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Scientific Article

Cost of Treatment for Brain Metastases Using Data From a National Health Insurance

Joseph Crooks, BS,[a,*] Oralia Dominic, PhD,[b] Matthew Shepard, MD,[c] Alexander Yu, MD,[c] Yun Liang, PhD,[d] Stephen M. Karlovits, MD,[d] and Rodney E. Wegner, MD[d]

[a]Department of Medicine, Drexel University College of Medicine, Philadelphia, Pennsylvania; [b]Medical Policy Research Department, Highmark Health, Pittsburgh, Pennsylvania; [c]Department of Neurosurgery, Allegheny Health Network, Pittsburgh, Pennsylvania; and [d]Department of Radiation Oncology, Allegheny Health Network, Pittsburgh, Pennsylvania

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Purpose: In the United States, brain metastases (BMs) affect 10% to 20% of patients with cancer, presenting a significant health care challenge and necessitating intricate, high-cost treatments. Few studies have explored the comprehensive care cost for BMs, and none have used real insurance claims data. Partnering with a northeastern health care insurer, we investigated the true costs of various brain-directed radiation methods, aiming to shed light on treatment expenses, modalities, and their efficacy.

Methods and Materials: We analyzed medical claims from Highmark Health-insured patients in Pennsylvania, Delware, West Virginia, and New York diagnosed with BMs (ICD-10 code C79.31) and treated with radiation from January 1, 2020 to July 1, 2022. Costs for radiation techniques were grouped by specific current procedural terminology claim codes. We subdivided costs into technical and physician components and separated hospital from freestanding costs for some modalities.

Results: From January 1, 2020 to July 1, 2022, 1048 Highmark Health members underwent treatment for BMs. Females (n = 592) significantly outnumbered males (n = 456), with an average age of 64.4 years. Each member had, on average, 5.309 claims costing $2015 per claim. Total cost totaled $10,697,749. Per-treatment analysis showed that hippocampal avoidance intensity modulated radiation therapy was the costliest treatment at $47,748, followed by stereotactic radiation therapy at $37,230, linear accelerator stereotactic radiosurgery (SRS) at $30,737, Gamma Knife SRS at $30,711, and whole-brain radiation therapy at $5225.

Conclusions: Whole-brain radiation therapy was the least costly radiation technique. Similar per-treatment prices for Gamma Knife and linear accelerator SRS support their use in treating BMs. Stereotactic radiation therapy in general was costlier on a per-use basis than SRS, prompting further scrutiny on its frequent use. Hippocampal avoidance intensity modulated radiation therapy was the costliest radiation therapy on a per-use basis by a moderate amount, prompting further discussion about its comparative cost effectiveness against other radiation modalities. This study underscores the importance of multiple considerations in treating BMs, such as tumor control, survival, side effects, and costs.

Introduction

In the United States, brain metastases (BMs) are a critical health issue, impacting a significant number of patients with cancer. Estimates show that 10% to 20% of all patients with cancer will be affected by BMs.[1] Lung cancer, breast cancer, and melanoma are the most common primary cancers responsible for the metastases.[2]

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Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

*Corresponding author: Joseph Crooks, BS; Email: jcc453@drexel.edu

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The financial burden of treating these malignancies is felt by both patients and the health care system as a whole. The total cost of treating BMs has remained largely unknown because few studies have incorporated insurance claims data into total cost of care analyses. One study analyzed cost effectiveness of stereotactic radiosurgery (SRS) alone compared with whole-brain radiation therapy (WBRT) plus SRS in treating 1 to 3 metastases and concluded that SRS alone is more cost effective than WBRT with SRS.[3] However, no studies to date have incorporated real payer data into a comparative analysis of the cost of using different radiation modalities to treat BMs.

A partnership with a major northeastern United States health care insurer has allowed us to gain a better understanding of the total cost of care for treating BMs with different forms of radiation therapy. Treatment often includes radiation therapy, chemotherapy, surgical resection, or a combination of multiple therapies. Common radiation modalities include WBRT, Gamma Knife (GK) and linear accelerator (LINAC) SRS and stereotactic radiation therapy (SRT), and hippocampal avoidance intensity modulated radiation therapy (HA-IMRT), which involves sparing the hippocampus of prescription doses of radiation because it is believed to play a key role in mediating neurocognitive recovery after brain-directed radiation.[4-6]

Multiple studies have sought to compare effectiveness between these radiation modalities. One such study found that combining WBRT with SRS did not improve survival for patients with 1 to 4 BMs compared with using SRS alone. However, individuals who did not receive WBRT experienced a significantly higher occurrence of intracranial relapse.[7] Others have shown a higher incidence of cognitive decline observed with WBRT in contrast to SRS, with no significant variation in overall survival between the 2 treatment modalities. SRS has emerged as a recommended standard of care, providing a less toxic yet equally effective alternative to WBRT.[8-10] These studies emphasize the importance of considering both the effectiveness and side effects of various brain-directed radiation techniques when treating BMs as well as the need for personalized treatment strategies based on individual patient needs.

