American College of Radiology
ACR Appropriateness Criteria®

SINGLE BRAIN METASTASIS

Expert Panel on Radiation Oncology–Brain Metastases: Andrew D. Vassil, MD[1]; Gregory M. M. Videtic, MD[2]; Elizabeth M. Gore, MD[3]; Jeffrey D. Bradley, MD[4]; John M. Buatti, MD[5]; Isabelle Germano, MD[6]; A. Paiman Ghafoori, MD[7]; Mark A. Henderson, MD[8]; Stephen T. Lutz, MD[9]; Gregory J. A. Murad, MD[10]; Roy A. Patchell, MD[11]; Samir H. Patel, MD[12]; Jared R. Robbins, MD[13]; H. Ian Robins, MD, PhD[14]; Franz J. Wippold II, MD[15]; Michael J. Yunes, MD.[16]

Summary of Literature Review

Introduction/Background

Brain metastases represent the most common adult intracranial tumor. Treatment for patients with a single brain metastasis remains controversial given the number of management strategies available and the strong opinions associated with each option. Despite class I evidence suggestive of best therapy, there is no clear consensus regarding optimal treatment for these patients.

Prognostic Factors

Clinical factors have been evaluated to guide treatment decisions. The Radiation Therapy Oncology Group (RTOG®) Recursive Partitioning Analysis of three consecutive phase III brain metastases trials [1] determined that the four most important factors were Karnofsky performance score (KPS), age, control of primary and status of extracranial disease. A more quantifiable scale, Graded Prognostic Assessment (GPA), from five phase III RTOG® trials demonstrated the importance of the number of lesions (1 vs 2-3 vs >3) in determining outcomes for patients with brain metastases [2]. The GPA has been further refined for specific diagnoses of non-small-cell lung cancer, small-cell lung cancer, melanoma, renal cell carcinoma, breast cancer, gastrointestinal cancer, and others [3].

Surgery

Advances in surgery and imaging have allowed for safer resection of brain metastases. If the patient is suffering from significant mass effect or has no pathologic confirmation of the primary, then surgical resection of the lesion, if feasible, is warranted. For patients with a single lesion who are relatively asymptomatic, the decision process may be more complicated. The decision to use aggressive therapy depends on the extent and activity of extracranial disease and the number of brain lesions, as well as the patient's general medical condition, performance status, and preference. For patients with stable or absent extracranial disease, two randomized studies have clearly shown the benefit of surgical resection followed by whole-brain radiotherapy (WBRT) [4,5]. The benefits are expressed not only in terms of freedom from neurologic progression but also in terms of overall survival. However, a third study by Mintz et al [6] failed to show a survival advantage with the addition of surgery, or an advantage in terms of quality of life. Thus, two of three randomized studies have shown a benefit of surgical resection and WBRT versus biopsy and WBRT alone.

Whole-Brain Radiation Therapy

The dose used with WBRT in patients with a single brain metastasis is based mainly on studies performed in patients with multiple brain metastases. Prospective, randomized phase III clinical trials in patients with multiple brain metastases have included doses of 1000 cGy in one fraction (1000/1), 1200/2, 1800/3, 2000/5, 3000/10,

---

[1]Principal Author, Cleveland Clinic, Strongsville, Ohio. [2]Panel Chair, Cleveland Clinic Foundation, Cleveland, Ohio. [3]Panel Vice-chair, Medical College of Wisconsin, Milwaukee, Wisconsin.[4]Washington University School of Medicine, St. Louis, Missouri. [5]University of Iowa Hospital, Iowa City, Iowa. [6]Mount Sinai School of Medicine, New York, New York, American Association of Neurological Surgeons/Congress of Neurological Surgeons. [7]University Medical Center Brackenridge, Austin, Texas. [8]Indiana University School of Medicine, Indianapolis, Indiana. [9]Blanchard Valley Regional Cancer Center, Findlay, Ohio. [10]University of Florida, Gainesville, Florida, American Association of Neurological Surgeons/Congress of Neurological Surgeons. [11]Barrow Neurological Institute, Phoenix, Arizona, American Academy of Neurology. [12]Mayo Clinic Arizona, Scottsdale Arizona. [13]Henry Ford Hospital, Detroit, Michigan. [14]University of Wisconsin, Paul P. Carbone Comprehensive Cancer Center, Madison, Wisconsin, American Society of Clinical Oncology. [15]Mallinckrodt Institute of Radiology, Saint Louis, Missouri, Chair, Expert Panel on Neurologic Imaging. [16]Baystate Medical Center, Springfield, Massachusetts.

