Egypt. J. Biophys. Biomed. Eng., **Vol. 23,** No. 1 pp.11-25 (2022)

Physical and Radiobiological Evaluation of Gamma Knife Radiosurgery Plans in the Treatment of Meningioma: Comparison between two isodose lines (50% and 75%)

Gad Elbaz[1], Hedaya Hendam[1], Elsayed M. Alashkar[2], Khiry. Ereiba[2], Ehab Attalla

[1].Gamma knife Damietta Center, Department of Neurosurgery, faculty of medicine, Damietta Al-Azhar university Hospital. ,[2].Biophysics Branch, Physics Department, Faculty of Science, Cairo Al-Azhar University and [3].National Cancer Institute, Cairo University. Cairo, Egypt.

THIS work explores how the choice of prescription isodose line (IDL) achieves a high probability of local tumor control (Tumor Control Probability, TCP) at low risk of normal tissue complications (Normal Tissue Complications Probability, NTCP) for Gamma Knife Radiosurgery at two different plans applying different isodose lines to evaluate the radiosurgical metrics, plan quality, and outcome probability in treatment of meningioma using Gamma Knife Radiosurgery (GKS).

The cross-sectional study included 10 patients (4 male and 6 female) with median age of 42 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. A quantitative approach has been conducted to evaluate and compare both plans. Dose-volume histogram was imported to MATLAB to compute tumor control probability (TCP), normal tissue complications probability (NTCP) values at 5 years for each plan, and physical indices such as coverage, selectivity, conformity, heterogeneity, and gradient indices.

Median target irradiated volume was 5.44 cm^3(0.59-23.72). TCP was significantly higher in the plan using 50% isodose line for the marginal dose than that using 75% isodose line (94.98%, 45.09%, p=0.0018, *Mann-Whitney test*). Brainstem and optic apparatus NTCPs were very low with median of 0.01% (0-0.03%) in the former plan and zero in the later one (p=0.005, *Mann-Whitney test*).

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

Keywords: Leksell Gamma Plan, Dose Volume Histogram, Tumor Control Probability, Normal tissue complication Probability, Physical indices

Introduction

The Leksell Gamma Knife is a particular treatment unit that enables a high-level stereotactic radiosurgery system to handle the tumor treatment process, vascular mutations, and pain disorders within the head. The main advantage of stereotactic target localization is that it only allows a minimum radiation dose to be imparted to adjacent organ at risk (OAR) [1,2,3].

Physically, there are several factors defined the range of a penumbra such as the design of the source and the collimation defines a geometric component while the energy of the beam along with the composition of the transport medium defines a radiological component [4].

Regarding supreme portion, the penumbra is likewise influenced by the decision of remedy Isodose line (IDL) where it is invaluable to recommend a line that exists in the portion angle. 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 tumble off external the objective[4].

Correspondsing author Email: gadelbaz@azhar.edu.eg
Received 27/11/2021 , accepted 30/1/2022

DOI :10.21608/ejbbe.2022.107953.1052

In this study, we explore fitting numerical details of normal tissue complication rate (NTCP) is like the plan of the tumor control probability (TCP), which addresses the likelihood that after a radiation therapy no malignant growth cell has made due in the irradiated area. Treatment 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 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.

This study aims to evaluate the biological differences in treatment plans with different Isodose lines on Gamma Knife Radiosurgery technique for Meningioma in terms of outcome probability and physical indices.

Materials and Methods

Patients and Materials

Subjects Included

Ten meningioma patients were treated in (Gamma knife Unit) from March 2019 to March 2021. They were 4 male and 6 female patients with median age of 42 years (21-66). The location of meningioma was variable (petro-clival 2, cavernous 2, sellar and suprasellar 3, petrous apex 1, supratentorial 1, frontal 1.). All patients have been evaluated bya multidisciplinary board for deciding the proper management modality. All patients have signed the informed consent afteran explanation of the procedure and treatment outcome possibilities.

Leksell Gamma Plan (LGP)

Leksell Gamma Plan version 10.1 is the simulation and planning of stereotactic Leksell Gamma Knife Perfexion® radiosurgery that is used to non-invasively treat brain lesions. It incorporates 192 fixed Cobalt-60 sources, which ensures the highest degree of accuracy during treatment due to the minimization of potential error from stationary sources based on tomographic and projection images. The program is capable of handling a range of different 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 collimator helmet tope used during treatment, and determining parameters of radiation shots to be delivered by Leksell Gamma Knife® [5].

MATLABR2013a

MATLAB is a handy language for technical computing as well as data visualization designed for finding solutions to scientific as well as mathematical problems. This development software has served as a useful tool for processing the pencil beam data sets (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].

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

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

Where The TCD50 is that the dose to control 50% of tumors once the tumor is homogeneously irradiated, 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 dose-response curve. EUD is calculated from equation (3) :

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

Where (Vi) is that the three-quarter organ volume that receives a dose (Di) and (a) may be a tissue-specific parameter describing the amount impact. during this study, the worth of (a) and different parameters TD_{50}, γ_{50}, and α/β for late response [5 years] were taken, as listed in Table (2) [9,10].

