Dosimetric verification of volumetric modulated arc therapy-based total marrow irradiation using Eclipse treatment planning: **An anthropomorphic phantom study**

Sawinee Sriklay, Pimolpun Changkaew, Siwaporn Sakulsingharoj,
Supaporn Srisuwan, and Puangpen Tangboonduangjit*

Master of Science Program in Medical Physics, Department of Diagnostic and Therapeutic Radiology,
Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, 10400, THAILAND

Abstract

Introduction: The application of volumetric modulated arc therapy (VMAT) to treat total marrow irradiation (TMI) requires several arc fields, which is possible to present hot and cold spots between the arcs and the junctions between each planning target volume (PTV) subvolume. The objective of this study was to determine the dosimetric accuracy of volumetric modulated arc therapy-total marrow irradiation technique (VMAT-TMI).

Material and methods: The treatment planning of Eclipse AAA algorithm version 13.6 with dose grid size of 2.5 mm was performed for VMAT technique. The PTV consisted of whole bone marrow from head to mid femur. Plans with 10 arcs were optimized for 6 MV photon beams with the dose prescription of 12 Gy in 6 fractions. This VMAT plan was evaluated by dosimetric verification using thermoluminescent dosimeter (TLD) to measure the radiation dose in the target of the anthropomorphic phantom. Gafchromic EBT3 films were also used to verify the planar dose at the overlapping regions and within some organs. The gamma criteria of 3%/3mm and 5%/5mm were applied for planar dose evaluation. All measurements were repeated 3 times.

Results: The average %dose difference from TLD measurement in the H&N region was -1.39%, the chest region was 1.80%, the pelvis region was 2.75%, the H&N-chest junction was 2.95% and the chest-pelvis junction was -1.56%. The average %passing rate for gamma criteria of 3%/3 mm and 5%/5 mm from Gafchromics EBT3 films measurement in lungs were 89.1 ± 5.3% and 96.8 ± 1.3% and at the chest-pelvis junction were 84.2 ± 2.7% and 96.0 ± 0.2%, respectively.

Conclusions: The results confirmed the accuracy of dosimetry for the gamma criteria of 5%/5mm. The VMAT-TMI plan could deliver radiation dose accurately and reliably with reasonable benchmark.

Keywords: Total marrow irradiation, Total body irradiation, Volumetric modulated arc therapy

บทคัดย่อ

หลักการและเหตุผล: การนำเทคนิคการฉายรังสีแบบปรับความเข้มหมุนรอบตัวมาใช้ในการฉายรังสีที่ไขกระดูกนั้น ต้องการหลายลำรังสีจึงอาจจะทำให้เกิดปริมาณรังสีส่วนเกิน (hot spot) และปริมาณรังสีส่วนที่ขาด (cold spot) ระหว่างบริเวณของลำรังสีและรอยต่อระหว่างแต่ละอวัยวะเป้าหมาย ในการศึกษานี้จึงต้องการตรวจสอบความถูกต้องของปริมาณรังสีในการฉายรังสีที่ไขกระดูกโดยใช้เทคนิคการฉายรังสีแบบปรับความเข้มหมุนรอบตัว

วัสดุและวิธีการทดลอง: ในการวางแผนการรักษาและคำนวณปริมาณรังสีใช้ Eclipse AAA algorithm version 13.6 ด้วยขนาด dose grid ที่ 2.5 มม. อวัยวะเป้าหมายประกอบไปด้วยไขกระดูกทั้งหมดจากศีรษะถึงกึ่งกลางกระดูกต้นขา โดยใช้ลำรังสีทั้งหมด 10 arcs โฟตอนพลังงาน 6 เมกกะโวลต์ ปริมาณรังสีที่แพทย์กำหนดคือ 12 Gy ใน 6 ครั้ง และการตรวจสอบปริมาณรังสีจะใช้ thermoluminescent dosimeter (TLD) วัดปริมาณรังสีในหลายตำแหน่งของอวัยวะเป้าหมายในหุ่นจำลองเสมือนมนุษย์ และในการตรวจสอบความถูกต้องของปริมาณรังสีจะใช้ Gafchromic EBT3 film ในการวัดปริมาณรังสีในแนวระนาบบริเวณรอยต่อต่างๆ รวมถึงพื้นที่ในอวัยวะต่างๆ เกณฑ์ในการประเมินผลจะใช้ gamma criteria 3%/3mm และ 5%/5mm โดยจะทำการวัดปริมาณรังสีซ้ำทั้งหมด 3 ครั้ง

