**A model to guide the management and decision of re-planning during radiotherapy for cervical cancer**

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**Background:** To establish a model to predict whether re-planning is needed in the process of cervical cancer radiotherapy.

**Methods:** We collected the clinical indexes of 132 patients diagnosed with cervical cancer receiving concurrent chemotherapy and radiotherapy, including 33 factors about tumor markers [carcinoembryonic antigen (CEA), cancer antigen 125 (CA-125), squamous cell carcinoma antigen (SCC)], tumor volume, rectal volume, bladder volume, volumes receiving 30–50 Gy in organs-at-risk (OARs), and the maximum dose (Dmax) received by 1–2 cc in OARs. We established a multivariate model for re-planning evaluation via principal component analysis, and then verified the model based on the internal data.

**Results:** We identified the dose index (P1), tumor size index (P2), and volumes receiving 30–50 Gy in OARs and the tumor (P3) as the three most weighted factors of the re-planning model. We set the cut-off for the re-planning modification requirement at 1. The model was consistent with $R = 0.12P1 + 0.21P2 + 0.31P3$, and it performed accurately that area under the test set characteristics curve (AUC) = 0.826.

**Conclusions:** Our proposed method can help to reduce image re-examination during treatment, decrease toxicities in OARs, shorten the radiotherapy course, lessen oncologists’ efforts, and save medical resources.

**Keywords:** Cervical cancer; radiotherapy; re-planning; model

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**Introduction**

Cervical cancer is one of the most common malignant tumors in women worldwide (1). Radiotherapy is a major treatment for cervical cancer (2). The protection of organs-at-risk (OARs) during radiotherapy is essential to prevent side effects (3). Intensity-modulated radiotherapy (IMRT) has superior dose distributions that conform to the shape of the target volume, and most of all, yield lower acute and late radiation toxicities (4). Nevertheless, a study has confirmed that after using IMRT, the radiation toxicities of normal tissue are reduced, but the effect is limited, and the problem cannot be solved completely. For example, Cheng et al. (5) reviewed 222 patients who were treated with IMRT. They demonstrated that the most common toxicity was vaginal stricture (grade 2, n=59, 26.6%; grade 3, n=4, 1.80%), followed by proctitis (grade 2, n=24; 10.8%; grade 3, n=7; 3.20%) and cystitis (grade 2, n=5, 2.3%; grade 3, n=2; 0.90%), and only 5 patients (grade 2, 2.3%) were found to have colitis.
The question remains as to why a toxic reaction of OARs still occurs in IMRT treatment. It has been previously considered that the change in tumor size affects the toxicity of OARs. For example, Chen et al. (6) studied cone-beam computed tomography (CBCT) to measure the tumor changes in 16 patients with cervical cancer, including 23.05 (8.8–46.7), 40.35 (10.3–57.0), 55.57 (25.2–76.6), 64.06 (46.9–82.0) and 70.85 (54.2–87.4) cm$^3$ at 9 Gy/5 f, 18 Gy/10 f, 27 Gy/15 f, 36 Gy/20 f, and 48.6 Gy/27 f, respectively. The results showed that tumor regression was most obvious at 27 Gy/15 f irradiation. For 36 Gy/20 f, tumor regression was not obvious after 20 rounds of radiotherapy. Nam et al. (7) used magnetic resonance imaging to measure the regression of tumor volume in 81 patients with cervical cancer during radiotherapy. The results showed that the tumor regression at 36–45 Gy determined the tumor control rate.

To further reduce the increased toxicity caused by tumor changes, our hospital used re-planning in radiation. However, several reports are inconsistent, suggesting that not all patients need a second plan. Therefore, it is necessary to establish a reliable model to predict whether re-planning is required. Meanwhile, the re-planning prolongs the course of treatment and potentially affects the prognosis. Herein, we pooled the clinical-pathological characteristics and physical parameters of radiotherapy into a principal component analysis and established a mathematical model to guide clinical decisions. We present the following article in accordance with the MDAR reporting checklist (available at https://dx.doi.org/10.21037/tcr-21-2545).

Methods

Patients

In this study, 132 patients diagnosed with cervical cancer according to the International Federation of Gynecology and Obstetrics (FIGO) guidelines in 2009 (8) and received image-guided radiotherapy (IGRT) with 4–6 cycles of platinum chemotherapy weekly between May 2017 and December 2019 were included.

