A Dosimetric Study of Conformal Radiotherapy and Two dimensional conventional Radiotherapy in craniospinal irradiation for Medulloblastoma Patients

Mohamed Abdelgawad, MD; Eman Ibrahim Ismail, MD; Mohamed Abd elwahab Badwy, MD

Department of Clinical Oncology, Faculty of Medicine, Zagazig University, Egypt

Corresponding Author: Dr Mohamed Abdelgawad
Clinical Oncology Department, Faculty of Medicine
Zagazig University, Egypt
Email: gawad2@yahoo.com

Key words: Dosimetric, Conformal, Conventional, Craniospinal, Medulloblastoma.

ISSN: 2070-254X

Abstract

Background and purpose: There has been an evolution from two dimensional (2D) to three dimensional (3D) planning.Our aim was to compare dosimetically the dosimetric outcomes for target coverage and organs at risk

Patients and methods: Twelve patients of meduloblastoma. In 3DCRT clinical target volume (CTV) for craniospinal irradiation is the entire craniospinal axis. Three posterior coplanar beams were used to treat the spinal PTV. The CTV posterior fossa boost volume encompass the entire posterior fossa. Organ at risk OARs outlined on planning CT. In Conventional(2D) planning radiotherapy we used osseous reference marks as performed in routine practice. The dose according to risk (23.4 Gy, 36 Gy) to the craniospinal axis and dose to the PTVpf up to be 54.0, 55.8 Gy.

Results: There was no statistical difference in PTV coverage when comparing 3D to conventional 2D planning. The mean of dose to OAR were all decreased when comparing 3D to 2D planning as follows: LT lens RT lens, Thyroid, Dental area, and Heart, with statistical difference in thyroid and heart. While mean dose to OAR were all increase when comparing 3D to 2D as follows lt eye, rt eye, Lung, kidneys, bladder, and liver with statistical difference in kidneys and Lt eye.

Conclusion: No statistical difference in mean dose of PTV coverage, and was noted to have reductions in maximum dose of PTV and some selected organs at risk. Further study comparing 3D conformal radiotherapy (3DCRT) planning with IMRT is needed to analyse the dose uniformity in CSI.

Introduction

Medulloblastoma comprises approximately 20% of pediatric CNS tumors, although one third of medulloblastomas occur in adults.[1]

Today, CSI followed by chemotherapy is the standard of care for both average- and high-risk children ages 3 and older. In average-risk disease (defined as gross totally resected tumor without severe anaplasia, and no metastases), 23.4 Gy to the craniospinal axis, plus a boost to 54 Gy to the posterior fossa, followed by adjuvant chemotherapy, is standard and has resulted in 5-year survival of 80% or better.[2] Areas of active investigation in average-risk disease are lowering of the craniospinal dosage to 18 Gy, conformal posterior fossa radiotherapy to the tumor volume, and intensification of chemotherapy with autologous peripheral blood stem cell support.[3] In high-risk disease (defined as subtotally resected tumor, severely anaplastic histology, or presence of metastases), 36 Gy craniospinal plus a boost at the posterior fossa to 54 Gy, followed by chemotherapy is standard, and results in 5-year survival rates of 50% to 70%. [4] Three-dimensional (3D) conformal radiation therapy (CRT) promises high precision in dose delivery and allows ~30-40% reduction of the normal tissue included in the high-dose volume compared with conventional 2D planning [5].

Field shaping for CSI has evolved from traditional bony landmarks using two-dimensional (2D) planar radiographs to the more recent CT simulation techniques [7-6].In most of these techniques, field shaping and matching of cranial and spinal fields are done geometrically with no attempt to compute the dose–volume data of the target and/or organs at risk (OARs). Various modifications to treatment planning and delivery have been made in an effort to improve target volume coverage, dose homogeneity and conformity. Parker et al have recently reported the feasibility of conventional linear accelerator (LA)-based intensity-modulated radiotherapy (IMRT) for CSI in small children[8].

Purpose

Craniospinal irradiation (CSI) is a technically difficult and time consuming radiation therapy technique. Dose inhomogeneity and long term sequelea, especially in the pediatric population, from CSI is of concern. There has been an evolution fromConventional two dimensional (2D) to three dimensional (3D) planning.Our aim was to compare dosimetrically the dosimetric outcomes for target coverage and organs at risk.

