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Research Article

Stereotactic Body Radiation Therapy (SBRT) for Non-Small Cell Lung Cancer (NSCLC) Therapy

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Abstract

For patients with early-stage non-small cell lung cancer (NSCLC) who cannot undergo surgery, stereotactic body radiotherapy (SBRT), also known as stereotactic ablative radiotherapy (SABR), usually achieves good therapeutic effects. This new treatment method has the characteristics of low toxicity and high efficacy for peripheral lung cancer. However, in central type lung cancer, especially in lesions near structures such as bronchial trees or mediastinum, there is an increased risk of severity. This review summarizes the following areas: (1) the methods and indications of using SBRT to treat NSCLC patients in different areas; (2) the principle and advantages and disadvantages of targeted MRI linear accelerators; (3) the diagnostic and evaluation process of targeted MRI linear accelerator therapy for lung cancer; (4) the clinical process of targeted MRI linear accelerator treatment for lung cancer; (5) tracking and monitoring of targeted MRI linear accelerator therapy for lung cancer; (6) pulmonary MRI disorders may include the following situations; (7) how to evaluate stage I-IV non-small cell lung cancer with targeted MRI linear accelerator; (8) how to locate central and peripheral lung cancer using targeted MRI linear accelerators; (9) increase safety of SBRT in central locations.

Keywords

Non-Small Cell Lung Cancer, Stereotactic Body Radiotherapy, Stereotactic Ablative Radiotherapy, Central Type Lung Cancer, Peripheral Lung Cancer

1. Introduction

Lung cancer is the cancer with the highest global cancer mortality rate. According to GLOBOCAN 2020 statistics, lung cancer accounts for 18% of the total deaths from male and female cancers [1, 2]. The most common type of lung cancer (85% of cases) is non-small cell lung cancer (NSCLC).

The main pathological subtypes of NSCLC include adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Small cell lung cancer (SCLC), which accounts for only 15% of the total incidence rate of lung cancer, is an uncommon tumor [3].

For patients with early NSCLC (stages I and II, T1-2N0M0), surgical treatment is the standard treatment method [4]. For a large group of patients who cannot undergo surgery or refuse surgery, the application of a new treatment method, namely stereotactic body radiotherapy (SBRT), also known as stereotactic ablation radiotherapy (SABR), can achieve good therapeutic effects and low toxicity.

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In this review, we summarized the SBRT treatment methods and dose grading schemes, as well as how to avoid the associated toxicity in the early treatment of peripheral, central, and hypercenter NSCLC.

2. The Principle and Advantages and Disadvantages of Targeted MRI Linear Accelerators

Targeted MRI linear accelerator is an advanced radiotherapy technique used for the treatment of non-small cell lung cancer. Some basic information about targeted MRI linear accelerator therapy for non-small cell lung cancer:

The principle of targeted MRI linear accelerator treatment for non-small cell lung cancer: Targeted MRI linear accelerator combines magnetic resonance imaging (MRI) and linear accelerator techniques, allowing for real-time monitoring of tumor location and morphological changes. Through precise positioning and radiation planning, high-dose radiation can be accurately delivered to tumor tissue, minimizing damage to surrounding normal tissues [5].

Targeted MRI linear accelerator therapy for lung cancer has many advantages, but there are also some drawbacks. The following are the advantages and disadvantages of this treatment method:

Advantages:

1. Accuracy: Targeted MRI linear accelerators can provide high-precision radiation therapy, ensuring the accuracy and safety of radiation by real-time monitoring of tumor location and morphological changes.
2. Personalized treatment: Based on the tumor characteristics and physical condition of each patient, personalized design can be carried out to ensure the accuracy and effectiveness of treatment.
3. Maximizing protection of surrounding normal tissues: Targeted MRI linear accelerators can minimize radiation damage to surrounding normal tissues and improve patient tolerance.
4. Efficiency: Compared to traditional radiotherapy methods, targeted MRI linear accelerator therapy usually requires a shorter time and makes the treatment process more comfortable for patients.

Disadvantages:

1. High equipment and technical requirements: Targeted MRI linear accelerator therapy requires doctors and technicians with high professional levels, as well as advanced equipment and technical support.
2. High cost: The equipment and technology used to treat lung cancer with targeted MRI linear accelerators are expensive, which may increase the treatment costs for patients.
3. Limited therapeutic indications: Targeted MRI linear accelerator therapy for non-small cell lung cancer may not be suitable for all types of lung cancer patients, and some patients may not be able to receive this treatment due to their own conditions.

