Operations Research and Planning of Radiation Therapy

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Reference to Radiation Therapy

Most pictures and films in this talk from:

**Wolfgang Schlegel and Andreas Mahr:**

**3D Conformal Radiation Therapy:**
A multimedia introduction to methods and techniques,
2001 (Springer Book and CD ROM)
Intensity Modulated Radiation Therapy (IMRT)
Geometry Problem: Where does the gantry stop?
Intensity Problem: How much radiation is sent off?
Realization Problem: How is the radiation modulated?
Contents of this talk

Part I: Horst W. Hamacher
  • Geometry Problem

  • Intensity Problem:
    Multicriteria Approach - First Model

  • Realization Problem:
    Sweep Technique and Linear Time Algorithm
    Technical Restrictions and Network Flow Solutions

Part II: Alexander Scherrer
  Algorithms and Numerics
  Online Treatment Planning - A Decision Support Tool
Geometry Problem: Where does the gantry stop


M. Ehrgott and R. Johnston, Optimisation of Irradiation Directions in IMRT Planning, OR Spectrum 2003 (Talk at this conference)

Mangalika Jayasundara, Spherical location problem (Current Research)
Intensity Problem

Which intensity profiles give the best conformal picture of tumor?
Intensity Problem

Conflicting criteria:
• high radiation in target volume (cancer cells should be killed)
• low radiation in organs at risk (organs should stay functional)

OR Solution Approach:
Compute set of 600 - 1,000 radiation plans which are Pareto solutions of multicriteria linear programs

(Hamacher, Küfer: Discrete Applied Mathematics, 2002 “Inverse Radiation Therapy Planning - A Multicriteria Approach”)
Calculation of Dose Distribution

Discretize

- radiation beams into beam elements (bixels)
- body parts into volume elements (voxels)
Dose Volume Calculation

- $P(i,j) =$ dose in voxel $i$ irradiated from bixel $j$ under unit intensity.

- dose volume $D =$ $P \times (x_j =$ radiation intensity in bixel $j$)

- partitioned into target volume $(k=1)$
  
  $D_1 =$ $P_1 \times$

  and organs at risk $(k=2,\ldots,K)$

  $D_k =$ $P_k \times$
Given: Dose bounds \( L_1 \geq 0 \) and \( U_k \geq 0, \ k = 2, \ldots, K \)

Find: Intensity vector \( x \geq 0 \) satisfying the system of linear inequalities

\[
\begin{align*}
D_1 &= P_1 x \geq L_1 e & \text{(target condition)} \\
D_k &= P_k x \leq U_k e, \ k = 2, \ldots, K, & \text{(risk conditions)}
\end{align*}
\]

System is in general inconsistent !
Such an \( x \) does in general not exist !
Penalize violation of constraints

minimize $\mu_1 F_1(x) + \ldots + \mu_K F_K(x)$ for given weights $\mu_1, \ldots, \mu_K > 0$

- Bortfeld, Schlegel, Brahme, Gustafsson ...

  $F_1(x) = \| L_1 e - P_1 x \|_2$
  $F_k(x) = \| (P_k x - U_k e)_+ \|_2$, $k = 2, \ldots, K$

  \textit{Least square approach}

- Holmes, Mackie, Burkard, ...

  $F_1(x) = \| (L_1 e - P_1 x)_+ \|_\infty$
  $F_k(x) = \| (P_k x - U_k e)_+ \|_\infty$, $k = 2, \ldots, K$

  \textit{Minimax approach}

Disadvantage:
- time consuming
- unsatisfying results
Pareto intensity profile - Simple Model

minimize \(( t_1, t_2, \ldots, t_K )\)

such that

\[ P_1 x + t_1 L_1 e \geq L_1 e \]
\[ P_k x - t_k U_k e \leq U_k e, \quad k = 2, \ldots, K \]

\[ t = ( t_1, t_2, \ldots, t_K ) \geq 0 \]
\[ x \geq 0 \]

• Consistent system
• Too many Pareto solutions!
Pareto intensity profile - Advanced Model

Allow that part of risk organs are destroyed:

\[ EUD = \text{Equivalent Uniform Dose} \]

**Linear model**

- \[ EUD_i(D_i) = (1-\alpha_i) \|D_i\|_{\text{mean}} + \alpha_i \|D_i\|_{\text{max}} \]
  Thieke, Küfer, Bortfeld (2001)

More:  Part II of this presentation!
Realization Problem:  
Integer and Combinatorial Optimization

How are the intensity profiles generated?
Modulate uniform radiation field using Multileaf Collimator (MLC)
Multileaf Collimators: Mechanics
Multileaf Collimators in Action
(Strict) C1P Matrices

\[ Y = \begin{pmatrix} 1 & 1 & 1 \\ 1 & 1 & 1 \\ 1 & 1 \end{pmatrix} \]

Various applications of C1P matrices:

- stops in public transportation
- radiation therapy
C1P-Decomposition of Integer Matrices

Given: Non-negative integer \( m \times n \) matrix \( I = (I_{ij}) \)

Find: „Good“ decomposition of \( I \) into C1P matrices

\[
I = \sum_{t \in T} \alpha_t Y_t
\]

with \( \alpha_t \geq 0 \) for all \( t \).

