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Clinical implementation of Total Body Irradiation with Tomotherapy: from imaging to dose delivery

Implementação clínica da Irradiação de Corpo Total com Tomotherapy: da imagem ao tratamento

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Resumo

A Irradiação de Corpo Inteiro tem sido, por muitos anos, utilizada como parte do regime de condicionamento para transplante de medula óssea. Com os avanços tecnológicos, a Radioterapia de Intensidade Modulada começou a ser aplicada com esse propósito, com o objetivo de potencialmente reduzir toxicidade, uma vez que permite redução de dose nos órgãos em risco e uma distribuição de dose mais homogênea. A Tomotherapy® tem sido utilizada para tratamentos modulados de corpo inteiro e representa um método sofisticado, seguro e de alta qualidade. O principal objetivo deste artigo é apresentar um método para a implementação clínica de Irradiação de Corpo Inteiro utilizando a Tomotherapy, fornecendo métricas de distribuição de dose, baseados em nossa experiência clínica. A metodologia apresentada consistiu na descrição dos acessórios de imobilização utilizados e a apresentação de um fluxo de trabalho detalhado do planejamento do tratamento e de tratamento. Os resultados apresentados de 20 pacientes mostraram boa uniformidade de dose e cobertura no alvo; as médias dos desvios calculados foram inferiores a 5 mm e a dosimetria in-vivo mostrou boa concordância com a dose prescrita. As métricas fornecidas podem ser utilizadas como um guia para instituições com interesse em implementar esta modalidade de tratamento com Tomotherapy.

Palavras-chave: corpo inteiro, tomoterapia, planejamento de tratamento, administração de dose, garantia de qualidade específica para o paciente.

Abstract

Total Body Irradiation (TBI) has been used as part of conditioning regimens pre-bone marrow transplantation for several years. With technology advances, IMRT started to be applied to this purpose, aiming potentially less toxicity by allowing OAR sparing and more homogeneous dose distribution. Tomotherapy® equipment has been used for modulated TBI and represents a sophisticated, safe and high quality method for this purpose. The main purpose of this paper is to present a methodology to clinically implement TBI treatments using Tomotherapy and to provide metrics of dose distribution based in our clinical experience. The presented methodology includes in a description of the immobilization accessories used and presenting a detailed workflow for treatment planning and delivery. Results of 20 patients showed good uniformity and target coverage, registration offsets averages inferior to 5 mm and in-vivo dosimetry with good agreement with the prescribed dose. The provided metrics could be used as a guide for those institutions that are willing to implement TBI with Tomotherapy.

Keywords*: total body, tomotherapy, treatment planning, dose delivery, patient-specific quality assurance.*

1. Introduction

Total Body Irradiation (TBI) has been used as part of conditioning regimens pre-bone marrow transplantation for several years. To cover the whole patient's body, the most common technique uses two parallel-opposed beams at extended distance from conventional linear accelerators (1). Despite the low implementation cost and relatively higher availability, this approach has some limitations such as limited organ-at-risk sparing and difficulty to produce an homogenous dose distribution. With technology advances in the radiation therapy, intensity modulated beams are become reality and as the IMRT benefits were being published for all anatomical sites, it was natural that, although the results of the conventional TBI has been well established, the clinical community started to create methods to use IMRT also for treating the whole body, aiming potentially less toxicity, by allowing OAR sparing and more homogeneous dose distribution (2-4).

Tomotherapy® equipment has been used for modulated TBI (5,6) and represents a sophisticated, safe and high quality method for this purpose.

The main purpose of this paper is to present a methodology to clinically implement TBI treatments using Tomotherapy and to provide metrics of dose distribution based in our clinical experience.

