เปรียบเทียบปริมาณรังสี ที่ฐานกะโหลกส่วนหน้าและแอ่งสมองส่วนกลาง จากการฉายรังสีแบบคลุมเยื่อหุ้มสมองทั้งหมด โดยใช้จุดศูนย์กลางที่ตำแหน่งต่างกัน

DOSIMETRIC COMPARISON AT CRIBRIFORM PLATE AND MIDDLE CRANIAL FOSSA BETWEEN DIFFERENT ISOCENTERS IN WHOLE SUBARACHNOID IRRADIATION

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บทคัดย่อ

หลักการและเหตุผล : การฉายรังสีแบบคลุมเยื่อหุ้มสมองทั้งหมดในผู้ป่วยที่มีแนวโน้มจะมีโรคมะเร็งกระจายไปตามช่องน้ำเลี้ยงไขสันหลัง มีตัวแปรสำคัญของการกลับเป็นซ้ำ และอัตรารอดชีวิตคือ การครอบคลุมขอบเขตมะเร็งอย่างเพียงพอ ตำแหน่งที่พบว่ามีความคลาดเคลื่อนบ่อยได้แก่ ฐานกะโหลกส่วนหน้า และ แอ่งสมองส่วนกลาง

วัตถุประสงค์ : เพื่อเปรียบเทียบความครอบคลุมของปริมาณรังสีที่ cribriform plate และ middle cranial fossa ระหว่างการฉายรังสีป้องกันการลุกลามที่สมองโดยใช้ศูนย์กลางอยู่ที่ขอบกระบอกตาด้านข้างกับกึ่งกลางสมอง

วัสดุและวิธีการ : ศึกษาในผู้ป่วยที่ได้รับการทำเอ็กซเรย์คอมพิวเตอร์สมองเพื่อจำลองการฉายรังสีตั้งแต่มกราคม 2554 ถึงกุมภาพันธ์ 2555โดยวางแผนการฉายรังสีแบบ two lateral opposed whole subarachnoid จากภาพเอ็กซเรย์คอมพิวเตอร์ด้วยศูนย์กลางลำรังสีที่แตกต่างกันคือ กึ่งกลางสมอง (ตำแหน่ง A) สำหรับแผน A และขอบกระบอกตาด้านข้าง (ตำแหน่ง B) สำหรับแผน B ด้วย Varian Eclipse treatment planning system version 8.0 จากนั้นประเมินปริมาณรังสีที่ cribriform plate, middle cranial fossa และเลนส์ตาของแต่ละแผน

ผลการศึกษา : ผู้ป่วยทั้งสิ้น 44 ราย อายุเฉลี่ย 38 ปี เพศชาย 26 คน (59.1%) เพศหญิง 18 คน (40.9%) วินิจฉัยเป็นโรคเนื้องอกสมองมากที่สุด (63.64%) พบว่าแผน B ทำให้ปริมาณรังสีต่ำสุดของขอบเขตมะเร็งทางคลินิก (clinical target volume) และการวางแผน (planning target volume) เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ (p-value =0.001 และ 0.002 ตามลำดับ) ส่วนปริมาณรังสีไปยังเลนส์ตาในแผน B ก็เพิ่มขึ้นจากแผน A 3.6 %

ข้อสรุป : การฉายรังสีโดยให้ศูนย์กลางลำรังสีอยู่ที่ขอบกระบอกตาด้านข้างเพื่อป้องกันการลุกลามที่สมองเพิ่มความครอบคลุมของปริมาณรังสีต่ำสุดที่สมองได้มากกว่า

Abstract

Backgrounds : For whole subarachnoid irradiation in patients with CSF seeding tumor, an important factor of tumor recurrence and survival rate is adequate tumor coverage. The two common missing area are cribriform plate and middle cranial fossa.

Objectives : To compare dose coverage at cribriform plate and middle cranial fossa from prophylactic cranial irradiation between using lateral orbital rim isocenter and mid-brain point isocenter technique.

Materials and Methods : The study was performed in patients having undergone cranial CT simulation from January 2011 to February 2012. Two-lateral-opposed whole subarachnoid irradiation was planned on CT brain images using two different points of isocenters, i.e. at mid-brain point (point A) for plan A and at lateral orbital rim (point B) for plan B. The Varian Eclipse planning system version 8.0 was applied. Isodose distributions were assessed at cribriform plate, middle cranial fossa and eye lenses for each plan.

