Total marrow and lymphoid irradiation with helical tomotherapy: A practical implementation report

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Methodology

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Abstract

Objective To standardize the technique and resources for total marrow and lymphoid irradiation (TMLI) as part of the conditioning regimen before allogenic bone marrow transplantation (ABMT) using helical tomotherapy.

Methods We used this technique in our first 5 patients requiring TMLI. Patients were immobilized using a mask and a whole-body vacuum cushion. CT scanning was performed in head first supine (HFS) and feet first supine (FFS) orientations with an overlap at mid-thigh. Target consisted of the entire skeleton, spleen, sanctuary sites and major lymphatics whereas lungs, kidneys, aero-digestive tract, bowel, parotids, heart and liver were defined as organs at risk (OAR). Treatment was performed in two parts based on 2 different plans generated in HFS and FFS orientations with an overlap at the mid thigh. Patients along with the immobilization device were manually rotated by 180° to change the orientation after the delivery of HFS plan. The dose at the junction was contributed by a complementary dose gradient from each of the plans. Plan was to deliver 95% of 12Gy to 98% of CTV with dose heterogeneity < 10% and pre-specified OAR doe constraints. Megavoltage-CT was used for position verification before each fraction. Patient specific quality assurance and an in-vivo film dosimetry to verify junction dose were performed in all patients.

Results Treatment was delivered in two daily fractions of 2Gy each for 3 days with at least 8-hours gap between each fraction. The target coverage goals were met in all the patients. The average person-hours per patient were 16.5, 21.5 and 25.75 for radiation oncologist, radiation therapist and medical physicist respectively. Average in-room time per patient was 9.25 hours with an average beam-on time of 3.32 hours for all the six fractions.

Conclusion This report comprehensively describes technique and resource requirements for TMLI and would serve as a practical guide for departments keen to start this service. Despite being time and labor intensive, it can be implemented safely and robustly. We will be using this methodology in a prospective phase II trial to study safety and feasibility of dose escalated TMLI as part of conditioning regimen before ABMT.

Introduction

The total body irradiation (TBI) with extended source-to-skin distance (SSD) is a simple and robust technique to deliver myeloablative treatment as part of the conditioning regimen for allogeneic bone marrow transplant (ABMT) for myeloid and lymphoid leukemia. However, this modality does not spare organs at risk (OAR) except lungs and results in large heterogeneities in radiation dosage across the body.

Total marrow irradiation (TMI) is emerging as an alternative to TBI as it has shown reasonable safety and efficacy in phase I/II trials [1–6]. Addition of lymphoidal irradiation to TMI (TMLI) has the potential to reduce the rejection against the lymphocytes in donor marrow. Currently several groups are evaluating its

role in standard and high-risk acute leukemias [7]. TMLI targets the entire skeleton and lymphoid tissues while sparing the organs at risk such as parotids, oral cavity, lens, thyroid, lungs, heart, bowel, kidneys, liver, breast, etc. thereby significantly limiting potential toxicities associated with irradiation of these structures. Hereby, we report our initial experience with the detailed technique, resource and time requirements for TMLI using Helical Tomotherapy (HT) (Accuray Inc, USA) at our center.

Materials And Method

This report aimed to standardize the methodology for simulation, target delineation, treatment planning, optimization, patient-specific quality assurance, in-vivo dosimetry, pre-treatment image verification, setup and treatment. Patients were considered for this procedure after due discussions in the multi-disciplinary tumor board in close co-ordination with the haemato-oncology team. Feasibility for TMLI in these patients was based on the ability and willingness to lie down on the treatment couch for at least 1.5 hours. All patients signed an informed consent document before the procedure. Our experience of treating the first five consecutive adult patients (age >18 years) has been used in this practical implementation report.

Simulation

Simulation was done after the insertion of all catheters or venous access as deemed fit by the hemato-oncology team. Patients were positioned supine in a large vacuum bag encompassing the entire body in a neutral position and a 3-clamp thermoplastic mask on a standard neck support was made to immobilize the head and shoulder. The arm, forearm and hands were placed closely touching the lateral aspect of the body. The knees were placed in a comfortable position and the height was adjusted on the vacuum bag. In males, the scrotum was strapped to the lower abdomen and marked. The firm impression of heel and toes on the vacuum bag was captured. Before acquiring CT imaging, a thin copper wire was placed over the mid-thigh bilaterally. Lines were drawn horizontally over upper and lower limbs with corresponding lines over the vacuum bag to aid reproducibility.
As HT unit can treat till a maximum length of 135cm, two sets of CT scans (on AcquillonLB, Toshiba, Japan) of 5mm slice thickness in free breathing were acquired for each patient. The first scan was acquired from vertex to distal thigh (at least 5cm beyond the wire placed over mid-thigh) in the headfirst supine (HFS) position. Then the patient along with the immobilization was rotated by 180° and a second CT scan was acquired from toes (entire vacuum bag to be included) to the upper thigh (at least 5cm beyond the wire placed over mid-thigh) in feet first supine (FFS) position. Both scans encompassed the entire thigh to aid in registration for the evaluation of the summated plan. For the HFS scan the CT reference point was marked over the chin and for the FFS scan over the knee.

