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Nearly Half of Metastatic Brain Disease Patients Prescribed 10 Fractions of Whole-Brain Radiation Therapy Die Without Completing Treatment

To the Editor

Since 1954, whole-brain radiation therapy (WBRT) has been an integral palliative treatment modality for brain metastases.[1] For over 40 years, the standard palliative WBRT regimen in the U.S. has been 30 Gy in 10 fractions over two weeks, although shorter regimens have been reported.[2-4] Although prolonged (≥10 fractions) WBRT regimens have historically been favored owing to a perceived improvement in neurocognitive side effect profile, hypofractionated WBRT is equally effective for disease control[2,3] and reduces the burden of prolonged treatment on patients and caregivers near the end of life. In addition, some patients cannot finish planned WBRT owing to declining performance status; however, the likelihood of failing to complete standard-fractionation WBRT has not been rigorously evaluated. To address this void, the following analysis was performed to allow for improved objective quantifying of this commonly used palliative modality.

Methods

An IRB-approved prospective institutional database identified 52 patients receiving WBRT (30 Gy/10 fractions) for brain metastases between April 2015 and December 2018. Functional independence was defined as Karnofsky Performance Status (KPS) ≥70; 30-day

Table 1
Clinical Characteristics of Patients Who Did Versus Did Not Complete WBRT

Patient Demographic	Failed WBRT Completion (*n* = 23)	Completed WBRT (*n* = 29)	*P*-value
Age (mean)	58.0	58.2	0.966
Male	11 (47.8%)	11 (37.9%)	0.576
Female	12 (52.2%)	18 (62.1%)	
Inpatient	14 (60.1%)	12 (41.4%)	0.264
Outpatient	9 (29.9%)	17 (58.6%)	
KPS ≥ 70	4 (17.4%)	13 (44.8%)	0.043
Death within 30 days of final fraction	16 (69.6%)	9 (31.0%)	0.011

WBRT = whole-brain radiation therapy; KPS = Karnofsky Performance Status.

mortality was defined as death within 30 days immediately after final radiation treatment. Statistical analyses were performed in SPSS version 24 (IBM Corp., Armonk, NY). $P < 0.05$ was considered statistically significant.

Results

Of 52 patients who began WBRT, 29 (55.8%) completed prescribed therapy; demographics are depicted in Table 1. Patients completing WBRT were significantly more likely to be functionally independent at baseline and had lower 30-day mortality. Mean treatment duration for patients completing WBRT was 15.3 days. Of the 23 patients failing to complete standard WBRT, 30-day mortality was nearly 70%.

Discussion

Brain metastases carry a poor prognosis; median survival after WBRT is three to four months.[2,3,5] However, this relatively long anticipated survival after WBRT has historically provided practitioners with confidence that prolonged treatment regimens will not adversely affect QOL. Our results indicate this widespread presumption may be incorrect. The large minority (nearly 50%) of patients prescribed standard 10-fraction WBRT who died without completing treatment suggests that a large subset of this patient population may not live as long as generally presumed. Consequently, adjustments to clinical practice of both prescribing and requesting WBRT should be considered, particularly because the data originally establishing 10-fraction WBRT as the standard of care demonstrated no significant difference in survival or local control between 30 Gy in 10 fractions, 20 Gy in five fractions, and 10 Gy in one fraction.[2-3] In addition, Level I evidence has demonstrated no neurocognitive advantage of prolonged WBRT.[6] For the significant proportion of WBRT patients with less than four weeks to live, any reduction in treatment time represents a meaningful reduction in the rigors of

daily traveling for a treatment that confers no survival advantage over shorter schedules.

Furthermore, the modern WBRT patient population is likely enriched for poor-KPS patients and those with a larger disease burden, as more favorable patients (i.e., those with oligometastatic disease) are increasingly likely to receive stereotactic radiosurgery instead. Median survival after WBRT in the modern era may therefore actually be shorter compared with historical data collected before stereotactic radiosurgery was considered standard of care for good KPS patients with one to three brain metastases.

Limitations of this study include its small sample size, retrospective nature, and single-institution source of data, each of which independently limit the scope of our conclusions. However, the relative standardization of WBRT practice increases the applicability of our findings.

Conclusions

Over 40% of patients prescribed standard 10-fraction WBRT regimens are unable to tolerate the full duration of treatment. With nearly half of patients dying within 30 days of standard 10-fraction WBRT, hypofractionated (i.e., one- or five-fraction) regimens may reduce the physical and financial burden of treatment on this population and should be strongly considered by clinicians, especially in poor-performance status patients.

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Disclosures and Acknowledgments

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