Original Article

A mathematical model to predict the different isodose volumes using TRAK value in HDR intracavitary brachytherapy for revised Manchester and ICRU-89 based Point A plans using computer tomography images

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ABSTRACT

Purpose: To find out the simple relationship between Total Reference Air Kerma (TRAK) and various isodose volumes. Calculated isodose volumes were compared with experimental data for revised Manchester and International Commission on Radiation Units and measurements (ICRU)-89 Point A-based treatment plans. The accuracy of the formula was compared with the results of other relationships available in the literature.

Materials and Methods: Dosimetric data from 62 intracavitary brachytherapy (ICBT) treatment plans of 31 patients with cervical cancer were studied. Each patient had treatment plans normalized to revised Manchester and ICRU-89 Points A (A_{flange} and A_{icru89}). For each treatment plan, TRAK values, $V_{350,}$ V_{700}, $V_{1050,}$ and V_{1400} were obtained. The modeling curve was plotted between Isodose volume (V_d) and the ratio of d/TRAK obtained from A_{flange} plans to get a mathematical relation. The results of this formula were compared with the experimental data and outcomes of other formulas available in the literature. A paired-sample *t*-test was performed to assess the statistical significance.

Results: In the case of revised Manchester-based A_{flange} normalization plans, the mean isodose volume of V_{350}, V_{700}, $V_{1050,}$ and V_{1400} were 285.98 ± 32.3 cm^3, 101.96 ± 10.63 cm^3, 52.71 ± 4.72 cm^3, and 31.44 ± 2.33 cm^3 respectively. Likewise, for ICRU-89 based A_{icru89} normalization plans, the mean isodose volumes of V_{350}, V_{700}, $V_{1050,}$ and V_{1400} were 304.11 ± 26.17 cm^3, 108.88 ± 8.29 cm^3, 56.62 ± 3.69 cm^3 and 34 ± 2.23 cm^3 respectively. The mean difference was significant. The Mathematical relationship developed was $V_d(cm^3) = e^{\left(-0.1054\left(ln\left(\frac{d}{TRAK}\right)\right)^2 - 0.0544\left(ln\left(\frac{d}{TRAK}\right)\right)+10.521\right)}$. No correlation was found between TRAK and $D_{0.1cm}{}^3$,$D_{2cm}{}^3$ for organs at risk.

Conclusions: The developed formula calculated isodose volumes within the accuracy of ± 3% in ICBT plans.

KEY WORDS: American Brachytherapy Society, cervical brachytherapy, ICRU, intracavitary brachytherapy, isodose, total reference air kerma

INTRODUCTION

Treatment of cervical cancer patients includes external beam radiotherapy (EBRT) with a boost using high dose rate (HDR) brachytherapy.[1,2] The brachytherapy boost contributes higher doses to the tumor region and spares surrounding normal tissues.[3]

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Initially, radium sources were used for the treatment of cervical cancer through intracavitary brachytherapy (ICBT).[4,5] The two major parameters used for prescription in ICBT were milligram hours and dose to Point A.[6,7] With the advent of technology, different artificial radionuclides had been developed as an alternative to radium sources and therefore they were specified in milligram radium equivalent instead of milligram hour. Currently, the output of source strength is specified in terms of Reference Air Kerma Rate (RAKR) because this term includes a correction for attenuation and scattering.[8,9]

Total Reference Air Kerma (TRAK) is the integral of the RAKR from all radioactive sources at a distance of 1m from the source over the total treatment duration.[10,11]

Point A has been extensively used for dose prescription and reporting in ICBT. Primarily, Point A was used in the Manchester system defined by Tod and Meredith in 1938 and revised in 1953, so that Point A could be localized for individual patients using radiographic film.[7,12] The revised Manchester Point A was defined as 2 cm superior from the tandem flange and 2 cm lateral from the center of the intrauterine tandem. The ovoid surface edges were not clearly visible on radiographs. Therefore, the basis of localizing Point A was proposed from the lowermost position of the radioactive source or tandem flange. The revised Manchester system is still used for dose prescription in ICBT.

In ICBT, International Commission on Radiation Units and Measurements (ICRU) Report 38 recommendations are used for assessment and reporting of absorbed dose to the ICRU bladder, rectum points, pelvic wall, and lymphatic trapezoid.[10] Besides, TRAK value, description of the 60 Gy reference volume with height, width, and thickness were recommended on the orthogonal radiographs. Point A was not recommended in ICRU report 38 because of its occurrence in a high absorbed-dose gradient region, failure to locate ovoid surface on radiographs, and its position changes with intracavitary applicators instead of anatomical structures.[13-15]

With the availability of different intracavitary applicators, radioisotopes, and computer-assisted treatment planning systems (TPS), many radiation oncologists started using cervical os for locating Point A, which resulted in a larger variation in absorbed dose to Point A depending on the method used for localizing. To overcome this problem the American Brachytherapy Society (ABS) recommended a new definition of Point A with relation to the applicator, which was later amalgamated in the ICRU-89 report.[16,17] The reason to include Point A in the ICRU-89 report for dose reporting was to compare the clinical outcome of the earlier patients treated with dose prescription to Point A in ICBT and cervical cancer patients treated with volume-based planning.

