Robust optimization: PTV reduction for rigid body deformations

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Outline

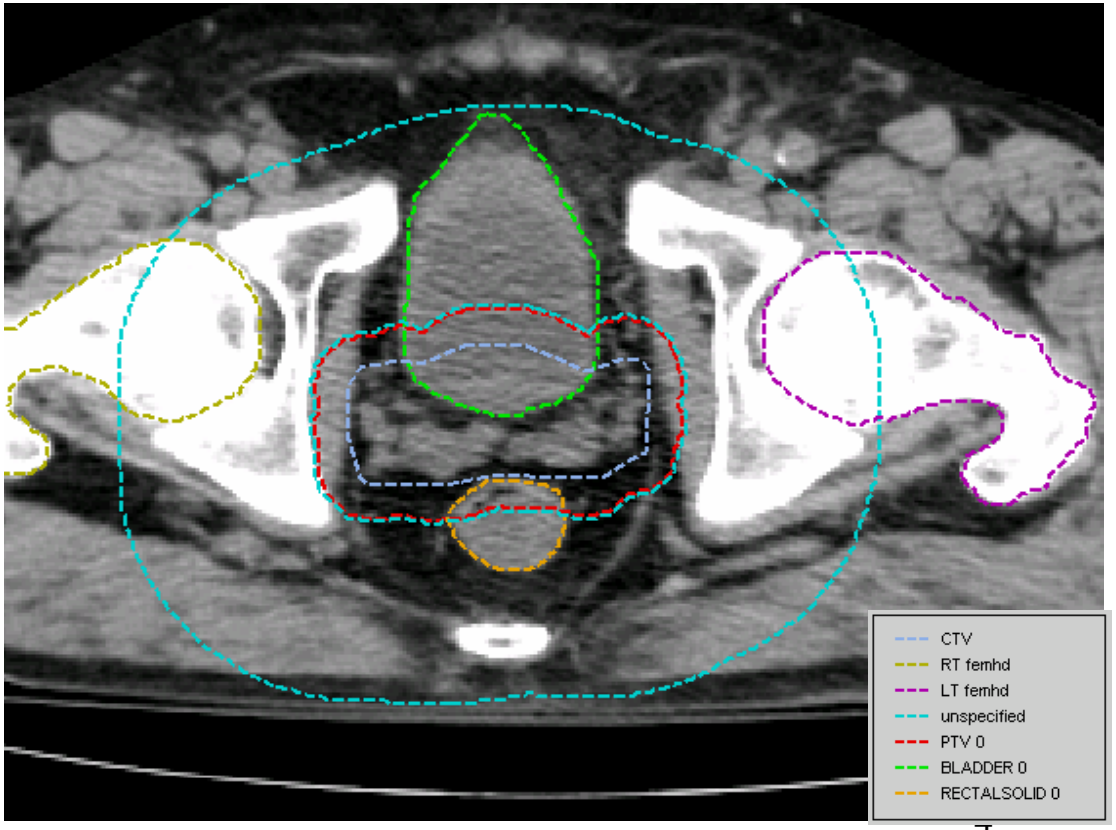
- Problem overview
- Traditional/robust comparison
- Robust approach in detail
- Towards clinical standards

Problem overview

Treatment planning

Goal: Choose beam angles and beamlet intensities that **kill tumor** and **spare healthy tissues**

- Take CT scan
- Delineate
- Discretize body into "voxels"
- Formulate & solve a mathematical program to find a "good" plan



Princess Margaret Hospital

Problem addressed

Find: beamlet intensities

Assuming:

- beam angles are given
- influence (dose) matrix is given
- dose to a voxel "adds up"
- any beamlet configuration possible

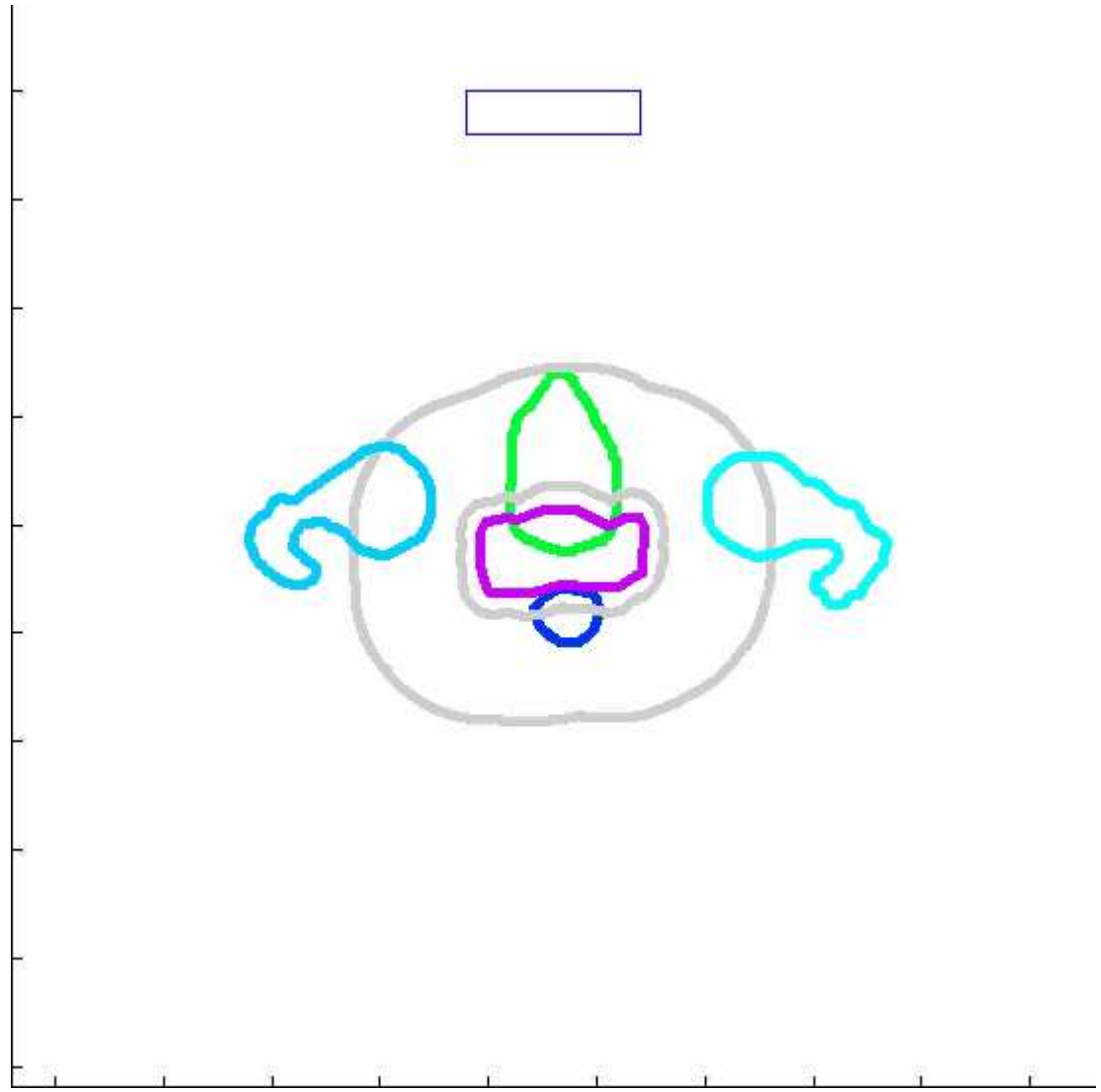
Calculating dose delivered

Dose delivered to voxel:

$$Dose(v) = \sum_{b \in B} w(b) Dose(b, v)$$

w(b) = intensity of beamlet b (decision variable)

