Evaluation of proton and carbon ion beam models in TReatment Planning for Particles 4D (TRiP4D) referring to a commercial treatment planning system

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Abstract

Purpose: To investigate the accuracy of the treatment planning system (TPS) TRiP4D in reproducing doses computed by the clinically used TPS SyngoRT.
Methods: Proton and carbon ion beam models in TRiP4D were converted from SyngoRT. Cubic plans with different depths in a water-tank phantom (WP) and previously treated and experimentally verified patient plans from SyngoRT were recalculated in TRiP4D. The target mean dose deviation ($\Delta D_{mean,T}$) and global gamma index (2%–2 mm for the absorbed dose and 3%–3mm for the RBE-weighted dose with 10% threshold) were evaluated.
Results: The carbon and proton absorbed dose gamma passing rates (γ-PRs) were $\geq$99.93% and $\Delta D_{mean,T}$ smaller than -0.22%. On average, the RBE-weighted dose $D_{mean,T}$ was -1.26% lower for TRiP4D than SyngoRT for cubic plans. In TRiP4D, the faster analytical 'low dose approximation' (Krämer, 2006) was used, while SyngoRT used a stochastic implementation (Krämer, 2000). The average $\Delta D_{mean,T}$ could be reduced to -0.59% when applying the same biological effect calculation algorithm. However, the dose recalculation time increased by a factor of 79–477. $\Delta D_{mean,T}$ variation up to -2.27% and -2.79% was observed for carbon absorbed and RBE-weighted doses in patient plans. The γ-PRs were $\geq$93.92% and $\geq$91.83% for patient plans, except for one proton beam with a range shifter (γ-PR of 64.19%).
Conclusion: The absorbed dose between TRiP4D and SyngoRT were identical for both proton and carbon ion plans in the WP. Compared to SyngoRT, TRiP4D underestimated the target RBE-weighted dose; however more efficient in RBE-weighted dose calculation. Large variation for proton beam with range shifter was observed. TRiP4D will be used to evaluate doses delivered to moving targets. Uncertainties inherent to the 4D-dose reconstruction calculation are expected to be significantly larger than the dose errors reported here. For this reason, the residual differences between TRiP4D and SyngoRT observed in this study are considered acceptable.
The study was approved by the Institutional Research Board of Shanghai Proton and Heavy Ion Center (approval number SPHIC-MP-2020-04, RS).

Keywords: particle radiotherapy; treatment planning; dosimetric comparison

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1 Introduction

The treatment planning system (TPS) plays a vital role in the development of Charged particle therapy (CPT) [1]. TPSs for charged particle beams such as SyngoRT [2–4], XiO [5], Raystation [6], Eclipse [7], Pinnacle3 [8], and several in-house developed TPSs [9,10] were generally utilized in CPT facilities under clinical operation.

SyngoRT Planning treatment planning system (Siemens AG Healthcare, Germany) is a commercially available TPS for pencil beam scanning (PBS) proton and carbon ions. It is used in clinical operations at Heidelberg Ion Beam Therapy Center (HIT), Marburg Ion Beam Therapy Center (MIT), Centro Nazionale Adroterapia Oncologica (CNAO), and Shanghai Proton and Heavy Ion Center (SPHIC). SyngoRT uses pencil beam-based dose calculation algorithm. It calculates the RBE-weighted dose by applying a fixed RBE of 1.1 for proton beams and utilizes the Local Effect Model I (LEM I) [11] for calculating the variable RBE of carbon ion beams. Clinical application of SyngoRT commenced in 2009 [12].

Development and clinical application of advanced methods such as robust calculation and evaluation in TPS are essential for achieving accurate CPT. Currently, SyngoRT has some limitations regarding advanced dose optimization and dose evaluation abilities ,for instance, the lack of robust planning and evaluation. A particular need resides in infrastructure for planning CPT of moving targets, which is still a great challenge, especially for scanning particle beams [13]. Advanced approaches for handling target motion at the time of irradiation in CPT, such as rescanning, 4D treatment planning, tumor tracking, and 4D dose reconstruction, are not available in SyngoRT.

TRiP98 (TReatment planning for Particles) has served as the standard treatment planning system for the GSI (Gesellschaft für Schwerionenforschung, Darmstadt, Germany) radiotherapy project from 1997 to 2008 [11,14]. It covered the optimization of the physical absorbed dose and RBE-weighted dose for carbon ion beams during the clinical operation of GSI carbon ion treatment [15]. Since then, TRiP has been continuously expanded as a research TPS. The current version of TRiP98, denoted TRiP4D, provides full modeling of 4D dose calculation, including calculating the interplay effects for regular and irregular patient motion and a framework for delivered dose computation considering the actual beam delivery and patient motion data available for the fraction irradiation. TRiP4D also features several options in 4D treatment planning [16], such as the capability to evaluate the robustness of 4D treatment plans [17], to handle 4D-Internal Target Volume (ITV)-based intensity modulated particle therapy (IMPT) for multiple targets [18], robust 4D-optimization [19], to synchronously deliver the beam with the motion of a moving planning target volume (PTV) using a multi-phase 4D delivery approach [20].

