High-precision radiotherapy for craniospinal irradiation: evaluation of three-dimensional conformal radiotherapy, intensity-modulated radiation therapy and helical TomoTherapy

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ABSTRACT. This study aimed to establish the feasibility of intensity-modulated radiation therapy (IMRT) in craniospinal irradiation (CSI) using conventional linear accelerator (IMRT_LA) and compare it dosimetrically with helical TomoTherapy (IMRT_Tomo) and three-dimensional conformal radiotherapy (3DCRT). CT datasets of four previously treated patients with medulloblastoma were used to generate 3DCRT, IMRT_LA and IMRT_Tomo plans. A CSI dose of 35 Gy was prescribed to the planning target volume (PTV). IMRT_LA plans for tall patients were generated using an intensity feathering technique. All plans were compared dosimetrically using standardised parameters. The mean volume of each PTV receiving at least 95% of the prescribed dose ($V_{95\%}$) 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. In conclusion, 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 motion and whole-body integral doses.

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Medulloblastoma is the most common malignant neoplasm of the central nervous system in children, constituting approximately 20% of all paediatric brain tumours [1]. The last two decades have witnessed tremendous advances in technology and biology, resulting in an improved outcome for these children [2–4] owing to refinements in micro-neurosurgery, more effective chemotherapy regimens and modern radiotherapy techniques. A more mature understanding of the biology of disease has led to a contemporary clinicobiological risk stratification system for assigning prognosis and deciding treatment [5]. The current standard of care consists of maximal safe resection followed by radiotherapy and chemotherapy, yielding a 5-year survival rate of $>80\%$ for average-risk medulloblastoma and $>50\%$ for high-risk disease [4].

Radiotherapy for medulloblastoma entails irradiation of the entire neuraxis, *i.e.* craniospinal irradiation (CSI) with a homogeneous dose. This still remains one of the

most technically challenging processes in radiotherapy planning and delivery because of the need to irradiate a very large and complex shaped target volume uniformly. With continuous improvements in long-term survival, particularly in children with average-risk medulloblastoma, there is a growing concern regarding treatment-related long-term side effects. These include neurocognitive decline, hearing impairment, growth retardation, endocrine dysfunction, cataract formation, cardiomyopathy, impaired fertility and second malignancies. The majority of these late effects are dose- and volume-related, and form the basis of reduced dose CSI (23.4 Gy) for average-risk disease in conjunction with chemotherapy [6], and are the clinical motivation for investigating sophisticated emerging radiotherapy techniques to reduce doses to non-target tissues to ameliorate toxicity.

Field shaping for CSI has evolved from traditional bony landmarks using two-dimensional (2D) planar radiographs to the more recent CT simulation techniques [7, 8]. 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

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been made in an effort to improve target volume coverage, dose homogeneity and conformity. Parker et al [9] have recently reported the feasibility of conventional linear accelerator (LA)-based intensity-modulated radiotherapy (IMRT) for CSI in small children. However, even with this advanced technique, matching of cranial and spinal fields is an unavoidable situation in LA-based IMRT for CSI. This problem is further compounded in older children and adolescents, in whom the spinal lengths often exceed the allowable maximum field sizes, necessitating a second spinal–spinal junction. Helical TomoTherapy has emerged as a revolutionary and novel approach to radiation treatment, whereby a 6 MV LA mounted on a ring gantry continuously rotates around the patient to deliver radiation in helical mode as the patient is transported through the ring, allowing treatment to large cylindrical volumes of up to $40 \times 160 \text{ cm}^2$. This unique feature of TomoTherapy has been explored for CSI [10, 11], with promising dosimetric results. However, to the best of our knowledge, no formal dosimetric comparison has been made between conventional three-dimensional conformal radiotherapy (3DCRT) and IMRT, either with conventional LA (IMRT_LA) or Helical TomoTherapy (IMRT_Tomo), for CSI using the same patient dataset. The aim of this study was to establish the feasibility of performing IMRT using conventional LA for CSI in medulloblastoma patients of differing spinal lengths and to compare it dosimetrically with 3DCRT and Helical TomoTherapy.

Methods and materials

The CT datasets of four paediatric and adolescent female patients (mean age, 9 years; range, 5–14 years) with medulloblastoma previously treated with 6 MV photons employing conventional 2D bony landmark-based field shaping were included into this retrospective dosimetric study. All patients were immobilised in the prone position using customised thermoplastic masks on an adjustable prone head rest (MedTec, Orange City, IA) for head support and vacuum cradle for body support. Planning CT images were acquired from the vertex to the coccyx on a Somatom Sensation multislice CT scanner (Siemens Medical System, Erlangen, Germany) with 5 mm contiguous slice thickness and then transferred via a network to a Coherence Dosimetrist contouring workstation (Siemens Medical System), where the target volumes and OARs were outlined. Target volume delineation was performed in accordance with internationally accepted guidelines [12]. Brain and spinal targets volumes were contoured separately and not as a single volume. This was necessary to maintain uniformity and consistency in planning across the three chosen techniques. The clinical target volume (CTV) of the brain (CTV_brain) included the entire brain and meninges, whereas the CTV of the spine (CTV_spine) included the entire spinal canal until the termination of the thecal sac, including the cerebrospinal extension to the spinal ganglia. The planning target volumes (PTVs) of the brain (PTV_brain) and spine (PTV_spine) were generated by growing a uniform volumetric margin of 5 mm in all directions over the corresponding CTVs. OARs outlined included the eyes, thyroid, heart, lungs, oesophagus,

liver and kidneys. The ovaries were not contoured in any of these four patients as they were difficult to identify in the CT scans of the two younger patients.