Dose(b,v) = dose to voxel v from unit intensity beamlet b (parameter)



Types of models

- Common objectives:
  - Maximize the minimum dose to the target
  - Minimize deviations from prescribed dose
- Common constraints:
  - Homogeneity
  - Maximum dose constraints
  - Dose-volume constraints

Remark: Optimization = Feasibility

Traditional formulation

minimize: total penalty

subject to:

Dose to voxel v in healthy structure k $\leq U_k$

$U \geq$ Dose to voxel v in tumor $\geq L$

w(b) = beamlet intensities ≥ 0

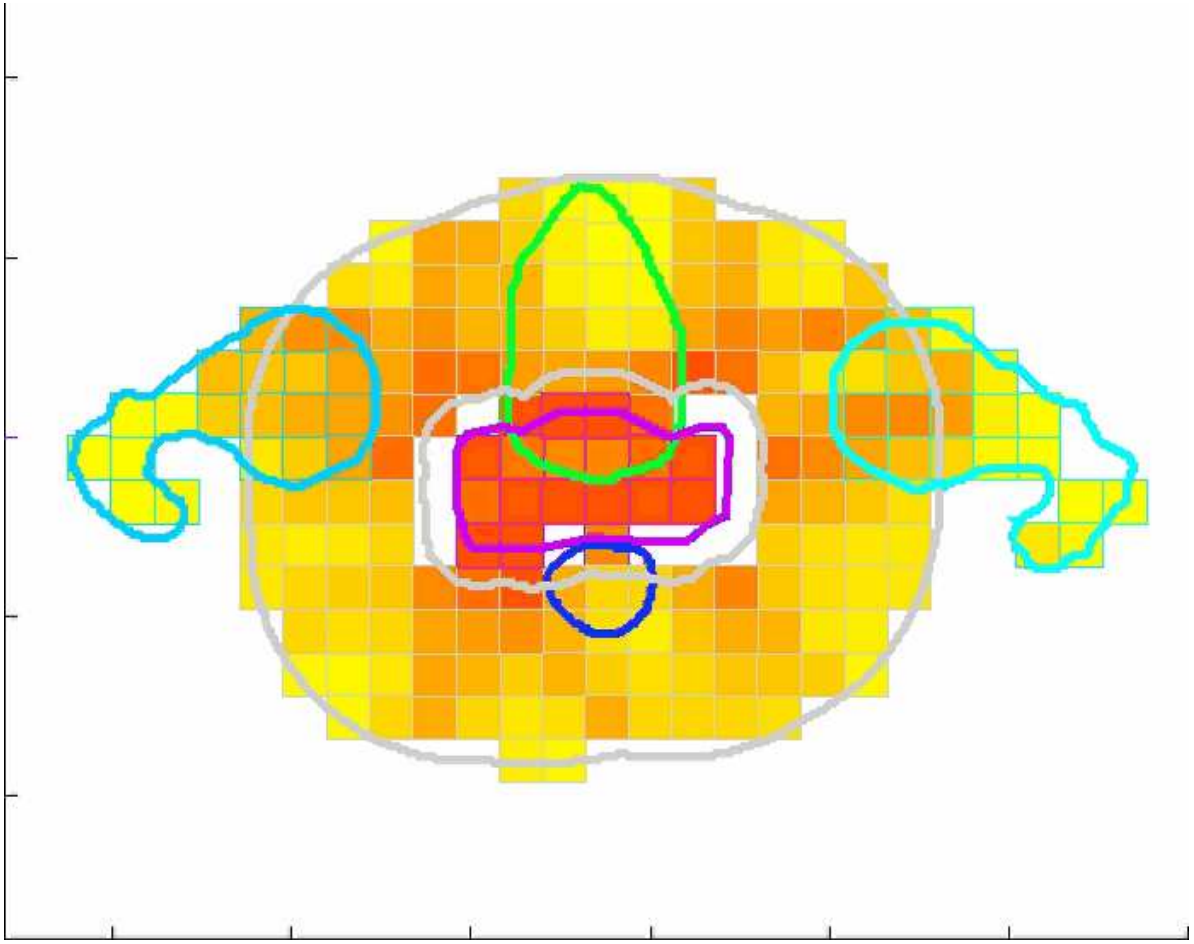
"Approximate" dose-volume constraints

Uncertainties

- Inter-fractional
  - Setup errors
  - Structural changes (e.g., weight loss)
- Intra-fractional
  - Patient motion
  - Organ motion (breathing, cardiac, etc.)

A direction: rescan to eliminate *some* of these errors

Plans and uncertainty



Traditional approach

Add a safety margin:

- Gross Tumor Volume (GTV) = solid tumor
- Clinical Target Volume (CTV) = GTV + suspected regions of subclinical disease
- Planning Target Volume (PTV) = CTV + margin for uncertainties

Robust approach

Constrain cumulative dose to each voxel

"No matter where CTV, structures fall"

within reason

minimize: penalty objective

subject to:

Pr(Dose to voxel v in healthy structure k $\leq$ U_k) $\geq$ 0.95

Pr(U $\geq$ Dose to voxel v in tumor $\geq$ L) $\geq$ 0.95

Pr(DVH-alternative constraints hold) $\geq$ 0.95

w(b) = beamlet intensities $\geq$ 0

Dose delivered

- Let $D_v(w)$= Dose delivered to voxel v in N fractions with beamlet intensities w

$$D_v(w) = D_{v,1}(w) + D_{v,2}(w) + \ldots + D_{v,N}(w)$$

- Typically, N = 30 - 45
- Assume $D_{v,i}(w)$ are i.i.d.
- By CLT,

$$\boxed{D_v(w) \sim \mathbf{Normal}(\mu(w), \sigma(w)^2)}$$

Probabilistic constraints

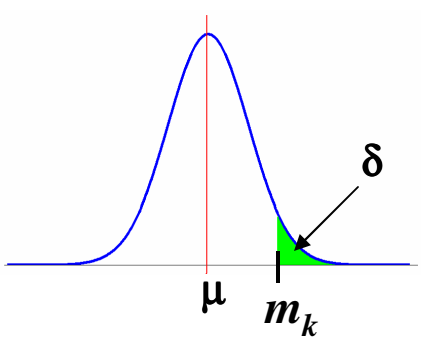
- Constraints to be violated with low probability, e.g., $\delta = 0.05$
- For voxel v in healthy structure H_k, want:

$$\Pr(D_v(w) > m_k) \le \delta$$

$$\Pr\left(\frac{D_v(w) - \mu(w)}{\sigma(w)} > \frac{m_k - \mu(w)}{\sigma(w)}\right) \le \delta$$

