Stereotactic Radiotherapy for Multiple Lung Metastases: Early Clinical Outcomes

Çoklu Akciğer Metastazları İçin Stereotaktik Radyoterapi: Erken Klinik Sonuçlar

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ABSTRACT

Introduction: Oligometastatic lung cancers are usually small in size and high doses of radiation increase the chance of local control. In this study, it was aimed to treat patients with stereotactic body radiotherapy (SBRT) technique and to examine the early effects of treatment in order to control these tumors of patients whose primary tumor was controlled but 3 and 4 metastases developed in their lungs.

Methods: Computed tomography (CT) images of seven patients with three to four lung metastases were acquired using 2 mm sections. Treatment plans were prepared to deliver a total of 48 Gray (Gy) in four fractions at two isocenters. All plans were created using the Monaco treatment planning system (TPS) and the MonteCarlo algorithm at a filter-free 6MV energy (6FFF - dose rate: 1600 MU/min). During all these processes, the exact target was irradiated through active breathing control (ABC). Patients were administered a pulmonary function test (PFT) before and after the treatment and the results were compared.

Results: 100% of the intended dose was prescribed to the tumor volumes of the patients. Critical organ doses met the TG101 standards. The maximum dose of the plans was kept below 120%. All treatment plans reached desired values and were clinically accepted.

Conclusion: Local control was achieved in the patients and there was no grade 3-4-5 radiation pneumonia (RP). In particular, patients with severe pulmonary comorbidities should be carefully monitored for RP during the few months of follow-up after SBRT. Depending on the patient's condition (holding the breath, being stable, etc.) or the characteristics of the linear accelerator, SBRT can be safely administered to metastases at two or three isocenters and the metastases can be controlled when patients with locally controlled primary tumors develop multiple distant metastases in the lungs.

Key words: Multiple lung metastases, SBRT, high MU, radiation pneumonia (RP)

ÖZET

Giriş: Oligometastatik akciğer kanserleri genellikle küçük boyuttadır ve yüksek radyasyon ile lokal kontrol şansı artmaktadır. Bu çalışmada primer tümörü kontrol altına alınmış fakat akciğerlerinde 3 veya 4 metastaz gelişen hastaların bu tümörlerini kontrol altına almak için stereotaktik beden radyoterapi (SBRT) tekniği ile hastaların tedavi edilmesi ve tedavinin erken etkilerinin incelenmesi amaçlanmıştır.

Yöntemler: Akciğerinde 3 ve 4 metastaz bulunan 7 hastanın tomografi (CT) görüntüleri 2mm kesitlerle çekildi. Tedavi planları iki izomerkezde 4 fraksiyondan toplamda 48 Gray (Gy) olacak şekilde hazırlandı. Bütün planlar Monaco tedavi planlama sistemi (TPS) ile MonteCarlo algoritması kullanılarak filtresiz 6MV enerjide (6FFF - doz hızı 1600MU/dk) oluşturuldu. Planlar hazırlanırken istenilen dozun %100'ü, tümör hacminin %100'üne reçete edilmesi amaçlandı. Hastalara tedavi öncesinde ve sonrasında solunum fonksyon testi (SFT) yapılarak sonuçları karşılaştırıldı.

Bulgular: Tümör hacmine istenilen dozun %100'ü reçete edildi. Kritik organ dozları TG101 standartlarını karşıladı. Planların maksimum dozları 120%'nin altında tutuldu. Tüm tedavi planları istenilen dozları karşıladı ve klinik olarak kabul edilebilir durumdaydı.

Sonuç: Hastalarda lokal kontrol sağlandı ve herhangi bir grade 3-4-5 radyasyon pnomonisi (RP) izlenmedi. Özellikle ciddi pulmoner komorbiditeleri olan hastalar, SBRT sonrası takip döneminde birkaç ay içinde RP'nin açısından dikkatle izlenmelidir. Hastanın durumuna (nefesini tutması, sabit kalabilmesi vb) veya lineer hızlandırıcının özelliklerine göre primer tümöründe lokal kontrol sağlanmış hastaların akciğerlerinde birbirine uzak birden fazla metastaz oluşması durumunda iki veya üç izomerkezle bu metastazlara güvenle SBRT tekniği uygulanabilir ve metastazların kontrolü sağlanabilir.

