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Lung Locations Most Affected by Dose-Calculation Algorithms in CyberKnife Stereotactic Body Radiotherapy

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ABSTRACT CyberKnife is a robotic stereotactic body radiotherapy (SBRT) system that precisely delivers large radiation doses to a target. Tissue heterogeneity and shape can be problems. The treatment -planning system allows for use of the Monte Carlo (MC) or fundamental Ray Tracing (RyTc) algorithms for ultimate dose calculation. The MC is more accurate but consumes more computer resources and time. We compared radiation dose calculations for lung targets between the MC and RyTc algorithms. We placed a prosthetic marker at different thorax sites in a Rando phantom to compare the calculation results. The peripheral sites followed by the diaphragm showed the greatest significant differences in parameters for evaluating the treatment quality. For gross tumor volume dose, peripheral lung targets were the most critical for the calculation algorithm. The MC mean doses were lower than the RyTc mean doses and generally demonstrated better conformity. However, the deviation between conformal index (CI) and new CI at the peripheral location was large. The coverage differences between the RyTc and MC were most obvious at the peripheral lung site. The MC algorithm for radiation dose calculation in the lungs was indispensable in SBRT using CyberKnife for accurate dose evaluation, especially at the peripheral and diaphragm locations.

INDEX TERMS Stereotactic body radiotherapy (SBRT), cyberknife, Monte Carlo (MC), lung, ray tracing (RyTc).

I. INTRODUCTION

Stereotactic radiosurgery is a precision form of radiation therapy that focuses energy on a small area of the body. It was originally defined by the Swedish neurosurgeon Lars Leksell, who directed a stereotactical single high-dose fraction of radiation to an intracranial lesion [1]. The first device for radiosurgery was the Gamma Knife®, which typically contains 201 cobalt-60 sources, each located in a hemispheric array in a heavily shielded assembly. The patient should be fixed with a specialized helmet to the skull surgically; therefore, Gamma Knife cannot be used to perform radiosurgery on the body. A linear accelerator (Linac) produces x-rays by electric power without isotopes. With a Linac, the patient lies on a gantry and treatment couch that moves in space to change the radiation delivery angle. These treatments now use a thermoplastic cast to fix the patient and align the x-ray beam for imaging. The cast is both comfortable for the patient and accurate, and radiosurgery can be used to treat body lesions, including fractionally, besides skull lesions.

Going a step further, a robot arm has been applied to this technology.John R. Alder—a Stanford University professor of neurosurgery and radiation oncology—and the Peter and Russell Schonberg of Schonberg Research Corporation developed a frameless robotic radiosurgery system called the

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CyberKnife® [2], [3]. A compact X-band Linac is mounted on the robot, which allows near-complete freedom of the radiation incidence to the patient. The radiation can be collimated either by using fixed tungsten collimators, which are referred to as 'cones,' or variable-aperture collimators, which use two offset banks of six prismatic tungsten segments to form a blurred regular dodecagon field of variable size referred to as the 'IRIS', A multileaf collimator for irregular fields is also available in the modern generation of CyberKnife. X-ray imaging cameras are located on supports around the patient, which allows instantaneous image guidance [4]. The frameless nature and freedom for the radiation incidence of CyberKnife increases the clinical applicability. Radiosurgery can be used to not only treat intracranial lesions but also body lesions in any location.

Unlike cranial tissue, body compositions are more complex. Radiosurgery for extracranial sites encounters the problems of tissue heterogeneity and shape. Stereotactic body radiotherapy (SBRT) refers to a type of therapy in which accurate computational methods for dose–volume analysis are used to ensure that critical structures are adequately spared while delivering ablative doses to the lesions. However, uncertainty may still be introduced by the inaccuracy of the algorithm. The treatment -planning system of CyberKnife, which is called MultiPlan®, provides the option of using the Monte Carlo (MC) algorithm in addition to the fundamental Ray Tracing (RyTc) algorithm for ultimate dose calculation. For thoracic treatment, which has inhomogeneous tissue density (air and soft tissue) and requires small fields, the MC algorithm has been shown to be more accurate than the RyTc for dose calculation [5]–[7]. However, the MC algorithm consumes more computer resources and time, which reduces the treatment effectiveness and delivery efficiency. Therefore, understanding the calculation difference between the MC and RyTc algorithms according to treatment site is important in deciding if the MC algorithm is necessary for the final dose calculation.

