

Field in Field Technique (FIF) Technique With Intra-fractionally Modulated Junction Shifts for Cranio-spinal Irradiation (FSI) Planning With 3D-CRT.

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Abstract

Background

To plan craniospinal irradiation (CSI) with “field-in-field” (FIF) homogenization technique in combination with daily, intra-fractional modulation of the field junctions, to minimize the possibility of spinal cord overdose. Photon-based techniques for CSI may result in dose inhomogeneity within the treatment volume and usually require a weekly manual shift of the field junctions to minimize the possibility of spinal cord overdose. Nowadays FIF technique is used to feather out the dose inhomogeneity caused by multiple fields. We have started using this technique after acquiring advanced technology machines in recent years.

Methods and Materials:

16 patients treated with 3D-CRT for CSI were retrospectively chosen for analysis. These patients were treated during 2016–2017. Contouring of PTV and OAR were done and planning done on Eclipse™ TPS (Varian). These patients were planned with Lateral cranio-cervical fields and posterior spinal fields using a forward-planned, FIF technique. Field junctions were automatically modulated and custom-weighted for maximal homogeneity within each treatment fraction. Dose volume histogram (DVH) was used for analysis of results. A corresponding plan without FIF technique was planned and maximum dose at the junction was noted for each patient with both plans and the readings were evaluated.

Results

Plan inhomogeneity improved with FIF technique. It provided consistent dose delivery during each fraction of treatment across the junctions. The maximum doses calculated at the junction were higher in the CSI plans without FIF compared to those with FIF technique.

Conclusion

This paper hence proves that FIF technique is better in planning CSI.

Background

Medulloblastoma is the most common malignant neoplasm of the central nervous system in children, constituting approximately 20% of all paediatric brain tumors. [1] Recently tremendous advances in technology and biology have been witnessed, resulting in an improved outcome for these children owing to refinements in micro-neurosurgery, more effective chemotherapy regimens and modern radiotherapy techniques. [2] The current standard of care for these patients consists of maximal safe resection

followed by radiation and chemotherapy, yielding a 5-year survival rate of > 80% for average-risk medulloblastoma and > 50% for high-risk disease. [3]

Radiotherapy for medulloblastoma and other central nervous system (CNS) neoplasms that are prone to cerebrospinal fluid dissemination, like ependymoma, intracranial germinoma (ICG) and primitive neuroectodermal tumor (PNET) entails irradiation of the entire neuraxis, i.e. craniospinal irradiation (CSI) with a homogeneous dose. Neuraxis includes those areas drained by Cerebrospinal fluid, that is the Brain and the spinal cord upto the level of the thecal sac. Planning CSI still remains one of the most technically challenging processes in radiotherapy planning and delivery because of the need to irradiate a very large and complex shaped target volume uniformly. [1]

Generally in planning Craniospinal irradiation two laterally opposed cranial fields, are matched to a posterior spine field with the potential for dose inhomogeneity at the junctions. Both the fields are matched either by gap junction method or by rotating couch and collimator ("Exact-match" technique). Elder children and adults frequently require two posterior spine fields, which lead to additional junctions and planning complexity. The classical method of field edge matching is being followed in most of the radiation centers while performing CSI. In this traditional method, the junction between cranium and spine field and between spine fields shall be shifted twice with an extension of 0.5-1 cm upon delivering every 9 Gray (Gy) or 5 fractions. This shifting of the junction is called as feathering technique by which the inferior margin of the cranial field is shortened and the superior and inferior portions of spine field edges is extended.

These techniques for craniospinal irradiation (CSI) may result in dose inhomogeneity within the treatment volume. A new planning methodology was developed in Eclipse™ Treatment Planning system (TPS) recently worldwide. The aim of this planning is to introduce a simple method of field edge matching, thereby easy to achieve the homogeneous dose distribution in the entire PTV for CSI and to reduce the overall treatment duration. Plans were evaluated using Dose Volume Histogram (DVH) and Dose Color wash 3D Dose Distribution. This is called Field-in-field (FIF) technique. To deploy FIF, multiple lower-weighted reduction fields are created on the basis of the primary field. The reduction fields contain blocked segments strategically placed to reduce the highest isodose areas and to force greater homogeneity and conformity to the target volume.