The American College of Radiology seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply individual or society endorsement of the final document.

Reprint requests to: Department of Quality & Safety, American College of Radiology, 1891 Preston White Drive, Reston, VA 20191-4397.

3600/6, 4000/20, 5000/20, and 5440/34 (160 cGy BID) [7-13]. None of these regimens has proved superior in terms of survival or efficacy (about half of patients have an improvement in their neurologic symptoms). However, 3000 cGy in 10 fractions or 3750 cGy in 15 fractions represent the most frequently used dose/fractionation schedules. WBRT alone can provide excellent palliation for many patients with brain metastases. Most patients with radiosensitive histologies such as small-cell lung cancer, leukemia, lymphoma, and germ cell tumor can be managed with WBRT alone. (See Variant 1 and Variant 2.)

Surgery versus Stereotactic Radiosurgery

Whether stereotactic radiosurgery (SRS) is as effective as surgical resection has not been evaluated within a large phase III randomized trial for patients with a single brain metastasis. Auchter et al [14] performed a multi-institutional outcome study on patients treated with radiosurgery and WBRT who met the same entry criteria as the patients treated in the two positive randomized trials of surgery and WBRT versus WBRT alone. The results of this nonrandomized study indicate that radiosurgery plus WBRT produces the same local control, freedom from neurological deterioration, and overall survival as surgery plus WBRT. Another retrospective study from Bindal et al [15] showed improved median and 1-year survival for those undergoing surgery as compared to SRS. The rates of local recurrence and neurologic death were lower in the surgery group. Studies have suggested that the results of SRS and WBRT are equivalent to those of surgery and WBRT [16-19]. For tumors >4 cm in greatest diameter or causing significant mass effect, surgery rather than SRS is the preferred treatment. (See Variant 3.)

Brachytherapy

Studies looking at stereotactic interstitial brachytherapy for patients with single lesions indicate that control rates are similar to those obtained with radiosurgery [20,21]. However, brachytherapy is an invasive procedure and requires hospitalization. A phase II trial evaluating balloon brachytherapy demonstrated local control rates of 80%, but higher rates of radiation necrosis [22]. Given the invasive nature of brachytherapy, this approach is not routinely practiced.

Surgery With or Without Whole-Brain Radiation Therapy

The use of WBRT for patients with a single metastasis has been a subject of growing controversy [23]. The question of whether surgical resection can be performed without the addition of WBRT was investigated in phase III randomized trials [19,24]. These trials demonstrated an improvement in local and distant brain recurrence rates with the addition of WBRT, but no improvement in survival. The study published by Patchell et al [24], however, was not powered to detect such a difference. (See Variant 4 and Variant 5.)

Stereotactic Radiosurgery With or Without Whole-Brain Radiation Therapy

The analogous question of whether radiosurgery can be performed without the addition of WBRT has been studied in a phase III trial conducted in Japan randomizing patients with one to four brain metastases between radiosurgery and radiosurgery plus WBRT. This study demonstrated significantly improved local and distant brain control in the WBRT plus radiosurgery arm [25]. Since the primary end point of the study was local control and not overall survival, it was not powered properly to evaluate survival differences.

Similar results were found in a phase III study of WBRT versus observation after radiosurgery or surgical resection for patients with one to three brain metastases [19]. An intergroup phase III trial involving patients with one to three brain metastases comparing the results of SRS versus SRS followed by WBRT is ongoing. (See Variant 6.)

