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Monte Carlo simulation for verification of lung stereotactic treatment plans delivered with an Elekta beam modulator collimator systems

S. Herwiningsih[1*] and A.L. Fielding[2]

[1]Physics Department, Faculty of Mathematics and Natural Sciences, Universitas Brawijaya, Jl. Veteran 1, Malang, East Java, 65145, Indonesia

[2]School of Chemistry and Physics, Faculty of Science, Queensland University of Technology, 2 George Street, GPO Box 2434, Brisbane, Queensland, 4001, Australia

► ***Original article***

***Corresponding author:**
Sri Herwiningsih, Ph.D.,
***E-mail:** herwin@ub.ac.id*

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ABSTRACT

Background*:** This paper makes use of Monte Carlo (MC) simulation to verify the dosimetric accuracy lung SBRT treatment plans delivered with an Elekta beam modulator multileaf collimator (MLC) system. ***Materials and Methods: Treatment plans of twenty early stage non-small cell lung carcinoma (NSCLC) patients were retrospectively re-calculated using the collapsed cone convolution (CCC) algorithm of the Pinnacle treatment planning system (TPS). Dose distributions were also calculated using the BEAMnrc and DOSXYZnrc MC user codes. A comparative analysis of target volume and organ at risk (OAR) dosimetry was performed between the TPS and MC dose calculation. A statistical analysis of the two dose distributions and parameters generated by the TPS and MC was performed to examine the significance of any differences. ***Results:*** The results showed that the TPS matched within 6% of the MC calculations for the planning treatment volume (PTV) coverage, mean and maximum PTV doses, and conformity index. The differences over all plans for the PTV were not statistically significant. For the organ at risk, the TPS overestimated the mean dose parameters over all patients but was only statistically significant for some organ at risks including the mean lung dose (MLD), V_{20Gy} to the lung and V_{30Gy} to the chest wall. ***Conclusion:*** The TPS dose calculation of lung SBRT using CCC Pinnacle[3] algorithms is relatively closer to the MC calculation, however there may be inaccuracies in the TPS dose calculation for some patients, manifesting in some of the key dosimetric parameters that are used as correlates for irradiation related complications.

INTRODUCTION

Stereotactic Body Radiotherapy (SBRT) is increasingly used to treat thoracic cancers such as lung cancer [1-3] as well as abdominal tumour sites [4, 5]. The aim of SBRT is to deliver a large dose / fraction in fewer fractions (hypo-fractionation), resulting in a higher biologically equivalent dose compared to conventional fractionation schemes. In SBRT, the toxicity to healthy tissues is minimised by high dose conformality to the target volume as well as a sharp gradient in dose around the target volume. Highly conformal hypo-fractionated treatments also require accurate targeting that is achieved through image guidance in the treatment room [6]. These characteristics of SBRT results in a requirement for an increase in the confidence of the accuracy of each stage of the planning and delivery. SBRT typically involves the delivery of very small fields of radiation to one of the most heterogeneous and low-density sites in the body, the lung. The dose calculation is made even more challenging as the tumour volume will be subject to respiratory motion. These factors make dose calculations during the treatment planning process particularly challenging such that even the most advanced analytical algorithms may no longer give an accurate representation of the delivered three-dimensional (3D) dose distribution [7]. This potential reduction in accuracy in the treatment planning system (TPS) dose calculation can have important consequences on the clinical planning protocols.