This technique is common in other parts of the globe but has not been in practice in our country commonly but recently we at our institute have begun planning CSI using a multi-segmented, intensity-modulated "field-in-field" (FIF) and automated "junction-shift" techniques. This paper will describe about the cases we have treated using this method and will guide the readers about this better planning technique for CSI.

Material And Methods

As this is a planning study only and there is no direct contact with patients so a waiver was obtained from the ethical review board of the primary institution Ziauddin University Karachi, Pakistan. 16 patients (2 adults and 14 children) treated with 3D-CRT for craniospinal irradiation were retrospectively chosen for this analysis. 14 of these patients were diagnosed cases of medulloblastoma while one patient had Atypical Teratoid Rhabdoid tumor (ATRT) while another had Germ cell Tumor of Brain. These patients were planned and treated during 2016–2017.

• **CT Simulation:**

Planning Computed Tomography (CT) scans of these patients were done with Intravenous contrast on The Siemens™ SOMATOM Definition AS Open CT Simulator. Patients, which included mostly children, were positioned supine with a hyper-extended neck rest so as to avoid divergence of the PA field through the oral cavity. Thermoplastic facemask with extended neckline was used for head immobilization and shoulder retractor was used for retracting the shoulder as low as possible to extend the lateral cranio-cervical fields. Furthermore a leg-separator was used to immobilize the lower body. Some of the younger children needed anesthesia for CT planning and an anesthetist was called for it. Planning CT images of each patient were acquired from the vertex to the coccyx. After performing the CT Simulation with all its requirements, DICOM (Digital Imaging and Communications in Medicine) images with 3mm thickness were transferred to the VARIAN Eclipse™ Treatment Planning System version 13.0.

• **Image Registration, Contouring and Approval:**

Previous (preoperative) diagnostic MRI Brain and spine images of the patients were retrieved from local PACS (Picture Archiving and communication system) system of the institution. These images were registered with the CT Simulation images using the Registration option of the TPS. Target volume delineation was performed in accordance with internationally accepted guidelines. [4] Gross tumor volume (GTV) in this case would only be any postoperative residual area and it will be of help only in the 2nd Phase of Radiation i.e. Posterior fossa Boost. Contouring of the Clinical Target volume (CTV) includes the Brain, meninges and Spinal Cord up to the thecal sac, which ends at S2 vertebrae and includes region of the optic nerve, exiting nerve origins in the base of skull and posterior dorsal nerve roots, which are the areas of CSF drainage. These volumes were drawn with the help of the previous MRI images and consultation with the Radiologist of the institution. The planning target volume (PTV) was generated by growing a uniform volumetric margin of 5 mm in all directions over the corresponding CTVs. OARs outlined included the eyes, heart, lungs, esophagus, liver and kidneys. These contours were first prepared by the Postgraduate residents of Radiation Oncology program, which were then reviewed by the Attending Radiation Oncologist. Later all the volumes were peer-reviewed finally by the whole Radiation Oncology team including the Planners i.e. the dosimetrist and medical physicist for any final change in contours.

• **3D-CRT Planning with FIF Feathering Technique at the Junction:**

Planning was done on VARIAN Eclipse™ Treatment Planning System version 13. All of these patients were planned with lateral cranio-cervical fields and posterior spinal fields using a forward-planned, FIF technique. Another plan was made using non-FIF technique. The cranio-cervical fields used were parallel opposed and asymmetric jaws were used to block the half beam, isocenter was kept at the cervical spine. In addition, multi leaf collimators (MLC) were used to conform the field to the PTV and to shield the critical organs. Half beam was blocked from the isocenter to provide a non-divergent junction with the posterior spine field with couch and collimator rotations.

