Dosimetric comparison of three-field conformal spinal radiation and single posterior spinal field in craniospinal irradiation

การศึกษาเปรียบเทียบปริมาณรังสีระหว่างการฉายรังสีบริเวณไขสันหลังด้วย 3 ลำรังสี และ 1 ลำรังสี ในการฉายรังสีบริเวณสมองและไขสันหลัง

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ABSTRACT

Background: Craniospinal irradiation (CSI) is technically challenging because of the need to cover complex clinical target volume. There are innovative techniques improving target volume coverage such as intensity-modulated radiotherapy (IMRT), tomotherapy, and proton therapy. However, 3D conformal radiotherapy (3D-CRT) is still used in limited-resource institutions.

Objectives: To compare the radiation dose to organs at risk (OARs), conformation number (CN), and homogeneity index (HI) between 3-field conformal spinal radiation (3F-SPINE) and single posterior spinal field (1F-SPINE).

Material and methods: From June 2011 to December 2012, 10 patients with high risk of craniospinal involvement underwent CT simulation with supine position and replanned CSI with 3F-SPINE and 1F-SPINE. Prescription dose was 36 Gy to 95% of the PTV. The parameters were V25Gy of heart, V20Gy of lung, mean lung dose, V20Gy of kidneys, mean liver dose, CN, and HI.

Results: 3F-SPINE showed a significant reduction of V25Gy of heart within QUANTEC threshold compared to 1F-SPINE (3.03% vs 42.48%). However, doses to other OARs were within QUANTEC threshold in both techniques. 3F-SPINE showed better results in V20Gy of lung and CN than 1F-SPINE (V20Gy of lung of 9.83% vs 12.59%; and CN of 0.75 vs 0.70, respectively). In contrast, 1F-SPINE showed better results in mean lung dose, V20Gy of kidneys, and HI than 3F-SPINE (mean lung dose of 6.27 Gy vs 8.53 Gy, V20Gy kidneys of 11.24% vs 13.02%, and HI of 1.16 vs 1.17, respectively). There was no significant difference between 3F-SPINE versus 1F-SPINE for mean liver dose (9.03 Gy vs 9.16 Gy).

Conclusion: 3F-SPINE reduced V25Gy of heart to be within QUANTEC threshold. Doses to other OARs were within QUANTEC threshold in both techniques.

Keywords: 3D conformal radiotherapy, craniospinal irradiation, three-field conformal spinal radiation

บทคัดย่อ

หลักการและเหตุผล: การฉายรังสีบริเวณสมองและไขสันหลังใช้เทคนิคซับซ้อน ปัจจุบันมีเทคนิคที่มุ่งเป้าได้ดี เช่น ฉายรังสีปรับความเข้ม ฉายรังสีเกลียวหมุน ฉายโปรตอน แต่การฉายรังสีสามมิติยังใช้ในหลายสถาบันที่ขาดแคลนเครื่องมือ

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบปริมาณรังสีที่อวัยวะข้างเคียงได้รับ conformation number (CN) และ homogeneity index (HI) ระว่างการฉายรังสีบริเวณไขสันหลังด้วย 3 ลำรังสี และ 1 ลำรังสี

วัสดุและวิธีการ: ตั้งแต่มิถุนายน2554 ถึงธันวาคม 2555 มีผู้ป่วยที่ต้องฉายรังสีบริเวณสมองและไขสันหลังจำนวน 10 คน ผู้ป่วยรับการทำเอกซเรย์คอมพิวเตอร์ในท่านอนหงาย และนำภาพมาวางแผนฉายรังสีด้วย 3 ลำรังสี เปรียบเทียบกับ 1 ลำรังสี ด้วยปริมาณรังสี 36 Gy โดยตัวแปรที่วิเคราะห์ในงานวิจัยประกอบด้วย V25Gyของหัวใจ V20Gyของปอด รังสีเฉลี่ยของปอด V20Gyของไต รังสีเฉลี่ยของตับ CN HI

