CASE REPORT

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Craniospinal Irradiation in Adult Medulloblastoma: A Case Report and Analysis of Treatment Planning Comparing Volumetric Modulated Arc Therapy and Three-Dimensional Conformal Radiotherapy

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ABSTRACT

Introduction: Adult medulloblastoma is a very uncommon case. Multimodal treatment, including surgery, radiation therapy, and chemotherapy, has led to an improvement not only in long-term survival but also in major-related toxicity.

Case Presentation: We report the case of a 24-year-old man with medulloblastoma who underwent surgery followed by volumetric modulated arc therapy (VMAT) craniospinal irradiation (CSI) three weeks after resection. The radiation dose was 36 Gy in 20 fractions to the craniospinal axis, with an 18 Gy boost dose in 10 fractions to the posterior fossa. Three-dimensional conformal radiotherapy (3D-CRT) planning was done to compare the dosimetric results of VMAT and 3D-CRT.

Conclusion: The VMAT CSI technique delivers a better dose of homogeneity, conformity, and OARs-sparing than 3D-CRT.

INTRODUCTION

Medulloblastoma is the most common and aggressive embryonal tumor originating from the posterior cranial fossa and spreading through the cerebrospinal fluid [1–3]. The tumor has a preferential manifestation in young children. The incidence of medulloblastoma in post-pubertal patients and adults or the elderly is rare, accounting for less than 1% of adult central nervous system tumors, with an incidence rate of about 0.5 per million [4–6].

Based on the 2021 World Health Organization Classification of Central Nervous System Tumors (WHO CNS5), medulloblastoma is molecularly classified into four groups: 1) WNT-activated, 2) SHH-activated and TP53 wild type, 3) SHH-activated and TP53 mutant, and 4) non-WNT/non-SHH. Histologically, medulloblastoma is divided into four types: 1) classic, 2) desmoplastic/nodular (DN), 3) extensive nodularity (MBEN), and 4) Large Cell/Anaplastic. Those four histological types were classified as "medulloblastoma, histologically defined [7,8]."

The best option for treating medulloblastoma is a combination of multimodal treatment, including maximally safe resection, chemotherapy, and craniospinal irradiation (CSI). With multimodal treatment and appropriate risk stratification, patient survival can increase to 70–80% [7].

Available evidence suggests that maximally safe resection should remain the initial surgical goal. Aggressive resection that is expected to cause high neurological morbidity, for example, if there is damage to the brain stem, is not recommended. Postoperative MRI is recommended within 48 hours to measure the extent of resection, determine residual tumor volume, and obtain baseline imaging for further follow-up. A second operation may be considered if the remaining tumor is more than 1.5 cm² on postoperative imaging [6,9].

Further treatment for both standard-risk and high-risk patients is radiation therapy. Craniospinal irradiation with a booster to the posterior fossa or tumor bed is standard radiation therapy for medulloblastoma. CSI is usually given at full dose (36 Gy) with a booster of 18.8 Gy to the posterior fossa (up to 54–55.8 Gy). In standard-risk adult patients, dose-reducing CSI (23.4 Gy) combined with chemotherapy is still under study. Craniospinal irradiation is recommended starting 3–6 weeks after surgery to obtain better outcomes [6,9].

To date, several radiation techniques have been developed for CSI, including three-dimensional conformal techniques (3D-CRT), Intensity Modulated Radiation Therapy, Volumetric Modulated Arc Therapy (VMAT), helical tomotherapy, and proton beam therapy [10].

Medulloblastoma is a chemosensitive tumor. Adult patients with medulloblastoma should be treated with systemic therapy in addition to resection and radiotherapy. Evidence suggests that adjuvant chemotherapy is associated with improved survival compared to radiation alone in high-risk patients. In standard-risk patients, the meta-analysis results showed that chemotherapy (neo- or adjuvant) given as first-line significantly improved survival and the chances of long-term survival [6,9].

