ANTICANCER RESEARCH *41*: 3153-3159 (2021)
doi:10.21873/anticanres.15101

Impact of Multileaf Collimator Width on Dose Distribution in HyperArc Fractionated Stereotactic Irradiation for Multiple (5-10) Brain Metastases

SHINGO OHIRA[1,2], YOSHIHIRO UEDA[1], NAOYUKI KANAYAMA[1], MASARU ISONO[1], SHOKI INUI[1], RIHO KOMIYAMA[1], HAYATE WASHIO[1], MASAYOSHI MIYAZAKI[1], MASAHIKO KOIZUMI[2], TERUKI TESHIMA[1] and KOJI KONISHI[1]

[1]*Department of Radiation Oncology, Osaka International Cancer Institute, Osaka, Japan;*
[2]*Department of Medical Physics and Engineering, Osaka University Graduate School of Medicine, Suita, Japan*

Abstract. *Background/Aim: To assess the impact of the width of multileaf collimator (MLC) on dose distributions on HyperArc fractionated stereotactic irradiation for multiple (5-10) brain metastases. Patients and Methods: Twenty-one HyperArc (HA) plans were generated using the high definition (HD) MLC (2.5 mm) to deliver 30-35 Gy in 3-5 fractions (HA-HD). The HyperArc plans using Millennium (ML) MLC (5 mm) were retrospectively generated (HA-ML) using the same planning parameters with HA-HD. Dosimetric parameters between the planning target volume (PTV) and organs at risk (OARs) were compared. Results: The conformity index was significantly higher ($p<0.0001$) in the HA-HD plans (0.95±0.04) than that in the HA-ML plans (0.92±0.06). The HA-HD provided significantly lower ($p<0.0001$) gradient index (5.6±2.5) than HA-ML (6.2±3.5). For the brainstem and retina (right), a statistically significant difference ($p<0.05$) was observed between the HA-HD (12.8±10.9 and 2.8±1.7 Gy, for brainstem and retina, respectively) and HA-ML (13.6±11.1 and 3.0±1.8 Gy) plans. For the brain tissue, the HA-HD plans statistically significantly reduced dosimetric parameters ($p<0.0001$) in all evaluated dose range (V_{6Gy}-V_{28Gy}). Conclusion: The narrower MLC provided significantly higher conformity, steeper dose gradient, and better normal tissue sparing.*

Owing to the improvement of systemic therapy and the advances in magnetic resonance imaging modality, the incidence of the brain metastases, which can be a direct cause of death, is increasing (1). Whole brain irradiation has been considered to be standard radiotherapy, while, approximately 90% patients showed impairment of one or more neurocognitive tests at baseline (2). The stereotactic irradiation (STI), which delivers high dose radiation in small fractions, is expected to reduce radiation-induced side effect without compromising treatment outcome (3-5). Yamamoto *et al*., showed that the overall survival for patients with 5-10 brain metastases was non-inferior to those with 2-4 brain metastases and they concluded that the STI might be a suitable alternative approach to the whole brain irradiation (6).

The volumetric imaging with the cone-beam computed tomography and the continuous movement of gantry and multileaf collimator (MLC) can achieve the precise and highly conformal STI using the C-arm linear accelerator (7, 8). Because brain metastases are surrounded by normal brain tissues, the rapid dose falloff from the target surface is required for the STI. For multiple brain metastases, the recent advanced treatment approach, named HyperArc, using the C-arm linear accelerator has advantages for of reducing the treatment time and delivering the conformity dose for targets compared with the other treatment units such as GammaKnife and CyberKnife (9-11).

To generate the complicated dose distribution, the width of leaves projected to the isocenter is quite important. Dhabaan *et al*. demonstrated that the narrower width of MLC provided higher conformity dose for targets and lower radiation dose for normal tissues in the dynamic conformal arc therapy for intracranial lesions (12). Similar results were reported by Abisheva *et al*. in volumetric modulated arc therapy (VMAT) for multiple brain metastases (13). Because HyperArc utilized more complex MLC patterns than conventional VMAT to generate the steep dose gradient for multiple targets (9), the narrower MLC has potential for providing the ideal dose distribution.

Correspondence to: Shingo, Ohira, Ph.D., Department of Radiation Oncology, Osaka International Cancer Institute, 3-1-69 Otemae, Chuo-ku, 537-8567 Osaka, Japan. Tel: +81 669451181, Fax: +81 669451900, e-mail: oohira-si@mc.pref.osaka.jp

Key Words: Multilead collimator, MLC, hyperarc, stereotactic irradiation, brain metastases, dose distribution.

The aim of this study was to assess the impact of the width of MLC on the dosimetric parameters for targets and OARs in the HyperArc plans (fractionated STI) for patients with multiple (5-10) brain metastases.

Patients and Methods

Patients and simulation. This retrospective study included twenty-one patients with multiple (5-10) brain metastases who underwent fractionated STI, and was approved by the ethics committee of our institution. Table I lists the patients' characteristics. For simulation, the patient was immobilized using the thermoplastic mask, and was scanned using a dual-energy computed tomography (DECT) system (Revolution HD; GE Medical Systems, Milwaukee, WI, USA). The following scanning parameters were used: tube voltage of 80/140 kVp, tube current of 550-600 mA, gantry rotation speed of 0.8 s/rot, helical pitch of 0.531:1. The virtual monochromatic images (VMIs) at 77 keV were reconstructed with a slice thickness of 1 mm and a field of view of 320 mm.

