Abstract

Purpose: InCise™ multileaf collimator (MLC) was introduced for CyberKnife® (CK) Robotic Radiosurgery System (CK-MLC) in 2015, and finite size pencil beam (FSPB) was the only available dose computation algorithm for treatment plans of CK-MLC system. The more advanced Monte Carlo (MC) dose calculation algorithm of lnCise™ was initially released in 2017 for the CK Precision™ treatment planning system (TPS) (v1.1) with new graphic processing unit (GPU) platform. GPU based TPS of the CK offers more accurate, faster treatment planning time and intuitive user interface with smart three-dimensional editing tools and fully automated autosegmentation tools. The MC algorithm used in CK TPS simulates the energy deposited by each individual photon and secondary particles to calculate more accurate dose. In the present study, the dose disparities between MC and FSPB algorithms for selected Stereotactic Ablative Radiation Therapy (SABR) CK-MLC treatment plans are quantified. Materials and Methods: A total of 80 CK-MLC SABR plans computed with FSPB were retrospectively reviewed and compared with MC computed results, including plans for detached lung cancer (or tumors fully surrounded by lung tissues, n = 21), nondetached lung cancer (or tumor touched the chest wall or mediastinum, n = 23), intracranial (n = 21), and pancreas lesions (n = 15). Dosimetric parameters of each planning target volume and major organs at risk (OAR) are compared in terms of normalized percentage deviations (Ndev). Results: This study revealed an average of 24.4% overestimated D95 values in plans using FSPB over MC for detached lung (n = 21) and 14.9% for nondetached lung (n = 23) lesions. No significant dose differences are found in intracranial (0.3%, n = 21) and pancreatic (0.9%, n = 15) cases. Furthermore, no significant differences were found in Ndev of OARs. Conclusion: In this study, it was found that FSPB overestimates dose to inhomogeneous treatment sites. This indicates, the employment of MC algorithm in CK-MLC-based lung SABR treatment plans is strongly suggested.

Keywords: Conformity Index, CyberKnife, finite size pencil beam, homogeneity index, Monte Carlo, stereotactic ablative radiation therapy, tissue heterogeneity

Introduction

InCise™ Multileaf Collimator (MLC) of CyberKnife® (CK) Robotic Radiosurgery System (Accuray Inc, Sunnyvale, CA, USA) with significantly improved treatment efficiency was released to clinical use in 2015. An overwhelmed concern was related to the dose discrepancies in the treatment plans computed with the then-available finite size pencil beam (FSPB) algorithm and those computed using industry well-accepted algorithms including the Monte Carlo (MC) dose algorithm.

The shorter treatment delivery time and experience with MC planning encouraged the clinical implementation of CK-MLC to stereotactic radio surgery (SRS) and stereotactic ablative radiation therapy (SABR) taking the existing advantages of the unique dynamic motion management powered by its robotic system.

The robotic arm empowered CyberKnife® consists of three types of beam collimator: Discrete fixed collimators to stereotactic radio surgery (SRS) and stereotactic ablative radiation therapy (SABR) taking the existing advantages of the unique dynamic motion management powered by its robotic system.

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(5–50 mm), Iris variable aperture collimators, and InCise MLCs for variably shaped dose-intensity-modulated beamlets.[6–8] The capability of respiration synchronized real-time motion tracking enabled the CK effectively deliver dose to a moving target, such as for lung SABR with high precision.[9–11] Otherwise much larger treatment margins have been used in such treatments.[12]

This Synchrony® Respiratory Tracking System of CK establishes a prediction three-dimensional model of moving target based on a series of paired orthogonal X-ray images correlated with the body surface motion due to respiration. During dose delivery, the synchronization model is periodically verified and adjusted to ensure its accuracy.[11,13] The clinical efficacy and reliability of CK-MLC have been demonstrated in multiple studies.[8,14,15]

