Comparison of physical dose distributions of a carbon ion radiotherapy treatment plan obtained from matRad treatment planning system and PHITS Monte Carlo simulation

การเปรียบเทียบการกระจายปริมาณรังสีกายภาพจากแผนการรักษาด้วยการฉายลำอนุภาคคาร์บอนที่ได้จากโปรแกรมวางแผนการรักษา matRad และโปรแกรมมอนติคาร์โล PHITS

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Abstract

Background: In carbon ion radiotherapy (CIRT) treatment planning, dose prescription is done in term of relative biological effectiveness (RBE)-weighted dose in the unit of Gy(RBE). There are two major biophysical models used in CIRT: the microdosimetric kinetic model (MKM) and the local effect model (LEM). For the same prescribed dose, both RBE models can lead to different physical dose distributions in the patient. Therefore, it is not possible to directly compare clinical data using different RBE models. In the past, the conversion factors between MKM and LEM prescribed doses were evaluated using two treatment plans calculated based on both models. However, direct conversion from a treatment plan to the other based on the underlying biophysical model has not been performed. The latter approach requires the information of the physical dose distribution from a treatment plan and the resulting voxel-by-voxel energy spectra of primary and secondary charged particles, which can be obtained by Monte Carlo simulation.

Objectives: To compare physical dose distributions obtained by Particle and Heavy Ion Transport code System (PHITS) Monte Carlo simulation and matRad treatment planning system, to be used for the conversion of CIRT prescribed doses between the LEM and the MKM.

Material and methods: A virtual water phantom with the size of 50 x 35 x 50 cm3 was generated. The target was defined as a spherical volume with a radius of 3 cm, centered at 7 cm water-equivalent depth from the entrance surface of the phantom. Treatment planning of the target was performed with an open-source treatment planning system matRad with the prescribed dose of 4.3 Gy(RBE). The parameters from matRad including number, position, energy and width of carbon ion beam spots were used to define sources in PHITS. Physical dose distributions from matRad and PHITS were compared using the gamma analysis method.

Results: The differences between the Bragg peak positions from matRad and PHITS for monoenergetic carbon ion beams were approximately 1 mm. By shifting the water phantom 1 mm upstream of the beam entrance in the Monte Carlo simulation, the gamma passing rates at 3%/3mm between both sets of physical dose distributions were averagely 99% and 90% in the target region and all regions, respectively.

Conclusion: The combination of matRad and PHITS can be applied to evaluate the conversion factors between LEM and MKM treatment plans, especially in the target region.

Keywords: Carbon ion radiotherapy, treatment planning, Monte Carlo simulation, matRad, PHITS

บทคัดย่อ

หลักการและเหตุผล: การรักษามะเร็งด้วยการฉายลำอนุภาคคาร์บอนใช้ปริมาณรังสีถ่วงน้ำหนักด้วยผลทางชีววิทยาสัมพัทธ์ (RBE-weighted dose) ในการวางแผนการรักษา แบบจำลองที่นิยมใช้สำหรับคำนวณค่า RBE ของลำอนุภาคคาร์บอน ได้แก่ แบบจำลอง microdosimetric kinetic model (MKM) และ local effect model (LEM) อย่างไรก็ดี การกำหนดปริมาณรังสีจากแบบจำลองทั้งสองชนิดนี้อาจทำให้การกระจายปริมาณรังสีกายภาพในผู้ป่วยต่างกัน จึงไม่สามารถเปรียบเทียบผลการรักษาได้โดยตรง ในอดีตการแปลง RBE-weighted dose ระหว่างแบบจำลอง LEM และ MKM ทำโดยการเปรียบเทียบแผนการรักษาที่ได้จากแบบจำลองทั้งสองชนิดนี้ แต่ยังไม่เคยมีการแปลงโดยตรงจากแผนการรักษาหนึ่งไปเป็นอีกแผนการรักษาโดยใช้แบบจำลองชีวฟิสิกส์พื้นฐาน การดำเนินการดังกล่าวต้องใช้ข้อมูลการกระจายปริมาณรังสีกายภาพจากแผนการรักษาแบบใดแบบหนึ่ง และสเปกตรัมพลังงานของอนุภาคปฐมภูมิและทุติยภูมิในแต่ละ voxel ซึ่งคำนวณได้จากโปรแกรมมอนติคาร์โล

