Optimization of Gamma Knife Radiosurgery and Beyond

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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

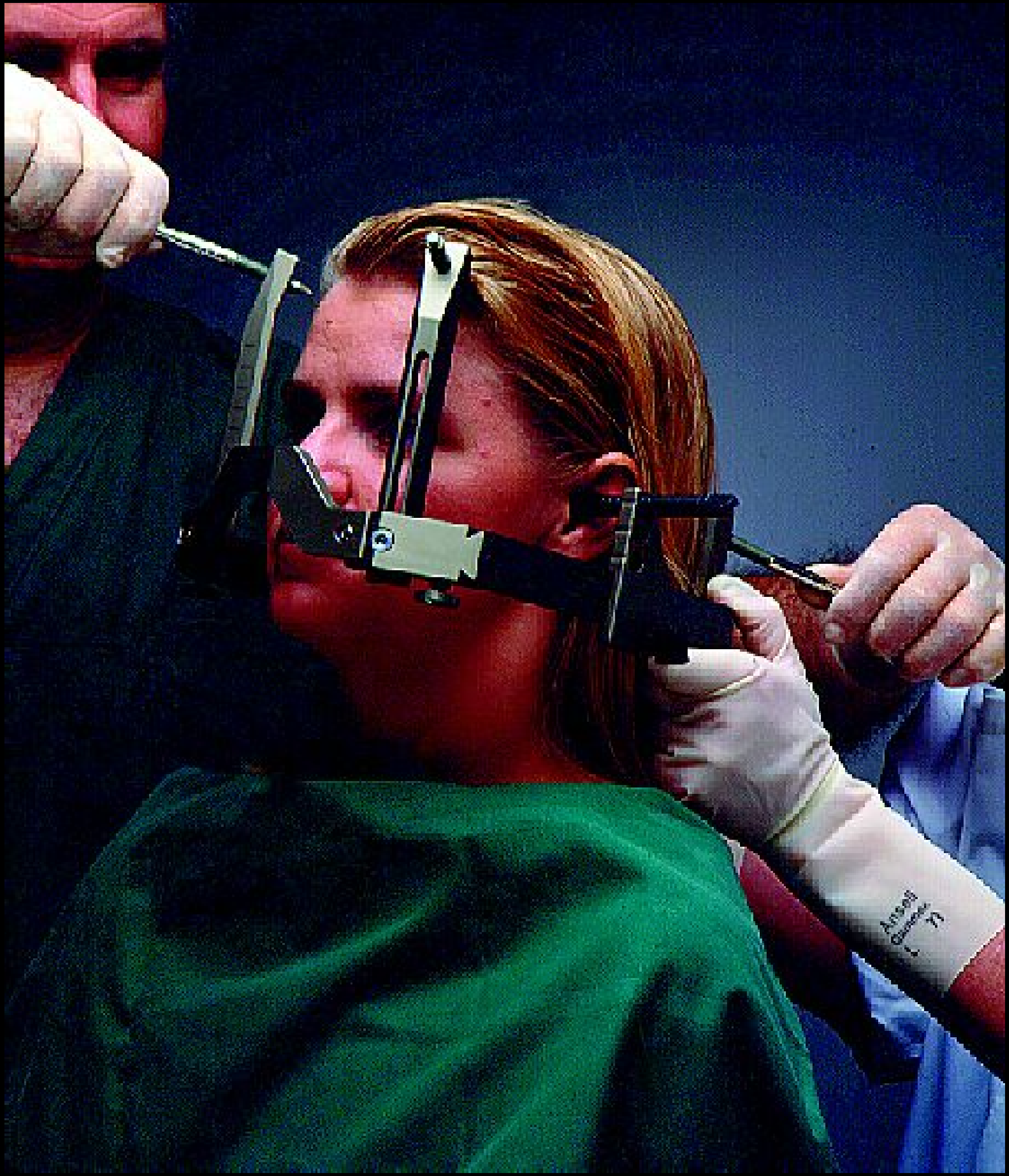
Stereotactic radiosurgery?

- Stereotactic - orginated from the Greek words stereo meaning three dimensional and tactus 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!)

The Gamma Knife

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

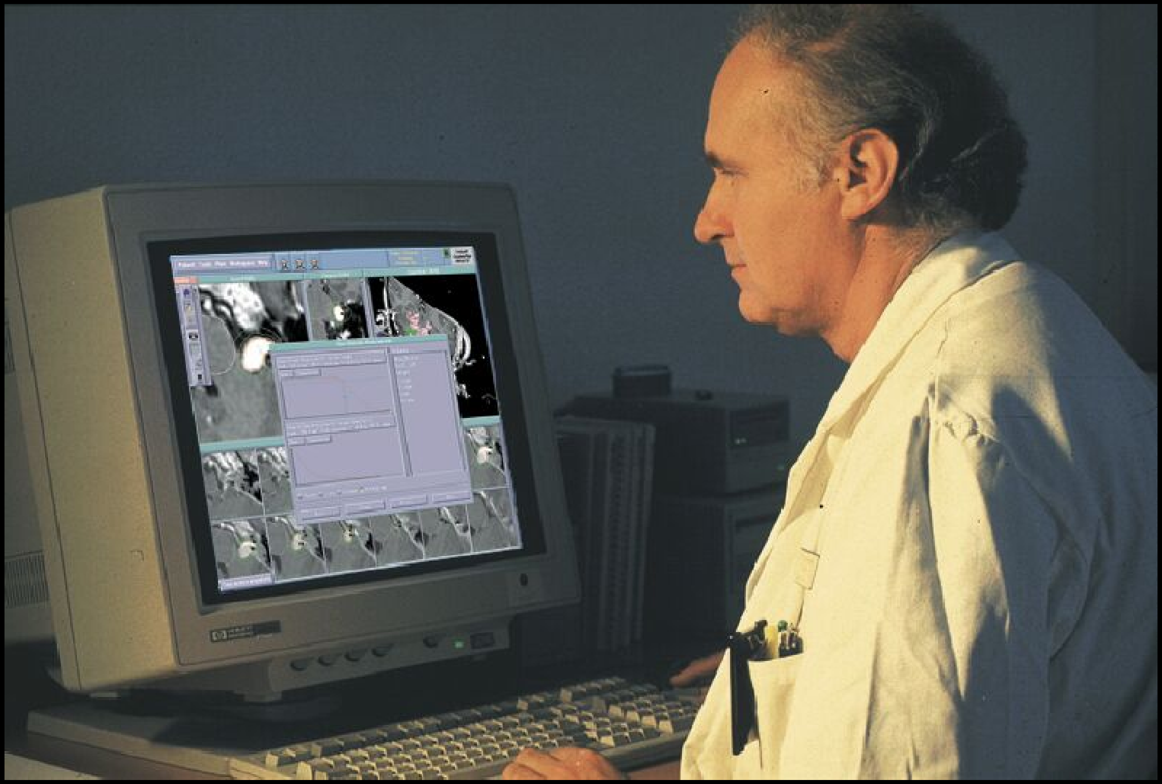
The patient’s head is positioned within the Gamma Knife so that the tumor is in the focal point of the gamma rays.



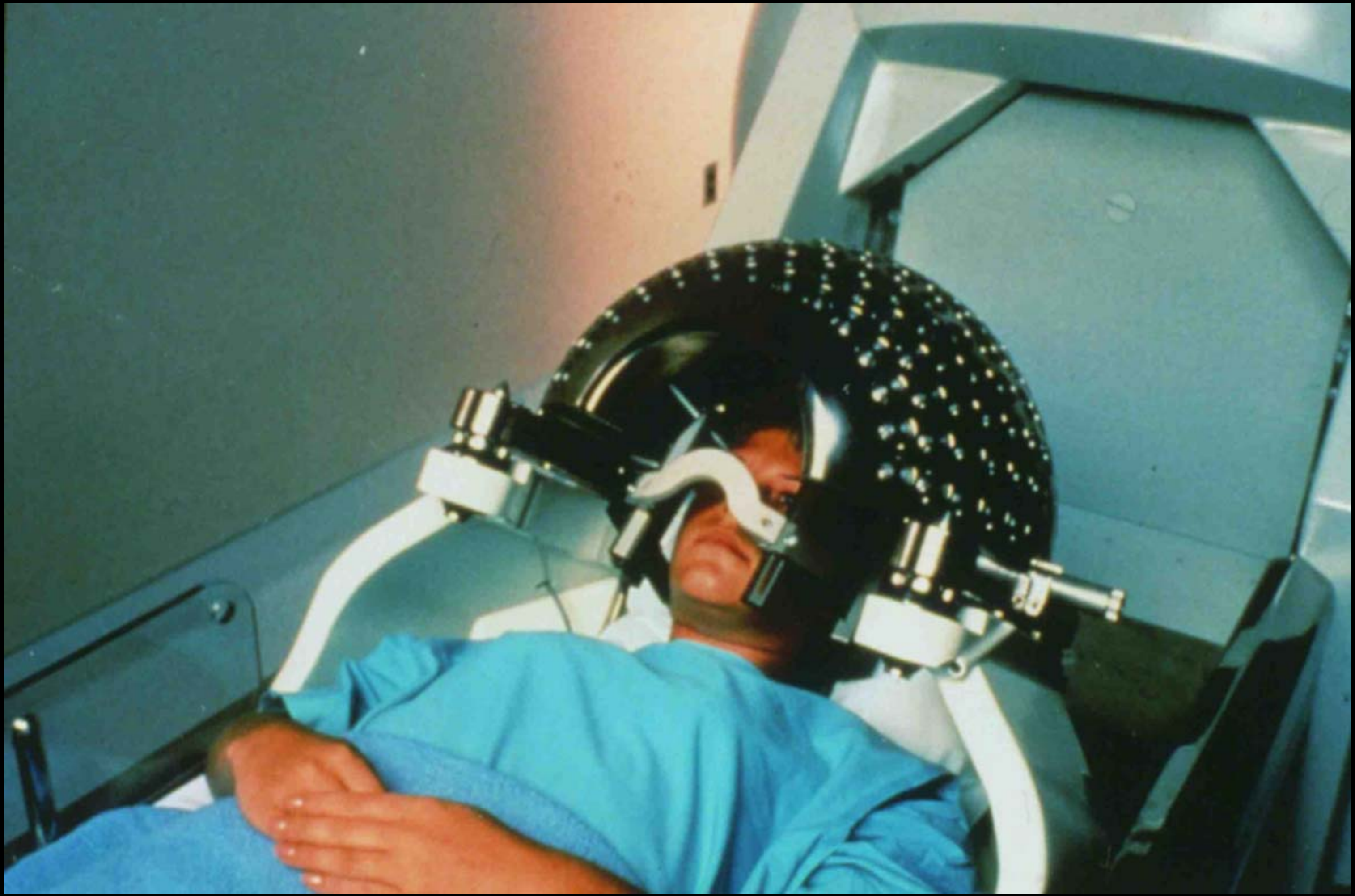
How is Gamma Knife Surgery performed?

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

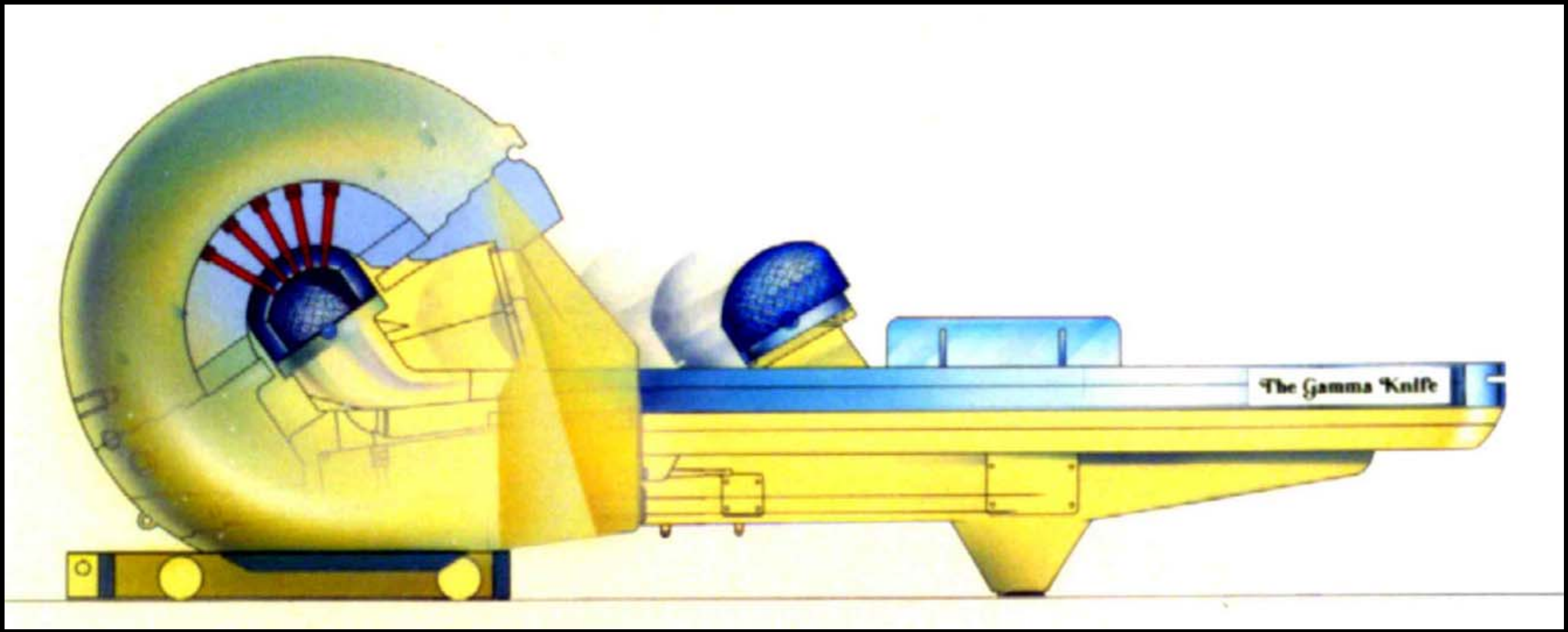
Step 2: The head is imaged using a MRI or CT scanner while the patient wears the stereotactic frame.



