Evaluation of Lung Density and Its Dosimetric Impact on Lung Cancer Radiotherapy: A Simulation Study

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ABSTRACT

Background: The dosimetric parameters required in lung cancer radiation therapy are taken from a homogeneous water phantom; however, during treatment, the expected results are being affected because of its inhomogeneity. Therefore, it becomes necessary to quantify these deviations.

Objective: The present study has been undertaken to find out inter- and intra-lung density variations and its dosimetric impact on lung cancer radiotherapy using Monte Carlo code FLUKA and PBC algorithms.

Material and Methods: Density of 100 lungs was recorded from their CT images along with age. Then, after PDD calculated by FLUKA MC Code and PBC algorithm for virtual phantom having density 0.2 gm/cm^3 and 0.4 gm/cm^3 (density range obtained from CT images of 100 lungs) using Co-60 10 x10 cm^2 beams were compared.

Results: Average left and right lung densities were 0.275±0.387 and 0.270±0.383 respectively. The deviation in PBC calculated PDD were (+)216%, (+91%), (+)45%, (+)26.88%, (+)14%, (-)1%, (+)2%, (-)0.4%, (-)1%, (+)1%, (+)4%, (+)4.5% for 0.4 gm/cm^3 and (+)311%, (+)177%, (+)118%, (+)90.95%, (+)72.23%, (+)55.83% ,(+)38.85%, (+)28.80%, (+)21.79%, (+)15.95%, (+)1.67%, (-) 2.13%, (+)1.27%, (+)0.35%, (-)1.79%, (-)2.75% for 0.2 gm/cm^3 density mediums at depths of 1mm, 2mm, 3mm, 4mm, 5mm, 6 mm, 7 mm, 8mm, 9mm,10mm, 15mm, 30mm, 40mm, 50mm, 80mm and 100 mm, respectively.

Conclusion: Large variations in inter- and intra- lung density were recorded. PBC overestimated the dose at air/lung interface as well as inside lung. The results of Monte Carlo simulation can be used to assess the performance of other treatment planning systems used in lung cancer radiotherapy.

Keywords

PBC, Monte Carlo Code FLUKA, Variation in Lung Density, Virtual Phantom, Computed Tomography.

Introduction

Success of radiotherapy depends on the accurate dose delivery to the tumor and at the same time minimum dose to normal tissues. To achieve this, knowledge of accurate density of organs coming into the treatment beams is necessary. Human body consists of a variety of tissues and cavities with different physical and radiological properties. Most important among these are tissues and cavities that are radiologically different from water such as lungs and oral cavities. The

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dose distribution is affected by these tissue inhomogeneities due to difference in density and atomic number compared to water. The presence of inhomogeneity in the path of photon beam will produce increased/decreased transmission depending upon the density and atomic number of inhomogeneity. These decreased/increased photon scatter and the loss of electronic equilibrium result in increased or decreased dose near and inside the inhomogeneity. Lung tissues have different density compared to other organs. Also, lung is one of the most heterogeneous organs in itself. Therefore, it creates more problems as far as lung cancer radiotherapy concerns [1].

A number of methods have been devised to correct these inhomogenieties such as; equivalent tissue air ratio method, isodoe shift, Batho power law, etc. These conventional factor-based algorithms are found not to be able to predict accurate dose distribution in all clinical situations. Several modifications have been incorporated to increase the accuracy of these methods time to time [2-4].

Since its innovation, Computed Tomographic (CT) scanner has been the best tool for density determination. It is the CT data that is used in the treatment planning system (TPSs) for the dose calculation in modern era.

Among current algorithms used in radiotherapy planning, Monte Carlo method is only able to take care of all aspects of interaction of radiation with matter [5]. Along with these features, Monte Carlo simulation code facilitates features of creation of virtual inhomogeneous phantom as found in real practice, and measurement can be performed without measuring equipment. Several Monte Carlo codes are used in radiotherapy treatment planning calculation. In this work, Monte Carlo FLUKA code was used to assess the impact of variation in lung density on dose delivery in lung cancer radiotherapy [6-10].

Aim

The present study has been undertaken to evaluate the inter- and intra-lung density variations and its dosimetric impact on lung cancer radiotherapy using Monte Carlo code FLUKA and pencil beam convolution (PBC) algorithm.

Material and Methods

Patients registered in the department of radiotherapy were enrolled in this study. Figure 1 depicts the age distribution of 50 patients included in this study. All enrolled patients had undergone Computed Tomography (CT) scan in the supine position breathing normally as in the normal radiotherapy procedure. The CT scan (Somatom, Siemens Healthcare; US) images of inter slice thickness 3 mm were taken. These images were stored at the console of CT to evaluate lung density taking three transverse sections one each from the apex, middle and the base of the lung as in Figures 2-4. The same criterion was used for both left and right lungs of each patient. Further, to investigate the intra-lung density variation in the anterior-posterior direction, four planes were selected and average density was calculated using Hounsfield unit as given in equation (1):

$$D = 1.000+0.001N_{CT} \qquad (1)$$

Where D is the electron density (gm/cm^3) of lung tissue relative to water and N_{CT} is HU