Target Delineation:

CT images were transferred to RayStation Treatment Planning System (TPS, V7.0, RaySearch labs, Stockholm), which is the preferred system for target delineation in our department. Clinical target volume (CTV) included entire bony skeleton, brain, testes spleen and major lymphatics. CTV defined on HFS and

FFS scan included bones auto-segmented based on grey level (Hounsfield units-HU) thresholding ranging between 250-1700 HU and edited appropriately. Bony CTV was split into multiple segments (skull, chest, upper/lower limbs, vertebra, and pelvis) to enable differential planning target volume (PTV) margins. Mandible, hyoid bone, patella and larynx were excluded from CTV. PTV margin of 3mm, 5mm, 7mm, 10mm, 5mm were given to CTV skull, vertebra, chest/spleen, upper limb (and lower limb for FFS scan), and pelvis (and scrotum) respectively. For patients with maximum lateral separation exceeding 45cm, an additional margin was created for PTV upper limbs since the field of view (FOV) of megavoltage CT (MVCT) was limited to 40cm. Lymphatics delineated included cervical, supraclavicular, mediastinal, axillary, entire para-aortic chain, external and internal iliac, and inguinal nodes. A uniform PTV margin of 5mm was applied to generate lymph nodal PTV. Individual PTV's generated were summated to create PTV. Organs at risk (OAR) delineated were eyes, lens, midline mucosa (oral, pharyngeal, laryngeal, tracheal and esophageal mucosa), lungs, heart, liver, bowel, kidneys, parotids, thyroid, breast, and ovaries. Dose Prescription and dose constraints have been summarized in table-1.

Treatment planning, plan evaluation and patient-specific quality assurance (PSQA):

We used the Precision planning system (iDMS version 1.1.1.1, Accuray Inc, USA) for optimization and dose calculation purposes. For planning and optimization, the entire target volume contoured in HFS & FFS images series was divided into three parts namely PTV-upper, PTV-lower and PTV-Junction [Fig-1]. The length of the junction volume was kept at 10cm (typically located between the upper thigh corresponding to the distal end of the fingers and knee) and it was divided into five sub-volumes in each CT image series to create a dose gradient. They were labeled as PhyUG2Gy, PhyUG4Gy, PhyUG6Gy, PhyUG8Gy, PhyUG10Gy, PhyLG2Gy, PhyLG4Gy, PhyLG6Gy, PhyLG8Gy, and PhyLG10Gy. The copper wires placed on the left and right mid-thigh were used as common reference markers to correlate the axial positions from both HFS & FFS CT image series. Using this common reference marker the extension and location of the three PTV's were verified in both the CT image series.
As a standard protocol CT tabletop in the image series was replaced by the Radixact couch model. The patient position was set using a green laser in such a way that the entire body was fit within the field of view. Two separate treatment plans were generated on each of the scans (HFS and FFS) to cover the entire target including the junction between the two plans [Fig-2a and 2b].
Plan setup parameters were chosen to meet the clinical goals of the target. Pitch from 0.3 – 0.43, field width of 5cm, modulation factor of 2.5 – 3.5 for HFS orientation and 2.15- 2.5 for FFS were used. A higher heterogeneity was accepted near the upper limbs especially near the forearm and hands. Pitch values were optimized to have minimal thread effect and good target coverage. Higher modulation factors were used for initial iterations and subsequently modified to have efficient beam delivery time. The final plans generated on both the CT's were summated [Fig-3a] and the dose profile across the junction [Fig-3b] was evaluated on RayStation TPS (due to limitation in summating plans generated on two differently referenced CT's on Precision TPS). As part of the PSQA, we measured the dose using a cylindrical cheese phantom (Accuray Inc, USA) with the A1SL ion chamber (Sun Nuclear, USA). Since the target volume exceeded 120cm, multiple point doses (3 for HFS plan and 2 for FFS plan) were measured

to cover the entire target. Each point dose measurement was associated with a specific QA plan and a laser position co-ordinate for phantom placement. Before each measurement phantom position was verified using MVCT image registration with planning CT.

Treatment delivery and In-vivo dosimetry:

Pre-treatment imaging and treatment delivery were divided as the patient was treated in both HFS and FFS positions as described in the pictogram [Fig-4]. Treatment was interrupted each time after a pre-specified time. In HFS treatment, the first MVCT scan was obtained from mid-chest to upper abdomen level to correct any significant longitudinal and yaw errors manually. The 2nd MVCT was acquired from the vertex to the mid-chest level. After applying the necessary lateral and vertical corrections, patient was treated up to the upper abdomen. The third MVCT scan was obtained encompassing the entire abdomen up to mid-thigh, the position of scrotum was verified and the rest of the patient treatment was completed for HFS plan. Subsequently, the patient was rotated by 180 degrees (in yaw plane) with the same immobilization and alignment in place for FFS treatment plan. The fourth MVCT was acquired from ankle to thigh, couch corrections were applied (including the longitudinal corrections since the patient was moved manually) and treatment was delivered with FFS plan. The dosimetric accuracy of the junction was verified using GafChromic ebt3 film placed over the junction during the first treatment fraction.

Results

Five patients (3 males; 2 females) with a median age of 36 years (range 25-49 years) underwent this procedure from the 7th-5th day before ABMT. The median patient height was 167cm (range 160-178cm).

