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Comparison with conventional arc and split-partial arc techniques of volumetric modulated arc therapy in terms of planning efficiency for stereotactic radiotherapy treatment of multiple brain metastases

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Abstract

Aim: In stereotactic radiotherapy of multiple brain metastases (BM), Conventional Arc (CA) of the volumetric modulated arc therapy (VMAT) technique with a single isocenter is a frequently used technique using Linac (Linear Accelerator) treatment devices. Reducing the dose of healthy brain tissue as well as improved delivery efficiency in SRT treatment of BM is important to reduce possible treatment toxicity. Therefore, multileaf collimator (MLC) movements in wide arcs of CA technique may result in non-optimal dose distribution and increasing low-dose volume in the brain. Improvement of the protection of brain tissue by using SPA technique which has reduced field sizes and minimizes physical limitations of MLCs is evaluated.

Materials and Methods: 28 patients with 3≤, ≥6 of multiple BM included in this retrospective planning study. All plans were generated 27 Gy in 3 fractions using conventional arcs with automated width of fields and split partial arcs with the manual arrangement of fields according to localizations of tumors in the brain. Dosimetric parameters included tumor coverage, conformity index (CI), gradient index (GI), V_{4Gy}, V_{10Gy} and V_{12Gy} volumes of brain from both techniques were compared by Wilcoxon signed-ranked tests.

Results: Both techniques satisfied clinical requirements in coverages of PTV and CI. CA technique had a significantly higher GI than SPA of VMAT (GI; 4.19 vs. 3.58; $p < 0.001$). SPA technique was found significantly lower V_{4Gy} (18.50 vs. 21.30 cm^3, $p < 0.001$), V_{10Gy} (30.71 vs. 40.76 cm^3, $p < 0.05$) and V_{12Gy} (213.32 vs. 305.71 cm^3, $p<0.05$) volumes.

Conclusion: Due to rapid MLC modulation and less tongue-and-groove effect in arcs with smaller field widths, SPA technique can reduce OAR and brain dose radiation exposure in brain stereotactic radiotherapy for different tumor localizations in the brain. This technique may be the first choice compared to the CA technique for SRT of BM having distant and scattered targets.

Introduction

Brain metastases, which develop in approximately 15-35% of cancer patients during the course of their disease, are the most common intracranial malignancies. Especially 25-40% of patients with multiple BM have a high mortality rate as a result of poor local control [1-3]. Stereotactic radiosurgery or radiotherapy (SRC/SRT) is a common treatment option for multiple brain metastases (BM) using different dose schedule protocols with different treatment techniques such as conformal dynamic arc, static arc, fixed gantry 3D conformal radiotherapy (3DCRT), intensity modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT) [4-8]. Nowadays, the most common approach in the treatment of BM's SRS/SRT is the VMAT technique, which has a complex process due to the synchronization of the gantry, dose rate and multi-leaf collimator (MLC) modulation rate. For VMAT where the dose is given by the simultaneous dynamic movement of the MLC leaves, dose rate, MLC speed and gantry speed need to be synchronized unlike other techniques [6, 9]. These variables, which are determined according to the patient's treatment planning, are determined by the optimization method in the treatment planning system. The optimization method tries to establish a dose distribution

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taking into account some mechanical Linac (Linear Accelerator) constraints such as MLC leaf position limits and MU weights [7, 8, 10].

In theory, target volumes which are uniformly localized from the beams eye view, the VMAT is capable of delivering a fractional dose in a single arc. However, multiple arcs are required both to reduce the effect of the MLC movements constraints on field width and to target volumes that are uneven and at the edge of the irradiation field [11]. An MLC movement of the current VMAT implementation does not allow repositioning the width of the jaws in each arc according to targets of irradiation localization during delivery [7, 8, 12, 13]. In additional the width of the jaws in each arc is required to be automatically open to cover all targets for each arc to be used for delivery during the plan optimization [7, 8, 10, 12, 13]. Therefore In order to irradiate metastases, which usually consist of small volumes in a different part of the brain, the size of the jaws must be opened to cover the entire cranium [14]. Many studies have investigated the effect of collimator angle and size of the jaws to make treatment more efficient, such as target coverage, normal tissue protection, monitor units (MUs), and have emphasized irradiation-specific collimator angle and field sizes for different target regions [14, 15]. In VMAT optimization, the physical limitations of the machine, such as the MLC leaf positions and length, as well as the maximum leaf speed, can directly affect the optimization process [12, 15-17]. It becomes especially important for the treatment of BM of targets located in different localizations in the brain. For example, high definition leaves on Varian Truebeam (Varian Medical Systems, Palo Alto, CA, USA) Linac used in the study are 15 cm long (iso-center), so two opposing MLC leaves moving parallel to their x-jaws can only cover 30 cm of the area. In addition, when the x-jaw opening of a VMAT field is more than 15 cm, a leaf cannot reach the opposite end of the field. This situation may damage the quality of the plan and sometimes cause undesirable irradiation of healthy tissue.

