Study on the improved internal feedback system of Rapidplan model

Kuo Li  
Shandong Tumor Hospital

Pan Yang  
Linzi District People's Hospital

Xinqiang Zhang  
Shandong Tumor Hospital

Shuang Yu  
Qilu Hospital of Shandong University

Cheng Tao  
Shandong Tumor Hospital

Changsheng Ma (machangsheng_2000@126.com)  
Shandong Tumor Hospital

Research Article

Keywords: Rapid Plan, cervix cancer, knowledge-based model, dose, intensity modulated radiation therapy

DOI: https://doi.org/10.21203/rs.3.rs-286925/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Objective: To study whether an interactive improved internal feedback system with the model can be established, we aimed to compare the plans generated by two automatic planning models generated under the same conditions.

Methods: 70 cases of pelvic patients were selected. Intensity modulated radiation therapy (IMRT) plans (P0) generated by clinical model (M0) were imported into Rapidplan model, in order to establish dose volume histogram (DVH) predicted model through automatic planning model in clinical used, and the new Rapidplan model (M1) was generated by training and structure matching settings. 70 new IMRT plans (P1) were generated by M1, and new Rapidplan model (M2) was training by P1. By the same way, 70 IMRT plans (Plan2) were generated by M2. Dosimetric differences between P1 and P2 were compared and analysed.

Results: From the inside of the model, the values of $R^2$ and $X^2$ in P2 were higher than those in P1, and the CD values of bladder, right femoral head and rectum in P1 were higher than those of corresponding organs in P2. The SR value of bladder and the SR and DA values of left femoral head and right femoral head in P1 were lower than those of P2. In terms of planning, the $D_2$, $D_{98}$ and HI in P1 were better than those in P2 (P<0.01), the bladder V10 and left femoral head V40 in P2 were lower than those in P1 by 0.08% and 0.15%, respectively (P<0.05), the others in P2 were higher than those in P1 (P<0.05) except the bladder V20, $D_{mean}$, rectum V10, V20, V30, right femoral head V10 and V40; and the MUs of P2 was lower than that of P1 for 132.2 (P<0.05).

Conclusion: The stability of M2 is stronger than that of M1. Therefore, it can be considered that the interactive improved internal feedback system within the model of "plan-model-plan-model" is feasible and meaningful.

Introduction

The optimization of radiation treatment plan is a process of trial and error that obtains satisfactory dose distribution between the planning target volume (PTV) and organs at risk (OARs). Under the condition that the PTV and dosage are determined, the quality of plans has a great relationship with angle and optimization conditions given by the physicist. Due to the different experiences and levels of different physicists in different hospitals, there are great differences in the radiotherapy plans designed for the same case. The radiotherapy planning design of "knowledge-based radiation therapy" (KBRT) which was proposed by the research team of Duke University\textsuperscript{[1]} is a good method to solve this problem.

KBRT, as a typical representative of artificial intelligence and big data application in radiotherapy, has been well known, accepted and recommended by the industry. At present, each mainstream planning system also has its own KBRT. The Eclipse planning system of Varian Company has launched its own
automatic planning system Rapid Plan, which is commonly referred to as rapid planning or automatic planning. Eclipse 13.5 version 13.5 and later can turn on this feature. This study uses Eclipse version 13.6.

For the newly established model, further examination and analysis are needed to eliminate the problems that may be caused by data import, PTV and organ structure matching, prescription dosage and other steps. The following parameters are mainly checked: (1) residual scatter plot reflects the difference between the real value and predicted value of dose volume histogram (DVH); (2) Regression curve reflects the relationship between main geometric features and DVH; (3) The box map of the geometric distribution of OARs reflects the anatomical features used in the model training plan; (4) The distribution of DVH in the field reflects the correlation between the real value and the predicted value of DVH in the field; (5) Training log files record statistical characteristics of fitting results. To detect outliers or strong influence points, set the following thresholds: Cook’s distance value (CD) > 4; modified Z-score (MZ) > 3.5; Studentized residual (SR) > 3; Areal difference of estimate (DA) > 3. Based on the above, we established a new rapid planning model and explored its clinical practicability.