2. Methods and Material

The modulated TBI implementation was performed in a Tomotherapy HD linear accelerator. This machine is equipped with a 6MV FFF photon beam with constant dose rate of 850 MU/min and a binary multi-leaf collimator containing 64 leaves with 0.625 cm width each. The maximum nominal field size is 40 cm x 5 cm, with the target longitudinal coverage being achieved through continuous couch translation during irradiation. Patient immobilization is performed with the combination of a thermoplastic open face mask and a whole-body vacuum cushion (Orfit Solutions, Belgium). Patient CT images were acquired in a

Discovery RT® CT-simulator (GE Healthcare Systems) and the treatment planning system (TPS) used was Precision® (Accuray, Madison, WI). Detailed information on each step of the process is presented in the following subsections.

2.1. Patient immobilization

Patients' positioning and immobilization devices should be chosen with the goal of achieving an optimal compromise of immobilization effectiveness, setup reproducibility and patient comfort. Currently, patients were positioned in the supine position over a whole-body vacuum cushion extending from the upper thorax to the bottom of the feet, and an open-face thermoplastic mask placed over the head, neck and shoulders (Fig.1). Both devices are indexed over an Orfit base plate. The mask is removed when treating the patient's lower body, which improves comfort without compromising accuracy. The arms are positioned alongside the body as close as possible of the patient's body to reduce the total lateral width. Care was taken with the proper positioning of the vacuum cushion to avoid blocking the mask's should fixation on the base plate and to have enough cushion to mold the patient's feet contour properly. The legs and feet are elevated as needed to keep the as level as reasonably achievable with the torso. Several reference marks were done on the patient's skin, mask and cushion to assist in the correct positioning of the patient in the treatment room.

The first two patients were immobilized with an additional thermoplastic mask covering the abdomen and pelvis, which caused discomfort in the patients' breathing and difficulties in arm positioning, thus this setup was discontinued.

2.2. Image acquisition and contouring

At the CT-simulator, with the patient immobilized, we acquired a set of images with 5 mm thickness, field-of-view (FOV) of 65 cm and maximum longitudinal scan length. If the maximum scan length (≈160 cm) is not enough to cover the entire patient, a second scan is necessary. This second studyset image was taken with the patient at the supine feet-first position and with the scan encompassing from the feet to the pelvis. The two scans are then merged into a single studyset covering the entire patient's body using the Eclipse® TPS (Varian Medical Systems, Palo Alto, CA).

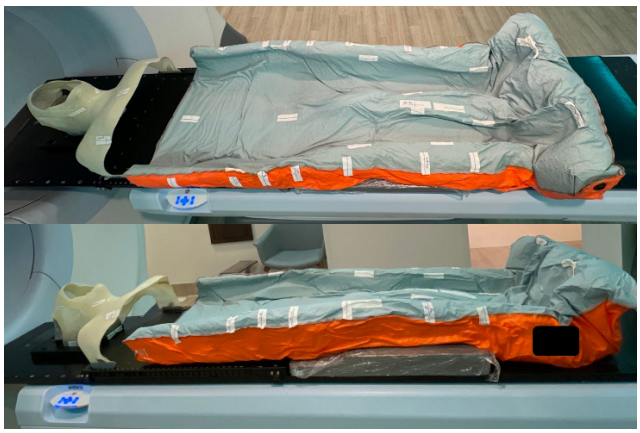

Figure 1: Patient immobilization with open-face mask for head and shoulder regions and whole-body vacuum cushion

The total PTV was defined as the patient's body with an internal margin of 2 mm, to prevent high fluency at the skin surface (Fig.2a). A virtual bolus of 10 mm surrounding the PTV is assigned, was created to produce a skin flash assuring that even with small patient's shifts from the patient planned position (Fig. 2b). To create fluency at the bolus region, a ring of 7 mm external to the PTV was defined (Fig.2c).

