University of Colorado
Anschutz Medical Campus

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

JS Song, JL Steiner, D Niemann, AM Griesinger, AM Pierce, MS Brown, NK Foreman, NJ Serkova
Department of Radiology, Anschutz Medical Campus

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.

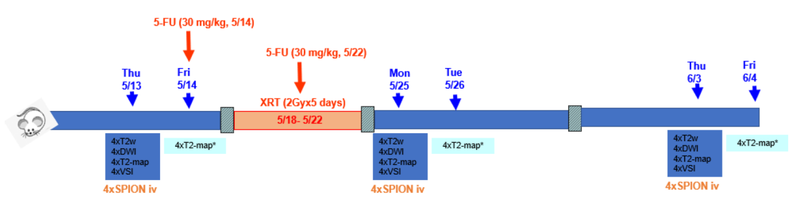
OBJECTIVE

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 T2maps (qT2) (before and 24hr after ferumoxytol injection) and vessel size imaging (VSI) modeling

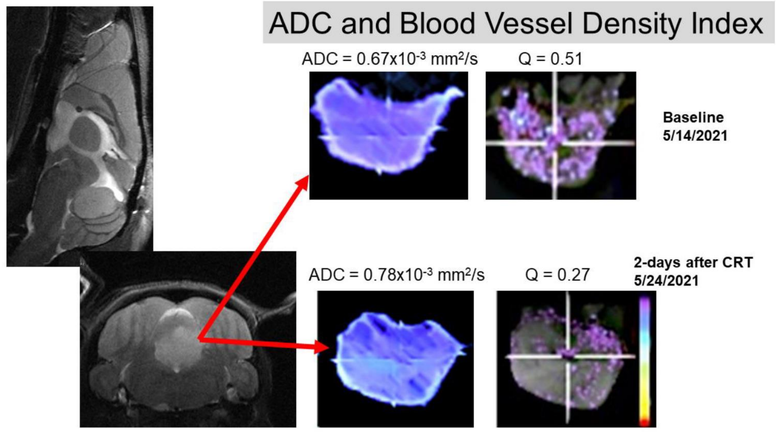


Analysis:
Analysis performed in ParaVision NEO Software and in house MATLAB simulations.

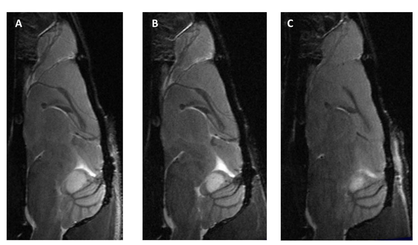
RESULTS

BASELINE
- All EPN PDX were inoculated in the correct location: cerebellum
- Median Tumor Volume: 21±12 mm^3
- Increased Blood Vessel Densities: Q=0.54±0.12
- ADC values low at $0.67x10^{-3}$ mm^2/s

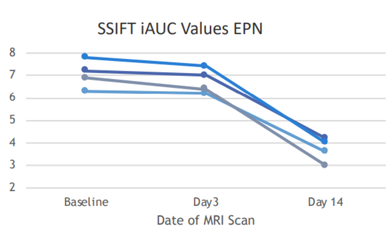
EARLY RESPONSE TO TREATMENT
- Appreciated as early as 2 days after CRT
- Decreased blood vessel density
- Increased presence of inflammatory macrophages and microglial cells



LATE RESPONSE TO TREATMENT
- Appreciated 2 weeks after CRT
- Decrease in tumor volume: mean 12.24 mm^3 to 4.05 mm^3 (P<0.01)
- Increased ADC values from 0.67 to 1.25 (P=0.01)
- Decreased fitted cellularity: $8.5x10^3$ to $5.2x10^3$ mm^{-2}
- Decreased SSIFT iAUC from 7.1 to 4.2 (P=0.001)



A = Baseline B = 2 days post CRT C = 2 weeks post CRT



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 vasculature 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.

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DISCLOSURES

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

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