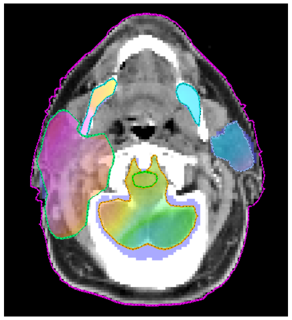


RADIATION THERAPY

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

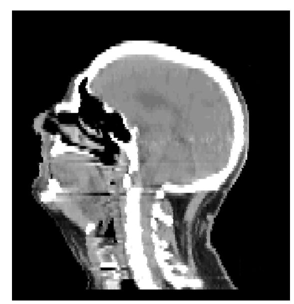
- Cancer can be treated using radiation therapy (RT)
- In RT, beams of high energy photons are fired into the patient that are able to kill cancerous cells
- In the United States, about **half of all cancer patients** undergo some form of radiation therapy

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**



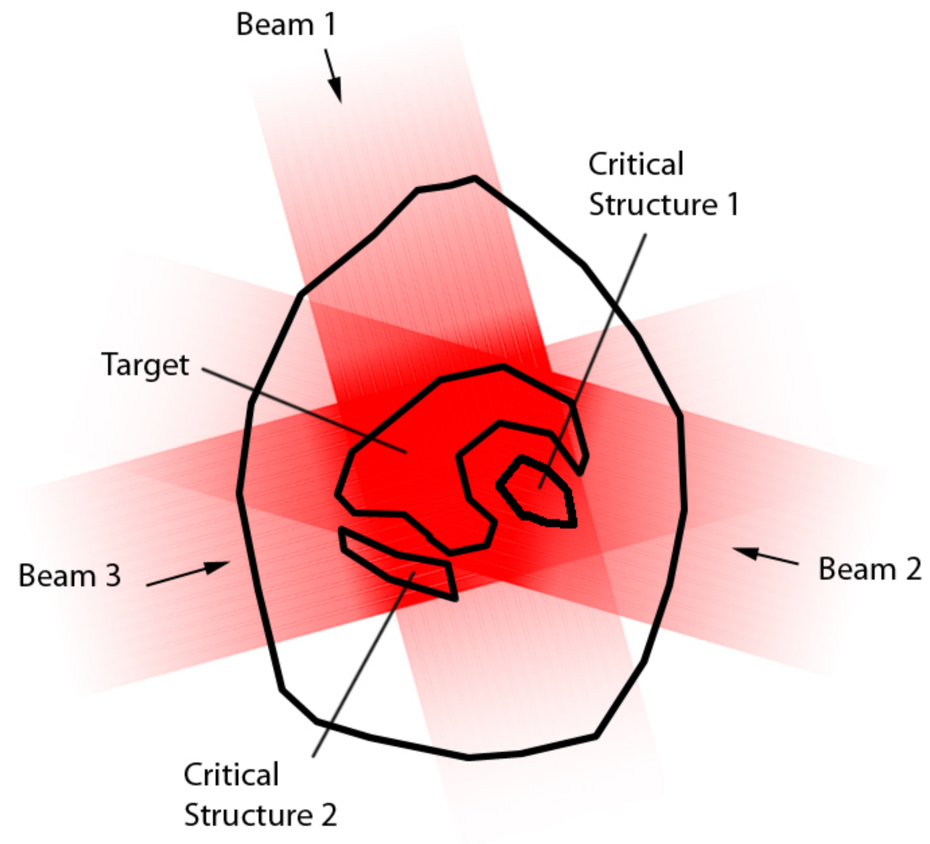
IMRT

- 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

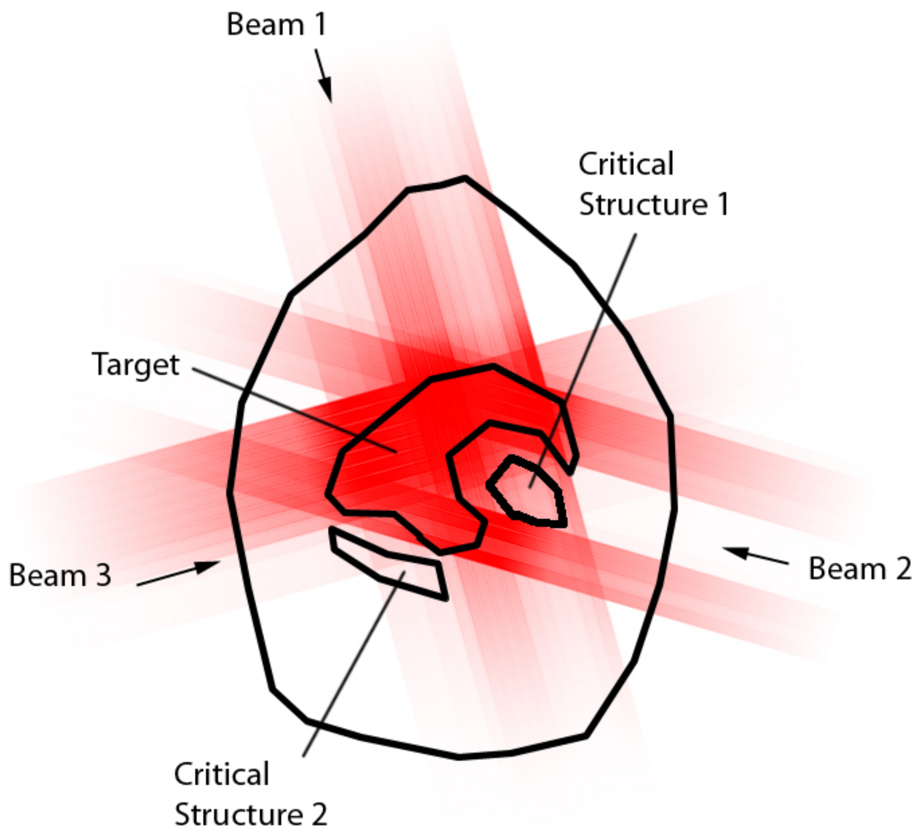
IMRT

- 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

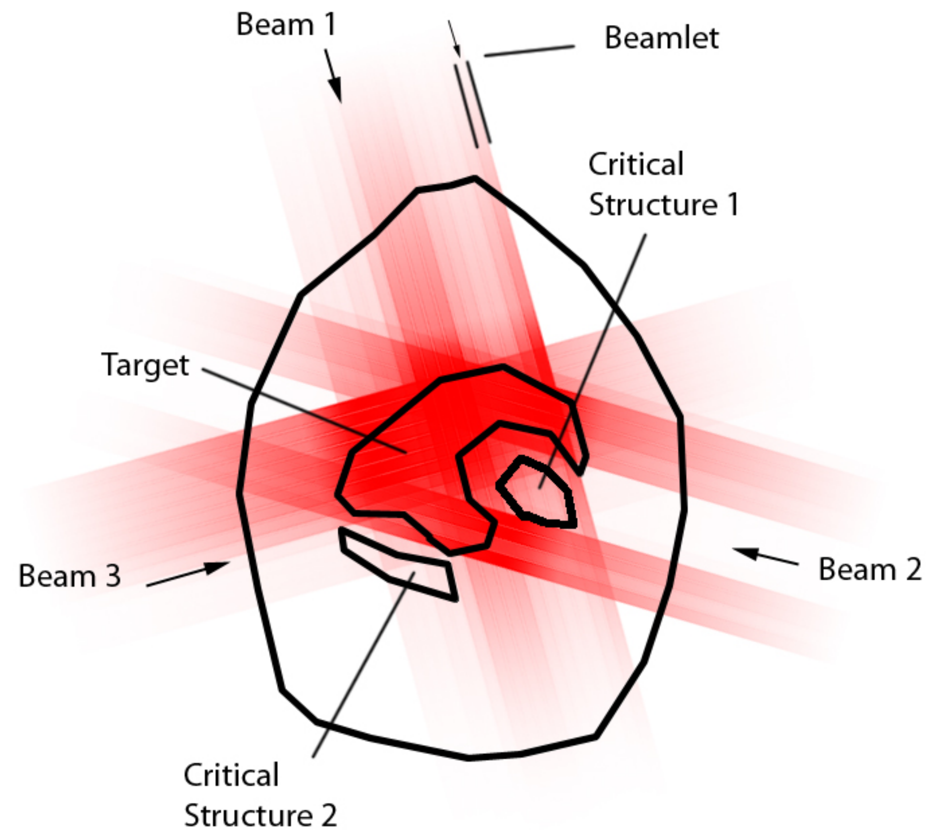
Using Traditional Radiation Therapy



Using IMRT


Beam 1
Critical
Structure 1
Target
Beam 3
