Evaluation of contrast agent dispersion in cerebral arteries using CFD simulations: influence on CBF quantification

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INTRODUCTION First-pass dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) can be used to quantify the perfusion of brain tissue, which is of considerable clinical importance, e.g., for stroke diagnosis[1] and tumor grading[2]. One of the main challenges for brain perfusion quantification is the accurate measurement of the arterial input function (AIF), i.e. the amount of contrast agent (CA) entering the cerebral tissue at time *t*. From the point of AIF measurement to the examined brain tissue, the CA can undergo delay and/or dispersion[3]. While delay-related errors can be accounted for by using specialized deconvolution techniques[4], dispersion effects are more challenging. Although different techniques to determine the correct 'local' AIF such as independent component analysis[5], factor analysis[6], or heuristic approaches[7] have been presented, the precise degree to which CA dispersion affects brain perfusion studies is still unclear. Here we analyze CA dispersion effects in the brain using Computational Fluid Dynamics (CFD) simulations in a high-detailed 3D model of the arterial tree following the middle cerebral artery (MCA).

METHODS To create the 3D vascular model, volunteer brain data were acquired using a high-resolution time-of-flight angiography sequence (TE=3.98ms, TR=23ms, FA=18°, BW=185Hz/px, voxel size 200x200x320 μm^3) on a 3T MR scanner (Prisma, Siemens Medical Solutions, Germany) using a 64-channel head coil. Afterwards, a standard 2D phase-contrast flow measurement was performed in the left MCA to acquire the velocity profile at the inlet. The 3D vascular model was then extracted from the angiography data using the the open-source software vascular modeling toolkit (Fig. 1), and a hexahedral mesh containing 2,851,804 elements was created using commercial software (ICEM CFD 14, Ansys, Darmstadt, Germany). Blood flow and transport of the CA were then simulated using the open-source software package OpenFOAM (OpenFOAM 2.1.0, OpenCFD Ltd., ESI Group, Bracknell, United Kingdom) on the High Performance Cluster Elwetritsch (Elwetritsch, RHRK, TU Kaiserslautern, Germany) using 32 processors. The structured tree model was used as outlet boundary condition[8], and CA concentration at the inlet (AIF_{in}) was modeled as a gamma-variate function.

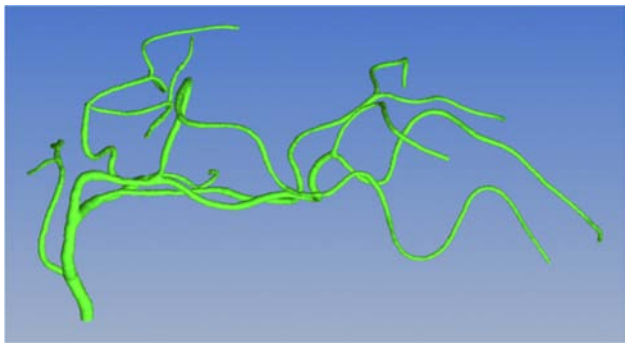

Fig. 1. The 3D vascular model that was extracted from the angiography data. The vessel in the lower left is the left MCA. The radius of the smallest vessels is approximately 0.3 mm.

To investigate the influence of CA dispersion on CBF quantification, the calculated AIFs at the outlets were used to obtain tissue concentration curves c_{tissue} using a Lorentzian residue function[3], a reference CBF value of 60 ml/100 g/min [9] and a mean transit time of MTT=4s [7]. To eliminate delay-related CBF errors, the curves were shifted to a common time origin. The undispersed AIF_{in} and the c_{tissue} were then employed to quantify CBF values using the truncated singular value decomposition (TSVD) approach with a truncation level of 10% [9].

Outlet	1	2	3	4	5	6	7	8	9	10	11
ΔCBF	-2.2%	-3.0%	-1.3%	-1.3%	-1.4%	-4.1%	-3.3%	-2.0%	-0.3%	-2.1%	-7.9%

Tab. 1. CBF errors that arise if dispersion is neglected for all outlets of the 3D vascular model.

RESULTS Fig. 2 depicts three representative outlet concentration-time curves that exhibit different degrees of dispersion. While the obtained AIFs showed clearly discernable delays, only very limited dispersion was observed. The resulting dispersion-related CBF errors are listed for all outlets in Tab. 1. Consistent with previous studies, dispersion led to an underestimation of CBF. Due to the limited degree of dispersion, however, CBF underestimation was relatively small (-0.3% to -7.9%).

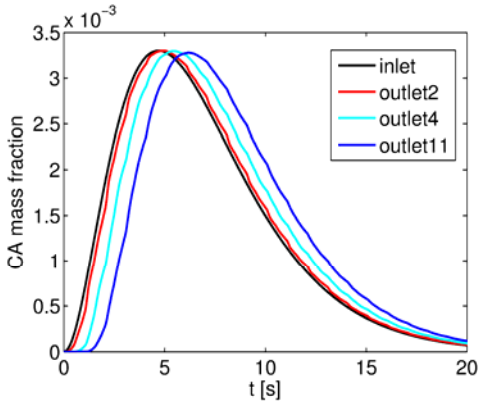

Fig. 2. Three representative AIFs that were obtained at outlet 2 (smallest dispersion), at outlet 4 (medium dispersion), and at outlet 11 (strongest dispersion).

DISCUSSION Our results suggest that high-detailed CFD simulations are a valuable tool to investigate transport phenomena in cerebral arteries. Our analysis shows that CA dispersion in cerebral arteries of healthy subjects may be smaller than previously thought. This is consistent with previous simulations in the coronary arteries that showed much stronger dispersion effects, because blood flow velocities are much higher in the cerebral arteries, which is known to reduce dispersion[10]. CBF errors due to dispersion may be increased in patients with atherosclerotic lesions, where collateral circulation can occur. Future studies should, thus, include geometries with vascular pathology. Furthermore, the CFD technique may be applied to clarify whether it is acceptable to measure the AIF even more distant to the brain tissue, e.g., in the carotid arteries to avoid partial volume effects. Further research is, however, needed to validate the presented CFD simulations, e.g., using high-resolution PC-MRI flow measurements. The technique may then be compared to recently published local AIF algorithms[5,6,7].

ACKNOWLEDGMENTS This work was supported by a Carl Zeiss Foundation Dissertation Fellowship for Karsten Sommer and by the Max Planck Graduate Center with the Johannes Gutenberg-Universität Mainz (MPGC).

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