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Craniospinal Irradiation of Pediatric Medulloblastoma, Dosimetric Comparison between Helical Tomotherapy, and Conventional Radiation Therapy

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Abstract

Background: Dosimetric comparison between 3D-conformal radiation therapy (3D-CRT) and helical tomotherapy (HT) in pediatric Medulloblastoma (MB) receiving craniospinal irradiation (CSI).

Method: This was a retrospective dosimetric study on five pediatric male patients diagnosed as MB, who were planned to receive CSI post-surgery. Treatment plans for 3D-CRT and HT were generated. Comparison was made in terms of planning target volume (PTV) coverage, homogeneity index (HI), conformity index (CI), organs at risk (OAR) dose, and treatment time (TT).

Results: HT increased the minimum dose up to PTV (81% vs. 74%) with better CI and HI (1.024 vs. 0.36 and 1.078 vs. 1.21, respectively). HT decreased the mean and maximum dose to OAR, except for higher mean dose of larynx, oral cavity, pharynx, and comparable V5 of lungs. TT of 3D CRT was shorter than HT (76 seconds vs. 545 seconds).

Conclusion: HT was found to be a better treatment option in all the MB cases receiving CSI regarding PTV, conformity, homogeneity, and most of OAR, while TT was shorter in 3D-CRT plan.

Keywords: Pediatric, Medulloblastoma, Craniospinal irradiation, Dosimetry

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Introduction

Medulloblastoma (MB) is one of the most prevalent tumors in children with peak age incidence between 5-6 years.[1] Approximately 30% of the cases were diagnosed with metastatic disease.[2, 3] Gene profiles have been recently used several years back to define the MB prognosis.[4-7]

The standard of care for average risk MB consists of entire craniospinal irradiation (CSI) to a dose of 23.[4] Gy in 13 fractions with concurrent vincristine followed by

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posterior fossa boost to reach 54Gy, as a total dose,[8] with a five-year survival rate of 85%.[9]

The average risk of MB with anaplastic variant has a survival rate of around 73%,[9] while the high-risk survival rate is 30%-60%.[10,11]

The boost dose to the primary tumor may be given to whole posterior fossa as the standard of care or tumor bed involved field without increased local failure rates.[12,13]

Helical tomotherapy (HT) is one of the recent advances of intensity modulated radiation therapy (IMRT) with a high therapeutic ratio and image guidance creation via mega voltage computed tomography (MVCT) scan.[14]

The present study aimed to show which technique has a better dosimetric distribution HT or 3D conformal radiation therapy (3D-CRT).

Patients and Methods

Study design

This was a retrospective dosimetric study of five pediatric male patients diagnosed as MB, who were planned to receive CSI post-surgery at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia. The Research Ethics Committee approved this project via Research Advisory Council number of 2221001 and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki; however, for retrospective review of the data with less than the minimal risk for the patients, no consent was required from the Ethics Committee. Brain, spinal cord, and meninges were contoured as clinical target volume (CTV). Isotropic of 3-5 mm was added to CTV in order to create planning target volume (PTV). Cribriform plate was considered as a part of target volume to prevent increased relapse rate. Thecal sac was identified to be below the second sacral spine in most cases via magnetic resonance imaging.

We contoured the organs at risk (OAR) (globe, lens, thyroid, and oral cavity and pharynx, larynx, parotid, esophagus, heart, lung, liver, kidney, and scrotum). The prescribed dose was 23.4Gy in 13 sessions. We expressed the target and critical organ doses as absolute dose.

In this study, the plans were created using two different planning systems, namely TomoTherapy Hi Art planning system (Helical IMRT) and Varian Eclipse planning system for 3D plans.

Tomotherapy planning

HT cases were planned using 5.0 y-jaw width in order to minimize the treatment time (TT). Although dose conformity is better with smaller field widths (2.5cm and 1cm), an acceptable conformal dose could be achieved via a 5-cm jaw width for such cases with the minimum modulation factors. With the moving couch, one single plan can cover the whole PTV without patient reposition or beam junction risk.