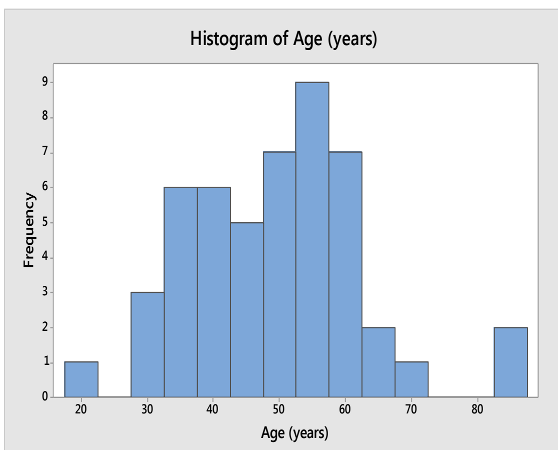

Figure 1: Age Distribution

Figure 2: Transverse section of Upper lung along with the four points (circles) to record the intra lung density of right and left lungs

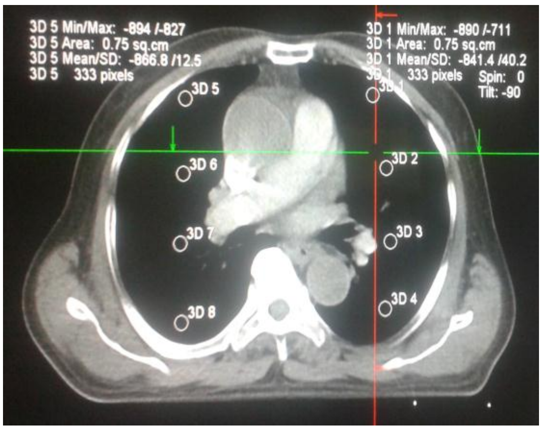

Figure 3: Transverse section of Upper lung along with the four points (circles) to record the intra lung density of right and left lungs

which can be defined in terms of the attenuation coefficients of the material under investigation and water [11].

Monte Carlo Simulation

For simulation purposes, we have used FLUKA, a general purpose Monte Carlo code capable of handling KV range to cosmic ray energy. FLUKA code can be used in various fields including medical and accelerator physics. It is widely used for simulation of transportation of particles and interaction of

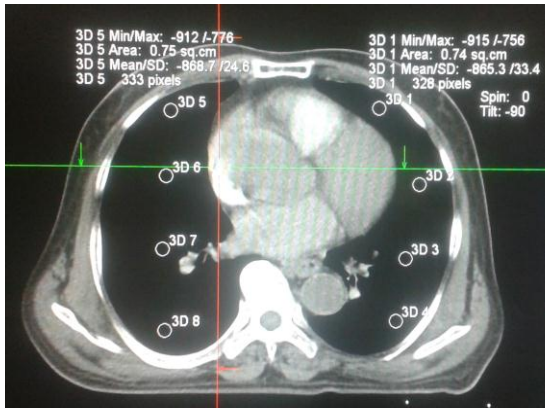

Figure 4: Transverse section of Lower lung along with the four points (circles) to record the intra lung density of right and left lungs

radiation with matter, calorimetry, cosmic ray interaction, radiation protection, detector design, target design dosimetry, space mission, radiobiology, radiotherapy, beam-machine interaction, etc. FLUKA can handle as many as 60 different particles including photon and electron ranging from Kev to TeV and can handle very complex geometry using combinational geometry package. FLUKA works on physical models and performs electron transport using multi-scattering approach.

The problem geometry provided in Figure 5 has been incorporated into Monte Carlo code FLUKA. A conical photon beam emitted by Co-60 source at a distance of 80 cm from detector (phantom) surface has been used in simulation. The average energy of the photon beam emitted from Co-60 source is assumed to be 1.25 MeV. The beam is collimated from the starting of the detector surface to a field size of 10 cm x 10 cm. Various materials have been used to fill the phantom of 30 cm x 30 cm x 30 cm. EM-CASCA default option was selected for the particle transport. USRBIN cards have been used for dose scoring in the phantom at bin size of 1 mm. Number of primary particles has been selected in such a way that relative errors in the estimated doses were <1%.

