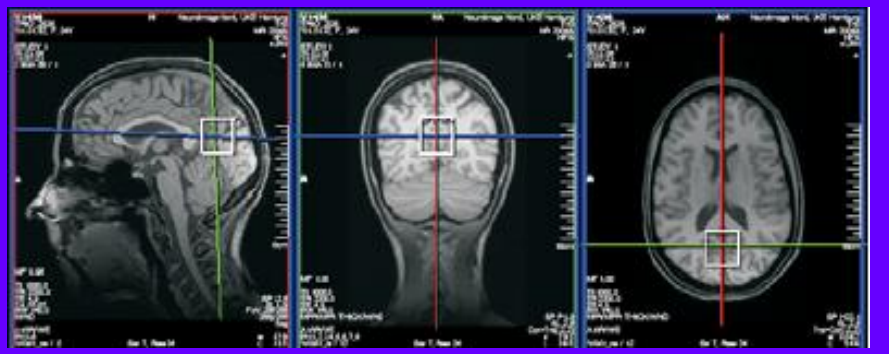


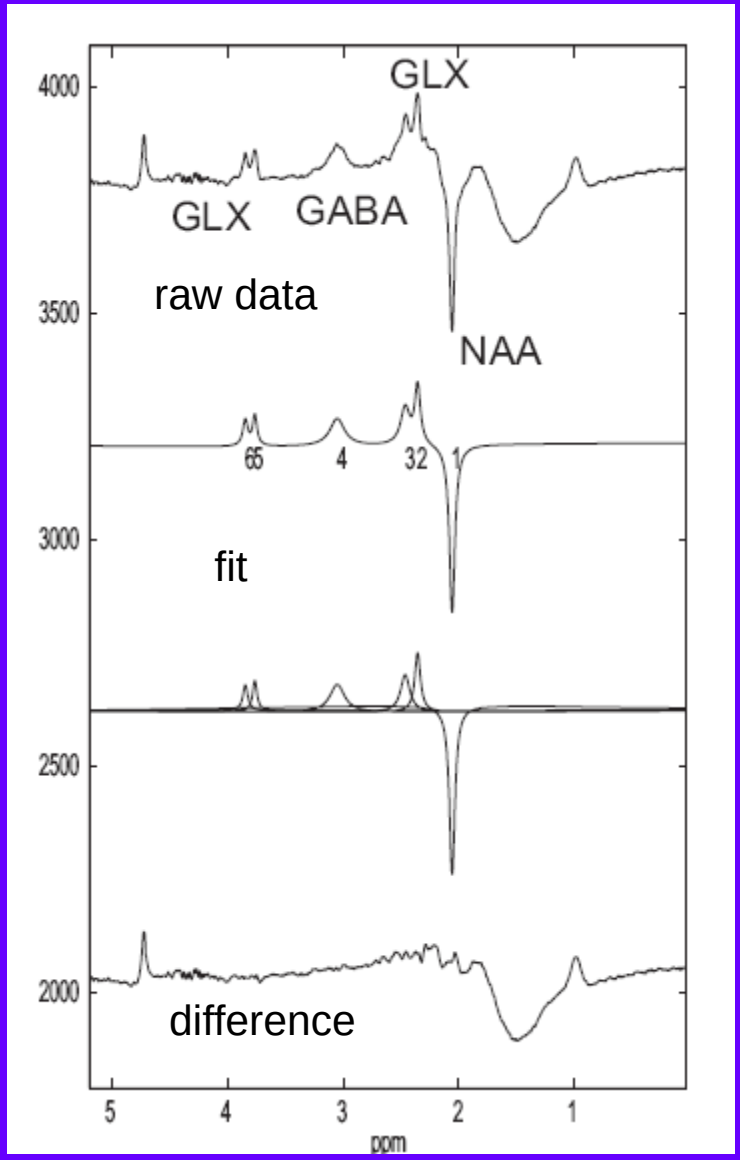
TE = 69 ms TE = 136 ms

voxelsize = 27 cc, TA = 6’24 min

MAGNETOM Trio: GABA Editing

- **svs_se_edit**
- **by Mescher, Merkle, Kirsch, Garwood, Gruetter**
- ***In vivo spectral editing (MEGA, 2-shot)***
- **TE 68 ms**
- **voxelsize = 27 cc**
- **TA = 6'24min**
- **8-Channel Array Coil and offline signal combination**
- **fitting with MRUI**