Conventional 3D planning

For Varian Eclipse plans, patient setup is usually done with prone position. For making a highly accurate plan comparison, we made the plans to be on supine position. Multiple abutting fields with different plan isocenters were used to cover the whole PTV. Two lateral beams were utilized to cover brain and one or two Postero-Anterior beams (depending on PTV length) for spine. The selection of collimator angles, field sizes, and location of beam junctions is crucial to prevent PTV hot or cold spots. Multiple plans for every five fractions and every patient were created with different beam junction locations to move hot and cold spot positions; accordingly, the effect of hot or cold spots could be minimized.

Treatment plan evaluation

Dose-volume histogram statistics were analysed concerning target and critical organs, conformity index (CI), homogeneity index (HI), and TT in order to compare the treatment plans.

Statistical analysis

All the data were collected, tabulated, and statistically analyzed using SPSS 22.0 for windows (IBM Inc., Chicago, IL, USA). Continuous Quantitative variables were expressed as the average ± standard deviation and median (range). Continuous data were checked for normality employing Shapiro Walk test. Wilcoxon singed ranks test was used to compare the two dependent groups of non-normally distributed data. All the tests were two-sided. P-value < 0.05 was considered to be statistically significant.

Table 1. Planning DVH characteristics of the five patients

	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5	
	HT	3D	HT	3D	HT	3D	HT	3D	HT	3D
PTVn%	100	101.7	99.4	103.1	99.7	101.4	99.7	98.1	100	100.8
PTVx%	109.4	111.1	108.1	106.7	108.1	110.3	109.4	111.7	106.4	116.9
PTVm%	83.6	69.4	75.8	72.2	83.3	75	79.2	77.8	83.3	75
Rt lung mx%	72.8	101.7	82.2	107.5	72.8	103.1	80	103.6	76.7	107.2
Mean%	16.1	23.6	17.8	38.3	15.8	29.4	16.9	34.4	16.9	30.3
V20%	0.7	18.9	2.5	36	0.5	26.7	1.8	30.8	1.5	27.7
V10%	11.3	24.3	14.8	43.5	11	32.8	13.8	38.2	13.5	33.4
V5%	40.7	35.4	45	53.6	40.3	44	41.4	47.8	42.8	44
Lt lung mx%	75.6	104.4	83.9	108.3	76.4	105	80	102.8	83.1	106.7
Mean%	16.1	23.1	17.5	32.2	16.1	25.3	16.7	25	16.9	14.7