Treatment planning

The CT datasets along with the contours of each patient were exported to an Eclipse (V 7.3.1; Varian Associates, Palo Alto, CA) treatment planning system (TPS) and TomoTherapy Planning Station (V 2.2.4; TomoTherapy Inc., Madison, WI) using a Dicom RT protocol. Of the four patients included, two were relatively tall with measured PTV_spine lengths of 38.5 cm and 48 cm. The Eclipse TPS used for the planning has been configured and commissioned for 6 MV X-rays from a Clinac 6EX LA (Varian Associates, Palo Alto, CA) equipped with a Millennium 120 multi-leaf collimator (MLC). The 60 pairs of the MLC with variable projected leaf widths of 0.5 cm and 1 cm at the isocentre can define a maximum field size of $40 \times 40 \text{ cm}^2$ and support intensity modulation in dynamic MLC mode. It uses an iterative method for the inverse optimisation and convolution–superposition for dose computation [13, 14]. TomoTherapy supports only helical IMRT planning for 6 MV X-rays using a binary MLC with 0.625 cm projected leaf width at the isocentre and uses an inverse treatment planning process based on iterative least squares minimisation of an objective function [15]. As part of the optimisation, the dose is calculated using a superposition–convolution algorithm [16, 17].

For each patient, three separate treatment plans — a conventional 3DCRT plan, an IMRT plan on conventional LA (IMRT_LA) and a TomoTherapy plan (IMRT_Tomo) on Helical TomoTherapy — were generated. In all plans, a total dose of 35 Gy in 21 fractions with 1.67 Gy per fraction was prescribed such that at least 95% of the volume of both PTVs (PTV_brain and PTV_spine) received at least 95% of the prescription dose, while restricting the maximum dose limit to 107% as recommended by the International Commission on Radiation Units and Measurements Report 50 (ICRU-50) [18]. Moreover, considerable efforts were made to reduce the dose to all OARs.

3DCRT planning

Conventional 3DCRT plans were generated for each patient on an Eclipse TPS using 6 MV X-rays. A fixed-beam geometry was used, employing two bilateral half-beam blocked cranial fields, collimated to match the divergence of the direct posterior spinal field. The details of the fixed geometry planning technique used in our study have been described previously [8]. Cranial bilateral beams and spinal fields were shaped based on the three-dimensional shape of both PTVs (PTV_brain and PTV_spine) using a Millennium MLC. MLC positions were edited to reduce the dose to the OARs without compromising the target coverage. Dose was prescribed and normalised to the reference point at the geometric centre of the PTV_brain. The spinal field was weighted to achieve optimal coverage of the PTV_spine. For both

patients with large spinal lengths, two adjacent direct spinal fields were dosimetrically matched to cover the entire spinal length.

IMRT_LA planning

IMRT using conventional LA (IMRT_LA) is the summation of two separate plans — one for PTV_brain and the other for PTV_spine — using 6 MV photons on an Eclipse TPS. The spinal PTV was first planned using a five-field inverse planning technique using five posterior fields with gantry angles of 0° , $\pm 20^\circ$ and $\pm 50^\circ$. The isocentre was set at the geometrical centre of the PTV_spine in the cranio-caudal direction (Y) and at the midline and midplane at the level of the C2–C3 vertebral body for the depth (Z) and lateral (X) position. A total dose of 35 Gy was prescribed and normalised to the spinal isocentre. In the absence of availability of benchmark dose-volume constraints, the optimisation was driven until the OAR dose could be reduced without compromising on target volume coverage or increasing hot spots. Once an optimum IMRT plan was achieved for PTV_spine, a separate plan was created for the cranial target. The isocentre for the cranial fields was set at the most inferior slice of the PTV_brain while maintaining the depth (Z) and lateral (X) co-ordinates of the PTV_spine plan. Lateral opposed half-beam blocked fields each individually shaped to the beam's-eye-view projection of the target with a MLC were used in this plan. While shaping the cranial fields, a uniform margin of 1 cm was added around the PTV_brain, except for the caudal direction, to account for penumbra and thereby improve target coverage. MLC positions were graphically edited to reduce the dose to the OARs without compromising target coverage. The dose distribution was calculated and the dose was prescribed and normalised to the reference point at the geometric centre of the PTV_brain. Appropriate collimator angles were used to match the dose gradient from the IMRT spine plan. Both spinal and cranial plans were summated dosimetrically to achieve the composite final plan (IMRT_LA) for the entire craniospinal axis.

In the two tall patients, the entire spinal length was split in four sections, as shown in Figure 1. IMRT plans (P1 and P2) were created separately for the upper and lower spine using the same beam geometry (five fields), as described for the shorter patients, and intensity feathering technique. In this technique, component beams overlap with each other by a small pre-specified amount, and the intensity in the overlap region gradually decreases for one field component and increases for the other. Thus, the middle two sections, MS1 and MS2, were used to create a contemporary dose gradient from both plans P1 and P2, such that the dosimetric sum represents the composite IMRT plan for PTV_spine and achieves a homogeneous dose in the abutment region. PTV_brain was planned using a separate forward plan (P3), as described earlier. Sufficient care was taken to match the cranial and spinal plans dosimetrically with acceptable dose variation. The dosimetric summation of P1, P2 and P3 represents the IMRT_LA plan for taller patients.