ผลการศึกษา: ค่าเฉลี่ยความแตกต่างของปริมาณรังสีจากการวัดปริมาณรังสีด้วย TLD ในบริเวณศีรษะและลำคอเท่ากับ -1.39%, บริเวณทรวงอกเท่ากับ 1.80%, บริเวณเชิงกรานเท่ากับ 2.75%, บริเวณรอยต่อระหว่างศีรษะและลำคอและทรวงอกเท่ากับ 2.95% และบริเวณรอยต่อระหว่างทรวงอกและเชิงกรานเท่ากับ -1.56% ในการวัดปริมาณรังสีด้วย Gafchromics EBT3 films ค่า gamma ที่ได้เมื่อใช้ criteria ที่ 3%/3mm และ 5%/5mm ในบริเวณทรวงอกเท่ากับ 89.1 ± 5.3% และ 96.8 ± 1.3% ตามลำดับ และในบริเวณรอยต่อระหว่างทรวงอกและเชิงกรานเท่ากับ 84.2 ± 2.7% และ 96.0 ± 0.2% ตามลำดับ

ข้อสรุป: ผลที่ได้จากการศึกษาแสดงถึงความถูกต้องของปริมาณรังสีสำหรับ gamma criteria 5%/5mm การฉายรังสีที่ไขกระดูกโดยใช้เทคนิคการฉายรังสีแบบปรับความเข้มหมุนรอบตัวแสดงถึงความถูกต้องของปริมาณรังสีซึ่งอยู่ในเกณฑ์ที่ยอมรับได้

คำสำคัญ: การฉายรังสีที่ไขกระดูก, การฉายรังสีทั่วทั้งตัว, การฉายรังสีแบบปรับความเข้มหมุนรอบตัว

Introduction

Total body irradiation (TBI) is commonly used with chemotherapy for patient treatment with hematologic malignancy before stem cell transplantation. The purpose of TBI is to destroy malignant cell or cell with genetic disorders and suppress immune of the patient to prevent the rejection of the donor stem cell. The conventional TBI technique has been developed in order to achieve dose homogeneity within ±10% at the patient's mid-line[1]. There are two commonly-used TBI techniques with delivered in parallel opposed fields[2] i.e., anterior-posterior/posterior-anterior (AP/PA) fields and right-left lateral (RL LAT) fields. Patient was positioned from 3 – 5 meters from gantry isocenter and treated whole body with sparing some normal tissues. The problem of TBI technique is the variation of body thickness facing difficulty to make uniform dose distribution and long treatment time. The most significant toxicity was lung toxicity causing the major limit dose to TBI technique. Patients treated with TBI technique increases risk for radiation toxicity. For example, lungs with large radiation dose can lead to interstitial pneumonitis which was a major cause of mortality[3]. Therefore, the method to get rid of lung toxicity is to use lungs shielding. Nevertheless, the

problem of using lungs shielding are decreasing the radiation dose to bone marrow and making dosimetric error because of inaccurate position of lung shielding. So the total marrow irradiation (TMI) has been developed to irradiate for only bone marrow. Due to innovation in radiotherapy technique, the therapeutic ratio can be improved by obtaining tighter target coverage and reducing radiation dose to normal tissue. Volumetric modulated arc therapy (VMAT) has been developed by using customized algorithm to deliver intensity modulated radiotherapy (IMRT) in dynamic arc rotations around the patient. For each arc, shape of beam aperture is defined by multileaf collimators (MLC) while intensities are modulated by varying gantry speed and dose rate that improved dose conformality to target, decreased radiation dose to normal tissue and the important one, reduced the treatment time. The treatment plan for VMAT-TMI is separated for three PTV subvolumes: head and neck (H&N), chest, and pelvis. However, the VMAT plan requires several arc fields, it shows hot and cold spots between the arcs and the junctions between each planning target volume (PTV) subvolume. Dosimetric verification was performed to verify the accuracy of radiation dose in VMAT-TMI plan.

Material and methods

Simulation

An anthropomorphic Rando phantom (Radiology Support Devices, Inc., CA, USA) was scanned using the GE optima 580 CT simulator (GE Healthcare, Chicago, IL, USA) with 512 × 512 pixels per slice. The CT images were scanned from vertex of the skull to mid-thigh of the phantom with slice thickness of 5 mm.

