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Comparison of Diffusion tensor imaging and magnetic resonance perfusion imaging in differentiating recurrent brain neoplasm from radiation necrosis

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Abstract

Rationale and Objectives—To compare differences in diffusion tensor imaging (DTI) and dynamic susceptibility-weighted contrast-enhanced (DSC) MR perfusion imaging characteristics of recurrent neoplasm and radiation necrosis in patients with brain tumors previously treated with radiotherapy with or without surgery and chemotherapy.

Methods and Materials—Patients with a history of brain neoplasm previously treated with radiotherapy with or without chemotherapy and surgery who developed a new enhancing lesion on

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post-treatment surveillance MRI were enrolled. DSC perfusion MR imaging and DTI were performed. Region of interest (ROI) cursors were manually drawn in the contrast enhancing lesions, in the perilesional white matter edema, and in the contralateral normal-appearing frontal lobe white matter. DTI and DSC perfusion MR indices were compared in recurrent tumor versus radiation necrosis.

Results—Twenty-two patients with 24 lesions were included. Sixteen (67%) lesions were placed into the recurrent neoplasm group and 8 (33%) were placed into the radiation necrosis group using biopsy results as the gold standard in all but 3 patients. Mean ADC values, mean parallel eigenvalues, and mean perpendicular eigenvalues in the contrast enhancing lesion were significantly lower and relative cerebral blood volume was significantly higher for the recurrent neoplasm group compared to the radiation necrosis group ($p<0.01$, $p=0.03$, $p<0.01$, and $p<0.01$ respectively).

Conclusion—The combined assessment of DTI and DSC MR perfusion properties of new contrast enhancing lesions is helpful in distinguishing recurrent neoplasm from radiation necrosis in patients with a history of brain neoplasm previously treated with radiotherapy with or without surgery and chemotherapy.

Introduction

Conventional MRI is not reliable in distinguishing radiation necrosis from recurrent brain neoplasm in patients with brain tumors previously treated with radiation therapy and surgery (1–4). Stereotactic biopsy and resection remain the most reliable methods for classifying enhancing lesions that develop in the post treatment period (2). In recent years, dynamic susceptibility-weighted contrast-enhanced (DSC) MR perfusion imaging and diffusion tensor imaging (DTI) have been used to evaluate post-treatment brain tumor patients. Multiple studies have shown significantly higher relative cerebral blood volume (rCBV) in the contrast enhancing lesions of patients with recurrent tumor compared to those of patients with radiation necrosis (4–10). While some studies have shown enhancing lesion apparent diffusion coefficient (ADC) values or ratios to be lower in recurrent neoplasms as opposed to radiation necrosis (7, 9–13), other studies have shown contradictory findings (14, 15). Few studies have published findings specifically examining the diffusion tensor imaging characteristics (fractional anisotropy, eigenvalues) of these lesions (7, 11–14).

Our study prospectively analyzes both DSC MR perfusion and diffusion tensor imaging characteristics of new enhancing lesions in patients with brain tumors previously treated with radiation therapy with or without surgery and chemotherapy.

Materials and Methods

Institutional review board approval was obtained for this prospective cohort study. Informed consent was obtained from all subjects.

Subjects

The study population consisted of 22 subjects with 24 enhancing lesions (mean age: 51 years, range: 18–78 years; 8 females [mean age: 58 years, range: 34–78 years]; 14 males

[mean age: 47 years, range: 18–69 years]) with a history of treated primary or secondary brain neoplasm who developed a new enhancing lesion on conventional MRI in the post-treatment period. Enrollment of patients occurred between January 2007 and August 2014. Inclusion criteria were 1) a history of histologically confirmed brain neoplasm treated with radiation therapy (including radiosurgery) with or without surgery, 2) the development of a new contrast enhancing lesion with a size of 1 cm or more on conventional brain MRI after treatment, 3) an age 18 years or older. Exclusion criteria were 1) pregnancy, 2) an inability to undergo MRI, 3) the presence of metallic or ferromagnetic prostheses that would obscure imaging results or cause significant artifact. Frequency of conventional MRI examinations for identification of potential study candidates was at the discretion of the clinical service. All screening examinations were standard hospital protocol. Patient demographics are detailed in table 1. Two subjects, each with two distinct enhancing lesions occurring at separate time points, were enrolled in the study twice.

