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Carbon Radiotherapy For Head and Neck Cancer: Dosimetric Comparison with Photon Plans

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ABSTRACT

Radiation therapy is one of the most widely used treatment methods for tumors. The therapeutic use of carbon ions is more advantageous than other radiotherapy techniquies especially photon-based irradiation due to its physical properties and radiobiological effects, and therefore it has received more attention. One of the most important reasons for that carbon ion beams are more effective than photon beams while minimizing the dose in the normal tissues around the target, it offers an improved dose distribution that leads to sufficient dose concentration in tumors. In addition, the carbon beam reaches its maximum at the end of its range, which increases with depth, and due to this feature, it provides a higher biological efficiency. In radiotherapy studies, Monte Carlo simulation is widely used to determine the dose distributions and to obtain the correct properties of the beams. With MC simulation, it helps to understand the relative biological efficiency as well as the spatial model of energy storages. In this study, a geometry with critical organs (skull, brain, nasopharynx and thyroid) based on a MIRD phantom was modeled with the Monte Carlo simulation tool GATE (vGATE 9.0). In this experiment, the tumor was irradiated with different carbon beam energies and photon beams. The aim is to calculate the energy accumulations in the region and surrounding organs with the MC method, and as a result, to show the dosimetric advantages of carbon radiotherapy over photon radiotherapy.

Keywords: Breast cancer, Proton therapy, Photon therapy, GATE, Monte Carlo .

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Introduction

Among the head and neck cancers, nasopharyngeal cancer makes surgical intervention impossible due to its epidemiological and histological features, as well as its anatomical localization, and therefore it shows sensitivity to radiotherapy and chemotherapy, which are effective treatment methods in order to destroy the tumor [1]. For this reason, radiotherapy is the main treatment method for nasopharyngeal cancer. New radiotherapy techniques allow the preservation of brain areas with low tolerance to radiation, such as the pituitary gland and brain.

During the application of radiotherapy, some healthy cells may be affected by radiation, but they can repair themselves faster than cancer cells or cause side effects and secondary cancer formation as a result of exposure to high doses. With a good treatment planning, it is critical to protect the healthy tissues around the target volume at the highest level by giving the highest dose to the target volume.

Carbon ion therapy, which is a new radiotherapy method recently, has given very successful results in cancer treatment. Carbon ion therapy is a new form of radiation that fights to the extent that it destroys the unwanted mass by damaging the DNA in the cancer cell [2]. It is a modern treatment method based on the interaction of heavy ion beams such as carbon with living tissue. In photon radiotherapy, the rays are scattered by Compton scattering as they move through the living tissue and when they reach the cancerous area, they leave most of their energy on the healthy tissue, in which case it damages the healthy tissue. The carbon radiotherapy method ensures that the target cancer cells are destroyed by leaving minimal effects on the surrounding healthy tissue [3].

The use of the Monte Carlo (MC) method in radiotherapy dosimetry has increased exponentially recently, and even this computer simulation technique has been taken as a reference and has become a common tool in treatment plans and dosimetry calculations [4]. The most accurate way to calculate the dose distribution in treatment planning is the geometry of the source, the transport of energy to the desired tissue and the monitoring of energy accumulation by using the particle transport MC method. Geant4 (GEneration ANd Tracking) is software that can simulate particles interacting with and passing through matter [4]. Geant4 is a widely used MC code in health physics for various applications such as dosimetry, imaging, nuclear medicine and radiation protection. This code library is constantly evolving, so Geant4 is a fully automated system for health physics that compares this MC code with reference data and performs regression testing. The tests performed in Geant4-med are carried out on the CERN computing infrastructure by using the geant-val web application developed for Geant4 testing at CERN [5].

In this study, the dosimetric advantages of carbon radiotherapy over photon radiotherapy for head and neck cancers were investigated with the MC method in terms of the rays exposed to the healthy tissues around the malignant tumor cells.

Materials and Methods

GATE is open source software, developed jointly by the world's leading medical physics laboratories, that allows simulating medical physics using the Geant4 code library.. Geant4 is an object-oriented and C++ programming language that simulates particle transition in matter and simulates real-world processes or systems very close to reality. Geant4 (C++) is a software package developed in 1998 after Geant3 (based on Fortran), which was developed at CERN (European Nuclear Research Council) in 1993 for high energy physics experiments [6]. By using the Geant4 simulation, the possible interactions of the particle with the atom and nucleus of the target material during its progression in the matter and physical events such as position and energy in this process can be monitored.

