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BİLATERAL SÜRRENAL METASTAZLI HASTALARDA FARKLI ARK TEDAVİ PLANLARININ DOZİMETRİK KARŞILAŞTIRMASI

DOSIMETRIC COMPARISON OF DIFFERENT ARC TREATMENT PLANS IN PATIENTS WITH BILATERAL SURRENAL METASTASES

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ÖZET

AMAÇ: Bilateral adrenal bez metastazlarının (AGM) tedavisinde ablatif stereotaktik vücut radyoterapisinin (SBRT) etkinliğini ve güvenilirliğini araştırmak için farklı ark tedavi planlarının dozimetrik karşılaştırılması amacıyla retrospektif bir çalışma tasarlanmıştır.

GEREÇ VE YÖNTEM: Ekim 2006'dan Ocak 2017'ye kadar AGM 84 ve Karnofsky performans skoru ≥70 olan 14 hastada (12 erkek, 2 kadın) tekli (S-VMAT) ve çoklu (M-VMAT) izocenter ark VMAT'ı SBRT tedavileri için optimize edilmiştir. Kritik organlar olarak böbrek, karaciğer, omurilik, aort, mide, duodenum, pankreas, deri ve tüm vücudun belirli hacimlerdeki maksimum dozları, ortalama dozları ve maksimum organ dozları incelenmiştir. Ayrıca tedavi planlama sisteminde tedavi süresine karşılık gelen MonitorUnit değerleri arasındaki farklar istatistiksel olarak analiz edilmiştir.

BULGULAR: S-VMAT planları, M-VMAT ile karşılaştırıldığında %4'lük bir nispi iyileşme ile daha iyi bir doz coverage indeksi (COI) ile sonuçlanmıştır. Bu fark anlamlıydı (p=0.02). Benzer şekilde, S-VMAT planları, %13,8'lik bir göreli iyileşme ile M-VMAT'tan önemli ölçüde daha yüksek bir HI sergilemiştir (p=0.001). S-VMAT planları, M-VMAT'a kıyasla sırasıyla %8,7 ve %6,9 oranında daha iyi bir UI ve GI ile sonuçlanmıştır (p=0.02). Fraksiyon başına ortalama MU değerleri S-VMAT'ta 2755,21±388,72 ve M-VMAT'ta 4848,79±491,06 olarak hesaplanmıştır. S-VMAT planları, fraksiyon başına MU'larda %76 azalma ile sonuçlanmıştır (p=0.01).

SONUÇ: S-VMAT, M-VMAT tekniğine kıyasla hedef kapsama alanından taviz vermeden OAR'ları önemli ölçüde korumuştur. Bir S-VMAT planı hazırlamak için ortalama süre, bir M-VMAT planı hazırlamak için ortalama sürenin yaklaşık dört katı olmasına rağmen, bu plan, daha kısa tedavi süresi ve daha az monitör unit (MU) dahil olmak üzere birçok doğal avantaj sergilemiştir. Sonuç olarak M-VMAT plan kalitesini düşürmekte ve risk altındaki organların (OAR) dozlarında artışa sebep olmuştur. Ayrıca toplam MU sayısında da artışa sebep olduğu için tedavi süresi uzamakta ve hastaya verilen MU artmıştır.

ANAHTAR KELİMELER: Bilateral, Adrenal Gland Metastazlar, SBRT, VMAT.

ABSTRACT

OBJECTIVE: A retrospective study was designed for dosimetric comparison of different arc treatment plans to investigate the efficacy and safety of ablative stereotactic body radiotherapy (SBRT) in the treatment of bilateral adrenal gland metastases (AGM).

MATERIAL AND METHODS: In 14 patients (12 males, 2 females) with AGM of 84 and Karnofsky performance score ≥70, we optimised single-volumetric arc therapy (S-VMAT) and multiple-volumetric arc therapy (M-VMAT) isocentric arc VMAT for SBRT treatments from October 2006 to January 2017. The maximum and mean organ doses in specific volumes of critical organs were examined. The differences between the monitor unit values were statistically analysed.