ผลการศึกษา: การฉายรังสีด้วย 3 ลำรังสีลด V25Gyของหัวใจได้ตามเกณฑ์ของ QUANTEC เมื่อเทียบกับ 1 ลำรังสี (3.03% เทียบกับ 42.48%) ส่วนอวัยวะอื่นได้รับรังสีตามเกณฑ์ของ QUANTEC ในทั้ง 2 เทคนิค โดย 3 ลำรังสีได้ผลดีกว่า 1 ลำรังสีด้าน V20Gyของปอด (9.83% เทียบกับ 12.59%) และ CN (0.75 เทียบกับ 0.70) ขณะที่รังสีเฉลี่ยของปอด (8.53 Gy เทียบกับ 6.27 Gy) V20Gyของไต (13.02% เทียบกับ 11.24%) และ HI (1.17 เทียบกับ 1.16) ของ 1 ลำรังสีได้ผลดีกว่า 3 ลำรังสี ส่วนรังสีเฉลี่ยของตับไม่แตกต่างกันในทั้ง 2 เทคนิค (9.03 Gy เทียบกับ 9.16)

ข้อสรุป: 3F-SPINE ลด V25Gyของหัวใจได้ ส่วนอวัยวะอื่นได้รับรังสีตามเกณฑ์ของ QUANTEC ในทั้ง 2 เทคนิค

คำสำคัญ: รังสีสามมิติ การฉายรังสีบริเวณสมองและไขสันหลัง การฉายรังสีบริเวณไขสันหลังด้วย 3 ลำรังสี

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Introduction

Craniospinal irradiation (CSI) has been used as an important part of brain tumors treatment. It is indicated in group of patients with high risk of craniospinal axis involvement such as medulloblastoma, ependymoblastoma, pineal-oblastoma, atypical teratoid/rhabdoid tumors (AT/RT), and supratentorial primitive neuroecto-dermal tumors. The current standard of care consists of maximal safe resection followed by radiotherapy and chemotherapy. Although survival rate is continuously improved, there is a growing concern regarding long-term treatment-related side effects.

CSI is technically challenging because of the need to cover a complex clinical target volume (CTV) including whole brain, whole length of spinal axis, and covering meninges. In most radiotherapy departments, CSI is delivered to patients in prone position using lateral opposed fields to cover whole brain and direct posterior fields to cover spinal axis. The junctions between the fields are feathered during the course of treatment. The supine position provides numerous advantages such as comfort and reproducibility. For the patients who need anesthesia, airway protection is easily monitored by supine position.[1,2]

The standard CSI technique is three-dimen-sional conformal radiotherapy (3D-CRT). The use of CT simulation decreases simulation time and increases planning accuracy.[1, 2] There are many innovative techniques such as intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), tomotherapy, and proton therapy to improve target volume coverage, dose homogeneity, and conformity.[3] The estimated risks of all adverse effects by IMRT technique were less than 3D-CRT technique. For

example, the estimated risk of heart failure was lower because IMRT had multiple fields and delivered tightly-focused radiation beams to target volume. However, the estimated risk of secondary cancer was increasing by IMRT technique. Proton therapy was better than 3D-CRT and IMRT in term of adverse effects and secondary cancer.[4]

Because of restricted access to IMRT in many institutions, this study mimicked IMRT by planning 3D-CRT with multiple spine fields. Three-field conformal spinal radiation (3D-SPINE) was compared to single posterior field (1F-SPINE) to avoid organs at risk (OARs) such as heart, lung, kidneys, and liver. Furthermore, this study compared homogeneity index (HI) and conformation number (CN) between 3F-SPINE and 1F-SPINE.

Materials and methods

This study was approved by the Research Ethics Review Committee of the faculty of medicine, Chulalongkorn university. A retrospective study was conducted by retrieving the information of dosimetry from CT simulator database from June 2011 to December 2012. Patients with high risk of craniospinal involvement who underwent CT simulation in supine position, neck extension, and shoulder depression were included. CSI was replanned with 6 MV photon, using Eclipse Planning System Version 11 (Varian Medical System, Palo Alto, CA), to compare between 3F-SPINE and 1F-SPINE.

Radiation volume included CTV of brain and spine. CTV of brain was defined as brain and meninges down to foramen Magnum which included meninges around optic nerve and disc. CTV of spine was defined as spinal cord and meninges down to thecal sac, including meninges in neural foramen. Planning target volume (PTV) of brain and spine were defined as CTV of brain plus 0.5 cm and CTV of spine plus 1 cm, respectively. The radiation dose from 3F-SPINE and 1F-SPINE covered whole vertebra. OARs included heart, lung, liver, and bilateral kidneys.