Matching the upper border of the spine field to the lower border of the cranial field requires strict attention to achieve the accuracy, overlapping of the spinal field to cranium (i.e. overdosing) may lead to catastrophic outcomes for the patient. Uncertainty of dose distribution in this sensitive region is eliminated by adopting half-beam blocked fields and then eliminating the under and over-dosage with feathering techniques.

Field junctions were modulated and custom-weighted for maximal homogeneity within each treatment fraction. At the craniospinal match in the low neck, multileaf collimator leaf adjustments were used at the junction field edges; and these were shifted by successive 1-cm increments during each treatment session. Three approximately weighted control points were used, with two successive 1-cm shifts in each fraction of treatment. More control points were used as needed so as to homogenize the dose distribution across the junction. To assess the predicted coverage in the plan evaluation, thecal sac volumes were contoured with 1-cm margins around the superior and inferior borders of the modulated segments. Plans were optimized and the assigned physicist/dosimetrist evaluated the plan so that it can be practically reproduced on the treatment machine. (Fig. 1)

• Plan Evaluation and Treatment delivery:

Dose volume histogram (DVH) was used for analysis of results. Maximum dose to spinal cord and lens was evaluated to be within tolerance and was observed that maximum dose to spinal cord is less than 44 Gy and lens maximum dose less than 5 Gy. Treatment plans were reviewed by the Radiation Oncologist. As per department protocol, after the primary attending physician, plans were put on a weekly Planning review meeting and were approved by the whole Oncology team including the oncologists and Medical Physicists. Portal dosimetry was also done to assess the actual dose delivered at the modulated junctions. Treatment was then executed in the Varian Trilogy™ machine.

For this study a corresponding plan without FIF technique was planned and maximum dose (in terms of volume of the PTV covering $\geq 100\%$, $\geq 110\%$ and $\geq 120\%$) at the junction was noted for each patient, then mean was calculated by averaging all values and dividing with the total reading in each volume with both plans and the readings were evaluated. (Fig. 2)

Results

- **Improvement in dose conformality and reduced inhomogeneity:**

Field-in-field technique improved conformality of dose to the thecal sac, intra-fractional modulation of doses at the field junction also helped reducing the maximum dose on the thecal sac. Without FIF or modulated junctions, the volume receiving 110% of the prescribed dose ranged from 39–74% (mean: 62.12%) and volume receiving 120% dose ranged from 8–28% (mean: 17.68%). Whereas with FIF and modulated junctions, the thecal sac volume receiving 110% of dose ranged from 2–18% (mean: 11%) and volume receiving 120% ranged from 0–2%. (Table 1)

- **Practical Implementation of modulated junction shifts:**

A single consistent cranial setup point was used throughout the entire radiation course due to which treatment was shortened and simplified and the delivery process was made less prone to manual errors in setup of the junctions. Secondly portal dosimetry confirmed the safety of modulated treatment delivery, with no point in the junction region in the lower spine reaching > 80% of the prescription dose measured in the coronal plane or > 99% measured in the axial plane. Dose was delivered as planned.

Table 1

Dose to thecal sac evaluated with and without FIF technique and modulated junction shifts.

Serial No.	Patient Diagnosis	Volume of Thecal Sac at $\geq 100\%$, $\geq 110\%$, and $\geq 120\%$ of the prescribed dose					
		Without FIF Technique			With FIF Technique		
		$\geq 100\%$	$\geq 110\%$	$\geq 120\%$	$\geq 100\%$	$\geq 110\%$	$\geq 120\%$
1.	Medulloblastoma	99	71	16	98	18	0
2.	Medulloblastoma	99	68	21	99	15	0
3.	Medulloblastoma	98	72	6	99	15	0
4.	Atypical Teratoid Rhabdoid Tumor	99	74	15	97	10	0
5.	Medulloblastoma	97	73	25	99	11	0
6.	Medulloblastoma	99	55	10	97	6	1
7.	Medulloblastoma	98	71	20	99	10	0
8.	Germ Cell Tumor Brain (Germinoma)	99	69	26	97	15	2
9.	Medulloblastoma	99	68	28	99	5	0
10.	Medulloblastoma	98	67	18	98	2	0
11.	Medulloblastoma	97	54	27	99	11	0
12.	Medulloblastoma	98	40	19	98	9	0
13.	Medulloblastoma	99	65	15	99	12	1
14.	Medulloblastoma	97	39	8	97	14	0
15.	Medulloblastoma	98	45	12	96	13	0
16.	Medulloblastoma	99	63	17	99	10	1

