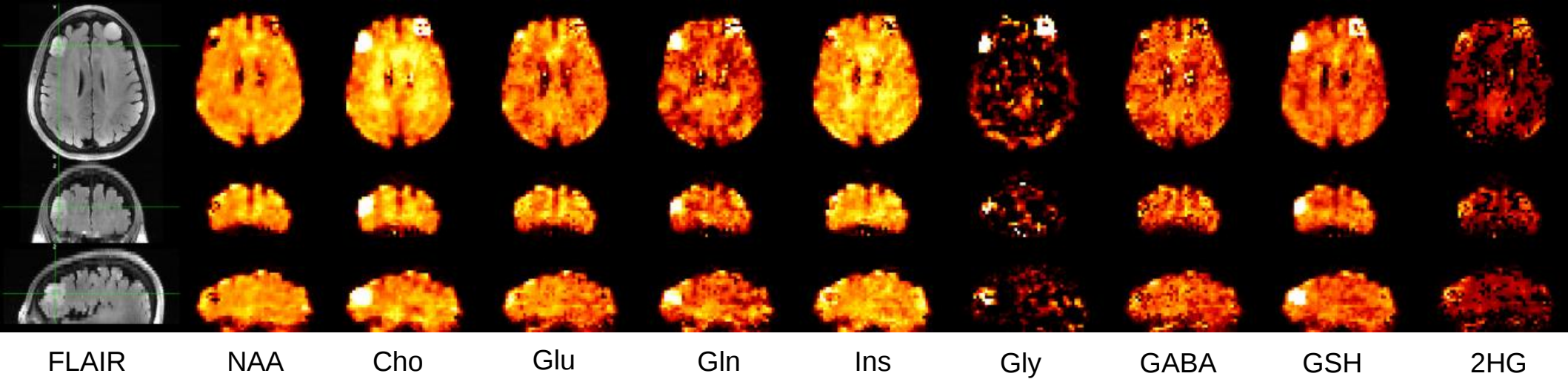




Fast Magnetic Resonance Spectroscopic Imaging and Reconstruction Techniques

Antoine Delattre-Klauser, PhD
On-Site Scientist

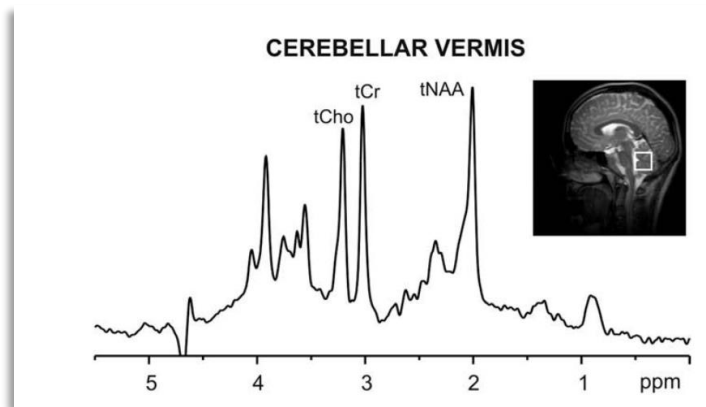


Advanced Clinical Imaging Technology

What message I want to you take home:

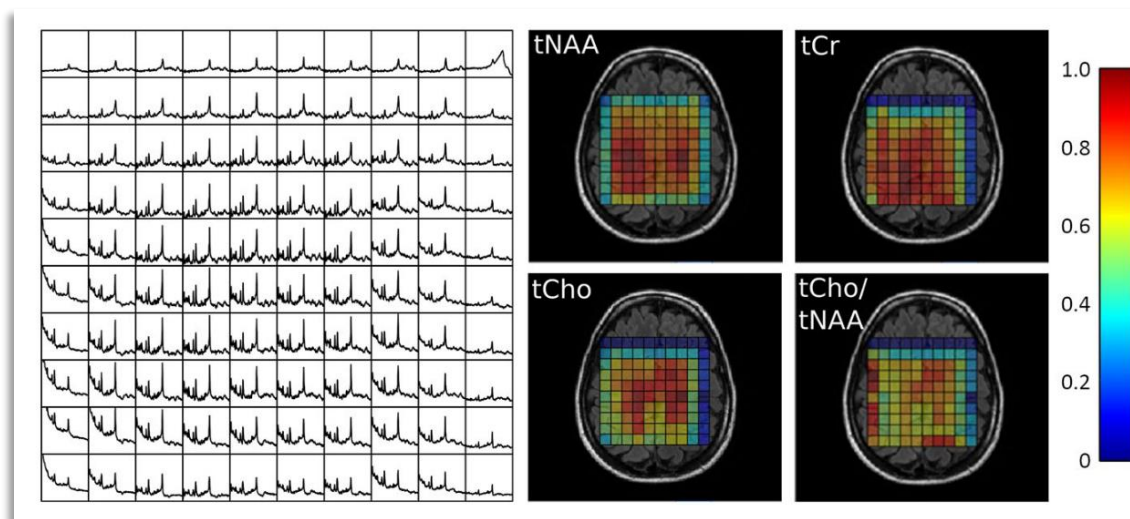
- What are the general limitations with MRSI
- How we can tackle these limitations
- Why do we need to push for higher-resolution full brain MRSI

From classical magnetic resonance spectroscopy...



Consensus* acquisition parameters:

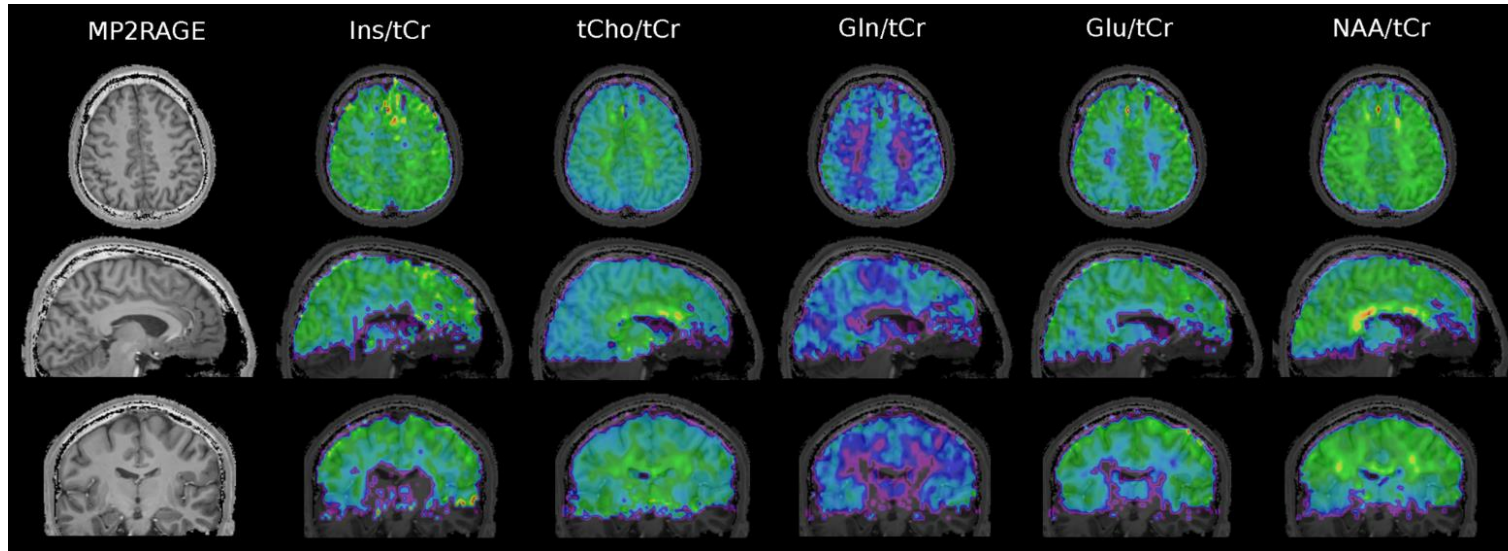
- Voxel 25x25x25mm³
- 5min Acq. Time



- Voxels 10x10x15mm³
- 20x20 FOV (2D)
- 13min Acq. Time

*Wilson, M., et al. (2019). Methodological consensus on clinical proton MRS of the brain: Review and recommendations. MRM, 82(2), 527–550.

... To High-Resolution Whole-Brain magnetic resonance spectroscopic imaging



State-of-the-Art H-R W-B MRSI
Parameters *:

- Voxels 3 x 3 x 3 mm
- 80 x 80 x 47 matrix (3D)
- No volume selection
- 15min Acq. Time

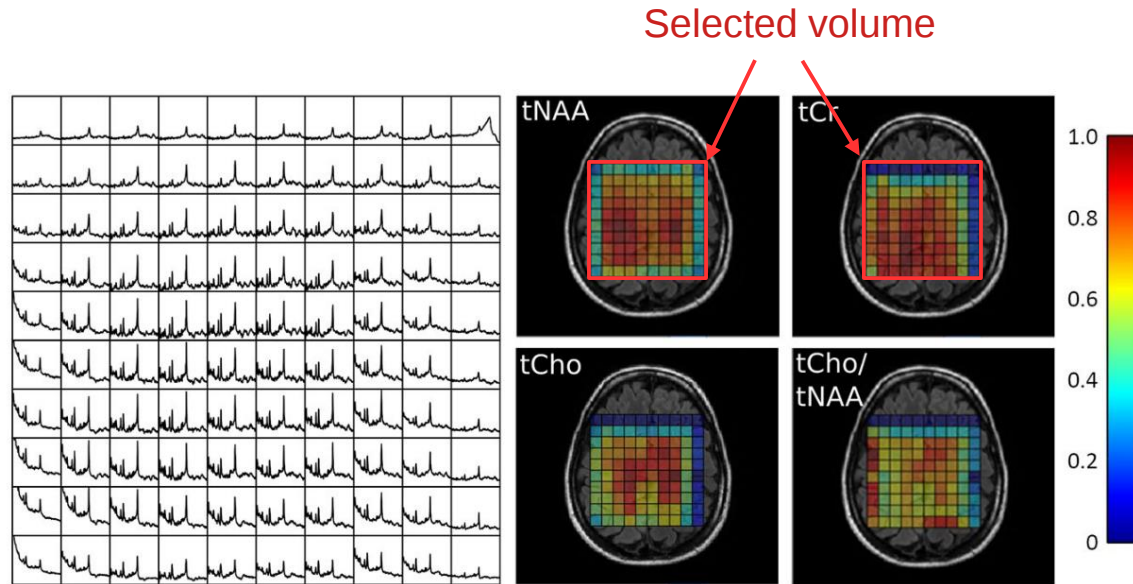
*Hingerl, L. et al. (2019). Clinical High-Resolution 3D-MR Spectroscopic Imaging of the Human Brain at 7 T. *Investigative Radiology*,

➤ Magnetic Resonance Spectroscopic Imaging (MRSI):
What are the limitations?

- Fast and High resolution MRSI:
Key ingredients
- Reconstruction as solution to the inverse-problem
- Few applications

Magnetic Resonance Spectroscopic Imaging (MRSI): What are the limitations?

