Producing IMRT plans robust to uncertainty in lung motion

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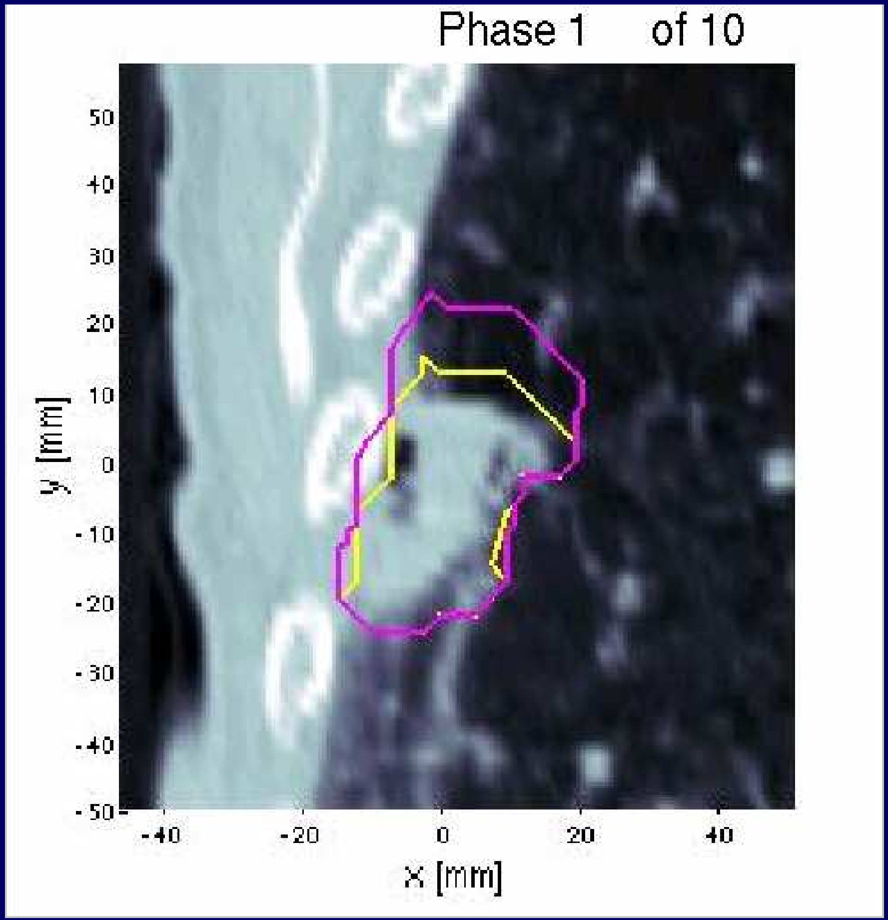
The Main Idea

- We consider beamlet weight/intensity optimization in IMRT
- Uncertainty is introduced in the form of irregular breathing motion (intrafraction)
- How do we ensure that we generate "good" plans in the face of such uncertainty?

Tumor motion



- What do we do if motion is irregular?

Outline

- Uncertainty induced by irregular breathing
- Robust optimization background
- Robust IMRT formulation

How to mitigate uncertainty

- In general, one can use a margin
  - The good: uniform dose to tumor
  - The bad (and ugly): healthy tissue overly irradiated
- What if the uncertainty is induced by motion?
  - Model the motion and include it intelligently in the optimization: "motion pdf"
  - Assumption: "the motion … is reproducible and stable during the treatment delivery"
  - This motivates the use of robust optimization
    - As opposed to uncertainty due to motion, we focus on uncertainty in the motion itself

Robust Optimization

- Optimizing objective function over constraints with uncertain data (modeled)

- Goal: Want an optimal “robust” solution (feasible under all realizations of uncertainty)

- Our formulation is linear (e.g. objective: mean or max dose; constraints: dose >= …)

Robust Optimization

- Uncertainty: imprecise measurements, future info, etc.
- Want optimal solution to remain feasible under all realizations of uncertain data

$$\begin{array}{rll} \min & \mathbf{c}'\mathbf{x} & \\ \text{st} & \mathbf{A}\mathbf{x} \geq \mathbf{b} & \forall \mathbf{A} \in \mathcal{U} \end{array}$$

- Want *robust counterpart* to be efficiently solvable
- Complexity depends heavily upon choice of uncertainty set
- Classification, image reconstruction, scheduling, options pricing, supply chain, portfolio selection, truss design …

Linear IMRT model

- Basic problem: Minimize total dose delivered, subject to tumor receiving at least some prescribed dose

Dose to voxel v from unit intensity of beamlet b

Intensity of beamlet b

Desired dose to voxel v

$$
\begin{aligned}
\text{min} \quad & \sum_{v \in \mathcal{V}} \sum_{b \in \mathcal{B}} D_{v,b} w_b \\
\text{st} \quad & \sum_{b \in \mathcal{B}} D_{v,b} w_b \geq \theta_v && \forall\, v \in \mathcal{T} \\
& w_b \geq 0 && \forall\, b \in \mathcal{B}
\end{aligned}
$$

- To incorporate motion, convolve pmf with *D* matrix…

Warm-up to robust formulation

- Nominal problem:

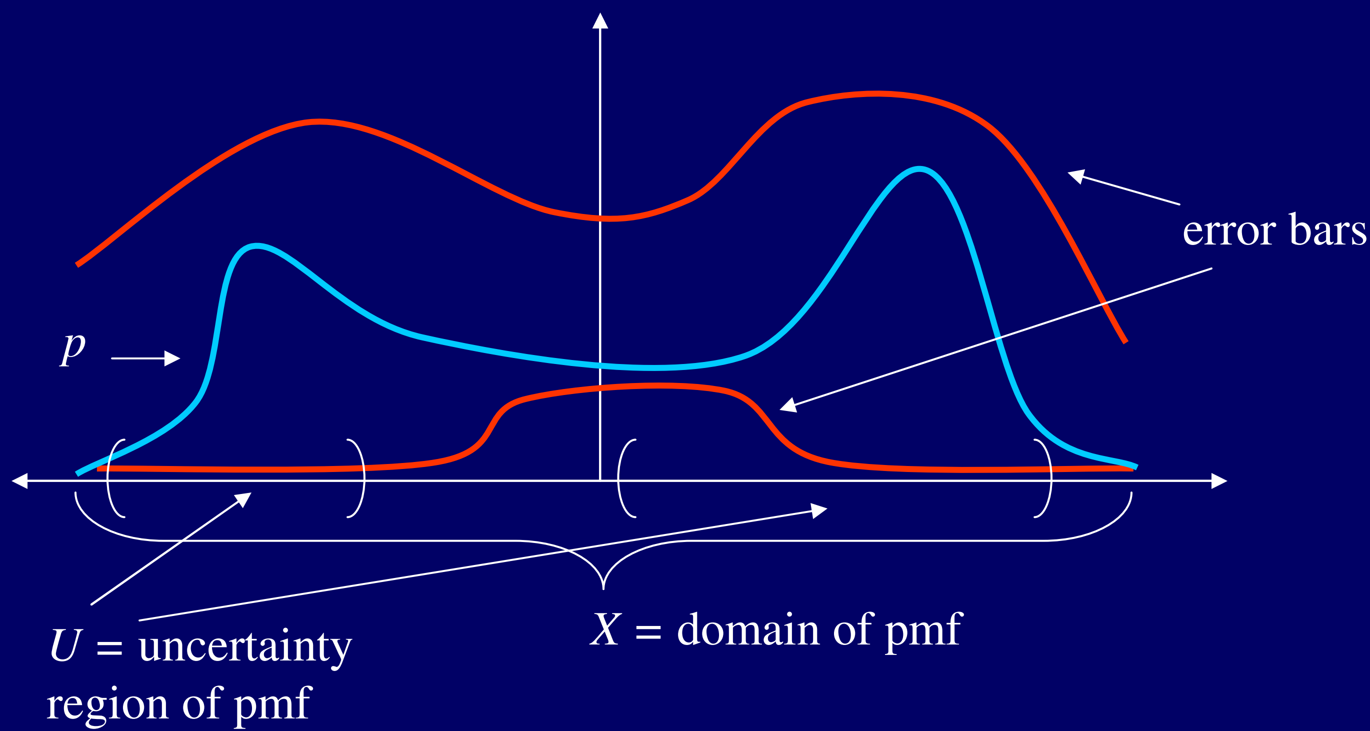
Dose from unit intensity of beamlet b to voxel v shifted by x

Nominal pmf (frequency of time tumor spends at x)

$$\begin{aligned} \text{min} \quad & \sum_{v \in \mathcal{V}} \sum_{b \in \mathcal{B}} \sum_{x \in X} \Delta_{v,x,b} p(x) w_b \\ \text{st} \quad & \sum_{b \in \mathcal{B}} \sum_{x \in X} \Delta_{v,x,b} p(x) w_b \geq \theta_v \qquad \forall\, v \in \mathcal{T} \\ & w_b \geq 0 \qquad \forall\, b \in \mathcal{B} \end{aligned}$$

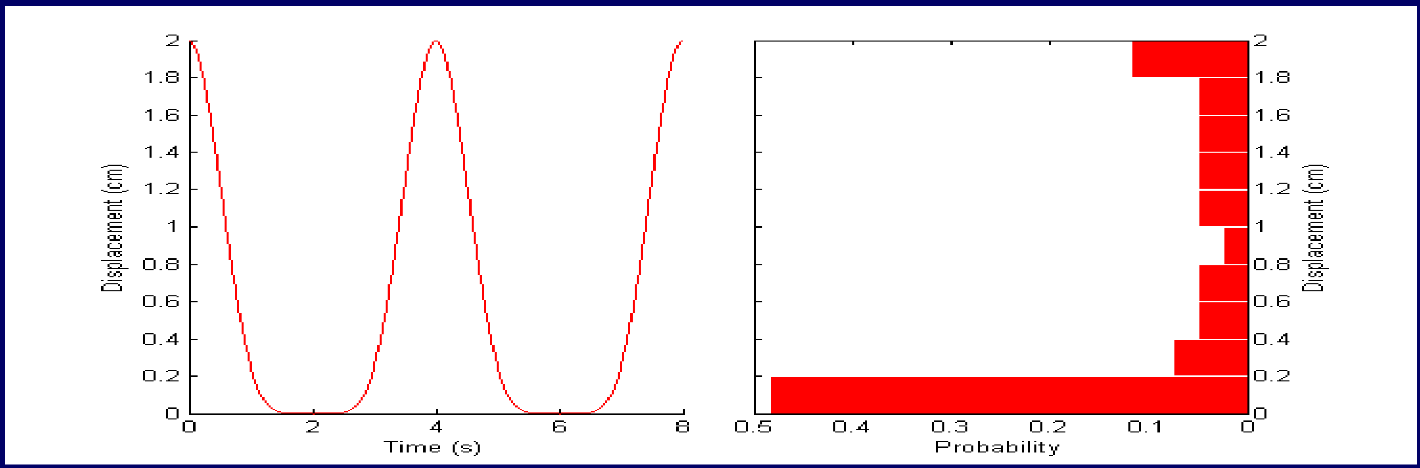
- Introduce uncertainty in *p*…

Model of uncertainty

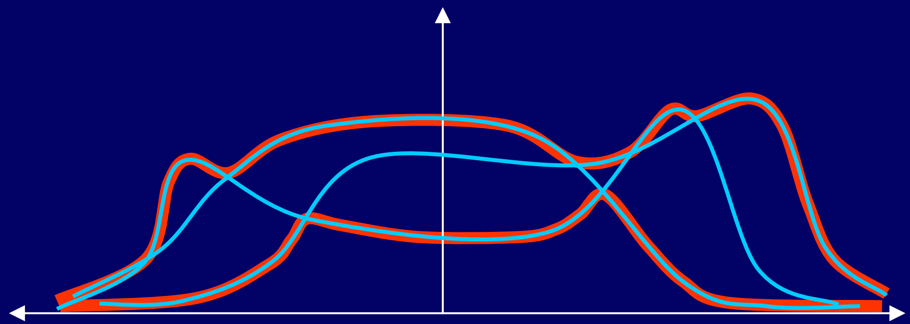


PMF from motion data

- We can get a pmf from sinusoidal data by "horizontal binning"