Original tumor histology was confirmed by pathology report or by clinic note. Nine (41%) of the tumors were glioblastoma multiforme (GBM), 4 (18%) were oligodendroglioma, 1 (5%) was anaplastic glioma, 3 (14%) were astrocytoma, 2 (9%) were mixed oligoastrocytic neoplasm, and 3 (14%) were metastatic tumor (2 lung and 1 breast primary tumors). Nineteen (86%) of the subjects were treated with an initial surgical approach, 1 subject (5%) was treated with chemotherapy and radiotherapy alone, and 2 subjects (9%) were treated by stereotactic radiosurgery alone. All tumors undergoing initial resection were completely removed. Patients undergoing fractionated radiotherapy received an average radiation dose of 63.6 gray (range: 54–81 gray) for treatment of their index brain neoplasm. Mean interval time between initial brain tumor diagnosis and development of an enhancing lesion on MRI was 2.2 years (range: 0.3–5.6 years) excluding 4 outlier patients with interval times greater than 10 years.

MRI Technique

All patients underwent MRI utilizing a 3 Tesla scanner (Achieva MRI system, Philips, Best, Netherlands) with a dedicated head coil. The following sequences were obtained: axial T2-weighted TSE (SENSE, TR shortest, TE 80ms, flip angle 90, slice thickness 4 mm, FOV 240, acq. matrix 400x314, scan time 1:42 minutes), axial fluid attenuated inversion recovery (FLAIR) (TR 11000ms, TE 125ms, TI 2800ms, slice thickness 4ms, FOV 240, acq. matrix 352x173, scan time 3:40 minutes), T1-weighted 3D TFE before and after intravenous gadolinium-based contrast administration (SENSE, TR shortest, TE shortest, flip angle 8, number of slices 210, FOV 250, acq. matrix 252x240, scan time 5:40 minutes), diffusion weighted imaging (EPI, TR 4000ms, TE 75ms, flip angle 90, b=0, b=1000, b=2000, b=4000, slice thickness 4mm, FOV 240, acq. matrix 128x98, time 4:00 minutes), and diffusion tensor imaging (EPI, TR 6400ms TE 62ms, directions: 16, b=0, b=800, flip angle 90, slice thickness 2mm, FOV 224, acq. matrix 112x110, scan time 5:01 minutes). Nineteen of the patients included in the study additionally underwent DSC perfusion MR imaging (SSEPI gradient echo, TR 1500ms, TE 50ms, flip angle 40, dync scans 45, slice thickness 4.4mm, scan time 1:12 minutes). Gd-DTPA (20 mL) was intravenously administered (injection rate of 2 cc/sec) prior to the contrast enhanced sequences. Perfusion data was not obtained for 5 of the lesions.

Data Acquisition and Post Processing

Imaging data was post-processed with a software developed in-house using MATLAB (MathWorks, Natick, MA, USA). Axial T1-weighted gadolinium-enhanced images were used to aid in region of interest (ROI) placement. ROI cursors were manually drawn in the contrast-enhancing lesion, in the perilesional white matter edema, and in the contralateral normal-appearing frontal lobe white matter on both the DSC MR perfusion (when available) and DTI maps for each patient. All ROIs comprised an area of 40–60 mm². All enhancing lesion ROIs were drawn in the location felt to best represent the lesion in question and areas of frank necrosis were excluded from measurement. Mean ADC values, mean fractional anisotropy (FA) values, mean parallel eigenvalues (λ_1), and mean perpendicular eigenvalues ($\lambda_{\perp}$) were measured and recorded for each ROI on the diffusion maps. The λ_1 value reflected the eigenvalue parallel to the direction of greatest diffusivity, and the $\lambda_{\perp}$ value was calculated by computing the average of the two eigenvalues perpendicular to the direction of greatest diffusivity. Mean cerebral blood volume (CBV) values were measured and recorded for each ROI on the perfusion maps. Relative CBV (rCBV) values were calculated as the ratio of the mean CBV measured in the contrast-enhancing lesion and the mean CBV measured in the contralateral normal-appearing frontal lobe white matter. Areas of necrosis were excluded from measurement. All data was acquired prospectively prior to surgical biopsy or resection of the enhancing lesion. Post-processing and ROI placement was performed by a senior radiology resident who was blinded to the histologic results. Example images and ROI placements may be seen in figures 1 and 2.

