Research Article

Chuou Yin, Peng Yang, Shengyuan Zhang, Shaoxian Gu, Ningyu Wang, Fengjie Cui, Jinyou Hu, Xia Li, Zhangwen Wu, and Chengjun Gou*

A self-adaptive prescription dose optimization algorithm for radiotherapy

<https://doi.org/10.1515/phys-2021-0012>

received December 23, 2020; accepted February 11, 2021

Abstract

Purpose – The aim of this study is to investigate an implementation method and the results of a voxel-based self-adaptive prescription dose optimization algorithm for intensity-modulated radiotherapy.

Materials and methods – The self-adaptive prescription dose optimization algorithm used a quadratic objective function, and the optimization engine was implemented using the molecular dynamics. In the iterative optimization process, the optimization prescription dose changed with the relationship between the initial prescription dose and the calculated dose. If the calculated dose satisfied the initial prescription dose, the optimization prescription dose was equal to the calculated dose; otherwise, the optimization prescription dose was equal to the initial prescription dose. We assessed the performance of the self-adaptive prescription dose optimization algorithm with two cases: a mock head and neck case and a breast case. Isodose lines, dose–volume histogram, and dosimetric parameters were compared between the

conventional molecular dynamics optimization algorithm and the self-adaptive prescription dose optimization algorithm.

Results – The self-adaptive prescription dose optimization algorithm produces the different optimization results compared with the conventional molecular dynamics optimization algorithm. For the mock head and neck case, the planning target volume (PTV) dose uniformity improves, and the dose to organs at risk is reduced, ranging from 1 to 4%. For the breast case, the use of self-adaptive prescription dose optimization algorithm also leads to improvements in the dose distribution, with the dose to organs at risk almost unchanged.

Conclusion – The self-adaptive prescription dose optimization algorithm can generate an ideal clinical plan more effectively, and it could be integrated into a treatment planning system after more cases are studied.

Keywords: intensity-modulated radiotherapy, dose optimization, self-adaptive prescription dose optimization algorithm, molecular dynamics

1 Introduction

Compared with conventional conformal radiotherapy, intensity modulated radiotherapy (IMRT) increases the dose of tumor and decreases the dose of organs by adjusting the intensity distribution of radiation field [1–4]. IMRT is the mainstream of radiotherapy technology at present. Inverse planning is the foundation of IMRT, and its performance determines the success of IMRT [5,6]. There are two kinds of inverse optimization techniques in IMRT: organ-based optimization and voxel-based optimization. In the organ-based optimization, the prescription dose and weight parameters are given to the organ, and all the voxels in an organ are combined and treated equally in the objective function. Because there is no clear relationship between the dose and weight parameters and the final dose distribution, the determination of these parameters is essentially a “guessing game;”

* **Corresponding author: Chengjun Gou**, Key Laboratory of Radiation Physics and Technology of Ministry of Education, Institute of Nuclear Science and Technology, Sichuan University, Chengdu 610064, China, e-mail: GOUCJSCU720@scu.edu.cn

Chuou Yin, Peng Yang, Shengyuan Zhang, Shaoxian Gu, Ningyu Wang, Fengjie Cui, Zhangwen Wu: Key Laboratory of Radiation Physics and Technology of Ministry of Education, Institute of Nuclear Science and Technology, Sichuan University, Chengdu 610064, China

Jinyou Hu: Key Laboratory of Radiation Physics and Technology of Ministry of Education, Institute of Nuclear Science and Technology, Sichuan University, Chengdu 610064, China; Department of Radiotherapy, Cancer Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China

Xia Li: Cancer Center, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, Chengdu 610072, China

therefore, many trial-and-error are needed, and the plan quality heavily depends on the clinical experience of the planner [7,8]. On the contrary, voxel-based optimization directly adjusts the parameters related to each voxel in the objective function [9–12]. Previous studies showed that compared with organ-based optimization, voxel-based optimization obtained better dose distribution [13–18].

