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Formulation of normal tissue irradiation volumes in Co-60 and Ir-192 HDR ICBT of Ca cervix using Total Reference Air Kerma (TRAK)

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ABSTRACT

Aim: The aim of this study was to formulate isodose volume relations encompassed by isodose surfaces in Co-60 and Ir-192 HDR intracavitary brachytherapy (ICBT) of cervix carcinoma using the Total Reference Air Kerma (TRAK).
Background: The TRAK and isodose volumes are radioactive source related. The formulated relations can easily estimate the irradiated isodose volume if the TRAK and dose are known. The C0-60 can also be used for brachytherapy because of its longer half life and comparable OAR doses to Ir-192.
Materials and methods: Isodose volumes encompassed by different isodose surfaces and TRAK were obtained from 22 Ca cervix ICBT treatment plans in Co-60 and Ir-192 HDR brachytherapy with 9 Gy prescription to point A. Isodose volume relations were formulated both for Co-60 and Ir-192 brachytherapy source from the slopes and intercepts of the linear fit in the plot between isodose volumes and TRAKs.
Results: The TRAK value of Co-60 was higher than Ir-192 by about 7.16%. The isodose volumes at low doses for Co-60 were higher than Ir-192. But no significant differences in the dose to the bladder and rectum were observed due to these sources. For dose to 2 cm^3 bladder and rectum volume, the differences were 1.07% and 0.75%, respectively. The correlation coefficient with the 2-tailed significance of correlation (p value) between TPS measured isodose volume and calculated isodose volumes using the formulated relations at different dose values were statistically significant as $p < 0.05$.
Conclusion: Results show different isodose volumes for both sources but the dose to the bladder and rectum are nearly the same.

1. Background

Brachytherapy is a radiation therapy technique in which radioisotopes are placed very close to the tumour. The word brachytherapy was derived from Greek. It refers to a short range therapy and has been described as the first form of conformal radiation therapy.[1] The advantages of placing radiation sources very close to the tumour are to deliver a very high radiation dose to the tumour and very low radiation

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dose to the normal tissue due to its rapid dose fall off. This is the aim of radiotherapy. So, it is very important to know the tissue volume encompassed by isodose surfaces of various doses, particularly of prescription dose and low doses. Earlier, some authors have studied the relationship between isodose volume and Total Reference Air Kerma (TRAK). The TRAK is the sum of the products of the reference air kerma rate and the irradiation time for each source. It is an important quantity which should be reported for all brachytherapy applications. It is a quantity that is simple to calculate and on which there can be no ambiguity. It is analogous to the milligram hour (mg.hr) of radium.[2] Authors, like Wilkinson and Ramachandran, DD Deshpande et al. and NR Datta et al. gave relationships between isodose volume and TRAK at any dose, respectively as[3–5]:

$$V(\text{cm}^3) = 4965\left(\frac{\text{TRAK}}{\text{dose}}\right)^{1.5} \quad (1)$$

$$V(\text{cm}^3) = 156\left(\frac{\text{TRAK}}{\text{dose}}\right)^{1.55} \quad (2)$$

and

$$V(\text{cm}^3) = 5661.65\left(\frac{\text{TRAK}}{\text{dose}}\right)^{2} + 1295.99\left(\frac{\text{TRAK}}{\text{dose}}\right) - 23.09 \quad (3)$$

where TRAK is in mGy. m^2 and dose in Gy.

Eqs. 1 and 2 were derived for Cs-137 source used in the Low Dose Rate (LDR) brachytherapy whereas Eq. 3 was for the Ir-192 source in the High Dose Rate (HDR) brachytherapy. Nowadays, most of the LDR brachytherapy units in different hospitals have been replaced with HDR brachytherapy units. The most commonly used radioisotopes of HDR brachytherapy units available in the market at present are Ir-192 and Co-60. The Co-60 emits gamma photons of average energy 1.25 MeV which are highly penetrating. It has specific gamma ray constant of 13.2 R-cm^2/hr-mCi. Whereas Ir-192 emits gamma photons of average energy 0.38 MeV with specific gamma ray constant 4.8 R-cm^2/hr-mCi. So Co-60 requires more shielding because of its higher photon energy compared to Ir-192. For example, the equilibrium TVL of Co-60 and Ir-192 are, respectively, 210 mm and 139 mm of concrete.[11] The advantage of Co-60 over Ir-192 lies in the logistical aspect as Co-60 has a longer half-life (5.26 years) compared to Ir-192 (73.83 days). Hence, during the useful life of Co-60, which is its one half-life, about 20 source exchanges are required for the Ir-192 source.[12] Apart from this, it is also necessary to know the amount of normal tissue volume irradiated by these sources, particularly at low doses. The relations mentioned above cannot be applied for all types of radioactive sources used in brachytherapy. For example, the isodose volume due to Co-60 radioactive source used in BEBIG HDR MultiSource cannot be estimated using the above relations (Eqs. 1–3). It is because the volume encompassed by a particular isodose surface is dependent upon the TRAK. This can be seen from Fig. 1 that the TRAK value of Co-60 is more than the Ir-192 source when all the plans were made with the same prescription dose of 9 Gy to point A and the same pattern of source loading. So, there are requirements of different relations based on the type of radioactive source used.

