Tanzania Journal of Science 49(1): 108-115, 2023
ISSN 0856-1761, e-ISSN 2507-7961

Dosimetric Comparison Between Two and Six Beams Conformal Radiotherapy Plans for Paediatric Wilm's Tumour Patients at Ocean Road Cancer Institute, Tanzania

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Received 10 Nov 2022, Revised 9 Feb 2023, Accepted 17 Feb 2023 Published Mar 2023

DOI: https://dx.doi.org/10.4314/tjs.v49i1.10

Abstract

This study aimed to compare the dose distributions of three-dimensional conformal treatment planning using two and six radiation beams among paediatric patients receiving radiotherapy for Wilms tumour at Ocean Road Cancer Institute. CT scans of 53 patients were used to generate 106 treatment plans, 53 plans for two beams, and 53 plans for six beams. Planning target volumes and organs at risk parameters were compared between both plans using paired samples t-test. A *p-value* < 0.05 was considered statistically significant. The findings showed that the $D_{95\%}$ and D_{mean} of the target are better with six beams than with the two-beam plans *($p < 0.001$).* The conformity index and monitor unit are significantly better with two-beam plans than with six-beam plans *($p < 0.001$).* No volume of the contralateral kidney received more than 12 Gy for both two and six plans. There were no differences in D_{max} for the spinal cord *($p = 0.208$),* while D_{mean} was observed to be lower in two compared to six beams *($p < 0.001$)* for the liver. Six beam plans have good target coverage, while two beam plans have good conformity index and monitor unit. The observed doses to the organs at risk in both plans were lower than their normal tolerance.

Keywords: Wilm's tumour, Three-dimensional conformal radiotherapy, whole abdomen radiotherapy, paediatric radiotherapy, Dosimetry.

Introduction

Childhood cancers constitute about 1% of all cancers and contribute significantly to disease-related deaths in children (Bhutani et al. 2021). The incidence of childhood cancers in most populations globally has been increasing since the 1980s in children aged 0–14 years (Steliarova-Foucher et al. 2017). However, there is no global estimate of incidence, survival and mortality for children with cancer in most lower and middle-income countries (LMICs) (Bhakta et al. 2019). Wilm's tumour (WT) also known as nephroblastoma is the most common cancer in childhood (Bahoush and Saeedi 2020). WT is ranked second among frequently diagnosed childhood cancers in Tanzania (Nyagabona et al. 2020).

Radiotherapy (RT) plays an essential role in the management of WT. Whole abdomen radiotherapy (WART) is usually done using different RT techniques. At Ocean Road Cancer Institute (ORCI), three-dimensional conformal radiotherapy (3D CRT) with an opposed antero-posterior and posterior-anterior (AP/PA) beams are usually used to treat WT. This technique has limitations of poor coverage of the target area as well as higher doses of the organs at risk (OAR) (Paulino et al. 2000, Breslow et al. 2006).

A dosimetric comparison between AP/PA and multiple beams 3D CRT for WART reveals that the use of multiple beams 3D CRT has better target coverage and OAR sparing than AP/PA technique radiotherapy plans (Morganti et al. 2013). It has been reported that there is a 60% clinical benefit to the OAR when using multiple fields in comparison with AP/PA (Mul et al. 2021). However, other studies have found no difference in OAR sparing between two and multiple field plans, although the multiple fields were superior to AP/PA in tumour coverage (El-Hossiny et al. 2009, Morganti et al. 2013).

During WART for WT, the contralateral kidney is the most important critical organ which needs to be protected from a higher dose of radiation. WART also needs to deliver good dose coverage to the planning target volume (PTV). Studies have shown that the use of an AP/PA radiotherapy plan typically results in high toxicity to the OAR (Jereb et al. 1994, Paulino et al. 2000, Breslow et al. 2006).

