Advanced Vessel- and Cell-Size MRI to Assess Chemo-Radiation Treatment Response in Pediatric Ependymoma Models

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Purpose: Ependymoma (EPN) is an aggressive pediatric brain tumor that contributes significantly to poor overall outcomes in children. The purpose of this study is to develop and optimize an advanced MRI protocol to characterize the phenotype and chemo-radiation treatment (CRT) response in an orthotopic mouse of patient-derived xenografts (PDX) of pediatric EPN.

Methods: Severely immune deficient (SCID) female mice inoculated with EPN tumors (n=22). In the chemo-radiation treatment (CRT) group (n=6), mice were treated with 10 Gy radiation plus 30 mg/kg 5-fluorouracil. For each MRI session, the animal was inserted into a Bruker 9.4 Tesla BioSpec MRI scanner with a Bruker mouse head array RF cryo-coil. The MRI images were analyzed for tumor volume, tumor necrosis (apparent diffusion coefficient (ADC)), edema, and degrees of inflammation using ParaVision NEO software and in house MATLAB simulations. This protocol was performed before CRT, immediately after CRT, and two weeks after CRT.

Results: The median tumor volumes at baseline was 21±12 mm^3. These tumors also revealed increased blood vessel densities, high SSIFT iAUC indicative for EPN cell size of 14±3 microns, and low ADC values in EPN as compared to the normal cerebellum. The 5-day CRT resulted in a significant decrease in the tumor volumes, accompanied by the increased ADC values and decreased SSIFT iAUC and cell size two weeks after CRT. Interestingly, the most immediate response, seen as soon as 2 days after the CRT, was a decreased blood vessel density and an increased presence of inflammatory macrophages and microglial cells.

Discussion: Orthotopically implanted PDX EPN xenografts closely mimic histological features, anatomical location and radiologic features of the primary tumors. Our advanced mpMRI protocol followed by novel MATLAB algorithm analysis allows for a unique characterization of pediatric EPN as well as assessing the tumor response to a clinically relevant CRT protocol in a mouse model.