MRI PRACTICALS ON CIBM PRECLINICAL IMAGING SYSTEMS

BASICS OF MRSI

Cristina Cudalbu

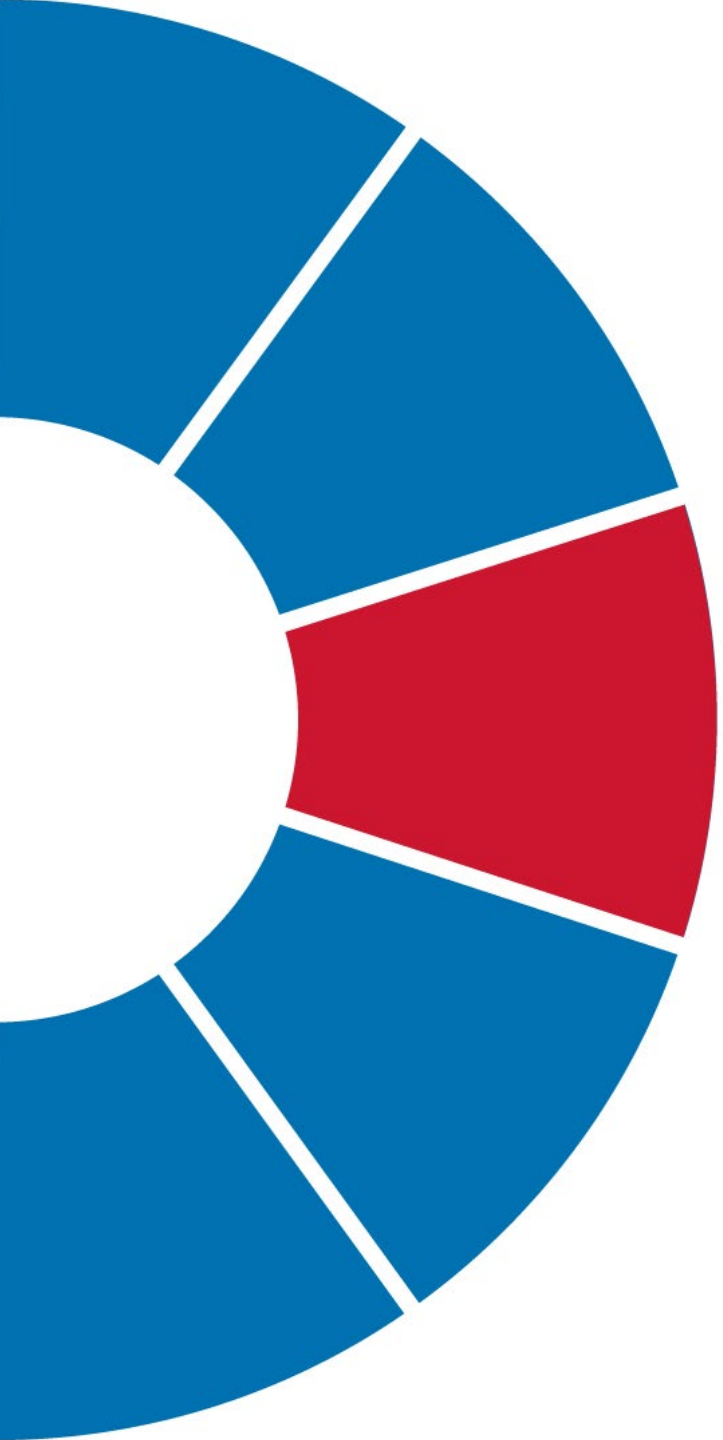
CIBM PCI EPFL

Master Course 2025-2026

cristina.cudalbu@epfl.ch

OUTLINE

- From MRS to MRSI – the magic formula
- Spatial encoding for MRSI
- MRSI advantages and challenges
- From square maps to full brain coverage

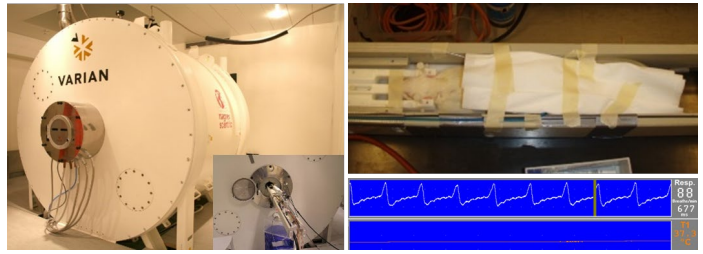


FROM MRS TO MRSI – THE MAGIC FORMULA

WHAT DO WE MEASURE: ^{1}H MRS ?

- ***in vivo***
- **non invasively**
- **localized in hippocampus**

- **at high magnetic field (9.4T)**
- **ultra short TE (2.8ms)**



Neurochemical Profile at 9.4T

>18 Markers of :

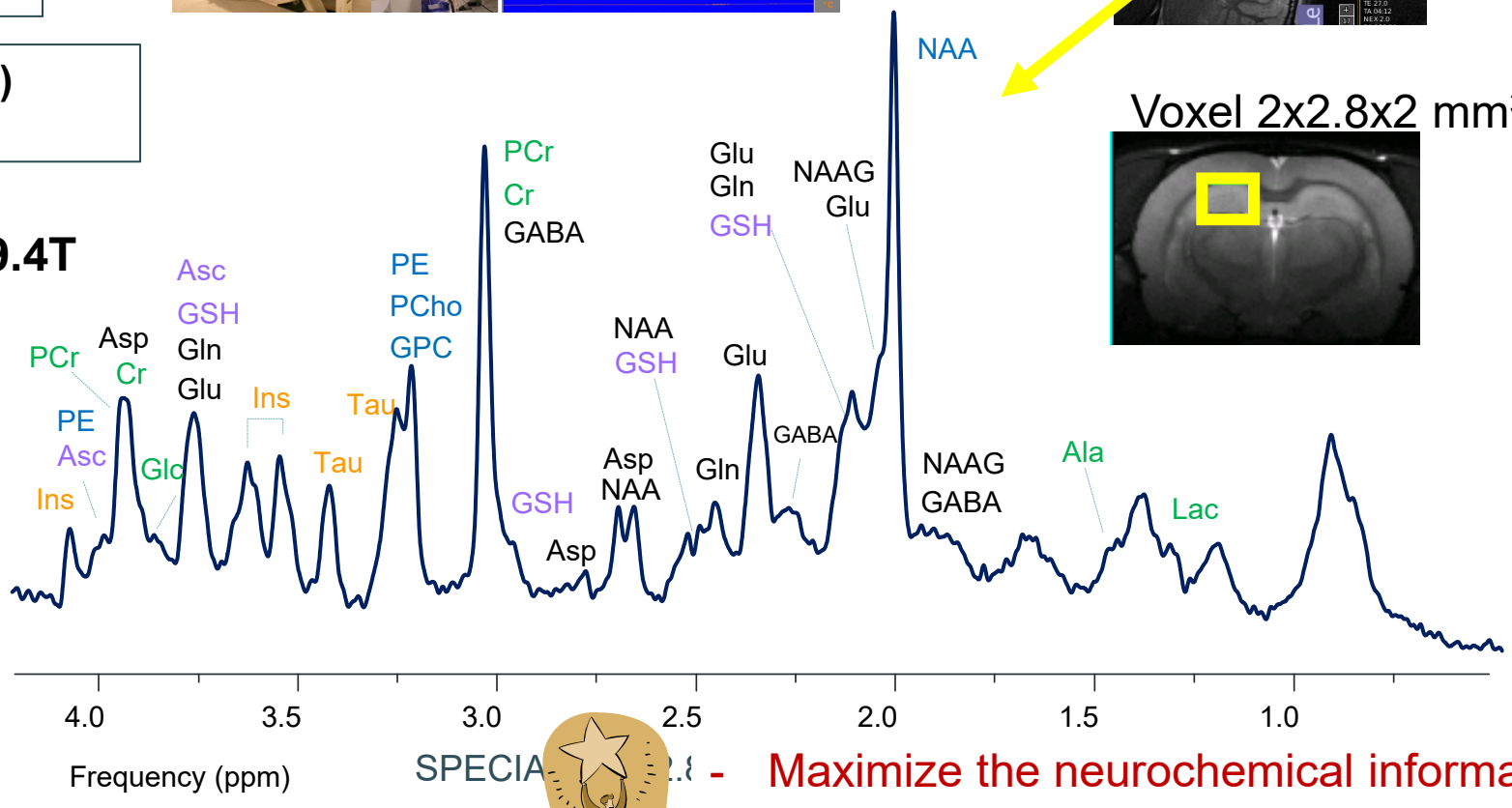
Myelination/Cell proliferation

Energy metabolism

Osmoregulation

Neurotransmitter metabolism

Antioxidants



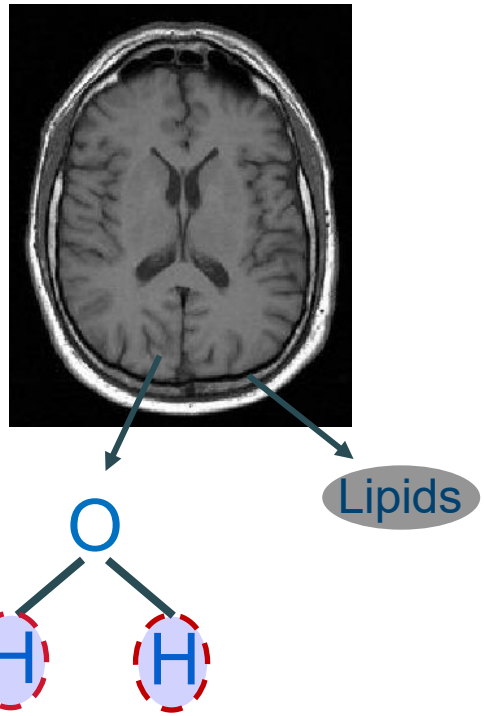
- Maximize the neurochemical information
- Increase precision, accuracy – quantification
- Increase the reliability of obtained concentrations

CD Rae et al, Anal Biochem. 2017; CD Rae .Neurochem Res. 2014; V Račkayová et al 2017; Lanz et al, 2017

cristina.cudalbu@epfl.ch

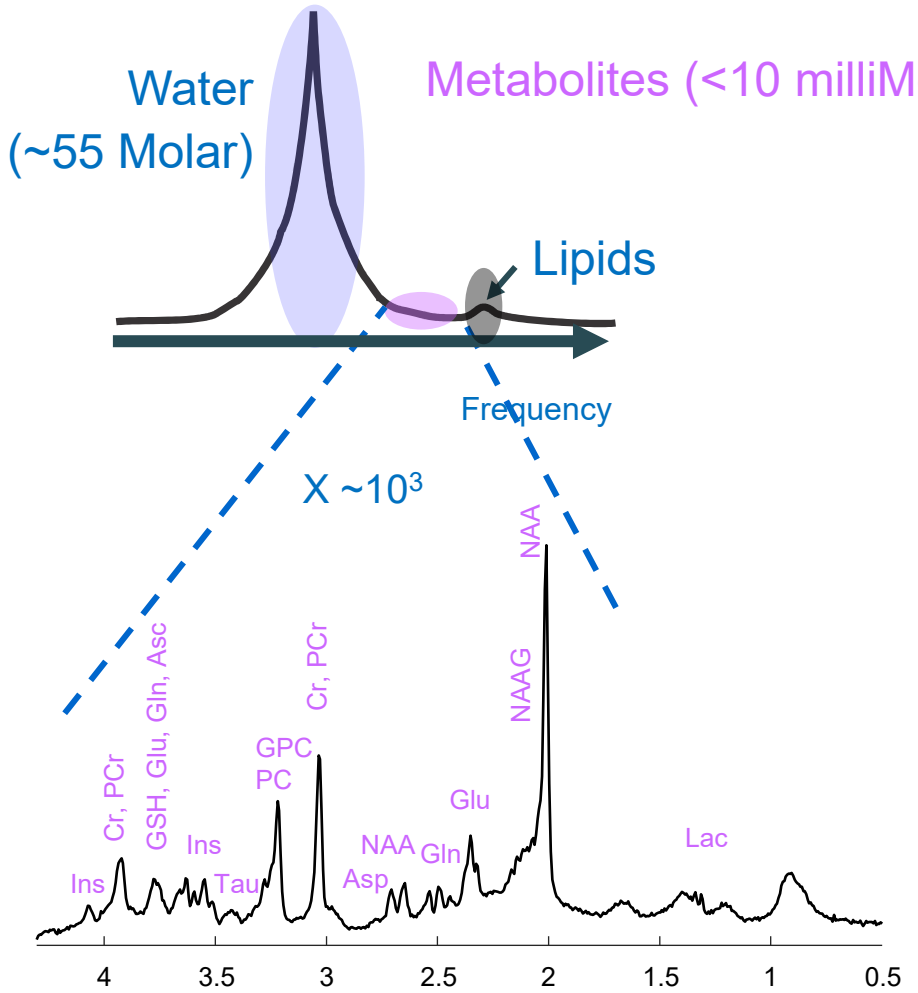
BASICS OF MRS

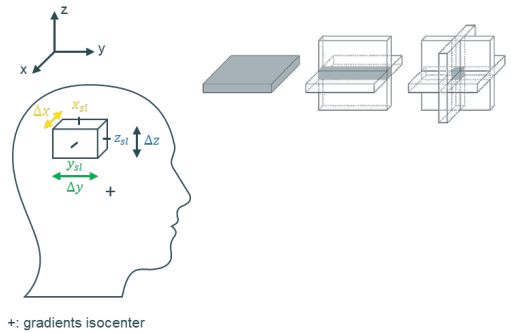
MRI

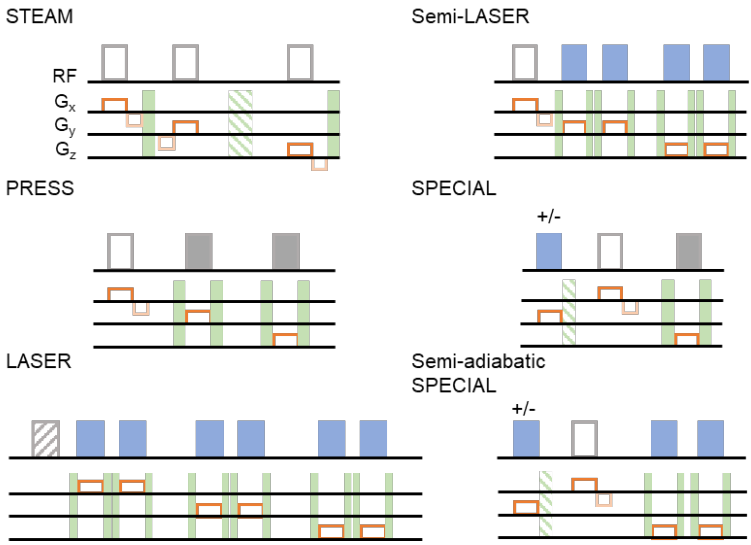


Ivan Kirov, ENIGMA-U
https://www.youtube.com/playlist?list=PL1TaL2CueZ-DOznKgKWdg_mHRK9UUiQoJ

^{1}H MRS







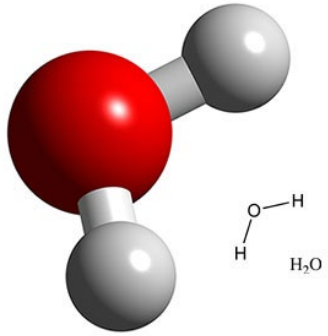
BRAIN METABOLISM – *in-vivo* and non-invasively

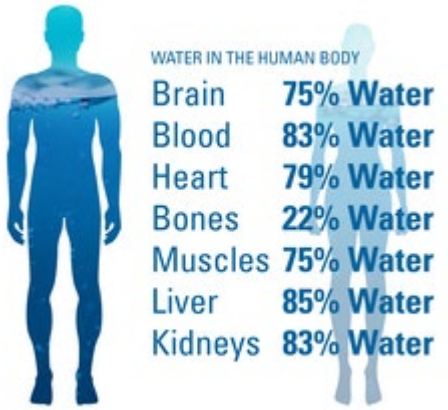
J Mosso

cristina.cudalbu@epfl.chc

MAGNETIC RESONANCE IMAGING -> SPECTROSCOPY

MRI:
Imaging ^{1}H of water

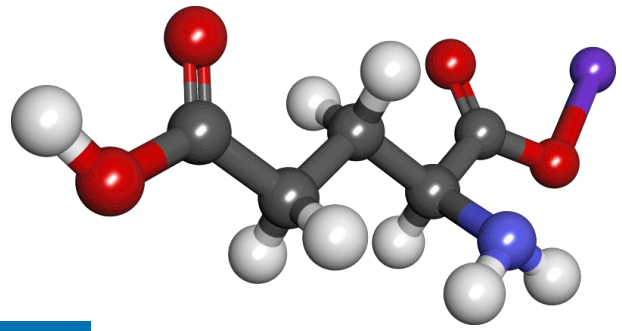




usgs.gov

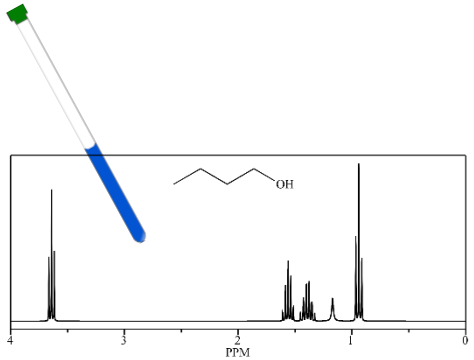
~ 55 M

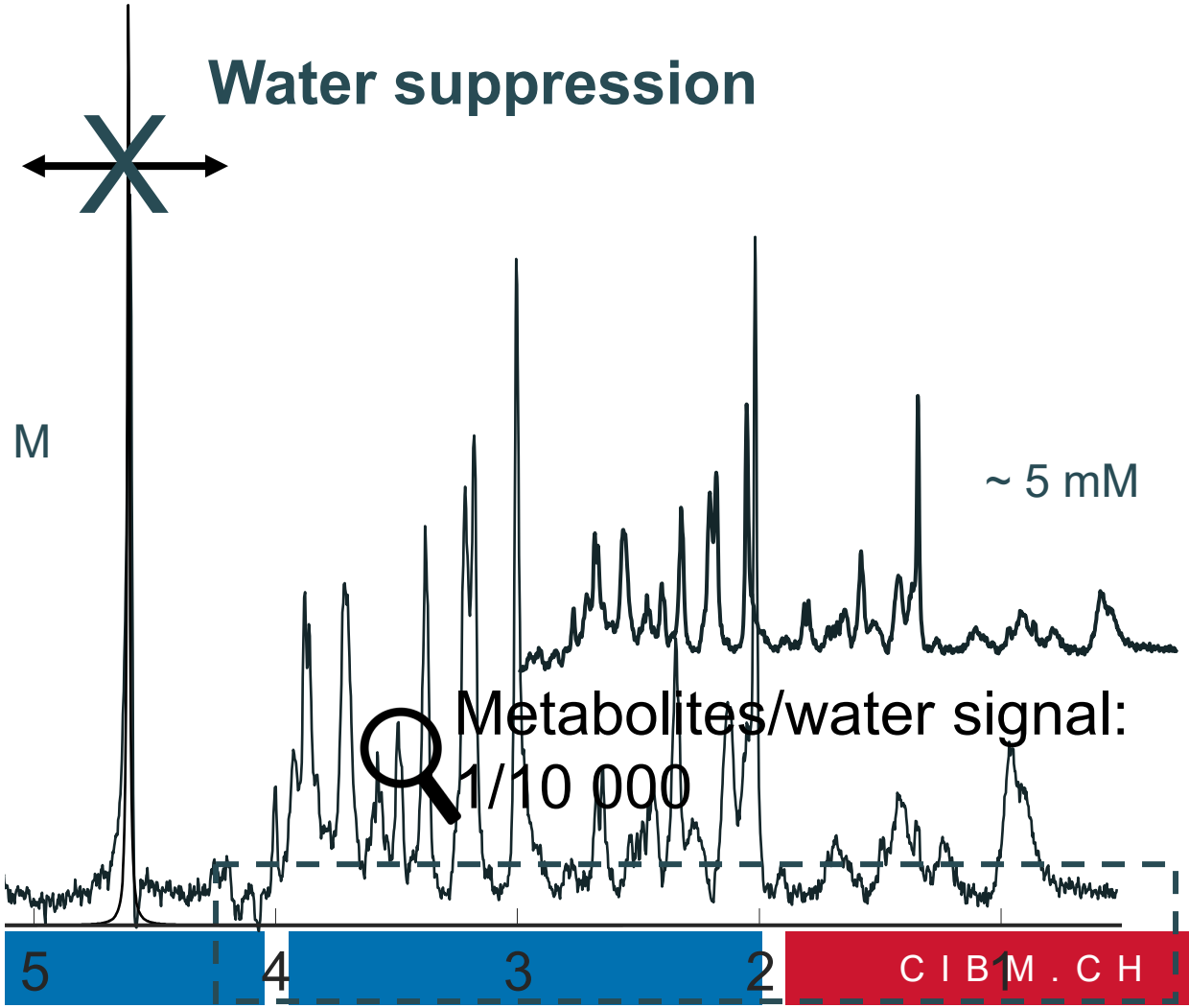
MRS:
Measuring ^{1}H of biomolecules



glutamate

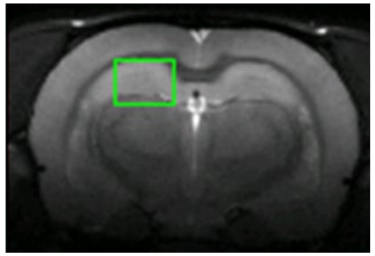
As chemical NMR…
but *in vivo*



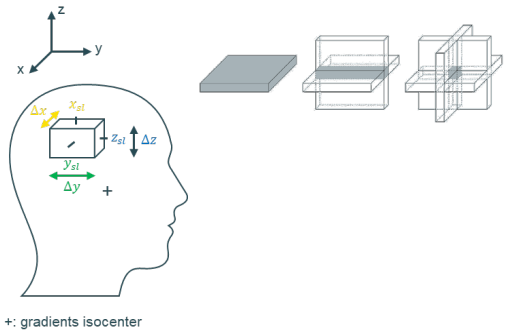


Courtesy of J Mosso

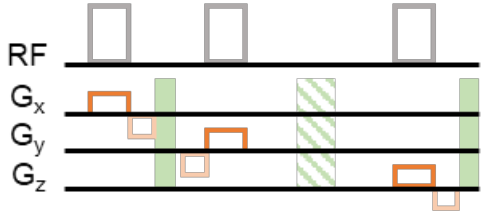
UNTIL NOW



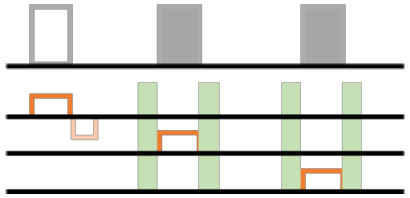
T_2 weighted image of the rat brain: VOI in the hippocampus



