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Original Article

Dose Assessment of Eye and Its Components in Proton Therapy by Monte Carlo Method

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Abstract

Introduction
Proton therapy is used to treat malignant tumors such as melanoma inside the eye. Proton particles are adjusted according to various parameters such as tumor size and position and patient's distance from the proton source.
The purpose of this study was to assess absorbed doses in eyes and various tumors found in the area of sclera and choroid and the adjacent tissues in radiotherapy while changing most important proton therapy parameters such as moderators thickness (1.5-1.9 cm), exposure radius (0.5-0.8 cm), and proton energy beam (53.5-65 MeV).
Materials and Methods
A proton therapy system of Laboratori Nazionali del Sud-INFNwas simulated by Monte Carlo method. Moreover, the eye and its components were simulated using concentric spheres. To obtain a more accurate results, real density of eye components such as cornea and lens, were applied for simulation. Then, the absorbed dose of eye and eye tumor, in choroid and sclera areas, were calculated by Monte Carlo method.
Results
The absorbed dose in tumoral region of eye was calculated to be about 12.5 ±0.006Gy in one day with energy 62 MeV for a therapy session, which is suitable for treatment. However, normal eye cells received at most 11.01 Gy which is high.
Conclusion
The amount of absorbed dose in tumoral cells is noticeable. Therefore, accurate treatment planning, patient immobility and fine calibration of proton-therapy system and its simulator are very important to reduce the absorbed dose of healthy cells.

Keywords: Absorbed Dose; Melanoma; Monte Carlo Method; Proton Therapy.

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1. Introduction

1.1. Eye anatomy

In general, the eyeball is composed of three coating layers which from outside to inside are listed below and are shown in Figure 1:
Outer layers or the sclera
The middle layer or grapes or Uvea
The inner layer of the eyeball or retina
The middle layer of the eyeball is the distance between the sclera and the retina, which is composed of three parts: the iris, ciliary body, and choroid. The total weight of both eyes is about 15 g in the International Commission on Radiological Protection (ICRP) Publication 23. The eye structure is like a sphere with an average diameter of 24 mm. Each of the sclera and the choroid has an average thickness of 1 mm. There is a transparent window in the front part of the sphere, called the cornea. The eye focuses the lights received from the outside on the retina very clearly, so that the light from the outside environment enters cornea and reaches the retina after passing through the pupil and lens. The retina sends these images to the brain as nerve impulses and the brain interprets them. The sclera protects the internal components and prevents deformation of the eyeball. [1-4]

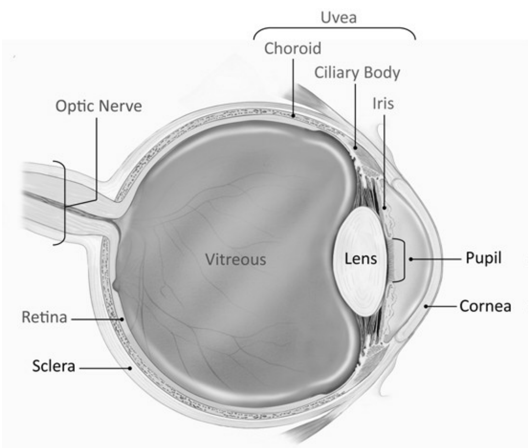

Figure 1. Human eye and its components. Uvea is comprised of three parts: ciliary body, iris, and choroid [1].

1.2. Eye tumors

The most common malignant tumors of the eye can be divided into two categories: melanoma and retinoblastoma. These tumors are classified depending on what age they occur.
Melanoma is originated by the pigmented cells of uvea and seen in adults usually at the age of 60 to 70. However, retinoblastoma is common in children under 7 years [5]. A typical image of choroidal melanoma is shown in Figure 2. The tumors have different sizes and shapes and they can be divided into three categories based on their size.Small tumors with volume of less than 400 mm^3, mean tumors with volume of 400-1000 mm^3, and large tumors with volume of more than 1000 mm^3. [6] The eye and brain tumors are relatively common in modern societies [7, 8]. The use of proton beam has been proposed for the treatment of these tumors in recent years, and some researches have been conducted in this respect in the developed countries [9, 10].