This report presents a case of a 24-year-old man with a right cerebellopontine mass diagnosed as medulloblastoma based on histopathological and immunohistochemical examinations. It was the first adult medulloblastoma patient treated with the VMAT technique at Mochtar Riyadi Comprehensive Cancer Center (MRCCC) Siloam Hospital. VMAT is one of the advanced techniques in radiotherapy, while 3D-CRT is a conventional one that is still widely used, especially in Indonesia. We compared and analyzed the radiation therapy planning between VMAT and 3D-CRT CSI to prove that the VMAT planning had better homogenous target coverage while reducing radiation dose to several organs at risk (OARs) than the 3D-CRT, especially for adult patients with medulloblastoma.

CASE PRESENTATION

A 24-year-old man was referred from the Neurosurgery Department to the Radiation Oncology Department of MRCCC Siloam Hospital in February 2019 with medulloblastoma post-surgical resection. He complained of intermittent headaches for two months, accompanied by loss of balance, which improved after resection. Examination of the cranial nerves was normal, with no deficits in sensory and motor functions.

According to Magnetic Resonance Imaging (MRI) of the head and whole spine (before resection), the imaging results showed a 4.3 x 3.2 x 3.4 cm mass on the right cerebellopontine angle with mild tonsillar herniation and no metastasis to other sites.

Ventriculoperitoneal (VP) shunt procedure and craniotomy tumor removal were performed on this patient in January 2019. Histopathological and immunohistochemical analysis revealed medulloblastoma, World Health Organization (WHO) grade IV. Magnetic resonance imaging evaluation showed a 3 x 2.3 x 1.7 cm residual mass after resection on the right cerebellopontine angle.

Craniospinal irradiation was delivered to this patient three weeks after resection with the VMAT technique. RapidArc® (RA) volumetric modulated arc therapy (VMAT) is a technique in radiotherapy using dynamic rotational therapy to give a highly conformal and homogenous radiation dose to the target volume [11]. This technique is often called rotational intensity-modulated radiotherapy (IMRT), in which the gantry continuously rotates around the patient. In VMAT, the positions of the multileaf collimator (MLC), gantry speed, and dose rate continuously change, thus enabling more rapid treatment times during treatment delivery and generating a similar dose distribution with other helical radiotherapy techniques [12]. The radiation dose was 36 Gy in 20 fractions to the craniospinal axis, with an 18 Gy boost dose in 10 fractions to the posterior fossa. During radiation therapy and one month after treatment, the patient complained about mild headaches and hair loss, which improved over time.

We generated 3D-CRT planning to analyze and compare the dosimetric results of VMAT and 3D-CRT for this case report **(Figure 1). Table 1** shows the parameters evaluated for Planning Target Volume (PTV) for both techniques.

Patient simulation

The computed data of a patient diagnosed with medulloblastoma treated in 2019 were included in this retrospective dosimetric study and analyzed postradiotherapy. The patient was simulated in a supine position; a VacLoc vacuum bag was used for body

Table 1. Parameters evaluated for planning target volume (PTV) using 3D-CRT and VMAT

Technique /parameters	3D-CRT	VMAT
PTV		
D98% (in Gy)	53.72	53.8
D2% (in Gy)	56.63	56.04
D50% (in Gy)	55.13	55.01
D95% (in %)	99.7	100
D107% (in %)	0.007	0.002
D110% (in %)	0	0
Conformity Index	0.96	1.92
Homogeneity Index	0.08	0.25