The phantom was placed on the x, y, z coordinates with the dimensions of 2.0 x 2.0 x 2.0 m^3. The average sized skull, brain, nasopharynx and thyroid organs of an adult human were scaled and defined inside the world geometry created in the Cartesian coordinate system. Maximum x, y and z lengths were measured as 20.00 21.20 12.80 cm for the skull, 7.00, 3.50, 11.20 cm for the brain, 4.00, 4.50, 3.00 cm for the nasopharynx, and the skull volume is 5.427.2 cm^3 [7]. Thyroid with 0.83, 1.85, 4.50 cm dimensions were defined in the phantom created. Materials and tissues to fill the phantom volume were selected over the textures defined in the GateDatabase.db file based on the NIST Standards [8].

In this study, the vGATE 9.0 version of GATE was used and the teleportation was performed on a personal computer with 10 million events. Figure 1 below shows the image of the created geometry and Figure 2 shows the image formed during irradiation.

DoseActors with voxel dimensions of 1.0 mm x 1.0 mm x 1.0 mm were attached to the organs defined in the simulation code. The targeting of the cancerous area was completed by sending carbon ion beams and photon beams from different points for typical MeV values of each irradiations shown in Table 1. Radiation exposure of surrounding organs was measured with DoseActor. The dose value (Gy) stored in DoseActor was saved by taking the output files in root format. Cut regions for each tissue and each particle (electron, positron, gamma) has been set to 0.01 mm.

Table 1: Doses absorbed by organs (Gy) for each energy levels (MeV) with 1M events using a particle filter.

Energy For Carbon(MeV)	Energy For Photon(MeV)	Carbon DoseActor (Gy)		Photon DoseActor (Gy)	
		Nazofarengeal	3.9122 e-08	Nazofarengeal	1.7570 e-08
160 MeV	12 MeV	Brain	7.1320 e-10	Brain	4.2980 e-08
		Thyroid	3.6452 e-10	Thyroid	3.1052 e-08
		Nazofarengeal	4.6213 e-08	Nazofarengeal	9.4296 e-09
140 MeV	10 MeV	Brain	1.8312 e-10	Brain	3.3480 e-09
		Thyroid	5.2590 e-11	Thyroid	4.0096 e-09
		Nazofarengeal	3.7962 e-08	Nazofarengeal	2.2865 e-07
120 MeV	9 MeV	Brain	2.1590 e-10	Brain	3.0870 e-07
		Thyroid	3.7125 e-11	Thyroid	4.4290 e-10
		Nazofarengeal	3.0596 e-08	Nazofarengeal	5.1355 e-08
110 MeV	8 MeV	Brain	6.1599 e-10	Brain	3.3012 e-09
		Thyroid	3.6500 e-10	Thyroid	7.1230 e-08
		Nazofarengeal	3.0713 e-08	Nazofarengeal	9.3361 e-09
100 MeV	7 MeV	Brain	6.1560 e-10	Brain	4.3000 e-08
		Thyroid	5.2031 e-11	Thyroid	3.9810 e-10

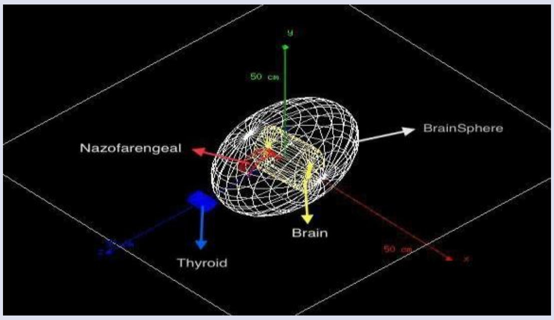

Figure 1. Geometric shape designed with the help of Gate simulation package [8]

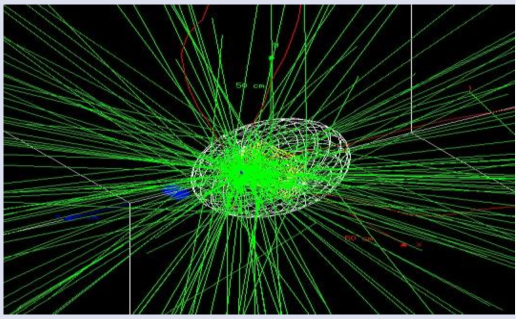

Figure 2. Schematic view of particle beams interacting towards the nasopharynx.

