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Vorwort

Das Tätigkeitsfeld des Fraunhofer-Instituts für Techno- und Wirtschaftsmathematik ITWM umfasst anwendungsnahe Grundlagenforschung, angewandte Forschung sowie Beratung und kundenspezifische Lösungen auf allen Gebieten, die für Techno- und Wirtschaftsmathematik bedeutsam sind.

In der Reihe »Berichte des Fraunhofer ITWM« soll die Arbeit des Instituts kontinuierlich einer interessierten Öffentlichkeit in Industrie, Wirtschaft und Wissenschaft vorgestellt werden. Durch die enge Verzahnung mit dem Fachbereich Mathematik der Universität Kaiserslautern sowie durch zahlreiche Kooperationen mit internationalen Institutionen und Hochschulen in den Bereichen Ausbildung und Forschung ist ein großes Potenzial für Forschungsberichte vorhanden. In die Berichtreihe sollen sowohl hervorragende Diplom- und Projektarbeiten und Dissertationen als auch Forschungsberichte der Institutsmitarbeiter und Institutsgäste zu aktuellen Fragen der Techno- und Wirtschaftsmathematik aufgenommen werden.

Darüber hinaus bietet die Reihe ein Forum für die Berichterstattung über die zahlreichen Kooperationsprojekte des Instituts mit Partnern aus Industrie und Wirtschaft.

Berichterstattung heißt hier Dokumentation des Transfers aktueller Ergebnisse aus mathematischer Forschungs- und Entwicklungsarbeit in industrielle Anwendungen und Softwareprodukte – und umgekehrt, denn Probleme der Praxis generieren neue interessante mathematische Fragestellungen.

Prof. Dr. Dieter Prätzel-Wolters
Institutsleiter

Kaiserslautern, im Juni 2001

A dynamic algorithm for beam orientations in multicriteria IMRT planning

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Abstract. For the last decade, optimization of beam orientations in intensity-modulated radiation therapy (IMRT) has been shown to be successful in improving the treatment plan. Unfortunately, the quality of a set of beam orientations depends heavily on its corresponding beam intensity profiles. Usually, a stochastic selector is used for optimizing beam orientation, and then a single objective inverse treatment planning algorithm is used for the optimization of beam intensity profiles. The overall time needed to solve the inverse planning for every random selection of beam orientations becomes excessive. Recently, considerable improvement has been made in optimizing beam intensity profiles by using multiple objective inverse treatment planning. Such an approach results in a variety of beam intensity profiles for every selection of beam orientations, making the dependence between beam orientations and its intensity profiles less important. We take advantage of this property to present a dynamic algorithm for beam orientation in IMRT which is based on multicriteria inverse planning. The algorithm approximates beam intensity profiles iteratively instead of doing it for every selection of beam orientation, saving a considerable amount of calculation time. Every iteration goes from an N-beam plan to a plan with $N + 1$ beams. Beam selection criteria are based on a score function that minimizes the deviation from the prescribed dose, in addition to a reject-accept criterion. To illustrate the efficiency of the algorithm it has been applied to an artificial example where optimality is trivial and to three real clinical cases: a prostate carcinoma, a tumor in the head and neck region and a paraspinal tumor. In comparison to the standard equally spaced beam plans, improvements are reported in all of the three clinical examples, even, in some cases with a fewer number of beams.

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1. Introduction

The main goal of intensity-modulated radiation therapy (IMRT) planning is to find an optimal compromise between the two conflicting goals: delivering a high dose to the tumor and sparing the critical structures from unnecessary overdosages. Finding the optimal IMRT treatment plan is, in fact, a large scale optimization problem as a consequence of the many possible parameter configurations. In order to solve it in reasonable time, its decision variables are split into two clusters: beam orientation, determined by a set of gantry and table angles, and beam intensity profiles.