The performance of FLUKA code was validated by comparing the PDDs along central

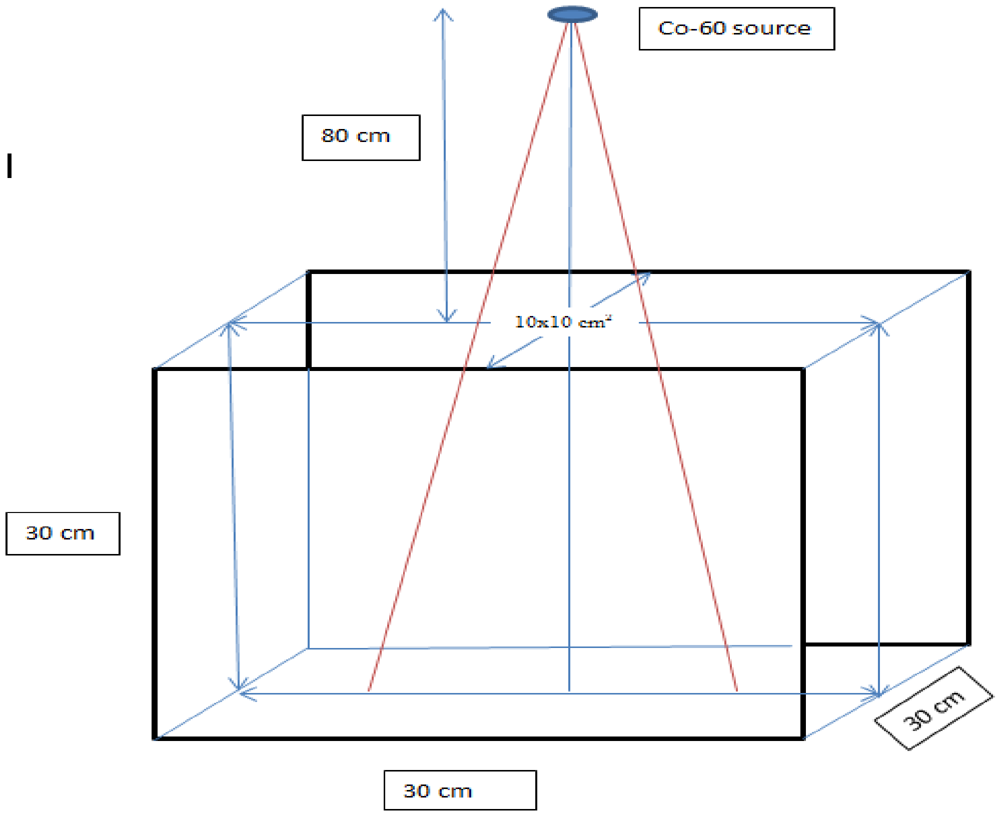

Figure 5: Phantom setup for the calculation of PDD for medium having (1) Water equivalent (2) 0.4 gm/cm3 (3) 0.2gm/cm^3 density

axis generated from the simulation of 10x10 cm^2 field size of C0-60 employed to irradiate the 30x30x30 cm^3 water phantom and PDD of 10x10 cm^2 from BJR supplement 25 data [12]. Simulations were also performed by replacing water with another medium having density 0.2 gm/cm^3, 0.27 gm/cm^3 and 0.4 gm/cm^3, respectively.

TPS Measurement

To assess the dose calculation accuracy of commercially available PBC algorithm based TPS (Eclipse V 8.6) on variation in lung density. Eclipse TPS (V 8.6) provides the feature of assigning a particular density value to phantom created inside it. To validate the results from TPS, virtual phantom of dimension 30x30x30 cm^3 was created assigning water equivalent density and PDD was obtained along the central axis and was compared with standard BJR report. To assess the impact of variation in lung density on PDD, a virtual phantom of dimension 30x30x30 cm^3 was created and assigned lung equivalent densities of 0.2 gm/cm^3 and 0.4 gm/cm^3 that were obtained from 100 lungs using the above-mentioned procedure.

Results

The variation in lung density with age was found. We have found a relationship between age and respective density of lung. Interestingly, there is slight variation in relationship between age and lung density for left and right lungs for the same patient.

$$Y= -0.0012x+0.3341 \quad \text{(left lung)}$$
$$Y= -0.0015x+0.3424 \quad \text{(right lung)}$$

Figures 6 and 7 demonstrate the variation of lung density with age. Average left lung density for the sample was found 0.275±0.387 and

