High-resolution imaging of vessels in the isolated rat brain

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Introduction: While several atlases are available depicting the spatial distribution of various parameters either measured with MRI or from histological section, no comparable comprehensive data exists for the distribution of vessels in the rat brain. Angiography is able to use the blood flow in the brain of the living rat to display the largest arteries, while SWI can visualize veins down to medium size. The aim of this study was to obtain a full picture of vessels even down to relatively small size in the isolated rat brain perfused with contrast agents at ultra-high field.

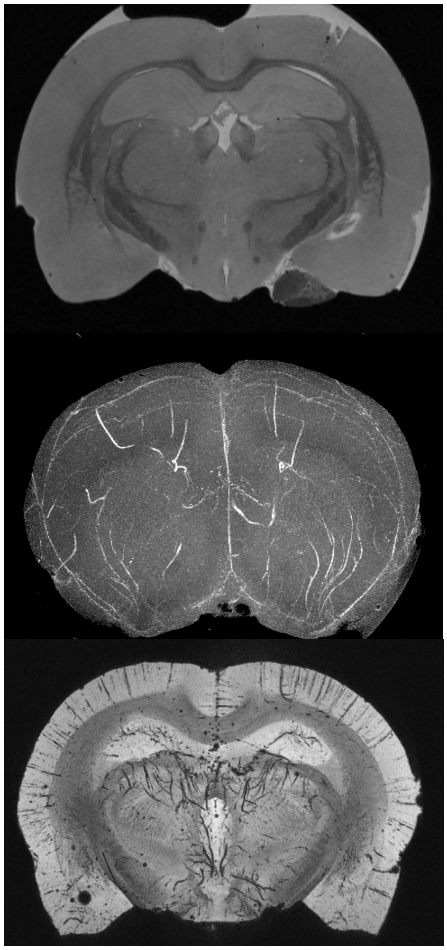

Fig.1: Slices from rat brains with different contrast agents: A: Gd-DTPA shows no vessel contrast. B: Gd-DO3A-HAMP highlights large vessels (maximum intensity projection over 6.25 mm). C: FeO contrast agent shows large number of veins and arteries (minimum intensity projection over 2.5 mm)

Methods: The rats were perfused using a mixture of fluorescent dye labeled Gelatine gel [1] with either a Gd-based contrast agent or an agent containing iron-oxide particles. The gel was allowed to congeal for 4 hours. The brain was isolated and the vascular surface was scanned for fluorescence signal using a Zeiss Imager microscope with a 5x objective. Then it was placed into a test tube filled with fluorocarbon fluid for susceptibility matching. MR Images were acquired at a horizontal 16.4 T scanner with a homemade microstrip volume coil, using gradient echo sequences with isotropic spatial resolutions of 50 µm (FeO) and 45 µm (Gd) for between 5 and 12 hours. Afterwards the brain was cut and processed for histochemistry (Cytochrome oxidase).

Results: Images acquired with Gd-DTPA, Gd-DO3A-HAMP and FeO as contrast agents are shown in Fig. 1. Using Gd-DTPA does not enhance the vessels due to the breakdown of the Blood-Brain-Barrier, causing a distribution of the contrast agent over the entire tissue. Gd-DO3A-HAMP binds specifically to polar macromolecules [2], preventing diffusion out of the vessel and thus making it possible to identify large and medium sized veins and arteries (Fig. 1b). Suspending the brain in a susceptibility-matched but MR invisible fluid makes it even possible to clearly see the surface vessels and overlay them on histological reconstructions (Fig. 2). The ironoxide-based contrast agent causes an apparent amplification of the vessel size, making it possible to view vessels with a significantly smaller diameter than the voxel size. Thus, these images clearly depict a large number of arteries and veins (Fig. 1c). Especially striking are the high density of outward vessels in the cortex (Fig. 3) that are visualized with high detail.

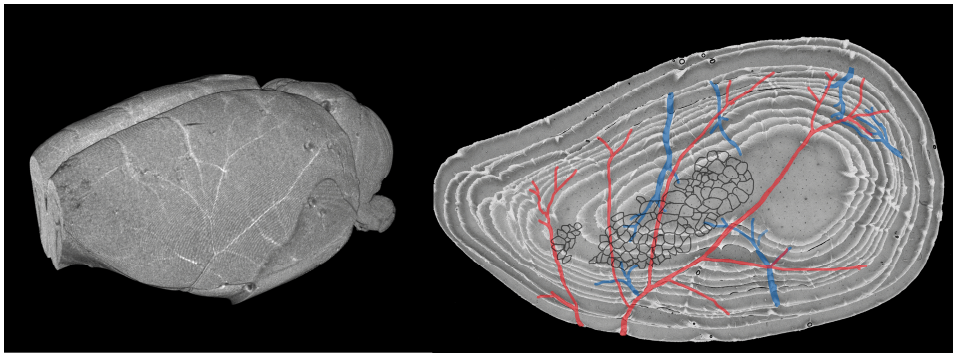

Fig. 2: Surface vessels can be identified clearly on the Gd-enhanced MR image (top). For comparison, arteries, veins and barrel field contours on the brain surface as found from CytOx-stained sections (different animal).

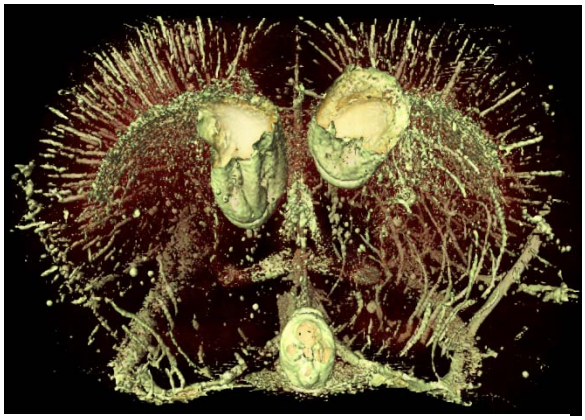

Fig. 3: 3D-surface plot of vessels enhanced with FeO.

Conclusions: Using dedicated contrast agents for perfusing the animals makes it possible to obtain highly resolved images of the vessel distribution in the rat brain. Further optimization in contrast agent concentrations and post-processing of the image data will make it possible to compile a complete atlas of brain vessels down to relatively small size. The resulting vessel maps can be used as a highly detailed framework that spans through the entire cortex and enable an up to now unreached precise and individual alignment of volumetric MR datasets to histological preparations.

References:

[1] P. Tsai et al, J. Neurosci 29, 14553 (2009)
[2] I. Mamedov et al, ACS Chem. Neurosci. (epub 2010)