Improved Lung and Gonadal Sparing during Total Body Irradiation using a VMAT technique

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Background

- Pulmonary toxicity and infertility has a paramount influence on the quality of life of the patients undergoing Total Body Irradiation (TBI).
- Reproductive toxicity is common following total body irradiation even at doses as low as 1 Gy and has major quality of life implications for patients[1].

Objectives/Aims

- We report on implementation of the Volumetric Arc Therapy (VMAT)-based TBI technique aimed at achieving improved lung and gonadal sparing.
- Gonadal sparing is demonstrated here for two pediatric patients with aplastic anemia (one in each gender).

Methods

- From October 2019 to July 2020 ten patients were treated with a VMAT TBI technique on C-arm LINAC.
- Patients were treated with the range of doses (2 Gy – 12 Gy) depending on the protocol.
- For dosimetric comparison between conventional 2D and VMAT approaches, a simulated 2D plans replicating our current clinical setup with lung blocks, chest-wall boosts and hypothetical testes/ovaries shields were created for two pediatric patients, an 8-year-old boy (**Patient 1**) and a 3-year-old girl (**Patient 2**) with aplastic anemia requiring hematopoietic stem cell transplantation (HSCT) and receiving 2Gy TBI.

Rotational Couch-Top

- As the patients were treated on C-arm LINAC to switch from Head First Supine (HFS) to Feet First Supine (FFS) treatment positions without re-positioning the patient, an in-house-developed rotational couch-top was used enabling 180°-patient rotation.

Figure 1. In-house developed rotational couch-top enabling patient position transition from HFS to FFS.

Methods: Simulation and Treatment Planning

- **Simulation:** Patients were immobilized in HFS position in a Civco long vac-lok bag on the in-house-made rotational platform. Patients' necks were extended resting on the Civco Timo neck support, arms tight close to the body, and the Civco knee fix and feet fix were placed under patients knees for comfort and leg position reproducibility. For 4 patients with the height <115cm enabling the treatment in HFS position only, rotational platform was not used. The full body CT scans were performed on Siemens Biograph PET/CT scanner with 5mm slice thickness and extended field of view to include arms in the scan.
- **Treatment Planning:** Treatment planning was performed using Eclipse v15.6 Treatment Planning System (Varian Medical Systems, Palo Alto) with 6MV or 10MV energy delivered by TrueBeam linear accelerator (Varian Medical Systems, Palo Alto).
- VMAT plans were generated with 3 isocenters (head, chest/abdomen, pelvis/upper legs) in head first supine (HFS) position and if needed, with additional AP-PA plans with 1-2 isocenters in feet first supine (FFS) position.
- Lower body AP-PA plans and the VMAT plan were matched on skin with field-in-field generated to improve homogeneity of the dose distribution. Upper body VMAT plans were optimized with all three isocenters included in one plan with at least 2cm overlap between the fields and using AP-PA Upper Leg plan as a baseline dose to homogenize the dose distribution in the matchline area. Auto-feathering optimization option was turned on to create smooth dose gradients in the field overlapping areas and prevent extreme dose heterogeneity in the event of larger setup variations.
- The VMAT plan was optimized to achieve at least 90% of the whole body PTV cropped 3mm from skin and critical normal structures to be covered by the prescription dose. **Table 1** shows the plan objectives for treatment planning.
- Plans for Patients 9-10 were created using an in-house developed Eclipse API VMAT TBI auto-planning script enabling automatic generation of optimization structures, insertion of treatment fields and optimization.

Structure	Dosimetric parameter	Limit (2 Gy Rx)	Limit (12 Gy Rx)
PTV_Body	D90%>=	200 cGy (100%)	1200 cGy (100%)
	Dmax<=	240 cGy (120%)	1440 cGy (120%)
	V110%<=	5%	5%
Lungs_Eval (Lungs-1cm)	Dmean<=	90 cGy (45%)	540 cGy (45%)
Lungs	Dmean<=	120 cGy (60%)	720 cGy (60%)
Kidneys	Dmax<=	210 cGy (105%)	1260 cGy (105%)
	Dmean<=		720 cGy (60%)
Bowel	Dmax<=	210 cGy (105%)	1260 cGy (105%)
Lenses	Dmax<=	180 cGy (90%)	1080 cGy (90%)
Testes/ovaries	Dmean<=	50 cGy (25%)	
	Dmax<=	ALARA (required <100 cGy)	
Brain_Eval (Brain-1cm)	Dmean<=	150 cGy (75%)	
Thyroid	Dmean<=	150 cGy (75%)	

Table 1. Plan objectives for VMAT TBI.

- For **Patient 1 and 2**, the VMAT TBI plans were compared to 2D plans assuming 5 cm lead shield for testes/ovaries with 5 mm margin and 1 cm water bolus (to decrease back scatter). Conventional AP/PA technique uses 15 MV beams at ~608 cm SSD with the compensator to homogenize the dose distribution along 7 positions on CAX, 50% transmission lung blocks, and electron chest-wall boosts prescribed to 1 Gy at depth of maximum dose.

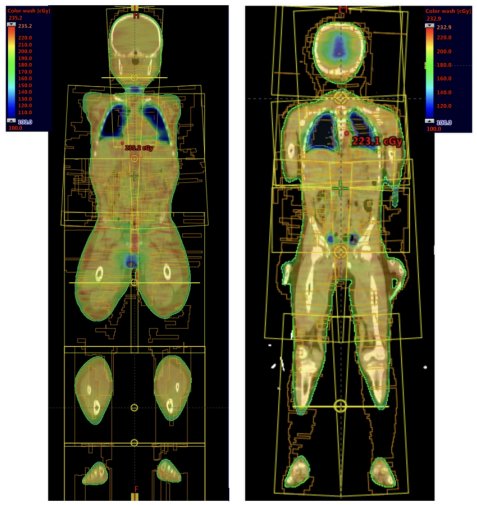

Figure 2. VMAT TBI beam arrangement and dose distribution on coronal view for **Patient 1** (left) and **Patient 2** (right).

