Anisotropic Tensor Total Variation Regularization For Low Dose Low CT Perfusion Deconvolution

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Abstract. Tensor total variation (TTV) regularized deconvolution has been proposed for robust low radiation dose CT perfusion. In this paper, we extended TTV algorithm with anisotropic regularization weighting for the temporal and spatial dimension. We evaluated TTV algorithm on synthetic dataset for bolus delay, uniform region variability and contrast preservation, and on clinical dataset for reduced sampling rate with visual and quantitative comparison. The extensive experiments demonstrated promising results of TTV compared to baseline and state-of-art algorithms in low-dose and low sampling rate CTP deconvolution with insensitivity to bolus delay. This work further demonstrates the effectiveness and potential of TTV algorithm's clinical usage for cerebrovascular diseases with significantly reduced radiation exposure and improved patient safety.

1 Introduction

Cerebrovascular disease, or stroke, is the second leading cause of death worldwide after cancer. CT perfusion (CTP) is one of the most widely used imaging modality for disease diagnosis and assessment of treatment response in cerebrovascular diseases. However the radiation exposure in CTP is has caused significant concerns in the community [1].

Numerous efforts have been proposed to reduce the necessary radiation dose to meet the "as low as reasonably achievable" (ALARA) principle, including lowering the radiation dose level, reducing the exposure time, using effective shielding for the patients and increasing the distance between the body and the radiation source.

Recently, tensor total variation (TTV) regularization algorithm has been proposed for robust low-dose CTP deconvolution [2] by reducing the tube current-exposure time product measured in mAs, which varies linearly with the radiation dosage. TTV has shown promising results in correcting the over-estimation of cerebral blood flow (CBF) and under-estimation of mean transit time (MTT) at significantly reduced radiation level (8%) compared to commercially available methods, such as standard singular value decomposition (sSVD) [3], block-circulant singular value decomposition (bSVD) [4], Tikhonov regularization (Tikh) [5], as well as the state-of-art learning-based method sparse perfusion deconvolution (SPD) [6]. However, the robustness of TTV to bolus delay, contrast preservation and low sampling rate has not been fully explored.

In this paper, we use both synthetic simulation and in-vivo clinical data to extensively evaluate TTV algorithm in low-dose, low-sampling rate CTP data with bolus delay. Block-circulant TTV algorithm shows encouraging performance in various tasks,

including contrast preservation, estimation at reduced sampling rate and robustness to tracer arrival time in arterial input function. This work further demonstrates the effectiveness and potential of TTV algorithm's clinical usage in cerebrovascular diseases with significantly reduced radiation exposure and improved patient safety.

2 Anisotropic Tensor Total Variation Regularized Deconvolution

TTV algorithm regularizes the convolution model with tensor total variation term to reduce the oscillation and error in the recovered residue functions.

Let's denote $A \in \mathbb{R}^{L\times L}$ as the block-circulant Teoplitz matrix of the zero-padded arterial input function $c_{art}(t) \in \mathbb{R}^{T\times 1}$, $C \in \mathbb{R}^{L\times N}$ as the zero-padded contrast concentration curves $c_{voi} \in \mathbb{R}^{T\times 1}$ in the region of interest (ROI) with N voxels, and $K \in \mathbb{R}^{L\times N}$ as the flow-scaled residue impulse functions, where $L \geq 2T$, and T is the time length of the measured signal. $\|\cdot\|_{TV}$ is the total variation norm. To estimate K, TTV algorithm optimizes

$$K_{ttv} = \underset{K\in\mathbb{R}^{T\times N}}{\arg\min}\,(\frac{1}{2}\|AK - C\|_2^2 + \|K\|_{TV}) \tag{1}$$

Here we use anisotropic weighting for the tensor total variation term, instead of isotropic weighting in [2]. It is based on the assumption that the piecewise smooth residue functions in CTP should have small total variation, and the smoothness in the temporal and spatial dimensions should be different. The tensor total variation term is defined as

$$\begin{aligned}\|K\|_{TV} = \sum_{t,i,j,k} \Big[&\gamma_t|\tilde{K}_{t+1,i,j,k} - \tilde{K}_{t,i,j,k}| + \gamma_x|\tilde{K}_{t,i+1,j,k} - \tilde{K}_{t,i,j,k}| \\ &+ \gamma_y|\tilde{K}_{t,i,j+1,k} - \tilde{K}_{t,i,j,k}| + \gamma_z|\tilde{K}_{t,i,j,k+1} - \tilde{K}_{t,i,j,k}|\Big]\end{aligned} \tag{2}$$