$$\frac{m_k - \mu(w)}{\sigma(w)} \ge z_{1-\delta}$$

$$\boxed{\sigma(w) \le \frac{m_k - \mu(w)}{z_{1-\delta}}}$$



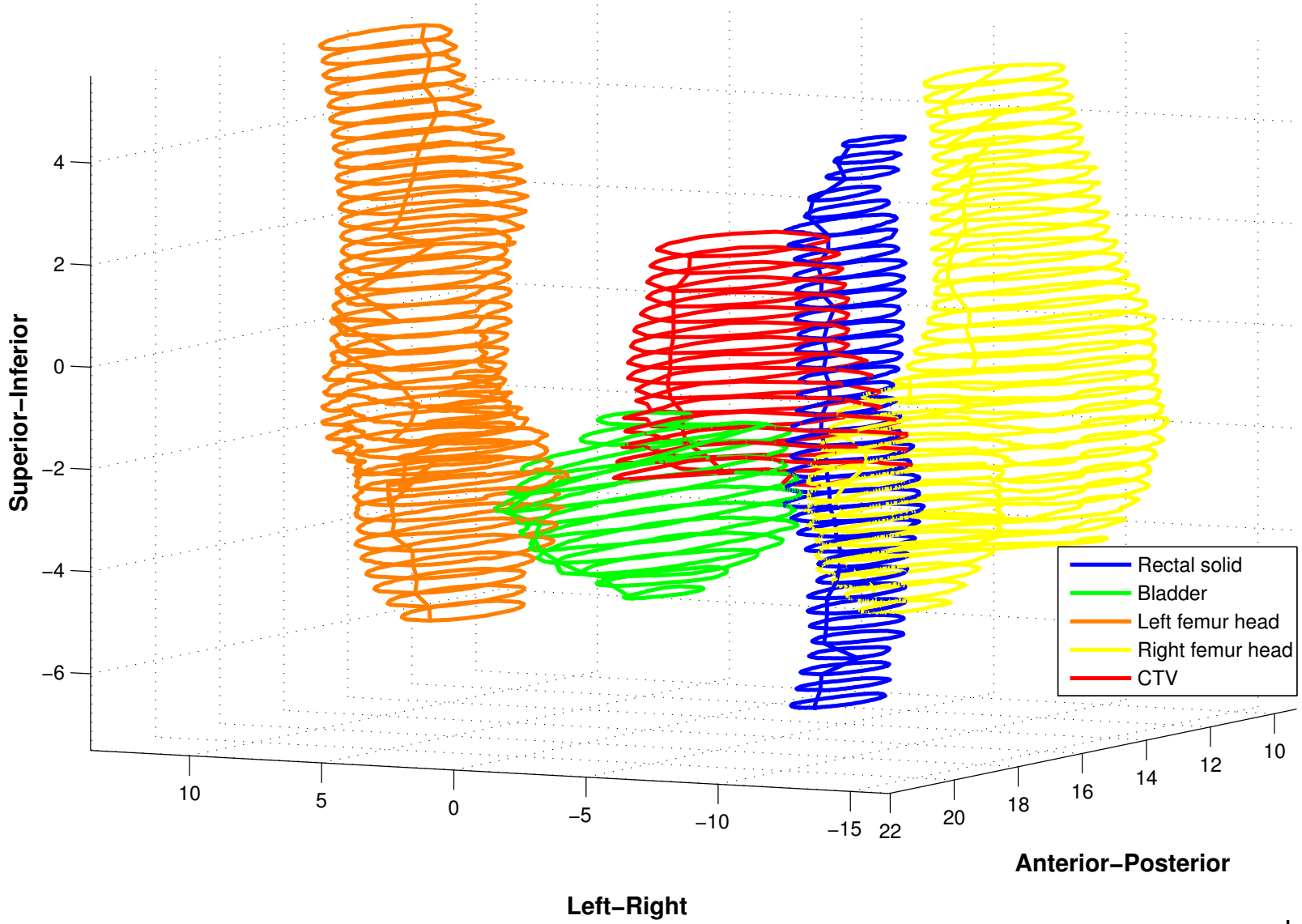
where

$$\Pr(Z > z_{1-\delta}) = \delta$$

$$Z \sim N(0,1)$$

Traditional/robust comparison

CTV
RT femhd
LT femhd
unspecified
PTV 0
BLADDER 0
RECTALSOLID 0


Superior−Inferior
4
2
0
−2
−4
−6
10
5
0
−5
−10
−15
Left−Right
22
20
18
16
14
12
10
Anterior−Posterior
Rectal solid
Bladder
Left femur head
Right femur head
CTV

