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Interactive multiobjective optimization for IMRT

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Abstract

In this paper, interactive multiobjective optimization for radiotherapy treatment planning is studied. The aim of radiotherapy is to destroy a tumor without causing damage to healthy tissue and treatment planning is used to achieve an optimal dose distribution. In intensity modulated radiotherapy (IMRT), the intensity of the incoming radiation flux can be modulated using some aperture such as a multileaf collimator. Radiotherapy goals are conflicting and it is impossible to satisfy all the targets simultaneously. Therefore, an interactive multiobjective optimization method for IMRT is used. With this method, the best compromise can be found for all the conflicting targets. Results of numerical studies indicate that in this way a radiotherapy expert, called as a decision maker, can conveniently utilize one's knowledge and expertize and direct the solution process interactively and iteratively in order to find the best feasible radiotherapy treatment plan. This approach decreases the number of uninteresting solutions computed and the best solution can be selected in a case specific way by using the decision maker's expertize.

Key words: Interactive multiobjective optimization, Intensity modulated radiotherapy treatment planning optimization

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1 Introduction

In radiotherapy treatment planning, a model is needed to compute the absorbed dose distribution within a patient to ensure a desired treatment outcome. The dose calculation models are typically referred to as radiotherapy forward problems. During the years, these mathematical models have improved and physical and biological responses are better known (Smith 1995, Ahnesjö and Aspradakis 1999). In external radiotherapy, so called pencil beam models are typically used for photon dose calculation. Alternatively, one could use Monte Carlo (Andreo 1991) or deterministic Boltzmann transport equation based models (Boman et al.2005). In conformal radiotherapy, the aim of the treatment planning is to achieve a dose distribution, that conforms the tumor as closely as possible while healthy tissue does not receive too high a dose. For these purposes the intensity modulated radiotherapy (IMRT) can be utilized (Bortfeld 2006). In IMRT, the intensity of the incoming beam is modulated using apertures such as multileaf collimators (MLC).

Radiotherapy treatment planning is in fact an inverse problem. The problem is to find treatment settings such that the aims of the treatment planning are met. The use of IMRT increases remarkably the number of different settings and alternatives in treatment planning and some optimization algorithm has to be used to find the best possible treatment plan (Brahme 2000, Bortfeld 1999, Censor and Zenios 1997). Although optimization in the radiotherapy treatment planning has been widely studied, see for example Palta and Mackie 2003 and Brahme 1995, still, clinical applications typically use a more or less trial and error sequence, in which a radiotherapist seeks for the best treatment plan based on his/her intuition and knowledge. In IMRT optimization, the number and orientation of beams and/or flux intensities are usually the decision variables which control the dose distribution during the optimization. Traditionally, approaches used in radiotherapy are based on optimizing one objective function and the objective function is often defined as a weighted sum of quadratic penalties where the idea is to fulfill some predefined dose limits specified for different organs and tumors, see e.g. Shepard et al.1999, Tervo and Kolmonen 2000 and Carlsson and Forsgren 2006. However, let us point out that the actual goal is to fulfill the given dose limits and minimize the harmful dose, simultaneously. Then, in the methods widely used in the literature, all the targets are scaled or summed as one objective, but it is typically hard to predefine priorities or weights of the optimization targets in an optimal way. Furthermore, sometimes information about objectives and even practical relevance of the objective functions can be lost because of mixing the objectives as a sum. To avoid this, we present an alternative method for radiotherapy optimization.

In this paper, we integrate a dose calculation model of IMRT with the interactive multiobjective optimization method NIMBUS (Miettinen and Mäkelä 2006) and discuss the results of the studies. The aim of radiotherapy is to destroy the tumor (or the planning target volume (PTV)) without causing damage to healthy tissue (often divided to the dose sensitive volume organ at risk (OAR), and normal tissue (NT)). Naturally, these targets are conflicting, that is increasing the dose in the tumor also increases the unwanted dose in the surrounding healthy tissue. Thus, it is impossible to satisfy these criteria at the same time. When one target is optimized, some other will suffer. This trade off is complex and optimization tools capable of handling multiple and conflicting objectives are required. Traditional optimization is not enough. Our approach is to use interactive multiobjective optimization for IMRT. Although multiobjective optimization has already been applied in radiotherapy treatment planning, see e.g. Küfer et al.2000, Cotrutz et al.2001, Lahanas et al.2003 and Schreibmann et al.2004, the approach presented in this paper is different since it does not use objective weights defined beforehand or evolutionary algorithms. As mentioned above, there are some obvious difficulties in defining the weighting coefficients. Furthermore, evolutionary algorithms have their own drawbacks. For example, they are very time consuming because a large set of uninteresting solutions together with the interesting ones need to be generated before a desired solution can be found. In our iterative solution process, the interactive role of the radiotherapy expert, called a decision maker, and his/her knowledge is emphasized. The presented multiobjective optimization approach is user friendly, intuitive and iterative when optimizing the conflicting objectives simultaneously. It uses the decision maker's knowledge to direct the solution process in order to find the most preferred compromise, so called Pareto optimal solution, between the conflicting criteria. As can be seen from results of the numerical studies, the approach presented helps the decision maker to understand and learn about the interrelationships between the objectives and the decision maker can choose the best possible solution by case according to his/her knowledge. In addition, the number of uninteresting solutions calculated decreases. This makes the optimizing process very fast and the desired solution is easy to choose.

