UDC: 539.16.047:615.015.3
Professional paper

DOSIMETRIC COMPARISON OF THREE DIFFERENT EXTERNAL BEAM PARTICLES USING TREATMENT PLANNING SYSTEM MATRAD

Nermine MURADI[1], Gazmend NAFEZI[2], Fadil AJREDINI[1], Bashkim ZIBERI[1]

[1]Department of Physics, Faculty of Natural Sciences and Mathematics, University of Tetova, Ilinden bb, 1200 Tetovo, R.N. Macedonia*
[2] Department of Physics, Faculty of Mathematics and Natural Sciences, University of Prishtina "Hasan Prishtina", 10000, Prishtina, Kosovo
[*]Corresponding Author: e-mail: nermine.muradi@unite.edu.mk

Abstract

In recent decades, valuable clinical experience in particle therapy has been gained worldwide. Along with the development of new technologies, especially for the application of radiation and technologies related to treatment planning, every day there is a wider use of heavy particle and ion radiotherapy in clinical settings to make optimal use of physical and biological properties of protons and heavy ions.
Dose confirmation is called the possibility to concentrate the radiation dose to the tumor while sparing the surrounding normal tissue, which is the aim of radiotherapy. Before the irradiation of each patient, different complex models for treatment planning are used in Radiotherapy. One of these systems is mated, an open-source TPS - Treatment Planning System based on Matlab programming language where optimal plans are calculated in advance, following the prescribed dose to cover tumor volume, while keeping constraints to limit dose for the irradiation of Organs at risk – healthy cells. The software has a dual education and research purpose with the possibility to create treatment plans, calculate and optimize doses for different modalities as for photons, protons and carbon ions. In this work, different treatment plans are created for the TG119 phantom and an exemplary prostate patient case with two beams in the optimal angles of 90° and 270°. The treatment plans are compared for three different modalities of radiation: photons, protons, and carbon ions. The goal was to minimize the dose to healthy cells while delivering 50 Gy to the TG119 case target, and 68 Gy to the target on the prostate case in 30 fractions. From the present study has been concluded that the main advantage of proton and carbon ions compared to photons is the reduction of the integral dose in healthy tissues and the delivery of a higher dose in the tumor side.

Keywords: Treatment planning system, particle RT, cancer treatment simulation, matRad, Prostate cancer.

1. Introduction

The study and use of ionizing radiation began with three important discoveries: X–rays by Wilhelm Röntgen in1895, natural radioactivity by Henri Becquerel in 1896, and radium by Marie and Pierre Curie in 1898 (Podgoršak, 2016). These discoveries were the starting point of the development of radiology, radiotherapy, and medical physics. Radiology and radiotherapy developed very rapidly, both relying on physicists for the routine use of radiation as well as for the development of new techniques and equipment.

H. Sung et al (2021) reported cancer is a significant global health problem that caused nearly 10 million deaths in 2020. Female breast cancer has surpassed lung cancer as the most commonly diagnosed cancer, with an estimated 2.3 million new cases (11.7%), followed by lung (11.4%), colorectal (10.0 %), prostate (7.3%), and stomach (5.6%) cancers. Lung cancer remained the leading cause of cancer death, with an estimated 1.8 million deaths (18%), followed by colorectal (9.4%), liver (8.3%), stomach (7.7%), and female breast (6.9%) cancers. After the discovery of X-rays by Rontgen, immediately their potential benefit was used in medicine to generate images of tissues and structures inside the body, and also used as treatment of cancer with external radiation.

During the last two decades, most of the developments in radiation in medicine have been related to the integration of computers in image acquisition, the development of digital diagnostic imaging techniques, and the incorporation of computers into high-energy delivery technologies.
Today almost half of cancer patients are treated with radiation in many medical centers in different countries of the world. This method of treatment uses a rather complex technology that also includes radiation with acceleration voltages, which reach values up to millions of volts. Therefore, the treatment requires great care, to avoid both mistakes in the treatment of the patient and the exposure of the workers to radiation.
Radiotherapy aims to deliver a high dose of radiation to the tumor cells, and at the same time to keep to a minimum the dose received by the healthy cells near the tumors, i.e. to the neighboring healthy organs, which usually are called Organs at risk (OAR). Planning Target Volume – PTV is a geometric concept that is determined in such a way as to select the appropriate beam arrangements, considering the net effect of all possible geometric variations, to ensure that the prescribed dose is absorbed from the tumor, cancer cells in the surrounding and also eliminate the possibility of an error (ICRU Report 50, 1993).
Different computer programs and platforms are used to calculate the doses received from the tumor as well as from the healthy cells, contouring and all the steps necessary to make a protocol. These platforms do the localization of tumors, the positions of organs in the vicinity and also of the organs that are at greater risk, and then also the way the position of the radiation beams, that presents the treatment plan, which is currently marked TPS or Treatment Planning System.
In the TPS – Treatment planning systems it is now possible to simulate plans with different radiations and to pre-calculate the dose received by the tumors, as well as the dose received by the other surrounding organs. In addition to the dose received by certain volumes using TPS, is it also possible to see the biological efficiency and other important parameters in radiotherapy, which minimizes side effects, and technical errors and reduces toxicity from radiotherapy.
The majority of patients who are treated with radiotherapy are using photon radiation, but in the last decade, the number of patients who are also treated with particle radiation such as protons and heavy ions such as carbon ions, helium ions, etc. has increased every year.
The reason that the number of medical centers that use heavy particle radiation is now increasing is that proton or carbon ion beams enable the prescribed dose to be delivered to the tumor, as well as provide better biological efficiency at the entry point into the body, therefore minimal dose is delivered to the organs at risk compared to photon radiation.
Treatment planning requires a three–dimensional geometric model of accurate patient treatment positioning, along with a three–dimensional coordinate system for accurate transfer to the treatment machine. For these reasons, CT – computed tomography can be considered the most appropriate modality for radiotherapy treatment planning (Mayles, P., Nahum, A. and Rosenwald, 2022).
All these patient anatomical data from different imaging modalities should be combined into a dataset. These data can be transferred to the treatment planning system, where in addition to direction, dose distribution is optimized in advance. The oncologist must decide on the treatment volumes, positioning, and beam parameters, and together with the medical physicist create treatment planning and verify that the created plans cover the target volume and at the same time spare the healthy tissue.

