# R2\*, R1, and proton density age variations in subcortical structures in young adults at 7T

Poster No:

3580

Submission Type:

Abstract Submission

Authors:

<u>Mikhail Zubkov</u><sup>1</sup>, Kerrin Pine<sup>2</sup>, Pierre-Louis Bazin<sup>3</sup>, Nasrin Mortazavi<sup>4</sup>, Siya Sherif<sup>5</sup>, Puneet Talwar<sup>5</sup>, Laurent Lamalle<sup>5</sup>, Christophe Phillips<sup>6</sup>, Fabienne Collette<sup>7</sup>, Anneke Alkemade<sup>8</sup>, Evgeniya Kirilina<sup>9</sup>, Nikolaus Weiskopf<sup>2</sup>, Gilles Vandewalle<sup>5</sup>

# Institutions:

<sup>1</sup>University of Liège, Liège, Liège, <sup>2</sup>Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, <sup>3</sup>Full brain picture Analytics, Leiden, Zuid Holland, <sup>4</sup>GIGA-Institute, CRC-In Vivo Imaging Unit, University of Liège, Liege, Liege, <sup>5</sup>Sleep and Chronobiology Lab, GIGA-Institute, CRC-In Vivo Imaging Unit, University of Liège, Liège, Belgium, <sup>6</sup>University of Liège, Liège, Belgium, <sup>7</sup>University of Liège, Liège, Liège, Liège, <sup>8</sup>University of Amsterdam, Amsterdam, Netherlands, <sup>9</sup>Max Planck Institute, Leipzig, Germany

First Author:

Mikhail Zubkov University of Liège Liège, Liège Co-Author(s): Kerrin Pine Max Planck Institute for Human Cognitive and Brain Sciences Leipzig, Germany Pierre-Louis Bazin Full brain picture Analytics Leiden, Zuid Holland Nasrin Mortazavi GIGA-Institute, CRC-In Vivo Imaging Unit, University of Liège Liege, Liege Siya Sherif Sleep and Chronobiology Lab, GIGA-Institute, CRC-In Vivo Imaging Unit, University of Liège Liège, Belgium Puneet Talwar Sleep and Chronobiology Lab, GIGA-Institute, CRC-In Vivo Imaging Unit, University of Liège Liège, Belgium Laurent Lamalle Sleep and Chronobiology Lab, GIGA-Institute, CRC-In Vivo Imaging Unit, University of Liège Liège, Belgium Christophe Phillips, Prof

University of Liège Liège, Belgium Fabienne Collette, Prof University of Liège Liège, Liege Anneke Alkemade University of Amsterdam Amsterdam, Netherlands Evgeniya Kirilina Max Planck Institute Leipzig, Germany Nikolaus Weiskopf Max Planck Institute for Human Cognitive and Brain Sciences Leipzig, Germany **Gilles Vandewalle** Sleep and Chronobiology Lab, GIGA-Institute, CRC-In Vivo Imaging Unit, University of Liège Liège, Belgium

#### Introduction:

Ultra-high field (UHF) MRI and its ability to provide high resolution data is progressively entering the clinical application stage and provides promising advances for brain imaging. Small subcortical structures can now be appropriately imaged in hope of mapping their function in healthy population, and their role in neurodegenerative disorders (1,2). UFH MRI comes, however, with altered contrast, instrumental biases, and still lacks established imaging protocols. Quantitative MRI (qMRI) has the potential to mitigate these issues via estimating parameters related to the biophysical properties of tissues (relaxation rates R1, R2, and R2\*, proton density, magnetization transfer etc.) and using calibration maps to correct for the protocol-and scanner-dependency.

The critical issues for qMRI are currently the reproducibility, the incoherence in parameter mapping approaches, and the consequential lack of consensus on normal values of tissue parameters. The latter presents an aggravating issue for possible disorder diagnostics, when inter-individual (3) and inter-site differences are poorly accounted for. We present a preliminary evaluation of variation of a number of qMRI parameters with age within a sample of young and healthy volunteers for a multiparameter mapping (MPM) qMRI protocol at 7T.

#### Methods:

21 healthy volunteers (4 males) with age ranging from 18 to 29y (median of 21) underwent the scanning at 7T Terra MRI (Siemens Healthineers, Erlangen, Germany) with a 1-Tx/32-Rx head coil (Nova Medical, Wilmington, MA, USA).

The MPM protocol (4) comprised three (T1-weighted, PD-weighted, MT-weighted) whole-brain 3D FLASHbased multi-echo sequences with similar isotropic resolution of 0.6 mm (TR 19.5 ms, FA PDw/MTw/T1w 5/5/20°, six equispaced echoes with TE ranging from 2.3 to 14.2 ms for PDw and T1w and 4 equispaced echoes for MTw with TE ranging from 2.3 to 9.44, GRAPPA with acceleration factor R=2 in each in the two phase encoding directions, and B1 mapping for transmit field correction (5).