Anahtar Kelimeler: Çoklu akciğer metastazları, SBRT, yüksek MU, radyasyon pnomonisi (RP)

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INTRODUCTION

Oligometastasis refers to the state of disease in which cancer cells spread beyond the primary tumor site, but are not yet diffuse metastatic. Emerging evidence in patients with a limited oligometastatic burden suggests that treating all sites of disease with ablative therapies can improve patient outcomes, including overall and progression-free survival (1). Many studies have defined the oligometastatic state as the presence of one to three or one to five metastatic lesions. Some studies considered the presence of metastatic lesions up to nine as the oligometastatic state (2).

Oligometastatic lung cancers are usually small in size and high doses of radiation increase the chance of local control. Therefore, oligometastatic lung cancers are treated with radiosurgery that is more commonly known as stereotactic body radiotherapy (SBRT) (3). While developments in radiotherapy have positively changed cancer treatment in the last decade, developments that can be considered cutting-edge technology have become available in the routine practice of most centers, one of which is SBRT (4). SBRT is a technique that prescribes high doses to the tumor and provides a highly conformal dose distribution (5,6). In recent years, SBRT has been used as an effective treatment method in inoperable patients with lung tumors and metastases. Remarkable local controls for lung tumors and metastases have been reported with SBRT (5-8).

Preparation of SBRT treatment plans has increased the interest in FFF beams because the characteristics of FFF beams are different from those of filter (FF) beams. The dose rate of FFF beams is very high compared to FF beams and a high dose rate means a short duration of treatment. A short duration of treatment improves patient comfort and reduces uncertainties in dose distribution that may occur due to organ movements. Since it is filter free, there is no photon hitting the filter, thereby also reducing the out-of-field doses that will arise from the contamination of electrons scattered from and formed in the device. In addition, the low average energy and different penumbra width allow reducing dose scattering to the critical organs around the tumor, which makes FFF beams unique for SBRT (4,9-12).

We know that studies have been conducted on patients with multiple lung metastases. Bernand et al. conducted a study on a patient with seven metastases in one lung and recommended the use of SBRT, especially in metastatic patients with a high possibility of survival (13). Kelly et al. demonstrated that lungs could be re-irradiated by SBRT up to three metastases in patients who were administered primary treatment to the thorax, and reported no Grade 3 or 4 toxicity (14). Okunieff et al. irradiated patients with ≤ 5 metastases by SBRT and observed a high rate of local control with low toxicity (7). Li et al. irradiated two patients with ≥ 5 metastases by SBRT and showed that the technique was fast, precise, and tolerated by the patient (15).

However, these studies had single-center treatment plans and selected metastases with close proximity. Therefore, it was easy to define the dose to the target and secondary cancer risks were not emphasized. In patients with a high possibility of survival, it is necessary to focus on the organs that can easily turn into secondary cancer, such as the lungs and breast (16,17). Intensity-modulated radiation therapy (IMRT), especially with gantry rotation or helical motion, is of concern because normal tissues exposed to radiation will increase in volume, meaning that the risk of secondary cancer will be higher than the treatment with three-dimensional conformal radiotherapy (3D-CRT) (18). In their study conducted in 2016, Chunhui et al. stated that treatment plans with 3D-CRT would increase the risk of secondary cancer in one lung compared to rotational IMRT while decreasing such risk for the contralateral lung (19).

In the present study, we aim to investigate the possible side effects of the treatment plans at two and three isocenters that include a high number of monitor units

(MU) on patients who had a primary tumor previously locally controlled but developed three to four lung metastases, to follow up pulmonary functions, and to monitor local control.

METHODS

Patients

This study selected seven patients who were previously given radiation to the primary tumor, resulting in local control but developed multiple lung metastases. All patients received treatment in 2020, and seven patients had a total of 24 metastases. The primary tumor was in the lung in three patients, colon in two patients, rectum in one patient, and endometrium in one patient. There were three, three, and four metastases in the patients with primary lung tumors, four metastases in the patient with a primary rectal tumor, three and four metastases in the patients with primary colon tumors, and three metastases in the patient with primary endometrial tumor (the total number of metastases was 24). The patients were aged 83, 75, 68, 61, 49, 45, and 66 years, respectively. Three patients were male and four were female (Table 1).

Table 1. Demographic characteristics of the patients

	Primary Tumor	Number of Metastases	Age	Sex
Patient 1	Lung	3	83	Female
Patient 2	Lung	3	75	Male
Patient 3	Lung	4	68	Male
Patient 4	Rectum	4	61	Male
Patient 5	Colon	3	49	Female
Patient 6	Colon	4	45	Female
Patient 7	Endometrium	3	66	Female

The treatment was administered to the patients using the ABC system to induce breath-holds. During the tomography scanning of the patients, the ABC system was set to 25 s, and images of the patients were acquired with the full lung for 25 s using a 2-mm section thickness. During the treatment, the breath-holding time was kept shorter depending on the patient's condition so that the patient would not get tired.