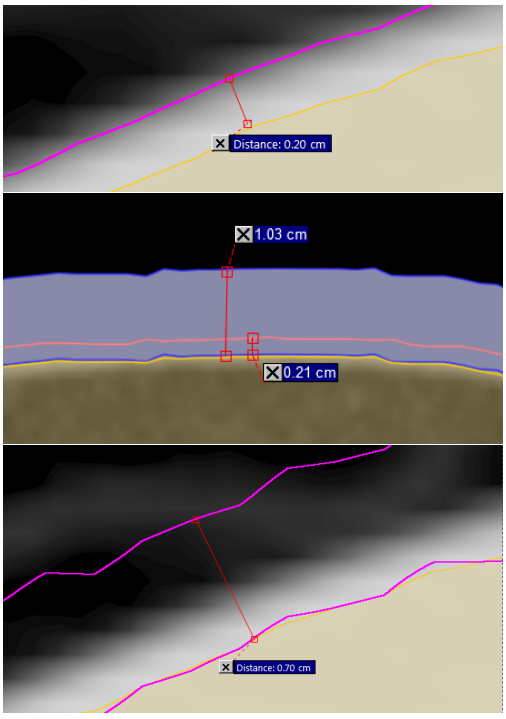

Figure 2: Structures used to define the target area: PTV_total (yellow), virtual bolus (blue) and ring (pink) structures to create a skin flash margin

In order to have better control while optimizing regions with different thickness along the body, the total PTV is divided into: PTV_head; PTV_arms; PTV_thorax_abd; PTV_pelvis and PTV_inf. Every portion of the PTV had its own ring of 7 mm to be optimized separately (Fig. 3).

Figure 3: Target structures used to better optimize the whole body. Ring structures are visualized at the right

The maximum allowable longitudinal treatment length for a single plan in Tomotherapy is 135 cm. Considering a fixed jaw setting of 5 cm and the flash fluence extension of 0.5 cm in both superior and inferior directions, the total PTV longitudinal length is limited to 129 cm. To ensure a safe setup margin (considering the discrete couch indexing positions and image verification errors), our standard practice is to use a PTV length of approximately 110 cm, with the length limit of no more than 120 cm for any single plan. For larger targets, two separate plans are generated for the superior (PTV_Sup) and inferior (PTV_Inf) regions of the patient that share a common dose gradient region to minimize the effect of setup errors in the transition zone between the two PTVs.

The dose gradient region is comprised of three 5 cm thickness bands of partial doses objectives, with 25% reduction steps (PTV_75%_grad, PTV_50%_grad, PTV_25%_grad) and two 2.5 cm thickness at the matching region extremities to smooth the dose gradient (PTV_95% _grad and PTV_5%_grad). Each portion of the PTV_grad has a ring of 7 mm to be optimized separately (Fig.4). During CT simulation, a radiopaque marker is placed at a distance of approximately 100 cm from the top of the patient's head (usually in the patient's thighs), which is used as a reference location for the center of the region. For male patients, the gradient region may be displaced inferiorly as needed to avoid placing the scrotum in this transition zone to minimize the risk of potential underdose, though it might not be possible for taller patients due to the longitudinal extension limitation.

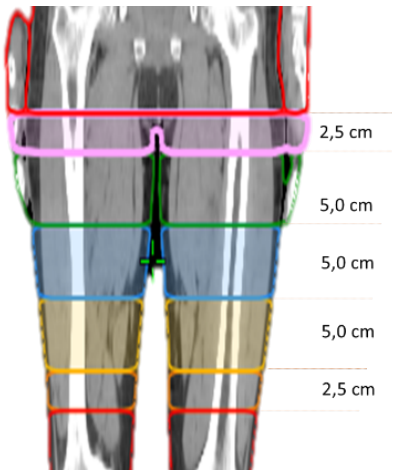

Figure 2: Dose gradient regions used for the junction between superior and inferior plans

Organs-at-risk were contoured to report doses, as recommended by ICRU-83 (heart, lung, liver, kidneys).

