High Throughput Computing and Sampling Issues for Optimization in Radiotherapy

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Outline

- Introduce a medical application
- Describe a sampling solution approach
- Convert the serial approach to parallel and/or distributed computing.
- Speculation about the resurrection of the service bureau

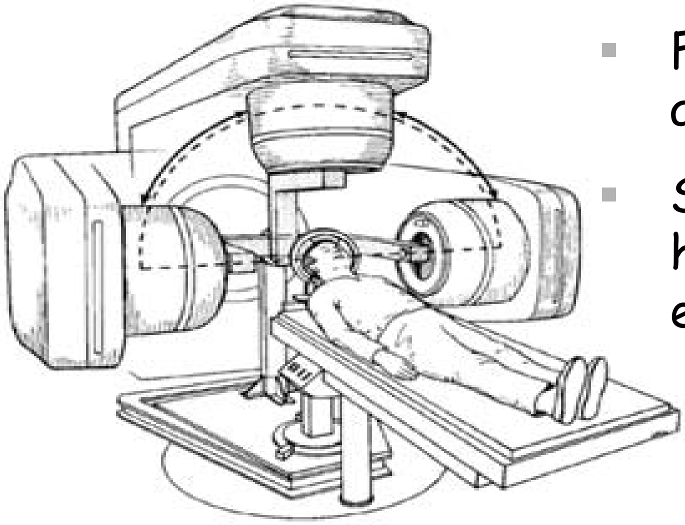
Radiation Treatment Planning

- Cancer is the 2nd leading cause of death in U.S.
  - Only heart disease kills more
- Expected this year in the U.S. (American Cancer Society)
  - New cancer cases = 1.33 million (> 3,600/day)
  - Deaths from cancer = 556,500 (> 1,500/day)
  - New brain/nerv. sys. cancer cases > 18,300 (> 50/day)
- Cancer treatments: surgery, radiation therapy, chemotherapy, hormones, and immunotherapy

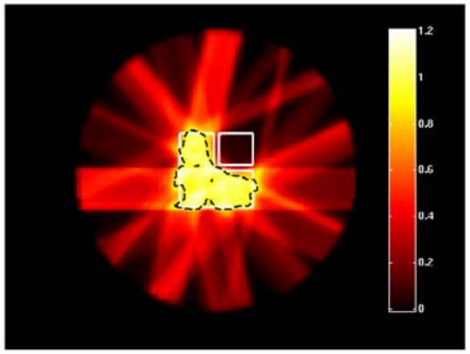
Radiation As Cancer Treatment

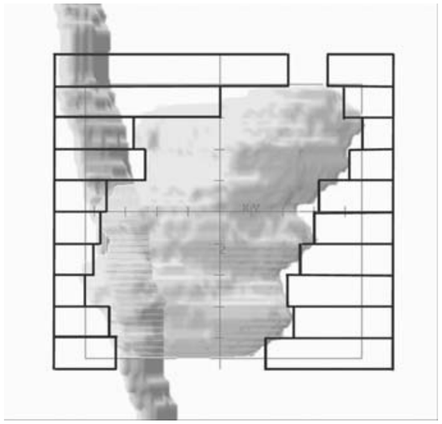
- Interferes with growth of cancerous cells
- Also damages healthy cells, but these are more able to recover
- Goal: deliver specified dose to tumor (PTV) while avoiding excess dose to healthy tissue and at-risk regions (organs)

Conformal Radiotherapy

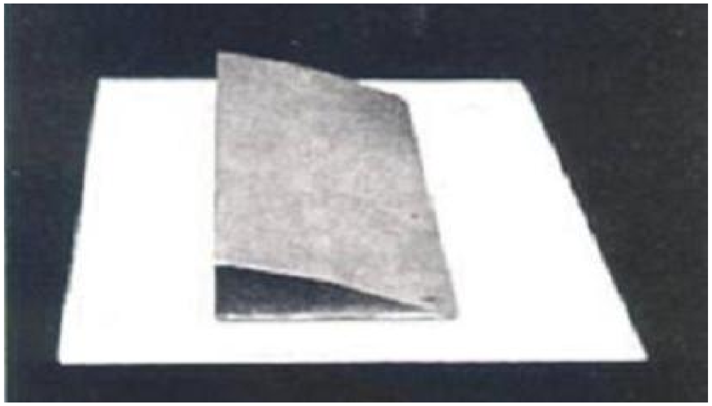


- Fire from multiple angles
- Superposition allows high dose in target, low elsewhere