TRiP4D holds the potential for evaluating the robustness of previously treated patient plans generated by SyngoRT, reconstruction of 4D doses for moving target plans, and developing and implementing motion compensation strategies. Although physical and biological dose calculation algorithms in SyngoRT were initially based mainly on TRiP98 [21], the vendor has proprietary rights to the final software product. The algorithms' internal details are not disclosed. Therefore, a dosimetric comparison study is necessary to fully validate the functions in TRiP4D for evaluating treatment plans generated by SyngoRT. This work recalculated simple cubic dose distributions in water and different patient plans generated by SyngoRT with TRiP4D. Dose distributions calculated by the two TPSs were compared.

2 Methods

2.1 Creating the beam model for TRiP4D

Before the comparison studies, it was necessary to create the beam model for TRiP4D. The beam data for carbon with a 3 mm ripple filter (RiFi), carbon with 6 mm RiFi, and proton pencil beams from SyngoRT (VC13C, SIEMENS, Germany) at the Shanghai Proton and Heavy Ion Center (SPHIC) were converted into a TRiP4D beam model. The beam data in SyngoRT was commissioned in 2014 before the clinical operation of SPHIC, and it has been used clinically since then

The integrated depth dose distributions (IDDs) of 290 and 291 energies for proton and carbon ion beams in SyngoRT were identical in the TRiP4D beam database.

The SyngoRT in-air spot size data includes seven planes relative to the isocenter plane: −112.6, −80, −40, 0, +20, +40, and +80 cm. In total, four focus levels for proton beams and five for carbon ion beams are available for each energy. The in-air spot size at the isocenter plane was imported to the TRiP4D database since TRiP4D currently only considers the beam spot in air at the isocenter plane.

SyngoRT and TRiP4D use a double-Gaussian scattering model to describe the lateral fluence distribution [4]. SyngoRT beam data provides double Gaussian σ values of 8 energies located at different water equivalent depths relative to the Bragg peak. The σ values were interpolated to 290 and 291 energies for proton and carbon ion beams, respectively, for TRiP4D, which requires the input of double Gaussian σ values for each particle energy.

RBE-weighted dose calculation for carbon ion plans is based on the local effect model I (LEM I) [22]. Fragment spectra are necessary for the RBE-weighted dose calculation of carbon ion beams. SyngoRT and TRiP4D share the same fragment spectrum file format, so the fragment spectrum

files were identical for the two TPSs. The conventional constant RBE of 1.1 was used for proton plans in SyngoRT and TRiP4D.

The Hounsfield unit (HU) to stopping power calibration curve, virtual source position, and water equivalent thickness of nozzle devices were identical for the two TPSs.

2.2 Cubic targets plans in water-tank phantom

Five cubic targets with a distal beam range of 7, 11, 13, 19, and 27 cm (R7, R11, R13, R19, R27) and a side length of 6 cm (S6) were optimized on a Water Tank Phantom (WP). SyngoRT generated single beam plans with a prescribed dose of 2 Gy and 4 Gy(RBE) for proton and carbon ion, respectively. In addition, carbon beam plans with prescribed doses of 3.0, 3.5, and 4.5 Gy(RBE) were also generated for the R11S6 cubic target. The DICOM RT plan file of all plans was imported into TRiP4D. The plans were recalculated on the same WP. For RBE-weighted dose calculation, two methods are implemented in TRiP4D. The "stochastic implementation" which samples particle data randomly by Monte Carlo techniques (hereafter referred to as Classic) [11] and the analytical "low dose approximation" (hereafter referred to as Low-dose) [23]. The latter improved the calculation efficiency. SyngoRT used a method analogous to the former, though the exact implementation is not disclosed. Both methods were applied for the RBE-weighted dose recalculation for cubic target carbon plans in TRiP4D. Other dose calculation parameters were kept consistent. For example, the dose sampling grid was set to 3 mm or 2 mm according to the original SyngoRT plan; the dose cut-off value 3.5σ of spot size was used.

