Optimization of Gamma Knife Radiosurgery

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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 while avoiding excess dose to healthy tissue and at-risk regions (organs)

Commonalities

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

Stereotactic radiosurgery?

- Stereotactic - orginated from the Greek words stereo meaning three dimensional and tactos meaning touched
- Stereotactic – fixation system (Leksell, 1951)
  - Bite on dental plate to restrict head movement
  - Or screw helmet onto skull to fix head-frame in position
  - Treatment almost always to head (or neck)
- Multiple radiation fields from different locations
- Radiosurgery – one session treatment
  - High dose, single fraction (no movement errors!)

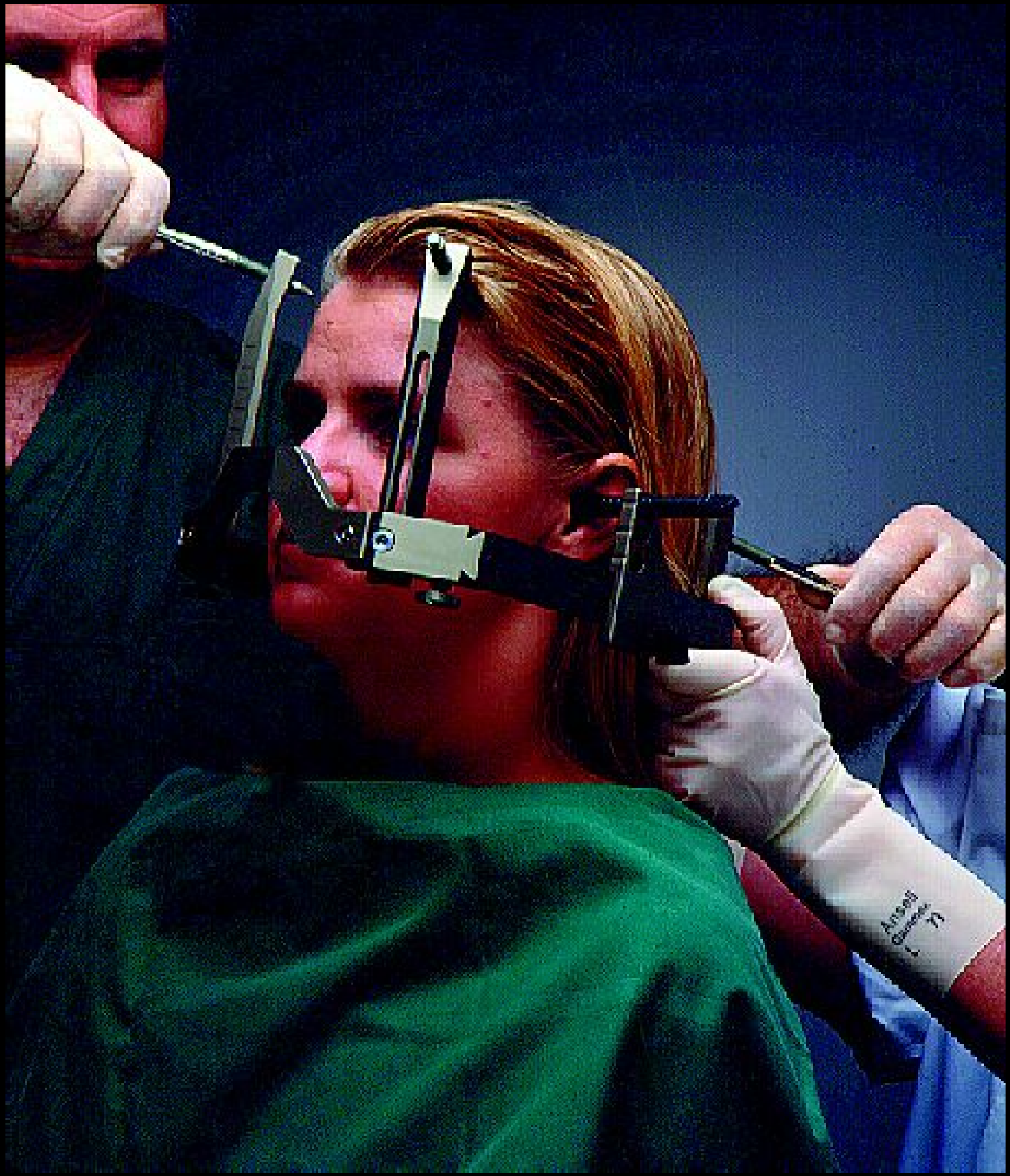
Types

- Particle beam (proton)
  - Cyclotron (expensive, huge, limited availability)
- Cobalt60 based (photon)
  - Gamma Knife (focus of this talk)
- Linear accelerator (x-ray)
  - (Tumor size) cone (12.5mm – 40mm) placed in collimator
  - Arc delivery followed by rotation of couch (4 to 6 times)

The Gamma Knife

201 cobalt gamma ray beam sources are arrayed in a hemisphere and aimed through a collimator to a common focal point.

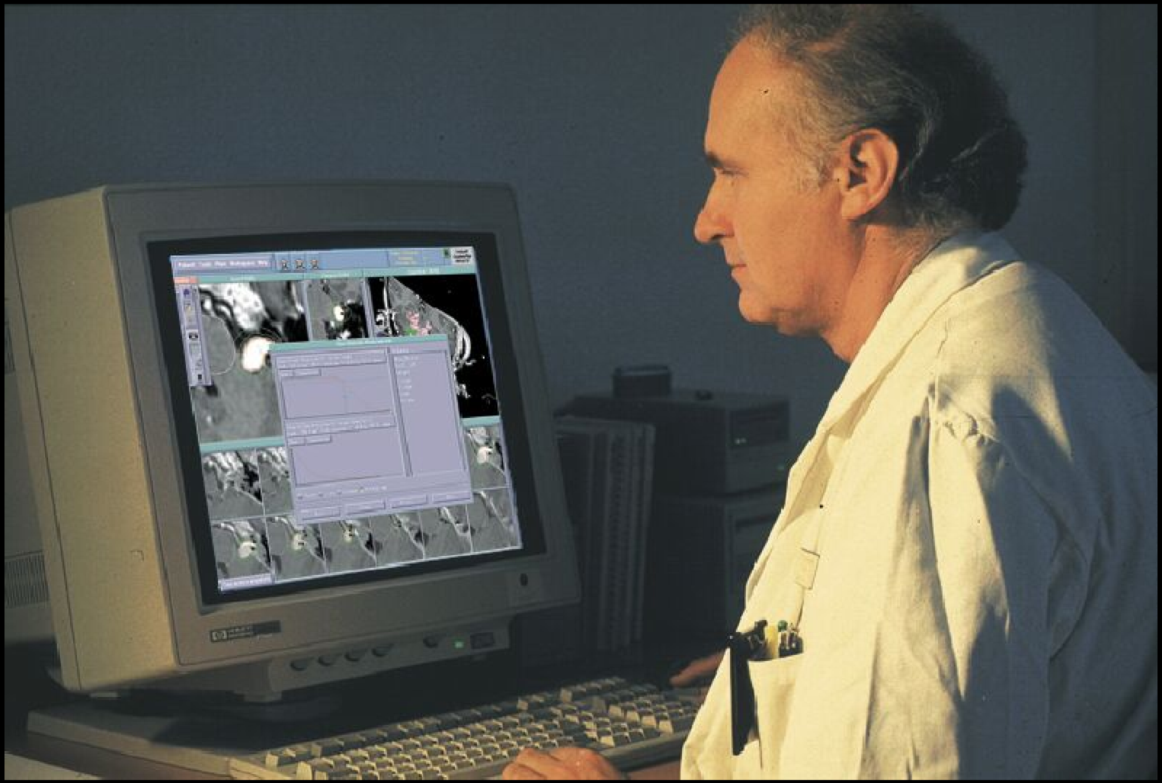
The patient’s head is positioned within the Gamma Knife so that the tumor is in the focal point of the gamma rays.



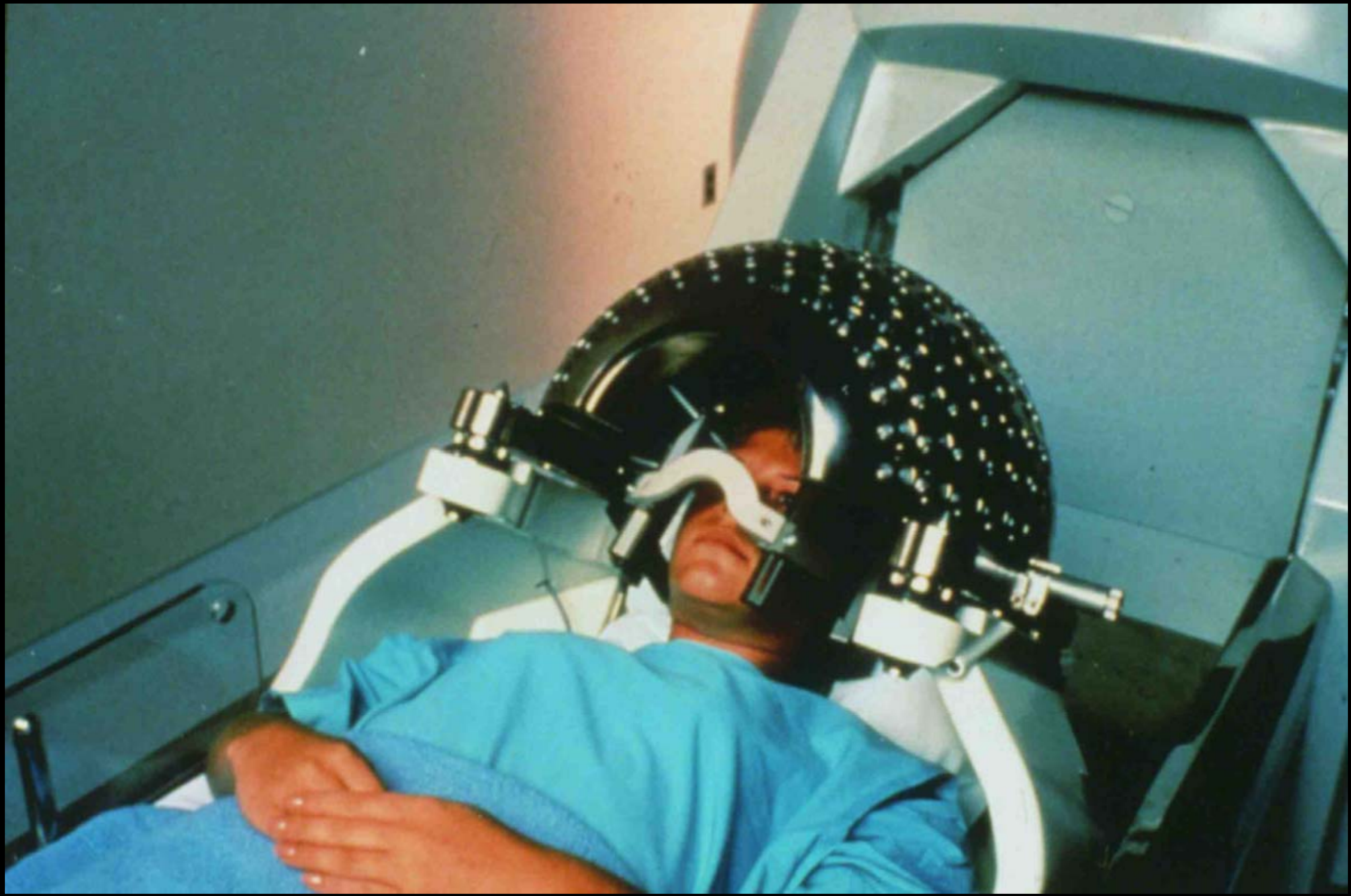
How is Gamma Knife Surgery performed?

Step 1: A stereotactic head frame is attached to the head with local anesthesia.

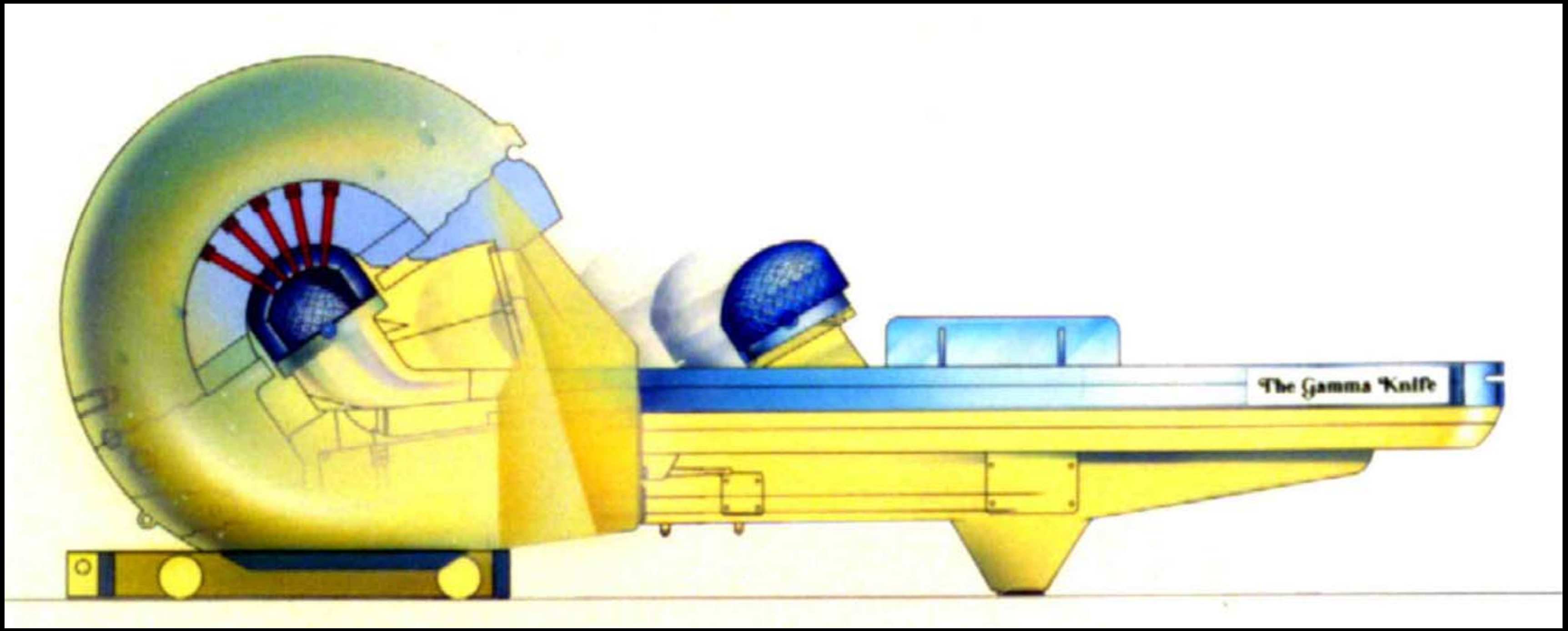
Step 2: The head is imaged using a MRI or CT scanner while the patient wears the stereotactic frame.



Step 3: A treatment plan is developed using the images. Key point: very accurate delivery possible.



Step 4: The patient lies on the treatment table of the Gamma Knife while the frame is affixed to the appropriate collimator.

