Human gray matter microstructure mapping using NEXI and 300 mT/m gradients

Quentin Uhl[1], Tommaso Pavan[1], Malwina Molendowska[2], Derek Jones[2], Marco Palombo[2,*] & Ileana Jelescu[1,*]

[1]Dept. of Radiology, CHUV, Lausanne, Switzerland, [2]CUBRIC, Cardiff University, UK, *Equal contribution

Introduction

We aimed to **quantify microstructure parameters** in the human cortex in vivo using the NEXI model of two exchanging compartments[1,2].

NEXI parameters are the **exchange time** t_{ex}, the **intra and extra-neurite apparent diffusivities** D_i and D_e and the **intra-neurite signal fraction** *f*.

We wanted to estimate the **reliability of NEXI estimates** by comparing t_{ex} to that obtained from time-dependent kurtosis K(t), and by comparing intra-subject (scan-rescan) to inter-subject variability of microstructure estimates in the cortex.

We also wanted to investigate whether a **three-compartment declination** of NEXI would better explain our data, allowing for an extra parameter[2] capturing a possible Rician bias or 'dot' compartment.

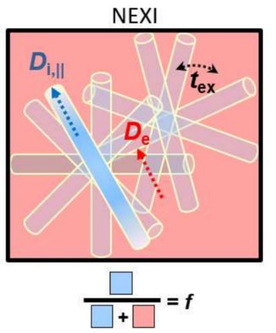


FIGURE 1. NEXI parameters

Methods

Four healthy volunteers were scanned, 3 rescanned.

Acquisition:

- DWI acquired on a 3T Siemens Connectom system
- PGSE EPI sequence with b-values of 1, 2.5, 4, 6 and 7.5ms/µm², Δ=20, 29, 39 and 49ms, δ=9ms, 15 b=0 images per Δ, 700 total dwi, at 1.8-mm isotropic resolution, total scan time: 45min.

Preprocessing:

- Multi-shell multi-diffusion time data preprocessed jointly.
- Preprocessing steps : MP-PCA magnitude denoising[4], Gibbs ringing correction[5], distortion and eddy current correction[6], average over all the directions and normalization by the mean value of the *b*=0 volumes.

Processing:

- Fitting the NEXI model using non-linear least squares.
- DKI fitting to extract Mean Diffusivity (MD) and Mean Kurtosis (MK) for each Δ using b-values up to 2.5ms/µm².
- Fitting of $K_{KM}(t)$ to MK to provide an alternative estimation of t_{ex}[1,3].
- Segmentation of the cortical ribbon ROI on the anatomical MPRAGE image using FastSurfer[7] and transformation into diffusion native space using linear registration[8] of *b*=0 images to MPRAGE images.

NEXI parametric maps

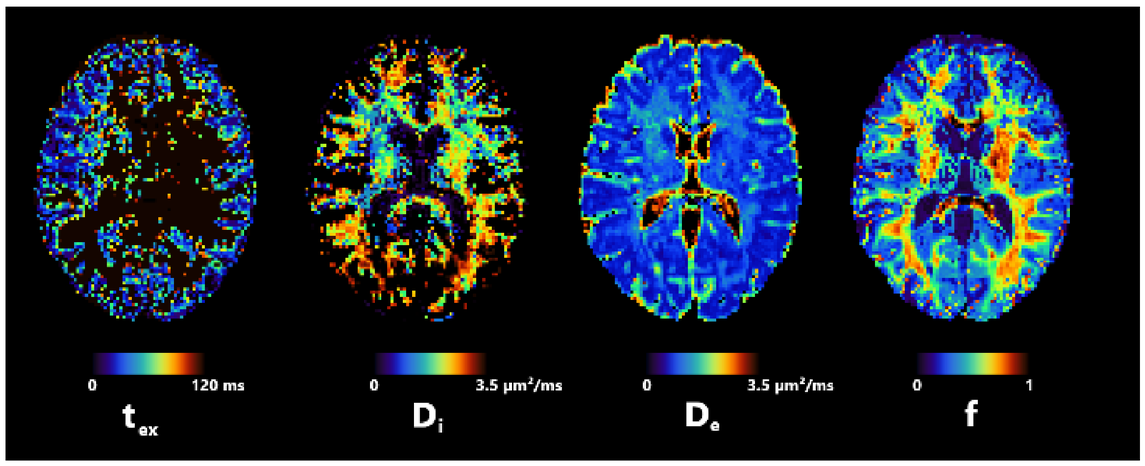


FIGURE 2. Axial slice of NEXI parametric maps in one subject.

- t_{ex} **and** D_e **are consistent throughout the cortex**, but t_{ex} is presumably longer in the WM and **cannot be reliably estimated** using available diffusion times.
- *f* displays the expected anatomical pattern in white vs gray matter.
- D_i **shows large variability** across voxels, while hitting its upper bound frequently.