Each treatment plan consisted of brain fields, upper spine fields, and lower spine fields. Feathering technique was used to match brain fields and upper spine fields at C-spine level 5 to 7 and match upper spine fields and lower spine fields at L-spine level 2 to 3. Junctions were shifted 1 cm everyday as shown in **figure 1**. Brain fields utilized lateral opposing beams and rotated collimators to match with divergence of superior border of upper spine beams as shown in **figure** 1. Upper spine fields and lower spine fields were planned in both technique. 3F-SPINE utilized gantry with 150, 180, and 210 degrees and 1F-SPINE utilized gantry with 180 degrees as shown in **figure 2.**

For embryonal tumors with high risk of craniospinal involvement, the standard CSI dose is 36 Gy. Therefore, the prescription dose in this study was 36 Gy to 95% of the PTV (1.8 Gy per fraction per day). The data was collected in data record form and analyzed the difference between two techniques in aspect of dose to OARs, HI, and CN. QUANTEC studies and COG long-term follow-up guidelines reported complication from radiation.[5] The parameters

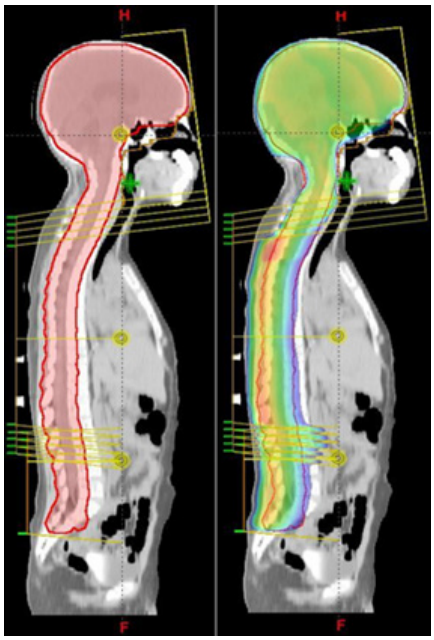

Figure 1: Feathering technique and collimator rotation of brain fields to match with divergence of superior border of upper spine fields

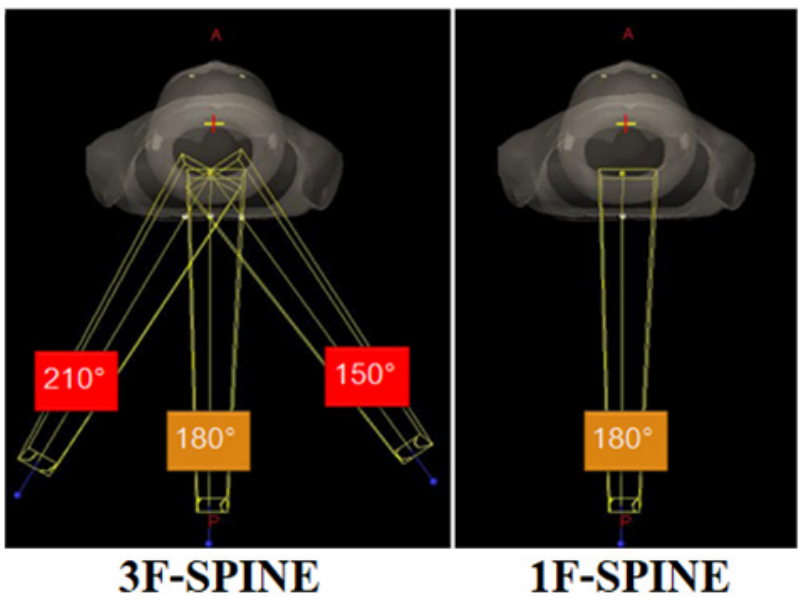

Figure 2: Spine fields using 3 beams compared to single posterior beam

from 2 studies were quite similar but QUANTEC studies had clear-cut threshold dose as shown in **table 1**. HI and CN were other parameters in this study. RTOG defined HI as maximum isodose in the target divided by reference isodose. van't Riet A defined CN as following equation.[6] CN = (TVRI / TV) * (TVRI / VRI)

TVRI = target volume covered by the reference isodose

TV = target volume

VRI = volume of the reference isodose

Wilcoxon matched-pair signed-rank test was used to compare the results between 3F-SPINE and 1F-SPINE. All tests were two-sided with p-value ≤ .05 for significant level. Statistical analysis was processed using SPSS version 20.0. This study was approved by the Research Ethics Review Committee of the faculty of medicine, Chulalongkorn university.