Treatment planning technique

The Eclipse treatment planning of Anisotropic Analytical Algorithm (AAA) algorithm version 13.6 (Varian Medical System Inc., Palo Alto, CA, USA) using dose calculation grid size of 2.5 mm was performed for RapidArc technique (Varian Medical System Inc., Palo Alto, CA, USA) with the prescribed dose of 12 Gy in 6 fractions. The clinical target volume (CTV) was consisted of whole bone marrow from skull to mid-thigh of femurs and then margin of 2 mm was added to generate PTV. The organs at risks (OARs) included lungs were contoured by a radiation oncologist. The PTV was divided into 3 subvolumes i.e., H&N, chest, and pelvis subvolumes as shown in Figure 1. The H&N and chest region were separated at C6 vertebral level and chest, while pelvis region was separated at L1 vertebral level. For the first arc, the range of the gantry started from 181 to 179 degree, 185 to 175 degree and 181 to 179 degree for H&N plan, chest plan, and pelvis plan, respectively. The second arc of each plan was overlapping at minimum of 2 cm to prevent hot and cold spot between arcs. The H&N plan, chest plan, and pelvis plan were used 3,

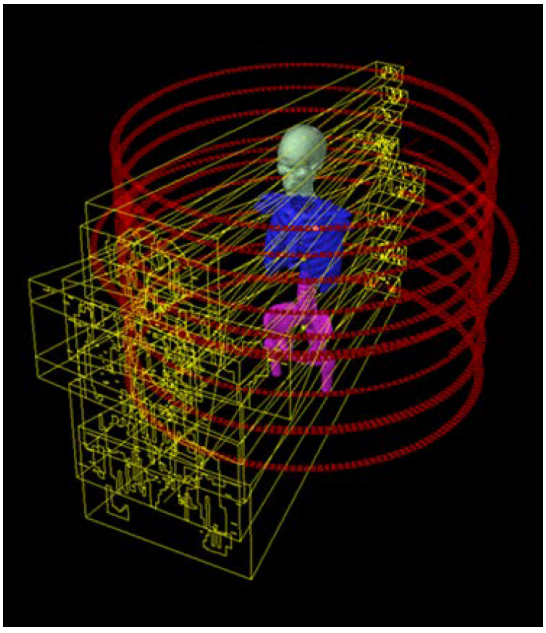

Figure 1 Three subvolumes (green region for head & neck, blue region for chest, and pink region for pelvis subvolumes) in VMAT-TMI planning with 10 arcs and multiple isocenters.

4, and 3 arc fields, respectively. The collimator was set to 90 degree except in chest subvolume that the planning collimator was set to 10 degree. The 6 MV photon beams was used in optimization with 10 arcs and multiple isocenters. The chest subvolume was selected as the first subvolume of planning, which was based plan for H&N and pelvis subvolumes to reduce the hot and cold spot between junctions. The dose constraint for evaluation of VMAT-TMI plan was that the volume of PTV received 12 Gy radiation dose was more than or equal to 90%. The maximum radiation dose of 130% was accepted and the OAR at the upper dose limit (mean dose) for lungs was less than 8-9 Gy.

Dosimetric verification

Point dose measurement

TLD calibration. The TLD-100 was used in this study. The TLDs were annealed at 400°C for 1 hour and 100°C for 2 hours. The TLDs reading were performed with Harshaw 5500 TLD reader (ThermoFisher Scientific, Waltham, MA, USA). The sensitivity of each TLD was estimated by radiation dose of 2 Gy with 1.25 MeV gamma ray of Co-60 machine at field size of 15 cm × 15 cm for source to surface distance (SSD) of 80 cm. The bolus of 0.5 cm was added on TLDs. The calibration factor of TLDs was calculated from the sensitivity exposure of TLD in order to convert charge reading form TLDs to radiation dose.

Dosimetric verification plan using TLDs. To verify accuracy of radiation dose, TLD-100 was used to measure the radiation dose in the anthropomorphic Rando phantom. TLDs were positioned in 52 difference locations and spread throughout the target (bone marrow) and lungs in anthropomorphic Rando phantom. The number of TLDs were 16, 18, and 8 in H&N, chest, and pelvis region, respectively. Furthermore, 10 TLDs were used for measurement in the junctions of H&N-chest and chest-pelvis region to verify the accuracy of radiation dose and dose homogeneity.

