Dose Comparison between Eclipse Dose Calculation and Fast Dose Calculator in Singleand Multi-Field Optimization Intensity-Modulated Proton Therapy Plans with Various Multi-Beams for Brain Cancer

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Abstract

The purpose of this study was to grasp current potential problems of dose error in intensity-modulated proton therapy (IMPT) plans. We were interested in dose differences of the Varian Eclipse treatment planning system (TPS) and the fast dose calculation method (FDC) for single-field optimization (SFO) and multi-field optimization (MFO) IMPT plans. In addition, because some authors have reported dosimetric benefit of a proton arc therapy with ultimate multi-fields in recent years, we wanted to evaluate how the number of fields and beam angles affect the differences for IMPT plans. Therefore, for one brain cancer patient with a large heterogeneity, SFO and MFO IMPT plans with various multi-angle beams were planned by the TPS. Dose distributions for each IMPT plan were calculated by both the TPS's conventional pencil beam algorithm and the FDC. The dosimetric parameters were compared between the two algorithms. The TPS overestimated 400 - 500 cGy (RBE) for minimum dose to the CTV relative to the dose calculated by the FDC. These differences indicate clinically relevant effect on clinical results. In addition, we observed that the maximum difference in dose calculated between the TPS and the FDC was about 900 cGy (RBE) for the right optic nerve, and this quantity also has a possibility to have a clinical effect. The major difference was not seen in calculations for SFO IMPT planning and those for MFO IMPT planning. Differences between the TPS and the FDC in SFO and MFO IMPT plans depend strongly on beam



arrangement and the presence of a heterogeneous body. We advocate use of a Monte Carlo method in proton treatment planning to deliver the most precise proton dose in IMPT.

Keywords

Fast Dose Calculator, Monte Carlo, Intensity-Modulated Proton Therapy, Single-Field Optimization (SFO), Multi-Field Optimization (MFO)

1. Introduction

Proton beam therapy is one of the most advanced technologies in cancer care [1]. Its main advantage over conventional photon beam therapy is that it provides an enhanced possibility of tumor control while minimizing irradiation to surrounding normal tissues due to the proton's Bragg peak with a sharp distal fall-off. Currently, pencil beam scanning (PBS) techniques [2] [3] [4] are the most precise forms of proton therapy that have been developed, and they are utilized clinically in several facilities. Among these techniques, intensity-modulated proton therapy (IMPT) [5] [6] delivers the most conformal dose.

In order to realize these precise therapies, proton dose distributions in the patient's body with heterogeneities have to be predicted with considerable accuracy in treatment planning. Currently, the treatment planning system for the PBS routinely uses a pencil beam algorithm [7] [8] because of the short computation time and because the pencil beam algorithm can perform well for homogeneities. However, it is common knowledge that the algorithm's accuracy deteriorates for targets with large heterogeneities [9] [10] [11].

In contrast, the full Monte Carlo (MC) methods [12] such as GEANT4 [13] and MCNPX [14] can provide accurate dose estimations in even the presence of large heterogeneities because they take into account the basic physical processes in medium and track paths of individual primary protons and secondary particles. However, the MC methods require computation times of hundreds of CPU hours, and are not appropriate in clinical use.

Therefore, simplified Monte Carlo [9] [10] [11] methods and VMC pro [15] dedicated to proton beam therapy have been developed to reduce the calculation time. Yepes *et al.* also developed the fast dose calculator (FDC) [16] [17], which used a Monte Carlo track-repeating algorithm based on GEANT4. This FDC has been already validated by GEANT4 for IMPT plans [18]. Yepes *et al.* reported that the FDC can calculate dose distributions in less than 5 minutes per patient and is suitable for routine clinical work.

At The University of Texas MD Anderson Cancer Center, IMPT plans are planned by the Varian Eclipse treatment planning system (TPS; version 13.5, Varian Medical Systems, Inc., Palo Alto, CA), which adopts a pencil beam algorithm as a dose calculation algorithm. It is obvious that the pencil beam algorithm produce errors in the boundary region of a thick heterogeneous material having an edge parallel to the beam central axis [9]. This means that dose error depends on a location of a target, the presence of a heterogeneity and beam direction. Dose differences between the TPS and actual irradiation in these plans are expected [19].