Legend: This table shows the dose at the thecal sac with and without FIF technique and it proves that with field-in-field technique and modulated junctions, doses $\geq 110\%$ and $\geq 120\%$ are recorded very much less to the thecal sac as compared to non-FIF technique.

Discussion

Cranio-spinal irradiation (CSI) is a mode treatment in many pediatric and some adult brain tumors. Mostly done in cases of medulloblastoma, other areas where CSI is used include anaplastic Ependymoma, Intracranial germinoma, Primitive Neuro-ectodermal tumor (PNET) and others. Medulloblastoma is the most common type of malignant brain tumor in childhood with an incidence of

18–20% of all brain tumors. [4] As most patients in this study are cases of Medulloblastoma, we need to know about it. For treatment purposes, patients with medulloblastoma are divided into two prognostic groups: children over 3–5 years of age with non-metastatic disease and minimal residual disease (< 1.5 cm²) post-operatively comprise the standard-risk group. Other patients with a sub-total resection, or metastatic disease and younger patients below 3–5 years of age comprise the high-risk group. [5] Irrespective of the risk group, cranio-spinal irradiation (CSI) with or without chemotherapy is the standard of treatment for medulloblastoma. [6] In standard-risk disease (defined as gross totally resected tumor without severe anaplasia, and no metastases), 23.4 Gy to the craniospinal axis, plus a boost to 54 Gy to the posterior fossa, followed by adjuvant chemotherapy, is standard and has resulted in 5-year survival of 80% or better. [7]

Craniospinal irradiation still remains one of the most technically challenging processes in radiotherapy planning and delivery because of the need to irradiate a very large and complex shaped target volume homogeneously. With continuous improvements in long-term survival, particularly in children with average-risk medulloblastoma, there is a growing concern regarding treatment-related long-term side effects. Some of these side effects include neurocognitive decline, hearing impairment, growth retardation, endocrine dysfunction, cataract formation, cardiomyopathy, impaired fertility and second malignancies. [8] Other than the long-term complications, PTV coverage is equally important in terms of high incidences of neuraxial recurrences, which is supported by many studies [9].

Before the advent of CT based radiation treatment planning CSI was done in a very old fashioned way. Patients were set to prone position and 2 plans with different isocenters were used to treat cranium and whole spinal cord. The first plan with right and left lateral beams covered the cranium and the upper cervical vertebrae till the shoulder clearance. Taking the maximum neck area in the lateral fields gives a chance to save the oral cavity and oropharynx in getting treated with high doses of radiation. The second field covers the remainder of the spine with PA projection; the junction of both plans is kept at the neck level where the cold spot towards posterior and hot spot towards anterior side are created due to the divergence of the junction fields. For adults' patients or tall children the posterior spinal field cannot cover the whole remaining spine in a single field due to mechanical limitations of 40 cms and there were two PA fields used, junction of these fields were to be matched and feathered as well. Lead shielding is applied to the cranio-cervical field, blocking the orbits, oral cavity and oropharynx with keeping margins to the target spinal cord area. For feathering gap junction shifting is done i.e. for every 9 Gy or 5 fractions, extend the cranial field superiorly by 1 cm, shift the upper spine field superiorly by 1 cm, and extend the lower spine field by 1 cm.