Whole-Brain Radiation Therapy With or Without Stereotactic Radiosurgery

Another question, whether patients receiving WBRT for a single brain metastasis benefit from the addition of radiosurgery, has been answered in an RTOG® randomized trial involving patients with one to three brain metastases [26]. In patients with a single brain metastasis, the addition of radiosurgery increased median survival time from 4.9 months to 6.5 months (P=0.04). Local control was significantly improved for all patients. Based on the results of this trial, the RTOG® started a phase III trial (RTOG® 0320) for patients with non-small-cell lung cancer with one to three brain metastases, but it closed secondary to poor accrual. (See Variant 7.)

Neurocognitive Effect of Whole-Brain Radiation Therapy

Concerns of neurocognitive deterioration from WBRT have received much attention and scrutiny. As part of a phase III trial evaluating the use of a novel radiation sensitizer with WBRT, all patients underwent evaluation of neurocognitive function using a battery of tests [27]. Baseline neurocognitive testing demonstrated that 91% of patients had a significant decline in at least one domain prior to WBRT. Further analysis of the 208 patients in the WBRT arm of the study demonstrated that WBRT-induced tumor shrinkage correlated with better survival and neurocognitive function [28]. In addition, neurocognitive deterioration preceded quality-of-life declines, which suggests that strategies that delay neurocognitive decline appear worthwhile [29]. Strategies including neuroprotective medications and hippocampal avoidance during WBRT are being investigated through the RTOG®. When Mini-Mental Status Examination (MMSE) was used to evaluate neurocognitive function as part of the phase III trial of SRS versus SRS plus WBRT for patients with one to four brain metastases, the omission of WBRT led to faster time to neurologic deterioration based on MMSE [30]. In addition, the omission of WBRT significantly increased the risk for tumor recurrence and decline in neurologic function. A pilot study of neurocognitive function in patients with one to three brain metastases treated with SRS alone showed that 60% of the patients had impairment at presentation [31]. A recent phase III trial demonstrated worse neurocognitive outcomes at 4 months as measured by the Hopkins Verbal Learning Test (HVLT) for patients randomized to the WBRT and SRS arm versus those in the SRS alone arm [32]. Results from a phase III study showed no significant differences in global cognitive function (MMSE) or quality of life after prophylactic cranial irradiation, but there was a significant decline in memory (HVLT) at 1 year [33].

Stereotactic Radiosurgery to Resection Cavity

In an effort to avoid the potential toxicity of WBRT, the use of SRS to the resection cavity has also been investigated to aid in local control; however, published randomized trials are not available. Reports of SRS to the resection cavity are small in sample size, are retrospective, and use a wide range of SRS dosing and schedules. Rates of distant brain metastasis are similar to those in studies of surgery alone. A study of 106 patients treated with SRS to the resection cavity showed a 1-year local control rate of 80% with a 1-year distant brain failure rate of 64.6% [34]. A study of 112 patients showed expansion of the resection cavity with a 2-mm margin to be associated with improved 1 year local control rates of 3% with expansion versus 16% without expansion [35]. In this study, 54% of patients experienced distant brain failure at 1 year. Taken together, these studies show that approximately 2.8%-3.6% of patients may require surgery for radiation-related toxicity. An ongoing intergroup phase III trial of adjuvant SRS versus WBRT for patients with one to four brain metastases that have been removed surgically is addressing this topic; the primary endpoints are overall survival and neurocognitive function.

Long-Term Survival after Surgery or SRS

More aggressive treatment with surgery or SRS has led to a greater number of patients being long-term survivors. A retrospective review of patients undergoing SRS reported that 6.5% survived at least 4 years [36]. Another review of long-term survivors showed that 2.6% of patients in a large single-institution database survived a minimum of 5 years [37].