Figure 1. The split of PTV_spine into four components to generate the contemporary intensity gradient in IMRT_LA planning using intensity feathering. US, upper spine; LS, lower spine; MS1, upper middle spine; MS2, lower middle spine; PTV, planning target volume; IMRT, intensity-modulated radiation therapy; LA, linear accelerator.

IMRT_Tomo planning

IMRT plans based on Helical TomoTherapy (IMRT_Tomo) were generated for all four patients on a TomoTherapy planning workstation. In all TomoTherapy plans, a fan beam thickness (FBT) of 2.5 cm, pitch of 0.3 and a modulation factor of 3 were used during optimisation and dose computation, based on previously published data [10, 11]. A total dose of 35 Gy was prescribed to both the PTV_brain and PTV_spine. The optimiser in TomoTherapy uses a different algorithm from Eclipse, hence an identical set of dose-volume constraints was not applied. However, an attempt was made to keep the constraints similar and the optimisation was implemented until OAR doses could not be reduced any further without compromising coverage or increasing hot spots. As TomoTherapy can plan long fields, the spinal fields were planned using a single

PTV_spine even for the two tall patients. The directional blocking option available on TomoTherapy was used to partially block some of the OARs, such as the eyes and kidneys. The planning process, inverse planning algorithm and optimisation parameters for TomoTherapy have been described previously in detail [15, 19].

Plan evaluation

The dosimetric outcomes of 3DCRT, IMRT_LA and IMRT_Tomo were compared qualitatively and quantitatively using standardised dose–volume indices in terms of target volume coverage, dose homogeneity, dose conformity, OAR sparing and integral doses (IDs). Target volume coverage and dose homogeneity were assessed as the volume of the PTV receiving at least 95% ($V_{95\%}$) and 107% ($V_{107\%}$) of the prescribed dose, respectively. Dose homogeneity was evaluated quantitatively using the dose homogeneity index (DHI), defined as the ratio between the doses to 95% (D_{95}) and 5% (D_5) of the volume of the PTV. The conformation of therapeutic dose volume to the target volume was estimated using the conformity index (CI) as defined by Paddick [20]:

$$CI = (V_{T,Pi} \times V_{T,Pi}) / (V_T \times V_{Pi}) \quad (1)$$

where $V_{T,Pi}$ is the volume of target enclosed by the prescription dose, V_{Pi} is the volume of tissues including the target covered by the prescription dose, and V_T is the volume of the target. This CI also takes into account the location of the prescription dose volume relative to the target volume. The volumes of each OAR receiving $\geq 80\%$ (high; $V_{80\%}$), $\geq 50\%$ (intermediate; $V_{50\%}$), $\geq 30\%$ (low; $V_{30\%}$) and $\geq 10\%$ (low; $V_{10\%}$) of the prescribed dose were compared among the three techniques for every patient. The ID of both the target volumes and various OARs was calculated using the equation:

$$ID_j = \rho_j V_j D_j \quad (2)$$

where ρ_j , V_j and D_j are the density, volume and mean dose of the organ, respectively, for subvolume j [21]. For this study, we assumed that the organ had a density equal to its mean density and that all subvolumes of the organ received mean dose D .

Results

Dose coverage, uniformity and conformity to target

The sagittal dose distributions resulting from 3DCRT, IMRT_LA and IMRT_Tomo for one of the representative

Figure 2. Mid-sagittal dose distributions with (a) 3DCRT, (b) IMRT_LA and (c) IMRT_Tomo for one of the representative cases having a large spinal length of 48 cm. Red represents 107%, green 95%, yellow 50% and blue 30% of the isodose line. 3DCRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiation therapy; LA, linear accelerator; Tomo, TomoTherapy.

cases with a large spinal length are shown in Figure 2. The cribriform plate was covered by the 95% isodose line in all three techniques. Among the three techniques, 3DCRT shows the highest dose heterogeneity and substantial exit doses along the spinal column. The IMRT_Tomo plan seems to deliver highly homogeneous and conformal doses throughout the craniospinal axis compared with 3DCRT and IMRT_LA.

