HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2022.04372
Haydarpasa Numune Med J 2022;62(4):447–453

hnhtipdergisi.com

ORIGINAL ARTICLE

Dosimetric Phantom Consistency of TMR-10 Protocol in Homogeneous and Inhomogeneous Regions in Gamma Knife Radiosurgery Planning

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Abstract

Introduction: The algorithms used in the GammaPlan treatment planning system are "Tissue Maximum Ratio (TMR) classical," "TMR 10," and "convolution" algorithms, respectively. In this study, the consistency of dosimetric measurements with the TMR 10 protocol used in SRC (stereotactic radiosurgery) planning in lesions located in homogeneous and inhomogeneous regions in different intracranial location scenarios was investigated.

Methods: In this study, the accuracy of administration of multiple metastasis treatment on the Gamma Knife Perfexion device was investigated. Computed tomography was performed with 1 mm cross-section intervals of CIRS brand Atom randofantoma. Critical organs and three different brain metastases located in homogeneous and heterogeneous regions, which are not on the same plane with each other, were drawn on the phantom. Planned target volume (PTV) volumes were created without margining the drawn gross tumor volumes, and three separate plans were made for three different PTV volumes. All plans were calculated using the TMR 10 algorithm. Critical organ doses were kept below the brain-SRC criteria for all calculated plans. Gafchromic EBT-3 film was placed on the sections with the target volume drawn on the phantoms and irradiated (1600 cGy, 50% isodose area). Measurements were made three times. The measured film results and the doses calculated from the planning were compared with gamma index analysis for different tolerance values.

Results: In our study, for three different lesions planned and irradiated with different gradient index values, a difference of 2.11–9.58% was observed between the values calculated with the TMR-10 protocol and the values obtained in the dosimetric measurement. A decrease in consistency was observed, especially in inhomogeneous region placements.

Discussion and Conclusion: There may be inconsistency between the TMR-10 protocol and actual dosimetric measurements, especially around inhomogeneous intracranial structures. We hope that this inconsistency will decrease in the future with the developing dose calculation protocols.

Keywords: Dosimetry; gamma knife; gammaplan; radiosurgery; TMR-10 algorithm.

Gamma knife radiosurgery is an exclusive treatment modality that has been used successfully in the treatment of various intracranial lesions since 1968[1]. Algorithms used in "Gamma Plan" treatment planning system from past to present are "Tissue Maximum Ratio (TMR)-classic", "TMR 10," and "convolution" algorithms, respec-

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Submitted Date (Başvuru Tarihi): 10.11.2021 **Revised Date (Revize Tarihi):** 10.11.2021 **Accepted Date (Kabul Tarihi):** 14.01.2022

tively. TMR algorithms do not take into account the fact that bone structures and air cavities have different electron densities, therefore, do not take into account the effect of inhomogeneity in dose calculation. Instead, TMR algorithms assume that the patient's head is composed of only the water equivalent of matter. Convolution algorithm, on the other hand, takes into account the different effects of different structures such as bone, air, soft tissue, on dose attenuation by taking into account the electron densities obtained from the computed tomography (CT) data, and makes more realistic calculations, especially in inhomogeneous regions. The effect of inhomogeneous structures is more evident especially in small areas and at the inhomogeneity interface with different densities (e.g., bone, air, and soft-tissue interfaces)[2]. In this study, the consistency of dosimetric measurements with the TMR 10 protocol used in SRS (stereotactic radiosurgery) planning was investigated in lesions located in homogeneous and inhomogeneous regions in different intracranial location scenarios.

Materials and Methods

In this study, the accuracy of administration of multiple metastasis treatment on the Gamma Knife Perfexion (Elekta Instruments, Stockholm, Sweden) was investigated. CT was performed on CIRS Atom RANDO phantom (CIRS, Inc., Norfolk, VA, USA) using Philips Brilliance Big Bore CT (Philips Medical Systems, Cleveland, OH, USA) with 1 mm slice thickness. Critical organs and three different brain metastases located in homogeneous and heterogeneous regions, which are on different planes with each other, were contoured on the phantom. Planned target volumes (PTVs) were created without margining the plotted gross tumor volume and three separate plans were made for three different PTV volumes.

