A NOVEL METHOD TO DETERMINE THE TIKHONOV REGULARIZATION PARAMETER FOR PULMONARY PERFUSION QUANTIFICATION WITH MRI

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INTRODUCTION: The assessment of pulmonary perfusion by dynamic contrast enhanced MRI requires deconvolution of the arterial input function. In the presence of noise this is an ill-posed problem which leads to strongly oscillating, unphysical solutions when it is solved without regularization [1]. In this study a novel method to determine the parameter for Tikhonov regularization based on a model of the residue function is introduced and compared to the classical L-curve criterion.

METHODS: Perfusion quantification: The contrast agent concentration in a tissue is $C_{tissue}(t)=PBF*[C_{aif}(t)\bullet R(t)]$ sampled at $t=t_1,..,t_n$. $C_{aif}(t)$ is the concentration in the arterial input which is convolved with the tissue residue function R(t) and PBF is the pulmonary blood flow. In discrete form this is a linear system of equations $Ak=C_{tissue}$ with the unknown $k(t)=PBF*R(t)$. General form Tikhonov regularization $k=argmin\{ \|Ak-C_{tissue}\|^2 + \lambda^2*\|Lk\|^2 \}$ with a first-order difference matrix L is used to solve for k. The PBF and the mean-transit-time (MTT) can be determined from k: $PBF=max(k)$; $MTT=\int k(t)dt / max(k)$.

Residue function model: In order to determine the optimal parameter λ our new model uses the negative slope and positive function values of k(t) as a priori knowledge. Only minor deviations from these requirements are allowed. 200 values for λ are selected which are distributed logarithmically between 1% and 100% of the maximum singular value of A. For each λ the regularized solution $k(t)=PBF*R(t)$ is computed and checked if it fulfills the acceptance criterion. The accepted solution k(t) which belongs to the smallest λ is assumed to be the optimal solution (Fig. 1). Acceptance criterion: p is defined as the index of the first zero-crossing of k(t) (Fig. 1). The index of the maximum that occurs before the first zero crossing is called m. In order to be accepted as a solution each difference $k_{i+1}-k_i$ (i=m,..p-1) must not exceed a small positive constant α and each norm $\|k_j\|$ (j=p,..,n) must be below a small positive constant β.

Simulation: Synthetic perfusion data are generated with $C_{aif}(t)$ modeled as a gamma-variate function as in [1,2]. $C_{aif}(t)$ is sampled from 0 s to 60 s at an interval of Δt=1 s and convolved with $k(t)=PBF*exp(-t/MTT)$ to yield $C_{tissue}(t)$. Gaussian distributed noise is added to $C_{tissue}(t)$ and $C_{aif}(t)$. In the first data set MTT takes the values [3;6;9;12] s with SNR=30. In the second data set MTT is 6 s and SNR takes the values [20;30;40;50;60;70]. In both sets PBF equals 180 ml/min/100ml. Regularization is performed with determination of λ according to the residue function model (RFM), setting $\alpha=(0.01*max(k)*\Delta t)$ and $\beta=(0.1*max(k))$, and the L-curve criterion (LCC) [3]. The LCC determines λ as the corner point in a plot of $log(\|Ak-C_{tissue}\|)$ against $log(\|Lk\|)$. The simulation is repeated 500 times for each configuration with different noise and the medians of the relative errors of the estimated PBF and MTT are calculated.

MRI data: Dynamic contrast enhanced data of pulmonary perfusion are measured in 4 healthy volunteers using a 2D FLASH technique during end-inspiratory breath-hold (TE/TR=0.73 msec/1.73 msec; α=40°; GRAPPA, factor 3; FOV: 500x500 mm; matrix: 192x144; slice thickness: 20 mm; 100 measurements with Δt=400 ms were acquired after the administration of 0.04 mmol/kg Gd-DTPA).

RESULTS: Simulation: Results from the first data set are shown in table 1 and from the second data set in figure 2. MRI data: Figure 3 shows a typical estimate of k(t) from one measurement. For all measurements the RFM method determined a smaller parameter λ and estimated higher PBF and lower MTT values than the LCC method. The relative differences of the estimates with the two methods were below 10%.

Table 1: Relative errors of the estimated PBF and MTT with simulated data using the RFM and LCC methods for parameter determination.

