

# Improved Organ Sparing Using Auto-Planned Stanford Volumetric Modulated Arc Therapy for Total Body Irradiation (VMAT-TBI) Technique

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May 10, 2023

## Abstract

**Purpose/Objectives:** To evaluate dosimetric differences between auto-planned Volumetric Modulated Arc Therapy (VMAT) Total Body Irradiation (TBI) technique and 2D AP/PA TBI technique. **Methods:** Ten pediatric patients treated with VMAT-TBI on Varian c-arm linac were included in this study. VMAT-TBI plans were generated using our in-house developed and publicly shared auto-planning scripts. For each VMAT-TBI plan, a 2D AP/PA plan was created replicating the institution's clinical setup with the patient positioned at extended SSD with a compensator to account for differences in patient thickness, 50%-transmission daily lung blocks and electron chest-wall boosts prescribed to 50% of the photon prescription. Clinically relevant metrics were analyzed and compared between the VMAT and 2D plans. **Results:** All VMAT-TBI plans achieved PTV D90% [?]100% of prescription. VMAT-TBI PTV D90% significantly increased ( $6.2\% \pm 2.4\%$ ,  $p < 0.001$ ) compared to the 2D technique, whereas no differences were observed in global Dmax ( $p < 0.2$ ) and PTV V110% ( $p < 0.4$ ). Compared to the 2D plans, significant decreases in the Dmean to the lungs ( $-25.6\% \pm 11.5\%$ ,  $p < 0.001$ ) and lungs-1cm ( $-34.1\% \pm 10.1\%$ ,  $p < 0.001$ ) were observed with the VMAT plans. The VMAT technique also provided additional sparing to other organs: for 12Gy prescription, kidneys Dmean of  $64.7\% \pm 3.3\%$ ; for 2Gy prescription, testes/ovaries (Dmean of  $31.6\% \pm 10.7\%$ ), brain (Dmean of  $74.8\% \pm 1.6\%$ ) and thyroid (Dmean of  $72.5\% \pm 3.5\%$ ). **Conclusions:** Superior lung sparing with improved target coverage and similar global Dmax were observed with the VMAT plans as compared to 2D plans. In addition, VMAT-TBI plans provided greater dose reductions in gonads, kidneys, brain, and thyroid.

## INTRODUCTION

Total body irradiation (TBI) is a well-established conditioning regimen used in bone marrow or stem cell transplantation during which the whole body is irradiated with the intention of eliminating malignant cells and preventing the rejection of donor cells through immunosuppression. Even though this regimen is effective<sup>1</sup>, it is associated with significant side effects including pulmonary toxicity (approximately 25% of patients),<sup>2,3</sup> cataracts (30-40% of patients)<sup>4</sup>, gonadal failure<sup>5</sup>, thyroid and kidney dysfunction<sup>6,7</sup> and decreased bone mineral density<sup>8</sup>. Based on the most recent Children Oncology Group (COG) survey on TBI techniques<sup>9</sup>, most conventional AP/PA TBI techniques use partial transmission lung blocks of non-patient-specific thickness to limit the lung toxicity. However, lateral TBI techniques rarely incorporate lung blocks, resulting in lung dose that is equal to or higher than the prescription dose. In addition, inconsistent lung dose reporting, and manual monitor unit calculation in a homogenous medium based on patient thickness measurements limit accuracy in lung dose determination. The importance of reduction of lung dose in decreasing the risks of pneumonitis and potentially lethal pulmonary toxicity has been demonstrated, with recent

studies have demonstrated that mean lung doses below 8 Gy are needed to decrease lung toxicity risks and improve overall survival<sup>10</sup>.

The Children’s Oncology Group survey of 152 COG institutions on the practice patterns in pediatric TBI in 2020-21 found that 100% of physician respondents were interested in refining the conventional TBI techniques to lower lung dose and 75% of physicians were interested in implementing VMAT or Tomotherapy TBI<sup>9</sup>. But, as shown by the survey, the supply does not meet the demand: only 14% of institutions adapted VMAT-TBI and Tomotherapy TBI.