The MC algorithm of lnCise™ was approved for clinical use in the new graphic processing unit (GPU) platformed Precision™ treatment planning system (TPS) (v1.1) in 2017. In this TPS, FSPB dose calculations are primarily based on the effective path length, while the MC particularly addresses the tissue heterogeneity effects on primary and scatter doses to give a more accurate dose calculation.[10,16,17] It has been widely accepted in the literature that MC shall be used in treatment planning of regions with substantial density variation, such as a tumor in the lungs or near the sinus air cavities.[16,18] Accuracy of dose calculation is an important factor to ensure that adequate dose can be delivered leading to a better clinical outcome in radiation therapy.[16,20]

The main objective of this study is to quantify the dosimetric differences between MC and FSPB dose calculation algorithms for CK-MLC plans for lung SABR and other selected anatomical sites. Initially, the beam commissioning for the MC algorithm was processed for the CK-MLC M6 system using the Accuray Precision™ TPS (v1.1). The dose calculation results report the dosimetric accuracy of MC algorithm for the CK-MLC included in the GPU platformed Precision™ TPS. Furthermore, the selected dose points of organs at risk (OAR) for critical volumes were recorded for both algorithms of each treatment plan and compared. Moreover, the quality of the treatment plans was evaluated by calculating the Radiation Therapy Oncology Group (RTOG) Conformity Index (CI) and Homogeneity Index (HI).

**Materials and Methods**

**The Monte Carlo beam commissioning for CyberKnife Precision treatment planning system**

Beam commissioning for the MC dose calculation algorithm with MLC collimators of the CyberKnife® M6 system was processed using the Accuray Precision System. Each secondary collimator type (Fixed, Iris and MLC) of CK requires independent source model.[10] The Gaussian distribution source model was selected for the system with initial full width at half maximum (FWHM) of 1.8 mm and related modeling functions for source distribution, fluence distribution, and the energy spectrum. During further tuning, MC calculated off centre ratio (OCR) and tissue phantom ratio (TPR) were compared with the measured values for all depths and field sizes with 0.2% uncertainty and the source model parameters (FWHM and energy spectrum) were adjusted accordingly. The final FWHM was determined to be 2.0 mm with 7.0 MeV energy spectrum. The computed output factors were compared with the measured values with 0.2% uncertainty. All the MC calculations are subjected to a statistical uncertainty with a trade-off between calculation time and spatial resolution.

**Treatment plan selection, dose calculation, plan comparison, quality of treatment plans and evaluation tools**

A total of 80 CK-MLC SABR treatment plans from the selected institution that had been computed with FSPB were retrospectively reviewed and recomputed with MC dose calculation algorithm. All the MC dose calculations were performed with 1% uncertainty and resolution was matched with the FSPB plans with same monitor units settings. Treatment plans included detached lung cancer (tumors fully surrounded by lung tissues, n = 21), nondetached lung cancer (tumor touched the chest wall or mediastinum, n = 23), intracranial (n = 21), and pancreas lesions (n = 15). Detached lung cancer was defined when the closest edge of tumor is 0.5 cm away from the chest wall, or mediastinum at its closest view. The prescription doses (Rx) ranged from 5000 to 6000 cGy in 5 consecutive fractions for the lung SABR, 1400–2400 cGy for intracranial single fractional SRS, and 3500–4000 cGy in 5 fractions for pancreas cases. Planning target volume (PTV) D95 coverage in all the treatment plans was 90% or greater.

The FSPB plans were compared with MC computed plans in regard to dose distribution in PTVs and OARs for each treatment site. Recorded dose parameters for each treatment site include dose to 95% (D95) volume of PTV, mean (Dmean), prescription dose (Rx), and maximum (Dmax) dose to the PTV. In addition, maximum dose to 0.03 cc of OAR for each treatment was recorded. Furthermore, selected dose points in OAR for critical volumes were recorded. Mean values for dose parameters were calculated to evaluate the effect of tissue inhomogeneity on dose calculation for MC and FSPB algorithms. The quality of the treatment plans was evaluated by calculating RTOG CI, and the HI.