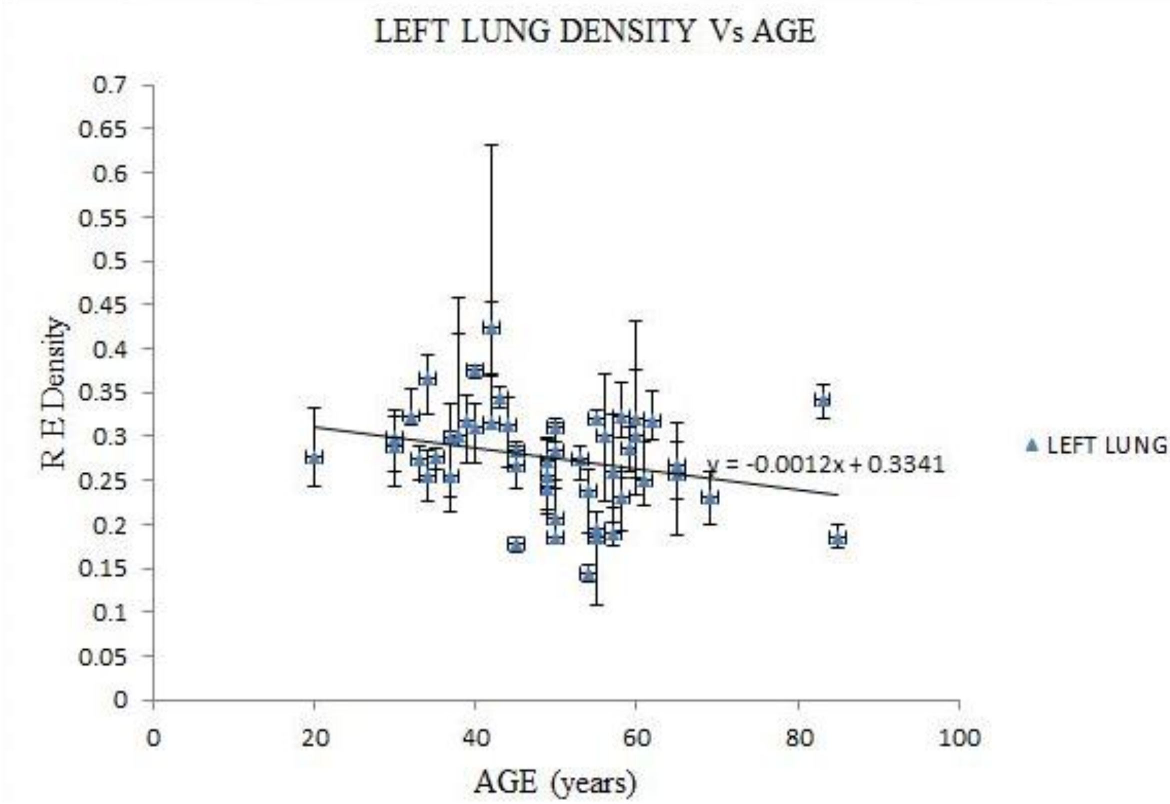

Figure 6: Variation of left lung density with age

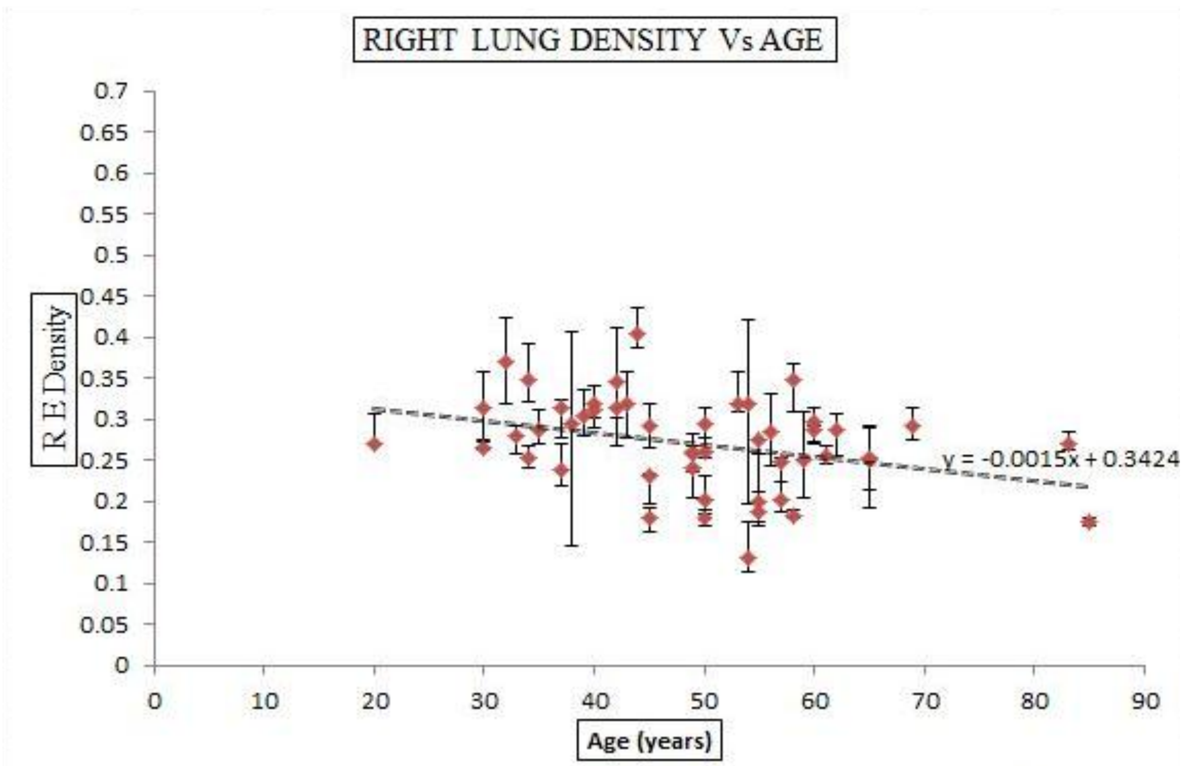

Figure 7: Variation of right lung density with age

correlation coefficient with age was -0.2765. Similarly, average right lung density was found 0.270±0.383 with correlation coefficient -0.3478. The correlation coefficient between the density of left and right lung was 0.8258. From these density data, a relationship between age and lung density was established using the least square fit method [13]. Table 1 contains the calculated lung density using the relationship found from the least square fit method for a particular age.