Histologic Analysis

After MRI, 21 (88%) of the enhancing lesions were biopsied or resected. These were subdivided into group 1: recurrent neoplasm, or group 2: radiation necrosis, based on review of their surgical pathology report. Patients with pathology reports describing viable tumor cells or significant tumor cells in a background of radiation necrosis were placed into group 1. Patients with pathology reports describing either complete radiation necrosis or few tumor cells in a background of extensive radiation necrosis were placed into group 2. Representative images of both group 1 and group 2 lesions may be seen in Figures 1 and 2. Three (12%) of the lesions did not undergo surgical biopsy or resection. Two of these were classified into group 1 based on progressive enlargement over multiple subsequent conventional MRI examinations spanning a course of at least 6 months. One of these was classified into group 2 based on spontaneous resolution on subsequent MRI without recurrence in 4 years of follow-up.

Data Analysis

Comparative analysis between group 1 and group 2 was performed using student's T-test. Various MRI indices were compared to one another using scatter plots (Figures 3–5).

Results

Sixteen (67%) lesions were classified into the recurrent neoplasm group (group 1) and 8 (33%) lesions were classified into the radiation necrosis group (group 2). Fourteen group 1 patients and 5 group 2 patients had DSC MR perfusion data. Patient demographics are

presented in Table 1. Mean enhancing lesion ADC values were significantly lower for group 1 lesions ($1.01 \times 10^{-3} \pm 0.19$) compared to group 2 lesions ($1.26 \times 10^{-3} \pm 0.08$; $p < 0.01$). The mean ADC values measured in group 1 lesions, despite being significantly lower than those of group 2 lesions, had a wider range of values (group 1 range: $0.72 \times 10^{-3} - 1.27 \times 10^{-3}$; group 2 range: $1.13 \times 10^{-3} - 1.37 \times 10^{-3}$). The mean FA values measured in group 1 lesions (0.23 ± 0.10) were not significantly different than those measured in group 2 lesions (0.16 ± 0.06 ; $p=0.07$). The mean parallel eigenvalues (λ_1) measured in group 1 lesions ($1.25 \times 10^{-3} \pm 0.24$) were significantly lower compared to those of group 2 ($1.46 \times 10^{-3} \pm 0.11$, $p = 0.03$). The mean perpendicular eigenvalues ($\lambda_{\perp}$) measured in group 1 lesions ($0.89 \times 10^{-3} \pm 0.19$) were significantly lower compared to those of group 2 ($1.15 \times 10^{-3} \pm 0.09$, $p < 0.01$). No significant between-group differences were observed for the mean ADC values, mean parallel eigenvalues (λ_1), mean perpendicular eigenvalues ($\lambda_{\perp}$), or mean FA values measured in the perilesional white matter edema or contralateral normal-appearing frontal lobe white matter.

The mean rCBV values for the group 1 lesions (3.76 ± 1.95) were significantly higher compared to group 2 lesions (0.99 ± 0.25 ; $p < 0.01$). No significant between-group differences were observed for the mean rCBV values measured in the perilesional white matter edema ($p=0.17$). Mean values and p values for all measurements obtained are in Table 2. Scatter plots of mean ADC values versus mean rCBV values, mean ADV values versus mean λ_1 values, and mean λ_1 values versus mean rCBV values are in Figures 3–5.

Discussion

Distinguishing radiation necrosis from recurrent neoplasm in patients with brain tumors previously treated with radiation therapy presents an important clinical dilemma. The two conditions overlap in clinical symptoms and imaging characteristics, however, treatment options differ (1, 16, 17). The ability to non-invasively separate these two entities would expedite appropriate therapy without the risk of morbidity inherent to surgical biopsy or resection for lesions where surgical resection is not indicated. While conventional MRI imaging is not reliable for distinguishing these two entities (1–4), other imaging techniques and modalities such as diffusion imaging, MR perfusion imaging, MR spectroscopy, positron emission tomography, and single photon emission CT have been studied (5–14, 18–20). Our study focused on the evaluation of diffusion tensor imaging and DSC MR perfusion imaging.

