Calibration of cerebral blood oxygenation and perfusion MR imaging in mice by invasive micro probe measurements.

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Target Audience: Physicists, biologists, technologists and physicians interested in MR imaging of cerebral blood oxygenation.

Purpose: To validate quantitative MR imaging methods sensitive to cerebral blood oxygenation and perfusion by different respiratory stimuli and subsequent invasive micro probe measurements.

Methods: Sixteen C57BL/6 mice (m, age: 12wks, weight: 25g), anesthetized by injecting 200µl of a ketamine-xylazine-acepromazine mixture i.p. (10-2-0.4 mg/ml concentration), were imaged on a 7T small animal MRI applying stimuli of air, 100% O_2 and air+10% CO_2 for 30 min each. ASL-CBF was measured by Q2TIPS (TI1/TI2/SS = 900/1400/1375ms and 45 control-label pairs). R2* was measured by 3D FLASH (TEs = 3, 8, 13, 18, 23, 28, 33ms). Phase images were used to correct R2* for macroscopic field inhomogeneities [1]. R2 of venous blood was assessed by the QUIXOTIC sequence [2]: TI = 725ms, velocity sensitization gradients (amplitude-duration-separation = 15Gauss/cm-2ms-17ms), T2 prep times = 20, 40, 60 ms and 30 control-label pairs. After MRI, animals were reinjected with 200µl of anesthetic to maintain anesthesia for the invasive micro probe measurements. Two combined pO_2 and laser Doppler flow probes were inserted 3 mm deep into the brain (Fig. 1). After micro probe measurements, animals were euthanized by 100% CO_2.

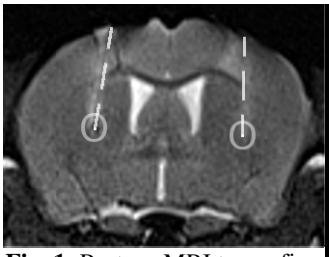

Fig. 1: Post-op MRI to confirm the location of the micro probes.

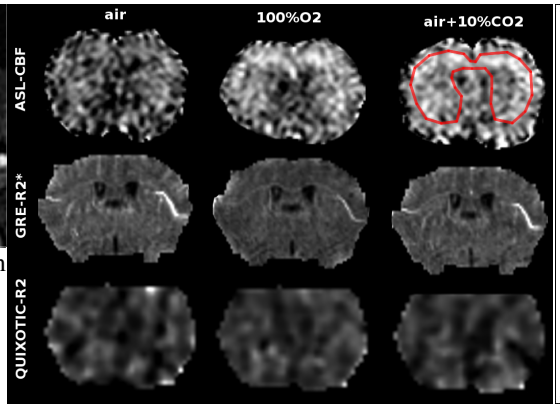

Fig. 2: Quantitative parameter maps of the different stimuli, scaled equally for better comparison. Brain tissue ROI (red) was defined on the underlying raw data of each method by excluding ventricles and areas close to the skull.

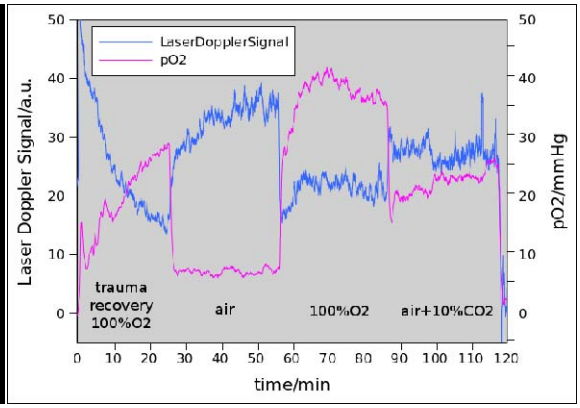

Fig. 3: Exemplary micro probe measurements of one animal. 100% CO_2 were applied at 120 min.

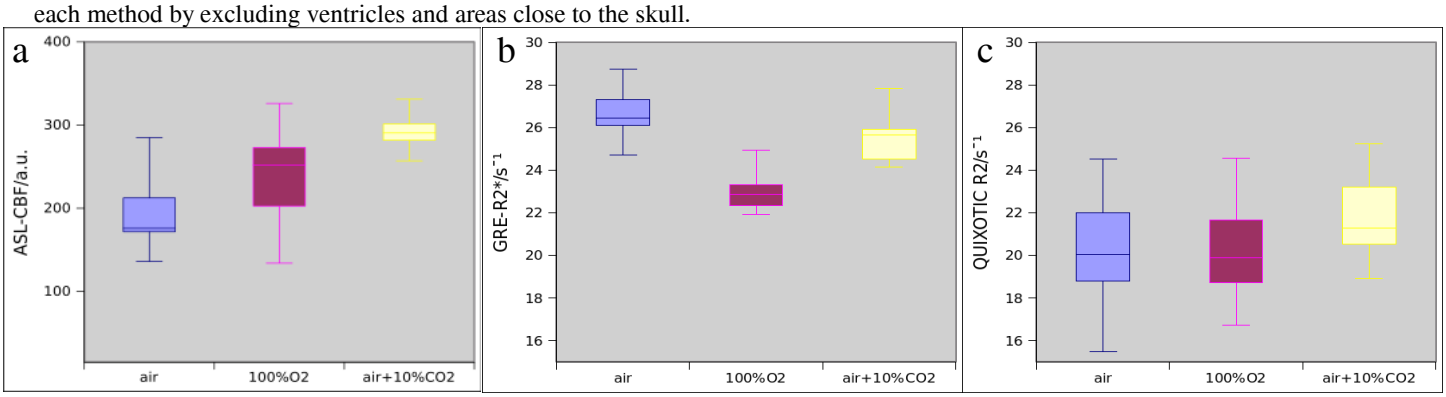

Fig. 4: Box plots of the ROI analysis of 16 mice for the different stimuli and MR methods.

Results and Discussion: Quantitative parameter maps of the measurements are shown in **Fig. 2**. The increase in cerebral perfusion during the 10% CO_2 stimulation is clearly visible in ASL-CBF and laser Doppler measurements (**Fig. 3** at 90-120 min and **Fig. 4a**). Perfusion during air and 100% O_2 breathing showed high variability in MRI, most likely due to adverse effects of the anesthesia which was applied shortly before. Micro probe measurements additionally suffered from trauma recovery causing inconsistent results between animals and first stimuli. Estimation of blood oxygenation showed high R2*, i.e. low blood oxygenation at air, low R2*, i.e. high blood oxygenation at 100% O_2 and intermediate R2* values at 10% CO_2 stimulation (**Fig. 4b**). This is consistence with micro probe tissue pO_2 measurements (**Fig. 3**). Direct measurements of venous blood R2 (QUIXOTIC) showed high variability and no apparent trend with respect to the applied stimuli. This may be caused by suboptimal sequence settings for mouse MRI which need further optimization.

Conclusion: We found reasonable consistency between MRI and micro probe measurements. However, adverse effects of anesthesia and trauma during micro probe insertion have to be solved in further experiments.

References: [1] Fernández-Seara MA and Wehrli FW. Magn Reson Med. 2000 Sep;44(3):358-66. [2] Bolar DS et al. Magn Reson Med. 2011 Dec;66(6):1550-62.