Beam 2
Critical
Structure 2

Using IMRT


Beam 1
Beamlet
Critical
Structure 1
Target
Beam 3
Beam 2
Critical
Structure 2

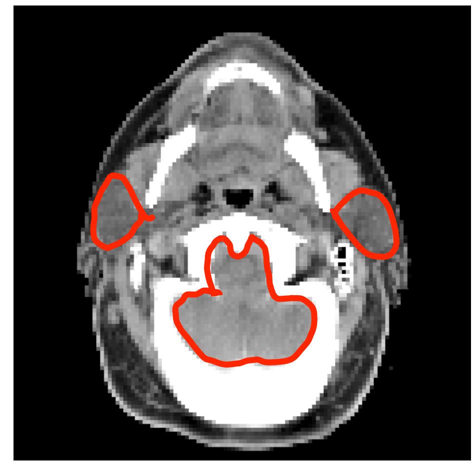
Designing an IMRT Treatment

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

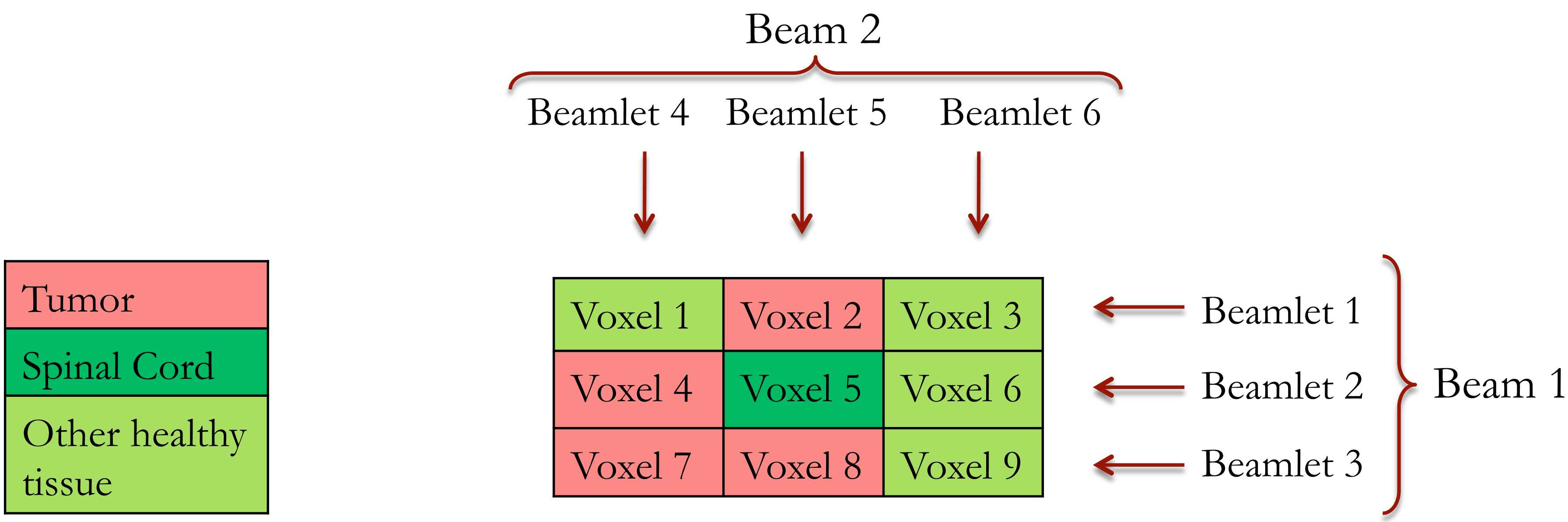
The Data

- 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	← Beamlet 1
1	2	2.5	← Beamlet 2
1.5	1.5	2.5	← Beamlet 3

