



Original Article

Multi-Detector *in Vivo* Dosimetry of Volumetric Arcs of Total Body Irradiation: An Institutional Comparative Study

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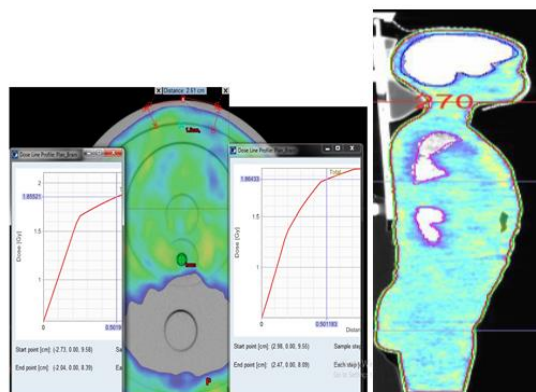
ABSTRACT

Background: The purpose of this study was to evaluate the dosimetric difference in calculated and measured doses for volumetric modulated arc therapy enabled total body irradiation (VMAT-TBI) technique. The study also aims to find the uniformity of doses delivered at the junction region of two adjacent isocentric arcs using three different detectors. **Material and Methods:** This phantom study was performed on arc phantom and contains three different detectors: Gafchromic films, silicon diodes, and 0.6cc ionisation chamber. Measured doses using Gafchromic films and silicon diodes were the representative of skin surface doses and the 0.6cc chamber measured the mid plane doses at each isocenter. Ten (10) selected patients from the data base were the representative for this retrospective dosimetric analysis, verification and in-vivo dosimetry, however, the pre-treatment verification of all VMAT-TBI plans were already completed using EPIQA and Octavious phantom. Epson 1100 flatbed scanner was used for film scanning. The Gamma analysis and average dose difference between TPS calculated and measured with different dosimeters were found.

Results: The found dose difference in surface doses measured using Gafchromic film is in the range from 0.044 to 0.204 cGy and for diodes the range is from 0 to 0.112 cGy with respect to planned values. The point doses at each arc isocenter were within 3% of TPS calculated.

Conclusion: The diodes, gafchromic films and used ionisation chamber are in good agreement with the TPS doses. Hence, it can be concluded and suggested that any available detector is good for dose determination in TBI.

GRAPHICAL ABSTRACT



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Introduction

The blood cancer in India has a high prevalence along with other blood-related disorders like thalassemia or aplastic anemia. In every five minutes, someone in India is diagnosed with blood cancer as per report of Deutsche Knochenmarkspenderdate or German Bone Marrow Donor Center - Bangalore Medical Services Trust (DKMS-BMST) foundation India along with other cancer incidences in India [1, 2]. As per Leukemia & Lymphoma Society (LLS) every third person in United States (US) is diagnosed with blood disorders. The common diseases are leukemia, lymphoma, or myeloma [3].

Chemotherapy drugs and some pro-drugs have a role in cancer along with radiation [4, 5].

Blood circulation and marrow forming sites are in the whole body, so total body is conditioned with a radiation dose of 12-14 Gy in 6-8 fractions. Total body irradiation (TBI) is a special radiotherapy procedure and pre-conditioning regimen for patients (pts) with hematological malignancies having low immune system that undergo bone marrow transplant (BMT). Just like the other treatment sites like breast, and pelvic malignancies, the role of modulated treatments has increased due to advent of technological changes [6].

An alternative to intensity modulated radiation therapy (IMRT) is volumetric modulated arc radiation therapy (VMAT), where dose is delivered by continuously moving the radiation source through 360°. The TBI delivery significantly changed due to multiple technological innovations such as imaging modalities, dose planning, delivery technology, *in vivo* dosimeters, and measurement methods. Newly technological innovation has led to a path towards highly conformed dose delivery, reduces dose to normal tissues or organ at risk and minimize the risk of toxicity, morbidity, and secondary malignancies. Springer *et al.* reported the clinical benefit of treating whole body with the VMAT technique and selectively reducing the dose to the lungs, kidneys, heart, liver, and brain (if necessary) [7]. There is a scope of dose escalation if OARs could be spared. TBI using

VMAT is a new approach to our center for the patients who undergo BMT. The feasibility of the volumetric modulated arc therapy enabled total body irradiation (VMAT-TBI) treatment with C series linear accelerator started in March 2015 in the Department of Radiotherapy and Oncology of our Institute using Varian Trilogy.