2. Aim

The aim of this study was to formulate isodose volume relations encompassed by isodose surfaces in Co-60 and Ir-192 HDR intracavitary brachytherapy (ICBT) of cervix carcinoma using the Total Reference Air Kerma (TRAK).

3. Materials and methods

For the study, CT series of twenty-two (22) patients were selected from the database of the treatment planning system (TPS, HDR Plus version 3.0.6.0 of Eckert and Ziegler BEBIG, Germany). The patients underwent intracavitory applications for cancer of uterine cervix in Co-60 HDR brachytherapy (MultiSource, Eckert and Ziegler BEBIG, Germany). All these patients were treated with the prescription of 9 Gy (normalised to point A) per fraction in two fractions. Depending upon the length of the tandem (Fletcher suit), the source loading was different and depending upon the source loading and length of the applicator, the Total Reference Air Kermas (TRAKs) were also different. The sources were loaded in a step size of 2.5 mm with default offset value of 4.8 mm. We followed our departmental source loading protocol. For example, the tandem and ovoids loading pattern for the 6 cm tandem was 1,3,5,7,9,12,15,18, 21, 24; 3,4,5,6; 3,4,5,6. The TRAK values (in cGy.m^2) and isodose volumes encompassed by 3 Gy, 5 Gy, 8 Gy, 9 Gy, 10 Gy, 13 Gy, 15 Gy, 18 Gy, 23 Gy, 25 Gy, 40 Gy and 50 Gy isodose surfaces were recorded from all the 22 treatment plans from the HDR Plus TPS. The same CT datasets of these 22 patients were exported from the Co-60 HDR Plus TPS and imported in the Ir-192 HDR TPS (Oncentra, version 4.3 of Nucletron, Netherlands). Then they were used to make similar plans with the same pattern of source loading and prescription dose in the Oncentra TPS as those in Co-60 HDR Plus TPS. From the TPS, TRAK values and isodose volumes encompassed by 3 Gy, 5 Gy, 8 Gy, 9 Gy, 10 Gy, 13 Gy, 15 Gy, 18 Gy and 25 Gy isodose surface were also recorded from all the 22 plans. Those TRAK values from both TPS were compared and the comparison was shown in Fig. 1 using Microsoft excel. The isodose volumes encompassed by different isodose surfaces (Fig. 2) and the dose to 0.1 cm^3 and 2 cm^3 of the bladder and rectum volumes were compared (Fig. 3) for both sources. From the collected data, scatter plots were made between the TRAK and isodose volumes for Co-60 and Ir-192 from both TPS (Fig. 4). All the data points in the plots followed the linear pattern at different dose values. In these two plots of Fig. 4, the best fitted curves were the equations of lines with different slopes and intercepts depending upon the dose values. Also, the slopes and intercepts of these fitted lines of different dose values followed a certain pattern. They were found to be increased with doses. If the slope and intercept of a particular dose value is known then it would be possible to find out the isodose volume encompassed by that particular isodose surface. To find the relationship of slope and intercept with dose for both the sources, plots of dose vs. slopes and dose vs. intercepts were made (Fig. 5). Using MATLAB curve fitting tool, the best fitted curve of these four plots was found out and it was found to be a power function curve. The equations of these power function curves that

