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PHYSICS TRANSLATIONAL INVESTIGATION

Evaluation of ray tracing and Monte Carlo algorithms in dose calculation and clinical outcomes for robotic stereotactic body radiotherapy of lung cancers

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Purpose/Objective: Dose calculation in treatment planning must account for tissue heterogeneity, especially for tumors within low-density lung tissues. While Monte Carlo (MC) calculation methods are the most accurate, Ray Tracing (RT) methods are also commonly employed. We evaluated dose calculation differences between the RT and MC algorithms in central and peripheral lung tumors treated with CyberKnife SBRT to determine which planning parameters may predict dose differences. We also examined clinical outcomes of local-regional control (LRC) and long-term treatment-related toxicity as a function of calculation method.

Materials/Methods: A retrospective series of 70 patient plans (19 central and 51 peripheral lung lesions) treated between 2009 and 2011 were analyzed. Among those, 33 were primary lung cancer and 37 were metastatic lesions. Thirty-three treatment plans were developed with the RT method, and 37 plans used MC. Groups were recalculated with the reciprocal method for dose comparison. Parameters examined to quantify dose differences between the two algorithms included: dose delivered to 95% (D95) of the planning target volume (PTV), dose heterogeneity, and dose to organs at risk (OAR). Dose differences were analyzed as a function of target volume, distance to soft tissue, and fraction of target overlap with soft tissue. For the subset of primary lung tumors, LRC was assessed radiographically at a median follow-up of 19 months (mo) (range, 2 to 41 mo).

Results: Compared to MC, the RT algorithm largely overestimated the dose delivered to the PTV. The dose difference between RT and MC plans correlated to the volume of PTV overlapping with soft tissue; the smaller the overlap volume, the larger the dose differences between RT and MC. Compared to MC, the RT algorithm overestimated the dose delivered to 10% of the ipsilateral lung (D10%). Evidence of local progression was noted in only one of the 31 patients treated for primary lung malignancy. DFS and OS were not significantly different between RT and MC plans.

Conclusion: There is a significant range of discordance between MC and RT dose calculations for SBRT treated peripheral lung tumors. While variation is correlated to target size and proximity to soft tissue, no single parameter can reliably predict dose differences. Ultimately, local control and long-term toxicity appear independent of the dose calculation method.

Keywords: Monte Carlo, Ray Tracing, Heterogeneity, Dose Calculation, SBRT, Lung Cancer

1. INTRODUCTION

Stereotactic body radiation therapy (SBRT) is increasingly used for treatment of lung tumors in select

patient populations, with institutional studies demonstrating excellent local control rates of 85-97% [1-4]. These early patient populations were characterized by older age, debilitation, and multiple comorbidities. The first RTOG-sponsored randomized SBRT trials were directed at early-stage medically inoperable peripheral lung tumors [5, 6], and subsequently extended to more central lesions [7]. More recently, SBRT has also been employed in the treatment of metastatic lung tumors with results demonstrating good local control with minimal treatment related toxicity [8, 9].

Historically, non-small cell lung cancer (NSCLC) has demonstrated a dose-dependent response in terms of improved local-regional tumor control [10, 11]. Preliminary SBRT studies suggested greater clinical efficacy of doses at BED >100 Gy, to limit repair and repopulation [12]. These dosing considerations have now been established in SBRT, with BED in the range of 83.2 to 146 Gy regarded as reasonable [13-15]. SBRT planning allows for high dose conformality to maximize tumor control probability. However, there is concern for toxicity in the compact intermediate dose region, a special consideration in medically inoperable patients with comorbidities including compromised cardiopulmonary function. In conventional external beam radiotherapy, the recent results of RTOG 0617 demonstrated that dose escalation did not improve overall survival and resulted in increased toxicity [16]. Studies investigating the optimal dose schedule to maximize therapeutic efficacy with SBRT are ongoing [17].

Valid dose calculation in hypofractionated radiation therapy planning, as employed in SBRT, must account for tissue heterogeneity. This consideration is particularly important in low-density tissues, such as the lung, where particle disequilibrium occurs, yielding decreased dose deposition at the lung-tumor interface. Traditional dose calculation techniques employing equivalent path (EPL) length corrections or pencil beam (PB) algorithms fail to adequately account for tissue heterogeneity. Dose calculation methods based on Monte Carlo probabilities are generally regarded as the most accurate, although other modern algorithms such as the convolution-superposition approach are also recognized as superior to EPL or PB [18, 19]. Significant differences between RT and MC dose distribution in SBRT-treated lung cancer patients have been reported [20-23]. In particular, scaling the prescription dose according to tumor size has been recommended for MC plans [23, 24].

We evaluated dose calculation differences between two calculation algorithms utilized in SBRT-treated peripheral and central lung tumors: Ray Tracing (RT) and Monte Carlo (MC). In this study, we compared RT and MC plans to determine which planning characteristics predicted the greatest likelihood of dose differences and explored the feasibility of adjusting the prescription dose based upon those factors. Additionally, we compared the clinical outcomes of locoregional control (LRC), disease free survival (DFS), overall survival (OS) and long-term treatment-related toxicity as a function of the calculation method.