During the carbon-ion and photon simulations, we considered 2D circular shaped mono-energetic beam with 2 mm σ_x and 2 mm σ_y distribution targeting the centre of the phantom assuming the cancer cells are not larger than the beam size. For the physical interactions, built-in physics lists are used together as QGSP_BERT_HP and FTFP_BERT_HP within the Geant4 code. Statistical outputs showed that 1K events correspond to 2.235 minutes of irradiation without initializations in photon simulations while 7.16 minutes of irradiation in carbon simulations.

Results

In this study, we calculated the radiation absorbed by the cancerous mass and neighboring organs with the help of virtual dosimetry called doseActor in GATE. Carbon ion beams with energies of 160 MeV, 140MeV, 120MeV, 110MeV and 100 MeV were delivered to the target mass and five different simulations were performed. We also delivered the photon beams with energies of 10 MeV, 9 MeV, 8 MeV and 7 MeV. Then the dose values are calculated by the voxel algorithms for each simulation from the 2D and 3D absorbed dose distributions formed in the phantom that we designed to use together with the photon and carbon simulation as in Figure 3 and Figure 4.

The amount of doses stored in each organ and the percentage of doses absorbed are given in Table 2. As expected, carbon doses absorbed a very high percentage of the total dose in the target organ, the nasopharynx, while the percentile of doses absorbed by organs outside the area remained below 2%. It has been observed with the data that the organs adjacent to the target organ, the nasopharynx, absorb photon doses close to the nasopharynx or even more. With the data obtained by simulation, the organs outside the target mass were found to be very low compared to the photon doses, and it was listed in Table 2.

Table 2. Doses and percentages received by organs at the end of treatment.

Energy for carbon(MeV)	Energy for photon(MeV)	Carbon DoseActor (Gy)		Percentiles	Photon DoseActor (Gy)		Percentiles
160 MeV	12 MeV	Nazofarengeal	12.8	%20	Nazofarengeal	6.75	%15
		Brain	0.2335	%0.36	Brain	16.4915	%36.65
		Thyroid	0.1192	%0.19	Thyroid	11,90	%26.45
140 MeV	10 MeV	Nazofarengeal	12.8	%20	Nazofarengeal	6.75	%15
		Brain	0.0510	%0.08	Brain	2.3908	%5.31
		Thyroid	0.0149	%0.02	Thyroid	2.8663	%6.36
120 MeV	9 MeV	Nazofarengeal	12.8	%20	Nazofarengeal	6.75	%15
		Brain	0.0730	%0.11	Brain	7.4250	%16.5
		Thyroid	0.0125	%0.02	Thyroid	0.0131	%0.03
110 MeV	8 MeV	Nazofarengeal	12.8	%20	Nazofarengeal	6.75	%15
		Brain	0.2581	%0.40	Brain	0.4342	%0.96
		Thyroid	0.1532	%0.23	Thyroid	9.3685	%20.81
100 MeV	7 MeV	Nazofarengeal	12.8	%20	Nazofarengeal	6.75	%15
		Brain	0.2564	%0.40	Brain	31.1093	%69.13
		Thyroid	0.0216	%0.03	Thyroid	0.2879	%0.64

