Center for Biomedical Imaging

QUANTIFICATION OF MR SPECTRA

Cristina Cudalbu

CIBM PCI EPFL

Master Course 2025-2026

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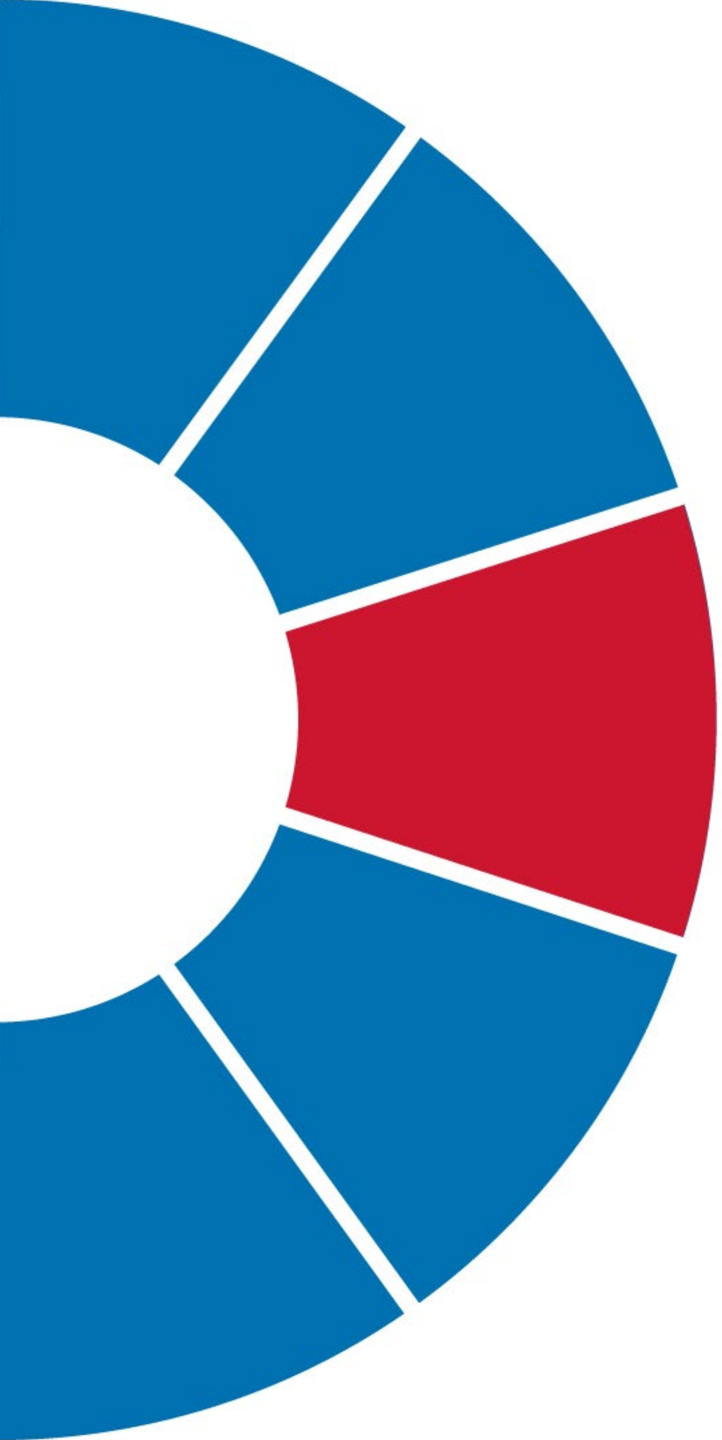
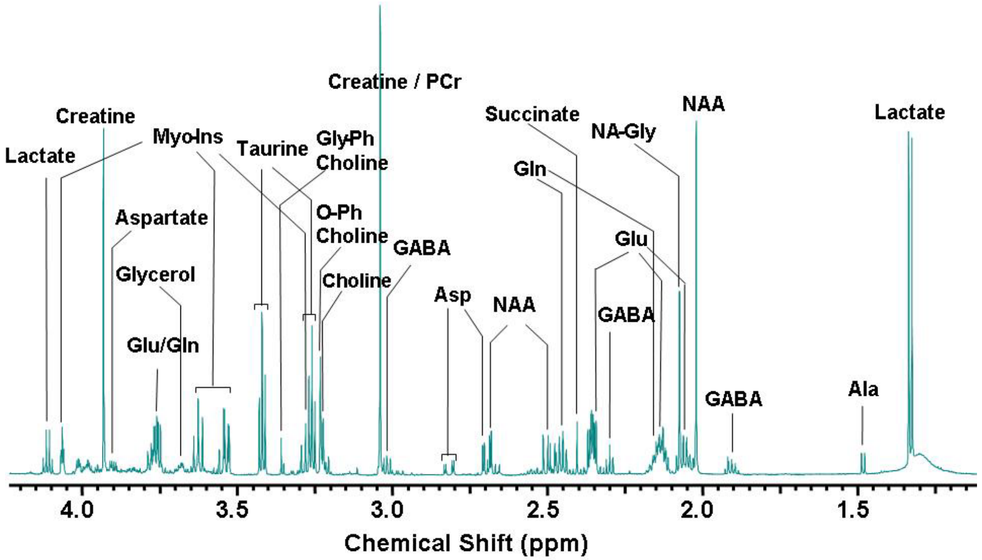


QUANTIFICATION

MAGNETIC RESONANCE SPECTROSCOPY

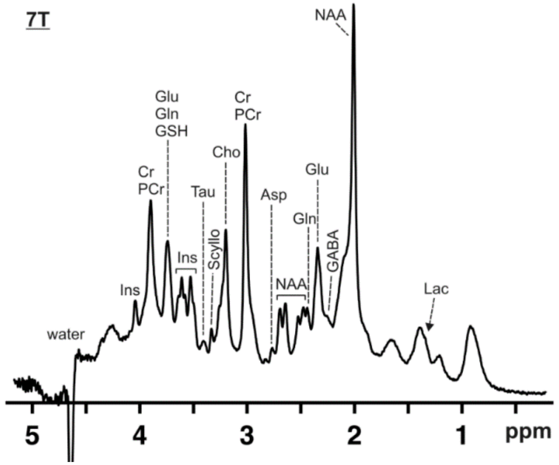
- NMR Spectroscopy

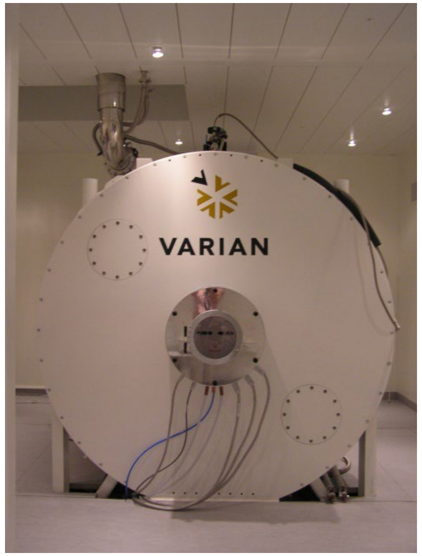


MAGNETIC RESONANCE SPECTROSCOPY

In Vivo MR spectroscopy (MRS)

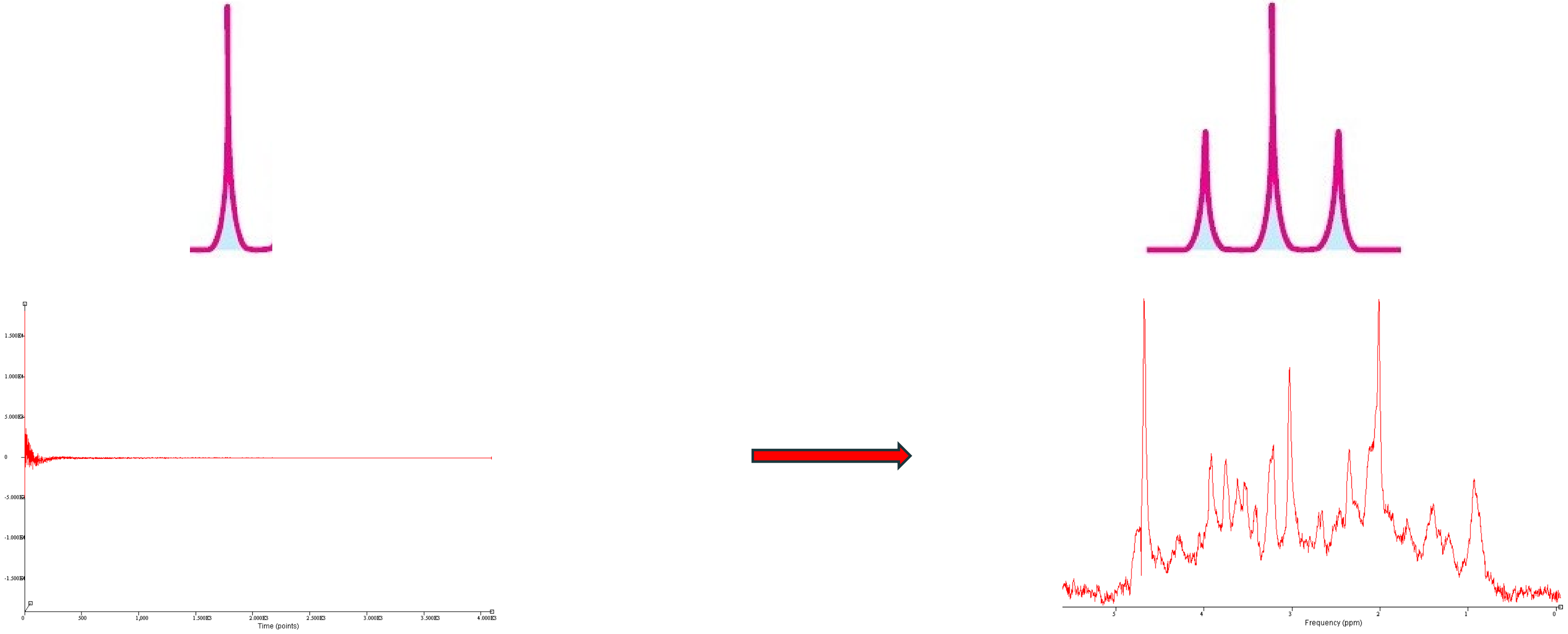
- Measurement of different metabolites- metabolism
- Different organs
- Different nuclei: 1H, 13C, 31P, 15N, ..
- Different magnetic fields
- Different acquisition parameters





QUANTIFICATION

- MRS – principal goal – quantification of changes in concentration of known metabolites



- Frequencies
- Amplitudes
- Damping factor
- Phase
- Beginning time

- Frequencies
- Surface
- Linewidths
- Zero order phase.
- first order phase

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WHY IN VIVO 1H MR SPECTROSCOPY ?

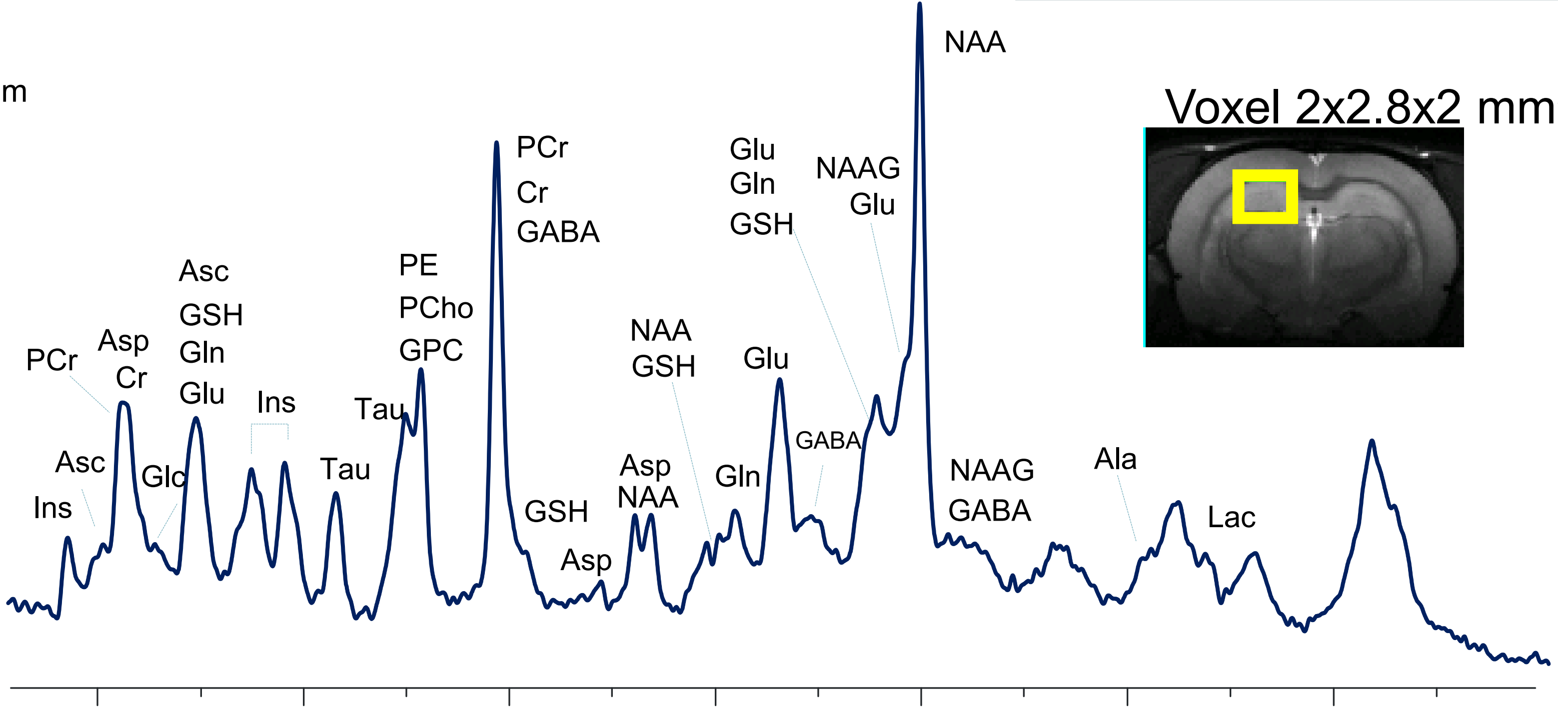
Neurochemical Profile at 9.4T

>18 Markers of :

Myelination/Cell proliferation
Energy metabolism
Osmoregulation
Neurotransmitter metabolism
Antioxidants

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

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



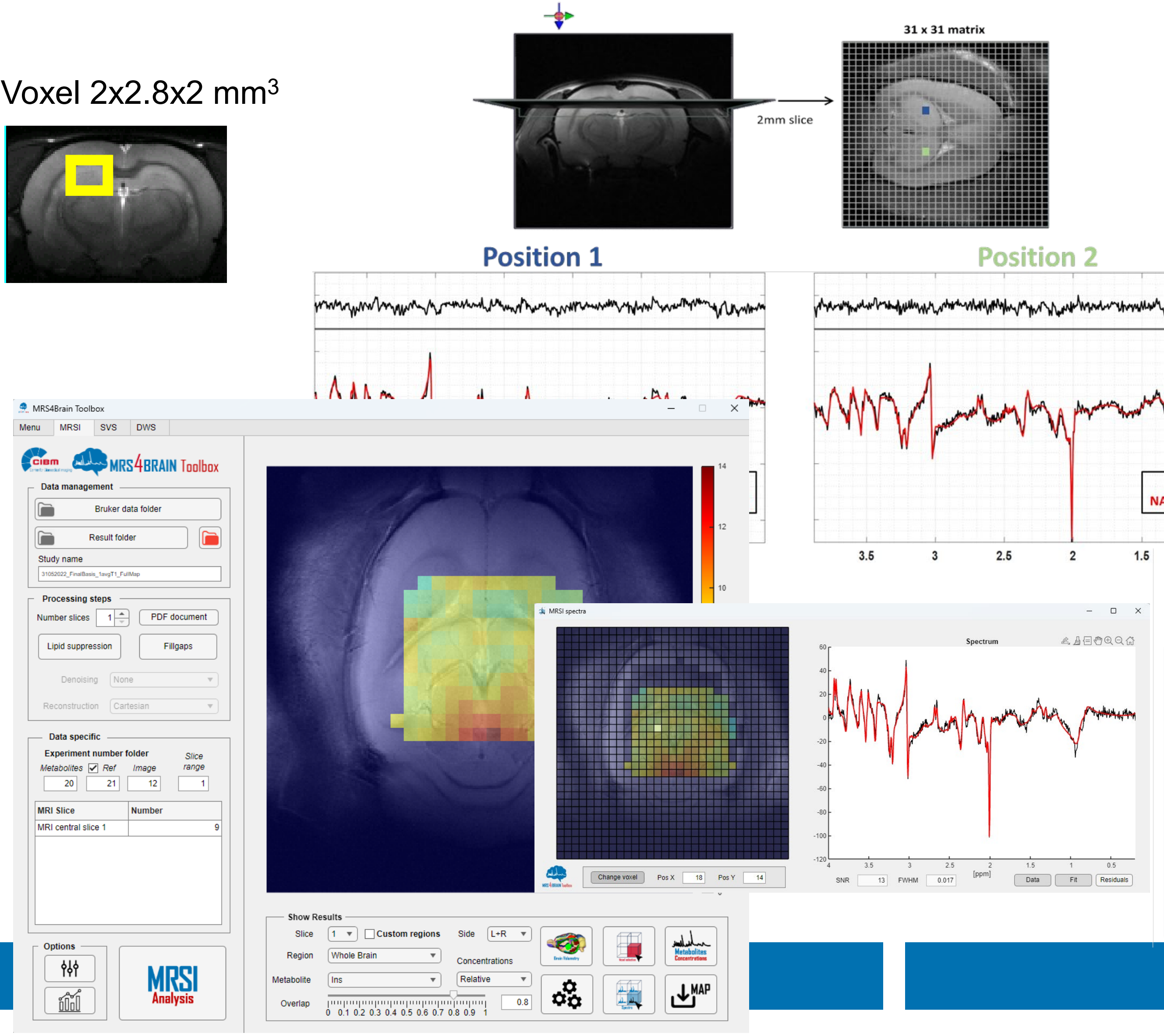
Voxel 2x2.8x2 mm^3

- 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; JMN Duarte 2012

METABOLIC MAPPING via MRSI


B Alves


Voxel 2x2.8x2 mm^3

MRS4Brain Toolbox

Data management

Bruker data folder

Result folder

Study name: 31052022_FinalBasis_1avgT1_FullMap

Processing steps

Number slices: 1

PDF document

Lipid suppression

Fillgaps

Denoising: None

Reconstruction: Cartesian

Data specific

Experiment number folder

Metabolites: 20 | ☑ Ref: 21 | Image: 12 | Slice range: 1

MRI Slice	Number
MRI central slice 1	9

Options

MRSI Analysis

Show Results

Slice: 1 | ☐ Custom regions | Side: L+R

Region: Whole Brain

Concentrations: Relative

Metabolite: Ins

Overlap: 0.8

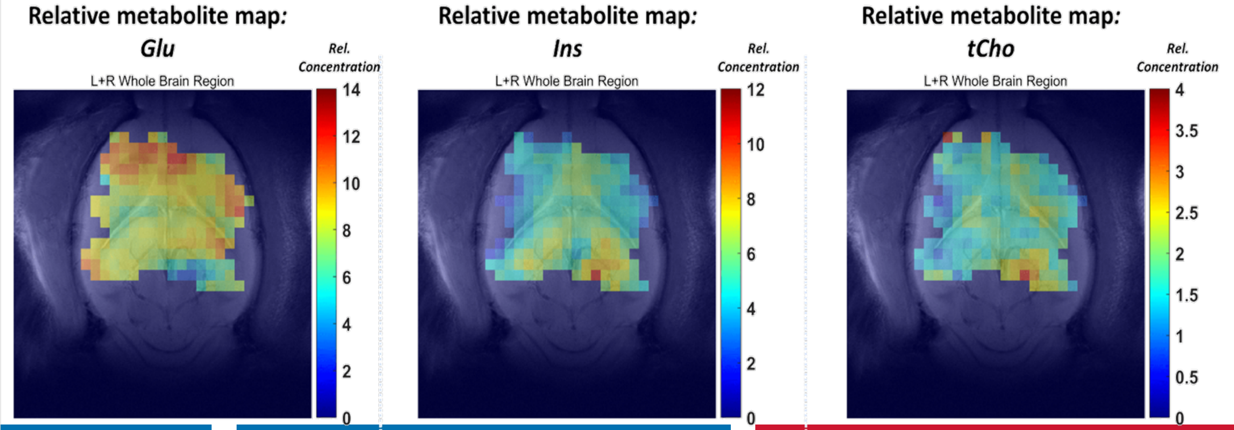
MRSI spectra

Change voxel | Pos X: 18 | Pos Y: 14

SNR: 13 | FWHM: 0.017

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

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


Relative metabolite map: *Glu*

Relative metabolite map: *Ins*

Relative metabolite map: *tCho*

C I B M . C H

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

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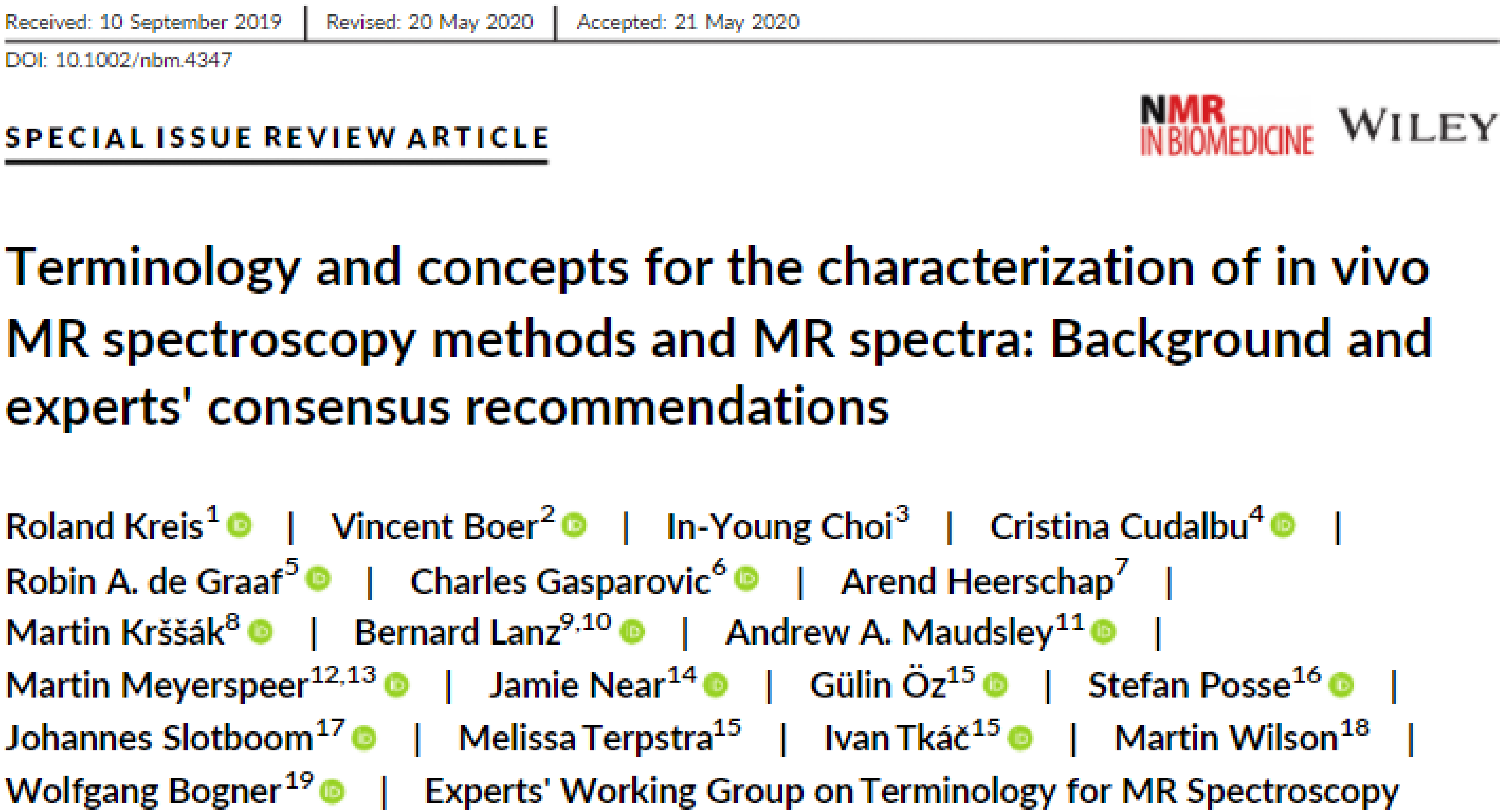

Received: 10 September 2019 | Revised: 20 May 2020 | Accepted: 21 May 2020
DOI: 10.1002/nbm.4347

SPECIAL ISSUE REVIEW ARTICLE

NMR IN BIOMEDICINE WILEY

Terminology and concepts for the characterization of in vivo MR spectroscopy methods and MR spectra: Background and experts' consensus recommendations

Roland Kreis[1] | Vincent Boer[2] | In-Young Choi[3] | Cristina Cudalbu[4] | Robin A. de Graaf[5] | Charles Gasparovic[6] | Arend Heerschap[7] | Martin Krššák[8] | Bernard Lanz[9,10] | Andrew A. Maudsley[11] | Martin Meyerspeer[12,13] | Jamie Near[14] | Gülin Öz[15] | Stefan Posse[16] | Johannes Slotboom[17] | Melissa Terpstra[15] | Ivan Tkáč[15] | Martin Wilson[18] | Wolfgang Bogner[19] | Experts' Working Group on Terminology for MR Spectroscopy

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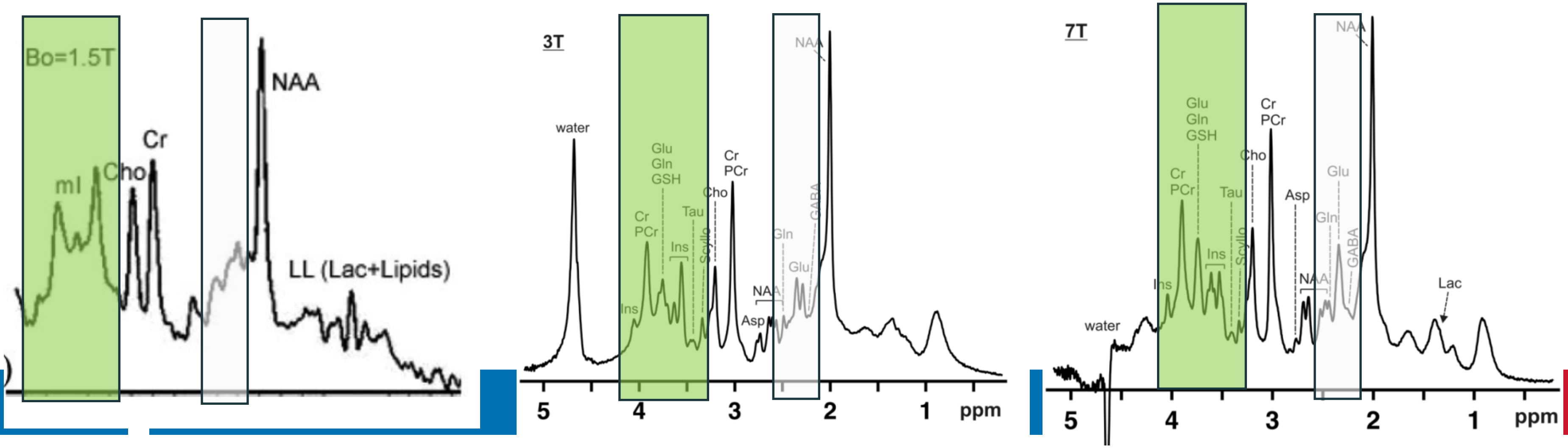
WHY HIGH MAGNETIC FIELD ?

