RefleXion X1 Treatment Planning Feasibility Study for Cranio-Spinal Irradiation (CSI)

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October 30, 2023

Abstract

Purpose: The first clinical biology-guided radiation therapy (BgRT) system – RefleXion ^{TM} X1 - was installed and commissioned for clinical use at our institution. This study aims at evaluating X1 treatment planning feasibility of complex craniospinal targets for pediatric medulloblastoma patients and comparing plan quality to multi-isocenter linac-based VMAT plans. **Methods:** Five pediatric patients treated with multi-isocenter craniospinal irradiation (CSI), planned using Eclipse VMAT and delivered using Varian Trilogy C-arm linac, were selected for this retrospective study. All PTV targets had a craniocaudal length<50cm (current X1 TPS limit) and received 36 Gy in 20 fractions. The target volumes and organs-at-risk (OARs) used for VMAT plans were used to generate plans using RefleXion X1. The near maximum dose to PTV (PTV D2%), OARs Dmean and Dmax, and treatment times were collected for analysis. A paired-sample t-test was performed to detect significance at $p < 0.05$. **Results:** All five RefleXion X1 CSI plans were successfully generated and were clinically acceptable for treatment. PTV D2% was higher for X1 compared to VMAT plans at 41.3 Gy and 39.2 Gy, respectively, ($p = 0.08$). For the X1 plans, the average Dmean to the bowel, cochleas, heart, kidneys, lungs, and oral cavity were 10.4 Gy, 38.5 Gy, 12.5 Gy, 18.2 Gy, 13.7 Gy, and 16.0 Gy, respectively. The difference was not found to be statistically significant ($p>0.05$) compared to VMAT plans which showed Dmean to the bowel, heart, kidneys, lungs, and oral cavity at 11.7 Gy, 38.4 Gy, 11.6 Gy, 15.6 Gy, 13.3 Gy, and 15.0 Gy, respectively. The average treatment beam-on time for X1 plans was 16.7 min versus 3.6 min for VMAT plans ($p<0.01$). However, RefleXion X1 platform enabling one-isocenter treatment and 90 cm long kVCT scan has a potential to decrease the setup/imaging time, and thus the total treatment time compared to multi-isocenter linac-based VMAT where the total treatment time up to 43.5 min was observed. **Conclusion:** Apart from a higher maximum dose to PTV, X1 plans showed comparable dosimetry to multi-isocenter VMAT plans. Although the average beam-on time with X1 was longer, there is a potential for a more streamlined setup and IGRT using a single-isocenter plans.

INTRODUCTION

Medulloblastoma is the most common childhood malignant central nervous system (CNS) tumor [1]. Peak incidence occurs at age 7 with slightly greater incidence in males [1,2]. A large proportion of medulloblastoma patients have craniospinal fluid (CSF) spread at the time of diagnosis. The standard of care for medulloblastomas involves surgical resection, craniospinal irradiation (CSI), and chemotherapy [3]. For average-risk patients the 5-year survival rate is over 80% while high-risk patients have a 5-year survival rate of less than 50% [2,4].

CSI presents challenges due to its large target volume which extends beyond the 40 cm x 40 cm field size limitation of a commonly used C-arm linear accelerator collimator opening [5, 6]. Therefore, the use of multiple plan isocenters provides a solution to this limitation by dividing the target volume into three fields—the whole brain, the upper spine, and the lower spine. CSI is commonly performed using 3D conformal radiation therapy (3D-CRT) technique which is prone to errors due to the complexity of the planning and the treatment delivery setup [7-12]. This technique results in dose inhomogeneity and non-conformality which yields significant dose to the anterior of the spine target volume. 3D CSI also requires feathering the junctions resulting in multiple plan pairs, gap calculation and couch rotations, making the planning and treatment procedures complex and cumbersome and prolonging treatment times.