There is an opportunity to use multiple fields of planning using existing equipment and software; these are CT simulation, linear accelerator machine and eclipse for radiotherapy planning, although this would require more time for planning. However, the difference between the dosimetric parameters of the two planning techniques (AP/PA vs multiple beams) has not been evaluated in our settings. Hence, there is a need to evaluate the doses to the target and OAR between these plans and take measures to reduce the probability of these disadvantages of AP/PA 3D CRT. The use of a larger number of fields can potentially improve both target coverage and OAR sparing during treatment planning thereby improving treatment outcomes.

Materials and Methods

Contoured 3D images of all patients who were planned for WART between Jan 2021 to December 2021 were used to create a pair of conformal radiotherapy plans including two beams AP/PA and six beams (Antero-Posterior, Posterior-Anterior, Left Anterior Oblique, Left Posterior Oblique, Right Anterior Oblique and Right Posterior Oblique) using Eclipse treatment planning system (version 15.5.11, Triple A Algorithm, Varian medical systems, Palo Alto, USA). The total prescribed dose was 18.0 Gy in 12 fractions for all patients. All patients were immobilized with a thermoplastic mask around the abdomen while lying in supine with both arms extended above the head and underwent contrasted computed tomography (CT) simulation with three reference points placed on the sagittal and right lateral and left lateral of the patients using a dedicated CT simulator (Siemen healthiness, Gmbh, Germany). The 3 mm CT cuts were taken and the dataset was transferred to the treatment planning system.

Target volume and organ at risk delineation

After the CT simulation of the patients who were included in the study, images in digital imaging and communication in medicine (DICOM) format were transferred to the eclipse (Varian medical system Palo Alto CA, USA) treatment planning system for dose planning (Serarslan et al. 2017, Aras et al. 2019). All the WT patients in this study received post-surgery radiotherapy after undergoing a nephrectomy to remove the affected kidney and therefore the gross tumour volume (GTV) was not included for contouring. The clinical tumour volume (CTV) corresponded to the entire abdominal cavity from the dome of the diaphragm to the pelvic floor, and then the 0.5 mm margin was applied to the CTV to define the planning target volume (PTV) following Sheltered Instruction Observation Protocol (SIOP) (Van Den Heuvel-Eibrink et al. 2017). The contralateral kidney, spinal cord and liver were contoured following the Radiation Oncology Group (RTOG) guidelines (Mul et al. 2021). All the contouring was done by attending radiation oncologist.

Treatment planning and dose definition

Two different treatment plans for WT patients were performed in this study. The 6 MV photon beams were used to create two fields AP/PA at gantry angles of 0° and 180°, respectively as well as six beam plans at gantry angles of 0°, 60°, 120°, 180°, 240°, and 300°. The PTV was planned to receive a total dose of 18.0 Gy in 12 fractions (1.5 Gy/ fraction). The planning goal for both types of plans was 100% volume of the PTV to be covered by a 95% isodose line and OAR constraints were specified using Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC). Dose-volume histograms (DVH) were generated and used to extract target and OAR parameters.

The conformity index (CI) was defined as CI = TV/PTV where the treatment volume (TV) is the treated volume covered by 95% isodose and the PTV is the corresponding PTV following the International Commission on Radiation Unity and Measurement (ICRU) report 50. The calculated values range between 0 and 1, where a value close to 1 indicates higher dose conformity to the target. The homogeneity index (HI) was defined as

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}}$$

where D_2%, D_{98}% and D_{50}% are defined as dose taken 2%, 98% and 50% of total volume. The value should be < 15 for an acceptable plan. A lower HI closer to one means more homogeneity in dose distribution (Rastogi et al. 2018, Ige and Adewole 2020). All patients were eventually treated following departmental protocol (AP/PA) using a vital beam linear accelerator (LINAC) machine installed in late 2017, using a beam energy of 6 MV while the patient lying in supine and immobilized with a thermoplastic shell.