$\left.\begin{array}{l}\text{Beamlet 1}\\ \text{Beamlet 2}\\ \text{Beamlet 3}\end{array}\right\}$ Beam 1

Dose to Each Voxel – Beamlets 4, 5, 6

Beam 2

Beamlet 4	Beamlet 5	Beamlet 6
1	1	1
2	2	2
1	1	1

Small Example – The Model

1	2	2	← Beamlet 1
1	2	2.5	← Beamlet 2
1.5	1.5	2.5	← Beamlet 3

Beamlet 4 ↓	Beamlet 5 ↓	Beamlet 6 ↓
1	1	1
2	2	2
1	1	1

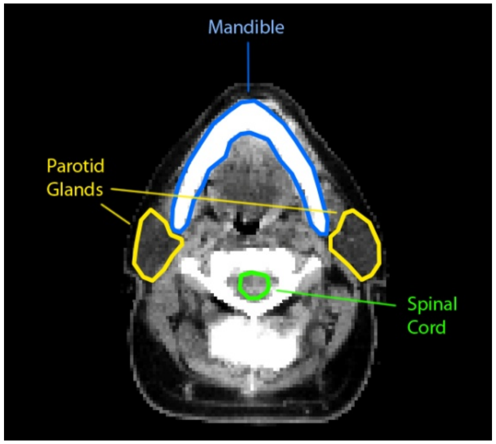
Decisions: $x_1, x_2, x_3, x_4, x_5, x_6$

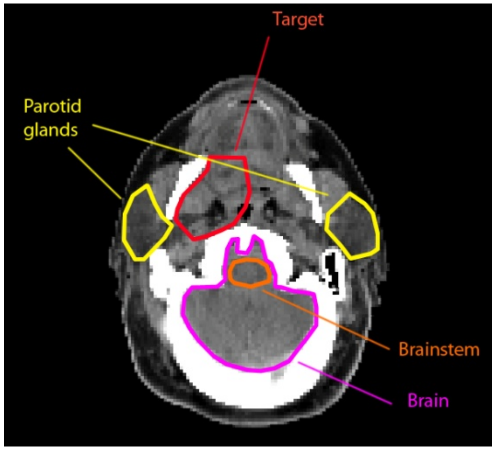
minimize $(1+2)x_1 + (2+2.5)x_2 + 2.5x_3 + x_4 + 2x_5 + (1+2+1)x_6$

$$2x_1 + x_5 \geq 7$$
$$x_2 + 2x_4 \geq 7$$
$$1.5x_3 + x_4 \geq 7$$
$$1.5x_3 + x_5 \geq 7$$
$$2x_2 + 2x_5 \leq 5$$
$$x_1, x_2, x_3, x_4, x_5, x_6 \geq 0$$