One of the practical difficulties in the voxel-based optimization model is that the number of adjustable parameters increases dramatically, and therefore it is difficult to adjust them manually. In this study, a new algorithm is introduced to automatically adjust the dose prescription of voxels in the optimization process. We call it the voxel-based self-adaptive prescription dose optimization algorithm (SAPDOA). Two cases were used to evaluate the SAPDOA performance.

2 Materials and methods

2.1 Self-adaptive prescription dose optimization algorithm

The optimization engine in this study was molecular dynamics. The implementation detail of conventional molecular dynamics optimization algorithm (CMDOA) has been reported in references, and therefore it is only briefly introduced here [19–21]. The CMDOA used a weighted quadratic objective function defined by

$$O(I) = \sum_i^{NO} w_i (D_c - D_p)^2, \quad (1)$$

where O is the objective function, I is the beamlet intensity, NO is the total number of organs, w_i is the penalty weight, D_c is the calculated dose, and D_p is the prescribed dose.

The D_c was calculated through the formula given in equation (2):

$$D_c = \sum_j^{NB} I_j d_j, \quad (2)$$

where NB is the total number of beamlet, and d is the dose contribution matrix of one-unit beamlet intensity.

The SAPDOA also used the weighted quadratic objective function, which was the same as the CMDOA we have implemented, but the objective function was redefined as follows:

$$O(\vec{I}) = \sum_k^{NV} w_k \left(\sum_{NB}^j I_j d_j - D_{m,k} \right)^2, \quad (3)$$

where NV is the total number of voxels, and D_m is the self-adaptive prescription dose.

In CMDOA, the D_p did not change with the number of iterations. However, the D_m may change at every step of the optimization iteration in SAPDOA. The change of D_m follows the following rules:

- (1) For the target volume, if the D_c was within a certain range ($\pm 5\%$) of the prescription dose D_p , $D_m = D_c$, else $D_m = D_p$.
- (2) For an organ at risk (OAR) volume, if the D_c was smaller than the prescription dose D_p , $D_m = D_c$, else $D_m = D_p$.

Rule 1 allowed us to improve the dose uniformity of the target volume, and rule 2 to avoid the problem of low planning quality caused by excessive prescription dose of OARs.

2.2 Test cases

We evaluated the SAPDOA algorithm with two cases, one of them was from the AAPM TG-119 (mock head and neck) [22], and the other one was a clinical case (breast). We first used the CMDOA to make a reasonable plan (C-plan), and then we used the SAPDOA to get a new plan (S-plan). To make a fair comparison of the two plans, we kept all optimization parameters unchanged except the optimization algorithm. The test process was carried out on the Fonics (Qilin Company, Chengdu, China) treatment planning system (TPS).

For the mock head and neck case, nine 6 MV IMRT beams at 0° , 40° , 80° , 120° , 160° , 200° , 240° , 280° , and 320° were chosen. The dose prescription was PTV $D_{90\%} = 50$ Gy. The evaluation parameters including $D_{99\%}$ and $D_{20\%}$ for PTV and $D_{50\%}$ for normal structures were used for parotid, and maximum dose was used for cord. In the breast case, a setup with four 6 MV IMRT beams at 122° , 135° , 295° , and 342° was used. The dose prescription was PTV $D_{97\%} = 50$ Gy. The sensitive structures included lung and heart. We first assessed the plan quality by the dose volume histogram (DVH) for the two cases, and then dosimetric parameters were used to evaluate the difference between the plans using different optimization algorithms. To facilitate the plan comparison, all plans were normalized to the dose prescription.

Figure 1: DVHs of the mock head and neck plans obtained using the self-adaptive prescription dose optimization algorithm (solid curves) and the CMDOA (dashed curves).