RESULTS: S-VMAT plans had a better dose conformity index (COI) than M-VMAT plans, with a relative improvement of 4% (p=0.02). Similarly, S-VMAT plans had a significantly higher homogeneity index (HI) than M-VMAT plans, with a relative improvement of 13.8% (p=0.001). S-VMAT plans resulted in better UI and GI compared with M-VMAT, with relative improvements of 8.7% and 6.9% respectively (p=0.02). Mean MU per fraction was 2755.21±388.72 in S-VMAT and 4848.79±491.06 in M-VMAT. The S-VMAT schedules reduced MU per fraction used by 76% (p=0.01).

CONCLUSIONS: S-VMAT has significantly protected OARs without compromising target coverage compared to the M-VMAT technique. Although the average time to prepare an S-VMAT plan is approximately four times that of an M-VMAT plan, this plan has demonstrated several inherent advantages, including a shorter treatment duration and fewer monitor units (MU). Consequently, it has reduced the quality of M-VMAT plans and caused an increase in the doses to organs at risk (OARs). Furthermore, as it has also caused an increase in the total number of MUs, the treatment duration has been extended and the number of MUs delivered to the patient has increased.

KEYWORDS: Bilateral, Adrenal Gland Metastases, SBRT, VMAT.

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INTRODUCTION

Adrenal gland metastases (AGM) are frequently encountered in patients with primary lung, liver, kidney, colorectal and lymphoma tumors (1). Although not very common, adrenal insufficiency in patients with bilateral adrenal metastases may lead to more severe outcomes by decreasing the quality of life (QOL) of the patient (2). Salvage chemotherapy and surgery with severe complications are commonly used in the treatment of AGM. In these cases, pathologic examination is required to administer chemotherapy regimens (3). In addition, in case of failure of the first chemotherapy regimen, an increase in toxicity with the second chemotherapy regimen is inevitable (4). Although surgical resection is another alternative, adrenal insufficiency and accompanying morbidities are possible (3). For all these reasons, radiotherapy is considered a new alternative treatment with high efficacy and low side effects (3). With the developing technology, ablative stereotactic body radiotherapy (SBRT) is the new treatment option for adrenal metastases where resection is difficult or impossible (5-7). In addition, since the ablative dose given with SBRT (BED10, $\alpha/\beta = 10$) is highly effective, local control and survival are significantly increased (5, 8, 9). In the meta-analysis results of Chen et al., 2-year local control (LC) rates of 47.8%, 70.1% and 85.6% and overall survival (OS) rates of 34.0%, 47.2% and 60.1% were emphasized for 60 Gy, 80 Gy and 100 Gy BED10 values (5). However, it increases the risk of toxicity to organs at risk (OAR) during targeted delivery of ablative dose (10,11); thus, good use of current radiotherapy technology is an important parameter for both local control and survival.

Stereotaxy is the determination of the 3D position of a given point in free space in a limited coordinate system determined within an external rigid frame. Contrary to conventional treatment schemes, it is a method applied for the ablation of relatively small volume lesions by giving a high radiation dose in 1-5 fractions. Radiobiological and radiophysical studies have shown that the SBRT condition can be achieved when the lesion size is a maximum of 4 cm (12). Currently, survival is improved with SBRT for metastatic lesions. SBRT is preferred in treatments with serious complication risk such as adrenalectomy because of its low complication risk (13-15). SBRT is frequently used in the treatment of lung cancer, liver cancer, pancreatic cancer and prostate cancer (16-19). Despite its increasing use, clinical data and treatment outcomes of AGM treatment with SBRT are among the rare studies. Due to the limited number of such studies in the literature, we conducted this study to evaluate the efficacy and safety of volumetric modulated arc therapy (VMAT) SBRT plans under AGM management.