Validation of TPS and FLUKA Code

For the validation purposes, FLUKA MC Code derived PDD of water equivalent medium were compared with BJR supplement 25 values. As shown in Table 2, difference of less than 0.5 % was found between two PDDs. Moreover, Pearson's correlation coefficient was found 0.997 for FLUKA PDDs and BJR PDDs values with p value 0.00001. Similarly, negligible difference between TPS calculated PDD and BJR PDDs value was found with Pearsons's correlation coefficient 1.

Table 1: Lung density calculated by least square fit method for different ages.

Age	Calculated Lung Density
5	0.331
10	0.253
15	0.318
20	0.310
25	0.305
30	0.299
35	0.292
40	0.286
45	0.279
50	0.273
55	0.266
60	0.260
65	0.253
70	0.247
75	0.240
80	0.234

Comparison of PBC Algorithm and FLUKA MC Code

The difference in FLUKA calculated PDD for water and lung equivalent medium(s) of density 0.2 gm/cm^3 (0.4 gm/cm^3) were 21.75% (16.18%), 41.54(13.39), 9.64(-3.26), -3.07(-0.85), -6.80(-2.44), -9.96(2.39), -8.6(-7.38) at 1 mm, 5 mm, 10 mm, 15 mm, 20 mm, 25 mm, 30 mm depths (Figure 8).

PDDs for the mediums having density 0.2 gm/cm^3 and 0.4 gm/cm^3 were generated for 10x10 cm^2 field size using FLUKA code and PBC algorithm-based TPS (Eclipse V 8.6). Significant difference in PDDs from these two was observed. With increase in density, PDD was found decreasing; however, PDDs corresponding to depths less than depth of maximum dose (Dmax) Figure 2 showed an opposite trend. At 5 mm depth, PDDs were 99.00% and 86.61% from PBC algorithm and FLUKA code respectively for medium having density 0.4 gm/cm^3. Similarly, for medium having density 0.2 gm/cm^3, the PDDs were 100% and 58.46% from PBC algorithm and FLUKA code respectively at depth 5 mm. However, opposite

Table 2: Comparison of PDDs generated by MC Code FLUKA with BJR report.

Depth (cm) in Water	PDD		Difference
	MC	BJR	
1	96.74	98.1	0.01%
2	93.37	93.7	-0.35%
3	88.31	88.7	-0.43%
4	83.55	83.7	-0.18%
5	78.8	78.8	0%
6	74.36	73.9	-0.60%
7	69.70	69.3	-0.57%
8	64.78	64.7	0.12%
9	60.53	60.5	0.00%
10	56.41	56.4	0.00%