Statistical analysis

The maximum dose, minimum dose and mean dose, $D_{95\%}$, CI, and HI in the PTV were extracted from the DVH. OAR parameters include contralateral kidney V_{12}, maximum dose (D_{max}), minimum dose (D_{min}), the mean dose (D_{mean}), spinal cord D_{max} and the liver D_{95}, D_{max}, D_{min} and D_{mean}. The PTV and OAR dosimetric parameters between the two types of plans were statistically analyzed by using paired samples t-test. The Statistical Package for Social Sciences (SPSS version 23) was used for statistical analysis. A *p-value* of < *0.05* was considered to be statistically significant.

Results

Socio-demographic characteristics

Table 1 represents the social demographic and clinical information of Wilm's tumour patients. The patients involved in this study were aged 1–15 years, whereby 64.2% of all the patients were aged 1–5 years. 52.8% of the participants were females, 77.4% were disease stage III and 88.7% of the patients received curative treatment.

Table 1: Socio-demographic characteristics and clinical information (N = 53).

Variable		Frequency	Percentage
Age	1–5	34	64.2
	6–10	15	28.3
	11–15	4	7.5
Sex	Male	25	47.2
	Female	28	52.8
Indication	Curative treatment	47	88.7
	Palliative treatment	6	11.3
Stage of the disease	I	1	1.9
	II	3	5.7
	III	41	77.4
	IV	8	15.0

Treatment planning for planning target volume

Table 2 presents dosimetric parameters for the PTV using two and six beams. The PTV doses at 95% and D_{mean} are higher in six beams than in two beam plans, and this difference is statistically significant (3.80 Gy vs 1.65 Gy, $p < 0.001$; 15.05 Gy vs 14.22 Gy, $p = 0.001$, respectively). The CI is higher and the monitor unit (MU) is lower in two beam plans than with six beam plans (0.71 vs 0.54, $p = 0.004$; 166.47 vs 183.51, $p < 0.001$, respectively). There is no significant difference in D_{max} (19.90 Gy vs 19.83 Gy, $p = 0.898$), D_{min} (0.46 Gy vs 0.59 Gy, $p = 0.069$) and HI (1.05 vs 1.06, $p = 0.627$) between two and six beam plans.

Table 2: Treatment planning evaluation for planning target volume between two plans (two and six beams with 3D CRT radiotherapy plans)

Plan parameters	Two beams (Mean ± SD)	Six beams (Mean ± SD)	*P-value*
D_{95} (Gy)	1.65 ± 1.78	3.80 ± 1.74	*<0.001*
D_{max} (Gy)	19.90 ± 0.95	19.83 ± 2.69	*0.868*
D_{min} (Gy)	0.46 ± 0.64	0.59 ± 0.57	*0.069*
D_{mean} (Gy)	14.22 ± 1.59	15.05 ± 1.81	*0.001*
HI	1.05 ± 0.23	1.06 ± 0.42	*0.627*
CI	0.71 ± 0.79	0.54 ± 0.58	*0.004*
MU	166.47 ± 22.34	183.51 ± 13.25	*<0.001*

Figure 1 shows beam arrangement and the dose colour wash of the same CT slice in three-dimensional conformal between two beams and six beam plans.