2. Methods

In radiotherapy, the most widely used commercial TPS such as Raysearch (RaySearch Medical Laboratories AB, Stockholm, Sweden), Eclipse (Varian Medical Systems, Palo Alto, CA, USA), XiO (Elekta AB, Stockholm, Sweden), or Syngo RT (Siemens, Erlangen, Germany) employ semi-analytical pencil beams algorithms for dose calculation. Even though these TPS offer a variety and different options, they cannot be used without a license or outside the organization, in most cases outside of the hospital.

This work has used matRad, an open–source TPS based on the Matlab programming language, language (The MathWorks, Inc., Natick, Massachusetts, United States), developed by the German Cancer Center (DKFZ) for IMRT and particle therapy (protons and Carbon ions) (Wieser et al, 2017). Therapeutic dose distributions are calculated by inverse treatment planning. Basic information, such as treatment modality and irradiation geometry, as well as a set of dose objective and constraint functions, are introduced by the user, and the TPS adjusts pencil beam fluence to produce the desired dose distribution.

The matRad has a DICOM (Digital Imaging and Communications in Medicine) import module which allows the conversion of data such as sets of CT and RT structures, into the matRad format. Patient data only needs to be converted once.

The matRad source code includes basic radiation modeling data for photons, protons and carbon ions.

Photons: For the photon dose calculation algorithm, the base data is obtained from the clinically approved engine for photons Dose calculation PDC++ and describes the decomposed lateral scattering kernels and depth dose components as detailed in work of K. Parodi (2012) for a 6 MV linear accelerator for multiple source to surface distances (SSDs). A singular value decomposed pencil beam algorithm is facilitated by matRad to calculate dose deposition

For the charged particles according to the work of Cabal, F.P. A (2020) matRad assumes an active spot scanning dose application and features the conventional dose-to-water-pencil beam algorithm. For every single pencil beam delivered dose is calculated and the product of a 2 – dimensional lateral component and depth component is defined. The source code, for both protons and carbon ions, for calculating physical dose is the same.

Wieser et al (2017) give the parameters for Protons: The calculations run for protons depth dose in water approximately for 114 proton beam energies, starting from 31.72 MeV to 236.1 MeV which correspond to peak positions from (7 mm to 347 mm), Carbon ions: Depth dose profile for integrated carbon ion are based on FLUKA Monte Carlo simulations describing interactions of carbon ions and their fragments with a generic beam line considering a ripple filter of 3 mm, 121 carbon ion depth dose profiles are used from 115.23 MeV to 398.84 MeV depicting peak position from 32mm to 294mm. First step for calculating the dose distribution is the choosing of optimal pencil beans to hit the tumor or the target volume. By means of a ray-tracking method, for each voxel is determined the corresponding WET (Water equivalent thickness). So the energies are determined for each pencil beam, so the spread out Bragg peak will cover the target volume. When the pencil beam grid configuration is ready with the corresponding energy positions, the energy delivered by each beam is calculated in the entire CT 3D matrix (Muradi N, 2023).

Finally, various optimization functions are used to calculate the final beam fluences that ensure an appropriate distribution of the therapeutic dose. An ideal treatment plan should ensure dose distribution in all corresponding voxels in the target volume as close as possible to the prescribed value and at the same time adjust the fluences of the individual bundles to meet the dose requirements of the penalty and constraint functions that are set during the planning of the treatment.