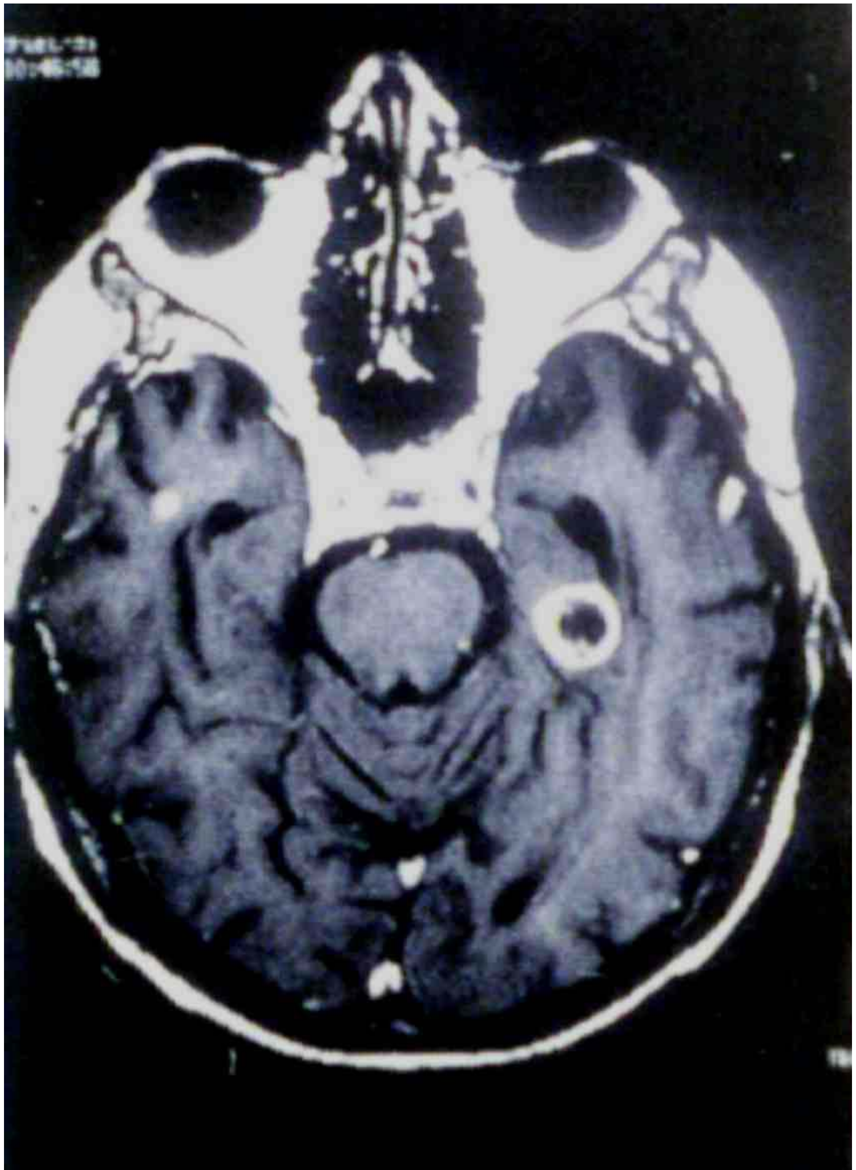


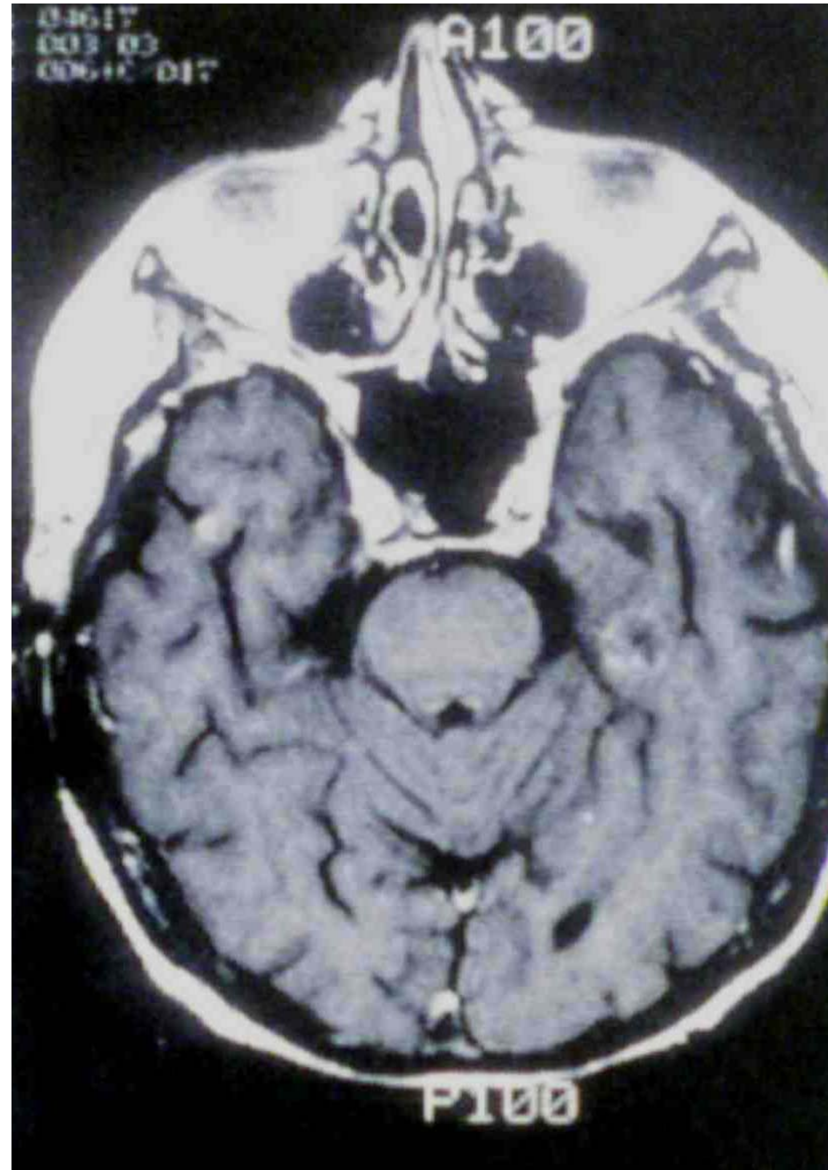
Step 5: The door to the treatment unit opens. The patient is advanced into the shielded treatment vault. The area where all of the beams intersect is treated with a high dose of radiation.

Procedure

- Placement of head frame
- Imaging (establish coordinate frame)
- Treatment planning
- Treatment
  - Multiple arcs of radiation
  - Multiple shots from Gamma Knife
- Frame removal


4
4
8
8
14
14




A100
P100

What disorders can the Gamma Knife treat?

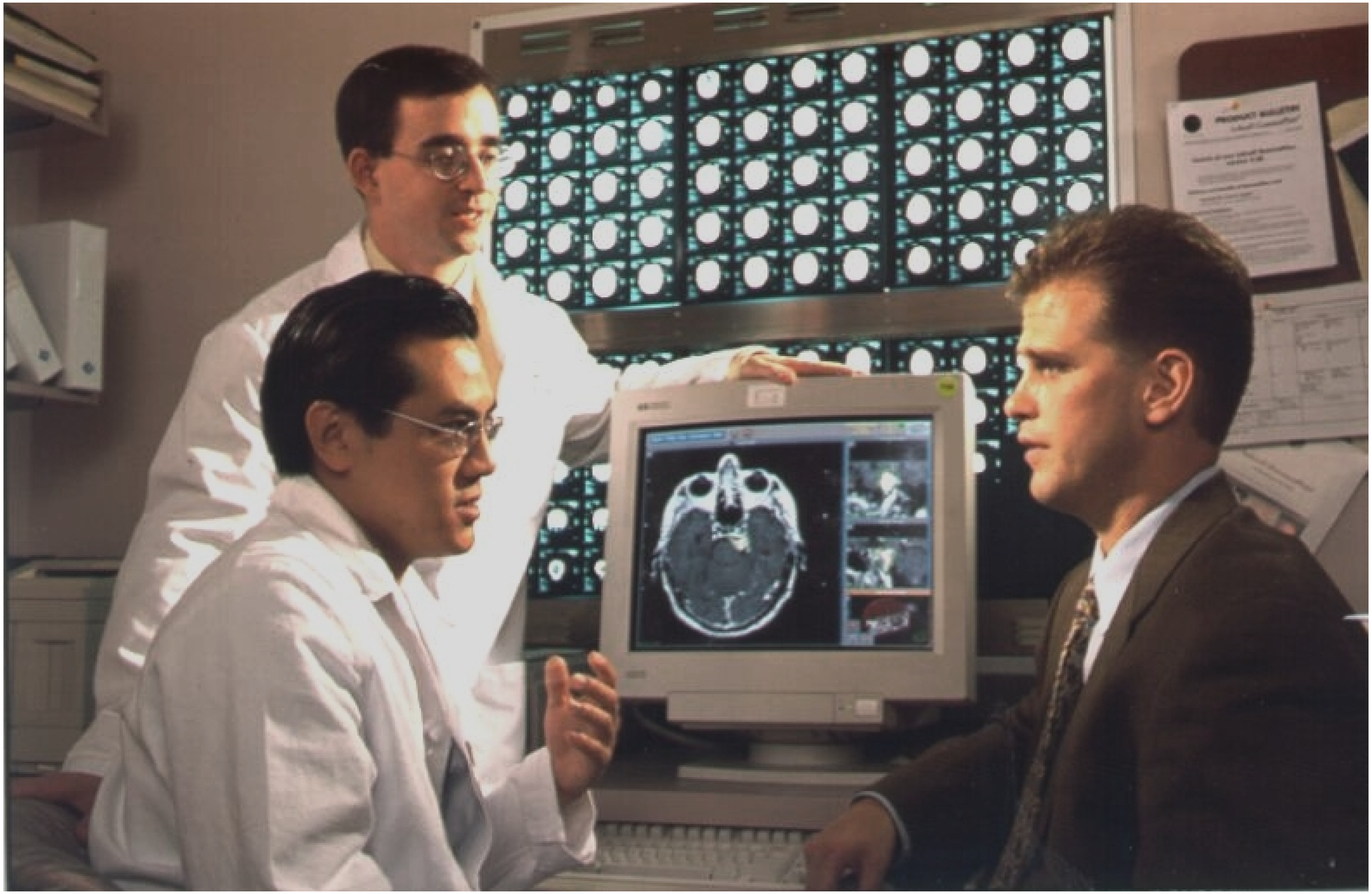
- Malignant brain tumors
- Benign tumors within the head
- Malignant tumors from elsewhere in the body
- Vascular malformations
- Functional disorders of the brain
  - Parkinson's disease

Gamma Knife Statistics

- 120 Gamma Knife units worldwide
- Over 20,000 patients treated annually
- Accuracy of surgery without the cuts
- Same-day treatment

- Expensive instrument

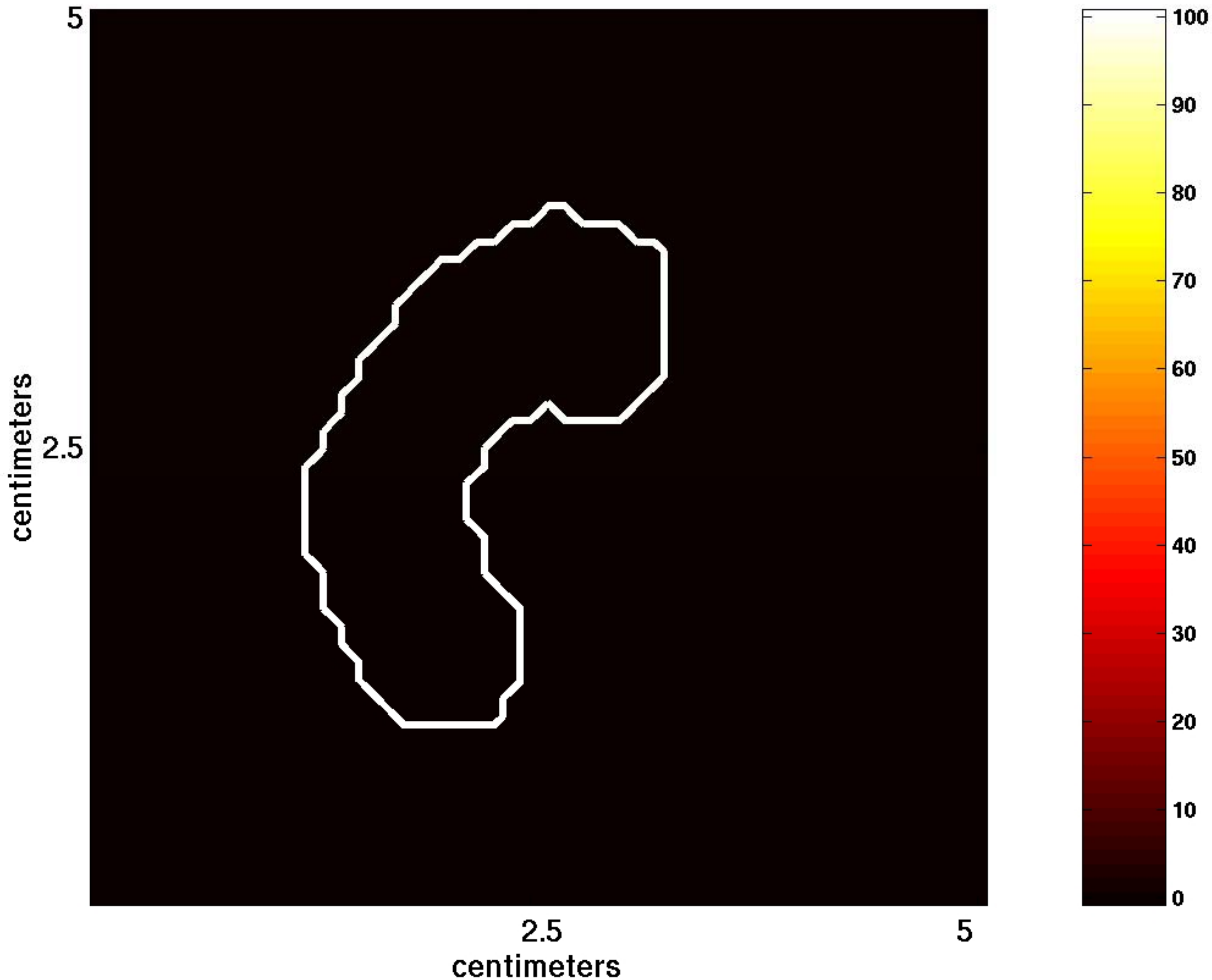
Treatment Planning



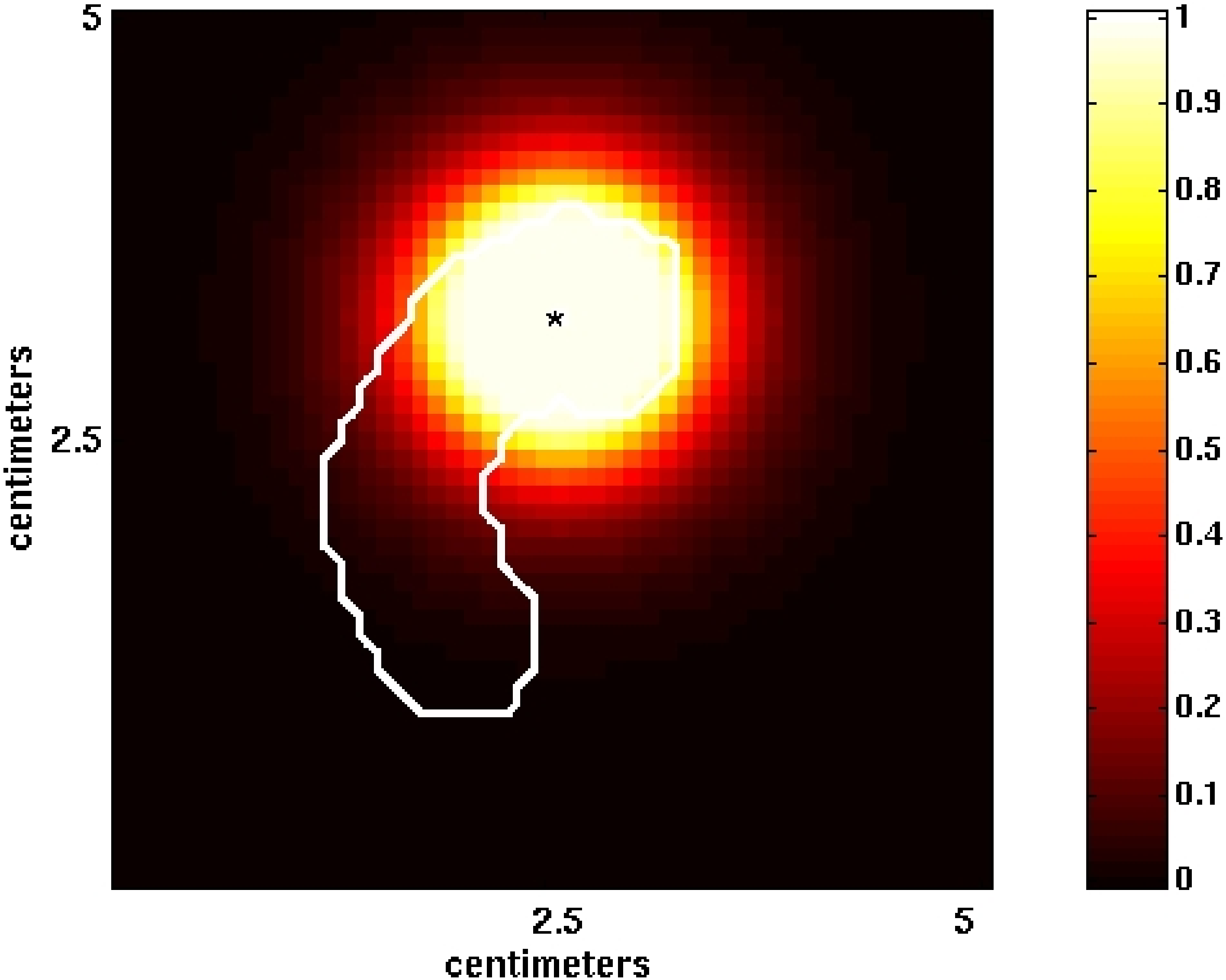
Treatment Planning

- Through an iterative approach we determine:
  - the number of shots
  - the shot sizes
  - the shot locations
  - the shot weights
- The quality of the plan is dependent upon the patience and experience of the user

