

# Methodology of dose calculation for external beam radiation combined with high dose rate brachytherapy in the era of 3-dimensional treatment planning system

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## Abstract

Intracavitary application of brachytherapy (BT) sources followed by external beam radiation is essential for the local treatment of carcinoma of the cervix, prostate, and nasopharynx. Dose distribution of external beam radiation plus BT can be challenging for the planning system because of their dose calculation by 2 different treatment planning system (TPS). The aims of this study were to introduce a novel iterative method of dose calculation performed in the Pinnacle plan and evaluate a combined dose distribution for external beam radiation and BT.

Because it is often the goal of the planner to produce plan with uniform dose throughout the target volume and normal tissue, we present an Iridium-192 calculation program using American Association of Physicists in Medicine Task Group 43 formula and export it to other commercialized TPS though the combined dose distribution of external beam radiation and BT can be shown. To illustrate such an improved procedure, we present the treatment plans of 2 patients treated with external beam radiation plus BT.

Dose distribution of the single BT source were calculated with the Plato post loading TPS and the program model, and the results of 2 methods were similar. A nasopharyngeal case and a cervical case were shown in Pinnacle with this program. The total dose distribution of BT combined with EBRT was showed in compute tomography images. And the corresponding dose volume histogram figures could be displayed correctly in Pinnacle TPS.

We demonstrated a novel iterative method of dose calculation performed in the Pinnacle plan to produce a combined dose distribution for external beam radiation and BT. We used it to evaluate the dose of target volume and normal tissues in the treatment of external beam radiation plus BT.

**Abbreviations:** 3-D = 3-dimensional, BT = brachytherapy, CT = compute tomography, DVH = dose volume histogram, EBRT = external beam radiotherapy, HDR = high dose rate, IMRT = intensity-modulated radiotherapy, LDR = low dose rate, NPC = nasopharyngeal carcinoma, TPS = treatment planning system.

**Keywords:** American Association of Physicists in Medicine Task Group 43, brachytherapy, combined dose distribution, external beam radiotherapy

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WF and JC contributed equally to this work.

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### 1. Introduction

In the last decade, technological improvements in radiotherapy have been significant and consequently the use and importance of radiotherapy in cancer treatment have increased greatly. Between the various available techniques, brachytherapy (BT) is an advanced form of radiotherapy where a radiotherapy source is placed inside or next to the volume requiring treatment and important treatment modality for carcinoma of the uterine cervix, prostate, and nasopharynx.<sup>[1-3]</sup> Because this treatment is characterized by a steep dose gradient, it can deliver a high dose to the tumor while minimizing doses to the surrounding normal tissue. The few randomized trials comparing low dose rate (LDR)- and high dose rate (HDR)-BT have demonstrated comparable survival and toxicity rates.<sup>[4-7]</sup> Our center had already been using HDR-BT and decided to integrate external beam radiation (EBRT) with it in 1995. Pinnacle or Raystation treatment planning system (TPS) was used for the EBRT and PLATO TPS for the BT. Now, no TPS was used for combined EBRT and BT. We present an iridium-192 calculation program using American Association of Physicists in Medicine (AAPM) Task Group (TG)-43UI formula<sup>[8,9]</sup> and export it to Pinnacle TPS though the combined dose distribution of EBRT and BT can be shown. And the cumulative dose distribution of combined internal and external radiation therapy can be evaluated by Dose Volume Histogram (DVH) and equal dose distribution.

### 2. Instrumentation and method

We described the methodology of dose calculation for EBRT combined with HDR BT in the era of 3-dimensional (3-D) TPS. This study was approved by the Medical Ethics Committee and the institutional reviewed board of Cancer Hospital of the University of Chinese Academy of Sciences (Zhejiang Cancer Hospital).

#### 2.1. Source description

BT irradiation is performed by means of a microseletron (Nucletron) HDR remote after-loading device. The facility is provided with an Ir-192 radioactive source that has an active length of 3.6 mm and a diameter of 0.65 mm. The source is sealed inside a capsule that is welded to one end of flexible steel and the treatment unit positions the source at the required dwell positions by means of a cable drive unit. The steel capsule has an active length of 4.5 mm and a diameter of 0.9 mm.

