Co-registration of DTI Tractography with Gd-enhanced T1 imaging in evaluation of CED studies in the Rhesus Macaque

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Introduction: Recent advances in white matter fiber tracking methods using diffusion tensor imaging have a wide range of potential applications. DTI tractography can non-invasively extract information about the shape of white matter fibers. In the case of direct drug infusions to the brain, and specifically convection-enhanced delivery (CED), this information could be beneficial in choosing a precise target zone for the infusion that will potentially minimize diffusion away from the target region along white matter tracts. With the specific goal of evaluating distribution of a CED agent to the putamen in the rhesus macaque, we here propose a systematic landmark-based registration of diffusion tensor images and a series of T1-weighted anatomical images showing the progress of enhancement as a Gd-mixture is infused into the putamen during a CED procedure. We then use the area of enhancement as a seed region to perform tractography, in order to observe the effect of white matter tracts in the area of the putamen on the distribution of the infusate.

Methods: *1) Data acquisition and tensor calculation:* Individual rhesus macaques were each scanned (on a GE Discovery MR750 3T system) in one session to acquire "baseline" images, which included a T1-BRAVO sequence and a diffusion-weighted EPI sequence with 55 gradient-encoding directions with b=3000 and 10 b=0 scans. On a second session at a later date, an infusion experiment with a Gd agent of concentration 1mM/mL was performed on the same animal. Images acquired included T1 scans with f.a.=34 taken at 10-minute intervals during the infusion. After performing eddy current correction and fieldmap correction we used CAMINO [1] for non-linear tensor fitting. *2) Cross-modality coregistration:* This challenging step was solved by resampling the T1-BRAVO image of a single animal to match the 3D resolution of the DTI data (0.589mmx0.589mmx2.5mm) from the same animal, and 21 slices were extracted from both the T1 and FA images that covered the same regions of the brain. Using ITK-SNAP [2], 3D regions of interest were hand-drawn around the left and right putamen, and a small sphere in a central white matter tract, to serve as a total of 3 landmark regions in each image. Then, using the methods described in [3] with the ANTS program, the transformation (using both point-set guided and pure cross-correlation metrics) of the FA image to the T1 image was calculated, and the inverse transformation applied to the T1 image to warp it into the space of the diffusion tensor image. *3) Tractography of infusion sequence:* In a selection of 9 of the 71 T1 images acquired during the infusion, a region of interest was hand-drawn covering the area of contrast enhancement to use as a seed for the tractography algorithm. We then performed tractography using Tensor Deflection algorithm [4]. Viewing the tractography overlaid on the T1 images demonstrates the correspondence of infusion volume with white matter fibers.

Results: Figures 1, 2, 3, and 4 show the white matter tracts which pass through the infused area at selected increasing time points during the study. In Fig. 1, we are mid-way through infusing the right putamen. In Fig. 2, we have finished infusing the right putamen and begun with the left. In Fig. 3, we have almost completed infusion of the left putamen and for clarity of presentation have omitted tractography through the completed right putamen.

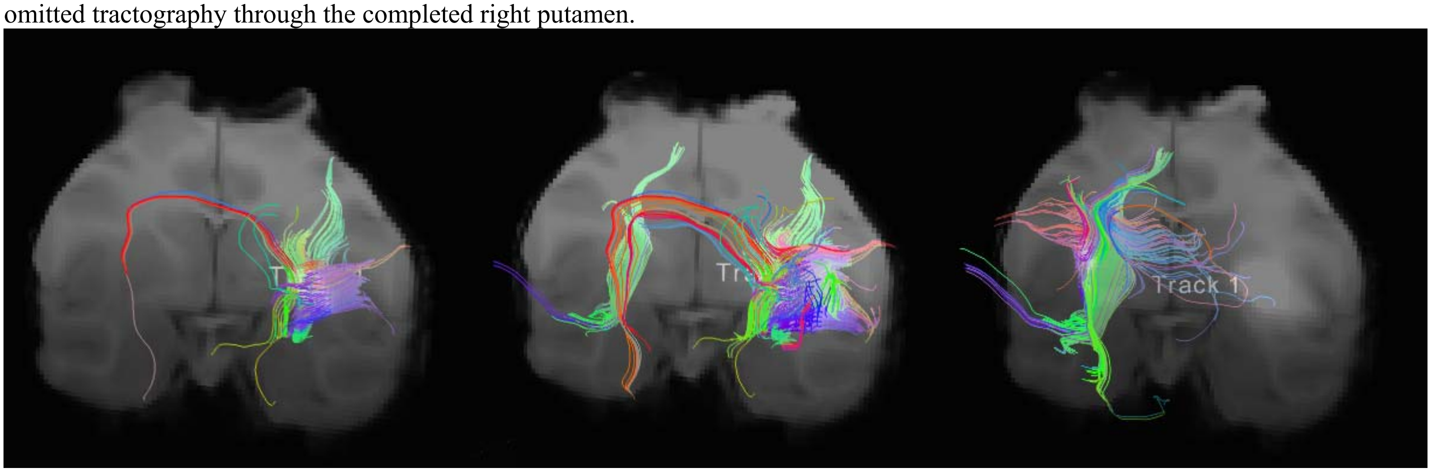

Fig.1 Fig. 2 Fig. 3

Discussion: The co-registration, region of interest drawing, and DTI Tractography performed on this animal has provided a proof of concept for this potentially informative procedure. During ROI drawing, it was noted that infusate had begun to spread outside of the left putamen, and Fig. shows a central white matter tract along the path of the infusate. In the future, the potential to coregister and overlay these 3D views with MR Angiography data may help better guide surgeons during target placement for CED studies monkeys, and eventually of Parkinson's Disease drugs in humans.

References: [**1**] P. A. Cook, et al. Camino: Open-Source Diffusion-MRI Reconstruction and Processing, 14th Scientific Meeting of the ISMRM, Seattle, WA, USA, p. 2759, May 2006. [**2**] Paul A. Yushkevich, et al. User-guided 3D active contour segmentation of anatomical structures: Significantly improved efficiency and reliability. Neuroimage. 2006 Jul 1;31(3):1116–28. www.itksnap.org [**3**] http://www.picsl.upenn.edu/ANTS/ [**4**] Lazar M, et al. White matter tractography using diffusion tensor deflection. Hum Brain Mapp. 2003 Apr;18(4):306-21. [**5**] Melhem ER, et al. Diffusion Tensor MR Imaging of the Brain and White Matter Tractography. AJR:178, Jan. 2002.