The inclusion criteria were as follows: (I) female, 30–80 years old; (II) cervical squamous cell carcinoma was confirmed histologically or pathologically; (III) Karnofsky performance scale $>70$; (IV) expected survival $>3$ months; (V) radiotherapy 29.12 Gy/17 f to 36 Gy/19 f; (VI) patients treated with platinum-based chemotherapy lasting 4–6 cycles; and (VII) the white blood cells $>3.5 \times 10^9$/L, neutrophil $>1.5 \times 10^9$/L, platelet $>100 \times 10^9$/L, hemoglobin $>90$ g/L, total bilirubin $<1.5$ times the upper limit of the normal value, alanine aminotransferase and aspartate aminotransferase $<2.5$ times the upper limit of the normal value, and creatinine $<1.5$ times the upper limit of normal value.

The exclusion criteria were as follows: (I) patients with mental illness and those unable to cooperate; (II) patients with severe heart, liver, kidney, lung, and other visceral diseases; (III) patients with blood system diseases; (IV) FIGO stage: patients without radiotherapy pointer; (V) patients with other malignant tumors; (VI) patients with leukocytosis caused by infection, immunity, and other diseases. The endpoint of the study was defined as when OARs enter the clinical target volume (CTV), the target area needed to be modified. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was performed in the Affiliated Hospital of Inner Mongolia Medical University and approved by the institutional ethics board of Affiliated Hospital of Inner Mongolia Medical University [No. WZ(2021050)] and individual consent for this retrospective analysis was waived.

Radiation procedures

Positioning scheme

Patients received oral administration of the compound meglumine diatrizoate before positioning, kept bladder filling and rectal emptiness, were in the supine position, had their hands in front of their foreheads, maintained relaxation of the body, had their legs straightening naturally, thermoplastic film fixed position, and laser lamp calibrating phantom three markers. Next, the cases underwent enhanced CT scanning (scanning thickness: 5 mm; scanning range: from the diaphragm to middle femur). The last CT images were transferred to the treatment planning department.

Target delineation

Gross target volume (GTV) was defined as a cervical mass that invaded the uterine body and vagina. Lymph node metastasis (GTV-nd) was defined as para-aortic, iliac vascular, pelvic, and inguinal lymph node metastasis. CTV was defined as the drainage area of the uterus, cervix, vagina, and lymph nodes. Planning target volume (PTV) was defined as the expansion of CTV in anterior/posterior, superior/inferior, right/left direction by 7, 10, and 7 mm (9).
Restriction of OARs
Rectum V45 Gy ≤50%; bladder V45 Gy ≤50%; femoral head V45 Gy ≤5%; the Dmax of spinal cord ≤45 Gy; small intestine V25 Gy ≤50%, V54 Gy ≤2 cc.

Plan evaluations
95% of PTV met the prescribed dose of the target area. PTV accepted 110% of the prescription dose (PD)-volume <20%. PTV accepted 93% of the PD-volume <3%. There was no more than 110% PD anywhere outside the PTV.

Treatment procedures
After positioning by CT (LightSpeed RT 16, GE, USA), the patient received radiotherapy (1.8–2 Gy/f, 5 fractions per week to 48.5–50 Gy) via a 6 MV high-energy X-ray linear accelerator (Trilogy, Varian, USA). We used CBCT to verify the position and calibrate the settings first, and four cycles of platinum-based chemotherapy were synchronized with radiotherapy once weekly. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013).

Secondary CT evaluation and re-planning
CT was used to re-examine all patients after 18 fractions. CT images were matched with the previous plan. If any OAR was included inside the CTV, we re-delineated GTV, CTV, and OARs to adopt the new tumor condition. The dosage of the two-step-plan also accumulated to 48.5–50 Gy.