Researchers in the field have treated the problem using two approaches. The formal one was based on optimizing some single objective function that evaluates the treatment plan and assigns a number to it. Mainly due to the contradictory goals of the treatment plan, this single number was not able to determine the quality of the plan properly. Thus, the result of such an approach is often suboptimal. The most recent approach, which is more accurate to the structure of the problem, models it as a multi-criteria optimization problem with conflicting objectives ([Küfer *et al.*, 2000], [Cotrutz *et al.*, 2001], and [Küfer *et al.*, to appear in 2006]). However the both approaches calculate the beam intensity profiles under the assumption of a fixed preselected set of beam orientations. In fact, optimizing the set of beam orientations may play a considerable role during the search for the best possible compromise [Pugachev *et al.*, 2001]. Unfortunately, the influence of a beam set on the final dose distribution can not be determined unless an optimal solution of the intensity profiles is found, and coupling between beam orientations and beam profiles to formulate the complete problem will turn the objective function in either approach into a nonconvex function preventing the usage of gradient based methods ([Bortfeld and Schlegel, 1993]). Thus, most of the studies that have addressed the problem of beam orientation in IMRT equipped the formal approach with some stochastic optimization algorithm where the optimization of beam intensity profiles is performed for every individual selection of beam orientations ([Pugachev *et al.*, 2001], [Bortfeld and Schlegel, 1993] and [Stein *et al.*, 1997]). These methods require performing the optimization process that calculates the intensity profiles many thousand times, each time for a different beam selection. The time needed for this purpose, especially in the 3D situation, is not acceptable in practice. Moreover, it is not practicable to apply these stochastic methods in the multi-criteria approach where the optimization process of the beam intensity profiles results in a set of Pareto optimal solutions for each choice of beam orientations. The planner then needs to search through the Pareto set manually to decide on an optimal solution ([Küfer *et al.*, to appear in 2006]). This manual search which is required for every set of beam orientations is inconvenient for computerized beam orientation. Hence, in real life, beam orientation in IMRT is still a time consuming trial-and-error search scheme that is based on intuition and empirical knowledge.

This work is devoted to introduce an efficient algorithm that focuses on determining a proper set of beam orientations for the multi-criteria optimization approach in IMRT planning. In contrast to the preceding approaches where the computation of the intensity profiles assumes a fixed set of beam orientations, the presented algorithm works under the assumption of fixed beam intensity profiles. The intensity for each beamlet of every possible beam is optimized using an empirical objective function that was especially designed to adhere to the treatment goals, taking into account the new conditions that the algorithm applies iteratively. This optimization process is performed once for each iteration rather than for each set of beam orientations. In each iteration, after approximating and fixing the intensity profiles, every possible beam is evaluated by using a score function that measures the deviation from the prescribed dose over the target. The beam with the minimum deviation score will then be selected and added to the set of beam orientations if it passes a reject-accept procedure. Therefore, the set of beam orientations is enlarged by one beam in every iteration. Finally, the algorithm ends when the required number of beams is reached.

2. Materials and methods

In this work we use the inverse treatment planning system KonRad (developed at DKFZ Heidelberg, commercially distributed by Siemens) for performing the dose calculation which is the input for our algorithm presented below.

2.1. Algorithm

For a given beam space, $\mathbb{B} = \{b_1, \ldots, b_n\}$ where $n \in \mathbb{N}$, we are seeking a set of beam orientations $B \subseteq \mathbb{B}$ which is able to produce fluence profiles with dose distributions as close as possible to the desired prescribed dose. For technical reasons we assume that it is an ordered set. The algorithm is based on two steps repeated recursively until the desired number of beams is achieved. The first step is performed at the beginning of each iteration where the intensity for each beamlet is approximated using the optimization problem

$$\min \frac{w_T}{N_T} \sum_{i \in T} [D^p - (D_i^d + x d_i)]^2 + \frac{w_R}{N_R} \sum_{i \in R} (D_i^d + x d_i)^2 \tag{1}$$

where w_T and w_R are the importance factors assigned to the target and organ at risk, D_i^d corresponds to the dose delivered to voxel i by the beams that have been already selected and added to the set B, D^p is the target prescribed dose and N_V is the number of voxels belonging to the volume V. If the resulting intensity x of the considered beamlet is negative, it is set to zero.

The construction of the optimization problem (1) was gained empirically through the intuitive consideration which was aimed to capture the main features of the treatment goals through the iterative developments of the algorithm. We should emphasize here that the obtained fluence profiles are intended to be used only during the search for an optimal set of beam orientations. They may actually be very different from the optimal intensity profiles, which are calculated using a completely different technique.

After the fluence profiles have been approximated for all the beams, the algorithm starts the second step, in which the complement of the orientation set ($B^{\complement} = \mathbb{B} \backslash B$) is exhaustively searched in order to find the best beam to be moved into the set B. To do this, the dose distribution for the set B coupled with each individual beam $b \in B^{\complement}$ is calculated, and its deviation score $S_{B \cup \{b\}}$ is evaluated using the quadratic function

$$S_{B \cup \{b\}} = \sum_{i \in T} (D^p - D_i)^2, \tag{2}$$

where $D_i = \sum_j x_j d_{ij}$ is the total dose value absorbed by voxel i and delivered by the beams belonging to the set $B \cup \{b\}$.

