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Quality of Radiosurgical Plans by Leksell Gamma Knife Perfexion in the Treatment of Meningioma: Comparison between two isodose lines (50% and 75%)

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ABSTRACT

Introduction: Radiosurgery is a well-established available technique for treating many diseases and indications. Planning quality assessment is a crucial step in the procedure itself and outcome probabilities; either control or complication probability. Several physical indices and methodology have been developed to describe any plan. Accordingly, plan quality and outcome could be compared with other plans. In current study, the aim was to compare two plans with different isodose line using radiobiological model, tumor control probability (TCP), normal tissue complication probability (NTCP) and plan's physical indices.

Material and Methods: The cross-sectional study included 20 patients (5 male and 15 female) with median age of 44 years (21-66) and presented with radiologically diagnosed meningioma. Two radiosurgical forward plans were applied with same marginal dose of 12Gy at two different isodose lines of 50% and 75% isodose alternatively using Leksell Gamma Plan of single session GKS. Dose-Volume Histogram (DVH) was imported to MATLAB to compute TCP, NTCP values at 5 years for each plan, and physical indices such as coverage, selectivity, conformity, heterogeneity, and gradient indices.

Results: Median target irradiated volume was 7.5 cm^3 (0.588 -23.72). TCP was significantly higher in the plan using 50% isodose line for the marginal dose than that using 75% isodose line (95.05%, 49.44%, p<0.05, *Independent Samples t-Test*). Brainstem and optic apparatus NTCPs were very low 0.01% (0-0.045%) in the former plan and zero in the later one (p =0.001, Mann-Whitney test).

Conclusion: Radiobiological models and physical indices could be used for the optimum plan selection of GKS.

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Introduction

The Leksell Gamma Knife is a well-established treatment modality that uses the radioactive source and stereotactic technique to deliver high dose to the target and very low dose towards the surrounding normal tissues. Such target could be tumor, vascular malformation, or other pathologies. The main advantage of stereotactic target localization is that it only allows a minimum radiation dose to be imparted to adjacent organs at risk (OAR) [1-2-3]. The process of stereotactic delivery of the high do

se of radiation is a complex of several sequential steps. Planning is a crucial step coming after neuroimaging on the frame-affixed head and before the execution of the plan using the radiosurgery machine itself. Isodose line and prescription physical dose are the most common parameters to be exported and evaluated which are not enough to cover all radiobiological aspects, and to compare with other plans efficiently.

Physically, there are several factors defining the range of a penumbra such as the design of the source, collimation, and the isodose line (IDL) [4]. For GK-based conveyance, the 50% IDL is the most well-known determination to a great extent dependent on chronicled point of reference and the presumption that endorsing to the 50% IDL gives the steepest portion [4].

In this study, fitting numerical details of normal tissue complication rate (NTCP) is like tumor control probability (TCP), which addresses the likelihood that after a radiation therapy no malignant growth cell has made. Treatment decision expects to accomplish a TCP esteem that merges or is close to one. While the TCP is worried about the harm to destructive tissue, the harm of encompassing normal tissue cells is

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excluded from a TCP model, the NTCP, and we use the current TCP models as rules for the progression of NTCP models for normal tissue.

The aim of this study was to evaluate the biological differences in treatment plans with different isodose lines using Gamma Knife Radiosurgery technique for meningioma in terms of radiobiological model, outcome probability, physical indices.

Materials and Methods

Patients and Materials

Subjects Included and Pathology Specifications

Twenty meningioma patients were treated with Gamma Knife between March 2019 and March 2021. They were 5 male and 15 female patients with median age of 44 years (21-66). The anatomical location was variable (petro-clival 3, CPA 2, cavernous 4, sellar and suprasllar 4, Sphenoid wing 3, petrous apex 1, supratentorial 1, Pineal body 1, frontal 1.). All patients were diagnosed on the common radiological characteristics of the meningioma depending on brain CT and MRI. The lesion was slightly hyperdense in non-contrast CT and brightly and homogeneous contrast enhancement with characteristics dural tail, with or without nearby hyperostosis. It was also isointense to grey matter in T1-weighted image with intense and homogeneous enhancement with contrast study. The T2-weighted image showed isointense / hyperintense to grey matter and restricted diffusion in DWI/ADC. All patients have been evaluated by multidisciplinary board for deciding the proper management modality. All patients have signed the informed consent after explanation of the procedure and treatment outcome possibilities.

Leksell Gamma Plan (LGP)

Treatment Planning System of stereotactic Leksell Gamma Knife Perfexion® radiosurgery, which is used to treat brain lesions without surgery, is done with Leksell Gamma Plan version 10.1.The use of 192 fixed Cobalt-60 sources minimizes any potential inaccuracy from stationary sources based on tomographic and projection images, ensuring the highest level of precision throughout treatment.The application has the ability to work with a variety of imaging modalities. Images from tomographic sources such as Computer Tomography (CT), Magnetic Resonance (MR). In this study, the treatment planning application can plan a patient's treatment protocol on images from MR based on a single target or multiple targets. The basic elements of treatment planning are defining a cranial target or targets, devising the configurations of the collimator helmet tope used during treatment, and determining the parameters of the radiation shots to be Leksell Gamma Knife® conveyed the message [5].Current gamma knife radiosurgery uses a "ball-packing" planning strategy and a "step-and-shoot" delivery method to "pack" various-sized spherical high-dose volumes (referred to as "shots") into a tumour volume.We adapted the collimators to different diameters by contouring of each meningioma; 4mm, 8mm, and 16mm with several way of plugging sectors to adapt and avoid the OAR.

MATLAB R2013a

MATLAB is a practical language for technical computing and data visualization created for solving issues in science and mathematics. The pencil beam data sets have been processed effectively using this development program (Math Works, Inc., Natick) [6].