Additionally, for the cases were it was necessary to restrict doses at lungs and kidneys, other PTVs were created (Fig.5):

- PTV ribs: a 1cm-ring external to the lungs, cropped 1 cm from the heart and excluding regions inside the diaphragm;
- PTV_lung_out: a 1 cm-ring internal to the lungs;
- PTV_lung_inner: total lung cropped 3 mm from the PTV_lung_out;
- PTV_kidneys: sum of left and right kidneys.

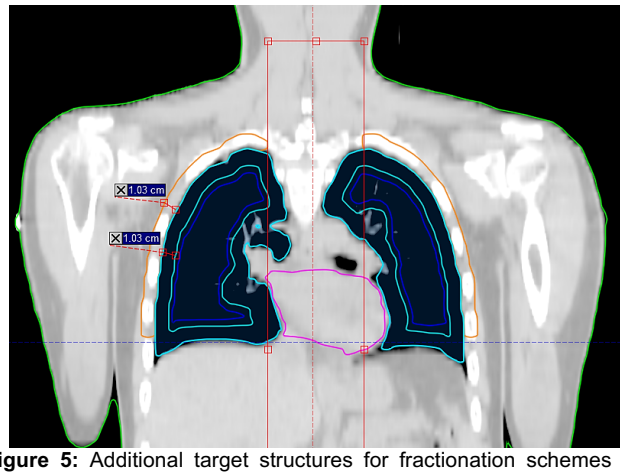

Figure 5: Additional target structures for fractionation schemes where sparing lung and kidneys are necessary

2.3. Treatment planning

2.3.1 Beam geometry

Inverse-planning was performed using Precision TPS. A relative electronic density of 1.0 was assigned to the virtual bolus.

Both TomoDirect® and TomoHelical® delivery were used on different patients to treat the superior portion of the target. The inferior portion was treated with TomoHelical in all cases. For TomoDirect, six beams were employed and a skin flash of 3 MLC leaves was added to each beam (Fig.6). Gantry angles could differ slightly between cases in order to involve the

entire patient's body (Fig.7). For the TomoHelical treatment planning, a pitch of 0.42-0.43 was used for the superior region, while for the inferior region the average pitch was 0.40 (0.287-0.43). All plans used a Y-jaw setting of 5 cm.

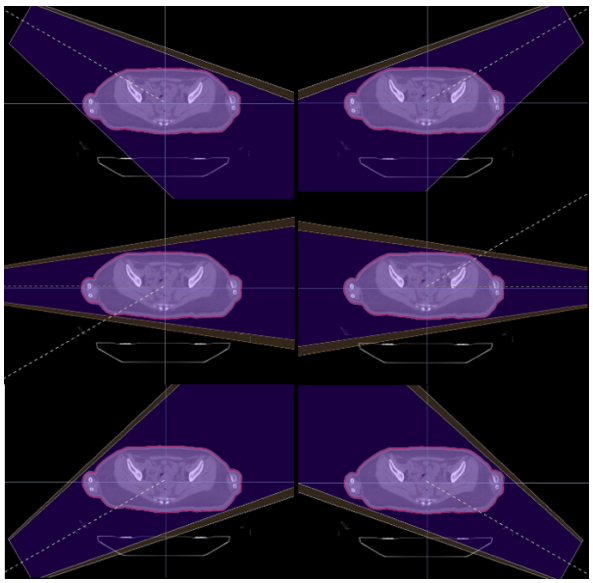

Figure 6: Example of a TomoDirect delivery beam geometry. Gantry angles are typically set as 60°, 90°, 120°, 240°, 270° and 300°

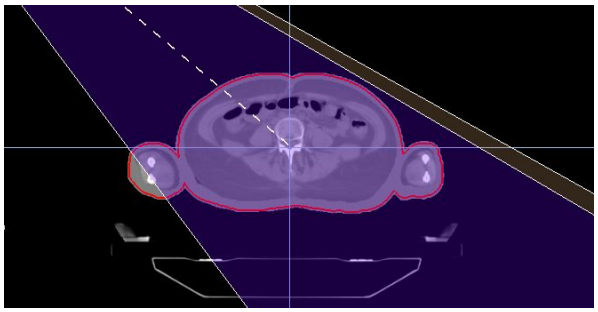

Figure 7: In some cases, the axial field size limitation of 40 cm requires slight modifications of the gantry angles to improve the coverage of the patient's body