Quantitative dosimetric parameters related to target coverage, homogeneity and conformity resulting from the three techniques are presented in Table 1. For each technique, dosimetric data are reported as the mean of all four datasets, along with its standard deviation (SD). All plans yielded a comparable mean dose (D_{mean}) to the PTV_brain (~35.5 Gy) and PTV_spine (~36 Gy). The target volume coverage represented by $V_{95\%}$ was >98% in all plans. The best target coverage was seen with the IMRT_Tomo plan, with a mean $V_{95\%}$ (SD) of 99.33% (0.37%) for PTV_brain and 99.88% (0.18%) for PTV_spine. For PTV_brain, the high dose volume within the target represented by $V_{107\%}$ was negligible for all three techniques: mean $V_{107\%}$ was 0% (0%) for 3DCRT; 0.07% (0.08%) for IMRT_LA; and 0.27% (0.07%) for IMRT_Tomo. For PTV_spine, the IMRT_Tomo plan yielded the lowest mean $V_{107\%}$ of 0.24%, compared with 3.04% for IMRT_LA and 34.61% for 3DCRT. All of the three techniques resulted in an homogeneous dose distribution to PTV_brain with a mean (SD) DHI of 0.93 (0.02) both for 3DCRT and IMRT_LA and 0.96 (0.01) for IMRT_Tomo. In the case of the PTV_spine, IMRT_Tomo showed the highest dose homogeneity with a mean DHI (SD) of 0.96 (0.01), compared with 0.91 (0.01) for IMRT_LA and 0.84 (0.03) for 3DCRT. The volume of tissues including the target covered by the prescription dose V_{pi} was comparable (~1715 cm³) between 3DCRT and IMRT_LA plans for PTV_brain, but slightly less (1664 cm³) in the IMRT_Tomo plan. The mean values of V_{pi} for PTV_spine were 630 cm³ for 3DCRT, 171 cm³ for IMRT_LA and 233 cm³ for IMRT_Tomo plan. The difference in V_{pi} among the three techniques primarily led to variation in the mean CI. The best conformation for PTV_brain was achieved with IMRT_Tomo, with a mean CI of 0.96. For PTV_spine, IMRT_LA provided the best conformity, with a mean CI of 0.83. The poorest dose conformation to the target volume (mean CI = 0.23) was observed with 3DCRT for the PTV_spine.

Dose to the OARs

The dose statistics in terms of the maximum (D_{max}) and mean (D_{mean}) dose for each OAR from the three planning techniques of 3DCRT, IMRT_LA and IMRT_Tomo are shown in Table 2. The IMRT_Tomo plan was better with regard to reduction of doses (both D_{max} and D_{mean}) to all OARs except the lungs, for which 3DCRT and IMRT_LA achieved marginally better sparing. The D_{max} to all individual OARs except the lungs was 1.30–2.77 (mean, 2.03) times higher in 3DCRT and 1.21–1.63 (mean, 1.44) times higher in IMRT_LA when compared to IMRT_Tomo. Except for the lungs, D_{mean} to all other OARs was 1.86–3.70 (mean, 2.96) times higher in 3DCRT and 1.18–3.49 (mean, 1.94) times higher in IMRT_LA when compared with IMRT_Tomo. For both lungs, D_{mean} from 3DCRT was 0.7–0.8 times the corresponding values from IMRT_Tomo. The D_{mean} to lungs from IMRT_LA was also marginally better (0.78–0.85 times) than from IMRT_Tomo.

The percentage volumes of each OAR receiving high ($V_{80\%}$), intermediate ($V_{50\%}$) and low doses ($V_{30\%}$ and $V_{10\%}$) of radiation from the three different treatment planning techniques are presented in Tables 3 and 4. IMRT_Tomo was superior to other techniques with regard to reduction of the volume of each OAR irradiated to a certain dose level (percentage of prescribed dose) except for the 10% dose ($V_{10\%}$). The high ($V_{80\%}$) and intermediate ($V_{50\%}$) dose volume of all OARs was almost negligible for IMRT_Tomo. Even the low dose volume ($V_{30\%}$) was considerably reduced for all OARs with IMRT_Tomo, except for the lungs, which was similar to other techniques. The lowest dose volume ($V_{10\%}$) chosen in this study was highest with IMRT_Tomo for most of the OARs. IMRT_LA and IMRT_Tomo plans were comparable in terms of $V_{80\%}$ to most OARs, except for the eyes, whereas $V_{50\%}$ from IMRT_LA was significantly higher for the eyes, thyroid and oesophagus.

Integral dose

The mean ID to the targets and various OARs from the three planning techniques is shown in Table 5. ID to both PTVs was comparable for all three techniques.

Table 1. Dose–volume indices for the three different treatment techniques. All values represent the mean of four patients

Parameters	PTV_Brain			PTV_Spine		
	3DCRT	IMRT_LA	IMRT_Tomo	3DCRT	IMRT_LA	IMRT_Tomo
D_{max} (SD)	37.4 (0.2)	38.6 (1.3)	38.5 (0.5)	42.3 (1.5)	39.2 (1.2)	36.9 (0.3)
D_{min} (SD)	18.5 (6.5)	22.6 (2.0)	18.5 (5.3)	31.8 (1.7)	30.0 (3.4)	31.1 (2.3)
D_{mean} (SD)	35.5 (0.1)	35.5 (0.1)	35.9 (0.2)	37.0 (0.8)	36.3 (0.8)	35.9 (0.2)
$V_{95\%}$ (SD)	98.2 (0.6)	98.3 (0.7)	99.3 (0.4)	99.5 (0.2)	98.8 (1.1)	99.9 (0.2)
$V_{107\%}$ (SD)	0.0 (0.0)	0.1 (0.1)	0.3 (0.1)	34.6 (16.4)	3.0 (1.4)	0.2 (0.5)
DHI (SD)	0.9 (0.0)	0.9 (0.0)	1.0 (0.0)	0.8 (0.0)	0.9 (0.0)	1.0 (0.0)
V_{pi} (SD)	1713 (79)	1715 (89)	1664 (200)	630 (231)	171 (52)	233 (74)
CI (SD)	0.9 (0.1)	0.9 (0.1)	0.9 (0.0)	0.2 (0.0)	0.8 (0.1)	0.6 (0.1)

PTV, planning target volume; D_{max} , maximum dose; D_{min} , minimum dose; D_{mean} , mean dose; SD, standard deviation; $V_{95\%}$, volume covered by 95% of prescription dose; $V_{107\%}$, volume covered by 107% of prescription dose; DHI, dose homogeneity index; V_{pi} , volume covered by prescription isodose; CI, conformity index; 3DCRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiation therapy; LA, linear accelerator; Tomo, TomoTherapy.

