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A method for standardizing intensity modulated radiation therapy planning optimization for nasopharyngeal carcinoma

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► ***Short Report***

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ABSTRACT

Background: To investigate a method for standardizing intensity modulated radiation therapy (IMRT) optimization for nasopharyngeal carcinoma (NPC), in order to reduce the influence of subjective factors. ***Materials and Methods***: This study is based on example IMRT plans for NPC, which were randomly divided into data acquisition and data verification groups. Organs at risk (OARs) were analyzed for various sub-organs. The data acquisition group was used for statistical evaluations of the mean value of the normalized mean doses of sub-organs. The data validation group was used to validate the findings. ***Results:*** Significant negative correlations were observed between the normalized mean doses of sub-organs for each OAR and the shortest distance between sub-organs and the target region surface. For each OAR, there was no statistically significant difference in the normalized mean doses of sub-organs between the data acquisition and verification groups ($p > 0.05$). ***Conclusion:*** The influence of subjective factors can be reduced by using the normalized mean doses of sub-organs for each OAR as the evaluation parameter for standardizing. This method is relatively simple; a majority of radiotherapy centers can apply the model for standardizing IMRT planning optimization based on the existing planning system.

Keywords: *IMRT, planning optimization, standardize.*

INTRODUCTION

In recent years, intensity modulated radiation therapy (IMRT) has become widely used in radiotherapy. IMRT has allowed the dosage to the tumor target region to be increased, while also allowing the dosages of organs at risk (OARs) to be decreased, thereby improving tolerability and greatly increasing the quality of life of patients [1-5]. Plan quality variability can be a result of planner and physician experience, institutional experience, the complexity of IMRT goals, and differences in patient anatomy. Typically, physicians provide planners with optimization goals determined from population-based data, RTOG guidelines, or clinical knowledge and intuition. Stable and high -quality IMRT plans are challenging [6, 7]. There has recently been considerable interest in methods of standardizing IMRT optimization, such as the overlap volume histogram (OVH) or distance to target histogram (DTH) method [8-11]. For OVH method, if the volume of the OAR and the target region is zero, accurate prediction of the OAR dose may not be performed. For DTH method, need special software to extract OAR sampling point dose. Compared with these methods, we obtained the mean dose of sub-organ for each OAR in a simple way, and chose these mean doses of sub-organs to be the standardizing optimization parameters. This method is simple, regardless of whether the OAR intersects with the target region and does not need to extract the distance of each sampling point of OAR. A majority of radiotherapy centers can apply the model for standardizing IMRT

planning optimization based on the existing planning system.

MATERIALS AND METHODS

The following sites were selected for inclusion in the study: the inner ear, oral cavity, parotid glands, larynx, postcricoid region of the hypopharynx, and esophagus in patients with NPC.

Patient information

Patients (Chinese race) who had NPC and who received IMRT planning at our department were randomly selected and divided into data acquisition and data verification groups. The data acquisition group included 70 patients with NPC. The data verification group included 30 patients with NPC.

Target delineation and prescription dose regions

According to International Commission on Radiation Units and Measurements (ICRU) Reports 50 and 62 [12, 13], a radiotherapist delineated the gross tumor volume (GTVnx; the visible primary tumor location and its range of invasion on imaging and clinical examination), lymph node metastasis to the pharynx and larynx (GTVrnp), lymph node metastasis to the neck (GTVnd), CTV = CTV1 (GTVnx + 5–10 mm + corresponding sites in the nasopharyngeal mucosa and 5 mm from the submucosa), CTV2 (including CTV1, the posterior region of the nasopharyngeal cavity, the posterior region of the maxillary sinus, the pterygopalatine fossa, part of the posterior ethmoid sinus, the parapharyngeal space, skull base, part of the cervical spine, and clivus according to the location and scope of tumor invasion), and CTVnd (GTVnd + the neck lymph node drainage area requiring shielding from radiation). Three-millimeter expansions of GTV and CTV were regarded as the planning target volumes (PGTV and PCTV, respectively).

