

Letter to the Editor

Role of Re-irradiation in Salvage Treatment of Glioblastoma Multiforme

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Dear Editor

Glioblastoma multiforme (GBM) is the most common and aggressive primary brain tumor in humans, accounting for 12-15% of all brain tumors. The first therapeutic approach in this tumor is to perform maximal surgical resection with preserving neurologic functions. Currently, adjuvant radiotherapy (combined with chemotherapy or alone) following surgery is the standard treatment with proven positive effects on the local control and survival in GBM. Goal of radiotherapy is reducing the possibility of local recurrence and increasing tumor control. Maximal survival advantage can be obtained with adequate doses of radiotherapy. However, despite this advantage mean survival differs between 1 to 2 years and there is almost no surviving patient in the long term (Shapiro et al., 2012; Clark et al., 2014).

Despite advancements in neurosurgery with neurological imaging and in chemotherapy with novel agents and radiotherapy techniques, recurrence is observed in more than 50% of patients within 1-2 years because of the infiltrative nature of glial tumors. Clinical and autopsy studies conducted report that more than 80% of recurrences develop within the area at 2 cm distal to gross tumor. Surgery or chemotherapeutic agents is the first administered salvage treatment in patients who develop recurrence. Surgery can be performed in limited cases due to high risk of morbidity and infiltrative nature of the tumor. Whereas the use of chemotherapy agents can also be limited because of bone marrow suppression. This increases the efforts to seek for more effective new chemotherapeutic agents and radiotherapy techniques in treatment of recurrences (Shapiro et al., 2012; Clark et al., 2014; Kirkpatrick and Sampson, 2014).

Because re-irradiation would increase late radiation damage (toxicity) like radionecrosis in recurrence, there are no prospective studies previously conducted on this subject. With newly developed RT techniques, imaging modalities better determining the target and understanding better tolerance dose of the brain, re-irradiation has become a current issue again (Shapiro et al., 2012). Therefore, clinical radiotherapy techniques providing optimal tumor control with minimal radiation damage have gained importance. Since GBM is a radioresistant tumor; re-irradiation (conformal RT, brachytherapy, fractionated stereotactic RT and radiosurgery) combined with radiosensitizers, altered fractionation or localized dose escalation have gained currency. There is still not a

standard therapeutic approach in the studies because of quite different techniques used in re-irradiation, various dose intervals and volumes applied (Ballangrud et al., 2011; Shapiro et al., 2012; Kirkpatrick and Sampson 2014). The most crucial criteria in toxicity related to RT include dose, volume and the period between two cures. It has been reported that, no increase was observed in the incidence of radionecrosis up to the total cumulative dose of 100 Gy.

Today effectiveness of various targeted agents is being investigated for use concurrently with radiotherapy in re-irradiation. In the clinical trials conducted in patients with high-grade glial tumors, bevacizumab showed efficacy against these tumors, positively affected the neurological functions of patients and either did not change or improved quality of life. While survival advantage of bevacizumab has been demonstrated in previous studies, it has been recognized as a part of both the standard treatment and concurrently administered RT in recurrent GBM (Ballangrud et al., 2011; Shapiro et al., 2012; Kirkpatrick and Sampson, 2014).

In conclusion; malignant gliomas are progressive brain tumors. Quick introduction of effective and reliable treatments in recurrence is of benefit when assessing patient with malignant glioma. Although there is still not a standard therapeutic approach in terms of the total dose, fractionated dose and treatment volumes in re-irradiation, total cumulative dose can be given up to 100 Gy. In addition, combining RT with bevacizumab and/or temozolomide increases rate of response to treatment. Treatment planning in these patients should be made considering the risk for tissue necrosis, mental damage and late radiation damage (toxicity) related to the side effects of previously received radiotherapy and chemotherapy.

References

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