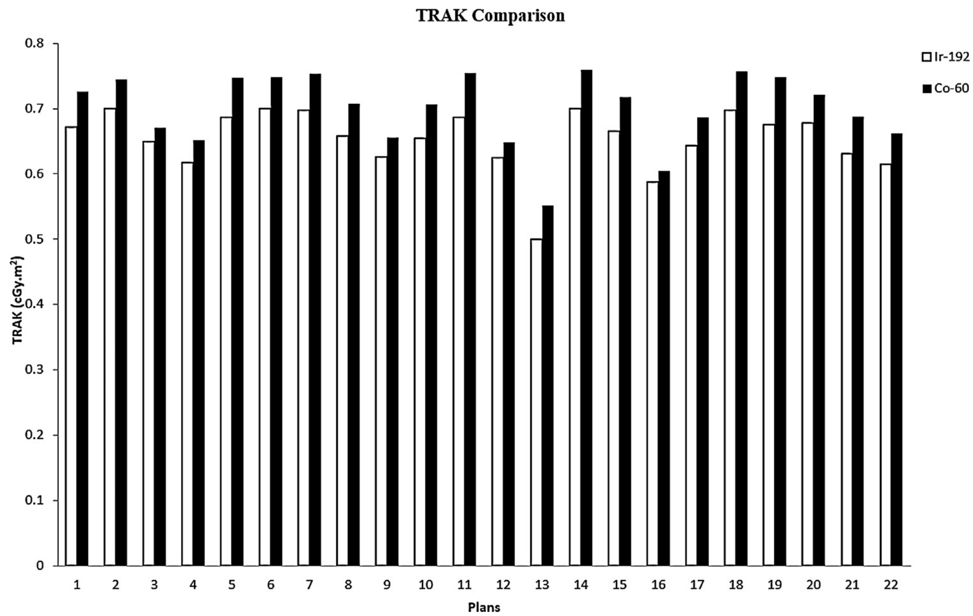

Fig. 1 – The comparison of TRAK values for Co-60 and Ir-192 sources from 22 HDR ICBT plans of Ca cervix.

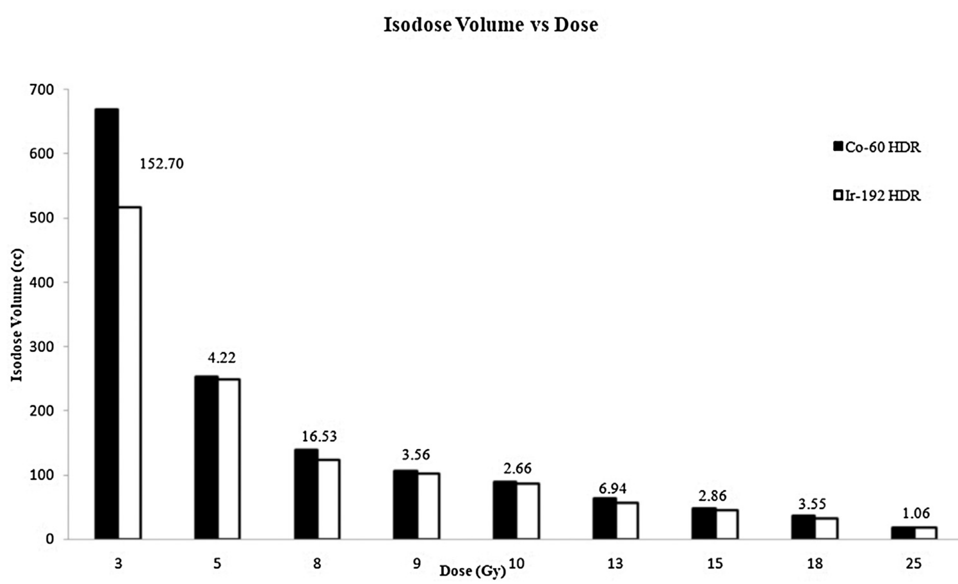

Fig. 2 – Comparison of average isodose volumes of 22 treatment plans at different dose values of Co-60 and Ir-192 sources with the isodose volume difference when 9 Gy was prescribed to point A.

relate slopes and intercepts as function of dose are given in Table 1.

So, the generalised equations of the isodose volume of both sources were given as:

Isodose volume (cm^3) = Slope × TRAK – Intercept

Case 1(Co-60 source):

$$\text{Isodose volume}(cm^3) = (8641 \times \text{dose}^{-1.709}) \times \text{TRAK} - (1801 \times \text{dose}^{-1.754}) \quad (4)$$

Case 2(Ir-192 source):

$$\text{Isodose volume}(cm^3) = (6621 \times \text{dose}^{-1.594}) \times \text{TRAK} - (1872 \times \text{dose}^{-1.876}) \quad (5)$$

where TRAK is in cGy. m^2 and dose in Gy.

To check the accuracy of the above equations, ten ICBTs of Ca cervix plans were selected at random from both Oncentra and HDR Plus TPS. From those plans the TRAK values and isodose volumes encompassed by various isodose surfaces were