MATERIALS AND METHODS

For this retrospective study, 14 randomly selected cases of bilateral AGM were included. A slice thickness of 2mm was used for CT scans in patients immobilized in the supine position with a vacuum mattress. Gross tumor volume (GTV) was determined by the volume of the lesion clearly visible on imaging examinations. All scans delineated the right and left kidney, liver, pancreas, stomach, doudenum, spinal cord, aorta, body and a planning target volume (PTVSingle (S-VMAT) and multiple (M-VMAT) isocenter arc VMAT SBRT 6MV beam energy treatment plans were created in Eclipse TPS version 13.6. The geometric center was used at the isocenter of the S-VMAT plans **(Figure 1)**.

Figure 1: Beam geometry the single-isocenter VMAT plan for a typical surrenal stereotactic body radiation therapy case

In the other planning technique, M-VMAT plans, a double isocenter was used **(Figure 2)**.

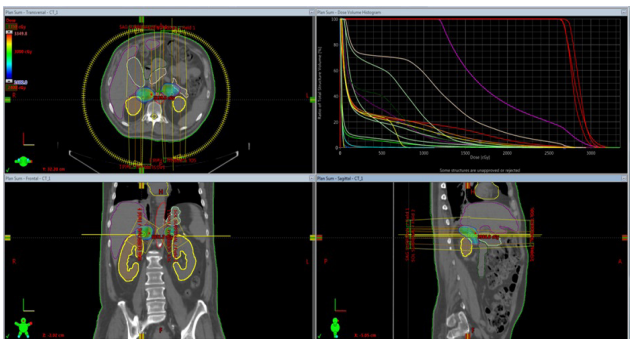

Figure 2: Beam geometry the dual-isocenter VMAT plan for a typical bilateral AGM stereotactic body radiation therapy case.

Here, it was replanned by placing it at the approximate geometric center of the total PTV. The prescription dose was determined as 24 Gy in 3 fractions. Analytic Anisotropic Algorithm (AAA) with a 2.5 mm dose grid matrix was used in all plans. In all plans, the prescription dose was created to receive ≥95% of the prescribed dose to a minimum of 100% of the PTV. At the maximum dose, the PTV was optimized to receive ≥110% of the dose. The Eclipse treatment planning system (TPS) (Varian Medical Systems, Palo Alto, CA, USA) was used for all SBRT plans. The dosimetric analysis of these S-VMAT and M-VMAT plans had been made using dose-volume histogram (DVH) analysis. For the PTV quality comparison, dosimetric indices like coverage index (COI) (20), homogeneity index (HI) (21), conformity index (CI) (22), uniformity index (UI) (23), and gradient index (GI) (24) were calculated as stated below. The COI was defined as:

$$COI = \frac{\mathrm{Dp}}{\mathrm{D95\%}}$$

Where DP is the prescription dose and D95% is the dose received by 95% of the PTV. The CI was calculated as:

$$CI = \frac{\mathrm{VPTV}}{\mathrm{PTVref}} \mathrm{x} \frac{\mathrm{Vref}}{\mathrm{PTVref}}$$

Where VPTV is the volume of PTV, VPTVref is the reference isodose (95%) volume within the PTV, and Vref is the volume of reference isodose (95%). The HI was calculated as:

$$HI = \frac{\mathrm{PTV\ max.}}{\mathrm{Dp}}$$

Where PTV max. is the maximum dose of the planning target volume and DP is the prescription dose. The UI was calculated as:

$$UI = \frac{\mathrm{D5\%}}{\mathrm{D95\%}}$$

Where D5%, D95% are the doses received by 5%, 95% of the PTV respectively. The GI was defined as:

$$GI = \frac{\mathrm{V50\%}}{\mathrm{VPTV}}$$

Where V50% is 50% isodose volume and VPTV is the volume of PTV. The ideal value for COI, CI, UI, and GI is 1 and, a plan with a value closer to 1 indicates a superior plan. In addition, total monitor units (MU) were noted to assess the delivery efficiency.

Ethical Committee

Approval for this study was obtained from Afyonkarahisar Health Sciences University, Faculty of Medicine, Ethics Commit¬tee with decision 04.02.2021 2021/04 by the principles of the Declaration of Helsinki.