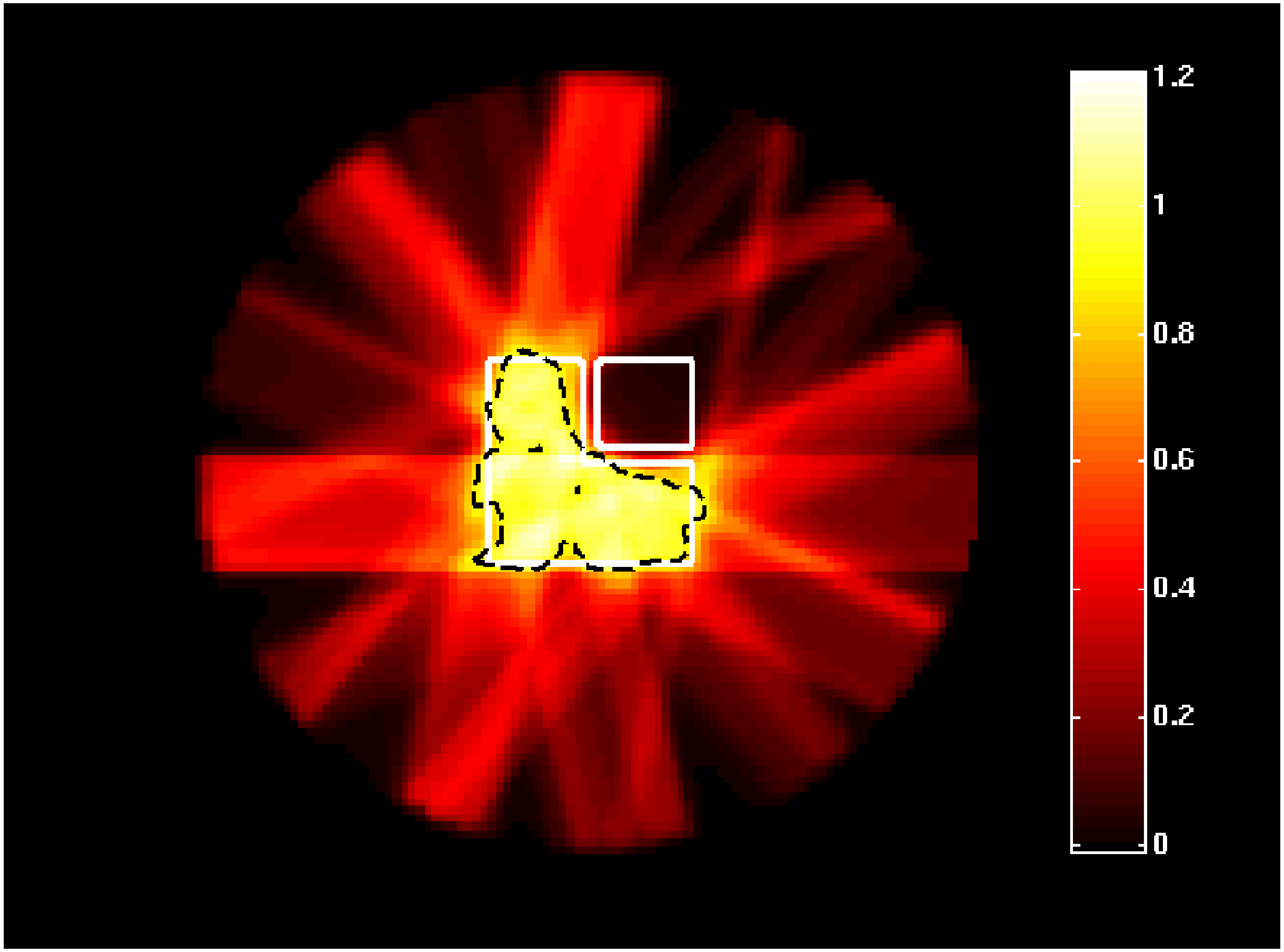


- Beam shaping via collimator
- Gradient across beam via wedges



Conformal Radiotherapy

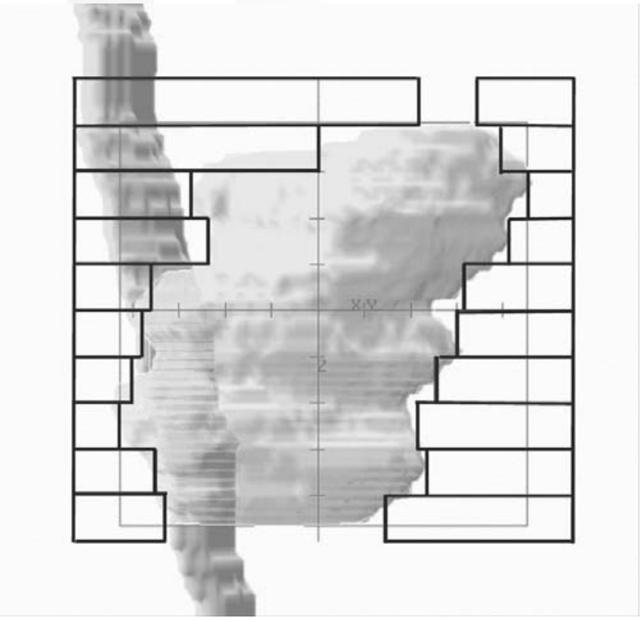
Example

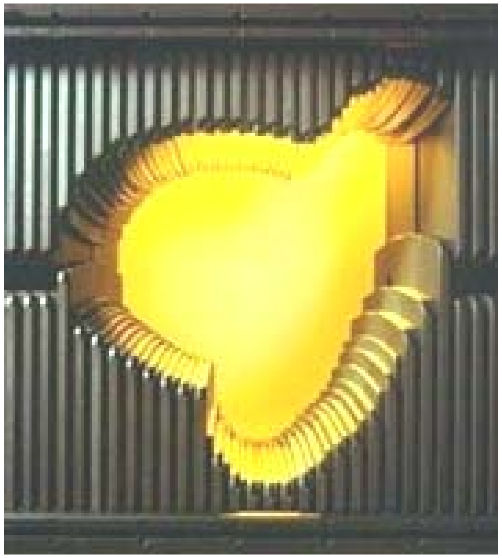


Beam’s eye view

- Beam’s eye view at a given angle is determined based upon the beam source that intersects the tumor

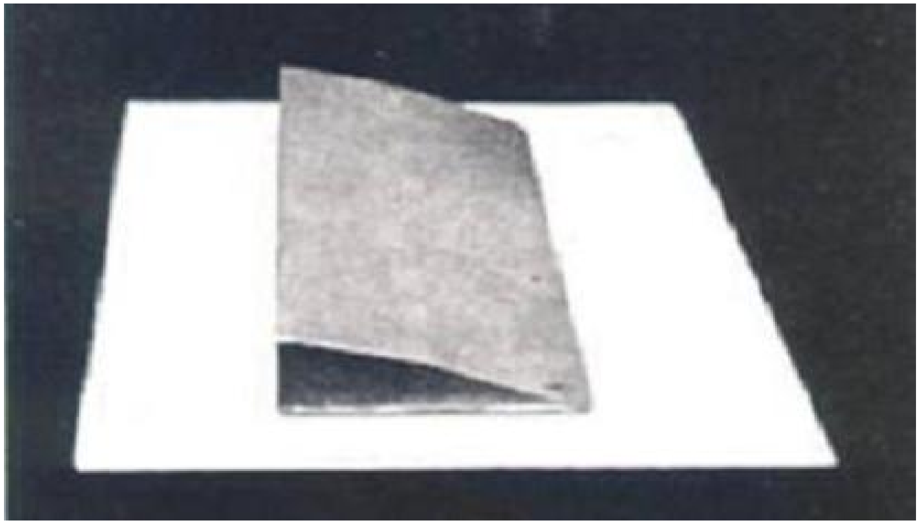
- The view is constructed using a multi-leaf collimator





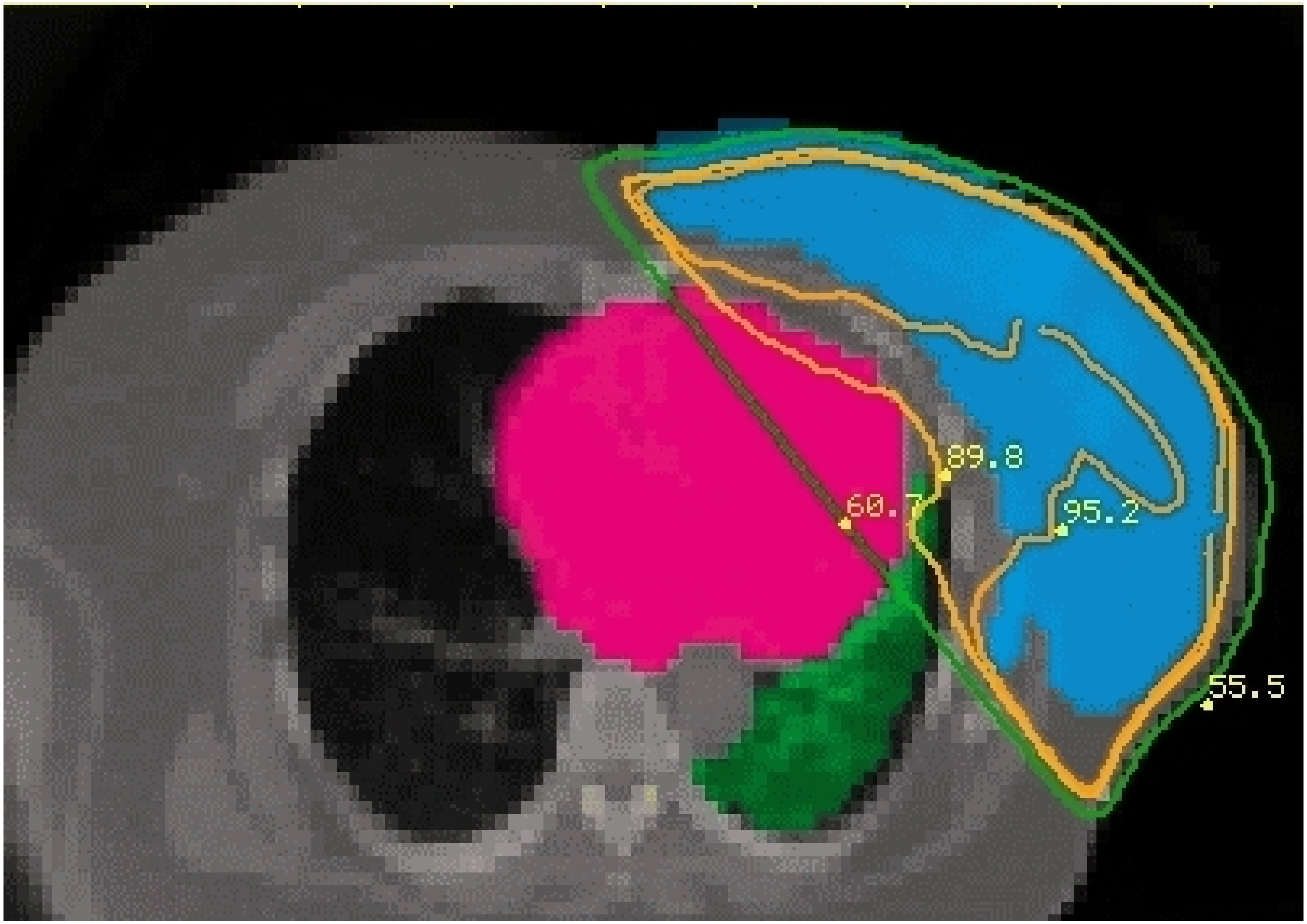
Wedges

- A metallic wedge filter can be attached in front of the collimator.
- It attenuates the intensity of radiation in a linear fashion from one side to other.
- Particularly useful for a curved patient surface



- 5 positions considered: Open, North, East, South, and West.

