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

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BACKGROUND

• Ependymoma (EPN) is an aggressive pediatric brain tumor
• After radiation therapy and surgery, EPN recurs in 23-66% of patients. Benefits of chemotherapy are not well defined.
• EPN is characterized by high tumor cellularity, cytological anaplasia, high mitotic index, tumor necrosis, and inflammatory cells such as M2-type myeloid cells.

OBJECTIVE

To develop and optimize an advanced mpMRI protocol to characterize the phenotype and chemo-radiation treatment (CRT) response in an orthotopic mouse of patient-derived xenografts (PDX) of pediatric EPN.

METHODS

Mouse Models:
• Female severe immunodeficient mice (n=22)
• CRT group (10 Gy radiation plus 30 mg/kg 3-fluorouracil) (n=6)

MRI protocol:
• High resolution T2w turboRARE (sagittal and axial) for tumor volume
• Diffusion weighted imaging (DWI) for tumor necrosis, edema, and selective size imaging
• Quantitative T2 maps (qT2) (before and 24hr after ferumoxytol injection) and vessel size imaging (VSI) modeling

Analysis:
Analysis performed in ParaVision NEO Software and in house MATLAB simulations.

RESULTS

BASELINE
• All EPN PDX were inoculated in the correct location: cerebellum
• Median Tumor Volume: 21±12 mm³
• Increased Blood Vessel Densities: Q=0.54±0.12
• ADC values low at 0.67x10⁻² mm²/s

EARLY RESPONSE TO TREATMENT
• Appreciated as early as 2 days after CRT
• Decreased blood vessel density
• Increased presence of inflammatory macrophages and microglial cells

LATE RESPONSE TO TREATMENT
• Appreciated 2 weeks after CRT
• Decrease in tumor volume: mean 12.24 mm³ to 4.05 mm³ (P<0.01)
• Increased ADC values from 0.67 to 1.25 (P=0.01)
• Decreased fitted cellularity: 8.5x10³ to 5.2x10³ mm⁻²
• Decreased SSIFT iAUC from 7.1 to 4.2 (P=0.001)

CONCLUSIONS & IMPLICATIONS

• Limitation: current focus is on one type of EPN (PFA1 vs PFA2 vs PFB)
• Our PDX models closely mimic histological features, anatomical location and radiological features of the primary tumors
• Early response to CRT: Significant decrease in vascularity and increase in inflammatory cells
• Late response to CRT: Decreased cellularity and cell shrinkage.
• Future studies will further characterize the pathology of these models and investigate the response of PDX EPN to other treatment modalities.

REFERENCES


DISCLOSURES

The authors have no financial affiliations or relationships. There was no off-label use of pharmaceuticals in human subjects.

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