Original article

Dosimetric comparison of helical tomotherapy (HT) with intensity modulated radiotherapy (IMRT), three-dimension conformal radiotherapy (3D-CRT) and conventional two-dimension radiotherapy (2D) for craniospinal axis irradiation (CSI)

Bongkot Supawongwattana,[1] Thikhamporn Hoonghual,[2] Imjai Chitapanarux,[1] Somsak Wanwilairat,[1] and Patrinee Traisathit[3]

[1]Department of Radiology, Faculty of Medicine, Chiang Mai University, [2]Udon Thani Cancer Hospital, [3]Department of Statistics, Faculty of Science, Chiang Mai University

Objective Helical tomotherapy (HT) can provide a radiation beam for a longer treatment field without a matching junction. The goal of this study was to evaluate the feasibility and potential dosimetric benefit in HT when compared with intensity modulated radiotherapy (IMRT), three-dimension conformal radiotherapy (3D-CRT) and two-dimension radiotherapy (2D).

Methods Twelve newly diagnosed central nervous system (CNS) tumors requiring craniospinal axis irradiation (CSI) were treated with HT. The same computed tomography (CT) image datasets were re-planned with IMRT, 3D-CRT and 2D. Target dosimetric comparisons were categorized into the brain, spine and tumor boost planning target volume (PTV), and performed by an analysis of homogeneity index (HI) and conformity index (CI). The percentage of prescription and integral dose to the spinal cord and whole body (ID), respectively, were compared as well.

Results HT achieved the best dosimetric distribution for brain PTV with a mean HI of 44.51% (p <0.001) and CI of 0.984 (p <0.001). The result of tumor boost PTV was almost identical to that of brain PTV. Regarding the spinal portion, HT and IMRT revealed an equal HI, while the CI was highest in HT (p <0.001) and compatible with the lowest prescription dose of 122.22% to the spinal cord. The ID of HT was comparable to the 2D technique (p =0.272) and significantly inferior to 3D-CRT (p =0.034), while IMRT planning showed the highest ID (p <0.05). The mean overall treatment time was 40 days. Grade 3-4 hematologic toxicity was the only adverse event that caused a treatment break.

Conclusion HT was feasible with shorter overall treatment time, and it also gave an excellent dosimetric distribution. Regarding ID, HT was inferior to 3D-CRT. Longer follow-up is required to evaluate this concerning issue. **Chiang Mai Medical Journal 2015;54(1):17-28.**

Keywords: craniospinal axis irradiation, helical tomotherapy, dosimetric comparison

Address correspondence to: Bongkot Supawongwattana, M.D., Department of Radiology, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200 Thailand. E-mail: phung_nemo@hotmail.com
Received: October 2, 2014, Accepted: December 7, 2014.

Introduction

Craniospinal axis irradiation (CSI) is a challen-ging technique for radiation oncologists in the treatment of intracranial tumor with potential leptomeningeal dissemination. Previous techni-ques typically applied a carefully calculated field junction between the cranial and spine field, or perhaps an additional matching at the upper and lower spinal field, owing to an excess of allowable maximal field size[1]. These field junctions are considered cautiously in order to minimize over- or under-dosage, which is sometimes inevitable. The heterogeneity of dose in this region translates to compromise target coverage, and reduce the required therapeutic dose in order to limit constraints on normal tissue dosage. Otherwise, CSI traditionally places the patients in a prone position, which provides unavoidably difficult airway management and discomfort[2].

The helical tomotherapy (HT) system was developed at the University of Wisconsin-Madison by professor Thomas Rockwell Mackie, Ph.D[3]. The impressive advantage of this technique is its ability to radiate a longer treatment field without a matching junction; which may lead to improve target homogeneity and reduce doses to organs at risk (OARs)[4]. HT also allows supine position for patients, which is more convenient and enhances airway management.

The standard guideline for CSI is still under development; dose per fraction and total dose delivered depending on the type of primary malignancy and practice of an individual institute (dose 1.6-2.0 Gy/Fx, total dose 23.4-36 Gy CSI, 40-45 Gy for spinal disease and 54-55.8 Gy for tumor bed)[5–10].

In March 2012, the Division of Therapeutic Radiology and Oncology, Faculty of Medicine, Chiang Mai University, was the first institute in Thailand to implement an HT machine. This study present the feasibility of CSI with HT as the simultaneous integrated boost technique (SIB). This was because the first computed program installed in the machine had limitations (HiArt 4.1.2.1), which made it ineffective in summarizing the accumulated dose on a sequential technique. We also performed a dosimetric comparison between the four different radiation treatment plans; HT, intensity modulated radiotherapy (IMRT), three-dimensional conformal radio-therapy (3D-CRT) and conventional two-dimensional radiotherapy (2D).

Methods

Patient population

Patients newly diagnosed with primary central nervous system (CNS) tumor, and required post-operative CSI, were recruited prospectively and treated with HT from May 2012 to August 2013. Complete spinal staging by magnetic resonance imaging (MRI) of the spine, and cerebrospinal fluid (CSF) cytology, also were requested for possible spinal boost. Computed tomography (CT) simulation was started within 1-week post enrolment.

Simulation and patient setup

The patients were placed in the supine position. CT simulation images from the skull vertex to whole pelvic bone were acquired with uniform slice thickness and spacing of 5-mm on a CT simulator (Asteion, Toshiba).

