Calculating Efficient Plans in Radiotherapy Planning

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Abstract

The challenge in radiotherapy planning is to achieve a high dose of radiation in the tumour while keeping the dose in the surrounding healthy organs as low as possible. This goal is contradictory in nature and is the motivation to use a multicriteria problem to model the radiotherapy planning problem. The ideal plan, where desired ideal dose limits are respected, will however be mostly unachievable. The aim with the multi-criteria formulation is to build a set of plans that are a good representation of the whole solution space, all possible combinations of dose deviations while being efficient, where plans are contained.

From here with an appropriate navigational tool the doctor can search for an appropriate plan for the individual patient through a database of pre-calculated plans guided by their own preferences, without any knowledge of the physical parameters involved. The appropriate representation of possible solutions will be focused on the area of most interest, where comparable deviations from ideal dose limits are achieved, rather than satisfying one dose bound and having another far from optimal.

Contained in the set of solutions is a designated starting point for the search, ideally being a balanced solution were the maximum deviation is minimised and all deviations are of a similar value, this will minimise the expected time for an appropriate plan to be found.

1 Introduction

Radiation therapy has been proved successful in cancer treatment. It is one of the major forms of treatment besides chemotherapy and surgery. The fact that cancerous cells are more sensitive to radiation than normal cells means that irradiating the tumour is often used in the treatment of cancer.

The major task of clinical radiation treatment planning is to realize, on the one hand, a high level dose of radiation in the cancer tissue in order to obtain maximum tumour control. On the other hand, it is obvious that it is absolutely necessary to keep the unavoidable radiation in the surrounding organs at risk as low as possible.

These two objectives of treatment planning have a contradictory nature and thus present a difficult problem for those planning the treatment. Unfortunately, it will in general, not be possible to produce an ideal plan, which achieves both these goals simultaneously. Therefore there is the need to compromise between overdosing the organs at risk and under-dosing the tumour.

2 Current Methods

2.1 Parameters

There are 2 main classes of parameters involved in radiation therapy planning – Medical parameters and Physical parameters.

Medical Parameters

Medical parameters are based on and set by doctor and specialist recommendation. The most important, involving the inverse strategy, being.

- Dose bounds on the tumour and healthy organs at risk. A radiation therapy planning problem is formulated with the help of desired ideal dose bounds: a lower bound for the dose level in the cancer tissue, L_1, which was proven successful in the past with respect to a high tumour control probability, and upper bounds for doses in organs at risk, U_k $k \in (2,\ldots,K)$ K = number of organs defined in model, that guarantee a low normal tissue complication probability.

Physical Parameters

Physical parameters are set by the radiation therapy planner, the dosimetrist and in the aim of achieving the medical targets set by the specialist. These combine to form the set up of the radiation machine, which produce the radiation beams. These include:

- The number and position of the radiation beams. The set-up of the beams being used has a huge impact on the quality of the plan able to be produced and is assumed to be given in this context. A fixed beam set-up is considered.

- The intensity profile of the radiation beams. The intensity profiles arise from the differing levels of radiation produced across the head of the beam.

2.2 Assumptions

Important assumptions involving in the model are:

- There will be K well defined parts of the body being affected by the irradiation, where the target volume (i.e. the tumour) is indexed with k = 1, and the healthy organs at risk are indexed with k = 2,…,K. Typically K will be of the order 3 –7.

- Introduce the model in discretized form. This is done two-fold:
    1. Each radiation beam is divided into equally sized elements called bixels, each of these bixels is able to provide a different radiation intensity which combine to form the intensity profile of the beam. The total number of bixels N is equal to the number of beams multiplied by the number of bixels per beam.
    2. The K body parts defined are divided into equally sized volume elements called voxels. This is based on MRI or CT scans, which are 2-dimensional cross-sections of the body in the area of the tumour. A 3-dimensional picture is able to be built using these cross-sections. The total number of voxels M, can be made up of $M_1 + \ldots + M_K$, where M_k represents the number of voxels in organ k.

