Cerebral MR angiography in mice with a new blood pool agent (P792)

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Introduction: Magnetic resonance angiography (MRA) in mice is classically performed using Time of Flight methods[1] (TOF). Image quality may however be improved by using intravascular contrast agents[2]. In this study, we evaluated a new blood pool agent, P792 (Vistarem®, Guerbet, France), to perform cerebral angiography in mice. Angiograms acquired after injection of P792 were compared to TOF images and to those acquired after injection of Gd-Dota contrast agent (Dotarem®, Guerbet, France). In addition, two injection sites were tested: the retro-orbital sinus and the tail vein.

Materials and methods: Swiss mice (OF1 Charles River laboratories, mean weight 27g, n=5) were used. In vivo cerebral MRA images were recorded on a 4.7 Tesla Bruker Biospec system using a surface coil actively decoupled from the transmitting birdcage probe. P792 (45µmol/kg) and Gd-Dota (100µmol/kg) were injected manually outside the magnet. Injections in the tail vein were done via a catheter. The mean time between injections and the beginning of acquisition was 2 min. Images with and without contrast agents were recorded by using 3D gradient echo sequence with the following parameters: repetition time (TR)=19 ms, echo time (TE)=4.4ms, flip angle (α)=30°, field of view (FOV)=15x20x15mm^3, acquisition matrix: 144x192x104, acquisition time 12min 41s. Brain tissues were manually extracted using Amira 3.1® software and angiograms were obtained by generating Maximum Intensity Projections (MIP matrix: 256x352x256).

Results: Images recorded after injection of Gd-Dota showed a signal increase in the tissue around the skull, related to extravasation of the contrast agent in the tissue due to its small molecular weight. No signal increase was noticed within parenchymal brain tissue. Signal increase within head tissues was barely noticed after injection of the P792 compound. Angiograms reconstructed after head tissue removal were however very similar for both contrast agents: both angiograms displayed arteries and veins and despite a slightly higher contrast with P792, the number of the detected vessels was not increased with this agent (figure). In addition, we did not notice any difference between images recorded after retro-orbital or tail vein injection. TOF angiograms only showed arteries (figure). Some of their ramifications (for example for the posterior cerebral artery or the more distal parts of the azygos pericallosal artery) were slightly better visible on angiograms after injection of P792, than on TOF angiograms.

Conclusion/Discussion: By comparison with 3D TOF angiography, contrast enhanced angiography in mice allowed to detect veins, and (for some animals) more distal parts of arteries. Despite a slightly better contrast of vessels with P792, visual inspection of Dotarem and Vistarem enhanced angiography suggested that the two methods provided similar results, as the number of the detected vessels was not increased. One drawback of Dotarem was however its extravasation in the body, that increased signal in extracerebral tissues, but this could be worked around by brain extraction prior to angiograms reconstruction.

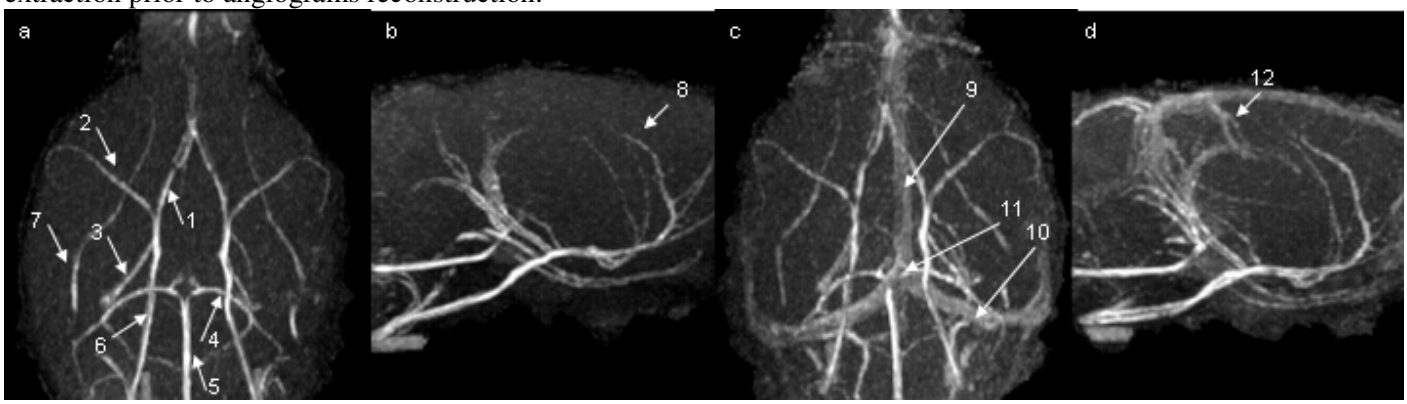

Figure: Cerebral angiograms of the same swiss mouse before (a,b) and after injection of P792 (c,d). The detected vessels were: 1. anterior, 2. middle, 3. posterior cerebral arteries, 4. superior cerebellar artery, 5. basilar artery, 6. internal carotid artery, 7. pterygopalatine artery, 8. azygos pericallosal artery, 9. superior sagittal sinus, 10. transverse sinus, 11. caudal confluence of sinuses, 12. straight sinus.

Reference: 1. Beckmann N et al., The Journal of Neuroscience. 23(24):8453-9; 2003; **2.** Kiessling F.M. et al., Proceedings of the ISMRM meeting, 2005, p. 173.

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