HHS Public Access

Author manuscript

J Radiat Oncol. Author manuscript; available in PMC 2018 November 09.

Published in final edited form as:

J Radiat Oncol. 2018 September ; 7(3): 241–246. doi:10.1007/s13566-018-0353-8.

Stereotactic radiosurgery practice patterns for brain metastases in the United States: a national survey

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Abstract

Background—Stereotactic radiosurgery (SRS) has emerged as an important modality for the treatment of intracranial metastases. There are currently few established guidelines delineating indications for SRS use and fewer still regarding plan evaluation in the treatment of multiple brain metastases.

Methods—An 18 question electronic survey was distributed to radiation oncologists at National Cancer Institute (NCI) designated cancer centers in the USA (60). Centers without radiation oncologists were excluded. Physicians who indicated that they do not prescribe SRS were excluded from the remaining survey questions. Sign test and Chi-square test were used to determine if responses differed significantly from random distribution.

Results—One hundred sixteen of the 697 radiation oncologists surveyed completed the questionnaire, representing 51 institutions. Sixty-two percent reported treating patients with brain metastases using SRS. Radiation oncologists prescribing SRS most commonly treat CNS (66.2%) and lung (49.3%) malignancies. SRS was used more frequently for < 10 brain metastases (73.7%; $p < 0.0001$) and whole brain radiation therapy (WBRT) for > 10 brain metastases (82.5%; $p < 0.0001$). The maximum number of lesions physicians were willing to treat with SRS without WBRT was 1–4 (40.4%) and 5–10 (42.4%) ($p < 0.0001$ compared to 11–15, 16–20 and no limit). The most important criteria for choosing SRS or WBRT were number of lesions ($p < 0.0001$) and performance status ($p = 0.016$). The most common margin for SRS was 0 mm (49.1%; $p = 0.0021$). The most common dose constraints other than critical structure was conformity index (84.2%) and brain V12 (61.4%). The LINAC was the most common treatment modality (54.4%)

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent is not required. This is approved by our institutional IRB.

and mono-isocenter technique for multiple brain metastases was commonly used (43.9%; p = 0.23). Most departments do not have a policy for brain metastases treatment (64.9%; p = 0.024).

Conclusions—This is one of the first national surveys assessing the use of SRS for brain metastases in clinical practice. These data highlight some clinical considerations for physicians treating brain metastases with SRS.

Keywords

SRS; Stereotactic radiosurgery; Brain metastases; Practice patterns

Introduction

Brain metastases are a significant cause of morbidity and mortality among oncologic patients, affecting 20–40% of this population [1]. Several therapeutic strategies for intracranial metastases exist, including stereotactic radiosurgery (SRS), whole brain radiotherapy (WBRT), surgical resection, and supportive care with steroids, though systemic therapy remains an option for patients with selected cancers [2]. WBRT was historically the treatment modality of choice for brain metastases with or without surgical resection [3, 4]. Technological improvements in Gamma Knife and LINAC-based SRS coupled with data indicating decreased cognitive toxicity with SRS [5] have led to increased utilization of SRS [6]. Although evidence-based clinical practice guidelines exist for the use of SRS for brain metastases [7–12], there are comparatively fewer reports that study specific aspects of SRS plan evaluation or if current use reflects the recommendations of professional societies. In that context, the current study represents one of the few national surveys which specifically investigates these issues to clarify the role of SRS for intra-cranial metastases in clinical practice.

Materials and methods

Study design

An 18 question, non-incentivized electronic survey was distributed to radiation oncologists at National Cancer Institute designated cancer centers in the USA (60). Centers without radiation oncologists were excluded. The total number of physicians contacted was 697. Physicians who reported not prescribing SRS were not invited to complete remaining survey questions. Per institutional policy, this study was IRB-exempt.

Statistical analysis

Depending on type of question, 95% confidence interval (estimate of proportion), sign test (difference from expected mean), or Chi-square test (difference from expected distribution) were used to determine if responses differed significantly from random distribution. All data analyses were completed using Stata software and a p value < 0.05 was considered to be statistically significant.