2.3 Dose Calculation Formula

The Dose calculation formula is introduced in every model describing radiation therapy planning, it approximately calculates the absorbed dose of radiation in the patients tissue for unit beam intensity and unit treatment time. The dose calculation formula is

$$D = Px$$

P is an M by N matrix such that P_{ij} denotes the dose in voxel i resulting from unit intensity in bixel j.

D = $(d_1,\ldots,d_M)$ is a vector of size M representing the Dose volume vector, the dose of radiation received in each voxel defined in the model. The vector can be made up of smaller vectors D = $(D_1,\ldots,D_K)$ where D_k represents the doses absorbed in the voxels corresponding to organ k [1].

x = $(x_1,\ldots,x_n)$ is a vector incorporating n vectors, with total entries N, representing the intensity profiles of the beams, n is the number of beams.

The linear relationship between the radiation intensity and the absorbed dose in a volume element of the human body is a good approximation of the true behaviour.

2.4 Design-Reuse Strategy

Currently, radiation therapy plans being implemented on patients at Auckland Hospital and most other hospitals world-wide are being sought using the *design-reuse* strategy. That is, existing treatment plans, that have proved successful in the past, are reused as an initial plan for incoming patients with clinically similar conditions. The plan is then modified by the experienced planner to better suit the incoming patient. Although this is an accepted way of developing plans for the new patient it doesn't take into account the uniqueness of the new patients situation where seldom is the tumour and organs in the same locations. The *design – reuse* or *forward* strategy makes prior assumptions about the best method of treatment, including the number and location of the radiation beams being used and the level of radiation that they produce, which need not be accurate.

The process of modifying the plan to better accommodate the needs of the incoming patient is based on a trial and error process. In the case of complicated anatomical situations the forward strategy is time consuming and produces unsatisfactory results, where the therapy plan is far from being the best possible for the patient.

2.5 Inverse Strategy

In recent years, therapy planning problems have been modelled by some using a more sophisticated method of an *inverse* or *backward strategy*, that is, given the desired dose bounds L_1 and U_k, the intensity profiles, are found with the help of a computerised decision support system.

The *inverse-strategy* currently being used formulates the problem as an LP. The assumptions and parameters are the same as in the *design-reuse-strategy*

$$\begin{aligned} &\text{Minimise} && F(\mu,T) := \mu_1 T_1 + \ldots + \mu_K T_K \\ &\text{Subject to} && D_1 = P_1 \cdot x \geq L_1(1 - T_1)e \\ &&& D_k = P_k \cdot x \leq L_k(1 - T_k)e, \quad k=2, \ldots,K \\ &&& x \geq 0,\ T_j \geq 0,\ \mu_j \geq 0,\ j = 1,\ldots,K \end{aligned}$$

T is the maximum measured dose deviation from the desired dose bound and $\mu = (\mu_1, \ldots,\mu_k)$ is a vector of weights, where $\mu_1 + \ldots + \mu_K = 1$, assigned to the dose deviations. These weights signify the importance of keeping a low deviation level in the respective

organs and help to control the dose deviation values obtained. The problem now becomes one of finding a set of weights that produce an appropriate plan.

3 Multi-criteria Approach

3.1 Formulation

The idea to use a multicriteria Linear Program (MCLP) approach is in direct consequence to the observation that achieving a high level of dose in the tumour while keeping a low level of dose in the surrounding healthy organs is contradictory in nature. The formulation is:

$$\begin{aligned} &\text{Minimise} && T = (T_{1,} \ldots, T_K) \\ &\text{Subject to} && D_1 = P_1 \cdot x \geq L_1(1 - T_1)e \\ & && D_k = P_k \cdot x \leq L_k(1 - T_k)e, \quad k = 2, \ldots, K \\ & && x \geq 0,\ T_k \geq 0,\ k = 1, \ldots, K \end{aligned}$$

The multi-criteria formulation considers each of the dose deviations as a separate objective function and there is now no optimal solution to the Radiation therapy problem, but a set of efficient solutions.

A solution is called efficient if there is no other solution dominating it. That is, there is no other solution, which is at least as good for all objectives and strictly better for a least one. These are the only solutions that we are interested in.

The *inverse-strategy* formulation is the scalarised version of the MCLP where each of the objective functions is given a weight of importance and incorporated into the same objective function producing an LP. Because of this the set of efficient solutions produced by the two formulations is exactly the same when considering all possible combinations of strictly positive weights for the scalarised problem.

