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Original Article

Dosimetric comparison of helical tomotherapy using different techniques, simultaneous integrated boost and sequential boost for craniospinal irradiation: a single institution experience

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Abstract

Purpose: Craniospinal irradiation (CSI) has become an important and challenging radiation technique for radiation oncologists. Helical tomotherapy (HT) seems to have dosimetric advantage for CSI compared with other radiation modalities. The purpose of this study was to compare dosimetric data between two different HT plans; simultaneous integrated boost (SIB) and sequential boost (Sq).

Method: Twelve previously treated CSI contoured datasets by SIB technique were replanned. Dosimetric comparative parameters of targets were conformity index (CI) and homogeneity index (HI). For organ at risk (OARs), the mean dose of parallel organs, D2% of serial organs and whole body integral dose (ID) were also investigated.

Result: SIB plan significantly provided more conformed dose to CSI and tumour boost while resulting in a similar CI in spinal boost region compared with Sq plan. The HI showed no differences between two plans. Radiation exposure to serial organs and ID were also significantly lower in SIB plan.

Conclusion: CSI treatment using HT, SIB technique was feasible and had more target coverage while minimising the radiation dose to healthy tissues.

Keywords: craniospinal irradiation; dosimetric comparison; helical tomotherapy

INTRODUCTION

Many malignant central nervous system (CNS) tumours that tend to develop leptomeningeal dissemination require craniospinal irradiation (CSI) as a part of the mandatory treatment. CSI is considered to be a challenging technique for radiation oncologist in order to provide homogeneous and

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conformal dose distribution to planning target volume (PTV) while minimising the radiation dosage to organ at risks (OARs). Historical data used conventional two-dimension (2D) radiation technique which is composed of two lateral opposing radiation beam at cranial region and direct posterior beam at spinal region. After the improvement of computed tomographic (CT) simulation, radiation modalities were shifted to three-dimension conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT). However, these techniques still require gap junction between cranial and spinal field which usually causes a heterogeneity of dose painting in this area, resulting in overdose on spinal cord while providing underdose to the target. Various techniques were applied to solve this problem.[1,2]

According to our previous study,[3] one of the sophisticated modalities for CSI that can eliminate the gap junction is helical tomotherapy (HT). In this technique, the couch can continuously move up to 160 cm with helical delivery of photon radiation by IMRT. HT achieved the best dosimetric distribution in terms of homogeneity index (HI) and conformity index (CI) for both PTV brain and spine compared with 2D, 3D-CRT and IMRT.[3] The feasibility of CSI treatment using HT in the supine position, which was suitable for paediatric patients who required sedation during radiation course, was also reported. Nevertheless, the important limitation of the study was the first installed calculating program, HiArt 4·1·2·1, was unable to evaluate the radiation dose in the sequential boost plan (Sq). The radiation schedule based on equivalent dose (EQD) and Biological effective dose (BED) concept to set the CSI protocol with simultaneous integrated boost (SIB) plan was carefully calculated. However, published data to support the use of SIB technique in CSI plan was not commonly found.

After the HiArt program was updated to version 4.2.3.9, the appropriate CSI technique for the patients was determined. The purpose of this study was to compare between dose distribution to the target and unavoidable radiation dose to selected reported OARs in CSI treatment using tomotherapy with SIB and Sq plans.

METHOD

Patient populations

There were 12 patients with primary CNS cancers who required CSI treatment with HT, SIB technique admitted during May 2012 to August 2013 at the Faculty of Medicine, Chiang Mai University. Eligibility criteria consisted of pathologic-confirmed of intracranial tumour with potential leptomeningeal dissemination, Eastern Cooperative Oncology Group performance status 1–2,[4] and good bone marrow function. Patients who had extra-CNS metastasis and previously received radiation therapy at any site were excluded. Patient characteristics were summarised in Table 1. Six of the 12 patients

Table 1. *Patient characteristics*

No.	Age (years)	Diagnosis	Target length (cm)	Mean beam on time (minutes)	Follow-up
1	8	Medulloblastoma, T-spine metastasis	58·1	8·1	Alive
2	5	Medulloblastoma, diffuse spinal metastasis	50·7	7·4	Death
3	19	Medulloblastoma, residual tumour >1·5 cm^2	77·2	11·9	Alive
4	4	Pineoblastoma, T-spine metastasis	55·7	8·2	Death
5	3	Retinoblastoma, diffuse spinal metastasis	48·9	7·2	Death
6	22	Multifocal germinoma, 4^{th} ventricle metastasis	77·8	12·0	Alive
7	3	Medulloblastoma, presenting at second-year of age	54·0	7·9	Alive
8	10	Medulloblastoma, residual tumour >1·5 cm^2	60·5	8·9	Alive
9	12	Supratentorial primitive neuroectodermal tumour, diffuse spinal metastasis	68·3	11·6	Death
10	19	Ependymoma, conus medullaris metastasis	70·3	11·4	Alive
11	9	Medulloblastoma, spinal metastasis	59·9	7·9	Alive
12	15	Supratentorial primitive neuroectodermal tumour, residual tumour >1·5 cm^2	78·1	11·4	Death

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(50%) were medulloblastoma; all of them were classified as high risk according to the Chang system.[5] Other diagnoses were retinoblastoma, supratentorial primitive neuroectodermal tumour, pineoblastoma, multifocal germinoma and ependymona with spinal metastasis. Eight patients (67%) were found to have craniospinal fluid (CSF) dissemination before starting radiation treatment and two patients were diagnosed with a malignant tumour at 2 years of age. Most of the patients received neo-adjuvant and adjuvant chemotherapy but none had concurrent chemoradiation.

