Whole Brain Irradiation With Hippocamus Protection On Tomotherapy HDA Device

PEPELE, Eda Kaya¹, NALBANT, Nilgül², DEMİRTAŞ, Mehmet³

¹ Turgut Özal University Yesilyurt Vocational School Biomedical Device Technology Malatya, Turkey

² Acibadem University Atakent Hospital Radiation Oncology Istanbul, Turkey

³ Turgut Özal Medical Center Radiation Oncology Department Malatya, Turkey

Correspondence:

Eda KAYA PEPELE Turgut Özal University Yesilyurt Vocational School Biomedical Device Technology Malatya, Turkey eda.pepele@ozal.edu.tr

Received: 11 December 2024 Revised: 4 October 2025 Accepted: 16 January 2025

ABSTRACT

Purpose: In this study, treatment planning and hippocampus dose were evaluated by hippocampus-protected radiotherapy planning in whole brain irradiation with Helical Tomotherapy plan. Materials and Methods: In the study, magnetic resonance and computed tomography images were used to contour the PTV, the whole brain, hippocampus and structures at risk (OAR). The optimization volume was drawn by giving a 5 mm margin to the hippocampus. Planning parameters were 1.25 cm jaw width, 3 modulation factors and 0.215 pitch factors. Direction block definitions were entered for the right and left lenses from the structures at risk. Dose calculation was made with the fine dose grid. The dose prescription for the PTV was defined as 30 Gy in 10 fractions. In the PTV evaluation; while the dose received by the 95% volume, Homogeneity Index (HI) and Conformity Index (CI) were evaluated for homogeneity, the RTOG 0933 (Radiation Therapy Oncology Group) protocol was taken as a reference for the structures at risk, and the maximum and median doses of the hippocampus were evaluated considering the reference studies for the hippocampus. Findings and Conclusion: In the whole brain irradiation performed with the helical tomotherapy device while preserving the hippocampus, it was observed that 95% of the PTV volume covered the targeted dose. The parameters indicating the quality of the plan were calculated as HI= 0.21 and CI=1.05. It was observed that the eyes and lenses were below the tolerance doses specified in RTOG. It was found that the maximum and mean doses of the hippocampus were high compared to the reference studies. Since the tomotherapy device allows rapid dose reduction and target dose homogeneity, the hippocampus can be preserved in whole brain irradiation.

Keywords: Tomotherapy, Whole brain irradiation, Hippocampus.

INTRODUCTION

Whole brain radiotherapy (RT) is a method applied to patients with many brain metastases originating from various malignancies [1]. In whole brain irradiation, the hippocampus is one of the critical organs in whole brain irradiation, along with critical structures such as the brainstem and chiasm. The hippocampus is located in the medial part of the temporal lobe in an area adjacent to the temporal horn of the lateral ventricle [2]. The functions of the hippocampus have been investigated for many years. However, both the complexity of the hippocampus structure and its close relationship and intense connection with many regions in the brain make it difficult to fully explain its functions. Therefore, it is more accurate to work on the role of the hippocampus in complex functions rather than defining its functions alone [2,3]. Whole brain radiotherapy can lead to various side effects such as the development of cerebellar dysfunction, short-term memory and decreased learning ability,

Interruption of neurogenesis in the subgranular region can cause memory damage [6]. The function of the hippocampus is negatively affected due to radiation damage [7]. In the study conducted by Gondi and colleagues, the hippocampus dose was reduced both in average and maximum values in whole brain radiotherapy with a 30 Gy/10 fraction prescription while preserving treatment the hippocampus. [8]. Comparison with historical data of regularly treated patients indicated that there was significant memory protection for brain metastases with a phase II-RTOG0933 trial on preservation of the hippocampus in whole brain irradiation. [9]. Recent advances in radiotherapy techniques have made it possible to have a hippocampal-protected WBRT. Three-dimensional conformal radiotherapy (3DCRT) and more advanced techniques such as intensity-modulated radiotherapy (IMRT), imageguided radiotherapy (IGRT) and the unique irradiation technique Tomotherapy are widely used

and disorders in neurocognitive functions [4,5].

methods in radiotherapy applications. The concept of hippocampal-protected whole-brain radiotherapy has been proposed and studies have been conducted to avoid some of the observed neurocognitive toxicity. In whole-brain radiotherapy treatments, a sufficient dose is required for the brain tissue remaining in the target tumor in hippocampus-protected plans. Several studies have shown that the risk of metastasis in the hippocampal region is low [10,11]. Dosimetric studies conducted with the Tomotherapy technique in hippocampus-protected radiotherapy techniques show that this technique is used [12,13]. In this study, hippocampus-protected radiotherapy planning was performed in whole brain irradiation with Helical Tomotherapy device, and the planned target volume (PTV) of the treatment plan, dose homogeneity of the treatment plan and hippocampus dose were evaluated.