Statistical analysis
The R Programming Language x64 3.6.2 (University of Auckland, New Zealand) is selected for all statistical analyses. The original data was normalized to form new data named data, and the relationship between 33 variables (Table 1) in the data and R (we set R as the output value to define re-planning situation at a cutoff =1) was then analyzed. Combined with the principal component analysis (data 1), the main factors affecting the re-planning were identified, and the model was subsequently established. Next, the related problems were explained by polychotomous logistic regression, and finally, the feasibility of the model was verified.

| Table 1 Variable interpretation |
|--------------------------------|
| **Abbreviations** | **Full name** |
| C (CEA) | Carcinoembryonic antigen |
| CA (CA-125) | Cancer antigen 125 |
| S (SCC) | Squamous cell carcinoma antigen |
| L1 (long diameter 1) | Long diameter of pre-radiotherapy |
| L2 (long diameter 2) | Long diameter of peri-radiotherapy |
| S1 (short diameter 1) | Short diameter of pre-radiotherapy |
| S2 (short diameter 1) | Short diameter of peri-radiotherapy |
| T1 (tumor volume 1) | Tumor volume of pre-radiotherapy |
| T2 (tumor volume 2) | Tumor volume of peri-radiotherapy |
| R1 (rectal volume 1) | Rectal volume of pre-radiotherapy |
| R2 (rectal volume 2) | Rectal volume of peri-radiotherapy |
| B1 (bladder volume 1) | Bladder volume of pre-radiotherapy |
| B2 (bladder volume 2) | Bladder volume of peri-radiotherapy |
| ED | External dose |
| PX (PTV Dmax) | Maximum planned target dose |
| RX (rectal Dmax) | Maximum rectal dose |
| BX (bladder Dmax) | Maximum dose of bladder |
| PM (PTV Dmin) | Planned target minimum dose |
| RM (rectal Dmin) | Rectal minimum dose |
| BM (bladder Dmin) | Bladder minimum dose |
| PN (PTV Dmean) | Planned target mean dose |
| RN (rectal Dmean) | Rectal average dose |
| BN (bladder Dmean) | Mean bladder dose |
| R3 (rectal V30) | Volume of rectum 30 Gy |
| R4 (rectal V40) | Volume of rectum 40 Gy |
| R5 (rectal V50) | Volume of rectum 50 Gy |
| B3 (bladder V30) | Volume of bladder 30 Gy |
| B4 (bladder V40) | Volume of bladder 40 Gy |
| B5 (bladder V50) | Volume of bladder 50 Gy |
| RC1 (rectal D1cc) | Maximum dose of rectal 1 cc |
| BC1 (bladder D1cc) | Maximum dose of bladder 1 cc |
| RC2 (rectal D2cc) | Maximum dose of rectal 2 cc |
| BC2 (bladder D2cc) | Maximum dose of 2 cc in bladder |
Results

Characteristics of patients

One hundred and thirty-two patients with cervical cancer were enrolled in this study, of which 99 were assigned to the training set, and 33 were assigned to the testing set. We collected the patients’ characteristics, which are shown in Table 2. The comparison of the patients’ tumors, rectums, and bladders pre and peri-radiotherapy is shown in Table 3, and the doses of the rectum, bladder, and tumor are shown in Table 4.

Some variables were involved in re-planning in radiotherapy

Polychotomous logistic regression was performed to explore the relationship between 33 variables and re-planning (Figure 1). The three criteria show that most of the information of the data set can be preserved by selecting three principal components (Figure 2).

Three indexes were defined to predict the re-planning

By analyzing the results of the program, we find three main influencing factors. The relationship between them is as shown in Figure 3. We find that: the first index was mainly related to “PN”, “PX”, “BC1”, “RX”, “RC1”, and “RC2”, which we defined as the “dose index”. The second index was mainly related to “L2”, “S2”, “S1”, “T2”, “L1”, and “T1”, which we defined as the “tumor size index”. The

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### Table 2 Characteristics of patients

| Characteristics     | N=132, n (%) |
|---------------------|-------------|
| Age (years)         |             |
| Range 31–80         | 30–40       |
| 9 (6.81)            |
| 25 (18.94)          |
| 53 (40.15)          |
| 37 (28.03)          |
| 8 (6.06)            |
| Stage (FIGO, 2009)  |             |
| IB 5 (3.79)         |
| IIA 12 (9.09)       |
| IIB 81 (61.36)      |
| IIIA 2 (1.51)       |
| IIIB 29 (21.97)     |
| IVA 3 (2.27)        |
| External dose       |             |
| 46 Gy/25 f 29 (21.97) |
| 50 Gy/25 f 56 (42.42) |
| 50.96 Gy/28 f 47 (35.61) |
| Re-planning         |             |
| Yes 24 (18.18)      |
| No 108 (81.82)      |
| FIGO, International Federation of Gynecology and Obstetrics. |

