Shielding in whole brain irradiation in the multileaf collimator era: Dosimetric evaluation of coverage using SFOP guidelines against in-house guidelines

ABSTRACT

Aim: Compare the planning target volume (PTV) coverage in three different shielding techniques in cranial irradiation.

Settings and Design: Tertiary care center, prospective study.

Materials and Methods: The whole brain and meninges were contoured in ten planning CT scans, and expanded by 5 mm for the PTV. Shielding was designed using the French Society of Pediatric Oncology (SFOP) guidelines (SFOP plan), in-house recommendation (with 1 cm margin from the orbital roof and sphenoid wing) on digitally Reconstructed Radiograph (DRR) and a third plan was generated using a 3D conformal radiation technique (3DCRT). The coverage of the PTV was noted using the isodose covering 95% of the PTV (D95), minimum dose within the PTV (Dmin), and maximum dose within the PTV (Dmax). The location of PTV not covered by the 95% isodose curve was noted. The median dose and maximum dose (Dmax) to both eyes and maximum dose (Dmax) for the lens were noted.

Statistical Analysis: General linear model method repeated the measure of analysis of variance test (ANOVA).

Results: PTV coverage was significantly poorer in the SFOP and in-house plans as compared to 3DCRT plan (P=0.04). Median volume of PTV not covered by 95% isodose curve was 4.18 cc, 1.01 cc, and 0 cc in SFOP, in-house, and 3DCRT plan, respectively.

Conclusions: In the absence of volumetric planning techniques, SFOP guidelines lead to inadequate coverage and the in-house method is recommended.

KEY WORDS: Brain metastasis, cranial irradiation, radiotherapy planning

INTRODUCTION

In the management of many malignant neoplasms, whole brain with its meningeal covering forms a part of the clinical target volume (CTV). Common indications of conformal whole brain radiation when administered with curative intent include craniopharyngioma for medulloblastomas, and prophylactic cranial irradiation (PCI) in acute lymphoblastic lymphoma (ALL), and small cell lung cancer. While the dose, time, and fractionation in each setting may differ, the delivery technique remains essentially the same. Parallel opposed, two lateral portals are utilized, with added customized shielding to protect the surrounding critical structures.

The area around the cribriform plate is considered to be gravity-related sanctuary site. However, due to its proximity to the ocular structures, it often gets shielded in cranial radiation. In medulloblastoma and ALL, nearly 15-20% of recurrences occur at this site which is attributed to overzealous shielding. This emphasizes the importance of a proper technique for designing the shield in cranial radiation. There are various techniques reported in the literature of designing the shield. The standard German helmet technique has been criticized as it leads to inadequate coverage of the cribriform plate. In 1999, SFOP (French Society of Pediatric Oncology) gave guidelines for design of cranial shielding in medulloblastoma, which have been subsequently adapted for use in other indications where whole brain radiation is required. A similar but modified guideline for design of cranial shield is used at our center.

The use of 3D conformal radiation technique (3DCRT) for whole brain radiation has been studied, as it uses the 3D dataset designing of the beam portals and the shield in cranial radiation is near perfect. However, the resources required for this method of radiation are not widely available.

The study was designed to compare the adequacy of PTV coverage and dose delivered to the ocular...
structures by using the shielding technique recommended by the SFOP, shielding technique developed in-house and that designed by three-dimensional conformal planning.

MATERIALS AND METHODS

Planning CT (computed tomography) scans of whole brain of ten patients who had been treated for various intra-cranial malignancies were retrieved from the database. Care was taken to preserve patient anonymity by copying these CT scans in a protocol-specific dataset after purging data pertaining to identification of the patient.

All planning CT were helical scans with 2.5 mm slices at 120 KvP and 250–300 mA, acquired in the CT simulator Light Speed® VFX-16 (GE Health Care Ltd, Waukesha, WI, USA). Six patients were immobilized with a three-point thermoplastic cast (Efficast, Meditrons) and the rest with a five-point. Four scans were acquired in the prone position, while remaining scans were in the supine position. The neck was in the extended position in all the scans selected for the purpose of the study.