A PFT was administered to the patients two months before and after the treatment (Table 3). The patients were screened by CT of the lung at months one and three after SBRT and at every three months during the first year, even in the absence of clinical symptoms, to detect potential RP.

Radiotherapy Planning

A total dose of 48 Gy in four fractions was prescribed to each patient. To date, several reports have mentioned local control and survival in oligometastatic lung tumors, but a standard dose or fraction has not yet been defined for oligometastatic lung tumors (20,21). However, the prescribed doses for lung metastases were reduced in the SABR-COMET-3 trial after radiation-related toxicities in the SABR-COMET-10 trial (1,22).

It was intended to prescribe 100% of the dose to 100% of the tumor volume and 95% of the planning target volume (PTV) with a 0.2-mm margin. Treatment plans were optimized not to exceed 120% of the intended dose. 6FFF beams were used in the treatment plans. The dose rate of 6FFF beams is 1800 MU/min in the Elekta Verse HD linear accelerator. Distant metastases were collected in two and three groups, and treatment plans were created at a total of two and three isocenters, one for each group, by a single physicist in the Monaco treatment planning system (TPS). Since FFF beams are filter free, they have a different structure, and the dose given to the tumor decreases as the beams move away from the center. Therefore, filter-free beams should be exactly defined to the tumor. The grid space was chosen as 2 mm for all patients and the angles as 360 degrees double arc. TG101 was used for dose constraints for organs at risk (23).

Table 2. Target volume and critical organ doses

		PTV					Lung (cGy)		Spinal Cord (cGy)	Heart (cGy)		MU
Patients	Number of Met	CI	HI	D100 (cGy)	D95 (cGy)	D2 (cGy)	1000 cc	1500 cc	max	max	15cc	
Patient 1	3	0.19	1.11	4479.5	5038.5	5637.2	807.7	535.5	2097.8	2452.6	1414.3	4482.69
Patient 2	3	0.21	1.11	4801.5	5127.3	5716.3	512.1	359.4	817.3	928.9	509.2	7435.35
Patient 3	4	0.11	1.09	5009.3	5258.1	5787.7	667.4	410	1193.6	1878.4	1437.2	9715.69
Patient 4	4	0.1	1.07	4931.8	5061.5	5448.1	943.5	733.9	1044.6	1196.1	937.4	7295.45
Patient 5	3	0.11	1.1	4878	5029.8	5583.1	488.9	275.5	1056.4	932	437.4	9021.98
Patient 6	4	0.28	1.14	4654.7	4871.9	5590.4	566.1	395.6	1316.8	1887.8	1096.9	10268.07
Patient 7	3	0.21	1.17	4316.9	4892.4	5779.8	371.7	242.2	1613.6	3880.2	1212.6	13732.25

All treatment plans aim for the patient to complete the treatment in the most effective way. While creating treatment plans, the duration of treatment was kept short, and critical organ doses were never exceeded. Likewise, the treatment plans were optimized in a way that the low doses that the patient might be exposed to could lose their energy as soon as possible. The patients completed these treatments by receiving them every other day.