For comparative aim, the values for TCD_{50} and γ_{50} for adjuvant radiotherapy and curative aim were investigated to evaluate TCP-values

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 Year	Diagnosis	Target Volume TV(cc)	Prescription isodose volume [PIV] (cc)	TCD50 (Gy)	Dose per fraction [DPF] (Gy)	Max dose [MD] (Gy)	Number of isocenter shots
1	Female	47	RT cavernous and seller meningioma	7.78	7.55	16.2	12	24	22
2	Female	66	LT Pertrous apex meningioma	3.546	3.55	16.5	12	24.3	24
3	Male	27	LT cavernous and petrous apex meningioma	6.41	4.48	13.8	12	24.8	26
4	Female	48	Sup frontal meningioma	7.58	4.56	13.3	12	24	19
5	Female	29	Post operative supratentorial meningioma	21.52	13.32	13.4	12	24	32
6	Male	65	RT supaseller Meningioma	0.588	0.557	17.1	12	24	6
7	Male	21	RT petro clival Meningioma	2.62	2.37	16.7	12	26	7
8	Male	40	Residual Supraseller Meningioma	23.72	15.25	14.1	12	24.3	12
9	Female	39	RT cavernous sinus meningioma	2.91	2.8	17	12	24	24
10	Female	47	RT petro clival Meningioma	4.47	4.23	16.5	12	24.9	20

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

with physical indices from DVH. These equations square measure written in MATLAB to analyze DVH for each patient using specific program. Save this get into MATLAB as EUDMODEL (DVH), wherever DVH may be a 2-column matrix similar to the accumulative, not%, dose-volume Histogram. First column corresponds to increasing absolute dose and second column to the corresponding absolute volume. The matrix should have a minimum of 2 rows, and both columns should be of equal length[11].

Second: Physical Indices of GKR:

Dosimetry parameters included in the study were as follows: prescribed dose, prescription isodose volume, maximum dose. Coverage index is defined as the proportion of target volume (TV) that is covered by prescription isodose volume (PIV): Volume (PIV⌒TV)/Volume (TV), Selectivity index is defined as the proportion of prescription isodose volume (PIV) that is inside the target volume (TV): Volume (PIV⌒TV)/ Volume (PIV), CIn, HIn, GIn, number of isocenters [5,13]. Volumes and doses were determined with the use of dose-volume histograms [DVH]. The following were used to calculate CIn, HIn, Gin, [14]:

Conformity Index = (Prescription Isodose volume)/

(Target Volume)

Heterogeneity Index = (Maximum Dose)/

(Prescription Dose)

Gradient Index = (Value of half the Prescription Isodose)/

(Value of the entire Prescription Isodose)

Treatment Plans for Intracranial Meningioma's characteristics by Ehsan H. Balagamwala, A.B., John H study are shown in Table 3[15].

Treatment protocol:

This work was designed so that it supports the analysis of DVH. We have participated in all different 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:

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[12]
	Brain Stem	7	3	15	2	Roman.liscak[3]

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.

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

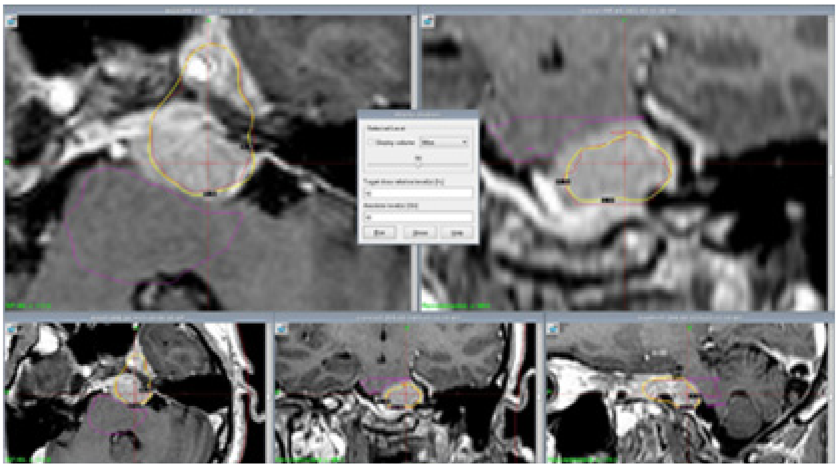


Fig.1. Dose Distribution in Benign Intracranial Meningioma treatment, Isodose line 50% and Brain stem is OAR.

Generally, in Benign Intracranial Meningioma treatment, organs at risk "OAR "are Brain stem or right and left optic nerve. The technique developed in LGP software was standard, when prescription isodose has been set, it is only possible to change the selected isodose level temporarily by keeping left mouse button pressed while moving the Selected level slider. [3,4].

The prowess was used for LGP of the patients enrolled in this study. The imported patients were treated using two techniques for all target volumes. (PTV, brain stem, and optic nerve). The two plans are done for each patient. And value of Isodoseline was changed for each of the two plans (IDL50% and IDL75%) for each plan.

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 (DICOM) Images were done run around of the area was located Tumor, PIV at IDL 75% in Figure (2).

To determine the optimal plan, in this case, clinicians may need to rely on relatively vague notions of dose-volume characteristics of different tissues. A natural application of radiobiological modeling to radiotherapy is the ranking of treatment plans through a more explicit calculation of TCP and NTCP values using models that automatically incorporate available clinical data regarding the dose-volume characteristics of different tissues [16,17] then compute the NTCP and TCP for each plan for all patients and compute the Physical indices [18].

Results and Discussion :

Equivalent Uniform Dose (*EUD*) is the absorbed dose that, if homogeneously delivered to a lesion, causes the same expected number of clonogens to survive as the actual non-homogeneous absorbed dose distribution does. Clonogen survival is a stochastic magnitude governed by Poisson statistics, and *EUD* is obtained as an expectation value.

EUD is a simplified parameter to make comparisons among alternatives plans easy, when irradiations are non-homogeneous. The underlying assumption is that homogeneous irradiation of a target with absorbed dose D, and any non-homogeneous irradiations with EUD equal to D are equivalent in a biological sense. The biological effect is considered equal as long as the mean surviving fraction of clonogens is the same.

One of the advantages pointed out in the article by Niemierko, who first defined the *EUD* concept, was its robustness, i.e. its slow variation with radiobiological parameters. McGary *et al*., studied this issue further and reported non-negligible dependence of *EUD* with linear-quadratic model parameters when large-dose inhomogeneities are present [14].

