MODEL SELECTION FOR DCE-MRI APPLIED TO SUBTLE BLOOD-BRAIN BARRIER DISRUPTION

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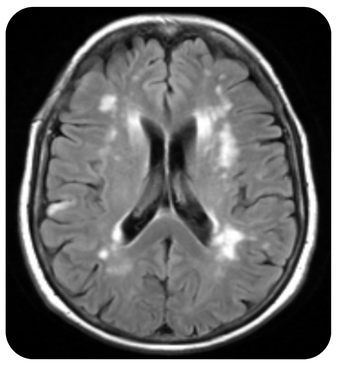
Abstract

The purpose of this study was to choose a suitable pharmacokinetic model to quantify subtle blood-brain barrier (BBB) permeability using dynamic-contrast enhanced MRI (DCE-MRI). 201 mild stroke patients underwent DCE-MRI; three nested models were fitted to the data and ranked according to the Akaike information criterion. The Patlak model proved to be the most suitable model under the conditions of this experiment, providing the best trade-off between goodness-of-fit and model complexity.

Introduction



FLAIR image of a mild stroke patient with white matter disease

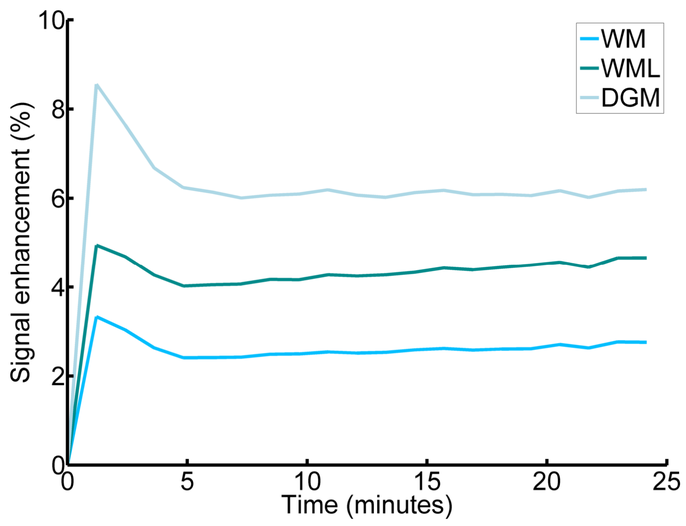
- Many brain pathologies, such as tumours, cause an opening of the BBB.
- Quantitative information about the functional integrity of the BBB can be gained by performing DCE-MRI.
- There has been growing interest in the application of permeability imaging to pathologies associated with subtle BBB disruption, such mild stroke [1].
- A wide range of pharmacokinetic models have been proposed for fitting DCE-MRI data [2].
- It is important to recognise the assumptions built into these models and assess their likely validity for a given pathology and acquisition protocol.

Objectives

Choose a suitable pharmacokinetic model from a set of three nested models to quantify BBB permeability in normal-appearing white matter (NAWM), white matter lesions (WML) and deep grey matter (DGM)

Imaging

- DCE-MRI performed in 201 patients with mild stroke
- Intravenous injection of contrast agent (0.1 mmol/kg Gd-DOTA)
- Repeated acquisition of T1-weighted images (1.5T, spoiled gradient echo, TR/TE/FA=8.2ms/3.1ms/12°) over 23 minutes (Δt = 73 seconds); additional acquisition with FA=2° for T1 estimation
- Segmentation of tissue types [3] and extraction of a vascular input function from the superior sagittal sinus