#### 2.2. Dose distribution calculassions

**2.2.1. Application of American Association of Physicists in Medicine Task Group 43 dosimetry formalism.** At present the dose distribution of BT seeds is described in terms of dose rates. The AAPM TG 43<sup>[8]</sup> and its update<sup>[9]</sup> comprise the currently accepted protocol for calculation of dose to water in Ir-192 BT for a reference air-kerma strength  $S_k$  measurement. The dose rate is given by Eq 1.

$$\dot{D}(r, \theta) = S_k \cdot \Lambda \cdot \frac{G_L(r, \theta)}{G_L(r_0, \theta_0)} \cdot g_L(r) \cdot F(r, \theta) \quad (1)$$

Where  $\gamma$  is the radial distance along the transverse axis of the source,  $\theta$  is the polar angle to the sources longitudinal axis,  $(\gamma_0, \theta_0)$  is the reference point located at (1 cm,  $\pi/2$ ),  $S_k$  is the sources air-kerma strength,  $\Lambda$  is the dose rate constant of the BT source,

$g_L(\gamma)$  is the radial dose function,  $F(\gamma, \theta)$  is the anisotropy function,  $G_L(\gamma, \theta)$  is the geometry function accounting for the sources radioactive material distribution, defined as:

$$G_L(r, \theta) = \begin{cases} \frac{\beta}{Lr \sin \theta} & \text{if } \theta \neq 0 \\ (r^2 - L^2/4) & \text{if } \theta = 0 \end{cases} \quad (2)$$

Figure 1 shows dose calculation of the Ir-192 BT source. The dose rate at a point  $P(\gamma, \theta)$ , at the radial distance  $\gamma$ , and the polar angle  $\theta$ , from a cylindrically symmetric line source centered at the origin of the water phantom, is used to calculate the radial dose function, the anisotropy function, geometry function, dose rate constant and air-kerma strength.

**2.2.2. The adapted formalism.** In the adapt formalism, we calculate basic dosimetry parameters defined in the dose calculation formalism recommended in the AAPM TG43 and its update.<sup>[8,9]</sup> These dosimetry parameters such as  $S_k$ ,  $\Lambda$ ,  $g_L(x, y, z)$ ,  $F(x, y, z)$ ,  $G_L(x_0, y_0, z_0)$ ,  $G_L(x, y, z)$  originate from PLATO TPS. But the grid matrix of Cartesian coordinate system is used in Pinnacle external radiation TPS. Namely we can find out the corresponding dose according to the point in mould. So we firstly transform the polar coordinates into Cartesian coordinates, namely:

$$r = \sqrt{x^2 + y^2 + z^2}$$

$$\theta = \arcsin \frac{\sqrt{x^2 + y^2}}{\sqrt{x^2 + y^2 + z^2}} \quad (3)$$

Thence, the dose rate  $\dot{D}(x, y, z)$  is given by Eq 4 too.

$$\dot{D}(x, y, z) = S_k \cdot \Lambda \cdot \frac{G_L(x, y, z)}{G_L(x_0, y_0, z_0)} \cdot g_L(x, y, z) \cdot F(x, y, z) \quad (4)$$

Where  $x, y, z$  are the distances along  $x, y, z$  axis of the source, respectively.

The total dose is the sum of the individual dose rate.

$$D(x, y, z)_{total} = \sum_{i=1}^n t_i \dot{D}(x, y, z)_i \quad (5)$$

where  $n$  is the number of the presence of the radioactive source,  $t_i$  is the time of the I presence

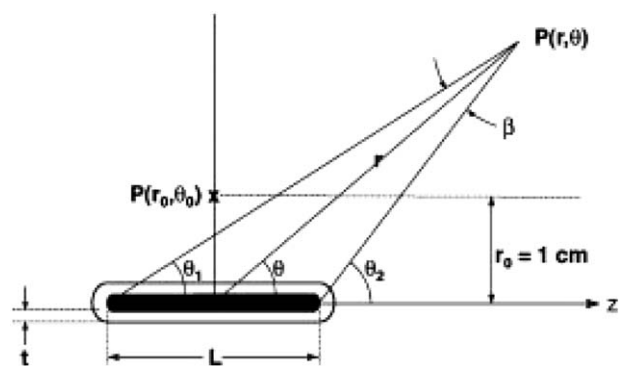


Figure 1. Methodology for dose.

**2.3. The position reconstruction of applicator based on the compute tomography coordinates**

The spatial location of each applicator can be determined by the orthogonal X-ray image captured from an ordinary simulator or C-arm machine. The position of the donor can also be determined by CT scans. However, the spatial coordinates of the donor obtained by these methods are different from those of the established EBRT planning. They are going to transfer between them.

