

Stereotactic Radiosurgery for Central Nervous System Parenchymal Metastases: Prognostic Factors for Survival



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Purpose/Objective:

To determine factors independently predicting for improved or worsened survival in patients who presented for their first treatment with Gamma Knife stereotactic radiosurgery (SRS) for brain metastases.

Methods:

Data were abstracted from hospital records and the Connecticut Tumor Registry on 334 patients with parenchymal central nervous system (CNS) metastases treated with initial SRS between 1998 and 2004. A multivariate analysis was used to identify factors independently affecting survival. Analyzed variables included age, sex, race, histology, systemic disease control, number of metastases, total volume and location of metastases, the use of surgical resection, the use of whole-brain radiation therapy (WBRT), and the use of chemotherapy before and after SRS.

Table 1: Cox Regression Survival Analysis – entire cohort

Variable	Unadjusted*		Adjusted Multivariate Model**	
	Hazard Ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value
N=334				
Age (years)	1.01 (0.999, 1.02)	0.075	1.01 (0.999, 1.02)	0.091
≥ 4 CNS metastases	1.53 (1.16, 2.01)	0.003	1.50 (1.13, 2.00)	0.005
Total CNS tumor volume <5.0 cc	0.67 (0.52, 0.85)	0.001	0.68 (0.53, 0.88)	0.003
Systemic control	0.47 (0.36, 0.62)	<0.001	0.51 (0.39, 0.67)	<0.001
Breast cancer	0.55 (0.40, 0.77)	<0.001	0.60 (0.43, 0.84)	0.003
Esophageal cancer	2.64 (1.17, 5.98)	0.020	2.24 (0.98, 5.1)	0.055

CI=Confidence interval
 * Unadjusted hazard ratios and P values based on simple Cox regressions.
 ** Adjusted hazard ratios and P values from final multivariate Cox regression model. Overall P<0.001 for final multivariate Cox regression model.
 Note: Hazard ratios <1 indicate a decreased risk of death during any period of observation; conversely, hazard ratios >1 indicate an increased risk of death during any period of observation

The authors report no conflicts of interest

Results:

The age range was 20-87 (median 57.3) years, and 1-36 (median 2) metastases were treated in the first SRS session. Tumor histologies included non-small cell lung cancer (36%), breast (17%), melanoma (16%), small cell lung cancer (8%), renal cell (7%), esophageal (2%), and other (16%). Three-hundred patients (90%) had confirmed deaths, with a median survival after SRS of 8.1 months.

Patients with 1-3 metastases had an improved survival (median 8.5 months) compared to those with ≥4 metastases (median 6.3 months; HR=1.50, p=0.005). In the subgroup with 1-3 metastases, systemic control (HR=0.49, p<0.001), breast cancer (HR=0.57, p=0.003), and total tumor volume <5.0 cc (HR=0.65, p=0.002) were independently associated with increased survival; esophageal cancer (HR=2.36, p=0.042) patients had a decreased survival.

In the ≥4 metastases subgroup, only age <45 years was independently associated with increased survival (HR=0.39, p=0.006), and melanoma (HR=2.32, p=0.008) and use of chemotherapy (HR=2.59, p=0.077) with a decreased survival. Total tumor volume was not significantly different between the 1-3 metastases subgroup (mean = 4.5 cc) versus the 4+ subgroup (mean = 4.9 cc, p=0.458). Race, sex, metastasis location, surgical resection, WBRT before/after SRS, and chemotherapy did not affect survival.

Table 2: Survival Estimates Following SRS for CNS Metastases – entire cohort

Variable	N (%)	Unadjusted*		Adjusted Multivariate Model**	
		Median Survival (months)	P value	Median Survival (months)	P value
Female	185 (55%)	9.2	0.001	#	
Male	149 (45%)	7.3			
1-3 CNS metastases	264 (79%)	8.5	0.003	8.6	0.005
≥4 CNS metastases	70 (21%)	6.3		6.6	
Total CNS tumor volume <5.0 cc	231 (69%)	9.2	0.001	9.1	0.003
Total CNS tumor volume ≥5.0 cc	103 (31%)	6.3		6.8	
Systemic control	98 (29%)	12.9	<0.001	12.4	<0.001
No systemic control	236 (71%)	6.7		7.3	
Breast cancer	56 (17%)	15.7	<0.001	12.0	0.003
Other 1° cancer	278 (83%)	7.7		7.8	
Melanoma	53 (16%)	4.7	0.010	#	
Other 1° cancer	281 (84%)	8.4			
Esophageal cancer	6 (2%)	3.7	0.020	4.2	0.055
Other 1° cancer	328 (98%)	8.1		8.2	

