The Influence of Contrast Agent Bolus Dispersion in Contrast-Enhanced Myocardial Perfusion MRI: A Computational Fluid Dynamics Simulation Study on Influencing Factors and Different Methods of Quantitative Analysis

Regine Schmidt[1], Dirk Graafen[1,2], Karsten Sommer[1], Hanns-Christian Breit[1], and Laura Maria Schreiber[1,3]

[1]*Section of Medical Physics, Department of Radiology, Johannes Gutenberg University Medical Center, Mainz, Germany,* [2]*Department of Radiology, Johannes Gutenberg University Medical Center, Mainz, Germany,* [3]*Department of Cellular and Molecular Imaging, Comprehensive Heart Failure Center (CHFC), Wuerzburg, Germany*

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

Purpose: Myocardial blood flow (MBF) can be determined using T1-weighted contrast-enhanced first-pass myocardial perfusion MRI. This method requires the estimation of the arterial input function (AIF), which should be measured inside a supplying vessel as close as possible to the tissue of interest (TOI). In myocardial perfusion MRI the AIF is usually estimated from the blood pool signal of the left ventricle (LV) for technical reasons. However, dispersion (deformation) of the contrast agent bolus might occur between the LV and the myocardium. The negligence of this dispersion can result in a systematic error of the MBF and the myocardial perfusion reserve (MPR). The dispersed AIF can be described mathematically as the convolution of the AIF of the LV and a vascular transport function (VTF)[1]: $AIF_{TOI}=VTF \otimes AIF_{LV}$. The variance σ^2 of this VTF can be seen as a quantitative measure of the dispersion[1]. Graafen *et al.* and Schmidt *et al.* observed an underestimation of the MBF and an overestimation of MPR inside idealized coronary artery geometries with the help of computational fluid dynamics (CFD) simulations[2-6]. The aim of this study was to further investigate the results of the latter study by comparing different quantitative evaluation methods (the tracer kinetic model MMID4 and the Fermi function model[7,8]). In addition, the influence of the erythrocytes (main part of the cellular components of blood) on the diffusion coefficient of the contrast agent[9] and the resulting dispersion of the contrast agent bolus has been investigated at further CFD simulations.

Methods: An idealized bifurcation geometry model of the left main coronary artery (LMCA) to the left anterior descending (LAD), which includes a stenosis, and the left circumflex (LCX) was created[4,5,6]. Two sets of simulations corresponding to two different flow conditions through the stenotic branch have been performed: first, full autoregulation of the pressure drop across the stenosis by vasodilation of the downstream vessels, and second, limited autoregulation, and therefore, reduced flow through the stenotic branch[4,5,6,10]. CFD simulations have been performed using the Fluent software package (Fluent 14, Ansys, Darmstadt, Germany) at the High Performance Cluster ‚Elwetritsch' (RHRK, TU Kaiserslautern, Germany). The first quantitative analysis of the errors in MBF and MPR due to negligence of bolus dispersion was performed using the tracer kinetic model MMID4. The quantitative analysis using the Fermi function model was accomplished with the help of the software MATLAB (MATLAB R2014a, MathWorks, Natick, MA, USA). Thereby, the data was superimposed by noise of typical magnitude for a more realistic analysis. Furthermore, the variation of the diffusion coefficient of the contrast agent according to the local shear rate due to the influence of the erythrocytes of blood was implemented at the CFD simulations via a user defined function (UDF).

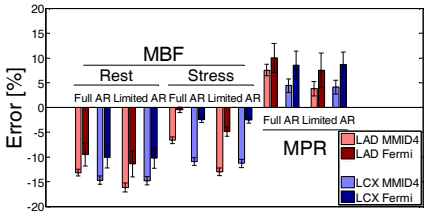

Figure 1: Errors in MBF and MPR due to the negligence of bolus dispersion for both quantitative evaluation methods for full and limited autoregulation (AR).

Results: A systematic underestimation of the MBF of up to -16.1% and -11.4% for analysis using MMID4 and the Fermi function model was observed (Fig. 1). The larger underestimation at the resting condition results in an overestimation of the MPR of up to 7.5% for MMID4 and up to 10.0% for the Fermi function model, respectively. The variation of the effective diffusion coefficient of contrast agent due to the influence of the erythrocytes has a non-negligible influence on the dispersion of the contrast agent bolus at low flow velocities as presented in Fig. 2.

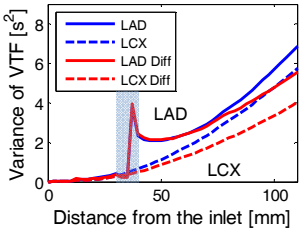

Figure 2: The variance of the VTF for the effective diffusion coefficient of Gd-DTPA due to the influence of the erythrocytes (red) compared to the results for the original simulation settings with fixed diffusion coefficient (blue: Gd-DTPA, $D=1.5*10^{-10}$ m^2/s). The position of the stenosis is highlighted in gray.

Discussion and Conclusion: The errors in MBF for the analysis using MMID4 found in this study are in the order of the variation (interquartile range) typically observed in myocardial perfusion MRI (±20% in healthy volunteers[11]). Thus, bolus dispersion may influence MR perfusion imaging to some extent. Furthermore, MBF errors using the MMID4 model are larger compared to the errors for the analysis via the Fermi function model. However, due to the small errors for stress, the overestimation of the MPR is larger for the Fermi function model compared to the MMID4 model. The influence of the erythrocytes on the diffusion of the contrast agent includes two effects: on one hand diffusion in stagnant blood is slightly obstructed by the erythrocytes compared to the diffusion in pure blood plasma, but on the other hand erythrocytes introduce motion and a local mixing in flowing blood which enhances the effective diffusion coefficient[9]. Due to this enhanced effective diffusion the bolus dispersion is reduced compared to the results of the original simulation settings. This correlation (the larger the diffusion coefficient, the smaller the bolus dispersion) has already been observed in a previous study[6]. Simulations considering the effective diffusion coefficient due to the influence of the erythrocytes are currently performed in a realistic geometry of the right coronary artery (RCA) for more realistic results. In worst case, negligence of the observed bolus dispersion might cause a false assessment of a patient. For example, if the MMID4 model is used for quantification, the underestimation of the MBF can lead to a false positive assessment of a patient, and if the Fermi function model is used, the overestimation of the MPR might cause a false negative classification of a patient, respectively.

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