# Optimization of radiation therapy treatment plans

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# Outline

1. Radiation therapy treatment planning
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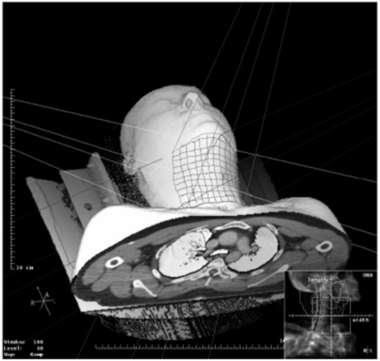
# Radiation therapy and cancer

- Each year, more than 10 million people worldwide are newly diagnosed with cancer
    - about 50-65% of these will be treated by some form of radiotherapy
    - about half of these will benefit from *external beam conformal radiotherapy*
- Despite sophisticated radiation therapy delivery technology
    - many patients still die from their disease
    - others suffer significant side-effects of their treatment
- Better treatment planning and treatment paradigms have the potential to significantly improve patient outcomes

# Radiotherapy treatment

- During radiotherapy, beams of radiation pass through a patient, killing not only cancerous but also normal, healthy cells



# Radiotherapy side effects

- Head-and-neck cancer
    - Delivering too much dose across the spinal cord has the same effect as cutting it
    - Preserving salivary gland function is very important to the quality of life of the patient as well
        - this function allows eating, speaking, maintaining oral hygiene

- Prostate cancer
    - Bowel complications (bleeding, inflammations) should be avoided

- Lung cancer
    - Overdosing the lung may cause a fatal buildup of fluid

# Radiotherapy goals

- The goal is to design a treatment plan that
  - delivers a prescribed dose to *targets*
  - while sparing, to the greatest extent possible, *critical structures*
- Radiation therapy therefore seeks to conform the geometric shape of the delivered dose distribution to the targets

# Radiotherapy delivery technique

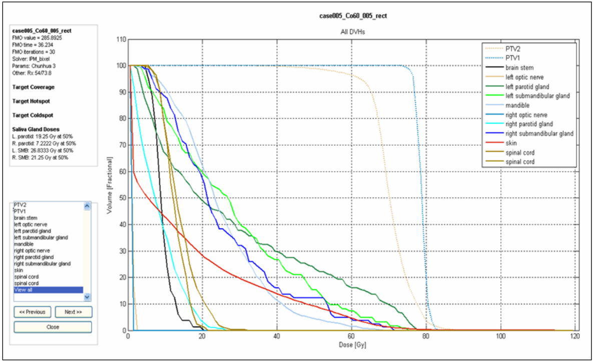
- The currently most widely used delivery technique is called *Intensity Modulated Radiation Therapy (IMRT)*
  - This technique has been used in clinics since 1994
- We will discuss how to build optimization models that can help in the design of a high-quality treatment plan for individual patients
  - Quantifying treatment plan (dose distribution) quality
  - Representation of technological abilities and constraints
  - Radiation vs. dose

# Evaluation of dose distribution (1D)

- The physician specifies a collection of measures that summarize the dose distribution *in a given structure* by a single value
- For a target, we may consider
  - minimum dose
  - dose homogeneity (e.g., ratio of maximum to minimum dose)
  - probability of tumor control
- For a critical structure, we may consider
  - (generalized) mean dose
  - maximum dose
  - probability of normal tissue complication

# Evaluation of dose distribution (2D)

- The *dose-volume histogram (DVH)* specifies, for each dose value, the fraction of a structure that receives at least that amount of dose



**case005_Co60_005_rect**
FMO value = 285.8925
FMO time = 36.234
FMO iterations = 30
Solver: IPM_bixel
Params: Chunhua 3
Other: Rx 54/73.8

**Target Coverage**

**Target Hotspot**

**Target Coldspot**

**Saliva Gland Doses**
L. parotid: 19.25 Gy at 50%
R. parotid: 7.2222 Gy at 50%
L. SMB: 26.8333 Gy at 50%
R. SMB: 21.25 Gy at 50%

