Radiation Treatment Planning: Fractionation

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Dose Distribution

- Experts determine an "ideal dose distribution" for a particular target
  - Covers tumor
  - Limits radiation to healthy/at-risk regions
- Delivery plan = optimization problem

Delivery Plan

$$\begin{array}{ll} \text{min} & \|Dose(i) - T(i)\| \\ \text{subject to} & Dose(i) = \sum_A w_A D_A(i) \\ & Dose(Sens(k)) \leq U(k) \\ & L \leq Dose(Target) \\ & w_A \geq 0 \end{array}$$

plus some integrality constraints

Commonalities

- Target (tumor)
- Regions at risk
- Maximize kill, minimize damage
- Homogeneity, conformality constraints
- Amount of data, or model complexity
- Mechanism to deliver dose

Day-to-day planning

- Dose delivered in a series of treatments over many days
  - Limits burning
  - Allows healthy tissue to recover
- Current approach: apply a constant policy
  - Divide target dose distribution by number of treatments
- Attempt to deliver same amount each time (only requires one optimization)

Error sources

Displacement of tumor from target region and uncertainty about its exact position and extent caused by:

1. Delivery errors or differences between planned and actual delivered dosages;

Error sources

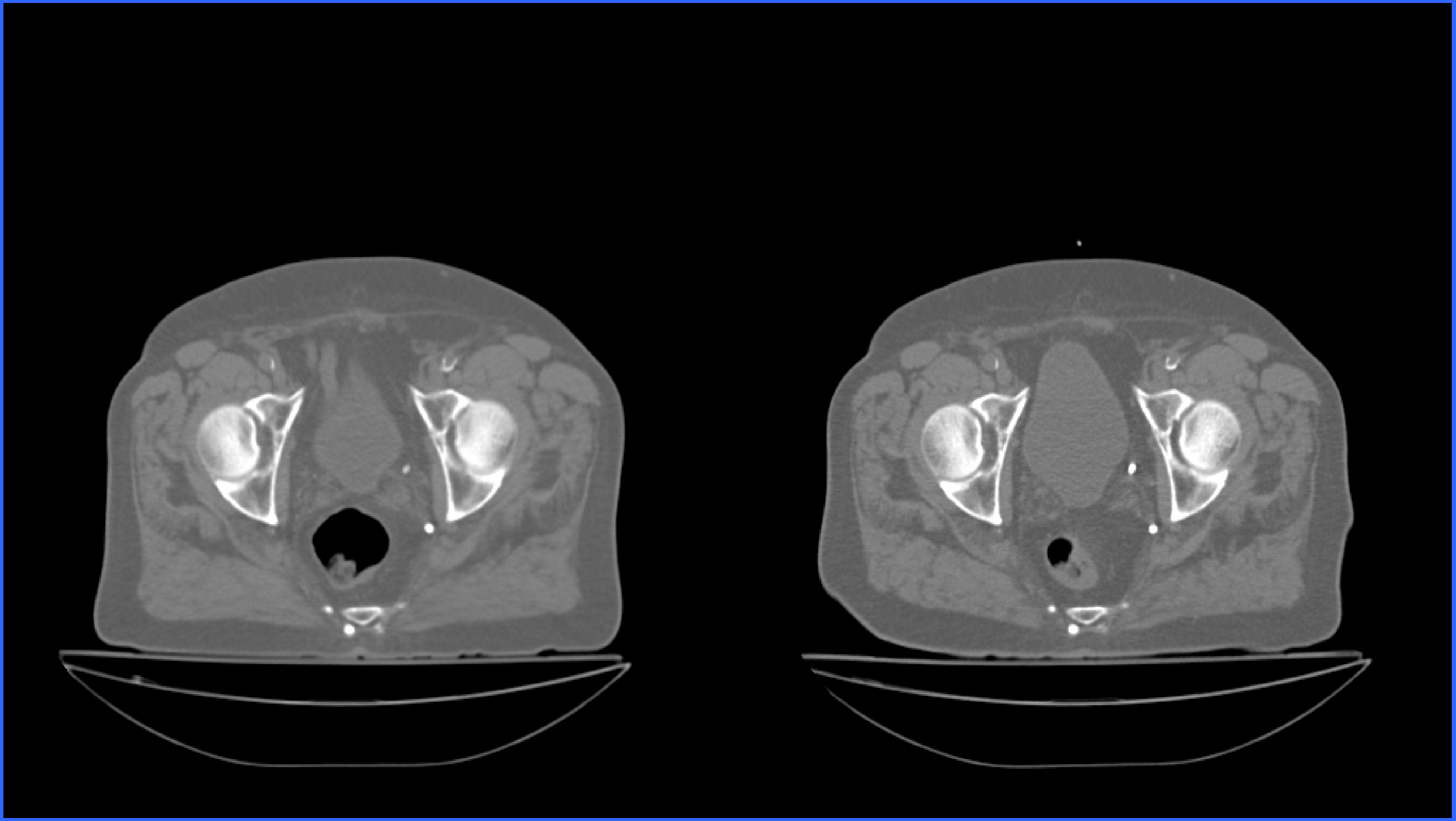
2. Errors in setting up (registering) the patient on the treatment device;
3. Patient movement (usually due to breathing) while the dose is being delivered.
4. Mistakes in interpretation of imaged data, or presence of microscopic extensions of the tumor not viewable by current imaging technology;
5. Movement and/or shrinkage of patient internal organs from day to day, between treatment sessions;

Example: Breast case

The breast cannot be positioned exactly the same from day to day.

Also, breathing motion can move the breast out of the treatment field if this motion is not accounted for properly in the planning and delivery.

CT Fraction 1 | CT Fraction 9



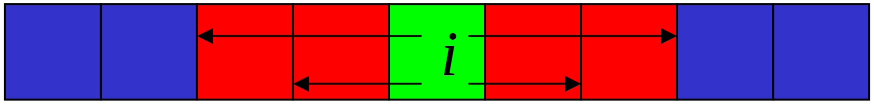
Current Solution

- Add safety margin to GTV: CTV
- CTV modified to form PTV

- Synchronize beam with breathing, breathing control, motion adaptation
- Statistical approaches
- Adaptive radiotherapy

Model Problem

- Consider one-dimensional example
- Consider simple shifts and N=20:
  - Shift to the left or right
  - Shift by 0, 1, or 2 voxels
- 5 probabilities need to be assigned