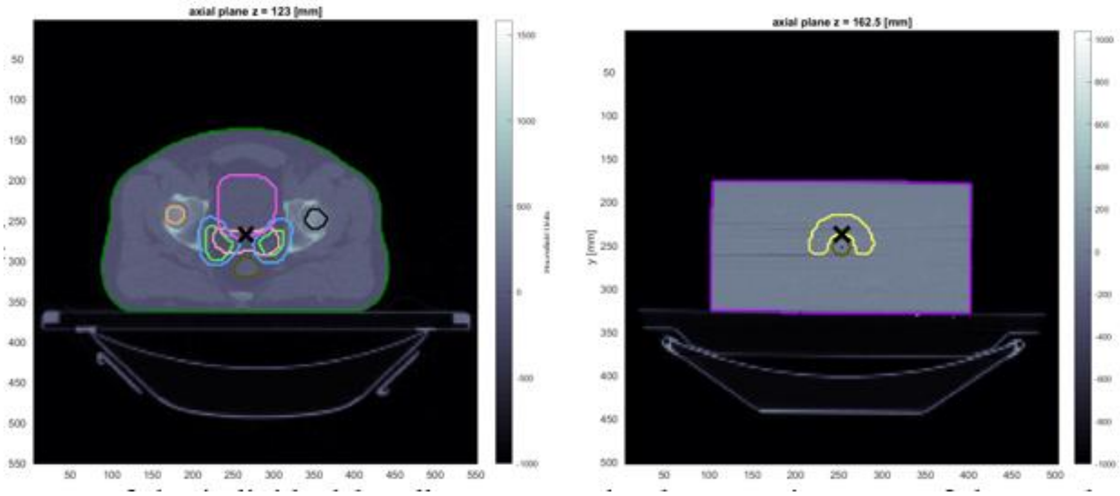


Figure 1. a) Prostate case b) TG119 Phantom case

Different treatment plans were calculated for the TG119 phantom and an exemplary prostate patient case. These patient DICOM data were used from the CORT dataset (Craft D., 2014) as shown in figure 1.

Treatment plans for the two cases are optimized with clinical goals such as the maximum dose to go on the tumor mass and minimal dose, within tolerance doses, at organs at risk. Specifics and other information about the plan specifications and parameters, as well as the dose/volume constraints for the targets and organs at risk (OAR) are summarized in Table 1.

Table 1. Treatment plan parameters used in matRad for dose calculation, giving details about selected gantry angles (GA) in degree, the number of fractions (NF), the volume of interest (VOI) and prescribed dose objectives for optimization in Gray.

Patient case	GA (deg)	NF	VOI	VOI Type	Dose objective	Dose (Gy)
TG119 Phantom	90,270	30	Outer target	Target	Sq. deviation	50
			Core	OAR	Sq. overdosing	25
			Body	OAR	Sq. overdosing	30
Prostate case	90, 270	30	PTV	Target	Sq. deviation	68
			Bladder	OAR	Sq. overdosing	50
			Rectum	OAR	Sq. overdosing	50
			Body	OAR	Sq. overdosing	30

Three plans were created for the prostate case, one treatment plan with photon beams, one plan with proton beams and one plan with carbon ions beam using the same angles 90° and 270°. For the TG119 are created 3 plans, treatment planning with beams in two different angles 90° and 270° with the three different beam particles photon, proton and carbon ions.

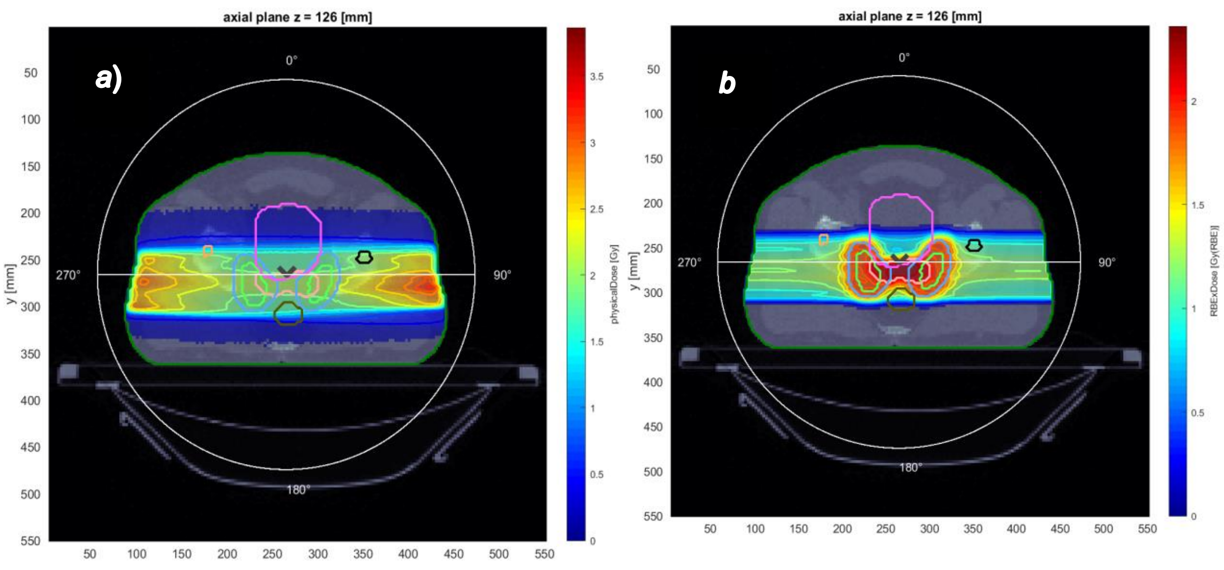
3. Results

For the prostate case are created three treatment planning, first one with photon beam, second one with proton beam and third one with carbon ion beam in two different angles 90° and 270°.

