AbstractID: 14333 Title: Intracranial murine tumour investigation of radiation and anti-angiogenic agents using serial MRI

Purpose: This study investigates the feasibility and utility of serial magnetic resonance imaging (MRI) to guide the design, delivery and evaluation of a murine intracranial(IC) tumour experiment of radiation(RT) and anti-angiogenic(AA) therapy.

Method and Materials: U87 glioma cells were injected IC into 58 NOD SCID mice. MRI with gadolinium(gad) via tail vein were acquired day 0(7days post-IC), 3,7,10,14, 21. Mice with day 0 MRI visible tumours were stratified by tumour size to: (1)placebo(CTRL) (2)RT+placebo(RT) (3)Sunitinib(SU) (4)RT+SU(SURT). Cone-beam CT(CBCT)-guided RT with day 0 MRI was used to deliver 8Gy/1 fraction to tumour on day 1. SU 0.8mg or placebo was given for 7 days starting day 1. Serial MRI included: (1)T2 (2)Quantitative T1 (3)Dynamic contrast enhanced(DCE) (4)Diffusion weighted(DWI) (5) T1-gad. RT dose to tumour was evaluated on fused images of CBCT and day 0 MRI.

Results: Mean day 0 tumour size was similar in all arms: $0.60\pm0.04 mm^3$[Range: $0.09\text{-}1.6 mm^3$]. No mice died with serial MRI. All irradiated tumours received >90% prescribed dose. Tumour growth rate was slower for SURT vs placebo($p<0.001$) or SU($p=0.003$) but similar to RT($p=0.4$). By day 3, DCE(iAUC60) decreased in SURT 31% but increased in CTRL16%($p=0.00009$), RT 34%($p=0.0008$), SU 15%($p=0.0004$). Percent change in ADC relative to tumour volume change at day 3 was greater for SURT $131\%/mm^3$ and RT $393\%/mm^3$ compared with SU $40\%/mm^3$ or CTRL $3.5\%/mm^3$.

Conclusion: This study demonstrates serial MRI studies are feasible and augments investigation of RT and AA in murine IC tumour models by providing temporal, spatial and physiological information. Serial MRI identified promising biomarkers and their optimal timing: decline in iAUC60 and composite metric of ADC and tumour volume change at day 3. This helps focus future preclinical studies that evaluate underlying pathophysiology and guides timing of clinical biomarker evaluation.

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