Patients and methods

Study included 12 patients diagnosed with primary meduloblastoma. between August 2008 and May 2011, in Clinical Oncology Department, Zagazig University, Egypt. Eligibility criteria included age range between 3-15 years, histologically was confirmed as medulloblastoma and patients were to have no

evidence of disseminated disease on magnetic resonance imaging of the entire brain and spine. The patient was placed in prone position, hyperextend the neck. Following mask application with thermoplastic, CT scans was taken from the flash region over the head to obturator foramen. Conventional and 3D-CRT were performed on an Percise treatment planning station. Parallel opposed beams were used to treat the brain.

Three dimensional (3D) planning included Cranial fields which contain CTV for CSI (CTV csi) is the entire craniospinal axis. PTV margins was 1.0 cm. The whole-brain field extended anteriorly and include the entire frontal lobe, including the cribriform plate region. The volume cover the superior orbital tissues to ensure coverage of the cribriform plate; A margin of at least 0.5 cm below the base of skull and foramen magnum is recommended for CTVcsi. PTVcsi should be defined to account for setup error. The caudal border of the whole-brain field placed superiorly enough to allow for two junction shifts during treatment with a matching posterior spinal field.

The spinal target volume included the entire thecal sac. CTVcsi for the spinal field should extend laterally to cover the recesses of the vertebral bodies; with 1-cm PTVcsi margin added on either side to account for setup variation and uncertainty. The superior border is the junction with the whole-brain field. The inferior border of the treatment volume placed 2 cm below the termination of the subdural space as seen on a spinal MRI. Generally, the inferior border of the spinal field extends to the S2–S3 interspace, but may be lower. If the entire spinal target volume cannot be adequately covered with a single posterior field, two spinal fields should be used with an appropriately matched junction between them. In 3D-CRT, 3 posterior coplanar beams (180°, 145°, 215°, 6 MV) were used to treat the spinal PTV.

The CTV posterior fossa (CTVpf) boost volume encompass the entire posterior fossa. The CTVpf extends from the foramen magnum inferiorly, to the bony walls of the occiput and temporal fossae posteriorly and laterally, and superiorly to the tentorium cerebelli. The anterior borders of the brainstem and midbrain bind the posterior fossa contents anteriorly. The PTV posterior fossa (PTVpf) consists of a 0.3- to 0.5-cm geometric margin around the CTVpf and accounts for day-to-day setup variation. Again, PTVpf should be limited to the bony confines of the skull, except at the foramen magnum where it extends to the level of C1. The PTVpf should extend anteriorly to the posterior clinoids, excluding the pituitary gland, and inferiorly to the C1-C2 junction. Three-dimensional treatment planning is highly recommended to define these volumes.

Organ at risk OARs outlined on planning CT included lt eye, rt eye, rt lens, lt lens, thyroid, dental area, heart, lung, kidneys, bladder and liver.

Conventional (2D) planning radiotherapy were created using digital reconstructed radiographs (DRR). We designed the fields using osseous reference marks as performed in routine practice.

Whole cranial border included superiorly flash the skin, inferiorly 0.5–1 cm on cribiform plate, 1 cm on middle cranial fossa. One centimerer anterior to the vertebral bodies, 2–2.5 cm posterior to eye markers. gantry to align eyelid markers to avoid radiation to the lens.

Gap shift = For every 9 Gy, extend the cranial field inferiorly by 1 cm, shift the upper spine field inferiorly by 1 cm, and shorten the lower spine field by 1 cm. Need to recalculate couch angle each time. PF boost: use 3DCRT

Spinal field border included superiorly C2 without exiting through mouth, inferiorly bottom of S2 or lowest level of the thecal sac as seen on MRI. In conventional treatment, a direct posterior field was used to treat the spine laterally 1 cm lateral to the lateral edge of pedicles,increase by 1–2 cm in sacrum to cover sacral foramen inferiorly.

Patients with average-risk medulloblastoma are treated to the craniospinal axis to a dose of 23.4 Gy using conventional fractionation (1.8 Gy/fraction) and receive an additional boost of 30.6 to 32.4 Gy. The cumulative dose to the PTVpf be 54.0 55.8 Gy. When using a 3-D conformal technique, the 95% of the PTVpf should receive at least 95% of the prescription dose. No part of the PTVpf should receive a dose less than 50.0 Gy. High-risk medulloblastoma patients are treated to 36.0 Gy to the craniospinal axis (1.8 Gy/fraction) followed by a boost of 18.0 to 19.8 Gy to achieve posterior fossa doses of 54.0 to 55.8 Gy.OAR evaluated included eye ball,lens, heart, thyroid, liver, lung, kidney and. Dose volume histograms were used to assess the plans and time spent per plan was recorded.