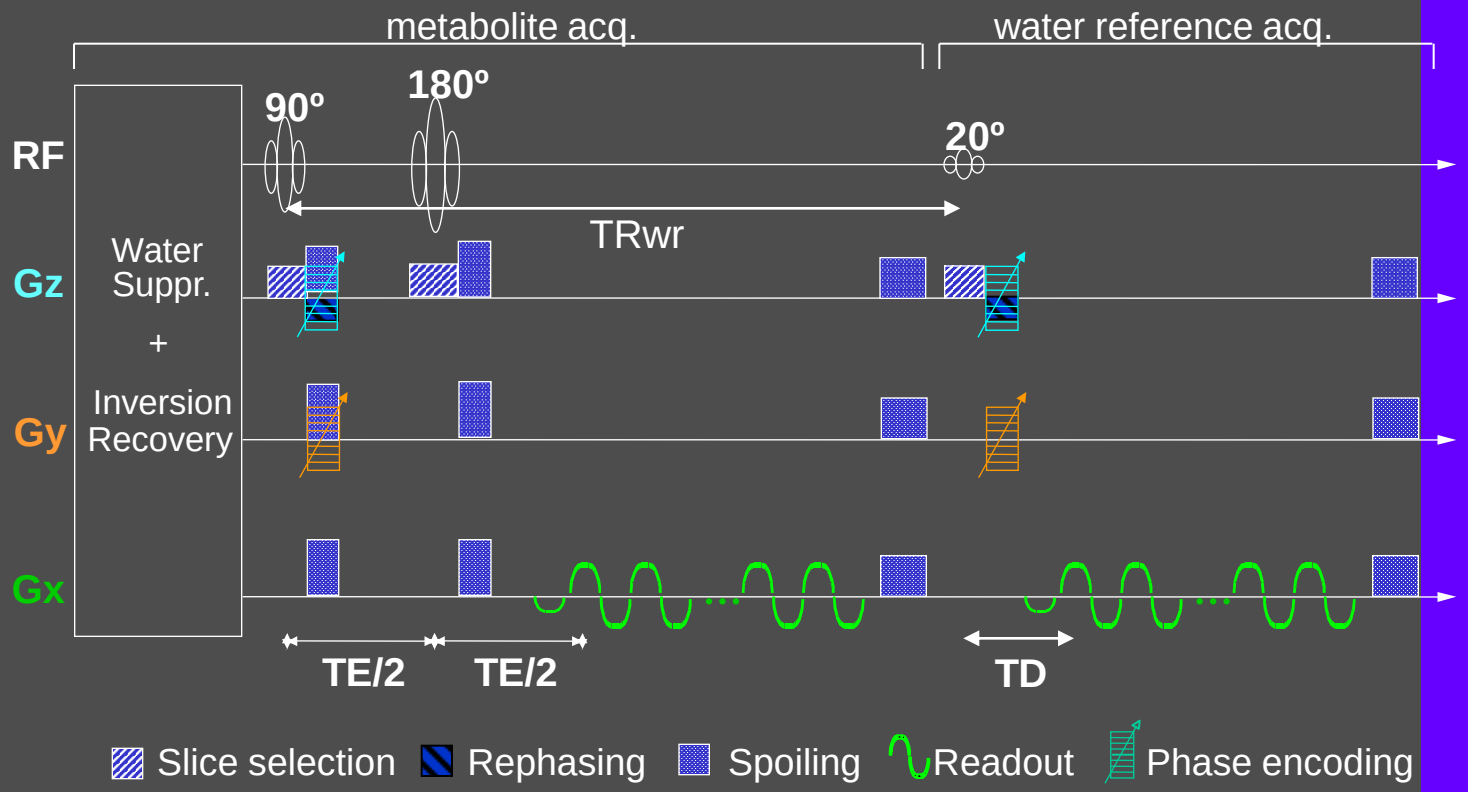




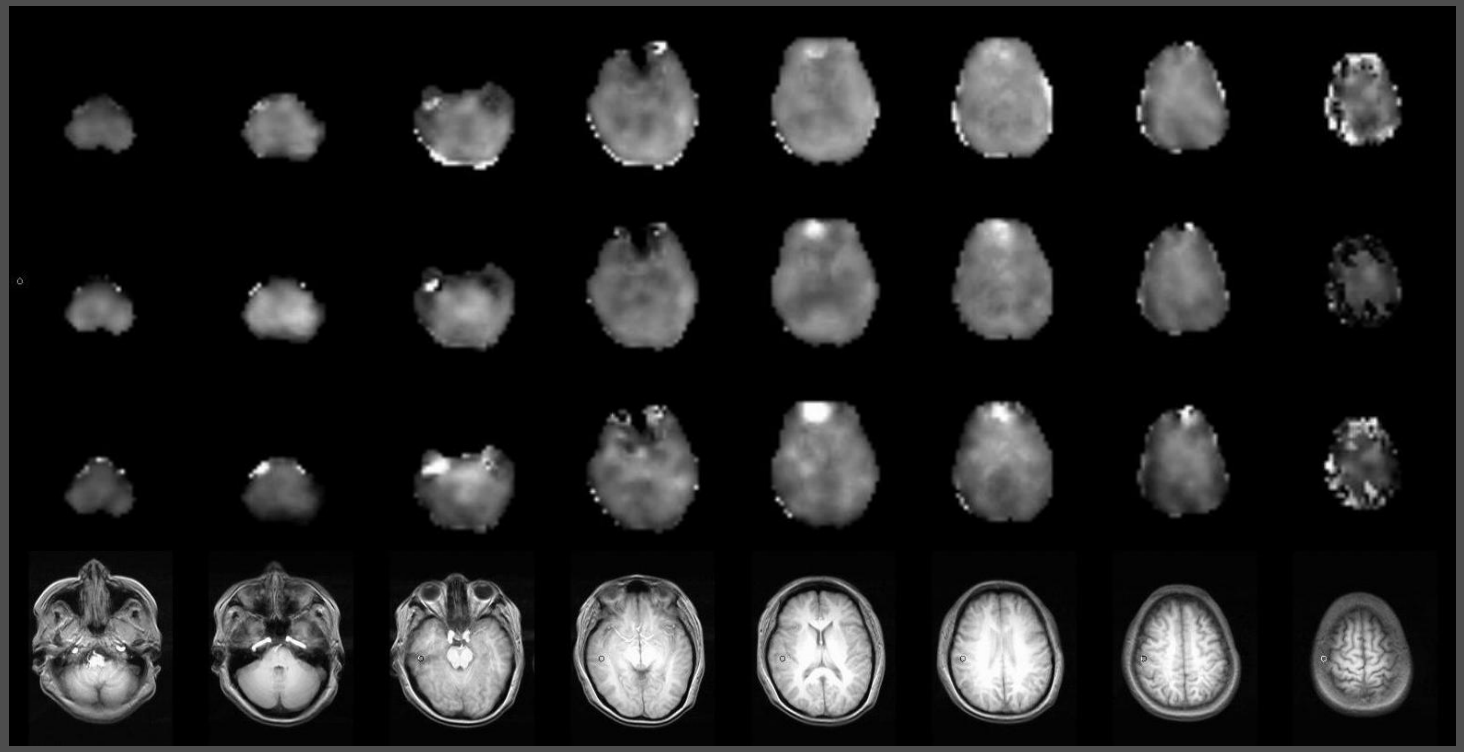
The GABA user group

Works in Progress:
Echo-Planar Spectroscopic Imaging

3D EPSI with interleaved water reference



Volumetric High Resolution (64 x 64) EPSI on the MAGNETOM Trio



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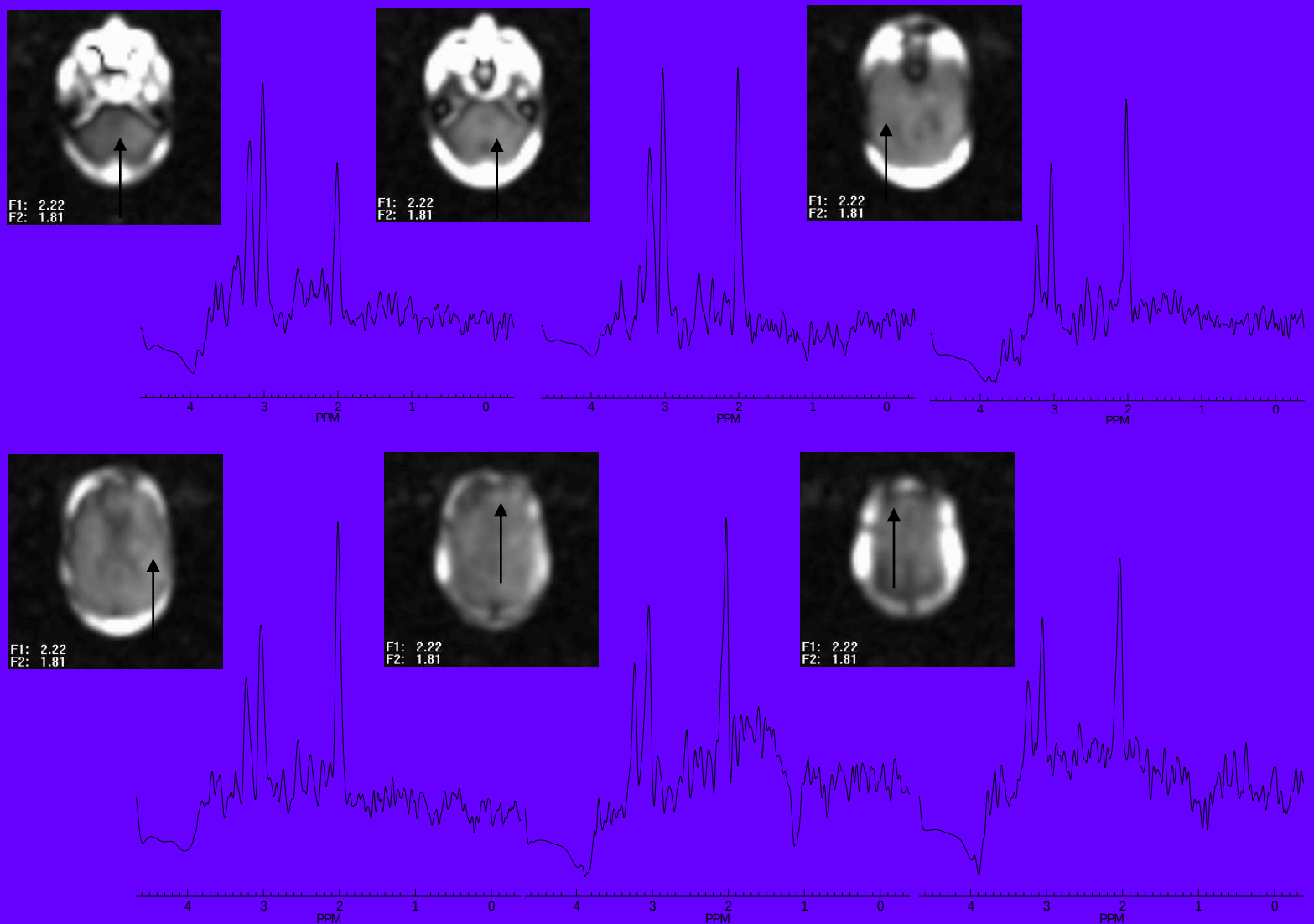


Works in Progress:
Steady State Free Precession Techniques

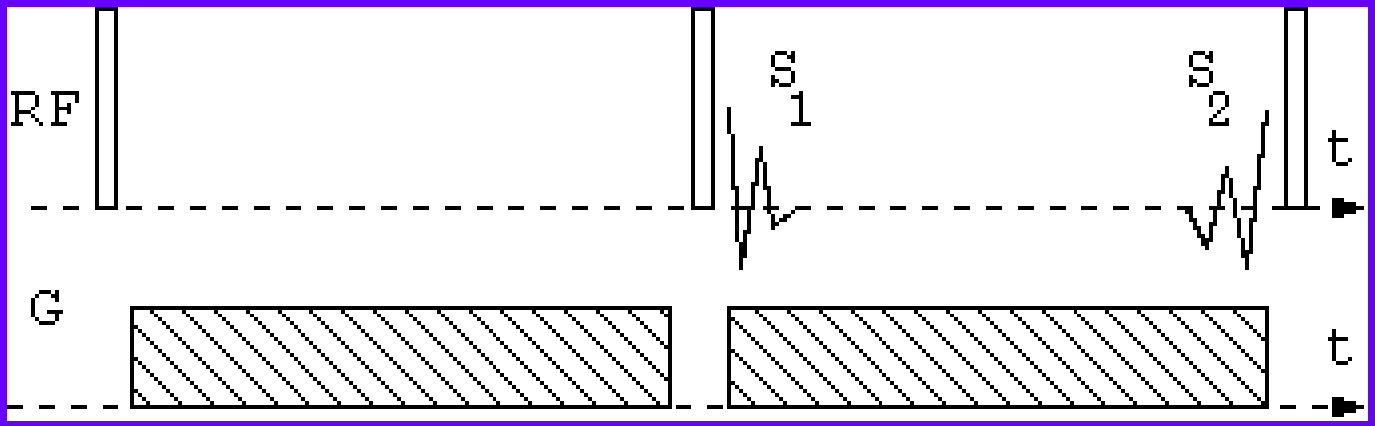
SSFP-based Pulse Sequences I

- **SSFP = steady state free precession**
- **fast sequence of RF-pulses, TR < T_2, T_1**
- **constant gradient net effect**

→ formation of 2 echo types

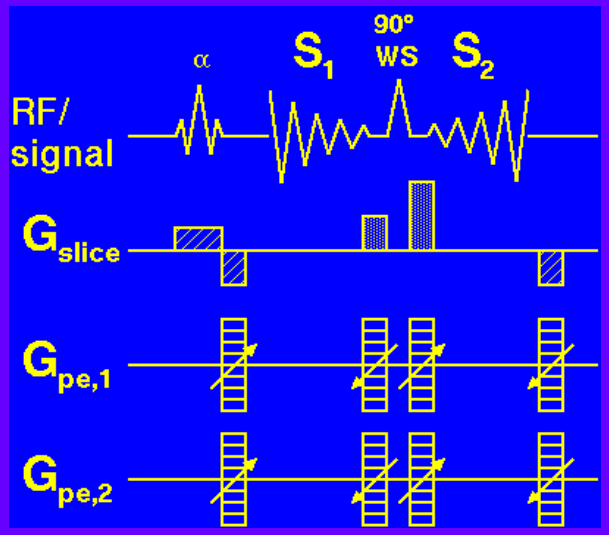
– fid-type of signal S1

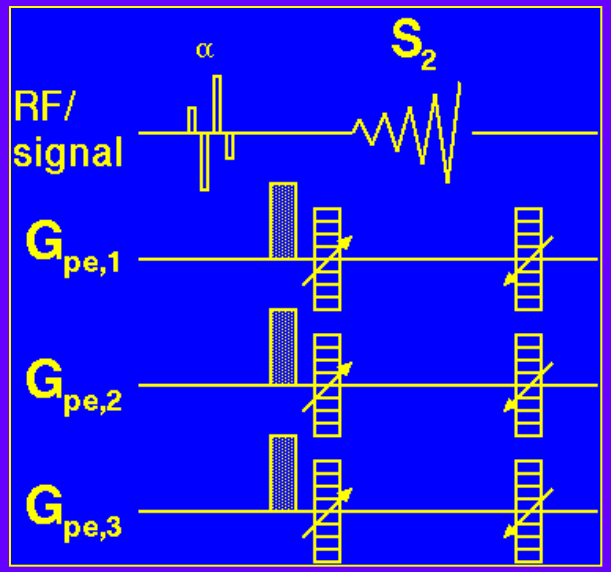
– echo-type signal S2



SSFP-based Pulse Sequences II

- **4 sequence types**
- **True-FISP = coherent combination of S1 and S2**
  - **FAST = detection of only S1**
  - **CE-FAST = detection of only S2**
  - **FADE = separate detection of S1 and S2**
- **Usage in MRI**
  - **suggested already in the 80s**
  - **since end of the 90s: broad usage due to short TA_{min} and high efficiency**
- **Usage for MRS to be explored**
  - **is spectral resolution sufficient?**
  - **can water suppression be integrated?**
  - **what sequence type to be preferred?**
  - **how do J-coupled spins behave?**