For the purpose of the study, the CTV delineation was performed on Advantage Sim Workstation 4.3 (GE Medical Systems, Waukesha, WI, USA) using setting for Head CT (window width 100 and Mean 40). Whole of the brain with its meninges was designated as the CTV. As the meninges are not visualized in CT, whole of brain till the inner cortex of the skull was included in the CTV as shown in Figure 1. The CTV was contoured till second cervical vertebra. The cribriform fossa was taken as a part of the cranial CTV which also included the thin bony orbital roof. No special attempt was made to contour the gross tumor volume (GTV). Both eyes and lens were also contoured separately as avoidance structures. PTV was generated from the CTV with an isotropic margin of 5 mm. This margin was selected based on our departmental assessment audit and was specific for the patients with brain tumors both in supine and prone positions. These scans and structure set were transferred to the Eclipse treatment planning system version 8 for planning and dose calculation.

Two parallel opposed lateral cranial portals were placed using an isocentric technique with the isocenter placed in the patients’ midline. Three different types of cranial shielding were designed in the digitally reconstructed radiographs in the Eclipse planning system in the lateral cranial fields in each of these patients for the study purpose.

1. First technique (SFOP plan): Here the shielding was designed in accordance with SFOP guidelines. The guidelines specify a block margin of 0.5 cm below the roof of the orbit, 1 cm in front of the anterior most projection of the greater wing of sphenoid, 0.5 cm below the base of skull, 0.5 cm in front of the anterior edge of the upper two cervical vertebrae and 1 cm from the outer table of the skull in the remaining directions6 [Figure 2].

2. Second technique (in-house plan): In the in-house plan, a block margin of 1 cm below the roof of the orbit and 1 cm in front of the anterior most projection of the greater wing of sphenoid are given. Remaining margins are similar to SFOP guidelines as mentioned above [Figure 2].

3. Third technique (conformal plan): Shielding designed by using the multileaf collimators (MLCs) fit and shield software in the Eclipse treatment planning system with a block margin of 0.7 cm from the PTV. MLC leaves were constrained to intersect outside the margin during this planning process in order to ensure that excess shielding of the PTV did not occur due to the jagged nature of the MLC-defined field border.

All shielding was done with MLC Varian Millennium 80 MLC

Figure 1: Depicting the delineation of CTV (brain till inner cortex) and PTV. Note that the PTV has gone nearly as far as the anterior compartment of the eyes

Figure 2: (Panel A) SFOP shielding used. (Panel B) In-house shielding used. The distance of orbital roof from the shielding (A) was 5 mm and 10 mm in SFOP and in-house plan, respectively. The distances B, C and D were 10 mm, 10 mm, and 5 mm, respectively, in both plans.
which provides 40 leaves with a projected width of 1 cm at the isocenter. In all plans, the MLC were placed outbound.

Dose calculation was done in the midline at the plane of maximum cranial separation and the coordinates of the point of calculation being kept same for each patient for all the three techniques.

The minimum isodose surface which covered the 95% of PTV, minimum dose ($D_{\text{min}}$) in PTV, maximum dose ($D_{\text{max}}$) in PTV, and the volume of the PTV which was not covered by 95% of the prescribed dose were noted.

The volume within the PTV within the 95% isodose envelope was converted into a dummy structure which then was subtracted from the PTV using the Boolean operator feature in the Eclipse treatment planning system. The location of remaining PTV (PTV miss) was noted for all the three plans. The $D_{\text{max}}$ and the median dose to both eyes and lens were recorded

Statistical analysis
Comparison of the dosimetric and volumetric parameters noted above in between the three plans was done by the GLM method repeated measure ANOVA test using SPSS version 12. A $P$ value of less than 0.05 was taken as statistically significant. Greenhouse-Geisser correction and Huynh-Feldt corrections were performed when the assumption of sphericity were violated. Corrections were applied when the value of epsilon, which is a measure of sphericity, was less than 1. The Greenhouse-Geisser correction was done when the epsilon value was below 0.75 and Huynh-Feldt correction when it was more than 0.75.

