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Modulated volumetric arc therapy for total marrow irradiation: A feasibility study in the oncology hospital of CMN SXXI from a medical physics approach

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ABSTRACT

Aim: The objective of this study is to explore the use of volumetric arc therapy (VMAT) to perform total marrow irradiation (TMI) and compare its results to the standard TBI technique in the Mexican public health system.

Background: The standard total body irradiation (TBI) technique is used with chemotherapy as a method of a pre-transplant conditioning of the bone marrow. In this technique, the whole body of the patient is considered to be PTV and irradiated generating toxicities and raising concerns about possible development of radio-induced tumors.

Materials and methods: Through the use of simulation tomography of 12 patients previously treated with TBI, twelve different treatment plans were created with the proposed TMI technique and compared with the conventional protocol, the treatment plans were evaluated with a dose volume histogram analysis and quality assurance was evaluated with a portal dosimetry system using the gamma index criteria 3%/3 mm.

Results: Experimental results show an increasing dose to 99% of PTV of up to 41.1% by using TMI with the VMAT technique. The mean average dose to PTV was increased up to 19.3%. The use of the new TMI technique caused an improvement in the mean average dose to 99% of the PTV as well the homogeneity of the dose distribution prescribed at the PTV while leading to a better reproducibility of the treatment. The Qa of all the plans met the criterion of gamma index 3 mm-3%.

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Conclusion: The results analysis shows that the proposed TMI technique is feasible and applicable in the Mexican public health system.

1. Background

Total body irradiation (TBI) is used in conjunction with chemotherapy as a method of a pre-transplant conditioning of the bone marrow. In this technique, the whole body of the patient is considered PTV and irradiated with a prescription dose of 12 Gy with the objective of obtaining a sufficient modular ablation to improve the chances that the bone marrow transplant is satisfactory,[1,14,16–20] the total body irradiation protocol used in our center consists of a pair of opposing parallel irradiation fields between which the patient is placed at a distance of 4 m skin surface distance (SSD) so that the divergence of the radiation beam is able to irradiate the entire PTV.[21] This implies irradiation of radio-sensitive organs (OAR) that surround the PTV, generating toxicities, limiting the possibility of escalation of doses and raising concerns about the possible development of radio induced tumors.[14–17] The search for new options to replace this technique has created different proposals, one of them is total marrow irradiation; a technique to irradiate only the areas where the bone marrow has production peaks of hematopoietic cells (the bone system of the skull to the middle third of the femur, excluding the jaw and arms) (Fig. 1). In the literature, a helical tomotherapy equipment has been used (TomoTherapy Inc., Madison, WI) with a limited number of patients and has been reported to be able to significantly reduce the doses to tissues and organs at risk (OAR). In addition to maintaining or improving the homogeneity of the dose and coverage of the planning target volume (PTV),[2–4,8] in the bibliographic review there was no reference to the use of a conventional linear accelerator to perform the TMI technique in Mexico or Latin America and the number of patients reported in this work exceeds the average number in similar studies in other countries. The objective of this study is to investigate the feasibility of using the TMI technique by proposing and evaluating the VMAT technology (Varian medical Systems, Palo Alto, CA) and comparing it with the TBI technique, applying the protocol of our center using the data obtained by the TPS Eclipse version 13.6.

2. Materials and methods

For the present study, computed tomography images were used of 12 patients who had received total body irradiation with conventional technique used in the oncology hospital of CMN SXX. The clinical target volume (CTV) consisted of all the bones contained in the body from the skull to the middle third of the femurs, excluding the bone of the jaw and both arms, including a margin around the bone marrow, finally to obtain the planning treatment volume (PTV) an additional margin of 3 mm was added to the CTV (Fig. 1). To facilitate planning, three isocenters were placed in the anatomical regions corresponding to the head and neck, chest and abdomen, pelvis and middle third of the femur. A total of two dynamic arcs were placed in the first isocenter (head and neck), four in the second one (thorax and abdomen) and 3 in the third one (pelvis and middle third of the femur) using a methodology similar to that described by Aydogan et al.[22]