Statistical Analysis

Because of small sample size and non-normality distribution, non-parametric tests were used to compare the effect of changing the plan from 50% to 75% IDL (Wilcoxon Signed-Rank Test, two-sided). The significant p-value was considered to be below 0.05. All descriptive data are shown in Table 1.

Methods, Treatment Planning Evaluation

First: Radiobiological Evaluation of GKR Plan

The EUD (equivalent uniform dose model) based mathematical model is simple because it is based mainly on 2 equations, and versatile because the same model may be used for both TCP and NTCP calculations from equation (1), (2) [7,8].

$$TCP=\frac{1}{1+(\frac{TCD50}{EUD})^{4\gamma 50}} \quad (1)$$

$$NTCP=\frac{1}{1+(\frac{TD50}{EUD})^{4\gamma 50}} \quad (2)$$

Where The TCD50 is that the dose to control 50% of the tumors once the tumor is homogeneously irradiated, The TD50 is that the tolerance dose for a 50% complication rate at a selected amount [e.g., five years within the Emami et al. traditional tissue tolerance knowledge, ɣ50 describes the slope of the dose-response curve. EUD is calculated from equation (3):

$$EUD = (\sum v_i D_i^{a})^{1/a} \quad (3)$$

Where (a) may be a tissue-specific characteristic defining the magnitude of the impact, (Vi) is the three-quarters of the organ volume that receives a dose (Di), and The value of (a) and the various parameters TD50, γ_{50} and α/β for the late response period [5 years] were taken throughout this study, as listed in Table (2) [9,10].

Table 1a. Patient's treatment plans and their information, (a) represents a decreasing value of the isodose line (IDL 50%).

Patiens group a	Gander	Age [Y]	Diagnosis	Target Volume TV(cc)	Prescription isodose volume [PIV] (cc)	TCD50 (Gy)	Max dose [MD] (Gy)	Number of isocenter shots
1	Female	47	RT cavernous and seller Meningioma	7.78	7.55	16.2	24	22
2	Female	66	LT Pertrous apex Meningioma	3.546	3.55	16.5	24.3	24
3	Male	27	LT cavernous and petrous apex Meningioma	6.41	4.48	13.8	24.8	26
4	Female	48	Sup frontal Meningioma	7.58	4.56	13.3	24	19
5	Female	29	Post operative supratentorial Meningioma	21.52	13.32	13.4	24	32
6	Male	65	RT supaseller Meningioma	0.588	0.557	17.1	24	6
7	Male	21	RT petro clival Meningioma	2.62	2.37	16.7	26	7
8	Male	40	Residual Suprasellar Meningioma	23.72	15.25	14.1	24.3	12
9	Female	39	RT cavernous sinus Meningioma	2.91	2.8	17	24	24
10	Female	47	RT petro clival Meningioma	4.47	4.23	16.5	24.9	20
11	Female	54	Residual LT petro clival Meningioma	14.5	11.8	14.7	25	19
12	Female	45	LT parasellar Meningioma	6.3	6	17	27.4	18
13	Female	47	residual RT cavernous sinus Meningioma	5.12	4.9	16.9	27	24
14	Male	30	RT middle sphenoid cavernous sinus Meningioma	4.2	4.1	17.6	24	17
15	Female	58	recurrent intro-orbital suprasellar Meningioma	5	4.9	17.3	24.6	12
16	Female	53	Pineal body Meningioma	12.8	11.3	16	24.7	15
17	Female	46	Recurrent Lt CPA Meningioma	5	4.7	16	24	16
18	Female	35	residual RT sniddle 1/3 sphenoid Meningioma	9.9	9.88	16	24.3	17
19	Female	59	RT Sphenoid wing Meningioma	5	4.88	17	24	16
20	Female	21	RT CPA Meningioma	1.52	1.49	17	24.2	8

Table 1b. Patient's treatment plans and their information. (b) represents Increasing value of the isodose line (IDL 75%).

Patients group (b)	Prescription isodose volume [PIV] (cc)	Max dose MD (Gy)	Tumor Control Dose (50%) TCD50 (Gy)	Number of isocenter shots
1	1.6	16.2	10.7	22
2	1.13	16.33	11	24
3	0.6239	16	9.2	26
4	0.9495	16.5	8.9	19
5	2.48	16	8.9	32
6	0.245	16.9	11.4	6
7	1.27	19	12	7
8	4.54	16.2	9.4	12
9	1.09	16.6	11.3	24
10	1.39	16.6	11	20
11	1.77	16	9.8	19
12	1.52	16.5	10.3	18
13	2.08	17.3	11.3	24
14	1.9	16	11.7	17
15	2.1	16.4	11.6	12
16	3.7	16.5	10.6	15
17	2.01	16	10.5	16
18	2.98	16.2	10.8	17
19	1.93	16	11.4	16
20	1.52	16	11.3	8

Table 2. Radiobiological parameters used to calculate NTCP and TCP

Structures		a	γ_{50}	TD_{50} (Gy)	α/β	References
Tumor	Meningioma	2	2.5	--	3	Niemierko[8]
Organs at risk QAR	Optic nerve	25	3	10	2	Emami et al[10]
	Brain Stem	7	3	15	2	liscak, R [3]

In order to compare the TCP-values with physical indices from DVH, the values for TCD50 and γ_{50} for adjuvant radiation and curative purpose were examined. These MATLAB equations were created to examine the DVH for every patient utilizing the particular application. Save this data into MATLAB as EUDMODEL (DVH), where DVH is a 2-column matrix that resembles the cumulative dose-volume histogram rather than the percent dose-volume histogram. rising absolute dose is represented by the first column, and corresponding absolute volume is represented by the second column. The matrix must have a minimum of two rows and two equal-length columns [11].

