Multi-objective optimization of inverse planning for accurate radiotherapy*

CAO Rui-Fen(曹瑞芬)[1,2] WU Yi-Can(吴宜灿)[1,2,3] PEI Xi(裴曦)[1,2] JING Jia(景佳)[1,3,5]
LI Guo-Li(李国丽)[4] CHENG Meng-Yun(程梦云)[1,2] LI Gui(李贵)[1,2] HU Li-Qin(胡丽琴)[1,2]

[1] Institute of Plasma Physics, Chinese Academy of Sciences, Hefei 230031, China
[2] Engineering Technology Research Center of Accurate Radiotherapy, Hefei 230031, China
[3] School of Nuclear Science and Technology, University of Science and Technology of China, Hefei 230027, China
[4] Zhejiang University of Technology, Hangzhou 310014, China
[5] Hefei University of Technology, Hefei 230009, China

Abstract: The multi-objective optimization of inverse planning based on the Pareto solution set, according to the multi-objective character of inverse planning in accurate radiotherapy, was studied in this paper. Firstly, the clinical requirements of a treatment plan were transformed into a multi-objective optimization problem with multiple constraints. Then, the fast and elitist multi-objective Non-dominated Sorting Genetic Algorithm (NSGA-Ⅱ) was introduced to optimize the problem. A clinical example was tested using this method. The results show that an obtained set of non-dominated solutions were uniformly distributed and the corresponding dose distribution of each solution not only approached the expected dose distribution, but also met the dose-volume constraints. It was indicated that the clinical requirements were better satisfied using the method and the planner could select the optimal treatment plan from the non-dominated solution set.

Key words: inverse planning, multi-objective optimization, accurate radiotherapy

PACS: 87.53Tf, 87.53Kn, 81.40Wx **DOI:** 10.1088/1674-1137/35/3/019

1 Introduction

Radiotherapy has been applied to the treatment of tumors for almost a century, but the multi-objective character of inverse planning optimization was only fully recognized about ten years ago. Inverse planning optimization is a multi-objective optimization problem whose solution is known as the Pareto solution set. However, most currently used inverse planning systems translate the multi-objective optimization problem into a single objective optimization problem by computing the weighted summation of each objective, and then optimize it using an stochastic algorithm or an analytic method. There are two shortcomings of this approach. First, the weighting factors should be determined before optimizing, also known as "priori method". However, as the optimum weighting factors are unknown before optimizing, the optimization procedure is a trial and error process, resulting in a waste of manpower and planning time. Second, its applicability is limited, because the method is acceptable only for convex multi-objective optimization problems and cannot guarantee that the obtained solution is a Pareto solution when the optimization problem is non-convex. In fact, most clinical cases are non-convex problems. Only the optimization of radiation field weighting factors is a single-extreme problem. However, if the intensity map of each beam, the beam angels and the beam numbers are all optimized simultaneously, the inverse planning optimization is a non-convex problem [1], so the Pareto solution can not be obtained with the "priori method". To obtain the Pareto solution set of a multi-objective optimization problem, many multi-objective evolutionary algorithms including the fast and elitist multi-objective Non-dominated Sorting Genetic Algorithm (NSGA-Ⅱ), have recently been proposed. They have been applied in many fields because of their high efficiency, while for the multi-objective optimization of inverse planning, they are seldom used.

Received 4 May 2009, Revised 9 November 2010

* Supported by National Natural Seience Foundation (30900386) and Anhui Provincial Natural Science Foundation (090413095, 11040606Q55)

In this study, multi-objective optimization of inverse planning was studied based on inverse planning research by the Advanced/Accurate Radiation Therapy System (named ARTS) [2–8]. First, the mathematical modeling was presented, in which the clinical requirements for a treatment plan were transformed into a multi-objective optimization problem with multiple constraints. Then, the NSGA-II was introduced to optimize the model. Lastly, a clinical example was tested. The results showed that an obtained set of non-dominated solutions were distributed uniformly. Then, the corresponding dose distribution of each solution in the non-dominated solution set not only approached the expected dose distribution, but also satisfied the dose-volume constraints. It was indicated that the clinical requirements were better satisfied and that the planner could select the optimal treatment plan from the non-dominated solution set. With the method we proposed, the planner has no need for a trial and error process to find the optimum plan, so efficiency will be highly improved.

