

Deviation From Delivery Of Radiation Therapy To Childhood Cancer Patients: A Retrospective Audit

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Abstract

Background The delivery of Radiation therapy (RT) needs a level of coordination and planning which can be challenging in resource-limited settings. In this retrospective study we describe the profile of children undergoing radiation and analyze deviation from accepted norms. **Procedure** Data on all children (< 18 years age) with cancer who completed RT from Jan 2009 to Dec 2019 were retrieved. Diagnostic groups with more than 5 patients, were included in the analysis for deviations in RT (Time to start (TTS); total dose delivered (TDD) in Grays; and time to complete (TTC)). We investigated reasons for deviation. **Results** 207 received RT as front-line treatment (68% Indian, 59% male and 32% received treatment preceding RT outside). Most common diagnosis were brain tumors (44%), lymphoma (13%). leukemia and soft tissue sarcoma (10% each). 23.6% had deviation in TTS, 6.0% in TDD and 24.7% in TTC while 43.4% had at least one deviation in any of these three parameters. Deviation in TTS varied significantly by location of preceding treatment and by cancer (greatest deviation in sarcomas) with issues around access to healthcare the most common reason. Deviation in TTC varied significantly by cancer (greatest deviation in sarcomas and medulloblastoma) with myelotoxicity the most common reason. **Conclusions** Our study adds to the limited literature on RT quality for children with cancer in LMIC. Certain cancers (sarcomas and medulloblastoma) and patient groups (preceding treatment outside our institute) had the maximum deviation. Barriers to accessing care and myelotoxicity were the two main reasons for this deviation.

TITLE PAGE

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Deviation From Delivery Of Radiation Therapy To Childhood Cancer Patients: A Retrospective Audit

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Abbreviations

RT	Radiotherapy
TTS	Time to start
TDD	Total dose delivered
TTC	Time to complete
LMIC	Low and middle-income countries
ICCC	International Childhood Cancer Classification

Background

The delivery of Radiation therapy (RT) needs a level of coordination and planning which can be challenging in resource-limited settings. In this retrospective study we describe the profile of children undergoing radiation and analyze deviation from accepted norms.

Procedure

Data on all children (< 18 years age) with cancer who completed RT from Jan 2009 to Dec 2019 were retrieved. Diagnostic groups with more than 5 patients, were included in the analysis for deviations in RT (Time to start (TTS); total dose delivered (TDD) in Grays; and time to complete (TTC)). We investigated reasons for deviation.

Results

207 received RT as front-line treatment (68% Indian, 59% male and 32% received treatment preceding RT outside). Most common diagnosis were brain tumors (44%), lymphoma (13%). leukemia and soft tissue sarcoma (10% each). 23.6% had deviation in TTS, 6.0% in TDD and 24.7% in TTC while 43.4% had at least one deviation in any of these three parameters. Deviation in TTS varied significantly by location of preceding treatment and by cancer (greatest deviation in sarcomas) with issues around access to healthcare the most common reason. Deviation in TTC varied significantly by cancer (greatest deviation in sarcomas and medulloblastoma) with myelotoxicity the most common reason.

Conclusions

Our study adds to the limited literature on RT quality for children with cancer in LMIC. Certain cancers (sarcomas and medulloblastoma) and patient groups (preceding treatment outside our institute) had the maximum deviation. Barriers to accessing care and myelotoxicity were the two main reasons for this deviation. **Introduction**

The role and need for radiation therapy (RT) of childhood cancer treatment is well established.(1) Despite declining trends of use over time,(2) it remains a critical part of multimodality treatment for several childhood cancers.(1) Modern treatment protocols are complex and multidisciplinary and often prescribe in detail the indication, the timing, the field and the dose of RT with additional guidance on managing toxicity.

The delivery of RT thus needs a level of coordination and planning which can be challenging in resource-limited settings.(3) This is because globally access to RT is not uniform and there are deficiencies in availability of RT machines, trained staff, as well as aspects of quality like input of interdisciplinary RT teams, treatment planning protocols, and quality assurance.(3,4) This is an under-researched area in low and middle-income countries (LMIC) including India where most of the childhood cancer cases occur.

In this retrospective study we audit the profile of children undergoing RT at our centre and analyze deviation from accepted norms during their treatment. This information will provide us guidance on how to further improve the delivery of our RT services.

