

CIBM Annual Symposium 2022 30th November Campus Biotech, Geneva

# Variability and reproducibility of multi-echo T<sub>2</sub> reproducibility: Insights from multi-site, multi-session and multi-subject MRI acquisitions

E. Fischi-Gomez<sup>1,2</sup>, G. Girard<sup>1,3,4</sup>,P.J. Koch<sup>5,6,7,8</sup>,T. Yu<sup>1,9</sup>,M. Pizzolato<sup>1,10</sup>,J. Brügger<sup>5,6</sup>, G. Piredda<sup>1,4,9</sup>, T. Hilbert<sup>1,4,9</sup>, A.G. Cadic-Melchior<sup>5,6</sup>, E. Beanato<sup>5,6</sup>, C-H. Park<sup>5,6</sup>, T. Morishita<sup>5,6</sup>, MJ. Wessel<sup>5,6,11</sup>, S. Schiavi<sup>12,13</sup>, A. Daducci<sup>13</sup>, T. Kober<sup>1,4,9</sup>, E.J. Canales-Rodriguez<sup>1</sup>, F.C.Hummel<sup>5,6,14</sup>, J-P.Thiran<sup>1,3,4</sup>

<sup>1</sup>Signal Processing Laboratory 5 (LTS5), École Polytechnique Fédérale de Lausanne, Switzerland, <sup>2</sup>Translational Machine Learning Lab, Department of Radiology, Centre Hospitalier Universitaire Vaudois, University of Lausanne, Lausanne, Switzerland, <sup>3</sup>CIBM Center for Biomedical Imaging, Lausanne, Switzerland, <sup>4</sup>Department of Radiology, Centre Hospitalier Universitaire Vaudois, University of Lausanne, Lausanne, Switzerland, <sup>5</sup>Defitech Chair for Clinical Neuroengineering, Neuro-X Institute (NIX) and Brain Mind Institute (BMI), École Polytechnique Fédérale de Lausanne (ÉPFL), Lausanne, Switzerland, <sup>6</sup>Defitech Chair of Clinical Neuroengineering, Neuro-X Institute (NIX) and Brain Mind Institute (BMI), École Polytechnique Fédérale de Lausanne (ÉPFL Valais), Clinique Romande de Réadaptation, Sion, Switzerland, 7Department of Neurology, University of Lübeck, Lübeck, Germany, <sup>8</sup>Center of Brain, Behavior and Metabolism (CBBM), University of Lübeck, Lübeck, Germany, <sup>9</sup>Advanced Clinical Imaging Technology, SiemensHealthineers International AG, Lausanne, Switzerland, <sup>10</sup>Department of Applied Mathematics and Computer Science, Technical University of Denmark, Kongens Lyngby, Denmark, <sup>11</sup>Department of Neurology, University Hospital and Julius-Maximilians-University, Wuerzburg, Germany, <sup>12</sup>Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, Italy, <sup>13</sup>Diffusion Imaging and Connectivity Estimation (DICE) Lab, Department of Computer Science, University of Verona, Verona, Italy, <sup>14</sup>Clinical Neuroscience, University Hospital of Geneva (HUG), Geneva, Switzerland

## BACKGROUND

Quantitative magnetic resonance imaging (qMRI) can increase the specificity and sensitivity of conventional weighted MRI to underlying pathology. However, estimation methods are limited by their sensitivity to the underlying noise. Moreover, estimating the model's parameters is challenging because the resulting inverse problem is ill-posed, requiring advanced numerical regularization techniques. As a result, the estimates from distinct regularization strategies are different. This study focuses on multi-echo  $T_2$  relaxometry, which probes the tissue microstructure by differentiating compartment-specific  $T_2$  relaxation times.

