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Stereotactic Body Radiotherapy for Lung Cancer: Insights from an Institutional CyberKnife Study

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Abstract

This retrospective study aimed to evaluate the treatment plans and analyse the dosimetric parameters for stereotactic body radiotherapy (SBRT) using the CyberKnife® system in patients with inoperable primary or metastatic lung cancer. Ten lung cancer patients treated with SBRT using the CyberKnife® were included in the study. Treatment plans were designed using the Precision 3.3.1.2 treatment planning system, with optimization performed using the Monte Carlo algorithm. Two tracking methods were employed: fiducial markers with Synchrony® in five cases and direct tumor visualization using Xsight® Lung in the remaining five cases. Patient-specific quality assurance (QA) was conducted using SRS MapCHECK® and StereoPHAN™ phantom, with gamma analysis performed using 2%/2 mm criteria and a 10% threshold.

Results demonstrated that the dose distribution for the planning target volume (PTV) and surrounding organs at risk (OARs) met clinical prescription requirements. The target conformity index (CI) and new conformity index (nCI) for PTV were 1.03 ± 0.103 and 1.09 ± 0.10, respectively. The dose gradient index (GI) was 3.412 ± 1.108, and the homogeneity index (HI) was 1.2 ± 0.13. Doses to OARs were minimal, indicating effective sparing of normal tissues. The study concluded that CyberKnife®-based SBRT plans for lung cancer achieve clinically acceptable dosimetric outcomes for both PTV and OARs, ensuring optimal treatment efficacy while minimizing risks to surrounding structures.

Keywords: CyberKnife, Stereotactic body radiotherapy, Real-time tracking; fiducial markers; stereotactic radiotherapy, lung cancer

Introduction:

Cancer remains one of the most pressing global public health challenges, with lung carcinoma standing out as one of the most prevalent and deadly malignancies. It is the leading cause of cancer-related mortality in both China and the United States, affecting men and women alike. Among the diverse manifestations of lung cancer, multiple primary lung cancers (MPLC) represent a unique and clinically significant subgroup. First described in the 1920s, MPLC can arise following curative resection of bronchogenic carcinoma, presenting as unilateral or bilateral, synchronous or metachronous tumors. Reported incidences range from 0.5% to 10%, underscoring the need for effective management strategies.

Historically, surgery has been the cornerstone of treatment for MPLC. However, advancements in radiotherapy technology have expanded therapeutic options, particularly for patients deemed inoperable due to medical comorbidities or tumor characteristics. Stereotactic body radiotherapy (SBRT)[1,3] has emerged as a groundbreaking curative approach for early-stage non-small cell lung cancer (NSCLC) in patients who are either unwilling or unable to undergo surgery. SBRT delivers highly precise, ablative doses of radiation with minimal margins, making it an attractive alternative to surgical resection[2]. Moreover, its application in treating lung metastases, though less extensively documented, shows promising potential.

The precision of SBRT is further enhanced by advanced radiotherapy systems such as the CyberKnife® (Accuray Incorporated, Sunnyvale, CA, USA). Unlike traditional linear accelerators, the CyberKnife® employs a robotic arm and sophisticated image-guided radiotherapy (IGRT) capabilities, including a dual kV X-ray imaging system and real-time tumor tracking via the Synchrony® system. This innovative technology compensates for tumor motion caused by respiration, ensuring submillimeter accuracy during treatment. The system's ability to monitor tumors in real time—either through implanted fiducial markers (e.g., gold markers or vascular coils) or direct visualization using Xsight® Lung—sets a new standard for precision in radiation oncology.

The integration of real-time tracking and adaptive targeting not only improves treatment accuracy but also minimizes radiation exposure to surrounding healthy tissues, thereby reducing the risk of complications. As a result, the CyberKnife® has become an increasingly favored modality for SBRT in lung cancer, offering hope for patients with limited treatment options. This study explores the dosimetric and clinical outcomes of CyberKnife®-based SBRT, highlighting its potential to redefine the standard of care for lung cancer patients.

