RADIATION ONCOLOGY: BIOLOGY & PHYSICS; CLINICAL APPLICATIONS

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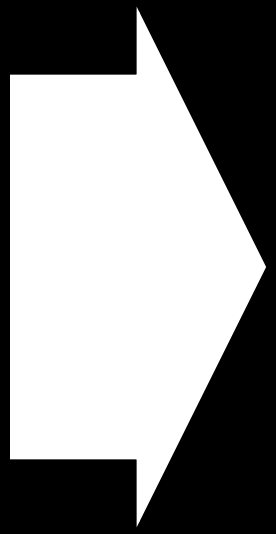
INTRODUCTION

Radiation Oncology is Based on...

- Clinical Oncology
- Medical Physics
- Imaging/Technology
- Radiobiology



Treatment

Present Status of Radiotherapy

- After surgery, radiotherapy (RT) is the most effective cancer treatment.
- Around 40% of the population will develop cancer and 60% will require RT.
- Of patients having RT, 60-70% are treated with curative intent.

Trends in 5-Year Survival for Adult Cancer Patients in the US (1975-2005)

Tumor site	1975-77	1999-2005
Prostate (male)	69%	100%
Breast (female)	75%	90%
Rectum	49%	69%
Lung	13%	16%

(Cancer Facts and Figures. American Cancer Society 2010)

Trends in 5-Year Survival for Pediatric Cancer Patients (<19 yr-old males) in the US (1975-2000)

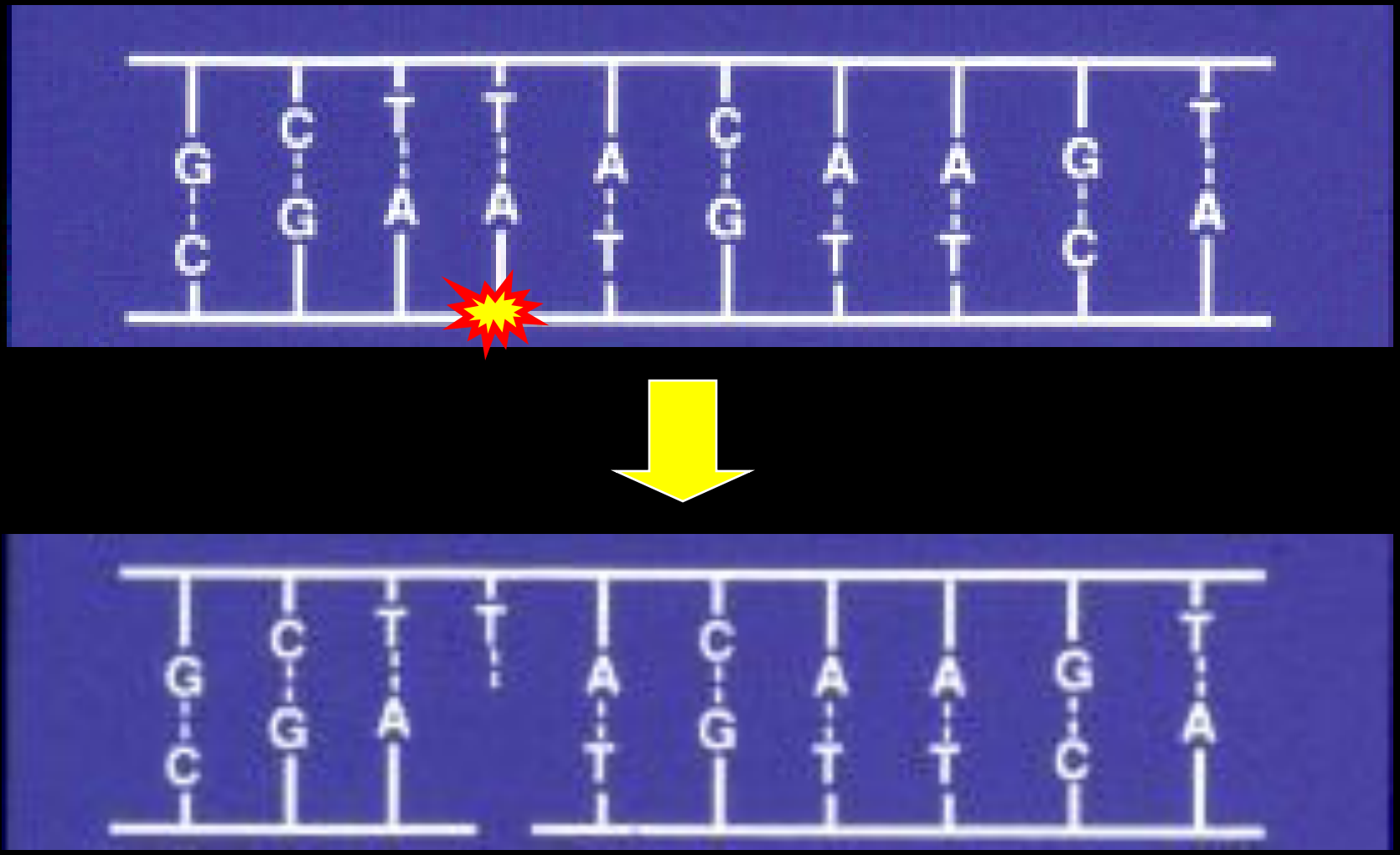
Tumor site	1975-79	1995-2000
CNS	57%	72%
Soft tiss. sarcoma	62%	73%
Hodgkin	86%	96%
All sites	**58%**	**77%**

(Annual report to the Nation, Cancer, July 2004)

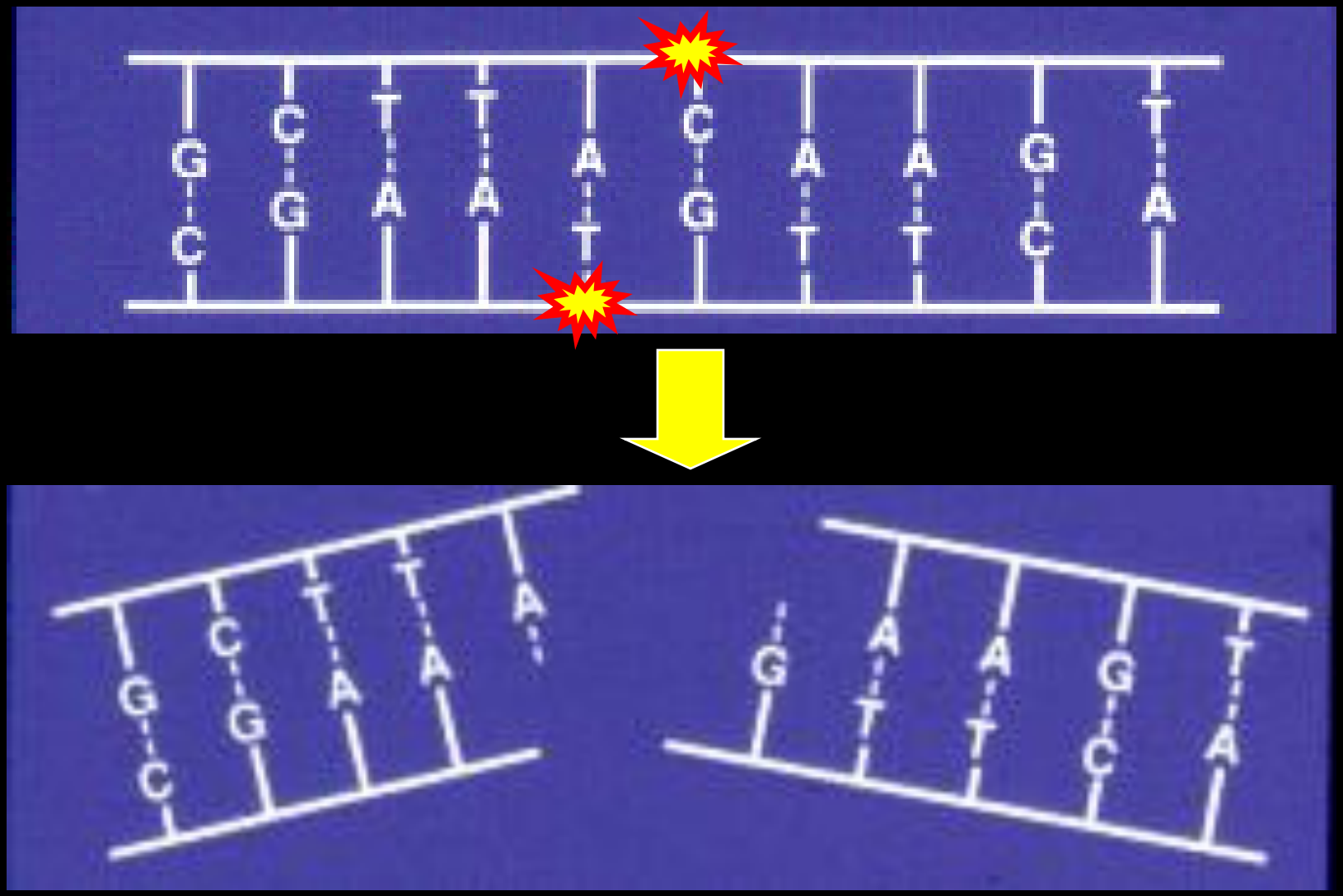
BIOLOGY

Cell killing effect

- Radiation interacts with DNA: DNA breaks.
- DNA breaks trigger cellular repair actions.
- DNA double strand breaks may lead to cell-kill.



Single strand break



Double strand break

PHYSICS

RT Modalities

- External RT:

  Radiation source outside the patient (radiation beams: *X-rays*, e^-, H^+,...)

- Brachytherapy:

  Radiation source inside the patient (*Ir, Cs, I, Au, Pd*,...)

Standard Dose Parameters

- *Standard fractionation:*
  1.8-2 Gy/fraction; 1x day; 5 days/week.

- *Total dose:*

low	(20-30 Gy):	seminoma, Hodgkin,...
medium	(45-55 Gy):	subclinical disease,...
high	(65-80 Gy):	prostate, sarcoma,...

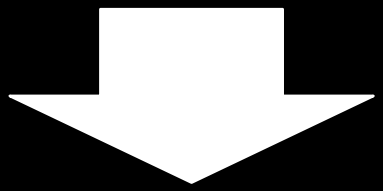
Present Limitation of RT

1/3 of patients still fail
locally after curative intent RT

How to overcome post RT Failures?

- State of the art equipment & high quality imaging
- Quality assurance programs
- Biology: altered fractionation, sensitizers,...
- **Improve dose distribution: dose escalation**

To improve dose distribution in order to safely escalate the dose

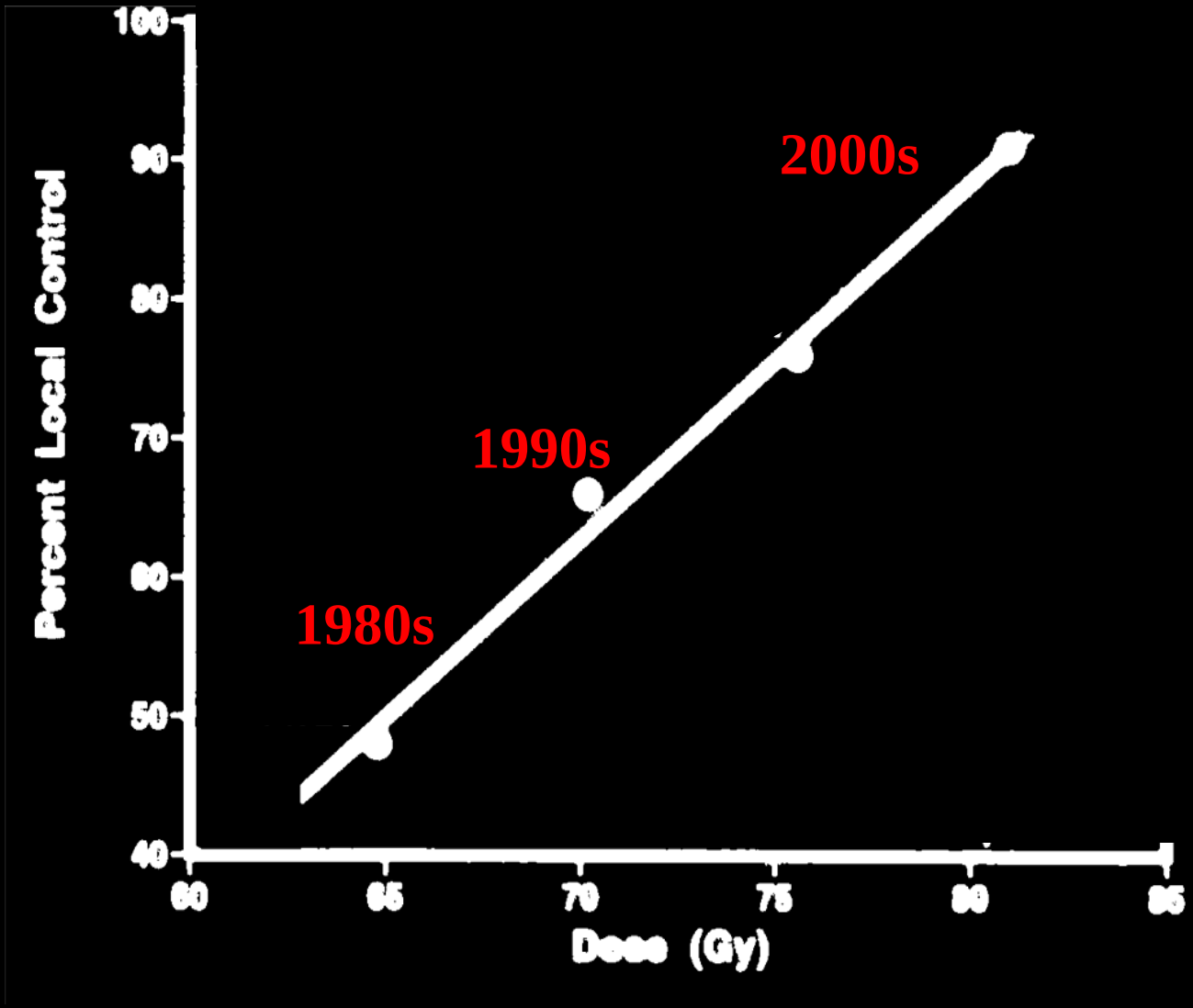


3-D conformal RT

Dose escalation studies

- Prostate
- CNS
- Base of skull & paranasal sinus
- Non-extremity soft tissue sarcomas