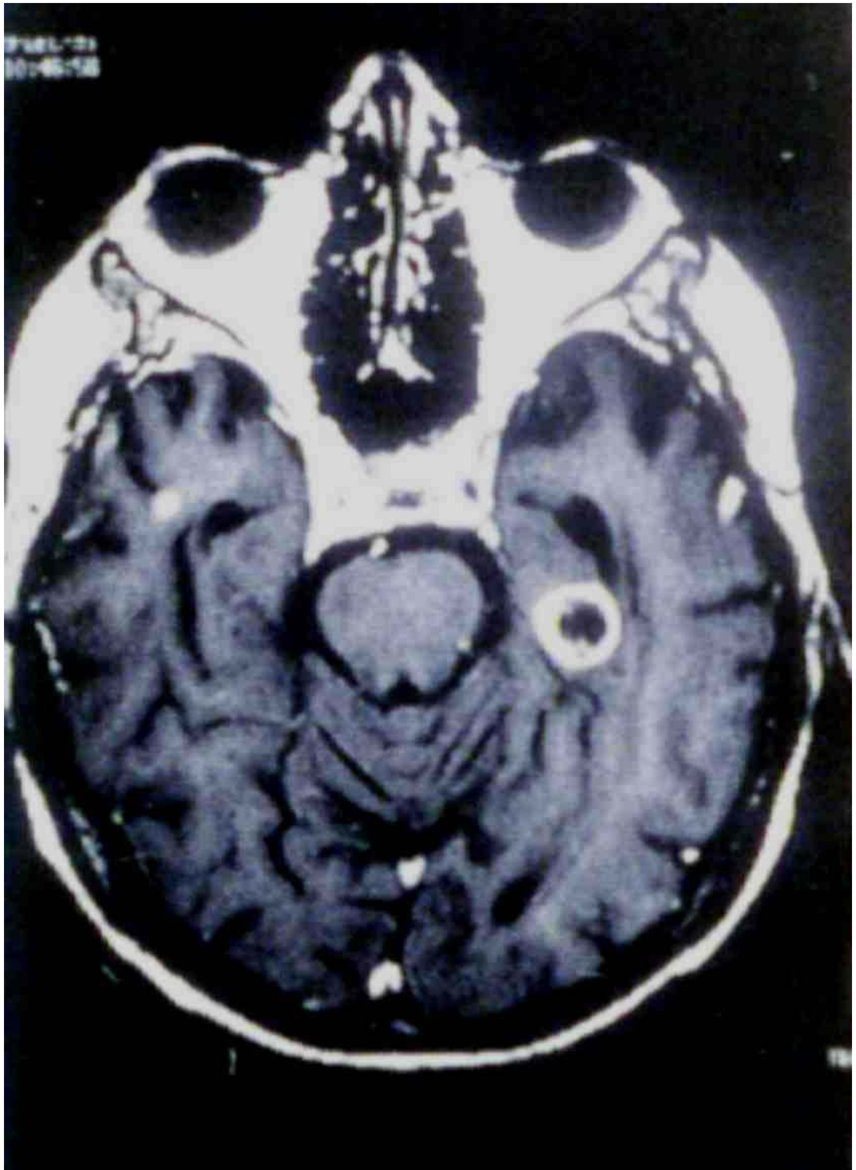
Step 3: A treatment plan is developed using the images. Key point: very accurate delivery possible.

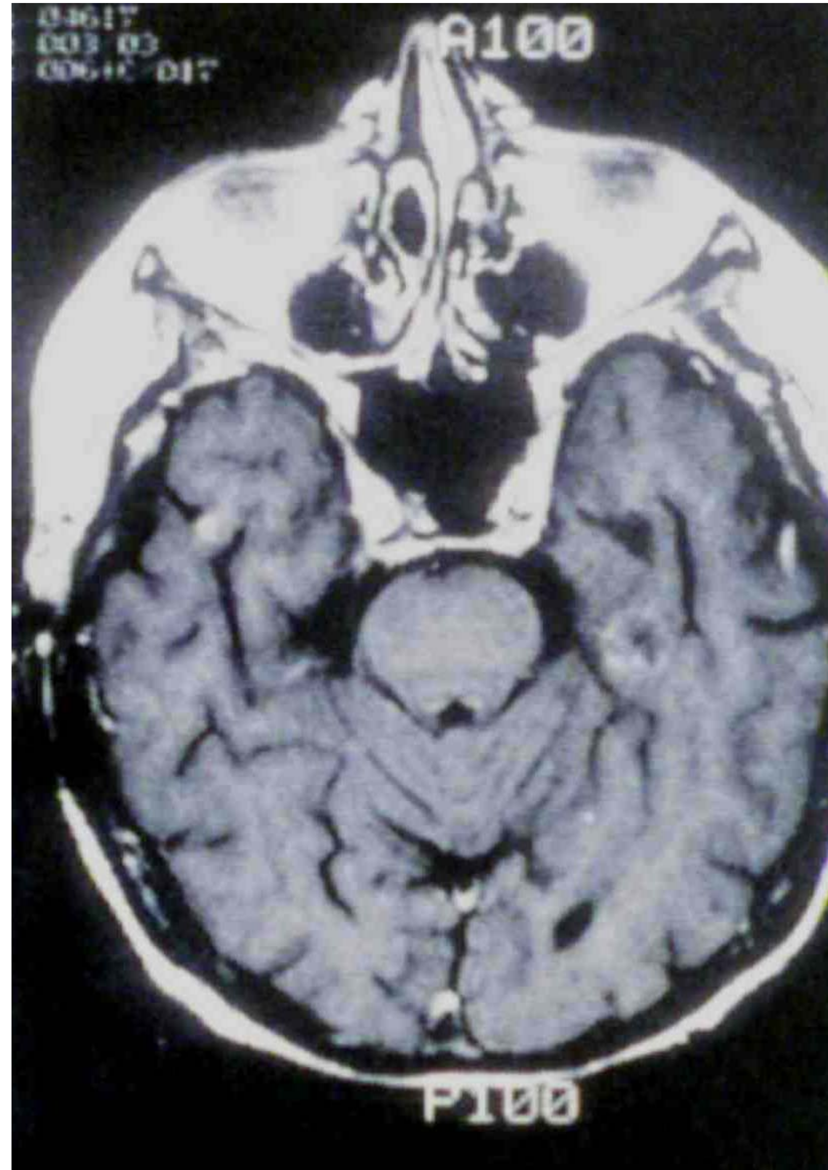


Step 4: The patient lies on the treatment table of the Gamma Knife while the frame is affixed to the appropriate collimator.



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.




A100
P100

What disorders can the Gamma Knife treat?

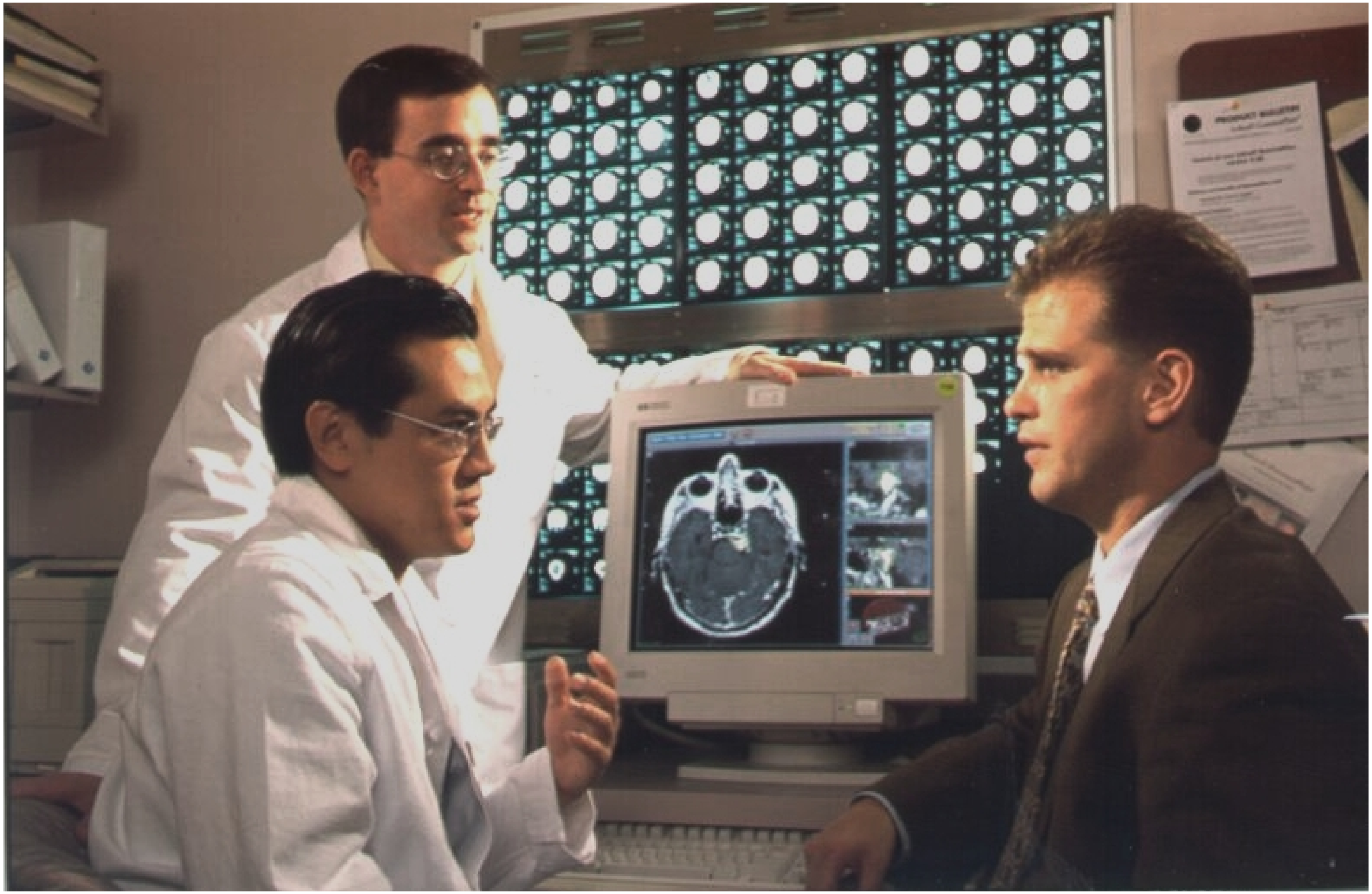
- Malignant brain tumors
- Benign tumors within the head
- Malignant tumors from elsewhere in the body
- Vascular malformations
- Functional disorders of the brain
  - Parkinson's disease

Procedure

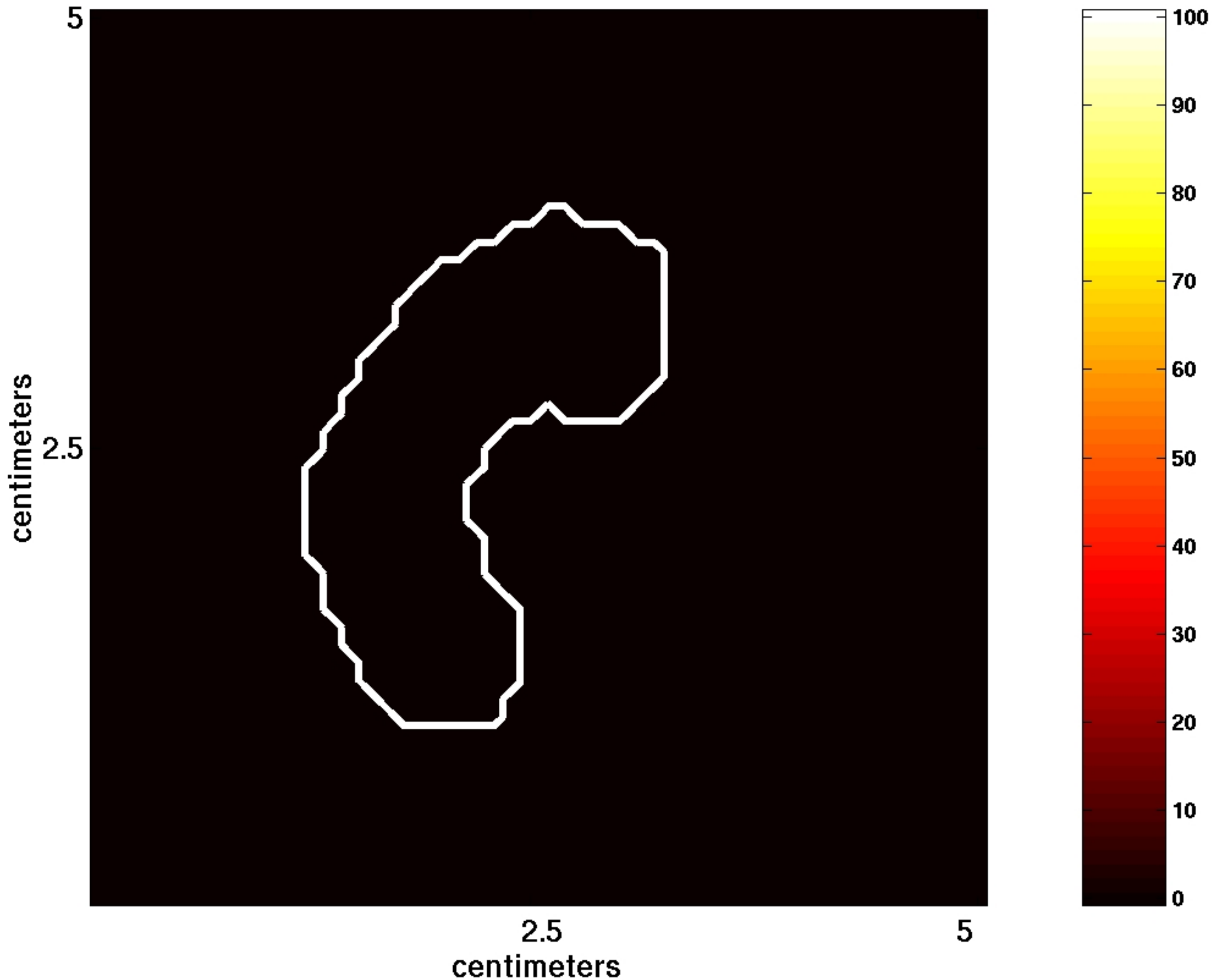
- Placement of head frame
- Imaging (establish coordinate frame)
- Treatment planning
- Treatment
  - Multiple arcs of radiation
  - Multiple shots from Gamma Knife
- Frame removal


