Imaging Tasks Useful in Convection-enhanced Drug Delivery in the Brain: Depicting Distal Cerebral Vasculature

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INTRODUCTION: Convection-enhanced delivery (CED) [1] can drive therapeutic agents (infusates) through catheters and may one day slow or reverse neurodegenerative diseases like Parkinson's disease (PD). Research efforts have concentrated on quantifying the localized concentration of infusate delivered under the high pressure used during CED [2]. The high pressure delivery often increases the open, perivascular space running along the exterior of small, distal arteries in the target zone shown in green in Fig. 1a, creating unwanted escape routes for the infusate. Depicting this vasculature, and later correlating infusate concentration near it during CED, is thus of interest.

We present a visualization platform to simplify the simultaneous viewing of T1-weighted brain roadmaps with vascular 3D data from the desired target zone. Current clinical imaging efforts seldom focus on these small (< 500 um diameter) perforating arteries, so we investigate two protocols to image them – balanced SSFP (bSSFP) and Time Of Flight (TOF). The end goal of the platform is to help the interventionalist choose a catheter trajectory that is as distant as possible from local vasculature to minimize loss of infusate.

METHODS: Using a 3T GE scanner and 32-channel head coil, a high-resolution 3D T1-weighted image volume is first acquired whose gray/white matter contrast is used to identify the desired treatment region. We focus on a gray matter region, the putamen. The roadmap is pulled into Vurtigo, an open-source visualization platform, developed at the University of Toronto and the affiliated Sunnybrook Research Institute [3]. We modified Vurtigo to allow us to render vascular data from constrained regions near the target simultaneously with the T1 roadmap. The Vurtigo-based visualization is compatible with a Vurtigo plug-in used to direct real-time targeting and monitoring in CED treatments [4].

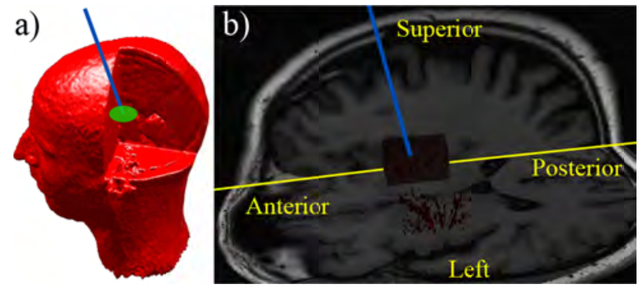

Figure 1: a) *CED Illustration: catheter (blue) used to deliver infusate to a brain region (green).* **b)** *Sagittal and axial T1-weighted cut planes with superimposed MIPs of putamen vasculature (imaged via bSSFP as in Figure 2). The dark box shows the restricted volume of the far MIP.*

Time of Flight (TOF) is a diagnostic standard for imaging the relatively large, high velocity feeding vessels crucial for perfusion of the brain. Imaging the much smaller, slower flow in the perforating vessels in the putamen led us to explore a comparison of three TOF protocols of varying resolution with a balanced steady-state free precession (bSSFP) acquisition in five healthy volunteers. Scan parameters were chosen to create TOF scans of similar and longer duration to the bSSFP scans, with the longest scan having similar resolution to the bSSFP scan. We acquired a bSSFP volume with 0.47 x 0.47 x 0.5 mm (64 slices total) with a 40 degree flip angle and 3 signal averages in a scan time of 6:16. The three TOF protocols utilized a 15 degree flip angle to image 2 slabs (50 slices total) to cover the putamen with voxel dimensions of a) 0.86 x 0.86 x 0.8mm (5:18), b) 0.57 x 0.57 x 0.6 mm (6:45), and c) 0.5 x 0.5 x 0.5 mm (8:11). The inferior face of the imaging slabs was prescribed to maximize fresh inflow into the putamens in each case.

RESULTS: As a reference of the putamen vasculature, high resolution (200 um) atlas X-ray images of thin, fixed slices after iodinated contrast was injected in a cadaver are shown in the sagittal (top) and coronal planes (bottom) of Fig. 2 [5]. The shrub-like appearance of the putamen's perforating vessels in the sagittal is clearly more visible with bSSFP than in the best depiction of the TOF data, found in the high resolution scan, in a selected volunteer. The coronal frame bSSFP depiction also has much higher contrast than TOF, but the bright cerebrospinal fluid in bSSFP images complicates the rendering – hence the use of restricted MIP volumes in Figure 1. In one volunteer, dental work created dropout artifacts that required higher order shim correction, a capability not found on all magnets.

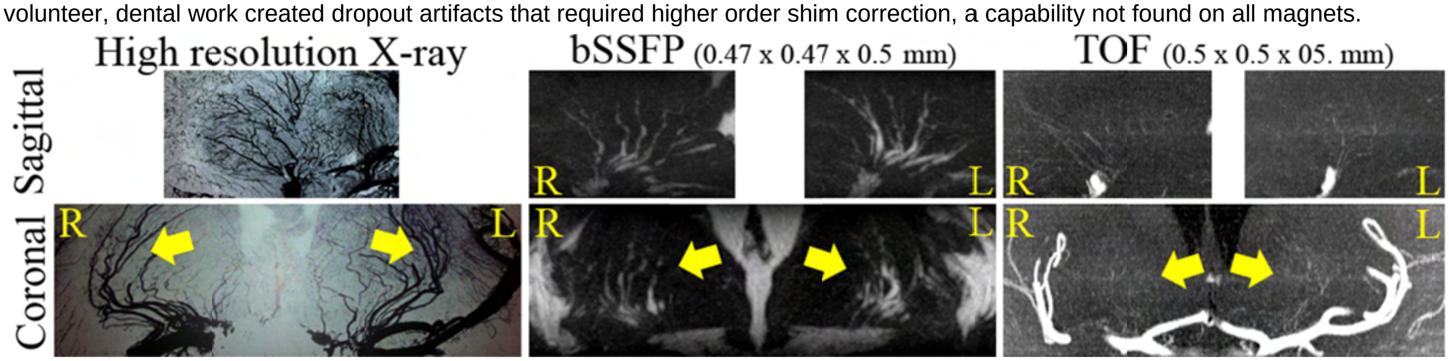

Figure 2: Arterial *comparison of cadaver X-ray reference (left), bSSFP (center) and TOF (right) of the putamen in the sagittal (top) and coronal plane (bottom). bSSFP better depicts the vascular appearance (shrub-like in sagittal, at heads of yellow arrows in coronal).*

CONCLUSION: A visualization platform has been developed for simultaneously visualizing brain structures and small vessels in the target area for CED. This platform is fully compatible as a planning stage for a real-time targeting platform [4]. The limited slab thickness required to cover CED target regions allows bSSFP to better exploit inflow for imaging distal cerebral vasculature than the standard clinical method, TOF. We now aim to test the imaging methods on a cohort of patients presenting to our Parkinson's service.

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REFERENCES: **1)** Bankiewicz KS, et al. Exp Neurol. 2000 Jul;164(1):2-14. **2)** Emborg et al. Soc. For NeuroSci, 2010. **3)** Radau et al. "VURTIGO: Visualization platform …", Proc. 2011 MICCAI, Sept. 22, 2011. (in press) **4)** Brodsky et al. MRA Club, 2011. **5)** Salamon G. "Atlas of the Arteries of the Human Brain", 1973.