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Comparison of doses received by the hippocampus in patients treated with single isocenter– *vs* multiple isocenter–based stereotactic radiation therapy to the brain for multiple brain metastases

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ABSTRACT

To investigate the doses received by the hippocampus and normal brain tissue during a course of stereotactic radiation therapy using a single isocenter (SI)–based or multiple isocenter (MI)–based treatment planning in patients with less than 4 brain metastases. In total, 10 patients with magnetic resonance imaging (MRI) demonstrating 2-3 brain metastases were included in this retrospective study, and 2 sets of stereotactic intensity-modulated radiation therapy (IMRT) treatment plans (SI *vs* MI) were generated. The hippocampus was contoured on SPGR sequences, and doses received by the hippocampus and the brain were calculated and compared between the 2 treatment techniques. A total of 23 lesions in 10 patients were evaluated. The median tumor volume, the right hippocampus volume, and the left hippocampus volume were 3.15, 3.24, and 2.63 mL, respectively. In comparing the 2 treatment plans, there was no difference in the planning target volume (PTV) coverage except in the tail for the dose-volume histogram (DVH) curve. The only statistically significant dosimetric parameter was the V_{100}. All of the other measured dosimetric parameters including the V_{95}, V_{99}, and D_{100} were not significantly different between the 2 treatment planning techniques. None of the dosimetric parameters evaluated for the hippocampus revealed any statistically significant difference between the MI and SI plans. The total brain doses were slightly higher in the SI plans, especially in the lower dose region, although this difference was not statistically different. The use of SI-based treatment plan resulted in a 35% reduction in beam-on time. The use of SI treatments for patients with up to 3 brain metastases produces similar PTV coverage and similar normal tissue doses to the hippocampus and the brain when compared with MI plans. SI treatment planning should be considered in patients with multiple brain metastases undergoing stereotactic treatment.

Introduction

Brain metastases are the most common presentation of central nervous system tumors. The incidence of brain metastases varies with the location and histology of the primary tumor. For tumors such as adenocarcinoma of the prostate, the risk of brain metastases is relatively low, in the range of 5% or less, whereas for other histologies, such as small cell lung cancer and metastatic melanoma, the risk can be high, in the range of 20% to 50%.[1,2] In addition to pathologic features relating to the primary tumor, the extent of systemic disease, the number of brain lesions, and the size and location of brain lesions can all affect the overall prognosis for the patient. With the improvement in systemic therapy that has occurred over the past decade, the prognosis for patients with brain metastases has continued to improve,[3] with a resulting emphasis on quality of life as well as duration of survival.

One way of improving quality of life in the treatment of brain metastases is to use more limited fields as opposed to whole-brain treatments. Stereotactic treatments for brain metastases have been used for several decades, with high control rates in the treated lesion.[4,5]

In addition, RTOG 0933 was recently reported in an abstract form and demonstrated decreased decline in neurocognitive function when doses to the hippocampus were reduced by using a hippocampal-sparing whole-brain radiation regimen. Although

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Table 1
Patient and tumor characteristics

	n	Median	Mean	Range
Patient				
Male	4			
Female	6			
Age (y)	10	58	57	31 to 81
PTV volume (mL)				
Per lesion	23	3.15	10.02	0.42 to 51.67
Per patient	10	15.17	24.06	2.00 to 56.24
Hippocampus volume				
Right (mL)	10	3.24	3.04	1.85 to 3.76
Left (mL)	10	2.63	2.65	2.06 to 3.09
Brain volume (mL)	10	1364	1350	1223 to 1587

this study was performed in patients undergoing whole-brain radiation therapy, the suggestion was that certain parts of the hippocampus play a significant role in neurocognitive function, and limiting the radiation doses to these regions could reduce the potential neurocognitive deficits after radiation therapy.

Based on this, we wanted to determine whether using a single isocenter (SI)–based stereotactic treatment would increase doses to the hippocampus when compared with multiple isocenter (MI)–based stereotactic treatments. The purpose of our study was to evaluate the doses received by the hippocampus for patients undergoing linear accelerator–based stereotactic radiation therapy using a SI- *vs* MI-based treatment planning.

Methods and Materials

The records of 10 patients with multiple brain metastases treated with stereotactic radiation therapy were reviewed. This study was approved by the University of Oklahoma Health Sciences Center Institutional Review Board.

Before the start of therapy, all patients underwent treatment planning computed tomographic (CT) and magnetic resonance imaging (MRI) scans. Treatment planning CT scans were obtained on a Discovery 590RT CT scanner (General Electric Healthcare, Milwaukee, WI). Axial CT imaging was used to scan all patients using a brain protocol. Both precontrast and postcontrast images were obtained at 1.25-mm slice thickness. Treatment planning MRI was performed on a General Electric (General Electric Healthcare, Milwaukee, WI) 3-Tesla Discovery 750-W MRI unit. Various sequences including T1 + C, T2, and SPGR were obtained and fused with the treatment planning CT scan.