V20%	0.9	18.5	2.3	28	1.2	20.8	2	19.6	2.1	9.2
V10%	10.7	22.7	15.2	34.4	11.5	24.9	13.3	24.4	13.2	13.3
V5%	40.4	30.6	44.6	43.9	40.1	33.6	40.7	33	43.3	20.6
Rt parotid mx%	66.7	83.6	77.5	105.3	85.6	101.4	70	99.4	74.2	99.2
Mean%	43.6	61.7	42.5	57.2	47.8	26.4	42.5	88.9	43.3	37.5
Lt parotid mx%	66.7	101.7	79.4	105.6	92.5	102.2	74.2	101.1	71.9	101.4
Mean%	45.3	59.4	44.2	59.2	48.1	29.7	45.6	94.2	45.8	54.4
Rt lens mx%	22.2	76.1	20	57.2	16.7	25.3	20.3	35.3	20.8	76.9
Mean%	16.1	30.6	16.4	25	13.6	15.3	16.7	20.6	16.1	37.2
Lt lens mx%	22.2	93.1	20	81.7	15.6	23.1	21.1	42.8	18.1	80.6
Mean%	16.4	39.2	16.7	38.1	13.3	13.1	17.5	26.9	14.4	42.8
Rt globe mx%	83.9	102.2	84.4	104.7	79.2	102.5	83.1	102.5	85.3	101.2
Mean%	38.9	53.9	46.9	65.8	36.9	50.6	46.9	56.9	43.6	61.4
Lt globe mx%	84.2	102.5	86.7	104.7	76.7	102.5	84.4	102.8	91.4	102.1
Mean%	40.3	58.6	48.1	65.8	33.6	43.9	49.4	73.6	40.3	66.1
Larynx mx%	70.3	90	65.3	63.9	51.9	51.9	67.5	88.9	68.1	93.1
Mean%	40.8	28.3	32.8	20.8	31.1	18.6	40.3	27.8	42.2	37.8
Ph&O.C mx%	83.6	97.2	90	98.3	88.3	91.7	95.6	97.8	90	92.2
Mean%	33.1	15	33.1	15	33.6	9.2	34.4	21.9	33.6	13.3
Thyroid g. mx%	42.8	72.2	45.3	91.4	37.8	85.3	51.4	78.1	44.7	87.2
Mean%	30	44.2	29.7	86.1	27.8	76.7	30.3	56.4	30.8	77.2
Esophagus mx%	63.3	93.1	90.8	94.4	67.8	88.1	90.3	92.8	78.9	90.8
Mean%	51.9	87.2	72.5	89.4	52.5	82.8	69.7	88.1	59.7	85.6
Heart mx%	52.8	89.2	71.1	93.1	51.4	90.8	67.2	89.7	60.8	88.1
Mean%	28.1	67.5	32.5	70.1	27.8	52.5	33.3	64.2	30	43.1
V30%	0.0	9.9	0.0	17.2	0.0	4.7	0.0	9.8	0.0	2.6
Liver mx%	43.3	91.9	51.9	91.7	50.8	93.3	54.4	96.7	55.3	92.8
Mean%	18.3	24.2	18.3	27.8	18.3	27.5	18.6	31.1	20	26.7
V30%	00	2	00	3.6	0.0	2	0.0	3.9	0.0	2.7
Rt kidney mx%	43.6	99.2	63.6	98.3	53.1	99.2	59.7	100.6	56.4	96.9
Mean%	21.4	26.7	22.2	28.6	21.9	27.8	21.7	40	21.7	12.5
V20%	00	21.9	00	23.6	0.0	23.5	0.1	38	0.0	5.6
Lt kidney mx%	41.9	96.4	57.2	101.9	53.9	98.3	59.7	100	53.9	93.6
Mean%	21.7	23.1	21.7	30	21.9	20.8	21.9	39.7	21.9	13.1
V20%	00	17.6	00	25.8	0.0	15.1	0.2	37	0.0	6.6
Scrotum mx%	0.9	2.8	0.56	2.7	0.28	1.9	2.2	4.6	0.28	1.3
mn%	0.6	2.1	0.4	2.5	0.2	0.8	1.5	3.6	0.2	1.0
CI	1.03	0.4	1.05	0.3	1.01	0.4	1.01	0.3	1.02	0.4
HI	1.09	1.2	1.08	1.4	1.07	1.19	1.09	1.2	1.06	1.06
TT(seconds)	577	95	489	71	565	71	559	71	535	71