MR Spectroscopic Imaging (MRSI, also CSI / Multi-voxel MRS)



2D MRSI 10x10x15mm, 13min Acq. time

- Technique that combines
 - Rectangular VOI selection (MRS)
 - Spatial 2D/3D phase encoding (MRI)
- But
 - Signal only in the Rectangular VOI
 - Slow acquisition of the 3D/4D (k,t)-space:
 - 2D ~10min
 - 3D ~20-30min
 - Low resolution (> 10mm)

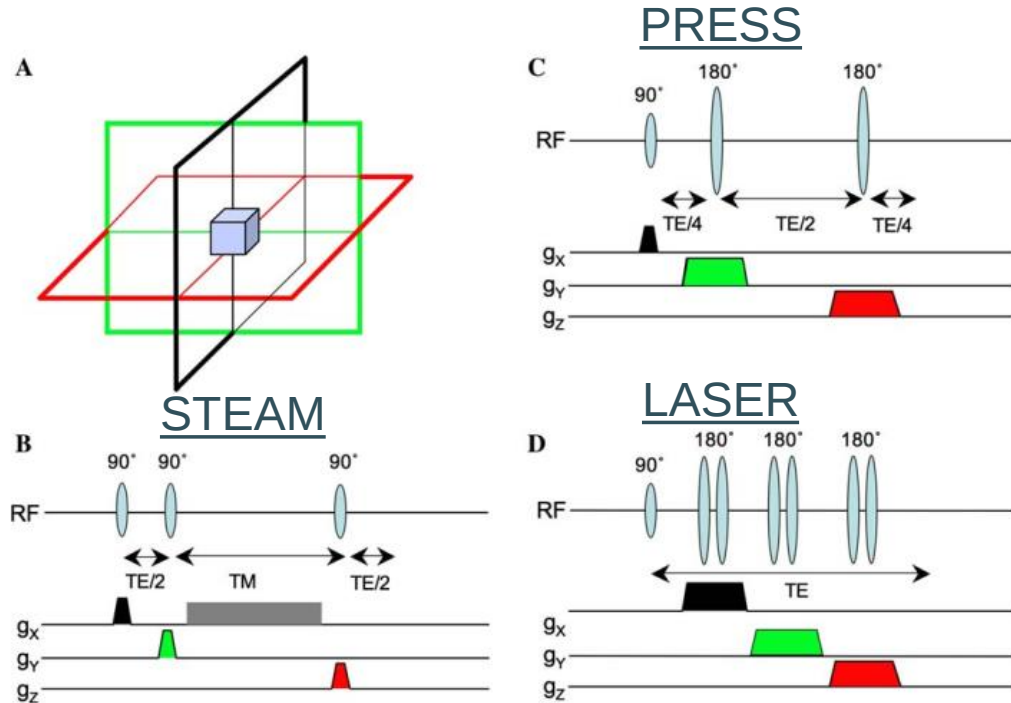
Magnetic Resonance Spectroscopic Imaging (MRSI): What are the limitations?

Sequences with volume selection

- To measure spectrum from this location only
- To prevent signal contamination by other part of the brain (or body)

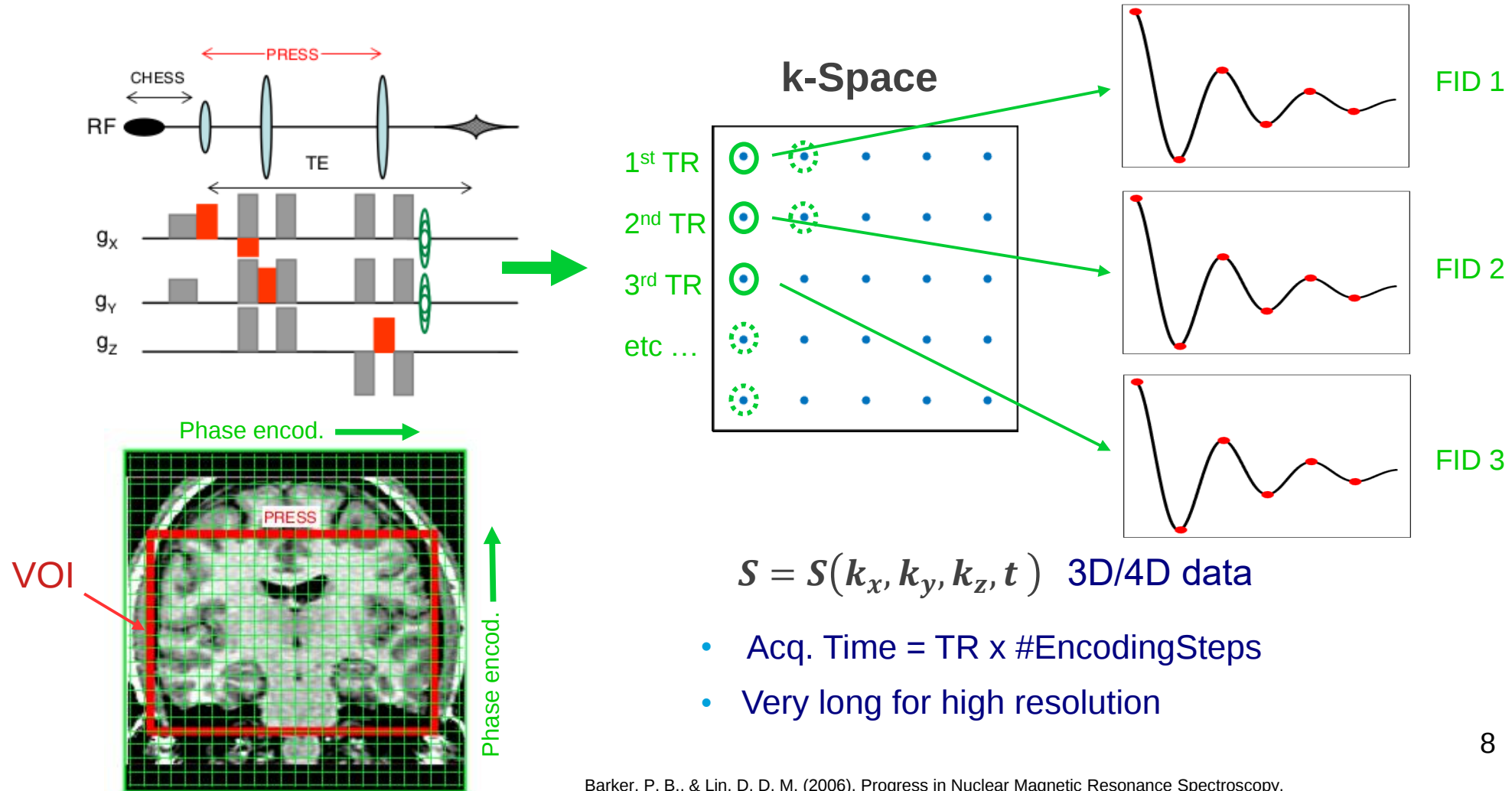
But

- Take some time (long TE, long TR)



Barker, P. B., & Lin, D. D. M. (2006, September 30). In vivo proton MR spectroscopy of the human brain. Progress in Nuclear Magnetic Resonance Spectroscopy.

Magnetic Resonance Spectroscopic Imaging (MRSI): What are the limitations?



Magnetic Resonance Spectroscopic Imaging (MRSI): What are the limitations?



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Contents lists available at ScienceDirect

NeuroImage

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

Ultra-high resolution brain metabolite mapping at 7 T by short-TR Hadamard-encoded FID-MRSI[☆]

Gilbert Hangel^a, Bernhard Strasser^a, Michal Považan^b, Eva Heckova^a, Lukas Hingerl^a,
Roland Boubela^a, Stephan Gruber^a, Siegfried Trattnig^b, Wolfgang Bogner^{a,*}

^a High Field MR Center, Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Austria

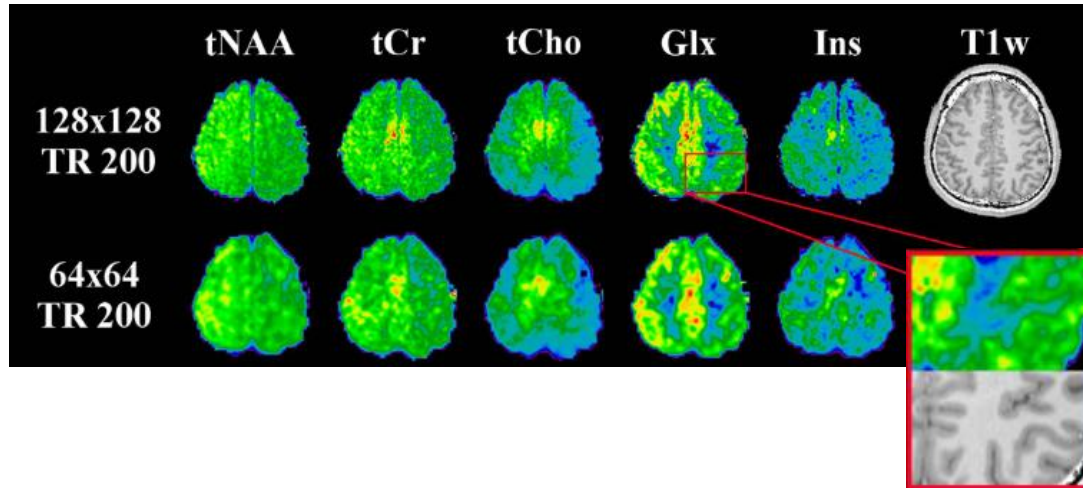
^b High Field MR Center, Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Christian Doppler Laboratory for Clinical Molecular MR Imaging, Austria

High and ultra-high resolution metabolite mapping of the human brain using ¹H FID MRSI at 9.4T

Sahar Nassirpour^{a,b,*}, Paul Chang^{a,b}, Anke Henning^a

^a Max Planck Institute for Biological Cybernetics, Spemannstr. 41, Tübingen 72076, Germany

^b IMPRS for Cognitive and Systems Neuroscience, Eberhard Karls University of Tübingen, Tübingen, Germany

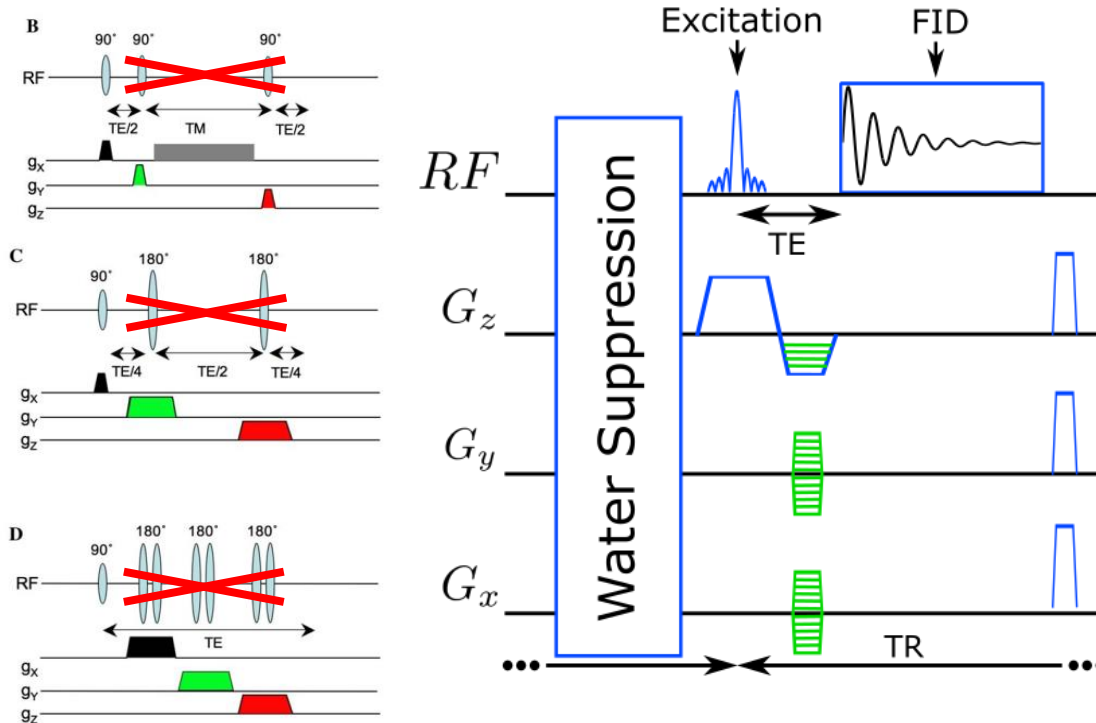


- FID-MRSI sequence (short TR)
- Ultra-High Field MRI (≥ 7 T)
- **2D** MRSI in High-resolution:
 $2 \times 2 \times 10 \text{ mm}^3$
- Whole-Brain coverage

- Magnetic Resonance Spectroscopic Imaging (MRSI):
What are the limitations?
- Fast and High resolution MRSI:
Key ingredients
- Reconstruction as solution to the inverse-problem
- Few applications

Key ingredients : the sequence

- Acquisition Time = $\text{TR} \times \text{\#EncodingSteps}$



FID-MRSI Sequence:

- Short TR (200-500ms)
- Low Excitation Flip Angle
- Ultra short TE (~ 1ms)

But:

- No VOI selective excitation for full brain acquisition, solution needed for lipid contamination
- No Spin Echo
- Possible T_1 weighting in signal

- Henning, A. *et al.* (2009). Slice-selective FID acquisition, localized by outer volume suppression (FIDLOVS) for (1)H-MRSI of the human brain at 7 T with minimal signal loss. *NMR Biomed*, 22(7), 683–696.
- Bogner, W. *et al.* (2012). High-resolution mapping of human brain metabolites by free induction decay 1H MRSI at 7 T. *NMR in Biomedicine*, 25(6), 873–882.