This paper is organized as follows: In Section 2, we examine the radiotherapy dose calculation model and define a feasible solution for radiotherapy. Section 3 introduces multiobjective optimization and presents the optimization method used. We also give a short review of decision support aids. In Section 4, we describe and discuss a numerical example of a C-shaped tumor case. We define objective functions and also study and discuss our interactive multiobjective optimization process. Finally, Section 5 is devoted to conclusions and future directions and challenges.

2 IMRT treatment planning problem and optimization

2.1 Dose calculation in a patient space and inverse problem

Optimization in IMRT treatment planning can be categorized into two areas. On the one hand, in which the treatment settings are solved directly (Tervo et al.2003), and on the other hand, in which the field intensities are solved and the treatment settings are determined afterward from the solved intensities. The direct method has some benefits, but for simplicity we concentrate here on the latter case.

Let us assume that the treatment geometry consists of L different fields S_l ($l = 1, \ldots, L$) with given gantry α_l, couch β_l and collimator θ_l angles. The treatment space U_l of the field S_l is discretized into voxels $u_{i,j,l} := [u^l_{1,i-1}, u^l_{1,i}] \times [u^l_{2,j-1}, u^l_{2,j}]$, where $i = 1, \ldots, I_l$ and $j = 1, \ldots, J_l$ such that $U_l = \sum_{i,j} u_{i,j,l}$. Denote $u = (u_1, u_2)$ to be a point in U_l.

For the forward problem, we use a pencil beam model, in which the dose distribution $D(x)$, where $x = (x_1, x_2, x_3)$ is a point in the patient space V, thus $x \in V$, for L different fields U_l is given as an integral (known as the first kind of Fredholm integral equation)

$$D(x) = \sum_{l=1}^{L} \int_{U_l} h_l(x, u)\psi_l(u)\mathrm{d}u, \tag{1}$$

where $h_l(x, u)$ is a dose deposition kernel and $\psi_l(u)$ is the intensity of the field S_l. The treatment space U_l and the patient space V are illustrated in Figure 1.

For simplicity, the dose deposition kernel $h_l(x, u)$ for each field $l = 1, \ldots, L$ is chosen to model a photon pencil beam in water equivalent media. The kernel is given in Ulmer and Harder 1995 and 1996 as

$$h_l(x, u) = I(x_3) \sum_{k=1}^{3} \frac{c_k}{\pi\sigma_k(x_3)^2} \exp\left[\frac{-((x_1 - u_1)^2 + (x_2 - u_2)^2)}{\sigma_k(x_3)^2}\right], \tag{2}$$

where $I(x_3)$ is a function representing a relative depth dose and $\sigma_k(x_3)$ is a depth dependent mean square radial displacement. These values and parameter c_k are tabulated in Ulmer and Harder 1995. This kernel corresponds to the situation where the origin of the patient coordinate system is at the point O_l and the x_3-axis is perpendicular to the plane U_l. Other directions $A_l x$ are obtained using general coordinate transformations for the patient space V co-

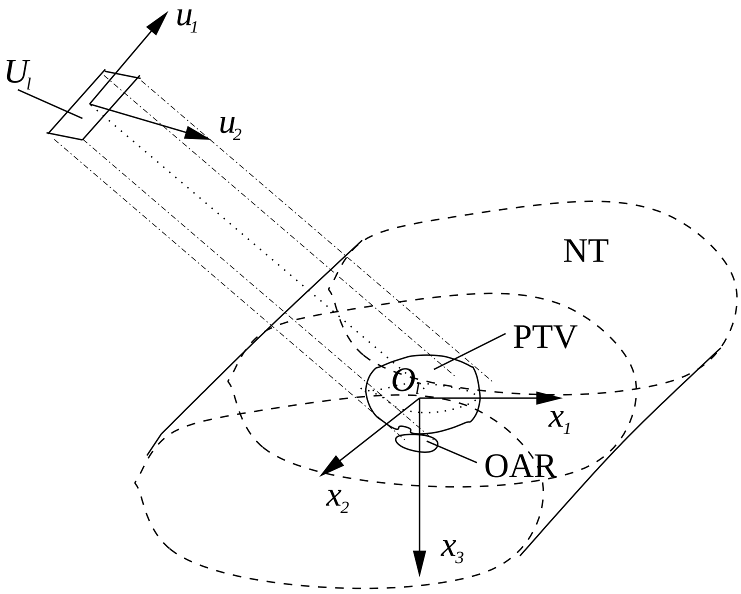

Figure 1. Coordinate systems in dose calculation. Plane U_l is the treatment space. The radiation field comes to the patient space V and isocenter is O_l. The patient space V includes regions PTV, OAR and NT.

ordinates, i.e., $A_l x = R_1(\theta_l)R_2(\beta_l)R_3(\alpha_l)(x - O_l)^T$, where T is the transpose of a matrix and R_1, R_2 and R_3 are appropriate rotation matrices. In the present form, the kernel used does not take into account the tissue inhomogeneities and the real patient geometry. These model simplifications are assumed to be irrelevant to demonstrate the applicability of the optimization method proposed.