All patients received two daily fractions of 2Gy each for 3 days with a minimum gap of 7 hours between each fraction. The mean beam-on-time per fraction was 33.25 minutes with a dose rate of 1051MU/minute. The resources and time requirements for the treatment planning and delivery procedure have been summarized in table-2.
The desired target coverage and OAR sparing was satisfactorily achieved in all patients. The dose-volume parameters achieved have been summarized in table-3. The dose homogeneity was acceptable with a mean homogeneity index of 0.170 (range 0.147-190) for the combined PTV (PTV-upper + PTV-lower + PTV-junction). A higher inhomogeneity was accepted only for PTV upper limbs (mean HI=0.327, range 0.197-0.441). The mean of lung D50, kidney D50, heart D50, liver D50 and max dose to mucosal structures achieved were 8.15Gy, 7.5Gy, 8.17Gy, 7.41Gy and 12.48Gy respectively. The liver was included in the target volume for the patient-2, which led to a higher lung D50. For the calculation of average D50 for liver, this patient was excluded (Table 3).

Setup errors were minimal in all patients based on MVCT verification [table 4]. After the initial verification with the first MVCT and manual re-positioning if required, none of the patients required additional re-positioning since most of the errors noted were corrected by necessary couch translations.

The PSQA results achieved for all the patients were satisfactory as per our institutional thresholds and have been summarized in table-5. On qualitative comparison of TPS calculated dose profile and measured dose profile (in-vivo film dosimetry) at the same level no abnormal spikes in dose were observed in all the patients [Fig-5].
All patients completed their treatment with no Grade 2+ acute toxicities (CTCAE V5). Subsequently, all patients were successfully engrafted and no late toxicities were observed at a median follow-up of 7 months (range 2.5-8 months).

Discussion

After a considerable experience with extended SSD TBI for last several years, we evaluated this methodology of TMLI, with an aim to eventually study the feasibility and safety of dose escalation in selected patients. Our objective with this study was to standardize the procedure, plan resources and time requirements for this procedure in our department. We preferred HT for magna-field irradiation as it offers a high degree of conformity, homogeneity of target coverage dose and significant sparing of OAR with optimal treatment efficiency, without the need for multiple junctions. This is possibly the reason why several groups have extensively evaluated it for TBI and TMI/TMLI [8–14]. Recently VMAT has also been evaluated in this setting to a reasonable success [15,16]. Although we have used HT to treat our patients, the same principles can be broadly applied for VMAT as well.

The target delineation for both TMI and TMLI has been varied in literature. Exclusion of mandible, maxilla, bones in the forearm, small bones of the hands and feet from the target has been diverse [1–6]. We have included the entire skeletal system excluding mandible, hyoid, laryngeal cartilage and patella. Similarly inclusion of nodal groups varied with some authors not explicitly mentioning the nodal groups that are intentionally irradiated [8–10]. We have included cervical, mediastinal, para-aortic, pelvic and inguinal nodal chains and have excluded Waldeyer's ring and porta-hepatic nodal groups in order to limit the doses to oropharyngeal mucosa and liver/bowel respectively. There is also a discrepancy when it came to inclusion of liver, which was part of the target in some and was an OAR in a few series [8–10,17]. Patients will be followed up to validate the appropriateness of our approach.

We have used two sets of CT scans and plans with complementary dose gradient across the junction similar to the one described by Haraldsson, et al [18] for TMI. Planning and optimization processes were similar except that we allowed a lengthier junction to ensure plan robustness. The target delineation, final plan summation and evaluation were performed on one TPS, whereas the optimization and dose calculation were carried out on another TPS. The dose coverage and homogeneity met our pre-specified dose constraints except in upper limbs where the inhomogeneity exceeded our thresholds. This is expected with HT delivery for peripherally located targets due to increased thread effect and limited beamlet views for this region.

Lung D50 achieved in our patients was relatively higher compared to other published series of TMLI [8–10,17] and this is possibly due to differences in target delineation, margins and differences in target

coverage goals. Varying margins to the chest wall target have been used by investigators which were based either on geometric expansion ranging from 0-10 mm [9,18] or based on chest wall motion [18]. Our coverage goal of 95% of dose to 98% of CTV was higher than the 85% set by others (9) possibly explaining higher lung D50. However, lung D50 achieved for TMLI in our cohort was comparable to that achieved by Haraldsson, et al for TMI. We intend to aggressively limit lung D50 in future, especially when we escalate TMLI doses by relaxing the target coverage goals in the upper chest (our current mean CTV chest D98 was 99.6%). We already have reduced our mean lung D50 constraint from 8.5Gy to 7Gy for our last patient.

We have used MVCT alone as a guide for patient setup verification, which mandated diligent patient immobilization and systematic imaging protocol to minimize patient repositioning. The first MVCT (lower neck to chest) in our imaging protocol was done to manually correct any longitudinal and yaw errors before proceeding with the rest of the procedure. This step `significantly reduced the magnitude of couch corrections and the need for repositioning. Special attention was given to extremities and scrotal position during immobilization and daily set up to minimize the repeated image verifications. The robustness of the dose at the junction was reaffirmed with the help of film dosimetry.

