Dynamic susceptibility Contrast MRI: Improved Discrimination of Hypoperfused Tissue

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Introduction: Perfusion measurement by DSC-MRI is becoming increasingly important as a tool for clinical assessment of hypoperfusion and as an endpoint in therapeutical trials. In acute stroke, interest is in identifying thresholds for tissue mean transit time or cerebral blood flow (CBF) values to guide the selection of patients for thrombolysis. In pursuing this, perfusion measurements must be optimized to detect and distinguish subtle levels of hypoperfusion, and standardized to allow comparison and application of results across subjects and centers. The precision (random noise) and accuracy (systematic bias) of perfusion values depend on the noise regularization used in deconvolution. Precision and accuracy are in competition: Deconvolution schemes, which are optimal for accuracy [1-4] does not provide the highest possible precision and vice versa. We analyse this issue in detail in (Abstract submitted to this Meeting, submission number 2539) and [5] presenting the method 'Truncation FT' optimized for precision. Here we consider consequences of the resulted intra- and intersubject variability. We propose to compromise accuracy for the precision yielding a better delineation of hypoperfused tissues in individuals and in group studies.

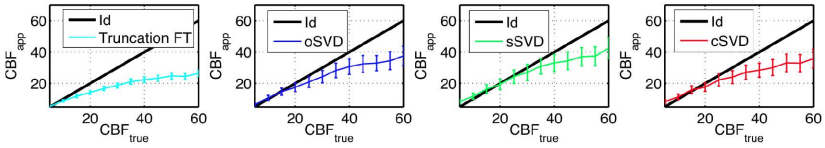

Figure 1: Estimated (apparent) CBF vs true CBF. SNR = 20 and TR = 1.5s. Increased precision on the costs of accuracy is evident for Truncation FT.

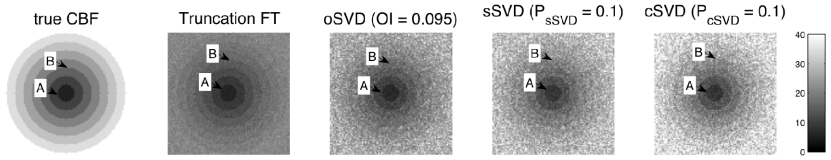

Figure 2: Simulation of infarct region (CBF). A and B indicate the border for CBF below true CBF = 10 ml/100g/min and below true CBF = 20 ml/100g/min, respectively. SNR = 20, TR = 1.5s.

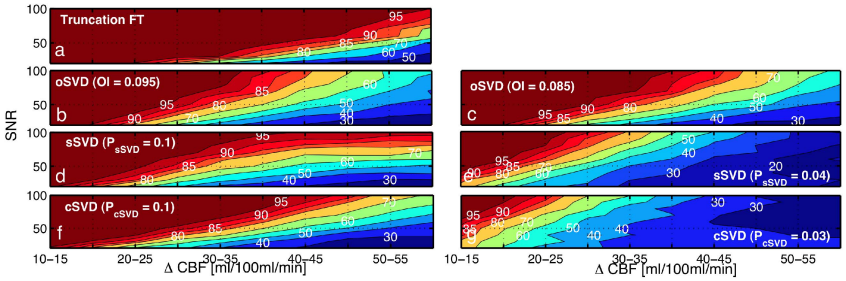

Figure 3. Intra-subject discrimination vs SNR and CBF levels. Contour map of the power (in percent) vs SNR and different CBF levels from CBF = 10ml/100ml/min to 60ml/100ml/min in steps of 5ml/100ml/min. The simulation is performed with TR = 1.5s, CBV = 0.04 and AIF width 3s. AIF mean of five noise realizations.

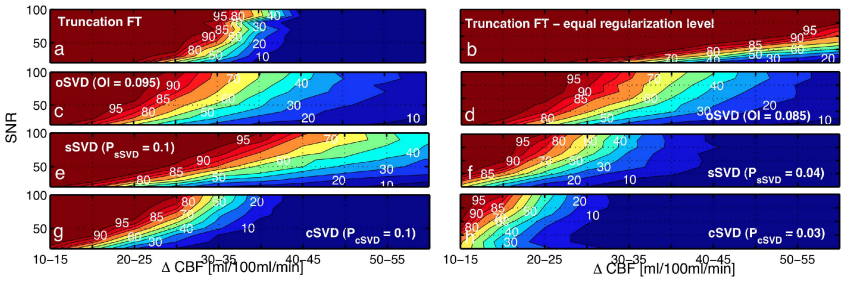

Figure 4. Multi-subject discrimination vs SNR and CBF levels. Simulation values as in figure 3.

Methods: Perfusion simulations were performed as in [2,5]. AIF was modeled as a gamma variate function and the residue function modeled as an exponential function. To test the ability of the methods to discriminate CBF values within a subject, we generated 16 tissue concentration curves (4x4 voxels with equal CBF) for a range of CBF- and SNR levels. Deconvolution was performed with the 4 methods and a two sample t-test (significance level 0.05) was performed between neighboring CBF levels. The simulation was repeated 500 times, and we registered the number of times the wrong hypothesis of equal means was rejected (N_{reject}). Power = N_{reject}/500 which gives the probability of rejecting a false hyphothesis. The regularization levels used in oSVD, sSVD and cSVD were found in [2]. To assess multi-subject discrimination paralleling group studies, we repeated the above simulation, but with different AIFs for the 16 tissue concentration curves. AIFs were modeled as gamma variate functions drawn from an empirically defined distribution. The regularization level was 1) optimized to the individual AIF width, 2) fixed on a value obtained from a broad AIF, in order to investigate the gain of equal regularization level in a multi-subject comparison [5].

Results: The increased precision and decreased accuracy of CBF for 'Truncation FT' is shown in figure 1. In figure 2, the enhanced discrimination ability is shown in simulation images of an infarct: the infarct was simulated using concentric shells with CBF decreasing towards the center. The threshold for irreversible tissue damage at CBF < 12 ml/100ml/min is indicated at letter 'A' and the threshold for reversible tissue damage is indicated at letter 'B'. The discrimination ability is shown as the statistical power in contour plots for the different deconvolution methods (fig. 3). The proposed methods show a markedly improved discrimination (larger red area in the figure) as compared to the existing methods as visually confirmed in figure 2. Moreover, Truncation FT with equal threshold showed excellent discrimination ability in the multi-subject simulation (fig 4b).

Discussion: The simulations suggest that the proposed method improves separation of CBF levels within subject as well as between subjects when a common regularization level is used. We therefore speculate that the proposed technique will lead to better delimination of hypoperfusion areas in stroke and will increase the efficacy of clinical trials with CBF as endpoint.

References: [1] Østergaard et al, MRM 36:715-725 1996 [2] Wu et al, MRM 50:164-174 2003 [3] Liu et al, MRM 42:167-172 (1999) [4] Carpenter et al, MRM 55:1342-1349 (2006) [5] Kjølby et al submitted to NeuroImage.