medical imaging,
MRI, brain perfusion

Bartosz KARCZEWSKI*, Jacek RUMIŃSKI*

VALIDITY OF MRI BRAIN PERFUSION IMAGING METHOD

Brain perfusion imaging using Dynamic Susceptibility Contrast Magnetic Resonance Imaging is very promising method since it can be easily implemented as a standard contrast-based MRI procedure. Quantitative brain perfusion description by DSC-MRI data post processing requires validation. Different validation analysis was performed to verify the influence of a bolus dispersion, delay, low SNR and calculation procedures on final perfusion parameter values. The results indicate that quantitative description of brain perfusion using DSC-MRI is possible and can be acceptable with accuracy about 10%.

1. INTRODUCTION

Parametric images represent values of reconstructed parameters for assumed tissue/activity model. This includes DSC-MRI [3], Arterial Spin Labelling (ASL) MRI [5], dynamic Positron Emission Tomography (PET) [1], dynamic active thermography [4], etc. In DSC-MRI imaging, after injection of a bolus of contrast agent (e.g. Gd-DTPA), a series of images are measured. Obtained signals (for each point/pixel) present local voxel activity of contrast/blood flow and distribution. It is assumed, that measured MRI signal values are proportional to the contrast concentration. Contrast concentration as a function of time is also measured for chosen brain artery, which is estimated as the arterial input function (AIF). The AIF is not an ideal impulse function (due to dispersion and delay); additionally signals are measured not from the venous output but from a tissue volume of interest (VOI) therefore deconvolution is required to calculate a VOI impulse response *F*R(t)*:

$$C_t(t) = \frac{\rho}{Kh}\int_0^t C_a(\tau)\cdot\big(F\cdot R(t-\tau)\big)d\tau\,, \qquad (1)$$

where: $C_a(t)$ - contrast concentration in the artery (e.g., Middle Cerebral Artery) – AIF, $C_t(t)$ - contrast concentration in the tissue VOI, $\frac{\rho}{Kh}$ - a scaling factor (in quantitative description), *F*R(t)* – scaled fractional tissue concentration (*R(t)*).

Assuming that contrast material remains intravascular and the first pass of the contrast bolus can be eliminated from the concentration function a set of perfusion related parameters can be calculated (using deconvolution to find *R(t)*). Since *R(t=0)* should be equal to 1, then

* Department of Biomedical Engineering, Gdansk University of Technology

$$F \cdot R(t=0) = F = rCBF \text{ (regional Cerebral Blood Flow).} \quad (2)$$

Regional cerebral blood volume (proportional to the normalised total amount of a tracer) and mean transit time (average time required for any given particle of a tracer to pass through the tissue after an ideal bolus injection) can be estimated as

$$rCBV = \left(\int_0^\infty C_t(\tau) d\tau \right) / \left(\frac{\rho}{Kh} \int_0^\infty C_a(\tau) d\tau \right); \; rMTT = rCBV/rCBF. \quad (3)$$

The aim of this study was to estimate the influence of the contrast bolus dispersion and delay as well as the signal noise levels on perfusion parameter values. This validation is important to assess either the quantitative parametric imaging method using DSC-MRI is acceptable or not for brain perfusion estimation.

In experiments simulation and clinical data were used. Image sequences for in-vivo measurements were collected using 1.5T MRI scanner (SE-EPI with: 12 slices, 50 samples, TR=1.25-1.61s; TE=32-53ms; slice thickness 5-10 mm; 60 series - 3000 images). Using own, created software (written in Java) we extracted signals and concentration curves used further to reconstruct rCBF, rCBV and rMTT parametric images.