Statistical Analysis

For statistical analysis, IBM SPSS (version 19; SPSS Inc., Chicago, IL, USA) was used and Kruskal-Wallis H test was applied at a statistical significance level of $p<0.05$ to evaluate the differences between treatment parameters that did not show normal distribution. All statistical tests were two-sided, and all data presented are recorded as mean ± standard deviation.

RESULTS

In this study, we have compared single and multiplizocenter VMAT SBRT for the treatment of locally advanced surrenal cancer patients. All plans were clinically applicable, including target coverage and organs at risk. In both planning techniques, the prescription was applied for at least 95% PTV volume receiving 100% of the prescribed dose. The mean ± standard deviation (SD) of volumes of PTV129,5±113,7 cm3. PTV results for all plans are summarized in **Table 1**. The S-VMAT (PTV; max (2593.8±40.5) and mean (2457.8±46.7) and M-VMAT(PTV; max. (2968.3±214.5) and mean (2645.8±127.4) plans were statistically significant differences among all S-VMAT plansfor the PTV coverage ($p = 0.02$). There was no statistically significant difference between the PTV min. dose values of the S-VMAT (PTVmin. (2266.1±42.0)) and M-VMAT (PTVmin.(2331.4±127.5))plans.

Table 1: Comparison Results of Planning Target Volume Parameters

Planning Technique/ Critical Organs	S-VMAT (Mean±SD)	M-VMAT (Mean±SD)	p Value
PTV Volume (cm^3)	129,5±113,7	129,5±113,7	-
PTV Max. (cGy)	2593,8±405	2968,3±214,5	0,02#
PTV Min. (cGy)	2266,1±42,0	2331,4±127,5	0,06
PTV Mean (cGy)	2457,8±46,7	2645,8±127,4	0,04#
D5	2488,18±37,98	2825,68±185,29	0,01#
D95	2414,23±32,38	2521,87±78,57	0,01#
V50	859,24±539,57	957,00±562,60	0,35

COI, Coverageindex; CI, Conformityindex; HI,Homogeneity index; UI, Uniformityindex; GI, Gradientindex; MU, Monitorunit; #, statistically significant result

Dosimetric Parameters Results for Planning Efficiency for all plans are summarized in **Table 2**.

Table 2: Dosimetric Parameters Results for Planning Efficiency

Planning Technique/ Critical Organs	S-VMAT (Mean±SD)	M-VMAT (Mean±SD)	p Value
COI	0,99±0,01	0,95±0,03	0,02#
HI	1,08±0,01	1,23±0,10	0,001#
UI	1,03±0,02	1,12±0,06	0,01#
GI	1,01±0,01	0,94±0,64	0,02#
MU	2755,21±388,72	4848,79±491,06	0,01#

COI, Coverageindex; CI, Conformityindex; HI,Homogeneity index; UI, Uniformityindex; GI, Gradientindex; MU, Monitorunit; #, statistically significant result

The S-VMAT plans resulted in a better dose COI compared with M-VMAT, with a relative improvement of 4%. This difference was significant (p=0.02). Similarly, the S-VMAT plans exhibited a significantly higher HI than the M-VMAT, with a relative improvement of 13,8%. (p=0.001). The S-VMAT plans resulted in a better UI and GI compared with M-VMAT, with a relative improvement of 8,7 and 6,9%, respectively (p=0.02). The mean values of MUs per fraction were 2755,21±388,72 in S-VMAT and 4848,79±491,06 in M-VMAT. The S-VMAT plans resulted in a 76% reduction in MUs per fraction consumed (p=0.01). When evaluated in terms of PTV quality score in the study, it was concluded that S-VMAT plans were better than M-VMAT plans.A summary of the OAR values of all plans is given in **Table 3**.