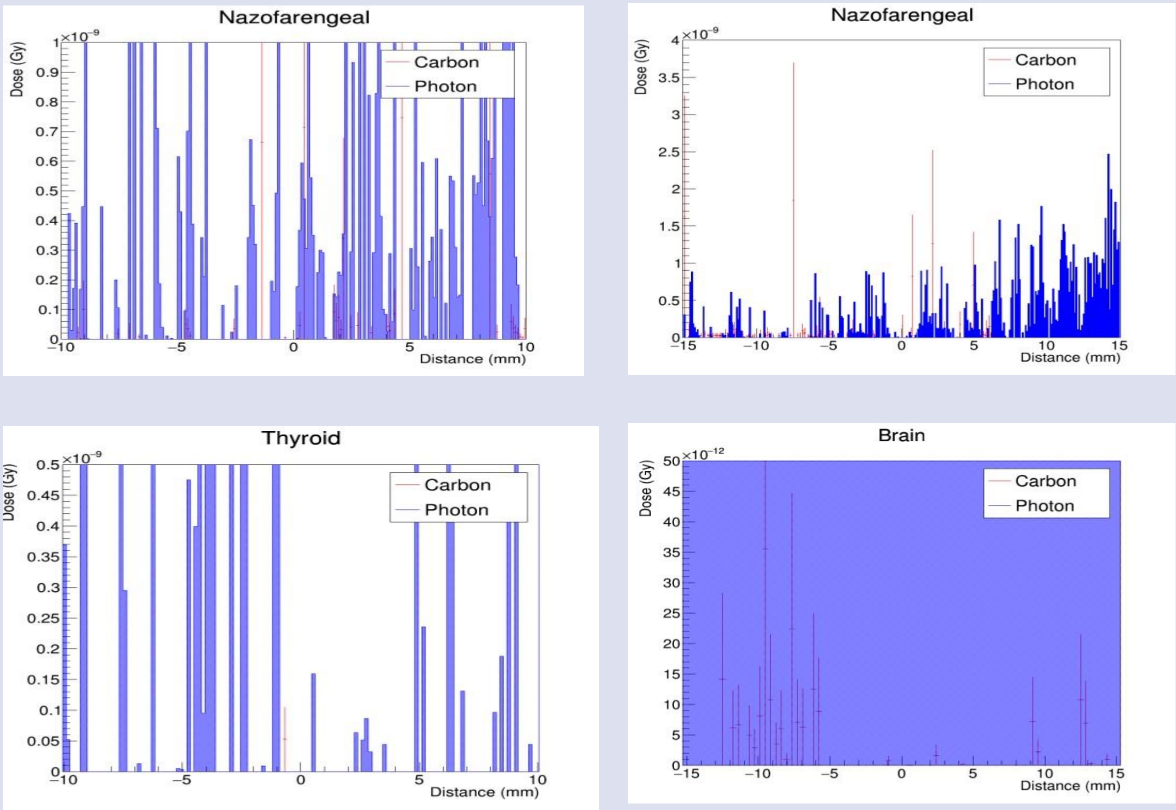

Figure 3. 2D dose distribution plots absorbed in the nasopharynx, thyroid, and brain phantom with applied particle filter. Photon rays with blue color spread over a wider area, therefore a wider area is exposed to the dose. The carbon rays shown with red color spread in a smaller area and create a more dose effect on the target. It is seen that photon rays cause more dose units on both the target audience and critical organs than carbon rays.

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During the simulations, insignificant amounts of secondary particles are observed. While the observed types were only the electrons, positrons and gammas for photon irradiations, a wider spectrum of secondary particle types was observed for carbon irradiations including carbon-12(^{12}C) ion, protons, electrons, gamma, alphas, ...etc. In order the perform a fair comparision in Table-1, we have applied a particle filter excluding all secondary particles. However, that limitation caused a decrease in the total dose for carbon irradiation by the factor 2 approximately.

First results revealed that carbon and photon irradiations have quite separate characteristics due to their different nuclear substructure and interactions. In our simulations, that resulted as : *i.* wider dispersion, *ii.* rather randomized penetration features, *iii.* less dose deliverance for photons through out all the tissues in comparsion with carbon-ion irradiation as summarized in Table 3.

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Table 3. Statistical outputs from photon and carbon simulations of Figure 4 for 10M hit data.

Statistical Parameters	Carbon	Photon
Mean x	1.152	37.8
Mean y	1.6	7.23
Std. Deviation for x (σx)	0.5282	27.68
Std. Deviation for y (σy)	2.022	14.25
Skewness x	11.71	-1.416
Skewness y	-0.004	-0.5