4
4
8
8
14
14

Treatment Planning

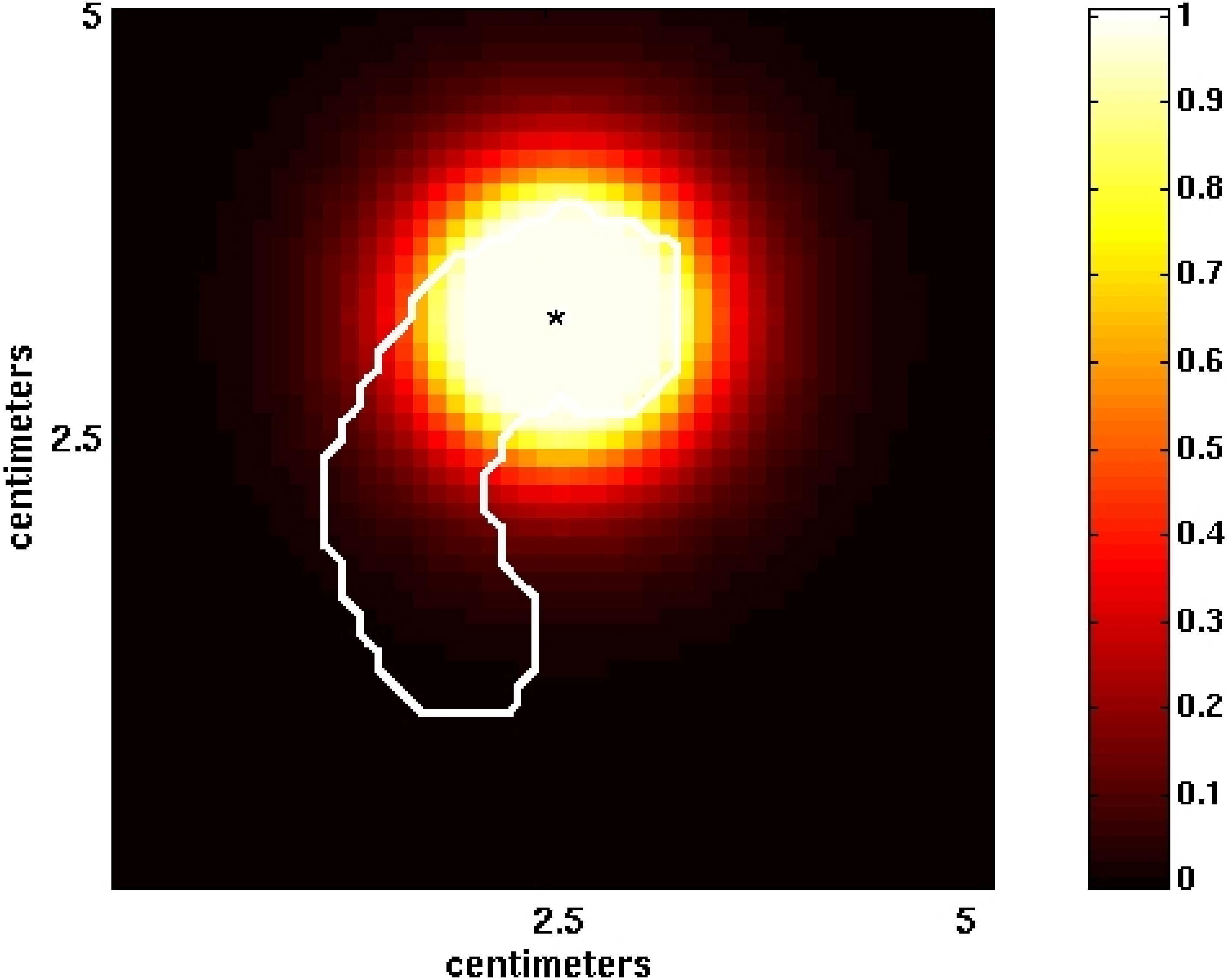


Target

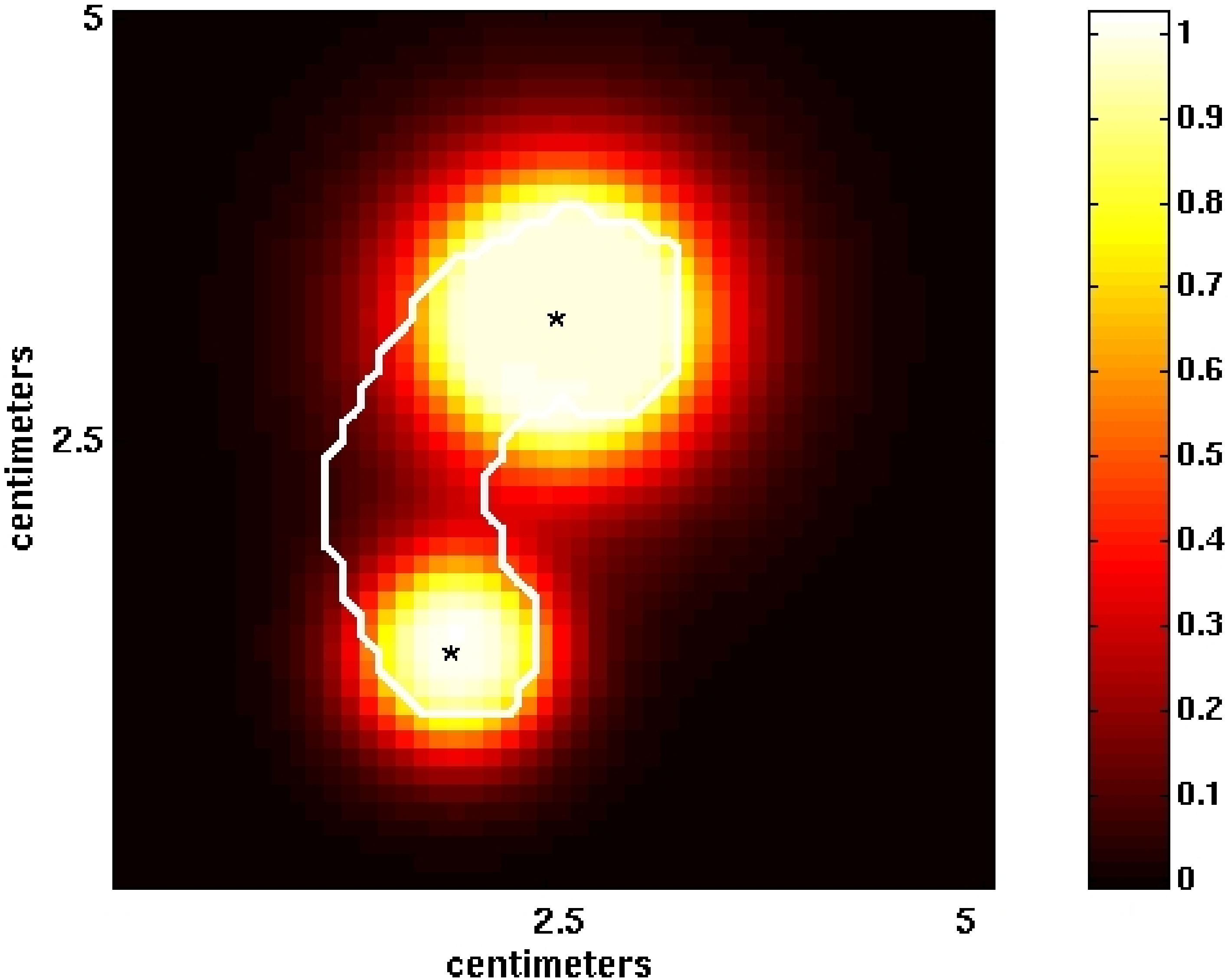


5
2.5
centimeters
2.5
5
centimeters
100
90
80
70
60
50
40
30
20
10
0

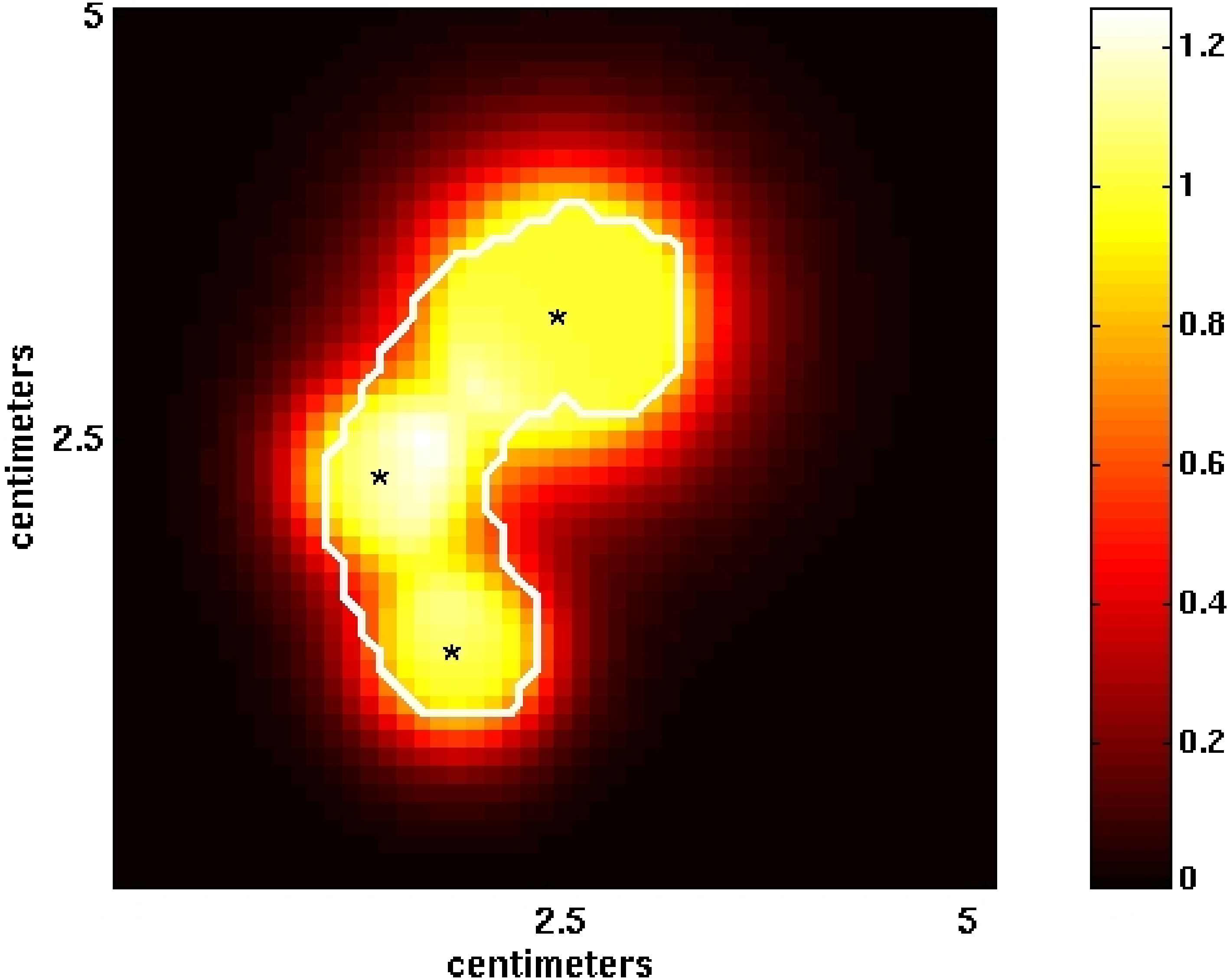
1 Shot



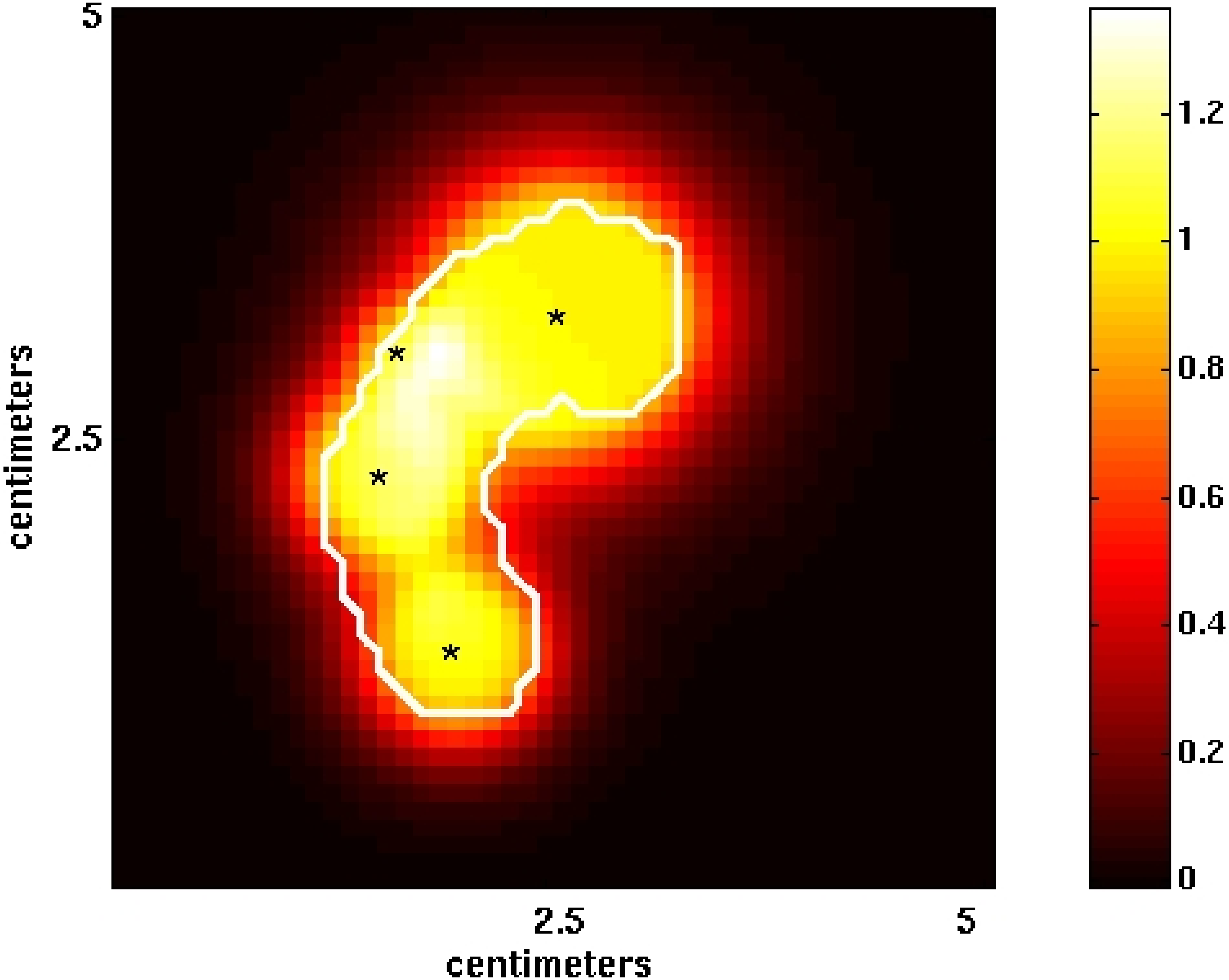
2 Shots



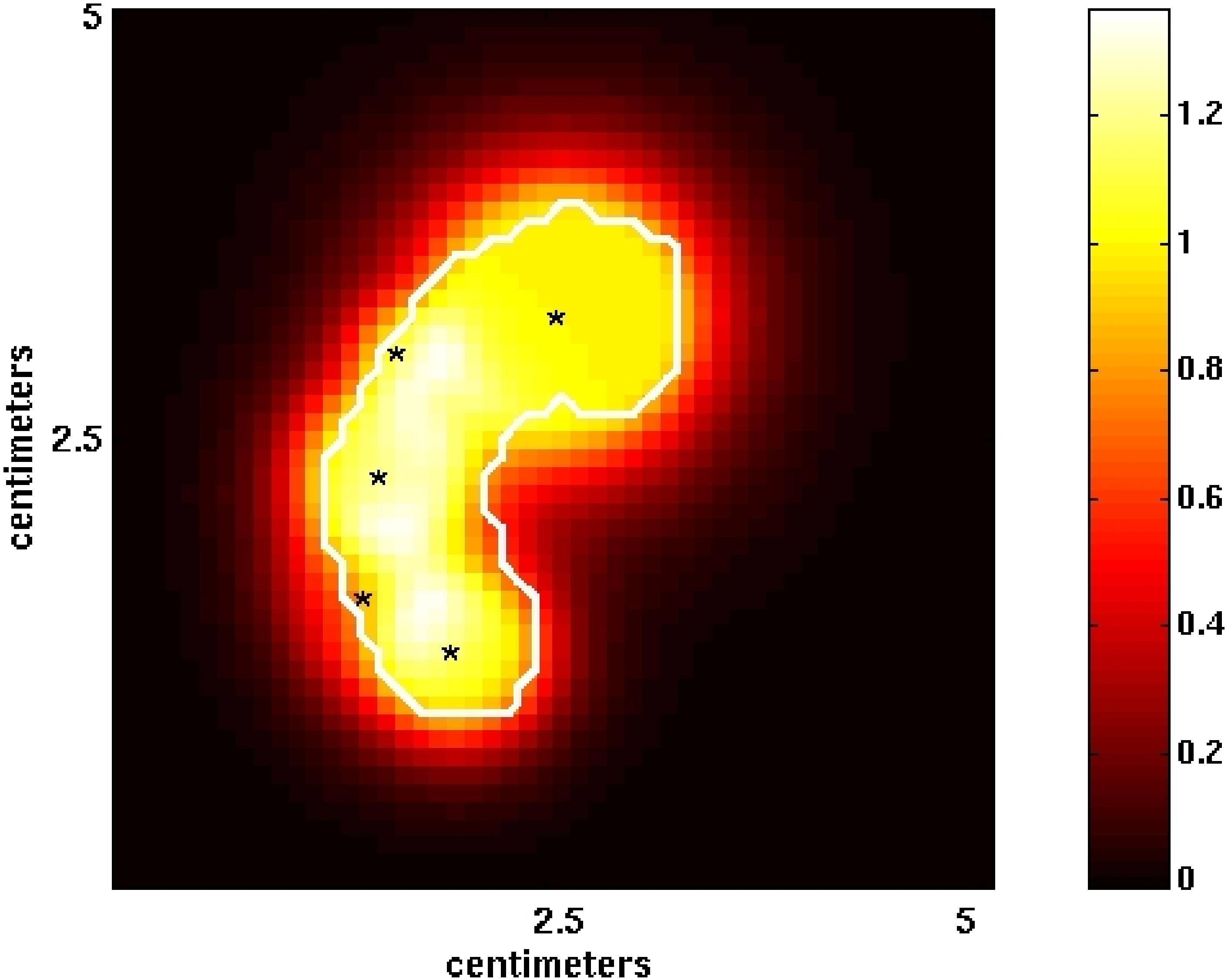
3 Shots



4 Shots



5 Shots



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

Ideal Optimization

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

subject to

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

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

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

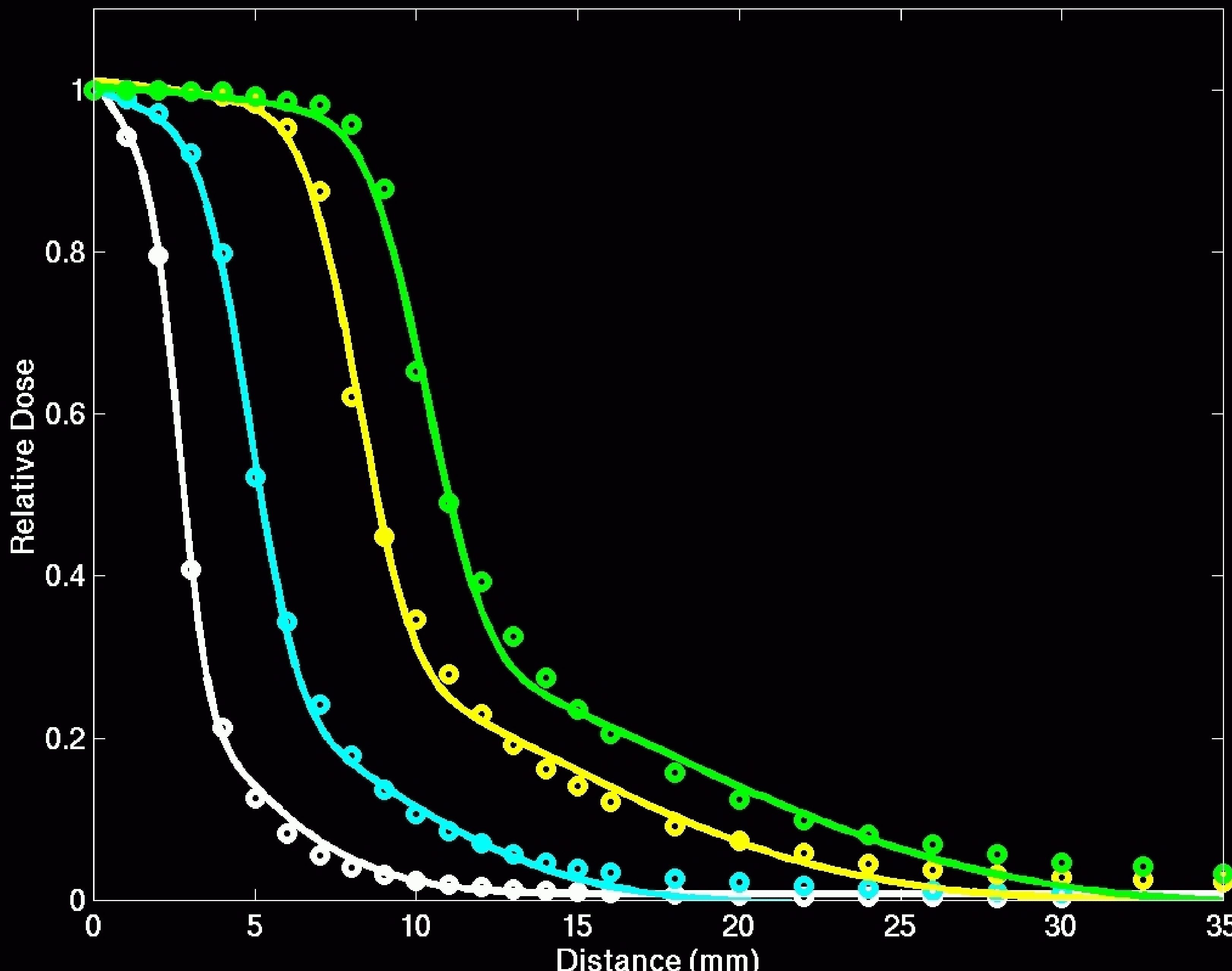
$$|S| \leq N$$

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

Solution methodology

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



Relative Dose
1
0.8
0.6
0.4
0.2
0
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?

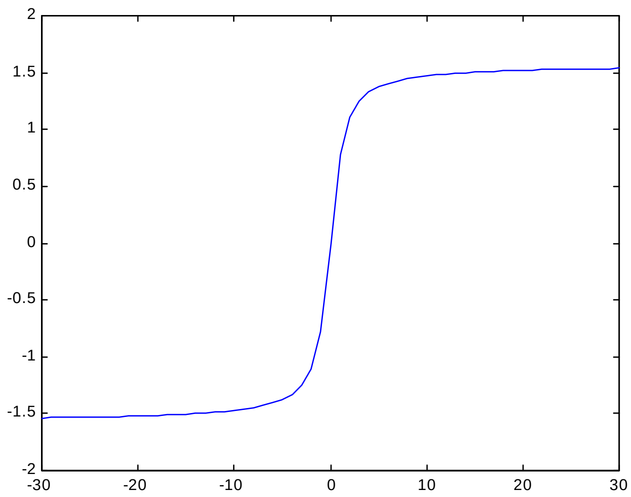
$$\psi_{s,w} = \begin{cases} 1 & \text{if shot s is width w} \\ 0 & \text{else} \end{cases}$$

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

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

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?