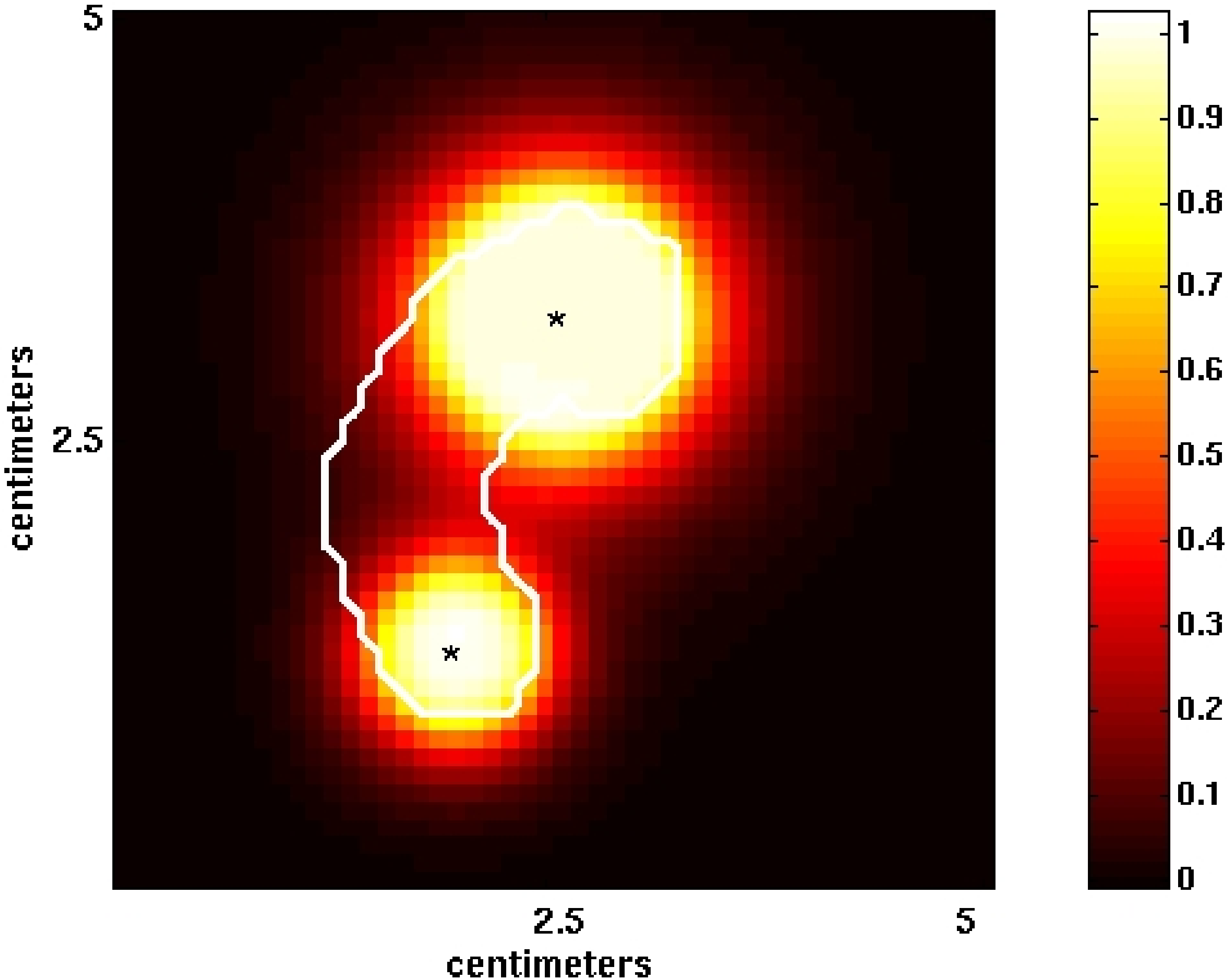
Target


5
2.5
centimeters
2.5
5
centimeters
100
90
80
70
60
50
40
30
20
10
0

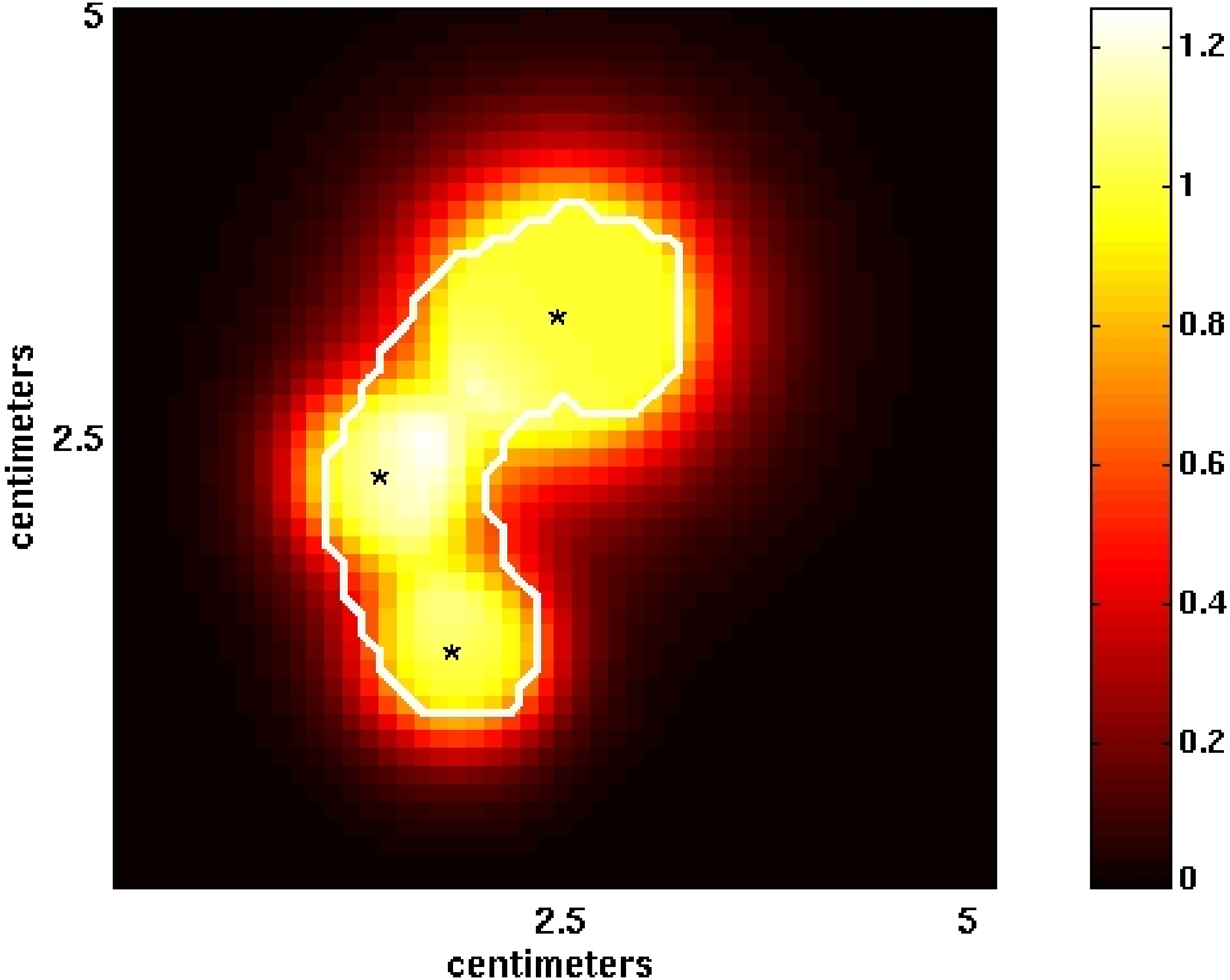
1 Shot



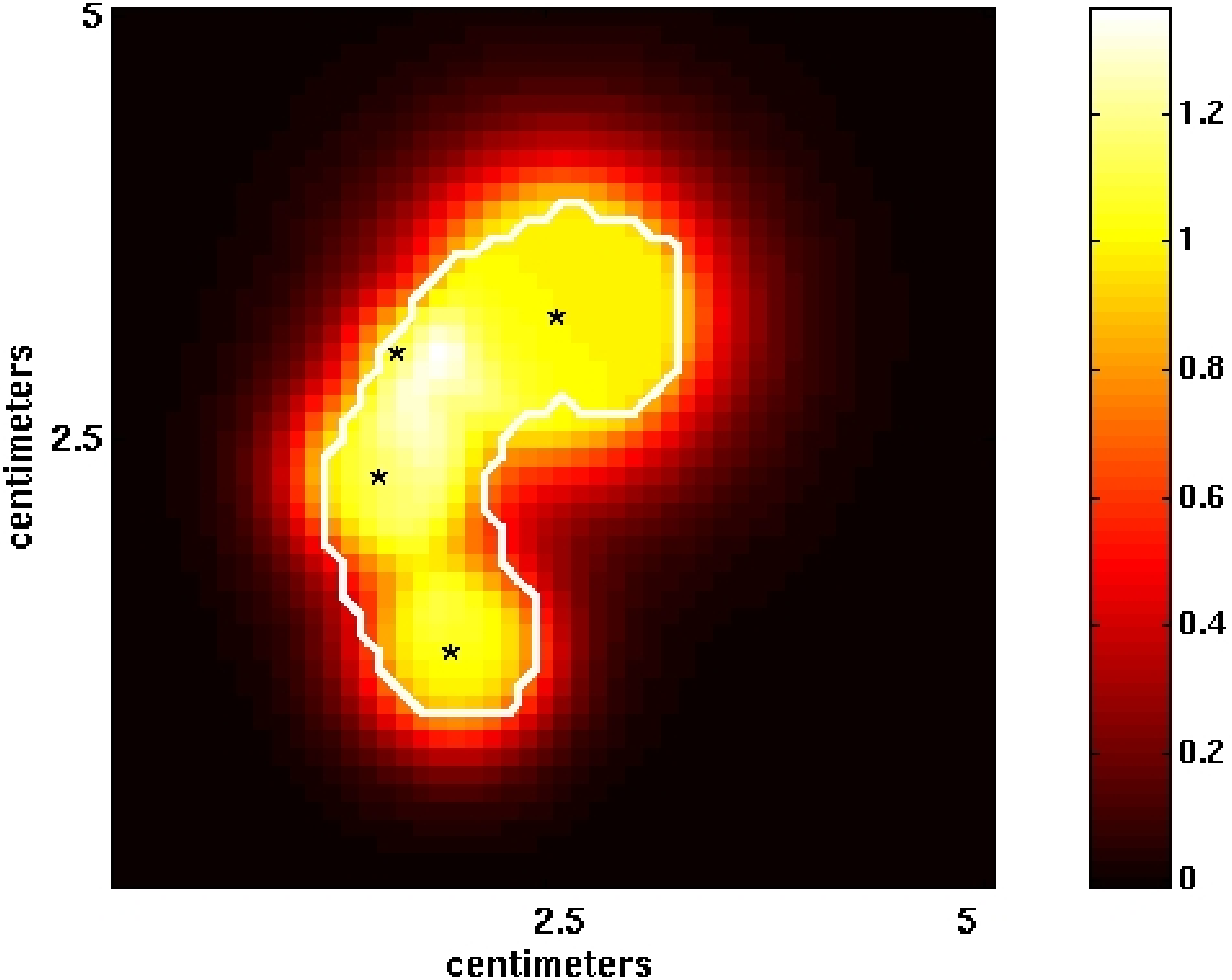
2 Shots



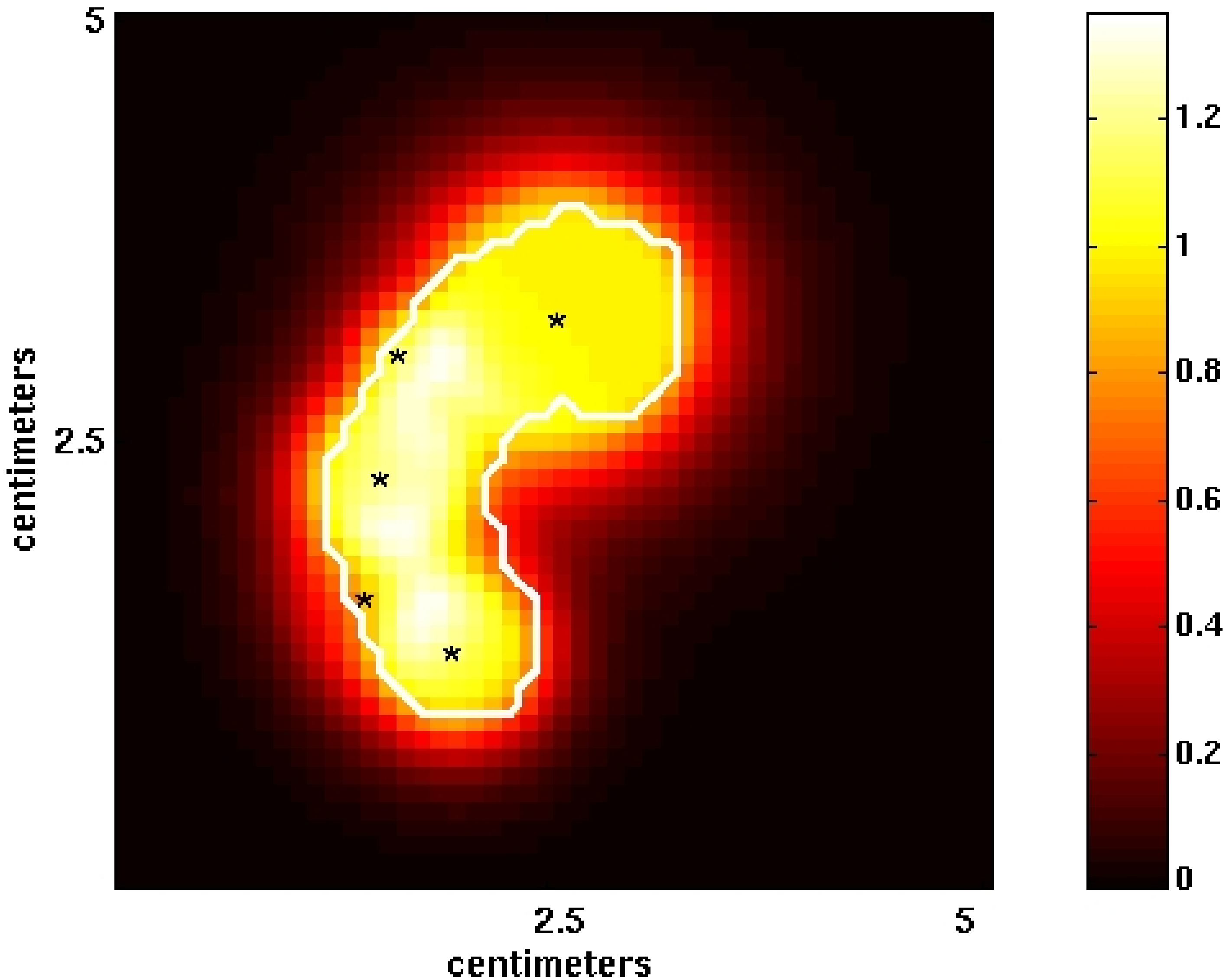
3 Shots



4 Shots



5 Shots



Inverse Treatment Planning

- Develop a fully automated approach to (Gamma Knife) treatment planning
- A clinically useful technique will meet three criteria: robust, flexible, fast

- Benefits of computer generated plans
  - uniformity, quality, faster determination

Computational Model

- Target volume (from MRI or CT)
- Maximum number of shots to use
  - Which size shots to use
  - Where to place shots
  - How long to deliver shot for

  - Conform to Target (50% isodose curve)
  - Real-time optimization

Summary of techniques

Method	Advantage	Disadvantage
Sphere Packing	Easy concept	NP-hard Hard to enforce constraints
Dynamic Programming	Easy concept	Not flexible Not easy to implement Hard to enforce constraints
Simulated Annealing	Global solution (Probabilistic)	Long-run time Hard to enforce constraints
Mixed Integer Programming	Global solution (Deterministic)	Enormous amount of data Long-run time
Nonlinear Programming	Flexible	Local solution Initial solution required

Ideal Optimization

$$\min_{t_{s,w}, x_s} Dose(NonTarget)$$

subject to

$$Dose(i) = \sum_{s \in S, w \in W} t_{s,w} D_w(x_s, i)$$

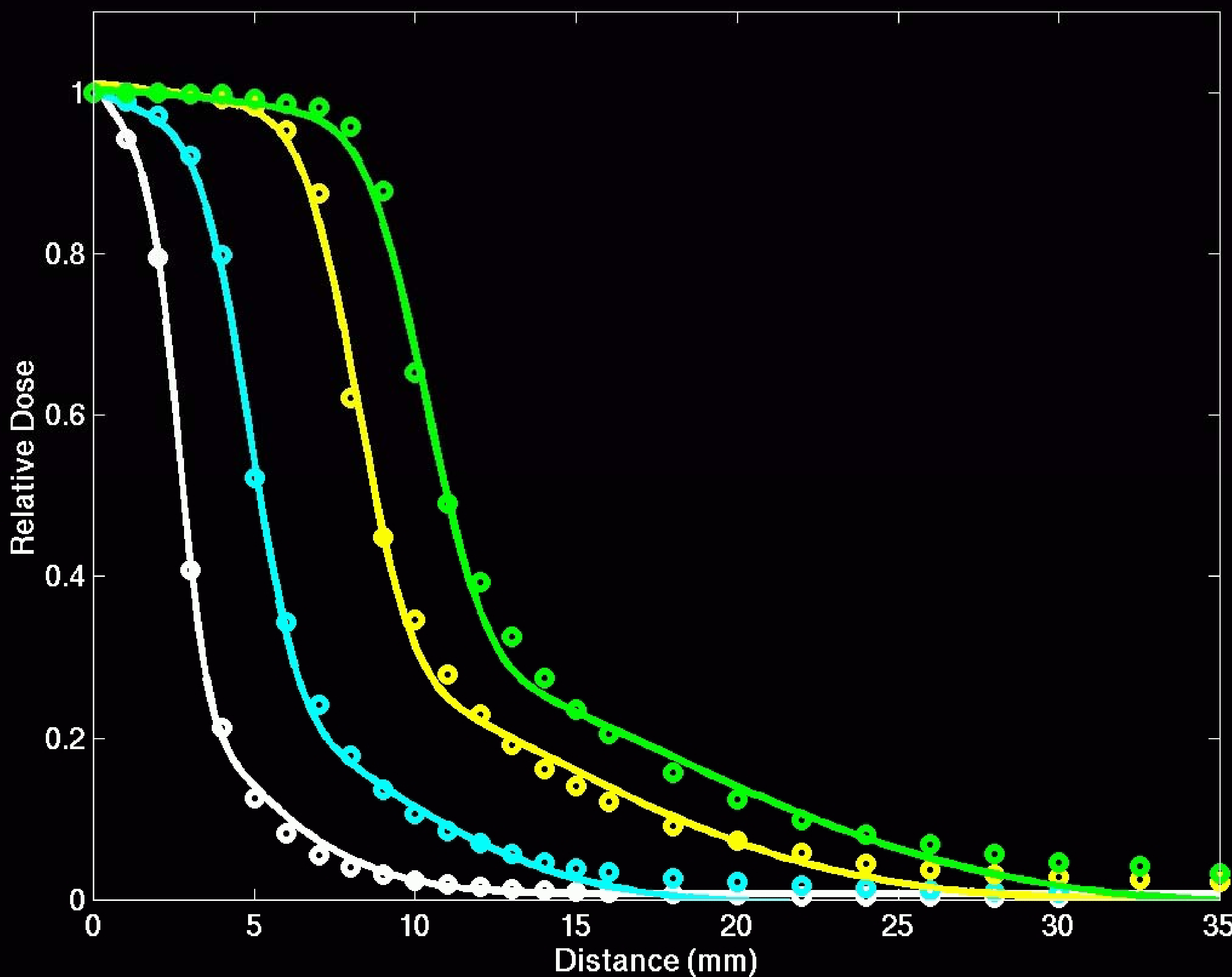
$$0.5 \leq Dose(Target) \leq 1$$

$$t_{s,w} \geq 0$$

$$|S| \leq N$$

Solution methodology

- Detail dose distribution calculation
- Describe nonlinear approximation
- Outline iterative solution approach
- Starting point generation
- Modeling issues
- Examples of usage


Relative Dose
0
0.2
0.4
0.6
0.8
1
0
5
10
15
20
25
30
35
Distance (mm)

Dose calculation

- Measure dose at distance from shot center in 3 different axes
- Fit a nonlinear curve to these measurements (nonlinear least squares)
- Functional form from literature, 10 parameters to fit via least-squares

$$m_1 \; erf(\frac{d_1(x)-r_1}{\sigma_1}) + m_2 \; erf(\frac{d_2(x)-r_2}{\sigma_2})$$

Nonlinear Approach

Let x_s be the variable locations

$$s = 1, 2, \ldots, N$$

$D_w(x_s, i)$ is nasty nonlinear function

What width shot to use at x_s?