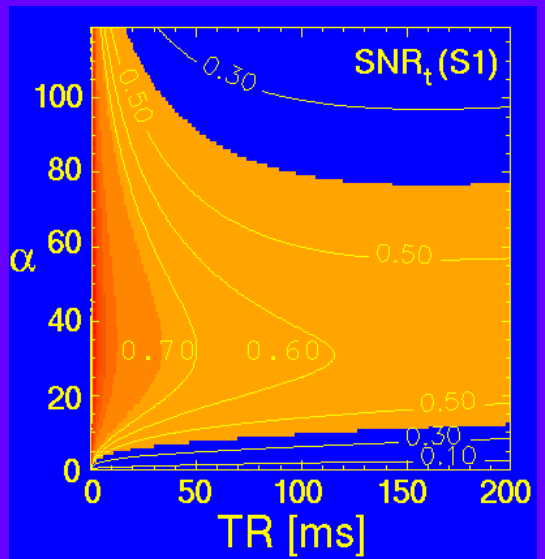


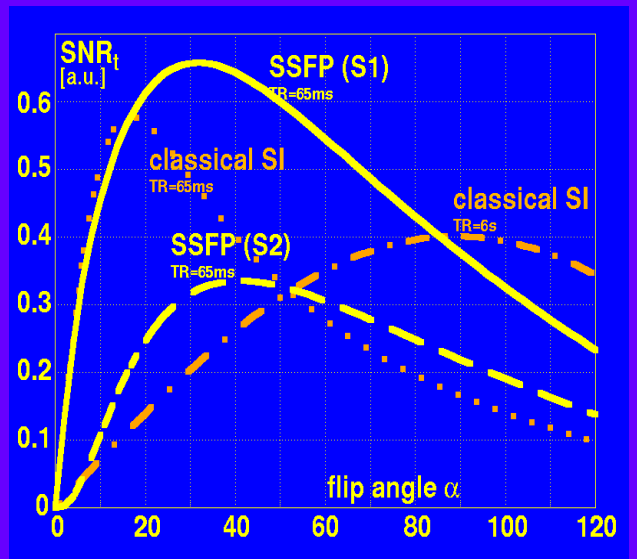


SSFP-based Pulse Sequences III

sequence efficiency

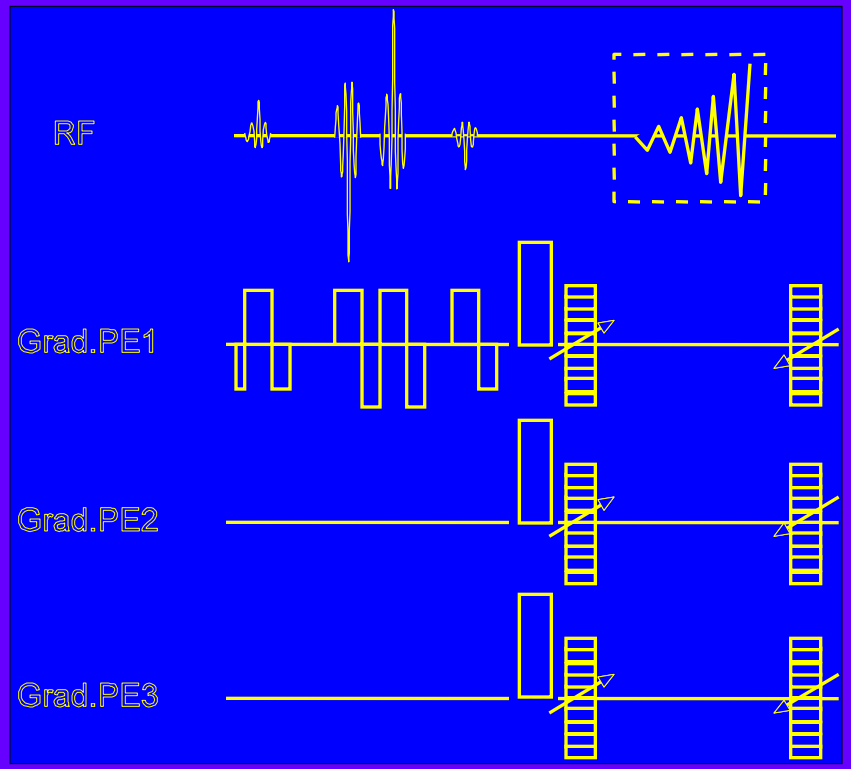
- **W. Dreher et al., *Magn. Reson. Med.*, 50: 453-460(2003)**
  - **utilizing high sequence efficiency**
  - **avoiding interferences between S1 and S2**
    - **FAST = detection of only S1**
    - **CE-FAST = detection of only S2**
    - **FADE = separate detection of S1 and S2**
  - **acquiring complete spectra**





CE-FAST using spatial-spectral selective RF-pulses

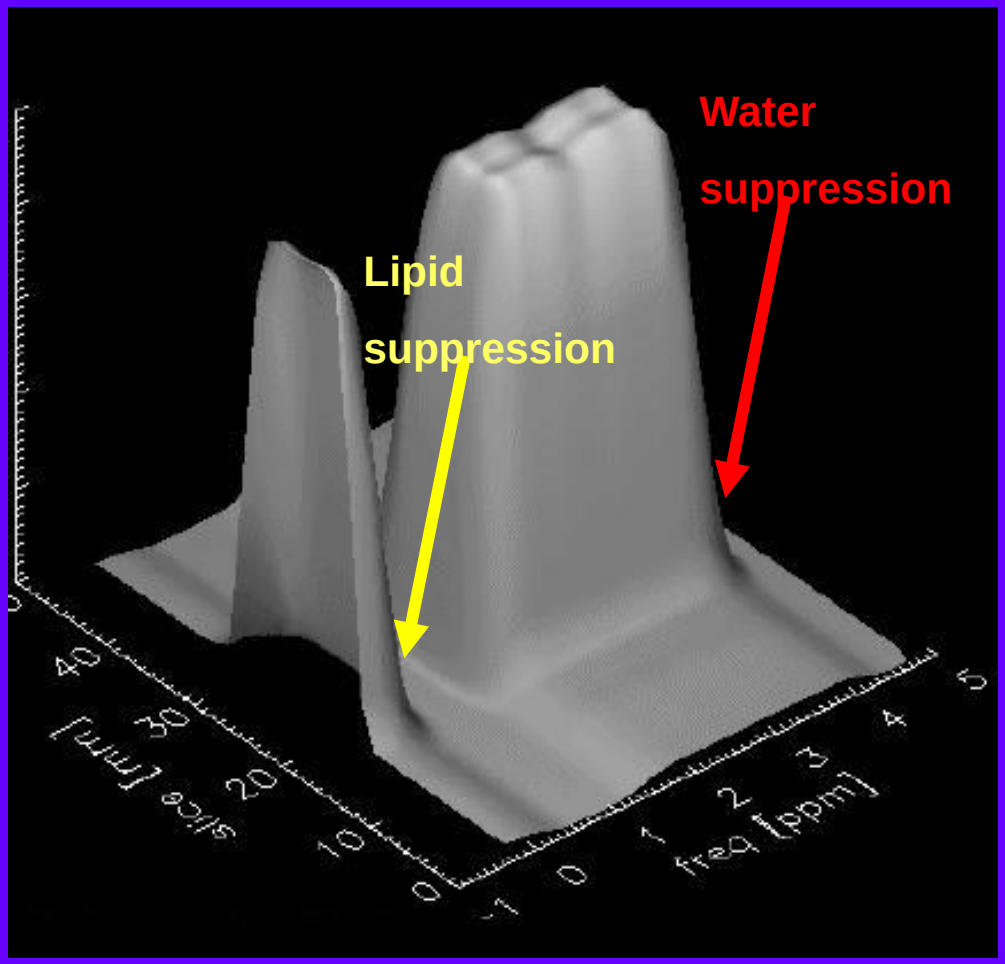
- **2D RF-pulses, selecting**
  - a spectral dimension
  - a spatial dimension [1,2]
- composite pulse of
  - hard-pulses
  - slice-selective pulses [3]
  - timing 1-2τ-5.4-τ-5.4-2τ-1



[1] Meyer et al, MRM 15(2), 1990
[2] Spielman et al, MRM 18(2), 1991
[3] Schick et al, JMRI 8(4), 1998