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

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

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

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

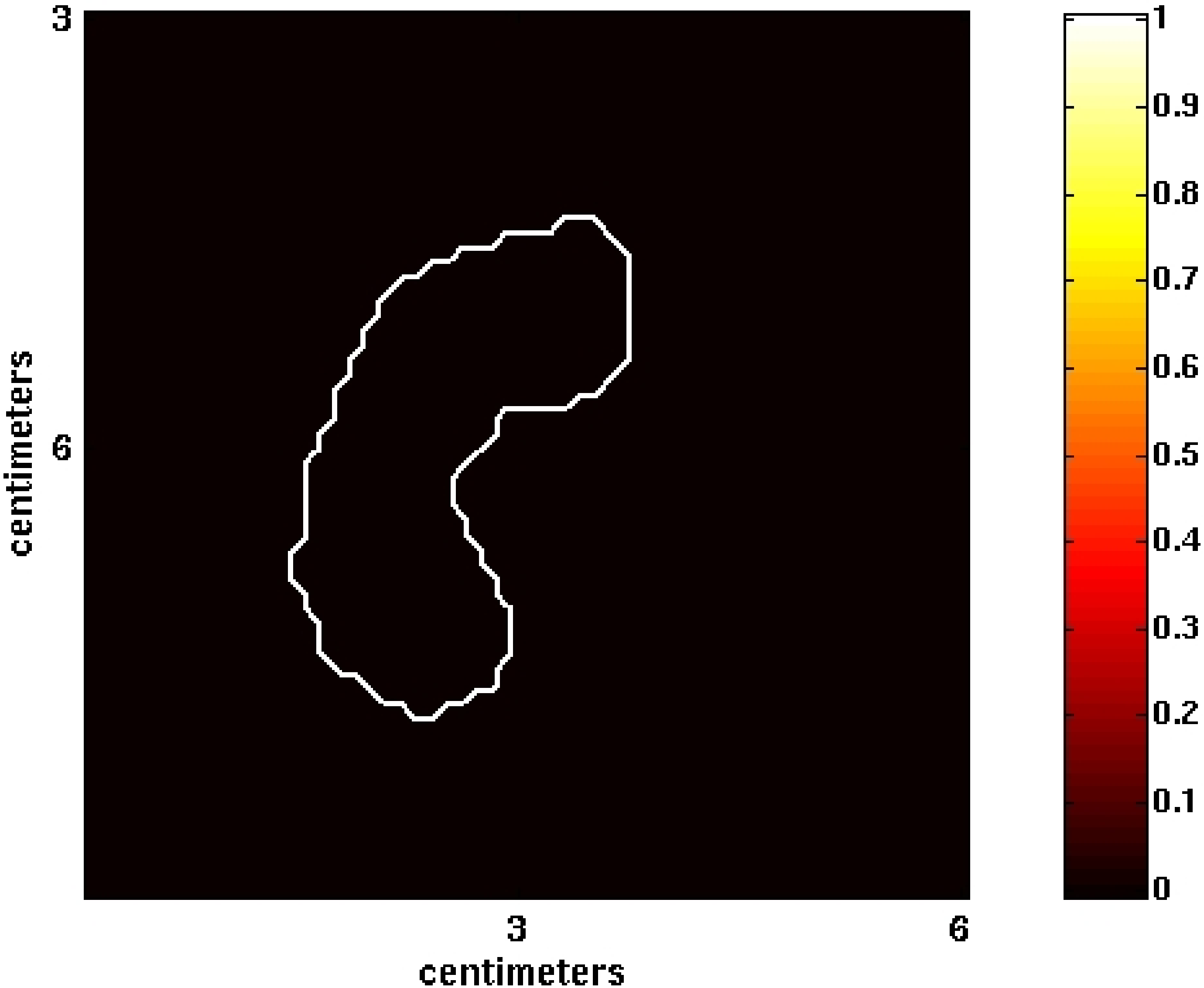
$$D_{s,w}(i) := D_w(x_s, i)$$

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

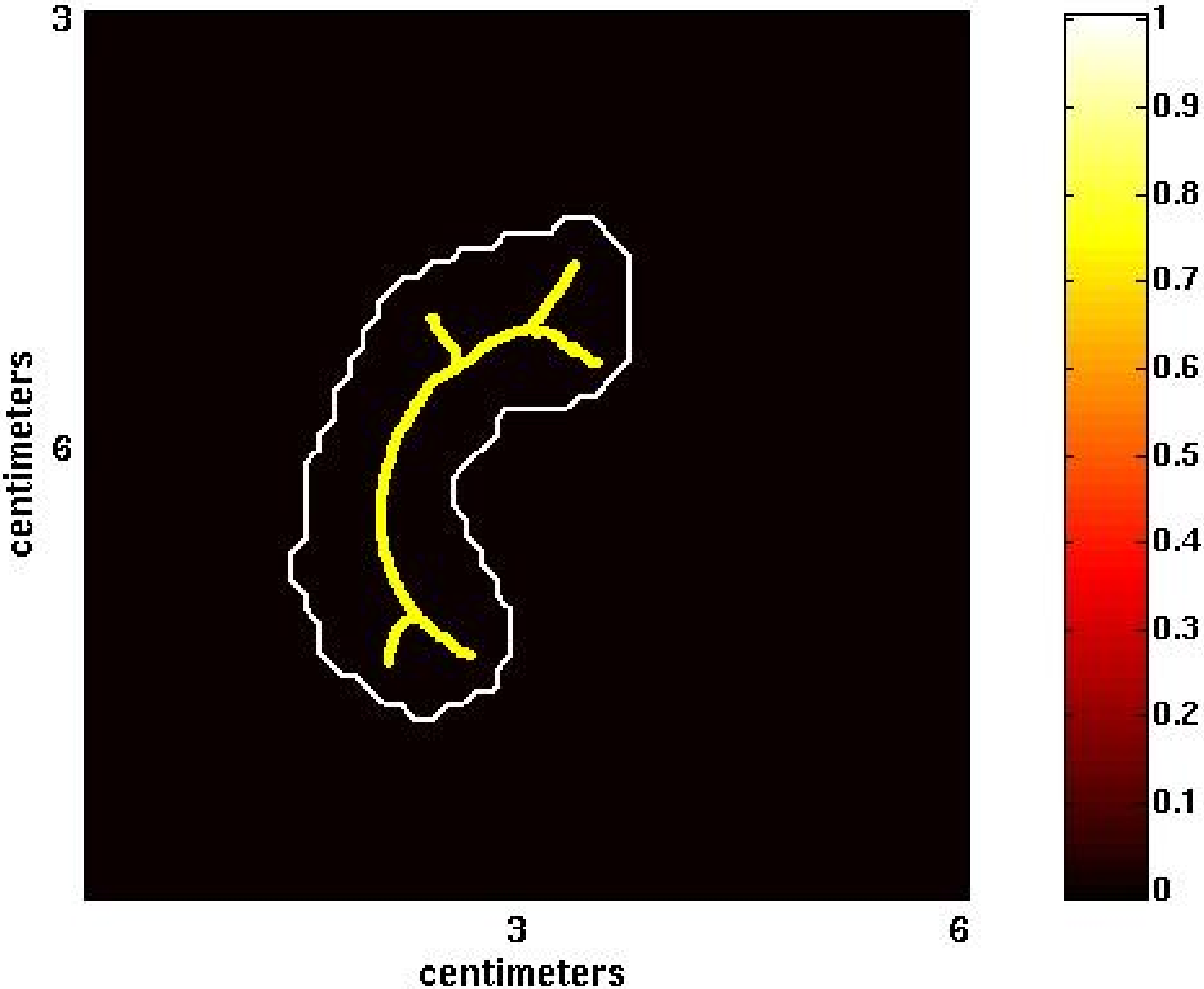
MIP Problem

$$
\begin{aligned}
\min_{t_{s,w},\psi_{s,w}} \quad & Under(Target) \\
\text{s.t.} \quad & Dose(i) = \sum_{s\in S, w\in W} t_{s,w} D_{s,w}(i) \\
& 0 \leq Under(i) \geq 1 - Dose(i) \\
& Dose(Target) \;\geq\; P \sum_{s,w} t_{s,w} \overline{D_w} \\
& \underline{T}\psi_{s,w} \leq t_{s,w} \leq \overline{T}\psi_{s,w} \\
& \sum_{s\in S, w\in W} \psi_{s,w} \leq N
\end{aligned}
$$