Results

Response and demographic data

All survey results are reproduced in Table 1. Of 697 physicians surveyed, 118 (16.9%) responded, with 28.7% reporting that they do not treat brain metastases with SRS. Respondents represented 51 different institutions across 28 states with varying years of practice experience.

Indications and use in practice

Respondents primarily treated CNS (66.2%, 95% CI [54–77%]); lung was numerically the second most commonly treated disease site (49.3%). SRS (73.7%) was used more frequently than WBRT (10.5%) for < 10 brain metastases ($p < 0.0001$) while WBRT (82.5%) was used more frequently than SRS (5.3%) for ≥ 10 brain metastases ($p < 0.0001$). The maximum number of lesions physicians were willing to treat with SRS without WBRT in the treatment session was 1–4 (40.4%) and 5–10 (42.4%) ($p < 0.0001$; compared to 11–15, 16–20, and no limit). Most physicians reported they would not treat more than 10 lesions over multiple sessions with SRS (43.9%; $p = 0.0003$) but 19.3% reported there was no limit to the number they would treat. Physicians indicated that their practice had changed in the past 5 years by more frequently using SRS without WBRT (84.2%) and SRS without other treatments (i.e., surgery or WBRT; 82.5%). Criteria used to determine SRS versus WBRT use were number of lesions ($p < 0.0001$), histology ($p = 0.0014$), performance status ($p = 0.016$), and location ($p < 0.0001$) as determined by sign test. Leptomeningeal disease was statistically significant versus all other choices as the predominant contraindication to prescribing SRS without WBRT (93%; CI [83–98%]).

Treatment modality and planning

LINAC (54.4%) was more commonly used than the CyberKnife (14.0%) or Gamma Knife (31.6%) for SRS treatment ($p = 0.0009$). The mono-isocenter technique for multiple brain metastases was commonly used (43.9%; $p = 0.23$). The most common margin for SRS was 0 mm (49.1%; $p = 0.0021$), with 38.6 and 12.3% prescribing a 1- and 2-mm margin, respectively. The most common dose constraints other than critical structure were conformity index (84.2%) and V12 (61.4%). Diameter, volume, and histology of lesion were all ranked as significant in determining the SRS prescription dose (sign test, $p < 0.0001$, $p = 0.001$, and $p < 0.0001$, respectively). Notably, most departments do not have a policy in place for treating brain metastases with SRS (64.9%; $p = 0.024$).

Discussion

Despite increasing use of SRS to treat brain metastases, little exists in terms of guidance for physicians using this modality. Moreover, our data indicate that most departments do not have policies governing SRS use. Importantly, no clear guidelines exist regarding the maximum number of metastases for which SRS is recommended, despite a historically used cutoff of 4 in clinical trials [5, 13, 14]. In this study, 42.4% of respondents reported using SRS for patients with 5–10 metastases and 17.5% of respondents offering it for more than 10 lesions without WBRT. Thus, a significant number of respondents are using SRS for more

than the standard 4 lesions. In total, 73.7% of respondents reported using SRS more often for < 10 metastasis, and 82.5% used WBRT more often for > 10 lesions. These physicians may be influenced by a shifting paradigm towards SRS alone for a greater than 5 or greater than 10 lesions [15–17]. Indeed, the majority of respondents reported increasing their use of SRS over the last 5 years. While the survey did not evaluate the role insurers play in physicians' decision-making, private insurance typically recognizes the role of SRS in treating multiple brain metastases with no clear maximum identified [18]. Additionally, citing a growing body of literature regarding safety and efficacy, current National Comprehensive Cancer Network (NCCN) recommendations for SRS alone do not specify a maximum number of lesions [19].

