Optimization in Intensity Modulated Radiation Therapy (IMRT)

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OUTLINE

• Radiation therapy
• Intensity modulated radiation therapy
• Key planning problems
  – Fluence map optimization
  – Beam angle optimization
  – Multi-leaf collimator optimization
Radiation Therapy

- Radiation therapy (also called radiotherapy, x-ray therapy, or irradiation) is the use of ionizing radiation to kill cancer cells and shrink tumors.
- About half of all cancer patients are treated with radiation therapy.
- Radiation therapy injures or destroys cells in the area being treated (the “target tissue”) by damaging their genetic material, making it impossible for these cells to continue to grow and divide.
- Although radiation damages both cancer cells and normal cells, most normal cells can recover from the effects of radiation and function properly.
- Radiation therapy may be external or internal. External radiation, the type most often used, comes from a machine outside the body. Internal radiation is implanted into or near the tumor in small capsules or other containers.
- Radiation therapy planning: Determine dose delivery so as to damage as many cancer cells as possible, while limiting harm to nearby healthy tissue.

Radiation Oncology in a Nutshell

CT Simulation → Planning → Delivery/Verification
Anatomy Map → Create personalized treatment plan → Deliver the radiation plan over 6 weeks
IMRT

- A form of external beam therapy
- Radiation delivered from a linear accelerator
- Beam head can swivel and bed can move offering many degrees of freedom
- Beam head has a mask called a “multileaf collimator” (MLC) which can be used to shape the beam
- By several deliveries overlaying different shapes with different intensities we can get desired dosage of the tumor
MLC

MLC in Action
Beamlets

- Since the beam can be positioned at many different angles, we can imagine we have several “stationary” beams
- Conceptually MLC discretizes each beam into several small “beamlets”
- Furthermore, by possibly overlaying, we can control the intensity of each beamlet independently

![Desired dose intensity](image1)

\[
\begin{array}{ccc}
0 & 0 & 1 \\
0 & 3 & 1 \\
0 & 3 & 5 \\
0 & 0 & 0 \\
\end{array}
\]

\[
\begin{array}{ccc}
1 & 1 & 1 \\
1 & 1 & 1 \\
2 & 2 \\
2 & 2 \\
2 \\
\end{array}
\]

Delivered by overlaying doses of varying intensities and shapes

Is this best way? This is an interesting optimization problem which we will discuss later… first we will discuss how to come up with the desired beamlet intensities to match prescription.

Planning Process

- Several CT scan slices of the tumor area are taken
- Clinician marks tumors and critical organs and prescribes dosage limits
  - e.g. Dose on target volume should be at least 70 Gray (Joules/Kg)
- Dose calculation:
  - CT scan slices are used to construct a 3D model of the tumor volume
  - The volume is discretized into “voxels”
  - Each beam (angle) is discretized into “beamlets”
  - Physics models are used to compute the dose deposition per intensity for each voxel-beamlet pair

Dose volume matrix

\[D_{ij} = \text{Dose deposited in voxel } i \text{ per unit intensity of beamlet } j\]
IMRT Planning Problem

- Beam angle optimization: What are the best beams (angles)?
- Fluence map optimization: For a given set of beams (angles), what is the intensity of each beamlet?
- MLC optimization: Given a fluence map, what are the best MLC “shapes” to deliver it?

So that the prescription requirements for the tumor and critical organs are satisfied.

A simple FMO model

For a given set of beams, find beamlet intensities so as to satisfy dose restrictions on tumor and critical organs while minimizing total dose deposited to normal structures.

Decision variables: beamlet intensities

Constraints:  
dose on tumor >= required dose  
dose on critical organs <= maximum dose  
non-negativity

Objective: total dose on normal structures
**LP Formulation**

**Sets**
- $I$: Set of all voxels
- $T$: Set of tumor voxels ($T \subseteq I$)
- $C$: Set of critical organ voxels ($C \subseteq I$)
- $J$: Set of beamlets

**Variables**
- $x_{j}$: Intensity of beamlet $j$
- $z_{i}$: Total dose deposited on voxel $i$

**Parameters**
- $d_{ij}$: Dose/intensity for voxel $i$ and beamlet $j$
- $d_{T}$: Minimum dose required on tumor voxel
- $d_{C}$: Maximum dose allowed on critical voxels

\[
\begin{align*}
\text{min} & \quad \sum_{i \in I \setminus T} z_{i} \\
\text{s.t.} & \quad z_{i} = \sum_{j \in J} d_{ij} x_{j} \quad \forall \ i \in I \\
& \quad z_{i} \geq d_{T} \quad \forall \ i \in T \\
& \quad z_{i} \leq d_{C} \quad \forall \ i \in C \\
& \quad x_{j} \geq 0 \quad \forall \ j \in J
\end{align*}
\]

**Problem Size**

- Each beam (position) has a rectangular aperture of size 10cmX10cm to 20cmX20cm which is discretized into beams of size 1cmX1cm
  \(\Rightarrow\) 100 to 400 beamlets/beam X 4 to 10 beams = 400 to 4000 beamlets
- Each voxel is typically 4mmX4mmX4mm to 8mmX8mmX8mm
  \(\Rightarrow\) 10,000 to 100,000 voxels
- Resulting LP has tens – hundreds of thousands of variables and hundreds of thousands of constraints
- Typically can be solved using standard packages on standard desktops in order of 1-3 minutes.
Dose deposition