The organs at risk were delineated by the radiation oncologist according to the guidelines used in our hospital. The TMI treatment plans used in this study were made using the VMAT system provided within the Eclipse planning system version 13 (Varian Medical System, Palo Alto, CA). The photon optimizer algorithm version 13.6.23 was used for the optimization and anisotropic analytical algorithm version 10.0.28 for the calculation of treatment plans. Three isocenters were used with a total of nine dynamic arcs that ran between the 179–180.1 angles with a combination of clockwise and anti-clockwise rotations, 10-degree collimator turns for clockwise rotations and 350° for anti-clockwise rotations (Fig. 2). For the generation of the TBI treatments, the same tomographic images were used as in the TMI where we applied a pair of opposite parallel fields, beams with an energy of 10 MeV (photons) to a SSD of 4 m with a collimator opening of 40 cm × 40 cm and a collimator rotation of 45°. The TBI plans were normalized in such a way that the monitor units (UM) calculated by the TPS coincided with those calculated by the method used in our hospital, the TMI plans were normalized in such a way that the 95% of the PTV received 12 Gy. The analysis of the dosimetric data was made using the information provided by the volume dose histograms of each treatment. For the verification of the plans, we worked with the Dosimetry Portal system of Varian Medical Systems obtaining a cumulative dose plane for the total rotations in each isocenter and comparing it with the one generated in the planning system and in this way evaluated the criterion gamma index 90% 3 mm-3%. The difference between the two techniques (TMI and TBI) was evaluated applying the Student *T*-test to the data obtained from the OAR and PTV.

3. Results

A representative dose distribution in 3D solid color of the proposed VMAT-TMI is shown in Fig. 2, the axial dose distribution for the isocenter corresponding to the head and neck is shown in Fig. 3a, the isocenter of the chest in Fig. 3b and the dose curve of prescription obtained in which OARs are successfully protected as shown in Fig. 3c, d. A representative volume dose histogram is shown in Fig. 4. Table 1 shows the doses corresponding to 99% of the volume of the PTV at 1% of the volume of it and its average dose. The average dose corresponding to D99 is 11.14 Gy, the average D1 is 15.27 Gy while its average dose is 13.12 Gy. The average doses of the OAR evaluated are shown in Table 2. These were generally lower

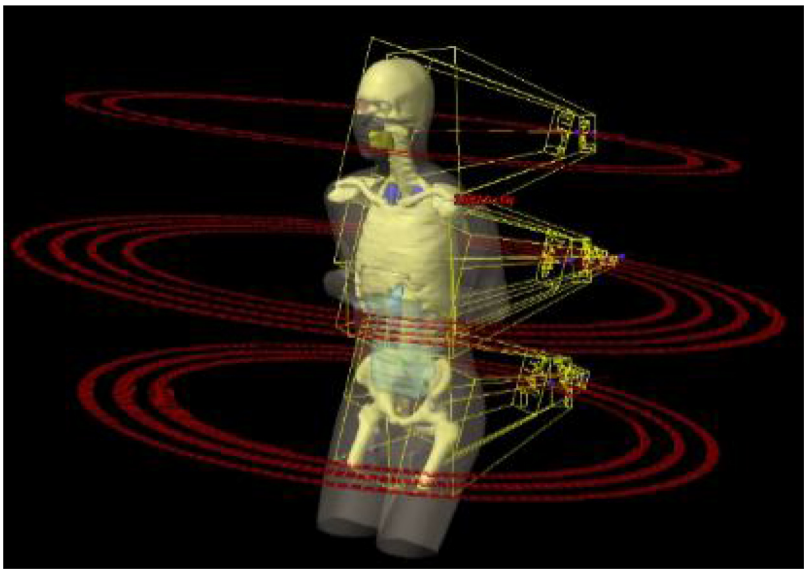


Fig. 1 – Volumetric arc therapy total marrow irradiation plan consisting of nine arcs.