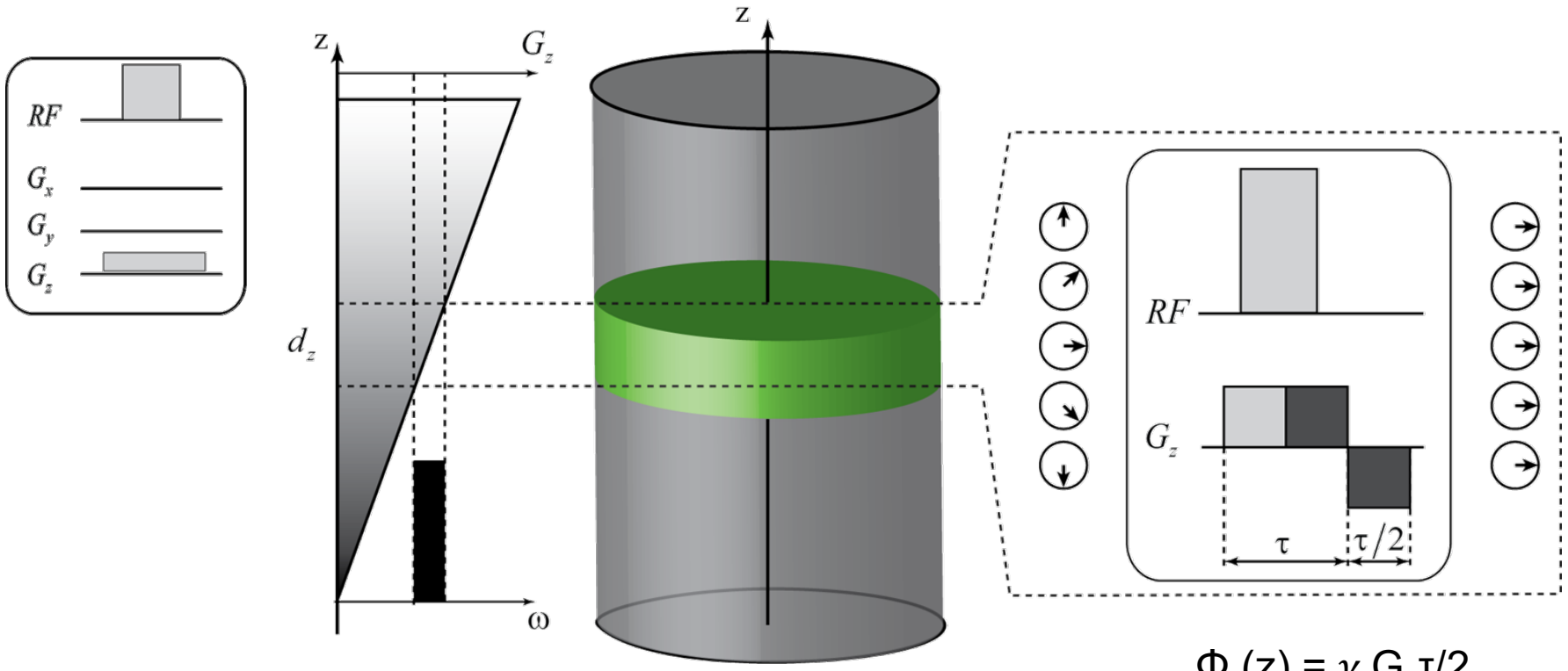
STEAM



PRESS



SPATIAL ENCODING – SLICE SELECTION



$$S \propto \iint_{slice} \rho(x,x)dx\,dy$$

$$\delta z = \frac{BW_{RF}}{\gamma G_z}$$

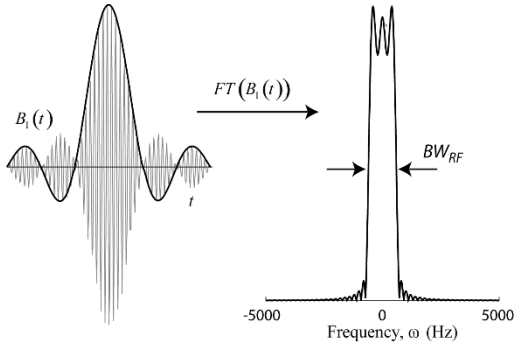
$$\Phi(z) = \gamma G_z \tau/2$$

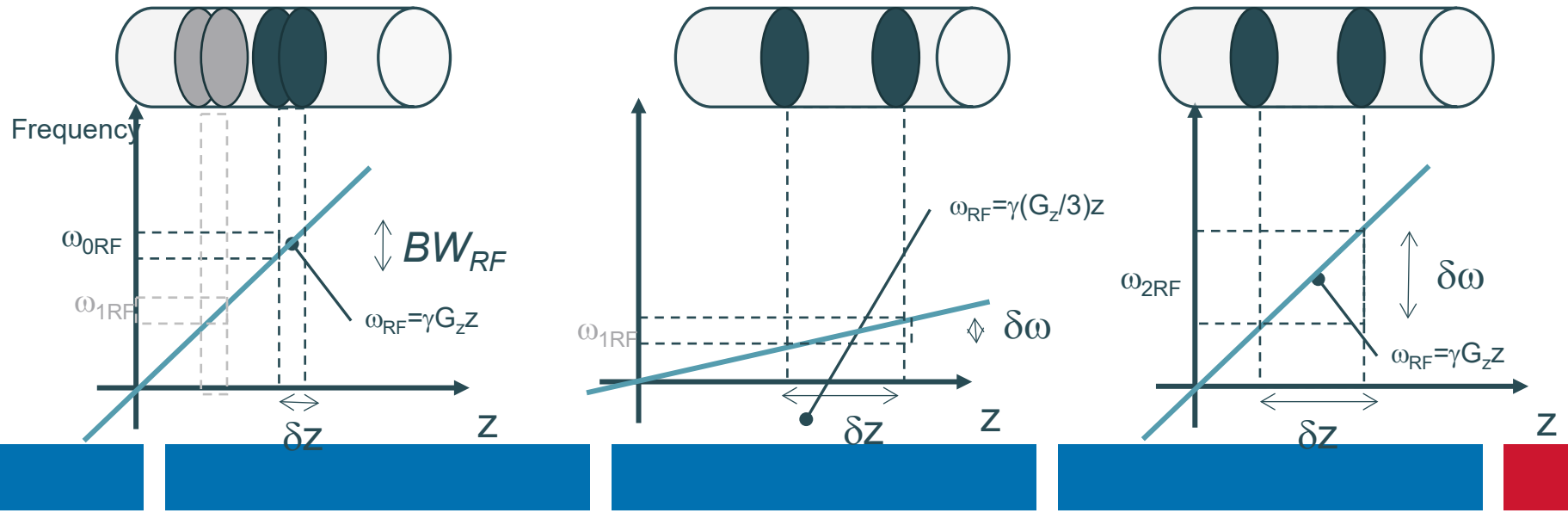
SLICE SELECTION

- Gradient is applied during an RF-pulse, which is characterized by its excitation bandwidth (BW_{RF})

$$\delta z = \frac{BW_{RF}}{\gamma G_z}$$

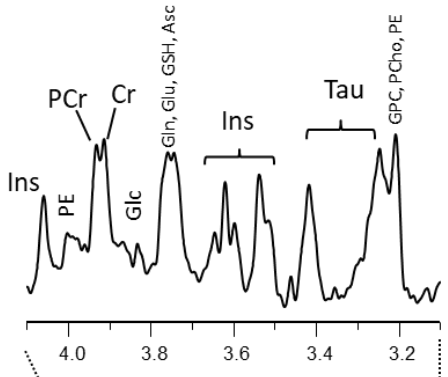
- The slice thickness can be changed either by adjusting the pulse length or the gradient amplitude

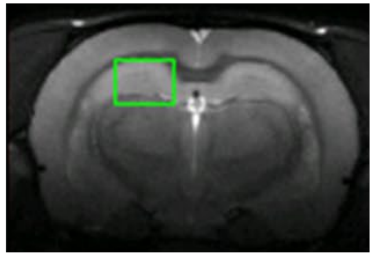




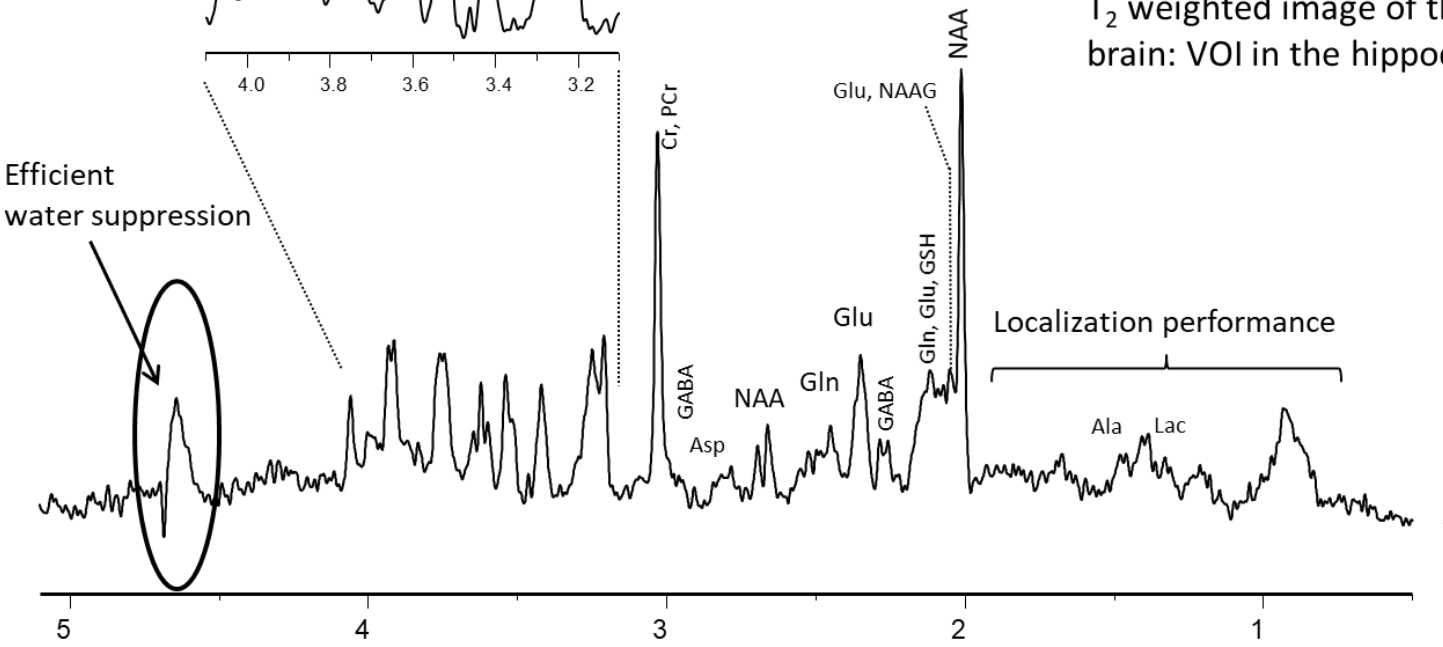
UNTIL NOW

High spectral resolution



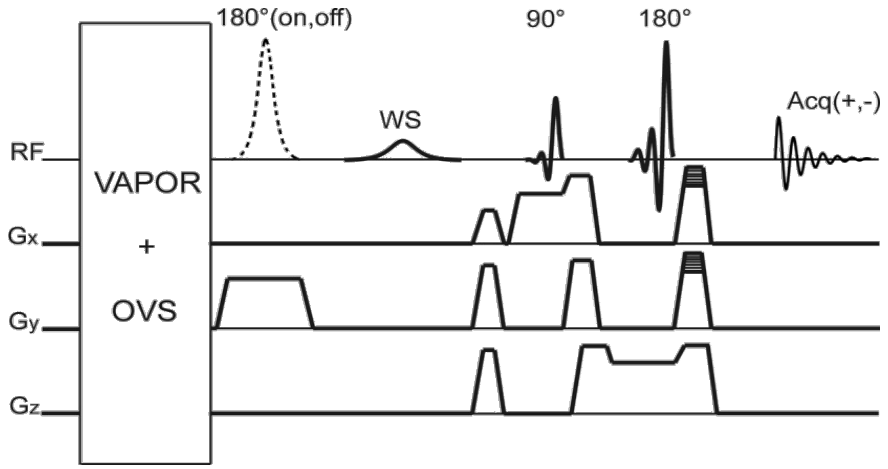


T_2 weighted image of the rat brain: VOI in the hippocampus

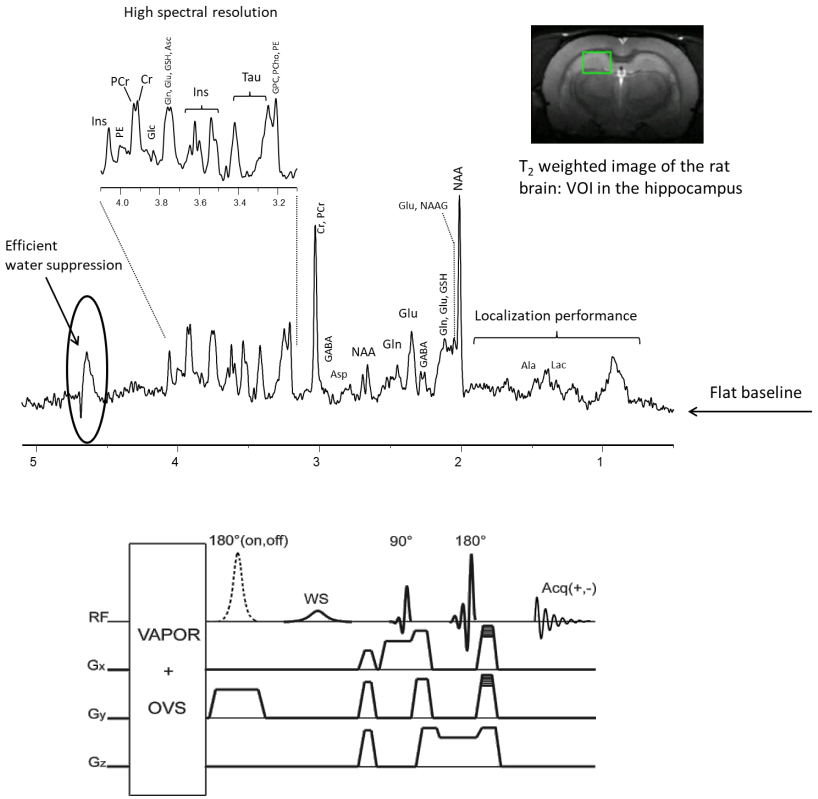


Flat baseline

SPECIAL sequence

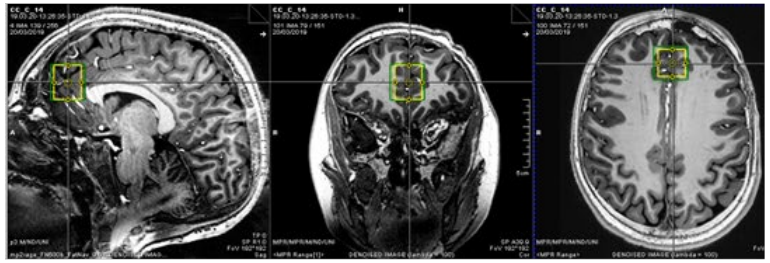


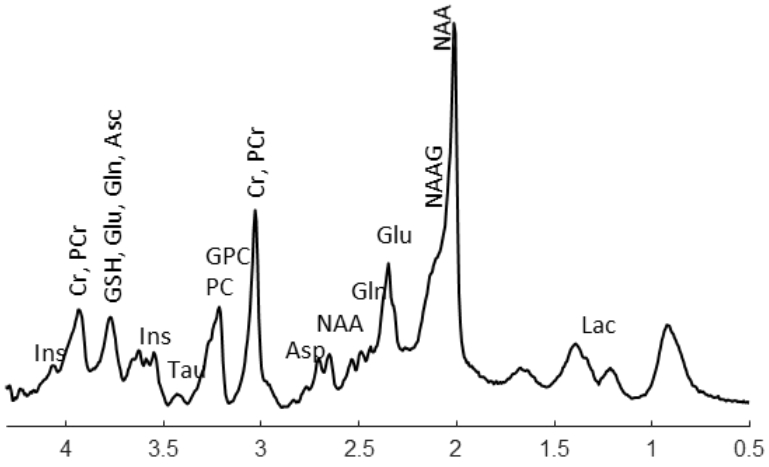
UNTIL NOW



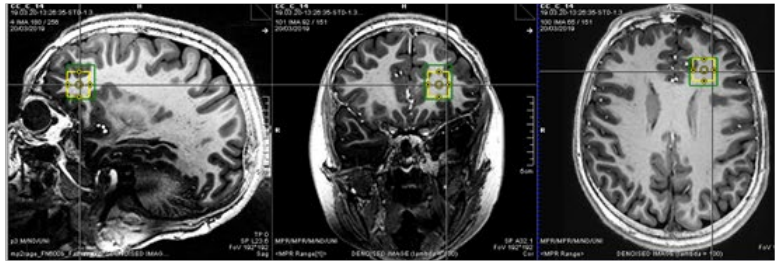
T_2 weighted image of the rat brain: VOI in the hippocampus

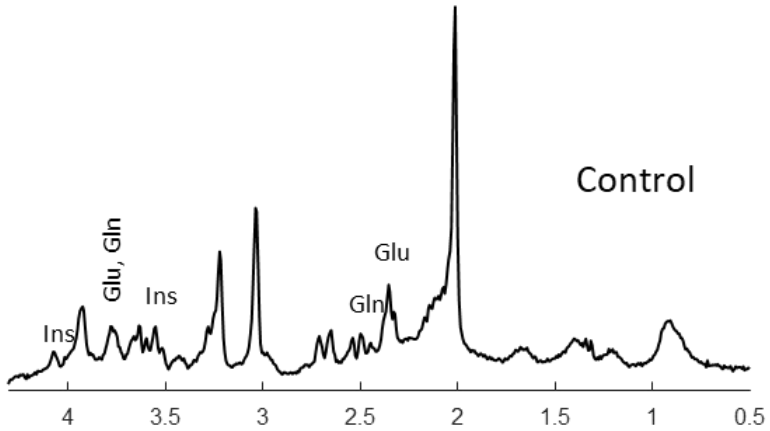
Gray Matter



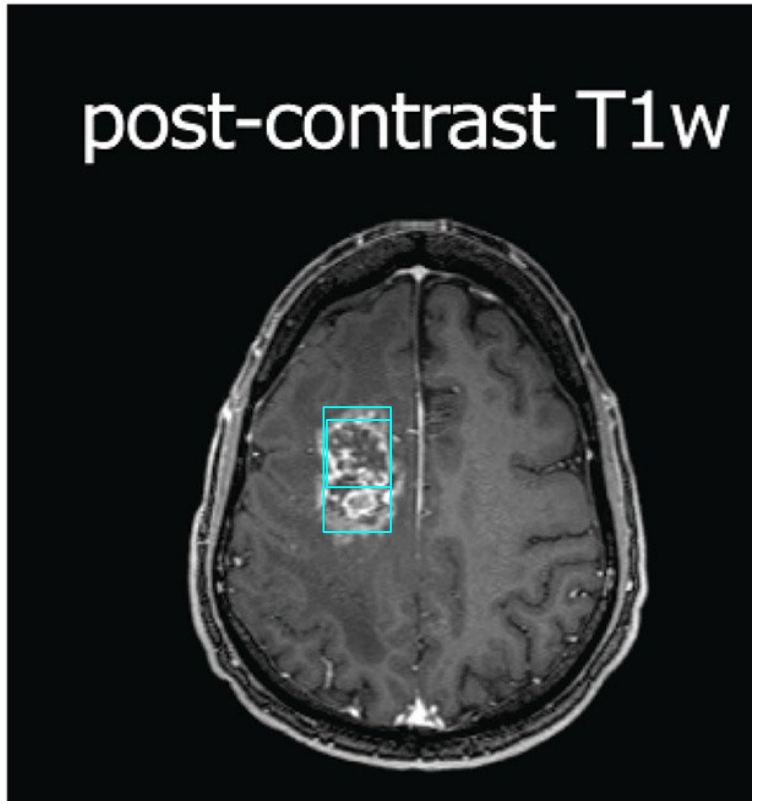


White Matter





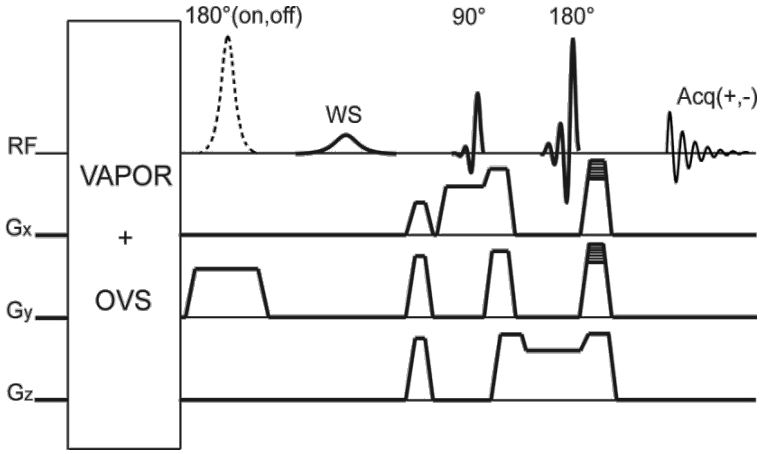
BUT WHAT IF …..



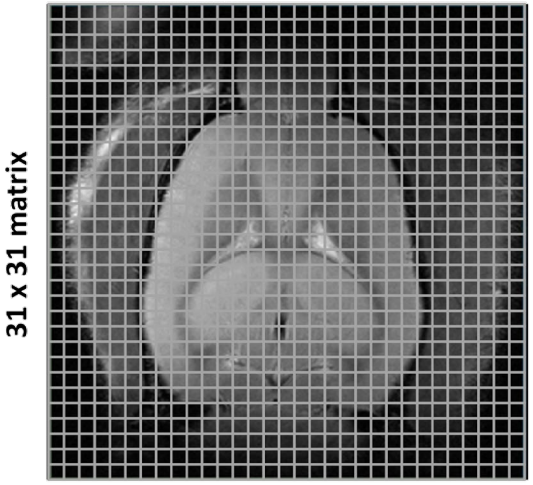
What to do –any idea ?

Multiple voxels? With multiple spectra inside ?