Planar dose measurement

Film calibration. The calibration curve in dose range of 0, 0.2, 0.4, 0.8, 1.0, 1.2, 1.6, 1.8, 2, 2.2, 2.4, and 2.6 Gy for 6 MV photon beams were measured using Gafchromic EBT3 films LOT number 09071603 (Gafchromic, International Specially Products, Wayne, NJ, USA), at depth of 10 cm of solid water phantom. The reader of pixel value was performed using VIDAR'S DosimetryPRO Advantage (Red) (VIDAR, Herndon, VA, USA) with 71 resolutions and 16 bits depth. The known radiation dose of 1 Gy and 2 Gy were exposed at the same time to confirm the accuracy of the measurement using both ionization chamber and Gafchromic EBT3 films. Omnipro I'mRT software (Omnipro Systems Inc, San Francisco, CA, USA) was used to analyze the film results.

Dosimetric verification plan using films. Gafchromic EBT3 films were used to verify at the chest-pelvis junction and chest. The measurement was repeated 3 times. The planar dose results were evaluated using 2 gamma criteria, including 3 mm distance to agreement and 3% dose difference and 5 mm distance to agreement and 5% dose difference. The former criteria was selected in order to follow the protocol from Task Group number 119 and the latter one was used also to compare with the study from Mancosu *et al*.[4]

Results

The VMAT-TMI plan for measurement in anthropomorphic Rando phantom was the plan sum of H&N plan, chest plan, and pelvis plan. A total number of monitor units (MU) in H&N plan, chest plan, and pelvis plan were 973 MU, 1301 MU, and 1232 MU, respectively. The VMAT-TMI plan dose distribution is shown in Figure 2. The H&N axial,

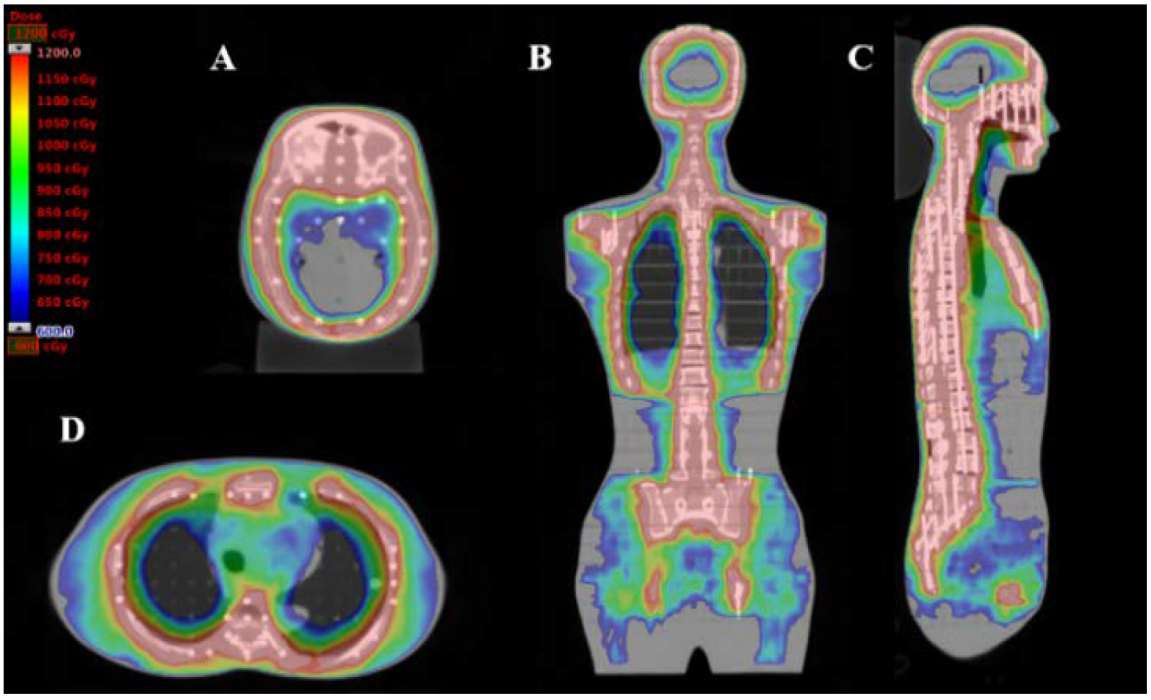

Figure 2 Isodose distribution of VMAT-TMI plan for an anthropomorphic Rando phantom in dose range of 6 Gy to 12 Gy in (A) H&N axial plane (B) coronal plane (C) sagittal plane and (D) lung axial plane.

