

# First Experience of Standard Linac, Rapid Arc and Dose-drop Scheme Based Total Body Irradiation

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## Research

**Keywords:** total body irradiation, rapid arc, positioning related dose deviation, quality assurance

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# Abstract

**Background and purpose:** To introduce a standard linac with true attachment free, rapid arc and dose-drop scheme for positioning related dose deviation control based total body irradiation(TBI).

**Materials/Methods:** One eight years old girl diagnosed with acute lymphocytic leukemia underwent TBI in 2020. Target volumes and organs at risk were contoured after CT simulation. Total sixteen ARC and four AP-PA from five isocenters were designed. A dose-drop scheme on both sides of adjacent region were performed to reduce positioning-related dose deviation. A series of quality assurance before radiotherapy and real-time dose monitoring during radiotherapy were carried out.

**Results:** The average on board imaging (OBI) time of per fraction was 40.3 min, the average beam on time of per fraction was 37.2 min, the average time to change from head first to feet first position was 18.4 min. The average mean lung dose was 9.89 Gy, the maximum lens dose was 7.60 Gy, the mean PTV\_total dose was 12.17Gy, 98.23% PTV\_total volume was covered by 90% of the prescription dose. The maximum dose (Dmax) of PTV\_total was 13.65Gy. Dmean and V10.8 of PTV\_total are only slightly different(0.49% - 1.89% and 0.26% - 1.04% respectively) even with an error of 5 - 20mm longitudinal misalignments. Gamma passing rate(3mm/ 3% Gamma criteria) are between 93.5% and 100%. Real-time dose monitoring showed an overall deviation of  $-3.9\pm 5.51\%$ .

**Conclusions:** Standard linac, rapid arc and dose-drop for positioning-related dose deviation control based total body irradiation is feasible, accurate, and reliable. It is worthy of clinical application.

## Introduction

<sup>1-3</sup>TBI is frequently used as a component of hematopoietic stem cell transplant (HSCT). <sup>4</sup>The techniques of TBI vary widely from institution to institution. Conventional TBI often use two or three dimensional radiotherapy techniques, for example opposing anterior and posterior fields or lateral fields. Disadvantages of conventional TBI include: 1. attachment devices and long source skin distance needed. 2. shielding specific organs are not precise. 3. poor dose uniformity. The inverse-planned intensity-modulated radiation therapy(IMRT) based TBI technique was developed to improve these shortcomings. But many IMRT TBI studies also need some special attachment and rare positioning related dose deviation control techniques. Now we report a standard linac with true attachment free, rapid arc and dose-drop positioning related dose deviation control based total body irradiation.

## Materials And Methods

One eight years old girl diagnosed with acute lymphocytic leukemia underwent allogenic stem-cell transplantation following TBI and VP16 chemotherapy treatment at Hongkong university Shenzhen hospital in 2020. Patient was informed about the treatment and it`s possible adverse events and about necessary diagnostics prior to treatment. Written consent by the patient herself and parents was obtained.

## Positioning, immobilization and simulation

Simulation occurs on a computed tomography scanner (Philip Brilliance CT Bigbore) with a setting of 120kVp, 3 mm slice. The scan length is limited to 1.15meters. Both upper limbs are placed at the bilateral sides of the body. Head & neck and shoulders thermoplastic mask, head rest and moldable head and neck support are used to fix the head and neck and shoulders. Whole body thermoplastic cast and whole body evacuated vacuum bags are used to fix thorax, abdomen, and limbs. The patient was positioned on a total body base board, in order to connect all above positioning devices as a whole unit as shown in Fig. 1. Prior to CT acquisition, radiopaque markers are placed near the umbilicus to serve as origin(Fig. 2) and a merge point of the two scans. The overlap area of two scanned images should be longer than 7cm(5 cm for minimized dose gradient at radiation fields junctions, 2 cm for scattered dose calculation at radiation fields edge). If the patient is taller than 1.15 meters, two scans will be performed, the first scan (upper body) goes from the top of the head to pelvis with head first position, the second scan (lower body) goes from the bottom of the feet to the pelvis with feet first position. Both scans include the above origin markers. To allow for quality assurance (QA) measurements during radiotherapy, total eight 0.5 cm bolus are also scanned along with the patient, eight metal oxide semi-conductor field effect transistor (MOSFET) will be placed under bolus for timely treatment dose monitoring as shown in Fig. 1.