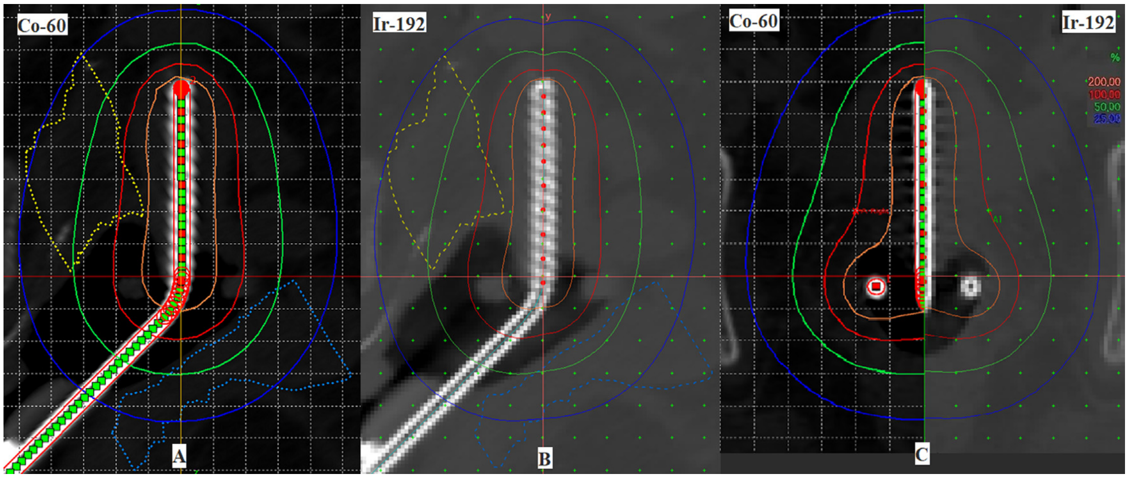

Fig. 3 – The isodose comparison between Co-60 and Ir-192 HDR brachytherapy sources. The inset figures A, B and C were of Co-60, Ir-192 and composite of the two at isodose level 200%, 100%, 50% and 25%.

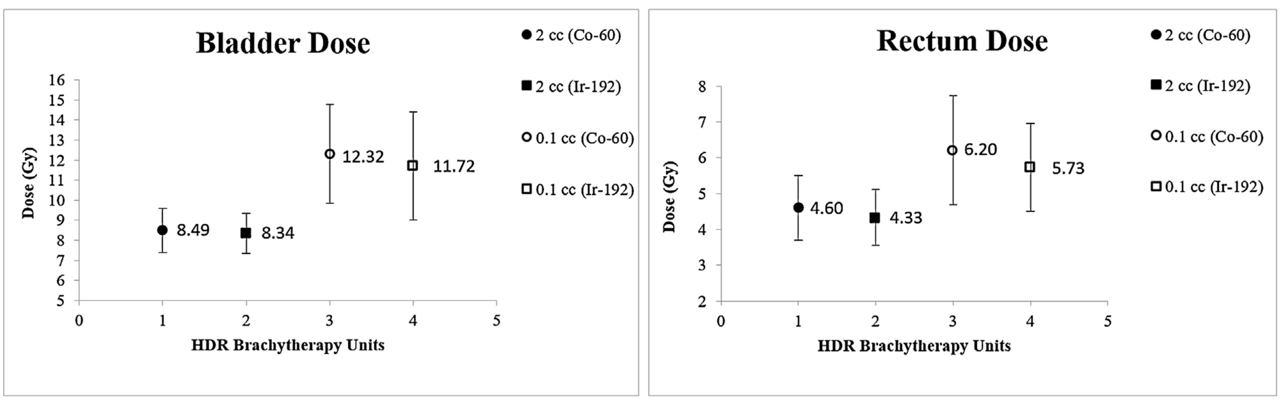

Fig. 4 – The mean and standard deviation dose at 2 cm^3 and 0.1 cm^3 volumes of bladder and rectum from 22 ICBT of Ca cervix treatment plans due to Co-60 and Ir-192 HDR brachytherapy sources (Inset figures A and B for bladder and rectum respectively).

