Radiation therapy treatment plan optimization

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MOPTA – Lehigh University
August 18–20, 2010

Outline

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   - Treatment planning
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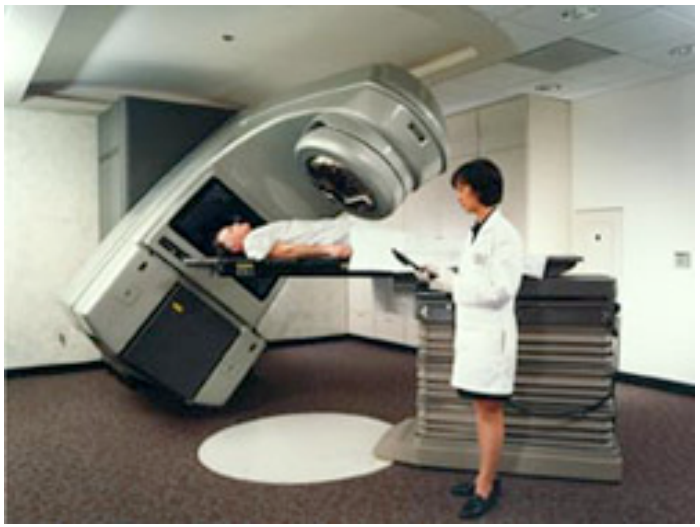
Radiation Therapy

- Each year, about 1.5 million people in the U.S. and 10 million worldwide are newly diagnosed with cancer
  - about 50-65% of these will be treated by some form of radiation therapy
  - about half of these will benefit from *external beam conformal radiation therapy*
- We will discuss optimization problems dealing with the design of *effective* and *efficiently deliverable* radiation therapy treatment plans

Radiation Therapy Delivery

- The most common form of external beam radiation delivery is using a gantry-mounted radiation source generating a rectangular beam of high-energy photons
  - linear accelerator: (megavoltage) X-rays
  - Cobalt source: γ rays



- The radiation source has constant output (intensity)

Radiation Therapy Delivery

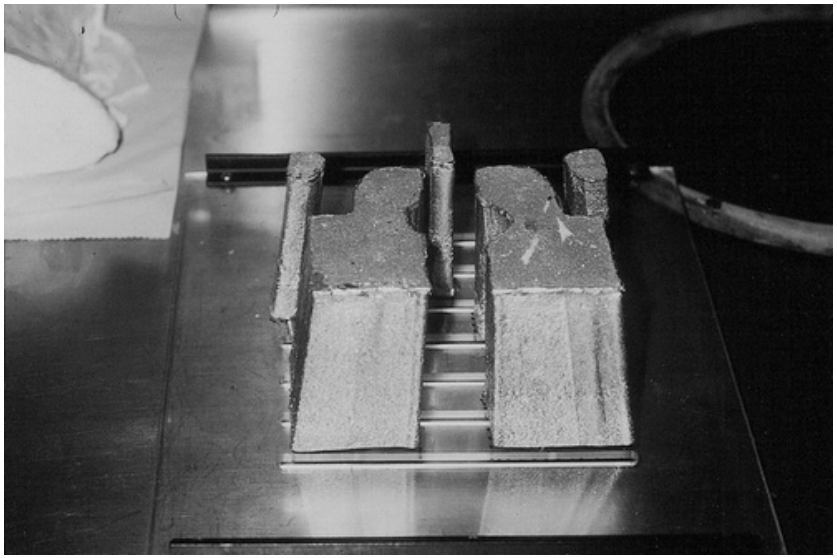
- Patients are generally treated
  - with beams from *multiple directions* by rotating the gantry around the patient
  - using non-rectangular (partially blocked) beams
  - daily over a period of 5–8 weeks to allow healthy cells to recover from radiation damage
- Regarding the latter:
  - We will mostly assume that *patient geometry is stationary* and *patients are motionless*
  - We will (briefly) discuss the issue of associated uncertainties later

Radiation Therapy Delivery

- Techniques for partially blocking beams:
  - 3D/Conventional Conformal Radiation Therapy (3DCRT)
    - wedge filters
    - physical apertures (cerrobend)
  - Intensity Modulated Radiation Therapy (IMRT)
    - multileaf collimator (MLC) system
  - Volumetric Modulated Arc Therapy (VMAT)
    - variant of IMRT

3DCRT

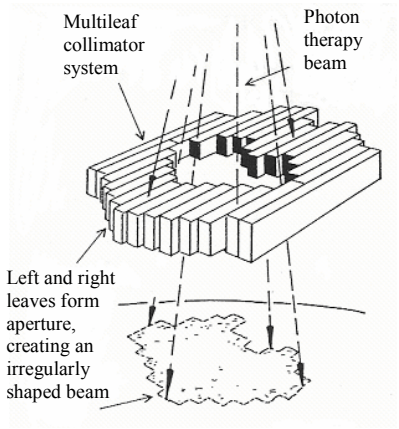
- Cerrobend block:



  - In 3DCRT, only a few apertures or filters, typically one from each of a small number of beam orientations, is used

IMRT and VMAT

- A *multi-leaf collimator* (MLC) system consists of leaves that can dynamically block part of a beam to form different *apertures*:



  - In IMRT, several different apertures are formed at each of a relatively small number of beam orientations
  - In VMAT, the gantry rotates continuously while the beam is on and the MLC leaves form apertures