All treatment planning was performed on the iPlan (BrainLab, Inc., Westchester, IL) treatment planning system. Both thin-slice CT images and MRI scans were imported into the treatment planning system and fused with each other. The gross tumor volume was contoured and a planning target volume (PTV) determined by the treating physician. A 2- to 3-mm expansion around the PTV was used for treatment plan optimization. An intensity-modulated radiation therapy (IMRT)-based, MI treatment plan with 8 to 10 noncoplanar fields per isocenter was used for each metastatic lesion. Critical structures considered in plan optimization included but were not limited to the brainstem, optic nerve, optic chiasm, and orbits. Appropriate treatment plans were generated to maximize the tumor coverage while minimizing the dose to critical structures. The prescribed dose to the metastases was 25 Gy in 5 fractions, with at least 95% of the target volume receiving 95% of the prescribed dose. Treatment plans were created following these dose constraints: the maximum dose to each critical structure was required to be $<$ 800 cGy (pituitary), $<$ 800 cGy (optic chiasm and optic nerves), $<$ 600 cGy (orbits), $<$ 200 cGy (lens), and $<$ 1200 cGy (brain stem). All plans were approved by the treating physician before the patient underwent treatment.

For the purposes of this study, a second plan was generated for these patients. The plan contained 10 to 14 fields using a SI-based treatment plan. All of the prior contours including the Gross Tumor Volume (GTV), hippocampus, and other critical structures were kept the same. SI plans used an isocenter location that was centroid or near-centroid to the metastatic lesions. Treatment plans used IMRT with noncoplanar field arrangements. As there were fewer isocenters, the SI plans used different field geometry with fewer total beams when compared with the MI treatment plans. Each plan was reviewed by a single physician and approved as acceptable for treatment. The resulting dose-volume histograms (DVHs) for the metastatic lesion as well as the hippocampus were compared between the 2 plans. Various dosimetric parameters including V_{10} (percentage of volume getting 10% of the prescribed dose), V_{20}, V_{40}, V_{60}, V_{80}, V_{100}, D_{100} (dose received by 100% of the volume), D_{90}, D_{80}, D_{50}, D_{30}, and D_{10} were evaluated. XLStat v 2013 (Addinsoft, Paris-l'hopital, France) was used for all statistical analysis. A 2-tailed paired t test analysis was performed for comparing the various dosimetric parameters derived from the MI and SI treatment plans.

Results

A total of 23 lesions in 10 patients were evaluated. Patient characteristics are shown in Table 1, and the metastatic lesion location and proximity to each other are shown in Table 2. There were 6 female and 4 male patients. Median patient age was 58 years. Overall, 7 patients had 2 metastases, and 3 patients had 3 metastases. The mean size and median size of the brain metastases were 10.7 and 3.15 mL, respectively. The median hippocampal sizes were 3.24 and 2.63 mL for the right and left side, respectively. For SI plans, 10 noncoplanar fields were most commonly used for treatment planning. The median number of total fields used for MI plans with 2 brain metastases was 18 and for MI plans with 3 metastases was 30.

Figure 1 shows the averaged DVH plots for PTV coverage from all of the treated tumors. In comparing the SI and MI treatment plans, there was no difference in the PTV coverage until the tail end of the curve. When specifically looking at the V_{95}, the V_{98}, and the V_{100}, the only statistically significant parameter was the V_{100}, where the PTV coverage was lower for the SI plan (Table 3). None of the other evaluated dosimetric parameters were different for PTV coverage when comparing the SI and the MI plans.

Critical structure dose constraints were met for all the plans. When comparing the DVH parameters for the hippocampus, there were no significant differences noted between the SI and the MI plans (Fig. 2). This was the case whether the right and left hippocampal doses were compared individually, or combined into a single analysis. In general, the MI plans appeared to treat larger volume of hippocampus in the lower dose region of the curves, and lower volume of hippocampus in the higher dose regions. However, the difference was only a few percentage points and was not statistically significant.

Figure 3 shows the DVH for the entire brain volume as well as the brain sub-PTV volume. Overall, the SI plan resulted in slightly larger volume of brain tissue receiving some dose of radiation. This appeared especially to be the case in the low-dose region. However, the difference between the SI and the MI plans was small and not statistically significant.

Table 2
Location of metastatic tumors and their proximity to each other

Patient no.	No. of target	Location of metastases	Minimum/maximum distance between targets (mm)
1	2	Left temporal and left inferior cerebellar	30.0
2	2	Left parietal and Left parieto-occipital	32.5
3	2	Right and left occipital	26.1
4	2	Right frontal and right parietal	63.6
5	2	Posterior brainstem and posterior chiasm	25.1
6	2	Left temporal and left optic chiasm	$<$ 8.0
7	2	Left cerebellar and left frontal	68.5
8	3	Left temporal, left parietal, and right temporal	42.3 / 81.7
9	3	Left anterior frontal, left thalamic, and Left occipital	10.9 / 67.1
10	3	Left parietal, left cerebellar, and right temporal	69.5 / 92.9

All distance measurements are from the nearest edge of the targets to each other.