Results : All 44 patients were enrolled in this study. The median age of patients was 38 years. Male patients were 26 (59.1%) and female patients were 18 (40.9%). The most common diagnosis was CNS tumor (63.64 %). The study found that plan B significantly improved the minimum doses at CTV and PTV (p-value = 0.001 and 0.002, respectively). Mean lens dose in plan B was more than in plan A by 3.6 percentage points of the prescribed dose.

Conclusions : Using isocenter at lateral orbital rim for prophylactic cranial irradiation increased the dose coverage of the minimum dose at whole brain, especially in the area of cribriform plate and middle cranial fossa comparing with using mid-brain point isocenter technique.

Key word : Dosimetric comparison, whole subarachnoid irradiation, cribriform plate, middle cranial fossa

Introduction

Whole subarachnoid irradiation is generally used as prophylaxis and treatment for cancers with a predilection for cerebrospinal fluid (CSF) seeding, including medulloblastoma, high-risk acute lymphocytic leukemia, central nervous system (CNS) germ cell tumors, pinealoblastoma, CNS lymphoma, malignant ependymoma, malignant choroid plexus tumor, and small-cell lung cancer after complete remission. More patients who are anticipated to have excellent systemic control and have high risk for developing CNS metastases receive prophylactic cranial irradiation (PCI) for improving survival. The effect of dose inhomogeneity in whole brain radiotherapy

(WBRT) is unknown, but was suspected to contribute to disease recurrence and late sequelae[1].

The particular important area is the cribriform plate at anterior cranial fossa, which has been called a possible gravity-related sanctuary for tumor cells.

From the study of Gripp et al., the patients who were treated by two dimension radiotherapy for whole subarachnoid irradiation, the cribriform plates were not completely included in the radiation fields for about 10% of cases[2].

In our institution, the radiation coverage and dose distribution at cribriform plate by using helmet field technique according to ICRU-50 criteria were evaluated and analysed.

According to our treatment planning methods, we followed the standard landmarks guideline for 2D treatment planning. Nevertheless, the cribriform plate was sometimes not entirely included in the treatment fields for quite considerable proportion (10% of our patients). So, the modifications of the irradiation technique to improve dose coverage had been proposed e.g. additional anterior boost field, either by photons or electrons, to increase the dose to the subfrontal region[3]. With this technique, however, a uniform dose distribution still can hardly be achieved, especially at the edges of the anterior field[2]. Due to beam divergence, the setting of the central ray at a mid-brain point might increase dose to the inferior edges of the treatment field. Therefore, it may be a contributing factor to the irradiation of the clinical target volume[4]. To account for divergence, the central axis of the radiation beam may be set to the bony canthus (lateral orbital rim) or may be angled posteriorly away from the eyes. By this method, the scattered dose to the ocular lens is effectively diminished. However, if the subarachnoid space extends beneath the level of the ocular lenses, this modification would not solve the problem[2]. Most importantly, there has been no research study in Thailand to investigate whether shifting isocenter technique from mid-brain point to lateral orbital rim would enhance the whole subarachnoid irradiation to adequately cover the cribriform plate and middle fossa.

Materials and Methods

This experimental study was performed at Division of Radiotherapy, Department of Radiology, Faculty of Medicine, Khon Kaen University, Thailand, from January 2011 to February 2012. This project has been approved by the Human Ethics Committee of Khon Kaen University (HE 551003). Inclusion criteria were patients who have undergone cranial CT simulation at Srinagarind Hospital and volume of CT scanning covered from the vertex of skull down to the second cervical vertebrae. Exclusion criteria were patients who had skull defect due to previous surgery and patients with congenital cranial or brain abnormalities. The statistical analysis was performed by using the STATA software version 10.0. A *p*- value of less than 0.05 was considered statistically significant. Sex, primary tumor and location of minimum dose and maximum dose were described by proportion. Age was described

by median and range. Minimum, maximum and mean dose of each organ, and received dose at 95% CTV and 5% eye lens volume were described by median and range. Doses at each organ and region treated by the different techniques were compared by Wilcoxon signed-rank test.

Patients who participated in this study were treated with the specific procedures as these followings

1. Transfering their images to the Varian Eclipse treatment planning system version 8.0.

2. Contouring the target volume, organs and determining the center point of each plan. The Clinical target volume (CTV) in this study was defined as the brain and meninges with caudal border at second cervical vertebra. The Planning target volume (PTV) was generated by expanding the CTV by 1 cm in all directions.