VMAT technique may be used as the first choice in patients with multiple brain metastases with very scattered localization. However, the limited geometric and physical capacities of the jaw and MLC structure of the treatment machine may cause a decrease in the quality of this technique. This study was designed to evaluate the dosimetric efficacy of Split-Partial Arc (SPA) technique, which minimizes physical limitations with MLC move of narrow jaws compared to standard VMAT technique which name is Conventional Arc (CA) technique having field width size are automatically adjusted during planning, for BM.

Materials and Methods

Patients selection

This retrospective study was carried out in The Koç University Committee on Human Research (KUCHR) Ethics Committee approval from the KUCHR (Date: 06.05.2022 No: 2022. 159.IRB1.062). A total of 28 BM cancer patients, who were treated at American Hospital of MD Anderson in İstanbul, Turkey with the four full CA technique using HD MLC of Varian TrueBeam Linac between 2019 and 2022 were chosen for this retrospective dosimetric investigation. All patients with characteristics displayed in Table 1, were generated according to protocol of 27 Gy in 3 fractions for number 3≤, ≥6 of BM in different localizations of brain. All cases used in this study had an average of 3,882 cc (range 5.04 cc to 2.01 cc) per tumor volume. For Treatment Planning, Computed Tomography (CT) imaging with a slice thickness of 1 mm was obtained in the simulation, and then T1-weighted and T2-weighted Magnetic Resonance Imaging (MRI) with contrast at 1 mm slice thickness was obtained for target determination in all cases. Gross tumor volume (GTV) and the organs at risk (OAR) volumes were generated by the radiation oncologist in the Pinnacle treatment planning system (Brain LAB AG, Munich, Germany) based on the fused images of CT and MR. For unbiased comparison, the planning target volume (PTV) of all cases were established by extending the GTV uniformly by 0.2 cm. For unbiased comparison, the planning target volume (PTV) of all cases were established by extending the GTV uniformly by 0.2 cm.

The same structures included GTV, PTV and OAR were used for both CA and SPA techniques.

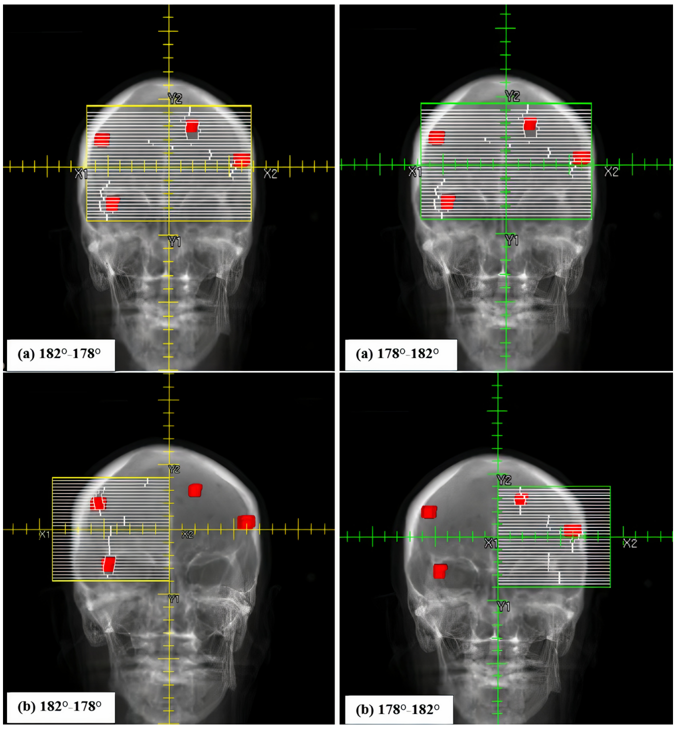

Figure 1. DRR images registration of cranial in VMAT plans performed with different field width sizes. (a) A beam's eye view DRR of a fully opened field size of CA technique with MLC to sufficiently cover all PTVs from a clockwise and counterclockwise arc angle between 182° and 178°. (b) A beam's eye view DRR of A half-opened field size of SPA technique with MLC to cover part of right and left PTV's from a clockwise and counterclockwise arc angle between 182° and 178°. The red color volumes is four PTV's of BM on different location of head.