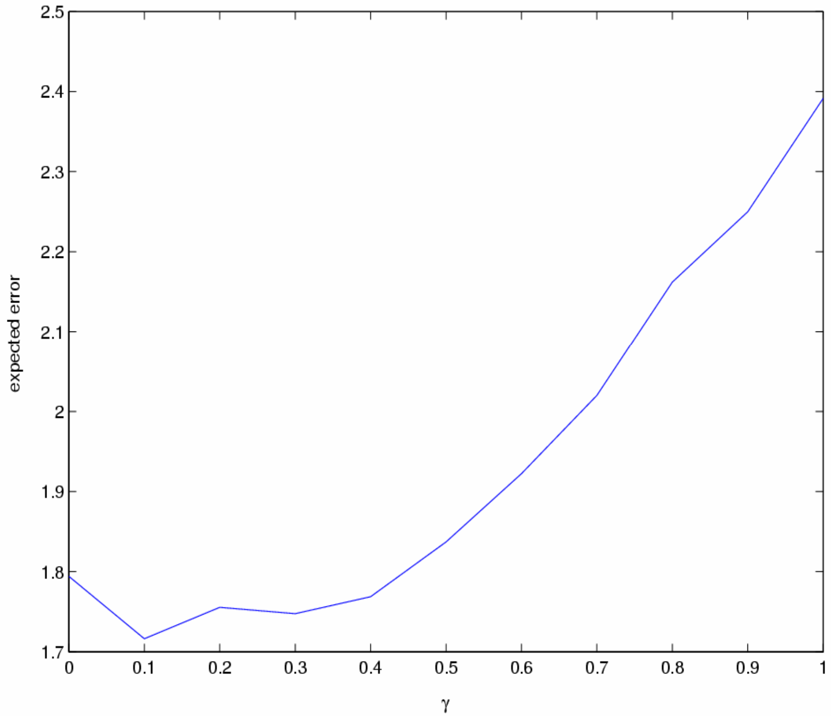


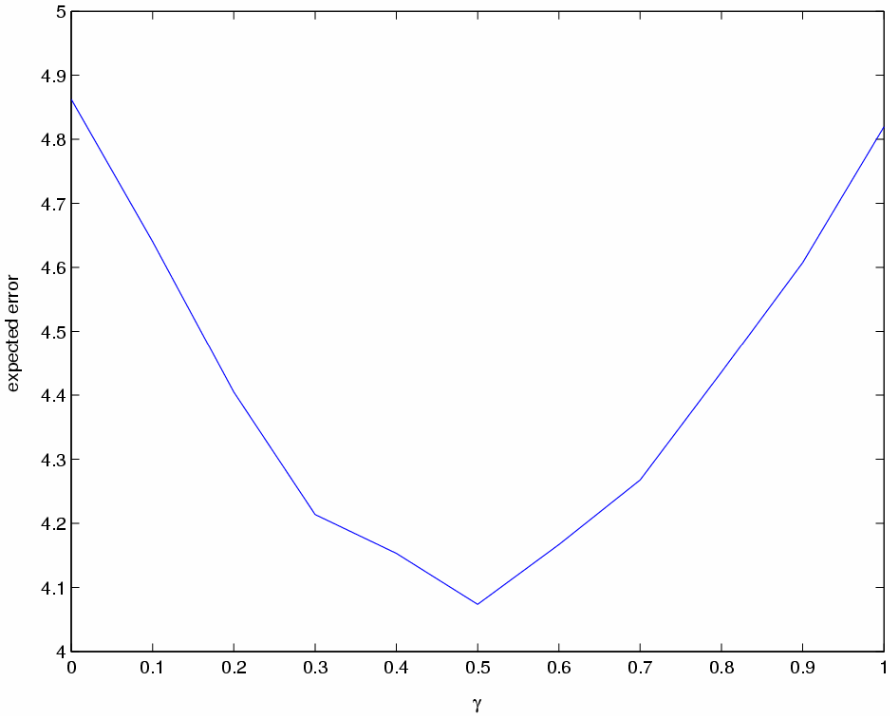
Could Use Expectation

- Assume deliver same dose every period, known error distribution
- After N periods, dose delivered approximately equal to expected dose
- Plan so expected dose = "ideal dose"
- Modified constant policy delivers:

$$u = (1-\gamma)u_{expected} + \gamma u_{constant}$$

Modified Constant Policies

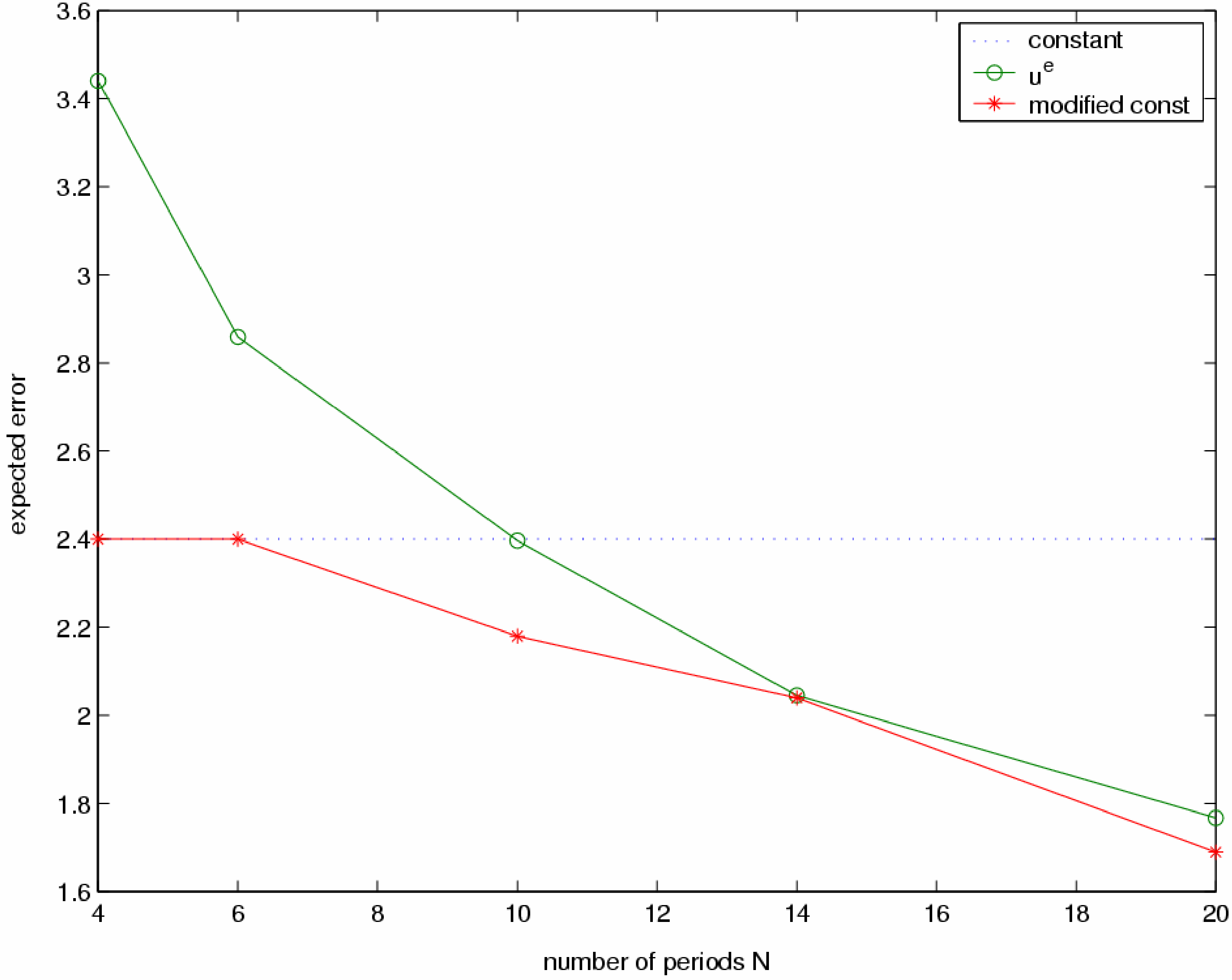




Low volatility

High volatility

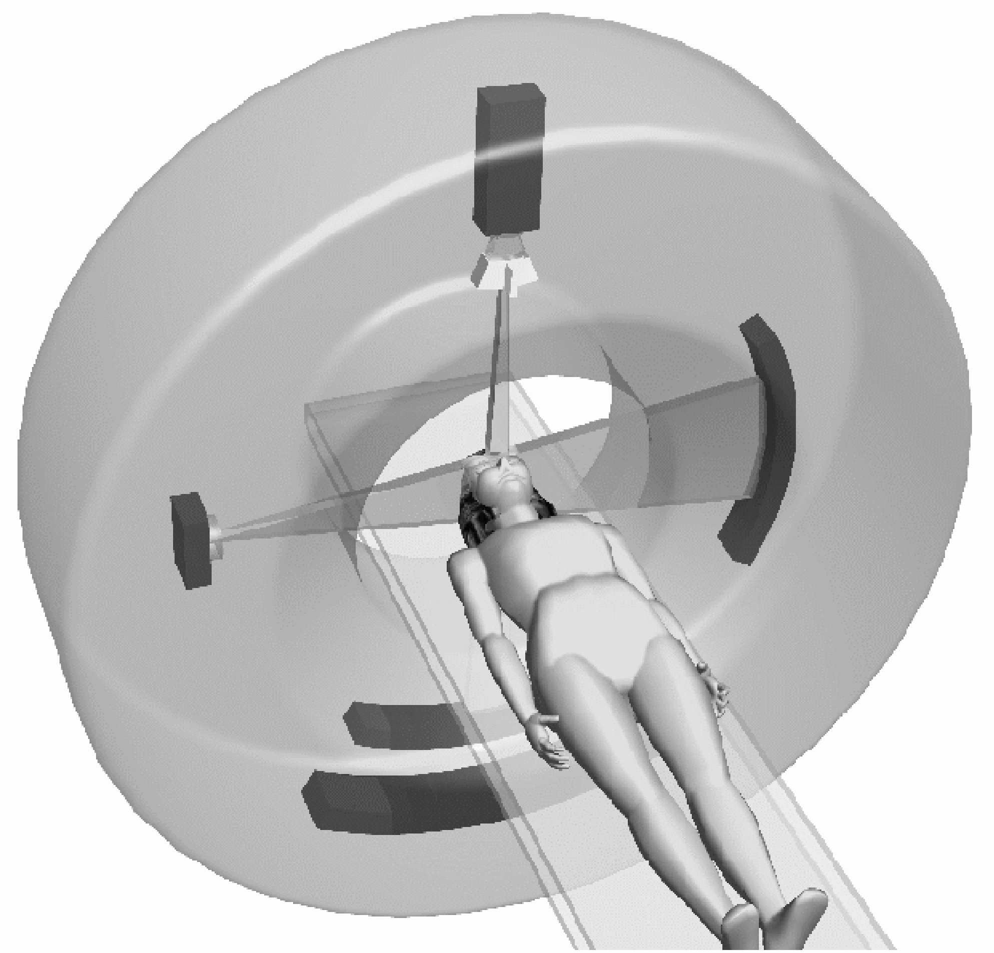
Error with stages N



Dose Delivery

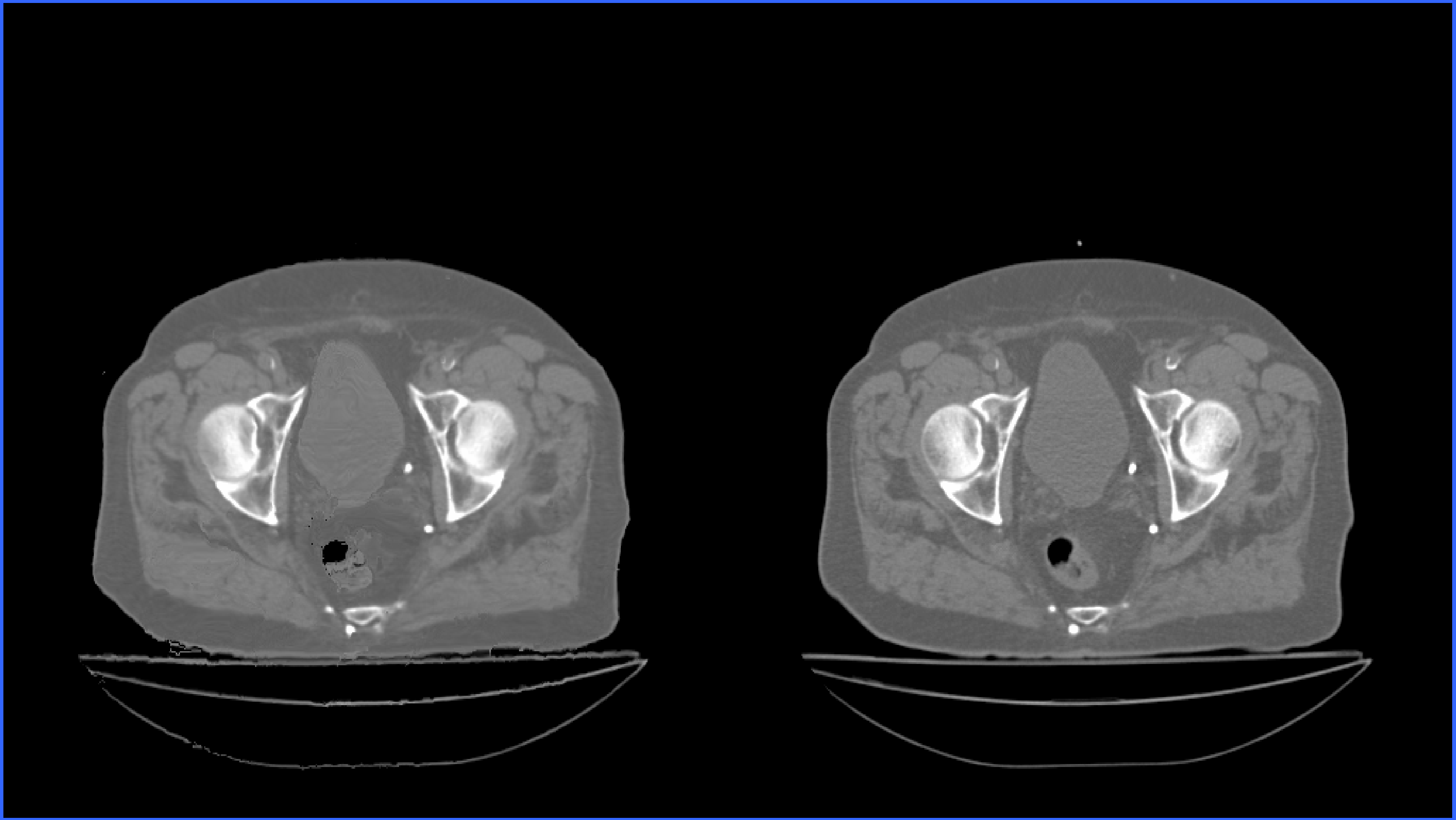
- Errors:
  - Organ movement
  - Registration of patient on machine
  - Movement of patient during treatment
  - Planning/mechanical error
- New option: True dose delivered can be measured during individual treatments
  - Update (reoptimize) treatment plan day-to-day
  - Compensate for errors

Tomotherapy Machine



Original CT Deformed

CT Fraction 1 CT Fraction 9



Control Problem

Develop an adaptive treatment:

- Given:
  - Total number of treatments (N)
  - Number of the current treatment (k)
  - Target dose (T)
  - Accumulated dose already delivered (x_k)
- Determine:
  - Dose (u_k) to apply to minimize final error

Modeling assumptions

- Divide the target into voxels
- Assume errors (w_k) are shifts
  - Spatially correlated, independent over time
- Assign probabilities to each shift
- Stochastic optimal control problem

$$x_{k+1}(i) = x_k(i) + u_k(i + w_k)$$

Mathematical Formulation

Stochastic Linear Program:

min $\quad E(\|x_N - T\|) = G(x_N)$

subject to $\quad x_{k+1}(i) = x_k(i) + u_k(i + w_k)$

$u_k \geq 0$

with x_0 given.

