Original Research Article

Dosimetric Comparison of Stereotactic Body Radiotherapy in Lung Cancers: CyberKnife Versus Helical Tomotherapy Versus Volumetric Modulated Arc Therapy

ABSTRACT

Aim: *Stereotactic body radiotherapy (SBRT) is widely used in the treatment of early stage lung cancer. There are several SBRT techniques. We aimed to compare three planning techniques: CyberKnife (CK), Helical Tomotherapy (HT), and Volumetric Modulated Arc Therapy (VMAT).*
Material and Methods: *This study included 15 patients with early stage lung cancer who were treated in our clinic. For this study, their images were recountured and replanned in CK, HT, and VMAT. Treatment plans were compared in terms of target volume doses and organ-at-risk doses.*
Results: *The HT plan differed significantly from the other plans in terms of CI, and GI (p<0.001). There was a significant difference between the plans in terms of HI in favor of HT (p<0.001). VMAT plan reduced the monitor unit per fraction and beam on time per fraction values (p < 0.001). The lowest lung V5 (22,7%, p = 0.046),* $D_{maximum}$*, and the dose of 5 cc of trachea (499.4 cgy, 252.4 cgy; p=0.017, p=0.034) and esophagus (673.9 cgy, 237.3 cgy; p=0.014 and p=0.08) were observed with the VMAT plan.*
Conclusions: *All plans met the organ-at-risk dose constraints and target volume doses with acceptable limits. Each clinic should select an appropriate technique based on the available resources and experience.*

Keywords*: Lung cancer, Stereotactic body radiotherapy, CyberKnife, Helical tomotherapy, Volumetric modulated arc therapy*

INTRODUCTION

Lung cancer is the leading cause of cancer-related death (18%) globally.[1] Currently, stereotactic body radiotherapy (SBRT) is the standard treatment for medically inoperable early-stage lung cancers. High SBRT doses can be safely delivered with advanced techniques that provide high coherent target coverage and strict adjacent normal tissue protection. Lee et al. reported that these techniques provided better local control with high biologically effective dose values.[2] Using SBRT, prospective multi-institutional trials have demonstrated local control and overall survival rates of approximately 85% and 60%, respectively.[3-5] SBRT is a treatment option that dose not compromise the patients quality of life, has tolerable toxicity, and has a high rate of local control (rate ≥ 90%).[6] A study evaluated the cost-effectiveness of treatment modalities in patients with stage I non-small cell lung cancer (NSCLC) and revealed that SBRT was more cost-effective in marginally operable patients, whereas lobectomy was more cost-effective in clearly operable patients.[7]

CyberKnife (CK) is a robotic arm-mounted 6-MV linear accelerator image-guided radiotherapy system. Moving tumors can be treated with sub-millimeter accuracy while patients are breathing normally with this system. Helical tomotherapy (HT) is a technology that delivers image-guided intensity-modulated radiotherapy (IMRT), and treatment plans are generated in the Tomotherapy Hi-Art planning system using 6-MV photons. Volumetric modulated arc therapy (VMAT) is an arc-based therapy that is delivered by a conventional linear accelerator.

This study aimed to compare the dosimetric differences between SBRT plans delivered with CK, HT, and VMAT in terms of quality and planning rationality for patients with early-stage NSCLC.

MATERIAL AND METHODS

In this study, the treatment of 15 patients with peripheral early-stage NSCLC who had previously undergone SBRT in our radiation oncology department was replanned using three treatment planning systems (CK, HT, and VMAT) based on the same planning tomography. Patients breathed freely and consistently. Treatment planning computed tomography (CT) with a four-dimensional technique and 1.5-mm slice thickness was obtained for the delineation of target volumes and organ-at-risk (OARs) using a multislice CT scanner (Philips Big Bore Brilliance). After CT scanning, the CT data were sorted into 10 breathing phases. The obtained CT dataset was sent to CK's planning system. All patients were treated with CK. These CT data were transferred to the HT and VMAT planning systems in this study. The version of HT is Hi-ART 5.1.4. All target volumes and OARs were recontoured for each patient by same radiation oncology. Gross tumor volume (GTV) indicated the tumor defined in radiological screenings. All patients undewent Positron emission tomography (PET) CT before treatment, and GTV was contoured using PET CT fusions. Internal target volume (ITV) was defined for all patients using the sorted breathing phases on planning CT. Subsequently, for all plans, planned target volume (PTV) was generated with 5-mm margins in all directions to ITV. The lungs, esophagus, rib, heart, proximal bronchial tree, trachea, great vessels, and spinal canal were all at risk. Radiotherapy plans in the planning systems were performed by physicist who were familiar with the systems used in this study. Three plans were performed for each patient CK, HT, and VMAT. The prescription dose was 50 Gy in 5 fractions. The PTV was optimized to cover at least 95% of the volume with 100% of the prescription dose. Treatment plans were designed to meet Timmerman's normal tissue dose constraints.[8]

CK plans were generated using sequential optimization in Multiplan version 3.5. Two fixed circular collimators and two to three shell constraints were used for each plan. The 76% to 80% isodose line interval was given treatment doses. During treatment, the tumor was tracked using the X-sight lung tracking method.