**Statistical analysis**

The percentage normalized deviation

\[ \text{dev} = \left(\frac{|\text{MC} - \text{FSPB}|}{\text{FSPB}} \right) \times 100\% \]

for all dose parameters was calculated to express the percentage changes from MC to FSPB. Paired two sample t-tests with null hypothesis and Wilcoxon signed rank nonparametric test were accomplished with significance level α = 0.05 to determine the significant statistical dissimilarity between the MC and FSPB dose calculation algorithms. Spearman correlation coefficient test was carried out to determine the effect of PTV size on the normalized deviation of each dose parameter.
RESULTS

Monte Carlo commissioning for the multileaf collimator

Good agreement was found for FWHM of 2.0 mm with 7.0 MeV energy spectrum between measured and MC calculated OCR/TPR for all the field size ranges from 7.6 mm × 7.7 mm to 115.0 mm × 100.1 mm at all depths. Figure 1a presents the calculated and measured TPRs for all field sizes as a function of depth. The difference between measured and calculated TPR for all the field sizes versus depth are presented in Figure 1b. The MC calculation statistical uncertainties were 0.2% and 0.2% for the smallest and largest field size, respectively.

Figure 2 presents the x (left) and y (right) OCR profiles at 100.0 mm depth (a) for the smallest field size, 7.6 mm × 7.7 mm, and (b) for the largest field size, 115.0 mm × 100.1 mm. The average statistical uncertainty of MC calculation for the smallest and largest field size at the 100 mm depth is 0.07% and 0.07%, respectively.

MC calculated and measured output factors are compared in Figure 3. The MC calculation had an average statistical uncertainty of 0.2%. The output factor is defined as ratio of the absorbed dose at a particular field size to the absorbed dose by 60 mm fixed collimator size at 800 mm source-axis distance (SAD). All the OF for MLC are measured only at 800 mm SAD using Sun Nuclear Edge detector™.

Dosimetry comparison of Monte Carlo and finite size pencil beam computed dose distributions

The percentage normalized deviation

\[
N_{\text{dev}} = \left( \frac{\text{MC} - \text{FSPB}}{\text{FSPB}} \right) \times 100\%
\]

between MC and FSPB dose calculations was calculated for each dose parameter of all 80 treatment plans. The averaged normalized deviations for each PTV dose parameter of all treatment plans are listed in Table 1. The paired sample t-test and Wilcoxon signed-rank nonparametric tests were carried out to evaluate the significant differences in dose parameters between MC and FSPB dose calculations. The calculated P values and sign rank P values are also included in Table 1.

Figure 4 presents the comparison of \(N_{\text{dev}}\) of dose parameters through the selected treatment sites. FSPB plans of CK-MLC overestimate \(D_{95}\) of PTV by an average of 24% compared to the MC computed plans in detached lung cases, and 15% in nondetached lung cases. No significant normalized dose deviations were found for the intracranial or pancreas treatment plans. Intracranial treatment plans have \(N_{\text{dev}}\) of 0.3% and pancreas treatment plans have \(N_{\text{dev}}\) of 0.9%. Note that percentage deviation >7% is considered clinically significant.[21]

The largest differences between MC and FSPB dose calculations of the \(D_{\text{mean}}\) PTV dose parameter were found for the lung treatment plans. Specifically, ~19% for the
detached lung treatment plans and ~12% for the nondetached lung treatment plans. Intracranial ($N_{\text{dev}} = 0.6\%$) and pancreas ($N_{\text{dev}} = 0.7\%$) treatment plans have no significant differences. The $D_{\text{max}}$ of PTV has lower significant differences (<7%) between MC and FSPB dose calculation for all four treatment sites.

Overall, MC dose calculated plans show significantly reduced values ($P < 0.00001$) for lung treatment plan that are in close agreement with previous studies.\cite{21,22,23} The lung SABR plans encompass the situation with the largest tissue density heterogeneity among all the groups, especially those for detached lung tumors where the disadvantage of FSPB results to the largest percentage normalized deviation in dose computations as expected.\cite{21,22,25} These differences emphasize the lack of photon scatter correction at low tissue densities in FSPB algorithm where dose calculations are primarily based on the effective path length, while the MC dose calculation considers the heterogeneity effects on scatter dose.\cite{10,16,25}