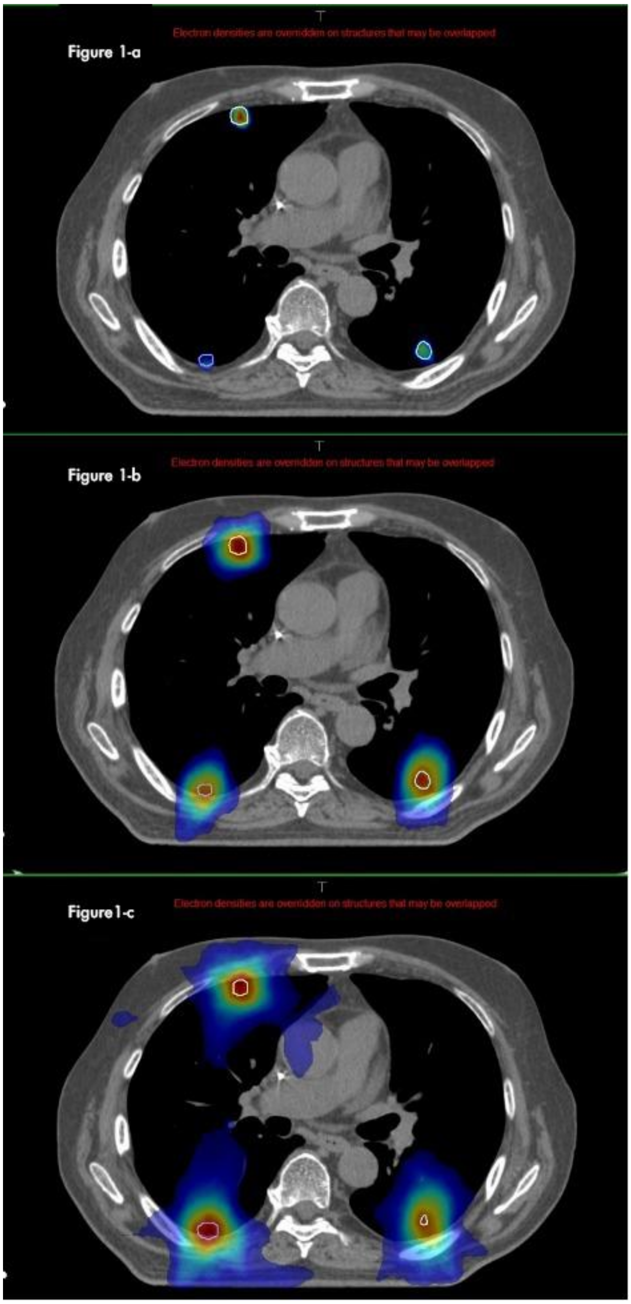

Figure 1a,b,c. Distributions of 100%, 50%, and 25% of the prescribed dose

The above figures 1a, 1b, and 1c belong to the same patient, showing 100%, 50%, and 25% of the prescribed dose, respectively. As is seen in the figures, treatment plans were created in a way that the 25% dose would not overlap with each other. As we were most afraid of the effects of low doses on patients, we tried to limit low doses as much as possible. As seen in Figures 2.a. and 2.b., although the patient had two metastases in both the right and left lobes of the lung, low doses were kept minimum.

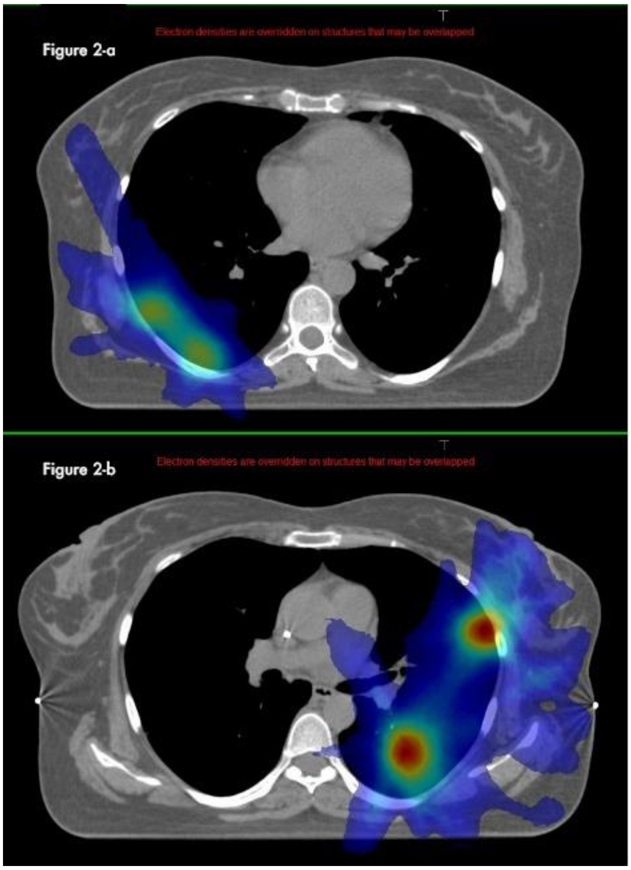

Figure 2a,b. 25% distribution of the prescribed dose

CBCT and image matching

Image-guided radiotherapy (IGRT) was performed for image verification. After CBCT imaging by the kV imaging system XVI (figure 3a,b), our patients were positioned using the six-dimensional table HexaPOD and then treated. This procedure was repeated for both two and three treatment centers.

During the treatment, the lung fullness limits in the simulation were entered and the patients were asked to hold their breath. Since the CBCT imaging would take much longer than the breath-holding of the patients, the patients were asked to hold their breath at 20-second intervals and the kV imaging system was manually stopped at the end of this time. This procedure was completed every 20 seconds.