To cover whole body from cranial to caudal height of patient up to mid-thigh, multiple successive isocenters were taken. The positional change is only in longitudinal shifts. The main focus in our study is the upper body as lower body has no critical organs so treated with conventional open AP/PA fields. In VMAT-TBI, selected dose schedule to deliver 12Gy/6#, 2Gy/#, and 2#/day with six-hour gap between two fractions. The six-hour gap is for the normal tissue repair between two fractions and treatment of patient continues three consecutive days for those who undergo bone marrow transplantation. For those patients who undergo haploidentical transplantation with non-ablative conditioning single fraction of 2Gy is delivered. The calculation of dose for multiple isocenters with overlapping arcs may cause non-trivial solutions; the doses verification along with machine specific quality assurance tests is the primary requirement and compulsory procedure. In addition, large field treatment, long treatment time, changing body separation along patient's height, and the patient movement may increase the possibility of errors. Hence, dose homogeneity due to the large variation in body contour and tissue densities may be affected, so *in vivo* dosimetry should be performed to find consistency in dose delivery with respect to the calculated TPS. Internationally accepted *in vivo* accuracy is within $\pm 10\%$ for different used dosimeters as the whole body dose homogeneity is difficult due to varying thickness in body contour [8].

Before treatment all VMAT-TBI plans are verified using EPIQA to assess clinically relevant differences between planned and delivered doses as well as plan accuracy was evaluated using GAI of 3%/3 mm [9].

This means the considered acceptance criteria is the dose difference and distance-to-agreement (DTA) [10].

Furthermore, the pre-treatment verification of VMAT plan is done using PTW 4D Octavius phantom. The multiple active and passive detectors, as well as the phantoms have been studied and reported in the literature which could be used for *in vivo* dosimetry [11, 12]. Consequently, the use of Gafchromic films for dosimetry is well defined [13, 14] and a dosimetry study also reported by Su *et al.* using gafchromic films that achieved 4.1% agreement [15].

However, measuring the doses at the junction of different arcs offers some difficulties. Thus, the aim of this study is to verify the dose difference at isocenter and also at the field edges or the junction's of adjacent arcs using three different dosimeters such as 0.6 cc farmer ion chamber, diodes, and Gafchromic films.

Material and Methods

Patient selection and target delineation

The CT images of ten patients selected randomly from data base treated with rapid arc VMAT-TBI were included in the study. The complete patient's details are listed in Table 1. The first set CT images included head to mid-thigh in head first supine position and the second set contains images from mid-abdomen to fall off of the feet in feet first supine position having 512×512 pixels with 5 mm slice thickness. After registration of two CT image data sets, planning target volume (PTV) was delineated and cropped 3 mm from the external body contour including arms and

other extremities. The PTV delineation is easy as the whole body is the target. The target is cropped 3 mm inside to avoid the interface dose calculation errors [16]. To perform a meaningful comparison and evaluation a PTV-Phy excluding critical structures (brain, lungs, heart, liver, and kidneys) was also contoured. The total time of delineation was approx. 1.5 hr/patient using interpolation and automatic/semi-automatic methods of contouring.

Table 1: Patients information included in the study

No. of Patients	10
Gender	M-7, F-1, & C-2
Mean Age	26.7 years (8pts) C-8.5 years

M: male, F- female, C- children, and pts-patients.

Planning technique

The cranio-caudal length ranges from 65 cm (children) to 110 cm (adults). The measured length is from head to the mid-thigh. PTV was optimized as a single target with multi isocentric arcs. The flowchart for plan methodology and execution is displayed in Figure 1. Mainly three to four isocenters (Figure 2a and b) were used according to patient height. The set isocenters were initially at neck region, second in thorax/abdomen region, and third in abdomen/pelvic area. The PTV should be optimally covered and for the PTV coverage, the constraints for OAR used in VMAT optimization are only for major organs b/l lungs, liver, heart, and b/l kidneys and brain (if no cranial boost is necessary).

