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Evaluation of Auto-planning for Left-side Breast Cancer After Breast-conserving Surgery Based on Geometrical Relationship

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Abstract

Purpose: This study aimed to evaluate (1) the performance of the Auto-Planning module embedded in the Pinnacle treatment planning system (TPS) with 30 left-side breast cancer plans and (2) the dose-distance correlations between dose-based patients and overlap volume histogram-based (OVH) patients.

Method: A total of 30 patients with left-side breast cancer after breast-conserving surgery were enrolled in this study. The clinical manual-planning (MP) and the Auto-Planning (AP) plans were generated by Monaco and by the Auto-Planning module in Pinnacle respectively. The geometric information between organ at risk (OAR) and planning target volume (PTV) of each patient was described by the OVH. The AP and MP plans were ranked to compare with the geometry-based patients from OVH. The Pearson product-moment correlation coefficient (R) was used to describe the correlations between dose-based patients (APs and MPs) and geometry-based patients (OVH). Dosimetric differences between MP and AP plans were evaluated with statistical analysis.

Result: The correlation coefficient (mean R = 0.71) indicated that the AP plans have a high correlation with geometry-based patients from OVH, whereas the correlation coefficient (mean R = 0.48) shows a weak correlation between MP plans and geometry-based patients. For different indicators, the dose distribution of V_{5Gy}, V_{10Gy}, V_{20Gy} in the ipsilateral lung (AP: mean R = 0.82; MP: mean R = 0.58) is more relevant to geometry-based patients compared to the dose distribution of V_{5Gy} in the heart (AP: mean R = 0.4; MP: mean R = 0.19). The dosimetric comparison revealed a statistically significant improvement in ipsilateral lung V_{5Gy} and V_{10Gy} and in the heart V_{5Gy} of AP plans compared to MP plans.

Conclusion: The overall results of AP plans were superior to MP plans. The dose distribution in AP plans was more consistent with the distance-dose relationship described by OVH. After eliminating the interference of human factors, the AP was able to provide more stable and objective

plans for radiotherapy patients.

Background

Breast cancer is the most common malignant tumor in women, ranking first in both morbidity and mortality (1). As a standard treatment for early breast cancer, whole-breast irradiation after breast-conserving surgery can effectively improve the local control rate and long-term survival rate (2). With the development of radiation therapy technology for breast cancer treatment, intensity modulated conformal radiation therapy (IMRT) and volume arc intensity modulated radiation therapy (VMAT) are proposed. Compared to traditional techniques, IMRT and VMAT can provide more-uniform dose distribution in the target area and offer better protection to organs at risk (OAR) (3-4). Moreover, compared to the IMRT plan, the VMAT plan can provide better homogeneity of planning target volume (PTV), protect the endangered organs (especially the lung and heart) with a lower absorbed dose, and reduce monitor units (MUs) and treatment time. With better performance during the radiotherapy treatment process, the VMAT technology has become the first choice for most patients with early breast cancer after breast-conserving surgery (5-8). However, clinical manual planning (MP) is very time-consuming, and its optimization results mainly depend on personal performance and experience. The results of the same manual plan may fluctuate with different planners due to differences in skills, habits, and methods (9-11).

In recent years, the rapid development of Auto-Planning (AP) has become the focus of radiotherapy treatment. The AP aims to reduce the manual time required for optimization and automatically optimize the objective function to achieve the desired effect. Moreover, the implementation of an automatic process can potentially reduce the objective differences between physicists as well as the overall planning quality. Current research on applying AP to different types of cancer shows that while AP produces a high-quality clinically acceptable plan, it can improve the efficiency of the optimization process and the quality of the plan while eliminating the need to repeat experiments during manual planning (12-15). However, most of that researches focusing on the dosimetric comparison between manual plans and automatic plans to demonstrate the superiority of the AP.