Extract each metabolite and have a color map



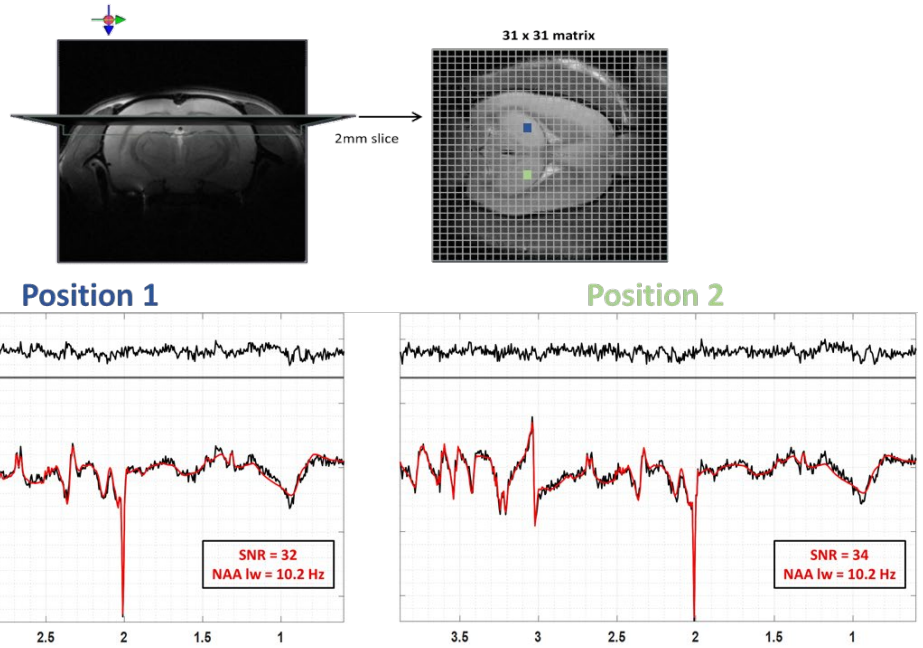
Mlynárik V, et al, MRM 2008

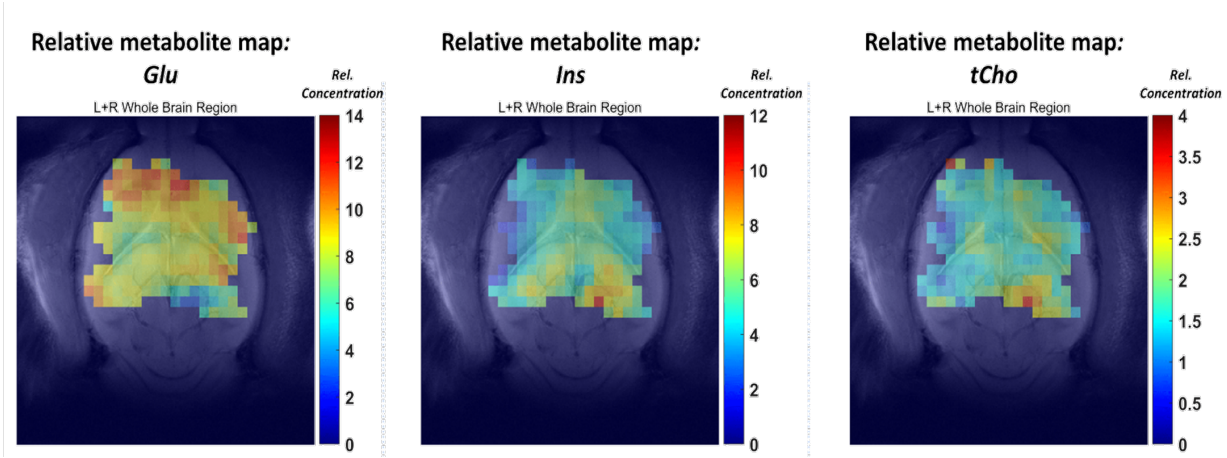


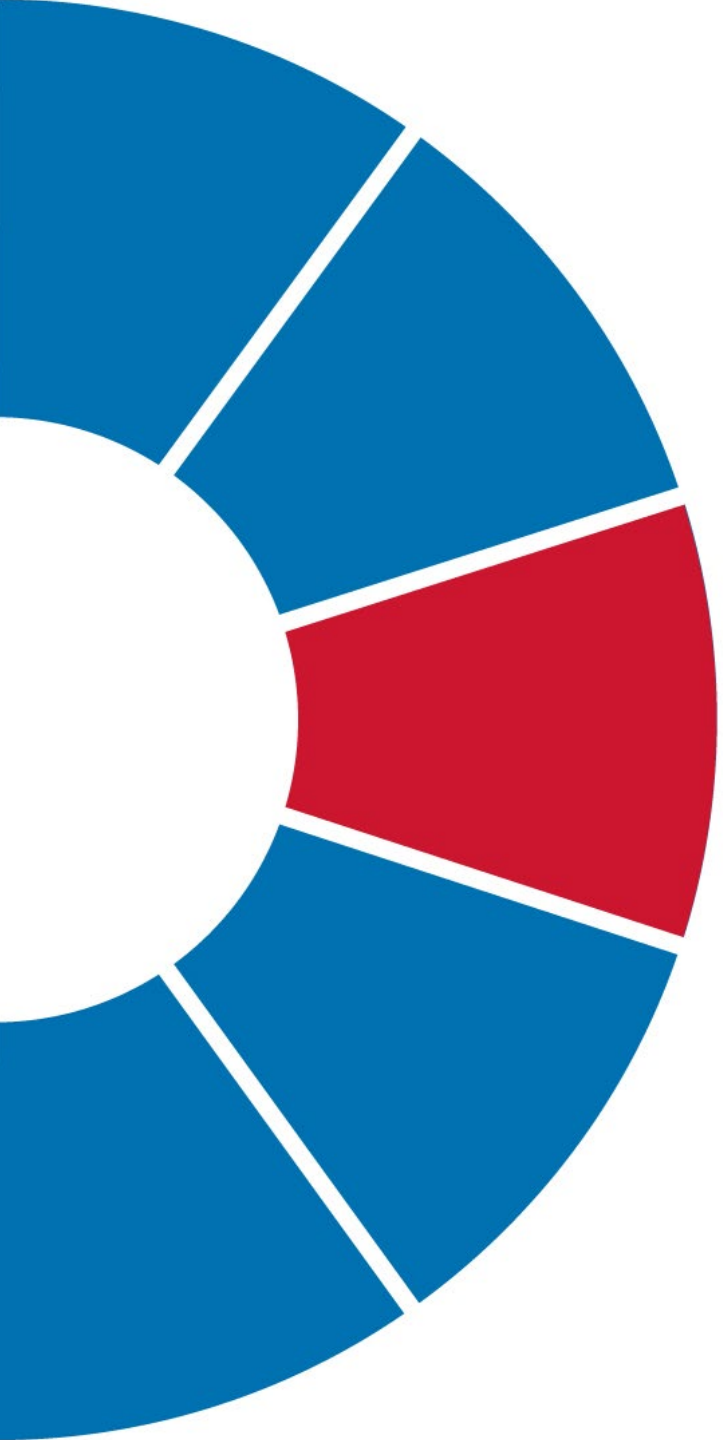
Advanced magnetic resonance spectroscopic neuroimaging: Experts' consensus recommendations - Maudsley - 2021 - NMR in Biomedicine - Wiley Online Library

BUT WHAT IF …..

Extract each metabolite and have a color map





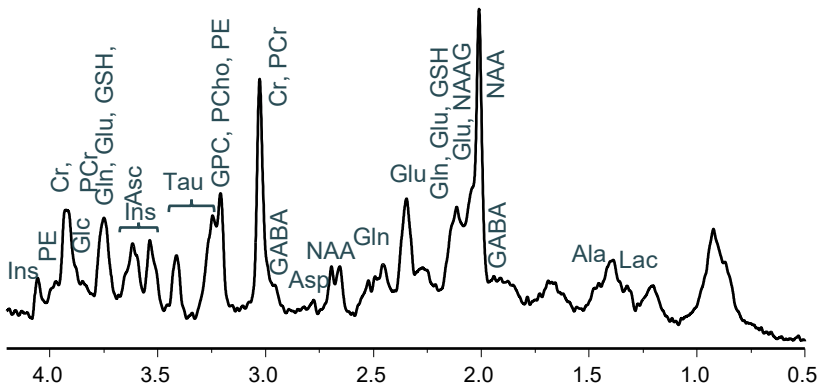


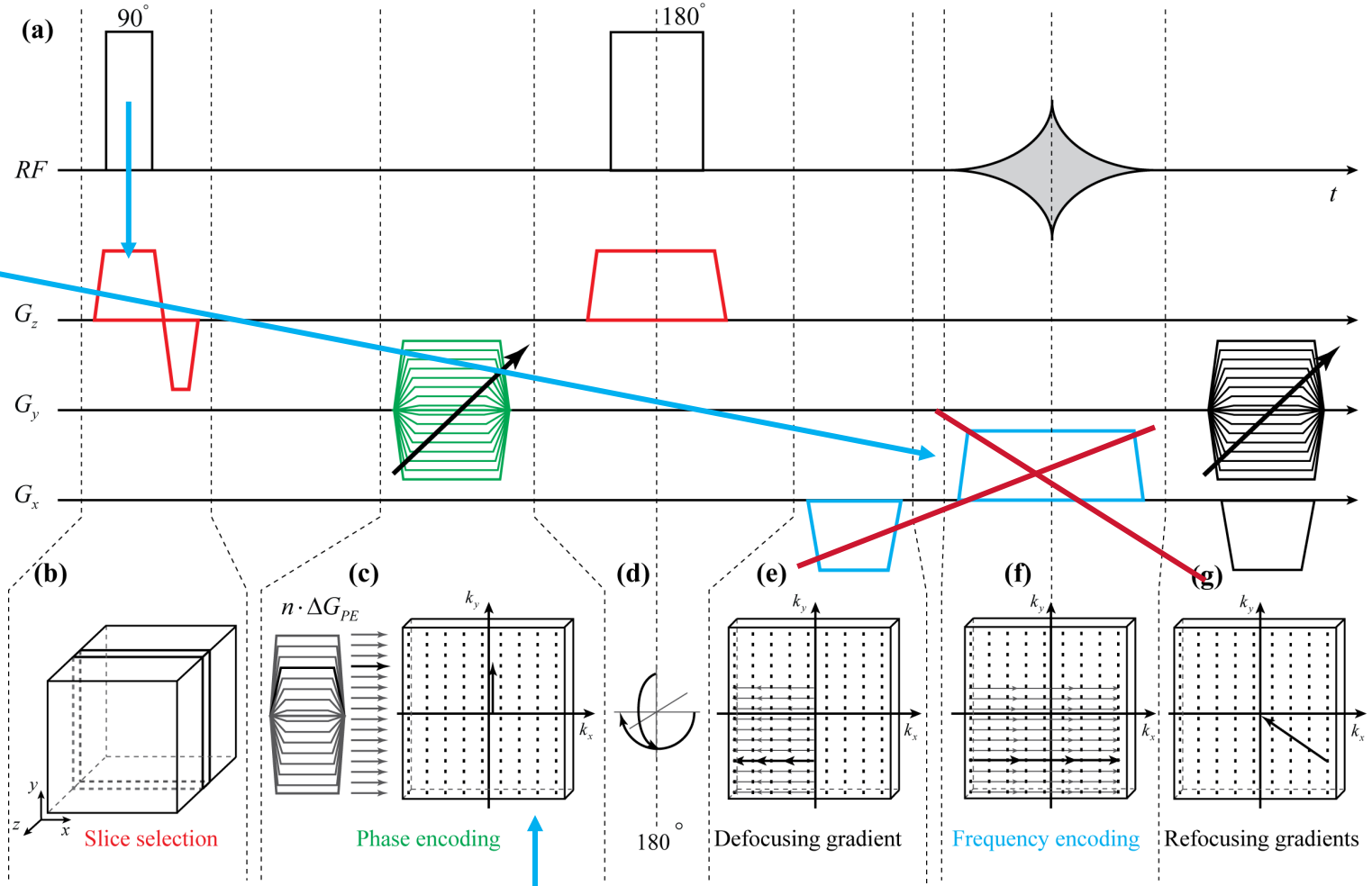
SPATIAL ENCODING FOR MRSI

BASICS OF MRI

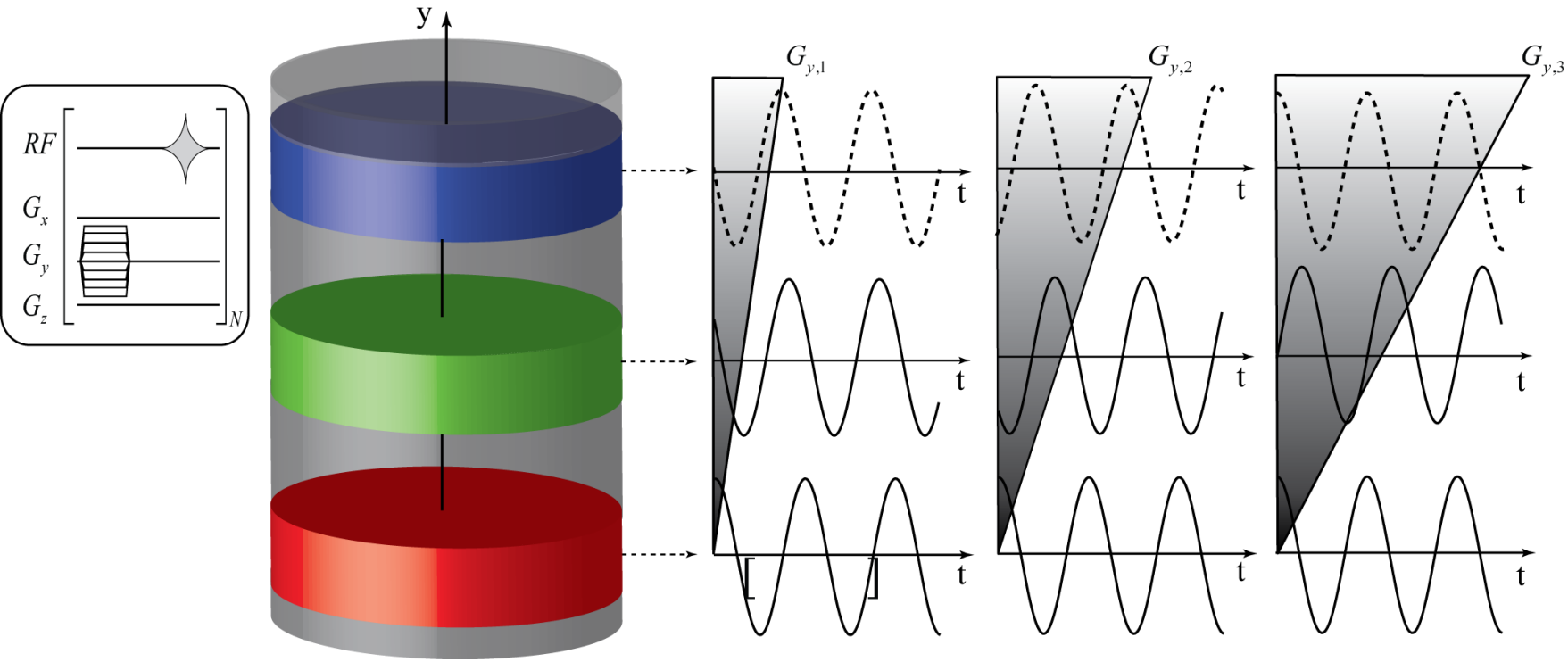
Conventional 2D acquisition

MR spectrum – frequency encoded





SPATIAL ENCODING – PHASE ENCODING

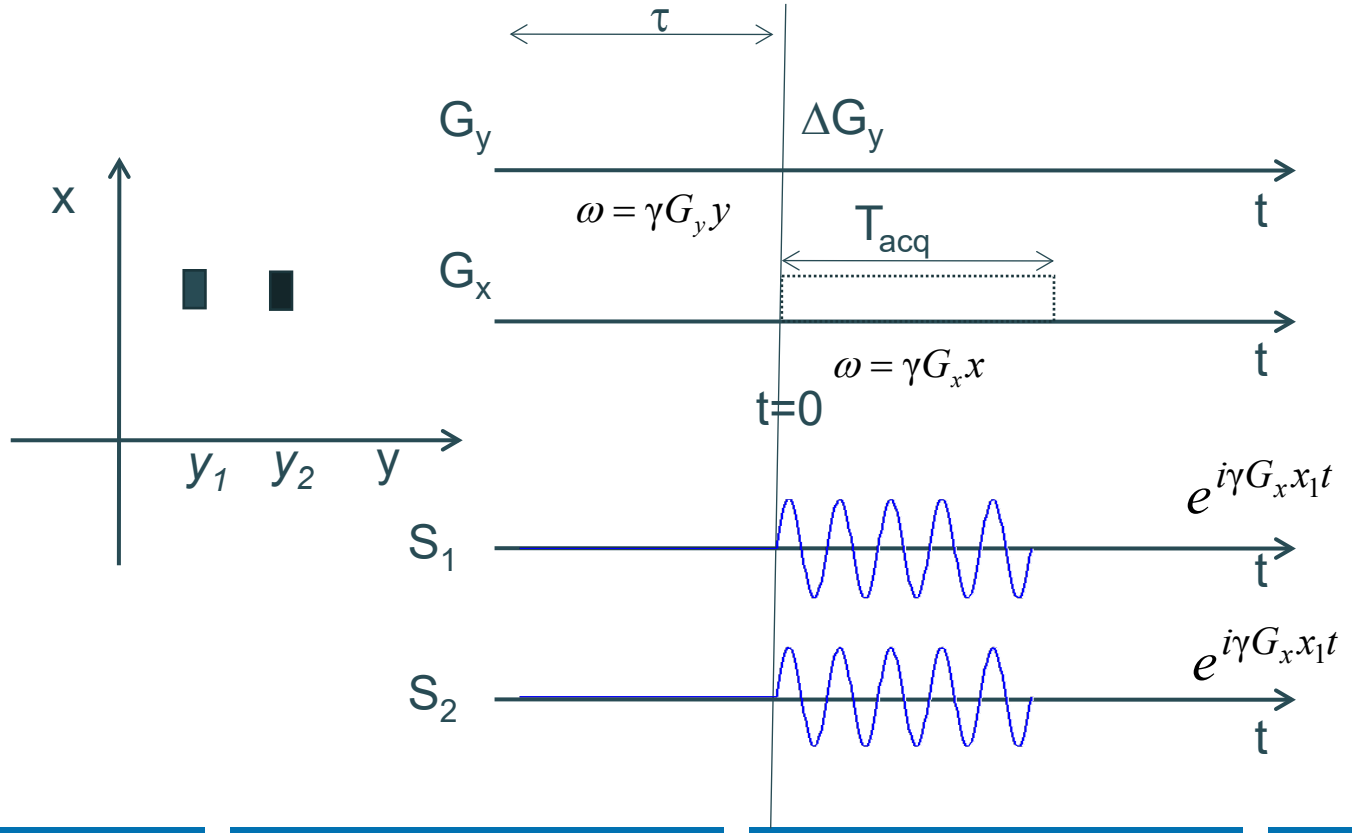


$$\phi\,(y) = \omega_y \cdot \tau_{pe} = \gamma \cdot y \cdot G_y \cdot \tau_{pe}$$

$$S(G_y, \tau_{pe}) \propto \iint_{slice} \rho(x,y) e^{-j\gamma G_{yy}\,\tau_{pe}} dx\,dy$$

PHASE ENCODING

– In a single acquisition, frequency encoding indicates the position in one dimension. Encoding 2nd and 3rd dimension is usually accomplished via phase encoding (position is encoded in the phase of the NMR signal)



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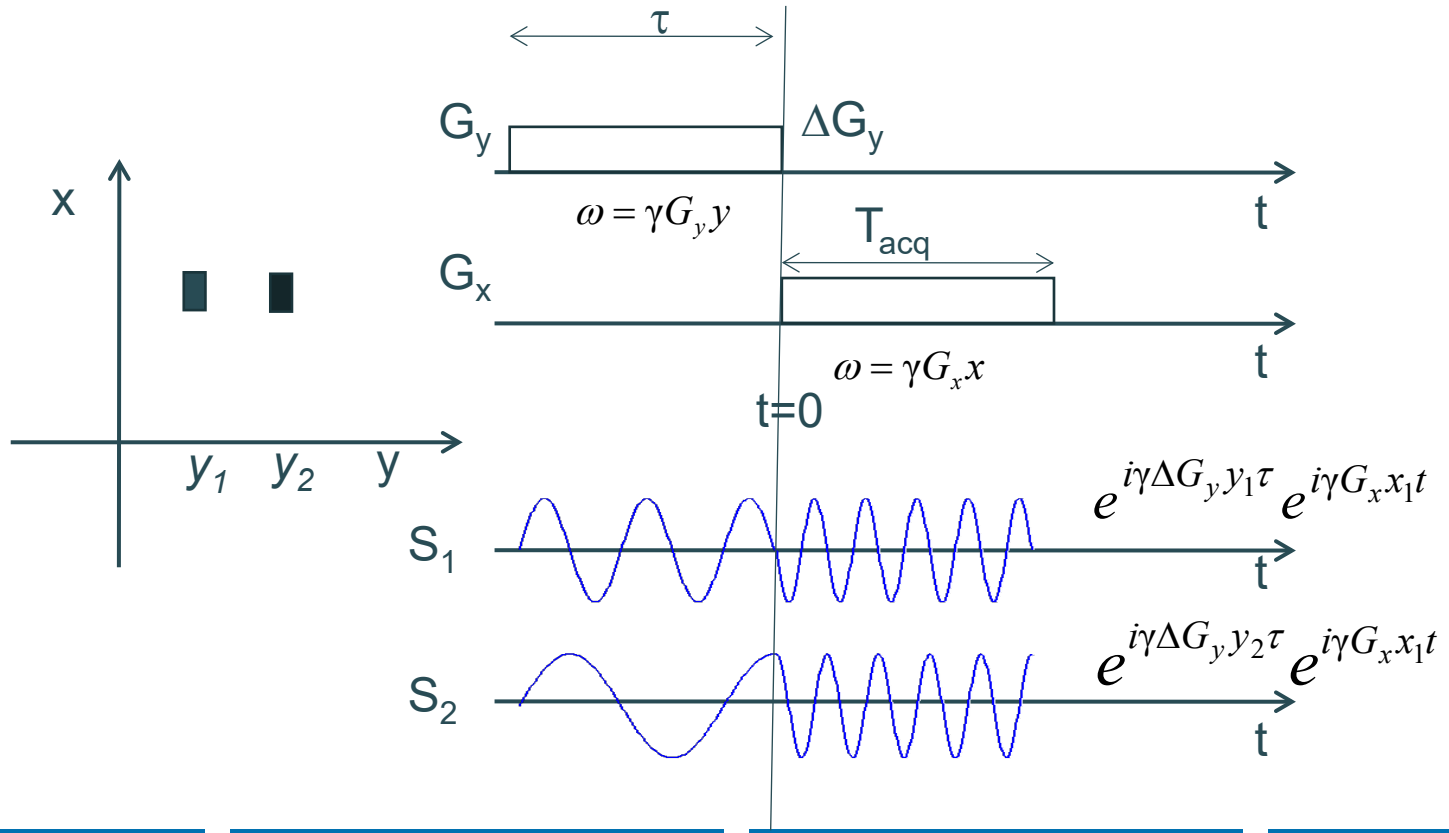
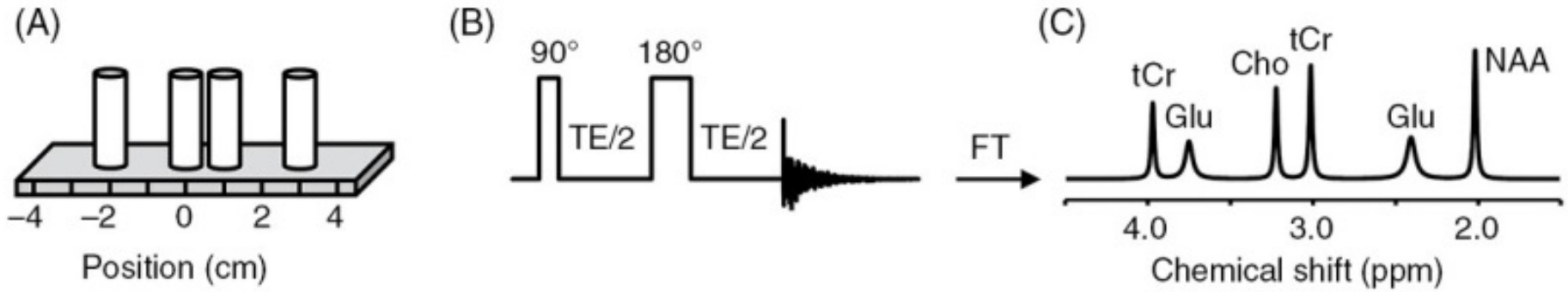
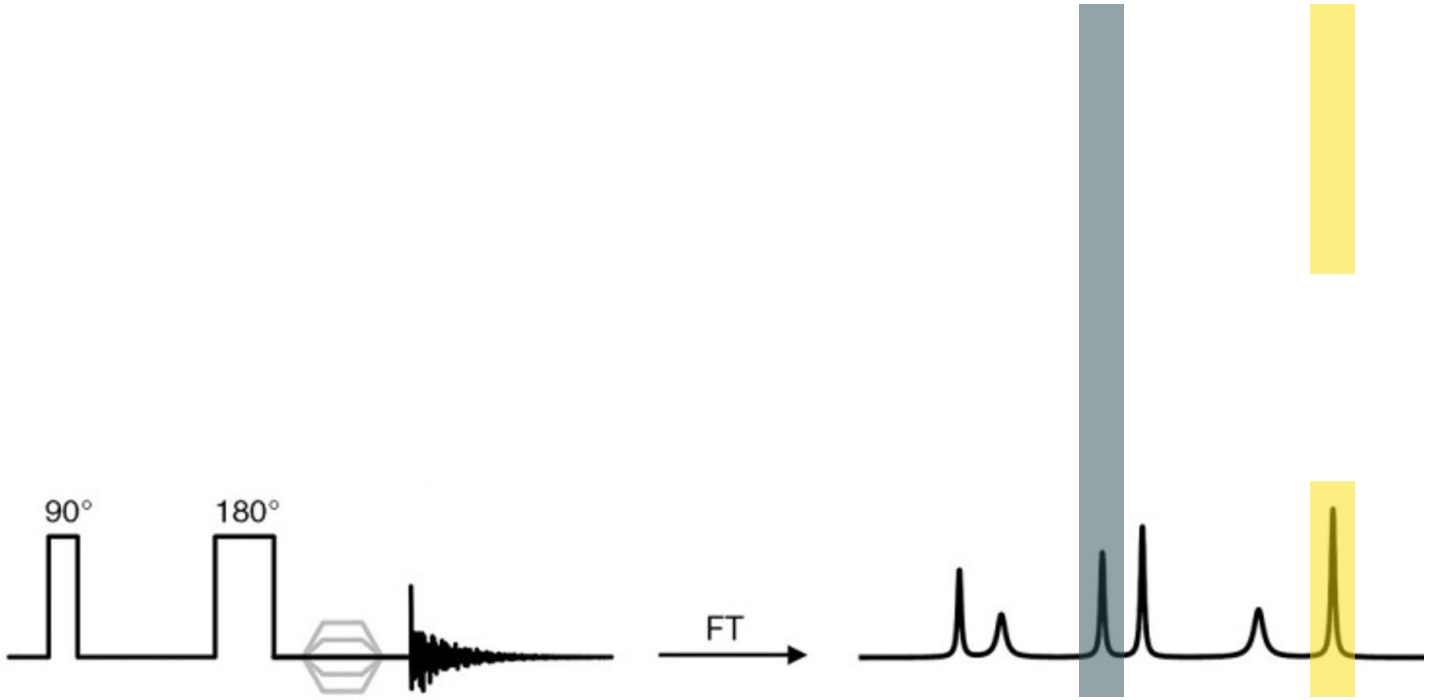