Table 3: Comparison Results of Organs at Risk Dosimetric Parameters

Planning Technique/ Critical Organs	S-VMAT (Mean±SD)	M-VMAT (Mean±SD)	p Value
Right KidneyMean	442,5±172,4	420,5±145,2	0,06
Right Kidney 130cc	98,2±81,9	77,3±72,9	0,09
LeftKidneyMean	372,0±162,5	381,5±151,2	0,02#
LeftKidney 130cc	39,2±72,9	55,9±25,7	0,02#
BilateralKidney	408,6±137,0	394,9±108,3	0,286
BilateralKidney 200cc	104,7±72,3	114,2±59,8	0,01#
LiverMean	618,6±553,3	618,6±553,3	0,359
Liver 700cc	353,9±183,6	353,9±183,6	0,245
PancreasMax.	2449,8±181,9	2582,2±444,2	0,297
Pancreas 5cc	1735,7±516,5	1947,7±599,2	0,04#
StomachMax.	2188,5±705,8	1958,7±600,2	0,01#
Stomach 10cc	1121,6±494,9	1157,0±370,5	0,01#
DuodenumMax	1801,9±1038,5	1881,3±903,4	0,647
Duodenum 5cc	1100,9±653,3	1078,8±670,9	0,463
Duodenum 10cc	820,6±585,3	759,3±572,9	0,133
SpinalCordMax.	1069,8±208,7	1060,4±312,4	0,925
Aorta Max.	2433,0±169,8	2675±270,3	0,013#
Body Max.	2615,1±111,1	2977,7±239,5	0,04#

COI, Coverageindex; CI, Conformityindex; HI,Homogeneity index; UI, Uniformityindex; GI, Gradientindex; MU, Monitorunit; #, statistically significant result

M-VMAT doses were lower than S-VMAT doses in right, left and bilateral kidney 130cc doses, but statistical significance was obtained in left and bilateral kidney 200cc doses. Similarly, the liver mean, stomach maximum, stomach 10cc, duodenum 5cc, duodenum 10cc and spinal cord maximum doses were significantly less in the M-VMAT plans. Both the S-VMAT and M-VMAT plans liver 700cc dose were the same. In contrast, left kidney mean and pancreas 5cc dose were significantly less in the S-VMAT plans. The maximum doses of aorta and body were significantly less in the S-VMAT plans.

DISCUSSION

Since treatment planning depends on differences in TPS, calculation algorithm, treatment equipment and most importantly the skill level of the planner, this study aimed to normalise the process of radiotherapy plans. S-VMAT and M-VMAT plans were created for each patient under the same constraint conditions. Each plan was designed by the same radiotherapy physicists and approved by the same radiotherapy oncologist.

In VMAT, there is no need to use different isocenters and arc(s) for each target when a single isocenter can provide the same coverage as the plan (25). As can be seen from the results of the study, M-VMAT plans are not better than S-VMAT plans in terms of plan quality and OAR. LINAC-based VMAT SRS treatment applications have become widespread due to the rapid and practical applicability of single-center SRS (26). For this reason, planning with the M-VMAT technique did not provide a significant difference in fast and practical treatments.

When Scorsetti et al. (27) evaluated the acute outcomes of treatment of abdominal primary or metastatic tumors with S-VMAT, they emphasized that local control and acute toxicity were promising. The main reason for this is the planning quality and success in OAR protection, which is also emphasised in our study. On average, nVMAT (non-coplanar) plans gave higher kidney doses than cVMAT (coplanar) plans in their study by Woods et al. (28). Similarly, it gave OAR doses in M-VMAT plans. The most important conclusion of the study is that S-VMAT is superior to M-VMAT in VMAT SBRT treatments to preserve OARs without compromising target coverage. Preparing the M-VMAT plan takes less time than preparing

the S-VMAT plan. Because it will take time to manage the plan by taking into account the OARs in S-VMAT optimization and evaluating them with insights and experience. But MU and treatment time will also be shorter than M-VMAT. In addition to all these, the reduced treatment time increases patient comfort and reduces interfractiton tumor movement. As a result, M-VMAT plans are summed, and cumulative doses are overlapped. This leads to overlapping of OAR doses and decreased plan quality.

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