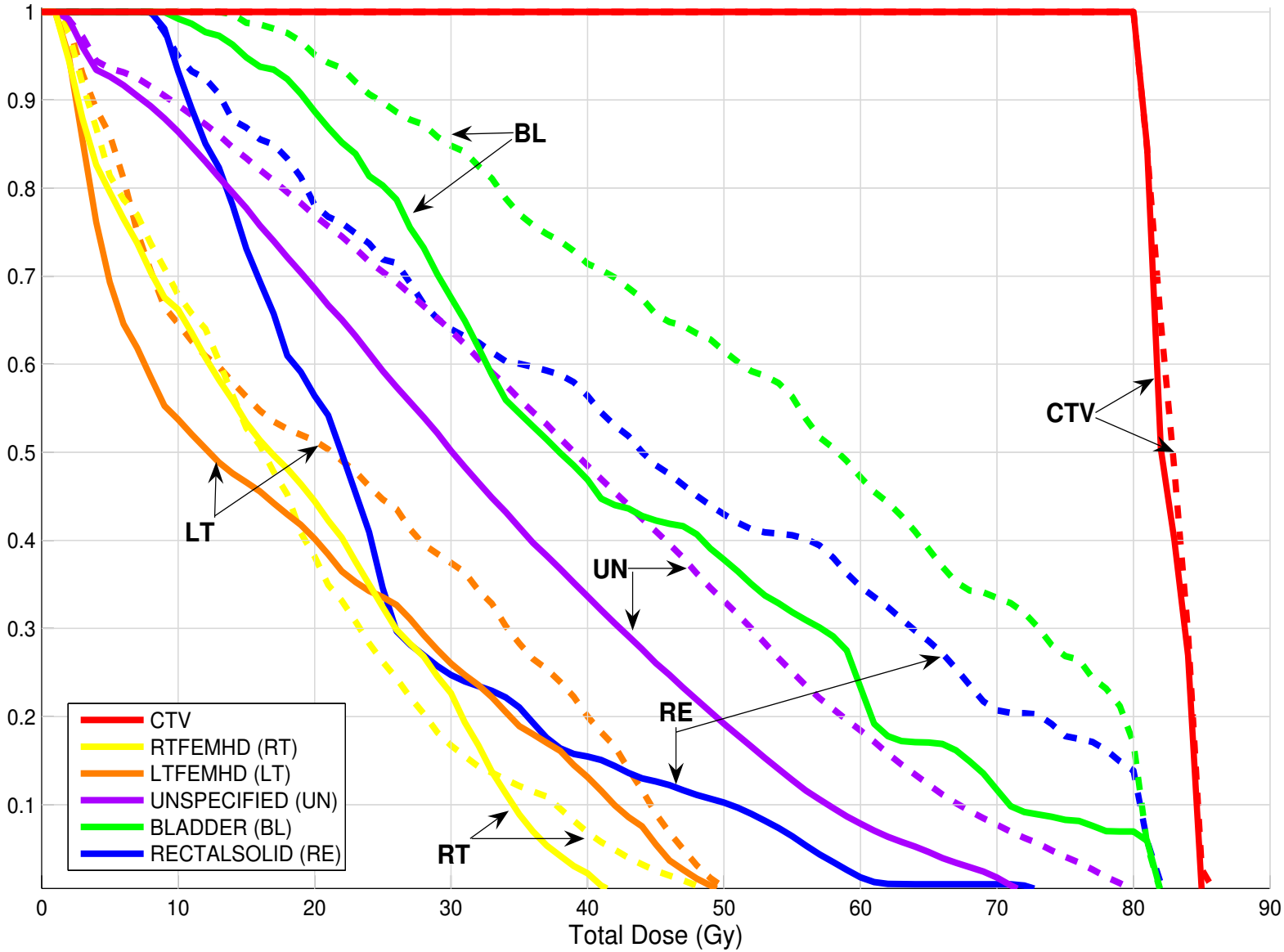
Uncertainty

Simple shifts (rigid body deformations):

Direction	Shift	Probability
None	0 mm	0.250
Anterior	5 mm	0.125
Posterior	3 mm	0.125
Left	2 mm	0.125
Right	2 mm	0.125
Inferior	3 mm	0.125
Superior	4 mm	0.125

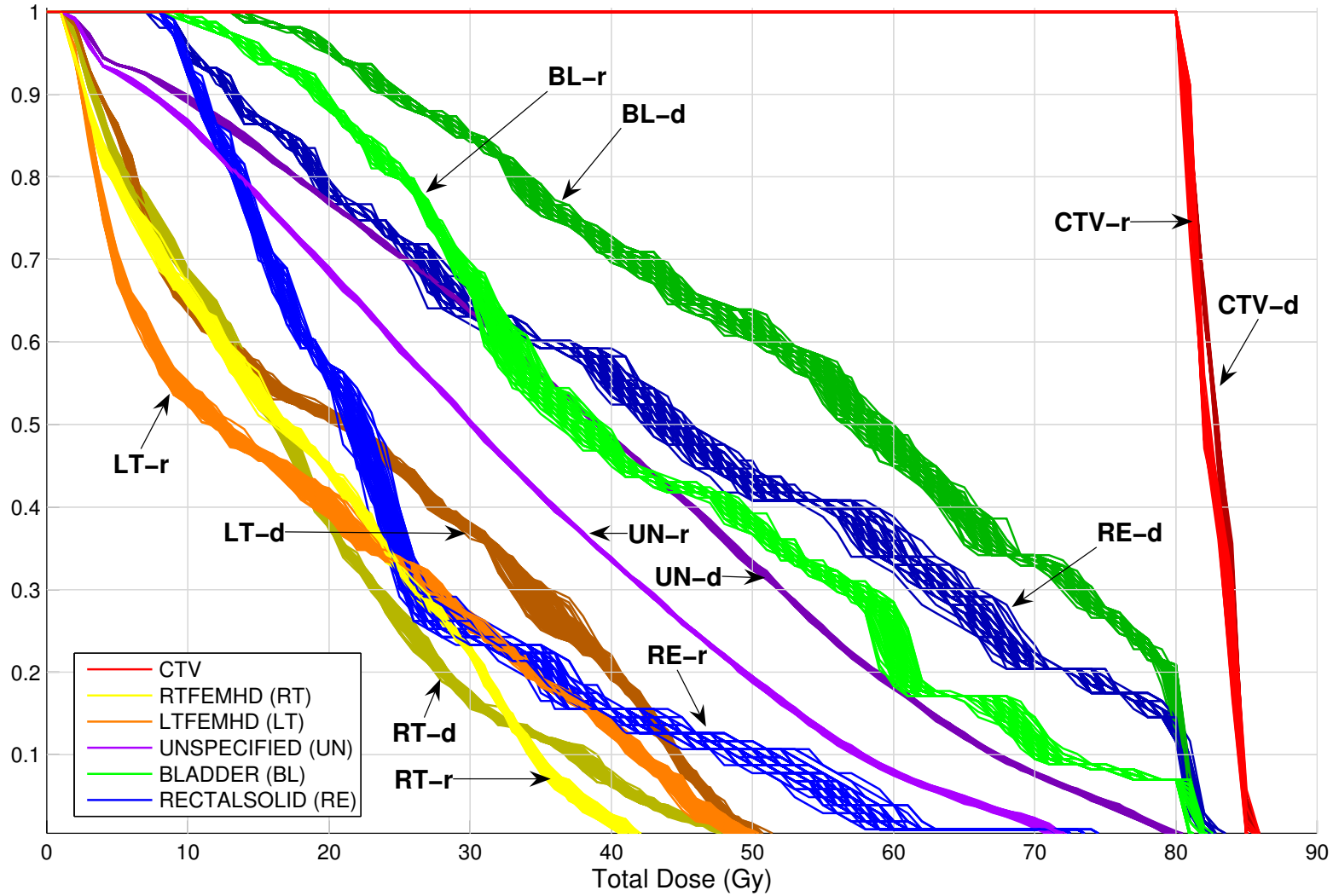
Side-by-side comparison

- 8 mm voxel size
- shift patient randomly each fraction
- compute cumulative dose for a patient (45 fractions, adds up over ~6 weeks)
- plot DVH for the expected cumulative dose



Dose-Expected VH:

- robust – solid curves,
- deterministic – dashed.

