RESEARCH ARTICLE

Hippocampal Sparing Whole Brain Radiotherapy and Integrated Simultaneous Boost vs Stereotactic Radiosurgery Boost: A Comparative Dosimetric Planning Study

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Abstract

Background: Whole brain radiotherapy (WBRT) and stereotactic radiosurgery were frequently used to palliate patients with brain metastases. It remains controversial which modality or combination of therapy is superior especially in the setting of limited number of brain metastases. The availability of newer medical therapy that improves survival highlighted the importance of reducing long term radiation toxicity associated with WBRT. In this study, we aim to demonstrate the hippocampal sparing technique with whole brain and integrated simultaneous boost Materials and Methods: Planning data from 10 patients with 1-5 brain metastases treated with SRS were identified. Based on the contouring guideline from RTOG atlas, we identified and contoured the hippocampus with 5mm isocentric expansion to form the hippocampal avoidance structure. The plan was to deliver hippocampal sparing whole brain radiotherapy (HSWBRT) of 30 Gy in 10 fractions and simultaneous boost to metastatic lesions of 30 Gy in 10 fractions each. Results: The PTV, hippocampus and hippocampal avoidance volumes ranges between 1.00 – 39.00 cc., 2.50 – 5.30 cc and 26.47 – 36.30 cc respectively. The mean hippocampus dose for the HSWBRT and HSWBRT and SIB plans was 8.06 Gy and 12.47 respectively. The max dose of optic nerve, optic chiasm and brainstem were kept below acceptable range of 37.5 Gy. Conclusions: The findings from this dosimetric study demonstrated the feasibility and safety of treating limited brain metastases with HSWBRT and SIB. It is possible to achieve the best of both worlds by combining HSWBRT and SIB to achieve maximal local intracranial control while maintaining as low a dose as possible to the hippocampus thereby preserving memory and quality of life.

Keywords: Hippocampal sparing - simultaneous integrated boost - whole brain radiotherapy - brain metastases -

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Introduction

Whole brain radiotherapy (WBRT) was initially introduced in the 1950s and frequently utilized as a form of palliative treatment for patients with brain metastases otherwise only treated symptomatically. This modality became a key component among patients with metastatic brain lesions as a result of improved survival outcome. Stereotactic radiosurgery (SRS) has been utilized upfront in limited brain metastases instead of WBRT owing to concerns of neurocognitive impairment. Recently, phase II results of RTOG 0933 has shown that hippocampal sparing WBRT (HSWBRT) technique led to significant improvements in memory preservation. Central to this belief was the presence of radiosensitive neural stem cells in the subgranular zone of the hippocampal dentate gyrus which may lead to neurocognitive function (NCF) impairment specifically short term memory function. In this study, we aim to demonstrate the hippocampal sparing technique with whole brain and integrated simultaneous boost.

Materials and Methods

The planning CT and MRI data from 10 patients with 1-5 brain metastases treated with SRS were identified. We then contoured the hippocampus based on the contouring guideline from RTOG atlas with 5mm isocentric expansion to form the hippocampal avoidance structure. Our aim was to deliver hippocampal sparing whole brain radiotherapy of 30 Gy in 10 fractions and simultaneous boost to metastatic lesions of 30 Gy in 10 fractions each. Based on isoeffective LQ model, we calculated our dose/fractionation for brain metastases as 60 Gy in 10 fractions (BED 78 Gy10 or 150 Gy2).

Dosimetric planning was completed using Tomotherapy® planning station 4.2.3.9 and all dose constraints were within acceptable limits of RTOG 0933.

Detailed palnning parameters were as detailed below: *i*). Fan beam thickness: 1 or 2.5 cm, *ii*). Pitch: 0.214, *iii*). Modulation factor: 3.5, *iv*). Normal calculation grid: 0.468 mm^3.