Local control *vs* dose in prostate



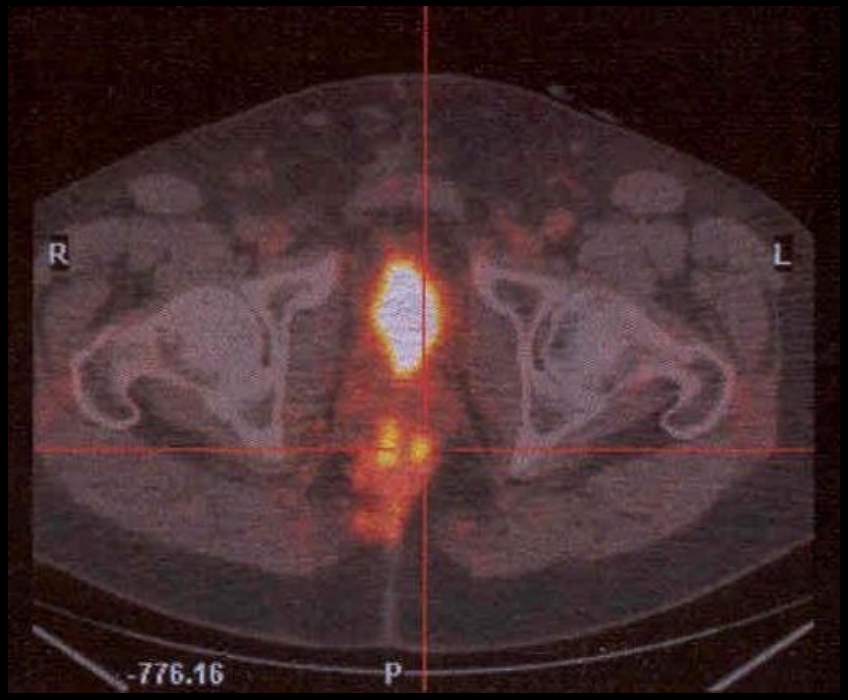
Fuks et al, MSKCC 2000

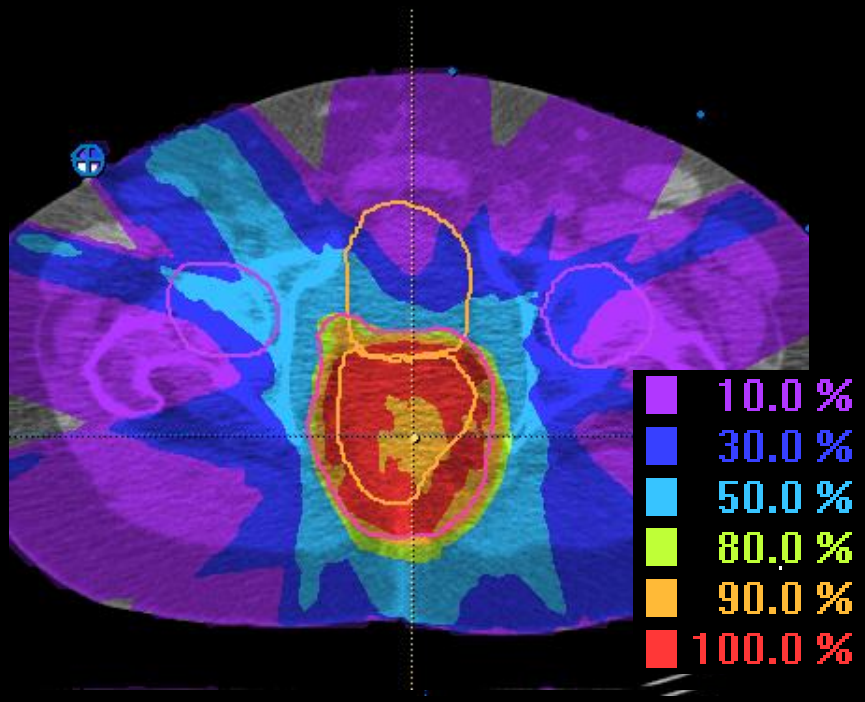
Treatment optimization

- Imaging (CT, MRI, PET) and IGRT (image guided RT)
- Treatment planning sytems: 3-D dosimetry
- Intensity Modulated RT (& inverse planning)
- Protons: in depth conformation

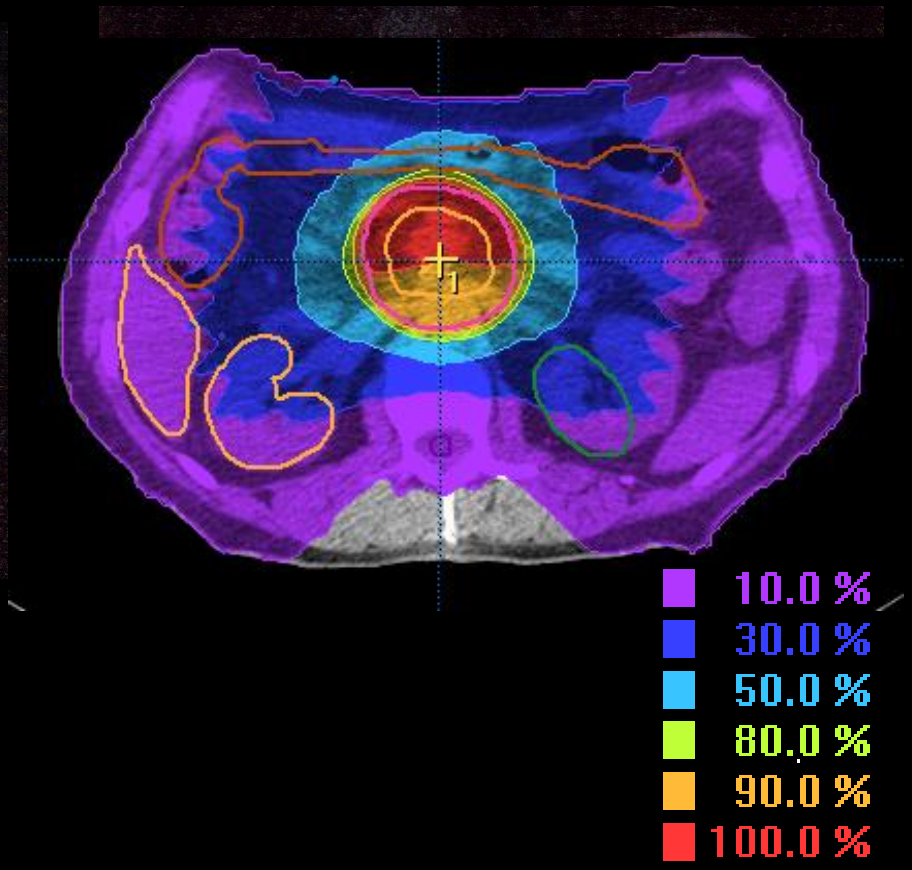
Convergence of imaging
&
accuracy in treatment plannig

^{18}F-deoxyglucose PET for rectal cancer: postsurgical local relapse

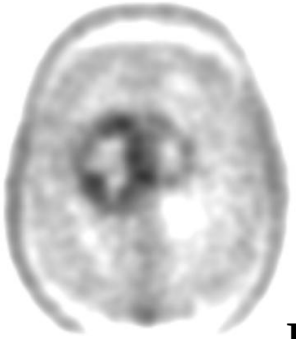




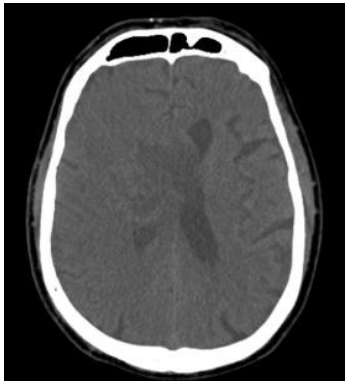
^{18}F-deoxyglucose PET for pacreatic cancer: postsurgical residual disease



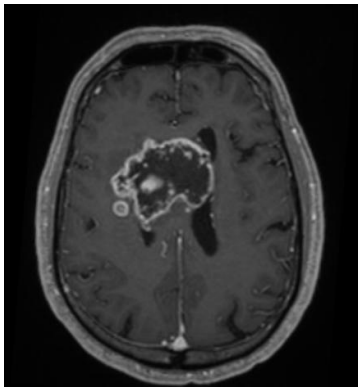
PET imaging
F_{18} - Tyrosine (FET)



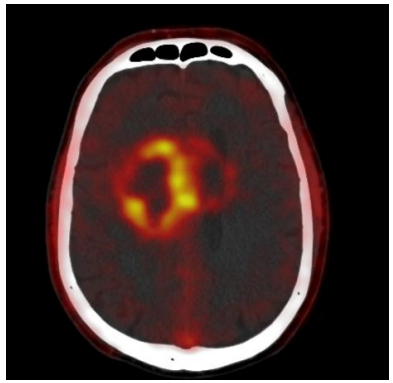
PET



CT



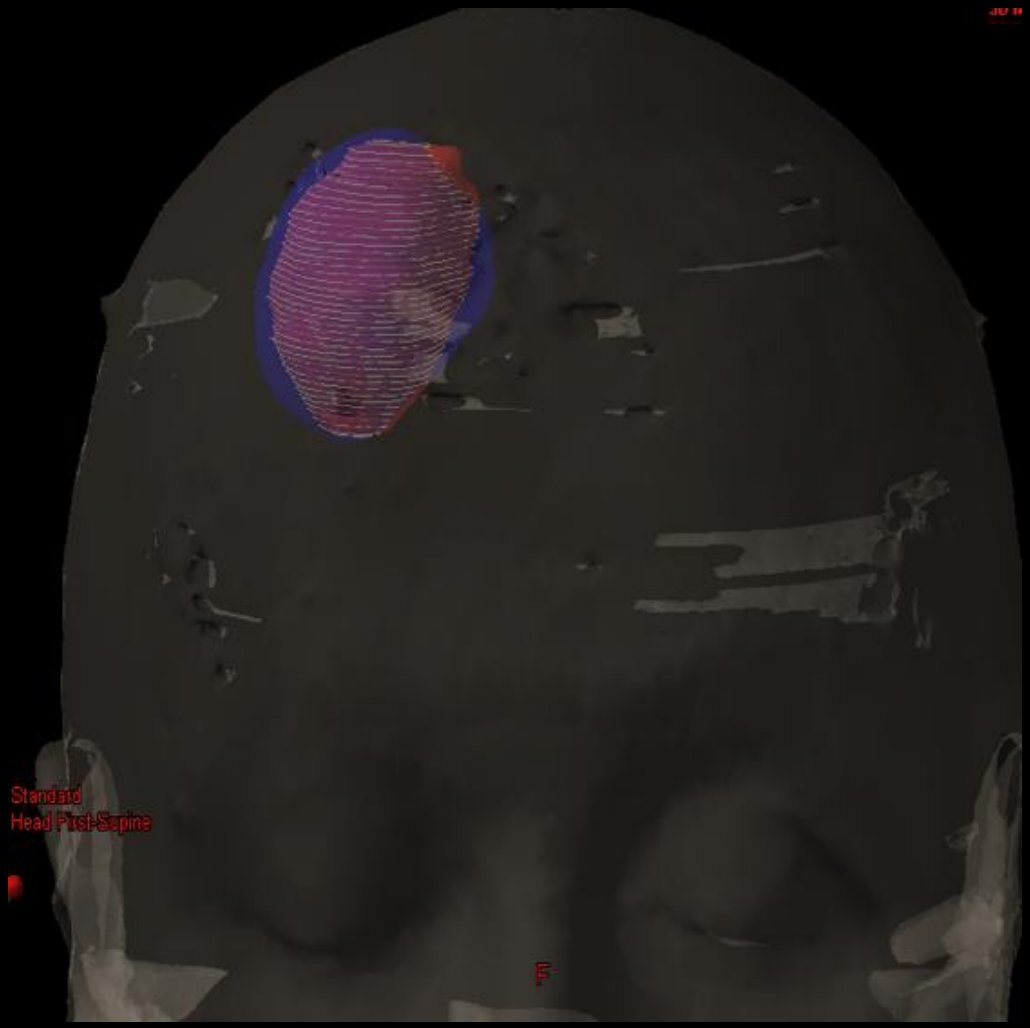
MRI



PET-CT

Applications: - Brain tumours (glioblastoma)