The prescription dose and plan evaluation were selected according to the regulations of the RTOG 0225 and RTOG 0615 trials [14, 15]; the per fraction doses of PGTVnx and PGTVrnp were 2.10–2.25 Gy with an integral dose of 66.0–70.0 Gy. The per fraction and integral doses of PGTVnd were 2.00–2.25 and 66–70 Gy, respectively. The per fraction and integral doses of PCTV1 were 1.80–2.05 Gy and 60.0–66.0 Gy, respectively. Finally, the corresponding per fraction and integral doses of PCTV2 and PCTVnd were 1.80 and 54.0–56.0 Gy, respectively.

Limits for OARs

For NPC, the limits for OARs were as follows: mean dose of the unilateral inner ear ≤45 Gy, mean dose of the oral cavity ≤Gy, mean dose of the parotid glands ≤26 Gy (when the overlapped area of the parotid glands and PCTV2 was too large, we specified that $D_{50\%}$ should be <30 Gy or the dosage should be as low as possible), mean dose of the larynx ≤45 Gy, mean dose of the hypopharynx ≤45 Gy, and mean dose of the esophagus ≤45 Gy.

Preparatory work for IMRT planning

All IMRT plans were planned and designed using the Pinnacle^3 8.0 m (Philips, Fitchburg, WI) treatment planning system. For NPC and cervical cancer, direct machine parameter optimization was used to design a 6-MV plan. Before the plan optimization, the PCTV2 was expanded outwards by 0.3 cm in multiple rings. Among them, $ring_1 \cap OAR$ was defined as $sub\text{-}organ_1$, and this definition was applied iteratively until we reached the definition of $ring_n$ OAR as $sub\text{-}organ_n$. Figure 1 shows the right parotid gland sub-organs of Patient 10 in the data acquisition group.

IMRT plan design for the data acquisition group

We chose the sub-organs to be the optimization parameter in the data acquisition group. The dosage of OARs was kept to the minimum possible value through repeated adjustments of the size and weight of the uniform doses of various sub-organs in the patient, under the condition that the dosage for the target region had to satisfy the evaluation requirements. As the number of sub-organs

considered during optimization was large, the weight parameters were adjusted until the weight value of the corresponding target region was smaller. Finally, the mean values of the normalized mean doses were calculated along with $D_{sub\text{-}organ\ mean}/D_{prescription}$, where $D_{sub\text{-}organ\ mean}$ is the mean dose of the sub-organs and $D_{prescription}$ is the prescription dose at PCTV2 of the NPC. The sub-organs of the investigated OARs were used to provide statistical evaluations for the data acquisition group.

IMRT plan design for the data verification group

Optimization was carried out on 30 patients with NPC using the methods in the data verification group: the treatment dosage for the target region and OARs had to satisfy the evaluation requirements, and two or more planners had to repeatedly adjusted the optimized parameters of the target area and OARs to ensure that the dosages of each OAR was as low as possible.

Statistical analysis

Using SPSS 20 software, statistical differences were determined using a two sided paired t test. Differences with a p value of <0.05 were considered significant.

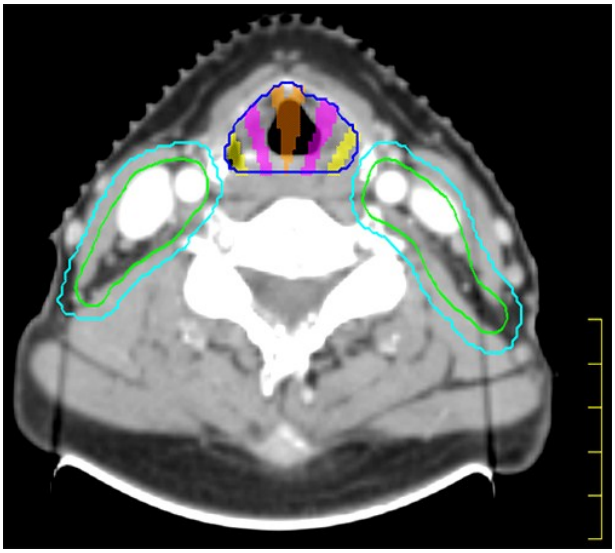

Figure 1. CTV2: green line, PCTV2: cyan line, and larynx: blue line. The yellow shadow represents the overlapping region of ring2 and the larynx (sub-larynx2), the pink shadow represents the overlapping region of ring4 and the larynx (sub-larynx4), the orange shadow represents the overlapping region of ring6 and the larynx (sub-larynx6).