In general, targeted MRI linear accelerator therapy for lung cancer has the advantages of radiation accuracy and safety, but also has disadvantages such as high cost and technical requirements. When determining the treatment plan, it is necessary to consider the specific situation of the patient and the availability of medical resources [6].

It is important to note that the specific treatment plan should be determined based on the patient's specific situation and the doctor's advice. Patients with non-small cell lung cancer are advised to consult a professional doctor for accurate diagnosis and treatment advice.

The targeted MRI linear accelerator is an advanced medical device that can be used to treat lung cancer. This device combines MRI imaging and linear accelerator radiation therapy technology to more accurately locate tumors and perform radiotherapy [7].

The treatment process usually includes the following steps:

1. Diagnosis and evaluation: The patient will first undergo MRI imaging to determine the location, size, and surrounding tissue of the tumor. The doctor will conduct a detailed evaluation based on the MRI imaging results and develop a personalized treatment plan.
2. Positioning and planning: Before the treatment begins, patients need to undergo CT scan or PET-CT scan to help doctors accurately locate the tumor and develop a treatment plan. The doctor will determine the specific radiotherapy plan based on the location and morphology of the tumor to ensure the accuracy and effectiveness of the treatment.
3. Treatment process: During the treatment, the patient lies on the treatment bed and aligns the tumor's position with the radiation beam of the linear accelerator through a positioning system. At the same time, the MRI imaging system can monitor the tumor's position and morphological changes in real time, helping doctors adjust the treatment plan to ensure the accuracy and safety of radiation.
4. Radiation therapy: Once the tumor is accurately located, a linear accelerator will release high-energy particle beams that directly irradiate the tumor tissue, damaging the DNA of cancer cells and preventing their growth and spread. The MRI imaging system can monitor the location of tumors in real time, ensuring that the radiation beam accurately irradiates the tumor site and maximally protects surrounding normal tissues from damage.
5. Tracking and monitoring: After the treatment is completed, doctors will regularly follow up and check the condition of the tumor, and evaluate the treatment effect. Patients also need to undergo regular MRI imaging and other imaging examinations to ensure that the tumor does not recur or metastasize.

Overall, targeted MRI linear accelerator therapy for lung cancer has the characteristics of precise positioning, real-time monitoring, and efficient treatment, which can minimize damage to surrounding normal tissues and improve the safety and effectiveness of treatment.

3. The Diagnostic and Evaluation Process of Targeted MRI Linear Accelerator Therapy for Lung Cancer

1. Clinical evaluation: The doctor will first conduct a clinical evaluation of the patient, including medical history inquiry, physical examination, and evaluation of related symptoms, to understand the patient's health status and symptoms [8].
2. Imaging examination: Patients usually need to undergo multiple imaging examinations to help doctors determine the location, size, and condition of surrounding tissues of lung cancer. This includes X-ray chest X-ray, CT scan, MRI imaging, and PET-CT scan.
3. Pathological examination: If the lesion is small or unclear in shape, pathological examination may be necessary to determine the type and grading of the tumor through biopsy or cytological examination, in order to develop a more accurate treatment plan.
4. Staging evaluation: Doctors will evaluate lung cancer based on the examination results to determine the size of the tumor, lymph node metastasis, and the presence of distant metastasis, in order to guide the development of subsequent treatment plans.
5. Evaluation of treatment plan: Based on the specific situation of the patient and the characteristics of the tumor, the doctor will combine imaging and pathological examination results, comprehensively consider factors such as the patient's age, physical condition, personal preference, etc., and develop the most suitable treatment plan for the patient, including surgery, radiotherapy, chemotherapy, etc.
6. Targeted MRI linear accelerator treatment plan: If the decision is made to use a targeted MRI linear accelerator for treatment, the doctor will develop a detailed treatment plan, including establishing treatment goals, designing radiation plans, selecting appropriate doses and radiation plans, etc.

Overall, the diagnosis and evaluation of targeted MRI linear accelerator therapy for lung cancer is a comprehensive process that requires doctors to comprehensively consider the patient's clinical manifestations, imaging and pathological examination results, in order to develop the most suitable treatment plan and ensure the accuracy and effectiveness of treatment [9].