Summary

- Compelling evidence suggests that aggressive local therapy for patients with a single brain metastasis is beneficial for survival and quality of life.
- If patients have no evidence of progressive extracranial disease, surgical resection or radiosurgery is appropriate therapy. While it appears that the addition of WBRT does not add to survival or duration of functional independence, it does reduce the risk of further intracranial failure and delays neurocognitive decline, particularly for those patients whose tumors have responded to WBRT.
- Recently completed and ongoing studies will help address the impact of WBRT on neurocognitive function and quality of life, which have been major reasons why WBRT is being omitted despite class I evidence supporting the use of WBRT after surgery or SRS.
- Since much controversy exists regarding optimal treatment for a patient with a single brain metastasis, patient participation in clinical trials is important to evaluate best treatment. For those patients who do not participate in clinical trials, the roles of surgery and SRS in improving outcomes for patients with a single lesion are evident.

Supporting Documents

- ACR Appropriateness Criteria® Overview
- Evidence Table

References

1. Gaspar L, Scott C, Rotman M, et al. Recursive partitioning analysis (RPA) of prognostic factors in three Radiation Therapy Oncology Group (RTOG) brain metastases trials. *Int J Radiat Oncol Biol Phys.* 1997;37(4):745-751.
2. Sperduto PW, Berkey B, Gaspar LE, Mehta M, Curran W. A new prognostic index and comparison to three other indices for patients with brain metastases: an analysis of 1,960 patients in the RTOG database. *Int J Radiat Oncol Biol Phys.* 2008;70(2):510-514.
3. Sperduto PW, Kased N, Roberge D, et al. Summary report on the graded prognostic assessment: an accurate and facile diagnosis-specific tool to estimate survival for patients with brain metastases. *J Clin Oncol.* 2012;30(4):419-425.
4. Noordijk EM, Vecht CJ, Haaxma-Reiche H, et al. The choice of treatment of single brain metastasis should be based on extracranial tumor activity and age. *Int J Radiat Oncol Biol Phys.* 1994;29(4):711-717.
5. Patchell RA, Tibbs PA, Walsh JW, et al. A randomized trial of surgery in the treatment of single metastases to the brain. *N Engl J Med.* 1990;322(8):494-500.
6. Mintz AH, Kestle J, Rathbone MP, et al. A randomized trial to assess the efficacy of surgery in addition to radiotherapy in patients with a single cerebral metastasis. *Cancer.* 1996;78(7):1470-1476.
7. Borgelt B, Gelber R, Larson M, Hendrickson F, Griffin T, Roth R. Ultra-rapid high dose irradiation schedules for the palliation of brain metastases: final results of the first two studies by the Radiation Therapy Oncology Group. *Int J Radiat Oncol Biol Phys.* 1981;7(12):1633-1638.
8. Chatani M, Matayoshi Y, Masaki N, Inoue T. Radiation therapy for brain metastases from lung carcinoma. Prospective randomized trial according to the level of lactate dehydrogenase. *Strahlenther Onkol.* 1994;170(3):155-161.
9. Chatani M, Teshima T, Hata K, Inoue T. Prognostic factors in patients with brain metastases from lung carcinoma. *Strahlenther Onkol.* 1986;162(3):157-161.
10. Haie-Meder C, Pellae-Cosset B, Laplanche A, et al. Results of a randomized clinical trial comparing two radiation schedules in the palliative treatment of brain metastases. *Radiother Oncol.* 1993;26(2):111-116.
11. Harwood AR, Simson WJ. Radiation therapy of cerebral metastases: a randomized prospective clinical trial. *Int J Radiat Oncol Biol Phys.* 1977;2(11-12):1091-1094.
12. Kurtz JM, Gelber R, Brady LW, Carella RJ, Cooper JS. The palliation of brain metastases in a favorable patient population: a randomized clinical trial by the Radiation Therapy Oncology Group. *Int J Radiat Oncol Biol Phys.* 1981;7(7):891-895.
13. Murray KJ, Scott C, Greenberg HM, et al. A randomized phase III study of accelerated hyperfractionation versus standard in patients with unresected brain metastases: a report of the Radiation Therapy Oncology Group (RTOG) 9104. *Int J Radiat Oncol Biol Phys.* 1997;39(3):571-574.
14. Auchter RM, Lamond JP, Alexander E, et al. A multiinstitutional outcome and prognostic factor analysis of radiosurgery for resectable single brain metastasis. *Int J Radiat Oncol Biol Phys.* 1996;35(1):27-35.
15. Bindal AK, Bindal RK, Hess KR, et al. Surgery versus radiosurgery in the treatment of brain metastasis. *J Neurosurg.* 1996;84(5):748-754.
16. O'Neill BP, Iturria NJ, Link MJ, Pollock BE, Ballman KV, O'Fallon JR. A comparison of surgical resection and stereotactic radiosurgery in the treatment of solitary brain metastases. *Int J Radiat Oncol Biol Phys.* 2003;55(5):1169-1176.
17. Rades D, Kueter JD, Veninga T, Gliemroth J, Schild SE. Whole brain radiotherapy plus stereotactic radiosurgery (WBRT+SRS) versus surgery plus whole brain radiotherapy (OP+WBRT) for 1-3 brain metastases: results of a matched pair analysis. *Eur J Cancer.* 2009;45(3):400-404.
18. Schoggl A, Kitz K, Reddy M, et al. Defining the role of stereotactic radiosurgery versus microsurgery in the treatment of single brain metastases. *Acta Neurochir (Wien).* 2000;142(6):621-626.
19. Kocher M, Soffietti R, Abacioglu U, et al. Adjuvant whole-brain radiotherapy versus observation after radiosurgery or surgical resection of one to three cerebral metastases: results of the EORTC 22952-26001 study. *J Clin Oncol.* 2011;29(2):134-141.
20. Bernstein M, Cabantog A, Laperriere N, Leung P, Thomason C. Brachytherapy for recurrent single brain metastasis. *Can J Neurol Sci.* 1995;22(1):13-16.
21. Ostertag CB, Kreth FW. Interstitial iodine-125 radiosurgery for cerebral metastases. *Br J Neurosurg.* 1995;9(5):593-603.