Shorthand $x_{k+1} = f(x_k, u_k(x_k), w_k)$

Difficulty in Finding Optimal Policy

Size!

- 4 time stages: 18k eqs, 14k vars, 25 secs
- 5 time stages: 91k eqs, 70k vars, 3 mins
- 6 time stages: 457k eqs, 352k vars, 1 hr

- Parallel computing
- Scenario reduction techniques (lower bound)

Dynamic Programming

- State evolving over time
- Decisions applied at each time stage
- Each decision affects future decisions
- Cost-to-go:

$$J_k(x_k) = \mathrm{E}[G(x_N)]$$

where $x_{k+1} = f(x_k, u_k, w_k)$

- Also becomes intractable

Design Approach: NDP

- Approximate the exact cost-to-go function using simulation
- Update decisions using rollout policy:
  - From current state, consider all possible decisions u
  - Approximate cost-to-go function J for each decision using simulation and base policy
  - Choose decision that gives the best result

Policy Choices

- Constant
- Reactive (base policy)

$$\max\{0, T - x_k\}/(N - k)$$

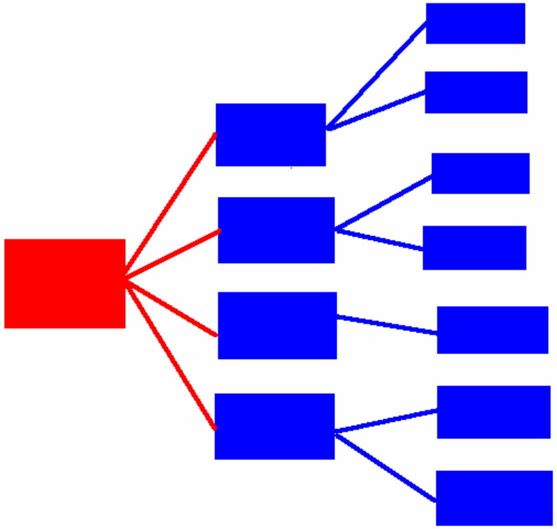
- NDP

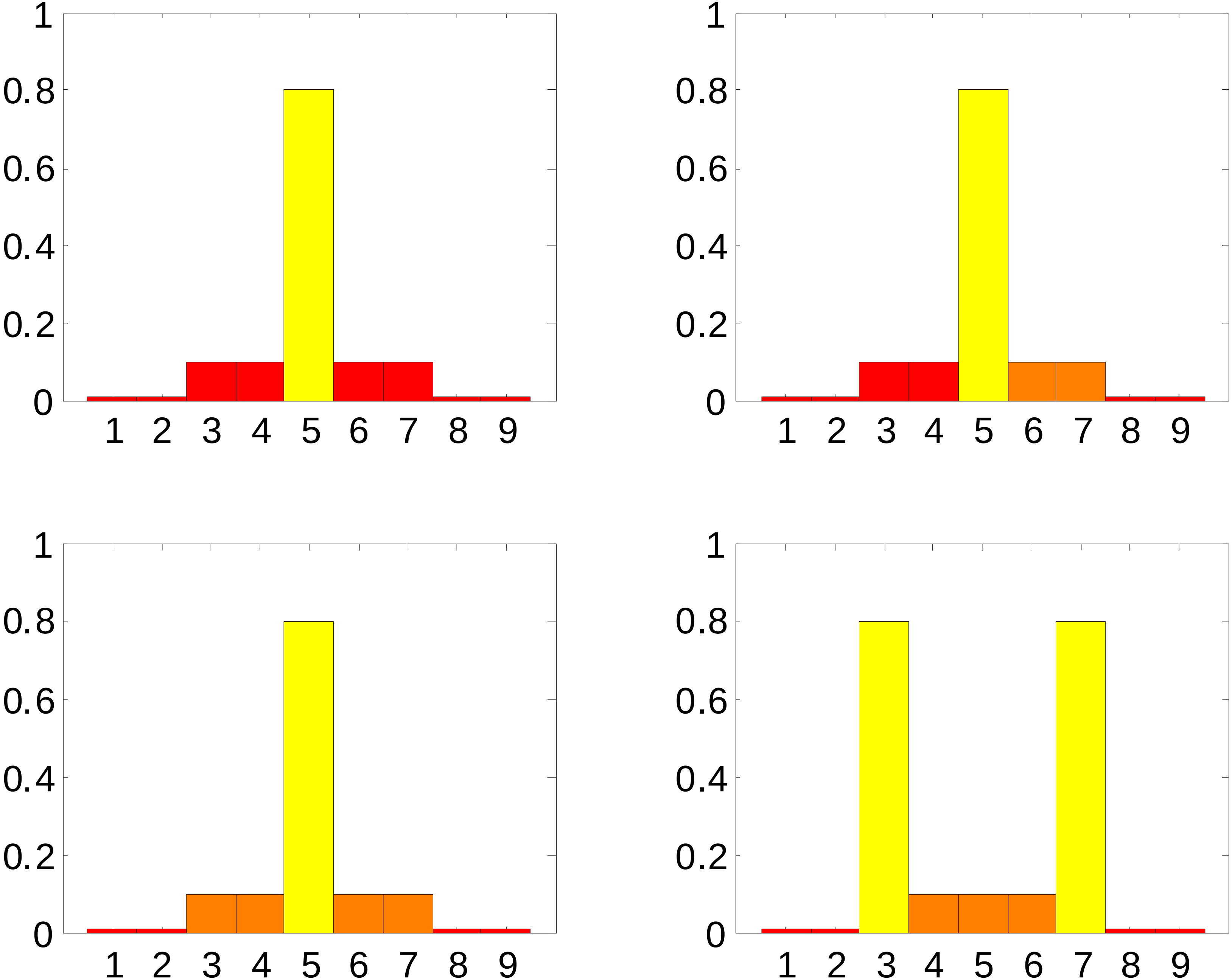
$$\alpha \max\{0, T - x_k\}/(N - k)$$

NDP in Control Problem

- Choose a good heuristic (base) policy
- Choose finite number of policies
- Evaluate using simulation in future
- Choose best choice right now