The localization and planning of targeted MRI linear accelerator therapy for lung cancer are very important steps in the treatment process, mainly including the following:

1. Positioning: Before undergoing radiotherapy, it is necessary to accurately locate the location of the lung tumor. This can be achieved through high-resolution imaging techniques such as MRI imaging and CT scanning. These imaging techniques can help doctors determine the size, shape, and surrounding tissue of tumors, thereby developing more accurate radiotherapy plans.
2. Image fusion: While performing localization, doctors may perform fusion of different image modalities, such as fusing MRI and CT images, to obtain more comprehensive and accurate tumor information.
3. Radiation therapy planning: Based on the location, morphology, and individual characteristics of the tumor, doctors will design a personalized radiation therapy plan. This plan needs to consider factors such as the size and location of the tumor, protection of surrounding normal tissues, distribution of radiation dose, and treatment time.
4. Targeted therapy: When using a targeted MRI linear accelerator for radiotherapy, doctors ensure that the radiation beam accurately targets the tumor tissue while minimizing damage to surrounding healthy tissues. This usually requires real-time monitoring in conjunction with MRI imaging systems to ensure the accuracy and safety of radiation.
5. Individualized treatment: Each patient's tumor characteristics and physical condition are different, so radiation therapy planning needs to be personalized based on the patient's specific situation to ensure the accuracy and effectiveness of treatment.

Overall, localization and planning are crucial steps in the targeted MRI linear accelerator treatment of lung cancer. They provide accurate targets and refined plans for subsequent radiation therapy, while maximizing the protection of surrounding normal tissues and ensuring the safety and effectiveness of treatment [10].

4. The Clinical Process of Targeted MRI Linear Accelerator Treatment for Lung Cancer

The process of targeted MRI linear accelerator treatment for lung cancer usually includes the following steps [11]:

1. Preoperative preparation: Before undergoing radiotherapy, patients need to undergo a series of examinations, including CT scans, MRI imaging, etc., to help doctors determine the location, size, and surrounding tissue condition of the tumor.
2. Treatment plan formulation: Based on the specific situation of the patient and the characteristics of the tumor, doctors will develop personalized treatment plans and determine the goals and plans of radiation therapy.
3. Localization and labeling: Before starting treatment, patients need to perform localization and labeling to

ensure that the location of the tumor can be accurately located. This can be achieved through MRI imaging systems and other imaging techniques [12].

4. Radiation therapy: Patients lie on the treatment bed, and a linear accelerator releases high-energy particle beams that directly irradiate tumor tissue, destroying the DNA of cancer cells and preventing their growth and spread. At the same time, the MRI imaging system can monitor the location of tumors in real time, ensuring that the radiation beam accurately irradiates the tumor site, and maximizing the protection of surrounding normal tissues from damage.
5. Treatment cycle: Usually, patients need to undergo multiple rounds of radiotherapy, and the specific dosage and frequency of each radiotherapy will be adjusted according to the specific situation, usually requiring several consecutive weeks [13].
6. Tracking and monitoring: After the treatment is completed, the doctor will conduct follow-up and examination to track the condition of the tumor and evaluate the treatment effect. Patients also need to undergo regular MRI imaging and other imaging examinations to ensure that the tumor does not recur or metastasize [14].

Overall, targeted MRI linear accelerator therapy for lung cancer is a precise and complex process that requires the collaboration of doctors, radiation therapy technicians, and imaging experts to ensure the accuracy and effectiveness of treatment. This treatment method has the precision and safety of radiation, which can minimize damage to surrounding normal tissues and improve the effectiveness and safety of treatment [15].

Targeted MRI linear accelerator radiation therapy for lung cancer is a precise radiation therapy method that uses high-energy particle beams to directly irradiate tumor tissue to achieve the goal of killing cancer cells. This treatment method has the following points [16]:

1. Positioning and Planning: Before performing radiation therapy, doctors will accurately locate the location of lung tumors using techniques such as MRI imaging, and develop personalized radiation therapy plans. This plan needs to consider factors such as the tumor's location, surrounding normal tissue preservation, radiation dose distribution, and treatment time.
2. Real time monitoring: Targeted MRI linear accelerators can ensure the accuracy and safety of radiation therapy by monitoring the location and morphological changes of tumors in real time. This helps to minimize damage to the surrounding normal tissues to the greatest extent possible [17].
3. Precision irradiation: Linear accelerators release high-energy particle beams that can accurately irradiate tumor tissue, destroy the DNA of cancer cells, and prevent their growth and spread. Meanwhile, this treatment method can maximize the protection of surrounding normal tissues from damage.
4. Precision irradiation: Linear accelerators release high-energy particle beams that can accurately irradiate tumor tissue, destroy the DNA of cancer cells, and prevent their growth and spread. Meanwhile, this treatment method can maximize the protection of surrounding normal tissues from damage [18].