Before optimizing dose delivery to the patient space V, a discrete inverse problem needs to be formulated from equation (1). Function $\psi_l(u)$ is assumed to be a constant $w_{i,j,l}$ at each sub domain $u_{i,j,l}$. Thus,

$$\psi_l(u) = w_{i,j,l}, \tag{3}$$

when $u \in u_{i,j,l}$. Then equation (1) is of the form

$$\begin{aligned} D(x) = {} & I((A_l x)_3) \sum_{k=1}^{3} \frac{c_k}{\pi\sigma_k((A_l x)_3)^2} \sum_l \sum_i \sum_j w_{i,j,l} \\ & \cdot \int\limits_{u_{i,j,l}} \exp\left[\frac{-(((A_l x)_1 - u_1)^2 - ((A_l x)_2 - u_2)^2)}{\sigma_k((A_l x)_3)^2}\right] \mathrm{d}u \qquad (4) \\ = {} & \sum_l I((A_l x)_3) \sum_{k=1}^{3} \frac{c_k}{\pi\sigma_k((A_l x)_3)^2} \sum_i \sum_j w_{i,j,l} \end{aligned}$$

$$\cdot \int_{u^l_{1,i-1}}^{u^l_{1,i}} \exp\left[\frac{-((A_l x)_1 - u_1)^2}{\sigma_k((A_l x)_3)^2}\right] \mathrm{d}u_1$$
$$\cdot \int_{u^l_{2,j-1}}^{u^l_{2,j}} \exp\left[\frac{-((A_l x)_2 - u_2)^2}{\sigma_k((A_l x)_3)^2}\right] \mathrm{d}u_2. \tag{5}$$

The error function erf_τ is defined by an integral

$$\mathrm{erf}_\tau(x) = \frac{1}{\sqrt{\pi}\tau} \int_{-\infty}^{x} \exp\left[\frac{-s^2}{\tau^2}\right] \mathrm{d}s, \tag{6}$$

and one can find that

$$\begin{aligned} D(x) = \sum_l I((A_l x)_3) \sum_{k=1}^{3} c_k \sum_i \sum_j w_{i,j,l} \\ \cdot \left[\mathrm{erf}_{\sigma_k}(-((A_l x)_1 - u^l_{1,i})^2) - \mathrm{erf}_{\sigma_k}(-((A_l x)_1 - u^l_{1,i-1})^2)\right] \\ \cdot \left[\mathrm{erf}_{\sigma_k}(-((A_l x)_2 - u^l_{2,j})^2) - \mathrm{erf}_{\sigma_k}(-((A_l x)_2 - u^l_{2,j-1})^2)\right]. \end{aligned} \tag{7}$$

Let us denote $\boldsymbol{w} := (w_{1,1,1}, \ldots, w_{I_l,J_l,L})^T$ and thus, we have $D(x, \boldsymbol{w}) := D(x)$.

This model is used in our multiobjective optimization approach for IMRT in dose calculations and the intensities $w_{i,j,l}$ needed in optimization can be solved from equation (7) as an inverse problem.

2.2 A feasible solution for radiotherapy treatment planning

Our approach is based on the fact that the dose $D(x, \boldsymbol{w})$ in the PTV, must be as close as possible the desired dose D_{PTV}, which is case specific depending on the type of the tumor. Nevertheless, a few per cent deviation from the desired dose D_{PTV} is acceptable. At the same time the dose in the OAR and in NT should be as low as possible. These regions are illustrated in Figure 1. In real life, there is an upper bound for dose in the OAR and in NT that should not be violated. We denote these limits D_{OAR} and D_{NT}, respectively. Our goal is to find the intensities $w_{i,j,l}$ so that the above-mentioned criteria hold.

We divide the patient space V into separate regions V_p, p=1,2,3. Let $x_p \in V_p$ and define the union $I = I_1 \cup I_2 \cup I_3$ such that

$$I_1 = \{p \in I | x_p \in \mathrm{PTV}\},$$

$I_2 = \{p \in I | x_p \in \text{OAR}\}$,
$I_3 = \{p \in I | x_p \in \text{NT}\}$.

Now we can define a feasible objective set, which is in fact know as a feasible solution in radiotherapy treatment planning. Thus, we try to find the intensities for which the inequalities

$$\begin{array}{lll} d\%\ D_{PTV} \le D(x_p, \boldsymbol{w}) \le D\%\ D_{PTV}, & & p \in I_1, \\ D(x_p, \boldsymbol{w}) & \le D_{OAR}, & p \in I_2, \\ D(x_p, \boldsymbol{w}) & \le D_{NT}, & p \in I_3 \end{array}$$

are at least satisfied, but in optimization, we want to minimize the unwanted dose at the same time. Coefficients $d\%$ and $D\%$ are the case specific accepted deviation from the desired dose D_{PTV}.

As one can easily understand, when optimizing the treatment plan, the targets are conflicting. Thus, all the treatment planning targets can not reach their minima at the same time. Achieving the wanted dose D_{PTV} in the PTV is not possible without affecting some dose to unwanted regions because the radiation must travel through NT to reach the PTV, for example.