Good matching between the PET/CT-target and the MRI target

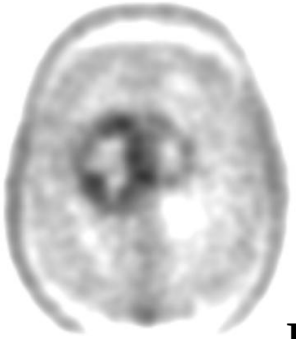


Weber DC et al, Radiat Oncol 2008

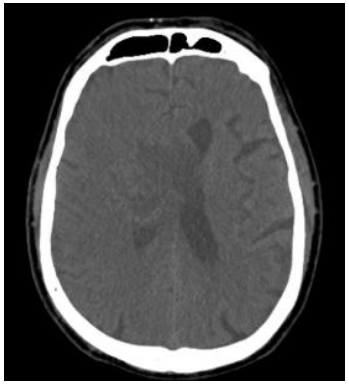
Substantial mismatch between the PET/CT-target and the MRI-target

Weber DC et al, Radiat Oncol 2008

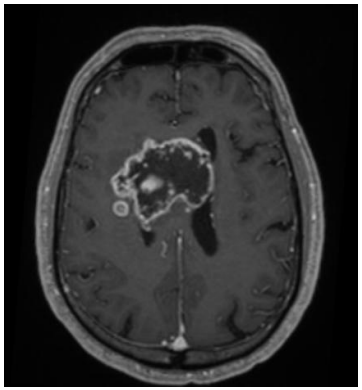
PET imaging
F_{18} - Tyrosine (FET)



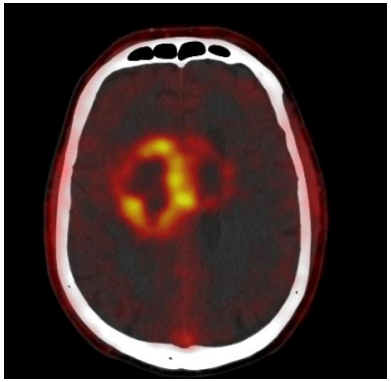
PET



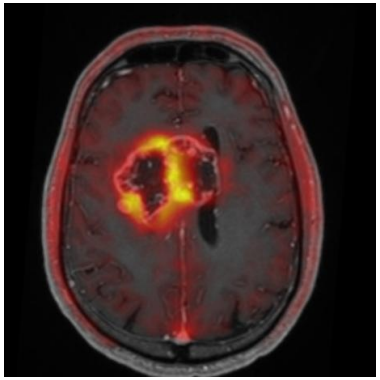
CT



MRI



PET-CT



PET-MRI

Applications: - Brain tumours (glioblastoma)

PET-MRI in Geneva

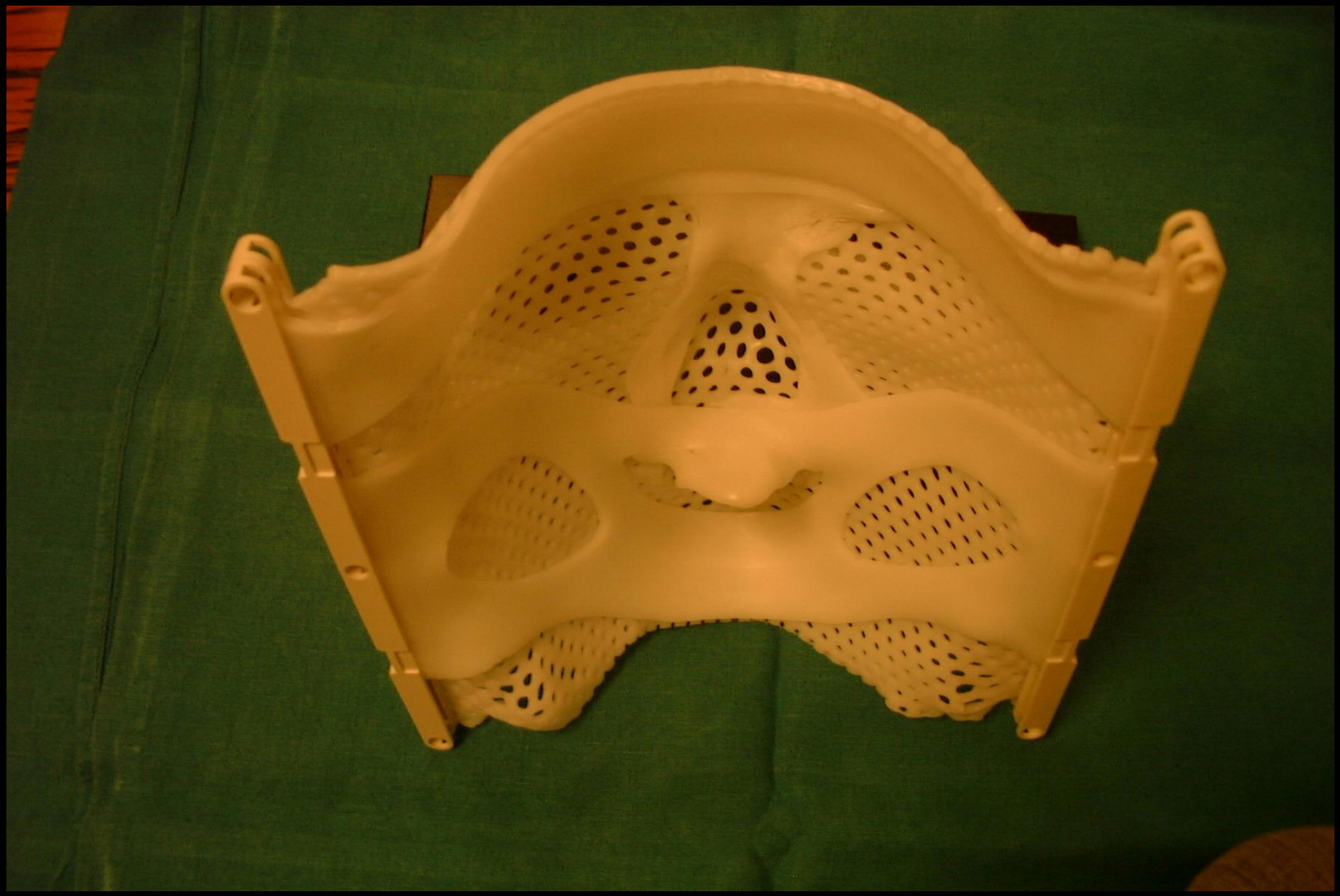
Optimization of treatment precision…

- Improvement in patient's repositioning
- Reduction of internal organ motion

External immobilization

- Thermoplastic mask
- Customized vacuum body cast
- Stereoatactic extracranial infrared guided repositioning system
- Treatment set-up tune-up: bone registration

Positioning / Patient fixation



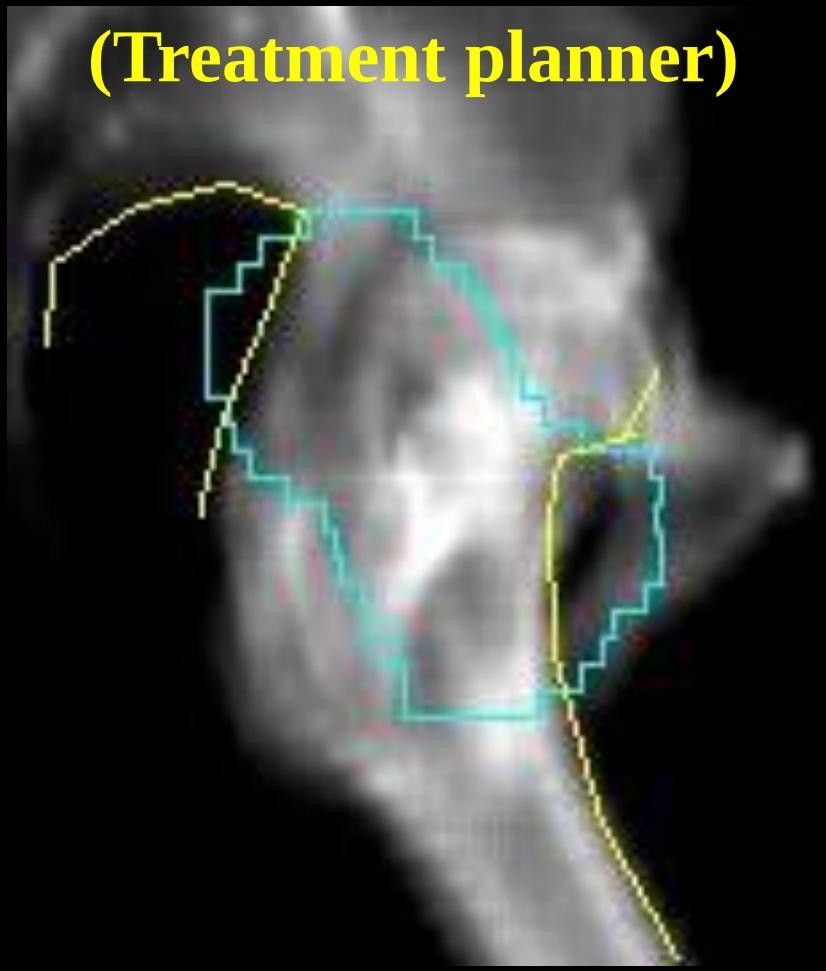
Customized vacuum body cast

Repositioning system for extracranial stereotactic radiotherapy

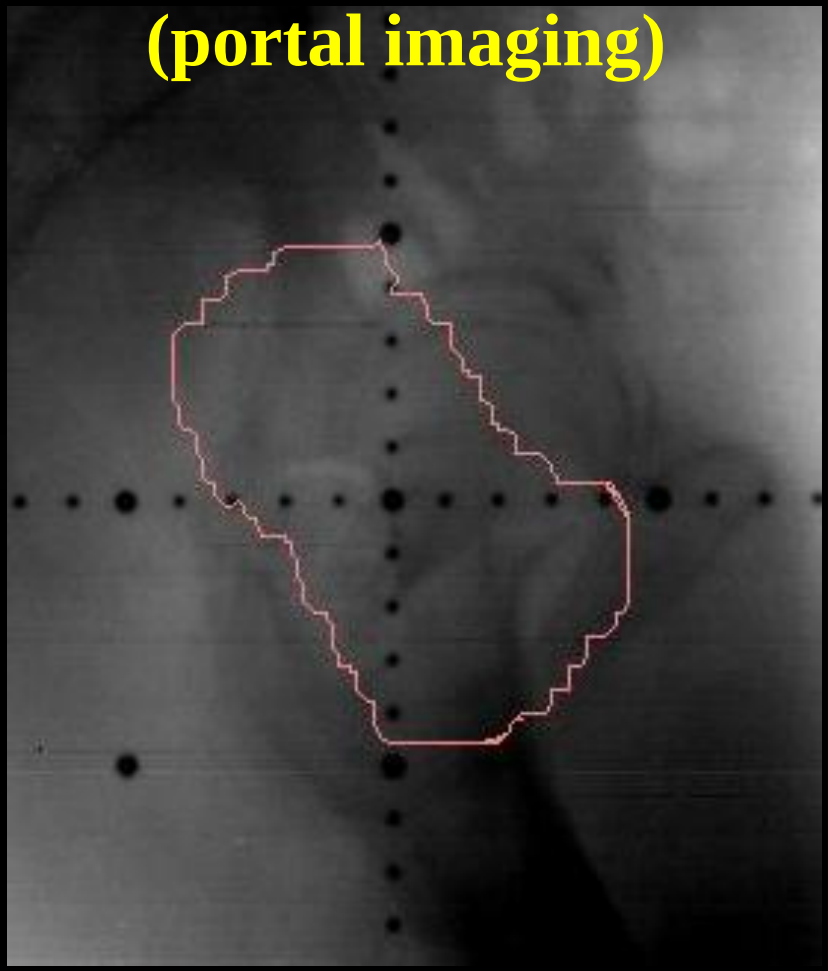

Calibration
Load Patient
Position Patient
New Patient
Store Position
Ultrasound
Video
Exit
View
Live
Ref. Image + Live
Ref. Image - Live
Reference Image
Body Shape
current
target
Objects
current
Store Image
Reference
Document
Done
Press Enable Button
MATCH
ACCURACY
Vertical
-000.77
Longitud.
+000.22
OK
Lateral
-000.38
OK
Table
+000.32°
OK

On-line treatment verification: electronic portal imaging devices

DRR lateral field
(Treatment planner)