	MTT = 3 s		MTT = 6 s		MTT = 9 s		MTT = 12 s	
	LCC	RFM	LCC	RFM	LCC	RFM	LCC	RFM
‖ ΔPBF / PBF ‖ [%]	16.8	13.2	13.1	10.7	11.4	9.3	10.1	8.2
‖ ΔMTT / MTT ‖ [%]	23.2	18.5	15.1	12.6	12.9	10.6	10.1	8.1

DISCUSSION: The results from the simulated data in table 1 and figure 2 show that the RFM method leads to less relative errors in the estimated PBF and MTT than the LCC method. Compared to the LCC method, which is a model-free approach, the RFM method includes physiologically motivated a priori knowledge. With this knowledge the amount of regularization is minimized to an adequate level. That may explain why the estimated perfusion quantities are estimated more accurately with the RFM method.

Applied to the measured MRI data both methods gave meaningful and similar estimates of PBF and MTT. The maximum at t>0 in figure 1 is associated with bolus dispersion. Because the exact underlying perfusion parameters are not known it is difficult to assess the accuracies of these estimates. But in all four measured data the RFM method determined a lower λ value than the LCC method which shows that it indeed minimizes the amount of regularization. The smoothness of k(t) depends mainly on the threshold parameter α. This fixed threshold values may not be confused with a fixed value of the parameter λ. The value of α determines how much deviation from a residue function with only negative slope is permitted. In this study only one value for α was used and a further investigation with different α values may be performed. The main advantage of the RFM method is that the amount of regularization is determined in a well interpretable manner and over-smoothing of the solution k(t) is avoided.

CONCLUSION: The novel method is an alternative to the classical L-curve criterion. The amount of regularization is minimized by a priori knowledge of the residue function. Results from simulated data show that the novel method leads to more accurate estimates of the perfusion parameters. Investigations with measured pulmonary perfusion data show that it produces stable solutions with a lower amount of regularization than the L-curve criterion.

REFERENCES: [1] Calamante F. et al (2003), MRM 50:1237-1247. [2] Sourbron S. et al (2004), Phys. Med. Biol. 49:3307-3324. [3] Hansen P.C. (1992), SIAM Rev. 34:561-580.

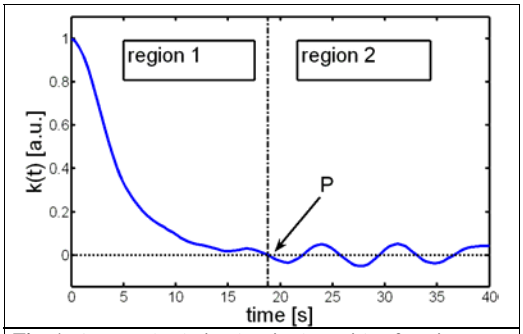

Fig. 1: Accepted solution k(t) in the residue function model. In region 1 the differences $(k_{i+1}-k_i)$ are be below a constant α. In region 2 the norms $\|k_j\|$ are below a constant β. P is the index of the first zero-crossing.

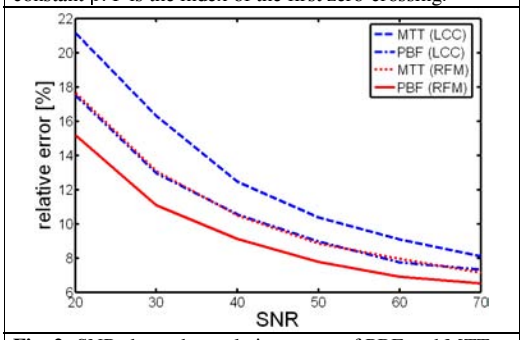

Fig. 2: SNR-dependent relative errors of PBF and MTT with simulated data using the RFM and LCC methods.

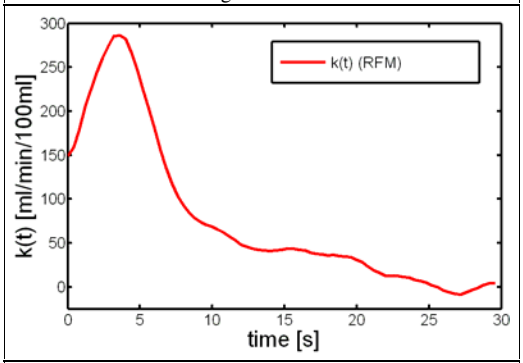

Fig. 3: Typical estimated k(t) from one MRI measurement using the novel RFM method (PBF=286 ml/min/100ml, MTT=6.9 s).