### METHODS

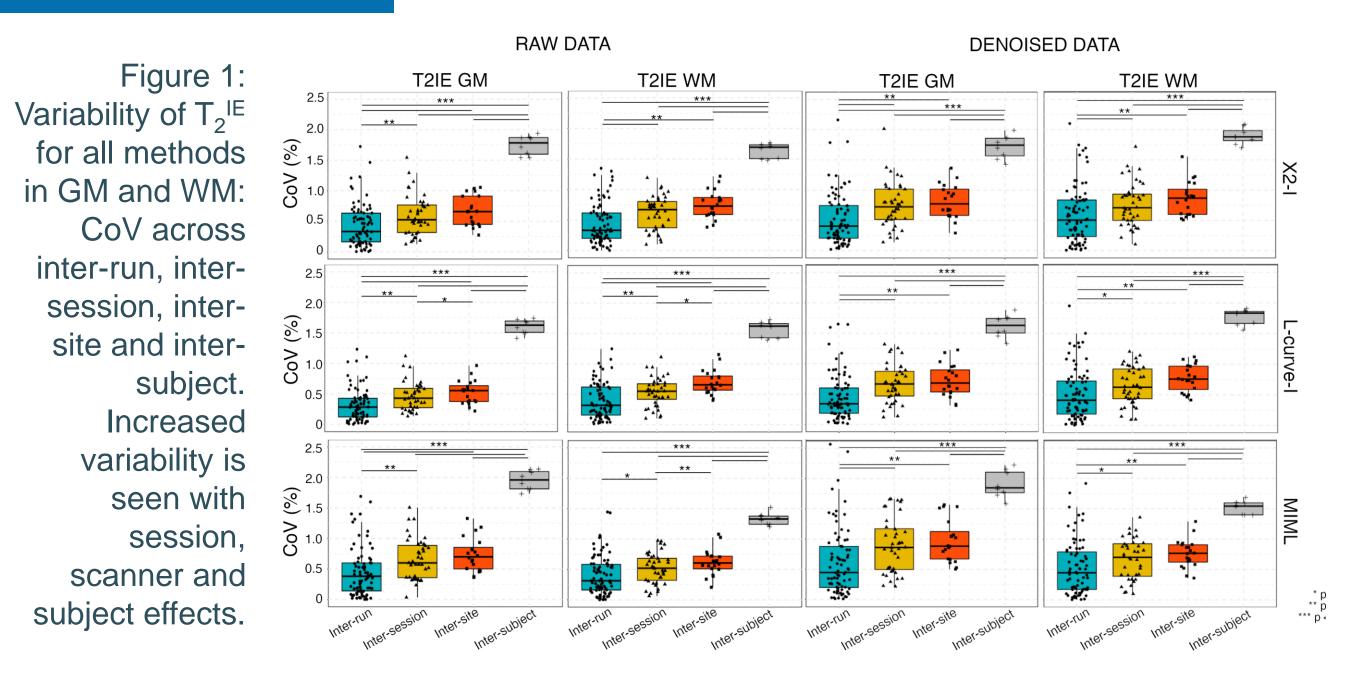
MRI protocol: <u>3D multi-echo gradient and spin-echo (GRASE) prototype</u> w/ CAIPIRINHA [1]: minTE= 10.68ms; #echoes = 32;  $\Delta$ TE=10.68ms; TR=1s; prescribed FA=  $180^\circ$ ; res=1.6mm<sup>3</sup> iso #slices=84; AF=3x2(1); #averages =1;AT=10:30min. 144×126×134; 3D MPRAGE: TR = 2300ms; TI=7.1ms; TE=2.96ms; FA=9°; res=1mm<sup>3</sup> iso; #slices=192; FoV=256×256mm<sup>2</sup>.

**Population and scanning design**: 20 healthy subjects (11M, 9F,

## AIMS

In this work, we aimed to investigate the variability and reproducibility of different techniques for estimating the transverse relaxation time of the intra- and extra-cellular space  $(T_2^{IE})$  in gray (GM) and white matter (WM) tissue in a clinical setting, using a multi-site, multi-session and multi-run  $T_2$  relaxometry dataset

## RESULTS



age=27+/-3 years [24-33]). Each subject was scanned in two MRI scanners (MAGNETOM Prisma, Siemens) at Geneva University Hospital and Sion Hospital (sites) at two different time points (sessions). At each session, each subject was scanned twice (runs). Between runs, subjects were repositioned, followed by a new shimming. Eight scans were obtained per subject, for a total of N=160 scans.

 $T_2$  estimation: 3 different techniques for  $T_2$  spectra estimation were used: two regularized non-negative least squares methods (X<sup>2</sup>-I and L-Curve-I) and a machine learning approach (MIML) [2].

**Analysis:** Two independent analyses were performed to study the effect of different reconstruction methods using both raw and denoised data:

- Variability analysis: 4 effects were studied by means of the coefficient of variation (CoV) for WM and GM: inter-run (same session, same subject, same scanner), inter-session (different sessions, same subject, same scanner), inter-site (different sessions, same subject, different sites) and inter-subject (different subjects, different sessions, same scanner)
- Reproducibility analysis: For each reconstruction method the agreement of multiple assessments of the same subjects was computed via the Intraclass Correlation Coefficient (ICC)