Modern radiotherapy TPS, such as Pinnacle, make use of 3D convolution algorithm to calculate the dose to a volume in the patient [8, 9]. However, the most accurate dose calculation algorithms for heterogeneous and low-density regions have been shown to be the Monte Carlo (MC) techniques [10-12]. For many years the MC based algorithms, although limited by longer computation time and a requirement for significant computational resources, have been used to investigate that accuracy of clinical dose calculations. The challenges of calculating dose accurately for lung radiotherapy has motivated

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several studies using MC algorithms [13–20]. More recently the interest in hypo-fractionated lung SBRT treatments has increased the importance of the dose calculation accuracy and the use of MC algorithms. Aarup *et al.* [21] investigated the effect of the dose calculation accuracy on tumour volume coverage for pencil beam and more advanced convolution algorithms in the Varian Eclipse and Oncentra Masterplan commercial TPS. In their study the EGSnrc code was used to calculate the dose distribution in an in-silico lung phantom with different densities of lung tissue. The different densities aimed to model the lung density changes that can occur over the respiratory cycle during an SBRT treatment. The pencil beam algorithms were shown to overestimate the dose with the effect increasing as the lung tissue density decreased. The Advanced Analytical Algorithm (AAA) of the Eclipse TPS and Collapsed Cone Convolution (CCC) algorithm of the Oncentra TPS were found to have clinically acceptable agreement with the reference MC calculated dosimetry. Panettieri *et al.* [22] performed a similar study, comparing different commercial dose calculation algorithms with the dose distributions calculated using the PENELOPE MC code. They also included respiratory motion effects in their analysis and a spatial variation in the differences between the TPS and MC. Differences of up to 10% were reported in the lung tissue close to the tumour periphery and smaller differences of 2-3 % in the central part of the tumour volume. Lax *et al.* [23] performed an in-silico phantom study of the TPS dose calculation accuracy compared to a reference MC dose calculation in the presence of respiratory motion. They found for a static case that the CCC algorithm gave better agreement than a pencil beam algorithm. Respiratory motion effects were introduced to the MC dose distribution through convolution of a motion probability density function with the static dose distribution. More significant differences between the TPS and the MC were found in the presence of respiratory motion.

We have previously reported the development of a MC model of the Elekta Axesse linear accelerator equipped with the Beam Modulator micro-collimator system [24]. This current work aims to use this MC model to investigate the dosimetric accuracy of lung SBRT plans created in the Pinnacle^3 Treatment Planning System (Philips, Stockholm, Sweden) and delivered using the Elekta Beam modulator collimator system (Elekta AB, Stockholm, Sweden). This work shows the application of an independent calculation based on Monte Carlo modelling for real clinical multiple-fields patient plans for a specific combination of the Pinnacle TPS and the Elekta Beam modulator collimator system [25]. The work evaluated the accuracy of the clinical treatment plans of non-small cell lung cancer (NSCLC) as a prelude to the implementation of SBRT, by comparing the dose distribution calculated from the TPS with the dose distribution calculated from BEAMnrc/DOSXYZnrc Monte Carlo simulation.

MATERIALS AND METHODS

This work was a retrospective study of early stage NSCLC clinical treatment plans (Stage IA/B or IIA N0M0). Institutional ethics approval was obtained prior to the start of the research work (Registration number QUT1400000993, Registration Date: 11/02/2015).

Treatment plans

Twenty clinical patient treatment plans were retrospectively evaluated in this study. The tumour diameters were all less than 5 cm, a requirement for eligibility for SBRT. The Planning Target Volumes (PTV) for the twenty plans had a median value of 29.42 cm^3 (range 18.48 to 83.80 cm^3) with 80% of the patients having a PTV volume <50 cm^3. The tumours were mostly located in the right lung and the PTV extended into the chest wall in ten plans.

All patients were treated using an Elekta Axesse™ linear accelerator with a built-in Beam Modulator™ collimator system (Elekta AB, Stockholm, Sweden). The collimation system equipped with a mini-MLC, enabled the creation of the small radiation fields required for contemporary modulated and SBRT treatments [25]. A 3D conformal technique was used for plan design, employing ten radiation beams, which had been optimised as part of a previous study on SBRT implementation. The beams were arranged as a combination of coplanar and non-coplanar beams, resulting in a conformal dose distribution to the target [26].