3.2 Building a set of representative Efficient Solutions

The focus of this paper is to build a set of solutions that are a good representation of all the possible efficient solutions. Having said this we will be more interested in the area for which an appropriate plan will most likely be chosen, where all organs have similar deviations rather than having one satisfied and another far from optimal.

From here the doctor, with an appropriate online tool, will be able to search through the pre-calculated plans guided by his or her preferences, without any knowledge of the actual planning parameters.

3.3 Calculating Efficient Solutions

Multi-criteria Simplex Algorithm

This is an extension on the Simplex Algorithm to deal with Multicriteria problems. It finds all efficient solutions produced from the formulation. In the context of Radiotherapy planning, knowing all efficient solutions is of no interest as many solutions will differ so slightly that from a practical point of view can be thought of as the same, also many solutions will be out of the area of most interest. However, because of the methodology of the paper it is important to know the efficient solution space of an example radiotherapy problem to affirm that a method that calculates a subset of solutions is of any worth.

3.3.1.1 Example Radiotherapy Problem

An example problem was considered from a software package introduced in prototype form that first introduced using multicriteria LP's to model Radiotherapy [2]. It involves a tumour located in the nasal cavity with the healthy organs being the left and right eye and optical nerves. The desired lower bound on the tumour is 30 grey, while the upper bound on both the healthy organs is 10 grey. This software makes a further assumption that the irradiated area is 2-D. The T values of the efficient extreme points produced by the multicriteria Simplex Algorithm included in the software ADBASE available from its author [3] are shown in figure 1. With another program available from the department I was able to build the convex efficient solution space that contains all efficient solutions, also shown in figure1. What can be seen is that there are no solutions produced in the area of most interest.

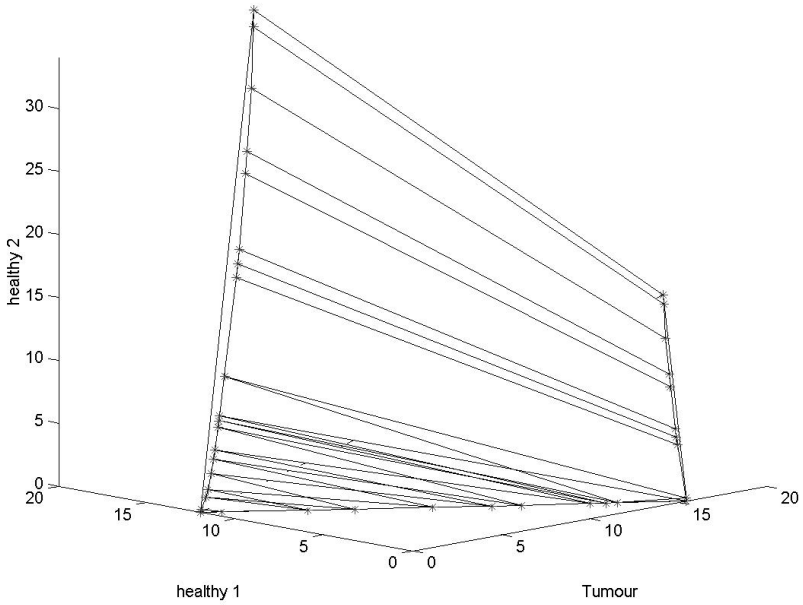

Figure 1: Efficient solutions of the Multicriteria Formulation and resulting convex efficient solution space

Finding new efficient Solutions

From what is seen above in figure 1, new efficient solutions need to be created through the multicriteria formulation inside the boundaries of the convex efficient solution space.

3.3.1.2 The ε-constraint Method

Apart from the scalarisation formulation the most well known method in solving Multicriteria problems is by the ε-constraint method. This is achieved by formulating an LP by leaving one organ in the objective and adding constraints to the problem which bounds the values for which the other organs can take. This is able to trap an efficient solution produced in a certain area of interest. The formulation is:

$$\begin{aligned} &\text{minimise} \quad Ti \qquad x \in X \\ &\text{subject to} \quad T_j \leq \varepsilon_j \quad j = 1,\ldots,K\backslash i \end{aligned}$$

or subsequently $T_j \geq \varepsilon_j$ or a combination of both. This was the approach considered with the prototype software in the aim of building a set of representative solutions [2].

