DSC-MRI PERFUSION IN HIGH GRADE CEREBRAL TUMORS: SOLUTION OF LEAKAGE EFFECTS IN A SIMPLE CLINICAL IMAGE PROCESSING PROTOCOL.

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BACKGROUND: Dynamic-Susceptibility-Contrast (DSC) Magnetic Resonance Imaging (MRI) represents the widespread approach in neuroradiology for perfusion weighted imaging (PWI) of cerebral tumors. First-pass bolus tracking analysis, with an appropriate kinetic model, provides information on cerebral hemodynamic through the evaluation of quantitative maps of cerebral blood flow (CBF), volume (CBV) and mean transit time (MTT). The use of such maps, as indicators of tumor aggressiveness, contrasts with the limits of the underlying cerebrovascular model which requires as an assumption that the tracer remains completely intravascular during its passage. Blood-Brain-Barrier (BBB) breakdown, often associated to high grade cerebral tumors, reduces the reliability of the traditional DSC parameters in the voxels occupied by the injury, making an accurate delineation of tumor boundaries difficult on perfusion images. The purpose of this methodological study is to evaluate the feasibility of a modified voxel-wise quantitative analysis of perfusion signals to improve the accuracy of the classification of brain tissue in the presence of BBB disruption.

MATERIALS AND METHODS: MR imaging was performed on 30 consecutive untreated patients affected by glioma: 7 females and 23 males ranging in age from 23 to 80 years (mean age 58.2 ± 15.3 ys). Of these, 15 patients were affected by a grade VI glioma and 3 patients by a grade III glioma. For 13 of the grade IV patients and 2 of the grade III patients histopathologic analysis of the resected tissue confirmed the diagnosis and grading of the tumor. 12 patients were diagnosed with a grade II glioma by means of MRI and clinical follow-up and were included in the study. All patients provided signed informed consent. The MRI scanning protocol included a DWI EPI-SE, a FLAIR, a T1-weighted SE, a T1-weighted 3D FFE and DSC imaging acquired using a T_2^*-PWI 3D PRESTO sequence (PRinciples of Echo Shifting with a Train of Observations). All scans were acquired axially. A voxel-wise analysis of the perfusion T_2^* relaxivity curves, adopting a higher number of parameters than standard, was performed with the purpose of increasing the sensitivity to cerebral hemodynamic alterations, particularly in regions where BBB injury occurs. Estimated parameters included, together with the conventional CBF, CBV, MTT and TTP, signal peak height (Cmax = max(C(t)), where C(t) is the local tissue concentration of the contrast material), peak position (Tmax = time-at(max(C(t))), Full Width at Half Maximum (FWHM) and Maximum Slope of C(t) (MS = max(dC(t)/dt)), as well as the Wash-in Time (defined as the time interval between the exam start time, t0, and the bolus arrival time, t_washin, WiT = t_washin – t0), the Wash-out Time (defined as the time interval between t0 and the time at which the bolus passage ends, t_washout, WoT = t_washout – t0), the T_2^* Negative Integral (calculated as $T_2^*NI = \int_0^T S(t)dt$, where S(t) is the PWI signal intensity) and the T_2^* velocity (T_2^*Vel = min(S(t))/S0). In addition, the perfusion MR dataset was prepared including several pre-processing steps, such as single-value decomposition (SVD) filtering and image oversampling, to assess the effects of a more sophisticated pre-analysis on the sensitivity of PWI to pathology.