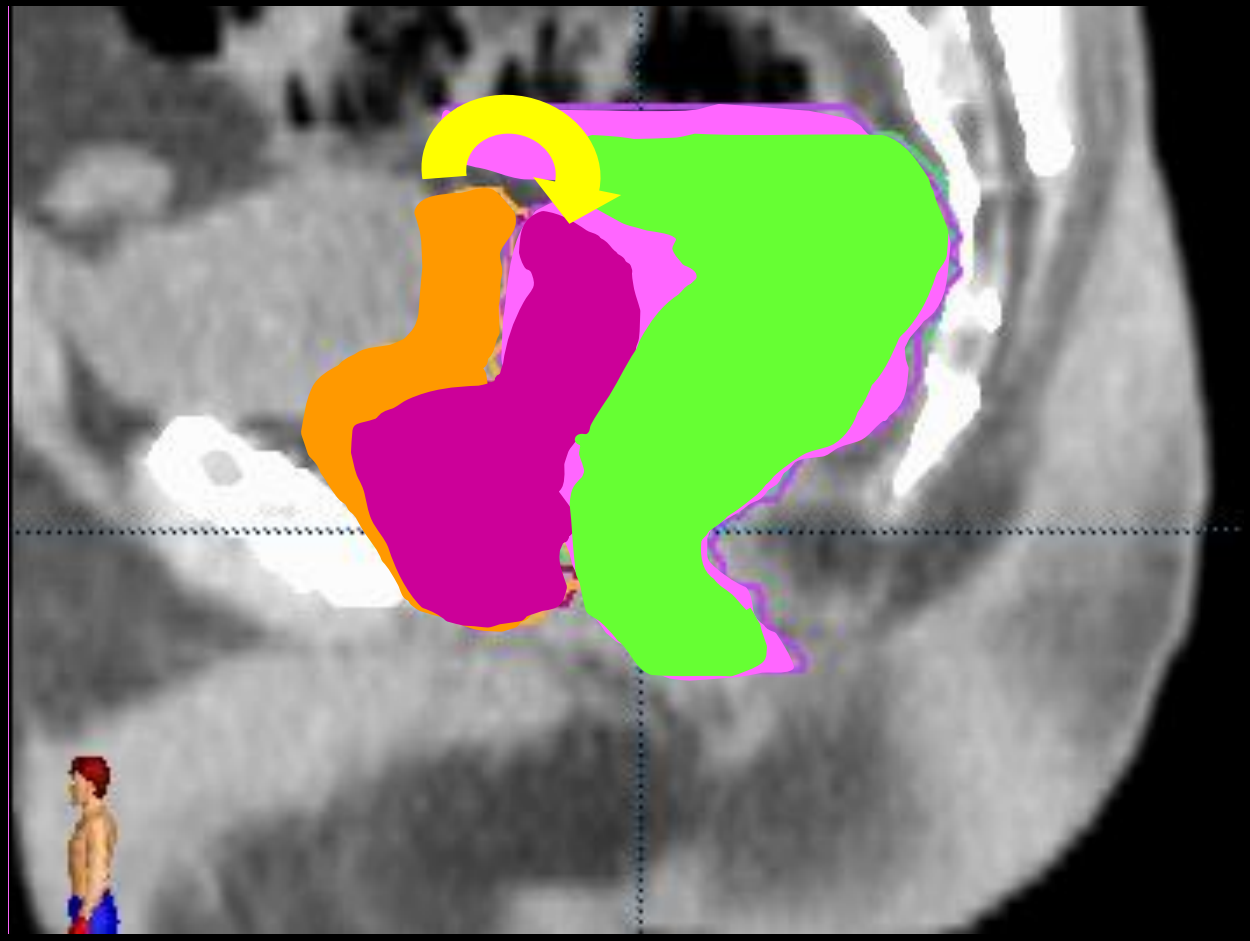
Amorphous silycon
(portal imaging)



Internal organ immobilization

- Magnetic resonance imaging endorectal probe inflated with 60 cc air
- Fiducial marker registration

Apex centered sagittal rotation



CTV at planning

CTV on-treatment

Rectum at planning

Rectum on-treatment

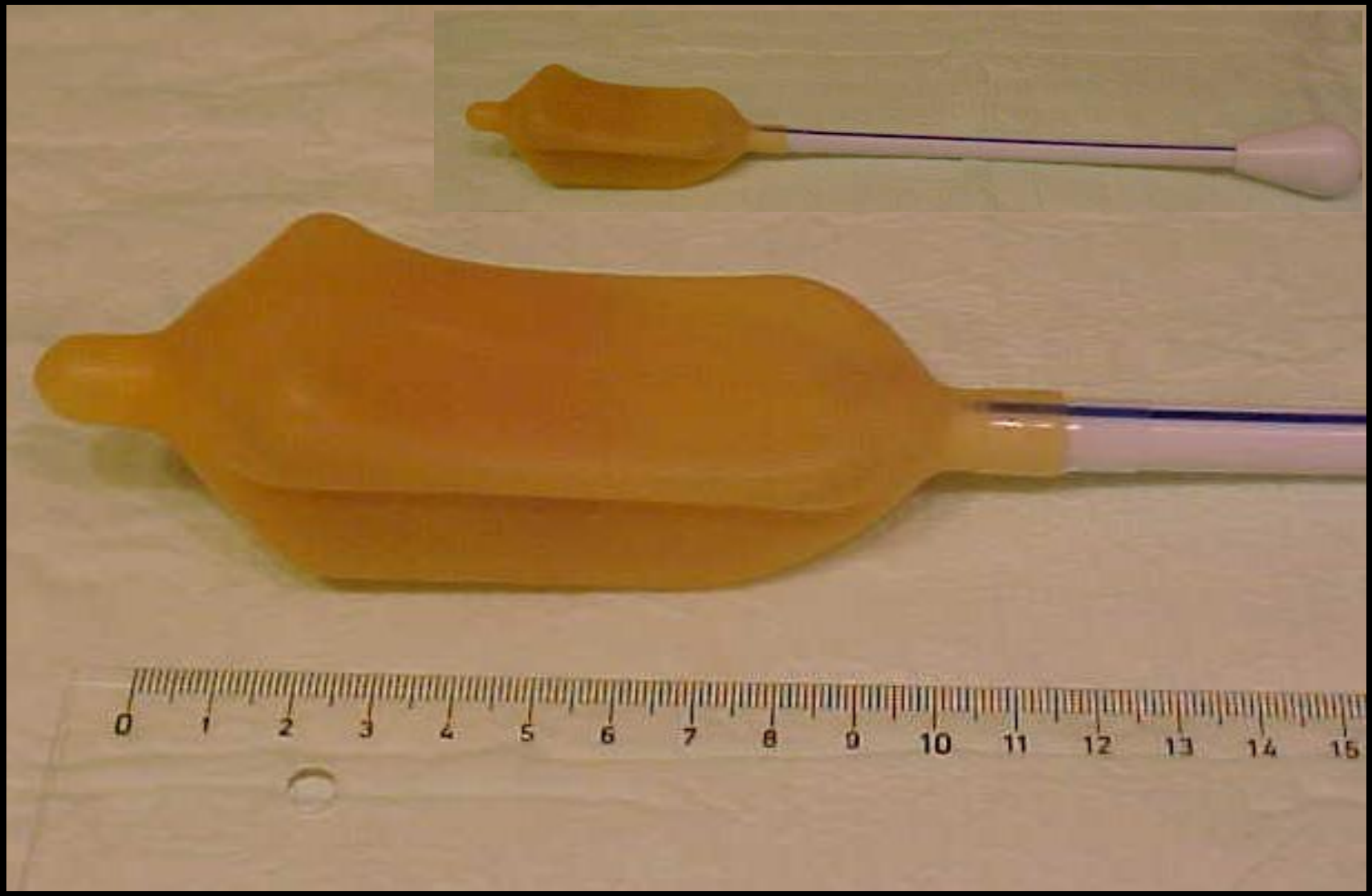

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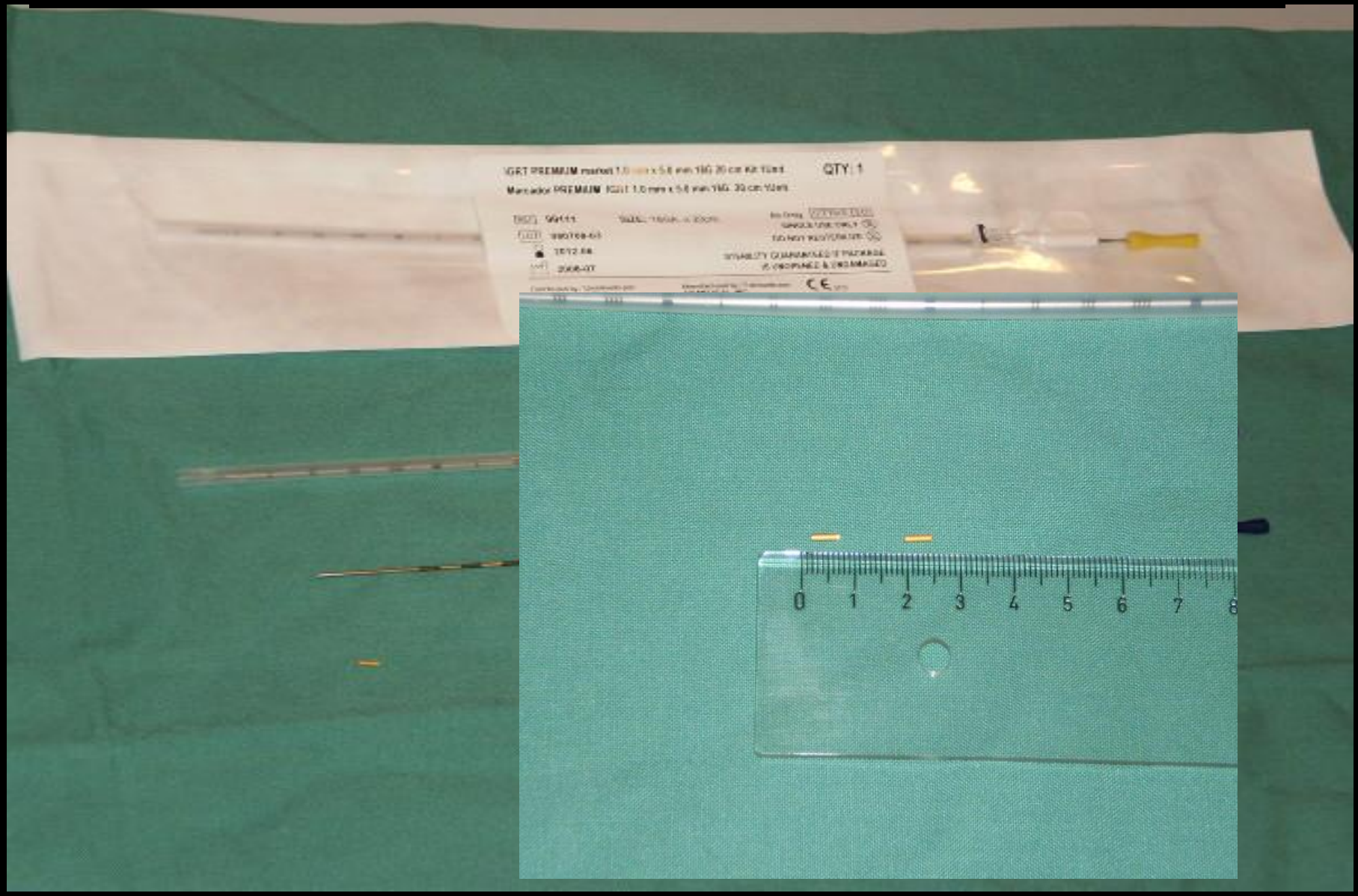
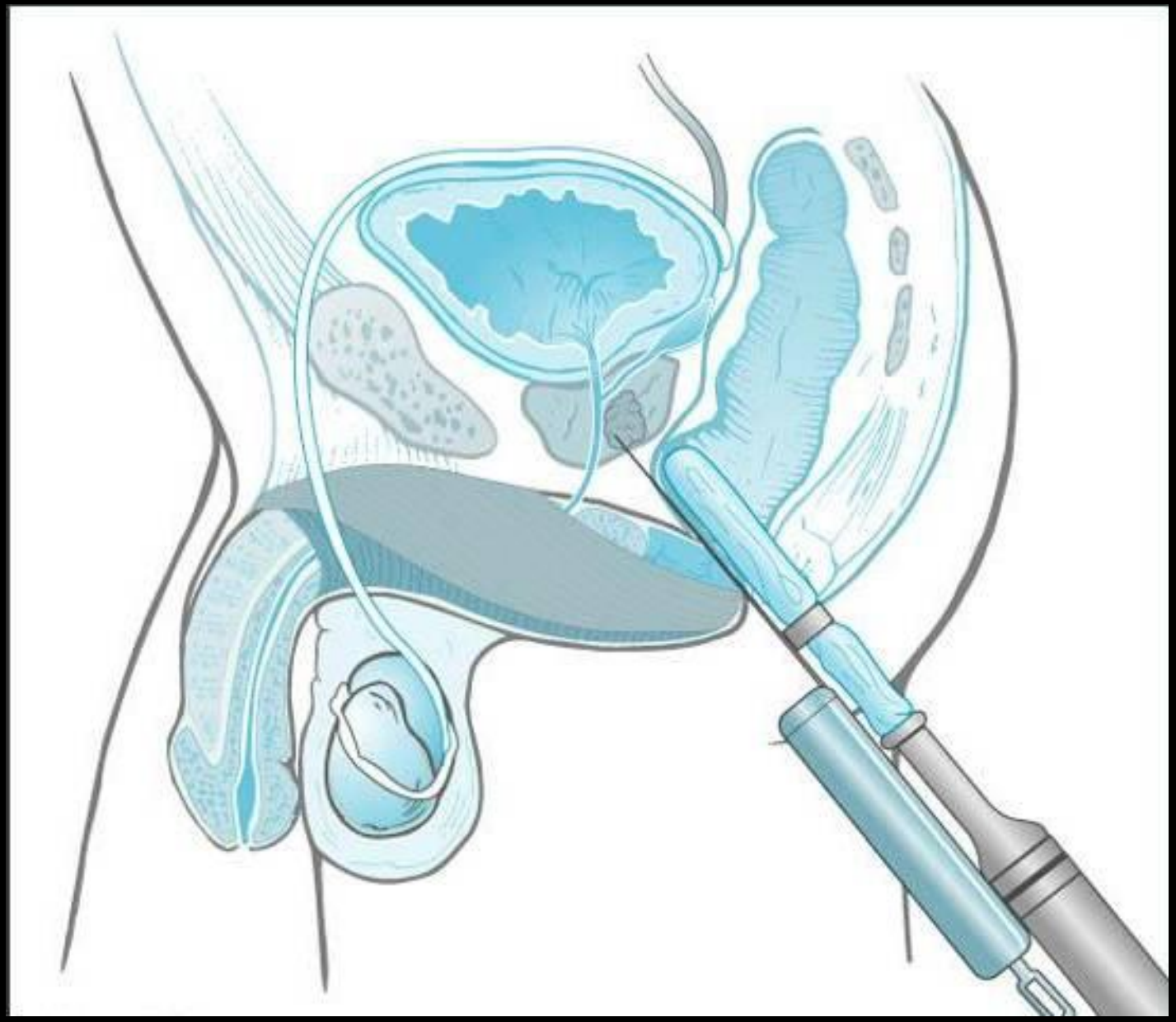
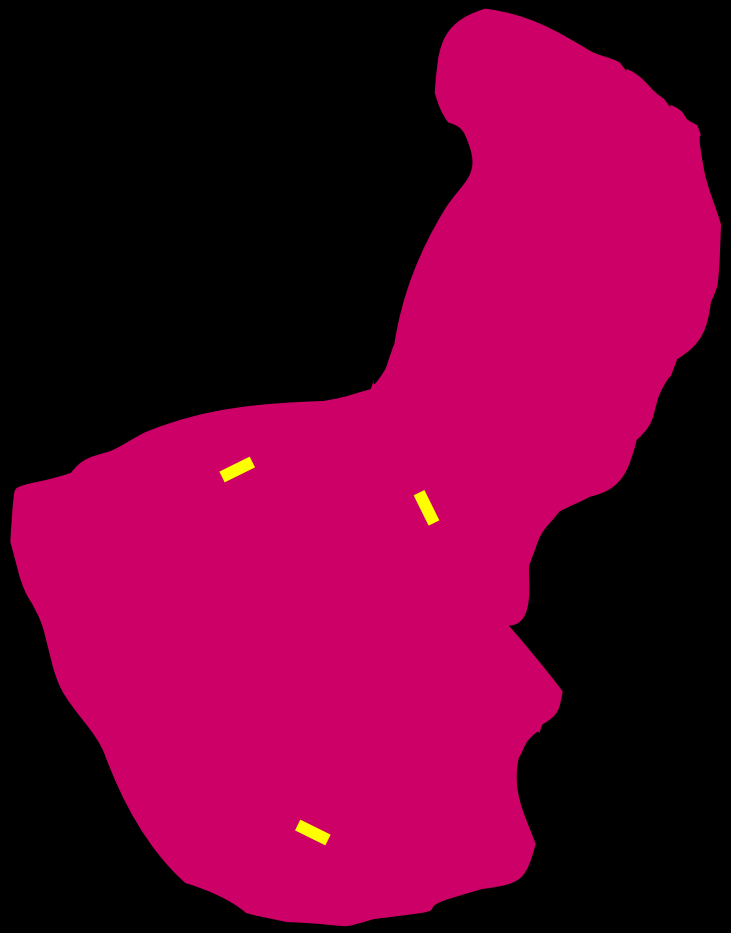
Image Guided Radio Therapy (IGRT)