In the present study, we evaluated dose differences of the TPS and the FDC in single-field optimization (SFO) and multi-field optimization (MFO) IMPT [20] for brain cancer with heterogeneity, in order to grasp current potential problems of dose error in IMPT plans designed by the TPS. Additionally, because a proton arc therapy with ultimate multi-fields has dosimetric benefit [21] [22], we wanted to know how the number of fields and beam angles affect the differences for IMPT plans. Therefore, SFO and MFO IMPT plans with various multi-angle beams were also evaluated by the FDC.

2. Materials and Methods

A patient treated with passively scattered proton therapy at the University of Texas MD Anderson Cancer Center was selected for the study from a sample of typical cases. The clinical case with critical organs adjacent to the target and target surrounded by a heterogeneity which consists of bone, cavity, and soft tissue was that of a patient with grade III anaplastic astrocytoma.

Figure 1 shows the outlining of the target volumes and organs at risk (OARs) for the brain cancer treatment plan on a computed tomography slice. The prescribed doses were 5700 and 5000 cGy (RBE) (RBE = relative biological effectiveness) to the gross tumor volume (GTV) and clinical target volume (CTV), respectively, in 30 fractions. The maximum dose constraint for the chiasma, both optic nerves,



Figure 1. Contours of the GTV, CTV, and organs at risk (brainstem, optic chiasm, left optic nerve, and right optic nerve) have been drawn on this CT slice for the actual brain cancer IMPT plan.

and the brainstem was 5400 cGy (RBE). The optic chiasma, left optic nerve, and brainstem were at the edge of the target volumes.

Proton beam irradiation needs to sacrifice GTV and CTV coverage to maintain normal tissue constraints and avoid or minimize end of range in these critical structures. SFO and MFO IMPT planning were done with the same optimization conditions on the TPS. We used coplanar beams of 3, 4, 5, 6, and 9 treatment fields in the SFO and MFO IMPT plans, as shown in **Table 1**. Left anterior oblique beams from 40 degrees to 160 degrees were mostly used because of the locations of the target, optic chiasm and brainstem. Plan F and L were considered extreme cases because of the large number of beams and the 40-degree beam angles. The RBE value we used was the conventional uniform RBE value of 1.1. The FDC algorithm [16] [17] uses a database of pre-generated tracks to calculate IMPT dose distributions in any material, as described previously [18].

In order to evaluate the difference of dose calculation algorithms, SFO and MFO IMPT plans designed by the TPS were compared with those designed by the FDC. The comparative analysis for each dose distribution in regions of interest was done using the following dosimetric parameters: minimum dose, maximum dose, mean dose. For the CTV, doses to 95% and 5% of the clinical target volume (D95 and D5), heterogeneity index (HI), and conformity index (CI) were also added. HI and CI were proposed by the Radiation Therapy Oncology Group in 1993 [23], and described as HI = maximum dose in CTV/prescription dose and CI = prescription isodose volume/volume of CTV.

3. Results

Figure 2 shows (a) minimum, maximum, and mean dose, (b) D95 and D5, and (c) HI and CI obtained by the TPS and the FDC for the CTV in the SFO IMPT plans. In **Figure 2(b)**, the dosimetric parameters except for minimum dose by the FDC did not depend on the number of fields. On the other hand, differences for minimum dose depend on it, and the difference in plan F was 119 cGy (RBE) of the minimum difference. Minimum doses calculated by the TPS were smaller than 390 cGy (RBE) whereas those calculated by the FDC were always higher. Average differences of maximum and mean dose between the two algorithms were -16 ± 66 (1 SD) and 81 ± 20 cGy (RBE), respectively.