The CT images were transferred to a contouring workstation (Oncentra, Philips). Contouring the treatment volume and OARs was performed by the principle investigator and confirmed by radiation oncologist staff.

Delineation of target volumes and normal tissue structure

The CSI volume was contoured on a similar program, but the target volume had varying delineation according to the primary tumor. The OARs outlined included the brainstem, optic apparatus, temporal lobe, globe, lens, head and neck mucosa, parotid, mandible, cochlea, spinal cord, thyroid, larynx, esophagus, heart, lung, gut, kidney and liver, and they were constrained [11–13]. The whole body was identified as the external contour of the body covering the whole treated volume.

Dose schedule

As the Tomotherapy planning system was limited, as described above, this study created a CSI treatment protocol to treat all target volumes, using the simultaneous integrated boost (SIB) technique in accordance with Biological effective dose (BED) and Equivalent dose (EQD) concepts, and a dose per fraction of 1.8 Gy as a standard fractionation. A new total dose and dose per fraction were calculated, providing the same BED for each target dose could be delivered by the SIB technique, as shown in Table 1.

Table 1. Dose schedule for a total of 23 fraction treatments

Target dose (Gy)	55.8	54	50	45	40	36
BED-tumor	65.84	63.72	59.00	53.10	47.20	**42.48**
Dose/Fx	2.32	2.26	2.12	1.93	1.75	**1.59**
Total delivery dose	53.36	51.98	48.76	44.39	40.25	**36.57**

Radiation therapy planning

After target-OARs were delineated on the contouring workstation, the structure datasets were sent to a planning workstation (HiArt, Tomotherapy). The same CT Dicom images were transferred to a particular treatment planning workstation to generate a comparison with the IMRT, 3D-CRT and 2D plan.

1. Conventional-2D plan (Pinnacle, Philips)
   - CSI cranial field and tumor bed boost : two-lateral opposing technique
   - CSI spine field and spine boost : direct PA field
   - Field junction: Cranial-spinal junction at C3-C4, upper-lower spinal junction at T10-T11, use of sliding junction technique, matching with the skin at 1.5-cm distance
2. 3D-CRT plan (Pinnacle, Philips)
   - CSI cranial field: Two-lateral opposing beams
   - CSI spine field and spine boost : Three-field (225^{o}, 180^{o} and 135^{o} with 60-degree virtual wedge)
   - Tumor bed boost: Five-field technique (60^{o}/ 120^{o}/ 180^{o}/240^{o} and 300^{o})
   - Field junction: Matching area calculation was at the posterior border of the spine planning target volume (PTV), with 1-cm distance from the three-sliding junction (line A, B, C)
3. IMRT plan (Konrad, Siemens)
   - CSI cranial field: Two-lateral opposing beams
   - CSI spinal field and boost: Five-beams (230°, 205°, 180°, 155° and 130°)
   - Tumor bed boost: Seven-beams (318^{o}, 272°, 226°, 180°, 134°, 88° and 42°)
   - Field junction: Two-sliding junction of 1.0-cm distance with field matching at the posterior border of the spine PTV
4. Helical Tomotherapy plan (HiArt, Tomotherapy)
   - Treatment with the SIB technique in 23 fractions
   - No need for field junction

Plan evaluation

At least 95% of the target volume received 100% of the prescribed dose, which was considered as an acceptable plan in all four treatment techniques. The dosimetric parameters were compared using the dose conformity index (CI), homogeneity index (HI), and integral doses (IDs).

Conformity index (CI)

$$CI = \frac{V_{TR}}{TV}$$

V_{RI} = Volume of target enclosed by the reference isodose

TV = The target volume

Homogeneity index (HI)

$$\mathrm{HI} = \frac{\mathrm{D}_2 - \mathrm{D}_{98}}{\mathrm{D}_\mathrm{P}} \times 100\%$$

D2 = The dose to 2% of the target volume

D98 = The dose to 98% of the target volume

Dp = Prescribed dose

Integral dose (ID)

$$ID = V \times D$$

V = Volume of the organ (L)

D = Mean dose to the organ (Gy)

Daily localized pre-treatment with a megavoltage computed tomography (MVCT) scan was acquired for treatment verification during CSI. This facility enabled physicians to correct any detected deviation by automated fusion, and manually adjust the couch position before radiation delivery. This study applied the whole target volume length by setting up MVCT once a week and alternating between the cranial-upper spinal and mid-lower spinal area every other day.

A weekly complete blood count was obtained during the treatment period. All toxicities were graded according to the Radiation Therapy Oncology Group (RTOG) acute radiation morbidity scoring criteria.

Treatment time definition

Definition of the actual CSI treatment time with HT was performed as follows:

Daily treatment time: start from patient entering the room to finishing treatment

Beam on time: radiation delivery time in each fraction

Setup time: time taken to setup patient and verify by daily calculation of treatment time minus beam on time

Overall treatment time: begin from the starting date of radiation to the time of last fraction

Statistical analysis

The SPSS Statistics 20.0 was used for data analysis. The Friedman Test determined the difference between the datasets of HT, IMRT, 3D-CRT and 2D. Dosimetric comparison between two techniques was detected by the Wilcoxon Signed Ranks test. A probability value < 0.05 was consi-dered statistically significant.