Methods

This audit was conducted at three units of Max Institute of Cancer Care (MICC) Saket, Patparganj and Vaishali which are all healthcare establishments in the private sector located in Delhi National Capital Region. RT in these units was delivered on the Linac accelerator by different techniques. Thermoplastic mould and Vac-loc were used as immobilization device for simulation and treatment for each patient. Patients received five fractions of external beam radiotherapy each week. CT based planning for treatment was done for every patient irrespective of the technique. Anaesthesia for immobilisation and radiation delivery for young children was used as per requirement.

Children with cancer (< 18 years of age) treated with RT from 1st January 2009 to 31st December 2019 in these units were identified. Those who received RT in a relapsed/refractory setting were excluded as were those where the RT was given to the metastatic site only (e.g. lung metastasis). Relevant demographic, clinical and RT data was retrieved from RT records, clinical notes and the pediatric hospital based case registry. Patients were categorized as per International Childhood Cancer Classification (ICCC).(5)

From this cohort, we further selected those ICCC categories and sub-categories where there were at least 5 patients to analyze deviation from accepted norms during their treatment. We looked at three specific parameters in these patients: Time to start (TTS) RT calculated as the time interval between date of diagnosis and start of RT; total dose delivered (TDD) in Grays; and time to complete (TTC) RT which is the interval between the first fraction and the last fraction of the scheduled RT.

For the purpose of this audit, we had to create a standard. Two of the authors (RA and RSA) examined recommendations of contemporary national and international protocols as well as a standard textbook of radiation oncology.(6) From this standards on TTS and TDD were created. These were then reviewed by the other two authors (VG and AKA) and finalised (Table 1). Deviation was defined as

- For TTS – If greater than standards in Table 1 unless preceding surgery or chemotherapy was delayed or treatment toxicity occurred which then impacted on TTS.
- For TDD - If dose of radiation was lesser or greater than standards in Table 1.
- For TTC – If the duration of radiation was 5% more than the total number of fractions prescribed with allowance for weekends.

We further examined association deviation with demographic (age, gender, nationality), disease (diagnosis) and treatment (whether preceding treatment was done at MICC or not) variables. Excel sheet was used for data collection and chi square test was applied to see association between variables. P value less than or equal to 0.05 was considered significant. We also examined any reasons for deviation which could be identified through searching of RT records and clinical notes. The analysis was descriptive and results were tabulated for display.

As this was a retrospective audit, patient consent was not required.

Results

A total of 275 children with cancer (< 18 years of age) received RT from 1st January 2009 to 31st December 2019 in the three MICC units. Of these 68 (24.7%) were excluded (RT was given for refractory/relapse disease (n=64), for palliation of metastatic site (n=3) and for lung metastasis (n=1)) and 207 were included (59% male, mean age 9.3 years, 68% from India, 67% received preceding treatment at MICC). The most common ICCC categories were CNS tumours (44%), lymphomas (13%), leukemias and soft tissue sarcomas (10% each), bone sarcomas (8%) and all others (15%).

Of the 207 included patients, 182 were examined for deviation of TTS, TDD and TTC as they belonged to the 13 diagnoses in which there were more than five patients (table 2 and table 3). The mean TTS, TTD and TTC are displayed in table 2. 43 children (23.6%) had deviation in TTS, 11 (6.0%) in TDD and 45 (24.7%) in TTC while 79 children (43.4%) had at least one deviation in any of these three parameters. Deviation from these and their association with age, gender, nationality, type of cancer and preceding treatment are displayed in Table 3. Type of cancer was significantly associated with deviation in all three parameters. TTS deviations were greatest in Ewing sarcoma and nonrhabdomyosarcoma soft tissue sarcoma, and renal tumours; TDD deviations were greatest in brain stem gliomas; and TTC deviations were greatest in nonrhabdomyosarcoma soft tissue sarcoma, medulloblastoma and primitive neuroectodermal tumour, and Ewing sarcoma. In addition location of preceding treatment and nationality were also significantly associated with deviation of TTS.

Table 4 lists the reasons attributed to these deviations. TTS was mostly impacted by issues around accessing care like preceding treatment outside our centres, logistical challenges of finance or approval for treatment, and travelling home or for second opinion. No specific reason was identified for TDD deviations. Myelotoxicity was the most common reason for deviations in TTC but we could not establish the reason in a third of the patients.

Discussion

Quality assurance is integral to modern day delivery of RT and focusses on metrics related to processes, logistics and timing. RT protocol compliance is one aspect of quality assurance and adult and paediatric studies have confirmed that RT protocol deviation leads to increased treatment failure (7,8). There is no accepted universal definition of deviations and this varies by cancer and protocol but would generally include one or more of the following; dose, volume, field, timing of start and overall treatment time (7,8).

