Journal of Gastrointestinal Cancer (2019) 50:879–887
https://doi.org/10.1007/s12029-018-0170-8

ORIGINAL RESEARCH

Stereotactic Body Radiation Therapy (SBRT) Using CyberKnife in Oligometastatic Cancer Patients; Retrospective Evaluation, Single Institution Experience

Abdullah Alsuhaibani[1] · Ahmed Elashwah[2,3] · Abdullah Alkafi[2] · Camelia Constantinescus[2] · Faisal ALzorkany[2]

Published online: 6 October 2018

Abstract

Objectives We retrospectively evaluate local control rate at 6 months and 1 year in oligometastatic cancer patients treated with SBRT using CyberKnife.

Methods Total of 21 patients with 24 treatment sites from February 2014 till June 2017 who were treated with SBRT in our institution were included in this study.

Results Eleven patients were males, 10 patients were females, median age at diagnosis was 63 years, and colorectal cancer is the most commonly diagnosed cancer in 18 patients. The abdomino-pelvic lymph nodes were the commonest treatment site in 11 (45.8%), average PTV volume of 46.4 cc. All the patients received SBRT with average (BED) of 97 GY, 7 treatment sites received BED of < 100GYgroup 1, and 17 received BED ≥ 100GY group 2. No reported G3 or G4 acute or chronic toxicity. The 6 months and 1 year local control (LC) were 95.8 and 88.2%, respectively. After a median follow-up of 16.8 months, 19(90.5%) patients were alive; among them, local progression was observed in 1 (4.1%) treatment site, while systemic progression in 4 (16.6%), and two (9.5%) patients died; they had both local and systemic failures. The 1-year local PFS rate was 82%. In univariate analysis, PTV volume was significantly correlated with LC rate at 6 months ($p = 0.001$), while the site of metastasis appeared to significantly correlate with PFS ($p = 0.03$).

Conclusion SBRT using CyberKnife is feasible, safe, and effective treatment for oligometastatic sites. Six months and 1 year local control rate is 95.8 and 88.2% respectively in our patients cohort, treatment regimens with higher BED resulting in better 1-year local PFS, although it was not statistically significant. A larger cohort of patients and longer follow up is required for better evaluation.

Keywords Oligometastatic · Cancer · Radiation · Sterotactic · SBRT · CyberKnife · Metastatic disease · Local control

Introduction

The concept of oligometastases in cancer management was first introduced in 1995 by Hellman and Weichselbaum. It was introduced as a distinct clinical entity of limited metastatic disease as an intermediate stage of cancer spread between localized and disseminated disease [1]. Multiple studies had demonstrated long-term survival rates in this subset of patients when treated with aggressive local therapy including surgery and radiotherapy [2–4]. No consensus definition of oligometastatic disease. Milano et al. [5] defined cases with oligometastatic disease as those with no more than five detectable metastases. Salama et al. [4] similarly defined oligometastatic disease as one to five metastatic sites; however, other institutions have limited their eligibility for SBRT to patients with no more than three metastatic sites [6].Various radiation regimens have been used for the treatment of oligometastases. The use of high doses of single-session stereotactic radiosurgery has been used and well established in the management of brain metastases [7–9], a similar approach has been used with either a hypofractionated treatment

✉ Abdullah Alsuhaibani
asuhaibani@gmail.com

[1] Oncology Center, University Medical City, King Saud University, Riyadh, Saudi Arabia

[2] Radiation oncology department King Faisal specialized hospital and research center, Riyadh, Saudi Arabia

[3] Kasr Aleini center of clinical oncology and nuclear medicine (NEMROCK), Cairo University, Cairo, Egypt

regimen using limited numbers of fractions with increasing daily fraction dose or single-session regimens with ablative doses of radiation delivered to extracranial disease sites. This approach is termed stereotactic body radiotherapy (SBRT) [10]. The lung, liver, and spine metastases are the most commonly treatment sites using SBRT. SBRT is often the preferred radiation treatment option for sites of oligometastatic disease due to the limited radiation dose delivered to normal tissues with highly conformal treatment planning and limited number of fractions needed for treatment [11, 12].

In this review, we retrospectively evaluate local control rate at 6 months and 1 year in oligometastatic cancer patients treated with SBRT using CyberKnife.

Materials and Methods

Total of 21 patients with 24 treatment sites from February 2014 till June 2017 who were treated with SBRT in our institution were reviewed in this study.

All the patients had initial baseline CT chest, abdomen and pelvis, and PET-CT whole body. At time of CT simulation, planning CT images are taken with 1–2-mm slice thickness. Patient immobilization to ensure accurate tumor targeting was achieved by a body frame (body fix) holding the patient accompanied by a vacuum pillow to form a tight, reproducible seal around the patient. Additional devices have been utilized to limit and track tumor motion in the treatment of lung and liver metastases. This has been achieved using four-dimensional treatment planning software, allowing tumors to be tracked during the respiration cycle and restricting treatments to particular phases of the respiratory cycle [19]. In case of liver metastasis, we used fiducial marker inserted under ultrasound guidance for proper tumor tracking. Abdominal compression was used in cases with abdominal metastasis to limit the motion of the diaphragm during treatment [11]. Daily set-up verification with KV image to ensure adequate treatment positioning for each high dose of delivered treatment [12].

