Radiation Oncology and Optimization

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Previous Reviews


- The Radiation Oncology & OR web site: www.trinity.edu/aholder/HealthApp/oncology/


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Model Parameters

Optimization models depend on

- Where dose is calculated,
- Where the isocenter is placed,
- What couch angle(s) are allowed, and
- What gantry angle(s) are used.

**bold** decisions are mandatory, others can be addressed within the optimization model.

The examples and images are from the academic treatment system RAD, lagrange.math.trinity.edu/rad.

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Calculating Dose

A naive grid distribution:
Dose is calculated on a uniform grid (1 cm spacing).

A judicious initial placement:
We define a swath to place dose points and then only add points in normal tissue to avoid hot spots.
Model Parameters

**Dose Placement** This is the most crucial decision required to build a model. Treatment and technique comparisons are directly related to this decision.

**Isocenter Placement** There is typically a single isocenter placed near the center of mass of the target. There is no reason to believe that this is an ‘optimal’ placement.

**Couch Angle(s)** Couch Angles should be decided by the optimization model, but is currently not done. We expect the user to define couch angles.

**Gantry Angles** Optimal selection of gantry angles is single biggest problem in the field. Selection is currently required by commercial systems.
Allow only a finite number of beams, sub-beams, and patient pixels. These sub-beams are elementary beams, but pencils, which radiate from a single point source, are also common.
The following vectors are the minimum needed to form a prescription.

- **$TUB$** - vector of upper bounds on the tumor (target volume).
- **$TLB$** - vector of lower bounds on the tumor.
- **$CUB$** - vector of upper bounds for the critical structures.
- **$GUB$** - vector of upper bounds for the good tissue.

The dose to tissue is linear in time, and we let $x \mapsto Ax$ be the transformation that maps exposure times ($x$) into deposited dose ($Ax$). The rows of $A$ are separated as indicated.

\[
A = \begin{bmatrix}
A_T \\
A_C \\
A_G
\end{bmatrix} \quad \leftarrow \text{tumor pixels}
\]

\[
\quad \leftarrow \text{critical structures}
\]

\[
\quad \leftarrow \text{good tissue}.
\]
The simplest linear models are feasibility models*. These models attempt to satisfy

\[ A_T x \geq TG, \quad A_C x \leq CUB, \quad A_N x \leq NUB, \text{ and } x \geq 0. \]

Consistency is not guaranteed because physicians are often overly demanding, and many authors have complained that infeasibility is a shortcoming. In fact, the argument that feasibility alone correctly addresses treatment design is that the region defined by these constraints is relatively small, and hence, optimizing over this region does not provide a significant benefit.

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Linear Models

- Maximize Aggregate Dose to Tumor
  \[ \max \{ e^T A_T x : A_T x \geq TG, A_C x \leq CUB, A_N x \leq NUB, x \geq 0 \} \]

- Minimize Aggregate Dose to Critical Structures
  \[ \min \{ e^T A_C x : A_T x \geq TG, A_C x \leq CUB, A_N x \leq NUB, x \geq 0 \} \]

- Maximize the Minimum Dose to the Tumor
  \[ \max \{ z : A_T x \geq TG + z e, A_C x \leq CUB, A_N x \leq NUB, x \geq 0, z \geq 0 \} \]

- Minimize the Maximum Dose to the Critical Structures
  \[ \min \{ z : A_T x \geq TG, A_C x \leq CUB - z e, A_N x \leq NUB, x \geq 0, z \geq 0 \} \]
Objectives that consider both target and critical structures*:

- Maximize the difference in the integral doses of target and critical structures
  \[ \max\{e^T A_T x - e^T A_C x : A_T x \geq TG, A_C x \leq CUB, A_N x \leq NUB, x \geq 0\} \]

- Maximize the difference in the minimum tumor dose and the maximum critical structure dose
  \[ \max\{z - q : A_T x \geq TG + ze, A_C x \leq CUB - qe, A_N x \leq NUB, x \geq 0, z \geq 0, q \geq 0\} \]

---

An elastic model that removes the threat of infeasibility *

\[
\min \{ \omega \cdot l^T \alpha + u_C^T \beta + u_N^T \gamma : TLB - L\alpha \leq A_T x \leq TUB, \\
A_C x \leq CUB + U_C \beta, A_N x \leq NUB + U_N \gamma, -CUB \geq U_C \beta, \\
0 \leq U_N \gamma, 0 \leq x \} 
\]  

(1)

This model has a nice theoretical results

**Theorem** The linear model and its dual are strictly feasible, meaning that each of the constraints can simultaneously hold without equality.

**Theorem** Allowing \((x^*(\omega), \alpha^*(\omega), \beta^*(\omega), \gamma^*(\omega))\) to be an optimal solution for a particular \(\omega\), we have that \(l^T \alpha^*(\omega) = O(1/\omega)\).

---

Most nonlinear models are p-norm extensions of the previous linear models*.