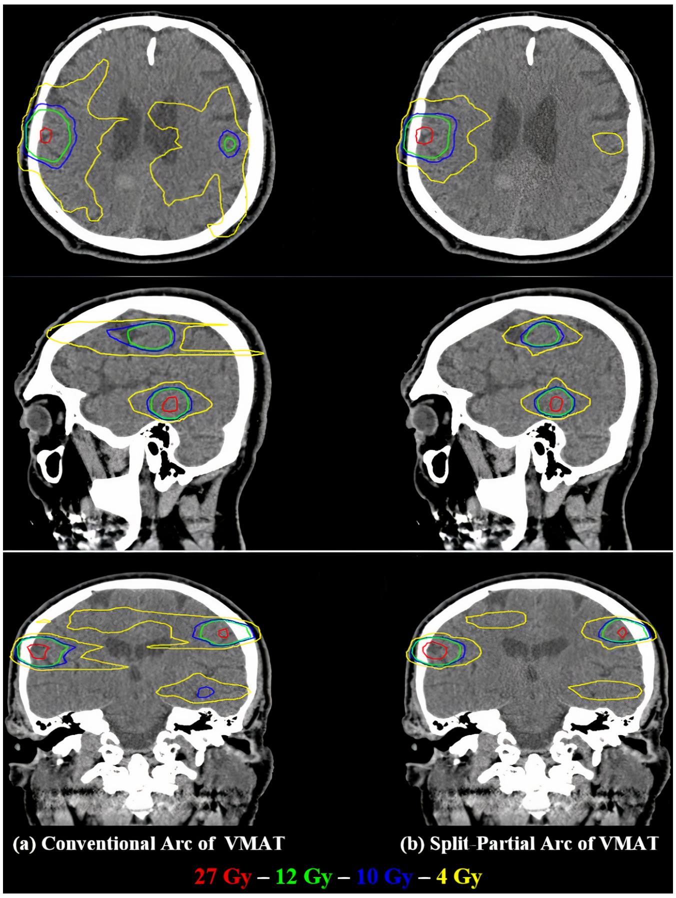

Figure 2. Plans of CA and a SPA techniques on images of example case. The panel from top to bottom shows axial, sagittal and coronal views of isodose distribution of (a) CA technique (left), (b) SPA technique (right).

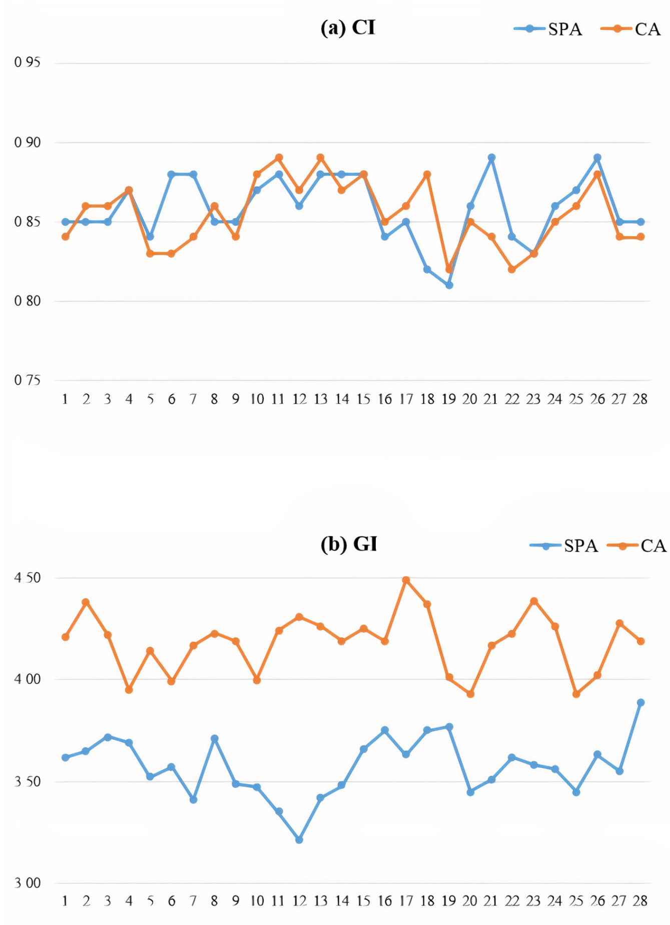

Figure 3. Treatment quality parameters (a) CI, and (b) GI of all plans, for SPA and CA techniques.