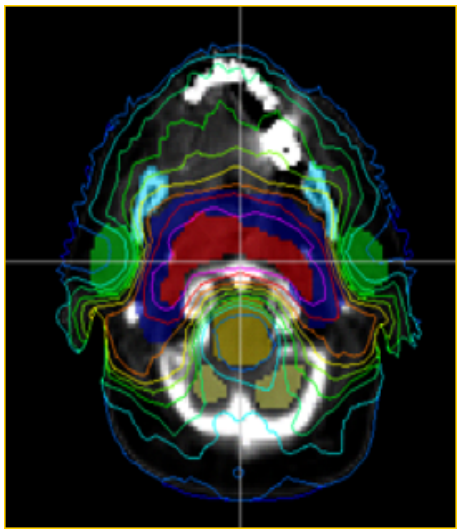
Treatment planning

- We will next focus on two main components:

1. *Treatment plan evaluation*
   - Quantifying the quality of a treatment plan (delivered dose distribution)
2. *Treatment plan delivery*
   - Determining a collection of apertures (and/or wedges) with corresponding intensities

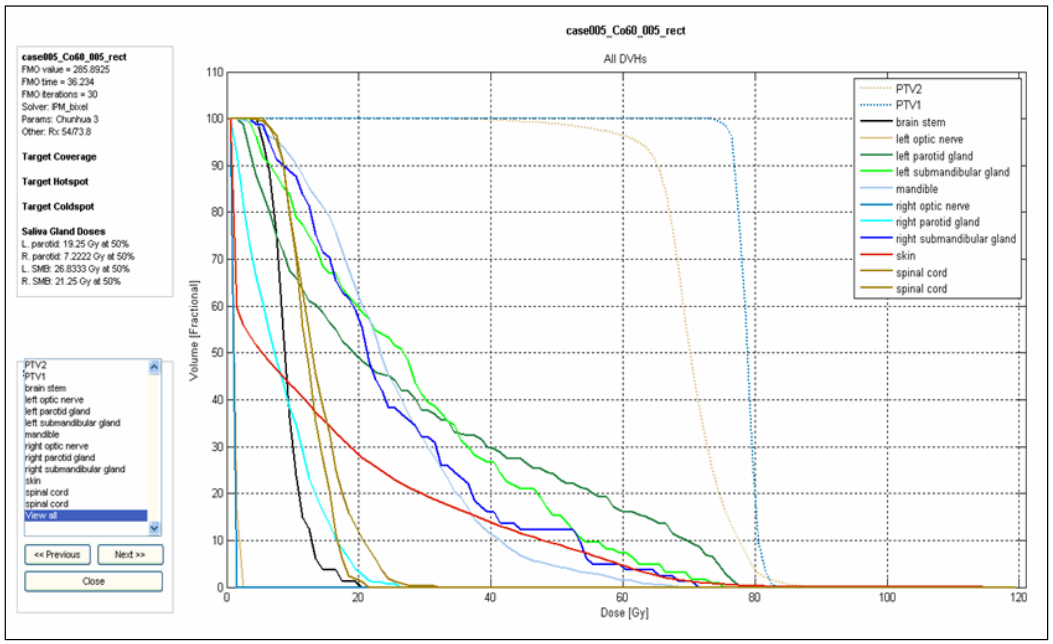
Radiotherapy goals

- 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



Evaluation of a dose distribution

- A physician typically considers the dose distribution received by each individual structure
  - The *dose-volume histogram (DVH)* is an important tool that specifies, for each dose value, the fraction of a structure that receives at least that amount of dose



Evaluation of a dose distribution

- Rephrasing the goal of treatment plan design: we wish to identify a treatment plan that has
  - a *desirable* dose distribution in the targets
  - an *acceptable* dose distribution in the critical structures
- Let the random variable D represent the dose (rate) at a uniformly generated point in a structure in the patient
  - Letting F_D denote the cumulative distribution function of D, the DVH of the structure is simply the function $1 - F_D$
- This suggests a connection between (financial) *risk management* and *treatment planning*
  - In both fields, we wish to control the shape of the probability distribution of one or more random variables

[1] Romeijn and Dempsey (TOP, 2008)

Criteria

- Broadly speaking, we wish to penalize
  - overdosing of areas in both target and critical structure
  - underdosing of areas in target
- Physical criteria are therefore often of the form

$$\mathcal{E}\left(u(D)\right)$$

for an appropriately chosen function u

  - In the context of risk management the function u would be a utility function, its shape depending on risk preferences
  - In radiation therapy treatment planning the function u depends on the biological properties of the underlying structure being evaluated

Criteria for underdosing

- *Target*, underdosing
  - u decreasing, usually convex
  - when $u(d) = e^{-\alpha d}$ (with $\alpha > 0$) the expected utility is a monotone transformation of a measure of *tumor control probability* (TCP)

$$\text{TCP} = \exp\left(-N\mathcal{E}\left(e^{-\alpha D}\right)\right)$$

    - $N =$ number of clonogen cells in the target
    - $\alpha =$ rate of cell kill per unit dose

Criteria for overdosing

- *Target or critical structure*, overdosing:
  - u increasing, but shape depends on biological response of tissue to radiation
    - serial: high dose to a small fraction of the structure can destroy its functionality
    - parallel: sparing a part of the structure will preserve its functionality
  - u convex
    - when $u(d) = d^k$ (with $k \geq 1$) the expected utility is a monotone transformation of the so-called *equivalent uniform dose* (EUD)

$$\text{EUD} = \left(E(D^k)\right)^{1/k}$$

  - u "S-shaped"

Criteria

- Other special cases are
  - mean excess or mean shortfall criteria:

$$u(d) = \max\{0, d - T\} \quad \text{or} \quad u(d) = \max\{0, T - d\}$$

    - A related measure is the so-called *Conditional Value-at-Risk*
    - i.e., the upper or lower tail average of the dose distribution

