Reliability of Deconvolution Methods and Parameter Formulas For DSC-MRI Brain-Perfusion Maps

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PURPOSE: Previous research has shown that brain perfusion parameters of acute stroke patients can identify the location, extent and severity of brain tissue ischemia and can help identify patients who would benefit from advanced reperfusion therapies over conservative treatment regimes. While the utility of individual parameters is still a subject of ongoing research and some controversy, the literature suggests that CBV, CBF, MTT and T_{max} values can play an important role in the clinical workup of patients. Since accuracy, precision and potential confounders are highly relevant for treatment decisions, exact knowledge about what influences these parameters is important. From our experience with clinical and simulation data we have seen that different computation methods can provide profound differences for the same data set depending on which method was used. In order to provide a robust and reliable perfusion data analysis package that works in a clinical setting one has to identify the most reliable and stable methods. The objective of this study was therefore to evaluate from simulated DSC-MRI data: i) different deconvolution methods and ii) different formulas for computation of CBV, CBF, MTT and T_{max} from DSC-MRI datasets. The simulations were designed to also address the problems with anatomic or pathologic confounders (e.g. delay, dispersion and recirculation) and noise. They were also taking into account specific control parameters for deconvolution algorithms and integration methods (i.e. thresholds for singular values (SV) in SVD-based methods, residue cut-off).

METHODS: To assess the properties of the deconvolution algorithms and formulas, numeric simulations were executed with varying delay, dispersion, recirculation, SNR, tissue MTT (MTT_{tis}) and SVD threshold values using IDL environment (RSI, Boulder, CO). The arterial input function *AIF(t)* was simulated using a gamma-variate function $c = A(t - t_0)^{\alpha} e^{-(t-t_0)/\beta}$. The residue functions *R(t)* were simulated either as exponential-decay or box functions using tissue MTT from 4s to 20s. The tissue concentration curves $C_{tis}(t)$ were obtained by convolving the *AIF(t)* with the residue function *R(t)*. For deconvolution, both non-parametric (non-parametric FT (NP-FT), truncated SVD (tSVD), circular SVD (cSVD)) as well as parametric methods were tested. The parametric deconvolution (P-FT) was performed by fitting gamma-variate curves to both the AIF and tissue concentration profiles followed by a Fourier-Transform based deconvolution. All simulations were conducted with different amount of noise added to individual time points (baseline SNR ranged from 120 to 20). We determined the perfusion parameters by evaluating different formulas available in the literature. Finally, the parameter values were compared against the ground truth data.

Table 1: Properties of brain perfusion parameter formulas under simulated conditions. $R_0(t)$ is the original deconvolved residue function, whereas $R_1(t)$ is circularly shifted $R_0(t)$ such that $max(R_0(t)) = R_1(0)$. The t_{max} is the time span of the simulated profiles.

Formula	Ref	Formula Properties
$CBV_1 = \int_0^{t_{max}} C_{tis}(t)dt \Big/ \int_0^{t_{max}} AIF(t)dt$	[4]	Stable under all circumstances.
$CBV_2 = \int_0^{t_{max}} R_1(t)dt$	[2] [4]	Formula delivers worse results in the presence of noise, particularly when the NP-FT method is used since the noise in residue function is integrated. SVD-based methods have higher CBV estimates with increasing noise levels. P-FT performed well if the parametric model was capable to correctly capture the concentration profile. The formula is susceptible to higher SVD thresholds (due to energy loss of such filtering process), which leads to CBV underestimation. In the presence of negative delays the tSVD will yield incorrect results.
$CBF_1 = R_1(0) = R_{1max} = R_{0max}$	[3] [4]	For typical physiological values of MTT (e.g. 6s) and TR of 2s, all the methods underestimate flow by ~30%. This is due to a low pass-filtering nature of the FT/SVD methods that lack proper characterization of fast processes. The formula is also susceptible to higher SVD thresholds due to energy loss of filtering, which leads to further underestimation. In the presence of negative delays the tSVD will yield incorrect results.
$CBF_2 = CBV_1 / MTT_2$	[2]	This formula delivers good results if only a small amount of noise is present. It is less prone to underestimation due to a low-pass filtering/energy loss effect compared to CBF_1, but is more susceptible to noise.
$MTT_1 = CBV_1 / CBF_1$	[1]	Errors can be introduced by errors in the CBF_1 estimation.
$MTT_2 = \int_0^{t_{max}} R_1(t)dt \Big/ R_{1max}$	[2]	The formula delivers better results than MTT_1 when little noise is present. Possible CBF_1=R(0)=R_{max} error seems to be compensated by the error in the nominator (=CBV_3). The results are better in comparison with MTT_1 if $MTT_{tis} \rightarrow TR$, but became worse if a higher noise/oscillation is present in the residue function (see discussion for CBV_2). The error grows more steeply with rising levels of noise. In the presence of negative delays the tSVD will yield incorrect results.
$MTT_3 = \int_0^{t_{max}} th(t)dt \Big/ \int_0^{t_{max}} h(t)dt$	[4]	The function *h(t)* is defined as $h(t) = -dR/dt$. Due to the differentiation this formula is very susceptible to noise and oscillations that appear later in the residue function are weighted more in the numerator integration. Therefore this formula is not applicable in concert with the evaluated FT or SVD methods in the presence of any noise or oscillations in *R(t)*. In the presence of negative delays the tSVD will yield incorrect results.
$T_{max} = where(R_{0max})$	[4]	If T_{max} is detected past t_{max}, it indicates an negative delay for cSVD, P-FT and NP-FT methods (see below) and delay is then determined as $T_{max}' = t_{max} - T_{max}$; in such the tSVD will yield incorrect results.. In the presence of noise, NP-FT will yield incorrect results due to an incorrectly estimated residue function.

RESULTS: We found that the deconvolution techniques performed as follows: 1) the tSVD method proved to be stable under most conditions, only lacking the capability to model negative delays, 2) the cSVD delivered stable results in all modeled situations, 3) the NP-FT delivered most often worse results; this was mostly due to noise (even in presence of filtering in frequency domain) and 4) the P-FT performed similar to SVD-based methods, in case the fitting of gamma-variate function to AIF and C_{tis} was feasible and appropriately modeled the profiles. Interestingly, the results were often even better due to lower amount of oscillations in the final residue functions due to the analytic approach (Table 1).

CONCLUSION: Our results indicate that the most reliable parameter estimates for CBV, CBF and MTT are CBV_1, CBF_1 and MTT_1 (Table 1), respectively. However, if low noise/oscillation is present in the residue function, then the formulas for CBF_2 and MTT_2 can deliver more accurate results. The preferred method for deconvolution is the cSVD method, possibly combined with compensation for "energy loss" from thresholding of SV. The tSVD can introduce significant errors if negative delays are present. Negative delays are physiologically not meaningful but can occur in the presence of incorrect slice timing or stenotic feeding vessels in combination with collateral supply. The P-FT will fail if the tissue concentration profiles can not be correctly approximated by the fitted parametric model, such as in regions with long tissue MTTs (e.g. stroke); the NP-FT method is highly susceptible to noise.

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