- We can get "error bars" as upper/lower envelopes of many pmfs



Robust formulation

$$\begin{aligned}
\text{min} \quad & \sum_{v\in\mathcal{V}}\sum_{b\in\mathcal{B}}\sum_{x\in X} \Delta_{v,x,b}\, p(x) w_b \\
\text{st} \quad & \sum_{b\in\mathcal{B}}\sum_{x\in X} \Delta_{v,x,b}\, p(x) w_b + \beta_v(\boldsymbol{w}) \geq \theta_v \qquad \forall\, v \in \mathcal{T} \\
& w_b \geq 0 \qquad \forall\, b \in \mathcal{B}
\end{aligned}$$

where

$$\begin{aligned}
\beta_v(\boldsymbol{w}) = \text{min} \quad & \sum_{b}\sum_{x\in U} \Delta_{v,x,b}\, \widehat{p}(x) w_b \\
\text{st} \quad & \sum_{x\in U} \widehat{p}(x) = 0 \\
& -\underline{p}(x) \leq \widehat{p}(x) \leq \overline{p}(x) \qquad \forall\, x \in U
\end{aligned}$$

- Robust counterpart stays LP

Robust formulation

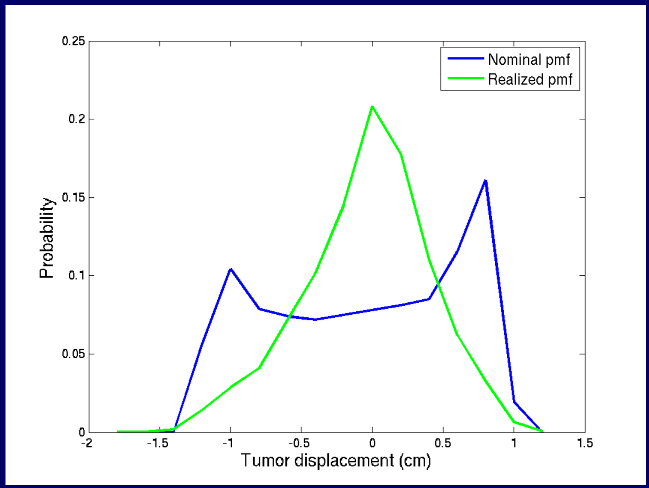
$$\beta_v(\boldsymbol{w}) = -\sum_{b\in\mathcal{B}}\sum_{j>j^*}(\Delta_{v,x(j),b} - \Delta_{v,x(j^*),b})\underline{p}(x(j))w_b$$
$$-\sum_{b\in\mathcal{B}}\sum_{j<j^*}(\Delta_{v,x(j^*),b} - \Delta_{v,x(j),b})\overline{p}(x(j))w_b$$

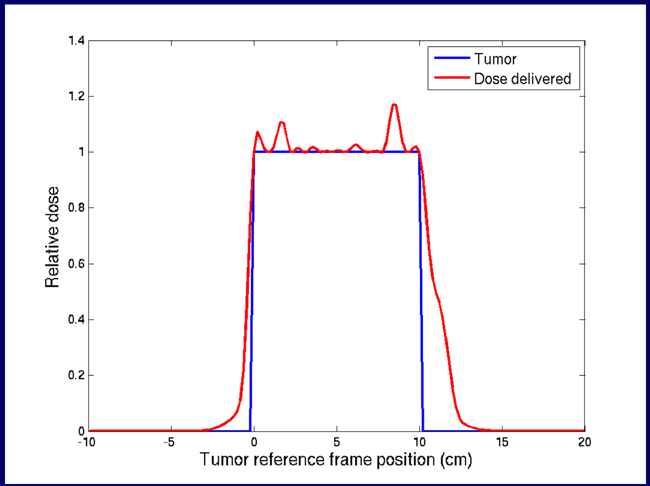
- Idea: Protect against voxels in tumor from spending too much time in low dose region and too little time in high dose region of static dose distribution

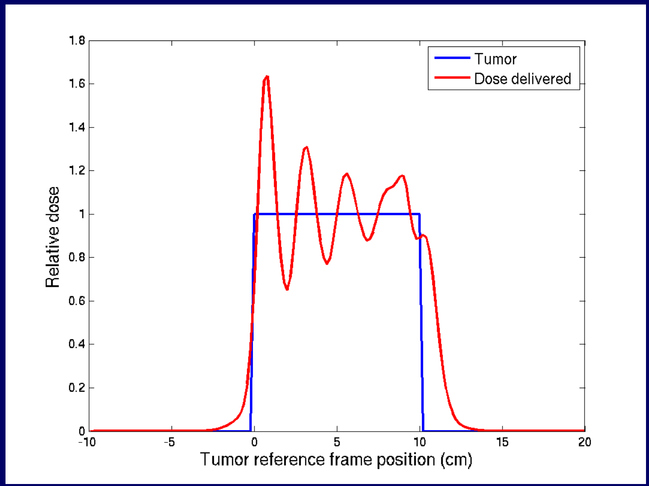
Motivation re-visited

- Nominal problem

$$
\begin{aligned}
\text{min} \quad & \sum_{v \in \mathcal{V}} \sum_{b \in \mathcal{B}} \sum_{x \in X} \Delta_{v,x,b}\, p(x) w_b \\
\text{st} \quad & \sum_{b \in \mathcal{B}} \sum_{x \in X} \Delta_{v,x,b}\, p(x) w_b \geq \theta_v \qquad && \forall\, v \in \mathcal{T} \\
& w_b \geq 0 && \forall\, b \in \mathcal{B}
\end{aligned}
$$