Treatment planning. The VMIs were loaded into a treatment planning system (Eclipse, version 15.6; Varian Medical Systems, Palo Alto, CA, USA). Gross tumor volume (GTV) was delineated referring to a T1-weighted magnetic resonance image (slice thickness of 1 mm) with contrast enhanced medium (gadolinium). A planning target volume was formed by adding a 1 mm isotropic margin to the GTV. The clinical HyperArc plans were designed based on a TrueBeam STX or Edge linear accelerator equipped with a high-definition MLC with a leaf width of 2.5 mm (HA-HD) (14), and a photon energy of 6X (flattening filtered or flattening filter free) was used. The prescription dose of 30-35 Gy was delivered in 3-5 fractions to cover the 95% volume of the combined PTV. The position of isocenter, collimator angles and non-coplanar beam arrangement were automatically determined. In the optimization process, the inhomogeneity dose within the PTV was allowed and the doses to brain tissue were reduced as low as possible. Optimal resolution of 1.25 mm, dose calculation grid size of 1.25 mm and analytic anisotropic algorithm dose calculation algorithm were used.

Retrospectively, the clinical HyperArc plans (HA-HD) were modified to generate the HyperArc plans using a Millennium MLC with a leaf width of 5 mm (HA-ML) (15). Except for the width of MLC, the same treatment planning parameters (prescription dose, isocenter, collimator angles, optimization parameter, *etc*.) as the HA-HD plans were used for generating the HA-ML.

Data analysis. To assess the impact of MLC width on dose distributions, dosimetric parameters for the targets and organs at risk (OARs) between the HA-HD and HA-ML were compared. The conformity index (CI) was defined as follows: $CI=TV_{pr}/BV_{pr}$, where TV_{pr} and BV_{pr} indicate the volume of the target and body covered by the prescription dose, respectively (16). The gradient index (GI) was calculated as: $GI=BV_{50\%}/BV_{pr}$, where $BV_{50\%}$ represents the volume of 50% of the prescription isodose. The homogeneity index (HI) was calculated as: D_{max}/D_{pr}, where respective Dmax and Dpr denote the maximum dose and prescribed dose (17). For OARs (brainstem, optic chiasm, optic nerves, retinas and lens), the D_{max} was assessed. For brain tissue excluding the PTV, the volumes receiving a specific dose ranging from 6 Gy to 28 Gy (V_{6Gy}-V_{28Gy}), in 2 Gy increments, were evaluated. Subsequently, differences in dosimetric parameters for brain tissue were calculated for each patient.

Table I. *Patient characteristics*.

Number of patients, n	21
Male/female, n	11/10
Age [median (range)], years	68 (28-84)
Number of metastases (5/6/7/8/9/10), n	3/3/8/1/1/5
Treatment plan	
Prescription dose (30/35 Gy), n	10/11
Number of fractions (3/5 fractions), n	9/12
Beam energy (6X, 6X-FFF), n	5/16
Total PTV volume [median (range)], ml	5.3 (0.7-22.4)

PTV: Planning target volume; FFF: flattening filter free.

The dosimetric parameters for the PTV and OARs between the HA-HD and HA-ML were compared using the paired Wilcoxon' signed-rank test (SPSS, version 27; IBM, Armonk, NY, USA). A value of $p<0.05$ was considered to be statistically significant.

Results

The direct comparison of the physical characteristics of the individual treatment plans between the HA-HD and HA-ML are shown in Figure 1. The CI was statistically significantly higher ($p<0.0001$) in the HA-HD plans (0.95±0.04) than that in the HA-ML plans (0.92±0.06). Moreover, the HA-HD provided a statistically significantly lower ($p<0.0001$) GI (5.6±2.5) than HA-ML (6.2±3.5), which indicated that a steeper dose gradient was generated in the HA-HD plans. The comparable HI (1.7±0.3 *vs*. 1.7±0.2 for HA-HD and HA-ML plans, respectively, $p=0.54$) and MU (4,735±1,203 *vs*. 4,715 ±1,390 MU, $p=0.77$) were obtained between the two treatment planning approaches.

Figure 2 illustrates the comparison of the dose distributions between the HA-HD and HA-ML plans for patients #4, 14, and 21. HA-HD provided complicated shape of dose distribution, and the dose bridge in the 10-20 Gy isodose line was reduced (arrow). Table II summarizes the dosimetric parameters for the PTV and OARs. The dosimetric parameters for the PTV were comparable ($p>0.1$) between the HA-HD (54.8±11.3, 40.0±4.5 and 28.1±2.8 Gy for D_{max}, D_{mean} and D_{min}, respectively) and HA-ML (54.8±10.2, 40.2±4.3 and 27.9±2.6 Gy) plans. For the brainstem and retina (right), a statistically significant difference ($p<0.05$) was observed between the HA-HD (12.8±10.9 and 2.8±1.7 Gy, for brainstem and retina, respectively) and HA-ML (13.6±11.1 and 3.0±1.8 Gy) plans. The dosimetric parameters were comparable ($p>0.05$) for the optic chiasma, optic nerves, retina (left) and lens. For the brain tissue, the HA-HD plans statistically significantly reduced dosimetric parameters ($p<0.0001$) in all evaluated dose ranges (V_{6Gy}-V_{28Gy}). Figure