3 Optimization approach

3.1 Multiobjective optimization

In general, a multiobjective optimization problem can be defined as follows (Miettinen 1999)

$$\begin{array}{ll} \min & \{f_1(\boldsymbol{w}), f_2(\boldsymbol{w}), \ldots, f_k(\boldsymbol{w})\} \\ \text{subject to } \boldsymbol{w} \in S, & \end{array} \tag{8}$$

where $\boldsymbol{w}$ is a vector of decision variables from the feasible set $S \subset \boldsymbol{R}^n$ defined by box, linear and nonlinear constraints. We can denote a vector of objective function values or an objective vector $\boldsymbol{f}(\boldsymbol{w}) = (f_1(\boldsymbol{w}), f_2(\boldsymbol{w}), \ldots, f_k(\boldsymbol{w}))^T$. We denote the image of the feasible set by $\boldsymbol{f}(S) = \text{Z}$ and call it as a feasible objective set. If some objective function f_i is to be maximized, it is equivalent to consider minimization of $-f_i$.

In multiobjective optimization, optimality is understood in the sense of Pareto optimality (Miettinen 1999). A decision vector $\boldsymbol{w}^* \in S$ is Pareto optimal, if there does not exist another decision vector $\boldsymbol{w} \in S$ such that $f_i(\boldsymbol{w}) \leq f_i(\boldsymbol{w}^*)$ for all $i = 1, \ldots, k$ and $f_j(\boldsymbol{w}) < f_j(\boldsymbol{w}^*)$ for at least one index j. These Pareto optimal solutions constitute a Pareto optimal set. From a mathematical point of view, all of them are equally good and they can be regarded as equally valid compromise solutions of the problem considered. Because vectors cannot be ordered completely, there exists no trivial mathematical tool in order to find the most satisfactory solution in the Pareto optimal set.

Because all the solutions are equally good, an expert of the problem known as a decision maker is typically needed in order to find the best or most satisfying solution to be called the final one. The decision maker can participate in the solution process and in one way or the other, determine which one of the Pareto optimal solutions is the most desired to be the final solution. It is often useful for the decision maker to know the ranges of objective function values in the Pareto optimal set. An ideal objective vector gives lower bounds for the objective functions in the Pareto optimal set and it is obtained by minimizing each objective function individually subject to the constraints. A nadir objective vector giving upper bounds of objective functions in the Pareto optimal set is usually difficult to calculate, and, thus, its values are usually only approximated, for example, by using pay-off tables, see for more Miettinen 1999.

Sometimes, the many methods developed for multiobjective optimization are divided into four classes according to role of the decision maker (Miettinen 1999). First, there are methods where no decision maker is available and where the final solution is some neutral compromise solution. The three other classes are a priori, a posteriori and interactive methods, where the decision maker participates in the solution process before it, after it or iteratively, respectively. We concentrate on the last-mentioned class in this paper, because an interactive multiobjective optimization method is ideal for radiotherapy optimization. It makes possible the decision maker to control the solution process iteratively and learn about the conflicting radiotherapy targets during optimization. An interactive approach also provides shorter computing times, because the decision maker directs the solution process the way he/she wants and only such solutions he/she is interested in are generated.

3.2 NIMBUS - an interactive multiobjective optimization method

Our main idea is to integrate the radiotherapy model together with an interactive multiobjective optimization method. The method we are using is NIMBUS (Miettinen and Mäkelä 2006, Miettinen 1999) and so far we have been able to prepare a preliminary integration. The NIMBUS method was selected because it has been successfully used in other applications in optimal control and shape design, for example, in Miettinen et al.1998, Hämäläinen et al.2003, Hakanen et al.2005 and Heikkola et al.2006.

In interactive multiobjective optimization methods, it is important that the information given to and asked from the decision maker is easily understandable. The NIMBUS method is based on the idea of classification of objective functions. From a cognitive point of view, classification can be considered as an acceptable task for human decision makers (Larichev 1992). In NIMBUS, the decision maker participates in the solution process continuously and iteratively. Finally, he/she decides, which one of the Pareto optimal solutions is the most desired one. During the solution process, the decision maker classifies objective functions at the current Pareto optimal point into up to five classes, which are the following:

(1) Functions whose values should be improved,
(2) Functions whose values should be improved until a desired aspiration level,
(3) Functions whose values are satisfactory at the moment,
(4) Functions whose values can be impaired until a given bound,
(5) Functions whose values can change freely.

Because the solutions obtained are Pareto optimal, the decision maker can not make a classification where all the objective function values are improving without allowing at least one of the objective functions to impair. While the decision maker classifies the objective functions, he/she is asked to specify the aspiration levels and the bounds if they are needed. By classifying the objective functions the decision maker gives preference information about how the current solution should be improved and, based on that, a scalarized single objective optimization problem, also know as a subproblem, can be formed. The subproblem generates a new Pareto optimal solution that satisfies the preferences given in the classification as well as possible. The decision maker can use any solution obtained that far as a starting point for a new classification. Alternatively, the decision maker can generate a desired number of intermediate solutions between any two Pareto optimal solutions. He/she can also save interesting solutions in a database which enables him/her to return later to these solutions and continue the solution process from any of them.