Results

There were 10 patients enrolled in the period of this study. Median age was 9 years (range 5-33 years old). Embryonal tumors consisted of high-risk medulloblastoma 80%, pinealoblastoma 10%, and AT/RT 10%. There were 6 males (60%) and 4 females (40%). The median PTV length was 55.15 cm and mean PTV length was 57.46 cm (range 46.57- 77.18 cm) as shown in **table 2**. The PTV dose was 36 Gy in all patients. The volume and dose to OARs, HI, and CN were shown in **table 3.**

Table 1: The parameters of organs at risk from QUANTEC[5]

Organs at risk	Parameters	Toxicities
Heart	V25Gy < 10 %	Long term mortality < 1 %
Lung	V20Gy ≤ 30 %	Symptomatic pneumonitis < 20 %
	Mean < 13 Gy	Symptomatic pneumonitis 10 %
Kidneys	V20Gy ≤ 32 %	Clinical dysfunction < 5 %
Liver	Mean < 30 Gy	Radiation-induced liver disease < 5 %

Table 2: Patients characteristics

Patients characteristics (N = 10)		
Age (years)	Median	9
	Mean ± SD	12.10 ± 8.49
	Range	5 - 33
Disease	High-risk medulloblastoma	8 (80 %)
	Pinealoblastoma	1 (10 %)
	Atypical teratoid/rhabdoid tumor	1 (10 %)
Sex	Male	6 (60 %)
	Female	4 (40 %)
Length of planning	Median	55.15
Target volume (cm)	Mean ± SD	57.46 ± 9.97
	Range	46.57 – 77.18

Table 3: The volume and dose to organs at risk, homogeneity index, conformation number

Parameter	3F-SPINE (mean ± SD)	1F-SPINE (mean ± SD)	p value
Heart: V_{25Gy}(%)	3.04 ± 1.58	42.48 ± 6.91	< .005
Lung: V_{20Gy}(%)	9.83 ± 2.48	12.59 ± 4.36	< .005
Mean dose (Gy)	8.53 ± 1.43	6.27 ± 1.43	< .005
Kidneys: V20Gy (%)	13.02 ± 6.03	11.23 ± 5.43	< .005
Liver: Mean dose (Gy)	9.03 ± 1.09	9.16 ± 1.18	.169
Homogeneity index	1.17 ± 0.04	1.16 ± 0.04	.014
Conformation number	0.75 ± 0.08	0.70 ± 0.11	< .005

Abbreviations: 3F-SPINE = 3-field conformal spinal radiation, 1F-SPINE = single posterior spinal field

V_{25Gy} of the heart in 3F-SPINE was decreased and within the QUANTEC threshold while V_{25Gy} of heart in 1F-SPINE was over the QUANTEC threshold (3.03 ± 1.58 % vs 42.48 ± 6.91 %; $p < .005$) as shown in **figure 3.**

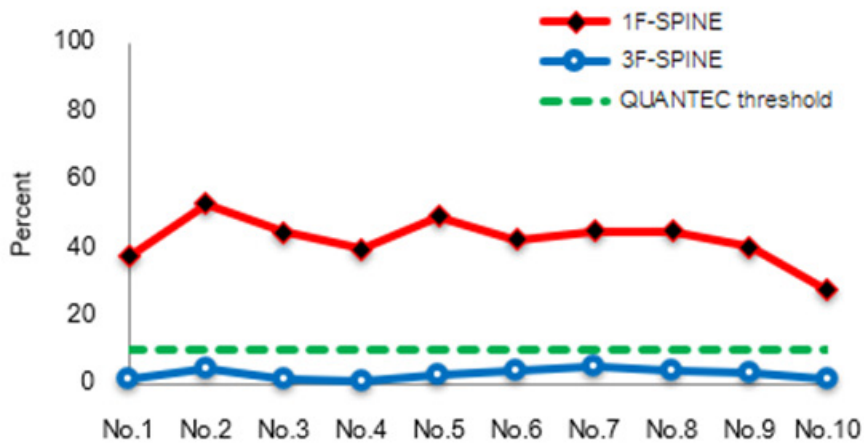

Figure 3: V25Gy of heart

Abbreviations: 3F-SPINE = 3-field conformal spinal radiation, 1F-SPINE = single posterior spinal field

