

The choice of arterial input function in perfusion-weighted MR imaging - size matters in terms of saturation-like effects

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Introduction Dynamic susceptibility-contrast (DSC)-MRI is the most widely used method for perfusion imaging (PI) in brain e.g. to visualize the hypoperfused tissue in stroke¹. For that purpose dynamic T2*-weighted imaging is performed after administration of a bolus of a contrast agent (CA). Perfusion parameter maps can then be calculated depending on the arterial input function (AIF) which is usually extracted from a voxel showing an early and steep dynamic contrast change. Finally, for each voxel cerebral blood flow and volume can be estimated by deconvolution making the results independent from the individual bolus shape. However, the indicator-dilution theory behind this assumes at least the availability of the relative CA concentration which can be principally estimated from T2*-contrast. Theoretical considerations about the relationship between signal change and tracer concentration refer to a network of capillaries. They do not necessarily apply to an individual large vessel which is targeted while estimating the AIF. Attempts were made to also describe the latter case utilizing a simplified (cylindrical) model for the artery, especially for describing partial volume effects (PVE)². In clinical research, however, extracting the AIF directly from imaging data is still the method of choice. The objective of the present study is to examine the impact of this technique on the accuracy of DSC-MRI. Especially, the influence of the chosen arterial segment on the observed peak signal and the level of linearity in comparison to the microvascular signal are investigated.

Methods As a sub-trial of the 1000Plus study (clinicaltrials.gov - NCT00715533) 246 patients with suspected stroke and at least one PI scan within 24 hours from symptom onset were screened. 35 patients had to be excluded for several reasons. The remaining 211 patients (93 female) had a median age of 68 years (interquartile range (IQR) 58 to 78). PI was performed on a 3 T MRI scanner (TRIO TIM; Siemens AG, Germany) using a gradient echo single-shot echo-planar imaging (GE-EPI) sequence (TE = 29 ms; TR = 1390 ms; matrix size = 128 x 128; field-of-view = 230 mm; slice thickness = 5 mm). For perfusion measurements a dosage between 4 and 5 mL 1 M Gadobutrol (> 100 kg: 6 mL; < 50 kg: 4 mL) was injected at a rate of 5 mL/s using a power injector, followed by 20 mL saline flush. In every patient and for each of the three segments (M1, M2, and M3) of the middle cerebral artery (MCA) three AIFs were chosen contralaterally to the suspected ischemia³. Besides auxiliary, quality-related parameters like signal-to-noise ratio (SNR) the relative peak signal drop ($\Delta S(t) = 1 - S(t)/S(0)$) and concentration ($c(t) = -\log(S(t)/S(0))$) were estimated.

Results The median dosage of contrast agent was 0.059 mmol/kg BW (IQR 0.051 to 0.067). The mean relative peak concentration from the whole slice at M2 (which serves as a reference level) exhibited a strong linear relationship to another level (at M3), which was expressed by a high correlation coefficient (Spearman's $r = .967$; $p < 0.01$) (Fig 1A). The level of the linearity between this reference slice – dominated by a microvasculature signal – and the AIFs was still fair for M3 and M2, although the scatter plot is widened for higher peak concentrations ($r = .547 / .555$, respectively, $p < 0.05$, Fig 1B-C). For AIFs from M1 segments the correlation was no longer significant ($r = .114$, n.s., Fig 1D). Similar findings were made investigating the relative peak signal drop (Fig 2). Summarizing, a decoupling between arterial and microvascular signal drop has been observed. This effect has risen with the diameter of the targeted artery.