where $\tilde{K} \in \mathbb{R}^{T\times N_1\times N_2\times N_3}$ is the 4-D volume obtained by reshaping matrix K based on the spatial and temporal dimension. Here $N = N_1 \times N_2 \times N_3$. The tensor total variation term here uses the forward finite difference operator using L_1 norm. The L_1 norm here imposes sparsity in TV regularization term, which imposes smoothness while preserving the edges. The regularization parameter $\gamma_i, i = t, x, y, z$ controls the regularization strength for the temporal and spatial dimension, and the larger the γ_i, the more smoothing the TV term imposes on the residue function in i^{th} dimension.

We propose an algorithm to efficiently solve the problem in Eq. 1 inspired by the framework of [7], as described in Algorithm 1.

3 Experiments

3.1 Synthetic Evaluation

Because the clinical CTP does not have ground truth perfusion parameter values for comparison, we first use synthetic data to evaluate the proposed algorithm, using the synthetic experiment setup in [4].

Algorithm 1 The framework of TTV algorithm.

Input: Regularization parameters γ_i, $i = t, x, y, z$
Output: Flow-scaled residue functions $K \in \mathbb{R}^{T\times N_1\times N_2\times N_3}$.
$K^0 = 0$
$t^1 = r^1 = K^0$
for $n = 1, 2, \ldots, N$ **do**
(1) Steepest gradient descent

$$K_g = r^n + s^{n+1}(A^T(C - Ar^n))$$

where $s^{n+1} = \frac{Q^T Q}{(AQ^T)(AQ)}$, $Q \equiv A^T(Ar^n - C)$
(2) Proximal map:

$$K^n = \text{prox}_\gamma(2\|K\|_{TV})(K_g)$$

where $\text{prox}_\rho(g)(x) := \arg\min_u \left\{ g(u) + \frac{1}{2\rho}\|u - x\|^2 \right\}$
(3) Update t, r

$$t^{n+1} = (1 + \sqrt{1 + 4(t^n)^2})/2$$

$$r^{n+1} = K^n + ((t^n - 1)/t^{n+1})(K^n - K^{n-1})$$

end for

Bolus Delay In Arterial Input Function: Circular deconvolution has been used to correct the delay effect using circular representation of c_{art} and c_{voi}, but with limited improvement, as shown in Fig. 1, where the arterial input function is delayed by 5 s. bSVD and TTV use the block-circulant version of c_{art} and c_{voi}, while sSVD and Tikhonov use standard deconvolution. Though bSVD shows relatively improved performance compared to sSVD and Tikh, the estimated CBF (the maximum value of residue function) is still over-estimated to be around 30 mL/100g/min. On the other hand, TTV is able to correct the bolus delay and estimate accurate residue function.

Uniform Region Variability: From the recovered residue function, perfusion parameters CBF and MTT can be estimated. We generate a small region containing 40×40 voxels with the same perfusion characteristics, and compute the mean and standard deviation of the perfusion parameters over this region.

1) The ideal variability of the uniform region should be zero. Fig. 2 shows the estimated perfusion maps of the reference and four methods on the uniform region. While the baseline methods behave poorly in recovering the smooth region, TTV results in uniform perfusion maps for all three parameters at PSNR = 15. SPD reduces the noise level in estimating the three perfusion parameter maps compared to other baseline methods, but the over-estimation in CBF and under-estimation in MTT could not be corrected using SPD. In comparison, TTV not only decreases the noise standard deviation in the

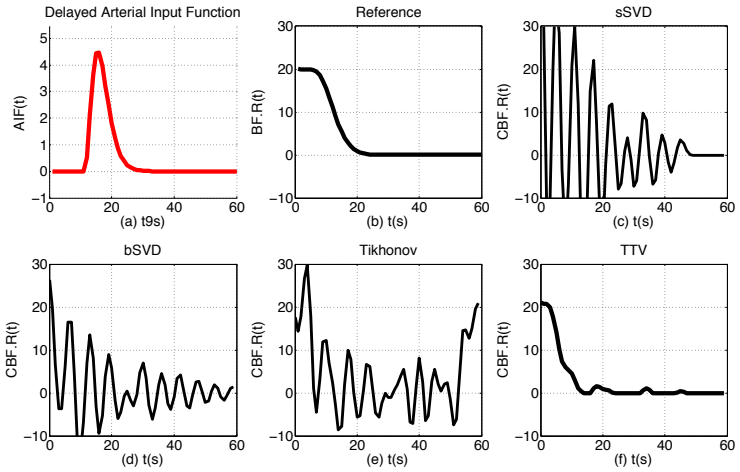


Fig. 1. (a) The delayed arterial input function with 5 s delay compared to tracer arrival at the tissue. (b)-(f) The recovered residue functions by baseline methods and TTV. The parameters used for residue function recovery are the simulation is CBV = 4 mL/100 g, CBF = 20 mL/100 g/min, PSNR=25.