As compared to TBI, TMLI is a time and resource-intensive procedure. We observed that for one patient to be successfully treated, the department would have to allocate nearly 27 physicist-hours, 21.5 therapist-hours and 16.25 radiation oncologist-hours (table-2). Significantly higher person-hours and in-room time as compared to other magna-field irradiations can potentially lead to stress on work-timings for all the personnel involved especially in busy radiation oncology departments. The mean in-room time of 9.25hrs per patient over 3 days, could potentially lead to significant changes in treatment schedules for other patients. We chose weekends and public holidays to treat our patients to minimize interruptions to the department’s routine. Our beam-on time was higher compared to that reported for TMI using HT and VMAT [16], but comparable to others for TMLI using HT [8–10,17]. Our time for target delineation, treatment planning and QA was comparable to that reported by others for TBI [19]. We believe that further optimization of total in-room time can be achieved with growing experience.

Since the aim of the study was to standardize our methodology and plan resource requirements, we chose to publish this report after treating the initial 5 patients. However, the dosimetric data is limited due to the small sample size and hence we may have to optimize the target and OAR dose constraints in the future on a case to case basis. All our patients were young and had healthy lung volumes enabling us to achieve desirable lung D50, however this could be challenging in patients with poor lung volumes. The robust set-up and minimal couch corrections noted in our study may not be possible to achieve in more challenging patients and hence may either require a more liberal margin recipe or a compromise on dose constraints. Our average beam-on-time of 9.25hrs per patient may pose a significant challenge while treating pediatric patients, although the need for junction would not arise in such patients (<135cm).

Conclusion

TMLI results in significant sparing of OAR and provides an opportunity for safe dose escalation despite being a time and resource-intensive procedure. Our comprehensive report on the detailed methodology, resource and time requirements to implement TMLI would help departments planning to commission this procedure and plan their resources. We will be using this methodology in a prospective phase II trial to study the safety and feasibility of dose-escalated TMLI as part of the conditioning regimen before ABMT.

List Of Abbreviations

TMLI: Total marrow and lymphoid irradiation

ABMT: allogeneic bone marrow transplantation

OAR: Organs at risk

SSD: Source to skin distance

HFS: Head first supine

FFS: Feet first supine

FOV: Field of view

CT: Computed Tomography

CTV: Clinical target volume

PTV: Planning target volume

TBI: Total Body Irradiation

PSQA: Patient specific quality assurance

TPS: Treatment planning system

MVCT: Megavoltage-CT

Declarations

Ethics approval and consent to participate

Voluntary written informed consent was obtained from the patients to study and publish their clinical data anonymously

Consent for publication

Voluntary written informed consent was obtained from the patients to study and publish their clinical data anonymously

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

Not applicable

Authors' contributions

SC was the chief treating radiation oncologist and was involved in the entire treatment, analysis and manuscript preperation; SS was the senior registrar involved in entire treatment, analysis and manuscript preperation ; RT was the medical physicist involved in treatment planning and dosimetry; JE was the Chief Haemato-Oncologist involved during the treatment; MS was the associate medical physicist involved during treatment planning and collection of data; GK was the medical physicist involved in patient specific quality assurance(PSQA) tests; PKP was involved in data collection, analysis and manuscript preparation; DS is the head of medical physics department and has significantly contributed for the treatment planning, PSQA and dosimetry analysis; RJ has contributed significantly during treatment planning and manuscript writing.

All authors read and approved the final manuscript

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Tables

Table-1: Dose volume constraints and planning goals.

Structure	Planning Objective
CTV	98% of CTV to receive at least 95% of 12Gy Dose to 2% < 110% of prescription dose Dose to 98% > 90% of prescription dose
PTV	95% of PTV to receive 95% of prescription dose
Lungs	Mean dose <8.5 Gy
Kidneys	Mean dose to each kidney<8.5Gy
Heart	Mean dose <8.5Gy
Liver	Mean dose <8.5Gy
Lens	Mean dose<3Gy
Mucosal structures, Esophagus, Bowel	Max dose <105% of prescription dose

Table-2: Time, resource requirements for the TMLI. (as per local practice)

Process	Time (Median)	Resource
Simulation and image acquisition	1.5 hrs	2 Radiation therapists Verified by Medical Physicist and Radiation oncologist
Target Delineation	6 hrs	1 Radiation Oncologist
Optimization and dose calculation	44 hrs (effective working hours spent by physicist- 12 hrs)	Medical Physicist 1 hr verification by second medical physicist (partially shared time with other activities)
Plan evaluation	1 hr	Medical Physicist Radiation Oncologist
Patient specific Quality assurance	1.5hr	2 medical Physicists
Treatment delivery fraction1	1.75 hrs	2 Radiation therapists Medical Physicist Radiation Oncologist
Treatment Delivery subsequent fractions (5#)and In vivo dosimetry	1.5 hrs	2Radiation therapists, Medical Physicist Radiation Oncologist
Summary of person hours		
Therapist	21.5 hrs	
Medical Physicist	26.75 hrs	
Radiation Oncologist	16.25 hrs	
In-room time for all fractions	**9.25 hrs per patient***	
*This excludes the treatment room preparation time which is about 15 min before each fraction		