Table 2. Calculated mean dose for the PTV and some OAR for the prostate case for 30 fractions

	Mean dose (Gy)		
VOI (structure color countour) / Modality	Photons	Protons	Carbon Ions
Rectum (dark green)	36.24	26.52	25.62
Penile bulb (orange)	4.95	2.46	1.95
Lymph Nodes (light green)	56.58	56.91	56.94
Rt femoral head (light orange)	48.66	19.16	14.97
Prostate bed (dark blue)	67.17	67.92	67.95
PTV_68 (light pink)	66.69	67.74	67.77
PTV_56 (light blue)	56.94	57.24	57.27
Bladder (pink)	30.54	23.76	23.37
Body (green)	10.41	5.56	4.83

In the table 2 are shown the mean dose calculated for the prostate case when is irradiated in two different angles with different beam modality particles.
The dose distribution visually is shown in Figure 2, a) photon beam, b) proton beam, and c) carbon ion beam, while graphically it is shown in DVH – Dose volume histograms 1, 2, and 3, for photon beam, proton beam, and carbon ion beam respectively. Colors of the contours corresponding to the VOI structures are shown also in the table. In the histograms, the vertical axis shows volume in percentages, while the horizontal axis reads the received dose from the volume of interest. The curves for each volume are presented in the same colors as in the contours. Should be noted that the doses presented in the DVH obtained by mated are doses only for one fraction. For the total dose absorbed by each volume, the value of the mean dose is multiplied by the number of fractions that were used in the planning, which in this case is 30 the NF.
From the average dose values that are obtained, and also from the dose distribution fgures, it can be seen that the treatment plan with proton and carbon ion beams deliver most of the dose to the tumor and in the same time deliver minimur or much smaller dose to OAR comparing ith the treatment plans with photon beams. Therefore, treament planning with protons or carbon



ion beams are more than enough to achieve the goals of optimal plans even when we are using less number of radiation beam.

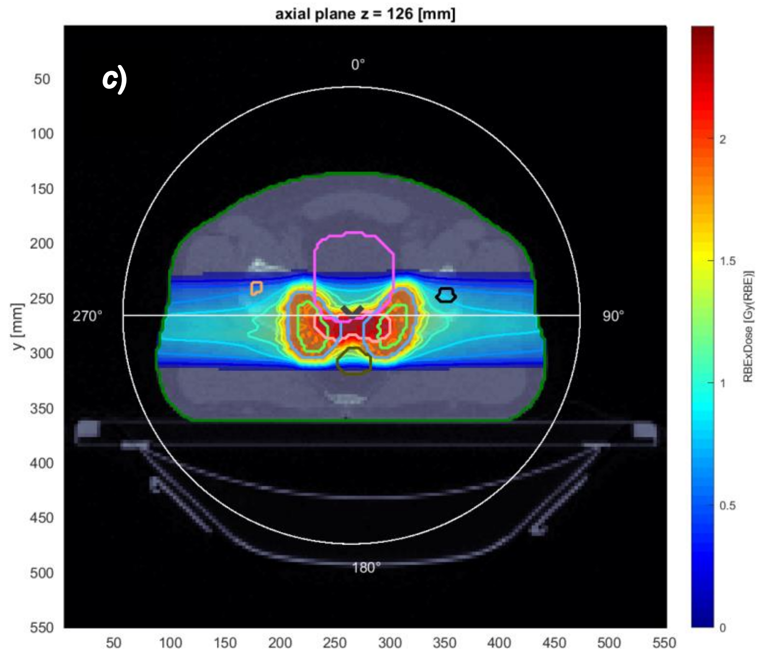


Figure 2. Dose distribution at oristate case: a) Treatment plan with photon beams in two angles b) Treatment plan with proton beams in two angles c) Treatment plan with carbon ion beams in two angles

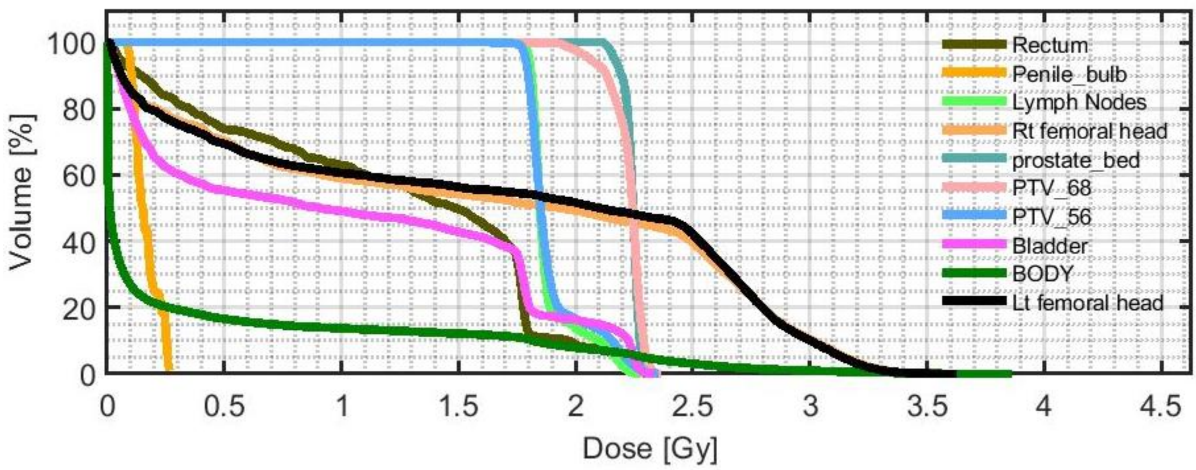


Figure 3. Dose volume histogram DVH for radiation of prostate case with photon beam in two angles 90° and 270°