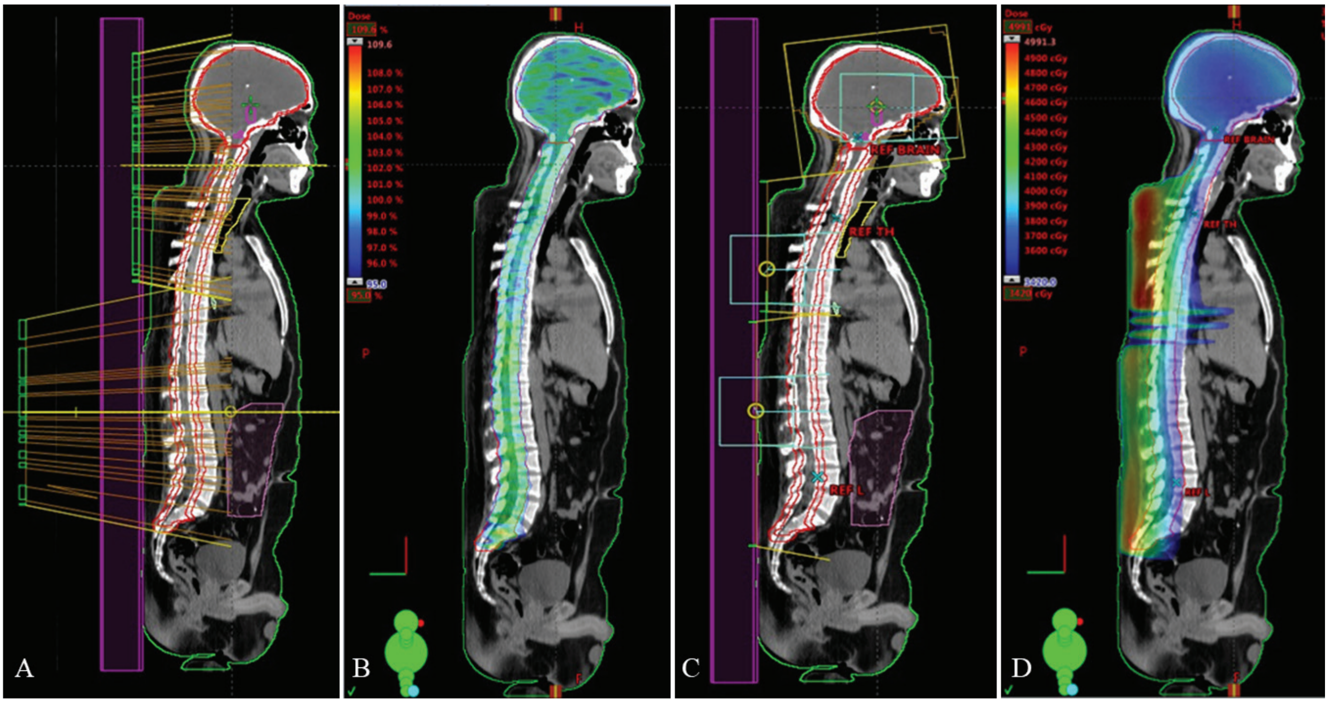

Figure 1. Plan comparisons between VMAT and 3D-CRT. (A & B) Beam arrangement and 95% dose coverage in VMAT; (C & D) Beam arrangement and 95% dose coverage in 3D-CRT

Table 2. Dosimetric comparison of OARs using 3D-CRT and VMAT

OARs	3D-CRT					VMAT				
	Dmax (Gy)	Dmean (Gy)	V10 (%)	V20 (%)	V30 (%)	Dmax (Gy)	Dmean (Gy)	V10 (%)	V20 (%)	V30 (%)
Left lens	5.47	4.04	-	-	-	5.35	4.53	-	-	-
Right lens	6.65	4.30	-	-	-	5.37	4.66	-	-	-
Left eye	31.75	7.31	20.55	3.11	-	23.45	7.61	32.21	3.58	-
Right eye	32.50	8.27	24.4	7.17	-	13.27	6.36	21.42	-	-
Optic chiasm	36.07	35.96	100	100	100	37.14	36.21	100	100	100
Left optic nerve	36.33	33.08	100	99.9	48.03	33.43	22.72	100	88.72	1.76
Right optic nerve	35.91	30.17	100	88.84	33.54	33.95	22.96	100	81.28	8.45
Brainstem	37.42	36.22	100	100	100	37.93	36.35	100	100	100
Left cochlea	37.53	36.70	100	100	100	37.33	36.22	100	100	100
Right cochlea	36.80	36.30	100	100	100	36.52	35.71	100	100	100
Esophagus	41.87	35.59	100	100	61.49	36.02	23.46	100	78.67	0.03
Thyroid	32.15	30.42	100	100	0.4	25.86	18.09	100	26.26	-
Heart	40.9	20.23	66.07	60.9	4.83	29.46	11.9	65.74	3.56	-
Left lung	38.31	12.45	2.66	1.25	-	32.18	9.26	30.69	1.22	-
Right lung	40.93	14.03	7.85	5.21	-	34.5	10.13	38.5	4.81	-
Liver	40.94	10.33	28.67	20.08	-	23.91	8.1	24.07	0.19	-
Left kidney	6.67	1.31	66.71	4.74	-	22.23	9.72	42.59	0.37	-
Right kidney	8.31	1.41	27.68	-	-	18.33	8.37	22.77	-	-
Bowel	28.9	7.71	28.78	23.39	0.3	21.66	8.79	32.54	0.08	-
Testicle	1.1	0.41	-	-	-	0.85	0.24	-	-	-

