Supplementary material to *Achieving High-Resolution $^1$H-MRSI of the Human Brain with Compressed-Sensing and Low-Rank Reconstruction at 7 Tesla.*

Further details about the methods and results of the main manuscript are presented in this document.

## I. MODEL ALTERNATIVES

In fig.S3, 2D MRSI dataset from volunteer 3 and the high-resolution phantom dataset (described in the main manuscript) are reconstructed with several alternative models. With the notation defined in the methods section of the main manuscript, we recall the forward model

$$s = \mathcal{F} CBUV,$$

with the assumption that the signal is partially as $\rho = UV$.

The fig.S3 left shows the reconstruction result for fully-sampled 2D MRSI dataset. The alternative models used for reconstruction are defined as follows

| Reconstruction | Formula |
|----------------|---------|
| **Adjoint op.** | $\rho = B^*C^*F^*s$ (with $X^*$ the adjoint of the operator $X$) |
| **SENSE** | $\arg\min_\rho \|s - \mathcal{F}CB\rho\|_2^2$ |
| **SENSE + LR** | $\arg\min_{UV} \|s - \mathcal{F}CBUV\|_2^2$ |
| **SENSE + TGV** | $\arg\min_\rho \|s - \mathcal{F}CB\rho\|_2^2 + \lambda \sum_{t=1}^T TGV^2 \rho(r,t)$ |
| **SENSE + TGV + LR** | $\arg\min_{UV} \|s - \mathcal{F}CBUV\|_2^2 + \lambda \sum_{c=1}^K TGV^2 \{U_c\}$ |

The Adjoint op. reconstruction applies the forward-model adjoint operator as reconstruction operator, also often referred as Direct Fourier transform reconstruction. The reconstruction SENSE + TGV + LR is the CS-SENSE-LR reconstruction used in the original manuscript.

The fig.S3 right presents the performance of the reconstruction alternative for acceleration by retrospective undersampling factor 3. The Adjoint op. reconstruction is not performed at this point because this direct operation is not suited for undersampled dataset (missing k-space data resulting in signal aliasing).

A spectrum from a location designated by the red arrow is shown for each reconstruction alternative. In both cases, the complete model SENSE + TGV + LR reconstruction, show the best denoising performance for the metabolite maps and the sample spectrum. The spectral denoising effect of the CS-SENSE-LR model is less pronounced for the phantom dataset as the original data contain higher SNR. However, in the resulting metabolite maps, the reconstruction by complete model SENSE + TGV + LR enables the clear distinction of the smallest 2mm tubes.

## II. FILTERED DATA FIDELITY

In fig.S4, we demonstrated that a Hamming filter applied on the data fidelity term can improve the reconstruction result. Also we show that this improvement is different than applying a spatial hamming filter on the measured data and does not increase the effective voxel size. The MRSI data were either reconstructed by adjoint operator or by the CS-SENSE-LR model reconstruction. Defining the spatial Hamming filter operator $H$, the different reconstructions read
In the Data Filter Model, the Hamming filter is applied to the measured data $\mathbf{s}$ and the solution of the reconstruction inherits the characteristics of the usual spatially filtered data: improved SNR but increased effective voxel size. For the Fidelity Filter Model, the filter is applied on both term of the data fidelity. In absence of regularization ($\lambda = 0$), the solution is identical with or without $\mathcal{H}$ and is computed by the Penrose pseudo-inverse of the forward operator: $\rho = (\mathcal{F}CB^*)^{-1}\mathcal{F}CB^*\mathbf{s}$. For a reconstruction with regularization ($\lambda > 0$), Fidelity Filter Model corresponds to a filtering of the data fidelity contribution in the convergence process. Following the filter profile, the data fidelity is fully preserved at the center of the k-space but is lowered on the outer k coordinates. The convergence process is therefore less affected by low SNR data points at the k-space periphery. Also, the data fidelity contribution being attenuated on the outer k-space, this is equivalent to applying a stronger TGV regularization for higher spatial frequencies.

