Volumetric Modulated Arc Therapy Based Total Body Irradiation – Five Year Clinical Experience

Elizabeth R Zhang, David Parsons, Jun Tan, Mindy Joo, Robert Reynolds, You Zhang, Pam Lee,
Xuejun Gu, Eric Chambers, Neil B. Desai, Tu D. Dan, and Kiran A. Kumar
Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX

UTSouthwestern
Harold C. Simmons
Comprehensive Cancer Center
Radiation Oncology

Introduction

In this poster we share our clinical experience and treatment outcome on a volumetric arc-therapy based TBI (VMAT-TBI) technique developed in our institution. The goal of developing VMAT-TBI technique was to realize a comfortable supine position in a standard size vault, while satisfying TBI dosimetric requirement with homogenous dose (within ±10%) to the body and lower dose, e.g. 75% of the prescription dose (Rx) to the lungs. With this goal, we have been developing, implementing, and improving VMAT-TBI technique since 2014. To date, more than 50 patients have been simulated and planned with VMAT-TBI technique, and more than 40 patients have been treated and followed.

Materials & Methods

Data (Table 1) were retrospectively collected from 44 patients (20 children and 24 adults) who were treated with VMAT-TBI between 2014 and 2020. 39 patients received TBI for malignant indications (leukemia or lymphoma), whereas 5 patients received TBI for benign indications.

Simulation: Computed tomography (CT) based treatment simulation is conducted with the aid of home-developed rotational body frame (Figure 1). **Treatment planning:** Target and OARs defined for planning are listed in Table 2. Depending on patient size, as shown in Figure 2, typically 5-7 isocenters are typically utilized, 3-4 for VMAT arc fields of the upper body and 2-3 for AP-PA fields of the lower body. All arc fields have collimator rotated 90°, such that the MLC leaves travel along the superior-inferior (SI) direction for better field modulation. Special attention required for the chest isocenter, which is shared by two 21x40 cm^2 arc fields with 2 cm overlap. A third 30x40 cm^2 arc with 5º collimator rotation maybe needed for larger patients. In general, brain, abdomen and pelvic isocenters host one arc field per each isocenter. An additional arc can be added to chest, abdomen and pelvic isocenter for larger patients, which will increase dose uniformity. **Treatment delivery:** A couch-shift document that contains the frame coordinates and corresponding treatment table positions of each isocenter is made during treatment planning. During treatment, the couch-shift document is used to guide all couch shifts relative to user origin/chest isocenters, in which this location is determined through CBCT image guidance.

Table 1: Patient characteristic and survival outcome.

	Pediatric		Adult	
	Low dose (2 patients, 3 treatments)	High dose (18 patients)	Low dose (10 patients)	High dose (14 patients)
Age	8 (6-11)	14 (3-17)	57 (25-68)	29 (20-47)
Malignant	0 (0%)	18 (100%)	7 (70%)	14 (100%)
KPS	90 (80-100)	100 (70-100)	80 (60-100)	85 (80-100)
OS	21.1 months (100%)	19.6 months (72%)	6.5 months (100%)	39.0 months (71%)
PFS	NA	15.4 months (61%)	6.3 months (86%)	33.1 months (57%)

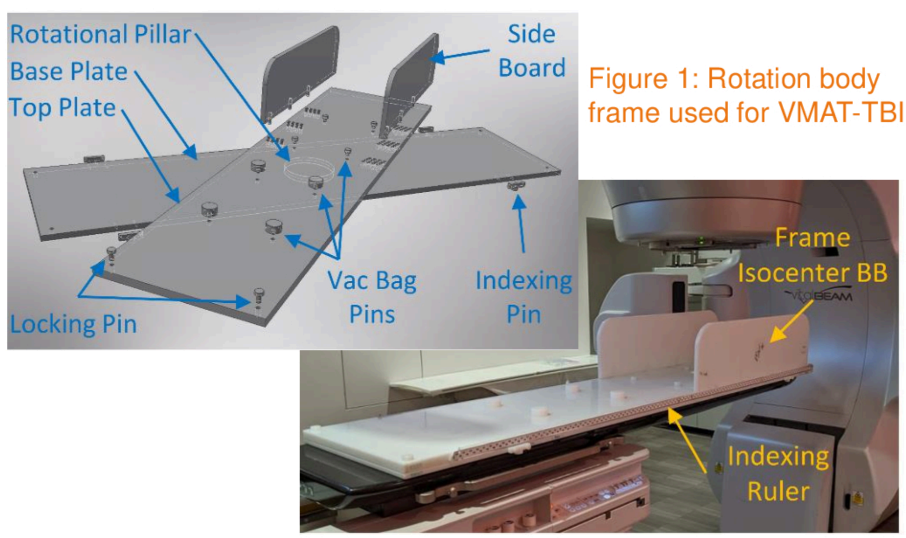

Figure 1: Rotation body frame used for VMAT-TBI.