22. Rogers LR, Rock JP, Sills AK, et al. Results of a phase II trial of the GliaSite radiation therapy system for the treatment of newly diagnosed, resected single brain metastases. *J Neurosurg.* 2006;105(3):375-384.
23. Brown PD, Asher AL, Farace E. Adjuvant whole brain radiotherapy: strong emotions decide but rational studies are needed. *Int J Radiat Oncol Biol Phys.* 2008;70(5):1305-1309.
24. Patchell RA, Tibbs PA, Regine WF, et al. Postoperative radiotherapy in the treatment of single metastases to the brain: a randomized trial. *Jama.* 1998;280(17):1485-1489.
25. Aoyama H, Shirato H, Tago M, et al. Stereotactic radiosurgery plus whole-brain radiation therapy vs stereotactic radiosurgery alone for treatment of brain metastases: a randomized controlled trial. *Jama.* 2006;295(21):2483-2491.
26. Andrews DW, Scott CB, Sperduto PW, et al. Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: phase III results of the RTOG 9508 randomised trial. *Lancet.* 2004;363(9422):1665-1672.
27. Meyers CA, Smith JA, Bezjak A, et al. Neurocognitive function and progression in patients with brain metastases treated with whole-brain radiation and motexafin gadolinium: results of a randomized phase III trial. *J Clin Oncol.* 2004;22(1):157-165.
28. Li J, Bentzen SM, Renschler M, Mehta MP. Regression after whole-brain radiation therapy for brain metastases correlates with survival and improved neurocognitive function. *J Clin Oncol.* 2007;25(10):1260-1266.
29. Li J, Bentzen SM, Renschler M, Mehta MP. Relationship between neurocognitive function and quality of life after whole-brain radiotherapy in patients with brain metastasis. *Int J Radiat Oncol Biol Phys.* 2008;71(1):64-70.
30. Aoyama H, Tago M, Kato N, et al. Neurocognitive function of patients with brain metastasis who received either whole brain radiotherapy plus stereotactic radiosurgery or radiosurgery alone. *Int J Radiat Oncol Biol Phys.* 2007;68(5):1388-1395.
31. Chang EL, Wefel JS, Maor MH, et al. A pilot study of neurocognitive function in patients with one to three new brain metastases initially treated with stereotactic radiosurgery alone. *Neurosurgery.* 2007;60(2):277-283; discussion 283-274.
32. Chang EL, Wefel JS, Hess KR, et al. Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: a randomised controlled trial. *Lancet Oncol.* 2009;10(11):1037-1044.
33. Sun A, Bae K, Gore EM, et al. Phase III trial of prophylactic cranial irradiation compared with observation in patients with locally advanced non-small-cell lung cancer: neurocognitive and quality-of-life analysis. *J Clin Oncol.* 2011;29(3):279-286.
34. Jensen CA, Chan MD, McCoy TP, et al. Cavity-directed radiosurgery as adjuvant therapy after resection of a brain metastasis. *J Neurosurg.* 2011;114(6):1585-1591.
35. Choi CY, Chang SD, Gibbs IC, et al. Stereotactic radiosurgery of the postoperative resection cavity for brain metastases: prospective evaluation of target margin on tumor control. *Int J Radiat Oncol Biol Phys.* 2012;84(2):336-342.
36. Kondziolka D, Martin JJ, Flickinger JC, et al. Long-term survivors after gamma knife radiosurgery for brain metastases. *Cancer.* 2005;104(12):2784-2791.
37. Chao ST, Barnett GH, Liu SW, et al. Five-year survivors of brain metastases: a single-institution report of 32 patients. *Int J Radiat Oncol Biol Phys.* 2006;66(3):801-809.