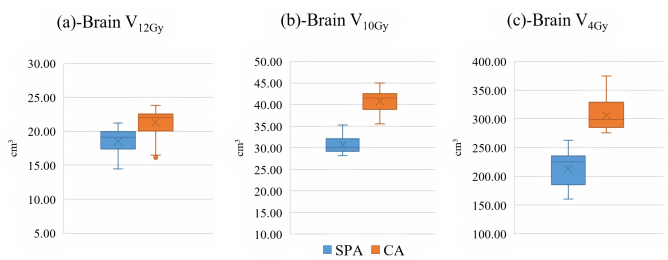

Figure 4. The Box-Whisker Plot of Brain (V12Gy, V10Gy and V4Gy = cm3) according to SPA and CA techniques.

Treatment Planning

Conventional Arc (CA) technique of VMAT

All plans of each cases were designed with the collapse cone convolution (CCC) algorithm of the Philips Pinnacle Therapy Planning System (TPS) 9.10 (Philips Medical Systems Inc., Cleveland, OH) according to Varian TrueBeam having a "high resolution" 120-sheet multi-leaf collimator (HD MLC). Treatment head of the TrueBeam Linac with HD MLC is equipped with two banks of 60 tungsten leaves which are 15 cm long (at isocenter), so two opposite MLC leaves, moving parallel to the x-jaws, can only cover up to maximum 30 cm of the field during delivery. Therefore, this leaf length of HD MLC limits the field width sizes of the VMAT fields, the x-jaw aperture. Field width sizes of the arcs also include different margins such as penumbra, set-up errors. Plans having CA technique were generated with four arcs having the same isocenter rotating clockwise and counter clockwise starting from 182° and 178°, respectively with used automatic field width size to cover all PTV according to the standard approach of our clinical practice. Field width sizes of the arcs also include different margins such as penumbra, set-up errors. Multiple control points for each arc that provide dose distribution in the brain with gantry rate, dose rate, total delivery time, and leaf movement rates, were created using algorithm during optimization. The objectives/constraints on Pinnacle TPS during the optimization in order to coverage and sparing of PTV&OAR were used on both techniques of VMAT.

Split-Partial Arc (SPA) technique of VMAT

SPA technique was based on the use of split-partial arcs having half field width size according to localization of PTVs on brain during optimized in Pinnacle TPS. In this technique, the arcs having field width size to cover all PTV for CA technique were manually re-adjusted. Half field plans, which were call SPA technique in this study, were generated from full field plans by blocking half of the fields. To get half-blocked fields, one of x-jaw was closed at the center of the field. The same x-jaw was blocked whenever possible to avoid high and low dose regions at the junctions. Half-blocked fields have reduced field widths; therefore, MLC leaves travel shorter distance and reach higher modulation capability. SPA technique benefits from the advantages of moving MLC with less geometric limitation on half blocked fields. The SPA technique has the same gantry rotation direction and the same number of arcs as CA technique, except for the width of the arc areas. Digitally reconstructed radiography (DRR) images reconstruction of the concept of conventional arcs and split partial arcs with a start of 182° and 178° beam's eye view (BEV) were shown detailed in Figure 1.

Plan comparison

Plan quality parameters were calculated by Pinnacle TPS for all plans made using both techniques, and doses of the brain were measured from dose-volume histogram (DVH) analysis. For values in volume of healthy brain without gross tumor volumes receiving more than low brain dose 4 Gy (V_{4Gy}), medium brain dose 10 Gy (V_{10Gy}), and high brain dose 12 Gy (V_{12Gy}), were determined by analysis of DVH. For plan quality parameters, values of PTV, mean dose (D_{mean}), maximum dose as $D_{98\%}$, minimum dose as $D_{2\%}$, conformality index (CI = V_{Rx} / V_{PTV}, as V_{RX}, RX is the volume of PTV covered by the prescription isodose line and VPTV is the volume of the PTV) and Gradient Index (GI = $V_{50\%Rx}$ / V_{Rx}, as $V_{50\%Rx}$ is the volume of the 50% of prescription isodose line and V_{PTV} is the volume of the PTV) were compared according to both treatment techniques.