The Pinnacle^3 Radiotherapy TPS version 9.6 (Philips Medical System, Stockholm, Sweden) was used to create the treatment plans. All twenty patients received a four dimensional (4D) respiratory gated Computed Tomography (CT) simulation in the supine treatment position. CT slice thickness was 2 mm, as recommended for lung SBRT [27]. The Gross Tumour Volume (GTV) from 10 respiratory phase bins of the 4D CT was combined to create an Internal Target Volume (ITV). A uniform margin of 5 mm was added to ITV to create the PTV as per the clinical protocol. The dose distribution of the Pinnacle TPS plans were calculated using CCC algorithms with a 2 mm dose grid. The prescribed dose was 54 Gy delivered in 3 fractions as used in the Trans-Tasman Radiation Oncology Group (TROG) 0902 Chisel trial [28]. The plan objective was to deliver the prescribed dose to more than 95% of the PTV ($PTV_{54\ Gy}$) and 99% of the PTV should be covered by 90% of the prescribed dose ($PTV_{48.6\ Gy}$). For OARs, the dose constraints adopted the RTOG (Radiation Therapy Oncology Group) 1021 protocol [29], except for the

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ribs and chest wall constraints, which adopted from the work by Fitzgerald *et al.* [26].

Linear accelerator

The design of Elekta Axesse™ linear accelerator from the Bremsstrahlung target to the mirror is the same as other Elekta linear accelerator platforms such as the Synergy. For the Axesse system, there is an addition of a secondary collimator above the Beam Modulator micro-MLC (multi leaf collimator) and the replacement of moveable back up jaws with fixed inner and outer diaphragms. The Beam Modulator has the projected leaf spacing of 4 mm at the isocenter. It consists of 40 leaf pairs made of tungsten alloy with a rounded end and a straight leaf side which is designed to produce the small radiation fields typically required for contemporary modulated and SBRT treatments [25]. Interleaf leakage is minimized by defocusing the leaves slightly from the central axis and target. The beam transmission through a gap between a 'closed' leaf pair is minimized by positioning the unused leaf pair behind the fixed outer diaphragm of the opposed leaf bank. The collimation system is able to produce a maximum field size of 21 cm × 16 cm.

MC Modelling of the linear accelerator head

This study used the BEAMnrc user code of the general purpose EGSnrc MC code (National Research Council, Canada) [30] to simulate the transports of a 6 MV photon beam within the treatment head of the Elekta Axesse linear accelerator. The full MC model of the linear accelerator head started from the Bremsstrahlung target to the exit window of the linear accelerator head. As already mentioned, the upper part of the linear accelerator model was taken from a previously commissioned model of the Elekta Precise linear accelerator [31, 32]. The modification to the Synergy model included the secondary collimator, Beam Modulator and fixed diaphragm components.

The BEAMnrc simulation was performed to model the radiation transport of a 6 MV photon beam in the linear accelerator head with the phase space file scored at 55 cm distance from the target. The DOSXYZnrc code (National Research Council, Canada) was used to simulate the dose deposition in a cubic water phantom with a dimension of 50 cm in all directions. The surface to source distance of the model water phantom was 100 cm. The optimal incident electron energy was 6.2 MeV with an elliptical full width at half maximum (FWHM) 0.2 cm in the leaf-side direction and 0.3 cm in the leaf-end direction as reported previously [24]. The simulated dose profiles were then compared against the measured dosimetry data to validate the linear accelerator model.

Patient treatment simulations

The treatment plans were exported from the Pinnacle TPS in DICOM format consisting of patient CT images, the patient contour structures, plan data, and dose information. The simulation employed the EGSnrc/BEAMnrc codes and DOSXYZnrc codes to simulate the transport of the radiation within the linear accelerator head and the dose deposition in the patient geometry, respectively. The BEAMnrc patient treatment simulations used an electron and photon cut-off energy of 0.7 MeV and 0.01 MeV, respectively, and implemented directional bremsstrahlung splitting (DBS) to improve efficiency of the Bremsstrahlung x-ray production in the target (splitting number N_{DBS} = 1000) [33]. The simulated history was ~ 10^8 particle. A field size specific DBS splitting radius parameter was chosen to completely include the conformal radiation fields. Input files containing the Beam Modulator leaf positions for the conformal fields were created using in-house code that read the information from the DICOM RTPLAN file.