4 A balanced Solution

For a successful navigation to take place among the representative efficient solutions a starting solution needs to be specified. The role of the starting solution is to represent a balanced plan, one where there is no bias towards any single dose deviation. This will mean achieving similar deviations from desired dose levels in all organs rather than achieving a desired dose level in one organ while another is far from its optimal. From the balanced solution, the search time can be expected to be minimised, as it encompasses no preconceptions as to what the final chosen plan will be.

4.1 Scalarisation With Equal Weights

When considering the scalarisation formulation one might think that the appropriate way to achieve the solution that best conforms to that of the balanced solution would be to consider equal weights for all organs [2], but this is not the case. The formulation with equal weights does not take into account the geometry set-up of the radiation beams. Differing beam set-ups are going to affect the level of radiation differently in each of the organs and therefore the dose deviations. Unless the weights take into account the beam set-up geometry, which is incidentally very hard to capture, the solution found will always be biased with the use of equal weights.

As mentioned before when solving the scalarisation problem with equal weights the solution obtained is restricted to the set of solutions produced by the MCLP. But as seen above the solutions produced, by the example problem being considered, are all biased solutions. This makes for a futile effort formulating the problem in such a way to produce a balanced solution, as one does not exist.

4.2 Lexicographic Max-ordering

An unbiased solution will not have extremely high deviations in any one organ while others will have no or small deviation values. To achieve this we minimise the largest of the deviation values T_k using a mini-max model.

$$\begin{aligned} &\text{Minimise:} \quad W \\ &\text{Subject to:} \quad P_1 \cdot x \geq L_1(1 - t_1)e \\ &\qquad\qquad P_k \cdot x \leq L_k(1 + t_k)e, \quad k = 2, \ldots, K \\ &\qquad\qquad W \geq T_k \quad k = 1, \ldots, K \\ &\qquad\qquad X \geq 0, \quad T \geq 0 \end{aligned}$$

But also saying this, we are only interested in an efficient solution. In obtaining this from the mini-max solution we also need to consider the second largest, third largest values etc. in case of ties. This concept is an extension of the mini-max model known as Lexicographic max-ordering in the context of MCLP [4], which will always produce an efficient solution. The solution is then found through a sequence of K optimisation problems the first of which is as follows.

Assume the solution $T^* = (T_1^*, \ldots, T_j^*, \ldots T_k^*)$ is produced. We then identify the index j of the largest T_k^* value and the corresponding constraint $W \geq T_j^*$ is replaced by $W = T_j^*$. This process is now repeated K – 1 times until all W surplus constraints have been replaced with equality constraints.

Results

Both the approaches were applied and compared with each other on the example being considered. The solution found by the scalarisation, figure 2, with equal weights of 1/K produced the deviation values of 0 for both the left and right eye and optical nerves and 15.48 for the tumour.

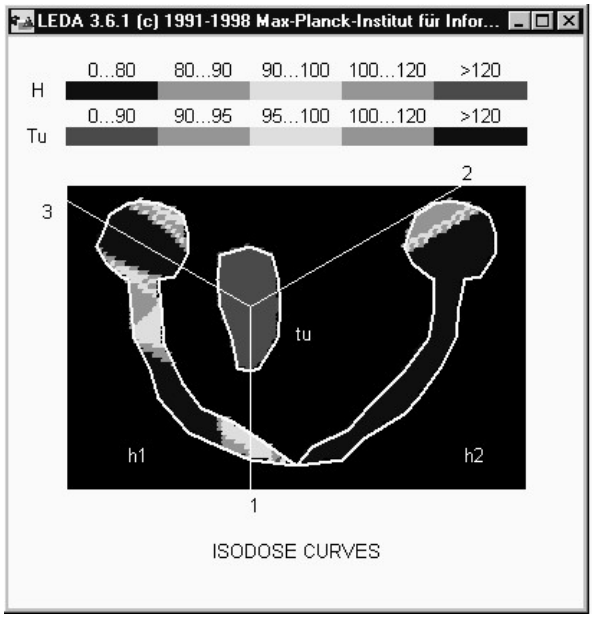

Figure 2: Scalarisation with equal weights of 1/K, T = (15.48, 0, 0)