In the so-called synchronous NIMBUS method used here, there are four different subproblems available (see Miettinen and Mäkelä 2006, Miettinen and Mäkelä 2002), and thus, the decision maker can choose if he/she wants to see one to four new solutions after each classification. Each of the subproblems generates a solution taking the classification information into account in a slightly different way. The scalarized subproblems are solved with appropriate single objective optimizers. For more about NIMBUS scalarizations used as well as ways of aiding comparison with different visualizations, see Miettinen and Mäkelä 2006.

4 Numerical example and discussion

4.1 Objective functions and multiobjective optimization of a C-shaped tumor case

In this multiobjective optimization example, a two dimensional simulation was made in an artificial phantom geometry describing water. For dose computations, the Fredholm integral equation with the 8 MV photon pencil beam kernel in a two dimensional homogeneous water domain was used as described in Section 2.1 (neglecting the third dimension in the patient space V and the second dimension in the treatment space U_l). Five incoming radiation fields were used at the angles 0°, 72°, 144°, 216° and 288°. The field intensities $\psi_l(u)$ (l=1,. . .,5) were divided into 10 subintervals and in each interval the intensity was assumed to be constant $w_{i,l} \in [0, 1]$. Thus, we had $\boldsymbol{w} = (w_{1,1}, \ldots, w_{10,1}, \ldots, w_{1,5}, \ldots, w_{10,5})^T$, and therefore, the number of the decision variables was 50. The problem contained box constraints for the decision variables, but it did not have any inequality or equality constraints. Simulation were carried out with the mathematical software Matlab® and all the simulation and optimization calculations were made with a personal computer (Pentium® 4 CPU 3.00 GHz with 2 GB central memory).

In the simulation, the pentagonal phantom consists of three different structures as presented in Section 2.2: a non-convex PTV area, an OAR area next to the PTV and a surrounding NT. In this case, the decision maker defined three objective functions characterizing an optimal solution. According to the hopes of the the decision maker, three objective functions were defined as

$$f_1(\boldsymbol{w}) = \max_{p \in I_1}(|D(x_p, \boldsymbol{w}) - D_{PTV}|), \tag{9}$$

$$f_2(\boldsymbol{w}) = \frac{1}{|I_2|} \sum_{p \in I_2} D(x_p, \boldsymbol{w}) \tag{10}$$

and

$$f_3(\boldsymbol{w}) = \frac{1}{|I_3|} \sum_{p \in I_3} D(x_p, \boldsymbol{w}), \tag{11}$$

which were minimized simultaneously. The optimization problem followed

$$\begin{aligned} &\min && \{f_1(\boldsymbol{w}), f_2(\boldsymbol{w}), f_3(\boldsymbol{w})\} \\ &\text{subject to } \boldsymbol{w} \in [0,1], \end{aligned} \tag{12}$$

where $\boldsymbol{w}$ was a vector of decision variables.

The objective functions chosen describe how the dose behaves in separate regions V_p in the presented patient space V. The objective function f_1 describes the maximum dose deviation from a desired dose D_{PTV} in the PTV and we want to minimize the maximum deviation from the desired dose D_{PTV}. The objective functions f_2 and f_3 are the averaged doses in the OAR and NT, respectively, to be minimized, too. The desired dose D_{PTV} was scaled to 100%.

Using his/her expertise and knowledge of radiotherapy, the decision maker with an analyst (responsible for the mathematical and methodological side of the solution process) can define as many interesting case specific objective functions $f_1, ..., f_k$ as he/she wants. The decision maker's knowledge of radiotherapy can be used to select an appropriate combination of the objective functions to be used in solving the treatment planning problem. This is because the decision maker is an expert on his/her field and the expert is assumed to know best the interesting objective functions that suit the case considered. The expert selects objective functions by case and he/she can learn about the problem during the solution process. This enables the expert to modify the case and define the objective functions better during the treatment planning process if needed.

Problem formulation (12), with conflicting objectives, was used for the demonstration of the proposed interactive multiobjective optimization method for IMRT. An implementation of the NIMBUS method, called IND-NIMBUS (Miettinen 2006), with a local optimizer based on the proximal bundle method (Mäkelä and Neittaanmäki 1992, Miettinen and Mäkelä 2006), was used in optimization.

4.2 Solution process

In this example, we consider the multiobjective optimization of the radiotherapy treatment planning problem described. The aim of the planning is to ensure the wanted dose D_{PTV} and dose distribution in the PTV and minimize the unwanted dose in the OAR and in NT.

In this optimization problem, the interactive solution process was guided by preference information of a radiotherapy expert, who was acting as a decision maker. At the beginning, objective functions had the initial values $f_1 = 37.66, f_2 = 33.78$ and $f_3 = 22.29$, presented also in Table 1. The initial solution $\mathbf{f}(\boldsymbol{w}^1)$ was produced with typical values of the decision variables and it was projected on the Pareto optimal set by NIMBUS. The initial solution values are shown as contours describing the dose distribution in the phantom area in Figure 2. As said, the decision maker had preference information that the desired dose D_{PTV} in the PTV is 100%, but 5% deviation from the desired dose D_{PTV} in the PTV is acceptable in this case. Thus, we could set $d\% = 95\%$ and $D\% = 105\%$. Also, according to the preferences of the decision maker, in the OAR and in NT the average dose D_{OAR} and D_{NT} should be under 60% and 40% of the D_{PTV}, respectively.