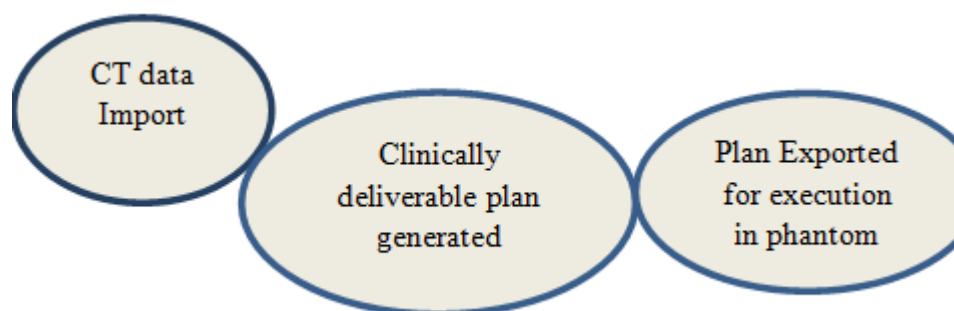


Figure 1: Flowchart for plan methodology and execution



Figure 2: Beam isocenters yellow circles written with red text and dose coverage [17]

All the plans were generated in the eclipse treatment planning system 11.0.3 having PRO3 optimization and anisotropic analytical algorithm (AAA) dose calculation algorithm on a Dell precision T 5400 series workstation from Varian Palo alto. To cover the PTV with uniform dose coverage of more than 90%, a pair of arcs one clock wise and counter clockwise at each isocenter with an additional arc at thorax and abdomen region were used. The eclipse planning system took approximately 5-7 hour for single optimization with dose calculation and average time of planning on eclipse was 15-20 hour to get good clinically deliverable plan [17]. Dose color wash is depicted in Figure 2c and d.

Plan evaluation

The visual inspection of the planned doses in the axial view was evaluated very carefully to prevent any high dose region in OAR's and low dose regions in the target area. A maximum dose of 110% was accepted globally except in OAR's region. The mean dose, D_2 (the maximum), D_{98} (the minimum) criteria were chosen in addition of global maximum. Furthermore, the mean doses of the brain, B/L lungs, liver, heart, and B/L kidneys were accepted below 10 Gy.

Plan verification

The pre-treatment verification and *in vivo* dosimetric study was divided into three parts:

- (1) Pre-treatment verification using an EPIQA and Octavious phantom.
- (2) Point dose measurement at the Arc Isocenter using 0.6 ccs Ionisation Chamber (IC).
- (3) Surface dose measurement at the junction of adjacent arcs using Gaf-Chromic films and EDP-15 p-type diodes.

Before *in vivo* dosimetry, the machine's output was verified and the plan verification using Octavious phantom was performed. The dose verification using arc phantom was performed for three different detectors, as illustrated in Figure 3a, b and c and Figure 4a, b and c. The Gaf-chromic films of 4 cm in the longitudinal direction (more than or equal to junction overlapping region 4 cm/3 cm) were used for dose measurement while point doses were measured by diode and 0.6 cc FC65G ion chamber. A total of three set of measurements for each detector were taken. Films were scanned using an EPSON 1100 flatbed scanner.



Figure 3: (a) Arc Phantom, (b) EDP-15 p-type diode, and (c) axial view

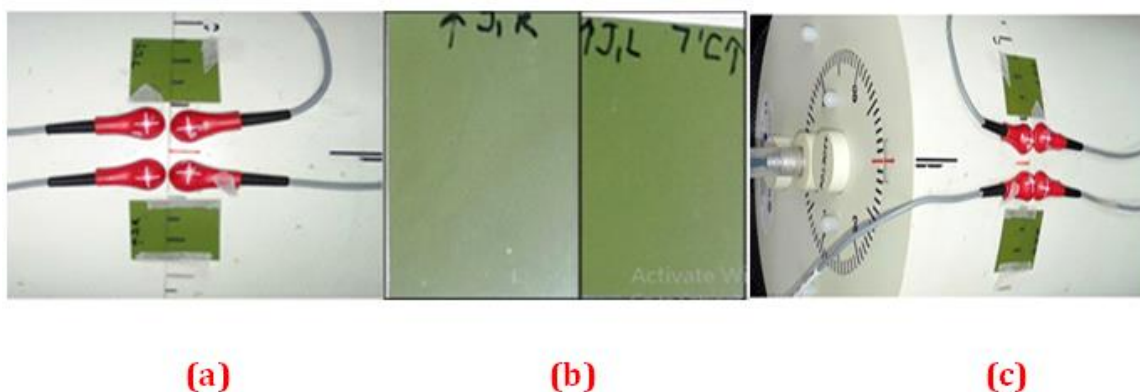


Figure 4: (a) Placement of diodes, (b) Gafchromic films, and (c) ion chamber

On scanning of the film, the values for darkness are measured using image viewer in Eclipse TPS. The Gamma analysis and average dose difference at the skin surface between TPS calculated and measured using different dosimeters were found.