This is the first study investigating Radiobiological evaluation of Gamma Knife treatments by using MATLAB program, through importing real clinical data from DVHs allows assisting to radioncologist and medical physicists in the evaluation of treatment planning. It is an accessible program for everyone user. Biological constants are available in papers for use in this

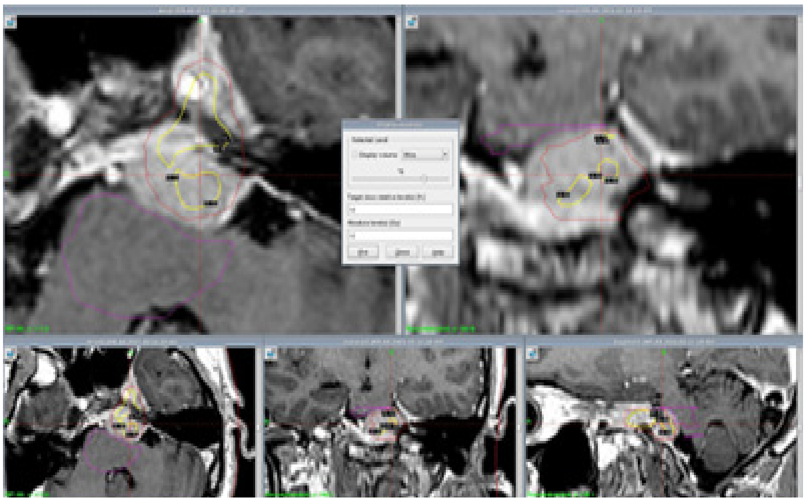


Fig.2. Snapshots of treatment plan and dose distribution in intracranial meningioma using isodose line 75%, and brain stem is OAR.

program. Then investigate relationship between (conformity, heterogeneity, gradient, Coverage, Selectivity) indices and development of toxicity in patients treated with Gamma Knife radiosurgery for intracranial meningiomas.

First: Radiobiological Evaluation of Gamma Knife Radiosurgery:

In this radiobiological model response study, we compared the radiobiological impact of IDL 50% and IDL 75% plans within LGP for a single session of Intracranial Meningioma .There were differences in the TCP values between the IDL 50% and IDL 75% plans, and the EUD difference between the IDL50% and IDL75% plans for the meningioma tumor were within 0.01%. For OARs, the IDL50% plans produced higher EUD by about 0.01-0.75% in comparison to the IDL 75% plans. The NTCP values of Brain stem (0.017%vs. 0.0005%) and optic nerve (0.017%vs. 0.0003%) were comparable in the IDL 50% and IDL 75%, whereas the IDL 50% plans , 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 opticnerve.

Published studies show 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 [19].

TCP Model:

In this study, all the results showed that the average TCP% of PIV of the plans that contain isodose line 50% is 94.98% while in other plans that contain isodose line 75 % is 45.09%. Mean± SEM of the group (a) is 94.98%± 0.817while in group b is 45.09%± 4.7, N=10. 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=0.0018, Mann-Whitney test).

NTCP Model:

While the Mean± SEM of a group (a) of NTCP of OARs(optic nerve and Brain Stem) is 0.017% ±0.006. While in a group (b) is 0.0005%±0.003meaning that complication of some normal tissue such as Brain Stem is less with increasing the Isodose line such as (IDL 75%) there is a slight decrease in complication means less damage to normal tissue but Brainstem and optic apparatus NTCPs were very low with a median of 0.01% (0-0.03%) in the former plan and zero in the later one (*p*=0.005, *Mann-Whitney test*), Figure 3 (a, b and c) show the effect 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% [19]; and Rana S, Cheng CY. Within ±3.32% [20].

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

No of cases	PIV(CC)			EUD (Gy)		Δ(%)	TCP(%)	
	IDL(50%)	IDL(75%)		IDL(50%)	IDL(75%)		IDL(50%)	IDL(75%)
1	7.55	1.6	0.04	21.24	10.2	0.01	93.75%	37.51%
2	3.55	1.13	0.02	23.20	11.06	0.01	96.8%	51.44%
3	4.48	0.6239	0.04	17.41	8.36	0.01	91.07%	27.81%
4	4.56	0.9495	0.04	17.24	8.27	0.01	93.04%	32.48%
5	13.32	2.48	0.04	16.83	8.088	0.01	90.72%	27.76%
6	0.557	0.245	0.003	24.96	11.87	0.01	97.77%	60.05%
7	2.37	1.27	0.01	24.27	13.26	0.01	97.67%	73.1%
8	15.25	4.54	0.02	18.77	9.09	0.01	95.2%	41.76%
9	2.8	1.09	0.02	24.28	11.56	0.01	97.24%	55.75%
10	4.23	1.39	0.02	23.04	10.9	0.01	96.58%	43.21%
Average	5.87	1.53	0.03	21.12	10.27	0.01	94.98%	45.09%
SD	4.8	1.21	0.17	3.26	1.76	0.11	2.58	14.9

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

No of cases	EUD (Gy)		Δ(%)	NTCP(%)	
	ID(50%)	ID(75%)		ID(50%)	ID(75%)
2	4.54	2.27	1	0.01%	0.0002%
4	2.062	1.49	0.4	0.01%	0.0001%
5	2.28	1.184	0.9	0.002%	0.00%
7	7.91	6.156	0.3	0.04%	0.002%
8	2.12	1.09	0.9	0.01%	0.00%
10	5.155	2.51	1	0.03%	0.0005%
Average	4.01	2.45	0.75	0.017%	0.0005%
SD	2.33	1.09	2.01	0.014	0.001
P-value	0.23			0.005	

Abbreviations: EUD= Equivalent uniform dose; NTCP= Normal Tissue complication probability; IDL= isodose line; SD= Standared deviation; ([IDL (50%)- IDL(75%)]/ IDL(75%).