## Contouring

Body was contoured using search body automatic tool, then manually modified to include all the outer body contour.

Even with a well-positioned devices, given the movement of the chest wall and ribs, The planning target volume (PTV) was contoured using the outer body contour minus bilateral lungs (except 3 mm margin of lung tissue adjacent to the ribs and chest wall to ensure full dose coverage of the ribs and chest wall). PTV\_upper and PTV\_lower were contoured on upper body and lower body scans respectively. PTV\_total is equal to PTV\_upper plus PTV\_lower. PTV\_crop was equal to PTV\_total shrinks by 3 mm in the three-dimensional direction. The right, left and bilateral lungs were contoured using the pulmonary windows separately according to RTOG atlases for Organs at Risk (OARs) in Thoracic Radiation Therapy.

Due to protection of lung tissues and dose coverage of chest wall, helping structures PTV\_chestwall\_1 cm was defined as the extrapulmonary three-dimensional area within 1 cm. In order to ensure adequate skin dose coverage, the area with PTV\_upper and PTV\_lower expansion of 3 mm were named PTV\_upper\_3 mm and PTV\_lower\_3 mm respectively. At the same time, in order to reduce the actual dose coverage error caused by the positioning error, five sections of dose-drop transition zone were drawn continuously at the junction, the length of each section was 1 cm, five sections were named as Step\_12Gy-10Gy, Step\_10Gy-8Gy, Step\_8Gy-6Gy, Step\_6Gy-4Gy and Step\_4Gy-2Gy respectively as shown in Fig. 2. The parts of PTV\_total in the dose-drop region was named PTV\_drop. However, for dose statistics and dose volume histograms(DVH), the anatomical lungs are the relevant structures. The right, left and bilateral kidneys were contoured if pre-existing renal insufficiency. Additional helping structures within the overlapping regions were contoured and used for steering the optimizer leading to an improved

dose distribution in those areas. Other OARs were not routinely contoured and involved in dose optimization.

### Treatment planning and irradiation

The full-body CT scan was imported into Eclipse treatment planning system, version 15.0. Isocenter was created for treatment planning of each scan. The total prescription dose was 12 Gy, 2 Gy per fraction, two fractions per day, the minimum interval was 6 h. Irradiation was delivered at linac (Triology, Varian) based photon energy of 6 MV over three consecutive days. The elevator and linear accelerator room were routinely disinfected before each fraction radiotherapy. The dose constraint is as follows: The minimum dose ( $D_{min}$ ) of PTV is more than or equal to 90% of prescription dose; The  $D_{max}$  of PTV is less than or equal to 130% of prescription dose; The volume of PTV covered by 120% of the prescription dose should be less than 10%. The mean dose of both lungs is less than or equal to 10 Gy; The mean dose of both kidneys is less than or equal to 10 Gy if renal insufficiency, no special dose limitation for both kidneys if normal renal function.

As shown in Fig. 2, total sixteen ARC and four AP-PA from five isocenters were designed. For upper body treatment planning, total 12 ARCs were designed with three iso-centers because of the collimator field limitation is 40 cm X 40 cm. For lower body treatment planning, four AP-PA fields in fields were designed for bilateral shanks with a isocenter firstly. Then, another four ARCs with another isocenter were used to cover other parts of lower body. For the convenience of positioning, the coordinate values of each iso-center point are only different in the longitudinal direction. The connection between each rapid arc plan at each isocentric point was administrated by the function module of Base Dose Plan Compensation (BDPC).

Regarding the adjacent region dose distribution between upper and lower body radiotherapy, slight errors may cause significant hot and cold spots if conventional radiotherapy plans. Therefore, we designed a dose-drop scheme on both sides of adjacent region, which decreased from the prescribed dose (12 Gy) to 2 Gy within a length of 5 cm.

We can treat upper body first with head first position, but re-position was needed with feet first position due to the limitation of the length of the linear accelerator treatment bed. For image guidance, kilo-voltage on broad imaging was used to collect images at anterior and right lateral directions for head and neck, abdomen, pelvis and lower limbs, and right lateral oblique directions for thorax to avoid obstruction by the arms. Online matching of the images with digital reconstruction radiograph (DRR) from the planning CTs were performed. Radiotherapy was permitted only if the senior physician and senior therapist confirm that the position error in each direction was less than 2 mm. Treatment team will monitor the whole process with audio and video.