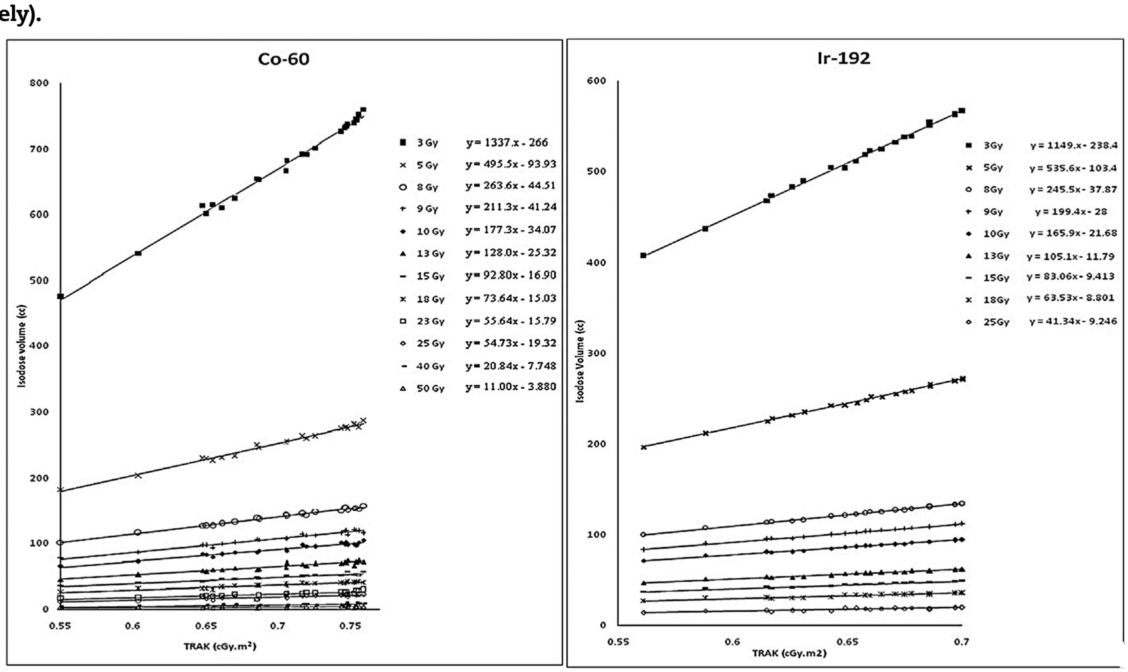

Fig. 5 – The plots of TRAK and isodose volumes for Co-60 and Ir-192 sources and the regression lines with governing equations.

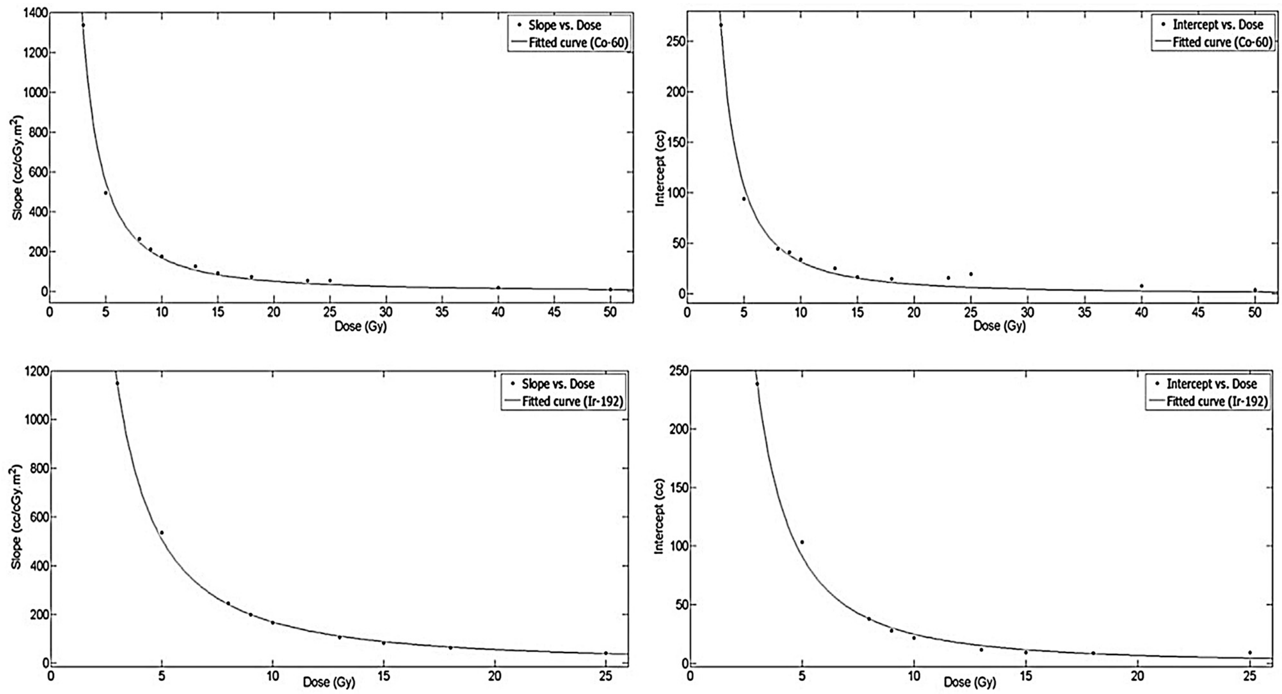

Fig. 6 – Fitted curves of the plots between dose vs slope and dose vs intercept for Co-60 and Ir-192 sources from regression lines in Fig. 3.

Table 1 – Fitted relations of slope and intercept as a function of dose for both Co-60 and Ir-192 sources from Fig. 4.