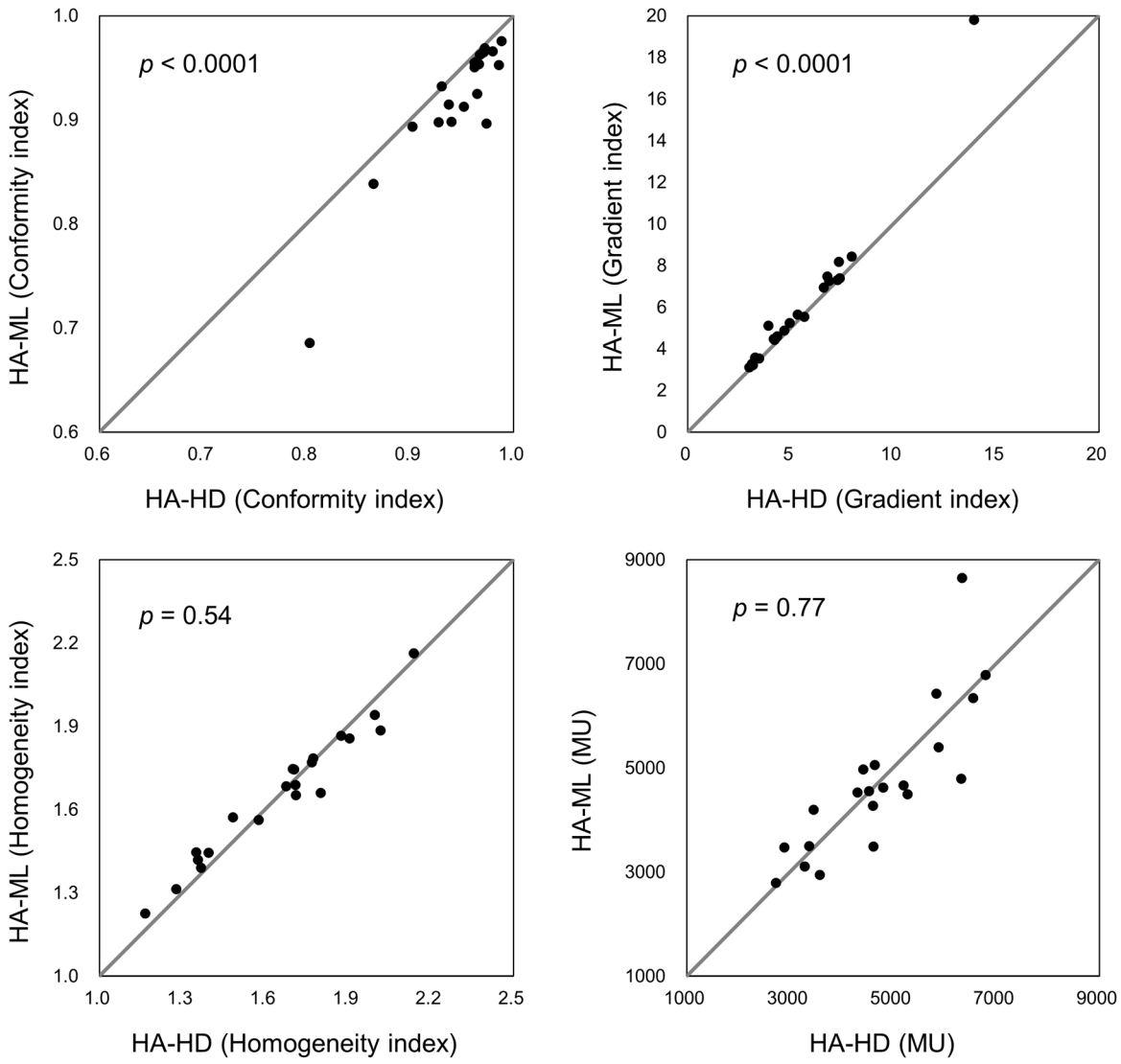

Figure 1. *Direct comparison of the physical characteristics of the individual treatment plans between HyperArc (HA) plans using the High definition (HA-HD) multileaf collimator (MLC) and Millennium (HA-ML) MLC.*

3 shows the differences in dosimetric parameters for brain tissue in each patient. For almost all cases, the narrower MLC resulted in better brain tissue sparing in all evaluated ranges. The differences in V_{10Gy} and V_{20Gy} were 10.8±11.2 and 1.8±2.6 ml, respectively.