Second: Physical Evaluation of Gamma Knife Radiosurgery:

In this physical evaluation response study, we compared the physical indices of IDL 50% and IDL 75% plans within LGP for a single session of Intracranial Meningioma. There were differences in coverage index values between the IDL 50% and IDL 75% plans within 0.025% 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 - 0.165%. This shows that there isn't 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 0.01%. means that

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

No of cases	EUD (Gy)		Δ(%)	NTCP(%)	
	ID(50%)	ID(75%)		ID(50%)	ID(75%)
1	2.86	1.49	0.01	0.03%	0.001%
3	2.92	1.09	0.02	0.03%	0.0003%
6	3.051	1.57	0.01	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	0.01	0.001%	0.00%
Average	2.3	1.15	0.01	0.017%	0.0003%
SD	0.74	0.32	0.031	0.014	0.0004
P-value	0.006			0.005	

Abbreviations: EUD= Equivalent uniform dose; NTCP= Normal Tissue complication probability; IDL= isodose line; SD= Standared deviation; ([IDL (50%)- IDL(75%)]/ IDL(75%).

Mean± SEM of group (a) 94.98%± 0.817

Mean± SEM of group (b) 45.09%± 4.7(p=0.0018, Mann-Whitney test)

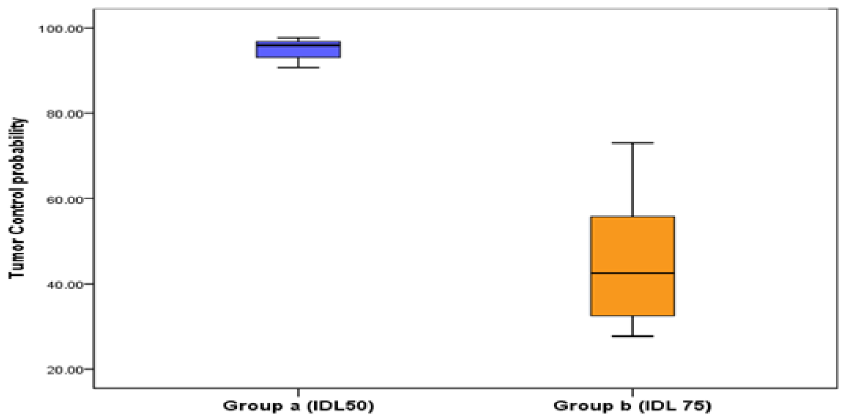


Fig. 3a. shows the effect of the value of isodose line on Meningioma brain tumor and normal tissue on PIV for both group a and b which (IDL 50%) and (IDL 75%), respectively.

Mean± SEM of group (a) 0.017% ±0.006

Mean± SEM of group (b) 0.0005%±0.003 (p= 0.005, Mann-Whitney test).

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 0.03%. 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), 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).

Coverage index:

In this study, all the results showed that the average Coverage index of PTV of the plans that contain isodose line 50% is 0.82 while in other plans that contain isodose line 75 % is 0.25. Mean± SEM of the group (a) 0.82± 0.05while in group(b) is 0.25± 0.042. 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 = 8.1×10^{-8}, Independent Samples T- Test).

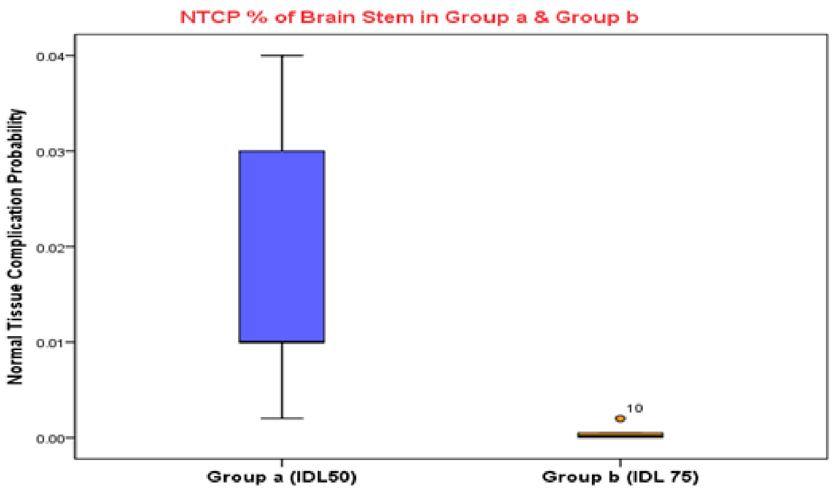


Fig. 3b. shows the effect of the value of isodose line on tumor and normal tissue on the Brain Stem for both group a and which (IDL 50%) and (IDL 75%), respectively.

Mean± SEM of group (a) 0.017% ±0.006

Mean± SEM of group (b) 0.0003%±0.0002(p= 0.005, Mann-Whitney test).

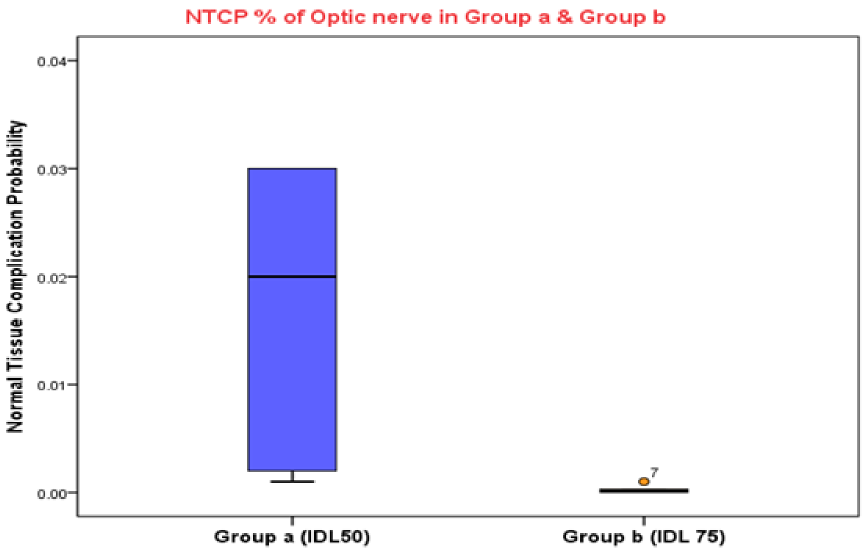


Fig. 3c. shows the effect of the value of isosdose line on tumor and normal tissue on the Optic Nerve for both group a and b which (IDL 50%) and (IDL 75%), respectively.

