RADIOTHERAPY PLANNING SYSTEM WITH DOSE CONSTRAINTS

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ABSTRACT

Intensity Modulated Radiotherapy is a technique used in the treatment of cancer based on the use of different spatially distributed X-Ray beams. The task of treatment planning is to determine the dose quantity that each beam of radiation should deliver, and for each spatial direction, and so determining a specific dosage distribution for the patient. In this paper a conditional optimization problem is studied, proposing a new reduction method for the dimensions of this problem. The procedure proposed has been used in the planning of the treatment for a real of prostate cancer case, where satisfactory results have been obtained.

1. INTRODUCTION

Treatment planning for intensity modulated radio therapy (IRMT) requires the intensity masks for each one of the beams of radiation to be obtained; with the objective of attaining a dose distribution across the area of the tumour which best matches the dose prescribed by the medical specialist [1].

To solve this problem a mathematical model must to be established, for this model the volume to be treated and the beams of radiation are considered discrete elements. On one side, the patient volume is divided into small three-dimensional cubes, called voxels. On the other side, the beams radiation are divided into small two-dimensional cells, perpendicular to the beam of radiation, in such a way that the radiated intensity in each spatial direction is described by a fluence map or weight matrix. The dose received in a given voxel of the patient is obtained as the sum of the contributions of each of the beams of radiation, a contribution which depends also on the direction of each ray within the beam and is a function of the distance that the ray travels inside the patient.

Once a mathematical model has been obtained relating the fluence matrix to the dose obtained in the interior volume of the patient, it is possible to deal with the treatment plan (the inverse problem). The objective is to obtain a set of weights such that the dose prescribed by the specialist is reached in the targeted volume. The optimization process meets two fundamental purposes: achieve a high dose which is homogeneous across the tumour, and protect the rest of the healthy tissue. These aims are inherently contradictive, and so a compromise must be reached between them. The consideration of a weighting factor in the error function allows more or less aggressive treatments on the healthy tissue to be achieved.

One of the main difficulties when resolving the inverse problem is the possibility of multiple solutions which can result in local minimums of the error function [2].

2. BASIC CONCEPT OF THE METHOD

Therapy with X-Rays requires a mathematical model to be established that describes the relation between the dose radiated by the beams and the dose distributed over the affected volume of the patient.

The dose that each of the voxels of the volume receives is determined by the relation:

$$D_o^{\,i} = \sum_{j=1}^{n} f_{ij} w_j \qquad i = 1, \ldots, m$$

where n is the number of weights of the set of the fluence matrices, m is the number of voxels in which the treated volume is divided, w_j is the value of the j^{th} weight and f_{ij} is the attenuation suffered by the X-Rays from the j^{th} cell of the grid to the i^{th} voxel.

The reordering of the weights w_i of the fluence matrices in a vector w allows the previous expression to be expressed as a matrix,

$$D_o = F \cdot w$$

Where F is a *mxn* matrix whose elements are the coefficients f_{ij} being D_o a vector of dimensions m that contains the dose in the different voxels of the volume. Each one of the weights w_j of each beam has an influence over a region of the volume, determined by a conical surface of revolution. Consequently, once the regions of the volume radiated by each weight are delimited, the dose obtained for a specific intensity mask can be found directly.

Where the matrix F is obtained calculating the attenuation suffered by the X-Ray beams from the position occupied by the jth weight up to the isocentre of the i^{th} voxel according to the expression:

$$\frac{1}{d_{ij}^{\,2}} e^{-\mu p_{ij}}$$

Being p_{ij} the distance travelled by the beam in the interior of the patient and μ the coefficient of attenuation.

The inverse problem for the radiotherapy treatment planning is based on the knowledge of F, and implies the seeking of the weight vector w that approximates the dose prescribed by the oncology specialist. With this finality, an error function G(w) has been considered constructed by the sum of the quadratic terms, where the error produced in the different structures of the affected volume are weighted with a coefficient P_k.