Greater values of the standard deviations were found for all the dose parameters of selected treatment sites, indicating that the data points are broadly distributed. This may be attributed to the small sample size for each treatment site. Similar standard deviations were found in the dose comparison study by Kim et al. for the lung and breast treatment sites.\cite{25}

### The performance of planning target volume size

Normalized percentage deviations of all dose parameters between MC and FSPB were compared as a function of the PTV size for all treatment plans. The results are presented in Figure 5. Spearman correlation coefficient was carried out to represent the PTV size dependency of the $N_{\text{dev}}$ for all treatment plans.
From Figure 5a and b, dose parameters of PTV \((D_{95}, D_{\text{mean}}, D_{\text{max}})\) show larger normalized percentage deviation for the smaller PTV size of lung treatment plans. The largest % discrepancy (−53%) was found for PTV volume 17.3 cc [Figure 5b] for the case of detached lung PTV where tissue inhomogeneity is greater compared to the other treatment sites.\(^{[21,24,25]}\) For the PTV \(D_{\text{mean}}\), the largest discrepancy (42%) was found at detached lung PTV at the same tumor volume 17.3 cc as shown in Figure 5b. The largest difference (8.7%) of the PTV \(D_{\text{max}}\), was found at PTV size of 16.5 cc also located at detached lung tumor.

Table 2 lists the mean Spearman correlation coefficient values of all dose parameters of all treatment plans. The RHO values closer to ±1 show perfect relation between the \(N_{\text{dev}}\) and PTV size and closer to zero indicate that \(N_{\text{dev}}\) has weaker dependency on PTV size. No significant dependency of \(N_{\text{dev}}\) on PTV size were found for pancreas [Figure 5c] and intracranial [Figure 5d] treatment plans. \(P\) values indicate the statistically significant relation between \(N_{\text{dev}}\) and PTV size. Our results show that PTV size has weaker dependency on the \(N_{\text{dev}}\) for all dose parameters of all treatment sites.

### Radiation Therapy Oncology Group Conformity Index and Homogeneity Index

The RTOG CI and HI were calculated with both dose calculation algorithms by using the following equations:

\[
CI = \frac{V_p}{PTV} \\
HI = \frac{D_{\text{max}}}{D_p}
\]

\(V_p\) is the volume covered by the prescription isodose line, \(D_{\text{max}}\) is the maximum dose, and \(D_p\) is the prescribed dose.\(^{[26,27]}\)

The results of CI as a function of the PTV size are plotted in Figure 6. Triangles represent the CI for the treatment plans computed with the MC algorithm, and dots represent the same treatment plans calculated with the FSPB algorithm.

Plans with CI in the range of 1.0 and 2.0 are complying with RTOG protocol. Plans with CI between 0.9–1.0 and 2.0–2.5 are within minor deviations, while plans with CI >2.5 or CI <0.9 have major violations, but nevertheless acceptable.\(^{[26-30]}\) CI <1...
means that the PTV is not covered by the reference dose, and C1 >2 means that the entire PTV is covered by the reference dose, but healthy tissues are also included into the high-dose irradiation which is not negligible.\[28\]

It is found that 71.8% of the MC computed treatment plans had major deviations with CI <0.9 where the largest contribution was found in detached lung cancer treatment plans. 15.4% had no deviation from the RTOG protocol, while minor deviations occurred for 12.8%. A CI$_{\text{max}}$ = 2.8 was found in intracranial treatment plans with PTV size of 1.14 cc [Figure 6d]. The CI$_{\text{min}}$ = 0.1 was found for detached lung treatment plan [Figure 6b] and pancreas treatment plan [Figure 6c]. For the detached lung plan CI$_{\text{max}}$ occurred at three PTV sizes, 13 cc, 14 cc, and 21 cc. For the pancreas treatment plans, the CI$_{\text{min}}$ was found at PTV size of 110.9 cc.

Among all treatment plans computed with the FSPB algorithm, 91% fall within RTOG protocol. 7.7% of treatment plans show major deviations while minor deviations occur only for 1.3% of all FSPB computed treatment plans. CI$_{\text{max}}$ = 4.2 was found for the detached lung treatment plan [Figure 6b] with PTV size of 6.16 cc. The CI$_{\text{min}}$ = 0.5 appeared for the nondetached lung treatment plans with PTV size of 11.4 cc [Figure 6a].