Gross target volume (GTV) is usually contoured in planning CT taking in consideration the information obtained from diagnostic CT and PET-CT. The GTV is contoured in the different phases of respiratory cycle and labeled as internal target volume (ITV); 3–5 mm margin is usually added to ITV as a planning target volume (PTV). Different dose range was prescribed (range 30–60 Gy/3–5 fractions).

The biological equivalent dose (BED) is a very important concept in the SBRT treatment, which is a term describing the biological effect of a delivered dose to a tumor taking into account the number of radiation treatments, the total dose delivered, and the α:β ratio. The (BED) delivered to a tumor is a mathematical formula based on the linear quadratic model: $nd\ (1 + d/\alpha/\beta)$, where n = the fractionation number, d = the daily dose, and α/β that is used to describe the curvature of the cell survival curve after radiation. Low α/β ratios characterize late-responding tissues and high α/β ratios delineate early-responding tissues [13].

In this study, we used α/β ratios of 10 Gy for the different treatment sites and divide the treatment sites into two groups according to the BED (whether ≥ 100 GY or < 100 GY) as in many reports, SBRT intensive regimens of BED ≥ 100 GY are associated with significantly better local control and survival than less intensive regimens in primary lung cancer [14–17].

Planning Techniques and Objectives

The CyberKnife machine used in this study is a G4 v10.1 which is capable of delivering 800 MUs/Min using Mutiplan® v5.1 planning system. The sequential optimization algorithm was used to plan the patients. The planning approach was to use a full path. At least two shells were used to improve the conformality of the plan and decrease the dose spillage. The number of beams was reduced to have a minimum of 10 MUs per beam per fraction and a maximum of 200 MUs per beam per fraction.

For plan approval, efforts were always made to minimize the dose to all normal tissues as much as possible; we follow these dose constraints summarized in Table 1 according to the University of Texas Southwestern [18] and the University of Virginia [19].

Follow-Up, Response, and Toxicity Assessment

After completion of treatment, all the patients underwent follow up CT CAP and PET-CT at 3, 6, and 12 months post-SBRT. The Common Toxicity Criteria Adverse Events version 4.0 was used.

For reporting the treatment-related toxicities, acute toxicities were defined as adverse events occurring within 3 months after SBRT, and late toxicities were those occurring after 3 months.

Tumor response was assessed using response evaluation and criteria in solid tumors (RECIST). Complete disappearance of the tumor was defined as a complete response (CR), and a partial response (PR) was defined as a decrease of > 30% in the longest diameter and/or SUV-FDG activity of the target tumors. A decrease of < 30% or no change was defined as stable (SD), and progression of > 20% was defined as progressive disease (PD). Local control was defined as being free from the development of a new lesion or an increase in tumor size or SUV-FDG activity within the treated PTV volume. Systemic progression is defined as development of new metastatic lesions outside the treated areas.

Table 1 Summary of suggested dose constraints for various critical organs

Serial tissue	Max critical volume above threshold	One fraction		Three fractions		Five fractions		End point (grade3)
		Threshold dose (Gy)	Max point dose Gy	Threshold dose (Gy)	Max point dose Gy	Threshold dose (Gy)	Max point dose Gy	
Esophagus	< 5 cc	11.9	15.4	17.7	25.2	19.5	35	Stenosis/fistula
Brachial plexus	< 3 cc	14	17.5	20.4	24	27	30.5	Neuropathy
Heart/pericardium	< 15 cc	16	22	24	30	32	38	Pericarditis
Great vessels	< 10 cc	31	37	39	45	47	53	Aneurysm
Trachea and large bronchus	< 4 cc	10.5	20.2	15	30	16,5	40	Stenosis/fistula
Bronchus-smaller airways	< 0.5 cc	12.4	13.3	18.9	23.1	21	33	Stenosis with atelactasis
Rib	< 1 cc	22	30	28.8	36.9	35	43	Pain or fracture
Stomach	< 10 cc	11.2	12.4	16.5	22.2	18	32	Ulceration/fistula
Duodenum	< 10 cc	11.2	12.4	16.5	22.2	18	32	Ulceration
Jejunum/ileum	< 5 cc	11.9	15,4	17.7	25.2	19.5	35	Enteritis/obstruction
Colon	< 20 cc	14.3	18.4	24	28.2	25	38	Colitis/fistula
Rectum	< 20 cc	14.3	18.4	24	28.2	25	38	Proctitis/fistula
Bladder wall	< 15 cc	11.4	18.4	16.8	28.2	18.3	38	Cystitis/fistula
Renal hilum/vascular trunk	< 2/3 volume	10.6	18.6			23		Malignant hypertension
Parallel tissue								
Lung (right or left)	1500 cc	7	N/A	11.6	N/A	12.5	N/A	Basic lung function
Lung (right or left)	1000 cc	7.4	N/A	12.4	N/A	13.5	N/A	Pneumonitis
Liver	700 cc	9.1	N/A	19.2	N/A	21	N/A	Basic liver function
Renal cortex (right or left)	200 cc	8.4	N/A	16	N/A	17.5	N/A	Basic renal function

Statistical Analysis

Descriptive statistics was performed for all available categorical variables. The outcomes studied were local control (LC), local progression-free survival (PFS), and progression-free survival (PFS). A linear regression model was used to identify independent predictors of control and survival. The PFS was calculated from the date of SBRT. The difference in distributions between the two treatment groups was tested using Pearson's chi-squared test or Fisher exact test. The Kaplan-Meier methodology was used to estimate survival probability (expressed as a mean with a range and two-sided 95% confidence interval). All statistical tests were two-tailed and differences were considered to be statistically significant for a p value less than 0.05. All statistical analyses were performed using a software package (SPSS version 20, Inc., Chicago, IL, USA).

