Utility of Non-model based 'Semi-quantitative' Indices derived from Dynamic Contrast Enhanced T1-weighted MR Perfusion in Differentiating Treatment Induced Necrosis from Recurrent Progressive Brain Tumor.

J. Narang[1], R. Jain[1,2], S. A. Arbab[3], and A. Babajani-Feremi[3]
[1]Neuroradiology, Henry Ford Health System, Detroit, MI, United States, [2]Neurosurgery, Henry Ford Health System, Detroit, MI, United States, [3]Radiology, Henry Ford Health System, Detroit, MI, United States

Purpose: To assess the utility of non-model based 'semi-quantitative' indices derived from dynamic contrast-enhanced T1-weighted magnetic resonance perfusion (DCET1MRP) in differentiating treatment induced necrosis (TIN) from recurrent/progressive tumor (RPT).

Background/Introduction: Dynamic contrast-enhanced T1-weighted magnetic resonance perfusion (DCET1MRP) is being increasingly used in various clinical trials involving brain tumors. It allows characterization of the vascular microenvironment in tumors by measurement of a range of parameters, such as K_{trans}, K_b , V_e, and V_P (1) that reflect specific physiologic characteristics and relate to various aspects of tumor biology. However, the biggest hurdle in obtaining these pharmacokinetic quantitative metrics is the use of complicated multi-compartment physiological models to derive these metrics. On the contrary, various non-model based 'semi-quantitative' indices derived from DCET1MRP, which don't have much physiologic specificity, but have been successfully used in the past in evaluation of prostate, breast, cervical, and pancreatic cancers (2-4). However, these 'semi-quantitative' indices have not been used much in the evaluation of brain tumors. In a treated brain tumor patient with a recurrent or progressive enhancing lesion, it is imperative to differentiate RPT from TIN as the prognosis and treatment for both these entities differs significantly. Both entities often manifest as an enlarging mass lesion with varying degrees of surrounding edema and progressive enhancement on serial MR images which is usually very difficult to differentiate based on conventional morphologic imaging alone (5). This is further complicated by the fact that most of these recurrent or progressive enhancing lesions are mixtures of variable degrees of tumor and treatment effects and rarely have either pure tumor or necrosis. Various metabolic (MR spectroscopy, PET) and physiologic (DWI, diffusion tensor imaging and perfusion imaging) imaging techniques have been used in the past with variable success (6). However, most of the clinically available imaging tools suffer from some limitation not just due to the limited resolution but also due to the complexity of the tissue microenvironment. We in this study propose the use of these non-model based indices in differentiating these two enteties.

Materials and Methods: 23 patients with previously treated brain tumors who showed recurrent or progressive enhancing lesions on follow-up magnetic resonance imaging and also underwent DCET1MRP were included in the study. Another 8 patients with treatment-naïve, high-grade gliomas who underwent DCET1MRP were included as controls in the study. Semi-quantitative indices were derived from DCET1MRP enhancement curves which included maximum slope of enhancement in the initial vascular phase (MSIVP), normalized maximum slope of enhancement in the initial vascular phase (nMSIVP), normalized slope of the delayed equilibrium phase (nSDEP), initial area under the normalized time-intensity curve (nIAUC) at 60 and 120 secs ($nIAUC_{60}$ and $nIAUC_{120}$). These indices were calculated using in house MATLAB-based software as described in Fig1.

Results: 15 patients were diagnosed with RPT, and 8 patients had TIN. There was a statistically significant difference between the two groups (p value < 0.01), with the RPT group showing higher mean MSIVP (16.20 versus 7.88), mean nMSIVP (0.0468 versus 0.028), mean $nIAUC_{60}$ (33.42 versus 25.35) and mean $nIAUC_{120}$ (80.38 versus 65.25) compared with the TIN group. nSDEP was significantly lower in the RPT group (7.45 $\times 10^{-5}$ versus 15.1 $\times 10^{-5}$) compared with the TIN group. Plots of mean and SD of these indices in RPT, TIN and controls is shown in Fig 2. Receiver operating characteristic (ROC) curve analysis showed nMSIVP to be the best single predictor of RPT with very high (100%) sensitivity and high (75%) specificity using a cut point of 0.031 and nSDEP as the most specific predictor of TIN with a very high specificity (100%) and sensitivity (87%) using a cut point of 11.89. Representative examples of RPT and TIN are shown in Fig 3and Fig 4.