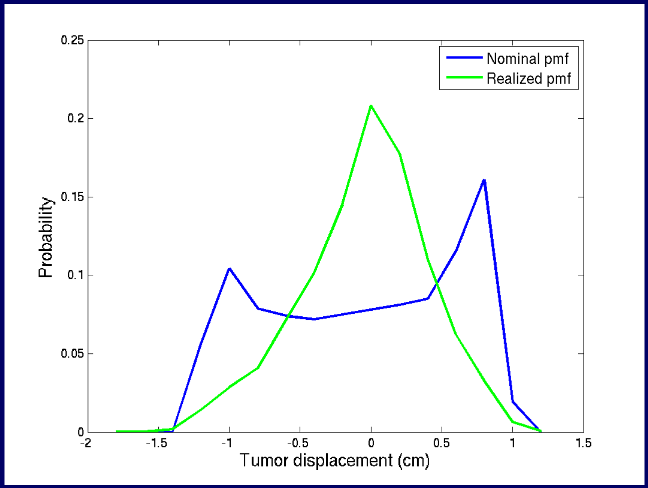


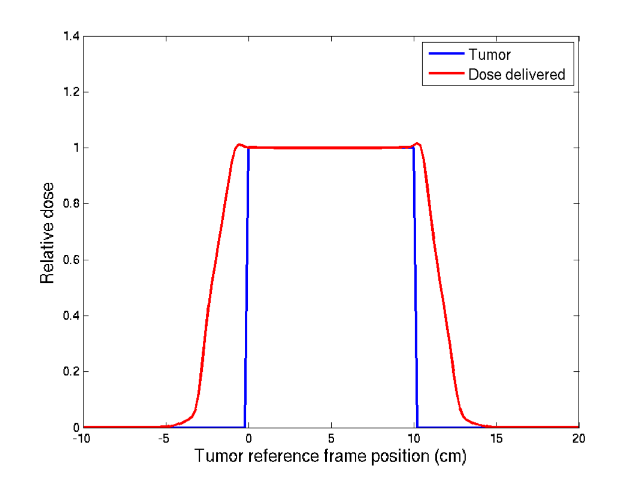


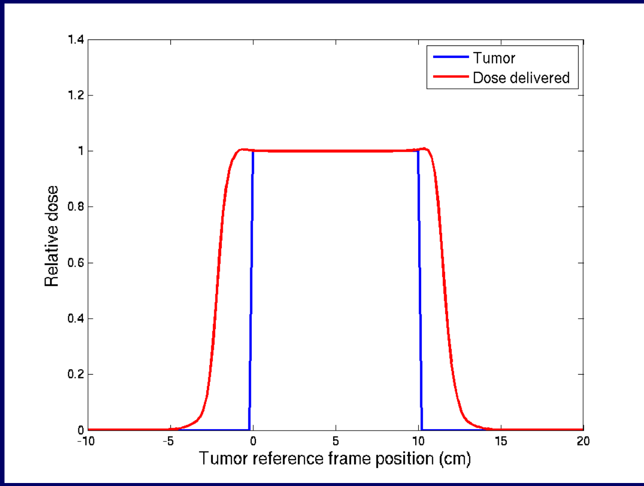


Margin illustration

$$
\begin{array}{lll}
\text{min} & \displaystyle\sum_{v \in \mathcal{V}} \sum_{b \in \mathcal{B}} \Delta_{v,x,b} p(x) w_b & \\
\text{st} & \displaystyle\sum_{b \in \mathcal{B}} D_{v,b} w_b \geq \theta_v & \forall\, v \in \mathcal{T} \\
 & \displaystyle\sum_{b \in \mathcal{B}} D_{v,b} w_b \geq \mu_v & \forall\, v \in \mathcal{M} \\
 & w_b \geq 0 & \forall\, b \in \mathcal{B}
\end{array}
$$

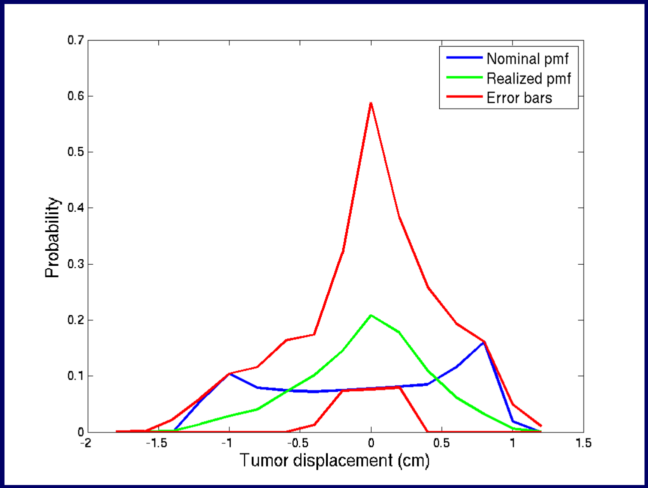


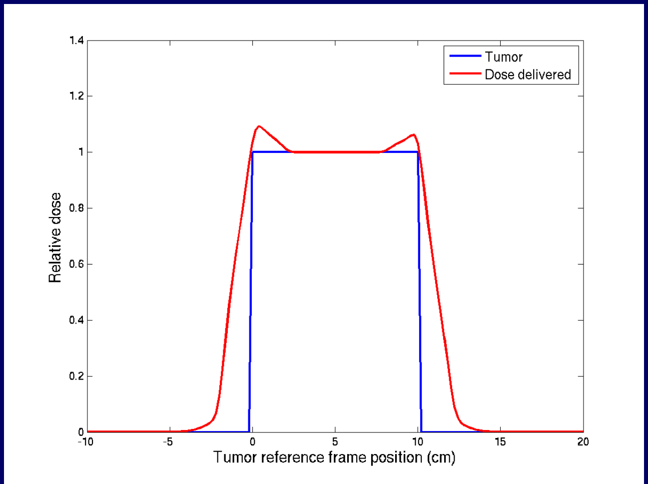


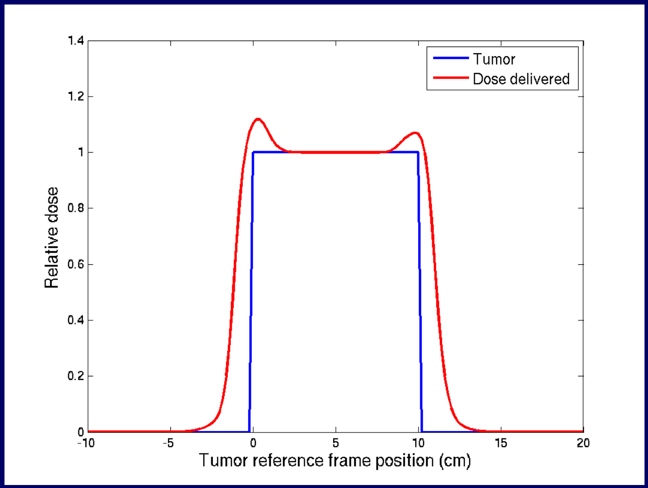


Robust formulation results

- Robust problem
  - Protects against uncertainty unlike nominal formulation
  - Spares healthy tissue better than margin formulation



