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Evaluation of Target Definition for Stereotactic Reirradiation of Recurrent Glioblastoma

Beyzadeoglu M, Sager O*, Dincoglan F and Demiral S

Medical Faculty, Department of Radiation Oncology, University of Health Sciences, Ankara, Turkey

***Corresponding author:** Sager O

omersager@gmail.com

Medical Faculty, Department of Radiation Oncology, University of Health Sciences, Ankara, Turkey.

Tel: +90 312 304 4683

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Abstract

Background and purpose: Glioblastoma multiforme (GBM) constitute the most prevalent brain tumor in adults. The prognosis of GBM is typically bleak, with eventual recurrence in an overwhelming majority of the patients despite multimodality management including surgery, radiation therapy (RT), and systemic treatment. Vast majority of patients develop recurrence within or in close vicinity of the initial RT field, which limits the reirradiation dose to be delivered for recurrent tumor. Accurate target definition is critical for stereotactic reirradiation of recurrent glioblastoma. Multimodality imaging with computed tomography (CT), magnetic resonance imaging (MRI) and molecular imaging techniques may be used for detection of recurrence. In this study, we assessed the utility of multimodality imaging in target volume determination for stereotactic reirradiation of recurrent glioblastoma.

Patients and methods: Sixteen patients receiving radiosurgery at our institution for recurrent glioblastoma were identified for comparative evaluation of target definition based on CT imaging only and CT-MR fusion based imaging.

Results: CT-only imaging and CT-MR fusion based imaging for radiosurgery target definition was comparatively evaluated for 16 patients treated with radiosurgery at our institution for recurrent glioblastoma. Comparative assessment revealed that target definition based on CT-MR fusion based imaging was optimal and identical to the consensus decision of treating physicians in majority of the treated patients.

Conclusion: Incorporation of MRI may improve target definition for recurrent glioblastoma radiosurgery despite the need for further supporting evidence.

Keywords: Recurrent glioblastoma; Radiosurgery; Target volume; Magnetic Resonance Imaging (MRI)

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Introduction

Glioblastoma multiforme (GBM) constitutes the most prevalent brain tumor in the adult population [1,2]. The prognosis of GBM is typically bleak, with eventual recurrence in an overwhelming majority of the patients despite multimodality management including surgery, radiation therapy (RT), and systemic treatment. In the setting of recurrence, repeated surgery, reirradiation, systemic agents, or a combined modality treatment may be selected for individualized management of the patients based on several factors including age, performance status, time from diagnosis, response to previous therapies, size and location of the recurrent tumor, and availability of treatment resources. Considering the performance status, best supportive care may also be an option for selected patients.

While the role of RT has been well established in management of newly diagnosed patients with glioblastoma, its utility in the setting of recurrence is still being refined. Vast majority of patients develop recurrence within or in close vicinity of the initial RT field, which limits the reirradiation dose to be delivered for recurrent tumor [3,4]. Stereotactic irradiation in the form of stereotactic radiosurgery (SRS), fractionated stereotactic

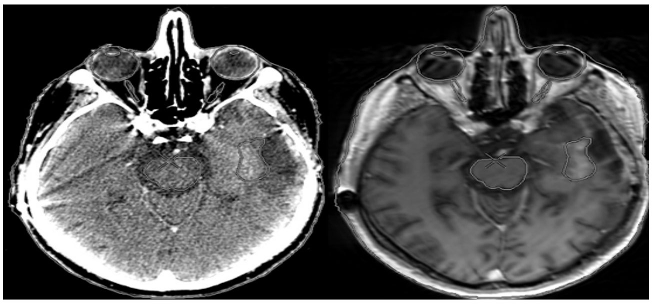

Figure 1 Axial planning CT and MR images of a patient with recurrent glioblastoma demonstrating the delineated target volume and critical structures including the brainstem and optic apparatus.

radiotherapy (FSRT), hypofractionated stereotactic radiotherapy (HFSRT), and stereotactic body radiation therapy (SBRT) has been used for management of several benign or malignant conditions throughout the body with encouraging therapeutic outcomes [5-21]. Primary advantage of stereotactic irradiation is the ability to deliver high doses to the well-defined tumors with typically steep dose gradients around the target volume which may improve normal tissue sparing. However, limited margins are used to expand the defined targets on radiosurgery planning images to account for sub-microscopic spread, and rigid immobilization with a stereotactic head frame and image guidance is typically used for elimination of setup margins. In this regard, accurate target definition is critical for stereotactic reirradiation of recurrent glioblastoma. Multimodality imaging with computed tomography (CT), magnetic resonance imaging (MRI), and molecular imaging techniques may be used for detection of recurrence. In this study, we assessed the utility of multimodality imaging in target volume determination for stereotactic reirradiation of recurrent glioblastoma.