Selectivity index:

While the Mean± SEM of a group (a) of Selectivity index (Sin) of PTV is 0.86± 0.04. while in a group (b) is 0.97± 0.02(p = 0.024, 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.

Conformity index:

Also, in another index such as the Conformity index (CIn) Mean±SEM of a group (a) is 0.83± 0.07. while in a group (b) is 0.26± 0.04.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%)

(p =1.41×10^{-6}, Independent Samples T- Test).

TABLE 6a. 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	0.005	1	0.2	0.04
2	2	1.35	0.005	1	0.31	0.02
3	2.025	1.33	0.005	0.9	0.1	0.08
4	2.067	1.37	0.005	0.6	0.12	0.04
5	2	1.33	0.005	0.37	0.12	0.02
6	2.075	1.41	0.004	0.95	0.42	0.01
7	2.16	1.5	0.004	0.9	0.48	0.01
8	2.07	1.35	0.005	0.64	0.19	0.02
9	2	1.36	0.005	0.96	0.37	0.02
10	2.07	1.38	0.005	0.95	0.31	0.02
Average	2.04	1.37	0.0048	0.83	0.26	0.03
SD	0.05	0.05	0.0004	0.21	0.14	0.02
P-value	1.16×10^{-16}			0.005		

TABLE 6b. 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	0.04	3.04	14.1	0.01	0.65	0.80	-0.63
2	0.94	0.30	0.02	2.6	6.66	0.01	0.70	0.95	-0.26
3	0.70	0.10	0.04	3.41	15.83	0.01	0.90	1.0	-0.1
4	0.60	0.13	0.04	2.86	8.81	0.01	0.99	1.0	-0.01
5	0.62	0.12	0.04	2.9	9.32	0.01	1.00	1.0	0
6	0.95	0.39	0.003	2.65	4.61	0.01	0.82	1.0	-0.18
7	0.91	0.48	0.01	2.84	7.7	0.01	0.78	0.92	-0.22
8	0.64	0.19	0.02	2.72	5.54	0.01	0.99	1.0	-0.01
9	0.96	0.38	0.02	2.66	4.68	0.01	0.89	1.0	-0.11
10	0.95	0.29	0.02	2.56	5.67	0.01	0.87	1.0	-0.13
Average	0.824	0.254	0.025	2.82	8.29	0.01	0.86	0.97	-0.165
SD	0.16	0.133	0.014	0.26	3.89	0	0.12	0.064	0.19
P-value	8.1×10^{-8}			3.16×1^{0}-4			0.024		

Gradient Index:

Also in another index such as Gradient Index Mean±SEM of a group (a) is 2.82± 0.08. while in a group (b) is 8.29± 1.22. 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%, ($p = 3.16\times10^{-4}$, Independent Samples T- Test).

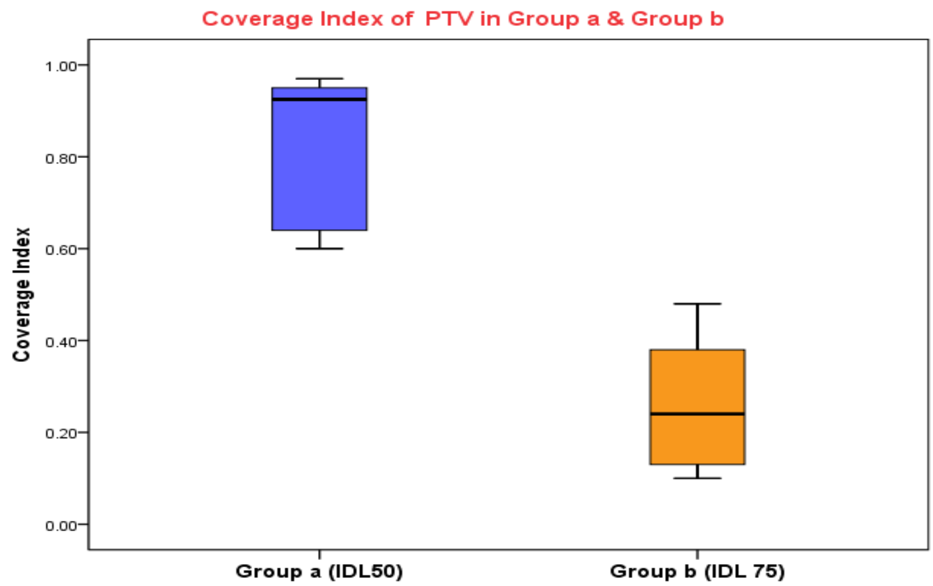
Heterogeneity Index:

Also, in another index such as the Heterogeneity Index Mean±SEM of a group (a) is 2.04± 0.016. while in a group (b) is 1.37± 0.016. 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%, ($p = 1.16\times10^{-16}$, Independent