	Slope	Intercept
Co-60	f(x) = a_1*x$\hat{b}_1$, where **x** = dose in Gyfigure* Coefficients (with 95% confidence bounds):figure* a_1 = 8641 (7512, 9770)figure* b_1 = -1.709 (-1.809, -1.608)figure* **Goodness of fit**:figure* SSE: 5098figure* R-square: 0.9966figure* Adjusted R-square: 0.9963figure* RMSE: 22.58	f(x) = a_2*x$\hat{b}_2$, where **x** = dose in Gyfigure* Coefficients (with 95% confidence bounds):figure* a_2 = 1801 (1409, 2192)figure* b_2 = -1.754 (-1.923, -1.585)figure* **Goodness of fit**:figure* SSE: 517.9figure* R-square: 0.9911figure* Adjusted R-square: 0.9902figure* RMSE: 7.196
Ir-192	f(x) = a_3*x$\hat{b}_3$, where **x** = dose in Gyfigure* Coefficients (with 95% confidence bounds):figure* a_3 = 6621 (6384, 6858)figure* b_3 = -1.594 (-1.621, -1.567)figure* **Goodness of fit**:figure* SSE: 204.9figure* R-square: 0.9998figure* Adjusted R-square: 0.9998figure* RMSE: 5.41	f(x) = a_4*x$\hat{b}_4$, where **x** = dose in Gyfigure* Coefficients (with 95% confidence bounds):figure* a_4 = 1872 (1483, 2261)figure* b_4 = -1.876 (-2.042, -1.71)figure* **Goodness of fit**:figure* SSE: 198.9figure* R-square: 0.9957figure* Adjusted R-square: 0.9951figure* RMSE: 5.33

recorded. The isodose volumes so obtained from the two TPS were compared to those obtained using the above two relations (Eqs. 4 and 5).

4. Results

From the Fig. 1 it was found that on an average Co-60 has higher TRAK values with respect to Ir-192 by about 7.16%. Also, the isodose volumes at low doses were higher in the case of Co-60 compare to Ir-192. The average of 3 Gy isodose volume of the 22 treatment plans in Co-60 was about 152.70 cm^3 more than Ir-192. This difference in the isodose volume between Co-60 and Ir-192 decreased at a higher dose isodose volume (Fig. 2).

The isodose comparison of the two sources is shown in Fig. 3. The inset figures A, B and C of it were, respectively, of Co-60, Ir-192 and composite of the two. Fig. 4 shows the dose to 0.1 cm^3 and 2 cm^3 bladder and rectum volume due to the two different types of sources. Reporting of doses to these volumes is recommended according to many authors.[3,7–10] The doses to 2 cm^3 bladder due to the Co-60 and Ir-192 sources were 8.49 Gy and 8.34 Gy, respectively, while to 0.1 cm^3 they were 12.32 Gy and 11.72 Gy, respectively. Similarly, for the same volumes and sources, the doses to the rectum were 4.60 Gy, 4.33 Gy, 6.20 Gy and 5.73 Gy, respectively. In the two plots between TRAK and isodose volumes of different doses, the best fitted curves were found to be the lines (Fig. 5). The inset figures show the equations of these lines of both sources for different dose values. The slopes and intercepts of these fitted lines of both sources decrease with the increase in dose. The slopes were more in the case of Co-60 than the Ir-192 source for the same dose value and it appeared that it converged to zero at a very high dose. The plots of dose vs. slope and dose vs. intercepts of the fitted lines are shown in the Fig. 6. Then the best fitted curves of these plots were found to be of power law relations (Table 1, Fig. 6). The values of isodose volume of various dose ranges (low to high) calculated using the above derived relations were comparable with those obtained in the respective TPS (Oncentra for Ir-192 and HDR Plus for Co-60). Tables 2 and 3 show the comparison between calculated isodose volumes using the above relations and the TPS estimated isodose volumes of ten randomly selected patient treatment plans from both TPS. It was found that the percentage deviations of these isodose volumes calculated using the derived relations from the TPS isodose volumes increases with the increase in dose. The average (mean) of the percentage errors with standard deviations (SD) for the doses 3 Gy, 9 Gy, 15 Gy and 20 Gy were respectively −1.59 ± 1.32%, −1.84 ± 3.22%, −2.64 ± 4.62% and −1.11 ± 12.87% for the Co-60 source and for the Ir-192 source for the doses 3 Gy, 9 Gy, 15 Gy and 18 Gy, the average of percentage errors was −0.06 ± 0.44%, −2.19 ± 0.46%, 3.15 ± 1.57% and 6.96 ± 2.58%, respectively. The correlation coefficient with 2-tailed significance of correlation (p value) between TPS measured and calculated (fitted) isodose volumes in the above dose values were, respectively, 0.998 (0.000), 0.988 (0.000), 0.986 (0.000) and 0.933 (0.000) for Co-60 and 0.998 (0.000), 0.997 (0.000), 0.972 (0.000) and 0.94 (0.000) for the Ir-192 sources. These correlations were statistically significant as the 2-tailed significance value $p < 0.05$ (Table 2 and 3)