Materials and methods

Simulation:

This retrospective study evaluated ten patients with single lung cancer lesions treated using the CyberKnife® system (Accuray Incorporated, Sunnyvale, CA, USA) at our institution. To account for tumor motion caused by respiration, patients with tumor respiratory motion exceeding 10 mm underwent placement of two to three fiducial markers near the tumor using bronchoscopy and four-dimensional computed tomography (4D-CT)[4,9]. For radiotherapy planning, all patients underwent high-resolution computed tomography (CT) scans of the chest and abdomen using a GE LightSpeed 16 scanner. Patients were immobilized using a Civco Vac-Lock cushion (CIVCO Medical Solutions, Iowa, USA) to ensure reproducibility and stability during treatment. Chest CT scans were acquired at 1.25-mm slice thickness to assess tumor motion and define target volumes accurately. When necessary, 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) images were fused with CT scans to enhance target delineation.

Target volumes were defined using the Precision 3.3.1.2 treatment planning system (TPS). The gross tumor volume (GTV) was delineated as the visible tumor on lung window settings of the planning CT images, and the clinical target volume (CTV) was considered equivalent to the GTV. To account for uncertainties such as respiratory motion[9,10], organ movement, and setup errors, a 10 mm margin was uniformly expanded around the GTV to create the planning target volume (PTV). Critical organs at risk (OARs) were meticulously contoured to ensure that incidental radiation exposure was minimized. These OARs included the lungs, heart, spinal cord, ribs, bronchi, Esophagus, great vessels, and carina.

Treatment planning:

Following target and OAR delineation, the Precision 3.3.1.2 TPS was utilized to design stereotactic body radiotherapy (SBRT)[3,5,6] plans based on the CT images. Dose optimization was performed using the Monte Carlo algorithm, which is recognized for its accuracy in modeling physical processes, including secondary electron distributions. Although computationally intensive, the Monte Carlo algorithm was chosen for its precision in dose calculation. Two tracking methods were employed: fiducial markers with the Synchrony® respiratory tracking system in five cases and direct tumor visualization using Xsight® Lung in the remaining five cases. The choice of tracking method was based on the characteristics of each tumor. Multileaf collimation (MLC) was used to shape the radiation beams, and a single path was selected for beam delivery.

The prescribed dose to the PTV was 50 Gy delivered in five fractions. A 6 MV flattening filter-free (FFF) photon beam was used at a dose rate of 800 MU/min. Volumetric optimization was performed to ensure that 100% of the prescribed dose covered 99% of the GTV and 95% of the PTV. The treatment plans were designed to deliver a highly conformal dose distribution while sparing surrounding healthy tissues.