Sample Display



Notation

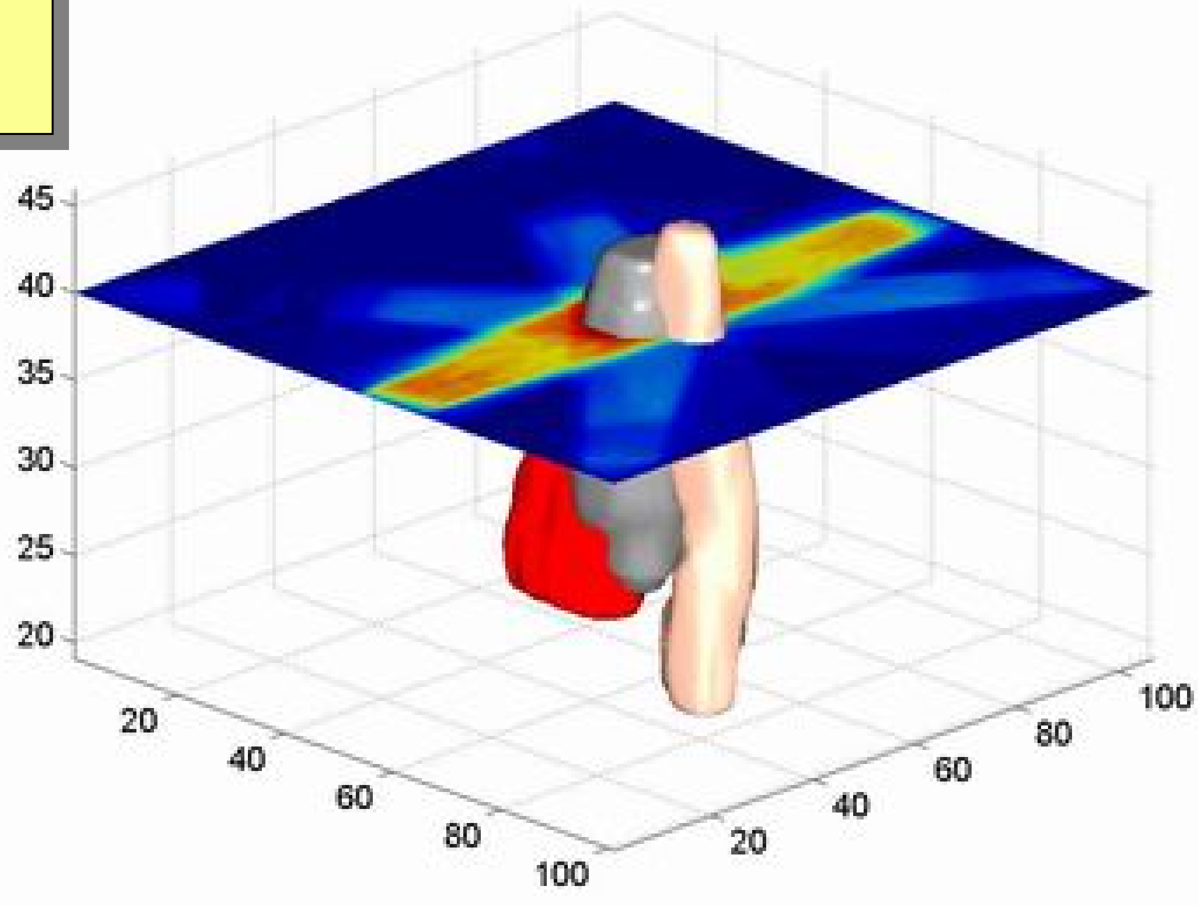
Dose delivered by a beam of unit weight to voxel (i,j,k) by an angle A

Dose Distribution

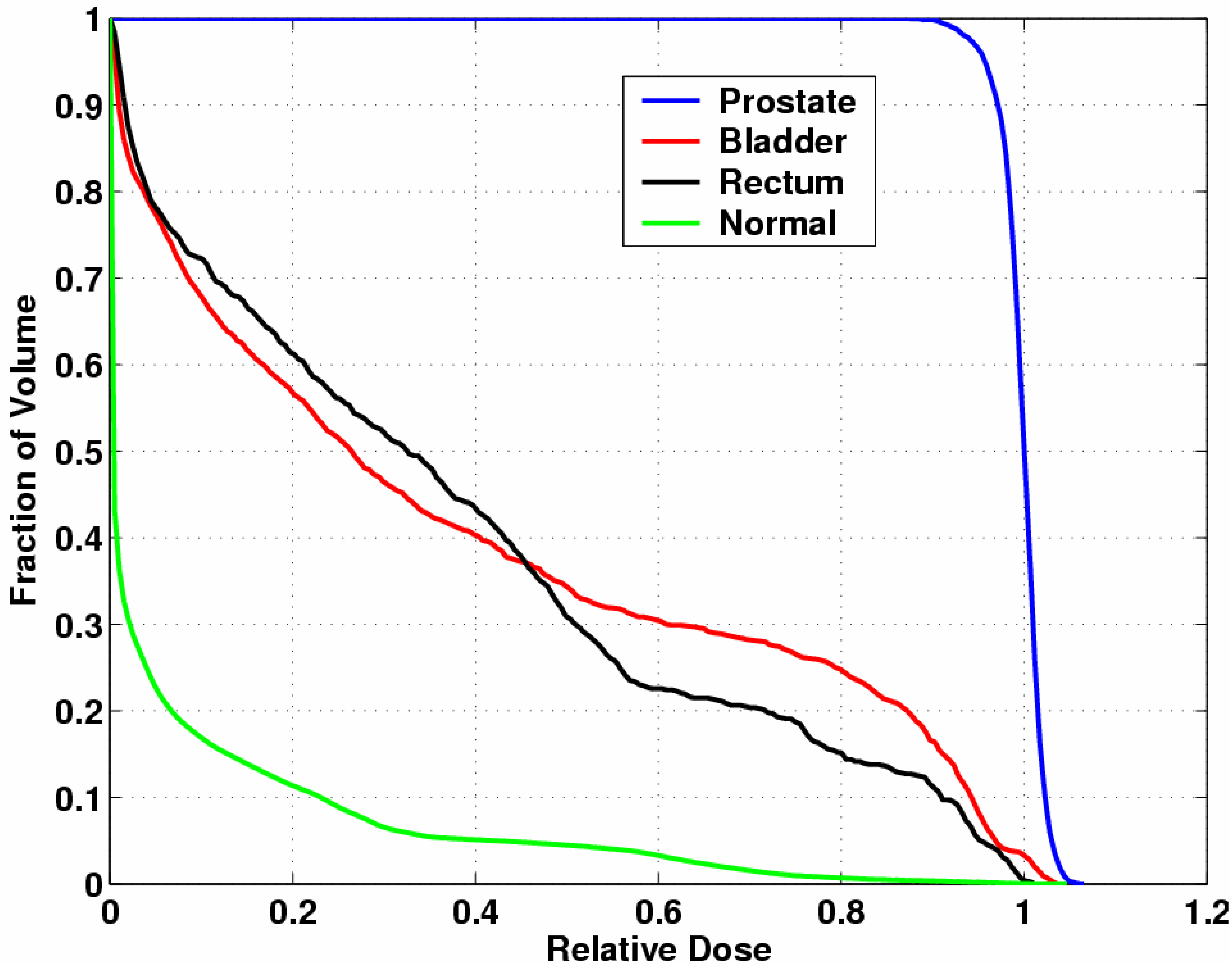
- Experts determine an ideal dose distribution for a particular target
  - Covers target (tumor)
  - Limits radiation to healthy/at-risk regions
- Delivery plan = optimization problem