Overall, Volumetric Modulated Arc Therapy (VMAT) CSI has been observed to create plans with better dose conformality, better dose homogeneity, greater normal tissue sparing, low sensitivity to positioning errors, and shorter treatment time compared to 3D-CRT CSI [13-17]. While VMAT can produce clinically favorable plans even with setup errors of up to 3 mm margin, accurate patient alignment with minimal setup remains important. A multicenter study conducted by Gram et al. showed daily image guidance with 6-DoF couch corrections was found optimal in significantly reducing positioning errors and uncertainties for pediatric CSI patients [11].

While daily image guidance and 6-degrees of freedom couch corrections can assist in optimizing patient setup, the inherent risks for positioning errors and uncertainties cannot be eliminated for VMAT CSI due to the use of multiple isocenters and field matching. Helical-delivery radiation treatment techniques such as Tomotherapy™ can reduce these risks associated with multi-center CSI treatments by using a ring-based gantry to deliver a single field CSI treatment as the patient moves into the treatment ring [18-20]. A study by Lee et al. reported Tomotherapy CSI to have acceptable inter-fractional and intra-fractional errors, and setup verification based on the measurements and evaluations of treatment setup for 83 patients [19]. In addition, Tomotherapy CSI techniques have been demonstrated to produce highly conformal and homogeneous treatment plans compared to 3D CSI [21,22].

RefleXion™ (RefleXion Medical Inc., Hayward, CA) is a novel Positron Emission Tomography (PET) treatment modality that similarly utilizes a ring-based gantry for axial step-and-shoot IMRT delivery. The first clinical installation of RefleXion X1 was recently conducted at our institution [23,24]. The RefleXion X1 design provides potential advantages to CSI treatments using a single isocenter which can potentially decrease complexity of planning, image guidance and delivery reducing risk of shift and localization errors. This study aims to test the feasibility of treatment planning of X1 CSI and compare the plan quality and beam-on time to the current standard of care at our institution – VMAT CSI planned in Eclipse and delivered using Trilogy linear accelerator (Varian Medical Systems, Palo Alto, CA).

METHODS

Patient selection and simulation

Of 81 patients previously treated with VMAT CSI at our institution during 2012-2022, only five patients had PTV length less than 50 cm in the cranio-caudal direction (current RefleXion X1 Treatment Planning System (TPS) limitation). These five patients were included in the planning feasibility study. Patients were simulated using Siemens CT scanner (slice thickness 2 mm) in the head-first-supine (HFS) position with arms by side, immobilized in 5-point head and neck mask and AccuForm cushion (CIVCO) in the neutral neck position. All patients were treated under anesthesia.

VMAT CSI planning

VMAT CSI plans were generated on Eclipse v15.6 (Varian Medical Systems, Palo Alto, CA) using 6 MV energy beams, Photon Optimization (PO) algorithm, Analytical Anisotropic Algorithm (AAA) dose calculation, and a calculation grid of 2.5 mm. Two full arcs were used to treat the brain and a single arc was used to treat the spine, with an overlap of at least 2 cm between the brain and spine fields. Brain and Spine isocenters were placed such that there was only longitudinal shift between them. Auto-feathering was enabled during optimization to create smooth dose gradients in the overlapping areas between fields. The spine arcs used avoidance sectors to limit dose entering through the arms. VMAT CSI plans were normalized at 95% PTV coverage by the prescription dose of 36 Gy.

RefleXion X1 linac

RefleXion X1 is the first Biology-guided Radiotherapy (BgRT) system consisting of a 6MV flattening-filter-free (FFF) linear accelerator mounted on the 85 cm gantry ring rotating at 60 rpm and delivering the treatment using one isocenter in axial fashion advancing the couch every 2.1 mm. Modulation is achieved using 64 binary pneumatically-driven multi-leaf fast-transitioning collimators (MLC). Two sets of jaws, positioned above and below the MLCs, are used to set the maximum field extent in the patient superior-inferior direction: either 1 cm or 2 cm at isocenter. The X1 is also equipped with fan-beam kilovoltage computed tomography (kVCT) of near-diagnostic image quality, megavoltage portal, and positron emission tomography (PET) imaging subsystem.