Several studies showed the benefit of modern treatment planning and treatment delivery approaches to TBI, including helical tomotherapy<sup>11-12</sup> or volumetric modulated radiation therapy (VMAT)<sup>13-15</sup> allowing for superior organ sparing and more comfortable patient positioning during treatment. However, these treatment techniques require expertise and special equipment, which has limited their accessibility, and relatively little data regarding dosimetric comparisons has been reported. We have developed the Stanford auto-planned VMAT-TBI technique<sup>13,16-17</sup> and shared the auto-planning scripts with the public to make VMAT-TBI more wide-spread (<https://github.com/esimiele/VMAT-TBI>). Our technique was also included as a basis for VMAT-TBI methodology among 2D and Tomotherapy TBI techniques on the Children Oncology Group (COG) ASCT2031 trial. In this work, we report the comparison between our auto-planned VMAT-TBI for myeloablative and nonmyeloablative regimens and our 2D-conventional TBI technique. These results are relevant for institutions intending to switch from 2D to VMAT-TBI technique and can be beneficial for creation of future analysis and dosimetric correlatives for Children Oncology Group (COG) ASCT2031 trial.

## METHODS AND MATERIALS

Ten pediatric patients (age range, 3 – 17 y.o.) treated with the VMAT-TBI technique on the Varian TrueBeam from November 2019 to August 2020 were included in this IRB approved study. Patients were treated with either non-myeloablative (2 Gy in one fraction) or myeloablative (12 Gy in six fractions) regimens. Corresponding 2D plans replicating our current clinical setup with lung blocks and chest-wall boost were created for all ten patients for dosimetric comparison between the 2D and VMAT techniques.

For VMAT-TBI, patients were simulated head-first supine (HFS) position in a CIVCO long vac-lok bag positioned on the in-house developed rotational platform. Patients’ necks were extended resting on the AccuForm cushion (CIVCO) neck support, arms tightly clasped straight alongside the body, and the CIVCO knee fix and/or feet fix were placed under patient’s knees for comfort and leg position reproducibility. The in-house-developed auto-planning script within Eclipse v15.6 Application Programming Interface (API) was used for treatment planning<sup>16</sup>. The VMAT plans were auto-generated with three isocenters (head, chest/abdomen, pevis/legs) in HFS position. Additional AP/PA plans with 1 to 2 isocenters in the feet-first supine (FFS) position were used if patient height exceeded 115 cm (due to the longitudinal table limit in HFS position). Upper-body VMAT plans using 6 MV or 10 MV were optimized with all isocenters included in one plan with at least 2 cm overlap between the fields. The AP/PA Upper Leg plan was used a baseline dose in the optimization to homogenize the dose distribution near the matchline area. The auto-feathering optimization option was turned on to create smooth dose gradients in the fields’ overlapping areas and to prevent extreme dose heterogeneity in the event of larger setup variations. The VMAT plans were optimized and normalized to achieve at least 90% coverage of the whole body PTV with the prescription dose. The PTV volume was created by cropping 3 mm from skin and critical normal tissues.

For each VMAT-TBI plan, a simulated 2D plan was developed in Eclipse based on the VMAT-TBI CT scan. The 2D plan fields were setup for AP/PA technique at an extended SSD (~608 cm), collimators at 45° and 135°, field sizes set to 40 x 40 and 15 MV energy. Umbilicus was used as the isocenter. Screen-to-skin distance, separation and off-axis measurements that are typically acquired during clinical setup were measured based on the CT scan. The compensator layers were re-created on the CT scan to homogenize dose distribution based on the following midline points: head, chin, neck, suprasternal notch (SSN), xiphoid, umbilicus, hip/pubis, thigh, knee, calf, and ankle. Lung blocks were generated using the lung contour contracted by 1 cm (lungs-1cm) and 1 cm below clavicle with the constant thickness of 2.5 cm of Cerrobend for every patient. The

block transmission measurements in the middle of 10 cm thick lung slab sandwiched in-between two 4-cm thick solid water slabs was 50% for 15 MV beam. Electron chest wall (CW) boost fields were created for all patients prescribed to 50% of TBI photon prescription to depth of maximum dose. The accuracy of the dose calculation was verified using the ion chamber measurement in the phantom composed of the lung slab sandwiched between the solid water slabs.

The clinically relevant metrics in this study, including plan global Dmax, PTV D90%, PTV V110%, lungs and lungs-1cm Dmean, were analyzed and compared between the VMAT-TBI and simulated 2D plans. For gonadal sparing comparison, the VMAT-TBI plans were compared to 2D plans for a girl (Patient 4) and a boy (Patient 3) assuming 5 cm lead shield for testes/ovaries in front of the patient with 5 mm margin. All dosimetric comparisons between the VMAT and 2D plans were made with the dose expressed as a percentage of the prescription dose and the volume expressed as a percentage of the PTV volume. Paired t-test was used to compare the dosimetric indices between the VMAT and 2D TBI plans with p-values less than 0.05 considered to be statistically significant.