- Do it!
- Repeat process for next time stage





1
0.8
0.6
0.4
0.2
0
1 2 3 4 5 6 7 8 9
1
0.8
0.6
0.4
0.2
0
1 2 3 4 5 6 7 8 9
1
0.8
0.6
0.4
0.2
0
1 2 3 4 5 6 7 8 9
1
0.8
0.6
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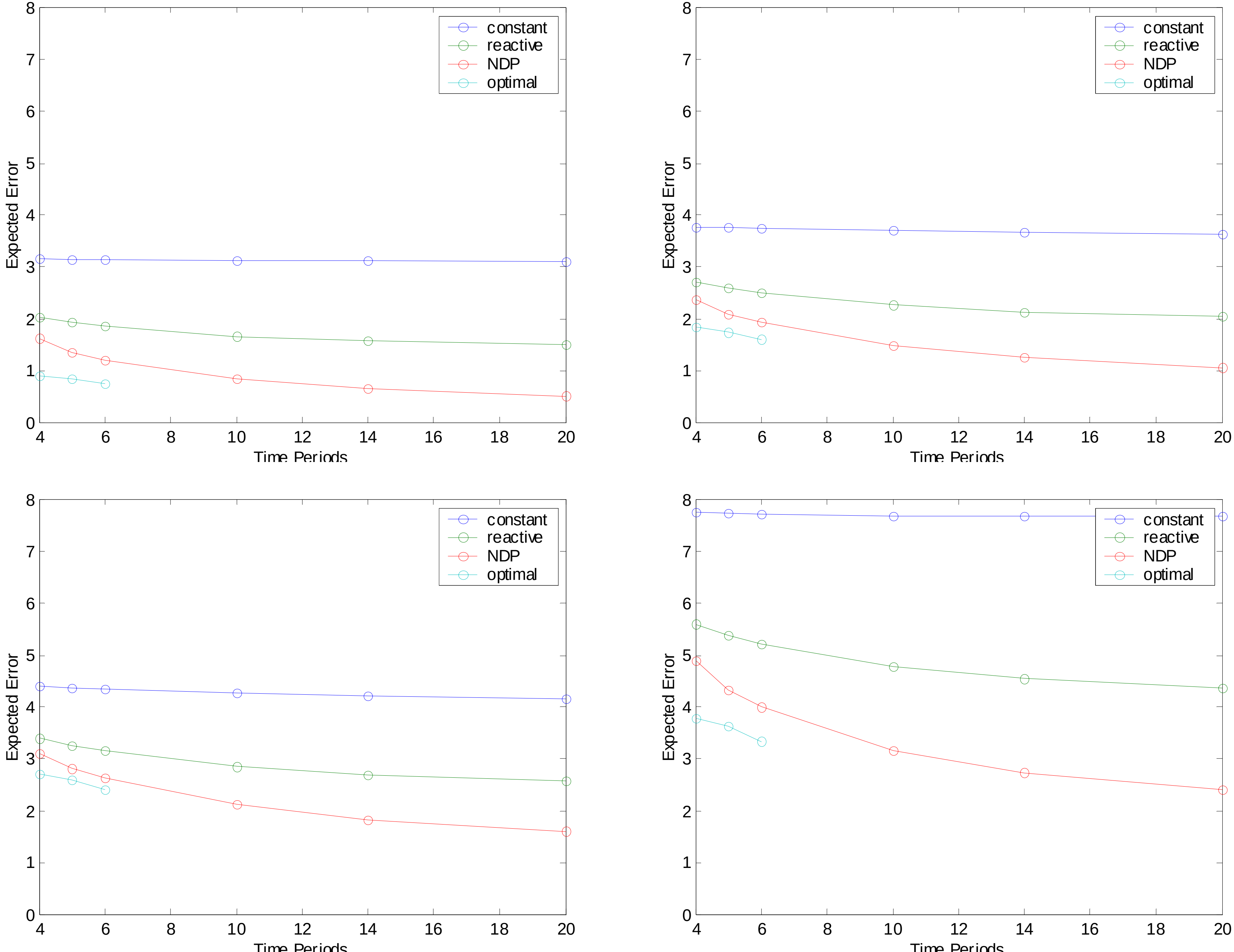
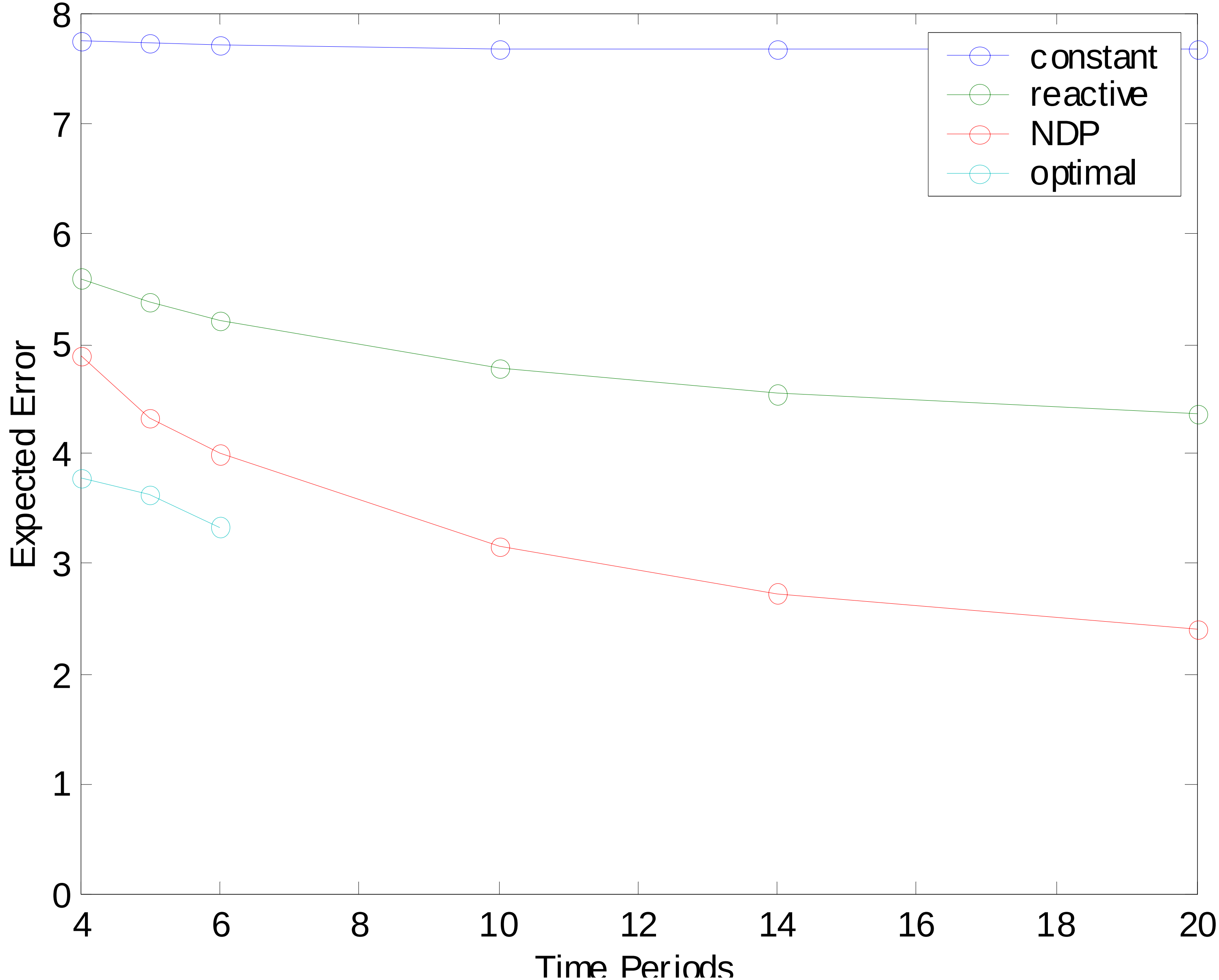
0.2
0
1 2 3 4 5 6 7 8 9



constant
reactive
NDP
optimal
Expected Error
Time Periods
0
1
2
3
4
5
6
7
8
4
6
8
10
12
14
16
18
20



constant
reactive
NDP
optimal
Expected Error
Time Periods
0
1
2
3
4
5
6
7
8
4
6
8
10
12
14
16
18
20

Expected Errors (low vol)