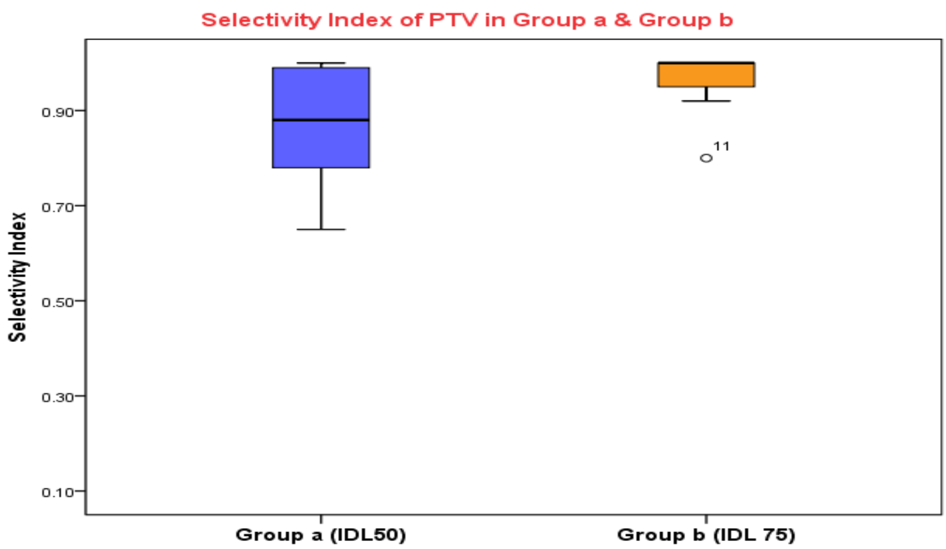
Samples T- Test). Figure 4 [a, b, c, d, and e]. show the effect of the value of isodose line on tumor and normal tissue on the physical indices of PTV for both group a and b which (IDL 50%) and (IDL 75%), respectively. Our results agree with Ehsan H. Balagamwala, A.B., *John H which believe that the 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 [3,15].

Conclusion

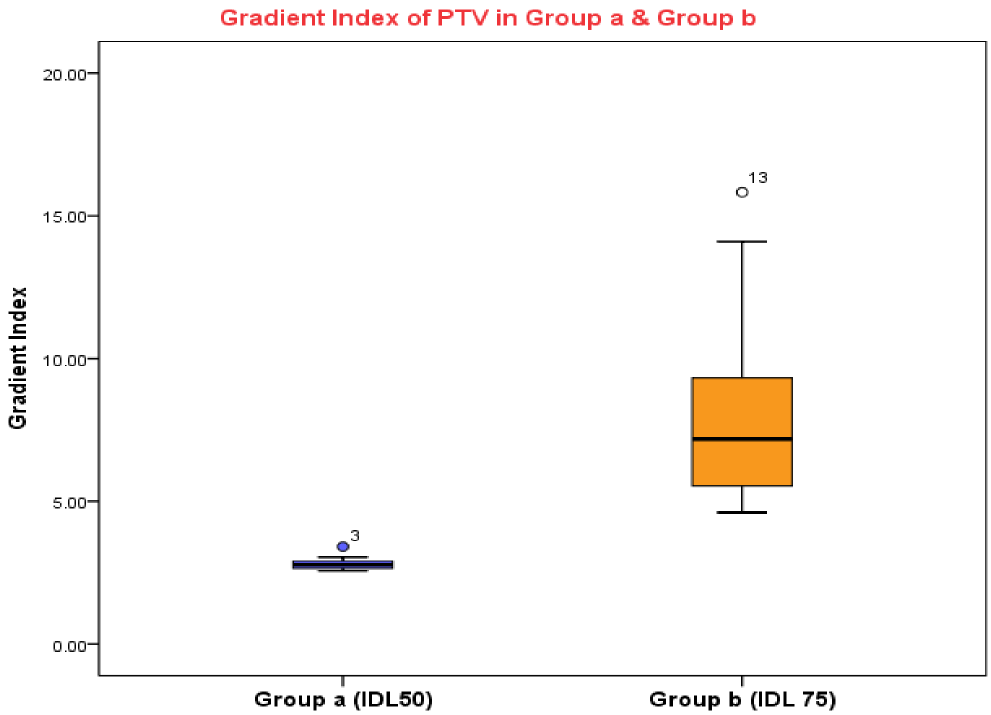
Comparison of two isodose lines normalization showed that radio oncologists and medical physicists could be advised to decide on treatment through the accurate values of TCP and NTCP, and this is achieved via testing plans by the MATLAB program within computing the physical indices. Further studies and quantitative models on other radiosurgery modalities may be also useful for more comprehensive conclusion.



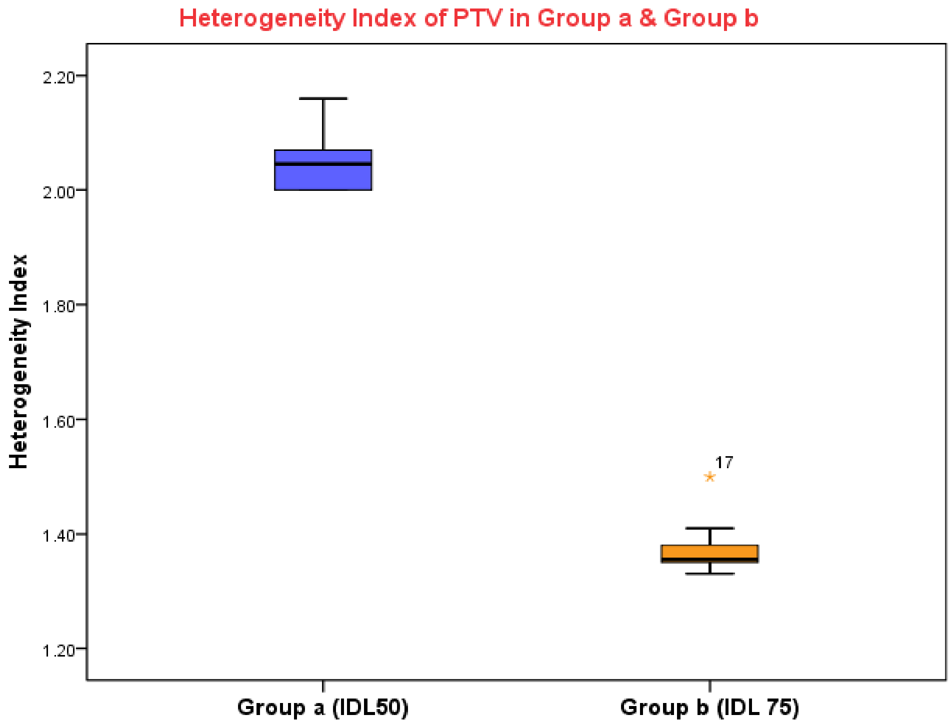
Mean± SEM of a group (a) 0.82± 0.05.
Mean± SEM of a group (b) 0.25± 0.042. (p = 8.1×10-8, Independent Samples T- Test).