A patient model (an EGSPHANT file) in DOSXYZnrc with a uniform voxel size of 2 mm was created using an in-house variation of the CTCREATE code [34]. Computed Tomography (CT) Hounsfield units in each voxel were converted to four materials (air, lung, soft tissue and bone) as well as mass densities using a widely accepted method [35]. Each DOSXYZnrc simulation used ~5×10^8 particle histories with electron and photon cut-off energies of 0.521 and 0.01 MeV respectively resulted in statistical uncertainties of 0.4%. Photon splitting (splitting factor 10) and range rejection (ESAVE of 2 MeV) were used in the DOSXYZnrc simulations. The PRESTA-II and PRESTA-I electron step and boundary crossing algorithms were used respectively. All simulations were performed using a high-performance computing cluster environment that facilitated parallel processing of each radiation field in a batch of 10.

The dose calculated by DOSXYZnrc is in units of Gray/number of incident particles used in the simulation, while the TPS calculates the dose in Gray per Monitor Unit (MU). Direct comparison of the dose distributions was facilitated through an absolute dose calibration of the MC dose [36]. A BEAMnrc and DOSXYznrc simulation was performed that modelled the clinical absolute dose calibration setup to determine an absolute dose (to water) calibration factor for the MC dose distribution. Each patient simulation resulted in multiple 3D dose distributions $D(x,y,z)$, one for each beam. The dose at each point in the 3D grid was converted to absolute dose using equation 1 [36].

$$D(x,y,z)_{abs} = D(x,y,z)\left(\frac{D(x,y,z)_{abs}^{cal}}{D(x_{ref},y_{ref},z_{ref})^{cal}}\right)\cdot MU \qquad (1)$$

$D(x,y,z)$ is the dose at each point in Gy/incident particles for a single beam calculated by the DOSXYZnrc simulation, $D(x,y,z)_{abs}^{cal}$ is the absolute dose for the calibration set-up (normally 1 cGy/MU),

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and $D(x_{ref},y_{ref},z_{ref})^{cal}$ is the dose at the calibration reference point in Gy/incident particles calculated by the DOSXYZnrc simulation. The resulting multiple BD dose distributions were then Summed and Weighted by the number of MU, producing an integrated single 3D dose distribution that could be compared directly wrth the treatment planning system dose calculation.

Analysis

Analysis of the MC and TPS dose distributions was performed in MATLAB using the open-source CERR software toolkit (Version 4.6) [37] to ensure a consistent analysis of both dose distributions. Comparison of the MC and TPS dose distributions was performed by fast 3D gamma calculation with the acceptance criteria of 3% for the local reference dose and a distance to agreement of 3 mm [38]. The gamma calculation included the point dose larger than 10% of maximum reference dose. Dosimetric evaluation was performed for the PTV and organ at risk (OAR) by using cumulative dose volume histograms (DVHs). Target volume coverage was assessed through the volume of the target receiving 100% of the prescribed dose (PTV-$_{54\text{ -Gy}}$) and the target volume receiving 90% of the prescribed dose ($PTV_{48.6\text{ Gy}}$). The dose constraint to normal lung was evaluated using $V_{11.4Gy}$ (lung volume that received dose larger than 11.4 Gy) for the clinical endpoint of pneumonitis, $V_{10.5Gy}$ with an endpoint of grade 3 basic lung function, and V_{20Gy}. The dose constraint for the rib was evaluated using V_{40Gy} and maximum point dose to the ribs, while for the chest wall the constraint was V_{30Gy}.