2.3 Patient cases

The patient study included 29 clinical treatment plans from 22 previously treated thoracic patients (lung cancer and trachea adenocarcinoma). The median target volume was 159.2 cm^3 (range 15.8–522.6 cm^3). Of these, 22 were carbon, and 7 were proton plans. The prescribed dose ranged from 3 Gy(RBE) to 7 Gy(RBE) for carbon plans and 2.2 Gy (RBE) for proton plans. Each plan had 2–4 beams. In total, 56 and 20 beams were included for carbon ion and proton plans. Of the carbon ion beams, 21 used a 3 mm ripple filter (RiFi), and 35 used a 6 mm RiFi. The beams' median water equivalent depth was 83.7 mm (43.4–133.2 mm). One proton and two carbon beams used a range shifter (RS). Detailed information is reported in Table A.1 in Appendix A. The DICOM RT plan file of all plans was imported into TRiP4D. The plan was recalculated on the same patient CT image sets. The RBE-weighted dose for patient carbon plans was recalculated using the LEM-I RBE model with the Low-dose algorithm.

2.4 Data analysis

The dose distribution of each beam between the two TPSs was compared using gamma analysis (criteria: physical dose 2 mm/2% of global max, carbon RBE-weighted dose 3 mm/3% of global max, 10% threshold). The difference $\Delta D_x = (D_x\ [TRiP4D] - D_x\ [SyngoRT])/D_x\ [SyngoRT]$ was computed with x representing: (1) The target mean dose ($\Delta D_{mean,T}$) and D95% (ΔD95%) for each plan, (2) Lungs mean dose ($\Delta D_{mean,Lung}$) of each plan (for patient plans only). In addition, a comparison of one-dimension (1D) depth profiles (for cubic carbon plans only). For carbon plans, if applicable, comparisons were performed for both physical absorbed and biological RBE-weighted doses.

3 Results

3.1 Cubic plans

The $\Delta D_{mean,\ T,}$ and gamma passing rates (γ-PRs) for cubic plans are summarized in Fig. 1. For proton plans, the largest $\Delta D_{mean,\ T}$ was −0.22%. For absorbed dose distribution of carbon plans, the maximum $\Delta D_{mean,\ T}$ was found for the R7S6-4Gy(RBE) cubic plan, which was −0.44%. The γ-PRs were always ≥99.93% for both proton and carbon absorbed doses.

For the RBE-weighted dose distribution of carbon plans using the Low-dose method, the $\Delta D_{mean,\ T}$ varies from −1.91% to −0.83%. The ΔD95% varies from −2.36% to −1.02%. The lowest γ-PR was 94.32% (R27S6-4Gy(RBE) plan). The calculated target mean RBE-weighted dose was lower for TRiP4D than SyngoRT, with an average deviation of –1.26%.

The target mean RBE-weighted dose deviation was −0.83%, −1.15%, −1.20%, −1.50%, and −1.91% for R7S6, R11S6, R13S6, R19S6, and R27S6 4Gy(RBE) plans, respectively, indicating a decreasing trend with the increase of the beam range. The shallow located cubic, R7S6 showed the smallest target mean biological dose deviation.

The target mean RBE-weighted dose deviation was −1.28%, −1.14%, −1.15%, and −1.06% for R11S6 3, 3.5, 4, and 4.5 Gy(RBE) plans, respectively. No clear trend as a function of the prescribed doses was observed.

A comparison of RBE-weighted dose deviations between the Classic and Low-dose methods is shown in Fig. 2. For the RBE-weighted dose distribution of carbon plans using the Classic method, the average $\Delta D_{mean,\ T}$ was reduced to −0.59%. The maximum $\Delta D_{mean,\ T}$, and ΔD95% were −0.72% and −0.94%. The γ-PR was never below 99.22%. The recalculation time for the Classic method varied from 1626.5 s to 9977.4 s, while for the Low-dose method, it ranged between 13.9 s and 30.4 s. The dose recalculation time increased by a factor 79–477 with the Classic RBE dose calculation strategy.