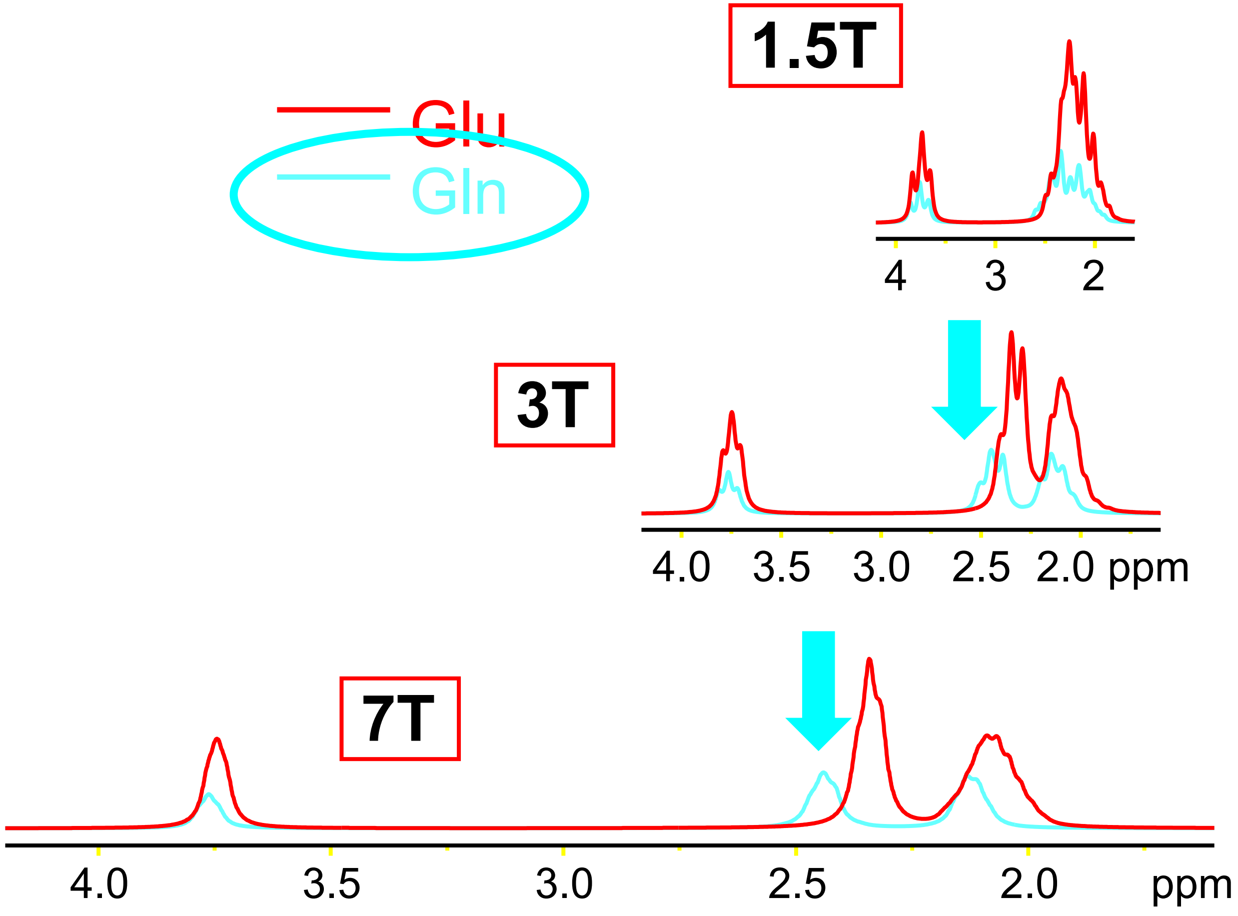
- More signal
- More spectral resolution
- And more sensitivity



Ralf Mekle et al, (2009) MRM 50: 1279

WHY HIGH B_0?

- Enormous progress
  - ↑ SNR 🙂
  - ↑ chemical shift dispersion – ↑ resolution 🙂
  - decreased strong J-coupling effects
  - Improve quantification precision and accuracy
  - ↓ T_2^* - ↑ spectral lw in Hz ☹

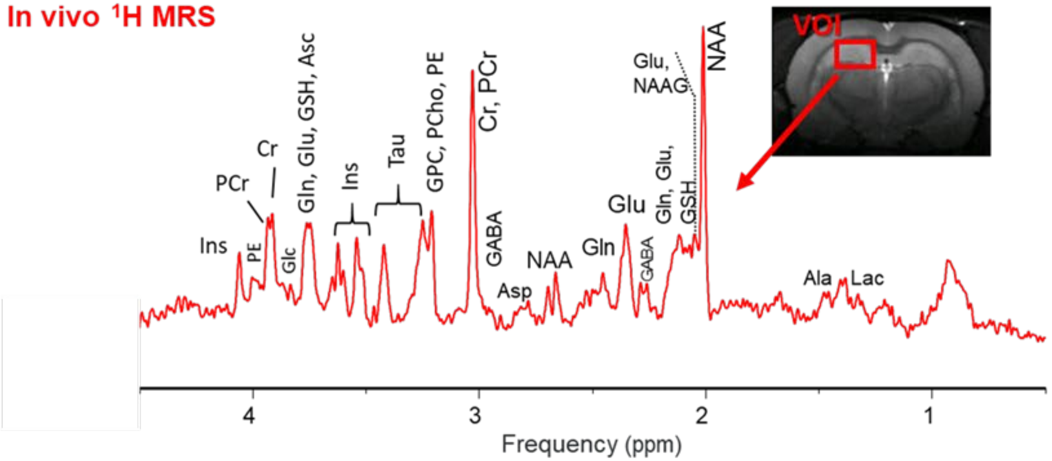


Courtesy of I Tkac

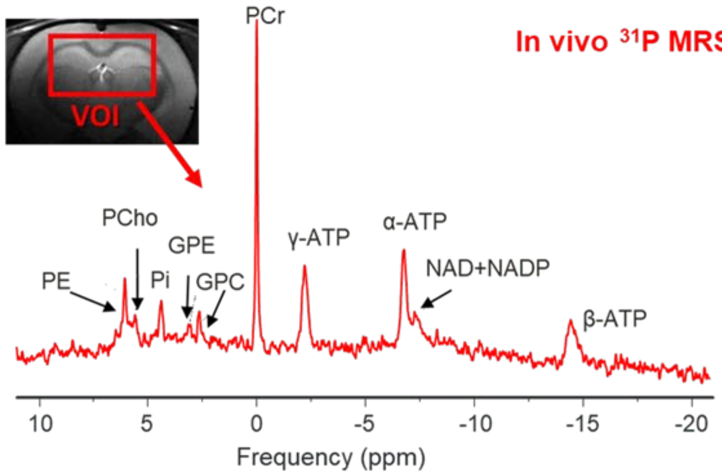
Oz G, et al., Clinical proton MR spectroscopy in central nervous system disorders. Radiology. 2014
Wilson M, et al., Methodological consensus on clinical proton MRS of the brain: Review and recommendations. Magn Reson Med. 2019

X NUCLEI MRS – 9.4T

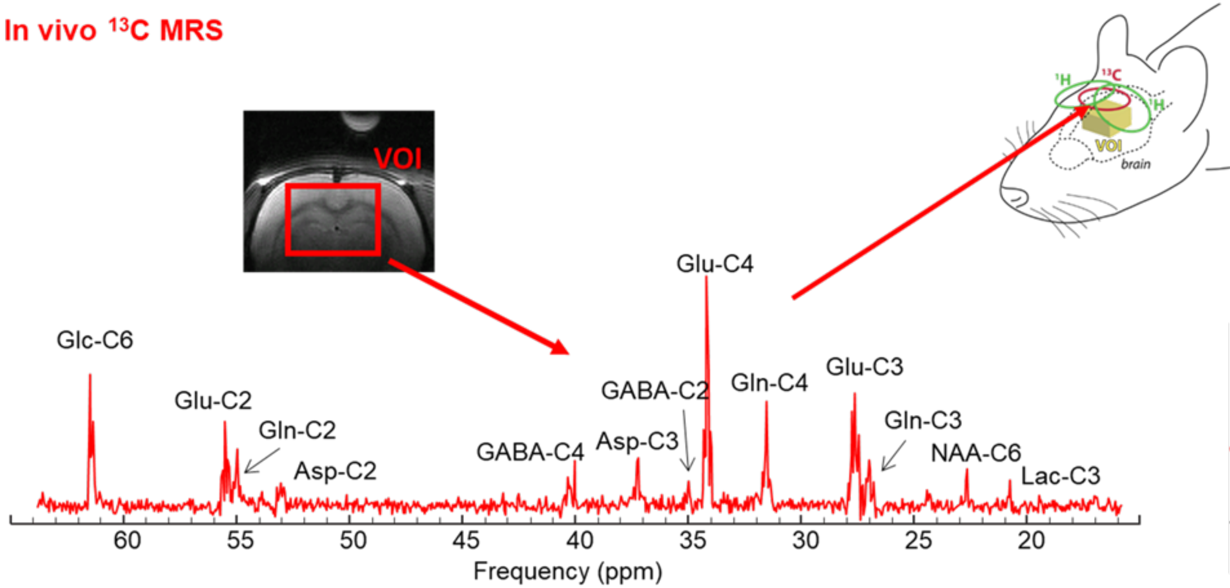
In vivo ^{1}H MRS



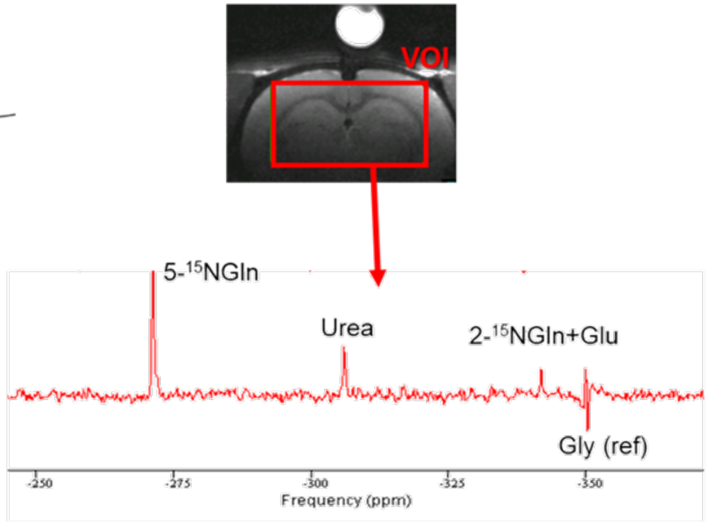
In vivo ^{31}P MRS



In vivo ^{13}C MRS



In vivo ^{15}N MRS



Lanz et al, 2017, 2020; Cudalbu et al 2021;

CLINICAL VS PRECLINICAL DATA

	Preclinical	**Clinical**
Subjects	Animal (rat/mouse) - anesthesia	Human – no anesthesia
Motion	☺	? ☹
Time for scanning	☺ Shim, WS, OVS, …	☹
@scanner	MRS experts	Not necessary MRS experts
Amount of data	+++	+++++++

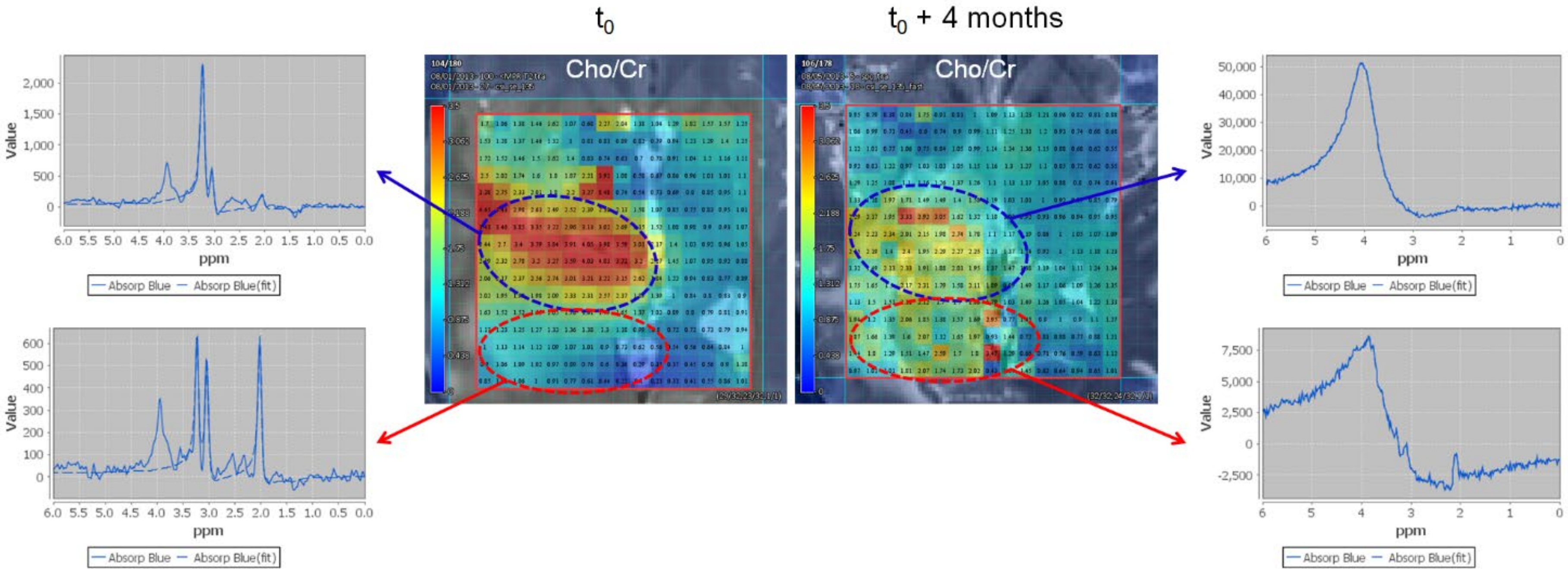
(Lots) Data with sometimes artifacts

- Need to be identified
- Corrected or data discarded
- Preprocessed
- Quantified

Clinicians

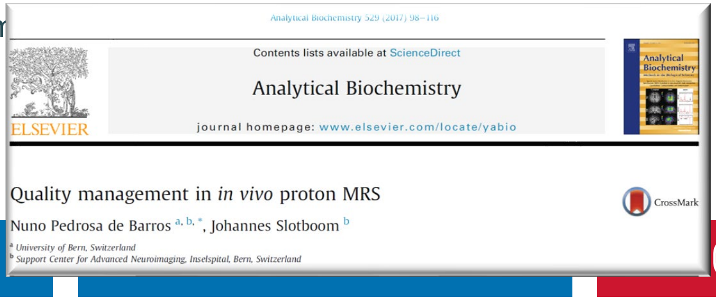
☹ Draw incorrect decisions
☹ Standard quantification software – NO quality check
☹ CRLB …..

CLINICAL VS PRECLINICAL DATA



Example showing two Cho/Cr maps of a Glioma patient acquired 4 months apart.
Siemens Aera 1.5 T, 2D-PRESS, 12x12 interpolated to 32x32, TE/TR 135/1500m

From N Barros et al, Analytical Biochemistry, 2017



Analytical Biochemistry 529 (2017) 98–116

Contents lists available at ScienceDirect

Analytical Biochemistry

journal homepage: www.elsevier.com/locate/yabio

ELSEVIER

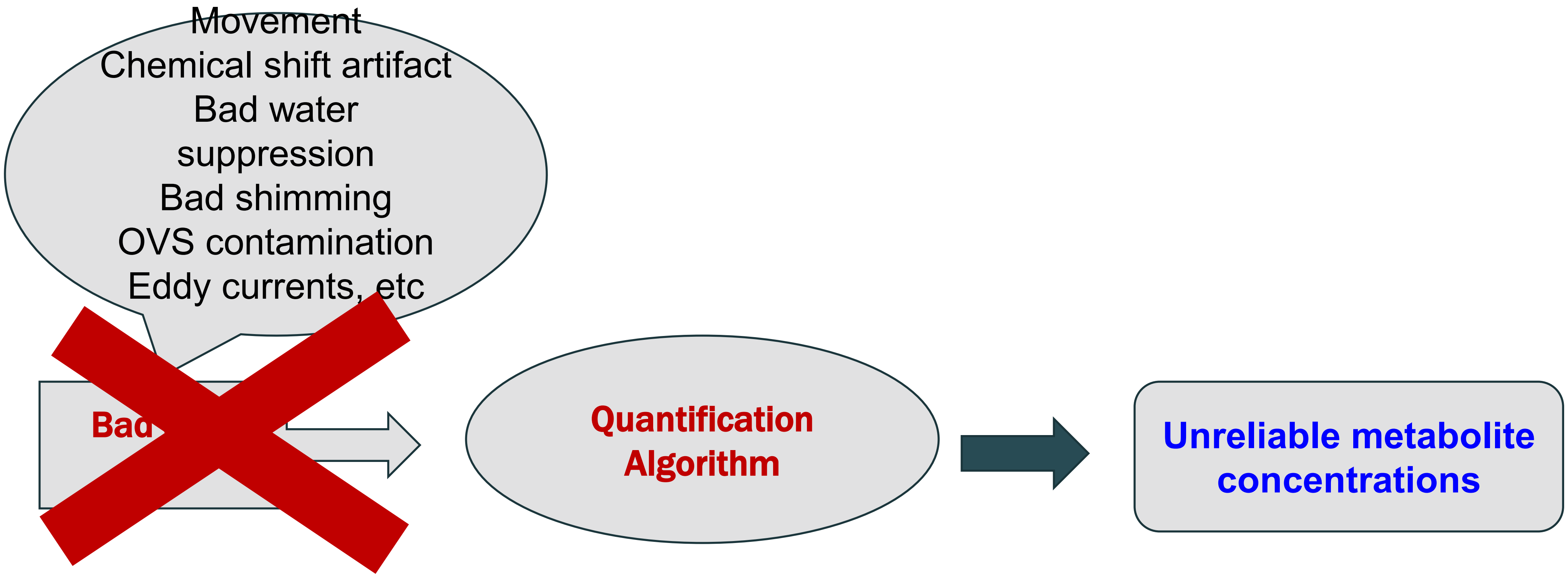
Quality management in *in vivo* proton MRS

Nuno Pedrosa de Barros [a, b, *], Johannes Slotboom [b]

[a] University of Bern, Switzerland
[b] Support Center for Advanced Neuroimaging, Inselspital, Bern, Switzerland

CrossMark

ARTIFACTS IN 1H MRS



Movement
Chemical shift artifact
Bad water suppression
Bad shimming
OVS contamination
Eddy currents, etc

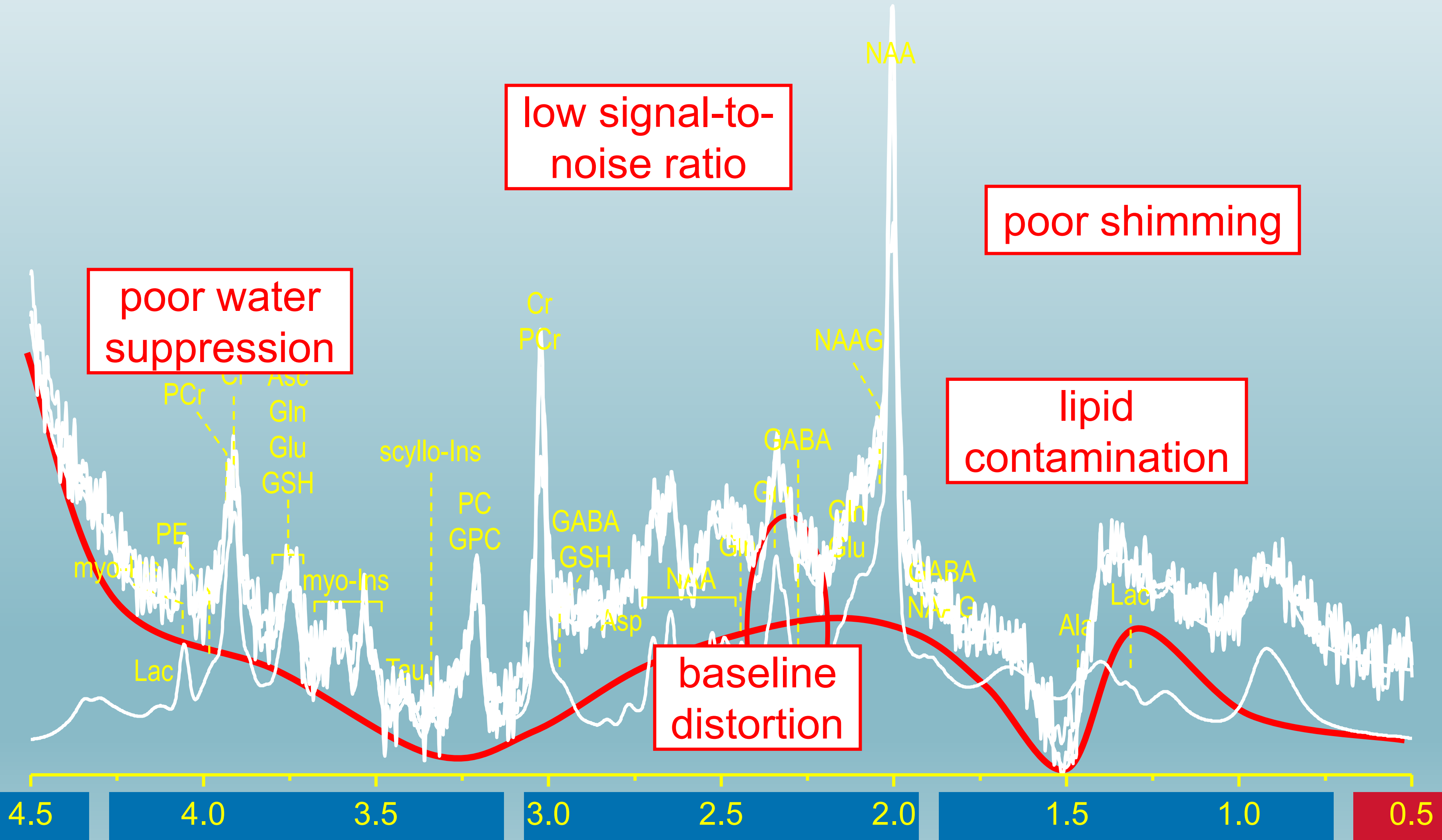
~~Bad~~

Quantification Algorithm

Unreliable metabolite concentrations

ISMRM 2010, Potentials and Challenges at High Field MRS
R Kreis, NMR Biomed 2004, 17:361
Tkáč I, et al, Appl Magn Reson. 2005 29:139.