- As the radiation from a beamlet passes through the dose dissipates
- For each organ (set of voxels) and a beamlet we have a dose distribution over the voxels

![Graph showing dose distribution]

Ideal

- No critical organ voxel should receive more than 10 Gy
- All tumor voxels should receive at least 70 Gy

Actual

- 45% of the critical voxels receive more than 10 Gy
- Only 75% of the tumor voxels receive more than 70 Gy
Dose Volume Histogram (DVH) Constraints

- Need to sacrifice some critical tissue to guarantee tumor destruction
- Most common physician prescription are constraints such as
  “At least 95% of the tumor voxels should receive >= 70 Gray”
  “No more than 30% of critical organ voxels should receive >= 10 Gy”

Integer Programming Formulation

- The DVH constraints can be imposed by introducing binary variables.
  E.g. “No more than 30% of critical organ voxels should receive >= 10 Gy” can be modeled as:

\[
10y_i \leq z_i \leq 9.99(1 - y_i) + 10^{0.9} y_i \quad \forall i \in C
\]

\[
\sum_{i \in C} y_i \leq 0.30 |C|, \quad y_i \in \{0,1\} \quad \forall i \in C
\]

- Need to introduce as many binary variables as the number of voxels, 10000-100000!!!
- The resulting IP is extremely difficult to solve.
“Borrowing” from the finance world

- A standard financial constraint: “The probability that the loss of my portfolio exceeds 10 million should be less than 30%”
- In other words: The 70% quantile of the losses (known as 70% value at risk) should be less than 10 million
- Constraint: 70% VaR ≤ 10 Million

Conditional Value at Risk

- CVaR = Conditional expectation over the right tail of VaR

- VaR ≤ 10 Million can be enforced by CVaR ≤ 10 Million
- The CVaR constraint can be enforced using linear programming
Beam Angle Optimization

- How to select the set of beam (angles) to use in the FMO problem?
- Enumerate:
  - 360 possible angles
  - Chose 20 positions
  - Possibilities = 3.2E32 (320 nonillion) > no. of stars = 7E22
  - For each possibility, we need to solve an FMO LP
  - If each LP takes 0.0001secs we would need 1E22 years > age of the universe (1.3E10) to pick the best configuration

BAO: A scoring approach

- Assume all 360 beams are used, and solve the FMO LP
- For each beam, calculate the total dose delivered to tumor and the total dose delivered to critical organs
- Solve an integer program to select the subset of 20 beams to maximize dose on tumor and restrict the dose on critical organs to some threshold
- This IP solves in a few minutes
- Other scores for the beams can also be used
- Solve the FMO for the final set of beams to get the final beamlet intensities

\[
\max \sum_{k=1}^{360} T_k y_k \\
\text{s.t.} \quad \sum_{k=1}^{360} C_k y_k \leq M \\
\sum_{k=1}^{360} y_k = 20 \\
y_k \in \{0,1\} \quad \forall k
\]
MLC Optimization

- For each of the selected beams (by BAO) we have the needed intensity required for each beamlet (by FMO)
- We need the MLC shapes to deliver this intensity profile

```
0 0 0 1
0 3 3 1
0 3 5 1
0 0 0 0
```

Desired dose intensity e.g. required intensity of beamlet (2,2) is 3 units.

```
1 1 1
1 1 1
```

Delivered by overlaying doses of varying intensities and shapes

A Network Approach

- Solve each row separately (this is a simplification)

Possible shapes

<table>
<thead>
<tr>
<th>Possible shapes</th>
<th>A possible solution</th>
<th>Another possibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 4 1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

```
2 4 1
```

"Beam-on Time" = 7

```
2 4 1
```

"Beam-on Time" = 4

```
2 4 1
```

= 2 4 1

= 2 4 1
A Network Flow Formulation

• One node for each cell + one last dummy node
• Add arc \((i,j)\) if there is a shape that is open in cell \(i\) and first closes in cell \(j\) \((i<j)\)
• The supply at node 1 is the required intensity in cell 1, the supply in the last dummy node is 0
• The supply at node 2 is the required intensity at 2 – required intensity at 1
• … the supply at node \(j\) is the required intensity at \(j\) – required intensity at \((j-1)\)
• The cost/unit flow on each arc is 1

A possible solution

```
A possible solution
2 2 2 2
4 4 4 4
1 1 1 1
0 0 0 0
0 0 0 0
= 2 4 1
```

Possible shapes

```
(1,2)
(2,3)
(3,4)
(1,3)
(2,4)
(1,4)
```

Another possibility

```
Another possibility
0 0 0 0
1 1 1 1
0 0 0 0
2 2 2 2
1 1 1 1
0 0 0 0
= 2 4 1
```

A Network Approach

• Solving a minimum cost network flow problem over the constructed network solves the minimum beam on time problem for a single row
MLC Optimization

- The network flow problem (for the one row case) can be solved extremely fast
- Constraint link the rows together so we cannot really solve them separately
- A decomposition scheme is used to

Concluding Remarks

- Optimization models and algorithms are routinely used for IMRT planning and delivery
- A key challenge is the large scale nature of the problem
- Ideally we would like to solve the full problem in an integrated manner but is impossible with current algorithmic and computational technologies
- The decomposed scheme gives very good solutions
- New equipment capabilities give rise more challenging and interesting problems
  - VMAT: The beam head swivels around the patient continuously while delivering radiation