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Comparison of the Tofts and the Shutter Speed Model for DCE-MRI in patients with Brain Glioma

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Synopsis

DCE-MRI allows interrogation of patho-physiological insular micro-environments through the passage of contrast agents and model-based pharmacokinetic analysis. In this study, we analysed data from 14 patients with suspected primary glioma who underwent DCE-MRI. Using both the Tofts model and the shutter speed model (SSM), we evaluated the performance and variability of each extracted parameter. We then analysed the ability of the two models to discriminate between tumour and healthy tissue to test the differences between the two methods. Results showed higher performance for the SSM, with a high robustness for the mean capillary water molecule lifetime τ_i.

Abstract

Introduction

Dynamic contrast-enhanced (DCE) MRI allows tissue perfusion quantification with the acquisition of T1-weighted images before, during and after injection of a gadolinium-based contrast reagent (CR). Data is frequently modelled by the Tofts model (TM), which embeds the implicit assumption that equilibrium transcytolemmal water exchange is infinitely fast[1]. The effect of water exchange on the MRI signal amplitude is incorporated by the shutter speed model (SSM), which introduces a further pharmacokinetic parameter τ_i, the mean intracellular water lifetime[2]. The Tofts pharmacokinetic assumes a linear dependence of R_1 on [CR]. However, tissue parenchyma cannot be considered as a single homogeneous solution. A voxel in MR will contain different tissue compartments which may affect the signal and are considered in the modification for the SSM[3]. We assess the robustness of the two methods by studying them in tumour lesions and contra-lateral white matter (CWM).

Methods

14 patients (7 male, 7 female; aged 23-73 years, mean 40 years) with suspected primary supratentorial glioma were recruited to this study. Ethical approval was given by the local ethics committee and informed consent was obtained from all patients. MR images were acquired on a 3T Siemens Verio MRI system using a 32 channel head coil; including pre- and post-contrast T1-weighted images, T2-FLAIR images and a DCE sequence with a variable flip angle pre-contrast T1 map acquisition. VOIs were drawn by a Radiologist and confirmed by a Consultant Neuroradiologist for each patient around T2-FLAIR hyperintense regions and on a 2cm diameter circular region on CWM. 3 patients with bilateral disease were excluded from the analysis.

Pharmacokinetic analysis was performed with TM and SSM and resulted with 3D parametric maps of K_{trans} (contrast agent plasma/interstitium transfer rate constant), K_{ep} (intravasation rate constant), v_e (extravascular and extracellular volume fraction) and τ_i (mean capillary water molecule lifetime), in the tumour and the CWM. A Wilcoxon Rank sum test was performed to assess for statistical difference between mean values for the pharmacokinetic maps evaluated with the two models in the lesion and the CWM. Receiver operating characteristic curve (ROC) analysis was then computed for both pharmacokinetic models to further investigate their ability in the classification of the tissue.

Results

Parametric maps of TM and SSM estimates of K_{trans} and τ_i for one axial slice of a non-enhancing and an enhancing tumour are shown in Fig.1. Boxplots of TM and SSM K_{trans} and τ_i evaluated in the CWM are shown in Fig.2. Fig. 3 shows the boxplot of mean values of K_{trans} (TM and SSM) and τ_i maps in tumour and CWM. Results for the ROC analysis are shown in Fig 4. Results showed a strong statistical difference between tumour and CWM for the Tofts' K_{trans} ($p<0.01$) and for the SSM K_{trans} and τ_i ($p<<0.01$).

Discussion

The feasibility of the SSM DCE-MRI pharmacokinetic analysis in brain was previously investigated on 6 healthy, 6 multiple sclerosis and 5 glioblastoma subjects[4]. Cerebral τi maps were found to represent metabolic activity in the brain[4]. However, to our knowledge the importance of τ_i and a comparison between the TM and the SSM in brain tumours hasn't been carried out. In this work, we presented the results of the application of TM and SSM to primary glioma. The analysis of the CWM showed a high variability for the K_{trans} (TM: coefficient of variation (CV) 108%; SSM: CV 122%) while τ_i CV was low at 5% (Fig.2). Comparing tumour and CWM, both models were found to statistically discriminate between the two ($p<0.05$), however the TM-K_{trans} showed some overlapping values (Fig. 3). ROC analysis confirmed the higher performance of the SSM with an AUC=0.987 for K_{trans} and an AUC=0.939 for τ_i.