coronal, sagittal, and lung axial planes are shown in Figure 2A, 2B, 2C and 2D, respectively. The figures demonstrate remarkably successful dose coverage to the target and sparing normal tissue. For the target volume, the mean dose (Dmean), 95% of PTV volume that received radiation dose (D95) and maximum dose (Dmax) were 11.32 Gy, 11.83, and 14.87 Gy, respectively. For the OAR (lungs), the mean dose was 7.06 Gy. The readings of TLDs confirmed the accuracy of radiation dose. The good agreement was observed in TLDs measurement. Table 1 shows average %dose difference between dose calculation from treatment planning and radiation dose measurement from TLDs. The results of average %dose difference in all TLDs position were within 5%. The average %dose difference in the H&N region was -1.39% (range: -7.87% to 7.77%), the chest region was 1.80% (range: -4.33% to 8.41%), and the pelvis region was 2.75%

Table 1 The dose differences between dose calculation from treatment plan and dose measurement from TLDs.

Regions	Average dose difference (%)
H&N	-1.39 ± 0.68
Chest	1.80 ± 2.91
Pelvis	2.75 ± 1.52
H&N-chest junction	2.95 ± 4.68
Chest-pelvis junction	-1.56 ± 1.42

Dose difference (%) = (Calculated – Measured)/Measured × 100

(range: 0.28% to 6.01%). The dose measurement in each junction showed excellent agreement for %dose difference of 2.95% (range: 1.20% to 5.74%) and -1.56% (range: -3.77% to 0.74%) in H&N-chest and chest-pelvis junctions, respectively. The range of standard deviation relative to the average dose in each region of TLD measurement for H&N region was 0.27% to 1.32%, the chest region was 0.07% to 5.52%, the pelvis was 0.47% to 4.95%, the H&N-chest junction was 4.08% to 5.89% and the chest-pelvis junction was 0.74% to 1.99%.

The Gafchromic EBT3 film was used to verify planar dose distribution at the chest-pelvis junction and chest region. Figure 3A demonstrates example gamma results according to 3%/3mm criteria for lung plan evaluation and profiles along Y-axis for the treatment plan and delivered dose comparison is shown in Figure 3B. Table 2 reports the averaged %passing rate for gamma criteria of 3%/3mm and 5%/5mm in chest region which were 89.1 ± 5.3%, and 96.8 ± 1.3%, respectively, while the corresponding rates for chest-pelvis junction were 84.2 ± 2.7% and 96.0 ± 0.2%, respectively.

Discussion

TBI is an important treatment for hematologic malignancies in conjunction with intensive chemotherapy. The commonly-used technique was extended SSD with parallel opposed fields including: AP/PA field and bi-lateral field. These TBI techniques encounter difficulty to obtain dose distribution for the homogeneity of ±10% at mid-line because of the variation of patient's body thickness. The conventional TBI technique uses external shielding in normal tissue to decrease radiation dose. However, the limitation of using the conventional TBI technique is lung

Figure 3 Planar dose verification using Gafchromic film. (A) example of the gamma result using 3% /3mm criteria evaluation in lung region: in blue region showed area were less than 3%/3mm and in red color regions reported points which did not pass the criteria (the gamma evaluations were more than 3%/3mm) and (B) profiles in horizontal axis from figure 3A comparison between profile from the treatment planning (green color) and the delivered dose (red color).

Table 2 The passing rate of lungs and chest-pelvis junction when using Gafchromic EBT3 films for measurement compared with treatment planning system.

