

RADIATION THERAPY

An Application of Linear Optimization

15.071x – The Analytics Edge

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

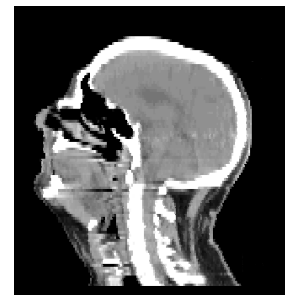
History of Radiation Therapy

- 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



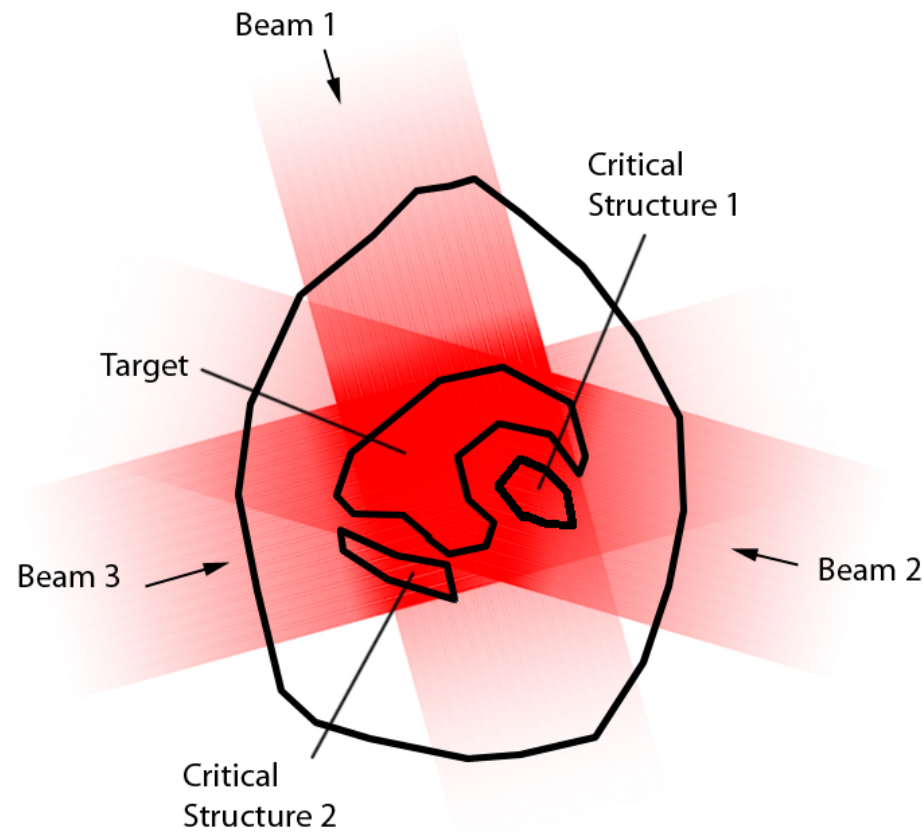
- To reach the tumor, radiation passes through healthy tissue, and damages both healthy and cancerous tissue
- Damage to healthy tissue can lead to undesirable side effects that reduce post-treatment quality of life
- We want the dose to “fit” the tumor as closely as possible, to reduce the dose to healthy tissues