PHASE ENCODING FOR MRSI



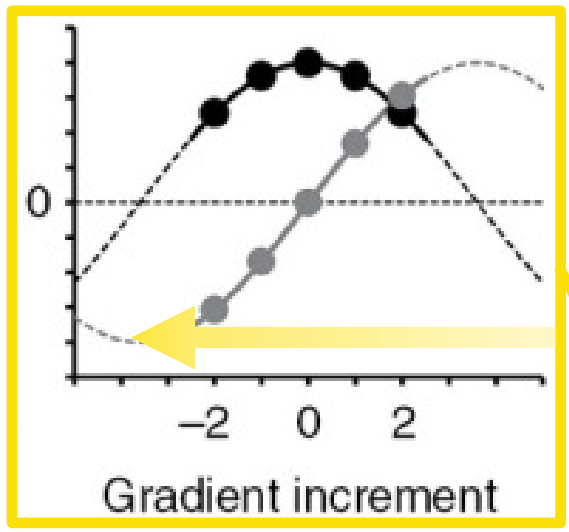
- Frequency encodes metabolites – we cannot encode spatial position with frequency, but …
- … we can convert any MRS sequence into an MRSI sequence by adding phase encoding gradients!

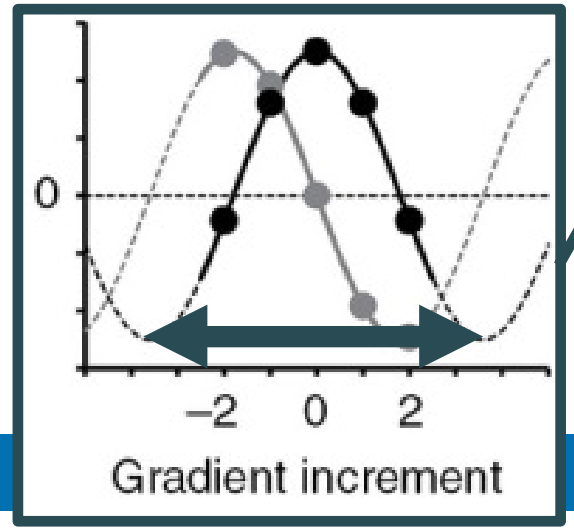
PHASE ENCODING FOR MRSI- QUALITATIVE EXPLANATION

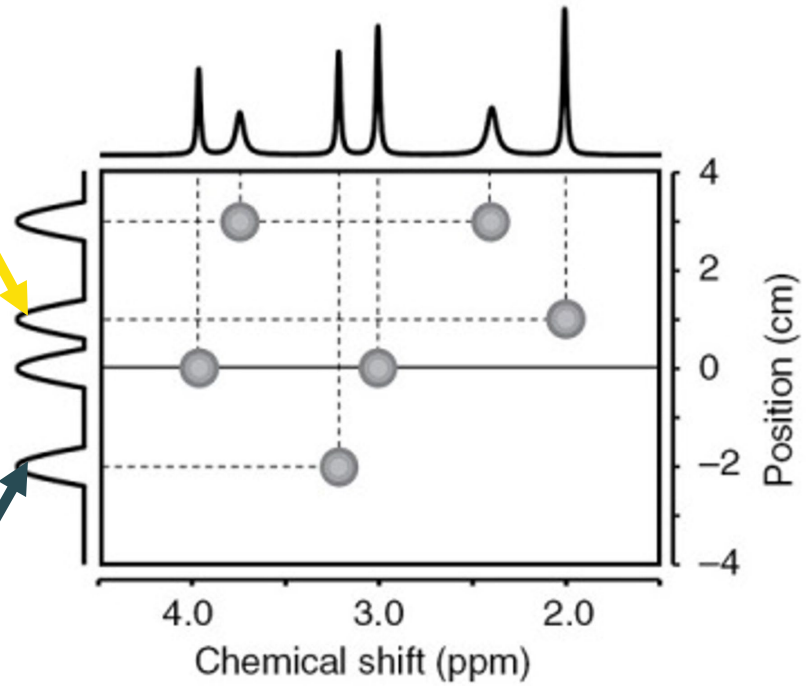


$$\phi(y) = \gamma y G_y t$$

2D FOURIER TRANSFORM







$$F(G,\omega) = \int_{-\infty}^{+\infty} f(r,\omega) e^{i\gamma rGt} dr$$

$k = \gamma Gt$ ⬇ k-space formalism

$$F(k,\omega) = \int_{-\infty}^{+\infty} f(r,\omega) e^{ikr} dr$$

⬇ Fourier transformation

$$f(r,\omega) = \int_{-\infty}^{+\infty} F(k,\omega) e^{-ikr} dr$$

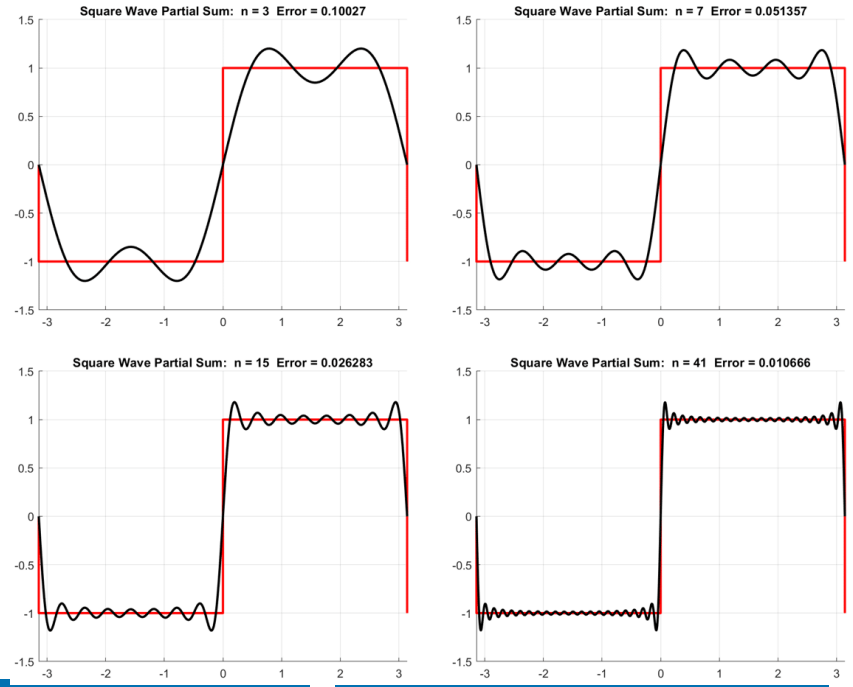
SAMPLING –K_{SPACE}- FT

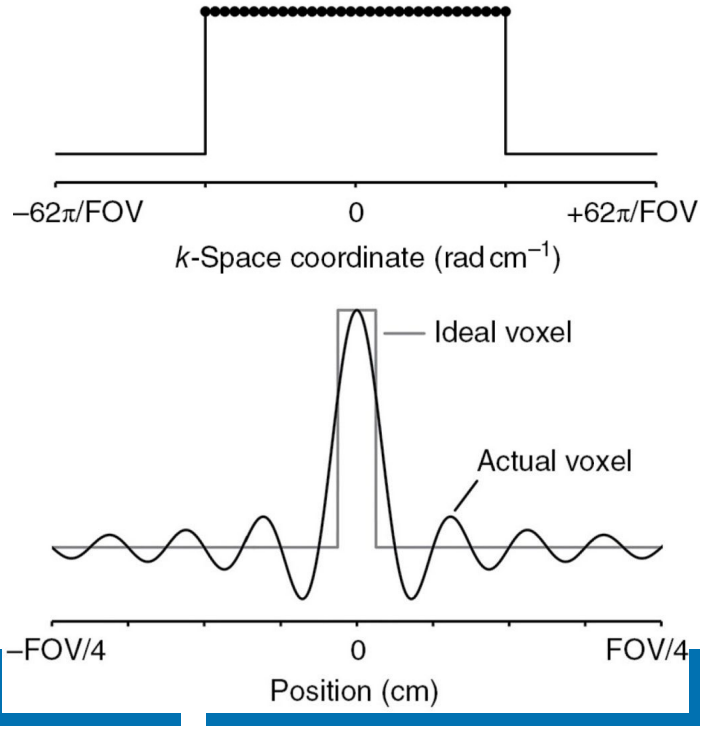
- The signal is not continuously sampled in the k-space
- Digitalization rate in the spatial frequency– phase encoding steps -- if too many – too much time ☹
- Nyquist sampling criterion – avoid aliasing maximum phase shift between two gradient increments over the whole FOV needs to be 2π
- $2\pi = \gamma\, FOV\, \Delta G\, t \quad \rightarrow \quad FOV = \frac{2\pi}{\gamma \Delta G t} = \frac{2\pi}{\Delta k}$
- $\Delta V = \frac{FOV}{N}$ - nominal voxel size

SPATIAL RESOLUTION &PSF

- We cannot efficiently collect a large *k* space grid in a reasonable time
- Small number of *k* space frequency components cause ripples in spatial localization (described by the Point Spread Function)
- signal is contaminated with the signals from other nominal voxels

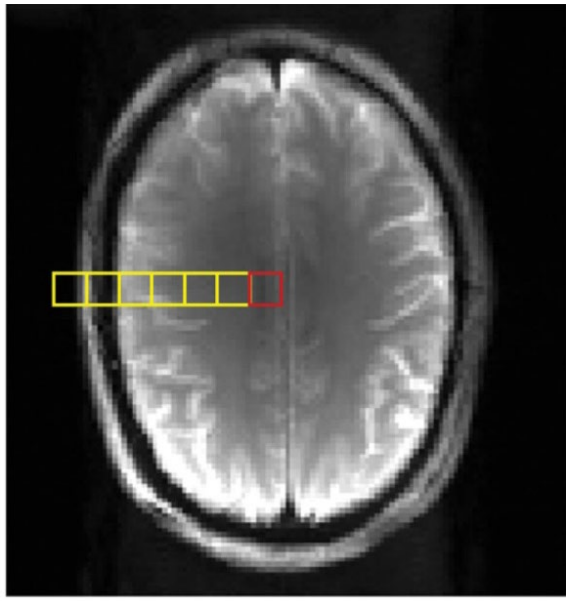
Image credit: gaussianwaves.com

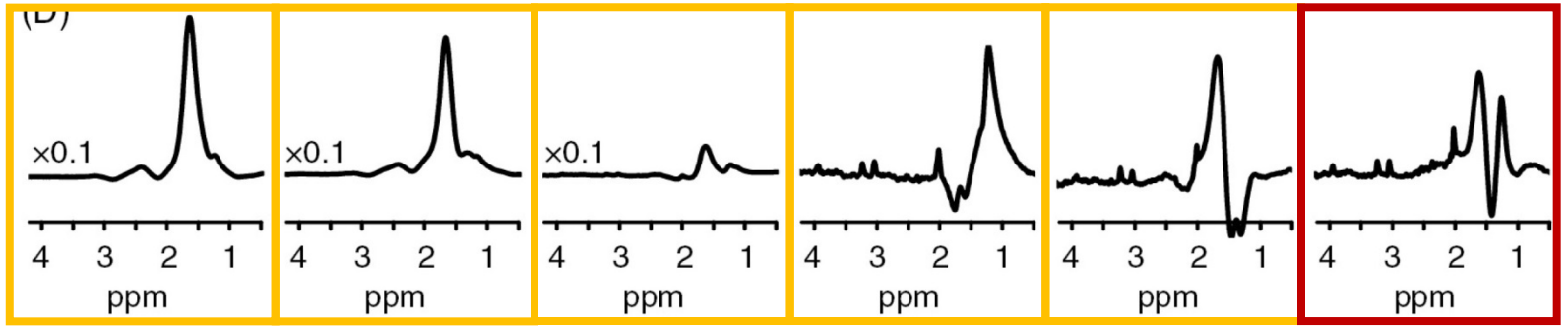


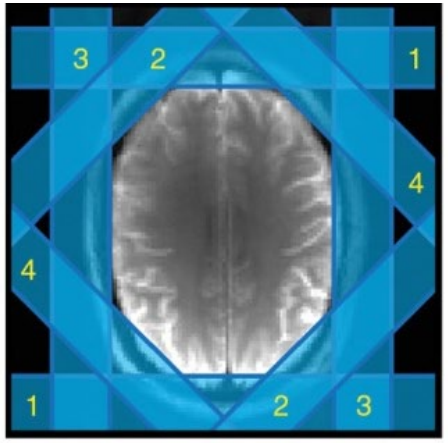


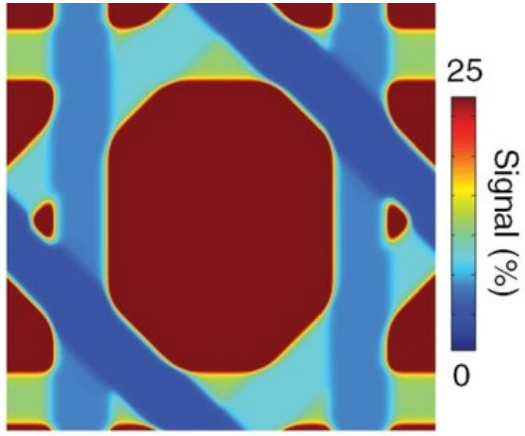
SPATIAL RESOLUTION

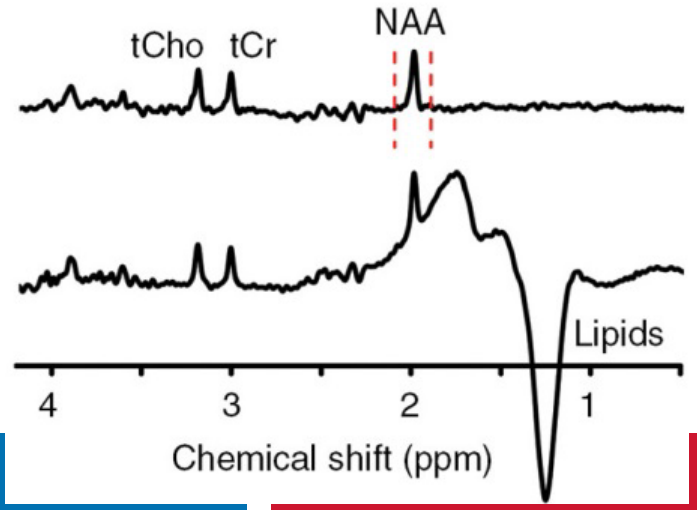
Extracranial lipids 'leak' even into center-brain voxels due to PSF!





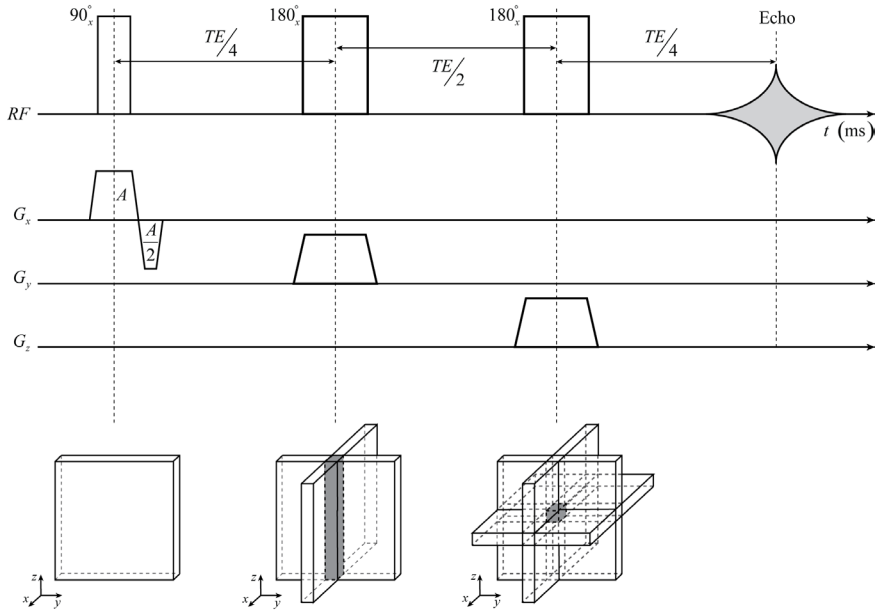




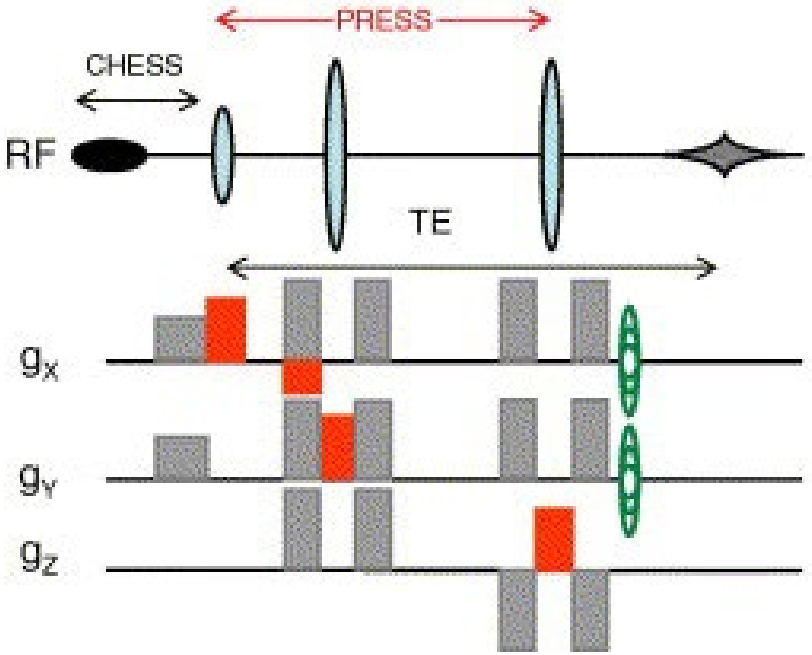


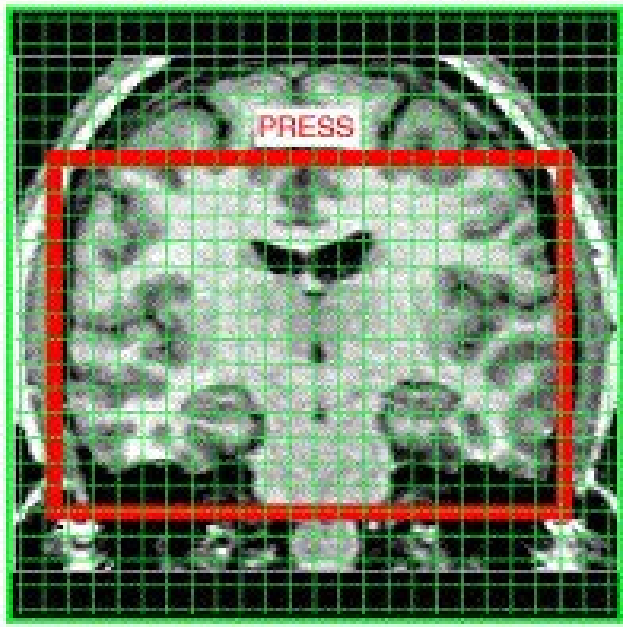
WHAT SEQUENCES TO USE

Any type of sequence to which you add phase encoding gradients



- 3RF pulses – traditional SVS localization techniques
- 2 RF pulses – what will you be selecting here?
- 1RF pulse – what will you be selecting here?
- 2 pe gradients but you can also have 1pe gradient ☺



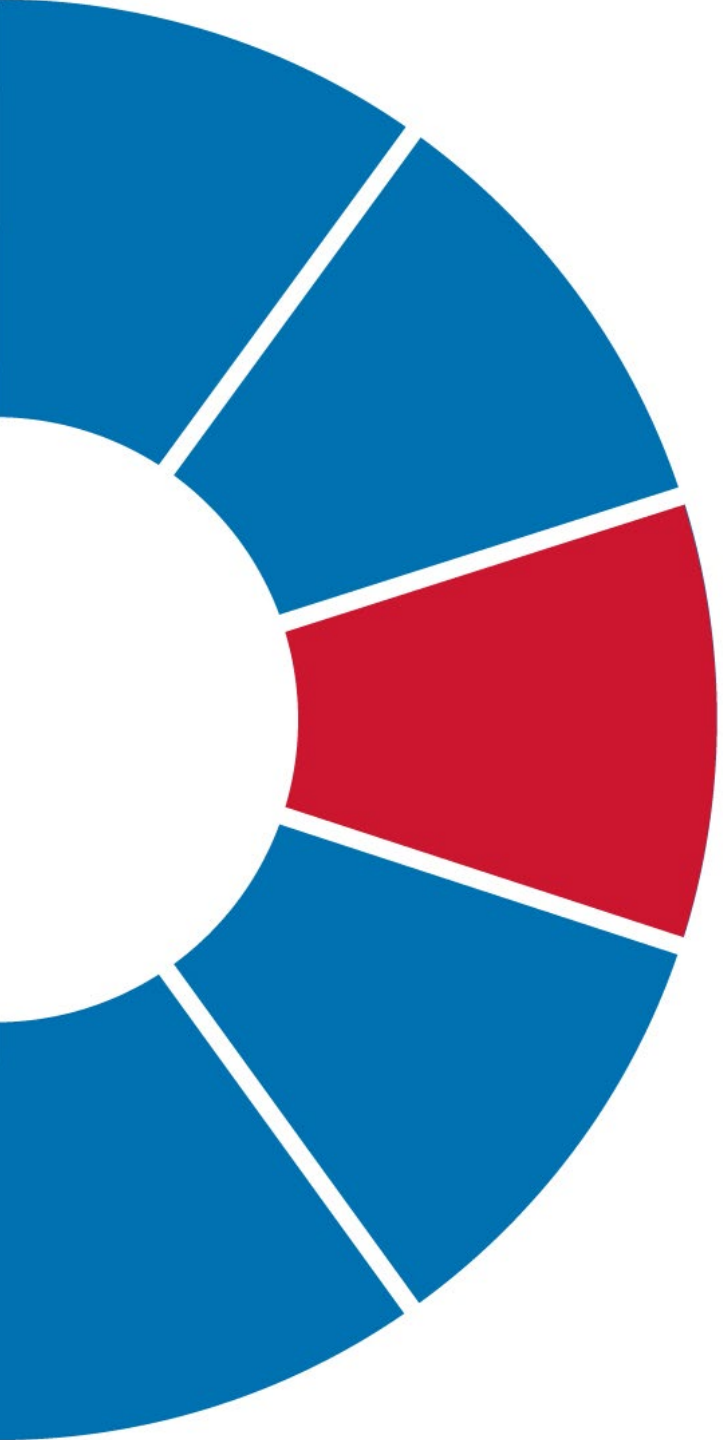


In vivo proton MR spectroscopy of the human brain - ScienceDirect

TEMPORAL RESOLUTION

- $T_{measurement} = NA \times N_x \times N_y \times TR$
  - 1.5T, 16x16x16, NA=1, TR=2000ms --- 136min
  - 32x32 – 34min
- SNR is defined as signal per one SD of the noise
  - Effective voxel volume and no of averages
  - No of phase encoding x NA --- 32x32 with 1NA = 1024 averages as the entire VOI is excited each time
- SNR unit of time= $\frac{SNR}{\sqrt{Ttot}}$