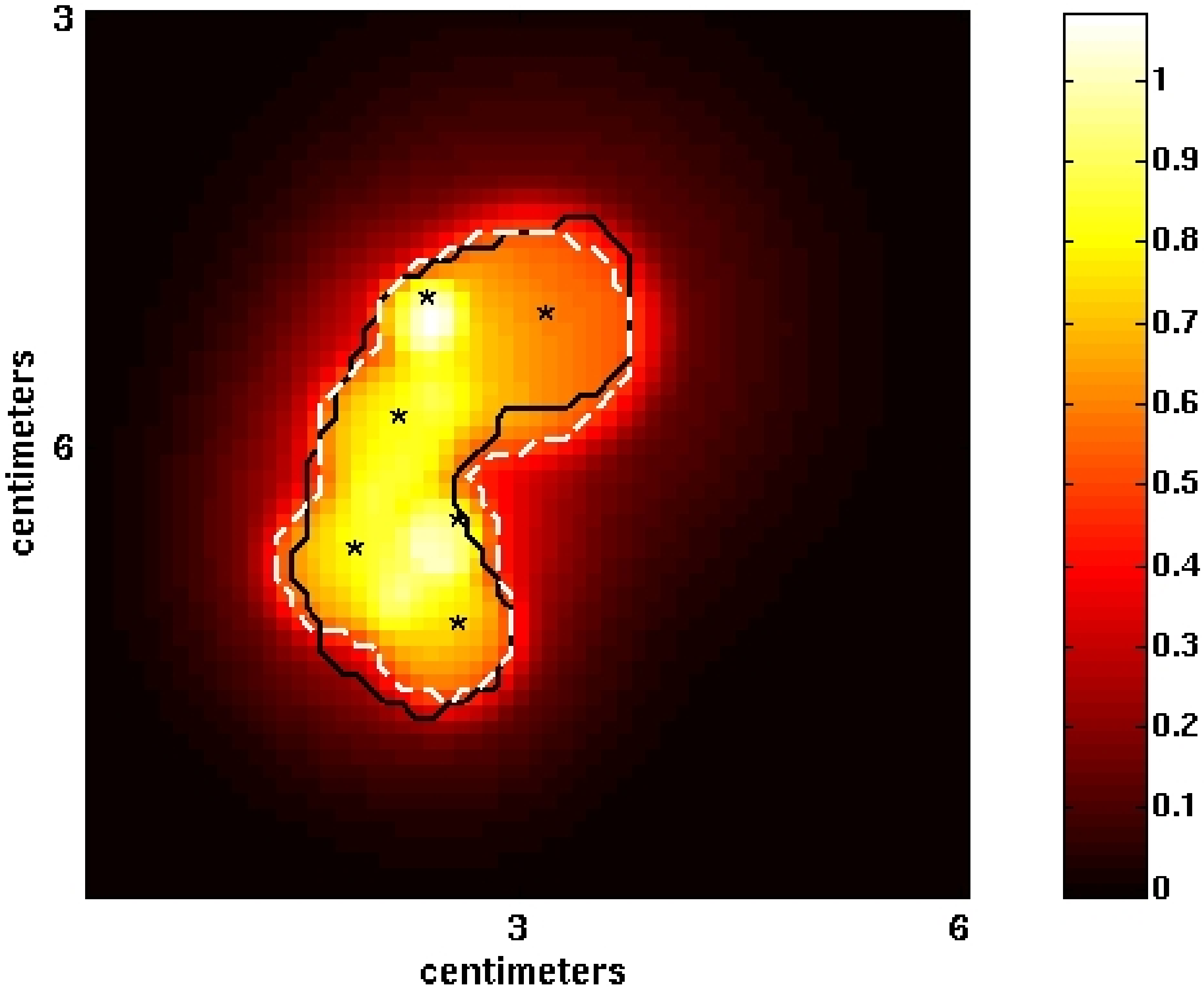
Target



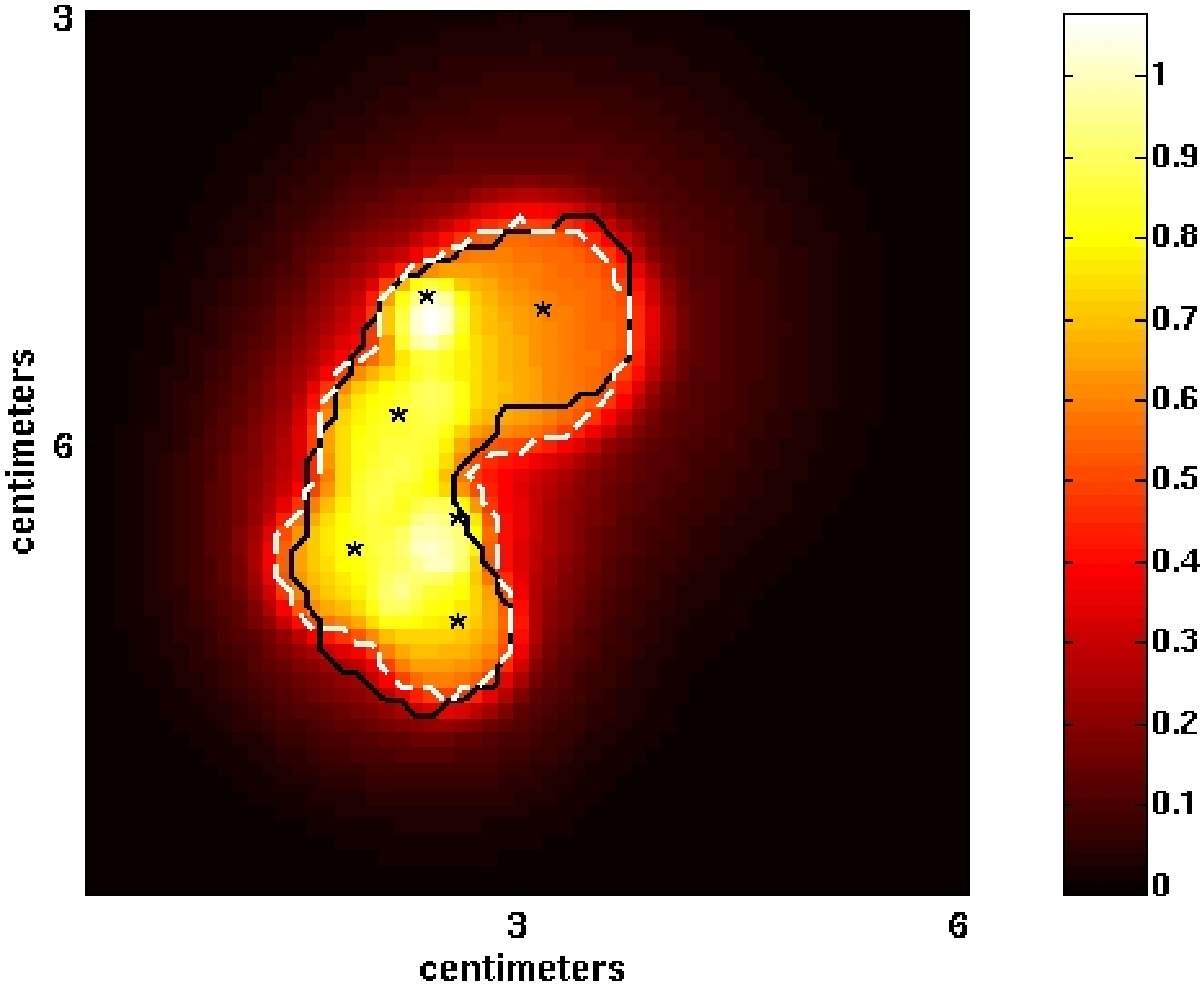
Target Skeleton is Determined



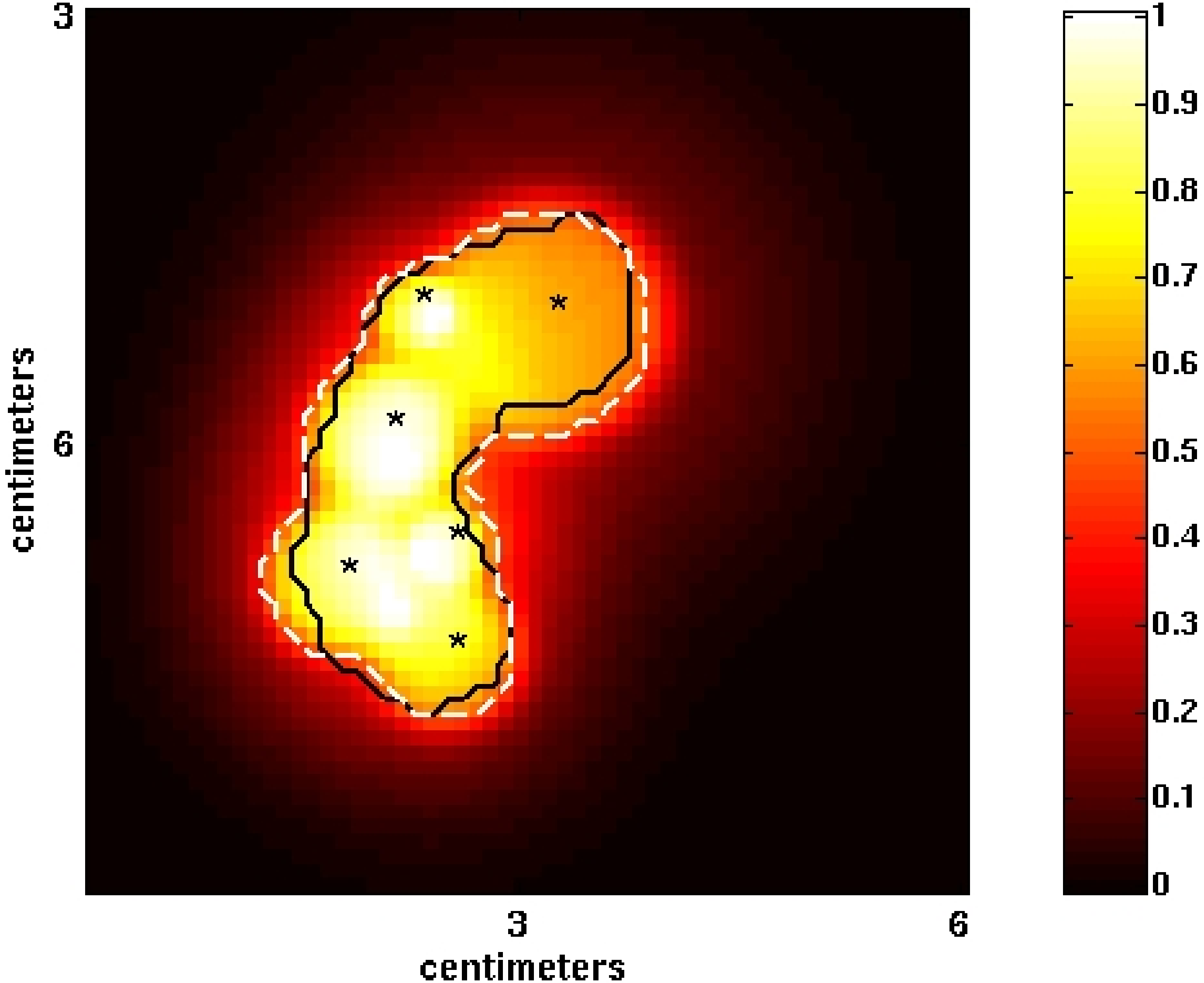
Sphere Packing Result



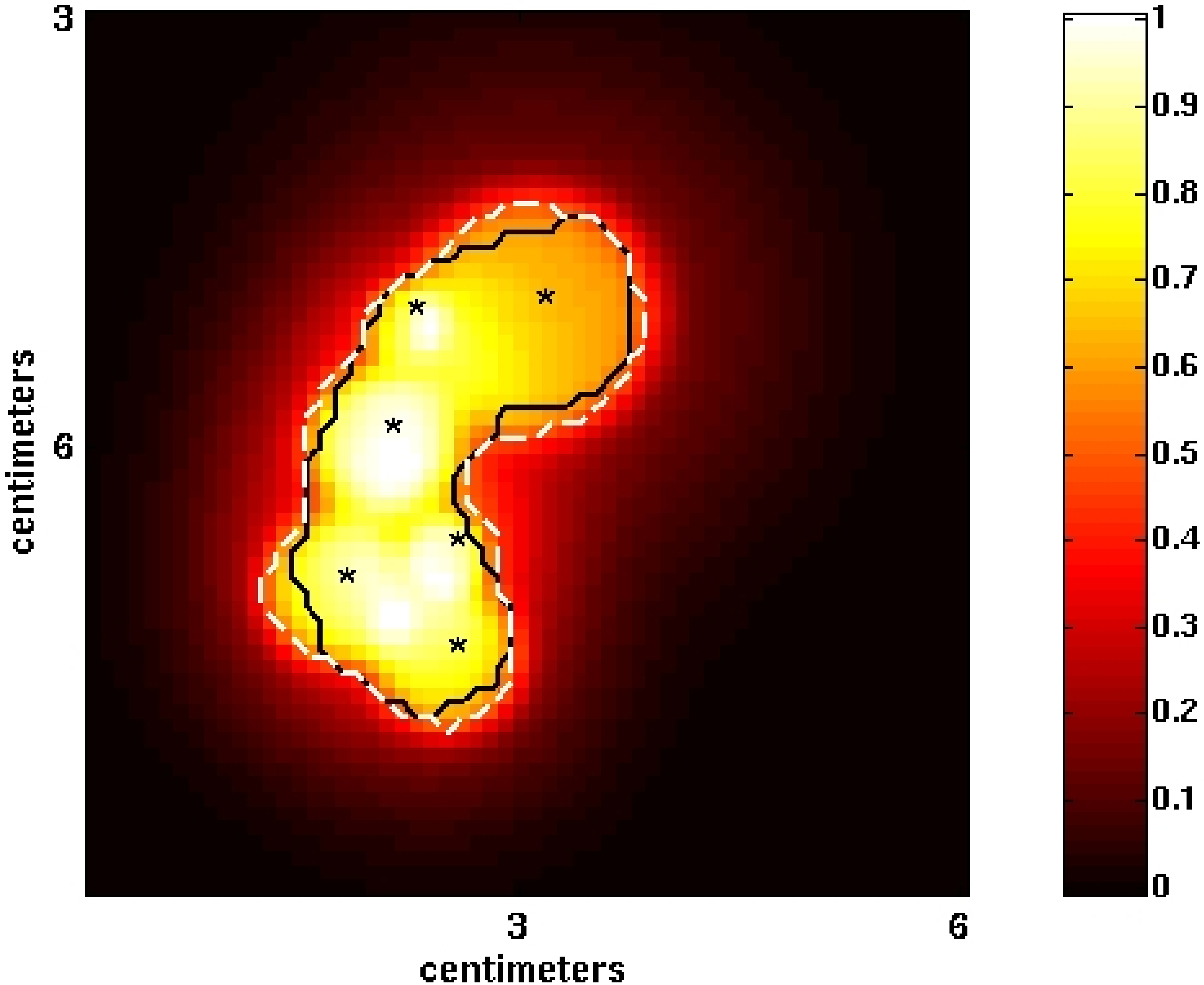
10 Iterations



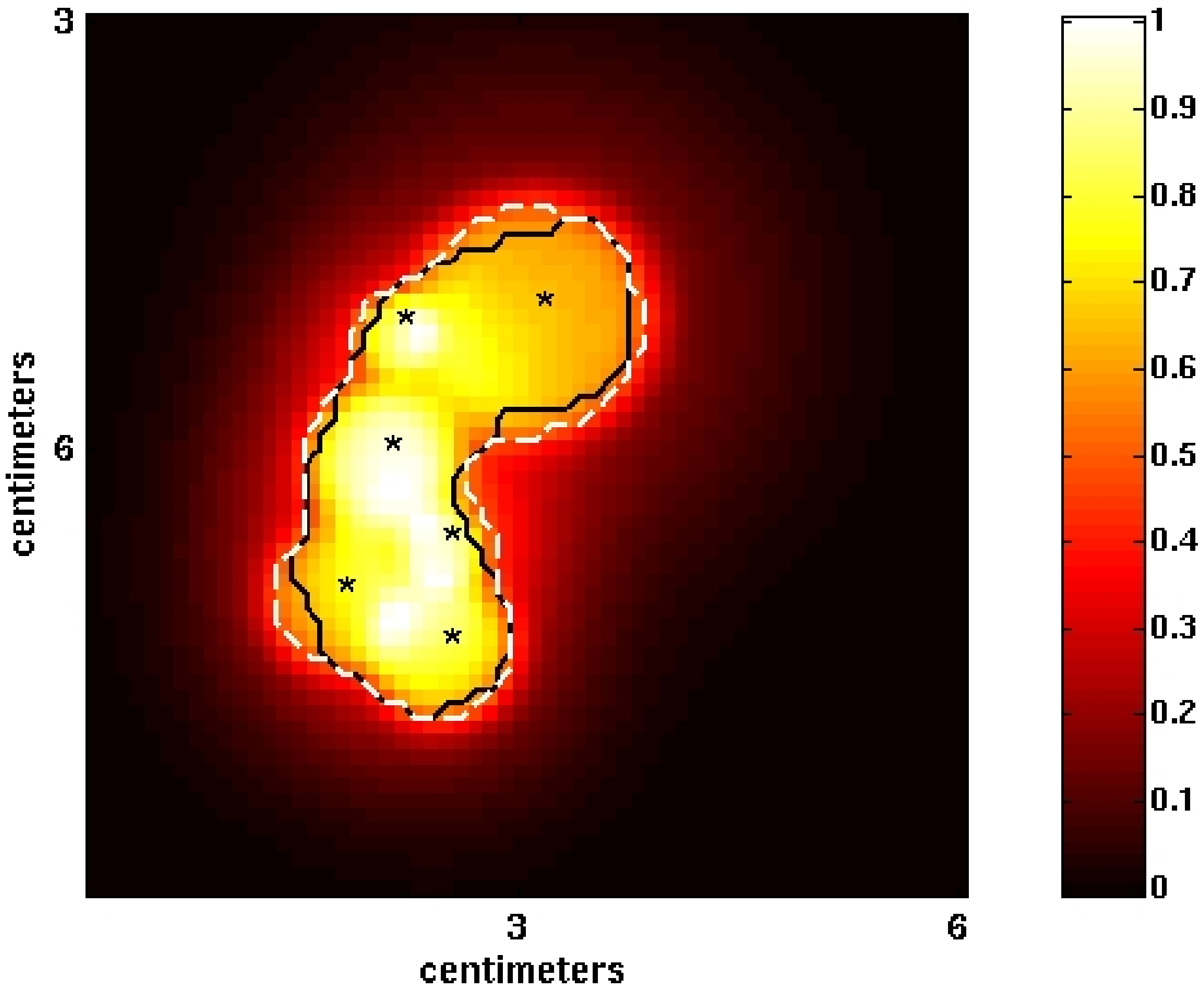
20 Iterations



30 Iterations



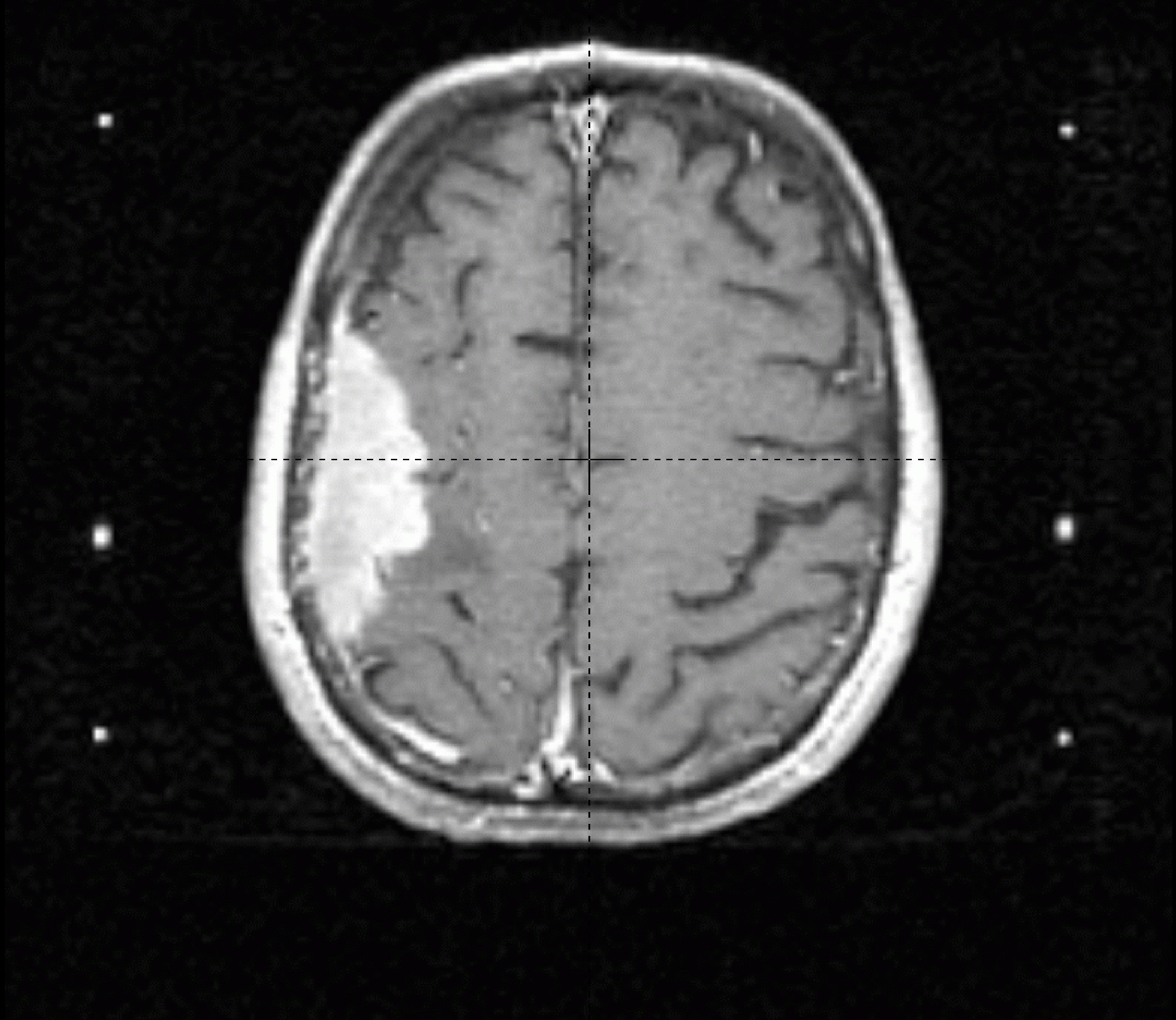
40 Iterations



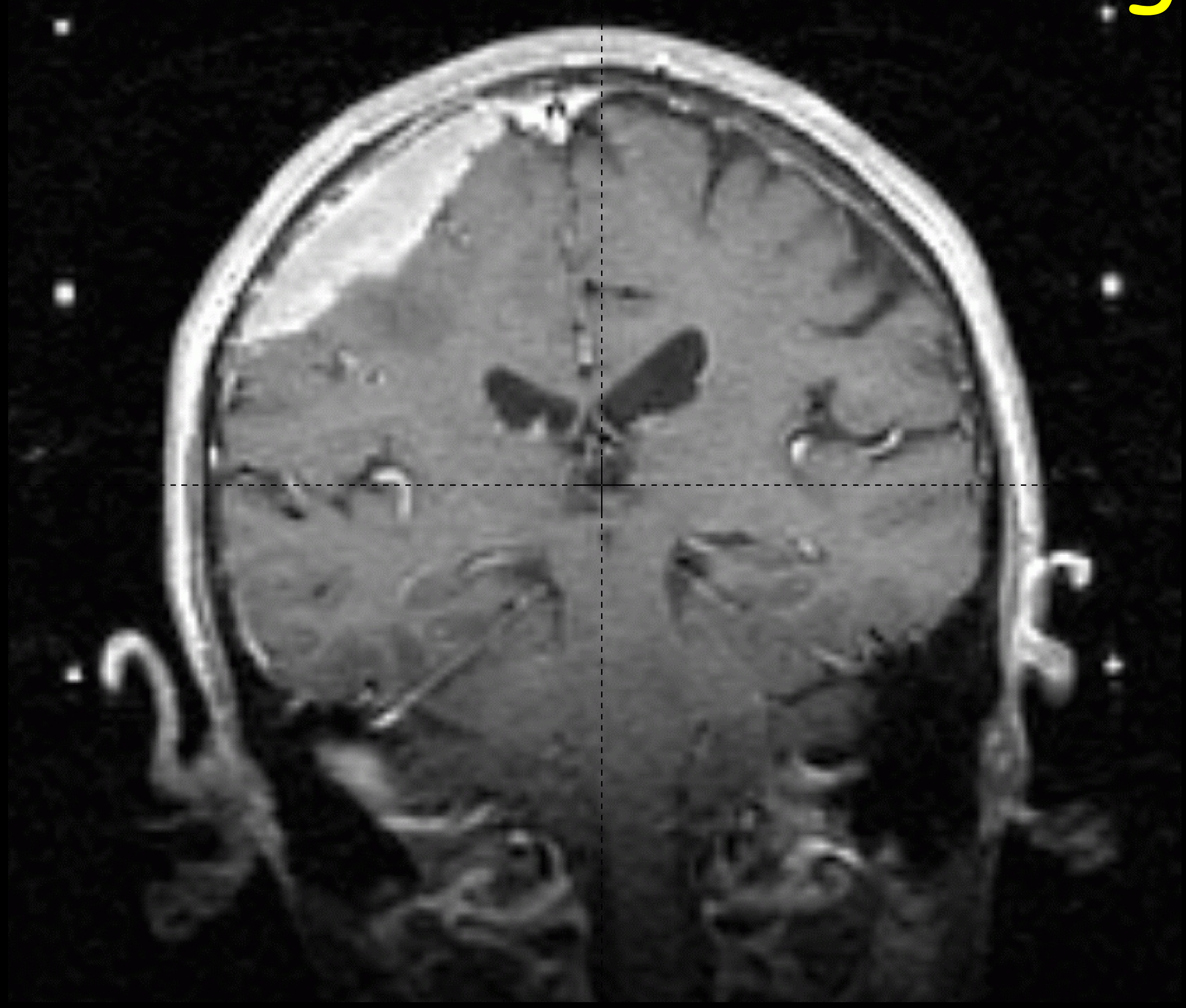
Status

- 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

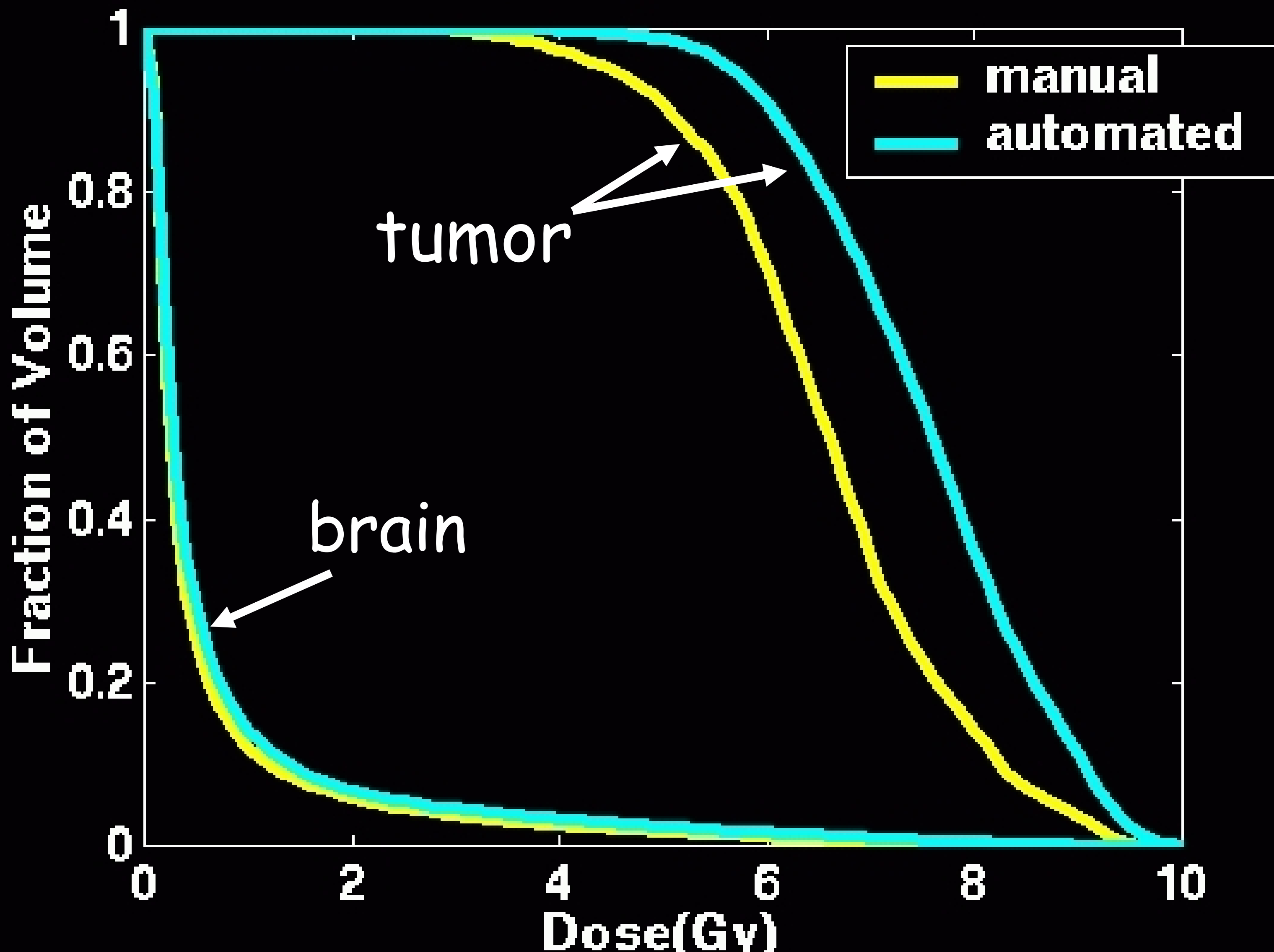


Patient 1 - Coronal Image

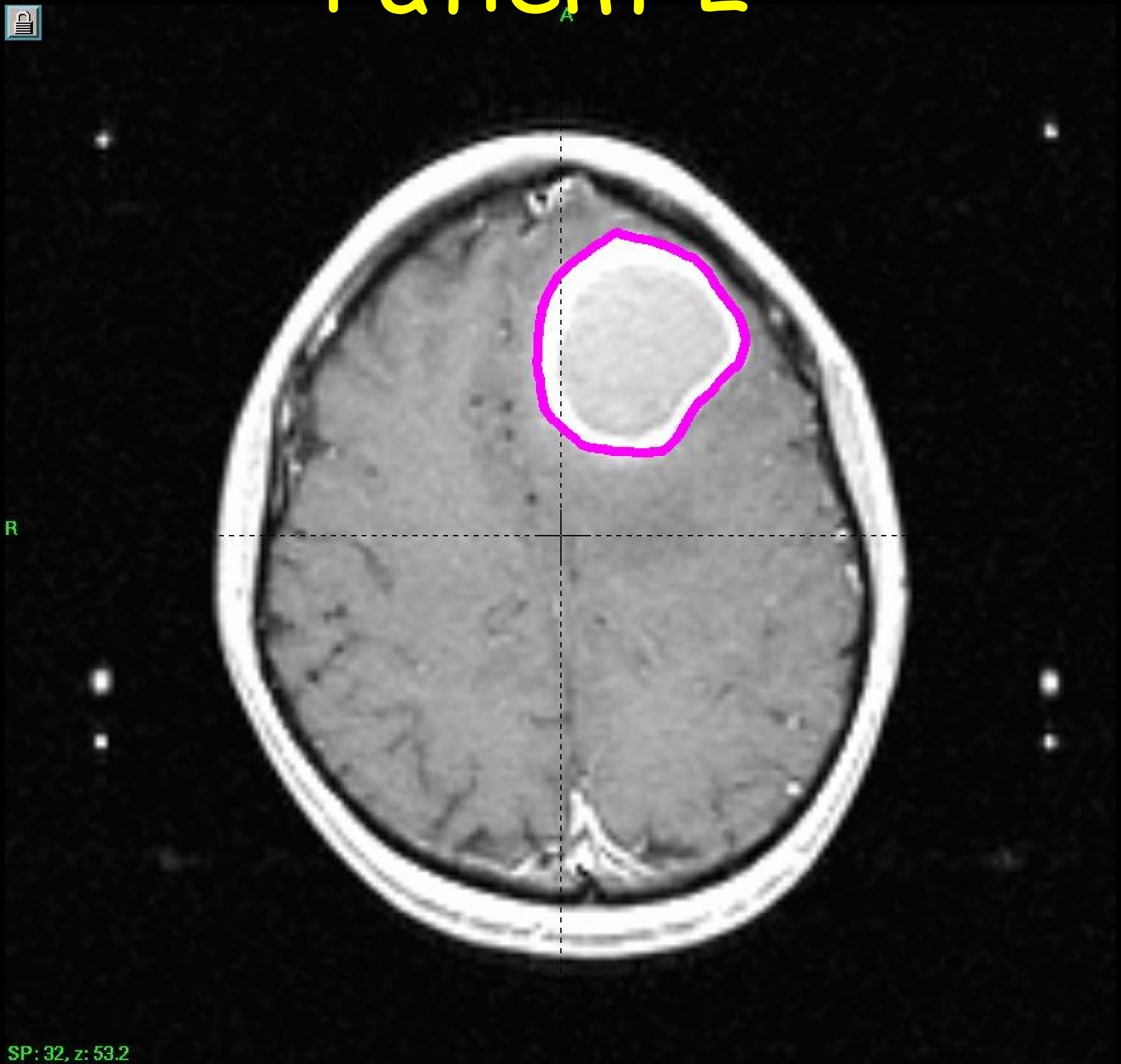


manual

optimized


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

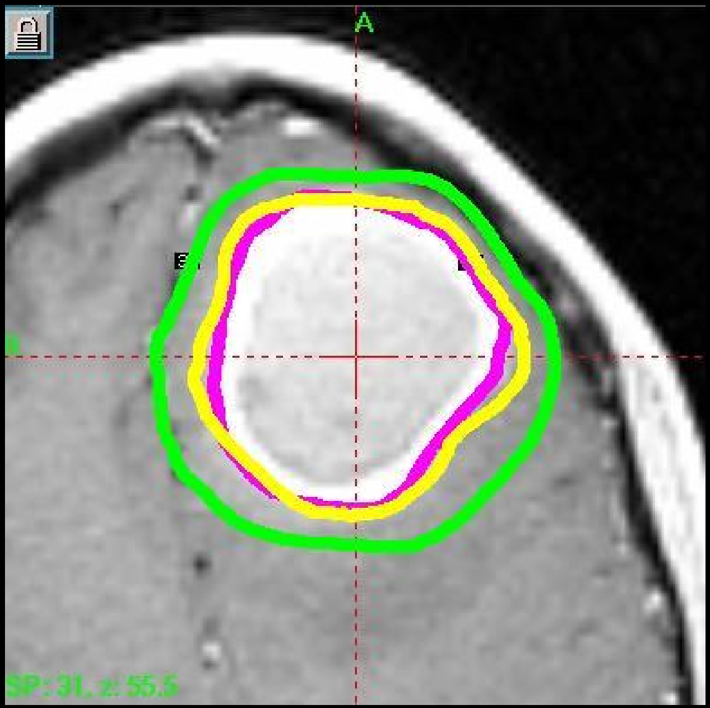
Patient 2



Patient 2 - Axial slice

15 shot manual

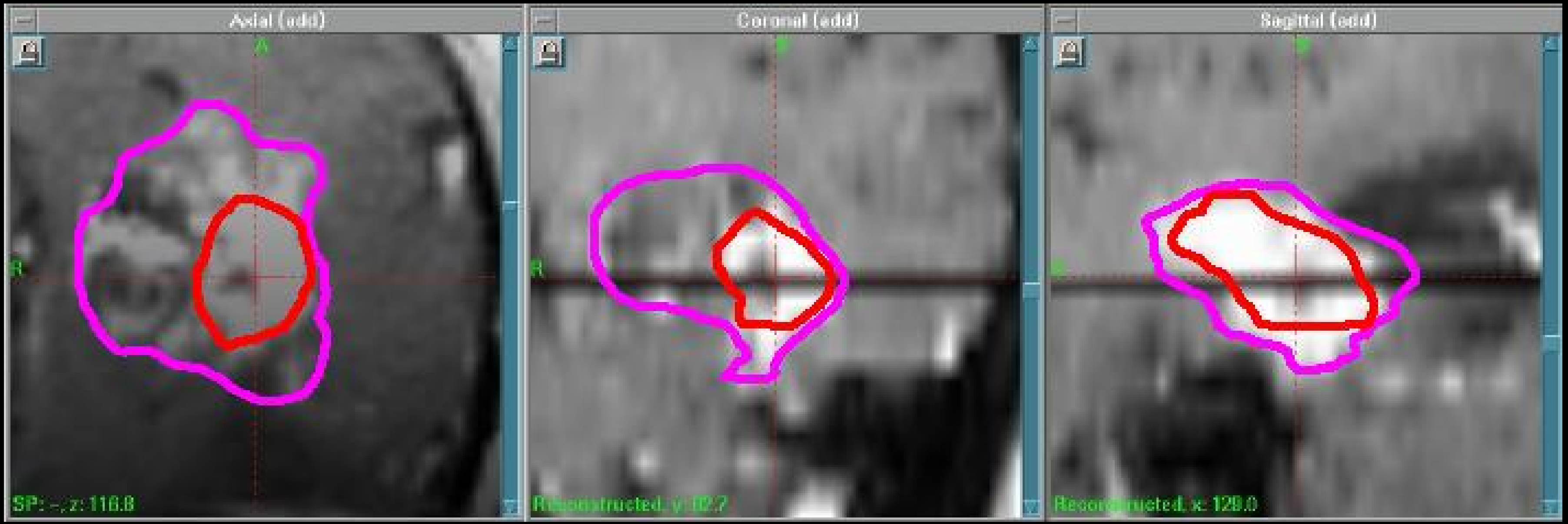
12 shot optimized

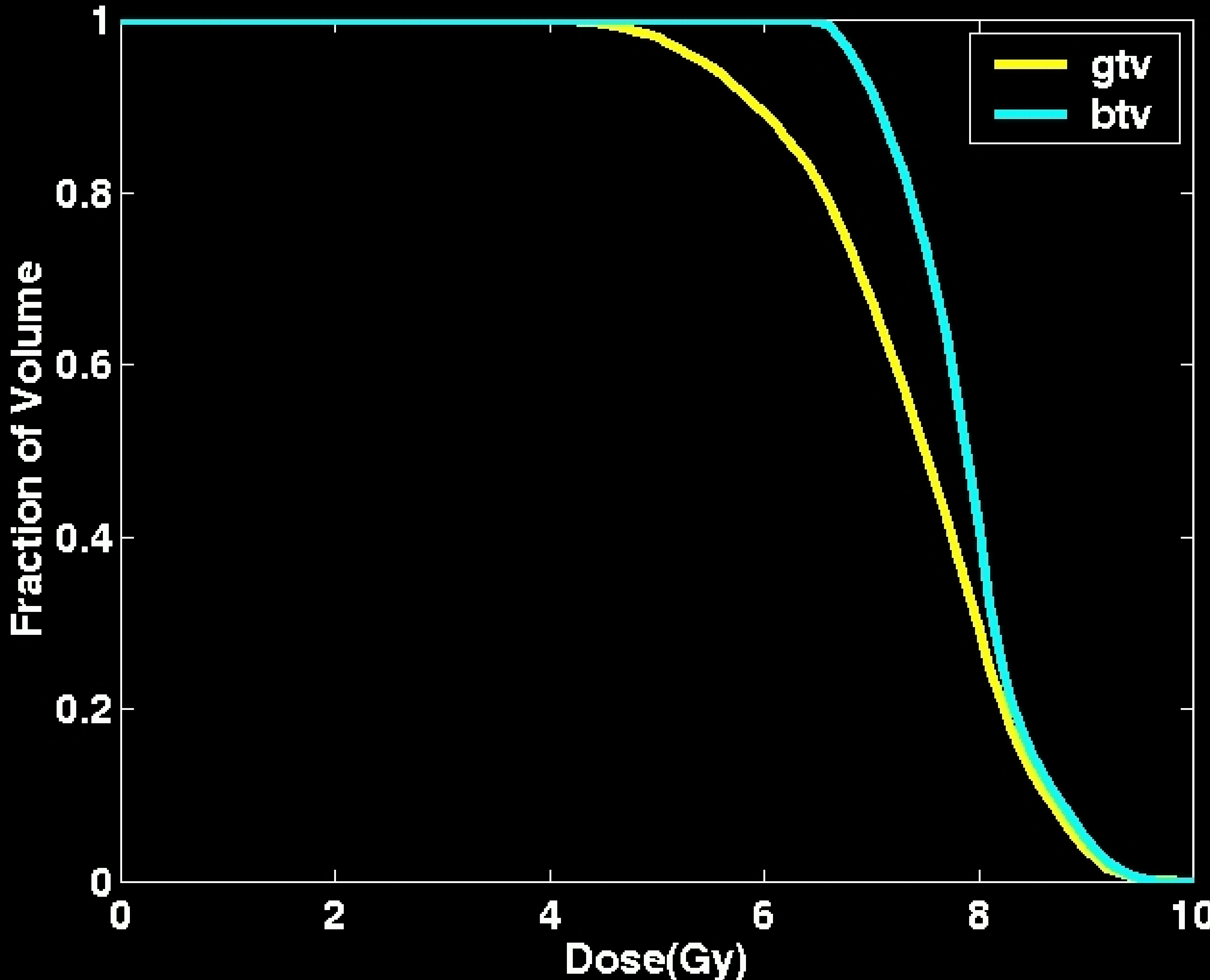


Localized Dose Escalation

- 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