Authorization by consent was obtained from the adoles-cent or adult patients, or parents of the younger patients. This study was approved by the Ethics Committee of Maharaj Nakorn Chiang Mai Hospital (RAD-13-1429-FB).

Results

Patient characteristics

A total of 12 patients were enrolled from November 2012 to September 2013. Medulloblastoma was the most common cancer in this study, and all of its patients were classified as high risk. Other cancers were retinoblastoma, S-PNET, pineoblastoma, multifocal germinoma and ependymoma.

All of the patients received HT irradiation with the SIB technique, using a field width of 5-cm, pitch of 0.43 and modulation factor of 2.0-3.0. The mean field length was 63.3 cm (48.9-78.1 cm). The mean daily treatment time, beam on time and setup time was 24 minutes (19.5-28.6 minutes), 9.5 minutes (7.2-12.0 minutes) and 14.2 minutes (11.3-17.3 minutes), respectively. The mean overall treatment time was 40 days (32-53 days).

CSI in supine position was well tolerated by and reproducible for the patients, including anesthetized children. Grade 3-4 acute hematologic toxicity was the main cause of treatment interruption.

Dosimetric comparison of the targets

Isodose distribution for each radiotherapy modality was performed, as shown in Figure 1. The CI and HI of the brain, spine and tumor bed boost PTV were compared in the four treatment plans by using the Friedman test (Table 2), and the differences were statistically significant. The CI and HI were compared also between two treatment plans by the Wilcoxon test (Table 3). HT seemed to deliver an excellent homogeneous and conformal dose distribution.

Brain PTV

HT had the best homogeneous dose distribution, followed by IMRT, 3D-CRT and 2D, consecutively, while IMRT and 3D-CRT had negligible results. Conventional 2D was the

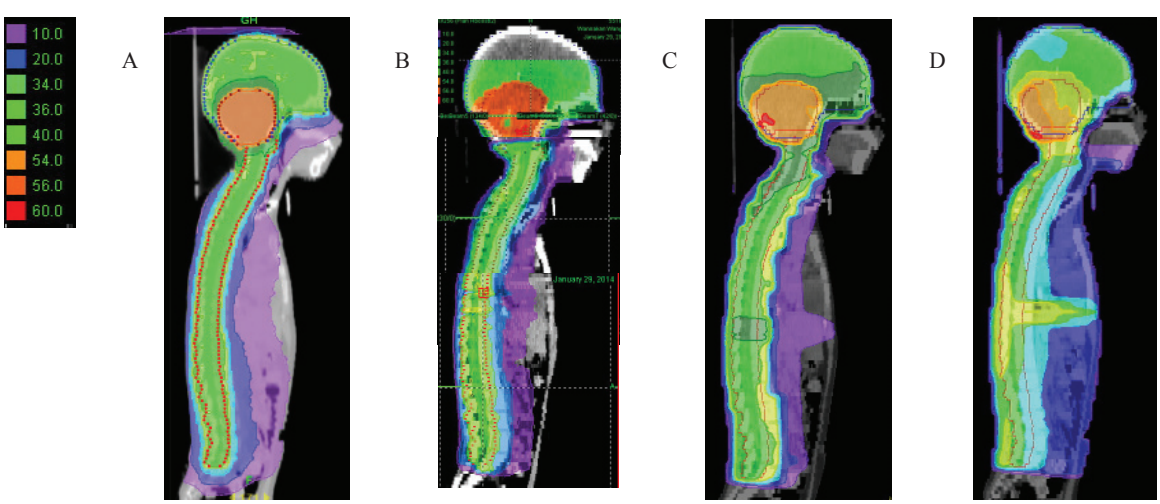

Figure 1. Case of a 10-year old girl with high-risk medulloblastoma (residual tumor > 1.5 cm^2). Sagittal isodose distribution of Helical Tomotherapy (A), IMRT (B), 3D-CRT (C) and 2D (D) techniques.

Table 2. Dosimetric parameters of the target for the four different treatment plans: all dosimetric values represent the mean value of twelve patients

Treatment plan modality		HT	IMRT	3D-CRT	2D	*p*
Brain PTV	HI	44.51%	54.92%	56.07%	86.32%	< 0.001
	CI	0.984	0.955	0.976	0.830	< 0.001
Spine PTV	HI	22.43%	22.20%	41.44%	59.24%	< 0.001
	CI	0.978	0.917	0.929	0.753	< 0.001
Tumor boost PTV	HI	6.35%	10.62%	8.31%	11.44%	0.008
	CI	0.965	0.870	0.931	0.269	< 0.001

Friedman analysis, statistical significance; $p < 0.05$

least homogeneous. HT also delivered more conformal doses than IMRT and 2D, while yielding a comparable mean CI to 3D-CRT. IMRT had a conformity index lower than 3D-CRT, but higher than the 2D plan.

Spine PTV

HT and IMRT seemed to have an identical homogenous dose distribution, but it was signi-ficantly better than in the other two treatment plans. The 2D plan yielded the lowest dose of homogeneity. The HT plan also provided the best conformity, while the lowest was observed in the 2D plan.