As can be seen, the score function (2) does not consider the dose delivered to organs at risk. Including this dose will not play a considerable role in the algorithm since the construction of the optimization problem (1) takes care of reducing the dose delivered to the target if the corresponding beamlet hits an organ at risk, especially if a relatively large weight was assigned to this organ. Consequently the deviation score of the orientation set containing the beamlet will increas.

During the first iteration, when the set B is still empty and hence $D_i^d = 0$, the optimization problem (1) is solved for every single beamlet in each beam $b \in B^{\complement} = \mathbb{B}$. Then the deviation scores of the beams are sorted and stored for reordering purpose concerning further iterations. Choosing the beam with the minimum deviation to be added to our orientation set B will terminate this iteration.

This first iteration is somewhat similar to the BEVD and pBEV techniques ([Pugachev and Xing, 2001a] and [Pugachev and Xing, 2001b]). What makes our approach distinguitioable from the BEVD and pBEV is that the upcomming itrations consider the interplay among multiple beams. Every further iteration is meant to move the beam which contributes with the maximum missing target dose from the set $B^{\complement}$ to the set B. Each time the algorithm starts a new iteration, the fluence profiles are modified in the following manner.

First we consider the beams belonging to the set B, taking into account these two points:

- Since the optimization problem (1) depends on the delivered dose, changing the order of the beams, in the set B, will result in different solutions. To overcome this situation we arrange the beams according to the order found in iteration number one.

- Moreover, problem (1) considers the beamlet being processed as the last to be used to irradiate the tissue. This will result in a relatively high fluence if there are still more beams to be added. In such a case, a low fluence will be assigned to the beamlets which intersect the current one and belong to the beams that will be processed later on. To guarantee a better approximation of the fluence profiles, we consider a beam share system of the target prescribed dose. If, for instance, B contains two beams, we multiply the prescribed dose in the optimization problem (1) by 2/3 when calculating the fluence for the first beam. The fluence of the second beam, which is the last in this case, will then be approximated using the full prescribed dose.

After the fluence profiles of the set B are modified, we start resolving problem (1) for each beamlet in every beam $b \in B^{\complement}$, taking into account the dose delivered by all the beams contained in B.

Now the second step of the algorithm, where the dose distribution of every set $B \cup \{b\}$ for all $b \in B^{\complement}$ is computed and scored, is perform again. Finally, and unlike in iteration one, where the best scored beam is directly moved into the set B, the selection criteria is slightly complicated. Here the beam with the best score b^* is not moved into B immediately. Instead it is tested through a reject-accept procedure, which is accomplished by the following three steps:

1. The beams of the set $B \cup \{b^*\}$ are reordered.
2. The intensity profiles of the reordered set are reestimated and its score S^r is recomputed.
3. b^* is accepted if S^r is equal or better than S^*; otherwise it is rejected and replaced by the next best beam.

The testing procedure is performed several times until a couple of beams are accepted. The beam with the best score, among the accepted ones, is moved then into the set B.

The algorithm terminates when the recommended number of beams is achieved. A flow chart of the presented algorithm is found in figuer (1).

For a given set of beam orientations, the final optimal intensity profiles for IMRT treatment are computed using a multi-criteria solver developed in the optimization department of Fraunhofer Institute for Industrial Mathematics (ITWM), Germany. The solver generates a set of Pareto optimal solutions that minimize the vector function $F(\mathbf{x}) = (EUD_1(\mathbf{x}), EUD_2(\mathbf{x}), \ldots, EUD_K(\mathbf{x}))$, where K is the number of considered clinical structures and EUD represents the equivalent uniform dose measure of an organ. Next, the set of Pareto optimal solutions is searched manually by using a navigation tool, also developed at the ITWM, to determine the most desirable solution. For more about multi-criteria optimization in intensity modulated radiotherapy planning,