2. MATERIALS AND METHODS

A series of 70 lung tumors treated with robotic SBRT were analyzed. Patients primarily included early-stage non-small cell lung cancer and metastatic patients with oligometastatic lung lesions and/or designated for palliation and not appropriate for surgical resection. Depending on the individual patient characteristics, a range of prescription doses and fractionation schemes were employed for treatment. Lesions were categorized based on their location within the chest (central or peripheral) and size (small, medium and large). According to the definition by Timmerman et al. [25], lesions were categorized as *central* if they were located within 20 mm of the carina or main bronchus. Targets were categorized as *small* for planning target volume (PTV) ≤10 cc, *medium* for PTV >10 cc and ≤30 cc, and *large* for PTV > 30 cc. The tumor and patient characteristics are shown in Table 1 and Table 2.

Five of 19 central lesions and 17 of 51 peripheral lesions were treated with dynamic target tracking (fiducial tracking [26] or lung tumor tracking [27]), which enabled synchronization of radiation delivery to the continuously changing target position. The remainder of the patients were treated with a static tracking method (bony spine tracking [28]) using bony landmarks in the vertebral column for patient alignment. Patients with peripheral lesions were typically treated every day, while patients with central lesions were typically treated every other day.

Patients were simulated in the supine position with the arms along the torso. A simulation CT scan was acquired with a slice thickness of 1.5 mm and used as the primary image set for target delineation and dose calculation. The gross tumor volume (GTV) was contoured in the primary CT scan using lung windows. The PTV was created by expanding the GTV in 3 dimensions by 2-5 mm. However, for rare selected cases *ad hoc* margins ranging from 0 to 7 mm were applied. For patients treated using the static tracking method, an internal target volume (ITV), encompassing the entire range of target motion, was delineated. The ITV was contoured using two additional CT scans acquired at maximal inhalation and exhalation phases of respiration or more commonly, a 4D CT image set acquired over the entire respiratory cycle. In this case, the PTV

Table 1. Patient demographics.

	Peripheral	Central	Total
Cases, N (%)	51 (73%)	19 (27%)	70 (100%)
Patients, N (%)	41 (72%)	16 (28%)	57 (100%)
Median age (years)	70	60	65
Range	21-87	13-82	13-87
Median KPS*	80	70	70
Range	50-90	50-80	50-90
Median follow-up (months)	19	17	19
Range	2-40	3-41	2-41
Primary Lung Tumor			
Cases, N (%)	26 (37%)	5 (7%)	31 (44%)
Median diameter(cm)	3.9	4.2	4.2
Range	1.6-7.3	1.6-5.9	1.6-7.3
Metastases			
Cases, N (%)	25 (36%)	14 (20%)	39 (56%)
Median diameter(cm)	3.1	3.1	3.1
Range	1.1-7.6	1.8-10.3	1.1-10.3
Metastatic Histology, N			
Bladder	1	1	2
Colorectal	4	0	4
Esophageal	1	1	2
Laryngeal	1	0	1
Lung	3	7	10
Lymphoma	0	2	2
Melanoma	1	1	2
Ovarian	1	0	1
Renal	11	0	11
Sarcoma	2	0	2
Thymic	0	2	2
TOTAL	25	14	39
Treatment Calculation Method			
Ray Tracing	31	2	33
Monte Carlo	20	17	37

was created by expanding the ITV by 2-5 mm. Critical structures (spinal cord, esophagus, lungs, heart) were contoured on the primary CT scan.

Treatment plans were generated using 1 – 3 circular apertures and an average number of 148 (range 29 - 328) non-coplanar non-isocentric beams. The dose was typically prescribed to the isodose line covering 95% of the PTV volume.

For the purpose of comparison, the plans were first calculated in the Multiplan treatment planning software (Accuray Inc., Sunnyvale, CA) with either RT or MC, and then with the reciprocal method. The RT plans were calculated using a high-resolution grid, and the MC plans were calculated using a high-resolution grid and 1% uncertainty. In the recalculated plan, the dose was not re-prescribed or re-optimized. The MC and RT plans have therefore the same number of beams, beam directions, monitor units per beam and total monitor units.

The following parameters were used to quantify the magnitude of calculated dose differences between RT and MC:

Table 2. Dosimetric characteristics.

		Peripheral	Central
Cases, N (%)	Total	51 (73%)	19 (27%)
	Small	18 (26%)	2 (3%)
	Medium	14 (20%)	5 (7%)
	Large	19 (27%)	12 (17%)
PTV volume (cm)	Small	4.2 (0.8-9.8)	4.6 (3.3-5.9)
	Medium	22.8 (11-29.8)	15.1 (10.6-21.3)
	Large	64.7 (32.5-210.1)	144.9 (32.2-492.0)
Dose (Gy)	Small	32 (20-60)	34 (20-48)
	Medium	41 (12-60)	31 (16-50)
	Large	46 (20-60)	34 (10-60)
Number of Fractions	Small	1.6 (1-5)	3.0 (2-4)
Median (Range)	Medium	3.0 (1-5)	2.6 (1-5)
	Large	4.0 (1-5)	4.0 (2-5)

- Dose delivered to 95% of PTV (D95)
- Maximum PTV dose
- Mean PTV dose
- Maximum dose to the organs at risks (spinal cord, esophagus, heart)
- Dose received by 10% of ipsilateral lung (D10%)

Dose differences were analyzed as a function of target location (central or peripheral), and target volume (small, medium and large). Results were reported as a ratio between the RT dose and the MC dose. Ratio > 1 means that the RT dose is larger than the MC dose.