Our study serves to uncover the costs incurred by a major Northeast United States insurance company in both planning for and treating BMs using the aforementioned modalities of radiation. We also sought to distinguish the number of patients with BMs (ICD-10 C79.31) treated with various radiation techniques by year, age, sex, physical location where procedure was performed, specialty, and geography as well as determine cost per claim and cost per year (2020-2022).

Methods and Materials

This study was a secondary data analysis of the cost of care for BMs using medical claims data from commercial members insured by Highmark Health in Pennsylvania, Delaware, West Virginia, and New York. The use of deidentified patient data in this study was approved under Highmark Health's institutional review board number 2021 to 121 titled "Outcomes of Medical Policy CED/New Technology, QM &QA COVID-19 and Underlying Conditions, SDoH, Health Equity Program Mitigations Among Insured Members Using Claims Data."[11]

Patients with medical claims filed under the ICD-10 code C79.31 (secondary malignant neoplasm of brain) from January 1, 2020 to July 1, 2022 who received radiation treatment were included in the study. Patient demographic data were collected and totaled on the basis of year of treatment, age, sex, physical location, and geography. Total number of medical claims filed under C79.31 in the study date range was then tabulated, and an average number of claims filed per patient was calculated. The total cost for treating BMs across all covered patients was then calculated by totaling the cost of each individual claim. Average cost per claim was calculated by dividing the total cost by the number of individual claims.

To better understand how the costs of the individual components of each patient's radiation treatments factor into total cost of treatment across all patients, we devised a grouping system that sought to uncover how cost of care differed across various radiation modalities. Types of radiation modality used include GK SRS, GK SRT, LINAC SRS, LINAC SRT traditional WBRT, and HA-IMRT. This differentiation was accomplished by creating groups and assigning certain current procedural terminology (CPT) claim codes to each group. For example, only the CPT codes used to bill for GK SRS under the "Highmark Radiation Therapy Authorization Program"[11] guidelines were assigned to the GK SRS group. This same grouping protocol was applied to each individual radiation modality used to treat BMs in our patient cohort. These groups were then subdivided into subgroups based on type of service billed (technical component or physician component of treatment). For instance, certain CPT codes are used to bill for the technical components of radiation treatment such as CPT code 77290, "Therapeutic Radiology Simulation; complex,"[11] while others are used to bill for the physician components of radiation treatment such as CPT code 77263, "Therapeutic Radiology treatment planning; complex."[11] Multiple CPT claim code groups were created for the radiation modalities LINAC SRT, traditional WBRT, and HA-IMRT because they were implemented in both hospital and freestanding locations. This additional grouping allowed for the distinction of the cost of care in hospital versus freestanding settings.

Specific CPT code groupings can be found in Table 1. Claim counts for each CPT code were tallied and can be found in Table 2 along with individual CPT codes used in the study.

Table 1 Complete list of radiation modalities used to treat brain metastases in this study, as well as the current procedural terminology (CPT) codes used to bill for each radiation modality

Radiation Modality	Technical component CPT	Physician component CPT
GK SRS hospital	77290, 77280, 77295, 77334, 77370, 77300, 77371, 77470	77263, 77290, 77280, 77295, 77432, 77334, 77300, 77470
GK SRT hospital	77290, 77280, 77295, 77334, 77370, 77300, 77373, 77470, 77336	77263, 77290, 77280, 77295, 77435, 77334, 77300, 77470
LINAC SRS hospital	77301, 77338, 77334, 77300, 77372, 77470	77263, 77301, 77338, 77432, 77334, 77300, 77470
LINAC SRT hospital	77301, 77338, 77334, 77300, 77373, 77470, 77336	77263, 77301, 77338, 77435, 77334, 77300, 77470
LINAC SRT, freestanding	N/A	77301, 77338, 77300, 77334, 77373, 77470, 77336, 77263, 77435
Traditional WBRT, hospital	77290, 77334, 77307, 77280, 77412, 77336, 77417	77263, 77334, 77290, 77307, 77427, 77280
Traditional WBRT, free standing	N/A	77263, 77290, 77334, 77307, 77300, 77280, 77336, 77427, 77417, 77412, G6012
HA-IMRT, hospital	77334, 77301, 77338, 77300, 77386, 77336	77263, 77334, 77301, 77338, 77300, 77427, 77387, 77014
HA-IMRT, free standing	N/A	77263, 77334, 77301, 77338, 77300, 77427, 77336, 77386, G6017, 77387, 77014

Abbreviations: GK = Gamma Knife; HA-IMRT = hippocampal avoidance intensity modulated radiation therapy; LINAC = linear accelerator; N/A = not applicable; SRS = stereotactic radiosurgery; SRT = stereotactic radiation therapy; WBRT = whole-brain radiation therapy.
CPT codes are used to either bill for a technical component, such as for equipment or execution of radiation delivery, or for a physician component, such as for planning or continuing education, and are grouped accordingly.

