RADIATION THERAPY
An Application of Linear Optimization
Cancer

- Cancer is the second leading cause of death in the United States, with an estimated 570,000 deaths in 2013

- Over 1.6 million new cases of cancer will be diagnosed in the United States in 2013

- In the world, cancer is also a leading cause of death – 8.2 million deaths in 2012
Radiation Therapy

- Cancer can be treated using radiation therapy (RT)
- In RT, beams of high energy photons are fired into the patient that are able to kill cancerous cells
- In the United States, about half of all cancer patients undergo some form of radiation therapy
History of Radiation Therapy

• X-rays were discovered by Wilhelm Röntgen in 1895 (awarded the first Nobel Prize in Physics in 1901)
  • Shortly after, x-rays started being used to treat skin cancers

• Radium discovered by Marie and Pierre Curie in 1898 (Nobel Prize in Chemistry in 1911)
  • Began to be used to treat cancer, as well as other diseases
History of Radiation Therapy

• First radiation delivery machines (linear accelerators) developed in 1940

• Computed tomography (CT) invented in 1971

• Invention of intensity-modulated radiation therapy (IMRT) in early 1980s

Machines and MRI scan images removed due to copyright restrictions.
IMRT

• To reach the tumor, radiation passes through healthy tissue, and damages both healthy and cancerous tissue

• Damage to healthy tissue can lead to undesirable side effects that reduce post-treatment quality of life

• We want the dose to “fit” the tumor as closely as possible, to reduce the dose to healthy tissues
IMRT

- In IMRT, the intensity profile of each beam is non-uniform

- By using non-uniform intensity profiles, the three-dimensional shape of the dose can better fit the tumor

- Let’s see what this looks like
Using Traditional Radiation Therapy
Using IMRT
Using IMRT
Designing an IMRT Treatment

• Fundamental problem:
  • How should the beamlet intensities be selected to deliver a therapeutic dose to the tumor \textit{and} to minimize damage to healthy tissue?
The Data

• Treatment planning starts from a CT scan
  • A radiation oncologist contours (draws outlines) around the tumor and various critical structures
  • Each structure is discretized into voxels (volume elements) – typically 4 mm x 4 mm x 4 mm

• From CT scan, can compute how much dose each beamlet delivers to every voxel
Small Example – 9 Voxels, 6 Beamlets

- Minimize total dose to healthy tissue (spinal + other)
- Constraints: tumor voxels at least 7Gy (Gray), spinal cord voxel at most 5Gy
**Dose to Each Voxel – Beamlets 1, 2, 3**

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<thead>
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Beam 1

- Beamlet 1
- Beamlet 2
- Beamlet 3
### Dose to Each Voxel – Beamlets 4, 5, 6

#### Beam 2

<table>
<thead>
<tr>
<th>Beamlet 4</th>
<th>Beamlet 5</th>
<th>Beamlet 6</th>
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Small Example – The Model

Decisions: $x_1, x_2, x_3, x_4, x_5, x_6$

minimize

$$(1 + 2)x_1 + (2 + 2.5)x_2 + 2.5x_3 + x_4 + 2x_5 + (1 + 2 + 1)x_6$$

$2x_1 + x_5 \geq 7$

$x_2 + 2x_4 \geq 7$

$1.5x_3 + x_4 \geq 7$

$1.5x_3 + x_5 \geq 7$

$2x_2 + 2x_5 \leq 5$

$x_1, x_2, x_3, x_4, x_5, x_6 \geq 0$
A Head and Neck Example

- We will test out this approach on a head-and-neck case
  - Total of 132,878 voxels
  - One target volume (9,777 voxels)
  - Five critical structures: spinal cord, brain, brain stem, parotid glands, mandible (jaw)
- 5 beams; each beam ~60 beamlets (1cm x 1cm) for a total of 328 beamlets
Treatment Plan Criteria

- Dose to whole tumor between 70Gy and 77Gy
- Maximum spinal cord dose at most 45Gy
  - Significant damage to any voxel will result in loss of function
- Maximum brain stem dose at most 54Gy
- Maximum mandible dose at most 70Gy
- Mean parotid gland dose at most 26Gy
  - Parotid gland is a parallel structure: significant damage to any voxel does not jeopardize function of entire organ
The Optimization Problem

minimize Total healthy tissue dose

subject to $70\text{Gy} \leq \text{Dose to voxel } v \leq 77\text{Gy}$, for all tumor voxels $v$,

$\text{Dose to voxel } v \leq 45\text{Gy}$, for all spinal cord voxels $v$,

$\text{Dose to voxel } v \leq 54\text{Gy}$, for all brain stem voxels $v$,

$\text{Dose to voxel } v \leq 70\text{Gy}$, for all mandible voxels $v$,

$\frac{\text{Total parotid dose}}{\text{Num. parotid voxels}} \leq 26\text{Gy}$,

$w_b \geq 0$, for all beamlets $b$. 
Solution

![Graph showing radiation therapy dose response](image)

- **Brain**
- **Brain stem**
- **Mandible**
- **Parotid gland**
- **Spinal cord**
- **Target**

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Exploring Different Solutions

- Mean mandible dose was 11.3 Gy – how can we reduce this?
- One approach: modify objective function
  - Current objective is the sum of the total dose
    \[ T_B + T_{BS} + T_{SC} + T_{PG} + T_M \]
  - Change objective to
    \[ T_B + T_{BS} + T_{SC} + T_{PG} + 10 \times T_M \]
  - Set mandible weight from 1 (current solution) to 10
New Solution
Sensitivity

• Another way to explore tradeoffs is to modify constraints
  • For example: by relaxing the mandible maximum dose constraint, we may improve our total healthy tissue dose
  • How much does the objective change for different constraints?
Shadow Prices

<table>
<thead>
<tr>
<th>Organ</th>
<th>Highest shadow price</th>
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<tbody>
<tr>
<td>Parotid gland</td>
<td>0</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>96.911</td>
</tr>
<tr>
<td>Brain stem</td>
<td>0</td>
</tr>
<tr>
<td>Mandible</td>
<td>7399.72</td>
</tr>
</tbody>
</table>

- Parotid gland and brain stem have shadow prices of zero
  - Modifying these constraints is not beneficial
- Mandible has highest shadow price
  - If slight increase in mandible dose is acceptable, total healthy tissue dose can be significantly reduced
IMRT Optimization in Practice

• Radiation machines are connected to treatment planning software that implements and solves optimization models (linear and other types)
  • Pinnacle by Philips
  • RayStation by RaySearch Labs
  • Eclipse by Varian
Extensions

- Selection of beam angles
  - Beam angles can be selected jointly with intensity profiles using **integer optimization** (topic of next week)

- Uncertainty
  - Often quality of IMRT treatments is degraded due to uncertain organ motion (e.g., in lung cancer, patient breathing)
  - Can manage uncertainty using a method known as **robust optimization**
Efficiency

- Manually designing an IMRT treatment is inefficient and impractical

- Linear optimization provides an efficient and systematic way of designing an IMRT treatment
  - Clinical criteria can often be modeled using constraints
  - By changing the model, treatment planner can explore tradeoffs
Clinical Benefits

• Ultimately, IMRT benefits the patient

  • In head and neck cancers, saliva glands were rarely spared prior to IMRT; optimized IMRT treatments spare saliva glands

  • In prostate cancer, optimized IMRT treatments reduce toxicities and allow for higher tumor doses to be delivered safely

  • In lung cancer, optimized IMRT reduces risk of radiation-induced pneumonitis