VMAT plans were generated using the Varian Eclipse version 11.4 treatment planning system, and dose calculation was performed using the AAA algorithm. All plans were based on two coplanar partial arcs with multileaf collimators. The optimization resolution was 2.5 mm in all cases.

All contours and CT images for HT were transferred to the tomotherapy planning station (Accuray, Sunnyvale, CA). Then plans were generated, using a fixed jaw mode with a modulation factor of 2.0, a field width of 2.50 cm, and a pitch factor of 0.15–0.18 cm.

Target volume doses, organ-at-risk doses, and treatment plan quality were used to compare treatment plans. D2, D50, D98, $D_{minimum}$, $D_{maximum}$, and D_{mean} were calculated from the DVHs of all plans for the target (PTV). V5, V10, V20, and mean lung dose for the lung; the dose of 0.35 cc of spinal cord volume; $D_{maximum}$ and the dose of 5 cc of esophagus volume for the esophagus; $D_{maximum}$ and the dose of 15 cc of heart volume for the heart; $D_{maximum}$ dose of great vessel volume; $D_{maximum}$ and the dose of 5 cc for the trachea and proximal bronchial tree; $D_{maximum}$ and the dose of 5 cc for the rib were analyzed. The conformity index (CI), dose homogeneity index (HI), gradient index (GI), beam on time per fraction (BOT/fx), and monitor unit per fraction MU/fx were used to evaluate treatment plan quality.

The CI was calculated as follows:

$$CI = \frac{V_{Rx}}{TV_{Rx}},$$

where TV_{RX} indicates tumor volume receiving prescription dose and V_{RX} indicates prescription isodose volume.

The new CI (nCI) was calculated as follows:

$$nCI = \frac{TV}{TV_{RX}} x \frac{V_{Rx}}{TV_{Rx}},$$

where TV indicates tumor volume (cc), TV_{RX} indicates tumor volume receiving prescription dose, and V_{RX} indicates prescription isodose volume. [9] The reference value of CI and nCI is accepted as 1.

The dose HI was calculated to quantitatively evaluate dose heterogeneity in the target tumor using the following formula:

$$DHI= \frac{D_{maximum}}{D_{prescribe}},$$

where $D_{maximum}$ indicates maximum dose to the target volume and $D_{prescribe}$ indicates prescription dose to the target volume.[9]

The GI was calculated as follows:

$$GI = \frac{V_{\%50Rx}}{V_{Rx}},$$

where $V_{\%50Rx}$ indicates 50% of prescription isodose volume and V_{RX} indicates prescription isodose volume.[10]

Statistical analysis

Twenty-two packages of Social Science Statistical Package (SPSS, SPSS Inc., Chicago, IL) were utilized. From the target perspective, percentage and mean ± standard deviation (mean ± *SD*) in the course from the study perspective. The Shapiro–Wilk test was used to assess the normal application of continuous administrations. The reconstruction of the two alignments was performed using analysis of foci under normal conditions and analysis of variance for normal alignments. *P*-values of < 0.05 were considered to indicate statistical significance.

RESULTS

All patients had peripherally located tumors. Of the 15 patients, 6 patients had tumors on the right upper lobe, 3 on the right middle lobe, and 6 on the left upper lobe. The mean PTV volume was 41.8 ± 32.5 cc (min = 8.9, max = 124.5).

All OARs with comparable target coverage dose limitations met the Radiation Therapy Oncology Group [11] and/or Timmerman protocol limits.[8]

Significant differences were observed between the plans in terms of $PTV_{minimum}$ and PTV D98 ($P < 0.01$), which may be due to the difference between VMAT and other plans. Moreover, there were significant differences in PTV_{mean}, $PTV_{maximum}$, and PTV D2 ($P < 0.01$), which may be due to the differences in all plans. There was a significant difference between the plans in terms of PTV D50 ($P < 0.01$). This difference resulted from the difference between CK plan and the other two plans (Table 1).