Abbreviations: α/β=alpha beta ratio; TD_{50}= tolerance dose for 50% of complication; γ_{50} is a unitless model parameter that is specific to the normal structure or tumor.

Second: Physical Indices of GKR

The following dosimetry variables were examined: prescribed dose, prescribed isodose volume, and maximal dose. The percentage of the target volume (TV) that is covered by the prescribed isodose volume (PIV) is known as the coverage index: (PIV⌒TV)/ (TV), The percentage of the prescription isodose volume (PIV) that is contained inside the target volume (TV), (PIV⌒TV)/ (PIV) is the selectivity index. Number of isocenters, CIn, HIn, and GIn [5,13]. Using dose-volume histograms (DVH), volumes and doses were calculated. The CIn, HIn, and Gin, [14] were calculated using the following:

$$\text{Conformity Index} = \frac{\text{Prescription Isodose volume}}{\text{Target Volume}}$$

$$\text{Heterogeneity Index} = \frac{\text{Maximum Dose}}{\text{Prescription Dose}}$$

$$\text{Gradient Index} = \frac{\text{Value of half the Prescription Isodose}}{\text{Value of the entire Prescription Isodose}}$$

For instance, if the dose prescribed was 12 Gy to the 50% Isodose line, then the Gin would be: Treatment Plans for Intracranial Meningioma's characteristics by Ehsan H. Balagamwala, A.B., John H study are shown in Table 3 [14].

Table 3. Tumor and Treatment Characteristics

Characteristics	Median	Range
Tumor volume (cc)	4.3	0.12-22.4
prescribed dose (Gy)	12	10 -14
Isodose line (%)	51.1	50-92
Maximum dose (Gy)	25	17.2-48
Total isocenters	12	1-52
Conformity index	1.7	0.85-4.88
Heterogeneity index	1.95	1.09-2.83
Gradient index	3	2.33-4.81

Treatment protocol

The purpose of this work's design is to aid in the analysis of DVH. We have taken part in several diagnosis for Benign intracranial Meningiomas within different volumes which located near "OAR" Organ at risk such as (optic nerve and brainstem). Patients were treated by Leksell Gamma Plan (LGP) in a single session within prescribed dose 12 Gy and isodoseline 50%. DVHs of the treatment were imported from Leksell Gamma Plan to MatLab as shown in Figure 1.

Generally, in Benign Intracranial Meningioma treatment, organs at risk "OAR "are Brain stem or the right and left optic nerve. The technique developed in LGP software was standard, when the prescription isodose has been set, it is only possible to change the selected isodose level temporarily by keeping the left mouse while dragging the Selected level slider with the button depressed. [3,4]. The patients who participated in this study's prowess were used for LGP. Two strategies were used to treat the imported patients for all target volumes. (Optic nerve, brain stem, and PTV). Each patient receives one of the two plans. Additionally, for each of the two designs (IDL50 percent and IDL75 percent), the value of the isodose line was altered.

Since various treatment plans may prompt portion circulations having comparable gross portion measures (like mean portion), yet described by DVHs with altogether different shapes, they also show through Magnetic Resonance Images were done run around of the area was located Tumor, PIV at IDL75% in Figure 2. Clinicians might be forced to make decisions in this situation based on hazy assumptions about the dose-volume properties of certain tissues. The ranking of treatment plans through a more explicit calculation of TCP and NTCP values using models that automatically incorporate the available clinical data regarding the dose-volume characteristics of various tissues is a natural application of radiobiological modelling to radiotherapy [15,16]; Then compute the NTCP and TCP for each plan for all patients and compute the Physical indices [17].

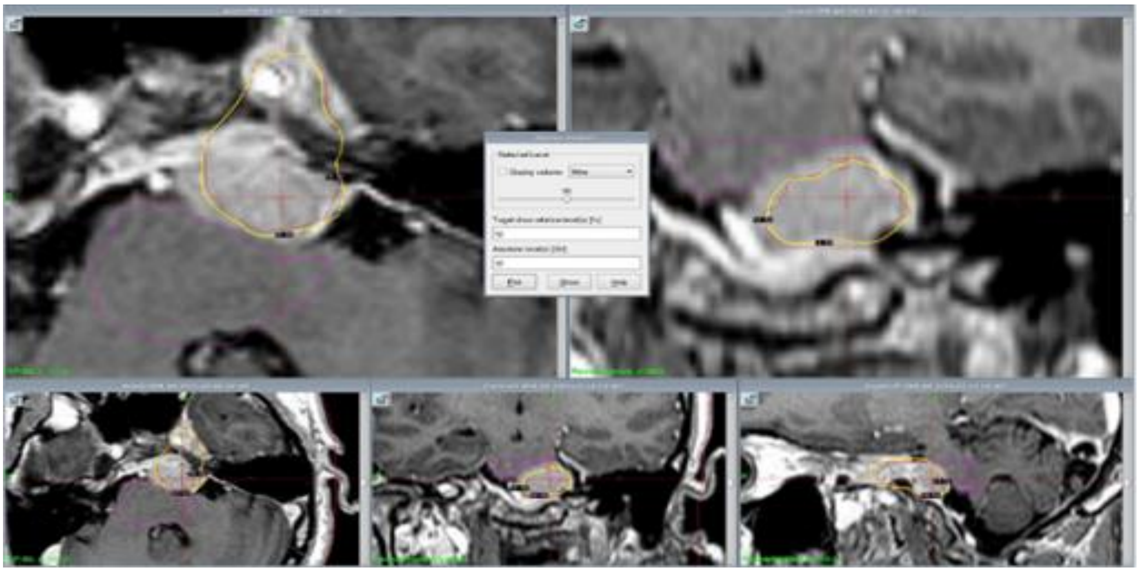


Figure 1. Dose Distribution in Benign Intracranial Meningioma treatment, Isodose line 50% and Brain stem is OAR.