IMRT

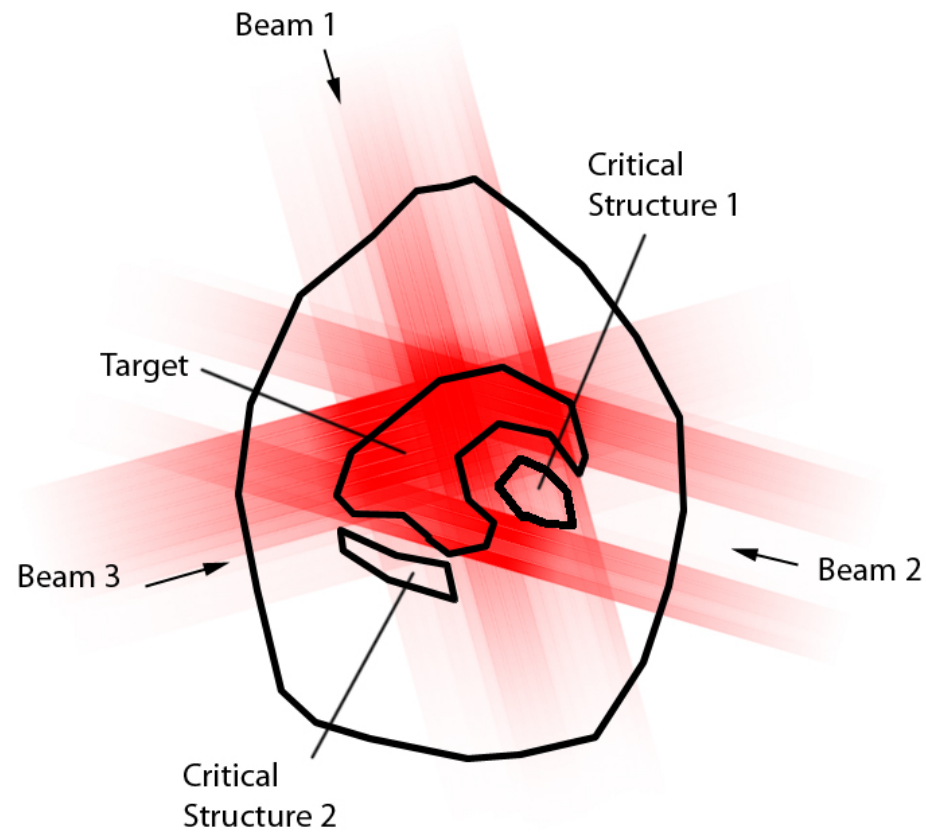


- In IMRT, the intensity profile of each beam is non-uniform
- By using non-uniform intensity profiles, the three-dimensional shape of the dose can better fit the tumor
- Let's see what this looks like