The following parameters were evaluated as predictors of dose differences:

- Minimum distance of PTV to soft tissue
- Volume of PTV overlapping with dense tissue (soft tissue, chest wall)
- Average target margin (GTV to PTV expansion)

The Kruskal–Wallis one-way analysis of variance test was used to determine whether changes between RT and MC were significantly different for the three tumor sizes. The Kruskal-Wallis test is a non-parametric method for determining whether more than two samples of unequal size originate from the same distribution. A Kruskal–Wallis p-value below 0.05 indicates a statistically significant difference between mean values of the data sets. The Pearson's correlation coefficient was used to measure the linear dependence between two variables.

Following SBRT, patients were followed radiographically by CT and/or PET for a median of 19 mos (range 2 to 41 mos) to assess local response to radiotherapy. Radiologist-reported imaging results were confirmed by the treating radiation oncologists. Only primary lung malignancy patients were included in the follow-up analysis, as the heterogeneous group of metastatic patients treated for oligometastatic disease or palliative intent was generally associated with poor prognosis and complicated by use of systemic therapy. Likewise, toxicity in metastatic patients was confounded by poorer performance status and more rapid systemic, including intrathoracic, progression, potentially leading to further compromised lung function. LRC, DFS, and OS of RT vs. MC generated treatment plans were compared by Kaplan-Meier actuarial survival analysis. LRC was scored as evidence of local or regional progression on interval imaging. DFS was defined as the absence of both LRC and distant recurrence outside of the radiation portal. Toxicities were graded by CTCAE v4.03.

3. RESULTS

3.1 Planning Dosimetry

The RT algorithm largely overestimates the dose delivered to the target.

Figure 1 shows an example of the dose distribution originally calculated with RT (left) and recalculated with MC (right). In the MC calculation, the prescription dose of 60 Gy (in orange) is considerably smaller, with the appearance of inadequate target coverage.

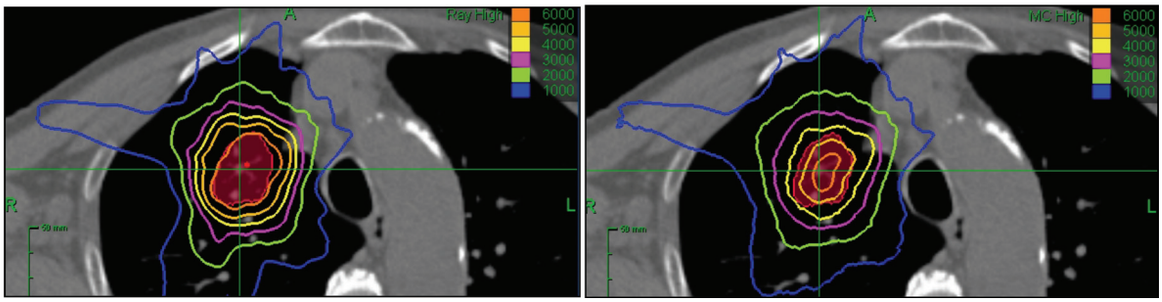

Figure 1. Example of dose distribution originally calculated with RT (left) and recalculated with MC (right).

For peripheral lesions, the ratio between the PTV D95 parameter calculated with RT and MC ranges from 1.04 to 1.60 (mean 1.32) for small targets, from 1.03 to 1.34 (mean 1.17) for medium targets, and from 1.01 to 1.34 (mean 1.11) for large targets. The difference in the D95 ratio among the three PTV sizes is statistically significant (p-value <0.0001). For central lesions, the ratio between the PTV D95 parameter calculated with RT and MC ranges from 0.97 to 1.27 (mean 1.08), with no significant differences among targets of different sizes (p-value >0.05).

Figure 2 shows a "box-plot" analysis for the ratio of PTV D95, mean PTV dose and maximum PTV dose in peripheral and central lesions. In this plot, the box has lines at the 25th percentile, 50th percentile, and 75th percentile values. For peripheral lesions, the difference in the calculated PTV doses depends significantly on the size of the lesion (p-value <0.0001 for D95, mean dose and max dose), while for central lesions, the differences in calculated dose are not statistically significant (p-value >0.05 for D95, mean dose and max dose).

Dose differences between RT and MC plans depend on the volume of PTV overlapping with dense tissue. Figure 3 shows the ratio between RT and MC D95 as a function of the overlap volume for small, medium and large size PTV. For all PTV sizes, the smaller the overlap volume, the larger the dose differences between RT and MC. In particular, in the large PTV group, the point corresponding to the largest D95 ratio (RT/MC ratio = 1.25, PTV volume =39.4 cc) has zero overlap volume; while in the small PTV group, the point corresponding to the smallest D95 ratio (RT/MC ratio = 1.05, PTV volume = 7.7 cc) has an overlap volume of 6.5 cc (i.e. 84.7% of PTV volume is in soft tissue). A correlation analysis indicated that the magnitude of dose reduction from RT to MC is associated with the volume of PTV overlapping soft tissue (Pearson correlation coefficient = -0.52). No correlation was observed between dose reduction and minimum distance to soft tissue or GTV to PTV margin.