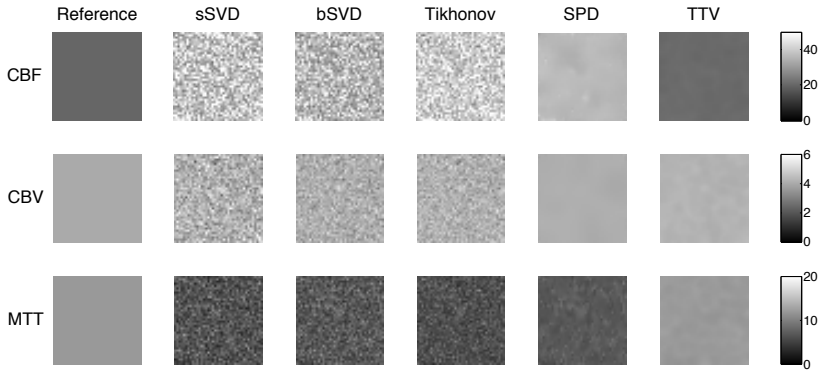


Fig. 2. Visual comparison in a uniform regions of perfusion parameter estimation using baseline methods and TTV. The ideal variation is 0. The reference is the ground truth at CBV = 4 mL/100 g, CBF = 20 mL/100 g/min, MTT = 12 s, PSNR = 15.

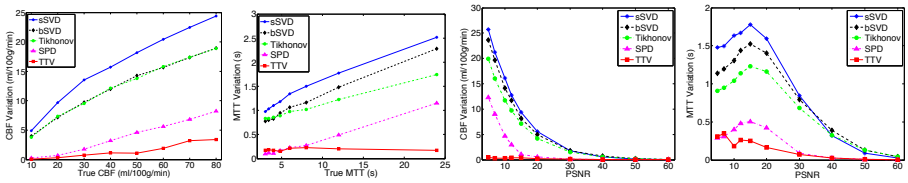
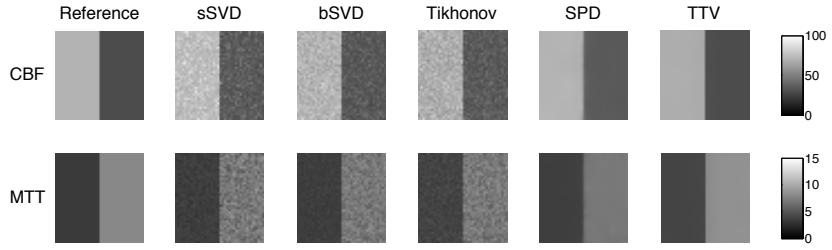


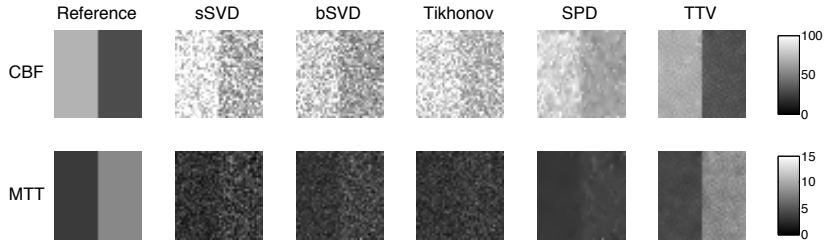
Fig. 3. Comparisons of reducing variations over homogeneous region of (a) CBF at different CBF values with PSNR = 15. (b) MTT at different true MTT values with PSNR = 15. (c) CBF at different PSNR values with true CBF = 20 mL/100 g/min. (d) MTT at different PSNR values with true MTT = 12 s.

estimated perfusion maps, but also estimatess the accurate quantitative parameters for CBF and MTT.