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fixation, and a thermoplastic mask was used for head fixation. Computed tomography (CT) simulation used a Philips Brilliance CT Big Bore.

Target volume delineation and dose prescription

Target volume delineation consisted of the whole brain and spinal cord. Various organs at risk (OAR) close to the target volume were delineated on the Eclipse contouring tab images, slice by slice. The PTV consists of PTV1 and PTV2. The whole brain and spinal cord were PTV1, while the posterior fossa would be boosted as PTV2. The total radiation doses for PTV1 and PTV2 were 36 Gy in 20 fractions, with 18 Gy in 10 fractions as boost doses, respectively.

Treatment planning

A series of consecutive CT slices would be the base for treatment planning. The patient was planned on Varian Eclipse version 13.6 using Millennium-120 MLCs for beam shaping. VMAT plan was generated for 6 MV photons with progressive resolution optimizer Version (PRO) and volume dose calculation by the anisotropic analytic algorithm (AAA) with a resolution of 2.5 mm. It consisted of 2 isocenters; the first isocenter would cover the whole brain and upper side of the cervical spinal cord with a double full arc (the first arc was from the angle of 181° to 179° clockwise, and the second arc was from 179° to 181° counter-clockwise); the second isocenter utilized a single 360° full arc (from 179° to 181° counter-clockwise) that covered the remaining spinal cords was derived from the lower part of the cervical, thoracic, lumbar, and sacrum. A three-dimensional conformal radiotherapy plan was generated for 6 MV and 10 MV photons and consisted of 3 treatment plans with three different isocenters: the first treatment plan covered the whole brain part using a radiation field from 90° fix gantry angle and an opposing field from 270° gantry fix rotation with isocentric technique; the second and third treatment plans covered the thoracal, lumbar, and sacrum region, consisted of single radiation field from 181° fix gantry angle with fixed SSD technique. Hot and cold spots occurred between 2 junctions adjacent to the thoracal and lumbar–sacrum treatment fields. Thus, we used interfraction moving field junctions to feather out any potential hot and cold spots.

Plan evaluation

Plans were analyzed for PTV dose coverage, organs at risk (OARs), dose sparing, conformity, and homogeneity index, and cumulative dose-volume histograms (DVHs) for PTV and OARs were computed for analysis.

Treatment delivery

Treatment was delivered on Varian Clinac iX (Varian Medical Systems, Palo Alto, USA) using dynamic MLCs. Radiotherapy for the craniospinal axis was delivered five fractions per week with a 1.8 Gy daily dose.

DISCUSSION

Medulloblastoma is a type of central nervous system tumor that is aggressive and malignant and arises from the cerebellar vermis in the fourth ventricle roof. In adults, the cerebellar hemisphere is the frequent site of tumor involvement. Therefore, the tumor predilection site in adults is more lateral than in children [13]. Medulloblastoma is seen more rarely in adults than in children, whereas late recurrences of medulloblastoma are more frequent in adults in the posterior cranial fossa [14].