- Minimize the 2-norm distance from the goal dose over the target
  \[
  \min \{ \| A_T x - TG \|_2 : A_C x \leq CUB, A_N x \leq NUB, x \geq 0 \}
  \]

- Minimize the 2-norm distance from prescription
  \[
  \min \{ \| A_T x - TG \|_2 + \| A_C x - CUB \|_2 + \| A_N x - NUB \|_2 : x \geq 0 \}
  \]

This model is most appropriate with \( CUB = 0 \) and \( NUB = 0 \).


Partition $C$ into $C^1, C^2, \ldots, C^K$, where $C^k$ contains the dose points within the $k$th critical structure. For each $k$, let $T^{k_1}, T^{k_2}, \ldots, T^{k_{\Lambda_k}}$ be the thresholds for critical structure $k$. We let $\alpha_p^{k\lambda}$ be a binary variable that indicates whether or not dose point $p$, which is in critical structure $k$, is below or above threshold $T^{k\lambda}$. The percentage of critical structure $k$ that is desired to be under threshold $T^{k\lambda}$ is $1 - \rho^{k\lambda}$. We now have the ability to allow for dose-volume constraints as follows.

$$
TLB \leq A_T x \leq TUB \\
A_{C_k} x \leq T^{k\lambda} e + \alpha^{k\lambda} M, \quad \text{for each } k
\\
\rho^{k\lambda} |C^k|, \quad \text{for each } k
\\
A_N x \leq NUB
\\
x \geq 0
\\
\alpha_p^{k\lambda} \in \{0, 1\} \quad \text{for each } p \in C^k.
$$
Binary Models & Dose-Volume Constraints

\[
\min w^1 \cdot e^T \beta + \sum_{k\lambda} w^{k\lambda} \cdot e^T \alpha^{k\lambda}
\]

If we add similar dose-volume const. \( A_T x \leq TUB \),

\( A_T x \geq TLB - \text{diag}(TLB)\beta \),

for underdosing \( e^T \beta \leq \gamma|T| \),

the target, this \( A_T x \leq TUB \),

model minimizes \( A_{Ck} x \leq T^{k\lambda} e + \alpha^{k\lambda} M \),

over and under dosing\*.

\( e^T \alpha^{k\lambda} \leq \rho^{k\lambda} |C^k| \),

\( A_N x \leq NUB \),

\( x \geq 0, \alpha_p^{k\lambda} \in \{0, 1\}, \beta_p \in \{0, 1\}, \quad p \in C^k, p \in T. \)


Morrill develops a biologically based model where the goal is to maximize the probability of a complication free treatment. The idea behind this model is that different organs react to radiation differently, and that there are probabilistic ways to measure whether or not an organ will remain complication free. To represent this model, we let $f(d^k)$ be the probability of critical structure $k$ remaining complication free, where $d^k$ is a vector of dose values in critical structure $k$, the optimization model is

$$\max \left\{ \prod_{k=1}^{K} f(d^k) : TLB \leq A_T x \leq TUB, \right.$$  

$$A_{C_k} x = d^k, \ k = 1, 2, \ldots, K, \ A_N x \leq NUB \right\}. \quad (2)$$

While the matrix coefficients of $A$ are different, the linear relationship between exposure time and deposited dose remains valid. The model proposed by Ferris, Lim and Shepard* is

$$
\min\{e^T u_T : d_T = A_T x, d_C = A_C x, \theta \leq u_T + d_T,
\begin{align*}
0 &\leq x \leq sM, \\
e^T s &\leq n,
\end{align*}
\begin{align*}
s_i &\in \{0, 1\}, 0 \leq u_T, 0 \leq u_C \}.
\end{align*}
$$

(3)

The constraint with $\rho$ ensures that the target dose is at least $\rho$ of the total dose. The authors approximate the binary constraints with

$$
\begin{align*}
0 &\leq x \leq sM, \\
e^T s &\leq n,
\end{align*}
\begin{align*}
s &\in \{0, 1\}
\end{align*}
$$

with

$$
\sum_{(c,i)} \tan^{-1}(\alpha x_{(c,i)}) \leq n.
$$

A different Gamma Knife model is suggested by Cheek, Holder, Fuss and Salter*. This binary model is is based on the over and under treatment ratios.

\[
\min \left\{ \sum_{i=1}^{I} w_i (1 - e_{TV}^T \Theta_i / e^T \Theta_i) + u_i (1 - (V/K)e_{TV}^T \Theta_i) : \right. \\
Ax = d, \text{diag}(d)ee^T \leq ee^T HD + M\Theta, 0 \leq x \leq M\beta, e^T \beta \leq L, \\
\beta_i \in \{0,1\}, \Theta_{(p,i)} \in \{0,1\} \right\}.
\]

This is a binary, global optimization problem and is solved with simulated annealing (but we hope to investigate other algorithms and heuristics).