Results

For the period of the study, January 1, 2020 to July 1, 2022, there were a total of 1048 Highmark Health members treated for BMs with the various radiation techniques previously described. There were significantly more females (n = 592) than males (n = 456) treated (P = .003), and the average age was 64.4 years. The number of medical claims per member was 5.309, and the average cost per claim was $2015. The combined total cost of treating BMs across the 4 states totaled $10,697,749.

In analyzing the total cost for each individual radiation modality and differentiating this cost by technical versus professional (physician) component, there was notable overlap in CPT code sharing. For example, many CPT codes billed under ICD-10 code C79.31 can be applied to multiple of the radiation modalities included in this study. Therefore, the calculation of total cost for each radiation modality includes an intrinsic redundancy so that the actual total cost across all modalities is lower than the sum of the cost of each radiation modality as calculated by totaling the cost of all CPT codes that apply to that modality. Using this protocol to calculate the cost of employing each radiation modality yields GK SRS (hospital) as the most expensive overall radiation treatment at $6,387,882, followed by GK SRT (hospital; $4,814,449), LINAC SRT (hospital; $4,032,990), LINAC SRS (hospital; $2,889,359), HA-IMRT (hospital; $2,724,946), traditional WBRT (hospital; $2,011,506), traditional WBRT (freestanding; $104,591), HA-IMRT (freestanding; $93,007), and LINAC SRT (freestanding; $87,688). Although GK modalities constituted the 2 most expensive overall treatment techniques, the most expensive physician components of any treatment modality came from LINAC SRS and SRT ($751,381 and $718,200, respectively), followed by HA-IMRT (hospital; $684,086), GK SRT and SRS ($522,189 and $507,513, respectively), and traditional WBRT (hospital; $472,907). The most expensive technical component across all radiation modalities was that for GK SRS ($5,880,369), and the least expensive technical component was for traditional WBRT (hospital; $1,538,599).

The most commonly billed CPT codes were 77334 (treatment devices; complex), 77300 (basic radiation dosimetry), 77263 (therapeutic radiology treatment planning; complex), 77295 (3-dimensional radiation therapy plan, including dose-volume histograms), and 77290 (therapeutic radiology simulation; complex). The entire list of CPT codes billed for along with their corresponding descriptions and billing frequencies can be found in Table 1.

Table 2 Complete collection of all current procedural terminology (CPT) codes used by the health insurer to bill for the planning and delivery of radiation treatments targeting brain metastases using various radiation modalities

CPT code	Description	Radiation modalities used	Number of claims
77014*	CT guidance for placement of radiation therapy fields	HA-IMRT*	360
77263	Therapeutic radiology treatment planning; complex	GK SRS, GK SRT, LINAC SRS, LINAC SRT, WBRT, HA-IMRT	1047
77280	Therapeutic radiology simulation; simple	GK SRS, GK SRT, WBRT	520
77290	Therapeutic radiology simulation; complex	GK SRS, GK SRT, WBRT	788
77295*	3D radiation therapy plan, including dose-volume histograms	GK SRS, GK SRT*	953
77300	Basic radiation dosimetry	GK SRS, GK SRT, LINAC SRS, LINAC SRT, WBRT, HA-IMRT	1313
77301	IMRT planning	LINAC SRS, LINAC SRT, HA-IMRT	335
77307*	Teletherapy isodose plan; complex (multiple treatment areas, tangential ports, the use of wedges, blocking, rotational beam, or special beam considerations), includes basic dosimetry calculation(s)	WBRT*	302
77334	Treatment devices; complex	GK SRS, GK SRT, LINAC SRS, LINAC SRT, WBRT, HA-IMRT	2158
77336	Continuing medical physics consultation	GK SRT, LINAC SRT, WBRT, HA-IMRT	368
77338	Multileaf collimator device(s) for IMRT, design and construction per IMRT plan	LINAC SRS, LINAC SRT, HA-IMRT	357
77370*	Special medical physics consultation	GK SRS, GK SRT*	149
77371*	Stereotactic radiosurgery treatment delivery, complete course of treatment of cerebral lesion(s) 1 session, multisource Cobalt 60 based	GK SRS*	208
77372*	Stereotactic radiosurgery treatment delivery, complete course of treatment of cerebral lesion(s) 1 session, LINAC based	LINAC SRS*	94
77373	Stereotactic body radiation therapy delivery per fraction 1 or more lesions; including image guidance not to exceed 5 fractions	GK SRT, LINAC SRT	225
77386*	IMRT delivery, includes guidance and tracking, when performed; complex	HA-IMRT*	59
77387*	Guidance for localization of target volume for delivery of radiation treatment delivery, includes intrafraction tracking, when performed	HA-IMRT*	218
77412*	Radiation treatment delivery, >1 MeV; complex	WBRT*	404
77417*	Therapeutic radiology port films	WBRT*	101
77427	Radiation treatment management, 5 treatments	WBRT, HA-IMRT	508
77432	Stereotactic radiation treatment management cerebral lesion(s) complete course of treatment consisting of 1 session	GK SRS, LINAC SRS	430
77435	Stereotactic body radiation treatment management per treatment course; 1 or more lesions, including image guidance entire course not to exceed 5 fractions	GK SRT, LINAC SRT	240