Results

Between August 2008 and May 2011, 12 patients were enrolled on this study. There was no statistical difference in PTV coverage when comparing 3D to conventional 2D planning, the mean dose of PTV 101.6 ±1.2, 101.1 ±1.6 respectively.While there is statistical difference when comparing 3D to 2D planning the maximum dose 111.36 ±7.68, 106.03 ±3.86 respectively.

The Mean dose to OAR were all decreased when comparing 3D to 2D planning as follows: LT lens 6.75%, RT lens 6.8%,Thyroid 47.2%, Dental area 4.85% and Heart 33.175% with statistical difference in thyroid (P =0.0004) and heart (P=0.01), while Mean dose to OAR were all increased when comparing 3D to 2D as follows LT eye 52.8%, RT eye 50.5%,lung 21.7%,kidneys 11.6%,bladder 5.5%,and liver 26% with statistical difference in kidneys(P =0.0002)and LT eye (P=0.008). Table 1.

Table 1: Mean dose of target and organ at risk

	Mean dose		
Organ	**Conventional Mean - SD**	**3D Mean - SD**	**P value**
PTV	101.6 ±1.2	101.1 ±1.6	0.39
LT eye	47.9 ±3.02	52.8 ±4.8	0.008
Rt eye	49.3 ±1.34	50.5 ±3.96	0.33
Rt lens	7 ±0.8	6.75 ±0.8	0.48
Lt lens	7.3 ±1.7	6.8 ±0.8	0.37
Thyroid	67.3 ±14.8	47.2 ±7.9	0.0004
Dental area	4.9 ±0.85	4.85 ±0.78	0.806
Heart	44.1 ±12.85	33.175 ±4.39	0.01
Lung	19.5 ±4.2	21.7 ±9.6	0.4
Kidneys	6.8 ±1.07	11.6 ±0.66	0.0002
Bladder	5.45 ±1.78	5.5 ±1.09	0.89
Liver	24.6 ±4.6	26 ±4.1	0.47

The mean of Maximum dose to OAR were all decreased when comparing 3D to 2D as follows: LT eye 95.8%,RT eye 94.8%,thyroid 85.73%, Dental area 7.8% with statistical difference in kidneys (P =0.04) and thyroid (P=0.037), while The mean of Maximum dose to OAR were all increase when comparing 3D to 2D as follows: LT lens 13.6%, RT lens 21.3%, and lung 100.5%,bladder%70.33and liver 97% with statistical difference in LT lens (P =0.001), RT lens (P =0.00004), and bladder (P =0.03). Table 2.

Table 2: Maximum dose of target and organ at risk

	Maximum		
Organ	**Conventional Mean - SD**	**3D Mean - SD**	**P value**
PTV	111.36 ±7.68	106.03 ±3.86	0.043
LT eye	97.46 ±3.86	95.8 ±5.12	0.46
Rt eye	96.3 ±5.94	94.8 ±5.94	0.52
Rt lense	7.6 ±1.3	13.6 ±5.41	0.001
Lt lense	10.33 ±1.7	21.3 ±7.25	0.00004
Thyroid	92.9 ±3.8	85.73 ±10.5	0.037
Dental area	8.6 ±1.39	7.8 ±1.61	0.22
Heart	89.36 ±2.1	85.96 ±8.9	0.21
Lung	99.03 ±0.85	100.5 ±4.26	0.23
Kidneys	81.4 ±1.8	71.9 ±1.1	0.04
Bladder	64.7 ±8.3	70.33 ±2014	0.03
Liver	92.66 ±7.92	97 ±2025	0.08

Discussion

In medulloblastoma irrespective of the risk group, cranio-spinal irradiation (CSI) with or without chemotherapy is the standard of treatment in postoperative setting [9-12,13,14-16].The use of radiation in medulloblastoma, is technically demanding and biologically critical with inadequate coverage of PTV leading to high incidences of neuraxial recurrences which is supported by many studies [17].In such situations, the use of a proper technique for the adequate coverage of PTV is of prime importance. Craniospinal irradiation (CSI) is a technically difficult and time consuming radiation therapy technique[18]. Homogeneous dose distribution remains one of the most technically challenging planning processes in radiation oncology owing to the excessively long field lengths and complex shape of the target volume[19].Dose in-homogeneity and long term sequlae, especially in the pediatric population, from CSI is of concern[18]. With rapid advancements in technology, 2D planar imaging has gradually been replaced by 3D CT-based volumetric imaging for radiation planning. The aim of our study was to investigate the dosimetric outcomes for target coverage and organs at risk (OAR) using these 2 different techniques for treatment planning.

