

Observation on the Clinical Effect of Stereotactic Body Radiotherapy in Patients with Oligometastatic Tumors

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Abstract: Objective: To observe the efficacy and safety of stereotactic body radiotherapy (SBRT) in the treatment of extracranial oligometastases. Method: A retrospective analysis of 70 patients with extracranial oligometastasis of malignant tumors who underwent SBRT in our hospital (Shaanxi Provincial People's Hospital) from January 2019 to December 2021 with \leq 5 metastases, \leq 3 metastatic organs, and metastases with diameters of \leq 5 cm. According to the clinical data of patients, the dose-fractionation mode of SBRT is mainly determined according to the pathology of the primary tumor, the location of the metastatic tumor, and the important structures around the tumor. The local control, survival and adverse reactions were observed. Results: A total of 219 oligometastatic lesions in 70 patients were treated with SBRT. The median follow-up time was 24 months (12-40 months). The local control rate (LCR) of all target lesions assessed 3 months after radiotherapy was 94.1%; the 1-, 2-, and 3-year LCRs were 88.6%, 74.6%, and 64.9%, respectively. The median progressionfree survival (PFS) was 11.8 months (95% CI, 8.9–14.7 months), and the 1- and 2-year PFS rates were 48.6% and 32.6%, respectively; the median overall survival (OS) was 31.9 month (95% CI 26.0-37.8 months), the 1-year OS rate was 84.3%. The local control time, PFS, and OS of patients with metastases ≤ 3 cm were significantly better than those with metastases > 3 cm, and the differences were statistically significant (P < 0.05). Acute adverse reactions after SBRT treatment in oligometastatic patients were mainly bone marrow suppression and gastrointestinal reactions, with incidence rates of 48.98% and 30.61%, respectively; chronic adverse reactions were mainly pain (bone, muscle), radiation enteritis, and radiation pneumonitis, with incidence rates of 38.57%, 30.00%, and 24.29%, respectively. The treatment-related adverse reactions were mainly grade 1, which were all improved after symptomatic treatment, except for one patient with bone metastases from lung cancer who had grade 4 myelosuppression. No grade 4 or 5 adverse events occurred in the other patients. Conclusion: The application of SBRT in the treatment of extracranial oligometastases is safe, effective, and has high tolerability.

Keywords: Stereotactic body radiotherapy; Extracranial oligometastases; Efficacy; Adverse reactions

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1. Introduction

The traditional medical view holds that as long as the tumor has metastasized, the treatment is limited to palliative reduction. Hellman first proposed the concept of "oligometastasis" of tumors in 1995, arguing that oligometastasis is a transitional stage between local primary tumor and extensive metastasis ^[1]. The

physical condition of a patient with oligometasis is still relatively good, the number of metastases is not many and are organ-specific, and the biological invasiveness is mild with no tendency for systemic dissemination. These properties of oligometastases determine the clinical significance of local therapy. Under the premise of ensuring a safe and effective systemic treatment, a positive and reliable local treatment mode for oligometastatic tumors needs to be developed through further clinical research. With the vigorous development of modern radiotherapy technology, the continuous innovation of radiotherapy equipment, and the change of the radiotherapy segmentation mode, the emergence and clinical application of stereotactic body radiotherapy (SBRT) technology has made the radiotherapy of oligometastatic tumors more effective. Technically possible. We used SBRT technology to treat oligometastatic tumors and achieved good clinical efficacy, which are reported as follows.