V_{20Gy} of the lungs in 3F-SPINE was less than 1F-spine (9.83 ± 2.48 % vs 12.59 ± 4.36 %; $p < .005$) but mean lung dose was higher (8.53 ± 1.43 Gy vs 6.27 ± 1.43 Gy; $p < .005$) as shown in **figure 4 and 5.**

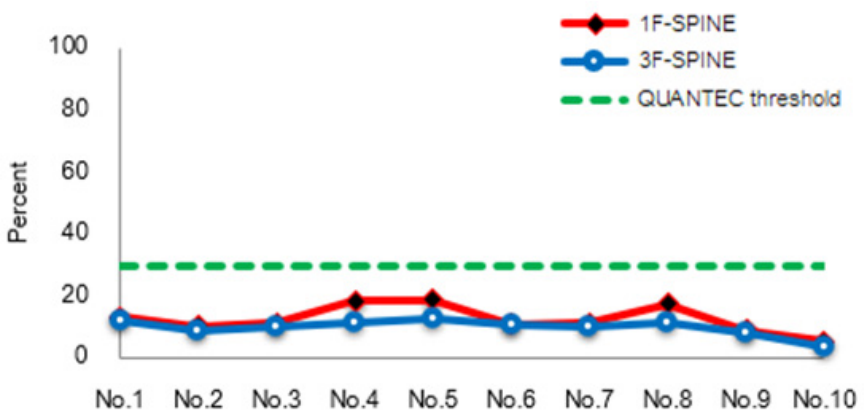

Figure 4: V20Gy of the lungs

Abbreviations: 3F-SPINE = 3-field conformal spinal radiation, 1F-SPINE = single posterior spinal field

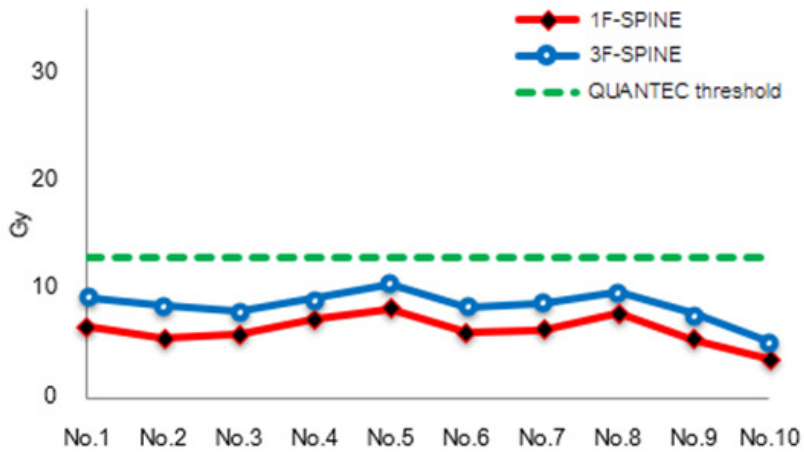

Figure 5: Mean lung dose (Gy)

Abbreviations: 3F-SPINE = 3-field conformal spinal radiation, 1F-SPINE = single posterior spinal field

V_{20Gy} of kidneys in 3F-SPINE was increased (13.02 ± 6.03 % vs 11.23 ± 5.43 %; $p < .005$) as shown in **figure 6.**

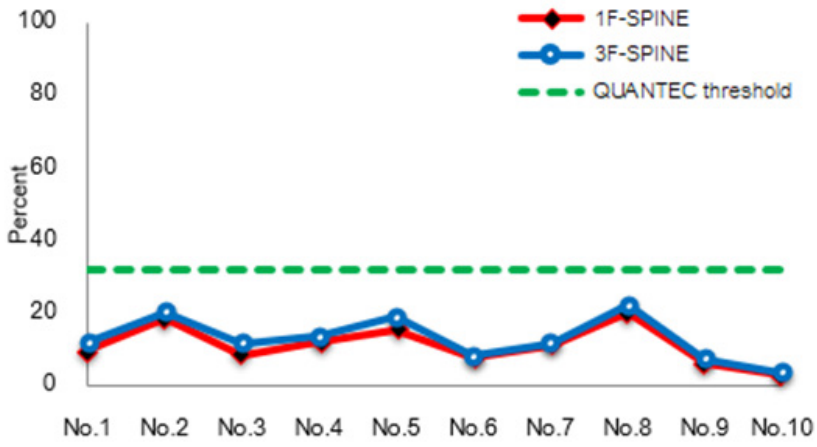

Figure 6: V_{20Gy} of kidneys

Abbreviations: 3F-SPINE = 3-field conformal spinal radiation, 1F-SPINE = single posterior spinal field