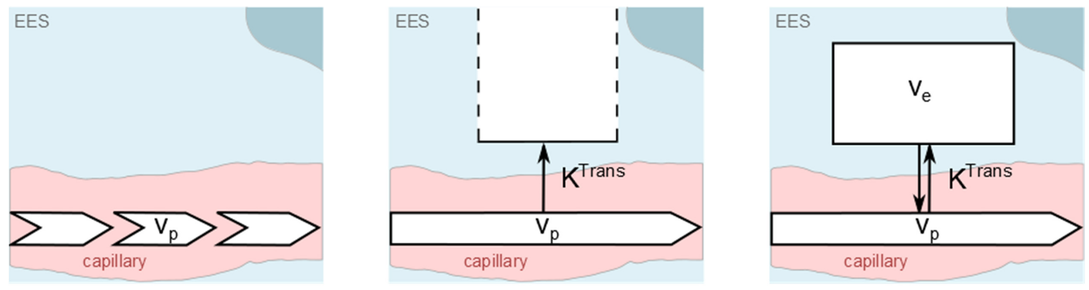
Population-averaged contrast agent concentration curves in NAWM, WML and DGM

- Measurement of averaged signal enhancement curves over time in each tissue type
- Calculation of contrast agent concentration profiles

Model selection

- Set of three nested models with increasing complexity

1) Steady State [2] 2) Patlak [4] 3) Modified Tofts [5]



v_p: fractional plasma volume, K^{Trans}: volume transfer constant, v_e: fractional volume of the extravascular extracellular space (EES)

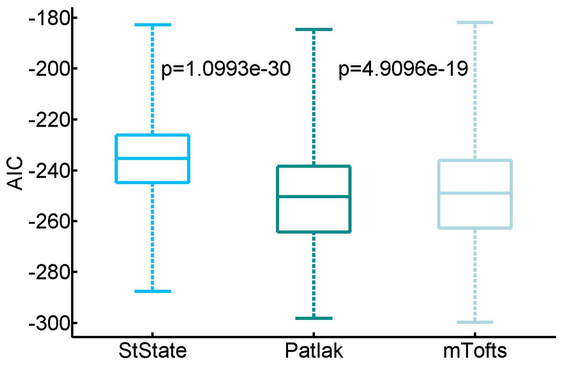
- Akaike information criterion (AIC) [6]:
  - Objective measure of model suitability
  - Accounts for goodness-of-fit and number of free model parameters

Results

- The pharmacokinetic parameters obtained with the three models are significantly different

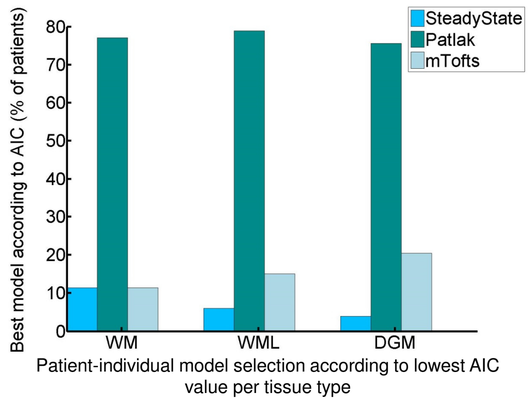
Pharmacokinetic parameters in normal appearing white matter (population average ± standard deviation)

Model	v_p ($\cdot 10^{-2}$)	K^{Trans} ($\cdot 10^{-4}$ min^{-1})	v_e
Steady State	1.15 ± 0.41		
Patlak	0.55 ± 0.33	2.79 ± 1.52	
Mod. Tofts	0.33 ± 0.35	6.37 ± 7.30	0.36 ± 0.42



AIC values in normal appearing white matter

- The steady state model does not provide adequate fits to the data
- Overall, the Patlak model produced the best (lowest) AIC values in all tissue types
- Hence, automatic selection of the best model according to AIC in each patient and tissue type results in the Patlak model being preferred in the vast majority of patients



Patient-individual model selection according to lowest AIC value per tissue type

Conclusions

- Steady state model not sufficient to describe the data
- Patlak model is the most suitable for the tissues of interest and given image acquisition
- Additional free parameter of the modified Tofts model does not significantly increases the goodness-of-fit, but introduces uncertainty in parameter estimation

SINAPSE

References:

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