Results

Eleven patients were male (52%),10 patients were females (48%), median age at diagnosis was 61 years, colorectal cancer is the most commonly diagnosed cancer in 18 patients (85.7%), 2 patients (9.5%) were diagnosed with cholangiocarcinoma, and 1 patient (4.8%) was diagnosed with gastric cancer. The abdomino-pelvic lymph nodes were the commonest site in 11 sites (45.8%), with average PTV volume of 46.4 cc. All the patients received SBRT with dose range from 30 to 60 GY/3–5 fractions with average BED of 97 GY (range 48–180 GY); 7 sites received a BED of less than 100 GY (group 1) and 17 received a BED of ≥ 100 GY (group 2) (Tables 2 and 3). The dose was prescribed to an isodose line covering the PTV which range from 75 to 81% and a maximum of conformality index (CI) 1.29 was achieved. The PTV/ITV was at least covered by 72% of the dose. Figures 1, 2, and 3 represent examples of three different treatment sites (Fig. 1 for lung, Fig. 2 for liver, and Fig. 3 for abdominal LN oligometastasis). No reported G3 or G4 acute or chronic toxicity. The 6-month local control rate was 95.8% (23/24 sites); 13 of them (56.5%) had shown complete metabolic response with no reported residual FDG activity in PET-CT. The 1-year local control rate was 88.2% (15/17), and 10 of them (71.4%) had shown complete metabolic response with no reported residual FDG activity in PET-CT. After a median follow-up of

Table 2 Patients and treatment characteristics

Median age at diagnosis	63 (41–76)
Gender	
Male	11(52%)
Female	10(48%)
Diagnosis	
Colo/rectal cancer	18(85.7%)
Cholangiocarcinoma	2(9.5%)
Gastric cancer	1(4.8%)
Treatment site	
Abdomino-pelvic LN	11(45.8%)
Liver	6(25%)
Lung	5(20.8%)
Tumor bed recurrence	2(8.4%)
Dose Gy	
30	2(8.3%)
35	2(8.3%)
40	1(4.2%)
48	3(12.5%)
50	15(62.5%)
60	1(4.2%)
NO fractions	3–5

16.8 months (range 6.1–44.7 months), 19(90.5%) patients were alive. Among them, local progression was observed in one (4.1%) site while systemic progression in four (16.6%) sites. Two (9.5%) patients died; they had both local and systemic failures. Internal comparison between group 1 and group 2 revealed no significant difference between two groups regarding age, gender, treatment sites, primary diagnosis, and PTV volume (Table 3). With reported 6 months and 1 year local control rate of 100% and 71.44, respectively, in group 1 vs 94.1 and 94.1% respectively in group 2, with 1 year local PFS of 67% in group 1 vs 87% in group 2 (p value 0.448) (Fig. 4).

In univariate analysis, correlation between LC rate at 6 months and 1 year with the following factors (age, gender, SBRT dose, treatment site, and PTV volume) was performed, and only PTV volume was significantly correlated with LC rate ($p = 0.001$); the patients with good LC had an average PTV volume of 43.5 cc (34.6) (range 2.4–201.9 cc), while the ones with local failure had an average PTV volume of 65.3 cc (92.2) (range 2.6–171.3 cc). The site of oligometastasis appeared to significantly correlate with PFS ($p = 0.03$) (Fig. 5).

Discussion

Various SBRT dosing schedules have been used to treat both lung and liver metastases [20–25]. However, the optimal dosing schedule that takes into account multi factors such as tumor volume, tumor location, primary histology, and biological response has yet to be determined. McCammon et al. suggested a dose-response relationship in the treatment of liver

Table 3 Comparison between BED1 and BED2 patients. All factors showed an even distribution

Characteristic		BED1 ($n = 5$)		BED2 ($n = 16$)		P	All ($n = 21$)	
Age at diagnosis (yrs)	Range	49–73		41–76		0.249[b]	41–76	
	Average	63		61			62	
	SD	10		12			11	
	Median	69		62			63	
Gender	Female	2	40%	8	50%	0.264[b]	10	47.6%
	Male	3	60%	8	50%		11	52.4%
primary diagnosis	Colo/rectal ca	3	60%	15	93.8%	0.28[a]	18	85.7%
	Cholangio	1	20%	1	6.2%		2	9.5%
	Gastric ca	1	20%	0	0%		1	4.8%
		BED1 ($n = 7$)		BED2 ($n = 17$)		P	All ($n = 24$)	
Site of oligometastases	LN	4	57%	7	41%	0.327[a]	11	45.8%
	Liver	0	0%	6	35.3%		6	25%
	Lung	2	28.5%	3	17.6%		5	20.8%
	Tumor bed	1	14.5%	1	6.1%		2	8.4%
PTV volume (cc)	Range	2.6–119		2.4–201.9		0.289[a]	2.4–171.3	
	Average	48.7		45.4			46.4	
	SD	36.1		47			43.2	