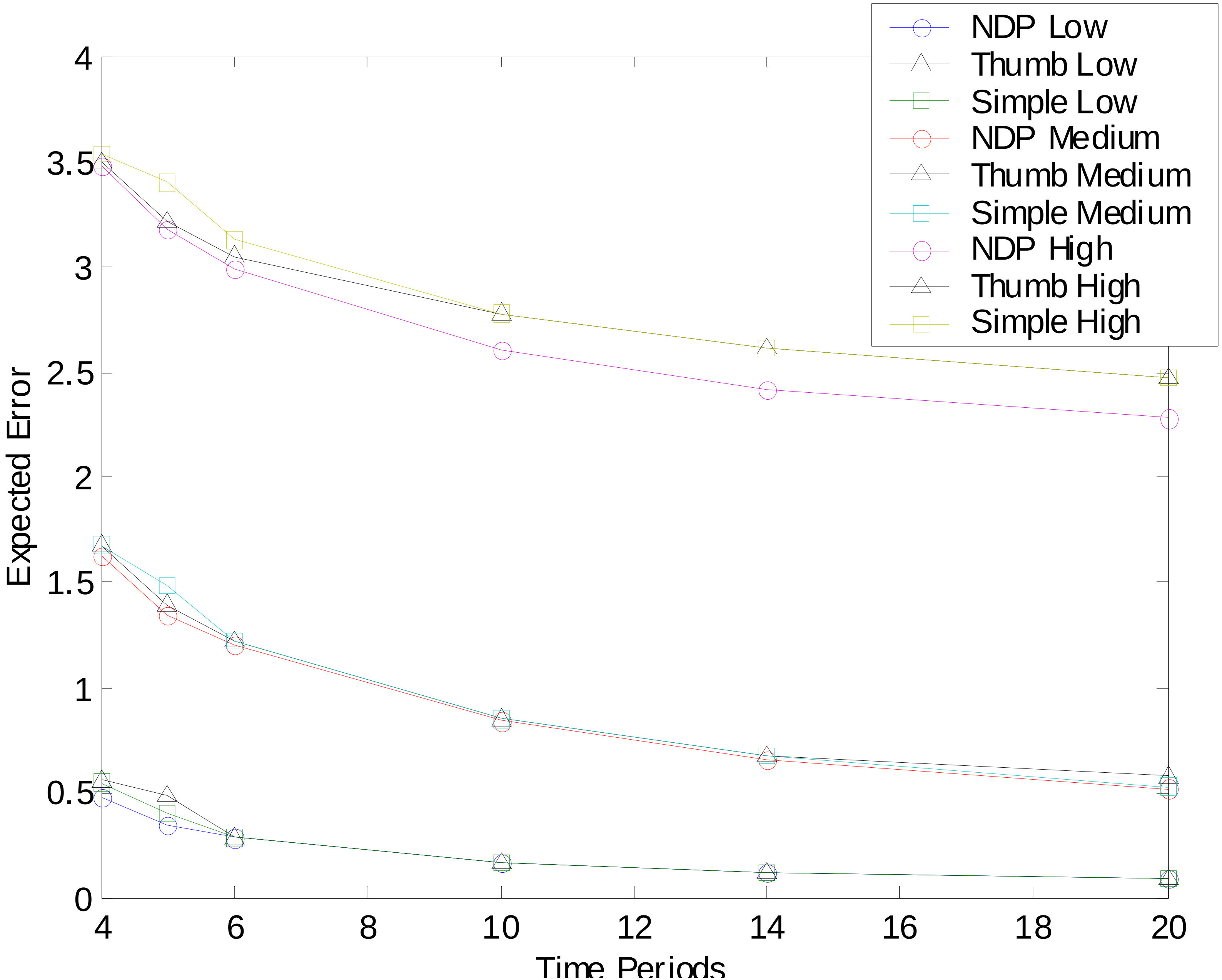
	Mean	Variance
Constant	2.40	0.81
Mod. Constant (0.2)	1.75	0.43
Reactive	0.74	0.10
Mod. Reactive (3.0)	0.56	0.16
NDP rollout	0.53	0.17

Summary of Results

- Constant policy performs poorly
  - Does not consider errors
- Reactive policy is significantly better
- NDP outperforms reactive policy
  - NDP can get close to optimal policy
  - NDP result is as easy to implement in real application
  - Case dependent policy is expensive to compute

