Survival Rate Prediction in Patients with Glioblastoma Multiforme, Using Dynamic Contrast Enhanced MRI and Nested Model Selection Technique

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Target Audience: Neuroradiologists, neurologists, and medical physicists who are interested in pharmacokinetic modeling and brain tumor studies.

Purpose: Dynamic Contrast Enhanced-Magnetic Resonance Imaging (DCE-MRI) is being widely used in research and the clinic for grading cancerous tumors of patients[1,2]. Glioblastoma Multiforme (GBM) is one of the most common and malignant brain tumor types[3]. The survival time of patients with GBM is up to15 months with best treatment, including temozolomide[3]. Prediction of survival can play an important role in treatment planning. Several studies have explored the diagnostic accuracy of different MRI-derived parameters with respect to glioma grading and survival[4-6]. In this study, using a pharmacokinetic nested model-Selection (NMS) technique[2] four different models (0, 1, 2 and 3) were constructed for estimating the following physiological parameters respectively: plasma volume (v_p), v_p and forward vascular transfer constant (K^{trans}), v_p, K^{trans} , reverse vascular transfer constant (K_{ep}) and extra-cellular extra vascular volume fraction ($v_e = K^{trans}/K_{ep}$)[2,7]. This pilot study investigates the predictive power of different permeability parameters estimated by the NMS technique[2] for survival of patients with GBM.

Methods: 20 treatment-naïve GBM patients were studied. A Variable-Flip-Angle(3D-Spoiled-Gradient Echo, flip angles: 2, 5, 10, 15, 20, and 25) pulse sequence was used for T_1 mapping using the Driven Equilibrium Single Pulse Observation of T1 (DESPOT1) method; this was followed by a DCE-T1 (3D-SPGRE, flip angle: 30 degree, TR/TE: 5.8/0.84ms, matrix size: 256×256, 5.31 sec temporal time, 16 slices, Magnevist: 0.1mol/kg,4ml/sec) experiment using a 3Tesla scanner (Signa Excite, GE healthcare). The time trace of the CA concentration (ΔR1) was calculated from pre-injection T_1 maps and dynamic data[2]. Arterial input functions (AIFs) were picked by a trained Neuroradiologist. NMS was used to estimate the physiological parameters (v_p, K^{trans} and K_{ep}) of Models 0, 1, 2 and 3. A Cox proportional-hazards regression (CPHR) model[8](P-value < 0.05, Confidence Level=%95) was used to analyze the survival time of the patients. All the estimated parameters for each model from different slices in each patient were averaged and used as independent features as for CPHR analysis[4].

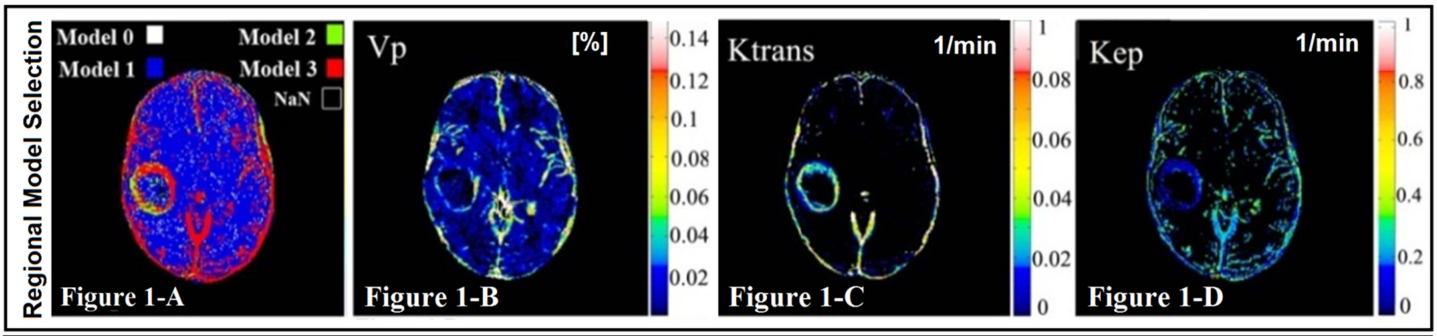
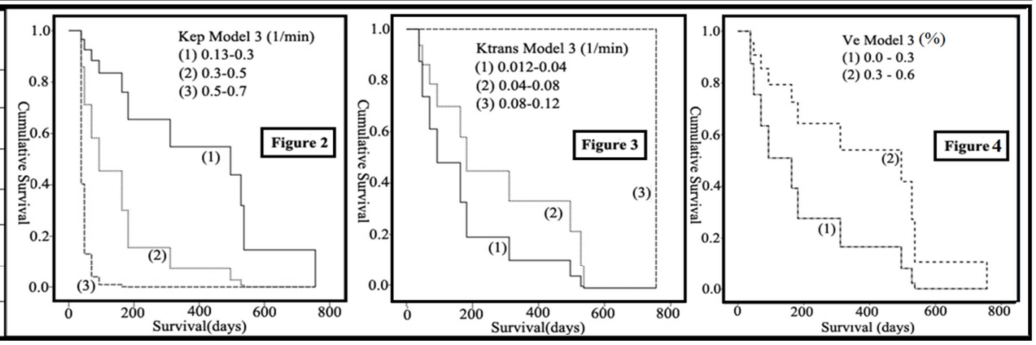


Table 1		
Model parameters	P-value	Wald test value
K^{trans} model 3	0.020	5.4
K_{ep} model 3	0.027	4.8
v_p model 3	0.269	1.2
K^{trans} model 2	0.118	2.4
v_p model 2	0.090	2.8
v_p model 1	0.175	1.8
ve model 3	0.025	5



Results: Figure 1-A illustrates the model choice map generated by the NMS technique[2] for one of the patients. Model 1 (blue color) which is predominated in this figure represents non-leaky or normal brain tissue while green and red colors represent the model 2 and 3 regions respectively. As shown in these figures, the rim-like lesion includes models 2 and 3 in which the model 2 regions are surrounded by the model 3 regions (the only region that K_{ep}, the transfer constant for CA concentration back-flux is measureable). Figures1-B,1-C and 1-D illustrate estimated maps of v_p, K^{trans} and K_{ep} respectively. The CPHR analysis for each individual parameter estimated by the NMS technique demonstrates the significance of each physiological parameter in the prediction of the overall survival time. Table 1 demonstrates the p-values and Wald test values estimated by CPHR analysis for all models' parameters. Figures 2, 3 and 4 demonstrate CPHR survival curves for different levels of K_{ep}, K^{trans} and v_e respectively. Figure 2 clearly shows an inverse relationship between K_{ep} and survival, while Figures 3 and 4 show a clear direct relationship between K^{trans} and v_e with survival (i.e., patients with higher values of $K^{trans}$and v_e showed improved survival).

Discussion and conclusion: According to the Wald test values (Table 1), the 2 transfer constants (K^{trans} and K_{ep}) and v_e in model 3 regions are the best predictors of survival time among the other parameters. In conclusion, using NM selection, this pilot study suggests a possible association between K^{trans},K_{ep}, v_e and survival in GBM patients that may be of considerable clinical importance. In addition, this study attests that DCE-MR data analysis using NMS technique provides useful information that can be used in treatment planning and studying cancerous tumors.

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