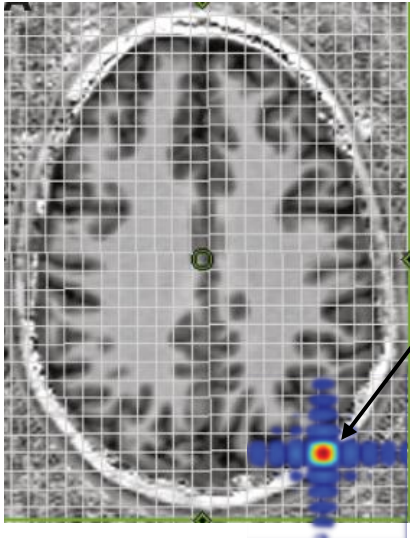
Key ingredients : the lipid signal suppression

Problem:

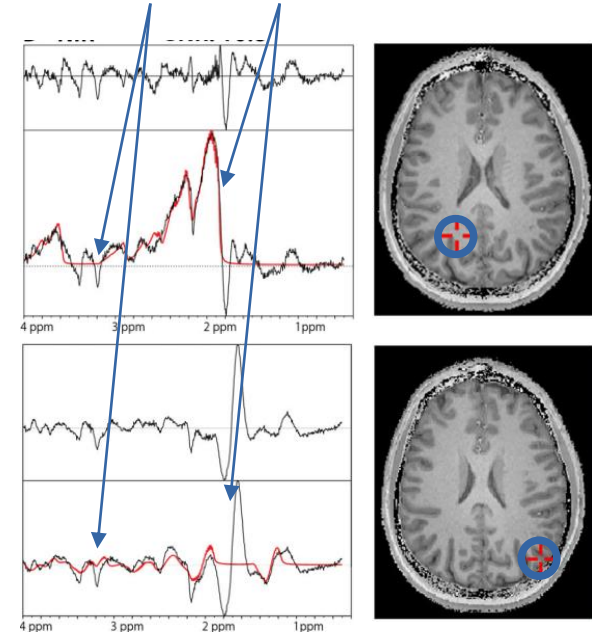
- Without VOI selective, whole slab is excited
- Lipid signal at the skull contaminates the entire FOV via point-spread-function (PSF)
- Metabolite signal ($\ll$ Lipids) fully overlapped

Solutions^{1,2}:

- RF-Pulses
- K-space filtering/extrapolation
- Model-based removal



Cre Lipids



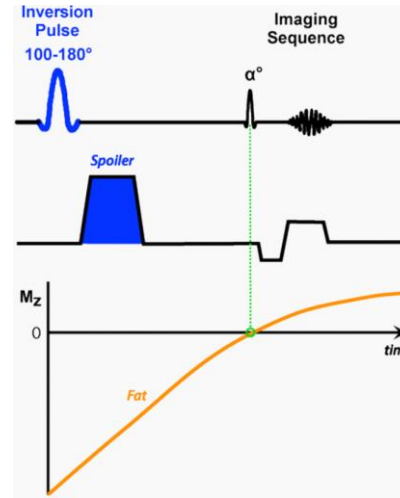
2D FID-MRSI, 7T, TE=1ms
Hangel G, et al (2015).
NMR Biomed;28(11):1413-1425.

1. Tkáč I, Deelchand D, Dreher W, et al. Water and lipid suppression techniques for advanced ^1H MRS and MRSI of the human brain: Experts' consensus recommendations. NMR Biomed. 2021;34(5). doi:10.1002/nbm.4459
2. Hangel G, Strasser B, Považan M, et al. Ultra-high resolution brain metabolite mapping at 7 T by short-TR Hadamard-encoded FID-MRSI. Neuroimage. 2018;168(October):199-210. doi:10.1016/j.neuroimage.2016.10.043

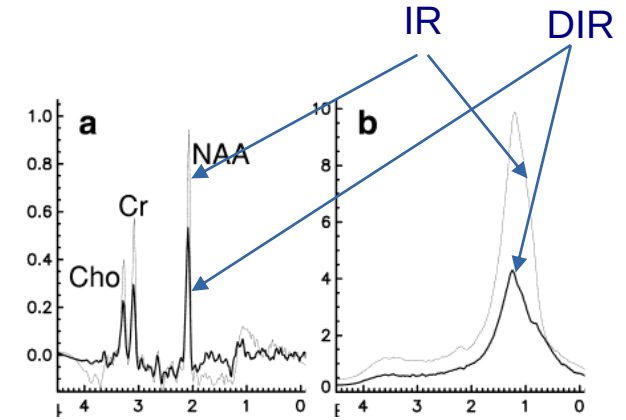
Key ingredients : the lipid signal suppression

Solution 1: RF Pulses

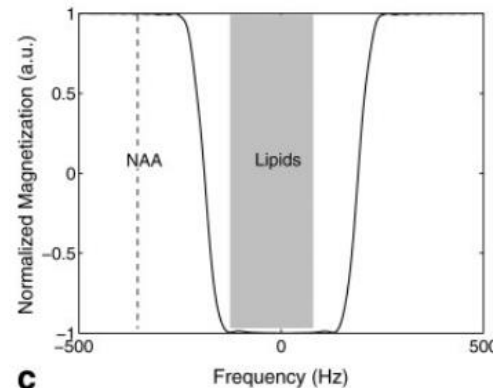
- Inversion-Recovery (IR), Double-Inversion-Recovery (DIR) schemes (but High SAR, Metabolite signal attenuation, might depends on B_1)
- Freq.-selective inversion RF-pulse (low SAR, but depends on B_0 shim quality)
- For both techniques : sequence TR increased by 200ms



<https://mriquestions.com/spir.html>



Ebel A, et al. (2003) Magn Reson Med. 2003;49(5):903-908.

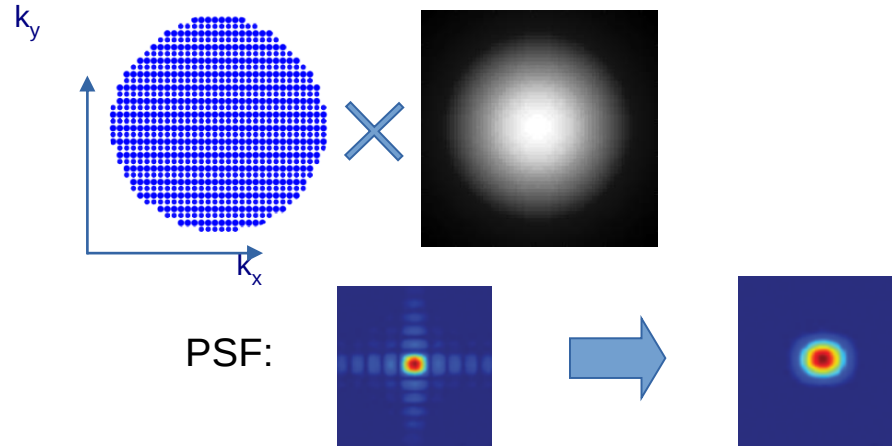


Balchandani P et al (2008). Magn Reson Med;59(5):980-988. doi:10.1002/MRM.21537

Key ingredients : the lipid signal suppression

Solution 2: k-space filter

- Apply filter on k-space data to truncate the PSF¹
- Optimize the encoding operator (forward model) to reduce range of the PSF²
- Implementation of Papoulis-Gerchberg algo. to extrapolate higher k-space values to null the lipid signal in the brain³



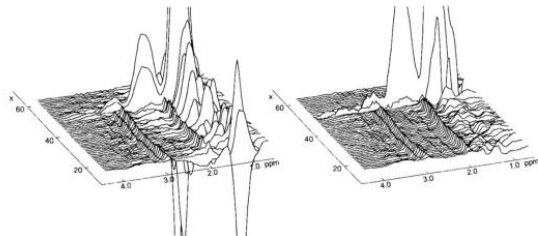
1. Bogner W, Gruber S, Trattnig S, Chmelik M. High-resolution mapping of human brain metabolites by free induction decay 1H MRSI at 7 T. NMR Biomed. 2012;25(6):873-882. doi:10.1002/nbm.1805

2. Kirchner T, Fillmer A, Tsao J, Pruessmann KP, Henning A. Reduction of voxel bleeding in highly accelerated parallel 1H MRSI by direct control of the spatial response function. Magn Reson Med. 2015;73(2):469-480. doi:10.1002/mrm.251851.

3. Haupt CI, Schuff N, Weiner MW, Maudsley AA. Removal of lipid artifacts in 1H spectroscopic imaging by data extrapolation. Magn Reson Med. 1996;35(5):678-687. doi:10.1002/mrm.1910350509

No Lip. Supp.

PG



Key ingredients : the lipid signal suppression

Solution 2: Model based methods^{1,2}

- Processing methods using metabolite-lipid orthogonality :

$$\int s_{metab.}(\omega) \cdot s_{lipid}(\omega) d\omega = 0$$

$$x_{LB} = \underset{x}{\operatorname{argmin}} \underbrace{\|F_{low}x - y_{low}\|_2^2}_{\text{data consistency}} + \lambda \underbrace{\sum_{i \in M_{brain}} \|L_{low}^H x_i\|_1}_{\text{lipid-basis penalty}}$$

Bilgic, B., et al. (2014). JMRI, 40(1), 181–191.

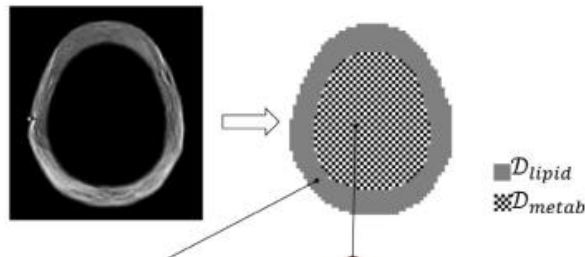
$$(\mathbb{1} - \tilde{\mathbf{P}}^c) \mathbf{s}_c = \mathbf{s}_c^{\text{LipFree}}$$

Tsai S, Lin Y, Lin H, Lin F. Magn Reson Med. 2019;81(3):1486-1498. doi:10.1002/mrm.27496

Klauser A, et al. Magn Reson Med. 2019;81(5):2841-2857. doi:10.1002/mrm.27623

- Or Lipid / Metabolite spatial support :

Scalp Segmentation & 2D Mask Generation



$$\rho(\mathbf{x}, t) = \rho_M(\mathbf{x}, t) + \rho_L(\mathbf{x}, t) + \rho_W(\mathbf{x}, t)$$

$$= \sum_{p=1}^{P_M} u_{M,p}(\mathbf{x}) v_{M,p}(t) + \sum_{p=1}^{P_L} u_{L,p}(\mathbf{x}) v_{L,p}(t) + \sum_{p=1}^{P_W} u_{W,p}(\mathbf{x}) v_{W,p}(t),$$

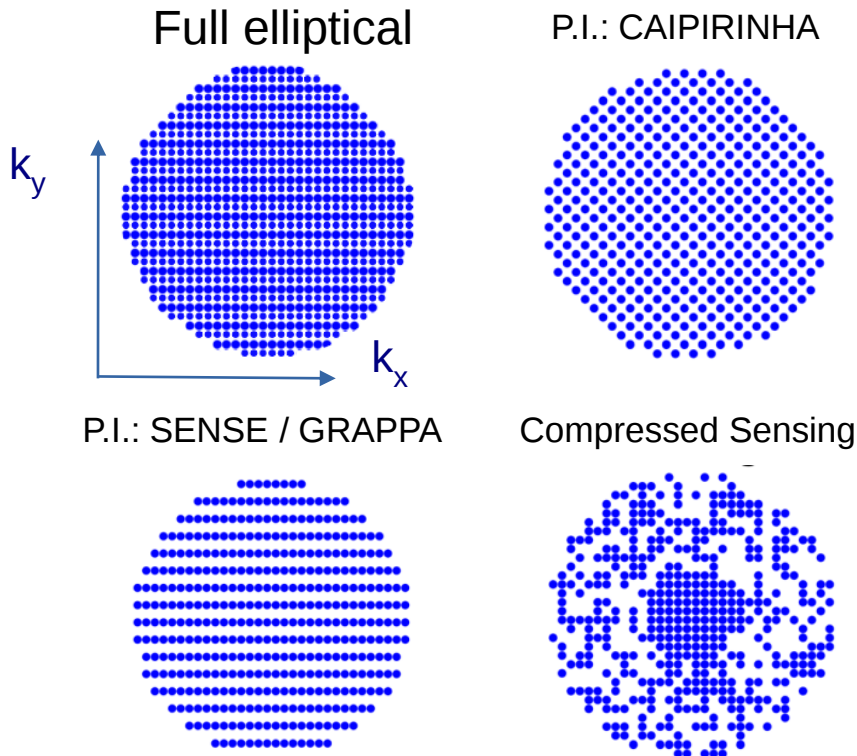
Ma C, Lam F, Johnson CL, Liang Z-P. Magn Reson Med. 2016;75(2):488-497. doi: 10.1002/mrm.25635