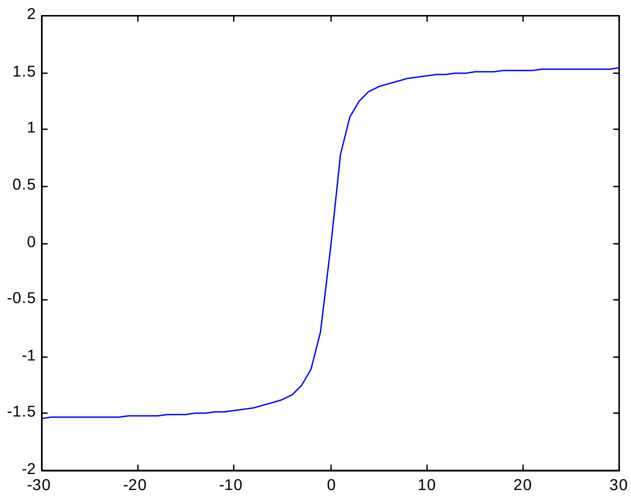
$$\psi_{s,w} = \begin{cases} 1 & \text{if shot s is width w} \\ 0 & \text{else} \end{cases}$$

$$\underline{T}\psi_{s,w} \le t_{s,w} \le \overline{T}\psi_{s,w}$$

$$\textstyle\sum_w \psi_{s,w} \le 1$$

Nonlinear approximation

- Approximate via "arctan"



$$\forall s \in S$$
$$\sum_{w} arctan(t_{s,w}) \leq \frac{\pi}{2}$$

- First, solve with coarse approximation, then refine and reoptimize

Difficulties

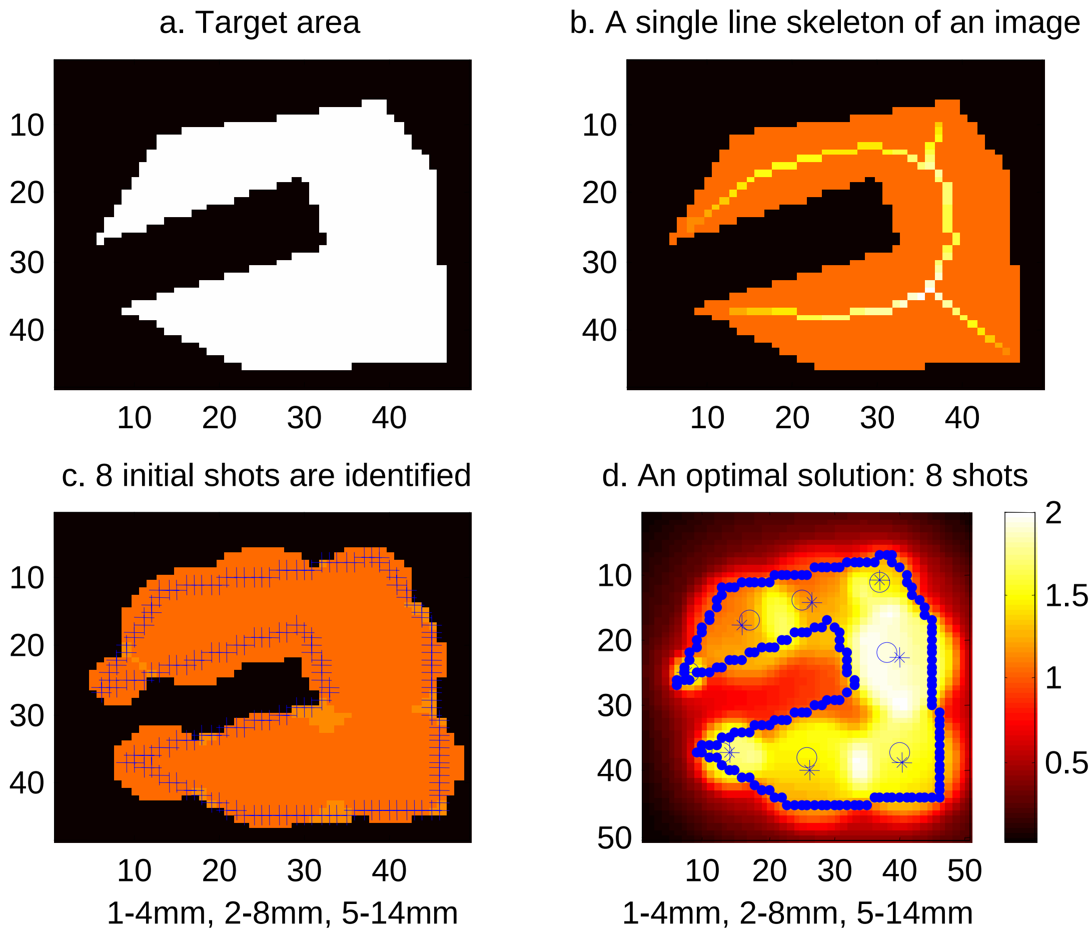
- Nonconvex optimization
  - speed
  - robustness
  - starting point
- Too many voxels outside target
- Too many voxels in the target (size)
- What does the neurosurgeon really want?

$$
\begin{aligned}
\min_{t_{s,w},x_s} \quad & Under(Target) \\
\text{s.t.} \quad & Dose(i) = \sum_{s\in S, w\in W} t_{s,w} D_w(x_s, i) \\
& 0 \leq Under(i) \geq 1 - Dose(i) \\
& Dose(Target)/(\sum_{s,w} t_{s,w}\overline{D_w}) \geq P \\
& \sum_{s,w} \mathrm{arctan}(t_{s,w}) \leq N \ \pi/2 \\
& 0 \leq Dose(i) \leq 1,\ 0 \leq t_{s,w}
\end{aligned}
$$

Iterative Approach

- Rotate data (prone/supine)
- Skeletonization starting point procedure
- Conformity subproblem (P)
- Coarse grid shot optimization
- Refine grid (add violated locations)
- Refine smoothing parameter
- Round and fix locations, solve MIP for exposure times

Skeleton Starting Points



Run Time Comparison

Average Run Time	Size of Tumor		
	Small	Medium	Large
Random (Std. Dev)	2 min 33 sec (40 sec)	17 min 20 sec (3 min 48 sec)	373 min 2 sec (90 min 8 sec)
SLSD (Std. Dev)	1 min 2 sec (17 sec)	15 min 57 sec (3 min 12 sec)	23 min 54 sec (4 min 54 sec)

MIP Approach

If we choose from set of shot locations

$$\psi_{s,w} = \begin{cases} 1 & \text{if use shot s of width w} \\ 0 & \text{else} \end{cases}$$

$$D_{s,w}(i) := D_w(x_s, i)$$

$$Dose(i) = \sum_{s \in S, w \in W} t_{s,w} D_{s,w}(i)$$

MIP Problem

$$\min_{t_{s,w},\psi_{s,w}} \quad Under(Target)$$

$$\text{s.t.} \quad Dose(i) = \sum_{s\in S, w\in W} t_{s,w} D_{s,w}(i)$$

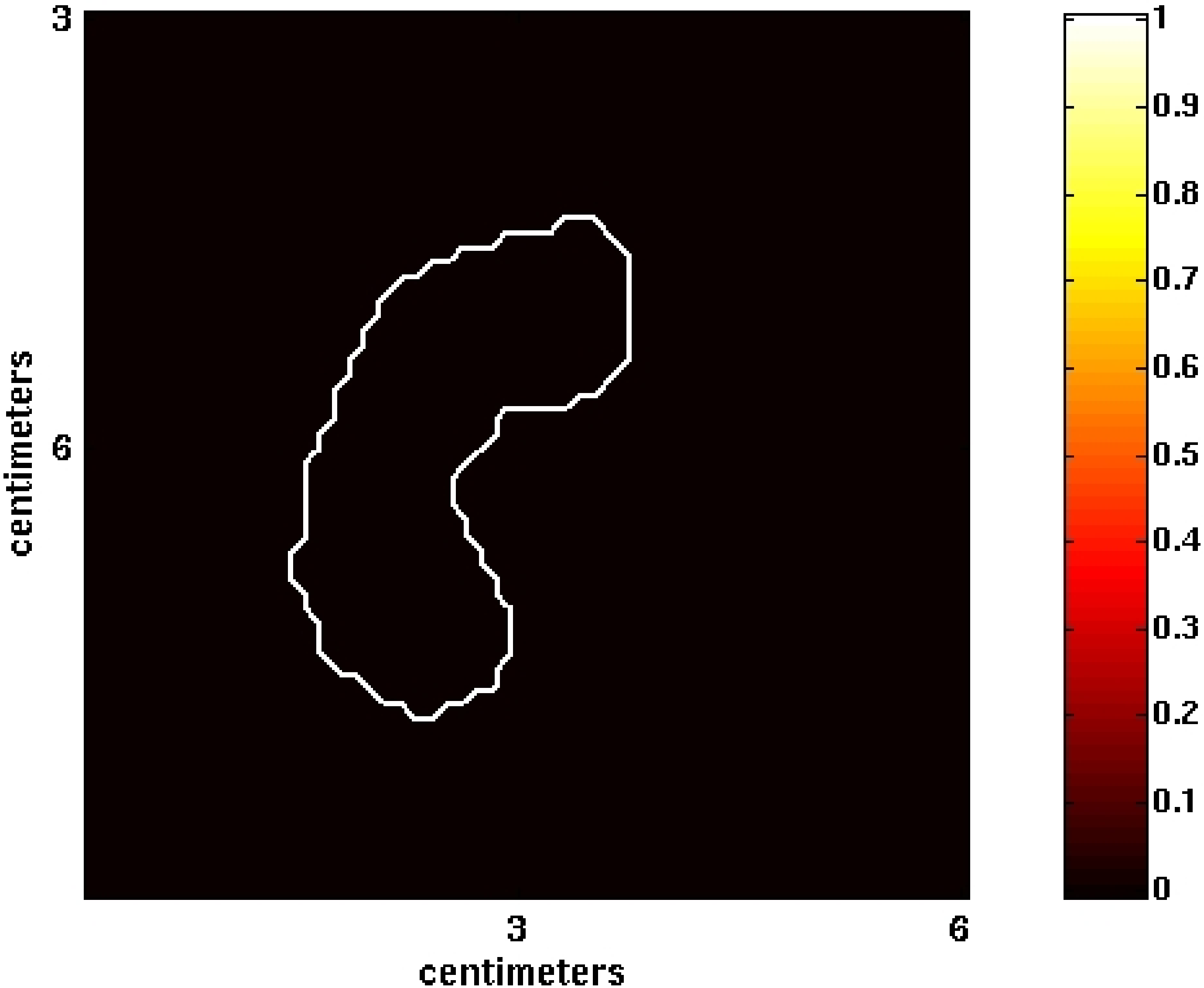
$$0 \leq Under(i) \geq 1 - Dose(i)$$

$$Dose(Target) \;\geq\; P \sum_{s,w} t_{s,w} \overline{D_w}$$

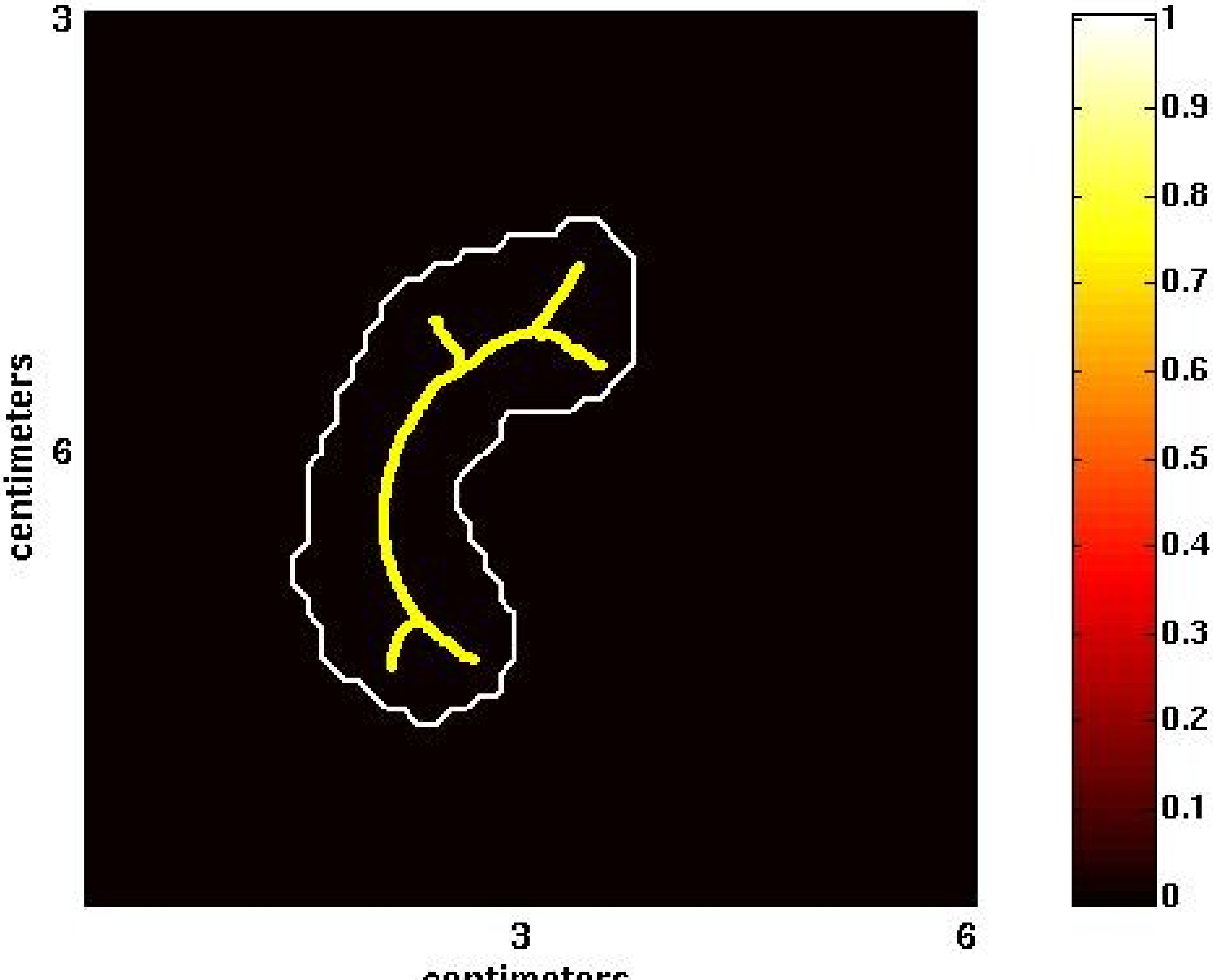
$$\underline{T}\psi_{s,w} \leq t_{s,w} \leq \overline{T}\psi_{s,w}$$