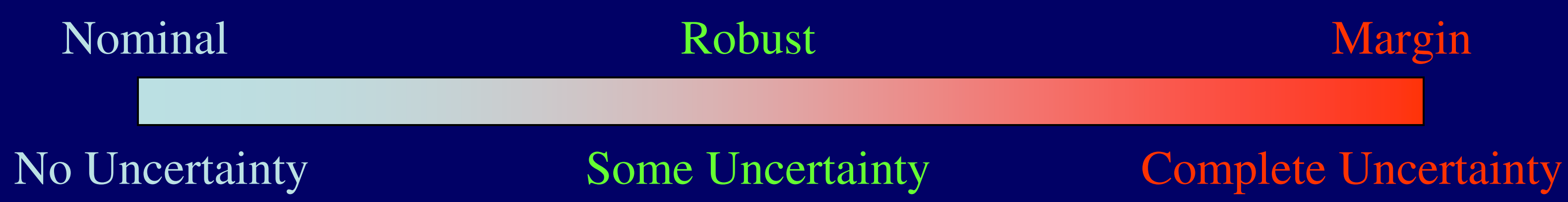




Numerical results

	Nominal	Robust	Margin
Total dose delivered	85.29 %	91.43 %	100.00 %
Dose to normal tissue	31.41 %	61.94 %	100.00 %

Continuum of Robustness



- Can prove this mathematically
- Flexible tool allowing planner to modulate his/her degree of conservatism based on the case at hand

Conclusions

- Introduced linear, robust formulation and "Continuum of Robustness"
- Illustrated results of robust formulation and compared it to nominal and margin
- Extensions: 3D, serial organs, other uncertainty
- Take home: Robust framework is flexible with advantages of both nominal and margin

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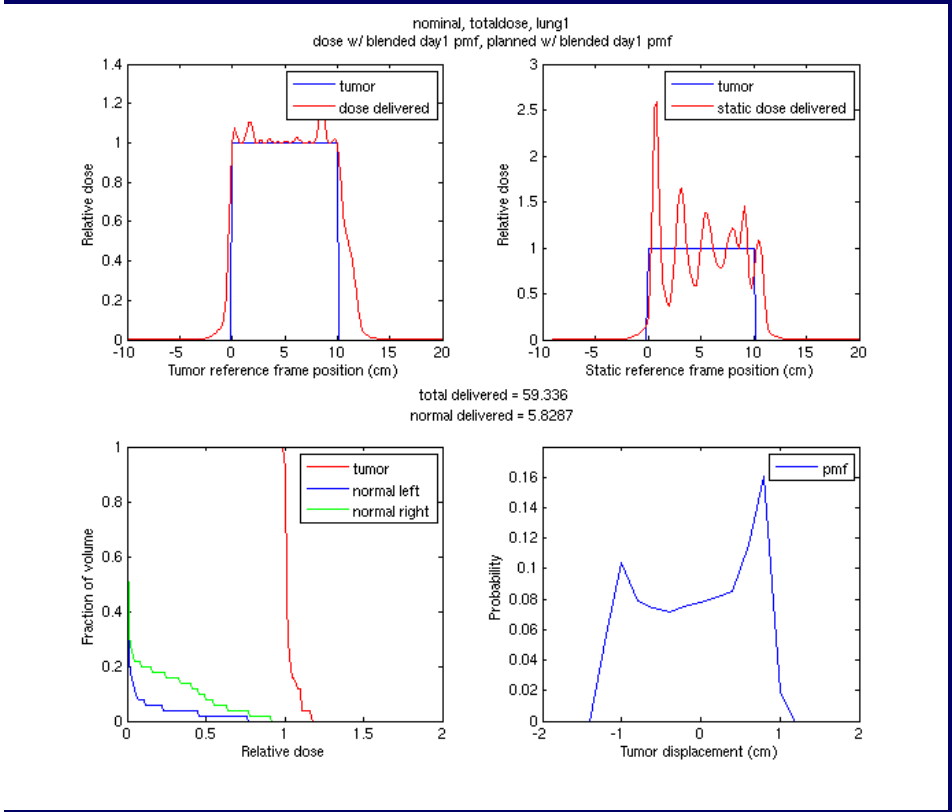
Linear formulation implemented