Overall, targeted MRI linear accelerator radiation therapy for lung cancer has the characteristics of precise positioning, real-time monitoring, and high treatment efficiency, which can minimize damage to surrounding normal tissues and improve the completeness and effectiveness of treatment. This treatment method plays an important role in the treatment of lung cancer, providing patients with a more precise and safe treatment option [19].

5. Tracking and Monitoring of Targeted MRI Linear Accelerator Therapy for Lung Cancer

Tracking and monitoring are crucial for evaluating treatment outcomes and patient health status after targeted MRI linear accelerator therapy for lung cancer. The following are general tracking and monitoring measures [20-25]:

1. Follow up and examination: Patients usually need to return to the hospital regularly for follow-up and examination to evaluate treatment effectiveness and monitor the condition of the tumor. These follow-up usually include physical examinations, imaging examinations (such as MRI imaging, CT scans, etc.), and blood tests.
2. Follow up and examination: Patients usually need to return to the hospital regularly for follow-up and examination to evaluate treatment effectiveness and monitor the condition of the tumor. These follow-up usually include physical examinations, imaging examinations (such as MRI imaging, CT scans, etc.), and blood tests.
3. Symptom assessment: Patients need to regularly inform their doctors if there are any new symptoms or discomfort after treatment, such as difficulty breathing, cough, chest pain, etc. This helps doctors to detect and deal with possible complications or recurrence in a timely manner.
4. Tumor marker detection: Sometimes doctors may require blood tests to detect specific tumor markers to help evaluate treatment efficacy and monitor the condition of the tumor.
5. Psychological and quality of life assessment: It is equally important to assess the patient's psychological and quality of life after treatment. This helps to understand the patient's psychological condition and quality of life, thereby providing necessary support and assistance.

Overall, tracking and monitoring are important aspects of targeted MRI linear accelerator therapy for lung cancer. They help evaluate treatment outcomes, identify and manage potential complications or recurrence, and provide necessary support and assistance to patients [26-28].

6. Pulmonary MRI Disorders May Include the Following Situations

1. The impact of respiratory movement: The lungs are organs with respiratory movement, which can cause image blurring and distortion during MRI scans. Respiratory movements can cause movement of lung tissue during the scanning process, leading to a decrease in image quality [29-33].
2. The influence of lung gas on MRI signals is mainly composed of gas in the lungs, while MRI signals are mainly generated by water molecules. Therefore, the air in the lungs can weaken the MRI signal, resulting in lower image contrast in the area.
3. The interference of the heart and blood vessels can lead to magnetic field interference caused by the proximity of the lungs to the heart and large blood vessels, which in turn can affect the quality of lung MRI images.
4. Lack of tissue contrast: Due to the fact that the lungs are mainly composed of gas, while MRI signals are mainly produced by water molecules, this may result in low contrast between lung tissues, making it difficult to distinguish the structure of the image.

In order to overcome these obstacles, medical imaging technology is constantly advancing. There are currently some technologies and methods that can be applied to address lung MRI obstacles, such as using different pulse sequences, adjusting scanning parameters, combining respiratory control techniques, and using special surface coils to improve the quality and reliability of lung MRI images [34-36].

Targeted MRI linear accelerators can determine tumor location, size, and surrounding tissue conditions through the following methods:

Magnetic Resonance Imaging (MRI): Targeted MRI linear accelerator combined with MRI technology can monitor the location and morphological changes of tumors in real-time. Before treatment, patients will undergo scanning to determine the location, size, and surrounding tissue condition of the tumor through high-resolution images.

Positioning system: Targeted MRI linear accelerators are equipped with precise positioning systems that can determine the location of tumors through patient anatomical structures or special markers (such as metal markers or reference points). The positioning system can register with MRI images to ensure the accuracy of radiation therapy.