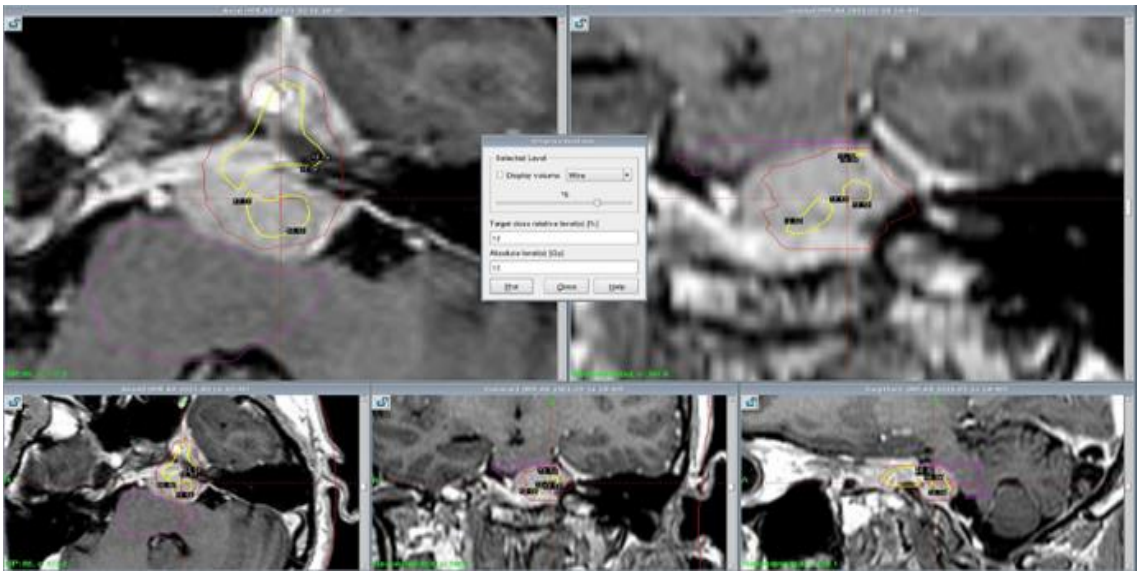


Figure 2. Snapshots of treatment plan and dose distribution in intracranial meningioma using isodose line 75%, and brain stem is OAR.

Results

Radiobiological Evaluation of Gamma Knife Radiosurgery

All results of EUD model of the two plans for each patient obtained are listed in the table (4) and table (5{a& b}), where (a) corresponding to NTCP of Brain Stem and (b) corresponding to NTCP of the optic nerve.

Table 4. EUD and TCP for Intracranial Meningioma in IDL (50%) and IDL (75%) Plans.

No of cases	PIV(CC)		Δ(%)	EUD (GY)		Δ(%)	TCP(%)	
	IDL (50%)	IDL (75%)		IDL (50%)	IDL (75%)		IDL (50%)	IDL (75%)
1	7.55	1.6	0.07	21.24	10.2	0.20	93.75%	37.51%
2	3.55	1.13	0.03	23.20	11.06	0.22	96.8%	51.44%
3	4.48	0.624	0.04	17.41	8.36	0.16	91.07%	27.81%
4	4.56	0.95	0.04	17.24	8.27	0.16	93.04%	32.48%
5	13.32	2.48	0.1	16.83	8.09	0.16	90.72%	27.76%
6	0.56	0.25	-0.04	24.96	11.87	0.24	97.77%	60.05%
7	2.37	1.27	0.01	24.27	13.26	0.23	97.67%	73.1%
8	15.25	4.54	0.14	18.77	9.09	0.18	95.2%	41.76%
9	2.8	1.09	0.02	24.28	11.56	0.23	97.24%	55.75%
10	4.23	1.39	0.03	23.04	10.9	0.22	96.58%	43.21%
11	11.8	1.77	0.11	18.78	9.01	0.18	87.64%	33.79%
12	6	1.52	0.1	21.5	10.3	0.2	93.13%	49.04%
13	4.9	2.08	0.04	24.2	11.5	0.23	97.32%	54.83%
14	4.1	1.9	0.03	25.6	12.2	0.25	95.29%	58.16%
15	4.9	2.1	0.04	25.32	12.04	0.24	95.47%	57.47%
16	11.3	3.7	0.1	22.05	10.5	0.21	93.20%	48.70%
17	4.7	2.01	0.04	24.96	11.87	0.24	98.84%	77.41%
18	9.88	2.98	0.1	22.64	10.8	0.22	96.99%	50.03%
19	4.88	1.93	0.04	24.4	11.6	0.23	97.40%	55.00%
20	1.49	1.52	0.01	24.06	11.46	0.23	96.99%	53.64%
Average	4.48	1.13	0.04	23.2	8.36	0.16	95.05%	49.44%
SD	3.96	0.98	0.04	2.83	1.42	0.03	0.286	0.134
P-value	0.0002			0.0001>			0.0001>	

Table 5a. EUD and NTCP for Brain Stem in IDL (50%) and IDL (75%) Plans.