In this study, we used a prosthetic marker at different sites of the thorax in a Rando phantom as the treatment target for CyberKnife to compare the calculation results between the RyTc and MC algorithms, with the goal of providing a reference for selecting the final dose calculation algorithm in the CyberKnife M6 system (Accuray Inc., Sunnyvale, CA).

II. MATERIALS AND METHODS

A. PHANTOM PREPARATION

The thorax part of the Rando phantom was used in the investigation. A 1.5-cm diameter prosthetic marker was placed in the Rando phantom to simulate the treatment target. The prosthetic marker was placed at the peripheral, middle, central and diaphragm regions of the lung to acquire computed tomography (CT) (LightSpeed RT16 CT simulator, GE Medical Systems, Milwaukee, WI, USA) imaging data for the treatment -planning system. Figure 1 shows a simple illustration of the locations of the prosthetic markers.

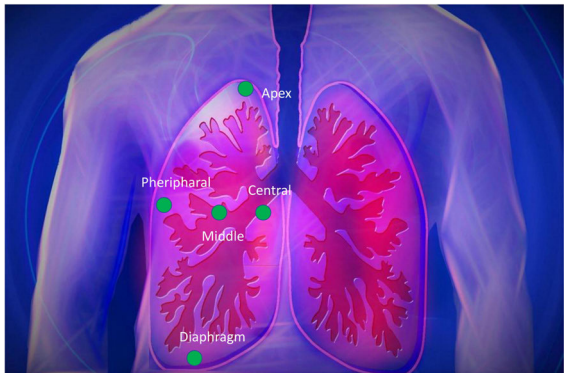


FIGURE 1. A simple illustration of the locations of the prosthetic markers.

B. COMPUTER TOMOGRAPHY SIMULATION

The Rando phantom was set up on a CT coach (GE LightSpeed RT®, GE Medical Systems, Milwaukee, WI, USA). The phantom was scanned from the low jaw to 10 cm below the diaphragm by using a 0.625 mm slice. The scanning was performed for each prosthetic marker location at the peripheral, middle, central and diaphragm regions of the lung. The CT imaging sets were then transferred to the Multiplan Treatment Planning Software (MTPS; version 5.1.3; Accuray Inc., Chesapeake Terrace, Sunnyvale, CA) for radiation dose calculation.

C. TREATMENT PLANNING

The prosthetic marker was segmented to represent the gross tumour volume (GTV), and an additional symmetrical 2-mm margin was appended for the planning target volume (PTV). The isocenter was set at the center of the GTV, and an isocentric full-path plan with a 20-mm cone collimator was established. The prescription was 10 Gy on a 75% isodose line. Therefore, the homogeneity index, which evaluates the uniformity of dose within the target volume, is defined as the maximum target dose/ prescription dose and is equal to 1.25. The treatment plan was calculated by both the RyTc and MC algorithms under the same beam arrangement for comparison.

D. DATA ANALYSIS

The plan was evaluated for the minimum, maximum and mean doses of the GTV and PTV. The conformal index (CI), new conformal index (nCI) and coverage were also checked. The CI is the prescription isodose volume (PIV)/tumour isodose volume (TIV), where PIV is the total three-dimensional (3D) volume of the isodose line and TIV is the tumour volume covered by the isodose volume. The nCI is the tumour volume (TV) $\times$ TV/(target isodose volume)^2. Coverage is determined as a percentage. The independent t-test was applied to examine the statistical significance of differences in the treatment plan parameters between the doses calculated by the RyTc and MC algorithms. A one-sample t-test was applied to check the significance of the differences among the doses at the target location calculated by the RyTc and MC algorithms.

A paired t-test was performed to determine the significance of differences in the doses between the RyTc and MC algorithms. The differences in the treatment plan parameters according to target site were analyzed using the one-sample t-test to evaluate the most critical treatment site for the RyTc and MC algorithms.

III. RESULTS

The results of the treatment plan using an isocentric full-path plan with a 20 mm cone collimator for different lung locations calculated by the RyTc and MC algorithms are presented in Table 1.

The coverage percentages for the GTV were 100% except for the lesion located at the periphery of the lung for both the RyTc and MC algorithms. A paired t-test for the treatment plan parameters demonstrated a significant difference in the mean GTV doses, minimal PTV doses, mean PTV doses and the CIs and nCIs of both the GTV and PTV(Table2).

The average with standard derivation and the maximum and minimum values for the evaluation parameters of the treatment plans calculated by the RyTc and MC algorithms are presented in Table 3.