2.3.2 Planning objectives

In general, the planning objectives were: PTV_sup; PTV_inf: 90% of the prescribed dose covering the whole body (no metrics defined, evaluated visually); minimize the volume receiving more than 110% of the prescribed dose. If the prescribed dose is higher than 8 Gy, the acceptance criteria followed the tolerances described in Table 1 below.

Table 1: Dose objectives for dose prescription higher than 8 Gy

Structure	Target value	Acceptable value
PTV*	Dmean (12Gy) ± 2% D98% > 11.4 Gy D2% < 13 Gy	Dmean (12Gy) ± 5% D95% >11.4 Gy D5% < 13 Gy
Ribs	D95% > 10Gy	D90% > 10 Gy
Lung R & L	V6Gy > 99% V8Gy < 40%	V6Gy > 90%
Kidney R & L	Dmean < 8Gy	-
Lens	Dmean < 8Gy	Dmean < 10Gy

Source: The Author (2024).
* PTV was cropped from PTV_ribs, PTV_lung_out, PTV_lung_inner and PTV_kidneys
Source: Loginova et al, 2022[5]

Because of Precision´s limitation in performing a plan summation from different studysets, both dose distributions (superior and inferior) were exported to Eclipse in order to evaluate the adequacy of coverage in the junction region (Fig.8). In order to visualize the dose distribution, both studysets should have the same calculation grid size. So, before starting the plans, both superior and inferior studysets were extended so that both have the same length.

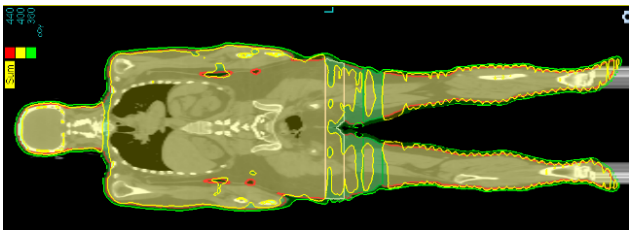

Figure 8: Typical dose distribution of a 2 x 200 cGy plan optimized using TomoDirect for the superior PTV and TomoHelical for the inferior PTV

2.4 Patient Specific Quality Assurance

After being approved by a certified radiation oncologist, all treatment plans were evaluated at the machine by irradiating a SunNuclear ArcCheck® (SunNuclear) device with a PinPoint 31014 (PTW) ionization chamber inserted. The measured dose distribution was compared to the calculated dose before delivering the plan to the patient.

A gamma analysis with 5%/3mm and 10% threshold was used and a 5% dose tolerance to the ionization chamber was considered acceptable. As the ArcCheck length is not enough to cover the entire body, the plan is irradiated more than one time to evaluate different regions of the target (head, thorax and gradient region, for example).

All patients were submitted to an in-vivo dosimetry at the first fraction using SunNuclear QED® (Fig.9).

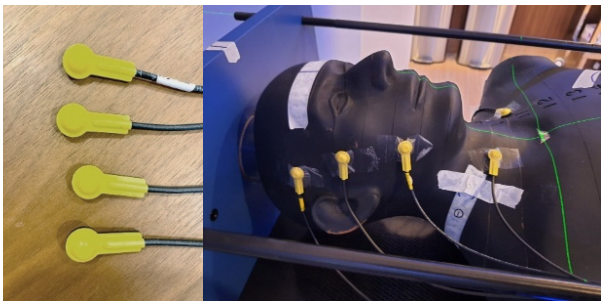

Figure 9: In-vivo dosimetry illustration

2.5 IGRT and dose delivery

A BODY_IGRT structure were defined as a body expansion of 5 mm. To assure the right positioning of the patient, an MVCT image was taken for each patient plan. Images are evaluated so that the entire patient is enclosed by the BODY_IGRT structure. For the superior plan, the image is usually acquired from the middle of the skull to the beginning of the dose gradient region, while for the inferior plan it is usually