Conclusions: Practical impact of DCET1MRP on routine neuro-oncologic imaging practice is restricted by the need of complicated multi-compartment physiological models and intensive computational requirements to derive pharmacokinetic metrics and the lack of an easy to use and yet robust commercially available software. We propose the use of these non-model based 'semi-quantitative' indices derived from DCET1MRP in differentiating RPT from TIN which are relatively easy to derive, robust, reproducible and do not require a complicated model- based approach for calculation. These indices even though don't have a specific physiologic basis, may still serve the purpose of a robust and easy to use clinical tool / noninvasive imaging biomarkers in day to day clinical practice which can help in quick and efficient decision making.

References:

[1] O'Connor JP et al. Br J Cancer. 2007 Jan 29;96(2):189-95.
[2] Alonzi R et al. Eur J Radiol. 2007 Sep;63(3):335-50.
[3] Kuhl CK et al. Radiology. 1999 Apr; 211(1):101-10.
[4] Zahra MA et al. Int J Radiat Oncol Biol Phys. 2009 Jul 1;74(3):766-73.
[5] Kumar AJ et al. Radiology 217:377–384, 2000.
[6] Jain R et al. J Neurooncol. 2010 Oct;100(1):17-29.

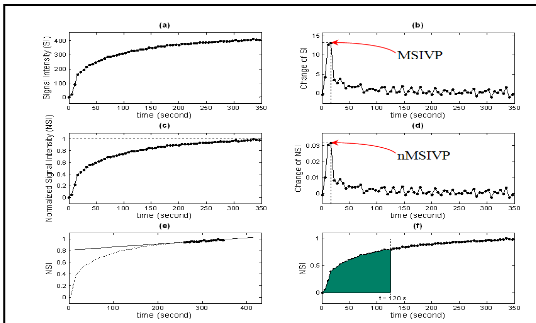

Figure 1: Calculation of various non-model based indices obtained from the signal intensity (SI)-time curve. (a) Representative SI-time curve of a tumor ROI. (b) Change of the SI per unit time that the maximum value in this figure represents MSIVP. (c) Normalized (to peak) SI. (d) Change of the normalized SI per unit time that the maximum value in this figure represents nMSIVP. (e) Slope of the fitted linear curve to the final 25% samples of the normalized SI represents nSDEP. (f) The area under the normalized curve within the time limits 0-120 represents $nIAUC_{120}$.

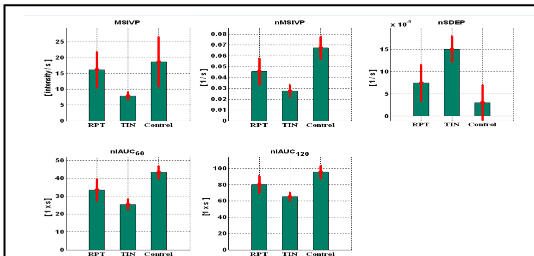

Figure 2: Plot of mean and standard deviation showing various non-model based 'semi-quantitative' indices derived from DCEMRP in TIN, RPT and control groups.

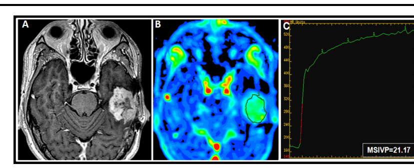

Figure 3: A 40 years old male with a recurrent enhancing lesion in the right temporal region (A). MSIVP parametric map B) and graph of MSIVP C) showed high MSIVP suggesting RPT, proven on histopathology.

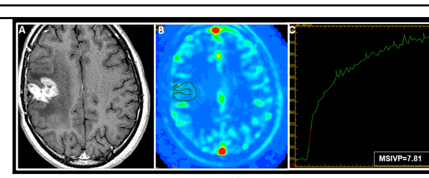

Figure 4. A 19 years old female with a recurrent enhancing lesion in left parietal region. (A). MSIVP parametric map B) and graph of MSIVP C) showed low MSIVP suggesting TIN, proven on histopathology.