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Original contribution

Comparison of actual with default hematocrit value in dynamic contrast enhanced MR perfusion quantification in grading of human glioma

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ABSTRACT

Purpose: Dynamic contrast enhanced (DCE) MRI is used to grade and to monitor the progression of glioma while on treatment. Usually, a fixed hematocrit (Hct) value for adults is assumed to be ~45%; however, it is actually known for individual variations. Purpose of this study was to investigate the effect of measured Hct values in glioma grading using DCE-MRI.

Materials and methods: Fifty glioma patients were included in this study. Kinetic and hemodynamic parameters were estimated for each patient using assumed as well as measured Hct values. To look the changes in Hct value over time, Hct was measured multiple times from 10 of these glioma patients who were on treatment. Simulation was done to look for the effect of extreme variations of Hct values on perfusion metrics. The data was compared to look for significant differences in the perfusion metrics derived from assumed and measured Hct values.

Results: The measured Hct value in patients was found to be (40.4 ± 4.28)%. The sensitivity and specificity of DCE-MRI parameters in glioma grading were not significantly influenced by using measured vis-a-vis assumed Hct values. The serial Hct values from 10 patients who were on treatment showed a fluctuation of 15–20% over time. The simulated data showed linear influence of Hct values on kinetic parameters. The tumor grading was altered on altering the Hct values in borderline cases.

Conclusion: Hct values influence the hemodynamic and kinetic metrics linearly and may affect glioma grading. However, perfusion metrics values might change significantly with large change in Hct values, especially in patients who are on chemotherapy necessitating its use in the DCE model.

1. Introduction

Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) is being increasingly used in glioma grading and monitoring the response to treatment. Several authors have demonstrated excellent correlations between glioma grade and DCE-derived perfusion parameters [1–3]. In practice, first pass analysis and tracer kinetic models are fitted to DCE-MRI derived concentration time curve to quantify hemodynamic and kinetic parameters [4–6]. First pass analysis gives the estimation of cerebral blood volume (*CBV*) and cerebral blood flow (*CBF*) that relates to tumor angiogenesis. Pharmacokinetic analysis facilitates the quantification of parameters like fractional plasma volume V_p, fractional extracellular extravascular space (EES) volume (V_e), volume transfer constant between plasma and EES (K^{trans}) and leakage rate from plasma to EES (λ^{tr}), related to blood brain barrier (BBB) disruption [4]. In DCE-MRI, the reliability of the model depends on many factors such as absolute pre-contrast absolute T_1 estimation (T_{10}), arterial input function (AIF), post-processing models (e.g., Patlak model, Toft Model, Leaky Tracer Kinetic Model etc.), fitting algorithms and also on blood hematocrit (Hct) values that may alter or influence the calculation of DCE parameters [7–9].

Over the years, a lot of developments have been made to improve the T_{10} quantification, kinetic modeling, and AIF estimation as the reproducibility and accuracy of kinetic parameters estimates are

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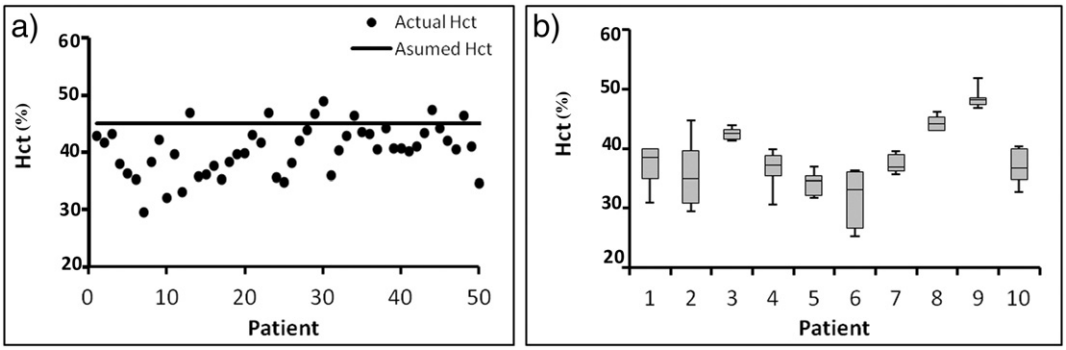


Fig. 1. Scatter plot shows the measured pre-treatment hematocrit (Hct) value of 50 patients (a), box plot shows the fluctuation in blood Hct value of 10 patients during the time interval of treatment (b).