Mean liver dose was not significantly different between two study arms (9.03 ± 1.09 Gy vs 9.16 ± 1.18 Gy; *p = .169*) as shown in **figure 7.**

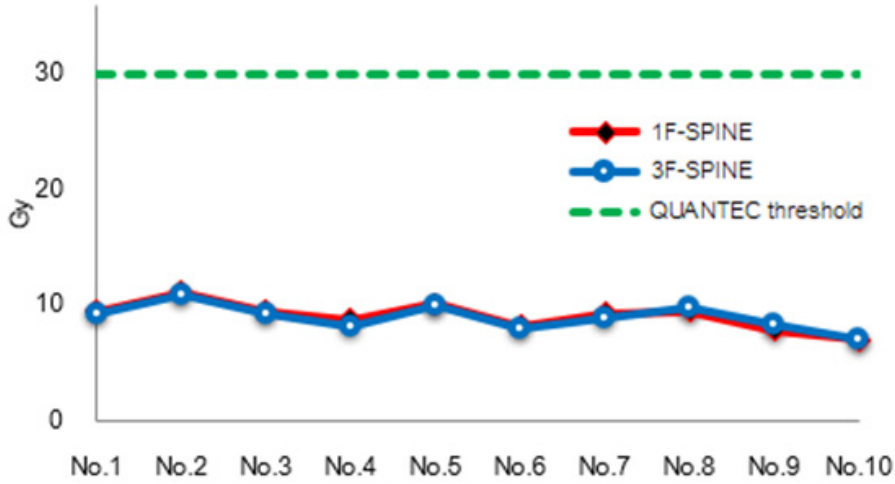

Figure 7: Mean liver dose (Gy)
Abbreviations: 3F-SPINE = 3-field conformal spinal radiation, 1F-SPINE = single posterior spinal field

HI in 3F-SPINE was worse (1.17 ± 0.04 vs 1.16 ± 0.04 %; *p = .014*) but HI was better (0.75 ± 0.08 vs 0.70 ± 0.11 %; *p < .005*) as shown in **figure 8 and 9**. The best CN and HI values were 1.

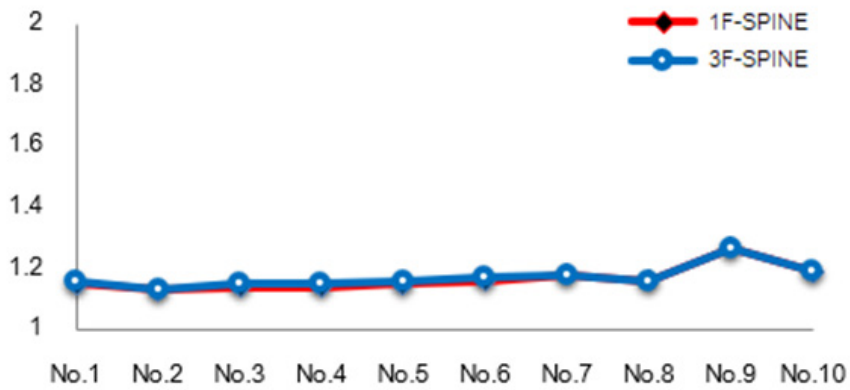

Figure 8: Homogeneity index
Abbreviations: 3F-SPINE = 3-field conformal spinal radiation; 1F-SPINE = single posterior spinal field