2. Materials and methods

2.1. Case data

Patients with oligometastatic malignant tumors who underwent SBRT in our hospital from January 2019 to December 2021 with complete data were collected for retrospective analysis. Inclusion criteria: (i) patients with stage IV solid tumor confirmed by histology or pathology; (ii) aged ≥ 18 years old; (iii) comprehensive imaging examination, with ≤ 5 metastases and ≤ 3 metastatic organs; (iv) each metastatic lesion can be assessed by imaging (computed tomography [CT], magnetic resonance imaging [MRI], electroconvulsive therapy [ECT], positron emission tomography-computed tomography [PET-CT]), with diameters \leq 5cm; (5) all oligometastatic tumors are suitable for SBRT treatment, and there is no history of radiotherapy in the lesion area; (6) Eastern Cooperative Oncology Group (ECOG) performance status score of 0-2; (7) Expected survival time > 3 months; (8) No vital organ dysfunction before treatment, bone marrow function, liver and kidney function, and cardiopulmonary function are normal; (9) voluntarily participated and signed a written informed consent. Exclusion criteria: (1) intolerable or metastatic lesions not suitable for SBRT treatment; (2) brain metastases; (3) pregnant or lactating women; (4) those with mental disorders who cannot complete the treatment; (5) those with acute infection and uncontrolled dysfunction of important organs such as the heart, liver, lung, and kidney. A total of 70 patients were finally eligible for inclusion, including 45 males and 25 females; the age of the patients ranged from 20 to 82 years old, with a median age of 62 years. The ECOG score was 0 in 7 cases, 1 in 24 cases, and 2 in 39 cases. The primary lesions included 19 lung cancers, 14 colorectal cancers, 8 breast cancers, 7 pancreatic cancers, 4 esophageal cancers, 3 renal cancers, 3 gastric cancers, 2 gallbladder cancers, 2 hypopharyngeal cancers, 2 cases of cervical cancer, and 6 cases of other tumors (endometrial cancer, ovarian cancer, submandibular adenocarcinoma, ureteral cancer, prostate cancer, and soft tissue sarcoma). There was 1 oligometastasis in 5 cases, 2 in 15 cases, 3 in 22 cases, 4 in 20 cases, 5 in 8 cases. The location of oligometasis were in liver in 29 cases, in the lung in 24 cases, in the bone in 22 cases, in the lymph node in 20 cases, in the adrenal gland in 9 cases, and in the soft tissue in 1 case. The metastases were registered according to the 6 anatomical sites of liver, lung, bone, lymph node, adrenal gland, and soft tissue. There were 219 metastases, including 64 liver metastases, 61 lung metastases, 48 lymph node metastases, and 35 bone metastases, 9 adrenal metastases, and 2 soft tissue metastases; the total number of metastases was 1 in 5 cases, 2 in 16 cases, 3 in 22 cases, 4 in 19 cases, and 5 in 8 cases. The largest diameter of oligometastatic tumor is \leq 3cm in 55 cases, >3 cm in 15 cases. See **Table 1** for more details.

Clinicopathological parameters	Number of cases (n)	Percentage (%)
Gender	70	100
Male	45	64.3
Female	25	35.7
Primary tumor type	70	100
Lung cancer	19	27.1
Colorectal cancer	14	20.0
Breast cancer	8	11.5
Pancreatic cancer	7	10.0
Esophageal cancer	4	5.7
Kidney cancer	3	4.3
Stomach cancer	3	4.3
Gallbladder cancer	2	2.9
Hypopharyngeal cancer	2	2.9
Cervical cancer	2	2.9
Endometrial cancer	1	1.4
Ovarian cancer	1	1.4
Submandibular adenocarcinoma	1	1.4
Ureteral cancer	1	1.4
Prostate cancer	1	1.4
Soft tissue sarcoma	1	1.4
Number of metastases at each site (number)	219	100
Liver	64	29.2
Lung	62	28.3
Lymph nodes	48	21.9
Bone	34	15.5
Adrenal glands	9	4.1
Soft tissue	2	0.9
Total number of metastases (pieces)	70	100
1	5	7.1
2	16	22.9
3	22	31.4
4	19	27.1
5	8	11.5
Maximum diameter of metastases	70	100
≤3cm	55	78.6
>3cm	15	21.4

Table 1. General clinical data of 70 patients with oligometastases

2.2. Treatment methods

2.2.1. SBRT

(1) CT positioning and image transmission processing

Patients were placed in the supine or prone position, fixed with a thermoplastic body film and/or a vacuum pad, and after marking the body surface markers, all patients were subjected to CT enhanced scanning positioning on a Philips large-aperture CT simulation positioning machine (Patients with allergies to iodine contrast agents and other related drugs were excluded), the slice thickness was \leq 5mm (if 4D-CT was performed, CT images of different phases were collected). During the positioning scan, the patient was instructed to breathe calmly, and an abdominal pressure plate was used to limit the breathing movement in patients with oligometastatic tumors in the chest and abdomen. When there are metastases in the brain, liver, and spine, it is necessary to perform enhanced MRI of the brain, liver, and spine again and record the images on a disc. The images were transmitted to Elekta through the network. In the Monaco treatment planning system, the physicist will fuse the images of the brain-enhanced MRI, liver-enhanced MRI and spine-enhanced MRI in the same position as the radiotherapy positioning with the positioning CT respectively.