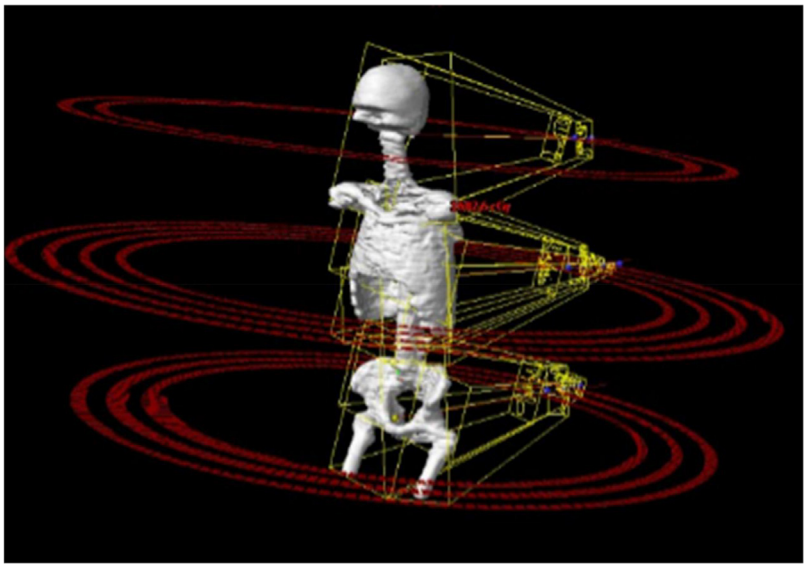


Fig. 2 – Volumetric arc therapy total marrow irradiation 1200 cGy dose and collimator rotations.

than the prescription dose and in the case of the lens, they were 7.5 Gy. Table 3 shows the maximum average doses, D1 and D99 of all the evaluated organs where none of the OAR receives the prescription dose in its entire volume. In the case of the TBI technique, Table 4 shows the doses corresponding to 99% of the volume of the PTV at 1% of the volume thereof and its average dose, the average dose corresponding to D99 is 7.89 Gy, the average D1 is 14.5 Gy while the average dose is 11 Gy (Table 5). The average doses of the OAR evaluated are shown in Tables 4 and 6, shows the maximum average doses, D1 and D99 of all the organs evaluated, the median and D99 dose for PTV is significantly reduced (Table 7). The average time in which the treatment is triggered in the linear accelerator is 18 min, which corresponds to 2 min per arc. The verification of the treatment plans was made using the Portal Dosimetry system (Varian medical Systems, Palo Alto, CA). In this test, all the plans satisfied the analysis criterion by gamma index 3 mm-3% in more than 90% of the points evaluated. The results of the Student *T*-test delivered a value of $p < .05$, for all organs at risk evaluated (with exception of the liver) and PTV values for D1, D99 and mean dose, which made us conclude that the variation is statistically significant.

4. Discussion

During the literature review we found that similar studies include only 5 patients on average. They do not offer