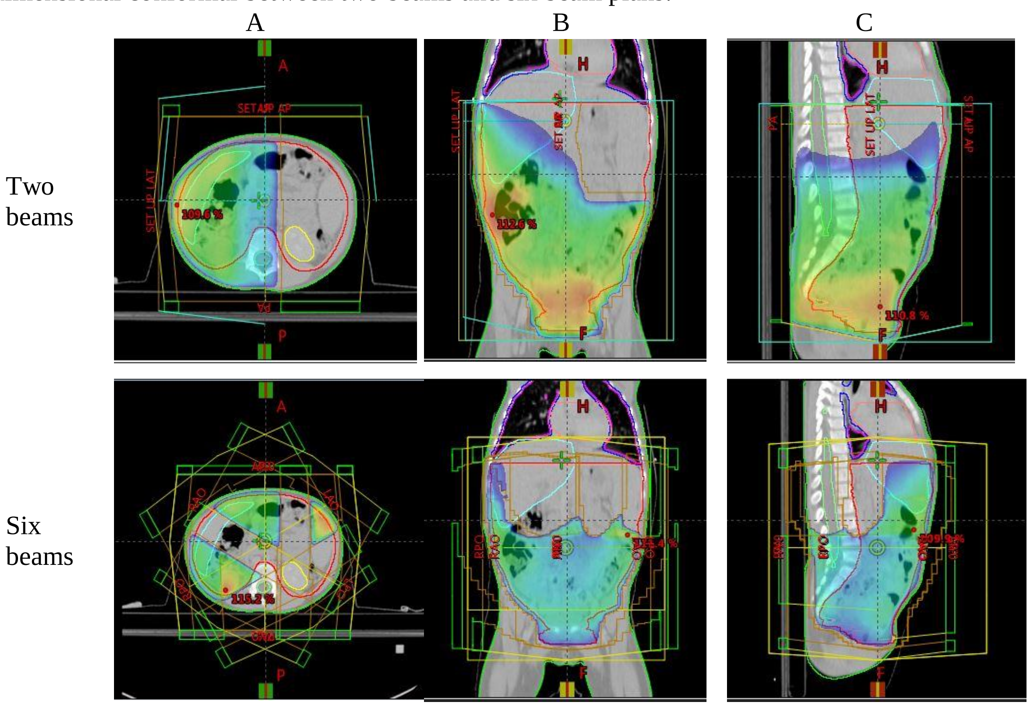

Figure 1: 3D dose distribution obtained for two and six-beams conformal radiotherapy plans. Dose colour wash representative plans for the same patient show dose distribution in three planes including cross-sectional (A), coronal (B) and sagittal (C).

Figure 2 is the DVH of two and six-beam plans.