วัตถุประสงค์: เพื่อเปรียบเทียบการกระจายปริมาณรังสีกายภาพของลำอนุภาคคาร์บอนที่ได้จากโปรแกรมมอนติคาร์โล PHITS และโปรแกรมวางแผนการรักษา matRad สำหรับใช้ในการแปลง RBE-weighted dose ระหว่างแบบจำลอง LEM และ MKM

วัสดุและวิธีการ: ภาพหุ่นจำลองน้ำเสมือนจริงขนาด 50 x 35 x 50 ลูกบาศก์เมตร ถูกนำมาใช้ในการวางแผนการรักษา โดยกำหนดให้ทรงกลมขนาดรัศมี 3 เซนติเมตร ซึ่งมีจุดศูนย์กลางอยู่ที่ความลึก 7 เซนติเมตร ในน้ำเป็นก้อนมะเร็งเป้าหมาย การวางแผนการรักษาใช้โปรแกรม matRad โดยกำหนด RBE-weighted dose เท่ากับ 4.3 Gy(RBE) ข้อมูลที่ได้จาก matRad ประกอบด้วย จำนวน ตำแหน่ง พลังงาน และขนาดของลำอนุภาคคาร์บอนถูกนำไปใช้กำหนดต้นกำเนิดรังสีใน PHITS จากนั้นปริมาณรังสีกายภาพที่คำนวณได้จาก matRad และ PHITS ถูกนำมาเปรียบเทียบโดยใช้เทคนิคการวิเคราะห์ค่าแกมมา

ผลการศึกษา: แบรกก์พีคของอนุภาคคาร์บอนที่ได้จาก matRad และ PHITS อยู่ในตำแหน่งต่างกันประมาณ 1 มิลลิเมตร การเลื่อนหุ่นจำลองน้ำขึ้นไปทางต้นกำเนิดรังสี 1 มิลลิเมตร ใน PHITS ทำให้การกระจายปริมาณรังสีกายภาพที่ได้จาก matRad และPHITS ผ่านข้อกำหนด 3%/3 มิลลิเมตร ของการวิเคราะห์ค่าแกมมา เฉลี่ย 99% และ 90% ในก้อนมะเร็งเป้าหมาย และทุกบริเวณ ตามลำดับ

ข้อสรุป: สามารถใช้โปรแกรม matRad ร่วมกับ PHITS ในการประเมินค่าการแปลง RBE-weighted dose ระหว่างแบบจำลอง LEM และ MKM ได้ โดยเฉพาะอย่างยิ่งในก้อนมะเร็งเป้าหมาย

คำสำคัญ: การฉายลำอนุภาคคาร์บอน, การวางแผนการรักษา, การจำลองมอนติคาร์โล, matRad, PHITS

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Introduction

Carbon ion radiotherapy (CIRT) is of increasing interest worldwide because of the outstanding characteristics of carbon ions for cancer treatment. The high linear energy transfer (LET) of carbon ions provides a high relative biological effectiveness (RBE) and a low oxygen enhancement ratio (OER). Furthermore, the sharp dose falloff behind the Bragg peak region and relatively small lateral scattering help to spare

normal tissues from radiation dose when delivering a high dose to the target. For CIRT treatment planning, dose prescription is done in terms of RBE-weighted dose in the unit of Gy(RBE), considering the biological effect of the radiation beam that is associated with the physical dose and the radiation quality.

To date, two biophysical models for the calculation of RBE-weighted dose have been used clinically in active scanning CIRT, namely, the microdosimetric kinetic model (MKM)[1, 2] and the local effect model (LEM)[3, 4]. Both models require the distribution of the radiation quality of the mixed radiation field as an input, namely, the lineal energy distribution and the specific energy distribution, respectively[5]. The MKM is used for treatment planning at the National Institute of Radiological Sciences (NIRS) in Japan, while the LEM is used by European particle therapy centers such as the Heidelberg Ion Beam Therapy center (HIT) in Germany and the National Center for Oncological Hadrontherapy (CNAO) in Italy. For the same prescribed dose, both RBE models can lead to different physical dose distributions delivered to the patient[6]. Therefore, it is not possible to directly compare clinical data from different institutes that use different RBE-weighted dose models.