[a] Pearson's chi-squared test

[b] Fisher exact test

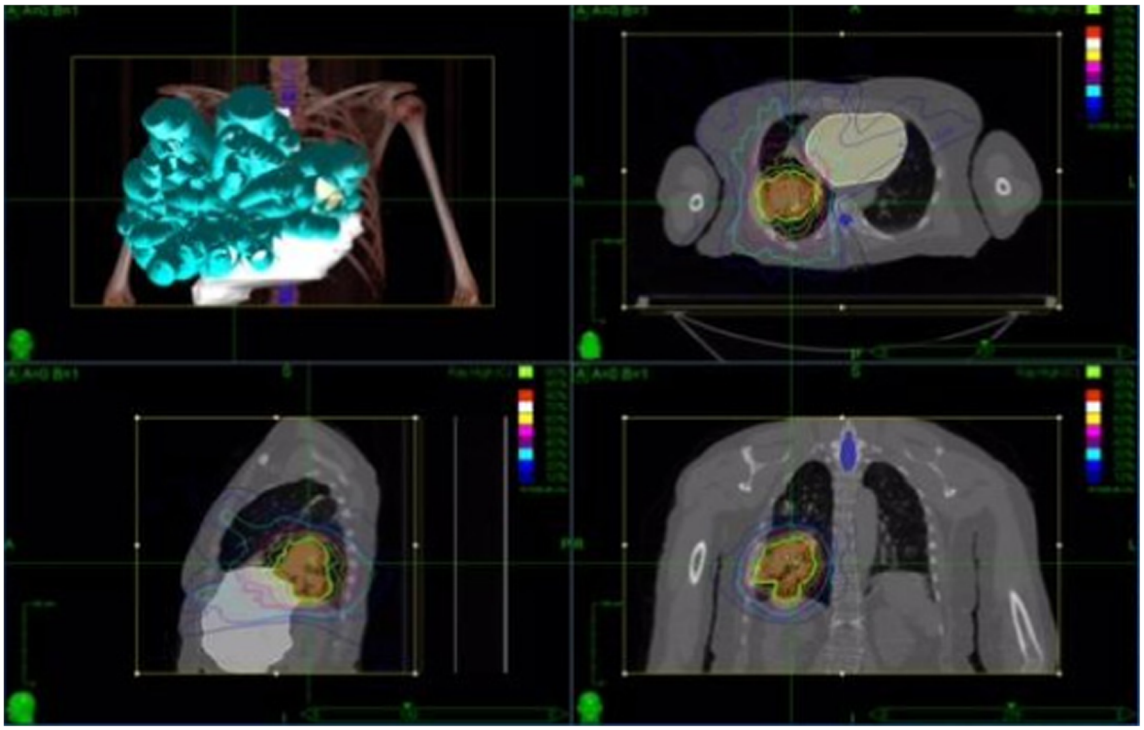

Fig. 1 Three-dimensional reconstruction and axial, sagittal, and coronal imaging for a lesion in the right lower lobe of the lung treated with 50 Gy in five fractions

and lung metastases. They reported on 246 lesions treated with SBRT for 3 fractions to a dose of at least 54 Gy and found 3-year local control rates of 89.3% compared with 59.0 and 8.1% for those treated to between 36 and 53.9 Gy and less than 36 Gy respectively [26].

Fumagalli et al. suggested a difference in outcome based on anatomical location. With an improved disease-free survival rate on univariate analysis was noted in patients with pulmonary metastases ($P = .02$) [25]. These results suggest a difference may exist in SBRT outcomes based on treatment

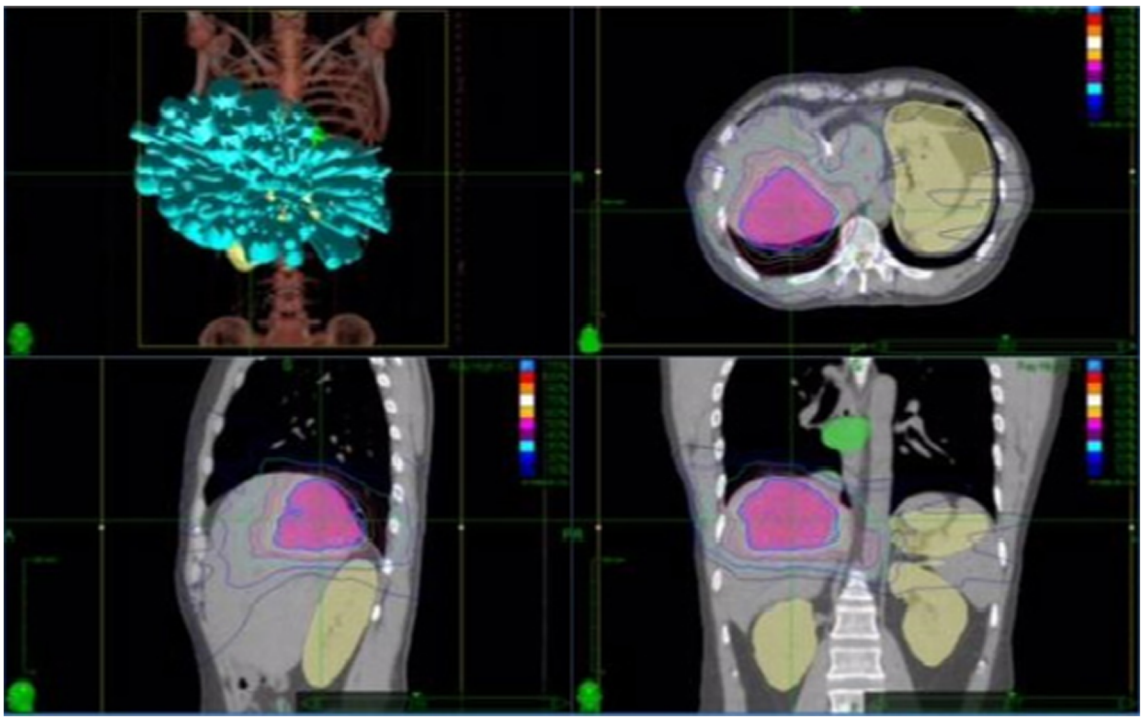

Fig. 2 Three-dimensional reconstruction (axial, sagittal, and coronal imaging for a liver lesion treated with 50 Gy in five fractions