DISTORTIONS OF 1H NMR SPECTRUM OF THE HUMAN BRAIN AT 7T



low signal-to-noise ratio

poor shimming

poor water suppression

lipid contamination

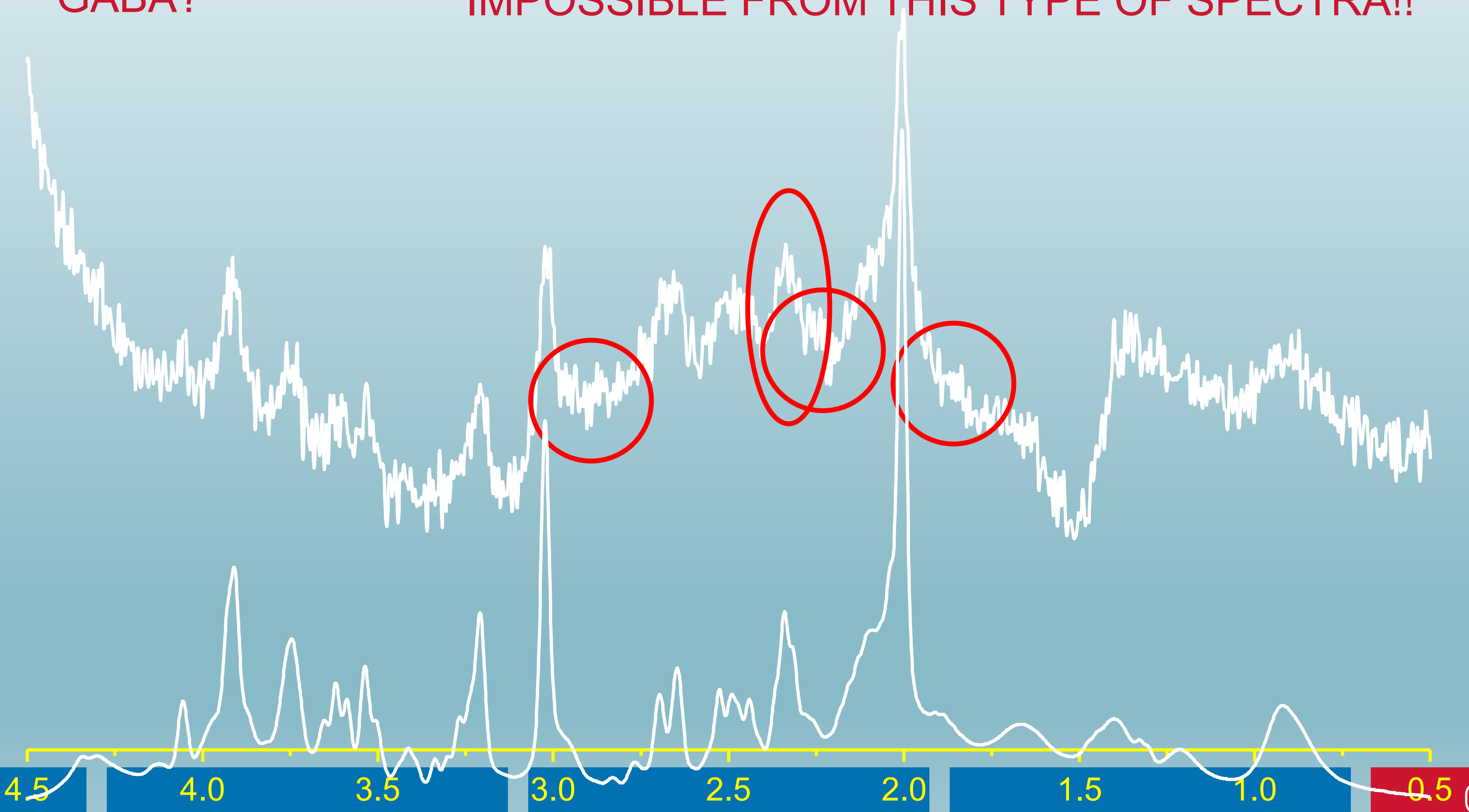
baseline distortion

TKAC, University of Minnesota

IS RELIABLE QUANTIFICATION OF GABA AND GLU POSSIBLE?

GLUTAMATE? DIFFICULT, LIMITED PRECISION

GABA? IMPOSSIBLE FROM THIS TYPE OF SPECTRA!!



TKAC, University of Minnesota

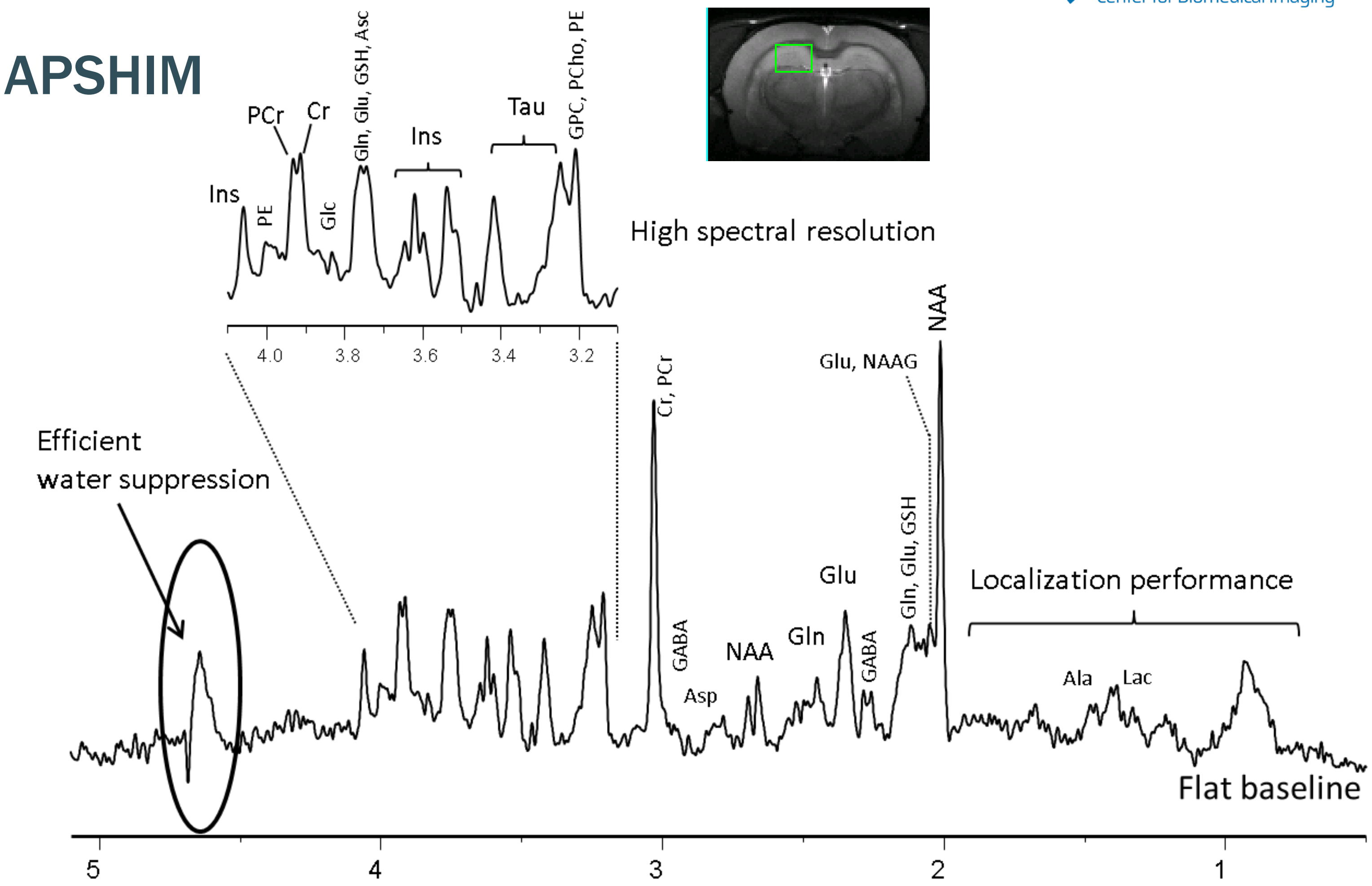
GOOD QUALITY DATA AT SHORT TE

- **Shimming: e.g. FASTMAP, MAPSHIM**
- **Pulse sequence at short TE**

Provide undistorted multiplets and no T_2 weighting

Increased no of metabolites

Improved quantification

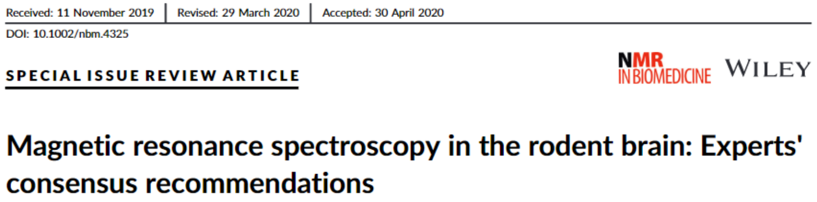


SPECIAL, TE=2.8ms, 10 min

R Kreis 2004; C Cudalbu 2013 (450) Quality of MRS/MRSI – YouTube - I Tkac

ACQUISITION SEQUENCES

- Reduced CSDE
- Good localization :
  - double : OVS+Seq or LASER
- Strong crusher gradients
- Good WS



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DOI: 10.1002/nbm.4325

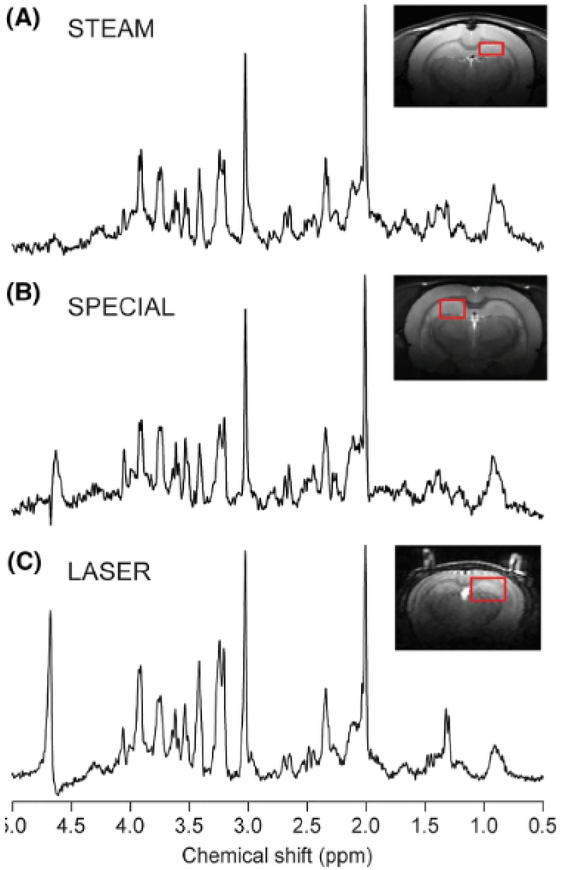
SPECIAL ISSUE REVIEW ARTICLE

NMR IN BIOMEDICINE WILEY

Magnetic resonance spectroscopy in the rodent brain: Experts' consensus recommendations

LANZ ET AL. NMR IN BIOMEDICINE WILEY 9 of 20

FIGURE 3 Example ^{1}H MR spectra obtained in rodent brains at 9.4 T with STEAM (A), SPECIAL (B) and LASER (C) sequences. A, STEAM spectrum: rat brain, 2.3 × 1.3 × 2.5 mm^3 voxel placed in the hippocampus, TR = 5 s, TE = 2 ms, TM = 20 ms, number of averages = 448. Spectrum is shown with Gaussian factor = 0.15. B, SPECIAL spectrum: rat brain, 2 × 2.8 × 2 mm^3 voxel placed in the hippocampus, TR = 4, TE = 2.8 ms, number of averages = 160. C, LASER spectrum: mouse brain, 1.7 × 2.25 × 2.25 mm^3 voxel placed in hippocampus, TR = 4 s, TE = 27 ms, number of averages = 384. The STEAM spectrum was provided by Ivan Tkáč



Received: 23 March 2020 | Accepted: 23 November 2020
DOI: 10.1002/nbm.4459

SPECIAL ISSUE REVIEW ARTICLE

NMR IN BIOMEDICINE WILEY

Water and lipid suppression techniques for advanced ^{1}H MRS and MRSI of the human brain: Experts' consensus recommendations

Ivan Tkáč[1] | Dinesh Deelchand[1] | Wolfgang Dreher[2] | Hoby Hetherington[3] | Roland Kreis[4] | Chathura Kumaragamage[5] | Michal Považan[6] | Daniel M. Spielman[7] | Bernhard Strasser[8] | Robin A. de Graaf[5]

Received: 15 March 2019 | Revised: 29 October 2019 | Accepted: 7 November 2019
DOI: 10.1002/nbm.4236

SPECIAL ISSUE REVIEW ARTICLE

WILEY NMR IN BIOMEDICINE

Advanced single voxel ^{1}H magnetic resonance spectroscopy techniques in humans: Experts' consensus recommendations

Gülin Öz[1] | Dinesh K. Deelchand[1] | Jannie P. Wijnen[2] | Vladimír Mlynárik[3] | Lijing Xin[4] | Ralf Mekle[5] | Ralph Noeske[6] | Tom W.J. Scheenen[7,8] | Ivan Tkáč[1] | the Experts' Working Group on Advanced Single Voxel ^{1}H MRS

RF COILS

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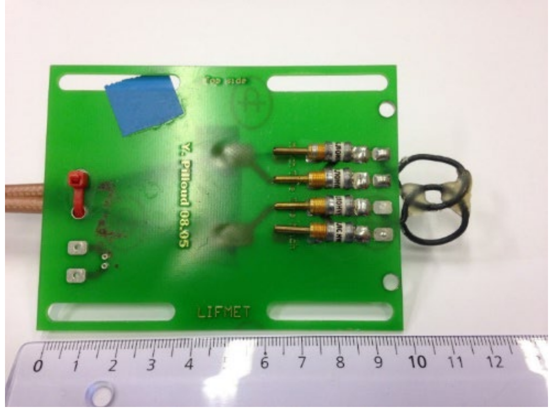

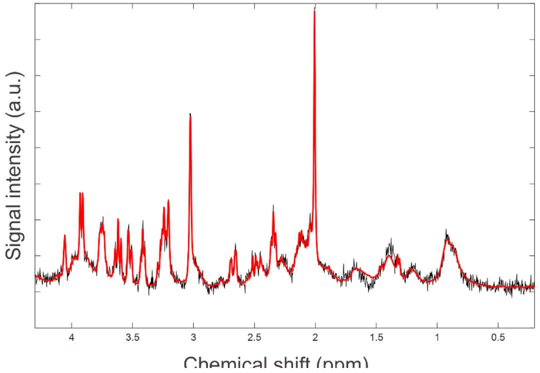

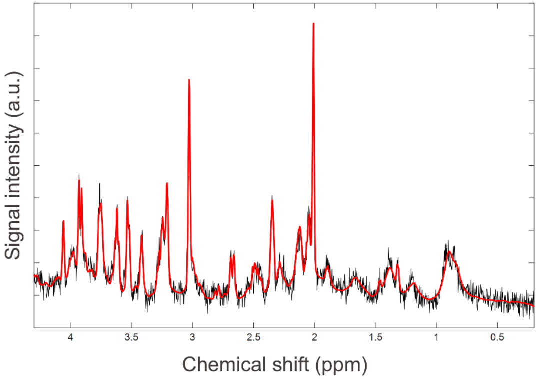

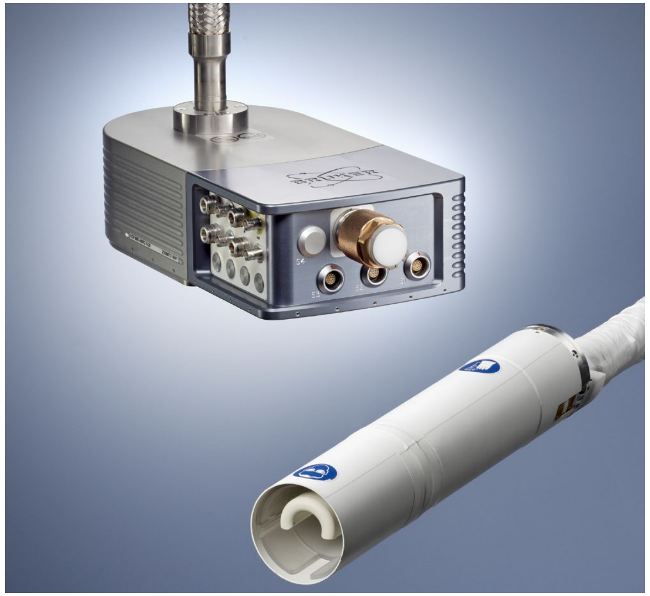

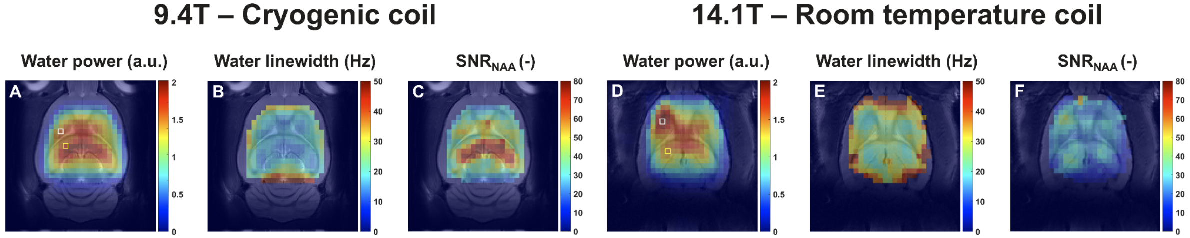

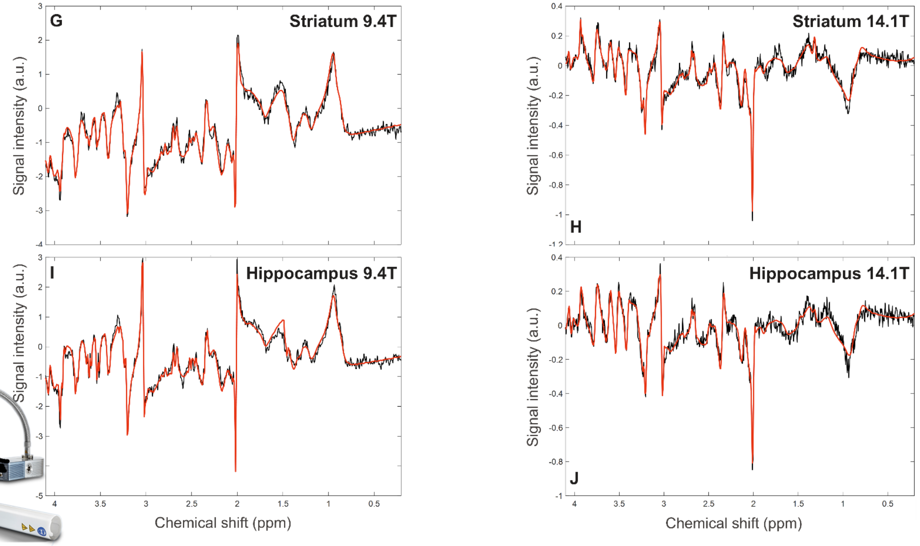

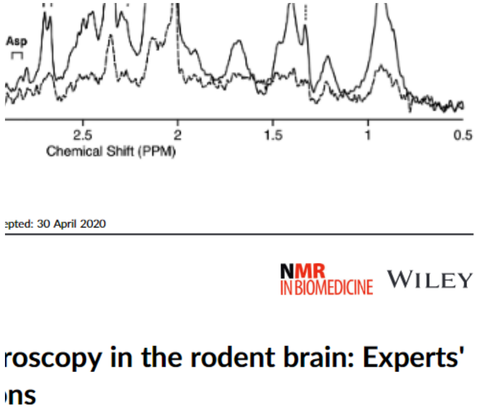

ɜpted: 30 April 2020

NMR IN BIOMEDICINE WILEY

ɾoscopy in the rodent brain: Experts'

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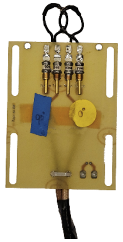

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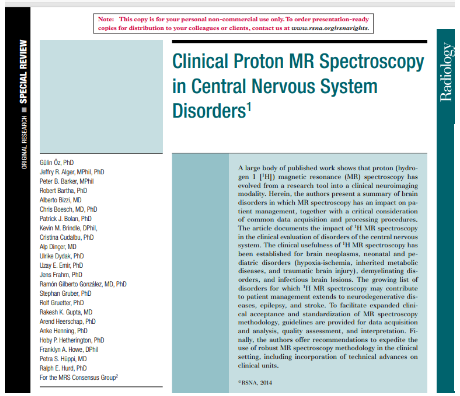
MINIMUM QUALITY CRITERIA



ORIGINAL RESEARCH ■ SPECIAL REVIEW

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Radiology

Clinical Proton MR Spectroscopy in Central Nervous System Disorders[1]

Gülin Öz, PhD
Jeffry R. Alger, MPhil, PhD
Peter B. Barker, MPhil
Robert Bartha, PhD
Alberto Bizzi, MD
Chris Boesch, MD, PhD
Patrick J. Bolan, PhD
Kevin M. Brindle, DPhil,
Cristina Cudalbu, PhD
Alp Dinçer, MD
Ulrike Dydak, PhD
Uzay E. Emir, PhD
Jens Frahm, PhD
Ramón Gilberto González, MD, PhD
Stephan Gruber, PhD
Rolf Gruetter, PhD
Rakesh K. Gupta, MD
Arend Heerschap, PhD
Anke Henning, PhD
Hoby P. Hetherington, PhD
Franklyn A. Howe, DPhil
Petra S. Hüppi, MD
Ralph E. Hurd, PhD
For the MRS Consensus Group[2]

A large body of published work shows that proton (hydrogen 1 [^{1}H]) magnetic resonance (MR) spectroscopy has evolved from a research tool into a clinical neuroimaging modality. Herein, the authors present a summary of brain disorders in which MR spectroscopy has an impact on patient management, together with a critical consideration of common data acquisition and processing procedures. The article documents the impact of ^{1}H MR spectroscopy in the clinical evaluation of disorders of the central nervous system. The clinical usefulness of ^{1}H MR spectroscopy has been established for brain neoplasms, neonatal and pediatric disorders (hypoxia-ischemia, inherited metabolic diseases, and traumatic brain injury), demyelinating disorders, and infectious brain lesions. The growing list of disorders for which ^{1}H MR spectroscopy may contribute to patient management extends to neurodegenerative diseases, epilepsy, and stroke. To facilitate expanded clinical acceptance and standardization of MR spectroscopy methodology, guidelines are provided for data acquisition and analysis, quality assessment, and interpretation. Finally, the authors offer recommendations to expedite the use of robust MR spectroscopy methodology in the clinical setting, including incorporation of technical advances on clinical units.