Table 1: Results of target dose comparisons and DVH Parameters for CK, HT, and VMAT plans

	CK	**HT**	**VMAT**	***P*-value**
	Mean ± SD	Mean ± SD	Mean ± SD	
$PTV_{minimum}$ (cGy)	4792.1 ± 109.7^{a}	4692.9 ± 179.1^{a}	4407.5 ± 156.5^{b}	**<0.001***
PTV_{mean} (cGy)	5483.1 ± 89.0^{a}	5128.2 ± 60.9^{b}	5225.7 ± 31.8^{c}	**<0.001***
$PTV_{maximum}$ (cGy)	6320.8 ± 130.7^{a}	5285.1 ± 92.8^{b}	5570.4 ± 101.7^{c}	**<0.001****
PTV D98(cGy)	4990.7 ± 76.7^{a}	4948.9 ± 37.7^{a}	4864.1 ± 65.4^{b}	**<0.001***
PTV D50(cGy)	5444.6 ± 92.7^{a}	5169.3 ± 112.4^{b}	5246.2 ± 23.6^{b}	**<0.001****
PTV D2(cGy)	6085.2 ± 124.3^{a}	5232.8 ± 88.2^{b}	5376.7 ± 53.6^{c}	**<0.001****

*One way analysis of variance, **Kruskal-Wallis analysis, a,b,c Statistically significant differences between the groups

Abbreviations: DVH: dose volume histogram, CK: CyberKnife, HT: Helical tomotherapy, VMAT: volumetric modulated arc therapy, PTV: planning target volume.

The HT plan differed significantly from the other plans in terms of CI, nCI, and GI ($P < 0.001$). There was a significant difference between the plans in terms of HI ($P < 0.001$). This difference resulted from the difference between the CK plan and other plans. There was a significant difference between the plans in terms of MU/fx and BOT/fx (min, $P < 0.001$). This difference was caused by the differences in all plans (Table 2).

Table 2: Dosimetric results of CI, nCI, HI, GI, MU/fx, and bot/fx

	CK	HT	VMAT	***P*-value***
	Mean ± SD	Mean ± SD	Mean ± SD	
CI	1.16 ± .04^{a}	1.25 ± .08^{b}	1.15 ± .15^{a}	**<0.001**
nCI	1.18 ± .05^{a}	1.33 ± .12^{b}	1.15 ± .05^{a}	**<0.001**
HI	1.27 ± .03^{a}	1.07 ± .06^{b}	1.11 ± .03^{b}	**<0.001**
GI	4.64 ± .53^{a}	6.35 ± 1.01^{b}	5.00 ± .72^{a}	**<0.001**
mu/fx (mu)	6625.1 ± 858.0^{a}	10071.9 ± 1692.6^{b}	3352.8 ± 618.0^{c}	**<0.001**
bot/fx(min)	35.8 ± 3.9^{a}	11.7 ± 1.9^{b}	6.4 ± .6^{c}	**<0.001**

*One way analysis of variance, **Kruskal-Wallis analysis, ^{a,b,c} Statistically significant differences between the groups

Abbreviations: CK: CyberKnife, HT: Helical tomotherapy, VMAT: volumetric modulated arc therapy, HI: homogeneity index, CI: conformity index, nCI: new conformity index, GI: gradient index, MU/fx: monitor unit per fraction, bot/fx: beam on time per fraction.

Significant differences were noted between the plans in terms of lung V5 ($P = 0.046$), trachea $D_{maximum}$ ($p = 0.017$), trachea 5 ($P = 0.034$), and esophageal 5 ($P = 0.008$), which was due to the difference between the CK and VMAT plans. There was a significant difference between the plans in terms of esophageal $D_{maximum}$ ($P < 0.014$). This difference resulted from the difference between the VMAT plan and other plans (Table 3).

Table 3: Dose comparison for OARs

	CK	HT	VMAT	***P*-value***
	Mean ± SD	Mean ± SD	Mean ± SD	
Mean lungs-ptv (cGy)	410.6 ± 223.0	448.5 ± 168.7	307.5 ± 149.5	0.104**
Lung V 5 (%)	34.3 ± 16.3^{a}	32.1 ± 12.2^{a,b}	22.7 ± 9.8^{b}	**0.046****
Lung V 10 (%)	20.4 ± 13.3	23.9 ± 9.8	16.6 ± 9.0	0.136
Lung V 20 (%)	20.9 ± 42.1	12.0 ± 6.3	8.3 ± 6.1	0.069
Spinal cord D 0.35 cc (cGy)	731.7 ± 507.1	598.0±468.2	700.7 ± 358.4	0.828
Heart $D_{maximum}$ (cGy)	847.1 ± 711.4	976.1 ± 1283.6	731.1 ± 1193.3	0.242
Trachea $D_{maximum}$ (cGy)	992.0 ± 534.5^{a}	790.5 ± 456.7^{a,b}	499.4 ± 340.4^{b}	**0.017****
Trachea D 5 cc (cGy)	600.3 ± 480.5^{a}	441.4 ± 336.8^{a,b}	252.9 ± 165.2^{b}	**0.034****
PBT $D_{maximum}$ (cGy)	727.7 ± 952.6	905.5 ± 633.8	800.3 ± 934.2	0.283
Rib $D_{maximum}$ (cGy)	4441.3 ± 1477.3	4918.5 ± 726.6	4858.3 ± 873.0	0.800
Rib D 5 cc (cGy)	2106.5 ± 1533.0	2361.9 ± 1316.2	2354.9 ± 896.7	0.824**
Esophagus $D_{maximum}$ (cGy)	1005.3 ± 422.8^{a}	998.6 ± 341.1^{a}	673.9 ± 209.1^{b}	**0.014****
Esophagus D 5 cc (cGy)	585.7 ± 360.8^{a}	445.8 ± 255.5^{a,b}	257.3 ± 171.5^{b}	**0.008****