DVH: Dose volume histogram, PTV: Planning target volume, n: Mean, m: Minimum, x: Maximum, g: Gland, Rt: Right, Lt: Left, Ph and O.C: Pharynx and oral cavity, CI: Conformity index, HI: Homogeneity index, TT: Treatment time; HT: Helical tomography

Results

Table 1 depicts PTV, OAR dose, CI, HI, and TT in seconds for the five patients. The percentage of the mean and maximum doses was calculated for the target and OARs. Table 2 represents the biostatistics for all the patients of both techniques in addition to the *P* value.

Target volume coverage

Both techniques achieved the dosimetric plan requirements regarding PTV coverage. HT significantly succeeded to increase the minimal dose to PTV (81.1% vs. 73.9%, $P = 0.042$).

Normal tissue sparing

Regarding OAR dose (heart, lung, kidney, parotid, eye, liver, thyroid, and scrotum), all of

Table 2. Patients' biostatistics (Continued)

	HT (N=5) Average ± SD	3D (N=5) Average ± SD	Test[a]	*P*-value
PTV				
Mean	99.80 ± 0.44	101 ± 1.87	-1.089	0.276
Maximum	108 ± 1.22	111.40 ± 3.64	-1.761	0.078
Minimum	81 ± 3.39	73.80 ± 3.42	-2.032	0.042
Other ttt parameters				
CI	1 ± 0	0 ± 0	-2.236	0.025
HI	1 ± 0	1 ± 0	0.000	1.000
TT (seconds)	545 ± 34.84	75.80 ± 10.73	-2.023	0.043
RT globe				
Maximum	83 ± 2.34	102.40 ± 1.51	-2.023	0.043
Mean	42.80 ± 4.60	57.80 ± 5.89	-2.023	0.043
LT globe				
Maximum	84.60 ± 5.12	102.80 ± 1.30	-2.032	0.042
Mean	42.20 ± 6.26	61.80 ± 11.27	-2.023	0.043
RT lens				
Maximum	20 ± 1.87	54 ± 23.57	-2.023	0.043
Mean	15.80 ± 1.09	25.80 ± 8.55	-2.023	0.043
LT lens				
Maximum	19.40 ± 2.40	64.40±29.89	-2.023	0.043
Mean	15.60 ± 2.07	32 ± 12.16	-1.826	0.068
RT parotid				
Maximum	75 ± 7.41	97.60 ± 7.98	-2.023	0.043
Mean	43.80 ± 2.48	54.40 ± 24.17	-0.674	0.500
LT parotid				
Maximum	76.80 ± 9.52	102.40 ± 2.07	-2.032	0.042
Mean	45.80 ± 1.48	59.20 ± 22.86	-0.944	0.345
Larynx				
Maximum	64.60 ± 7.26	77.60 ± 18.44	-1.461	0.144
Mean	37.40 ± 5.02	26.80 ± 7.46	-2.060	0.039
Pharynx				
Maximum	89.60 ± 4.33	95.40 ± 3.13	-2.032	0.042
Mean	33.60 ± 0.54	14.80 ± 4.71	-2.032	0.042
Thyroid				
Maximum	44.40 ± 4.66	82.60 ± 7.56	-2.032	0.043
Mean	29.80 ± 1.09	68 ± 17.36	-2.023	0.043
	HT (N=5) Average ± SD	**3D (N=5) Average ± SD**	**Test[a]**	***P*-value**
Esophagus				
Maximum	78.20 ± 12.63	91.80 ± 2.38	-2.032	0.042
Mean	61.20 ± 9.54	86.60 ± 2.30	-2.023	0.043
Right Lung				
Maximum	77 ± 4.0610	4.80 ± 2.58	-2.032	0.042
Mean	16.80 ± 0.83	31 ± 5.29	-2.032	0.042
V20	1.40 ± 0.89	28.20 ± 6.22	-2.023	0.043
V10	13 ± 1.87	34.40 ± 7.36	-2.023	0.043
V5	42 ± 2	45 ± 6.92	-1.214	0.225
Left Lung				
Maximum	79.80 ± 3.76	105.40 ± 2.07	-2.032	0.042
Mean	16.80 ± 0.83	24 ± 6.08	-1.753	0.080
V20	1.60 ± 0.54	19.20 ± 6.83	-2.023	0.043
V10	12.80 ± 1.48	23.80 ± 7.46	-1.826	0.068
V5	41.80 ± 2.16	32.60 ± 8.20	-2.023	0.043
Heart				
Maximum	60.80 ± 8.64	90.20 ± 1.92	-2.023	0.043
Mean	30.20 ± 2.28	59.40 ± 11.52	-2.023	0.043
V30	0 ± 0	9 ± 5.43	-2.032	0.042
Liver				
Maximum	51 ± 4.74	93.40 ± 2.07	-2.023	0.043
Mean	18.60 ± 0.89	27.60 ± 2.50	-2.032	0.042

Table 2. Patients' biostatistics (Continued)

	HT (N=5) Average ± SD	3D (N=5) Average ± SD	Test[a]	*P*-value
V30	0±0	3±1	-2.041	0.041
RT kidney				
Maximum	55.40±7.60	98.80±1.48	-2.032	0.042
Mean	21.80±0.44	27.20±9.98	-0.948	0.343
V20	0±0	22.80±11.36	-2.032	0.042
LT kidney				
Maximum	53.40±6.81	98±3.16	-2.032	0.042
Mean	22±0	25.40±10.16	-0.542	0.588
V20	0±0	20.60±11.41	-2.023	0.043
Scrotum				
Maximum	0.80±0.83	2.80±1.48	-2.060	0.039
Minimum	0.60±0.89	2±1.22	-2.070	0.038

PTV: Planning target volume, OAR Organs at risk, CI: Conformity index, HI: Homogeneity index, TT: Treatment time in seconds, V20: Volume receiving 20 Grey; HT: Helical tomography

them were statistically significant in favor of HT; however, the V5% of lungs was comparable to or better than that of 3D-CRT (right lung HT 42% vs. 45% and $P = 0.225$, left lung HT 41.8% vs. 32.3% and $P = 0.043$), which is a common finding over the recent radiation modalities (larger volume received lower doses than conventional techniques).