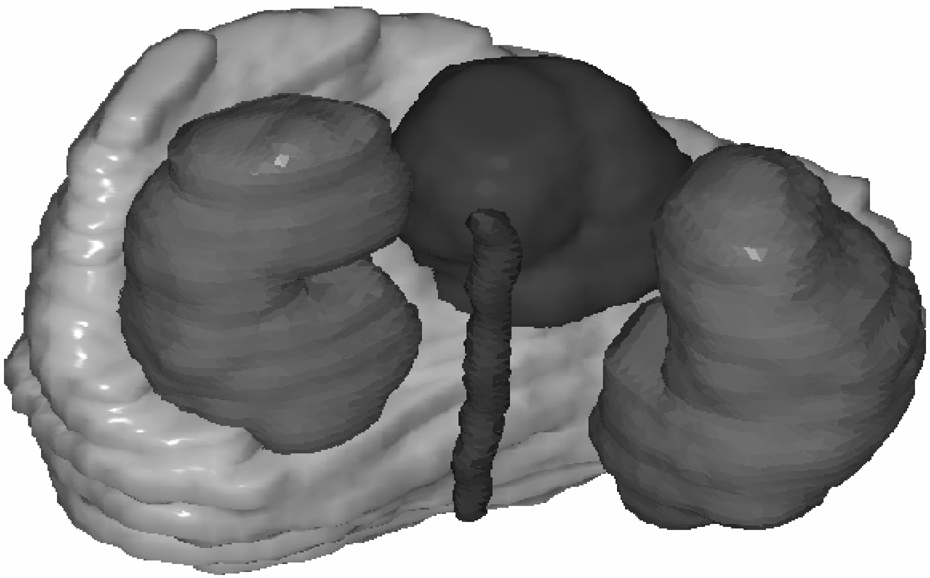
Simple rule of thumb

	1-14	15	16	17	18	19	20
α	2.0	1.8	1.6	1.4	1.025	0.9	0.5



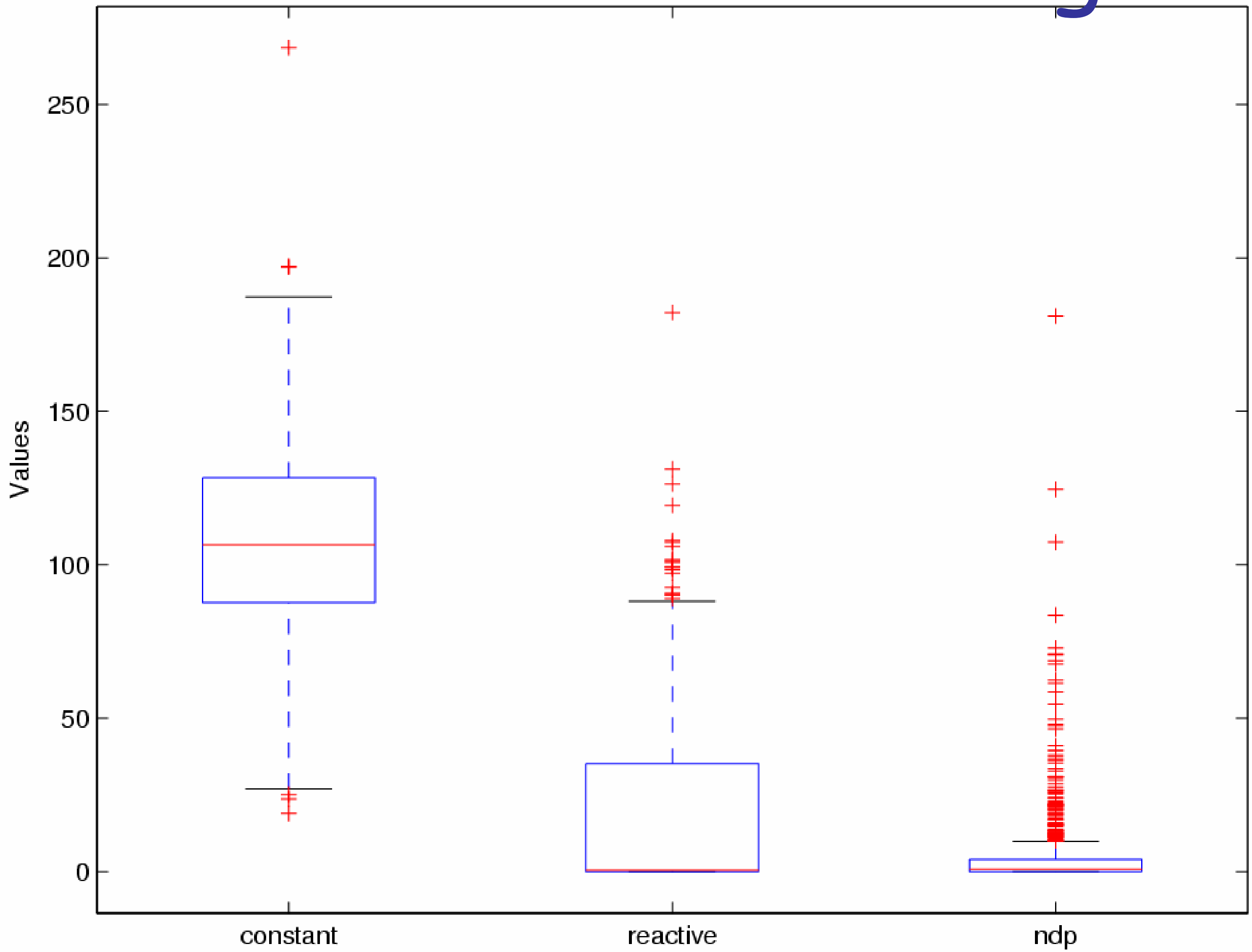
NDP Low
Thumb Low
Simple Low
NDP Medium
Thumb Medium
Simple Medium
NDP High
Thumb High
Simple High
Expected Error
Time Periods
0
0.5
1
1.5
2
2.5
3
3.5
4
4
6
8
10
12
14
16
18
20