The patients were treated with the breath-hold ABC system, and it was thereby tried to reduce breathing-related tumor movements to zero. Along with the ABC system, the Versa HD linear accelerator is equipped with a system that automatically starts irradiation when patients hold their breath and stops irradiation when they start breathing.

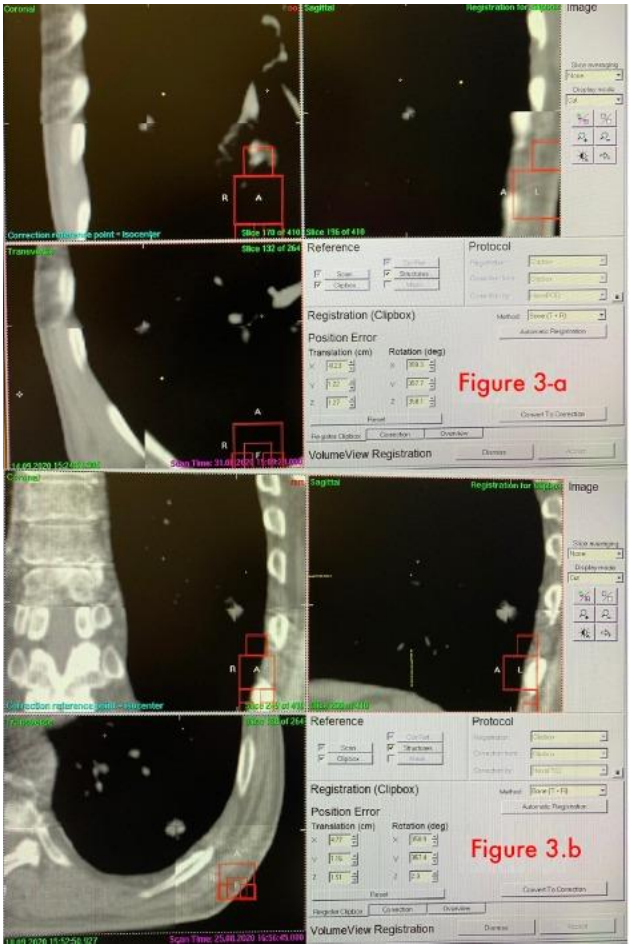

Figure 3a,b. Comparing CT and CBCT with XVI

Statistical Analysis

Data were analyzed using SPSS 24 software. First, the normality of the qualitative data was tested by the Shapiro-Wilk test. The Wilcoxon test, a non-parametric dependent two-sample test, was used for analyses. In addition, the t-test was used to analyze independent groups. A p-value of <0.05 was considered statistically significant for all statistical analyses.

Ethical Considerations

The study was approved by both the Turkish Ministry of Health and the ethics committee of Eskişehir Osmangazi University Faculty of Medicine (No: E-45403353-050.99-207787) and was conducted in accordance with the principles of the Declaration of Helsinki and all relevant regulations.

RESULTS

100% of the intended dose was prescribed to the tumor volumes of the patients. Critical organ doses met the TG101 standards (23). The maximum dose of the plans was kept below 120%. All treatment plans reached desired values and were clinically accepted (Table 2).

The MU, the sum of the different isocenters of the patients, was concerning, but the treatment was tolerated by all patients, including Patient 7. Three isocenters were used for Patient 7. Each isocenter corresponded to one metastasis. Metastases were treated on separate days so that the high MU value was somewhat distributed over the days.

CI and HI were close to each other in almost all patients. Although the maximum dose for the lung was high, the values 1000 cc and 1500 cc were close to each other. The biggest reason for this was that the metastases were small and the same dose was given to the patients. Since metastases were close to the heart and spinal cord in some patients, the maximum doses for these organs varied from patient to patient but were still kept within the TG101 standards. There was a great variation in the MU. Although the metastases were in close proximity in some patients, great efforts were made to achieve the doses for organs at risk. The difficulty in creating the treatment plan increased the MU. There were three isocenters for

Patient 7 and therefore the highest MU occurred in this patient.

The median follow-up after SBRT was 12 months (range: 9–14 months). PFTs of the patients were as seen in Table 3. The PFT results revealed a significant difference in forced expiratory volumes in 1 second (FEV1.0) and forced vital capacities (FVC) between pre-treatment and post-treatment measurements ($p = 0.001$ and $p = 0.002$). In this study, RP was developed in two patients: Grade 1 in Patient 2 and Grade 2 in Patient 7. These two patients with RP also had pulmonary comorbidity. Grade 3-4-5 severe RP was not observed in any patient. Patients who developed RP were given medical treatment and clinically improved. The high MU did not cause acute radiodermatitis and wound site infection on the skin of the patients.

