Dosimetric comparison of three-dimensional conformal radiotherapy, intensity modulated radiotherapy, and helical tomotherapy for lung stereotactic body radiotherapy

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ABSTRACT

To compare the treatment plans generated with three-dimensional conformal radiation therapy (3DCRT), intensity modulated radiotherapy (IMRT), and helical tomotherapy (HT) for stereotactic body radiotherapy of lung, twenty patients with medically inoperable (early nonsmall cell lung cancer) were retrospectively reviewed for dosimetric evaluation of treatment delivery techniques (3DCRT, IMRT, and HT). A dose of 6 Gy per fraction in 8 fractions was prescribed to deliver 95% of the prescription dose to 95% volume of planning target volume (PTV). Plan quality was assessed using conformity index (CI) and homogeneity index (HI). Doses to critical organs were assessed. Mean CI with 3DCRT, IMRT, and HT was 1.19 (standard deviation [SD] 0.13), 1.18 (SD 0.11), and 1.08 (SD 0.04), respectively. Mean HI with 3DCRT, IMRT, and HT was 1.14 (SD 0.05), 1.08 (SD 0.02), and 1.07 (SD 0.04), respectively. Mean R50% values for 3DCRT, IMRT, and HT was 8.5 (SD 0.35), 7.04 (SD 0.45), and 5.43 (SD 0.29), respectively. D<sub>2cm</sub> was found superior with IMRT and HT. Significant sparing of critical organs can be achieved with highly conformal techniques (IMRT and HT) without compromising the PTV conformity and homogeneity.

Key words: Helical tomotherapy; intensity modulated radiotherapy; lung stereotactic body radiotherapy; three-dimensional conformal radiation therapy; treatment planning

Introduction

Stereotactic body radiotherapy (SBRT) is a form of high-precision RT for tumor targets in extracranial sites, employing higher dose per fraction and fewer fractions than conventional RT.¹ SBRT delivers a much higher biological effective dose compared with conventional RT and has reduced local failure (<10%) comparable to the rates following surgery, in patients with early-stage nonsmall cell lung cancer (NSCLC).² SBRT has become a standard treatment to increase the local control for patients who either refuse surgery or are medically inoperable early lung cases. Compared to the standard fractionation schedules used with conventional three-dimensional conformal radiation therapy (3DCRT), SBRT has been shown to improve overall survival rates with excellent local control for stage I/II NSCLC. Various treatment modalities are available at present and must be evaluated for accurate delivery of SBRT.³ The multiple ways⁴ are discussed to deliver SBRT treatments to the peripheral lung including multiple noncoplanar beams with 3DCRT, intensity modulated radiotherapy (IMRT), helical tomotherapy (HT), and volumetric-modulated arc therapy (VMAT).

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The Radiation Therapy Oncology Group (RTOG) protocol 0236 established a common way for clinics to simulate, plan, and treat lung cancer patients with SBRT.\(^{9,10}\) For SBRT of the peripheral lung, there is much tissue inhomogeneity in the thorax, especially at the lung and chest wall interface where these peripheral lung tumors tend to develop. This inhomogeneity causes a decrease in plan quality which needs to be examined.\(^{11}\) Further investigations into the use of IMRT and HT for SBRT need to be done, and this study compares the ability of three modalities to utilize these technologies for SBRT delivery to the peripheral lung. An ideal modality of SBRT delivery should deliver fast and accurate treatments without sacrificing plan quality.

The goal of this study was to compare 3DCRT, IMRT, and HT dosimetrically in the SBRT of lung. Plans were assessed qualitatively and quantitatively.

### Materials and Methods

A retrospective, consecutive database of our initial 20 patients of early medically inoperable NSCLC were reviewed for dosimetric evaluation of treatment delivery techniques. All the target and organs at risk (OAR) delineation was done as per International Commission of Radiation Units and Measurements (ICRU)-62\(^{12}\) on the Eclipse (version 8.6, Varian Medical Systems, USA), treatment planning system (TPS). Planning and dose calculation were done on the free-breathing computed tomography (CT) scan.