Discussion

This study clearly demonstrated the impact of the width of MLC on dose distributions in fractionated STI using HyperArc for patients with multiple brain metastases. Because the thermoplastic mask is generally used for patient immobilization with the acceptable intra-fractional setup errors during the STI dose delivery using the C-arm linear accelerator, the dose fractionation can be performed easier than the invasive frame-based immobilization (18). The radiobiological advantage of the fractionated STI over the single fraction STI is that the dose fractionation may reduce the side-effects on normal tissue while maintaining tumor control (19). For large brain metastases (>2 cm), Minniti *et al*. reported that the 1-year cumulative local control rate was 77% in the single fraction STI (20% of patients experienced radionecrosis) while the local control rate was 91% in the fractionated STI (8% experienced radionecrosis) (20). Moreover, Lucia *et al*. demonstrated that the inhomogeneous dose distribution within the tumor in the fractionated STI

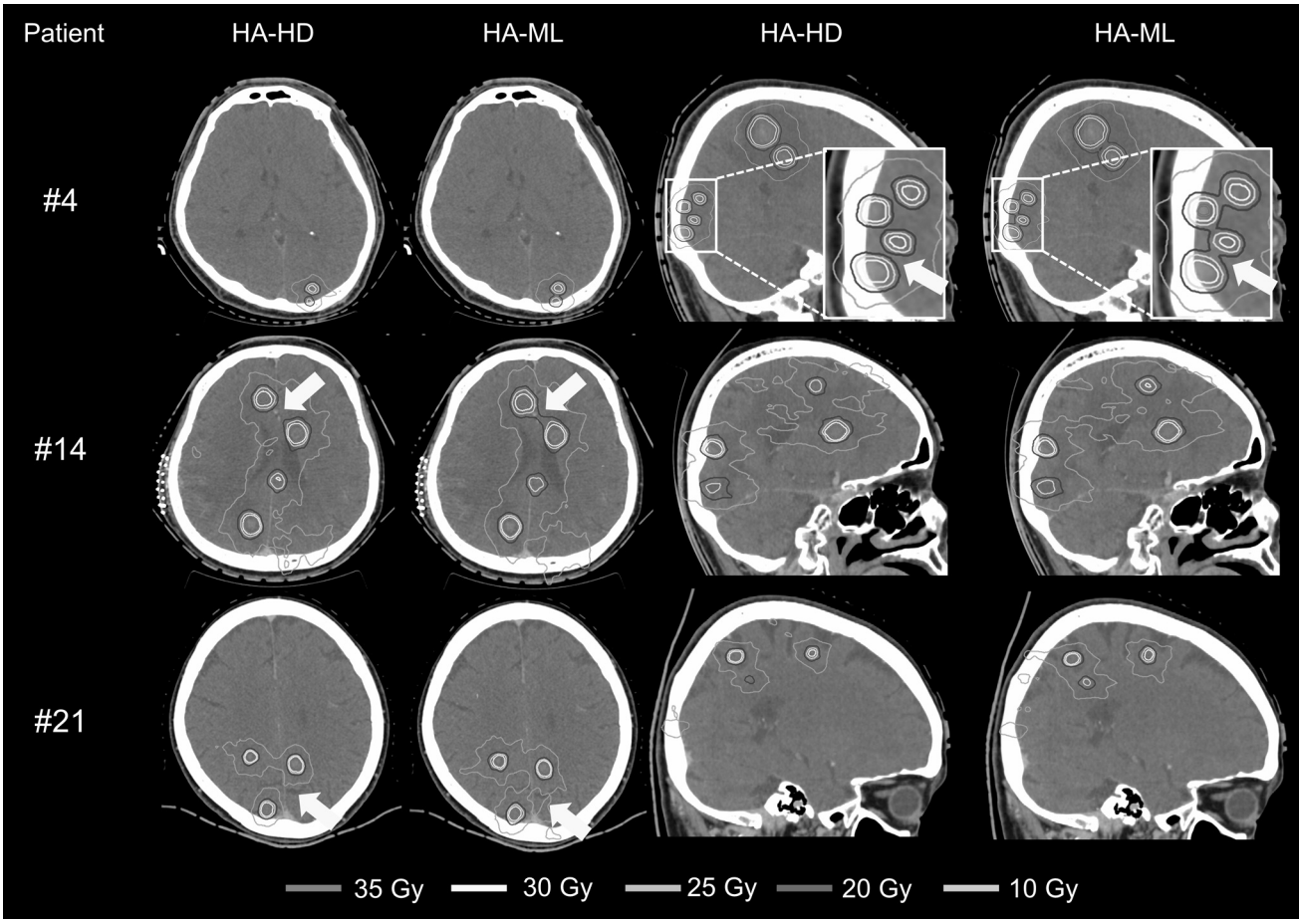

Figure 2. *Comparison of dose distributions between the HyperArc (HA) plans using the High definition (HD) multileaf collimator and Millennium (ML) multileaf collimator plans for patients #4, 14, and 21.*