Comparison of dosimetric parameters

Concerning CI, HT was non-significantly better than 3D-CRT (1.024 vs. 0.36, $P = 1.0$) and significantly better regarding HI (1.078 vs. 1.21, $P = 0.043$).

TT was significantly shorter in 3D-CRT (76 seconds vs. 545 seconds, $P = 0.043$).

Discussion

Craniospinal irradiation is a very sophisticated technique owing to the big target volume including brain and spinal cord in addition to most of critical organs of the body involved in this procedure. In our institution we are usually used the 3D-CRT in CSI to save the departmental resources and we may shift to HT plan, if complicated case is suspected due to poor target coverage or high critical organs dose which in turn lower the therapeutic ratio.

In this study, both techniques achieved comparable results in terms of target volume coverage; however, HT achieved better dose distribution and higher minimal dose to PTV.

Clair and colleagues reported the same findings regarding target coverage[15] and similar outcome noticed in different studies using IMRT.[16-18]

In this study, CI was better in tomotherapy arm compared with 3D-CRT (1.024 versus 0.36), while Myers et al.[19] reported CI of tomotherapy was 0.93 vs. 0.67 of 3D-CRT, also Sharma et al.;[20] noticed CI of tomotherapy was 0.96 vs. 0.23 of 3D-CRT and William et al.[21] found CI of tomotherapy was 1.28 vs. 1.61 of 3D-CRT.

Regarding HI in this study, tomotherapy was better than 3D-CRT (1.078 vs. 1.21), similar to Sharma et al.;[20] as HI of tomotherapy was 0.96 vs. 0.84 of 3DCRT, contrary to Myers et al.;[19] who found HI was comparable in both plans (1.15 vs. 1.13 for 3D-CRT) and other studies noticed the same comparable results.[21-24]

Regarding OARs, our study showed that HT decreased the mean and maximum dose in the majority of OARs, except for higher mean dose of larynx, oral cavity, pharynx, and comparable V5 of lungs; however, the outcome of reports is conflicting in this filed. This discrepancy may be due to contouring and PTV margin issues, but in general, recent IMRT techniques showed smaller volumes have received higher doses and those characterized by larger volumes received lower doses.[19-24]

Myers et al.[19] noted that HT has a lower maximum, but a higher mean dose for the majority of OAR and 3D-CRT has a higher maximum, but a lower mean dose to OAR on the contrary to our study.

Sugie et al.[22] reported that HT significantly increased the mean doses to the lung, kidneys,

and liver and V5 Gy of six OARs, including the lung, were contradictory to our findings.

In line with our study, Sharma et al.[20] showed that HT reduces the maximum and mean dose to almost all OARs, like heart, thyroid, and salivary glands, except for the lung, kidney, liver, lens, and stomach.

Parker et al.,[21] Yoon et al.,[23] and Muscarine et al.[24] obtained similar results to our findings.

All the studies have shown shorter beam on time by 3D-CRT than HT; however, daily Mega Voltage CT (MVCT) generated in HT is advantageous, which allows precise target monitoring resulting in higher therapeutic ratio.[19-24]

Finally, in our practice, we used 3D-CRT in most cases in order to save departmental resources. On the other hand, HT is usually used in children under general anesthesia as intrafraction immobilization occurs. One of the limitations of our study is the small sample size due to the more complicated technique of CSI which almost cover the whole body organs.

Conclusion

Both plans reached the required target coverage and OARs sparing in CSI. Meanwhile, HT plan provided a better dose conformity, homogeneity, and OARs sparing at the expense of exposing larger volumes of tissue to lower dose and longer beam on time compared with the three dimensional plans.

Conflict of Interest

None declared.

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