Improved Assessment of Regional Cerebral Blood Flow by Dynamic Susceptibility Contrast MRI Using a Kernel-based Deconvolution Approach

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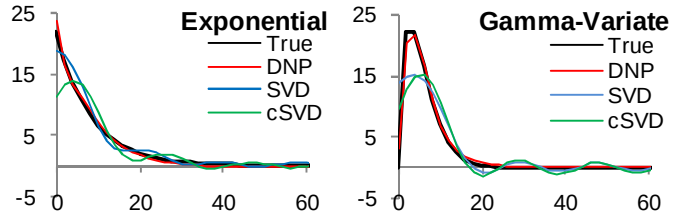
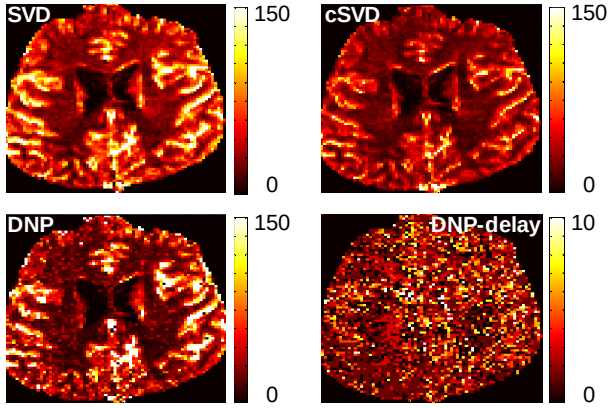
INTRODUCTION: In dynamic susceptibility contrast magnetic resonance imaging (DSC-MRI), in order to estimate the Cerebral Blood Flow (CBF), a deconvolution operation between the arterial input function (AIF) and the voxel concentration of contrast agent (C(t)) must be performed to obtain the residue function (R(t)) [1]. Here, we propose a kernel based deconvolution approach that tackles the problem in a fully Bayesian framework and includes information on both R(t) continuity and on the system BIBO stability. The algorithm proposed by **D**e **N**icolao & **P**illonetto (DNP) was validated on both simulated and clinical data and compared to the most common deconvolution techniques in DSC-MRI quantification, i.e. the singular value decomposition (SVD) [1] and the block-circulant SVD (cSVD) [2].

MATERIALS AND METHODS. Simulation: the simulated data set was generated by assuming TR=2s and using a gamma-variate function to model the AIF as in [1] and four different models for the R(t), as in [3]: Exponential and Lorentzian R(t) to simulate the dispersion absence and Gamma-variate and Dispersed Exponential R(t) to account for the dispersion. CBF and MTT values typically found in normal white matter were used as in [2](CBF: 22±3.5 ml/100g/min mean±SD; MTT: 6±1 sec. mean±SD). Delay was also simulated by translation of the voxel concentration curves of 0, 1, 2, 3, 4 samples. Finally, Gaussian noise with four Signal to-Noise Ratios (SNR=500-50-10-5) was added to data, where SNR=10 corresponds to the noise level generally present in clinical data. Simulations were repeated 100 times for each residue function type and SNR. Summarizing, the simulated data set contains 8000 situations (4 R(t) models × 100 CBF & MTT combinations × 5 delay × 4 SNR).
Clinical Data: 11 patients with severe atherosclerotic unilateral stenosis of the internal carotid artery (ICA) were investigated. Imaging was performed with a gradient echo EPI (on a Sigma Horizon CV 1.5 T GE Medical System; TR=1560ms, TE=51ms, FOV=230x230 mm, 5mm slice thickness). The bolus dose was 14 ml of Gd-DTPA, at a rate of 5 ml/s in the right antecubital vein. In total, 12 slices were obtained. In some subjects, examination was repeated 6 months after the surgery. In total, 18 different clinical cases were considered (i.e. 10 pre-surgery and 8 post-surgery). AIF was automatically extracted as reported in [4].
DNP: The key step in the deconvolution method proposed in [5] is the formulation of a Gaussian prior on the residue function. This latter is modeled as an integrated Wiener process, with zero initial value and arbitrary first-order derivative at zero, subject to a change of coordinates regulated by the time transformation $\tau=e^{-\beta t}$. This stochastic model contains information regarding the RH(t) continuity and the system BIBO stability. Under these assumptions, the minimum error variance estimate of R(t) is given by a Tikhonov estimator defined on a suitable **R**eproducing **K**ernel **H**ilbert **S**pace (RKHS). The RH(t) stochastic model contains the hyper parameters $p=[\lambda, \beta, \sigma, \Delta]$, where λ is the Wiener process variance, β characterizes the time transformation, σ is the data noise standard deviation and Δ is the delay between the AIF and the C(t). Such hyper parameters are estimated via maximum likelihood so that not only DNP is insensitive to delay, but it can also estimate it.



▲Figure 1: DNP, SVD and cSVD mean reconstructed R(t) compared to the true R(t) both in absence (left panel) and in presence (right panel) of dispersion. Results are obtained at SNR=10 and without delay between the AIF and the C(t).



►Figure 2: CBF maps obtained using SVD, cSVD and DNP deconvolution methods and delay map obtained by using DNP. Relative CBF values are normalized to the same reference region. Delay values are expressed in seconds.

RESULTS: Simulation: Estimated CBF percentage error and the root mean square error (RMSE) between the reconstructed R(t) and the true one have been computed. On the basis of the RMSE, R(t) obtained using DNP is closer to the true one than those provided by SVD and cSVD in 71% of the cases, whereas SVD and cSVD scores the best RMSE value in 11% and 18% of the cases, respectively. Moreover, DNP provides a smaller CBF percentage error than SVD and cSVD. Among the 8000 simulated situations, in 73% of the cases DNP provides the best CBF estimate, whereas SVD and cSVD provides the best result in 20% and 7% of the cases, respectively. R(t)s reconstructed using DNP have very small negative values and they do not present any oscillation, resulting in more physiological shapes than those provided by SVD and cSVD (fig. 1). In presence of dispersion, DNP overestimates the delay between the AIF and the C(t) (max 4 s) and the differences in DNP, SVD and cSVD performances become less marked, however DNP still provides the best RMSE and CBF percentage error results. Furthermore, DNP performances do not change significantly among the simulated noise levels.
Clinical Data: CBF map provided by DNP is comparable to those obtained using SVD and cSVD (fig. 2). DNP provides more physiological R(t) estimates than SVD and cSVD, whit very small and damped oscillations and small negative values. Moreover, delay map obtained using DNP shows higher delay values in the pathological region, in agree with the physician diagnosis (fig. 2).

DISCUSSION: In [6] a nonparametric population deconvolution (PD) method has been proposed and validated. The population approach is suitable for large voxel set analysis, but, in some occasions, the analysis of a small number of voxels is required or only a region of interest (ROI) mean curve has to be considered. In such situations, a pixel based deconvolution algorithm has to be used. DNP works on a fully Bayesian context and the prior defined for the R(t) include information on both the R(t) continuity and the system BIBO stability. Thus, DNP provides more accurate and more physiological estimates of R(t) than SVD and cSVD both on simulated and clinical data. Furthermore, DNP can estimate the delay between the AIF and the C(t), improving the quality of the information provided to the physician.
DNP is relatively computationally expensive, the estimated computation time of a 128x128 slice, using matlab© non optimized software on an Intel dual core Pentium® 2.0 GHz, is about 90 minutes.

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