All plans were calculated using the TMR 10 algorithm in GammaPlan software. Critical organ doses were kept below the brain-SRC criteria for all calculated plans. Gafchromic EBT-3 film (Ashland Specialty Ingredients, NJ, USA) was placed on the sections with the target volume drawn on the phantom, then irradiated. Measurements were made 3 times. The measured film results and the doses calculated from the planning were compared with gamma index analysis for different tolerance values.

CIRS Atom 702G Adult Female Phantom

The body tissue of the CIRS Atom RANDO phantom is designed in accordance with the structure of human tissues and cavities, and its bones are the equivalent of natural human bones. X-ray and electron absorption properties are equivalent to human tissue. It is a RANDO phantom plastic whose soft tissues are made of a synthetic material and hardened by heat. CIRS Atom RANDO phantom consists of 2.5 cm thick transverse sections.

Gamma Knife Perfexion Stereotactic Radiosurgery System

The collimator architecture of the Leksell Gamma Knife Perfexion is designed as cylindrical and it performs the treatment using three different sizes of circular collimators located in the radiation unit. The collimator part of the device consists of 8 sections (sectors) and there are 4, 8, and 16 mm collimator openings in each sector. There are 24 radioactive Co-60 sources that can act mechanically in each section. The total number of cobalt resources is 192. The half-life of the Co-60 source in Gamma Knife Perfexion is 5.26 years, and it decays into Ni-60 by making two different gamma irradiations of 1.33 and 1.17 MeV (mega electron volt) and two β-irradiations of 0.313 and 1.48 MeV. The average gamma energy of the source is 1.25 MeV. Since the rays coming from the sources in the Gamma Knife Perfexion device are combined in a single center, it creates a high dose region in the center. By positioning the high energy obtained at the junction of the sources with stereotactic coordinates, the target tissue is treated with the biological effect it creates. With the advantage arising from the geometric structure of the device, while the tumor is wrapped with a 50% isodose line to create a high target dose, a low dose region can be obtained in the normal brain tissue with a steep dose fall. This ensures that the normal tissue outside the target volume is exposed to a much lower radiation dose in the treatment with Gamma Knife. The dose rate is related to the activity of cobalt. While the dose rate decreases as it moves away from the center, this dose rate becomes half of the central one for the 50% isodose line. Therefore, as the dose efficiency decreases with the decreasing dose rate, an additional protection is provided for the surrounding tissues.

"Gamma Plan" Treatment Planning System

Gamma Plan treatment planning system allows planning on CT, MR, PET, and angiography images. The TMR 10 algorithm is often used for plans made on magnetic resonance images. Since this algorithm does not give any information about the bone structure, the skull shape is manually introduced to the planning system using a special cap called "bubble head frame" and measuring the distance to the scalp with a ruler (bubble measurement). Manual shot placement is used in planning to optimize tumor coverage rate, selectivity, and gradient index. In the current system, 4 mm, 8 mm, and 16 mm diameter collimators are used in planning. In addition, the geometric shape of the spherical isodose fields obtained from these collimators through 8 circularly placed sectors can be changed manually or automatically with the method called "beam shaping" or "dynamic shaping."

Film Dosimeters

The working principle of the film dosimeter is based on the relationship between the radiation dose to which the film is exposed and the degree of darkening. The irradiated radiation dose value and the corresponding optical density form the basis of film dosimetry. Optical density (OD) in the irradiated film is measured with a densitometer device. The amount of darkening in the film is found by calculating the optical density.

$OD = \log_{10} (I_0/I)$

I_0 = Initial light intensity

I = Light intensity passing through the film

Film dosimetry is a relative method. Therefore, a dose-calibration curve is needed. A dose-calibration curve is created by irradiating the films with previously known dose values and finding the corresponding ODs. The advantages of the film dosimeter are that it provides 2D information about the irradiated region with high spatial resolution, can be used for small and large area dosimetry, can be read repeatedly and the amount of absorbed radiation can be recorded.

Gafchromic® EBT3 Film

The nominal thickness of the active layer of the EBT3 films used in our study is 28 µm. The active layer is located between two polyester substrates of the same thickness (125 µm), and microscopic silica particles (less than about 10 µm in diameter) are embedded in the surface.