In **Figure 2(b)**, the D95 values calculated by the two algorithms tended to decrease slightly with the number of fields. D5s, however, were almost constant for each field number. Average differences of D95 and D5 between the two algorithms were 1.0% and 1.3%. In **Figure 2(c)**, HIs were almost constant for each number of fields, but CIs tended to improve considerably with the number of fields. The average difference in HI between the two algorithms was $-0.3\% \pm 1.2\%$. CI by the FDC decreased 3.2% $\pm 1.5\%$ as compared with those by the TPS.

Minimum, maximum, and mean dose obtained by the TPS and the FDC in SFO IMPT plans for the OARs are shown in **Figure 3**. In the brainstem, average differences of minimum, maximum, and mean dose between the two algorithms

Plan		Number of treatment	Poem angle (degrees)								
SFO	MFO	fields	beam angle (degrees)								
A	G	3	40	100	160	N/A	N/A	N/A	N/A	N/A	N/A
В	н	4	40	80	120	160	N/A	N/A	N/A	N/A	N/A
С	I	5	40	70	100	130	160	N/A	N/A	N/A	N/A
D	J	6	40	70	100	130	160	220	N/A	N/A	N/A
Е	К	9	40	70	100	130	160	190	220	250	280
F	L	9	20	60	100	140	180	220	260	300	340

Table 1. Treatment fields and beam angles for each single-field optimization (SFO) and multiple-field optimization (MFO) plan.



Figure 2. (a) Minimum, maximum, and mean dose; (b) D95 and D5; and (c) HI and CI for the CTV obtained by the TPS and the FDC in single-field optimization (SFO) IMPT plans.

were -3 ± 4 , 93 ± 42 , and 8 ± 24 cGy (RBE). Mean doses for the brainstem tended to increase with the number of fields because the number of beams that crossed the brainstem increased with the number of fields. In the optic chiasm,



Figure 3. Minimum, maximum, and mean dose obtained by the TPS and the FDC in single-field optimization (SFO) IMPT plans for the (a) Brainstem; (b) Optic chiasma; (c) Left optic nerve; and (d) Right optic nerve.

average differences of minimum, maximum, and mean dose were -30 ± 33 , 153 \pm 46, and -67 ± 48 cGy (RBE). In plan E, the TPS made a more than 219.2 cGy (RBE) estimate of the maximum dose to the optic chiasma.

In the left optic nerve, average differences of minimum, maximum, and mean dose were 17 ± 12 , -2 ± 65 , and 106 ± 13 cGy (RBE). In the right optic nerve, average differences of minimum, maximum, and mean dose were 25 ± 7 , 558 ± 90 , and 125 ± 29 cGy (RBE). These differences for the right optic nerve, on the unaffected side of the brain, were the most sensitive, and the TPS made a more than 600 cGy (RBE) estimate of maximum dose. This is because dose distributions in the right optic nerve were formed by the ends of the beams.

Figure 4 shows (a) minimum, maximum, and mean dose, (b) the D95 and D5 values, and (c) the HI and CI obtained by the TPS and the FDC for the CTV in MFO IMPT plans. Average differences of minimum dose except for plan L were



Figure 4. (a) Minimum, maximum, and mean dose; (b) D95 and D5; and (c) HI and CI for CTV by the TPS and the FDC in multiple-field optimization (MFO) IMPT plans.

 -476 ± 29 cGy (RBE). In contrast, that in plan L was 623 cGy (RBE). These differences between the algorithms were very large and depended strongly on beam arrangement. In contrast, average differences of maximum and mean dose were -97 ± 83 and 71 ± 12 cGy (RBE). Then, average differences of D95 and D5 were 1.6 ± 1.6 and $1.1\% \pm 0.3\%$. Average differences of HI and CI were -1.8 ± 1.7 and $2.3\% \pm 1.1\%$.