Further statistical analysis of the two dose distributions and parameters generated by the MC and TPS was conducted to investigate the significance of any differences. The analysis was performed using SPSS software version 23 (IBM). The mean and the standard deviation of distributions of the different parameters were determined over all twenty patients. The distribution of the dosimetric parameters was evaluated using the normality test [39]. For the normally distributed data, paired student t-test were performed with a 95% confidence interval [40], otherwise a related Wilcoxon test were used. The upper and lower levels of agreement between the TPS and MC dose distribution was determined using the Bland-Altman test [41]. Significance was defined as the result of a particular test having a P-value less than 0.05.

RESULTS

Comparative analysis of the dose to the PTV calculated using the MC and TPS was performed using the 3D gamma calculation with acceptance criteria of 3%/3 mm. This resulted in a mean pass rate for the 20 patient plans of 99.08% (ranging from 93.7% to 100%). The gamma pass rate for the OARs was >99% using the same 3%/3mm acceptance criteria. Figure 1 shows an example of the dose distribution comparison for a single SBRT plan. For this plan, the cumulative DVH to the PTV shows an overestimation of the dose to the PTV by the MC calculation compared to the TPS algorithm.

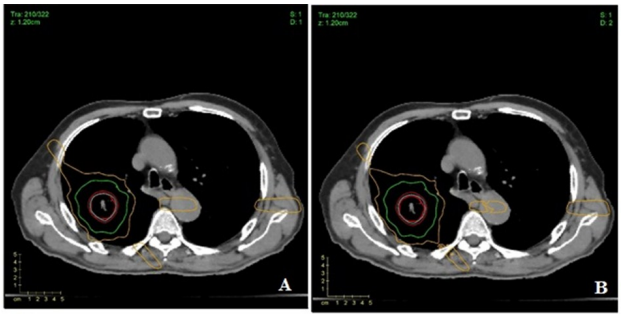


Figure 1. Isodose comparison in one of lung SBRT plans: **a)** the TPS calculation, **b)** the Monte Carlo calculation, from outer to inner lines: 20 Gy, 27 Gy, 48.6 Gy and 54 Gy. The red bold line indicates the PTV structure.

The comparison of the TPS and MC calculated dose distributions for the 20 patient SBRT plans showed here was n sIgnificant difference for the dose volume parameters to the PTV except for the maximum dose to the PTV. The TPS algorithm was found to overestimate the PTV_{54Gy} in 11 out of 20 plans, but the difference of the MC and TPS PTV_{54Gy} coverage across all plans was not statistically significant. The agreement of the PTV_{54Gy} was within ±6%. Improved agreement of ±2% was achieved for the PTV coverage of 90% of the prescribed dose ($PTV_{48.6Gy}$). For the minimum dose to the PTV, the difference for the MC and TPS for all 20 patient plans was up to -8.55%. A lower difference of ±3.5% between the TPS and MC plans was observed for the mean dose and maximum dose to the PTV.

Table 1. Dosimetric parameters to the PTV averaged over all 20 plans.

Parameters	TPS Mean± SD	Monte Carlo Mean±SD	% difference	Lower LOA	Upper LOA	p-value
D_{min} (Gy)	44.5±3.4	43.8±4.46	1.81	-6.37	9.98	0.12
D_{mean} (Gy)	64.7±3.8	64.6±4.25	0.09	-2.69	2.86	0.89
D_{max} (Gy)	79.4±10.4	78.8±10.7	0.73	-1.13	2.58	0.005
PTV_{54Gy} (%)	95.1±1.6	95.1±2.67	0.04	-4.82	4.89	0.97
$PTV_{48.6Gy}$ (%)	99.5±0.4	99.2±0.87	0.25	-0.9	1.40	0.07

SD: Standard deviation, Dmin: minimum dose to the PTV. Dmean: mean dose to the PTV Dmax: maxImum dose to the PTV, LOA: level of aqreements.