Table 3. Pulmonary function tests two months before and after SBRT

	Before RT		Two Months After RT	
	FVC /% Pred	FEV1.0 /% Pred	FVC /% Pred	FEV1.0 /% Pred
Patient 1	2.95 L / 97	2.41 L/ 92	2.74 L / 91	1.99 L / 77
Patient 2	2.78 L / 79	2 L / 76	2.21 L / 75	1.57 L / 60
Patient 3	3.06 L / 81	2.21 L / 75	2.31 L / 63	1.76 L / 62
Patient 4	3.48 L / 105	2.79 L / 98	3.26 L / 99	2.77 L / 98
Patient 5	3.41 / 84	2.87 / 90	2.86 / 71	2.42 / 77
Patient 6	1.71 / 73	1.41 / 79	1.54 / 65	1.13 / 63
Patient 7	1.94 / 82	1.43 / 73	1.36 / 71	1.24 / 79

DISCUSSION

The normal course of cancer begins with a primary tumor. It then spreads to the lymph nodes and metastasizes to distant organs. However, distant metastases are multiple even in the early stages of cancer. Doses administered to metastases are usually low and administered palliative. Today, patients with multiple lung metastases can be treated by SBRT because of the rapid developments in the software and treatment equipment of radiotherapy. It seems promising based on the encouraging results of randomized trials, mostly involving patients with one to three lesions, and single-arm studies evaluating ablative therapy patients with greater disease burden. However, as the number of metastases increases, the risk of distant metastasis (i.e. the development of additional metastases after SBRT) and the risk of toxicity from SBRT are likely to increase (1). In such patients, SBRT doses can be reduced or administered just before systemic therapy to reduce the risk of toxicity.

For multiple metastases, helical tomotherapy and robotic-arm linear accelerators can safely deliver the treatment. Sterzking et al. stated that helical therapies could be used for multiple lesions (24). However, these two devices are not available in all centers and treatment requires a very long time. Today, many linear accelerators (Elekta VersaHD, Elekta Axesse, Elekta Harmony, Varian TrueBeam, Varian Trilogy, etc.) can perform SBRT. Treatments are administered to the exact target via breath tracking systems or breath-holds, and IGRT and FFF beams, the treatment duration is relatively shorter. The short duration of treatment is important for patient comfort as well as organ movements. In our study, the duration of irradiation per fraction varied from patient to patient, depending on the patient's breath-holding time and resting between breath-holds. The duration varied from patient to patient as well as between the two fractions for a patient. Treatment durations were inconsistent to give a mean value, and therefore not included in the study. But the duration of treatment did not exceed the time tolerated by the patients. In addition, our study used the six-dimensional Hexapod table of Elekta linear accelerator was used for the IGRT method. The working principle of Hexapod was explained by Mayer et al. (25). Rotational motion is very important in radiotherapy. Table rotation is of great importance, especially when treating small-volume lesions. By using

Hexapod in our treatments, we administered treatment to the intended target with accuracy.

The lung is the organ in which most metastases can develop after the liver (26). It is a well-known fact that it is difficult to create treatment plans for patients with multiple lung metastases. Several studies performed treatments for multiple lung metastases, but selected metastases with close proximity and that could be irradiated at a single isocenter (7,13-15). The metastases were distant from each other in our patients and thus treated using two and three isocenters. Two- and three-isocenter treatment plans are viable options. The number of isocenters is at the discretion of the treating physician and the physicists creating the plan. In general, metastases can be treated using individual isocenters if they are distant and well separated from each other.

Kelly et al. showed that no grade 4 or 5 toxicity was observed in patients previously given irradiation to the thorax and treated with SBRT (14). In our study, the use of high-dose SBRT for three patients who had previously received radiotherapy to the thorax was concerning. After the treatments, no major toxicity occurred in these patients. Some metastases were close to the ribs, creating a risk for rib and sternal fractures. Kim et al. reported a mean time of 17 months to develop rib fractures due to SBRT in their patient series (27). None of our patients developed fractures or pain.

Milano et al. administered a dose of 50Gy in 10 fractions and reported that lung metastases were treated in 41%, lymph nodes in 21% of patients, with a two-year local control rate of 67%. (28). Similarly, Heidelberg et al. used SBRT at 12 to 30 Gy in a single fraction in 61 patients with 71 lung metastases and reported a two-year local control rate of 74% (29). Rusthoven et al. administered 48 to 60 Gy in three fractions to 38 patients with 63 lung metastases and reported a two-year local control rate of 96% (30). According to Rusthoven et al., local control might increase with escalating SBRT doses, although there were differences between the study patients. Our study, despite adverse factors such as metastases in different parts of the lung or previous radiotherapy to the lung, showed that high-dose SBRT could be safely used and local control could be achieved.