Table 2: Treatment planning objectives.

Structure	DVH metric	Objective	Notes
PTV Body	V_{Rx}	> 90%	Human body with a 5mm contraction and the lungs subtracted
PTV Lungs	Mean	75% Rx* (low-dose cohort) 75%-50% Rx (high –dose cohort)	1 cm contraction from the lungs. High-dose cohort started with 75% Rx in first three years and gradually lowered to 67-50% Rx in later years.
Spinal Cord	Dmax	< 125% Rx	Max 0.125cc; As homogenous as possible
Bowel	Dmax	< 125% Rx	Max 0.125cc
Kidney (individual)	Mean	< 108% Rx	
Oral Cavity	Dmax	< 125% Rx	Max 0.125cc
Whole Brain	Dmax	< 125% Rx	Max 0.125cc

*Rx: prescription dose

Follow-up and toxicity: Acute toxicities were graded by Common Terminology Criteria for Adverse Events version 5 (CTCAE v5). Acute toxicities were deemed likely related if there was no other etiology to explain the toxicity (such as a documented gastrointestinal infection at the time that a patient experienced diarrhea). Graft-versus-host-disease (GVHD) was scored by NIH Consensus Criteria.

Results and Discussion

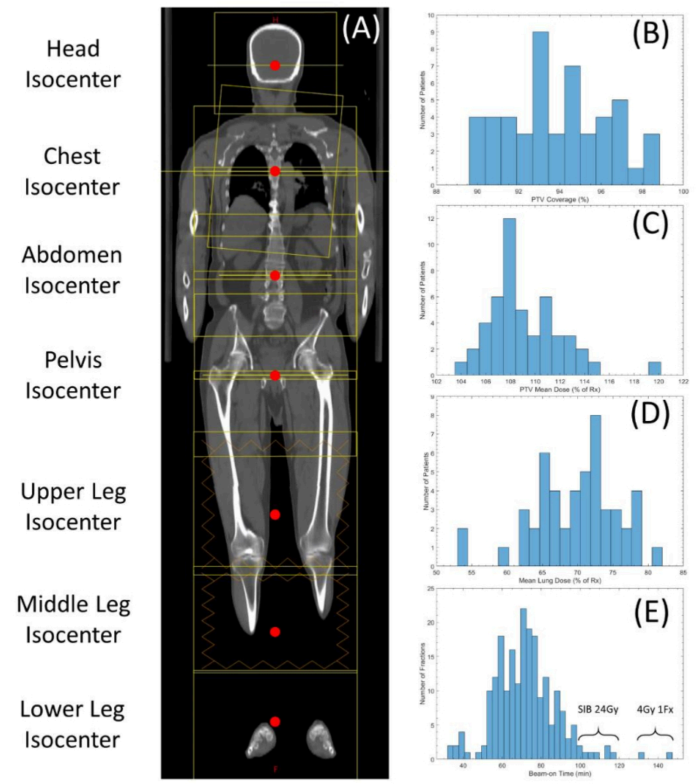

Figure 2: (A) Field arrangement used for VMAT-TBI, (B) PTV Body coverage, (C) PTV Body mean dose (D) PTV Lungs mean dose, (E) distribution of 44 patients' treatment time.

Figure 2B-D shows dosimetric statistics for PTV coverage, mean dose and lung mean dose relative to the Rx. Mean PTV coverage, PTV body dose and PTV lung dose is 93.9%, 109.2% of the Rx, 69.8% of the Rx, respectively. Our two most recent multi-fraction patients have a mean lung dose of 53% for an objective of 50% (6 Gy). Figure 2E shows fractional treatment delivery time ranged from 33-147 minutes with a mean of 72.2 minutes. The prolonged treatment time due to the conservative dose rate of 20 MU/min (pediatric) and 40 MU/min (adult) for the arc beams.