For peripheral lesions, the dose received by 10% of the ipsilateral lung (D10%) is on average 8% lower in MC calculated plans (average RT/MC ratio =1.08), compared to RT plans. Figure 4 shows the ratio between D10% calculated with RT and MC for peripheral lesions as a function of the PTV volume. As presented in Figure 5, a strong correlation exists between the RT D10% dose and the MC D10% (r^2=1.00). For central lesions, the ipsilateral lung D10% is on average 7% lower in MC calculated plans (average RT/MC ratio =1.07, range = 0.97-1.23), compared to RT plans, and the RT and MC D10% doses are strongly correlated (r^2=1.00)

For peripheral lesions, the maximum cord dose is on average 3% lower in MC calculated plans (average RT/MC ratio =1.03), compared to RT plans. Figure 6 shows the ratio between cord maximum dose calculated with RT and MC as a function of the PTV volume. As presented in Figure 7, a strong correlation exists between the RT and the MC max dose (r^2=0.99). For central lesions, the maximum cord dose is on average 1% lower in MC calculated plans compared to RT plans (average RT/MC ratio =1.01, range = 0.95-1.11), and the RT and MC D10% doses are strongly correlated (r^2=0.99)

Doses to heart and esophagus were reported for central patients. Compared to RT plans, the dose to 1 cc of heart is on average 4% lower in MC plans (average RT/MC ratio =1.04, range = 0.95-1.31), and the dose to 1 cc of esophagus is on average 1% lower in MC plans (average RT/MC ratio =1.01, range = 0.92-1.09).

Of note, organs at risk receiving low radiation doses were generally at a far distance from the target and MC calculation uncertainty in this area can be as high as 10%.

3.2 Clinical Outcomes

A total of 57 patients were treated within this study (31 primary non-small cell lung cancer, 26 metastatic), with 9 metastatic patients receiving concurrent or interval treatments for multiple lesions yielding a total of 70 treatment plans. As shown in Table 1, diverse patient

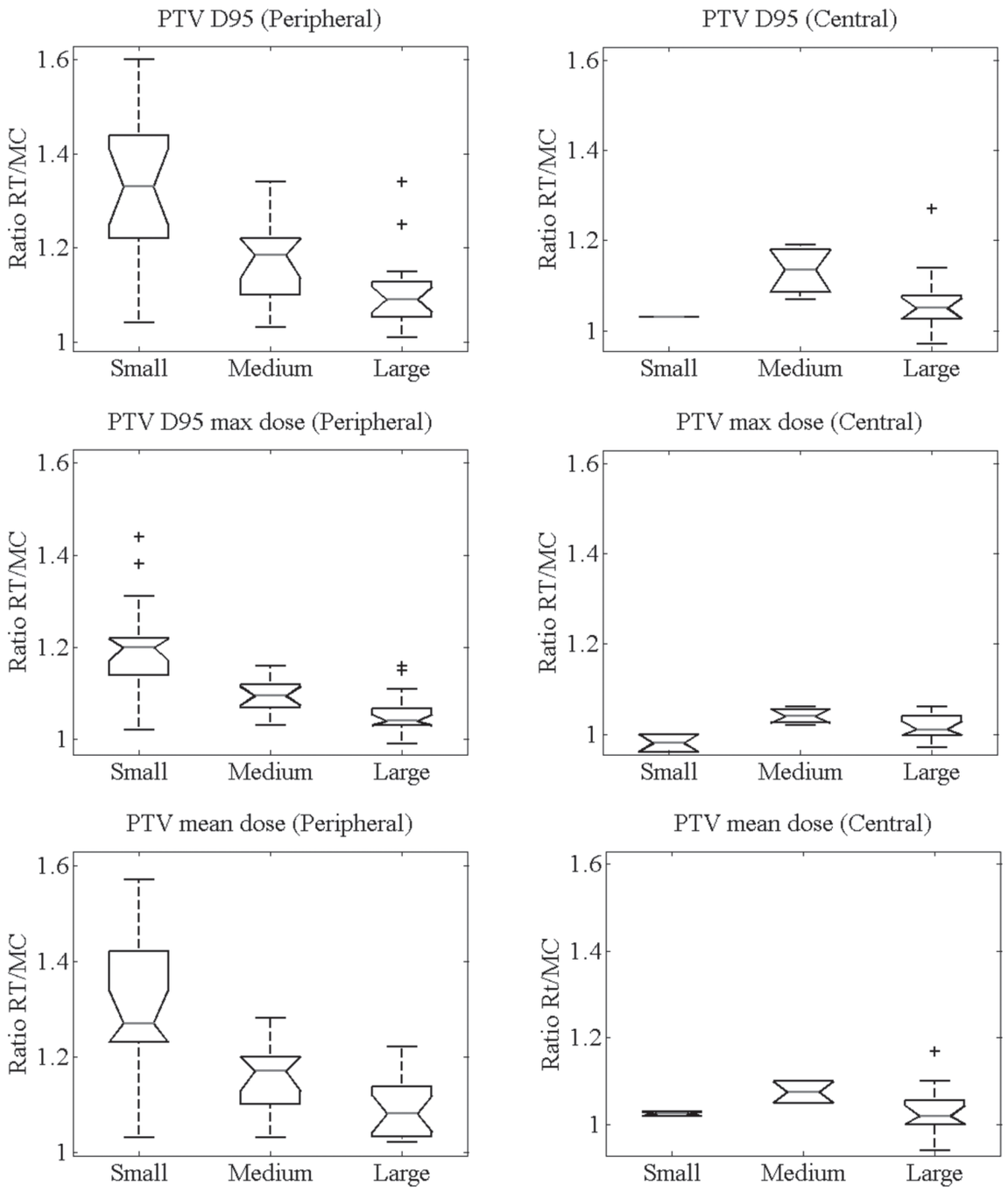

Figure 2. Box-plot analysis for the ratio of PTV D95, mean PTV dose and maximum PTV dose in peripheral and central lesions.