Table-3: Dose volume parameters achieved in the first 4 patients treated

Structure	Parameters	Patient 1 (Gy)	Patient 2 Gy	Patient 3 (Gy)	Patient 4 (Gy)	Patient 5 (Gy)	Mean	SD
CTV Skull	D98	11.96	11.79	11.62	11.93	11.88	11.84	0.137
	D2	12.59	12.89	12.98	12.68	12.56	12.74	0.186
CTV chest	D98	11.95	11.9	12.17	11.75	11.95	11.94	0.151
	D2	12.57	12.7	12.83	12.74	12.63	12.69	0.1
CTV Trunk	D98	11.76	11.73	12.11	11.81	11.98	11.88	0.162
	D2	12.97	12.89	13.68	12.74	12.66	12.99	0.406
CTV Upper limb	D98	12.02	10.82	10.72	11.49	11.52	11.31	0.541
	D2	13.76	13.99	13.95	12.89	13.11	13.54	0.507
CTV Lower limb	D98	11.77	11.81	11.73	11.9	11.45	11.73	0.17
	D2	12.57	13.02	12.7	13	12.70	12.8	0.201
	Planning Target Volume							
PTV Upper	D95	11.79	11.65	11.12	11.67	11.80	11.61	0.28
PTV Junction	D95	11.22	11.44	11.05	11.42	11.43	11.31	0.173
PTV Lower	D95	11.88	12.03	11.94	11.94	11.94	11.95	0.054
	Organs at risk							
Eyes	D50	8.92	7.1	6	4.5	9.53	7.21	2.069
Lens	D50	3.1	3.3	2.65	2.8	2.61	2.89	0.298
Midline mucosa	D50	9	10.88	10	11.58	8.76	10.04	1.204
Lungs	D50	8.15	8.75	8.4	8.45	6.99	8.15	0.682
Heart	D50	8.18	9.69	7.24	7.1	8.65	8.17	1.067
Bowel bag	D50	6.72	7.6	7.12	7.48	7.29	7.24	0.344
Liver	D50	5.31	11.76	4.65	8.19	7.13	7.41	2.812
Kidneys	D50	6.1	9.5	5.8	8.65	7.45	7.5	1.595

Table 4: Mean setup corrections (with standard deviations) in mm

Site	Lateral (x)	Longitudinal (y)	Vertical (z)
Head and Neck	-0.98 ± 3.68	-1.9 ± 2.67	-0.69 ± 2.5
Thorax	0.11 ± 3.86	0	1.32 ± 3.42
Abdomen	1.40 ± 3.91	0	2.26 ± 2.94
Legs	0.08 ± 3.99	-0.4 ± 2.3	-0.11 ± 2.17

Table-5: Patient Specific Quality Assurance results

Patient	Location	TPSCalc Dose (cheese) (cGy)	Measured Dose (cheese) (cGy)	Dose difference	% Dose difference
Patient 1	Brain	164	163.91	-0.09	-0.05
	Thorax	177	177.02	0.02	0.01
	Pelvis	191	190.77	-0.23	-0.12
	Upper leg	149	149.34	0.34	0.22
	Lower leg	141	141.26	0.26	0.18
Patient 2	Brain	165	166.47	1.47	0.88
	Thorax	193	193.86	0.86	0.44
	Pelvis	205	205.31	0.31	0.15
	Upper leg	172	172.54	0.54	0.31
	Lower leg	153	153.42	0.42	0.27
Patient 3	Brain	162	163.12	1.12	0.69
	Thorax	198	198.87	0.87	0.44
	Pelvis	201	202.23	1.23	0.61
	Upper leg	151	151.33	0.33	0.22
	Lower leg	149	149.48	0.48	0.32
Patient 4	Brain	164	162.09	1.91	-1.17
	Thorax	169	168.5	0.5	-0.30
	Pelvis	174	173.5	0.5	-0.29
	Upper leg	152	151.69	0.31	-0.20
	Lower	149	148.03	0.97	-0.66

	leg				
Patient 5	Brain	166	165.66	0.34	0.20
	Thorax	184	182.69	1.31	0.712
	Pelvis	191	193.34	-2.34	-1.22
	Upper leg	162	160.27	1.73	1.07
	Lower leg	150	149.67	0.33	0.22