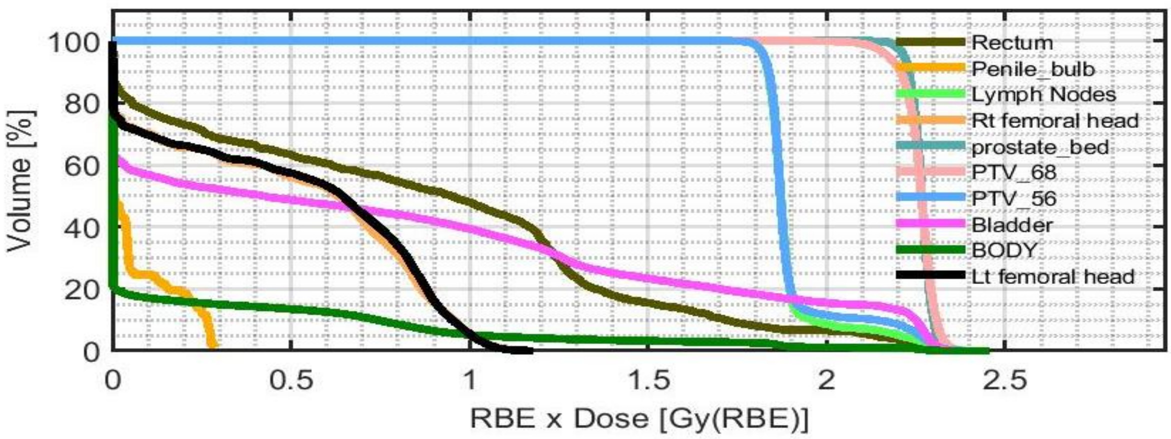


Figure 4. Dose – volume histogram DVH for radiation of prostate case with proton beam in two angles 90° and 270°

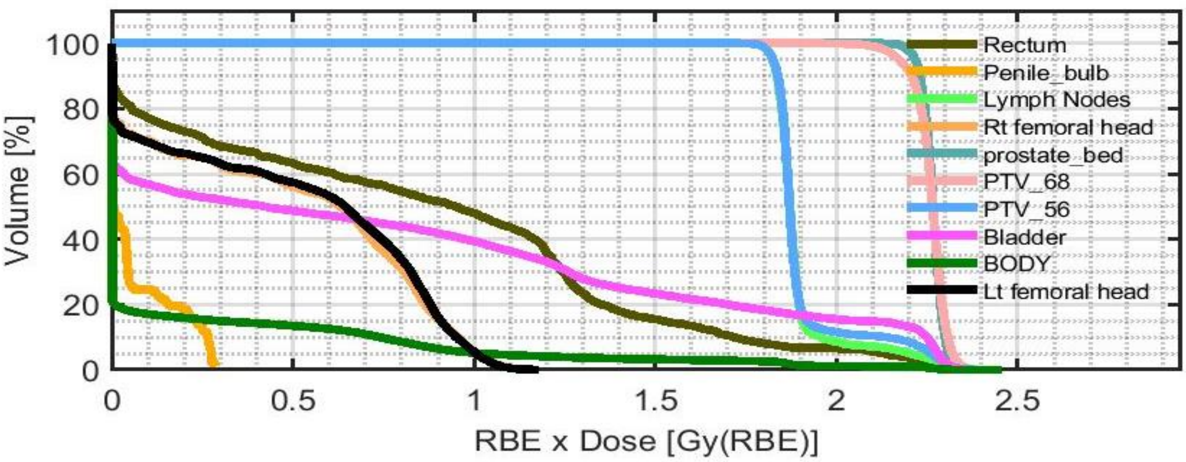


Figure 5. Dose – volume histogram DVH for radiation of prostate case with carbon ions beam in two angles 90° and 270°

In the table 3 are shown the mean dose calculated for the TG119 phantom case when is irradiated in two different angles with different beam modality particles.

Table 3. Calculated mean dose for the PTV and some OAR for the TG119 Phantom case for 30 fractions.

	Mean dose (Gy)		
VOI (structure color countour) / Modality	Photons	Protons	Carbon Ions
Core	34.58	17.48	19.34
Outer target	46.41	49.96	49.97
Body	5.72	3.06	2.51

The dose distribution visually is shown in figure 6, a) photon beam, b) proton beam and c) carbon ion beam, while graphically it is shown in DVH – Dose volume histograms 7, 8 and 9, for photon beam, proton beam and carbon ion beam respectively.