RESULTS

The normalized mean dose of sub-organs for each OAR and the volume for each OAR were not correlated. The normalized mean dose of sub -organs for each OAR and the shortest distance between sub-organs and the target region surface were significantly negatively correlated (all the correlation coefficients less than -0.95). The oral cavity, parotid glands, and larynx in the data acquisition group were selected as examples; table 1-3 show the normalized mean dose of sub-organs for the OARs (the oral cavity, parotid glands, and larynx). D1 represents the mean values of the normalized mean dose ($D_{sub\text{-}organ\ mean}/D_{prescription}$) of the first sub-organ (sub-OAR1), and Dn and so on.

Consider $\delta = [D_{plan} - D_{standard}] / D_{standard}$, where D_{plan} is the normalized mean dose of sub-organs of OARs obtained in the data verification group, and $D_{standard}$ is the mean value of the normalized mean dosage of corresponding sub-organs of OARs obtained in the data acquisition group. As D_{plan} and $D_{standard}$ approach each other, δ approaches 0. D_{plan} and $D_{standard}$ of each OAR are not significantly correlated ($p > 0.05$).

Table 1. The normalized mean dose of sub-organs for the oral cavity.

D	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D13	D14	D15	D16
mean	0.918	0.801	0.692	0.600	0.526	0.467	0.421	0.385	0.357	0.332	0.305	0.266	0.221	0.196	0.165
Standard deviation	0.027	0.029	0.032	0.036	0.037	0.036	0.030	0.028	0.0317	0.034	0.054	0.051	0.088	0.088	0.104

Table 2. The normalized mean dose of sub-organs for the parotid glands.

D	D1	D2	D3	D4	D5	D7	D8	D9	D10	D11	D12
mean	0.885	0.675	0.505	0.390	0.320	0.246	0.231	0.211	0.192	0.163	0.151
Standard deviation	0.023	0.040	0.044	0.0349	0.027	.0325	0.018	0.041	0.056	0.077	0.073

Table 3. The normalized mean dose of sub-organs for the larynx.

D	D1	D2	D3	D4	D6	D7	D8	D9
mean	0.892	0.772	0.659	0.578	0.479	0.439	0.403	0.374
Standard deviation	0.037	0.035	0.033	0.039	0.033	0.028	0.024	0.023

DISCUSSION

From the normalized mean doses of the sub-organs of each OAR and the shortest distance between the sub-organs and the surface of the target region, we can know that the dose of each OAR's sub-organ is traceable. So this study attempted to choose the mean dose of sub-organ for each OAR to be the standardizing optimization parameters for evaluating the dosages of OARs during IMRT planning, as a means of generating stable and high-quality radiotherapy plans, and thereby reducing the influences of subjective and experience-based factors on the quality of radiotherapy plans. In addition, when we use the dose volume optimization (DVO) optimization algorithm to implement IMRT optimization, the method of dividing the OAR into Sub-OARs can increase the sampling point of the OAR, which is more conducive to the optimization of the OAR.

The data verification group plans were used to validate the study findings from the data acquisition group. The D_{plan} and $D_{standard}$ of each OAR are not significantly correlated ($p > 0.05$), showing that findings from the acquisition group are accurate and effective.

In planning optimization, the δ threshold can be set for standardizing the dose of the sub-organ for each OAR, and the sub-organ of the δ value above the threshold can be optimized as a separate OAR until a satisfactory δ value is obtained under the condition of the target prescription evaluation. This reduces the influence of subjective factors. Conventional methods can be divided into multiple sub-organs, which is more time-consuming. However, this division can be achieved in a fully automated manner by the treatment planning system script program, greatly improve efficiency.

The limitations of this study include that the radiotherapy plans were obtained from a single center. In future research, it would be advantageous to add more radiotherapy centers, different radiotherapy planning systems, and larger samples of plans. Further, it would be beneficial to establish a radiotherapy plan sample database, and to provide access to more accurate the mean dose of sub-organs. The method that we have described is applicable to different treatment planning systems, different IMRT implementation technologies, and OARs for different diseases.

CONCLUSION

In this study, we proposed and verified a method that is choosing the mean dose of sub-organ for each OAR to be the standardizing optimization parameters for standardizing IMRT

optimization.

***Conflicts of interest*:** *Declared none.*

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