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





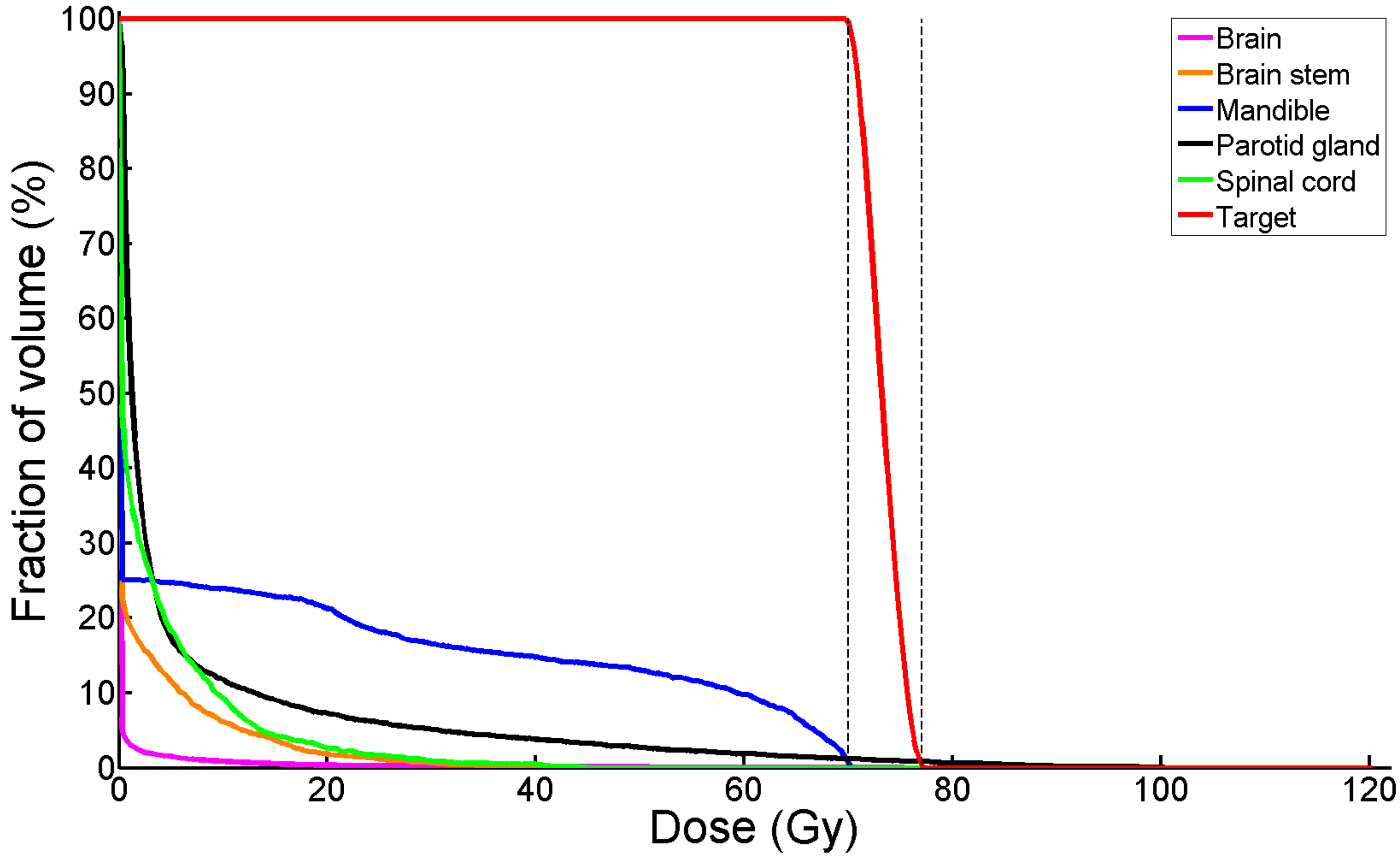
Treatment Plan Criteria

- 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

$$
\begin{aligned}
&\text{minimize Total healthy tissue dose} \\
&\text{subject to } 70\text{Gy} \leq \text{Dose to voxel } v \leq 77\text{Gy}, \quad \text{for all tumor voxels } v, \\
&\qquad \text{Dose to voxel } v \leq 45\text{Gy}, \quad \text{for all spinal cord voxels } v, \\
&\qquad \text{Dose to voxel } v \leq 54\text{Gy}, \quad \text{for all brain stem voxels } v, \\
&\qquad \text{Dose to voxel } v \leq 70\text{Gy}, \quad \text{for all mandible voxels } v, \\
&\qquad \frac{\text{Total parotid dose}}{\text{Num. parotid voxels}} \leq 26\text{Gy}, \\
&\qquad w_b \geq 0, \quad \text{for all beamlets } b.
\end{aligned}
$$

Solution



Fraction of volume (%)
100
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
120
Dose (Gy)
Brain
Brain stem
Mandible
Parotid gland
Spinal cord
Target