  - *DVH-criteria* that evaluate points on the DVH

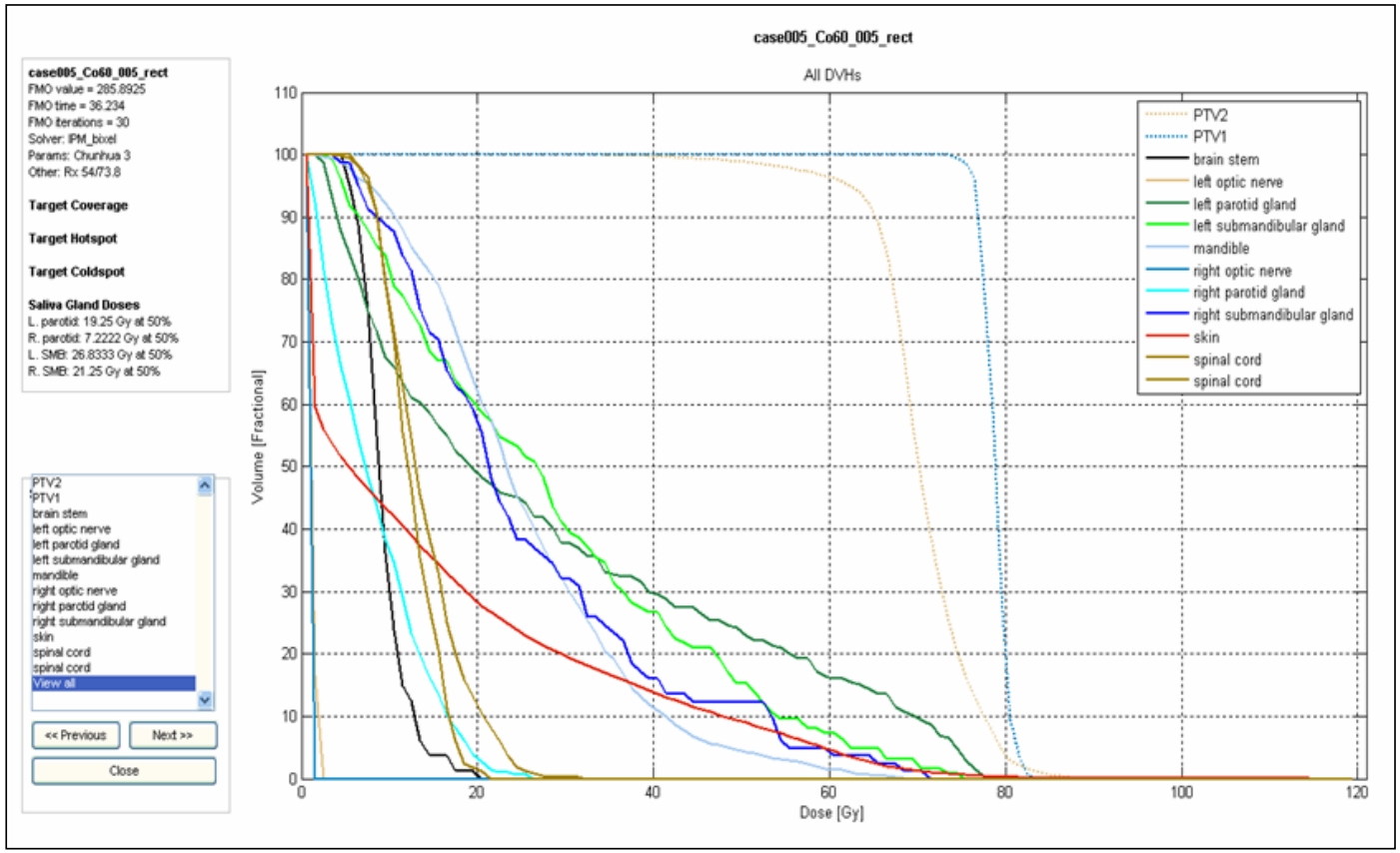
$$u(d) = 1_{[0,T]}(d) \quad \text{or} \quad u(d) = 1_{(T,\infty)}(d)$$

    - A related measure is the so-called *Value-at-Risk*
    - i.e., the dose level that is exceeded by (or not exceeded by) a given fraction of the structure

Criteria

- The latter are often used clinically, and referred to as *DVH criteria*
- Examples:
  - Target:
    - at least 99% of the volume should receive more than 93% of the prescribed dose
    - at least 95% of the volume should receive more than the prescribed dose
  - Saliva gland:
    - at most 50% of the volume should receive more than 30 Gy
    - none of the volume should receive more than 110% of the (target's) prescribed dose

Criteria


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%
PTV2
PTV1
brain stem
left optic nerve
left parotid gland
left submandibular gland
mandible
right optic nerve
right parotid gland
right submandibular gland
skin
spinal cord
spinal cord
View all
<< Previous
Next >>
Close
case005_Co60_005_rect
All DVHs
Volume [Fractional]
Dose [Gy]
0
10
20
30
40
50
60
70
80
90
100
110
0
20
40
60
80
100
120
PTV2
PTV1
brain stem
left optic nerve
left parotid gland
left submandibular gland
mandible
right optic nerve
right parotid gland
right submandibular gland
skin
spinal cord
spinal cord

Criteria

- More generally, a physician or clinician could specify a full DVH that should dominate the DVH of a structure (from above or below)
  - The bounding DVH corresponds to the c.d.f. of a random variable
  - The dominance constraint is called *first order stochastic dominance*
- A similar dominance could be defined with respect to tail means of the random variable and a bound on the corresponding curve
  - The dominance constraint is then called *second order stochastic dominance*
  - In optimization terms, a second order stochastic dominance constraint is the convex relaxation of a first order stochastic dominance constraint

Objective

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

$$G_\ell(z) : \ell \in L$$

expressed as a function of the dose distribution, i.e., the vector of voxel doses $z \in \mathbb{R}^{|V|}$