Terminology and concepts for the characterization of in vivo MR spectroscopy methods and MR spectra: Background and experts' consensus recommendations - Kreis - 2021 - NMR in Biomedicine - Wiley Online Library



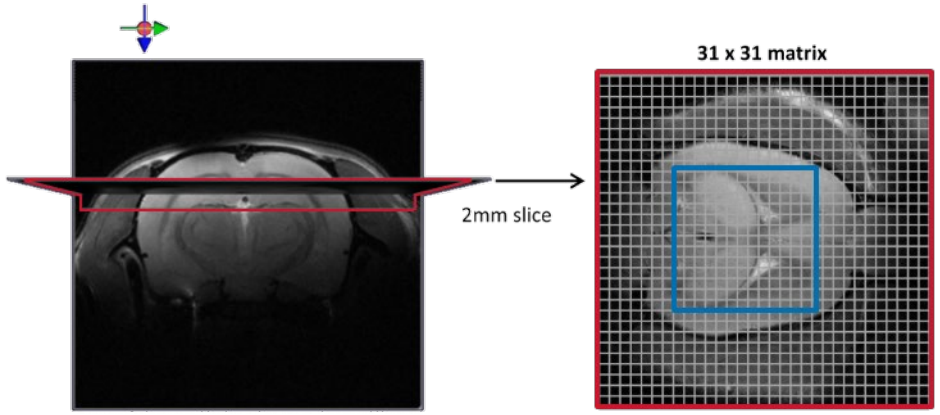
MRSI ADVANTAGES AND CHALLENGES

ADVANTAGES

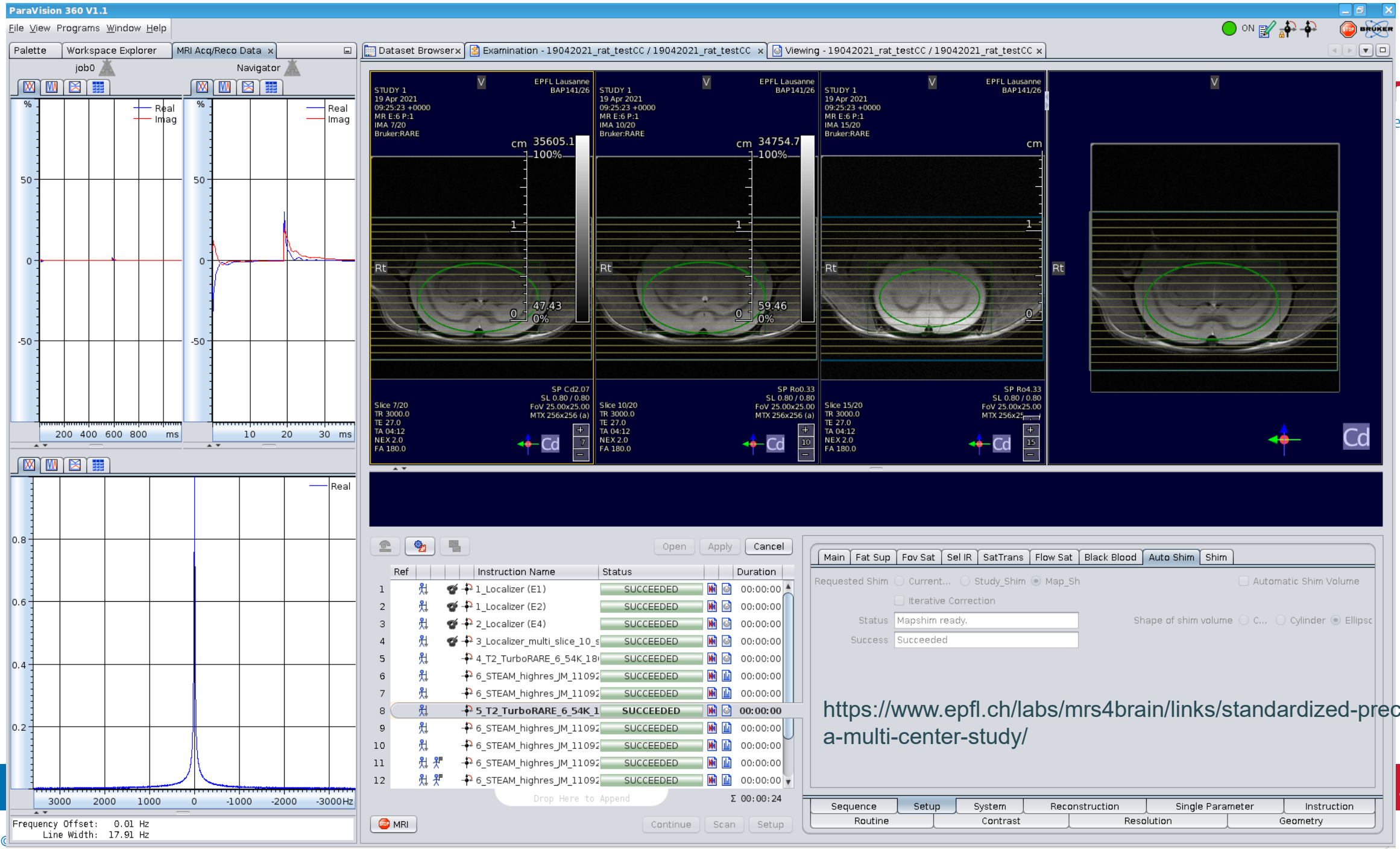
- Multiple locations in the same time / simultaneously
- Direct comparison of metabolic information from multiple regions of interest in a single scan
- 1H but also 31P, 2H, ….fMRSI, DW-MRSI, ….
- phase encoding gradient – no CSDA
- Can be full brain coverage and very fast – next talk

CHALANGES

- Bo shimming – shim larger regions – significant Bo inhomogeneities



B Alves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MRI Acq/Reco Data
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Viewing - 19042021_rat_testCC / 19042021_rat_testCC
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1_Localizer (E2)
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Automatic Shim Volume
Iterative Correction
Status
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Success
Succeeded
Shape of shim volume
Cylinder
Sequence
Setup
System
Reconstruction
Single Parameter
Instruction
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Contrast
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https://www.epfl.ch/labs/mrs4brain/links/standardized-preclinical-mrs-a-multi-center-study/
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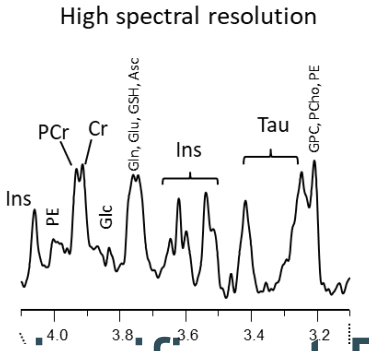
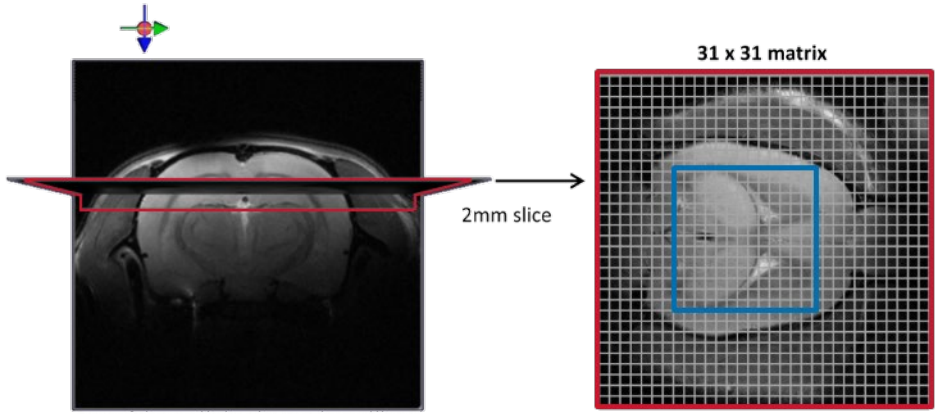
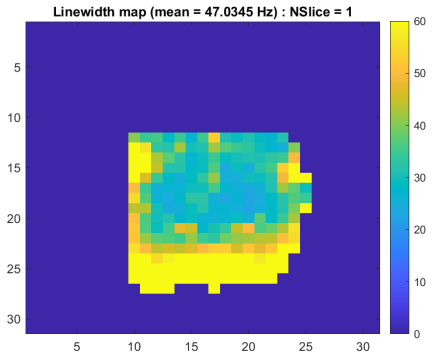
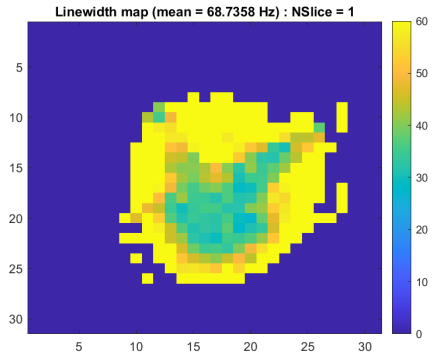
CHALANGES



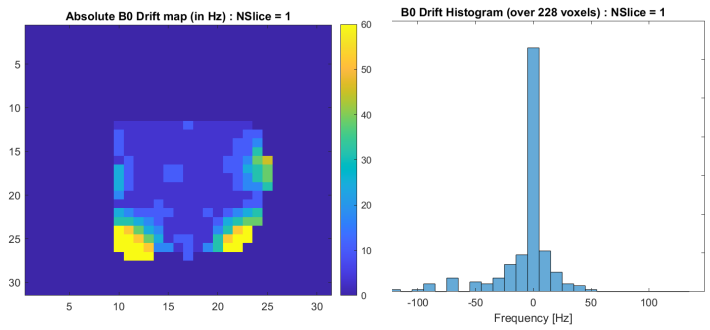
- Bo shimming – shim larger regions – significant Bo inhomogeneities

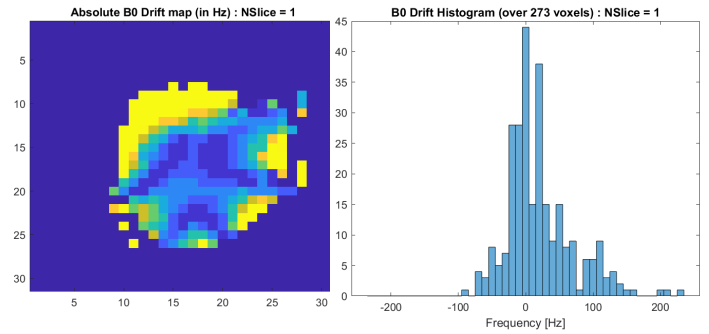






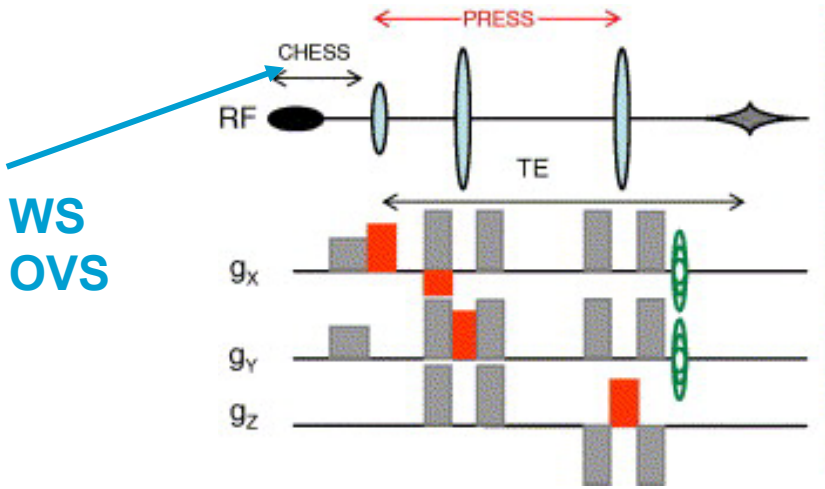
B Alves



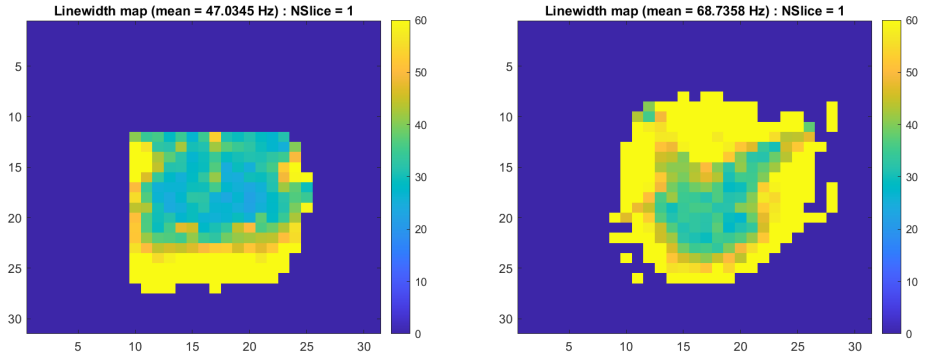


CHALANGES

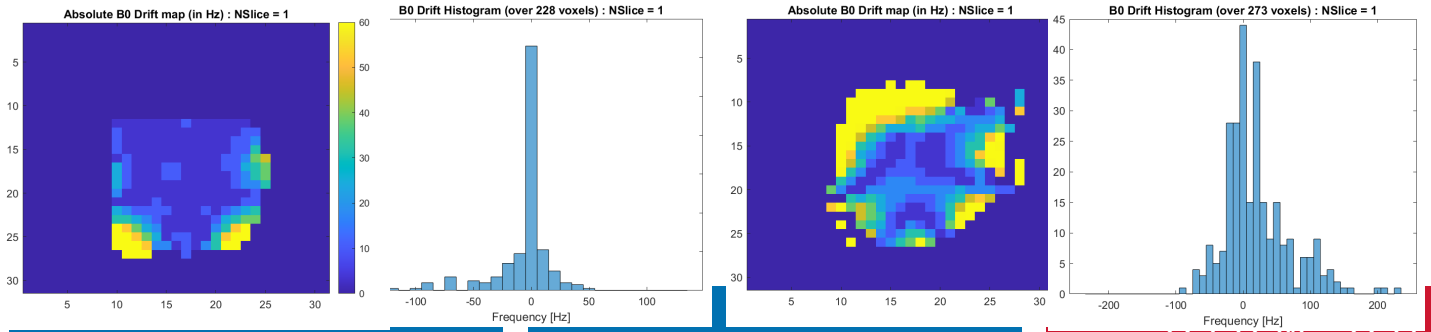
- Water suppression – is done on the signal coming from the entire organ where the resonant frequency (due to Bo inhom, Bo drifts, ..) can not be the best one

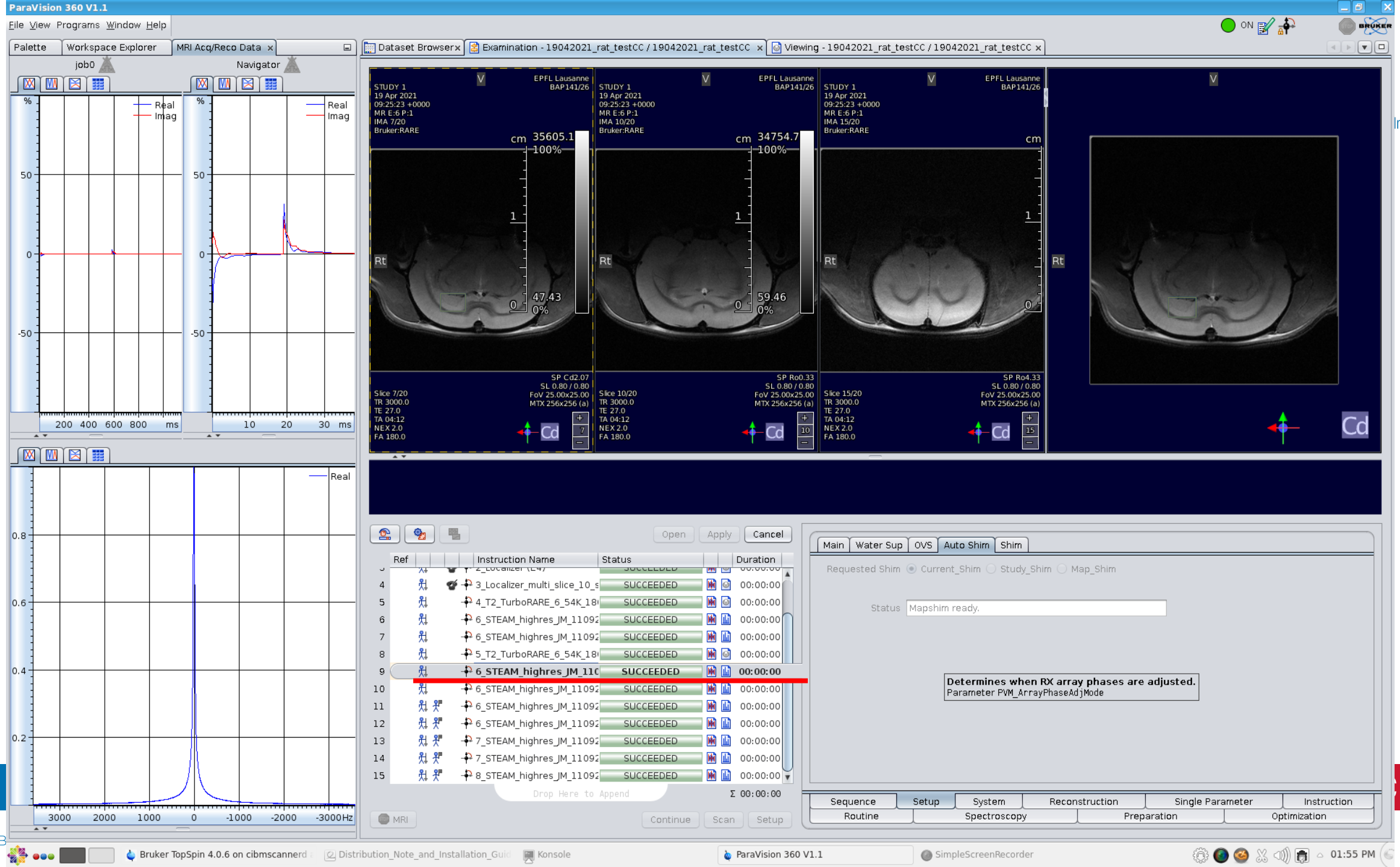


WS
OVS



B Alves

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Bruker:RARE
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BAP141/26
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0%
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TE 27.0
TA 04:12
NEX 2.0
FA 180.0
SP Cd2.07
SL 0.80 / 0.80
FoV 25.00x25.00
MTX 256x256 (a)
IMA 10/20
cm 34754.7
59.46
Slice 10/20
SP Ro0.33
IMA 15/20
Slice 15/20
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Determines when RX array phases are adjusted.
Parameter PVM_ArrayPhaseAdjMode
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Routine
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Imaging

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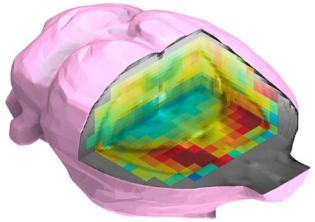
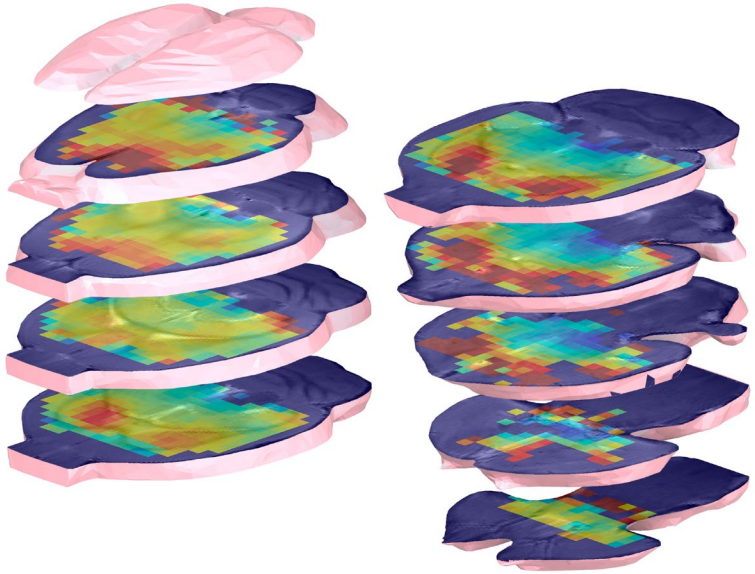
3D METABOLIC MAP

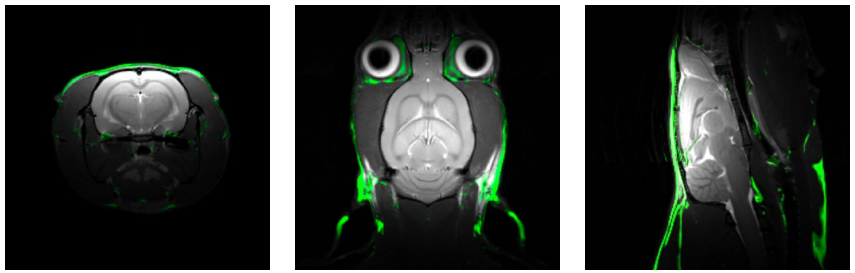


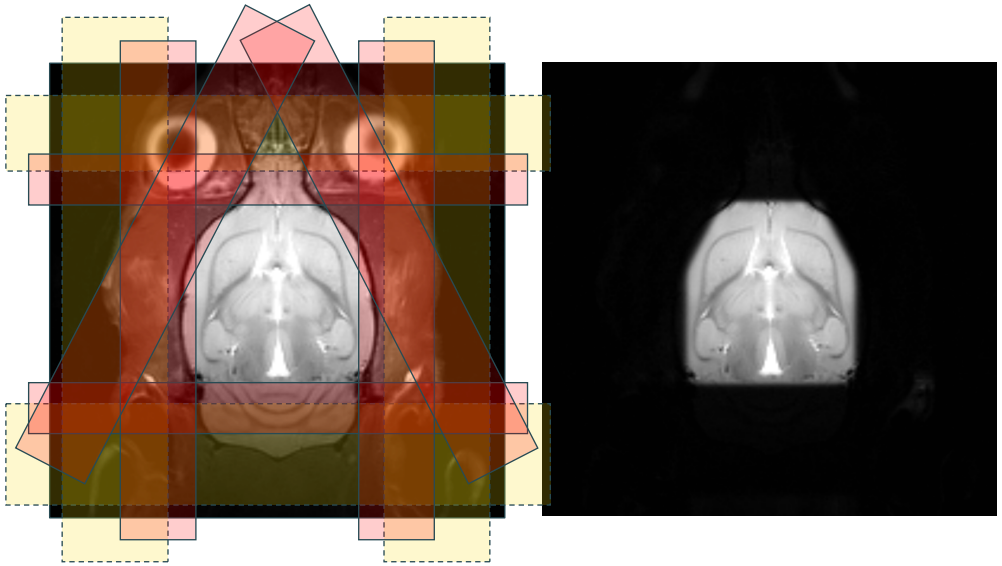
Tan Toi Phan

B Alves

T Le







- Time – CS (AF=4, 119min→28min), 1.19 µL to 0.59 µL
- PSF & Resolution
- Lipid contamination -- Saturation bands
- Post processing
- …