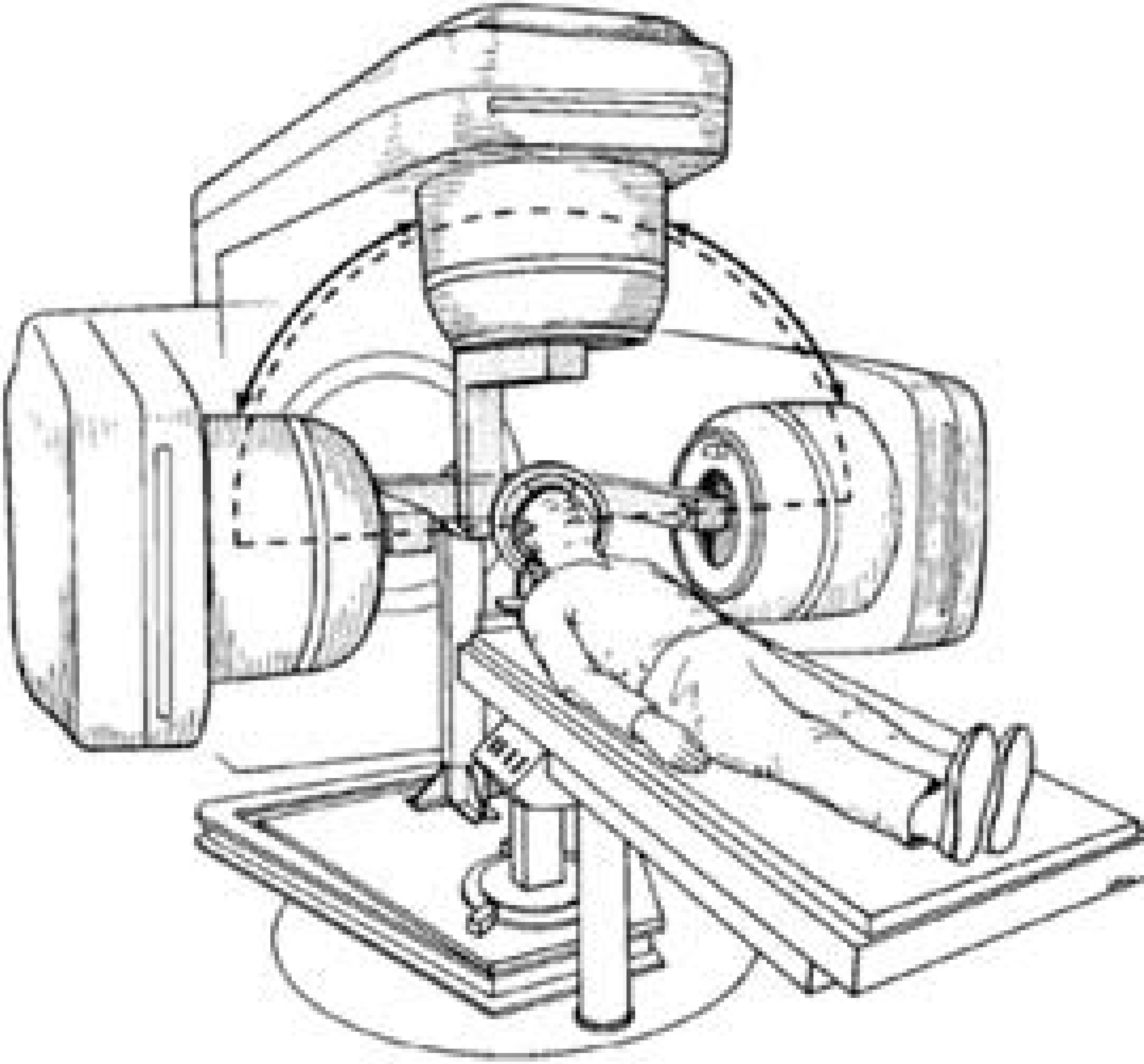

Fraction of Volume
Dose(Gy)
gtv
btv
0
0.2
0.4
0.6
0.8
1
0
2
4
6
8
10

Optimization as Model Building

- 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

Different Types of SRS

- 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)



Dose Painting

$$\min_{w_k \geq 0} \theta_T(Dose(Target)) + \sum_j \theta_j(Dose(O_j))$$

$$\text{subject to } Dose(i) = \sum_k w_k D_k(i)$$

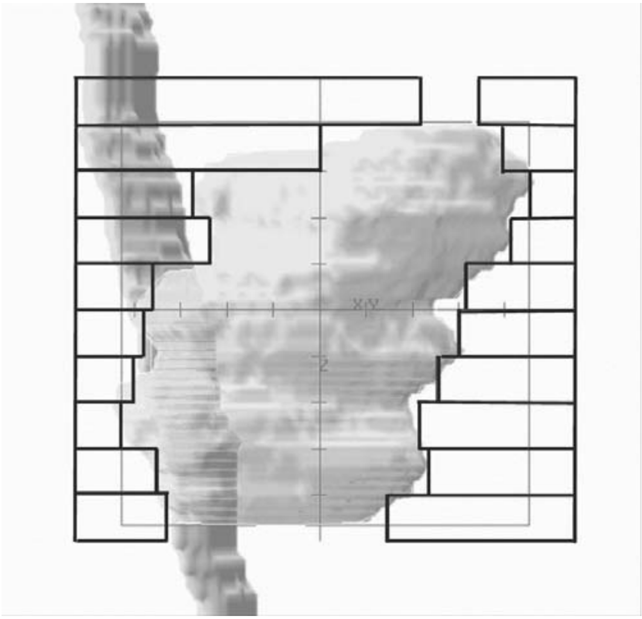
$$D_k \in X$$

- D_k is a beamlet (IMRT or Tomotherapy)
- Data generated via Monte-Carlo sampling
- X may represent discrete constraints:

e.g. Dose volume histogram, aperture setting

IMRT Planning

- Depicted: Beam's eye view at a given angle
- The view is constructed using a multi-leaf collimator
- IMRT allows multiple apertures per angle
- Can be modeled as a combination of network flow optimization (aperture) and nonlinear programming (fluence)
- Column generation



Dose/Volume Constraints

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