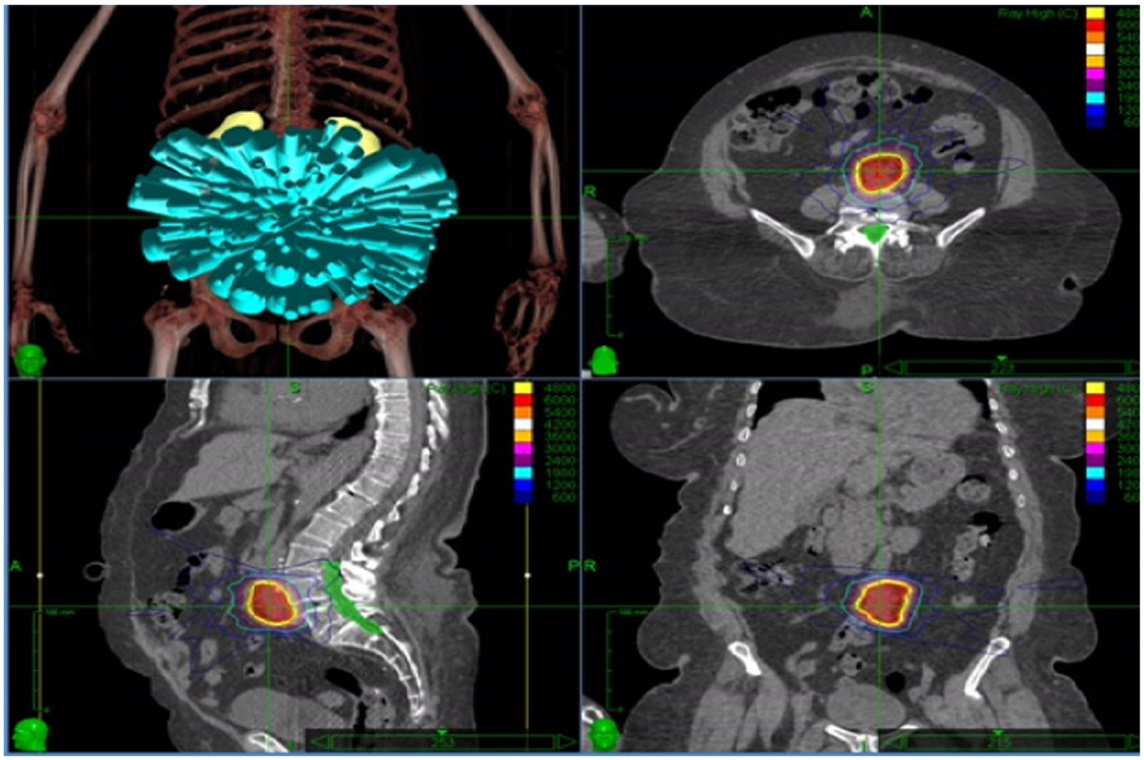

Fig. 3 Three-dimensional reconstruction (axial, sagittal, and coronal imaging for left common iliac lymph node treated with 50 Gy in five fractions

location, and eventually, dose selection plays an important role in achieving optimum control.

There is increasing clinical evidence suggesting that the management of oligometastases should be based on primary histology. A study conducted by Takeda et al. concluded that there is difference between the local control of oligometastatic lung lesions and primary lung cancers; in this study, they assessed 21 colorectal metastatic lung lesions, 23 lesions from