As V structures of the volume are considered, assigning an index T_k to each structure, and considering that in each structure there are N_{Tk} voxels, the desired function can de expressed as:

$$G(w) = \sum_{k \in V} \left(P_k \sum_{i \in T_k} \frac{\left(D_o^{\,i} - D_p^{\,i}\right)^2}{N_{T_k}} \right)$$

Or alternatively:

$$G(w) = \sum_{k \in V} \frac{P_k}{N_{T_k}} \left(\frac{1}{2} w^T Q_k\, w + R_k^{\,T}\, w + c_k \right)$$

And in matrix form:

$$G(w) = \frac{1}{2} w^T Q\, w + R^T\, w + c$$

Being:

$$Q = 2 \sum_{k \in V} \frac{P_k}{N_{T_k}} F_k^{\,T} F_k \qquad R = 2 \sum_{k \in V} \frac{P_k}{N_{T_k}} F_k^{\,T} D_{pk}$$

$$c = \sum_{k \in V} \frac{P_k}{N_{T_k}} D_{pk}^{\,T} D_{pk}$$

Where F_k is a matrix formed by the rows i of matrix F such that $i \in T_k$ and, likewise, D_{pk} is a vector formed by the elements i of D_p such that $i \in T_k$.

One possible election is to solely consider two structures on the volume, one of which contains the tumour (Clinical Target Volume CTV), and the other should contain the organs at risk (OAR), in which it is necessary to limit the quantity of radiation received.

When considering the rows of matrix F that belong to the structure that contains the organs at risk, matrix A is obtained. This is such that the limitation of the dose on these organs imposes:

$$A w \le L$$

Where L is a vector that contains the information of the maximum dose for the organs at risk.

Furthermore, given that the elements w_j of the fluence matrix represent radiation intensities, and these are positive quantities, to obtain a physically significant solution it is necessary to impose an additional restriction owing to the non-negativity of the weights (w≥0).

This allows the planning process to be described by a conditioned optimization problem:

$$\text{Minimise:} \quad \frac{1}{2} w^T Q\, w + R^T\, w + c$$

$$\text{Subject to:} \quad A w \le L \qquad w \ge 0$$

whose resolution has been carried out with the Lemke's algorithm for a linear complementary problem (LCP) and the Rosen gradient projection method [3]. Lemke's algorithm uses the simplex method as an effective solution to the LCP, but its complexity does not permit a mathematical explanation in this paper [4]. However, the more intuitive Rosen's method is based on the feasible directions theory, such that the search for a solution is carried out within the feasible region, through a direction that reduces the desired function and respects all the conditions.

The Rosen's method obtains the solution by an iterative process in which the solution w^k in the k^{th} iteration is updated following the expression:

$$w^{k+1} = w^k + \alpha\, \overline{d}$$

according to the search for the direction d which is most similar to the opposite of the gradient vector of the desired function in w^k

$$-\nabla G(w^k) = -\left(Q\, w^k + R\right)$$

and which also meets the feasibility and descent conditions. For the direction d to be descent, so that the value of the desired function is reduced, the following equation should be met.

$$\left.\frac{d}{d\alpha} G\left(w^k + \alpha \overline{d}\right)\right|_{\alpha \approx 0} = \overline{d}^T \nabla G\left(w^k\right) \le 0$$

Whilst the feasibility condition, assuming that the point w^k is feasible, requires that for all the active conditions in w^k (conditions that are within the limit of the equality of w^k) meet:

$$\left.\frac{d}{d\alpha}\left(a^i \left(w^k + \alpha \overline{d}\right) - L^i\right)\right|_{\alpha \approx 0} = \overline{d}^T a^i \le 0$$

where a^i are the rows of A that meet the condition $a^i\, w^k - L^i = 0$.

The parameter α represents the distance travelled along the length of the normalized search direction $\overline{d}$, and its value is either the distance to the intersection of the closest active condition, or the distance α^* that meets the condition

$$\frac{d}{d\alpha^*} G\left(w^k + \alpha^* \overline{d}\right) = \overline{d}^T \left(Q\left(w^k + \alpha^* \overline{d}\right) + R\right) = 0$$

The iterative process is repeated until it becomes impossible to find a feasible descent direction.

The methods for conditioned optimization are based on the Lagrange theory, and the difficulty of inequality conditions in conditioned optimization problems requires the introduction of slack and surplus variables [3].