(2) SBRT target volume delineation and prescribed dose

The target volume delineation should be done by senior radiotherapy physicians with reference to relevant imaging data. The target volume should be fully considered when delineating the target volume, especially for lesions located in the lower lungs, mediastinum, and large vessels, near the diaphragm, and other more active lesions. The appropriate window width and window level were selected on the 3D-CT image to delineate the gross tumor volume (GTV), which is GTV_{3D} , and was used in the 4D-CTMIP image. The inner target volume (ITV) was outlined and denoted as ITV_{MIP} . GTV_{3D} and ITV_{MIP} were integrated to generate ITV_{COMB} , and the ITV_{COMB} was expanded by 3-5 mm to form a planned target volume (PTV). The dose-fractionation mode was mainly determined according to the pathology of the primary tumor, the location of the metastatic tumor, and the important structures around the tumor, using 30-60 Gy/5-10 f, and Biological Effective Dose (BED) \geq 80Gy for non-bone metastatic lesions. 100 % of the prescribed dose is required to include 95% PTV, and the dose limits for organs at risk and normal tissues were based on the American Radiation Therapy Oncology Group (RTOG) Protocol No. 0236.

(3) Radiotherapy plan preparation, verification, and treatment

The radiotherapy plan preparation and dose calculation on the average density projection images were performed by a physicist in the Monaco treatment planning system. The plan was then evaluated by the and a radiotherapist. Radiation therapy was performed using either intensity-modulated radiation therapy (IMRT)-SBRT or volumetric rotational intensity-modulated radiation therapy (VMAT)-SBRT. Cone beam CT (CBCT) system was used for setup verification, and the error was controlled within 3mm. CBCT verification was performed before each treatment and the verification images were transmitted to the Monaco treatment planning system. SBRT was performed on the Elekta infinity linear accelerator as planned after the validation. During radiotherapy, blood routine, liver and kidney function and other indicators were regularly detected.

2.2.2. Systemic therapy

The treatment plan includes chemotherapy, targeted therapy and immunotherapy. The treatment plan was selected according to the histological type of the primary tumor, and was carried out before, during or after radiotherapy according to the actual situation of the treatment.

2.2.3. Necessary symptomatic treatment

When serious treatment-related toxicity occurs, corresponding symptomatic and supportive treatment (such as antiemetic, hemostasis, active correction of bone marrow suppression, and so on) was given.

2.3. Observation indicators and evaluation criteria

2.3.1. Local control status

The efficacy was evaluated according to the re-examination imaging data 3 months after SBRT, and the re-examination was performed every 3 months for 2 years thereafter, and once every six months after 2 years. The efficacy evaluation was divided into complete remission (CR), partial remission (PR), stable disease (SD) and progression disease (PD) according to the Response Evaluation Criteria in Solid Tumors (RECIST). Local control (LC) is defined as the absence of new or original lesions in or around the PTV after SBRT for oligometastatic lesions. Local Control Rate (LCR) = ([CR+PR+SD]/ [CR+PR+SD+PD]) × 100%.

2.3.2. Survival

Overall survival (OS) was observed and progression-free survival (PFS). OS was defined as the start of SBRT treatment on day 1 until the patient died or was lost to follow-up. PFS was defined as the start of SBRT treatment on day 1 until the patient's tumor progression or death or loss to follow-up.

2.3.3. Adverse reactions

Acute and chronic radiation injuries were graded according to the Radiation Therapy Oncology Group (RTOG) acute radiation injury grading criteria, and the National Cancer Institute (NCI) Common Adverse Events Evaluation Criteria (CTCAE) V4.0 was used. Treatment-related adverse events were evaluated.

2.3.4. Follow-up

The patients were followed up by visiting the hospital for re-examination or telephone, WeChat, etc. The patients were enrolled until May 31, 2021, and the follow-up was until June 31, 2022.

2.4. Statistical methods

SPSS 22.0 statistical software was used to process data, count data were expressed as percentage (%), and χ^2 test was used for comparison between groups. Survival curves were drawn by Kaplan-Meier method, and Log-rank test was used for survival analysis. *P* < 0.05 was considered to be statistically significant.

3. Results

3.1. Local control

All patients were followed up with a median follow-up time of 24 months (12-40 months). A total of 219 lesions in 70 patients completed SBRT treatment and were evaluated for short-term efficacy. Three months after radiotherapy, the LCR of all target lesions was 94.1% (206/219), including 16 CR, 23 PR, and 18 SD of liver metastases. LCR 89.1% (57/64) in liver metastases; 48 CR, 10 PR, 1 SD, 3 PD in lung metastases, LCR 95.2% (59/62) in lung metastases; 34 CR, 10 PR, 3 SD, and 1 PD in lymph nodes metastases, and the LCR of the lymph node metastases was 97.9% (47/48); 1 CR, 27 PR, 5 SD, 1 PD in bone metastases, and bone metastases LCR 97.1% (33/34); 6 CR, 2 PR, SD 0, PD 1 in adrenal metastases, and adrenal metastases LCR 97.1% (33/34); 0 CR, PR 0, SD 2, PD 0 in soft tissue metastases, and soft tissue metastases LCR 100% (2/2). The 1-, 2-, and 3-year LCR of the 70 oligometastatic patients were 88.6%, 74.6%, and 64.9%, respectively (see **Figure 1** for details). The local control time of patients with metastases ≤ 3 cm oligometastases was significantly better than that of patients with metastases > 3 cm oligometastases, and

the difference was statistically significant (P = 0.001) (see **Figure 2** for details).

