RADIOTHERAPY COMPENSATORS FOR AN UNSPECIFIED TARGET DOSE

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SUMMARY

An excessive dose received by healthy tissue during radiation cancer treatment may produce unwanted biological damage. Since a minimum prescribed dose to tumour tissue is to be delivered, one is concerned with the dose levels at various locations. The inhomogeneities of the human body cause the radiation beam to be attenuated unevenly, while the irregular shape of the body causes different path-lengths for different portions of the beam. Therefore, some compensation for these sources of uneven radiation effectiveness is needed. "Compensating filters", by selective pre-attenuation of parts of the beams, offer the potential of gaining higher control over the dose distribution. Thus for example, a filter with the wedge-like cross section applied over an inclined body surface, can compensate for that surface not being perpendicular to the beam axis. The wedge filter used in this situation is called the "missing-tissue" compensator, for it compensates for the shape of the human body not being box-like.

As it is unlikely that two patients have identical distribution of tissues and an identically located tumour, a given filter shape can not satisfy requirements in higher precision radiotherapy. More comprehensive design of filters is necessary for production of individualized "variable-thickness" compensators. Information on the body inhomogeneities (bone attenuates faster than lung) is available in a form of the CT-data stored in the computer that supports the scanner. Calculated filter thicknesses can be fed into a numerically controlled milling machine for automated manufacture of filters (usually lead plates below 20x20 cm).

Naturally, at least one radiation beam has to be applied for the irradiation to take place. For applications with the target zone (tumour) located deeper inside the body, a single beam arrangement is usually not suitable - the healthy tissues through which the beam has to pass on its way to the target zone would receive a higher dose than the tissue in the target zone. Therefore, multibeam radiation treatments have to be employed to allow concentration of a number of beams to the target area (allowing each individual beam to be of lower intensity and hence to cause fewer side effects to healthy tissues traversed by the

individual beams). This, however, introduces additional problem of adjusting the intensities of the applied beams relative to each other.

A number of attempts have been made to design radiotherapy compensators (1). A method to achieve the optimal design of radiation compensating filters in multibeam situations has been reported (1,2). That method optimized body dose distribution such that it spatially matched the prescription in the target zone, was minimized everywhere else, and did not exceed designated limits at selected vulnerable regions (regions where the dose limit is prescribed). It was a quadratic mathematical optimization method based on the minimization of the variance of doses received by tumour points relative to the prescription. Hence, a desired tumour dose (or its desired distribution in general) had to be prescribed. The "quadratic" method has been implemented into the commercial radiotherapy system ("Theraplan 300L", Theratronix International Ltd.).

This paper presents a method of solving a similar problem in those cases when the wanted tumour dose (distribution) is not known in advance. Therefore, instead of targeting a specific prescription over the tumour, which the quadratic approach did, the method presented in this paper is aiming at a general maximization of the tumour dose - subject to the same two additional criteria that i) provide that the dose at vulnerable regions is within designated limits, and ii) minimize the exposure of the healthy tissue. This method utilizes linear mathematical programming. The patient is represented via three sets of points fixed in space : healthy, vulnerable and tumour points. "Vulnerable" points are points which have a specified dose limit, and are either healthy or tumour points. Some or all tumour points may have a minimum or maximum (or both) required tumour dose prescribed, and some or all healthy points may have upper limit on tolerable dose prescribed. Clearly, imposed constraints on maximum allowed dose to designated points and minimum required dose to tumour points may constitute an over-constrained system with no solution, meaning that the proposed arrangement is physically impossible and corresponding compensators can not be designed. Alteration to imposed constraints on radiation dose or addition of a larger number of radiation fields may be necessary (the method will eliminate redundant fields or portions thereof). Upper limits to tumour dose may also be imposed if desired (for example in order to achieve tumour dose uniformity).

The linear method presented here is not meant to be a replacement, but a supplement to the said quadratic approach (2) since the application domains of the two complement each other. The two methods share a common basic concept and an analogous mathematical development.

THE CONCEPT

Incident radiation beams (further referred to as "basic" beams) are divided into a number of "elementary" beams. Appropriate mathematical optimization procedure is then performed utilizing these elementary beams. The results of such an optimization process are the desired intensities of these elementary beams. The calculated intensities indicate how much should each elementary beam be pre-attenuated relative to an adopted "reference-intensity" beam, thus specifying the needed filter thickness at the location of each elementary beam.