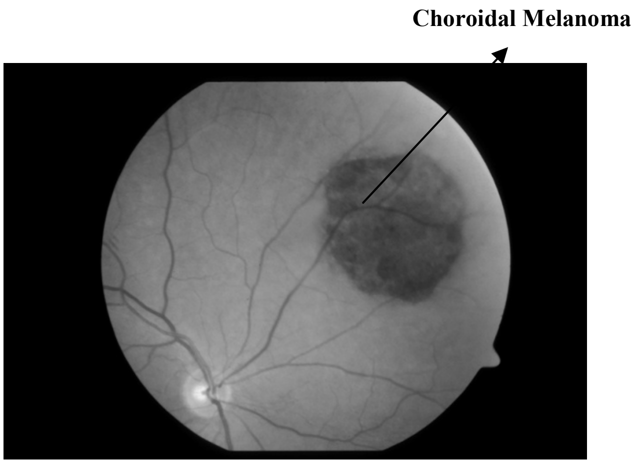

Figure 2. Choroidal melanoma of human's eye [5].

Using X-rays and γ-rays was the only treatment of the eye tumors until about 10 years ago, where many patients would suffer impaired vision or vision loss after treatment due to the large range of X-rays and γ-rays and its harmful effects on healthy cells of the eye. About 10 years ago, the use of nuclear particles was proposed for treating tumors in sensitive tissues such as brain and eye. [11-17]
Radiotherapy and hadron-therapy techniques use X-rays, γ-rays, β-, and

proton particles. These particles have some advantages such as they are non-invasive; the small dimensions of these particles and photons compared with cell dimensions. The most important advantages of proton therapy compared with other radiotherapy methods are: centrality of proton particles, appropriate Bragg peak, and relatively short range of proton particles. Currently, proton therapy is the best and most effective method to treat eye tumors. However, this treatment method still needs to be investigated and various research groups in developed countries are working on specific components of the proton therapy devices such as proton particles nozzle and also on calculation of received doses in the cancer and normal cells using simulation and analysis methods and have reported the results of their researches. [11, 18]

In this research, LNS-INFN proton particles device (Laboratori Nazionali del Sud - Istituto Nazionale di Fisica Nucleare, Italy) was simulated using Monte Carlo method. Since cancer incidence is most probable in the choroid and sclera area of the eye, therefore in this research, tumors of the eye in these two areas were considered and the received dose rates was calculated in different parts of the eye and also in both normal and cancer cells of these two areas of the eye.

2. Materials and Methods

2.1. Simulated proton therapy device specifications

LNS-INFN Specifications are as follows: The energy range of output particles was 50-250 MeV, moderator thickness is 1.5 cm and the output beam radius of the device was 0.5-1 cm.

MCNPX code was used to simulate the above proton therapy system. The tally number 6 (F6) in this program was used to calculate the deposited energy in each cell and the Number of histories for which source (NPS) of the followed particles was 10 million particles.

2.2. Simulated eye

The important parts of eye such as lens, cornea, optic nerve, choroid, sclera, and their internal parts were considered in simulated. The dimensions of the eye were replicated from the "Optics of the Human Eye" model [19]. The eye was appropriately made by the use of concentric spheres; the vitreous was placed behind the lens and the anterior in front of the lens and the optic nerve was simulated as a cylinder.

Sectors were made in the lateral wall of the model in order to calculate the dose in this region. The eye was made using concentric spheres in this simulation and the dimensions used are shown in Figure 3.

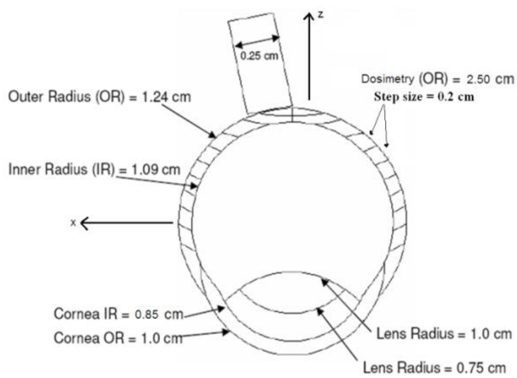

Figure 3. A schematic of the eye components and their sizes in XZ axis, which were used in the simulation. The coordinate axes specified in the figure are the same as those used in the simulation. The Y axis direction is toward the board.