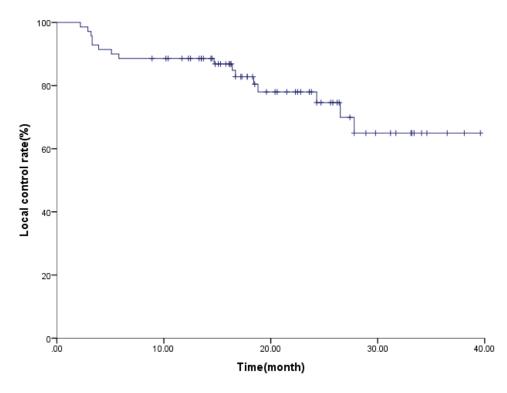


Figure 1. LC survival curve of patients with oligometastatic tumors treated with SBRT

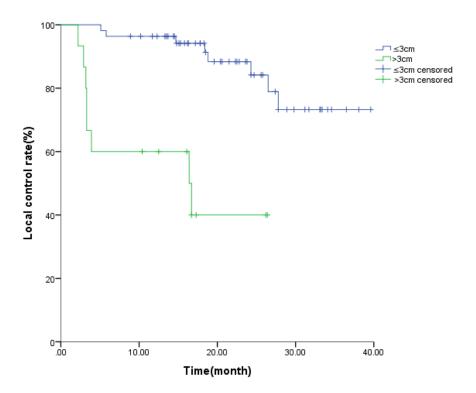


Figure 2. Comparison of LC survival curves in patients with oligometastatic tumors treated by SBRT with different metastatic foci sizes

3.2. Survival situation

During the follow-up period, a total of 52 (74.3%) of the 70 patients with oligometastases had disease progression, and the disease progression patterns are mainly as follows: the appearance of new distant metastases and the progression of the radiotherapy target area. Among the 52 patients with progressive diseases, 36 (69.2%) only developed new distant metastases, 8 (15.4%) only developed radiotherapy target lesions, and 8 (15.4%) had both conditions. Kaplan-Merier survival analysis showed that the median PFS of all patients was 11.8 months (95% CI 8.9–14.7 months), and the 1-year and 2-year PFS rates were 48.6% and 32.6%, respectively. Among them, the PFS of patients with metastases of \leq 3 cm was significantly better than the patients with metastases of > 3 cm, and the median PFS was 15.1 months (95% CI 13.0–17.2 months) and 6.2 months (95% CI 0.5–11.9 months), the difference was statistically significant (P = 0.000); the median OS of all patients was 31.9 months (95% CI 26.0–37.8 months). The 1-year OS rate was 84.3%, and the OS of patients with metastases of \leq 3 cm was significantly better than those with metastases of \geq 3.2.1 months (95% CI 27.2 to 37.0 months) and 17.3 months (95% CI 8.3 to 26.4 months), respectively, the difference was statistically significant (P = 0.001) (see **Figure 3, Figure 4, Figure 5, Figure 6**).

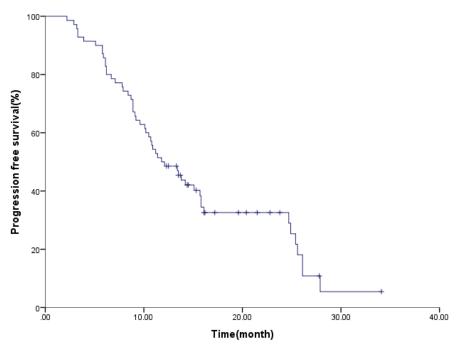


Figure 3. PFS survival curve of patients with oligometastatic tumor treated with SBRT