Kazhdan et al. (16) proposed a novel overlapping volume histogram (OVH), which describes the one-dimensional distance distribution of each endangered organ relative to the tumor. According to the OVH curve, the geometry of the organ relative to the tumor can be quickly identified (17). The geometry of the endangered organ and target area is used to identify patients with similar treatment plans. By comparing the geometric differences of different patients, the quality of a group of plans is expected to be estimated (18). In this study, we proposed an innovative method based on dose-distance relationship described by the OVH curve to evaluate the quality of AP plans and its correlation with the OVH curve.

Material and Method

Patient Selection

Thirty patients treated between 2018 and 2019 in our radiotherapy center after left-side breast-conserving surgery were selected in for this study. All patients were diagnosed with early breast cancer after breast-conserving surgery and did not have metastatic lymph nodes. The patients' plans were generated by an experienced medical physicist using the Monaco (version 5.10) treatment planning system (TPS) and satisfied clinical requirements. The plans were implemented by the VMAT technique with 6 MV photon beams on Elekta Synergy linear accelerator (Elekta AB, Stockholm, Sweden) or Elekta Versa linear accelerator respectively (Elekta AB, Stockholm, Sweden).

The patients were scanned using a large aperture computed tomography (CT) system (SOMATOM Sensation Open, Siemens, Germany) with a slice 5 mm thick. The clinical target volume (CTV) comprising the whole mammary gland was delineated on Pinnacle (Version 9.10) TPS. The planning target volume (PTV) was 4 cm extended in three-dimensional margins from the CTV and was contracted to 5 mm under the skin. The boundary of the PTV was not allowed to encroach into the ipsilateral lung. All (OARs, including ipsilateral lung, contralateral lung, heart, and contralateral breast, were delineated on Pinnacle TPS (Philips, Fitchburg, WI, USA), in accordance with the National Comprehensive Cancer Network guidelines 2018 and report 9804 of the Radiation Therapy Oncology Group. A prescription dose of 50 Gy in 25 fractions was specified for each patient.

According to the standards and experiences of OAR constraints in our radiotherapy center, constraints of OARs for whole breast radiotherapy (WBRT) after breast-conserving surgery are as follows:

PTV: $V_{50Gy} > 95\%$, $V_{55Gy} < 5\%$

Ipsilateral lung: $V_{20Gy} < 20\%$, $V_{10Gy} < 30\%$, $V_{5Gy} < 45\%$

Heart: $V_{10Gy} < 10\%$, $D_{mean} < 5Gy$.

Contralateral breast: $D_{mean} < 5Gy$.

The images and structures of each patient were transmitted to Monaco TPS for optimization. A tangent field that rotates clockwise and counterclockwise twice from a specific start and stop angle was set for each plan. The coordinates of the isocenter (ISO) was defined on the edge of PTV. The results of clinical plans were approved by a qualified oncologist and satisfied minimal clinical requirements.

Auto-Planning module

The AP plans can be achieved using the Treatment Techniques module embedded in Pinnacle 9.10 TPS. The module consists a Technique Library that provides a variety of templates for planners to apply to different types of patients. These templates are available for planners to revise or create with a group of parameter settings in the Technique Window. The constraints for the APs with left-side breast cancer after breast-conserving surgery have been listed in Table 1.

Besides the constraints for OARs, there are some initial parameters including the Tuning balance, Dose Fall-off margin, Hot-spot Maximum Goal, and Cold-spot ROIs that need to be set in the Technique Window. Tuning balance is a percentage of weight that can be adjusted between Target coverage and OAR sparing. Dose Fall-off margin represents how quickly the dose declines per unit distance. Hot-spot Maximum Goal and Cold-spot ROIs influence the uniformity and conformability of the target area. Other necessary settings, including machine type, coordinates of ISO, and beam start and stop angle, will remain the same as the clinical plan.

Ten experimental patients were planned prior to formal optimization in the AP module in order

to create a standard template as shown above for 30 APs' optimization. The PTV of a few plans were unable to achieve the requirement of $V_{50Gy} > 95\%$ in the first round of optimization due to unfavorable patient anatomy. For such cases, an increment of a small amount of MUs directly is acceptable under the condition of $V_{55Gy} < 5\%$.