The program can fuse different CT images of the same patient, and then reconstruct the position of the donor to the coordinates of the CT treatment plan of external radiotherapy. It does not take into account the patient’s change in position during the course of each treatment due to the change in the position of the target volume and the organs at risk. The translation and rotation of the coordinate system in the direction of X, Y, and Z is made only. Namely:

$$[x', y', z', 1] = [x, y, z, 1] \times T \tag{6}$$

Where T is the coordinate transformation matrix of  $4 \times 4$ . The CT fused images were finished with the Syntegra program of the Pinnacle TPS.

After the transformation, the spatial position of the donor can be mapped into the coordinate system of external irradiation treatment planning. In this way, it is possible to determine the location coordinate and the duration of the resident point for each radioactive source in the coordinate system of external irradiation TPS.

**2.4. Registration of the 3-dimensional dose distribution**

The overlap of 2 different dose distributions needs not only the 2 identical spatial coordinates, but also the same size of each volume, the same position and scale of the body elements in the spatial coordinates, as shown in Figure 2. When the 3-D dose distribution generated with using the source computing model, the parameters of 3-D dose grid, including the start coordinates ( $O(x, y, z)$ ), dimensions ( $l, m, n$ ) and voxel size ( $\Delta x, \Delta y, \Delta z$ ), were set according to the external radiation TPS (Pinnacle TPS was used in our hospital).

Namely : 
$$\begin{cases} O(x, y, z) = O'(x, y, z) \\ l = l', m = m', n = n' \\ \Delta x = \Delta x', \Delta y = \Delta y', \Delta z = \Delta z' \end{cases} \tag{7}$$

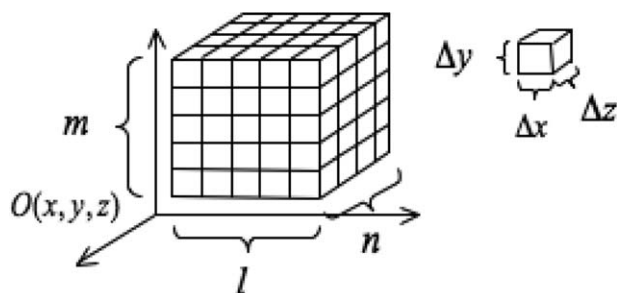


Figure 2. The network sketch of dose calculation.

**2.5. The total dose distribution of BT combined with EBRT**

The Pinnacle TPS used in our hospital is a simple EBRT TPS. It uses a voxel-based dose distribution expression, and its 3D dose distribution file can be obtained from the corresponding patient data file. The 3D dose distribution of BT, which is calculated by this program, is preserved according to the IEEE floating point representation defined by the Pinnacle TPS. A new field in the Pinnacle TPS was created before the dose file of BT was copied into Pinnacle TPS, then the dose file of BT replaced that of the new field. After that, the total dose distribution of BT combined with EBRT could be easily displayed in the Pinnacle TPS. It could not only display the 3D dose distribution in the Pinnacle TPS, but also set the prescription dose separately, evaluate the DVH curve and so on. In summary, the dose distribution of BT adding to EBRT could be seamlessly combined with the Pinnacle TPS. Figure 3 shows the flowchart of this methodology.

**2.6. Statistical analyses**

All data was analyzed by IBM SPSS Statistical software, version 19.0. And nonparametric tests (related samples) were used to compare the data of dose between 2 protocols. If P value < .05, the differences between groups were considered as statistically significant.

**3. Results**

**3.1. Comparison of dose distribution using Plato post loading treatment system and the program model calculated by the author**

The results of dose distribution of the single BT source were calculated with the Plato post loading TPS and the program model, respectively. And the results of dose distribution with 2 methods were shown in Table 1. Table 1a listed the dose distribution of the plane ( $Y=0$ ) calculated by the Plato TPS, which is obtained by the method of deriving the plane dose in the Plato post loading TPS. The columns in the table showed the X coordinates, and the rows represented the Z coordinates. Table 1b showed the results of dose distribution by the program model that is written by the author.

Table 2 listed the results of dose distribution in the plane ( $Z=0$ ) with 2 methods. Table 2a listed the dose distribution of the plane ( $Z=0$ ) calculated by the Plato TPS. Table 2b showed the results of dose distribution by the program model.