  - where smaller values are preferred to larger values

Optimization model

- Optimization model:
  - Objective:
    - single objective, by assigning appropriate weights to the different criteria
    - multi-criteria objective
  - Feasible region:
    - constraints on the value of one or more of the criteria
- An approach that combines these approaches is lexicographic optimization

Beams and apertures

- Let B denote the set of beam orientations used for delivery
  - In IMRT these beam orientations are often (but not necessarily) chosen by the physician or clinician
  - In VMAT we discretize the arc around the patient into a finite number of beam orientations
- The delivery constraints share the concept of an "aperture" (including wedges)
  - Let K_b denote the set of apertures that can be used at beam angle $b \in B$
  - Let $K = \cup_{b \in B} K_b$ be the set of all apertures that can be used for treatment

Data and decision variables

- Dose deposition coefficients:
  - Let $\mathcal{D}_{bkj}$ denote the dose deposited in voxel $j \in V$ from aperture $k \in K_b$ in beam $b \in B$ at unit intensity
- Decision variables:
  - Let y_{bk} denote the intensity of aperture $k \in K_b$, $b \in B$

Model

- Basic optimization model:

$$\text{minimize } G(z) = \sum_{\ell \in L} w_\ell G_\ell(z)$$

subject to

$$z_j = \sum_{b \in B} \sum_{k \in K_b} \mathcal{D}_{bkj} y_{bk} \qquad j \in V$$

$$y_{bk} \geq 0 \qquad k \in K_b,\ b \in B$$

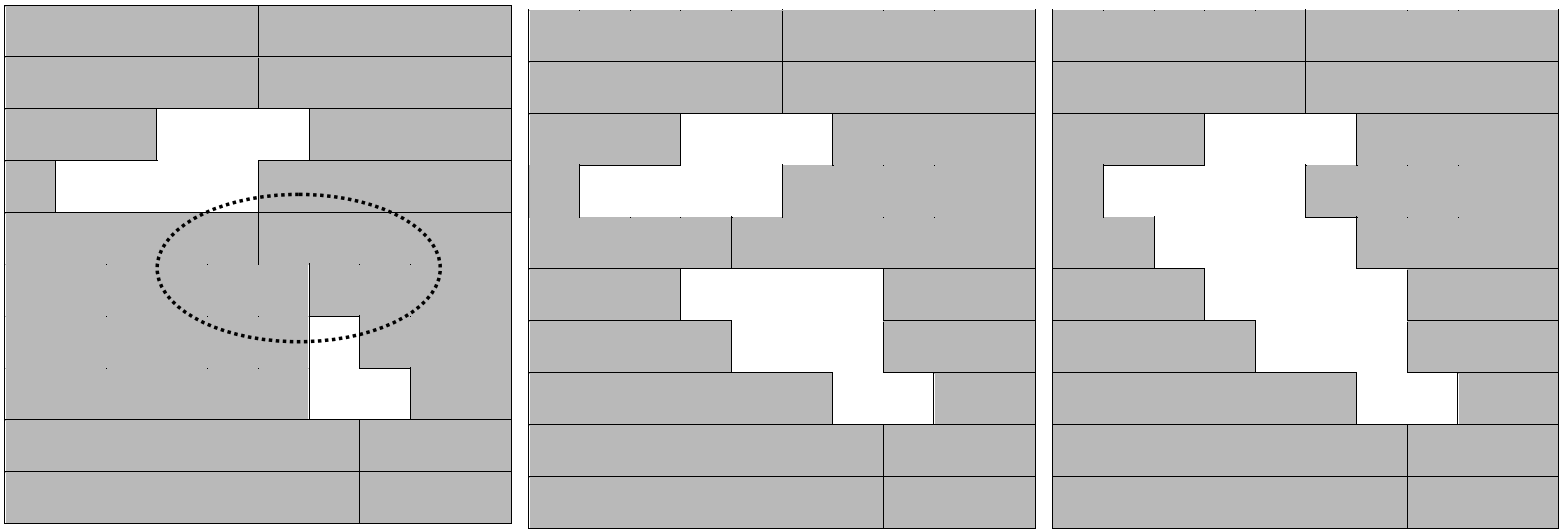
[2] Romeijn, Ahuja, Dempsey, and Kumar (SIAM Journal on Optimization, 2005)

Candidate apertures

- 3DCRT:
  - Usually “beam’s-eye-view” of target from a large number of candidate beam orientations
  - Wedge filters (angle, orientation)
- IMRT/VMAT:
  - Limited by MLC delivery constraints

MLC delivery constraints

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



Additional constraints

- VMAT:
  - Leaf motion constraints limit the sequence of apertures
  - Only a single aperture may be used at each beam orientation (at each gantry rotation)
  - It may be possible to vary the gantry speed and/or beam intensity

Additional criteria

- *Beam-on-time*
  - total amount of time the beam is “on”: sum of aperture intensities
- *Total treatment time*:
  - total amount of time the patient is being treated
  - approximated by a weighted sum of beam-on-time and number of apertures used

[3] Salari and Romeijn (in preparation)
[4] Taşkın, Smith, Romeijn, and Dempsey (Operations Research, 2010)
[5] Taşkın, Smith, and Romeijn (Annals of Operations Research, forthcoming)

Additional constraints

- 3DCRT
  - Only a small number of apertures is considered (can be enumerated)
  - Cardinality constraints (on the number of apertures used) are essential
- In the remainder we will focus on
  - IMRT
    - fixed set of beam orientations
    - no (hard) constraint on the number of apertures used
  - VMAT
    - no variation of gantry speed and/or beam intensity