Pre-established radiation plan: Before treatment begins, doctors will develop an individualized radiation plan based on MRI images and other imaging examination results. This plan will provide detailed guidance on the target area and dose distribution of radiation therapy to ensure maximum protection of surrounding normal tissues [37, 38].

Real time image guidance: During the treatment process, targeted MRI linear accelerators can monitor tumor location and morphological changes in real time. By continuously updating image guidance, precise radiation therapy can be performed on tumors to ensure accuracy and safety.

In summary, targeted MRI linear accelerators combine MRI technology and precise positioning systems to determine the location, size, and surrounding tissue conditions of tumors. This information will be used to develop personalized radiation therapy plans and be monitored and adjusted in real-time during the treatment process. This can minimize damage to surrounding normal tissues and improve treatment effectiveness.

7. How to Evaluate Stage I-IV Non-Small Cell Lung Cancer with Targeted MRI Linear Accelerator

Targeted MRI linear accelerators typically combine multiple imaging and clinical evaluation methods when evaluating stage I-IV non-small cell lung cancer. Here are some commonly used evaluation methods [39-41]:

Magnetic Resonance Imaging (MRI): MRI can provide high-resolution tumor images to help evaluate the size, location, infiltration range, and relationship with surrounding tissues of tumors. Through MRI images, doctors can determine the staging of tumors.

CT scan: CT scan is a commonly used imaging examination method that can provide detailed images of the anatomical structure of the lungs. Through CT scanning, doctors can evaluate the size, location, and lymph node metastasis of tumors, thereby determining the staging of tumors.

PET-CT scan: Positron emission computed tomography (PET-CT) combines positron emission tomography and CT scans to provide fusion images of metabolic activity and anatomical information. PET-CT scanning can help evaluate the metabolic activity and metastasis of tumors.

Lymph node biopsy: For lung cancer patients, lymph node metastasis is a common occurrence. Lymph node biopsy can determine the presence of tumor metastasis by sampling lymph node tissue.

Clinical evaluation: In addition to imaging evaluation, doctors will also conduct comprehensive evaluations based on the patient's medical history, symptoms, physical examination, and laboratory test results. These pieces of information help determine the staging of tumors and evaluate the overall condition of patients.

When using targeted MRI linear accelerators for lung cancer treatment, there may be some obstacles related to lung MRI [40-42]:

Respiratory movement: The lungs are located in the chest cavity and are greatly affected by respiratory movement. Respiratory movements can cause changes in lung position, posing challenges for precise tumor localization and radiation therapy. To overcome this problem, respiratory control techniques such as deep inhalation or exhalation pauses are usually used to reduce the interference of respiratory movements on treatment.

Image resolution: Lung tissue has lower density and contrast, which may lead to lower image resolution. This may pose certain difficulties for tumor detection and localization. To overcome this problem, image quality and resolution can be improved by increasing scanning time, optimizing image sequence parameters, or combining other imaging methods such as CT scanning or PET-CT scanning.

Mobile artifacts: Movement caused by breathing and other factors may result in the appearance of mobile artifacts in the image. These artifacts may interfere with the accurate localization and evaluation of tumors. To understand this issue, dynamic image acquisition techniques, breath gating techniques, or image post-processing methods can be used to reduce the impact of moving artifacts.

Airway and vascular movement: The lungs contain airways and blood vessels, and the movement of certain structures can also affect image quality and treatment plans. In the treatment plan, it is necessary to fully consider the movement of these structures to ensure the accuracy and safety of radiation therapy.

What is needed is that the above-mentioned obstacles are not absolute, but rather problems that may arise in certain situations. The medical team will develop corresponding strategies based on the specific situation and treatment needs of patients to overcome these obstacles and ensure the effectiveness and safety of treatment.