Both the heterosexual and radial functions are symmetrical along the Y axis, and the results are also symmetrical along the Y axis, so the results of the negative direction of the X axis are not shown. And nonparametric tests (related samples) were used to compare the data of dose between 2 protocols. The dose distribution in the plane ( $Y=0$ ) with the program model was similar with that using Plato TPS ( $P > .05$ ). Moreover, in the plane ( $Z=0$ ), similar dose distributions were obtained for both 2 protocols ( $P > .05$ ). The differences were not statistically significant.

**3.2. Dose distribution of EBRT combined with BT for cervical cancer**

In the planning of BT combined with EBRT, the dose distribution of BT was regarded as the dose distribution of a field, and the prescription dose of this field could be set in the Pinnacle TPS

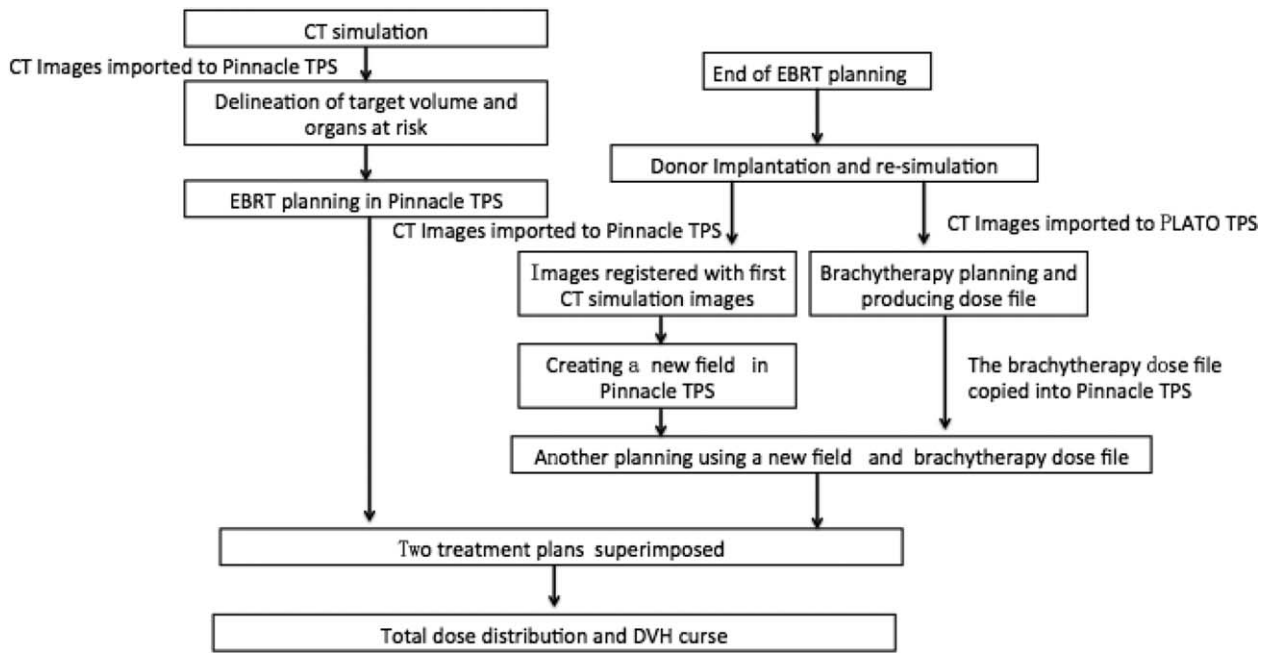


Figure 3. The flowchart of this methodology.

(Fig. 4A). The total dose distribution of BT combined with EBRT was showed in Figure 4B. And the corresponding DVH figures could be displayed correctly in Pinnacle TPS (Fig. 5).

**3.3. Dose distribution of intensity-modulated radiotherapy (IMRT) combined with brachytherapy for nasopharyngeal carcinoma (NPC)**

Figure 6 displays the plan of BT used for adding dose after IMRT in a patient with NPC. The positions of 2 CT scans were different and the plan of BT was finished in Plato TPS. The parameters reading from the Plato TPS included the resident position and duration of the radioactive source, and the air specific kinetic energy on the day of treatment. The resident position of the radioactive source was reconstructed in the Pinnacle TPS using the method of the coordinate reconstruction described in Section 1.4. Following that, the dose distribution of BT was computed and put into the Pinnacle TPS, then fused with IMRT plan.