Figures

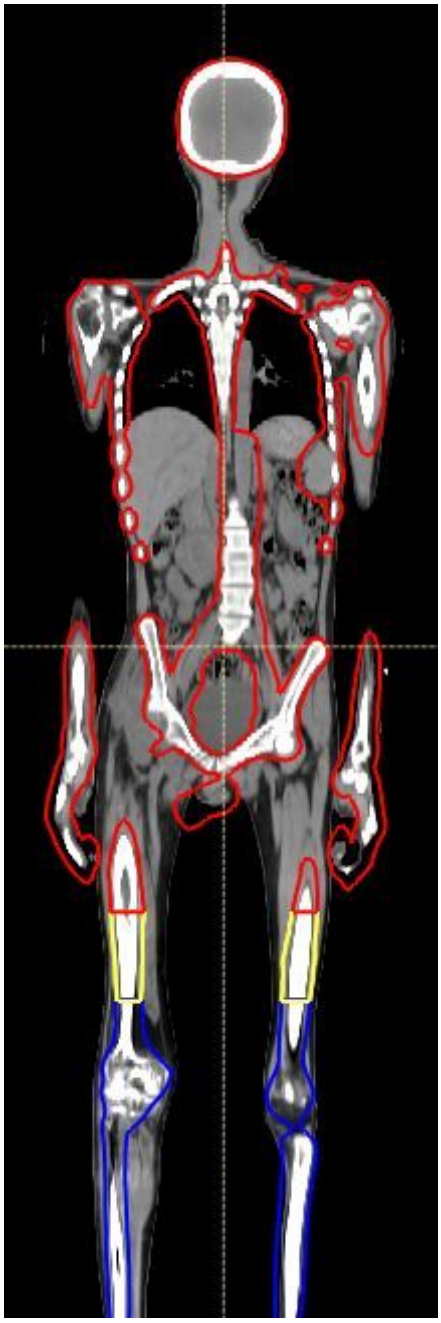

Figure 1

Figure displaying Planning PTV sub volumes

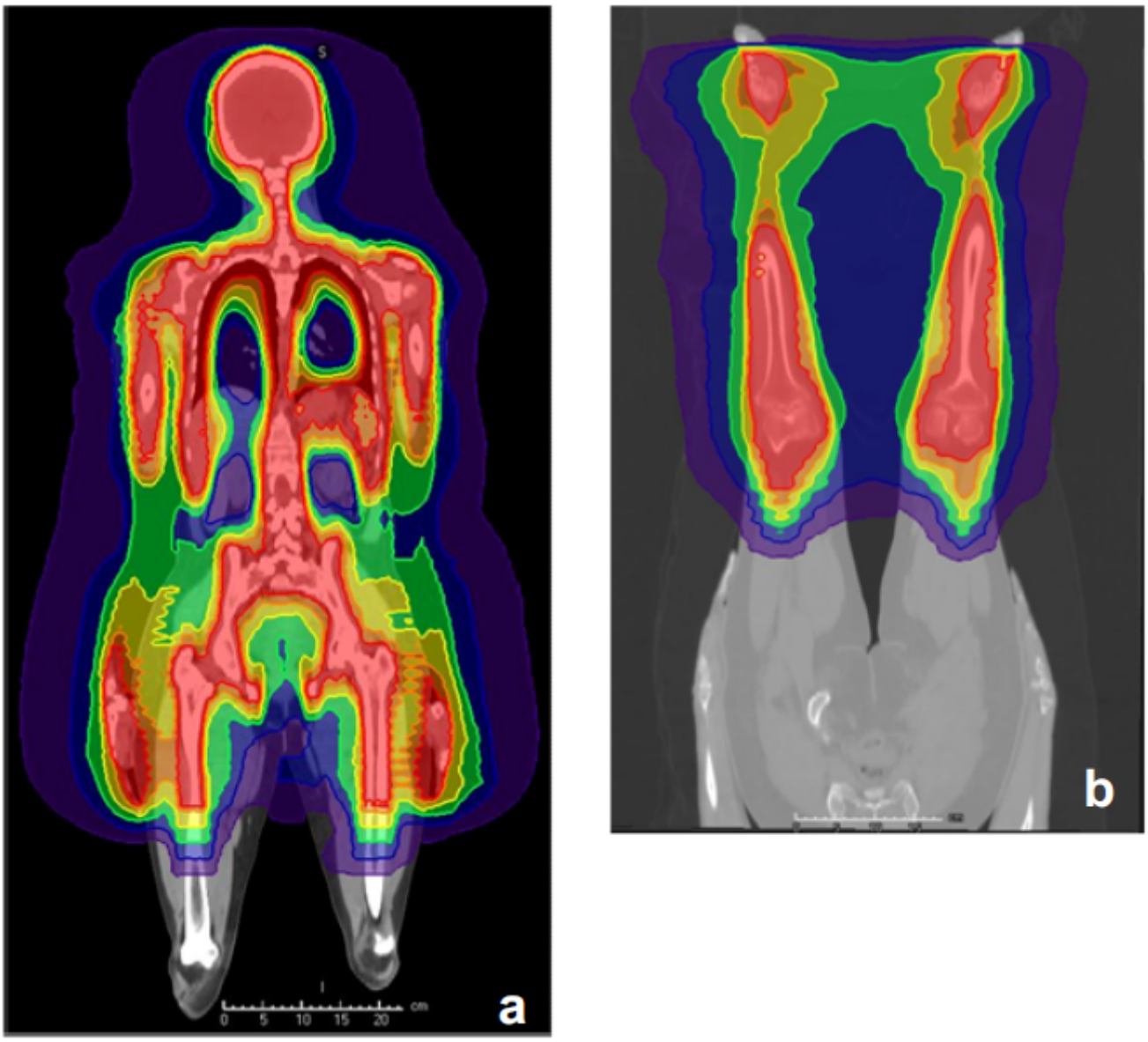

Figure 2

Figure displaying HFS and FFS plan