Point A and TRAK reporting is reproducible and helps the clinician to compare the present, past, and future clinical practice among different institutions for dose reporting. Therefore, in addition to the volumetric assessment, dose to Point A and TRAK value are now the minimum standard of reporting for ICBT treatment as per the ICRU-89.

Previously, in ICBT, treatment planning with orthogonal radiographs, recording, and reporting of reference isodose volumes was not a routine practice.[18] In the absence of DVH parameters for target and organs at risk (OARs), the isodose level volumes could help in understanding the risk factors for treatment-related toxicities and local disease failure. Therefore, there is a need for an alternative method to calculate the isodose volumes with the help of TRAK value and Point A dose. TRAK is a vital parameter and its value can be obtained from 2-D (radiographs based) as well as three-dimensional (3D) (computed tomography [CT]-based) ICBT treatment plans.

In the quest of finding a relationship between TRAK and isodose volumes in ICBT, several researchers have derived mathematical equations to calculate various isodose volumes using the value of TRAK.[19-23] However, the mathematical formulas of some authors were based on the revised Manchester Point A definition and others have used ABS/ICRU-89 Point A definition. The equations and terminologies used by them are complicated because of ambiguity in units of TRAK and dose used by them.

Therefore, in this study, we made an attempt to find out the simple relationship between TRAK and various isodose volumes. Furthermore, we calculated the isodose volumes using the mathematical formulas suggested by various authors and compared the outcome with actual isodose volumes of our revised Manchester and ICRU-89 Point A-based treatment plans.

MATERIALS AND METHODS

In this dosimetric study, we have taken treatment plans of 31 patients of cervical cancer treated with ICBT at our institute. All these patients were treated between March 2017 and February 2020. Clinical data of all the patients were collected according to the International Federation of Gynecology and Obstetrics staging system 2009, ranging from IB to IVA.[24] All these patients received a dose of 46 Gy in 23 Fraction (2 Gy per fraction, 5 fractions/week over a total duration of 5 weeks) by EBRT using 6 MV photon beam on Varian Unique Performance Linear accelerator (Varian Medical Systems Inc, California, USA) with weekly concurrent chemotherapy before ICBT. EBRT was delivered using either two fields, four fields or IMRT (Intensity Modulated Radiotherapy) technique. After completion of EBRT, all patients received 21 Gy in 3 fractions (7 Gy per fraction on a weekly basis) by HDR brachytherapy. Treatment was executed using an Iridium-192 (^{192}Ir) brachytherapy source using a remote afterloading microSelectron HDR v3.0 machine (Elekta AB, Stockholm, Sweden). Fletcher Williamson Asia Pacific ICBT applicator (Elekta AB, Stockholm, Sweden) consisting of

tandem and ovoids were used. The cervical stopper was used to decide the length of the intrauterine tandem. In all the patients, unshielded ovoid set was used.

Imaging and contouring

After insertion of applicators and Foley's catheter, 3D images were acquired using GE LightSpeed VCT (General Electric Medical Systems, Waukesha, Wisconsin) 64 Slice diagnostic CT scan machine. The 1.0 mm slice thickness images were obtained from umbilicus to mid-thigh. Acquired images were imported to Oncentra Brachy, v. 4.6.0 (Elekta AB, Stockholm, Sweden) TPS.

The radiation oncologist contoured the bladder, rectum, and sigmoid following the GEC-ESTRO guidelines on imported CT images in TPS.[25] The bladder was contoured from the bladder dome to the urethra. Contouring of the rectum began from 1 cm above the anus to the sigmoid flexure. The sigmoid was contoured from the recto-sigmoid flexure to the point at which the sigmoid extended into the anterior pelvis. To reduce the interpersonal error, all ICBT applicator insertion procedures and contouring were completed by the same radiation oncologist.

Treatment planning

The applicators were reconstructed and treatment was planned on Oncentra Brachy, v4.6.0 (Elekta AB, Stockholm, Sweden) TPS. In these previously treated patients, the dose was prescribed to Point A (A_{flange}) which was defined using the revised Manchester definition. Depending on the length of the tandem, source activation was done. In all the patient plans, radioactive sources were loaded with a step size of 2.5 mm and an offset of 6 mm.

All calculations were done using the TG-43 algorithm because the impact of heterogeneity corrected dose calculations for nonshielded applicators is small in cervical cancer patients.[26] As per established guidelines, the dose-volume parameters were used for reporting OAR doses of the bladder, rectum, and sigmoid.[17,25] Dose-volume parameters were estimated from the cumulative dose-volume histogram for OAR.

In all the treatment plans of 31 patients, a new Point A (A_{icru89}) was introduced as per ABS/ICRU-89 guideline and the dose was normalized to this new point without any other change in the source configuration, applicators, OARs, etc. Therefore, we were having a total of 62 treatment plans.

Isodose level volumes from treatment planning systems

For each treatment plan, TRAK value in cGy at 1m, V_{350} V_{700}, $V_{1050,}$ and V_{1400} (actual volumes encompassed by 350 cGy, 700 cGy, 1050 cGy, and 1400 cGy, respectively) were obtained when 100% dose (700 cGy) was prescribed at respective Point A (A_{flange} and A_{icru89}) as shown in Figure 1. These volumes were chosen because they were helpful in plan evaluation. A grid size of 200 mm × 200 mm × 200 mm in X, Y, Z-axis were used for isodose volume calculation to include all the voxels of isodose volumes.