Adany P, Choi I, Lee P. Magn Reson Med. August 2021:mrm.28949. doi:10.1002/MRM.28949

Key ingredients : the k-space acceleration

- Acquisition Time = $\text{TR} \times \text{\#EncodingSteps}$

2D k-space:



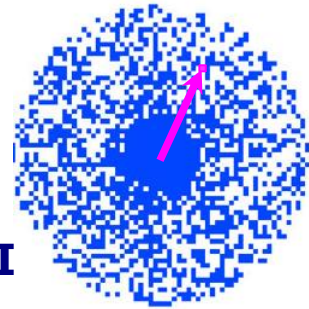
- Acceleration of the acquisition by x 2 – 4
- Calibration Data / Coil sensitivity profiles needed for SENSE / GRAPPA / CAIPI.
- Optimized SNR with Compressed Sensing

But:

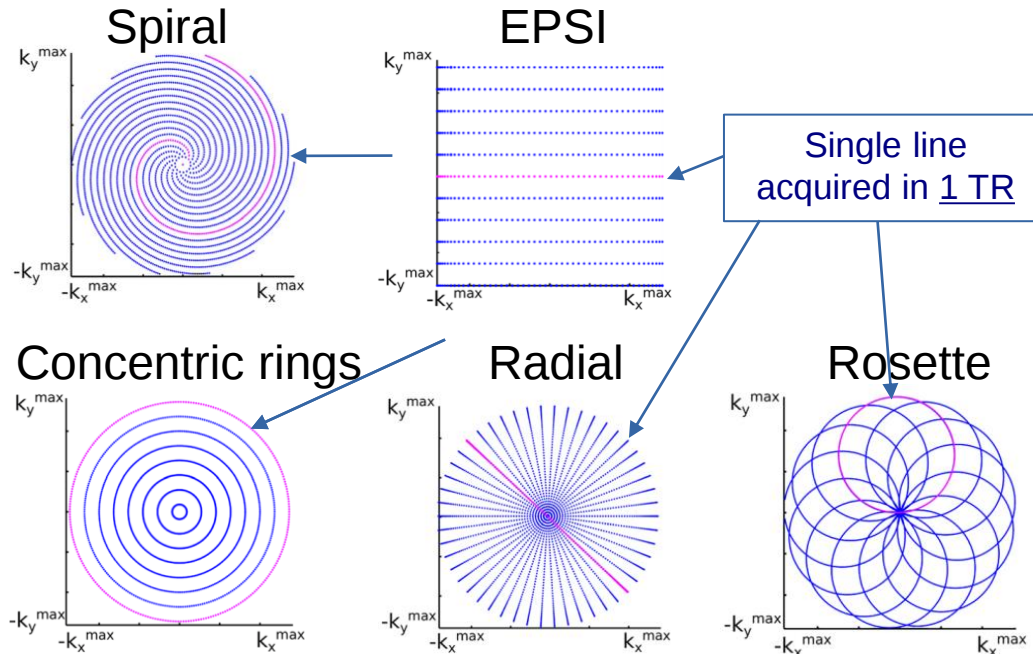
- Need for specific reconstruction with Compress Sensing that accounts for the random k-space undersampling

Key ingredients : the k-space acceleration

- **Cartesian MRSI** is inherently slow:
- **Spatial-Spectral Encoding (SSE) MRSI** provide a solution:



1 k-space FID acquired in 1 TR



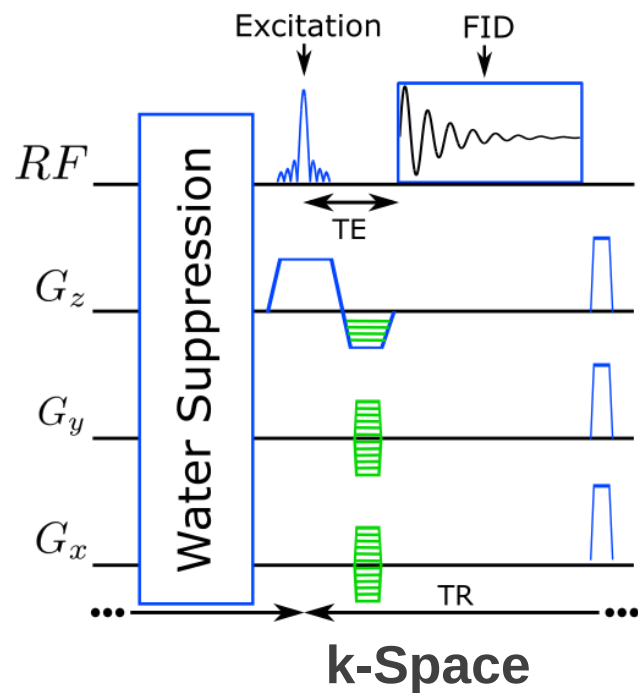
- Highly effective acceleration by x 10 – 100

But:

- Bandwidth necessary for acquisition is ~ 100 higher than conventional.
- SNR ~ 10 lower
- Several averages often necessary

Key ingredients : the k-space acceleration

Cartesian MRSI

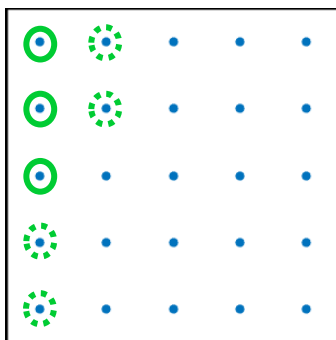


1st TR

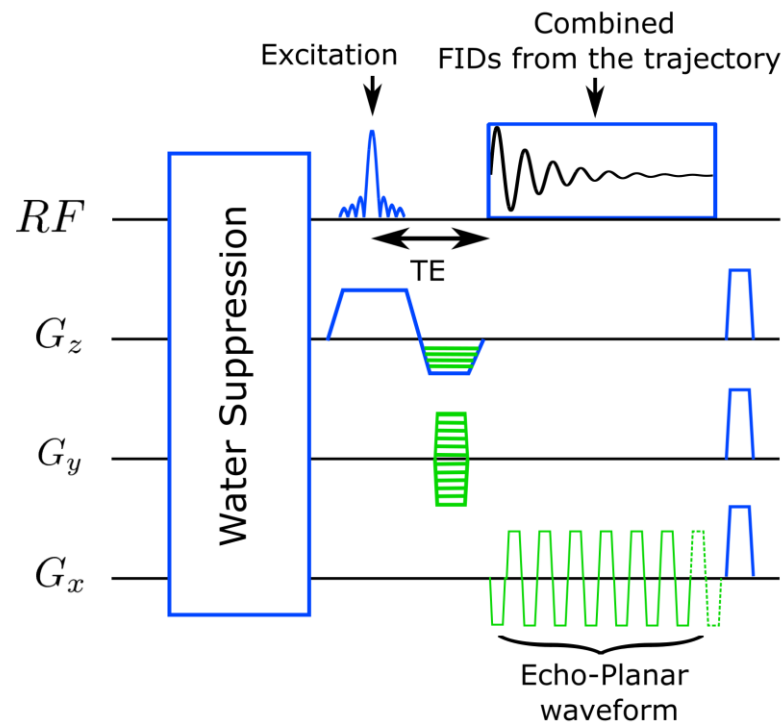
2nd TR

3rd TR

etc ...



Spatial-Spectral Encoding (SSE) MRSI



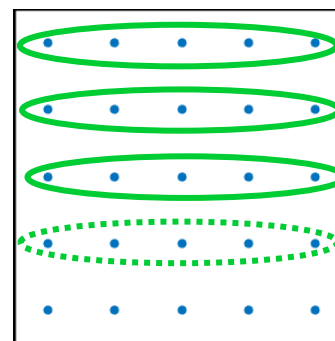
k-Space

1st TR

2nd TR

3rd TR

etc ...



Key ingredients : the k-space acceleration

- **Spatial-Spectral Encoding (SSE) MRSI**



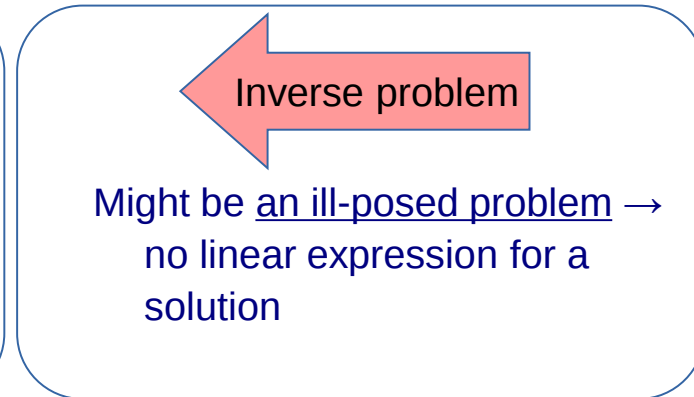
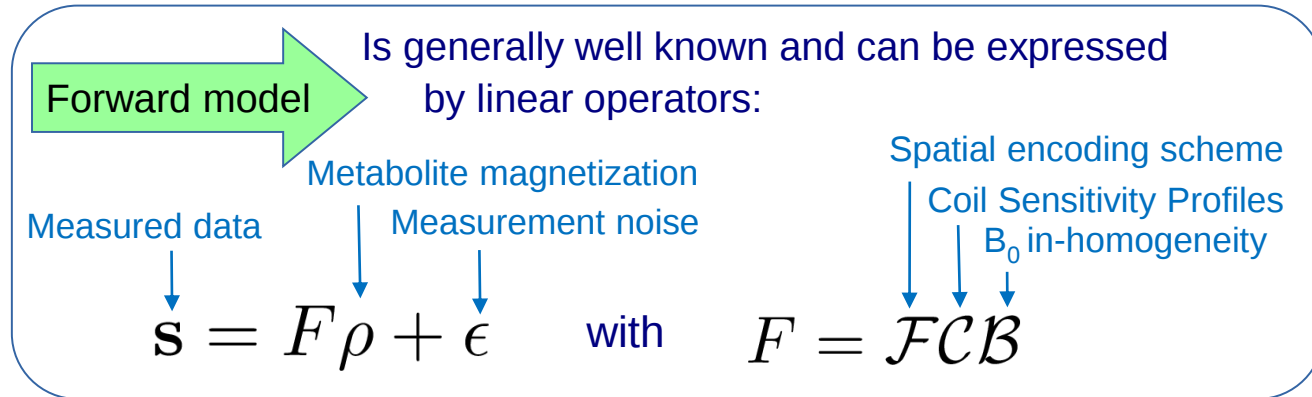
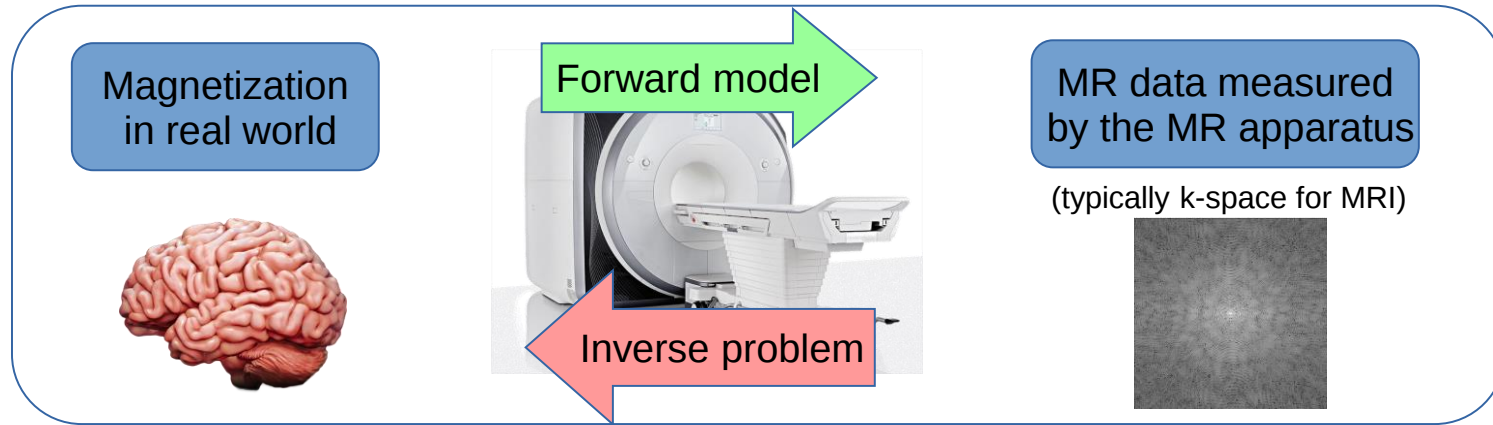
TR 1