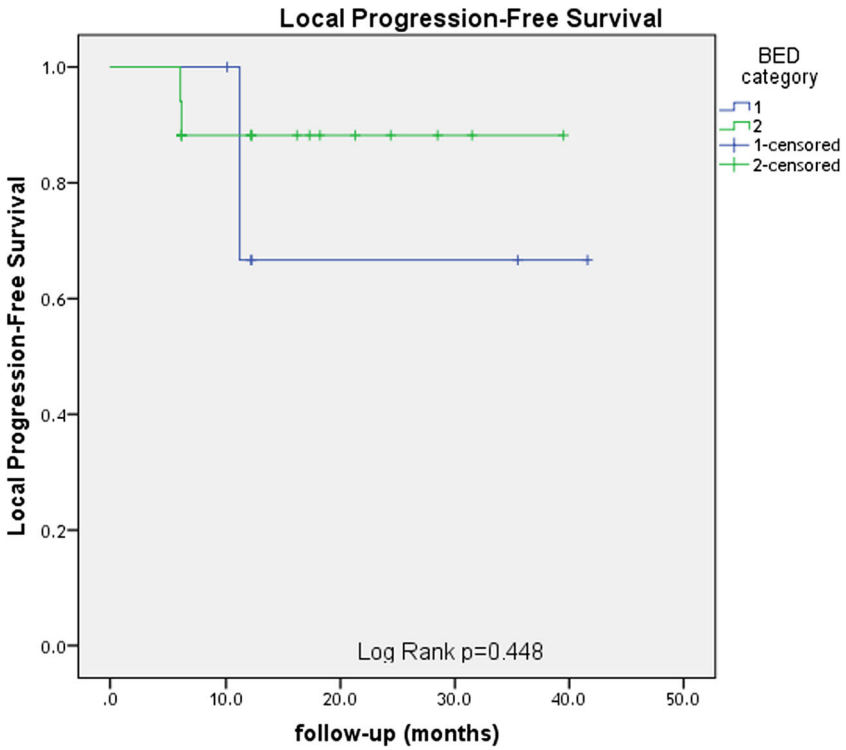

Fig. 4 local PFS for group 1 (treated sites with BED < 100GY) and group 2 (treated sites with BED≥100GY)

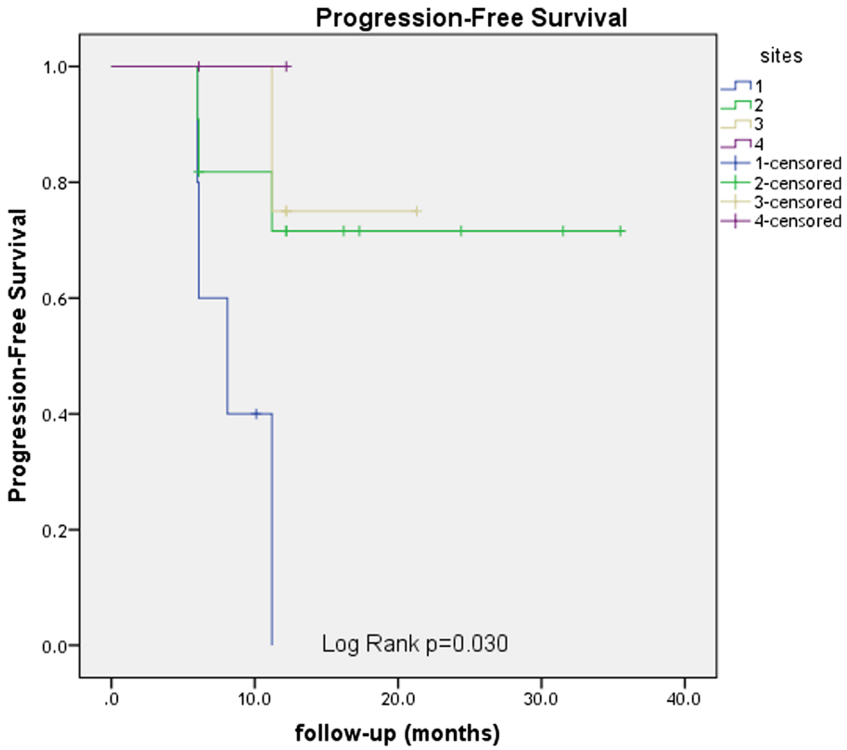

Fig. 5 Treatment site-specific PFS (1—lung, 2—LN, 3—liver, 4—tumor bed)

other origins, and 188 primary lung cancers treated with 50 Gy in 5 fractions. In multivariate analysis, the origin of the tumor was significantly correlated with local control ($P < .05$). The researchers reported 1-year local control rates of 80%, 94%, and 97% ($P < .05$) for colorectal primaries, oligometastases from other origins, and primary lung cancer, respectively [27].

The majority of treated sites in our study were abdominopelvic lymph node in 11 sites (45.8%), 10 of them have primary colorectal cancer and one has cholangiocarcinoma, average PTV volume of 33 cc, and average BED of 90 GY Table 4; no reported G3/G4 acute or chronic toxicity, with reported G2 acute toxicity in form of fatigue in 2 patients (18.1%). After median follow-up interval of 23.6 months, 6 months, and 1 year, local control rate was 100 and 90%, respectively (Fig. 6).

Five lung treatment sites, all from colorectal primary, were included in this study. The average PTV volume was 45.6 cc with average BED of 86.4 GY (Table 4), no reported G3/G4 acute or chronic toxicity, and only fatigue grade 2 developed in 40% as an acute toxicity. After median follow-up interval of 22 months, 6 months, and 1 year, local control rate was 80 and

Table 4 Average BED and PTV volume according to tumor site

Site (*n*)	BED GY(n)	Average BED(GY)	Average PTV volume cc
Tumor bed (2)	80	96.3	61
	112.5		
Lung (6)	60 (1)	86.4	45.6
	72 (1)		
	100 (3)		
Liver(6)	100 (2)	119.6	93.4
	112.5 (3)		
	180 (1)		
LN (11)	48 (1)	90	33
	60 (2)		
	72 (1)		
	100 (4)		
	112.5 (2)		
	124.8 (1)		