Change in total reference air kerma value with the distance of normalization

Variation in the TRAK value was obtained by recording the distance between the Point A_{icru89} and Point A_{flange} plans. The distance was taken positively when Point A_{flange} moved superior to Point A_{icru89} and negative for inferior displacement.

Relationship between total reference air kerma and organs at risk

To assess the relationship between OAR and TRAK, a linear fitting was performed for dose received to 0.1 cm^3 and 2 cm^3 volume, i.e. $D_{0.1cm}{}^3$ and $D_{2cm}{}^3$, of the bladder, rectum, and sigmoid with TRAK in revised Manchester and ICRU-89 plans. For OARs (i.e. bladder, rectum, and sigmoid), dose received to 0.1 cm^3 and 2 cm^3 volume i.e. $D_{0.1cm}{}^3$ and $D_{2cm}{}^3$ were calculated from the revised Manchester Point A plan denoted as $Bladder_{flange}$, $Rectum_{flange}$, and $Sigmoid_{flange}$, respectively. Similarly, the ICRU-89 Point A plan is denoted as $Bladder_{icru89}$, $Rectum_{icru89}$, and $Sigmoid_{icru89}$. Linear fitting was done to find out the correlation between TRAK and OARs (bladder, rectum, and sigmoid) for 0.1 cm^3 and 2 cm^3 volume in A_{flange} and A_{icru89} plans.

Modeling curve and predicted isodose volume from total reference air kerma

The modeling curve was plotted on a natural log-log scale between Isodose volume (V_d) and the ratio of d/TRAK obtained from A_{flange} and A_{icru89} plans. Where V_d is the isodose volume receiving d dose, d represents the X percent of the prescribed dose (PD) in cGy, X is a value for which isodose volume is to be calculated. V_{350}, V_{700}, V_{1050}, and V_{1400} represent the isodose volume in cm^3 for 350 cGy, 700 cGy, 1050 cGy, and 1400 cGy doses. A polynomial fitting was done on the data to obtain a mathematical equation for the isodose volume prediction from TRAK at a particular dose. From both the modeling curves, the one having R^2 value closer to 1.0 was chosen for further calculations.

Percentage error was calculated to see the accuracy of predicted isodose volumes with our formula and the mathematical equations given by other authors.

Statistical analysis

Statistical analysis was carried out using the IBM SPSS for Windows, version 20.0 (IBM Corp, Armonk, NY, USA). Descriptive Analysis was used to determine the mean ± standard deviation doses for the isodose volume of A_{flange} and A_{icru89} plans. A paired-sample *t*-test was performed to assess the statistical significance between A_{flange} and A_{icru89} plans. $P \leq 0.05$ was considered significant for statistical inference.

RESULTS

The isodose volumes (V_d) of different isodose levels obtained from TPS for revised Manchester and ICRU-89 based Point A plans are shown in Table 1. In the case of revised Manchester-based A_{flange} normalization plans, the mean isodose

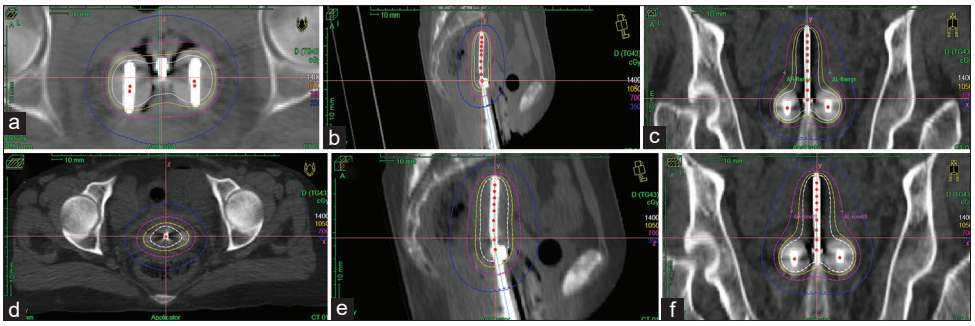

Figure 1: In treatment planning systems 700cGy (100%) dose prescribed to manchester Point A (A_{flange}) and ICRU-89 Point A (A_{icru89}) (a and d) Axial, (b and e) Sagittal, (c and f) Coronal computed tomography images with isodose level of 50%, 100%, 150% and 200% of prescribed dose i.e. 350 cGy, 700 cGy, 1050 cGy and 1400 cGy for A_{flange} and A_{icru89} Plans. V_d = Isodose volume (cm^3) receiving d dose, d = X percent of prescribed dose in cGy, X = Is a value for which isodose volume is to be calculated

volumes (V_d) of V_{350}, V_{700}, $V_{1050,}$ and V_{1400} were 285.98 ± 32.3 cm^3, 101.96 ± 10.63 cm^3, 52.71 ± 4.72 cm^3, 31.44 ± 2.33 cm^3, respectively. Likewise, ICRU-89 based A_{icru89} normalization plans, the mean isodose volumes (V_d) of V_{350}, V_{700}, $V_{1050,}$ and V_{1400} were 304.11 ± 26.17 cm^3, 108.88 ± 8.29 cm^3, 56.62 ± 3.69 cm^3, 34 ± 2.23 cm^3, respectively [Table -1]. The mean differences between revised Manchester and ICRU-89 plans for V_{350}, V_{700}, $V_{1050,}$ and V_{1400} were 18.13 cm^3, 6.92 cm^3, 3.91 cm^3, and 2.57 cm^3, respectively. It was found significant, as $P < 0.05$ [Table 1].