Simulation and contouring

CT simulation was undertaken in supine position, using 5 mm slice thickness. All patients were immobilised by using an individual thermoplastic mask and vacuum cushion. Target volumes and OARs delineations were contoured on the treatment planning system (Oncentra, Philips, Veenendaal, the Netherlands) by the radiation oncologist. The CSI volume covered the entire meninges, extending from brain to the end of thecal sac, and especially included cribiform plate. PTV were divided into PTV brain, PTV spine and PTV tumour boost in order to compare dosimetry among four-treatment plans (HT, IMRT, 3D-CRT and 2D).[3] In this study, contouring datasets from the previous study were selected to generate another HT plan for each patient deploying Sq technique.[3]

Treatment planning

The contoured CT datasets were transferred to the Tomotherapy planning workstation (HiArt, Tomotherapy). Both SIB and Sq techniques were planned by the same radiation physicist to achieve an acceptable radiation dosimetry. Each plan followed the International Commission on Radiation Units and Measurements ICRU 83[6]: the D50% close to a prescription dose, the D98% considered as a minimum radiation dose in PTV, and OARs constrained by the Quantitative Analyses of Normal Tissue Effects in the Clinic.[7] An equal penalty and important values calculation of each HT plan in the same patient were prescribed. According to widely published data, field width of 2·5 cm showed a nearly double beam on time compared with field width of 5·0 cm. This might be considered inconvenient for paediatric patients who received sedative procedures.[8–11] In this research, 5·0 cm field width with a pitch of 0·43 and modulation factor of 2·8 was used with all patients in both different tomotherapy plans. The SIB protocol was set, based on BED and EQD concepts of dose per fraction 1·8 Gy to total dose 23·4–55·8 Gy in 23 fractions (Fx),[3] while the Sq plan provided daily radiation dose 1·8 Gy Sq to 50·4–55·8 Gy.

Dosimetric comparison parameters

The plan was evaluated following the ICRU 83.[6] The dosimetric parameters of targets were compared referring to dose CI and HI.

Conformity index (CI):

$$\mathrm{CI} = \frac{V_{\mathrm{PTV}}}{V_{95}}$$

where V_{PTV} is the planning target volume, V_{95} the volume of PTV receiving 95% of the prescribed dose.

Homogeneity index (HI):

$$\mathrm{HI} = \frac{D_{2\,\%} - D_{98\,\%} \times 100}{D_{50\,\%}}$$

where $D_{2\%}$ is the dose to 2% of the volume of target, $D_{98\%}$ the dose to 98% of the volume of target, $D_{50\%}$ the dose to 50% of the volume of target.

The integral dose (ID) to the whole body was also concerned as a possible predictor for higher risk of developing secondary malignancy. Therefore, we calculated ID in all plans by utilising the following formula:

Integral dose (ID)[12]:

$\mathrm{ID} = V \times D$ where V is the volume of the whole body (L), D the mean dose to the whole body (Gy).

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) 16·0 was applied for analysing the dosimetric data. Comparisons between two plans were made by non-parametric Wilcoxon's

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signed-rank test. A p-value of <0·05 indicated the differences were statistically significant.

This study was approved by the Research Ethics Committee, Faculty of Medicine, Chiang Mai University.

RESULTS

Target comparison

The median values of CI for PTV CSI, tumour boost and spinal boost, including HI of PTV tumour boost and spinal boost, are presented in Table 2. The HI of PTV CSI could not be compared because four out of 12 patients were prescribed different doses between whole brain and whole spine from the diffuse spinal metastasis in each patient. SIB technique had significantly more conformed dose to PTV CSI and tumour boost than Sq plan while having a similar conformity to PTV spinal boost. Wilcoxon's signed-rank analysis showed an identical homogenous dose distribution on PTV tumour and spinal boost for both SIB and Sq techniques.

Table 2. *Conformity index (CI) and homogeneity index (HI) comparison*

	SIB technique		Sq technique		*p*-value
	Median	SD	Median	SD	
CI					
CSI	1·20	0·21	1·34	0·35	*0·002*
Tumour boost	1·38	0·16	1·82	0·43	*0·002*
Spinal boost	1·74	0·15	1·80	0·18	0·40
HI					
Tumour boost	3·94	1·50	4·36	1·18	0·64
Spinal boost	6·54	4·43	7·46	12·54	0·116

Abbreviation: CSI, craniospinal irradiation.
Italics: A statistical significant if p-value < 0.05.