EPSON Expression 11000 XL Scanner

The Epson Expression 11000 XL is a flatbed film scanner that offers very high scanning speed and high resolution. With 2400×4800 dpi resolution and 3.8 DMax high optical density, it offers scanning area even to A3 size. The scanner's maximum scanning resolution is 12800 dpi×12800 dpi and the color depth is 48-bit-color. The scanner is suitable for scanning all film types used for dosimetric controls.

SNC Patient™ Software

SNC Patient™ software from Sun Nuclear (Sun Nuclear, Melbourne, FL, USA) compares the planned dose with the measured dose points. In the gamma analysis method, dose distribution calculation accuracy is measured using DTA (distance between the calculated dose distribution showing the same dose and the measured data point) and DD (the difference between the calculation value and the measurement dose value at the same point).

Planning stages in GammaPlan System

After the stereotactic frame was attached to the phantom, stereotactic CT imaging was performed, skull measurements of the phantom were made using the Gamma Knife Bubble Head Frame and planning was started. Treatment plans were created using the 1 mm dose calculation grid and the TMR 10 dose algorithm. PTV volumes were selected at different anatomical locations.

- PTV 1: A parenchymal tumor at the level of the vertex with a volume of 2 cm^3
- PTV 2: Tumor adjacent to the nasopharyngeal cavity with a volume of 2 cm^3
- PTV 3: A tumor with a volume of 2 cm3 adjacent to the brain stem and chiasm.

Plans were made using separate calculation matrices for three different PTV volumes determined. 4 and 8 mm collimators were used in the plans. 8–13 different shots (isocenters) were used for each volume. The marginal dose was chosen as 1600 cGy in a single fraction. The target volume was normalized to the 50% isodose line to receive the entire dose. Tumor coverage percentage, selectivity, and gradient index values were calculated from the plans made (Fig. 1).

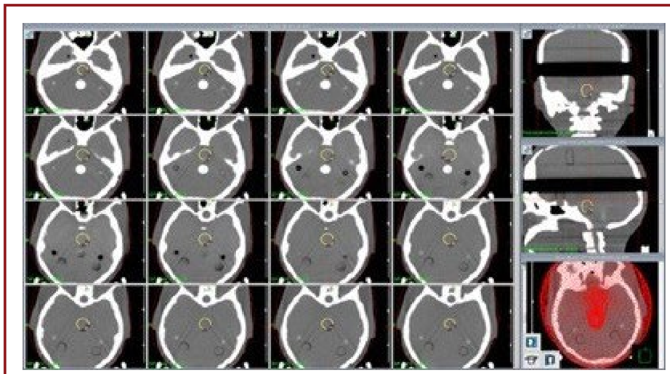

Figure 1. Screenshot of the treatment planning created for the planned target volume 3 volume.

Preparation of Gafchromic EBT-3 Films to be irradiated and Obtaining the Film Calibration Curve

To create the calibration of the Gafchromic EBT-3 films, a number of films corresponding to each MU value and the film to be used as the background were cut. To pay attention to the scanning direction due to the direction dependence of the films, a sign indicating the scanning direction was placed on the edge of each cut film with a pencil.

12 films of 4×5 cm^2 were attached to the Elekta Film holder. For the calibration curve, the films were irradiated with 0, 50, 100, 300, 500, 1000, 1500, 2000, 2500, 2700, 3000, and 3500 MU using a 16 mm collimator at a dose rate of 1.638 Gy/min. Three irradiation sessions were applied for each MU value. 24 h after the films were irradiated, each piece was scanned with the Epson Expression 11000 XL scanner in 48-bit depth color and 75 dpi resolution. In the film scanning process, attention was paid to ensure that the scanning direction of the scanner was the same as the direction previously marked on the film. Thus, the lateral response artifact caused by the direction dependency of the film was prevented. In addition, each scanned film was placed right in the center of the scanner. The films were scanned considering the orientation and position on the scanner bed to minimize the effect of optical irregularity. Each film was scanned 3 times to account for the warming effects of the scanner. The film calibration curve was created using SNC software (Fig. 2).