# Formal criteria

- The dose distribution is evaluated over a discretization of the irradiated area into a finite number of cubes (*voxels*)
- In particular, we consider a collection of treatment plan evaluation criteria:

  $$G_1(z), \ldots, G_L(z)$$

  expressed as a function of the dose distribution, i.e., the vector of voxel doses $z$
  - smaller values are preferred to larger values

# Optimization model: objective

- Multi-criteria optimization

$$\text{minimize } \{G_1(z), \ldots, G_L(z)\}$$

- Single-objective optimization

$$\text{minimize } \sum_{\ell=1}^{L} w_\ell G_\ell(z)$$

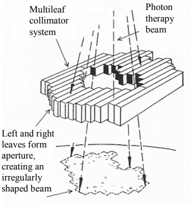
- We usually avoid imposing *hard constraints* on $z$

# IMRT delivery equipment

- Patients are generally treated on a *linear accelerator*
  - from *multiple directions*

# IMRT delivery equipment (2)

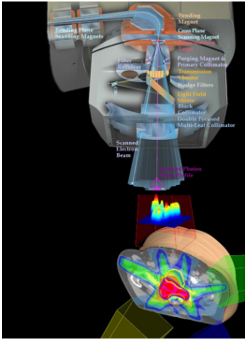
- The intensity (fluence) of the beams can be *modulated*
  - The accelerator is equipped with a *multi-leaf collimator (MLC) system*



  - This system can generate *apertures* that shape a beam by blocking part of the radiation

# Intensity profile or fluence map

- The superposition of the set of apertures and their intensities
  - corresponds to an *intensity profile* for each beam direction
  - generates a *dose distribution* in the patient



# Optimization problem: variables

- Each beam is decomposed into a collection of *beamlets (bixels)*
- Beamlet-based models:
  - optimize intensity profile: $x_i$ ($i \in N$)
  - then decompose the profile for each beam into apertures and intensities
- Aperture-based models:
  - optimize aperture intensities: $y_k$ ($k \in K$)

# Optimization problem: constraints

- We can predetermine the dose distribution generated by each individual beamlet (or aperture) at unit intensity
- Beamlet-based models:

$$\begin{aligned} z_j &= \sum_{i \in N} D_{ij} x_i && j \in V \\ x_i &\geq 0 && i \in N \end{aligned}$$

- Aperture-based models:

$$\begin{aligned} z_j &= \sum_{k \in K} \mathcal{D}_{kj} y_k && j \in V \\ y_k &\geq 0 && k \in K \end{aligned}$$

# Beamlet vs. aperture–based models

- The mathematical form of beamlet-based and aperture-based models is identical
- Beamlet-based models:
    - Pro: Fewer decision variables
    - Cons: Need for rounding and decomposition; approximate dose distribution
- Aperture-based models:
    - Pro: More accurate computation of dose distribution
    - Con: Large number of variables

# Beamlet vs. aperture–based models

- The models are equivalent if

  $$\mathcal{D}_{kj} = \sum_{i \in A_k} D_{ij}$$

  where $A_k$ is the set of beamlets exposed in aperture $k$
- However, this disregards (for example):
  - Transmission
  - Tongue-and-groove effect
- Moreover, using a beamlet-based approach it is not possible to make a formal trade-off between treatment tiime and quality

# Solving aperture-based models

- We can deal with the large number of decision variables (deliverable apertures) by using a column generation approach
  - provided that the treatment plan evaluation criteria are convex
- In this approach we iteratively
  - Solve a restricted problem with a relatively small number of apertures
  - Solve a pricing problem that
    - either determines that the current solution is optimal
    - or provides an aperture that may improve the solution

# Pricing problem

- The pricing problem takes the form

$$\max_{k \in K} \sum_{j \in V} \mathcal{D}_{kj} \hat{\pi}_j = \max_{k \in K} \sum_{i \in A_k} \left( \sum_{j \in V} D_{ij} \hat{\pi}_j \right)$$