RefleXion X1 planning

CT scans and structure sets used for VMAT CSI plan generation were imported to RefleXion X1 TPS for planning. The PTV_CSI target ranged between 48.1-49.3 cm and was the same for VMAT and X1 planning. All patients were planned on the RefleXion X1 v1.0.46 TPS using step-and-shoot IMRT technique with 6 MV FFF (energy, 2 cm jaws, accelerated proximal gradient based on FISTA algorithm and Collapsed Cone Convolution (CCC) superposition dose calculation algorithm, and a calculation grid of 2.1 mm. Plan isocenter was placed in the middle of the target. As plan dose normalization was not available in RefleXion X1 v1.0.46, each plan was optimized to allow for 95% of the PTV to receive the prescription dose (36 Gy in 20 fractions).

Plan comparison

Plans, created in Eclipse and RefleXion X1 for each patient, were evaluated for dose heterogeneity using dose to 2% of the PTV (D2%) and mean dose to critical structures. The critical structures evaluated and their dosimetric constraints are listed in Table 1. A paired sample t-test was then performed to evaluate these dosimetric quantities between the Eclipse and the RefleXion X1 plans for each patient, with statistical significance defined at $p<0.05$.

Beam-on time and Treatment time analysis

Beam-on time was collected from Eclipse and RefleXion X1 TPS and compared. Total treatment time from imaging to end of treatment session was recorded using Aria offline review for Eclipse VMAT plans for every fifth fraction for each patient. Institutional guidelines for VMAT CSI treatment include imaging all isocenters separately using kV/kV orthogonal pairs, shifting and adjusting positioning to obtain an accurate match for each isocenter position. CBCT is used for the first fraction and every 5th fraction or if alignment is problematic. After the imaging and adjustments, each isocenter position is confirmed with planar MV port added to the arc to confirm the accuracy of the shifts.

RESULTS

RefleXion X1 plans were successfully created for all 5 pediatric medulloblastoma patients. Figures 1 illustrates a comparison between axial, sagittal, and coronal dose distributions between an Eclipse VMAT plan and a RefleXion X1 plan.

Table 1 displays the summary of the average dosimetric indices and parameters achieved for VMAT and X1 plans. The dose to 2% of PTV (PTV D2%) was reported as 39.2 Gy for VMAT plans and 41.3 Gy for X1 plans. This difference was not found to be statistically significant ($p=0.08$). The OAR doses were comparable between the RefleXion X1 and Eclipse VMAT plans. Statistical significance was detected only for the difference in Dmean to the bowel bag, with RefleXion X1 plans reporting a lower average Dmean compared to Eclipse VMAT of 1.4 Gy ($p=0.04$).

The average beam-on time for Eclipse VMAT and RefleXion X1 plans were 3.6 min and 16.7 min, respectively ($p<0.01$). The average total treatment time from imaging to the end of treatment completion was also calculated for Eclipse VMAT as 29.2 min (range 16.3 – 43.5 min). No average total treatment time was acquired for RefleXion X1 because no treatment was delivered using this technology.

DISCUSSION

To our knowledge, this is the first treatment planning study of craniospinal irradiation using the RefleXion X1 system. We have previously reported on treatment planning comparison between RefleXion X1 and Eclipse VMAT for 42 patients across 6 cancer sites [25]. In this study, we tested the feasibility of CSI using RefleXion X1. We have successfully generated clinically acceptable RefleXion CSI plans for 5 pediatric medulloblastoma patients with target length less than 50 cm. Dosimetric indices were comparable between RefleXion X1 and Eclipse VMAT modalities except for statistically significantly improved bowel sparing with RefleXion X1.