Patient Example

- Grey – prostate
- Pink – rectum
- Red - bladder



Cumulative Dose Volume



Delivery Plan

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

plus some integrality constraints

Mixed Integer Approach

$$\psi_A = \begin{cases} 1 & \text{if use angle A} \\ 0 & \text{else} \end{cases}$$

$$0 \leq w_A \leq W\psi_A$$

$$\sum_A \psi_A \leq K$$

$$Dose(i) := \sum_A w_A D_A(i)$$

Dose/Volume Constraints

- e.g. no more than 5% of region R can receive more than U Gy

$$(\bar{U} - U) Viol(i) \geq Dose(i) - U$$

$$\sum_R Viol(i) \leq \frac{5|R|}{100}$$

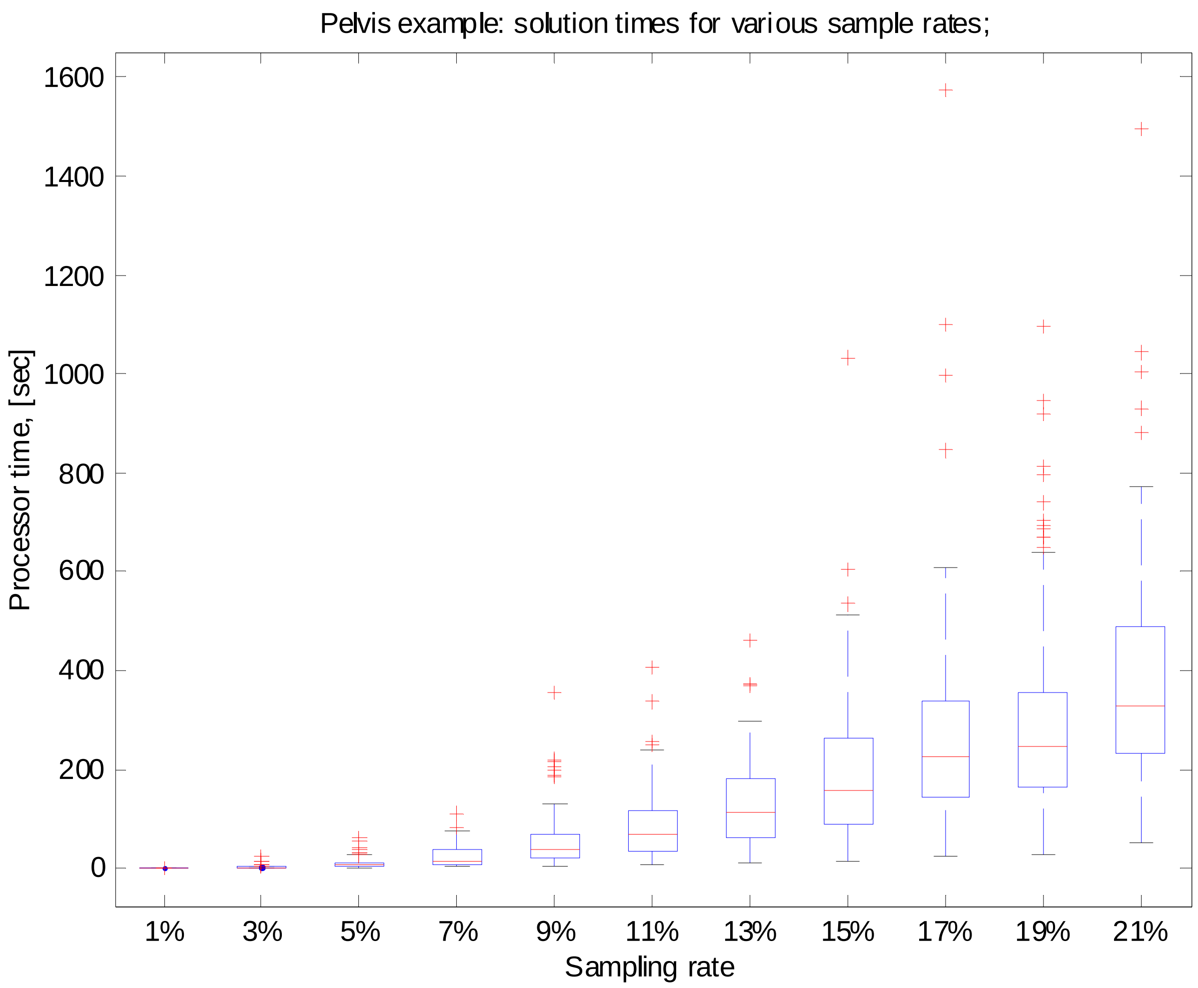
$$Viol(i) \in \{0, 1\}$$

Problems

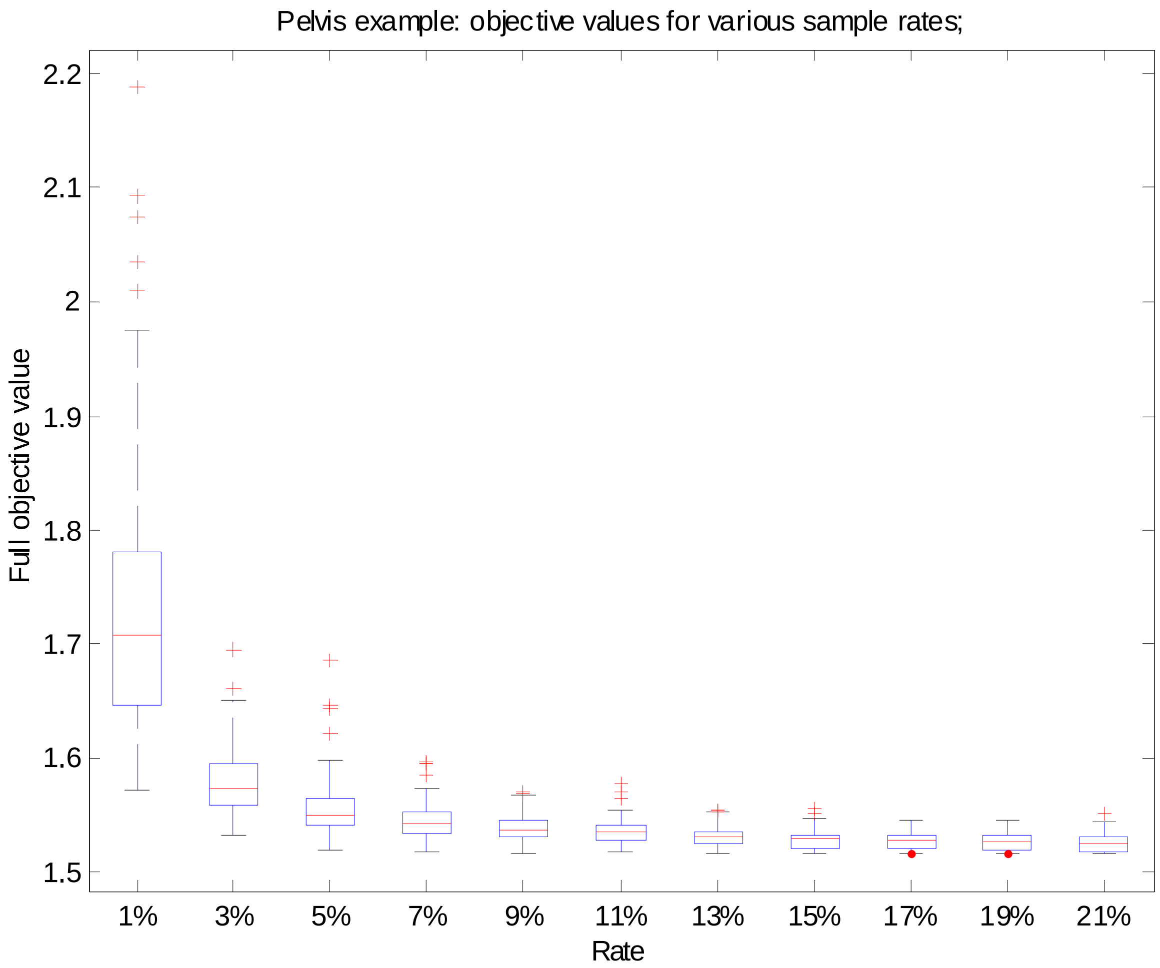
- Large computational times
- Large variance in computing times
- Ineffective restarts (what if trials?)
- Large amounts of data