There was no statistical difference in PTV coverage when comparing 3D to conventional 2D planning, the mean dose of PTV 101.6 ±1.2, 101.1 ±1.6 respectively. Similar results was obtained by[19] as there was no statistical difference in PTV coverage when looking at the mean, minimum, maximum, and median doses and the percent volume covered by 95% and 107% of the dose.While there is statistical difference,in our study, when comparing 3D to 2D the,maximum dose 111.36 ±7.68, 106.03 ±3.86.

The Mean dose to OAR were all decreased when comparing 3D to 2D with statistical difference in thyroid (P =0.0004)and heart (P=0.01), while Mean dose to OAR were all increase when comparing 3D to 2D with statistical difference in kidneys (P =0.0002)and LT eye (P=0.008).In Parhar et al study the Mean dose to OAR were all decreased when comparing 3D to 2D as follows: heart 5%, liver 13.5%, kidneys 31%, lungs 16.3%, bowel 28% but with no statistical significant results($p<0.05$),also their study showd that mean dose to OAR were all decreased when comparing IMRT to 3D as follows: heart 11.3%, liver 12%, thyroid 2%, kidneys 22%, bowel 8%($p<0.05$) [18]. In our study we have compared conventional plans against conformal. The conventional plan led to inadequate coverage of the PTV in all the patients with the median isodose covering the 95% PTV being 98.11%. The average minimum target dose (Dmin) in the PTV for conformal plans was 22.72% as against 51.67% for the conventional plans and 95.44% for conformal plans. In all patients, the area of miss was the cribriform plate.

Vijay M. Patil, et al compared plans generated using SFOP guidelines against an in-house developed shielding and a conformal plan based on segmentation of the CTV. The SFOP plan led to inadequate coverage of the PTV in all the patients with the median isodose covering the 95% PTV being 98.11%. However, the average minimum target dose (D min) in the PTV for SFOP plans was 22.72% as against 51.67% for the In-house.plans and 95.44% for conformal plans. In all patients, the area of miss was the cribriform plate[17].

D S SHARMA et al compared 3DCRT, IMRT_LA and IMRT_Tomo plans in previously treated patients with medulloblastoma the results of this comparison were the mean volume of each PTV receiving at least 95% of the prescribed dose (V95%) was.98% for all plans. All plans resulted in a comparable dose homogeneity index (DHI) for PTV_brain. For PTV_spine, IMRT_Tomo achieved the highest mean DHI of 0.96, compared with 0.91 for IMRT_LA and 0.84 for 3DCRT. The best dose conformity index was achieved by IMRT_Tomo for PTV_brain (0.96) and IMRT_LA for PTV_spine (0.83). The IMRT_Tomo plan was superior in terms of reduction of the maximum, mean and integral doses to almost all organs at risk (OARs). It also reduced the volume of each OAR irradiated to various dose levels, except for the lowest dose volume. The beam-on time was significantly longer in IMRT_Tomo. they concluded that IMRT_Tomo for CSI is technically easier and potentially dosimetrically favourable compared with IMRT_LA and 3DCRT. IMRT for CSI can also be realised on a conventional linear accelerator even for spinal lengths exceeding maximum allowable field sizes. The longer beam-on time in IMRT_Tomo raises concerns about intrafraction [19].

Conclusion

The study showed that no statistical difference in PTV coverage, and was noted to have reductions in maximum dose of PTV and some selected organs at risk (both eyes, thyroid, Dental area). Further study comparing 3DCRT planning with IMRT is needed to analyse the dose uniformity in CSI.