Minimum, maximum, and mean dose obtained by the TPS and the FDC in MFO IMPT plans for the brainstem, optic chiasm, and left and right optic nerves are shown in **Figure 5**. In the brainstem, average differences of each dosimetric parameter were -5 ± 2 , 64 ± 25 , and 15 ± 86 cGy (RBE). In the optic chiasm, minimum doses tended to increase with the number of fields because the number of beams that crossed the optic chiasm increased with the number of fields. Average differences of minimum and maximum dose were -67 ± 24 and 146 ± 33 cGy (RBE). Average differences of mean dose between the two algorithms, except



Figure 5. Minimum, maximum, and mean dose obtained by the TPS and the FDC in multiple-field optimization (MFO) IMPT plans for the (a) Brainstem; (b) Optic chiasma; (c) Left optic nerve; and (d) Right optic nerve.

for plan L, were -96 ± 20 cGy (RBE). Mean dose calculated by the FDC for plan L was 300 cGy (RBE) smaller than that calculated by the TPS.

Figure 5(c) shows that in the left optic nerve, average differences of minimum dose between the two algorithms except for plan L were 3 ± 21 cGy (RBE). Minimum doses by the FDC in plan L were 200 cGy (RBE) lower than those calculated by the TPS. Average differences of maximum dose except for plan L were -9 ± 9 cGy (RBE). Maximum dose by the FDC in plan L were less than about 400 cGy (RBE) as compared with that by the TPS. Average differences of mean dose between the algorithms were 89 ± 34 cGy (RBE). Mean doses by the FDC except for plan L were less than about 500 cGy (RBE) as compared with that by the TPS.

In **Figure 5(d)**, average differences of minimum and maximum dose between the algorithms were 19 ± 16 and 666 ± 162 cGy (RBE), respectively. Although average differences of mean dose between the algorithms except for plan L were 162 \pm 34 cGy (RBE), the TPS for plan L made a more than 260 cGy (RBE) estimate of mean dose for the right optic nerve.

4. Discussion

Basically, overestimating the dose to target and underestimating the maximum dose to critical organs by the TPS clinically poses a critical problem. In this analysis, the TPS overestimated 400 - 500 cGy (RBE) for the minimum dose to the CTV in the SFO and MFO IMPT plans. Dose difference of the TPS and the FDC for D95 in plan L was 4.8%, which is considered somewhat large. As shown in the red dashed circle region in **Figure 6**, we found considerable dose deterioration in front of the CTV in FDC for plan L. Since this region consisted of bone, cavity, and soft tissue and therefore had large heterogeneities, beams of 340° and 20° affected this difference between the TPS algorithm and the FDC.

We also observed a dose difference of about 1000 cGy (RBE) between the TPS and the FDC calculations for right optic nerve in plan G. Thus, these quantities are very large and cannot be ignored in clinical use. We therefore recommend that proton treatment planning be done using a Monte Carlo simulation method such as the FDC.

We were surprised to find that no major differences were seen between SFO IMPT planning and MFO IMPT planning. We have confirmed a one-to-one correlation for each difference between these two types of planning, but we did not observe any influence of the irradiation method ($R^2 = 0.7258$).

Results for plans F and L were different in nature from those of the other plans. We do not think these extreme plans are suitable for clinical use. However, it was obvious that dosimetric impact changed drastically with the beam selection in them. Therefore, these results reconfirm the importance of beam arrangement in IMPT planning. Further study should now be done to determine,



Figure 6. Comparison of isodose distributions obtained by the TPS (left) and the FDC (right) for plan L.

although beam angle optimization [24] and robust optimization techniques [25] may solve a problem of the beam arrangement.

On the other hand, since the FDC can also calculate linear energy transfer, the FDC is a powerful simulation tool in proton treatment planning. Namely, we can obtain a variable RBE by using the FDC. Therefore, we plan to evaluate incorporation of a variable RBE in IMPT plans by using these parameters in the near future.

5. Conclusion

We evaluated the dosimetric impact of the TPS and the FDC in SFO and MFO IMPT planning for a brain cancer patient. Large dose differences between the TPS and the FDC calculations were observed, and these depended on beam arrangement and the presence of a heterogeneous body. Because the magnitude of the dose differences was too large for clinical acceptability when the TPS calculations were used, we suggest that IMPT planning be done using a Monte Carlo method, such as the FDC.

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