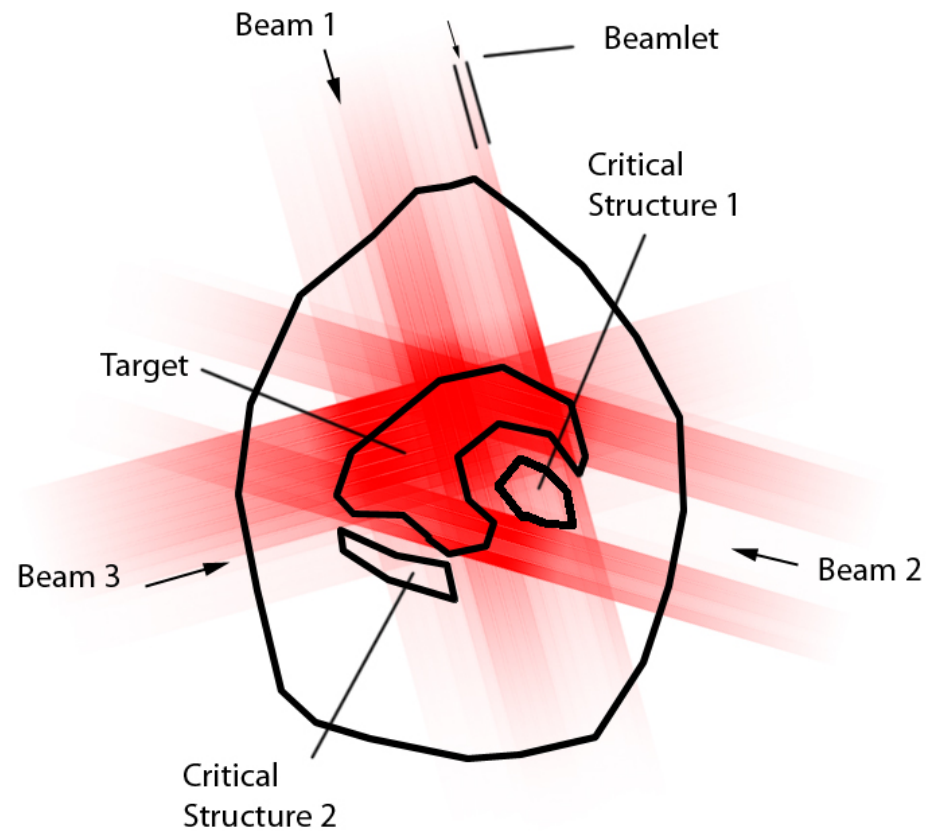
Using Traditional Radiation Therapy



Using IMRT



Using IMRT



Designing an IMRT Treatment



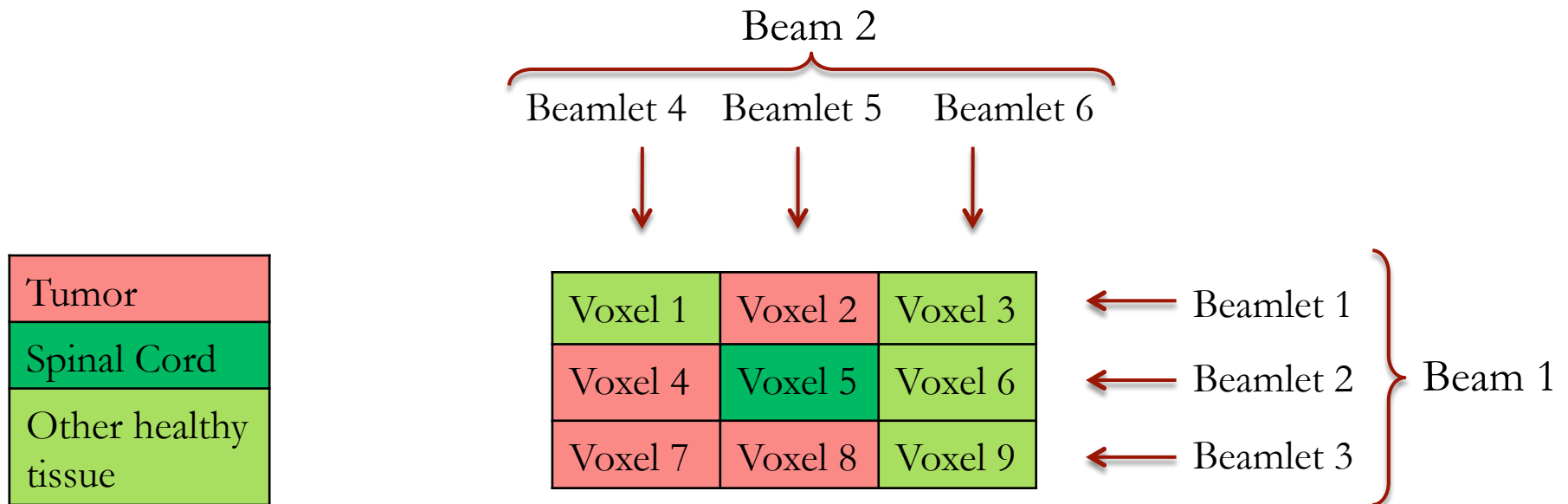
- Fundamental problem:
 - How should the beamlet intensities be selected to deliver a therapeutic dose to the tumor *and* to minimize damage to healthy tissue?