Regions	Gamma passing rate (%)	
	3%/3mm criteria	5%/5mm criteria
Lungs	89.1 ± 5.3%	96.8 ± 1.3%
Chest-pelvis junction	84.2 ± 2.7%	96.0 ± 0.2%

toxicity (interstitial pneumonitis) which related to the mean lung dose[1]. Nowadays, IMRT technique can deliver precise radiation dose to target and improve dose homogeneity therefore it can increase high radiation dose to target while reduce the radiation dose to normal tissue. Previous study of intensity modulated TMI (IM-TMI) reported that when compared to TBI, IM-TMI was better target coverage and dose reduction to normal tissue by 29 – 65%[5,6,7]. The major limitation of IMRT was that the maximum field size of 32 cm × 40 cm which was not enough to treat shoulder and upper extremities with long treatment time of 45-50 minutes[5]. The VMAT planning has shown excellent target coverage and lungs sparing, therefore the VMAT-TMI planning was also successful as shown in Figure 2. This plan consisted of 3 subvolumes: H&N, chest, and pelvis subvolumes for optimization with 10 arcs and overlapping fields to prevent hot and cold spots. This technique could decrease mean lung dose for sparing lung and critical organs. The result in Figure 2 shows that the mean lung dose was 7.06 Gy. Della Volpe, *et al*. reported that the risk of interstitial pneumonitis was decreased from 19% to 4% when lungs received dose below 9.4 Gy[3].

In this study, dosimetric verification between the dose calculation and dose measurement was investigated for VMAT-TMI planning technique. The TLDs were used for radiation dose measurement in target (bone marrow) and lungs. In some TLD position, the percentage dose difference was greater than 5% because it might be gradient of the dose profile which is sensitive to positional variation. Thus the variation of dose profile might affect the dose measurement by using TLDs. The largest percentage dose difference was 8.41% in the lung region as high standard deviation can be observed in this point also which was 5.52%.

Moreover, in our experiment, Gafchromic EBT3 films were also used for measurement in lung region and chest-pelvis junction. The planar dose distribution in lung region and junction were verified because lungs were inhomogeneity area and the junction was overlapping fields. These region and junction were needed to confirm the accuracy of dosimetric verification. The H&N-chest region was not measured by film in this experiment because this junction was located by stems of Rando phantom which is too narrow to insert the film. However, TLD could be used in this junction and it found that the maximum %dose difference from treatment planning calculation was 5.74%.

According to the gamma analysis using Gafchromic EBT3 film to compare with the treatment planning dose calculation, the gamma passing rate with criteria of 5%/5mm for both lung and chest-pelvis junction were more than 95%. The results showed that VMAT-TMI obtained good agreement in this planning technique for gamma criteria of 5%/5mm. However, when criteria of 3%/3mm is used, the % passing rate at lung region was 89.1% and at chest-pelvis junction was 84.3% instead. These results related to the study from Mancosu *et al*.[4] reported that dosimetric verification using Gafchromic EBT3 film to verify dose distribution in phantom and patient, the gamma passing rate with criteria of 5%/5mm and 3%/3mm were greater than 95% and 64% respectively. As expected for lung region, the accuracy of Eclipse using AAA algorithm which is convolution-superposition based algorithm could cause the differences up to 8% at low density tissue especially lung/soft tissue interface when compared with Acuros XB (AXB) (principle based algorithm which is closed to Monte Carlo based) reported by Han *et al*.[8] Moreover, dose at the chest-pelvis junction is the combination between dose from lung and pelvis regions which might cause hot and cold spots leading to high dose

gradient region, however, with the ability of dose smoothing technique as illustrated by Wilkie *et al*.[5], the hot and cold spots could be compromised. Nevertheless, the accuracy of dose calculation in this junction is still in controversy. Film's result at this junction shows the lowest value of %passing rate for the criteria of 3%/3mm which is 84.3% but TLD measurement shows the % dose difference of about 4% which sound agreeable.

All in all, the accuracy of treatment planning to calculate dose of VMAT-TMI technique was obtained within 3% indicated by TLD measurement except at lung region which showed 8% difference although the %passing rate of more than 95% for gamma criteria of 5%/5mm was achieved as evidenced by Gafchromic EBT3 film measurement. However, in order to fulfill more than 95% passing rate for gamma criteria of 3%/3mm, further work might not only be more careful selection of point dose measurement to avoid high dose gradient but also using the principle based algorithm for treatment planning dose calculation. Finally, to be more benefit to the patients with leukemia, TMI with VMAT could be verified and applied to the real clinical cases with care.

Conclusion

The results confirmed the accuracy of dosimetry for the gamma criteria of 5%/5mm. The VMAT-TMI plan could deliver radiation dose accurately and reliably with reasonable benchmark.

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