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CHENONCEAU: towards a novel mesoscopic (100/200 μ m) post-mortem human brain MRI atlas at 11.7T

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Introduction:

Actual human brain atlases rely either on optical microscopy at a microscopic scale[1,6,8], or on in-vivo MRI at a millimeter scale[2,3]. The development of ultra-high field MRI (UHF-MRI) motivates the creation of novel ex-vivo atlases targeting a few hundreds micrometers (100-200 μ m). The purpose of this work is to create a unique mesoscopic MRI atlas of the human left hemisphere, including anatomical and diffusion-weighted images at 100 μ m and 200 μ m respectively, to explore its structure, connectivity and microstructure using suitable advanced biophysical models.

Methods:

Acquisition- The two hemispheres of a formalin-fixed post-mortem human brain sample were cut into seven blocks. The 11.7T acquisition protocol included T2-weighted anatomical scans with the following parameters: isotropic resolution=100/150 μ m, TE=20/16ms, TR=500/6600ms, and diffusion-weighted (DW) 3D-segmented EPI sequences: 200 μ m isotropic, TE/TR=24.3/250ms, $\delta/\Delta=5/12.3$ ms, $b=1500/4500/8000$ s/mm², 25/60/90directions, $G=289/500/666$ mT/m, 30segments.

Preprocessing- DW images were filtered using a non-local means filter algorithm, resulting in a final SNR of 125, 81 and 69 respectively for $b=1500/4500/8000$ s/mm².

Reconstruction of the left hemisphere- A dedicated pipeline was developed to match and integrate all the FOV acquired at 11.7T into two 100/150 μ m anatomical datasets (42/12GBytes) and one 200 μ m HYDI dataset (891GBytes) corresponding to the entire left hemisphere. Connectivity- The HYDI dataset was used to compute Probability Density Functions (PDF) stemming from MAP-MRI model[4] as well as their inherited Orientation

Distribution Functions. Conventional quantitative maps stemming from the tensor model (FA, MD, CED maps) were also reconstructed. To explore the structural connectivity, a global spin glass-based tractography algorithm[5] was used with the following parameters: final number of spin glasses: 1.7 million, spin glass length: 0.16mm, internal energy weight: 30, curvature threshold: 30°, connection likelihood: 0.5.

Microstructure mapping- The HYDI dataset was used to infer NODDI[7] quantitative maps, fixing the local principal direction estimated from the jointly estimated DTI model and the diffusivities to $d_{\parallel}=3.10 \cdot 10^{-10} \text{m}^2/\text{s}$ (value giving the lowest Bayesian Information Criterion, Fig2.a) and $d_{\perp}=2.10 \cdot 10^{-9} \text{m}^2/\text{s}$.

Results:

Figure1.c shows the reconstructed left hemisphere, at 200, 150 and 100 μm . These images are compared with the anatomical scan obtained at 3T with a spatial resolution of 500 μm . The improved resolution reveals the lines of Baillarger in the cortical ribbon, in particular at 100 μm (pink and white arrowheads), and details of deep nuclei.

Figure1.b depicts anatomical scans, CED map, and the superposition of B4 with the blockface image acquired at 3T. White arrowheads highlight subcortical bundles visible on the CED map.

Figure2.a shows NODDI quantitative maps of B4, with the intracellular volume fraction, the concentration factor and the orientation dispersion (OD). Low OD values under the cortex reveal the presence of U-fibers.

Figure2.b presents the ODFs field of B4 superimposed on the FA map. ODFs' shape supports the hypothesis of sharp turns and U-fibers in subcortical white matter (white arrowheads). Moreover, ODFs inside the cortical ribbon are consistent with the existence of fibers running radial and tangential to the pial surface. Figure2.b depicts the reconstructed tractogram overlaid on B4, from which extract short association fibers were extracted.