Fiducial marker registration

Gold seed implants





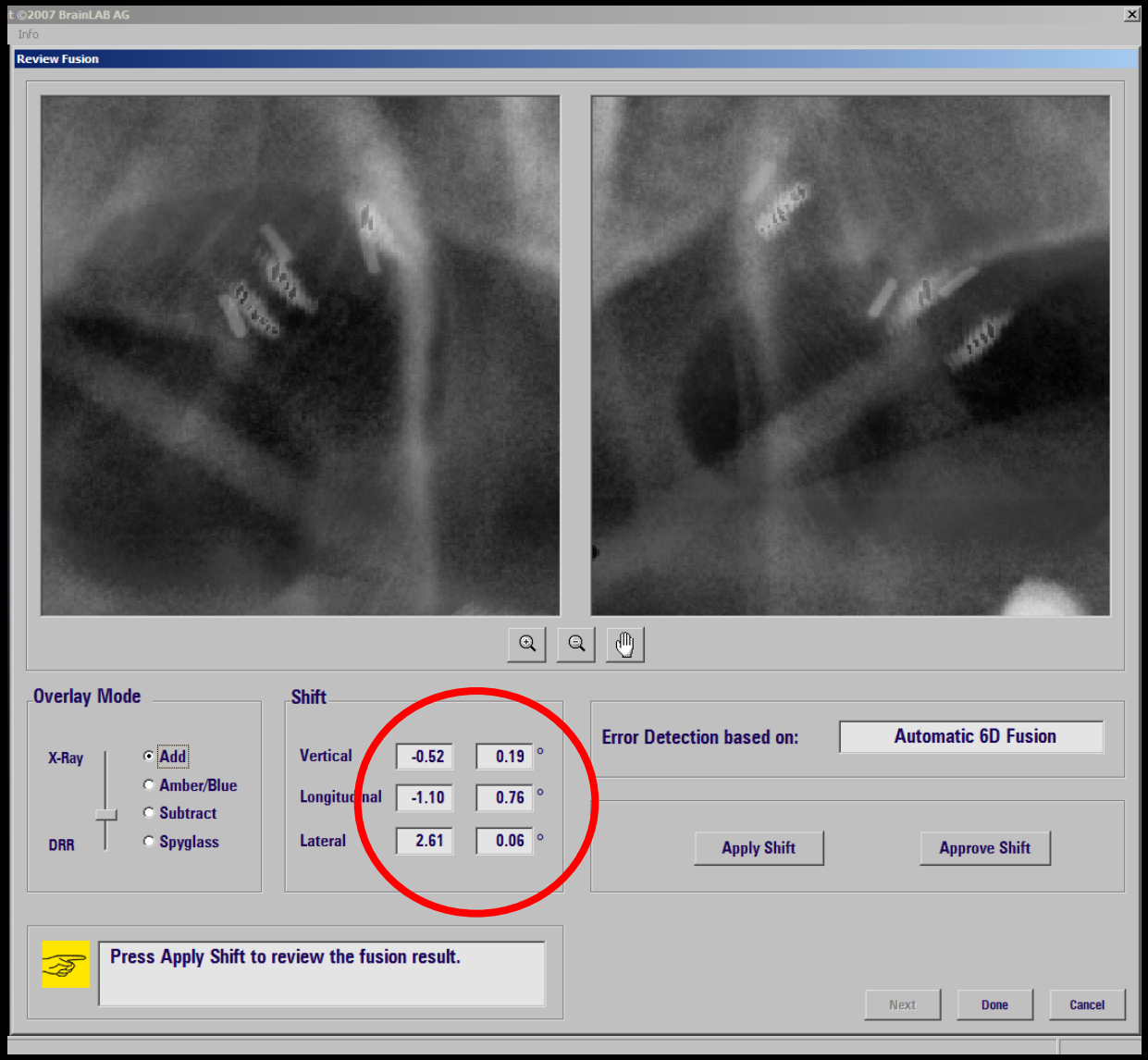


CT with fiducial markers

IGRT: automatic image verification

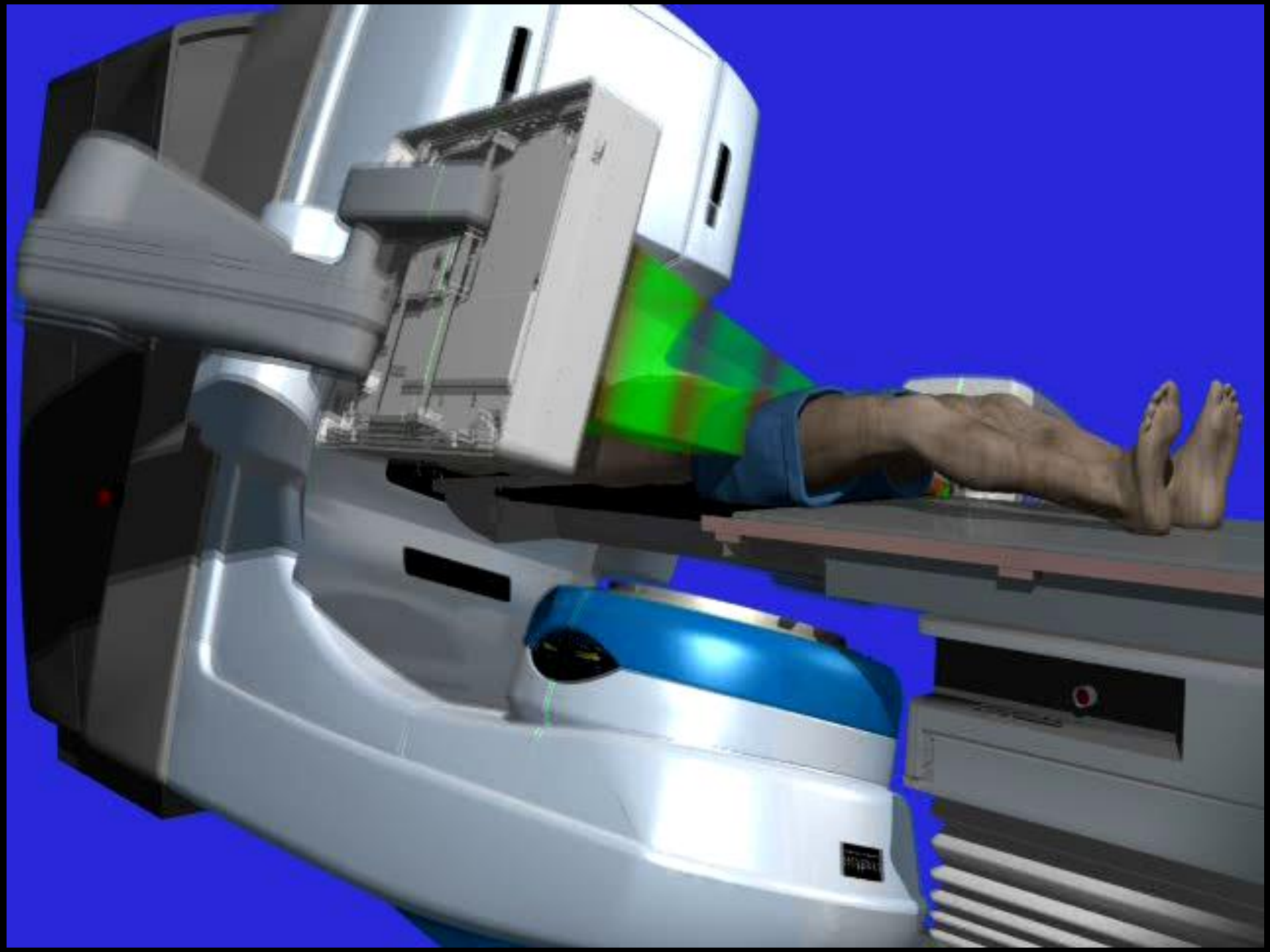
CT and X-ray image fusion

fusion verification followed by…



…automatic correction

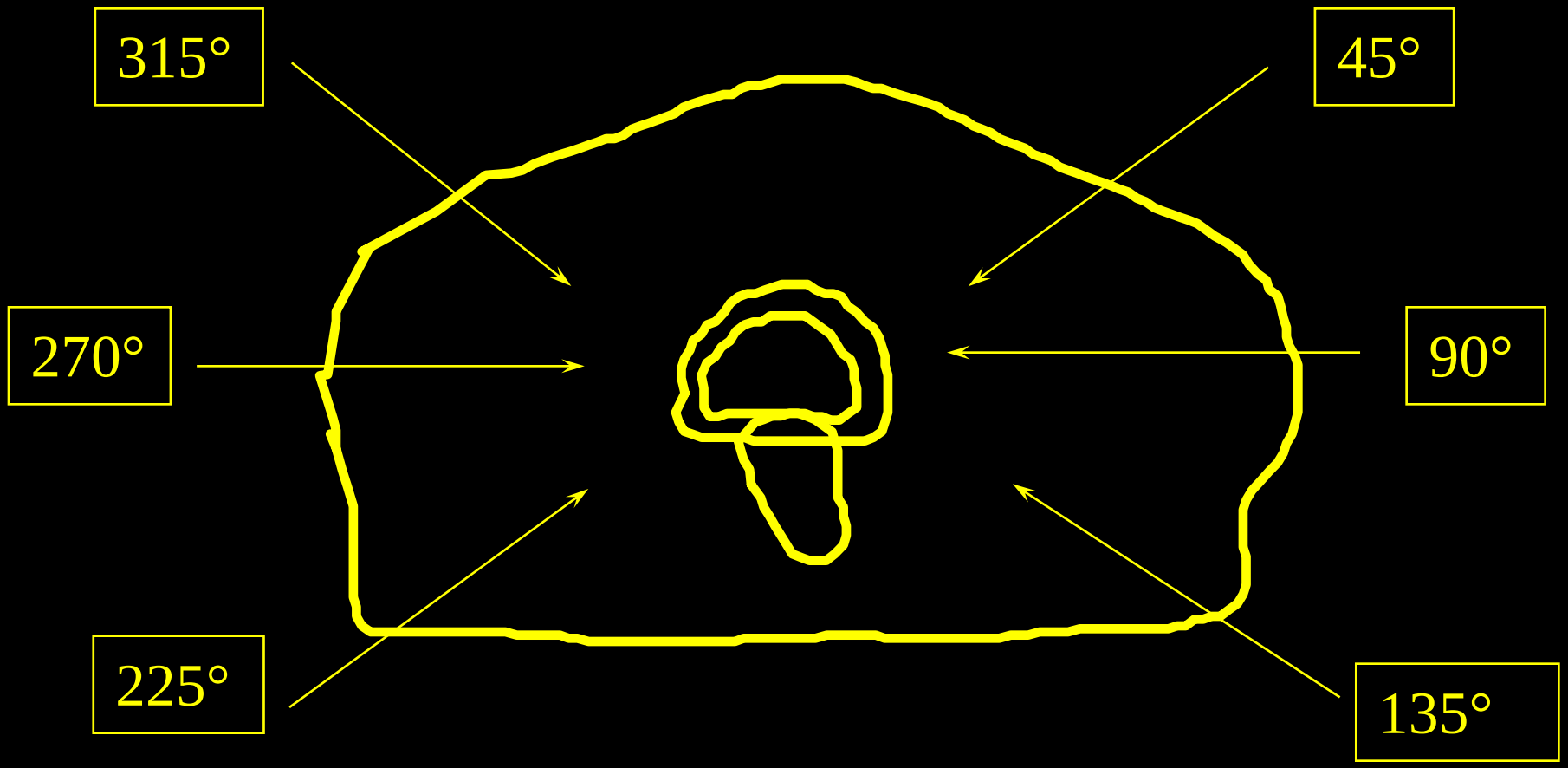
Cone Beam CT (CBCT)



