In vivo rapid 3D Microscopic DTI combining Super Resolution Reconstruction and Reverse Gradient correction method

Ulysse Gimenez[1], Antoine Triquet[1], and Hana Lahrech[1]

[1]*Clinatec, CEA, Grenoble, Rhones-Alpes, France*

Introduction: 3D isotropic high spatial resolution is still challenging on preclinical scanners. The objective of this work is to develop a rapid microscopic 3D DTI method for *in vivo* mouse brain experiments at high field. Here, a super-resolution reconstruction (SRR) is applied after reverse gradient (RG) distortion corrections.

Material and Methods: *In vivo* **MRI:** Experiments were performed at 9.4T (Bruker, 660mT/m) on wild type mice. One-shot EPI DTI was acquired twice in coronal, sagittal and axial orientations with opposite phase encoding directions (blip up and blip down). These six acquisitions were obtained using identical parameters: TE/TR=26/4000ms, NA=12, scan duration=5min36s, diffusion gradients (δ=4ms Δ=8.5ms) applied in six spatial directions with a b-value of 1500s/mm². T_2 weighted anatomical images were acquired using TURBORARE sequence: Rare factor=4, NA=4, scan duration=3min30s, TE_{eff}/TR=20/2500ms. In all acquisitions, field of view (FOV) and spatial resolution were set to 12.24*10.08*14.04 mm³ and 120*120*360 µm³ respectively. *Ex vivo* **MRI:** Experiments were performed at 7T (Bruker, 600mT/m). A 3D spin-echo DTI sequence (TE/TR= 16/90ms, NA=34) was applied with diffusion gradients (δ= 3.5 ms Δ=8 ms) in six spatial directions with a b-value of 1500s/mm². FOV and spatial resolution were set to 20x8.5x11.5 mm³ and 100x100x100 µm³ respectively with a total acquisition time of 59 hours. **RG correction:** RG method is used for image correction since EPI acquisitions suffer from severe distortions due to magnetic-susceptibility variations. For coronal, sagittal and axial acquisitions the "Topup" tool from FSL software[1] is applied on opposite blipped gradient acquisitions. A non-distorted image is then calculated by compensating opposite distortions.

SRR: SRR consists in reconstructing 3D high spatial resolution images from anisotropic « low resolution » acquisitions with different orientations[2]. Here, we used three orthogonal acquisitions to estimate a 3D isotropic volume of 120*120*120 µm³. The calculation was performed on homemade software using maximum a posteriori (MAP) estimation as previously described[2] and with improved dynamical minimization step. **Data analysis:** DTI parameters and fibertracking were constructed and analyzed using MedINRIA and Mrtrix softwares.

Results: Fig.1 shows RG method powerful ability to obtain undistorted images. One-shot EPI acquisitions suffer from severe distortions in the phase direction (dorsal-ventral), depending on the phase encoding orientation (A-B). The corrected image is then built (C), and can be compared to anatomical image (D). These corrections are computed on B0 images of coronal, sagittal and axial acquisitions, and applied to all diffusion weighted images. Using SRR, an *in vivo* 3D high spatial resolution DTI image is obtained for an acquisition time of 35 minutes. DTI parameters are then computed in the whole volume. Fig.2 shows an example of FA-color map in coronal orientation, before (A) and after SRR (B). Fibertracking is also computed on SRR 3D high spatial resolution and is compared to fibertracking obtained from undistorted and time-consuming *ex vivo* acquisitions. Fig.3 highlights that *in vivo* reconstruction (A) almost reproduces all details observable on *ex vivo* reconstruction (B) of the fornix bundle. Thus, the reconstruction of such small structure of the mouse brain validates our method at this stage.

Discussion / Conclusion: Compared to other techniques, SRR has several advantages. It can be easily applied in different facilities and it is a promising technique since it allows reaching isotropic high resolution images rapidly, exceeding limits of the slice thickness given by the maximum intensity of the magnetic gradient system. However, SRR needs accurate registration of low resolution images with different orientations. Traditional distortions corrections (using B0 map or Point Spread Function) are not sufficient to correct severe distortions observed on EPI acquisitions at high field. Here, we demonstrate that RG method effectively corrects EPI distortions. To our knowledge, this is the first time that SRR is applied *in vivo* in DTI imaging on mice. These results are promising for *in vivo* fibertracking longitudinal studies. Neurodegenerative diseases which imply the decrease of fine white matter structure may then be studied *in vivo* with a better accuracy.
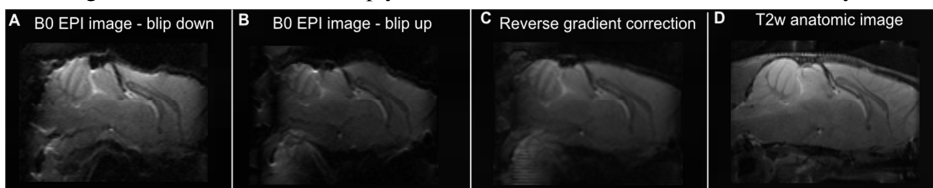

Fig1: RG method. Two EPI images acquired with opposite blipped directions (A-B). Compensating the opposite distortions, a corrected image is obtained from these 2 acquisitions (C), and compared to anatomical undistorted image (D).
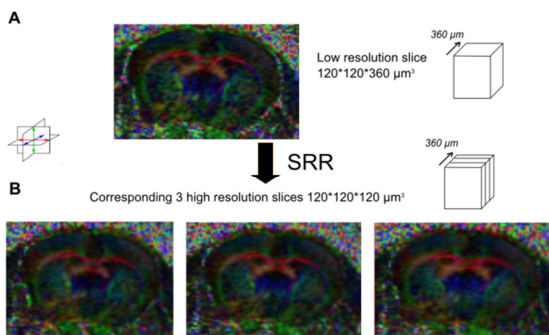

Fig2: FA-color map obtained from SRR. Low-resolution anisotropic (120*120*360 µm³) sagittal, coronal and axial DTI images are obtained from EPI acquisitions after Reverse Gradient correction. The SRR is then computed to obtain 3D isotropic high spatial resolution DTI image (120*120*120 µm³). FA-color map of low resolution coronal slice (A) is compared to the three corresponding high resolution slices (B).

Fig3: Sagittal view of fornix tractography obtained from 3D DTI data. (A) The fornix is constructed from *in vivo* 3D SRR DTI after reverse gradient correction. (B) The fornix is constructed from *ex vivo* spin echo 3D DTI.
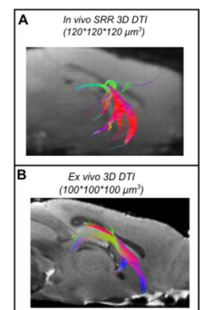
[1] Smith 2004, NeuroImage   [2] Scherrer 2012, Medical Image Analysis