The implied mathematical optimization is formulated such that the filters (compensators) modify the applied radiation beams according to the following three criteria :

1) dose to designated vulnerable regions is within the prescribed limits,

2) target dose is maximised, and

3) overall dose to the healthy region under consideration is minimised.

Shapes, sizes and weights of the beams do not have to be prescribed in advance, as they are determined by the technique. Incident radiation beams may have any penumbral characteristics and spacial inhomogeneities. Compensation for missing tissues and body heterogeneities is also possible.

Radiation quality must, however, be prescribed. Directions of radiation beams must be either prescribed or determined by another software module currently being developed (which will be reported separately).

The calculated filter thicknesses can be fed into a numerically controlled milling machine for automated fabrication, such as that of reference (3). Input into this calculation procedure is data from a selected dose calculation module for the unfiltered beams.

Figure 1 is a schematic representation of a simple treatment plan with basic beams divided into a set of elementary beams. The division is only fictitious, for the sake of mathematical manipulations. It is performed at equi-distant increments along both dimensions in the planes of all filters considered (although any division is acceptable and its frequency should correspond to the desired accuracy). Target zone, vulnerable regions, and healthy tissues of concern, are represented by a pre-selection of points of corresponding class.

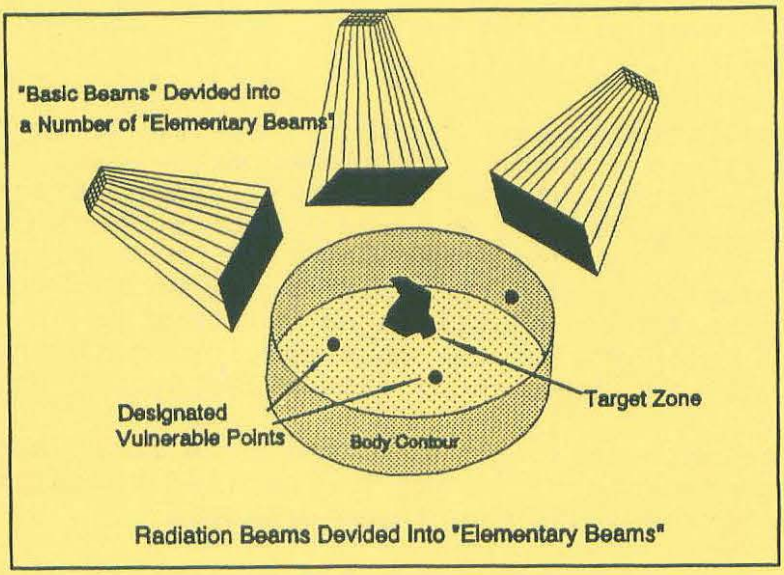

Figure 1

MATHEMATICAL FORMULATION

Attenuation of the filter at its i^{th} elementary beam location can be characterized by the ratio :

$$\frac{f_i^{(A)}}{f_i^{(B)}} = \frac{f_i^{(A)}}{f'}\frac{f'}{f_i^{(B)}} = w_i\frac{f'}{f_i^{(B)}} \quad , \quad i=1,2,\ldots n$$

where $f_i^{(A)}$ and $f_i^{(B)}$ are the i^{th} elementary beam intensities after and before the corresponding filter, f' is the adopted reference intensity, w_i is the "weight" of i^{th} elementary beam after the filter relative to the adopted reference intensity, and n is the total number of elementary beams.

Bounds on Variables w_i

To keep the ratios $f_i^{(A)}/f_i^{(B)}$ within their physically feasible bounds of unity and a value greater than zero (<1), the following bounds are introduced :

$$b_L \le w_i \le b_{U_i} \quad , \quad i = 1,2,3,\ldots n$$

where b_L ($0 < b_L < 1$) is a fixed quantity independent of i, and is a strictly positive lower bound (to preclude negative ratios

with no physical meaning, or large thicknesses for complete absorption of incident elementary beams), and $b_{Ui} = f_i^{(B)}/f'$, are n upper bounds having the values of unity in the case of ideal (uniform) beams ($b_{Ui} > b_L$ for any i=1,2,...n).