RESULTS: Considerable heterogeneity was observed in the shape of the dynamic concentration time curves for every tumor grading group. In agreement with the literature,[1-3] CBV and CBF ratios were observed to increase significantly in relation to the tumor grading score. CBV ratios showed a mean value which gradually and consistently increased from (131.82 ± 128.64)% for grade II to (614.10 ± 234.84)% for grade IV gliomas. Similarly CBF ratios increased from (121.70 ± 111.16)% for grade II to (589.11 ± 322.07)% for grade IV gliomas. The ANOVA test showed that the CBV ratio and CBF ratio significantly discriminate between low grade (LG) and high grade (HG) gliomas with $p < 0.001$, for data pre-processed with both the image oversampling and the SVD filtering algorithms. With the exception of WoT, FWHM and Tmax, all the non-conventional parameters calculated (WiT, Cmax, T_2^*NI, T_2^*Vel and MS) were able to differentiate among LG and HG groups with $p < 0.001$. In order to identify the correct sequence of processing steps to maximize the sensitivity and specificity of the perfusion maps, DSC-MRI dataset treated with four different processing schemes, of increasing complexity, were considered: 1) data without any processing; 2) perfusion volumes realignment; 3) perfusion volumes realignment and SVD filtering; 4) all of the former with a prior image oversampling. For each processing scheme conventional and non-conventional perfusion parameters were evaluated. Correlations with tumor grading were studied using Kendall's tau test for each generated dataset. Conventional perfusion maps, CBV and CBF ratios, were found to correlate significantly with the tumor grading ($p < 0.001$) for all of the four processing schemes. For both CBV and CBF ratios, the correlation coefficients were found to increase consistently from $r = 0.543$ ($p < 0.001$) and $r = 0.591$ ($p < 0.001$), respectively using perfusion data without any processing, to $r = 0.626$ ($p < 0.001$) and $r = 0.632$ ($p < 0.001$), respectively for the most sophisticated pre-processing scheme. A similar behavior was found for non-conventional parameters, Cmax, T_2^*NI, T_2^*Vel and MS ratios, which significantly correlated with tumor grading with $p < 0.001$ independently of the processing scheme considered. The TiW ratio correlated with the tumor grading with an increasing significance from $r = -0.472$ ($p = 0.0015$), using no pre-processing, to $r = -0.579$ ($p < 0.001$), using the most sophisticated pre-processing scheme. Similarly the Tmax ratio was found to correlate with tumor grading with increasing significance from $r = -0.387$ ($p = 0.01$), for unprocessed data, to $r = -0.495$ ($p < 0.001$), for the last dataset. The WoT ratio, in particular, displayed no correlation with tumor grading in the absence of any pre-processing, but with an increased level of sophistication of the pre-processing steps, the WoT data are found to correlate significantly with the tumor grading ($r = -0.365$ and $p = 0.014$). In conclusion, for each parameter which displayed a significant correlation with tumor grading, the correlation coefficient dropped slightly when the image oversampling step was included in the processing scheme.

CONCLUSIONS: Preliminary results demonstrate that the implementation of the multi-parametric approach for the perfusion time series analysis better characterizes cerebral tissues where leakage occurs, increasing both differences among different tumor grades and the correlation with the grading itself. The reported results also stress the relevance of an accurate pre-processing of the data to improve the correlation of PWI maps with tumor grading in glioma patients.

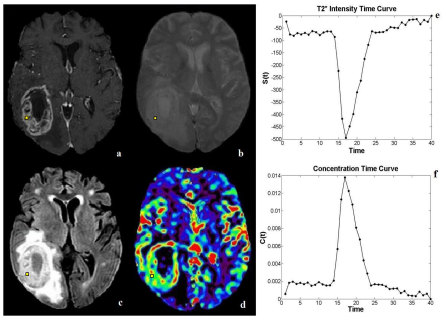

Figure 1: T1-weighted 3D GRE post-GAD injection, DP-SE, FLAIR, CBF map and corresponding Time intensity and concentration curves for a sample ROI on the GAD-enhancing lesion.

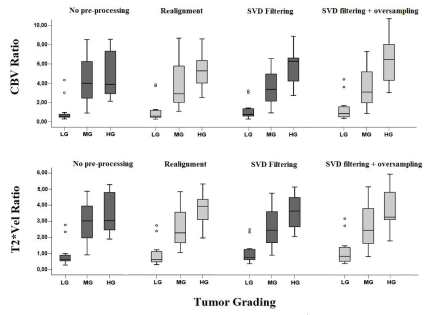

Figure 2: Box plots for the CBV and the T_2^*Vel measured values for the different tumor grades and dependence on the pre-processing approach.

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