2. INFLUENCE OF DISPERSION AND DELAY

In quantitative DSC-MRI it is crucial to exactly measure the AIF function. Based on the AIF the required signal ($F*R(t)$) is deconvolved and used for synthesis of quantitative maps. Theoretically the AIF describes concentration of contrast agent in the VOI feeding vessel. Practically it could be localized far away from the VOI (e.g. carotid artery, middle cerebral artery). The path between measured AIF source and true AIF localization is unknown. The AIF delay and dispersion can appear and can be modelled using [2]:

$$C_a^{true}(t) = C_a(t) \otimes h(t), \quad (4)$$

where: $\otimes$ - convolution operator, h(t) – vascular transport function, e.g.:

$$h(t) = \frac{1}{t_D} \cdot \exp\left(\frac{-t}{t_D} \right), \quad (5)$$

where: t_D - dispersion constant.

The influence of dispersion on final results (MTT or CBF) can be analysed performing the following test. First $C_a(t)$ and R(t) signals are modelled as

$$C_a(t) = \begin{cases} K(t-t_0)^\beta \cdot e^{-\alpha(t-t_0)}, t > t_0 \\ 0, t \le t_0 \end{cases}, \quad (6)$$

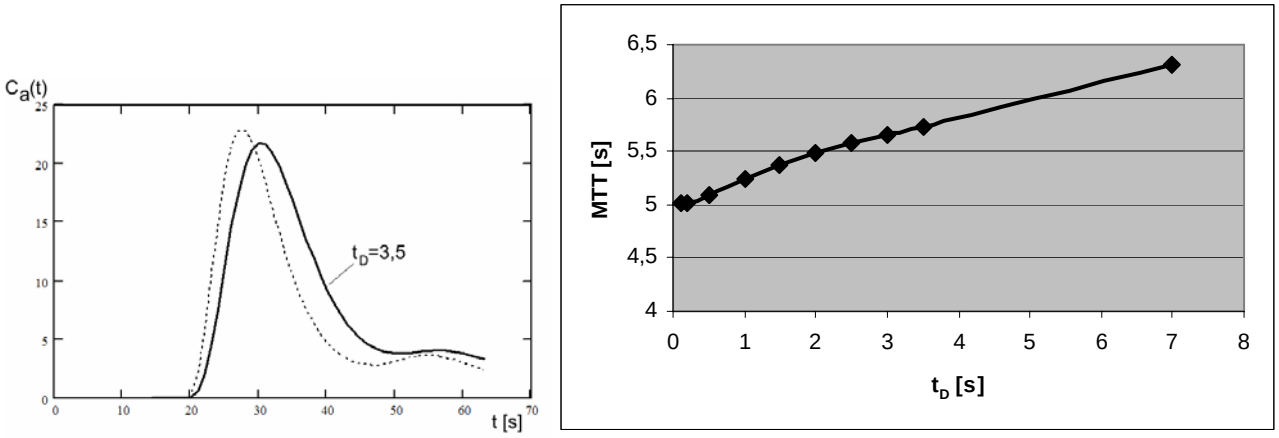
$$R(t) = \exp(-\frac{t}{MTT}), \quad (7)$$

where: K, α, β model parameters (used β=3, α=2/3), t_0 - bolus arrival time (BAT).

Then, the original $C_a(t)$ is convolved with the dispersion function using different values of the dispersion parameter t_D (eq. 5). Finally, dispersed $C_a(t)$ functions are convolved with R(t) producing a set of $C_t(t)$. Calculation of MTT/CBF requires to deconvolve the R(t) from $C_t(t)$, assuming $C_a(t)$. Performing deconvolution of R(t) for any $C_t(t)$ from the generated set, using the original (without dispersion) $C_a(t)$ can be used to analyse the influence of dispersion on MTT/CBF values. Similar analysis may be used to investigate the influence of $C_a(t)$ delay on final results. The delay in the test set was introduced using shift of samples. Other steps are identical as for dispersion analysis.

2.1. RESULTS

The influence of dispersion was estimated using 10 different values of t_D in the range of 0-7 seconds (typical MTT values for grey matter / white matter are 3-6s). Results (MTT as a function of t_D) are presented in Fig. 1b.



a) b)

Fig.1. a) Example of the dispersion effect on $C_a(t)$. b) MTT as a function of dispersion (t_D) – true value of MTT=5

In the range of the sampling period (in DSC-MRI usually 1-2s) the error caused by dispersion is 5-10%. This is a lower bound since for real signals (lower SNR) the influence of dispersion can be even higher. Analysing the role of delay, the shift in samples was used for the range: –2 to 5 samples (seconds). In Fig. 2a the results of analysis (MTT as a function of delay) are presented.