Only the CIs of the GTV were significantly different between the RyTc and MC algorithms, regardless of treatment target locations. Table 4 presents the results for the one-sample t-test for the significance of differences in the treatment plan parameters for each target site between the RyTc and MC algorithms. The greatest significant differences in the plan parameters were found for the peripheral sites followed by the diaphragm. For the dose of the GTV, the peripheral site treatment targets were the most critical for the calculation algorithm.

Figure 2 shows the mean dose for GTV and PTV with error bar for the minimum and maximum according to the target location. The mean doses calculated by the MC were lower than those by the RyTc, but the ranges were higher for the MC.

Figure 3 shows the CIs and nCIs for the RyTc and MC algorithms. The doses calculated by MC generally demonstrated better conformity than that of the doses calculated by the RyTc, which means that there was a smaller prescribed dose volume cover target. However, there was a large deviation between the CI and nCI at the peripheral location, which indicated that the dose coverage was not satisfactory.

Figure 4 illustrates the prescribed dose coverage according to target locations by the RyTc and MC algorithms. The coverage differences between the RyTc and MC algorithms were most obvious at the peripheral location.

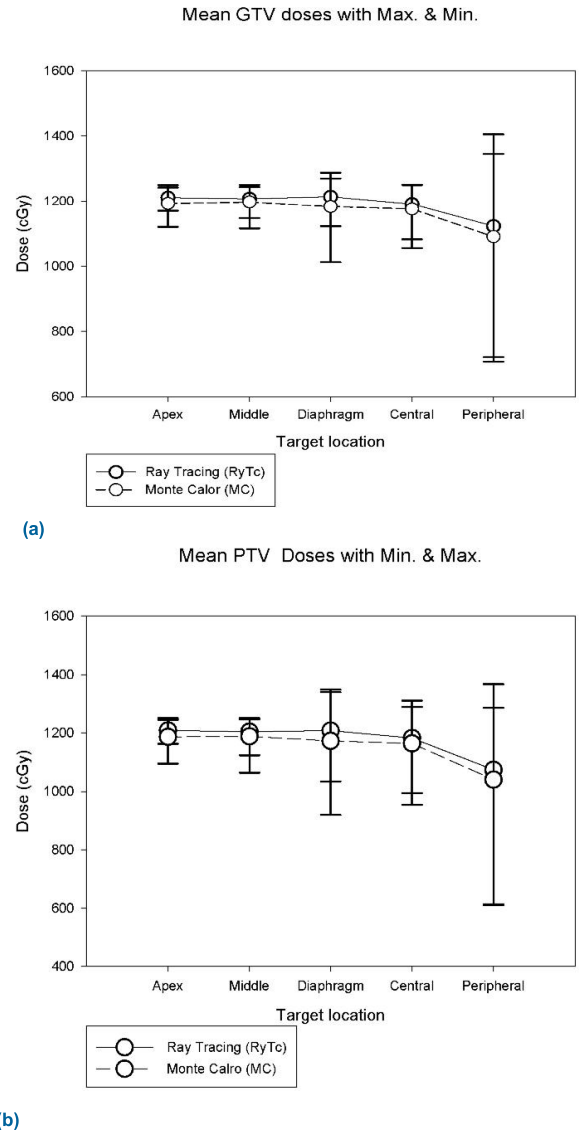


FIGURE 2. Mean dose with error bar for the minimum and maximum, according to the target location calculated by the Ray Tracing (RyTc) and Monte Carlo (MC) algorithms for (a) GTV and (b) PTV.

IV. DISCUSSION

Accurate dose calculation is the most important goal for radiation therapy treatment planning systems. The first high-energy photon beam dose algorithms were developed for the ultimate 'homogeneous' patient completely consisting of water [8]. They measured a set of generic dose functions for a set of regular treatment fields under reference conditions and then calculated by extrapolating these measurements to specific treatment files and applications of correction functions. These are the so-called 'correction-based methods'. However, a real human body is heterogeneous, and the radiation energy transport and deposition in tissues due to photon tissue interactions are a matter of course for realistic descriptions of the absorbed dose. With the progress in CT techniques, the heterogeneity of the patient anatomy would be represented by Hounsfield numbers that could provide high spatial information to check the absorbed energy in the patient for a more accurate description of radiation dose. An additional model for the radiation field emerging from the radiation source must be created for dose calculations and are referred to as 'model-based algorithms'.

Model-based algorithms constitute the standard algorithms in currently used commercial treatment planning systems.