Application of a Dose Calculation Module

Applying one of a number of available dose calculation methods (4-6), one can calculate the dose deposited to points of interest (vulnerable, tumour, and other healthy points), by each of the elementary beams temporarily assumed to be of the reference intensity. The division into elementary beams means a greatly increased number of beams to deal with. Practically, however, this does not require increased dose calculation efforts compared to "classical" procedures with basic beams. This is due to the fact that some form of integration over the volume is always needed, which implies a division analogous to the "elementary-beam" division - followed by the summation of the calculated dose contributions from these elementary beams (see reference 5 or 6, or the differential scatter-air ratios method in reference 4). This means, matrices **V**, **T**, and **U**,

$$\mathbf{V} = [v_{ij}] \ , \ i=1,2,...m_v \ , \ j=1,2,...n$$
$$\mathbf{T} = [t_{ij}] \ , \ i=1,2,...m_t \ , \ j=1,2,...n$$
$$\mathbf{U} = [u_{ij}] \ , \ i=1,2,...m_u \ , \ j=1,2,...n$$

can be calculated, where v_{ij} is the dose deposited to i^{th} vulnerable point by j^{th} elementary beam of the reference intensity, t_{ij} is the dose deposited to i^{th} tumour point by j^{th} elementary beam of the reference intensity, and u_{ij} is the dose deposited to i^{th} point of

the healthy tissue by the j^{th} elementary beam of reference intensity, m_v is the total number of considered vulnerable points, m_t is the total number of considered tumour points, m_u is the total number of considered healthy tissue points, and n is the total number of elementary beams.

The total dose deposited to a point under consideration by beams of intensities w_j relative to the reference intensity beam, j=1,2,..n, is

- dose to i^{th} vulnerable point

$$^{v}d_i = \sum_{j=1}^{n} v_{ij} w_j \ , \ i=1,2,...m_v$$

- dose to i^{th} tumour point

$$ {}^{t}d_i = \sum_{j=1}^{n} t_{ij} w_j \ , \ i=1,2,\ldots m_t $$

- dose to i^{th} healthy point

$$ {}^{u}d_i = \sum_{j=1}^{n} u_{ij} w_j \ , \ i=1,2,\ldots m_u $$

The above equations are well known (4-8). They show that the dose deposited to a point of interest, is a linear function of the beam intensity (2). For all i's, using matrix notation, the previous three equations can be rewritten in the form :

$$ {}^{v}\mathbf{D} = \mathbf{VW}, $$

$$ {}^{t}\mathbf{D} = \mathbf{TW}, $$

$$ {}^{u}\mathbf{D} = \mathbf{UW}, $$

where the bold variables **D** and **W** denote vectors of the corresponding components.

Constraints

Let vector **C** be the vector containing upper limits on dose set to vulnerable points. That these limits are not to be exceeded, can mathematically be formulated as ${}^{v}\mathbf{D} \leq \mathbf{C}$, or, $\mathbf{VW} \leq \mathbf{C}$. Let vector **B** be the vector containing lower limits on dose to tumour points. That these requirements must be satisfied, can be expressed as: ${}^{t}\mathbf{D} \geq \mathbf{B}$, or, $\mathbf{TW} \geq \mathbf{B}$.

Maximization of the Target Dose

In order to maximize the dose to tumour volume, the sum of doses received by m_t tumour points must be maximized. That is

$$ \chi_2^2 = \mathbf{Z}^T \, {}^{t}\mathbf{D} \quad \text{maximize.} $$

The vector **Z** is a unit vector (dimension m_t) if all tumour points are of the same significance. The i^{th} component of it may be assigned a positive value higher (or lower) than one if the increase in dose to this point is appreciated more (or less) than the same for other tumour points. χ_2^2 is actually a sum (which may be weighted if desirable) of doses delivered to each tumour point (2). Equivalently, it can be expressed as :

$$ \chi_2^2 = \mathbf{Z}^T\mathbf{TW}, \text{ maximize} $$

Dose Minimization to Points of the Healthy Tissue

The minimization of the overall total dose to the m_u healthy tissue points (which may include vulnerable points as well), can be expressed as :