References

1. Curran EK, Le GM, Propp JM, et al: Gender affects survival from medulloblastoma only in older children and adults: a study from the Surveillance Epidemiology End Results Registry. Pediatr Blood Cancer 2009; 52:60-64.
2. Packer RJ, Gajjar A, Vezina G, et al: Phase III study of craniospinal radiation therapy followed by adjuvant chemotherapy for newly diagnosed average-risk medulloblastoma. J Clin Oncol 2006; 24:4202-4208.
3. Gajjar A, Chintagumpala M, Ashley D, et al: Risk-adapted craniospinal radiotherapy followed by high-dose chemotherapy and stem-cell rescue in children with newly diagnosed medulloblastoma (St Jude Medulloblastoma-96): long-term results from a prospective, multicentre trial. Lancet Oncol 2006; 7:813-820.
4. Rutkowski S, Bode U, Deinlein F: Treatment of early childhood medulloblastoma by postoperative chemotherapy alone. N Engl J Med 2005; 352:978-986.
5. Kortmann RD, Timmermann B, Becker G, Kühl J, Bamberg M: Advances in treatment techniques and time/dose schedules in external radiation therapy

of brain tumours in childhood. Klin Pädiatr, 210: 220-226, 1998.
6. Mah K, Danjoux EC, Manship S, Makhani N, Cardoso M, Sixel KE. Computed tomographic simulation of craniospinal fields in pediatric patients: improved treatment accuracy and patient comfort. Int J Radiat Oncol Biol Phys 1998;41:997–1003.
7. Parker WA, Freeman CR. A simple technique for craniospinal radiotherapy in the supine position. Radiother Oncol 2006;78:217–22.
8. Parker W, Filion E, Roberge D, Freeman CR. Intensitymodulated radiotherapy for craniospinal irradiation: target volume considerations, dose constraints and competing risks. Int J of Radiat Oncol Biol Phys 2007;69:251–7.
9. Chojnacka M, Skowrońska-Gardas A. Medulloblastoma in childhood: Impact of radiation technique upon the outcome of treatment. Pediatr Blood Cancer 2004;42:155-60.
10. del Charco JO, Bolek TW, McCollough WM, Maria BL, Kedar A, Braylan RC, et al. Medulloblastoma: Time-dose relationship based on a 30-year review. Int J Radiat Oncol Biol Phys 1998;42:147-54.
11. Halperin EC. Impact of radiation technique upon the outcome of treatment for medulloblastoma. Int J Radiat Oncol Biol Phys 1996;36:233-9.
12. Jereb B, Krishnaswami S, Reid A, Allen JC. Radiation for\ medulloblastoma adjusted to prevent recurrence to the cribriform plate region. Cancer 1984;54:602-4.
13. Taylor RE, Bailey CC, Robinson KJ, Weston CL, Ellison D, Ironside J, et al. Impact of radiotherapy parameters on outcome in the International Society of Paediatric Oncology/United Kingdom Children's Cancer Study Group PNET-3 study of preradiotherapy chemotherapy for M0-M1 medulloblastoma. Int J Radiat Oncol Biol Phys 2004;58:1184-93
14. Miralbell R, Bleher A, Huguenin P, Ries G, Kann R, Mirimanoff RO, et al. Pediatric medulloblastoma: Radiation treatment technique and patterns of failure. Int J Radiat Oncol Biol Phys 1997;37:523-9.
15. Miralbell R, Fitzgerald TJ, Laurie F, Kessel S, Glicksman A, Friedman HS, et al. Radiotherapy in pediatric medulloblastoma: Quality assessment of Pediatric Oncology Group Trial 9031. Int J Radiat Oncol Biol Phys 2006;64:1325-30.
16. Uozumi A, Yamaura A, Makino H, Miyoshi T, Arimizu N. A newly designed radiation port for medulloblastoma to prevent metastasis to the cribriform plate region. Childs Nerv Syst 1990;6:451-5.
17. Vijay M. Patil, Arun S. Oinam, Santam Chakraborty, et al: Shielding in whole brain irradiation in the multileaf collimator era: Dosimetric evaluation of coverage using SFOP guidelines against in-house guidelines, J Cancer Res Ther - April-June 2010 - Volume 6 - Issue 2
18. P.K. Parhar,C. Hitchen,T. Duckworth,et al: Comparison of the Dosimetry of Spinal Fields in Craniospinal Irradiation using Two Dimensional, Three Dimensional and Intensity Modulated Radiation Therapy Planning Techniques, International Journal of Radiation Oncology * Biology * Physics Volume 72, Issue 1, Supplement, Page S211, 1 September 2008
19. D S SHARMA, MSc, DipRP, T GUPTA et al: High-precision radiotherapy for craniospinal irradiation: evaluation of three-dimensional conformal radiotherapy, intensitymodulated radiation therapy and helical TomoTherapy; The British Journal of Radiology, 82 (2009), 1000–1009

Conflict of Interest Statement: The authors declare that there are no competing interests. This research paper was financed totally by the authors of the study.