Conclusion

DCE-MRI methods hold great promise for quantitative in vivo evaluation of vascular properties under many different pathophysiological conditions. In our study, the higher performance of the SSM and the lower variability of its τ_i in the description of the CWM showed a more robust characterization of the lesion and we hypothesize that τ_i may reflect pathophysiology relevant to tumour. Furthermore, the lower variance of the SSM-K_{trans} may improve performance and tumour characterisation with less overlap in intra-tumoural values. Future studies will need to assess the textural features of the TM and SSM parameters in heterogeneous regions of the tumour.

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Figures

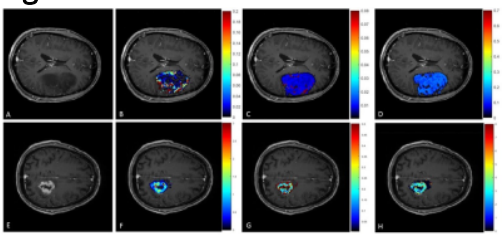

Figure 1: Parametric maps of K_{trans} and τ_i obtained with TM and SSM on VOIs of a non-enhancing tumour (WHO grade II, first row) and enhancing tumour (WHO grade IV, second row). A, E) post contrast sequence; B, F) TM K_{trans} ; C, G) SSM K_{trans}; D, H) τ_i.

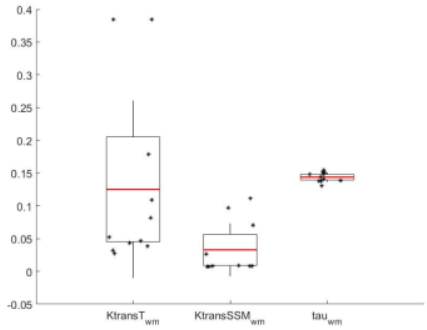

Figure 2: Boxplot of K_{trans} (TM and SSM) and τ_i in the contralateral white matter in 11 patients. A low variability is seen in the value of τ_i in CWM. The value of K_{trans} (SSM) was lower than that for K_{trans} (TM) and showed a lower range of values as compared to K_{trans} (TM).

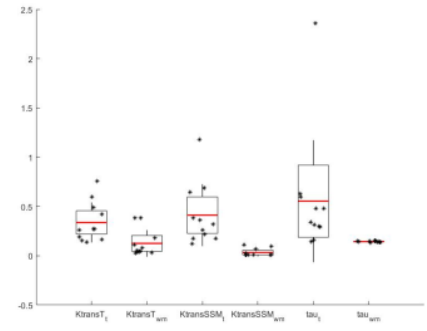

Figure 3: Boxplot of K_{trans} (TM and SSM) and τ_i in the tumour and CWM. The value of each parameter was higher in tumour than in CWM with the SSM parameters showing less overlap between tumour and CWM. The wide range of values in the lesion is indicative of the heterogeneity that exists in the tumours.

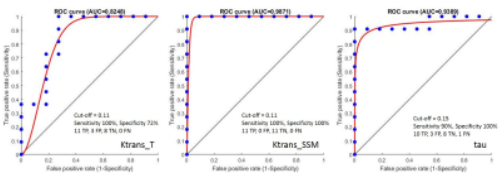

Figure 4: ROC analysis of TM and SSM K_{trans} and τ_i. TM K_{trans} resulted with an AUC of 0.8248 with a cut-off value of 0.11 (100% sensitivity, 72% specificity); SSM K_{trans} resulted with the same cut-off value but higher performance (100% sensitivity, 100% specificity, AUC = 0.9871). SSM τ_i resulted with an AUC of 0.9389 and a cut-off value of 0.15 (90% sensitivity, 100% specificity).

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