(*continued on next page*)

Table 2 (*Continued*)

CPT code	Description	Radiation modalities used	Number of claims
77470	Special treatment procedure (eg, total body radiation, hemibody radiation, per oral endocavity or intraoperative cone irradiation)	GK SRS, GK SRT, LINAC SRS, LINAC SRT	116
G6012*	Radiation treatment delivery, 3 or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 6-10MeV	WBRT*	1
G6017*	Intrafraction localization and tracking of target or patient motion during delivery of radiation therapy (eg, 3D positional tracking, gating, 3D surface tracking), each fraction of treatment	HA-IMRT*	0

Abbreviations: 3D = 3-dimensional; CT = computed tomography; GK = Gamma Knife; HA-IMRT = hippocampal avoidance intensity modulated radiation therapy; LINAC = linear accelerator; SRS = stereotactic radiosurgery; SRT = stereotactic radiation therapy; WBRT = whole-brain radiation therapy.
*Specific CPT codes and radiation modalities in the study that were uniquely used to bill for 1 type of radiation modality.

A more in-depth analysis of CPT codes revealed that a few of the CPT codes used to bill for treatment of BMs were unique to certain radiation modalities. The extremely narrow scope of these CPT codes allows for the direct comparison of the frequency of use of GK, LINAC, WBRT, and HA-IMRT. In addition, our CPT code analysis showed that a specific CPT code unique for GK SRS radiation treatment (77371) was billed 208 times while a specific CPT code unique for LINAC SRS radiation treatment (77372) was billed 94 times. It should still be noted that, altogether, 240 claims were made for delivery of SRT using the nonspecific CPT code 77435 ("Stereotactic body radiation treatment management per treatment course; 1 or more lesions, including image guidance entire course not to exceed 5 fractions"[11]) with a total cost of $8,935,127 and an average cost per radiation therapy of $37,230. However, difference in cost between GK SRT and LINAC SRT could not be determined directly given the aforementioned limitations of our data set. Given that GK SRS radiation cost a total of $6,387,882 across 208 suspected treatments, the average cost per treatment, including all other costs was approximately $30,711. Given that LINAC SRS radiation cost a total of $2,889,359 across 94 suspected treatments, the average cost per treatment including all other costs was $30,737. In addition, CPT codes 77307 and G6012 were billed a total of 405 times and were unique to only WBRT treatment delivery, while CPT code 77386 was unique to HA-IMRT treatment delivery and was billed 59 times. Given that the total overall cost for WBRT was $2,116,097, the total overall cost for HA-IMRT was $2,817,953, and that WBRT treatment was billed a total of 405 times compared with 59 times for HA-IMRT, it can be extrapolated that HA-IMRT is more expensive on a per-use basis, with WBRT costing $5225 per treatment including all other costs and HA-IMRT costing $47,748 per treatment including all other costs (Fig. 1). The remainder of the 1048 patients treated for BMs had radiation treatments billed 116 times under CPT code 77470 "Special Treatment Procedure (eg, total body radiation, hemibody radiation, per oral endocavity or intraoperative cone irradiation),"[11] a nonspecific code used to bill for both forms of SRS and SRT that yielded 116 claims.

A complete list of defined CPT codes used in the study as well as the number of times they were billed can be found in Table 1. CPT codes were associated with billing for a specific treatment type as outlined in Table 2 and defined by the health care insurer.