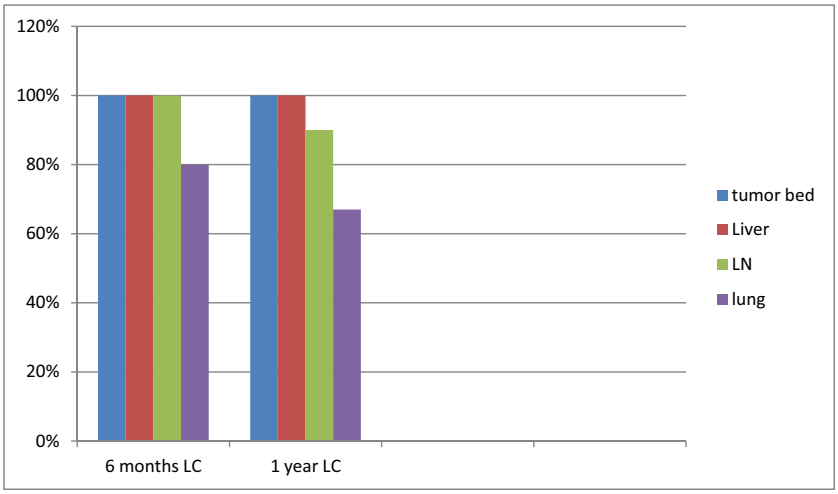

Fig. 6 LC rate at 6 months and 1 year follow up for different treatment sites

67%, respectively (Fig. 6), compared to a study conducted by Ricardi et al. in a series of 61 study patients with oligometastatic lung tumors. Dose selection was 26 Gy in 1 fraction in 51 study patients, 45 Gy in 3 fractions in 22 study patients, and 36 Gy in 4 fractions in 3 study patients. After a median follow-up interval of 20.4 months, local control rates at 2 and 3 years were 89 and 83.5% [28].

Six liver treatment sites were included in our study (five have colorectal primary and one with cholangiocarcinoma), average PTV volume of 93.4 cc and average BED of 119.6 GY (Table 4), no reported G3/G4 acute or chronic toxicity, with reported G2 acute toxicity in form of fatigue and nausea in 2 patients (33.3%). After median follow-up interval of 14.4 months, 6 months, and 1 year, local control rate was 100% with no reported local progression (Fig. 6).

A significant difference in the radio-sensitivity index (RSI) based on the anatomical location of metastases using SBRT, it was found that colon cancer metastasized to sites such as the ovary, abdomen, and liver were more radio resistant than when tumors are metastasized to sites such as the lung and lymph nodes ($P < .0001$) [29]. In comparison to our data in which the majority of cases have colorectal diagnosis (85.7%), we found better local control rate at 6 months, 1 year, and PFS in tumor bed recurrent lesion and liver than lung and LN sites in spite of larger PTV volume in both tumor bed recurrent and liver lesions that may be attributed to the higher average BED in tumor bed recurrent and liver lesions 96.3 and 119.6 GY, respectively, vs 90 and 86.4 GY for LN and lung sites, respectively (Table 4; Figs. 5 and 6).

In this study, we use α/β ratios of 10 Gy for the different treatment sites; however, a recent study conducted by Rainer J. Klement stated that for lung and liver metastasis from CRC, the estimated a/b ratio was 43.1 ± 4.7 Gy compared to 21.6 ± 7.8 Gy for non-CRC metastases. This study strongly recommends to take in consideration different dose regimens for liver and lung metastasis from CRC [30].

A statistically non-significant difference was found between the two groups of treatment sites (with better local PFS in group received BED ≥ 100 GY in comparison to those received BED < 100GY); this correlates with previous articles reporting that SBRT intensive regimens of BED ≥ 100GY are associated with significantly better local control and survival than less intensive regimens in primary lung cancer [14–16]; however, the statistically non-significant difference may be attributed to the small number of patients in this study.

Conclusion

SBRT using CyberKnife is feasible, safe, and effective treatment for oligometastatic sites. Six months and 1 year local control rate is 95.8 and 88.2%, respectively, in our patients' cohort. Treatment regimens with higher BED result in better 1 year local PFS, although it was not statistically significant. A larger cohort of patients and longer follow up is required for better evaluation.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Hellman S, Weichselbaum RR. Oligometastases. J Clin Oncol. 1995;13(1):8–10.
2. Casiraghi M, De Pas T, Maisonneuve P, et al. A 10-year single-center experience on 708 lung metastasectomies: the evidence of the "international registry of lung metastases.". J Thorac Oncol. 2011;6(8):1373–8.
3. Simmonds PC, Primrose JN. Colquitt JL, et al.Surgical resection of hepatic metastases from colorectal cancer: a systematic review of published studies. Br J Cancer. 2006;94(7):982–99.