Statistical analysis

In this study, there was not performed specific calculations for the sample size because of retrospectively analyzed dosimetric data using the two-tailed double-wise Wilcoxon signed sequential test of SPSS version 23.0 (IBM SPSS Statistics for Windows, IBMCorp Version 23.0. Armonk, NY), assuming a p value of <0.05 to indicate statistically significant differences. There was included the first 28 patients of brain metastases with a target volume of less than average of 8 cc. Comparison of an example patient according to SPA and CA techniques with different dose distributions in axial, sagittal and coronal sections is shown in Figure 2.

Results

CI, GI and values of all PTVs coverage as D_{Mean}, $D_{\%98}$ and $D_{\%2}$, are detailed with compared to both techniques in Table 2. While comparison of treatment effects, the mean value of CI was 0.84 ± 0.19 in SPA technique whereas this was 0.85 ± 0.29 in CA technique. The mean value of CI was found to be similar for both techniques ($p = 0.289$). The mean values of GI in SPA technique were 3.62 ± 0.41 and in CA technique 4.32 ± 1.24. These values were also found to be lower in SPA ($p<0.001$). The mean values of GI in SPA technique were 3.62 ± 0.41 and in CA technique 4.32 ± 1.24. These values were also found to be lower in SPA ($p<0.001$). For SPA and CA techniques, the Bar Plots of Treatment quality indexes (CI, GI) were showed in detailed with Figure 4.

Both techniques were acceptable and reached goal of clinically because of at least 95 % of PTV receiving 95 % of the prescribed dose [18]. Values of the D_{Mean} were found to be 28.42 ± 1.35 and 28.74 ±1.32; values of the $D_{\%98}$ were 27.14 ± 0.81 and 27.05 ± 0.73; values of the $D_{\%2}$ were 33.78 ± 1.62 and 33.82 ± 1.74 in SPA and CA techniques, respectively. These values were not statistically significant while comparison of both techniques (D_{Mean}; $p = 0.429$, $D_{\%98}$; $p = 0.518$, $D_{\%2}$; $p = 0.379$).

As shown details Table 3, all plans having SPA and CA techniques were compared in terms of doses received by the normal brain tissue. The results for the high dose of the brain doses comparison of SPA Brain-V_{12Gy} mean 19.95 ± 10.38 cm3 and CA Brain-V_{12Gy} mean 13.38 ± 11.06 cm^3 volumes, for the middle brain doses comparison of SPA Brain-V_{10Gy} mean 32.62 ± 13.54 cm^3 and CA Brain-V_{10Gy} mean 42.31 ±14.07 cm^3 volumes and for the low brain doses comparison of SPA Brain-V_{4Gy} mean 215.11± 58.26 cm^3 and CA Brain-V_{4Gy} mean 308.80 ±79.11 cm^3 volumes statistically significantly different ($p=0.022$, $p=0.012$, $p<.001$, respectively).

Discussion

Stereotactic treatment of BM in Linac can perform with wide variety techniques such as dynamic arc, static arc, and fixed gantry 3DCRT, IMRT or VMAT [19, 20]. Nowadays, the most preferred treatment technique in Linac stereotactic treatments is the VMAT technique [13]. VMAT is basically a rotational delivery technique in which MLC shapes are optimized to create effective dose distribution with synchronization of dose rate and gantry rotation speed [16]. Geometric and physical limitations of the machine such as gantry rotation speed, dose rate variation and maximum leaf speed are directly taken into account in the optimization process that creates dose distribution in VMAT plans. Geometric and physical limitations of the machine such as gantry rotation speed, dose rate variation and maximum leaf speed are directly taken into account in the optimization process that creates dose distribution in

Table 1. Patient's characteristics.

Gender	
Male	15
Female	13
Location	
Left temporal lobe	5
Right temporal lobe	6
Left occibital lobe	4
Right occibital lobe	4
Left parietal lobe	4
Right parietal lobe	5
Mean GTV (cc)	3.882
Range	5.04-2.01
Mean PTV (cc)	8.12
Range	12.31-5.67

Abbreviations: cc: cubic centimetre-volume, GTV: Gross target volume, PTV: Planning target volume.