### Table 3 Comparison of tumor, rectum, and bladder pre- and peri-radiotherapy

| Groups               | Tumor volume (cm³) | Long diameter (cm) | Short diameter (cm) | Rectal volume (cm³) | Bladder volume (cm³) |
|----------------------|--------------------|--------------------|---------------------|---------------------|----------------------|
| Pre-radiotherapy, mean ± SD | 69.25±35.90        | 5.582±1.238        | 3.807±1.100         | 66.74±25.52         | 375.71±154.72        |
| Peri-radiotherapy, mean ± SD | 28.87±15.02        | 3.610±1.207        | 2.437±0.823         | 74.05±22.71         | 271.32±121.5         |

The changes of tumor images before and after 17–19 rounds of radiotherapy were compared to evaluate the impact of the above indexes on re-planning.

### Table 4 Dose and volume of the rectum, bladder, and PTV

| Groups | V30 (%) | V40 (%) | V50 (%) | D1cc (cG) | D2cc (cG) | Dmin (cG) | Dmax (cG) | Dmean (cG) |
|--------|---------|---------|---------|-----------|-----------|-----------|-----------|------------|
| Rectal, mean ± SD | 0.92±0.07 | 0.36±0.14 | 0.01±0.02 | 4,796.8±338.96 | 4,725.4±351.78 | 2,287.5±604.05 | 5,045.6±423.74 | 3,778.4±219.59 |
| Bladder, mean ± SD | 0.86±0.08 | 0.49±0.09 | 0.16±0.11 | 5,425.2±362.0 | 5,338.7±353.32 | 2,222.7±317.08 | 5,593.3±462.94 | 4,008.3±259.58 |
| PTV, mean ± SD | –       | –       | –       | –         | –         | –         | –         | –          |

The mean ± SD of these indexes according to the pre-radiotherapy plan were calculated to evaluate the influence on re-planning.
Figure 1 Relationship between 33 variables and re-planning (R). (A) The negative correlation between C, R1, B1, PM, RM, BM, RN, R3, R4, B3, and re-planning was very weak; The positive correlation between L1, S1, RC1, RC2 and re-planning was stronger. (B) Other factors exhibited a weak positive correlation with re-planning. (C) S1, L1, T1, S2, L2, and T2 were positively correlated. (D) BC1, BC2, RC1, RC2, and ED were positively correlated. C, carcinoembryonic antigen; R1, rectal volume of pre-radiotherapy; B1, bladder volume of pre-radiotherapy; PM, planned target minimum dose; RM, rectal minimum dose; BM, bladder minimum dose; RN, rectal average dose; R3, volume of rectum 30 Gy; R4, volume of rectum 40 Gy; B3, volume of bladder 30 Gy; L1, long diameter of pre-radiotherapy; S1, short diameter of pre-radiotherapy; RC1, maximum dose of rectal 1 cc; RC2, maximum dose of rectal 2 cc; S1, short diameter of pre-radiotherapy; L1, long diameter of pre-radiotherapy; T1, tumor volume of pre-radiotherapy; S2, short diameter of peri-radiotherapy; L2, long diameter of peri-radiotherapy; T2, tumor volume of peri-radiotherapy; BC1, maximum dose of bladder 1 cc; BC2, maximum dose of 2 cc in bladder; RC1, maximum dose of rectal 1 cc; RC2, maximum dose of rectal 2 cc; ED, external dose.

Figure 2 The numbers of main components affecting radiotherapy re-planning. In the gravel test, this paper evaluated three eigenvalue standards based on the average eigenvalue (dotted line) from 200 random data matrices and the eigenvalue standard (horizontal line) greater than 1. PC, principal components; FA, factors.

third index was mainly related to “R3” and “B3”, which we defined as the “V30 index”. Their internal relationships are shown in Figures 4-6, respectively.