Problem dimension

- The number of available apertures will usually be too large to handle explicitly
- A column generation approach can be used to solve the (continuous relaxation of the) optimization model
  - attractive theoretical properties provided that the objective function G (and any additional constraints) are convex and well-behaved

Pricing problem

- Given an optimal solution to the (relaxed) problem with a limited number of apertures, the pricing problem is of the form:

$$\min_{b \in B} \left(\min_{k \in K_b} \sum_{j \in V} \mathcal{D}_{bkj} \pi_j \right)$$

  where $(\pi_j : j \in V)$ are the KKT multipliers corresponding to the dose definition constraints

- The efficient solvability of this problem depends on
  - The form of the set K_b
  - The dependence of $\mathcal{D}_{bkj}$ on k

Pricing problem

- The pricing problem is efficiently solvable
  - (i) for different models for $\mathcal{D}_{bkj}$
  - (ii) for many practical MLC delivery constraints
- We will illustrate this in the context of IMRT

IMRT

- Example of (i):
  - Discretize each beam orientation into a large grid of "beamlets" (N_b, $b \in B$)
  - Let A_{bk} denote the beamlets that are exposed in aperture $k \in K_b$ in beam $b \in B$
  - Precompute dose deposition coefficients for each beamlet: D_{bij}, $i \in N_b$, $b \in B$
  - Then we can, for example, let

$$\mathcal{D}_{bkj} = \sum_{i \in A_{bk}} D_{bij} + \varepsilon \sum_{i \in N_b \setminus A_{bk}} D_{bij}$$

    - accounts for *transmission* through the MLC leaves
    - other aspects of the MLC leaf architecture can be handled as well

[6] Men, Romeijn, Taşkın, and Dempsey (Physics in Medicine and Biology, 2007)
[7] Salari, Men, and Romeijn (submitted for publication)

IMRT

- Example of (ii):

$$\min_{k \in K_b} \sum_{j \in V} \sum_{i \in A_{bk}} D_{bij} \pi_j = \min_{u \in U_b} \sum_{i \in N_b} \left(\sum_{j \in V} D_{bij} \pi_j \right) u_i$$

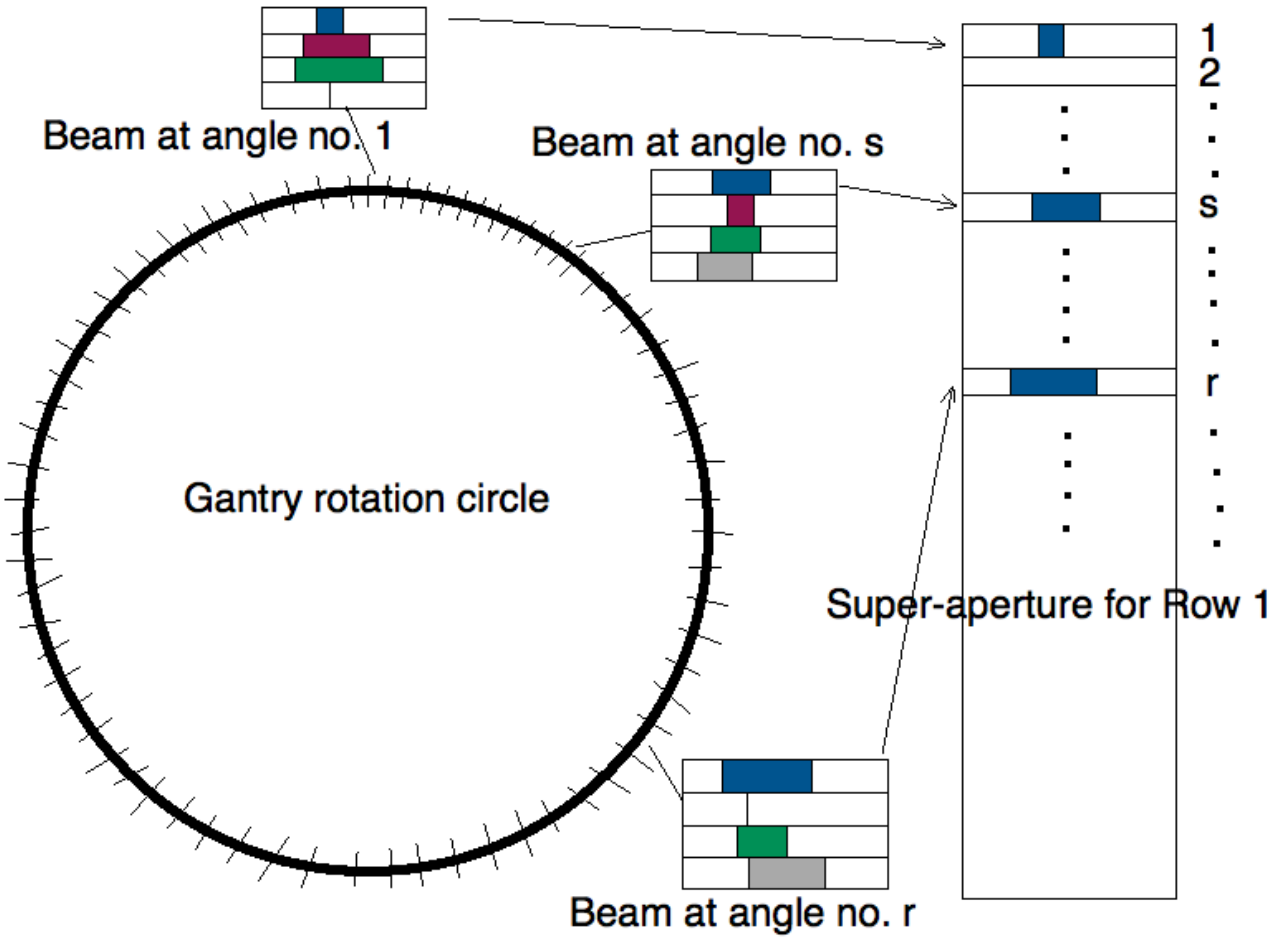
  - Suppose that all row-convex apertures are deliverable
    - Leaf pairs can move independently of one another
    - The pricing problem then decomposes by beamlet row
    - Can be solved in linear time in the number of beamlets in a row