Unfortunately, our study is unable to significantly elaborate on a cost-effectiveness analysis between the radiation modalities being discussed due to the fact that we lack individualized data on the subjects included in our study. Accessible data for use in this study did not include individual patient data on radiation modality received, survival duration, adjunct treatments received, or duration of therapy. Therefore, our study serves to uncover broader cost and spending trends in the treatment of BMs rather than a true cost-effectiveness analysis of each radiation modality.

Discussion

There are many factors to consider when choosing a radiation modality to treat BMs. Local control of the tumor, overall survival of patients after radiation treatment, side effect profile, and potentially even cost of

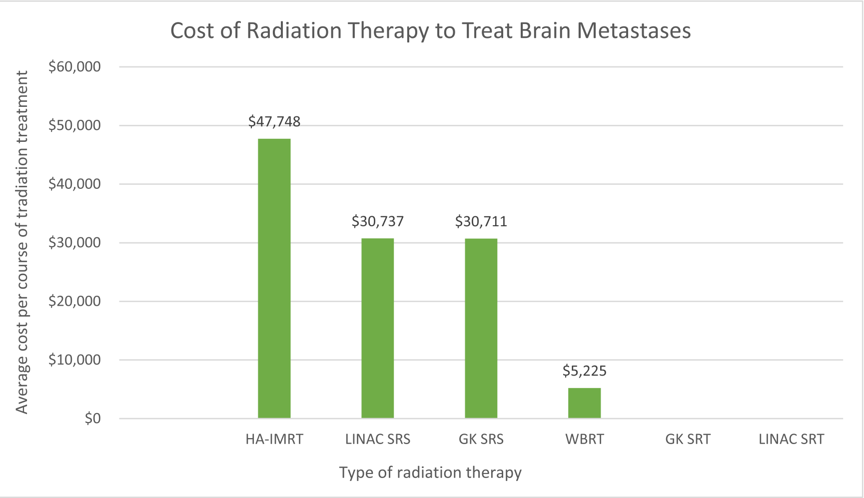

Figure 1 Average total cost per round of radiation therapy delivered across all radiation modalities used to treat brain metastases in the patient cohort. Average cost for Gamma Knife (GK) stereotactic radiation therapy (SRT) and linear accelerator (LINAC) SRT was unable to be calculated due to the lack of unique current procedural terminology codes, and therefore lack of clarity in claim count, pertaining to each treatment technique. *Abbreviations*: HA-IMRT = hippocampal avoidance intensity modulated radiation therapy; WBRT = whole-brain radiation therapy.

treatment are factors to consider when deciding on a brain-directed radiation treatment plan.

GK SRS and LINAC SRS have shown comparable levels of both local tumor control and patient overall survival posttreatment.[5,6] The similarity in effectiveness between these radiation modalities is significant enough to urge an analysis of the costs associated with their use in treating patients with BMs. In addition, a recent study comparing overall survival in patients receiving SRS or SRT for treatment of BMs found a nonsignificant difference in survival time between the 2 treatment strategies.[12] Considering our discovery that SRT has a higher average per-treatment cost than both GK SRS and LINAC SRS, and given that no significant differences in acute and late radiation-induced injury between the 2 fractionation methods has been observed,[13] further scrutiny is warranted to assess the clinical preference for SRT over SRS. One possible justification for using SRT over SRS is that SRS is typically used for lesions under 3 cm in diameter, while SRT becomes advisable when the tumor is larger or near critical structures like optic nerves. In such cases, the benefit of SRT is that the total radiation delivered is fractionated, allowing for better safety and preservation of surrounding tissues.[14]

Significantly more females compared with males were treated for BMs under health insurance coverage from the regional health care insurer used for this study, potentially indicating that more females than males are treated for BMs in general. Past studies have identified this disparity, 1 of which investigated the impact of sex on the presence of BMs at the time of diagnosis and subsequent survival in midlife patients (40-60 years old) with newly diagnosed malignancies. The study found that middle-aged females had a higher risk of developing BMs (odds ratio, 1.07) compared with males. However, females with BMs at diagnosis exhibited a lower risk of decreased all-cause mortality (hazard ratio, 0.86), indicating a survival advantage over middle-aged males with BMs.[15] This gender disparity can plausibly be attributed to the notion that breast cancer commonly metastasizes to the brain and has the highest incidence among all cancers in women, while prostate cancer rarely metastasizes to the brain and has the highest incidence among all cancers in men. The findings of our study support the logical trend that females are more frequently treated for BMs than males.[16,17]

Our study sought to compare the costs of these treatment techniques to determine whether cost of care should be taken into consideration when choosing a treatment technique. Data from a large regional health care insurer showed that GK SRS was the most expensive radiation modality of those included in the study. It also showed that GK required the most expensive technical component of spending, while LINAC required the most expensive physician (ie, professional) component. It is important to note that radiation oncologists and neurosurgeons bill for SRS with discrete CPT codes, and that billing data pertaining to these neurosurgeon-specific CPT codes (61796-61800) were neither included nor analyzed in our study. As a result of this omittance, the calculated overall cost for the treatment of BMs may be slightly underestimated.