A

B

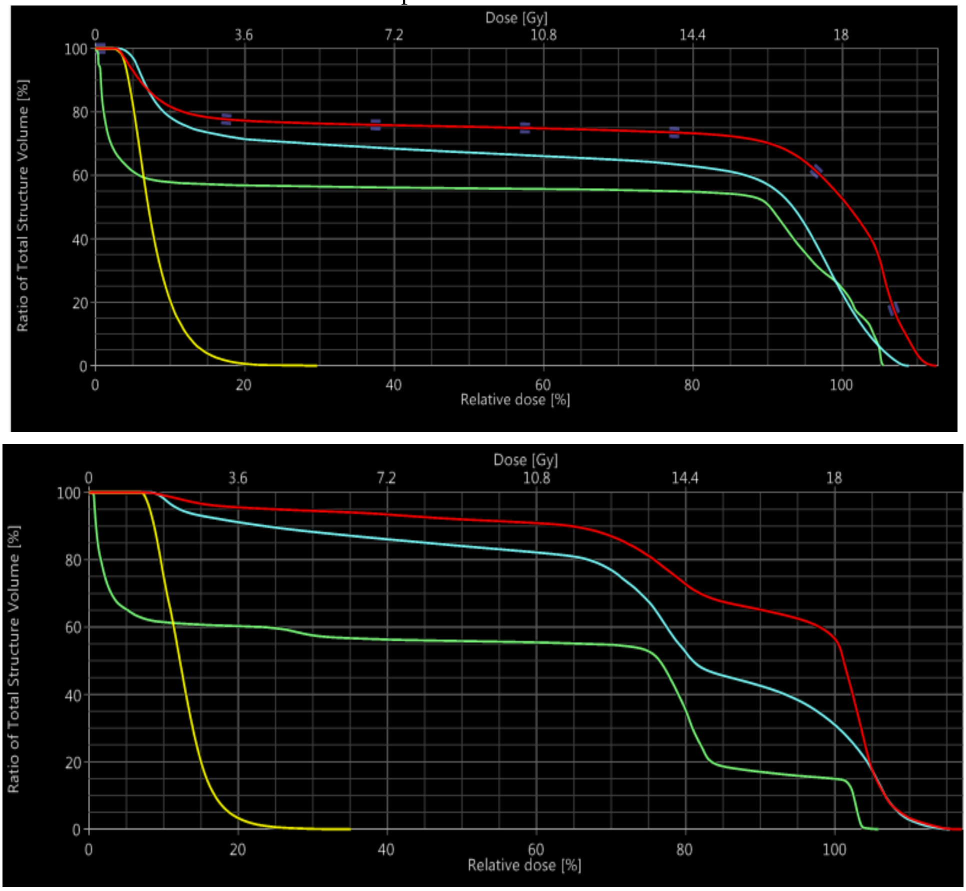

Figure 2: DVH curves for two beams (A) and six beams (B) with different colour lines. Red-PTV, yellow-contralateral kidney, cyan-liver and green-spinal cord.

Treatment planning evaluation for organs at risk

Table 3 shows dosimetric parameter for OAR in both two and six beams radiotherapy plans.

Contralateral kidney: The D_{max} on the contralateral kidney is lower in the two beams than in the six-beam plans (6.46 Gy vs 7.83 Gy, $p < 0.001$). The D_{min} and the D_{mean} have no significant differences between the two and six beams (1.20 Gy vs 1.24 Gy, $p = 0.770$; 2.11 Gy vs 2.08 Gy, $p = 0.899$, respectively).

Spinal cord: The D_{mean} in the spinal cord is lower in the two beams than in the six beam plans (11.64 Gy vs 10.08 Gy, $p < 0.001$). The D_{max} and D_{min} have no significant differences between the two and six beam plans (18.86 Gy vs 18.56 Gy, $p = 0.208$; 0.18 Gy vs 0.20 Gy, $p = 0.167$, respectively).

Liver: All the parameters of the liver; $D_{95\%}$, D_{max}, D_{min} and D_{mean} are significantly lower in two beams than in six beams (3.25 Gy vs 7.33 Gy, $p < 0.001$; 18.99 Gy vs 19.71 Gy, $p = 0.001$; 0.95 Gy vs 3.10 Gy $p < 0.001$; 11.74 Gy vs 14.18 Gy, $p < 0.001$, respectively).

Table 3: Treatment planning evaluation for organs at risk between two and six beams with 3D CRT technique

OAR		Two beams	Six beams	*P-value*
		Mean ± SD	Mean ± SD	
Contralateral Kidney	D_{max} (Gy)	6.46 ± 2.02	7.83 ± 1.99	*<0.001*
	D_{min} (Gy)	1.20 ± 1.13	1.24 ± 0.18	*0.770*
	D_{mean} (Gy)	2.11 ± 1.56	2.08 ± 0.36	*0.899*
Spinal cord	D_{max} (Gy)	18.86 ± 0.99	18.56 ± 1.38	*0.208*
	D_{min} (Gy)	0.18 ± 0.33	0.20 ± 0.40	*0.167*
	D_{mean} (Gy)	11.64 ± 2.90	10.08 ± 2.15	*<0.001*
Liver	D_{95} (Gy)	3.25 ± 4.87	7.33 ± 4.78	*<0.001*
	D_{max} (Gy)	18.99 ± 1.61	19.71 ± 1.37	*0.001*
	D_{min} (Gy)	0.95 ± 0.60	3.10 ± 3.27	*<0.001*
	D_{mean} (Gy	11.74 ± 4.53	14.18 ± 2.06	*<0.001*