METHODS

In the study, the planned target volume (PTV) and critical organ (OAR) contouring was performed using computed tomography images of a 70-year-old male patient who had previously undergone whole brain irradiation. The hippocampus was drawn using the patient's magnetic resonance (MR) and computed tomography (CT) images. The target volume and critical organs were made by a specialist physician at the Velocity brand contouring station.

Treatment Planning

Contourings were transferred to the Accuray brand HI-ART 5.1.4 version treatment planning system of the HI-ART model Tomotherapy device via DICOM. for the treatment plan, the field width (FW) was defined as 2.5, Pitch factor as 0.287 and modulation factor as 3.00 from the parameters specific to the Tomotherapy planning system. PTV whole brain dose was prescribed as 30 Gy/10 fraction treatment dose. 6 MV photon beam was used. The treatment plan was optimized so that 95% of the PTV whole brain would receive the prescribed dose.

Dosimetric Plan Quality Assessment

In the planned target volume assessment of the treatment plan, the planning target volume (PTV) was evaluated as recommended in the RTOG 0933 protocol, taking the Radiation Therapy Oncology Group 0933 (RTOG) protocol as reference.

Critical Organ Assessment

The maximum dose received by the hippocampus was examined in the evaluation. The maximum doses for the eyes, lenses, optic nerve, chiasm and brainstem were evaluated by reference to the dose limitations given in the RTOG 0933 protocol.

RESULTS

When we look at the results given in Table 1, it is seen that PTV whole brain provides the maximum dose and D%95 of the criteria determined for planning. The maximum dose was found to be 108% and the maximum dose was found to be within the target volume. It was seen that the doses received by the brainstem, optic chiasm, optic nerves, eyes, lenses, chiasm, pituitary, and cochleas met the maximum dose criteria.

Table 1. PT	TV whole brain	and OAR values.
-------------	----------------	-----------------

PTV/OAR	Criteria	Findings (Gy)
	D%95	28.50
PTV whole brain	D%98	24.86
	D%2	31.28
	Dmax	33.23
Hippocampus	Maximum Dose	17.65
Hippocampus	Mean Dose	12.10
Brainstem	Maximum Dose	31.20
Lenses	Maximum Dose	4.15
Eyes	Maximum Dose	23.15
Optic Nerves	Maximum Dose	30.74
Chiasma	Maximum Dose	30.69
Cochleas	Maximum Dose	29.75
Pituitary	Maximum Dose	31.69
Body	Maximum Dose	33.23

It can be seen Dose Volume Histogram (DVH) and dose distribution for coronal, sagittal and axial in the Figure 1. Yellow and red lines indicates the hippocampus and PTV, respectively.



Figure 1: Dose Volume Histogram (DVH) and dose distribution for coronal, sagittal and axial of treatment planning: Yellow and red lines indicates the hippocampus and PTV, respectively in DVH and Blue area is 30 Gy and purple area is 28.5 Gy in dose distributions.

DISCUSSION and CONCLUSION

In this study, target volume and critical organ doses were evaluated by hippocampus protection in whole brain irradiation in Tomotherapy HI-ART model Tomo Edge, Volo Ultra, PreciseArt system featured planning unit. According to the planning criteria determined for the target volume, acceptable RTOG 0933 range was taken into account for treatment plans [14]. While the dose received by the hippocampus and OARs was tried to be reduced, the necessary dose was tried to be given to the whole brain PTV. In hippocampus protected whole brain planning, providing the desired optimization conditions in dose coverage of the target volume is a complex process. While low dose is given to the hippocampus, a balance must be provided between target coverage and maximum dose for the planned target volume. Optimization parameters are updated until the targeted dose is achieved in these criteria. After each optimization process, new volumes should be defined to include cold and hot spots in the optimization until the best result is obtained in the planning [15]. According to the RTOG 0933 report, it is stated that 98% of the target volume should receive at least 25 Gy to avoid cold spots that may cause an increase in local relapse (LR) in the brain. In hippocampus-protected whole [7]. brain radiotherapy planning, dose reductions occur in regions close to the hippocampus. These low-dose regions may cause an increase in LR in whole brain radiotherapy [16]. This situation should be taken into