Tumor boost PTV

The highest homogeneity index in this study was achieved by the HT plan; followed by 3D-CRT, IMRT and 2D plans, consecutively. The conformity of dose distribution was comparable between HT and 3D-CRT plans, which were significantly better than the IMRT and 2D plans.

Dose for OARs

The doses and comparisons for OARs are presented in Table 4 (Friedman test) and 5 (Wilcoxon test), respectively. HT had the lowest spinal cord dose followed by IMRT, 3D-CRT and 2D, consecutively. The conventional 2D plan had a significantly maximal integral dose to the heart in this study. IMRT had the lowest integral dose to both lungs, while the HT dose was comparable to 3D-CRT and 2D doses for the right lung. The highest integral dose for the whole body was observed in the IMRT plan, while the 3D-CRT plan had the lowest. The whole body dose in the HT and 2D plan was comparable.

Treatment result

The mean follow up time was 8.75 months (1-18 months). Patients without diffuse spinal or intraventricular metastasis at initial diagnosis had a satisfactory outcome, and most of them had responded completely on a follow-up MRI scan. Poor responses were mainly in patients with initial diffuse spinal metastasis, and most of them had progression of disease approximately 6-months after complete irradiation.

Discussion

CSI plays an important role in several CNS malignancies. The principal goal for CSI is to achieve a satisfactory homogeneous and conformed dosimetric distribution. Historical data have used the technical gap or matching junction, owing to excessive field length. The featured junction, as an emergence of 3D-based CT simulation, was computed carefully in order to avoid a divergent radiation beam of the cranial and spinal field, and minimize critical normal structure doses without compromising the target coverage. Despite taking maximum precautions, a heterogeneous dose at the abutment region was unavoidable. In recent years, a novel HT techni-que has been able to provide a rotational fan beam to enable a longer treatment field; for up to 160 cm without requiring a discontinuous couch. This

Table 3. HI and CI comparison between two treatment plan modalities

Dosimetric parameters		HT vs IMRT	HT vs 3D-CRT	HT vs 2D	IMRT vs 3D-CRT	IMRT vs 2D	3D-CRT vs 2D
Brain PTV	HI	44.51% 54.92%	44.51% 56.07%	44.51% 86.32%	54.92% 56.07%	54.92% 86.32%	56.07% 86.32%
		$p = 0.002$	$p = 0.002$	$p = 0.002$	$p = 0.327$	$p = 0.002$	$p = 0.003$
	CI	0.984 0.955	0.984 0.976	0.984 0.830	0.955 0.976	0.955 0.830	0.976 0.830
		$p = 0.028$	$p = 0.136$	$p = 0.002$	$p = 0.041$	$p = 0.002$	$p = 0.002$
Spine PTV	HI	22.43% 22.20%	22.43% 41.44%	22.43% 59.24%	22.20% 41.44%	22.20% 59.24%	41.44% 59.24%
		$p = 0.583$	$p = 0.002$	$p = 0.002$	$p = 0.005$	$p = 0.002$	$p = 0.005$
	CI	0.978 0.917	0.978 0.929	0.978 0.753	0.917 0.929	0.917 0.753	0.929 0.753
		$p = 0.003$	$p = 0.002$	$p = 0.002$	$p = 0.347$	$p = 0.008$	$p = 0.007$
Tumor boost PTV	HI	6.35% 10.62%	6.35% 8.31%	6.35% 11.44%	10.62% 8.31%	10.62% 11.44%	8.31% 11.44%
		$p = 0.019$	$p = 0.117$	$p = 0.034$	$p = 0.084$	$p = 0.136$	$p = 0.456$
	CI	0.965 0.870	0.965 0.931	0.965 0.269	0.870 0.931	0.870 0.269	0.931 0.269
		$p = 0.002$	$p = 0.346$	$p = 0.002$	$p = 0.041$	$p = 0.002$	$p = 0.002$

Wilcoxon test, statistical signficance; $p < 0.05$

Table 4. Selected OARs for the four different treatment plans: all values represent the mean value of twelve patients

OARs	HT	IMRT	3D-CRT	2D	*p*
Spinal cord (% of prescription dose)	122.22%	127.80%	135.11%	148.22%	< 0.001
Heart: integral dose (Gy.L)	3.10	2.96	3.06	7.03	< 0.001
Lung Lt: integral dose(Gy.L)	5.16	3.71	5.33	4.46	< 0.001
Lung Rt: integral dose (Gy.L)	6.80	5.42	6.90	7.32	0.001
Whole body: integral dose (Gy.L)	264.48	310.24	256.43	270.82	0.008

Friedman analysis, statistical significance; $p < 0.05$

technique automatically eliminated inhomogeneous dosimetry of the previous junction area. Many published data demonstrated the feasibility of HT, with excellent target coverage, and superior normal tissue sparing[9,14,15].

