ET-07. DOES OSMOTIC BLOOD-BRAIN BARRIER DISRUPTION ALLOWS EFFLUX PUMP SUBSTRATES DELIVERY TO THE TUMOR AND CNS?
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Despite decades of research, the median survival of glioblastoma (GBM) patients remains 14.6 months. The presence of the blood-brain barrier (BBB) limits CNS antineoplastic drugs delivery. Many BBB characteristics are involved in the drug delivery limitation, amongst them the efflux pumps. Different delivery strategies, such as the osmotic blood-brain barrier disruption (BBBD) have been developed and used with success in GBM patients. In order to enhance BBBD efficacy, more information is needed about its dynamic process. The aim of this study was to determine if the BBBD procedure can enable the delivery of efflux pump substrates to brain parenchyma and glioma cells. Thirty-two F98-Fischer rats were randomly assigned to 6 groups: 1: control; 2: tariquidar (P-glycoprotein [PGP] inhibitor); 3: BBBD in tumor ipsilateral hemisphere; 4: tariquidar vehicle (n = 3); 5: BBBD negative control (n = 3); and 6: BBBD + tariquidar. An MRI scan was performed to allow PET-MRI images coregistration. A 1-h dynamic PET acquisition was obtained and, with $^{11}$C-Carvedilol (a PGP substrate) administered iv during the first minute of the scan. Four volumes of interest (VOI) were studied: tumor volume, distal volume to the tumor in the ipsilateral parenchyma and equivalent control VOIs in the contralateral hemisphere. $^{11}$C-Carvedilol uptake ratios of corresponding ipsilateral and contralateral VOIs were computed for every animal. $^{11}$C-Carvedilol uptake in tumors was significantly higher on average in tariquidar and BBBD + tariquidar groups compared to the control groups. When comparing $^{11}$C-Carvedilol uptake in parenchyma, there was no significant difference between the groups at study. However, only two out of six animals in the BBBD + tariquidar group did show higher $^{11}$C-Carvedilol uptake, indicating that the BBBD must be excellent for effective substrate delivery to CNS. These results demonstrate that the BBBD procedure does not allow significant delivery of efflux pump substrates to the CNS, unless excellent BBBD procedure is achieved.