Establishment of the predictive model for re-planning in radiotherapy

Given that the system of re-planning contained three indicators (dose index, tumor size index, V30 index), a multi-objective optimization model was first established as follows:

\[
\begin{align*}
\text{Max} R & = \sum_{i=1}^{3} \lambda_i P_i^j \\
\lambda_i & \geq 0 \\
\sum_{i=1}^{3} \lambda_i P_i & = 1
\end{align*}
\]

[1]

Model 1: re-planning index model

\( \lambda_i \) was the weighted coefficient of \( P_i \). \( P_i^j \) was the \( j^{th} \) principal
**Figure 3** Three principal components were obtained through analysis. (A) In $P_1$, “PTV Dmean” had the greatest influence on re-planning, and other influencing factors were arranged according to weight. (B) In $P_2$, “long diameter 2” had the greatest influence on re-planning, and other influencing factors were arranged according to weight. (C) In $P_3$, “rectal V30” had the greatest influence on re-planning, and other influencing factors were arranged according to weight. PTV, planning target volume; $P_1$, does index; $P_2$, tumor size index; $P_3$, volumes receiving 30 Gy in organs-at-risk (V30).

**Figure 4** Variable relationships within the “dose index”. The diagonal line represents the correlation between the comprehensive analysis of PN, PX, BC1, BC2, RX, RC1, and RC2. The other grids were the result of pairwise comparison based on the diagonal factors. The figure indicated that the factors in the “dose index” were non-linearly correlated. PN, planned target mean dose; PX, maximum planned target dose; BC1, maximum dose of bladder 1 cc; BC2, maximum dose of 2 cc in bladder; RX, maximum rectal dose; RC1, maximum dose of rectal 1 cc; RC2, maximum dose of rectal 2 cc.
**Figure 5** Variable relationships within the “tumor size index”. The diagonal line represents the correlation between the comprehensive analysis of L2, S2, S1, T2, L1, and T1. The other grids were the result of pairwise comparison based on the diagonal factors. The figure indicated that the factors in the “tumor size index” were non-linearly correlated. L2, long diameter of peri-radiotherapy; S2, short diameter of peri-radiotherapy; S1, short diameter of pre-radiotherapy; T2, tumor volume of peri-radiotherapy; L1, long diameter of pre-radiotherapy; T1, tumor volume of pre-radiotherapy.

**Figure 6** Variable relationships within the “V30 index”. The other grids were the result of pairwise comparison based on the diagonal factors. The figure indicated that the factors in the “V30 index” were non-linearly correlated. The diagonal line represents the correlation between the comprehensive analysis of B3 and R3. V30, volumes receiving 30 Gy in organs-at-risk; B3, volume of bladder 30 Gy; R3, volume of rectum 30 Gy.
Cervical cancer is a worldwide pandemic. Early stage re-planning in radiotherapy was as follows: the patients underwent re-planning). The final model for predicting re-planning in radiotherapy was as follows: R = 0.12P + 0.67P + 0.75P. The model verified the influence of the three indexes on re-planning and ranked them according to the weights (Table 5). The model also calculated the mostly affected factors in the “dose index” (Table 6), “tumor size index” (Table 7), and “V30 index” (Table 8). At the same time, the 95% confidence interval (CI) was used to limit each influencing factor (Table 9), which did not differ significantly (P>0.05).

The predictive ability of the model in the test set
We utilized the model on the patients in the test set. We randomly selected 33 patients into a test set for R Programming Language Verification. We calculated the accuracy at 0.826, indicating that the model performed well in the test set. Thus, this model is applicable to predicting re-planning in radiotherapy.

Discussion
Cervical cancer is a worldwide pandemic. Early stage component index (in this study, we drew the three principal component indexes). R was the re-planning index. Different patients had different λi. To standardize the data to P1, P2, and P3, we hypothesized that R was 1 (and that all of the patients underwent re-planning). The final model for predicting re-planning in radiotherapy was as follows: R = 0.12P + 0.21P + 0.31P. The model verified the influence of the three indexes on re-planning and ranked them according to the weights (Table 5). The model also calculated the mostly affected factors in the “dose index” (Table 6), “tumor size index” (Table 7), and “V30 index” (Table 8). At the same time, the 95% confidence interval (CI) was used to limit each influencing factor (Table 9), which did not differ significantly (P>0.05).

| Index          | P1  | P2  | P3  | R   |
|----------------|-----|-----|-----|-----|
| PTV Dmax       | 0.89| 0.08| −0.29| 0.89|
| Rectal Dmax    | 0.88| −0.06| 0.11| 0.444|
| PTV Dmean      | 0.87| 0.18| −0.23| 0.443|
| Bladder Dmax   | 0.85| 0.18| −0.20| 0.439|
| Rectal D2cc    | 0.82| −0.07| 0.14| 0.417|
| Rectal D1cc    | 0.83| −0.07| 0.09| 0.412|
| PTV Dmean      | 0.89| 0.08| −0.29| 0.411|
| Bladder D1cc   | 0.81| 0.16| −0.23| 0.407|
| Bladder D2cc   | 0.83| 0.12| −0.27| 0.397|
| Rectal Dmean   | 0.68| 0.20| −0.05| 0.390|