Plan verification using PTW Octavius

The volume analysis at the junction of different arcs was performed.

Plan verification using 0.6 cc IC

The point dose measurement along the central axis was performed using 0.6 cc IC and chamber was placed at the center of the arc phantom (as indicated in Figure 4c, which was a low dose gradient region. The difference in the planned and measured doses was calculated.

Doses measured using diode and Gafchromic films

Figure 4a and b shows the placement of diodes and Gafchromic films on the right and left sides of the junction. Both measurements were simultaneous and difference of measured and TPS dose was calculated.

Statistical analysis

A simple dose difference and percentage variation between two doses i.e. calculated and measured doses were estimated.

Results and Discussion

Plan verification using 0.6 cc IC

Table 2 presents the TPS calculated and IC based measured doses at three different iso-centers. A maximum percentage variation between two was 2.70% in the neck isocenter. This dose variation represents the point dose measurement at the isocenter position.

Table 2: Dose measured using ionization chamber

No. of patients	TPS calculated along central axis for three isocenter	Measured value along central axis	%age variation
1	2.018, 2.293, 1.914	2.010,2.319,1.923	0.40%, 1.13%,0.90%
2	2.09,2.231,1.927	2.117,2.264,1.94	1.29%,1.48,0.67%
3	2.015,2.252,1.925	2.033,2.225,1.939	0.89%,1.2%,0.73%
4	2.08, 2.35, 1.95	2.118,2.40,1.968	1.82%,2.12%,0.92%
5	1.98, 2.25, 2.014	1.962,2.275,1.989	0.90%,1.11%,1.24%
6	2.12,2.28,1.995	2.095,2.315,2.02	1.18%,1.53%,1.25%
7	2.06,2.229,1.954	2.079,2.189,1.975	0.92%,1.79%,1.07%
8	1.995,2.332,1.908	2.016,2.269,1.929	2.70% ,1.41%,1.10%
9	1.985,2.316,1.991	2.01,2.355,2.015	1.25%,1.68%,1.205%
10	2.08,2.195,1.946	2.115,2.228,1.966	1.75%,1.54%,1.02%

