

Efficacy and safety of image-guidance radiotherapy by helical tomotherapy in patients with lung cancer

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Abstract

This study aimed to explore the efficacy and toxicity of image-guided stereotactic body radiotherapy (IGSBR) by helical tomotherapy in patients with lung cancer among Chinese Han population.

A total of 21 patients with stage I lung cancer were included. They received a total of 60 Gy fractions IGSBR. The outcomes included complete response (CR), partial response (PR), stable disease (SD), progress disease (PD), overall response rate (ORR), and overall survival (OS). In addition, toxicities were also recorded in this study.

Three-year CR, PR, SD, PD, ORR, and OS were 47.6%, 38.1%, 9.5%, 4.8%, 85.7%, and 48.0 months, respectively. Additionally, mild toxicities were found in this study.

This study demonstrated that IGSBR is efficacious for patients with stage I lung cancer with mild toxicities among Chinese Han population.

Abbreviations: CR = complete response, GTV = gross tumor volume, IGSBR = image-guided stereotactic body radiotherapy, IOLC = inoperable lung cancer, ORR = overall response rate, OS = overall survival, PD = progress disease, PR = partial response, SD = stable disease, XVI = x-ray volumetric imaging.

Keywords: efficacy, lung cancer, stereotactic body radiotherapy, toxicity

1. Introduction

Lung cancer is one of the most common causes of cancer-related death in the world.^[1,2] Its early detection has been improved by using the examinations of computed tomography, and positron emission tomography.^[3] It has been reported that patients with lung cancer at early stage after the surgery often have encouraging effect with more than 90% local control rate, and 50% of 5-year survival.^[4] However, some patients are not available to have surgery, and they receive the management with radiotherapy.^[5–7] Previous studies have reported that conventional radiotherapy cannot control the primary lung cancer in more than 60% patient's population.^[8] In addition, more than 50% patients died from its progression ultimately with such kind of management.^[8]

Image-guided stereotactic body radiotherapy (IGSBR) is an advanced radiotherapy based on the conventional radiotherapy.^[9–13] It utilized advanced imaging techniques to deliver a targeted radiation dose to a tumor with a high degree of precision and steep dose gradients.^[9–10] Additionally, it can also minimize the dose to normal tissues, which can help preserve the healthy tissue for patients with lung cancer. It has been reported that IGSBR for the treatment of lung cancer achieved excellent effect of local control rates for primary tumors, and metastatic malignancies.^[14–17]

Presently, limited data of IGSBR for the treatment of patients in lung cancer at the early stage among Chinese population are available. In this study, we retrospectively analyzed the efficacy and toxicity of IGSBR in patients with lung cancer at the early stage among the Chinese population.

2. Patients and methods

In this retrospective study, 21 patients with the diagnosis of stage I lung cancer by computed tomography, or positron emission tomography were included, and were treated with IGSBR by helical tomotherapy. It was formally approved by the Medical Ethical Committee of The Affiliated Hongqi Hospital of Mudanjiang Medical University, and the informed consent was obtained from all patients. It was conducted at The Affiliated Hongqi Hospital of Mudanjiang Medical University from January 2013 to December 2015. The clinical characteristics are shown in Table 1. All patients were unavailable or declined to receive surgery. All patients aged from 40 to 82 years, with median age of 69 years. The mean tumor size was 2.5 ± 0.8 cm. All patients had central tumors. The histology included nonsmall cell lung cancer, squamous cell carcinoma, and adenocarcinoma. The status of Eastern Cooperative Oncology Group ranged from 0 to 2. The tumor, node, metastasis stage consisted of IA and IB.