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

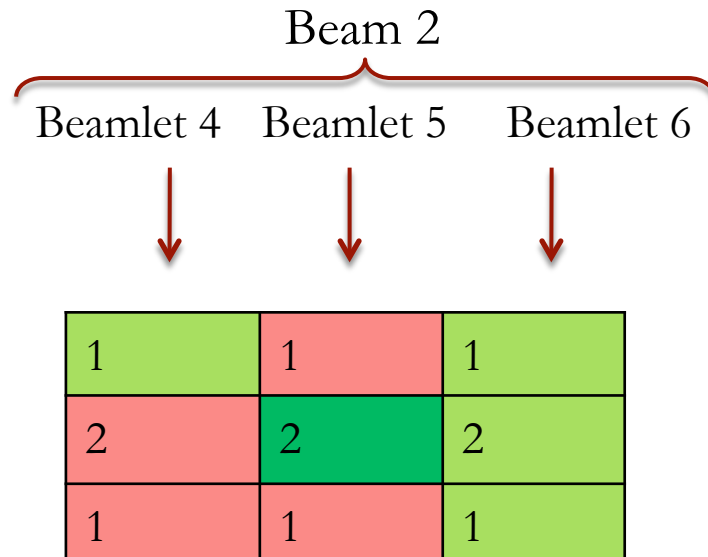
Dose to Each Voxel – Beamlets 1, 2, 3

1	2	2
1	2	2.5
1.5	1.5	2.5

← Beamlet 1
← Beamlet 2
← Beamlet 3

} Beam 1

Dose to Each Voxel – Beamlets 4, 5, 6



Small Example – The Model

1	2	2
1	2	2.5
1.5	1.5	2.5

← Beamlet 1

← Beamlet 2

← Beamlet 3

Beamlet 4 Beamlet 5 Beamlet 6

1	1	1
2	2	2
1	1	1

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

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

$$2x_1 + x_5 \geq 7$$

$$x_2 + 2x_4 \geq 7$$

$$1.5x_3 + x_4 \geq 7$$

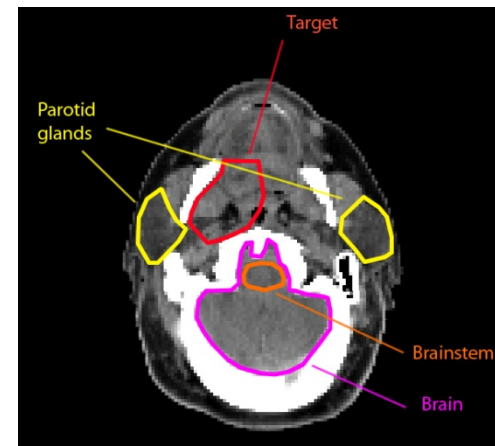
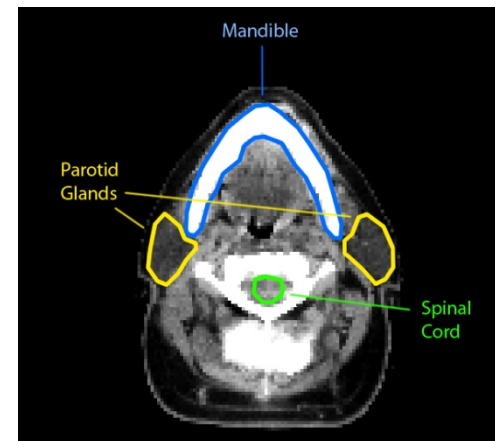
$$1.5x_3 + x_5 \geq 7$$