$$\sum_{s\in S, w\in W} \psi_{s,w} \leq N$$

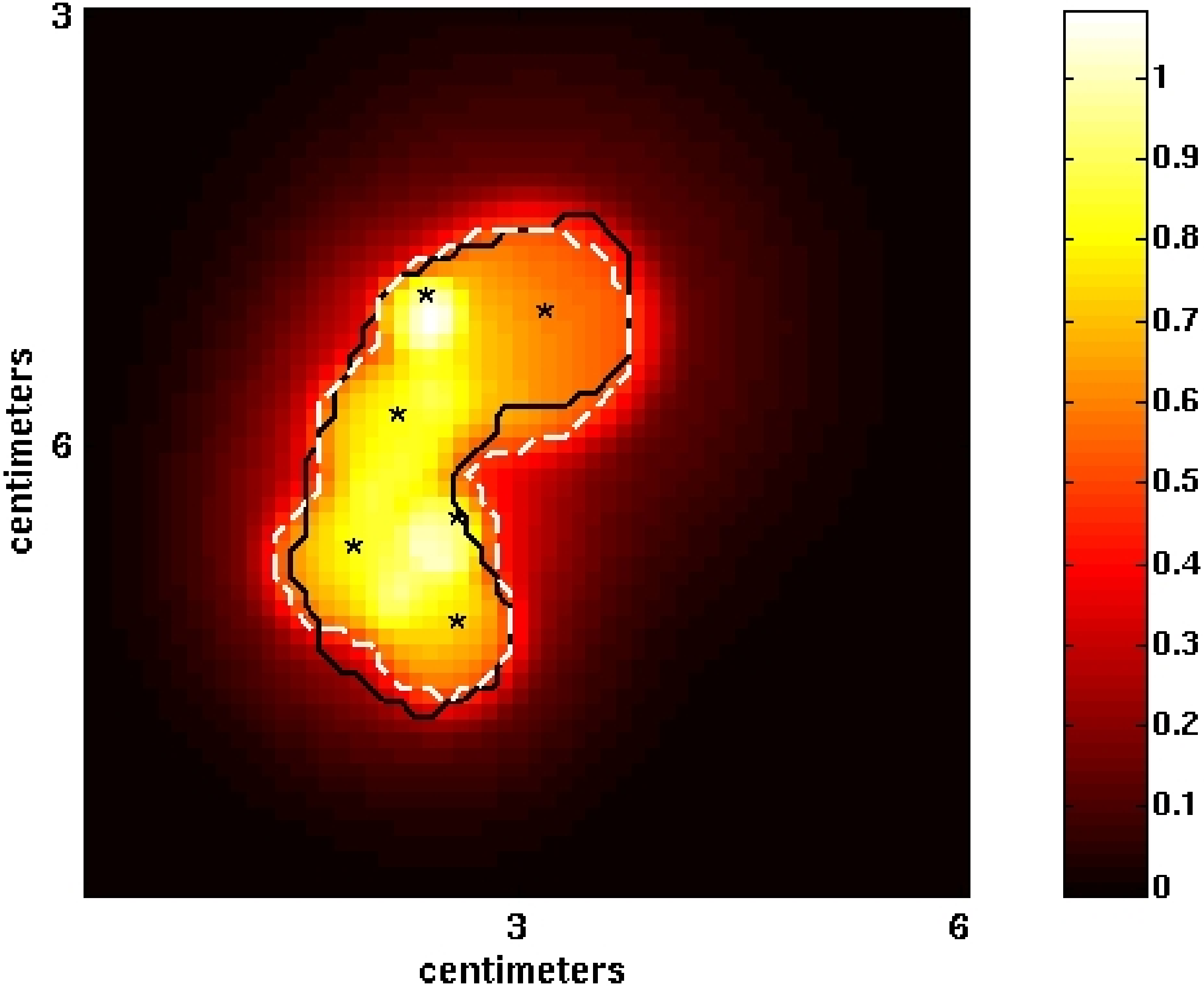
Target



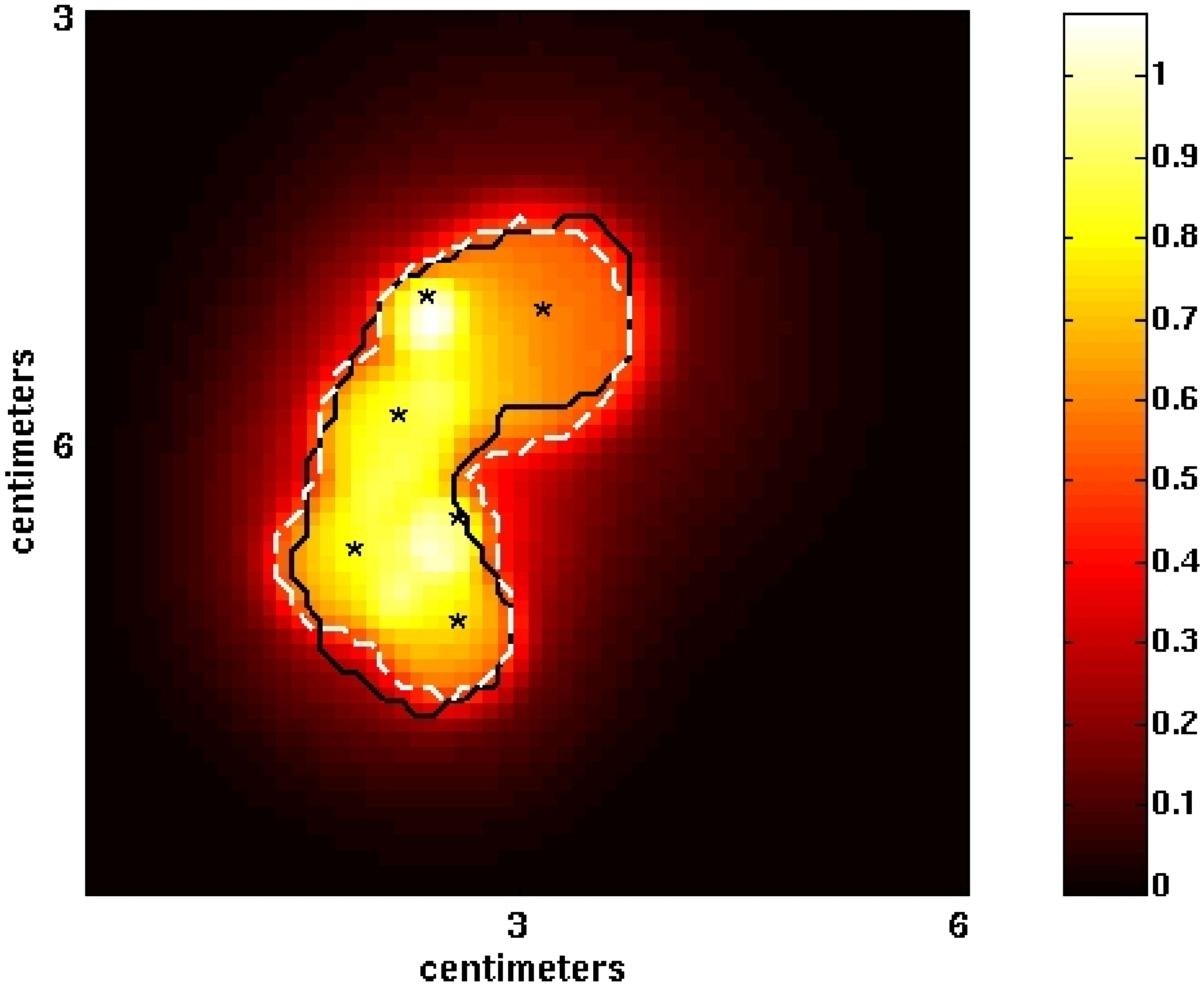
Target Skeleton is Determined



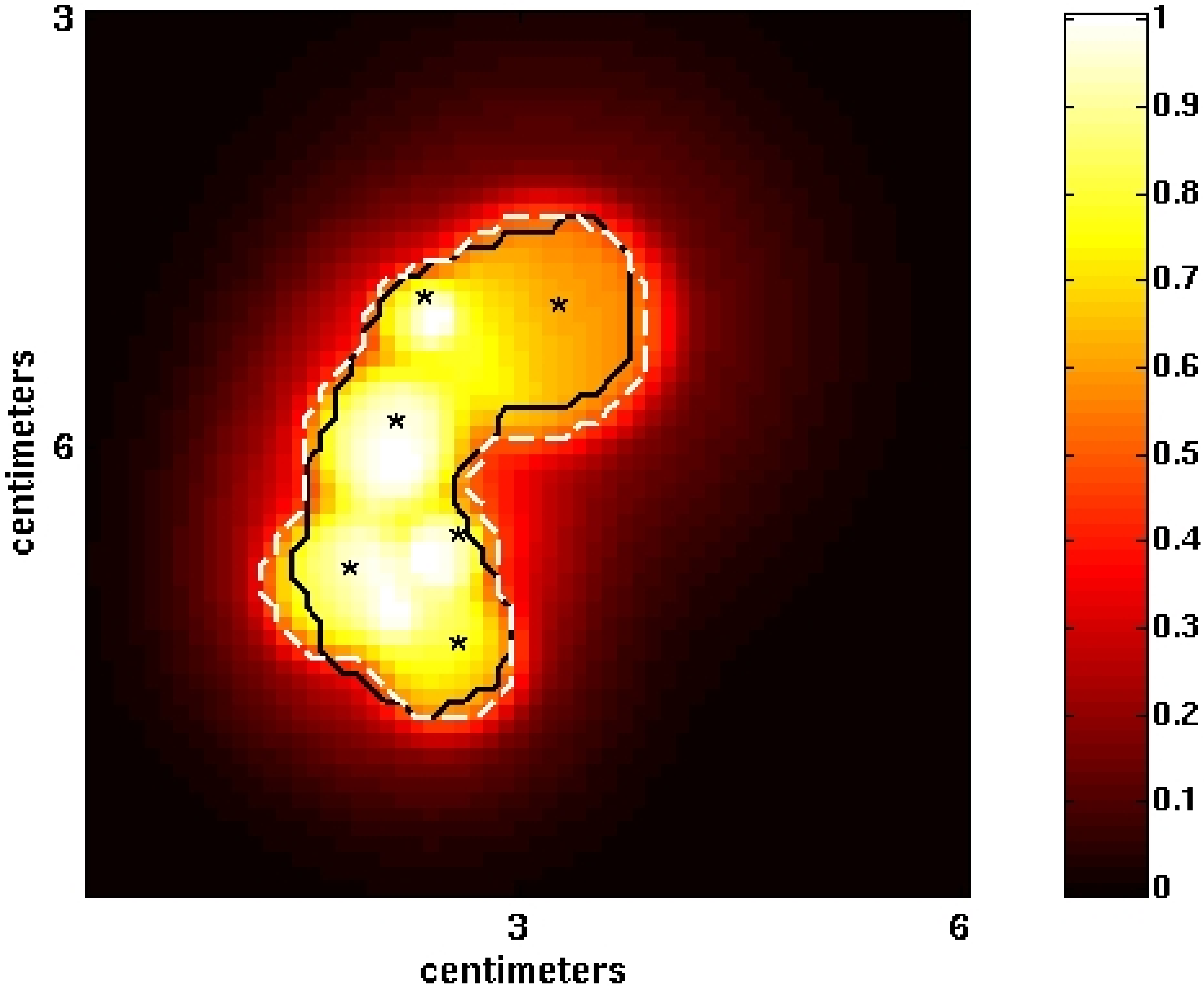
Sphere Packing Result



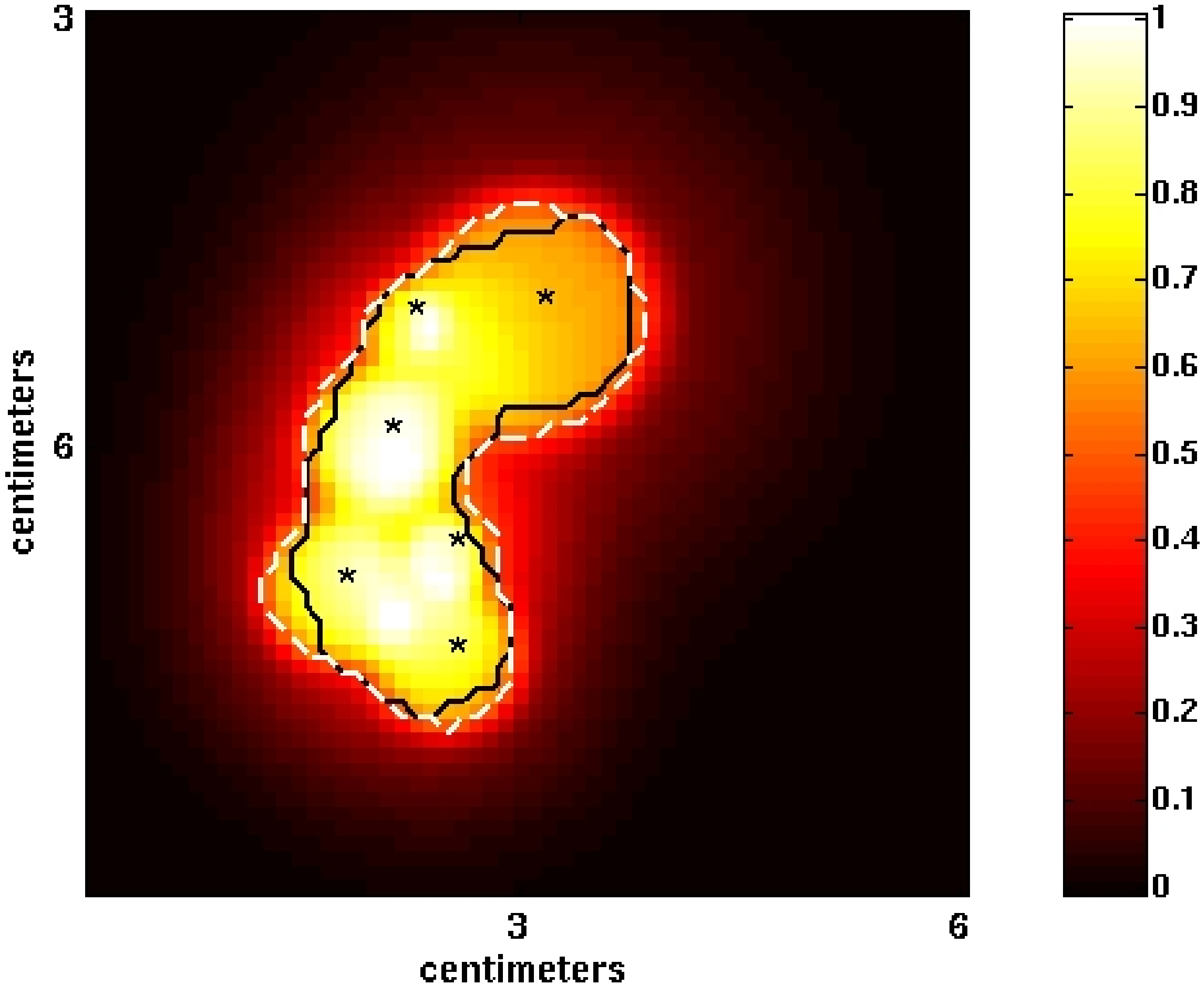
10 Iterations



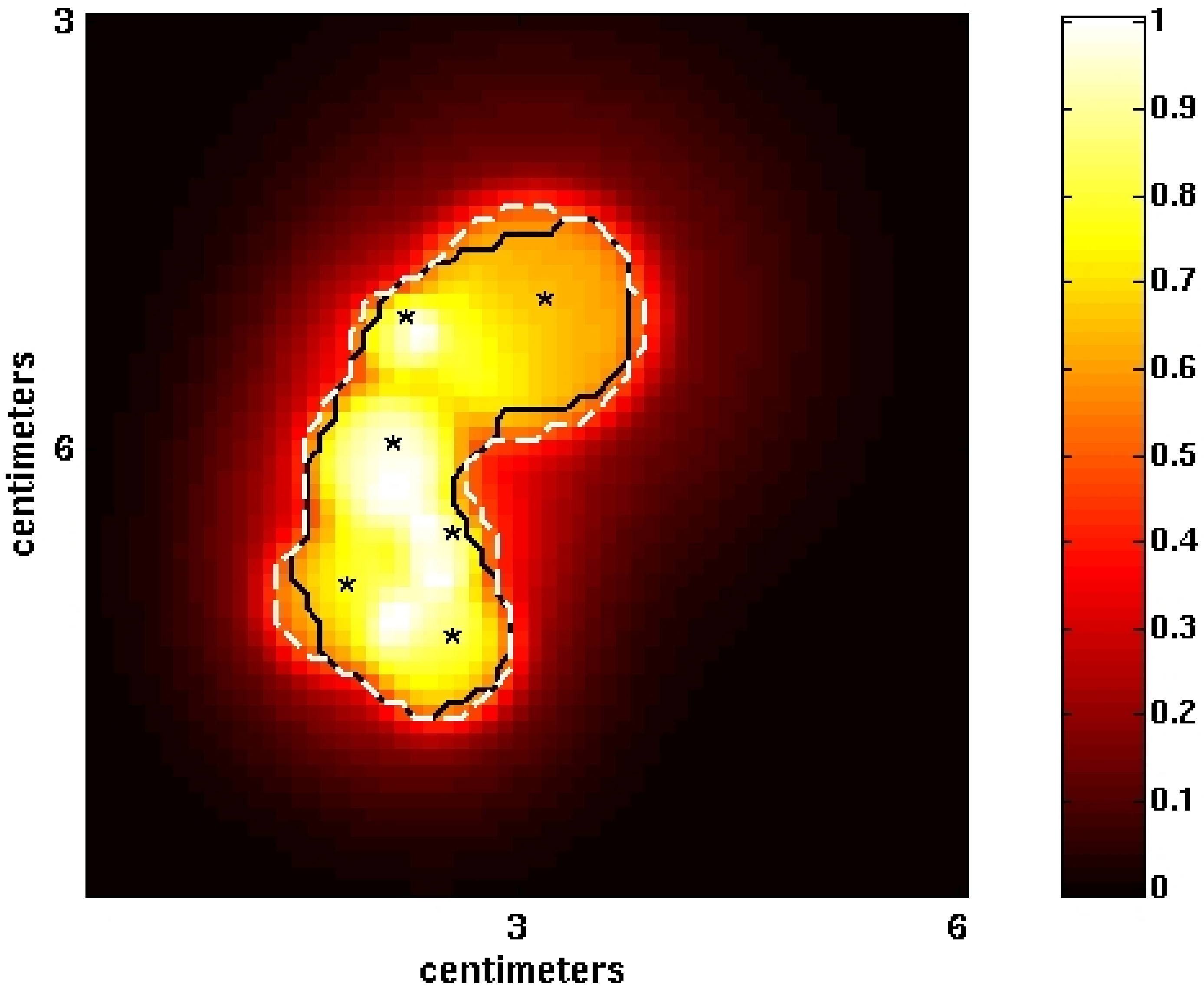
20 Iterations



30 Iterations



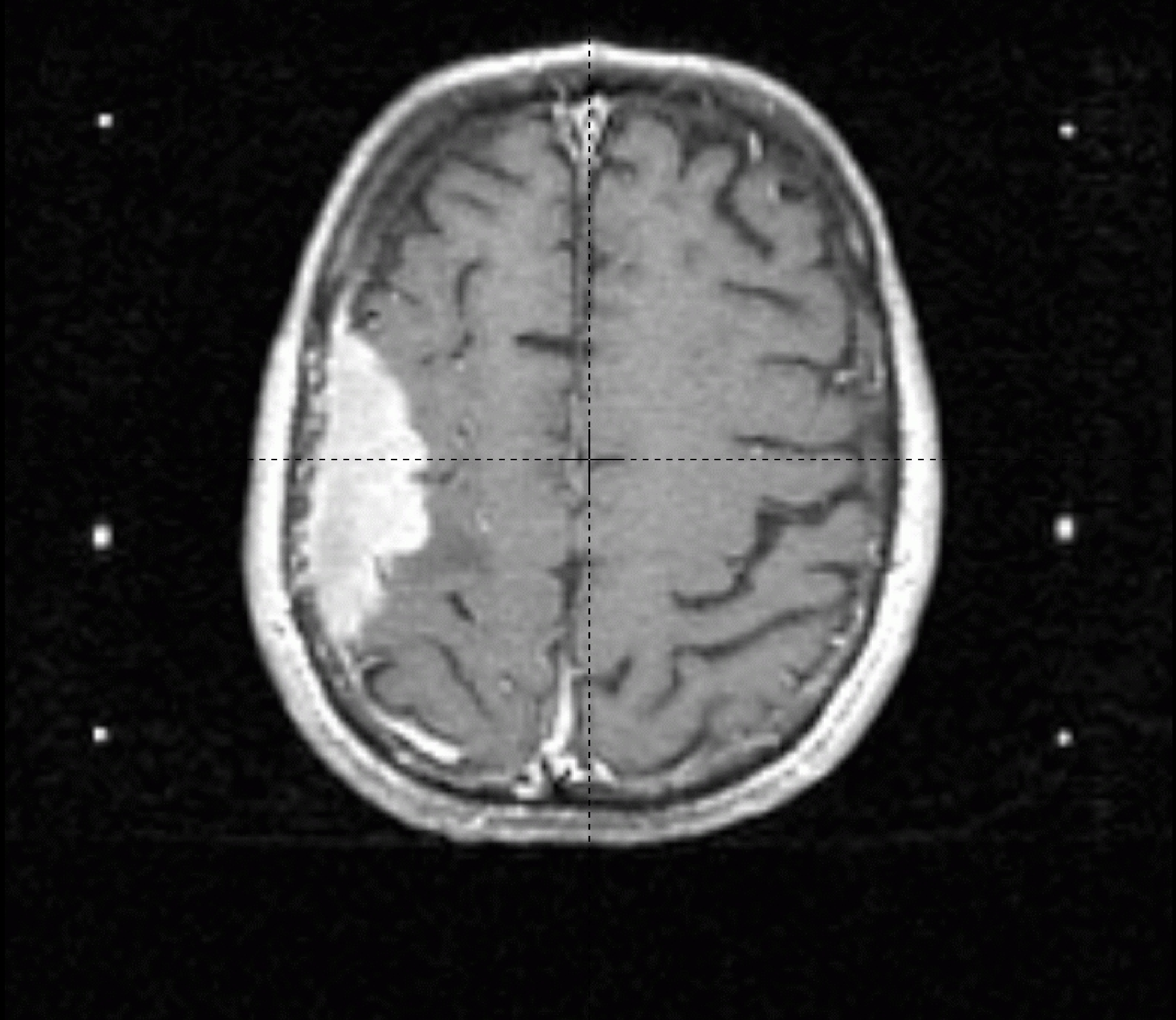
40 Iterations



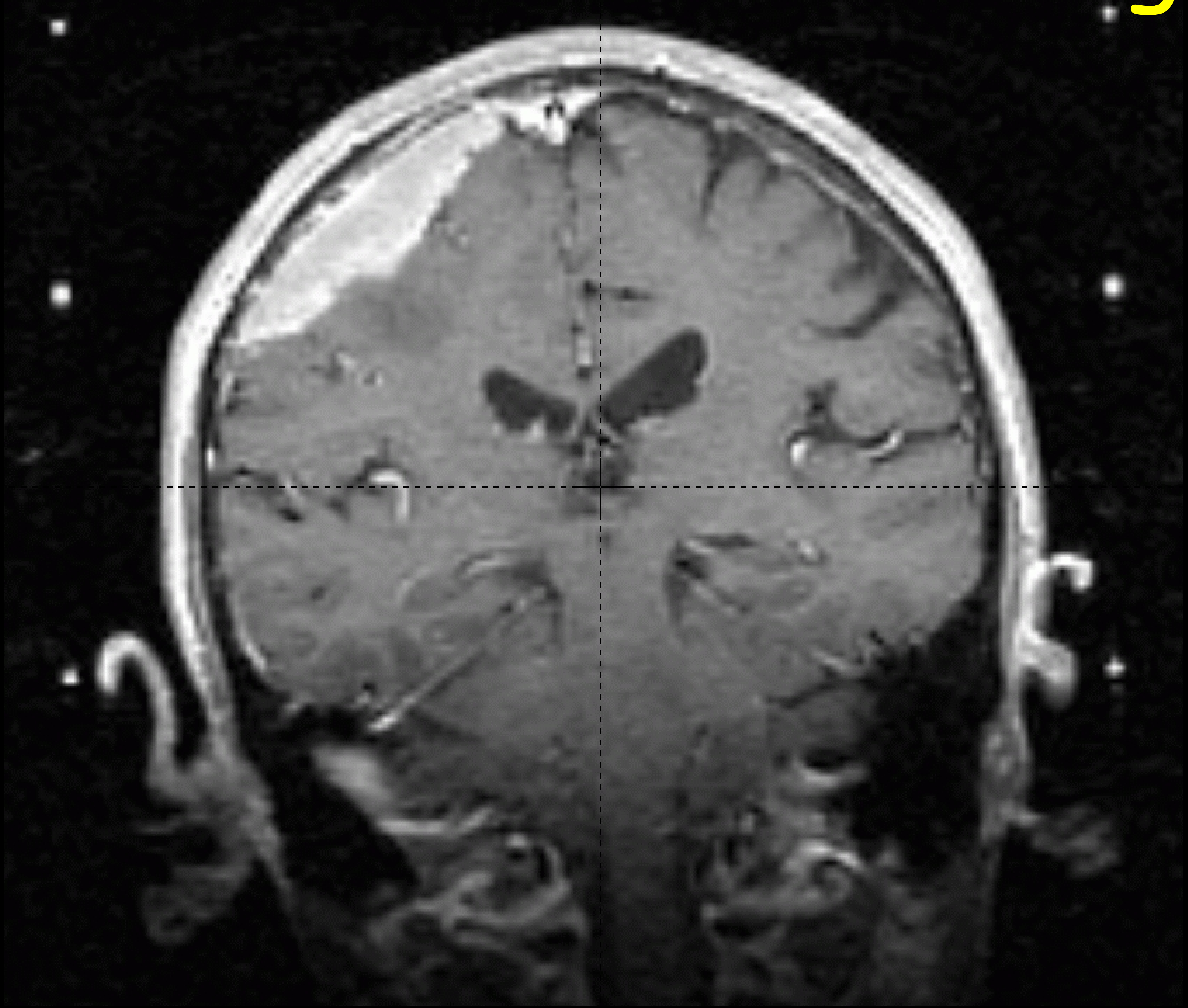
Status