Spatial-spectral selective RF-pulse profile

- **straightforward implementation**
- **8 ms duration**

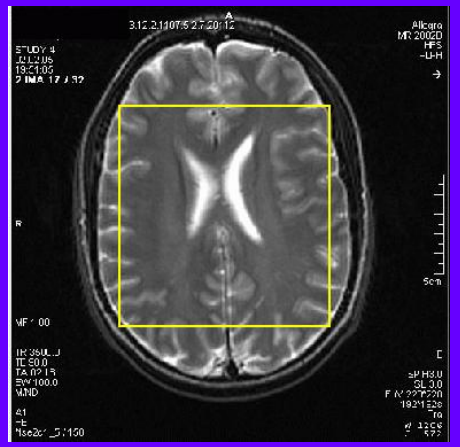


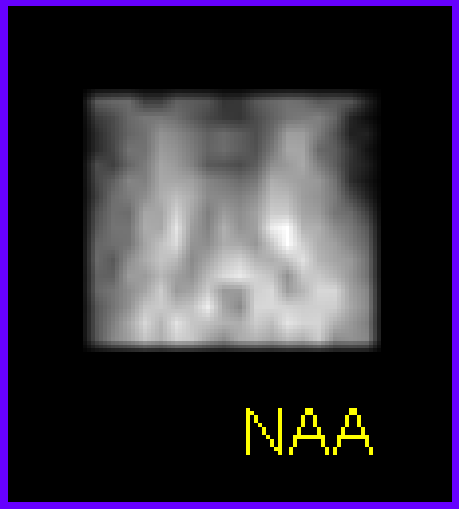
CE-FAST using spatial-spectral selective RF-pulses

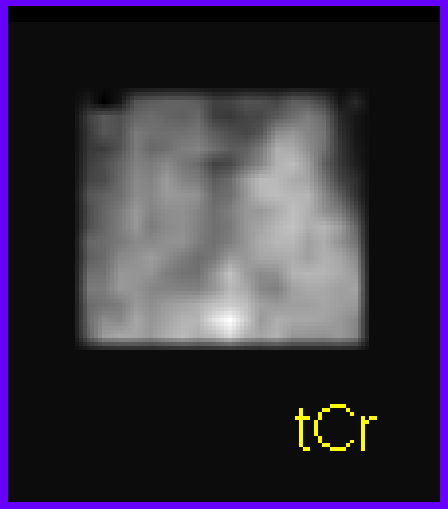
- **SSFP sequence**
- **TR = 83 ms. acqu. window = 64ms, α = 40°**
- **voxelsize = 1 cc, matrix 32 x 32, FoV 200**
- **TA = 1:29 min**

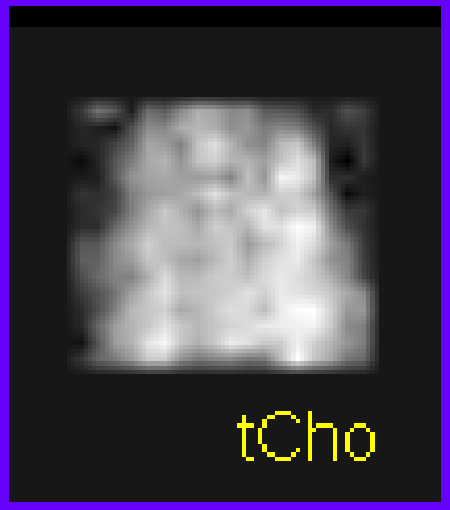
→ short acquisition time

→ high sequence efficiency







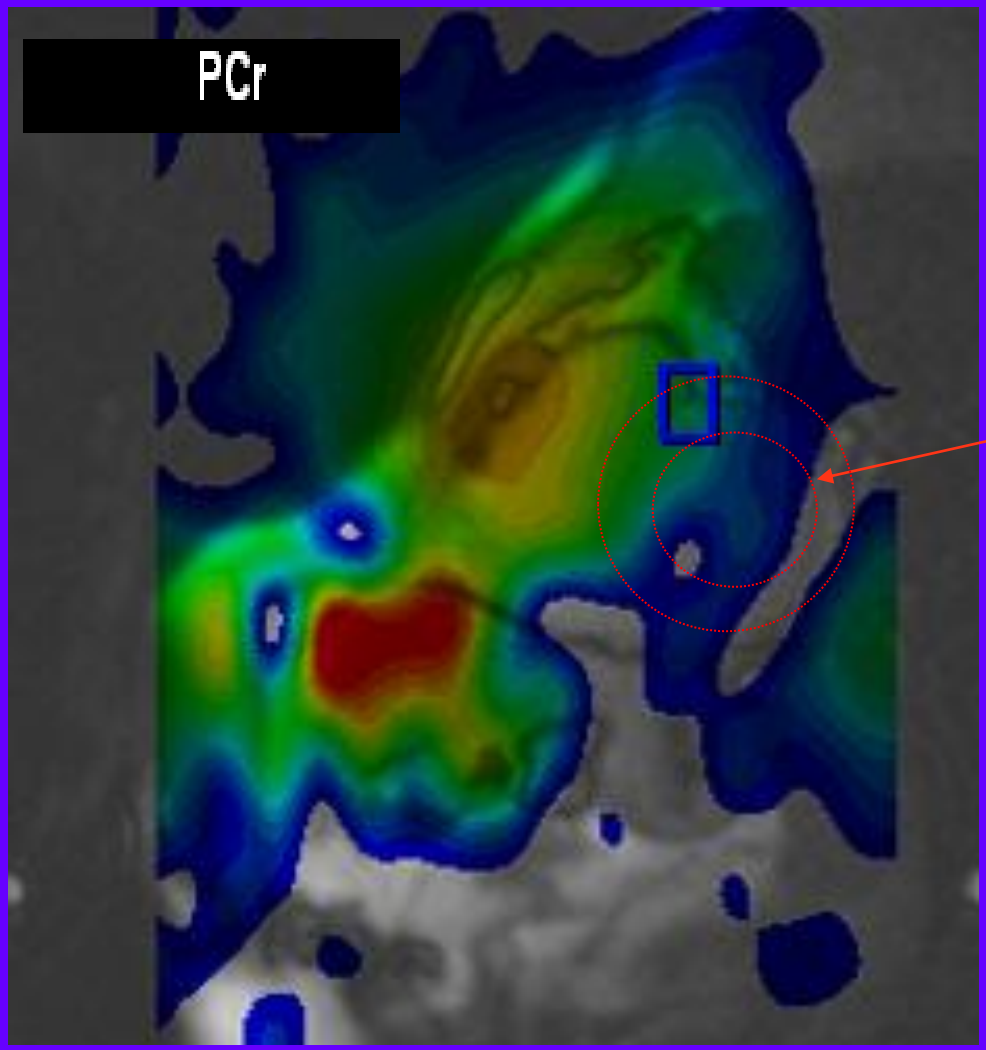


Works in Progress:
^{31}P Spectroscopy of the Heart:

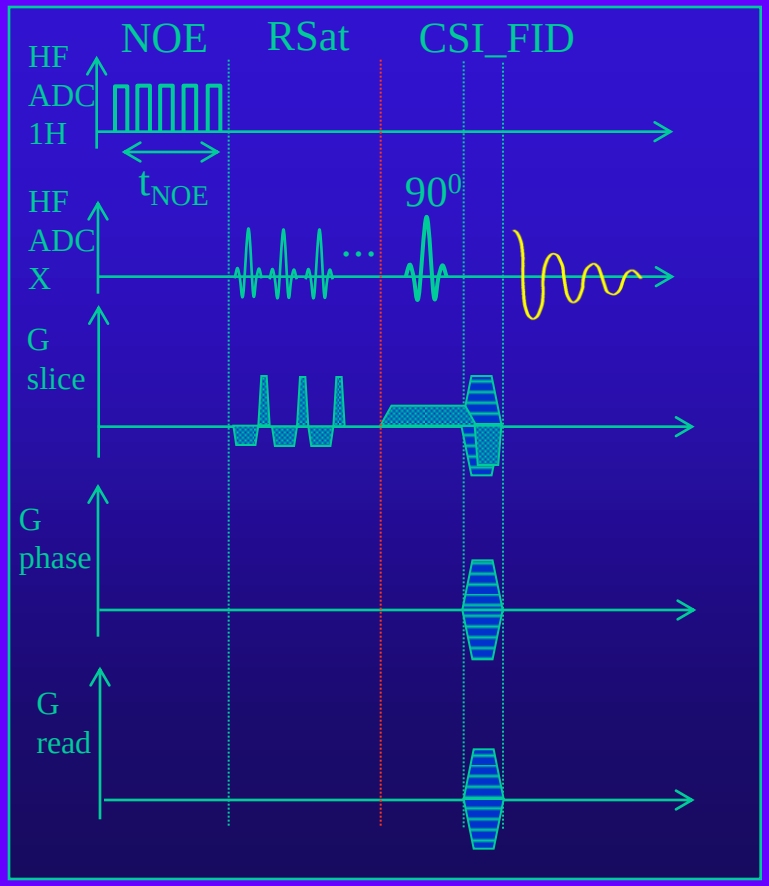
Improvements

PCr map of the control subject

shows the influence of the chest muscle



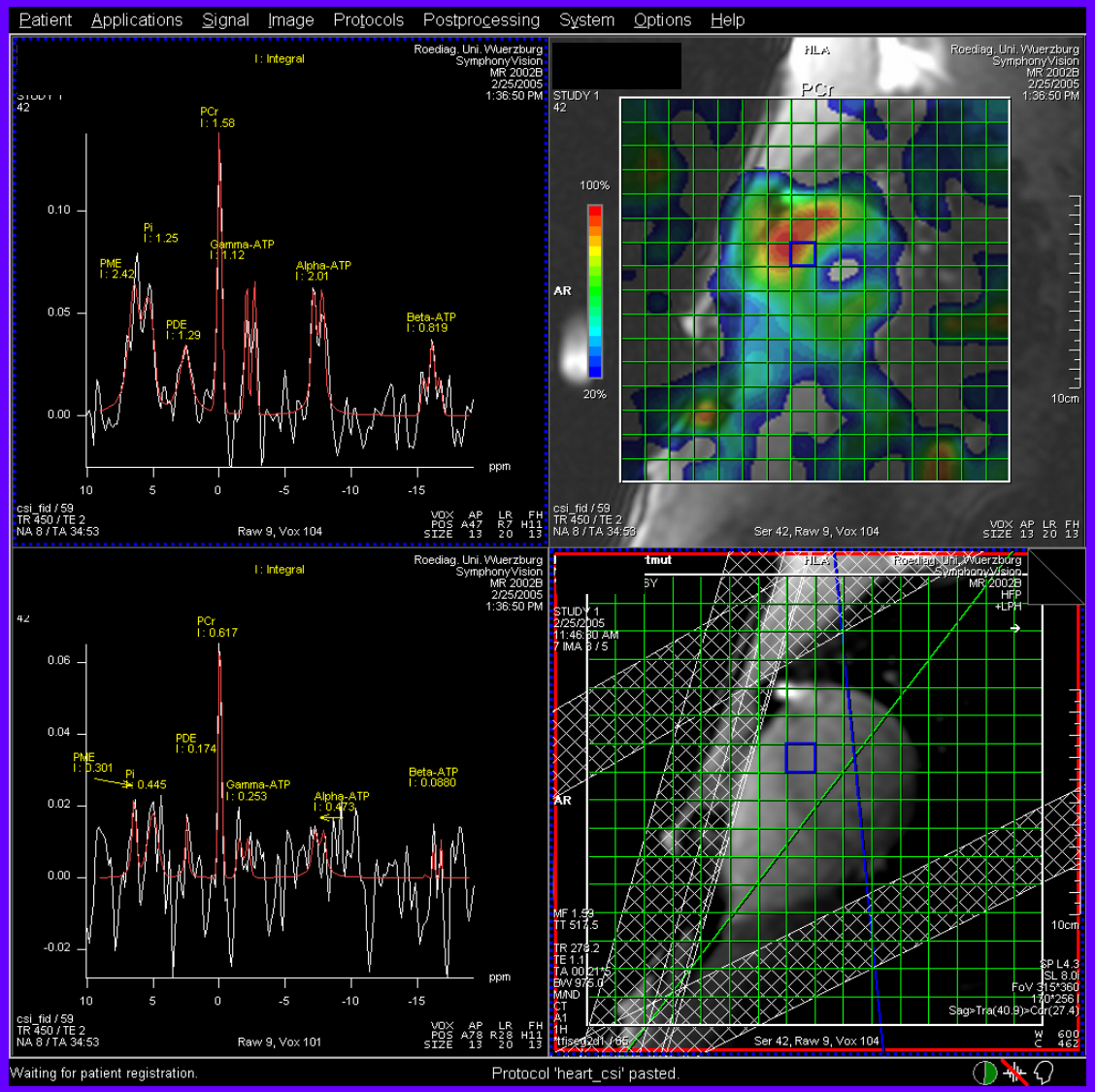
Work in Progress: csi_fid with regional saturation



RSat package:

- Up to 8 RSat pulses
- 1 repetition of each RSat pulse
- Pulse duration: 6400us
- (also available for 1H)