Subsequently, dosimetric parameters as below were

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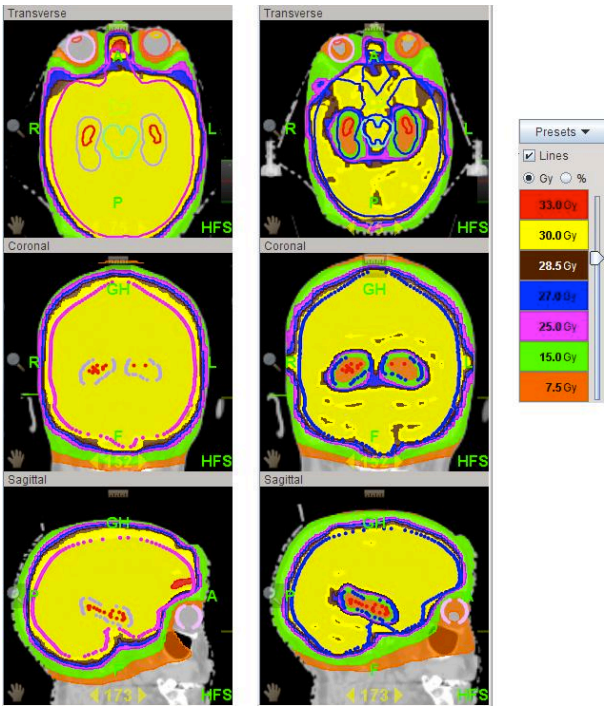

Figure 1. Representative HSWBRT Axial Isoose Distributions. The dark blue lines represent the hippocampal avoidance volume

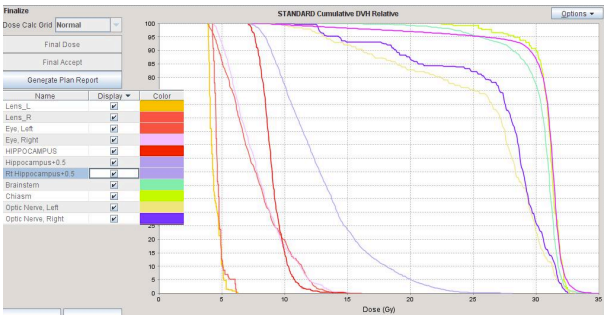

Figure 2. Representative Cumulative DVH for HSWBRT Plan

Table 1. Volumes in cc.

	PTV	H	HA	Brain	R*
1	25	4.64	36.3	1721.1	2.11
2	2.7	2.5	28.8	1386.2	2.08
3	1	3.46	30.88	1288.3	2.4
4	2.1	3.67	28.95	1371.3	2.11
5	39	5.3	35.96	1570.1	2.29
6	5.3	4.9	34.9	1171.4	2.98
7	29.9	3.12	28.74	1372.55	2.09
8	3.5	3.16	29.1	1492.3	1.95
9	18.7	3.02	27	1668.4	1.62
10	3.94	2.5	26.47	1152.6	2.3

calculated: *i*). PTV V95 Boost, *ii*). PTV V95 Brain, *iii*). Hippocampal maximum dose, *iv*). Hippocampal D100

v). Optic nerve maximum dose, *vi*). Optic chiasm maximum dose, *vii*). Brainstem maximum dose

Results

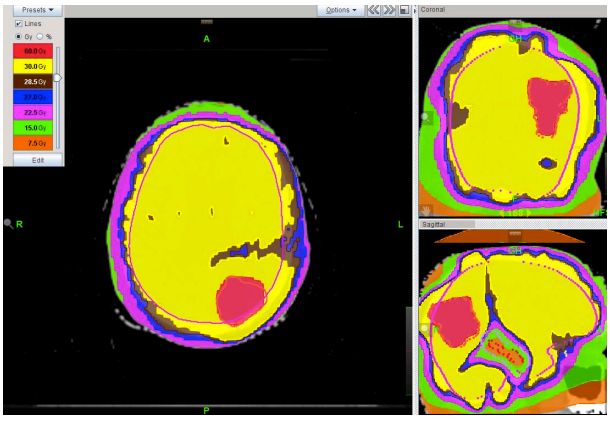

Figure 3. Representative HSWBRT + SIB axial isodose distributions. The dark blue lines represent the hippocampal avoidance volume