- Automated plans have been generated retrospectively for over 30 patients
- The automated planning system is now being tested/used head to head against the neurosurgeon
- Optimization performs well for targets over a wide range of sizes and shapes

Patient 1 - Axial Image

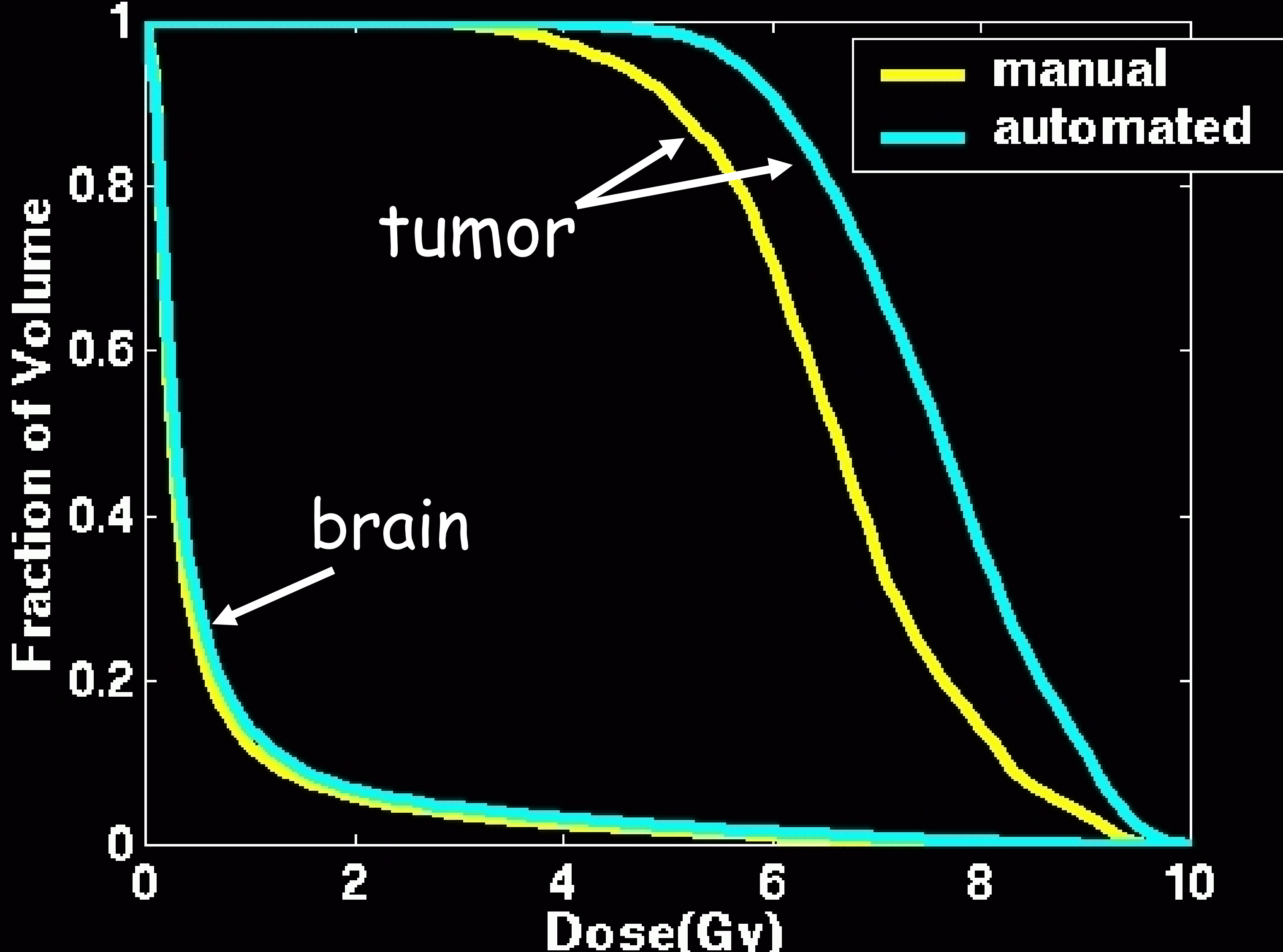


Patient 1 - Coronal Image



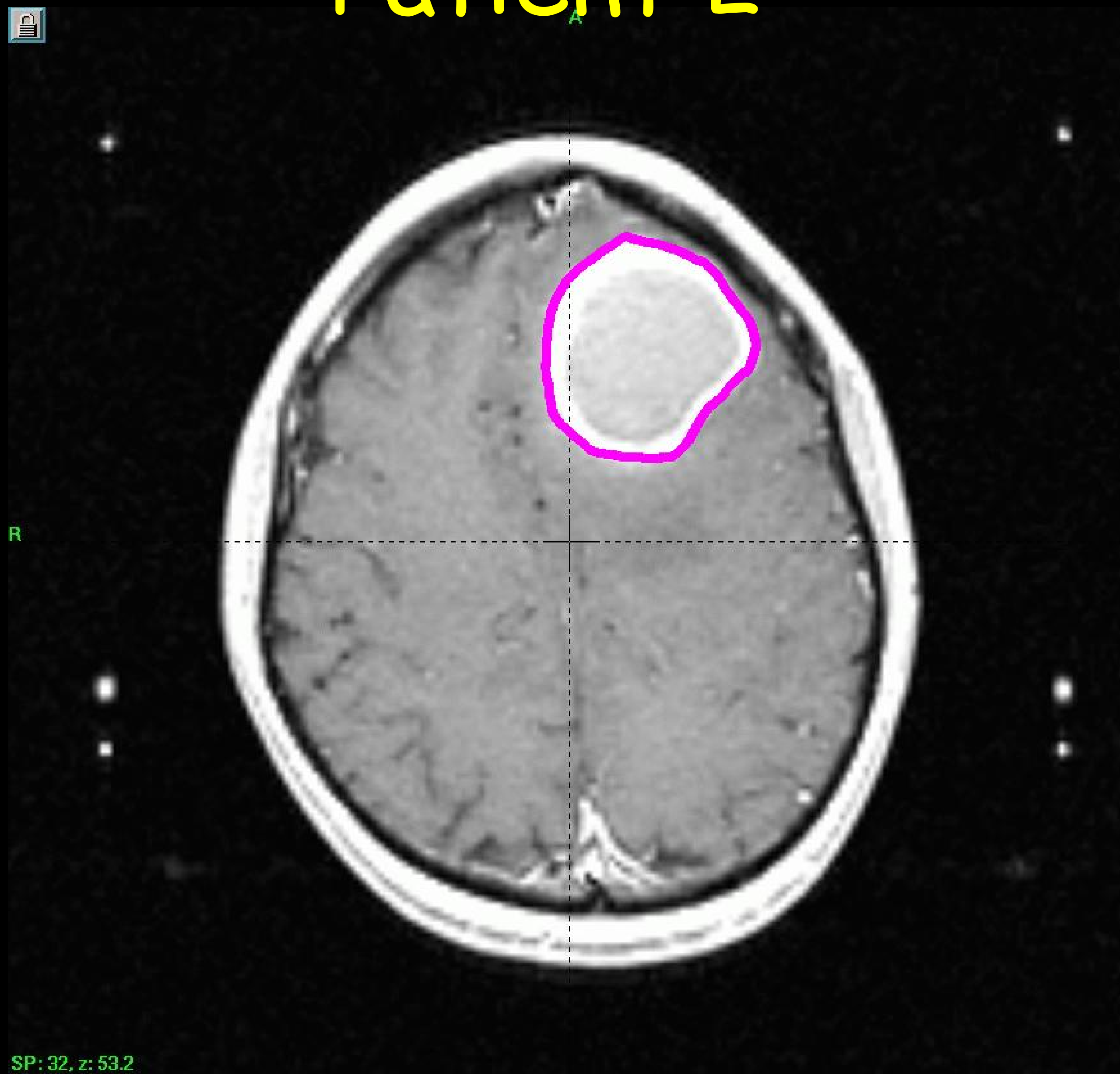
manual

optimized



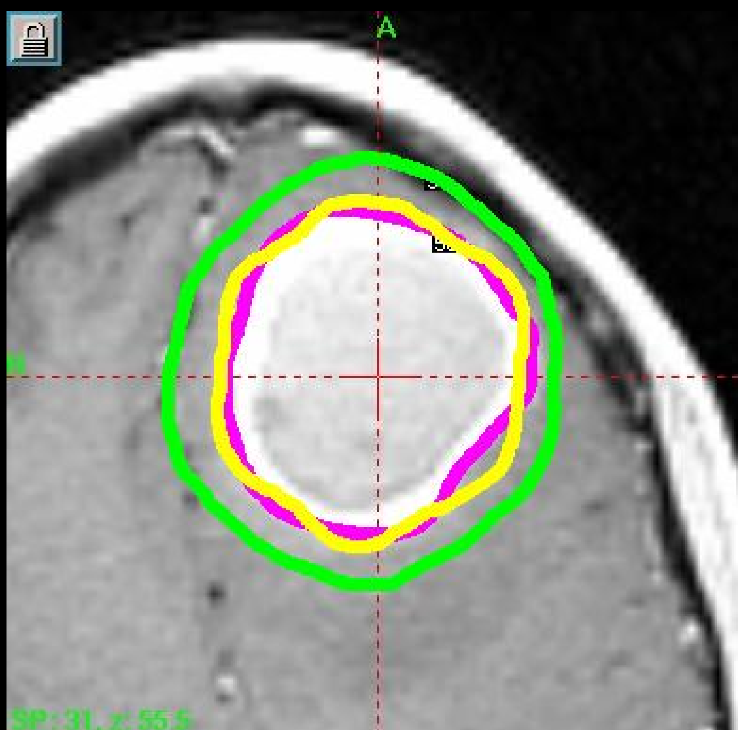
manual
automated
tumor
brain
Fraction of Volume
Dose(Gy)
0
0.2
0.4
0.6
0.8
1
0
2
4
6
8
10