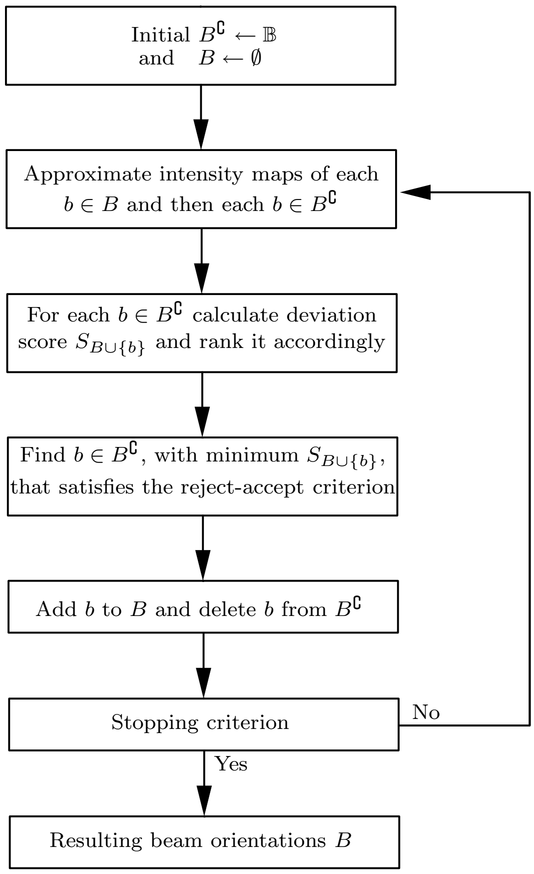


Figure 1. Flow chart of the dynamic algorithm.

see e.g. [Küfer *et al.*, to appear in 2006].

To illustrate the efficiency of the algorithm, it has been applied to one artificial example, where optimality is trivial, and three clinical cases: a prostate carcinoma, a tumor in the head and neck region and a paraspinal case. In all of the real clinical cases, the judgment of the algorithm's efficiency was based on the comparison between 2 types of optimization: (1) beam intensity profiles were optimized for coplanar equidistant beams; (2) beam intensity profiles were optimized for the coplanar orientation set which was found by the presented algorithm. To evaluate the quality of the treatment plan, a depiction of the dose distribution and dose-volume histogram (DVH) were used for the target and each of organs at risk.

3. Results

According to the International Electronical Commission (IEC) convention, every beam is specified by its couch and gantry angles. The algorithm presented in this work is applicable to non-coplanar beams, but in general, therapists are declined to move the couch, because it takes extra time and introduces some positional uncertainties. Hence we will consider in the following numerical examples only the coplanar situation.

3.1. An artificial example

The example consists of a cross shaped target surrounded by four squared critical structures located at the angles formed by the cross in a circular phantom. The beam space is given by the set $\mathbb{B} = \{b_i : 0 \leq i < 360, i \in \mathbb{N}\}$. For illustration, see figure (2).

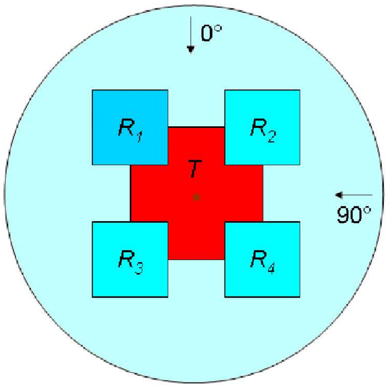


Figure 2. An rtificial example.

Importance factors and target prescribed dose are given in table (1).

Organ / Structure	w	D^p
Target	1.0	50
Organ at risk 1	0.6	
Organ at risk 2	0.5	
Organ at risk 3	0.5	
Organ at risk 4	0.5	
Unclassified tissue	0.2	

Table 1. Importance factors and ideal doses chosen for the target and organs at risk.

The result of applying the algorithm on the prescribed sample example is shown in figure (3) which contains four curves representing the deviation score for beam directions through four consecutive iterations. As can be seen, the curve representing iteration one shows global minima at beams with gantry angles 90° and 180°. This makes intuitive sense since theses beams are the most exposed to the target with minimum dose delivery to organ at risk R_1, which has the highest importance factor among all other organs at risk. Thus, the first iteration results in the beam orientations set $B = \{b_{90}\}$. The second curve resulted from iteration two shows a cut at beam b_{90}, since it was moved from $B^{\complement}$ to B. This movement allows beam b_{90} to contribute to the delivered