Recently, conversion between MKM and LEM prescribed doses was performed under the condition that the physical dose distribution and the radiation quality in both plans were as close as possible[7]. The conversion factors from MKM to LEM prescribed dose have been evaluated for targets with simple geometries[7] and patient cases[8]. It was found that for the simple geometries, the LEM I prescribed dose was higher than the MKM prescribed dose. In addition, the size, shape, depth and dose level of the target affected the conversion factor[7]. For patient cases, using different RBE models brought about different isodose volumes, which had an impact on surrounding normal tissue doses. For example, for prostate cancer, the MKM doses for targets and organs at risk (OARs) ranging from 0.18 Gy(RBE) to 4.55 Gy(RBE) per fraction were converted to the LEM doses with the conversion factors ranging from 2.72 to 1.06, respectively[8].

Until now, the conversion factors between MKM and LEM prescribed dose were evaluated using two parallel treatment plans calculated based on the MKM and the LEM, respectively. This approach is only feasible when the available TPSs use the MKM and the LEM for dose prescription. A direct conversion of CIRT prescribed dose using the underlying biophysical models has not been performed. The latter approach is particularly useful when the available treatment planning system (TPS) uses either one of the RBE models and the Monte Carlo simulation is used for characterizing the radiation quality of the mixed radiation field. In that case, both computational tools need to produce the same physical dose distribution for the same set of carbon ion pencil beams.

The aim of this study was to compare the physical dose distributions obtained from matRad treatment planning system (TPS)[9] and Particle and Heavy Ion Transport code System (PHITS).

MatRad is an open-source multimodality treatment planning system based on the LEM IV[10], while PHITS is capable of computing lineal energy distributions required for MKM biological dose calculation. Treatment planning for a spherical target was performed in matRad, providing a set of carbon ion pencil beams that was used as the input of the Monte Carlo simulation. The physical dose distributions from matRad and PHITS were compared by using the gamma analysis method[11].

Materials and methods

Target definition

A CT (computed tomography) image dataset of a virtual water phantom with the size of 50 x 35 x 50 cm3 was generated using RayStation treatment planning system version 8b (RaySearch Laboratories AB, Stockholm, Sweden). The CT dataset consisted of 260 slices, each of which had 260 x 185 voxels. The pixel spacing was 2 mm and the slice thickness was 2 mm. The target was defined as a spherical volume with a radius of 3 cm, centered at 7 cm water-equivalent depth from the beam entrance surface of the phantom. This spherical volume represented a head and neck tumor target similar to the study of Fossati et al[7].

Treatment planning

MatRad was used for active scanning CIRT treatment planning in this study. MatRad is based on generic treatment machines, completely written in the numerical programming language MATLAB (MathWorks, Inc, MA, USA), and supports DICOM data import for dose calculation and optimization[9].In matRad, the physical dose is calculated by the pencil beam algorithm, which scales the depth dose distribution according to the water-equivalent path length of tissues and calculates the lateral profile according to the Gaussian distribution.

DICOM-RT files of the virtual water phantom including CT images and contoured structures were imported into matRad. Users can manually specify the resolution of CT images. In this study, we used the original CT resolution of 2 mm.

The parameters used for treatment optimization are shown in **Table 1**. For particle therapy, matRad can perform only the multifield optimization, i.e. intensity modulated particle therapy. The details of the optimization technique has been described by Wieser et al[9]. The isocenter was automatically selected by matRad as the center of the target volume. Users can select the optimization parameters to suit their specific cases. In this work, we selected the bixel width (lateral spot spacing), the objective function and the penalty following Burigo et al [12], who made a treatment plan on a water phantom similar to this work. After optimization, the physical dose distribution and the weight for each pencil beam spot were stored in the output variable called “resultGUI”, while the number, position and energy of each spot were stored in the variable called “stf.ray”. The optimization resulted in 2771 carbon ion beam spots with 28 different energies ranging from 133.78 to 223.96 MeV/n (MeV/nucleon). The total number of carbon ions was 2.2×109 for this treatment plan. In addition, the parameters of

the generic machine such as the initial full width at half maximum (FWHM) of carbon ion beams at each energy was obtained from the database used by the program.