2) Quantitative comparison is shown in Fig. 3(a)-(b) (where CBF or MTT varies) and Fig. 3 (c)-(d) (where PSNR varies). All figures show that TTV produces lower CBF and MTT variations than the sSVD, bSVD and Tikhonov methods. SPD achieves lower variation than TTV in MTT estimation at different true MTT values in Fig. 3(c), but the mean estimated value of MTT in Fig. 2(b) shows under-estimation of MTT, compared to the ground truth.



(a) PCNR=1



(b) PCNR=0.2

Fig. 4. Comparisons of CBF and MTT estimated by the different deconvolution algorithms in preserving edges between two adjacent regions at PCNR=1 and 0.2. CBV is not shown because it is uniform in the region. True CBF is 70 and 30 mL/100 g/min on the left and right halves of the region. CBV is uniform in the region at 4 mL/100g. True MTT is 3.43 and 8 s on the left and right halves. Temporal resolution is 1 sec and total duration of 60 sec.

Contrast preserving: Contrast is an important indicator of how well two neighboring different regions can be distinguished. The contrast of perfusion parameters between the normal and abnormal tissue computed using the deconvolution algorithm from the noisy data should be comparable to that of the noise-free CTP data. To compare the performance of the baseline methods and TTV in preserving contrast, we generate synthetic CTP data spatially containing two 40×20 uniform regions with different perfusion characteristic. Peak contrast-to-noise ratio (PCNR) is defined as PCNR $= \max |I_1 - I_2|/\sigma$, where I_1 and I_2 are the perfusion parameter values of then two images to be compared for contrast.

Fig. 4 shows the estimated CBF and MTT by the different algorithms when PCNR=1 and 0.2. The corresponding σ=40 and 200. While baseline methods sSVD, bSVD and Tikhonov perform poorly at both PCNR levels, SPD and TTV yield improved CBF and MTT maps with regard to the reference. When the PCNR = 1 and the noise level is moderate, both SPD and TTV are capable of removing the noise and preserving the contrast. However the spatial resolution at the boundary of two regions is smoothed by SPD, compared to the clear-cut boundary using TTV. When the PCNR is as low as 0.2, the contrast to noise ratio is extremely low. sSVD, bSVD and Tikhonov generate severely biased perfusion parameters. SPD reduces the noise level to certain extent, but is unable to correct the estimation bias in CBF and MTT. TTV performs favorably compared to all baseline methods in preserving the edges between two adjacent regions in CBF and MTT, as well as accurate estimation of perfusion parameters.

3.2 Clinical Evaluations

Retrospective review of consecutive CTP exams performed on aneurysmal subarachnoid hemorrhage patients enrolled in an IRB-approved and HIPAA-compliant clinical trial from August 2007-Dec 2013 was used. Ten consecutive patients (9 women, 1 men) admitted to the Weill Cornell Medical College, with mean age (range) of 54 (35-83) years were included. 5 patients had brain deficits shown in the CTP images and the other 5 patients had normal brain images.

Because repetitive scanning of the same patient under different radiation levels is unethical, low-dose Perfusion maps are simulated from the high-dose 190 mAs by adding correlated statistical noise [8] with standard deviation of $\sigma_a = 25.54$, which yields PSNR=40. The maps calculated using bSVD from the 190 mAs high-dose CTP data is regarded as the "gold standard" or reference images in clinical experiments.

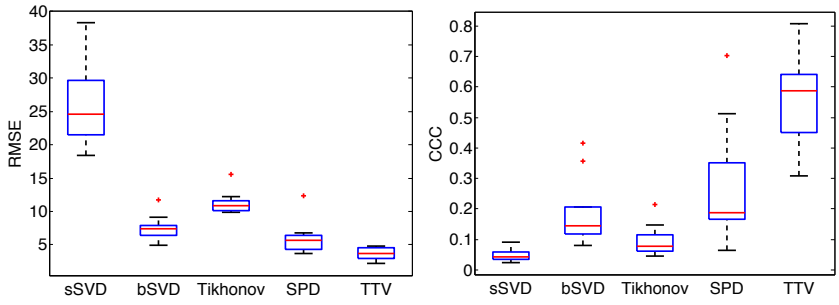


Fig. 5. Comparisons of RMSE and Lin's CCC among the four methods. TTV results in significant ($P < 0.001$) lower RMSE and higher Lins CCC compared with all the baseline methods.

Visual Comparison: At normal sampling rate of 1 s and reduced temporal sampling rate of 2 s and 3 s, the errors of CBF estimation in the four baseline algorithms increase, while TTV maintains accurate estimation for CBF value at all sampling rates.