populations were represented. Overall, patients were largely older adults (median age 65, range 13-87), with median KPS of 70. Primary lung cancer patients were generally medically inoperable or had tumors considered unresectable. Metastatic patients were of varied histologies, with the most common types being of renal (11/39), lung (10/39), and colorectal (4/39) origin. For consistency, lesion sizes were obtained from A-P measurement of tumors on treatment planning scans. Median tumor size was 4.2 cm for primary NSCLC patients, and 3.1 cm for metastatic patients. The majority of primary NSCLC patients had early-stage, T1 or T2 tumors, less than or equal to 7 cm. Of note, there was a single peripheral NSCLC patient with a measured tumor size

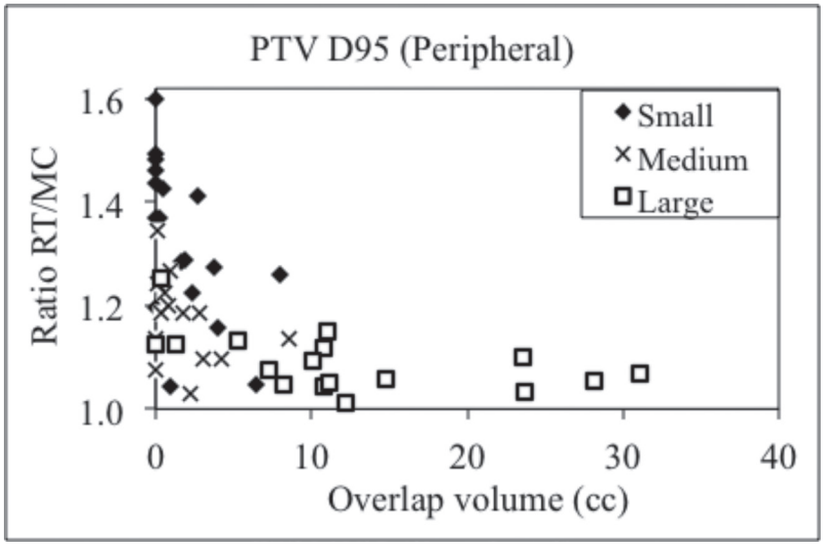

Figure 3. Ratio between RT and MC D95 as a function of the overlap volume for small, medium and large size PTV.

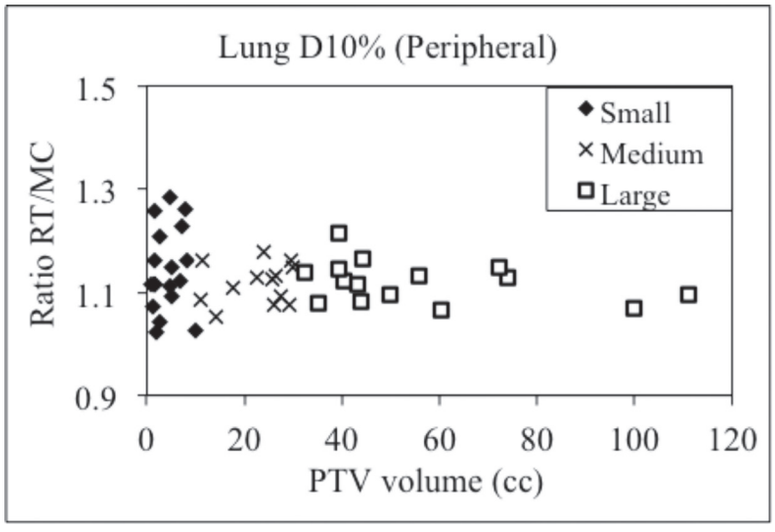

Figure 4. Ratio between ipsilateral lung D10% calculated with RT and MC for peripheral lesions as a function of the PTV volume.

of 7.3 cm on the treatment planning scan, due to slight interval growth from the time of staging scans to the time of treatment planning.

Overall, treatment was well tolerated among both primary and metastatic patients. Of the total 31 primary NSCLC patients, there were 16 RT and 15 MC plans generated. Median follow-up was 19 mo (range, 2-37 mo). The patient for whom follow-up was censored at 2 mo, expired from causes unrelated to his primary lung malignancy. Toxicity results are presented in Table 3. Three patients experienced grade 1 cough following SBRT. There was a single grade 2 event of radiation pneumonitis requiring steroids in one centrally treated lung cancer patient.