In addition, our CPT code analysis showed that a specific CPT code unique for GK SRS radiation treatment delivery was billed 208 times across all 1048 patients being treated for BMs. This particular CPT code 77371 is used to bill "SRS treatment delivery, complete course of treatment of cerebral lesion(s) 1 session, multisource Cobalt 60 based,"[11] which specifies a component unique to GK SRS. This indicates that either approximately one-fifth of patients being treated for BMs underwent this specific type of radiation delivery as part of their treatment, or that select patients required multiple treatment sessions before completion of their treatment course. Similarly, a specific CPT code unique for LINAC SRS radiation delivery was billed 94 times. This CPT code, 77372, is defined as "Stereotactic radiosurgery treatment delivery, complete course of treatment of cerebral lesion (s) 1 session, linac based."[11] It is unclear given the data set if these claims were spread across 94 patients or if select patients required multiple LINAC treatments billed under 77372. The average cost per GK SRS treatment including all other technical and physician costs was approximately $30,711, while the average cost per LINAC SRS treatment including all other costs was $30,737. The nearly identical cost-per-treatment for GK SRS and LINAC SRS prevents a conclusive judgment from being reached on the comparative costliness of these radiation modalities. Potential justification for electing to treat with LINAC over GK treatment may be attributed to the lower risk of radionecrosis associated with LINAC systems compared with GK systems with similar rates of effectiveness at treating BMs.[18]

While we lacked access to data describing the difference in cost between these 2 CPT code claims, the comparative frequency of claims paints the picture that GK SRS radiation treatments were used more than twice as frequently as LINAC SRS radiation treatments in this patient population and had the highest overall cost of implementation among the radiation treatment techniques studied. It is important to be aware of other factors that might influence the choice between using GK SRS and LINAC SRS systems. Smaller community treatment facilities likely find LINAC SRS more appealing because it does not require neurosurgical involvement, it is more widely applicable for nonintracranial targets than GK SRS, and the regulatory constraints and higher costs associated with cobalt-based machines like GK result in their use mainly in larger academic centers or private referral centers. A high concentration of large academic centers in the northeastern United States, where our study is focused, potentially explains the more frequent use of GK SRS compared with the LINAC SRS for the treatment of BMs.[19]

One study comparing treatment options for BMs showed that, compared with SRS with WBRT, SRS with observation alone had a higher average effectiveness (measured in life years saved), higher average cost, and resulted in an incremental cost-effectiveness ratio within the generally accepted cost-effectiveness range of $50,000 to $100,000 per quality-adjusted life year. The researchers concluded that SRS with observation, followed by neurosurgical management of recurrences, is a reasonable and cost-effective treatment modality for BMs.[20] The data available for our study was unequipped to elaborate on this cost-effectiveness analysis due to lack of information on which study subjects received only single-modality radiation therapy and which subjects received multimodal radiation therapy, nor does it provide individualized cost data for each study subject. While our analysis shows that WBRT costs an additional $5225 per treatment, it did not include an analysis on the cost of repeated neurosurgical interventions to treat metastases. Future analysis elaborating on per-treatment neurosurgery costs for managing BMs would add to the cost-effectiveness debate between using only SRS and WBRT versus SRS and neurosurgical management.

Our analysis showed that HA-IMRT is more expensive on a per-use basis than WBRT. Further analysis showed that HA-IMRT had both a more expensive physician and technical component than did traditional WBRT, supporting the hypothesis that HA-IMRT is more costly than traditional WBRT.[21] The use of HA-IMRT has increased in recent use due to its proposed neuroprotective effects. A prospective study by Tsai et al found a significant correlation between radiation therapy dose to the hippocampus and the occurrence of radiation-induced cognitive decline. To prevent radiation-induced cognitive decline, WBRT techniques were developed to spare the hippocampus' dentate gyrus and became known as HA-IMRT. The Radiation Therapy Oncology Group 0933 trial compared 40 patients treated with hippocampal avoidance WBRT (HA-WBRT) to a historical WBRT group and demonstrated reduced cognitive decline by 4 months post radiation therapy and improved quality of life after 6 months, confirming HA-IMRT's neuroprotective effect.[22−26] Increased cost associated with HA-IMRT may be linked to the supplemental use of memantine with HA-IMRT, an additional medication not commonly used in conjunction with stereotactic radiation techniques, which has demonstrated effectiveness in preventing cognitive impairment caused by radiation by counteracting deleterious synaptic changes.[27,28] However, our study did not directly observe the cost or frequency of use of memantine because a CPT code for memantine administration was not evaluated.