- Try sampling of voxels (size reduction)
- High level branching (choice reduction)

Solution Times



True Objective Values



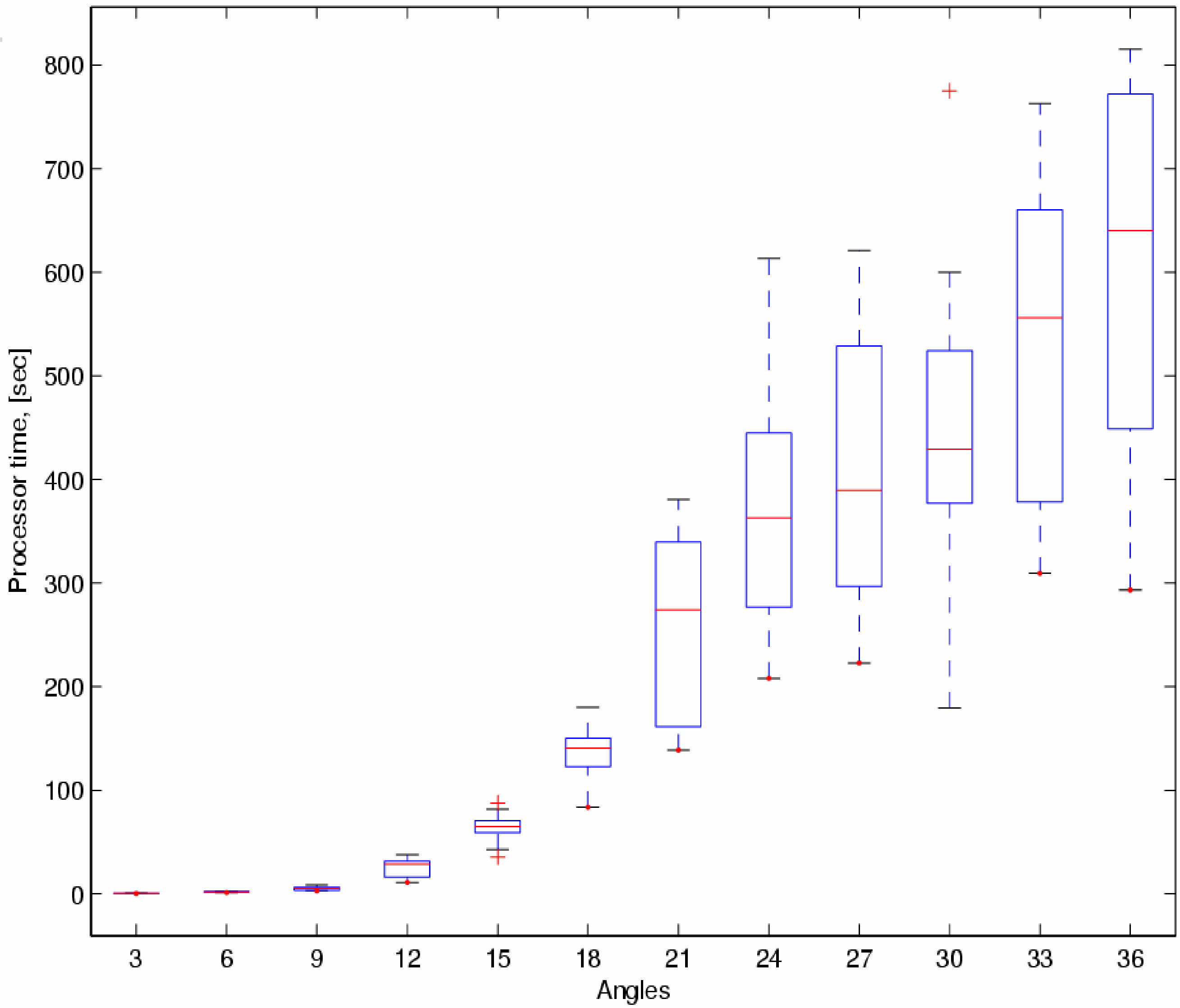
Naïve sampling fails

- Normal tissue
  - Huge numbers of voxels
  - Streaking effects undesirable (hot spots)
  - Use 5x sample on 2nd largest structure
- Small structures
  - Minimum sample size
- Homogeneity/min/max on PTV
  - 2x sample on PTV, rind sampling
- Large gradients on OAR's
  - 2x sample on OAR's
- Need adaptive mechanism