The images were processed with the open source hMRI toolbox (hMRI.info) v.0.5.0 (6), yielding R2\*, PD and R1 maps. Subcortical structures were automatically parcellated by Multi-contrast Anatomical Subcortical Structures Parcellation (MASSP) using all three parametric maps as input (7).

Median values for each of the parameters were extracted for the 27 subcortical structures with ventricles excluded from further analysis. A linear model was built for each of the median value sets with age, BMI and sex being the regressors. Each of the qMRI parameters was treated as a distinct measurement and multiple comparison correction was applied separately to each parametric map. The linear models with p-values for

age lower than 0.05 (false discovery rate-corrected) were deemed significant.

#### Results:

High quality, 0.6 mm resolution, co-aligned maps of gMRI parameters R2\*, PD, R1 were obtained in all participants. The resolution of the parametric maps and the contrast in cortical and subcortical anatomical structures allowed MASSP parcellations of subcortical structures across all 21 participants (e.g., Figure 1). The age dependency analysis showed no significant dependency in R1 versus age, the fornix showed significant (p<0.0004) proton density increase with age, while bilateral striatum (left: p<0.003 and right: p<0.0006) as well as the right subthalamic nucleus (p<0.0008) showed R2\* increase with age (Figure 2).



An example of subcortical structure segmentation overlaid on the R2\* parametric map



·Added variable plots for significant age-related dependencies

# Conclusions:

Despite the limited age-range and size of our sample (8), we provide a set of values that show age-variation in healthy young adults. The detected variations in R2\* can reflect age-related iron accumulation in the subcortical structures. The proton density dependency increase in the fornix is yet to be explained, as previous studies show no changes in proton density for young adults (9). This analysis will be complemented by a sample of older individuals allowing to assess if the detected age-related variations are also present over a larger age-range.

Lifespan Development:

Aging

Modeling and Analysis Methods:

Segmentation and Parcellation

Neuroanatomy, Physiology, Metabolism and Neurotransmission:

Subcortical Structures <sup>2</sup>

# Novel Imaging Acquisition Methods:

Anatomical MRI<sup>1</sup>

Keywords:

Aging HIGH FIELD MR MRI Segmentation STRUCTURAL MRI Sub-Cortical Other - qMRI

 $^{1|2}\mbox{Indicates}$  the priority used for review

Abstract Information

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation" study.

Resting state

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Structural MRI

For human MRI, what field strength scanner do you use?

7T

Which processing packages did you use for your study?

Other, Please list - Nighres

Provide references using author date format

1. Forstmann BU, de Hollander G, van Maanen L, Alkemade A, Keuken MC. Towards a mechanistic understanding of the human subcortex. Nat Rev Neurosci. 2017 Jan;18(1):57–65.

2. Keuken MC, Isaacs BR, Trampel R, van der Zwaag W, Forstmann BU. Visualizing the Human Subcortex Using Ultra-high Field Magnetic Resonance Imaging. Brain Topogr. 2018 Jul 1;31(4):513–45.

3. Callaghan MF, Freund P, Draganski B, Anderson E, Cappelletti M, Chowdhury R, et al. Widespread agerelated differences in the human brain microstructure revealed by quantitative magnetic resonance imaging. Neurobiol Aging. 2014 Aug 1;35(8):1862–72.

4. Weiskopf N, Suckling J, Williams G, Correia M, Inkster B, Tait R, et al. Quantitative multi-parameter mapping of R1, PD\*, MT, and R2\* at 3T: a multi-center validation. Front Neurosci. 2013; 7

5. Jiru F, Klose U. Fast 3D radiofrequency field mapping using echo-planar imaging. Magn Reson Med. 2006 Dec;56(6):1375–9.

6. Tabelow K, Balteau E, Ashburner J, Callaghan MF, Draganski B, Helms G, et al. hMRI – A toolbox for quantitative MRI in neuroscience and clinical research. NeuroImage. 2019 Jul 1;194:191–210.

7. Bazin PL, Alkemade A, Mulder MJ, Henry AG, Forstmann BU. Multi-contrast anatomical subcortical structures parcellation. Verstynen T, Frank MJ, Verstynen T, Neumann WJ, editors. eLife. 2020 Dec 16;9:e59430.

 8. Miletić S, Bazin PL, Isherwood SJS, Keuken MC, Alkemade A, Forstmann BU. Charting human subcortical maturation across the adult lifespan with in vivo 7 T MRI. NeuroImage. 2022 Apr 1;249:118872.
9. Hagiwara A, Fujimoto K, Kamagata K, Murata S, Irie R, Kaga H, et al. Age-Related Changes in Relaxation Times, Proton Density, Myelin, and Tissue Volumes in Adult Brain Analyzed by 2-Dimensional Quantitative Synthetic Magnetic Resonance Imaging. Invest Radiol. 2021 Mar;56(3):163.

# UNESCO Institute of Statistics and World Bank Waiver Form

I attest that I currently live, work, or study in a country on the UNESCO Institute of Statistics and World Bank List of Low and Lower-Middle Income Countries list provided.

No