The Effect of Bolus Dispersion in Semi-Quantitative and Quantitative Contrast-Enhanced Myocardial Perfusion MRI: A Computational Fluid Dynamics Simulation Study on Influencing Factors

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Target Audience: Researchers in the field of perfusion MRI, in particular of the heart

Purpose: Myocardial blood flow (MBF) can be measured via T1-weighted contrast-enhanced first-pass MRI. This method requires the measurement of the arterial input function (AIF), which should be estimated inside a supplying vessel as close as possible to the tissue of interest (TOI). Typically, the AIF is estimated from the blood pool signal of the left ventricle (LV) for technical reasons during myocardial MR-perfusion-measurement. Dispersion (deformation) of the contrast agent bolus can occur between the LV and the myocardium. Negligence of the dispersion could result in a systematic error of the MBF and the myocardial perfusion reserve (MPR). Dispersion can be characterized mathematically as convolution of the AIF of the LV and a vascular transport function (VTF): $AIF_{TOI}=VTF \otimes AIF_{LV}$. The variance of this VTF σ^2 can be used as a quantitative measure of the dispersion[1]. Graafen *et al.* found an underestimation of the MBF and an overestimation of the MPR in idealized geometries of a single coronary artery considering steady [2] and pulsatile[3] flow. Schmidt *et al.* observed an underestimation of the MBF and an overestimation of MPR inside a coronary bifurcation geometry for different flow conditions inside a stenosed branch as well[4, 5]. The aim of this study was to further investigate the results of the latter study by comparing semi-quantitative and quantitative analysis. Furthermore, continuative simulations have been performed to investigate the influence of different parameters on the contrast agent bolus dispersion, e.g. the non-Newtonian behavior of blood, different arrival times of the contrast agent bolus at the coronary arteries and the influence of different diffusion coefficients. Different diffusion coefficients correspond to different kinds of contrast agent, e.g. Gd-DTPA[2,3,4,5], Gd-DOTA[6] or USPIO molecules.

Methods: An idealized bifurcation geometry of the left main coronary artery (LMCA) to the left anterior descending (LAD), which includes a stenosis, and the left circumflex (LCX) was generated[4,5]. Two sets of simulations were performed to investigate two different outflow conditions through the stenotic branch: Full autoregulation of the pressure drop across the stenosis caused by vasodilation of the downstream vessels, and limited autoregulation and therefore reduced flow through the stenotic branch[4,5,7]. Computational fluid dynamics (CFD) simulations were performed using the Fluent software package (Fluent 14, Ansys, Darmstadt, Germany) at the High Performance Cluster ‚Elwetritsch' (RHRK, TU Kaiserslautern, Germany). The quantitative analysis of the errors in MBF and MPR due to negligence of bolus dispersion was accomplished using the MMID4 model. The semi-quantitative analysis was performed via measurement of the maximum upslope of the mass fraction-time curves[8]. The curves were superimposed by a random noise of typical magnitude for a more realistic evaluation, whereat this procedure was repeated 100 times. The upslope of the myocardial curves, which were generated using the MMID4 model, was normalized to the upslope of the curve inside the LV and the curves at the LAD and LCX outlets (normalized upslope = NUS), respectively. The errors in the corresponding MPR index (MPRI) due to bolus dispersion were calculated afterwards[8].
Furthermore, several parameters of the original CFD simulations, e.g. the diffusion coefficient of the contrast agent, have been varied to analyze the respective effect on bolus dispersion.

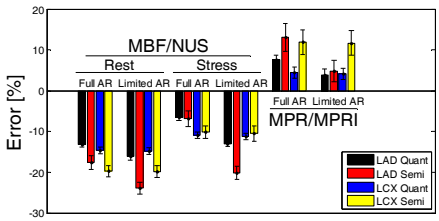

Figure 1: Errors in the MBF/NUS and the MPR/MPRI due to negligence of bolus dispersion. The acronym "AR" stand for autoregulation, „Quant" for quantitative analysis and „Semi" for semi-quantitative analysis.

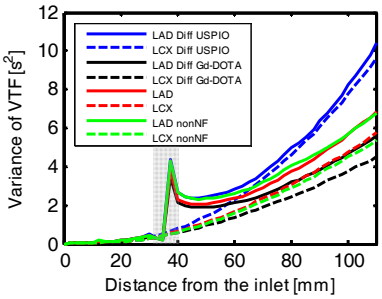

Figure 2: The variance of the VTF for different diffusion coefficients (blue: USPIO, $D=9.55*10^{-12}$ m^2/s and black: Gd-DOTA, $D=2.92*10^{-10}$ m^2/s) compared to the results for the original simulation settings (red: Gd-DTPA, $D=1.5*10^{-10}$ m^2/s), and the influence of the non- Newtonian behaviour of blood (green: nonNF). The position of the stenosis is highlighted in gray.

Results: A systematic underestimation of the MBF up to -16.1% for quantitative analysis and an average underestimation of the NUS up to -23.9% for the semi-quantitative analysis of the results were found (Fig. 1). The larger underestimation for rest compared to stress results in an overestimation of the MPR up to 7.5% for quantitative and of the MPRI up to 13.1% for semi-quantitative analysis. The diffusion coefficient of contrast agent seems to influence the bolus dispersion more compared to the influence of the non-Newtonian behavior of blood (Fig. 2).

Discussion and Conclusion: The MBF/NUS errors due to bolus dispersion found in this study are in the order of the interquartile range of myocardial perfusion MRI of about ±20% in healthy volunteers[9]. Therefore, bolus dispersion should not be neglected at MBF/NUS determination. Furthermore, most of the errors in NUS and MPRI for semi-quantitative analysis are significantly larger compared to the errors in MBF and MPR for quantitative analysis. This confirms that quantitative analysis should be preferred. Furthermore, the bolus dispersion for different kinds of contrast agent can vary significantly depending on their diffusion coefficient. The influence of the cellular ingredients of blood on the diffusion coefficient and therefore on the bolus dispersion is examined at the moment.

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