©RSNA, 2014

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DOI: 10.1002/nbm.4236

SPECIAL ISSUE REVIEW ARTICLE

WILEY NMR IN BIOMEDICINE

Advanced single voxel ^{1}H magnetic resonance spectroscopy techniques in humans: Experts' consensus recommendations

Gülin Öz[1] | Dinesh K. Deelchand[1] | Jannie P. Wijnen[2] | Vladimír Mlynárik[3] | Lijing Xin[4] | Ralf Mekle[5] | Ralph Noeske[6] | Tom W.J. Scheenen[7,8] | Ivan Tkáč[1] | the Experts' Working Group on Advanced Single Voxel ^{1}H MRS

jing

- SNR >3 for major resonances
- Linewidth - shimming
- Lineshape – symmetric
- WS
- No lipid contamination
- No other visible artifacts
    - Not so obvious artifacts (Chemical shift artifact, localization inaccuracies, signal cancellation, etc)
- CRBs
- Residuals with unexplained features

Signal

Quantification

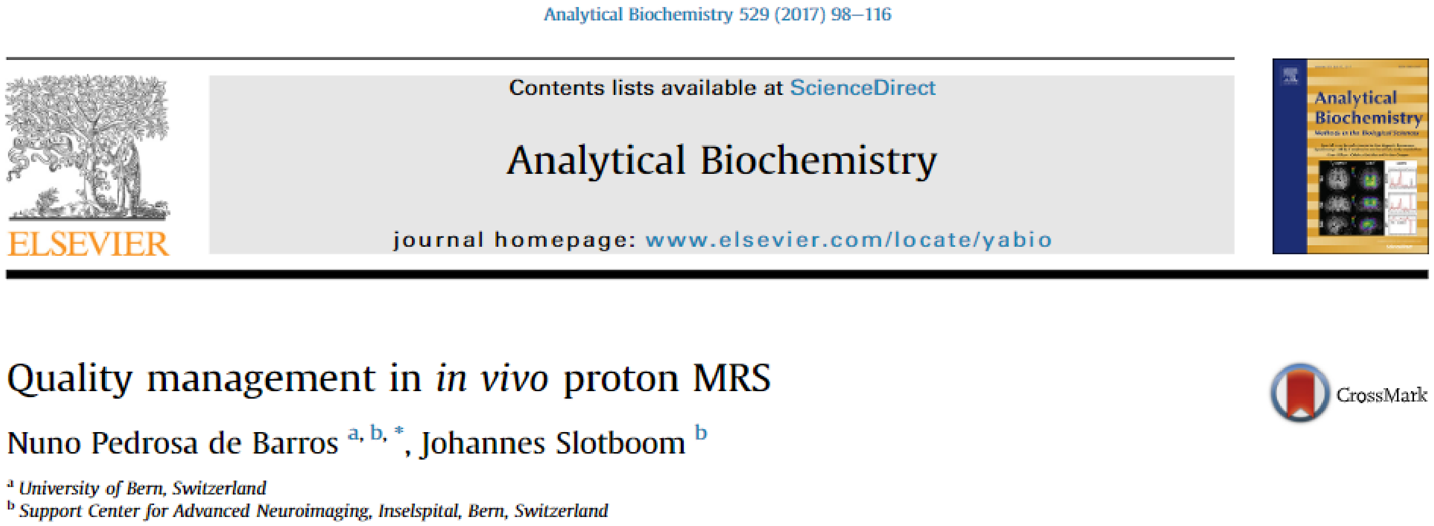
ISMRM 2010, Potentials and Challenges at High Field MRS
R Kreis, NMR Biomed 2004, 17:361
Tkáč I, et al, Appl Magn Reson. 2005 29:139.

http://www.ismrm.org/workshops/Spectroscopy16/program.htm
2nd TRANSACT Workshop, University Bern: Quality Issues in Clinical MRS 2014
The MRS Consensus Group. (2014), Radiology, 270(3):658-79.

QUALITY CONTROL

- **Quality Control – detection of artifacts (rejection or correction)**
  - **Signal Quality Control**
  - **Quantification Quality Control**
  - **Automatic (semi-automatic)**

https://mrs2022.cibm.ch/agenda/



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ELSEVIER

Quality management in *in vivo* proton MRS

Nuno Pedrosa de Barros [a, b, *], Johannes Slotboom [b]

[a] *University of Bern, Switzerland*
[b] *Support Center for Advanced Neuroimaging, Inselspital, Bern, Switzerland*

N Barros et al, Analytical Biochemistry, 2017

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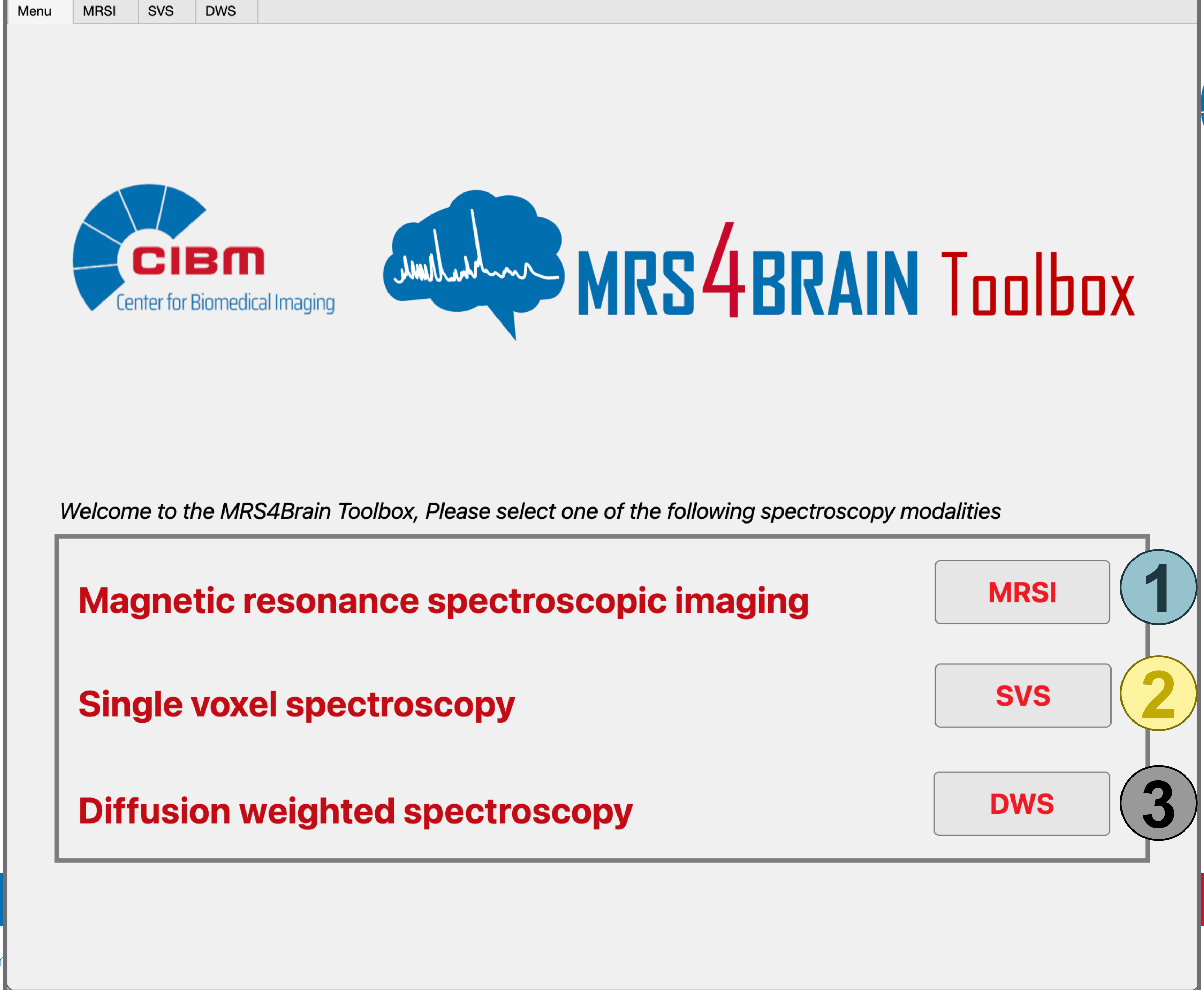
Center for Biomedical Imaging

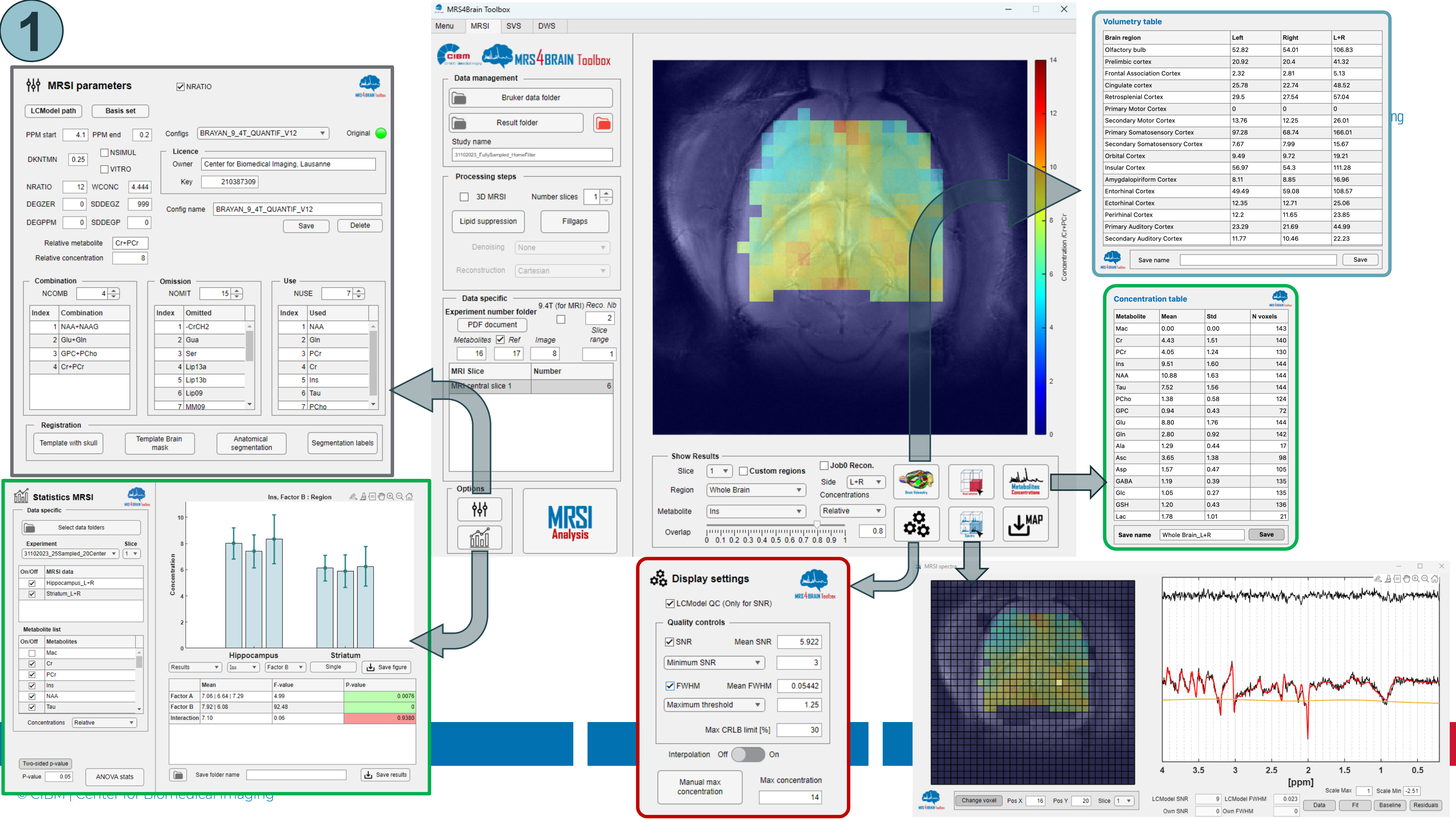


Welcome to the MRS4Brain Toolbox, Please select one of the following spectroscopy modalities

Magnetic resonance spectroscopic imaging

Single voxel spectroscopy

Diffusion weighted spectroscopy



MRSI parameters

☑ NRATIO

LCModel path | Basis set

PPM start 4.1 | PPM end 0.2 | Configs BRAYAN_9_4T_QUANTIF_V12 | Original

DKNTMN 0.25 | ☐ NSIMUL | ☐ VITRO

Licence: Owner Center for Biomedical Imaging, Lausanne; Key 210387309

NRATIO 12 | WCONC 4.444

DEGZER 0 | SDDEGZ 999

DEGPPM 0 | SDDEGP 0

Config name BRAYAN_9_4T_QUANTIF_V12 | Save | Delete

Relative metabolite Cr+PCr

Relative concentration 8

Combination: NCOMB 4

Index	Combination
1	NAA+NAAG
2	Glu+Gln
3	GPC+PCho
4	Cr+PCr

Omission: NOMIT 15

Index	Omitted
1	-CrCH2
2	Gua
3	Ser
4	Lip13a
5	Lip13b
6	Lip09
7	MM09

Use: NUSE 7

Index	Used
1	NAA
2	Gln
3	PCr
4	Cr
5	Ins
6	Tau
7	PCho

Registration: Template with skull | Template Brain mask | Anatomical segmentation | Segmentation labels

Data management

Bruker data folder

Result folder

Study name 31102023_FullySampled_HomeFilter

Processing steps

☐ 3D MRSI | Number slices 1

Lipid suppression | Fillgaps

Denoising None

Reconstruction Cartesian

Data specific

Experiment number folder | 9.4T (for MRI) ☐ | Reco. Nb 2

PDF document

Metabolites 16 | ☑ Ref 17 | Image 8 | Slice range 1

MRI Slice	Number
MRI central slice 1	6

Options

Show Results

Slice 1 | ☐ Custom regions | ☐ Job0 Recon.

Region Whole Brain | Side L+R

Metabolite Ins | Concentrations Relative

Overlap 0.8 (scale 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1)

Brain Volumetry | Voxel selection | Metabolites Concentrations | Spectra | MAP

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

Statistics MRSI

Data specific

Select data folders

Experiment 31102023_25Sampled_20Center | Slice 1

On/Off	MRSI data
☑	Hippocampus_L+R
☑	Striatum_L+R

Metabolite list

On/Off	Metabolites
☐	Mac
☑	Cr
☑	PCr
☑	Ins
☑	NAA
☑	Tau

Concentrations Relative

Two-sided p-value

P-value 0.05 | ANOVA stats

Results | Ins | Factor B | Single | Save figure

	Mean	F-value	P-value
Factor A	7.06 | 6.64 | 7.29	4.99	0.0076
Factor B	7.92 | 6.08	92.48	0
Interaction	7.10	0.06	0.9380

Save folder name | Save results

Display settings

☑ LCModel QC (Only for SNR)

Quality controls

☑ SNR | Mean SNR 5.922

Minimum SNR 3

☑ FWHM | Mean FWHM 0.05442

Maximum threshold 1.25

Max CRLB limit [%] 30

Interpolation Off ○ On

Manual max concentration | Max concentration 14

MRSI spectra

Change voxel | Pos X 16 | Pos Y 20 | Slice 1

LCModel SNR 9 | LCModel FWHM 0.023

Own SNR 0 | Own FWHM 0

Scale Max 1 | Scale Min -2.51

Data | Fit | Baseline | Residuals

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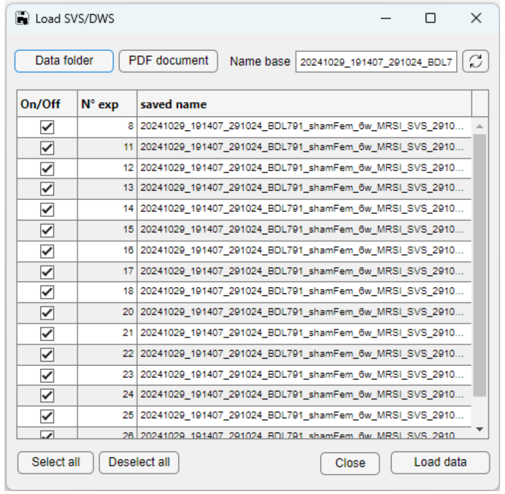
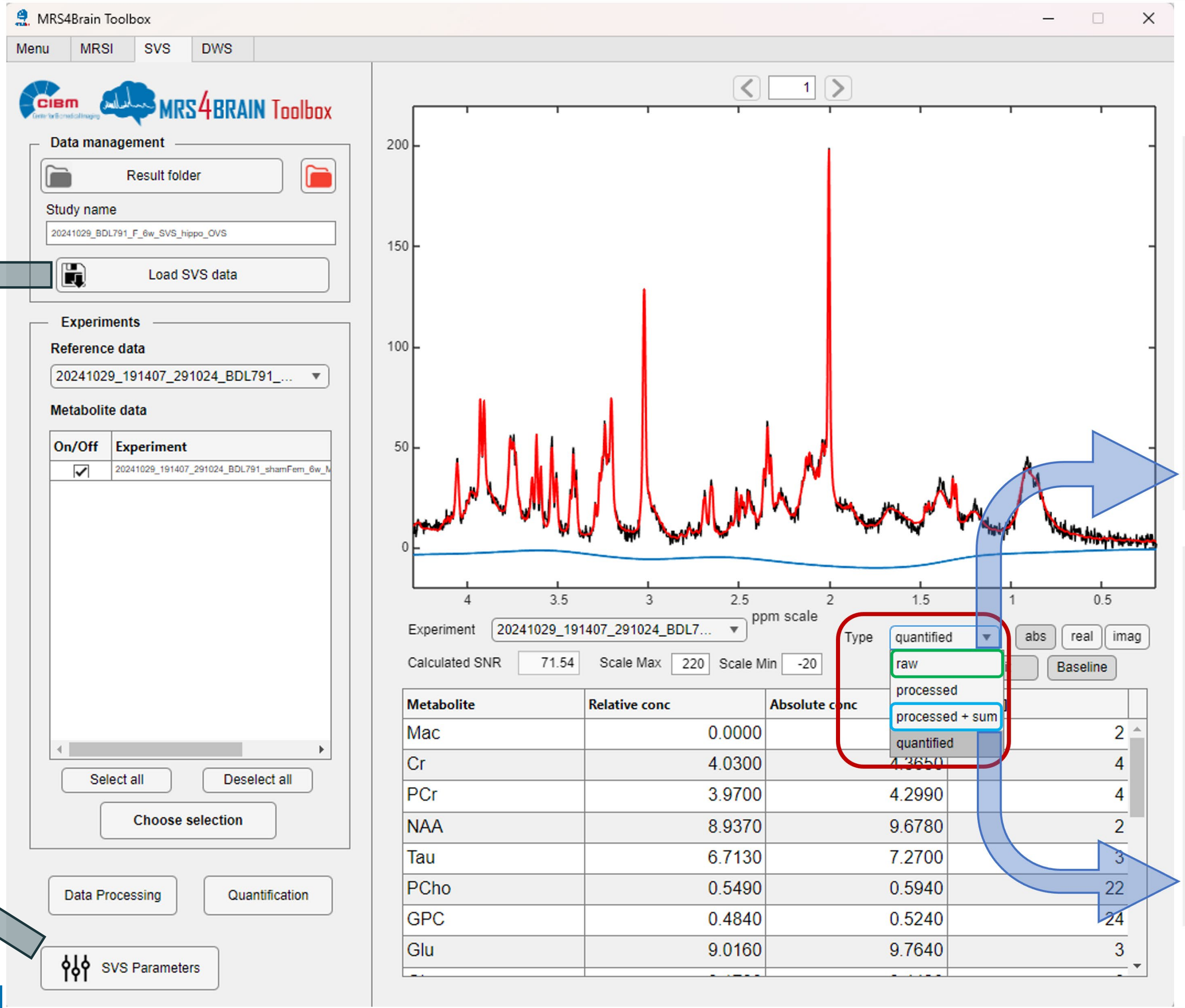
②



Name base 20241029_191407_291024_BDL7

On/Off	N° exp	saved name
☑	8	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	11	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	12	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	13	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	14	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	15	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	16	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	17	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	18	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	20	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	21	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	22	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	23	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	24	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	25	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910...
☑	26	20241029_191407_291024_BDL791_shamFem_6w_MRSI_SVS_2910



Study name 20241029_BDL791_F_6w_SVS_hippo_OVS

Reference data 20241029_191407_291024_BDL791_...

Metabolite data

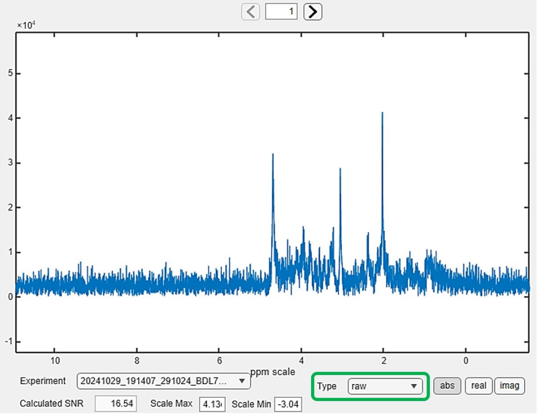
On/Off	Experiment
☑	20241029_191407_291024_BDL791_shamFem_6w_M

Experiment 20241029_191407_291024_BDL7...

Type quantified

Calculated SNR 71.54 Scale Max 220 Scale Min -20

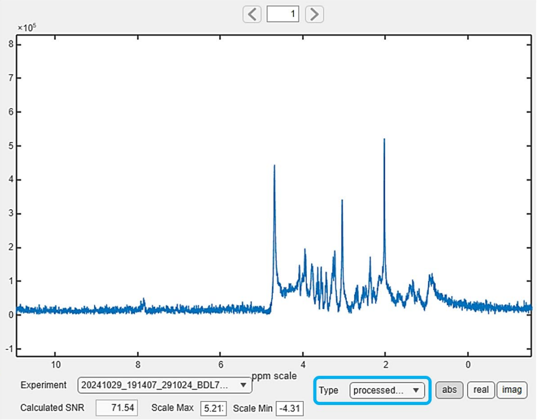
Metabolite	Relative conc	Absolute conc	
Mac	0.0000		2
Cr	4.0300	4.3650	4
PCr	3.9700	4.2990	4
NAA	8.9370	9.6780	2
Tau	6.7130	7.2700	3
PCho	0.5490	0.5940	22
GPC	0.4840	0.5240	24
Glu	9.0160	9.7640	3



Experiment 20241029_191407_291024_BDL7...

Type raw

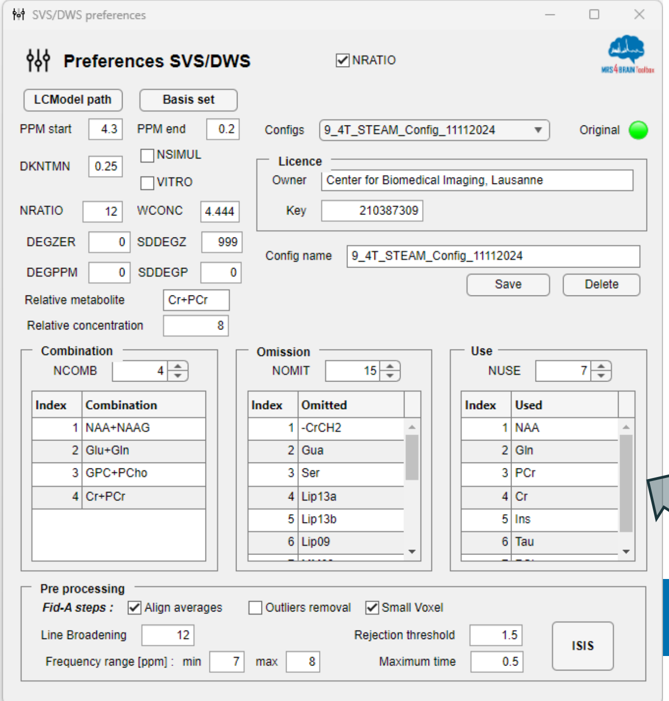
Calculated SNR 16.54 Scale Max 4.13 Scale Min -3.04



Experiment 20241029_191407_291024_BDL7...

Type processed...