Clinical Condition: **Single Brain Metastasis**

Variant 1: **77-year-old man, PET scan demonstrated widely metastatic melanoma with a 2 cm right thalamic lesion. Patient is symptomatic. Neurosurgeon believes surgery would be high risk. KPS 60. Patient refuses further systemic therapy.**

Treatment	Rating	Comments
Focal Therapy Alone		
Stereotactic radiosurgery (SRS) alone	7	Considerable debate regarding role of SRS for patient with KPS of 60. Some felt SRS alone provided quicker palliation compared to WBRT.
Surgical resection alone	1	
Whole Brain RT (WBRT) Alone		
2000 cGy/5 fractions	7	Debate regarding role of this fractionation scheme. Given low KPS and patient's refusal to receive further systemic therapy, short fractionation is deemed appropriate.
3000 cGy/10 fractions	8	
3750 cGy/15 fractions	5	Did not favor more prolonged WBRT schedule.
4000 cGy/20 fractions	1	
Combination Therapy		
SRS + WBRT	3	Aggressive therapy for patient with short life expectancy.
Surgery + WBRT	1	
Surgery + SRS to resection cavity	1	
Observation	6	Consider steroids and hospice care.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 2: **54-year-old man found to have widespread metastatic small-cell carcinoma to lung, bone, and liver by PET/CT imaging, with a 2 cm asymptomatic left anterior temporal lobe lesion. KPS 70. Systemic therapy is planned. No prior WBRT.**

Treatment	Rating	Comments
Focal Therapy Alone		
Stereotactic radiosurgery (SRS) alone	2	
Surgical resection alone	1	
Whole Brain RT (WBRT) Alone		
2000 cGy/5 fractions	5	
3000 cGy/10 fractions	8	
3750 cGy/15 fractions	8	
4000 cGy/20 fractions	2	
Combination Therapy		
SRS + WBRT	2	Considered too aggressive for radiosensitive tumor.
Surgery + WBRT	1	
Surgery + SRS to resection cavity	1	
Observation	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Single Brain Metastasis**

Variant 3: **68-year-old woman who received chemotherapy/radiotherapy and surgery for esophageal carcinoma. No evidence of extracranial disease. A 5 cm lesion in right anterior frontal lobe with 15 mm midline shift. KPS 90 on high-dose steroids.**