TABLE 1. The calculation results by an isocentric full-path plan with 20 mm cone collimator to different locations in the lung with Ray Tracing and Monte Carlo algorithms.

Parameter/ Target location, Target Volume, Algorithm	Minimal dose (cGy)	Mean dose of (cGy)	Maximal dose (cGy)	Conformality index (CI)	New conformality index (nCI)	Coverage (%)
Apex						
GTV						
Ray Tracing (RyTc)	1170.33	1210.94	1241.58	11.08	17.31	100.00
Monte Carlo (MC)	1121.24	1193.21	1250.00	15.66	15.66	100.00
PTV						
RyTc	1161.92	1208.24	1246.53	11.16	11.08	100.00
MC	1095.53	1186.75	1250.00	10.02	10.02	100.00
Middle						
GTV						
RyTc	1148.03	1207.53	1243.66	18.02	18.02	100.00
MC	1116.27	1197.61	1250.00	15.69	15.9	100.00
PTV						
RyTc	1123.51	1204.10	1246.53	11.16	11.1	100.00
MC	1064.42	1188.33	1250	9.71	9.71	100.00
Diaphragm						
GTV						
RyTc	1123.24	1231.67	1248.10	19.36	19.36	100.00
MC	1012.84	1183.54	1250.00	16.3	16.3	100.00
PTV						
RyTc	1034.34	1207.83	1249.44	9.39	9.39	100.00
MC	920.23	1172.73	1250.00	8.01	8.11	98.74
Central						
GTV						
RyTc	1083.00	1191.08	1239.88	18.75	18.75	100.00
MC	1056.15	1176.73	1250.00	16.99	16.99	100.00
PTV						
RyTc	9994.95	1182.57	1242.73	11.65	11.65	99.92
MC	954.51	1164.36	1250.00	10.99	10.99	98.71
Peripheral						
GTV						
RyTc	721.08	1123.15	1243.30	19.31	23.27	82.97
MC	707.61	1091.06	1220.66	18.14	23.77	76.29
PTV						
RyTc	610.22	1074.01	1245.31	12.75	17.97	70.97
MC	613.6	1040.54	1222.01	11.93	18.22	65.49

The simplest form is the pencil-beam algorithm that is still the standard, and it is a fast dose engine [9]–[11]. However, model-based algorithms rely on approximations and only partly describe the physical process involved in the microscopic absorption by the radiation. The most sophisticated approach that considers almost all known physical features about radiation–tissue interactions is the MC algorithm. The MC dose calculation consists of both a geometrical design of the treatment head for the machine and characteristic parameters from electrons to their respective radiations for input and simulation of the energy absorption and transport within the tissue of the patient. At present, the MC is the most sophisticated and accurate algorithm in radiation therapy planning systems [12], [13]. However, the long calculation times for the MC algorithm made this method impractical for routine clinical use. The development of fast code optimisation and computer processor techniques for reduced calculation times has made it possible for the MC to be used in practical radiation therapy treatment planning systems [14]–[16].

The RyTc algorithm used by the CyberKnife treatment planning system is a correction-based algorithm. The absorbed dose is calculated by assuming the effective depth

TABLE 2. Paired t-test for the treatment plan parameters between Ray Tracing and Monte Carlo algorithms.

Ray Tracing (RyTc)-Monte Carlo (MC)/Parameters	Pairs	Mean	Standard deviation	Standard error mean	95% confidence interval of difference	*p*-value
Minimum dose of GTV (cGy)	n = 5	46.31	38.03	17.00	−0.90–93.53	0.053
Mean dose of GTV (cGy)	n = 5	20.844	9.80	4.38	8.68 -33.01	0.009*
Maximum dose of GTV (cGy)	n = 5	-0.828	13.47	6.03	−17.56–15.90	0.897
Minimum dose of PTV (cGy)	n = 5	55.53	42.67	19.08	2.55–108.51	0.044*
Mean dose of PTV (cGy)	n = 5	24.80	8.90	3.98	13.75–35.86	0.003*
Maximum dose of PTV (cGy)	n = 5	1.36	12.51	5.59	−14.18–16.89	0.820
Conformal index (CI) of GTV	n = 5	1.99	0.72	0.32	1.09–2.89	0.004*
New conformal index (nCI) of GTV	n = 5	1.66	1.33	0.60	0.01–3.31	0.049*
Conformal index (CI) of PTV	n = 5	1.07	0.34	0.15	0.65–1.50	0.002*
New conformal index (nCI) of PTV	n = 5	0.84	0.68	0.30	0.00–1.68	0.050*
Coverage of GTV (%)	n = 5	1.34	2.99	1.34	−2.37–5.05	0.374
Coverage of PTV (%)	n = 5	1.59	2.26	1.01	−1.22–4.40	0.191

*p-value <0.05

TABLE 3. Differences between the Ray Tracing and Monte Carlo algorithms for the treatment plan evaluation parameters in an isocentric full-path plan with 20 mm cone collimator regardless of location.