3. Planning the treatment for the whole subarachnoid irradiation using different isocenters (plan A at mid-brain point and plan B at lateral orbital rim) applied to the same patient. For both plans, the field size and angles were also identically applied. The fields were designed using bony reference marks as performed in routine practice from digital reconstructed radiograph (DRR) without contour information on structures of the optimal dose coverage of the CTV, PTV, cribriform plate, middle cranial fossa and lens. Block contours according to osseous landmarks were used with a 5-mm distance from middle end of multileaf collimators (MLC) leaves to the frontobasis and the middle cranial fossa. The dose was prescribed to isocenter of the field. Field contours were digitalized to the planning system, which is equipped with a pencil beam algorithm.

4. Assessing minimum, maximum and mean dose at CTV, PTV, cribriform plate, middle cranial fossa and lens for each plan using cumulative dose - volume histograms. For each particular patient, the dose was normalized at 95% isodose of the CTV and 2% of transmission dose of the eye lenses was also calculated.

Results

Fourty - four patients were enrolled in this study. The patient baseline characteristics are listed in Table 1. The median age of patients was 38 years (range, 5-68 years). Of 44 patients, 59.1 % were men. The primary tumor included 28 of CNS, 12 of hematology and 4 of lung. Two different points of isocenters of portal beams were applied to the same patient on each planning. Doses at CTV, PTV, cribriform plate and middle cranial fossa are summarized in Table 2, doses at eye lens in Table 3 and location of minimum and maximum dose of PTV in Table 4.

The study suggested that 30 patients were able to receive more minimum doses at CTV in plan B than minimum doses in standardized plan A. Similarly, 24 patients could be improved the minimum doses at PTV in plan B. At the same time, 26 patients received more minimum doses at cribriform plate by plan B than plan A, as well as 27 patients also received more minimum doses at middle cranial fossa in plan B than plan A. Furthermore, 34 patients received a minimum of 95 % of prescribed dose at cribriform plate with

Table 1. Baseline characteristics

Characteristics		n = 44
Age	Median	38 years
	Range	5-68 years
Gender	Female	18 (40.9%)
	Male	26 (59.1%)
Primary tumor	Brain	28 (63.6%)
	Hematology	12 (27.3%)
	Lung	4 (9.1%)

Table 2. The minimum, maximum and mean doses for the CTV, PTV at cribriform plate and middle cranial fossa

Reference points		Plan A	Plan B	*P* –values
CTV	Minimum	41.8 (18.7-74.3)	70.9 (26.8- 97.4)	0.001
	Maximum	117.6 (117.0-119.2)	118.0 (116.7- 118.9)	0.802
	Mean	111.3 (110.9-111.8)	111.6 (110.8-112.7)	0.066
PTV	Minimum	5.7 (2.2-10.3)	8.0 (3.7-13.3)	0.002
	Maximum	120.5 (119.5-121.4)	120.4 (118.8-122.4)	0.779
	Mean	108.8 (106.3-109.9)	109.3 (107.4-111.0)	0.017
Cribriform	Minimum	103.6 (68.6-107.8)	105.3 (96.8- 107.1)	0.028
plate	Maximum	109.5 (108.1-111.4)	109.7 (108.6-111.2)	0.718
	Mean	107.5 (96.8-109.2)	107.8 (105.7-108.8)	0.342
Middle	Minimum	71.4 (39.4-98.1)	81.7 (57.9-103.3)	0.013
cranial	Maximum	112.3 (111.4-113.1)	112.0 (110.8-113.2)	0.327
fossa	Mean	107.8 (106.6-109.4)	107.5 (106.6-108.7)	0.153

**Data presented as percentages of the prescribed dose for each reference points*

Table 3. The minimum, maximum and mean doses at eye lens

Dose (%)	Plan A	Plan B	P-values
Minimum	6.2 (5.5-7.0)	6.5 (5.7-7.3)	0.108
Maximum	15.8 (9.1-31.5)	28.0 (14.6-45.6)	0.001
Mean	8.3 (6.9-13.1)	11.9 (8.0-16.7)	0.002