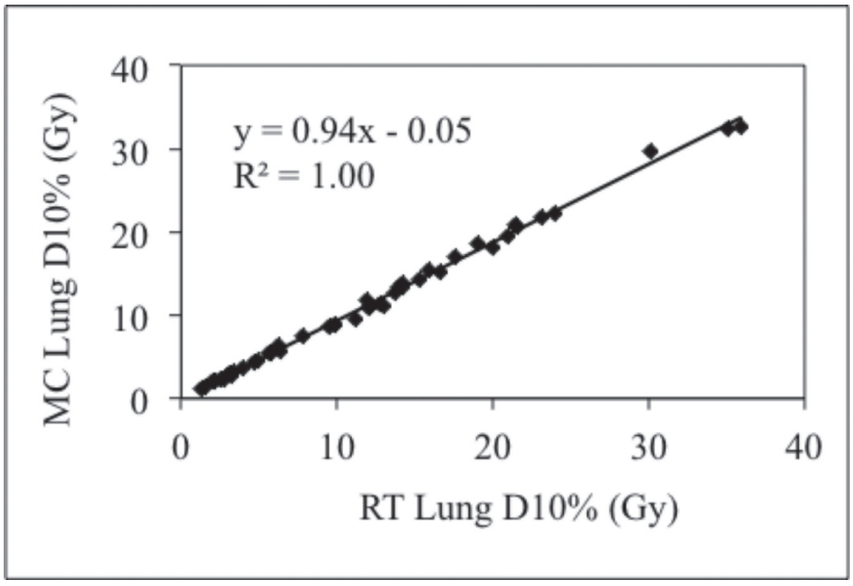

Figure 5. RT dose (D10%) as a function of MC dose for the ipsilateral lung in peripheral lesions.

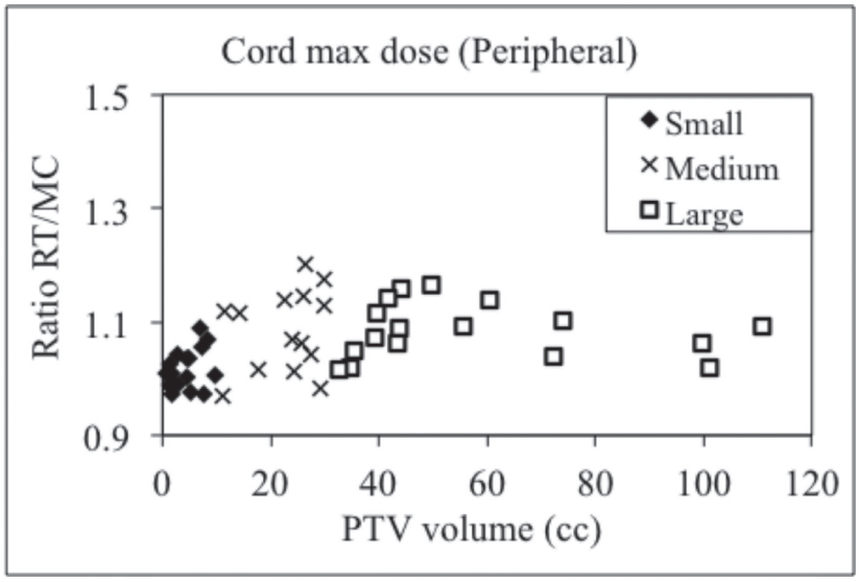

Figure 6. Ratio between cord maximum dose calculated with RT and MC for peripheral lesions as a function of the PTV volume.

Local-regional control was 93.7% for primary lung tumors, with no significant difference between RT and MC groups (Figure 8A, p=0.2568). Nine patients had no follow-up imaging due to loss of follow-up or death. There was a single peripheral T1b lung adenocarcinoma patient, treated to 50 Gy in 5 fractions with an MC calculated plan, who showed progression on interval imaging at 6 mos, with subsequent rapid progression to metastatic disease. Likewise, DFS was not significantly different between RT and MC groups (Figure 8B, 64.6% and 93.7% respectively, p=0.2498), with several patients developing metastatic disease during

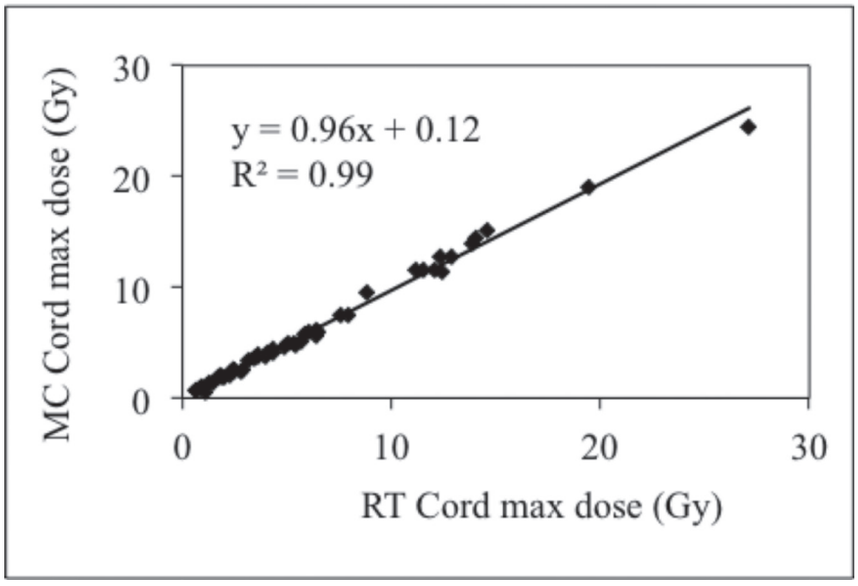

Figure 7. RT maximum dose as a function of MC maximum dose for the spinal cord in peripheral lesions.

follow-up. OS was similar at 46.3% and 55.9% for RT and MC groups, Figure 8C, p=0.5373. Furthermore, there was no relationship between RT and MC groups as a function of tumor size or location (data not shown).