Algorithm/parameters	Ray Tracing (RyTc)	Monte Carlo (MC)	*p*-value
Minimum dose of GTV (cGy)	1049.14 ± 186.23 (721.08–1170.33)	1002.82 ± 171.02 (707.61–1121.24)	0.693
Mean dose of GTV (cGy)	1189.27 ± 38.99 (1123.1–1213.60)	1168.43 ± 4401 (1091.00–1197.61)	0.682
Maximum dose of GTV (cGy)	1243.30 ± 3.08 (1239.88–1248.10)	1244.13 ± 13.12 (1220.6–1250)	0.332
Minimum dose of PTV (cGy)	985.19 ± 220.13 (610.22–1162.9)	929.66 ± 191.23 (613.6–1095.5)	0.532
Mean dose of PTV (cGy)	1175.35 ± 57.63 (1074.00–1208.2)	1150.54 ± 62.29 (1040.54–1188.3)	0.897
Maximum dose of PTV (cGy)	1245.76 ± 2.47 (1242.73–1249.44)	1244.13 ± 13.12 (1222.01–1250)	0.823
Conformal index (CI) of GTV	18.55 ± 0.88 (17.31–19.36)	16.56 ± 1.04 (15.6–18.14)	0.012*
New conformal index (nCI) of GTV	19.34 ± 2.33 (17.31–23.27)	17.68 ± 3.45 (15.6–23.77)	0.245
Conformal index (CI) of PTV	11.20 ± 1.21 (9.39–12.75)	10.13 ± 1.47 (8.01–11.93)	0.402
New conformal index (nCI) of PTV	12.25 ± 3.31 (9.39–17.97)	11.41 ± 3.95 (8.11–18.22)	0.724
Coverage of GTV (%)	96.59 ± 7.62 (82.97–100)	95.26 ± 10.60 (76.29–100)	0.825
Coverage of PTV (%)	94.18 ± 12.97 (70.97–100)	92.59 ± 15.16 (65.49–100)	0.863

*p-value <0.05

as determined by the density variation along the beam path and does not take into account effects caused by the variations in tissue heterogeneity and electronic disequilibrium at the tissue interface [17]. Therefore, the RyTc is regarded as a less accurate algorithm. Because the dose distribution tends to be more complicated in heterogeneous media, the

TABLE 4. One-sample t-test for differences in treatment plan parameters according to target sites between the RyTc and MC algorithms.