TR 1

TR 1

- Magnetic Resonance Spectroscopic Imaging (MRSI):
What are the limitations?
- Fast and High resolution MRSI:
Key ingredients
- Reconstruction as solution to the inverse-problem
- Few applications

Reconstruction: inverse-problem solution

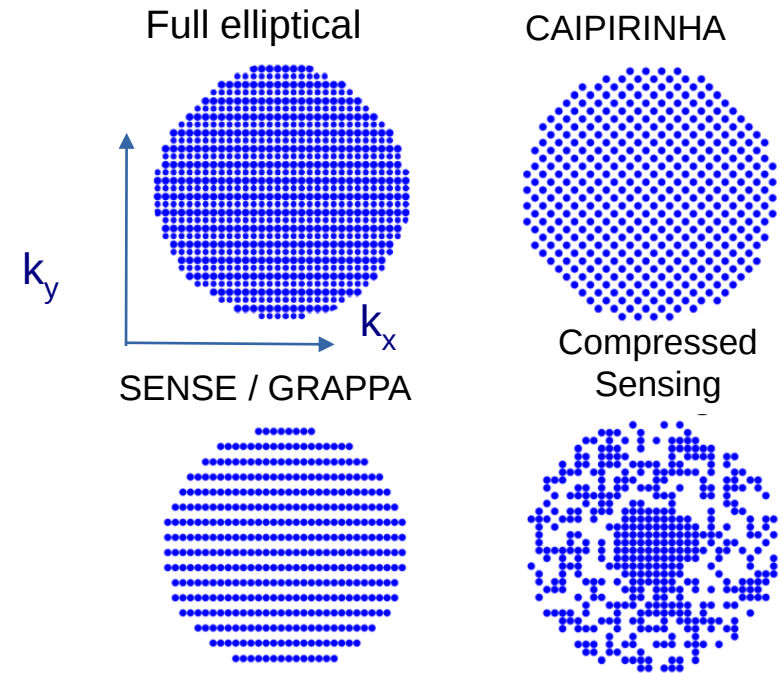


Reconstruction: inverse-problem solution

- When k-space is undersampled (e.g. for acceleration)
→ the problem is ill-posed (multiple solutions match the data)
- Retrieving the metabolite signal (the solution) is done by solving an optimization problem:

$$\arg \min_{\rho} \underbrace{\|s - F\rho\|_2^2}_{\text{Data fidelity}} + \underbrace{\lambda R\{\rho\}}_{\text{Regularization (prior knowledge)}}$$

Forward operator

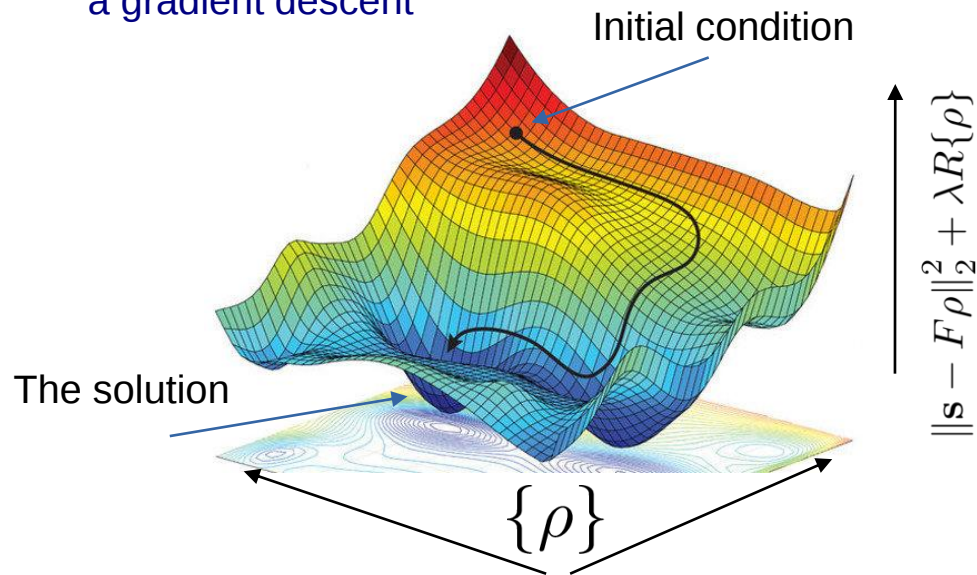


¹Lustig M, Donoho DL, Santos JM, Pauly JM. Compressed Sensing MRI. IEEE Signal Process Mag. 2008;25(2):72-82.

²Pruessmann KP, Weiger M, Börner P, Boesiger P. Advances in sensitivity encoding with arbitrary k-space trajectories. Magn Reson Med. 2001;46(4):638-651.

Reconstruction: inverse-problem solution

The minimization problem is solved by iteration:
a gradient descent



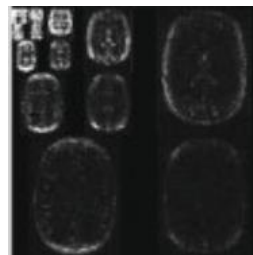
$$\arg \min_{\rho} \|s - F\rho\|_2^2 + \lambda R\{\rho\}$$

Data fidelity:
to keep solution close
to measured data

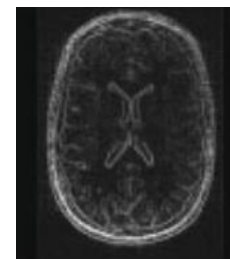
Regularization:
to penalize potential solution
with undesired features

For Compressed Sensing¹, regularization is:

Wavelet l_1 -norm



Finite difference l_1 -norm (TV)



¹Lustig M, Donoho DL, Santos JM, Pauly JM. Compressed Sensing MRI. IEEE Signal Process Mag. 2008;25(2):72-82.

²Pruessmann KP, Weiger M, Börner P, Boesiger P. Advances in sensitivity encoding with arbitrary k-space trajectories. Magn Reson Med. 2001;46(4):638-651.

Reconstruction: inverse-problem solution

Examples of accelerated Cartesian PE MRSI

Nassirpour S, Chang P, Avdievitch N, Henning A.

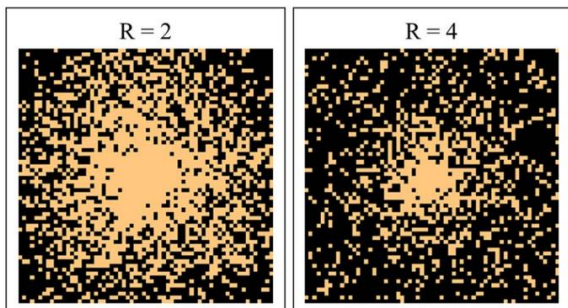
Compressed sensing for high-resolution nonlipid suppressed 1 H FID MRSI of the human brain at 9.4T.

Magn Reson Med. 2018;80(6):2311-2325.

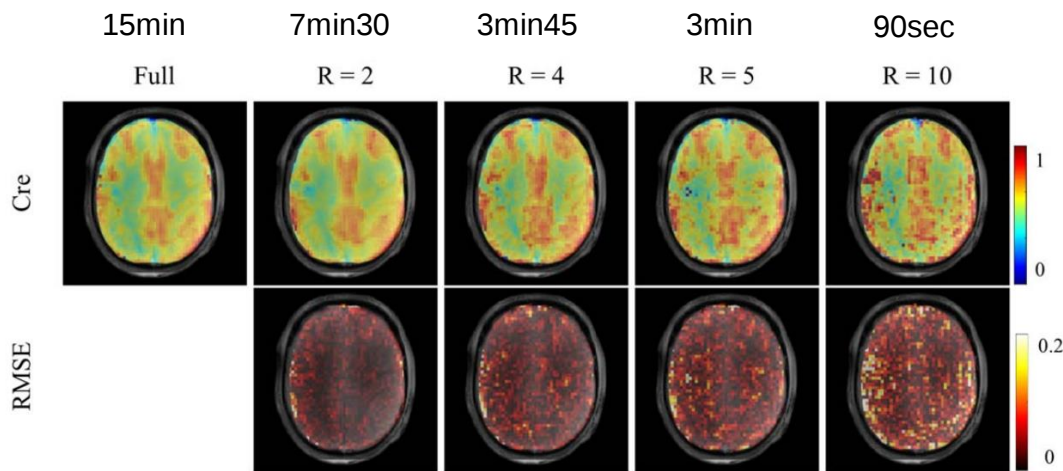
2D wavelet

3D (2D + Time) TV

$$\min_x \|\mathcal{F}_u x - y\|_2 + \lambda_1 \|\Psi x\|_1 + \lambda_2 \|TV(x)\|_1$$



7T 2D FID-MRSI : 3.4 x 3.4 x 10 mm³



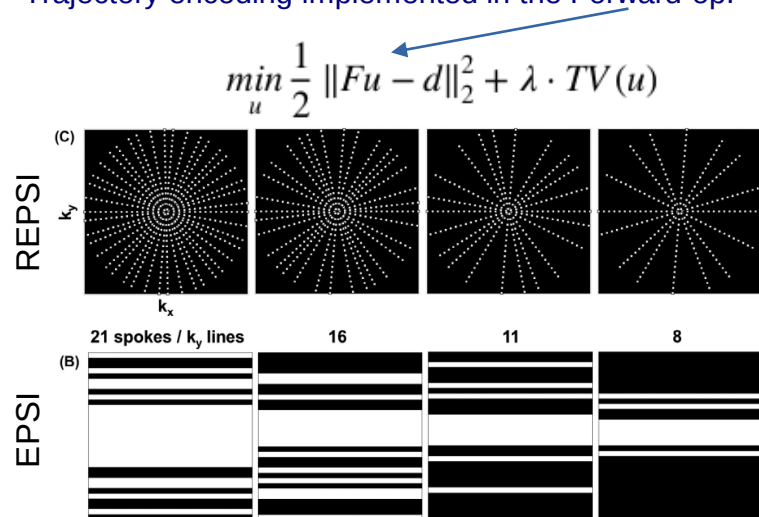
X **4-5** acceleration factor in-vivo

Reconstruction: inverse-problem solution

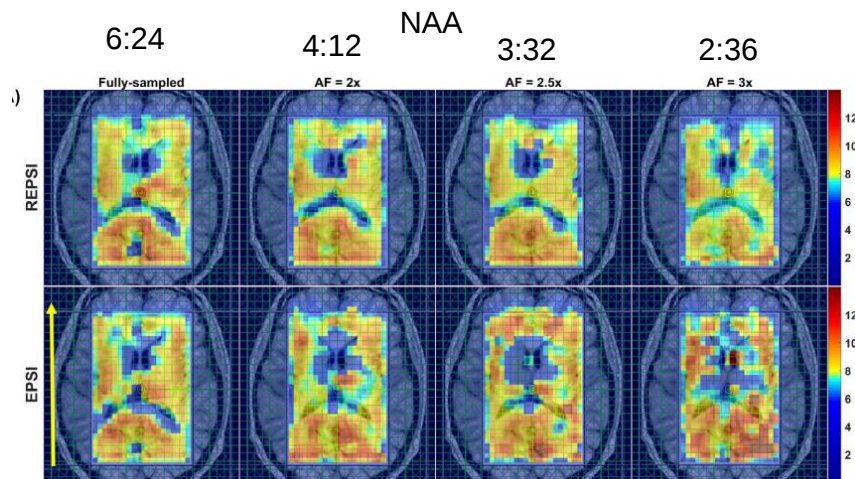
Examples of accelerated Cartesian PE MRSI

Saucedo A, Macey PM, Thomas MA. *Accelerated radial echo-planar spectroscopic imaging using golden angle view-ordering and compressed-sensing reconstruction with total variation regularization*. Magn Reson Med. 2021;86(1):46-61.