$$2x_2 + 2x_5 \leq 5$$

$$x_1, x_2, x_3, x_4, x_5, x_6 \geq 0$$

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 ,

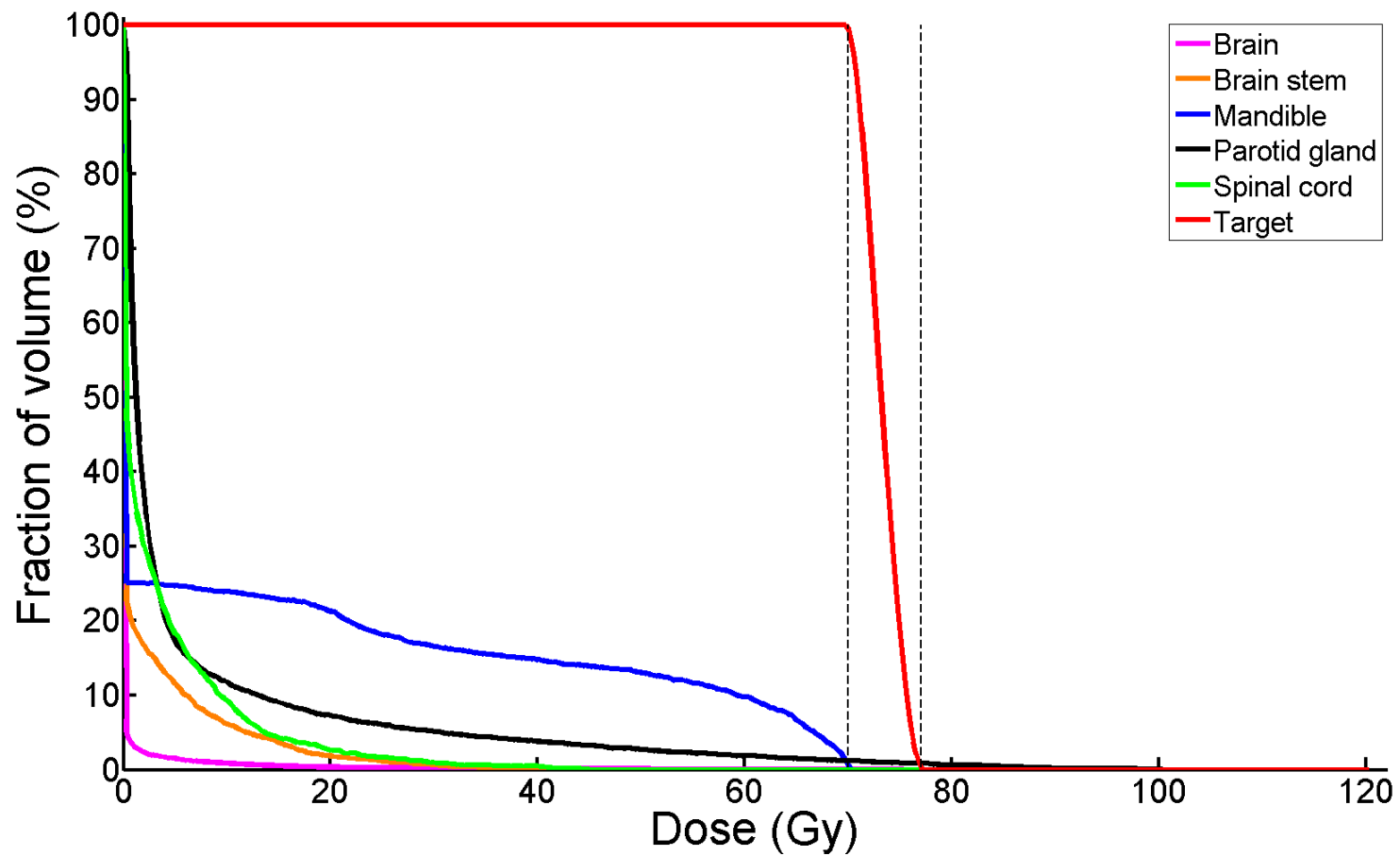
$\text{Dose to voxel } v \leq 54\text{Gy}$, for all brain stem voxels v ,

$\text{Dose to voxel } v \leq 70\text{Gy}$, 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 .