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* The Relationship Between the Number of Shots and the Quality of Gamma Knife Radiosurgeries, to appear in Optimization and Engineering.
Radiation Oncology and Optimization

An example of the isodose lines of a treatment from the previous model.
Suppose we want to divide a treatment into \( N \) smaller treatments. If \( d^k \) is the cumulative dose after \( k \) treatments, the problem is to decide how much dose to deliver in subsequent periods. This leads to a discrete-time dynamic system, and if we let \( u^k \) be the dose added in period \( k \) and \( w^k \) be the random error in delivering \( u^k \), then the system is

\[
d_{k+1} = d_k + u_k (1 + w_k).
\]

With this discrete model, Ferris and Voelker* consider

\[
\min \{ E(||w^T (d_N - D)||_1) : d_{k+1} = d_k + u_k (1 + w_k), u_k \geq 0, w_k \in W \}.
\]

---

Suppose we have optimally decided that the exposure times, in the beams-eye-view, are

\[
I = \begin{bmatrix}
0 & 0 & 2 & 2 & 2 & 0 \\
0 & 1 & 1 & 3 & 1 & 0 \\
0 & 0 & 2 & 2 & 1 & 0 \\
1 & 2 & 2 & 2 & 1 & 0 \\
0 & 1 & 2 & 3 & 2 & 1 \\
0 & 1 & 2 & 2 & 2 & 2
\end{bmatrix}.
\]

The question arises as to how best achieve this fluency pattern with a multileaf collimator. Boland, Hamacher and Lenzen* have addressed how to most efficiently adjust the collimator to achieve a known fluency pattern.

* Minimizing beam-on time in cancer radiation treatment using multileaf collimator, in review.
For each row $i$ and time step $t$ we let

$$l_{ijt} = \begin{cases} 1, & \text{if the left leaf in row } i \text{ is positioned in column } j \text{ at time } t \\ 0, & \text{otherwise} \end{cases}$$

$$r_{ijt} = \begin{cases} 1, & \text{if the right leaf in row } i \text{ is positioned in column } j \text{ at time } t. \\ 0, & \text{otherwise.} \end{cases}$$

The nonlinear, binary model studied is

$$\min \left\{ \sum_t \alpha_t : \sum_j l_{ijt} = 1, \forall i, t; \sum_j r_{ijt} = 1, \forall i, t, \right\}$$

$$y_{ijt} = \sum_{k=0}^{j-1} l_{ikt} - \sum_{k=1}^{j} r_{ikt}, \forall t; \sum_{k=0}^{j} l_{ikt} \geq \sum_{k=1}^{j} r_{ikt}, \forall t,$$

$$\sum_t \alpha_t y_{ijt} = I_{ij}, \forall i, j; l_{ijt}, r_{ijt}, y_{ijt} \in \{0, 1\}, \forall i, j, t; \alpha_t \geq 0, \forall t \right\}.$$}

This problem is shown by Boland, Hamacher and Lenzen to polynomial.
A quantizer, $Q$, is the composition of an encoder and a decoder.

Encoder

$$f : V \rightarrow \{1, 2, \ldots, n\}$$

Partitions $V$

Decoder

$$g : \{1, 2, \ldots, n\} \rightarrow V$$

Assigns Codevectors

The quantizer is $Q(x) = g(f(x))$, where $x$ is a random variable over the vector space $V$.

The design problem is to find a partition of $V$ and a collection of codevectors, called the codebook, that “quantize” the realizations of $x$ so that distortion is minimized.
The error for any realization of $x$ is

$$\varepsilon = d(x, Q(x)),$$

where $d$ is a metric over $V$. The typical error is $\|x - Q(x)\|_2$. A quantizer’s distortion is the average distortion

$$D = Ed(x, Q(x)) = \int_{-\infty}^{\infty} d(x, Q(x))p(x)dx.$$

Our error measure is $\|Ax - A'Q(x)\|_2$ —i.e. we match the dose distribution in the patient. This error measure is NOT simple, as we are quantizing angles but using a linearly transformed, altered optimal solution to measure distortion.
Beam Selection

**Known Codebook** The partition must satisfy the nearest neighbor condition.

**Known Partition** The codevectors are the centers of mass for each region.

A quantizer is **regular** if it satisfies the nearest neighbor condition, and is **uniform** if the length of each neighborhood is the same.

For us, the support set of the probability function is $[0, 2\pi]$, the number of sets in the partition is $n$, and $\Delta = (b - a)/n$. 
The first figure shows a tumor with desired dose of 80Gy ±3%. The critical structures are restricted to 40Gy, 30Gy, and 20Gy. The second figure shows the contour plot of the dose distribution, there are no hot spots and the tumor and critical structure bounds are satisfied. The dose distribution is in the third figure.
The problem with the Uniform Quantizer is that at every iteration we are assuming that we have no patient information, but this is simply not the case.

The dose distribution at the gantry is a good indicator of favorable angles, and we can normalize this to form a probability distribution. To get a non-uniform quantizer we evenly partition the accumulative dose distribution (at the gantry) to form a code book.
We uniformly subdivide the range of the accumulative distribution and project back to find a non-uniform codebook. The optimality conditions require that the codevectors be the centers of mass.
The quality of the plans is high throughout, and the lesser angle plans are significantly improved over the Uniform approach.

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Thank You For Your Time
Please Ask Questions