Diffusion tensor imaging, a form of diffusion weighted imaging, examines the mobility of water protons in tissue as well as their directionality. Water protons that only move in one direction are said to be anisotropic and have a fractional anisotropy equal to 1. Water protons that are equally likely to move in any direction are said to be isotropic and have a fractional anisotropy equal to 0. Eigenvalues (λ_1 , λ_2 , and λ_3) measure the degree of diffusion in 3 perpendicular axes. The principal eigenvalue, or λ_1 , describes the degree of diffusivity in the direction that it is greatest. The λ_2 and λ_3 values, often averaged to form $\lambda_{\perp}$, describe the degree of diffusivity in the two axes perpendicular to λ_1 . Currently, DTI is most frequently used for white matter tract mapping prior to brain tumor resection (21). Highly cellular tumor with a small extracellular space might be expected to have low diffusivity and low

anisotropy, whereas tumor infiltrating brain (especially in white matter where fibers tend to be parallel) might be expected to have relatively normal diffusivity with high anisotropy. In radiation necrosis, where cellular death and myelin loss are prominent features (16, 17), one might expect high diffusivity with low anisotropy.

Our data demonstrate significantly increased diffusivity in the contrast enhancing lesions of patients with radiation necrosis compared to patients with recurrent tumor, with significantly higher mean ADC, λ_1 , and $\lambda_{\perp}$ values measured in the radiation necrosis lesions ($p < 0.01$, $p = 0.03$, and $p < 0.01$ respectively). This increased freedom of diffusion would be expected in regions of necrosis and cell death as opposed to regions of cellular tumor tissue. While no significant between-group differences were observed in mean fractional anisotropy values, the recurrent tumor group had higher mean FA values (0.23) in comparison to the radiation necrosis group (0.16). This suggests a higher a proportion of maintained white matter tracts in the enhancing recurrent neoplasm lesions with resulting increased directional preference of diffusion.

While significantly higher diffusivity was observed in the recurrent tumor group, there was heterogeneity among the mean ADC values measured (range: 0.73×10^{-3} to 1.27×10^{-3}). The range of mean ADC values observed in recurrent tumor is more than double that observed in radiation necrosis (range: 1.14×10^{-3} – 1.37×10^{-3}). Additionally, many of the mean ADC values measured in the recurrent tumor lesions had significant overlap with those measured in the radiation necrosis lesions. In 5 out of 16 (31%) recurrent tumor lesions, the mean ADC values were within 1 standard deviation of mean of the radiation necrosis lesions. Heterogeneity in tumor histology and in tumor subtype may, in part, account for the wide range of ADC values observed in recurrent tumor lesions. Bauer, et al (18) examined 30 brain tumor patients with DSC perfusion MR and DTI and found differences in DTI and perfusion characteristics among GBMs and brain metastases. Verhaak, et al (22) in 2010 and Dunn et al (23) in 2012 described molecular heterogeneity in various subtypes of GBM. In our study population, there was no observable correlation between tumor histology and mean enhancing lesion ADC value. Many of the extreme mean ADC values observed, both high and low, were in glioblastoma patients.

Based on our data, high ADC and eigenvalues did not reliably predict radiation necrosis. However, we found that low ADC values readily predicted recurrent tumor. Nine out of 16 (56%) patients in the recurrent tumor group had enhancing lesion mean ADC values that were less than 1.10×10^{-3} (2 standard deviations below the mean for radiation necrosis lesions). In lesions with similarly low ADC values, recurrent tumor should be considered slightly more likely.

Significantly higher enhancing lesion mean rCBV values were observed in the recurrent tumor lesions (3.76 ± 1.95) compared to the radiation necrosis lesions (0.99 ± 0.25 , $p < 0.01$). In comparison to our diffusion tensor imaging data, there was substantially less overlap in mean contrast enhancing lesion rCBV values between the two groups. Twelve out of 14 (86%) lesions in the recurrent tumor group had mean rCBV values at least 3 standard deviations above the mean for the radiation necrosis group. There were two aberrantly low rCBV values (0.63 and 0.81) observed in the recurrent tumor lesions (one a metastatic lung

cancer, the other a glioblastoma). Despite these outliers, our data showed that elevated enhancing lesion rCBV values were highly predictive of recurrent tumor. The overwhelming majority of patients in the recurrent neoplasm group (86%) had rCBV of 2.5 or greater. The highest rCBV value measured in a radiation necrosis group patient was 1.30.