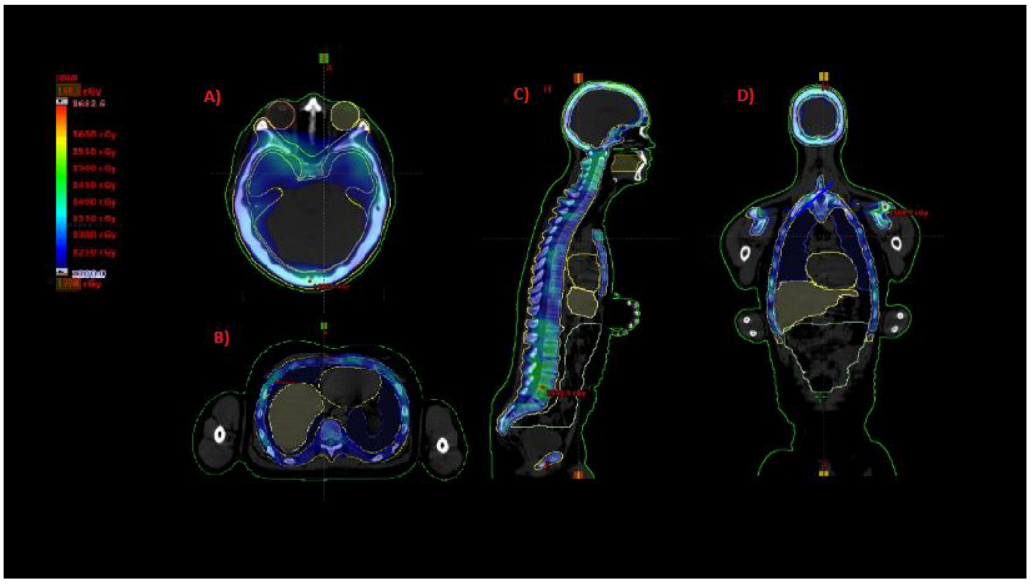
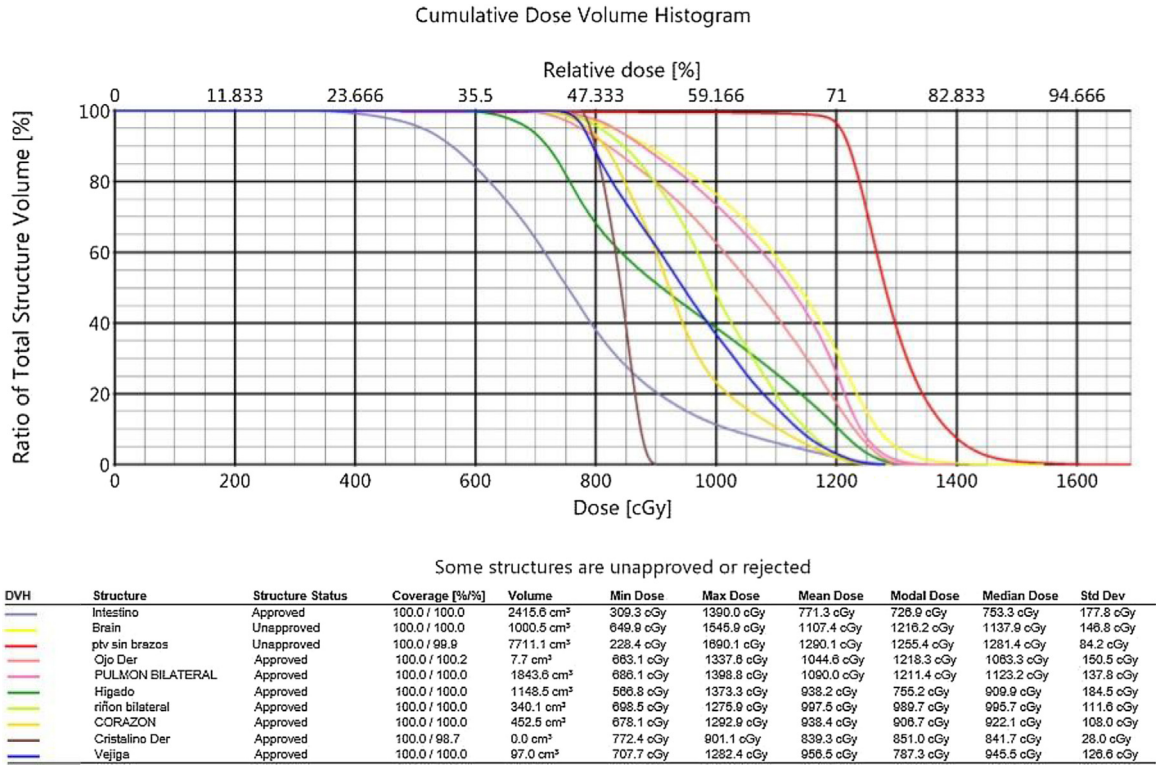


Fig. 3 – RapidArc volumetric arc therapy total marrow irradiation isodose distributions in colorwash: (a) head and neck axial, (b) chest axial, (c) sagittal, and (d) coronal view.