2 Method

2.1 Mathematical modeling

The aim of mathematical modeling is to establish the objective function of optimization, which measures the effectiveness of a selected plan, and its choice is crucial for radiotherapy treatment planning optimization. There are two different types of objective function, the 'physical' objective function and the 'biological' objective function. The 'physical' objective function, which establishes a link between the output dose distribution and the input beam parameters, is widely used in the commercial Treatment Planning System (TPS). In fact, the biological effects of radiation on tumors and normal tissues not only have a relation with the received dose value, but also have connections with the volume of different dose values. So dose-volume constraints are also widely used in clinical applications. In this investigation, difference between the calculated and expected dose, and the dose-volume constraints were both considered. The mathematical formulations of the inverse planning are shown as follows:

$$\left.\begin{aligned} \min f_1 &= \frac{1}{N_{\mathrm{PTV}^2}}\sum_{i=1}^{N_{\mathrm{PTV}}}(d_i^{\mathrm{PTV}}-D^{\mathrm{PTV}})^2, \\ \min f_2 &= \frac{1}{N_{\mathrm{NT}}}\sum_{i=1}^{N_{\mathrm{NT}}} d_i^{\mathrm{NT}}. \end{aligned}\right\} \tag{1}$$

Subject to:

$$\left.\begin{aligned} & V_{\mathrm{PTV}}^{\mathrm{L}} > V_{\mathrm{PTV}}^{\prime\mathrm{L}}, \quad V_{\mathrm{OAR}}^{D_{\mathrm{H}}} < V_{\mathrm{OAR}}^{\prime D_{\mathrm{H}}}, \\ & D_{\mathrm{avg}}^{\mathrm{OAR}} = \frac{1}{N_{\mathrm{OAR}}}\sum_{i=1}^{N_{\mathrm{OAR}}} d_i^{\mathrm{OAR}} < D_{\mathrm{avg}}^{\prime\mathrm{OAR}}, \end{aligned}\right\} \tag{2}$$

here d_i^{PTV} and d_i^{NT} are the calculated dose at the point of i in the Planning Tumor Volume (PTV) and Normal Tissue (NT) respectively; D^{PTV} is the prescribed dose of the PTV; N_{PTV} and N_{NT} are the calculated point numbers at the PTV and NT, respectively. Therefore, the optimization objectives can be expressed as: 1) the calculated dose of all the points in PTV must approximate D^{PTV}; 2) the smaller the average dose of NT is, the better the corresponding plan will be.

In Eq. 2, $V_{\mathrm{PTV}}^{\mathrm{L}}$ and $V_{\mathrm{PTV}}^{\prime\mathrm{L}}$ are the calculated volume and the least allowed volume where the dose is higher than L, respectively. $V_{\mathrm{PTV}}^{\prime\mathrm{L}}$ and L are given by clinical doctors according to the cancer type, expected treatment results and clinical experiences. $V_{\mathrm{OAR}}^{D_{\mathrm{H}}}$ and $V_{\mathrm{OAR}}^{\prime D_{\mathrm{H}}}$ are the calculated volume and the objective volume where the dose is higher than D_{H}, which is the allowed dose of the Organ At Risk (OAR), respectively. d_i^{OAR} is the calculated dose of the point i in the OAR. N_{OAR} is the point number in the OAR. $D_{\mathrm{avg}}^{\prime\mathrm{OAR}}$ is the highest allowed average dose of the OAR. So the constraints formulated by Eq. 2 can be expressed as: 1) not less than $V_{\mathrm{PTV}}^{\prime\mathrm{L}}$ of the volume of the PTV received a dose of higher than L; 2) not more than $V_{\mathrm{OAR}}^{\prime D_{\mathrm{H}}}$ of the volume of the OAR received a dose of higher than D_{H}; 3) the average dose of the OAR must be less than $D_{\mathrm{avg}}^{\prime\mathrm{OAR}}$. From Eq. (1) and Eq. (2) it is evident that the dose and dose-volume constraints were both considered.

2.2 Optimization algorithm based on NSGA-II

Evolutionary algorithms are popular for solving multi-objective optimization problems because they are characterized by a population of solution candidates and can produce a set of approximate solutions in a simulated run. As a representative of the multi-objective evolutionary algorithms, the NSGA-II has been applied to many areas due to its validity [9]. Therefore, the NSGA-II was introduced to the inverse planning in this paper. The procedures were as follows:

1) Initialization: the population size (N) and the maximum evolutionary generation were set and then N individuals of a parent population (P_0) were randomly generated;

2) N groups of field parameters were obtained by decoding the population P_0 and then the point dose

values in the PTV, OAR and NT were calculated in order to compute the objective functions and constraint values according to Eq. (1) and Eq. (2);