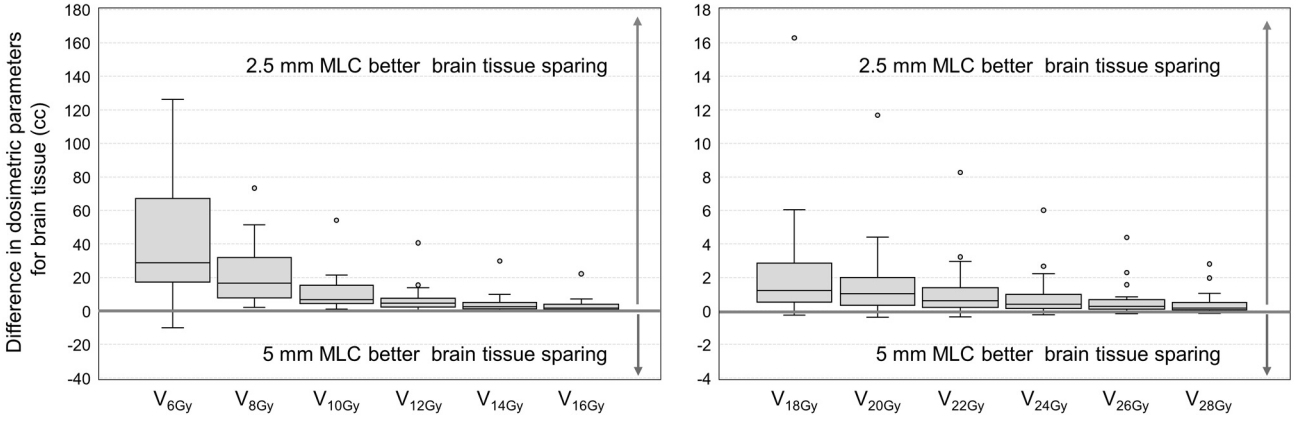

Figure 3. *Box plots of differences in dosimetric parameters between the HyperArc-high definition (HA-HD) and HyperArc-Millennium (HA-ML) plans for brain tissue. Boxes: median value, and upper and lower quartiles; Whiskers: maximum and minimum values within a 1.5× inter-quartile range; Dots: outliers located outside the whiskers.*

Table II. *Comparison of dosimetric parameters for PTV and OARs.*

Structure	Dosimetric parameter	HA-HD		HA-ML		*p*-Value
		Mean	SD	Mean	SD	
PTV	D_{max} (Gy)	54.8	11.3	54.8	10.2	0.59
	D_{mean} (Gy)	40.0	4.5	40.2	4.3	0.14
	D_{min} (Gy)	28.1	2.8	27.9	2.6	0.46
Brainstem	D_{max} (Gy)	12.8	10.9	13.6	11.1	0.001
Optic chiasma	D_{max} (Gy)	4.5	2.2	4.8	2.4	0.11
Optic nerve left	D_{max} (Gy)	3.5	1.8	3.6	1.9	0.31
Optic nerve right	D_{max} (Gy)	3.6	1.9	3.8	2.0	0.23
Retina left	D_{max} (Gy)	2.5	1.3	2.6	1.2	0.77
Retina right	D_{max} (Gy)	2.8	1.7	3.0	1.8	0.013
Lens left	D_{max} (Gy)	1.6	0.9	1.5	0.9	0.52
Lens right	D_{max} (Gy)	1.7	1.1	1.8	1.3	0.31
Brain	V_{28Gy} (ml)	3.8	4.1	4.2	4.3	<0.0001
	V_{26Gy} (ml)	5.6	5.1	6.3	5.6	<0.0001
	V_{24Gy} (ml)	7.9	6.7	8.8	7.4	<0.0001
	V_{22Gy} (ml)	10.7	8.9	11.9	9.8	<0.0001
	V_{20Gy} (ml)	14.4	11.9	16.2	13.2	<0.0001
	V_{18Gy} (ml)	19.4	16.2	21.9	17.9	<0.0001
	V_{16Gy} (ml)	26.6	22.5	29.9	24.8	<0.0001
	V_{14Gy} (ml)	37.3	32.1	41.9	35.1	<0.0001
	V_{12Gy} (ml)	54.4	48.0	61.3	52.4	<0.0001
	V_{10Gy} (ml)	85.8	79.7	96.6	84.5	<0.0001
	V_{8Gy} (ml)	150.5	140.7	171.6	145.5	<0.0001
	V_{6Gy} (ml)	300.0	240.8	345.3	251.5	<0.0001

PTV: Planning target volume; OARs: organs at risk; HA-HD: HyperArc-high definition; HA-ML HyperArc-Millennium.

resulted in better local control and lower risk of radionecrosis compared to homogeneous distribution (21).

The quality of dose distribution depends on the characteristics of the MLCs, and there are commercially available MLCs (leaf width of 2.5-10 mm) developed by the various vendors with specific design characteristics (22-26). Lafond *et al*. compared the dose distributions in VMAT plans generated using 10 mm MLC with those using 4 mm MLCs for patients with head and neck cancers (27). In that report, both MLCs achieved satisfactory dose distributions for complex target, while, the 4 mm MLC provided the better dose sparing especially for the brainstem and spinal cord. Moreover, Park *et al*. simulated the extremely narrow MLC (1.25 mm) in the VMAT plans for patients with prostate cancer, and treatment plans using the 1.25 mm MLC provided better dose homogeneity inside the target volume, better target conformity and less dose to normal tissue near the target volume than those using 2.5 mm MLC (28). These facts imply that a narrower MLC is suitable for generating the ideal dose distributions in the VMAT plans.