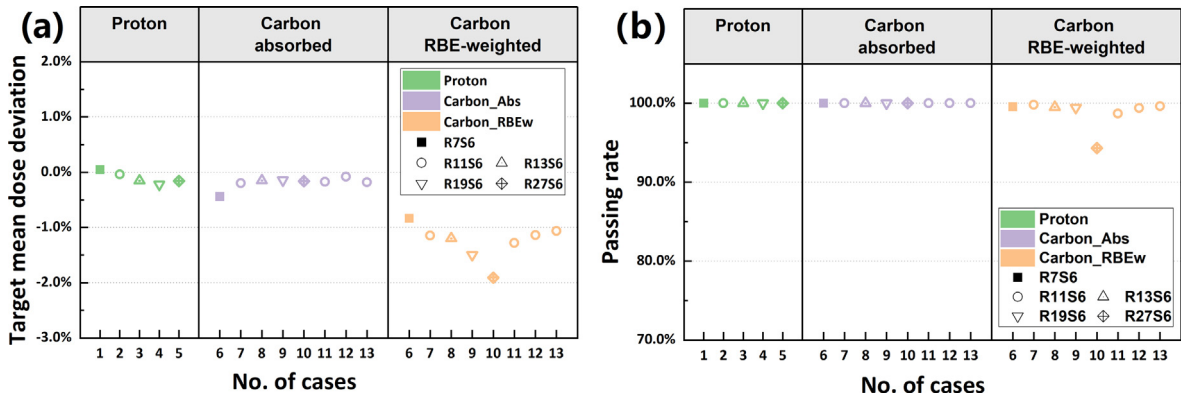

Figure 1. Target mean dose deviation (a) and Gamma passing rate (b) between TRiP4D and SyngoRT cubic plans on the WP. Gamma criteria of 2%/2 mm and 3%/3 mm was applied for absorbed dose and carbon RBE-weighted dose, respectively. Dose threshold ≥10% of the global maximum dose. Cases 1–5 are proton plans for target R7S6, R11S6, R13S6, R19S6, and R27S6, respectively. Cases 6–10 are carbon plans with a prescribed dose of 4Gy(RBE), and cases 11–13 are carbon plans with a prescribed dose of 3, 3.5, and 4.5 Gy(RBE) for target R11S6. The green, purple, and orange color represents the proton absorbed dose, the carbon absorbed dose, and the carbon RBE-weighted dose, respectively.

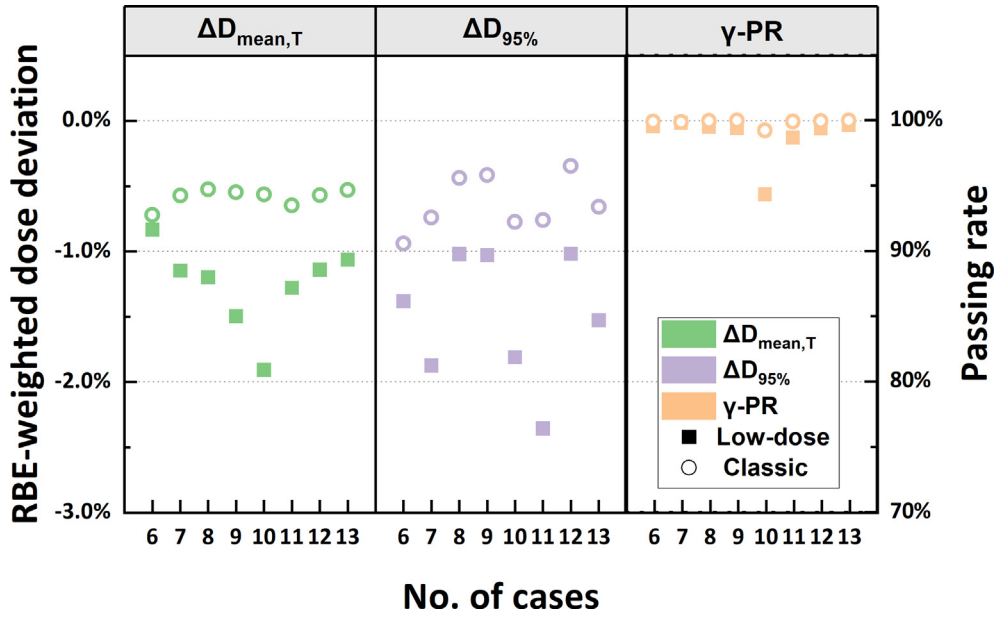

Figure 2. Comparison of RBE-weighted dose deviations of carbon plans between Classic and Low-dose method. The green, purple, and orange color represent the target mean dose deviation, the target dose of 95% volume, and the gamma passing rate, respectively.

Fig. 3 shows the physical and RBE-weighted depth dose profile along the axis of the beam direction for carbon 4Gy (RBE) plans of cubics R7S6, R11S6, R13S6, R19S6, and R26S6.

3.2 Patient plans

As is shown in Fig. 4, the average $\Delta D_{mean,\ T}$ was −0.73%, −0.59%, and −0.88% for proton absorbed, carbon absorbed, and carbon RBE-weighted doses, respectively. The average $\Delta D_{95\%,\ T}$ was −1.04% and −1.03% for all proton and carbon plans, respectively. $\Delta D_{mean,\ T}$ of all proton and carbon ion plans were within −1.60%, except for one carbon plan from patient No. 21. The absorbed and RBE-weighted $\Delta D_{mean,\ T}$ were −2.27% and −2.79% for this case. The maximum deviation of $\Delta D_{95\%,\ T}$ was −2.59% from patient case 21. Fig. 5 shows an example of SyngoRT and TRiP4D re-calcluated RBE-weighted dose distribution.