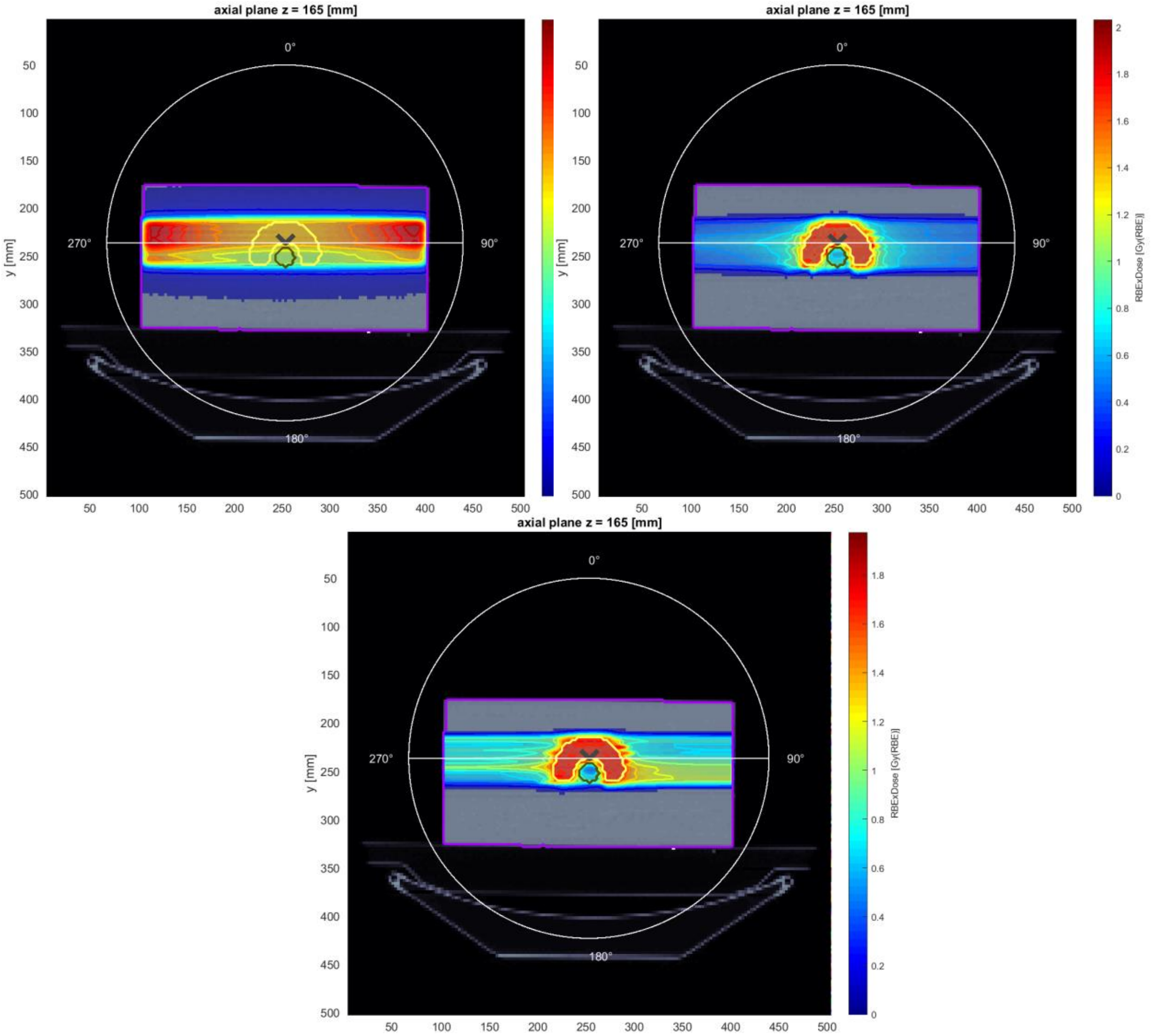


Figure 6. Dose distribution at TG119 phantom case: a) Treatment plan with photon beams in two angles b) Treatment plan with proton beams in two angles and *c) Treatment plan with carbon ion beams in two angles*

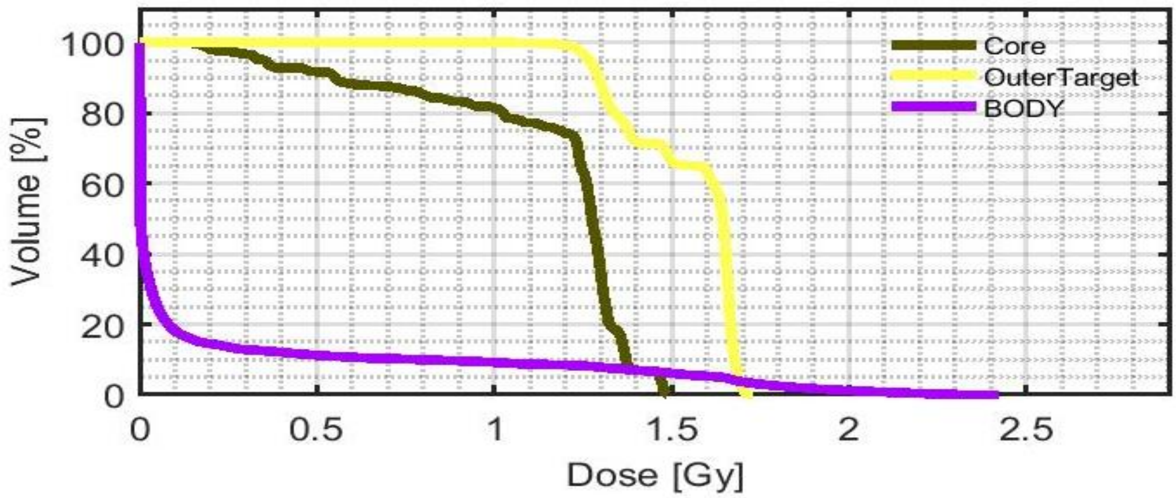


Figure 7. Dose – volume histogram DVH for radiation of TG119 phantom case with carbon ions beam in two angles 90° and 270°