Algorithms/target locations	Difference between Raytracing (RyTc) and Monte Carlo (MC)	Mean difference of other sites	95% confidence interval of difference sites	*p*-value
Apex				
Mmumini dose of GTV	49.09	−3	−73.28–66.34	0.884
Mean dose of GTV	17.73	3.89	−13.82–21.61	0.535
Maximum dose of GTV	−8.42	9.49	−14.01–32.99	0.289
Minimum dose of PTV	67.38	−14.82	−92.26–62.63	0.586
Mean dose of PTV	21.49	3.70	−12.31–19.70	0.515
Maximum dose of PTV	−5.22	8.22	−13.75–30.19	0.319
Conformal index (CI) of GTV	1.65	0.43	−0.85–1.71	0.365
New conformal index (nCI) of GTV	1.65	0.01	−2.43–2.46	0.988
Conformal index (CI) of PTV	1.06	0.02	−0.61–0.65	0.935
New conformal index (nCI) of PTV	1.06	−0.27	−1.50–0.95	0.529
Coverage of GTV	0	1.67	−3.64–6.98	0.391
Coverage of PTV	0	1.99	−1.83–5.81	0.196
Middle				
Minimum dose of GTV	31.76	18.19	−50.06–86.44	0.459
Mean dose of GTV	9.92	13.66	−0.42–27.73	0.054
Maximum dose of GTV	−6.34	6.89	−17.21–30.99	0.430
Minimum dose of PTV	59.05	−4.45	−82.77–73.86	0.884
Mean dose of PTV	15.77	11.30	−2.18–24.77	0.076
Maximum dose of PTV	−3.47	6.03	−16.41–28.48	0.455
CI of GTV	2.23	−0.42	−1.71–0.87	0.375
nCI of GTV	2.23	−0.84	−3.18–1.51	0.339
CI of PTV	1.45	−0.47	−0.97–0.03	0.058
nCI of PTV	1.45	−0.76	−1.83–0.31	0.110
Coverage of GTV	0	1.67	−3.64–6.98	0.391
Coverage of PTV	0	1.99	−1.83–5.81	0.196
Diaphragm				
Minimum dose of GTV	110.4	−80.11	−103.54 to −56.68	0.002*
Mean dose of GTV	30.13	−11.61	−26.87–3.65	0.094
Maximum dose of GTV	−1.9	1.34	−23.39–26.07	0.874
Minimum dose of PTV	114.11	−73.23	−123.48 to −22.97	0.019*
Mean dose of PTV	35.1	−12.87	−25.35 to −0.377	0.046*
Maximum dose of PTV	−0.56	2.40	−20.51–25.30	0.761
CI of GTV	3.06	−1.33	−2.09 to −0.57	0.011*
nCI of GTV	3.06	−0.84	−3.18–1.51	0.067
CI of PTV	1.38	−0.38	−0.93–0.16	0.112
nCI of PTV	1.28	−0.55	−1.71–0.61	0.230
Coverage of GTV	0	1.67	−3.64–6.98	0.391
Coverage of PTV	1.26	0.41	−3.73–4.55	0.317
Central				
Minimum dose of GTV	26.85	24.33	−42.62–91.28	0.331
Mean dose of GTV	14.35	8.12	−8.60–24.84	0.220
Maximum dose of GTV	−10.12	11.61	−11.23–34.46	0.204
Minimum dose of PTV	40.44	18.86	−57.99–95.71	0.492

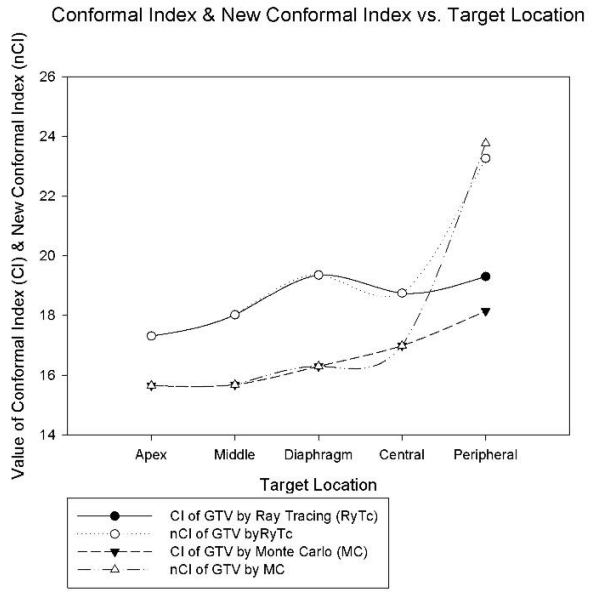
TABLE 4. ***(Continued.)*** **One-sample t-test for differences in treatment plan parameters according to target sites between the RyTc and MC algorithms.**

Mean dose of PTV	18.21	8.25	−6.64–23.14	0.176
Maximum dose of PTV	−7.27	10.78	−10.43–32.00	0.204
CI of GTV	1.76	0.29	−1.02–1.60	0.529
nCI of GTV	1.76	−0.13	−2.57–2.32	0.881
CI of PTV	0.66	0.52	0.05–0.98	0.038*
nCI of PTV	0.67	0.22	−1.02–1.45	0.617
Coverage of GTV	0	1.67	−3.64–6.98	0.391
Coverage of PTV	1.21	0.48	−3.66–4.61	0.739
Peripheral				
Minimum dose of GTV	13.47	27.68	−33.51–88.86	0.246
Mean dose of GTV	32.09	−14.87	−28.67 to −1.06	0.042*
Maximum dose of GTV	22.64	−29.34	−34.99 to −23.68	<0.001*
Minimum dose of PTV	−3.38	73.64	23.78–123.49	0.018*
Mean dose of PTV	33.47	−10.827	−24.56–2.90	0.087
Maximum dose of PTV	23.3	−27.43	−31.95 to −22.91	<0.001*
CI of GTV	1.17	1.03	0.00–2.06	0.050
nCI of GTV	−0.5	2.70	1.67–3.73	0.004*
CI of PTV	0.82	0.32	−0.26–0.89	0.177
nCI of PTV	−0.25	1.37	0.83–1.90	0.004*
Coverage of GTV	6.68	0	0–0	<0.001*
Coverage of PTV	5.48	−4.86	−6.00–3.73	0.001*