The three main influencing indexes were obtained, and the effects of the three indexes were comprehensively considered, namely, λ1 = 0.5; λ2 = 0.3; λ3 = 0.2. Among them, P1, P2, and P3 are the “dose index”, “tumor size index”, and “V30 index”, respectively. PTV, planning target volume.

| Index          | P1  | P2  | P3  | R   |
|----------------|-----|-----|-----|-----|
| Short diameter 1| 0.16| 0.83| −0.03| 0.83|
| Short diameter 2| 0.02| 0.81| 0.20| 0.81|
| Long diameter 2 | −0.11| 0.80| 0.09| 0.80|
| Tumor volume 1  | 0.16| 0.77| 0.09| 0.77|
| Long diameter 1 | 0.06| 0.76| 0.10| 0.76|
| Tumor volume 2  | 0.24| 0.75| 0.07| 0.75|

Rule out other factors, only consider the effect of dose index on re-planning; that is, λ1 = 1; λ2 = 0; λ3 = 0, in which P1, P2, and P3 are the “dose index”, “tumor size index”, and “V30 index”, respectively. PTV, planning target volume.

| Index          | P1  | P2  | P3  | R   |
|----------------|-----|-----|-----|-----|
| Rectal V30     | −0.08| −0.02| 0.74| 0.74|
| Bladder V30    | −0.12| 0.34| 0.69| 0.69|
| Rectal Dmean   | 0.35| 0.00| 0.67| 0.67|
| Bladder Dmin   | −0.18| 0.09| 0.57| 0.57|
| Rectal Dmin    | −0.11| 0.04| 0.50| 0.50|
| Bladder Dmean  | 0.11| 0.47| 0.46| 0.46|
| Rectal V40     | 0.42| −0.14| 0.37| 0.37|
| Bladder V40    | −0.15| 0.43| 0.34| 0.34|

Rule out other factors, only consider the effect of V30 index on re-planning; that is, λ1 = 0; λ2 = 0; λ3 = 1, in which P1, P2, and P3 were “dose index”, “tumor size index”, and “V30 index”, respectively.
patients may be treated by surgical, other patients may be treated by radiotherapy or chemotherapy (10). Radiation treatment is performed using IMRT techniques (volumetric arc, conventional IMRT, or tomotherapy) and three-dimensional planned conventional techniques use 6 MV-X photons (11). Cisplatin 40 mg/m$^2$ body surface area is given in 5 weekly applications to a total dose of 200 mg/m$^2$ during external beam radiation. In case of contraindication to cisplatin, carboplatin (area under curve 2-weekly) is applied (12). Even the radiation technique used was IMRT, genitourinary and gastrointestinal toxicity had hurt patients. In order to reduce these damage, we established a mathematical model to guide secondary planning during radiotherapy for cervical cancer.

In this paper, notably, “dose”, “tumor size”, and “V30” were found to be the major impacting factors in evaluating the necessity of re-planning. Furthermore, the model performed well in the test set. The goal of radiation oncologists is to deliver a high dose X-ray to foci and minimize the X-ray uptake of normal tissue. Meantime, the radiation-induced injuries of OARs are restricted. So, it is imperative to understand the relative anatomical position between the tumor and paracancerous tissue both pre- and peri-radiotherapy. However, the relative position of OAR tends to move during radiotherapy as tumors shrink.

Therefore, in this study, we typically performed two-stage CT during radiotherapy (18 times; 30.6–34 Gy/17 f) to evaluate the necessity of secondary planning of radiotherapy, in order to determine the tumor volume, location changes, and OARs. As previously reported, CBCT is limited and cannot solve the problem completely (13,14). Meanwhile, some studies have concluded that CBCT is an effective means to reduce positioning error and directly evaluate the axial and horizontal position changes of the tumor, bladder, and rectum during treatment (15-17). So, the most important subsidiary condition is that CBCT is applied weekly for every patient. However, Mason et al. (18) used the Dice similarity coefficient and measured contour-to-contour distance to evaluate spatial image changes, so as to improve the treatment accuracy of cervical cancer by adaptive radiotherapy. CBCT has a small, lightweight, and open architecture, which can be directly integrated into the linear accelerator (19). However, it is unable to reduce the dosage distribution in OAR (20,21).