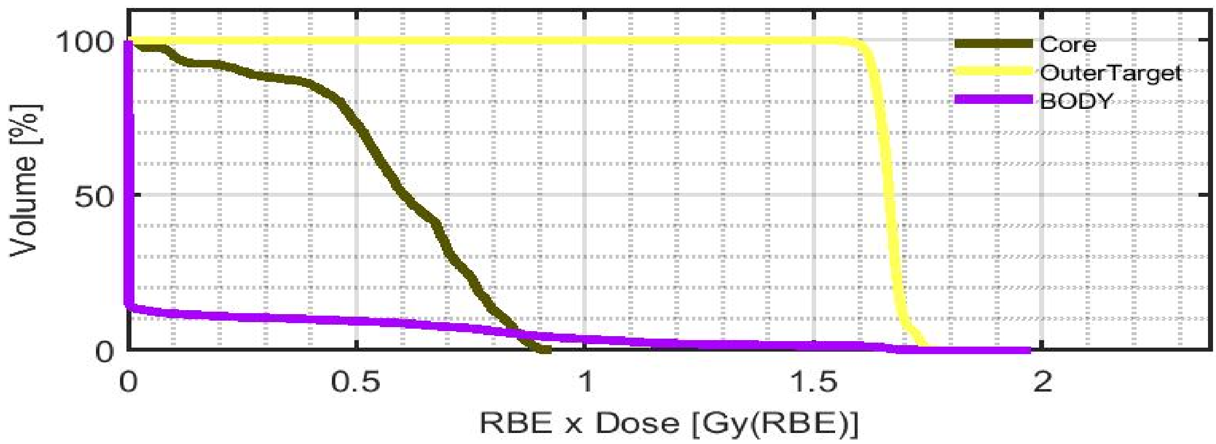


Figure 8. Dose – volume histogram DVH for radiation of TG119 phantom case with carbon ions beam in two angles 90° and 270°

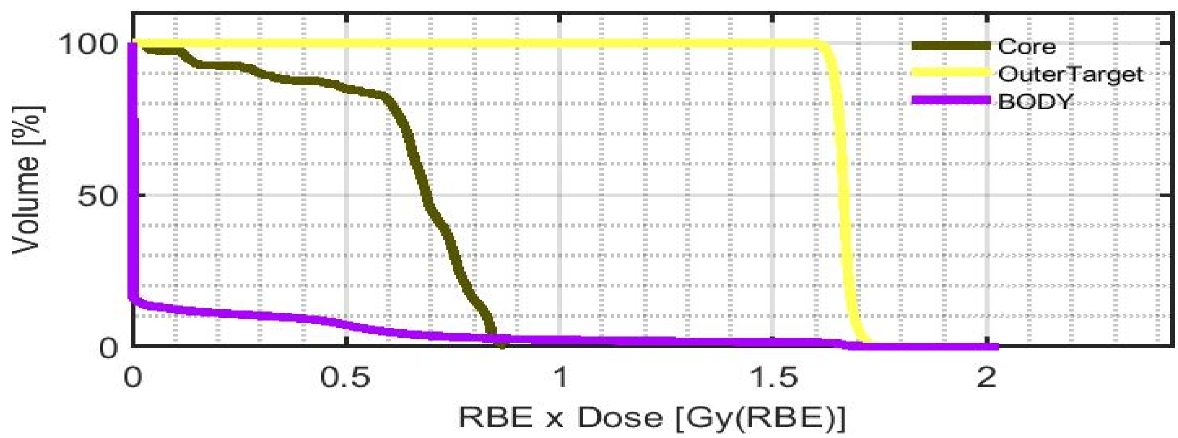


Figure 9. Dose – volume histogram DVH for radiation of TG119 phantom case with carbon ions beam in two angles 90° and 270°

4. Discussion and conclusions

Different treatment plans created with the same number of beams and optimal angles were compared between different radiation modes such as photon beam, proton beam, and carbon ion beam, to see which mode gives the highest dose to tumor mass, i.e. cancerous cell and at the same time to spare and deliver the minimum possible dose to the organs at risk. Additionally, in a visual way in the figures with dose distribution obtained in the software matRad, the plans are quantitatively compared in terms of the mean dose in the main OARs, and also compared for the PTV coverage in percent in both cases, in the prostate case and TG119 phantom case.
Mean dose reduction (Marc, L. et al, 2021) (MDR – mean dose reduction) achieved with proton beam plans as well as carbon ion plans are presented as relative reductions compared to the treatment planning created by simulation photon beam radiation as the mode treatment reference:

$$MDR = \frac{D_X^{VOI} - D_Y^{VOI}}{D_{fotone}^{VOI}} \tag{1}$$

where D_X^{VOI} represent mean dose to volume of interest (VOI) for a given treatment modality X compared to another treatment modality Y.
First, treatment planning with photon beams was compared with treatment planning with proton beams and carbon ion beams. In all cases, it has been observed that proton beam and carbon beam treatment planning provide more conformal dose distribution in the target area and cover the target volume, but at the same time provide protection and dose reduction in risk structures and normal tissue.
In the prostate case with two parallel beams of radiation, it can be seen that photons coming in opposite directions do not deliver most of the dose to the target, and that dose is delivered to the surrounding tissues (Figure 2a). Proton beam and carbon ion beam, deposit most of the dose to the tumor (Figure 2b and 2c respectively), and it appears in the figure that the dose receiver by the organs at risk and surrounding healthy cells is very small. So, proton and carbon ion beams reduce the dose absorbed by the healthy cells, without compromising the covering dose of the target.
Mean dose reduction MDR comparing the treatment planning with photons and that with protons has been achieved at 26.82% for the rectum, 22.2% for the bladder, 46.57 % for the body, 50.30 for the penile bulb, and 60.62% for RT femoral head. While the mean dose received by PTV compared, it can be seen that with photon beam is delivered 98% of the prescribed dose to the PTV, and with protons beam is delivered 99.6% of the prescribed dose to the PTV.
In comparison, photon beam radiation and carbon ion beam radiation have been seen that with carbon ion radiation the dose is reduced to OAR, so the MDR is 29.3% for the rectum, 60.62% for the penile bulb, 69.24% for RT femoral head, 23.4% for bladder and 46.57% for body. Meanwhile, the carbon ion beam delivers 99.6% of the prescribed dose to the PTV.
While comparing proton and carbon ion the difference is light, but yet carbon ion reduces the dose to the OAR, instead of using proton beam.
The reason that treatment planning with protons and carbon ions gives lower doses in OAR and higher doses in PTV compared to photons is that the photons lose most of their energy on the way before the radiation reaches the target, which is also seen in the DVH figure 3, that organs at risk for larger volume in percent receive higher doses, while PTV receives lower dose in high percentage compared to proton and carbon ion radiation presented in the DVH figure 4 and figure 5, respectively.

