Does deconvolution in DSC-MRI deliver bolus-shape independent results, or why noise is the limiting factor in DSC-MRI?

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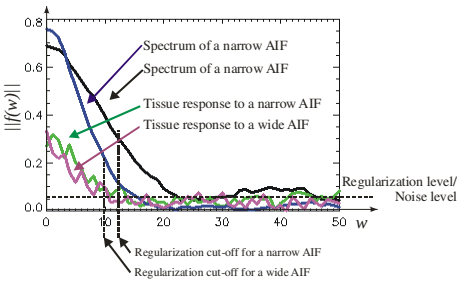

Fig. 1: Spectra of narrow and wide AIF and respective tissue responses are shown. as regularization level (noise level) is constant, the regularization cut-off frequency at which power of signal frequency component fall below power of noise/regularization differs for narrow and wide AIF case. Only components below cut-off contribute to IRF computation, thus more high-frequency components are missing in its reconstruction, cause CBF underestimation.

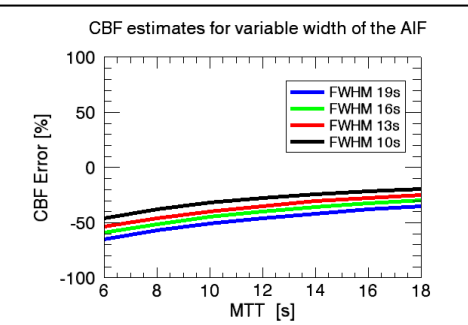

Fig. 2: Graphs shows differences in CBF estimates when different width of AIF is used. Wider AIF lead to higher errors, due to lower cut-off frequency (see Fig. 1). Also, CBF estimates from IRF with shorter MTT have higher error, due to larger portion of high frequency components being cut off [3].

Purpose: Estimation of perfusion parameters using gadolinium-based DSC-MR PWI has evolved into a clinically usable tool that is important in acute stroke and other cerebro-vascular diseases. To obtain quantifiable perfusion parameters, the deconvolution approach [1] is used to suppress the influence of the bolus shape which depends on injection speed, cardiac output, etc. Using deconvolution, the dynamic characteristic of a system is obtained by measuring response of the system (tissue curves) versus a known input signal (the arterial input function – AIF). The ratio of the input and output signals' frequency spectra yields the impulse response function (IRF). In theory, for linear systems the deconvolution should estimate the same IRF regardless of the shape of the input signal. Practically, regularization is needed in the deconvolution step to suppress instabilities, which occur due to the fact that the spectra of real PWI signals have large portions of frequency components with lower power and are therefore subject to noise. Regularization stabilizes the solution by suppressing frequencies whose power is comparable to the power of the noise. Typical DSC-MRI signals have monotonically decreasing spectra, hence regularization tends to be a strong low-pass filtering, manifesting a regularization cut-off frequency. Since frequencies above the cut-off are not used in computation, the shape of the recovered IRF is smoothed and leads to CBF underestimation. The range of frequencies usable for deconvolution is therefore limited by shape of the signals' spectra and noise level. The variance of noise in DSC-MRI is constant, related to variance of thermal and device noise only, and independent of the baseline SNR of the MR-acquisition. Therefore, the threshold under which the frequency components are excluded is given; either the noise level is assumed to be known (number related to AIF spectrum components in truncated SVD) or it is estimated from signals (Tikhonov regularization, Wiener filtering). With the noise level held constant, the range of frequencies used in deconvolution analysis depends only on the shape of the spectrum. If the shape of spectra of input and output signals change, either by scaling or due to different amounts of various frequency components, the range of frequencies recovered in IRF will also change. That is, possibly containing more or less high frequencies and is reflected in a change of the estimated CBF. Hence, fundamental questions arise:

1) For a given IRF, does deconvolution with given regularization allow one to recover the same CBF values if different inputs signal are used (i.e. narrow vs. wide AIF)?
2) If regularization and shape of input signal is kept constant but attributes of the underlying IRFs (e.g. their MTT) vary, will the particular IRFs be estimated with the same error?
3) If regularization level will differ (e.g. in multicenter trials), will be the CBF (for given IRF) estimated identically?