### Quality assurance

Before radiotherapy, dose verification was performed on each isocentric rapid arc or AP-PA plan and each radiation fields using ScandiDos Delta4PT 3D QA phantom. PTW Octavius 4D QA phantom was used for Gamma passing rate (3 mm/ 3% Gamma criteria) at intersection of each two isocentric rapid arc plans of upper body. Point dose deviation at bilateral lower limbs and the junction of upper body and lower body were verified by a 60 cm(length) X 30cm(width) X 10 cm(height) solid water phantom, PinPoint 0.015 cc and UNDOSE electrometer. During the process of each fraction radiotherapy, total eight interest point sites dose monitoring were needed using MOSFET. Points of interest include forehead, bilateral chest, navel, perineum, bilateral knee and unilateral foot.

## Results

OBI time of per fraction was 40.3 min, the average beam on time of per fraction was 37.2 min, the average time to change from head first to feet first position was 18.4 min. The average mean lung dose was 9.89 Gy, the maximum lens dose was 7.60 Gy, the mean PTV\_total dose was 12.17 Gy, 98.23% PTV\_total volume was covered by 90% of the prescription dose. The Dmax of PTV\_total was 13.65 Gy. The mean PTV\_crop dose was 12.23 Gy, 99.38% PTV\_crop volume was covered by 90% of the prescription dose, the Dmax of PTV\_crop was 13.65 Gy. Dose distribution of TBI was shown in Fig. 2.

The mean PTV\_drop dose was 12.13 Gy, 98.29% PTV\_drop volume was covered by 90% of the prescription dose. The Dmax of PTV\_drop was 13.31 Gy. The mean PTV\_drop\_crop dose was 12.17 Gy, 99.54% PTV\_drop\_crop volume was covered by 90% of the prescription dose. The Dmax of PTV\_drop\_crop was 13.31 Gy.

When plans were recalculated with longitudinal misalignments, DVH parameters of PTV\_total and PTV\_crop such as Dmax and Dmax difference(%), Dmean and Dmean difference(%), V10.8 and V10.8 difference(%) were obtained respectively. Table 1 showed that Dmean and V10.8 are only slightly different even with an error of 5–20 mm longitudinal misalignments. Considering that the positioning error of OBI verification can be controlled smaller than 2–5 mm, the change of Dmax is also acceptable.

Table 1  
Dosimetry parameter if an error of 5–20 mm closer longitudinal misalignments

Table 1		Dmax	Dmax difference(%)	Dmean	Dmean difference(%)	V10.8	V10.8 difference(%)
No shift	PTV_total	13.65	0.00	12.17	0.00	98.24	0.00
	PTV_crop	13.65	0.00	12.23	0.00	99.37	0.00
5 mm closer	PTV_total	16.79	23.00	12.23	0.49	97.98	-0.26
	PTV_crop	16.79	23.00	12.30	0.57	99.24	-0.13
10 mm closer	PTV_total	19.83	45.27	12.27	0.82	97.30	-0.96
	PTV_crop	19.83	45.27	12.35	0.98	98.65	-0.72
15 mm closer	PTV_total	20.90	53.11	12.34	1.40	97.31	-0.95
	PTV_crop	20.90	53.11	12.42	1.55	98.66	-0.71
20 mm closer	PTV_total	20.93	53.33	12.40	1.89	97.22	-1.04
	PTV_crop	20.93	53.33	12.48	2.04	98.62	-0.75

Table 2 showed dose verification of each isocentric rapid arc or AP-PA plan and each radiation fields were in compliance with the requirements perfectly. Gamma passing rates (3 mm/ 3% Gamma criteria) at intersection of each two isocentric plans of upper body were 98.4% and 95.9% respectively, the standard requirements have been well passed. Point dose deviation at bilateral lower limbs and the junction of upper body and lower body were from 1.5–3.38%, the values were also meet the standard requirements.