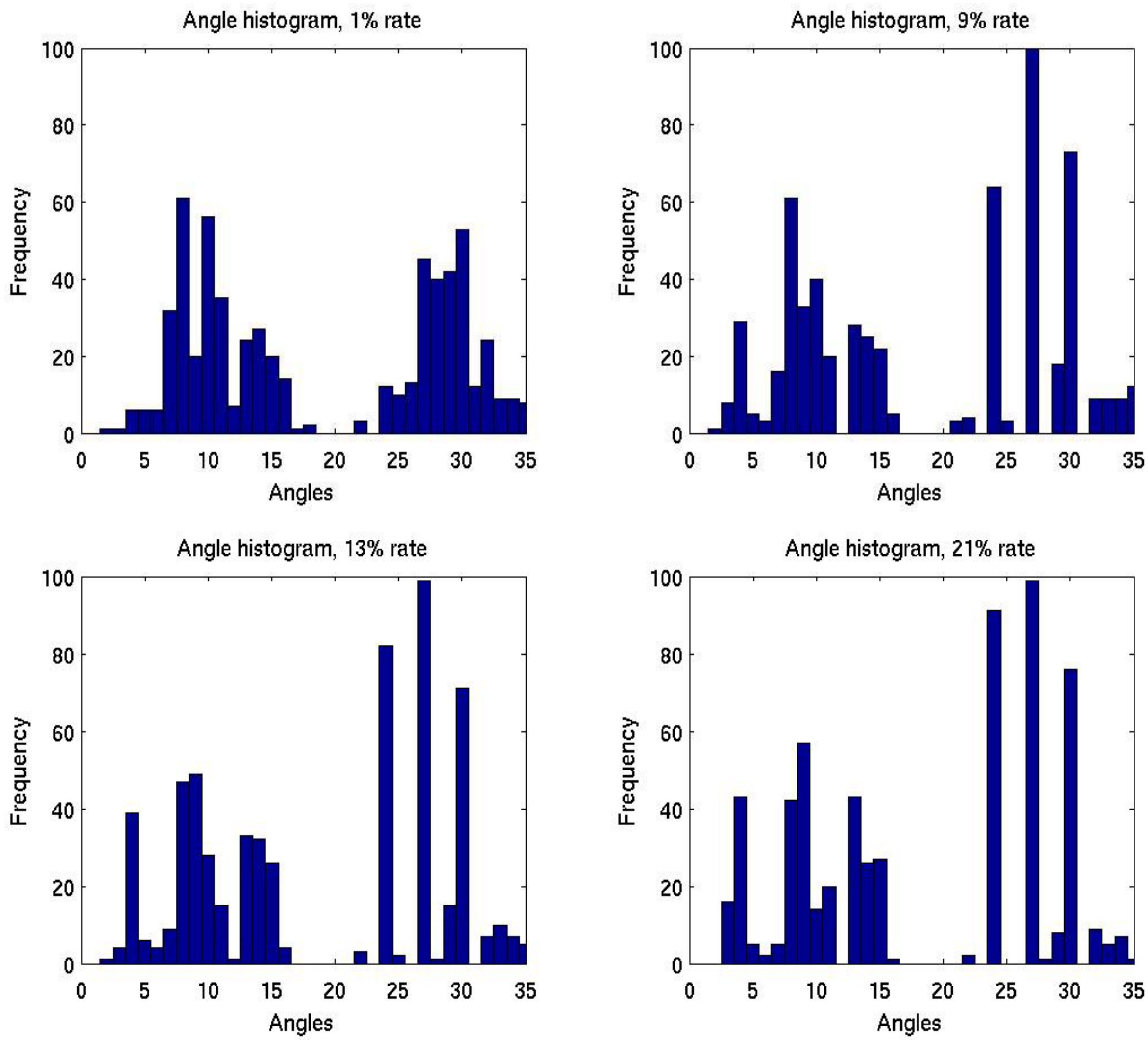
Sampling Issues

- For Details see: Sampling Issues for Optimization in Radiotherapy, by Michael C Ferris, David Shepard, Rikhardur Einarsson and Ziping Jiang. Preprint from ferris@cs.wisc.edu).
- Three Phase adaptive Sampling proved to be very successful
- We will only hint at sampling issues

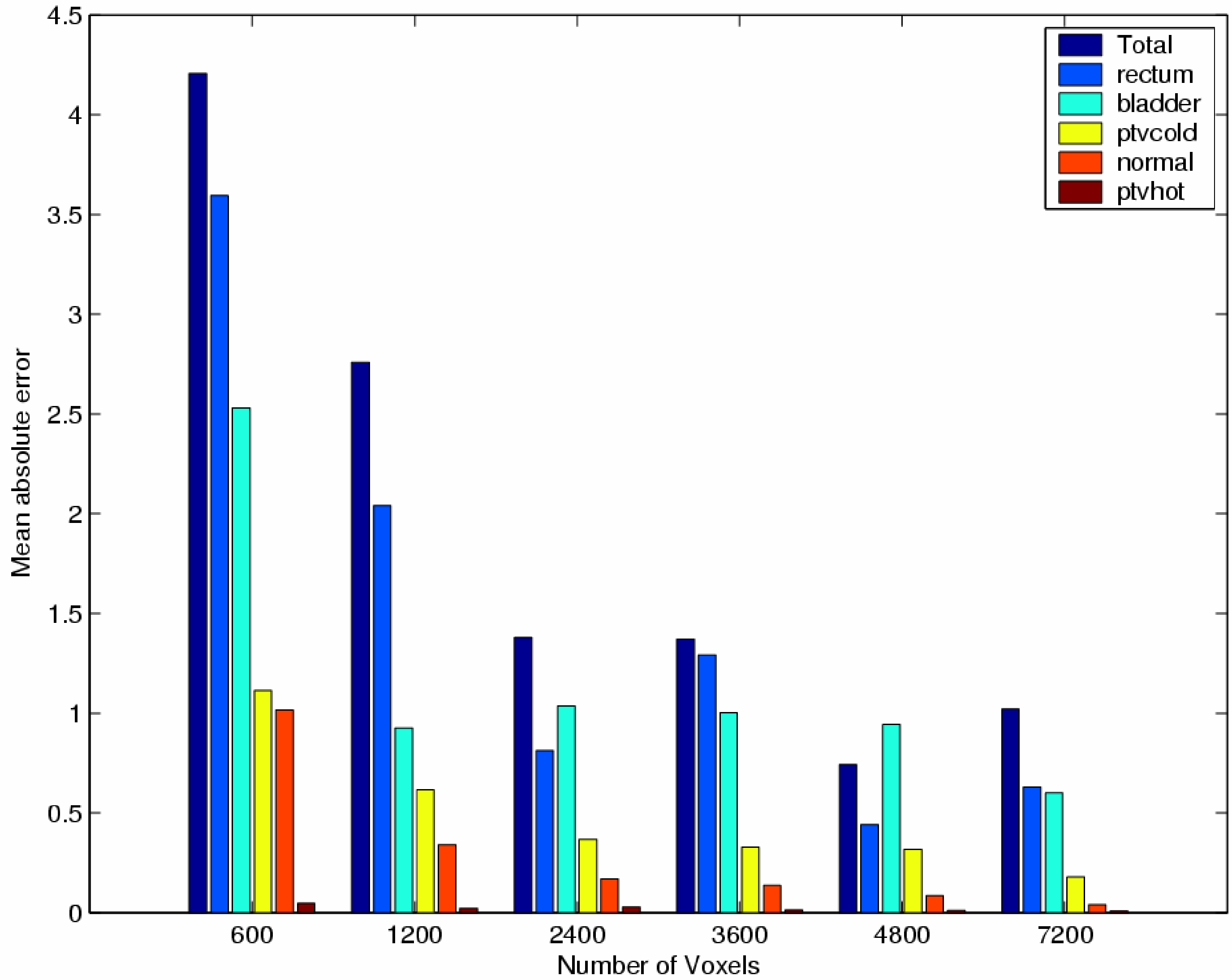
Processing Time



Angle Histograms



Proportional Sampling



Three Phase Sampling

- Reduce solution time without compromising quality
- Phase I:
  - Sample 10 times at low rate to predict angles to use
  - Each structure sampled proportionally with largest structure sample limited
  - Determine angles used in “best few” solutions
- Phase II:
  - Increase sample rate, using only proposed angles
- Phase III:
  - Increase sample rate, fix angles and wedge orientations

Sampling Process

- Determine initial sample size
- Phase I: use all angles
  - 10 sample LP’s used to adapt sample
  - 10 adapted sample LP’s solutions determine $\mathcal{A}_{\mathcal{I}}$
- Phase II: use reduced set of angles
  - 10 sample MIP’s determine $\mathcal{A}_{\mathcal{II}}$
- Phase III: use further reduc
  - Refine sample, solve single MIP, highly accurate solution