In addition, in a study of cost-effectiveness traditional radiation therapies such as WBRT were found to be cost effective for patients with shorter prognoses (3 and 6 months), while HA-WBRT and SRS plus HA-WBRT demonstrated cost effectiveness for cohorts with longer prognoses (12 and 24 months).[29] The study underscores the significance of considering patient life expectancy in determining the cost effectiveness of different treatments and in highlighting the value of controlling late brain toxicity with novel therapies.

On a per-use basis, WBRT costs far less than HA-IMRT, GK SRS, LINAC SRS, and SRT. Cost-effectiveness analyses have shown that both SRS alone and SRS plus WBRT were both found to be cost effective compared with WBRT alone. It would be of great value to understand if SRS and WBRT were being used in isolation or in conjunction to treat BMs in our patient population; however, our data set is limited to cost data rather than individualized treatment courses. While our study cannot directly comment on cost effectiveness accounting for patient life expectancy, it does provide a real-world look into how spending is currently being allotted to different radiation techniques.

Conclusion

In conclusion, the choice of radiation modality for treating BMs should account for factors such as local tumor control, overall patient survival, side effect profile, and cost of treatment. SRS, including GK LINAC-based systems, have become standard treatment options, offering fewer side effects and comparable overall survival rates to WBRT. Moreover, HA-IMRT has gained popularity due to its neuroprotective effects, reducing cognitive decline and improving quality of life posttreatment.

Our comprehensive analysis of BM treatment costs presents a nuanced understanding of the challenges in balancing clinical efficacy and economic considerations. Our deduction of true per-treatment costs associated with HA-IMRT, WBRT, SRS, and SRT prompts a careful reevaluation of each modality's cost effectiveness. While our study acknowledges limitations in the data set that prevent us from conducting such an analysis on our study cohort, it provides valuable insights into current spending patterns for different radiation techniques. This pragmatic exploration highlights the need for informed decision making, considering both clinical outcomes and economic efficiency in the landscape of BM treatment.