Methods: To answer the questions posed above we performed numerical simulations. AIFs were simulated as gamma-variate functions ($y = A(t-t_0)^{\alpha}\exp(-(t-t_0)/\beta)$,$\alpha\in\{2.0, 3.5, 5.0\}$, $\beta=3.0$, $t_0=10.0$, with A scaled so that all AIFs have the same area under the curve, resulting in AIFs with peak levels {44.0, 34.0, 28.0} [a.u.] and FWHM $\in$ {10, 13.5, 16.0}[s]. The IRF was modeled as a simple exponential decay with a MTT of 6-24s. Tissue response curves were obtained by numerical convolution of AIF and IRF with $\Delta t=0.1$s. Then, the AIF and tissue curves were resampled to a temporal resolution 2.0s. The 'measured' IRFs (hence the CBF estimates) were obtained by block-circulant SVD [2] deconvolution with a threshold of 20% of the largest singular value. To answer the third question, the deconvolution was performed also with a threshold of 15% and 25%. In all numerical simulations, noise was not modeled as it considered irrelevant for the analysis.

Results: Fig. 1 shows CBF estimates for IRFs with different MTTs when the AIF shape varied. As discussed above, the deconvolution with regularization recovers a variable range of IRF frequencies. Therefore, different errors in CBF (IRF peak) estimation will occur. An explanation for this behavior can be seen on Fig. 1, where wider AIFs have more power in lower frequencies, therefore a lower regularization cut-off occurs. Thus, the answer to question 1 is no as long as regularization cut-off frequency depends on the input or output signal spectrum. If this dependency is avoided, i.e. the same number of frequency components is used in IRF reconstruction independent of signal spectra, then the IRF will be reconstructed with the same error independent of the AIF shape. As this is normally not the case, the typical error due to change in AIF width can be up to 25% of the true CBF value (50% of the estimated CBF value). The answer to question 2 can be also seen from Fig.1, where IRFs with shorter MTT will have a higher error in estimated values. This is because with regularization, the IRFs with shorter MTT contain more high-frequency components which in turn will be discarded [3]. Here, this behavior is because in truncated SVD the threshold is relative to the spectrum of AIF and fixed. However, a very similar effect is manifested for all regularized deconvolution methods [2]. The answer to question 3 is also no, where the obvious explanation is the variable low-pass filtering induced by the regularization. In reality, the error with respect to 15, 20, and 25% threshold was approx. 10% of the true CBF value (20% of the CBF estimate), with lower errors towards long MTT IRFs (results not shown).

Discussion: Whereas DSC MRI perfusion measurement is an important clinical tool, its application in regular clinical routine is still questionable. There are multiple confounders significantly influencing quantitative values. While some of these effects have a huge impact on the computed CBF values (bulk blood correction), these might pose a great possibility for a robust correction. Other effects, e.g. errors arising from deconvolution might have less predicable impact, although being smaller magnitude. Deconvolution was aimed to address possible dependence of perfusion parameters on bolus shape, but noise inherently present in measurements sets limits on the quality of the reconstructed IRF. As the deconvolution results depend on the signal spectrum shape and the underlying IRF, one should be aware of errors possibly arising from this variability. It is also worth noting that to lower the influence of noise (hence the influence of the regularization), changes the baseline SNR (e.g. by changing TR of the acquisition) has no effect. The noise level in gadolinium-based DSC-MR PWI is related to CNR and therefore depends on echo-time of the imaging sequence, concentration of the tracer in the bolus (determined by injection speed and molarity of the tracer) and strength of the magnetic field. Higher concentration or stronger field will possibly lead to more severe clipping of the signals in vessels, where longer TR or multi-echo sequences [4] might be helpful.

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[3] Straka, M et al: Electronic Poster ISMRM 2007, Berlin, Germany [4] Newbould RD et al, Magn Reson Med. 2007 Jul;58(1):70-81

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