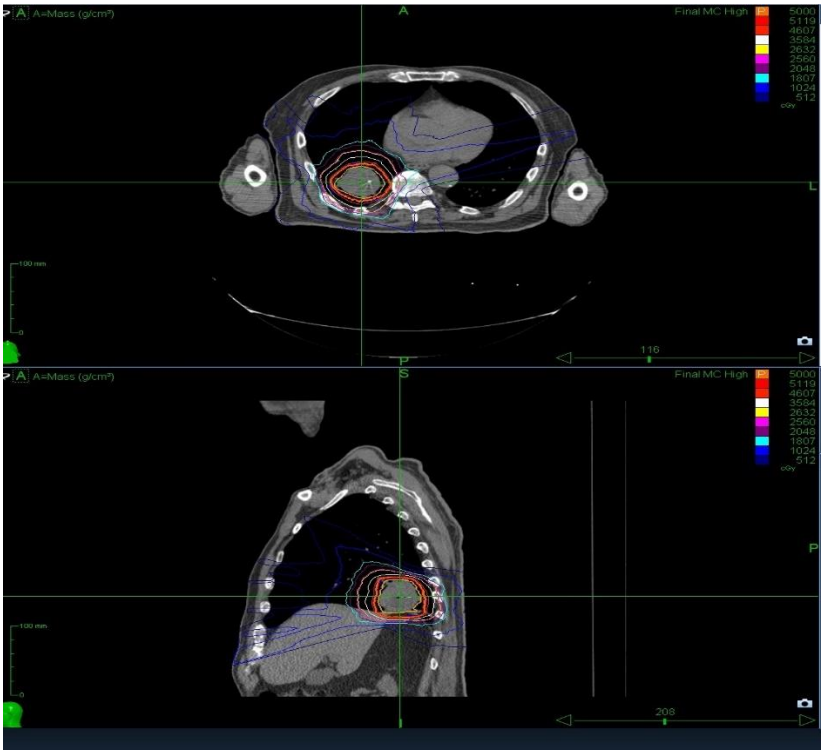

Fig.1- The transverse and coronal section isodose line distribution.

Dosimetric Parameters for Plan evaluation

The treatment plans were evaluated using a comprehensive set of dosimetric parameters to ensure clinical efficacy and safety. For the PTV, key metrics included coverage (defined as the percentage of the target volume receiving the prescribed dose), maximum dose (Dmax), mean dose (Dmean), conformity index (CI), new conformity index (nCI), homogeneity index (HI), and gradient index (GI). The CI and nCI assessed how well the prescribed dose conformed to the target volume, while the HI

evaluated dose uniformity within the PTV. The GI quantified the steepness of the dose falloff outside the target, reflecting the plan's ability to spare adjacent normal tissues.

For OARs, specific dose constraints were applied to minimize radiation exposure. For the combined lungs, parameters included mean dose (Dmean), V5 (volume receiving 5 Gy), V20 (volume receiving 20 Gy), V<12.5 Gy, and V<13.5 Gy. The heart was evaluated based on Dmean and Dmax, while the spinal cord was assessed using Dmax, D0.25cc (dose to 0.25 cc volume), and D1.25cc (dose to 1.25 cc volume). The esophagus was evaluated using Dmean and V19.5 (volume receiving 19.5 Gy), and the ribs were assessed based on Dmax and D1cc. The great vessels and liver were evaluated using Dmax and Dmean, respectively.

These dosimetric parameters ensured that the treatment plans met clinical requirements, balancing target coverage with the protection of critical structures. The results of this evaluation are presented in the subsequent sections, demonstrating the feasibility and precision of CyberKnife®-based SBRT for lung cancer.

Results:

The dosimetric analysis of the treatment plans demonstrated that the CyberKnife®-based stereotactic body radiotherapy (SBRT) for lung cancer achieved clinical prescription requirements for both the planning target volumes (PTVs) and organs at risk (OARs). The dose distribution was highly conformal, with optimal coverage of the PTV and effective sparing of surrounding critical structures. Representative transverse and coronal isodose line distributions for one treatment plan are illustrated in Figure 1, highlighting the precision of dose delivery to the target while minimizing exposure to adjacent tissues.

Target Volume Dosimetry: The coverage of the PTV, defined as the percentage of the target volume receiving the prescribed dose, was 95.3 ± 2.5%. Key dosimetric indices for the PTV were evaluated to assess plan quality, as summarized in Table 1. The maximum dose (Dmax), mean dose (Dmean), and minimum dose (Dmin) were analyzed to ensure adequate dose delivery to the target. The conformity index (CI) and new conformity index (nCI) were 1.03 ± 0.103 and 1.09 ± 0.10, respectively, indicating excellent dose conformity to the PTV. The homogeneity index (HI), which measures dose uniformity within the target, was 1.2 ± 0.13, while the gradient index (GI), reflecting the steepness of dose falloff outside the target, was 3.412 ± 1.108. These results confirm that the treatment plans achieved high precision in dose delivery, meeting clinical standards for SBRT.