Table 2. Descriptive statistics and comparisons according to SPA and CA techniques of VMAT.

SPA	$\bar{x}$±s	Median	CA	$\bar{x}$±s	Median	p-value
SPA_{CI}	0.84±0.19	0.86	CA_{CI}	0.85±0.29	0.85	0.289
SPA_{GI}	3.62±0.41	3.58	CA_{GI}	4.32±1.24	4.19	<.001*
SPA_{Mean}	28.42±1.35	27.28	CA_{Mean}	28.74±1.32	27.41	0.429
$SPA_{D98\%}$	27.14±0.81	26.70	$CA_{D98\%}$	27.05±0.73	26.60	0.518
$SPA_{D2\%}$	33.78±1.62	32.15	$CA_{D2\%}$	33.82±1.74	32.22	0.379

p*<0.001 CA: Conventional arc technique, CI: Conformality Index, D98%: 98% dose of PTV, D2%: 2% dose of PTV, GI :Paddick Gradient Index, SPA: Split-partial arc technique, Mean: mean dose of PTV.

Table 3. Descriptive Statistics and Comparisons of Brain according to SPA and CA techniques.

SPA	$\bar{x}$±s	Median	CA	$\bar{x}$±s	Median	p-value
BRAIN						
$SPA_{V12Gy=cm^3}$	19.95±10.38	18.50	$CA_{V12Gy=cm^3}$	13.38	11.06±21.30	0.022*
$SPA_{V10Gy<1cm^3}$	32.62±13.54	30.71	$CA_{V10Gy<1cm^3}$	42.31	14.07±40.76	0.012*
$SPA_{V4Gy = cm^3}$	215.11±58.26	213.32	$CA_{V4Gy = cm^3}$	308.80	79.11±305.71	<.001**

p*<0.05, p**<0.001 CA: Conventional arc technique, SPA: Split-partial arc technique, Gy: Gray, VxGy: Volume on X% dose.

VMAT plans. However, one of the most important limitations, especially in according to the shape, size and localization of the irradiation targets, is the MLC leaf length & mobility capacity in the irradiation regions. Especially for large irradiation areas such as pelvis, head and neck, and irradiation areas of very small multiple targets, MLC leaf length and mobility are the most important factors that directly affect dose distribution [10, 15-17]. In addition, there has been shown in many studies that the low dose area in surround area may increase in around the target according to other treatment techniques, and to reduce this, hybrid treatments based on combining with different treatment techniques have been proposed. In addition, it has been shown in many studies that the low dose area in surrounding area may increase according to other treatment techniques because of geometric and physical limitations of MLC, and to reduce this, hybrid treatments based on combining with different treatment techniques have been proposed [21, 22]. The results of our study showed that CI and PTV with values suitable for clinical acceptance conditions were similar for BM lesions in SPA and CA techniques. However, the SPA technique revealed that it is lower brain doses (V_{4Gy}, V_{10Gy}, V_{12Gy}) and value of GI compared to the CA technique due to minimize geometric and physical limitations of MLC using a split-partial jaw in the X-direction.

In brain radiotherapy, especially in high fraction dose treatments such as SRT and SRS, studies of healthy brain doses and side effects have been an interesting subject [23-25]. These studies have been emphasized that the main variables affecting the development of radiation necrosis were connected from radiation dose, fraction number and irradiation volume of the brain excluding the target. Maxime Loo et. all. have been reported that the volume of healthy tissue irradiated is a clear prognostic factor for radionecrosis in Stereotactic Radiotherapy for Brain Metastases in spite of more comfortable and safer the use of radiation modalities with increase technical capacity in recent years [23]. Michael T Milano et. all. have been shown that the risk of radionecrosis may be correlated with a function of dose and volume treated. In addition, choosing SRT than SRS was emphasized to decrease the risks of radionecrosis for cases with larger treatment volumes or multiple target volumes [25]. Lawrence et al. have been shown that for single fraction radiosurgery, a clear correlation bring about between the target size in the risk of adverse events regarding effect of radiotherapy [26]. In our study, since the number of multiple brain metastases and the total treatment volume were relatively large, the SRT treatment scheme, which was prescribed a total dose of 27 Gy in 3 fractions, was preferred. We have demonstrated in result of our study, it was better for SPA technique for low (V_{4Gy}), medium (V_{10Gy}), and high (V_{12Gy}) of brain doses because of faster dose fall-off (lower GI) compared to CA technique. Although the "brain volume receiving 12 Gy" in the treatment of SRS is within acceptable limits for both treatment techniques, it has been shown that the SPA technique is superior in cases of multiple and diffuse BM due to the reduction of brain doses.