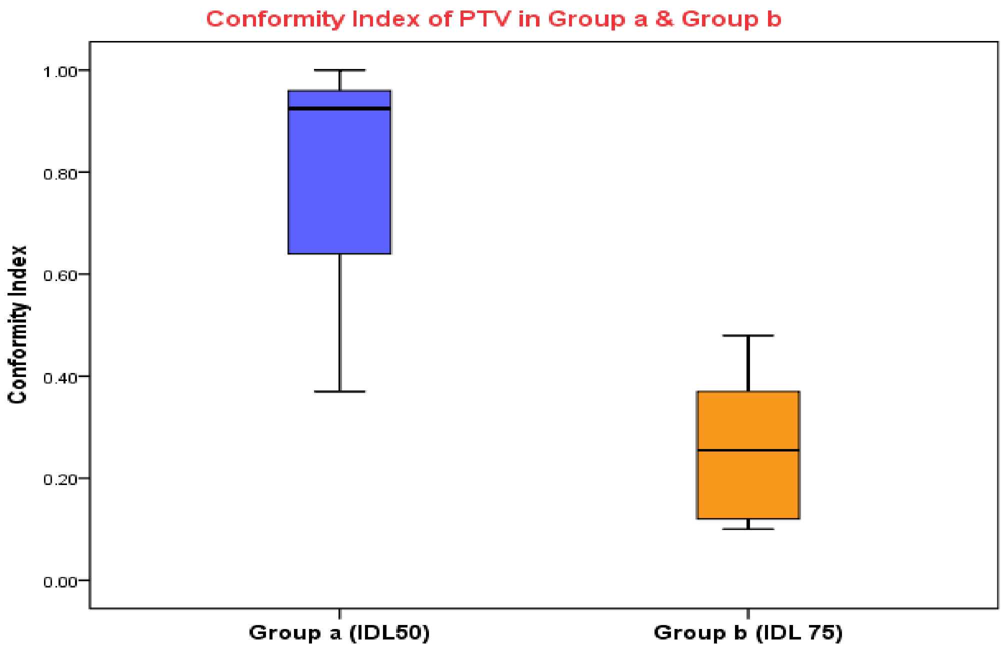
Mean± SEM of a group (a) 0.86± 0.04.
Mean± SEM of a group (b) 0.97± 0.02. (p = 0.024, Independent Samples T- Test).



Mean± SEM of a group (a) 2.82± 0.08
Mean± SEM of a group (b) 8.29± 1.22 (p =3.16×10-4,Independent Samples T- Test).



Mean± SEM of a group (a) 2.04± 0.016
Mean± SEM of a group (b) 1.37± 0.016 (p =1.16×10-16,Independent Samples T- Test).



Mean± SEM of a group (a) 0.83± 0.07
Mean± SEM of a group (b) 0.26± 0.04(p =1.41×10-6,Independent Samples T- Test).

Fig. 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.

Acknowledgment

Authors would like to thanks to Mohamed Osama, Biomedical designing and President of Medical Company, Faculty-of designing Helwan-University, for his incredible endeavors and ultimate support in the methodology section.

Conflict of Interest Statement

Authors have nothing to declare regarding any conflict of interest.

References

1. Pignol, J.-P., & Keller, B. M. (2009). Electron and photon spread contributions to the radiological penumbra for small monoenergetic x-ray beam (≤ 2 MeV). *Journal of Applied Physics*, *105*(10), 102011.

2. Ferris, M. C., & Shepard, D. M. (2000). Optimization of gamma knife radiosurgery. *Discrete Mathematical Problems with Medical Applications*, *55*, 27-44.

3. liscak, R. (2013). Gamma knife Radiosurgery. *Nova science Publishers*.

4. Johnson, P. B., Monterroso, M. I., Yang, F., & Mellon, E. (2017). Optimization of the prescription isodose line for Gamma Knife radiosurgery using the shot within shot technique. Radiation Oncology, 12(1), 1-9.

5. AB, E. I. ((2011-10). LGP 10 Leksell Gamma Plan®. Online Reference Manual, 1023200 Rev. 01.

6. Oldham, M., Khoo, V., Rowbottom, C., Bedford, J., & Webb, S. (1998). A case study comparing the relative benefit of optimizing beam weights, wedge angles, beam orientations and tomotherapy in stereotactic radiotherapy of the brain. *Physics in Medicine & Biology*, *43*(8), 2123.

7. Niemierko, A. (1999). A unified model of tissue response to radiation. In *Proceedings of the 41th AAPM annual meeting* (Vol. ١١٠٠). Nashville: Wikipedia.

8. Gay, H. A., & Niemierko, A. (2007). A free program for calculating EUD-based NTCP and TCP in external beam radiotherapy. *Physica Medica*, *23*(3-4), 115-125.

9. Willner, J., Baier, K., Caragiani, E., Tschammler, A., & Flentje, M. (2002). Dose, volume, and tumor control prediction in primary radiotherapy of non-small-cell lung cancer. *International Journal of Radiation Oncology* Biology* Physics*, *52*(2), 382-389.