Sphere center of the lateral wall of the lens was adjusted at 3.3 cm on the Z-axis and sphere center of the internal wall of the lens was adjusted at 2 cm on the Z-axis and at radiuses of 0.75 cm and 1 cm, respectively, as shown in Figure 3. Spheres which formed cornea, each were adjusted at 3.1 cm on the Z-axis and at radiuses of 1 cm and 0.85 cm, respectively. The optic nerve was simulated appropriately as a cylinder from the posterior pole of the eye with a radius of 0.25 cm and length of 0.2 cm along the X-axis and height of 1 cm along the Z-axis.

Moreover, choroid was divided into 0.2 cm parts by the use of dose measurement spheres in order to be able to obtain the accurate dose of each part of the choroid and sclera that may possibly have tumor.

2.3. Materials used in the simulated eye

Constructive elements of different eye regions were selected according to the data from International Commission on Radiation Protection (ICRU) Report 46 [20]. This report investigated various tissue groups of the body and identified their density and elemental composition for radiation dose measurement purposes. The density of tumor is different from tissues surrounding, Density of tumor is 1.0299 g/cm3 [18]. Recent studies have shown that the characteristics of vitreous and anterior liquid are similar to lymph properties which are mentioned in ICRU46 [20]. The choroid and the sclera are essentially an interlocking soft tissue, so they were modeled just the same, as a soft tissue.

2.4. Treatment protocol

Patient with eye tumor refers to the hospital for treatment. First, the tumor is diagnosed and then the size of the tumor and other parts of the eye are determined precisely. Then, the shape and location of the tumor are marked by an ophthalmologist using tantalum marker clips which are sewn to the outside of the sclera. One to two weeks after the insertion of surgical clips, the patient refers to hospital for further treatment. A block-bite and individual mask are made for the patient so that the components of patient's head and face are not damaged during the eye proton therapy and also the patient's head remains constant during the treatment. These two instruments are shown in Figure 4.

Figure 4. Individual mask and block-bite for stabilizing the patient's head during treatment.

The block-bite is a piece of material which the patient bites down on during the treatment. It is custom-made to fit the individual patient's teeth, ensuring consistent placement in the patient's mouth as he/she bites down on the block. Likewise, the individual mask is a form-fitting mesh that fits over the individual's face and is anchored behind the head.

The mask is set firmly against the patient's face and head and protects other parts of head and face against radiation-induced damages. Finally, these two segments determine the placement of the patient for treatment.

When the patient is immobilized in a position, a set of diagnostic X-rays are irradiated to the eye for precise measurement of the clamps locations in the eye in order to determine the position of the patient and proton therapy device. After placement of the patient in the determined position, medical radiologist revises the diagnostic images (MRIs, CTs, sonograms, and patient placement X-rays) and finally plans the desired dose of proton and the desired angle of the eye for treatment.

A minor light is put in front of the patient during treatment in order to maintain a steady angle of patient's eye to one direction. Stabilizing the patient's look can help reducing the dose reaching the main components of the eye. For example, in treatment of a posterior melanoma, it may be possible for the patient to fix their gaze looking toward the ceiling, effectively moving the cornea and lens out of the proton treatment path.

A picture of the method of stabilizing the angle of the patient's eye is shown in Figure 5. After considering all these aspects, a complete revision will be performed and then the patient is ready for treatment. Placement of the patient in front of the eye proton therapy device is shown in Figure 6.

Figure 5. Positioning the patient in front of the proton therapy system.

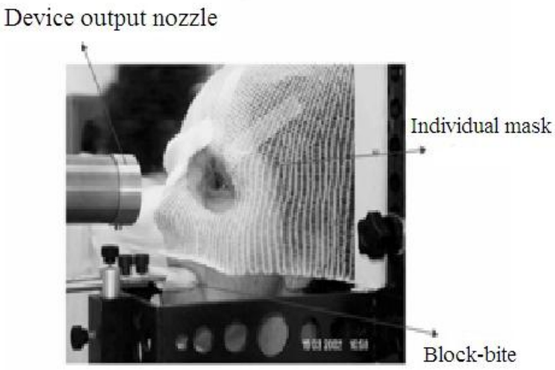

Figure 6. Positioning the patient in front of the proton therapy system by using block-bite and individual mask.