**Materials And Methods**

1.1 Basic Information

Intensity modulated radiation therapy (IMRT) planning for 70 pelvic tumors in Shandong Tumor Hospital were randomly selected, regardless of age, sex, disease type and stage. All plans were performed with 6MV FF X-rays at a dose rate of 400MU/minute. Different types of accelerators were allowed to be selected for different cases, and the requirements for the type and radiation fields of the same case were the same. This is a retrospective and offline study. So it is not necessary to need information regarding ethics approval for the study, nor does it contain written informed consent from participants (Table 1).

1.2 Model Establishment and Generation Plan

By using the existing Rapid Plan clinical model M0 generated by the clinical plan and the DVH prediction model, the structural conditions are uniformly matched, the plan optimization is automatically completed, and the completed IMRT plan is named Plan0. Plan0 of 70 cases was re-imported into Varian Rapid Plan model library, and training and structure matching settings were carried out to generate a new Rapid Plan model M1 as the primary model. Structural matching is uniformly limited to PTV, bladder, rectum and femoral heads.

The newly generated automatic planning model M1 was selected to continue the preparation of the new IMRT plan for 70 cases, 6MV FF X-ray and 400MU/minute dose rate were also selected. We will name the new IMRT plan generated by the automatic plan model M1 Plan1 (P1 group). Through the same method, Plan1 were used to establish a new Rapid Plan model M2 as a secondary model, and the same training and structure matching as M1 were carried out. By using model M2, the same conditions as Plan1 were selected to generate a new IMRT plan, which is named Plan2 (P2). (Fig. 1)
In order to reduce the human interference in the process of automatic plan optimization and ensure the consistency of optimization conditions, we will set Rapid Plan models M1 and M2 in a unified way. In the optimization process, no matter to what extent each target condition is reached and whether a single plan optimization result is well, no human adjustment will be made in the process of plan completion. The same normalization method will be adopted after the plan was completed.

1.3 Plans

P1 generated by M1 were taken as the first group and P2 generated by M2 were taken as the second group. The automatic planning of the same case keeps the same algorithm, angle, prescription dose. The plan between different cases may have different angles and dose (single dose of 1.8Gy or 2.0Gy, total dose of 50Gy or 50.4Gy). The reason why P0 generated by the clinical model M0 was not used is that M0 was established by the clinical plan. Although we set the same conditions and did not make manual adjustment, because the model was established by the manual plan, the P0 generated by M0 was inevitably influenced by human fine-tuning factors and tends to people's ideal dose index.

1.4 Plan Evaluation

Using DVH statistics to evaluate the planned organ-threatening parameters of each group, bladder/rectum/femoral heads V10, V20, V30, V40, D_{mean}; The MU (Monitor unit, sum of all field hops in a certain plan), maximum dose D_2, minimum dose D_{98}, target dose HI (Homogeneity Index) and CI (Conformability Index) of the two plans were evaluated. The maximum exposure dose D_2 is defined as the exposure dose received by 2% of the PTV; The lowest exposure dose D_{98} is defined as the exposure dose received by 98% of the PTV. Hl=(D_2-D_{98})/D_{pres}, where D_{pres} is the prescription dose, the smaller the Hl value, the better the uniformity of the PTV.\[1\] CI = (VT, ref/vt) * (vt, ref/Vref), vt, ref is the PTV enclosed by the reference isodose line, vt is the PTV, Vref is the total volume under the reference isodose line.\[2\]

1.5 Statistical Method

SPSS 19.0 was used for data analysis. DVH data were extracted from Eclipse and imported into the analysis software in tabular format. The comparison mean-paired sample T test was used, and the difference was statistically significant (P < 0.05).

Results

Model

2.1 R^2 and X^2

In addition to comparing the targets between P1 and P2, we also need to analysis from the inside of the model to see which model is better. Like the regression coefficient R^2 of bladder in two models, R^2 of bladder in M2 is 0.935, which is higher than that in M1 (0.892). On the whole, as shown in the figure
below, the $R^2$ value of M2 is higher than that of M1, indicating that the better convergence of M2, the more stable the result and the better the robustness. In addition, $X^2$ in M2, the value of $X^2$ in both single organ and whole body is higher than that of $X^2$ in M1. It can be understood that M2 is more likely be interrelated than M1, and more closer to our requirements for model setting, reflecting our requirements for model training, or to be closer to the requirements of the clinical plan for model generation, and the better its stability (Fig. 2).