Table 2. Maximum ($D_{\max}$) and mean (D_{mean}) doses to various organs at risk when prescribing 35 Gy to the whole craniospinal axis in the three different treatment techniques. All values are the mean of four patients

Organs at risk	$D_{\max}$ in Gy (SD)			D_{mean} in Gy (SD)		
	3DCRT	IMRT_LA	IMRT_Tomo	3DCRT	IMRT_LA	IMRT_Tomo
Left eye	36.3 (0.5)	36.3 (0.5)	18.9 (2.5)	21.3 (4.9)	21.3 (4.9)	8.1 (0.7)
Right eye	36.3 (1.7)	36.3 (1.7)	19.1 (1.3)	19.4 (6.7)	19.4 (6.7)	8.2 (0.6)
Heart	33.1 (1.8)	17.1 (4.2)	11.9 (1.8)	17.8 (2.1)	7.5 (1.0)	5.0 (1.0)
Right lung	35.7 (2.5)	24.5 (3.4)	27.5 (2.5)	4.8 (2.2)	5.2 (1.4)	6.7 (7.3)
Left lung	32.2 (3.2)	26.7 (1.6)	27.0 (3.2)	5.3 (2.4)	5.7 (0.9)	6.7 (3.8)
Thyroid	32.9 (1.9)	17.4 (6.3)	12.0 (1.9)	30.5 (2.5)	12.2 (4.8)	8.3 (2.9)
Right kidney	28.1 (5.9)	17.7 (2.4)	12.2 (5.9)	3.1 (1.7)	5.3 (1.7)	4.5 (0.6)
Left kidney	29.2 (10.8)	19.2 (2.9)	13.7 (10.8)	3.2 (1.5)	5.7 (1.1)	4.5 (0.5)
Liver	31.0 (1.4)	17.9 (2.2)	14.8 (1.4)	7.2 (1.4)	5.3 (0.6)	3.9 (0.6)
Oesophagus	33.1 (2.2)	27.9 (1.5)	17.1 (2.2)	32.7 (2.3)	18.7 (1.8)	9.1 (0.3)

3DCRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiation therapy; LA, linear accelerator; Tomo, TomoTherapy.

IMRT_Tomo plan reduced ID to the majority of OARs, including the eyes, heart, thyroid, liver and oesophagus when compared with 3DCRT and IMRT_LA. The mean ID to the eyes was higher by a factor of 2.64 (left) and 2.36 (right) in 3DCRT and IMRT_LA, whereas the mean ID to the heart was higher by a factor of 3.58 in 3DCRT and 1.50 in IMRT_LA, when compared with IMRT_Tomo. 3DCRT and IMRT_LA plans also resulted in 3.7 and 1.48 times higher ID to the thyroid when compared with IMRT_Tomo. In the 3DCRT plan, ID was higher by a factor of 1.86 for the liver and 3.61 for the oesophagus when compared with the IMRT_Tomo plan. The IMRT_Tomo plan showed an increase in ID to the lungs and kidneys compared with 3DCRT but only the lungs if compared with IMRT_LA. When compared with IMRT_Tomo, the mean ID to lung was reduced by a factor of 0.71 (right) and 0.80 (left) in 3DCRT and 0.78 (right) and 0.85 (left) in IMRT_LA. The 3DCRT plan reduced the mean ID to the kidneys by a factor of 0.7, whereas IMRT_LA increased it by 1.18 times (right) and 1.26 times (left), when compared with IMRT_Tomo.

Time

During treatment, the radiation beam is continuously on in helical TomoTherapy as the ring gantry rotates around the patient who translates through the bore, allowing radiation to be delivered from 51 projections

and resulting in longer beam-on times. This is in contrast to a conventional LA in which the beam is switched off intermittently to allow setting up of different fields. Using a FBT of 2.5 cm, pitch 0.3 and modulation factor 3, the average beam-on time for CSI was 21.80 min (range, 16.79–29.14 min) for IMRT_Tomo. This was significantly higher than IMRT_LA (mean, 2.17 min; range, 1.69–2.77 min) and 3DCRT (mean, 1.56 min; range, 1.25–1.91 min). We have not investigated room-in to room-out times, which may be different between the three techniques, as the treating technologist has to go inside the treatment room several times for LA-based treatment to set up different fields, unlike for TomoTherapy.