DVH	Structure	Structure Status	Coverage [%/%]	Volume	Min Dose	Max Dose	Mean Dose	Modal Dose	Median Dose	Std Dev
	Intestino	Approved	100.0 / 100.0	2415.6 cm³	309.3 cGy	1390.0 cGy	771.3 cGy	726.9 cGy	753.3 cGy	177.8 cGy
	Brain	Unapproved	100.0 / 100.0	1000.5 cm³	649.9 cGy	1545.9 cGy	1107.4 cGy	1216.2 cGy	1137.9 cGy	146.8 cGy
	ptv sin brazos	Unapproved	100.0 / 99.9	7711.1 cm³	228.4 cGy	1690.1 cGy	1290.1 cGy	1255.4 cGy	1281.4 cGy	84.2 cGy
	Ojo Der	Approved	100.0 / 100.2	7.7 cm³	663.1 cGy	1337.6 cGy	1044.6 cGy	1218.3 cGy	1063.3 cGy	150.5 cGy
	PULMON BILATERAL	Approved	100.0 / 100.0	1843.6 cm³	686.1 cGy	1398.8 cGy	1090.0 cGy	1211.4 cGy	1123.2 cGy	137.8 cGy
	Higado	Approved	100.0 / 100.0	1148.5 cm³	566.8 cGy	1373.3 cGy	938.2 cGy	755.2 cGy	909.9 cGy	184.5 cGy
	riñon bilateral	Approved	100.0 / 100.0	340.1 cm³	698.5 cGy	1275.9 cGy	997.5 cGy	989.7 cGy	995.7 cGy	111.6 cGy
	CORAZON	Approved	100.0 / 100.0	452.5 cm³	678.1 cGy	1292.9 cGy	938.4 cGy	906.7 cGy	922.1 cGy	108.0 cGy
	Cristalino Der	Approved	100.0 / 98.7	0.0 cm³	772.4 cGy	901.1 cGy	839.3 cGy	851.0 cGy	841.7 cGy	28.0 cGy
	Vejiga	Approved	100.0 / 100.0	97.0 cm³	707.7 cGy	1282.4 cGy	956.5 cGy	787.3 cGy	945.5 cGy	126.6 cGy

Fig. 4 – Dose volume histogram for the planning target volume (PTV) yellow and several organs at risk.

Table 1 – TMI planning target volume dose.

Variable	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	Average	STDV
D99	1050	1070	1084	1153	1097	1077	1063	1174	1144	1129	1174	1153	1114	41.66
D1	1530	1557	1520	1494	1622	1487	1620	1457	1568	1507	1491	1482	1527.91	49.31
Mean dose	1315	1345	1320	1290	1329	1304	1338	1292	1333	1300	1302	1285	1312.75	18.57

Abbreviation: Dn, radiation dose (cGy) delivered to *n* percentage of the planning target volume.

Table 2 – TMI median doses for organs at risk.

Organ at risk (OAR)	Median dose (cGy)													
	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	Average	STDV
Lungs	1210	1212	1167	1090	1235	1184	1238	1045	1121	1101	1144	1088	1152.92	59.16
Heart	1108	1151	1211	938	1138	1037	1031	950	946	955	994	870	1027.42	95.90
Kidneys	1117	1175	929	997	1166	1154	1091	934	992	979	1088	973	1049.58	84.47
Liver	1081	1229	1119	938	1164	1075	1048	818	1004	988	1037	898	1033.25	105.11
Bowels	1033	1067	1052	771	972	888	984	950	796	859	817	697	907.17	111.00
Brain	1364	1404	1405	1107	1426	1320	1390	1098	1124	1123	1164	1086	1250.92	131.87
Eyes	1024	1105	1045	1016	1068	1066	1062	867	998	905	975	1003	1011.17	63.59
Lenses	729	834	783	814	809	796	810	593	773	658	735	780	759.50	65.38
Body	909	917	908	972	979	878	709	774	922	927	868	858	885.08	71.27

Abbreviation: OAR, organ at risk.

Table 3 – TMI average doses for organs at risk.

OAR	Maximum (cGy)	D1(cGy)	D99(cGy)
Lungs	1467.41	1355.66	853.16
Heart	1361.16	1266.08	799.16
Kidneys	1317.08	1240.25	818.16
Liver	1446.08	1343.16	721.5
Bowels	1446.25	1320.41	534.83
Brain	1565.16	1455.33	986.66
Eyes	1376.16	1336.58	602.16
Lenses	785.66	831.416	688.58
Body	1586.1	1466.08	33.75

Abbreviation: OAR, organ at risk.

Table 6 – TBI Average doses for organs at risk.