RESULTS

The median of the percentage isodose curve which covered the 95% of the PTV were 98.11, 98.22, and 98.22 in the SFOP plan, in-house plan, and conformal plan, respectively. The details of coverage of the PTV for each patient are given in Table 1.

A repeated measure ANOVA with Greenhouse-Geisser correction conducted indicated that there was a statistically significant difference in the percentage isodose curve which covered 95% of PTV in the three plans with $F(1.06,9.55) = 10.95, P=0.008, R^2 = 0.55, \eta^2=0.55$. Means of the percentage isodose curve which covered the 95% of the PTV was 98.04%, 98.17%, and 98.16% in the SFOP plan, in-house plan, and conformal plan, respectively, suggesting that the coverage was poor with the SFOP plan.

The median values of the $D_{\text{max}}$ in the PTV were 16.35%, 61.55%, and 95.5% in the SFOP plan, in-house plan, and conformal plan, respectively. A repeated measure ANOVA with Huynh Feldt correction indicated that there was a statistically significant difference in the $D_{\text{max}}$ in the PTV in the three plans, $F(1.52,13.70) = 4.06, P = 0.04 , R^2 = 0.31, \eta^2=0.31$. Means of the $D_{\text{max}}$ in the PTV were 22.72, 51.67, and 95.44 in the SFOP plan, in-house plan and conformal plan, respectively, suggesting that the minimum dose in the PTV was lower with SFOP plans and in-house plan.

The median values of the $D_{\text{max}}$ in the PTV were 107.35% in all three plans. A repeated measure ANOVA with Greenhouse-Geisser correction conducted indicated that there was no statistically significant difference in the $D_{\text{max}}$ in the PTV in the three plans, $F(1.00, 9.01) = 0.56, P=0.818, R^2=0.006, \eta^2=0.006$. Means of the $D_{\text{max}}$ in the PTV were 107.09, 107.13, and 106.99 in the SFOP plan, in-house plan, and conformal plan, respectively, suggesting that the maximum dose in the PTV was nearly similar in the three plans.

The mean volume of the PTV contoured was 1631.66 cc (range 1481.90-1887.30). The location of PTV miss is shown in Figure 3. There was miss in all of SFP and in-house plans, while there were none in conformal plans. The PTV miss was located over and near the cribriform plate in all the SFOP and in-house plans. The median volumes of the PTV miss were 4.18 cc and 1.01 cc respectively in SFOP and in-house plans. A repeated measure ANOVA with Greenhouse-Geisser correction conducted indicated that there was a statistically significant difference in the volume of the PTV miss in the three plans, $F(1.19, 10.70) = 26.40, P<0.001, R^2=0.746, \eta^2=0.746$. Mean

### Table 1: Showing the PTV coverage parameters. The values of $D_{\text{max}}$ and $D_{\text{min}}$ are in terms of percentage of the prescribed dose

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>SFOP plan</th>
<th>In-house plan</th>
<th>Conformal plan</th>
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</table>
volumes of the PTV miss were 3.96 cc, 1.14 cc, and 0 cc in the SFOP plan, in-house plan, and conformal plan, respectively, suggesting again that the coverage was poor with the SFOP plan.

The median dose and the maximum dose received by the eyeball and lens are shown in Table 2. The conformal plans as can be seen in the table have lead to an increased dose to the ocular structures. The median dose and the $D_{\text{max}}$ is more in conformal plan. Also the $D_{\text{max}}$ for lens are higher and well above the TD5/5 for cataract if a prescription above 18 Gy is given in the conformal plans.\[14\]

Comparison of the $D_{\text{max}}$ and median dose to the eye showed a statistically significant difference between the three plans with $P$ values of 0.008 and < 0.001, respectively. The $D_{\text{max}}$ of the lens also varied significantly between three plans with a $P$ value of < 0.001. The examination of the means for doses received in the ocular structures from Table 2 indicates that higher dose was received by the ocular structures in conformal plans.