3) The non-dominated rank and crowding distance of individuals in population P_0 were computed according to the objective functions and the constraint functions [9, 10];

4) Considering the individual's non-dominated rank and the crowding distance, the binary tournament selection was adopted to select N individuals into the next population Q_0;

5) Individuals in Q_0 implemented an evolutionary process (including crossover and mutation) and then performed steps 2) and 3) again for Q_0, when finished, the process proceeded with step 6);

6) The parent population (P_0) and the offspring population (Q_0) were combined into a population Q of $2N$ individuals, and then N individuals of the parent population of the next generation were generated by the tournament selection from the individuals of Q;

7) If the iterative times or the other conditions were satisfied, the optimization process would be terminated and the obtained Pareto solutions (field parameters) were exported, otherwise the process would go to step 2).

The selection is a crucial evolutionary strategy. However, the selection based on fitness that is common used by the evolutionary algorithm is not suitable for the multi-objective optimization problem because fitness cannot be computed as a single-objective optimization problem. The selection of the NSGA-II proposed in the paper was based on the constraint values, the non-dominated rank and the crowding distance of the individuals, and was not necessary to calculate the fitness. The steps are shown as follows:

1) Two individuals were selected randomly and their feasibility was judged by the following rules: the individual satisfying Eq. (2) was a feasible solution, otherwise it was not a feasible solution (an infeasible solution). If only one of the two individuals was a feasible solution, it would be selected into the next pop; if both of the individuals were infeasible solutions, then their C(the degree of deviation from the constraints) would be computed according to Eq. (3) and the individual with less C was selected; if the C of the two individuals were the same or both were feasible solutions, then step 2) would be implemented.

2) The dominated relations were compared. The individual that was not dominated by the other one was selected. If they couldn't be compared, step 3) would be followed.

$$\left.\begin{aligned} &C_1=\max\{(V'^{\mathrm{L}}_{\mathrm{PTV}}-V^{\mathrm{L}}_{\mathrm{PTV}}),0\},\\ &C_2=\max\{(V^{D_{\mathrm{H}}}_{\mathrm{OAR}}-V'^{D_{\mathrm{H}}}_{\mathrm{OAR}}),0\},\\ &C_3=\max\left\{\left(\frac{1}{N_{\mathrm{OAR}}}\sum_{i=1}^{N_{\mathrm{OAR}}}d_i^{\mathrm{OAR}}-D'^{\mathrm{OAR}}_{\mathrm{avg}}\right),0\right\},\\ &C=C_1+C_2+C_3.\end{aligned}\right\} \tag{3}$$

3) The crowding distances of the two individuals were compared and the individual with a smaller crowding distance was selected; if their crowding distances were the same, step 4) would be performed.

4) One individual was selected randomly.

Feasibility, non-domination and diversity (uniformly distributed) of solutions are the three key evaluation criteria for a multi-objective optimization algorithm. From the investigation selection process it was shown that feasibility and non-domination of solutions were first considered. Meanwhile, retaining the diversity of the solutions was also considered. The constraints were satisfied by the solution's feasibility. The minimized objective function values were guaranteed by non-domination calculated according to objective functions. The smaller the individual's non-dominated rank was, the higher the probability that it would be selected into the next generation. Retaining diversity was guaranteed by the crowding distance calculated according to a number of other solutions around the solution. The smaller the individual's crowding distance, the higher the probability that it would be selected into the next generation. So the corresponding treatment plan solution could kill the tumor cells at an optimal level, while the surrounding organs at risk and other normal tissues were effectively protected.

2.3 Test example

LSM, a patient with a clinical head tumor with 18 CT (Computer Tomography) slices was chosen to test the method. The PTV and OAR were contoured as shown in Fig. 1. The radiation source was a Varian photon beam. Three beams with different orientations were adopted: anti-clockwise direction with the vertical 90°, clockwise into 60° and 120°.

The Source to Surface Distances of the three beams were all set to 100 cm. The parameters to be optimized were the beam weight, the field size (A/cm), the collimator angle (roat/(°)) of each beam and x_{f}/cm, y_{f}/cm of each beam's central axis offset.

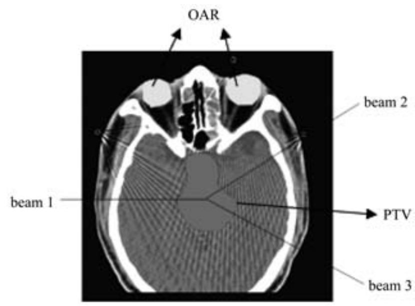

Fig. 1. Contour of PTV and OAR.