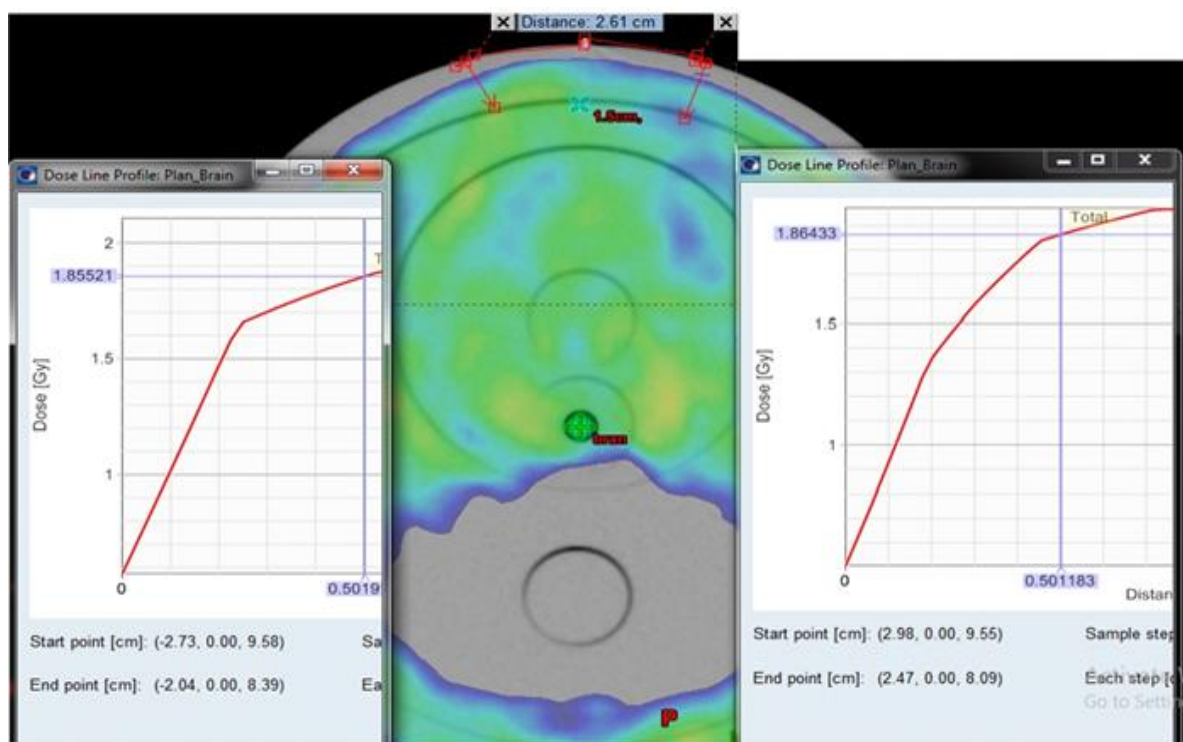


Figure 5: Treatment planning system (TPS) calculated dose at right and left sides of the isocenter

Table 3: Mean measured dose range (min-max)

Ion chamber	Variation ranges from 0.40%-2.70% at iso-center				The maximum variation is within 3%
Gafchromic films	J1_RT	0.131-0.104cGy	J1_LT	0.044-0.095cGy	The maximum variation is within 5%
	J2_RT	0.092-0.102cGy	J2_LT	0.107-0.098cGy	
	J3_RT	0.084-0.79cGy	J3_LT	0.173-0.102cGy	
Sillicon diodes	J1_RT	0.030-0.068cGy	J1_LT	0.036-0.084cGy	The maximum variation is within 5%
	J2_RT	0.09-0.10cGy	J2_LT	0.10-0.112cGy	
	J3_RT	0.0 -0.068cGy	J3_LT	0.09-0.042cGy	
PTW Phantom	Average Gamma Index at 3%, 3 mm for all isocentric arcs was calculated and it was > 96%.				

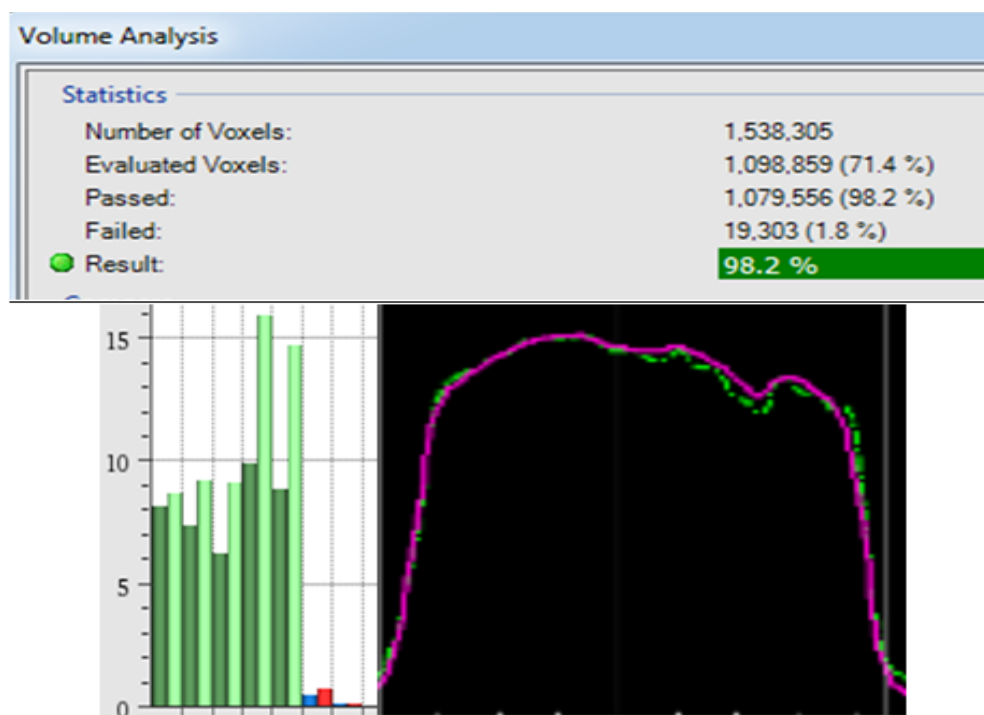


Figure 6: Octavius screenshot showing volume analysis, gamma, and dose distribution agreement