DISCUSSION

The use of whole brain radiation (WBI) in brain metastasis and as PCI in ALL is associated with improvement in quality of life and survival.\[1,5,15\] In medulloblastoma irrespective of the risk group cranio-spinal irradiation (CSI) with or without chemotherapy is the standard of treatment in postoperative setting.\[3,4,6-10,13,16-18\] In such situations, the use of a proper technique for the adequate coverage of PTV is of prime importance.

The use of radiation in medulloblastoma especially is technically demanding and biologically unforgiving with inadequate coverage of PTV leading to high incidences of neuraxial recurrences which is supported by studies in Table 3. Similar studies have been reported in ALL too. The importance of coverage of the cribriform plate has been stressed by Chatani et al.\[19\] An improved method of cranial radiation was proposed by Pla et al, in ALL in which the importance of not only inclusion of retro-orbital tissue but also treatment of this region with same dose as whole of the brain was stressed.\[11\]

It is noticeable that trials post 1999 have used shielding design similar to that suggested by SFOP for quality assurance purpose. In some studies distance of the block margin from the temporal bones was reduced but the distance of orbital roof from the shielding block was 5 mm.\[3,6,13,17\]

In the study by Chojanacka et al, out of evaluable patients, 27% of patients had a supratentorial failure in spite of correct shielding.\[7\] Similar result can be seen in SIOP/UKCCSG PNET 3 study reported by Taylor et al, where in spite of fields been labeled accurate in nearly 78% of patients, 15.5% of these patients failed in the region of the cribriform plate.\[13\] The distance of 5 mm between the shielding block and cribriform plate does lead to under coverage of the PTV as seen in the present study which may be an explanation for these results.

In our study we have 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 ($D_{\text{min}}$) in the PTV for SFOP plans was 22.72% as against 51.67% for the In-house
Table 2: Dose in terms of % of the dose prescribed received. The $D_{\text{max}}$ and median doses of the eye are average of the $D_{\text{max}}$ and median doses received by left and right eye, respectively. The $D_{\text{max}}$ dose of the lens is an average of the $D_{\text{max}}$ of left and right lens.

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Table 3: Details of various studies dealing with impact of target deviation in cranial portals in medulloblastoma

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*Used SFOP shielding design near cribriform plate for quality assurance; Figures within parentheses are percentages; NA: not assessed.

The biological consequences of this miss can be better appreciated if we consider the dose response curves of medulloblastoma and ALL cell lines. Halprein et al have demonstrated that the surviving fraction increases from 0.29 to 0.33 in medulloblastoma human cell line D283($D_0=1.2$ Gy), when the dose delivered per fraction is reduced from 1.5 to 1.35 Gy. Extrapolating these to more radioresistant cell lines of medulloblastoma($D_0=1.8$ Gy), the impact of this sparing effect would be further amplified. Use of proper radiotherapeutic techniques is thus of foremost importance in radiosensitive tumors in order to achieve good clinical results, and cranial radiation in medulloblastoma and ALL is no exception to this rule.

The failures caused by the improper technique of radiation in both medulloblastoma are difficult to salvage. In the series reported by Lal et al, all seven patients with recurrence eventually succumbed to it. In a recent analysis by Massimino et al, it was concluded that cure with second-line myeloablative schedules still remains a myth, despite the responses which are obtained by these second line schedules. In this series, out of 14 assessable patients 12 had a response; however, only one patient survived over 13 months. These responses came at a cost of substantial toxicity as highlighted by the same study in which grade 4 neutropenia was observed universally.

Bowers et al have further showed that in children older than 3 years who receive radiation, site of tumor progression was an independent prognostic factor determining survival. Patients having recurrence in posterior fossa fared better than those in the supratentorial region ($P=0.017$ on log rank analysis).

In ALL, the salvage of cranial recurrence has been more successful with Kumar et al reporting 10 out of 18 patients successfully salvaged, however, it came at the cost of substantial toxicity which were well managed in this trial. The ability of managing such toxicities in a third world health setup is questionable.

