ESTIMATORS FOR KINETIC MODELING OF DYNAMIC CONTRAST-ENHANCED MAGNETIC RESONANCE DATA FROM SPOILED GRADIENT ECHO PULSE SEQUENCES

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Abstract

In this work, the influence of the estimator was investigated on the accuracy and reproducibility of kinetic modeling of dynamic contrast enhanced MRI (DCE-MRI) data from spoiled gradient echo pulse sequences (SPGRE). The commonly used least square (LSQ) estimator was compared with a LSQ and a maximum likelihood estimator (MLM) both corrected for concentration bias. It was shown that the MLM estimator can reduce the kinetic parameter bias up to a factor 28, and decrease the width of its confidence interval with 12%.

Keyword: modeling of physiological systems

1 Introduction

Kinetic modeling of DCE-MRI data is increasingly used in tumor diagnosis, in the evaluation of novel anti-angiogenic therapies or for the monitoring of tumor response to treatment. The Tofts model describes the extravasation of contrast agent (CA) from the plasma to the tumor as a function of the extracellular extravascular space fraction v_e and the transendothelial transfer constant K^{trans}:

$$C_t(t) = K^{trans} \int_0^t C_p(t') \cdot \exp\left[-\frac{K^{trans}}{v_e}(t-t')\right] dt'$$

When the arterial input function (C_p) is known, K^{trans} and v_e are fitted from the MR-measured concentration curve C_t. Several studies have shown a strong positive correlation between K^{trans} and physiological properties as permeability and perfusion, or a significant reduction of K^{trans} after successful therapy. However, the technique suffers from low accuracy and weak reproducibility of these transfer constants estimates. This work investigates the influence of the estimator on the accuracy and the reproducibility of the kinetic parameters, fitted from DCE-MRI data from SGPRE pulse sequences.

2 Methods

Due to the non-linearity between the CA concentration and the SPGRE signal intensity, SPGRE-measured concentration data are biased and heteroskedastic. Therefore we have compared 3 estimators: the commonly used LSQ estimator (LSQ1), a LSQ estimator with a correction for the bias (LSQ2), and a MLM estimator with a correction for the bias (MLM1). The concentration bias correction was calculated from a taylor expansion of the SPGRE equation. Simulations were performed in Matlab, to compare these estimators for their kinetic parameter bias and their uncertainty (linearly related to the width of the confidence interval).

3 Results

$K^{trans}[min^{-1}]$ / v_e	Bias in K^{trans} [%]			Bias in v_e [%]		
	LSQ1	LSQ2	MLM	LSQ1	LSQ2	MLM
0.03/0.3	3.5	0.5	0.7	4.8	1.7	1.6
0.03/0.5	2.8	0.2	0.1	5.5	3.6	4.2
1.2/0.3	2.1	0.6	0.6	1.7	0.2	0.2
1.2/0.5	2.4	0.7	0.7	1.5	0.2	0.2

$K^{trans}[min^{-1}]$ / v_e	K^{trans}-uncertainty [%]			v_e-uncertainty [%]		
	LSQ1	LSQ2	MLM	LSQ1	LSQ2	MLM
0.03/0.3	10.4	10.3	10.3	11.1	11.1	11.1
0.03/0.5	8.7	8.6	8.6	16.4	16.4	16.4
1.2/0.3	16.6	16.3	14.8	3.2	3.2	3.0
1.2/0.5	13.9	13.6	12.4	2.3	2.3	2.2

The bias correction reduces K^{trans}-bias with a factor 3 up to 28 and the v_e-bias with a factor 1.5 to 8.5. Regarding uncertainty, the MLM performs better than the LSQ estimators and reduces the width of the confidence intervals of high K^{trans} up to 12%.

4 Conclusion

The accuracy and the reproducibility of kinetic parameter estimates, fitted from DCE-MRI data from SPGRE pulse sequences, can be significantly increased by using maximum likelihood estimators, with a correction for concentration bias.