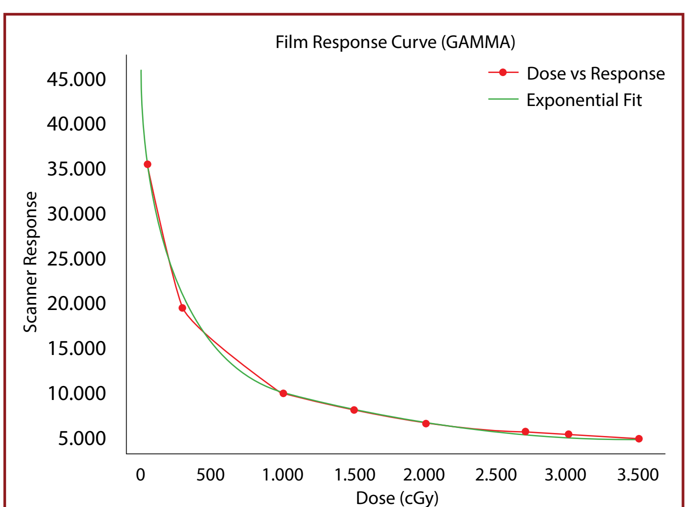

Figure 2. Film calibration curve of EBT 3 film obtained from Gamma Knife Perfexion.

Irradiation of Plans Created in GammaPlan Treatment Planning System (TPS)

The images were transferred to the GammaPlan Treatment Planning system after the CT scan of the CIRS Atom RANDO phantom, whose stereotactic localization was provided by the CT indicator box and fixed with the frame, was taken. Before starting the planning, fiducial marker measurement was performed for the accuracy of the imaging system. A bubble head frame was attached to the stereotactic frame attached to the phantom, and the distance between the helmet surface and the phantom scalp was measured at 24 reference points, and the values were introduced to the planning system. Target volumes with a diameter of 2 cm were determined in the sections where the film will be placed. For these target volumes, the dose of 1600 cGy was defined to the 50% isodose line. After the created plans were approved, they were sent to the treatment station. Then, for each tumor, the phantom was fixed on the treatment table, and the created plans were irradiated 3 times, respectively.

Evaluation of Irradiated Films

After the irradiation of the plans made in the Gamma Knife Perfexion device, the irradiated films were kept in a dark place for 24 h. Then, the irradiated films were scanned by following all the procedures applied in film calibration in the scanner. After the film scanning process was completed, a file with the extension ".tif" was created for each film. These ".tif" files were converted into ".flm" files using the film calibration curve. For each plan calculated in the GammaPlan treatment planning system, the dose distributions in the section where the film was placed and the dose distributions measured with the EBT 3 film were compared with the gamma index analysis method using SNC Patient Software. Gamma analysis evaluation criteria of the calculated and measured plans were determined as DTA=± 3 mm, DD=± 3%; DTA=±2 mm, DD=±2%, and DTA=±1 mm, DD=±1% (Fig. 3).

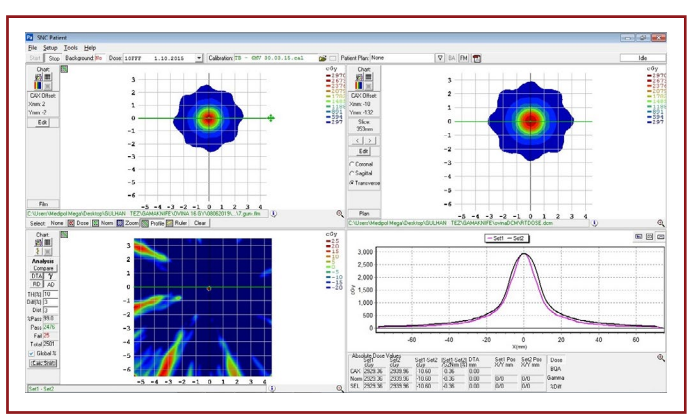

Figure 3. Gamma index analysis result determined as ±% 3/3 mm.

Results

Dosimetric Evaluation of Plans Made in Treatment Planning Systems

In all plans made in GammaPlan treatment planning systems, the PTV volume was ensured to receive 100% of the prescribed dose. While these criteria were met, critical organ doses were kept at or below the accepted limits in all plans. As a result of the data obtained from planning DVHs (dose-volume histogram), dose-volume parameters of critical organs and selectivity, tumor coverage ratio and GI (gradient index) values were compared (Table 1).