Results

- For **Patient 1**, **Table 2** and **Figure 3** show the comparison between VMAT TBI and 2D Conventional TBI plans. The testes were spared to the maximum dose of 71.9 cGy and mean dose of 44.7 cGy, lungs were spared to the mean dose of 110 cGy (55% of Rx) with VMAT TBI plan compared to 89% of Rx with 2D plan. Global Dmax was 235.2 cGy (117.5%). Dose rate was set as 100 MU/min for upper VMAT plans and 600 MU/min for lower AP/PA plans. The average dose rate at lungs was 12.06 cGy/min.

Structure	Dosimetric parameter	2D Conventional plan	VMAT plan
PTV_Body	D90%=	190.5 cGy (95.3%)	200 cGy (100%)
	Dmax=	246.4 cGy (123.2%)	235.2 cGy (117.5%)
	V110%=	0.5%	5%
Lungs_Eval (Lungs-1cm)	Dmean=	168 cGy (84%)	91.4 cGy (45.7%)
Lungs	Dmean=	178 cGy (89%)	110 cGy (55%)
Testes	Dmean=	135.5 cGy (67.8%)	44 cGy (22.3%)
	Dmax=	156.0 cGy (78%)	71.9 cGy (35.9%)
Thyroid	Dmean=	205.2 cGy (102.6%)	142.5 cGy (71.3%)
Lenses	Dmax=	189.2 cGy (94.6%)	138.5 cGy (69.3%)

Table 2. Dosimetric comparison between 2D Conventional and VMAT TBI plans for **Patient 1**.

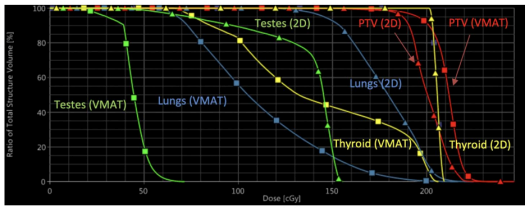

Figure 3. DVH comparison between 2D Conventional and VMAT TBI plans for **Patient 1**.

- For **Patient 2**, the ovaries were spared to the maximum dose of 87.8 cGy and mean dose of 64.8 cGy with VMAT plan (compared to 2D plan of 147 cGy and 150 cGy, respectively), lungs were spared to the mean dose of 60% of Rx (compared to 83.5% of Rx with 2D plan), lenses were spared to maximum dose of 198.6 cGy, brain was spared to mean dose of 152.6 cGy. Global Dmax was 232.9 cGy (116.5%). PTV coverage was also improved in the VMAT TBI plan versus the AP/PA plan (2 Gy D90% versus 1.9 Gy D90%, respectively). Dose rate was set as 100 MU/min for upper VMAT plans (head/chest, abdomen/pelvis) and 600 MU/min for leg plan. The average dose rate at lungs was 18.3 cGy/min.

Results

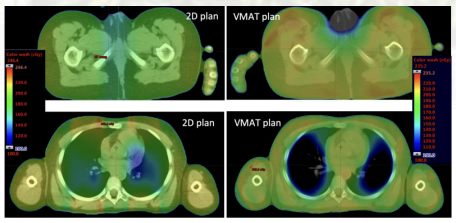

Figure 4. Dose distribution on axial slices for 2D conventional plan (left) and VMAT plan (right) for **Patient 1.**

- With VMAT TBI technique for all 10 patients, the mean dose to lungs and kidneys was 62.6%±5.7% and 66.8%±12.4% of Rx, respectively. Four pediatric aplastic anemia patients undergoing 2Gy-TBI regimen received mean doses to testes <0.4Gy, ovaries <0.6Gy, brain <1.5Gy, thyroid <1.4Gy. In addition, for one pediatric patient undergoing 12Gy-TBI regimen, liver received 7.4 Gy mean dose.

Treatment

- Since the auto-feathering optimization option was turned on, the plan robustness testing resulted in only 2.5% global Dmax increase for VMAT TBI plan for **Patient 1** when the isocenters were shifted ±5 mm.
- The dose measurements based on Optically stimulated luminescent dosimeters (OSLDs) placed on the match-line and testes were within 5% of the planned dose.

Figure 5. Cone-beam CT was acquired in the chest area to verify the positioning of **Patient 1** before treatment (left). Dosimetric shifts were applied to shift the patient to consequent isocenter positions, MV ports were acquired to verify the match after each shift (right)

- Beam-on time was 18.8 min for **Patient 1** and 15.0 min for **Patient 2**. Patient 1 patient was watching a movie during treatment using the AVATAR system[2], **Patient 2** patient was under anesthesia during treatment.

Conclusions

- This preliminary report suggests that VMAT TBI exhibited improved lung and gonadal sparing compared to the conventional approach.
- The present study can serve as a proof-of-concept for further prospective studies evaluating this technique for wider applications in populations receiving TBI.

[1]Hammond, C., Abrams, J. R. & Syrjala, K. L. Fertility and risk factors for elevated infertility concern in 10-year hematopoietic cell transplant survivors and case-matched controls. *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* **25**, 3511–3517 (2007).
[2] Hiniker SM, Bush K, Fowler T, et al. Initial clinical outcomes of audiovisual-assisted therapeutic ambience in radiation therapy (AVATAR). *Pract Radiat Oncol.* **7(5),** 311-318 (2017).

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