Our data suggest that DSC MR perfusion imaging and DTI used together may be superior in differentiating radiation necrosis from recurrent tumor than either modality alone. As seen in the scatter plots, patients with radiation necrosis tend to cluster together with relatively higher ADC and λ_1 values and lower rCBV values. Elevated rCBV values in lesions with equivocally high diffusion indices (i.e. ADC and λ_1 values within the range commonly seen in the radiation necrosis lesions) helped distinguish many lesions as recurrent tumor.

Our results are concordant with prior published works. In 2014, Alexiou et al (7) prospectively examined 30 patients with high grade gliomas treated with surgical resection, radiation and chemotherapy compared DTI, DSC MRI, and ^{99m}Tc -Tetrofosmin brain single-photon emission computed tomography (SPECT) in differentiating recurrent neoplasm from treatment induced necrosis. These authors reported significantly higher rCBV values and significantly lower ADC values in subjects with recurrent neoplasm compared to subjects with treatment-induced necrosis. They also reported that a cutoff rCBV value of 2.2 yielded 100% sensitivity and 100% specificity in differentiating tumor recurrence from treatment induced necrosis. Our data likewise demonstrated high specificity of elevated contrast enhancing lesion rCBV for the diagnosis of recurrent tumor. Twelve out of 12 (100%) lesions in our study with $\text{rCBV} > 2.2$ were found to have recurrent tumor. These authors additionally reported higher mean FA values in recurrent tumor lesions, however, this did not reach significance ($p = 0.072$).

A prospective trial by Hu et al (6) in 2009 evaluated 42 patients with primary brain neoplasms with DSC MRI and found subjects with treatment-related non-tumoral lesions to have rCBV values from 0.21–0.71 and subjects with recurrent tumor to have rCBV values from 0.55–4.64. Radiation necrosis lesions in our study were found to have a similar narrow range of low rCBV values, however, more than 1/3 of these lesions had $\text{rCBV} > 1$. Though rCBV analysis is clearly helpful in differentiating recurrent tumor from radiation necrosis, the presence of such outliers limits the ability of DSC MR perfusion to accurately distinguish radiation necrosis from recurrent tumor. To further increase sensitivity and specificity for the differentiation of recurrent neoplasm from radiation necrosis in the daily clinical setting, a multi-sequence, multi-modality approach including MR spectroscopy and positron emission tomography (PET) may be helpful (7, 19, 20, 24, 25). The evaluation of such imaging techniques/modalities were beyond the scope of this study.

Our study had several limitations. Many of the index brain tumors were treated at a medical facility outside the institution, and complete details of steroid and chemotherapy administration were not always available to the researchers. There was substantial histologic heterogeneity in the central nervous system neoplasms evaluated, particularly given the inclusion of metastatic lesions, and there is emerging evidence that DTI and DSC perfusion MR characteristics may vary with tumor histology (18, 26, 27). The various mutations/gene expressions of various glioblastomas (22, 23) were not evaluated in our GBM cohort.

Furthermore, three patients did not undergo surgical resection or biopsy of the brain lesion under study; although the evidence from follow-up strongly indicated the diagnosis, the diagnosis was not proven in these three patients. Additionally, isolated tumor or radiation necrosis is rare. Often times there is a combination of both processes, and dividing all lesions into two distinct groups is inherently problematic. For our study, the presence of radiation necrosis or recurrent neoplasm was determined from the clinical pathology reports. The histologic samples were not reported by a single pathologist or in a standardized manner. Undisclosed variation in pathologic interpretation may have influenced our data in unforeseen ways.

In summary, we found that the combination of DTI (ADC, λ_1 , and $\lambda_{\perp}$ values) and DSC MRI (rCBV) characteristics of new enhancing lesions in patients with brain neoplasms treated with radiation with or without surgery and chemotherapy to be helpful differentiating recurrent neoplasm from radiation necrosis, particularly in the lesions with elevated rCBV and diminished ADC values. In this setting, the likelihood of recurrent neoplasm is exceedingly high.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Representative enhancing lesion ROI placements on A) T1-weighted post-gadolinium, B) T2-weighted FLAIR, C) ACD map, D) FA map, E) color coded map of mean diffusion direction, and F) CBV map images in a patient with biopsy proven recurrent tumor (Group 1).

