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
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 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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Beamlet 1
Beamlet 2
Beamlet 3

Beam 1
Dose to Each Voxel – Beamlets 4, 5, 6

Beam 2

Beamlet 4  Beamlet 5  Beamlet 6

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**Small Example – The Model**

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<td>Beamlet 2</td>
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<td>2</td>
<td>2.5</td>
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<td>Beamlet 3</td>
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Decisions: $x_1, x_2, x_3, x_4, x_5, x_6$

**minimize**

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


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<th>Beamlet 4</th>
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<tr>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td>Beamlet 5</td>
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<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td>Beamlet 6</td>
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Constraints:

$2x_1 + x_5 \geq 7$

$x_2 + 2x_4 \geq 7$

$1.5x_3 + x_4 \geq 7$

$1.5x_3 + x_5 \geq 7$

$2x_2 + 2x_5 \leq 5$

$x_1, x_2, x_3, x_4, x_5, x_6 \geq 0$
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 \( v, \)
\( \frac{\text{Total parotid dose}}{\text{Num. parotid voxels}} \leq 26\text{Gy}, \)
\( w_b \geq 0, \) for all beamlets \( b. \)
Solution
Exploring Different Solutions

• Mean mandible dose was 11.3Gy – 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

![Graph showing dose-response curves for different structures in radiation therapy.](image)
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>
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<th>Organ</th>
<th>Highest shadow price</th>
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<tr>
<td>Parotid gland</td>
<td>0</td>
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<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>
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- 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