Table 1: Dosimetric parameters for evaluating PTV.

Dosimetric Parameter	Mean ± SD
MU	24836.7±512
PTV100%	95.3±2.5
Dmax (Gy)	55.13±3.2
Dmin(Gy)	48.1±1.20
Dmean (Gy)	54.26±1.1
Conformity Index (CI)	1.03±0.103
new conformity index(nCI)	1.09±0.10
Homogeneity index (HI)	1.2±0.13
Gradient Index (GI)	3.412±1.108

Organs at Risk (OARs) Dosimetry: The dosimetric parameters for OARs demonstrated effective sparing of normal tissues, ensuring patient safety. For the combined lungs, the mean dose (Dmean) was 7.42 ± 1.8 Gy, with V5 (volume receiving 5 Gy) and V20 (volume receiving 20 Gy) values of 44 ± 2.5% and 8.1 ± 3.1%, respectively. The protected lung volumes receiving less than 12.5 Gy and 13.5 Gy were 1500 ± 130 cc and 1000 ± 145 cc, respectively, indicating minimal radiation exposure to healthy lung tissue.

Table2: Dosimetric parameters for plan Evaluation-OARs.

Structure	Parameter	Mean ± SD
combined Lungs	Dmean (Gy)	7.42±1.8
	V5(%)	44±2.5
	V20(%)	8.1±3.1
	V<12.5 (cc)	1500±130
	V<13.5Gy (cc)	1000±145
Heart	Dmean (Gy)	6.63±2.14
	V32Gy (cc)	14.4±2.31
Spinal cord	Dmax (Gy)	3.71±2.92
	D0.25cc(Gy)	13.21±3.91
	D1.25cc(Gy)	10.08±2.17
Esophagus	Dmean (Gy)	10.44±2.32
	V19.5(cc)	0.14±0.05
Gtreat Vessel	Dmax (Gy)	16.26±2.18
Rib	Dmax (Gy)	23.11±3.16
	D1cc(Gy)	31.4±5.17
Liver	Dmean (Gy)	4.89±3.15

For the Esophagus, the mean dose (Dmean) was 10.44 ± 2.32 Gy, and the volume receiving 19.5 Gy (V19.5) was 0.14 ± 0.05 cc. The heart received a mean dose of 6.63 ± 2.14 Gy, with a V32 (volume receiving 32 Gy) of 14.4 ± 2.31 cc. The spinal cord was well-protected, with a maximum dose (Dmax) of 3.71 ± 2.92 Gy, a D0.25cc (dose to 0.25 cc volume) of 13.21 ± 3.91 Gy, and a D1.25cc (dose to 1.25 cc volume) of 10.08 ± 2.17 Gy.

The great vessels received a maximum dose of 16.26 ± 2.18 Gy, while the ribs were exposed to a maximum dose of 23.11 ± 3.16 Gy and a D1cc (dose to 1 cc volume) of 31.4 ± 5.17 Gy. The liver received a mean dose of 4.89 ± 3.15 Gy, well below tolerance limits. These results are summarized in Table 2, demonstrating that the treatment plans effectively minimized radiation exposure to critical structures while maintaining therapeutic efficacy.Patient-specific quality assurance (QA) was conducted (Figure2) using SRS MapCHECK® and StereoPHAN™ phantom, with gamma analysis performed using 2%/2 mm criteria and a 10% threshold.

In summary, the dosimetric evaluation confirmed that the CyberKnife®-based SBRT plans for lung cancer met clinical prescription requirements for both target coverage and OAR sparing. The high conformity, homogeneity, and gradient indices, along with the low doses to critical structures, underscore the precision and safety of this treatment approach. These findings highlight the potential of

CyberKnife® SBRT as a highly effective and patient-friendly option for lung cancer treatment, particularly for inoperable cases or those requiring precise dose delivery.