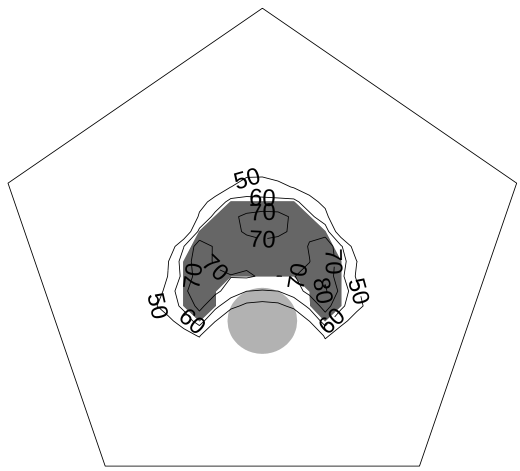

Figure 2. The initial solution. The light grey circle is the OAR and the dark grey C-shaped area is the PTV.

In brief, throughout the optimization process, the decision maker had the following aims. He wanted to obtain such a solution in which the dose deviation from the D_{PTV} in the PTV is minimized. He found very important that the 5% dose deviation from the D_{PTV} should not be violated. At the same time the dose in both areas, in the OAR and in NT, should be as low as can be reached, but at least under the desired threshold values, D_{OAR} and D_{NT}, respectively. As can be seen from the initial objective function values, the f_1 value is now certainly too high. This can be seen also in Figure 2. In the initial solution, the objective functions f_2 and f_3 are in a good level, thus the harmful dose in the OAR and in NT is low, but at the same time the deviation from the D_{PTV} in the PTV is high. In other words, the objective function f_1 is not in a good level, the dose in the PTV is too low and the tumor will not be treated properly. Thus, the decision maker wanted to search for a better solution in an iterative way. The decision maker was able to get 4 solutions for every classification, and all the solutions obtained are presented in Table 1.

4.2.1 *First classification*

In the first classification, the decision maker wanted to improve the values of f_1 and f_2: decrease the deviation from the desired dose D_{PTV} in the PTV and decrease the dose in the OAR. Simultaneously, he let the NT dose (f_3), to change freely. That is because he wanted to protect the OAR more efficiently than NT. Therefore, the decision maker classified f_1 and f_2 to class (i) and f_3 to class (v).

The decision maker obtained four new solutions. He obtained some improvements, all the new solution had the objective function values f_1 and f_2 in a better level than in the initial solution. At the same time, the objective function f_3 got worse. The changes were in the right direction, but the changes were minor. The best one of the solutions obtained according to the decision maker's knowledge was $\mathbf{f}(\boldsymbol{w}^2)$, where $f_1 = 20.41, f_2 = 19.47$ and $f_3 = 29.64$. The solution is shown in Figure 3. As can be seen, the dose in the PTV is jagged and non-uniform and the deviation from the desired dose D_{PTV} is too high, although it is much better than in the initial solution. Because the solution was not yet in a desirable level, the decision maker wanted to classify the objective functions again. He used the presented solution as a starting point of a new classification.

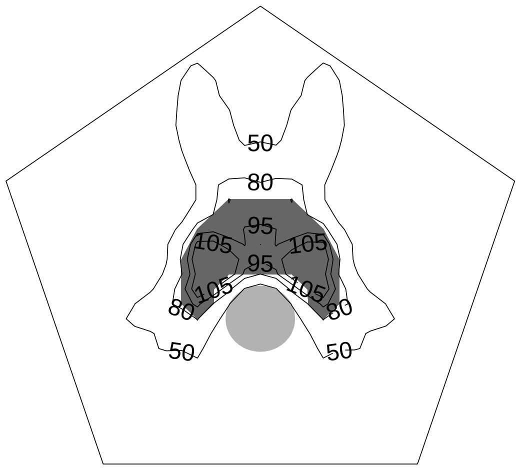

Figure 3. The best solution obtained after the first classification.

4.2.2 *Second classification*

All the improvements gained after the first classification were fair, but the changes were small. That is why the decision maker furthermore wanted to improve the objective function f_1. The decision maker did an almost the same kind of classification than the first classification was. Now he classified the objective function f_1 to improve (class (i)), simultaneously he let the objective function f_2 to impair until a specific bound (class (iv)), that is 33.33. The objective function f_3 was let to change freely (class (v)) just like in the first classification.

After the second classification, the decision maker obtained four new solutions in which the objective function values changed more dramatically. He obtained solutions, in which the objective function f_1, which he considered to be very important, was in an acceptable level but also some solutions, where it was not good enough. In other words, if the objective function f_1 was in a good level, the objective functions f_2 and f_3 were too poor and vice versa. Therefore, the decision maker wanted to produce intermediate solutions between two Pareto optimal solutions obtained after the second classification. He decided to produce five intermediate solutions between solutions $\mathbf{f}(\boldsymbol{w}^6)$ ($f_1 = 9.95$, $f_2 = 33.33$ and $f_3 = 34.30$) and $\mathbf{f}(\boldsymbol{w}^8)$ ($f_1 = 2.16$, $f_2 = 83.81$ and $f_3 = 42.22$).