Reliability

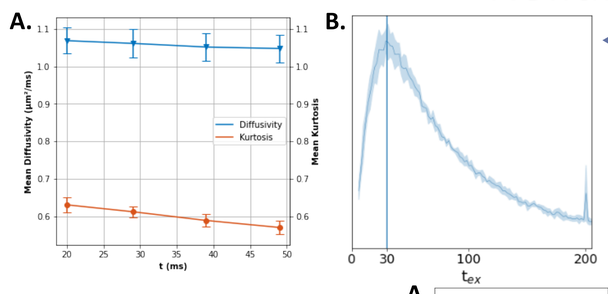


FIGURE 3.

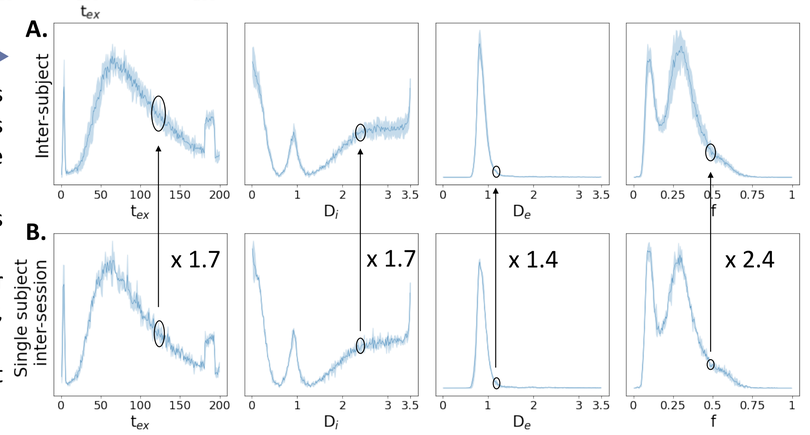
A. Time-dependent MD and MK in the cortex, averaged over the four subjects. **B.** Distribution of $t_{ex}^{K(t)}$ estimates across the cortex voxels.

- Estimated $t_{ex}^{K(t)}$ (30ms) is **shorter** yet **comparable** to t_{ex} from NEXI (65ms).

FIGURE 4.

Distributions of NEXI estimates across the cortex of the 4 subjects (**A**) and between two scans of the same subject (**B**).

- Consistency of these estimations with the rat cortex.
- Inter-subject variability is higher than intra-subject variability, particularly for *Di* and *f*.
- Multi-peak for *f* and *Di* : different solutions may be optimal ?



Dot compartment

	t_{ex} (ms)	Di (µm²/ms)	De (µm²/ms)
NEXI	**64.49** [37.16, 105.12]	**2.13** [1.00, 2.73]	**1.02** [0.85, 1.44]
NEXI_dot	**44.29** [5.28, 87.08]	**2.59** [1.68, 3.11]	**0.99** [0.83, 1.47]

	f	f_{dot}	AICc
NEXI	**0.37** [0.24, 0.58]	-	**41.13** ± 4.57
NEXI_dot	**0.33** [0.25, 0.45]	**0.022** [0.011, 0.0365]	**53.14** ± 3.66

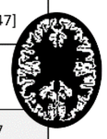


TABLE 1. Median and quartiles of NEXI estimations on the cortical ribbon, across voxels and all subjects. The last column shows the mean corrected Akaike Information Criterion (AICc) for each model.

- The **dot compartment** was found **negligible**, while **penalizing the AICc** with an additional parameter.

Summary

- We **quantified microstructure parameters** in the human cortex in vivo using the NEXI model and found consistencies with previous findings in the rat cortex.
- **These estimates are reproducible** from scan to rescan of the same subject and shows **sensitivity to individual differences**.
- Adding an **additional dot compartment** to NEXI was **not favored** by our data.

References

[1] Jelescu, NeuroImage 2022 [2] Olesen, NeuroImage 2022 [3] Jensen, NMR in Biomed 2010 [4] Veerart, NeuroImage 2016 [5] Kellner, MRM 2016 [6] Andersson, NeuroImage 2016 [7] Henschel, NeuroImage 2020 [8] Avants et al., Insight j, 2009, [9] Lee, NeuroImage 2020 [10] Lee, ISMRM Diffusion Day 2021

QU, TP and IJ are supported by SNSF Eccellenza grant PCEFP2_194260. MP is supported by UKRI Future Leaders Fellowship MR/T020296/2. The data were acquired at the UK National Facility for In Vivo MR Imaging of Human Tissue Microstructure funded by the EPSRC (grant EP/M029778/1), and The Wolfson Foundation. DKJ is supported in part by a Wellcome Trust Investigator Award (096646/Z/11/Z) and Wellcome Trust Strategic Award (104943/Z/14/Z).

UNIL | Université de Lausanne
Faculty of Biology and Medicine

Microstructure Mapping Lab

quentin.uhl@chuv.ch