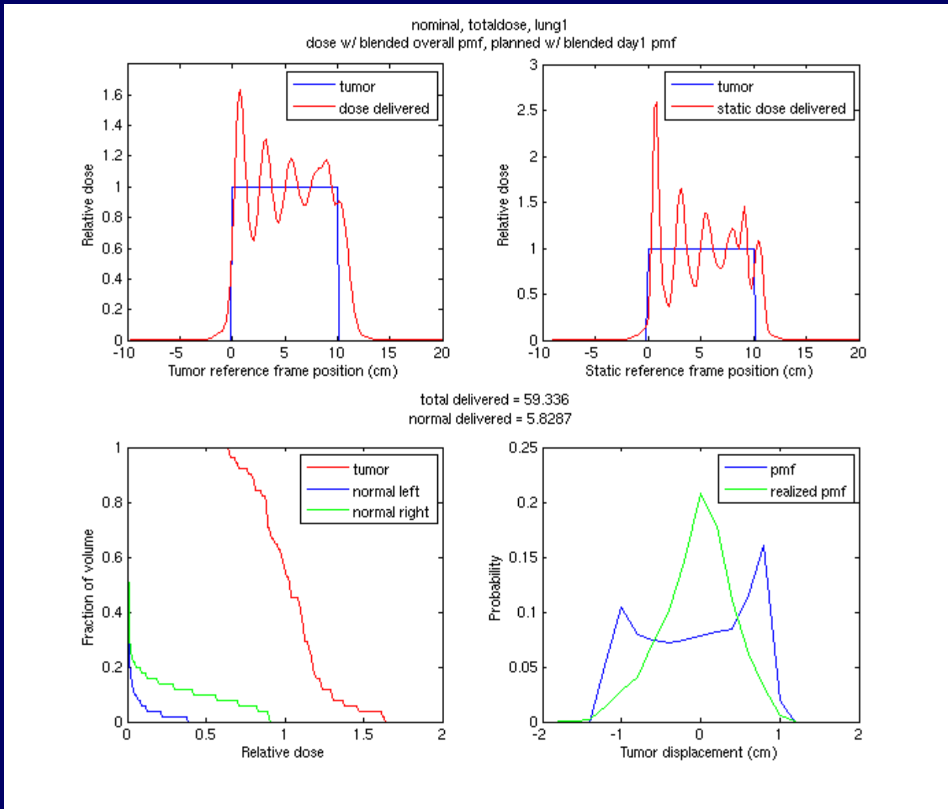
$$
\begin{array}{lll}
\text{min} & \displaystyle\sum_{v\in\mathcal{N}}\sum_{b\in\mathcal{B}}\sum_{x\in X}\Delta_{v,x,b}p(x)w_b & \\
\text{st} & \displaystyle\sum_{b\in\mathcal{B}}\sum_{x\in X}\Delta_{v,x,b}p(x)w_b-\sum_{b}\sum_{x\in U}\Delta_{v,x,b}\underline{p}(x)w_b+\sum_{x\in U}\underline{p}(x)q_v-\sum_{x\in U}r_{v,x}\geq\theta_v & \forall\, v\in\mathcal{T} \\
 & \displaystyle(\overline{p}(x)+\underline{p}(x))q_v-r_{v,x}\leq\sum_{b}\Delta_{v,x,b}(\overline{p}(x)+\underline{p}(x))w_b & \forall\, v\in\mathcal{T},\forall\, x\in U \\
 & q_v \ \text{free} & \forall v\in\mathcal{T} \\
 & r_{v,x}\geq 0 & \forall\, v\in\mathcal{T},\forall\, x\in U \\
 & w_b\geq 0 & \forall\, b\in\mathcal{B}
\end{array}
$$

What about…

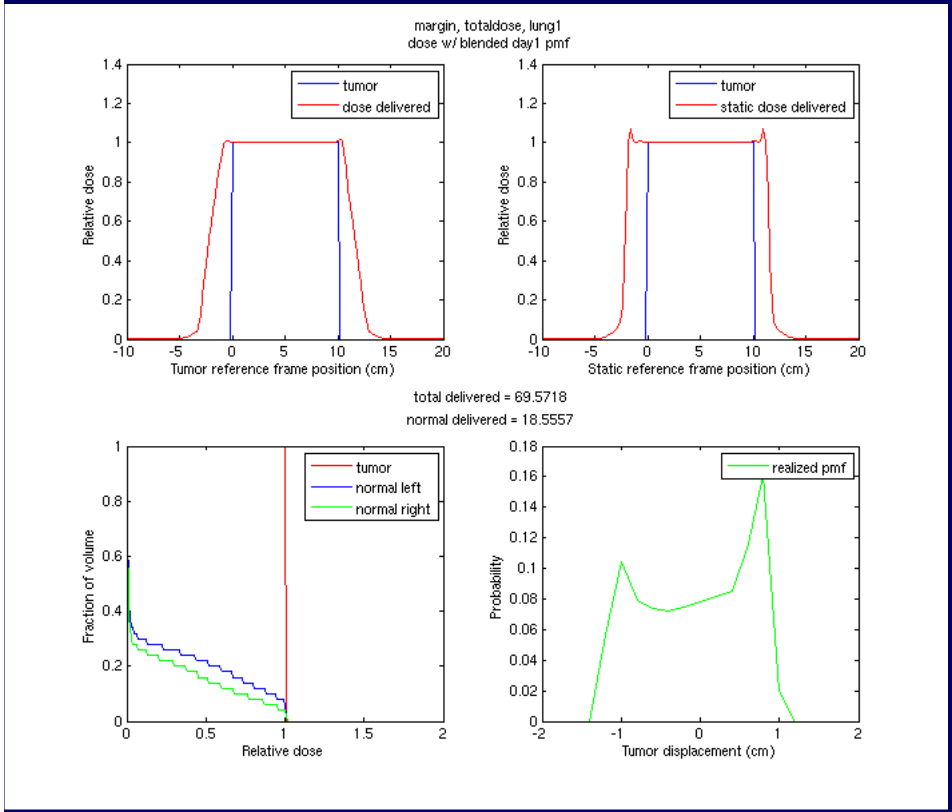
- We live in a non-linear world
  - Modeling tool, can approximate non-linear equations
- Complexity of robust plan
  - Add constraints to limit complexity
- Amplitude uncertainty
  - Choose U and error bars appropriately
- Rigid-body motion
  - Include pmf p_v for each voxel v
- Overly general approach
  - Can include distributional "guesses"