In our audit of children with cancer who received RT at our institute we found that approximately one in two children had a deviation in one parameter with one in four children having deviation in TTS and TTC but only one in 17 having deviation in TDD. A recent study from the Dominican Republic with a relatively smaller sample size (19 children with Wilms tumour, rhabdomyosarcoma, retinoblastoma and nasopharyngeal carcinoma) is the only other study from LMIC which has previously studied this and found that 95% of children had at least one deviation (they also examined an additional parameter of field) with greatest deviation in TTC 79% followed by TTS 53% and finally TDD 42%.(9)

These findings are concerning because the published literature provides evidence to the importance of these parameters. Delay in starting RT impacts outcome of children with Ewing sarcoma(10-12), Wilms tumour(13) and medulloblastoma(14) and excess time taken to complete RT has an adverse impact on children with medulloblastoma.(15) Similarly dose deviations have had an adverse impact in children with rhabdomyosarcoma(16), medulloblastoma(17) and Ewing sarcoma.(18) A limitation of our study is that we did not have follow-up for each patient to determine if deviations had an impact on outcomes but it would not be incorrect to assume some detrimental impact.

Factors associated with deviations may be demographic, disease or treatment related. We found the greatest deviations in TTS in sarcomas in comparison to leukemia, lymphoma and CNS tumours. This may be due to involvement of both, surgery and chemotherapy as modalities before radiation and toxicities related to these modalities. In carcinoma nasopharynx and brainstem glioma, in which radiation was primary mode of

treatment, treatment was started within days of diagnosis.

Additionally, healthcare related factors, which may be specific to our institution as well as the wider context of healthcare delivery in the country, may impact these deviations. 31% of the children who received RT had their preceding treatment (surgery and/or chemotherapy) outside our institute and their deviation in TTS was double of those who had preceding treatment at our institute. This highlights the lack of access to RT and the need to move to different locations, compromising delivery of quality care. Once RT commenced at our institute, preceding treatment ceased to be a significant factor in deviation of TTC as our infrastructure is geared to deliver uninterrupted treatment if the child remains well.

Similarly deviations in TDD were only around 6% and less likely to be impacted by any of the factors mentioned above. Although most of our patients are not on prospective clinical studies, we do use national and international recommendations and protocols to deliver the correct doses. Our data does show that there was TDD deviation in brainstem gliomas which received a mean dose of 52.6 Gray against a recommended dose of 54 to 60 Gray. We are now putting in guidelines to correct this.

We did see significant association of cancer type with TTC with the high degree of deviation seen in medulloblastoma where craniospinal irradiation (CSI) would lead to myelotoxicity. This challenge has also been highlighted in another publication from India where 73% of patients had interruptions in CSI.(19) In contrast experience from USA suggests that interruptions even in this group of patients can be as low as 2.5%.(20) We plan to review our practice of CSI including thresholds for interrupting RT and use of growth factors to address this.

In conclusion, our study adds to the limited literature on RT quality for children with cancer in LMIC. It highlights that one in four children have deviation in TTS and TTC RT and provides us areas to improve within our practice. Our work is limited by the fact that we did not examine the parameter of volume or field. Also our study is retrospective and dependent on the quality of record keeping and so we cannot comment on the individual circumstances which may have led to the deviation (e.g. site and stage of tumour, treatment intensity, etc.).

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Conflict of Interest statement

All the authors have no conflict of interest to declare

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Legends

Table 1 Radiation Reference Doses and Timing for Childhood Cancers

Table 2 Mean time to start radiation, dose of radiation and time to complete radiation by type of cancer

Table 3 Association of deviation of mean time to start radiation, dose of radiation and time to complete radiation with different variables

Table 4 Reasons attributed to deviation of time to start radiation, dose of radiation and time to complete radiation

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Table 1 Radiation Reference Doses and Timing for Childhood Cancers.pdf available at <https://authorea.com/users/407426/articles/517741-deviation-from-delivery-of-radiation-therapy-to-childhood-cancer-patients-a-retrospective-audit>

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Table 2 Mean time to start radiation.pdf available at <https://authorea.com/users/407426/articles/517741-deviation-from-delivery-of-radiation-therapy-to-childhood-cancer-patients-a-retrospective-audit>

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Table 3 Association of deviation of mean time to start radiation.pdf available at <https://authorea.com/users/407426/articles/517741-deviation-from-delivery-of-radiation-therapy-to-childhood-cancer-patients-a-retrospective-audit>

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