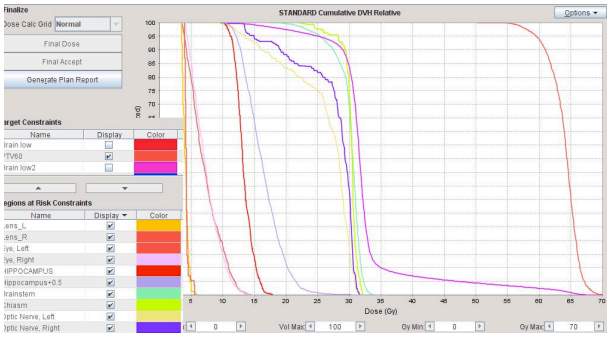

Figure 4. Representative Cumulative DVH for HSWBRT + SIB Planning

Table 2. Dosimetric Data for HSWBRT

Dosimetric parameter	Mean	Range
Dmax	35.02	33.40 – 38.77
PTV D95	28.61	27.70 – 29.80
Hippocampal max dose	14.11	12.70 – 14.90
Hippocampal D100	7.5	6.50 – 8.79
Hippocampal mean dose	8.06	8.11 – 9.75
Optic nerve max dose	32.65	30.65 – 36.41
Optic chiasm max dose	32.39	31.66 – 33.59
Brainstem max dose	33.23	32.22 – 36.18

Table 3. Dosimetric Data for HSWBRT + SIB

Dosimetric parameter	Mean	Range
Dmax	67.82	63.00 – 72.33
PTV D95	58.81	50.90 – 65.40
Hippocampal max dose	18.01	15.41 – 23.50
Hippocampal D100	10.43	8.10 – 11.60
Hippocampal mean dose	12.47	9.42 – 14.50
Optic nerve max dose	33.75	31.06 – 36.86
Optic chiasm max dose	33.85	32.16 – 37.30
Brainstem max dose	34.45	32.08 – 36.94

Table 1 shows the volumes of the planning target volume (PTV), hippocampus, hippocampal avoidance, brain and ratio of hippocampal avoidance to brain. The volume of PTV ranges between 1.00 - 39.00 cc. The hippocampus and hippocampal avoidance volume ranges between 2.50 - 5.30 cc and 26.47 - 36.30 cc respectively. The ratio of the avoidance volume to whole brain volume does not exceed 3%.

Table 2 - 3 shows the volumes and outcomes for

HSWBRT and HSWBRT + SIB plans, including the mean dose and dose range for PTV, hippocampus, optic nerve, optic chiasm and brainstem. For the HSWBRT plans, the mean hippocampus dose was 8.06 Gy. The mean PTV D95 was 28.61 Gy. For the HSWBRT + SIB plans, the mean hippocampus dose was 12.47 and PTV D95 was 58.81 Gy. The max dose of optic nerve, optic chiasm and brainstem were kept below acceptable range of 37.5 Gy.

Representative axial isodose distributions and corresponding DVH for HSWBRT are shown in Figure 1 and 2 respectively. Figure 3 and 4 demonstrate representative axial isodose distributions and corresponding DVH for HSWBRT + SIB.

Discussion

Both WBRT and SRS played important roles in management of brain metastases. An IPD meta analysis of SRS with or without WBRT for 1 to 4 brain metastases has demonstrated improved local and distant control although there was no significant overall survival benefit. However, recent secondary analysis of the JROSG 99-1 RCT demonstrated improved survival for patient s with DS GPA of 2.5-4.0 with combined WBRT and SRS. It is possible to achieve the best of both worlds by combining HSWBRT and SRS to achieve maximal local intracranial control while maintaining as low a dose as possible to the hippocampus thereby preserving memory and quality of life. However, based on the above results, patient selection based on DS GPA and availability of effective systemic therapy is important to achieve survival benefit.

The feasibility of hippocampal sparing depended on several factors. Based on the RTOG contouring guideline, we were able to demonstrate that the hippocampal avoidance volume only consisted of a small volume of the total brain/CNS volume. Studies to assess the likelihood of hippocampal metastases also showed that only a small number of metastases occur in this region even for small cell lung carcinoma. The possible explanation for this phenomenon may be due to limited vascular distribution or different local microenvironment leading to relative sparing of this region deemed appropriate for hippocampal sparing techniques.

The introduction of effective systemic therapy especially targeted therapy has also changed the landscape of treatment of brain metastases. Some of these agents including immunotherapy has shown good and prolonged responses. Availability of disease specific graded prognostic assessment helps to guide the treating physician to choose the most appropriate treatment.

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