2.5. Dose calculations

In addition to the simulation of the tumor, the eye and other optical components of it were also simulated and the received dose of the tumor and its surrounding healthy areas were calculated. In this study, after the simulation of the proton therapy device, some parameters such as source energy, the diameter of the exiting proton particles from the nozzle (source), moderator thickness, the distance between the source and the patient's head, and the irradiated area were regarded and the results of these changes were calculated and evaluated. A schematic of the eye-tumor therapy by the proton therapy device is shown in the Figure 7.

Most melanomas of the eye occur in choroid and sclera areas [18]. Therefore, the treatment design was regarded for five samples of melanoma in these areas within a radius of 0.26-0.3 cm, and in the cells number 20, 23, and 25 to 27 which have been marked in Figure 8. Furthermore, proton particles were irradiated toward the tumor with an energy range of (53.5-65) MeV, moderator thickness range of (1.5-1.9) cm, and beam radius range of (0.5-0.8) cm.

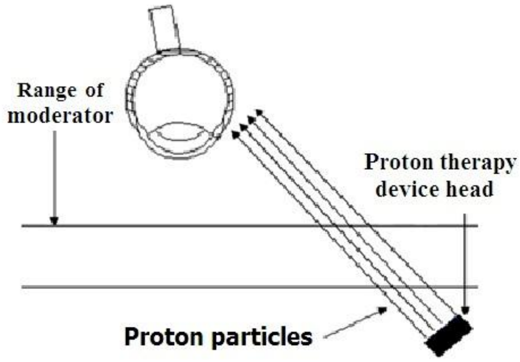

Figure 7. A schematic of the eye-tumor therapy by the proton therapy device.

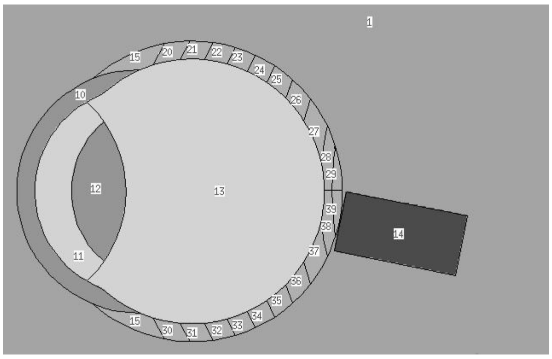

Figure 8. A schematic cell layout of the simulated eye and its components. Cell No. 10 in the cornea region, cell No. 11 in the anterior chamber, cell No. 12 inside the lens, cell No. 13 inside the vitreous humor, cell No. 14 in optic nerve and other cells from No. 20 to 39 in the choroid and sclera region represent the used dose measurement volumes in this study.

The received dose in proton therapy of the eye and hence treatment of its melanoma depends on many parameters such as proton energy, moderator thickness, selected radius of proton beam, distance between patient and the device, energy distribution of the source, and direction of the output beam. Thus, in order to achieve the most appropriate treatment setting, the above parameters should change and be selected individually.

3. Results

After validation of the results that has been listed in Table 1, tumors with a radius of 0.26-

0.3 cm were placed in different cells in the choroid and sclera regions of the eye in order to obtain a dose measurement in all parts of the eye. These regions are more probable to develop cancer and amounts of absorbed dose in the tumor and its surrounding regions were calculated.

Table 1. Results of calculated dose distribution, for treatment of the case that the tumor is located in the cell 26 of choroid and sclera regions, including calculated error and comparison with the results of previous simulations.

Dose volume	The calculated total dose during a period of four days treatment (Gy)	Total dose (Gy) [18]	Percent of relative error
Cornea	2.4±0.008	2.41	0.41
Anterior Liquid	0.36±0.044	0.37	2.7
Lens	0.35±0.044	0.36	2.7
Vitreous humor	19.72±0.062	19.73	0.05
Optic nerve	0.016±4.24	4.26	0.46
Cell 20	0.004±44.04	44.02	0.045
Cell 21	0.004±43.44	43.45	0.023
Cell 22	0.005±44	40.99	0.024
Cell 23	0.005±38.84	38.85	0.025
Cell 24	0.006±38.68	38.70	0.051
Cell 25	0.006±42.04	42.02	0.047
Cell 26	0.006±50	50.01	0.019
Cell 27	0.008±40.88	40.89	0.024
Cell 28	0.025±6.24	6.23	0.16
Cell 29	0.35±0.08	0.09	11.11
Cell 30	0.2±0.08	0.06	33.33
Cell 31	0.23±0.04	0.04	0
Cell 32	0.29±0.04	0.03	33.33
Cell 33	0	0	0
Cell 34	0	0	0
Cell 35	0	0	0
Cell 36	0	0	0
Cell 37	0	0	0
Cell 38	0	0	0
Cell 39	0	0	0