Table 2  
Dose verification of each isocentric rapid arc or AP-PA plan and each radiation field

	<b>Isocenter</b>	<b>Gamma passing rate (3 mm/ 3% Gamma criteria)</b>	<b>Fields</b>	<b>Gamma passing rate (3 mm/ 3% Gamma criteria)</b>	
Upper body	Isocenter 1	100%	1	100%	
			2	100%	
			3	100%	
			4	100%	
	Fields 1–4			5	99.9%
				6	100%
				7	99.4%
				8	100%
	Isocenter 2	99.3%		9	99.8%
				10	100%
				11	99.4%
				12	100%
Fields 5–8			13	99.8%	
			14	100%	
			15	100%	
			16	100%	
Isocenter 3	95.3%		17	100.0%	
			18	99.1%	
			19	100%	
			20	98.4%	
Fields 9–12					
Lower body	Isocenter 4	93.5%	13	99.8%	
			14	100%	
			15	100%	
			16	100%	
	Fields 13–16			17	100.0%
				18	99.1%
				19	100%
				20	98.4%
Isocenter 5	95.2%				
Fields 17–20					

During the process of each fraction radiotherapy, total eight interest point sites dose monitoring were done, then all the isocentric accumulative doses were added and analyzed, the results showed an overall deviation of  $-3.9\% \pm 5.51\%$ .

## Discussion

<sup>5,6</sup>TBI is mainly used for leukemia, followed by malignant lymphoma, myelodysplastic syndrome, multiple myeloma and other malignant diseases. It is also used for benign diseases such as aplastic anemia. <sup>7-11</sup>Outcomes after fractionated TBI were superior as compared with chemotherapy based conditioning with regard to overall survival, leukemia-free survival, relapse incidence, and non-relapse mortality. TBI in conjunction with chemotherapeutic agents has proven useful for eradicating residual malignant cells and for immunosuppression before HSCT. Unique features of TBI that make it a valuable component of transplant preparative regimens include: 1. No sparing of “sanctuary” sites such as testes and the central nervous system. 2. Dose homogeneity to the whole body regardless of blood supply. 3. Less chance of cross-resistance with other antineoplastic agents (chemotherapy). 4. No problems with excretion or detoxification. 5. Ability to tailor the dose distribution by shielding specific organs or by “boosting” sites. It is essential that the complicated treatment and care of the patient receiving TBI be well coordinated among the various subspecialties (medical oncology, radiation oncology, etc.) and caregivers (physicians, nurses, physicists, therapist psychologists, dieticians, etc).

<sup>12</sup> Most centers use opposing anterior and posterior fields with the patient standing upright several meters from the source and the beam pointed horizontally, thickness variations have less effect on dose homogeneity for This approach; however, the typical standing positioning can be strenuous with poor tolerance. <sup>13</sup>Patients also can be irradiated with lateral fields in a sitting or partly reclining position with better tolerance, but variations in patient thickness can cause large dose heterogeneities, especially if compensators are not utilized during treatment. Most importantly, these above conventional large-field techniques require an extended source-to skin distance (SSD) that may not be available in standard-sized Linear accelerator room. <sup>14</sup>Petra M. Härt et al introduced a sweeping beam technique for total body irradiation in standard treatment rooms and for standard linear accelerators. The patient is positioned on a low couch on the floor, the longitudinal axis of the body in the rotational plane of the linac. The sweeping beam technique needs the couch on the floor with the Makrolon plate on top. The inverse-planned IMRT based TBI technique was developed to improve upon these shortcomings, <sup>15,16</sup>a benefit could be demonstrated with regard to dose distribution and homogeneity and the selective dose-reduction to organs at risk.

<sup>17</sup> Patients taller than 120 cm cannot be treated in one position due to the limited cranial-caudal couch shift capacities of the linac. Therefore, patients are usually turned from a head-first supine position (HFS) to a feet-first supine position (FFS) to overcome this limitation. Losert C et al showed a newly developed rotatable tabletop consists completely of carbon fiber, including the ball bearing within the base plate of the rotation unit. The patient can be turned 180° from a HFS to a FFS position within a few seconds, without the need of repositioning. <sup>18</sup>Treatment plans with an indexed rotational immobilization system had multi-isocentric volumetric modulated arc therapy (VMAT) beams to the upper body and parallel opposed fields to the lower body, with a 12 Gy prescription dose to > 90% of the body and mean lung dose ~8 Gy. In the end-to-end test, point dose measurements had < 10% error. Compared to conventional TBI, the VMAT-based TBI technique increased the mean dose to the body by ~1.0–1.5 Gy and decreased the mean dose to the lung by ~1.0–1.5 Gy. The main problem of this approach is additional use of the