SRS Doses for Critical Organs

The total dose values of the plans created in the GammaPlan treatment planning system were evaluated considering the brain-SRS criteria (Table 2).

Film Calibration Curve

The calibration curve of the films irradiated with Co-60 γ-energy in Gamma Knife Perfexion is shown in Figure 3.

Findings Obtained from Plans Created in Treatment Planning Systems

After the irradiation of all plans created in the GammaPlan Treatment Planning System, the dose distributions obtained from the EBT3 film and the dose distributions obtained from the planning were compared. All plans were evaluated using ±3%/3 mm ±2%/2 mm and ±1%/1 mm gamma index analysis passing criteria (Table 3).

The calculated plans for each PTV were irradiated 3 times and the mean, standard deviation and % dose difference of these 3 measurements are given in Table 4.

The absolute dose difference in the center of the drawn PTVs was calculated with the following formula using the planning and measured values.

$$\%\ \text{Dose difference} = \%\ \frac{\text{Measured dose} - \text{Calculated dose}}{\text{Measured dose}}$$

Table 1. Values calculated by TMR-10 algorithm following irradiation of CIRS Atom randophantom with Gamma Knife

	PTV* 1	PTV 2	PTV 3
Treatment dose rate	1.610 Gy/min	1.610 Gy/min	1.610 Gy/min
Beam-on time	25.9 mins	35.2 mins	42.3 mins
Number of isocenters	8	11	13
Tumor coverage	1	1	1
Selectivity	0.98	0.98	0.99
GI (Gradient index)	2.40	2.80	2.61

*PTV: Planned target volume.

Discussion

In the GammaPlan system used for GammaKnife Perfexion, the plans of the CIRS atom RANDO phantom for three different tumor locations were made using the TMR 10 algorithm to meet the Brain SRS criteria. The tumor coverage ratio of the plan made for the PTV 1 volume located in the homogeneous region was found to be 1, its selectivity was

Table 3. Gamma index analysis passing criteria of the film results measured in the Gamma Knife Perfexion treatment and the dose distributions of the plans calculated with the TMR-10 algorithm in the GammaPlan treatment planning system

Criteria	3/3 mm ± %	2/2 mm ± %	1/1 mm ± %
PTV 1	99.0	98.7	97.2
PTV 2	91.2	88.6	77.2
PTV 3	98.7	97.2	96.4

Table 4. Dose differences of plans calculated and measured in Gamma Knife Perfexion

	Planning	Measurement +/- SD	% Dose difference
PTV 1	2939.96	2879.14 + 13.9	-2.11
PTV 2	3195.12	2915.78 + 24.7	-9.58
PTV 3	3030.58	2913.65 + 18.6	-4.01

Table 2. Critical organ dose values obtained from the average of the three plans made in GammaPlan

Critical Organ	Volume (mL)	Criteria (Gy)		Planned value (Gy)	
		Maximum volume dose	Maximum point dose	Maximum volume dose	Maximum point dose
Chiasm	<0.2	8	10	6.08	9.98
Right optic nerve	<0.2	8	10	6.08	9.98
Left optic nerve	<0.2	8	10	6.08	9.98
Brainstem	<0.5	10	15	8.22	13.20
Right lens	<0.1	5	10	0.12	0.40
Left lens	<0.1	5	10	0.08	0.11

0.98, and the gradient index was 2.40. The rates of passing the final dose distribution for this plan were 99.0%, 98.7%, and 97.2% for the pass criterion ±3/3 mm, ±2%/2 mm, and ±1%/1 mm DD and DTA values, respectively. These values were obtained as 91.2%, 88.6%, and 77.2% with the same evaluation criteria for the PTV 2 volume located in the inhomogeneous region close to the nasopharyngeal cavity. The tumor coverage, selectivity, and gradient index values of the plan for this volume were 1, 0.98, and 2.80, respectively. The penetration rates were found to be 98.7%, 97.2%, and 96.4% for the PTV 3 volume, which is located in a homogeneous region even though it is close to the critical organs. The plan for the PTV 3 volume had a tumor coverage ratio of 1, a selectivity of 0.99, and a gradient index of 2.61.