\( T \) ... index set of all C1P matrices
Sample Decomposition

\[ I = \sum_{t \in T} \alpha_t Y_t \]
C1P-Decomposition in Cancer Therapy
Objective Function of C1P-Dec

\[
\begin{pmatrix}
5 & 3 \\
3 & 5 \\
\end{pmatrix} = 5 \begin{pmatrix}
1 & 0 \\
0 & 0 \\
\end{pmatrix} + 3 \begin{pmatrix}
0 & 1 \\
0 & 0 \\
\end{pmatrix} + 3 \begin{pmatrix}
0 & 0 \\
1 & 0 \\
\end{pmatrix} + 5 \begin{pmatrix}
0 & 0 \\
0 & 1 \\
\end{pmatrix}
\]

\[
\begin{pmatrix}
5 & 3 \\
3 & 5 \\
\end{pmatrix} = 3 \begin{pmatrix}
1 & 1 \\
1 & 1 \\
\end{pmatrix} + 2 \begin{pmatrix}
1 & 0 \\
0 & 1 \\
\end{pmatrix}
\]

Beam-on time: 16
Set-Ups: 4

Beam-on time: 5
Set-Ups: 2
Objective Function of C1P-Dec

minimize \( \sum_{t \in T'} \alpha_t \) (decomposition time)

such that

\[ \sum_{t \in T'} \alpha_t Y_t = I \]

\[ \alpha_t \geq 0 \]

\( Y_t \) C1–matrix

\( T' \subseteq T \)
C1P-Dec is easy if $T' = T$

- C1P is separable into $m$ independent row problems
- Each row problem is equivalent to min cost network flow problem (solvable in linear time: $O(mn)$)

Ahuja, Hamacher 2003

show transparencies
C1P-Dec is easy if $T' = T$

Bortfeld and Boyer (1993): Sweep algorithm
C1P-Dec with $T' \neq T$

- No collision (interleaf motion) between adjacent leaf pairs

- Minimal radiation width: $\text{dist} > \delta$
C1P-Dec with Technical Constraints

Boland, Hamacher, Lenzen, NETWORKS 2003
“Minimizing Beam-On Time in Cancer Radiation Treatment Using Multileaf Collimators”
Definition of Variables

\( l_{it} \in \{0,\ldots,n\} \) \quad \text{position of left leaf in row } i

\( r_{it} \in \{1,\ldots,n+1\} \) \quad \text{position of right leaf in row } i

\[
y_{ijt} = \begin{cases} 0 & 0 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 & 1 & 0 & 0 \end{cases}
\]

Constraints:
\[ r_{it} \geq l_{it} + \delta + 1 \] (radiation width)
\[ r_{i+1,t} \geq l_{it} + 1 \quad \text{and} \quad r_{i-1,t} \geq l_{it} + 1 \] (interleaf motion)
\[ y_{ijt} = 1 \quad \text{iff} \quad l_{it} < j < r_{it} \] (radiation)
Path Representation of C1P

Graph $G = (V,E)$ with

- nodes $V = \{(k,l,r) : r \geq l+\delta+1, k = 1,...,m, l = 0,...,n, r = 1,...,n+1\}$
- edges $E$ satisfying interleaf motion constraints
  
  $(k,l,r) \rightarrow (k+1,p,q)$ if $p \leq r-1$ and $q \geq l+1$

- plus super source and super sink
Source-sink paths correspond to feasible C1P matrices