Table 1. Treatment planning parameters used in matRad for dose calculation and optimization.

Bixel width or lateral spot spacing (mm)	5
Gantry angle	0
Couch angle	0
Radiation mode	Carbon
Isocenter (mm) (The Left, Posterior, Superior (LPS) coordinate system for matRad)	x = 262.1 y = 81.60 z = 262.4
Source to axis distance (mm)	10000
Dose (Gy(RBE))	4.3
Number of fractions	1
Type of optimization	LEMIV_RBE
Volume of interest name	Sphere 6 cm
Volume of interest type	Target
Objective function	Squared Deviation
Penalty (p)	800

Monte Carlo simulation

PHITS is a general-purpose Monte Carlo particle transport simulation code. It can be used to simulate almost all particles, including neutrons, protons, heavy ions, photons and electrons[13]and is freely available to users within specific terms and conditions. The code has been applied for the calculation of RBE-weighted dose for heavy ion radiotherapy[13]. The calculations of physical dose, biological dose and RBEs for heavy ion radiotherapy by using PHITS coupled with the MKM have been reported[14].

The same CT image dataset as used for the matRad treatment planning was imported to PHITS by using DICOM2PHITS program[15]. At first, the coordinates used by matRad and PHITS were different. Therefore, a transformation (rotation and displacement) of CT images was required. A graphical display of the simulated objects was used to verify the consistence

between the coordinates used by PHITS and matRad. The outputs and parameters from matRad including number (or weight), position, energy and FWHM of each carbon ion beam spot were used to define multiple sources in the Monte Carlo simulation. The physical dose distribution was calculated by PHITS using the same CT resolution as that used in the matRad treatment planning system. The schematic of the Monte Carlo model defined in PHITS is shown in **Figure 1**. In total, 1.09×108 histories were simulated yielding the standard deviations of the calculated physical doses of lower than 5%. The computing time using 32 cores of Intel Xeon E5-2600 v4 at 3.2 GHz was approximately 18 hours.

The result of the Monte Carlo simulation was given in the unit of the calculated quantity (in this case, physical dose in Gy) per source particle. The total number of carbon ions used for the treatment plan (2.2×109 particles) was multiplied to the Monte Carlo simulated results to give the absolute values of physical doses.

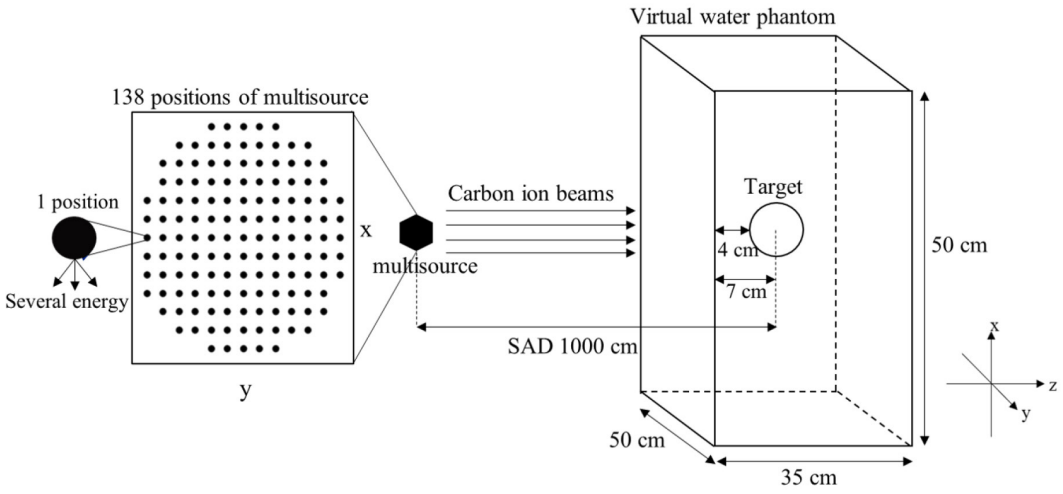

Figure 1. The schematic of the Monte Carlo model used in this study.