Since proton energy, moderator thickness, and beam radius are the most important parameters which affect the amount of received dose in proton therapy, these parameters and the dose were calculated in the above-mentioned regions of the eye. The results are shown in Figures 9 to 13.

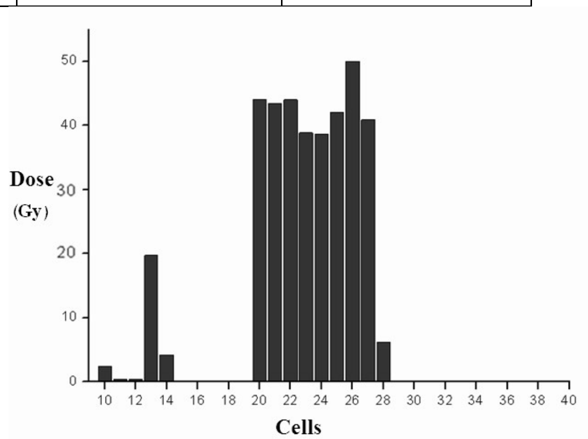

Figure 9. A histogram of deposited energy in the specified cells in the eye, during treatment a tumor with a radius of 0.26 cm in cell No. 26.

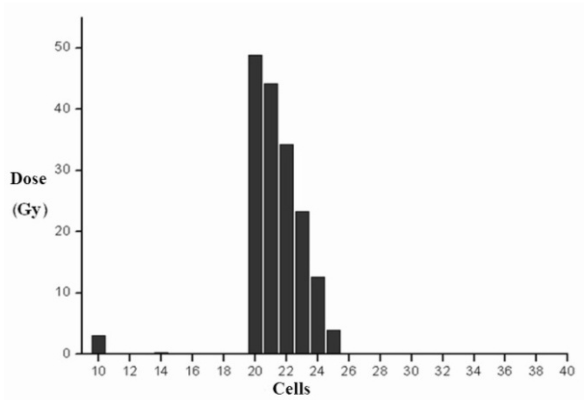

Figure 10. A histogram of deposited energy in the specified cells in the eye, during treatment a tumor with a radius of 0.3 cm in cell No. 20, which was located close to the sensitive cornea.

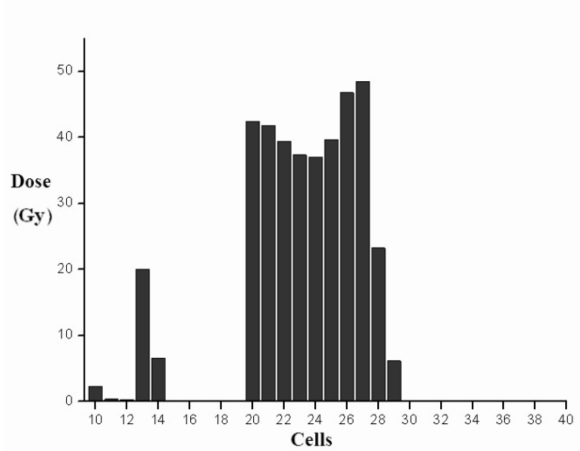

Figure 11. A histogram of deposited energy in the specified cells in the eye, during treatment a tumor with a radius of 0.26 cm in cell No. 27, which was located close to the sensitive optic nerve.

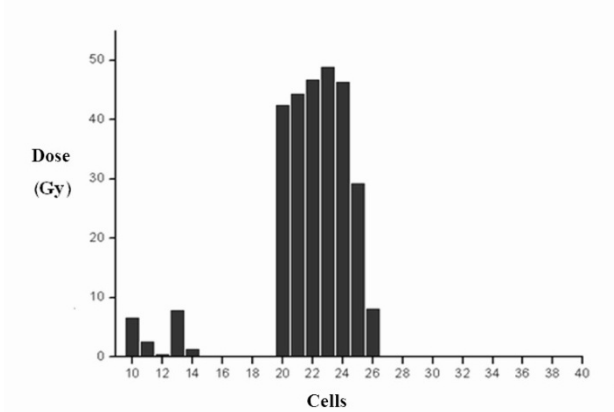

Figure 12. A histogram of deposited energy in the specified cells in the eye, during treatment a tumor with a radius of 0.28 cm in cell No. 23, which was located close to the sensitive cornea.