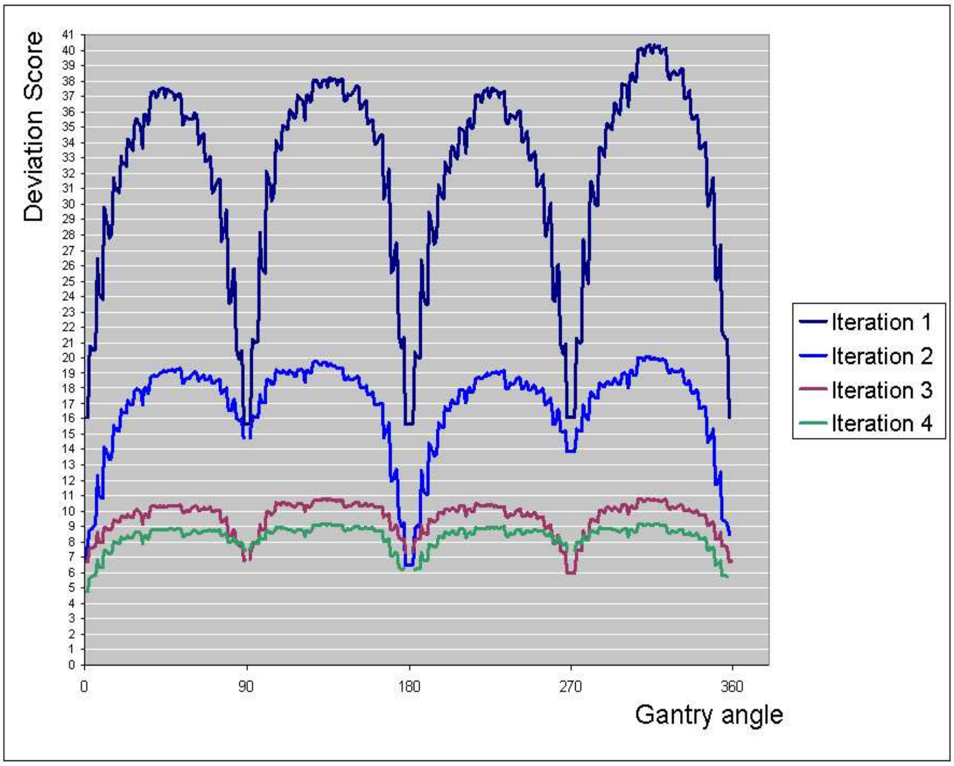


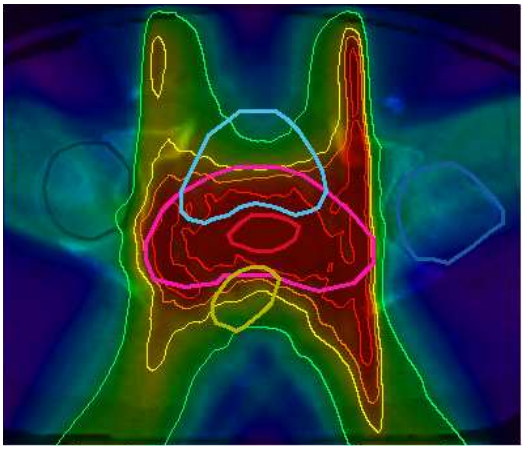
Figure 3. Deviation scores for gantry angles resulted from applying the algorithm on the sample artificial example.

dose which in turn reduces the competition level of beam b_{270} as can be easily seen in the corresponding curve. Moreover, the curve shows a a global minimum at beam b_{180} which is again meaningful for the same reasons mentioned for the first iteration. The remaining curves corresponding to iterations three and four show global minimum at beams b_{270} and b_0 respectively. Thus the algorithm results in the following set of beam orientations: $B = \{b_{90}, b_{180}, b_{270}, b_0\}$ which is obviously optimal.

One point that deserves mentioning here is that increasing the importance factor for the unclassified tissue avoids opposite directions in the final beam configuration.

3.2. Prostate carcinoma

In this study the irradiated volume contained two targets (boost and target) grown in the prostate area and surrounded by four organs at risk; the bladder, rectum, right femur and left femur. The couch angle was set to 0°, whereas the gantry angle was allowed to vary from 0° to 360° with 5° of increments. Five equiangular spaced beams plan were used in comparison with the five coplanar beams plan optimized by using the algorithm presented above. The dose distributions and the dose volume histograms of the both plans are shown in Fig (4) and Fig. (5) respectively.



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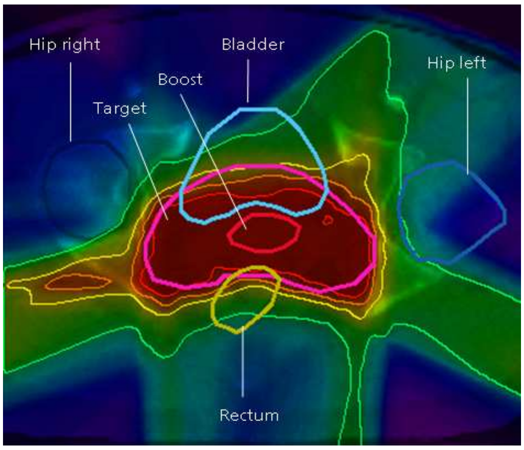

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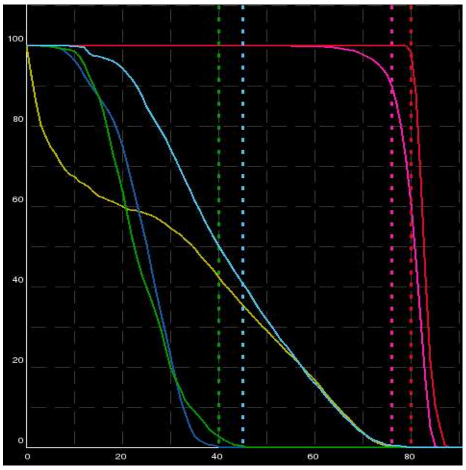
Figure 4. The dose distribution of two multicriteria IMRT prostate tumor treatments corresponding to (a) five equiangular spaced beams, (b) five optimized beams obtained by the algorithm presented above and (c) isodose levels.