At a median follow-up of 22.7 months, 35 of 44 patients were alive (overall survival 80%). Of the 9 patients who had died, 6 died of sepsis in the setting of subsequent immunosuppression, 1 died of gastrointestinal bleeding from gut GVHD, 1 died of ARDS (with possible component of radiation pneumonitis), and 1 died of encephalopathy caused by pneumonitis), and 1 died of encephalopathy caused by tumor lysis syndrome in the setting of progression. Notably, no deaths were observed in the low-dose (2-4 Gy in 1-2 fractions) cohort (Table 1). Skin and gut GVHD were observed in 48% and 18%, respectively of the 44 treated patients. Lung and liver GVHD were less common at 9% and 16%, respectively. Most cases of GVHD were mild and successfully managed with immunosuppression, but one pediatric patient treated with high-dose TBI experienced stage 4 gut GVHD which resulted in a lethal gastrointestinal bleed. The most common toxicities among the 44 treated patients were fatigue (77%), mucositis (82%), and diarrhea (89%).

9% of patients developed pneumonitis, of which all cases were severe (grade 3+). All observed cases were in the high-dose cohort (Table 3). One case was felt to be likely related to radiation, whereas the remaining 3 cases were in the setting of documented respiratory infection and likely multifactorial. One patient died of Acute Respiratory Distress Syndrome (ARDS), which we considered a possibly related grade 5 pneumonitis. The observed cases of nephrotoxicity (6 patients, 13%) were similarly all severe (grade 3-4), though all occurred in the setting of other etiologies such as shock and nephrotoxic medications and were considered multifactorial.

Table 3: Patient toxicities and GVHD.

	Pediatric						Adult					
	Low dose			High dose			Low dose			High dose		
Toxicities	Total	Grade 3+	Onset (days)	Total	Grade 3+	Onset (days)	Total	Grade 3+	Onset (days)	Total	Grade 3+	Onset (days)
Pneumonitis	0 (0%)	0 (0%)	NA	3 (17%)	3 (17%)	205	0 (0%)	0 (0%)	NA	1 (7%)	1 (7%)	79
Nephrotoxicity	0 (0%)	0 (0%)	NA	2 (11%)	2 (11%)	165.5	2 (20%)	2 (20%)	15.5	2 (14%)	2 (14%)	201.5
Fatigue	0 (0%)	0 (0%)	NA	15 (83%)	0 (0%)	6	9 (90%)	0 (0%)	2	10 (71%)	0 (0%)	4
Diarrhea	0 (0%)	0 (0%)	NA	16 (89%)	0 (0%)	8	10 (100%)	0 (0%)	4.5	13 (93%)	0 (0%)	4
Nausea	1 (33%)	0 (0%)	0	9 (50%)	0 (0%)	2	1 (10%)	0 (0%)	0	10 (71%)	0 (0%)	1
Erythema	0 (0%)	0 (0%)	NA	0 (0%)	0 (0%)	NA	0 (0%)	0 (0%)	NA	4 (29%)	0 (0%)	1.5
Xerostomia	0 (0%)	0 (0%)	NA	4 (22%)	0 (0%)	5	0 (0%)	0 (0%)	NA	3 (21%)	0 (0%)	3
Pre-transplant mucositis	1 (33%)	0 (0%)	0	14 (78%)	5 (28%)	7	0 (0%)	0 (0%)	NA	2 (14%)	0 (0%)	10.5
Post-transplant mucositis	3 (100%)	3 (100%)	4	18 (100%)	18 (100%)	10	3 (30%)	1 (10%)	6	12 (86%)	9 (64.3%)	10
GVHD												
Skin	1 (33%)		60	6 (33%)		62.5	3 (30%)		35	11 (79%)		30
Liver	0 (0%)		NA	4 (22%)		112.5	0 (0%)		NA	3 (21%)		68
Lung	0 (0%)		NA	1 (6%)		192	0 (0%)		NA	3 (21%)		188
Gut	0 (0%)		NA	5 (28%)		41	0 (0%)		NA	3 (21%)		98

Conclusions

VMAT-TBI provide a safe TBI dose delivery for both pediatric and adult patients. The overall workflow is well-aligned with routine VMAT treatment and achieves great efficiency. The dose modulation capability of VMAT-TBI techniques could lead to new treatment strategies, such as simultaneous boost and critical organs sparing, for better malignant cell eradication, immune suppression, and lower toxicities.