To the authors' knowledge, this is the first study to analyze dosimetric comparison of four different treatment planning techniques. Traditionally, the junction of cranial and spinal fields shaped and matched based on the 2D bony landmark. The advent of CT simu-lation permits better radiation coverage and improved treatment field definition. Radiation delivery by 3D-CRT provides dosimetry superior to that by 2D in terms of better HI and CI, as well as a dose reduction to OARs. The percentage of prescribed doses to the spinal cord, which represent an overdose, is diminished dramatically by utilizing volumetric based CT planning. IMRT has clinical impact on a potentially better homogeneous dose to the spine PTV, and significantly enhances sparing of healthy tissue when compared with 3D-CRT and 2D. This finding is in agreement with the report by D.S. Sharma and W. Parker, who used a single direct posterior spinal beam in the 3D-CRT technique. In this study, policy application of two oblique and one direct posterior spinal fields on 3D-CRT translated to a negligible conformation of spine PTV between IMRT and 3D-CRT[5,16]. The use of five-field inversely planned IMRT has demonstrated identical dose homogeneity to HT. In actual fact; other dosimetric parameters to the targets and sparing of critical tissue have always been excellent with the HT technique.

The 3D-CRT plan, with a direct posterior spinal field, was reported as being homogenously and conformably worse than HT[5]. Three fields of spinal radiation in this study were supported by Jose et al, who demonstrated a dosimetric HT that was preferable to 3D-CRT[6]. Bauma *et al,* allowed re-planning of previous 3D-CRT data, with highly conformal and homogeneous HT[9]. Parker also report a dosimetric advantage over 3D-CRT and commented that HT is considered as an acceptable option for CSI treatment[14].

There are limited published data comparing between IMRT and HT. Sharma *et al*, presented superior HI in HT over IMRT and 3D-CRT for brain and spine PTV, as well as better CI for brain PTV. Spine PTV in this study achieved the highest conformity through the IMRT plan, which could be from using a directional block to bilateral kidneys in HT reduced CI for spine PTV.

In general, HT seems to have superior target coverage, better homogeneous dose and excellent critical tissue sparing. This may be typical of allowing numerous beam angles to be delivered around the patient, together with continuous couch motion of up to 160 cm, and optimization by adjusting the field width, pitch and modulation factor. Theoretically, a narrower fan beam with an increasing modulation factor can facilitate conformal ability. Bauman et al achieved better coverage at the cribiform plate, and similar target coverage with a field width of 1 cm, compared to 2.5 cm, but sometimes at the expense of nearly double beam on times[9]. Another study was concerned about longer radiation delivery of up to 40 minutes

Table 5. OAR dose comparison between two treatment plan modalities

OARs	HT vs IMRT		HT vs 3D-CRT		HT vs 2D		IMRT vs 3D-CRT		IMRT vs 2D		3D-CRT vs 2D	
Spinal cord	122.22%	127.80%	122.22%	135.11%	122.22%	148.22%	127.80%	135.11%	127.80%	148.22%	135.11%	148.22%
(% of prescription dose)	*p* = 0.034		*p* = 0.023		*p* = 0.002		*p* = 0.019		*p* = 0.010		*p* = 0.023	
Heart: integral dose	3.10	2.96	3.10	3.06	3.10	7.03	2.96	3.06	2.96	7.03	3.06	7.03
(Gy.L)	*p* = 0.814		*p* = 0.695		*p* = 0.002		*p* = 0.456		P = 0.002		*p* = 0.002	
Lung Lt: integral dose	5.16	3.71	5.16	5.33	5.16	4.46	3.71	5.33	3.71	4.46	5.33	4.46
(Gy. L)	*p* = 0.003		*p* = 0.638		*p* = 0.003		*p* = 0.002		P = 0.028		*p* = 0.004	
Lung Rt: integral dose	6.80	5.42	6.80	6.90	6.80	7.32	5.42	6.90	5.42	7.32	6.90	7.32
(Gy.L)	*p* = 0.003		*p* = 0.583		*p* = 0.182		*p* = 0. 003		P = 0.005		*p* = 0.610	
Whole body:	264.48	310.24	264.48	256.43	264.48	270.82	310.24	256.43	310.24	270.82	256.43	270.82
Integral dose (Gy.L)	*p* = 0.005		*p* = 0.034		*p* = 0.272		*p* = 0.005		P = 0.012		*p* = 0.041	

by using a field width of 1 cm, which was considered to be unacceptable for a child being treated with daily sedation[10]. This study did not investigate the impact of adjusting those three parameters for the HT plan, but instead used a constant protocol. Parker *et al*, reported a preferable beam on time range from 10 to 15 minutes in a 5 cm field width, with a history of approximately more than 20 minutes in the 2.5 cm field width[9,10,14].

A pretreatment MVCT scan can locate a target volume more precisely with minimal effect on a total radiation dose; MVCT provided approximately 2 cGy daily, while a linear accelerator (LINAC) portal image gave up to 6 cGy per image. This study did not verify the post treatment MVCT scan for measuring any possible intra-fraction movement. The data from Parker showed a minimal difference of less than 3 mm shift on the post-treatment MVCT scan[14].

There is no supporting data on the SIB technique for CSI. This study attentively computed the target BED, based on the $\propto/\beta$ ratio and designed treatment, with a total of 23 fractions; dose per fraction 1.6-2.3 Gy. A slightly hypofractionated irradiation remains a concern as it is critically experimental. There is no data published on agreement of newly diagnosed CSI applying hypofractionation. However, F. Saran investigated patients having recurrent medulloblastoma or S-PNET, and being treated with hypofractionated stereotactic conformal therapy doses of 30-40 Gy in 6-8 fractions, which showed effective local control and acceptable toxicity[17]. Prophylactic ondansetron was not given in this study, as is usually taken in other techniques for the management GI toxicity. Only manageable acute hematologic toxicity was found, which caused a treatment break. This study did not examine the neurological questionnaire evaluation during the follow up period, as all live patients had equally or slightly improved neurological function.