Discussion

CSI with a homogeneous dose 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. With rapid advancements in technology, 2D planar imaging has gradually been replaced by 3D CT-based volumetric imaging for radiation planning. Traditionally, CSI is planned with two appropriately collimated lateral cranial fields shaped with MLCs or conformal blocks matched geometrically onto the beam divergence of direct posterior spinal field(s). The junction of the cranial and spinal fields, which occurs mostly at the C2–C3

Table 3. Volume of organs at risk receiving high ($\geq 80\%$) and intermediate ($\geq 50\%$) doses

Organs at risk	$V_{80\%}$			$V_{50\%}$		
	3DCRT	IMRT_LA	IMRT_Tomo	3DCRT	IMRT_LA	IMRT_Tomo
Left eye	43.4	43.4	0.0	64.4	64.4	0.7
Right eye	28.1	28.1	0.0	50.0	50.0	0.5
Heart	23.2	0.0	0.0	60.0	0.2	0.0
Right lung	6.0	0.0	0.0	10.6	2.2	0.6
Left lung	4.1	0.0	0.0	7.7	1.8	0.5
Thyroid	91.6	0.0	0.0	100.0	8.6	0.0
Right kidney	0.7	0.0	0.0	4.2	0.1	0.0
Left kidney	1.1	0.0	0.0	4.3	0.5	0.0
Liver	1.5	0.0	0.0	23.3	0.1	0.0
Oesophagus	100.0	0.2	0.0	100.0	65.0	0.0

3DCRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiation therapy; LA, linear accelerator; Tomo, TomoTherapy.

Table 4. Volume of organs at risk receiving low ($\geq 30\%$ and $\geq 10\%$) doses

Organs at risk	$V_{30\%}$			$V_{10\%}$		
	3DCRT	IMRT_LA	IMRT_Tomo	3DCRT	IMRT_LA	IMRT_Tomo
Left eye	77.4	77.4	19.4	95.4	95.4	100.0
Right eye	65.1	65.1	18.9	90.0	90.0	100.0
Heart	64.8	13.5	0.1	73.7	93.9	72.9
Right lung	13.9	12.3	11.8	20.5	60.6	91.0
Left lung	10.0	11.3	11.3	16.5	56.5	88.5
Thyroid	100.0	75.0	8.3	100.0	100.0	100.0
Right kidney	8.3	11.9	3.2	17.0	58.5	71.0
Left kidney	7.5	11.7	2.8	18.5	61.7	45.4
Liver	26.6	4.7	0.3	32.4	72.6	42.7
Oesophagus	100.0	100.0	21.4	100.0	100.0	100.0

3DCRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiation therapy; LA, linear accelerator; Tomo, TomoTherapy.

level, is generally feathered to minimise over- or under-dosage across the junction as an additional safeguard to avoid radiation myelopathy. In the majority of centres, including our own, field shaping and matching are performed based on the bony landmarks seen on the high-definition real-time fluoroscopic images on a conventional simulator in routine clinical practice. The advent of CT simulators and virtual simulation allows better field definition for improved coverage and better OAR sparing. Patients are treated using these planned fields without actually computing the dose distribution on a 3D TPS. Nevertheless, this 3D dataset is now increasingly being used to provide missing tissue compensation in the form of either physical compensators or electronic compensation. This technique, although used for the past few years, does not provide any estimate about the dose-volume relationships of targets and OARs. As the treatment-related long-term side effects become a growing concern for the paediatric population, there is certainly a need to evaluate systematically the dose-volume relationships of the intended treatment plan.

The main clinical impetus behind exploring IMRT for CSI has been the potential for better sparing of healthy tissue. The beam geometry and MLC shaping used in this study for PTV_brain was identical in the 3DCRT and IMRT_LA plans. This was done to avoid complexity that

would arise if a multifield IMRT plan was generated for the brain to match dosimetrically with the spinal IMRT plan. The moderately higher dose to the optic apparatus (eyes and optic nerves) resulting from shaped lateral cranial fields is widely accepted clinically. Consequently, the dosimetric outcome from 3DCRT and IMRT_LA plans was very similar for the cranial target. A minor difference in the mean value of $D_{\max}$ and $D_{\min}$ could be due to the dosimetric variation in the cranial and spinal field junctions. For the spinal target, the highest dose heterogeneity, with a mean DHI of 0.84 and $V_{107\%}$ of 34.61%, was observed in the 3DCRT plan, which is primarily a function of a single direct posterior field, further accentuated by contour irregularity, depth of prescription and natural spinal curvature. Periodic junction shifts have been routinely applied in conventional CSI to reduce uncertainty in abutment dosimetry and dose heterogeneity. Contemporary state-of-art technology available for radiotherapy planning and delivery has also been investigated for designing sophisticated and novel treatment strategies to reduce the dose to non-target tissues. Forward planned segmented field IMRT and inverse planned IMRT have been proposed for the spinal component of CSI [22, 23]. As these techniques were mainly aimed at improving the target coverage and dose homogeneity, the dose-volume relationship to the underlying normal tissues was not addressed. In addi-

Table 5. Integral dose to the targets and various organs at risk resulting from the three different treatment planning techniques of 3DCRT, IMRT_LA and IMRT_Tomo. All values are the mean of four patients