Knisely et al. first examined the use of SRS in clinical practice several years ago; physicians at two conferences hosted by national stereotactic radiosurgery societies were asked to fill a questionnaire, with a majority of respondents considering it "reasonable" to treat greater than 5 metastases with SRS alone [20]. More recently, Sandler et al. evaluated practicing physicians' "cutoff" for treating brain metastases with SRS alone versus WBRT, among other scenarios[21]. Importantly, they found CNS specialists to be comfortable treating a mean of 8.1 lesions compared to 5.6 and 5.1 lesions for low-volume CNS specialists and non-CNS specialists respectively [21]. While our survey did not stratify SRS use according to specialization, our results reflect a similar trend among physicians at a national level for treating greater than five lesions with SRS alone.

Notably, recent American Society for Therapeutic Radiology and Oncology (ASTRO) Choosing Wisely guidelines recommend against using adjuvant WBRT with SRS, and instead recommend SRS monotherapy for brain metastases [12, 22]. However, no guidance is provided regarding the SRS plan evaluation. The present study identifies several parameters in current SRS use for brain metastasis in practice, including the use of 0-mm margins, conformity index, brain V12, and the mono-isocenter technique for multiple brain metastases. While our survey did not specifically assess the values used for each parameter, retrospective data indicate that V12 greater than 10.9 cm^3 is associated with a 51% 1-year risk of radionecrosis [23]. Likewise, other treatment parameters appear to play an important role in the development of a safe and effective treatment plan.

The overall response rate was relatively low for this study (< 20%), introducing the potential for response bias. Despite this potential limitation, emerging research suggests that low response rates are not inherently associated with inaccurate results or nonresponder bias [24, 25]. Moreover, the wide geographic spread and distribution of practice experience among respondents suggests that the current sample was representative of the academic field at large. Despite these qualifications, we cannot definitively rule out bias in the study based on the observed response rate. There are other potential sources of bias as well. Because this survey was distributed to physicians practicing at NCI-designated cancer centers, the responses may not be reflective of the patterns of SRS use in non-academic and private practice settings. Additionally, the survey was only distributed to NCI-designated cancer centers that contain radiation oncologists; therefore, responses may not be reflective of practice patterns at NCI-designated centers without on-site radiation oncologists. Another potential limitation of the survey was that it did not account for patient volume per

institution, which may be a surrogate for expertise in SRS and could influence aggressiveness in treating multiple brain metastases. Furthermore, individual practitioners were not asked about their patient volumes, which may be a surrogate for clinical versus research time in an academic setting and therefore influence management preferences. Future studies will be needed to continue to address these issues and refine clinical practice.

Conclusions

To our knowledge, this is among the first national assessments of the use of SRS for brain metastases in clinical practice in the USA. The data indicate that radiation oncologists are increasingly using SRS for the treatment of intracranial lesions, even in situations which were historically treated with WBRT. Treatment parameters considered most by respondents include 0-mm margins, conformity index, brain V12, and a mono-isocenter technique for multiple brain metastases. These data may reveal areas that require guidance and instruction from cooperative group committees.

Acknowledgments

Funding E.S.B. received an F30 Ruth Kirschstein MD-PhD Fellowship Award (CA180500).

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J Radiat Oncol. Author manuscript; available in PMC 2018 November 09.

Table 1

Survey questions and responses. Listing of the 18 survey questions with associated responses. Responses are percentages for discrete answers, and rating averages for rank-order questions