Mean TRAK value for the revised Manchester and ICRU-89 plan was 0.50 ± 0.04 cGy and 0.53 ± 0.03 cGy, respectively when 700 cGy (100%) dose was prescribed to the respective Point A (A_{flange} and A_{icru89}).

In Figure 2a, the blue line represents the percentage difference between A_{icru89} and A_{flange} Point for the TRAK Value and the orange line represents the change in distance of A_{flange} point with respect to A_{icru89} point for all patients. Whereas, in Figure 2b, Green and Gray line represents the total treatment time (in sec) and TRAK (in cGy) value of A_{icru89} Plans. Purple and Yellow line represents the total treatment time (in sec) and TRAK (in cGy) value of A_{icru89} Plans as shown in Figure 2b.

The mean doses to 0.1 cm^3 of OAR volumes, i. e bladder, rectum, and sigmoid were 820.79 ± 207.47 cGy, 599.4 ± 155.63 cGy, and 816.53 ± 455.66 cGy, respectively. Likewise, dose to 2 cm^3 of OAR were 588.91 ± 136.35 cGy, 450.38 ± 104.32 cGy, and 541.23 ± 178.74 cGy in revised Manchester Point A (A_{flange}).

For ICRU-89 (A_{icru89}) plans, dose to 0.1 cm^3 of OAR i. e bladder, rectum and sigmoid were 860.52 ± 222.72 cGy, 631.2 ± 170.54 cGy, 852.6 ± 471.3 cGy, respectively. Likewise, the doses to 2 cm^3 volume of OARs were 610.26 ± 148.38 cGy, 469.61 ± 120.89 cGy, and 555.58 ± 209.0 cGy [Figure 3].

The scatter graph shows the relationship between Isodose volume (V_d) and d/TRAK ratio for A_{flange} plans on the natural log-log scale for the modeling curve [Figure 4]. To derive a relationship between isodose volume and TRAK at different doses, a mathematical equation was derived with the help

Table 1: Isodose volume for different isodose levels in revised manchester and ICRU - 89 Point A plan with their statistical significance

Isodose level (cGy)	V_d (cm^3), mean±SD		V_d mean difference (cm^3)	*P*
	A_{flange}	A_{icru89}		
350	285.98±32.30	304.11±26.17	18.13	<0.05
700	101.96±10.63	108.88±08.29	6.92	<0.05
1050	52.71±04.72	56.62±03.69	3.91	<0.05
1400	31.44±02.33	34.00±02.23	2.57	<0.05

Prescription dose to Point A was 700 cGy. V_d=Isodose volume receiving d dose, d=X percent of the prescribed dose in cGy, X is a value for which isodose volume to be calculated, SD=Standard deviation, A_{flange}=Plan normalize according to revised manchester Point A definition, A_{icru89}=Plan normalize according to new ICRU-89 Point A definition, ICRU=International Commission on Radiation Units and measurements

of polynomial fitting. We got a second-order polynomial that is a quadratic equation (Eq. 1). This mathematical equation represents the relationship between isodose volume and d/TRAK.

$$V_d(cm^3) = e^{\left(-0.1054\left(ln\left(\frac{d}{TRAK}\right)\right)^2 - 0.0544\left(ln\left(\frac{d}{TRAK}\right)\right) + 10.521\right)} \quad \text{(Eq. 1)}$$

R-square or coefficient determination (R^2) =0.9975. For simplification of the mathematical calculations, the units of V_d is cm^3, d is cGy, TRAK in cGy at 1m distance and ln represents the natural logarithm. The above equation was used to find out the isodose volumes (V_{350} to V_{1400}) from known values of TRAK in cervical cancer patients when 700 cGy dose was prescribed to Point A (A_{flange} and A_{icru89} plans).

The isodose volumes V_{350}, V_{700}, V_{1050}, and V_{1400} were predicted using a mathematical equation (Eq. 1) derived by us . These results were compared with the isodose volumes predicted with the formulas suggested by other authors for A_{flange} and A_{icru89} based plans [Tables 2 and 3].