**4. Discussion**

Today, BT is still essential for certain tumor, specially cervical cancer, NPC, and so on,<sup>[1-3]</sup> although 3-D conformal radiotherapy and IMRT were widely used. Because the accuracy of 3-D conformal radiotherapy and IMRT was likely to be affected by the patient’s posture and organ movement, BT can well overcome these shortcomings. Once the donor is implanted into the body of the patient, the relative position of the radioactive source and organs is determined and a better-shaped dose distribution can be produced in the tumor volume, while little effect on normal tissue around. Thence, in the radiotherapy of some tumors, such as cervical cancer, the combination of EBRT and BT has become the standard treatment option.

Now there are many brands of TPS used in radiotherapy, which have their own advantages in both internal and external radiation planning design, but they have few advantages in both aspects. Some planning systems that can synthesize internal and external radiation doses are often expensive, and most of the

**Table 1**

**Comparison of dose distribution in the plane (Y=0) with Plato treatment planning system and the program model.**

cGy Z (cm)	Results of Plato TPS X (cm)						Results of the program model X (cm)						P
	0	0.4	0.8	1	1.2	1.6	0	0.4	0.8	1	1.2	1.6	
-1.6	23.72	29.20	28.30	26.25	23.86	19.16	23.72	29.20	28.30	26.25	23.86	19.16	1.00
-1.2	42.14	52.55	45.31	39.51	34.00	24.89	42.14	52.55	45.31	39.51	34.00	24.89	1.00
-1	61.10	75.38	58.61	48.95	40.56	28.10	61.11	75.38	58.61	48.94	40.56	28.10	1.00
-0.8	98.89	114.75	76.52	60.37	47.86	31.39	98.91	114.75	76.52	60.37	47.86	31.39	.317
-0.4	485.68	311.65	124.48	86.17	62.76	37.18	486.18	311.65	124.48	86.16	62.76	37.18	.655
0		593.59	155.34	100.00	69.75	39.47		593.58	155.33	100.00	69.75	39.46	.083
0.4	547.40	311.52	124.38	86.13	62.70	37.11	547.96	311.52	124.38	86.13	62.70	37.10	.655
0.8	107.34	114.99	76.29	60.22	47.75	31.33	107.36	114.99	76.29	60.22	47.75	31.33	.317
1	65.90	76.06	58.50	48.82	40.45	28.04	65.91	76.05	58.50	48.82	40.45	28.04	.655
1.2	45.41	53.24	45.27	39.48	33.95	24.82	45.41	53.23	45.26	39.48	33.95	24.82	.157
1.6	25.50	29.71	28.41	26.28	23.88	19.15	25.50	29.70	28.40	26.28	23.88	19.15	.157

1a 1b.

**Table 2**  
**Comparison of dose distribution in the plane (Z=0) with Plato treatment planning system and the program model.**

cGy Y (cm)	Results of Plato TPS X (cm)						Results of the program model X (cm)						P
	0	0.4	0.8	1	1.2	1.6	0	0.4	0.8	1	1.2	1.6	
-1.6	39.47	37.17	31.65	28.48	25.38	19.85	39.46	37.17	31.65	28.48	25.38	19.85	.317
-1.2	69.75	62.85	48.47	41.39	35.12	25.38	69.75	62.85	48.47	41.38	35.12	25.38	.317
-1	100.00	86.37	61.33	50.39	41.39	28.48	100.00	86.37	61.33	50.39	41.38	28.48	.317
-0.8	155.34	124.67	78.37	61.33	48.47	31.65	155.33	124.67	78.37	61.33	48.47	31.65	.317
-0.4	593.59	305.79	124.67	86.37	62.85	37.17	593.58	305.79	124.67	86.37	62.85	37.17	.317
0		593.59	155.34	100.00	69.75	39.47		593.58	155.33	100.00	69.75	39.46	.083
0.4	593.59	305.79	124.67	86.37	62.85	37.17	593.58	305.79	124.67	86.37	62.85	37.17	.317
0.8	155.34	124.67	78.37	61.33	48.47	31.65	155.33	124.67	78.37	61.33	48.47	31.65	.317
1	100.00	86.37	61.33	50.39	41.39	28.48	100.00	86.37	61.33	50.39	41.38	28.48	.317
1.2	69.75	62.85	48.47	41.39	35.12	25.38	69.75	62.85	48.47	41.38	35.12	25.38	.317
1.6	39.47	37.17	31.65	28.48	25.38	19.85	39.46	37.17	31.65	28.48	25.38	19.85	.317

2a 2b.