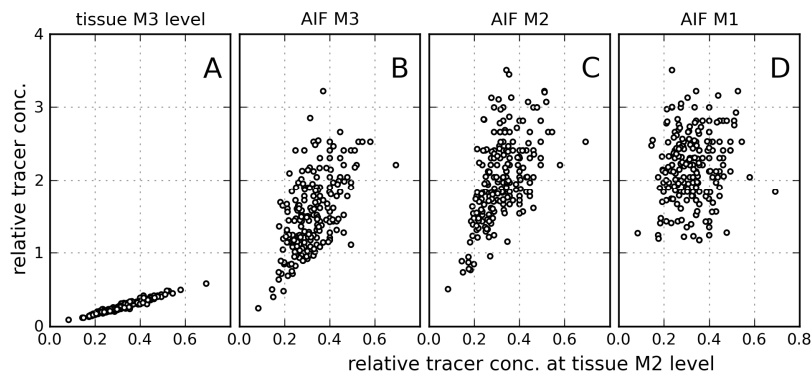


Figure 1: Scatter plots for the correlation between relative CA concentration averaged over the whole slice at middle cerebral artery level M2 against whole slice signal from M3 level (A) and against the AIF peak concentration in the M3 (B), M2 (C), and M1 segments (D) of the middle cerebral artery (MCA) (n = 211). A dependence from the microvascular signal drop can still be observed for the signal drop at M3 and M2 AIFs, but no longer at M1 AIFs.

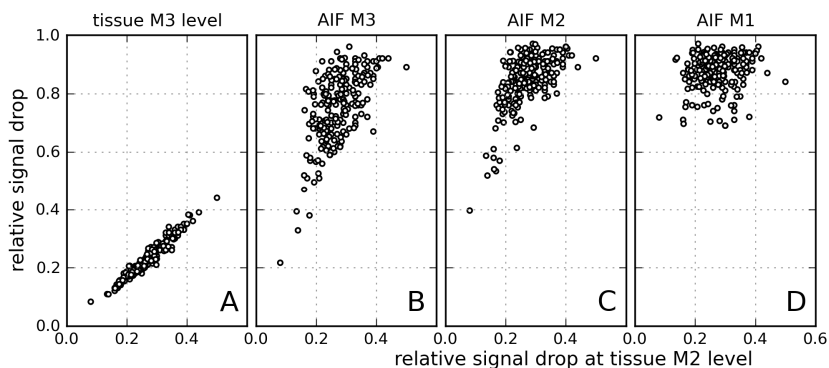


Figure 2: Scatter plots similar to Fig 1 but now depicting the correlation between the relative signal drop averaged over the whole slice at M2 level against M3 level (A) and against the relative signal drop in the M3 (B), M2 (C), and M1 segments (D) of the middle cerebral artery (MCA) (n = 211). A saturation-like behavior can be observed with an increasing diameter of the corresponding MCA branch.

Discussion The mean signal drop in two different whole slices acquired in the same examination correlated strongly (Fig 1A; 2A). In whole slice data most voxels are dominated by the microvasculature compartment. Averaged over many voxels and thereby representing a mixture from different tissue types this high level of linearity was to be expected. For signal drops from the arteries, correlation to the microvascular reference was degrading with increasing diameter of the vessel from which the AIF was derived (Fig 1B-D; 2B-D). In particular, for AIFs derived from M1 branches the correlation was no longer significant (Fig 1D; 2D). We concluded that even for low concentrations of Gadobutrol as used in our study (<0.1 mmol/kg BW) saturation-like effects can be observed, at least in larger arteries. The given dosage range especially excludes overdosage as an explanation. Probably the observed behavior is due to the strong and long-ranging dephasing patterns around these vessels in 3 T MRI, consequently leading to PVE and signal nulling in their vicinity. This obvious decoupling of AIF and tissue signal drop might render quantification of perfusion parameters problematic. It means in effect that an important precondition for the application of the indicator-dilution theory is no longer valid. This also sounds a note of caution to alternative post-processing strategies such as local AIFs. Given the limited representation of AIFs for tracer concentrations, efforts to improve AIF definitions with a customized sequence seem warranted⁴. In case only standard imaging techniques are available, we recommend the usage of more distal arterial branches.

References

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