2.2 geometric outliers

There is the concept of strong influence point in the model, which is generally identified by CD. It is the point that strongly influences the regression model. The strong influence point is not necessarily the abnormal point, but it influences the result of the regression model. CD indicates the strong influence point in the regression model. The larger the value is, the greater the influence it has on the model. It has a threshold setting. Compared with two models, the CD (CD1) values of bladder, right femoral head and rectum in M1 were higher than those of corresponding organs in M2. Because we described earlier that the human positive factor in P0 was higher than P1. Combined with the fact that CD1 is greater than CD2, the effect of CD1 was greater than that of CD2. This is the reason why some indexes in P1 were higher than that in P2. The geometric outliers MZ in the model. MZ (MZ1) of bladder, left femoral head and rectum in M1 were higher than those in M2. MZ represents the geometric characteristics of a structure and other geometric outliers of the same structure in the model (Table 2).

2.3 Over optimization

We can also use SR and DA to check whether a plan is over optimized. SR = standard deviation of residuals. If one plan is over optimized, the dose distribution will be much better than another plan. In the two models we studied, the SR values of bladder and femoral heads in M1 were lower than the corresponding values in M2; the DA values of bladder and rectum in M1 were higher than the corresponding values in M2; the DA values of femoral heads in M2 were higher than the corresponding values in M1, and the DA predicted the actual DVH. (Fig. 3)

2.4 Comparison of Target Dose Parameters Planned by Two Models

As shown in the Table1, the CI of P2 generated by M2 was better than that of P1 generated by M1, and the difference was statistically significant ($P < 0.01$). $D_2$, $D_{98}$ and HI in P1 were better than those in P2, and the differences were all statistically significant ($P < 0.01$) (Fig. 4).

2.5 Comparison of Dose Parameters of OARs Planned by Two Models

Compared with various parameters of OARs planned by the two models, all datas were shown in Table 3 and Fig. 5. Dosage parameters of some OARs, such as bladder V20, $D_{mean}$, rectum V10, V20, V30, right femoral head V10, V40, showed no significant differences ($P > 0.05$).
2.6 MU

As shown in the Table 3, the MU of P2 was significantly lower than that of P1 in the two plans, and the difference was statistically significant (P < 0.01).

Discussion

KBRT has been proved its advantages and reliability, and has been accepted for planning in practical work. Mainly includes the establishment of DVH prediction model and model training.[5–9] The establishment of DVH prediction model is to calculate the Geometry—Based Expected Dose (GED) of each organ in the provided treatment plan. GED is to evaluate the volume of the PTV and the OARs, the distance between them and the dose distribution at this distance. The training of the model uses the principal component analysis method to carry out regression analysis on the planned GED and DVH to obtain the DVH and geometric condition related parameters of each anatomical structure. When designing a new plan, the DVH prediction model calculates the possible DVH fluctuation range of the plan result through the correlation parameters according to the mutual positional relationship between the PTV on the patient image and the normal tissue, and selects its lowest dose limit as the target optimization condition.

This paper mainly discusses whether a "plan-model-plan-model" internal feedback system with interactive improvement can be formed in the closed-loop state. The results showed that the P2 is better than P1 in MU, CI, bladder V10, left femoral head V40. Aside in other aspects, the difference is also very small. Among them, left femoral head V10, V20, V30 and right femoral head V20, V30, Dmean index change is more obvious; bladder V30, V40, rectum V40, Dmean and other indicators change little; especially bladder V40, rectum Dmean index change less than 0.5%. Because plan optimization is multi-objective optimization, there will be some improvement of indicators, some indicators have not improved or even become worse, but overall can be controlled within the required range, its changes are floating within the required range.

The larger the chi square value of the model, the smaller the probability of independence and the greater the probability of correlation. In this study, the chi square value of the organ index of M2 is greater than that of M1. It showed that the closer it is to the requirements set by us for the model, the better it can reflect the plan we use to train the model. The M2 is relatively stable, and it can better reflect the requirements of the clinical plan.