Historically, the STI for brain metastasis (single isocenter for single target) was performed using multiple static/arc conformal beams using the C-arm linear accelerator, and the narrower MLC could adjust the leaf aperture to the shape of the PTV in the beam's-eye view resulting in better PTV conformity and surrounding tissue sparing (29, 30). Recent advances in the irradiation techniques such as VMAT allows simultaneous irradiation of multiple brain metastases, and is increasingly introduced in clinical practice owing to the acceptable target conformity and tissue sparing with its short treatment time (31). The HyperArc plan is one of the most complex irradiation techniques (non-coplanar irradiation, complex MLC movement and so on) in modern radiotherapy, and the HyperArc plans provides significantly higher conformity and rapid dose falloff with respect to the conventional VMAT plans (9). In this study, we firstly demonstrated that the width of MLC had significant impact on dose distributions in HyperArc plans, and narrower MLC could generate better treatment plan quality. In this regard, the narrower MLC is supposed to be better for tumor fitting in adjacent targets resulting in less dose bridge (Figure 2). Regarding radiation necrosis after the fractionated STI (three and five fractions), Inoue *et al*. reported that the dosimetric parameter of V_{14Gy} for the brain tissue could be a useful indicator for the risk evaluation of radiation necrosis (32, 33). In the report by Minniti *et al*., V_{18Gy} and V_{21Gy} were the most predictive independent risk factors for radiation necrosis in the fractionated STI (three fractions) (34). Because the

HA-HD significantly reduced doses to brain tissue in the range from V_{6Gy} to V_{28Gy} (Table II), the narrower MLC might be suitable for HyperArc planning for multiple brain metastases to minimize radiation-induced side effects.

Several limitations of this study warrant mention. First, although the brain metastases occur at various sites in the brain and vary enormously in size, in depth analysis of the effect of tumor size and distance between the metastases on dose distributions was not performed in this study due to the limited number of patients. Second, the same optimization parameters between the HA-HD (clinical plan) and HA-ML were used in this study, whereas better HA-ML plans might be generated using different optimization parameters. Finally, the impact of the width of MLC was assessed in patients with 5-10 brain metastases in this study, whereas in clinical practice, more than 10 brain metastases can be treated with the C-arm. Despite these limitations, our quantitative data can provide useful information for selecting the suitable treatment machine for patients with multiple brain metastases.

In conclusion, our results demonstrated that the HA-HD (2.5 mm MLC) provided significantly better tumor conformity (CI) and steeper dose gradient (GI) than those in the HA-ML plans (5 mm MLC). Moreover, doses for normal brain tissue were significantly reduced by using the narrower MLC.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

Authors' Contributions

All the Authors participated in the writing this article and take responsibility for its content. The Authors confirm that the content of the manuscript has not been published, or submitted for publication elsewhere.

Acknowledgements

This study was supported by JSPS KAKENHI Grant (Grant-in-Aid for Scientific Research (C) 21K07742).

References

1 Soffietti R, Rudā R and Mutani R: Management of brain metastases. J Neurol *249(10)*: 1357-1369, 2002. PMID: 12382150. DOI: 10.1007/s00415-002-0870-6

2 Meyers CA, Smith JA, Bezjak A, Mehta MP, Liebmann J, Illidge T, Kunkler I, Caudrelier JM, Eisenberg PD, Meerwaldt J, Siemers R, Carrie C, Gaspar LE, Curran W, Phan SC, Miller RA and Renschler MF: Neurocognitive function and progression in patients with brain metastases treated with whole-brain radiation and motexafin gadolinium: results of a randomized phase III trial. J Clin Oncol *22(1)*: 157-165, 2004. PMID: 14701778. DOI: 10.1200/JCO.2004.05.128

3 Chang EL, Wefel JS, Hess KR, Allen PK, Lang FF, Kornguth DG, Arbuckle RB, Swint JM, Shiu AS, Maor MH and Meyers CA: Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: a randomised controlled trial. Lancet Oncol *10(11)*: 1037-1044, 2009. PMID: 19801201. DOI: 10.1016/S1470-2045(09)70263-3

4 Sperduto PW, Yang TJ, Beal K, Pan H, Brown PD, Bangdiwala A, Shanley R, Yeh N, Gaspar LE, Braunstein S, Sneed P, Boyle J, Kirkpatrick JP, Mak KS, Shih HA, Engelman A, Roberge D, Arvold ND, Alexander B, Awad MM, Contessa J, Chiang V, Hardie J, Ma D, Lou E, Sperduto W and Mehta MP: Estimating survival in patients with lung cancer and brain metastases: an update of the graded prognostic assessment for lung cancer using molecular markers (Lung-molGPA). JAMA Oncol *3(6)*: 827-831, 2017. PMID: 27892978. DOI: 10.1001/jamaoncol.2016.3834

5 Brown PD, Jaeckle K, Ballman KV, Farace E, Cerhan JH, Anderson SK, Carrero XW, Barker FG 2nd, Deming R, Burri SH, Ménard C, Chung C, Stieber VW, Pollock BE, Galanis E, Buckner JC and Asher AL: Effect of radiosurgery alone vs radiosurgery with whole brain radiation therapy on cognitive function in patients with 1 to 3 brain metastases: a randomized clinical trial. JAMA *316(4)*: 401-409, 2016. PMID: 27458945. DOI: 10.1001/jama.2016.9839

6 Yamamoto M, Serizawa T, Shuto T, Akabane A, Higuchi Y, Kawagishi J, Yamanaka K, Sato Y, Jokura H, Yomo S, Nagano O, Kenai H, Moriki A, Suzuki S, Kida Y, Iwai Y, Hayashi M, Onishi H, Gondo M, Sato M, Akimitsu T, Kubo K, Kikuchi Y, Shibasaki T, Goto T, Takanashi M, Mori Y, Takakura K, Saeki N, Kunieda E, Aoyama H, Momoshima S and Tsuchiya K: Stereotactic radiosurgery for patients with multiple brain metastases (JLGK0901): a multi-institutional prospective observational study. Lancet Oncol *15(4)*: 387-395, 2014. PMID: 24621620. DOI: 10.1016/S1470-2045(14)70061-0