Trajectory encoding implemented in the Forward op.



3T, 2D semi-LASER, TE=40ms, 10x10x15mm³



Inverse-problem with Denoising

- Accelerated SSE MRSI is fast and whole-brain high-res MRSI can be measured quickly
- But with voxel size $< 5\text{mm}^3 \rightarrow$ low SNR

Solutions for denoising:

1. Low-Rank approximation² /

partial separability¹:

MRSI Data

Rank

$$\rho(\mathbf{r}, t) = \sum_{c=1}^K U_c(\mathbf{r}) V_c(t)$$

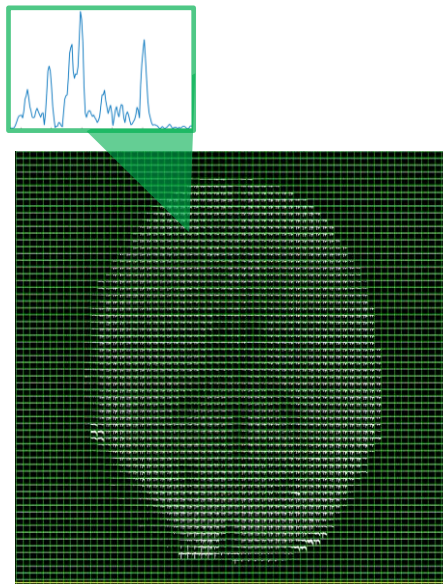
spatial components

temporal / spectral components

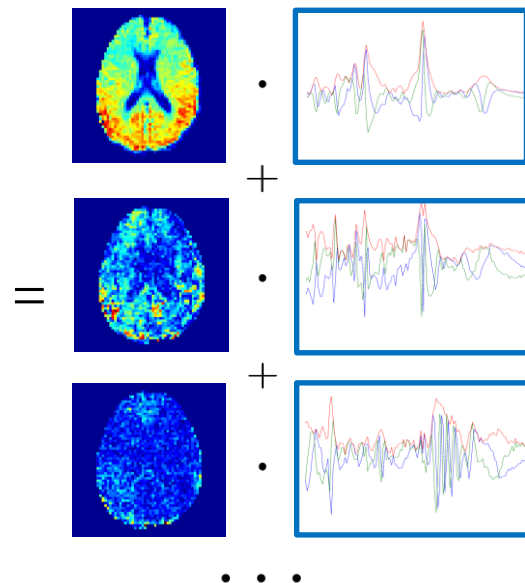
$$\arg \min_{\rho} \|\mathbf{s} - F\rho\|_2^2 + \lambda R\{\rho\}$$

$$\arg \min_{\mathbf{U}, \mathbf{V}} \|\mathbf{s} - F(\mathbf{U} \cdot \mathbf{V})\|_2^2 + \lambda R\{\rho\}$$

Much reduced DOF



Low-Rank $\rightarrow$ Keep first K components



¹ Nguyen HM, Peng X, Do MN, Liang Z-P. Denoising MR spectroscopic imaging data with low-rank approximations. *IEEE Trans Biomed Eng.* 2013;60(1):78-89.

² Kasten J, Lazeyras F, Van De Ville D. Data-Driven MRSI Spectral Localization Via Low-Rank Component Analysis. *Med Imaging, IEEE Trans.* 2013;32(10):1853-1863.

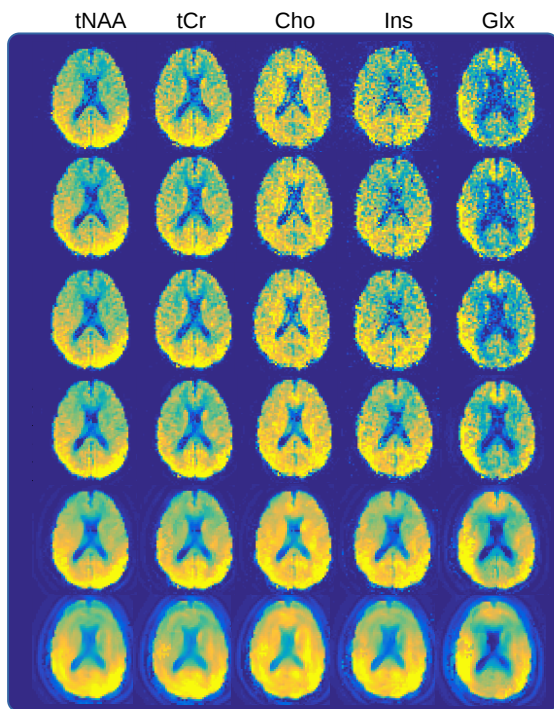
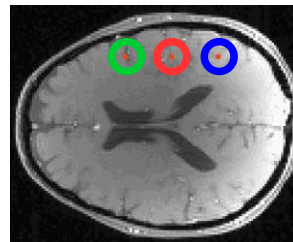
Inverse-problem with Denoising

Solutions for denoising:

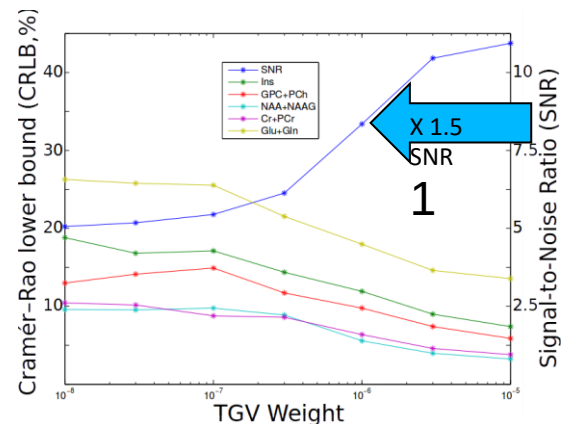
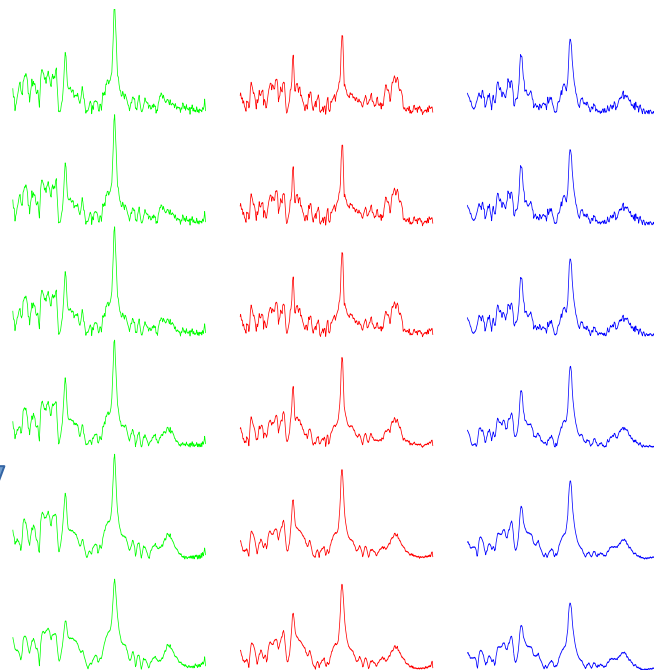
2. Regularization

2D FID-MRSI, 3T 3.5x3.5x10mm³
Cartesian, **fully** sampled (no acceleration)

$$\arg \min_{\rho} \|s - F\rho\|_2^2 + \lambda TGV_{spatial}\{\rho\}$$



TGV Regularization



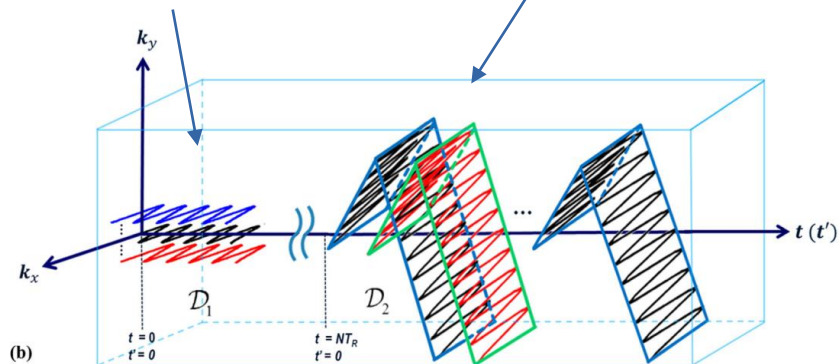
Inverse-problem with Denoising: SPICE

SPECTROscopic Imaging by exploiting spatiospectral CorrElation (SPICE),
a pioneer approach for Low-Rank Accelerated MRSI

2-steps acquisition^{1,2}:

1. High-temporal resolution acquisition to
determine the time components

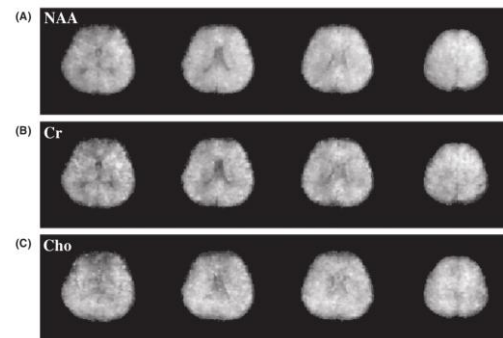
2. Fast and sparse k-space sampling to
determine the spatial components



Combine both acquisition in s Low-rank TV
Reconstruction⁶:

$$\hat{\mathbf{C}}_m, \hat{\mathbf{C}}_{MM} = \arg \min_{\mathbf{C}_m, \mathbf{C}_{MM}} \left\| \mathbf{d}_{\text{res}} - \Omega \{ \mathbf{FB} \odot (\mathbf{C}_m \Phi_m + \mathbf{C}_{MM} \Phi_{MM}) \} \right\|_2^2 + \lambda_m \left\| \mathbf{D}_w \mathbf{C}_m \right\|_F^2 + \lambda_{MM} \left\| \mathbf{C}_{MM} \right\|_F^2, \quad (4)$$

3D 2.4x2.4x3mm³ W-B MRSI in 5 min at 3T⁶



Many developments:

- FID / SE / Multi-Echo / J-resolved
- D₁ Acquisition replace by AI (autoencoder network)
- Different Sparse Sampling
- Different reconstruction model

¹ Lam F, Liang ZP. Magn Reson Med. 2014;71(4):1349-1357.

² Lam F, Ma C, Clifford B, Johnson CL, Liang Z-P. Magn Reson Med. 2016;76(4):1059-1070.

³ Peng X, Lam F, Li Y, Clifford B, Liang Z-P. Magn Reson Med. 2017;21(August 2017):13-21.

⁴ Ma C, Lam F, Ning Q, Johnson CL, Liang ZP. Magn Reson Med. 2017;77(2):467-479.

⁵ Lam F, Li Y, Clifford B, Liang Z-P. Magn Reson Med. 2018;79(5):2460-2469.

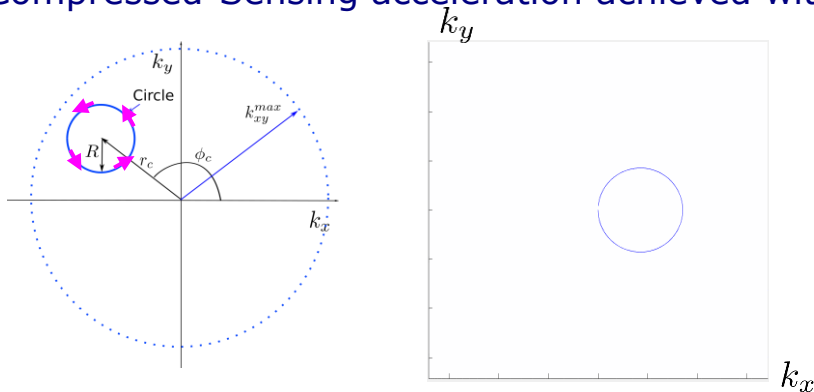
⁶ Lam F, Li Y, Guo R, Clifford B, Liang ZP. Magn Reson Med. 2020;83(2):377-390.

⁷ Wang Z, Li Y, Lam F. Magn Reson Med. 2022;87(3):1103-1118.