Protons and carbon ions, when they penetrate the tissue, reach the maximum energy deposition the Bragg peak and this causes the dose distribution to be localized, so it is given to the target and a very low dose is lost on the way or is deposited in the organs at risk.

This dose deposition in target now with the intensity modulation is even easier to control the depth where the Bragg peak occurs and this leads to greater homogeneity of the dose distribution which can also be seen in the graph that the dose deposition for the maximum volume gives the maximum dose homogeneous, that immediately after deposition there is an immediate drop in the curve indicating minimal dose in normal tissue.

In the second case, the TG119 phantom case, similar results have been obtained.

Mean dose reduction MDR comparing the treatment planning with photons and with protons has been achieved 49.43% for the core and 46.43% for the body. While the mean dose received by PTV i.e. outer target compared, it can be seen that with photon beam is delivered 92% of the prescribed dose to the PTV, and with protons beam is delivered 99.91% of the prescribed dose to the PTV.

In comparison, photon beam radiation and carbon ion beam radiation, has been seen that with carbon ion radiation the dose is reduced to OAR, so the MDR is 44.06% for the core and 56.09% for the body. The dose distributed by the photon beam can be also seen in figure 6a), where the reddish is the higher dose and is not delivered at tumor, but is left during the path to arrive at the tumor. In Figures 6b and 6c can be seen that most of the dose is given at target, and a very low dose, with blue color shown, is given to the healthy cell. Meanwhile, the carbon ion beam delivers 99.94% of the prescribed dose to the PTV.

Comparing the proton beam and carbon ion beam delivered dose, it can be seen that with protons less dose is given to the core, but carbon ion beam reduces the dose to the body. The difference in the values is very light.

In this work, only the mean doses received from the PTV and OAR have been investigated. In these analyses, it can be concluded that Treatment planning systems are very important in radiotherapy, especially in Particle Radiotherapy planning. Although treatment planning with proton and carbon ion radiation gives much better results than photon radiation, the centers that would enable these therapies are very expensive in terms of finances, and they also need a staff trained in many different fields to work, first in research laboratories and then in clinical application. Perhaps in the future, the combination of radiation or more extensive research will enable the selection of tumors for which type of cancer would be necessary to be treated with radiation with protons or carbon ions. Sometimes some tumors are radio-resistant to photons and as such it would be a perfect technique to use heavy particle radiation, proton, carbon ion beam, or maybe other ions.

In recent decades, valuable clinical experience in charged particle therapy has been gained worldwide. Along with the development of new technologies, especially for the application of radiation and technologies related to treatment planning, every day there is a wider application of heavy particle and ion radiotherapy in clinical settings to make optimal use of the physical and biological properties of protons and heavy ions.

References

[1] Cabal, F.P. *A dose calculation platform for treatment planning towards magnetic resonance image guided particle therapy*. Doctoral thesis. Medical University of Vienna, 2020

[2] D. Craft, M. Bangert, T. Long, D. Papp, and J. Unkelbach, 2014. Shared data for intensity modulated radiation therapy (IMRT) optimization research: the CORT dataset. GigaScience, 3(1):37

[3] International Commission on Radiation Units and Measurements, (ICRU), 1993. Prescribing, recording, and reporting photon beam therapy. International Commission on Radiation Units and Measurements, ICRU Report 50, ICRU, Bethesda.

[4] Marc, L. et al., 2021 Combined proton–photon treatment for breast cancer. *Physics in Medicine and Biology*, **66** (23).

[5] Mayles, P., Nahum, A. and Rosenwald, J.C., 2022 *Handbook of radiotherapy physics. Theory and practice.* 2nd ed, vol.1 and vol.2 . SHBA: Taylor & Francis Group.
[6] Muradi N., 2023, *Simulation of treatment planning with radiation at breast cancer and comparison with real cases.* Master thesis, University of Tetova
[7] Podgoršak, E.B. (2016) *Radiation Physics for Medical Physicists* . 3rd ed. Switzerland : Springer International Publishing
[8] 2] H. Sung, J. Ferlay, R. L. Siegel and F. Bray, 2021, "Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries", CA: Cancer J. Clinicians, vol. 71, no. 3, pp. 209-249
[9] Wieser, H.-P., et al, 2017.: Development of the open-source dose calculation and optimization toolkit matRad. Medical Physics. 44 Issue 6. 2017, 2556 – 2568.