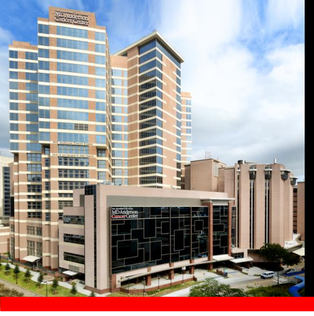

Cerebral Blood Volume Changes During Radiotherapy May Predict Pseudo-progression versus Disease Progression for Patients with High Grade Glioma

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Rationale

- Patients with high grade glioma (HGG) often demonstrate increased contrast enhancement following chemoradiation (CRT) that may represent pseudoprogression (PsP) or disease progression (DP)
- PsP occurs within 6 months following CRT, results from treatment-induced changes, and is associated with improved survival
- Diagnosis of PsP vs DP impacts clinical decision making
- Post-RT relative cerebral blood volume (rCBV) used as marker to differentiate PsP vs DP

Primary Objective

- Retrospectively determine if a change in rCBV within the first 3 weeks of CRT can predict PsP vs DP for patients with HGG

Secondary Objectives

- Determine if MGMT Methylation status predicts for PsP vs DP

Materials & Methods

Patient Eligibility

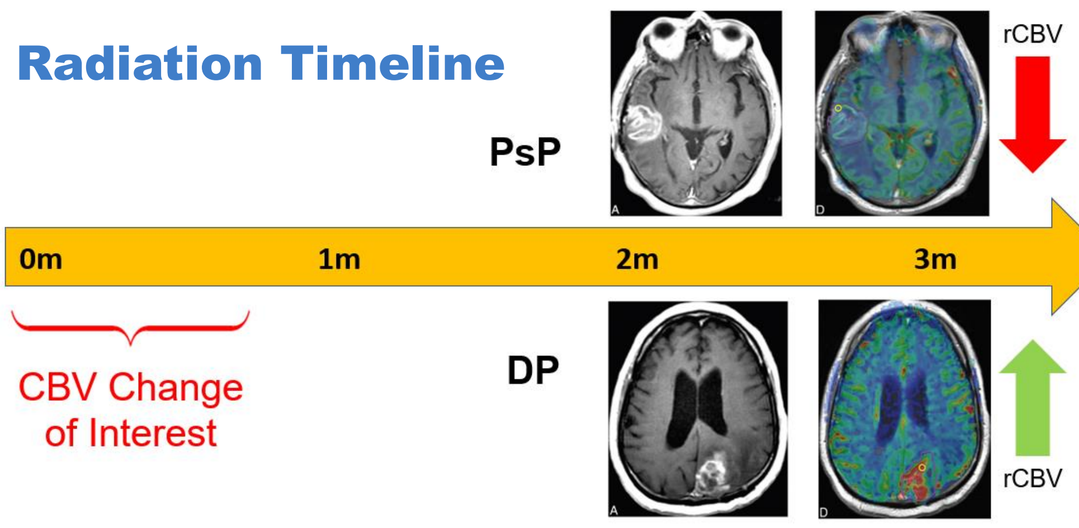
- Newly diagnosed HGG
- T1+C and DSC scans at MR Sim and 3-week F/U
- At least 6-month F/U

Tumor Segmentation & Post-processing

- Manual contouring on Axial MRIs using RayStation Non-Clinical – 10B DTK
- Leakage correction algorithm run on MATLAB 10a
- rCBV:

$$\frac{3\ week\ f/u\ Tumor\ rCBV}{3\ week\ f/u\ NAWM\ rCBV} - \frac{MR\ Sim\ Tumor\ rCBV}{MR\ Sim\ NAWM\ rCBV} = Change\ in\ rCBV\ During\ RT$$

Radiation Timeline



Patient Demographics

	All (n=26)	PsP (n=13)	DP (n=11)
Age, median (range), year	61 (28-74)	62 (28-74)	57 (48-67)
Gender, male (%)	15 (58)	9 (69)	6 (55)
MGMT Methylation Status			
Methylated (%)	8 (31)	5 (38)	3 (27)
Unmethylated (%)	14 (54)	5 (38)	7 (64)
Unknown (%)	4 (15)	3 (23)	1 (9)
Race, white (%)	24 (92)	13 (100)	9 (82)
KPS (%)			
≥ 70	24 (92)	13 (100)	8 (73)
< 70	2 (8)	0 (0)	2 (18)
Histology (%)			
GBM	22 (85)	9 (69)	11 (100)
Astrocytoma	3 (13)	3 (23)	0 (0)
Oligodendroglioma	1 (4)	1 (8)	0 (0)

Patient Categorization

Radiologist Impression	Neuro-Oncologist Tx Plan	PsP	DP	Stable/ Responding
Treatment-related changes	No treatment change	✓		
Disease progression	Treatment change		✓	
Inconclusive	Treatment change		✓	
Inconclusive	No treatment change	✓		
Stable	No treatment change			✓

Statistical Analysis

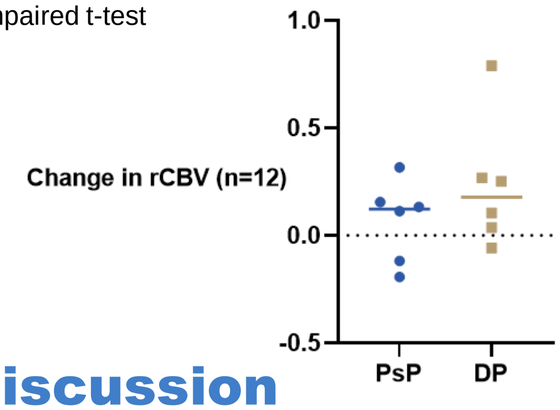
- Unpaired t-test to determine if early rCBV change and Fisher's exact test to determine if MGMT methylation status are significantly different between PsP and DP groups

Results

	All (n=14)	PsP (n=8)	DP (n=6)	*p-value	95% Confidence Interval
MR Sim rCBV				0.82	-1.12 – 0.90
Mean	0.85	0.81	0.92		
Median	0.51	0.37	0.67		
3-week rCBV				0.44	-1.51 - 0.70
Mean	0.92	0.74	1.15		
Median	0.63	0.51	0.85		
Change in rCBV				0.15	-0.71 – 0.12
Mean	0.06	-0.06	0.23		
Median	0.11	0.06	0.18		

	All GBM (n=12)	PsP (n=6)	DP (n=6)	*p-value	95% Confidence Interval
MR Sim rCBV				0.90	-1.10 – 1.23
Mean	0.95	0.98	0.92		
Median	0.67	0.72	0.67		
3-week rCBV				0.85	-1.24 – 1.05
Mean	1.10	1.05	1.15		
Median	0.84	0.75	0.85		
Change in rCBV				0.28	-0.49 – 0.16
Mean	0.15	0.07	0.23		
Median	0.12	0.12	0.18		

*Unpaired t-test



Discussion

- Preclinical literature in GBM mouse models suggests that radiation-induced microvascular changes take **time**
  - Angiogenesis inhibition and a significant decrease in perfusion seen at 2 weeks post-treatment (Seo et al. 2019, Kioi et al. 2010)
- Vascular changes may be delayed in human tumors comparative to animal models (Eberhard et al. 2000)

Future Directions

- Determine if a change in rCBV between MR Sim and **1-month post-CRT** predicts PsP vs DP
- Even if rCBV as an independent biomarker is not predictive, investigate whether it serves as useful input for a mechanistic mathematical model that forecasts tumor behavior

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