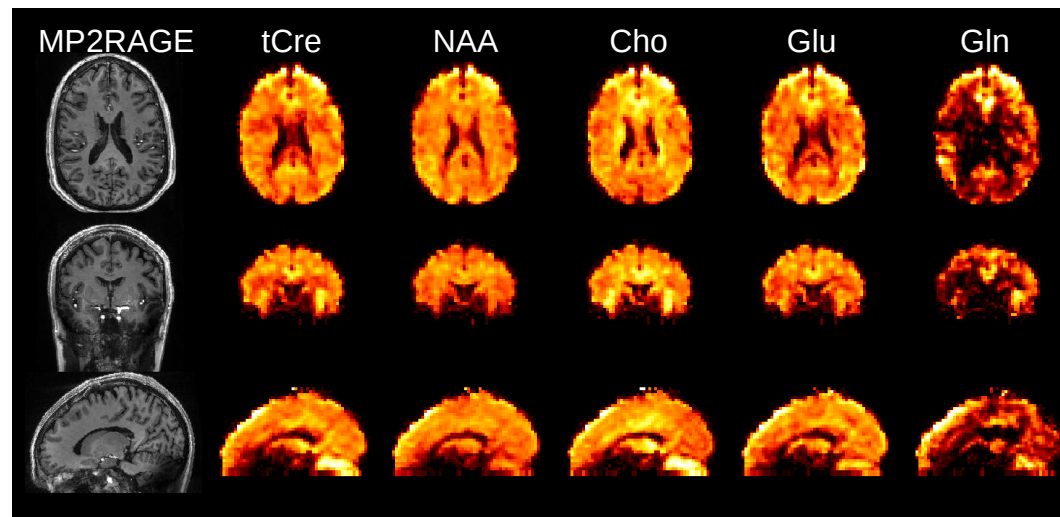
Inverse-problem with Denoising: ECCENTRIC

ECcentric Circle ENcoding TRajectories for Compressed-sensing (ECCENTRIC)¹

- High-Res MRSI at 7T, SSE requires high gradient slew-rate
→ Use small circles: lower slew-rate
- Compressed-Sensing acceleration achieved with circles randomly distributed



Whole-Brain 7T FID-MRSI
3mm iso, TA 9min



$$\arg \min_{\mathbf{U}, \mathbf{V}} \|\mathbf{s} - \mathcal{FSB}\{\mathbf{UV}\}\|_2^2 + \lambda \sum_{c=1}^{N_C} \text{TGV}^2\{U_c\} \quad [2]$$

Spatial Comp. Time Comp.
 ↑ ↑
 Acquired data B₀ inhomogeneity
 ↑ ↑
 Coil Sensitivity 1st and 2nd order
 ECCENTRIC encoding spatial derivative

¹ Klauser A, Strasser B, Bogner W, Hinger L, Schirda C, Thapa B, Cahille D, Batchelor T, Lazeyras F, Andronesi O

ISMRM 2021 Proceeding # 0835. ECCENTRIC: A fully random non-Cartesian sparse Fourier domain sampling for MRSI at 7 Tesla

² Kasten J, Lazeyras F, Van De Ville D. Data-Driven MRSI Spectral Localization Via Low-Rank Component Analysis. Med Imaging, IEEE Trans. 2013;32(10):1853-1863.

doi:10.1109/TMI.2013.2266259

- Magnetic Resonance Spectroscopic Imaging (MRSI):
What are the limitations?
- Fast and High resolution MRSI:
Key ingredients
- Reconstruction as solution to the inverse-problem
- Few applications

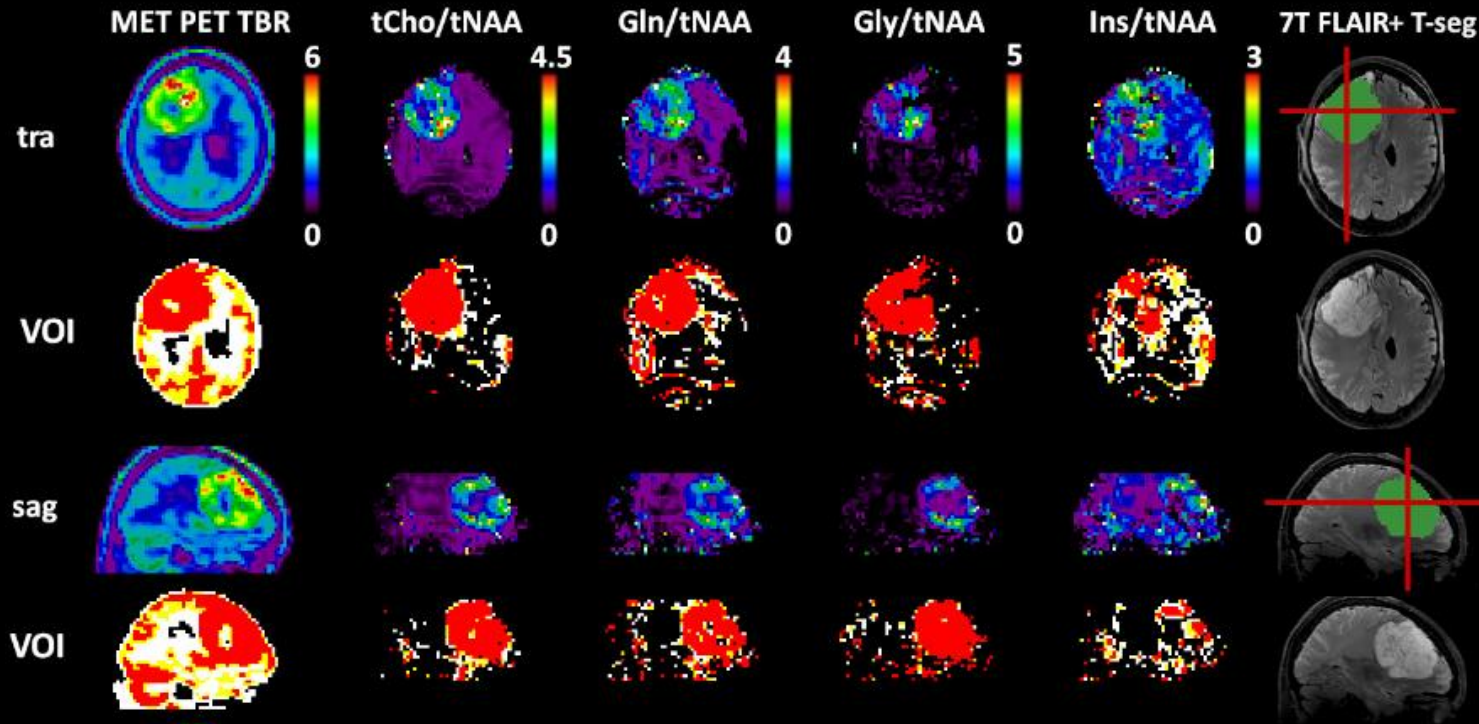
GALLERY OF APPLICATIONS

Article

7T HR FID-MRSI Compared to Amino Acid PET: Glutamine and Glycine as Promising Biomarkers in Brain Tumors

Gilbert Hangel ^{1,2,*}, Philipp Lazen ^{1,2}, Sukrit Sharma ¹, Barbara Hristoska ^{1,3}, Cornelius Cadrien ^{1,2}, Julia Furtner ⁴, Ivo Rausch ⁵, Alexandra Lipka ¹, Eva Niess ¹, Lukas Hingerl ¹, Stanislav Motyka ¹, Stephan Gruber ¹, Bernhard Strasser ¹, Barbara Kiesel ², Matthias Preusser ⁶, Thomas Roetzer-Pejrimovsky ⁷, Adelheid Wöhrer ⁷, Wolfgang Bogner ¹, Georg Widhalm ², Karl Rössler ², Tatjana Traub-Weidinger ⁸ and Siegfried Trattnig ^{1,9,10}

Ratio maps and thresholded VOIs in patient #1 - astrocytoma, IDH-mutant, grade 4



- Concentric-Rings (SSE) FID-MRSI 3.4 mm iso.
- Delineation with PET vs MRSI
- HR MRSI showed capability to replace PET as gold-standard

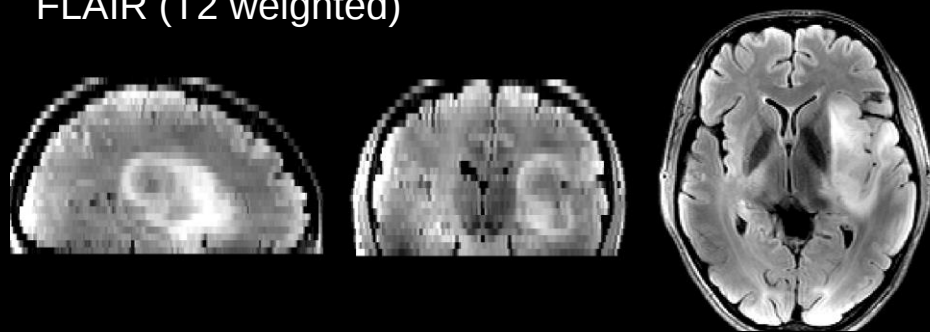
Hangel, G., ... Trattnig, S. (2022). 7T HR FID-MRSI Compared to Amino Acid PET: Glutamine and Glycine as Promising Biomarkers in Brain Tumors.

Cancers, 14(9), 2163. <https://doi.org/10.3390/CANCERS14092163>

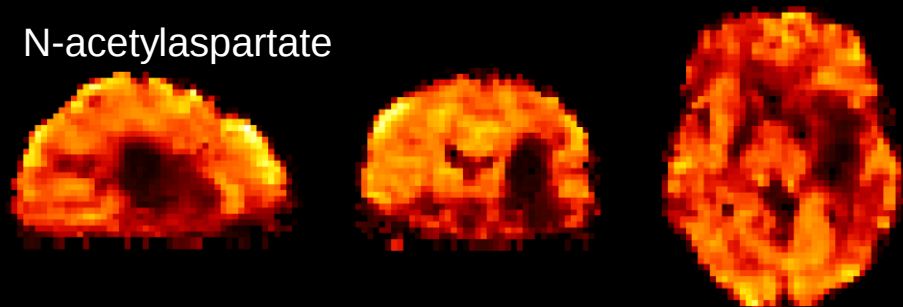
GALLERY OF APPLICATIONS

3D-ECCENTRIC FID-MRSI 3.4mm iso.:
Glioma, High-grade part highlighted in HR

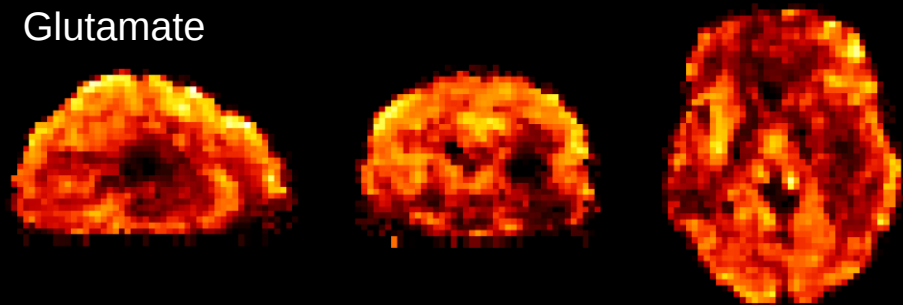
FLAIR (T2 weighted)