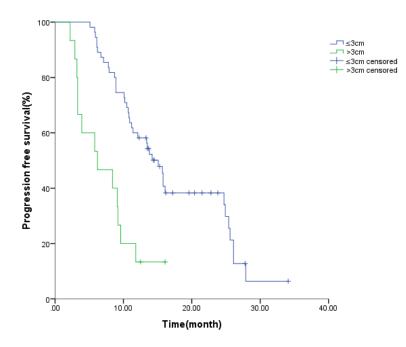


Figure 4. Comparison of PFS survival curves in patients with oligometastatic tumors treated by SBRT with different size of metastases

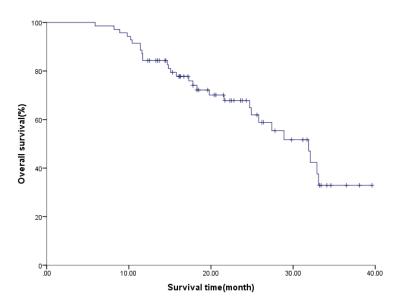


Figure 5. OS survival curve of patients with oligometastatic tumors treated with SBRT

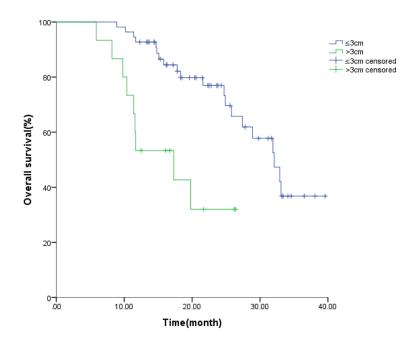


Figure 6. Comparison of OS survival curves in patients with oligometastatic tumors treated with SBRT by different metastatic foci sizes

3.3. Adverse reactions

Acute adverse reactions after SBRT treatment in oligometastatic patients were mainly bone marrow suppression and gastrointestinal reactions, with incidence rates of 48.98% and 30.61%, respectively, as shown in **Table 2**. Chronic adverse reactions were pain (bone, muscle), radiation enteritis, and radiation pneumonitis, with the incidence rates being 38.57%, 30.00%, and 24.29%, respectively, as shown in **Table 3**. The treatment-related adverse reactions of the patients were mainly grade 1, which were all improved after symptomatic treatment. Except for 1 patient with bone metastases from lung cancer who had grade 4 myelosuppression, no grade 4 or 5 adverse events occurred in the rest of the patients.

Table 2. Occurrence of acute adverse reactions after SBRT in 70 patients with oligometastatic disease

Adverse reactions	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
Myelosuppression	21	7	3	1	0	32
Gastrointestinal reactions	16	5	1	0	0	22
Radiation pneumonitis	8	3	1	0	0	12
Radiation enteritis	7	4	0	0	0	11
Abnormal liver function	6	0	0	0	0	6
Abnormal kidney function	3	1	0	0	0	4

Table 3. Chronic adverse reactions	after SBRT in 70	oligometastatic patients
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Adverse reactions	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
Pain	19	7	1	0	0	27
Radiation enteritis	15	5	1	0	0	21
Radiation pneumonitis	12	4	1	0	0	17

4. Discussion

Oligometastasis was first proposed by Hellman in 1995 and is considered to be a transitional stage between local primary tumors and extensive distant metastases ^[1]. Due to the relatively limited abnormal gene signal spectrum incorporated in the formation of oligometastases, there is no genetic predisposition to systemic dissemination, which determines its relatively mild biological properties, with small number of metastases and organ-specific. Subsequently, many literatures have also confirmed the existence of oligometastases. A clinical study on first-line systemic treatment of metastatic breast cancer found that about 50% of the enrolled patients initially had 2 or even fewer metastatic sites, up to 75% of patients had 4 or fewer metastatic sites ^[2], while similar findings were found in studies of non-small cell lung cancer ^[3], prostate cancer ^[4], and renal cell carcinoma ^[5]. At present, oligometastases still lacks a unified definition. Usually, the number of metastatic organs is limited to less than 3, and the total number of metastases is limited to 5 or less ^[6,7]. Different from multiple metastases in multiple organs, patients with oligometastatic status have less metastatic organs, and the tumors are less biologically invasive. Local treatments such as radiofrequency ablation may even lead to potential cures ^[8], and retrospective studies have confirmed that oligometastases have relatively good prognosis and survival advantages compared to patients with systemic multiple metastases ^[9,10], which undoubtedly challenges the traditional view of tumors.