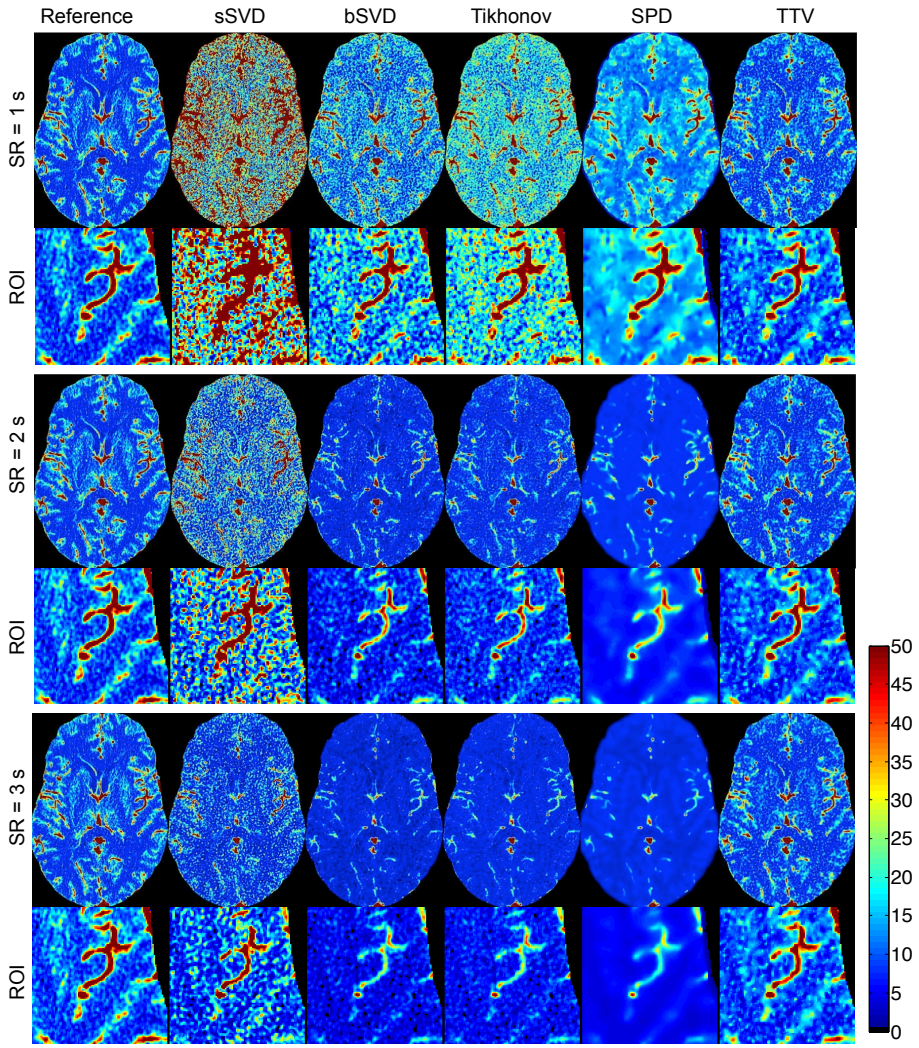
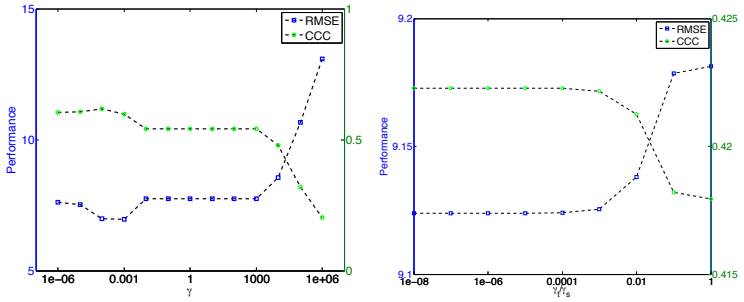


Fig. 6. The CBF maps with roomed ROI regions of a patient computed using different deconvolution methods at sampling rate (SR) of 1 s, 2 s and 3 s with 15 mAs tube current. At normal sampling rate 1 s, baseline methods over-estimate CBF values. At reduced sampling frequency 2 s, sSVD still over-estimate while bSVD, Tikhonov and SPD under-estimate CBF values. At reduced sampling rate of 3 s, baseline algorithms under-estimate CBF values. At all sampling rates, TTV accurately estimate the CBF values. (Color image)

Quantitative Comparison: Fig. 5 shows significant improvement in image fidelity between the low-dose CBF maps and the high-dose CBF maps by using the TTV algorithm compared to the baseline methods. On average, the root-mean-square-error (RMSE) decreases by 40%, Lin's CCC increases by 89% from the best performance by using the baseline methods. The quantitative values are computed with the vascular pixel elimination to exclude the influence of high blood flow values in the blood vessels.