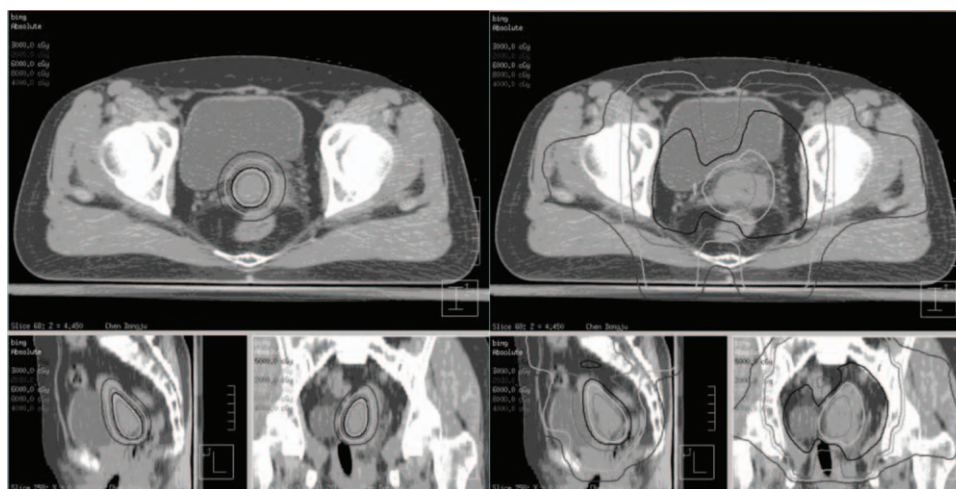
current internal and external beam radiotherapy planning systems belongs to different systems in hospitals. To solve the problem of dose superposition evaluation of internal and external irradiation plan, the following methods are adopted:

- (1) To display the dose distribution of internal and external irradiation on the third party software or to evaluate the dose of internal (external) irradiation. Distribution is imported into the external (internal) radiation therapy planning system to display and evaluate;
- (2) The compilation of the third party software displaying the superimposed dose distribution needs to run independently from the platform of the internal and external radiation TPS, and the internal and external radiation dose files cannot be modified once the guide is given;
- (3) Introducing the internal radiation dose distribution to the external radiation therapy meter. On the basis of internal irradiation, external irradiation can be used to supplement the under-dose area to superimpose, display and evaluate the internal and external irradiation dose on the same TPS platform. Cao et al imported the CT images of prostate planning into Eclipse TPS and delivered additional EBRT