The difficulty level of SRT or SRS treatments of BM tumors in different localizations of the brain can be divided into two groups; first of the groups could be into plans with distant targets to OARs: OAR non-challenge, second of the groups could be into plans with near targets to OARs: OAR-challenge [27]. If the tumor of BM is OAR non-challenge, it is not necessary to reduce the doses to the specific organ, but the dose spillage, which affects the normal brain parenchyma and may lead to tissue necrosis, should be reduced [27-29]. Whether OAR-challenged or unchallenged group, the content of radiotherapy technique such as isocenter, technique, arc geometry, beam weight and MLC shape selection are of great importance in the planning of BM's SRS/SRT in terms of reducing the dose spillage into the normal brain parenchyma [30-33]. The single isocentric VMAT treatment technique for SRS/SRT has gained popularity due to its rapid and effective treatment as well as its reduction in brain dose of multiple brain metastases [2]. Since our aim in our study was to reduce the dose spillage to the normal brain, a single isocenter four arcs geometry with 27 Gy in 3 fractions was used in all plans. Since our aim in our study was to reduce the dose spillage into the normal brain, single isocentric four arc geometries were used non-coplanar in both treatment techniques. Thus, we tried to reduce the dose taken by the healthy brain outside the target volumes that are far from the OAR in different localizations.

VMAT treatment technique has been the first treatment technique of choice for irradiation of different parts of the body with different treatment protocols, from lung SBRT to brain SRS/SRT and conventional prostate irradiation in recent years [6, 34]. However, it has been emphasized in many studies in the literature that the VMAT technique is not a perfect technique and has limitations of physical and geometric such as MLC speed, gantry speed, and dose rate in order to create an effective dose distribution.[7, 8, 10, 12]. Berat Tugrul Ugurlu et. all., in their study investigated the effect of field width on VMAT plan quality with virtual phantom, emphasized that the quality of the plan in the VMAT technique depends on the field width [15]. In addition, VMAT study performed with the half field technique in the whole pelvic radiation therapy , it was found that the GI values were better with OAR dose preservation in the VMAT plans optimized using the Hyunsoo Jang et all half beam technique [17]. With the SPA technique used in our study, the GI value was reduced by approximately 19% compared to the CA technique, resulting in a faster dose reduction from the target volume outward (values of GI: 3.62 ± 0.41 in SPA, 4.32 ± 1.24 in CA technique; $p<0.001$). This reduced the dose of spillage into the normal brain parenchyma (Table 3). This is mainly due to the additional dose modulation capability without geometric and physical limitations of MLC in the fields having smaller x- jaw apertures during delivery with HD MLC of Truebeam Linac. SPA Techniques in this study uses half-partial fields to reduce the field width of all arcs. In addition, our study was carried out using the Pinnacle treatment planning system on the Truebeam linac HD MLC treatment device. It is possible to work with other TPS on linac systems with different MLC structures.

Limitations

It has some limitations, as it is a retrospective dosimetric study involving a limited number of BM patients. We do not use the flattening filter (FFF) mode photon energy therapy techniques for BM patients as well as other SBRT/SRS treatment areas in our clinic, so our study excludes FFF mode for both techniques. We were unable to customize all of the arc geometry for all cases due to selected tumors away from OARs.

Conclusion

We found that SPA technique having half fields size of the arcs in VMAT can achieve clinically similar PTV quality, sparing brain doses when compared with standard VMAT technique which name is CA technique for tumors with appropriate localization on cranial. SPA technique for SRT treatments of BM is an available alternative to CA technique in this study because of without limited geometric and physical capacities of MLC on half field sizes of arcs. Although we cannot evaluate whether low dose spill area volume has a clinical effect on neurocognitive functions since it is a retrospective study, healthy brain tissue is better for low (40%), medium (25) and high (14%) brain doses due to approximately 19% less GI with new treatment technique approach that can be used in VMAT plans. It can be concluded that since it gives less radiation to the healthy brain, it can reduce toxicity.

Ethics approval

This retrospective study was carried out in The Koç University Committee on Human Research (KUCHR) Ethics Committee approval from the KUCHR (Date: 06.05.2022 No: 2022. 159.IRB1.062).

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