3 Results and discussion

Figure 1 compares the DVHs for the mock head and neck plan optimized with SAPDOA and CMDOA. The PTV coverage is the same ($D_{90\%} = 50$ Gy), but the sparing of OARs is greatly improved; especially in the high-dose regions, the dose of OARs of S-plan was obviously decreased. Figure 2(a) and (b) shows the isodose curves for the mock head and neck case optimized with SAPDOA and CMDOA, respectively. It is clearly seen that dose uniformity and conformity of PTV are also improved by adjusting the voxel prescription dose in the iterative

Figure 2: Isodose curves for the two cases: (a) and (b) are the isodose curves for the mock head and neck case optimized with SAPDOA and CMDOA, respectively; (c) and (d) are the isodose curves for the breast case optimized with SAPDOA and CMDOA, respectively. The isodose lines from the isocenter to the exterior are 110% (orange), 100% (red), 80% (pink), 60% (yellow), and 40% (green) of prescription dose, respectively.

Table 1: Dosimetric parameters of the mock head and neck case

Parameter	Plan goal (Gy)	Weight	SAPDOA (Gy)	CMDOA (Gy)
HN PTV $D_{90\%}$	>50	10	50	50
HN PTV $D_{99\%}$	>46.5	10	46.9	45.5
HN PTV $D_{20\%}$	<55	10	52.6	54.8
Cord maximum	<40	20	33.6	35.5
Left parotid $D_{50\%}$	<20	30	19.4	21.5
Right parotid $D_{50\%}$	<20	20	18.5	20.6

optimization process. In addition, the over-dose area is obviously decreased in PTV. In particular, the maximum dose to the spinal cord is reduced. Moreover, there is a ~10% reduction in the parotid $D_{50\%}$. The detailed dosimetric parameters are presented in Table 1.

For the breast case, a comparison of DVHs between the C-plan and the S-plan is shown in Figure 3. In this case, the DVH curve of the S-plan is improved. The CMDOA might cause excessive constraints on the target and OARs, which makes it difficult to meet all the optimization objectives. In the SAPDOA proposed in this article, the prescribed dose is automatically adjusted according to the calculated dose in the iteration process of optimization. The SAPDOA balanced the prescribed dose between the target and OARs and avoided the situation of over-constraints on the target and OARs effectively.

Figure 2(c) and (d) shows that the S-plan leads to an increased dose homogeneity and dose conformity within the target, and the over-dose area disappeared compared with the C-plan. The low-dose delivered to the left lung and heart has a tiny difference, ranging from -2.8 to 1.2%. However, the S-plan has a significant improvement for the OARs at the high-dose region (>45 Gy). The detailed dosimetric parameters are presented in Table 2.

Generally speaking, it is difficult for a treatment plan to meet the dosimetric requirements of target and OARs simultaneously. Therefore, it is usually necessary to adjust the optimization objectives many times to obtain an acceptable compromise solution. At this stage, organ-based inverse optimization is widely used in clinical practice. In organ-based inverse optimization, adding more dose-volume constraints can improve the plan quality, but it cannot change and expand the accessible solution space. Therefore, it is difficult to find a better solution. Different from this is that voxel-based inverse optimization increases

Figure 3: DVHs of the breast plans obtained using the self-adaptive prescription dose optimization algorithm (solid curves) and the CMDOA (dashed curves).

the accessible solution space [23]. Many study results showed that compared with the organ-based optimization method, the voxel-based inverse optimization method is easier to obtain qualified plans.