The dosimetric parameters to the normal lung, chest wall and ribs is presented in table 2. The dose constraints indicated were adopted from those specified by the RTOG 1021 protocol. This stUdy found that the $V_{10.5Gy}$ andV_{114Gy} constraints for the normalHung tissue were met for both the TPS dan MC

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dose calculations. The differences in $V_{11.4Gy}$ and $V_{10.5Gy}$ for TPS and MC calculated dose distributions were not found to be significant (p=0.45 and 0.55 respectively). The V_{20Gy} of normal lung was lower for the TPS calculation (p=0.002) although on average still well within the constraint of 15%. The V_{20Gy} was not outlined in the RTOG 1201 protocol [29] but included in the TROG 0902 CHISEL protocol [28] as it is considered a predictor for radiation pneumonitis.

The mean lung dose (MLD) was overestimated by the TPS compared to the MC (p <0.001) with an average difference of 2.81 %. The largest difference, 7.23%, was observed in plan 13, with the small PTV volume of 29.52 cm^3. However, it should be noted that for both the TPS and MC calculations the MLD was just over 4 Gy and the maximum MLD was observed in plan 5 with values of 5.44 and 5.26 Gy for TPS and MC respectively. These values are well below the MLD of 20 Gy recommended by the European Organization for Research and Treatment of Cancer (EORTC) for a hypofractionated SBRT regime [42].

Table 2. Dosimetric parameters for the normal lung, chest wall and ribs.

Critical organs	Dose constraint, unit	TPS Mean±SD	MC Mean± SD	P-value
Normal lungs	$V_{11.4Gy}$ < 1000 cm^3, cm^3	429.06±126.9	431.7±133.7	0.45
	$V_{10.5Gy}$ < 1500 cm^3, cm^3	469.4±134.04	471.4±141.8	0.55
	V_{20Gy} < 15%, %	4.30±1.53	4.37±1.53	0.002
	Mean Dose, Gy	4.11±0.18	4.01±0.19	<0.001
Chest wall	V_{30Gy} < 30 cm^3, cm^3	0.92±2.05	0.80±1.85	0.03
	V_{70Gy}< 70 cm^3, cm^3	37.87±20.00	35.44±18.61	0.001
Ribs	V_{40Gy} < 5 cm^3, cm^3	1.12±0.52	0.94±0.43	0.04
	D max < 50 Gy, Gy	45.79±15.97	45.57±19.95	0.38

Figure 2 shows the V_{30Gy} of the chest wall which was below the constraint of 30 cm^3 in eleven plans. This constraint was difficult to achieve in 7 plans which had the PTV overlapping with the chest wall, therefore the dose constraint was relaxed to 70 cm^3. The plans with the PTV overlapping the chest wall were also found to have a maximum point dose to the ribs that exceeded the constraint of 50 Gy as shown in figure 3.

This study shows that the TPS overestimated the V_{30Gy} parameter to the chest wall compared to the MC, in most of the plans with a mean difference of 50.1% when there was no PTV-chest wall overlap and 6.3% with PTV-chest wall overlap. The dose constraint for the chest wall used in this study was slightly higher from that defined by RTOG 1021 protocol. This because half of the plans used in this study had the PTV overlapping with the chest wall structure. The dose constraint of V_{30Gy} <30 cm^3 was used for the PTV that had no intersection with the chest wall and the dose constraint of V_{30Gy} <70 cm^3 was used for the PTV that overlapped the chest wall. The dose to the chest wall showed significant differences between the TPS and MC for both situations where the PTV overlapped and didn't overlap the chest wall.

A significant difference for the V_{40Gy} between the TPS and MC calculated dose was found for the ribs, while the maximum point doses did not differ significantly. The study found that the TPS overestimated the dose to the ribs in 12 plans, with the largest difference of 9.08% observed in one plan.

