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

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Abstract

Background: This study aimed to evaluate (1) the performance of Auto-Planning module embedded in Pinnacle treatment planning system (TPS) with 30 left-side breast cancer plans; (2) the dose-distance relations based on overlap volume histogram (OVH) curve.

Method: 30 patients with left-side breast cancer after breast-serving surgery were enrolled in this study. The clinical manual plan (MP) and the automatic plan (AP) were generated by Monaco and Auto-planning module respectively. The geometric relations between organ at risk (OAR) and planning target volume (PTV) of each patient were described by the overlap volume histogram (OVH). The patients were ranked according to the extension distance from PTV at a specific volume on the OVH curve. The MP and AP plans then were ranked to compare with the ranking of the OVH curves. Dosimetric difference between MP and AP plans were evaluated with statistical analysis.

Result: The comparative result shows a higher degree of correlation between AP and OVH curve. For different indicators, the dose distribution of V_{5Gy}, V_{10Gy}, V_{20Gy} in ipsilateral lung is more consistent with the distance-dose relation compared to the dose distribution of V_{5Gy} in heart. Dosimetric comparison shows a statistically significant improvement in ipsilateral lung V_{5Gy} and V_{10Gy}, and in heart V_{5Gy} of AP plans compared to MP plans. However, the result of ipsilateral lung V_{20Gy} of MP plans are better than that of AP plans.

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

Key words: VMAT, Auto-planning, OVH, breast cancer, geometrical relationship

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, intensity modulated conformal radiation therapy (IMRT) and volume arc intensity modulated radiation therapy (VMAT) are proposed. Compared with traditional techniques, IMRT and VMAT can provide more uniform dose distribution in the target area and have better protection to organ at risk (OAR) (3-4). Moreover, compared with 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 lower absorbed dose, and reduce monitor units (MUs) and treatment time. With better performance during radiotherapy treatment process, the technology of VMAT has become the first choice for most patients with early breast cancer after breast-conserving surgery. (5-8) However, clinically manual planning (MP) is very time-consuming, and its optimization results are mainly dependent on personal performance and experience. The results of the same manual plan may fluctuate from different planners due to their differences in skills, habits and methods. (9-11)

The rapid development of Auto-Planning (AP) has become the focus of radiotherapy treatment in recent years. The aim of the AP is to reduce the manual time required for optimization, and automatically optimize the objective function to achieve the desired effect. Besides, the implement of automatic process can potentially reduce the objective differences between physicists and possibly improve 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, and eliminates the need to repeat experiments during manual planning (12-15). However, most of those researches are focusing on dosimetric comparison between manually 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 difference of different patients, the quality of a group of plans is expected to be estimated. (18) In this study, we proposed a new method based on OVH curve to evaluate the quality of automatic and manually plans, and its correlation relation with OVH curve.

Material and Method

Patient Selection

Thirty patients treated from 2018 to 2019 in our radiotherapy center after left-side breast-conserving surgery were selected in this study. All patients were diagnosed as early breast cancer after breast-conserving surgery and did not have metastatic lymph nodes. The patients' plans were generated by experienced medical physicist using Monaco (version 5.10) treatment planning system (TPS) and satisfied for clinical requirements. Those plans were implemented by VMAT (Volumetric Modulated Arc Therapy) 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 large aperture computed tomography (CT) system (SOMATOM Sensation Open, Siemens, Germany) with slice of 5 mm thickness. The clinical target volume (CTV) comprised 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 5mm under the skin. The boundary of the PTV was not allowed to encroach into ipsilateral lung. All organs at risks (OARs) including ipsilateral lung, contralateral lung, heart, contralateral breast were delineated on Pinnacle TPS (Philips, Fitchburg, WI, USA) according to the National Comprehensive Cancer Network guidelines 2018 and the report no. 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 listed as followed:

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

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

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

Contralateral breast: D_{mean} < 5Gy.

The images and structures of each patient was 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 isocenter (ISO) was defined on the edge of PTV. The results of clinical plans were approved by a qualified physician and satisfied for 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 of 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 are listed in Table 1.

Besides the constraints for OARs, there are some initial parameters including 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 adjustment between Target coverage and OAR sparing. Dose Fall-off margin represents how quickly the dose decline per unit distance. Hot-spot Maximum Goal means and Cold-spot ROIs means influence the uniformity and conformability of the target area. Other necessary settings including machine type, coordinate of ISO, beam start and stop angle and constrain of leaf motion will remain the same as the clinical plan.

Ten experimental patient 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 the unfavorable anatomy of the patient. For those cases, increment of a small amount of MUs directly is acceptable under the condition of V_{55Gy}<5%.