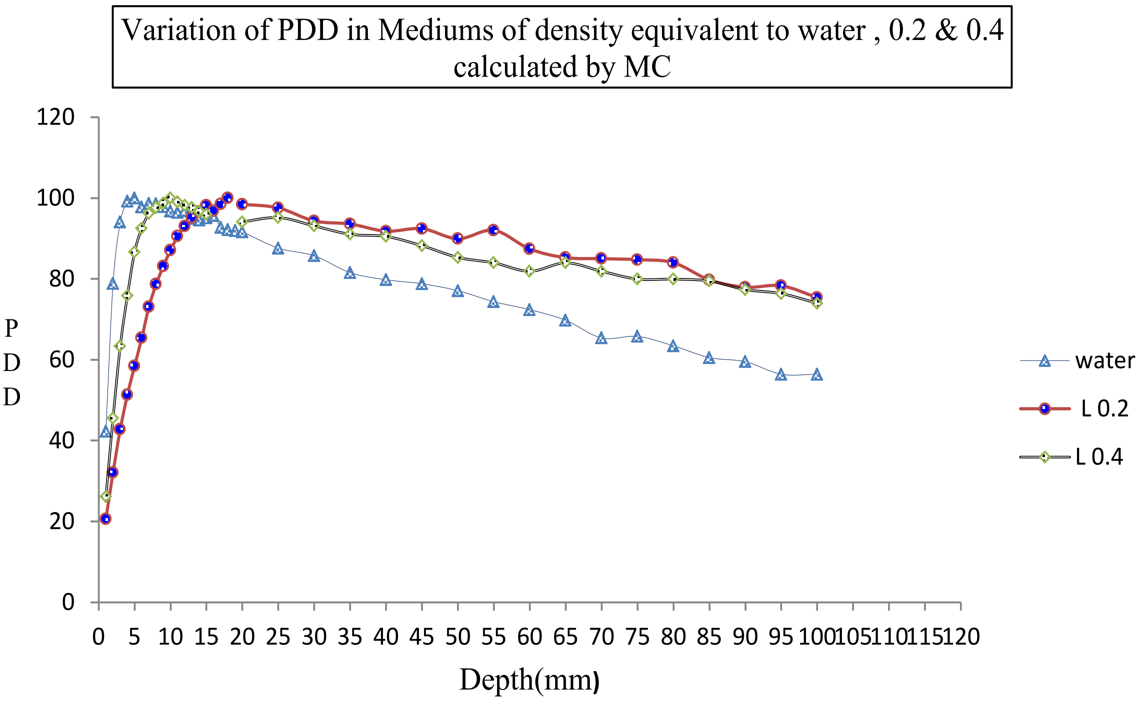

Figure 8: FLUKA MC Code generated PDD curve for the set up shown in Figure 6

to this trend, PDDs were 89.92% and 85.30% for density 0.2 gm/cm^3 and 0.4 gm/cm^3 produced by FLUKA MC Code. The percentage deviation in PBC calculated PDD compared to FLUKA code were (+)216%, (+91%), (+)45%, (+)26.88%,14%, -1%, 2%, -0.4%, -1%, 1%, 4%, 4.5% at 1mm, 2mm, 3mm, 4mm, 5mm, 10mm, 15mm, 30mm, 40mm, 50mm, 80mm and 100 mm, respectively in 0.4 gm/cm^3. In case of medium having density 0.2 gm/cm^3, the percentage deviations were 311%, 177%, 118%, 90.95%, 72.23%, 55.83%, 38.85%, 28.80%, 21.79%, 15.95%, 1.67%, -2.13%, 1.27%, 0.35%, -1.79%, -2.75% at 1mm, 2mm, 3mm, 4mm, 5mm, 6 mm, 7 mm, 8mm, 9mm ,10mm, 15mm, 30mm, 40mm, 50mm, 80mm and 100 mm, respectively.

Discussion

From the results, it was found that lung density varies. The range of lung density was found to be 0.45 to 0.2 with average 0.275gm/cm^3. A tendency of decrease in lung density with age was found. Fujisaki T et al. evaluated experimentally and theoretically the impact of change in lung density on dose distribution during lung cancer stereotactic radiotherapy by determining the relative electron density of 30 patients from their CT images, and similar to the present study, a decrease in lung density with age was recorded [14]. To validate the accuracy of CT, quality assurance tests were performed as recommended for clinical purposes and results were under tolerance.

The data used for the calculation of treatment time in manual as well as algorithm-based TPSs for cancer of lung (inhomogeneous in nature) treatment are taken from the measurements done on water phantom (homogenous) [15]. To quantify the impact of this ambiguity between inhomogeneous and homogeneous, authors recorded the PDD for the mediums having density 1 gm/cm^3 (water) and 0.20 gm/cm3 and 0.4 gm/cm^3 (lung equivalent).

Change in PDD from 78.80% to 87.05% and from 65.78% to 79.57% at 5 cm and 8 cm depth respectively was found due to the change in density from 1 gm/cm^3 to 0.275 gm/

cm^3 for 10x10 cm^2 Co-60 beams. RD Praveen kumar *et al.* conducted a study to estimate the inhomogeneity correction factors for Co-60 beam using Monte Carlo simulation. Results of current study also indicated that inhomogeneity correction factors should be applied in case of manual planning for accurate dose delivery [16].

The variation in density of lung along the path of radiation produces disequilibrium of electron transport. Additionally, the difference in density between body tissue and lung produces the same event. Monte Carlo (model-based) algorithms have shown the best performance in existing algorithms incorporating all these inhomogeneities [17]. The variation in lung density requires attention not only in manual planning but also in sophisticated TPS that uses algorithms for the dose distribution calculation taking variations in density including lung, different density tissues and bone.

In current study, to demonstrate the dosimetric impact of variation in lung density compared to water (approximately tissue equivalent) as well as variation in lung density itself, phantoms were created of dimension 30x30x30cm^3 (Figure 5) in Monte Carlo simulation code as well as in TPS. Phantoms of 0.4gm/cm^3 density & 0.2 gm/cm^3 density and tissue equivalent density were created. PDD was recorded from the dose calculated by MC code FLUKA for each density using 10x10 cm^2 field size beam of Co-60. Figure 8 demonstrates the PDD Vs Depth for different densities and depicts the fact that as depth of point of interest increases, the difference in PDD increases more rapidly. Table 3 illustrates difference of PDDs of water equivalent medium and medium having lung equivalent density. These differences cause overdosing (especially in manual planning) when not taken into consideration (Figure 9). However, at the surface of inhomogeneity like lung equivalent mediums electronic disequilibrium creates additional source of error [18].

As depicted in Figures 10 and 11, difference between PBC and FLUKA MC was the highest for the depths ranging from 1mm to ~20 mm.

Table 3: Comparison of PDDs for water equivalent and Lung equivalent mediums generated by MC code FLUKA

Depth (cm)	PDD		Difference
	Water Equivalent	Lung Equivalent (0.275gm/cm^3)	
1	96.74	91.93	-04.97%
2	92.37	95.78	03.69%
3	87.61	93.55	08.93%
4	81.55	90.65	13.31%
5	78.8	87.05	12.65%
6	74.36	83.94	15.53%
7	69.70	83.05	19.91%
8	65.78	79.57	20.96%
9	60.53	77.56	28.18%
10	56.41	74.51	32.08%

In the present study, the performance of PBC algorithms was compared with MC Code FLUKA. Overestimation of the range 300%-2% in 0.2 gm/cm^3 and 200%-1% in 0.4 gm/cm^3 density medium was produced by PBC algorithm compared to FLUKA MC Code [19].