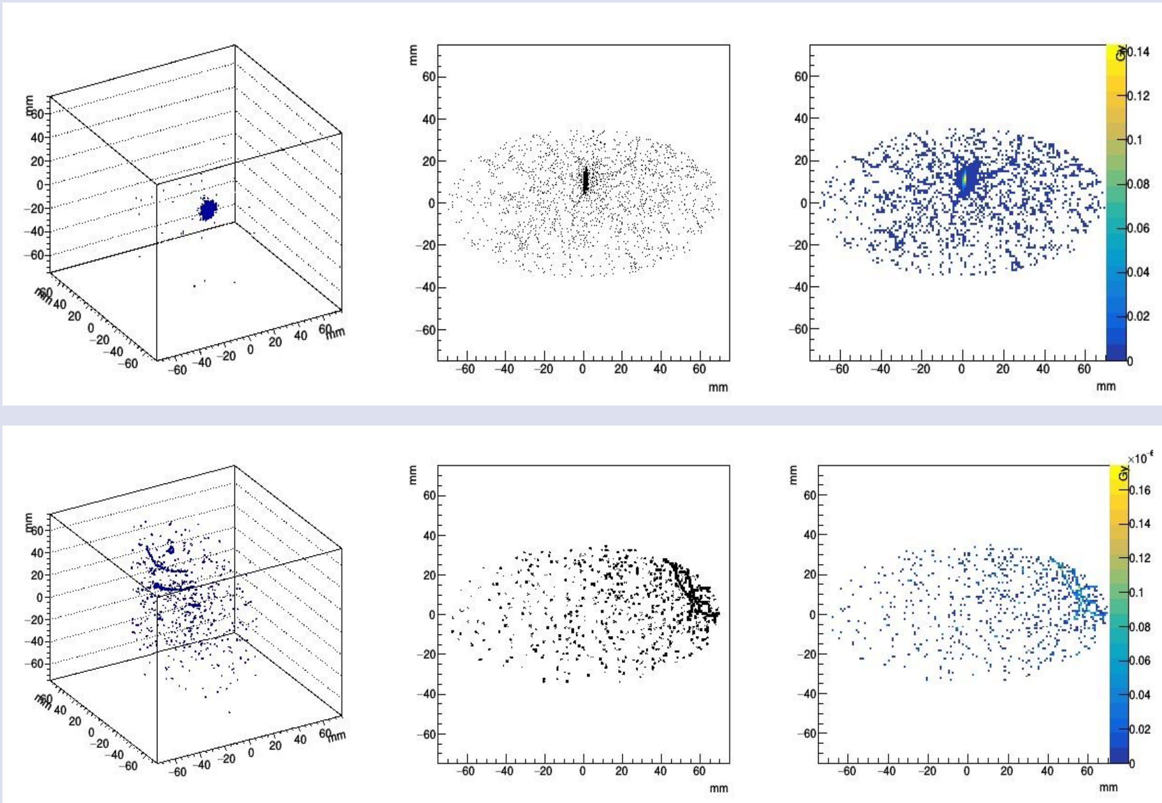

Figure 4. 3D dose distributions of carbon-ion (up) and photon (down) beams absorbed in the brain phantom with 1500 events and more than 10M hits.

Analysis

We applied χ2 -method on dose values as a statistical method in which goodness or inconsistencies between datasets are generally sought.Considering null hypothesis (H0) is "no significant dose difference between Carbon and Photon irradiations"(whereas alternate hypothesis is just the opposite),one can see that the total χ2 values at the order of ~10-7-10-9 corresponds to acceptance region of H0.

Table 4. χ^2 data.

Simulation No.	Nazofarengeal	Brain	Thyroid	Total
1	2.66e-08	4.15e-08	10.03e-08	1.38e-07
2	1.43e-07	2.99e-09	3.89e-09	1.49e-07
3	1.59e-09	3.07e-07	3.72e-10	3.09e-07
4	8.44e-09	2.18e-09	7.04e-08	8.10e-08
5	4.89e-08	4.18e-08	3.01e-10	9.10e-08
Total	2.28e-07	3.95e-07	1.45e-07	

However, one can realise from Table 3 that statistical dispersions based on the standart deviation of photon irradiations are huge by the factor of 55 and 7 of carbon standart deviations for x and y directions, respectively. Also, photon irradiation tends to give negative skewness for each directions. Inconsistent mean values of photon case reveals that the targeting of those particles are just failing due to their natural structure that can penetrate deeply in almost all of the tissues.

