



Is the Role of Whole-Brain Radiation Therapy Changing in the Era of Radiosurgery

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Keywords

Brain metastases; whole brain radiationtherapy; Radiosurgery

Short Communication

Brain metastases are the most common brain tumors in adults, developing in about 10% – 40% of adult cancer patients [1]. Lung cancer, melanoma, breast cancer, colorectal cancer, and renal cell cancer are the most common sources of brain metastases [2]. The aims of treatment are palliation of neurological symptoms, maintenance of Performance Status (PS), and local control of metastatic disease [3]. Whole Brain Radio Therapy (WBRT) is commonly used in order to improve neurological symptoms in multiple brain metastases and control the disease with in the brain [1,2,4-6]. Stereotactic radiosurgery is a good option for oligometastatic brain lesions and metastasectomy is also a treatment option especially to patients with favorable survival prognosis [5,7,8]. However, selection of local treatment only or WBRT depends on the performance of the patient, number of brain metastases and histology [9]. The benefit of radiosurgery is reduction of radiation to surrounding normal brain parenchyma, which may thereby reduce neurological toxicities when compared to WBRT or which may improve local control when used in conjunction with WBRT [3,5,10].

Regarding the histology of tumor, brain metastases prognosis differs and significance of WBRT is crucial. In the study of Greenspon et al. Including 167 non-small cell lung cancer patients with brain metastasis WBRT was the lowest, and Gamma Knife (GK)-only had a higher survival than the combined arm [11]. In another study including 720 lung cancer patients with brain metastasis, the GK-alone arm had a better survival than the combined arm, which was statistically in significant [12]. Incases of wild-type *EGFR* and *ALK* NSCLC, there are few effective systemic options, and therefore WBRT may have a more prominent role. Despite the current trend of preferring SRS alone, we need to carefully consider the important role of WBRT, especially for patients with brain metastases from NSCLC who have a favorable prognosis [13].

The median OS was highest among patients with breast cancer, compared to lung and other types of cancers [14,15]. In the study of Miller including 547 patients with breast cancer and brain metastasis, the median survival was not enhanced by hormone therapy in cases with positive hormone receptor (15.3-13.9 months, p=0.21). Use of both HER2 antibody drugs (17.9 vs. 15.1 months; p=0.04) and HER2/EGFR TKIs (21.1-15.4 months; p=0.03) increased the survival. Molecular sub types are prognostic for survival and determinant for the response to radiotherapy [16]. The used agents were believed to contribute to patients with breast cancer Page et al. Reported the median Over all Survival (OS) was 7.1 months for colorectal cancers [17]. The median OS was 12.8 months in patients with brain metastases for renal cell cancer, [18]. In the other studies, patients with melanoma had the shortest median OS [14,15]. The limitations were the small number of patients with brain metastases for breast, colorectal, urogenital cancer, melanoma in this cohort of patients.

Evidence based guide lines developed by multiple professional societies have established a role for whole brain radio therapy in the setting of multiple brain metastases. The limitation of WBRT is the four and six months decline in patient reported quality of life and deterioration of cognitive effects. To prevent these adverse effects of therapeutic and prophylactic cranial irradiation Intensity Modulated Radiotherapy (IMRT) have been developed to avoid conformally the hippocampal neural stem cell niche during WBRT often referred to hippocampal avoidance WBRT (HA-WBRT). In RTOG 0933 deterioration in 4 months was 19% comparing favorably with the former radiosurgery

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Received Date: 31 Mar 2018

Accepted Date: 27 Apr 2018

Published Date: 30 Apr 2018

Citation:

Baltalarlı B, Sagıncı H. Is the Role of Whole-Brain Radiation Therapy Changing in the Era of Radiosurgery. *Clin Surg*. 2018; 3: 1953.

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series. Building on the results of these studies National Cancer Institute approved phase II trial that will evaluate the potential combined neuro protective effects of hippocampal avoidance and prophylactic mement in enduring WBRT for brain metastases [19].

Despite the current trend of preferring SRS alone, we need to carefully consider the important role of WBRT, especially for NSCLC patients who have a favorable prognosis. These findings should be validated through prospective studies, not only for NSCLC but also for other primary cancers. In addition, further investigations targeting WBRT methods and drugs to preserve brain functions that result in less cognitive impairment with a reliable and durable neuro cognitive end point after treatment are warranted.

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