Purpose/Objective(s): Cell-cycle progression follows a circadian time structure that causes a nonlinear pattern of radiosensitivity. We examined outcomes of single-treatment GKRS for early (>10:00am <12:30pm) vs. late (>12:30pm <3:00pm) treatment times.

Materials/Methods: Fifty-eight pts. had early (<12:30pm) and 39 pts. had late (>12:30pm) GKRS between 1989 and 2008. RTOG Recursive Partition Analysis (RPA) categorization showed 23 pts. in class I, 72 pts. in class II, and 2 pts. in class III. Fifty-five pts. had a single met treated and 42 pts. had multiple mets treated. Prior whole-brain radiotherapy (WBRT) was used in 64 pts. The histology of the NSCLC was adenocarcinoma in 46, squamous cell carcinoma in 17, large cell carcinoma in 7, and unclassified NSCLC in 27 pts. The mean peripheral GKRS dose was 18.6 Gy. The mean tumor vol. was 7.3cc. MRI was used to score local control (LC) at 3 months. Cause of death (COD) was categorized as central nervous system (CNS, e.g. neurologic disease progression, stroke, brain death) or systemic (e.g. lung disease progression, extracranial disease progression).

Results: Demographic characteristics of the early vs. late treatment groups were found to be similar by Chi-square analysis (for categorical data) and Wilcoxon rank sum tests (for continuous data) in terms of gender, RPA class, KPS, cystic tumors, primary control, extra-cranial mets, prior WBRT, prior steroids, prior lung RT, histologic type, age, time from primary diagnosis to brain mets, time from brain met diagnosis to GK, no. of mets, no. of mets treated, total vol. of mets, vol. of largest met, vol. treated, and peripheral dose. LC at 3 months was achieved in 97% (35/36 pts.) with early GKRS compared to 75% (8/12 pts.) with late GKRS (Chi square, \( p = .014 \)). Early GKRS was associated with better post-GK survival (median = 9.5mo.) compared to late GKRS (median = 5mo.) (Kaplan-Meier log-rank, \( p = .025 \)). Factors contributing to a better survival in a Cox regression model included early treatment time (\( p = .004 \)) and RPA class (\( p < .001 \), but not gender (\( p = .11 \)), prior WBRT (\( p = .33 \)), total tumor vol. (\( p = .56 \), or peripheral dose (\( p = .28 \)). COD was cited in the early group as CNS-related in 6% (3/47 pts.) and systemic in 94% (44/47 pts.), whereas in the later group it was CNS-related in 24% (8/34 pts.) and systemic in 76% (26/34 pts.) (Chi square, \( p = .026 \)).

Conclusions: GKRS for mets of NSCLC resulted in poorer LC, worse survival, and more frequent CNS-related COD when given between 12:30pm and 3:00pm when compared to earlier times. These retrospective data should be considered hypothesis-generating and thereby alert clinicians to examine for a treatment time effect in other brain RS series and possibly in non-CNS treatment with SBRT.

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