8. How to Locate Central and Peripheral Lung Cancer Using Targeted MRI Linear Accelerators

The methods for locating central lung cancer and peripheral lung cancer differ when using targeted MRI linear accelerators. The following are the localization methods for these two types of lung cancer:

Localization of central lung cancer:

Carcinogenicity lung cancer refers to a tumor located in the main bronchus or near the main bronchi of the lung. For the localization of central lung cancer, the following methods can be used:

1) Use CT scans and MRI images to determine the location and extent of tumors. These images display the relationship between the tumor and the main bronchus, and help doctors determine the target area for radiation therapy;
2) Use bronchoscopy to directly observe the relationship between the tumor and the main bronchus. This can provide more accurate positioning information;
3) Place gold markers or catheters near the tumor for precise localization during the treatment process;

2. Localization of peripheral lung cancer:

Peripheral lung cancer refers to tumors located in the peripheral tissues of the lungs. For the localization of peripheral cancer, the following methods can be used:

(1) Using CT scans and MRI images to determine the location and size of tumors can help doctors determine the target area for radiation therapy.
(2) Use a navigation system for localization, using a needle or catheter to reach the tumor area to determine the target of radiation therapy.

Whether it is central or peripheral lung cancer, targeted MRI linear accelerators can provide real-time image guidance to ensure precise tumor localization and radiation delivery during the treatment process.

The specific positioning method should be determined based on the patient's specific situation and the doctor's advice. The medical team will develop personalized positioning plans based on the patient's imaging results, bed history, and other relevant information to ensure the accuracy and safety of treatment.

SBRT is a newly developed non-invasive targeted radiotherapy technique [5-7]. It can accurately irradiate cancer cell tissue with high radiation doses under the guidance of MRI, and minimize damage to normal lung tissue [5-7]. Recent literature has reported that the therapeutic effect and long-term survival rate of SBRT are the same as those of video-assisted thoracoscopic surgical (VATS) lobectomy with mediastinal lymph node dissection (VATS L-MLND) in patients with stage IA NSCLC who can undergo surgery [8].

The toxicity of SBRT therapy applied to the treatment of lung cancer are mainly related to the location of the lung cancer. SBRT is commonly used to treat peripheral tumors, including tumors with lesions>2 cm located in the following areas: from the central airway - trachea, carina, and main bronchus to the secondary bronchi [9].

The existing evidence (Level II) demonstrates that increasing the biologically effective dose (BED) (e.g. 3 x 20Gy) can significantly increase the incidence of grade 3 toxicity.

Due to the potential for over 10% of patients to develop grade 3 toxicity and associated higher toxicity (including death) during SBRT treatment, the optimal dose-fractionation allocation method should be selected for specific SBRT cases.

The definition of central located cancer is that the distance between the tumor lesion and the proximal bronchial tree is less than 2cm. In ultracentral tumors, the gross tumor volume (GTV) typically invades the proximal bronchial tree or mediastinal tissue.

9. Increase Safety of SBRT in Central Locations

In early phase II clinical trials using the SBRT method to treat NSCLC cases, central or extra central cancer locations were defined as "no fly zones" due to the excessive toxicity of the SBRT method to central or extra central cancers [10, 11]. Recently, the use of optimized dose grading techniques has increased the risk tolerance of central organ to radiation treatment, thereby enhancing the safety of SBRT therapy [12].

In the recent ISRS guidelines, it has been pointed out that when using SBRT to treat patients with ultracentral lung cancer, if the patient is selected appropriately and a reasonable design is achieved through combination therapy and radiation therapy, the use of SBRT method is safe [13].

Although there have been many reports on the use of SBRT for graded treatment of ultracentral lung cancer, the optimal treatment plan still needs further research and determination. Further determination is needed on the optimal treatment plan for SBRT: continuous treatment plan for several days, single treatment plan, or re-radiation treatment plan.

10. Conclusion

For patients with early NSCLC who cannot undergo surgery, SBRT has good efficacy and low toxicity. This article confirms that SBRT is safe and effective by summarizing relevant research reports on dose segmentation evidence of NSCLC patients in different locations. Further selection and design of combination therapy and comprehensive radiation therapy should be carried out through appropriate patient selection, in order to improve the therapeutic effect and minimize toxicity of SBRT.

Abbreviations

NSCLC	Non-Small Cell Lung Cancer
SCLC	Small Cell Lung Cancer
SBRT	Stereotactic Body Radiotherapy
SABR	Stereotactic Ablative Radiotherapy
MRI	Magnetic Resonance Imaging
CT	ComputerTomography
PET-CT	Positron Emission Tomography-ComputerTomography

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Author Contributions

Conceptualization, Z. L. and C. W.; data curation, Z. L.; writing—original draft preparation, Z. L.; writing—review and editing, C. W. All authors have read and agreed to the published version of the manuscript.

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The authors declare no conflict of interest.

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