Application of OVH Curve

The OVH describes the one-dimensional geometric relationships between OAR and Target, which is potentially related to the dose distribution of the plan (16). When a target T expanded a specific distance r, the proportion of the volume that overlaps with the OAR is defined as:

$$OVH_{O,T}(t) = \frac{|\{p \in O | d(p,T) \leq r\}|}{|O|} \tag{1}$$

Where $d(p, T)$ is the specific distance of p from the tumor's boundary, and $|O|$ signifies the volume of the OAR. (16)

The OAR absorbed dose is directly related to the extension distance from the target volume if the dose distribution of the target is relatively conformable to the target area. Fig. 1 shows an example of OVH for two OARs. The Y axis represents the volume of the target area that overlaps with the OAR after a certain distance expansion. The X axis represents the specific distance expanded from the target area. For the same percentage of overlap volume OVH(v) > 0, if the expanded distance $r_1 < r_2$, then the dose absorbed on OAR is concluded as $D_1 > D_2$.

In this study, 4 indicators, including V_{5Gy}, V_{10Gy}, and V_{20Gy} of ipsilateral lung and V_{5Gy} of heart, will be used as comparisons between the two plans (AP and MP) and OVH ranking. We will first select the 5 patients with the best results based on the results of 30 MP plans on Monaco. These 5 patients will serve as the basis for the subsequent OVH ranking. Then, the remaining 25 patients will be ranked and compared across different methods.

1. The first ranking is based on the optimized results obtained from MPs on Monaco.

2. The second ranking is based on the results of automatic optimization from APs on Pinnacle.

3. The third ranking is based on the size of the PTV extension distance obtained under a specific OVH volume.

For 30 patients with similar anatomical structures, OVH curves are prone to cross each other. In order to identify the ranking of OVHs for 25 patients, a specific volume on the OVH graph needs to be defined. In this study, we chose the average value of the top 5 plans as the representative volume to determine the ranking of OVHs for 25 patients. For example, to identify the ranking of 25 OVHs according to the indicator of the ipsilateral lung V_{5Gy}, we first ranked the 30 MPs on Monaco according to its volume of ipsilateral lung V_{5Gy}. Then, the top 5 plans were selected to calculate the average value (V_{mean}). On the OVH graph of the ipsilateral lung of the 25 patients, we were able to rank the PTV-extension distance d according to this V_{mean}. This ranking is supposed to correspond to the dose distribution of 5Gy in the ipsilateral lung of the 25 patients. According to the previously stated theory, the greater the extension distance d from the PTV, the lower the volume of V_{5Gy} of the ipsilateral lung in the plan. Then, the ranking of MPs and APs was compared with the ranking of OVH. Under the same conditions, it was estimated that the ranking results of the AP plans will be more consistent with the OVH ranking results.

Result

Overlap Volume Histogram (OVH) for 25 Patients

Thirty MPs were ranked first according to the V_{5Gy}, V_{10Gy}, and V_{20Gy} of the ipsilateral lung and V_{5Gy} of the heart. Then, the top 5 plans were selected and the average volume was calculated from the MPs ranking. The OVH of the remaining 25 patients of V_{5Gy}, V_{10Gy}, and V_{20Gy} of the ipsilateral lung and V_{5Gy} of the heart were generated in Fig. 2. The OVH graph shows that each patient's curve is very close to each other due to the anatomical similarity shared by the 25 patients with left-side breast cancer. Therefore, the OVH graph needs to be amplified at the average volume V_m in order to identify the ranking order of 25 patients.

According to the ranking of OVHs based on the extension distance d from PTV, the quality of a group of plans is expected to be identified. Then, the ranking of APs and MPs based on their dosimetric value is compared to the ranking of OVH for further assessment of the quality of the plans.