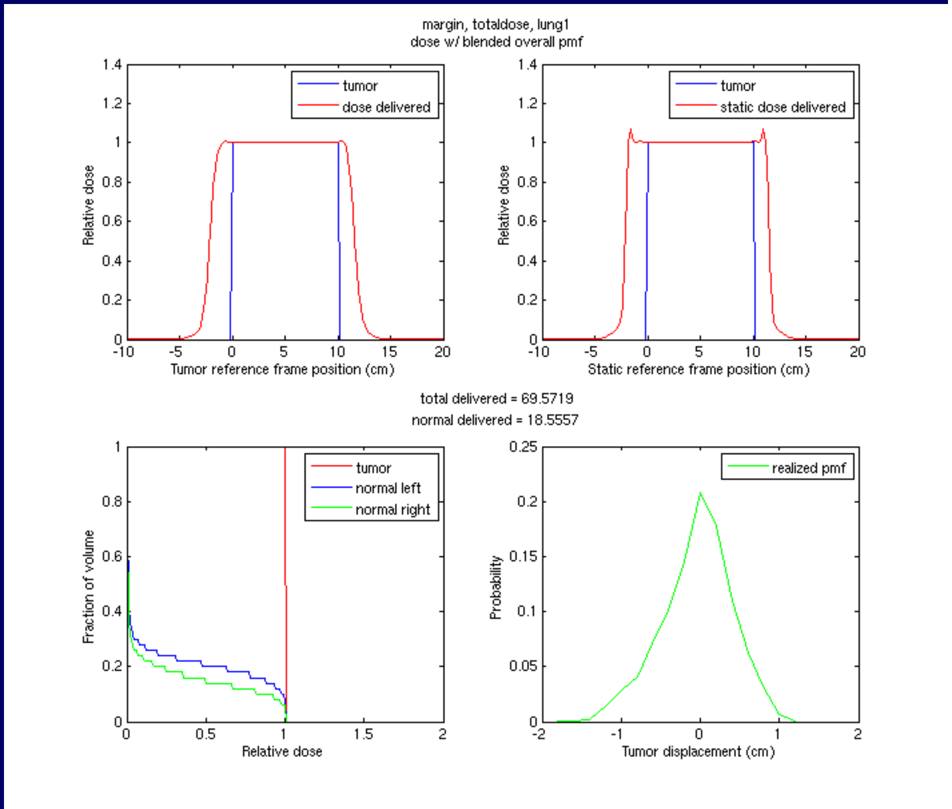
Nominal 4 subplots



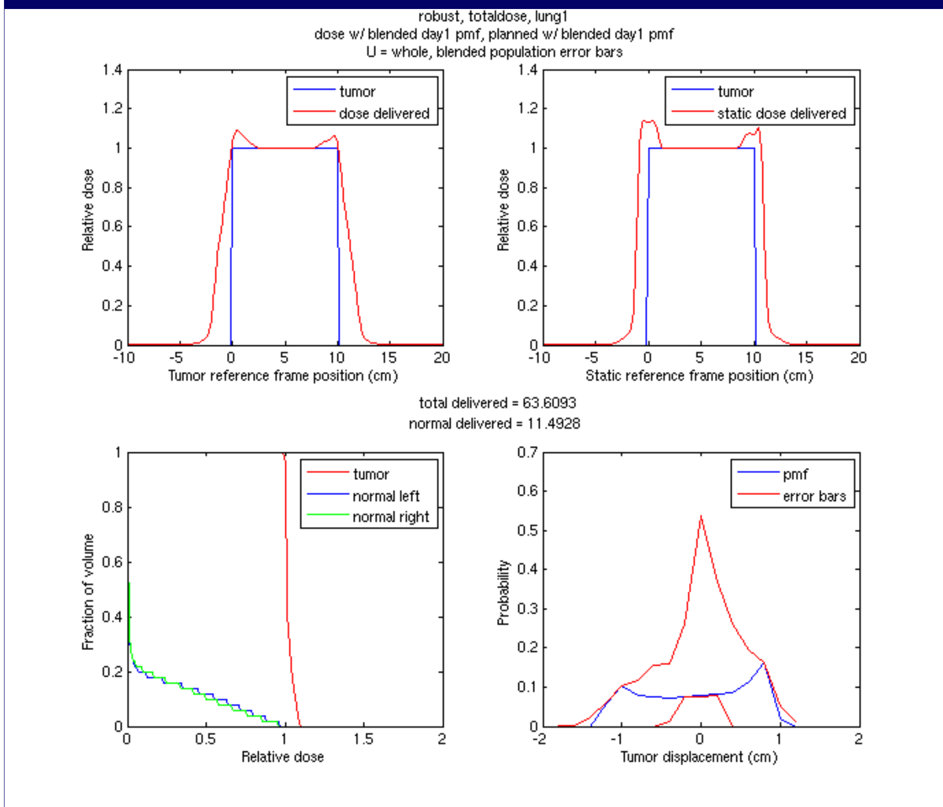


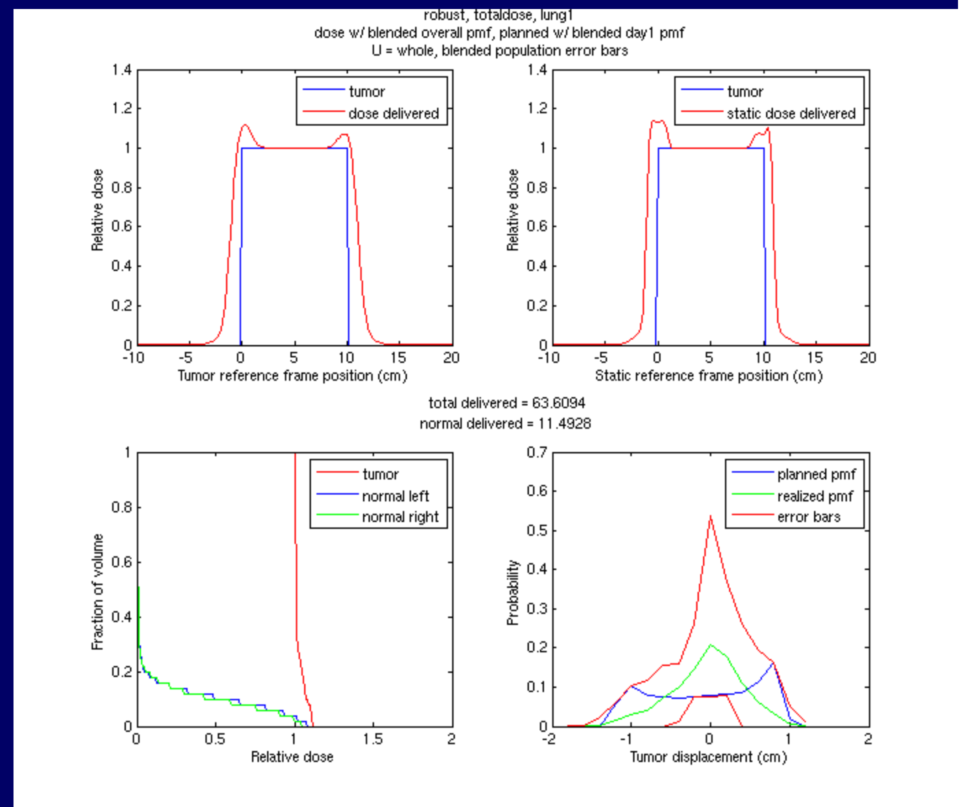
Margin 4 subplots





Robust 4 subplots





Numerical results

Relative increase in…	Margin : Nominal	Robust : Nominal	Margin : Robust
Total dose delivered	17.25 %	7.20 %	9.37 %
Dose to normal tissue	218.35 %	97.18 %	61.45 %

Numerical Results

- Nominal realized total: 59.336
- Margin realized total: 69.5719
- Robust realized total: 63.6094

- Nominal realized normal: 5.8287
- Margin realized normal: 18.5557
- Robust realized normal: 11.4928

Linear optimization basics

- Linear objective (eg. Mean or max dose) and linear constraints (eg. Dose >= ..)

$$\begin{array}{rlcrl} \min & \mathbf{c}'\mathbf{x} & \qquad & \max & \mathbf{p}'\mathbf{b} \\ \text{st} & \mathbf{A}\mathbf{x} = \mathbf{b} & & \text{st} & \mathbf{p}'\mathbf{A} \leq \mathbf{c}' \\ & \mathbf{x} \geq \mathbf{0} & & & \mathbf{p} \ \text{free} \end{array}$$

- Special case of “convex programming”
- Dantzig 1947 (OR’s Hounsfield?)
- 1950’s: explosion of mathematical programming (non-linear, networks, large-scale, stochastic, integer)

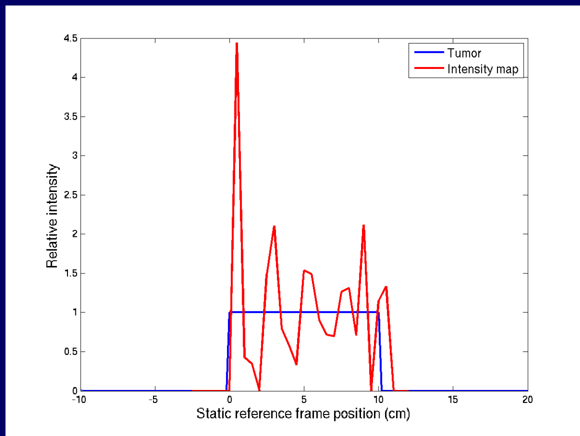
Linear optimization

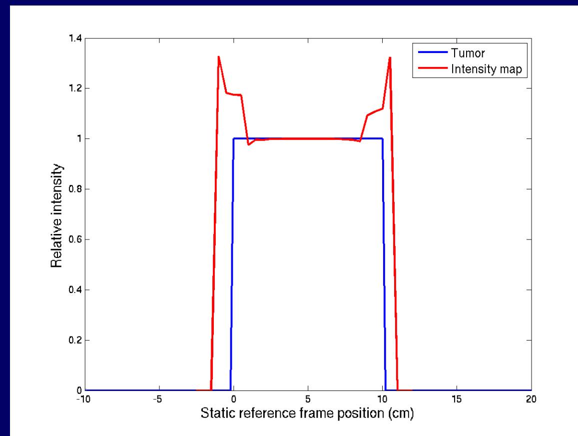
- Dantzig 1947 (OR's Hounsfield?)