The overall treatment time in the authors' previous traditional policy was usually around 2-months, in which two-separated radiation parts were divided. The first radiation was to the cranial and upper spine, then sequential irradiation to the lower spine together with the tumor bed boost field. Hematologic and nausea/vomiting problems occurred that caused treatment breaks, which occasionally extended the overall treatment time to almost 3-months, compare with the maximum 53 days of this study. The potential benefit of the SIB technique may offer an opportunity to improve local tumor control, with acceptable adverse events, as shown in the head and neck cancer treatment model[18].

The increased integral dose to the whole body (ID) is obviously an issue of concern. This study performed approximately 3.1% higher ID in the HT plan than in the 3D-CRT plan, which is the worldwide standard radiotherapy technique. This result was in agreement with data from J. A. Penagaricano, who reported 6.5% higher doses to the ID in the HT plan than in the 3D-CRT plan. Meanwhile, a subsequent update presented a study of three-patients, and found that the HT had 8% higher doses to the ID in two patients, which contrasted to a 2% lower dose in the other one, thus concluding that the clinical impact was still unknown[6,19]. Some authors indicated the potentially higher risk of secondary malignancy by accumulating a larger integral dose to the whole body[20]. In the IMRT era, several studies have estimated a higher rate of secondary malignancy by 1-9.9%, compared to 0.3-1.2% by conventional therapy[21,22]. Hall and Wuu concluded that IMRT would increase the risk of secondary malignancy from approximately 1-1.7% of patients surviving 10 years[23]. A later study from Hall performed a higher risk factor of 1.2-8% for IMRT[24]. On the other hand, Nguyen and Rubino reported that in their study the ID did not correlate to a good predictor for radiocarcinogenesis[25]. Nevertheless, IMRT data cannot be extrapolated to HT, as it is not multileaf collimator intensity modulated radiotherapy (MLC-IMRT), but it can illustrate the potential increased risk due to greater ID and handling the numbers of monitor units. Evaluation of relatively higher risk of radiation induced malignancy for HT obviously requires further study with a longer follow up. The concern about increased risk of

secondary malignancy, as a result of irradiated lower dose to a larger volume may be rectified by utilizing proton therapy; a charge particle that provides a radiation beam characteristic, with a rapid dose reduction to the distal target, consequently allowing a high conformity without increasing the theoretical risk of secondary malignancy. Even though proton therapy seems to have a more appropriate approach, especially for pediatric patients, it is not widely available, owing to its high cost and complicated treatment planning, which requires high specialization. While the proposed of improving clinical outcomes remains questionable.

Conclusion

HT seems to be ideally suited for radiation delivery to the craniospinal axis in terms of having excellent target coverage, and minimized radiation dose to critical structures, especially the spinal cord in the event of technically eliminating any field junction expediency and initiating dosimetric improvement at the abutment area. The daily pre-treatment of a MVCT scan provides radiation verification more precisely and reduces PTV expansion. The policy in this study was to treat the whole brain, entire spinal length and boost tumor simultaneously, in order to reveal feasibility with a shortened overall treatment time and more comfort while presenting only manageable grade 3-4 hematologic toxicity.

In comparison, HT also shows a satisfactory whole body integral dose that is significantly larger than the 3D-CRT in this study. Nevertheless, the potential increased risk of secondary malignancy, and uncertainty of delayed effect from applying a slightly hypofractionation need to be investigated further, and require a longer follow-up period. The upcoming Tomotherapy treatment planning system will allow an aggregation of OAR dose in sequential radiation planning, and may offer another interesting exploration of CSI, with a conventional fractionation scheme and tumor boost identical to the general radiation schedule.

However, clinical application must weigh up the possibility of adverse events with the impressive advantage of Helical Tomotherapy.