Discussion

Several studies have demonstrated the benefits of using 3D CRT with multiple fields in radiotherapy plans when compared to 3D CRT with AP/PA radiotherapy plans (El-Hossiny et al. 2009, Morganti et al. 2013). In this study, the volume of the PTV which intended to receive a 95% of the prescribed dose, minimum and mean doses were significantly better in the six beam plans compared to the two beam plans. These findings are similar to the study done by Leong et al. (2005) which shows that the conformal technique provides better coverage on the PTV with 99% of the PTV receiving 95% of the prescribed dose when compared with 93% when using the AP/PA technique. Furthermore, the percentage of PTV receiving 98% of the prescribed dose is 95% for the conformal technique and 71% for the AP/PA technique. However, other target dose parameters including the maximum dose, HI, CI and MU were better in the two beams plans compared to the six beams plans. The mean values of MUs were observed to be higher in six-beam plans when compared to the two-beam plans, the increased number of MU results in a larger total body dose due to more radiation fields, hence will increase the risk of other malignancies (Hall 2009). The higher MUs in six field plans could have negative implications on the risks of secondary malignancies, especially in children who will live long enough after their disease has been cured (Breslow et al. 2010, Leslie et al. 2022).

In children receiving WART for Wilm's tumour, sparing the contralateral kidney is of high priority to preserve renal function because they have only one kidney. In this study, the maximum dose to the contralateral kidney was lower in the two beams plans compared to the six beams plans, while the mean dose is higher in the two beams than in the six beams plans. However, in both types of the plans in this study, the volume of the contralateral kidney receiving more than 12 Gy was 0% and hence the dose to the contralateral kidney did not exceed the dose tolerance in both plans. Therefore, statistically significant differences observed in the maximum dose to the contralateral kidney between the two types of plans do not predict clinically significant differences in rates of renal complications. These findings are echoed in another study that compared AP/PA and multiple fields in operable stomach cancer which found that both radiotherapy plans doses were within the range of normal tissue tolerance although the multiple fields were statistically significantly superior to AP/PA fields (El-Hossiny et al. 2009).

Another important organ to consider is the spinal cord whereby statistically significant differences were found in the mean dose (11.64 Gy vs 10.08 Gy, $p < 0.001$) between two and six beams. There were no differences between the maximum and minimum doses between two and six beams (18.86 Gy vs 18.56 Gy, $p = 0.208$; 0.18 Gy vs 0.20 Gy, $p = 0.167$, respectively). Based on these findings, there are no clinical implications to the spinal cord because the doses were below tolerance (D_{max} < 50 Gy) as supported by Milano et al. (2007).

In this study, the D95%, maximum, minimum and mean doses to the liver were found to be significantly higher in six beams plans compared to two beams plans. This implies that the two beams' plans offer better liver protection than the six beams' plans. These results are similar to the findings of a previous study that found a significantly higher dose in the liver in the multiple beams compared to the two beams plans (Leong et al. 2005). However, regardless of the observed statistical differences between the two types of plans, both types of plans were within the QUANTEC constraints (Hessels et al. 2022). Therefore, no clinically significant differences in the probability of liver toxicity between the two types of plans.

Conclusion

The use of six beam plans in WART for WT improves the isodose line covering 95% of the prescribed dose to the PTV. However, the two beam plans have a better conformity index and monitor unit. The use of two beams has lower doses to the kidney and liver as compared to six beam plans. Nevertheless, the observed doses in both the two and six-beam plans were lower than the normal tolerance of the respective OAR. Therefore, both plans can be used for WART for WT, however, we suggest the continued use of the two-beam plan (AP/PA) since it saves time in planning.

Acknowledgement

The authors thank Dr Khamza Maunda and Dr Sikudhani Muya for their assistance, and also we thank the management of Ocean Road Cancer Institute for allowing us to use its facility to accomplish this study.

Ethical Committee Approval

The ethical clearance was obtained from the Institutional Review Board (IRB) of the Muhimbili University of Health and Allied Sciences (MUHAS). Permission to collect data was obtained from the Ethics and Research Committee of Ocean Road Cancer Institute.

Informed Consent: N/A

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declare that this study received no financial support.

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