CEA, CA-125, and SCC have been verified to be related to the tumor burden and could predict tumor progression (22,23). However, considering our limited sample size, we could not find the expression diversity of CEA, CA-125, and SCC in radiotherapy planning. So, we eliminated clinical-pathological characteristics to build our model.

“Short diameter 1”, as the most influencing factor of tumor regression, could be a potential factors affecting re-planning. As previously reported (24,25), the change of tumor volume affects the radioactive side effects to the bladder and rectum, which seems to indicate that the volume change of the bladder and rectum are negatively correlated with the change in tumor volume. This study found that the change in tumor size affected the patient’s original radiotherapy plan. Thus, we needed to modify the plan to reduce the damage to OARs.

“PTV Dmean” is a crucial factor in evaluating a radiation plan. Many scholars report that in an optimal plan, for the target area, the Dmin should be close to the PD, so that the PD coverage rate is close to 1 (26). Also, the maximum and average doses for normal tissue should be minimize to ensure that the smaller exposure volume is within the tolerance threshold points (27). Our findings partly confirm

| Table 9 Ninety-five percent CIs for 16 variables within the three indexes |
|-----------------------------|-----------------------------|-----------------------------|
| Index                       | 2.5%                        | 97.5%                       | Pr (>|z|)       |
| (Intercept)                 | −7.06                       | 10.37                       | 0.71         |
| Long diameter 1             | −2.10                       | 5.33                        | 0.38         |
| Short diameter 1            | −2.40                       | 6.53                        | 0.35         |
| Long diameter 2             | −2.38                       | 4.68                        | 0.51         |
| Short diameter 2            | −4.63                       | 2.96                        | 0.65         |
| Tumor volume 1              | −4.77                       | 2.73                        | 0.65         |
| Tumor volume 2              | −3.08                       | 3.84                        | 0.85         |
| PTV Dmax                    | −6.98                       | 3.83                        | 0.60         |
| PTV Dmean                   | −3.96                       | 6.92                        | 0.60         |
| Rectal Dmax                 | −5.77                       | 2.58                        | 0.46         |
| Bladder Dmax                | −2.38                       | 9.53                        | 0.27         |
| Bladder D1cc                | −8.71                       | 2.84                        | 0.46         |
| Bladder D2cc                | −8.07                       | 4.81                        | 0.51         |
| Rectal D1cc                 | −7.13                       | 5.19                        | 0.85         |
| Rectal D2cc                 | −1.13                       | 11.20                       | 0.15         |
| Rectal V30                  | −10.61                      | 5.63                        | 0.54         |
| Bladder V30                 | −12.27                      | 3.56                        | 0.30         |

The probability on the right side minus on the left gives the 95% CIs. The coefficient of regression equation is not significant (P>0.05). CI, confidence interval; PTV, planning target volume.
the above. We demonstrated that the average dose of PTV affects the related dose index of the rectum and has a significant positive correlation. Altogether, the “PTV Dmean” should be reduced in order to protect the rectum.

Besides the tumor size and “PTV Dmean”, “V30” was also found to be involved in re-planning (28). Qiao et al. (29) reported that the “V30” can predict injury to OARs, which can be reduced by reducing the “V30”. Previous studies have shown that the larger the “V30”, the more serious the side effects and the larger the intestinal volume (30-33). Unsurprisingly, “V30” affects enteritis and is significantly positively correlated to rectal volume. Therefore, the “V30” should be reduced in order to protect the rectum.

The model proposed in this paper has similar defects with a mass model, such as the end-to-end OARs segmentation model evaluated by Liu et al. (34), in providing accurate and consistent OARs segmentation results in much less time. The disadvantage of our model is that it is a single-center design, which means that the model would not apply to patients in other hospitals. Even though this model has achieved perfect results, it still required the collection of multiple data sources. However, the advantage of our model is that it can integrate medical knowledge and safely and reasonably evaluate whether the radiotherapy plan needs to be changed. Moreover, it can further reduce the damage of OAR. In short, modern radiotherapy needs to combine big data with medical treatment to deal with the uncertainty implied in radiotherapy and plan treatment more sensibly.

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