Plans were prescribed to planning target volume (PTV) with a dose of 8 Gy per fraction in 6 fractions, to deliver 95% of the prescribed dose to 95% volume of PTV. OARs included spinal cord, esophagus, heart, lung-PTV, and left and right lungs. For each SBRT patient, plans were evaluated for each of the three treatment modalities namely, 3DCRT, IMRT, and HT. Plans for all modalities used the same free-breathing CT image set, and all structure sets were contoured within Eclipse TPS. Since each patient had a 3DCRT plan used for treatment, only initial IMRT and HT plans needed to be created retrospectively.

All IMRT plans were created using the Eclipse TPS with 6 MV photons, taking into account inhomogeneity corrections. The 3DCRT and IMRT plans were created for delivery on a Trilogy (Varian Medical Systems Inc.,), a treatment machine. This machine has a 120 leaf millennium multileaf collimator (MLC) and an MLC leaf width of 5 mm at isocenter. The 3DCRT plans consisted of 4–6 fields using 6 MV/15 MV photon beams. IMRT plans consisted of seven coplanar 6 MV photon beams. Optimization was run in “beamlet mode” for approximately 350 iterations, at which point the cost function had converged. Following optimization of IMRT plans, final dose calculation was performed using the analytic anisotropic algorithm (AAA). The dose fractionation schedules were 48 Gy/6 fractions delivered on alternate days (2 Gy equivalence of above dose was 72 Gy). Dosimetric criteria mandated that 95% of the PTV was covered conformally by 95% of the prescription dose.

HT plans were created using the Hi·Art II treatment planning platform (version 4.2.3.9, TomoTherapy Inc., Madison, WI, USA) using 6 MV photons. For beam modulation, a 64-leaf binary MLC was used with a leaf width of 6.25 mm projected at isocenter. Longitudinal aperture size of 1.05 cm or 2.5 cm, a pitch of 0.3, and a modulation factor of 3 were used. Once initial parameters were set for each plan, a full beamlet dose calculation was run followed by 350 optimization iterations allowing for full convergence of the cost function. For final dose calculation, collapsed convolution superposition dose calculation algorithm was used.

### Plan evaluation

Plan quality was assessed using conformity index (CI) and homogeneity index (HI) for PTV. For all treatment plans, plan quality was evaluated by reviewing each dose distribution and calculating select dosimetric indices for the PTV and OARs from each dose-volume histogram (DVH). For the PTV, plan conformity was assessed using three indices. Conformality of the prescription dose to the target volume was assessed using the ICRU CI,

$$CIRI = \frac{\text{VRI}}{\text{TV}}$$  

(1)

Where VRI represents the volume of tissue covered by the reference isodose (RI = 95%), and TV represents the PTV. CI values closest to 1.0 indicate better conformity of dose to the target.

Intermediate dose spillage and falloff gradient beyond the PTV was assessed using two indices: R50% and D\(_{2\text{cm}}\). The R50% index is also calculated according to equation (1), with a reference isodose equal to 50% the prescription dose. D\(_{2\text{cm}}\) represents the maximum cumulative dose (as a percentage of the prescription dose) to any point located 2 cm away from the PTV. Mean intermediate dose spillage R50% (ratio of 50% isodose volume to PTV volume) and D\(_{2\text{cm}}\) were assessed. Lower R50% ratios and lower D\(_{2\text{cm}}\) doses indicate greater dose falloff and better plan conformity.

HI was also calculated for plan comparison as per equation (2). HI is defined as

$$\text{HI} \ 5/95 = \frac{D5}{D95\%}$$  

(2)

where D5% and D95% are the minimum doses delivered to 5% and 95% of the PTV, respectively. The values of HI closest to 1 indicate greater homogeneity within the target.