DISCUSSION

In many centers, HDR ICBT is planned with orthogonal radiographs, because 3D planning with CT images is expensive and time-consuming, whereas, 2D planning is simple, quick, and affordable. However, with 2D plans, it is not possible to

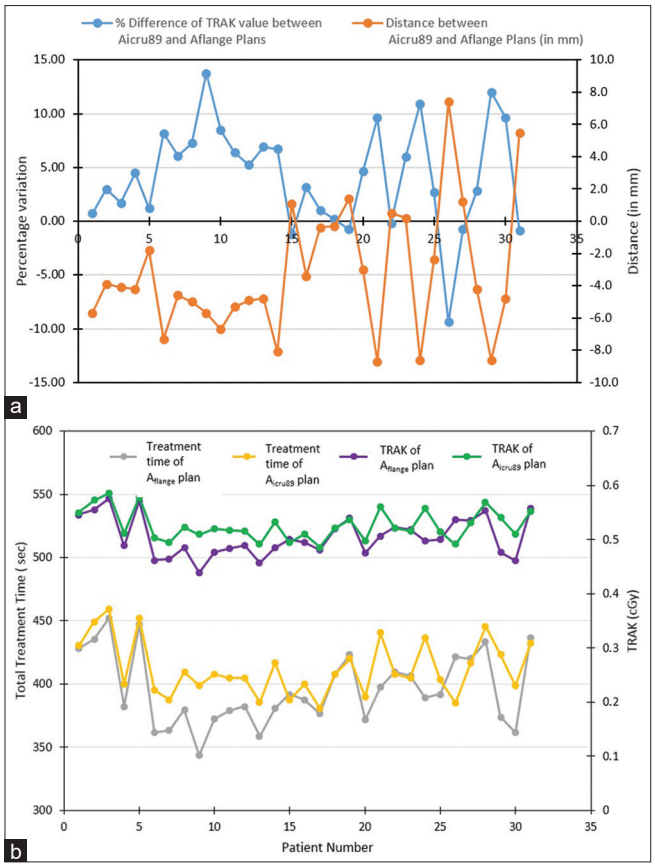

Figure 2: (a) Percentage difference in the Total Reference Air Kerma value of A_{flange} plans with respect to A_{icru89} plans (b) change in total treatment time and Total Reference Air Kerma value of A_{flange} plans with respect to A_{icru89} plans total

get the various isodose volumes but the value of TRAK can be obtained.

Therefore, relationship between TRAK and point A dose to calculate isodose volumes will enable the users to get absorbed dose volumes from the ICBT treatment plans accumulated over decades.

Several authors have given relationships between isodose volume and TRAK. The majority of authors gave power function relations and few authors suggested the quadratic equation. Previous suggested mathematical equations for the prediction of isodose volume were based on the Manchester prescribed Point A. However, in our study, we tried to find out an equation that can be used for isodose volume calculations from TRAK for revised Manchester, as well as ABS/ICRU-89, recommended Point A definition for dose reporting.

V_d in A_{flange} and A_{icru89}

The actual isodose volumes encompassed in Point A_{icru89} plans were higher as compared to Point A_{flange} revised Manchester plans [Table 1]. The difference between the two plans was found significantly larger in all isodose volumes. For Point A_{icru89} plans, isodose volumes V_{350}, V_{700}, V_{1050}, and V_{1400} were 6.34%, 6.79%, 7.42%, and 8.14% higher respectively, as compared to A_{flange} revised Manchester plans. Hence, for low isodose volume V_{350}, the amount of normal tissue irradiation was more in the case of Point A_{icru89} plans. In high isodose volumes V_{1050}, and V_{1400}, the relative amount of tumor was treated with a significantly higher dose as compared to Point A_{flange} plan. A higher standard deviation was observed in isodose volumes (V_d) obtained for A_{flange} as compared to A_{icru89}. It was because Point A_{flange} shifted above or below the ovoid surface, whereas the position of Point A_{icu89} is more stable.

Effect of distance on TRAK Value of A_{flange} plans with respect to A_{icru89} plans

When flange was below the surface of ovoids, the TRAK value of A_{flange} plans is less than A_{icru89} plans because Point A became closer to the ovoids, and required less dwell time to deliver the PD.

When flange was 5 mm above the surface of ovoid in A_{flange} plans, the TRAK value became more than A_{icru89} plans because Point A_{flange} plans moved away from the surface of ovoid. Hence to deliver the PD, the dwell time of activated sources increased.

In cases, where a flange is <2 mm above the ovoid surface, the percentage variation in TRAK value of ICRU-89 plans were within ±1% as compared to Manchester plans. TRAK value mostly remained unchanged when the position of Point A_{flange} and A_{icru89} was the same.

Total Treatment time and TRAK value of ICRU-89 plans were more than the Manchester plans in all patients except one patient, in that patient, shift in the flange was more than 5 mm. Moreover, if the superior shift was more than 5 mm, then the TRAK value of the manchester plan increases as compared to ICRU-89 plans, so percentage variation of ICRU-89 plan with respect to manchester plans became more in a negative direction (nearly 9%). Similar patterns were observed for treatment time in all patients. If the position of the sources remains unchanged, then the TRAK value depends upon the total treatment time.