The average $\Delta D_{mean,\ Lung}$ was comparable for proton and carbon plans (−0.74% and −0.69% for proton and carbon plans, respectively). However, a larger variation was

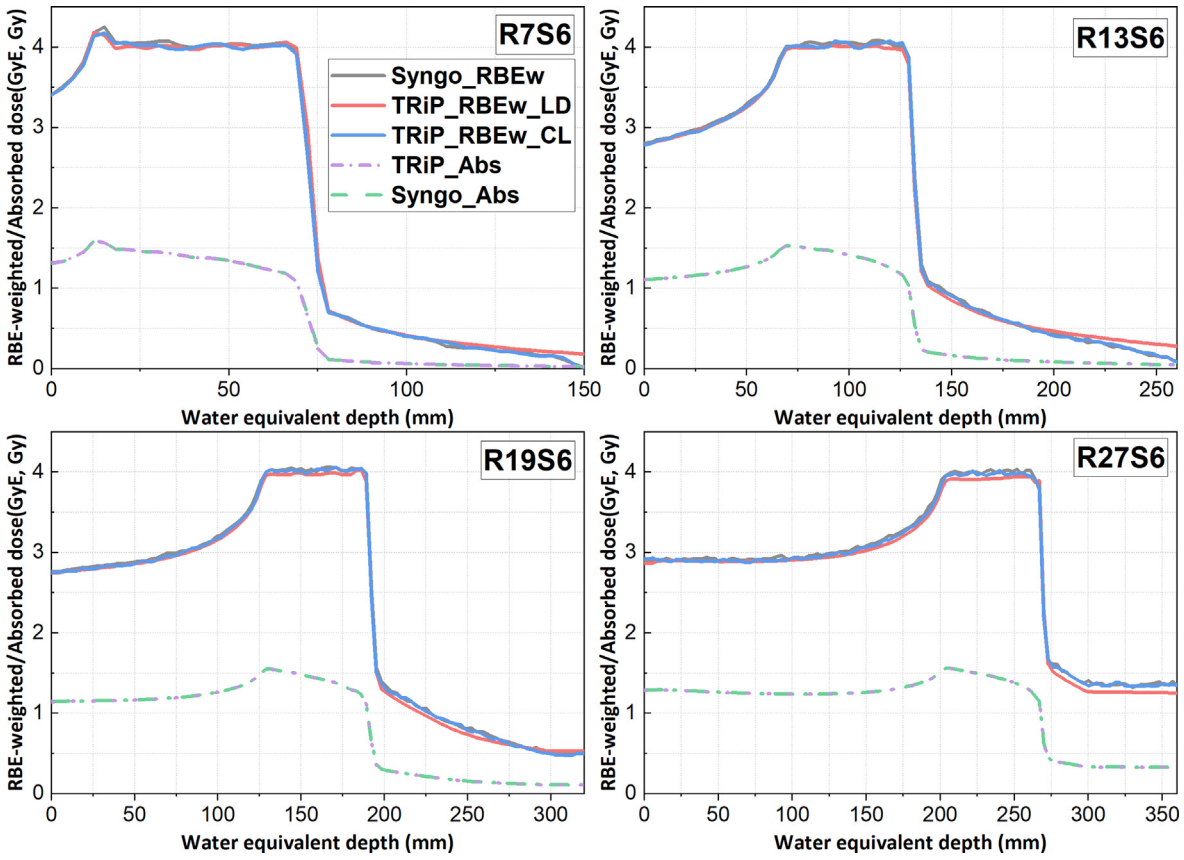

Figure 3. Absorbed and RBE-weighted depth dose profiles along the axis of the beam direction for carbon 4Gy(RBE) plans R7S6, R11S6, R13S6, R19S6, and R27S6. The solid lines in grey, red, and blue represent the SyngoRT RBE-weighted dose, TRiP4D RBE-weighted dose with the Low-dose algorithm, and TRiP4D RBE-weighted dose with the Classic algorithm. The dash-dotted lines in purple and light green represent the SyngoRT and TRiP4D absorbed dose.

observed for carbon plans than for proton plans. The standard deviation (SD), minimum and maximum of $\Delta D_{mean,Lung}$ was 0.54%, −1.74%, 0.06%, and 1.53%, −3.98%, 2.84% for proton and carbon plans, respectively.

The γ-PRs were always ≥93.92% and ≥91.83% for proton and carbon beams absorbed doses, except for one proton beam with RS. The γ-PR of this beam was 64.19%. The lowest γ-PRs of carbon RBE-weighted dose was 96.40%.