With respect to OARs, the maximum dose to the spinal cord, trachea, heart, esophagus, and ipsilateral chest wall was...
recorded; whereas for lung-PTV, mean dose and percent V20 and V5 were assessed. In addition, for lung-PTV, the doses to 1000 cc and 1500 cc were recorded. For ipsilateral chest wall, dose to 10 cc was also recorded. For heart, V20 and V5 were recorded. All the data were statistically validated with the two-tailed pair sampled t-test for estimating P value.

**Results**

Mean volume of the PTV for this patient group was 191.38 cc (range: 103–191.38) with a standard deviation (SD) of 62.04 cc. Axial, coronal, and sagittal isodose distributions from 3DCRT, IMRT, and HT plans are shown for one representative patient in Figure 1. PTV doses with SD and range for all three modalities are summarized in Table 1. Table 2 shows DVH-based analysis for lung-PTV with SD and range for these modalities. Table 3 shows DVH-based analysis for other OAR with SD and range for these modalities.

**Table 1: DVH based analysis for PTV for 20 patients**

| Organ | Parameter | 3DCRT         | IMRT         | HT            |
|-------|-----------|---------------|--------------|---------------|
| PTV   | CI        | 1.19 (0.9-1.41) | 1.18 (0.9-1.4) | 1.08 (1-1.19) |
|       | SD        | 0.13          | 0.11         | 0.04          |
|       | HI        | 1.14 (1-1.32) | 1.08 (1.01-1.32) | 1.07 (1-1.16) |
|       | SD        | 0.05          | 0.02         | 0.04          |
|       | R50%      | 8.50 (7.9-9.1) | 7.04 (6.3-7.7) | 5.43 (5-6)    |
|       | SD        | 0.35          | 0.45         | 0.29          |
|       | D2cm (%)  | 67.51 (64-71.6) | 75.53 (72.8-78.4) | 51.35 (47-56) |

CI: Conformity index, HI: Homogeneity index, R50%: Ratio of with a reference isodose equal to 50% the prescription dose to the PTV volume, D2cm: Percentage of the prescription dose to any point located 2 cm away from the PTV, SD: Standard deviation, DVH: Dose-volume histogram, 3DCRT: Three-dimensional conformal radiation therapy, HT: Helical tomotherapy, PTV: Planning target volume, IMRT: Intensity modulated radiotherapy.

Figure 2 shows mean CI for PTV with 3DCRT, IMRT, and HT for 20 patients. Mean CI with 3DCRT, IMRT, and HT was 1.19, 1.18, and 1.06, respectively. HT plans generated...
the most uniform dose distribution in the PTV. Figure 3 shows mean HI for PTV with 3DCRT, IMRT, and HT for 20 patients. Mean HI for 3DCRT, IMRT, and HT was 1.14, 1.08, and 1.07, respectively.

HT produced the most conformal plans, demonstrated by the R50% and D2cm. Mean R50% values for 3DCRT, IMRT, and HT were 8.59 (range: 8.2–9.1, SD 0.35), 7.11 (range: 6.3–7.6, SD 0.45), and 5.37 (range: 5–5.9, SD 0.29), respectively. D2cm was found superior with HT.

At a distance of 2 cm from the PTV, HT plans produced the lowest doses, indicating the least amount of intermediate dose spillage. On average, the D2cm for HT plans was 51.35% of the prescription dose. For 3DCRT and IMRT plans, the D2cm was 67.51% and 75.53%, respectively.
Mean lung-PTV doses for 3DCRT, IMRT, and HT were 5.87 Gy, 5.33 Gy, and 4.52 Gy, respectively. Percents V20 and V5 for lung-PTV were almost comparable with 3DCRT, IMRT, and HT. Mean percents V20 for 3DCRT, IMRT, and HT were 8.87, 9.02, and 8.7, respectively. Mean percents V5 for 3DCRT, IMRT, and HT were 3.86, 3.91, and 3.69, respectively. Mean doses received by 1500 cc lung-PTV with 3DCRT, IMRT, and HT were 2.41, 2.45, and 2.48, respectively.