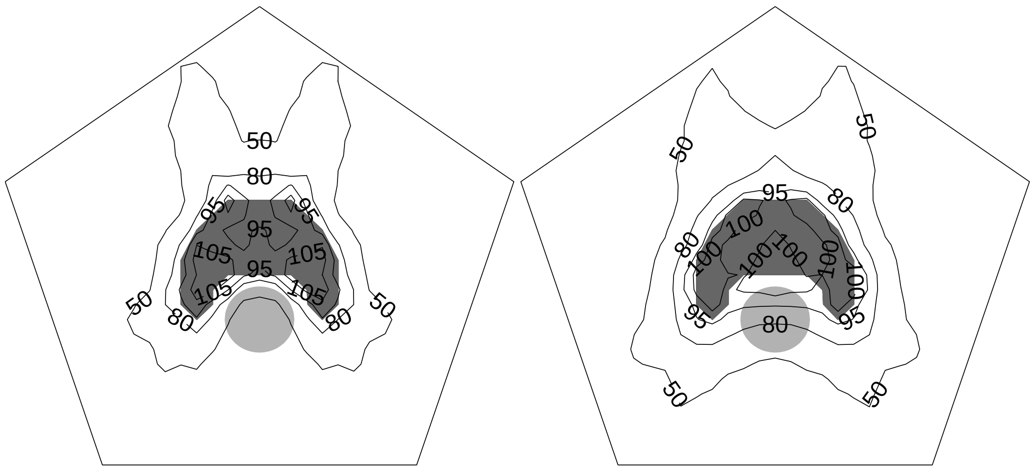

Figure 4. Two different solutions obtained after the second classification. Left, solution $\mathbf{f}(\mathbf{x}^6)$, good f_2 and f_3 values and right, solution $\mathbf{f}(\mathbf{x}^8)$, good function f_1 value.

4.2.3 Final solution and discussion

The decision maker was given five intermediate solutions. These intermediate solutions represented desired compromises between the conflicting targets. Many of the new solutions generated were quite satisfactory compromises and the decision maker felt he is able to make the final decision about which one of the solutions generated was the most satisfying to be the final solution. He was looking for a solution, in which the dose in the PTV is as uniform as possible and the preference information about dose limitations are valid. He achieved a solution in which the deviation from the desired dose D_{PTV} in the PTV was satisfactory (f_1=4.91) and simultaneously, the unwanted dose in the OAR (f_2=57.56) and in NT (f_3=37.72) was as small as it was reasonably achieved in the time he had. As can be seen in Figure 5, the 5% dose deviation from the D_{PTV} in the PTV was not violated and the average doses in the OAR and in NT were under the dose limits D_{OAR} and D_{NT}, respectively.

This solution $\mathbf{f}(\boldsymbol{w}^{12})$ was the most preferred one to be the final solution according to the decision maker's expertize. A summary of the solution process is presented in Table 1 including actions made by the decision maker and solutions selected at each iteration (denoted in bold face). In Table 1, we also give approximated information about objective function ranges in the Pareto optimal set as discussed in Section 3.1. The ranges of the Pareto optimal set were produced by NIMBUS and their values were updated during the solution process, whenever smaller or higher Pareto optimal function values were obtained during the solution process.

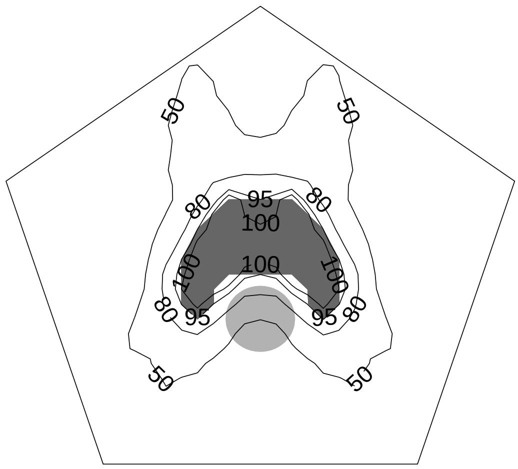

Figure 5. The final solution selected by the decision maker where 100% of the PTV gets the desired dose 95%-105% of the D_{PTV}.

In Table 1, we can study how the solution process progressed and how the new solution fulfills the decision maker's requirements after every iteration concerning the requirements of the radiotherapy process. This kind of additional information can be easily seen with the approach used and this enables the decision maker to learn and analyze the interrelationships of the objectives and compare solutions.

The solution process gave a new perspective to radiotherapy optimization. The approach differs from those used in the literature earlier since it does not use objective weights defined beforehand. The approach handles objectives in an understandable manner and the decision maker's interactive role and knowledge is emphasized in the iterative solution process. The above described optimization process did not only get the best radiotherapy treatment plan, but can also gave new understanding of the radiotherapy process. The interactive multiobjective optimization made possible for the decision maker to learn about the conflicting dose distribution targets and their interrelationships.

When the decision maker made his final decision and the best solution was found, the method presented gives not only the objective function values but

Table 1
Summary of solution process.