Volumes	Density (g cm ⁻³)	Volume (cm ³)	Mean dose (Gy)			Integral dose (Gy kg)			3DCRT/ IMRT_Tomo	IMRT_LA/ IMRT_Tomo
			3DCRT	IMRT_LA	IMRT_Tomo	3DCRT	IMRT_LA	IMRT_Tomo		
PTV_brain	1.1	1521.3	35.5	35.5	35.9	60.1	60.2	60.9	1.0	1.0
PTV_spine	1.1	143.6	37.0	36.3	35.9	6.0	5.9	5.8	1.0	1.0
Left eye	1.0	5.8	21.3	21.3	8.1	0.1	0.1	0.1	2.6	2.6
Right eye	1.0	5.4	19.4	19.4	8.2	0.1	0.1	0.1	2.4	2.4
Heart	1.1	208.1	17.8	7.5	5.0	3.9	1.7	1.1	3.6	1.5
Right lung	0.4	551.0	4.8	5.2	6.7	1.0	1.0	1.3	0.7	0.8
Left lung	0.4	508.4	5.3	5.7	6.7	1.0	1.0	1.2	0.8	0.9
Thyroid	1.1	5.7	30.5	12.2	8.3	0.2	0.1	0.1	3.7	1.5
Right kidney	1.1	60.4	3.1	5.3	4.5	0.2	0.3	0.3	0.7	1.2
Left kidney	1.1	64.1	3.2	5.7	4.5	0.2	0.4	0.3	0.7	1.3
Liver	1.1	455.1	7.2	5.3	3.9	3.5	2.6	1.9	1.9	1.4
Oesophagus	1.1	7.1	32.7	18.7	9.1	0.3	0.1	0.1	3.6	2.1

3DCRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiation therapy; LA, linear accelerator; Tomo, TomoTherapy; PTV, planning target volume.

tion, the adopted techniques do not reduce the dose to the underlying normal tissues and OARs because they use the same directly incident spinal field(s), as with 3DCRT in our study. The use of five-field inversely planned IMRT for the spinal target volume has demonstrated an improved dose homogeneity (DHI of 0.91 *vs* 0.84) and reduction of OAR doses when compared with 3DCRT. This is in agreement with the recent report by Parker et al [9]. When comparing our results with those of Parker et al [9], our mean value of $V_{107\%}$ was slightly lesser (34.61% *vs* 38%) in the 3DCRT plan but comparable (3.04% *vs* 3.0%) in the IMRT_LA plan. In the study by Parker et al, only short patients (spinal length <38 cm) were considered. As the target population for CSI includes older children and adolescents, LA-based IMRT for spinal fields exceeding the maximum allowable field size also needs to be investigated. We have for the first time demonstrated dosimetrically the feasibility of spinal IMRT planning even for taller patients. The maximum spinal length planned with IMRT_LA in our study was 48 cm, and our planning methods can be modified to plan patients of any heights. Irrespective of the methods adopted, cranial–spinal and cranial–spinal–spinal or spinal–spinal junctions are unavoidable on conventional LA for CSI planning owing to technical limitations, and extreme care regarding abutment dosimetry is warranted during the planning and delivery of treatment. Even after taking maximum precautions during planning, we still found small dose heterogeneity in the abutment region in IMRT_LA. Although periodic match-line junction shifts are proposed and implemented in several centres for conventional 2D techniques, the same may be difficult and resource-intensive in the case of IMRT_LA. Helical Tomotherapy offers a unique advantage in planning such extensively large and complex volumes with IMRT without any junctions. Our study demonstrated excellent target coverage (>99%), good dose homogeneity (0.96) and desirable OAR sparing with IMRT_Tomo compared with other techniques. The CI for brain target was highest for IMRT_Tomo, as the two other techniques used bilateral shaped fields. The reduction of CI with the IMRT_Tomo plan (0.62 *vs* 0.83 for IMRT_LA) for PTV_spine could be partly due to the use of directional blocks, which pull the prescription isodose in the anteroposterior direction at the location of the kidneys. More importantly, Tomotherapy plans are prescribed to the 100% isodose line compared with the 95% isodose line in LA-based planning. However, to maintain uniformity amongst the competing plans in this study, we decided to select 95% as the prescription isodose even for IMRT_Tomo plans, which could have resulted in a reduction in the conformity for PTV_spine. This statement is also supported by the increase in $V_{95\%}$ (>99% *vs* >98% for IMRT_LA). The lung dose was highest in the IMRT_Tomo plan and least in the 3DCRT plan. This could primarily be due to the relatively larger number of obliquely incident beams in IMRT_Tomo when compared with one direct and four oblique beams in IMRT_LA and a single direct beam in the 3DCRT plan. Our results are not directly comparable to any of the previously reported studies as none of them compared 3DCRT, IMRT_LA and IMRT_Tomo on the same datasets.

Penagaricano et al [10] in a single patient study reported the dosimetric advantage of the Tomotherapy plan over 3DCRT. The target coverage and inhomogeneity coefficient was comparable in the two plans, but the maximum and mean doses to various OARs, such as the heart, lung, thyroid and kidney, were lower in the Tomotherapy plan. Maximum doses to the optic apparatus (eyes and optic nerves) were higher for 3DCRT by 2–8 Gy, but the mean doses were lower by 1–6 Gy compared with IMRT_Tomo. It is possible that the authors did not use the option of directional block to avoid the direct incidence of beam on Tomotherapy for the eyes, which may have resulted in higher mean doses. We used directional blocks judiciously and achieved highly significant sparing of the optic apparatus without compromising on coverage or increasing hot spots. The mean values of $D_{\max}$ and D_{mean} to each OAR were much lower in our IMRT_Tomo plan when compared with the results of Penagaricano et al [10]. The possible reasons for this could (i) differences in contouring (both targets and OARs), (ii) optimisation parameters (hard and soft constraints), (iii) the use of directional blocks, and (iv) the number of patients. The authors further reported comparable IDs to the target, but the ID to all defined OARs was lower in IMRT_Tomo, except for the eyes and other non-contoured tissues. The total body ID was reportedly higher by 6.5% for Tomotherapy. In a subsequent update, the same authors compared the ID in conventional CSI delivery with helical delivery in three patients [24]. Overall ID was higher in CSI planned with IMRT_Tomo by 8% in two patients and lower by 2% in the third patient, leading to the conclusion that the clinical impact of such a modest increase in ID is unknown.