- Well-established algorithms to solve LPs to optimality
  - Simplex or interior points
- Beautiful theory of duality
  - Bounds and sensitivity analysis
- Robust versions remain tractable
- Computational progress
  - First LP solved in 1947 (9 cons. 77 vars.) took 120 person-days
    - First image reconstruction? Many hours scan, days to reconstruct 1972
  - Now can solve problems up to ~10^8 variables and constraints
    - Eg. 2003: production planning 400,000 cons. 1.6M vars. 59.1 s

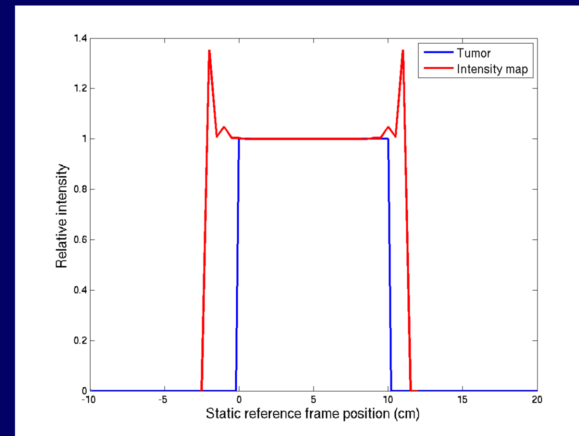
Robust Optimization

- LINEAR: Soyster 1973, Ben-Tal and Nemirovski 2000, Bertsimas and Sim 2004, Ben-Tal et al 2004
- DISCRETE: Bertsimas and Sim 2003
- CONIC: Ben-Tal et al 2002, Bertsimas and Sim 2006
- CONVEX: Ben-Tal and Nemirovski 1998, Ben-Tal et al 2006
- SDP: Ben-Tal and Nemirovski 2000, El Ghaoui et al 1998
- MDP: Nilim and El Ghaoui 2004
- Classification, image reconstruction, scheduling, options pricing, inventory, supply chain, portfolio selection, control, truss design, …

Continuum of Robustness







Nominal | Robust | Margin

No Uncertainty | Some Uncertainty | Complete Uncertainty

- Can prove this mathematically
- Flexible tool allowing planner to modulate his/her degree of conservatism based on the case at hand