## RESULTS

Table 1 shows the patient and dosimetric characteristics for VMAT-TBI plans. The mean global Dmax was  $118.8\% \pm 4.0\%$  and the PTV V110% ranged from 0.1% to 5.3%. All lung Dmean values were below 7.2 Gy and lungs-1cm Dmean was  $36.5\% \pm 4.8\%$ . For patients that required kidney sparing, the average kidney Dmean was  $67.5\% \pm 4.0\%$  of the prescription dose. Achieved testes/ovaries Dmean and Dmax were  $0.66 \pm 0.07\text{Gy}$  and  $0.90 \pm 0.03\text{Gy}$ , respectively. The average brain-1 cm Dmean was  $55.9\% \pm 3.7\%$ . Thyroid sparing was performed for two patients with Dmean =  $1.45\text{Gy} \pm 0.07\text{Gy}$ . Lenses were spared to 90% of prescription for all patients.

Table 2 shows the comparison between VMAT and 2D plans for target and lung dosimetric indices. The target coverage, PTV D90%, was significantly superior for VMAT plans as compared to 2D plans with a mean difference of  $6.1\% \pm 2.4\%$ ,  $p < 0.001$ . No significant difference was observed between the VMAT and 2D plans for global Dmax and PTV V110% (mean differences of  $-2.0 \pm 6.7\%$  and  $0.0 \pm 2.9\%$ , respectively). With the 2D plans, lungs received an average of 80.6% of the prescription dose (range: 72.0% - 90.0%). The average lungs-1cm Dmean for 2D TBI plans was  $70.6\% \pm 8.1\%$ .

The mean lungs and lungs-1cm dose for VMAT-TBI plans was significantly lower as compared to the 2D plans: reductions of  $-25.6\% \pm 11.5\%$  and  $-34.1\% \pm 10.1\%$ , respectively, were observed ( $p < 0.001$ ). In addition, VMAT-TBI plans spared kidneys, brain, thyroid, testes/ovaries, and lenses, while 2D plans delivered the prescribed dose to those organs.

Gonadal sparing between 2D and VMAT-TBI plans was compared for two patients (female - patient 4 and male - patient 3). For patient 4, Figure 1 shows the dose distribution comparison between the 2D and VMAT plans. The ovaries were spared to mean dose of 65.8 cGy and maximum dose of 87.8 cGy with the VMAT plan. Although gonadal sparing would not be practical with the 2D approach due to difficulties in ovary localization in the standing AP/PA treatment in the booth, the 2D plan was created for dosimetric comparison. With the 2D plan, the ovaries received 147.1 cGy Dmean and 150.0 cGy Dmax (prescription dose of 2 Gy). Figure 2 shows the DVH comparison between the VMAT and 2D Conventional TBI plans for patient 3. The maximum and mean doses to the testes were 71.9 cGy and 44.7 cGy, respectively, for the VMAT plan compared to 156.4 cGy Dmax and 136.2 cGy Dmean with the 2D plan.

All ten patients tolerated treatment well. The image guidance included CBCT at chest isocenter and MV portal images for the consequent isocenters. The average treatment time was 44.4 min, range: 25.1 min to 57.4 min. Three patients were treated under anaesthesia, and seven remaining patients were watching movies during radiotherapy.

## DISCUSSION

VMAT-TBI is a promising modality with increasing clinical utilization. In this study, we analyzed organ sparing using the VMAT technique in comparison to the conventional 2D technique. 2D and VMAT plans were generated for the same patients and directly compared. The VMAT-TBI treatment was well tolerated

and significant improvements in target coverage and lung sparing were achieved with the VMAT technique versus the 2D comparison plans. In addition, the VMAT technique provided the opportunity to spare other organs, such as kidneys, gonads, brain, thyroid, lenses when deemed appropriate. Other benefits of using VMAT-TBI technique are more comfortable patient positioning lying down, ability to treat TBI under anesthesia, more accurate dose calculation and image-guided treatment delivery, and the ability to treat TBI patients in a small vault.

The 2D conventional technique with lung blocks is the current standard of care. At our institution, lung blocks are created to allow, on average, 50% transmission at mid-lung point for an average-size patient. The size of the blocks are drawn to match the lungs–1cm contour and 1 cm below clavicle to enable dose coverage to the bones (clavicle and ribs). Therefore, a good portion of the lungs will still receive significant dose (>50% of the prescription dose). In addition, there is a dose contribution from chest wall boosts, adding up to a mean lung dose of 80.6% of the prescription.