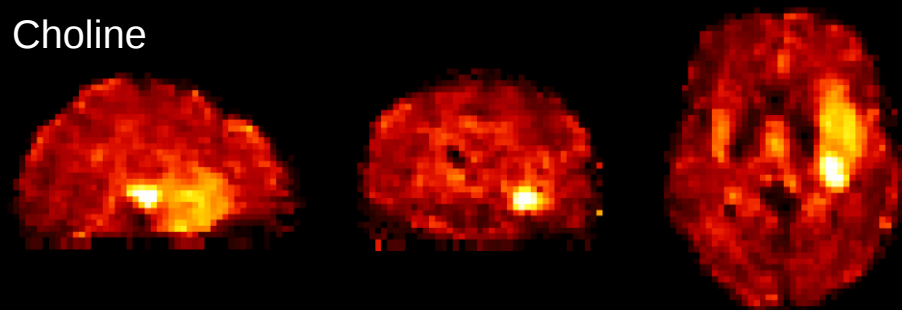
N-acetylaspartate



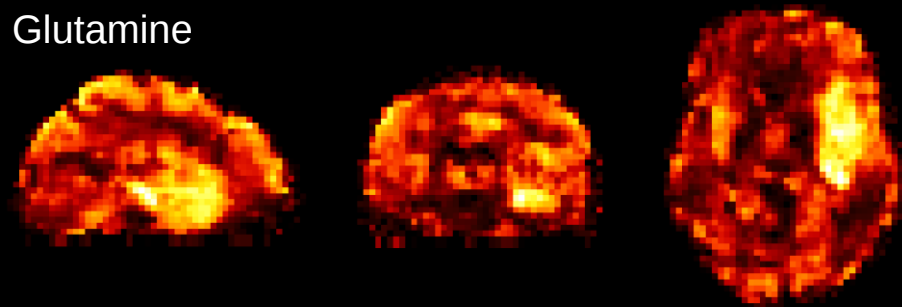
Glutamate



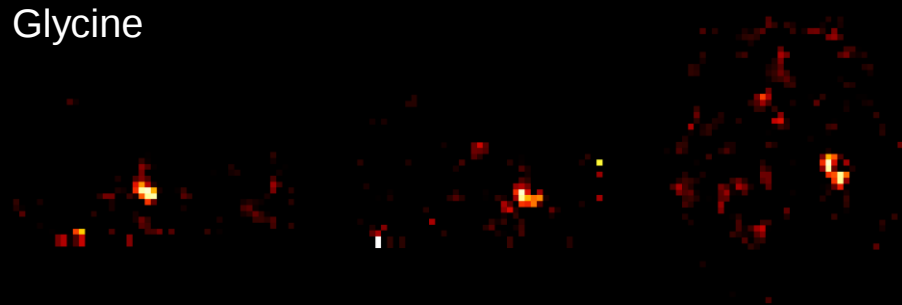
Choline



Glutamine



Glycine



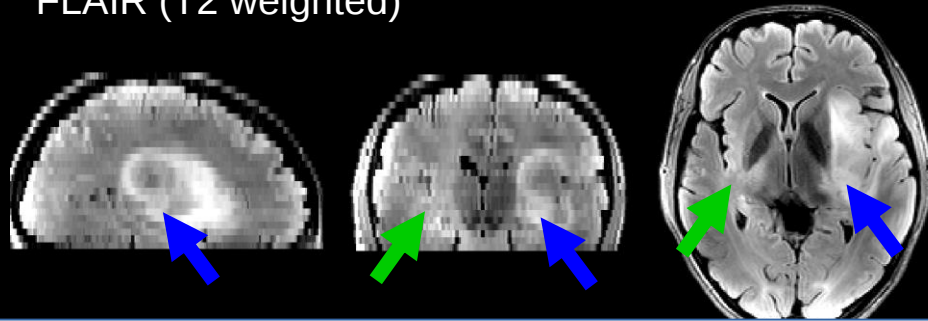
8 (NAA)
2 (Cho)
6 (Glu)
2 (Gln)
2 (Gly)
[I.U.]

0

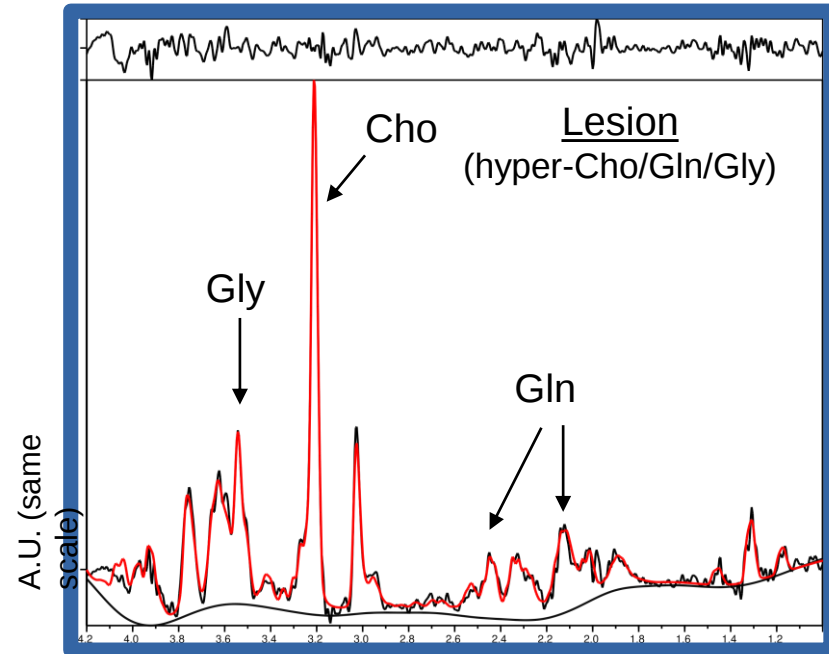
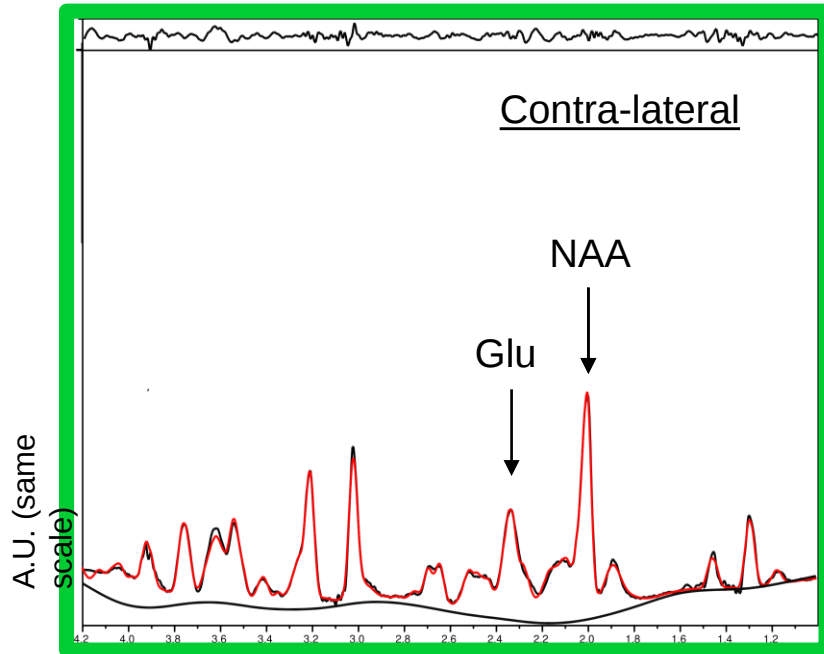
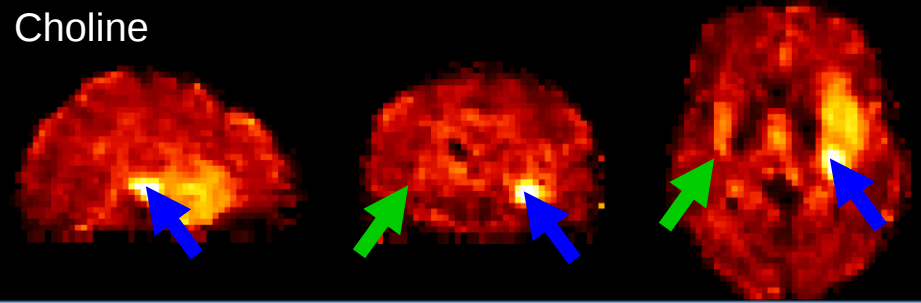
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Glioma, Grade 3, Prior to surgery,

FLAIR (T2 weighted)



Choline

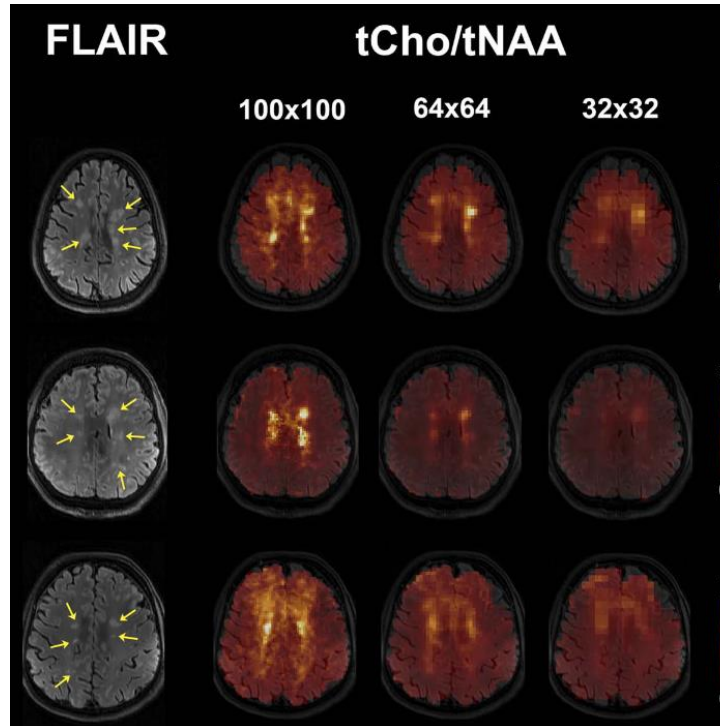
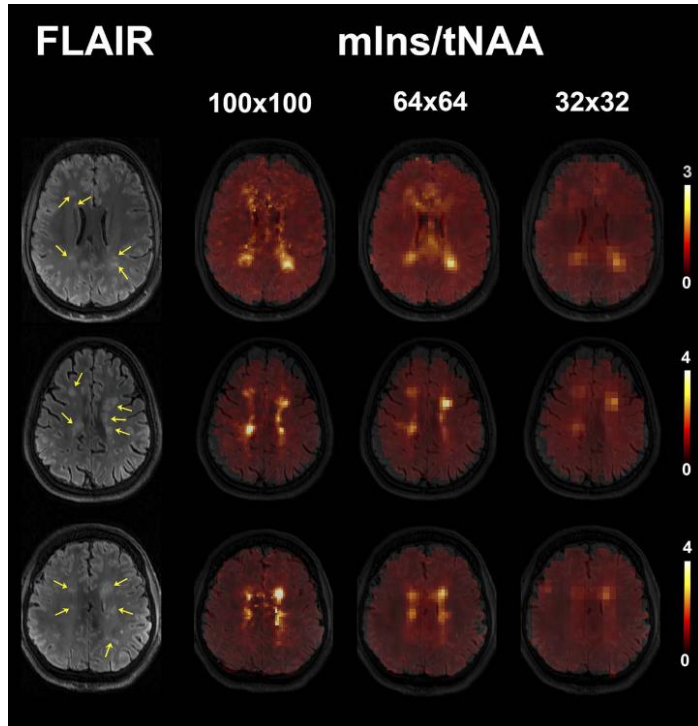


GALLERY OF APPLICATIONS

Multiple Sclerosis

7 T Magnetic Resonance Spectroscopic Imaging in Multiple Sclerosis *How Does Spatial Resolution Affect the Detectability of Metabolic Changes in Brain Lesions?*

Eva Heckova, MSc,* Bernhard Strasser, PhD,† Gilbert J. Hangel, PhD,* Michal Považan, PhD,‡§
Assunta Dal-Bianco, MD,|| Paulus S. Rommer, MD,|| Petr Bednarik, MD, PhD,* Stephan Gruber, PhD,*
Fritz Leutmezer, MD,|| Hans Lassmann, MD,¶ Siegfried Trattnig, MD,*# and Wolfgang Bogner, PhD*#



- Multiple-Sclerosis lesions
- 2D Hig-Res. FID-MRSI
- Increase contrast in
 - ↓ tNAA
 - ↑ Ins
 - ↑ Cho
- Lesions are better resolved, less partial volume

Conclusion

- *Fast MRSI and Reconstruction Techniques*
aim to tackle the classical limitations of MRSI (go high-res., whole-brain, fast)
- New sequence implementation are required:
 - FID-MRSI
 - k-space acceleration
 - Spatial-Spectral Encoding
- Technique generally required dedicated reconstruction
 - Enhance SNR
 - Suppress Lipid signal
 - Reconstruct CS acquisition
- First applications reveal the value of high-resolution metabolite maps

Advanced Clinical Imaging Technology

Thank you for your attention!

**Looking for a Master thesis/internship
in MRI / MRSI technique development and application?**

**Send me an email with CV :
Antoine.Delattre-Klauser@Siemens-Healthineers.com**