In the new era of radiotherapy, 2D treatments for CSI has now been minimized even in the developing nations and it has now been replaced with 3D-CRT at least followed by IMRT/VMAT where facilities are available. 3D CRT technique for CSI has been described in detail in the section above but the new variation in 3D CRT that is now being used for feathering in CSI is the filed-in-field technique (FIF) along with intra-fractional modulation. In this variation multiple sub-fields are created of a single field with different weightages and in a single fraction of radiotherapy doses are modulated as these sub-fields

ultimately creates feathered doses at the junctions, in this way setup variation at the junctions was minimized because each junction was self-feathering within each fraction [10]. This technique is also called forward planned IMRT. This variation of 3D CRT technique of CSI increases dose homogeneity in the target volume while decreasing the absorbed dose in the irradiated tissues outside the targeted tissue [11]. Furthermore, pediatric patients do not usually require the addition of many reduction fields because of the relatively uniform depth of the spinal column, but in adults several fields may be required; which can be weighted as much as 10–12% per field in the lower spine. As a forward-planned, step-and-shoot process, the use of FIF does not add substantially to the time and effort required for planning and treatment delivery [10].

Conclusion

This study concluded that the FIF technique used for CSI planning with 3D-CRT proved to be a good method to achieve a near to normal feathering at the junctions with lesser time to treatment in the machine. It is a good alternative to modern methods of radiotherapy like IMRT and VMAT.

Abbreviations

CSI	Cranio-spinal Irradiation
FIF	Field in field technique
3D-CRT	3D conformal radiotherapy
PTV	Planning target volume
OAR	Organ at risk
TPS	Treatment planning system
DVH	Dose volume histogram
CNS	Central nervous system
PNET	Primitive neuro-ectodermal tumor
ATRT	Atypical Teratoid Rhabdoid tumor
CT	Computed Tomography

PA
Postero-anterior
DICOM
Digital imaging and communications in Medicine
MRI
Magnetic resonance imaging
PACS
Picture archiving and communications system
GTV
Gross tumor volume
CTV
Clinical target volume
CSF
Cerebrospinal fluid
MLC
Multi leaf collimator
IMRT
Intensity modulated Radiation therapy
VMAT
Volumetric modulated arc therapy

Declarations

- *Ethics Approval and consent to participate:*

A waiver of informed consent was obtained from Ziauddin University institutional review board for this planning study, as there was no direct human participation and previous CT images was used for research purpose.

- *Consent for Publication:*

Not applicable.

- *Availability of data and materials:*

All relevant data are included in the same article. The data include table of the patient with the relevant data collected from each patients radiation plan.

- *Competing interests:*

The authors declare that they have no competing interests.

- *Funding:*

No funding needed in this radiation planning study.

- Authors contributions:

Dr. SH is the corresponding author and the major contributor towards writing of the manuscript. Dr. AH helped Dr. SH in the manuscript writing and literature review along with collection of data from patients radiation plan. Mr. RG and Ms. HN are the radiation planners (medical physicist and dosimetrist) who planned the corresponding plans with non-FIF technique along with interpretation and collection of results from the radiation plan. Dr. JM is the Radiation Oncologist who was responsible for approving all patients plan and he helped us review the whole manuscript along with doing corrections in the final discussion part of the article. Finally all authors have read and approved the final manuscript before submission.