7 Ruggieri R, Naccarato S, Mazzola R, Ricchetti F, Corradini S, Fiorentino A and Alongi F: Linac-based VMAT radiosurgery for multiple brain lesions: comparison between a conventional multi-isocenter approach and a new dedicated mono-isocenter technique. Radiat Oncol *13(1)*: 38, 2018. PMID: 29506539. DOI: 10.1186/s13014-018-0985-2

8 Hartgerink D, Swinnen A, Roberge D, Nichol A, Zygmanski P, Yin FF, Deblois F, Hurkmans C, Ong CL, Bruynzeel A, Aizer A, Fiveash J, Kirckpatrick J, Guckenberger M, Andratschke N, de Ruysscher D, Popple R and Zindler J: LINAC based stereotactic radiosurgery for multiple brain metastases: guidance for clinical implementation. Acta Oncol *58(9)*: 1275-1282, 2019. PMID: 31257960. DOI: 10.1080/0284186X.2019.1633016

9 Ohira S, Ueda Y, Akino Y, Hashimoto M, Masaoka A, Hirata T, Miyazaki M, Koizumi M and Teshima T: HyperArc VMAT planning for single and multiple brain metastases stereotactic radiosurgery: a new treatment planning approach. Radiat Oncol *13(1)*: 13, 2018. PMID: 29378610. DOI: 10.1186/s13014-017-0948-z

10 Ueda Y, Ohira S, Yamazaki H, Mabuchi N, Higashinaka N, Miyazaki M and Teshima T: Dosimetric performance of two linear accelerator-based radiosurgery systems to treat single and multiplebrain metastases. Br J Radiol *92(1100)*: 20190004, 2019. PMID: 31188018. DOI: 10.1259/bjr.20190004

11 Vergalasova I, Liu H, Alonso-Basanta M, Dong L, Li J, Nie K, Shi W, Teo BK, Yu Y, Yue NJ, Zou W and Li T: Multi-institutional dosimetric evaluation of modern day stereotactic radiosurgery (SRS) treatment options for multiple brain

metastases. Front Oncol *9*: 483, 2019. PMID: 31231614. DOI: 10.3389/fonc.2019.00483

12 Dhabaan A, Elder E, Schreibmann E, Crocker I, Curran WJ, Oyesiku NM, Shu HK and Fox T: Dosimetric performance of the new high-definition multileaf collimator for intracranial stereotactic radiosurgery. J Appl Clin Med Phys *11(3)*: 3040, 2010. PMID: 20717077. DOI: 10.1120/jacmp.v11i3.3040

13 Abisheva Z, Floyd SR, Salama JK, Kirkpatrick J, Yin FF, Moravan MJ, Giles W and Adamson J: The effect of MLC leaf width in single-isocenter multi-target radiosurgery with volumetric modulated arc therapy. J Radiosurg SBRT *6(2)*: 131-138, 2019. PMID: 31641549.

14 Borges C, Zarza-Moreno M, Heath E, Teixeira N and Vaz P: Monte Carlo modeling and simulations of the High Definition (HD120) micro MLC and validation against measurements for a 6 MV beam. Med Phys *39(1)*: 415-423, 2012. PMID: 22225311. DOI: 10.1118/1.3671935

15 Jang SY, Vassiliev ON, Liu HH, Mohan R and Siebers JV: Development and commissioning of a multileaf collimator model in monte carlo dose calculations for intensity-modulated radiation therapy. Med Phys *33(3)*: 770-781, 2006. PMID: 16878579. DOI: 10.1118/1.2170598

16 Feuvret L, Noël G, Mazeron JJ and Bey P: Conformity index: A review. Int J Radiat Oncol Biol Phys 64: 333–342, 2006. PMID: 16414369. DOI: 10.1016/j.ijrobp.2005.09.028

17 Shaw E, Kline R, Gillin M, Souhami L, Hirschfeld A, Dinapoli R and Martin L: Radiation Therapy Oncology Group: radiosurgery quality assurance guidelines. Int J Radiat Oncol Biol Phys *27(5)*: 1231-1239, 1993. PMID: 8262852. DOI: 10.1016/0360-3016(93)90548-a

18 Carminucci A, Nie K, Weiner J, Hargreaves E and Danish SF: Assessment of motion error for frame-based and noninvasive mask-based fixation using the Leksell Gamma Knife Icon radiosurgery system. J Neurosurg *129(Suppl1)*: 133-139, 2018. PMID: 30544303. DOI: 10.3171/2018.7.GKS181516

19 Marcrom SR, McDonald AM, Thompson JW, Popple RA, Riley KO, Markert JM, Willey CD, Bredel M and Fiveash JB: Fractionated stereotactic radiation therapy for intact brain metastases. Adv Radiat Oncol *2(4)*: 564-571, 2017. PMID: 29204523. DOI: 10.1016/j.adro.2017.07.006