CHALANGES

- low concentration of metabolites, long measurement times,
- low signal-to-noise ratio (SNR)
- hardware limitations (B_0 and gradient strength, RF coils, B_0 inhomogeneities)
- requirement for advanced pulse sequences that need to be developed in-house

CHALLENGES

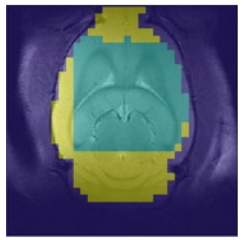
- CSDA is present as we localize the signal at some extend using slice selection gradients
- PSF - contaminations
  - Hamming filter
  - Increase the resolution
  - Weighted acquisitions, not necessary post-acquisition as they decrease the spatial resolution (increases the FWHM of PSF) and sensitivity per unit time (high Kspace coordinates are suppressed)
- Duration !!!!!!
  - Low concentration of metabolites
  - Phase encoding steps

MRS4BRAIN Toolbox

https://github.com/AlvBrayan/MRS4Brain-toolbox
https://www.epfl.ch/labs/mrs4brain/ressources/mrs4brain-toolbox/

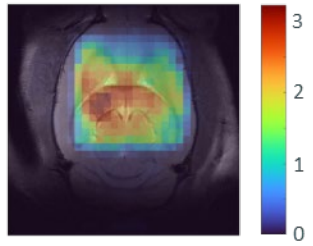
CIBM Center for Biomedical Imaging

1. **Read the Bruker MRSI data format**
2. **Brain mask** – Water power mask
3. **HSVD water removal**
4. **Lipid suppression**
5. Quick data assessment maps
   - → linewidth and ΔB_0 map (water signal)
   - → SNR map (NAA peak hight / σ noise)
6. **LCmodel (Version 6.3-1N)**
7. **Quality selection criteria**
   - → SNR (75% of $\overline{SNR}$), FWHM (125% of $\overline{FWHM}$) and CRLBs (<40%)
8. **Metabolic maps and atlas based automatic segmentation (SIGMA atlas)**

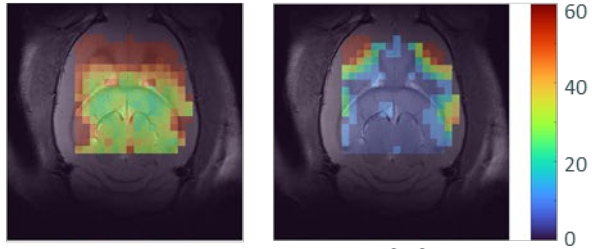


$$Power_{x,y} = \sum_{i=1}^{1024} |spectral\ point|$$

$$0 < Power_{x,y} - \overline{Power} \leftarrow Selection$$

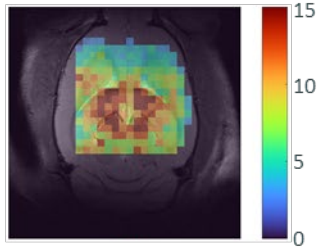


→ ΔB_0 and linewidth map (water signal)

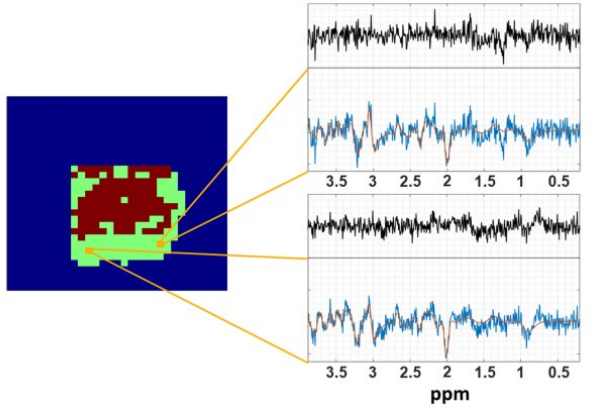


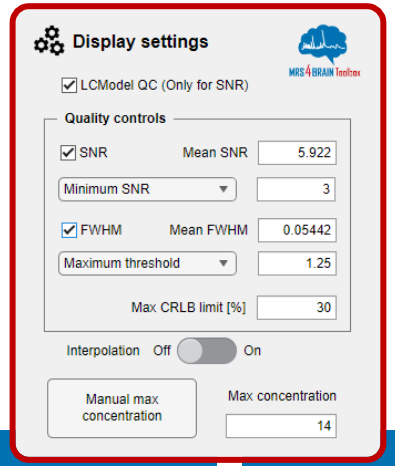
$|\Delta B_0 0|$ [Hz] LW [Hz]

→ SNR map (NAA peak hight / σ noise)



SNR



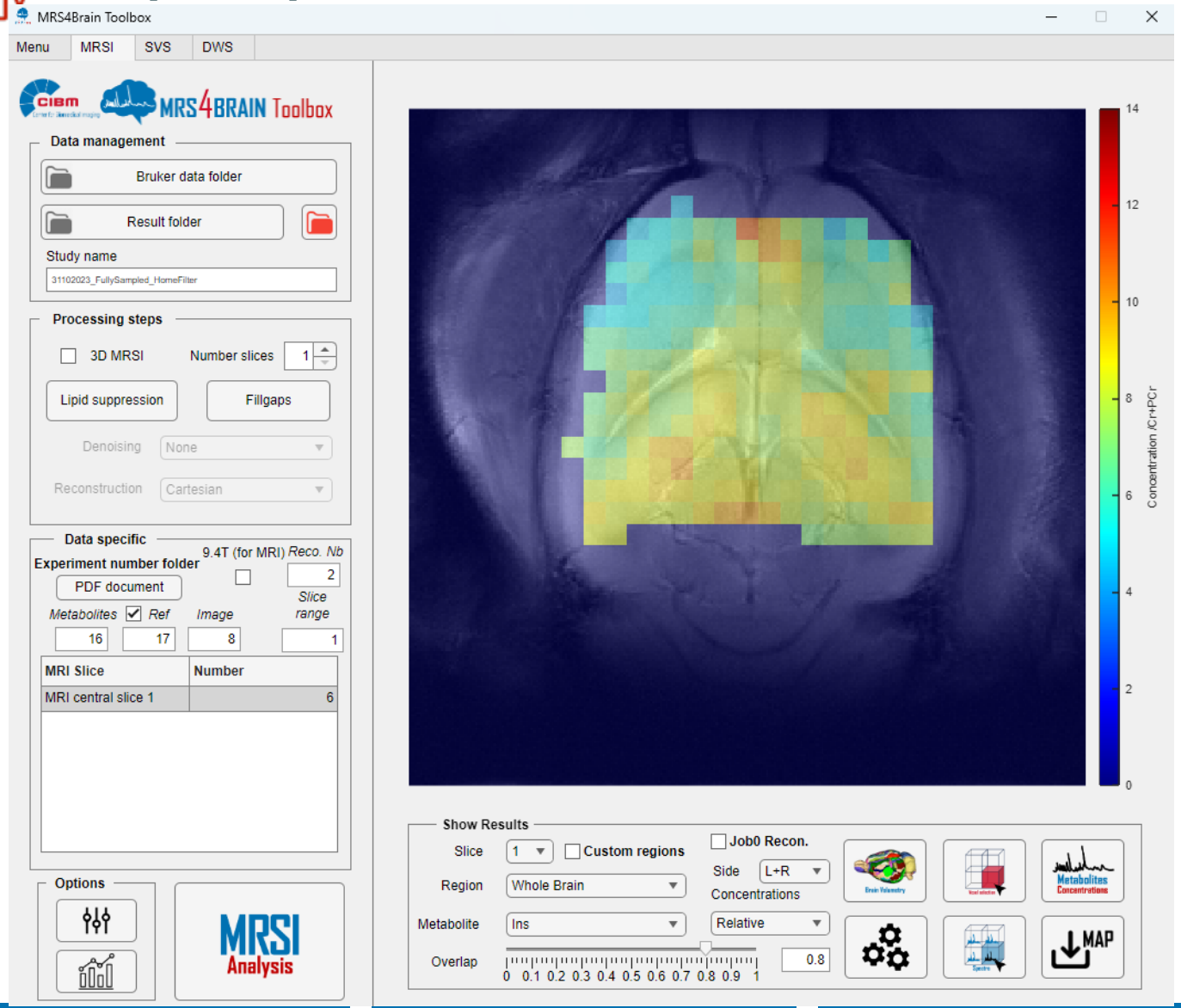


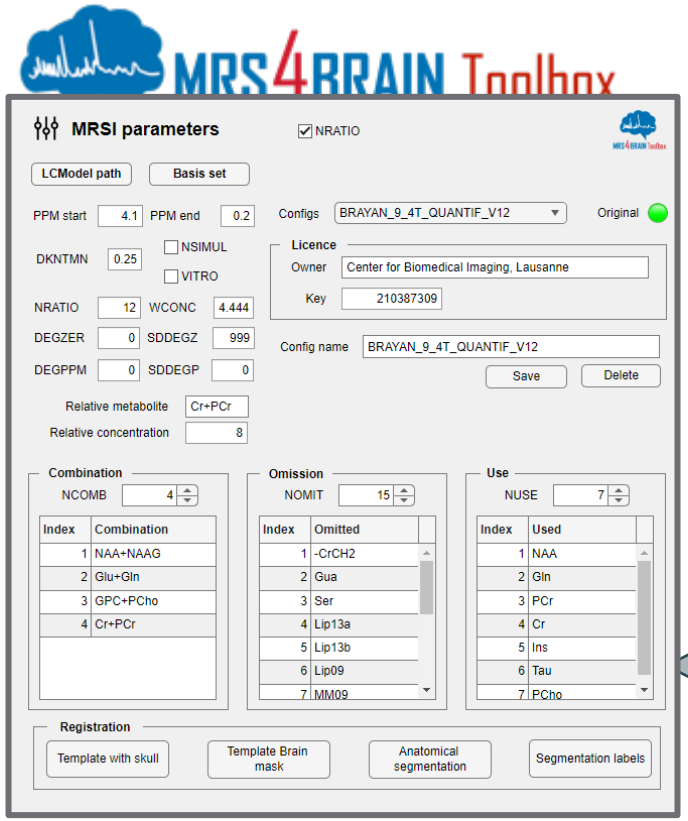
B Alves & G Briand

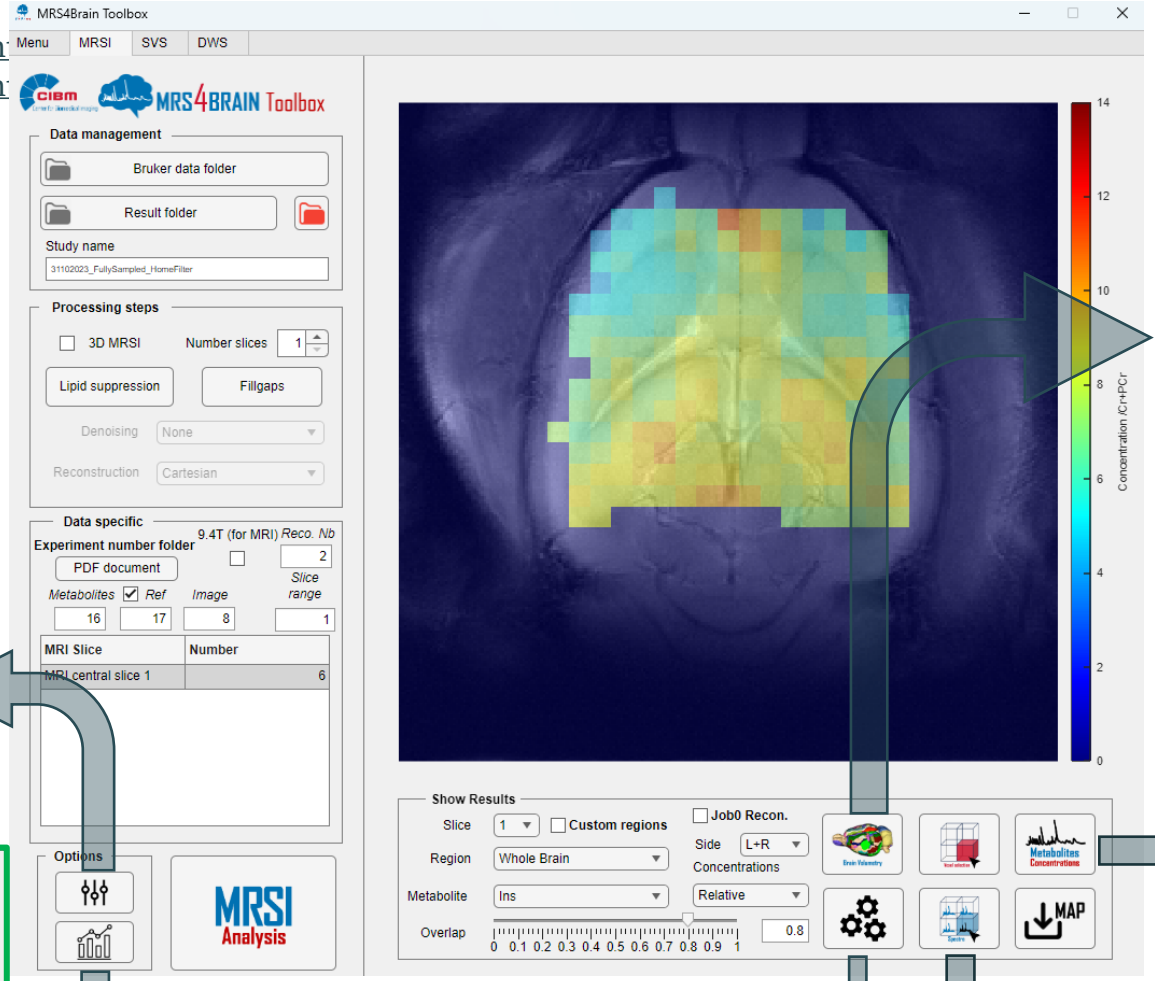
CIBM.CH

cristina.cudalbu@epfl.ch

https://github.com/AlvBrayan/MRS4Brain-toolbox
https://www.epfl.ch/labs/mrs4brain/ressources/mrs4brain-toolbox/







Volumetry table

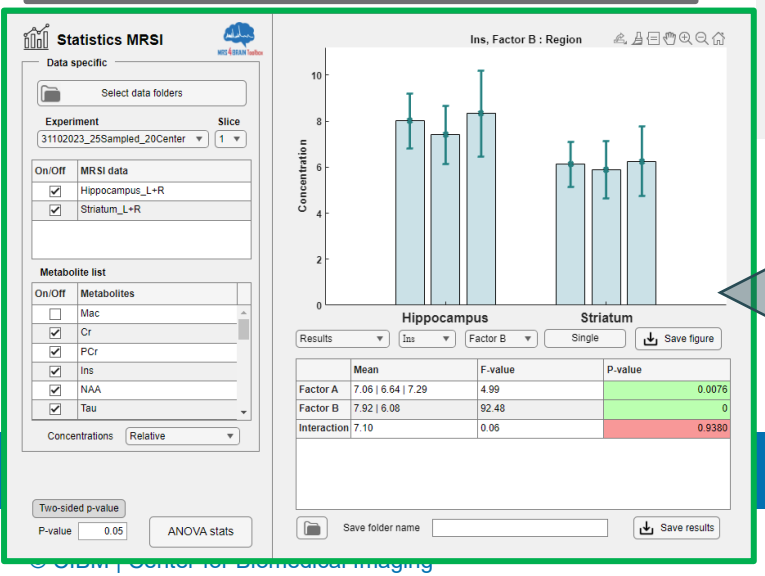
Brain region	Left	Right	L+R
Olfactory bulb	52.82	54.01	106.83
Prelimbic cortex	20.92	20.4	41.32
Frontal Association Cortex	2.32	2.81	5.13
Cingulate cortex	25.78	22.74	48.52
Retrosplenial Cortex	29.5	27.54	57.04
Primary Motor Cortex	0	0	0
Secondary Motor Cortex	13.76	12.25	26.01
Primary Somatosensory Cortex	97.28	68.74	166.01
Secondary Somatosensory Cortex	7.67	7.99	15.67
Orbital Cortex	9.49	9.72	19.21
Insular Cortex	56.97	54.3	111.28
Amygdalopiriform Cortex	8.11	8.85	16.96
Entorhinal Cortex	49.49	59.08	108.57
Ectorhinal Cortex	12.35	12.71	25.06
Perirhinal Cortex	12.2	11.65	23.85
Primary Auditory Cortex	23.29	21.69	44.99
Secondary Auditory Cortex	11.77	10.46	22.23

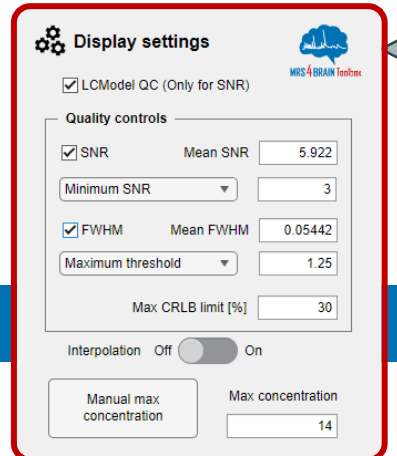
Save name | Save

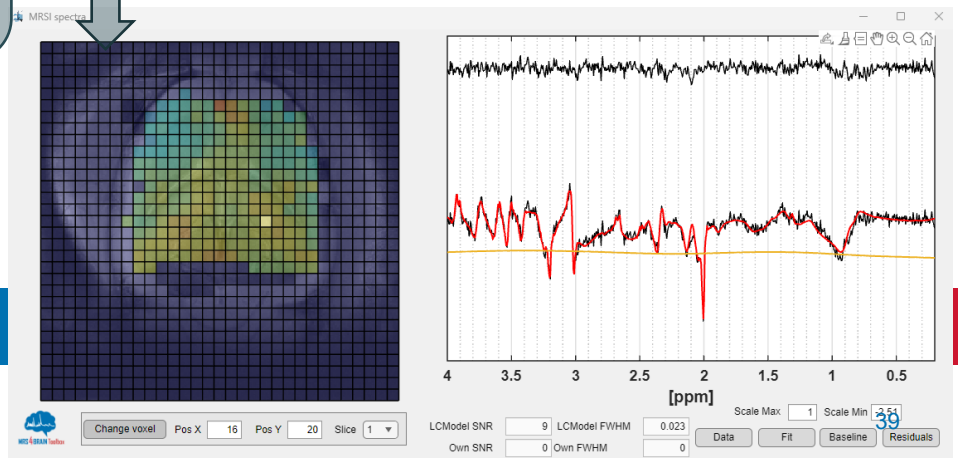
Concentration table

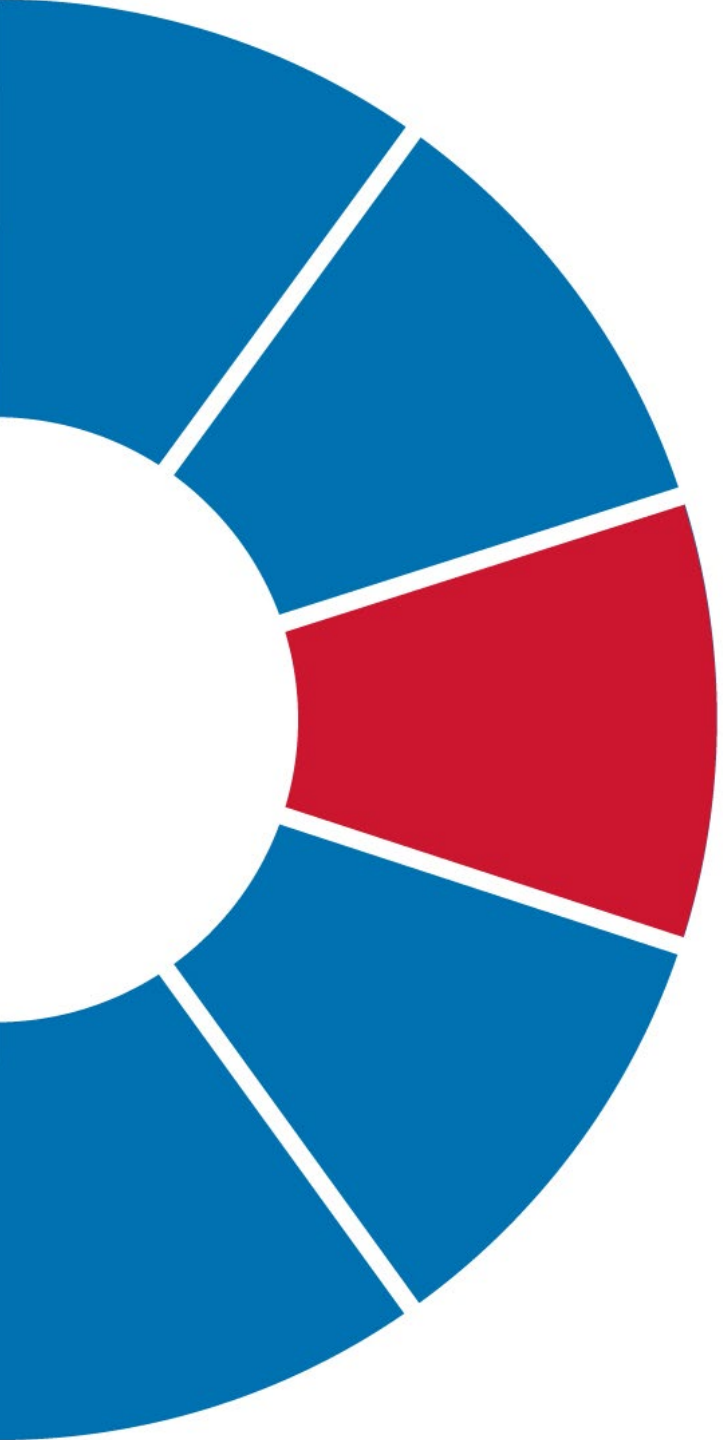
Metabolite	Mean	Std	N voxels
Mac	0.00	0.00	143
Cr	4.43	1.51	140
PCr	4.05	1.24	130
Ins	9.51	1.60	144
NAA	10.88	1.63	144
Tau	7.52	1.56	144
PCho	1.38	0.58	124
GPC	0.94	0.43	72
Glu	8.80	1.76	144
Gln	2.80	0.92	142
Ala	1.29	0.44	17
Asc	3.65	1.38	98
Asp	1.57	0.47	105
GABA	1.19	0.39	135
Glc	1.05	0.27	135
GSH	1.20	0.43	136
Lac	1.78	1.01	21