Statistical Analysis based on OVH Ranking

According to the volume of the ipsilateral lung V_{5Gy}, V_{10Gy}, V_{20Gy}, and heart V_{5Gy}, the rankings of 25 cases of AP and MP were obtained and compared with the rankings of 25 cases based on the OVH curve. The Pearson product-moment correlation coefficient was used to describe the degree of linear correlation between the dose-based and geometry-based patients. The scatter chart in Fig. 3 shows the ranking of three different methods according to the optimized result of AP plans, MP plans, and the extension distance d of OVH. The gray and yellow trend lines represent the degrees of linear correlation between automatic plans and manual plans respectively and the OVH ranking. The figure reveals that in all the results, the correlation degree (mean R = 0.71) between the AP ranking and the OVH-based ranking of 25 patients was higher than the correlation degree (mean R = 0.48) between the MP ranking and the OVH-based ranking. Such results indicate to a certain extent that after eliminating the interference of human subjective factors, the stability of AP is improved in comparison to that of MP optimized with subjective bias. In addition, whether it is in AP plans or MP plans, the degree of correlation (AP: mean R = 0.4; MP: mean R = 0.19) between the heart's ranking and the OVH ranking was lower than that of the ipsilateral lung (AP: mean R = 0.82; MP: mean R = 0.58). This probably because in the plan optimization, we artificially listed the ipsilateral lung as the priority target, so more constraints were applied to restrict the lung dose in both plans. This caused the dose in the lungs to follow the rule of dropping regularly as the distance from the target area increased.

Dosimetric comparison between AP and MP

Under the condition of PTV in both AP and MP plans reached $V_{50Gy} > 95\%$ and $V_{55Gy} < 5\%$, the dosimetric parameters of the ipsilateral lung and heart are listed and compared in Table 2. Statistical significance of differences was observed in all groups. Comparing the dosimetric parameters between AP and MP plans, V_{5Gy} and V_{10Gy} in the ipsilateral lung and V_{5Gy} in the heart of AP plans show a better result compared to MP plans, whereas V_{20Gy} in the ipsilateral lung of manually plans revealed a preferable results. Moreover, the standard deviation value of AP plans in all groups are smaller

than those of MP plans, which indicates a more stable and less scattered optimization result of the AP plans.

DISCUSSION

For the optimization process of manual plans, the planning and design of VMAT are based on the relative position of the target area and the OARs; some dosimetry constraints are manually added based on experience and then TPS is used for de-optimization. During this optimization process, the planner will repeatedly modify the parameters and try different dosimetry constraints according to the present result. This is an iterative process to obtain a treatment plan that meets clinical requirements. The trial-and-error process is very lengthy and time-consuming and prone to human error. This could be one of the reasons why the various indicators of OARs in APs are better than those in MPs in Table 3. Moreover, the standard deviation of various indicators in APs is also smaller than that in MPs, which shows that the result of AP plans is more stable. Similar results have been proven in many publications (12-15).

The geometric relationship between the target volume and OARs significantly affects the dose distribution in the physical plans. In many research articles, the effectiveness of the OVH method for plan evaluation and plan quality improvement has been described (18, 19). The distance-dose correspondence established by OVH can provide a general estimate of the plan quality before optimization (18, 20-22). Because of the relative objectivity and independence of the AP during the optimization process, the results obtained from it can reflect the correspondence more accurately between anatomical structure and dose distribution. This research verified the effectiveness of OVH and the superiority of AP through the comparison of three results: MPs, APs, and OVH prediction. In the previous results in Fig. 3, it was seen that in comparison to MPs, the results of APs show a more consistent correlation with OVH. This result illustrates the objectivity of the results of APs after reducing the interference of human factors. In addition, in the comparison of MPs and APs dosimetry, the results of V_{5Gy}, V_{10Gy} of the ipsilateral lung, V_{5Gy} of the heart in APs were significantly better than MPs. Only when comparing the V_{20Gy} of the ipsilateral lung were the results of APs slightly inferior to MPs. This is probably because the radiation oncologists in our department usually pay more attention to the dose of the ipsilateral lung in breast cancer patients. In order to make the dose lower, more constraints were applied to the ipsilateral lung when the medical physicist optimized the plan. The result of such plans may cause asymmetrical dose distribution in the patient.