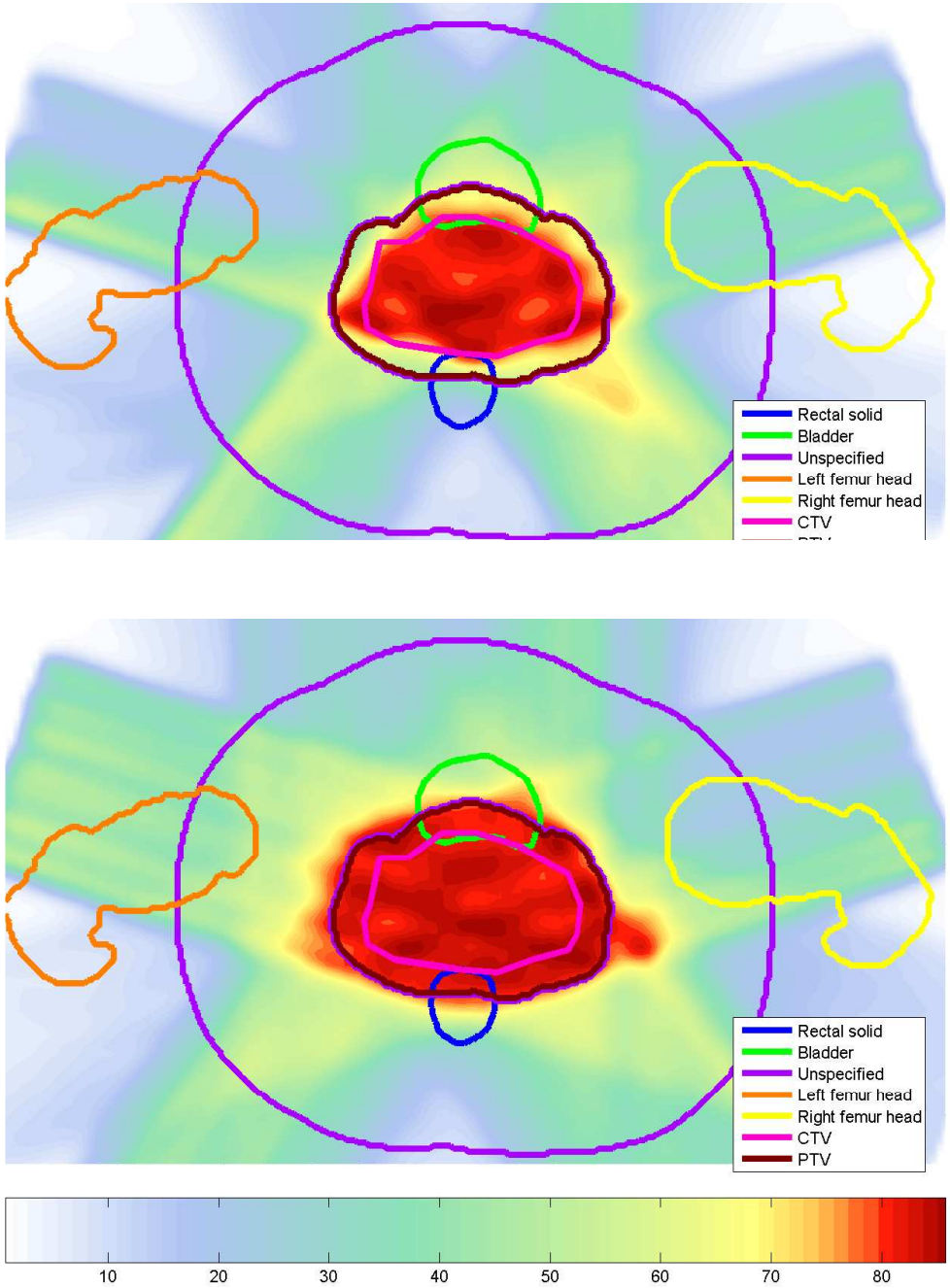


DVH "cloud" for 100 patients:

- robust – solid curves,
- deterministic – dashed.

2-D plot of cumulative dose:

- deterministic (bottom)
- robust (top)



Robust approach in detail

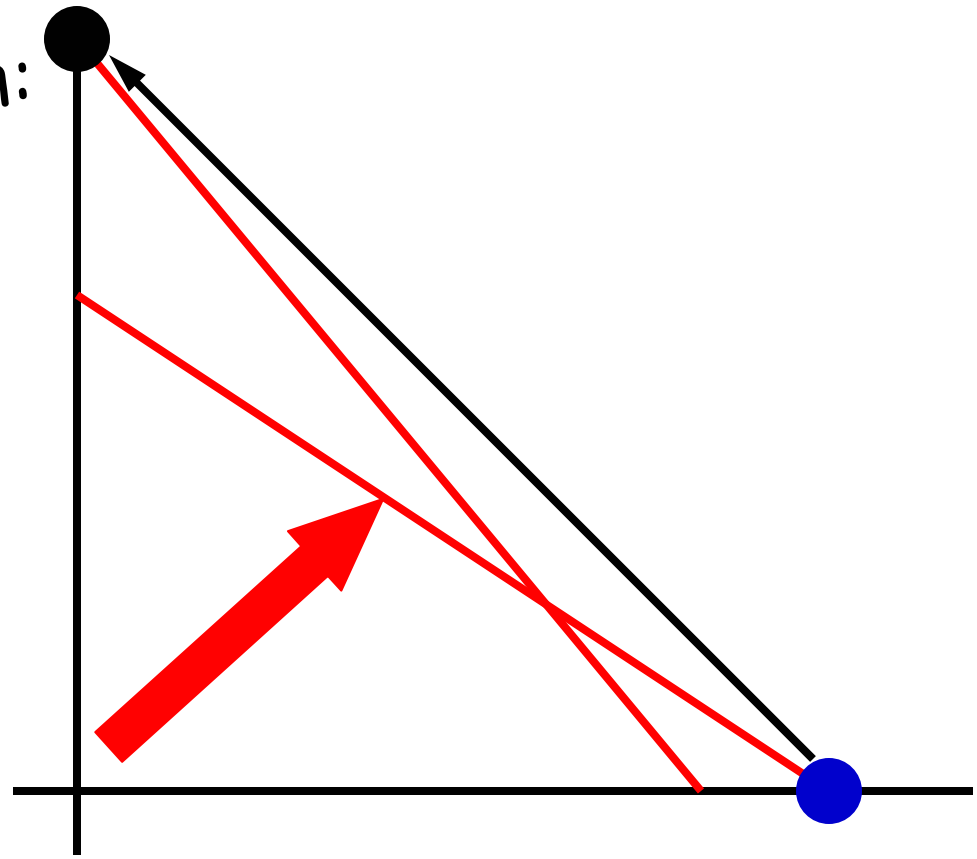
What can go wrong with LP?

Simple LP problem:

max $x + y$

s.t. $x + .99\,y \leq 1$

$x, y \geq 0$



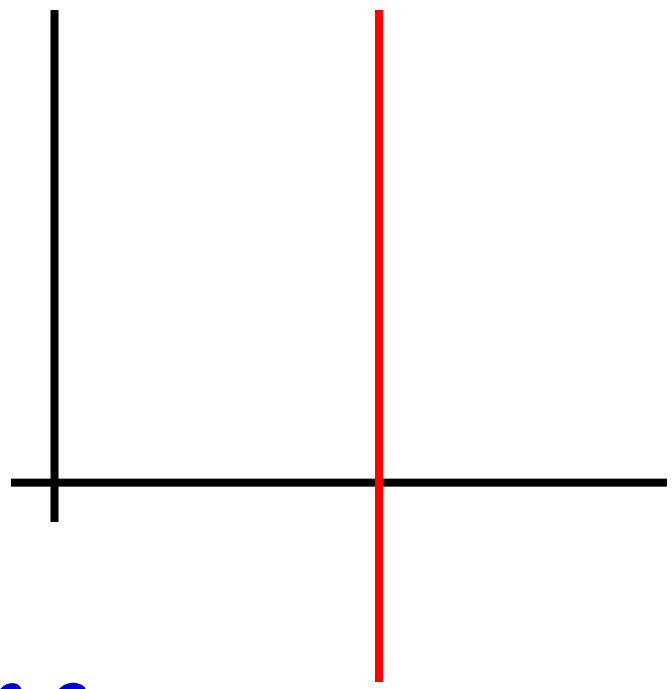
Robust linear programming

Simple linear constraint:

$$a\,x \leq 1$$
$$x \geq 0$$

with a "close" to 1,

$0 \leq a \leq 2$



Want x to work for all such a

How do we deal with it?