acquired from the sole of the feet to middle of the femurs. Example of typical IGRT images are shown in Figure 10. Verification is done every fraction before the treatment of each plan. Shifts can be performed with 4 degrees of freedom (translations and roll). All verification shifts were applied before treatment.

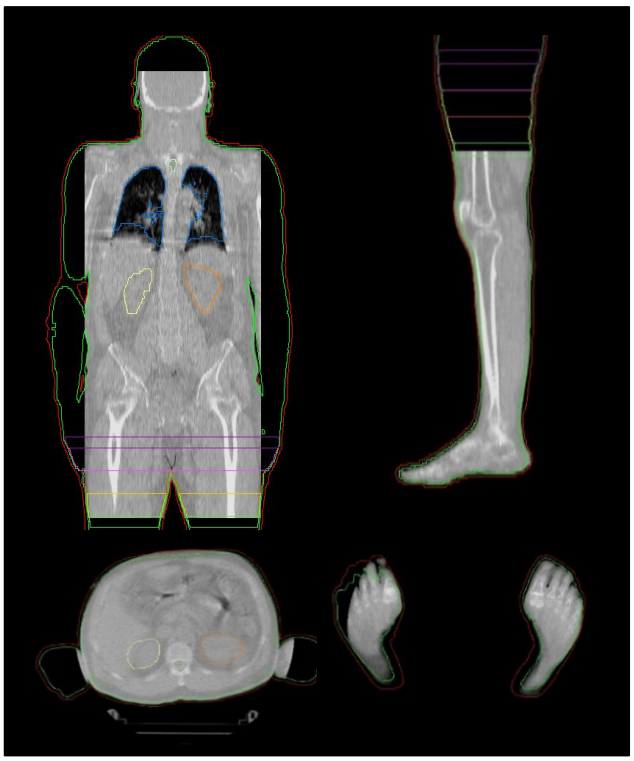

Figure 10: MVCT images from one patient showing good quality registration. It can be observed slight differences between treatment images (grayscale) and CT body contour (green line), but patient's body is still included at the IGRT_Body (red contour)

3. Results

From November 2019 to March 2024, 20 patients were planned and treated at our institution. Dose prescription varied from 2 Gy to 12 Gy (1 fx – 8 fx). The average target longitudinal extension was 1.73 (1.58-1.95) m. As all patients were higher than CT maximum scan length they needed two scans and two different treatment plans to cover the entire body.

3.1 Treatment planning

Average beam on times were 17.0 (13.5 – 20.2) min to treat the superior portion plus 13.8 (8.4 – 20.6) min to treat the inferior portion. Total beam on time can be roughly estimated (with an average error of less than 60 s) by multiplying the total longitudinal extension of the patient (in centimeters) by 11 s/cm. Metrics for coverage and homogeneity are reported in Table 2. Initial optimization objectives for different fractionations were saved as templates (Fig.11 and Fig.12) allowing the planning process to be more standardized and efficient.