It should be pointed out that only two OARs (ipsilateral lung and heart) were used as research objects in this research. Two other important OARs, the contralateral breast and the contralateral lung, were taken into the calculations of MP plans and AP plans but were not incorporated into the research results. One of the reasons is that the ipsilateral lung and the heart are the OARs oncologists in our department are most concerned about. For patients with left breast cancer after breast-conserving surgery, their target area is usually smaller than that of patients with advanced breast cancer. Therefore, the dose absorbed by the contralateral breast and the contralateral lung is very low due to their farther distanced position relative to PTV. Another – and possibly the most important – reason is that the dose distribution in patients is more compact when the OAR is close to the PTV. Typically, when the OAR is far from the PTV, the dose distribution becomes more

irregular. Thus, the distance-dose correspondence of OVH become meaningless when applied with the three OARs located further from PTV.

Although the results obtained in this study are consistent with our expectations, this does not mean that the same will hold true for other types of diseases. First, breast cancer after breast-conserving surgery is a relatively anatomically unique disease. For most patients, the shape of the PTV and the anatomical position of the PTV and OARs have relatively high similarities. Therefore, the dose distribution obtained after the plan optimization is more regular. (But it also proves the advantages of AP over MP from the negative side.) Secondly, although the optimization process of AP reduces the interference of human subjective factors, there are certain subjective factors in the initial settings of AP. For example, the modification of the restriction conditions in the template and the parameter setting of hot and cold spots will affect the result of the APs (23, 24). In addition, the number of patients enrolled in this study is limited. The result could be more conclusive with a larger sample size and more different type of diseases as the research object.

Conclusion

In conclusion, because of the distance-dose correspondence provided by OVH in this study, it is proven that the AP offers a fairer and more objective optimization result due to its independent and simple optimization process. When artificially optimizing the plan, we often pay too much attention to a certain index of OAR and ignore the dose distribution of other OARs, which can have side effects. The application of AP can potentially reduce human errors and save more time for medical physicists to devote to other tasks.

Abbreviation

TPS: Treatment Planning System; OVH: Overlap Volume Histogram; MP: Manual Planning; AP: Auto-planning; OAR: Organ At Risk; PTV: Planning Target Volume; CTV: Clinical Target Volume; IMRT: Intensity Modulated Conformal Radiation Therapy; VMAT: Volume Arc Intensity Modulated Radiation Therapy; MUs: Monitor Units; CT: Computed Tomography; WBRT: Whole Breast Radiotherapy; ISO: isocenter;

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Authors' contributions

YJL and HB proposed the original idea and method; YJL and DJH collected the data, performed the data analysis, and wrote the manuscript; all authors have read the manuscript and gave their personal advice for revision.

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Availability of data and materials

All research data are available for reasonable requests and will be supplied from corresponding author.

Ethics approval and consent to participate

The experimental procedures followed the ethical guidelines of the Helsinki Declaration (as revised in 2013) and were approved by the People's committee of the Third Affiliated Hospital of Kunming Medical University. The study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Legends

Fig.1. An example of OVH for two OARs, for the same volume V, the extended distance $r_1 < r_2$ means OAR2 located further from the target area than OAR1

Fig. 2. OVH of the ipsilateral lung for 25 patients ranked from (a) V_{5Gy}, (b) V_{10Gy} and (c) V_{20Gy}, and OVH of heart for 25 patients ranked from (d) V_{5Gy}. (a1), (b1), (c1) and (d1) is the magnified part of (a), (b), (c), and (d). The ranking of 25 patients from superior to inferior can be identified sequentially from right to left on the legend (a1), (b1), (c1) and (d1).

Fig. 3. Ranking of OVHs, APs, and MPs. R is the correlation coefficient between AP and MP ranking, respectively, and OVH-based ranking.

Tables

Table 1 Clinical constraints for APs

Table 2 Dosimetry comparison between AP and MP.