Comparison of dose distributions

The physical dose distributions obtained from matRad and PHITS were compared using the gamma analysis method. Both sets of physical dose distributions were compared slice-by-slice using 2D gamma analysis with the criteria of 3% dose difference and 3 mm distance to agreement (3%/3mm) using an in-house developed MATLAB program for the target and for all regions except voxels that received dose less than 10% of the maximum dose.

Results

Figure 2 shows the central-axis depth distributions of physical dose, RBE-weighted dose and RBE obtained from matRad for the prescribed dose of 4.3 Gy(RBE) in the target region. The physical dose decreased with depth as the RBE increased to yield a nearly constant RBE-weighted dose in the target region.

From a preliminary study, we found that the physical depth dose distributions of the treatment plan calculated by matRad and PHITS were slightly displaced at depths from 5 to 11 cm, corresponding to the Bragg peak positions of carbon ion beams in the energy range from 133.78 to 223.96 MeV/n. Therefore, in this work we first compared the physical depth dose distributions of monoenergetic carbon ion beams obtained from both programs in **Figure 3**.

As shown in **Figure 3**, the Bragg peaks from the PHITS simulation were 1-1.9 mm deeper than those from matRad for the carbon ion energies ranging from 133.78 to 192.43 MeV/n (examples in **Figure 3a** and **3b**), while good agreement of the Bragg peak positions was observed for the carbon ion energies ranging from 195.18 to 223.96 MeV/n (examples in **Figure 3c** and **3d**). These results led to a universal shift the virtual water phantom by 1 mm towards the beam source in the PHITS simulation. Consequently, the Bragg peak positions obtained from the PHITS

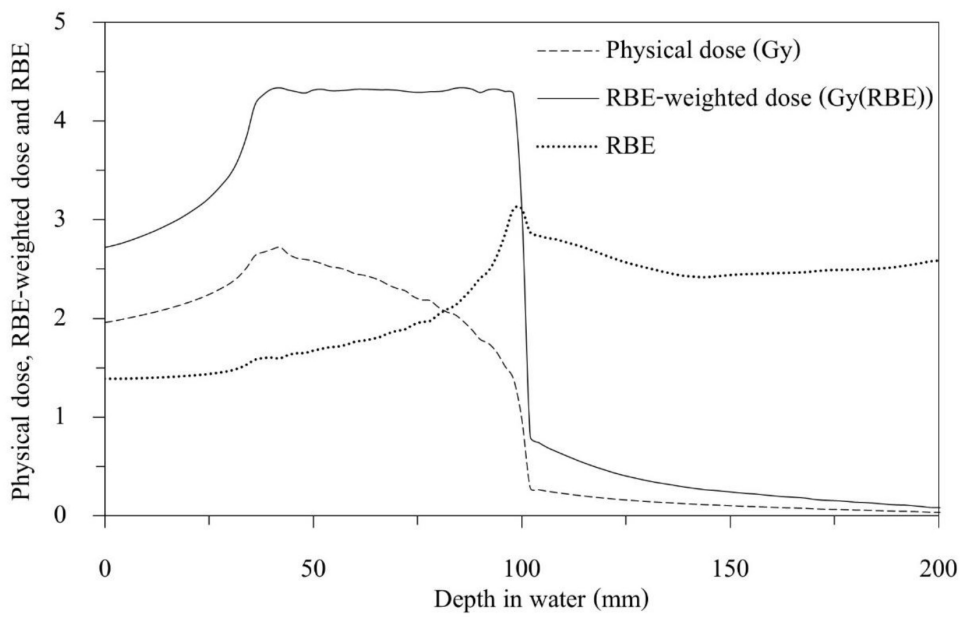

Figure 2. The central-axis depth distributions of physical dose (Gy), RBE-weighted dose (Gy(RBE)) and RBE obtained from matRad.

simulation were shifted towards the beam source and, in general, had better agreement with the Bragg peak positions obtained from matRad. It is to note that with 2 mm resolution of the CT images, the steep part and the position of the Bragg peaks may be distorted, especially when using the pencil beam algorithm as used in matRad. Thus, for some carbon ion energies, the Bragg peaks may appear to be wider than the nominal Bragg peaks, e.g., for 150.71 and 195.18 MeV/n energies using matRad, as shown in **Figure 3a** and **3c**.