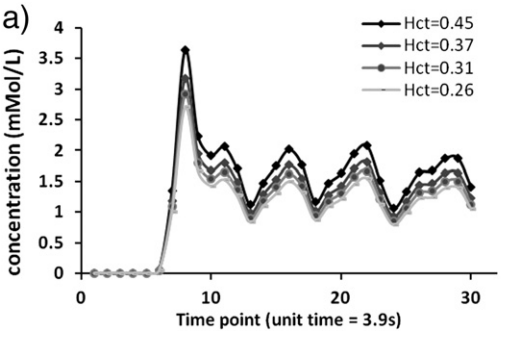
closely linked to these factors [7,10,11]. On the other hand, in general, the influence of Hct on AIF has been overlooked by considering it as a scaling factor of AIF in various DCE models. However, correction of the measured signal for blood Hct level is important to derive reliable estimation of the perfusion parameters since MRI contrast agents only occupy the blood plasma space and concentration of contrast measured at a voxel is the concentration in blood plasma (C_p) rather than the whole blood (C_b). Moreover, Hct relates to the measured C_b and C_p via the relationship $C_p = C_b/(1 - Hct)$ and thereby influencing the AIF [12,13]. Hct is mainly responsible for the viscosity of blood, and it has inverse relationship with the blood flow [14]. A change in Hct values can not only significantly affect *CBF* estimation [15,16], but also can affect K^{trans} estimations as it measures the result of combined effect of blood flow and permeability surface area product [17]. Furthermore, relaxation time T_1 for blood is strongly dependent on Hct [18]. Blood T_1 can influence the arterial input function (AIF) which is an important input for DCE-MRI parameters quantification [19] and the dependence of the accuracy of perfusion parameters on the errors in the AIF has previously been investigated [8]. In general, a fixed value of Hct in large vessels for adult human population is assumed to be 45% for DCE-MRI quantification [20]; however, the Hct values not only vary from patient to patient, Hct level may alter significantly during the treatment of cancer patients on chemotherapy [21]. Although it is quite evident that Hct has the potential to affect DCE-MRI based perfusion quantification, it has not been studied the influence of Hct on glioma grading and also the cutoff values of DCE parameters in a certain patient population with variable hematocrit values.

This study was designed to quantify the effect of measured Hct values in glioma grading in clinical practice using DCE-MRI model parameters and to compare it with assumed values used routinely in the model. To the best of our knowledge, this is the first such study in human gliomas.

2. Materials and methods

2.1. Patient selection

The study included a total of 50 treatment naïve patients with histologically confirmed glioma. MR examination of 50 patients (16 female and 34 male, aged 27–77 years old, mean age 48.92 ± 11.81 years old) included 38 patients with high grade glioma (33 glioblastoma, 3 anaplastic astrocytoma, 1 anaplastic oligodendroglioma, 1 anaplastic oligoastrocytoma) and 12 patients with low grade gliomas (7 astrocytomas, 1 oligodendroglioma, 4 oligoastrocytomas) classified on the basis of WHO classification were reviewed. All patients underwent conventional MRI and DCE-MRI. All these patients had imaging and routine hematological tests as a part of the pre-surgical requirement including the measured Hct values. It has been already reported that the Hct from venous system, arterial system and fingertips shows no significant difference [22], hence only the large vessel Hct level values were used in this study. Surgery was performed within 48 h of imaging. None of these patients had any obvious history of blood loss between imaging and surgery. We also measured hematocrit value multiple times in 10 of these patients who were undergoing chemotherapy post-surgery on the subsequent dates to understand how the Hct is influenced with treatment in the follow-up studies; however the DCE-MRI was not available for all follow-up studies. Written consent from each patient was obtained before MRI study. This retrospective study was approved by the institutional review board.



b)

	Hct	K^{trans}	K_{ep}	Vp	λ^{tr}
Default	0.45	0.169	3.814	0.042	0.070
1st study	0.37	0.194	3.834	0.048	0.080
After 20 Weeks	0.31	0.212	3.828	0.052	0.088
After 21 Weeks	0.26	0.227	3.825	0.056	0.094
After 25 Weeks	0.36	0.196	3.791	0.049	0.081

Fig. 2. Shows the effect of blood Hct value fluctuation on AIF (a) and kinetic parameter estimations (b) in a 59-year-old female patient with glioblastoma multiform. Here AIF and $C(t)$ of the first study were taken only the Hct value of subsequent study was used to quantify the kinetic parameters. 1st study was pre-surgical scan, after 20 week the patient got a surgery and radiation and chemo was started. When the patient was on chemo the Hct value drooped from 37% to 26% on 21st week. When the chemotherapy was stopped, the Hct reached to 37% at 25th week.