Discussion

The CyberKnife® system represents a paradigm shift in the delivery of stereotactic body radiotherapy (SBRT), particularly for lung cancer, owing to its unique combination of advanced robotic mobility, real-time imaging, and precision tumor tracking[7,8]. The system's robotic arm enables the delivery of highly focused radiation beams from multiple angles, ensuring optimal dose conformity to the target while minimizing exposure to surrounding healthy tissues. This capability is further enhanced by the system's state-of-the-art image-guided radiotherapy (IGRT) technology, which includes a dual kV X-ray imaging system and the Synchrony® Respiratory Tracking System. These features allow for real-time monitoring and compensation of tumor motion caused by respiration, a critical factor in lung cancer treatment where tumor movement can significantly impact treatment accuracy.

One of the standout features of the CyberKnife® is its ability to track tumors in real time using either implanted fiducial markers (via the Synchrony® system) or direct visualization of the tumor itself (via Xsight® Lung). This adaptability ensures submillimeter precision, even for tumors with complex motion patterns. The system's optical imaging capabilities also enable the tracking of external markers, which can predict tumor position and guide radiation delivery with exceptional accuracy. Additionally, the integrated kV X-ray imaging system allows for real-time correction of positioning and treatment errors, ensuring that the radiation beams are consistently aligned with the target throughout the treatment session. This level of precision is unparalleled in traditional radiotherapy systems and is a cornerstone of the CyberKnife®'s success in delivering SBRT.

The dosimetric results of this study underscore the clinical efficacy and safety of CyberKnife®-based SBRT for lung cancer. The planning target volumes (PTVs) achieved excellent dose coverage, with a mean coverage of 95.3 ± 2.5%, while maintaining high conformity (CI: 1.03 ± 0.103; nCI: 1.09 ± 0.10) and homogeneity (HI: 1.2 ± 0.13). The gradient index (GI: 3.412 ± 1.108) further demonstrated the steep dose falloff outside the target, highlighting the system's ability to spare adjacent normal tissues. These metrics collectively confirm that the CyberKnife® delivers highly precise and conformal radiation doses, meeting the stringent requirements of SBRT.

Equally important is the system's ability to protect organs at risk (OARs). The dosimetric analysis revealed that critical structures such as the lungs, heart, spinal cord, esophagus, ribs, great vessels, and liver received significantly lower doses, well within clinically acceptable limits. For instance, the mean dose to the combined lungs was 7.42 ± 1.8 Gy, with V5 and V20 values of 44 ± 2.5% and 8.1 ± 3.1%, respectively. Similarly, the spinal cord and esophagus received maximum doses of 3.71 ± 2.92 Gy and 10.44 ± 2.32 Gy, respectively, ensuring minimal risk of radiation-induced complications. These results demonstrate that the CyberKnife® not only achieves therapeutic efficacy but also prioritizes patient safety by minimizing radiation exposure to healthy tissues.

The findings of this study align with the growing body of evidence supporting the use of SBRT as a curative option for early-stage non-small cell lung cancer (NSCLC) and lung metastases, particularly for patients who are medically inoperable or refuse surgery. The CyberKnife®'s ability to deliver high-precision, image-guided radiotherapy makes it an ideal modality for such cases. Its real-time tracking and adaptive targeting capabilities address the challenges posed by respiratory motion, ensuring accurate dose delivery even for tumors in difficult-to-treat locations. Furthermore, the system's ability to track

and treat one tumor at a time enhances localization accuracy, making it particularly suitable for patients with synchronous or metachronous lung lesions.

One of the key advantages of the CyberKnife® is its ability to perform image-guided radiotherapy effectively, offering a non-invasive alternative to traditional surgical interventions. This is especially beneficial for patients with comorbidities or those who are otherwise unsuitable for surgery. The system's precision and adaptability also make it a valuable tool for treating recurrent or metastatic lung cancer, where preserving normal tissue function is critical.