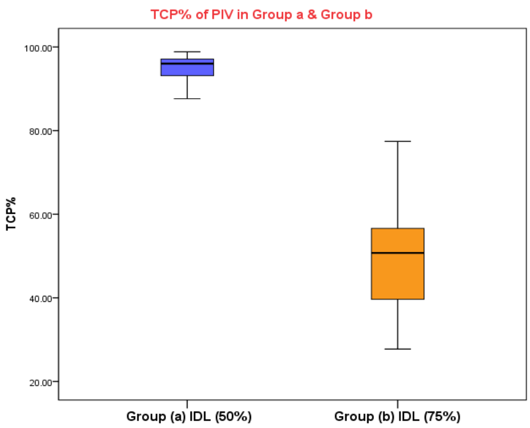
Brain Stem					
No of cases	EUD (GY)		Δ(%)	NTCP(%)	
	ID(50%)	ID(75%)		ID(50%)	ID(75%)
2	4.54	2.27	0.04	0.01%	0.0002%
4	2.062	1.49	0.01	0.01%	0.0001%
5	2.28	1.184	0.013	0.002%	0.00%
7	7.91	6.156	0.0٧	0.023%	0.002%
8	2.12	1.09	0.01	0.01%	0.00%
10	5.2	2.51	0.04	0.02%	0.0005%
11	3.63	1.84	0.03	0.0004%	0.00001%
12	1.77	0.92	0.01	0.00007%	0.00%
14	1.73	0.9	0.01	0.00005%	0.00%
16	2.53	1.39	0.02	0.0005%	0.00%
17	3.77	1.87	0.03	0.0006%	0.00001%
18	2.87	1.45	0.02	0.00002%	0.00%
20	3.58	1.76	0.03	0.0003%	0.00%
Average	2.12	2.51	0.03	0.0063%	0.0002%
SD	1.67	1.31	0.02	0.008	0.0006
P-value	0.024			0.001	

Abbreviations: EUD= Equivalent Uniform Dose; NTCP= Normal Tissue Complication Probability; IDL= Isodose Line; SD= Standard Deviation; Δ (%) = [IDL (50%)- IDL (75%)]/ IDL (75%).

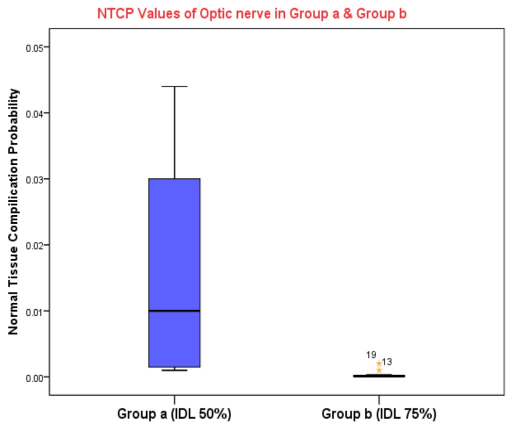
Table 5b. EUD and NTCP for Optic Nerve in IDL (50%) and IDL (75%) Plans.

Optic Nerve					
No of cases	EUD (GY)		Δ(%)	NTCP(%)	
	ID(50%)	ID(75%)		ID(50%)	ID(75%)
1	2.86	1.49	0.02	0.03%	0.001%
3	2.92	1.09	0.02	0.03%	0.0003%
6	3.051	1.57	0.02	0.01%	0.0002%
8	1.89	1.09	0.01	0.002%	0.0001%
9	1.759	0.95	0.01	0.001%	0.00%
10	1.31	0.72	0.003	0.001%	0.00%
11	4.41	2.24	0.03	0.045%	0.002%
12	3.87	1.97	0.03	0.001%	0.00003%
13	4.03	1.8	0.03	0.03%	0.00%
14	3.84	1.96	0.03	0.01%	0.00004%
15	3.48	1.79	0.02	0.01%	0.00002%
19	4.15	2.12	0.03	0.03%	0.00008%
Average	1.759	0.72	0.02	0.017%	0.0003%
SD	0.98	0.48	0.01	0.015	0.0006
P-value	0.0002			0.0001>	

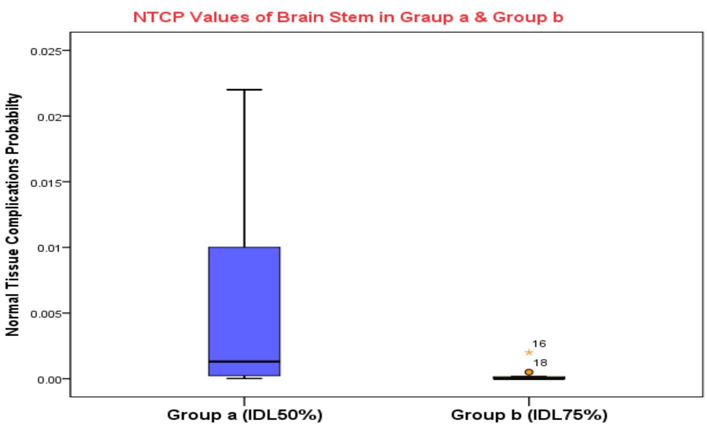
Abbreviations: EUD= Equivalent Uniform Dose; NTCP= Normal Tissue Complication Probability; IDL= Isodose Line; SD= Standard Deviation; Δ (%) = [IDL (50%)- IDL (75%)]/ IDL (75%).



(a)



(b)



(c)

Figure 3 The effect of the value of isodose line on Meningioma Via TCP% of PIV for both groups (a and b) as shown in fig (a) where the effect of the value of isosdose line on the Optic Nerve and brain stem via NTCP% for both groups as shown in fig (b) and fig (c) respectively.

Physical Evaluation of Gamma Knife Radiosurgery

All results of physical indices of the two plans for each patient obtained are listed in table [6(a, b)], where (a) corresponding to results of (coverage & selectivity) indices and Gin. while (b) corresponding to results of (Hin) and (Cin).

Table 6 a. Physical Indices for Intracranial Meningioma in IDL (50%) and IDL (75%) Plans.