$$\chi_1^2 = \mathbf{Y}^T {}^u\mathbf{D} \quad \text{minimize.}$$

Analogous to the **Z** vector, **Y** is a unit vector (dimension m_u) if all healthy points are of the same significance. The i^{th} component of it may be assigned a positive value higher (or lower) than one if the decrease in dose to this point is appreciated more (or less) than the same for other healthy points. χ_1^2 is a sum (which may be weighted if desirable) of doses delivered to each healthy point (2). It can be expressed as

$$\chi_1^2 = \mathbf{Y}^T\mathbf{U}\mathbf{W}, \quad \text{minimize.}$$

Instead of calculating the extreme of both functions, χ_1^2 and χ_2^2 separately, one can minimize their linear combination :

$$\chi = q\chi_1^2 - \chi_2^2 \text{ , minimize,}$$

where q is a constant positive scalar. With the choice of this scalar, one is able to adjust the relative importance (and priority) of the often contradictory requirements that χ_1^2 and χ_2^2 represent. (The choice of q is analyzed below).

Expanding, one obtains :

$$\chi = \mathbf{G}^T\mathbf{W}, \text{ minimize,}$$

where

$$\mathbf{G} = q\mathbf{U}^T\mathbf{Y} - \mathbf{T}^T\mathbf{Z}$$

is a gradient vector.

Estimation of the parameter q

The selection of elementary beam intensities which lowers the value function χ suggests a decrease in the component χ_1^2 and an increase in the component χ_2^2. However, a change of the elementary beam intensities that increases component χ_2^2 (tumour dose) will often result in an increase of another component, χ_1^2. The choice of the parameter q indicates whether or not such a change in beam intensities is regarded as an <u>overall</u> improvement of the situation since a multiplier q in χ scales changes in components χ_1^2 and χ_2^2 relative to one another. In other words,

with the choice of the scalar q in any particular situation, one is able to express one's preference for further tumour dose maximization over a possible reduction of doses everywhere else (or vice versa). This preference is obviously a subjective one, and is influenced by the particular situation. The parameter q, therefore, expresses one's personal judgement of what the "best" solution is. Hence, it cannot have a uniquely assigned value (one can always argue how much reduction in tumour dose is justifiable trade off for further reduction of doses within the healthy tissue). Even though the best value for the scalar q cannot be determined rigorously, some guidance in selecting it is needed.

The choice of q=0 is equivalent to the exclusion of the requirement for minimization of the dose to healthy tissue. A negative q would maximize doses to healthy tissue (subject to other criteria of higher priority such as limits to vulnerable points). Hence, q must have a nonnegative value ($q \geq 0$).

Too large q would place an undue emphasis on the reduction of doses to healthy tissue, with the accompanied consequence of low doses delivered to tumour. The upper limit for q will be evaluated by ensuring that a higher emphasis is placed on the tumour dose maximization criterium (χ_2^2) than on the minimization of doses to healthy tissue (χ_1^2) - one should not pursue with the irradiation otherwise. In terms of the gradient vectors of χ_2^2 and χ_1^2, $\mathbf{G}_2$ and $\mathbf{G}_1$, this can be expressed by :

$$\mathbf{G}_2 = \mathbf{T}^T\mathbf{Z} > q\mathbf{U}^T\mathbf{Y} = \mathbf{G}_1.$$

These n inequalities will all be satisfied if the most restrictive one is satisfied :

$$q < q_{max} = \min_i\{ (\mathbf{Z}^T\mathbf{T})//(\mathbf{Y}^T\mathbf{U}) \}, \quad i=1,2,...n,$$

where the "double slash" symbol denotes division of the corresponding components, and "$\min_i\{.\}$" the smallest of all component of the enclosed row vector.

Since the variables $\mathbf{Z}$, $\mathbf{T}$, $\mathbf{Y}$ and $\mathbf{U}$ are all known in advance, q can be chosen in the range $0 \leq q \leq q_{max}$ before performing the following mathematical optimization procedure.