$$a\,x \le 1,\ x \ge 0 \qquad \text{for all} \qquad 0 \le a \le 2$$

$$\Updownarrow$$

$$\max_{0 \le a \le 2,\ x \ge 0} a\,x \le 1,\ x \ge 0$$

$$\Updownarrow$$

$$2\,x \le 1,\ x \ge 0$$

$$\Updownarrow$$

$$x \le 1/2,\ x \ge 0$$

A slightly more involved example:

$$a\,x + b\,y \quad \leq \; 1$$

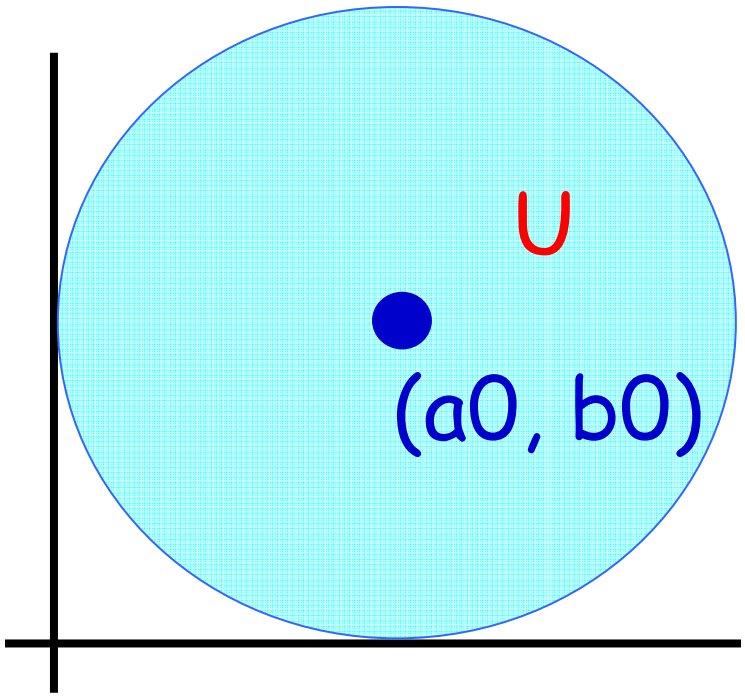
where (a, b) "close" to (1, 1),

in ellipsoidal "uncertainty" set U:

$(a, b) = (a_0, b_0) + (\Delta a, \Delta b)$

$(a_0, b_0) = (1, 1)$

$\Delta a^2 + \Delta b^2 \leq \; 1$



Want (x, y) to satisfy

$a\,x + b\,y \quad \leq \; 1,$

for all (a, b) from U

$$a\,x + b\,y \le 1 \qquad \text{for all} \qquad (a, b) \text{ in } U$$

$$\Updownarrow$$

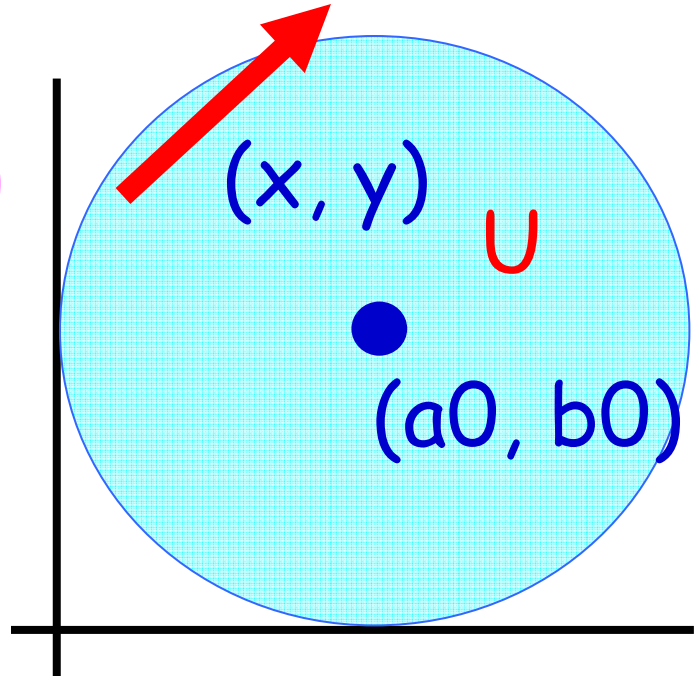
$$\max_{(a,\,b)\text{ in }U} \; a\,x + b\,y \le 1$$

What about $a\,x + b\,y$?

$$a\,x + b\,y = (a_0\,x + b_0\,y) + (\Delta a\,x + \Delta b\,y)$$

Think of (x, y) fixed

$$\max_{(a,\,b)\text{ in }U} \; a\,x + b\,y \quad (\leq 1\,?)$$



$$(a_0\,x + b_0\,y) \;+\; \max_{\Delta a^2 + \Delta b^2 \leq 1} \; (\Delta a\,x + \Delta b\,y) \quad (\leq 1\,?)$$

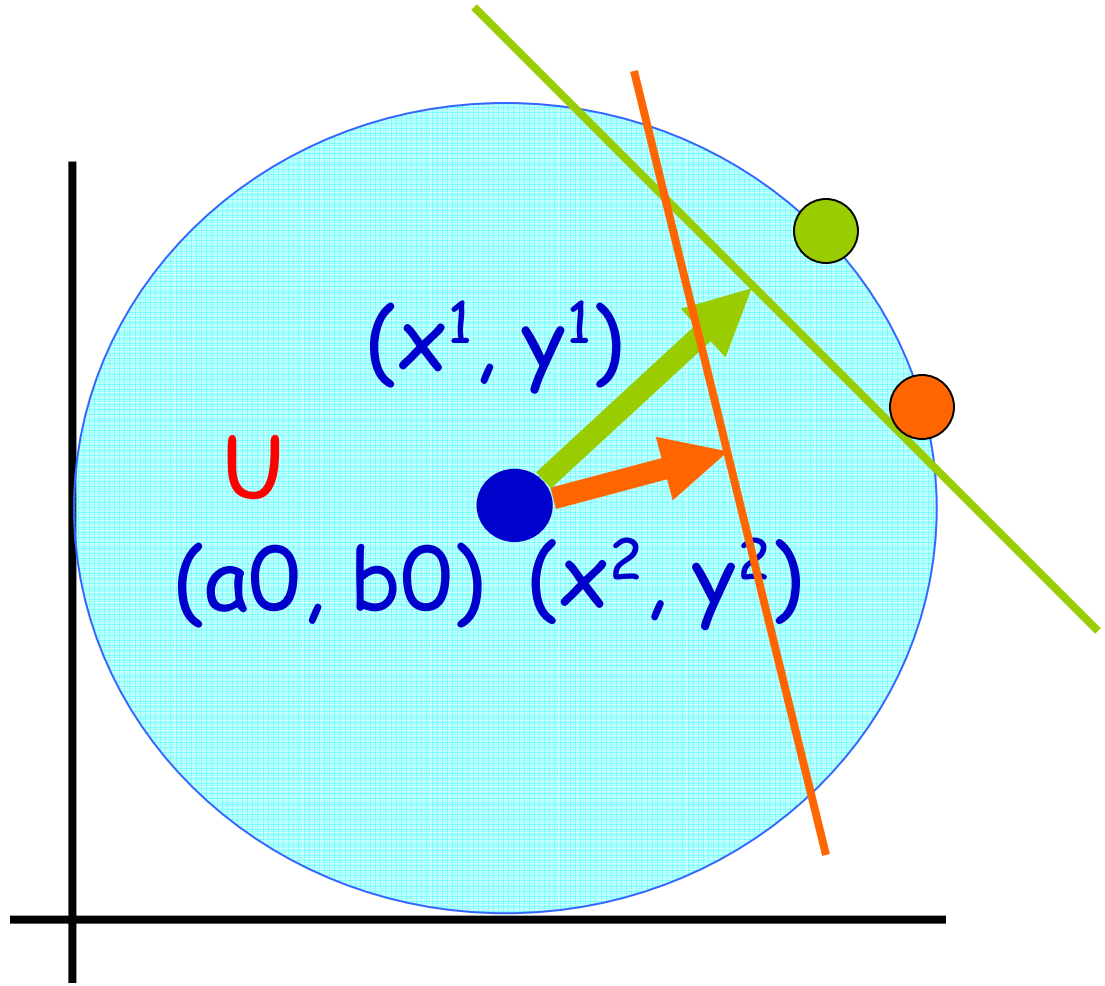
$$\max_{\Delta a^2 + \Delta b^2 \le 1} (\Delta a\, x + \Delta b\, y) \quad (\le 1 - (a_0 x + b_0 y)\ ?)$$