In another single patient study, Bauman et al [11] compared LA-based conventional CSI (using half-beam blocked cranial fields matched with the upper spinal field and a fixed longitudinal couch displacement for the lower spinal of 6 cm width) with Helical Tomotherapy. Dose–volume histogram analysis showed considerable heterogeneity in the target, particularly the spine (owing to a single posterior field with prescription at depth as well as two junctions). The doses to various OARs (although to smaller volumes) were also heterogeneous and high, sometimes reaching close to that at the target. The IMRT_Tomo plan achieved excellent target coverage and good conformity, as well as OAR sparing that was well within the specified constraints. The authors did raise concerns about the dose to the dentition (point doses to teeth of 9–10 Gy), dose variation across the vertebral bodies (36–24 Gy) and the increase in IDs to the body resulting from larger low-dose volumes (3–5 Gy) of normal tissues.

Kunos et al [25] investigated the role of Tomotherapy-based CSI in limiting dose to growing vertebral ring apophyses in four paediatric patients with medulloblastoma and compared it with conventional techniques. Helical Tomotherapy provided improved dose avoidance to growing vertebrae (2–14% of the vertebral volume exceeding 23 Gy) when compared with conventional CSI (33–44%). They also reported improved targeting of the craniospinal axis with Tomotherapy (mean dose 98.8% *vs* 76.8% for conventional radiotherapy). However, this was achieved at the potential

cost of large-volume low-dose radiation to non-target tissues. The cumulative whole-body dose exceeding 4 Gy was between 50% and 57% for TomoTherapy, compared with 25–37% for conventional CSI, thereby warranting a cautious approach to such technology.

The complexity and length of the treatment plan necessitates optimisation of the hard constraints on TomoTherapy to achieve clinically acceptable treatment times. By using a FBT of 1 cm (instead of the normally used 2.5 cm) and keeping the pitch and modulation factor constant, Bauman et al [11] could achieve better coverage at the cribriform plate with equivalent eye sparing, but at the expense of inordinately long treatment times (40 min *vs* 15 min). Penagaricano et al [26] also concluded that using a larger jaw width (FBT of 5 cm) or lower modulation factor, or both, substantially reduced the normalised beam-on time for CSI (by up to 61%) without compromising coverage or OAR sparing when compared with other plans. In their series of nine patients, minimum beam-on time was achieved with a FBT of 5 cm, pitch of 0.287 and modulation factor of 2.0. We have not investigated the impact of such modification in our patients, but instead used a constant FBT, pitch and modulation factor in all patients with excellent coverage, good OAR sparing and acceptable beam-on times (mean, 21.8 min; range, 16.79–29.14 min).

Two major concerns often raised over the use of IMRT, especially in children, are the increase in whole-body dose and the larger volumes of normal tissues irradiated at relatively lower radiation doses when compared with conventional radiotherapy. These two factors can potentially increase the risk of radiation-induced carcinogenesis, particularly in children and long-term survivors [27–31]. Very recently, Sharma et al [32] proposed the use of age- and gender-specific risk coefficients for estimating the risk of radiation-induced carcinogenesis. We have not attempted to estimate the risk of radiation-induced carcinogenesis for CSI in this study, but plan to do so in a subsequent report after enrolling more patients. Although most of the data pertaining to the risk of carcinogenesis are derived from conventional LA-based IMRT, it would be naïve to assume that such a relationship would not hold true for IMRT_Tomo. In fact, the relatively large number of monitor units associated with Helical TomoTherapy could result theoretically in a higher risk of secondary carcinogenesis than IMRT_LA. It is indeed reassuring to note that the IDs to most OARs in IMRT_Tomo were actually comparable to, or less than, IMRT_LA. Moreover, head leakage and collimator scatter, which are the main contributors to whole-body doses, are relatively small in Helical TomoTherapy when compared with LA. Although it may seem contradictory, OAR IDs are actually highest with conventional 2D CSI that employs a wide single posterior field for spinal irradiation.

Conclusions

CSI remains one of the most challenging processes in radiation planning, delivery and verification. Newer high-precision techniques have the potential to improve the benefit-risk ratio in CSI. Helical TomoTherapy seems to be ideally suited to plan such long and complex-shaped

target volumes, avoiding any junction, field-matching and abutment dosimetry. It also combines the inherent benefit of image guidance for precise dose delivery. IMRT_Tomo for CSI is favourable in terms of target volume coverage, dose homogeneity, conformity, OAR sparing and reduction of IDs to non-target tissues when compared with IMRT_LA and 3DCRT. In the case of non-availability of TomoTherapy, IMRT for CSI can be planned and delivered on a conventional LA even for spinal lengths exceeding the maximum allowable field sizes using appropriate intensity feathering with acceptable dosimetry. Although technically easier and potentially dosimetrically superior, IMRT_Tomo has significantly longer radiation beam-on times that raise concerns about intrafraction motion and whole-body IDs.

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