This is quite an obvious example of a biased solution, it is therefore a poor starting solution for the search process. The Lexicographic solution, figure 3, produced a deviation value of 6.32 for both organs at risk and the tumour. This is exactly conforms to what is expected from a balanced solution and is therefore a good starting solution as it encompasses no prior assumptions as to what the chosen plan will be. Because of the similar or equal deviations from ideal dose limits that are generated from the max-ordering solution it is therefore a clinically relevant solution itself to be considered by the doctor. It is obvious to see that the max-ordering solution is the more appropriate to be designated as a starting solution for the search.

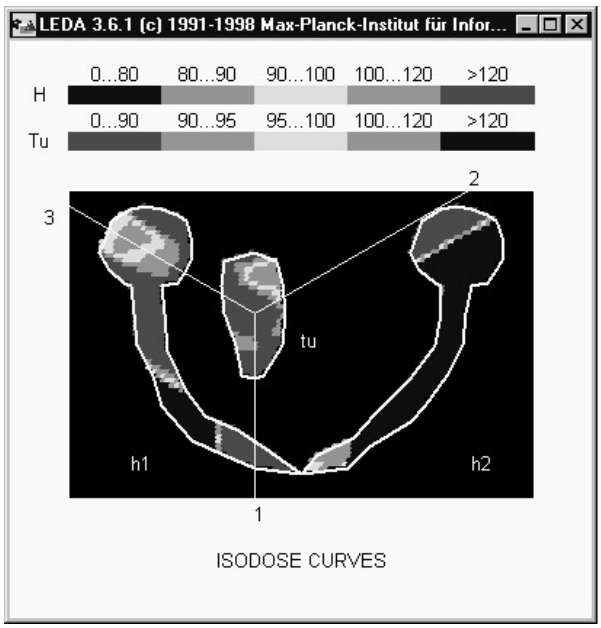

Figure 3: Lexicographic max-ordering, T = (6.32, 6.32, 6.32)

5 Calculating a set of Efficient Solutions

5.1 Formulation

To achieve the best possible coverage of the solution space by a set of representative solutions, I considered covering the projection of the solution space onto the healthy organs in a grid. The problem now becomes on of minimising the tumours deviation while restricting the healthy organs deviations to that of the defined grid points.
The formulation is now:

$$\begin{array}{lll} \text{minimise} & T_1 & \\ \text{subject to} & P_1 \cdot x \geq L_1(1 - t_1)e & \\ & P_k \cdot x \leq L_k(1 + t_k)e, & k = 2, \ldots, K \\ & T_k = g_k^{\,i} & i = \#\text{ grid points} \end{array}$$

5.2 Defining a Grid

To be able to grid the projection of the solution space, a box needs to be defined around the area in which will be the boundary of the grid. This will involve estimating the maximum and minimum deviations of each of the healthy organs. To find these deviations the scalarisation formulation is solved K times with the following weights:

$$\begin{array}{l} \{\ \ w_i = 1 - (K\text{-}1)*0.1 \\ \ \ \ w_j = 0.1\ j = 1,\ldots K \backslash i\ \ \} \ \ i = 1,\ldots k. \end{array}$$

If in this process one of the organs greatest deviations found was 0, it will be estimated as the maximum of the other healthy organ deviations found. As to achieve the maximum through the appropriate weights will require the weights to capture the set-up of the beams, which as explained earlier is very hard. An example of a grid to achieve this is showed below in figure 4.