Note:

$\Delta a\, x + \Delta b\, y$

$\le ||(x, y)||$

$= (x^2 + y^2)^{1/2}$



$$a\,x + b\,y \le 1 \qquad \text{for all} \qquad (a, b) \text{ in } U$$

$$\Updownarrow$$

$$\max_{(a,\,b)\text{ in } U} \; a\,x + b\,y \le 1$$

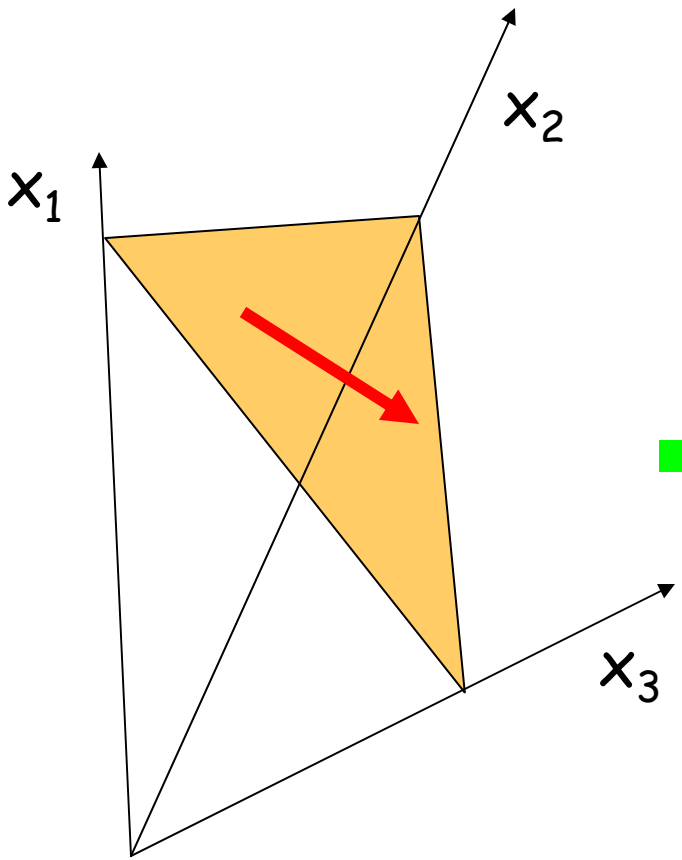
$$\Updownarrow$$

$$(a_0\,x + b_0\,y) + \max_{\Delta a^2 + \Delta b^2 \le 1} (\Delta a\,x + \Delta b\,y) \le 1$$

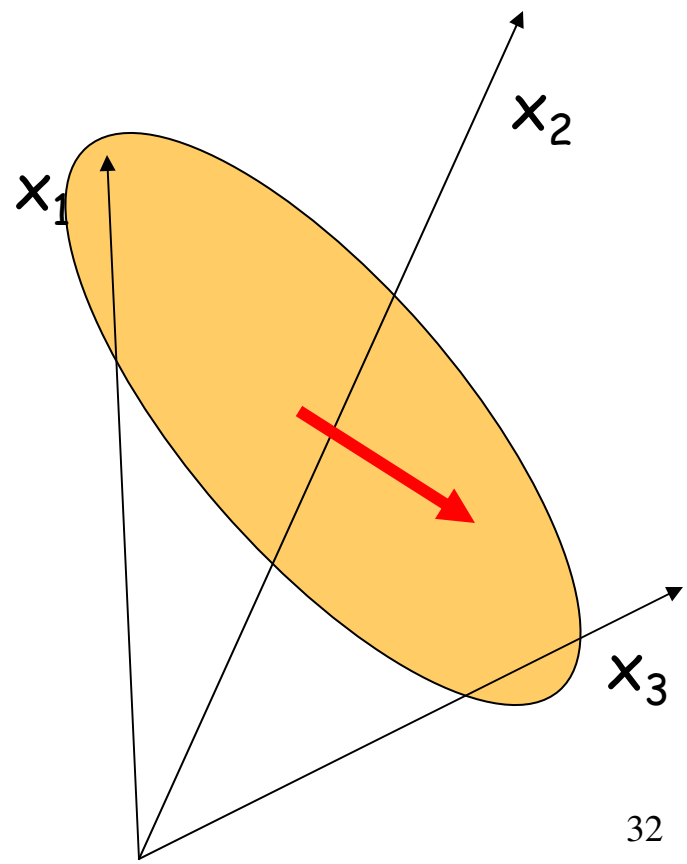
$$\Updownarrow$$

$$||(x, y)|| \le 1 - (a_0\,x + b_0\,y)$$

Robust LP geometrically



A robust LP: minimize over "Lorentz" cone



LP: minimize over nonnegative orthant

Alternative interpretations

Probabilistic constraint: $\Pr(A\, w(b) \le c) \ge \alpha$,

A taken from α-level set of a (multi-variate normal) probability distribution

SOCP equivalent:

$$\| R\, w(b) \| \le c - A_0\, w(b)$$

Can be solved "efficiently" — IPM!