Table 2: Metrics for target coverage and homogeneity from the treatment planning

Patient	Total dose (Gy)	Technique – superior region	D95%	D90%	D2%	Dmax
1	4	Helical	97.8	99.4	106.7	117.4
2	4	Helical	94.5	98.9	104.3	109.5
3	4	Direct	99.2	100.0	106.0	111.7
4	4	Helical	95.4	98.3	105.5	112.6
5	4	Helical	94.2	98.3	105.1	110.1
6	2	Direct	96.4	99.7	105.7	114.3
7	2	Direct	98.3	99.8	105.8	108.7
8	2	Direct	98.9	99.9	106.2	111.2
9	12	Helical	95.7	98.4	107.7	118.9
10	8	Direct	97.2	99.5	104.9	110.1
11	12	Helical	95.4	97.9	107.1	115.3
12	4	Direct	97.7	99.8	106.2	113.8
13	12	Helical	95.3	98.1	107.1	115.7
14	4	Direct	98.5	99.9	105.4	109.0
15	2	Direct	97.7	99.8	105.1	108.5
16	12	Helical	93.5	98.0	106.2	116.8
17	4	Direct	98.7	99.9	105.5	109.7
18	8	Helical	98.2	99.7	105.3	108.9
19	4	Direct	98.8	100.0	105.4	111.8
20	4	Direct	98.8	99.9	105.9	110.5
Mean	-	-	97.0	99.3	105.8	112.2

Source: The Author (2024)

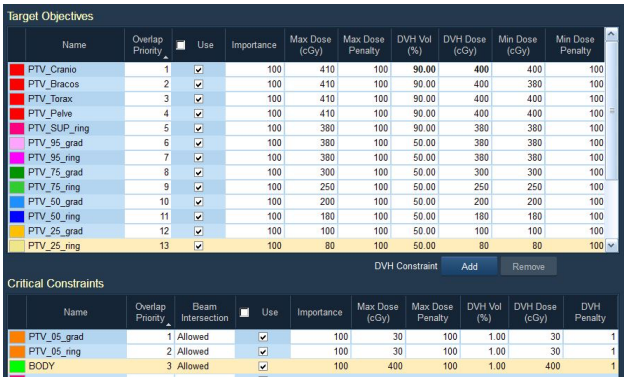

Figure 11: Initial dose objectives and critical constraints table for a 2 x 200 cGy plan (superior part)

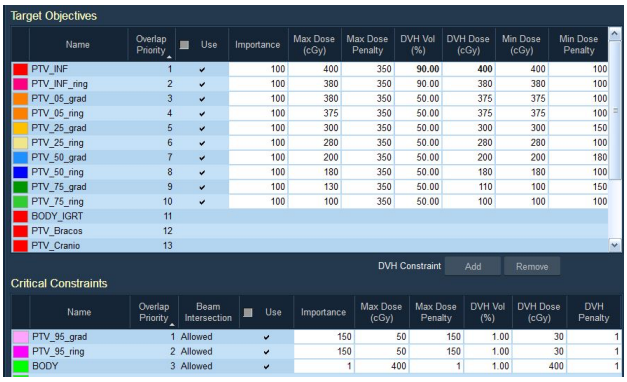

Figure 12: Initial dose objectives and critical constraints table for a 2 x 200 cGy plan (inferior part)

3.2 IGRT and verification shifts

An analysis of the positioning offset was performed for 62 fractions and the mean deviation for each patient was recorded. The average shifts for the superior portion of the target were 0.2 mm, -0.3 mm, 2.4 mm and 0.2º in the x (lateral), y (longitudinal), z (vertical) and roll directions, respectively. For the inferior portion, average shifts were 1.4 mm, -4.3 mm,

2.4 mm and 0° in x, y, z and roll, respectively. Box plots of the shifts are illustrated in Fig.13.

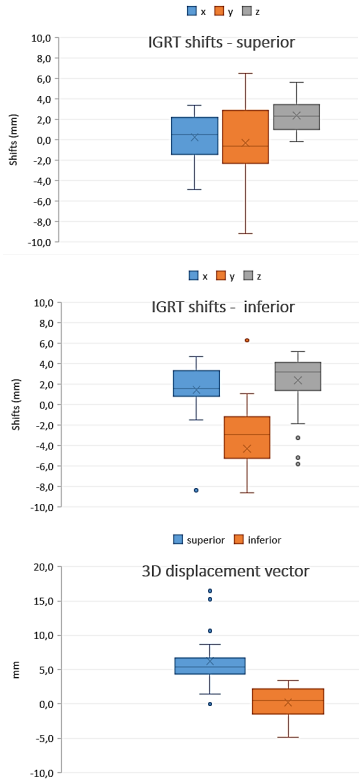

Figure 13: Shifts applied based on the IGRT images from the patients and the 3D vector displacement