The reason for this is that KBRT is to integrate the past treatment experience into the treatment of new patients. It uses a large number of previous similar plans to train fitting models. The verified model will be used to evaluate the anatomical structure and prescription dosage of new patients, especially the distance and interlacing between PTV and OARs. According to this, the model predicts the target parameters of DVH that the case may reach. The plan used to build the model affects the use effect of the model. In addition, in the process of using the model, due to the individual differences of cases and
different clinical requirements, and in order to achieve the effect of excellence, physicists sometimes have to make manual fine adjustments. In the process of establishing the experimental model, M1 is established based on P0, then P1 is generated, and then M2 is established through P1 to generate P2. From M1, P0 to M2, P2, the artificial influence factor of the automatic planning model is gradually weakened, but also a positive factor in the process of planning optimization is weakened, or the influence of this positive factor is an increasing trend for the forward model.

Varian KBRT divided the OARs into 4 parts: (1) shooting into the field and scattering; (2) The exposure dose between leaves is lower; (3) In the shooting field, the irradiated dose has obvious influence; (4) The PTV overlap, and the irradiated dose is equivalent to the PTV dose. This part has the most important influence on the PTV dose distribution. The process of establishing Rapid Plan model is to import the image, outline, dose, DVH, etc. of case intensity adjustment plan into Eclipse-Rapid Plan planning system for regression analysis of DVH curves of various OARs to create DVH prediction model. When a new plan is made by using the established model, after matching, the DVH prediction model will automatically generate the irradiation dose volume range of tissues and organs and give the optimal DVH curve satisfying the current plan, which will become the target center of the dose limit value for the next optimization. This calculation method is a two-dimensional algorithm, while the plan involves three-dimensional images, so the two-dimensional algorithm has its limitations in calculating the three-dimensional volume and dose distribution. It may be more appropriate to use a three-dimensional calculation method. The improvement of algorithm should play a more critical and core role in the improvement of Rapid Plan model.

The source plan on which M2 is built is in a non-advantageous state compared with the source plan used by M1, which we want to avoid but exist. However, even under such circumstances, the plan generated by M2 can be improved in some aspects. At the same time, the stability of M2 is better than M1.

### Conclusion

It can be considered that the interactive improved internal feedback system within the model of "plan-model" is feasible and meaningful. At the same time, for the model that has been used clinically, we should pay attention to the continuous improvement of the model by using the excellent clinical plan completed in the later stage of the model.

### Declarations

Ethics approval and consent to participate

This study was carried out in accordance with the recommendations of Ethics Committee Approval at Shandong Cancer Hospital and Institute. The protocol was approved by Ethics Committee of the Shandong Cancer Hospital and Institute. As the study is retrospective, the need for written informed consent from participants was waived.
Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Corresponding Author: Changsheng Ma, M.D. Email: machangsheng_2000@126.com

Competing interests

The authors declare that they have no competing interests

Funding

No fundings

Authors' contributions

Kuo Li and Pan Yang drafted conception and design and draft the manuscript. Xinqiang Zhang, Shuang Yu and Cheng Tao contributed to acquire, analyze, and interpret data. Changsheng Ma contributed to acquire data and enhanced its intellectual content. All authors read and approved the final manuscript.

Acknowledgements

This work was supported by Natural Science Foundation of Shandong Province (ZR2019MH136, ZR2017BH024, ZR2020QA089), Project funded by China Postdoctoral Science Foundation (2019M652356), The National Nature Science Foundation of China (81800156, 81974467, 12005119).

References

1. Yang Y, Ford EC, Wu B, et al. An overlap-volume-histogram based method for rectal dose prediction and automated treatment planning in the external beam prostate radiotherapy following hydrogel injection. Med Phys. 2013 Jan;40(1):011709.