With the development of oncology research, immunotherapy and other systemic treatments are on the rise, and the prognosis of tumor patients has gradually improved. Besides, with the improvement of tumor molecular detection levels such as markers, more and more advanced malignant tumors in patients with were found to be in a oligometastatic state ^[11–14]. With the goal of ensuring safe and effective systemic treatment, seeking a positive and reliable local treatment mode for oligometastatic tumors is a topic worthy of further clinical research. Research on oligometastatic tumors at home and abroad has been developing rapidly in recent years. Some studies have shown that surgical resection of oligometastatic lesions has cured some patients, such as liver metastases from rectal cancer^[15], lung metastases from various tumors^[16], and lung cancer. However, there are certain limitations to surgical treatment for patients with adrenal metastases, and most patients with oligometastases are not suitable for surgical treatment, especially for patients who cannot tolerate or refuse surgery, and also due to surgical anatomical location and technical limitations^[17]. With the vigorous development of modern radiotherapy technology, the continuous innovation of radiotherapy equipment, and modifications of the radiation therapy segmentation, the emergence and clinical application of SBRT technology make the radiotherapy of oligometastatic tumors technically feasible. SBRT is a modern, complex and highly precise radiotherapy technology. Compared to traditional conventional radiotherapy, SBRT has the characteristics of hypofractionation, short course of treatment, high precision, and little side effects. At the same time, SBRT can activate the immune response and induce T cell-mediated immune response, which kills unirradiated distant metastases and primary lesions. This "remote effect" makes SBRT local consolidation therapy for oligometastatic tumors highly effective. In recent years, much research has been done on SBRT in the field of oligometastatic tumors ^[18]. Some retrospective analyses from North America, Europe, and East Asia have shown an LCR of \geq 90% with SBRT for oligometastatic tumors ^[19,20]. Another study reported that the 1-year OS rate of SBRT in the treatment of oligometastatic tumors was over 80% ^[21,22]. The results of a multicenter randomized phase II clinical study reported by Gomez et al. showed that for patients with advanced non-small cell lung cancer with oligometastases, local consolidation therapy (such as radiotherapy) can improve PFS on the basis of maintenance therapy ^[23]. Results of a randomized, open-label Phase II study of SBRT-COMET conducted in 10 hospitals in Canada, the Netherlands, Scotland, and Australia were published in The Lancet recently. The study included Ninety-nine patients with oligometastatic tumors who were randomly assigned (1:2) to 33 (33%) in the control group receiving standard palliative care alone and 66 (67%) in the SBRT group receiving standard care plus SBRT for all metastatic disease. In patients with controlled primary tumors

and 1-5 metastatic lesions, SBRT improved the overall OS rate in patients with oligometastatic tumors, increasing the median OS by 13 months and doubling the PFS rate ^[24]. A multi-institutional analysis of 361 patients with 1-5 extracranial metastases treated with SBRT showed a median OS of 47 months, a median PFS of 10 months, and a 3-year LCR of 72% ^[25]. The results of this study also suggest that SBRT can achieve better curative effect in the treatment of extracranial oligometastatic tumors. The LCR at 1, 2, and 3 years was 88.6%, 74.6%, and 64.9%, respectively. The median PFS was 11.8 months, and the PFS at 1 and 2 years was 11.8 months. The OS rates were 48.6% and 32.6%, respectively, the median OS was 31.9 months, and the 1-year OS rate was 84.3%, which were basically consistent with the results reported in previous relevant literature. At the same time, this study found that 3 months after SBRT treatment, the LCR of all target lesions was 94.1 %, of which the LCR of soft tissue metastases was the highest (100%), the LCR of lymph node metastases was 97.9%, the LCR of bone metastases and adrenal metastases were both 97.1%, the LCR of lung metastases was 95.2%, and the LCR of liver metastases was the lowest (89.1%). The reasons for these results may be related to the small number of patients enrolled in this study, the big difference in the number of metastases in different parts, and the different tolerance of SBRT around the organs at risk around the metastases in different parts, the number of liver metastases in this study was the largest, reaching 64. When the liver metastases are adjacent to the stomach and duodenum, it is necessary to appropriately reduce the divided dose and increase the number of divisions to reduce the gastrointestinal damage that may be caused by excessive SBRT dose. The risk of perforation, ulcer, and bleeding in the tract results in a decrease in the local control rate, while the number of soft tissue metastases in the included cases was the least, only 2, and they were located in the subcutaneous soft tissue of the buttocks. The dose of SBRT was high, so the local control rate was the highest, up to 100%. The results of this study showed that the local control time, PFS and OS of patients with oligometastases with metastases less than 3 cm were significantly better than those with oligometastases with metastases > 3cm, suggesting that the size of metastases is one of the prognostic factors, which is basically consistent with the results reported in previous literature ^[26]. In terms of adverse events, the results of this study showed that acute adverse reactions after SBRT treatment in oligometastatic patients were mainly bone marrow suppression and gastrointestinal reactions, while chronic adverse reactions were mainly pain (bone, muscle), radiation enteritis, and radiation pneumonitis. All treatment-related adverse reactions were mainly grade 1, and all improved after symptomatic treatment. Except for 1 patient with bone metastases from lung cancer who had grade 4 myelosuppression, no grade 4 or 5 adverse events occurred in the rest of the patients.