Application of OVH Curve

The Overlap Volume Histogram (OVH) describe 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:

$$\mathrm{OVH}_{O,T}(t)=\frac{|\{p\in O|d(p,T)\leq r\}|}{|O|} \quad (1)$$

Where $d(p, T)$ is the specific distance of p from the tumor's boundary and $|O|$ is 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. Y-axis represents the volume of the target area that overlaps with the OAR after a certain distance expansion. 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 received 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 MP plans, AP plans 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 be the basis used for the subsequent OVH ranking. Then the remaining 25 patients will be ranked and compared in 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, their 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 choose 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 will first rank the 30 MPs on Monaco according to its volume of ipsilateral lung V_{5Gy}. Then the top 5 plans will be selected to calculate the average value (V_{mean}). On the OVH graph of the ipsilateral lung of the 25 patients, we are able to rank the PTV-extension distance d according to this V_{mean}. This ranking is supposed to be corresponding to the dose distribution of 5Gy in ipsilateral lung of the 25 patients. According to the previous theory, the larger 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 will be compared with the ranking of OVH. Under the same conditions, it is 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 its V_{5Gy}, V_{10Gy} and V_{20Gy} of ipsilateral lung and V_{5Gy} of heart. Then top 5 plans were selected and the average volume were calculated from the MPs ranking. The OVH of remaining 25 patients of V_{5Gy}, V_{10Gy} and V_{20Gy} of ipsilateral lung and V_{5Gy} of heart respectively were generated in Fig.2. The OVH graph shows the curve of each patient is very close to each other due to anatomical similarity of 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 are expected to be identified. Then, the ranking of APs and MPs based on its dosimetric value are compared to the ranking of OVH for further assessment for the quality of the plans.

Statistical Analysis based on OVH Ranking

According to the volume of its ipsilateral lung V_{5Gy}, V_{10Gy}, V_{20Gy} and heart V_{5Gy}, the ranking of 25 cases of AP and MP will be obtained and compared with the ranking of 25 cases based on OVH curve. The correlation coefficient is used to describe the degree of linear correlation between MP plans and AP plans, respectively, and OVH's ranking. 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 degree of linear correlation between automatic plans and manual plans, respectively, and OVH ranking. It has revealed from the figure that in all the results, the correlation degree between the AP ranking and the OVH-based ranking of 25 patients is higher than the correlation degree 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 better than that of MP optimized with subjective bias. In addition, whether it is in automatic plans or manual plans, the degree of correlation between the heart's ranking and the OVH ranking is lower than that of the ipsilateral lung. The reason for this result is probably that in the plan optimization, we artificially listed the ipsilateral lung as the priority target, so no matter in the automatic plan or the manual plan, more constraints were applied to restrict the lung dose. Thus causing the dose in the lungs to follow the rule of dropping regularly as the distance from the target area increases.

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 ipsilateral lung and heart are listed and compared in Table 2. Statistical significance of differences have been 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 manually plans, whereas V_{20Gy} in the ipsilateral lung of manually plans reveals a preferable results. Moreover, the standard deviation value of automatic plans in all groups are smaller than those of manually plans, which indicates a more stable and less scattered optimization results of the AP plans.

DISSCUSION

For the optimization process of manual plans, the planning and design of VMAT is based on the relative position of the target area and the OARs, manually adding some dosimetry constraints based on experience, and then using TPS for de-optimization. During this optimization process, the planner will repeatedly modify the parameters and try different dosimetry constraints according to present result. This is an iterative process in order to obtain a treatment plan that meets clinical requirements. The trial-and-error process is very lengthy and time-consuming accompanying human errors. 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 are also smaller than that in MPs, which shows that the result of AP plans is more stable. Similar results have been proved 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 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. The research in this article is to verify 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 is obviously seen that in comparison with 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 ofV_{5Gy}, V_{10Gy} of the ipsilateral lung, V_{5Gy} of the heart in APs are significantly better than MPs. Only when comparing the V_{20Gy} of the ipsilateral lung, the results of APs were 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 of breast cancer patients. In order to make the dose relatively low, more constraints are set to the ipsilateral lung when the medical physicist optimize the plan. The result of such plans may cause asymmetrical dose distribution in patient.

It should be pointed out that there are only two OARs (ipsilateral lung and heart) were used as research objects in this research. Another two important organs (contralateral breast, Contralateral lung) were taken into caculations of MP plans and AP plans but were not involved into research process. One of the reason is that the ipsilateral lung and the heart are the most concern OARs by oncologist in our department. For patients with left breast cancer after breast-conserving surgery, their target area are usually smaller than that of patients with advanced breast cancer. Therefore, the dose absorbed by contralateral breast and contralateral lung is very low due to the relatively further position to PTV. Another and possibly the most important reason is that the dose distribution in the patient is more compact when the OAR is close to the PTV. Relatively, when the OAR is far from the PTV, the dose distribution become 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 results will be presented in other types of diseases. Firstly, breast cancer after breast-conserving surgery is a relatively special 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 limited number of patients in this study is slightly lower. The result can be more convincing 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 proves from the side that the AP has a more fair and 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 may bring potential side effects to patients. 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 date anlysis and wrote the manuscript; all authors have read the manuscript and gave their personal advise for revision.

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Availability of data and materials

All research date are available for reasonable request 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 was approved by 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 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 OVH, APs and MPs. R is the correlation coefficient between AP and MP ranking, respectively, and OVH-based ranking.

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