Fujino et al. established no significant clinical or dosimetric factor to predict RP before treatment (31). Although RP is the most common complication after SBRT for lung tumors (32-34), it remains unclear how to limit these recommended dose-volume parameters. In our study, the FEV1.0 and FCV values of the patients decreased significantly after the treatment, but Grade 3-4-5 severe RP did not develop. This can be evaluated in relation to the treatment of multiple lung metastases by keeping the 1000 cc and 1500 cc of the lung below 10 Gy in treatment planning to predict RP.

CONCLUSION

In particular, patients with severe pulmonary comorbidities should be carefully monitored for RP during the few months of follow-up after SBRT. The correlation between dose and volume factors, which are risk factors for the RP incidence after SBRT, must be followed. Treatment plans with two and three isocenters can be safely used in multiple lung metastases.

Informed Consent: Informed consent was obtained from patients who participated in this study.

Conflict of Interest: Authors declared no conflict of interest.

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REFERENCES

1. Palma DA, Olson R, Harrow S, et al.Stereotactic ablative radiotherapy for the comprehensive treatment of 4–10 oligometastatic tumors (SABR-COMET-10): study protocol for a randomized phase III trial. BMC cancer.2019; 19(1), 1-15.

2. Ruers T, Van Coevorden F, Punt CJ,et al.Local treatment of unresectable colorectal liver metastases: results of a randomized phase II trial. JNCI: Journal of the National Cancer Institute.2017;109(9),1-10

3. Vassiliev ON, Peterson CB, Chang JY , Mohan RU. FFF beams to improve the therapeutic ratio of lung SBRT. Journal of Radiotherapy in Practice.2021; 20(4), 419-425.

4. Vassiliev ON, Kry SF, Chang JY, Balter PA, Titt U, Mohan R.Stereotactic radiotherapy for lung cancer using a flattening filter free Clinac. Journal of Applied Clinical Medical Physics.2009;10(1), 14-21.

5. Iyengar P, Timmerman RD.Stereotactic ablative radiotherapy for non–small cell lung cancer: rationale and outcomes. Journal of the National Comprehensive Cancer Network.2019;10(12), 1514-1520.

6. Senan S, Palma DA, Lagerwaard FJ. Stereotactic ablative radiotherapy for stage I NSCLC: recent advances and controversies. Journal of thoracic disease.2011;3(3), 189.

7. Okunieff P, Petersen AL, Philip A,et al.Stereotactic body radiation therapy (SBRT) for lung metastases. Acta oncologica.2006;45(7), 808-817.

8. Timmerman R, Paulus R, Galvin J,et al.Stereotactic body radiation therapy for inoperable early stage lung cancer. Jama2010;303(11),1070-1076.

9. Tambe NS, Fryer A, Marsden JE, Moore C, Beavis AW.Determination of clinically appropriate flattening filter free (FFF) energy for treating lung SABR using treatment plans and delivery measurements. Biomedical Physics & Engineering Express2016;2(6), 065016.

10. Fu W, Dai J, Hu Y, Han D, Song Y.Delivery time comparison for intensity-modulated radiation therapy with/without flattening filter: a planning study. Physics in Medicine & Biology.2004;49(8), 1535-1547

11. Xiao Y, Kry SF, Popple R,et al.Flattening filter-free accelerators: a report from the AAPM Therapy Emerging Technology Assessment Work Group. Journal of applied clinical medical physics.2015;16(3), 12-29.

12. Boda-Heggemann J, Mai S, Fleckenstein J,et al.Flattening-filter-free intensity modulated breath-hold image-guided SABR (Stereotactic ABlative Radiotherapy) can be applied in a 15-min treatment slot. Radiotherapy and Oncology.2013:109(3), 505-509.

13. Bernard ME, Critchfield L, Kudrimoti M. Safety of Stereotactic Body Radiation Therapy for Seven Ipsilateral Lung Lesions. Cureus.2020;12(6), e8759.

14. Kelly P, Balter PA, Rebueno N,et al.Stereotactic body radiation therapy for patients with lung cancer previously treated with thoracic radiation. International Journal of Radiation Oncology* Biology* Physics.2010;78(5), 1387-1393.

15. Li Q, Mu J, Gu W,et al.Frameless stereotactic body radiation therapy for multiple lung metastases. Journal of Applied Clinical Medical Physics.2014;15(4), 105-116.