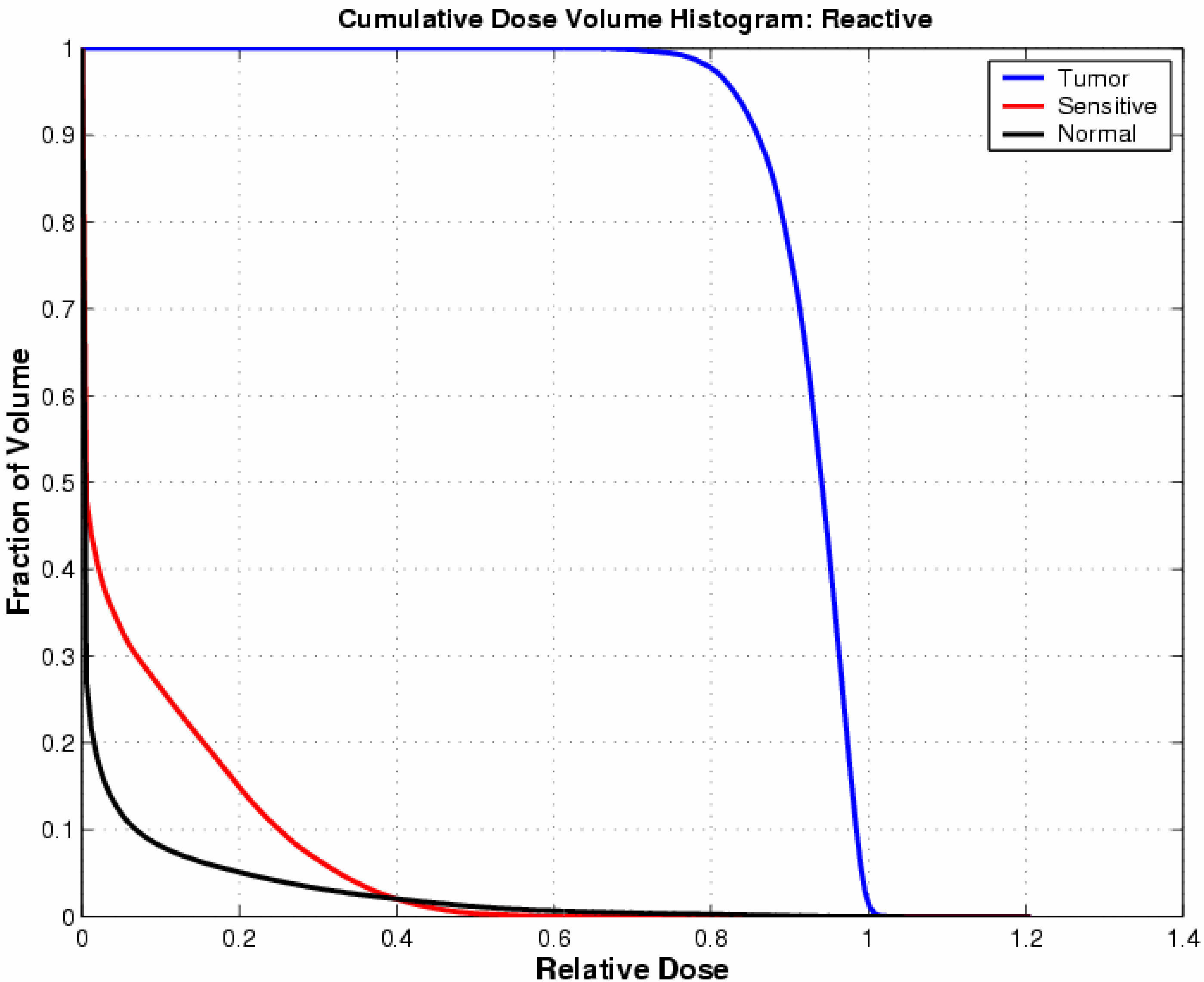
3D Patient Example



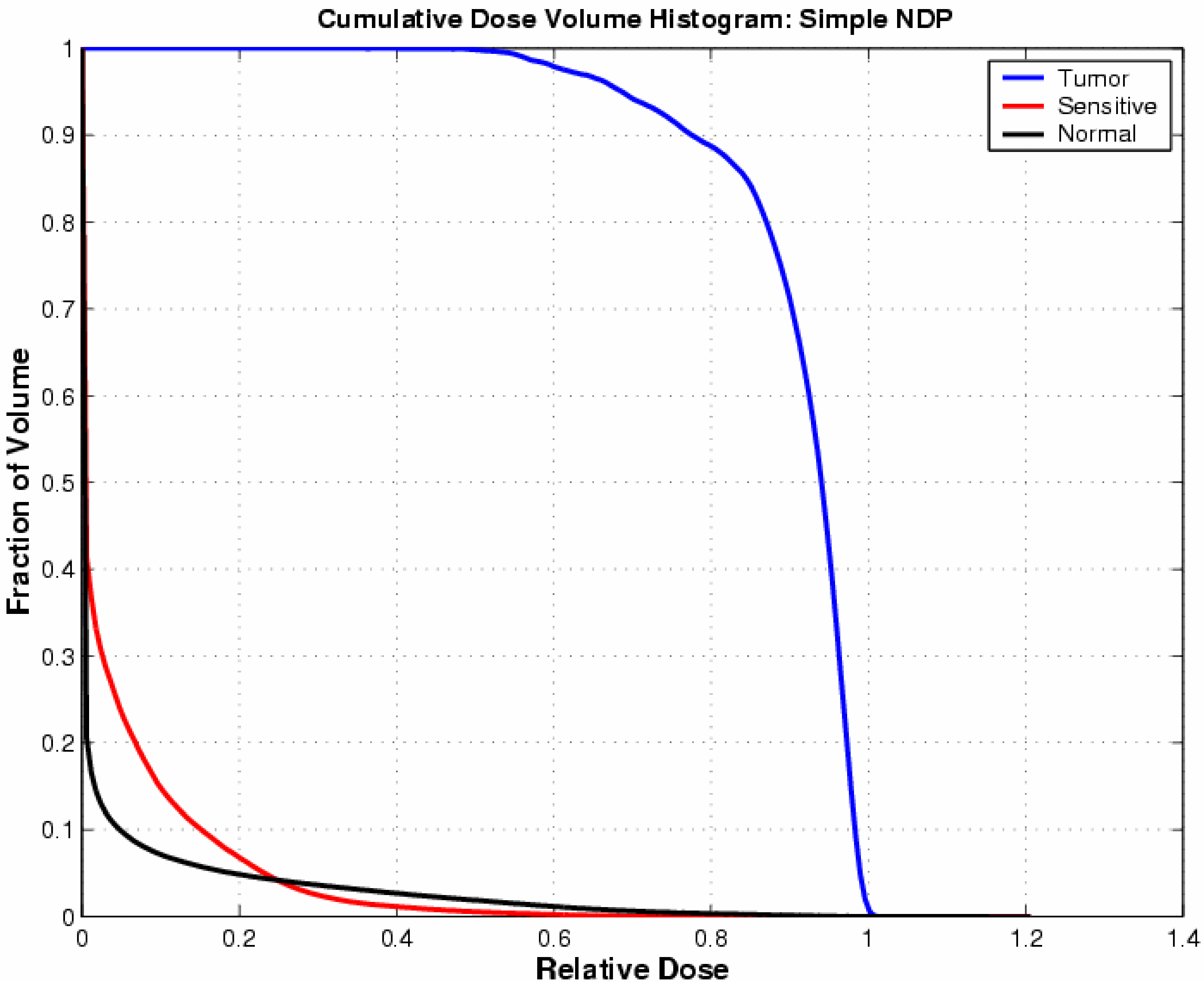
Tumor, Liver,Kidneys, Spinal Cord

Perfect Planning





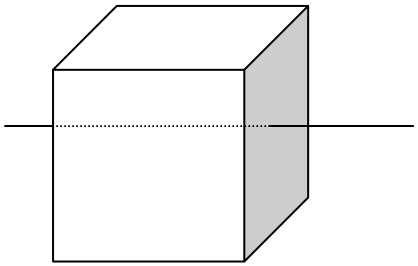
Cumulative Dose Volume Histogram: Reactive
Tumor
Sensitive
Normal
Fraction of Volume
Relative Dose
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
0.2
0.4
0.6
0.8
1
1.2
1.4

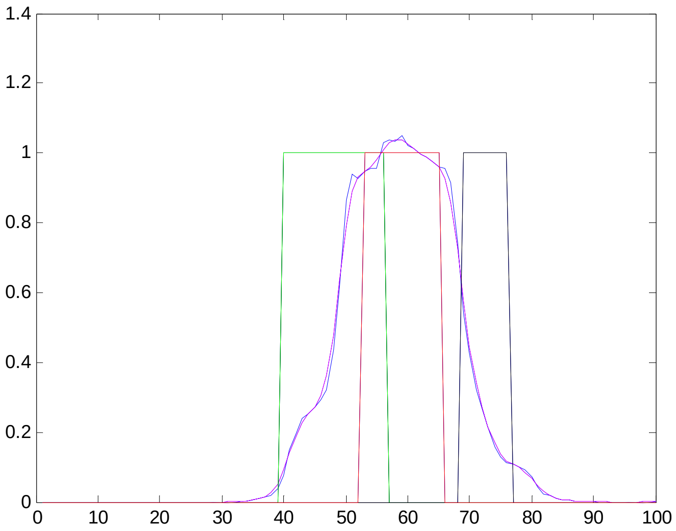


Cumulative Dose Volume Histogram: Simple NDP
Fraction of Volume
Relative Dose
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
0.2
0.4
0.6
0.8
1
1.2
1.4
Tumor
Sensitive
Normal

Effect of Fractionation

- Take a single line through 3D pelvis example
- Project tumor, sensitive structures and dose distributions onto line

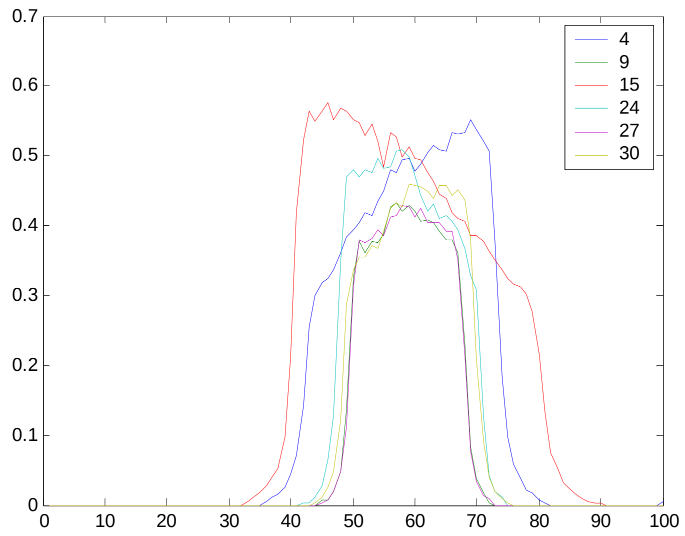




Realizable Delivery

- Exact delivery, constant policy, without shifts – 0.82
- Dose distributions from 6 angles
- Realizable delivery, constant policy without shifts – 2.05

With shifts 3.23



With shifts 1.74

Accuracy of Planning

- Parameterize between "exact" and "realizable" (3DCRT) using α

	0	0.1	0.3	0.5	0.7	0.9	1.0
W/o shifts	0.82	0.83	0.84	0.85	0.92	1.61	2.05
With shifts	1.26	1.29	1.32	1.42	1.55	1.69	1.74

Conclusions

- Reactive/NDP improve upon current policy
- NDP compared to reactive:
  - NDP better in perfect planning
  - NDP better in real planning (provided good)
- NDP useful for both improving treatments and planning treatments
  - On-line: run between treatments (overnight) to determine next policy
  - Off-line: "rules of thumb" suggest improvements for any planning tool

Issues for Future

- How do we quantify errors?
- Uncertain data – on-board imaging provides information – registration?

- How to generate map of organ movement?
- How to plan the (much more difficult) problems resulting from errors?

- Optimization – validation, robustness, design