2.4 Algorithm parameters

The objectives and constraints of the test example were set as follows: the objective dose of PTV was 92%; the dose of NT was as low as possible; the average dose of the OAR was lower than 20%; not less than 90% of the volume of the PTV received a dose of higher than 90%; not more than 15% of the volume of the OAR received a dose of higher than 30%. The calculated points were uniformly sampled and the point numbers of the PTV, the OAR and the NT were 417, 267 and 693, respectively.

The parameters of the algorithm were set as follows: the population size was 140; the max generation was 200; the crossover probability was 0.6; the mutation probability was 0.01; the variables were treated as the binary code; the binary bits of variables were different from each other according to the accuracy.

The point dose in Eq. (1) and Eq. (2) could be calculated by the Regular Beam Model (RBM), the Pencil Beam Model (PBM), etc. The RBM was adopted in the study.

3 Results and discussion

3.1 Results

As the test example had two contradicting objectives, there is no single optimal solution but instead a whole set of possible solutions of an equivalent quality (Pareto solutions). 36 Pareto solutions were obtained using the optimization. The distributions of the two objective values of 36 solutions are shown in Fig. 2. Three representations of the solutions were chosen: 1) Solutions 1: the first objective was minimized, which meant the dose of the PTV most approximated the expected dose; 2) Solutions 2: the second objective was minimized, which meant protecting the normal tissue was of utmost importance; 3) Solutions 3: compromises of the first objective and the second objective. The corresponding objective function values and beam parameters of the three solutions are shown in Table 1,

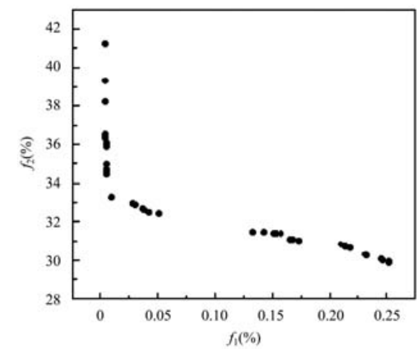

Fig. 2. Distribution of the pareto-front.

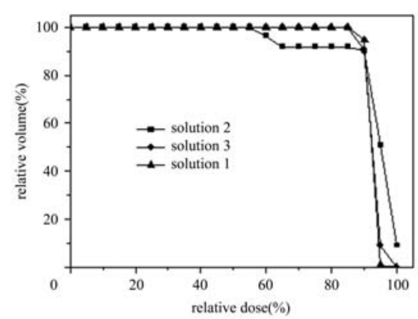

Fig. 3. Dose volume histogram of PTV.

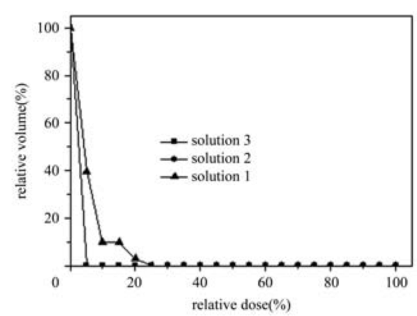

Fig. 4. Dose volume histogram of OAR.

Table 1. The parameters, constraint and objective values of three solutions.

		weight	A/cm	roat/(°)	x_f/cm	y_f/cm	f_1(%)	f_2(%)	V_{PTV}^{L}(%)	V_{OAR}^{Hd}(%)	D_{avg}^{OAR}(%)
	beam1	0.07	11	26	3.44	−2.68					
solution 1	beam2	0.8	5	112	−0.84	0.51	0.004	41.21	4.7	15	16.83
	beam3	0.40	9	−34	4.04	0.93					
	beam1	0.53	8	19	−1.38	3.58	0.252	29.91	0.168	15	21
solution 2	beam2	0.8	5	112	−0.51	0.51					
	beam3	0.07	7	163	3.6	−1.2					
	beam1	0.33	9	40	−1.56	−2.18					
solution 3	beam2	0.80	5	110	−1.52	0.51	0.01	33.21	0.647	15	21
	beam3	0.13	9	89	2.8	0.31					

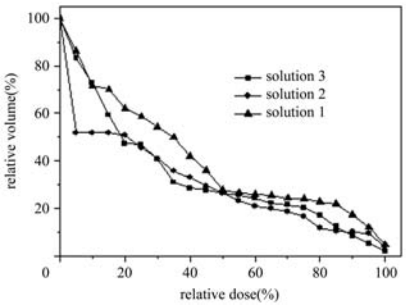

Fig. 5. Dose volume histogram of NT.

and the corresponding Dose Volume Histograms (DVH) of the PTV, OAR and NT are shown in Figs. 3–5.

