Understanding the Mechanism of Contrast Enhancement in Brain Tumors and Infections Through Dynamic Contrast Enhanced MRI

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Target Audience : Neuro surgeons, Radiologist, MR physicist, Neuro scientist

Purpose: Contrast enhancement (CE) has long been the de facto marker of intra-axial lesions (IALs) in a radiologist's armory; however, sometime it becomes challenging to differentiate common infections, e.g., Neurocysticerosis (NCC) from tumors such as gliomas by only evaluating contrast enhanced images. Although the mechanisms of contrast enhancement have not been yet entirely understood, it is commonly believed that the contrast enhancement in the brain lesion represents the lesion's vasculature and/or blood-brain barrier (BBB) breakdown[1]. Moreover, quantitative evaluation of the contributions from each of the above mentioned fractions in a particular lesion has also not been explored. On the other hand, dynamic contrast enhanced MRI (DCE) provides quantitative information of various pharmacokinetic parameters, and thus it may help to define the contribution of each fraction responsible for contrast enhancement in the lesion. The aim of this study is to explore and quantify the contributions of each pharmacokinetic parameter responsible for contrast enhancement of IALs. In addition, we sought to investigate differences in these CE contributing parameters in infections and tumors.

Materials and Methods: We have retrospectively analyzed 31 enhancing IALs (eIAL) patient data in accordance with the institutional ethical committee approval where 22 patients had histologically proven gliomas (16 high grade gliomas and 6 low grade gliomas) and 9 patients were diagnosed with NCC on the basis of scolex demonstration on susceptibility-weighted imaging (SWI) and balanced turbo spin echo (bTFE) images. DCE-MRI has already been performed for these patients using a three dimensional Fast Field Echo (FFE) sequence [TR/TE/flip angle/slice thickness/FOV/matrix size=5.0ms/1.4ms/10°/6mm/240×240mm/128×128mm] and at the fourth acquisition, Gd-BPOT was administered intravenously in the dose of 0.1 mmol/kg body weight through a power injector at 3 ml/sec, followed by 30ml saline flush. During retrospective data analysis, we extracted the concentration time curve $C(t)$ from the dynamic images. Kinetic parameters were estimated by fitting the recently developed leaky tracer kinetic model (LTKM)[2] for DCE MRI to $C(t)$ where $C(t) = C_{ps}(t) + C_{prs}(t) + C_{ls}(t)$ and C_{ps} , C_{prs} , C_{ls} are the concentration of contrast agent in plasma space, permeable space and leakage space per unit volume of tissue, respectively. Next, the relative plasma volume $\left(rPV = \left(\int C_{ps}(t)dt / \int C(t)dt \right) \times 100 \right)$ and relative EES volume$\left(rEV = \left(\int \left(C_{prs}(t) + C_{ls}(t) \right) dt / \int C(t)dt \right) \times 100 \right.$ were quantified. It is evident that $C(t)$ is a combination of three phases -- base line phase where no contrast is in the system, early post-contrast phase and late post contrast phase. In our analysis, the gradient of the late post contrast phase (slope2) was used for the segmentation of the enhancing lesions[3].

Region of interest (ROIs) in post-contrast images were drawn covering the area of pathological enhancement. All the voxels inside the ROI and with positive slope2 were selected for our analysis and the analyzed data was expressed as mean ± standard deviation (SD). The intergroup and intragroup difference between respective perfusion indices between tumor and NCC was analyzed using Student's independent sample T-test and paired T-test respectively in SPSS v.16. In all analyses we considered a P-value of 0.05 (two-sided) as being statistically significant.

Results: Intra-group comparison revealed significantly higher rPV than rEV in gliomas (40.16±10.87 vs. 59.83±10.88), and significantly higher rEV than rPV in NCC (75.06±11.13 vs. 24.94±11.13) (Figure 2a, b). Inter-group comparison demonstrated significantly higher rPV in gliomas than NCC (40.16±10.87 vs. 24.94±11.13) and higher rEV in NCC than tumors (75.06±8.13 vs.59.83±10.88) (Figure 2c, d). Figure-1 of similar appearing high-grade glioma (a) and NCC (d) on post-contrast T1WI shows similar contribution of plasma (b) and EES (c) fractions in tumor and visibly higher contribution of EES (f) than plasma (e) in NCC.

Discussion and Conclusion: To our knowledge, no literature evaluates the contribution of permeability and leakage to the total contrast enhancement. Our findings from analyzing the contribution of plasma and EES through pharmacokinetic parameters in the context of contrast enhancement are in conformance with the known literatures that demonstrate breakdown of BBB in both NCC and gliomas [4,5]. Moreover, our results compare favorably with known literature that shows significantly higher leakage in intracranial infection compared to neoplastic lesion[1] .and higher blood volume values in neoplastic lesions than infectious lesions[6]. Our analysis of DEC data sets confirms that both EES and plasma add up to the total contrast enhancement in tumor while contribution of EES fraction is significantly higher than plasma fraction in NCC.

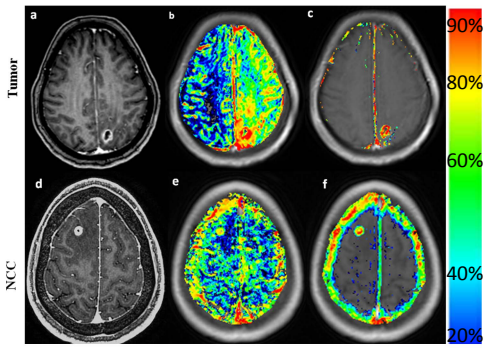

Figure 1: *a,b,c are the T_1 post-contrast 3D-T1, plasma volume map , leakage map of tumor (high grade glioma), respectively and d,e,f are the same images for NCC.*

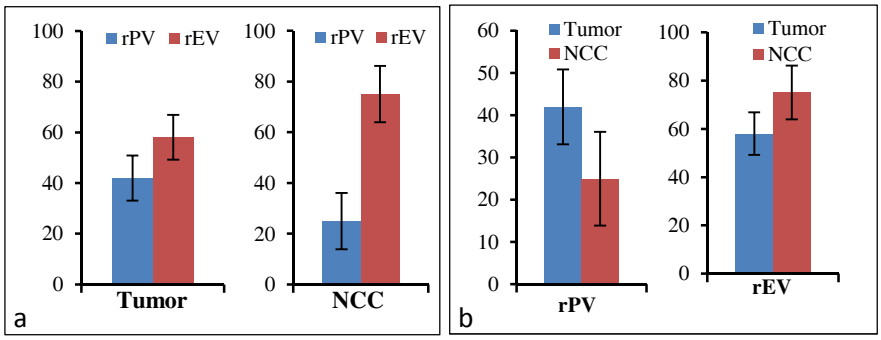

Figure 2: *(a) NCC and glioma separately demonstrate significantly higher relative contribution of leakage (rEV) to CE compared to the lesion vascularity (rPV). (b) Compared to gliomas, NCCs demonstrate higher relative contribution of BBB breakdown. Compared to NCC, gliomas demonstrate higher relative contribution of angiogenesis.*

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