Figure 2. Representative enhancing lesion ROI placements on A) T1-weighted post-gadolinium, B) T2-weighted FLAIR, C) ACD map, D) FA map, E) color coded map of mean diffusion direction, and F) CBV map images in a patient with biopsy proven radiation necrosis (Group 2).

Figure 3. Scatter plot of mean apparent diffusion coefficient (ADC) versus mean relative cerebral blood volume (rCBV) for recurrent neoplasm (group 1) lesions and radiation necrosis (group 2) lesions.

Figure 4.
Scatter plot of mean apparent diffusion coefficient (ADC) versus mean parallel eigenvalue
for recurrent neoplasm (group 1) lesions and radiation necrosis (group 2) lesions

Figure 5.
Scatter plot of mean parallel eigenvalue versus mean relative cerebral blood volume (rCBV)
for recurrent neoplasm (group 1) lesions and radiation necrosis (group 2) lesions.

Table 1

Patient Demographics:

Patient #	Sex	Age	Primary Tumor	Diagnosis	Time to lesion detection
1	Male	18	Diffuse astrocytoma	Tumor	42
2	Female	57	Metastatic breast cancer	Tumor	51
3	Male	41	Mixed glioma	Tumor	61
4	Male	42	GBM	Necrosis	14
5	Male	20	GBM	Tumor	10
6	Male*	28	Anaplastic glioma	Necrosis/Tumor	14, 28
7	Male	48	Anaplastic astrocytoma	Necrosis	11
8	Male	43	Metastatic lung cancer	Necrosis	41
9	Male	63	GBM	Tumor	12
10	Male	51	GBM	Tumor	18
11	Male	54	GBM	Necrosis	4
12	Male	69	Metastatic lung cancer	Tumor	8
13	Female	62	GBM	Tumor	17
14	Male*	62	Anaplastic oligodendroglioma	Necrosis/Tumor	173, 210
15	Male	68	Anaplastic oligodendroglioma	Tumor	395
16	Male	56	GBM	Tumor	23
17	Female	56	GBM	Necrosis	15
18	Female	51	Anaplastic astrocytoma	Tumor	68

Patient #	Sex	Age	Primary Tumor	Diagnosis	Time to lesion detection
19	Female	60	Mixed glioma	Tumor	8
20	Female	66	Oligodendroglioma	Tumor	146
21	Female	34	Anaplastic oligodendroglioma	Tumor	37
22	Female	78	GBM	Necrosis	50

Tumor = recurrent tumor; Necrosis = radiation necrosis; GBM = glioblastoma multiforme;

*patient included in study twice for 2 distinct lesions; Time to lesion detection is defined as time lapse (in months) from initial diagnosis of brain tumor to the development of a new enhancing lesion.

Table 2

Results:

	ADC	FA	λ_1	λ_L	rCBV
Group 1 (contrast enhancing lesion)	1.01 +/- 0.19	0.23 +/- 0.10	1.25x +/- 0.24	0.89x +/- 0.19	3.76 +/- 1.95
Group 2 (contrast enhancing lesion)	1.26 +/- 0.08	0.16 +/- 0.06	1.46x +/- 0.11	1.15x +/- 0.09	0.99 +/- 0.25
P Value (contrast enhancing lesion)	< 0.01	0.07	0.03	< 0.01	< 0.01
Group 1 (perilesional edema)	1.24 +/- 0.44	0.27 +/- 0.15	1.55 +/- 0.42	1.08 +/- 0.47	1.48 +/- 1.29
Group 2 (perilesional edema)	1.28 +/- 0.29	0.21 +/- 0.10	1.56 +/- 0.33	1.15 +/- 0.29	0.62 +/- 0.52
P Value (perilesional edema)	0.79	0.32	0.95	0.72	0.17
Group 1 (contralateral white matter)	0.80 +/- 0.08	0.56 +/- 0.08	1.35 +/- 0.19	0.52 +/- 0.08	n/a
Group 2 (contralateral white matter)	0.75 +/- 0.05	0.50 +/- 0.12	1.21 +/- 0.16	0.53 +/- 0.9	n/a
P Value (contralateral white matter)	0.18	0.23	0.09	0.93	n/a

Group 1 = Recurrent neoplasm, Group 2 = Radiation necrosis.

ADC values and eigenvalues are in units of $10^{-3} \text{ mm}^2/\text{s}$. FA and rCBV values are unitless.