C1P-matrix network (with $O(mn^2)$ nodes)
Optimal C1P Decomposition corresponds to minimal network flow problem

sending $\alpha_t$ units on path $P_t$ ↔
use C1P matrix $\alpha_t$ times

flow value ↔
decomposition time

minimal flow value = minimal decomposition time
Example

\[ D \]

\[
\begin{array}{cccc}
101 & 102 & 103 & 112 & 113 & 123 \\
201 & 202 & 203 & 212 & 213 & 223 \\
301 & 302 & 303 & 312 & 313 & 323 \\
401 & 402 & 403 & 412 & 413 & 423 \\
\end{array}
\]

\[ D' \]

\[
\begin{array}{cccc}
\alpha = 3 & \alpha = 2
\end{array}
\]

\[
3
\begin{pmatrix}
1 & 0 \\
0 & 1 \\
1 & 1 \\
0 & 1 \\
1 & 0 \\
\end{pmatrix}
+ 2
\begin{pmatrix}
0 & 1 \\
1 & 1 \\
1 & 0 \\
0 & 1 \\
\end{pmatrix}
= 
\begin{pmatrix}
3 & 2 \\
2 & 5 \\
5 & 3 \\
3 & 2 \\
\end{pmatrix}
\]
Which nodes contribute to $I_{ij}$?

Example: $I_{22} = 5$

Constraint:

$$\sum_{l=0}^{j-1} \sum_{r=j+1}^{n+1} \sum_{e \in E_-(i,l,r)} x_e = I_{ij}$$
Consequence

Minimum C1-Decomposition Time problem becomes a network flow problem with side constraints

\[
\sum_{l=0}^{j-1} \sum_{r=j+1}^{n+1} \sum_{e \in E_{-}(i,l,r)} x_e = I_{ij}
\]

Polynomially solvable!
Beam-On-Times of MLC

Instances

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Integrality is important

\[
\sum_{t=1}^{T} \alpha_t + \sum_{t=1}^{T-1} s_{\sigma(t)\sigma(t+1)} \quad \text{minimize delivery time} = \text{beam-on time} + \text{set-up time}
\]

\[
s_{\sigma(t)\sigma(t+1)} = \text{constant set up time}: \quad \sum_{t=1}^{T} \alpha_t + \tau(T - 1)
\]

Minimizing T is NP hard (Burkard 2002)
### Number of Shape Matrices

<table>
<thead>
<tr>
<th>Instance</th>
<th># Matrices</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
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<td>4</td>
<td>5</td>
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<td>14</td>
</tr>
<tr>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
</tr>
</tbody>
</table>

The bar chart above shows the number of shape matrices for each instance.
Delivery Time

![Bar chart showing delivery times for different instances. The chart compares the total delivery time across instances 1 to 15.]
How about integrality?

Flow Model I
137
258

Flow Model II
137\textsuperscript{1}

irradiation arcs

0 1 2 3 4 5 6 7
137\textsuperscript{2}

258\textsuperscript{1}

Side constraints are simpler as before:
outflow copy\textsuperscript{1} = inflow copy\textsuperscript{2}
Introduce
lower = upper bound = $I_{ij}$
on each irradiation arc
from (i,j-1) to (i,j)!

$I = \begin{pmatrix} 3 & 2 \\ 2 & 5 \\ 5 & 3 \\ 3 & 2 \end{pmatrix}$
Integral Solvability

Find flow with minimal value satisfying capacities and side constraint outflow copy\(^1\) = inflow copy\(^2\)

Solvable by negative “cycle” argument!

(Existence result - no combinatorial algorithm)
Find Algorithm with Improved Complexity

Algorithm of Baatar and Hamacher (2003)

Idea:

Represent each possible left leaf and each possible right leaf as node of a network \((2(m(n+1)))\) many nodes

Shape matrices = Paths in the network

Decomposition = Network flow
Example of Baatar Network

nodes:

1,1  1,2  1,3  potential left leaf position  in channel 1
1,1  1,2  1,3  potential right leaf position
2,1  2,2  2,3  potential left leaf position  in channel 2
2,1  2,2  2,3  potential right leaf position
3,1  3,2  3,3  potential left leaf position  in channel 3
3,1  3,2  3,3  potential right leaf position
4,1  4,2  4,3  potential left leaf position  in channel 4
4,1  4,2  4,3  potential right leaf position
Example of Baatar Network

edges:

1,1 → 1,2 → 1,3

2,1 → 2,2 → 2,3

3,1 → 3,2 → 3,3

4,1 → 4,2 → 4,3

leaf positions

1 2 3

cells

Example of Baatar Network
Example of Baatar Network

paths:

leaf positions

$$
\begin{bmatrix}
1 & 0 \\
0 & 1 \\
1 & 1 \\
0 & 1 
\end{bmatrix}
$$
Example of Baatar Network

flows:

\[
\begin{pmatrix}
1 & 0 \\
0 & 1 \\
1 & 1 \\
0 & 1
\end{pmatrix}
\]
Flow ⇒ Intensity Matrix

flows:

\[
\begin{pmatrix}
1 & 0 \\
0 & 1 \\
1 & 1 \\
0 & 1
\end{pmatrix} + 3 \begin{pmatrix}
0 & 1 \\
1 & 1 \\
1 & 1 \\
1 & 0
\end{pmatrix} = \begin{pmatrix}
2 & 3 \\
3 & 5 \\
5 & 5 \\
3 & 2
\end{pmatrix}
\]
Intensity Matrix ⇒ Flow

Integer matrix $I = (I_{ij})$ is given.