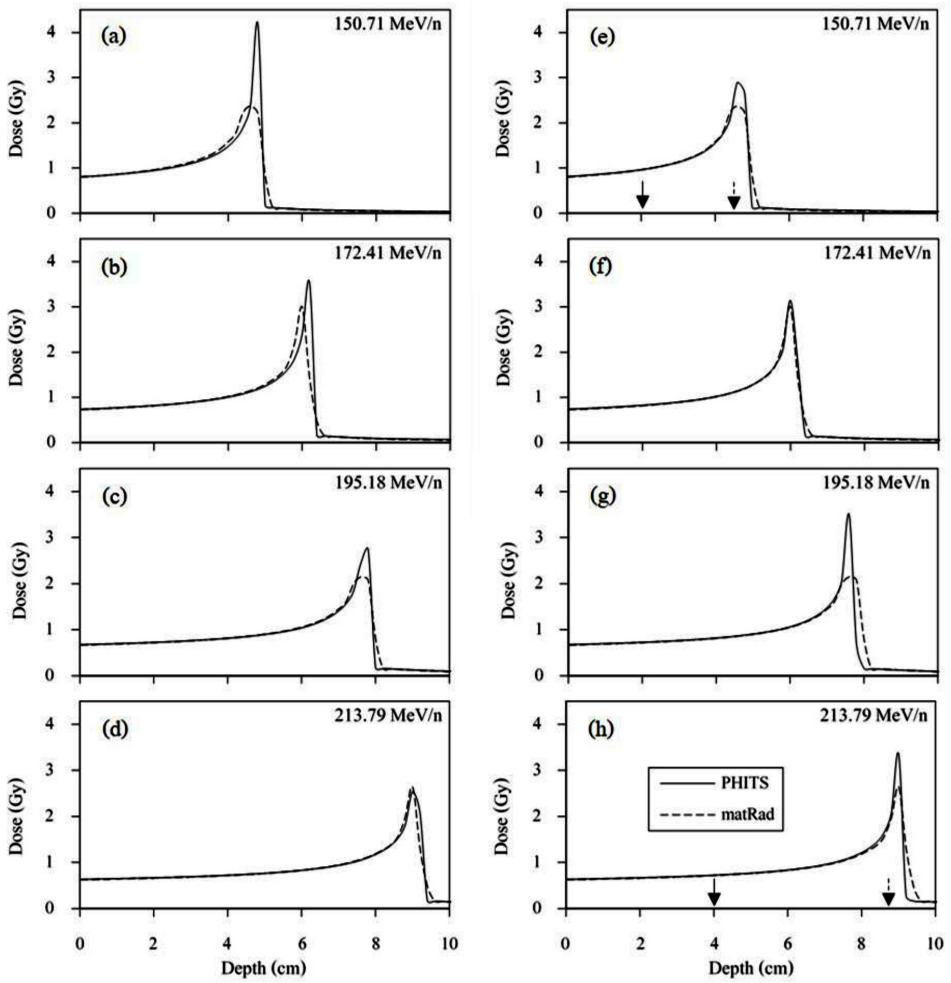

Figure 3. The physical depth dose distributions of monoenergetic carbon ion beams (106 particles) without (a, b,c and d) and with (e, f, g and h) 1 mm shift of the water phantom towards the beam source in the Monte Carlo simulation. The dashed lines and the solid lines were calculated by matRad and PHITS, respectively. The solid arrows and the dashed arrows indicated the depths at the entrance region and near the Bragg peak, respectively, that were used for the comparison of lateral profiles as shown in Figure 4.