4 Discussion

It is the first time TRiP4D has been benchmarked against a commercial TPS for calculating proton and carbon absorbed dose distributions and carbon RBE-weighted dose distributions. SyngoRT was selected as a reference because to date, it is one of the few clinically used TPSs that provides carbon ion RBE-weighted dose calculation. The accuracy and reliability of SyngoRT for both proton and carbon ion absorbed dose calculation were validated by measurements, as demonstrated in previous studies from several carbon ion therapy centers in Europe and China [2,24,25]. Our work focused on comparing the dose distribution between TRiP4D and SyngoRT using cubic plans with different depths in water and lung patient plans. This dosimetric validation presents a necessary step toward retrospective 4D delivered dose assessment for patient cases treated at SPHIC. Since 4D dose calculation is not supported in SyngoRT, this also provides a middle step towards independent benchmarking of 4D dose calculation provided by the Raystation (RaySearch Laboratories, Stockholm, Sweden) TPS, which is currently being commissioned for SPHIC.

Instead of generating TRiP4D basedata from direct commissioning, the SyngoRT beam basedata were directly converted and applied in TRiP4D. The TRiP4D basedata was kept consistent with SyngoRT for the IDDs, RBE table, HU to stopping power table, in-air spot size at isocenter, and fragment spectrum. However, differences in basedata exist because of the differences in the accepted data format between TRiP4D and SyngoRT. For example, SyngoRT has in-air spot sizes at 7 locations relative to the isocenter

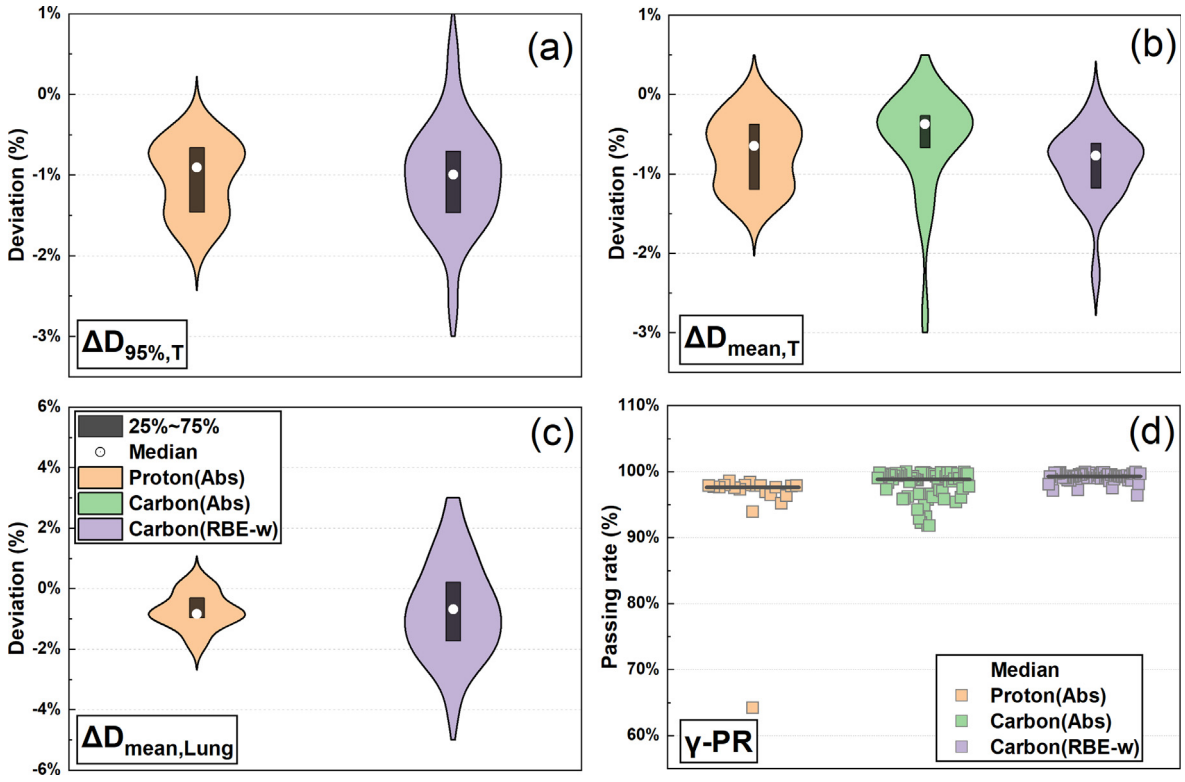

Figure 4. The target dose of 95% volume deviation (a), target mean dose deviation (b), lungs mean dose deviation for each patient plan (c) and the gamma passing rate for each beam of patient plans (d). The orange, green, and purple colors represent the proton absorbed dose, carbon absorbed dose, and carbon RBE-weighted dose, respectively. Please note that different scales were applied to each figure.

plane, while TRiP4D currently accepts only one at the isocenter plane. The double-Gaussian scattering beam model was applied in TRiP4D and SyngoRT to describe multiple Coulomb scattering in water. However, the SyngoRT basedata provides data for eight energies only, while TRiP4D needs data for all 290 energies, so interpolation of the data was necessary. Despite the possible bias in the basedata, we believe it does not have a decisive role in the dose comparison.