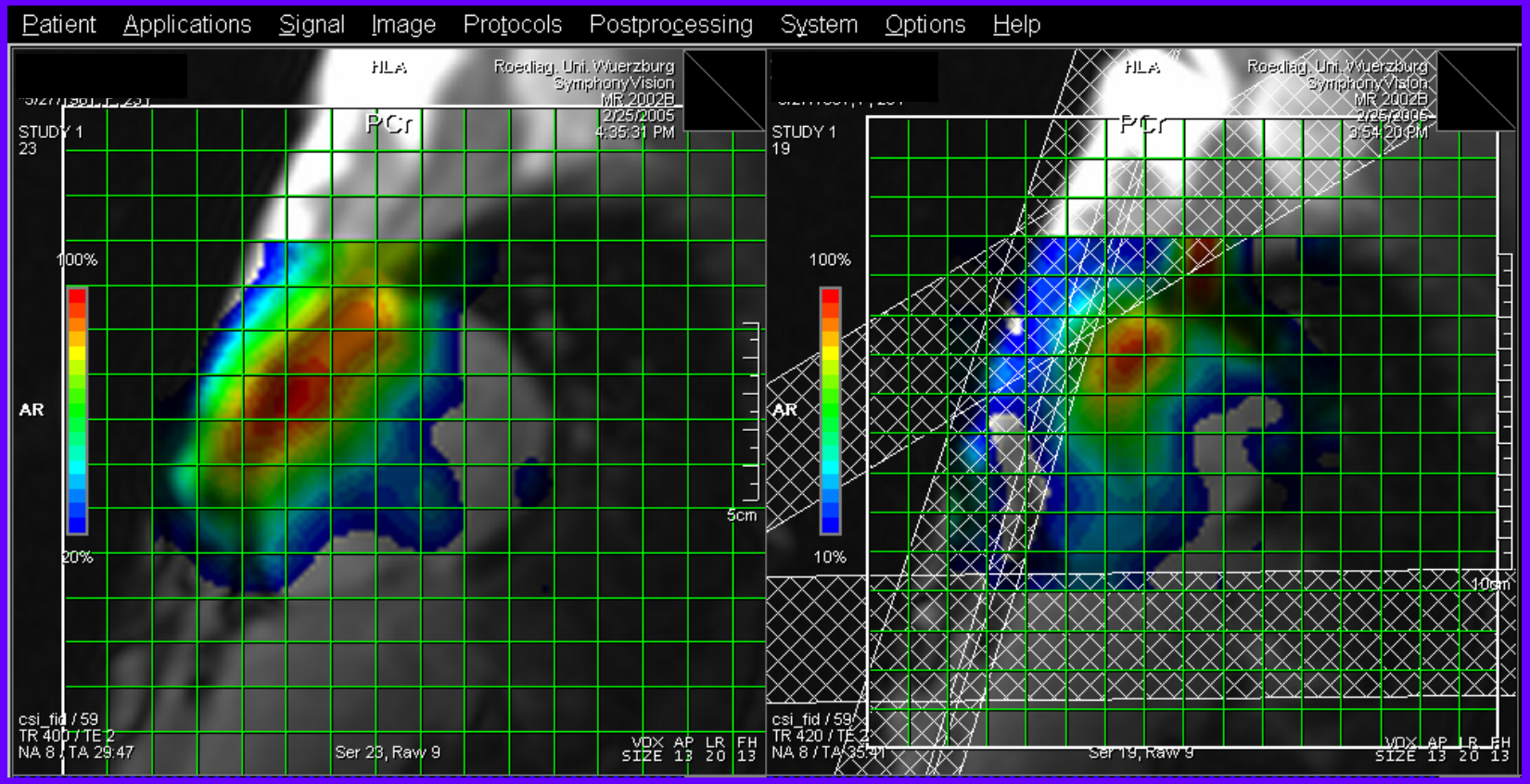
Volunteer PCr map with csi-fid RSat WIP



spectrum of saturated chest muscle

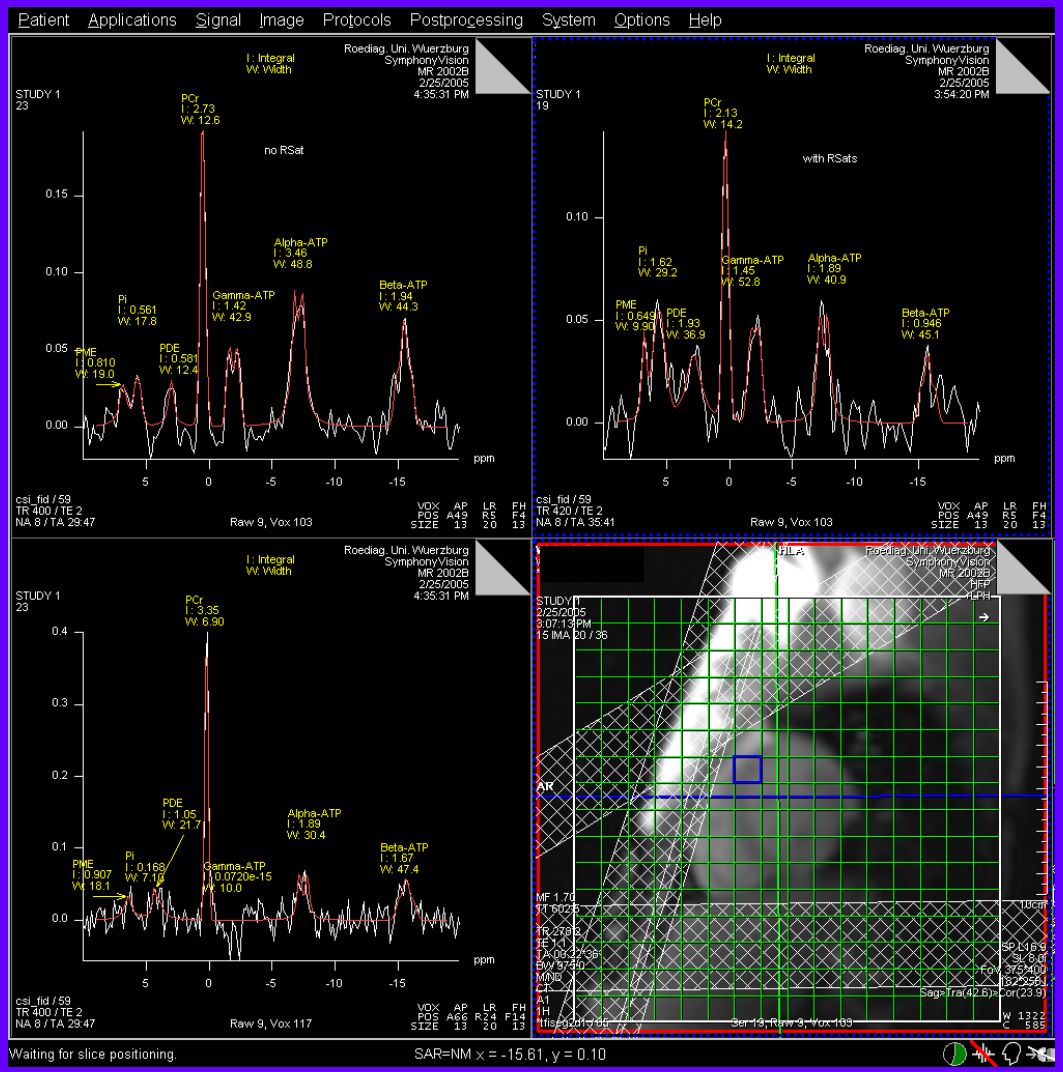
volunteer PCr map

without and with RSats



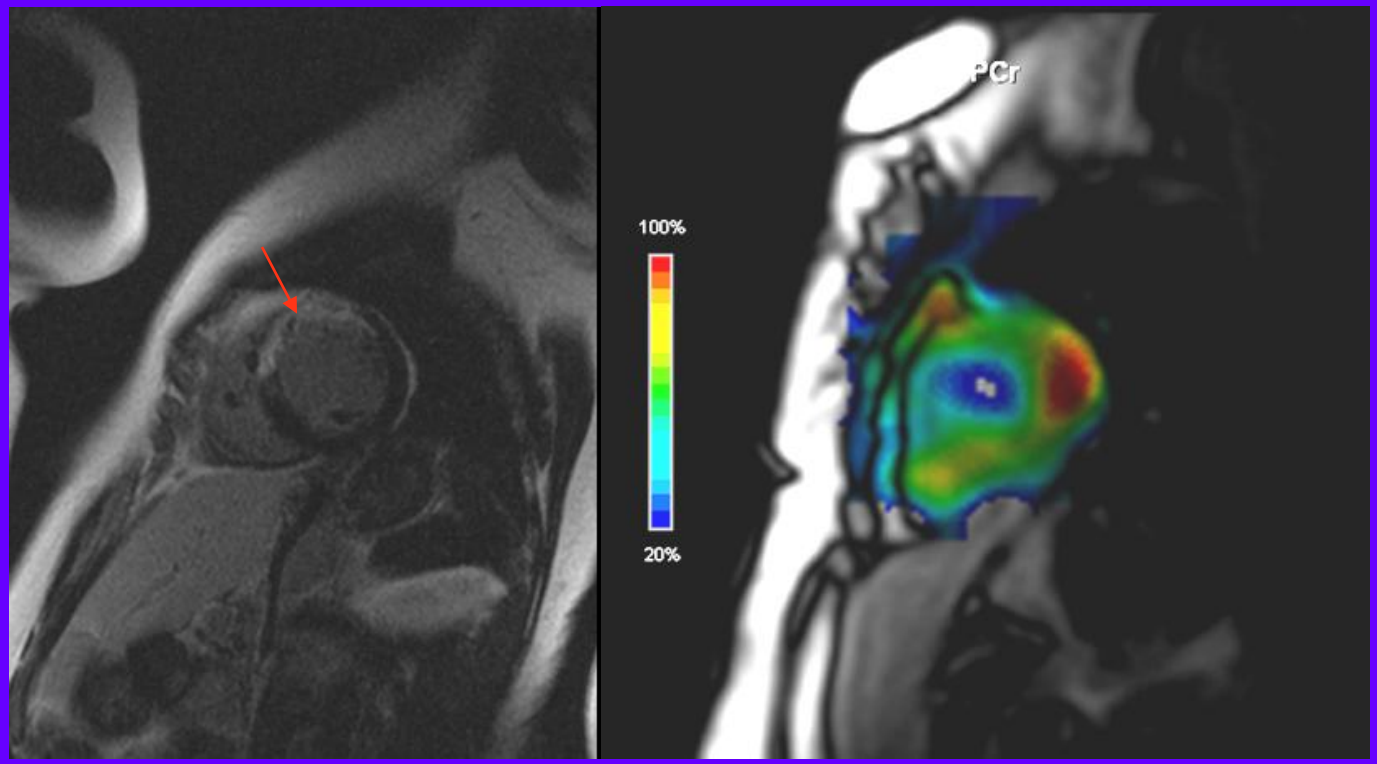
31P spectrum of the myocardium without and with RSats

chest muscle spectrum



^{31}P metabolite map of myocardial infarction

High correlation to late enhancement



Late enhancement shows the infarct region in the anterior septal wall

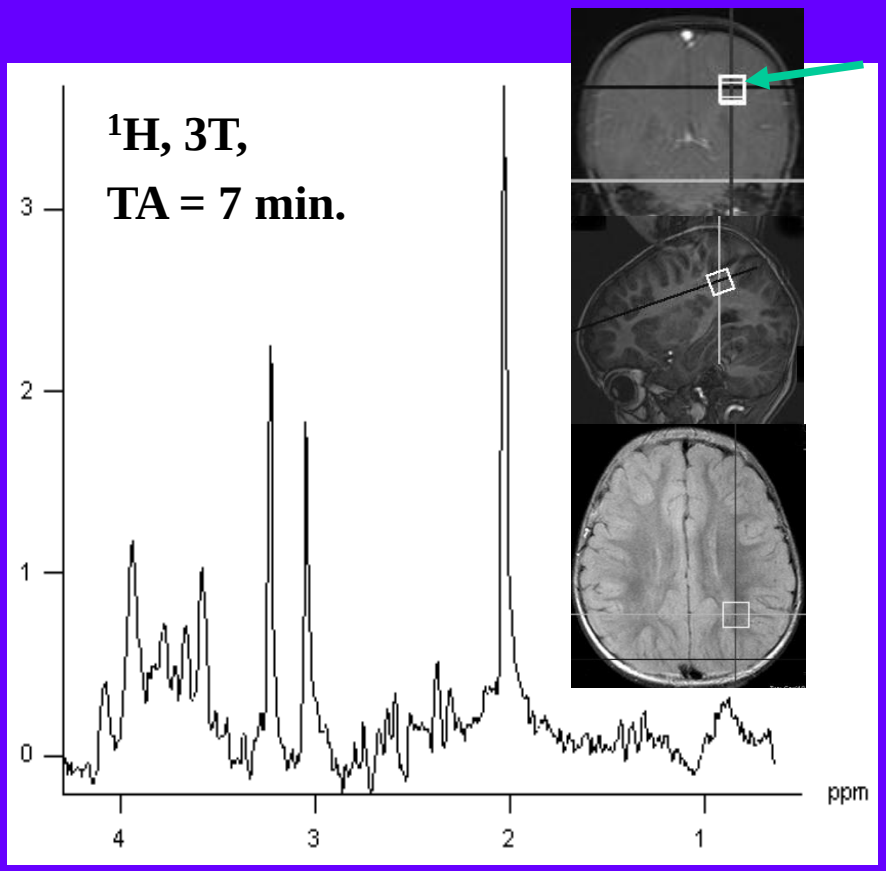
The metabolite map shows low PCr in the anterior septal region in good correlation with the late enhancement results

Works in Progress:

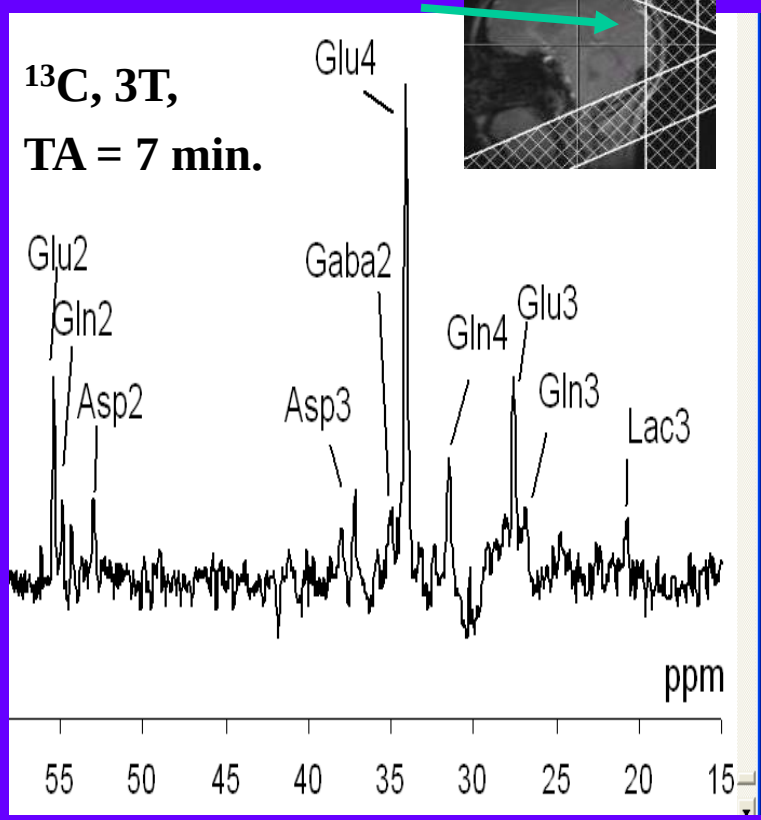
$^{1}H \rightarrow {}^{13}C$ Polarisation Transfer by DEPT

NMR sensitivity of ^{13}C vs. ^{1}H

- **identical B_0, identical conc. of nuclei**
  sensitivity of ^{1}H detection: 1
  sensitivity of ^{13}C detection *in vitro*: $\propto(\gamma_{13C} / \gamma_{1H})^3 = 0.016$
  sensitivity of ^{13}C detection *in vivo*: $\propto(\gamma_{13C} / \gamma_{1H})^2 = 0.06$