Patients usually complain of headaches, nausea, vomiting, and visual impairment. Papilledema can be found in the funduscopic examination. Cranial nerve deficits commonly happen when the tumor infiltrates the brainstem. Nerve IV or VI deficits have manifestations such as nystagmus and diplopia [2,13,15].

The management of medulloblastoma in children, including surgical resection of the tumor followed by CSI and boost irradiation to the posterior fossa with or without chemotherapy, is very well known and described in various literature [16]. This protocol is also used for the management of medulloblastoma in adults.

This case report showed the CSI technique with VMAT and 3D-CRT in adult patients. 3D-CRT CSI requires matching several radiation fields with different isocenters to achieve the desired target volume [17,18]. The beam geometry and field matching must be carefully considered because the radiation field is long in adult patients. Optimal patient positioning and correct junction placement are important to minimize dose inhomogeneity [19]. A feathering or manual junction shift technique can reduce dose inhomogeneity and inaccuracies in field junctions [20]. There are several disadvantages to this method. High dose gradients between fields can potentially create unintentional high and/or low doses in the spinal cord when even small setup errors occur. 3DCRT CSI patients are typically arranged in the prone position to provide direct visualization of multiple plane intersections. However, this position is often uncomfortable and can increase patient movement during radiation. Breathing becomes restricted when in the prone position, and the flexed head position is not conducive to radiation. Interfractional manual switching is complex enough to exacerbate patient setup errors and prolong the duration of radiation therapy [18].

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VMAT with a single or a combination of arcs with several isocenters can be used for CSI. VMAT CSI demonstrated its ability to achieve highly conformal and homogeneous dose distribution while limiting the dose to the surrounding OAR. VMAT contains overlapping fluence patterns between the brain and spinal field, which provides an additional advantage over 3DCRT, as it does not require an isocentric shift for smoothing purposes to match plane intersections. However, the technical advantages of the VMAT technique are also associated with an increased integral dose to nontarget tissue, which may be related to an increased risk of secondary malignancies [10].

In the current study, the CSI plan with VMAT achieved a highly conformal and homogenous radiation dose compared to 3D-CRT. **Table 1** shows that D95% of VMAT was 100% and 3D-CRT was 99.7%; D107% of VMAT was 0.002%, and 3D-CRT was 0.007%. These results revealed that the target volume covered with high doses in the VMAT plan was lower than in the 3D-CRT plan.

The analysis of the conformity index (CI) and homogeneity index (HI) showed that with the VMAT plan, CI was 1.92 and HI was 0.25; in the 3D-CRT plan, CI was 0.96 and HI was 0.08. These results show that the VMAT plan provided better homogeneity, conformity, and distribution of doses than the 3D-CRT plan.

The dosimetric comparison **(Table 2)** shows that VMAT has a better result than 3D-CRT. VMAT could reduce the max and mean dose in almost all OARs. VMAT has better sparing in V20 (left and right eye, left and right optic nerve, thyroid, esophagus, heart, lungs, bowel, liver, and left kidney), as well as V30 (left and right optic nerve, esophagus, thyroid, heart, and bowel). Unfortunately, we present only one case of adult medulloblastoma treated with VMAT CSI because it is a rare case in our center. New advanced radiotherapy techniques, e.g., proton beam therapy (PBT), may provide better planning results when compared to VMAT CSI. However, PBT is not yet available in our country**.**

CONCLUSIONS

Adult medulloblastoma is a rare case usually treated with surgical resection followed by craniospinal irradiation and chemotherapy. Generally, craniospinal irradiation is a complex and challenging technique in radiotherapy, especially in adult patients, because the target radiation volumes are usually longer than the maximum treatment field size. Hence, this technique will need more isocenters, which differ from pediatric patients. This case report showed that VMAT could be the first treatment selection for CSI in adult medulloblastoma since it could obtain better homogeneity, conformity, and dose distribution than 3D-CRT. Furthermore, VMAT allows more OARs sparing when compared to 3D-CRT.

DECLARATIONS

Ethics approval and consent to participate
Not applicable.

Competing interest
The authors declare no competing interests in this study.

Acknowledgment
Nothing to declare.

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