Leukoencephalopathy After Whole Brain Radiation Therapy Plus Radiosurgery Versus Radiosurgery Alone for Metastatic Melanoma to the Brain

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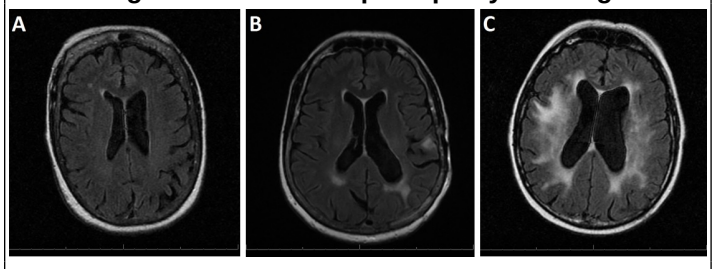
Introduction

Stereotactic radiosurgery (SRS) has proven a safe and effective alternative to whole-brain radiation therapy (WBRT) for the treatment of brain metastases[1]. WBRT has been linked to the delayed toxicity of leukoencephalopathy and cognitive dysfunction involving domains such as mood, memory, and executive function[2]. Advancements in systemic therapies for melanoma have prolonged patient survival and increased awareness of the delayed effects of therapy[3]. This study aims to evaluate the risk of leukoencephalopathy in patients receiving SRS with WBRT versus SRS alone in patients with brain metastases from melanoma.

Methods

We retrospectively compared 49 patients with metastatic melanoma to the brain who underwent SRS alone to 14 patients who received both WBRT and SRS who survived at least one year from initial treatment and had evaluable imaging. Leukoencephalopathy was graded on T2 and FLAIR sequences: (A) little or no increased signal change; (B) limited periventricular hyperintensity; and (C) diffuse white matter hyperintensity (Fig. 1).

Figure 1. Leukoencephalopathy Grading



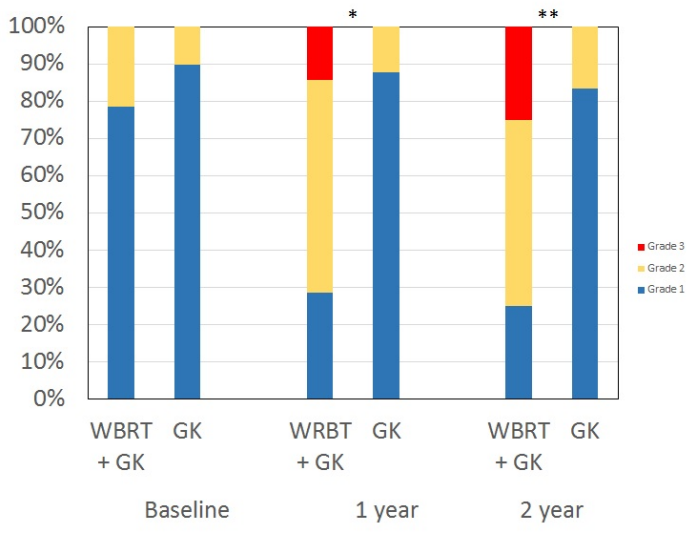
This figure shows representative FLAIR MRI images of a patient's brain at the time of WBRT with grade 1 findings, and following the development of grade 2 and 3 leukoencephalopathy at one and two years following treatment for brain metastases.

Table 1. Baseline Characteristics

	WBRT + SRS *n = 14*	SRS Only *n = 49*	p-value
Age, Mean (standard deviation)	59.7 (13.3)	57.9 (11.7)	0.615
Male	10 (71.4%)	34 (69.4%)	1.000
Prior chemotherapy	7 (50.0%)	15 (30.6%)	0.306
Prior extracranial radiation	0 (0.0%)	6 (12.2%)	0.390
n SRS treatments, Median (range)	1 (1-4)	2 (1-9)	0.015 *
n Mets treated at initial SRS, Median (range)	3 (1-11)	1 (1-8)	0.067
Gross tumor volume initially treated, cc Median (range)	2.8 (0.2-18.5)	1.5 (0.03-24.3)	0.417
Marginal SRS dose, Gy Median (range)	16 (15-20)	20 (14-22)	0.0002 *
Proximity of baseline MRI to treatment, mo Median (range)	0.8 (-0.7-4.4)	0.0 (-1.0-2.8)	0.145
Time to first graded imaging, mo Median (range)	11.2 (6.8-20.2)	12.2 (9.6-14.9)	0.203
Time to second graded imaging, mo Median (range)	23.9 (21.4-29.2)	24.4 (22.7-29.4)	0.712

* Statistically significant

Figure 2. White Matter Change in WBRT + SRS vs. SRS Only



Graph depicts changes in leukoencephalopathy grades between patients treated by WBRT + SRS vs. SRS only as a percentage of surviving patients. *1 year: p<0.0001; **2 year: p = 0.0458

Results

At the time of initial treatment the median leukoencephalopathy grades for SRS-only and combined therapy were 1 for both groups (p=0.36). At one year imaging follow-up, progression of leukoencephalopathy was seen in one patient (2%) receiving SRS alone. Sixty-four percent of patients receiving WBRT and SRS demonstrated evidence of leukoencephalopathy one year after treatment to grade 2 (p<0.0001). Two patients (14.3%) receiving WBRT and SRS progressed to grade 3 changes at one year. At the two year imaging follow-up, only 3 patients in the SRS only group demonstrated any changes in leukoencephalopathy grade from baseline, while 50% of patients treated with a combined regimen demonstrated grade 2 changes and another 25% demonstrated grade 3 changes.

Conclusions

Brain metastases from metastatic melanoma are radioresistant and WBRT is thus less effective. Moreover, this study demonstrates that there is a significantly increased risk of leukoencephalopathy following WBRT that can be avoided when patients are treated with SRS alone. These data support a re-evaluation of the reflexive, upfront use of WBRT in patients with melanoma brain metastases in light of evidence of delayed neurotoxicity and improved survival due new systemic therapies.

Learning Objectives

By the end of this session, participants should be able to:

1) discuss the delayed toxicities of WBRT
2) identify the WBRT-related leukoencephalopathy that is prevented through the use of SRS in brain metastases treatment.

References

1. Liew et al. *J. Neurosurg.* **2011**, *114*, 769.
2. Chang et al. *Lancet Oncol.* **2009**, *10*, 1037.
3. Knisely et al. *J. Neurosurg.* **2012**, *117*, 227.