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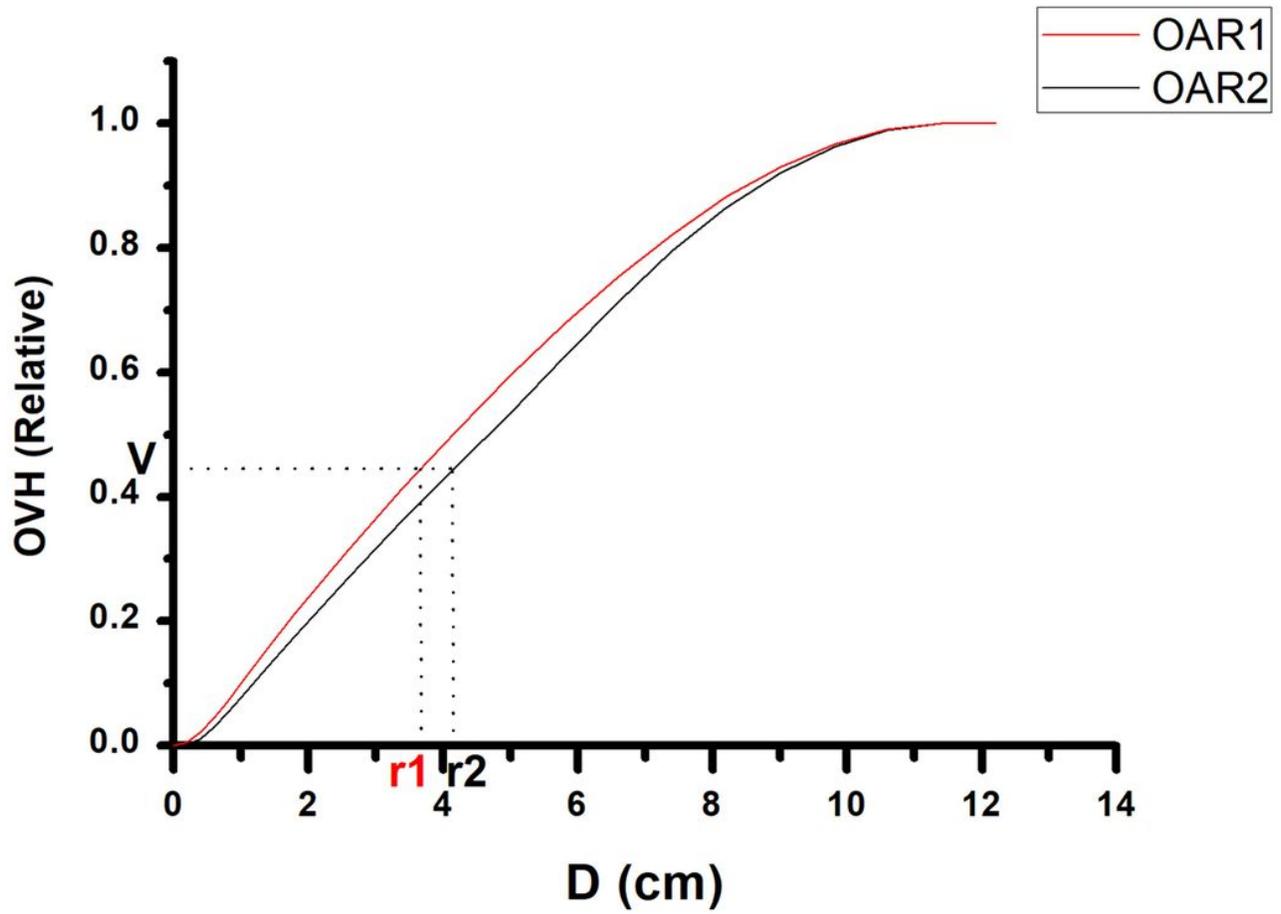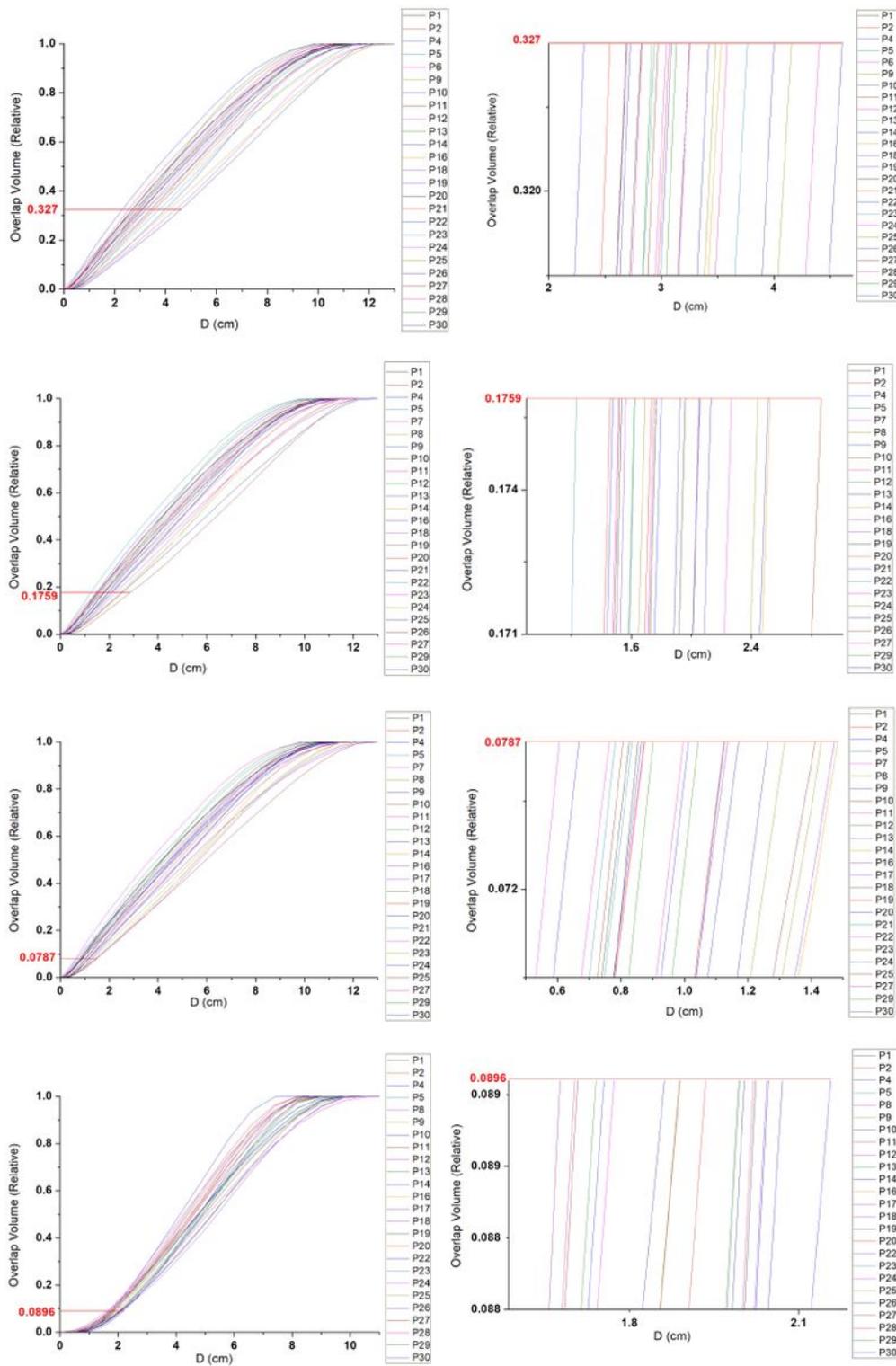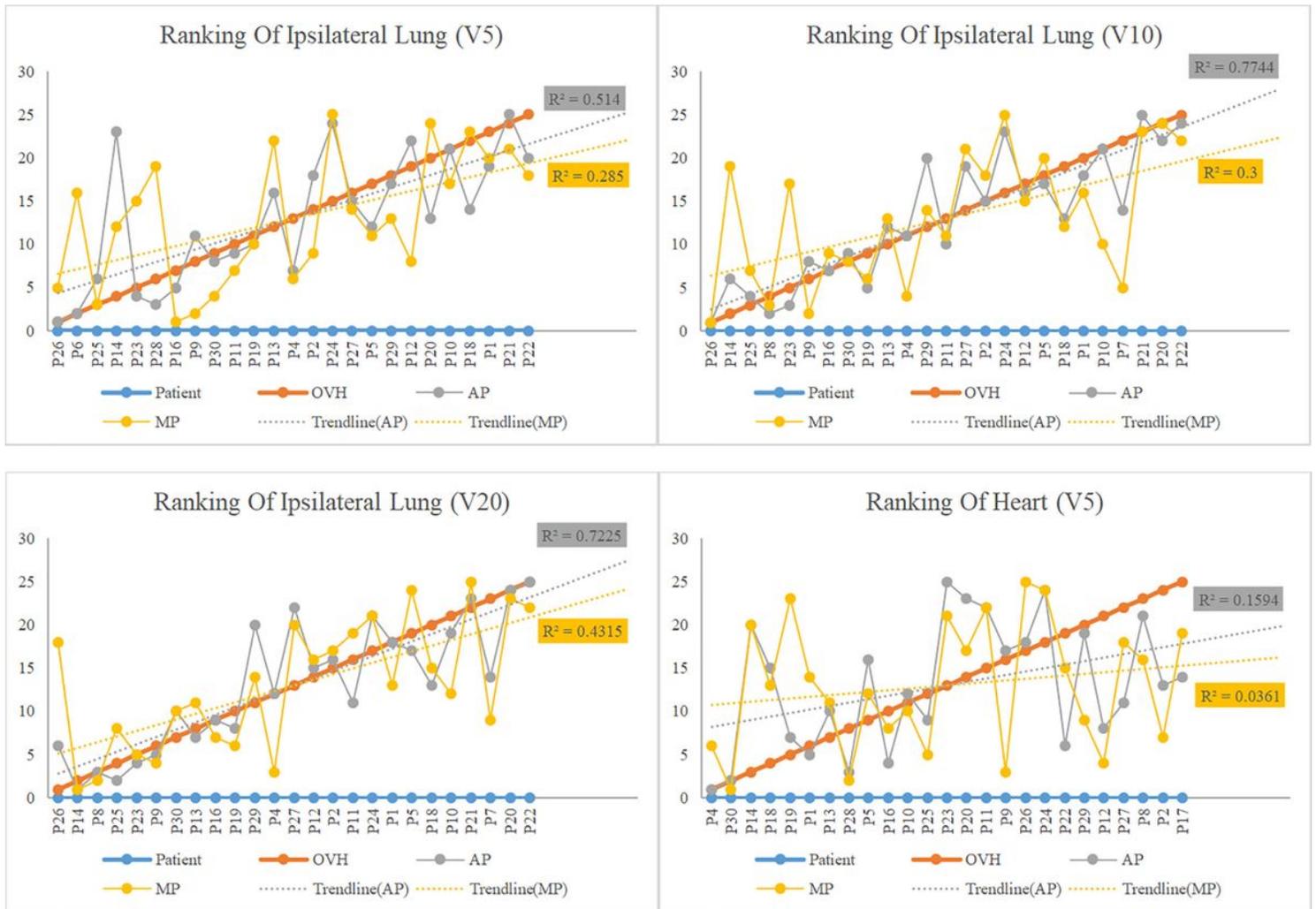
Figures

Figure 1

An example of OVH for two OARs, for the same volume V, the extended distance $r\_1 < r\_2$ means OAR2 located further from the target area than OAR1

Figure 2

OVH of the ipsilateral lung for 25 patients ranked from (a) V_5Gy, (b) V_10Gy and (c) V_20Gy, and OVH of heart for 25 patients ranked from (d) V_5Gy. (a1), (b1), (c1) and (d1) is the magnified part of (a), (b), (c), and (d). The ranking of 25 patients from superior to inferior can be identified sequentially from right to left on the legend (a1), (b1), (c1) and (d1).

Figure 3

Ranking of OVHs, APs, and MPs. R is the correlation coefficient between AP and MP ranking, respectively, and OVH-based ranking.

Supplementary Files

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- Table1.docx
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