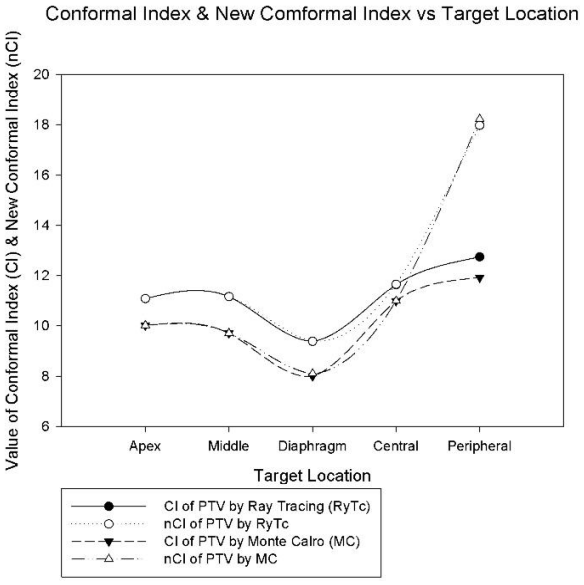
*p-value <0.05

calculation results of doses may show differences between different algorithms. The heterogeneous volume of tissue affects the results of planning doses that may affect clinical decisions and treatment responses. In the case of the RyTc algorithm for heterogeneous media that includes a low-density region, the dose tends to be overestimated relative to that estimated by the MC algorithm because it does not adequately describe the phenomenon of the spread-out electrons [18]. The MC algorithm is ultimately demanded for clinical use. However, the calculation time for the MC algorithm is much longer than that for the RyTc, and optimisation to achieve a satisfactory treatment plan is time consuming. Understanding the difference in calculation results between different algorithms is important, especially in heterogeneous organs, such as the lung.

According to our results, the average and maximum dose of the GTV and PTV were all higher when calculated by the RyTc than by the MC algorithm (Fig. 2). This result is consistent with the inference that the RyTc algorithm tends to overestimate the dose. The mean doses of the GTV and PTV were significantly different between the RyTc and MC algorithms. Additionally, the conformities according to the CI and nCI were also significantly different between the RyTc and MC algorithms, but the coverages were not (Table 2). These results suggest that although the coverage dose of the treatment target may not be significantly different between the RyTc and MC algorithms, the actual absorbed dose and dose conformity may be lower than expected from the treatment planning. Table 3 also shows that conformity is the major issue between the RyTc and MC algorithms regardless of treatment locations. On the other hand, the apex and middle locations of targets did not show significant differences among the absorbed dose parameters between the RyTc and MC algorithms for the different target locations. However, the greatest significant differences in the absorbed dose parameters were at the peripheral location, followed by the diaphragm, relative to the parameters at the other locations.



(a)



(b)

FIGURE 3. Conformal index (CI) and new conformal index (nCI) calculated by the Ray Tracing (RyTc) and Monte Carlo (MC) algorithms for (a) GTV and (b) PTV.

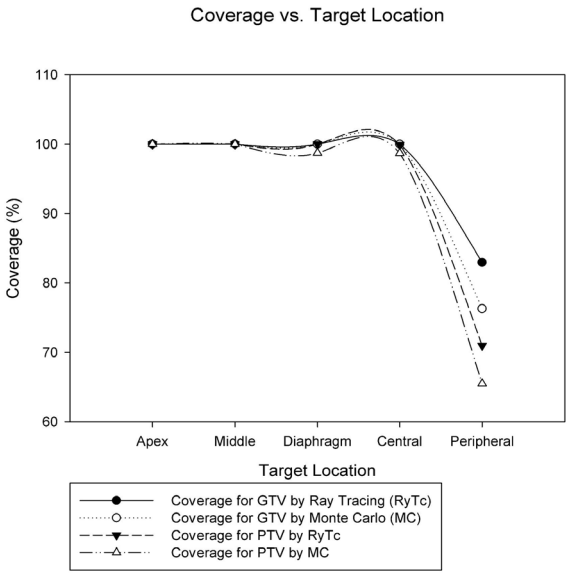


FIGURE 4. Dose coverage according to the target location calculated by the Ray Tracing (RyTc) and Monte Carlo (MC) algorithms for GTV and PTV.