Save name Whole Brain_L+R | Save





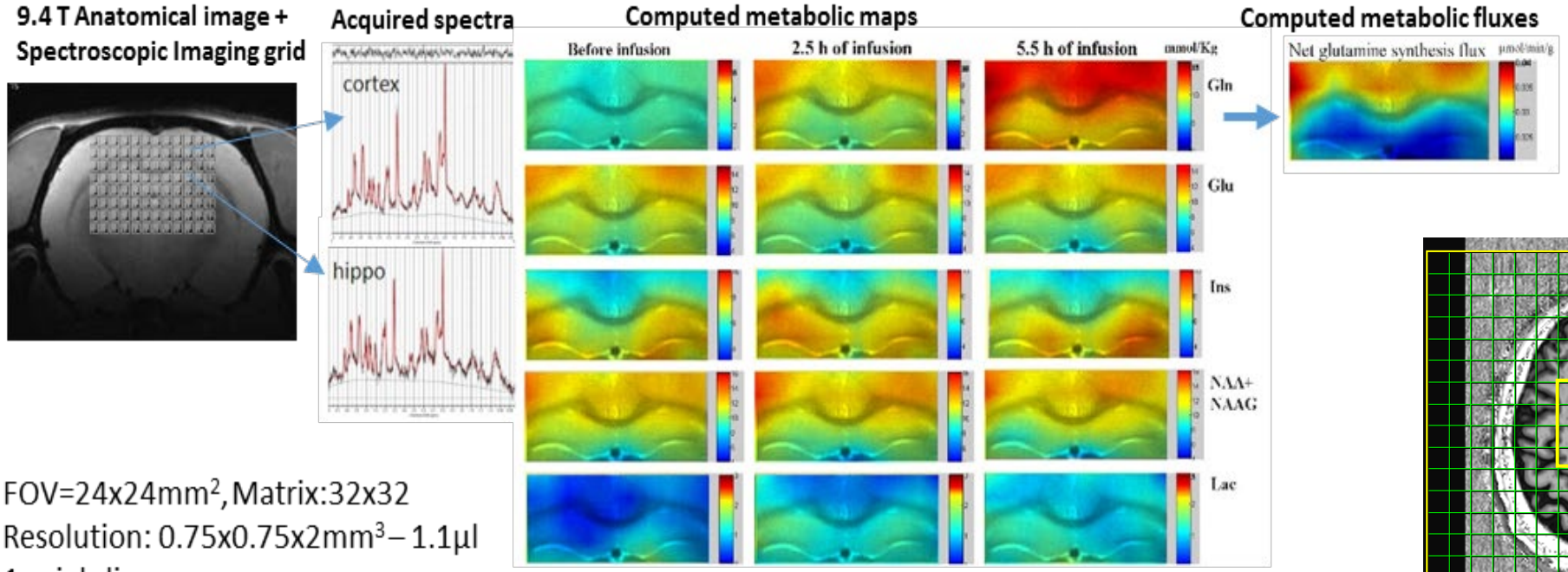




FROM SQUARE MAPS TO FULL BRAIN COVERAGE

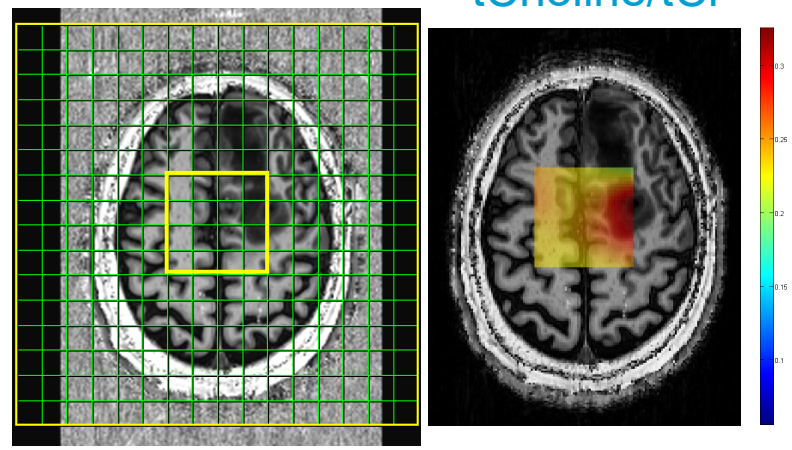
CHALLENGES

- Overall we still do not get full brain coverage and we are limited to squares inside the brain as we are using SVS localization techniques



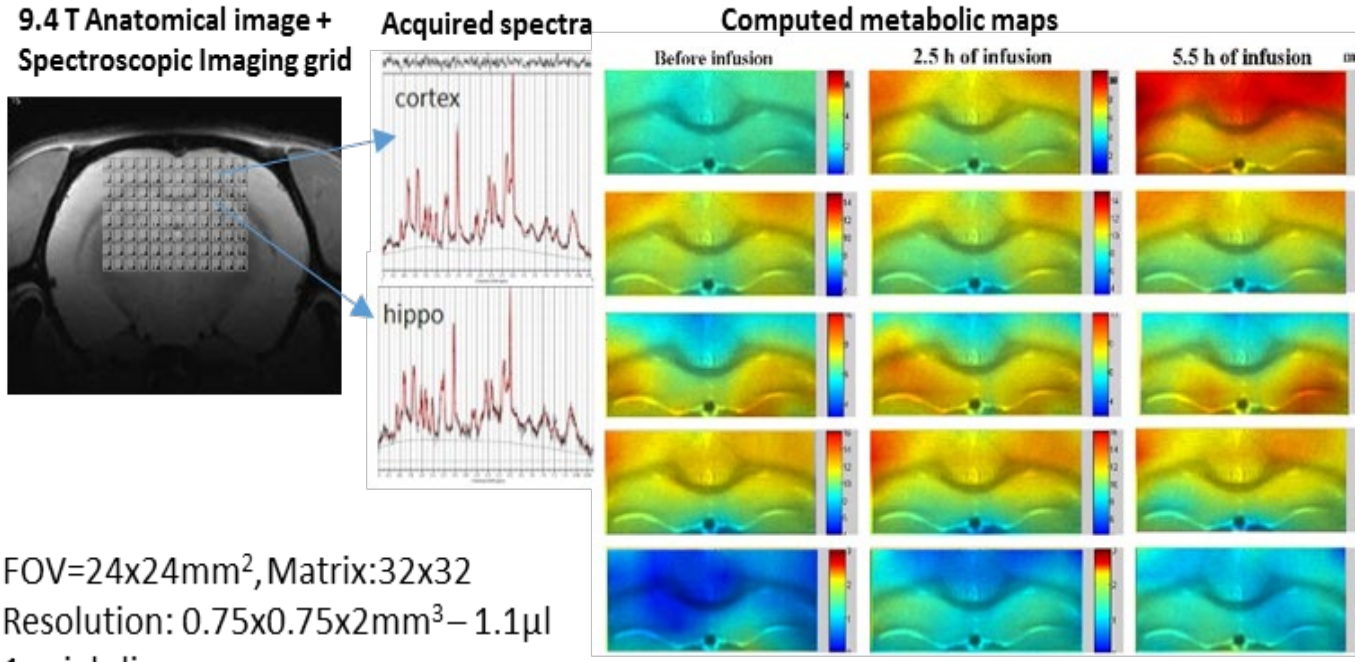
FOV=24x24mm^2, Matrix:32x32
Resolution: 0.75x0.75x2mm^3 – 1.1µl
1 axial slice
Acquisition time (metabolites+H_2O) = ~4h

tCholine/tCr



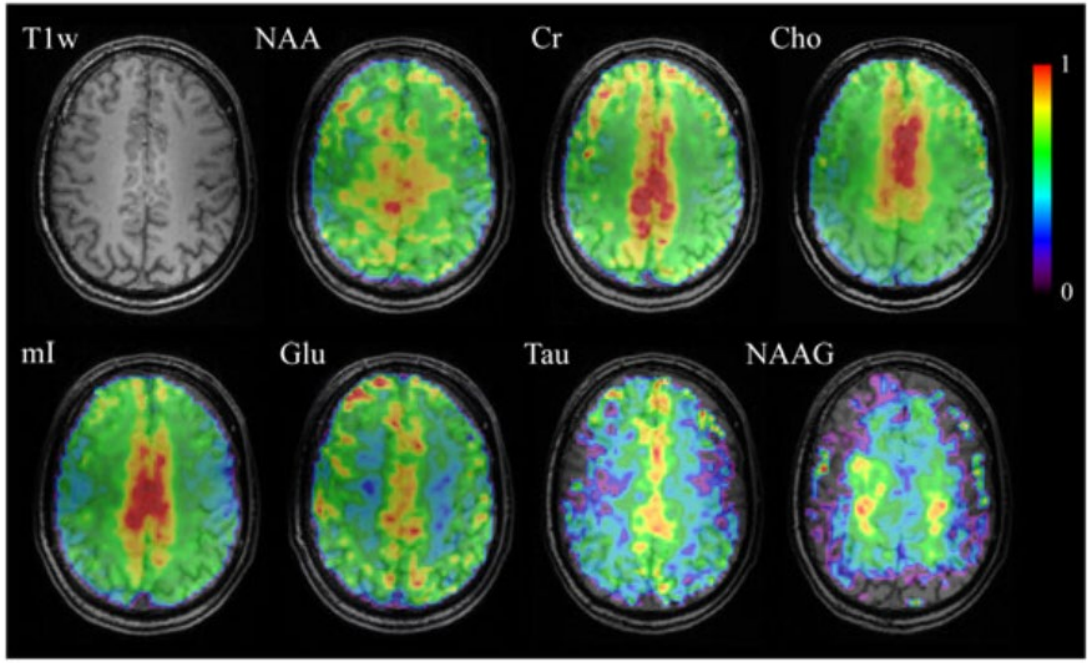
Lijing Xin

FROM SQUARE MAPS TO FULL BRAIN COVERAGE



FOV=24x24mm^2, Matrix:32x32
Resolution: 0.75x0.75x2mm^3 – 1.1µl
1 axial slice
Acquisition time (metabolites+H_2O) = ~4h

https://www.epfl.ch/labs/mrs4brain/ressources/live-demos/



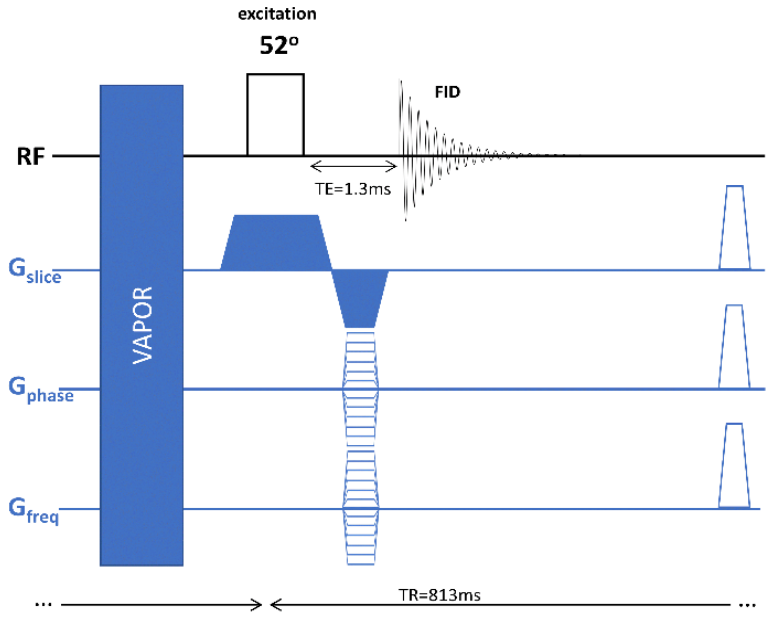
W Bogner et al, NMR Biomed , 2011
3.4x3.4x12 mm^3, within 30 min

FID-MRSI: negligible J-coupling and T_2 related signal loss, better suitability for fast MRSI at UHF in preclinical settings

cristina.cudalbu@epfl.ch

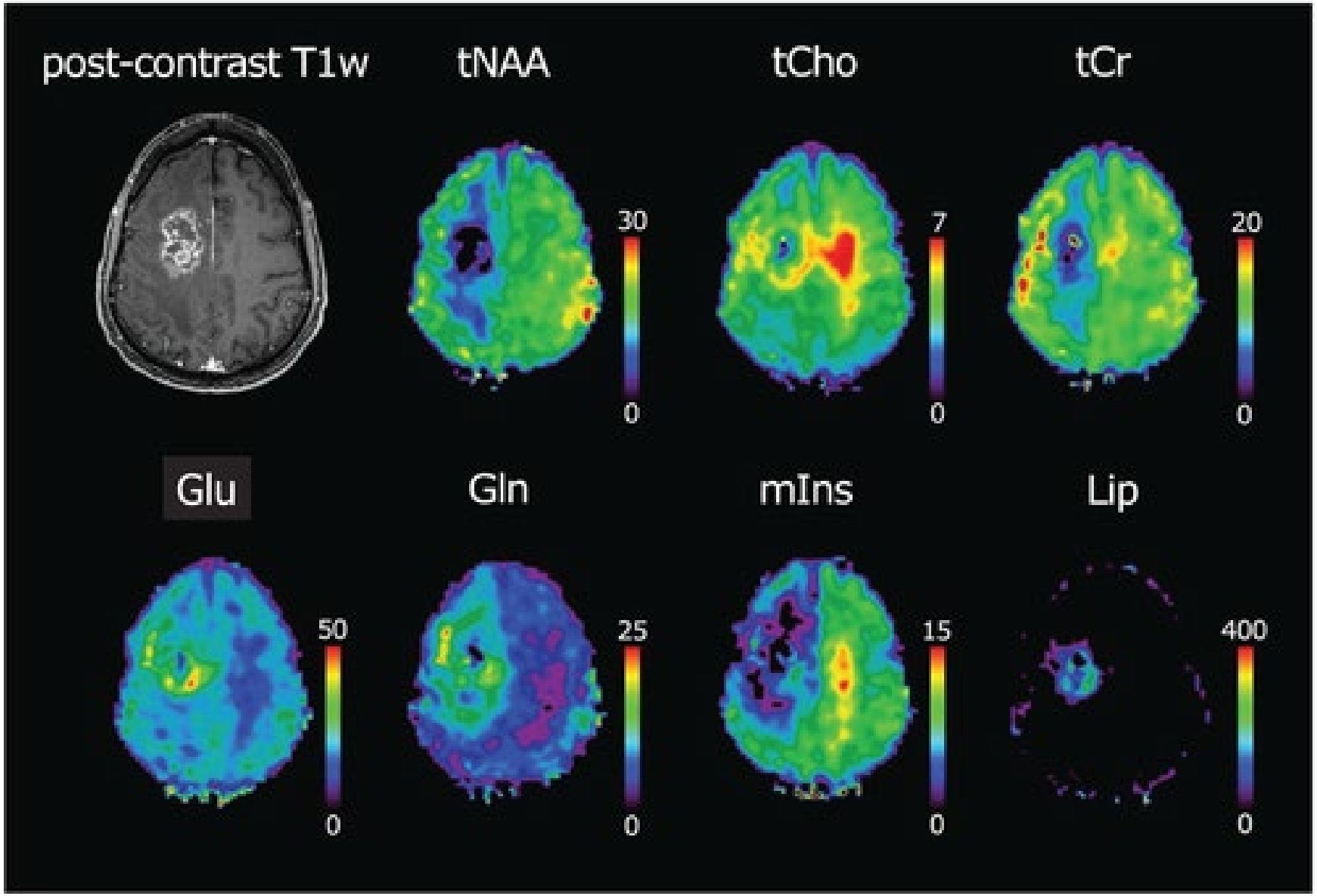
FID-MRSI

- Around 2009??
- Short TR (200-800ms) ----Low Excitation Flip Angle
- Ultra short TE (~ 1-1.3 ms) – no J evolution, not too much signal loss due to T2 relaxation, but 1st order phase in the spectra
- Short acquisitions – 13min (31x31 with TR=811ms) but can go even lower ---- increase number of phase encoding steps – better PSF
- in plane spatial resolutions of 1.7-10 mm for humans



https://www.epfl.ch/labs/mrs4brain/ressources/live-demos/

FID-MRSI: negligible J-coupling and T_2 related signal loss, better suitability for fast MRSI at UHF in preclinical settings



The single-slice FID-MRSI was acquired in 6 min with 6-fold accelerated phase-encoding, voxel size of 3.4 x 3.4 x 8 mm^3 and TR/AD of 600/1.3 ms.

Key clinical benefits of neuroimaging at 7 T - ScienceDirect

TEMPORAL RESOLUTION

MRSI

- $T_{measurement} = NA \times N_x \times N_y \times TR$
  - 1.5T, 16x16x16, NA=1, TR=2s →136min

Received: 26 November 2019 | Revised: 24 March 2020 | Accepted: 30 March 2020
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SPECIAL ISSUE REVIEW ARTICLE

NMR IN BIOMEDICINE WILEY

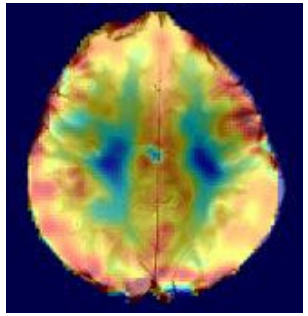
Accelerated MR spectroscopic imaging—a review of current and emerging techniques

Wolfgang Bogner[1] | Ricardo Otazo[2] | Anke Henning[3,4]

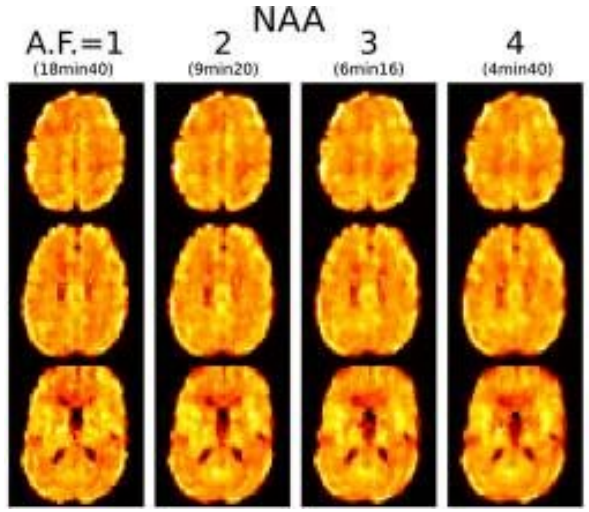
- short TR
- acquisition of multiple k-space points per TR (e.g. spatial-spectral encoding)
- k-space undersampling (e.g. PI, CS)
- data reconstruction using spectral or spatial prior knowledge

SVS

- $T_{measurement} = NA \times TR$
  - ~ 5min – human (cm)
  - ~10-15min – preclinical (mm, SE sequence)



Nassirpour S, et al, NeuroImage 2017



3.4x3.4x3.4mm^3

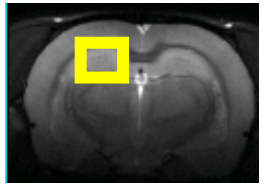
A Klauser, et al, 2024.

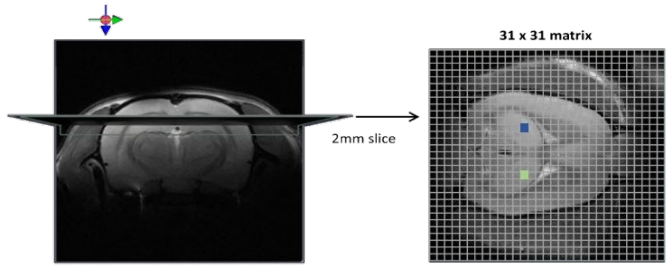
METABOLIC MAPPING via MRSI

Tan Toi Phan B Alves A Siviglia

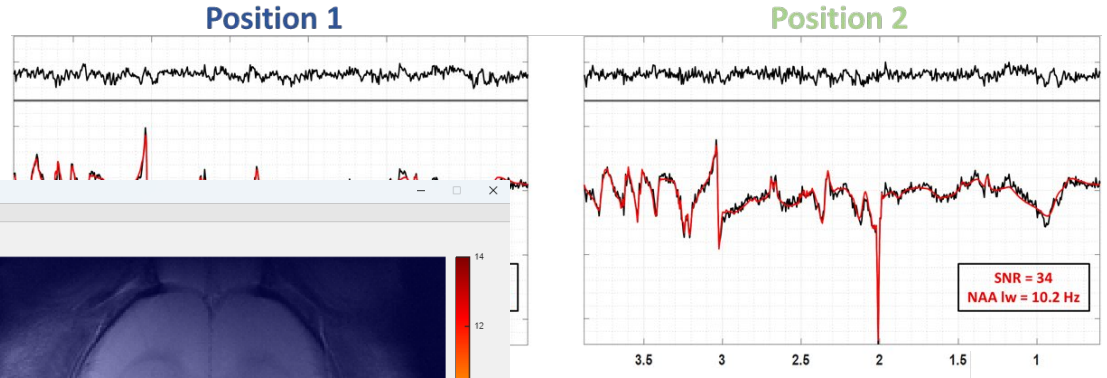
CIBM Center for Biomedical Imaging

Voxel 2x2.8x2 mm^3

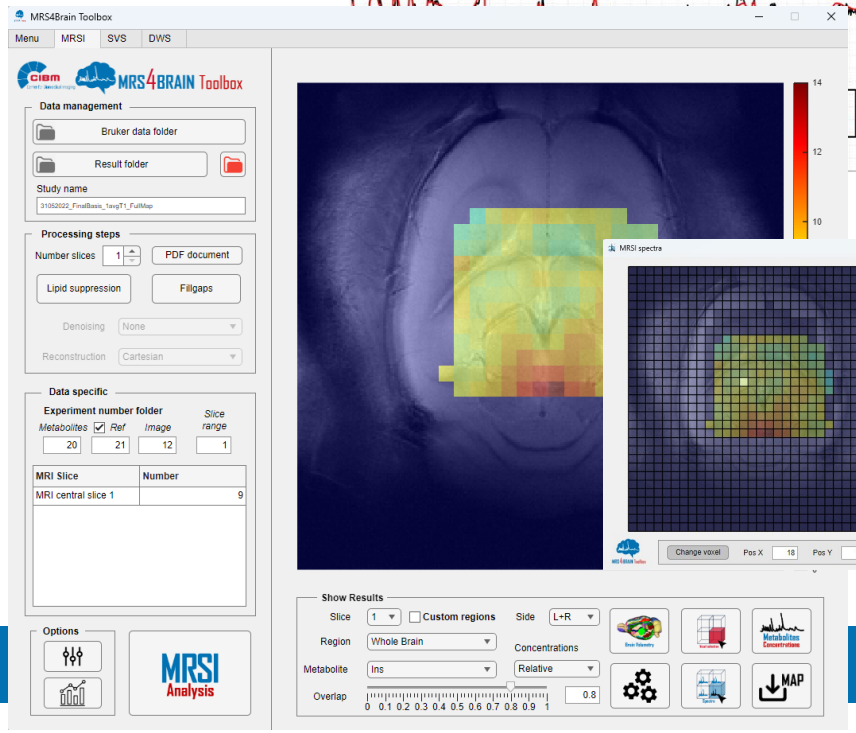


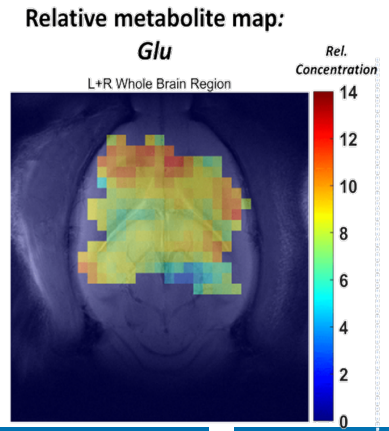


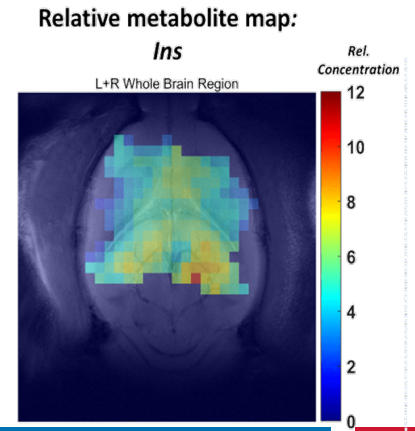
FID- MRSI
0.7x.0.7x2mm^3
13 min @14.1T

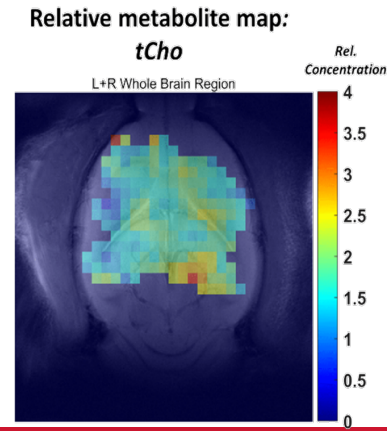


https://www.epfl.ch/labs/mrs4brain/ressources/mrs4brain-toolbox/









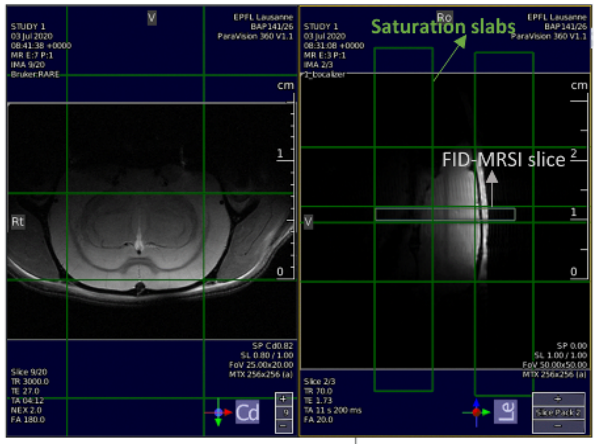
C I B M . C H

cristina.cudalbu@epfl.ch

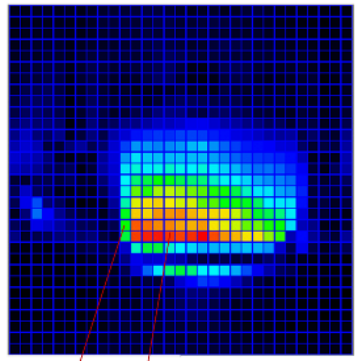
B Alves, et al, NMR Biomed, 2024; D Simicic et al, NMR Biomed 2025