Cubic plans were selected to cover water equivalent ranges from 7 to 26 cm, carbon plans prescribed doses from 3 to 4.5 Gy(RBE), and carbon plans' RBE-weighted dose (LEM I model) calculation was performed by using Classic and Low-dose methods. Overall, 21 doses were compared. The absorbed dose distribution in TRiP4D agreed with the calculation in SyngoRT for the proton and carbon ion plans. This is supported by the target mean dose deviation <0.5% and the γ-PRs $\geq$ 99.93% for the calculated plans. If the Low-dose method was used for the carbon ion RBE-weighted dose, the dose calculated by TRiP4D could be different with SyngoRT by up to −1.91% for the target mean dose. The differences could be reduced to be within −0.72% if the Classic method is applied. A trend can be seen in Fig. 4, where the discrepancy between TRiP4D and SyngoRT calculated RBE-weighted doses increases with higher beam energies. Meanwhile, the Low-dose method underestimated the dose for the target and right after the target but overestimated the dose after a certain distance downstream of the beam direction. Although a less than 2% difference in RBE-weighted dose seems reasonable due to the uncertainties stemming from the calculation of the RBE, from a consistency point of view, the TRiP4D Low-dose algorithm may need to be further improved. Nevertheless, improving computation efficiency makes it more suitable for 4D and robust optimization and evaluation, which eventually calculates a series of plans.

The patient plan cases were calculated with the Low-dose algorithm. As expected, the TRiP4D calculated RBE-weighted target mean dose was around 1-2% lower than what was predicted by SyngoRT. A large deviation of both absorbed and RBE-weighted dose was observed in patient No. 21. For this case, the $\Delta D_{mean,\ T}$ was −2.27% and −2.79% for the absorbed dose and RBE-weighted dose, respectively. Patient No.21 suffered from small-cell lung cancer. The target volume was 15.8 cm^3. This patient's plan contains two carbon ion beams with average ranges of

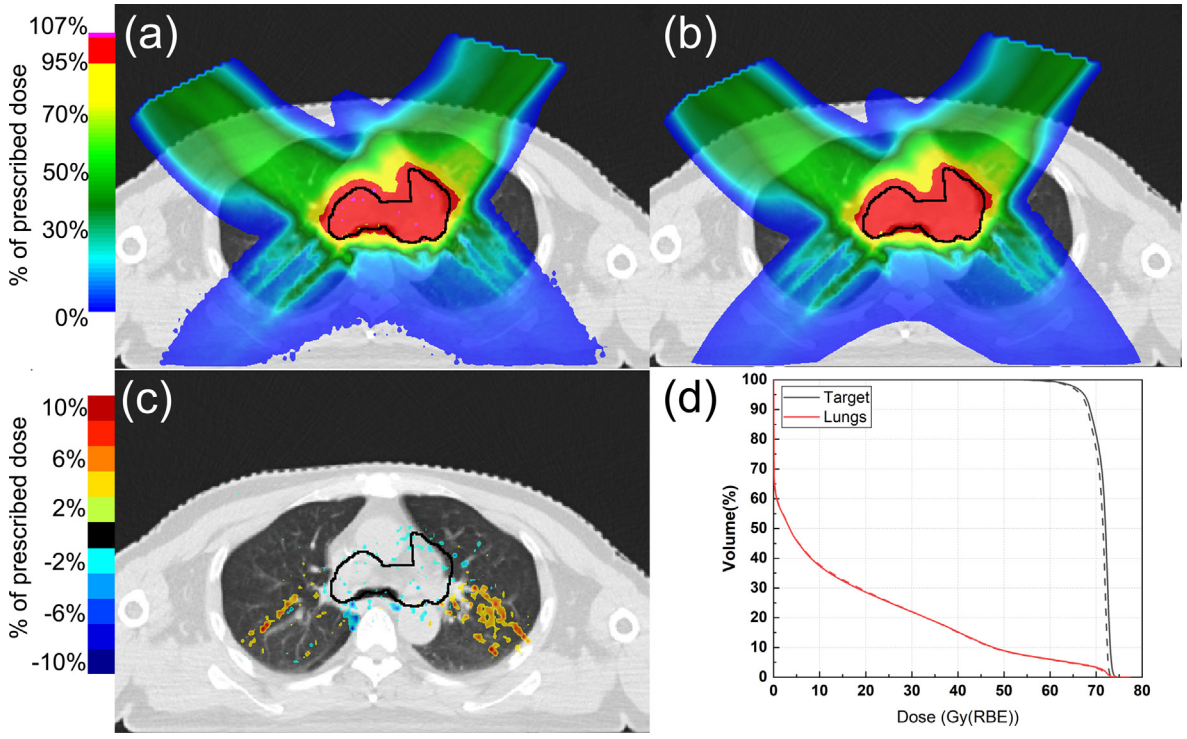

Figure 5. Example RBE-weighted dose distribution of SyngoRT (a) and recalculated using TRiP4D (b) for a clinical carbon patient case. The dose differences are shown in (c). Corresponding DVHs for the plan target volume and lungs are presented in (d).