Patient Case Results

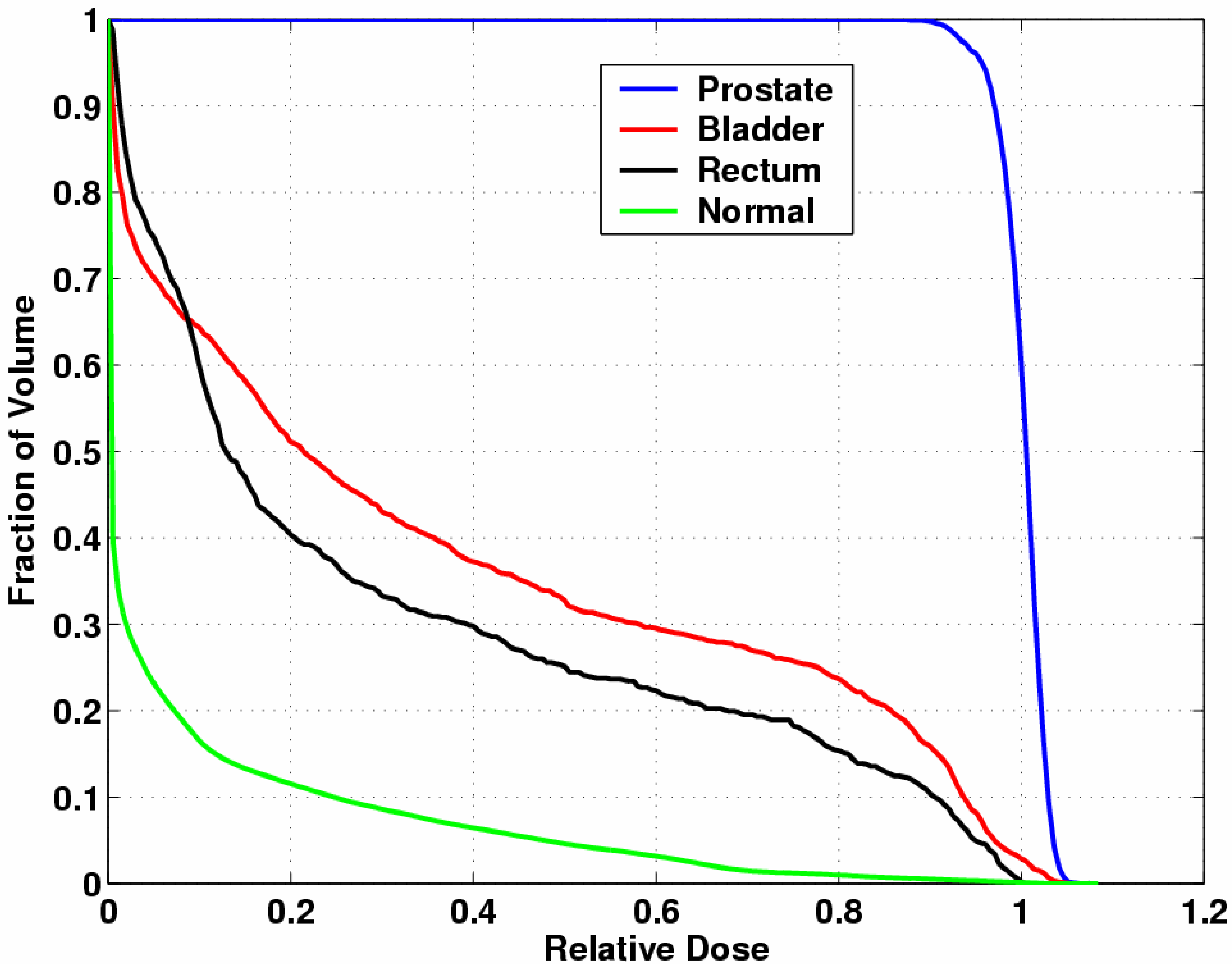
- Head/neck case:
  - Original time: 47,000 secs
  - Phase I time: 5.26 secs/sample
  - Phase II time: 51.21 secs/sample
  - Phase III time: 2.91 secs/sample
  - Solutions same: angles = 40, 140, 230 (+ wedges)
- Pancreas case:
  - Original time: 346,000 secs
  - Phase I time: 4 secs/sample
  - Phase II time: 77.31 secs/sample
  - Phase III time: 3.42 secs
  - Solutions same: angles = 80, 290, 350 (+ wedges)

GAMS

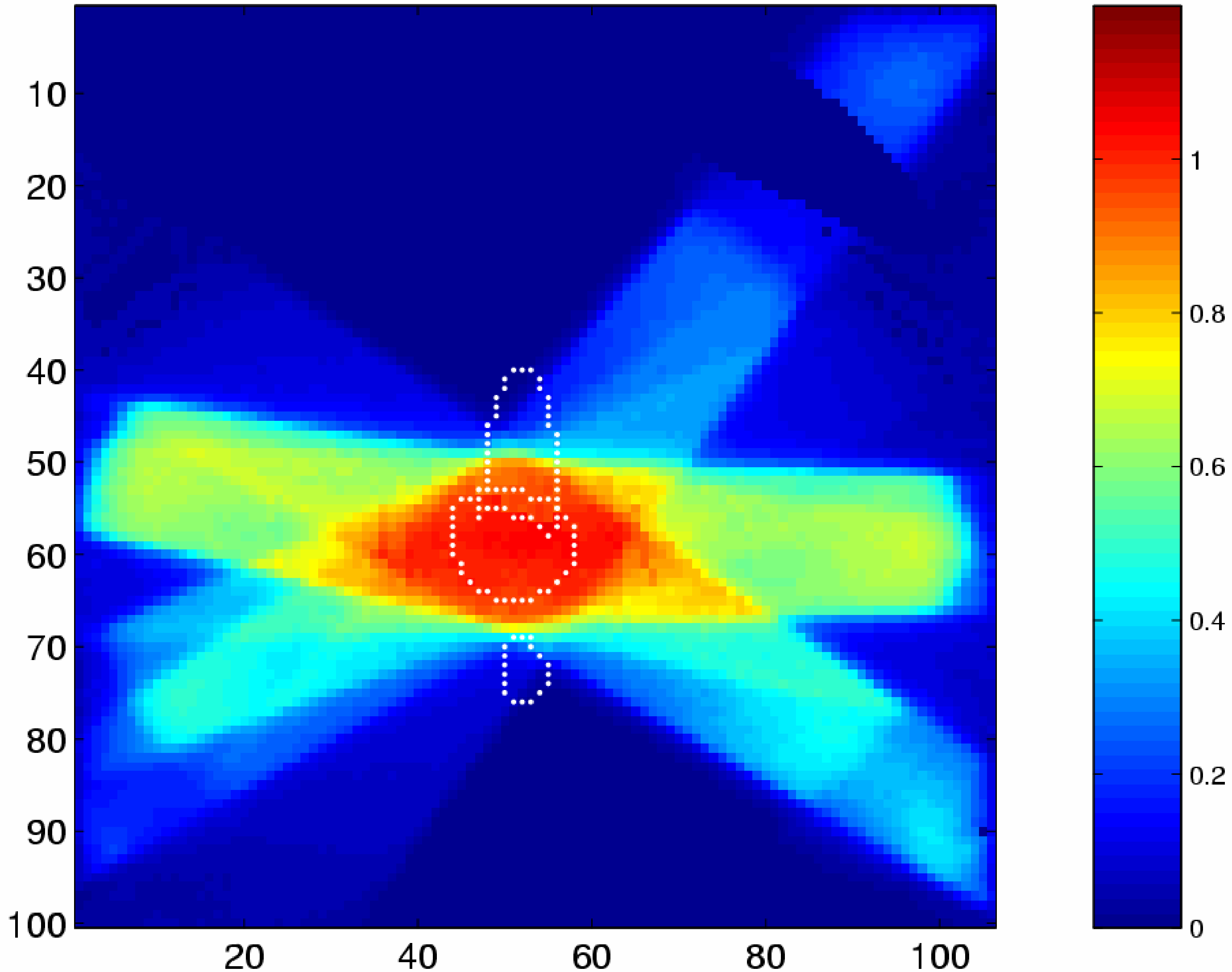
Pelvis case

- 3K prostate, 1.5K bladder, 1K rectum, 557K normal
- Time for “full problem”: 12.5K secs
- Time Phase I: 32 secs/sample
- Time Phase II: 18 secs/sample
- Time Phase III: 147 secs
- Solution: 80, 110, 130, 240, 270, 320

Dose Histogram



Axial Slice



Key contributions

- Use multiple (small) samples and multiple phases to determine plan
- Adaptive sampling via linear program solution
- High level branching via multiple samples and ranking
- Significant time reductions without loss in quality
- Applicable to more general treatment planning domains, and MIP applications

Remaining Issues

- Overall solution times still high
- Would like to consider more angles
- Work with higher sampling rates
- Use more samples
- Exhausted smart modeling
- Considerer high throughput computing
- How to convert from serial to parallel and distributed computing

New Opportunities

- The original model was implemented in GAMS and used CPLEX
- GAMS introduced an experimental grid computing facility
- High Throughput Computing via the Condor system and the SUN Grid Engine connected to GAMS
- Multi CPU desktop systems available

What is Grid Computing?