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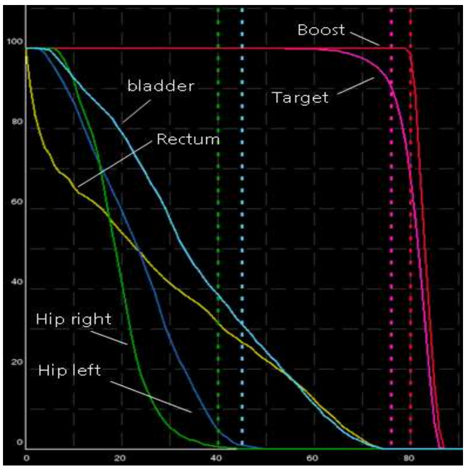


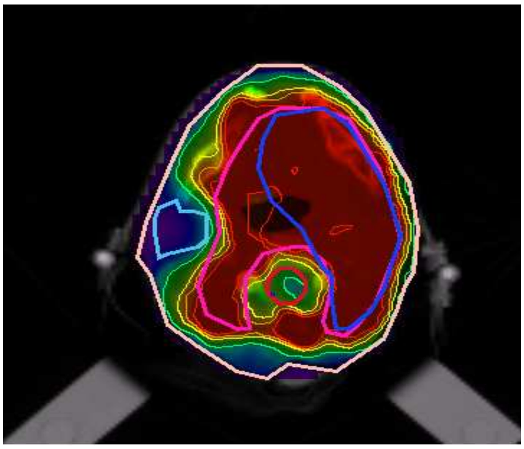
(*b*)

Figure 5. Dose volume histograms of two multicriteria IMRT prostate cancer treatments corresponding to (a) five equiangular spaced beams and (b) five optimized beams.

In comparison with the plan obtained using equiangular spaced beams, pronounced improvements in the dose distribution regarding all clinical structures were reported. As can be seen from Fig (5), the use of the optimized beams yielded a slightly better dose uniformity in the target. Furthermore the values of the organ EUDs in the multicriteria objective function were all reduced by 5%, 4%, 6% and 7% for the bladder, rectum, left femur and right femur respectively. Moreover,the shape of the dose distribution resulting from the optimized beams is better fitted to the shape of the tumor than the one obtained by the equiangular spaced beams as demonstrated in Fig (4).

3.3. Head and neck tumor

The irradiated volume, in this case, contained again two targets, spreading in the head and neck region among three organs at risk; spinal cord, brain stem, and parotid gland. Unlike the prostate case where the comparison was performed on two set of beam orientations with the same number of beams; in this case a seven coplanar equally spaced beams plan was compared with the plan obtained by using only six coplanar beams optimized using the presented algorithm. The dose distributions of these two plans and their dose volume histograms are shown in Fig. (6) and Fig. (7) respectively.



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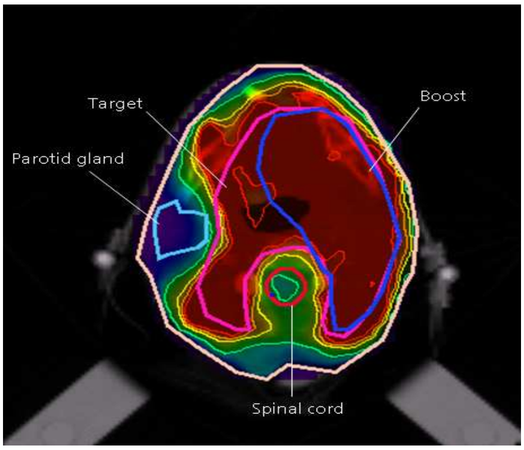

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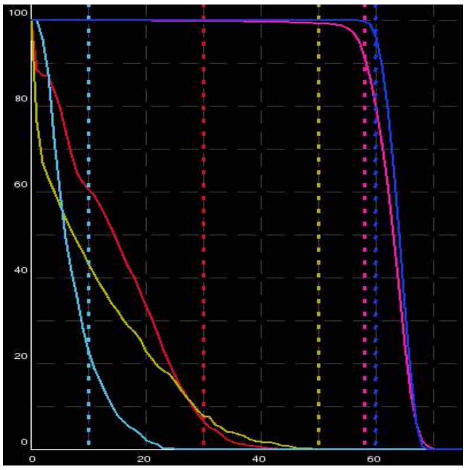
Figure 6. The dose distribution of two multicriteria IMRT treatments, for head and neck tumor, corresponding to (*a*) seven equiangular spaced beams, (*b*) six optimized beams obtained by the presented algorithm and (*c*) isodose levels.