As reported in earlier studies, PBC performs in poor way in case of lung tumor. PBC calculates dose taking a ray from the source of beam. To incorporate the density variations, each beam undergoes inhomogeneity corrections; however, the laxity of adjacent beams in dose deposition produces inaccurate results [20].

It was observed from the results that deviation was higher in 0.2 gm/cm^3 compared to 0.4 gm/cm^3 (Figure 8). The deviation in PBC calculated PDD was found in deeper point of interests as well as in depth of maximum dose (Dmax). The PBC calculated Dmax for 0.2 gm/cm^3 and 0.4 gm/cm^3 were 6 mm and 5 mm, whereas FLUKA produced 10 mm and 18 mm, respectively (Table 4). Such a type of

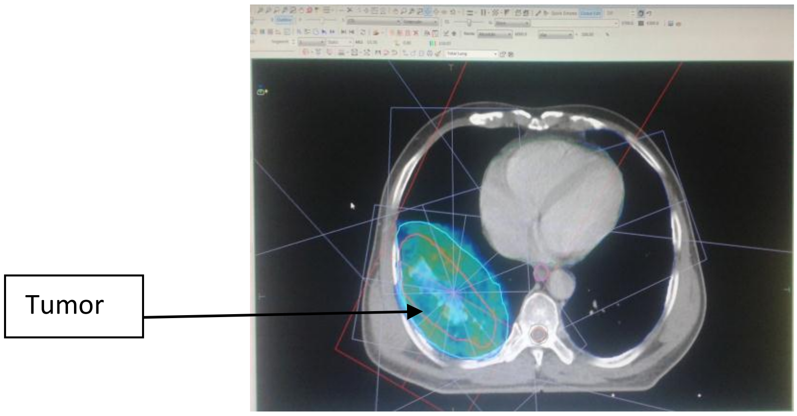

Figure 9: Transverse section of Thorax with tumor (contoured)

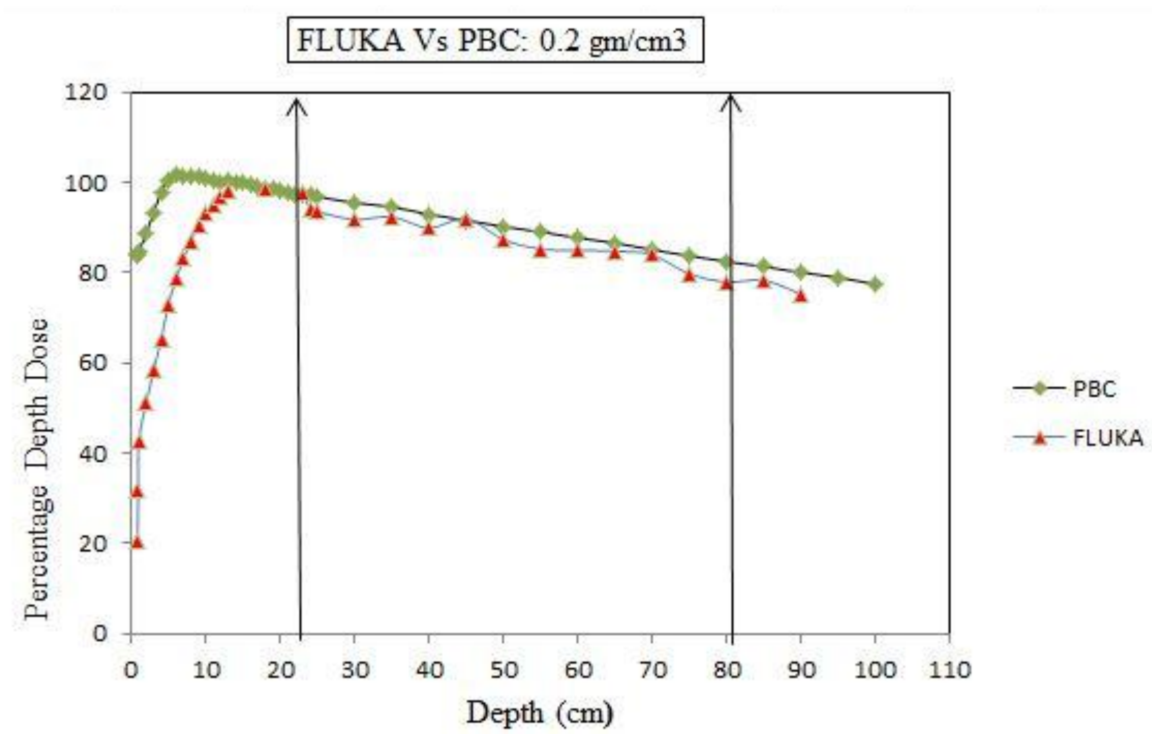

Figure 10: Variation of PDD with Depth calculated by FLUKA code and PBC for medium density 0.2 gm/cm^3.

variation can be favorable in clinical situations like tumor lying at the same depth equal to Dmax, and this can be favorable in delivering lesser dose to normal structure with maximum dose to tumor. However, this can result in under dosing of tumors such as that found just beyond the inhomogeneous surface along the beam (Figure 9). The performance (PDD) of both PBC and FLUKA code was found almost the same over the depth ranging from 2.5 cm to 7 cm in case of density 0.4 gm/cm^3; however, some deviations were recorded for 0.2gm/cm^3.