The limitation of the dose *in the i^{th} voxel* to a value L^i corresponding to an organ at risk is represented by:

$$\sum_{j=1}^{n} f_{ij}\, w_j \le L^i$$

Therefore, in the case in question, these variables must be incorporated to translate the unequal conditions into conditions of equality. This is such that introducing the slack variables, the previous equation is transformed into an equation of equality.

$$r_i^2 + \sum_{j=1}^{n} f_{ij}\, w_j = L^i$$

As r_i^2 is a positive term, the received dose by the i[th] voxel does not surpass the limit L^i established.
In the same way, the condition of non-negativity of the weights is solved, where surplus variables are used to translate.

$$w_j - s_j^2 = 0$$

This is such that the greater the number of restrictions on the dose, and the higher the number of weights, the greater the number of variables. In the application presented, the high number of variables needed, due in part to the restrictions of the voxels belonging to the OARs and also to the great number of weights of the fluence matrices, makes the resolution a priori unattainable. In the prostate case considered, this implies 8203 conditions in the OARs, and 266 variables to be determined assuming treatment with 5 beams. For this reason, in this article, a series of reductions are proposed which permit the problem to be solved.

3. REDUCTION OF THE DIMENSIONALITY

Firstly, with respect to the volume under treatment, an initial reduction has been made that consists in imposing dose conditions on those elements or voxels of the OARs that belong to the boundary area of these organs. Given that the dose limitation in these boundary areas means a limitation in the interior, due to the type of problem. With this objective, the voxels are selected that belong to the OARs and are adjacent to other organs to which restrictions are applied. In the considered case, 8203 voxels belong to OARs, and 2747 constitute the boundary area, with which the number of conditions is reduced considerable.
Regarding the reduction in the number of variables, the proposed beam tracing system calculates the size of the fluence matrices to adjust the opening of the distinct beams to the size of the tumour, even when the volume containing the tumour and the OARs is very large.
For this reason, if on the matrix *F*, there is any column j whose elements do not provide any radiation to the *voxels* of the tumour, this means that any positive valour of the j[th] weight could distribute radiation on healthy tissue sparing the tumour, so the j[th] column may be removed from the matrix and a null value assigned to the associated weight, allowing a reduction in the number of variables or weights to be determined. This will be:

$$w_j = 0 \qquad \left(\forall j \,:\, f_{ij} = 0 \,,\, i \in T_{CTV}\right)$$

with which the dose in any one of the voxels is independent of w_j , and this unknown can be excluded from the problem directly assigning to it a null value.

4. RESULTS

In this section results are shown for the proposed method, considering a real case of prostate cancer. The volume affected by the tumour comprises of the prostate (CTV), the rectum (OAR1), the bladder (OAR2) and unspecified healthy tissue
In order to solve this case a volume of 621 cm^3 has been considered, such that taking *voxels* with dimensions of 15 mm^2, it is composed of 39744 *voxels*, of which 1441 belong to the CTV, 2323 to OAR1 and 5880 to OAR2. In the discretisation of the beams, considering 5 beams and opening beamlets of 10mm, 266 weights are originated, and so the matrix *F* has dimensions of 39744×266. Considering an opening of 5mm originates 671 weights.
In the case of beamlets of 10mm this matrix F contains 76361 non-null elements, that imply 0.72% of the total elements. When eliminating the voxels that do not receive radiation from any of the weights, the dimension of the matrix becomes 23578×266. Of the useful 23578 *voxels*; 1155 belong to the OAR1, and 946 to the OAR2. Selecting only the voxels on the boundary area of the OARs, 982 *voxels* exist on which restrictions must be imposed. This means an important reduction with respect to the initial situation where it would have been necessary to impose restrictions on 8203 *voxels* related to the OARs.
In absence of dose restrictions the whole volume of the CTV practically receives the 60 Gy prescribed by the specialist.

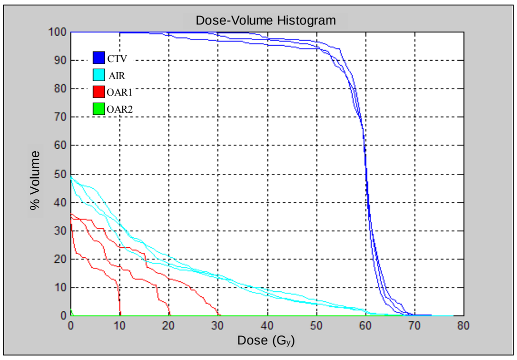

Fig. 1. *Dose-volume histograms with limitations of dose in the OARs for different values of* L_{OAR1} .