OARs comparison

The radiation doses and comparisons are shown in Table 3. The constraint dose for serial organs (spinal cord, brainstem and optic apparatus) followed ICRU-83 definition which was determined by D2%, while the parallel organs (lung, parotid gland and cochlea) were compared referring to Dmean. The radiation exposure to serial organs was significantly lower in SIB technique. In contrast, the radiation exposure to parallel organs, both techniques delivered an identical mean dose to lung and parotid glands whereas dose to bilateral cochlea were statistically significant higher in Sq plan. The whole body ID was also significantly lower when irradiated by SIB technique.

DISCUSSION

The developed HT equipted with a rotational fan beam that continuously releases the photon beam while the couch is moving, can generate an extensive radiation treatment field without a gap junction. CSI treated by HT achieved excellent dosimetric evaluation in terms of CI and HI of target volume while effectively minimised

Table 3. *Selected organs at risk comparison*

	SIB technique (Gy)		Sq technique (Gy)		*p*-value
	Median	SD	Median	SD	
Spinal cord	42·50	4·80	47·28	5·66	*0·004*
Brainstem	54·03	3·95	56·70	4·74	*0·002*
Optic chiasm	40·62	6·48	43·54	6·41	*0·003*
Optic nerve, right	39·96	5·76	42·29	5·45	*0·003*
Optic nerve, left	39·70	4·69	42·58	4·94	0·010
Lung, right	9·58	2·71	9·40	2·70	0·055
Lung, left	8·32	2·06	8·26	2·21	0·060
Parotid, right	16·78	2·83	17·15	5·32	0·071
Parotid, left	16·03	2·81	16·50	5·51	0·060
Cochlea, right	36·95	5·40	42·52	5·97	*0·008*
Cochlea, left	36·74	5·56	41·63	5·64	*0·002*
Whole body integral dose (Gy.L)	224·89	94·99	235·86	96·48	*0·004*

Italics: A statistical significant if p-value < 0.05.

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radiation dose to specific OARs compared with other techniques.[3,10,13–15] A total of 12 patients previously received CSI by HT, SIB technique in the previous study were selected and replanned to investigate the difference in dosimetry of another HT plan, Sq technique. As there are limited published reports on actually treating CSI by HT, the previous study undertaken by us is used as a reference study.[3] This previous study indicated that HT, SIB technique in CSI region reduced the overall treatment time compared with standard sequential technique and gave acceptable toxicities. Nonetheless, there are some limitations in this current study. One is that it is a retrospective single institution experience of previously treated CSI with a specific HT, SIB technique, rather than being treated prospectively. Another is that the small number of subjects in the study may limit a statistical power.

Dosimetric comparison in this study shows greater conformity of target as well as lower healthy tissue exposed to radiation in SIB technique; this is similar to the comparative results from other regions, such as head-and-neck cancer, lung cancer, and prostate cancer.[16,17] Whether the dose distribution advantage indicates the better clinical outcomes in terms of lower toxicity, a prospective study is required. In the protocol, SIB technique released radiation at the total of 23 Fx. According to the radiobiological point of view, this shortened overall treatment time (compared with around 27–31 Fx in Sq plan) and it may be assumed to reduce the risk of tumour clonogens regrowth and can improve local control, as seen in the head-and-neck cancer model.[16]

As the SIB plan slightly radiates hypofractionated radiation to the target which sometimes abuts the serious critical organ, such as brainstem and spinal cord, that have greater radiation sensitivity in larger doses per fraction, a sequential approach is preferable, to avoid fatal complications.

Irradiating the entire leptomeninges by SIB tomotherapy also improved whole body ID which is one of the concerning issues that helps evaluate the risk of second radiation-induced malignancy.[18] Although HT is theoretically assumed to provide more ID to whole body, the results from the previous study showed an equal dose between tomotherapy and conventional 2D technique. However, HT slightly irradiated more ID than 3D-CRT but less than step-and-shoot IMRT; this was supported by Penagaricano.[14,19] Several studies mentioned the higher estimated rate of secondary tumour with IMRT by 1–10% compared with conventional radiation delivery[20–22]; nevertheless, this result cannot be extrapolated to helical IMRT tomotherapy which is composed of multileaf collimator-IMRT. The matter of concern was greater normal tissue volume exposed to low radiation dose and the increase in the quantity of monitor units in HT. The most effective radiation modality proposed to reduce low dose volume of normal tissue and may decrease the risk of developing second cancer is a particle beam radiation; proton therapy appears to be one of the worldwide available options. Some authors report an approximate six time reduction of cancer risk in proton therapy compared with photon and electron modalities[23] but the clinical usefulness is still unclear.

CONCLUSION

CSI using HT, SIB technique was feasible and had better conformity to the target coverage; while minimising healthy tissue exposed to radiation. The whole body ID was also reduced by this technique. The advantage in shortening overall treatment time in SIB technique may affect the improvement of local tumour control which has been reported in the head-and-neck cancer model. However, irradiating a target that is attached to a serious critical structure, especially brainstem and spinal cord, by adopting SIB plan should be weighed with the exposure of a slightly hypofractionated radiation dose. The Sq plan may be considered as an appropriate modality approach in this situation.

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