Total reference air kerma and organs at risk

The scatter plot for bladder, rectum, sigmoid of 0.1 cm^3, 2 cm^3 dose volumes, and TRAK in Point A_{flange} and Point A_{icru89} based plans did not show any relation between them for dose-volume prediction. Because R^2 or coefficient of determination value was nearly zero for all the OAR dose volumes with respect to TRAK. The dose to the bladder, rectum and sigmoid depends upon their distance from the tandem, ovoid sources, vaginal packing and type of applicators used. Patient anatomy also influences the dose to these organs. Therefore, in our study, we did not find any mathematical relation between TRAK and OAR dose volumes for revised Point A_{flange} and Point A_{icru89} based plans. These results are in agreement with Datta *et al.*[21] However, Bockel *et al.*[27] in their study showed that TRAK

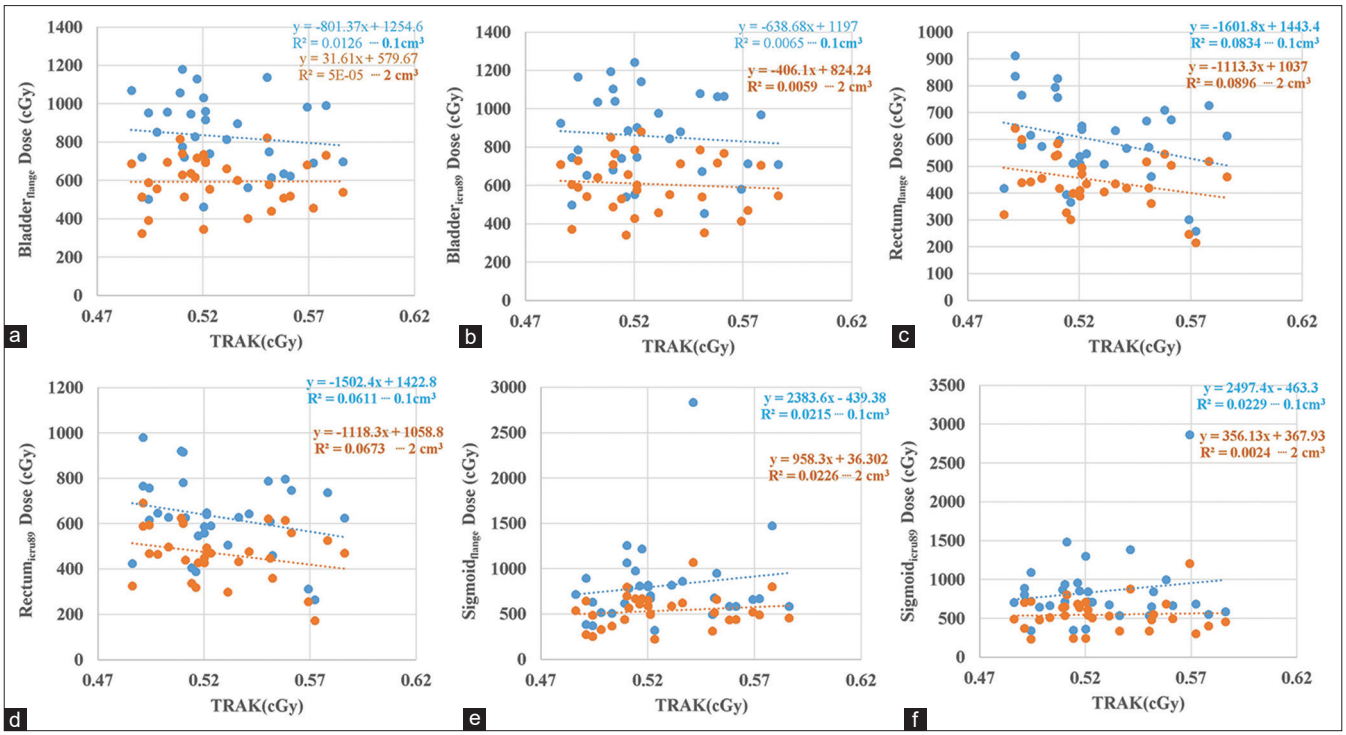

Figure 3: Scatter plot between organs at risk (bladder, rectum, and sigmoid dose volume) and TRAK for all patients. (a and b) for bladder, (c and d) for rectum, and (e and f) for sigmoid, 0.1 cm^3, 2 cm^3 dose volume, and Total reference air kerma relationship using revised Manchester and ICRU-89 plans for OARs

value ≥2 cGy was associated with a higher probability of late gastrointestinal toxicity (grade ≥2) in locally advanced cervical cancer.

Mathematical formula

We have derived the relationship between isodose volumes (V_d), TRAK, and the percentage of the prescribed dose (d). For simplification, the unit of d and TRAK was taken in cGy and the ratio of d/TRAK was greater than one. This would enable users to easily understand the empirical relation between d/TRAK and V_d as compared to other formulas where units for dose and TRAK were different.

In all other studies, the X-axis parameter was the TRAK/Dose ratio, and the unit of TRAK was different from the dose. The unit of TRAK value used by Wilkinson *et al.*,[19] Deshpande *et al.*[20] was mGy whereas, cGy was used by Datta *et al.*,[21] Nkiwane *et al.*[22] and Robert *et al.*[23] However, all the authors have used Gy for different isodose. This variation in the unit of TRAK and isodose may cause an error in calculations because we are trained to use uniform units. However, in our study, all the units were in cGy. Derivation of our equation from the calibration graph [Figure 4] is easy, less cumbersome, and predicted volumes with this equation are more accurate as compared to Robert *et al.*[23]

In revised Manchester plans, a range of mean percentage error between actual and predicted isodose volumes V_{350}, V_{700}, V_{1050}, and V_{1400} from our study were ranging from -0.87% to 2.70%. Whereas, predicted percentage error for Wilkinson *et al.*,[19] Deshpande *et al.*,[20] Datta *et al.*,[21] Nkiwane *et al.*,[22] and Robert *et al.*[23] range were −3.71% to 10.41%, −7.61% to 2.32%, −2.02% to -0.72%, 3.34% to 23.06%, and-3.74% to 16.23%, respectively in A_{flange} plans.