Patient 2

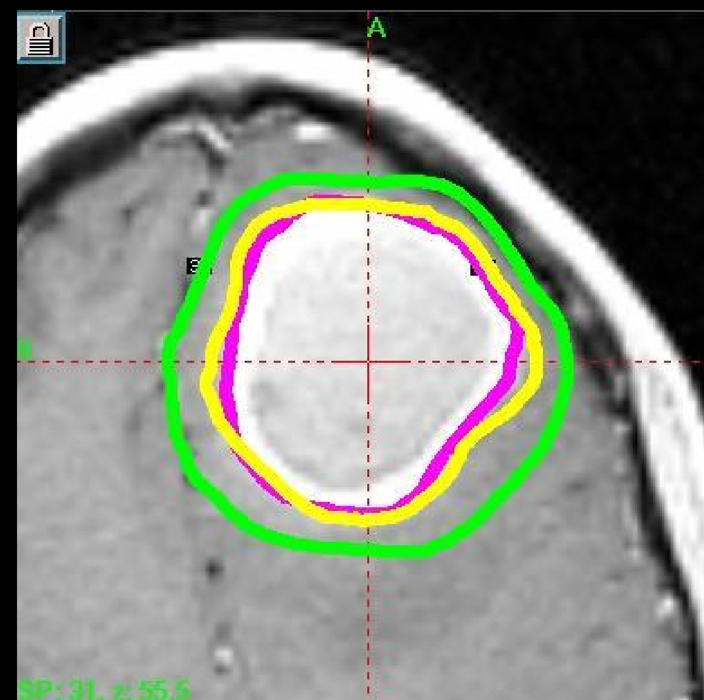


Patient 2 - Axial slice

15 shot manual



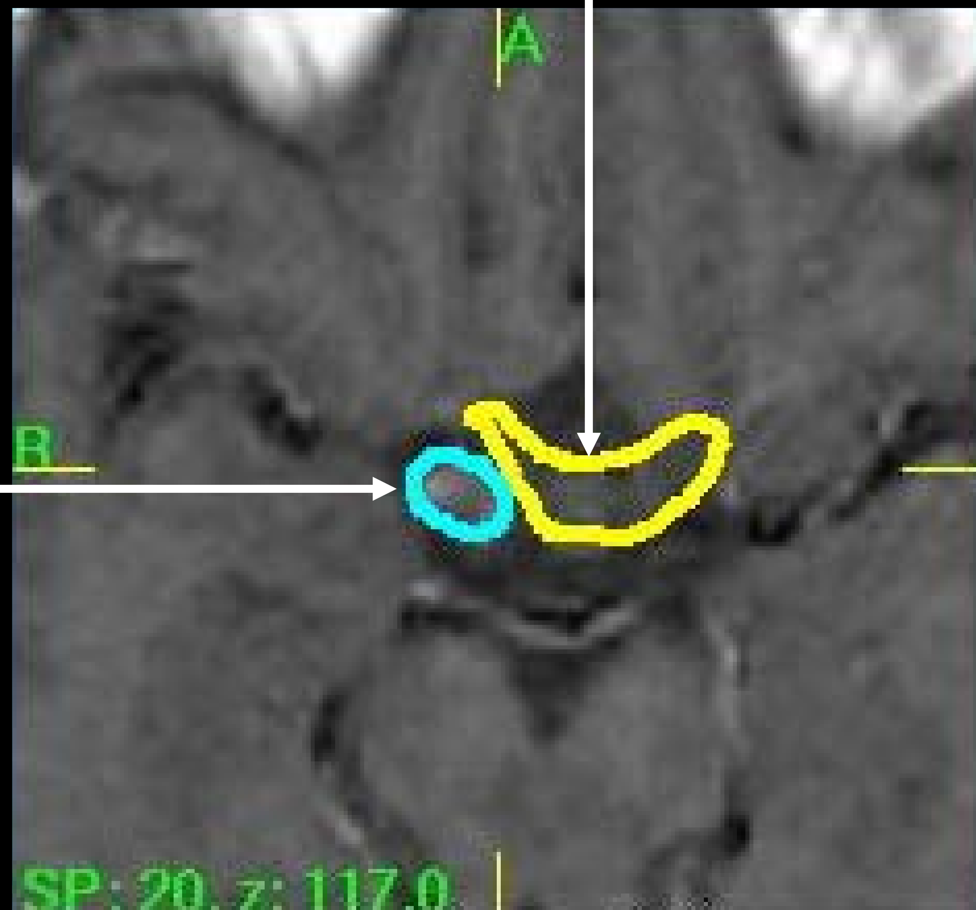
12 shot optimized

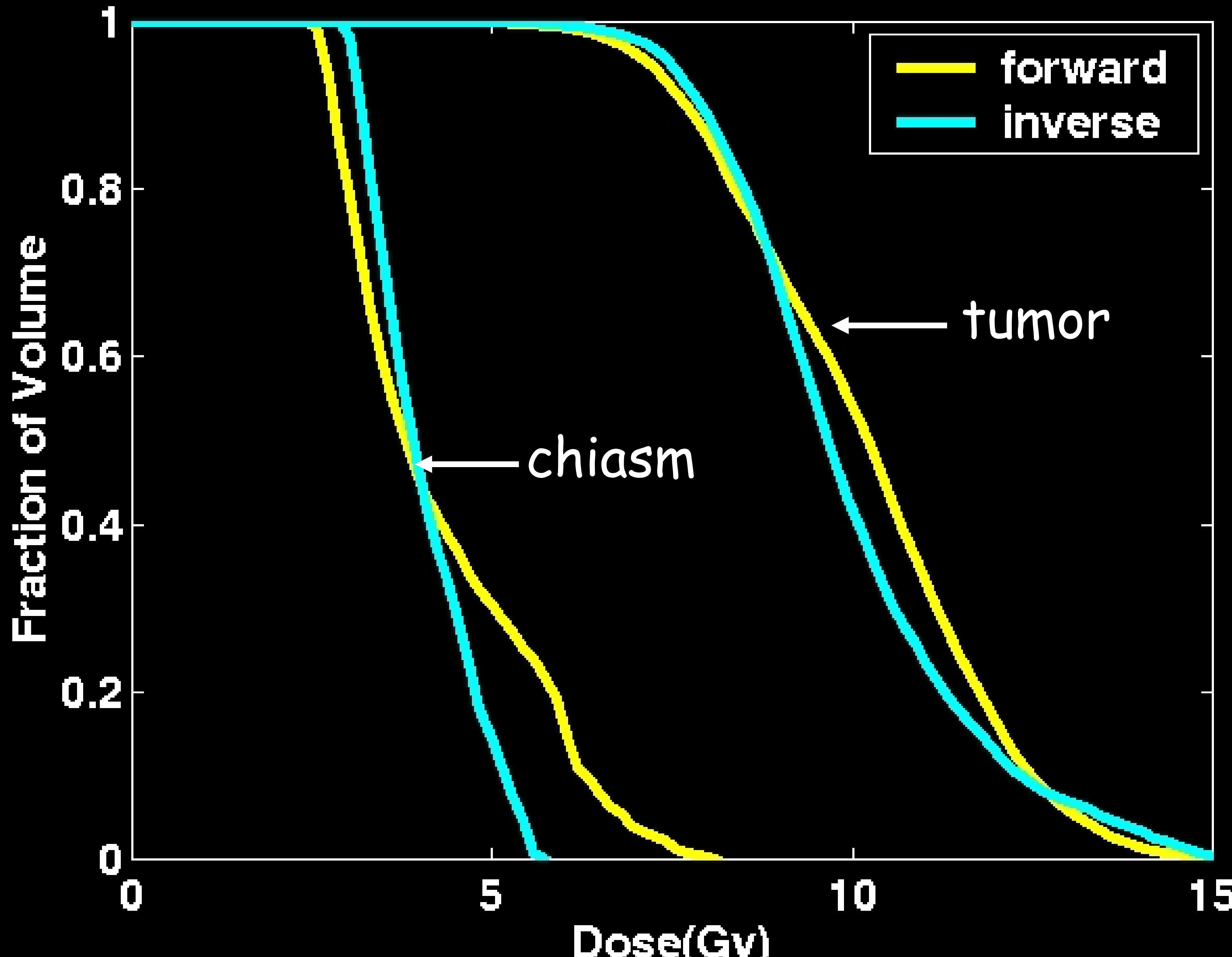


Patient 3

optic chiasm

pituitary adenoma

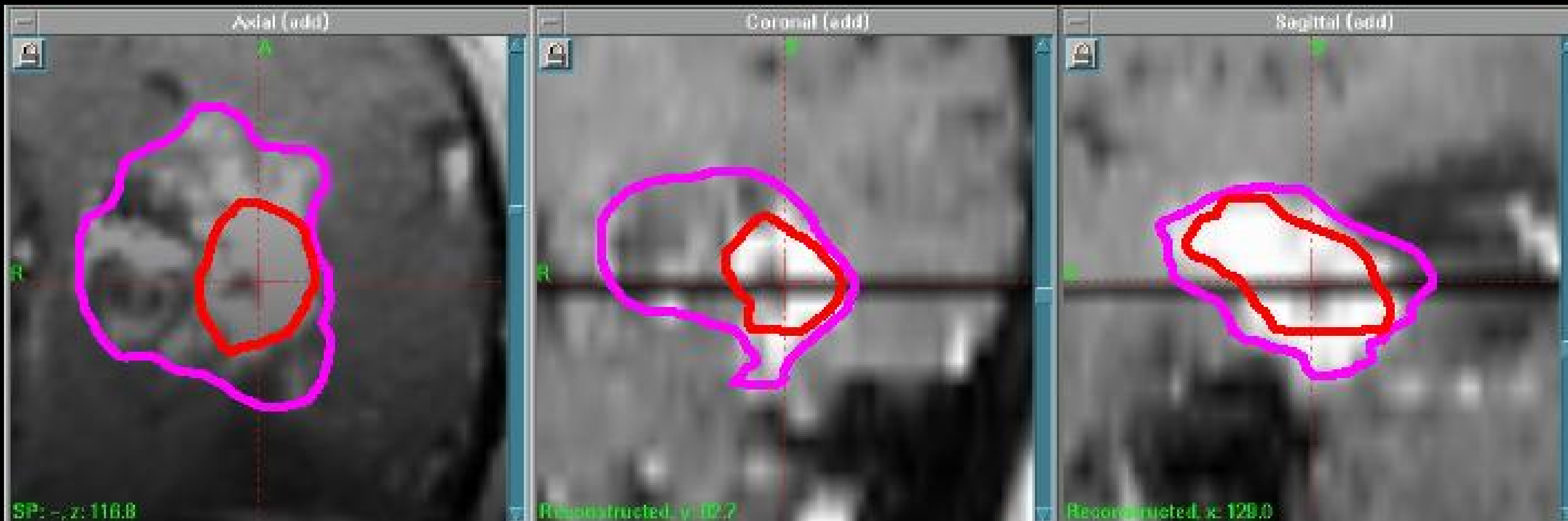


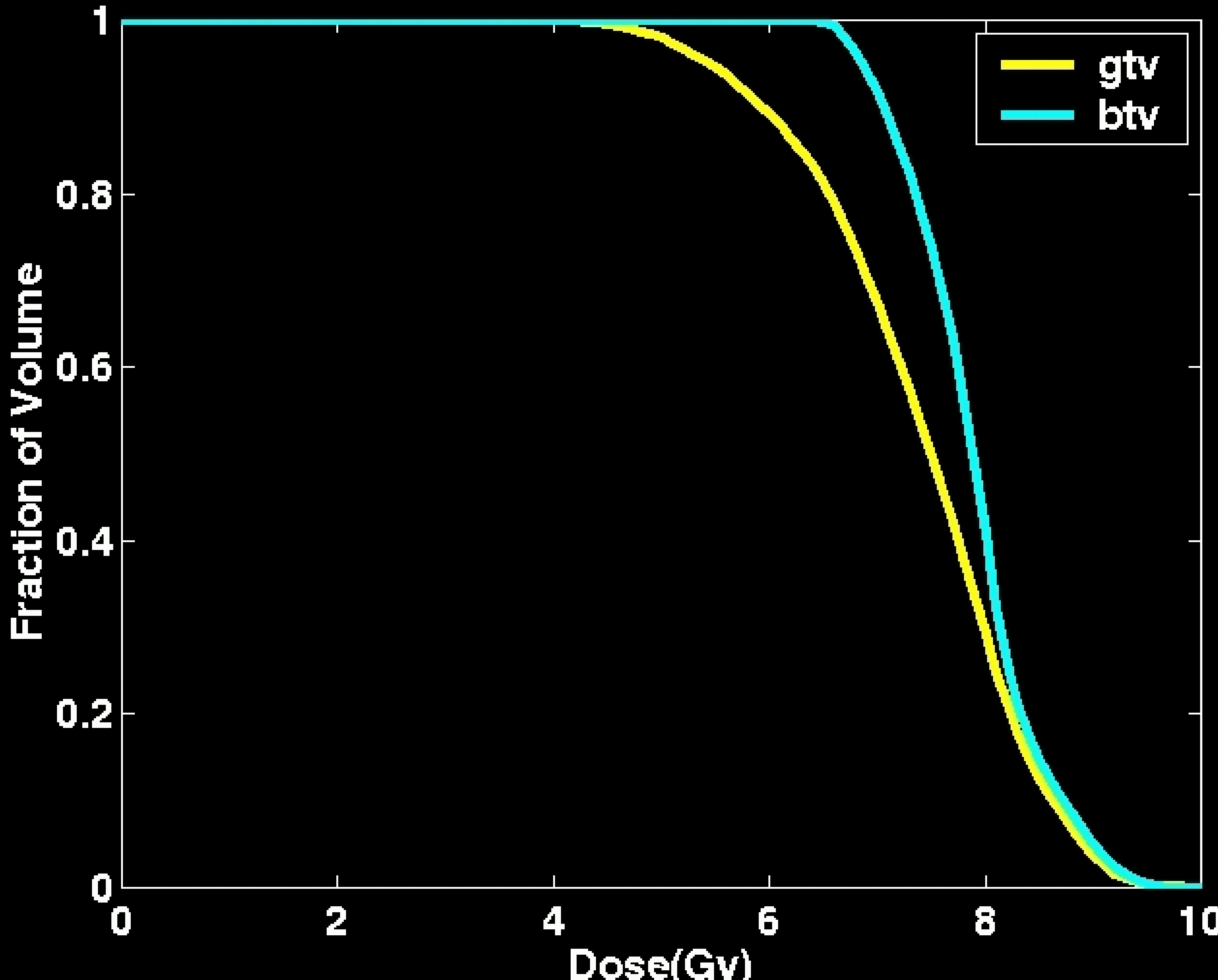

forward
inverse
tumor
chiasm
Fraction of Volume
Dose(Gy)
0
0.2
0.4
0.6
0.8
1
0
5
10
15

Localized Dose Escalation

- The dose to the active tumor volume or nodular islands can be selectively escalated while maintaining an acceptable normal tissue dose.
- Applicable to tumors such as cystic astrocytoma or glioblastoma multiforme that are nodular and permeative in nature

Localized Dose Escalation





gtv
btv
Fraction of Volume
Dose(Gy)
0
0.2
0.4
0.6
0.8
1
0
2
4
6
8
10

DSS: Estimate number of shots

- Motivation:
  - Starting point generation determines reasonable target volume coverage based on target shape
  - Use this procedure to estimate the number of shots for the treatment
- Example,
  - Input:
    - number of different helmet sizes = 2;
    - (4mm, 8mm, 14mm, and 18mm) shot sizes available
  - Output:

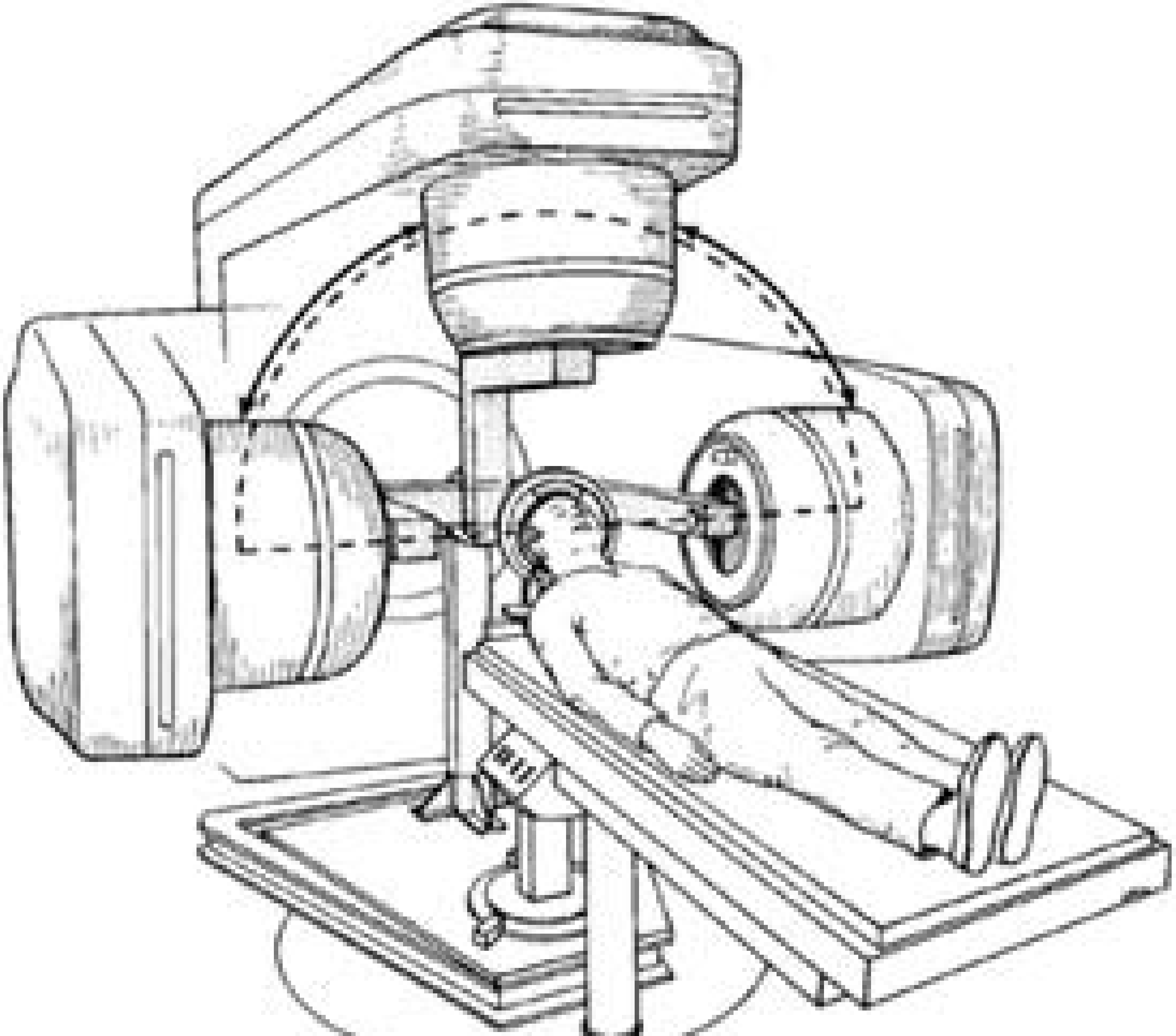
Helmet size(mm)	4 & 8	4 & 14	4 & 18	8 & 14	8 & 18	14 & 18
# shots estimated	25	10	9	7	7	7