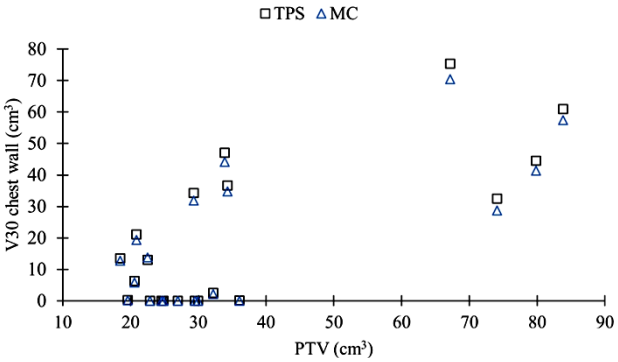


Figure 2. The V_{30Gy} of the chest wall for 20 plans. TPS: Treatment Planning System; MC: Monte Carlo

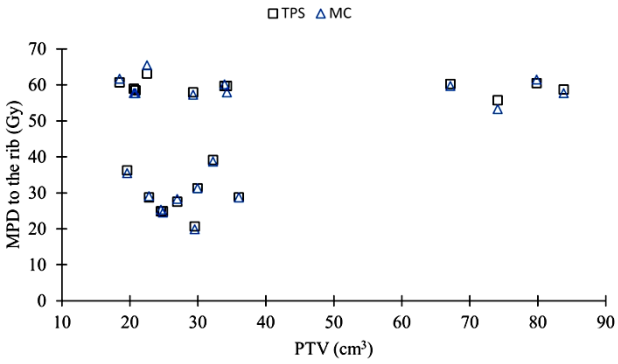


Figure 3. The maximum point dose to the ribs for the TPS and MC plans. TPS: Treatment Planning System; MC: Monte Carlo

DISCUSSION

The increasing use of SBRT for medically inoperable early stage non-small cell lung cancers requires a greater confidence in all aspects of the treatment planning as well as the delivery including the dose calculation. The use of ablative doses of greater than 10 Gy per fraction promises higher potential of local control but also may increase the risk of normal tissue complications. A further challenge is the mobility of thoracic tumours due to respiration that generally require larger target volume margin to accommodate movement during treatment delivery. This study has made use of the EGSnrc/BEAMnrc MC code to verify the accuracy of the collapsed cone convolution dose calculation algorithm implemented in the Pinnacle radiotherapy TPS for 6 MV photon treatments using an Elekta Axesse accelerator equipped with a Beam modulator

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micro-MLC.

This work shows that there was no significant difference for most dose volume parameters to the PTV between the TPS and MC calculation, except for the maximum dose to the PTV. The agreement of the TPS and MC calculation was within ± 9%. This finding is consistent with other studies where differences between the TPS and the MC calculations were 2 - 10% [13, 15-18, 43]. It is worth noting that some of these previous studies were for conventionally fractionated regimes with a lower number of treatment fields (3-7) than the plans in our current study. Calvo *et al.* [17] did study the CCC algorithm of Pinnacle against the EGSnrc MC code for 11 lung SBRT plans prescribing 45 Gy in 3 fractions using 5 coplanar IMRT beams. They found the agreement of mean dose to the PTV between the CCC algorithm and the MC of 5.6%. The difference of their study with the current work was on the technique used for radiation delivery, as our current work used a 10-field 3DCRT technique.

Analysis of the differences in the dose to selected OARs (normal lung, chest wall and ribs) showed a trend of the TPS overestimating the dose compared to the MC, exception for V_x parameters to normal lung and chest wall. The underestimation of the TPS calculation to V_{20Gy} of normal lung compared to the MC calculation was also reported by Li *et al.* [43]. Similar finding was reported by Calvo *et al.* [18] where the dose to the lung calculated by the Pinnacle TPS algorithms was lower than the MC calculation. However, the study by Fotina *et al.* [17] found that the enhanced CCC algorithm overestimated the dose to the lung. This study shows that the value of all the dose parameters to the lung were still below the dose constraints defined in the RTOG 1021 trial protocol. This indicates that the difference between the TPS and MC calculation might not be clinically significant.