In the range of the sampling period the error caused by delay is about 5%. In Fig. 2b the result of deconvolved $R(t)$ for dispersed (t_D =2s) and delayed (2s) $C_a(t)$ is presented (compare to (7)). In this analysis numerical deconvolution usually requires data matrix regularization (ill-posed matrix, build with $C_t(t)$ for linear deconvolution). The Tikhonov Singular Value Decomposition (TSVD) method was used [6]. In the range of the sampling period the error produced by both effects is up to 20%. However in clinical environment measured signals are affected by noise what can reduce the accuracy of CBF/CBV parameter values.

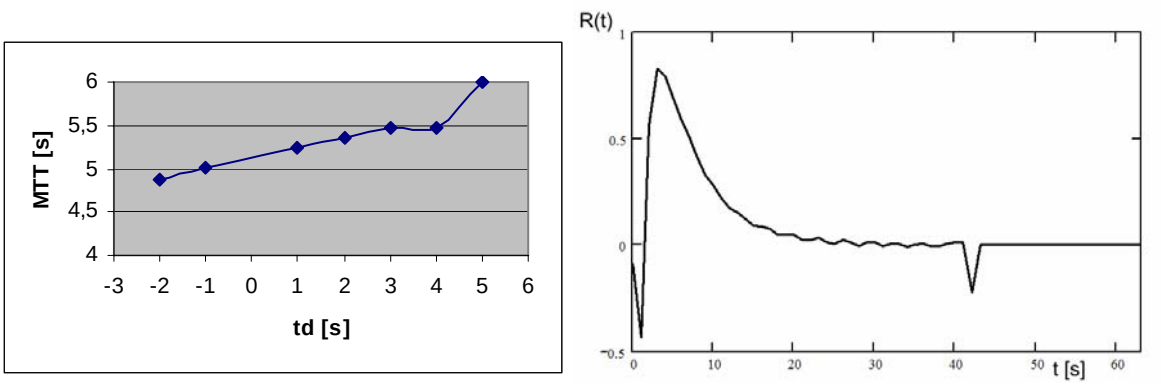


Fig.2. a) The influence of delay in $C_a(t)$ on MTT, true value of MTT=5s; b) deconvolved R(t) for dispersed (t_D =2s) and delayed (2s) $C_a(t)$

3. INFLUENCE OF A SIGNAL NOISE

The influence of a signal noise and regularisation factor values on perfusion parameters were investigated. Again the Gamma variate function (eq. 6) was used with $K=1$, $\alpha=1$, $\beta=1$, $t_0=0$, to generate *AIF*. In the case of the $R(t)$ function (eq. 7), a value of the MTT parameter was fixed to 5 (seconds). Signal $C_t(t)$ was distorted by a noise described by a normal distribution with a mean value fixed to zero and following values of a standard deviation [0, 0.01, 0.05, 0.1, 0.3, 0.5, 0.7, 1]. Additionally, to avoid dependency on fixed parameters K, α, β, t_0, F and MTT, a scale coefficient (a maximum value of $C_t(t)$) multiplied by a standard deviation value was used. Tests were repeated 100 times to obtain mean results. Quantitative comparison between true and calculated parameter values were described using:

$$RMSE\% = \frac{1}{p}\sqrt{\frac{\sum_{i=1}^{N}(p_i - p)^2}{N-1}}, \; Bias\% = \frac{1}{p}\sum_{i=1}^{N}\frac{(p_i - p)}{N}, \qquad (8)$$

where p is a true value of a parameter, p_i is an estimated value of a parameter in every step i, N - number of steps.

The goal of tests was to obtain Root Mean Square Error (*RMSE)* and *Bias* values as the function of introduced error (standard deviation), for *CBF* and *CBV* parameters.