4. Salama JK, Hasselle MD, Chmura SJ, et al. Stereotactic body radiotherapy for multisite extracranial oligometastases: final report of a dose escalation trial in patients with 1 to 5 sites of metastatic disease. Cancer. 2012;118(11):2962–70.
5. Milano MT, Katz AW, Muhs AG, Philip A, Buchholz DJ, Schell MC, et al. A prospective pilot study of curative-intent stereotactic body radiation therapy in patients with 5 or fewer oligometastatic lesions. Cancer. 2008;112(3):650–8.
6. Ahmed KA, Stauder MC, Miller RC, Bauer HJ, Rose PS, Olivier KR, et al. Stereotactic body radiation therapy in spinal metastases. Int J Radiat Oncol Biol Phys. 2012;82(5):e803–9.
7. Shaw E, Scott C, Souhami L, Dinapoli R, Bahary JP, Kline R, et al. Radiosurgery for the treatment of previously irradiated recurrent primary brain tumors and brain metastases: initial report of radiation therapy oncology group protocol (90-05). Int J Radiat Oncol Biol Phys. 1996;34(3):647–54.
8. Shaw E, Scott C, Souhami L, Dinapoli R, Kline R, Loeffler J, et al. Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: final report of RTOG protocol 90-05. Int J Radiat Oncol Biol Phys. 2000;47(2):291–8.
9. Bhatnagar AK, Flickinger JC, Kondziolka D, Lunsford LD. Stereotactic radiosurgery for four or more intracranial metastases. Int J Radiat Oncol Biol Phys. 2006;64(3):898–903.
10. Potters L, Kavanagh B, Galvin JM, Hevezi JM, Janjan NA, Larson DA, et al. American Society for Therapeutic Radiology and Oncology (ASTRO) and American College of Radiology (ACR) practice guideline for the performance of stereotactic body radiation therapy. Int J Radiat Oncol Biol Phys. 2010;76(2):326–32.
11. Heinzerling JH, Anderson JF, Papiez L, Boike T, Chien S, Zhang G, et al. Four-dimensional computed tomography scan analysis of tumor and organ motion at varying levels of abdominal compression during stereotactic treatment of lung and liver. Int J Radiat Oncol Biol Phys. 2008;70(5):1571–8.
12. Chen J, Morin O, Aubin M, Bucci MK, Chuang CF, Pouliot J. Dose-guided radiation therapy with megavoltage cone-beam CT. Br J Radiol. 2006;79(1):S87–98.
13. Fowler JF. 21 years of biologically effective dose. Br J Radiol. 2010;83(991):554–68.
14. Timmerman R, Paulus R, Galvin J,et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. 2010 17;303(11): 1070–6. doi: https://doi.org/10.1001/jama.2010.261
15. Bilal H, Mahmood S, Rajashanker B,et al. Is radiofrequency ablation more effective than stereotactic ablative radiotherapy in patients with early stage medically inoperable non-small cell lung cancer?. 2012 Aug;15(2):258–65. doi:https://doi.org/10.1093/icvts/ivs179. Epub 2012 May 10.
16. Gewanter RM, Rosenzweig KE, Chang JY,et al. ACR appropriateness criteria: nonsurgical treatment for non-small-cell lung cancer: good performance status/definitive intent. 2010;34(3):228-49. doi: https://doi.org/10.1016/j.currproblcancer.2010.04.001.
17. Kamran A. Ahmed, MD and Javier F.et al. Stereotactic body radiotherapy in the management of oligometastatic disease. Cancer Control January 2016, Vol. 23, No. 1.
18. Timmerman RD. An overview of hypofractionation and introduction to this issue of seminars in radiation oncology. Semin Radiat Oncol. 2008;18:215–22.
19. Dunlap NE, Cai J, Biedermann GB, et al. Chest wall volume receiving 30 Gy predicts risk of severe pain and/or rib fracture after lung stereotactic body radiotherapy. Int. J. Radiat. Oncol., Biol., Phys. 2009;76:796–801.
20. Rusthoven KE, Kavanagh BD, Cardenes H, Stieber VW, Burri SH, Feigenberg SJ, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for liver metastases. J Clin Oncol. 2009;27(10):1572–8.
21. Herfarth KK, Debus J, Lohr F, Bahner ML, Rhein B, Fritz P, et al. Stereotactic single-dose radiation therapy of liver tumors: results of a phase I/II trial. J Clin Oncol. 2001;19(1):164–70.
22. Ricardi U, Filippi AR, Guarneri A, Ragona R, Mantovani C, Giglioli F, et al. Stereotactic body radiation therapy for lung metastases. Lung Cancer. 2012;75(1):77–81.
23. Rusthoven KE, Kavanagh BD, Burri SH, Chen C, Cardenes H, Chidel MA, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for lung metastases. J Clin Oncol. 2009;27(10):1579–84.
24. Wulf J, Haedinger U, Oppitz U, Thiele W, Mueller G, Flentje M. Stereotactic radiotherapy for primary lung cancer and pulmonary metastases: a noninvasive treatment approach in medically inoperable patients. Int J Radiat Oncol Biol Phys. 2004;60(1):186–96.
25. Fumagalli I, Bibault JE, Dewas S, Kramar A, Mirabel X, Prevost B, et al. A single-institution study of stereotactic body radiotherapy for patients with unresectable visceral pulmonary or hepatic oligometastases. Radiat Oncol. 2012;7:164.
26. McCammon R, Schefter TE, Gaspar LE, Zaemisch R, Gravdahl D, Kavanagh B. Observation of a dose-control relationship for lung and liver tumors after stereotactic body radiation therapy. Int J Radiat Oncol Biol Phys. 2009;73(1):112–8.
27. Takeda A, Kunieda E, Ohashi T, Aoki Y, Koike N, Takeda T. Stereotactic body radiotherapy (SBRT) for oligometastatic lung tumors from colorectal cancer and other primary cancers in comparison with primary lung cancer. Radiother Oncol. 2011;101(2):255–9.
28. Ricardi U, Filippi AR, Guarneri A, et al. Stereotactic body radiation therapy for lung metastases. Lung Cancer. 2012;75(1):77–81.
29. Ahmed KA, Berglund AE, Hoffe SE, et al. Differences between colon cancer primaries and metastases utilizing a molecular assay for tumor radiosensitivity suggest implications for potential oligometastatic SBRT patient selection. Int J Radiat Oncol Biol Phys. 2015;92(4):837–42.
30. Rainer J. Klement radiobiological parameters of liver and lung metastases derived from tumor control data of 3719 metastases. Radiother Oncol. 2017;123:218–26.