Solution	$f_1[\%]$	$f_2[\%]$	$f_3[\%]$
Ideal	0.50	0	0
Nadir	100.00	97.35	59.92
Initial solution			
$\boldsymbol{f}(\boldsymbol{w}^1)$	**37.66**	**33.78**	**22.29**
1st classif.	(i)	(i)	(v)
$\boldsymbol{f}(\boldsymbol{w}^2)$	**20.41**	**19.47**	**29.64**
$\boldsymbol{f}(\boldsymbol{w}^3)$	20.79	19.86	31.35
$\boldsymbol{f}(\boldsymbol{w}^4)$	20.84	20.34	37.67
$\boldsymbol{f}(\boldsymbol{w}^5)$	20.47	19.57	30.04
2nd classif.	(i)	$(\text{iv})^{bound=33.33}$	(v)
$\boldsymbol{f}(\boldsymbol{w}^6)$	**9.95**	**33.33**	**34.30**
$\boldsymbol{f}(\boldsymbol{w}^7)$	7.57	40.20	35.98
$\boldsymbol{f}(\boldsymbol{w}^8)$	**2.16**	**83.81**	**42.22**
$\boldsymbol{f}(\boldsymbol{w}^9)$	7.91	38.10	35.59
Intermediate sol.	between	$\boldsymbol{f}(\boldsymbol{w}^6)$ and $\boldsymbol{f}(\boldsymbol{w}^8)$	
$\boldsymbol{f}(\boldsymbol{w}^{10})$	7.69	40.83	35.11
$\boldsymbol{f}(\boldsymbol{w}^{11})$	6.31	49.18	36.34
$\boldsymbol{f}(\boldsymbol{w}^{12})$	**4.91**	**57.56**	**37.72**
$\boldsymbol{f}(\boldsymbol{w}^{13})$	3.65	65.93	39.01
$\boldsymbol{f}(\boldsymbol{w}^{14})$	2.42	74.58	40.49

also the decision variable values, which are in our case the field intensities. With the mathematical software Matlab® also the contour plots of the dose distribution (isodose curve) and the dose volume histograms of the solutions are easily available. Computing times were short, only a few minutes per classification were needed (with PC). The optimization in NIMBUS took only a fraction of the total computing time. The Matlab® simulation was the most time consuming. With a faster dose calculation model this can be easily fixed, and that is why the optimization method (NIMBUS) is not a bottleneck for more complicated simulation models.

5 Conclusions

In this paper, we have successfully applied the interactive multiobjective optimization method NIMBUS for radiotherapy treatment planning and the numerical results obtained are promising. With this method, all the conflicting radiotherapy targets can be considered and optimized simultaneously without artificial simplifications. Results of the numerical studies indicate that the radiotherapy expert's knowledge and desires can be utilized to direct the solution process interactively and iteratively in order to find the best possible radiotherapy treatment plan. The most preferred treatment plan can be found by generating only few solution candidates and employing the decision maker's expertize.

With an interactive approach, the decision maker can learn about the problem and the interdependences between objective functions are clearly seen without any need of defining bounds for doses, object weights or sum of the objective functions beforehand. The decision maker can also select the interesting objective functions by case using his/her knowledge and if the decision maker feels that the current problem setting is not ideal, he/she can modify the problem setting considered. The method presented also gives an opportunity for the decision maker to play with the system. A curious decision maker can watch what happens if he/she directs the solution in different ways. Good, unique solutions can be found to satisfy the therapy plan, which are hard to find without this kind of a decision support aid. During and after the optimization process the decision maker can visualize the solutions generated and plot contour plots (isodose curves) or dose volume histograms for any Pareto optimal solution he/she wants. This makes the solutions more understandable, illustrative and easy to compare. Currently, treatment planning optimization is still rarely used at the clinics and trial and error procedure is dominating. The presented iterative and interactive multiobjective optimization method offers a slightly similar possibility for the radiotherapist to compare and choose the final treatment plan, but compared to the trial and error procedure used it enables the radiotherapist to select the *optimal* way to satisfy the treatment plan for each specific case.

As one can easily understand, radiotherapy treatment planning is complex for human mind and new, easy to use decision support aids are required. Because every case and user is unique, the decision support aid should be flexible for different types of usage and for different users. It should also be adjustable by case or by user. It is very important, that the solution processes is computationally efficient so that the interactive nature of the solution process will not suffer from excessive waiting times. The approach presented in this paper is a first step toward a decision support aid for the radiotherapy experts.

In the numerical example discussed, a simple dose calculation model was used. To take into account patient inhomogeneity and three dimensional geometry, more accurate dose calculation models have to be used. However, this simple example clearly shows that the system architecture presented is worth studying more and in the future we plan to combine the method presented with a more accurate dose calculation model or even with a treatment planning software. In this paper, field intensities were used as decision variables. In the actual treatment planning, this means that one should be able to form these intensities with some apertures such as a multileaf collimator. This is sometimes difficult and it can cause errors to the final dose distribution. Thus, direct leaf parameter optimization is more preferable and that is why one should use MLC parameters directly as decision variables in the optimization. In the future, we plan to combine the theories given in Boman et al.2005 and Tervo and Kolmonen 2000 with the presented method in order to use the MLC parameters directly as decision variables.

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