Patients and Methods

Sixteen patients receiving radiosurgery at our institution for recurrent glioblastoma were identified for comparative evaluation of target definition based on CT-only imaging and CT-MR fusion based imaging. Written informed consent was obtained for each patient before treatment. Treatment with radiosurgery was decided by a multidisciplinary team of experts from neurosurgery, radiation oncology, and neuroradiology. Contrast-enhanced planning CT images were acquired at CT simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) with immobilization of patients using a stereotactic head frame. Acquired images at CT simulation were sent to the contouring workstation (SimMD, GE, UK) for delineation of target volume and critical structures in intimate association with the recurrent glioblastoma lesion. Target volumes acquired from CT-only based imaging and CT-MR fusion based imaging were comparatively evaluated for each patient. Definition of ground truth target volume for all patients was decided after consensus, colleague peer review and collaboration of the treating physicians. Radiosurgery planning system was ERGO ++ (CMS, Elekta, UK) and treatment machine was Synergy (Elekta, UK) Linear Accelerator (LINAC).

Optimal target coverage and normal tissue sparing was provided by using a single 360-degree arc, double 360-degree arcs, or five 180-degree arcs along with the Arc Modulation Optimization Algorithm (AMOA) in radiosurgery treatment planning. An adjustment was made in the windows and levels of the planning CT simulation images to attain improved target and critical organ visualization. Axial, coronal and sagittal images were used for optimal contouring of the target and critical organs. Verification of isocenters and setup was performed under image guidance with kV-CBCT (kilovoltage Cone Beam CT) and XVI (X-ray Volumetric Imaging, Elekta, UK) system. All patients received intravenous dexamethasone with H2-antihistamines immediately after radiosurgery.

Results

CT-only imaging and CT-MR fusion based imaging for radiosurgery target definition was comparatively evaluated for 16 patients treated with radiosurgery at our institution for recurrent glioblastoma. Comparative assessment revealed that target definition based on CT-MR fusion based imaging was optimal and identical to the consensus decision of treating physicians in majority of the treated patients. **Figure 1** shows axial planning CT and MR images of a patient with recurrent glioblastoma.

Discussion

Glioblastoma remains to be a major health concern as the most common primary brain tumor in adults. Prognosis is poor even after combined modality management including maximal surgery, RT, and systemic treatments. Newer treatment approaches for glial tumors include immunotherapy and intensified management with several combinations of available therapies [22-26]. Despite all efforts, recurrence is almost inevitable in an overwhelming majority of the patients. Establishing standard management in the recurrent disease setting is complicated by several factors including limited RT dose tolerance due to initially administered RT doses and poor performance status of the patients due to previous treatments and aggressive tumor progression. Nevertheless, radiosurgery offers a non-invasive and viable therapeutic option as an outpatient procedure with a condensed treatment schedule. High dose gradients around the target allow for delivering high doses of radiation in one or a few treatment fractions. However, accurate target definition is an indespensable component of successful radiosurgery applications. In this context, multimodality imaging has been utilized for improving target definition accuracy for stereotactic reirradiation. Utility of MRI for high grade gliomas has been addressed in a comprehensive review [27]. MRI has been used for several purposes including lesion characterization, radiation treatment planning, evaluation of response to therapy, assessment of recurrence and adverse radiation effects [27]. In the context of target definition for stereotactic reirradiation of recurrent glioblastoma, MRI may provide valuable information for improving accuracy in target volume definition with its superior soft tissue contrast.

Treatment simulation for radiation treatment planning is typically performed by use of CT simulators in most RT departments. While CT is optimal for assessment of the bony anatomy, MRI provides superior soft tissue contrast. Combining imaging information from both modalities may thus facilitate optimal target definition and may also aid in delineation of relatively smaller structures of interest such as the optic pathway and hippocampus. Given the limited RT dose tolerance due to initially delivered RT for patients with glioblastoma, accurate determination of the target and critical structures becomes an important concern in the context of reirradiation. Every effort should be expended to refrain from excessive exposure of normal brain tissues during reirradiation of recurrent glioblastoma to avoid adverse radiation effects. In this context, we strongly suggest incorporation of all relevant imaging information of the patients in the radiation treatment planning process. Our study adds to the literature by indicating the importance of incorporating multimodality imaging for accurate target definition for precise stereotactic reirradiation of recurrent glioblastoma. Clearly, the concept of multimodality imaging should be further investigated in future trials for optimization of target definition for recurrent glioblastoma radiosurgery.

Conclusion

In conclusion, incorporation of MRI may improve target definition for recurrent glioblastoma radiosurgery despite the need for further supporting evidence. The risk factors related significantly with HCC mortality were BCLC stage, CP score, and treatment modality. The greater BCLC stage or Child-Pugh score is, the greater it is related to HCC mortality. Supportive treatment was associated with high HCC mortality. We suggest increasing HCC surveillance to detect earlier stages of HCC which can undergo curative treatment, has better prognosis and also lower mortality rate. For future studies, we recommend that other parameters can also be examined.

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