In general, there are two ways to adjust the objective function in voxel-based inverse optimization: one is to change the penalty weight of each voxel, and the other is to adjust the prescription dose of each voxel. Zarepisheh et al. [24] proposed a DVH guided intensity-modulated optimization algorithm that automatically adjusted the weight of voxels, and they applied the new algorithm to a head and neck case and a prostate case. The results showed that the voxel-based model is able to improve the plan quality in terms of the DVH at the reasonable price by exploring the parts of the Pareto surface missing in the organ-based models. Li et al. [8] developed an automatic two-loop algorithm to perform re-optimization of a treatment plan on the patient's new geometry by considering the original DVH as guidance. Automatic

voxel weighting factor adjustments avoided tedious trial-and-error schemes, and it is easier to find an acceptable compromise among different structures for re-planning. Lougovski et al. [25] established an inverse planning framework with the voxel-specific penalty. Substantial improvements were achieved in the final dose distribution by adjusting voxel prescriptions iteratively to boost the region where large mismatch between the actual calculated and desired doses occurs. Wu et al. [26] studied the two different modification schemes (weighting factors/dose prescription) based on Rustem's quadratic programming algorithms. Case studies demonstrated that the two modification schemes had the capability to fine-tune treatment plans.

In this study, our solution is to first determine the organ weight based on clinical experience, and then automatically determine the prescription dose according to the dose calculated in the iterative process. It can be seen from Section 2 that the principle of the SAPDOA algorithm is simple, and it is easily implementable in any existing inverse planning platform. The SAPDOA was tested on a head and neck case and a breast case. As compared with the CMDOA, the PTV experiences improved dose uniformity and the doses to OARs are also reduced. These results show that the SAPDOA provides room for further improvements of currently achievable dose distributions. Our approach could be integrated into a TPS after more case studies.

We acknowledge that the penalty weight of the SAPDOA is determined and adjusted by the planner based on his clinical experience, which limits the algorithm's ability to find the optimal solution in a larger solution space. The plan optimized by the algorithm finds the solution space corresponding to the set of penalty weight factors, and therefore the optimized plan may not be the global optimal solution. We are introducing an automatic optimization algorithm that combines voxel prescription dose optimization and penalty weight optimization, so as to effectively expand the solution space, navigate in the expanded solution space, and find the global optimal scheme. We hope that the research results could be published in the following years.

Table 2: Dosimetric parameters of the breast case

Parameter	Plan goal	Weight	SAPDOA	CMDOA
PTV $D_{97\%}$	>50 Gy	30	50 Gy	50 Gy
PTV $D_{99\%}$	>48.5 Gy	30	48.6 Gy	48.6 Gy
PTV $D_{5\%}$	<54 Gy	10	53.2 Gy	56.0 Gy
Left lung V_{20}	<25%	30	24.4%	23.5%
Left lung V_5	<40%	10	33.4%	35.7%
Right lung V_5	<1%	20	0.5%	<0.5%
Heart V_{30}	<20%	20	18.9%	18.4%
Heart V_5	<40%	10	37.8%	38.1%

4 Conclusion

Although organ-based inverse optimization is widely used in clinical practice at present, the quality of the plan obtained by organ-based optimization heavily depends on the experience of the planner. The continuous

trial-and-error process also leads to the inefficiency of planning. In this study, we investigated a new inverse optimization algorithm, SAPDOA, in IMRT. The results of the two test cases show that this algorithm can more effectively generate an ideal clinical plan. The SAPDOA algorithm is easy to implement on any existing inverse programming platform, and it could be integrated into a 3D TPS after studying more cases.

Acknowledgments: The authors sincerely thank all the teachers who helped in the process of this article.

Funding information: This work was supported by the National Key Research and Development Programme of China (grant no. 2016YFC0105103).

Conflict of interest: The authors declare that there is no conflict of interest.