In conclusion, the CyberKnife® system represents a significant advancement in the field of radiation oncology, particularly for lung cancer treatment. Its ability to deliver highly conformal and precise radiation doses, combined with its real-time tracking and adaptive capabilities, ensures optimal therapeutic outcomes while minimizing risks to surrounding healthy tissues. The dosimetric results of this study validate the clinical efficacy and safety of CyberKnife®-based SBRT, reinforcing its role as a leading modality for lung cancer treatment. As technology continues to evolve, the CyberKnife® is poised to further redefine the standards of care, offering hope and improved quality of life for patients with lung cancer.

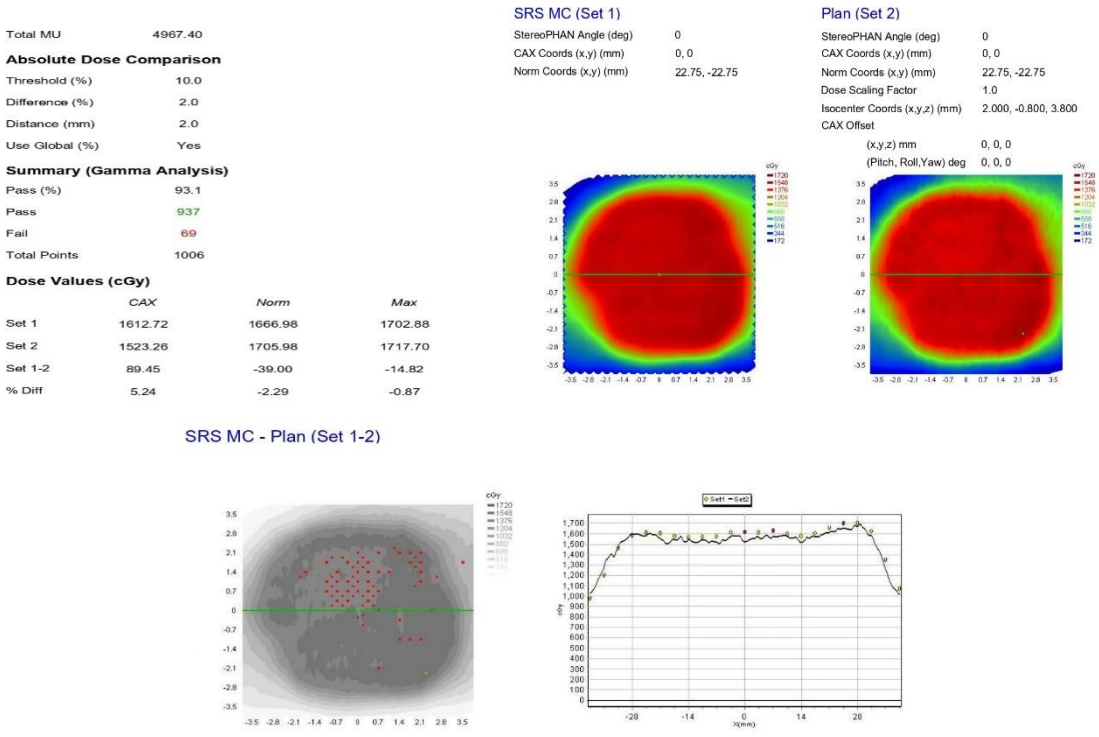

Fig.2: Patient Specific QA Analysis

Conclusion

In summary, this study demonstrates that CyberKnife®-based SBRT for lung cancer achieves exceptional dosimetric precision, meeting clinical prescription requirements for both target coverage and organ-at-risk (OAR) sparing. The system's advanced real-time tracking and adaptive capabilities ensure accurate dose delivery to the PTV while minimizing exposure to critical structures, making it a safe and effective option for inoperable patients. The results highlight the CyberKnife® as a leading modality for

lung cancer treatment, balancing therapeutic efficacy with patient safety. As technology advances, its role in transforming lung cancer care will continue to grow, offering hope and improved outcomes for patients worldwide.

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