Due to 2 cm field size and long PTV CSI targets, the average beam-on time was approximately 4.5 times greater using RefleXion X1 compared to Eclipse VMAT. For VMAT CSI delivery using 2-isocenter plans and treated on Varian C-arm linear accelerator, treatment times for the first fraction from start of pre-treatment imaging to the end of treatment session had a wide range of 16.3 – 43.5 min (mean, 29.2 min) signifying existing challenges in imaging and aligning each isocenter separately. RefleXion X1 has a capability of overcoming this challenge with imaging a long extent of the patient (up to 90 cm), localizing, and delivering the whole treatment using 1 isocenter in axial mode moving the couch in the cranio-caudal direction with 2.1 mm increments. This may potentially reduce beam matching and shifting errors which may arise from multi-isocenter delivery. In addition, X1 was recently upgraded to enable 1000 MU/min dose rate from the initial dose rate of 850 MU/min. This upgrade promises to improve the beam-on time but needs to be validated.

While there are currently no studies comparing RefleXion CSI and VMAT CSI, literature discussing Tomotherapy^{TM} delivering the treatment using 2.5 cm jaws in helical fashion may be useful as a comparison due to its similar delivery approach to X1. A study in 2019 by Sun et al. [26] comparing VMAT, IMRT, and Tomotherapy plans found that the Tomotherapy plans offered superior PTV homogeneity, conformity, and brainstem, optic chiasm, and optic nerve sparing compared to VMAT plans. IMRT was superior to VMAT and Tomotherapy in terms of OAR sparing in the mid body region (esophagus and heart). Results of this study by Sun et al. differed from the results of the current RFX study, which found difference in Dmean to the bowel bag as the only statistically significant dosimetric parameter. However, just as the average beam-on time for RFX plans were estimated to be longer than average beam-on time for VMAT plans in our study, delivery time of HT was found to be longer than the delivery time of VMAT for Sun et al.

Another study by Herdian et al. [27] found that differences in oral cavity Dmean, kidneys Dmean, and mean D2% to the spinal PTV were statistically significant between IMRT and Tomotherapy plans. Differences in oral cavity Dmean, kidneys Dmean, mean D2% to the cranial PTV, and mean D2% to the spinal PTV were also statistically significant between 3D-CRT plans and HT plans. Additionally, Tomotherapy plans resulted in longer mean beam-on time than both IMRT and 3D-CRT [27].

One limitation of this study is the small sample size (n=5) due to the maximum target length threshold of 50 cm. The vendor is planning to upgrade the system to enable treating targets greater than 50 cm in their next clinical release. This will enable us to expand the patient selection. Another limitation is that this study only focuses on comparison between VMAT and RefleXion X1 plans. It would be interesting to include Tomotherapy plans in the testing cohort. Based on our communication with the vendor, RefleXion Medical Inc will lift the maximum target length limit in the future software releases of X1 treatment planning system. This will enable us to include larger target sizes in the investigation and collect and analyze the treatment delivery times. This work shows the feasibility of CSI planning using RefleXion X1 paving the way to potentially use RefleXion X1 for CSI treatments. There is a potential benefit of single-isocenter treatment with near-diagnostic image-quality kVCT guidance enabling long scanning length of 90 cm. This can simplify the IGRT workflow and streamline the treatment delivery for CSI patients, especially important for pediatric patients treated under anesthesia.

CONCLUSION

Based on our limited dataset, we were able to demonstrate the feasibility of CSI treatment planning for RefleXion X1. The successfully generated RefleXion plans resulted in comparable dosimetric indices between

RefleXion X1 and Eclipse VMAT plans, as no statistically significant differences were detected in the PTV near maximum dose or average Dmean to critical structures except the bowel bag. Despite having longer average beam-on time than VMAT plans, RefleXion X1 utilizes a moving couch to allow for single-isocenter technique by encompassing the entire volume in one scan, potentially reducing translational and dosimetric match errors associated with multi-isocenter setups using C-arm linear accelerators.