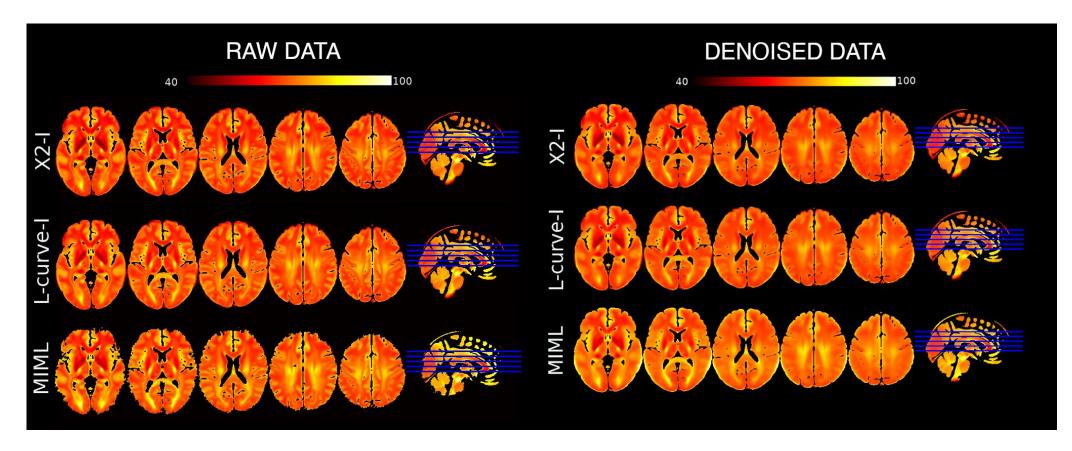


Figure 2: Voxel-wise regional variability: Whole-brain voxelwise T<sub>2</sub><sup>IE</sup> mean maps for the three reconstruction methods: X<sup>2</sup>-I, L-curve-I, and MIML. All methods showed consistent results, although MIML method displayed higher mean  $T_2^{IE}$  values. The values obtained with the NNLS methods were almost identical, with only slight differences mostly related to the smoothness of the solution.

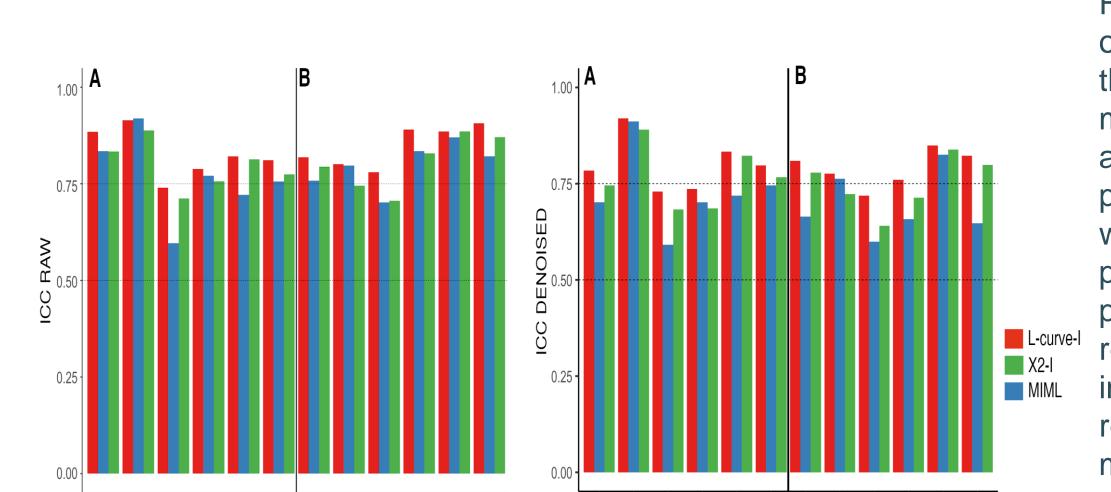
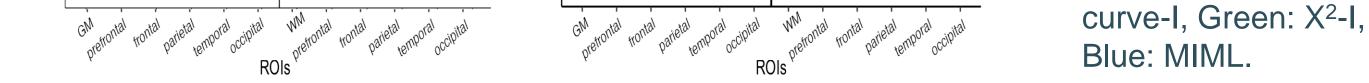


Figure 3: Regional ICC of mean  $T_2^{IE}$  for all three reconstruction methods for GM (A) and WM (B). In each panel, from left to right: whole-brain (GM/WM), prefrontal, frontal, parietal and temporal regions. Color bars indicate different reconstruction methods: Red: L-





We have acquired a unique multi-echo T2 MRI dataset to characterize the variability and reproducibility of the intra- and extra-cellular T2 relaxation time. We compared the estimates from three different reconstruction methods, including two classical algorithms based on regularized NNLS and a novel ML approach trained with synthetic data. The smallest source of variance is the run, followed by inter-session, inter-scanner, and inter-subject effects. Notably, there were no statistical differences between the inter-session and inter-scanner effects for any of the evaluated reconstruction techniques, suggesting that the acquisition sequence and employed methodology may be used in multi-site neuroimaging studies. This work has been published in [3].



References: [1] Piredda, G. F., et al. (2021) Fast and high-resolution myelin water imaging: Accelerating multi-echo GRASE with CAIPIRINHA. Magnetic Resonance in Medicine 85, 209–222. doi:10.1002/MRM.28427 [2] Yu, T., et al.(2021). Model-informed machine learning for multi-component T2 relaxometry. Medical Image Analysis 69 508101940. doi:10.1016/J.MEDIA.2020.10194 [3] Fischi-Gomez et al. Variability and reproducibility of multi-echo T2 relaxometry: Insights from multi-site, multi-session and multi-subject MRI acquisitions. Frontiers in Radiology doi: 10.3389/fradi.2022.930666

Financial support: Marco Pizzolato acknowledges the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No 754462. Erick J Canales-Rodríguez was supported by the Swiss National Science Foundation (Ambizione grant PZ00P2-185814). This study was supported by Personalized Health and Related Technologies grant (PHRT-2017-205) of the ETH Domain (to FCH) and by the Defitech Foundation (to FCH)