IGRT: respiratory gating

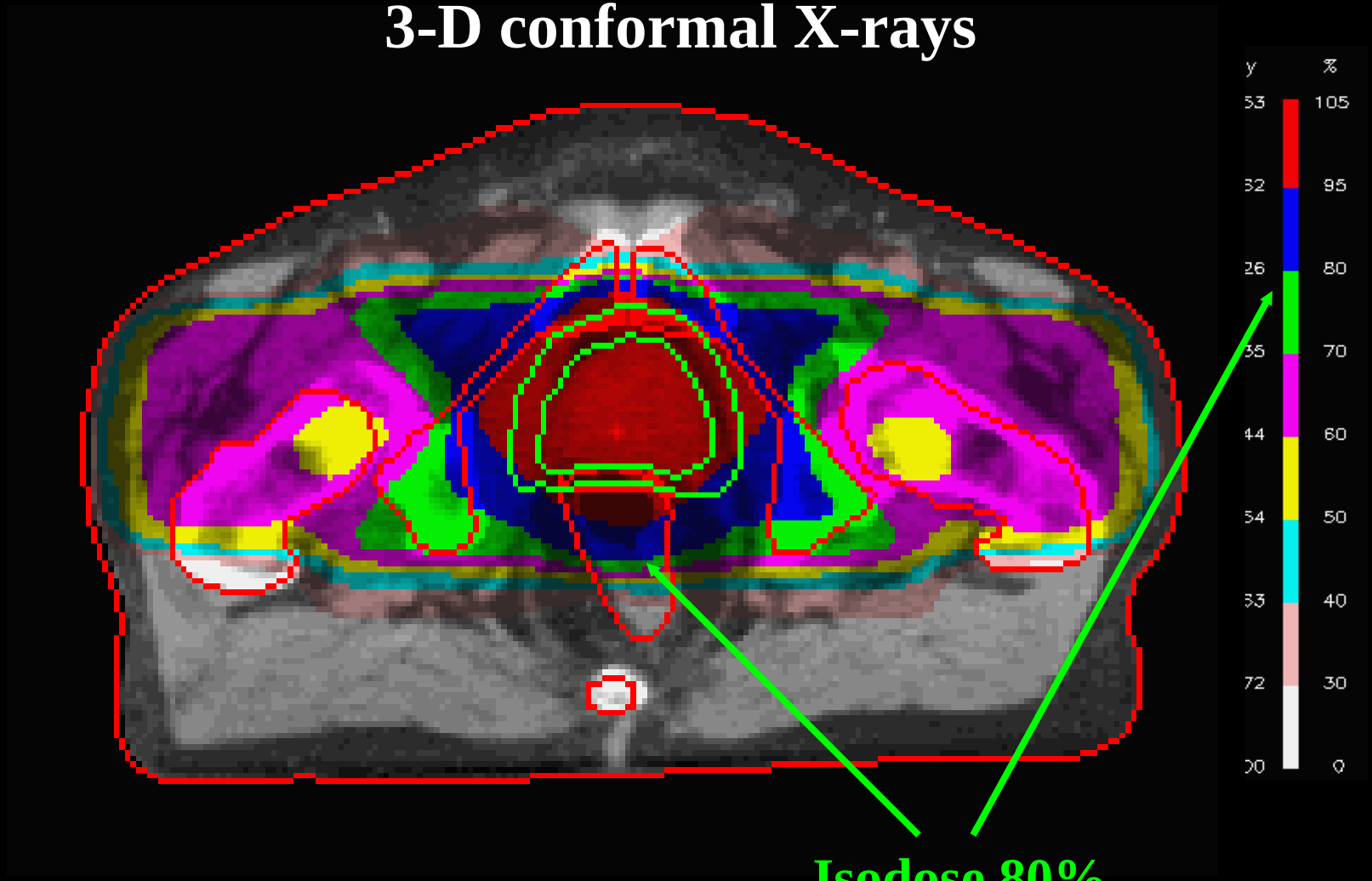
3-D conformal radiotherapy (forward planned)

X-rays



Prostate (100%: 81 Gy)

3-D conformal X-rays

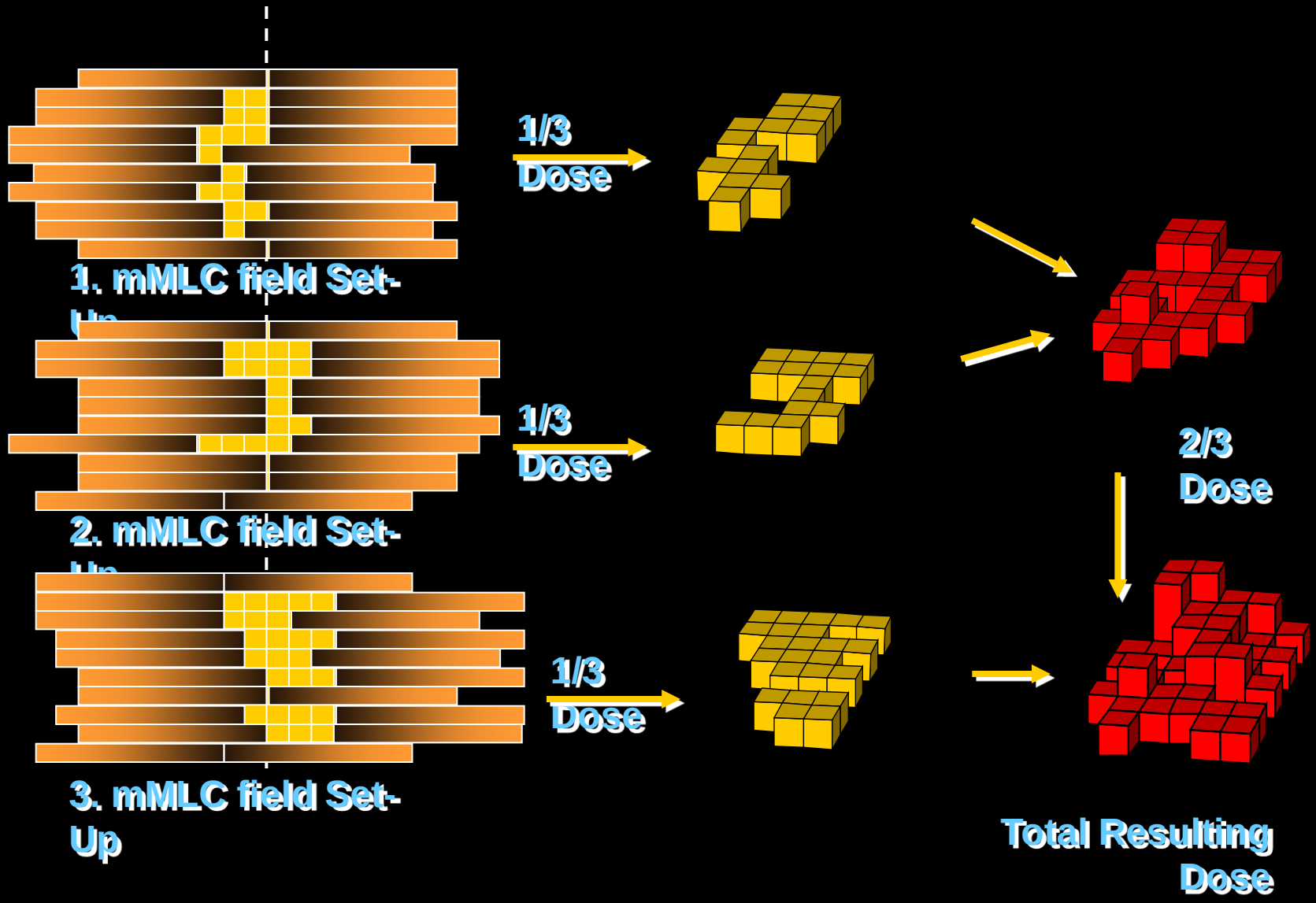


…is further optimization possible?

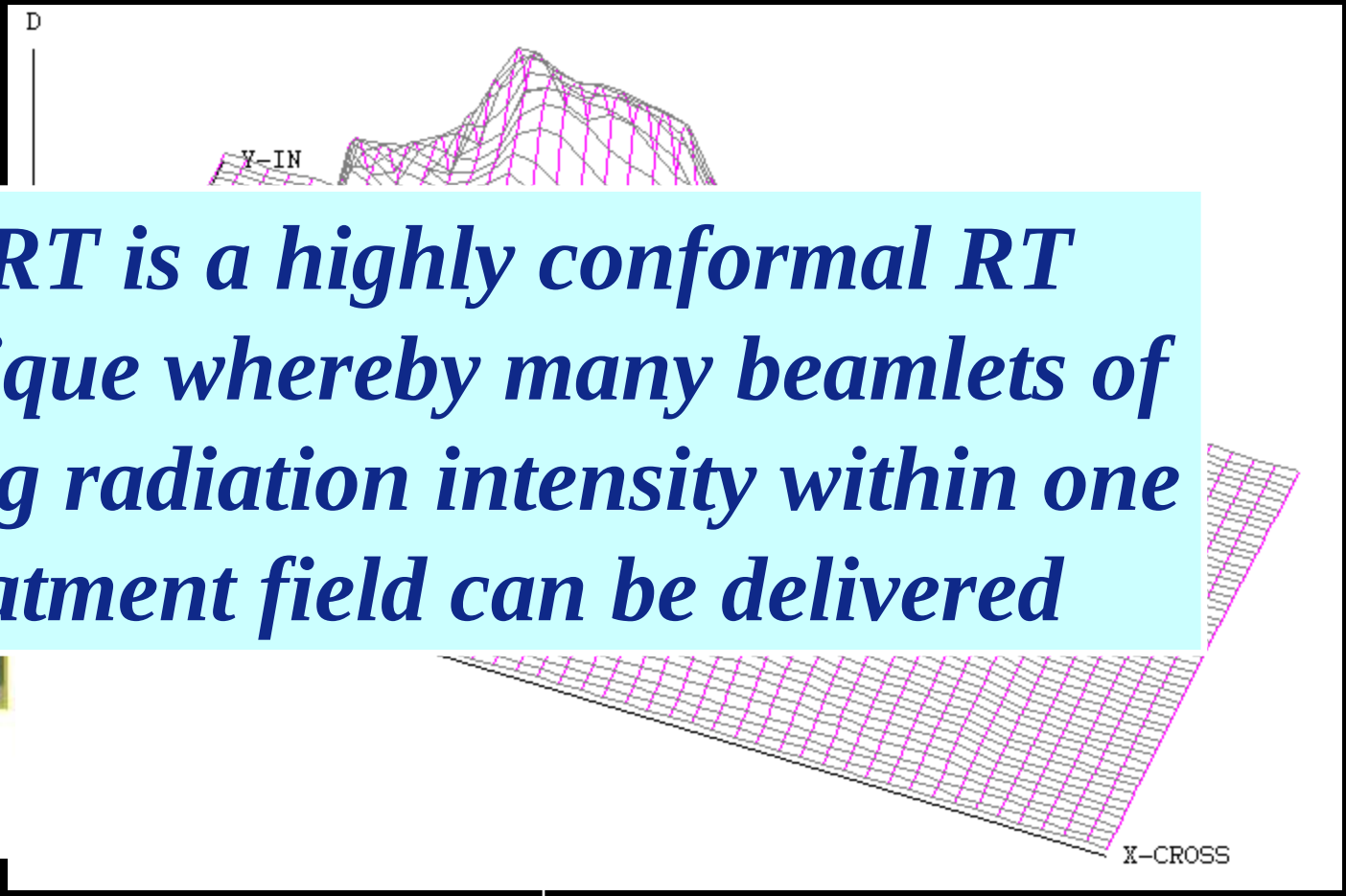
New treatment technologies such as **intensity modulated X-ray beams** and **proton beams** can provide an even superior dose distribution compared to conventional 3-D conformal RT

