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^{TM} (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 T_{2w}-imaging were performed before contrast agent injection with the following protocols: **(A)** flow-compensated GE: TR=27.2ms,TE=6.4ms,FoV=16x16x16mm^3,MT=512x512x128,t_{acq}=19min27s,res=31x31x125µm³), **(B)** T2w-SE: TR=3s,8echoes, TE_{min}=ΔTE=13.1ms,FoV=20x20mm^2,MT=384x384,t_{acq}=15min6s, res=52x52x500µm³). For Dynamic MRI, relaxation rate R_1=1/T_1 was measured during bolus injection (Gd-DOTA,0.1mmol/kg,t_{inj}=3.5s,V_{inj}=0.8mL) as described in [2] using the following protocol parameters: TR=17.4ms,TE_{min}=2.2ms,ΔTE=2.5m,TS$_1$=250ms,TS$_2$=600ms,FoV=20x20mm^2,MT=128x128,Δt=5.3s,t_{acq}=13min30s,res=156x156x1000µm. 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. 156x156x1000µm³. 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 relaxivitiy measured in phantom vials (4.9 mM^{-1}s^{-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 [1] Baltes C. et al. NMR Biomed (2009)22:834-842. [2] Heilmann M. et al. MAGMA (2007)20:193-203.
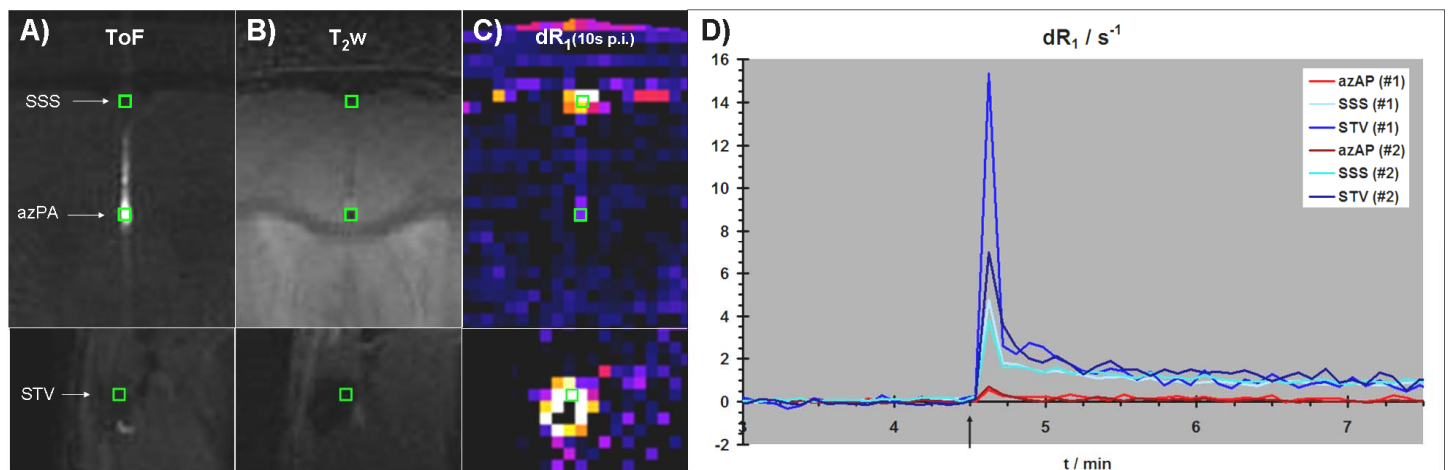
Fig. 1: R_1 changes were measured in a large artery (azPA) and a small (SSS) and a large (STV) vein. Single-voxel ROIs (green boxes) were positioned on the dynamic data sets by means of high-resolution T_{2w} images **(B)** and ToF angiographies **(A)**. The color-coded map of the R_1 variation **(C)** 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).

ROI	Vessel		dR$_1$ / s^{-1}				rel. dR$_1$ / %
	type	diameter / µm	mouse 1	mouse 2	mean	stdev	(Ref.: 11.1 s^{-1})
azAP	artery	~120	0.55	0.70	0.63	0.11	5.6
SSS	vein	~200	4.74	3.81	4.28	0.66	38.2
STV	vein	~1000	15.3	7.0	11.15	5.87	100.5

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.