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Table 1**Characteristics of included patients.**

Characteristics	Value
Mean age, years	71.4 (12.1)
Sex	
Male	17 (80.9)
Female	4 (19.1)
Ethnicity (Chinese Han)	21 (100.0)
Occupation	
Employed	2 (9.5)
Unemployed	3 (14.3)
Retired	16 (76.2)
Marital status	
Married	9 (42.9)
Divorced	2 (9.5)
Widowed	10 (47.6)
Tumor location	
Central	21 (100.0)
Mean tumor size, cm	2.5 (0.8)
Histology	
NSCLC	6 (28.6)
Squamous cell carcinoma	8 (38.1)
Adenocarcinoma	7 (33.3)
ECOG	
0	9 (42.9)
1	7 (33.3)
2	5 (23.8)
TNM stage	
IA	12 (57.1)
IB	9 (42.9)

Note: Data are present as mean \pm standard deviation or number (%); ECOG=Eastern Cooperative Oncology Group, NSCLC=non-small cell lung cancer, TNM=tumor, node, metastasis.

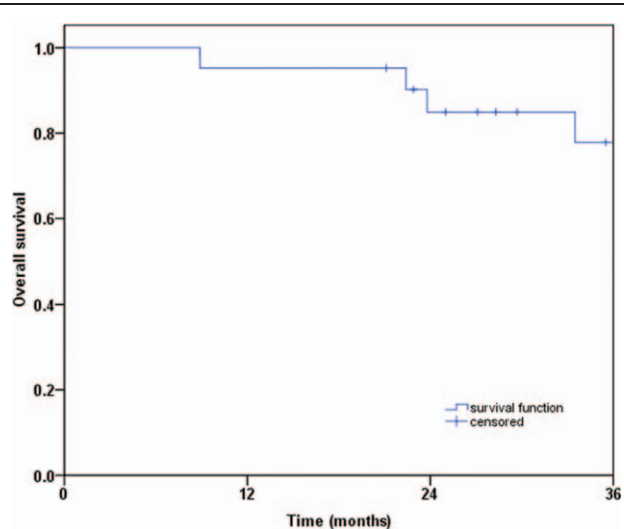
Before the IGSR treatment, all patients were positioned with supine to make sure that they were in a stereotactic body frame. The IGSR was performed by using Elekta Synergy S linear machine (Elekta, Stockholm, Sweden). Real-time tumor tracking was conducted to track the tumors motion, and other internal organs. The slices thickness was 3 mm. The target lesion was delineated as the gross tumor volume (GTV) on the planning computed tomography slices using a standardized computed tomography lung level setting. It was equal to the clinical planning target volume. If it is necessary, 18F-fluorodeoxyglucose positron-emission tomography/x-ray computed tomography was also used as optional. The attacked tumor regions were scanned daily. After that, the planning computed tomography scans and contours of each patient were transferred by Elekta x-ray volumetric imaging (XVI) software for treatment planning. The dose of risk-adapted fractionation scheme was applied. 60 Gy/10 fractions were delivered once daily, 5 days weekly.

In this study, all included patients were monitored and recorded daily for the acute and late treatment related toxicity. The standard of Response Evaluation Criteria in Solid Tumors 1.1 was used to measure each tumor size. In addition, complete response (CR) was defined as the total tumor disappearance.

Table 2**Response rate of all included patients.**

Value	CR	PR	SD	PD	ORR
Response rate	10 (47.6)	8 (38.1)	2 (9.5)	1 (4.8)	18 (85.7)

Note: Data are present as number (%); CR=complete response, ORR=overall response rate, PD=progress disease, PR=partial response, SD=stable disease.

**Figure 1.** Overall survival.

Partial response (PR) was defined as a $\geq 30\%$ decrease in the longest diameter of tumors. Stable disease (SD) was defined as a $< 30\%$ decrease or a $\leq 20\%$ increase of the longest tumor diameter. Progress disease (PD) was defined as a $> 20\%$ increase in the longest tumor diameter, or with the new lesion. Overall response rate consisted of CR and PR. Overall survival (OS) was calculated at the beginning of IGSR applied to the date of death with any reasons. OS were evaluated by the Kaplan–Meier method. Toxicities were assessed by using the Common Toxicity Criteria for Adverse Events (V4.0). The toxicity was defined from the first day to the 90th day from the beginning of the IGSR, and late toxicity was recorded after the 90th day. The log-rank test was conducted to perform univariate analysis. All data were analyzed by using SPSS software (SPSS Version 17.0, IBM Corp., Armonk, NY).