The average maximum doses (Gy) for spinal cord with 3DCRT, IMRT, and HT for 20 patients were 19.63 Gy, 18.06 Gy, and 17.71 Gy, respectively. For trachea, the average maximum doses with 3DCRT, IMRT, and HT were 23.35 Gy, 23.05 Gy, and 23.19 Gy, respectively. The average maximum doses to esophagus for 3DCRT, IMRT, and HT were 19.63 Gy, 18.06 Gy, and 17.71 Gy, respectively.

The average maximum doses to proximal bronchial tree for 3DCRT, IMRT, and HT were 27.08 Gy, 20.89 Gy, and 20.51 Gy, respectively. For ipsilateral chest wall, mean doses for 3DCRT, IMRT, and HT were 22.68 Gy, 18.73 Gy, and 15.70 Gy, respectively. The average maximum doses to heart for 3DCRT, IMRT, and HT were 36.66 Gy, 30.15 Gy, and 27.18 Gy, respectively. The percents V5 for heart with 3DCRT, IMRT, and HT were 14.35 Gy, 13.60 Gy, and 12.62 Gy, respectively. Table 4 shows the P value for OAR and PTV.

Mean ratios of monitor units (MUs) for IMRT/3DCRT, HT/3DCRT, and HT/IMRT were found to be 1.06 (SD 0.36), 6.63 (SD 2.59), and 6.64 (SD 2.16), respectively. MU increased nearly by a factor of six for HT compared to 3DCRT and IMRT, respectively.

**Discussion**

This study was undertaken to evaluate our initial experience with SBRT in NSCLC. Having used 3DCRT for a long time at our institution, dosimetric comparison for advanced modalities such as IMRT and HT was thought of. All the patients had variable PTV volumes and their volumes were large. So far, patients treated with 3DCRT had no significant toxicity. In this study, all three modalities were able to deliver highly conformal SBRT plans. The superior modality for each dosimetric criterion can vary based on patient anatomy, tumor location, and tumor size.

RTOG 236 recommends use of minimum six fields for treatment planning. In our study, 4 fields technique was used only for 2 patients (10% of patients). Of two, one was left lung cancer (mid lobe) patient (PTV volume of 154 cc) whereas other one was right lung cancer (lower lobe) patient (PTV volume of 113 cc). Shape of the PTV
was cylindrical. The beam directions were such that no major portion of the beam exits through the contralateral lung. V5 (lung-PTV) for these patients was well within the criteria (29.7% and 32%, respectively). The mean lung dose was 4.9 Gy and 9.7 Gy, respectively. Doses to all other OAR were minimal. The isodose wash of 50% and 50% was well-controlled. PTV dose coverage was achieved with the use appropriate use of beam weight, and the wedges and plans were reviewed by the radiation oncologists. However, 5 fields were used in 6 patients, 6 fields (4 patients), 7 fields (5 patients), and 8 fields (3 patients).

Videtic et al.\(^6\) validated the use of SBRT using IMRT beams for medically inoperable stage I lung cancer for 26 patients. The median conformity index was 1.38 (range: 1.12–1.8). The median heterogeneity index was 1.08 (range: 1.04–1.2). Mean CI for our study for IMRT was better 1.18 and for HT it was better than 1.06. The HI was also found to be better (as 1.08 for IMRT and 1.07 for HT) than their study.

Baumann et al.\(^1\) studied the impact of SBRT on 3 years progression-free survival of medically inoperable patients with stage I NSCLC which were analyzed in a prospective phase II study. Mean PTV volume in their study was 114 cc. They used a three-dimensional conformal multifield technique to deliver a dose of 15 Gy times three at about the 67% isodose to the periphery of the PTV, resulting in a central dose of about 22 Gy × 3. In our study the PTV was 191.38 cc and the treatment technique was similar. Number of beams used in our study varied from 3 to 8 beams. However in our study, prescribed dose was 48 Gy delivered in 8 fractions (6 Gy per fractions).