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Not applicable

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Figures

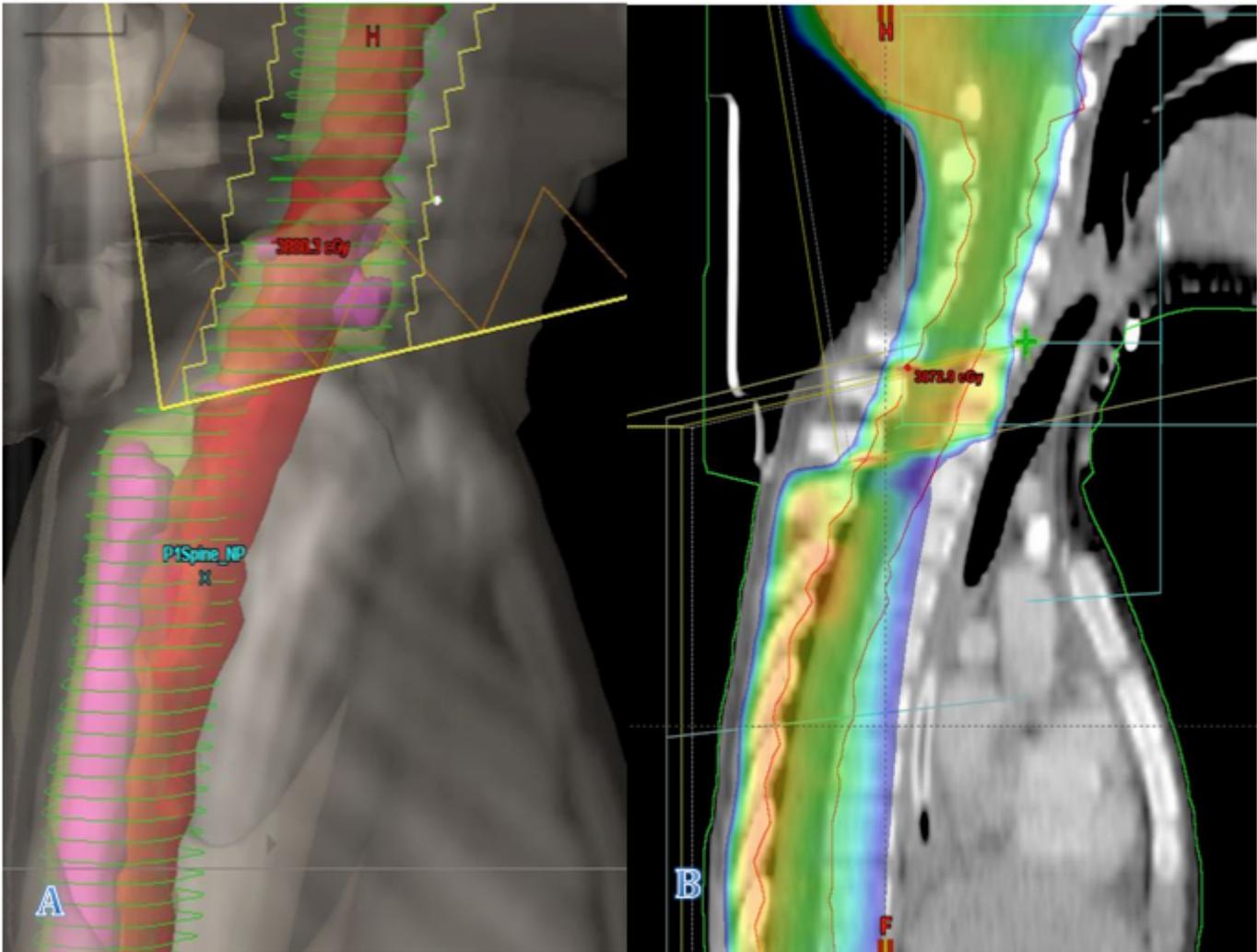


Figure 1

Figure 1

Comparison of two plans of a medulloblastoma child patient with and without FIF technique and modulated junctions. Legend: Part A: Sagittal DRR (Digitally reconstructed radiograph) of a Medulloblastoma child planned without field in field technique. Note the junction of the cranio-cervical field with the PA field showing deficient coverage of the anterior area of the PTV with 95% coverage (shown in green lines) of the prescribed radiation dose and the subsequent hot spot areas showed with purple colored dose distribution areas. Part B: Sagittal CT images of the same patient planned with field in field technique and modulated junctions and dose coverage showed in color wash. The junction can now be seen covered with $\geq 95\%$ coverage of the prescribed dose with minimum hot spot areas.