3.3 Parameters

In the TTV algorithm, there is only a single type of tunable parameter: the TV regularization weight. If the spatial and temporal regularization are treated equally, only one weighting parameter γ needs to be determined. Fig. 7(a) show the RMSE at different γ values. When $\gamma < 10^3$, RMSE does not change much. The optimal γ is between 10^{-4} to 10^{-3}.



(a) (b)

Fig. 7. Performace in terms of root-mean-square-error (RMSE) for different parameters (a) γ and (b) ratio γ_t/γ_s.

Since the temporal and the spatial dimensions of the residue impulse functions have different scaling, regularization parameters for t and x, y, z should be different too. We set the spatial $\gamma_s = \gamma_{x,y,z} = 10^{-4}$ since the spatial dimensions have similar scaling, and tune the ratio between the temporal weight γ_t and spatial weight γ_s. Fig. 7(b) shows that when the ratio $\gamma_t/\gamma_s < 10^{-4}$, the performance is stable. Compared to isotropic TTV, anisotropic TTV with the ratio of spatial and temporal regularization weight set to 10^{-4} output improved result from Fig. 7(b). Thus we set $\gamma_t = 10^{-8}$ and $\gamma_s = 10^{-4}$ for all experiments.

4 Conclusion

In this paper, we extended the tensor total variation regularized (TTV) deconvolution algorithm with anisotropic regularization weighting for the temporal and spatial dimensions. We evaluated TTV algorithm for bolus delay, uniform region variability and

contrast preservation on synthetic dataset, as well as for reduced sampling rate with visual and quantitative comparison on clinical dataset. The extensive experiments demonstrated the superiority of TTV compared to baseline and state-of-art algorithms in low-dose and low-sampling-rate CTP deconvolution with insensitivity to tracer arrival time. Future research include evaluation of TTV algorithm on larger-scale clinical datasets with acute stroke and other cerebrovascular diseases.

References

[1] Wintermark, M., Lev, M.: FDA investigates the safety of brain perfusion ct. American Journal of Neuroradiology **31**(1) (2010) 2–3

[2] Fang, R., Sanelli, P.C., Zhang, S., Chen, T.a.: Tensor total-variation regularized deconvolution for efficient low-dose ct perfusion. In Barillot, Golland, H.H., ed.: Medical Image Computing and Computer-Assisted Intervention MICCAI 2014. Lecture Notes in Computer Science. Springer Berlin Heidelberg (2014)

[3] Østergaard, L., Weisskoff, R.M., Chesler, D.A., Gyldensted, C., Rosen, B.R.: High resolution measurement of cerebral blood flow using intravascular tracer bolus passages. Part I: Mathematical approach and statistical analysis. Magnetic Resonance in Medicine **36**(5) (1996) 715–725

[4] Wu, O., Østergaard, L., Weisskoff, R.M., Benner, T., Rosen, B.R., Sorensen, A.G.: Tracer arrival timing-insensitive technique for estimating flow in MR perfusion-weighted imaging using singular value decomposition with a block-circulant deconvolution matrix. Magnetic Resonance in Medicine **50**(1) (2003) 164–174

[5] Fieselmann, A., Kowarschik, M., Ganguly, A., Hornegger, J., Fahrig, R.: Deconvolution-based CT and MR brain perfusion measurement: theoretical model revisited and practical implementation details. Journal of Biomedical Imaging **2011** (2011) 14

[6] Fang, R., Chen, T., Sanelli, P.C.: Towards robust deconvolution of low-dose perfusion ct: Sparse perfusion deconvolution using online dictionary learning. Medical image analysis (2013)

[7] Huang, J., Zhang, S., Metaxas, D.: Efficient mr image reconstruction for compressed mr imaging. Medical Image Analysis **15**(5) (2011) 670–679

[8] Britten, A., Crotty, M., Kiremidjian, H., Grundy, A., Adam, E.: The addition of computer simulated noise to investigate radiation dose and image quality in images with spatial correlation of statistical noise: an example application to x-ray ct of the brain. British journal of radiology **77**(916) (2004) 323–328