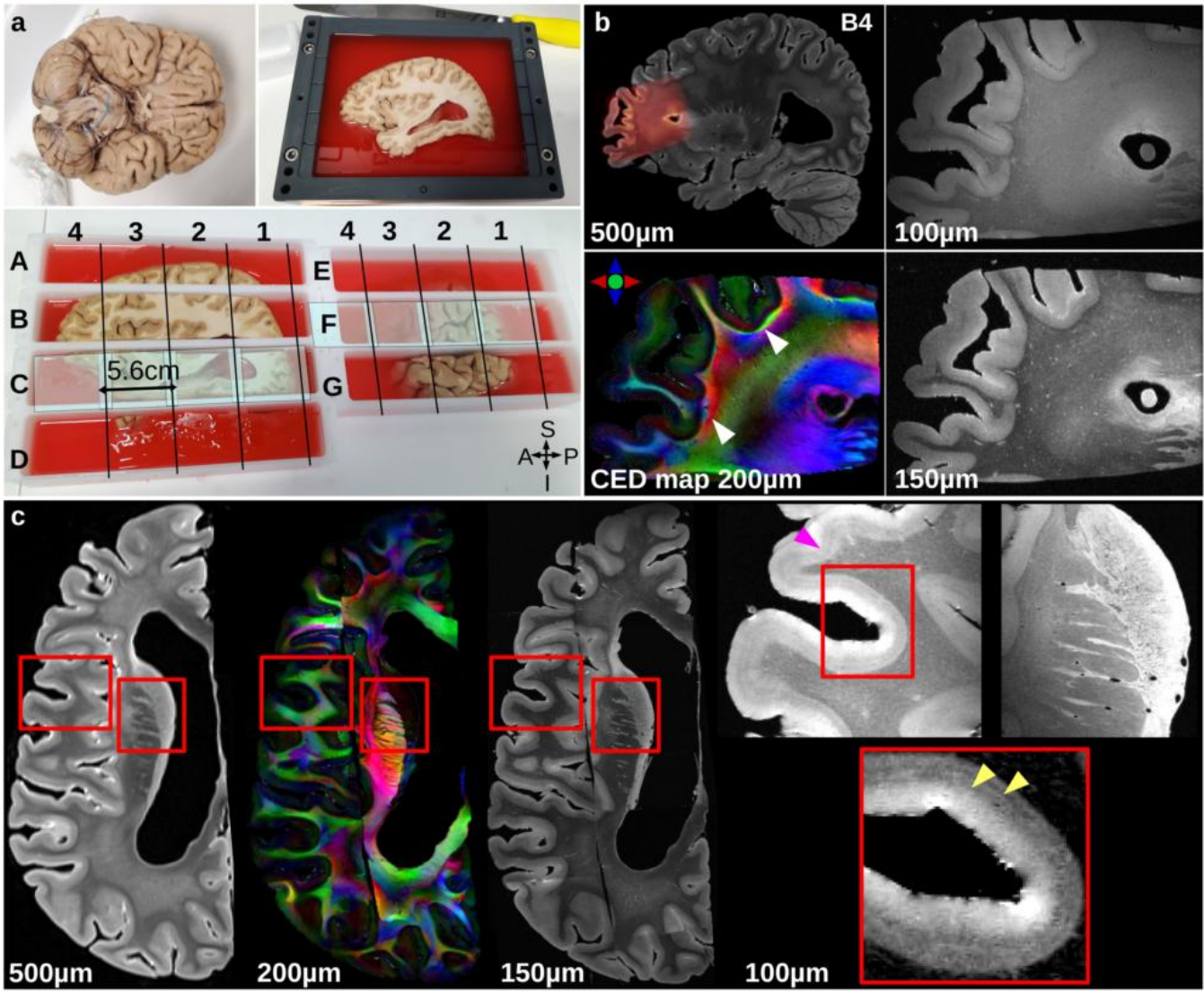
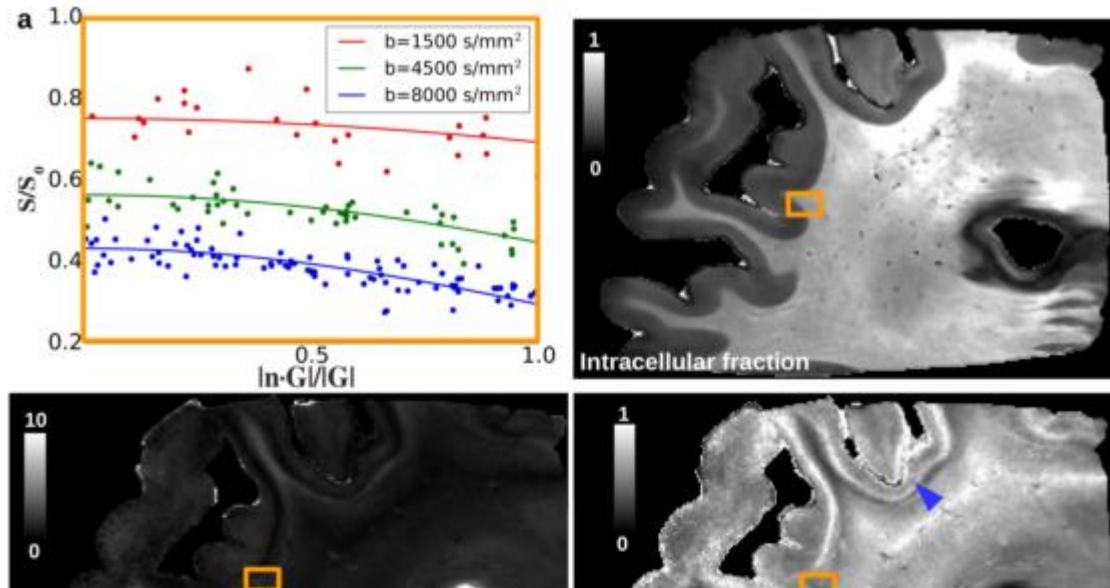