Figure 4 shows that the lateral profiles for 150.71 and 213.79 MeV/n carbon ions obtained from matRad and PHITS. Both calculations agreed well at the plateau region for both carbon ion energies (Figure 4a and 4b) and near the Bragg peak for 213.79 MeV/n carbon ions **(Figure 4d)**. However, the central axis doses for 150.71 MeV/n carbon ions from matRad and PHITS differed by 17%, due to the difference of the depth doses near the Bragg peaks for this carbon ion energy, as shown in **Figure 3a.**

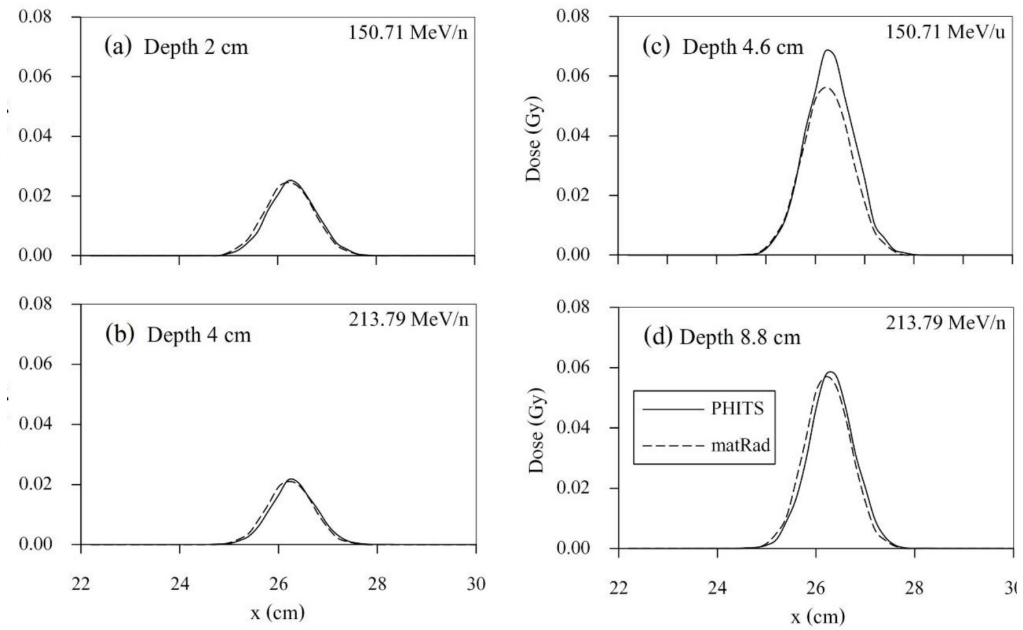

Figure 4. The lateral profile obtained from matRad and PHITS at the entrance region (a and b) and near the Bragg peak (c and d) for carbon ion energies 150.71 and 213.79 MeV/n (10^6 particles).

Figure 5 shows the examples of the physical dose distributions of the treatment plan calculated by matRad and PHITS. In general, both calculations yielded similar results with dose differences at some depths, including 4.6, 5.2, 7.8 and 9.6 cm, which corresponded to the Bragg peak positions of carbon ions with 150.71, 160.26, 195.18 and 218.91 MeV/n energies, respectively. For these carbon ion energies, matRad gave relatively different doses at the Bragg peaks than those obtained by PHITS, as shown in Figure 3e and 3g. The passing rates from the 2D gamma analysis (3%/3mm) for each slice ranged from 43% to 100% (averagely 90%) for all regions and from 94% to 100% (averagely 99.00%) for the target region. The slices with the relatively low passing rates were those outside the target region.