### Homogeneity Index

Figure 7 presents the HIs as a function of PTV size for all the treatment plans. All HIs were calculated with both MC and FSPB algorithms. Triangles mark the HI for the MC treatment plans and dots mark the HI for the FSPB treatment plans.

According to the RTOG protocol, treatment plans with HI $\leq$2.0 are considered to comply with it. Treatment plans with homogeneity indices between 2.0 and 2.5 have minor deviation, while major deviations occur for HI >2.5.\[26,31\]

As shown in Figure 7 the HI values for all MC calculated and FSPB calculated treatment plans are below 2.0, meaning that all the treatment plans are within the RTOG protocol. The HI$_{\text{max}}$ of 1.4 was found for the treatment plans computed with MC. This occurred at the nondetached lung treatment plan for two PTV sizes, 11.8 cc and 54.4 cc. The corresponding HI$_{\text{max}}$ for the treatment plans computed with
FSPB was also 1.4 and it was found at the same treatment plan, nondetached lung treatment plan with the same PTV size of 54.5 cc. In general, it was found that the HI values do not change significantly with the PTV size for both algorithms.

**DISCUSSION**

In this research we study the tissue homogeneity effect on dose calculation during the CK-MLC treatment planning. The MC algorithm is well known of its ability to consider homogeneity corrections to deliver an accurate dose calculation at low tissue density medium.\textsuperscript{[10,16,17]} The dosimetric parameters of CK-MLC plans computed with MC and FSPB algorithms are quantitatively compared. From our results, FSPB overestimates dose to the lung treatment plans where PTVs are surrounded by low-density inhomogeneous lungs. This overestimation is insignificant for the intracranial and pancreas treatment plans where the tumor location is in a homogeneous area. The dose deposited in low density medium is affected by the lack of photon scatter correction at low densities and the lack of electron equilibrium in heterogeneous geometries where these factors are considered during MC dose calculation.\textsuperscript{[32]} Thus, our results imply that the MC algorithms provide accurate and optimum dose to the PTV at inhomogeneous treatment sites.

Similar results have been published by multiple studies on different treatment machines.\textsuperscript{[21,22,33-36]} In Chen et al. study, PB algorithm overestimates the dose to the PTV significantly by an average of 22.9\% for the $D_{95}$ of PTV.

In addition, insignificant dose deviations were found between MC and FSPB for the OARs for all the treatment site which may be attributed to adjustment of the distance from the PTV. Perceptible differences were found only at spinal cord for lung treatment plan. This may be attributed to electron transport corrections at inhomogeneous tissue medium by the MC. Similar findings are published in studies by Zhuang et al.\textsuperscript{[21,34]}

From the RTOG CI study, our results show that MC dose calculation has low PTV coverage compared to the FSPB dose calculation algorithm. This is suggesting that MC computed treatment plans are not satisfied with RTOG protocol. Zhuang et al. also found that MC computed treatment plans are not satisfied with RTOG protocol.\textsuperscript{[37]} All the treatment plans had the ideal RTOG HI meaning that both MC and FSPB provide homogeneous dose to the PTV. Stanley et al. also found ideal HI for all 170 treatment plans in their study.\textsuperscript{[31]}

In summary, our CI study suggests that more plan optimization is required to have a superior PTV coverage for MC evaluated CK-MLC plans. This can be done during the treatment panning. However, this study suggests that the MC algorithm provides...
more accurate dose calculation in evaluating CK-MLC plans at low tissue density regions.

**Conclusion**

The findings in this study suggest that FSPB overestimates the dose in the interface region between soft-tissue density lung tumor and low-density lung. This occurs due to the scatter electron equilibrium is built up at low density regions and doses computed by MC algorithm improves accuracy. In CK-MLC-based SABR, the plans for high heterogeneous regions, such as lungs, it is strongly recommended that MC algorithm become standard.

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**Conflicts of interest**

There are no conflicts of interest.

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