Calculated SNR 71.54 Scale Max 5.21 Scale Min -4.31



☑ NRATIO

PPM start 4.3 PPM end 0.2

Configs 9_4T_STEAM_Config_11112024

DKNTMN 0.25

☐ NSIMUL

☐ VITRO

Owner Center for Biomedical Imaging, Lausanne

Key 210387309

NRATIO 12 WCONC 4.444

DEGZER 0 SDDEGZ 999

DEGPPM 0 SDDEGP 0

Config name 9_4T_STEAM_Config_11112024

Relative metabolite Cr+PCr

Relative concentration 8

NCOMB 4

Index	Combination
1	NAA+NAAG
2	Glu+Gln
3	GPC+PCho
4	Cr+PCr

NOMIT 15

Index	Omitted
1	-CrCH2
2	Gua
3	Ser
4	Lip13a
5	Lip13b
6	Lip09

NUSE 7

Index	Used
1	NAA
2	Gln
3	PCr
4	Cr
5	Ins
6	Tau

Fid-A steps : ☑ Align averages ☐ Outliers removal ☑ Small Voxel

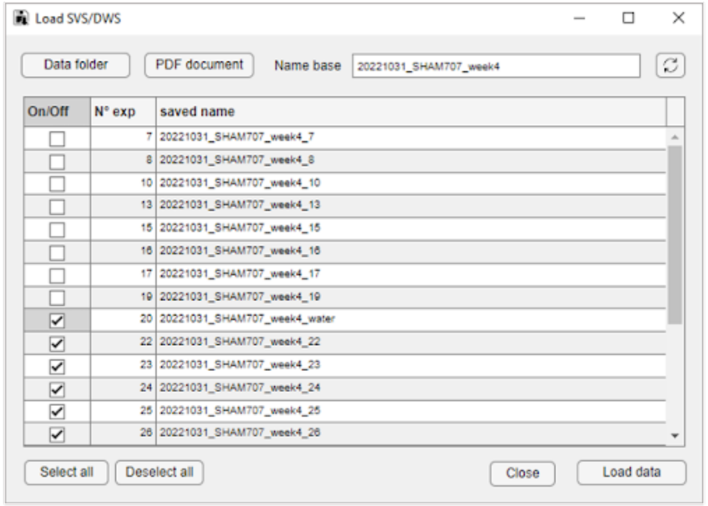
Line Broadening 12

Rejection threshold 1.5

Frequency range [ppm] : min 7 max 8

Maximum time 0.5

③



Name base: 20221031_SHAM707_week4

On/Off	N° exp	saved name
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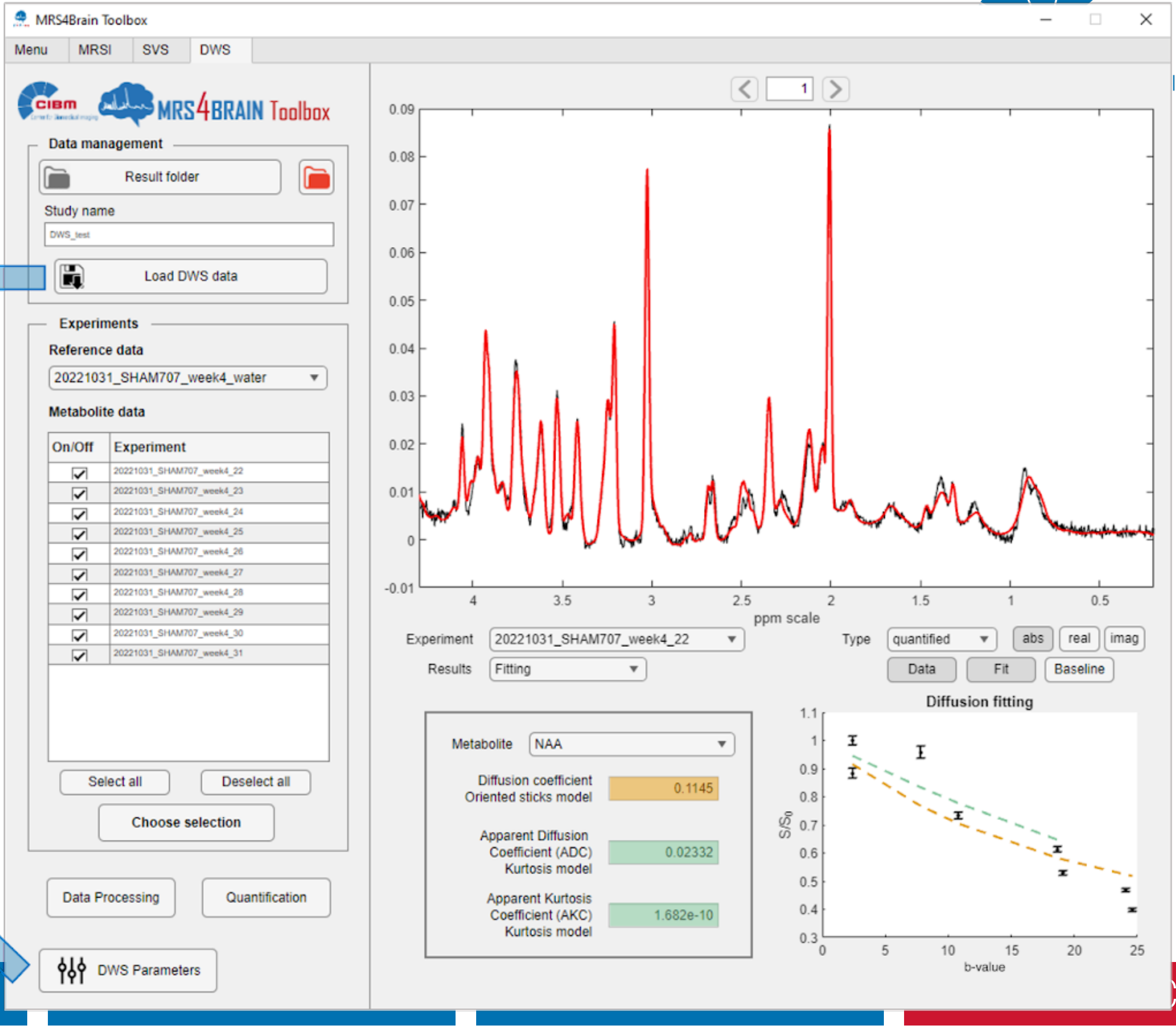
☐	8	20221031_SHAM707_week4_8
☐	10	20221031_SHAM707_week4_10
☐	13	20221031_SHAM707_week4_13
☐	15	20221031_SHAM707_week4_15
☐	16	20221031_SHAM707_week4_16
☐	17	20221031_SHAM707_week4_17
☐	19	20221031_SHAM707_week4_19
☑	20	20221031_SHAM707_week4_water
☑	22	20221031_SHAM707_week4_22
☑	23	20221031_SHAM707_week4_23
☑	24	20221031_SHAM707_week4_24
☑	25	20221031_SHAM707_week4_25
☑	26	20221031_SHAM707_week4_26



Study name: DWS_test

Reference data: 20221031_SHAM707_week4_water

Metabolite data

On/Off	Experiment
☑	20221031_SHAM707_week4_22
☑	20221031_SHAM707_week4_23
☑	20221031_SHAM707_week4_24
☑	20221031_SHAM707_week4_25
☑	20221031_SHAM707_week4_26
☑	20221031_SHAM707_week4_27
☑	20221031_SHAM707_week4_28
☑	20221031_SHAM707_week4_29
☑	20221031_SHAM707_week4_30
☑	20221031_SHAM707_week4_31

Experiment: 20221031_SHAM707_week4_22

Results: Fitting

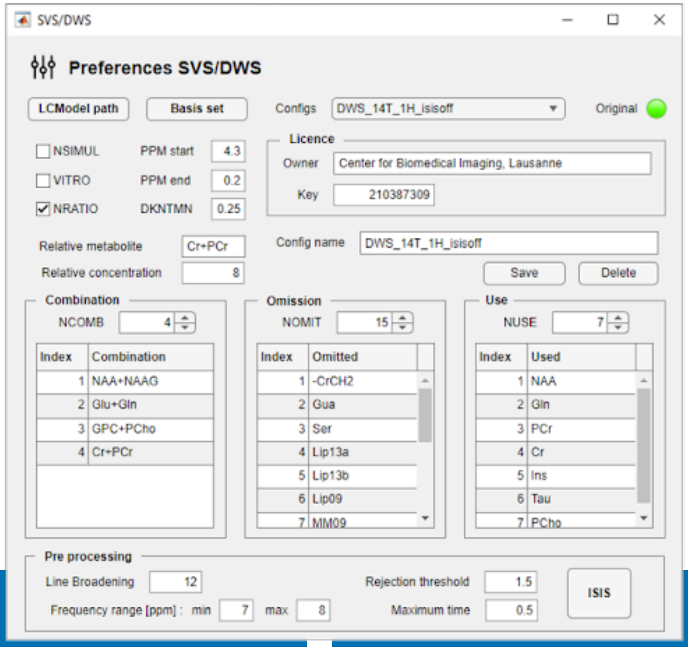
Type: quantified

Metabolite: NAA

Diffusion coefficient Oriented sticks model: 0.1145

Apparent Diffusion Coefficient (ADC) Kurtosis model: 0.02332

Apparent Kurtosis Coefficient (AKC) Kurtosis model: 1.682e-10



Preferences SVS/DWS

Configs: DWS_14T_1H_isisoff

☐ NSIMUL PPM start 4.3

☐ VITRO PPM end 0.2

☑ NRATIO DKNTMN 0.25

Licence

Owner: Center for Biomedical Imaging, Lausanne

Key: 210387309

Relative metabolite: Cr+PCr

Relative concentration: 8

Config name: DWS_14T_1H_isisoff

Combination

NCOMB 4

Index	Combination
1	NAA+NAAG
2	Glu+Gln
3	GPC+PCho
4	Cr+PCr

Omission

NOMIT 15

Index	Omitted
1	-CrCH2
2	Gua
3	Ser
4	Lip13a
5	Lip13b
6	Lip09
7	MM09

Use

NUSE 7

Index	Used
1	NAA
2	Gln
3	PCr
4	Cr
5	Ins
6	Tau
7	PCho

Pre processing

Line Broadening 12

Frequency range [ppm] : min 7 max 8

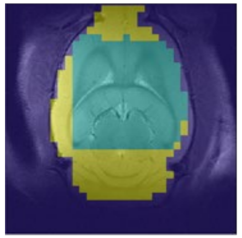
Rejection threshold 1.5

Maximum time 0.5

MRS4BRAIN Toolbox

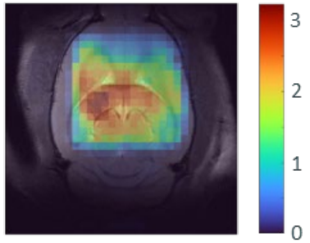
https://github.com/AlvBrayan/MRS4Brain-toolbox
https://www.epfl.ch/labs/mrs4brain/ressources/mrs4brain-toolbox/

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)**



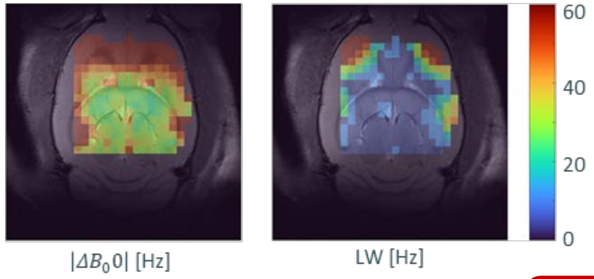
$$Power_{x,y} = \sum_{i=1}^{1024} |spectral\ point|$$

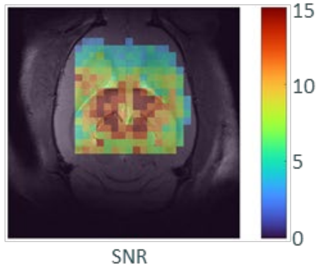
$$0 < Power_{x,y} - \overline{Power} \leftarrow Selection$$

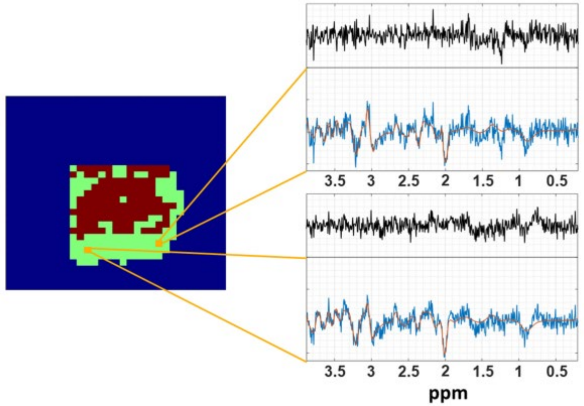


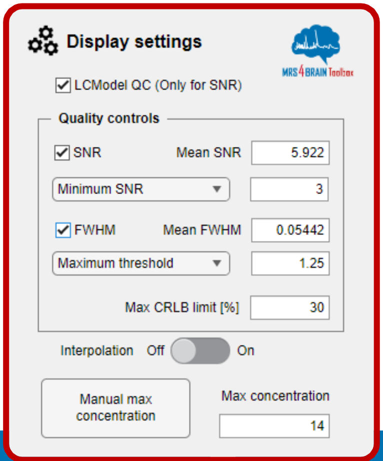
→ ΔB_0 and linewidth map (water signal)

→ SNR map (NAA peak hight / σ noise)









Display settings

☑ LCModel QC (Only for SNR)

Quality controls

☑ SNR Mean SNR 5.922
Minimum SNR ▾ 3
☑ FWHM Mean FWHM 0.05442
Maximum threshold ▾ 1.25
Max CRLB limit [%] 30

Interpolation Off ○ On

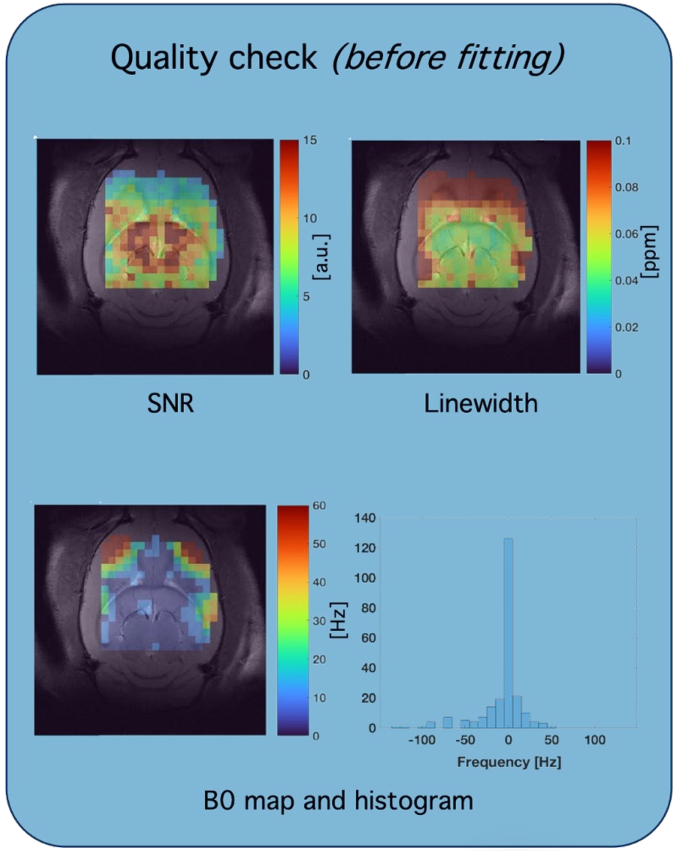
Manual max concentration
Max concentration 14

B Alves & G Briand

cristina.cudalbu@epfl.ch

MRS4BRAIN TOOLBOX : MRSI (QUALITY CONTROL)

CIBM
Center for Biomedical Imaging

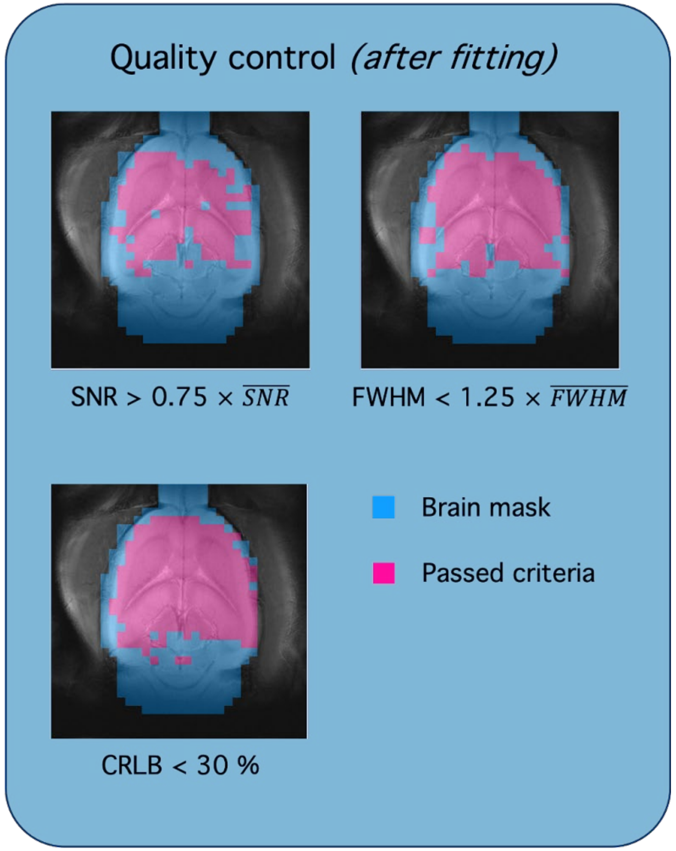


Quality check *(before fitting)*

SNR

Linewidth

B0 map and histogram



Quality control *(after fitting)*

$SNR > 0.75 \times \overline{SNR}$

$FWHM < 1.25 \times \overline{FWHM}$

CRLB < 30 %

🟦 Brain mask

🟪 Passed criteria

- 4 Quality Metrics reported : Signal-to-noise ratio (SNR), linewidth (lw or FWHM), B_0 shift & Cramer Rao lower bound (CRLB)
- Quality check before fitting (no masking)
- Quality control after fitting (masking of unwanted data)

MRS4BRAIN Toolbox

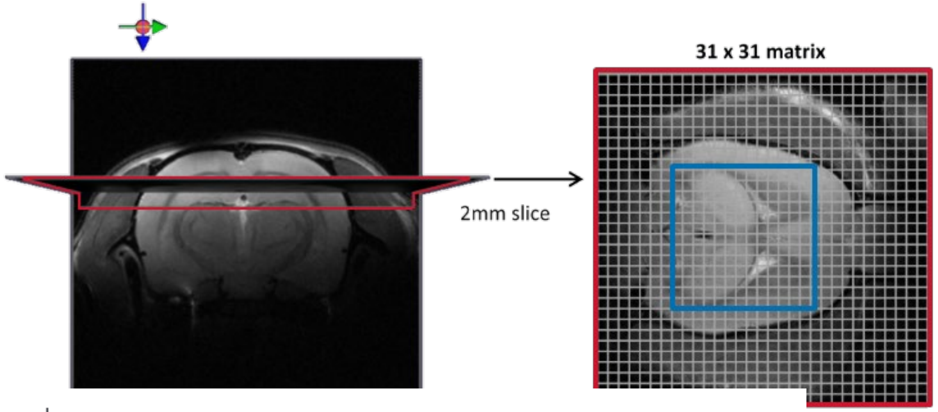
https://www.epfl.ch/labs/mrs4brain/ressources/mrs4brain-toolbox/

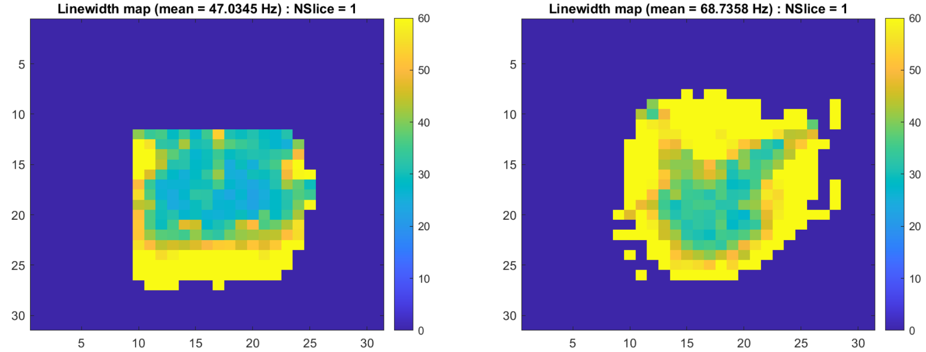
CIBM.CH

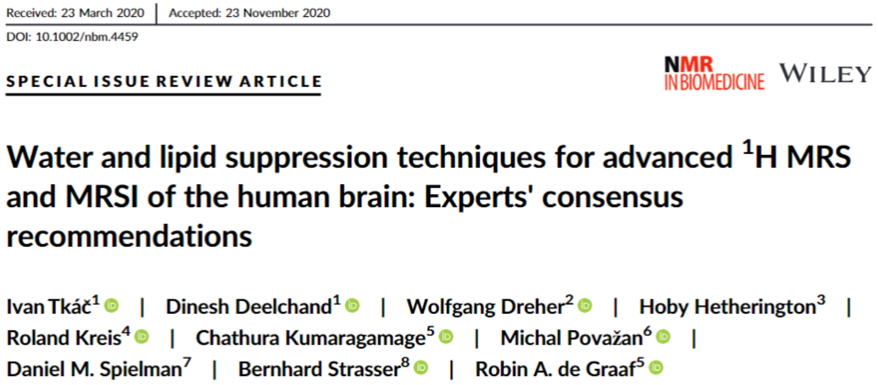
MRSI – quality control

B Alves

- Bo shimming – shim larger regions – significant Bo inhomogeneities







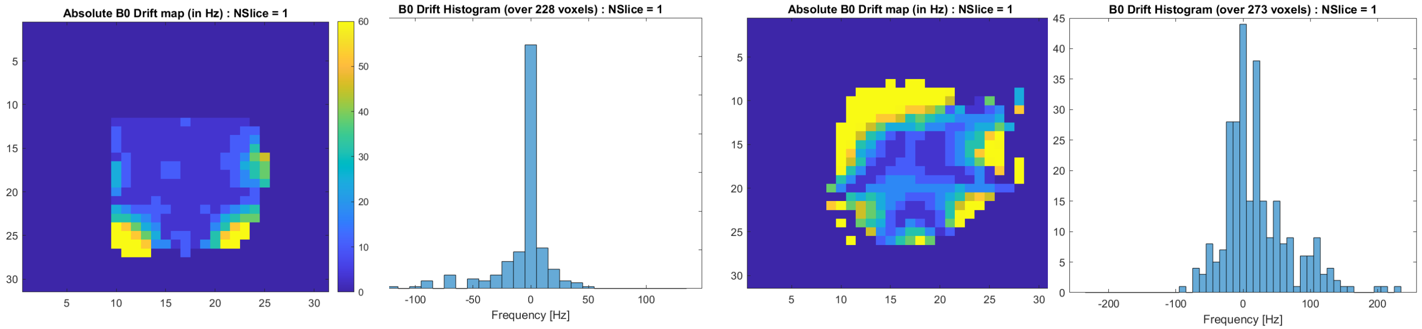
Received: 23 March 2020 | Accepted: 23 November 2020
DOI: 10.1002/nbm.4459

SPECIAL ISSUE REVIEW ARTICLE

NMR IN BIOMEDICINE WILEY

Water and lipid suppression techniques for advanced ^{1}H MRS and MRSI of the human brain: Experts' consensus recommendations

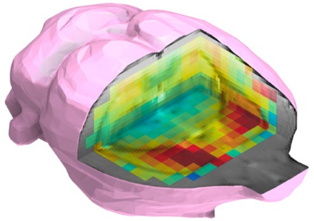
Ivan Tkáč[1] | Dinesh Deelchand[1] | Wolfgang Dreher[2] | Hoby Hetherington[3] | Roland Kreis[4] | Chathura Kumaragamage[5] | Michal Považan[6] | Daniel M. Spielman[7] | Bernhard Strasser[8] | Robin A. de Graaf[5]