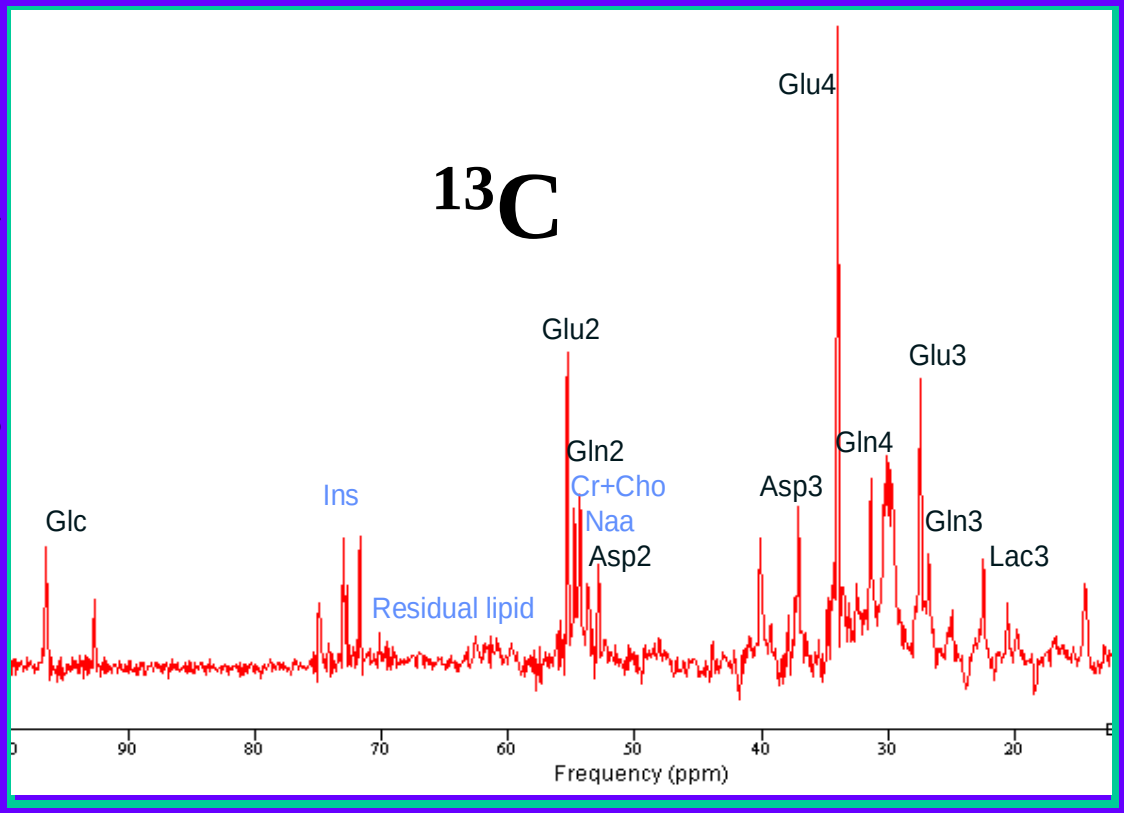


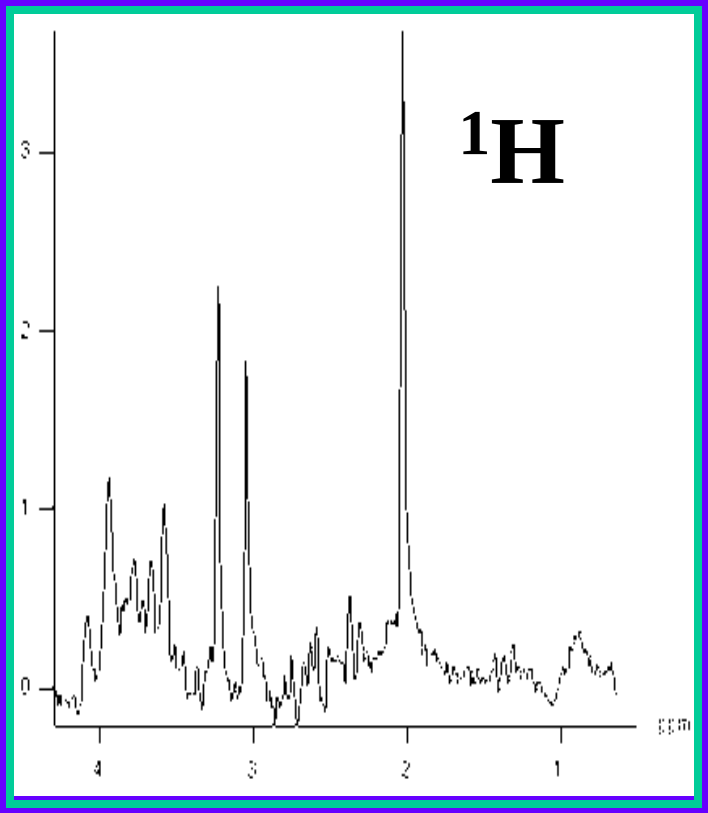
1ml vs. 500ml



Chemical dispersion ^{13}C vs. ^{1}H

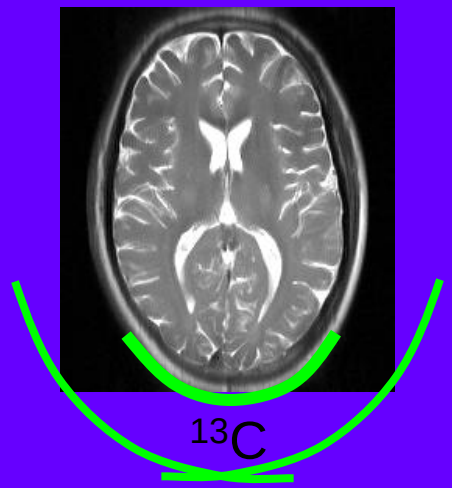
- dispersion ^{13}C = 20 x dispersion ^{1}H
  → shimming less important for ^{13}C applications
  → easier quantification
- ^{13}C spectra show wealth of biochemical information
- ^{13}C MRS can be used with labeled compounds
  → enables dynamic studies of biochemical fluxes

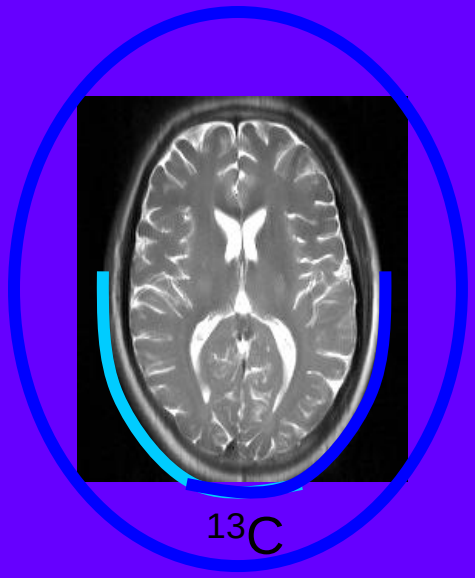




^{13}C spectroscopy: the quest for sensitivity Coil design

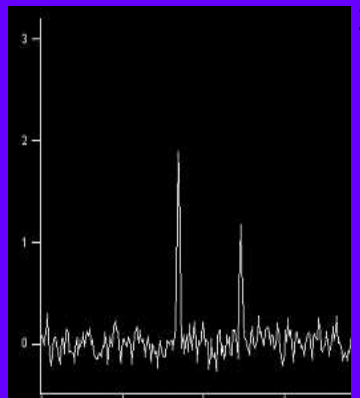
surface coil vs. ^{1}H volume & ^{13}C quad.



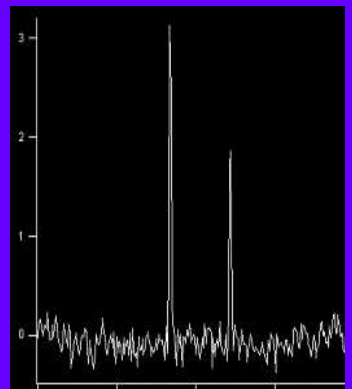


^{1}H

^{1}H (CP birdcage)



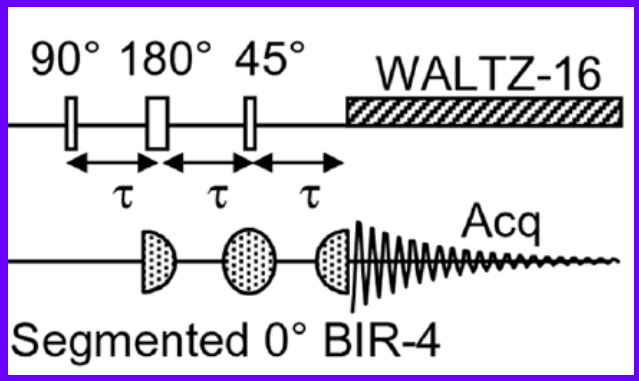
- **increased sensitivity**
- **homogeneous SAR**
- **homogeneous decoupling**