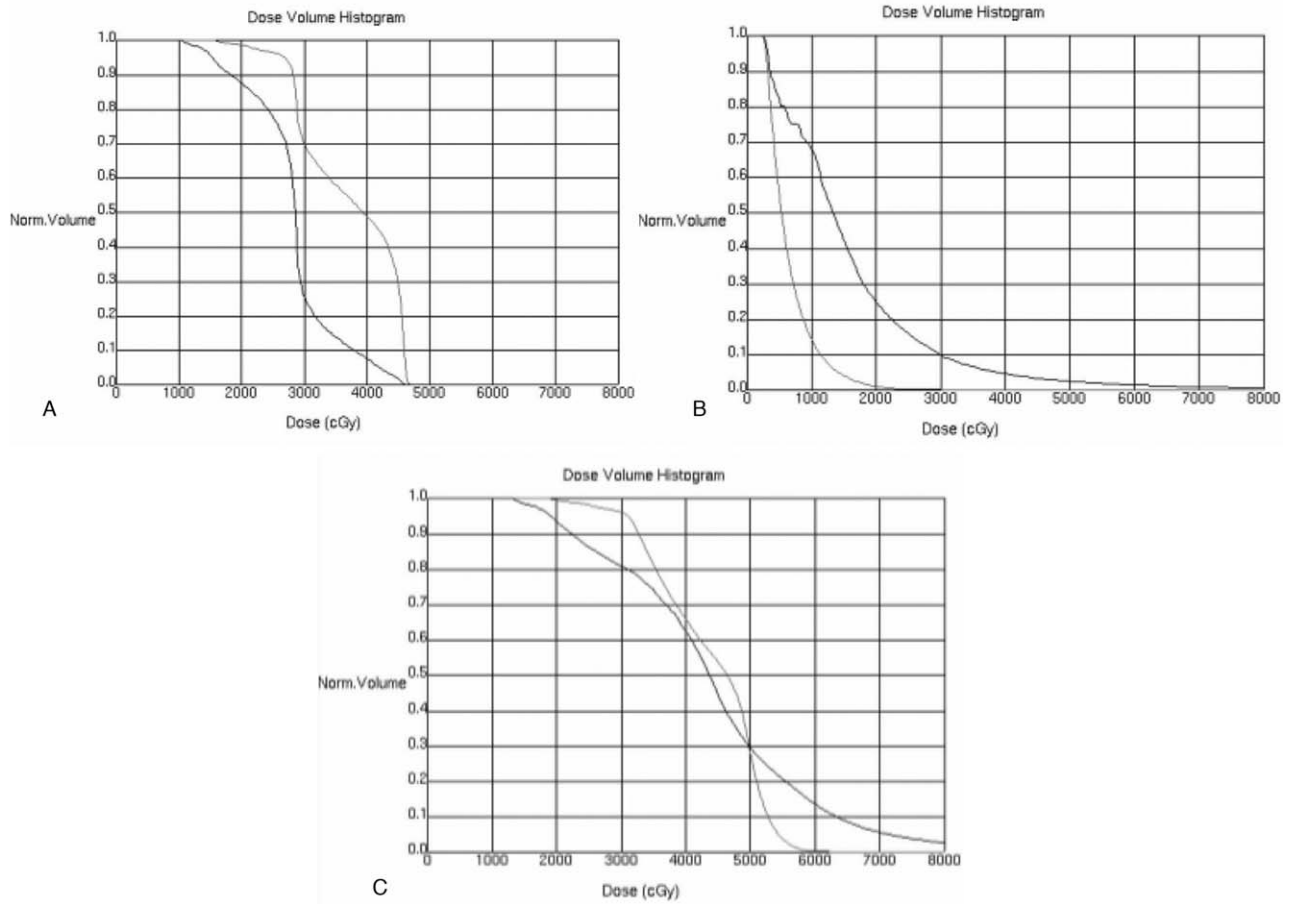
dose using IMRT for selected under-dose regions after BT.<sup>[10]</sup> The methods proposed by Pettersson et al used information from the EBRT DVH to estimate BT doses and assisted in assessing late toxicities with the limited dose data of EBRT and BT.<sup>[11]</sup>

Pinnacle TPS and Plato TPS were administered in our hospital, but both of these systems can only be used to calculate dose in separate modules and cannot display the cumulative dose of EBRT plus BT. The total dose cannot always be estimated accurately for 2 reasons:

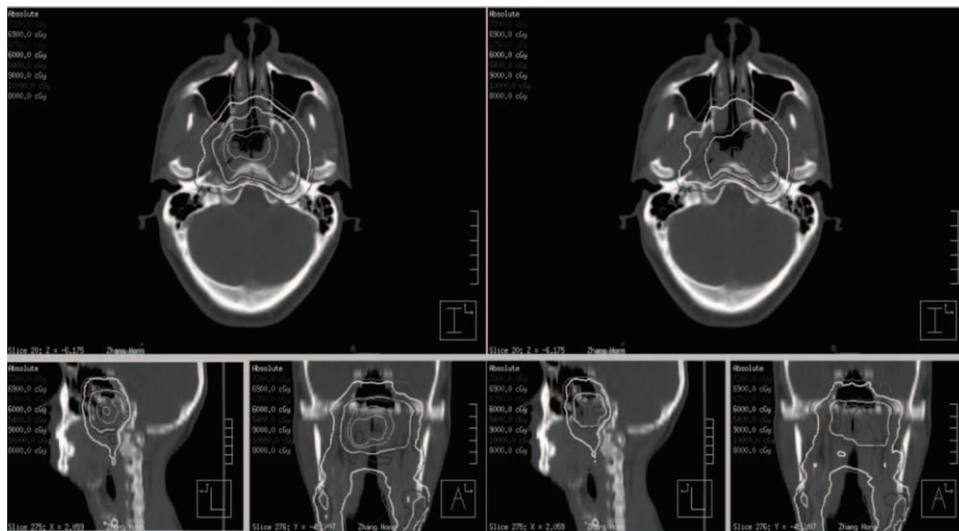
- 1) Each location of the applicator is different, so a single dose cannot be simply superimposed. The A- or B-point doses, which usually used in cervical cancer treated with BT, are only the dose at the certain distance point from the donor. Because the locations of A and B points change with the patients' position during each period of BT, the locations of A and B points cannot be exactly the same for the 2 treatment of BT. So it is not advisable to count the total dose of several fractions of BT and even to calculate