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

cristina.cudalbu@epfl.ch

3D METABOLIC MAP




B Alves


T Le

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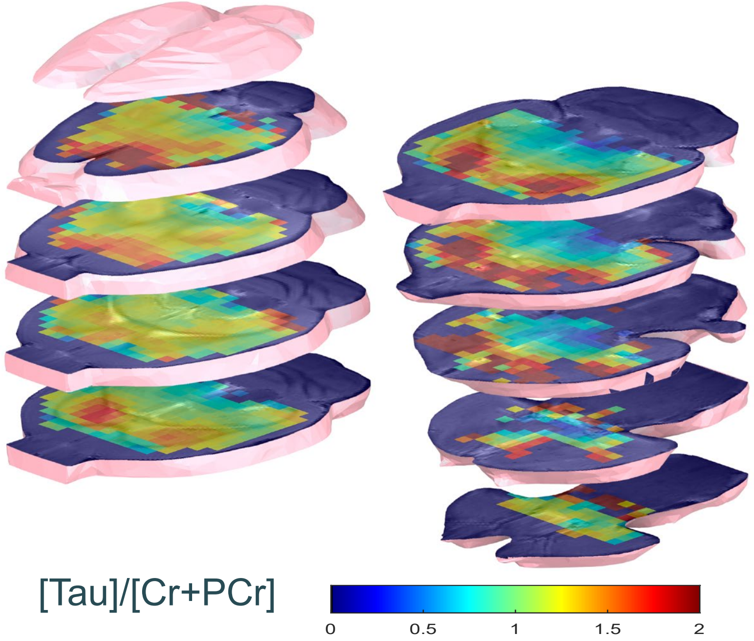
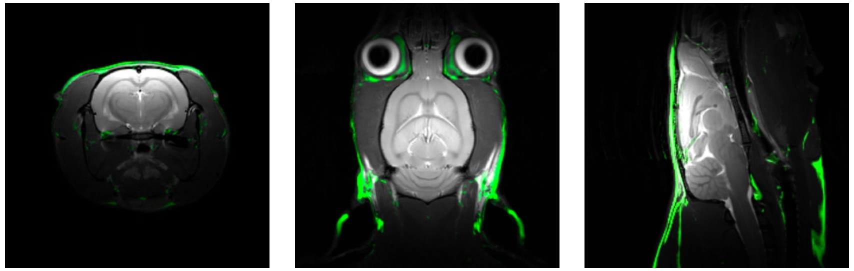
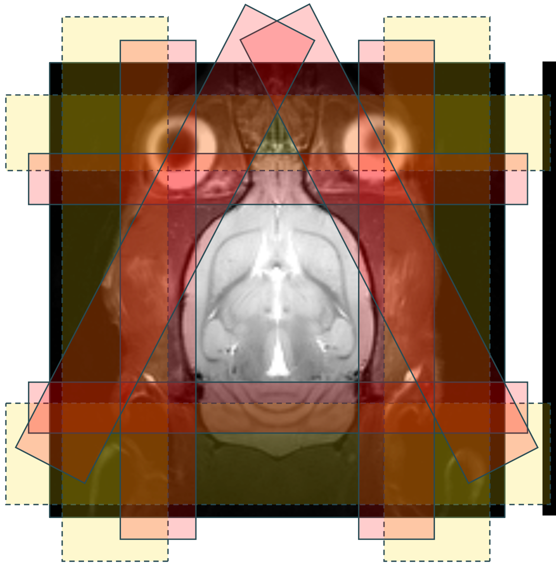
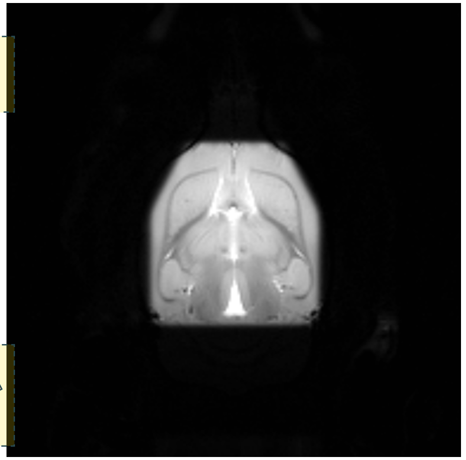
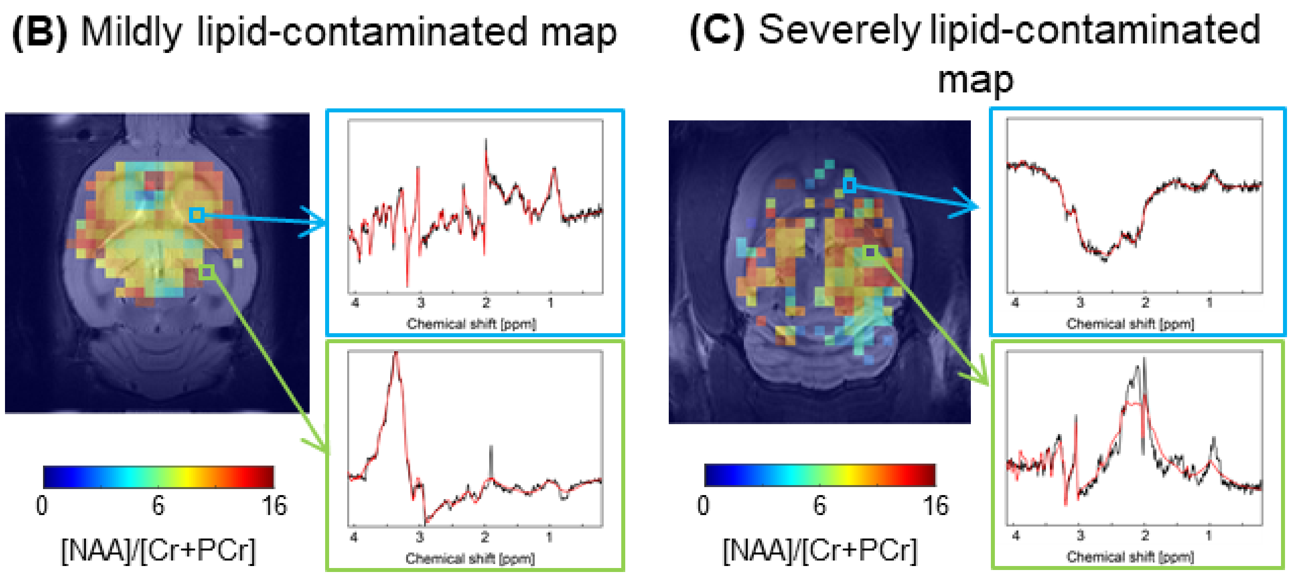




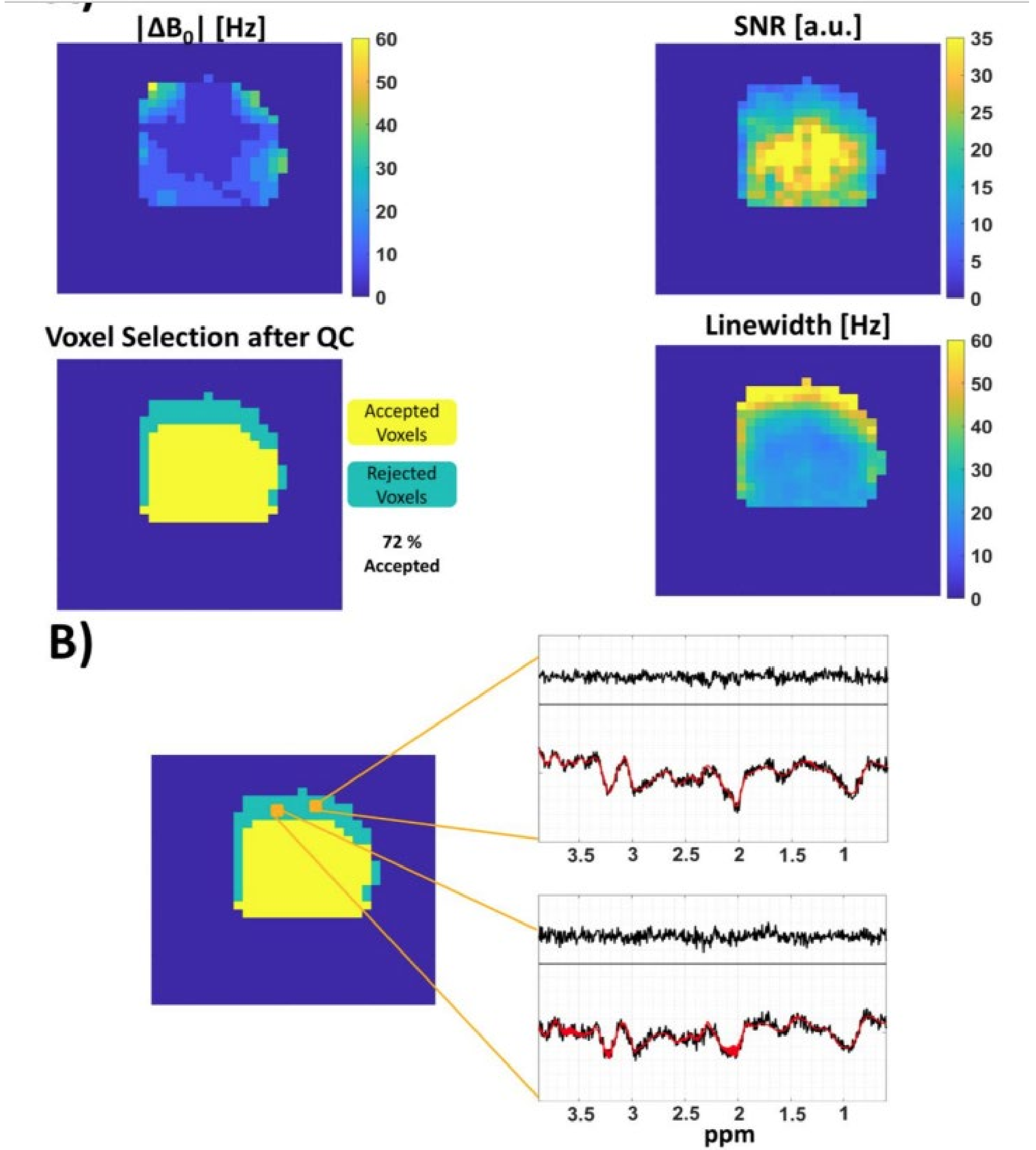




- Time – CS (AF=4, 119min→28min), 1.19 μL to 0.59 μL
- PSF & Resolution
- Lipid contamination -- Saturation bands
- Post processing
- …

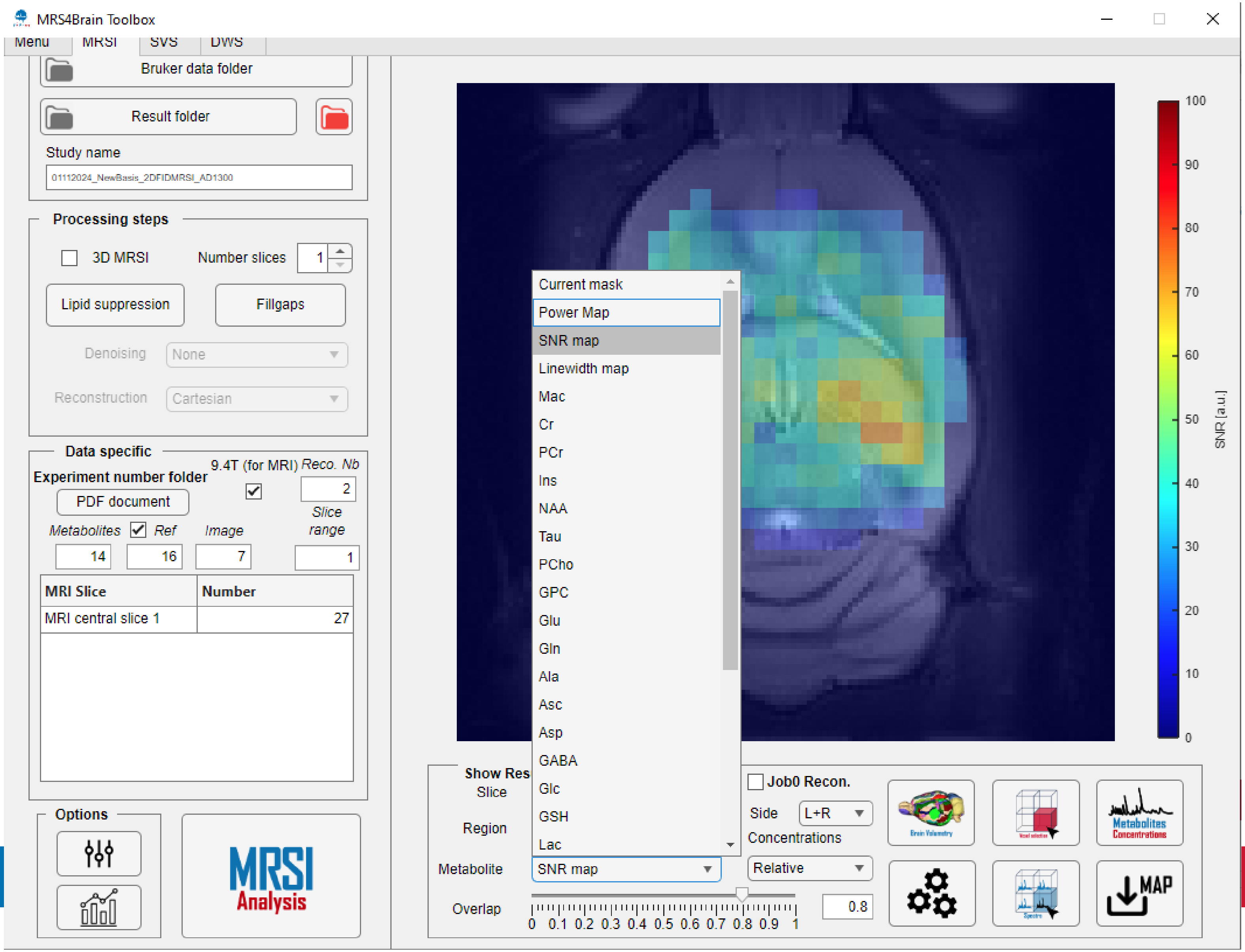

(B) Mildly lipid-contaminated map

(C) Severely lipid-contaminated map



QUALITY CONTROL IN MRS4BRAIN TOOLBOX

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



Study name: 01112024_NewBasis_2DFIDMRSI_AD1300

☐ 3D MRSI Number slices: 1

Denoising: None

Reconstruction: Cartesian

9.4T (for MRI) ☑ *Reco. Nb* 2

Metabolites 14 ☑ *Ref* 16 *Image* 7 *Slice range* 1

MRI Slice	Number
MRI central slice 1	27

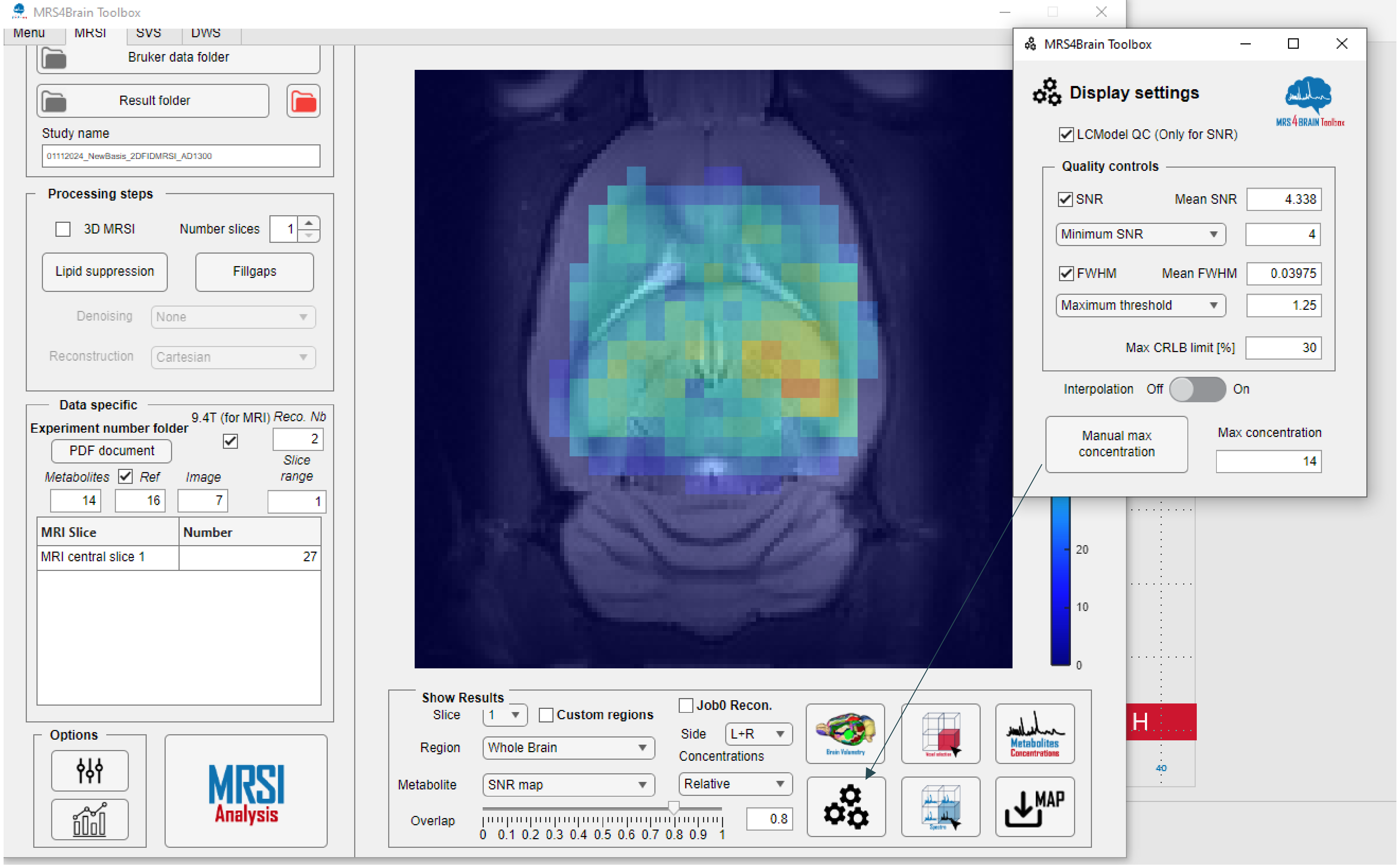
☐ Job0 Recon.

Side: L+R

Concentrations: Relative

Metabolite: SNR map

Overlap: 0.8



Study name: 01112024_NewBasis_2DFIDMRSI_AD1300

☐ 3D MRSI Number slices: 1

Denoising: None

Reconstruction: Cartesian

Experiment number folder

9.4T (for MRI) ☑ Reco. Nb: 2

Metabolites: 14 ☑ Ref: 16 Image: 7 Slice range: 1

MRI Slice	Number
MRI central slice 1	27

Slice: 1 ☐ Custom regions ☐ Job0 Recon.

Side: L+R

Concentrations: Relative

Region: Whole Brain

Metabolite: SNR map

Overlap: 0.8

Display settings

☑ LCModel QC (Only for SNR)

Quality controls

☑ SNR Mean SNR: 4.338

Minimum SNR: 4

☑ FWHM Mean FWHM: 0.03975

Maximum threshold: 1.25

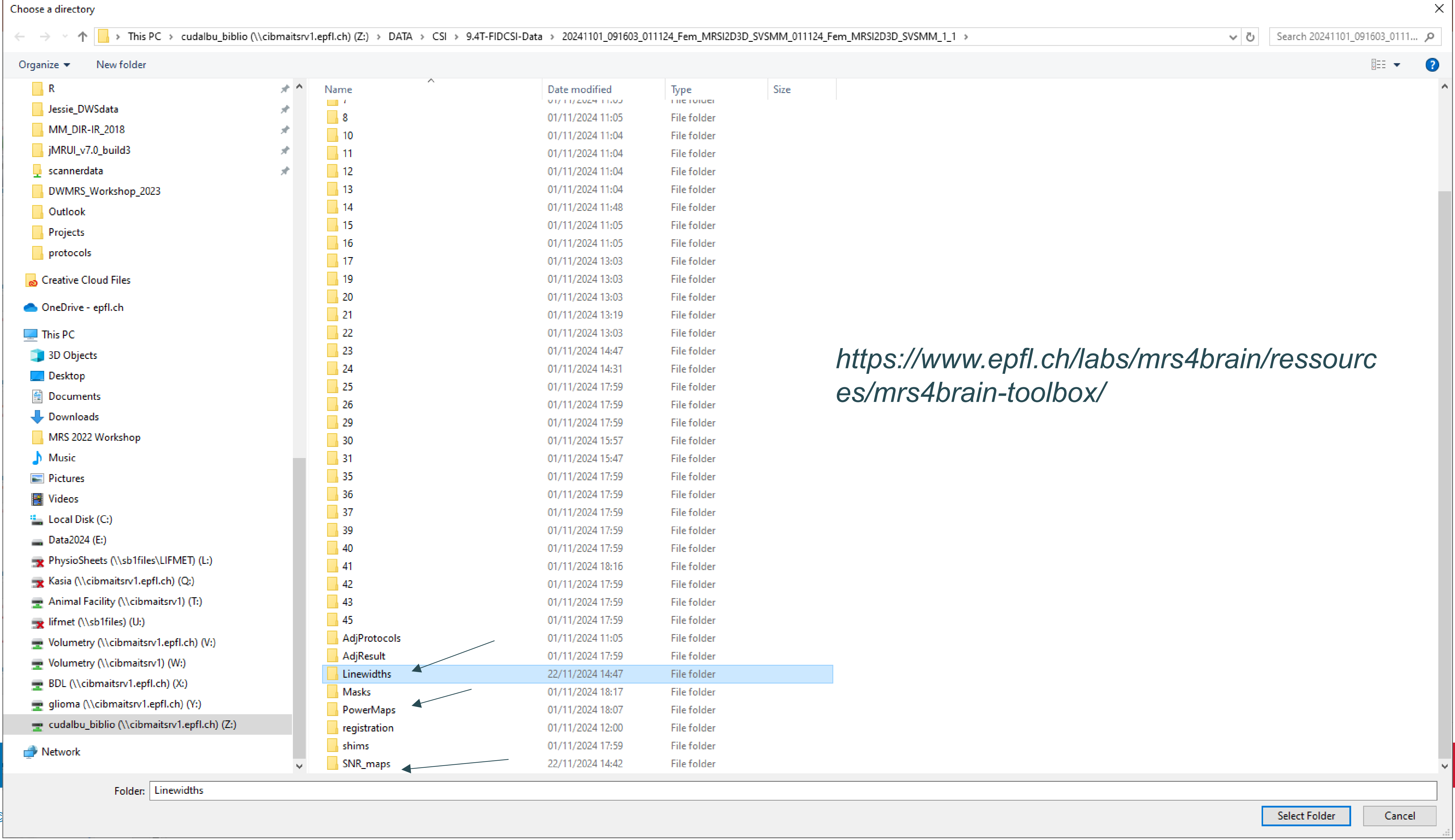
Max CRLB limit [%]: 30

Interpolation Off On

Manual max concentration

Max concentration: 14

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



Name	Date modified	Type	Size
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11	01/11/2024 11:04	File folder	
12	01/11/2024 11:04	File folder	
13	01/11/2024 11:04	File folder	
14	01/11/2024 11:48	File folder	
15	01/11/2024 11:05	File folder	
16	01/11/2024 11:05	File folder	
17	01/11/2024 13:03	File folder	
19	01/11/2024 13:03	File folder	
20	01/11/2024 13:03	File folder	
21	01/11/2024 13:19	File folder	
22	01/11/2024 13:03	File folder	
23	01/11/2024 14:47	File folder	
24	01/11/2024 14:31	File folder	
25	01/11/2024 17:59	File folder	
26	01/11/2024 17:59	File folder	
29	01/11/2024 17:59	File folder	
30	01/11/2024 15:57	File folder	
31	01/11/2024 15:47	File folder	
35	01/11/2024 17:59	File folder	
36	01/11/2024 17:59	File folder	
37	01/11/2024 17:59	File folder	
39	01/11/2024 17:59	File folder	
40	01/11/2024 17:59	File folder	
41	01/11/2024 18:16	File folder	
42	01/11/2024 17:59	File folder	
43	01/11/2024 17:59	File folder	
45	01/11/2024 17:59	File folder	
AdjProtocols	01/11/2024 11:05	File folder	
AdjResult	01/11/2024 17:59	File folder	
Linewidths	22/11/2024 14:47	File folder	
Masks	01/11/2024 18:17	File folder	
PowerMaps	01/11/2024 18:07	File folder	
registration	01/11/2024 12:00	File folder	
shims	01/11/2024 17:59	File folder	
SNR_maps	22/11/2024 14:42	File folder	

Folder: Linewidths

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

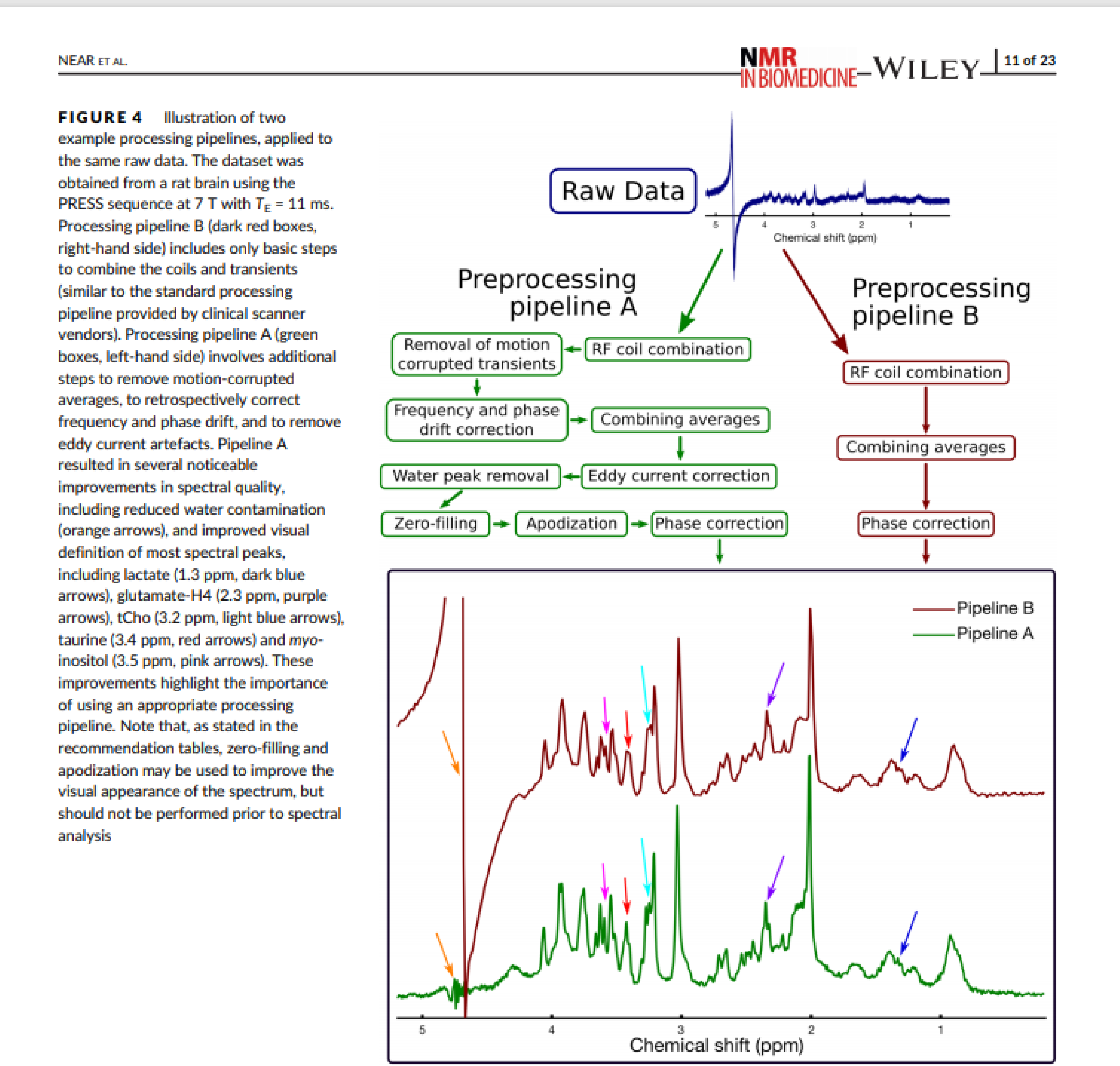
PREPROCESSING STEPS

- Phase offsets (0 and 1st order)
- Subject motion
- Scanner drift
- Eddy currents
- Alignment of spectra that need to be added/subtracted
- Water contamination
- …..