In the first case a constant value of regularization coefficient was used (= 10^{-2}) (*Test 1*). Next the optimal value of a regularisation factor was automatically calculated. It was performed for two configurations: *Test 2* - optimisation for *CBF*, *Test 3*- optimisation for *CBV*.

3.1. RESULTS

Selected results of tests (1-3) are presented in Tab. 1 –3.

Tab. 1. Results of Test 1 (fixed regularization value $\lambda = 10^{-2}$)

δ	RMSE [%] – CBF	RMSE [%] – CBV	Bias [%] - CBF	Bias [%] – CBV
0	0	0	-0.7473	0.7511
0.01	12.4	14.4	0.0572	0.3788
0.05	66.7	75	2.6068	3.1749
0.1	121.7	143.3	7.3263	8.067
0.3	368.2	430	21.2142	23.5769
0.5	647.8	735	39.1494	43.3167
0.7	865.9	996.3	49.7286	55.8438
1	1189.5	1374.4	77.3399	84.2707

Tab. 2. Results of Test 2 (optimization for CBF)

δ	RMSE [%] – CBF	RMSE [%] – CBV	Bias [%] - CBF	Bias [%] – CBV	λ
0	0	0.7511	-0.0164	-0.7473	0.01
0.01	0.0165	1.117	-0.0003	-1.0897	0.281
0.05	0.091	0.7639	-0.006	-0.4103	0.6355
0.1	0.1	1.4705	-0.0077	0.9641	0.8959
0.3	0.0994	6.1568	-0.0008	5.5812	1.6101
0.5	0.0901	10.955	0.0015	10.3718	2.0864
0.7	0.0832	15.6977	0.0005	14.8939	2.4954
1	0.0899	20.3769	0.0091	19.4394	2.985

Tab. 3. Results of Test 3 (optimization for CBV)

δ	RMSE [%] – CBF	RMSE [%] – CBV	Bias [%] - CBF	Bias [%] – CBV	λ
0	0.0165	0.7511	-0.0164	-0.7473	0.01
0.01	12.7627	0.2306	11.333	-0.133	0.0397
0.05	4.3126	0.0204	2.5405	-0.0021	0.5832
0.1	17.0457	0.0276	-1.625	0	0.9932
0.3	13.0668	0.0419	-12.1171	0.0007	2.0242
0.5	18.3853	0.0481	-17.6852	0.0005	2.6869
0.7	22.2841	0.0555	-21.5229	0.0043	3.2307
1	24.8288	0.0567	-24.1608	0.0121	3.947

The introduced noise has a large influence on the results in case of deconvolution using fixed value of regularization factor. The *RMSE* coefficient value reached maximum of 1400% for the *CBV* parameter (similarly, *CBF* is near 1200%). In the *Bias* case, situation is similar. The obtained values are lower, maximum 85%, but sufficiently large to eliminate them from further analysis.

Analyzing results for the best case of the regularization factor there is not possible to set a one, universal value that guarantee the best accuracy of both parameters (CBF/CBV). Optimal calculation of CBV (or MTT) and CBF requires repeating deconvolution process. Increasing the noise (a standard deviation value) corresponds to higher values of the regularization factor. However it seems that the influence of the noise (in analyzed range) is

not a critical factor in comparison to dispersion problems described earlier. Since the image sequence SNR can be controlled during measurement (high level of the noise, modelled here with $\delta>0.3$, is practically unacceptable) the more attention should be focused on appropriate AIF indication (to reduce dispersion/delay effects).

4. FINAL CONCLUSION

Performed tests indicate that using appropriate quality assurance procedures (to control SNR) and proper AIF extraction it is possible to reliable describe perfusion parameters using DSC-MRI. However, even in the controlled environment the error level can reach up to 10% of parameter values. In most applications (e.g. in cancer or stroke diagnosis) it can be acceptable because of high contrast in CBF/CBV parameter values between healthy and tumour tissues. Since the method assumes the typical contrast-based procedure it can be easily used with majority of MRI scanners. As the practical conclusion of the presented validation the software package (Java) was prepared for quantitative calculation of perfusion maps. In Fig. 3 an example of graphical user interface with EPI T2 image (first in the sequence measured during bolus tracking) and calculated rBAT, rCBV and rCBF images for a stroke case (limited perfusion in the observed left upper region) are presented.