References

- [1] Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin.* 2016;66(4):271–89. doi: 10.3322/caac.21349
- [2] Yue N, Roberts KB, Son H, Khosravi S, Pfau SE, Nath R. Optimization of dose distributions for bifurcated coronary vessels treated with catheter-based photon and beta emitters using the simulated annealing algorithm. *Med Phys.* 2004 Sep;31(9):2610–22. doi: 10.1118/1.1783533. PMID: 15487744.
- [3] Baskar R, Lee KA, Yeo R, Yeoh KW. Cancer and radiation therapy: current advances and future directions. *Int J Med Sci.* 2012;9(3):193–9. doi: 10.7150/ijms.3635. Epub 2012 Feb 27. PMID: 22408567; PMCID: PMC3298009.
- [4] Bortfeld T, Bürkelbach J, Boesecke R, Schlegel W. Methods of image reconstruction from projections applied to conformation radiotherapy. *Phys Med Biol.* 1990 Oct;35(10):1423–34. doi: 10.1088/0031-9155/35/10/007. PMID: 2243845.
- [5] Bogner L, Scherer J, Treutwein M, Hartmann M, Gum F, Amediek A. Verification of IMRT: techniques and problems. *Strahlenther Onkol.* 2004;180:340–50. doi: 10.1007/s00066-004-1219-0.
- [6] Ramar N, Meher SR, Ranganathan V, Perumal B, Kumar P, Anto GJ, et al. Objective function based ranking method for selection of optimal beam angles in IMRT. *Phys Medica.* 2020;69:44–51. doi: 10.1016/j.ejmp.2019.11.020. ISSN 1120-1797.
- [7] Bohoslavsky R, Witte M, Janssen T, van Herk M. 413 poster reducing trial-and-error with probabilistic IMRT planning for prostate cancer. *Radiother Oncol.* 2011;99(Suppl. 1):S164. doi: 10.1016/S0167-8140(11)70535-7. ISSN 0167-8140.
- [8] Li N, Zarepisheh M, Uribe-Sanchez A, Moore K, Tian Z, Zhen X, et al. Automatic treatment plan re-optimization for adaptive radiotherapy guided with the initial plan DVHs. *Phys Med Biol.* 2013 Dec 21;58(24):8725–38. doi: 10.1088/0031-9155/58/24/8725. Epub 2013 Dec 4. PMID: 24301071.
- [9] Ayala GB, Doan KA, Ko HJ, Park PK, Santiago ED, Kuruvila SJ, et al. IMRT planning parameter optimization for spine stereotactic radiosurgery. *Med Dosimetry.* 2019;44(4):303–8. ISSN 0958-3947. doi: 10.1016/j.meddos.2018.11.001.
- [10] Mescher H, Ulrich S, Bangert M. Coverage-based constraints for IMRT optimization. *Phys Med Biol.* 2017;62(18):N460–73. ISSN 1361-6560. doi: 10.1088/1361-6560/aa8132
- [11] Zarepisheh M, Uribe-Sanchez AF, Li N, Jia X, Jiang SB. A multicriteria framework with voxel-dependent parameters for radiotherapy treatment plan optimization. *Med Phys.* 2014 Apr;41(4):041705. doi: 10.1118/1.4866886. PMID: 24694125.
- [12] Li N, Zarepisheh M, Tian Z, Uribe-Sanchez A, Zhen X, Graves Y, et al. WE-G-BRCD-07: IMRT re-planning by adjusting voxel-based weighting factors for adaptive radiotherapy. *Med Phys.* 2012 Jun;39(6Part28):3966. doi: 10.1118/1.4736184. PMID: 28519641.
- [13] Breedveld S, Storchi PR, Keijzer M, Heemink AW, Heijmen BJ. A novel approach to multi-criteria inverse planning for IMRT. *Phys Med Biol.* 2007 Oct 21;52(20):6339–53. doi: 10.1088/0031-9155/52/20/016. Epub 2007 Oct 2. PMID: 17921588.
- [14] Lambin P, Petit SF, Aerts HJWL, van Elmpt WJC, Oberije CJG, Starmans MHW, et al. The ESTRO Breur Lecture 2009. From population to voxel-based radiotherapy: Exploiting intra-tumour and intra-organ heterogeneity for advanced treatment of non-small cell lung cancer. *Radiother Oncol.* 2010;96(2):145–52. doi: 10.1016/j.radonc.2010.07.001. ISSN 0167-8140.
- [15] Acosta O, Dreon G, Ospina JD, Simon A, Haigron P, Lafond C, et al. Voxel-based population analysis for correlating local dose and rectal toxicity in prostate cancer radiotherapy. *Phys Med Biol.* 2013;58(8):2581–95. doi: 10.1088/0031-9155/58/8/2581. ISSN 0031-9155
- [16] McIntosh C, Purdie Thomas G. Voxel-based dose prediction with multi-patient atlas selection for automated radiotherapy treatment planning. *Phys Med Biol.* 2016;62(2):415–31. ISSN 1361-6560. doi: 10.1088/1361-6560/62/2/415
- [17] McIntosh C, Welch M, McNiven A, Jaffray DA, Purdie TG. Fully automated treatment planning for head and neck radiotherapy using a voxel-based dose prediction and dose mimicking method. *Phys Med Biol.* 2017 Jul 6;62(15):5926–44. doi: 10.1088/1361-6560/aa71f8. PMID: 28486217.
- [18] Beaumont J, Acosta O, Devillers A, Palard-Novello X, Chajon E, de Crevoisier R, et al. Voxel-based identification of local recurrence sub-regions from pre-treatment PET/CT for locally advanced head and neck cancers. *EJNMMI Res.* 2019;9:90. doi: 10.1186/s13550-019-0556-z.
- [19] Hou Q, Wang J, Chen Y, Galvin JM. An optimization algorithm for intensity modulated radiotherapy—the simulated dynamics with dose-volume constraints. *Med Phys.* 2003 Jan;30(1):61–8. doi: 10.1118/1.1528179. PMID: 12557980.
- [20] Gou JJ, Yang XX, Wang G, Huang CY, Hou Q, Wu ZW. The study on an intensity modulated radiotherapy method-the simulated dynamics algorithm. *J Sichuan Univ (Nat Sci Ed).* 2011;48(1):109–15. doi: 103969/j.issn.0490-6756.2011.01.019. ISSN 0490-6756.
- [21] Hou Q, Wang Y. Molecular dynamics used in radiation therapy. *Phys Rev Lett.* 2001 Oct 15;87(16):168101.