Although the results of our study are basically consistent with previous related literature reports, the shortcomings and limitations of this study should still be considered. Clinical studies related to SBRT in the treatment of metastases often include patients with multiple tumor types ^[27]. This study performed SBRT treatment for multiple metastases in patients with oligometastatic tumors of various tumor types, which may be distributed in different organs and different anatomies. Different tumor types, different organs, different anatomical sites, and even the same patient may receive different SBRT dose-fractionated irradiation modes. Due to the limited sample size, no further studies were conducted on the effects of different dose-fractionated irradiation modes on the treatment toxicity and prognosis of patients. In addition, this study is a single-center retrospective study. The primary tumor types are mainly lung cancer and colorectal cancer, and the oligometastases are mainly concentrated in the liver, lung, bone and other parts. Most patients have 2-4 metastases, and most metastases were ≤ 3 cm in maximum diameter, which may lead to partial bias in the study results.

5. Conclusion

In conclusion, different from multiple organs and multiple metastases, patients with oligometastatic status have few metastatic foci or metastatic organs, and their biological invasiveness is in a relatively mild period.

The relatively good physical status of patients makes it possible for them to receive systemic therapy and to receive high doses of treatment. Timely SBRT treatment can better control primary and metastatic lesions, reduce tumor burden, improve local control rate, and then lead to higher survival rate and can act as a potential cure. This study confirmed that SBRT is a safe and effective local treatment for extracranial oligometastatic tumors. Due to the short observation time, small number of cases, and a single-centered retrospective study, SBRT is the best indication for the treatment of oligometastatic tumors. However, the optimal dose fractionation, the optimal tumor type, the optimal number of lesions, and many more need to be further explored. Prospective, multi-center, randomized, and controlled studies need to be carried out for stratified analysis and in-depth discussions.

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Disclosure statement

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References

- [1] Hellman S, Weichselbaum RR, 1995, Oligometastases. J Clin Oncol, 13(1): 8–10.
- [2] Dawood S, Broglio K, Gonzalez-Angulo AM, et al., 2008, Trends in Survival Over the Past Two Decades Among White and Black Patients with Newly Diagnosed Stage IV Breast Cancer. J Clin Oncol, 2008, 26(30): 4891–4898.
- [3] Mehta N, Mauer AM, Hellman S, et al., 2004, Analysis of Further Disease Progression in Metastatic Non-Small Cell Lung Cancer: Implications for Locoregional Treatment. Int J Oncol, 25(6): 1677-1683.
- [4] Tosoian JJ, Gorin MA, Ross AE, et al., 2017, Oligometastatic Prostate Cancer: Definitions, Clinical Outcomes, and Treatment Consideration. Nat Rev Urol, 14(1):15-25.
- [5] Loh J, Davis ID, Martin JM, et al., 2014, Extracranial Oligometastatic Renal Cell Carcinoma: Current Management and Future Directions. Future Oncol, 10(5): 761–774.
- [6] Milano MT, Katz AW, Zhang H, et al., 2012, Oligometastases Treated with Stereotactic Body Radiotherapy: Long-Term Follow-Up of Prospective Study. Int J Radiat Oncol Biol Phys, 83(3): 878– 886.
- [7] Palma DA, Salama JK, Lo SS, et al., 2014, The Oligometastatic State-Separating Truth From Wishful Thinking. Nat Rev Clin Oncol, 11(9): 549–557.
- [8] Ahmed KA, Caudell JJ, El-Haddad G, et al., 2016, Radiosensitivity Differences Between Liver Metastases Based on Primary Histology Suggest Implications for Clinical Outcomes After Stereotactic Body Radiation Therapy. Int J Radiat Oncol Biol Phys, 95(5):1399-1404.
- [9] Torok JA, Gu L, Tandberg DJ, et al., 2016, Patterns of Distant Metastases After Surgical Management of Non-Small-Cell Lung Cancer. Clinical Lung Cancer, 18(1): 57–70.
- [10] Dorn P, Meriwether A, Lemieux M, et al., 2011, Patterns of Distant Failure and Progression in Breast Cancer: Implications for the Treatment of Oligmetastatic Disease. Fuel and Energy Abstracts, 81(2): 643.