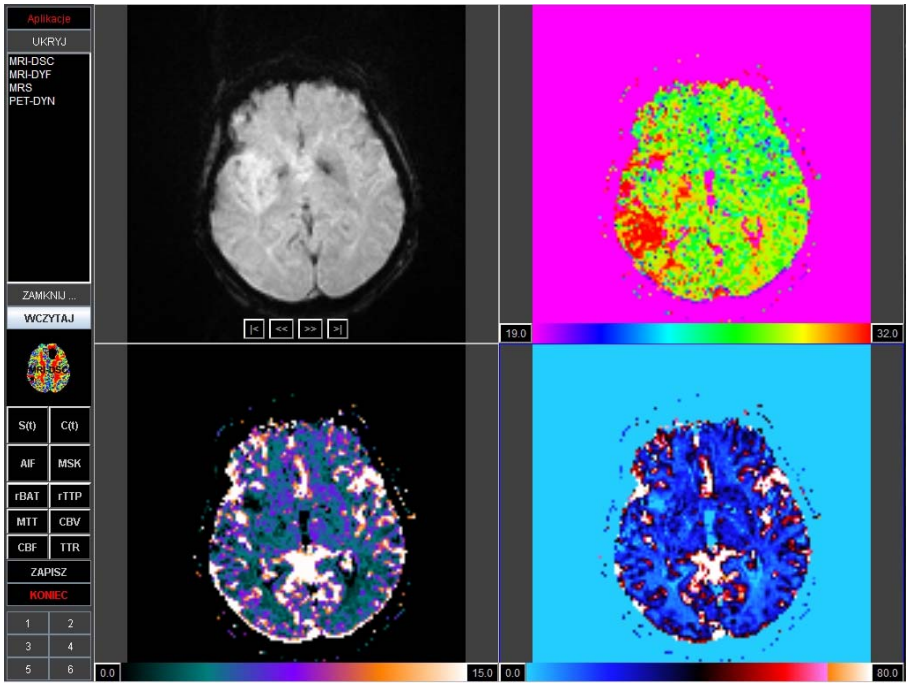


Fig. 3. An example of the graphical user interface with a set of images (from top left): EPI T2, calculated rBAT [s], rCBV [ml/100g] and rCBF [ml/100g/min] for a stroke case

ACKNOWLEDGEMENT

This work was partly supported by the grant of Polish State Committee for Scientific Research (2003-2006) 4 T11E 042 25.

BIBLIOGRAPHY

[1] CAI W., FENG D. D., FULTON R., Content based retrieval of dynamic PET functional images, IEEE Transactions on Information Technology in Biomedicine 4 (2)152-158, 2000.
[2] CALAMANTE F., GADIAN D. G., CONNELLY A., 2000 Delay and dispersion effects in dynamic susceptibility contrast MRI: simulations using singular value decomposition *Magn. Reson. Med.* **44** 466–73
[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: I. Mathematical approach and statistical analysis, II. Experimental comparison and preliminary results *Magn. Reson. Med.* **36** 715–36, 1996.
[4] RUMINSKI J., KACZMAREK M., NOWAKOWSKI A., Medical Active Thermography – A New Image Reconstruction Method, LNCS2124, Springer,2 74-281, 2001.
[5] WANG J., ALSOP D. C., LI L., LISTERUD J., GONZALEZ-AT J. B., SCHNALL M. D., DETRE J. A., Comparison of Quantitative Perfusion Imaging Using Arterial Spin Labeling at 1.5 and 4.0 Tesla, MRM 48:242–254, 2002.
[6] WU L., A Parameter Choice Method For Tikhonov Regularization, Electronic Transactions on Numerical Analysis. Volume 16, pp. 107-128, Kent State University, 2003.