**Figure 4.** A The dose distribution of brachytherapy calculated by this program in Pinnacle TPS. The dose distribution of brachytherapy combined with external beam radiotherapy. BT = brachytherapy, EBRT = external beam radiotherapy, TPS = treatment planning system.



**Figure 5.** A Dose volume histogram of rectum and bladder in external beam radiotherapy. B Dose volume histogram of rectum and bladder in brachytherapy. BT = brachytherapy, DVH = dose volume histogram. C. total dose volume histogram of brachytherapy and external beam radiotherapy. BT = brachytherapy, DVH = dose volume histogram, EBRT = external beam radiotherapy.



**Figure 6.** A Dose distribution of intensity-modulated radiotherapy for nasopharyngeal carcinoma. B Total dose distribution for intensity-modulated radiotherapy and brachytherapy. BT = brachytherapy, IMRT = intensity-modulated radiotherapy, NPC = nasopharyngeal carcinoma.

the cumulative dose of EBRT plus BT for individualized precise radiotherapy.

- 2) The point doses at both A and B could not satisfy with the concept of volume dose. The tumor control rate and the incidence of normal tissue complications were mostly evaluated with the relationship between dose distribution and target volume in modern radiation oncology. The key to success in cancer treatment is how much the dose exposing for certain tumor volume, such as D95 (the dose exposing for 95% of tumor volume). Likely, The incidences of normal tissue complications were determined by the relationship between irradiated dose and the volume of normal tissue exposed, such as TD5/5, TD50/5 and so on. It is not possible to reflect the relationship between dose distribution and target volume due to the point dose at both A and B points. So it is not probable to have an accurate perception of dose distribution in 3D space. It often led to false estimates, and affected the total précised dose of EBRT combined BT.

We developed this program to calculate the dose of BT. The location of the applicator during each treatment of BT could be determined by the patient's quadrature images using the common analog locator or C-arm machine, and CT scans. Using the method of set change described in Section 1.4, we can determine the 3D coordinated of the radioactive source in Pinnacle TPS. As a result, the plan of BT is correctly displayed in Pinnacle TPS, and it met the requirements of the individual BT plan evaluation. The 3D dose distribution of BT plan could be exhibited separately in the Pinnacle TPS. The superimposed dose distributions of several different BT plan combined with EBRT plan were also displayed in Pinnacle TPS. We could set separately the prescription dose and fractions for each BT plan and each EBRT plan, and assess the total dose distribution of EBRT plus BT. All evaluation tools included the equivalent scene line and DVH figure in the Pinnacle TPS were also used in the fusing plan of EBRT and BT.

However, there are inherent limitations in this study. First, from the radiobiological point of view, some question regarding the model of EBRT and BT were considered.<sup>[12]</sup> This program only calculated the combined physical doses of EBRT plus BT, but did not utilize the radiobiological parameters. Second, the images of EBRT planning were different from BT planning images although deformable image registration was used to accumulate the combined dose distribution of EBRT plus BT.<sup>[13–15]</sup> In this program, we did not use deformable image registration.

## 5. Conclusion

In conclusion, our study showed that 3-D dose distribution of BT planning could be displayed in the Pinnacle TPS separately, and the dose distributions of different BT plans plus EBRT plans could also be superimposed. The cumulative dose distribution of internal and external irradiation can be evaluated by setting a separate prescription dose and fraction times for each BT planning and EBRT planning. Internal and external radiation fusion plans can also use all available evaluation tools on Pinnacle TPS, including isodose curve and DVH.

## Author contributions

**Data curation:** Chuner Jiang, Weifeng Qin.

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**Investigation:** Zhimin Ye, Peng Wu.

**Methodology:** Kaiyuan Shi.

**Writing – original draft:** fangzheng wang.

**Writing – review & editing:** Zhenfu Fu, Yangming Jiang.

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