Question	Responses (Raw Numbers)							
1. Do you treat patients with brain metastases with SRS?	Yes 71.3% (72)				No 28.7% (29)			
2. How many years have you been a practicing radiation oncologist?	< 5 yrs 22.5% (16)	26.8% (19)	5-10 yrs 22.5% (16)	28.2% (20)	11-20 yrs		> 20 yrs	
3. What are the primary disease sites you treat? Choose as many as applicable.	Lung 49.3% (35)	CNS 66.2% (47)	GU 26.8% (19)	Breast 26.8% (19)	H&N 38% (27)	GI 28.2% (20)	Peds 12.7% (9)	GYN 11.3% (8)
4. Which modality do you more commonly prescribe for < 10 brain metastases?	SRS > WBRT 73.7% (42)	10.5% (6)	15.8% (7)	WBRT > SRS			SRS = WBRT	
5. Which modality do you more commonly prescribe for > = 10 brain metastases?	SRS > WBRT 5.3% (3)	82.5% (47)	12.3% (7)	WBRT > SRS			SRS = WBRT	
6. How have you changed your management of patients with multiple brain metastases in the past 5 years? Check all that apply.	I more frequently use SRS without WBRT I more frequently use SRS without WBRT				84.2% (48)			
	I more frequently use WBRT without SRS I more frequently use WBRT without SRS	0% (0)						
	The number of brain metastases I am willing to treat with SRS alone has increased The number of brain metastases I am willing to treat with SRS alone has decreased The size of brain metastases I am will to treat with SRS alone has increased The size of brain metastases I am will to treat with SRS alone has decreased My management of patients with multiple brain metastases has not changed				82.5% (47) 3.5% (2) 19.3% (11) 5.3% (3) 5.3% (3)			
7. What is the maximum number of brain metastases you would commonly treat with upfront SRS without offering WBRT?	1-4 40.4% (23)	5-10 42.1% (24)	11-15 7% (4)		16-20 7% (4)	No Limit 3.5% (2)	No SRS without WBRT 0% (0)	
8. Rank the following criteria by weight (first being most important) in determining the use of SRS vs WBRT at initial presentation (57 responses)	Diameter of metastases Number of metastases Volume of metastases Histology Performance status Status of extracranial disease Location (critical structures)				3.96 2.37 4.04 4.81 3.23 4.33 5.26			
9. Which of the following do you consider a contraindication to SRS without WBRT (not including size and number of metastases)?	Leptomeningeal disease Portion of brain stem involved Near or involving optic apparatus Local recurrence after prior SRS Intracranial progression after prior SRS Systemic disease progression 2-4	5-10	11-15		93% (53) 17.5% (10) 43.9% (25) 21.1% (12) 7% (4) 14.0% (8) 16-20		No Limit	

Question	Responses (Raw Numbers)				
10. What is the maximum number of simultaneous metastases you are willing to treat with SRS in one session?	31.6% (18)	40.4% (23)	15.8% (9)	7% (4)	5.3% (3)
11. What is the maximum number of simultaneous metastases you are willing to treat with SRS over multiple sessions?	2-4 12.3% (7)	5-10 43.9% (25)	11-15 10.5% (6)	16-20 14% (8)	No Limit 19.3% (11)
12. What margin do you prescribe for SRS?	0 mm 49.1% (28)		1 mm 38.6% (22)	2 mm 12.3% (7)	3 mm 0% (0)
13. Which factors do you consider in your evaluation of an SRS plan for a lesion that is not near critical structures? Check all that apply.	Brain V12 61.4% (35)		Conformity Index 84.2% (48)		Mean brain dose/integral dose 36.8% (21)
14. Rank the following criteria by weight (first being most important) in your determining radiation dose for a single brain metastasis without prior WBRT (57 responses).	Diameter 1.54		Volume 1.68		Histology 2.77
15. How do you generally prescribe your SRS dose for multiple brain metastases (> = 4)?	Based on size/volume only Based on uniform dose, such as 18 Gy or 20 Gy Based on size/volume, but reduced as compared to single brain metastasis Reduced dose based on V12 or other parameters I do not routinely treat > = 4 brain metastases simultaneously			54.4% (31) 8.8% (5) 19.3% (11) 3.5% (2) 14% (8)	
16. What is the primary modality you use to treat intracranial metastases?	Gamma Knife 31.6% (18)		LINAC 54.4% (31)		CyberKnife 14.0% (8)
17. If you use a LINAC based system, do you use a mono-isocenter technique for patients with multiple brain metastases?	Yes 43.9% (25)		No 26.3% (15)		N/A 29.8% (17)
18. Does your department have a policy for the treatment of brain metastases?	Yes 35.1% (20)			No 64.9% (37)	

J Radiat Oncol. Author manuscript; available in PMC 2018 November 09.