Disclosures

Author Oralia Dominic was employed by the Highmark Medical Policy Department at the time of manuscript creation. The authors have no other known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Lin X, DeAngelis LM. Treatment of brain metastases. *J Clin Oncol*. 2015;33:3475-3484.
2. Ostrom QT, Wright CH, Barnholtz-Sloan JS. Brain metastases: Epidemiology. Schiff D, van den Bent MJ, eds. Brain metastases: Epidemiology. *Handbook of Clinical Neurology. Vol 149. Metastatic Disease of the Nervous System*. 2018:27-42.
3. Kim H, Rajagopalan MS, Beriwal S, Smith KJ. Cost-effectiveness analysis of stereotactic radiosurgery alone versus stereotactic radiosurgery with upfront whole brain radiation therapy for brain metastases. *Clin Oncol*. 2017;29:e157-e164.
4. Kazda T, Jancalek R, Pospisil P, et al. Why and how to spare the hippocampus during brain radiotherapy: The developing role of hippocampal avoidance in cranial radiotherapy. *Radiat Oncol*. 2014;9:139.
5. Scorsetti M, Navarria P, Ascolese A, et al. OS03.4 Gammaknife versus Linac based (EDGE) radiosurgery (SRS) for patients with limited brain metastases (BMS) from different solid tumor: A phase III randomized trial. *Neuro-Oncology*. 2017;19(suppl 3):iii5-iii6.
6. Attia M, Menhel J, Alezra D, Pffefer R, Spiegelmann R. Radiosurgery − LINAC or Gamma Knife: 20 Years of Controversy Revisited. *Isr Med Assoc J*. 2005;7:583-588.
7. Aoyama H, Shirato H, Tago M, et al. Stereotactic radiosurgery plus whole-brain radiation therapy versus stereotactic radiosurgery alone for treatment of brain metastases: A randomized controlled trial. *J Am Med Assoc*. 2006;295:2483-2491.
8. Brown PD, Ballman KV, Cerhan JH, et al. Postoperative stereotactic radiosurgery compared with whole brain radiotherapy for resected metastatic brain disease (NCCTG N107C/CEC·3): A multicentre, randomised, controlled, phase 3 trial. *Lancet Oncol*. 2017;18:1049-1060.
9. Brown PD, Jaeckle K, Ballman KV, et al. Effect of radiosurgery alone versus radiosurgery with whole brain radiation therapy on cognitive function in patients with 1 to 3 brain metastases: A randomized clinical trial. *J Am Med Assoc*. 2016;316:401-409.
10. Yamamoto M, Serizawa T, Shuto T, et al. Stereotactic radiosurgery for patients with multiple brain metastases (JLGK0901): A multi-institutional prospective observational study. *Lancet Oncol*. 2014;15:387-395.
11. Highmark Inc. Highmark Radiation Therapy Authorization Program Administrative Guide. June 2016. Highmark Inc.; 2011-2016: 1-19. Accessed March 19, 2024. https://content.highmarkprc.com/Files/Region/PA/CareMgmtProg/RadAuthProg/rad-therapy-auth-admin-guide.pdf.
12. Ostdiek-Wille GP, Amin S, Wang S, Zhang C, Lin C. Single fraction stereotactic radiosurgery and fractionated stereotactic radiotherapy provide equal prognosis with overall survival in patients with brain metastases at diagnosis without surgery at primary site. *PeerJ*. 2023;11:e15357.
13. Li Y, Wu J, Liu F, et al. Single-fraction SRS and multiple-fraction SRT for brain metastases from colorectal cancer. *Front Oncol*. 2022;12: 1060570.
14. American Association of Neurological Surgeons. Stereotactic radiosurgery. Accessed March 19, 2023. https://www.aans.org/en/Patients/Neurosurgical-Conditions-and-Treatments/Stereotactic-Radiosurgery.
15. Che W, Wang Y, Wang X, Lyu J. Midlife brain metastases in the United States: Is male at risk? *Cancer Med*. 2022;11:1202-1216.
16. Nayak L, Lee EQ, Wen PY. Epidemiology of brain metastases. *Curr Oncol Rep*. 2012;14:48-54.
17. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: Incidence - SEER Research Data, 8 Registries, Nov 2021 Sub (1975-2020). Accessed April 24, 2023. https://seer.cancer.gov.
18. Sebastian NT, Glenn C, Hughes R, et al. Linear accelerator-based radiosurgery is associated with lower incidence of radionecrosis compared with gamma knife for treatment of multiple brain metastases. *Radiother Oncol*. 2020;147:136-143.
19. Park HS, Wang EH, Rutter CE, Corso CD, Chiang VL, Yu JB. Changing practice patterns of Gamma Knife versus linear accelerator-based stereotactic radiosurgery for brain metastases in the US. *J Neurosurg*. 2016;124:1018-1024.
20. Lal LS, Byfield SD, Chang EL, et al. Cost-effectiveness analysis of a randomized study comparing radiosurgery with radiosurgery and whole brain radiation therapy in patients with 1 to 3 brain metastases. *Am J Clin Oncol*. 2012;35:45-50.

21. Gondi V, Pugh SL, Tome WA, et al. Preservation of memory with conformal avoidance of the hippocampal neural stem-cell compartment during whole-brain radiotherapy for brain metastases (RTOG 0933): A phase II multi-institutional trial. *J Clin Oncol*. 2014;32: 3810-3816.
22. Gutiérrez AN, Westerly DC, Tomé WA, et al. Whole brain radiotherapy with hippocampal avoidance and simultaneously integrated brain metastases boost: A planning study. *Int J Radiat Oncol Biol Phys*. 2007;69:589-597.
23. Gondi V, Tolakanahalli R, Mehta MP, et al. Hippocampal-sparing whole-brain radiotherapy: A "how-to" technique using helical tomotherapy and linear accelerator-based intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys*. 2010;78:1244-1252.
24. Ghia A, Tomé WA, Thomas S, et al. Distribution of brain metastases in relation to the hippocampus: Implications for neurocognitive functional preservation. *Int J Radiat Oncol Biol Phys*. 2007;68:971-977.
25. Barani IJ, Benedict SH, Lin PS. Neural stem cells: Implications for the conventional radiotherapy of central nervous system malignancies. *Int J Radiat Oncol Biol Phys*. 2007;68:324-333.
26. Brown PD, Gondi V, Pugh S, et al. Hippocampal avoidance during whole-brain radiotherapy plus memantine for patients with brain metastases: Phase III trial NRG Oncology CC001. *J Clin Oncol*. 2020;38:1019-1029.
27. Duman JG, Dinh J, Zhou W, et al. Memantine prevents acute radiation-induced toxicities at hippocampal excitatory synapses. *Neuro-Oncology*. 2018;20:655-665.
28. Barbour AB, Jacobs CD, Williamson H, et al. Radiation therapy practice patterns for brain metastases in the United States in the stereotactic radiosurgery era. *Adv Radiat Oncol*. 2019;5:43-52.
29. Savitz ST, Chen RC, Sher DJ. Cost-effectiveness analysis of neurocognitive-sparing treatments for brain metastases. *Cancer*. 2015;121:4231-4239.