The present study contains the analysis of

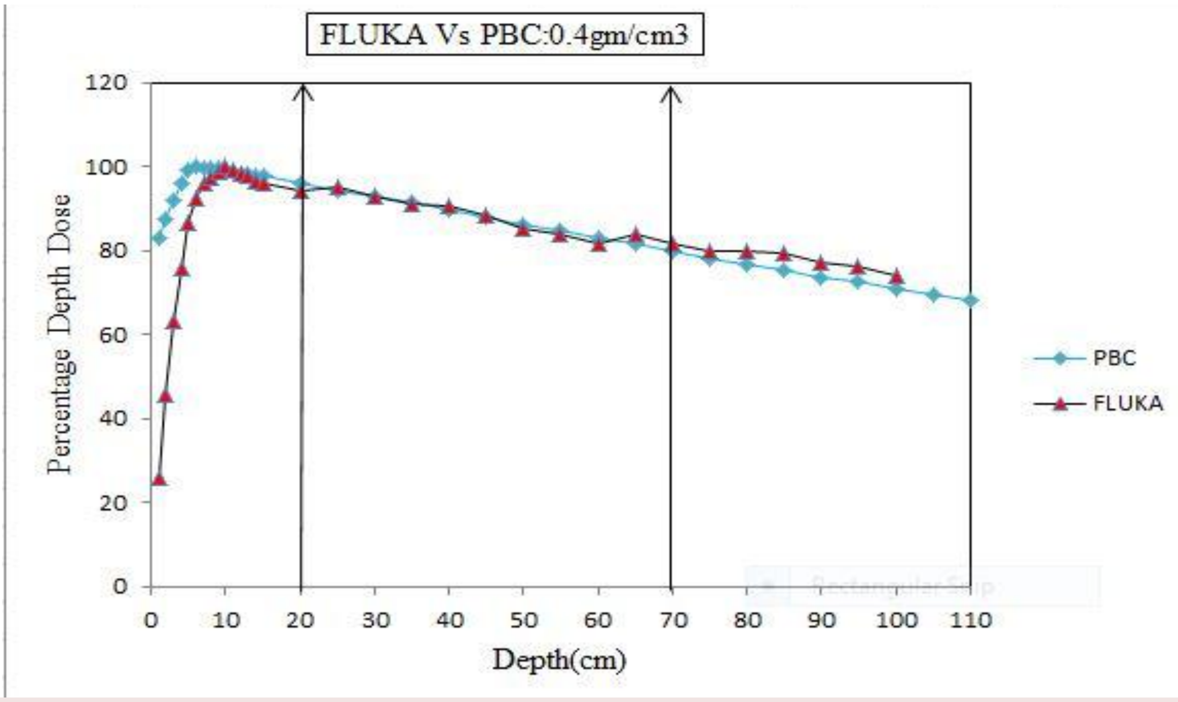

Figure 11: Variation of PDD with Depth calculated by FLUKA code and PBC for medium density 0.40 gm/cm³.

Table 4: Depth of Dmax for (Co-60) for different lung densities.

Medium	Water	0.4 gm/cm³	0.2 gm/cm³
Depth of Dmax (mm)	5	10	18

single anterior beam using PBC algorithm. Large differences between planned and delivered dose have been recorded in case of sophisticated treatment planning systems too. Hideharu Miura *et al*. studied the impact of lung density and tumor position on lung stereotactic body radiotherapy taking a range of lung density and found reduction in dose to PTV with a decrease in lung density. A difference of more than 20% was found between planned and delivered dose due to the change in lung density [21].

The authors in the present study employed only Co-60 photon beam as source of irradiation; however, similar deviations have been recorded for other photon beam used in lung cancer radiotherapy. To assess the difference in planned and delivered dose due to change in lung density, Lasse Rye Aarup et al. created a virtual lung phantom having lung and spherical tumor inside the cubical body. The performance of different algorithms including PBC for 6and 18 MV beams was evaluated in terms of target coverage having lung density ranging from 0.1 gm/cm³ to 0.45 gm/cm³ and similar to the present study, increase in PBC overestimation in the target dose with decrease in lung density was found. In case of lung cancer radiotherapy, these variations in lung density need to be considered [22]. The overestimation by TPSs used in lung cancer radiotherapy basically results in under dosing to the target and which can be a cause behind higher recurrence and mortality rate in lung cancer [23].

Conclusion

Large variations in inter-lung & intra-lung densities were observed. Lung density was found decreasing with age. In manual treatment time calculation for lung cancer radiotherapy, inhomogeneity correction factor should be used for a better dose delivery. Large overestimation in dose by PBC was found at air/lung interface as well as within the lung. The results of Monte Carlo simulation can be used to assess the performance of treatment planning systems used in lung cancer radiotherapy.

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Conflict of Interest

None

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