VMAT

- For VMAT we could explicitly add constraints on consecutive apertures to enforce leaf motion constraints
  - tractability of the resulting model is an issue
- However, we can use an approach that resembles the model for IMRT when all row-convex apertures are deliverable
  - Instead of viewing the leaf settings of the entire MLC as an "aperture", we group the leaf settings of a given leaf row as the gantry moves around the patient into an "aperture"
    - one aperture per (discretized) beam angle
    - constraints on the leaf speeds translate into constraints on consecutive pairs of leaf settings in a given row

[8] Peng, Epelman, and Romeijn (in preparation)

VMAT


Beam at angle no. 1
Beam at angle no. s
Gantry rotation circle
Beam at angle no. r
1
2
s
r
Super-aperture for Row 1

Beam vs. beamlet row arc

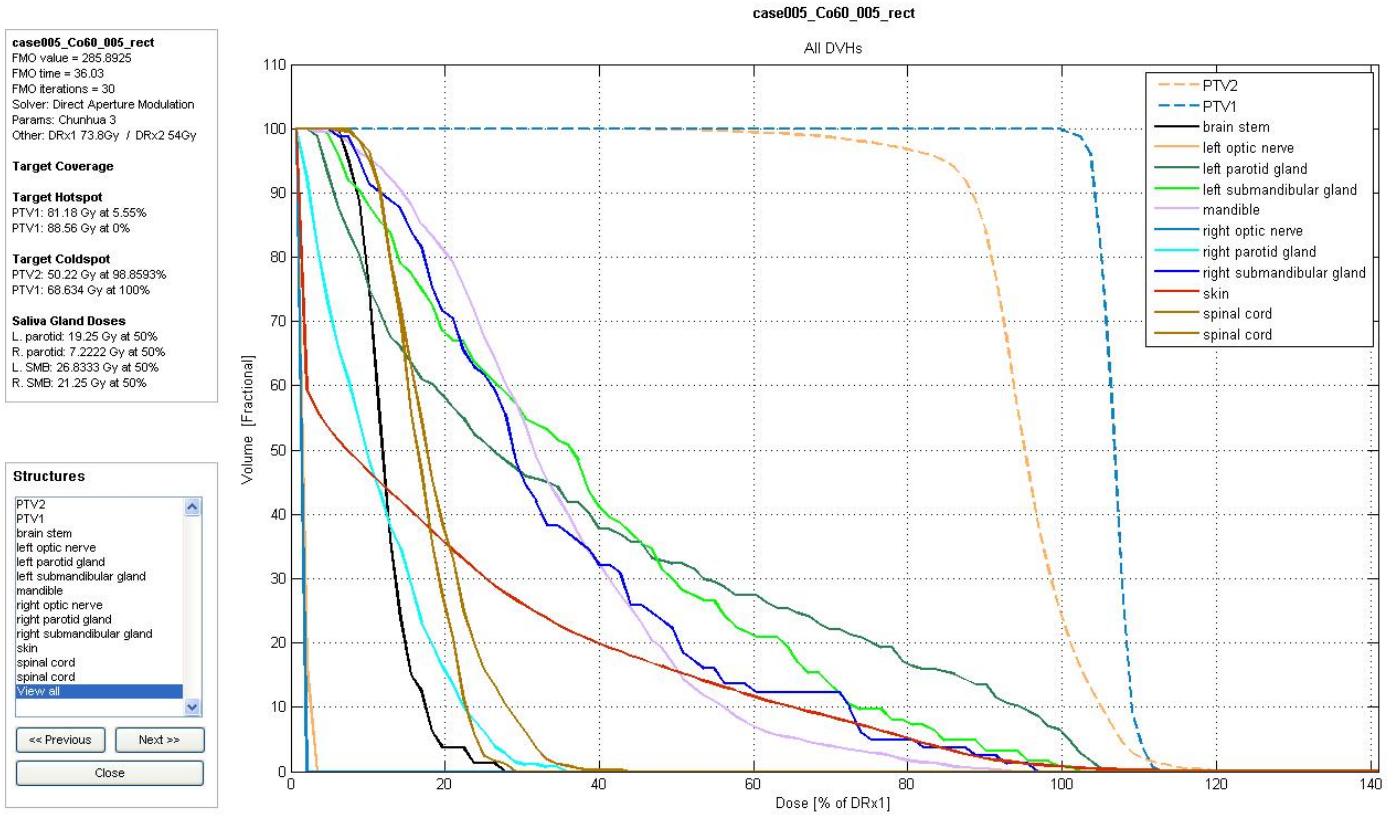
- In the model
  - b now indicates a beamlet row traversing an arc
  - k now indicates a sequence of leaf settings for a given beamlet row traversing an arc
  - The set K_b only contains "apertures" that satisfy the leaf motion constraints
- Pricing problem
  - Solvable in polynomial time using dynamic programming for each beamlet row
    - Stages: beam angles
    - States: pairs of leaf settings at a given beam angle
    - Arcs: connect leaf settings at consecutive angles that are compatible

Results

- Clinical patient cases
- Head-and-neck cancer
  - 2 targets (73.8 Gy and 54 Gy)
  - critical structures: saliva glands (4), spinal cord, brainstem, mandible, . . . (up to 10)

