Correlating Perfusion MRI Maps with Treatment Plans for Re-radiation Therapy in Brain Tumor Patients

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Abstract

Contrast-enhanced (CE) and Fluid attenuation inversion recovery (FLAIR) MRI are current standard of care tools for delineating radiation treatment targets in high-grade glioma (HGG) patients. However, in the setting of retreatment, tumor regrowth and therapy-related inflammation have identical MRI appearances. Dynamic Susceptibility-weighted Contrast-Enhanced Perfusion (DSC) MRI, can detect distinct characteristics of tumor and treatment effect through measurements of relative cerebral blood volume (rCBV). Our objective was to assess the extent to which rCBV maps correlate with re-radiation treatment plans in order to identify potential differences in treatment planning.

Eight previously treated HGG patients presenting for re-irradiation of suspected recurrent tumor were analyzed on an IRB-approved trial. All patients underwent DSC-MRI and routine MRI imaging, and underwent treatment as per routine clinical protocol. Following therapy, rCBV and radiation dose maps were overlaid on conventional MR to delineate differences in identified tumor burden.

Of the 8 patients, four rCBV images showed evidence of tumor outside of the RT planning volumes, while the other 4 showed fully treated tumor but with large volumes of uninvolved brain receiving radiation. Based on these results, DSC-MRI identified unique regions of potential tumor burden compared to conventional MRI and could be used to better tailor radiation treatment.

Introduction

CE-MRI is the current mainstay for monitoring HGG response to chemotherapy and RT. Gadolinium-based contrast agents can indicate the presence of blood-brain barrier disruption, which result in contrast-enhancement of tumors and other lesions.

CE-MRI is also used in conjunction with computed tomography (CT) for RT planning. However, early studies identified biopsy-proven tumor cells in the area of MRI FLAIR abnormalities outside CT abnormalities. Due to these concerns, FLAIR MRI, was soon incorporated into treatment planning.

Introduction cont'd

However, CE-MRI and FLAIR are both nonspecific tools for identifying recurrent tumor burden, in that therapy-induced injury, called Post-treatment Radiation Effect (PTRE), mimics its appearance on CE-MRI. It is paramount to distinguish these two as tumor regrowth indicates treatment failure, whereas PTRE represent treatment success.

DSC-Perfusion MRI detects variations in microvascular characteristics by measuring rCBV to detect differences in microvascular density (MVD), offering a promising adjunct to conventional MRI. PTRE reveals decreased capillary perfusion and MVD, while tumor growth typically reveals angiogenesis and increased MVD.

In this study, we focused on the plausibility of incorporating DSC-MRI the management of recurrent glioma patients. Our hypothesis is that rCBV maps may better define tumor burden within and possibly outside of these regions.

Methods

We recruited patients with recurrent HGG, undergoing re-radiation therapy. All study patients had previously undergone surgery and received temozolomide and radiation therapy.

We obtained pre- and postcontrast T1 and T2W stereotactic MRI data sets before DSC-MRI. T1 and T2 FLAIR were coregistered to produce an anatomic base. Anatomic CT scans and RT dosimetry were transformed into MR space. rCBV maps were generated from DSC-MRI by tracing hyperintense FLAIR lesions to generate a region of interest (ROI). An rCBV mask was applied to the ROI to produce an rCBV map, which combined with dosimetry, were fused to the T1/FLAIR base.

We analyzed the images by tracing the prescribed radiation dose and rCBV maps, to establish two volumes of interest (VOI). These were categorized into the following classes: 0) perfect alignment I) complete overlap but dose volume > rCBV volume II) complete overlap but rCBV volume > dose volume III) missed treatment volume. Each class also had 3 sub-categories of congruity, based on an overall volumetric assessment with A representing 75-100% congruity, B 25-50% and C 0-25%.

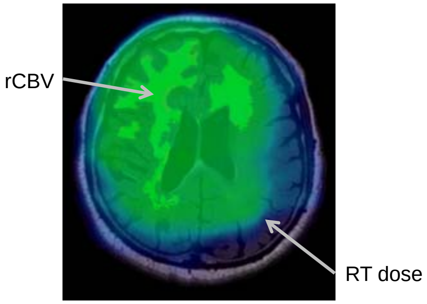

Figure 1: Example of Class 1B.
Image revealing overlap between radiation dose map and rCBV map with target vol > tumor vol

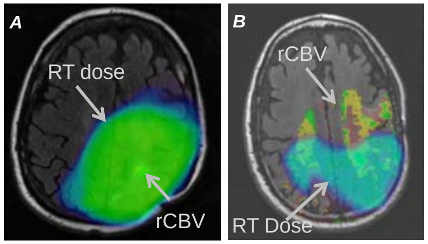

Figure 2: Examples of Class IC and IIIB.
A) Image reveals no missed treatment sites but radiation volume is much greater than rCBV volume. B) Image reveals missed treatment sites in bilateral parietal and left frontal lobes.

Patient Classes

Patient	Class
1	IB
2	IIIA
3	IIIA
4	IA
5	IB
6	IIIB
7	IIIB
8	IC

Table 1: Results of patient comparison image analysis

Results

DSC-MRI revealed regions of the rCBV map that did not overlap with treatment maps in four out of eight (50%) patients. Of these patients, two had large regions of potential tumor outside of the prescribed radiation dose volume.

The remaining 4 patients were judged to have complete overlap of treatment and rCBV maps but with a treatment volume larger than the rCBV-indicated tumor sites.

None of the patients were assessed to have either perfect alignment (Class 0) or complete overlap with rCBV volume greater than the treatment volume (Class II).

Discussion and Conclusions

DSC-MRI identified 4 patients who had potentially untreated tumor sites. The other 4 patients revealed treatment regions that fully encompassed tumor but also showed regions of irradiated normal brain. While DSC-MRI mostly correlates with radiation treatment plans, they appear to reliably identify regions of potentially untreated tumor. This suggests that DSC-MRI may be a viable tool to better delineate treatment targets during re-radiation therapy in recurrent HGG patients, identifying tumor missed by conventional MRI and sparing normal brain.

One important avenue to explore is if these regions of untreated tumor were 1) identified as sites of recurrence on follow up imaging and 2) if these differences contributed to any change in clinical outcome e.g. overall survival and quality of life. Ultimately these studies would be used to support the role of supplementing conventional MRI with DSC-MRI in routine clinical practice in order to more accurately treat tumors and improve outcomes.

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