47.6 mm and 43.4 mm, respectively, whereas the average range for all beams in this study was 81.1 mm. A 6 mm RiFi was used to reduce the necessary number of beam energy layers. Among the plans used in this study, each beam contained a median of 27 (range 5–49) different energies, while for this case, only 5 and 7 energies were used for the two beams. We performed three recalculations for this plan. We first recalculated the RBE-weighted dose using the Classic algorithm in TRiP4D. The RBE-weighted $\Delta D_{mean,\ T}$ was −1.73%. We then recalculated the two beams in a WP using TRiP4D and compared them with SyngoRT. The two beams' absorbed dose γ-PRs (criteria: 2 mm/2% of global max, 10% threshold) were 99.41% and 98.93% in WP compared to 92.24% and 91.83% in the patient CT. Finally, the preset system WED offset, which encompasses the WED of chambers in the nozzle and air between the vacuum window and patient, was shifted by −0.5 mm. Following this adjustment, we recalculated the two beams in the patient CT. The resulting $\Delta D_{mean,\ T}$ showed a reduction to −0.92% and −1.60% for the absorbed dose and RBE-weighted dose, respectively. One explanation for this finding may be attributed to the fact that Syngo adjusts the air WED value based on the patient's location relative to the isocenter and the body (the outline of patient contoured by planner), while disregarding CT pixels outside the body contour. In contrast, TRiP4D considers the system WED offset as a fixed value and takes into account the HU values of the full CT. As a result, TRiP4D may consider up to 20–50 cm of air twice, depending on the location of isocenter and beam angle. This feature will be fixed in a future version of TRiP4D. Our tests revealed that limited energy layers, differences in patient CT resolution, and discrepancies in the definition of the system WED offset between TRiP4D and SyngoRT may contribute to dose deviation of this case. Based on these findings, further evaluation of small, shallow-seated targets in TRiP4D may be beneficial, depending on the user's specific objectives.

One proton beam with a range shifter showed the lowest γ-PR among all the carbon and proton beams. For proton beams, SyngoRT considers the effect due to the scattering in the RS. This scattering also includes the beam broadening in the air gap between the range shifter and the patient entry point due to the additional beam divergence produced by the RS. It was not considered in the current version of TRiP4D but will be included in future software versions. The current version of TRiP4D should be used cautiously for calculating proton plans with RS.

It was reported that the MC dose algorithm's accuracy was superior to the PB algorithm in heterogeneous geometry [26]. Currently, the commissioning process of Raystation in

SPHIC is ongoing. Raystation provides both a PB and a Monte Carlo-based (MC) algorithm for proton beams. However, at present, Raystation provides only the PB algorithm for carbon ion beams. Ruangchan et al. reported large discrepancies behind the target in heterogeneous geometries for the carbon ion beam algorithm in Raystation [27]. The carbon beam algorithm in lung tissue needs to be further improved. TRiP4D is capable of advanced lung Bragg-peak modulation computation [28], which will be useful to better understand delivered doses in retrospective clinical studies for patients treated at SPHIC.

5 Conclusions

This work provides a first validation of TRiP4D calculated absorbed and RBE weighted dose distributions against the commercial TPS SyngoRT both in water and in patients. Dose comparison results showed that the absorbed dose between TRiP4D and SyngoRT was identical for both proton and carbon ion plans in the WP. Compared to SyngoRT, a slight underestimate of the target RBE-weighted dose in TRiP4D both in the WP and patient plans were observed. This was attributed to the use of the computationally more efficient Low-dose approximation to RBE-weighted dose calculation in TRiP4D, in contrast to the more accurate but computationally more demanding algorithm applied in SyngoRT. For a very small target volume, deviations between TRiP4D and SyngoRT calculated RBE-weighted doses were larger than for the bigger targets. TRiP4D will be used to evaluate doses delivered to moving targets. Uncertainties inherent to the 4D-dose reconstruction calculation are expected to be significantly larger than the dose errors observed here. For this reason, the residual differences between TRiP4D and SyngoRT observed in this study are deemed acceptable.

Data Availability Statement

The code used to extract the data is distributed by the authors as open-source. The patient data can be made available on request due to privacy/ethical restrictions.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.zemedi.2023.06.002.

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