Although the study improves upon the kidneys, brain, thyroid, lenses sparing, it is unclear that this benefit will be clinically meaningful, although the early outcomes and toxicity report is promising<sup>18</sup>. Despite this possibility, our institution generally abides by the ALARA (as low as reasonably achievable) principle, which would argue that lower organ doses are desirable in and of itself for patients without active disease; however, further studies will be necessary to elucidate the exact dose response of this lung toxicity at these lower observed doses.

## CONCLUSION

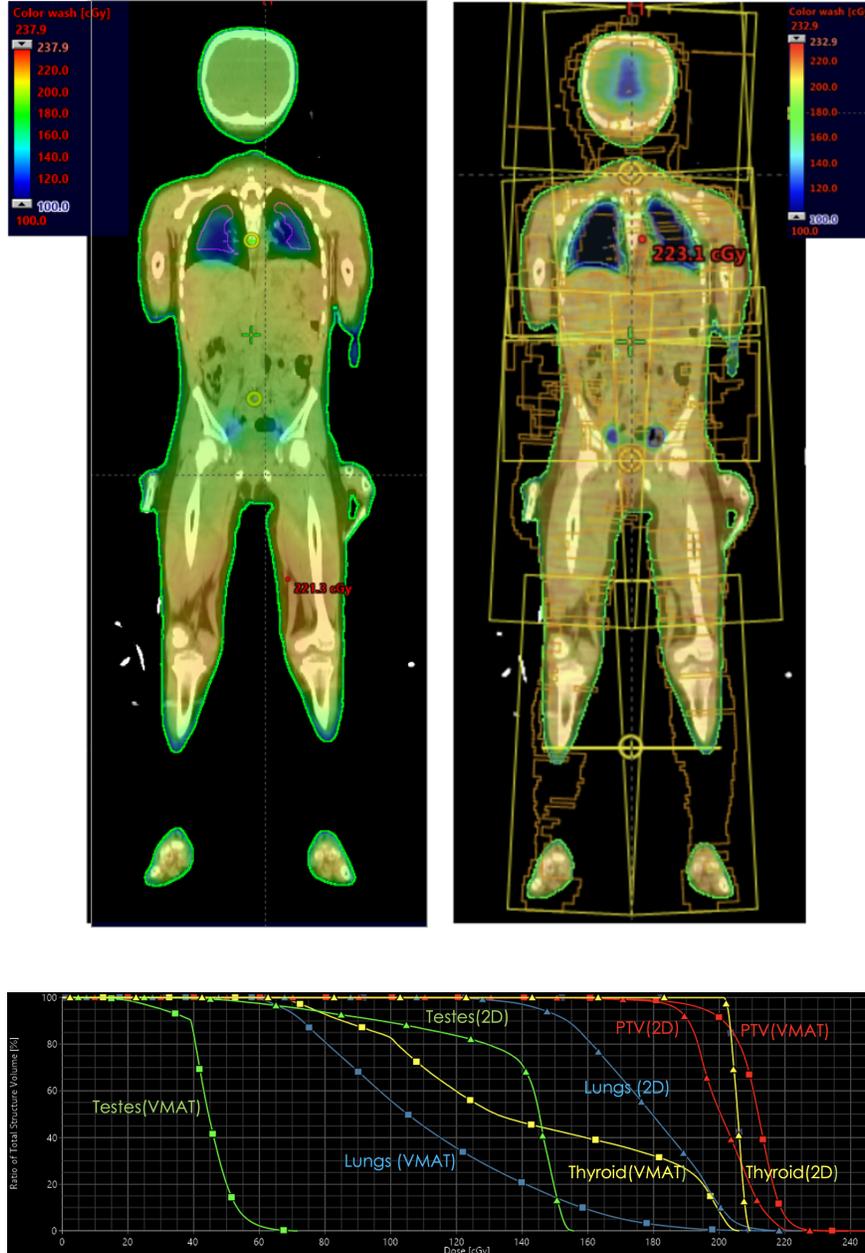
VMAT-TBI is a modern alternative to conventional 2D-TBI treatment, offering superior lung sparing with superior target coverage and similar global Dmax. In addition, VMAT-TBI plans using auto-planning scripts provided significant dose reductions in gonads, kidneys, brain, thyroid and lenses.

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Figure 1: Dose distribution on the coronal view for patient 4 with gonadal sparing for the 2D plan (left) and VMAT (right).

Figure 2: DVH comparison for the VMAT and 2D TBI treatment techniques for patient 3.



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Tables (1).docx available at <https://authorea.com/users/616398/articles/642423-improved-organ-sparing-using-auto-planned-standford-volumetric-modulated-arc-therapy-for-total-body-irradiation-vmat-tbi-technique>