Water map
NO FOV saturation

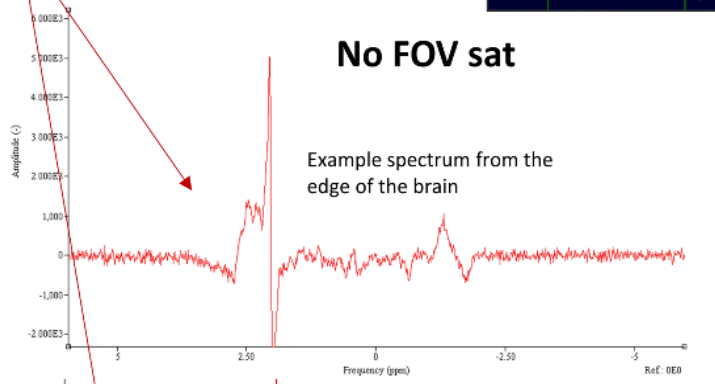
Addition of six 10mm thick saturation slabs



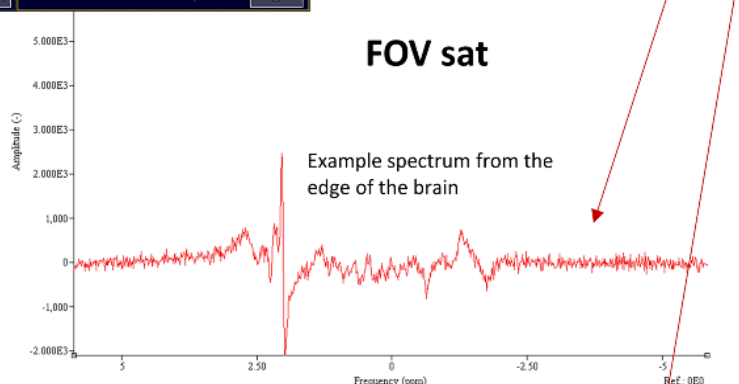
Water map
With FOV saturation



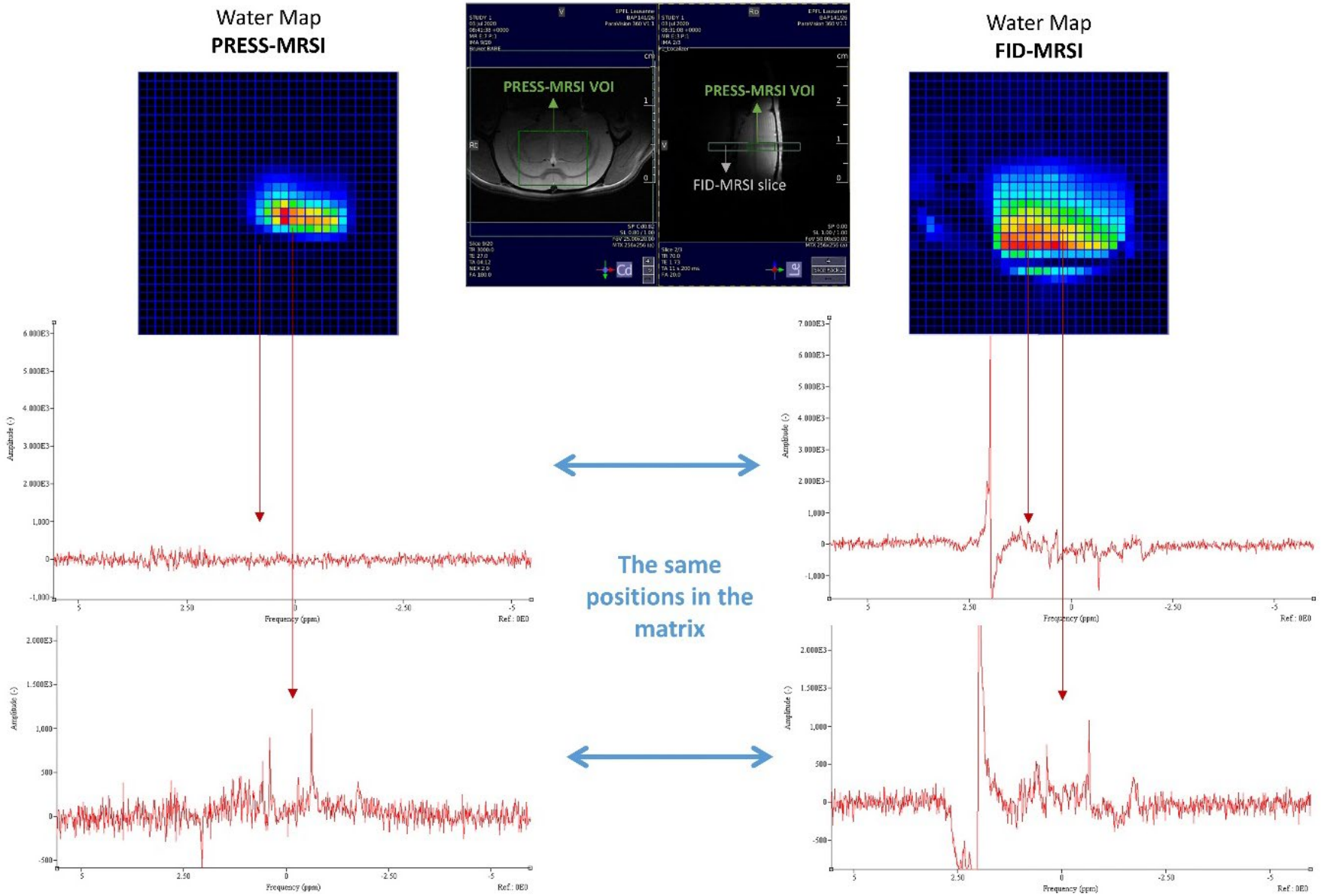
No FOV sat



FOV sat



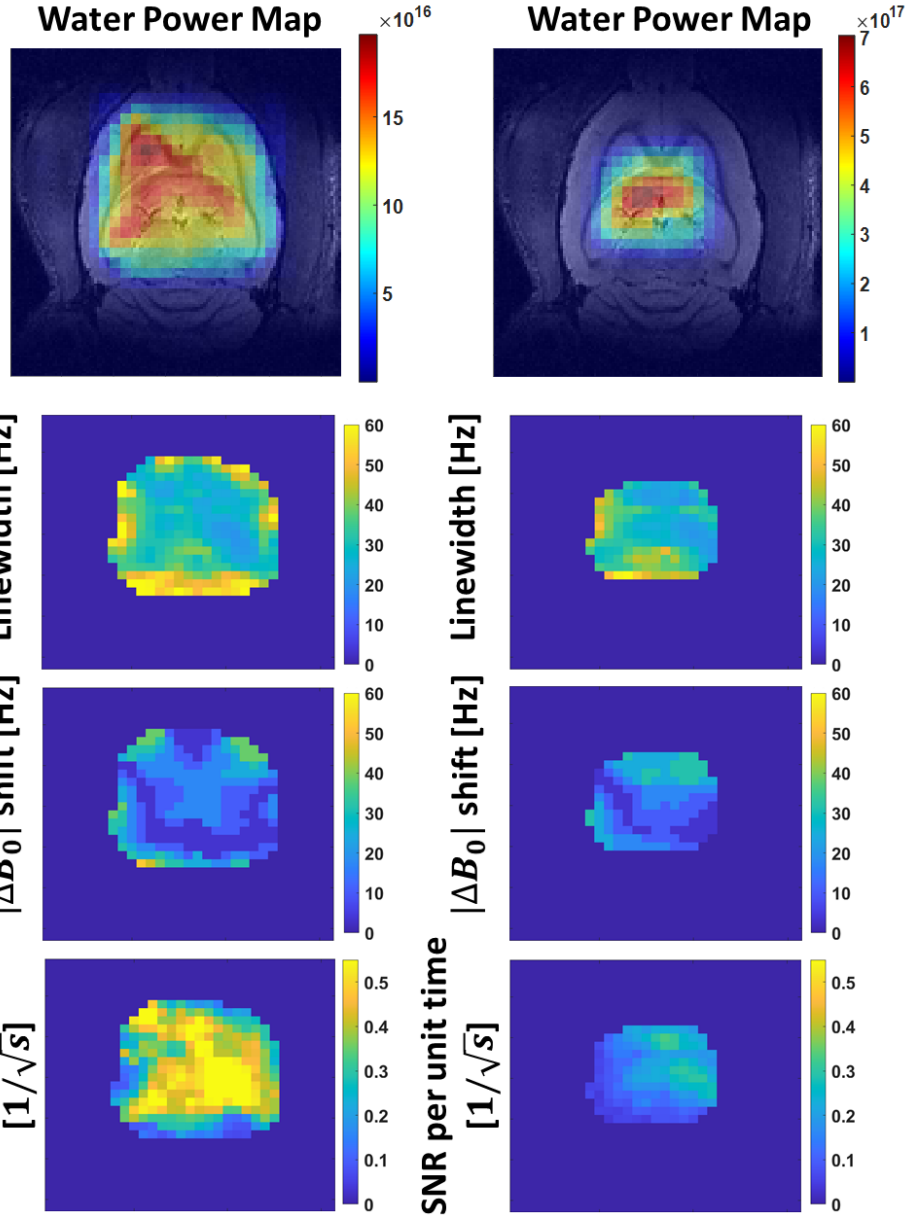
D Simicic
https://infoscience.epfl.ch/record/296066

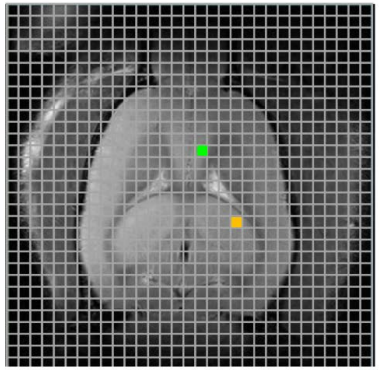


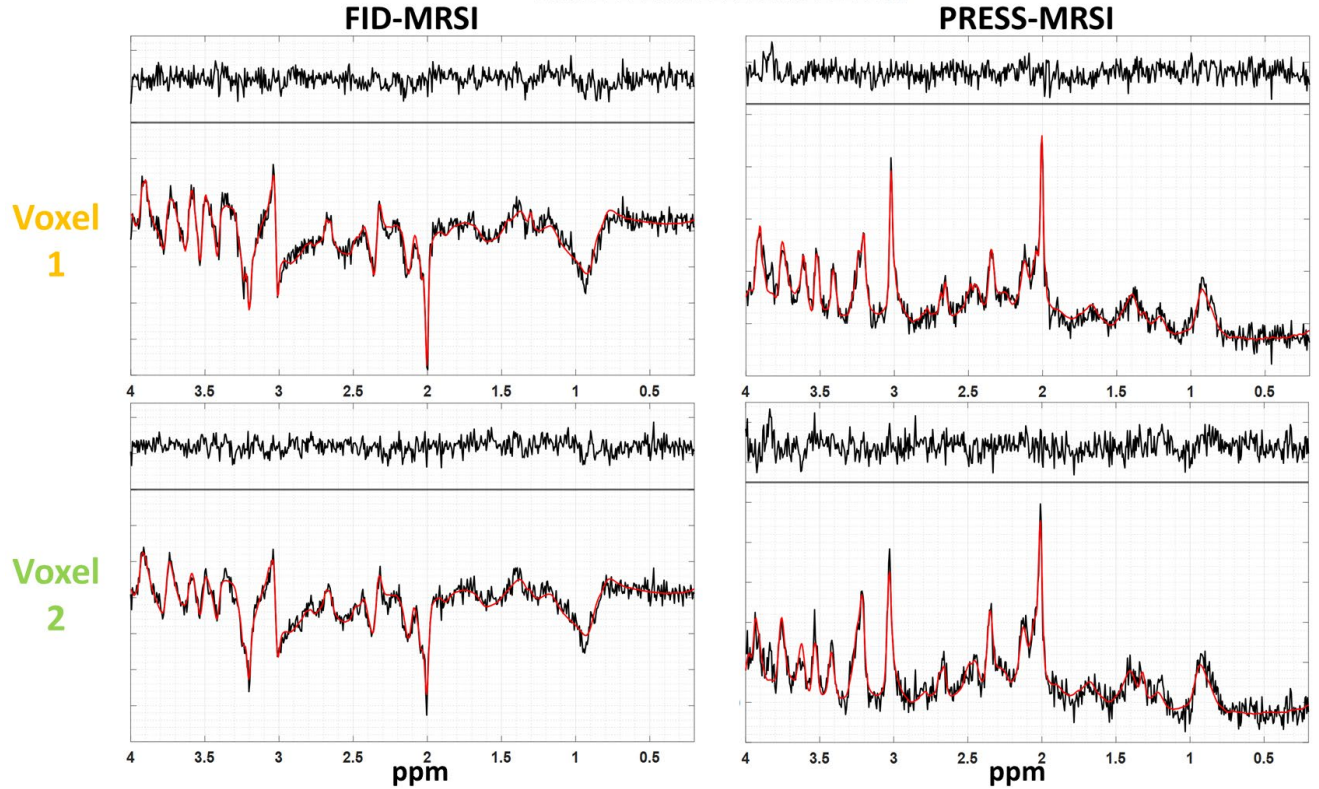
D Simicic
https://infoscience.epfl.ch/record/296066

FID-MRSI

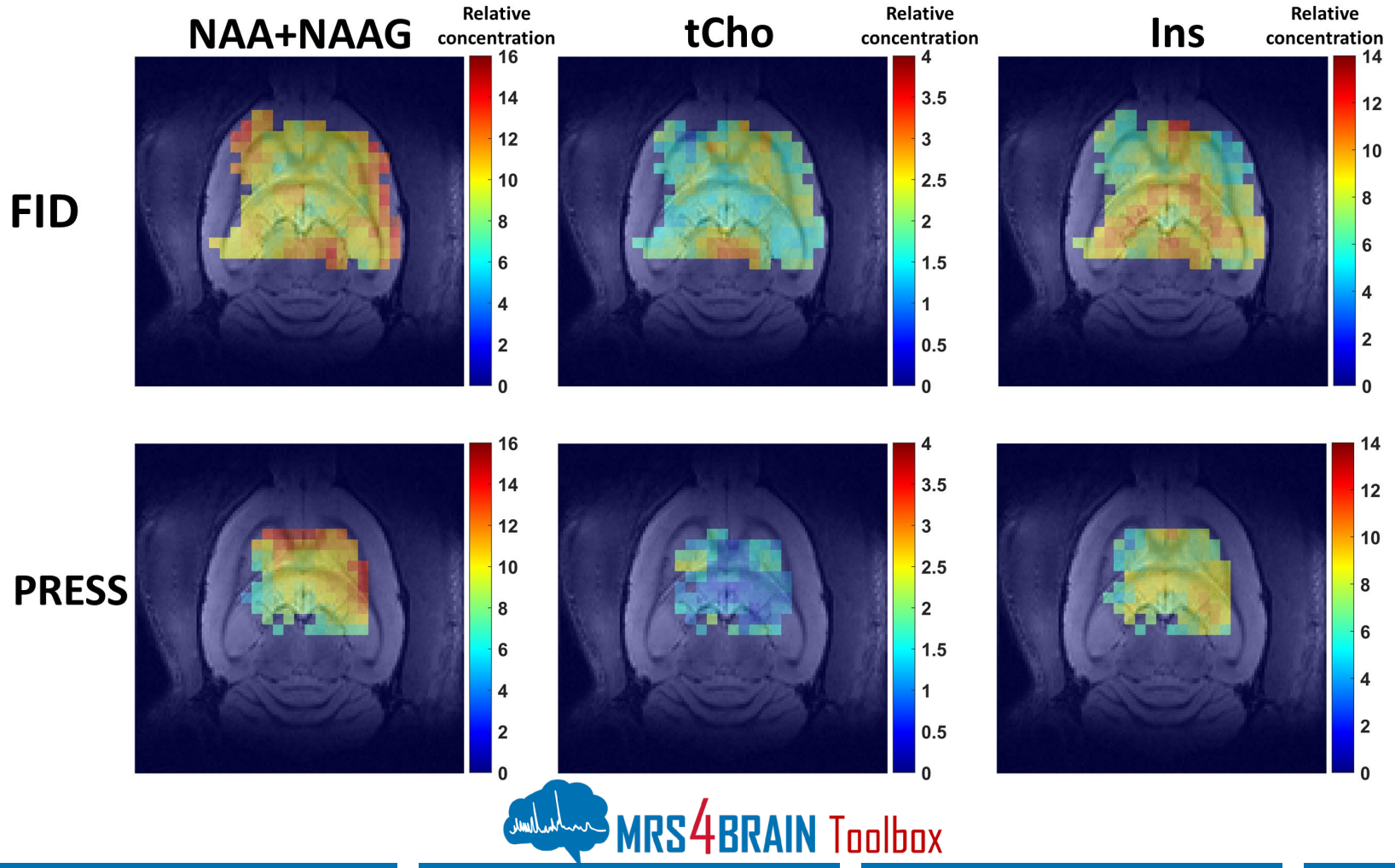
PRESS-MRSI





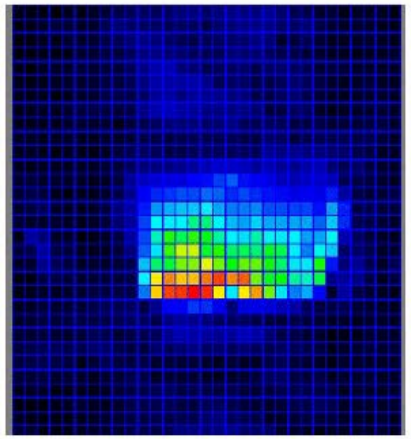


RESULTS : METABOLITE MAPS



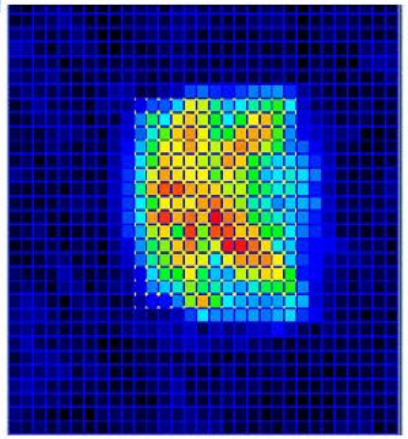
- FID-MRSI provided an increased brain coverage even after the application of quality control criteria (min. SNR, max. FWHM, max. CRLBs limits)
- Minor differences in metabolite concentrations were noted between the two sequences (underestimation for PRESS-MRSI) which might be related to the lack of metabolite T_1 and T_2 corrections, etc, something requiring further investigations.

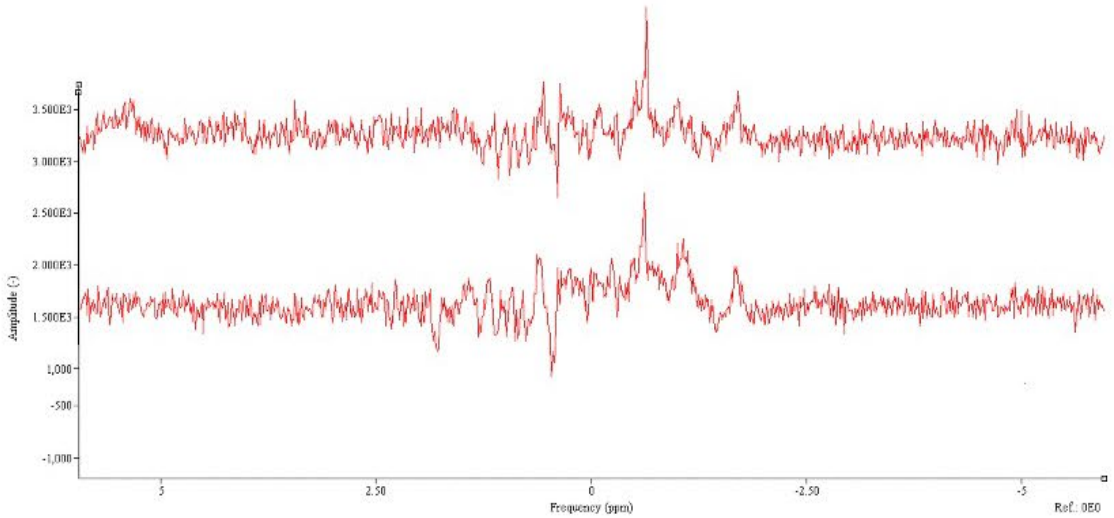
Axial slice – Water map



Surface coil

Coronal slice – Water map





→ Coronal slice orientation

→ Axial slice orientation

SUMMARY & ACKNOWLEDGMENTS

MRS & MRSI is incredibly rich & versatile ☺

THANK YOU – D Simicic and B Alves; B Lanz and G Briand

Thank you for listening! Questions?

For any question yon might have later on, please write me an email:

cristina.cudalbu@epfl.ch

THANK YOU FOR YOUR ATTENTION

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Fondation Leenaards