- [11] Thariat J, Marcy PY, Lagrange JL, 2010, Trends in Radiation Therapy for the Treatment of Metastatic and Oligometastatic Disease in 2010. Bull Cancer, 97(12): 1467–1476.
- [12] Hasselle MD, Haraf DJ, Rusthoven KE, et al., 2012, Hypofractionated Image-Guided Radiation Therapy for Patients with Limited Volume Metastatic Non-Small Cell Lung Cancer. J Thor Oncol, 7(2): 376–381.
- [13] Fumagalli I, Bibault JE, Dewas S, et al., 2012, A Single-Institution Study of Stereotactic Body Radiotherapy for Patients with Unresectable Visceral Pulmonary or Hepatic Oligometastases. Radiat Oncol, 7(1): 164.
- [14] Lussier YA, Xing HR, Salama JK, et al., 2011, MicroRNA Expression Characterizes Oligometastasis (es). PLOS One, 6(12): e28650.
- [15] Pawlik TM, Scoggins CR, Zorzi D, et al., 2005, Effect of Surgical Margin Status on Survival and Site of Recurrence After Hepatic Resection for Colorectal Metastases. Ann Surg, 241(5): 715–722.
- [16] Pastorino U, Buyse M, Friedel G, et al., 1997, Long-term Results of Lung Metastasectomy: Prognostic Analyses Based on 5206 Cases. J Thorac Cardiovasc Surg, 113(1): 37–49.
- [17] Strong VE, D'angelica M, Tang L, et al., 2007, Laparoscopic Adrenalectomy for Isolated Adrenal Metastasis. Ann Surg Oncol, 14(12): 3392–3400.
- [18] Lewis SL, Porceddu S, Nakamura N, et al., 2017, Definitive Stereotactic Body Radiotherapy (SBRT) for Extracranial Oligometastases: An International Survey of >1000 Radiation Oncologists. Am J Clin Oncol, 40(4): 418–422.
- [19] Iyengar P, Kavanagh BD, Wardak Z, et al., 2014, Phase II trial of Stereotactic Body Radiation Therapy Combined with Erlotinib for Patients with Limited but Progressive Metastatic Non-Small-Cell Lung Cancer. J Clin Oncol, 32(34): 3824–3830.
- [20] Hasselle MD, Haraf DJ, Rusthoven KE, et al., 2012, Hypofractionated Image-Guided Radiation Therapy for Patients with Limited Volume Metastatic Non-Small Cell Lung Cancer. J Thor Oncol, 7(2): 376-381.
- [21] Fanetti G, Marvaso G, Ciardo D, et al., 2018, Stereotactic Body Radiotherapy or Castration-Sensitive Prostate Cancer Bone Oligometastases. Med Oncol, 35(5): 75.
- [22] Dohopolski MJ, Horne Z, Clump D, et al., 2018, Stereotactic Body Radiation Therapy for Pulmonary Oligometastases Arising from Non-Lung Primaries in Patients without Extrapulmonary disease. Cureus, 10(2): e2167.
- [23] Gomez DR, Blumenschein GR Jr, Lee JJ, et al., 2016, Local Consolidative Therapy Versus Maintenance Therapy or Observation for Patients with Oligometastatic Non-Small-Cell Lung Cancer Without Progression After First-Line Systemic Therapy: A Multicentre, Randomised, Controlled, Phase 2 Study. Lancet Oncol, 17(12): 1672–1682.
- [24] Palma DA, Olson R, Harrow S, et al., 2019, Stereotactic Ablative Radiotherapy Versus Standard of Care Palliative Treatment in Patients with Oligometastatic Cancers (SABR-COMET): A Randomised, Phase 2, Open-Label Trial. Lancet, 393(10185): 2051–2058.
- [25] Hong JC, Ayala-Peacock DN, Lee J, et al., 2018, Classification for Long-Term Survival in Oligometastatic Patients Treated with Ablative Radiotherapy: A Multi-Institutional Pooled Analysis. PLOS One. 13(4): e0195149.
- [26] Oh D, Ahn YC, Seo JM, et al., 2012, Potentially Curative Stereotactic Body Radiation Therapy (SBRT) for Single or Oligometastasis to the Lung. Acta Oncol, 51(5): 596–602.
- [27] Andrews DW, Scott CB, Sperduto PW, et al., 2004, Whole Brain Radiation Therapy with or Without

Stereotactic Radiosurgery Boost for Patients with One to Three Brain Metastases: Phase III Results of the RTOG 9508 Randomised Trial. Lancet, 363(9422): 1665–1672.

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