3.2 Discussion

As shown in the DVH of the PTV (Fig. 3), the dose conformal of solution 1 is the best, followed by solution 3, while solution 2 is the worst. The reason for this is that the first objective's priority of the solution 1 is higher than the others. If the planner wants to effectively kill the tumor and the dose of the OAR and NT only need to meet the constraints, then solution 1 would be the preferred solution. From the DVH of the NT (Fig. 5) it can be seen that the corresponding DVH of solution 1 is the worst one, and the DVHs of the other two solutions are the same. As the second objective's priority (corresponding to NT) of solution 2 or 3 is higher than solution 1, and if the planner's expectation is to focus on minimizing the radiation exposure of the surrounding NT while the tumor receives a given radiation dose, then solution 2 or 3 would be the preferred solution.

All the Pareto solutions (shown in Fig. 2) meet the dose volume constraints, however, it can be seen from Fig. 4 that the DVHs of the OAR of solution 2 and 3 are both below the DVH of solution 1, which means that the volume that received a higher dose than every dose value in the OAR of solution 2 and 3 are less than that of the solution 1. Thus, the corresponding plan of the solutions 2 and 3 can protect the OAR better than solution 1. The planner can select the optimal plan from these Pareto solutions depending on what he wants (kill the tumor most or minimize the damage of the NT). In other words, multi-objective optimization based on the NSGA-II can obtain multiple Pareto solutions from which the planner can select the optimal plan according to the patient's situation, ease of implementation, clinical experiences and so on.

4 Conclusions

In this study, taking advantages of both the objective function based on the dose distribution and the objective function based on the dose-volume constraints, inverse planning optimization was mathematically modeled as a multi-objective optimization problem, and then a multi-objective evolutionary algorithm based on the NSGA-II was introduced to solve the problem. Clinical test results showed that multiple optimal solutions could be obtained, providing the planner with the best selection to tradeoff between different objectives and dose-volume constraints.

The commonly used optimization methods of inverse planning, which transform the multi-objective optimization problem into a single-objective optimization through weighted summation, can only obtain a balance between multiple objective functions and constraints. However, if the obtained solution does not satisfy the requirements, the optimization should be run again. Thus, the commonly used methods may waste more time. The proposed method in this paper provides a Pareto optimal solution set to be selected by the planners and does not force the user without any knowledge to import the weighting factors iteratively. Therefore, this method is more accurate and flexible for fulfilling practical clinical requirements.

References

1 Lahanas M, Baltas D, Zamboglou N. Med. Phys., 1999, **26**: 1904

2 WU Yi-Can, LI Guo-Li, TAO Sheng-Xiang et al. Chinese Journal of Medical Physics, 2005, **22**(6): 283 (in Chinese)

3 WU Yi-Can, SONG Gang, CAO Rui-Fen et al. Chinese Physics C (HEP&NP), 2008, **32**(Suppl. II): 177

4 LI Guo-Li. Study on Multi-objective Optimization Algorithm for Inverse Planning of External Radiation in ARTS. [PhD] Institute of Plasma Physics, Chinese Academy of Sciences. 2006

5 CAO Rui-Fen, LI Guo-Li, SONG Gang. Chinese Journal of Radiological Medicine and Protection, 2007, **27**(5): 467 (in Chinese)

6 LI Guoli, SONG Gang, WU Yi-Can. Nuclear Technology, 2007, **30**(3): 222 (in Chinese)

7 LI Guo-Li, WU Yi-Can, ZHANG Jian. Plasma Science and Technology, 2006, **8**(2): 234

8 LI Guo-Li, WU Yi-Can, SONG Gang, WANG Shi-Fang. Nuclear Physics Review, 2006, **23**(2): 233 (in Chinese)

9 Kalyanmoy Deb, Amrit Pratap, T Meyarivan. IEEE Transactions on Evolutionary Computation, 2002, **6**(2): 182–197

10 CAO R F, LI G L, WU Y. Advanced intelligent Computing Theories and Applications, Proceedings. 2007, **4682**: 553–564

11 SONG Gang. Hybrid Dose Calculation Research and Program Development for Accurate Radiotherapy. [PhD] Institute of Plasma Physics, Chinese Academy of Science. 2008