In ICRU-89 plans, a range of mean percentage error between actual and predicted isodose volumes V_{350}, V_{700}, V_{1050}, and V_{1400} from our study were -1.03% to 1.80%, respectively. Whereas, predicted percentage error for Wilkinson *et al.*,[19] Deshpande *et al.*,[20] Datta *et al.*,[21] Nkiwane *et al.*,[22] and Robert *et al.*[23] range were −3.93% to 8.75%, −7.64% to 0.99%, −2.13% to-0.75%, 3.38% to 21.12%, and-2.96% to 13.86%, respectively in A_{icru89} plans.

The predicted mean percentage error in isodose volumes with Wilkinson *et al.*[19] formula was less than 4% for V_{350}, IV_{700}, and IV_{1050}, while the mean percentage error was 10.41% for V_{1400} isodose volume. The higher percentage error in V_{1400} may be because their mathematical expression was derived from Cesium-137 sources. In their study, they suggested that if their formula is used for radionuclide other than Cs-137, the predicted isodose volumes may be more than 6% due to the absorption and scattering effect.

Deshpande *et al.*[20] used Cs-137 pellet sources to derive their formula for different combinations of intrauterine tandem length and colpostat diameters. They obtained slope from the graph of different tandem length and colpostat diameter combinations. Averaging of these slopes generated an isodose

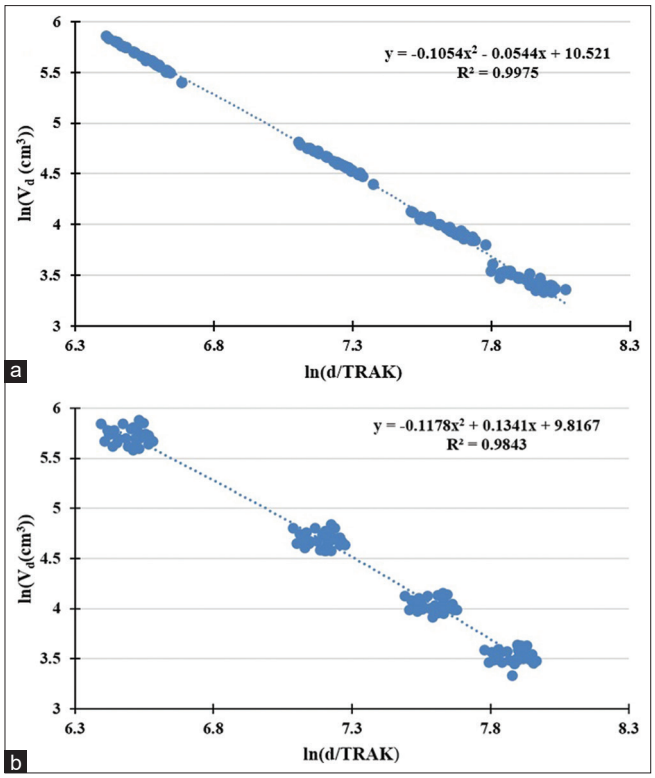

Figure 4: Modeling curve used to find the relationship between Isodose Volume (V_d) and d/TRAK ratio for (a) Manchester Point A_{flange} (b) ICRU-89 Point A_{icru89} normalization. The prescription dose to Point A_{flange} and A_{icru89} was 700 cGy. The fitted line shows a Quadratic Equation. V_d = Isodose volume (in cm^3) receiving d dose. d = X percent of the prescribed dose in cGy, X = is a value for which isodose volume to be calculated, ln stands for natural logarithm, TRAK = Total Reference Air Kerma

volume prediction equation as a power function. In their study percentage error for volumes enclosed by 10 Gy to 60 Gy, isodose was −8% to 9% for different tandem-colpostat combinations. In our study, using their expression, resulting percentage error for isodose volume prediction was −7.61% to 2.32% for A_{flange} and A_{icru89} plans. The variation in outcome may be because we have used the data from Ir-192 source. Still, the percentage error was higher with their formula as compared to our formula.

The percentage error between predicted and actual mean isodose volumes were small when Datta *et al.*[21] recommended mathematical equation was used. For revised Manchester-based Point A plans, mean isodose volumes V_{350}, V_{700}, V_{1050}, and V_{1400} were 282.08 cm^3, 99.90 cm^3, 52.33 cm^3, and 31.01 cm^3 respectively, with their formula and these values were close to the actual isodose volumes. However, they have not used similar units for TRAK (cGy) and dose levels (Gy) which may cause errors in calculations as we are trained to use uniform units while doing mathematical calculations.