5. Discussion

igure1, which shows the TRAK value comparison of the Co-60 and Ir-192 sources for the brachytherapy plans with the same pattern of source loading and applicator type, suggests that TRAK value is source related and Co-60 has a relatively higher TRAK value than Ir-192 by about 7.16%. The isodose volume encompassed by any dose value of Co-60 is higher than that of the Ir-192 isodose volume encompassed by the same dose value (Fig. 2). This difference of the isodose volume between these two isotopes was significantly larger at low dose. At 3 Gy, the difference was about 152.70 cm^3. Hence, the amount of normal tissue volume irradiated at low dose will be more in the case of Co-60 as compared to the Ir-192 source. The isodose of Ir-192 has dips towards the tip of the tandem while isodose of Co-60 do not have such feature (Fig. 3). This could be one of the factor for higher isodose volume of Co-60 compare to Ir-192. But the differences in the isodose volume due to these sources did not contribute a significant difference in the bladder and rectal dose (Fig. 4). The mean doses from the 22 treatment plans to 2 cm^3 bladder volume were 8.49 Gy and 8.34 Gy respectively for Co-60 and Ir-192 which is just 1.79% higher than the Ir-192 source. Similarly for the rectum, the mean doses were, respectively, 4.60 Gy and 4.33 Gy for Co-60 and Ir-192. For 0.1 cm^3 the differences in the dose to these organs due to these sources were about 0.6 Gy for the bladder and 0.27 Gy for the rectum. But the isodose volume relation using TRAK must be a source related one and relations derived from a particular source cannot accurately tell the isodose volume due to a different source. In Wilkinson and Ramachandran and Deshpande DD et al, studies, the

Table 2 – Comparison between TPS measured and calculated (Fitted) isodose volumes and their percentage deviations from TPS and correlation coefficient for Co-60 HDR brachytherapy sources.

Co-60	3 Gy				9 Gy				15 Gy				20 Gy			
Plans	TPS	Fitted	Fitted- TPS	% difference	TPS	Fitted	Fitted-TPS	%difference	TPS	Fitted	Fitted-TPS	% difference	TPS	Fitted	Fitted-TPS	% difference
1	641.29	627.10	−14.19	−2.21	99.70	97.86	−1.84	−1.85	43.08	41.24	−1.84	−4.28	28.31	25.34	−2.97	−10.47
2	750.80	741.96	−8.84	−1.18	119.78	115.43	−4.35	−3.63	51.77	48.58	−3.19	−6.17	31.74	29.83	−1.91	−6.01
3	492.84	469.14	−23.70	−4.81	70.28	73.70	3.42	4.86	28.91	31.15	2.24	7.73	15.57	19.17	3.60	23.13
4	752.22	746.19	−6.03	−0.80	121.79	116.08	−5.71	−4.69	51.58	48.85	−2.73	−5.30	38.69	30.00	−8.69	−22.46
5	622.93	618.64	−4.29	−0.69	101.26	96.57	−4.69	−4.64	39.81	40.70	0.89	2.23	21.65	25.01	3.36	15.54
6	612.11	600.79	−11.32	−1.85	93.78	93.84	0.06	0.06	40.34	39.56	−0.78	−1.94	24.87	24.32	−0.55	−2.22
7	621.18	617.32	−3.86	−0.62	96.85	96.36	−0.49	−0.50	43.10	40.61	−2.49	−5.77	25.61	24.96	−0.65	−2.53
8	671.47	670.45	−1.02	−0.15	107.42	104.49	−2.93	−2.73	47.71	44.01	−3.70	−7.76	29.27	27.04	−2.23	−7.62
9	616.95	607.14	−9.81	−1.59	94.17	94.81	0.64	0.68	40.60	39.96	−0.64	−1.57	24.03	24.56	0.53	2.22
10	587.92	575.94	−11.98	−2.04	95.74	90.04	−5.70	−5.96	39.40	37.97	−1.43	−3.63	23.50	23.35	−0.15	−0.66
Mean(SD)				**−1.59 (1.32)**				**−1.84 (3.22)**				**−2.64 (4.62)**				**−1.11 (12.87)**
Correl (p)	0.998 (0.000)				0.988 (0.000)				0.986 (0.000)				0.933 (0.000)			

Table 3 – Comparison between TPS measured and calculated (Fitted) isodose volumes and their percentage deviations from TPS and correlation coefficient for Ir-192 HDR brachytheray sources.