special rotatable tabletop at the linear accelerator, it is not available in most hospital around the world. <sup>16</sup>Bora Tas et al introduced total-body irradiation using linac-based volumetric modulated arc therapy, high-dose junction regions were eliminated after the registration of two CT sets via bias-dose properties of Monaco 5.11 TPS, Plan adaptation delivery while ensuring OAR tolerances never exceeded due to bias-dose planning because TPS considers dose distribution from previous plans while optimizing the cumulative dose distribution, but when plans were recalculated with each 3.0-mm, 6.0-mm, 9.0-mm, and 12.0-mm longitudinal misalignments, an average of  $2.0\% \pm 0.7$ ,  $3.7\% \pm 1.2$ ,  $6.5\% \pm 1.7$  and  $7.2\% \pm 1.7$  higher mean lung doses;  $2.6\% \pm 1.5$ ,  $9.9\% \pm 3.7$ ,  $15.1\% \pm 4.2$  and  $22.6\% \pm 3.1$  higher maximum lung doses and  $3.6\% \pm 1.3$ ,  $11.9\% \pm 3.2$ ,  $20.4\% \pm 3.6$  and  $22.0\% \pm 3.8$  higher point doses were obtained respectively. Our studies showed dose-drop positioning related dose deviation control technology can reduce dose distribution error.

<sup>19</sup> Naoya Ishibashi showed fractionated total body irradiation with myeloablative conditioning given at a lower dose ( $< 12$  Gy vs 12 Gy) did not decrease the incidence of adverse events. So the most common prescription dose is 12 Gy. <sup>11,20</sup>TBI can cause severe late-effects such as growth deficiency, sclerodermic chronic graft vs. host disease, osteonecrosis, impaired fertility, diabetes, pulmonary late effects, chronic renal insufficiency, cardiac late-effects, subsequent cancers, blindness and so on. More and more studies focus on late side effects. Pulmonary late effect is one of the main side effects. <sup>21</sup>Natia Esiashvili et al showed patients treated with mean lung dose  $< 800$  cGy had better outcomes. Lateral fields were associated with higher lung dose, and thus they should be avoided.

## Conclusion

Standard linac, rapid arc and dose-drop positioning error control based total body irradiation is safe and reliable. Advantages include: 1. a standard linac with true attachment free. 2. shielding specific organs and target volume dose coverage are precise by rapid arc. 3. excellent dose-drop scheme for positioning related dose deviation control. But good training in TBI-related techniques are needed first.

## Abbreviations

TBI, total body irradiation; OBI, on board imaging; AP-PA, anterior posterior; Dmax, maximum dose; Dmean, the mean dose; PTV, planning target volume; Dmin, minimum dose; HSCT, hematopoietic stem cell transplant; MOSFET, eight metal oxide semi-conductor field effect transistor; QA, quality assurance; OAR, organs at risk; BDPC, Base Dose Plan Compensation; DVH, dose volume histograms; DRR, digital reconstruction radiograph; HFS, head-first supine position; FFS, feet-first supine position; VMAT, volumetric modulated arc therapy.

## Declarations

Funding and Competing interests

This project is supported in part by Health Commission of Guangdong Province, China (NO. B2020100). The authors declare that they have no other competing interests.

Ethics approval  consent to participate and consent for publication

All patients signed, at hospital admission, consent for the use of their data for retrospective and scientific investigation. The paper has been performed in accordance with the declaration of helsinki and has been approved by the local ethics committee.

Availability of data and material

Not applicable

Competing interests

No

Funding

This project is supported in part by Health Commission of Guangdong Province, China (NO. B2020100). No other conflict of interest exists in the submission of this manuscript, and manuscript is approved by all authors for publication. I would like to declare on behalf of my co-authors that the work described was original research that has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed.