2. Varian Medical Systems. Eclipse Photon and Electron Instructions for Use. Palo Alto, CA;2014:183–213.

3. Varian Medical Systems. Eclipse Photon and Electron Reference Guide. Palo Alto, CA;2014:263–348.

4. Gown AM, Lazennec G, et al. Current issues in ER and HER-2 testing by IHC in breast cancer[J]. Mod Pathol, 2008, 21(2): S8

5. Bragg CM, Conway J, Robinson MH, et al. The role of intensity-modulated radiotherapy in the treatment of Parotid tumors[J]. Int J Radiat Oncol Biol Phys, 2002, 52(3): 729–738
6. Chanyavanich V, Das S, Lee W, et al. Knowledge based IMRT treatment planning for prostate cancer. Med Phys 2011;38:2515–2522.
7. Zhu X, Ge Y, Li T, et al. A planning quality evaluation tool for prostate adaptive IMRT based on machine learning. Med Phys 2011;38:719–726.
8. Lian J, Yuan L, Ge Y, et al. Modeling the dosimetry of organ-at-risk in head and neck IMRT planning: an inter-technique and inter-institutional study. Med Phys 2013;40:121704
9. Moore K, Scott Brame R, Low D, et al. Experience based quality control of clinical intensity modulated radiotherapy planning. Int J Radiat Oncol Biol Phys 2011, 81:545–551.
10. Appenzoller L, Michalski J, Thorstad W, et al. Predicting dose-volume histograms for organs-at-risk in IMRT planning. Med Phys 2012, 39:7446–7461.
11. David Good, MS Joseph Lo, PhD, et al. A Knowledge-Based Approach to Improving and Homogenizing Intensity Modulated Radiation Therapy Planning Quality Among Treatment Centers: An Example Application to Prostate Cancer Planning [J]. Radiation Oncol Biol Phys, 2013, 87(2):176–181.
12. Lulin Yuan, Yaorong Ge, W. Robert Lee, et al. Quantitative analysis of the factors which affect the inter-patient organ-at-risk dose sparing variation in IMRT plans[J]. Med. Phys, 2012, 39 (11):6868–6878.
13. Fogliata A, Po-Ming W, Francesca B, et al. Assessment of a model based optimization engine for volumetric modulated arc therapy for patients with advanced hepatocellular cancer[J]. Radiation Oncol 2014, 9(1):236–249.
14. D. Djajaputra, Q. Wu, Y. Wu, et al. Algorithm and performance of a clinical IMRT beam-angle optimization system[J] Phys. Med. Biol, 2003, 48:3191–3212.
15. Narayanan VK, Vaitheeswaran R, Bhangle JR, et al. An experimental investigation on the effect of beam angle optimization on the reduction of beam numbers in IMRT of head and neck tumors[J]. Appl Clin Med Phys, 2012, 13(4):3912.
16. Sung H K, Min Kyu Kang, et al. The impact of beam angle configuration of intensity-modulated radiotherapy in the hepatocellular carcinoma[J]. Radiat Oncol, 2012, 30(3):146–151.
17. Wu Hao, Jiang Fan, Yue Haizhen, et al. Treatment of statistical outliers and their dosimetric effects in varian rapid plan model training [j]. Chinese Journal of Medical Physics, 2016, 3(7):649–653. DOI:10.3969/j.issn.1005-202X.2016.07.001.

Tables

Table 1. Demographic characteristics of the cervix patients. FIGO: International Federation of Gynecology and Obstetrics.
| Patients, n | 70 |
| Age (Years) | Median 56 |
| Min - Max | 37-70 |
| Height, cm (average) | 159 |
| Weight, kg (average) | 61.6 |
| FIGO stage | 
| A | 31 |
| A | 17 |
| A | 17 |
| B | 5 |
| Histology | 
| Squamous Cell Carcinoma | 58 |
| Adenocarcinoma | 12 |

Table 2 Statistical Analysis of two groups of models (M1, M2)

| OAR(parameters) | M1 | M2 | t   | p  |
|----------------|----|----|-----|----|
| Bladder | CD 0.81±1.720 0.51±1.13 | 1.16 0.25 |
|           | mZ 1.43±0.63 1.40±0.61 | 0.25 0.81 |
|           | SR 0.62±0.65 0.7±0.54  | -0.85 0.40 |
|           | dA 0.85±0.47 0.85±0.40  | 0.07 0.95 |
| Rectum    | CD 0.84±1.07 0.75±1.19  | 0.32 0.75 |
|           | mZ 1.79±0.88 1.46±0.91  | 1.31 0.20 |
|           | SR 0.84±0.54 0.72±0.62  | 0.87 0.39 |
|           | dA 0.93±0.43 0.86±0.40  | 0.71 0.48 |
| Left femoral head | CD 0.71±1.26 0.92±1.67 | -0.81 0.42 |
|           | mZ 1.34±0.63 1.32±0.60 | 0.18 0.86 |
|           | SR 0.75±0.67 0.78±0.61 | -0.26 0.79 |
|           | dA 0.84±0.61 0.94±0.48 | -1.11 0.27 |
| Right femoral head | CD 0.70±1.33 0.69±0.93 | 0.05 0.96 |
|           | mZ 1.27±0.60 1.27±0.60 | 0.00 1.00 |
|           | SR 0.63±0.08 0.77±0.06 | 1.21 0.23 |
|           | dA 0.74±0.55 0.91±0.43 | -2.10 0.04 |