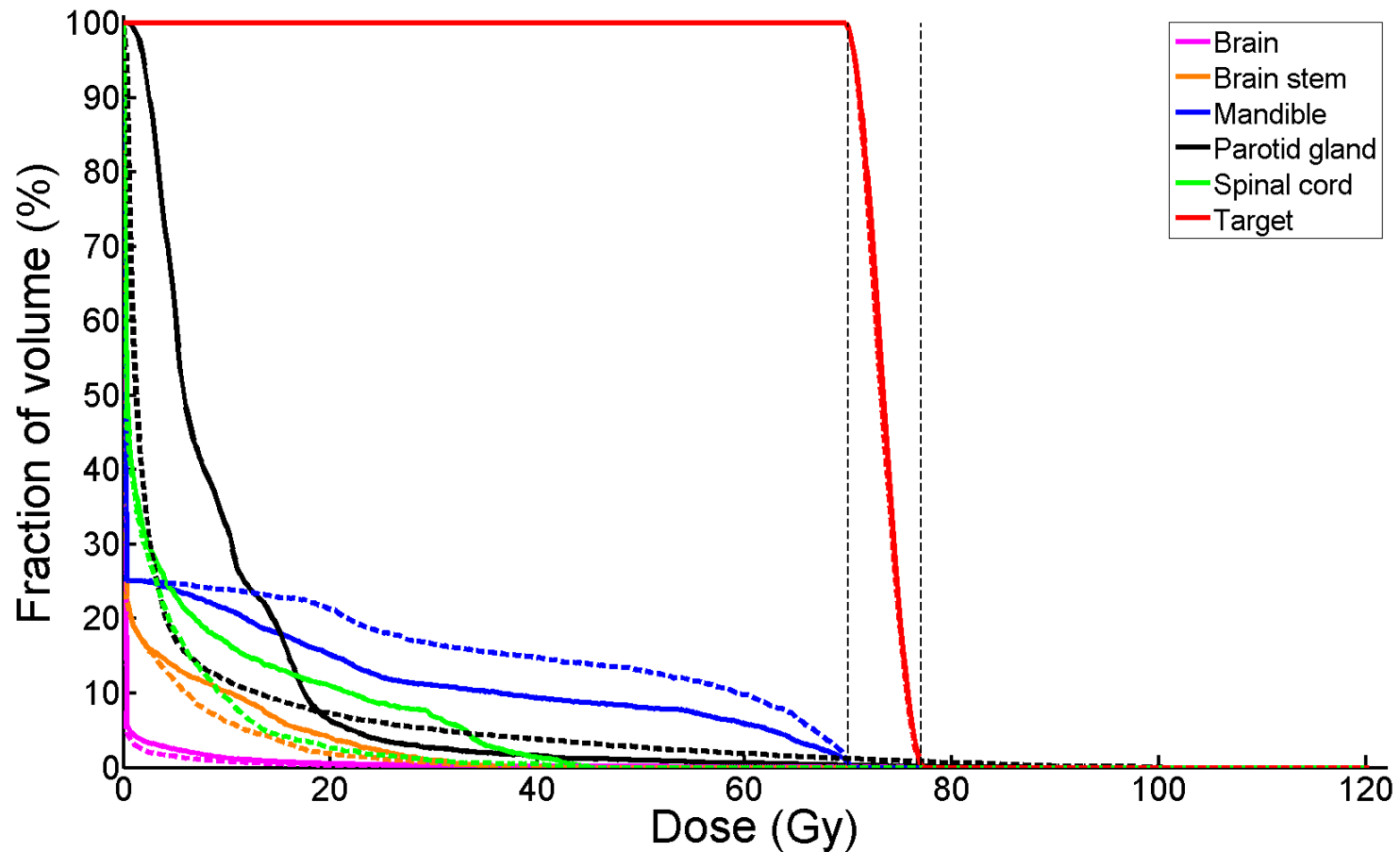
Solution



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



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

Organ	Highest shadow price
Parotid gland	0
Spinal cord	96.911
Brain stem	0
Mandible	7399.72

- 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 Phillips
 - 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