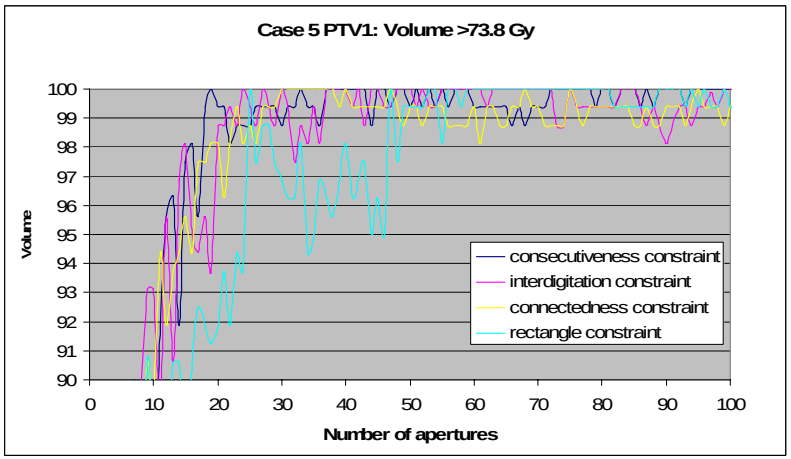
Presentation of results

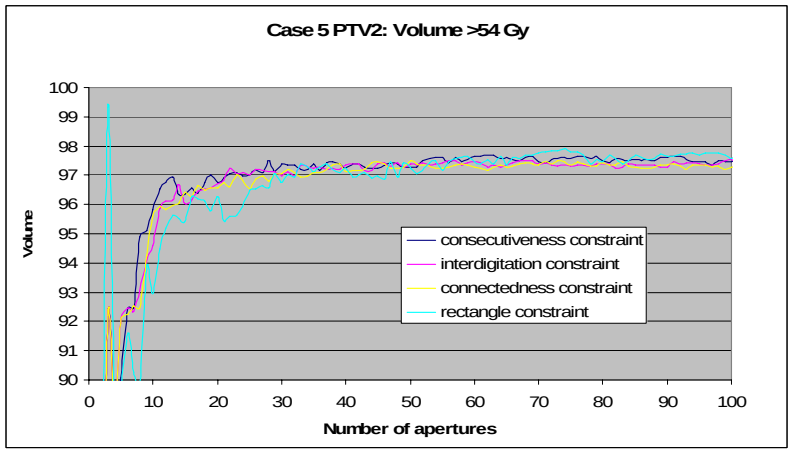
- Traditional: DVHs

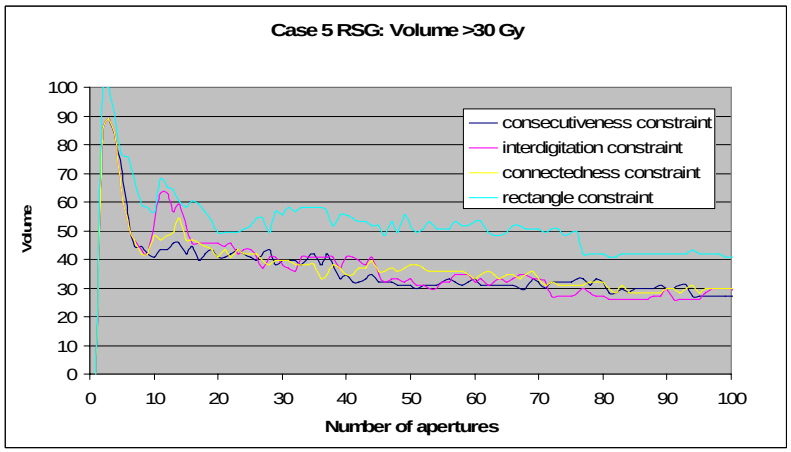


Presentation of results

- Delivery efficiency: clinical criteria vs. number of apertures

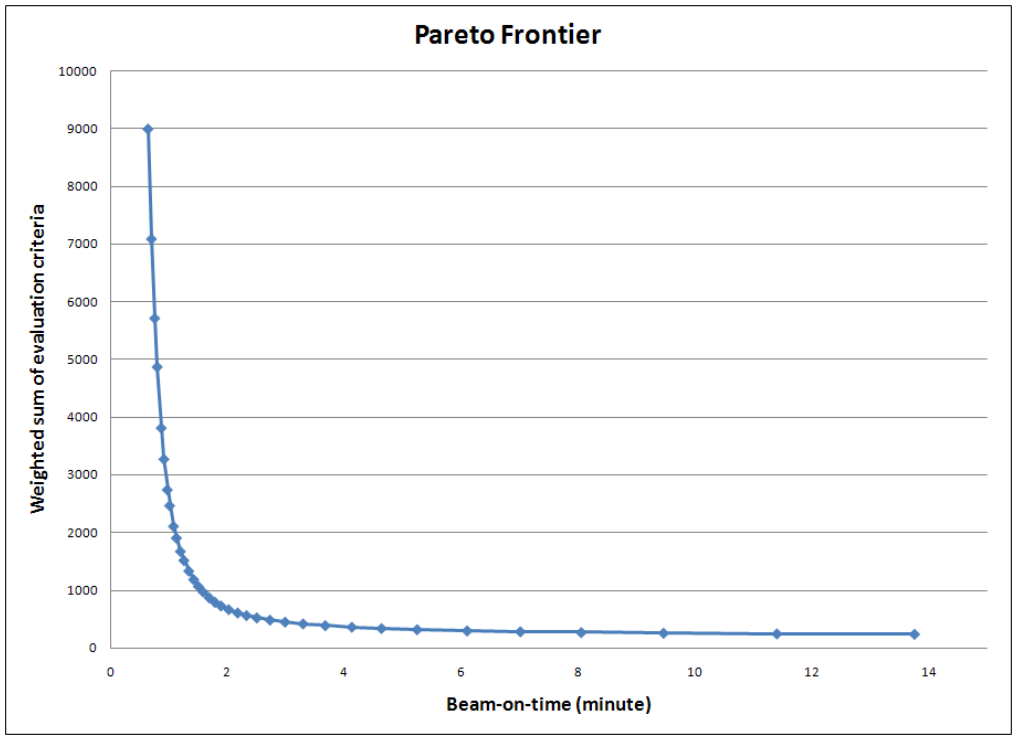






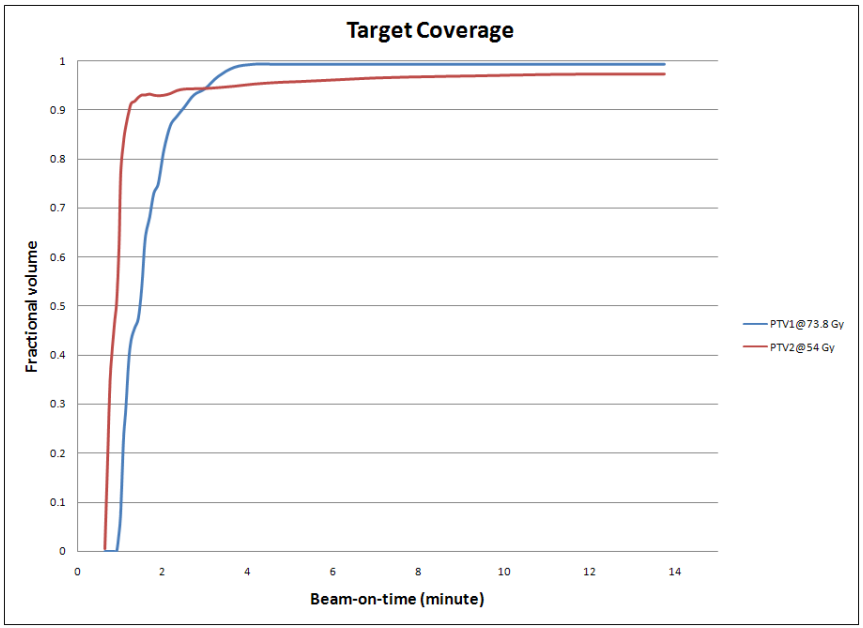
Presentation of results

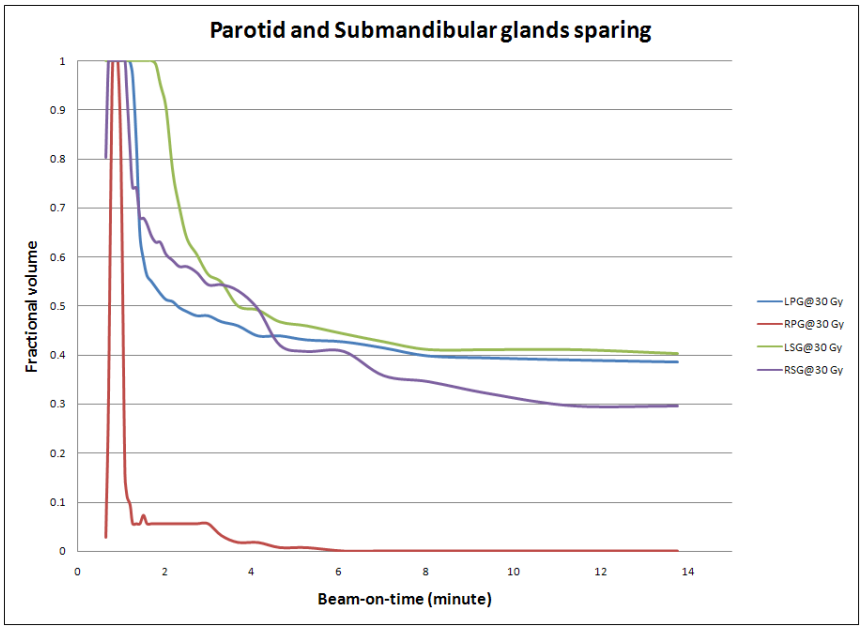
- Delivery efficiency: objective function vs. beam-on-time



Presentation of results

- Delivery efficiency: clinical criteria vs. beam-on-time





Uncertainties (or unknowns)

- Image segmentation (decomposition of V into structures)
  - Manual
  - Automatic
- Dose calculation
  - different models are used to “estimate” the values of D_{bij}, all of them approximate

Uncertainties (or unknowns)

- Treatment plan evaluation (functions G_ℓ)
  - Priorities/weights/tradeoffs
  - Parameter estimation
  - Differences in patient responses

Uncertainties

- Interfraction motion
  - Patient setup (systematic and random)
  - Tumor changes (e.g., shrinkage, growth)
  - Patient geometry changes
    - Structural: e.g., patient weight loss
    - Random: e.g., soft tissues
  - Assessing delivery of nonhomogeneous dose distribution over time
- Intrafraction motion
  - Breathing
  - Swallowing

Margins

- Currently, most of these “uncertainties” are dealt with by using margins to expand structures
- It is tempting to incorporate individual sources of uncertainty into the treatment planning process based on tractability
- It would be valuable to (first) study which of the uncertainties have the most impact on treatment quality

Research directions

- Efficiently exploring tradeoffs
  - between clinical evaluation criteria
  - between quality and efficiency
- Fast reoptimization
  - daily reoptimization based on
    - snapshot image taken before treatment fraction
    - 4D images taken during previous treatment fraction(s)
    - learning about individual patient response
- Intrafraction motion
  - modeling of patient motion
  - monitoring and reacting to patient motion