In fig.S4 left, MRSI fully-sampled data were simulated using an analytical phantom presented in [1] with an SNR level $\infty$, 4 or 2. The 3 sample spectra on the left illustrate the respective noise levels. The reconstructed Cr+PCr or Glu+Gln metabolite map was compared to the ground truth and the normalized root mean square error (NRMSE) 

$$\sqrt{\frac{\sum_{\mathbf{v} \in \text{brain voxels}} (C(v) - C_{\text{g.t.}})^2}{\sum_{\mathbf{v} \in \text{brain voxels}} C_{\text{g.t.}}^2}}$$

and Structural Similarity Index (SSIM) were computed for each model and SNR. The result at $SNR = \infty$ show a good agreement of the Adjoint op., No Filter Model and Fidelity Filter model with the ground truth. The Data Filter model shows more discrepancy due to the increased effective voxel size caused by the Hamming filtering applied on the data. This is clearly visible on both metabolites. As noise increases, the Adjoint op. reconstruction shows the lowest performance. The Fidelity Filter model shows the best NRMSE and SSIM, and produces less noisy metabolite maps in comparison to the No Filter model. The Data Filter model reconstruction shows better results than the Adjoint op. reconstruction with small apparent noise in the maps but there is a visible increase in effective voxel size in comparison with the Fidelity Filter and No Filter model reconstructions. In fig.S4 right, the three different models are compared for 2D MRSI dataset from volunteer 3 and the high-resolution phantom (described in main manuscript) at the proposed acceleration factor of 3. The volunteer data reconstructions show the better denoising performance with the Fidelity Filter model in comparison to the No Filter model. The difference with the Data Filter model is more subtle and the increase of effective voxel size is more difficult to observed than in the simulated data. At the opposite, in the phantom reconstructed metabolite maps, the difference in denoising between models is not distinct but the increased effective voxel size is clearly visible over the two smallest set of tubes for the Data Filter model reconstructions. Fidelity Filter model does not show any increase in effective voxel size in comparison to the No Filter model.

These results demonstrate that the Fidelity Filter model produces the best reconstruction in noisy dataset without increasing the effective voxel size contrarily to the Data Filter model. The Fidelity Filter model was used for the reconstruction of the 2D MRSI data for the main manuscript results.

### III. LCMODEL CONTROL PARAMETERS

LCModel [2] was performed with the controls parameters given here after. No macromolecules (MM) and lipid simulated signal were fitted with LCMRise (usimul = 0). This choice was consecutive to the observation that no MM nor lipid peaks were present in the MRSI signal after lipid suppression and reconstruction. The MM/lipid signal were supposedly removed like the scalp lipid signal by the lipid suppression by orthogonality. The non trivial control parameters were:

$sddegz = 999$. 
sddegp = 7.
ppmst = 4.2
ppmend = 1
nsimul = 0
hzppm = 297.0502
echot = 1.3
dows = T
deltat = 0.000125
degzer = 0.00
degppm = 0.00

IV. ATLAS-BASED ANALYSIS

To analyze the metabolite content of anatomical structures, the metabolite volumes were registered and analyzed with a brain anatomical atlas. Masks for the cerebral lobes were generated using the Standard atlas [3] in WFU PickAtlas toolbox (https://www.nitrc.org/projects/wfu_pickatlas/) and the gray and white matter compartments were segmented using the computational anatomy toolbox (CAT12; [4]). A general linear model was used to estimate the metabolite concentrations in each atlas structure [5]:

\[ Y = \sum_i \beta_i X_i + \beta_0 + \epsilon \]

where \( X_i \) is a vector containing all partial-volume estimate (a value between 0 and 1) with \( i \) the index of the anatomical structures, \( Y \) a vector made of the metabolite concentration in all voxels, \( \beta_0 \) is the concentration intercept and \( \epsilon \) represents normally distributed residuals. After fitting the general linear model on the MRSI data, \( \beta_i + \beta_0 \) provide the estimated metabolite concentration in each anatomical structure, intrinsically corrected for partial-volume.