3.3 In-vivo dosimetry

In 189 measurement points, 85.2% measured a dose that is within 90-110% of the prescribed dose. The overall mean deviation was 2.6%. The maximum deviation from the prescribed dose was 24.4% in a point located at the gradient region (around PTV_75%_grad) and a minimum measured dose of 20% inferior to the prescribed dose was measured in a pointed located in the arms region and for a TomoHelical delivery plan. In-vivo dosimetry results (mean and standard deviation) for each patient are illustrated in Fig.14.

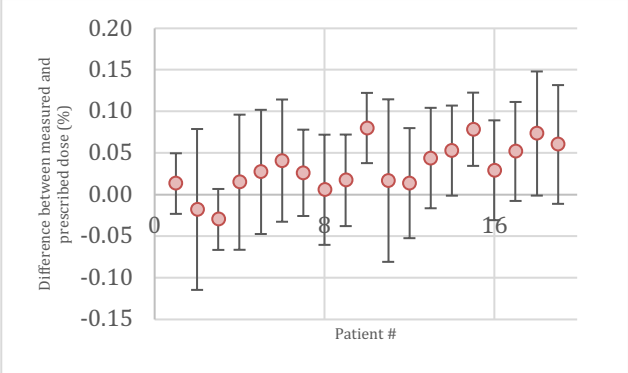

Figure 14: In-vivo doses reported as the difference from the prescribed dose

4. Discussion

Dose objectives were easily achieved using plan templates, with only minor adjustments needed.

TomoDirect was used for treatment planning of the superior target for 57% of patients. Compared to TomoDirect, TomoHelical delivery was correlated to a worse coverage (D98% = 85.2% vs 98.0%, p = 0,009) and higher heterogeneity (HI = 19,7 vs 6,6, p = 0,014) to the PTV_Arms. Coverage of the patients' arms can be technically difficult with both techniques due to the axial field size limitation of 40 cm. With TomoDirect, the loss is usually easily manageable to be within +/- 10% of the prescription dose. However, achieving this homogeneity with TomoHelical plans can be very challenging due to the thread effect, which is a ripple on the off-axis dose caused by the helical pitch (7). This effect is illustrated in Figure 15. For this reason, our current protocol favors using TomoDirect delivery for low dose treatments, with TomoHelical delivery for the superior region being preferred only in cases with a prescription dose higher than 8 Gy, in which a higher modulation capability is needed for the sparing of lungs and kidneys.

One disadvantage of TomoDirect delivery is that the patient goes out of the bore at the end of every beam instead of continuously and slowly moving inside the gantry a single time in TomoHelical delivery, which may cause some patient discomfort. Additionally, during quality assurance of TomoDirect plans with ArcCheck, the device's electronics are irradiated when measuring the centermost dose distribution.

Figure 15: Loss of coverage in the arms on a TomoHelical plan due to the helical thread effect

The average positioning offsets were below 5 mm for all directions, showing good reproducibility of the immobilization system. Some outliers could be observed, which might be related to insufficient skin marks or poor molding of the cushion vacuum.

In-vivo dosimetry reassures the system's capability of delivering a homogeneous dose distribution, but the presence of outliers warrants the need of using the gradient regions during treatment planning, since offsets could cause unacceptable dose deviations.

Despite the time spent to contour all the structures needed on the optimization process, dose distribution and patient experience is superior to traditional TBI treatment methods.

5. Conclusions

Modulated TBI treatments with Tomotherapy showed homogeneous dose distributions, with good target coverage. The metrics presented could be used as a guide to those institutions willing to implement TBI with Tomotherapy.

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