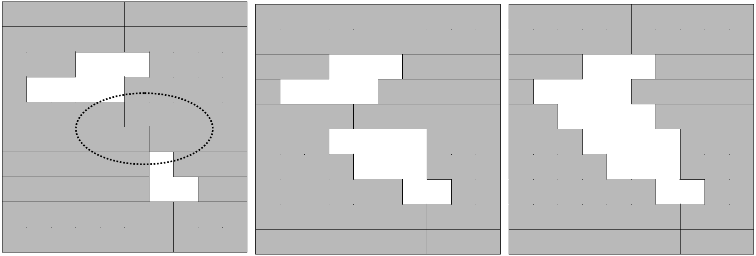
  where

$$\hat{\pi}_j = \sum_{\ell=1}^{L} w_\ell \frac{\partial G_\ell(\hat{z})}{\partial z_j}$$

  and $\hat{z}$ is the solution to the current restricted problem
- The pricing problem therefore identifies the aperture for which the rate of improvement in the objective function when increasing the aperture intensity is largest

# MLC delivery constraints

- Consecutiveness
- Non-interdigitation
- Connectedness
- Jaws-only



# Pricing problem (2)

- We can formulate a DP algorithm that solves the pricing problem in polynomial time
  - Associate a node with all possible leaf settings for all rows of the MLC
  - Connect nodes corresponding to adjacent leaves, maintaining feasibility
- In some cases (consecutiveness; jaws-only) a more efficient algorithm can also be found

# Pricing problem (3)

- Examples of extensions:
- *Transmission:*

$$\mathcal{D}_{kj} = \sum_{i \in A_k} D_{ij} + \epsilon \sum_{i \in \bar{A}_k} D_{ij}$$

- *Treatment efficiency:*
  Include a term in the objective that penalizes total beam-on-time:

$$\sum_{k \in K} y_k$$

# Current treatment paradigm

- *Day 1*
    - Image patient anatomy (CT, MRI, PET scan)
- *Days 2–5*
    - Contour targets and critical structures
    - Generate problem data
    - Determine “optimal” treatment plan
- *Day 6–40*
    - Treat patient in 35 daily *fractions*

# Interfraction motion

- Patient needs to be set up at the linear accelerator for each fraction
  - This cannot be done with complete precision
  - Setup errors mean that the actual delivered dose distribution on a given treatment day differs from the planned/optimized one
- Even if the patient could be repositioned *exactly* on each treatment day, the delivered dose distribution would still not be the same for each fraction
  - Organ motion
  - Tumor shrinkage/growth
  - Patient weight loss

# Interfraction motion (2)

- Periodic reoptimization:
    - Collect data by more frequently imaging patient
    - Process data after treatment
    - Re-plan based on delivered dose

# Unresolved issue

- How should dose be added between fractions?
    - Acute effects
    - Late effects
- New biological models are required to assess the effect of delivering nonstationary dose distributions

# Intrafraction motion

- Each treatment fraction takes about 10 minutes
- During a single fraction the patient moves because of
    - breathing
    - swallowing
    - bladder filling

# Intrafraction motion

- Currently the consequences of intrafraction motion is unknown
- We need so-called 4D image sets (“movies”) of the patient during treatment
- Tasks:
    - Assess effects of intrafraction motion for various disease sites
    - Modify treatment plan (optimization) accordingly where needed

# Image-guided radiotherapy

- By more frequently imaging the patient we may learn about motion and correct for it
- *Image-Guided IMRT (IGIMRT)*
- Several manufacturers are already offering radiation equipment that allows for more frequent imaging – but this is currently mainly limited to helping with patient setup

# Information

- More and more frequent imaging of patients will lead to a large amount of additional information
- How can we make the best use of this information, i.e., how can we find the *optimal* treatment plan (strategy) for each patient given this information?
- Which type(s) of information provide the largest benefit to the patient?

# Conclusions

- The problem of efficiently finding a high-quality *static* treatment plan based on a *single image set* and assuming *stationarity* of the patient is relatively well-solved

- However, we need to better deal with *uncertainties* and *nonstationarities*

- Operations research can help:
    - make optimal use of available technology
    - help assess which potential future technological enhancements are most valuable to the patient