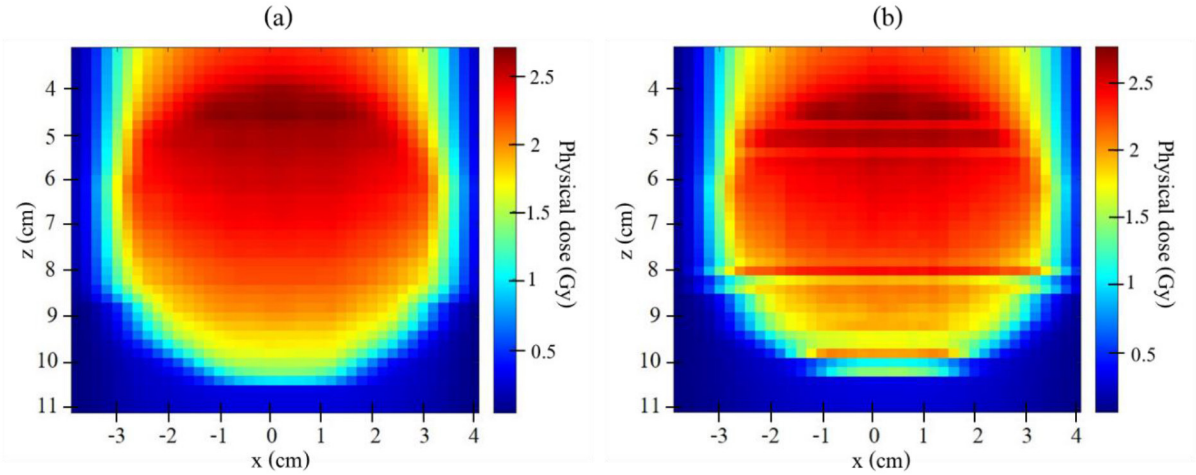

Figure 5. The physical dose distributions obtained from matRad (a) and PHITS (b) at the central-axis slice of the target. The comparison for this CT slice yielded the gamma passing rates (3%/3mm) of 98.6%.

Discussion

In this study, we simulated the active scanning CIRT treatment plan with the PHITS Monte Carlo simulation by using the information (position, energy, FWHM and weight) of the carbon ion pencil beams obtained from matRad treatment planning system. From the comparison of the physical depth dose distributions of monoenergetic carbon ion beams shown in **Figure 3**, it was found that the Bragg peak positions of monoenergetic carbon ion beams obtained from matRad and PHITS were displaced by about 1 mm for some carbon ion energies. For this reason, the water phantom in the Monte Carlo simulation was shifted by 1 mm toward the beam source. In general, the shift resulted in reasonable agreement between Bragg peak positions obtained by both programs. However, for high energy carbon ion beams (> 192.43 MeV/n) the shift of the water phantom caused a larger, but still considered to be minimal, displacement of the Bragg peaks, as shown in **Figure 3g** and **h.**

MatRad and PHITS gave slightly different physical dose distributions, which could be caused by several reasons. One of the reasons could be that both programs used the different methods for calculating physical doses. MatRad uses an analytical method based on the pencil beam algorithm[16], while PHITS uses the Monte Carlo method to mimic the random process of radiation interactions. In the pencil beam algrithm used in matRad, physical depth dose distributions of monoenergetic carbon ion beams were pre-calculated by FLUKA Monte Carlo simulation code[9]and used as the input of matRad for 3D dose calculation[17]. The uses of different MC simulation codes, namely, PHITS and

FLUKA, could yield some differences in the physical depth dose distribution[18]. Nevertheless, the 2D gamma analysis yielded the gamma passing rates at 3%/3mm of 43-100% with the average passing rate of 90% for all regions, while the passing rates for the target region reached 94-100% (averagely 99%). The reduction of gamma passing rates outside the target could arise from the fact that the Monte Carlo simulation took into account particle scattering explicitly while the pencil beam algorithm used by matRad considered particle scattering only approximately. Nevertheless, the results of this work indicated that the physical dose distributions for the treatment plan obtained from matRad and PHITS were in good agreement, especially in the target region. Therefore, the application of both programs to study the conversion between LEM and MKM prescribed dose should be feasible.

Conclusions

This study compared the physical dose distributions of an active scanning CIRT treatment plan obtained from matRad treatment planning system and PHITS Monte Carlo simulation. It was found that by shifting the water phantom by 1 mm towards the beam source in the Monte Carlo simulation, both computational programs could provide the physical dose distributions that were in good agreement with averagely 99% and 90% gamma passing rates at 3%/3mm in the target region and in all regions, respectively. Therefore, the combination of matRad and PHITS can be applied to evaluate the conversion factors between LEM and MKM RBE-weighted doses. In that case, matRad can be used to calculate the LEM treatment plan, while PHITS will be used to determine the lineal energy distribution specific to that treatment plan to be used for calculating the MKM RBE-weighted dose distribution.

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