However, on the other hand, an important proportion is obtained in the volume of the rectum (OAR1) that exceeds the recommended dose (10 Gy), for which this organ would be damaged.

When limitations are introduced on the dose in the boundary area of the organs at risk, so that the rectum (OAR1) does not exceed 10 Gy, the results shown in Fig. 1 are obtained. Included in this same figure are results obtained when considering the superior limit for the dose on the rectum of 20 Gy and 30 Gy, intended to contrast the benefits of the methods proposed in this work. It is observed that the curve in the OAR1 histogram falls down when the dose limit is reached for each case, and so meets the restriction. This results in some of the voxels of the CTV not reaching their prescribed dose, these correspond to prostate voxels close to the rectum, which is totally reasonable.

In the same way, it should be noted that the imposition of conditions in the bladder (OAR2) do not affect the results due to the fact that for the location of the beams considered none of the bladder voxels receive radiation. Furthermore, it can be seen that the number of prostate *voxels* that do not reach the prescribed dose increases when the dose limit imposed on the rectum is reduced.

A different way of solving this problem is imposing a minimum dose in the tumour while keeping the healthy tissue safe with a higher weight coefficient. In this case we employ a coefficient of 0.72 for the OAR's and a minimum dose of 100 Gy has been imposed on the bounds of the CTV obtaining the following results.

The histogram (Fig. 2) shows that the 100% of the CTV receives at least 90 Gy, while the OAR1 stays well protected.

Finally, a comparison has been drawn on the results obtained by Lemke's algorithm and those obtained by Rosen's gradient projection method. In Table 1, L_{OAR1} indicates the upper limit of the dose of OAR1 and U_{CTV} is the minimum dose required in the bounds of the CTV.

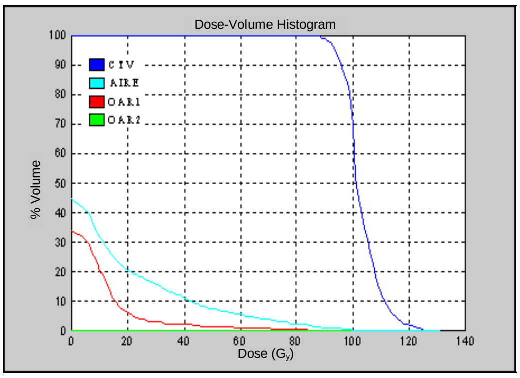

Fig. 2. Dose-volume histogram with limitation of minimum dose on the bounds of the CTV.

		L_{OAR1}	U_{CTV}	D_{CTV}	D_{OAR1}	D_{aire}	σ_{CTV}	σ_{OAR1}	σ_{aire}	*T (s)*
10mm	*Lemke*	-	-	59.45	7.52	9.56	1.64	12.89	13.99	1
		10	-	57.97	2.10	8.69	8.35	3.55	14.08	8
		-	60	64.32	5.94	10.25	4.12	11.56	15.69	126
	Rosen	-	-	59.45	7.52	9.56	1.64	12.89	13.99	193
		10	-	58.48	1.82	8.43	6.96	3.33	14.05	143
		-	60	61.71	4.28	9.42	8.72	8.76	14.52	83
5mm	*Lemke*	-	-	59.61	4.95	7.15	1.09	9.01	11.97	40
		10	-	58.71	1.57	6.61	6.27	2.92	12.21	180
		-	60	61.73	3.17	7.31	3.84	6.93	12.65	2400

Table 1. *Comparison of the results obtained.*

Where as D_{CTV}, D_{OAR1}, and D_{air} are the mean doses, expressed in Gy, obtained in the CTV, OAR1, and healthy tissue, respectively. In the same table, the standard deviations and the execution times (in seconds) of the algorithms developed in MatLab are included.

5. CONCLUSIONS

In this article, we show the advantages of employing conditioned optimization methods in the planning of intensity modulated radiotherapy for the treatment of cancer, which allows limits to be imposed on the dose received by organs at risk. The reductions proposed in the dimensions of the problem have shown their efficiency equally in the reduction of execution time of the algorithms, as well as in the protection of the volume of certain structures.

6. ACKNOWLEDGMENTS

The company Técnicas Radiofísicas S.L. for its collaboration in the development of this work.

7. REFERENCES

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