Buyyounouski et al.\(^4\) recommended in their report that the CI may be kept to <1.2 to minimize the volume of normal tissue receiving an ablative dose. CI in our study was within 1.2 for 3DCRT, IMRT, and HT. Intermediate-dose spillage, which is responsible for most of the toxicities associated with SBRT, was evaluated using one or both of the following methods, as follows: (1) By keeping the dose to any point 2 cm away from the PTV surface below a limit that is a function of PTV volume, and/or (2) by defining the region of intermediate-dose spillage as the ratio of 50% isodose coverage to the PTV volume. These concepts have been used in all of the RTOG multicenter lung cancer treatment studies to date, and constraints as a function of target volume can be viewed in the radiotherapy sections of these protocols ([http://www.rtog.org/members/active. html#lung]). The latter option was used in our study to evaluate intermediate-dose spillage. This is also known as CI50%.

Verbakel, et al.\(^5\) described the implementation of the RapidArc delivery technique in peripheral stage I lung cancer and compared the plans with those obtained with 10 static noncoplanar fields. They compared the plan quality by CI 80% and doses to OARs. The treatment time for both the techniques was also compared. In our study, ratio of MU among three techniques was compared. Mean ratios of MU for IMRT/3DCRT, HT/3DCRT, and HT/IMRT were found to be 1.06 (SD 0.36), 6.63 (SD 2.59), and 6.64 (SD 2.16), respectively. MU increased nearly by a factor of six for HT compared to 3DCRT and IMRT, respectively. They also evaluated V45 Gy (cc) and found minimal volumes receiving this dose with RapidArc. In our study, mean values of V45 Gy with 3DCRT, IMRT, and HT were 20 cc (SD 17.3), 14.2 cc (SD 17.1), and 13.6 cc (SD 15.5), respectively.

Ong et al.\(^6\) compared the dose distributions and delivery times between RapidArc and common delivery techniques in small (stage I) tumors. In 18 patients who completed RapidArc SBRT for tumors measuring <70 cc, new treatment plans were generated using noncoplanar three-dimensional conformal fields (conformal-SBRT) and dynamic conformal arc radiotherapy. RapidArc led to a small increase in V (5 Gy) to contralateral lung compared to conformal-SBRT (4.4 ± 4% vs. 1.2 ± 1.8%, P = 0.011). In our study, the mean dose to the ipsilateral chest wall was estimated and found to be the lowest for HT plans. There was slight increase in V 5 for 2–3 patients with IMRT and HT in our study as well. Overall, the values of V5 for IMRT and HT were comparable with 3DCRT when averaged over 20 patients.

Holt et al.\(^7\) demonstrated the potential of VMAT compared with IMRT techniques with a limited number of segments for SBRT for 27 early-stage lung cancer patients. The mean dose to the healthy lung was 4.1 Gy for VMAT and noncoplanar IMRT and 4.2 Gy for coplanar IMRT. The volumes of healthy lung receiving >5 Gy and >20 Gy were 18.0% and 5.4% for VMAT, 18.5% and 5.0% for noncoplanar IMRT, and 19.4% and 5.7% for coplanar IMRT, respectively. The dose conformities at 100% and 50% of the prescribed dose of 54 Gy were 1.13 and 5.17 for VMAT, 1.11 and 4.80 for noncoplanar IMRT, and 1.12 and 5.31 for coplanar IMRT, respectively. Our results of lung-PTV mean dose were comparable to Holt et al.\(^7\) Our IMRT plans were coplanar. CI for IMRT and HT were also comparable (in our study, CI50% was R50%).

Rao et al.\(^8\) compared VMAT to both HT and fixed field IMRT in terms of plan quality, delivery efficiency, and accuracy for six lung cancer patients. Their results demonstrated that both VMAT and HT were capable of providing more uniform target doses and improved normal tissue sparing as compared with fixed field IMRT. Our study also found the similar results of having benefit of IMRT and HT on minimizing the doses to OARs without compromising on the plan quality. As our 3DCRT plan involved wedges, the delivery efficiency (throughput) was slightly poorer compared to IMRT plans. Our study
found that HT plans achieved the best dose conformity of the PTV, as demonstrated by the conformity indices reviewed (CI, R50%, D_{2 cm}) where values were lowest for HT. In addition, HT plans were the most uniform in the PTV, with HI indices close to unity.