4. DISCUSSION

Accumulating evidence suggests SBRT outcomes are comparable to those achieved by limited surgical resection, with superior procedural recovery time and diminished toxicity [29-31]. As a result, SBRT of early-stage lung lesions has been increasingly employed, with accumulating evidence supporting its efficacy and safety [32]. Randomized studies investigating optimum dose-fractionation schedules are ongoing [33]. Accurate dose calculations will be pivotal in order to standardize outcomes analyses between centers, with the goal of maximizing tumor control and minimizing treatment-related normal tissue toxicity. Appropriate dosing may be especially important in elderly and fragile patient populations who are at increased risk for RT-related toxicities [34, 35].

Dose-calculation methods have not been strictly specified in recent clinical trials of lung SBRT, although MC-based methods are increasingly recognized as most appropriate. In this study, we demonstrate that there is a significant range of discordance, of up to 1.6, between MC and RT dose calculations for SBRT treated peripheral lung tumors. The level of variation in the calculated dose is inversely correlated to the target size and the degree of overlap with soft tissue. The increased dose difference seen for large-volumes peripheral tumors is most likely related to a substantial tissue heterogeneity along the calculated beam paths, especially pertinent at the lung parenchyma-tumor interface, the extent of which is most profound for smaller tumors surrounded by low-density lung tissue. Overlap with soft-tissue mitigates this heterogeneity. As such, in our study there appeared to be less heterogeneity overall in calculating doses to central lung lesions, which were predominantly larger and in proximity to structures with higher tissue density. However, no single parameter can reliably predict dose differences. Our results are in agreement with that of van der Voort van Zyp et al. [24] with respect to calculation method-dependent changes in both target dose and dose to the organs at risk. We similarly observed that the average magnitude of calculated dose differences is related to target size, although the range of the dose difference was very wide, particularly for small lesions. Moreover, a strong correlation between the RT and the MC dose was noted. For peripheral lesions, van der Voort van Zyp et al. recommend a conversion of the MC prescription dose to reflect the dose (3 x 20 Gy) that would have been delivered using the RT algorithm according to tumor size (3 x16 Gy for small tumors; 3 x 17 Gy for medium tumors; and 3 x 18 Gy for large tumors). However, we believe that our results do not provide a reliable basis for this conversion. Our practice at present is to use the MC algorithm exclusively for all tumors in the thorax.