*One way analysis of variance, **Kruskal-Wallis analysis, ^{a,b,c} Statistically significant differences between the groups

Abbreviations: OAR: organ at risk, PBT: proximal bronchial tree, CK: CyberKnife, HT: Helical tomotherapy, VMAT: volumetric modulated arc therapy

DISCUSSION

SBRT is a treatment option for medically inoperable lung cancer. With technological advancements, it is currently available in modern radiotherapy clinics. This study focused on three different SBRT techniques to determine target volume and critical organ doses.

Three different RT devices (CyberKnife®, Helical Tomotherapy®, and VMAT) were compared in another study evaluating the efficacy and toxicity of lung SBRT techniques. Their study compared the results of 111 patients, wherein compared with other plans (HT and VMAT), CK showed dosimetric benefit with reduced mean lung dose (2.6 vs. 4.1 Gy, $P < 0.001$), V5 (13.5% vs. 19.9%, $P = 0.002$), and V20 (2.3% vs. 5.4%, $P < 0.001$). The abovementioned study did not report a clear criterion for selecting techniques, and the obtained dosimetric parameters had no effect on toxicity.[12] Our study evauated all OARs and revealed statistically significant differences in lung V5, $D_{maximum}$, and dose of 5 cc of the trachea and esophageal volume. VMAT plan had lower lung V5 (P=0.046), $D_{maximum}$ and the dose of 5 cc of trachea (P=0.017, P=0.034) and esophagus (P=0.014, P=0.08) volume. However, we did not evaluate the toxicity, in order to evaluate the effect of dosimetric advantage on toxicity, a more comprehensive study evaluating the effect of dosimetric data can be done.

Desphande et al. conducted a comparative study and revealed that VMAT delivered higher maximum doses to the GTV and PTV and lower lung V5 than other plans. CK plans had higher CI than VMAT plans (median: 1.19 vs. 1.10, $P < 0.00001$), but VMAT plans had higher HI than CK plans (median: 1.30 vs. 1.25, $P < 0.001$).[13] In contrast to these findings, we reported higher CIs and HIs in HT and CKplans, respevtively. The CK and VMAT plans are more heterogeneous; therefore, the maximum dose and HI tend to increase as the dose is trapped more effectively in the PTV.

There have been numerous dosimetric comparison studies based on CK and VMAT plans on lung SBRT. When SBRT plans are evaluated in terms of time, Shao et al. compared CK and Eclipse plans for lung SBRT. They reported that MU/fx and BOT/fx values were statistically higher in VMAT plans. The BOT/fx for VMAT plans was 8 min shorter than that for CK plans ($t = 7.23$, $P = 0.000$).[14] Although VMAT plans showed a shorter treatment period in our study than CK plans, it is not preferred in clinical practice because of the absence of a tumor tracking system on the linear accelerator. In contrast, as CK has a real-time tumor tracking system, it is our clinic's first choice for SBRT.

Yu et al. compared treatment planning systems for lung SBRT using the CK Multiplan and Varian Eclipse treatment planning systems as well as VMAT and knowledge-based VMAT and revealed that CK plans showed the highest MUs ($P < 0.001$). HI was higher for CK plans than for other plans ($P = 0.003$ and $P = 0.006$). Conversely, OAR sparing was superior in VMAT than in CK plans.[15] Our results were consistent with this study.

CONCLUSION

All three treatment planning systems were optimal for the lung in this study. The OAR and target volume doses were comparable in all plans. Upon comparing the three planning methods, only lung V10 was significantly better than VMAT in OARs, but it remained within the range of dose constraints according to the guidelines for all plans. In our study patients, because the tumors were located in the periphery, the OAR values were within the limits stipulated by the guidelines and did not differ significantly when all three plans were compared. Thus, these techniques can be used safely. For the selection of SBRT technique, each clinic should consider dosimetric results and the available resources for lung SBRT. We prefer to use CK in lung SBRT since it has real time tumor tracking system in our clinic, and we recommend that clinics that have the opportunity evaluate CK primarly for lung SBRT.

ETHICAL APPROVAL

The study was approved by the Ethical Committee of Dr Abdurrahman Yurtaslan Oncology Training and Research Hospital (approval number 2022-05/109) on May 26, 2022.

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