consideration when optimizing treatment planning. In our study, it was observed that 98% of the target volume did not receive a dose below 24.86 Gy in PTV whole brain dose coverage. The maximum doses of critical organs met the acceptance criteria. In the study conducted by Gondi et al. using linac-based IMRT fields in hippocampus-protected whole brain radiotherapy, they created hippocampal avoidance zones by applying 30 Gy to the whole brain and using a 5 mm volumetric expansion around the hippocampus. According to their results, they found that the maximum dose received by the hippocampus was 15.3 Gy and the mean dose was 7.8 Gy [9]. When using nine fields in the Linac-based IMRT plan, Nevelsky et al. used only two different couch angles to reduce the treatment time. They reduced the maximum dose given to the hippocampus to 14.3 Gy compared to Gondi et al. [17]. In our study results, the maximum and mean doses of the hippocampus were found to be high compared to reference studies, and these values were obtained as 17.65 Gy and 12.10 Gy, respectively. The most important reason for the high hippocampus dose compared to reference studies is the attempt to meet the criteria for target volume coverage. Protection of the hippocampus during cranial irradiation creates significant technical difficulties in terms of contouring and treatment planning. In our study, since the protection of the hippocampus along with the whole brain target coverage and homogeneity causes a rapid dose decrease in the brain tissue close to the hippocampus, a balance must be achieved between target coverage and the maximum dose of the hippocampus. As a result, in our study, the target volume criteria were met while the critical organ doses were kept at the desired level in the whole brain irradiation with hippocampus protection by using the Tomotherapy planning unit. The maximum and mean doses of the hippocampus were found to be high compared to reference studies. The most important reason for the high maximum and mean doses is thought to be due to the optimization made for the PTV to reduce the low-dose area volumes.

Conflict of Interest

There are no conflicts of interest and no acknowledgements.

References

1. Nussbaum ES, Djalilian HR, Cho KH, Hall WA. (1996). Brain metastases. Histology, multiplicity, surgery and survival cancer;78:1781-8.

- İzci Y, Erbaş YC. (2015). Hipokampus: Yapısı ve Fonksiyonları. Türk Nöroşir Derg. Cilt: 25, Sayı: 3, 287-295.
- Collins P: Embryology and development. Williams PL (ed). Gray's Anatomy. 38. baskı. London: Churchill Livingstone, 1995: 249
- Du A, Jiang H, Xu L, An N, Liu H, Li Y, Zhang R: Damage of hippocampal neurons in rats with chronic alcoholism. Neural Regen Res 9(17):1610-5, 2014
- 5. Erdem A, Yaşargil G, Roth P: Microsurgical anatomy of the hippocampal arteries. J Neurosurg 79(2):256-265, 1993
- Ersoy AÖ, Tomar A, Köseoğlu E, Arman F, Karaman Y: Temporal lob epilepsili hastalarda hipokampal atrofi ve olaya bağlı endojen potansiyeller. Epilepsi 6(2): 104-109, 2000
- Başaran H, İnan G, Gül OV, Düzova M, Batur A. (2021) Tüm beyin radyoterapisinde yart tekniği ile hipokampus korumalı planların dozimetrik karşılaştırılması. Selçuk Üniversitesi Genel Tıp Derg. 31(1):76-81.
- 8. Gondi V, Tolakanahalli R, Mehta MP, et al. Hippocampalsparing whole brain radiotherapy: a "How-To" technique, utilizing helical tomotherapy and LINAC based intensity modulated radiotherapy. Int J Radiat Oncol Biol Phys. 2010;78(4):1244-52.
- Gondi V, Pugh SL, Tome WA et al. (2014). reservation 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
- 10. Grosu AL, Oehlke O, Sturm D. Whole-brain irradiation with hippocampal sparing and dose escalation on metastases:

Neurocognitive testing and biological imaging a phase ii prospective randomized multicentre study 2016:1–86.

- 11. Oehlke O, Wucherpfennig D, Fels F, et al. Whole brain irradiation with hippocampal sparing and dose escalation on multiple brain metastases. Strahlenther Onkol 2015;191:461-9.
- 12. Deng W, Saxe MD, Gallina IS, et al. Adultborn hippocampal dentate granule cells undergoing maturation modulate learning and memory in the brain. J Neurosci 2009;29:13532-42.
- Ghia A, Tomé W, Thomas S, et al. Distribution of brainmetastases in relationtothehippocampus: implications for neurocognitive functional preservation. Int J Radiat Oncol Biol Phys. 2007;68:971.
- 14. RTOG 0933 Protocol. A PhaseIi Trial of Hippocampal Avoidance During Whole Brain Radiotherapy For Brain Metastases. 31 March 2011.
- 15. Krayenbuehl J, Martino MD, Guckenberger M, Andratschke N. Improved plan quality with automated radiotherapy planning for whole brain with hippocampus sparing: a comparison to the RTOG 0933 trial. Radiation Oncology 2017;12:161.
- Harth S, Abo-Madyan Y, Zheng L, et al. Estimation of intracranial failure risk following hippocampal-sparing whole brain radiotherapy. Radiother Oncol. 2013;109:152–8.
- Nevelsky A, Ieumwananonthachai N, Kaidar-Person O, et al. Hippocampal-sparing whole-brain radiotherapy using the elekta equipment. J Appl Clin Med Phys. 2013;14:113–20.