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

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

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

Prostate seed implants (Bracytherapy)

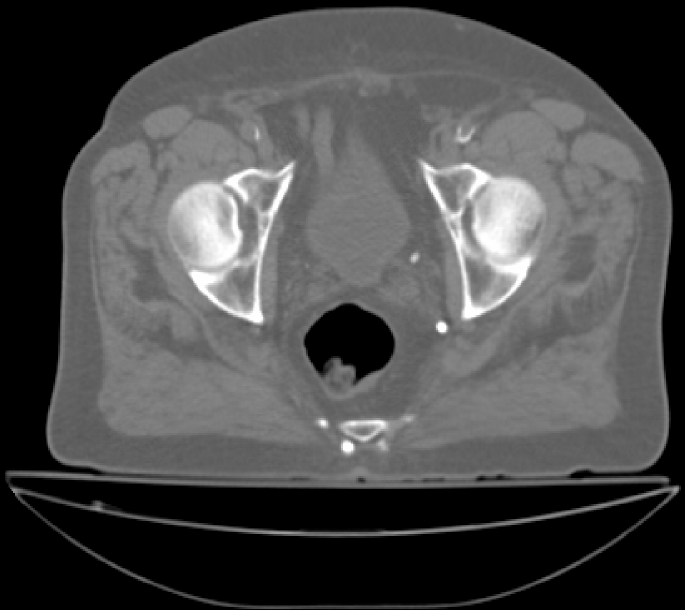
- Large numbers of treatments
- Long(er) term decay process
- Hard to deliver to precisely
- Physical constraints (in-line delivery)
- Large # of potential delivery sites

- Choose seed locations (on grid) - MIP

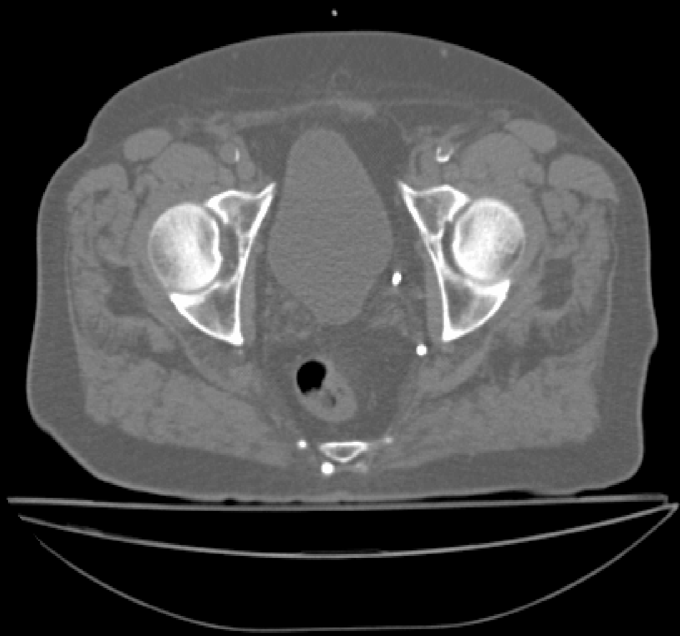
Fractionation

- 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
- Dynamic Programming / Optimal Control

CT Fraction 1



CT Fraction 9



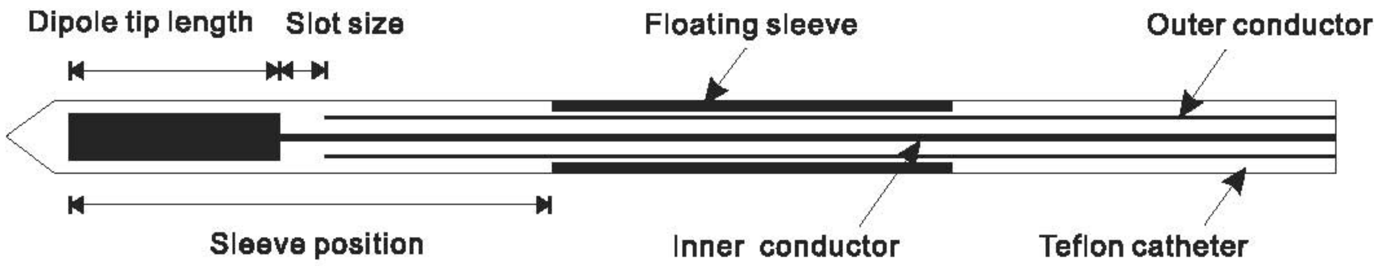
Uncertainty/movement

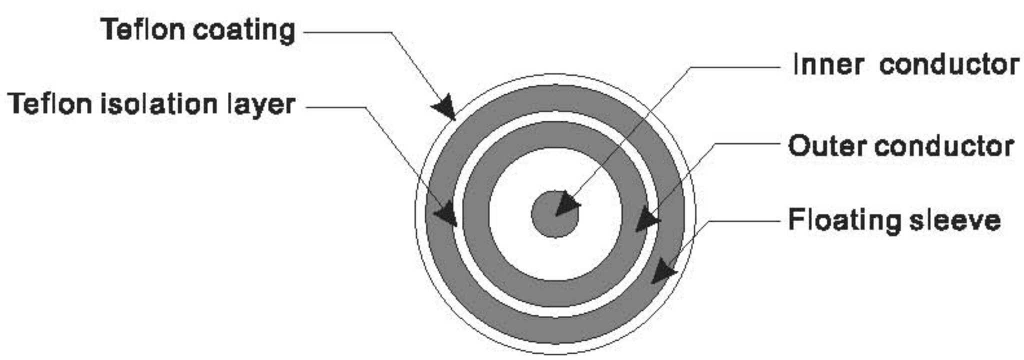
- Target may move (during or between deliveries), shrink, organ properties differ between patients (dielectrics)
- Robust (SOCP), stochastic, control optimization techniques applicable

- Image guided radiation therapy (IGRT)
- Replanning can use gradient optimization

Simulation Optimization for device design

- Liver ablation device (simulated via ODE)
- How do individual liver properties affect solution?





Problems and Technology

- Prescriptions are physician dependent
  - mathematical modeling, adaptive solution
- Complex, evolving delivery devices
  - physics/optimization
- Size of data for model precision
  - computational science
- Uncertainties due to fractionation, movement
  - Statistical modeling
  - Optimization (optimal control, stochastic, robust)
  - Computer science (reconstruction, imaging, feedback)

Conclusions

- Problems solved by models built with multiple optimization solutions
- Constrained nonlinear programming effective tool for model building
- Interplay between OR and Medical Physics crucial in generating clinical tool
- Radiotherapy: optimization has enormous promise to enable real-time implementation and models of increased integrity