Intensity Modulated X-ray Beams (IMRT)

IMRT


1/3
Dose
1. mMLC field Set-
1/3
Dose
2. mMLC field Set-
2/3
Dose
1/3
Dose
3. mMLC field Set-
Up
Total Resulting
Dose

*I*ntensity *M*odulated *R*adiation *T*herapy

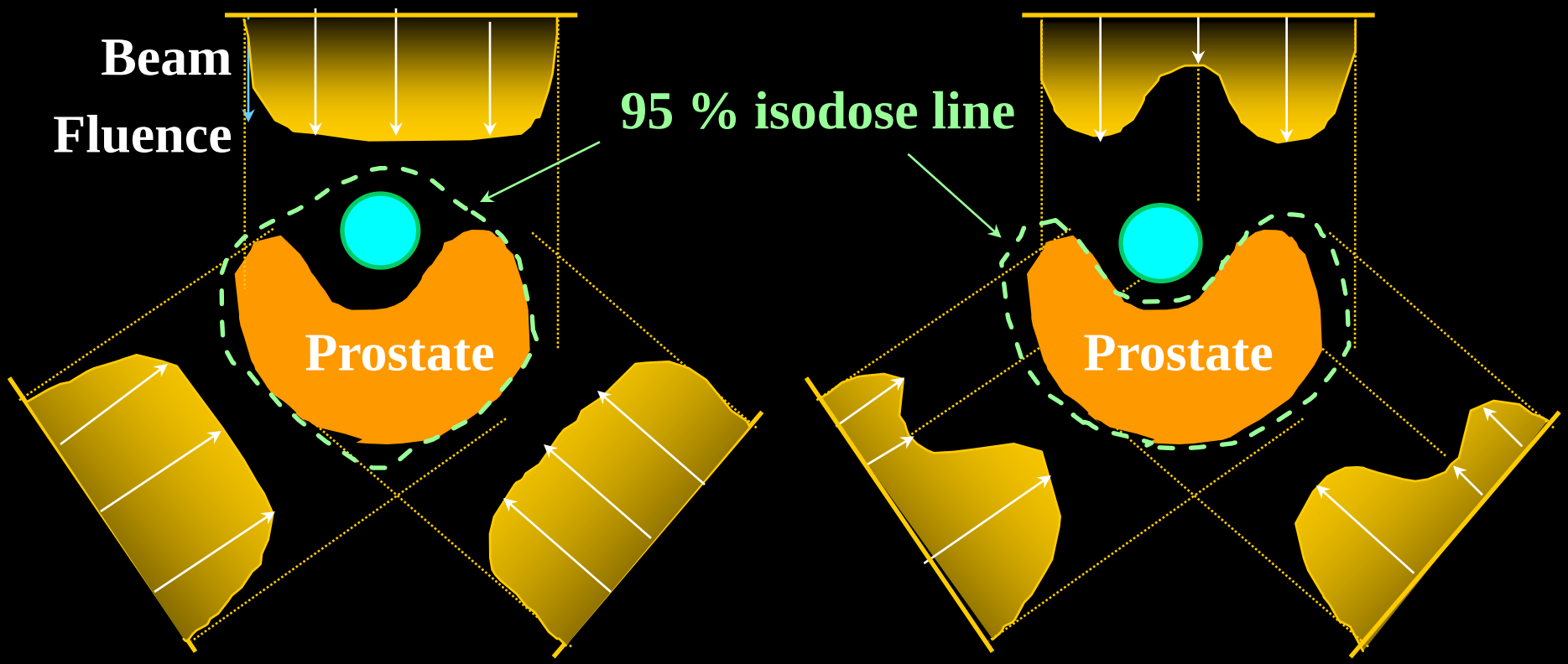


IMRT is a highly conformal RT technique whereby many beamlets of varying radiation intensity within one treatment field can be delivered

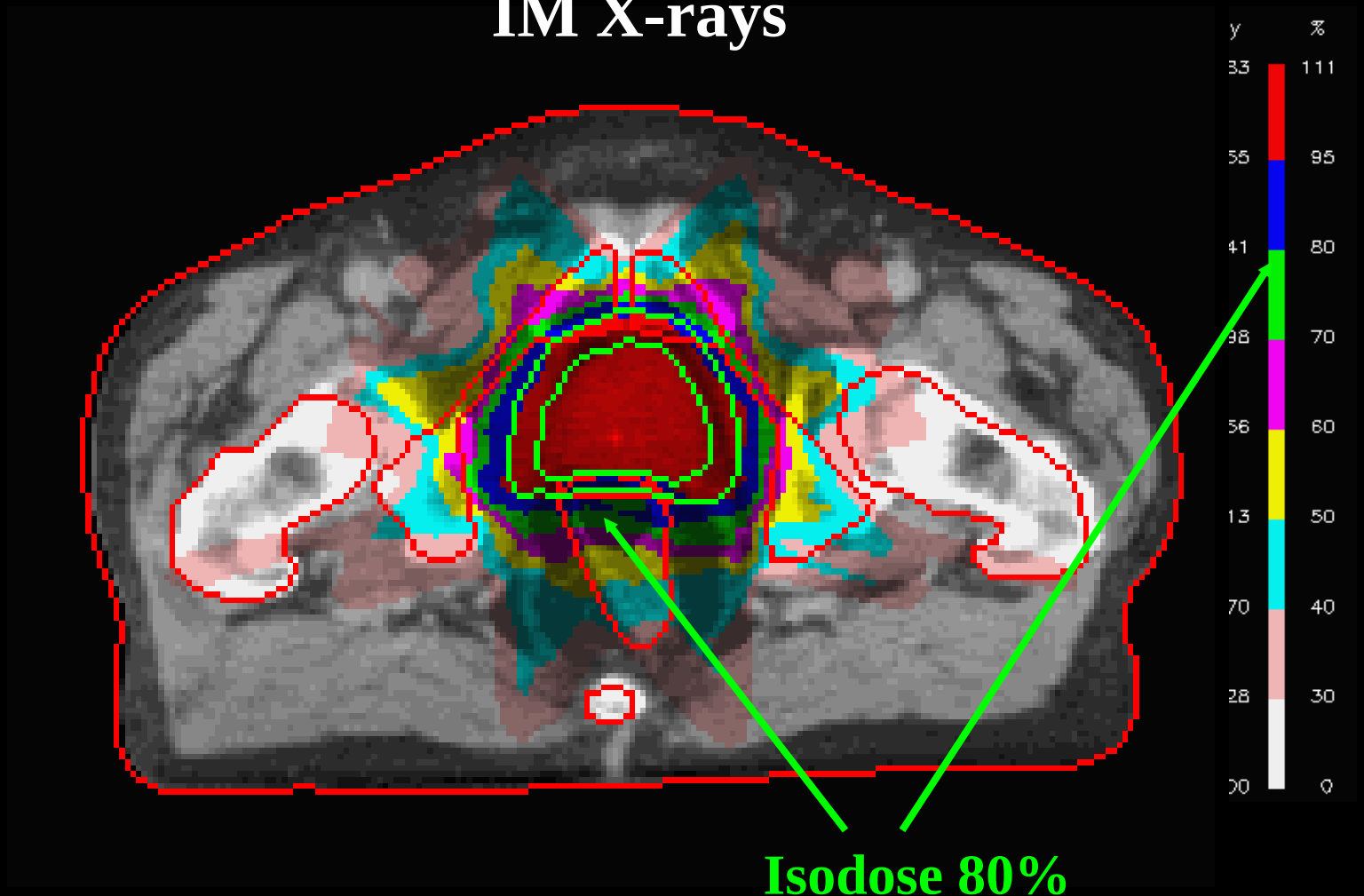
Fluence or Intensity Map

3D Dose Distribution

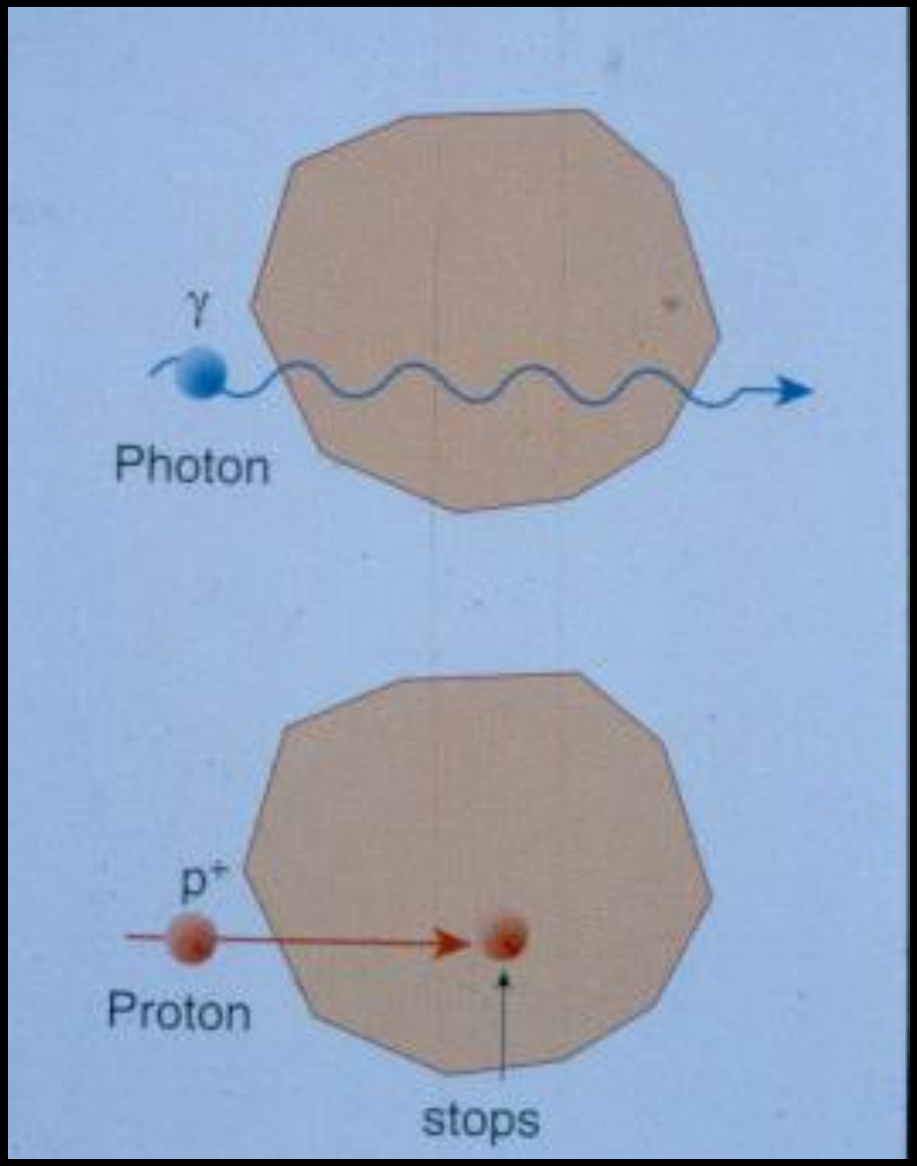
3D CRT vs. IMXT



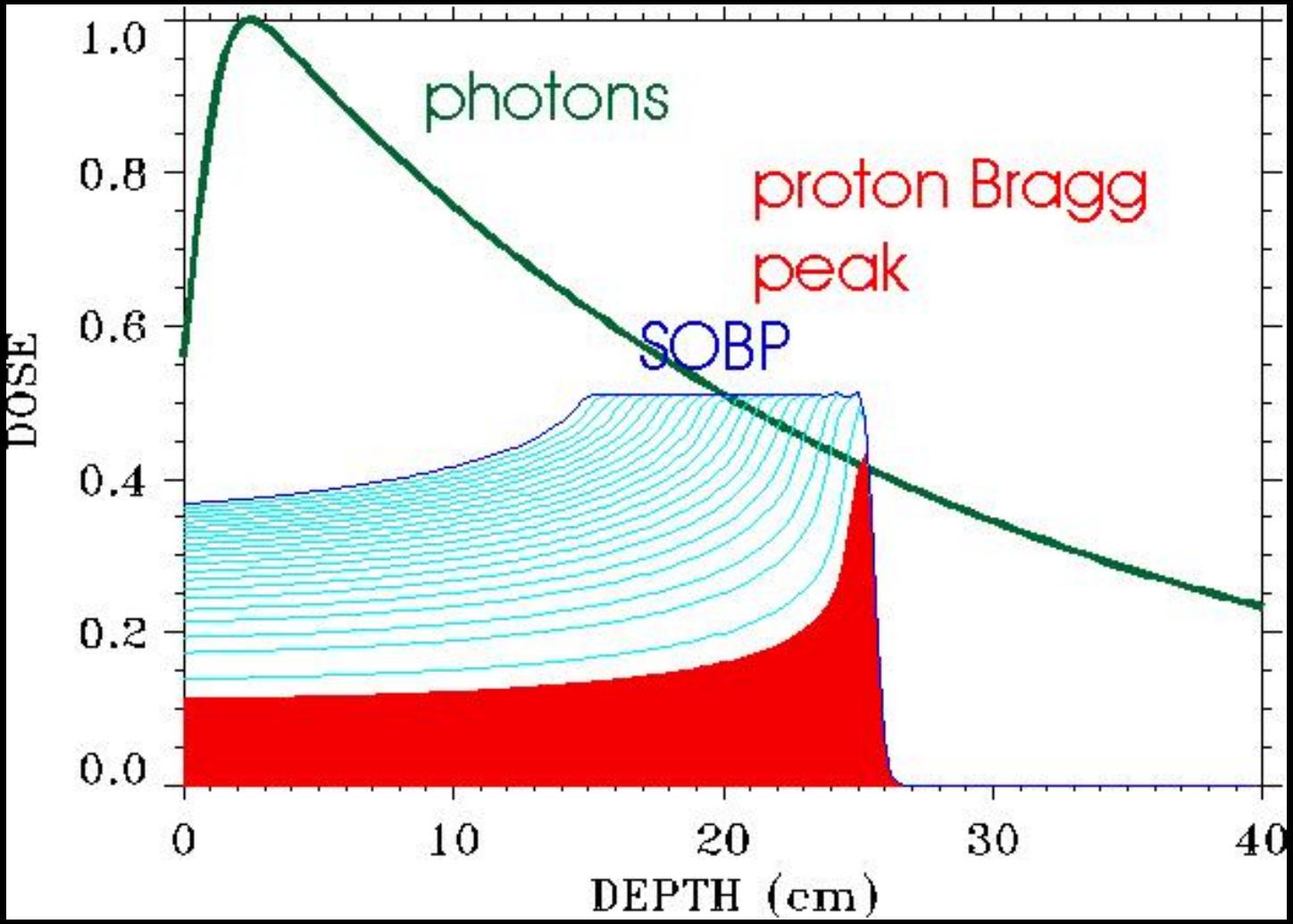
Prostate (100%: 81 Gy)