10. Emami, B., Lyman, J., Brown, A., Cola, L., Goitein, M., Munzenrider, J., Shank, B., Solin, L., & Wesson, M. (1991). Tolerance of normal tissue to therapeutic irradiation. *International Journal of Radiation Oncology* Biology* Physics*, *21*(1), 109-122.

11. Mansour, Z., Attalla, E. M., Sarhan, A., Awad, I. A., & Hamid, M. A. Study the Influence of the number of beams on radiotherapy plans for the hyopfractionated treatment of breast cancer using biological model.

12. Emami, B., Lyman, J., Brown, A., Cola, L., Goitein, M., Munzenrider, J., Shank, B., Solin, L., & Wesson, M. (1991). Tolerance of normal tissue to therapeutic irradiation. *International Journal of Radiation Oncology* Biology* Physics*, *21*(1), 109-122.

13. Stavrev, P., Stavreva, N., Niemierko, A., & Goitein, M. (2001). Generalization of a model of tissue response to radiation based on the idea of functional subunits and binomial statistics. *Physics in Medicine & Biology*, *46*(5), 1501.

14. Paddick, I., & Lippitz, B. (2006). A simple dose gradient measurement tool to complement the conformity index. *Journal of neurosurgery*, *105*(Supplement), 194-201.

15. Balagamwala, E. H., Suh, J. H., Barnett, G. H., Khan, M. K., Neyman, G., Cai, R. S., Vogelbaum, M. A., Novak, E., & Chao, S. T. (2012). The importance of the conformality, heterogeneity, and gradient indices in evaluating Gamma Knife radiosurgery treatment plans for intracranial meningiomas. *International Journal of Radiation Oncology* Biology* Physics*, *83*(5), 1406-1413.

16. Langer, M., Morrill, S. S., & Lane, R. (1998). A test of the claim that plan rankings are determined by relative complication and tumor-control probabilities. *International Journal of Radiation Oncology* Biology* Physics*, *41*(2), 451-457.

17. Moiseenko, V., Battista, J., & Van Dyk, J. (2000). Normal tissue complication probabilities: dependence on choice of biological model and dose-volume histogram reduction scheme. *International Journal of Radiation Oncology* Biology* Physics*, *46*(4), 983-993.

18. Shanei, A., Abedi, I., Saadatmand, P., Amouheidari, A., & Akbari-Zadeh, H. (2020). Comparison of 3D conformal and intensity modulated radiotherapy in early stage oral tongue cancer: Dosimetric and radiobiological evaluation. *International Journal of Radiation Research*, *18*(1), 33-42.

19. Santacroce, A., Walier, M., Régis, J., Liščák, R., Motti, E., Lindquist, C., Kemeny, A., Kitz, K., Lippitz, B., & Álvarez, R. M. (2012). Long-term tumor control of benign intracranial meningiomas after radiosurgery in a series of 4565 patients. *Neurosurgery*, *70*(1), 32-39.

20. Rana, S., & Cheng, C. (2014). Radiobiological impact of planning techniques for prostate cancer in terms of tumor control probability and normal tissue complication probability. *Annals of medical and health sciences research*, *4*(2), 167-172.

التقييم الفيزيائى والبيولوجى لخطط علاج الأورام السحائية بالجراحة الاشعاعية لمشرط جاما: (مقارنة بين خط جرعة ٥٠٪ وخط جرعة ٧٥٪) .

جاد الباز[١] , هداية هندام [١] , السيد محمد الأشقر[٢], خيرى عريبه [٣], إيهاب عطا الله [٤]
١- مركز الجاما نايف ، قسم جراحة المخ والأعصاب ، كلية الطب ، مستشفى جامعة الأزهر بدمياط.
٢- قسم الفيزياء ، كلية العلوم ، جامعة الأزهر.
٣- قسم جراحة المخ والأعصاب، كلية الطب ، جامعة طنطا.
٤- المعهد القومى للأورام ، جامعة القاهرة.

تستكشف هذه الدراسة كيف يحقق اختيار خط متماثل الجرعة (IDL) احتمالية عالية للتحكم المحلي في الورم (احتمالية التحكم في الورم ، TCP) مع انخفاض مخاطر حدوث مضاعفات الأنسجة الطبيعية (احتمالية مضاعفات الأنسجة الطبيعية ، NTCP) للجراحة الإشعاعية بسكين جاما عند تطبيق خطين مختلفين من خطوط الجرعة لكل خطة على حدة.

حيث أظهرت النتائج أن متوسط حجم الورم الهدف ٥,٤٤ سم ٣ (٠,٥٩ - ٢٣,٧٢) والذى كان قيمة احتمالية التحكم في الورم TCP أعلى فيه بشكل ملحوظ في الخطة الأولى ،والتى تطبق خط متساوي للجرعة بنسبة ٥٠٪ للجرعة مقارنة مع الخطة الثانية التي تطبق خط متساوي للجرعة بنسبة ٧٥٪ (٩٤,٩٨٪ ، ٤٥,٠٩٪ ، p = 0.0018 ، اختبار Mann-Whitney)؛ أما بالنسبة لقيمة إحتمالية مضاعفات الأنسجة الطبيعية NTCP مثل جذع الدماغ والعصب البصري منخفضة جدًا بمتوسط ٠,٠١٪ (٠-٠,٠٣٪) في الخطة الأولى وصفر في الخطة الثانية (p = 0.005 ، اختبار Mann-Whitney).

حيث أظهرت المقارنة أنه يمكن نصح أطباء الأورام والفيزيائيين الطبيين بإتخاذ القرار بشأن العلاج من خلال القيم الدقيقة لـ TCP و NTCP ، ويتم تحقيق ذلك من خلال نموذج الإختبار بواسطة برنامج ماتلاب، مع حساب المؤشرات الفيزيائية.