No of cases	Coverage index		Δ(%)	Gradient index (GIn)		Δ(%)	Selectivity index (SIn)		Δ(%)
	IDL (50%)	IDL (75%)		IDL (50%)	IDL (75%)		IDL (50%)	IDL (75%)	
1	0.97	0.16	-0.03	3.04	14.1	2.04	0.65	0.80	-0.63
2	0.94	0.30	-0.06	2.6	6.66	1.6	0.70	0.95	-0.3
3	0.70	0.10	-0.3	3.41	15.83	2.41	0.90	1.0	-0.1
4	0.60	0.13	-0.4	2.86	8.81	1.86	0.99	1.0	-0.01
5	0.62	0.12	-0.38	2.9	9.32	1.9	1.00	1.0	0
6	0.95	0.39	-0.05	2.65	4.61	1.65	0.82	1.0	-0.18
7	0.91	0.48	-0.09	2.84	7.7	1.84	0.78	0.92	-0.22
8	0.64	0.19	-0.36	2.72	5.54	1.72	0.99	1.0	-0.01
9	0.96	0.38	-0.04	2.66	4.68	1.66	0.89	1.0	-0.11
10	0.95	0.29	-0.05	2.56	5.67	1.56	0.87	1.0	-0.13
11	0.81	0.12	-0.19	2.91	11.7	1.91	0.97	1.0	-0.03
12	0.83	0.23	-0.17	2.8	6.1	1.8	0.96	1.0	-0.04
13	0.95	0.41	-0.05	2.7	4.41	1.7	0.90	1.0	-0.1
14	0.98	0.46	-0.02	2.52	3.68	1.52	0.85	0.98	-0.15
15	0.97	0.42	-0.03	2.46	4.1	1.46	0.89	1.0	-0.11
16	0.88	0.28	-0.12	2.62	4.93	1.62	0.97	1.0	-0.03
17	0.95	0.38	-0.05	2.75	4.55	1.75	0.83	0.99	-0.17
18	0.89	0.30	-0.11	2.62	5.04	1.62	0.93	1.0	-0.07
19	0.98	0.37	-0.02	2.7	4.41	1.7	0.91	1.0	-0.09
20	0.98	0.38	-0.02	2.7	4.9	1.7	0.81	0.93	-0.19
Average	0.87	0.29	-0.13	2.75	6.84	1.75	0.88	0.97	-0.13
SD	0.13	0.123	0.126	0.211	3.45	0.21	0.1	0.05	0.14
P-value	4.68×10^{-17}			0.0001>			0.0003>		

Table 6 b. Physical indices for Intracranial Meningioma in IDL (50%) and IDL (75%) Plans.

No of cases	Heterogeneity Index (HIn)		Δ(%)	Conformity Index (CIn)		Δ(%)
	IDL(50)	IDL(75)		IDL(50)	IDL(75)	
1	2	1.35	1	1	0.2	0
2	2	1.35	1	1	0.31	0
3	2.025	1.33	1.03	0.9	0.1	-0.1
4	2.067	1.37	1.07	0.6	0.12	-0.4
5	2	1.33	1	0.62	0.12	-0.63
6	2.075	1.41	1.8	0.95	0.42	-0.05
7	2.16	1.5	1.16	0.9	0.48	-0.1
8	2.07	1.35	1.07	0.64	0.19	-0.36
9	2	1.36	1	0.96	0.37	-0.04
10	2.07	1.38	1.07	0.95	0.31	-0.05
11	2.08	1.33	1.08	0.81	0.12	-0.19
12	2.03	1.38	1.03	0.83	0.24	-0.17
13	2.16	1.44	1.16	0.95	0.41	-0.05
14	2	1.33	1	0.98	0.46	-0.02
15	2.05	1.37	1.05	0.97	0.41	-0.03
16	2.05	1.37	1.05	0.88	0.3	-0.12
17	2	1.3	1	0.94	0.4	-0.06
18	2	1.35	1	0.89	0.3	-0.11
19	2	1.3	1	0.98	0.39	-0.02
20	2	1.3	1	0.98	0.38	-0.02
Average	2.04	1.36	1.041	0.89	0.30	-0.114
SD	0.05	0.048	0.05	0.13	0.123	0.123
P-value	0.0001>			0.0001>		