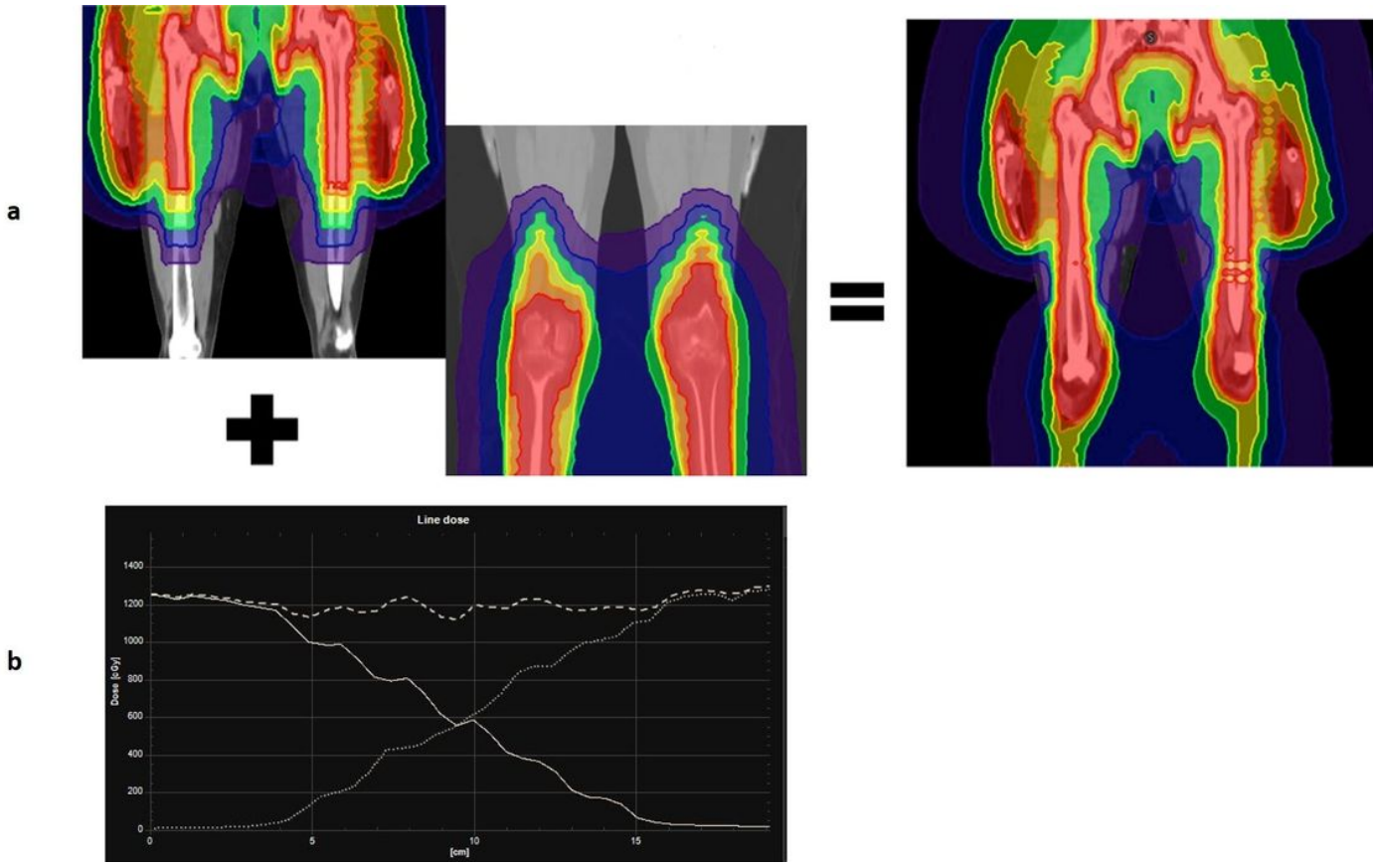

Figure 3

a: Figure displaying combined plan at the junction b: Figure displaying the dose profile across the junction after combining HFS and FFS plans