PREPROCESSING STEPS

- Why ?
  - quantification algorithms do not account for all of them
  - Lead to errors in the quantification process

- Requirements:
  - Automated methods
  - Included in the quantification software

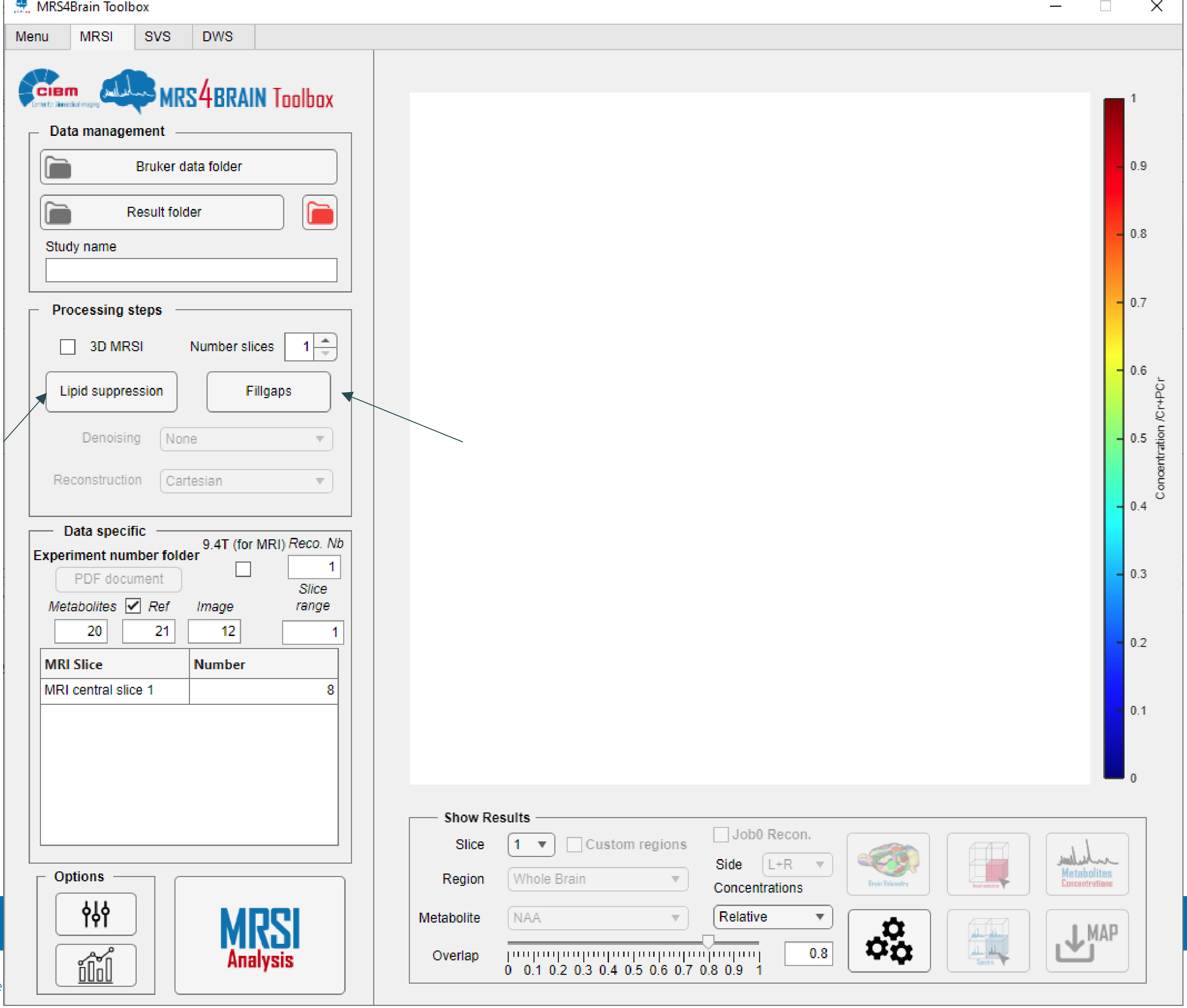


NEAR ET AL.

NMR IN BIOMEDICINE—WILEY | 11 of 23

FIGURE 4 Illustration of two example processing pipelines, applied to the same raw data. The dataset was obtained from a rat brain using the PRESS sequence at 7 T with T_E = 11 ms. Processing pipeline B (dark red boxes, right-hand side) includes only basic steps to combine the coils and transients (similar to the standard processing pipeline provided by clinical scanner vendors). Processing pipeline A (green boxes, left-hand side) involves additional steps to remove motion-corrupted averages, to retrospectively correct frequency and phase drift, and to remove eddy current artefacts. Pipeline A resulted in several noticeable improvements in spectral quality, including reduced water contamination (orange arrows), and improved visual definition of most spectral peaks, including lactate (1.3 ppm, dark blue arrows), glutamate-H4 (2.3 ppm, purple arrows), tCho (3.2 ppm, light blue arrows), taurine (3.4 ppm, red arrows) and *myo*-inositol (3.5 ppm, pink arrows). These improvements highlight the importance of using an appropriate processing pipeline. Note that, as stated in the recommendation tables, zero-filling and apodization may be used to improve the visual appearance of the spectrum, but should not be performed prior to spectral analysis

C I B M . C H



Study name:

☐ 3D MRSI

Number slices: 1

Denoising: None

Reconstruction: Cartesian

9.4T (for MRI) ☐

Reco. Nb: 1

Metabolites: 20

☑ *Ref*: 21

Image: 12

Slice range: 1

MRI Slice	Number
MRI central slice 1	8

Slice: 1

☐ Custom regions

☐ Job0 Recon.

Side: L+R

Region: Whole Brain

Concentrations: Relative

Metabolite: NAA

Overlap: 0.8

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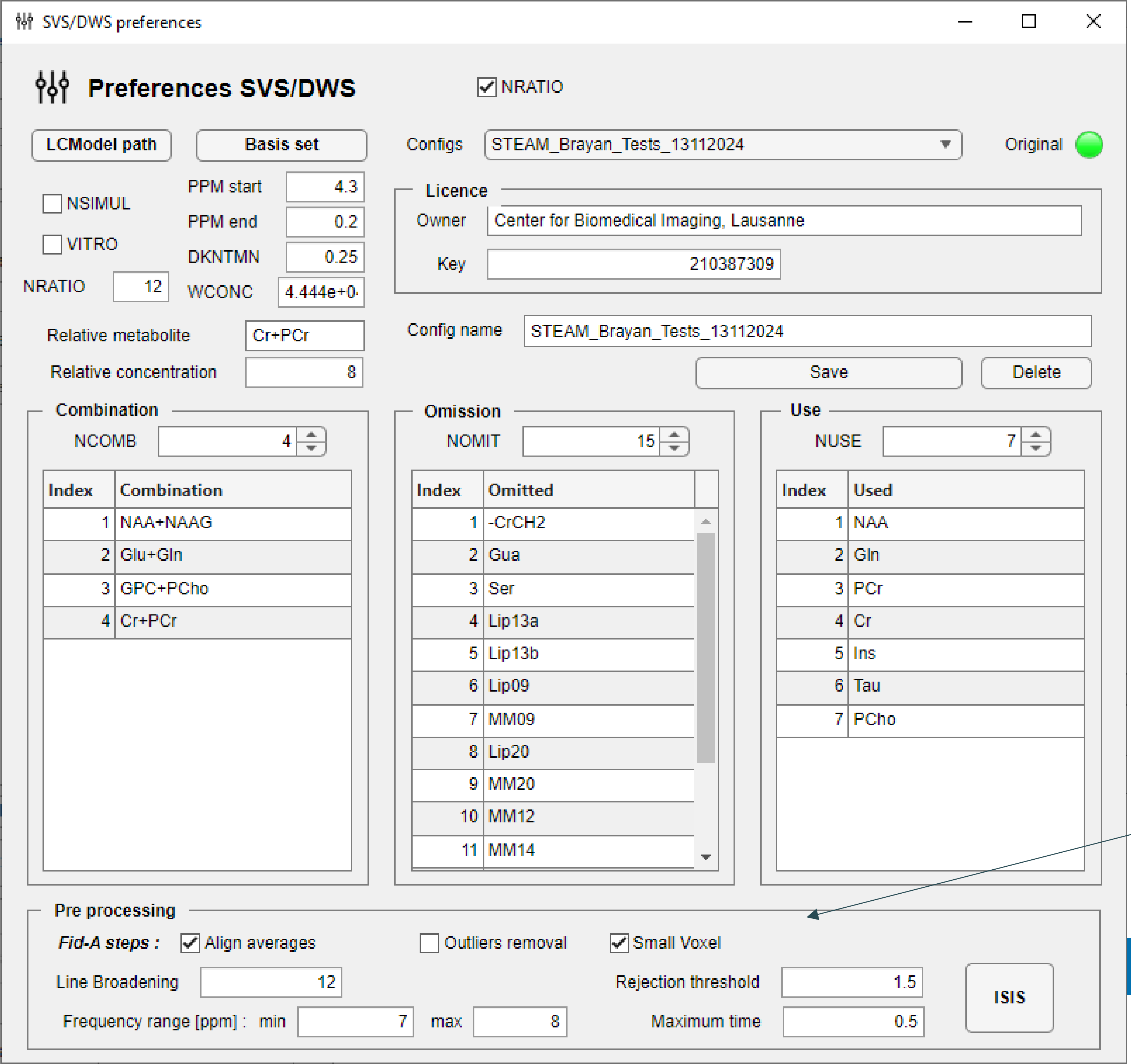
https://www.epfl.ch/labs/mrs4brain/resources/mrs4brain-toolbox/

CIBM.CH



Preferences SVS/DWS

☑ NRATIO

Configs: STEAM_Brayan_Tests_13112024

Original ●

☐ NSIMUL

☐ VITRO

NRATIO: 12

PPM start: 4.3

PPM end: 0.2

DKNTMN: 0.25

WCONC: 4.444e+0

Relative metabolite: Cr+PCr

Relative concentration: 8

Licence

Owner: Center for Biomedical Imaging, Lausanne

Key: 210387309

Config name: STEAM_Brayan_Tests_13112024

Combination

NCOMB: 4

Index	Combination
1	NAA+NAAG
2	Glu+Gln
3	GPC+PCho
4	Cr+PCr

Omission

NOMIT: 15

Index	Omitted
1	-CrCH2
2	Gua
3	Ser
4	Lip13a
5	Lip13b
6	Lip09
7	MM09
8	Lip20
9	MM20
10	MM12
11	MM14

Use

NUSE: 7

Index	Used
1	NAA
2	Gln
3	PCr
4	Cr
5	Ins
6	Tau
7	PCho

Pre processing

Fid-A steps : ☑ Align averages ☐ Outliers removal ☑ Small Voxel

Line Broadening: 12

Rejection threshold: 1.5

Frequency range [ppm] : min 7 max 8

Maximum time: 0.5

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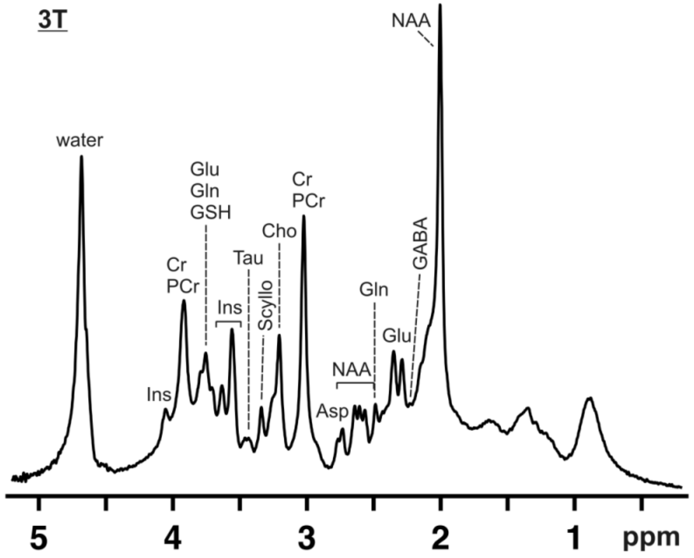
https://www.epfl.ch/labs/mrs4brain/resources/mrs4brain-toolbox/

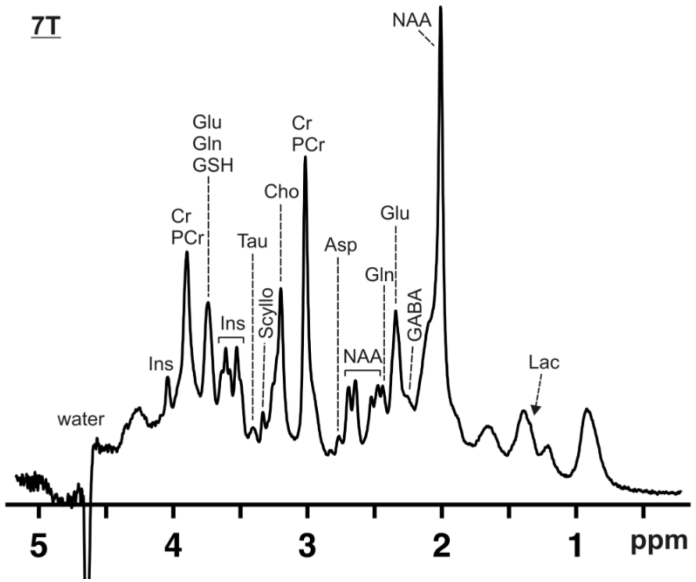
QUANTIFICATION SOFTWARE

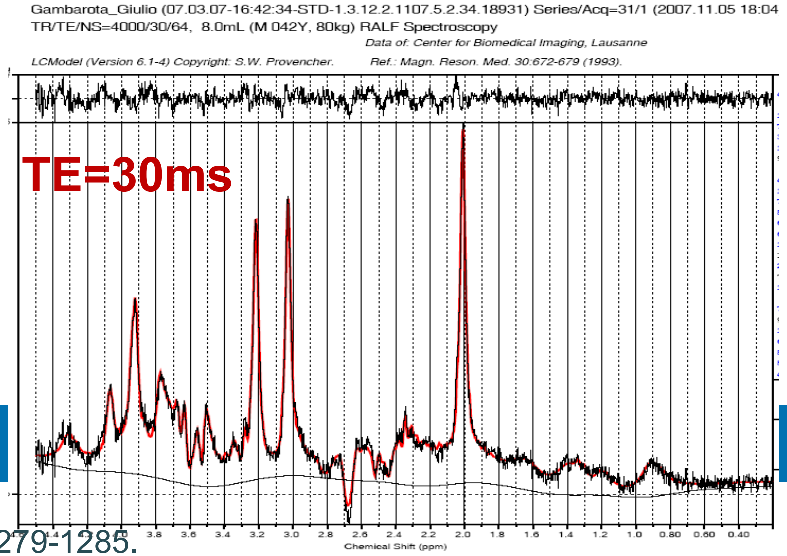
QUANTIFICATION

- MRS – principal goal – quantification of changes in concentration of known metabolites
- Accurate and precise quantification:
  - Signal quality
    - Hardware performance
    - Pulse sequence design & adjustment
  - Data (pre)processing (estimate the signal amplitude or peak area)
  - Quantification strategies (→ tissue content)
- Final Goal:
  - Maximize the neurochemical information
  - Increase the precision and accuracy of quantification
  - Maximize the reliability of neurochemical data

QUANTIFICATION






Gambarota_Giulio (07.03.07-16:42:34-STD-1.3.12.2.1107.5.2.34.18931) Series/Acq=31/1 (2007.11.05 18:04
TR/TE/NS=4000/30/64, 8.0mL (M 042Y, 80kg) RALF Spectroscopy
Data of: Center for Biomedical Imaging, Lausanne
LCModel (Version 6.1-4) Copyright: S.W. Provencher. *Ref.: Magn. Reson. Med. 30:672-679 (1993).*

TE=30ms

Mekle R, et al. Magn Reson Med 61, 1279-1285.

QUANTIFICATION

Signals are different (acq param, Bo, nucleus, etc)

– quantification is also different

THE ALGORITHMS ARE AUTOMATIC

BUT NOT FULLY PUSH-BUTTON

NEED TO BE ADAPTED

QUANTIFICATION

In vivo spectra - high B_0 → Increased - sensitivity
- spectral resolution

- short TE

is difficult:

- Complexity of the spectra:
  - many resonances
  - peak overlap
  - contribution of macromolecules and residual water

- Unpredictable lineshape :
  - residual eddy currents
  - field inhomogeneity
- Unpredictable baseline:
  - macromolecules
  - lipid signals
  - partially suppressed water

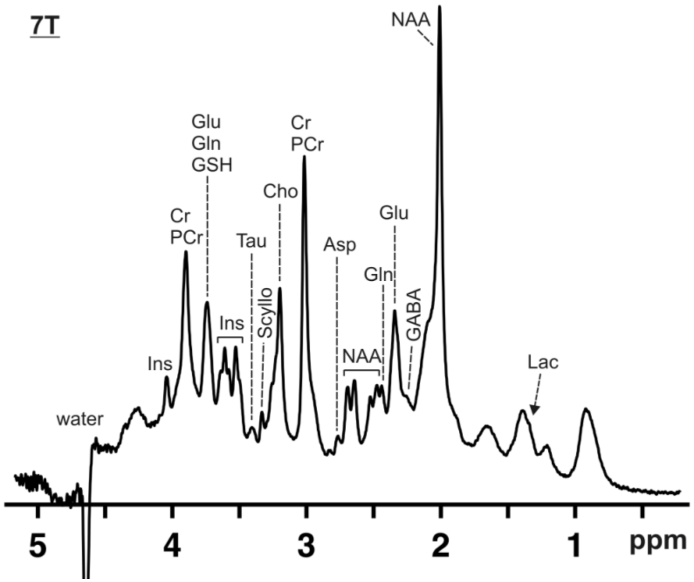
QUANTIFICATION

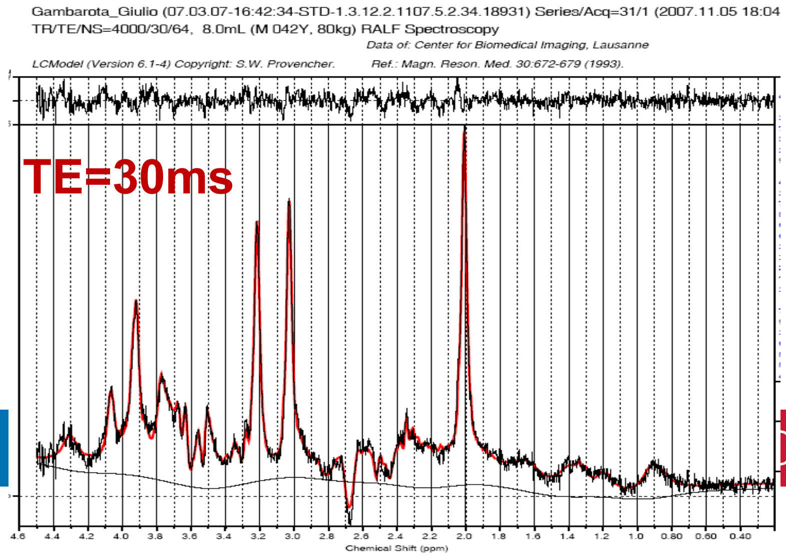
In vivo spectra - high B_0

- short TE

Increased - sensitivity

- spectral resolution





Gambarota_Giulio (07.03.07-16:42:34-STD-1.3.12.2.1107.5.2.34.18931) Series/Acq=31/1 (2007.11.05 18:04
TR/TE/NS=4000/30/64, 8.0mL (M 042Y, 80kg) RALF Spectroscopy
Data of: Center for Biomedical Imaging, Lausanne
LCModel (Version 6.1-4) Copyright: S.W. Provencher. *Ref.: Magn. Reson. Med. 30:672-679 (1993).*

Ralf Mekle & Giulio Gambarota

QUANTIFICATION

☹Vendors software - visualization of spectra

☹Peak fitting - !!!! Overlapping peaks ☹

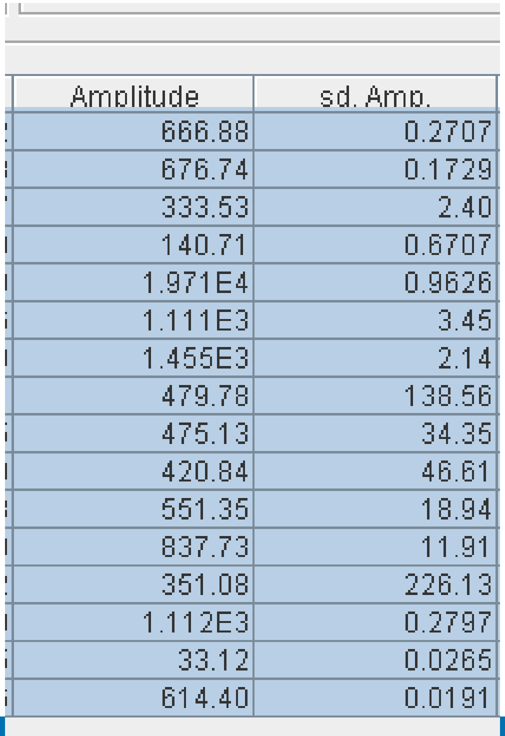
☺X nuclei

☺"Basis-set" fitting – In vivo MRS spectrum is modelled as a linear combination of individual metabolite basis spectra