For the dose parameters to the chest wall, the constraints were fulfilled in most of the plans, with an exception in one plan which had a V_{30Gy} >70 cm^3. This might associate with a higher risk of chest wall toxicity. The volume of the chest wallreceiving a hioh dose has been shown to be imnportant 44 as a predictor for an increased risk of toxiCIty ndludng pain and in extreme cases fractures. Knowing the chest wall dose accurately is therefore important. Important finding was also found in the maximum dose received by the ribs, where the maximum doses exceeded the dose constraints (i.e., 50 Gy) in 11 plans that had the PTV located at or close to the chest wall. Andolino *et al.* [44] reported that a dose larger than 50 Gy to the ribs cases a significant increase in chest wall toxicity. This indicates that the probability of the rib fracture and/or chest wall pain is higher for tumours located at the chest wall.

It is worth noting that the difference in scoring dose between the TPS and MC. The TPS calculates the dose to water in each voxel while the MC calculates the dose to medium [45-47]. In soft-tissue the difference would not be expected to be significant however in bone structures such as the ribs the dose-to-water would be expected to be higher than the dose-to-bone as reported by Andreo *et al.* [48]. This might cause uncertainty in the dose conversion from conversion of the Monte Carlo plan from dose-to-tissue to dose-to-water.

A common result of this study was that small significant differences were seen between the TPS and MC doses to the OARs, but the dose was still well within the clinical constraint. It could be argued that this makes the difference clinically insignificant. However, significant variations in differences between the TPS and MC dosimetry were seen at the individual patient level. Since the TPS calculations still satisfied the dosimetric requirement outlined in the RTOG 1021 protocol, the CCC algorithms implemented in the Pinnacle^3 TPS are still accurate enough for lung SBRT planning.

There are some limitations of this study which come from the use of small number of materials in the patient tissue composition in the Monte Carlo simulation and from the impact of Monte Carlo dose conversion from dose-to-tissue to dose-to-water. In this study the patient geometry was only defined using 4 materials, i.e., air, lung, soft tissue and bone. The adipose/fat and muscle tissues were not defined, which might have an impact to the calculation of the dose to the lung and other organs that might be composed by the adipose tissue.

CONCLUSIONS

This study has investigated the accuracy of the Pinnacle Collapsed Cone Convolution algorithm for modelling the dose delivered by an Elekta Axesse accelerator and integrated Beam Modulator micro-MLC for lung SBRT. It has been found that the MC calculations agreed to the TPS calculation to within 6% for the PTV coverage, PTV mean and maximum dose, and the conformity index. The dose received by the OARs was slightly higher in the TPS calculation, however the difference was only statistically significant for some OARS including the mean lung dose, V_{20Gy} to the lung, and V_{30Gy} to the chest wall which are all known to correlate with toxicity. The study indicated that some caution may need to be shown when considering the planned doses to the lung and chest wall/ribs for clinical SBRT. However, it is worth noting that even where differences were shown the doses were generally still within the RTOG 1021 protocol constraints. Additionally, more complex modulated deliveries such as IMRT and VMAT are increasingly being used and could introduce further inaccuracy into dose calculations by clinical treatment planning algorithms. Further research is recommended.

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***Conflict of Interest*:** There is no conflict of interest associated with this publication.

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***Ethical approval*:** This study is a part of PhD project titled "Dosimetric Verification of Stereotactic Body Radiotherapy Treatment Plans for Early Stage Non-Small Lung Cancer Using Monte Carlo Simulation" Approved by QUT Human Research Ethics Committee, QLD, Australia (Number 1400000993, Registration Date: 11/02/2015).

***Author contributions*:** We declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere. S. Herwiningsih and A. Fielding confirm contributions in the study conception and design, analysis and interpretation of results, manuscript preparation and editing. Data collection was conducted by S. Herwiningsih. All authors approved the final version of the manuscript.

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