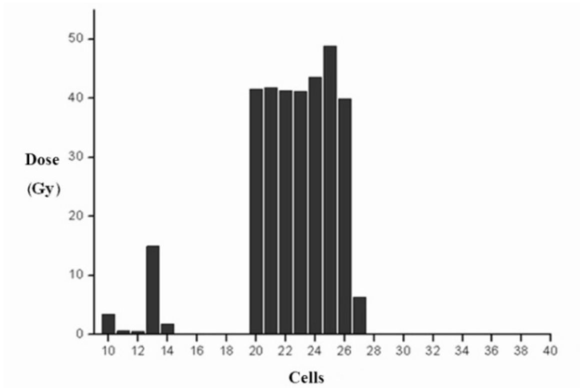

Figure 13. A histogram of deposited energy in the specified cells in the eye, during treatment a tumor with a radius of 0.27 cm in cell 25, which was located close to the sensitive choroid.

In Figure 9, the tumor has been located in cell No. 26 of the choroid with a radius of 0.26 cm and received the total dose of about 12.5 ±0.006 Gy for one day of treatment. Moreover, its surrounded healthy cells, i.e., cell No. 20 received the highest dose in one day with the amount of 11.01 Gy and cell No. 32 received the lowest dose in one day with the amount of 0.01 Gy. The amount of received dose by healthy cells adjacent to the cancerous cell No. 26 is in the ranges of 12.33% to 87.98% for cells No. 20 to 28 in comparison with the cell No. 26. It should be noted that cell No. 13 is in the vitreous region and exposed by relatively direct radiation, and so has received greater amounts of dose compared with its surrounding areas (10 to 14). The amount of received dose by non-adjacent healthy cells is in the ranges of 0.72% to 39.42% for cells No. 10 to 14.

For treatment of this tumor, proton particles energy of 62 MeV, moderator thickness of 1.5 cm, and beam radius of 0.5 cm were considered.

In Figure 10, the tumor has been located in the cell No. 20 of the choroid and close to the sensitive cornea with a radius of 0.3 cm. It received the amount of 12.42 Gy of radiation dose for one day of treatment. Moreover, its surrounded healthy cells, i.e., cell No. 21 received the highest dose in one day with the amount of 11.24 Gy and healthy cell No. 11 received the lowest dose in one day with the amount of 95E-5 Gy. The amount of received dose by healthy cells adjacent to the cancerous cell 20 is in the ranges of 8.05% to 90.49% for cells No. 21 to 25 in comparison with the cell 20. It was observed that during treatment, the sensitive cornea received only 3.04 Gy of radiation dose which is quite a harmless amount, because it is lower than the permitted limit of received dose for the cornea (15 Gy). The amount of received dose by non-adjacent healthy cells is in the ranges of 0.0077% to 6.11% for cells No. 10 to 14.

For treatment of this tumor, proton particles energy of 56 MeV, moderator thickness of 1.9 cm, and beam radius of 0.5 cm were considered.

In Figure 11, the tumor with a radius of 0.26 cm was located in cell No. 27 of the choroid region and close to the sensitive optic nerve. This cell received 12.34 Gy of radiation dose for one day of treatment. Moreover, its surrounded healthy cells, i.e., cell No. 26 received the highest dose in one day with the amount of 11.9 Gy and the lowest amount belongs to cell No. 37 which received the amount of 0.0013 Gy in one day treatment. The amount of received dose by healthy cells adjacent to the cancerous cell 27 is in the ranges of 12.64% to 96.43% for cells No. 20 to 29 in comparison with the cell No. 27 and the amount of received dose by non-adjacent healthy cells is in the ranges of 0.68% to 41.32% for cells No. 10 to 14. Moreover, during this treatment, the sensitive optic nerve received only 6.64 Gy of dose which is quite an inoffensive amount because it is lower than the permitted limit of received dose for the optic nerve (10 Gy).