Ir-192	3 Gy				9 Gy				15 Gy				18 Gy			
Plans	TPS	Fitted	Fitted-TPS	% Difference	TPS	Fitted	Fitted-TPS	% Difference	TPS	Fitted	Fitted-TPS	% Difference	TPS	Fitted	Fitted-TPS	% Difference
1	531.80	532.75	0.95	0.18	105.89	103.49	−2.40	−2.27	46.76	47.65	0.89	1.90	34.12	36.06	1.94	5.69
2	566.45	566.07	−0.38	−0.07	111.84	109.27	−2.57	−2.30	48.68	50.21	1.53	3.15	35.73	37.98	2.25	6.29
3	503.82	507.46	3.64	0.72	101.22	99.10	−2.12	−2.09	45.32	45.71	0.39	0.85	33.51	34.61	1.10	3.28
4	472.86	470.69	−2.17	−0.46	95.44	92.72	−2.72	−2.85	40.76	42.88	2.12	5.20	29.23	32.50	3.27	11.17
5	554.37	549.98	−4.39	−0.79	108.87	106.48	−2.39	−2.20	46.88	48.97	2.09	4.47	33.87	37.05	3.18	9.40
6	567.08	566.07	−1.01	−0.18	111.71	109.27	−2.44	−2.18	48.69	50.21	1.52	3.13	35.65	37.98	2.33	6.53
7	562.53	562.63	0.10	0.02	110.68	108.67	−2.01	−1.81	48.22	49.95	1.73	3.58	35.26	37.78	2.52	7.15
8	518.52	517.81	−0.71	−0.14	103.71	100.89	−2.82	−2.71	45.43	46.50	1.07	2.36	33.14	35.20	2.06	6.23
9	482.69	481.03	−1.66	−0.34	95.65	94.51	−1.14	−1.19	41.40	43.67	2.27	5.49	30.06	33.09	3.03	10.08
10	510.88	513.21	2.33	0.46	102.45	100.10	−2.35	−2.30	45.51	46.15	0.64	1.40	33.67	34.94	1.27	3.77
Mean(SD)				−0.06 (0.44)				−2.19 (0.46)				3.15 (1.57)				6.96 (2.58)
Correl (p)	0.998 (0.000)				0.997 (0.000)				0.972 (0.000)				0.941 (0.000)			

authors formulated isodose volume relations for Cs-137 used in LDR brachytherapy.[4,5] Their relations are generalised and applicable for all dose ranges. In NR Datta et al. study, the authors formulated isodose volume relations for the Ir-192 source used in HDR brachytherapy of ICBT of ca cervix and the isodose volume converge to negative value at a higher dose.[6] However, isodose volumes cannot be negative. Also, in their study they compared their results with those of Wilkinson and Ramachandran and Deshpande DD et al. studies. The comparison will not give appropriate results as the relations were derived for a different radioactive brachytherapy source. Co-60 as a HDR brachytherapy source has recently been introduced in the market and there is no such relation to estimate the isodose volume. So, there is a need to formulate an isodose volume relation for Co-60 and the Ir-192 source that is applicable for all the dose values. In our study we formulated generalised isodose volume relations for both the Co-60 and Ir-192 radioactive sources used in brachytherapy (relations 4 and 5).The slopes and intercepts of the regression line in the plot between isodose volume and TRAK for both the sources are source and dose dependent (Fig. 4). For a given dose value, the slope of Co-60 is more than the Ir-192 source and the slopes decreases with the increase in dose. As mentioned above, the fitted curve using MATLAB of the scatter plots between dose vs. slope and dose vs. intercepts followed power law relations (Fig. 5). The coefficient adjusted R-square of the fitted curve in dose vs. slope for the Co-60 and Ir-192 sources were respectively 0.9963 and 0.9998. Similarly, for dose vs. intercepts the values were 0.9902 and 0.9951, respectively, for the Co-60 and Ir-192 sources (Table1). The generalised isodose volume relations (in cm^3) derived using the slopes and intercepts followed power law (Eqs. 4 and 5). These relations were dose and TRAK dependent. The isodose volumes calculated using the above derived relations for ten patient plans, each for both sources, matched accurately with those measured from the TPS.

6. Conclusion

The TRAK is source dependent and hence the isodose volume relations using it are radioactive source related and are different for different brachytherapy sources. The relations formulated in our study for Co-60 and Ir-192 HDR brachytherapy using curve fitting can estimate the isodose volume accurately. Using these relations, the amount of tissue volume irradiated can be easily estimated if the TRAK and dose encompassing the isodose volume are known. Despite a larger isodose volume in the case of Co-60 than Ir-192 there were insignificant differences in the bladder and rectal dose due to these sources.

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The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript.

Conflict of interest

None declared.

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