Conclusion

Based on our analysis, one can conclude carbon ion radiotherapy is a promising treatment technique that can provide additional benefit to treat cancers that are difficult to treat with traditional methods, with the success achieved in studies on cancer patients in carbon radiotherapy centers in Germany and Japan recently for the treatment of tumors [9,10,11]. Carbon ion radiotherapy has the lowest level of toxicity compared to photon radiotherapy. It has a biological and physical superiority with its high degree of local control and a high degree of general controls. In photon radiotherapy, healthy tissues behind or in front of the targeted tumor are exposed to an overdose. Carbon ions, on the other hand, leave a significant part of their energy at the Bragg peak, and healthy tissues are exposed to the minimum dose due to the low energy accumulated in the entryway before and after the Bragg peak. Therefore, dose adjustment has a great importance in the quality of treatment. Therefore, carbon ion radiotherapy is a more advantageous, safe and effective treatment method. Comprehensive, prospective studies and long-term patient follow-up after treatment are needed to better define the role of CIRT.

Conflicts of interest

The authors declare that they have no conflict of interest.

References

[1] Yaprak G., Evaluation of radiological and biochemical methods in the late term toxicity of carotic artery, thyroid gland and temporal lob after radiotherapy in patients with nasopharyngeal cancer,master thesis,Ministry of Health-Dr.Lutfi Kırdar Kartal Training and Research Hospital, Radiology Oncology Department, (2007).

[2] Mohamad O., Sishc B.J., Saha J., Pompos A., Rahimi A., Story M.D., DavisA., Kim D.W.N., Carbon Ion Radiotherapy:A Review of Clinical Experiences and Preclinical,with an Emphasis on DNA Damage/Repair, DNA Repair Pathways in Cancer, 9 (6) (2017) 66.

[3] Kim J., Park J.M., Wu H.G.,Carbon Ion Therapy: A Review of an Advanced Technology, *Progress in Medical Physics*,31 (3) (2020) 71-80.

[4] Andreo P., Monte Carlo simulations in radiotherapy dosimetry, *Radiation Oncology* , 13 (2018) 121.

[5] Arce P., Bolst D., Bordage M.C., Brown J.M.C., Cirrone P., Cortés-Giraldo M.A., Cutajar D., Cuttone G., Desorgher L., Dondero P., Dotti A., Faddegon B., Fedon C., Guatelli S., Incerti S., Ivanchenko V., Konstantinov D., Kyriakou I., Latyshev G., Le A., Mancini-Terracciano C., Maire M., Mantero A., Novak M., Omachi C., Pandola L., Perales A., Perrot Y., Petringa G., Quesada J.M., Ramos-Méndez J., Romano F., Rosenfeld A.B., Sarmiento L.G., Sakata D., Sasaki T., Sechopoulos I., Simpson E.C., Toshito T., Wright D.H., Report on G4-Med, a Geant4 benchmarking system for medical physics applications developed by the Geant4 Medical Simulation Benchmarking Group, *Medical Physics*, 48 (1) (2021) 19-56.

[6] Amako K, On behalf of the Geant4 Collaboration, *Nuclear Instruments and Methods in Physics Research*, 453 (2000) 455-460.

[7] Karaca M., Chemoradiotherapy in nasopharyngeal cancer, master thesis, Ankara university, School of Medicine Department of Radiation Oncology, (2008).

[8] GATE Documentation, OpenGATE Collaboration, Available at:https://readthedocs.org/projects/gate demo/downloads/pdf/readthedocs/ Retrieved april 19,2022.

[9] Mizoe J., Hasegawa A., Jingu K., Takagi R., Bessyo H., Morikawa T., Tonoki M.,Tsuji H., Kamada T., Tsujii H., Okamoto Y., Organizing Committee for the Working Group for Head Neck Cancer, Results of carbon ion radiotherapy for head and neck cancer, *Gynecologic Oncology Reports*, 103 (1) (2012) 32-37.

[10] Malouff T.D., Mahaian A., Krishnan S., Beltran C., Seneviratne D.S., Trifiletti D.M., Carbon Ion Therapy:A Modern Review of an Emerging Technology, Frontiers in Oncology , 10 (82) (2020).

[11] Ebner D.K., Kamada T., The Emerging Role of Carbon-Ion Radiotherapy, Frontiers in Oncology,6 (140) (2016).