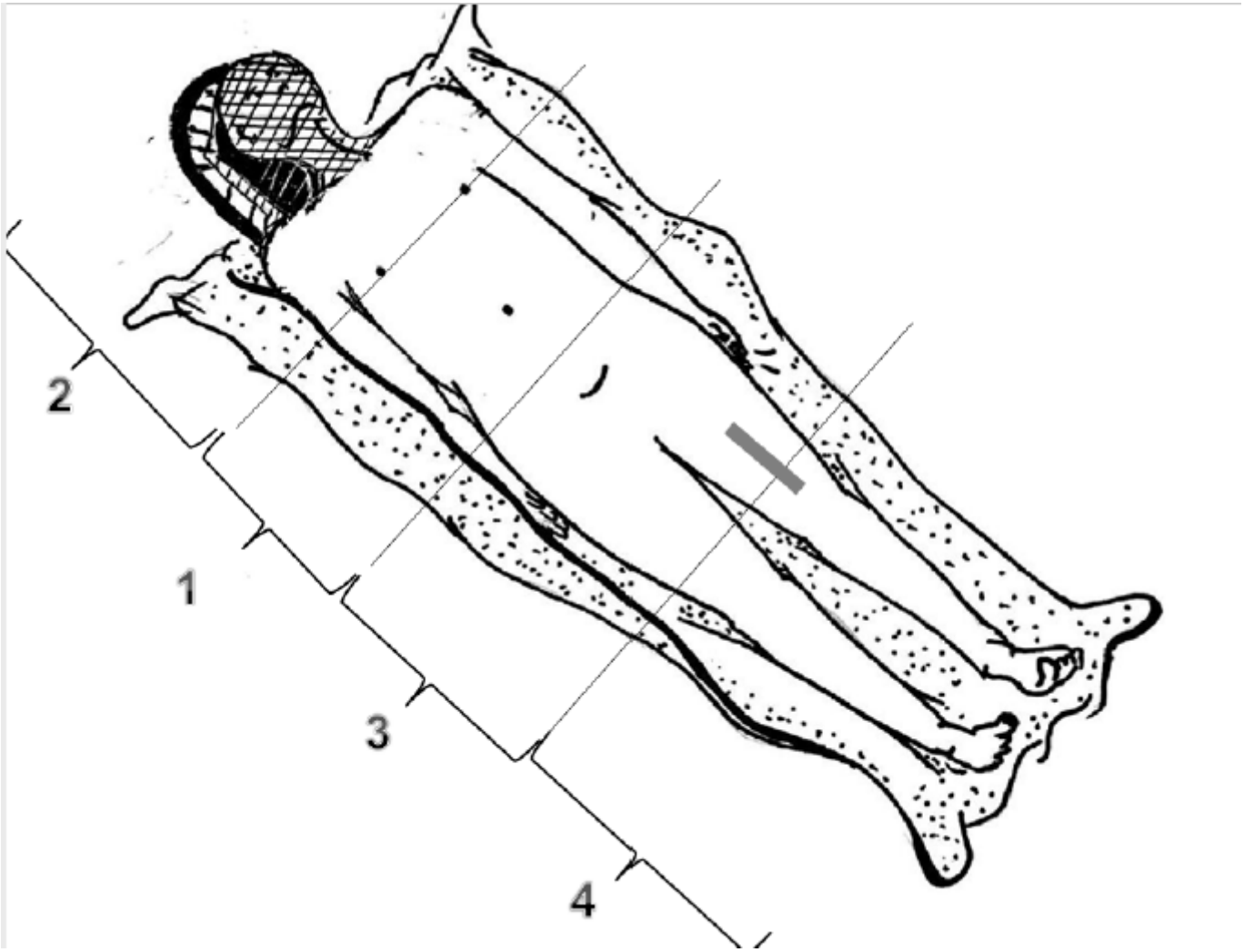

Figure 4

Figure displaying the sequence of pre-treatment imaging and the position of the film on thigh

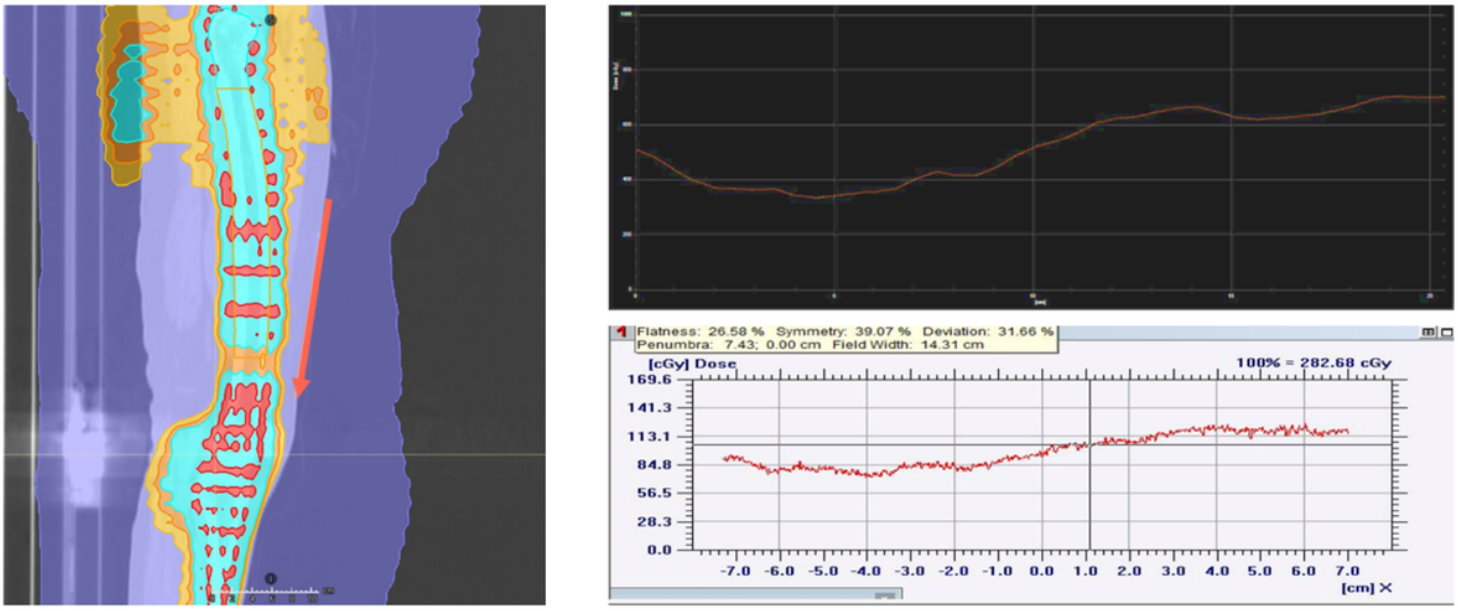

Figure 5

Figure displaying in-vivo junction dosimetry in a patient.