OAR	Maximum (cGy)	D1(cGy)	D99(cGy)
Lungs	1233.08	1167.66	869.91
Heart	1250.33	1228.66	1087
Kidneys	1134.75	1119.91	898.58
Liver	1250.5	1219.91	895
Bowels	1318.75	1275.25	983.75
Brain	1504.83	1454.83	1327.16
Eyes	1468.16	1461.33	1189.33
Lenses	1415.33	1410.5	1293.91
Body	1681	1482	790.25

information about the optimization algorithms and/or calculation they used and they were all performed in Europe and North America (the weights and sizes of their population vary significantly from those of the Mexican population). Studying the feasibility of this type of treatment for Latin America and Mexico is considered a priority. Among the main differences between this work and the literature is the number of patients evaluated (12 patients), which is twice the average in similar works. We offer a different technique than previously reported, a variation in the rotation of the multileaf collimator of $\pm 10^{\circ}$ (in order to eliminate the influence of the tongue and groove effect in the treatment) in contrast to the 90° for all the arcs. Despite these differences, our results are not quite similar to those reported but although the proposed technique is

Table 4 – TBI planning target volume dose.

Variable	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	Average	STDV
D99	822	840	823	835	815	792	778	742	741	784	758	743	789.41	34.40
D1	1578	1495	1452	1578	1630	1457	1399	1384	1364	1382	1353	1328	1450	92.20
Mean dose	1166	1118	1125	1168	1156	1077	1081	1073	1044	1100	1050	1052	1100.83	41.71

Table 5 – TBI median doses for organs at risk.

Organ at risk (OAR)	Median dose (cGy)													
	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	Average	STDV
Lungs	1042	984	1008	1017	1023	1003	967	1056	987	1053	1011	995	1012.16	25.55
Heart	1255	1150	1177	1249	1264	1129	1076	1220	1150	1216	1159	1078	1176.91	59.68
Kidneys	940	987	938	1099	989	911	946	1040	997	1012	1010	990	988.25	46.96
Liver	1121	1049	1144	1035	1163	1020	974	1112	1070	1058	1072	1023	1070.08	51.31
Bowels	1207	1136	1146	1249	1186	1119	1065	1167	1138	1166	1131	1097	1150.58	45.23
Brain	1520	1423	1362	1491	1541	1396	1345	1332	1426	1314	1287	1270	1392.25	82.84
Eyes	1561	1437	1365	1544	1578	1410	1369	1374	1289	1311	1345	1262	1403.75	97.99
Lenses	1521	1414	1325	1519	1551	1348	1347	1378	1244	1266	1314	1190	1368.08	105.61
Body	1166	1118	1125	1168	1156	1077	1081	1073	1085	1100	1044	1052	1103.75	39.40

Table 7 – TBI vs. TMI average doses for organs at risk.

OAR	TBI Maximum (cGy)	TMI Maximum (cGy)	TBI D1 (cGy)	TMI D1 (cGy)	TBI D99 (cGy)	TMI D99 (cGy)	TBI Median dose (cGy)	TMI Median dose (cGy)
Lungs	1233.08	1467.42	1167.67	1355.67	869.92	853.17	1012.17	1152.92
Heart	1250.33	1361.17	1228.67	1266.08	1087.00	799.17	1176.92	1027.42
Kidneys	1134.75	1317.08	1119.92	1240.25	898.58	818.17	988.25	1049.58
Liver	1250.50	1446.08	1219.92	1343.17	895.00	721.50	1070.08	1033.25
Bowels	1318.75	1446.25	1275.25	1320.42	983.75	534.83	1150.58	907.17
Brain	1504.83	1565.17	1454.83	1455.33	1327.17	986.67	1392.25	1250.92
Eyes	1468.17	1376.17	1461.33	1336.58	1189.33	602.17	1403.75	1011.17
Lenses	1415.33	785.67	1410.50	831.42	1293.92	688.58	1368.08	759.50
Body	1681	1586.1	1482	1466.08	790.25	33.75	1103.75	885.08

able to perform a TMI in a satisfactory manner and protect at-risk organs adjacent to the target volume while conserving or improving the quality of coverage and homogeneity, it is necessary to take into account the influence of using an average dose rate during the treatment in comparison with the fixed dose rate used in the TBI technique, in addition to the need to standardize the target volume and take into account the time necessary to carry out the planning and quality control in the TMI technique.