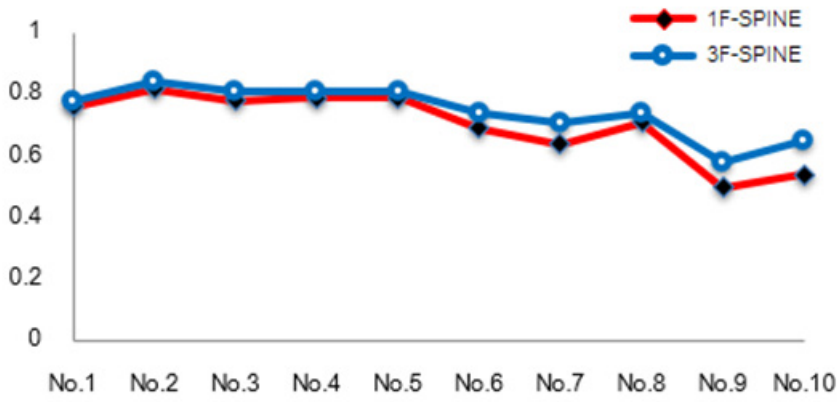

Figure 9: Conformation number

Abbreviations: 3F-SPINE = 3-field conformal spinal radiation, 1F-SPINE = single posterior spinal field

Discussion

CSI has been used as an important part of brain tumors treatment. It is indicated in group of patients with high risk of craniospinal axis involvement. This study used CT simulation in supine position with customized thermoplastic mask immobilization, neck extension, and shoulder depression. The advantage of supine position was more comfortable and reproducible.[1,2] Some pediatric patients required sedation, therefore airway protection was necessary. Delineation, fields placement, organ shielding, tumor boost, and 3D dose-calculation were accurately done under CT simulation.[7] Matching fields with feathering technique is required in our institution.[7] Tatcher et al. reported that feathering might be considered as a safety margin against spinal cord damage, overdosage, and underdosage.[8] Meanwhile, Tinkler et al. reported that stationary junction did not increase relapse or myelopathy when compared to other centers where feathering was used.[9]

Many studies concerned about long-term radiation-related complications. Single posterior spinal field increased risk of heart failure because mean heart dose increased, while IMRT and proton therapy reduced mean heart dose.[4] IMRT and tomotherapy reduced dose heterogeneity and exit doses along the spinal column.[10] Because of restricted access to sophisticated machines in many institutions, this study mimicked IMRT by planning 3D-CRT with multiple spinal fields instead of single posterior spinal field in order to decrease high dose to OARs. 3F-SPINE was compared to 1F-SPINE in the aspects of OARs, HI, and CN. Experimental arm was 3F-SPINE technique utilizing gantries of 150, 180, and 210 degrees. Standard arm was 1F-SPINE technique utilizing gantry of 180 degrees.[7] Cranial fields which consisted of lateral opposing fields were similar in both study groups.

Feathering technique for matching fields was used with the same junctions in both study groups. Therefore, cranial doses and gap doses were not reported in this study.

Radiation complication is deterministic effect. The severity varies with radiation dose and threshold. COG long-term follow-up guidelines for pediatric patients reported the parameters which were slightly different from QUANTEC.[5] Because QUANTEC had clear-cut threshold dose, this study used QUANTEC threshold to predict the risk of normal tissue injury. This study showed that 3F-SPINE reduced V25Gy of heart to be within QUANTEC threshold. Therefore, the clinical symptoms were expected to be decreased. From QUANTEC data, if V25Gy of heart was less than 10%, long-term mortality was less than 1%. This result was similar to the data reported by Brodin et al. that mean heart dose was significantly lower in IMRT compared to posterior single posterior spinal field technique (7.3 Gy vs 18.9 Gy). The estimated risk of heart failure increased 5 times in single posterior spinal field technique as compared to IMRT.[4] Sharma DS also reported that single posterior spinal field technique increased exit doses along the spinal column as compared to IMRT and tomotherapy. [10] Doses to other OARs were within QUANTEC threshold in both techniques, therefore the clinical symptoms might be sparse. V_{20Gy} of lung, mean lung dose, V_{20Gy} of kidneys, HI, and CN were minimally different.

Limitation of this study was dosimetric study. The results of these dose distribution might be surrogate markers for the estimated risks. The further clinical trials are necessary to calculate estimated risks and confirm this hypothesis. Results from patients treated with IMRT, VMAT, or tomotherapy may be different from this study.

Conclusion

This study showed that 3F-SPINE reduced V_{25Gy} of heart to be within QUANTEC threshold while 1F-SPINE increased V_{25Gy} of heart to be 32% over QUANTEC threshold. Doses to other OARs were within QUANTEC threshold in both techniques.

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