3. Results

The CR, PR, CD, PD, and ORR of the 3-year follow-up were 47.6%, 38.1%, 9.5%, 4.8%, and 85.7%, respectively (Table 2). The median OS was 48.0 months (95% confidence interval: 36.9–59.1 months) (Fig. 1).

The toxicity-related-treatment is shown in Table 3. The total toxicities were mild in this study, and all occurred in grade 1 and 2. No grade 3 or higher toxicities were recorded in this study. As

Table 3**Toxicities after IGSR treatment.**

Toxicities	Grade 1	Grade 2	Total
Acute			
Fatigue	3 (14.3)	2 (9.5)	5 (23.8)
Dyspnea	2 (9.5)	1 (4.8)	3 (14.3)
Radiation esophagitis	2 (9.5)	0 (0)	2 (9.5)
Pain	2 (9.5)	0 (0)	2 (9.5)
Late			
Pneumonitis	6 (28.6)	1 (4.8)	7 (33.4)
Chest pain	1 (4.8)	0 (0)	1 (4.8)
Rib fractures	0 (0)	0 (0)	0 (0)

Note: Data are present as number (%).

for acute toxicities, five (23.8%) patients were found to have acute fatigue; 3 patients had dyspnea (14.3%); and 2 patients occurred radiation esophagitis (9.5%), and pain (9.5%). As for late toxicities, 7 (33.4%) patients were recorded pneumonitis; and 1 (4.8%) patient was found chest pain. No patients were reported for rib fractures, as well as hematology toxicity.

4. Discussion

Previous studies have explored the efficacy and safety of IGSR in patients with lung cancer, and achieved promising outcome results. Two studies assessed the toxicity and efficacy of IGSR in a high-risk population of patients with early stage but medically inoperable lung cancer (IOLC).^[18,19] One concluded that patients with nonsmall cell IOLC received SBRT had a survival rate of 55.8% at 3 years.^[18] In addition, it also had high rates of local tumor control, and moderate treatment-related morbidity. The results of the other one demonstrated that IGSR allows for real-time tumor tracking and also the risk-adapted fractionation achieves satisfactory local control and low toxicity rates in patients with IOLC at early stage.^[19] The other study compared the effects between central and peripheral stage I lung cancer using IGSR by helical tomotherapy.^[20] It is found that helical IGSR for the treatment of central stage I lung cancer is safe and effective, when it is compared with the patients in peripheral stage I lung cancer.^[20] The another study analyzed the inter- and intrafractional changes in tumor volume with respect to both spatial and volumetric parameters among patients treated by IGSR for lung cancer.^[21] Its results demonstrated that interfractional IGSR is necessary for lung cancer.

The results of our study are consistent with the previous studies.^[18,20] Our study found that the efficacy and safe of image guidance radiotherapy via helical tomotherapy in patients with stage I lung cancer is encouraging. The ORR of 3-year follow-up was 85.7%. In addition, the median OS was 48.0 months. The total toxicities were mild without sever toxicities. The most frequencies toxicities were acute fatigue (23.8%), and late pneumonitis (33.4%).

This study has 3 limitations. First, this study had a relative small number of patients with lung cancer, which may affect the results of this study. Second, this study only explored the central lung cancer, thus patients with peripheral lung cancer still need to be explored. Third, all included patients are ethnicity of Chinese Han. Thus, the efficacy and safety of IGSR in patients of other ethnicities of Chinese population should also be focused in the future.

5. Conclusion

The results of this study demonstrated that IGSR is effective for patients with stage I lung cancer with mild toxicities among Chinese Han population.

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