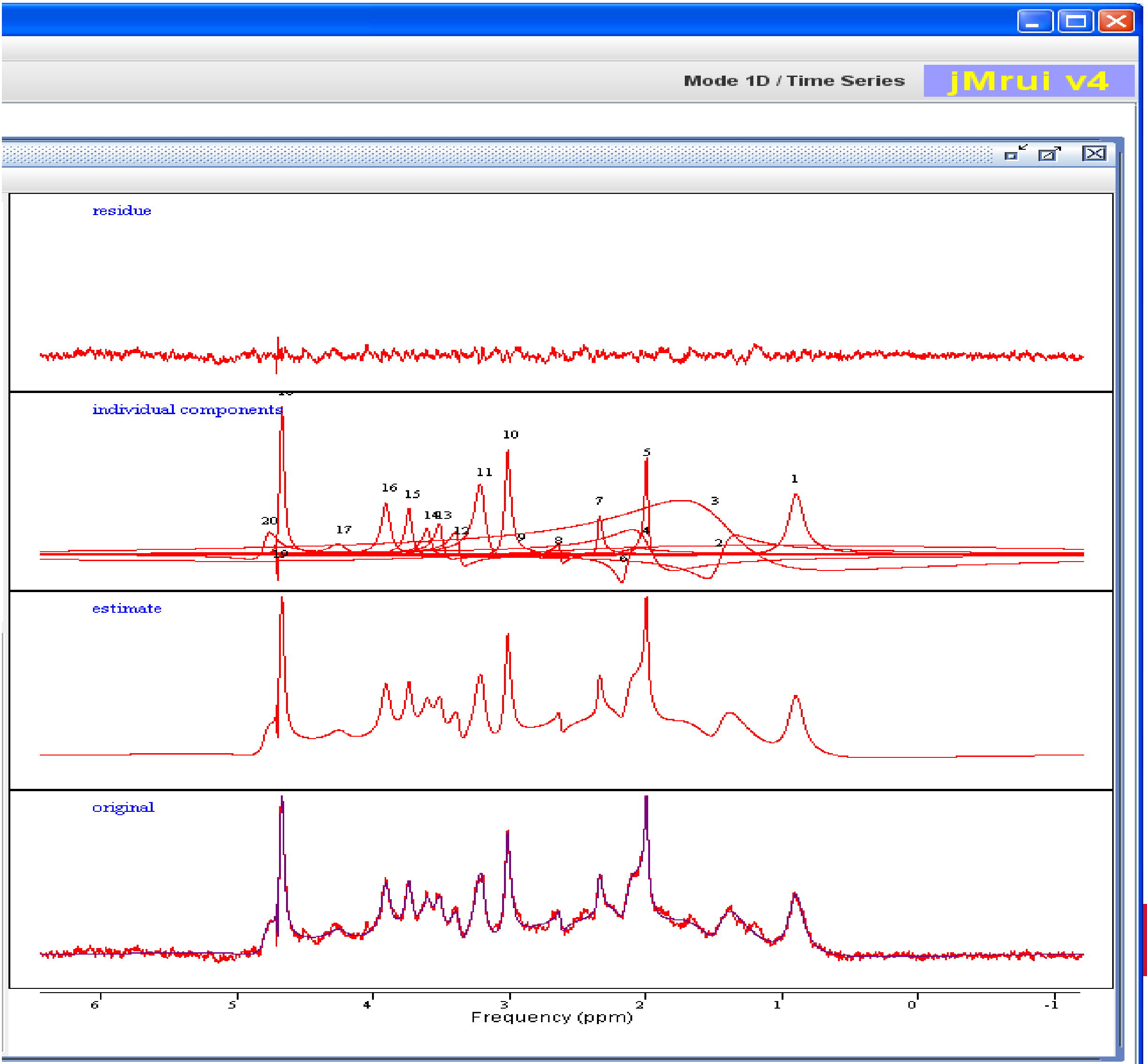
- Experimentally
- Simulated
  - User-friendly software packages: NMRScopeB, Vespa, GAMMA, GAVA, ….
- Macromolecules contribution
- Lipids contribution (i.e. malignant brain tumors)

SHORT DESCRIPTION OF THE ALGORITHMS

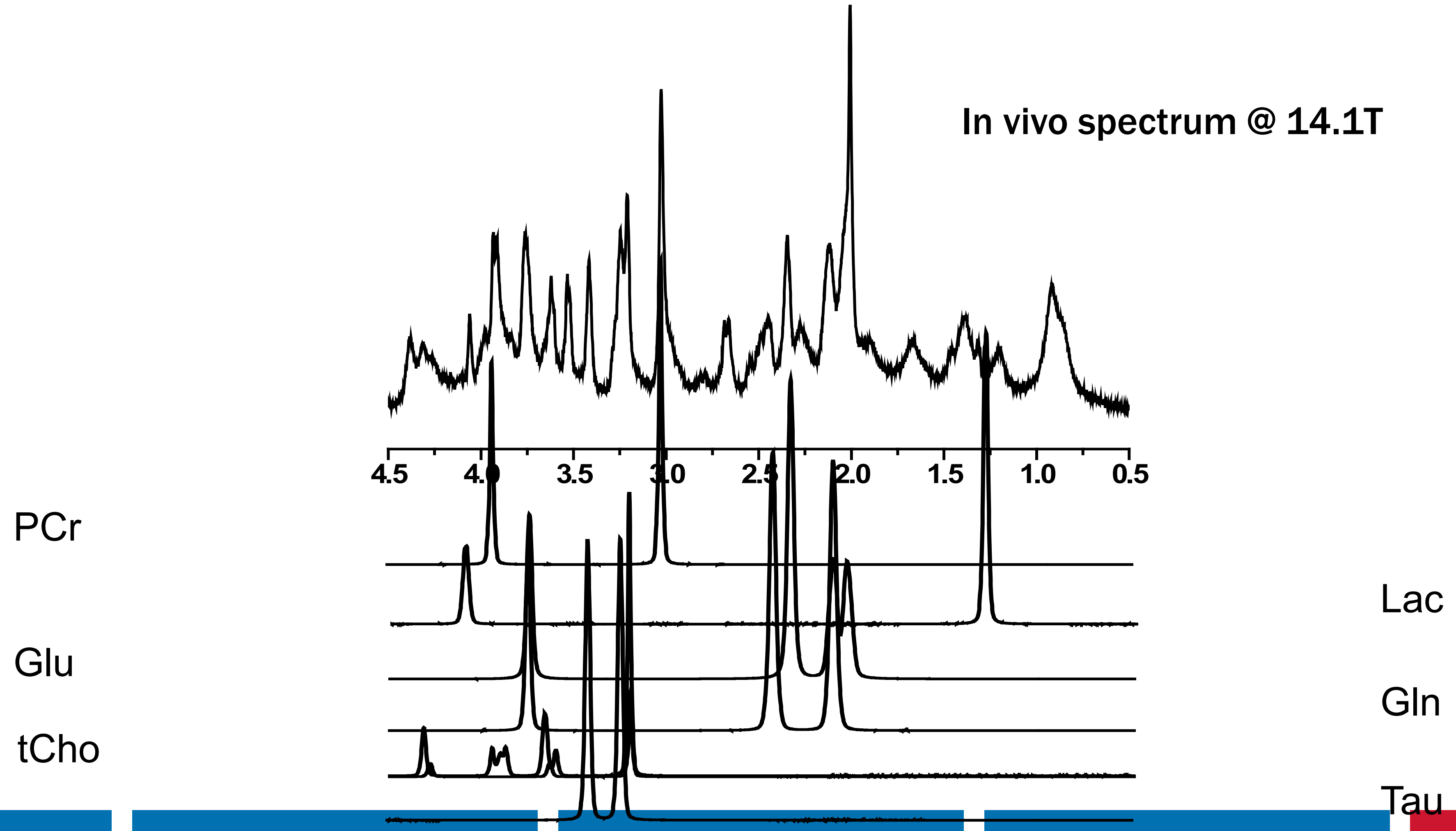
HLSVD quantification



Amplitude	sd. Amp.
666.88	0.2707
676.74	0.1729
333.53	2.40
140.71	0.6707
1.971E4	0.9626
1.111E3	3.45
1.455E3	2.14
479.78	138.56
475.13	34.35
420.84	46.61
551.35	18.94
837.73	11.91
351.08	226.13
1.112E3	0.2797
33.12	0.0265
614.40	0.0191



QUANTIFICATION WITH A BASIS SET



■ ■ ■ ■

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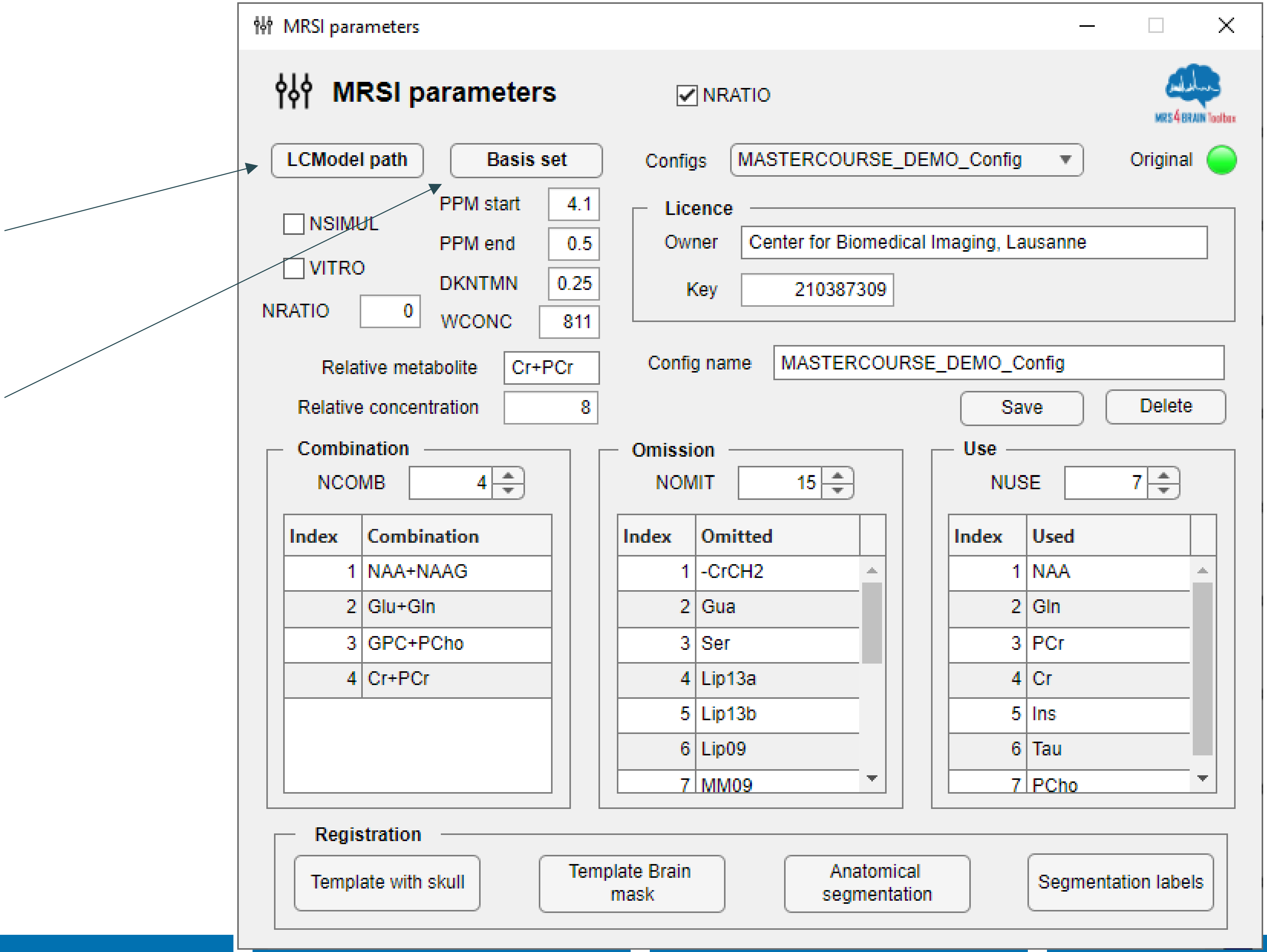

MRSI parameters

☑ NRATIO

Configs: MASTERCOURSE_DEMO_Config ▾

Original ●

☐ NSIMUL
☐ VITRO

NRATIO: 0

PPM start: 4.1
PPM end: 0.5
DKNTMN: 0.25
WCONC: 811

Licence
Owner: Center for Biomedical Imaging, Lausanne
Key: 210387309

Relative metabolite: Cr+PCr
Relative concentration: 8

Config name: MASTERCOURSE_DEMO_Config

Combination
NCOMB: 4

Index	Combination
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2	Glu+Gln
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Omission
NOMIT: 15

Index	Omitted
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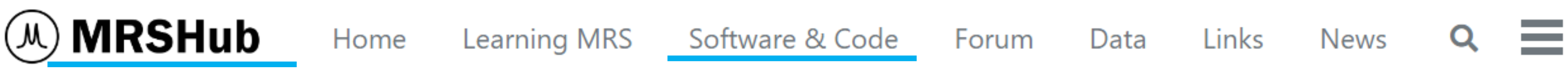
2	Gua
3	Ser
4	Lip13a
5	Lip13b
6	Lip09
7	MM09

Use
NUSE: 7

Index	Used
1	NAA
2	Gln
3	PCr
4	Cr
5	Ins
6	Tau
7	PCho

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

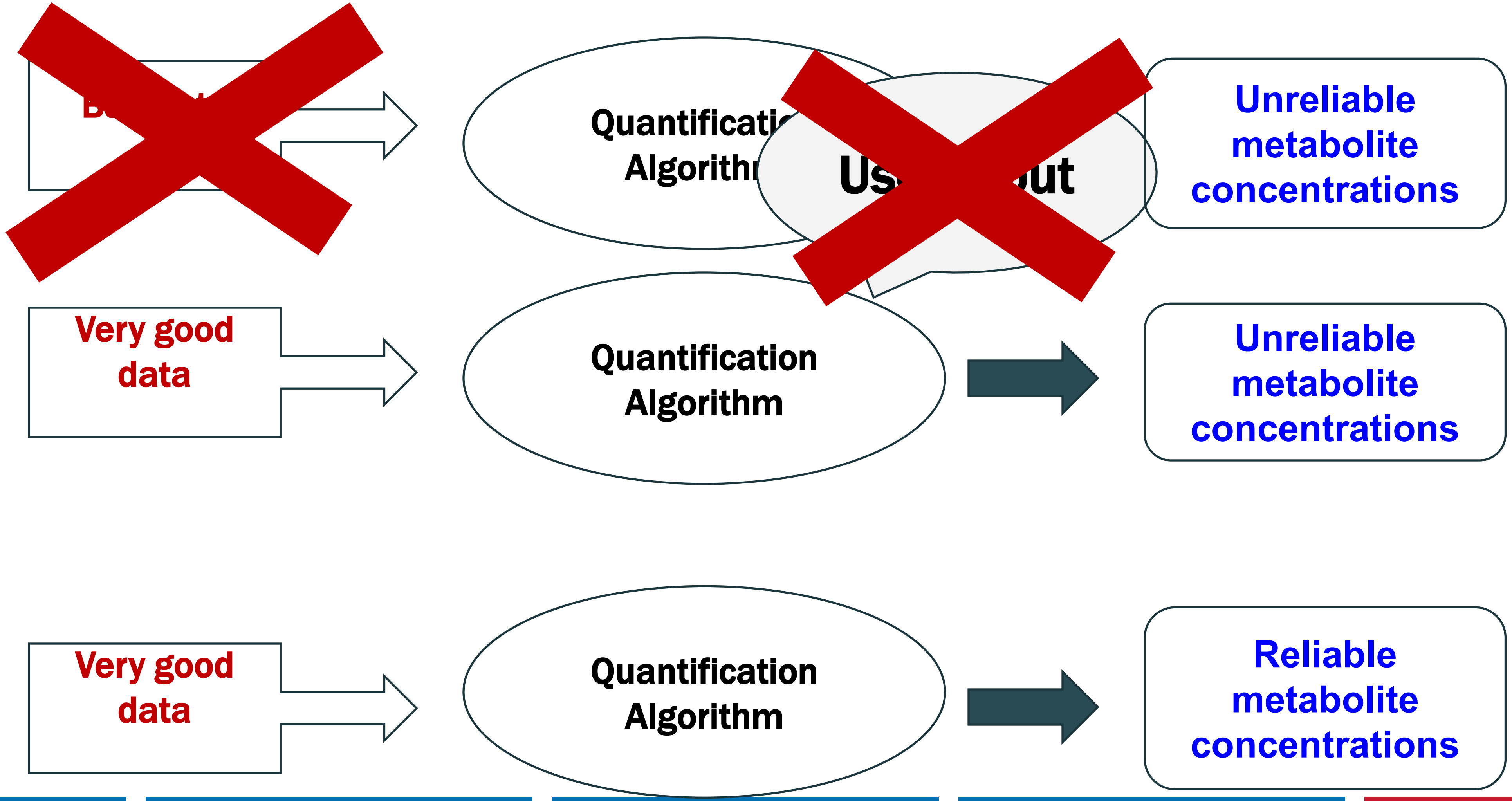
QUANTIFICATION SOFTWARE



	Cost	Type of data	Preprocessing	Simulations	Lineshape model	MM
Vespa	free	all	yes	yes	yes	yes
TARQUIN	free	all	yes	Yes – basic	Voigt	Baseline –TD Add
jMRUI	free	all	yes	yes	Lorentzian	Add TD
LCModel	Yes	all	yes	No Basis sets	estimated	Splines

Anke Henning. eMagRes, 2016, Vol 5: 981–994. DOI 10.1002/9780470034590.emrstm1472
Dirk van Ormondt, et al, eMagRes, 2015, Vol 4: 651–662. DOI 10.1002/9780470034590.emrstm1427
Jamie Near, Magnetic Resonance Spectrscopy Elsevier 2014
Jamie Near, et al, NMR Biomed, 2020 **https://doi.org/10.1002/nbm.4257**

https://mrs2022.cibm.ch/agenda/



B

Quantificati
Algorith

Us ut

Unreliable metabolite concentrations

Very good data

Quantification Algorithm

Unreliable metabolite concentrations

Very good data

Quantification Algorithm

Reliable metabolite concentrations

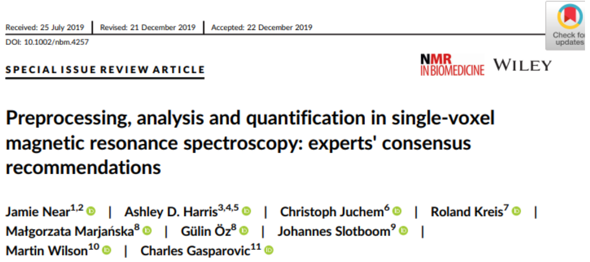
QUANTIFICATION (ABSOLUTE)

Signal amplitudes
Peak area

→

Concentrations
mmol/kg$_{ww}$

- External concentration reference
- Internal concentration reference
  - Ratios to tCr or NAA or Cho - They might change – disease
  - Water internal reference
    - Corrections for T1, T2 and water content
    - Very short TE – T2 correction could be neglected
    - Fully relaxed signals – long TR – T1 neglected
    - MT



Received: 25 July 2019 | Revised: 21 December 2019 | Accepted: 22 December 2019
DOI: 10.1002/nbm.4257

SPECIAL ISSUE REVIEW ARTICLE

NMR IN BIOMEDICINE WILEY

Preprocessing, analysis and quantification in single-voxel magnetic resonance spectroscopy: experts' consensus recommendations

Jamie Near[1,2] | Ashley D. Harris[3,4,5] | Christoph Juchem[6] | Roland Kreis[7] | Małgorzata Marjańska[8] | Gülin Öz[8] | Johannes Slotboom[9] | Martin Wilson[10] | Charles Gasparovic[11]

http://www.ismrm.org/workshops/Spectroscopy16/program.htm
2nd TRANSACT Workshop, University Bern: Quality Issues in Clinical MRS 2014
The MRS Consensus Group. (2014), Radiology, 270(3):658-79.

QUANTIFICATION QUALITY CONTROL

- CRLB – theoretical estimation
  - Assumes that the model is perfect
  - R Kreis, MRM 75, 2016 – CRLB % !!! – low conc metabolites
    - CRLB vs mean CRLB in normal cohort

- Fit residuals

QUANTIFICATION: RESULTS DISPLAY

Patient name : anonymous
Date of Birth :
Patient sex : M
Patient ID :

Accession number : 2699671
Study description : Kopf_12_Kanal
Study date : 20110630

Series description : svs_se_135_ws
Series number : 12
Series time : 155149.015000

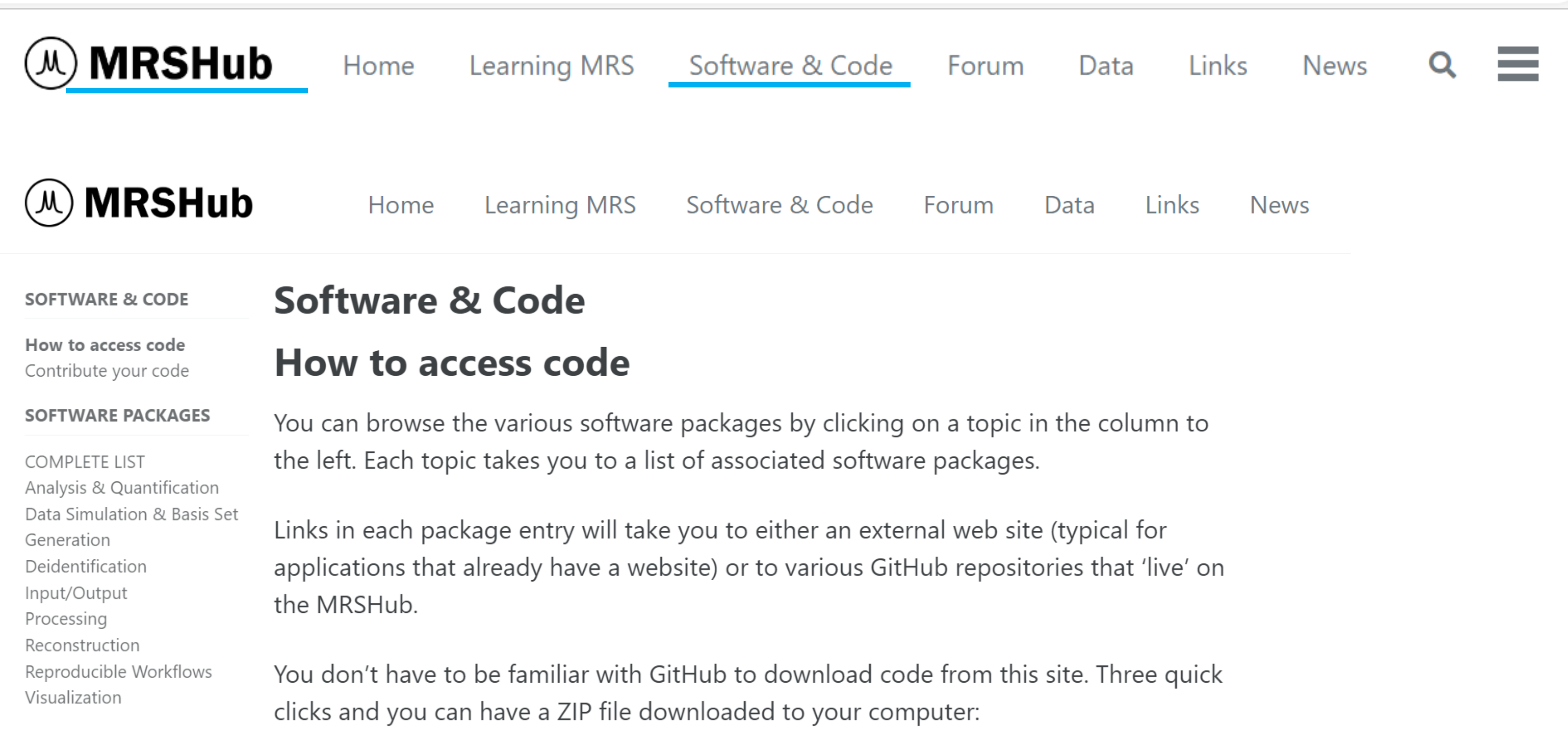
Scanner type : Verio
Echo time TE : 135000
Repetition time TR : 1500000
Voxel dimension : [15, 15, 15]

Metabolite Name	Concentrations (2 comp) [mmol/kg ww]	Normal (2 comp) [mmol/kg ww]
Choline (Cho)	8.8 ± 0.1	1.5 ± 0.1
Creatine (Cr)	7.7 ± 0.2	5.2 ± 0.1
Glutamate (Glu)	6.6 ± 0.4	3.7 ± 0.2
Glutamine (Gln)	4.4 ± 0.3	2.2 ± 0.1
Lactate (Lac)	1.2 ± 0.2	0.3 ± 0.1
Myo-inositol (m-Ins)	20.7 ± 1.2	7.8 ± 0.4
N-Acetyl Aspartate (NAA)	4.9 ± 0.2	7.5 ± 0.2

For scientific purposes only!
Report created with jMRUI.

Olivier Scheidegger et al, MRM 70:25–32 (2013)

FURTHER READING



Software & Code

How to access code

You can browse the various software packages by clicking on a topic in the column to the left. Each topic takes you to a list of associated software packages.

Links in each package entry will take you to either an external web site (typical for applications that already have a website) or to various GitHub repositories that 'live' on the MRSHub.

You don't have to be familiar with GitHub to download code from this site. Three quick clicks and you can have a ZIP file downloaded to your computer:

SUMMARY & ACKNOWLEDGMENTS

MRS & MRSI is incredibly rich & versatile ☺

Thank you for listening! Questions?

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

cristina.cudalbu@epfl.ch

CIBM
Center for Biomedical Imaging

THANK YOU FOR YOUR ATTENTION

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