Authors' contributions

Study design: Longhua Chen, Zhiyuan Xu, Li Yang. Literature research: Zhiyuan Xu, Li Yang. Data acquisition: Zhiyuan Xu, Li Yang, Tim Hui, Xiaoqin Jiang, Jacob Cheung, Jeff chan, Qian Wang, Eric Lee. Statistical analysis: Zhiyuan Xu, Li Yang, Tim Hui, Xiaoqin Jiang. Manuscript preparation: Zhiyuan Xu, Li Yang. Manuscript revision/review: Longhua Chen, Zhiyuan Xu, Li Yang, Tim Hui, Xiaoqin Jiang, Jacob Cheung.

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## Figures



**Figure 1**

Positioning and fixation device, ① - ⑧ shows MOSFET position diagram



Figure 1

Positioning and fixation device,  -  shows MOSFET position diagram

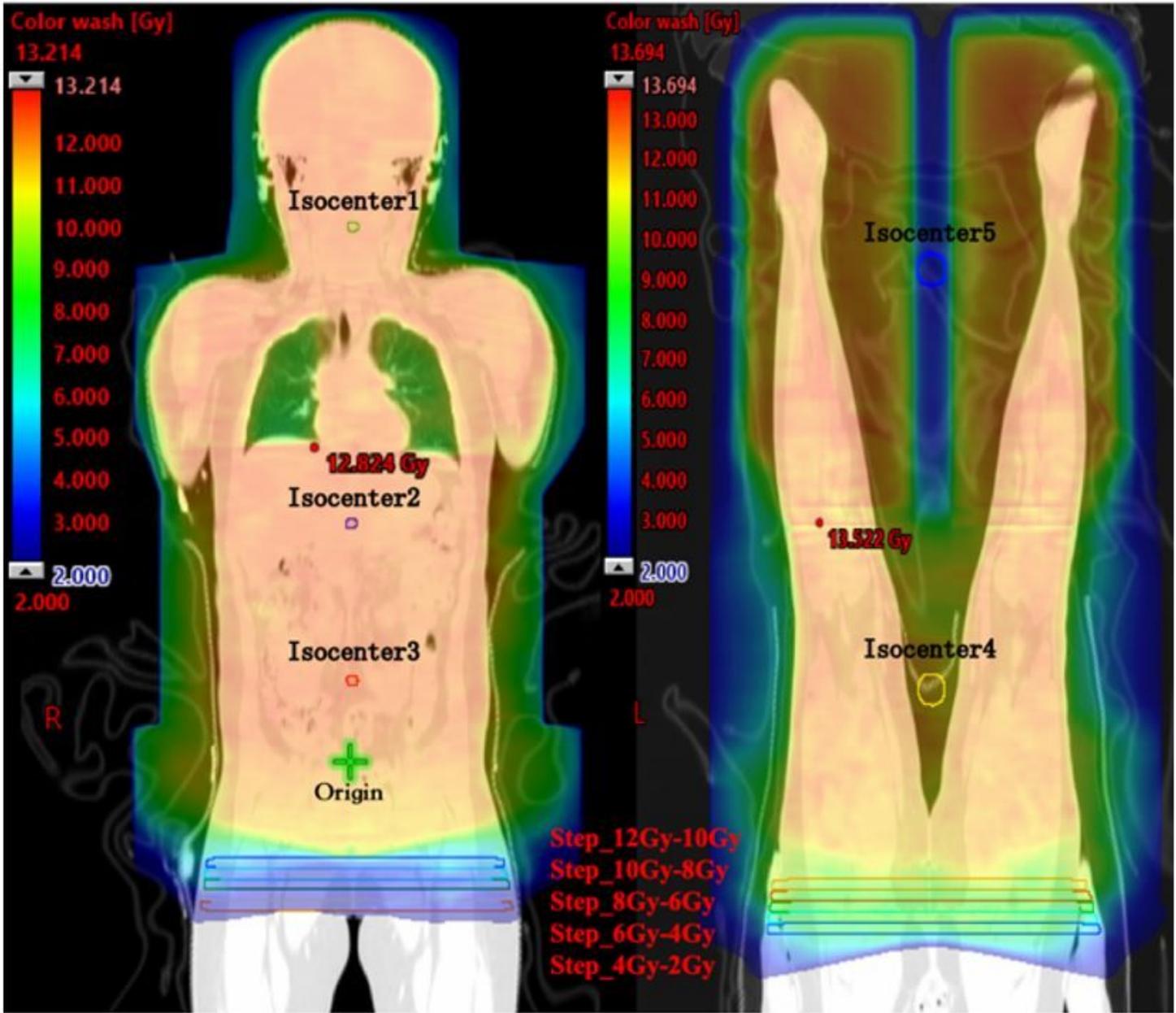


Figure 2

Dose distribution, five dose-drop sections and five isocenters.

