Blood contrast agent concentration measured by Dynamic MRI in intra- and extracranial mouse vessels at 9.4 Tesla using a novel cryogenic probe

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Introduction
Quantitative dynamic MRI requires the knowledge of contrast agent (CA) concentration in blood. Due to the small size of murine vessels, so far the so-called arterial input function (AIF) has only been measured in the mouse heart. Using a novel cryogenic probe at 9.4 T, we measured CA kinetics in three intra- and extra-cranial vessels in order to test their eligibility for serving as AIF in mouse brain perfusion studies.

Material and Methods
At 9.4 T (Biospec, Bruker, Germany) using a transmit-receive CryoProbe™ (Bruker), in a preliminary experiment two mice (21g) were examined. For optimal slice localization containing the vessels of interest, high-resolution 3D Time-of-flight (ToF) angiography and 2D T2w-imaging were performed before contrast agent injection with the following protocols:

\[(A)\] flow-compensated GE: \(TR=27.2\text{ms}, TE=6.4\text{ms}, \text{FoV}=16\times16\times16\text{mm}^3, MT=512\times512\times128, t_{\text{sec}}=19\text{min27s}, \text{res}=31\times31\times125\mu\text{m}^3\),

\[(B)\] T2w-SE: \(TR=3\text{s}, 8\text{echoes}, \Delta TE=13.1\text{ms}, \text{FoV}=20\times20\text{mm}^2, MT=384\times384, t_{\text{sec}}=15\text{min6s}, \text{res}=52\times52\times500\mu\text{m}^3\).

For Dynamic MRI, relaxation rate \(R_1=1/T_1\) was measured during bolus injection (Gd-DOTA, 0.1mmol/kg, \(t_{\text{inj}}=3.5\text{s}, V_{\text{inj}}=0.8\text{mL}\)) as described in [2] using the following protocol parameters: \(TR=17.4\text{ms}, \Delta T_E=2.5\text{ms}, TS_1=250\text{ms}, TS_2=600\text{ms}, \text{FoV}=20\times20\text{mm}^2, MT=128\times128, \Delta t=5.3\text{s}, t_{\text{sec}}=13\text{min30s}, \text{res}=156\times156\times1000\mu\text{m}\).

Calculation of \(R_1\) variations included a \(T_2^*\) correction and was performed with home-written software (IDL, USA). Regions-of-interest (ROIs) had the size of a single voxel in the dynamic data sets, i.e. \(156\times156\times1000\mu\text{m}^3\). They were defined on the high-resolution images (ToF, T2w) and afterwards copied to the parameter maps (Figs. 1A-C). \(R_1\) variations were measured in the azygos pericallosal artery (azPA), the sinus sagittalis superior (SSS), and the superficial temporal vein (STV) and plotted as a function of time.

Results and Discussion
In average, observed \(R_1\) changes (Fig. 1D, Tab.1) were highest in the STV (11.2 ± 5.9 s⁻¹) and lower in the SSS (4.3 ± 0.7 s⁻¹) and the azPA (0.6 ± 0.1 s⁻¹). Assuming a total blood volume in mice of 7-8 % of their body weight and a mean hematocrit of 0.44, the total plasma volume can be set to 0.88 mL. Due to an injection time, which was slow compared to the cardiac output rate of mice, the initial CA concentration (25mM) is supposed to be diluted homogeneously in the blood plasma, resulting in an initial blood concentration of 2.27 mM. Based on a CA relaxivity measured in phantom vials (4.9 mM⁻¹s⁻¹), \(R_1\) variations of 11.1 s⁻¹ were expected. Even though quite large inter-individual variations were observed in the STV, \(R_1\)-measurement in this vein allowed – at least in average – a quite well estimation of the blood CA concentration. In contrast in the smaller vessels, \(R_1\) variations reached only 38.2 % (SSS) and 5.6 % (azPA) of the expected value. In the latter case, where vessels are smaller than the dynamic MRI voxel, the partial volume effect can at least be estimated from the reduction factor of \(R_1\) variations with respect to the STV.

Conclusion
The use of a novel cryogenic probe at 9.4 T allowed to measure CA kinetics in different intra- and extracranial vessels of mice. Although inter-individual variations were high, the STV provided the best estimation of CA concentration in blood. Smaller vessels showed partial volume effects but were less prone to inter-individual variations. After further optimization of the dynamic MRI protocol regarding temporal resolution, evidence has to be adduced, to what extent mouse perfusion studies will benefit from AIF assessment in a single vessel compared to the heart.

References

Fig. 1: \(R_1\) changes were measured in a large artery (azPA) and a small (SSS) and a large (STV) vein. Single-voxel ROIs (green boxes) were positioned on the dynamic data sets by means of high-resolution \(T_2^*\) images (B) and ToF angiographies (A). The color-coded map of the \(R_1\) variation (C) shows the time-point of bolus passage. (D) Kinetics demonstrated highest \(dR_1\) values but also highest inter-individual variations after CA bolus (arrow) in the STV. However, in average, the STV value matches the expected value for pure blood (11s⁻¹). For smaller vessels, \(R_1\) changes were lower than the expected value (SSS: 38.2 %, azAP: 5.6 %), but they showed smaller inter-individual variations (Tab. 1).

<table>
<thead>
<tr>
<th>ROI</th>
<th>Vessel</th>
<th>(dR_1) / s⁻¹</th>
<th>rel. (dR_1) / %</th>
</tr>
</thead>
<tbody>
<tr>
<td>azAP</td>
<td>artery</td>
<td>0.65</td>
<td>5.6</td>
</tr>
<tr>
<td>SSS</td>
<td>vein</td>
<td>4.74</td>
<td>38.2</td>
</tr>
<tr>
<td>STV</td>
<td>vein</td>
<td>15.3</td>
<td>100.5</td>
</tr>
</tbody>
</table>

Tab. 1: Maximum \(R_1\) variations during bolus passage (\(dR_1\)) were measured in an artery (azPA) and two veins (SSS, STV). Relative variations (rel. \(dR_1\)) were calculated by normalization to the expected value (11.1 s⁻¹), which was calculated from the injected dose including assumptions for mean plasma volume, hematocrit, and CA relaxivity.