Compute for all $i=1,...,m$ and all $j=1,...,n+1$

$$\text{left}_{ij} = \max\{l_{ij} - l_{i,j-1}, 0\}$$

and

$$\text{right}_{ij} = \max\{l_{i,j-1} - l_{i,j}, 0\}$$

(with $I_{i0}=I_{i,n+1}=0$)
Intensity Matrix $\Rightarrow$ Flow

\[
left_{ij} = \max\{l_{ij} - l_{i,j-1}, 0\}
\]

\[
\begin{pmatrix}
3 & 2 \\
2 & 5 \\
5 & 3 \\
3 & 2
\end{pmatrix}
\]

\[
right_{ij} = \max\{l_{i,j-1} - l_{i,j}, 0\}
\]

\[
\begin{pmatrix}
0 & 1 & 2 \\
0 & 0 & 5 \\
0 & 2 & 3 \\
0 & 1 & 2
\end{pmatrix}
\]
Result:
Any MLC realization of a given intensity matrix $I$ can be written as flow in the Baatar network with

\( \text{supply left}_{ij} + w_{ij} \)
and

\( \text{demand right}_{ij} + w_{ij} \)
satisfying additional side constraints forbidding interleaf motion.
Intensity Matrix ⇒ Flow

\[
\begin{align*}
\text{min} & \quad T \\
\text{subject to} & \quad T = \text{left}_{i1} + \sum_{j=2}^{n} (\text{left}_{ij} + w_{ij}), \quad \forall i = 1, \ldots, m \\
& \quad \sum_{j=2}^{k} (\text{right}_{ij} + w_{ij}) \leq \text{left}_{i+1,1} + \sum_{j=2}^{k} (\text{left}_{i+1,j} + w_{ij}), \quad \forall i = 1, \ldots, m-1, \quad k = 2, \ldots, n \\
& \quad \text{left}_{i1} + \sum_{j=2}^{k} (\text{left}_{ij} + w_{ij}) \geq \sum_{j=2}^{k} (\text{right}_{i+1,j} + w_{i+1,j}), \quad \forall i = 1, \ldots, m-1, \quad k = 2, \ldots, n \\
& \quad w_{ij} \geq 0, \quad \forall i = 1, \ldots, m, \quad j = 2, \ldots, n \\
& \quad T \geq 0
\end{align*}
\]
Intensity Matrix ⇒ Flow

Result: Minimizing $\sum_j w_{ij}$

such that flow exists satisfying side constraints
yields minimal beam-on-time decomposition.

Solvable by a linear program with mn many variables!

• Solvable in polynomial time
• Faster than Boland-Hamacher network flow approach
Modifications Including Set-Up Times

\[
\sum_{t=1}^{T} \alpha_t + \sum_{t=1}^{T-1} s_{\sigma(t)\sigma(t+1)} \quad \text{minimize delivery time with constant set-up time (i.e. } s_{\sigma(t)\sigma(t+1)} = \text{const} \text{)}
\]

Use same approach with integer variables counting the number of shape matrices used.
Modifications Including Set-Up Times

\[ \sum_{t=1}^{T} \alpha_t + \sum_{t=1}^{T-1} \sigma(t) \sigma(t+1) \]

minimize delivery time with sequence dependent set-up time

Use arc-path formulation of flow

Use \( s_{\sigma(t)\sigma(t+1)} \) as data of a traveling salesman problem.

Current Research
Summary of Part I

• Several subproblems of radiation therapy have been successfully tackled
  • choice of radiation angle
  • representative system of Pareto solutions
  • minimizing beam on time

• Several results are interesting independent of application
  • integer solvability of C1 decomposition
  • NP completeness of cardinality decomposition

• Lots of open problems, e.g.
  • integrated system (angles + intensity profiles + realization)
  • efficient algorithms for (constant and variable) set-up time
KL - Literature:


- Boland, N., H.W. Hamacher, and F. Lenzen, 2002: “Minimizing beam-on time in cancer radiation treatment using multileaf collimators” *NETWORKS*