- doi: 10.1103/PhysRevLett.87.168101. Epub 2001 Sep 26. PMID: 11690247.
- [22] Ezzell GA, Burmeister JW, Dogan N, LoSasso TJ, Mechalakos JG, Mihailidis D, et al. IMRT commissioning: multiple institution planning and dosimetry comparisons, a report from AAPM Task Group 119. *Med Phys*. 2009 Nov;36(11):5359–73. doi: 10.1118/1.3238104. PMID: 19994544.
- [23] Shou Z, Yang Y, Cotrutz C, Levy D, Xing L. Quantitation of the a priori dosimetric capabilities of spatial points in inverse planning and its significant implication in defining IMRT solution space. *Phys Med Biol*. 2005 Apr 7;50(7):1469–82. doi: 10.1088/0031-9155/50/7/010. Epub 2005 Mar 16. PMID: 15798337.
- [24] Zarepisheh M, Long T, Li N, Tian Z, Romeijn HE, Jia X, et al. A DVH-guided IMRT optimization algorithm for automatic treatment planning and adaptive radiotherapy replanning. *Med Phys*. 2014 Jun;41(6):061711. doi: 10.1118/1.4875700. PMID: 24877806.
- [25] Lougovski P, LeNoach J, Zhu L, Ma Y, Censor Y, Xing L. Toward truly optimal IMRT dose distribution: inverse planning with voxel-specific penalty. *Technol Cancer Res Treat*. December 2010;629–36. doi: 10.1177/153303461000900611
- [26] Wu C, Olivera GH, Jeraj R, Keller H, Mackie TR. Treatment plan modification using voxel-based weighting factors/dose prescription. *Phys Med Biol*. 2003 Aug 7;48(15):2479–91. doi: 10.1088/0031-9155/48/15/315. PMID: 12953910.