For the treatment of this tumor, proton particles energy of 65 MeV, moderator thickness of 1.5 cm, and beam radius of 0.5 cm were considered.

In Figure 12, the tumor is inserted in cell No. 23 of the choroid area with a radius of 0.28 cm. It received 12.42 Gy dose for one day treatment and among its surrounding healthy cells, cell No. 22 received the highest dose in one day with an amount of 11.88 Gy and cell No. 31 received the lowest dose in one day of treatment with an amount of 87E-6 Gy. The amount of received dose by healthy cells adjacent to the cancerous cell No. 23 is in the ranges of 16.58% to 95.65% for cells No. 20 to 26 in comparison with the cell No. 23. The amount of received dose by non-adjacent healthy cells is in the ranges of 0.78% to 15.94% for cells No. 10 to 14.

For the treatment of this tumor, proton particles energy of 53.05 MeV, moderator thickness of 1.5 cm, and beam radius of 0.8 cm were considered.

In Figure 13, the tumor was located in cell 25 of the choroid area with a radius of 0.27 cm. It received 12.42 Gy dose for one day treatment and among its surrounding healthy cells, cell No. 24 received the highest dose in one day with an amount of 11.08 Gy and healthy cell No. 31 received the lowest dose in one day treatment with an amount of 0.0015 Gy. The amount of received dose by healthy cells adjacent to the cancerous cell No. 25 is in the ranges of 12.88% to 89.21% for cells No. 20 to 27 in comparison to the cell 25. The amount of received dose by non-adjacent healthy cells is in the ranges of 1.17% to 30.59% for cells No. 10 to 14.

For the treatment of this tumor, proton particles energy of 56.05 MeV, moderator thickness of 1.5 cm, and beam radius of 0.6 cm were considered.

The obtained results are shown in Table 2. These results can be utilized for treatment of tumors in these areas of the eye.

Table 2. Comparison of calculated results in different cells of the eye during proton- therapy.

Tumor Location	Tumor Radius (cm)	Output Beam radius (cm)	Moderator Thickness (cm)	Beam Energy (MeV)	Received Dose during Treatment (Gy)
Cell 26	0.26	0.5	1.5	62	50
Cell 27	0.26	0.5	1.5	65	49.36
Cell 25	0.27	0.6	1.5	56.5	49.68
Cell 23	0.28	0.8	1.5	53.5	49.68
Cell 20	0.3	0.5	1.9	56	49.68

4. Discussion

Results of this research showed that the amount of received dose for cancer cells is about 12.5 ±0.006% Gy for one day of treatment and therefore proton therapy is an effective method of treatment.

The extent of received dose of healthy tissues of the eye in various parts of the eye and particularly adjoining tumor is considerable, so that the total dose received by healthy tissue in one day was 5.7 Gy in a 20 mm distance from the tumor and 1.58 Gy in distances more than 4 mm from the surface of the tumor.

The results that were obtained during treatment for parts of eye in choroid and sclera areas were compared with the reference number 18 and were shown in Table 1. Furthermore percent of relative error calculated and show in Table 1. Percent of relative error were between 0.46-0.019. Highest error is for optic nerve and lowest error is for tumor. So results showed the calculated error adjacent to reference number 18 are appropriate.

So, the amount of received dose by healthy cells surrounding the cancer cells is important. Therefore, precise treatment design and adjustment of the proton therapy device, patient fixation, and using treatment planning simulator is of utmost importance in order to reduce the extent of received dose by healthy cells to the lowest amount.

5. Conclusion

In this study, tumor treatment by proton therapy was studied. The tumor was considered in 5 parts of eye in choroid and sclera areas within a radius of 0.26-0.3 cm.

Results showed that the amount of received dose depends on some parameters such as proton energy, moderator thickness, and radius of radiation. Furthermore, the effects of these parameters were calculated according to tumor location and size in this study as shown in Table 2. Therefore, it is recommended that in tumor treatment of the sensitive tissues such as eye, in addition to the usual calculations, treatment planning should be performed by Monte Carlo simulation method and necessary calculations be done to find the precise dose of moderator thickness, radiation beam, and energy so that the extent of received doses of tumor and healthy areas of the eye be optimized.

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