Figure 1. (a) Sample preparation, from the entire specimen to the division of the left hemisphere into seven blocks; (b) Block B4 acquired at 100/150/200µm and overimposed on the blockface image acquired at 3T at 500µm. White arrowheads highlight subcortical bundles visible on the color-encoded direction (CED) map; (c) Axial view of the left hemisphere reconstruction: from left to right : Images acquired at 500/200/150/100µm. Pink and white arrowheads show the two lines of Baillarger visible at 100µm

•Reconstruction of the left hemisphere



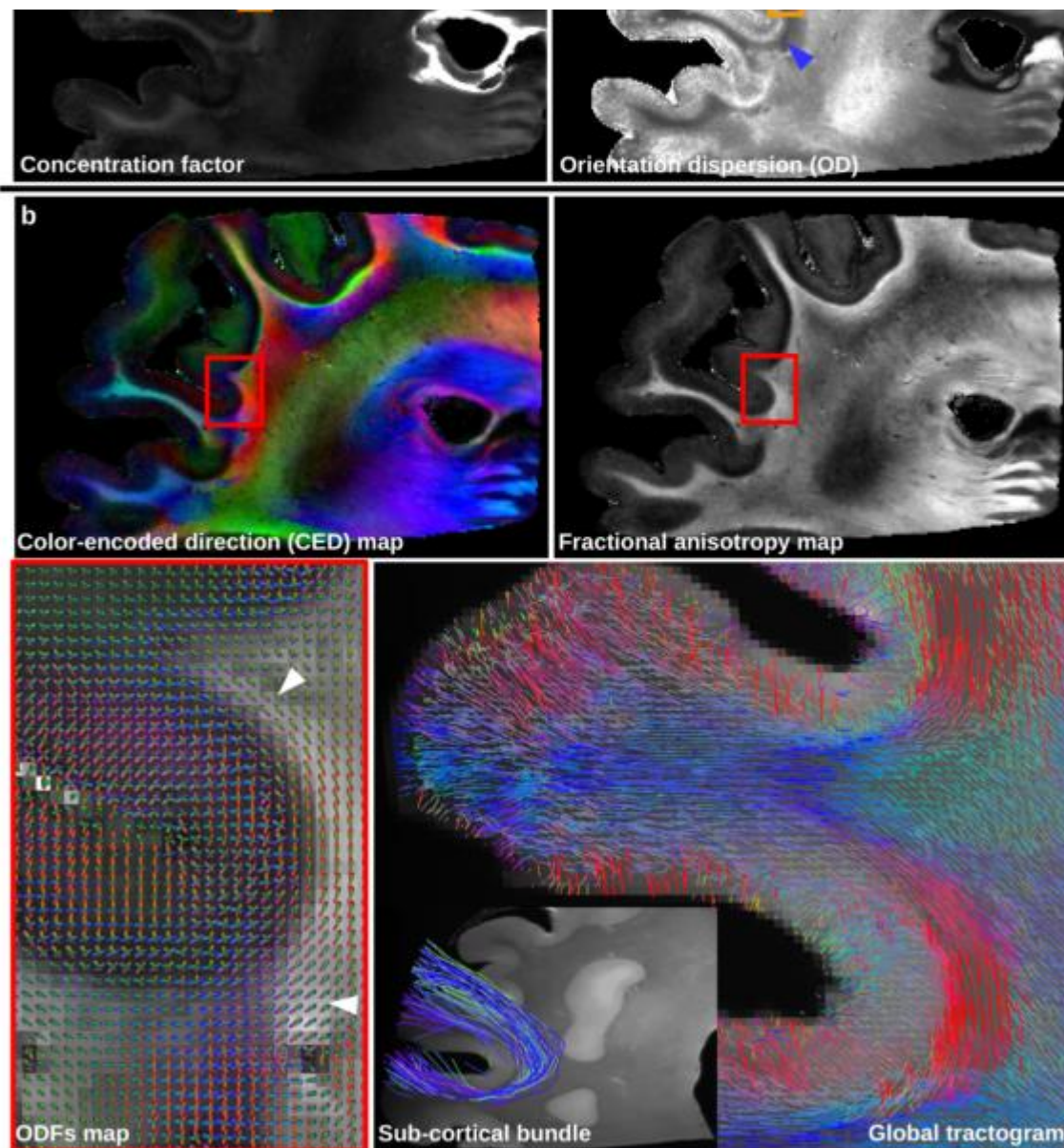


Figure 2- (a) B4 microstructure. Orange rectangles show the position of the voxel for which the fit quality was plotted, S/S_0 denotes the normalized signal attenuation, G the gradient direction, and $n \cdot G$ the dot product of the gradient direction and the mean fiber orientation. Blue arrowheads show low orientation dispersion values corresponding to subcortical bundles; (b) B4 connectivity. The red rectangles on the FA (upper left) and CED (lower left) maps highlight the position of the ODFs (middle) overimposed on the FA map. Their orientation supports the hypothesis of sharp turns and U-fibers in subcortical white matter. On the upper right is presented the global tractogram from which are extracted short association fibers

• Inference of the microstructure and connectivity of an acquired field of view

Conclusions:

This work provides new anatomical and HYDI datasets at mesoscopic resolutions on an entire human left hemisphere. Such unique dataset open the way to investigate not only the smallest brain structures invisible at lower resolution, but also the sub-cortical and inner-structure connectivity as well as the white matter microstructure and cortex cytoarchitecture, thus paving the way, after the acquisition of the right hemisphere, to the construction of a mesoscopic 11.7T human brain MRI atlas.

Imaging Methods:

Anatomical MRI
Diffusion MRI ²

Modeling and Analysis Methods:

Diffusion MRI Modeling and Analysis

Neuroanatomy:

Cortical Anatomy and Brain Mapping ¹

Cortical Cyto- and Myeloarchitecture

Keywords:

Acquisition

Cortex

Cortical Layers

STRUCTURAL MRI

Sub-Cortical

Tractography

White Matter

Other - diffusion MRI

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

My abstract is being submitted as a Software Demonstration.

No

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

Other

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.

Not applicable

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

Diffusion MRI

Postmortem anatomy

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

If Other, please list - 11.7T

Which processing packages did you use for your study?

Other, Please list - Connectomist

Provide references using author date format

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