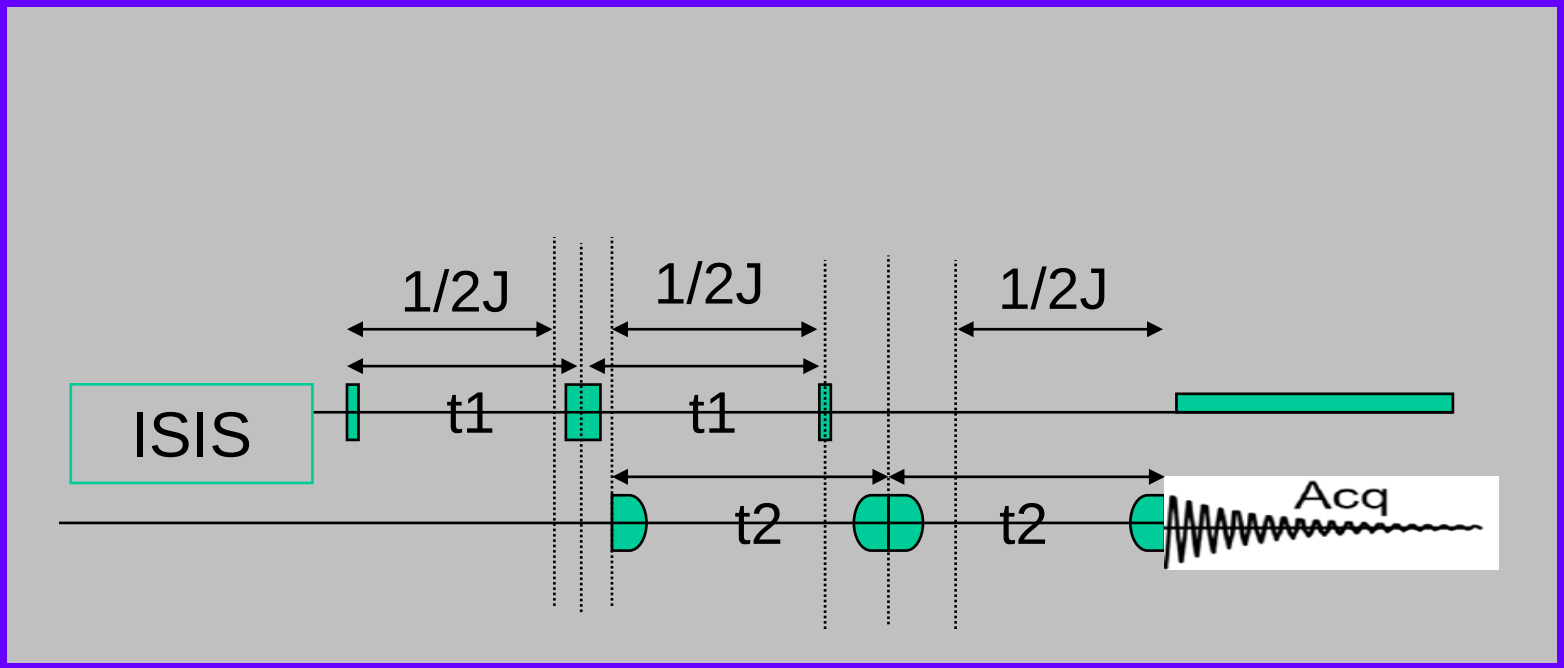
^{13}C spectroscopy: the quest for sensitivity

DEPT Polarisation Transfer

- classical simultaneous-Tx DEPT
- without localization

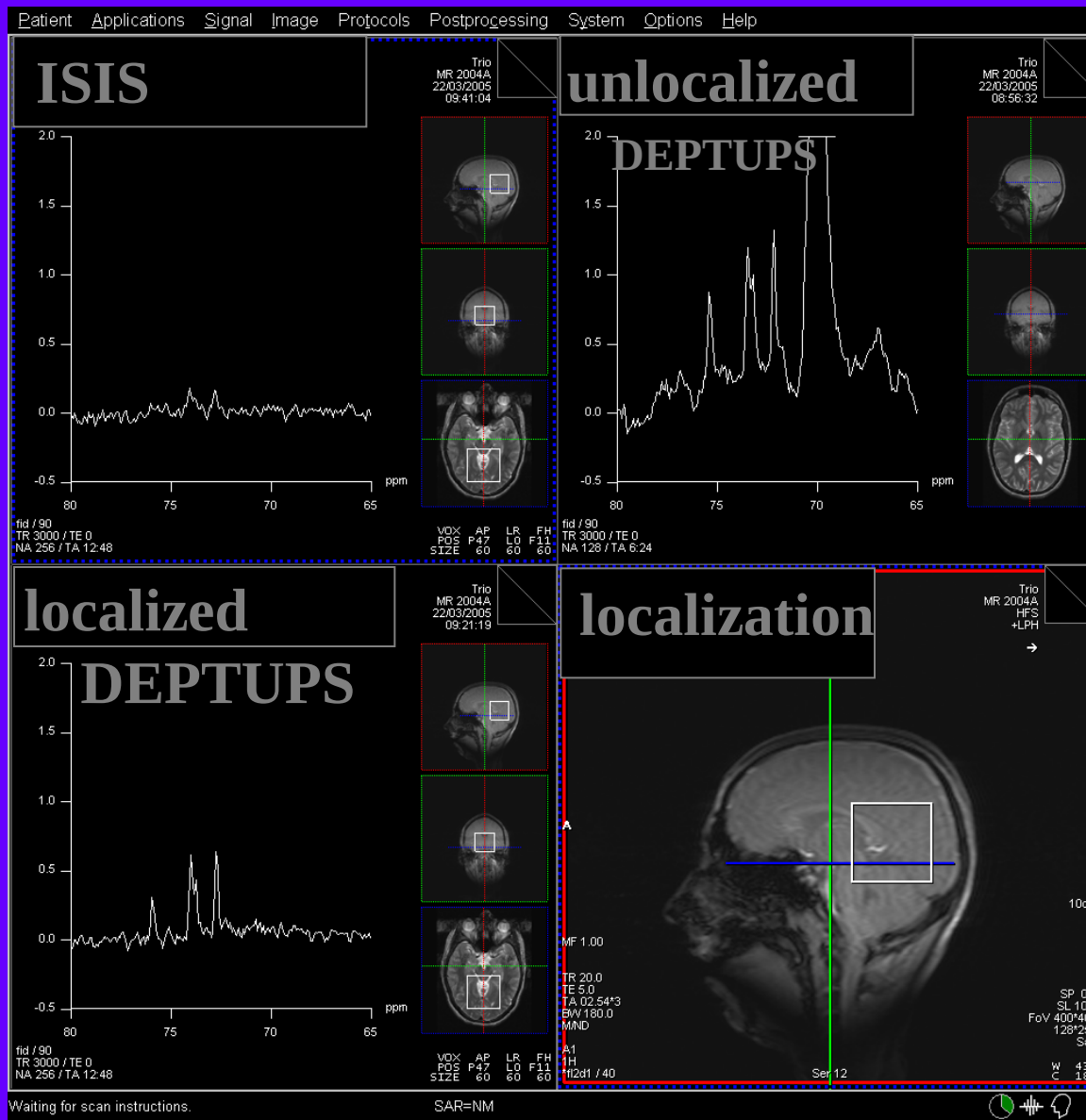


- localized DEPT Using Pulses Sequentially (DEPTUPS)



^{13}C spectroscopy: Sequential DEPT (DEPTUPS)
In vivo results MAGNETOM Trio

in vivo enhancement by DEPT Using Pulses Sequentially (DEPTUPS) reaches the theoretical upper limit !



Works in Progress:
Metabolite Report

Metabolite Report: New Spectroscopic Post-Processing

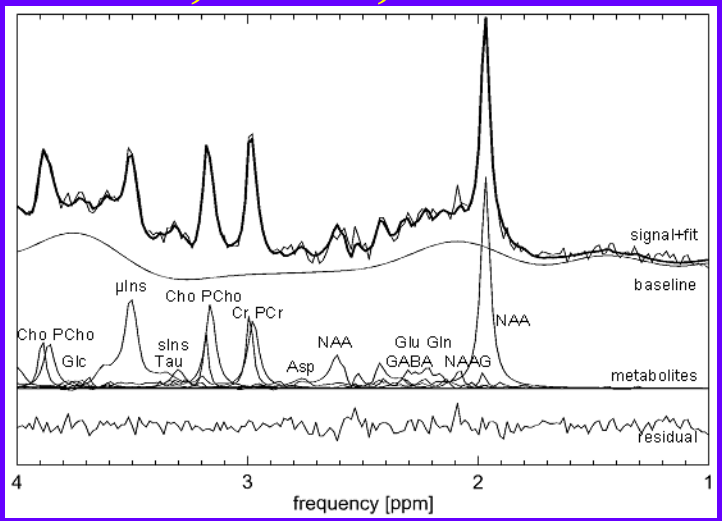
- **Algorithm:**
  - **Automated**
  - **Prior knowledge based**
  - **Complex time-domain fitting**
  - **With qualification of results**
- **Report generation:**
  - **Fully automated mode**
  - **No interaction for voxel/data selection or post-processing**
  - **Based on predefined settings**
- **Report format:**
  - **Structured Report**
  - **DICOM compatible**
  - **HTML compatible**

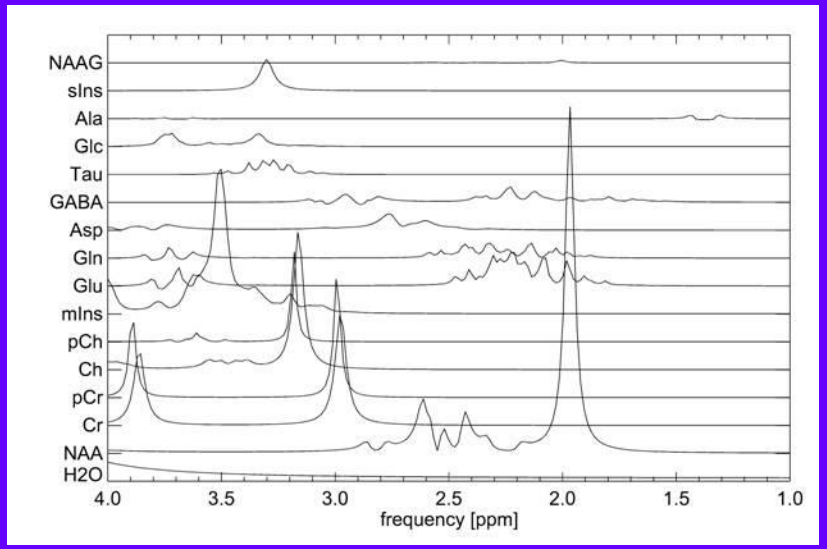
Algorithm: PRISMA

- **Complex fit in time-domain**

$$s(t,t_0,\varphi_0,A_i,\varpi_i,T_{2,i},T_{G,i}) = \sum_i^n A_i M_i \exp[-t/T_{2,i} - (t/T_{G,i})^2] \bullet \exp[-I\{\varpi_i(t-t_0)+\varphi_0\}]$$

- **Using model signals, based on analytical or simulated (GAMMA) models**
- **Gaussian, Lorentzian and Voigt lineshapes**
- **Result qualification based on Cramer-Rao-Bounds, SNR, …**





Fit of short TE in vivo data (SVS, SE, TE 30 ms)

Metabolite report includes

–patient info
–localization info
–metabolic info
–diagnostic info