References

1. **van Dyk J, Jenkin RD, Leung PM, Cunningham JR**. Medulloblastoma: treatment technique and radiation dosimetry. Int J Radiat Oncol Biol Phys 1977;2(9-10):993-1005.
2. **Hideghéty K, Cserháti A, Nagy Z, et al**. CNS radiotherapy A prospective study of supine versus prone positioning and whole-body thermoplastic mask fixation for craniospinal radiotherapy in adult patients. Radiother Oncol 2012;102:214-8.
3. **Mackie TR**. History of tomotherapy. Phys Med Biol 2006;51:R427-53.
4. **Latifa M, Raúl M, Sergey U, Immacolata M**. Helical tomotherapy in the treatment of pediatric malignancies: a preliminary report of feasibility and acute toxicity. Radiat Oncol. BioMed Central 2011; 6:102.
5. **Sharma D, Gupta T, Jalali R**. High-precision radiotherapy for craniospinal irradiation: evaluation of three-dimensional conformal radiotherapy, intensity-modulated radiation therapy and helical. Br J Radiol 2009;d:1000-9.
6. **Peñagarícano J, Papanikolaou N**. Feasibility of cranio-spinal axis radiation with the Hi-Art tomotherapy system. Radiother Oncol 2005;76:72-8.
7. **Peñagarícano J, Moros E, Corry P**. Pediatric craniospinal axis irradiation with helical tomotherapy: patient outcome and lack of acute pulmonary toxicity. Int J Radiat Oncol Biol Phys 2009;75: 1155-61.
8. **Hong JY, Kim GW, Kim CU, et al**. Supine linac treatment versus tomotherapy in craniospinal irradiation: planning comparison and dosimetric evaluation. Radiat Prot Dosimetry 2011;146:364-6.
9. **Bauman G, Yartsev S, Coad T**. Helical tomotherapy for craniospinal radiation. Br J Radiol 2005;78: 548-52.
10. **Mascarin M, Drigo A, Dassie A, et al**. Optimizing craniospinal radiotherapy delivery in a pediatric patient affected by supratentorial PNET: a case report. Tumori 2010;96:316-21.
11. **Marks LB, Yorke ED, Jackson A, et al**. Use of normal tissue complication probability models in the clinic. Int J Radiat Oncol Biol Phys 2010;76(3 Suppl):S10-9.
12. **Milano MT, Constine LS, Okunieff P**. Normal tissue tolerance dose metrics for radiation therapy of major organs. Semin Radiat Oncol 2007;17:131-40.
13. **Cella L, Conson M, Caterino M, et al**. Thyroid V30 predicts radiation-induced hypothyroidism in patients treated with sequential chemo-radiotherapy for Hodgkin's lymphoma. Int J Radiat Oncol Biol Phys 2012;82:1802-8.

14. **Parker W, Brodeur M, Roberge D, Freeman C**. Standard and nonstandard craniospinal radiotherapy using helical TomoTherapy. Int J Radiat Oncol Biol Phys 2010;77:926-31.
15. **Penagaricano JA, Yan Y, Corry P, Moros E, Ratanatharathorn V**. Retrospective evaluation of pediatric cranio-spinal axis irradiation plans with the Hi-ART tomotherapy system. Technol Cancer Res Treat 2007;6:355-60.
16. **Parker W, Filion E, Roberge D, Freeman C**. Intensity-modulated radiotherapy for craniospinal irradiation: target volume considerations, dose constraints, and competing risks. Int J Radiat Oncol Biol Phys 2007;69:251-7.
17. **Saran F, Baumert BG, Creak AL, et al**. Hypofractionated stereotactic radiotherapy in the management of recurrent or residual medulloblastoma/PNET. Pediatr Blood Cancer 2008;50:554-60.
18. **Dogan N, King S, Emami B, et al**. Assessment of different IMRT boost delivery methods on target coverage and normal-tissue sparing. Int J Radiat Oncol Biol Phys 2003;57:1480-91.
19. **Peñagarícano JA, Shi C, Ratanatharathorn V.** Evaluation of integral dose in cranio-spinal axis (CSA) irradiation with conventional and helical delivery. Technol Cancer Res Treat 2005;4:683-9.
20. **Aoyama H, Westerly DC, Mackie TR, et al**. Integral radiation dose to normal structures with conformal external beam radiation. Int J Radiat Oncol Biol Phys 2006;64:962-7.
21. **Verellen D, Vanhavere F**. Risk assessment of radiation-induced malignancies based on whole-body equivalent dose estimates for IMRT treatment in the head and neck region. Radiother Oncol 1999;53:199-203.
22. **Followill D, Geis P, Boyer A**. Estimates of whole-body dose equivalent produced by beam intensity modulated conformal therapy. Int J Radiat Oncol Biol Phys 1997;38:667-72.
23. **Hall EJ, Wuu C-S**. Radiation-induced second cancers: the impact of 3D-CRT and IMRT. Int J Radiat Oncol Biol Phys 2003;56:83-8.
24. **Hall EJ**. Intensity-modulated radiation therapy, protons, and the risk of second cancers. Int J Radiat Oncol Biol Phys 2006;65:1-7.
25. **Nguyen F, Rubino C, Guerin S, et al**. Risk of a second malignant neoplasm after cancer in childhood treated with radiotherapy: correlation with the integral dose restricted to the irradiated fields. Int J Radiat Oncol Biol Phys 2008;70:908-15.

การศึกษาความแม่นยำของการฉายรังสีบริเวณสมองและไขสันหลัง ด้วยเครื่องฉายรังสีภาพนำแบบเกลียวหมุน เปรียบเทียบกับการฉายปรับความเข้ม รังสี 3 มิติ และการฉายด้วยรังสี 2 มิติ

บงกช ศุภวงศ์วรรธนะ,[1] ทิฆัมพร ฮุ่งหวล,[2] อิ่มใจ ชิตาพนารักษ์,[1] สมศักดิ์ วรรณวิไลรัตน์,[1] และ ภัทรินี ไตรสถิตย์[3]

[1]ภาควิชารังสีวิทยา คณะแพทยศาสตร์, [2]โรงพยาบาลอุดรธานี, [3]คณะวิทยาศาสตร์ มหาวิทยาลัยเชียงใหม่