Even though we found important differences between the average doses to OAR obtained and those reported in similar studies, for example, by Aydogan et al.[22] we consider that our results represent an improvement and advancement against the TBI technique used in Mexico and Latin America. We are working on reproducing the results obtained by Aydogan et al.[22] and similar, based on improving the technique that we propose in this work.

5. Conclusions

The VMAT-TMI technique is capable of overcoming the gamma index test (standard quality control test in modulated intensity treatments), improves the average dose of PTV by 19.3% and its D99% by 41%, while generating coverage and homogeneity in the dose delivered to the target volume and adequately protecting the organs at risk as evaluated in Table 7. This makes it a feasible replacement from a physical point of view to the conventional TBI technique.

Conflict of interest

None declared.

Financial disclosure

None declared.

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REFERENCES

1. Bieri S, Helg C, Chapuis B, et al. Total body irradiation before allogeneic bone marrow transplantation: is more dose better? *Int J Radiat Oncol Biol Phys* 2001;**49**:1071–7.
2. Hui SK, Kapatoes J, Fowler J, et al. Feasibility study of helical tomotherapy for total body or total marrow irradiation. *Med Phys* 2005;**32**:3214–24.
3. Schultheiss TE, Wong J, Liu A, et al. Image-guided total marrow and total lymphatic irradiation using helical tomotherapy. *Int J Radiat Oncol Biol Phys* 2007;**67**: 1259–67.
4. Wong JY, Liu A, Schultheiss T, et al. Targeted total marrow irradiation using three-dimensional image-guided tomographic intensity-modulated radiation therapy: an alternative to standard total body irradiation. *Biol Blood Marrow Transplant* 2006;**12**:306–15.
8. Otto K. Volumetric modulated arc therapy: IMRT in a single gantry arc. *Med Phys* 2008;**35**:310–7.
14. Curtis RE, Rowlings PA, Deeg HJ, et al. Solid cancers after bone marrow transplantation. *N Engl J Med* 1997;**336**: 897–904.
15. HasegawaW, Pond GR, Rifkind JT, et al. Long-term follow-up of secondary malignancies in adults after allogeneic bone marrow transplantation. *Bone Marrow Transplant* 2005;**35**:51–5.
16. Thomas BC, Stanhope R, Plowman PN, et al. Growth following single fraction and fractionated total body irradiation for bone marrow transplantation. *Eur J Pediatr* 1993;**152**: 888–92.
17. Leiper AD. Late effects of total body irradiation. *Arch Dis Child* 1995;**72**:382–5.
18. Blaise D, Maraninchi D, Archimbaud E, et al. Allogeneic bone marrow transplantation for acute myeloid leukemia in first remission: a randomized trial of a busulfan-Cytoxan versus

Cytoxan-total body irradiation as preparative regimen: a report from the Group d'Etudes de la Greffe de Moelle Osseuse. *Blood* 1992;**79**:2578–82.
19. Ringden O, Remberger M, Ruutu T, et al., for the Nordic Bone Marrow Transplantation Group. Increased risk of chronic graft versus- host disease, obstructive bronchiolitis, and alopecia with busulfan versus total body irradiation: long-term results of a randomized trial in allogeneic marrow recipients with leukemia. *Blood* 1999;**93**:2196–201.
20. Socie G, Clift RA, Blaise D, et al. Busulfan plus cyclophosphamide compared with total-body irradiation plus cyclophosphamide before marrow transplantation for myeloid leukemia: long-term follow-up of 4 randomized studies. *Blood* 2001;**98**:3569–74.
21. AAPM American Association of Physicist in Medicine. *Report Task Group no. 17: The Physical Aspects of Total and Half Body Photon Irradiation, EUA*; 1986.
22. Aydogan B, Yeginer M, Kavak GO, Fan J, Radosevich JA, Gwe-Ya K. Total marrow irradiation with RapidArc volumetric arc therapy. *Int J Radiat Oncol Biol Phys* 2011;**81**(2): 592–9.