Treatment	Rating	Comments
Focal Therapy Alone		
Stereotactic radiosurgery (SRS) alone	1	
Surgical resection alone	2	
Whole Brain RT (WBRT) Alone		
2000 cGy/5 fractions	1	
3000 cGy/10 fractions	5	Consider if patient refuses surgery or is medically unfit for surgery.
3750 cGy/15 fractions	5	Consider if patient refuses surgery or is medically unfit for surgery.
4000 cGy/20 fractions	1	
Combination Therapy		
SRS + WBRT	1	
Surgery + WBRT	9	
Surgery + SRS to resection cavity	2	
Observation	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 4: **48-year-old man who received left upper lobe resection for NSCLC 1 year earlier, now with 3 cm right frontal lobe lesion. No clinical or radiographic evidence of extracranial disease. The right frontal lesion was completely resected, confirmed by contrast MRI scan 24 hours after surgery. Two weeks after surgery, KPS is 80.**

Treatment	Rating	Comments
Focal Therapy Alone		
Stereotactic radiosurgery (SRS) alone	5	No phase III trial demonstrating superiority over WBRT.
Whole Brain RT (WBRT) Alone		
2000 cGy/5 fractions	1	
3000 cGy/10 fractions	7	
3750 cGy/15 fractions	7	
4000 cGy/20 fractions	4	
Combination Therapy		
SRS + WBRT	1	
Observation	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Single Brain Metastasis**

Variant 5: **35-year-old woman with metastatic breast cancer to multiple bony sites with a 3 cm left parietal lesion. Systemic disease is no longer responding to chemohormonal therapy. Surgical resection was subtotal in nature, confirmed by postoperative MRI. KPS 90.**

Treatment	Rating	Comments
Focal Therapy Alone		
Stereotactic radiosurgery (SRS) alone	6	Concern that patient may live long enough to develop other brain metastases without use of WBRT.
Surgical resection (repeat)	2	
Whole Brain RT (WBRT) Alone		
2000 cGy/5 fractions	3	
3000 cGy/10 fractions	8	
3750 cGy/15 fractions	8	
4000 cGy/20 fractions	3	Prolonged course of WBRT is discouraged.
Combination Therapy		
SRS + WBRT	8	Since patient had subtotal resection, some recommend combination approach to maximize local control.
Surgery + WBRT	1	
Surgery + SRS to resection cavity	1	
Observation	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Single Brain Metastasis**

Variant 6: **49-year-old woman (nonsmoker) recently diagnosed with a 2 cm non-small-cell lung cancer in left upper lobe with no hilar and mediastinal lymphadenopathy, and asymptomatic 2 cm right frontal lesion. Abdominal CT and bone scans were negative. KPS 90.**

Treatment	Rating	Comments
Focal Therapy Alone		
Stereotactic radiosurgery (SRS) alone	7	
Surgical resection alone	5	
Whole Brain RT (WBRT) Alone		
2000 cGy/5 fractions	1	
3000 cGy/10 fractions	5	
3750 cGy/15 fractions	5	
4000 cGy/20 fractions	1	
Combination Therapy		
SRS + WBRT	8	
Surgery + WBRT	8	
Surgery + SRS to resection cavity	5	More data is needed for SRS to resection cavity.
Observation	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Single Brain Metastasis**

Variant 7: **42-year-old woman who had nephrectomy for renal cell carcinoma 6 years earlier presenting with a 1 cm lesion in the right lateral cerebellum found incidentally after MRI for head injury. Stereotactic biopsy was consistent with renal cell carcinoma CT of chest/abdomen and bone scan were negative. KPS 90.**

Treatment	Rating	Comments
Focal Therapy Alone		
Stereotactic radiosurgery (SRS) alone	7	
Surgical resection alone	4	
Whole Brain RT (WBRT) Alone		
2000 cGy/5 fractions	1	
3000 cGy/10 fractions	5	Some concern that WBRT would not sufficiently control renal cell carcinoma.
3750 cGy/15 fractions	5	Some concern that WBRT would not sufficiently control renal cell carcinoma.
4000 cGy/20 fractions	1	
Combination Therapy		
SRS + WBRT	8	
Surgery + WBRT	8	
Surgery + SRS to resection cavity	6	
Observation	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		