Table 3 Statistical Analysis of two groups of plans (P1, P2) generated by two models (M1, M2)
| Parameters | P1 | P2 | t     | p     |
|------------|----|----|-------|-------|
| **PTV**    |    |    |       |       |
| $D_2$      | 53.88±0.40 | 54.28±0.30 | -16.1740.000 |
| $D_{98}$   | 51.08±0.47 | 50.83±0.33 | 10.109 0.000 |
| HI         | 0.06±0.01  | 0.07±0.01  | -15.3340.000 |
| CI         | 0.70±0.08  | 0.81±0.07  | -30.411 0.000 |
| **MU**     |    |    |       |       |
|            | 1393.81±221.09 | 1261.61±190.86 | 19.795 0.000 |
| **Bladder**|    |    |       |       |
| $V_{10}$   | 99.72%±0.67% | 99.64%±0.85% | 2.719 0.008 |
| $V_{20}$   | 86.19%±8.21% | 86.38%±8.81% | -0.475 0.636 |
| $V_{30}$   | 54.30%±14.05% | 55.29%±14.61% | -2.472 0.016 |
| $V_{40}$   | 27.98%±12.45% | 28.46%±12.86% | -2.231 0.029 |
| $D_{\text{mean}}$ | 32.81±3.82 | 32.80±3.97 | 0.058 0.954 |
| **Rectum** |    |    |       |       |
| $V_{10}$   | 99.37%±1.62% | 99.36%±1.69% | 0.556 0.573 |
| $V_{20}$   | 93.74%±7.70% | 93.93%±8.21% | -0.870 0.388 |
| $V_{30}$   | 66.73%±17.17% | 67.38%±18.59% | -1.240 0.220 |
| $V_{40}$   | 33.10%±21.34% | 33.84%±21.39% | -2.526 0.014 |
| $D_{\text{mean}}$ | 35.36±5.73% | 35.53±5.79% | -2.367 0.021 |
| **Left femoral head** |    |    |       |       |
| $V_{10}$   | 93.82%±9.01% | 99.36%±1.69% | -2.000 0.049 |
| $V_{20}$   | 32.98±17.56% | 38.61%±17.89% | -13.438 0.000 |
| $V_{30}$   | 6.02%±7.00%  | 6.69%±6.42%  | -2.999 0.004 |
| $V_{40}$   | 0.56%±1.12%  | 0.41%±0.74%  | 2.502 0.015 |
| $D_{\text{mean}}$ | 18.39±3.08 | 19.03±3.04 | -9.555 0.000 |
| **Right femoral head** |    |    |       |       |
| $V_{10}$   | 97.20%±4.83% | 97.31%±4.98% | -0.715 0.477 |
| $V_{20}$   | 43.71%±14.52% | 48.17%±15.13% | -13.429 0.000 |
| $V_{30}$   | 7.78%±8.26%  | 8.34%±8.05%  | -2.274 0.026 |
| $V_{40}$   | 0.60%±1.07%  | 0.51%±0.95%  | 1.134 0.261 |
| $D_{\text{mean}}$ | 19.93±2.56 | 20.30±2.85 | -2.569 0.012 |

**Figures**
Figure 1

Flow chart of planning method

Figure 2

The R2 and X2 for M1 and M2
Figure 3

The value of CD, MZ, SR and DA for M1 and M2
Figure 4

The Dose Volume Histogram of OARs for P1 and P2

![Dose Volume Histogram](image)

Figure 5

The Mean Dose of OARs for P1 and P2

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- DoseParametersofPTVandOARsd1.xlsx
- modeld1.xlsx