- A pool of connected computers managed and available as a common computing resource
  - Allows parallel task execution
  - Allows effective sharing of CPU power
  - Licensing issues
  - Scheduler handles management tasks
  - Can be rented or owned in common
  - E.g. Condor, Sun Grid Engine, Globus

Economics of Grid Computing

- Yearly cost, 2-CPU workstation: $5200
  - Hardware - $1200
  - Software - $4000
- Hourly cost on the grid: $2
  - $1/hour for CPU time (to grid operator)
  - $1/hour for software (GAMS, model owner)
- 1 workstation == 50 hrs/week grid time
- Up-front vs. deferred, as-needed costs

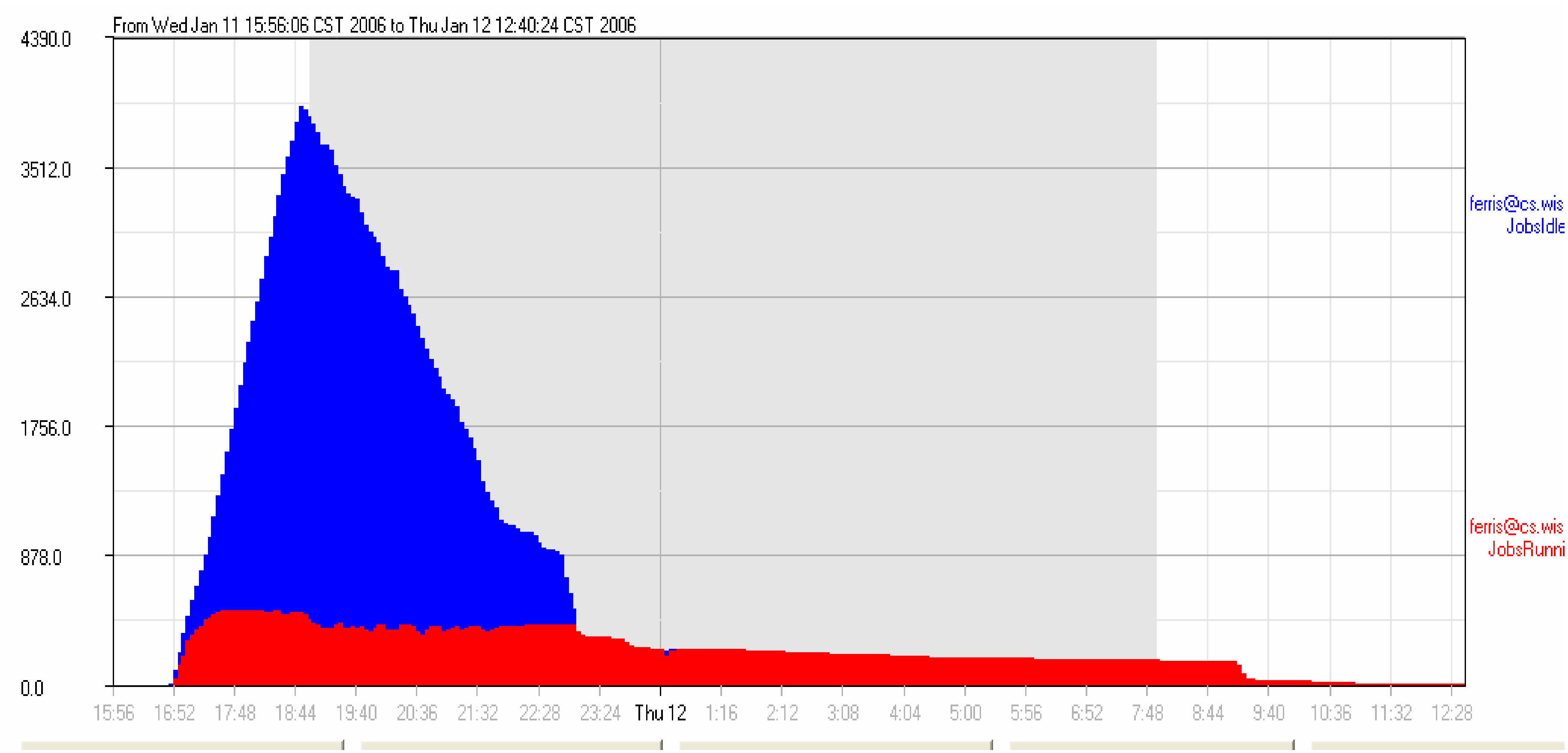
Use a GAMS Grid

- Solve the samples in parallel, e.g.
  - 200 CPUs: 15 minutes
- Marginal cost is $100
- No programming required (almost)
- Model stays maintainable
- Separation of model and solution maintained

Results for 4096 MIPS

- Submission start Jan 11 at 16:00 pm
- All job submitted by Jan 11 at 23:00 pm
- All jobs returned by Jan 12, 12:40 pm
  - 20 hours wall time, 5000 CPU hours
  - Peak number of CPUs: 500
- Different Instance:
  - 24 hours wall time, 3000 CPU hours

Condor Pool Statistics



Serial Solve Loop

```
loop(s,
  b(j) = dem(s,j);
  Solve tr using lp minimizing z;
  repx(s,i,j) = x.l(i,j);
  repy(s,'solvestat') = tr.solvestat;
  repy(s,'modelstat') = tr.modelstat );
```

Solve Submit Loop

parameter **h(s)** store the instance handle;

tr.**solvelink = 3**; // turn on grid option

loop(s,

  b(j) = dem(s,j)

  Solve tr using lp minimizing z;

  h(s) = tr**.handle**); // save instance handle

Solution Collection Loop

```
Repeat
  loop(s$h(s),
     if(handlestatus(h(s))=2,
        tr.handle = handle(s); execute_loadhandle tr;
        repx(s,i,j) = x.l(i,j); repy(s,'solvestat') = tr.solvestat;
        repy(s,'modelstat') = tr.modelstat;
        display$handledelete(h(s)) 'Could not remove handle';
        h(s) = 0) ) ; // indicate solution is loaded
   if(card(h), execute 'sleep 1');
until card(h) = 0 or timeelapsed > 100;
```

Grid Specifics Scripts

```
echo "#!/bin/bash"           > ${3}runit.sh
echo $1 $2                  >> ${3}runit.sh
echo gmscr_ux.out $2  >> ${3}runit.sh
echo mkdir ${3}finished  >> ${3}runit.sh
chmod 750 ${3}runit.sh
${3}runit.sh > /dev/null &
```

Sample Submit Script

```
@echo off                      > %3runit.cmd
echo %1 %2                    >> %3runit.cmd
echo gmscr_nx.exe %2          >> %3runit.cmd
echo mkdir %3finished         >> %3runit.cmd
echo echo exit                >> %3runit.cmd
start /b /BELOWNORMAL %3runit.cmd > nul
```

Conclusions

- Massive parallel and distributed computing environments are becoming available (SUN just introduced a 5000 node network in the US).
- Simple language extensions in existing modeling systems provide easy access
- Today's modeling languages are well suited to experiment with coarse grain parallel approaches for solving difficult problem.