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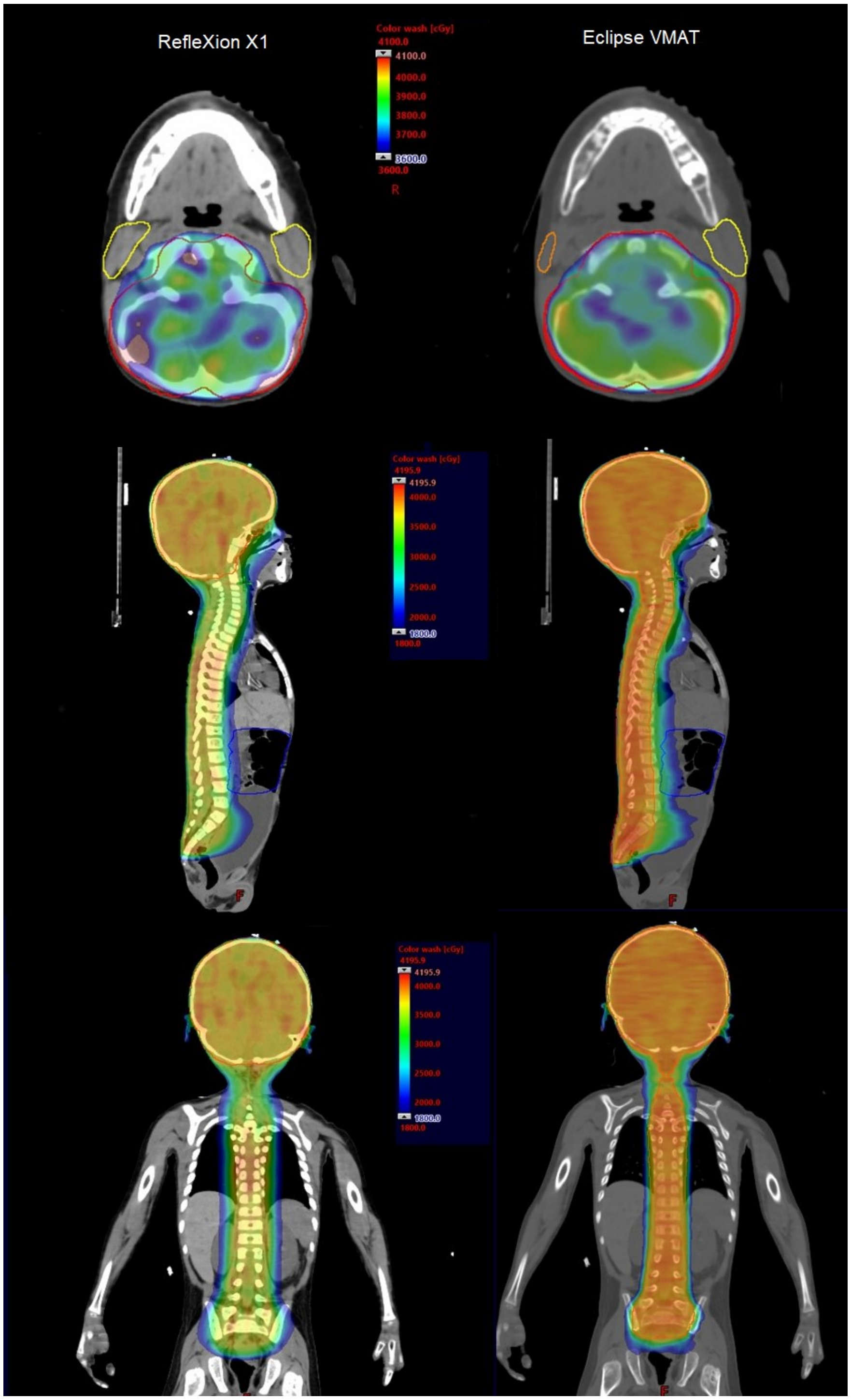

Fig. 1. Comparison of axial dose distributions between RefleXion X1 CSI plan (top) and Eclipse VMAT CSI plan (bottom). Minimum colorwash dose threshold of 3600 cGy (axial) indicating 100% of prescription dose and 1800 cGy (sagittal and coronal) indicating the 50% of prescription was used.

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