As can be seen from Fig (7), the use of the optimized beams resulted in reducing the maximum dose delivered to the spinal cord and brain stem against margin maximum dose increment delivered to the parotid gland. One can also see from Fig. (6) that some unnecessary hot spots in the irradiated volume were eliminated, allowing for better tumor dose shaping than the one produced using the equiangular spaced beams. Consistent results were reported by the numerical realization where the EUD values of the critical structures in the multicriteria objective function were improved by 4% and



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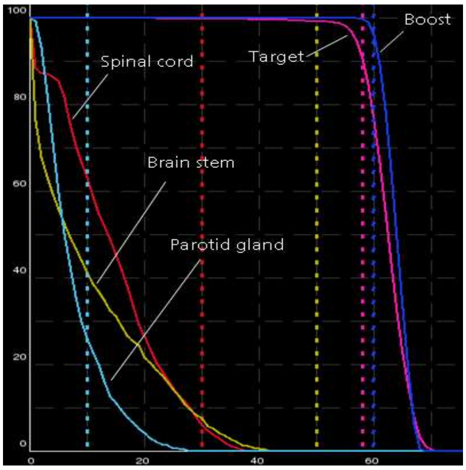


(*b*)

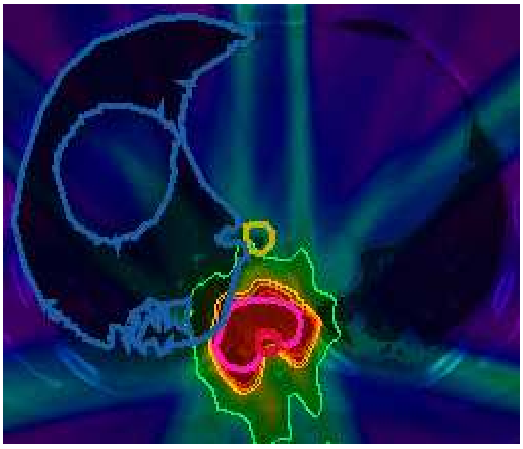
Figure 7. Dose volume histograms of two multicriteria IMRT treatments, for head and neck tumor, corresponding to (*a*) seven coplanar equiangular spaced beams and (*b*) six optimized beams.

5% for the spinal cord and the brain stem, respectively, against worsening the parotid gland by 9%.

Although optimizing the set of beam orientations in this case has not considerably improved the treatment plan, achieving a somewhat similar treatment plan with a fewer number of beams is a matter of improvement with respect to clinical and practical considerations. In fact, is always desirable to reduce the number of irradiating beams to its minimum without compromising the quality of the treatment. This allows for shorter treatment time, which in turn reduces potential errors in terms of patient movement and decreases patient discomfort.

3.4. Paraspinal case

In this example, the irradiated volume, contained one target, spreading around the spinal cord among three organs at risk; esophagus, left lung and right lung. Similar to the head and neck example, in this case, a plan with seven coplanar equally spaced beams was compared with the plan obtained by using six coplanar beams optimized using the algorithm. The dose distributions of these two plans and their dose volume histograms are plotted in Fig. (8) and Fig. (9) respectively.
As can be seen from these figures, significant improvements were reported in two organs at risk; esophagus and left lung where it is difficult to note any differences regarding the DVHs coresponding to right lung, the spinal cord or the target. EUDs improvements were reported as follows: 12% for the esophagus and 33% for the left lung where as all the others EUD values were almost equal.