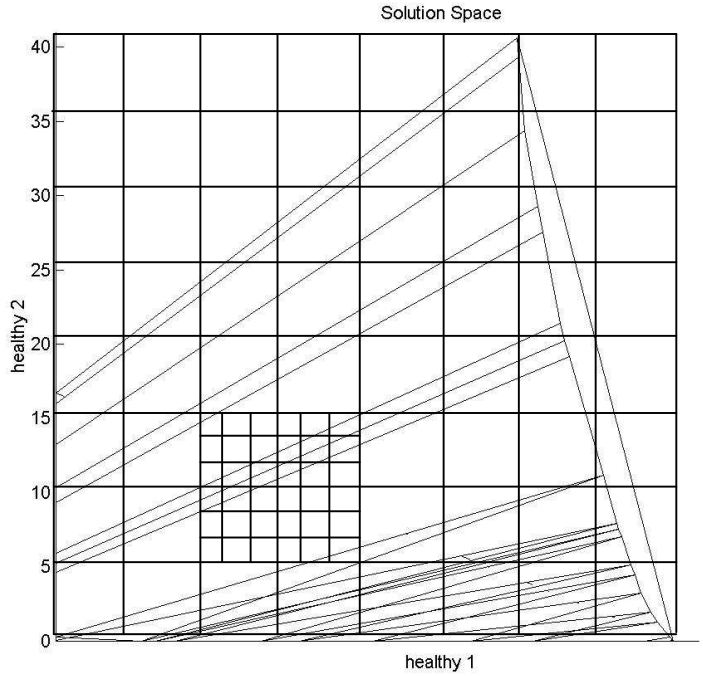

Figure 4: Example of a possible grid with finer representation around the area of most interest

The compromise with this method is that there is no way of knowing the exact solution space from the estimated maximum deviations and many of the grid points will subsequently lie outside the efficient solution space and produce non efficient solutions or infeasible problems. A non-efficient solution produced in this way is easily identified and can be discarded. As the minimum deviation possible is zero, a grid point that produces a tumour deviation value of zero is most probably a non-efficient solution as it is unlikely that a specific grid point describes an efficient solution with a tumour deviation value of exactly zero.

The number of grid points that produce non efficient solutions or infeasible problems can be kept to a minimum by a grid that defines larger boxes outside the area of interest where non efficient solutions are more likely to be produced. This also allows for the grid to be more finely defined in the area of most interest to produce a subset of solutions that better represent the area, which will surround the balanced solution.

5.3 Results

The set of solutions that were produced are shown below in figure 5. The box was defined in this example to have a maximum deviation in healthy organ 2 of 12 as a dose received higher than this will likely kill it and a chosen plan being contained in this part of the solution space will be highly unlikely. What can be seen is that the desired result was achieved were the solutions present an even distribution over the whole solution space interested in with the area of most interest more finely represented.

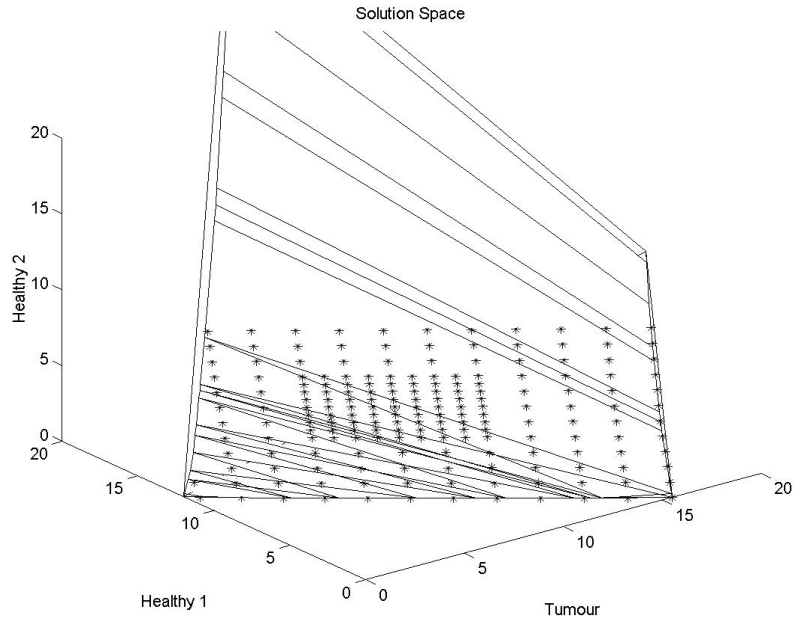

Figure 5: A representative set of efficient solutions calculated

6 References

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