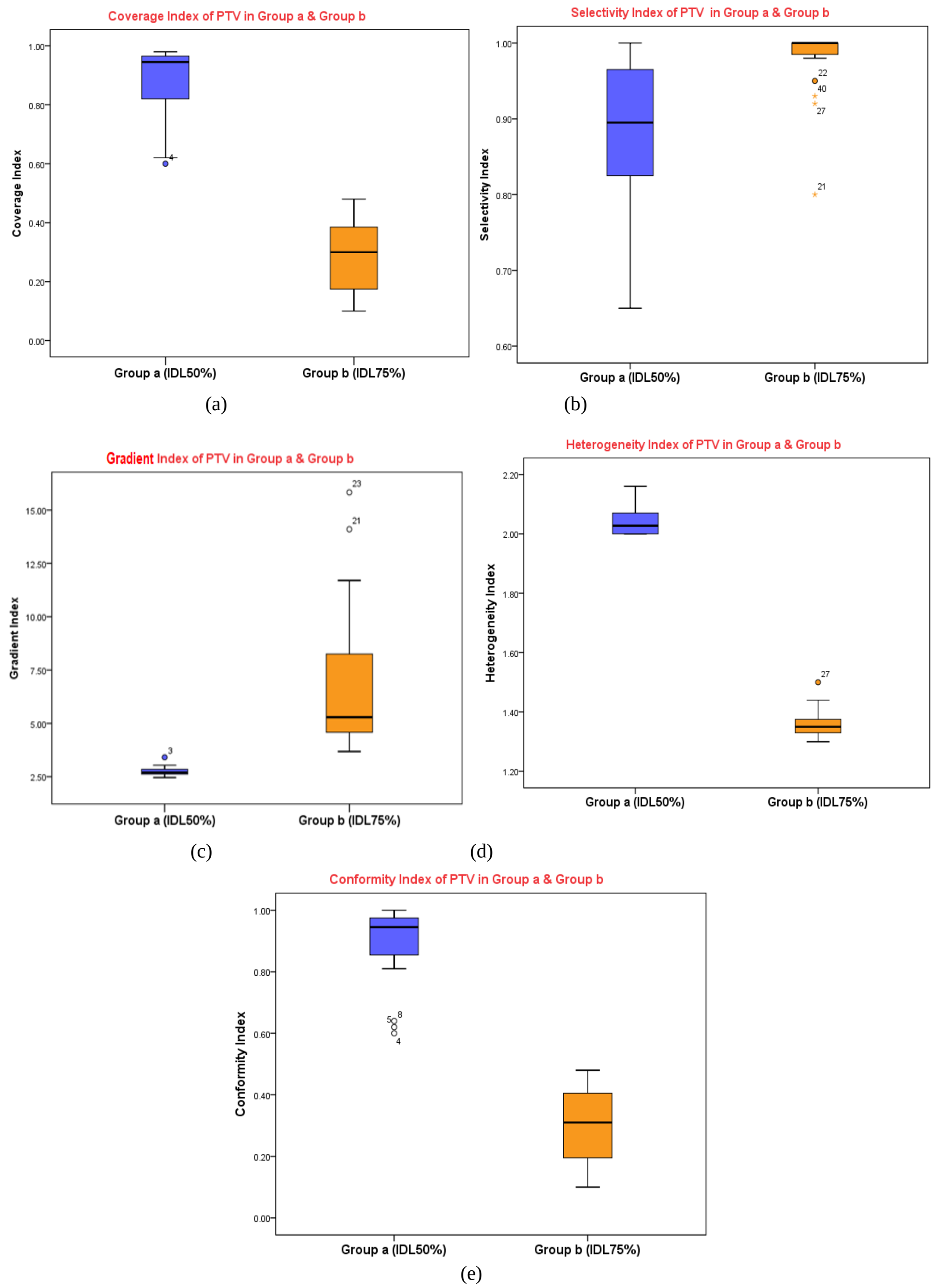


Figure 4. Show the effect of the value of isodose line on tumor and normal tissue for each on the (Coverage, Selectivity, Gradient, Heterogeneity and Conformity) indices in (a, b, c, d, e) of PTV for both group a and b which (ID 50%) and (ID 75%), respectively.

Discussion

The absorbed dosage that, if uniformly administered to a lesion, results in the same expected number of clonogens surviving as the actual non-homogeneous absorbed dose distribution does is known as an equivalent uniform dose (EUD).Clonogen survival is a stochastic quantity that is subject to Poisson statistics; an expected value for EUD is produced.

When irradiations are non-homogeneous, EUD is a simplified parameter to make comparisons between various schemes simple. The essential premise is that any non-homogeneous irradiations with EUD equal to D and homogeneous irradiations of a target with absorbed dose D are identical in a biological sense. As long as the mean clonogen surviving fraction is the same, the biological effect is regarded as equivalent. One of the benefits mentioned in Niemierko's essay, which introduced the EUD concept, was its robustness-more specifically, its gradual fluctuation with radiobiological parameters. When large-dose inhomogeneities are present, McGary et al. showed non-negligible dependence of EUD with linear-quadratic model parameters.

The use of eudmodel.m (a MATLAB tool) in this study's investigation of the radiobiological evaluation of Gamma Knife treatments enables radiologists and medical physicists to evaluate treatment planning by importing actual clinical data from DVHs. Everyone who uses the application can utilize it. This study provides biological constants for use in this application. We investigated the physical indices (conformity, heterogeneity, gradient, coverage, selectivity) as well as regarding the occurrence of toxicity in patients who underwent radiosurgery with the Gamma Knife for intracranial meningiomas.

We examined the radiobiological effects of IDL 50% and IDL 75% plans within LGP for a single session of intracranial meningioma in this radiobiological model response study. The EUD discrepancy between the IDL50% and IDL75% plans for the meningioma tumor was within 0.16 %, and there were differences in the TCP values between the IDL50% and IDL75% plans. In comparison to the IDL 75% plans, the IDL 50% plans provided EUD that was 0.02 to 0.03 percent greater for OARs. In the IDL 50% and IDL 75% plans, the NTCP values of the brain stem (0.006 % vs. 0.0002 %) and the optic nerve (0.017 % vs. 0.0003 %) were comparable, but not in the IDL 50% plans.

In this physical evaluation response study, we compared the physical indices of IDL 50% and IDL 75% plans within LGP. There were differences in coverage index values between the IDL 50% and IDL 75% plans within -0.13 % means that coverage of PTV by prescribed dose in IDL 50% Plan is higher than the coverage in IDL75% plan. This shows that there is a significance in a group (a) versus group (b). Also, there were differences in selectivity index values between the IDL 50% and IDL 75% plans within -0.13%. This shows that there is no significance between the IDL 50% and IDL 75% plans, also There were differences in gradient index values between the IDL 50% and IDL 75% plans within 1.75%.

Means that GIn of PTV by prescribed dose in IDL 75% Plan is higher than GIn in IDL50% plan. means that are not correlated with toxicity (dizziness) of the tumor by IDL 50 % is Less than IDL75%. Also, in another index such as CIn, there were differences in CIn values between the IDL 50% and IDL 75% plans within -0.11%. means that CIn of PTV by prescribed dose in IDL 50% Plan is higher than CIn in IDL 75% plan. This shows that there is a significance in group (a) versus group (b).

Published studies showed that tumor control rate or progression between 87% to 100%, the average being 95.5% and post-treatment neurological deficits of stereotactic radiosurgery are rarely disabling. The risk of temporary adverse effects ranges from 2.5% to 10% and permanent between 1.3% and 6.6% [3]. The most recent and the Largest Multicenter study by Santacroce et al. provided results in long-term results of Gamma Knife Treatment on Benign Meningiomas in 4.565 patients; It was 92.5% at the 5 years follow up and 88% at 10 years follow up [17].