It was observed that the penetration rates decreased as the evaluation criteria were decreased from ±3/3 mm to ±1%/1 mm. In addition, it was observed that one of the most important parameters affecting the penetration rates was the region of the tumor, and the rate of penetration decreased in places with organs with different densities, and this rate decreased to an unacceptable level especially in air cavities.

Although there are some studies examining the difference between GammaPlan algorithms in the literature, there is no consensus among the results of these studies.

Chung et al.[3] compared the dose distributions of the plans they made using the convolution algorithm on the RANDO phantom on GammaPlan with the film dosimetry. They reported that test plans using different isocenter numbers, measuring plane, location and collimator size had a pass percentage of ≥96.9%. As a result of their studies, they emphasized that both algorithms can be used.

Pipek et al.[4] compared the dose distributions calculated with three different algorithms (TMR classical, TMR 10 and convolution) in GammaPlan for Gamma Knife Perfexion with the Monte Carlo dose distribution they calculated using the Geant 4 code, and they did not find a significant difference between the three algorithms. Gamma index passing rates were found to be ≥99.9% for the ±3%/1 mm criterion for all three algorithms. As a result of their studies, they reported that the dose distributions calculated by the three algorithms were close to each other.

Choi et al.[5] in their study, compared the dose distributions calculated with the TMR 10 algorithm in GammaPlan for Gamma Knife Perfexion with the Monte Carlo dose distribution calculated using the Geant 4 code, and the TMR algorithm showed the dose to be 4% higher than the maximum dose for complex tumors close to the bone, they observed that the dose difference increased up to 11% in the plans made using small collimators in areas close to the air columns.

Xu et al.,[6] on the other hand, compared that the dose distributions calculated with three different algorithms (TMR classical, TMR 10, and convolution) in GammaPlan for the Gamma Knife Perfexion device. reported that the difference between classical and convolution algorithms was 11.5%.

In this study, plans were made for virtual PTV volumes in three different regions on CT images of CIRS Atom RANDO phantom in Gamma Knife Perfexion. A dose of 16 Gy in a single fraction has been prescribed. The plans were calculated with the TMR-10 calculation algorithm and the prescribed dose was defined to the 50% isodose line. The accuracy of dose distributions was investigated by gamma analysis evaluation method using EBT-3 film dosimeter. The obtained dose distributions were evaluated with tolerance criteria of ±1%/1 mm, ±2%/2 mm and ±% 3/3 mm, and the pass rates were examined. The results obtained from our study showed that the TMR 10 algorithm did not give satisfactory results, especially in the treatment of tumors located in the inhomogeneous region.

Conclusion

Geometric accuracy is an important requirement for stereotactic radiosurgery. It requires both precise target identification in three-dimensional space and precise delivery of radiation dose distributions that leave ablative doses to the target while minimizing the possibility of damage to surrounding healthy tissues and hence radiation.

Today, SRS/SRT systems play a solid role in the treatment of complex shape lesions, often adjacent to OARs. They also provide extremely steep dose gradients within the target. In SRS treatments with millimetric margins, it is very important to verify the criteria provided in the planning with measurement.

In this study, the dose calculation accuracy of the treatments and the algorithm used in the Leksell Gamma Knife applied in intracranial tumors with the SRS treatment method were investigated. For this, the dose differences between the dose distribution map taken from the section where the film coincides with the phantom from TPS and the dose distribution mapping on the irradiated films were investigated.

As a result of this study, although there was a similarity between the dose distributions calculated by the treatment planning system and the dose distributions measured with the EBT-3 film in homogeneous regions, it was observed that this similarity decreased in inhomogeneous regions. As a result, it was observed that the reliability of the TMR 10 algorithm was lower in regions with inhomogeneous anatomical structures.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: M.T., H.A.D.; Design: Ö.Y., H.A.D.; Data Collection or Processing: M.T., V.İ.; Analysis or Interpretation: Ö.Y., V.İ.; Literature Search: M.T., V.İ.; Writing: V.İ., Ö.Y.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study received no financial support.

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