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

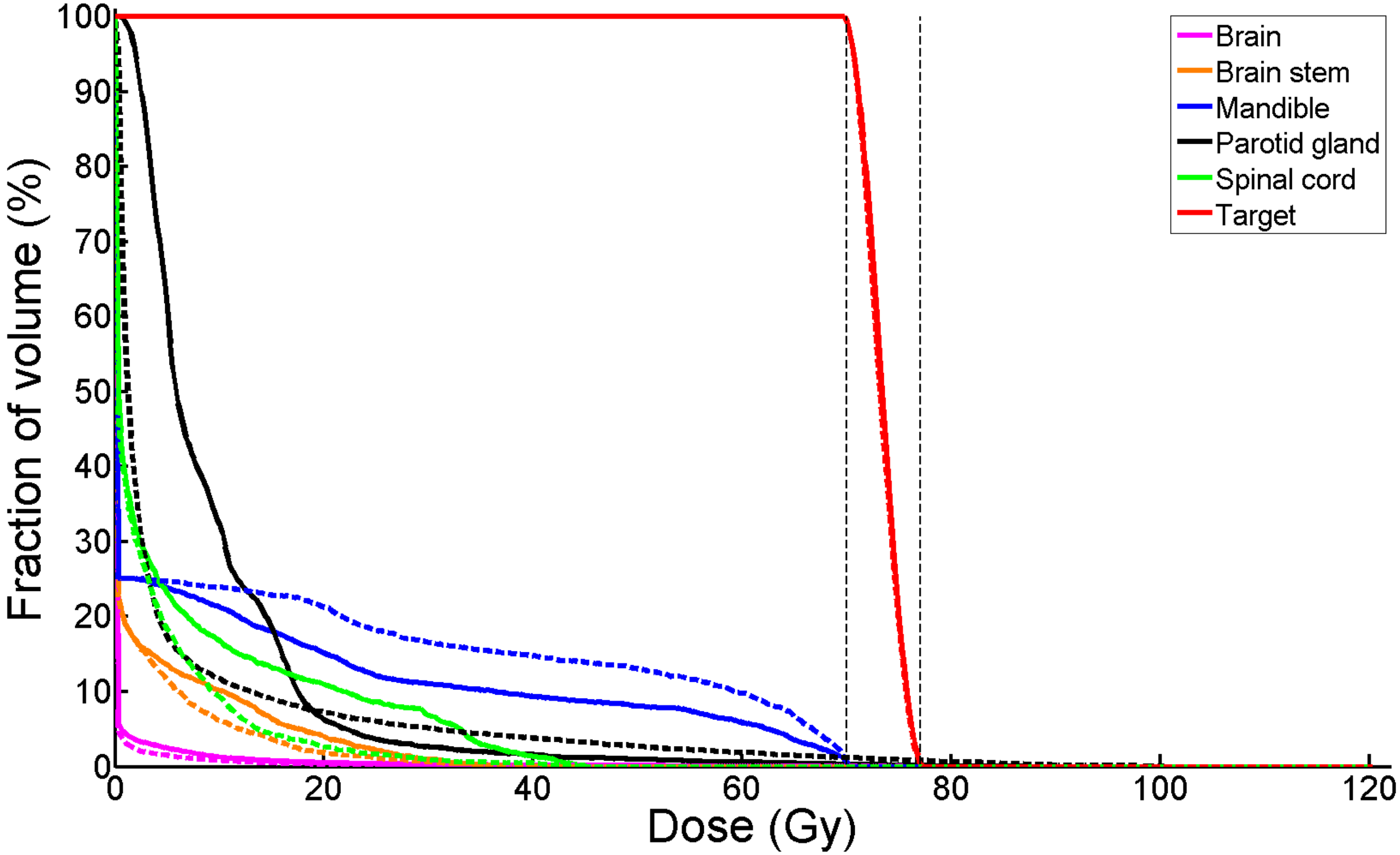
    $$T_{\mathrm{B}} + T_{\mathrm{BS}} + T_{\mathrm{SC}} + T_{\mathrm{PG}} + T_{\mathrm{M}}$$

  - Change objective to

    $$T_{\mathrm{B}} + T_{\mathrm{BS}} + T_{\mathrm{SC}} + T_{\mathrm{PG}} + 10 \times T_{\mathrm{M}}$$

  - 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 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