Doses measured using diode and Gafchromic films

Figure 5 shows the calculated doses at right and left sides of the iso-center and is at 5 mm depth. The depth measurement depicting the skin doses. Both the measurements were simultaneous and Table 3 provides the range from the minimum to the maximum dose difference with respect to prescribed dose for the gafchromic films and silicon diodes. The overall variation in all junctions was less than 6%.

Plan verification using PTW Octavius

The observed results of pre-treatment verification using phantom are more than 96% for 3%/3 mm DTA. Figure 6 demonstrates the volume analysis, gamma analysis, and dose distribution agreement of dose volume histogram (DVH) at abdomen/pelvic junction.

The whole body patient immobilization in nominal SSDs or old large field conventional/extended SSD methods is quite a difficult task. The long treatment time may increase the possibility of errors in dose delivery due to position discomfort. Hence, it necessitates the accuracy in delivery. On couch treatments offer us better correspondence between TPS calculated and real time measured doses using

film or delivered to the patient rather than large SSDs treatments. The different *in vivo* dosimeters for the measurement of entrance dose/skin doses to different points has also been reported like OSLD's, TLD's, Epiqa Software & EPID's, Gafchromic film and EBT2, MOSFET, and MAPCHECK [11, 18-20]. Surucu *et al.* used an anthropomorphic phantom and TLD to verify VMAT-TBI as well as demonstrated that VMAT is safe, accurate, and efficient way of delivery in junction regions from two different isocentric arcs and dose variation ranges from -4.3% - 6.6% [21].

In the present study, the arc phantom and three different dosimeters have been used and the reported results were consistent with the study conducted by Surucu *et al.* The results in Table 3 highlight the percentage variation using IC, the minimum to the maximum range of dose difference at junction and the pre-treatment verification measurements. The IC measurements are at the low gradient region confirming the point dose accuracy. The point doses measured with IC are + 3% with respect to the TPS calculated values [8].

The minimum to the maximum dose difference in the surface doses measured using Gafchromic film was in the range from 0.044 to 0.102 cGy and

is within $\pm 6\%$. For diodes at different junctions the minimum to the maximum range was from 0.0 to 0.112 cGy and the overall variation is within 5%. The observed value is in the good agreement with the results of mean percentage variation 3.5-8.5% as reported by *Arpita et al.* using MOSFET [22].

The gamma analysis of pre-treatment VMAT TBI verification plans at 3%/3 mm agreement is more than 96%, as illustrated in Figure 6. Tools and the in-house developed software for the 2D/3D gamma analysis have also been reported by number of researchers [23, 24]. *In vivo* measurements reported by Ganapathy *et al.* ranges from 6.5% -10% except at thigh region [25] and the other reported studies also show the dose uniformity over whole body within $\pm 10\%$ [26, 27]. The found results confirmed the accuracy of measurement and further validate a good positioning, reliability of set up, and delivery methods. Thus, the reported study on arc phantom is confirming the results using our own method of measurements. Hence, Gafchromic film seems to be a promising candidate for high-quality dosimetry in VMAT dosimetry along with the diodes and IC.

The limitation of the study is that it was a static phantom study for a ten limited number of patients; only clinical information could be related from our results. An elaborative clinical *in vivo* dosimetry study (consisting 70 patients) is in progress to assess the further scope for improved analysis.

Conclusion

The dose difference of $\pm 10\%$ using gafchromic films at the junctions shows the feasibility to use gafchromic films for VMAT TBI dosimetry. The measured dose difference between diodes and ionization chamber is in good agreement with the TPS calculated doses. Hence, diodes and gafchromic film seems to be a promising candidate for high-quality dosimetry in VMAT TBI.

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Disclosure Statement

No potential conflict of interest was reported by the authors.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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