16. Hancock SL, Hoppe RT.Long-term complications of treatment and causes of mortality after Hodgkin's disease. In Seminars in radiation oncology WB Saunders.1996;6(3),225-242.

17. Boice Jr, J D, Preston D, Davis, FG, Monson, RR.Frequent chest X-ray fluoroscopy and breast cancer incidence among tuberculosis patients in Massachusetts. Radiation research.1991;125(2), 214-222.

18. Hall EJ, & Wuu CS.Radiation-induced second cancers: the impact of 3D-CRT and IMRT. International Journal of Radiation Oncology* Biology* Physics,2003;56(1), 83-88.

19. Han C, Schultheiss, TE, Wong JY.Estimation of radiation-induced secondary cancer risks for early-stage non–small cell lung cancer patients after stereotactic body radiation therapy. Practical radiation oncology.2007;7(3), e185-e194.

20. Agolli L, Bracci S, Nicosia L, Valeriani M, De Sanctis V, Osti MF.Lung metastases treated with stereotactic ablative radiation therapy in oligometastatic colorectal cancer patients: outcomes and prognostic factors after long-term follow-up. Clinical colorectal cancer.2017;16(1), 58-64.

21. Singh D, Chen Y, Hare MZ,et al.Local control rates with five-fraction stereotactic body radiotherapy for oligometastatic cancer to the lung. Journal of thoracic disease.2014;6(4), 369.

22. Olson R, Mathews L, Liu M,et al.Stereotactic ablative radiotherapy for the comprehensive treatment of 1–3 Oligometastatic tumors (SABR-COMET-3): Study protocol for a randomized phase III trial. BMC cancer.2020;20(1), 1-12.

23. Benedict SH, Yenice KM, Followill D,et al.Stereotactic body radiation therapy: the report of AAPM Task Group 101. Medical physics.2010;37(8), 4078-4101.

24. Sterzing F, Welzel T, Sroka-Perez G, Schubert K, Debus J, Herfarth KK.Reirradiation of multiple brain metastases with helical tomotherapy. Strahlentherapie und Onkologie.2009;185(2), 89-93.

25. Meyer J,Wilbert J,Baier K,et al.Positioning accuracy of cone-beam computed tomography in combination with a HexaPOD robot treatment table. International Journal of Radiation Oncology* Biology* Physics.2007;67(4), 1220-1228.

26. Kanzaki R,Higashiyama M, Oda K,et al.Outcome of surgical resection for recurrent pulmonary metastasis from colorectal carcinoma. The American journal of surgery.2011;202(4), 419-426.

27. Kim SS, Song SY, Kwak J,et al.Clinical prognostic factors and grading system for rib fracture following stereotactic body radiation therapy (SBRT) in patients with peripheral lung tumors. Lung cancer.2013;79(2), 161-166.

28. Milano MT, Katz AW, Muhs AG,et al. A prospective pilot study of curative-intent stereotactic body radiation therapy in patients with 5 or fewer oligometastatic lesions. Cancer: Interdisciplinary International Journal of the American Cancer Society.2008;112(3), 650-658.

29. Hof H, Hoess A, Oetzel D, Debus J, Herfarth K.Stereotactic single-dose radiotherapy of lung metastases. Strahlentherapie und Onkologie.2007;183(12), 673-678.

30. Schefter TE, Rusthoven KE, Kavanagh BD, et al.Multi-institutional phase I/II trial of stereotactic body radiation therapy for lung metastases. Journal of Clinical Oncology.2009;27(10), 1579-1584.

31. Fujino M, Shirato H, Onishi H,et al.Characteristics of patients who developed radiation pneumonitis requiring steroid therapy after stereotactic irradiation for lung tumors. The Cancer Journal.2006;12(1), 41-46.

32. Nanda RH, Liu Y, Gillespie TW,et al.Stereotactic body radiation therapy versus no treatment for early stage non–small cell lung cancer in medically inoperable elderly patients: a National Cancer Data Base analysis. Cancer.2015;121(23), 4222-4230.

33. Nishimura S, Takeda, A, Sanuki N,et al. Toxicities of organs at risk in the mediastinal and hilar regions following stereotactic body radiotherapy for centrally located lung tumors. Journal of Thoracic Oncology.2014;9(9), 1370-1376.

34. Lu C, Lei Z, Wu H, Lu H.Evaluating risk factors of radiation pneumonitis after stereotactic body radiation therapy in lung tumor: meta-analysis of 9 observational studies. PLoS One.2018;13(12), e0208637.

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