วัตถุประสงค์ การรักษาด้วยเครื่องฉายรังสีภาพนำแบบเกลียวหมุน เป็นเทคโนโลยีที่สามารถกำจัดการต่อบริเวณที่ฉายรังสี (field junction) ได้ การศึกษานี้เพื่อประเมินการกระจายปริมาณรังสีและความแม่นยำของการฉายรังสี ในการฉายรังสีทั้งบริเวณสมองและไขสันหลัง (craniospinal axis irradiation: CSI) โดยใช้เครื่องฉายรังสีภาพนำแบบเกลียวหมุน เปรียบเทียบการกระจายปริมาณรังสีกับเทคนิคการฉายปรับความเข้ม, รังสี 3 มิติ และรังสี 2 มิติ

เครื่องมือและวิธีการศึกษา การศึกษานี้ได้รวบรวมผู้ป่วย 12 ราย ฉายรังสีด้วยเทคนิคภาพนำแบบเกลียวหมุน ภาพจำลองรังสีด้วยคอมพิวเตอร์ (CT simulation) ในผู้ป่วยแต่ละรายจะถูกนำไปวางแผนด้วยเทคนิคอื่น ๆ (รังสีปรับความเข้ม, รังสี 3 มิติ และ 2 มิติ) โดยจะทำการเปรียบเทียบการกระจายตัวและความแม่นยำของลำรังสีในบริเวณสมอง ไขสันหลัง และบริเวณก้อนเนื้องอกด้วยการประเมินจากค่าความสม่ำเสมอของรังสี (homogeneity index [HI]) และค่าความเข้ารูปของรังสี (conformity index [CI]) นอกจากนี้ยังได้ทำการเปรียบเทียบรังสีบริเวณไขสันหลังที่วัดเป็นเปอร์เซ็นต์ (percent [%]) ของค่าที่กำหนด และปริมาณรังสีที่กระจายไปยังร่างกายผู้ป่วยระหว่างสี่เทคนิคด้วย

ผลการศึกษา การรักษาผู้ป่วยกลุ่มนี้ด้วยเครื่องฉายรังสีภาพนำแบบเกลียวหมุนให้รังสีบริเวณสมองที่มีความสม่ำเสมอและเข้ารูปเมื่อเทียบกับเทคนิคอื่น ค่าเฉลี่ยของความสม่ำเสมอของลำรังสีด้วยรังสีภาพนำแบบเกลียวหมุนร้อยละ 44.51 (p <0.001) ค่าเฉลี่ยของความเข้ารูปคือ 0.984 (p <0.001) สำหรับรังสีที่ไปยังบริเวณก้อนเนื้องอกมีผลการศึกษาใกล้เคียงกับบริเวณสมอง ในบริเวณไขสันหลังนั้นพบว่าค่าความสม่ำเสมอของรังสีด้วยเทคนิครังสีภาพนำแบบเกลียวหมุนนั้นมีค่าเทียบได้กับเทคนิครังสีปรับความเข้ม ในขณะที่มีความเข้ารูปมากกว่า (p <0.001) ซึ่งสอดคล้องกับปริมาณรังสีที่ไปยังบริเวณไขสันหลังคือ ร้อยละ 122.22 นอกจากนี้พบว่ารังสีภาพนำแบบเกลียวหมุนและรังสี 2 มิติให้ค่าการกระเจิงรังสีไปยังทั่วร่างกายผู้ป่วยเทียบเท่ากัน (p =0.272) มีค่าสูงกว่ารังสี 3 มิติ (p = 0.034) ในขณะที่รังสีปรับความเข้มมีค่ารังสีสูงที่สุด (p <0.05) ผู้ป่วยทั้ง 12 คนสามารถรับการฉายรังสีได้ตามที่กำหนด ทนต่อการฉายรังสีด้วยเทคนิคภาพนำแบบเกลียวหมุนได้ดี ค่าเฉลี่ยของจำนวนวันที่ได้รับรังสี 40 วัน ผลข้างเคียงด้านโลหิตระดับ 3-4 เป็นผลข้างเคียงระยะสั้นเดียวที่ทำให้เกิดการหยุดฉายรังสีชั่วคราว

สรุปผลการศึกษา การรักษาด้วยการฉายรังสีภาพนำแบบเกลียวหมุนสามารถให้ลำรังสีไปยังบริเวณสมอง ไขสันหลัง และบริเวณก้อนเนื้องอกไปพร้อม ๆ กันได้ มีผลข้างเคียงจากการรักษาที่ยอมรับได้และระยะเวลารวมในการฉายรังสีอยู่ที่ระดับที่น่าพึงพอใจ เมื่อเปรียบเทียบกับเทคนิคอื่นแล้ว โดยรวมพบว่า เทคนิคภาพนำแบบเกลียวหมุนนี้ให้การกระจายตัวของลำรังสีอย่างสม่ำเสมอและเข้ารูปดี ในส่วนของรังสีที่กระเจิงไปยังบริเวณอื่น ๆ ของร่างกายนั้น พบว่าเทคนิคนี้จะแย่กว่ารังสี 3 มิติ แต่จะดีกว่ารังสีแบบปรับความเข้ม ผลของการกระเจิงนี้ยังต้องอาศัยการติดตามหลังการรักษาระยะยาวเพื่อประเมินผลข้างเคียงที่อาจจะเกิดขึ้นได้ **เชียงใหม่เวชสาร 2558;54(1):17-28.**

คำสำคัญ: craniospinal axis irradiation, helical tomotherapy, dosimetric comparison