Similar results of successful salvage of isolated CNS relapses post prophylactic cranial irradiation have been reported by Ritchey et al, where 100% of patient achieved second remission, as the 4 year event free survival was 71%. But with due consideration of the toxicity, the additional cost of repeated treatment and its psychological impact on the patient and family it should be a priority to ensure adequate coverage of the whole brain with its meninges while doing prophylactic cranial radiation itself.

In our study, MLCs were used for shielding as opposed to customized shielding blocks. Due to these step ladder pattern created by MLCs, there was a poor conformity between the intended area to shield and that achieved. However, care was
taken while designing the shields with MLC that minimum distances required in both SFOP and in-house design from bone land marks were obtained (outbound placement). The use of customized blocks is therefore better than use of MLC. However, use of MLC is a time, resource saving alternative and is proven to be equal to customized blocks in various studies.\[24,28\] In this era of MLCs, most of the institute use MLCs over customized shielding block due to their advantages highlighted in the previous line. The shielding in this study was designed on a digitally reconstructed radiograph. However, it is difficult to locate the cribriform plate on a digitally reconstructed radiograph or simulator films.\[26\] In addition, anatomical variation if any cannot be guessed from the bony landmarks. The point is well stressed by a study from Turkey by Erdem \textit{et al}, where the variation of the cribriform plate with respect to the roof of the ethmoids which is in close proximity to the roof of the orbit can vary from 1 to 15 mm.\[27\] Use of conformal planning in these cases is important, especially in young patients who are treated radically in whom the consequences of a PTV miss would be disastrous. The authors are also aware of the fact that using finer MLC might have resulted better conformity as compared to the use of 1 cm MLC. However, in our department all machines are equipped with 1 cm MLC, hence all plans were generated using the same MLC. However, using finer MLC is not likely to change the results as far as coverage is concerned as all leaves were placed in an out-bound setting. The benefit resulted from this is likely to be better shielding of the eyes and lens.

The importance of CT planning in WBRT and in medulloblastoma has been stressed by Gripp \textit{et al}, where the geographical miss in the subfrontal region was reduced from 28% to 0% when CT planning was done as opposed to 2D planning.\[29\] Kortmann \textit{et al} too showed that standard German helmet technique used by 2D planning missed in 52% of patients the CTV near the subfrontal region and middle cranial fossa, and in addition the set displacements around a 1 cm in either direction were noted. It was recommended to do CT examination for these patients and to give a safety margin of 1 cm for the set up errors.\[28\] Mah \textit{et al}, found that CT-based conformal planning is less time consuming, more accurate, and provides better dose homogeneity while planning craniospinal radiation.\[28\] Andic \textit{et al}, has reported a significant improvement in coverage of the retro-orbital area with 3D conformal radiation as opposed to the standard German helmet technique and D\textsubscript{20} of 59% with 2D plans as compared to 95% in 3D conformal plans.\[29\] It is to be noted that shielding guideline used in this study was not in accordance with the SFOP.

However, in developing countries, underdeveloped countries and even in some developed countries the facility of CT simulator is not often available.\[31,32\] In the absence of volumetric planning techniques, SFOP guidelines for shielding in CSI lead to an inadequate coverage, so the method of in-house shielding described in the present study may be recommended. Our recommendation differs from those given by Kortmann \textit{et al}, as a less margin is specified below the base of the skull and in front of the cervical vertebrae, which can potentially spare a greater volume of pharyngeal mucosa.

The dose to the lens in conformal and in-house plans was much higher than the tolerance limits.\[14\] But with the advancement in cataract surgery in children, the fear of this complication should not lead to inadequate coverage of PTV.\[33\] The dose delivered into whole brain in CSI in radical setting for medulloblastoma is in range of 3600 cGy and in metastasis in range of 4000 cGy. These are well below the tolerance limits of retina.\[14,34\] So concern for ocular toxicity is unjustifyable.

REFERENCES


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