20 Minniti G, Scaringi C, Paolini S, Lanzetta G, Romano A, Cicone F, Osti M, Enrici RM and Esposito V: Single-fraction versus multifraction (3 × 9 Gy) stereotactic radiosurgery for large (>2 cm) brain metastases: a comparative analysis of local control and risk of radiation-induced brain necrosis. Int J Radiat Oncol Biol Phys *95(4)*: 1142-1148, 2016. PMID: 27209508. DOI: 10.1016/j.ijrobp.2016.03.013

21 Lucia F, Key S, Dissaux G, Goasduff G, Lucia AS, Ollivier L, Pradier O and Schick U: Inhomogeneous tumor dose distribution provides better local control than homogeneous distribution in stereotactic radiotherapy for brain metastases. Radiother Oncol *130*: 132-138, 2019. PMID: 30017105. DOI: 10.1016/j.radonc.2018.06.039

22 Tacke MB, Nill S, Häring P and Oelfke U: 6 MV dosimetric characterization of the 160 MLC, the new Siemens multileaf collimator. Med Phys *35(5)*: 1634-1642, 2008. PMID: 18561638. DOI: 10.1118/1.2889782

23 Van de Walle J, Martens C, Reynaert N, Palmans H, Coghe M, De Neve W, De Wagter C and Thierens H: Monte Carlo model of the Elekta SLiplus accelerator: validation of a new MLC component module in BEAM for a 6 MV beam. Phys Med Biol *48(3)*: 371-385, 2003. PMID: 12608613. DOI: 10.1088/0031-9155/48/3/307

24 Belec J, Patrocinio H and Verhaegen F: Development of a Monte Carlo model for the Brainlab microMLC. Phys Med Biol *50(5)*: 787-799, 2005. PMID: 15798255. DOI: 10.1088/0031-9155/50/5/005

25 Ohira S, Takegawa H, Miyazaki M, Koizumi M and Teshima T: Monte Carlo modeling of the agility MLC for IMRT and VMAT calculations. In Vivo *34(5)*: 2371-2380, 2020. PMID: 32871762. DOI: 10.21873/invivo.12050

26 Vazquez-Quino LA, Massingill B, Shi C, Gutierrez A, Esquivel C, Eng T, Papanikolaou N and Stathakis S: Monte Carlo modeling of a Novalis Tx Varian 6 MV with HD-120 multileaf collimator. J Appl Clin Med Phys *13(5)*: 3960, 2012. PMID: 22955663. DOI: 10.1120/jacmp.v13i5.3960

27 Lafond C, Chajon E, Devillers A, Louvel G, Toublanc S, Olivier M, Simon A, De Crevoisier R and Manens JP: Impact of MLC leaf width on volumetric-modulated arc therapy planning for head and neck cancers. J Appl Clin Med Phys *14(6)*: 4074, 2013. PMID: 24257269. DOI: 10.1120/jacmp.v14i6.4074

28 Park JM, Park SY, Kim JH, Carlson J and Kim JI: The effect of extremely narrow MLC leaf width on the plan quality of VMAT for prostate cancer. Radiat Oncol *11*: 85, 2016. PMID: 27338929. DOI: 10.1186/s13014-016-0664-0

29 Monk JE, Perks JR, Doughty D and Plowman PN: Comparison of a micro-multileaf collimator with a 5-mm-leaf-width collimator for intracranial stereotactic radiotherapy. Int J Radiat Oncol Biol Phys *57(5)*: 1443-1449, 2003. PMID: 14630284. DOI: 10.1016/s0360-3016(03)01579-7

30 Tanyi JA, Kato CM, Chen Y, Chen Z and Fuss M: Impact of the high-definition multileaf collimator on linear accelerator-based intracranial stereotactic radiosurgery. Br J Radiol *84(1003)*: 629-638, 2011. PMID: 20923911. DOI: 10.1259/bjr/19726857

31 Wolff HA, Wagner DM, Christiansen H, Hess CF and Vorwerk H: Single fraction radiosurgery using Rapid Arc for treatment of intracranial targets. Radiat Oncol *5*: 77, 2010. PMID: 20836871. DOI: 10.1186/1748-717X-5-77

32 Inoue HK, Seto K, Nozaki A, Torikai K, Suzuki Y, Saitoh J, Noda SE and Nakano T: Three-fraction CyberKnife radiotherapy for brain metastases in critical areas: referring to the risk evaluating radiation necrosis and the surrounding brain volumes circumscribed with a single dose equivalence of 14 Gy (V14). J Radiat Res *54(4)*: 727-735, 2013. PMID: 23404206. DOI: 10.1093/jrr/rrt006

33 Inoue HK, Sato H, Seto K, Torikai K, Suzuki Y, Saitoh J, Noda SE and Nakano T: Five-fraction CyberKnife radiotherapy for large brain metastases in critical areas: impact on the surrounding brain volumes circumscribed with a single dose equivalent of 14 Gy (V14) to avoid radiation necrosis. J Radiat Res *55(2)*: 334-342, 2014. PMID: 24187332. DOI: 10.1093/jrr/rrt127

34 Minniti G, D'Angelillo RM, Scaringi C, Trodella LE, Clarke E, Matteucci P, Osti MF, Ramella S, Enrici RM and Trodella L: Fractionated stereotactic radiosurgery for patients with brain metastases. J Neurooncol *117(2)*: 295-301, 2014. PMID: 24488446. DOI: 10.1007/s11060-014-1388-3

Received April 13, 2021
Revised May 4, 2021
Accepted May 5, 2021