The MC dose calculation algorithm in the Multiplan system is sufficiently accurate for CyberKnife treatment planning, especially in heterogeneous media [19]. The MC algorithm is strongly recommended for heterogeneous media. The results of the actual measurements are more consistent with the dose calculation by the MC algorithm [20]. The maximum doses calculated by the RyTc for targets in the lung were uniformly larger than those calculated by the MC by up to a factor of 1.32. In addition, large differences in the dose coverage were observed. The MC algorithm should be consistently used for treatment plans of lung lesions and lesions near large air cavities, but the RyTc algorithm is adequate for treatment sites with less tissue heterogeneity [21]. A previous study compared the clinical outcomes of SBRT for lung tumours between the RyTc and MC algorithms. The outcomes were similar except for the response rates when the same apparent doses were prescribed, with the lower response rate in the RyTc group [22]. This result is consistent with the general concept that the RyTc algorithm overestimates the radiation dose in heterogeneous tissue. Furthermore, Braunstein et al. evaluated the RyTc and MC algorithms for dose calculations and clinical outcomes of CyberKnife treatment of lung cancers. Compared with the MC algorithm, the RyTc algorithm largely overestimated the delivered dose. The dose difference between the RyTc and MC plans correlated with the target volume overlap with soft tissue. Larger dose differences between the RyTc and MC correlated with smaller overlap volumes. The RyTc algorithm overestimated the dose delivered to 10% of the ipsilateral lung. However, disease-free survival and overall survival were not significantly different between the RyTc and MC treatment plan [23].

Wu et al. evaluated the influence of tumour location and size of dose calculations in the RyTc and MC algorithms for use with the CyberKnife. For peripheral lung cases, the RyTc produced significantly higher dose values at all reference points than those produced by the MC. For central lung cases, there were no significant reference and organ-at-risk dose differences between the RyTc and MC algorithms. The RyTc usually overestimated the dose. The RyTc was not recommended for peripheral lung tumours regardless of the target size [17]. Although peripheral lung targets have been considered to receive greater effects from radiation doses calculated by the RyTc algorithm, the effects on other lung targets have not been explicitly confirmed. In our report, the apex, middle and diaphragm locations were checked. The diaphragm location was the second most affected by the dose calculation

algorithm after the peripheral location. The radiation dose parameters for middle and apex locations were almost unaffected by the differences in the algorithms (Table 4).

The advantages of this study were the use of phantom and fixed-cone treatment planning that provided consistent radiation delivery and simplified possible variables that may be clinically useful. Moreover, we checked all lung target locations besides the peripheral and central locations that were mentioned in other reports. However, the limitations of our study were that we only checked the symbolic target locations in the right lung, and the phantom was not able to fully simulate all of the conditions of clinical treatment. However, our results should be relevant to clinical treatment.

The European Organization for Research and Treatment of Cancer recommendations for planning and delivery of high-dose high-precision radiotherapy for lung cancer indicate that advanced dose calculation algorithms (MC based) are strongly recommended for thoracic radiotherapy because they enable more accurate computation of dose distributions [24]. Although less sophisticated algorithms have been associated with more local recurrence [25], there is no consensus yet about the clinical acceptability and relevance of the differences in the dose calculation algorithms [26]–[28]. The MC algorithm is possibly more accurate for estimating doses for tumours at the periphery of the lung [29]. Considering the findings of other studies and our results, the MC algorithm for radiation dose calculation in the lungs is indispensable in SBRT using the CyberKnife, especially at peripheral and diaphragm locations.

AUTHOR CONTRIBUTIONS

CHLin, HHC, HMT, PJC, CHLiu and IHT: technical supports on data collection and analysis; and analysed the data and imaging processing, had provided valuable suggestions and revised the manuscript.

YJH and CCH: supported the characterization of the samples, had provided valuable suggestions and revised the manuscript.

YJH, CCH and TFL: supervised the project, had given valuable advices on the proceeding of this work, designed the concept and the experiment method of the research, wrote and revised the manuscript. All authors read and approved the final manuscript.

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We thank the provider for the lung image in Figure 1 which was courtesy from pixabay.com; Pixabay License: Free for commercial use, no attribution required. https://pixabay.com/illustrations/upper-body-lung-copd-disease-944557/

COMPETING INTERESTS

The authors declare no competing interests.

DATA AVAILABILITY

The data supporting the results of this article are included within this manuscript.

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