It was observed that CI for 4 patients with 3DCRT was the best, the being more regular shape of PTV which could confirm the best fit to MLCs to achieve the ideal CI. In addition, as mentioned earlier, the beam directions were appropriately selected with beam weights and wedges to avoid heterogeneity in the PTV. Moreover, six fields used were in those patients to achieve the best conformity. There was no other specific reason observed as such. However, we also observed that tomotherapy CI was very close to 3DCRT plans in these patients if compared on the numbers.

HI for IMRT patient number 18 is 30% higher than other two plans. The shape of the PTV was irregular and complex. Achieving minimal dose to the OAR in the vicinity was a great challenge. Hence, the modulation in IMRT plan was really high with no compromise on tumor coverage. Single planner was not involved in this study. The 3DCRT plans were done by 2–3 different planners. However, the plans were approved by single radiation oncologist. Thus, the objective was clear to make the best plan for the respective modality. IMRT and tomotherapy plans were generated by a single planner each. There was consistency in all the plans and the ultimate goal was to fulfill the RTOG criteria. The variations in the different patients were due to the shape of the tumor and the degree of modulation or the beam weighting due to restrictions on the OARs in the vicinity. Overall, the quality of plans was not compromised depending on the planner.

The uniformity of the HT plans was also evident by visual evaluation of isodose distributions, as shown in Figure 1. The HT planning system was able to create the most homogeneous and uniform distribution throughout the tumor, even in areas of great tissue inhomogeneity. The majority of plan hot spots were located within the PTV, which could be seen as an advantage by TG-101. The IMRT and 3DCRT plans were more likely to have hot spots located along the periphery of the PTV or partially outside of the PTV, slightly lowering plan quality. The maximum values of doses seen in the IMRT and 3DCRT plans were on average 7–8% higher than HT.

In Table 1, D_{2 cm} (%) shows higher values for IMRT. This was explored and may be due to the parameters settings in TPS. In TPS, the normal tissue tolerance value settings decide the nature of fall off. Optimal values were chosen to get desired dose fall off beyond PTV. In IMRT, volume of maximum D_{2 cm} was 0.3% and 40% D_{2 cm} was 1%. It was almost a long tail with range from 40% to 60% as D_{2 cm}. However, the max D_{2 cm} was recorded.

In plan optimization, the Eclipse and Hi·Art II TPSs use different optimization methods, as well as different cost functions. This means that planning constraints cannot be set exactly the same for the two planning systems. SBRT plans were originally created for 3DCRT delivery. It should be pointed out that the use of IMRT for SBRT planning of lung tumors is presently not straightforward as the optimization algorithm is based on convolution of spatially invariant point spread kernels, whereas the final dose calculation by the AAA better takes into account the tissue inhomogeneities. This difference between optimization and dose calculation could lead to a larger dose inhomogeneity in the PTV, though this often falls within our plan acceptance criteria.

For HT, the optimized DVH and the final dose calculated DVH are alike. To optimize the plans, the initial constraints for IMRT plans were kept similar to those used for the HT plan. In helical delivery, there are three main parameters used in planning. These are the longitudinal field size equal to the axial thickness of the fan beam, pitch equal to the distance the couch travels per gantry rotation relative to the field size at the axis of rotation, and the modulation factor equal to the maximum leaf opening time relative to the average leaf opening time.

Conclusion

For lung SBRT, all the three modalities (3DCRT, IMRT and HT) were evaluated. High-precision techniques like IMRT and HT were feasible in lung SBRT. Significant sparing of critical organs could be achieved with IMRT and HT without compromising on the PTV conformity and homogeneity. Now, we are gradually moving to use high-precision techniques (HT and RapidArc) for SBRT lung treatments to gain the dosimetric advantage.

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Conflicts of interest
There are no conflicts of interest.

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