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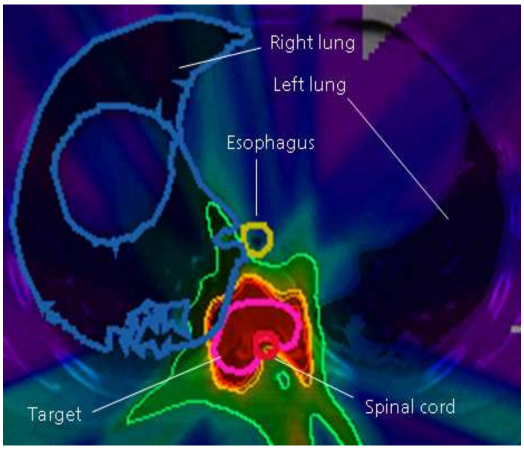

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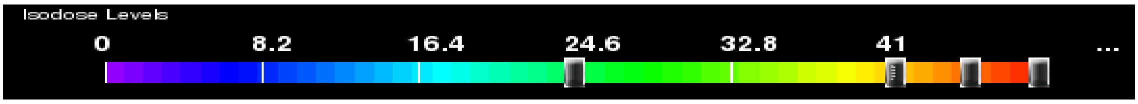

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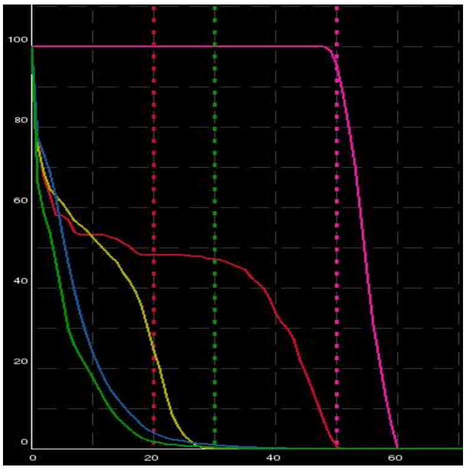
Figure 8. The dose distribution of two multicriteria IMRT treatments for paraspinal tumor, corresponding to (*a*) seven equiangular spaced beams, (*b*) six optimized beams obtained by the presented algorithm and (*c*) isodose levels.



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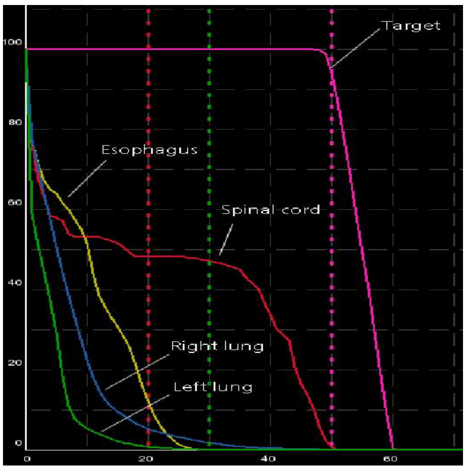

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Figure 9. Dose volume histograms of two multicriteria IMRT treatments for paraspinal tumor, corresponding to (*a*) seven coplanar equiangular spaced beams and (*b*) six optimized beams.

4. Discussion and conclusion

The choice of the beam orientations set in IMRT treatment planning is still a trial-and-error procedure based on intuition and empirical knowledge. This is due to the high nonconvexity level of the optimization problem in which the beam geometry and intensity profile variables are brought together simultaneously to formulate the objective function, resulting in an excessively enlarged search space. Accordingly, even with the aid of some stochastic optimization approach, the optimal solution is not achievable in practical time. In fact, such an approach requires optimizing beam intensity profiles for every random selection of beam orientations. Beam intensity profiles in IMRT are usually determined by using inverse treatment-planning methods that are controlled by either a single criteria or multicriteria objective function. On the first hand, using the single criteria approach often results in suboptimal intensity profiles with respect to the best clinical achievable solution, besides the excessive computational time required for optimizing the intensity profiles of the overall random beam orientations trials. On the second hand, using the multicriteria approach results in a Pareto set where a human interaction with the software is needed in order to find the optimal beam intensity profiles. Involving human interaction for every random selection is inappropriate.

In this work we have developed a dynamic algorithm to find an appropriate set of beam orientations for multi-criteria inverse planning in IMRT. Although the algorithm does not solve the problem of beam orientations completely, its deviation score function provides the planner with an efficient beam placement guideline which could be an alternative to the trial-and-error procedure. It was shown that the selection of beam orientations using the presented methods produces superior dose distributions to those obtained by equally spaced beams, even when, for some cases, a smaller number of beams was used. Moreover, the time complexity of the algorithm is efficient. Although the above calculation were performed using a normal workstation, the running time required by the algorithm was between three and four hours for all the presented clinical cases.

Finally, we mention that a current study based on merging the presented methods with the multicriteria solver mentioned above is in progress. We believe that this study, which aims at optimizing beam orientations in IMRT, may produce plans of high quality. In fact a good approximation of the intensity profiles is crucial for optimizing the orientation set accurately. For this reason the multicriteria solver is intended to be used once at the end of every iteration where the decision on the most desirable fluence profiles is left for the planner. We expect that this human guidance will help the algorithm to minimize the deviation from the optimal clinical solution.

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