Towards clinical standards

Uncertainty specification

- Appeal to probabilistic interpretation — scenarios for the influence matrix
- Pick scenarios based on the geometry
- Only few, e.g., 7, scenarios suffice
- Works well since the uncertainty is overestimated (voxels are not independent)

Computation

Import data: ADAC Pinnacle3 → RTOG format → CERR → MATLAB

Solve: use SeDuMi v. 1.1 (http://sedumi.mcmaster.ca)

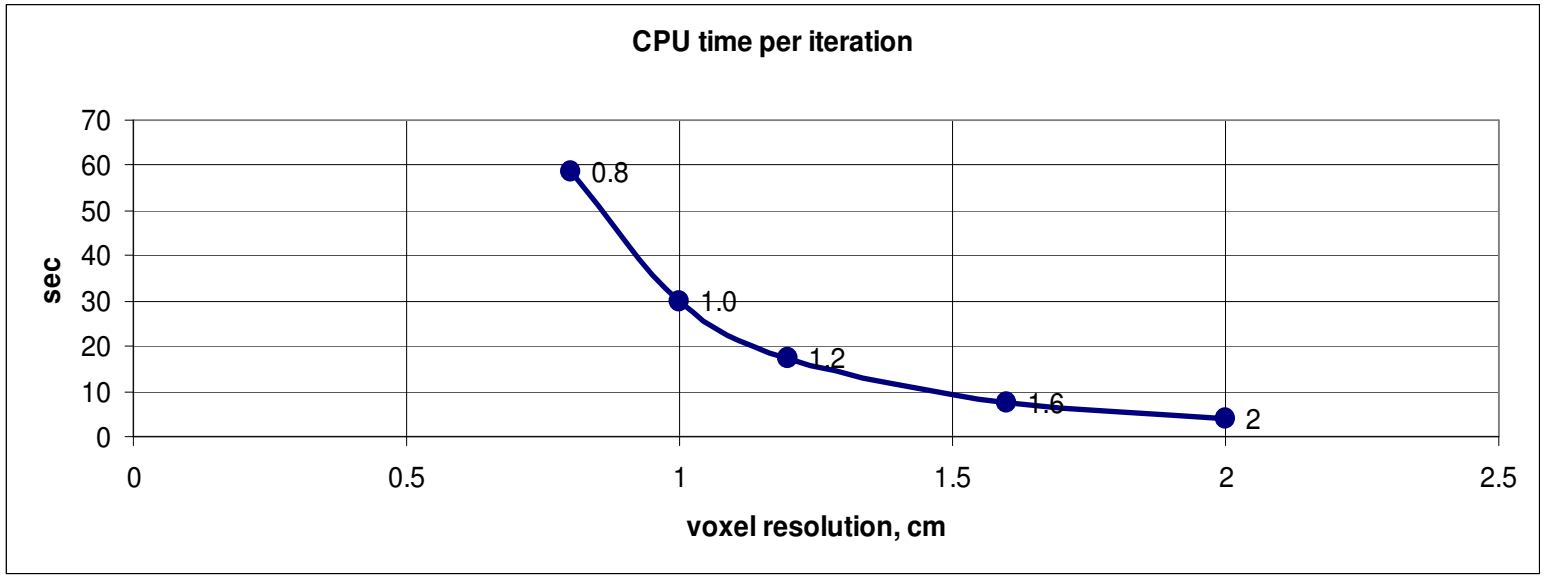
CPU time < 30 min

~3400 1cm-voxels, ~1000 beamlets, 7 scenarios, P4 3.2 GHz (or AMD), 2GB RAM, Linux/Windows

Clinically accepted: 2-3mm voxel resolution

Profiling

- Typically 50-60 iterations suffices
- Bottleneck: linear algebra (~1/(voxel size)^3)



80% time spent on matrix-matrix product

– highly parallelizable: on 4 PIII ~800MHz solve 2 times faster

Problem dimension reduction

- Few good scenarios
- Dose aggregation
- Voxel sampling

Not fully explored yet!

Conclusions

- Traditional approach: safety margin forces higher cumulative dose
- Robust approach: superior organ sparing
- Drawback: computational requirements
  - Dose aggregation, boundary sampling, etc.
- Plan evaluation tools need to address uncertainties
  - Dose-Expected VH, DVH clouds

Future work:

- More testing
- Scenario selection
- Algorithmic and modeling improvements

Spare slides

Robust LP formulation

max $c^T x$

s.t. $A^{(i)} x \leq b_i$, $i = 1,\ldots,m$

where

$c, x \in R^n$, $A^{(i)} \in R^{1 \times n}$, $A^{(i)} = A^{(i)}_0 + w_i P_i$

with

$w_i \in R^{1 \times k_i}$, $||w_i|| \leq 1$, $i=1,\ldots,m$, $P_i \in R^{k_i \times n}$

Sample computational results

Voxel Size	V	T	Iterations	Solve Time
2.0 cm	411	10	31	3 min
1.6	826	25	39	8
1.2	1934	56	61	30
1.0	3307	88	65	62
0.8	6569	191	97	199

Computational profile

Function Name	Calls	Total Time	**Self Time***	Total Time Plot (dark band = self time)
getada1 (MEX-function)	30	1275.000 s	1275.000 s	
getada2 (MEX-function)	30	116.470 s	116.470 s	
getsymbada	1	64.830 s	62.460 s	
Amul	285	46.580 s	46.580 s	
blkchol (MEX-function)	30	44.990 s	44.990 s	
wrapPcg	94	74.760 s	27.600 s	
getDAtm	30	24.730 s	14.770 s	
sedumi	1	1646.310 s	10.810 s	
ddot (MEX-function)	870	8.850 s	8.850 s	
wregion	30	64.600 s	6.500 s	
sddir	64	57.410 s	6.470 s	
…	…	…	…	

Parallelization

- Almost 80% of the time spent forming matrix-matrix product ADA'
- Not a standard BLAS call, but is highly parallelizable

Tools and equipment: OpenMP (e.g., Intel C), 4 PIII ~800MHz

Iteration	1CPU	2CPU	4CPU
1	327 s	248 s	135 s
2	327 s	250 s	135 s
3	327 s	248 s	135 s
4	327 s	249 s	136 s
Total time	**12733 s**	**10387 s**	**7017 s**

Memory requirements

- MATLAB manages memory poorly
- The most memory-expensive part is preprocessing
- Easy to bring down memory requirements to roughly twice the data storage

Example: 1cm-voxels ≈ 240MB, realistic target — solve on 396MB RAM laptop.

Dose-Volume constraints

- 0-1 var for each voxel: = 1 if dose is > d_k.
- Mixed integer program: Very Hard to solve!
- Alternative: upper bound the "excess" dose. For healthy structure H_k, we require:

$$\sum_{v \in H_k} (Dose(v) - d_k)_+ \leq g_k$$

linear constraints

Related work

- Optimization incorporating uncertainty
  - Replace dose with expected dose (Li & Xing 2000)
  - Physics approach: fluence profiles under uncertainty (Unkelbach & Oelfke 2004, 2005)
- Effects of uncertainty on:
  - Dose delivered (Beckham et al 2002, Lujan et al 1999)
  - Tumour control probability (Craig et al 2003, Van Herk et al 2002)
- Biology
  - Organ deformation (Brock et al 2003, Paganetti et al 2004, 2005)
  - Tumour growth during treatment (Wein et al 2000)
- Adaptive Radiation Therapy
  - (Löf et al 1998, Martinez et al 2001, Rehbinder et al 2004, Yan et al 1997)

Scenario selection

- Many studies on prostate motion during radiation therapy (Langen & Jones 2001)
- Prostate volume: no significant changes (Mechalakos et al 2002, Roeske et al 1995)
- Deformation: extent is small, relative to motion (Deurloo et al 2005)
- Rotations: about 4° along left-right axis (Van Herk et al 1995)

⇒ Motion: mainly shifts (Wong et al 2005, Balter et al 1995, Liu et al 2004, Lattanzi et al 1998)