In this study, all the results showed that the average TCP% of PIV of the plans that contain isodose line 50% is 95.05% while in other plans that contain isodose line 75 % is 49.44%. Mean± SEM of the group (a) is 95.05%±0.64 while in group b is 49.44% ± 3.0, N=20. This shows that there is significance in the group (a) (decreasing value of isodose line) versus group(b) (increasing value of isodose line) means that the tumor control probability by isodose line 50 % is larger than isodose line75%, (p=1.29×10-12, Independent Samples t-Test).

While the Mean± SEM of a group (a) of NTCP of the optic nerve is 0.017% ± 0.0043. Also, in other OAR such as Brain Stem Mean±SEM of a group (a) of NTCP of the brain stem is 0.0063% ± 0.0023; While in a group (b) is 0.0002%± 0.0002, ($p = 6.89\times10^{-5}$, Mann-Whitney test) and Mean±SEM of a group (b) of NTCP of the optic nerve is 0.0003%±0.0002, (p =0.001, Mann-Whitney test).

Meaning that with increasing the isodose line, such as (IDL 75 percent), there is a minor decrease in complications, which means less harm to normal tissue is caused to some normal tissue such as the brain stem and optic nerve. With a median of 0.01 % (0-0.045 percent) in the earlier plan and zero in the latter one (p = 0.001, Mann-Whitney test), the brainstem and optic system NTCPs were extremely low. Figures 3(a), 3(b), and 3(c) depict the impact of the value of isodose line on Meningioma brain tumor and normal tissue on PIV for both groups a and b. Our results agree with Santacroce et al. within ±2.48% [18]; and Rana S, Cheng CY. Within ±3.32% [19].

On the other side, the physical evaluation of Gamma Knife Radiosurgery plans for treatment of Meningioma Brain Tumors explained by clinical outputs and computing physical indices such as (Coverage index, selectivity index, CIn, GIn, and HIn).

In this study, all the results showed that the average of Coverage index (Cin) % of PTV of the plans that contain isodose line 50% is 0.87 while in other plans that contain isodose line 75 % is 0.29. Mean± SEM of the group (a) 0.87± 0.028 while in group(b) is 0.29± 0.027. This shows that there is a significance in the group (a) (decreasing value of isodose line) versus group (b) (increasing value of isodose line) means that the coverage of tumor by isodose line 50 % is larger than isodose line75%, ($p = 4.68\times10^{-17}$, Independent Samples t-Test).

While the Mean± SEM of a group (a) of Selectivity index (Sin)% of PTV is 0.88 ± 0.021. while in a group (b) is 0.97± 0.011. Meaning that the ratio of the target volume covered by the prescription isodose to prescription isodose volume (PIV) is less with decreasing the Isodose line such as (IDL 50%) there is a slight decrease in selectivity index (Sin) to Tumor, (p =

4.68×10^{-17}, Independent Samples t- Test). Meaning that the ratio of the target volume covered by the prescription isodose to prescription isodose volume (PIV) is less with decreasing the Isodose line such as (IDL 50%) there is a slight decrease in Selectivity index (Sin) to Tumor but also the results of group (a &b) are identical to with optimum value, Sin value should be at least SIn ≥ 0.70.

Also, in another index such as the conformity index (CIn) Mean ± SEM of a group (a) is 0.89 ± 0.028. while in a group (b) is 0.30 ± 0.027. This shows that there is a significance in the group (a) (decreasing value of isodose line) versus group(b) (increasing value of isodose line) meaning that the ratio of prescription isodose volume (PIV) to the target volume is less with Increasing the Isodose line by isodose line such as (IDL 75%) is less than isodose line50%, ($p = 2.21\times10^{-17}$, Independent Samples t- Test).

Also in another index such as gradient Index Mean±SEM of a group (a) is 2.75± 0.05. while in a group (b) is 6.84± 0.77. This shows that there is a significance in the group (a) decreasing value of isodose line) versus group(b) (increasing value of isodose line) means that are not correlated with toxicity (dizziness) of a tumor by isodose line 50 % is Less than isodose line75%, (p= 5.45×10-17, Independent Samples t- Test).

Also, in another index such as the Heterogeneity Index Mean±SEM of a group (a) is 2.04± 0.011. while in a group (b) is 1.36± 0.01. This shows that there is a significance in the group (a) (decreasing value of isodose line) versus group(b) (increasing value of isodose line) means that are not correlated with toxicity (dizziness) of a tumor by isodose line 50 % is larger than isodose line75%, ($p = 5.1\times10^{-34}$, Independent Samples t- Test). Figure 4 [a, b, c, d, and e]. show the effect of the value of isodose line on tumor and normal tissue on the physical indices of PTV for both group a and b which (IDL 50%) and (IDL 75%), respectively. Our results agree with Ehsan H. Balagamwala, A.B., *John H which believe that the target CIn should be ≤2.0, SI should be at least SIn ≥ 0.70, coverage index should be at least coverage ≥ 0.80, the HIn≤2.0 and the Gin ≤ 3.0 for intracranial meningiomas [3,14].

Conclusion

The importance of the isodose line in confirming control tumor and complications to normal tissue probabilities with the proposed planning necessitates that the medical physicist obtain the best plan based on TCP and NTCP from DVHs within Physical indices from clinical outcome data or equations in this paper. This expedites patient care and saves the medical physicist's time. As a result, the patient will greatly benefit from this study. Medical physicists and radio oncologists must make treatment decisions based on the precise values of TCP and NTCP, and this is accomplished through test plans by the MATLAB software within computing the physical indices. Further lager comparative studies are required to compare more plans with different stereotactic machines, models, and collimators.

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