Nkiwane *et al.*[22] have predicted isodose volumes with an accuracy of 10% in their study. However, when we used their formula to predict isodose volumes V_{350}, V_{700}, V_{1050}, and V_{1400} using our data the mean percentage error was ranging from 3% to 23.06% which was quite high. The mean percentage error increased with the increase in volume and it was 23.06% for V_{1400} for Manchester plan. This larger variation in higher isodose volume in Nkiwane *et al.* formula might be because they used advanced MRI image-based HRCTV optimized plans, including intracavitary and interstitial applicators, and incorporated Wilkinson *et al.*[19] formula in their equation with a different value of constant. The actual formula given by Wilkinson *et al.* was $V = 160(K/D)^{3/2}$ whereas, Nkiwane *et al.* have used $V = 4965(K/D)^{3/2}$.[28]

When we used Robert *et al.*[23] power-law relation formula to predict different isodose volumes, the mean percentage errors were ranging from −3.74% to 16.23%. However, in their study, they have predicted different isodose volumes within the accuracy of 7% between TPS measured and calculated isodose volumes. Their formula is complicated, did not produce an accurate result and the error was high at V_{1400}. Contrary to their results, in our study, Datta *et al.*[21] formula predicted isodose volumes with less mean percentage errors.

Actual isodose volumes in Point A_{icru89} (ICRU-89) based plan were larger as compared to Point A_{flange} (revised Manchester) plan. Isodose volumes predicted with our formula for Point A_{icru89} based plans had less percentage error than the isodose volumes predicted for Point A_{flange} based plans. This could be because of more accuracy in the method of locating Point A_{icru89} as compared to the location of Point A_{flange}. The position of revised Manchester Point A might change if the flange moves from its position during applicator insertion, packing, and patient shifting. The shift in Point A_{flange} would alter the shape and distribution of isodose volumes. The mean percentage error for predicted isodose volumes using formulas of all the authors in Point A_{flange} and Point A_{icru89} based plans were nearly the same.

The prediction of various isodose volumes from TRAK value is useful in the high workload department where planning is done either with radiographs or with dose prescription normalization to Point A on CT images. The outcome can be compared with the standard isodose surface volumes to know the accuracy of the treatment plan. If the first plan of the patient is done with volumetric imaging and the rest of the fractions are planned with radiographic images, then isodose volumes calculated for 2D plans can be compared with the outcome of the 3D plan. This relationship can be used to calculate the isodose volumes for old patients where TRAK value is available but data of isodose surface volumes is not available.

We successfully predicted isodose volumes from the TRAK value in revised Manchester and ICRU-89 plans. These volumes are useful for dose reporting and quality assurance in ICBT.

CONCLUSIONS

The formula developed by us to predict various isodose

Table 2: Prediction of isodose volumes at different isodose levels and percentage error between actual and predicted isodose volumes for revised Manchester plans

Revised Manchester plan parameters		Our study		Wilkinson and Ramachandran[19]		Deshpande *et al.*[20]		Datta *et al.*[21]		Nkiwane *et al.*[22]		Robert *et al.*[23]	
Isodose level (cGy)	Actual mean V_d (cm^3)	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error
350	285.98	286.58	0.21	277.69	−2.90	275.82	−3.55	282.08	−1.36	295.52	3.34	275.27	−3.74
700	101.96	101.07	-0.87	98.18	−3.71	94.20	−7.61	99.90	−2.02	107.10	5.05	101.68	−0.27
1050	52.71	52.47	-0.44	53.44	1.39	50.25	−4.67	52.33	−0.72	59.12	12.16	56.03	6.31
1400	31.44	32.29	2.70	34.71	10.41	32.17	2.32	31.01	−1.37	38.69	23.06	36.54	16.23

Prescription dose to Point A (A_{flange}) was 700 cGy. V_d=Isodose volume receiving d dose, d=X percent of prescribed dose in cGy, X is a value for which isodose volume to be calculated

Table 3: Prediction of isodose volume at different isodose levels and percentage error between actual and predicted isodose volume for ICRU - 89 plans

ICRU-89 plan parameters		Our study		Wilkinson and Ramachandran[19]		Deshpande *et al.*[20]		Datta *et al.*[21]		Nkiwane *et al.*[22]		Robert *et al.*[23]	
Isodose level (cGy)	Actual mean V_d (cm^3)	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error	Predicted mean V_d (cm^3)	Percentage error
350	304.11	303.85	-0.09	295.84	−2.72	294.45	−3.18	300.53	−1.18	314.40	3.38	295.10	−2.96
700	108.88	107.76	-1.03	104.60	−3.93	100.56	−7.64	106.55	−2.13	113.94	4.65	108.25	−0.57
1050	56.13	56.03	-0.87	56.93	0.56	53.64	−5.26	56.19	−0.75	62.90	11.10	59.47	5.04
1400	34.62	34.50	1.82	36.98	8.75	34.34	0.99	33.69	−0.92	41.19	21.12	38.72	13.86

Prescription dose to Point A (A_{icru89}) was 700 cGy. V_d=Isodose volume receiving d dose, d=X percent of prescribed dose in cGy, X is a value for which isodose volume to be calculated, ICRU=International Commission on Radiation Units and measurements

volumes from the TRAK value is simple and more accurate than the formulas available in the literature. This single formula could be used to calculate the various isodose volumes within the accuracy of ±3% from the TRAK value obtained from 2-D or 3-D ICBT plans. This single formula is valid for Point A_{flange} and points A_{icru89} based plans.

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Conflicts of interest
There are no conflicts of interest.

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