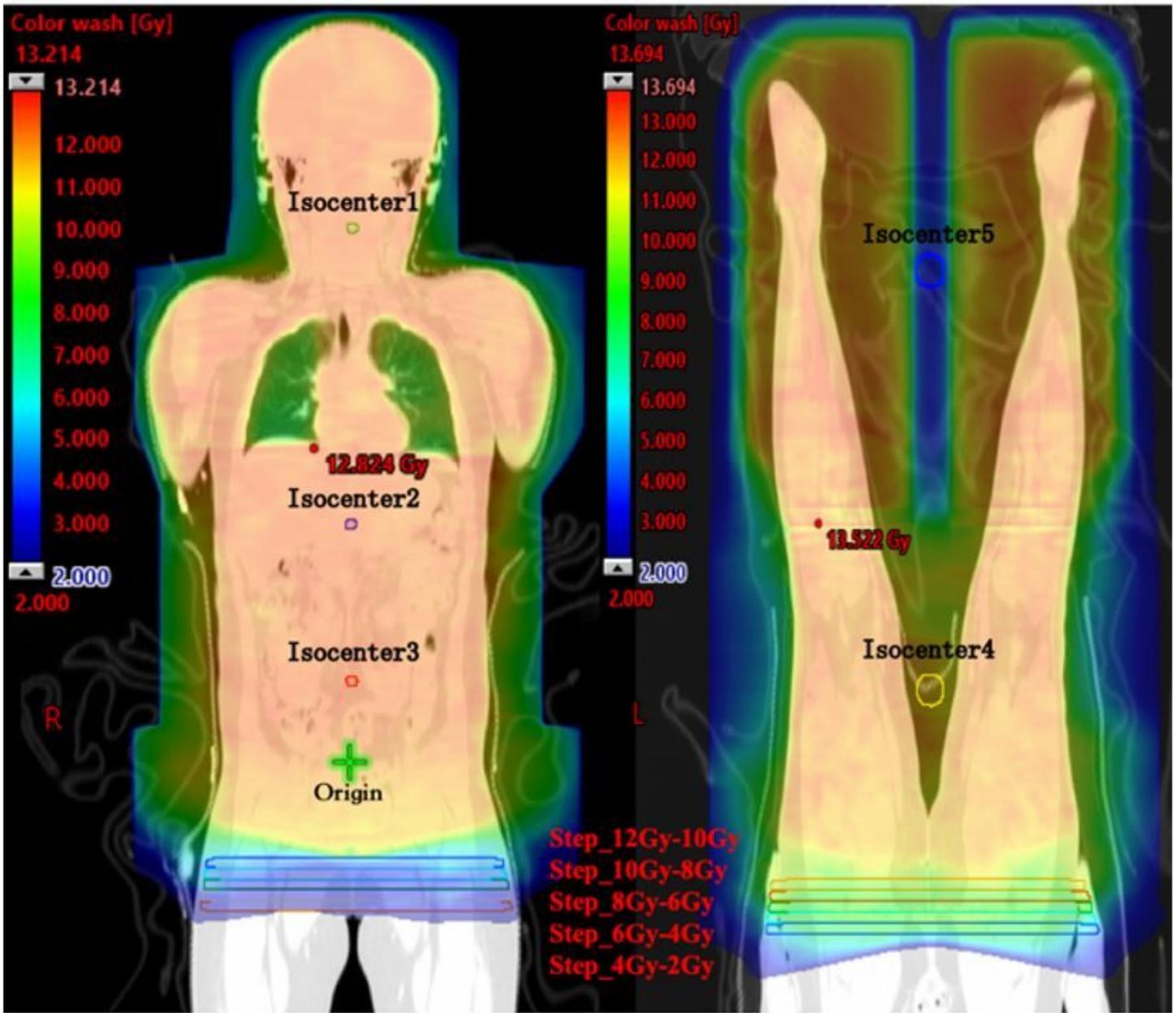


Figure 2

Dose distribution, five dose-drop sections and five isocenters.