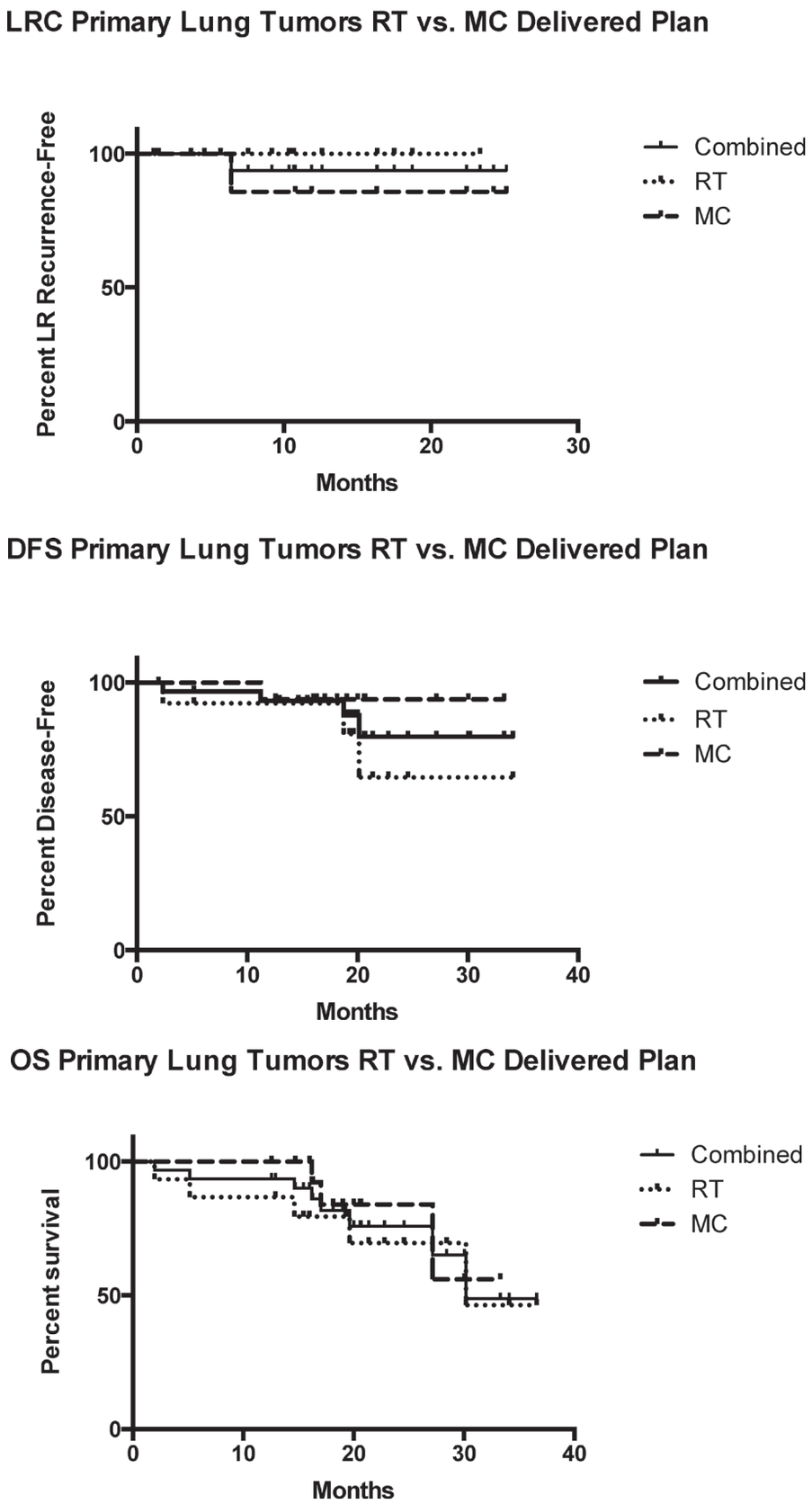

Figure 8. Clinical Outcomes for RT vs MC Radiographic LRC (A), DFS (B), and OS (C).

Table 3. Treatment related toxicity.

Symptom	Grade	Location	Total Dose (Gy)	Number of Fractions	Isodose line (%)	Dose Calculation Method
cough	1	peripheral	40	4	64	RT
cough	1	peripheral	54	5	64	MC
cough	1	peripheral	70	3	50	MC
pneumonitis	2	central	50	5	70	MC

Our results are also in agreement with those of Wilcox et al, where differences between RT and MC dose up to a factor of 1.63 are reported. However, there was no analysis of changes as a function of target size, or location of proximity to soft tissue. Those authors advocate that large discrepancies are linked to planning with smaller collimator sizes as well as the anatomical relationship of target and critical structures. We did not perform a multivariate analysis including these factors, but we recognize that dose difference may certainly be a function of the collimator size, since the collimator selection is related to the target size.

The two major advantages of lung SBRT are the excellent outcomes and overall low rate of severe treatment-related toxicity. In our study, the local-regional control and radiation-related toxicity results were excellent across the board, independent of the dose-calculation method. It must be noted that a major limitation of the outcomes comparison was the significant heterogeneity and limited long-term follow-up of our patient population. While outcome analysis was limited to the primary lung tumor subset, patients were not randomly assigned to RT and MC groups, and were unmatched for tumor and treatment characteristics, including tumor size and treatment dose.

As the target dose for MC-generated plans was on average 10-30% greater as a function of target volume and location, greater dose-dependent toxicity might have been expected as predicted from NTCP models [36]. However, there was no evidence of increased severe toxicity resulting from MC in this study. Ongoing dose escalation studies in SBRT suggest tolerance for high radiation doses to small volumes of normal lung parenchyma, and multiple studies support preserved lung function, with minimal toxicity for small tumors in patients undergoing SBRT [37-40]. Ultimately, clinically evident toxicity appears grossly independent of calculation method; tumor location may be the more relevant concern.

One challenge in follow-up assessment of SBRT-treated lesion has been the lack of established criteria for radiologic evaluation of treated lung tumors [41-44] While there was no established methodology for central imaging review as part of the study design, all follow-up scans were reviewed by the thoracic radiation oncologists. Moreover, in our cohort, the majority of patients had multiple interval follow-up imaging studies, revealing evolution in radiographic appearance of treated lesions and thus greater confidence in the assessment of treated lesion status. In any case, our observed low rates of local recurrence are consistent with previous reports, which demonstrate at least 90% local control rates for early stage NSCLC lung tumors treated with SBRT [45].

Finally, the modest overall DFS of 80% and relatively poor OS of approximately 50% are consistent with population-based data from previous surgical and SBRT series [34, 46, 47] and ultimately may be reflective of underestimation of distant disease extent at diagnosis, or non-cancer related mortality in an largely older and more afflicted population, despite excellent rates of local-regional control by SBRT. There also exists the possibility that improved LRC will be achieved through more routine use of MC-based higher target dose delivery, although this has yet to be widely reported. However, this study suggests a lack of impact of calculation method on clinical outcome of disease control irrespective of tumor characteristics, and may be due to significant tumor response over a wide range of BED [23].

Whereas the initial RTOG SBRT studies (0236 and 0618) precluded the use of heterogeneity corrections, the need to address particle non-equilibrium effects with modern dose calculation algorithms is now recognized. This study confirms a significant dose-difference between RT and MC calculation techniques. While in our study there was no discernible associated difference in toxicity or disease response, MC should be used for CyberKnife SBRT of lung patients, so that the actual dose delivered to the patient is reported. Today, MC is the only approved Cyberknife treatment planning algorithm for RTOG trials. Our results suggest

that small, isolated lung tumors may be subject to the greatest algorithm-dependent absolute dose-difference. This effect could be even further amplified in the case of lesions treated with high doses at a high conformality index. As SBRT approaches become increasingly common in the treatment of early stage NSCLC and oligometastatic disease, increased standardization of dose calculation methods and/or conversion algorithms will be essential such that optimal intrathoracic dosing parameters are properly identified.

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