Optimization as Knowledge Gathering

- Single problem, build model using sequence of optimization problems
- Many examples in literature
- Switch between different problem formats – LP, MIP, NLP
- Modeling system enables quick prototyping

Conclusions

- Problems solved by models built with multiple optimization solutions
- Constrained nonlinear programming effective tool for model building
- Interplay between OR and MedPhys crucial in generating clinical tool
- Gamma Knife: optimization compromises enable real-time implementation



Linac Based Radiosurgery

- Advantages
  - Cost/space
- Disadvantages
  - Machine time
  - Extensive QA procedures
  - Reliability issues

Linac model

$$\min_{t_{a,c},x^a} Dose(NonTarget)$$

subject to

$$Dose(i) = \sum_{a \in A, c \in C} t_{a,c} D_c(a, x^a, i)$$

$$0.5 \leq Dose(Target) \leq 1$$

$$t_{a,c} \geq 0$$

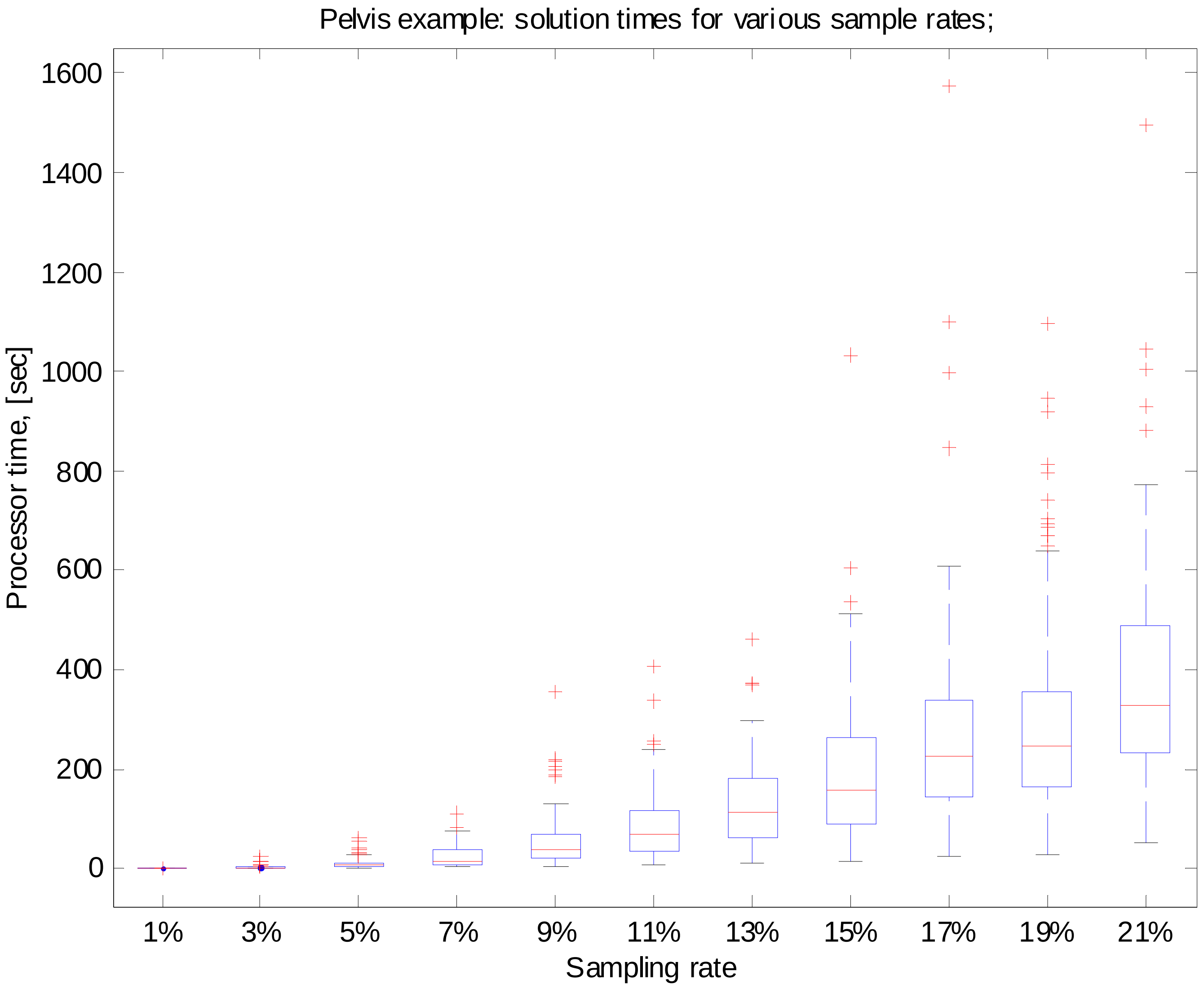
$$|A| \leq N$$

$$x^a \in W$$

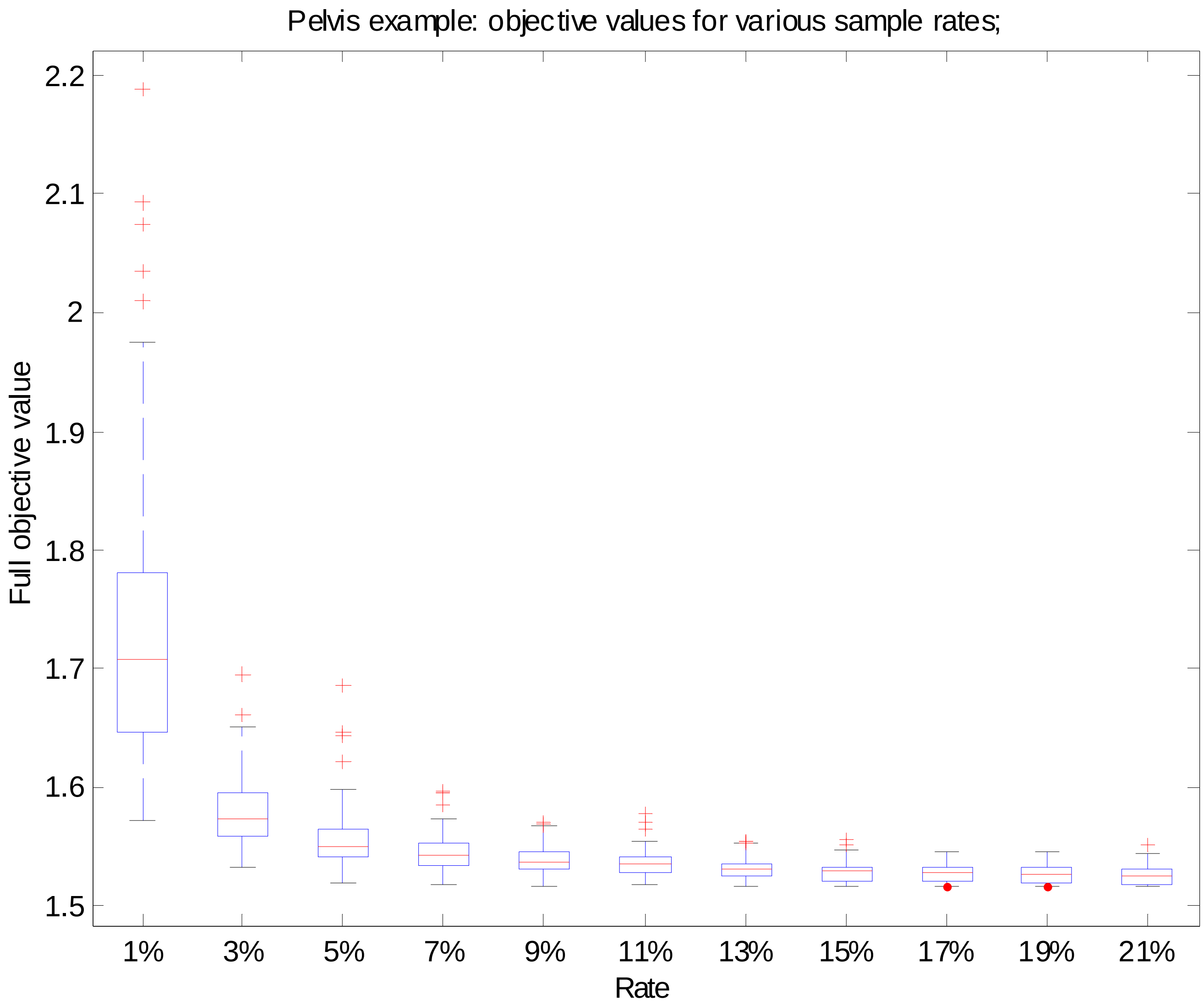
Problems

- Large computational times
- Large variance in computing times
  - 5000-12500 sec (for 60,000 voxel case)
- Ineffective restarts (what if trials?)
- Large amounts of data

- Try sampling of voxels (carefully)


Pelvis example: solution times for various sample rates;
Processor time, [sec]
1600
1400
1200
1000
800
600
400
200
0
1%
3%
5%
7%
9%
11%
13%
15%
17%
19%
21%
Sampling rate

Naïve sampling fails

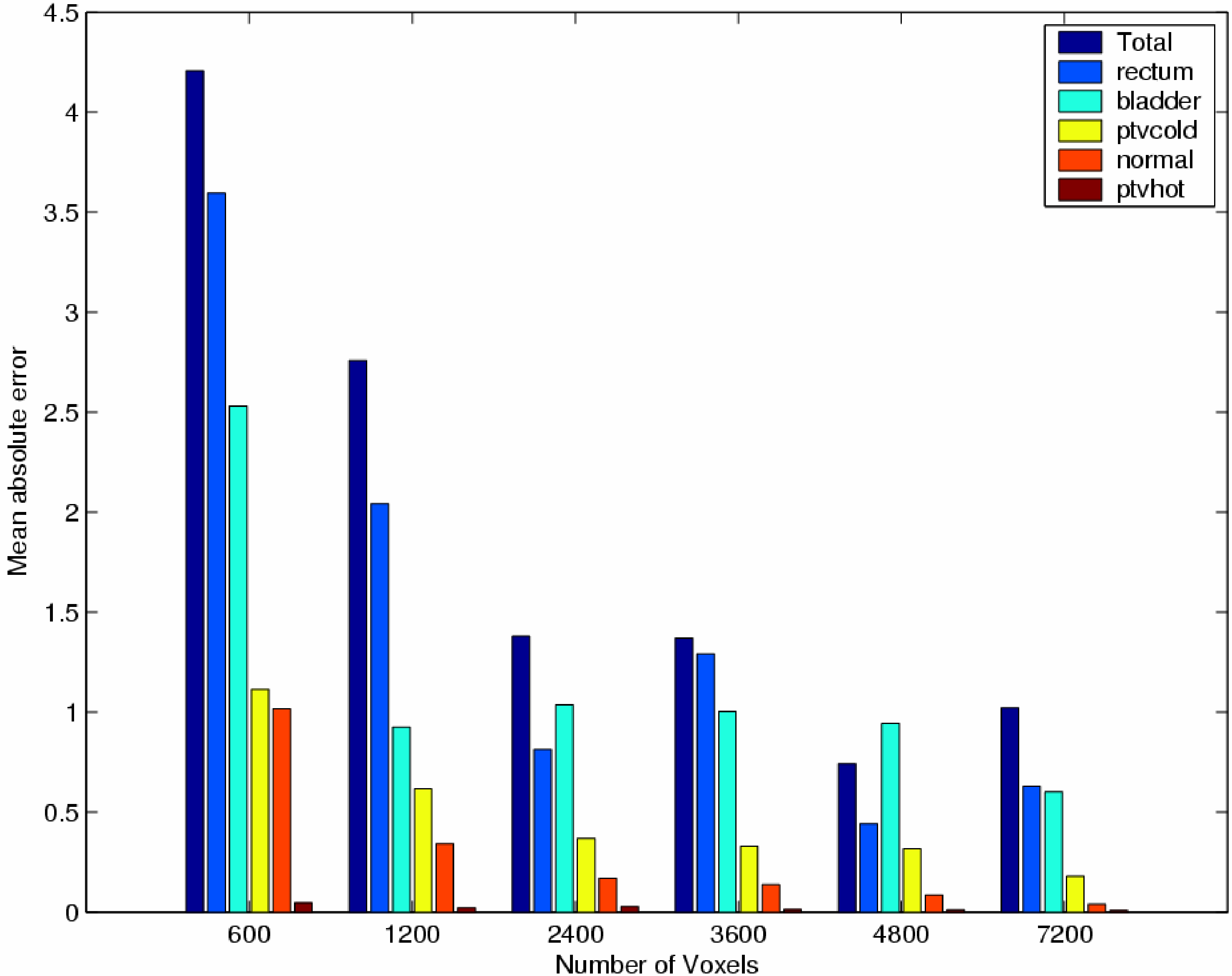


Multiple samples

- Generate K instances at very coarse sampling rate
- Use histogram information to suggest promising angles
- How many? (e.g. K=10)
- How to select promising angles? (frequency > 20%)

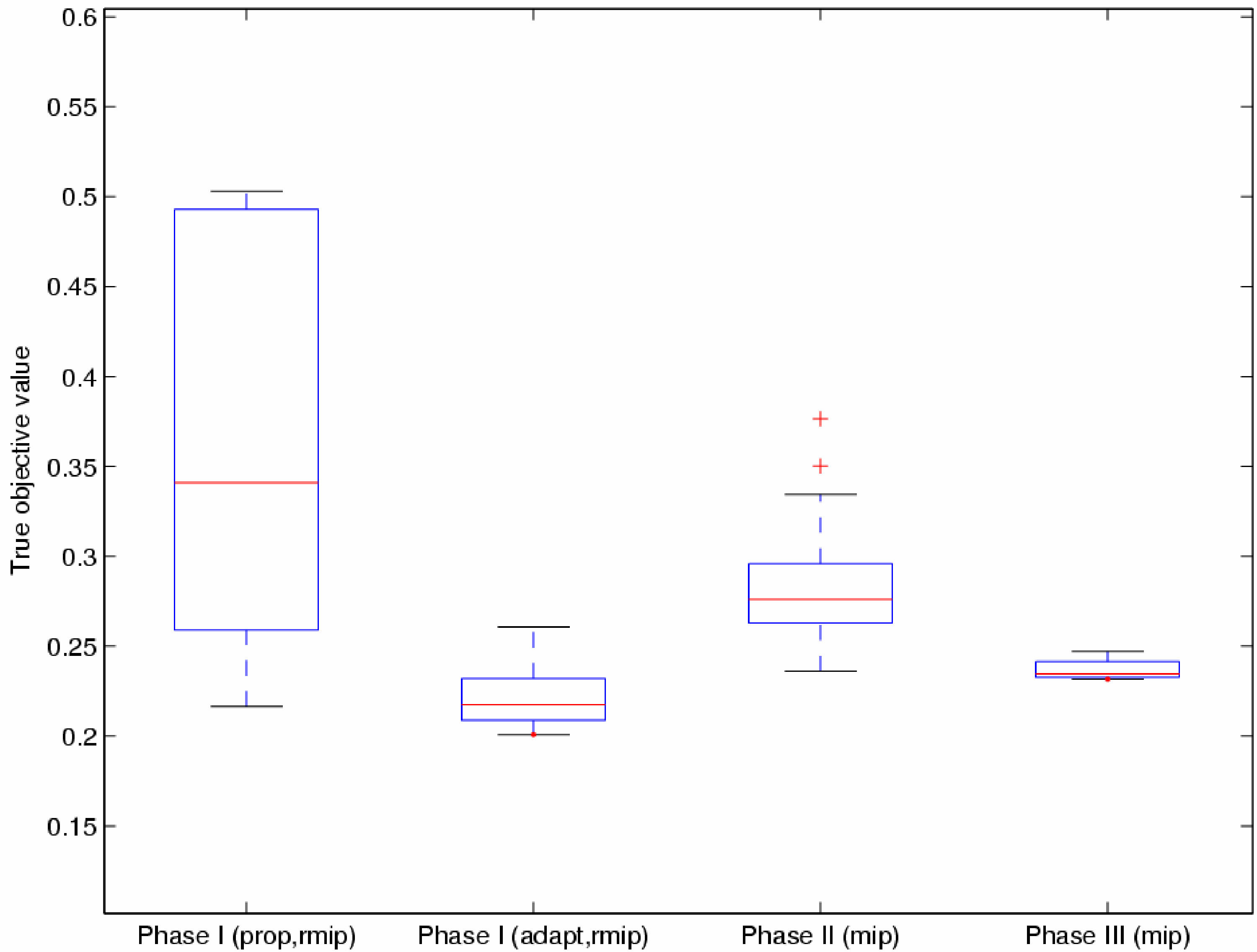
True Objective Value

- >20% scheme may lose best solution
- Can calculate the objective function with complete sample cheaply from solution of sampled problem
- Use extra information in 2 ways:
  1. Select only those angles that appear in the best "full value" solutions
  2. Refine samples in organs where discrepancies are greatest


Total
rectum
bladder
ptvcold
normal
ptvhot
Mean absolute error
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
600
1200
2400
3600
4800
7200
Number of Voxels

Sampling Process

- Determine initial sample size
- Phase I: use all angles
  - 10 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 reduced set
  - Increase sample rate, solve single MIP


0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
True objective value
Phase I (prop,rmip)
Phase I (adapt,rmip)
Phase II (mip)
Phase III (mip)

Conclusions

- Optimization improves treatment planning
- Adaptive sampling is effective tool for solution time reduction
- Future work needed for more complex delivery devices and for adaptive radiotherapy