Dropped from multivariate model – not a significant independent predictor of survival

Figure 1: a. Overall Survival after Stereotactic Radiosurgery; b. Survival Stratified by Number of CNS Metastases

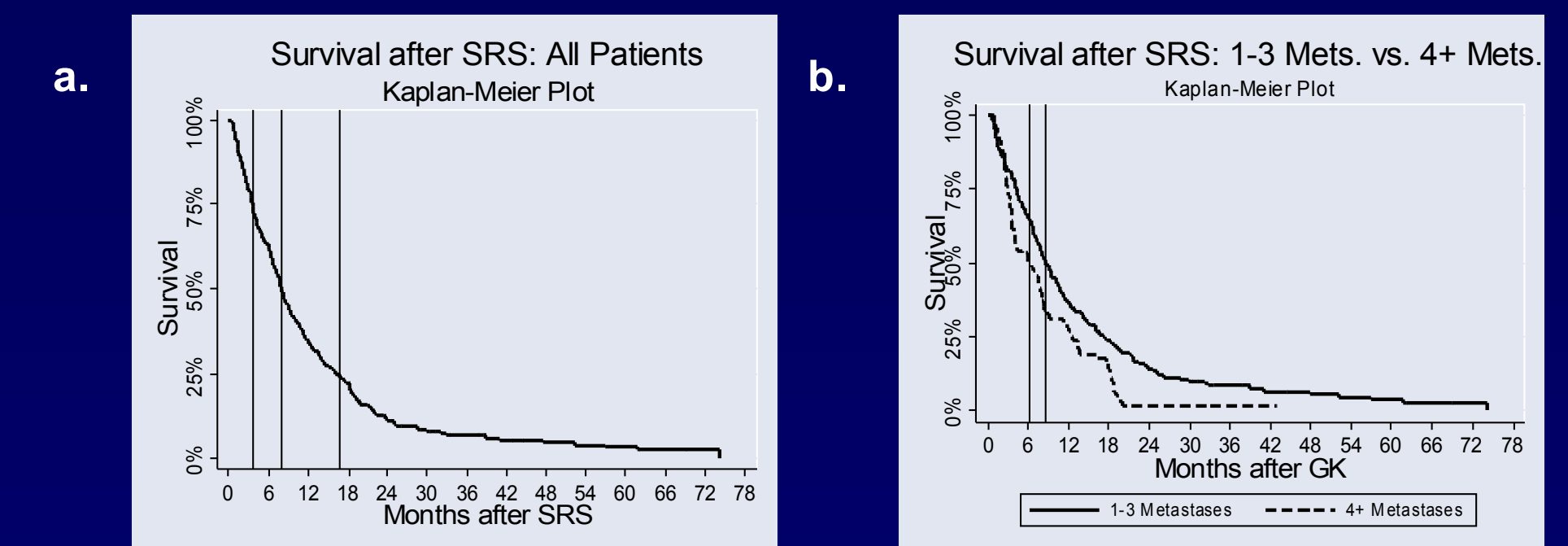
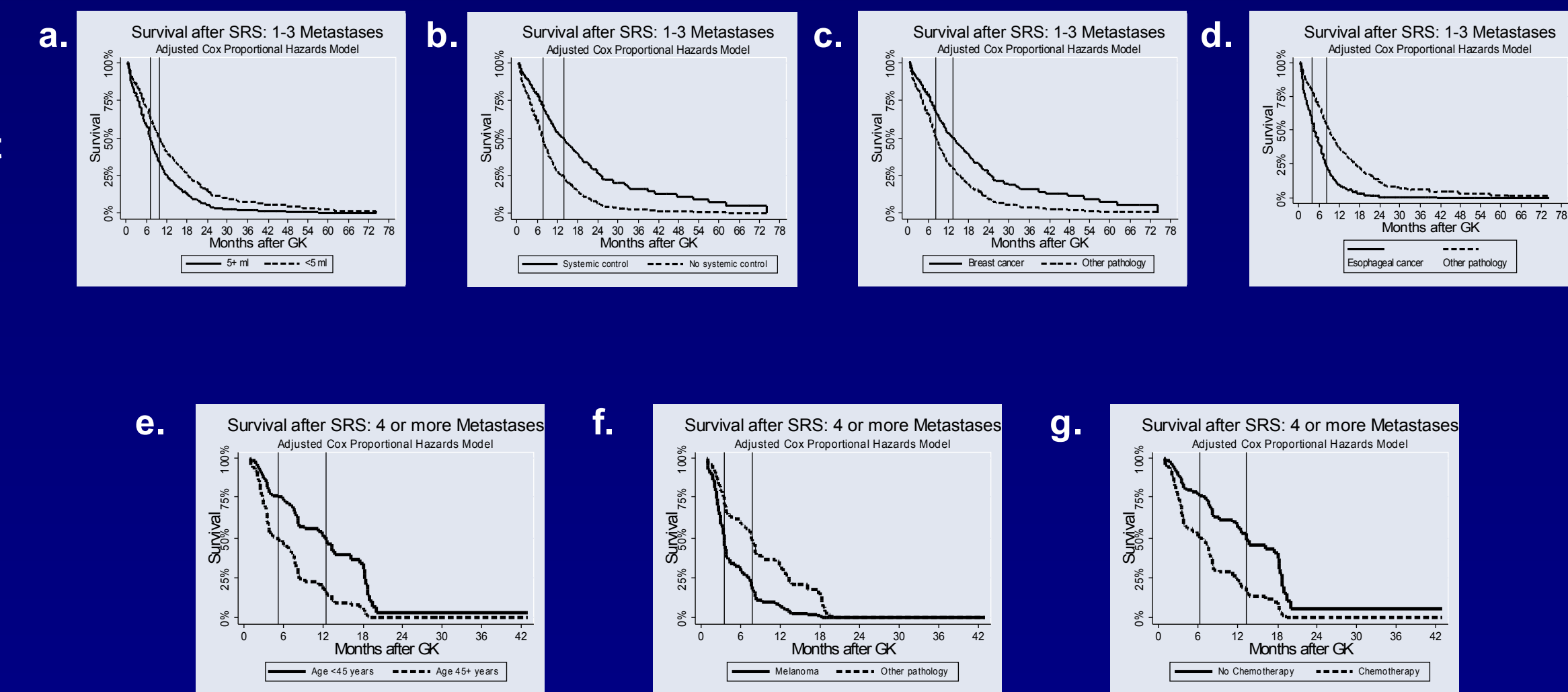


Figure 2: Subgroup Analysis Adjusted Survival—stratified by 1-3 CNS Metastases (a-d) vs. ≥ 4 CNS Metastases (e-g)

a. total tumor volume; b. systemic control; c. breast cancer; d. esophageal cancer; e. age; f. melanoma; g. chemotherapy.



Conclusions:

Despite more than twenty years of experience with SRS, no consensus exists for stratifying patients with CNS metastases for prognostication. Recommendations for individual patients are still based upon therapies developed for populations. Our data suggests that different factors affect outcomes in patients undergoing their first radiosurgical treatment depending on if they present with 1-3 versus 4+ metastases. Inherent genetic differences may exist between the malignancies of patients that present with 1-3 CNS metastases and the malignancies of patients that present with ≥4 CNS metastases.

Identifying informative genetic markers in primary tumors or other metastatic foci may allow predictive, personalized, and pre-emptive care to be delivered to patients with CNS metastases (if and when they develop), and may optimize the use of both WBRT and SRS.

The authors report that there are no financial disclosures or conflicts relevant to this poster communication.