**Data presented as percentages of the prescribed dose for both eye lenses*

Table 4. Location of minimum and maximum dose of PTV

Location		Plan A	Plan B
Minimum dose region of PTV	Cervical region	36.4 %	29.5 %
	Frontal region	20.5 %	14.5 %
	Ethmoid sinus	27.3 %	20.4 %
	Other	15.8 %	38.6 %
Maximum dose region of PTV	Frontal region	45.4 %	49.9 %
	Parietal region	27.3 %	27.3 %
	Occipital region	18.2 %	18.2 %
	Skin	6.8 %	2.3 %
	Third ventricle	2.3 %	2.3 %

plan B whereas 28 patients received a minimum of 95% of prescribed dose in plan A. Nineteen patients also had ≥ 95% of prescribed dose at middle cranial fossa with plan B while 12 patients had ≥ 95 % of prescribed dose provided by plan A.

By using DVHs, a mean dose of 95% of CTV and 5% lens volume for each plan can be calculated. The average dose received by 95% of CTV was 107 % (103-112) and 108% (100-112) when treated with standardized plan A and plan B, respectively. Conformity index did not appear to be significantly different between two plans ($p = 0.058$). Conversely, the mean of received dose of 5% lens volume significantly increased to 16% (6-80) of prescribed dose after shifting isocenter to the lateral orbital rim ($p = 0.008$).

Discussion

In this study, it was found that whole subarachnoid irradiation using the lateral orbital rim as isocenter significantly improved the minimum doses at CTV, PTV, cribriform plate and middle cranial fossa than mid-brain isocenter. The relevant reasons for such outcomes could be from lesser depth at frontal region than at mid-brain region, beam profile near central axis is deeper and less divergence than at periphery and more proximity of lateral orbital rim to cribiform plate. Meanwhile, lens doses were higher which may resulted from more scattered doses. But, the dose homogeneity of the whole brain of both techniques was not different.

The study of Weiss et al [5] studied 11 patients using 2cm-posterior to lens as isocenter, to evaluate dose coverage at cribriform plate and dose to eye lenses in 3D isodose distributions. The result showed increasing of minimum doses at cribriform plate from 65% to 95% after shifting eye blocks in caudal and ventral directions. Additionally, mean dose received by 5% of lenses was increased to 91% of the prescribed total dose in spite of sufficient lens shielding. Doses in the mentioned study were five times more than figures in our study. The main reason

for yielding much different outcomes is due to more beams in changing eye blocks technique.

Andic et al.[3] reported dosimetric data from two dimensional helmet field whole brain irradiation and three dimensional conformal radiotherapy (3D-CRT). Isocenters of their plans were located in the center of the brain and two opposed lateral fields were used. Even though there was inadequate space to arrange MLC leaves between ocular lenses and retro-orbital areas in 3D-CRT planning, the minimum doses for both retro-orbital areas were statistically higher for 3D-CRT plans than for 2D planning. By using same isocenter, the maximum doses at eye lenses were similar to our findings. He concluded that CT simulation in WBI is significantly superior to conventional simulation with respect to complete coverage of the target volume and protection of the eye lenses.

However, minimum doses at CTV and PTV from our study were not as much as the doses observed in study of Andic et al. A possible explanation for this result may be from the overlapping of PTV and MLC leaves. In our study, MLC leaves were specifically referred to the osseous landmarks and PTV was marginally wider, by a centimeter added to the CTV. In our study, the CTV of helmet field is defined as the whole brain and meninges with the caudal border at the second cervical vertebrae.

Other published data[6,7] revealed a correlation between survival and dose coverage for medulloblastoma. They also identified that missed areas were inferior part of frontal and temporal lobes. So, the improvement of minimum dose for the whole brain, especially at cribriform plate and middle cranial fossa, may improve survival and reduce recurrence rate in those patients but the doses to lenses were considerably increased. For the treatment of medulloblastoma, total dose of 36 Gy to the whole subarachnoid is required. So, the resulting dose of 5% to the lenses in patients would be about 3.5 Gy with the standardized helmet technique and approximately 5.8 Gy with our modified technique. Since, threshold of total doses to the lens by fractionated radiation therapy was about 5-6 Gy which was approximately the reported threshold doses for cataract formation.

Conclusions

Using isocenter at lateral orbital rim for prophylactic cranial irradiation increased the dose coverage of the minimum dose at whole brain, especially in the area of cribriform plate and middle cranial fossa comparing with using mid-brain point isocenter technique.

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