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[3] J. A. Maldjian, P. J. Laurienti, R. A. Kraft, and J. H. Burdette, NeuroImage (2003), ISSN 10538119.
[4] J. Ashburner and K. J. Friston, NeuroImage 26, 839 (2005), ISSN 1053-8119, URL https://www.sciencedirect.com/science/article/pii/S1053811905001102.
[5] N. Schuff, F. Ezekiel, A. C. Gamst, D. L. Amend, A. A. Capizzano, A. A. Maudsley, and M. W. Weiner, Magnetic Resonance in Medicine 45, 899 (2001), ISSN 07403194, NIHMS150003, URL http://doi.wiley.com/10.1002/mrm.1119.
FIG. S1: Left, 2D 2.5mm metabolite maps measured with CS-FID-MRSI and accelerated retrospectively with several acceleration factors. Scales are in institutional unit (common to all metabolites). Right, Corresponding T1-weighted image and three sample spectra are shown for acceleration factor 1, 3 and 5. Bottom right, the residuals root mean square (RMS) of the LCModel fit as function of the acceleration is shown as indicator of spectral quality. The normalized root mean square error (NRMSE) of each metabolite over the whole brain relative to the fully sampled map (A.F.=1) versus the acceleration factor. Metabolite decomposition of the voxel 1 fitting is presented in supplementary material fig.S6
FIG. S2: 3D CS-FID-MRSI metabolite volumes of the three healthy volunteers performed with acceleration factor of 4.5 for a total acquisition time of 20min. The colour scale goes from 0 till the 95th percentile for each metabolite separately. Right, the anatomical images show the MRSI slab positions.
FIG. S3: Model alternatives for 2D MRSI reconstruction (see text for detailed description)
FIG. S4: Effects of different Hamming filter methods combined with the CS-SENSE-LR reconstruction model. Left, 2D MRSI were simulated with three different noise levels. The reconstructed metabolite maps of Cr+PCr and Glu+Gln were compared to the ground truth with NRMSE and SSIM. Right, in vivo and tube-phantom 2D MRSI accelerated by factor 3 were reconstructed with CS-SENSE-LR and 3 filtering methods (See text for details).
Effect of regularization parameter on metabolite distributions

FIG. S5: Effect of the regularization parameter value on the reconstructed metabolite maps.
FIG. S6: Metabolite decomposition of the LCModel fitting for sample spectra. The spectra correspond to Fig.6 Voxel 1, A.F.=4.5 (3D in vivo), Fig.5 Voxel 1, A.F.=3 (2D in vivo) and Fig.2 spectrum nb. 3 (2D phantom).
FIG. S7: Retrospective acceleration was performed on 2D MRSI simulated dataset computed with 3 levels of SNR: $\infty$, 4 or 2. An illustration of the noise level in the spectra reconstructed by adjoint op. can be found in Fig.S2. The k-space undersampling corresponding to the acceleration factor are shown in the figure center, and the GPC+PCh and Glu+Gln maps resulting from the CS-SENSE-LR reconstruction are displayed for the three levels of SNR. The ground truth concentration maps are shown on the left. For each metabolite map, the normalized root mean square error (NRMSE) and Structural Similarity Index (SSIM) were computed (see supplementary material text for details about the simulation and computation of the NRMSE and SSIM).
FIG. S8: 2D Metabolite maps resulting from two consecutive acquisitions performed in volunteers 3, 4 and 5 with either no acceleration or acceleration factor (CS) 2.5, are presented. The absolute error between the two results is shown with a scale going from 0% to 100%. The normalized root mean square error (NRMSE) computed over the whole slice is defined in the main manuscript and compares to the values in fig.S1.
FIG. S9: 3D Metabolite volumes successively acquired in volunteers 1 and 4 with acceleration factor (CS) 2.5 and 4.5 are presented. The absolute error between the two results is shown with a scale going from 0% to 100%. The normalized root mean square error (NRMSE) over the whole slab follows the main manuscript definition and values compare to the values in fig.3.
FIG. S10: $B_0$ frequency shift correction and $B_1$ signal intensity correction computed from the low resolution water reference acquisition and reconstructed to MRSI high-resolution.