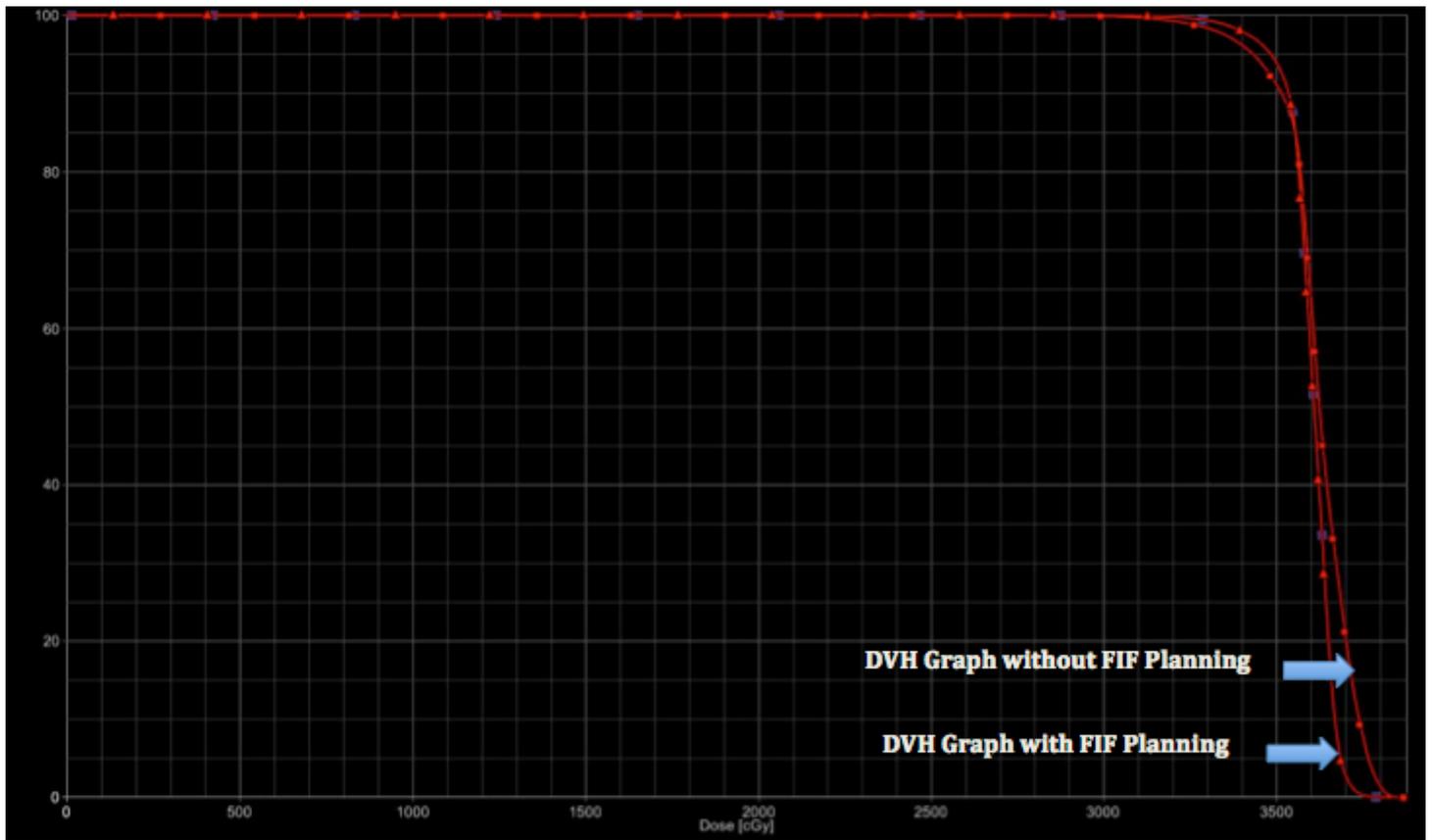


Figure 2

Figure 2

Comparison of DVH (Dose volume histograms) of same patient planned with and without FIF technique. Legend: The graph shows two curves, one without FIF technique and modulated junction, of which the curves shows deficient 95% coverage and along with that more hot spot. In contrast the 2nd curve with the FIF technique shows good 95% coverage with lesser hot areas.