OPTIMIZATION

The problem is reduced to calculation of the $\mathbf{W}$ vector which minimizes the "value function" χ:

$$\chi = \mathbf{G}^T\mathbf{W} \text{ minimize},$$

subject to a set of linear constraints,

$$\mathbf{VW} \leq \mathbf{C}$$

$$\mathbf{TW} \geq \mathbf{B}$$

and subject to the following bounds on variable **W**:

$$\{b_L\} \leq W \leq \{b_{U_i}\}, \quad i = 1,2,3,\ldots n$$

This problem can be recognized as the "linear programming" problem, and is well documented in the literature (9). A computer program has been developed for the numerical calculations of **W**. It makes use of the International Mathematical and Statistical Libraries (IMSL) computer library (10).

FILTER THICKNESSES

Vector **W** is the result of the described optimization process. Its components can be grouped into p vectors ${}^{j}\mathbf{W}$ of dimension n_j, ($\Sigma n_j=n$) $j=1,2,\ldots p$, to correspond to the p basic beams. For each of these, a component ${}^{j}w_{k(j)}$, $1 \leq k(j) \leq n_j$, can be determined, so that

$${}^{j}w_{k(j)} = \max_i\{{}^{j}w_i\}, \quad i=1,2,\ldots n_j.$$

In order to minimize filter thicknesses, vectors ${}^{j}\bar{\mathbf{W}}$ are formed by dividing all ${}^{j}\mathbf{W}$ by ${}^{j}w_{k(j)}$:

$${}^{j}\bar{\mathbf{W}} = ({}^{j}w_{k(j)})^{-1} \cdot {}^{j}\mathbf{W}$$

Each vector ${}^{j}\bar{\mathbf{W}}$ is actually vector ${}^{j}\mathbf{W}$ scaled down by its largest component. Hence, each vector ${}^{j}\bar{\mathbf{W}}$ has at least one component equal to unity, corresponding to a zero-thickness compensator. All basic beams should be assigned an individual weight ${}^{j}w_{k(j)}$, and therefore, this algorithm gives also the beam weights.

Vector ${}^{j}\tau$ with components equal to the thicknesses of the j^{th} filter can be calculated from:

$$\mu_j \, {}^{j}\tau = \ln\{\mathbf{F}\} - \ln\{f' \, {}^{j}\bar{\mathbf{W}}\}, \quad j=1,2,\ldots p,$$

where μ_j is the narrow beam linear attenuation coefficient (at the energy of the incident beam) for the material the j^{th} compensator is to be built from, "ln{.}" is a vector with components equal to the natural logarithm of the argument vector's components, and **F** is vector of incident elementary beam intensities.

Components of the resulting vectors ${}^{j}\tau$, j=1,2,...p, are the required thicknesses of the corresponding p filters. A computer file with these data can be fed directly into a numerically controlled milling machine, such as that of Ref. 3, for automated fabrication of the filters.

POST PROCESSING

With the above calculated filters assumed in place, one can predict the doses to all considered points (independent of whether or not the scaling of **W** had been performed):

$$ {}^{v}D = VW, $$

$$ {}^{t}D = TW, $$

$$ {}^{u}D = UW, $$

where ${}^{v}D$, ${}^{t}D$ and ${}^{u}D$ are vectors containing doses to vulnerable, target and healthy zones.

It should be emphasized that the input data for the presented mathematical procedure are the calculated doses for the unfiltered beams, whereas the output data contains doses that will result from application of the calculated beams and filters. There is no need to repeat the dose calculations.

In designing variable thickness compensating filters and determining the shape, size and weight of the photon beams, top priority is given to meeting the strict dose limits assigned to vulnerable regions. As a next important criterion, the target dose is maximized. Minimization of doses everywhere else, including the vulnerable regions, is considered next in importance. A computer program has been written to implement the described mathematical procedure.

CONCLUSION

Multibeam situation variable thickness compensating filters are optimised such that the target dose is maximized while the dose limits set to vulnerable regions are not exceeded, and the overall exposure is minimized. Not only the size, shape and relative intensity of the photon beams are determined, but detailed dose distribution for the optimized arrangement is also provided. The developed computer algorithm is efficient and flexible, as it allows easy evaluation of different planning arrangements. Work is continuing to implement the method into an existing radiotherapy system that already has the "quadrat ic" method (1,2) incorporated into it.

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