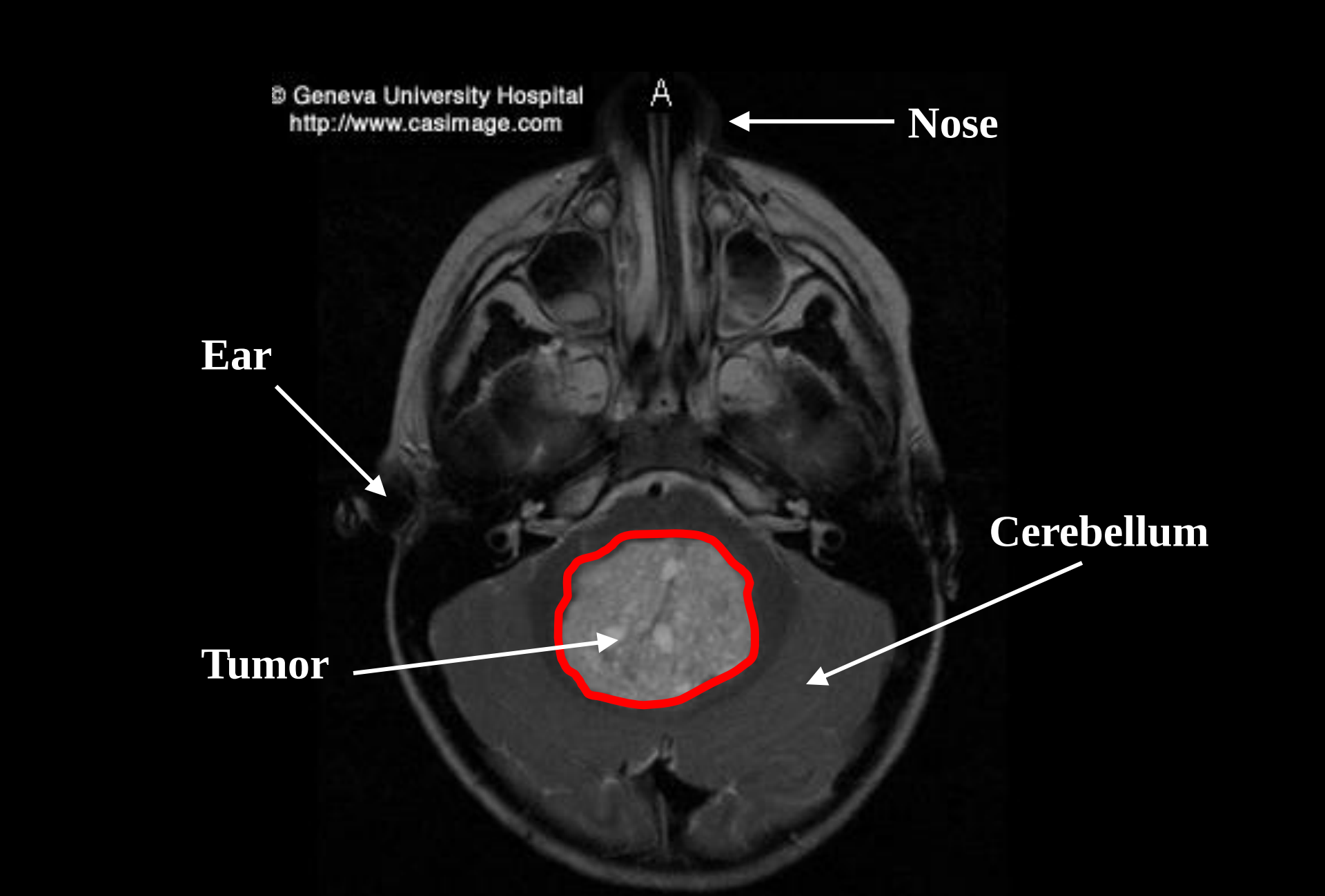


Proton Beams

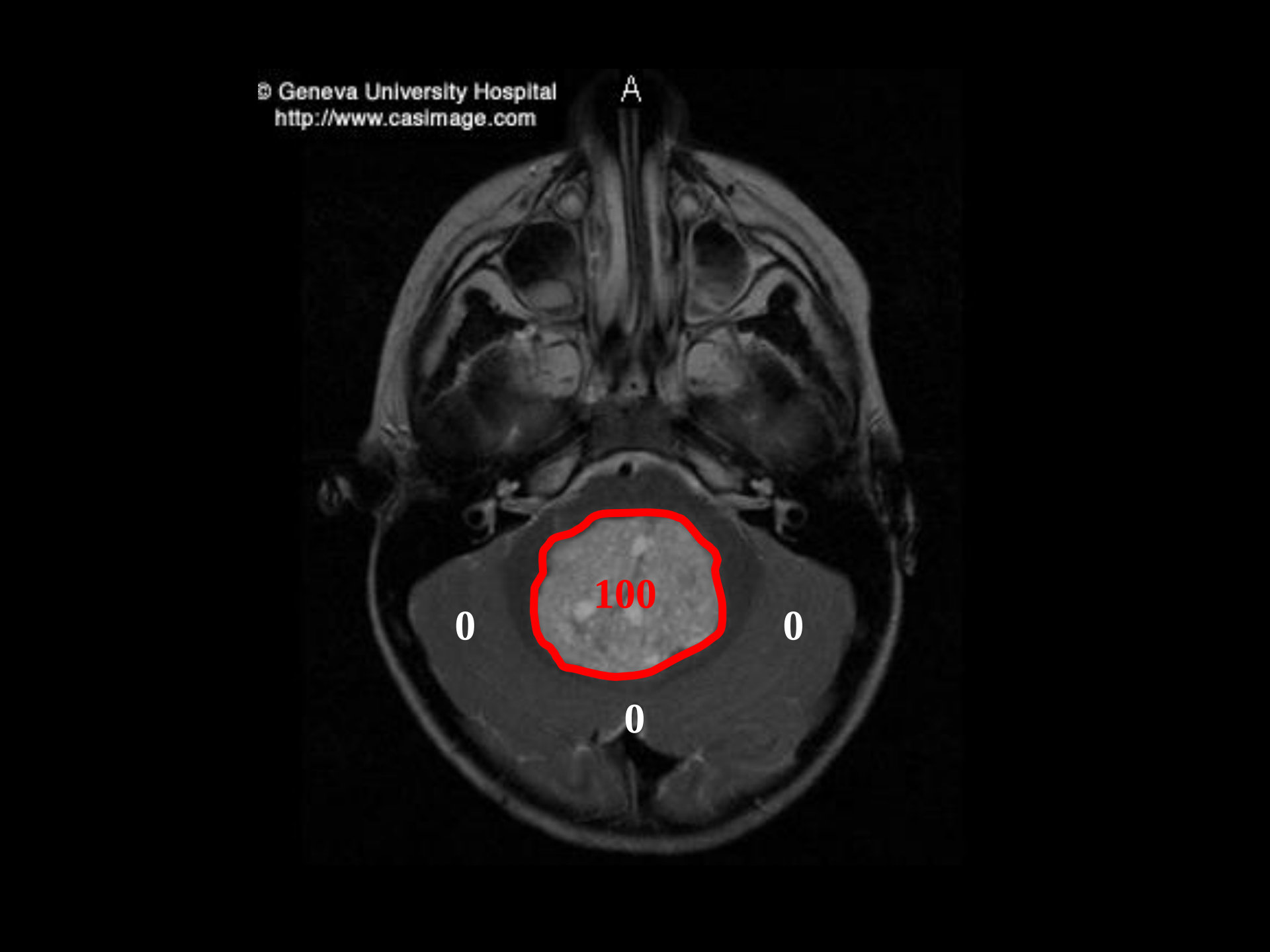

γ
Photon
p+
Proton
stops

Protons vs Photons





MRI: tumor of the Central Nervous System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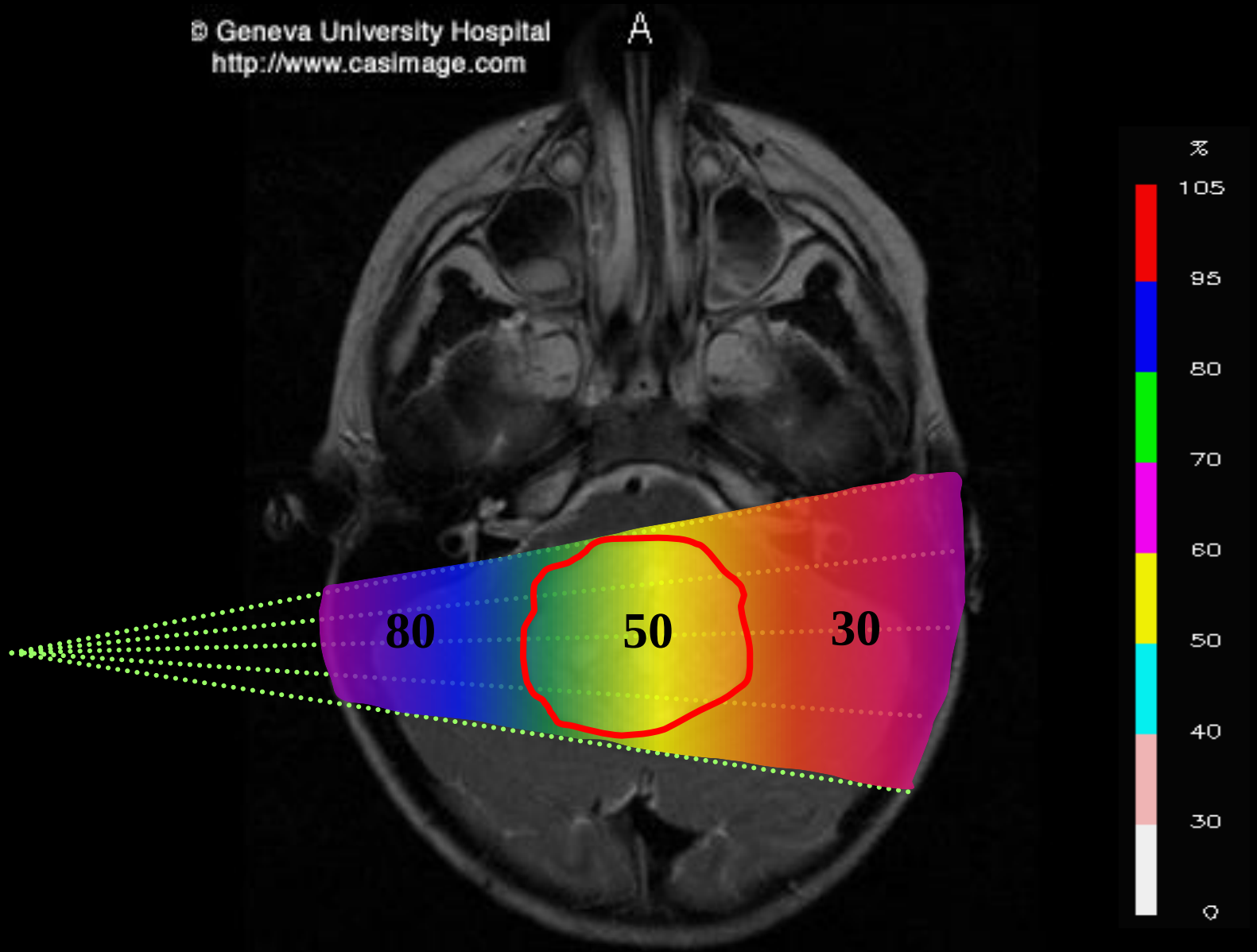
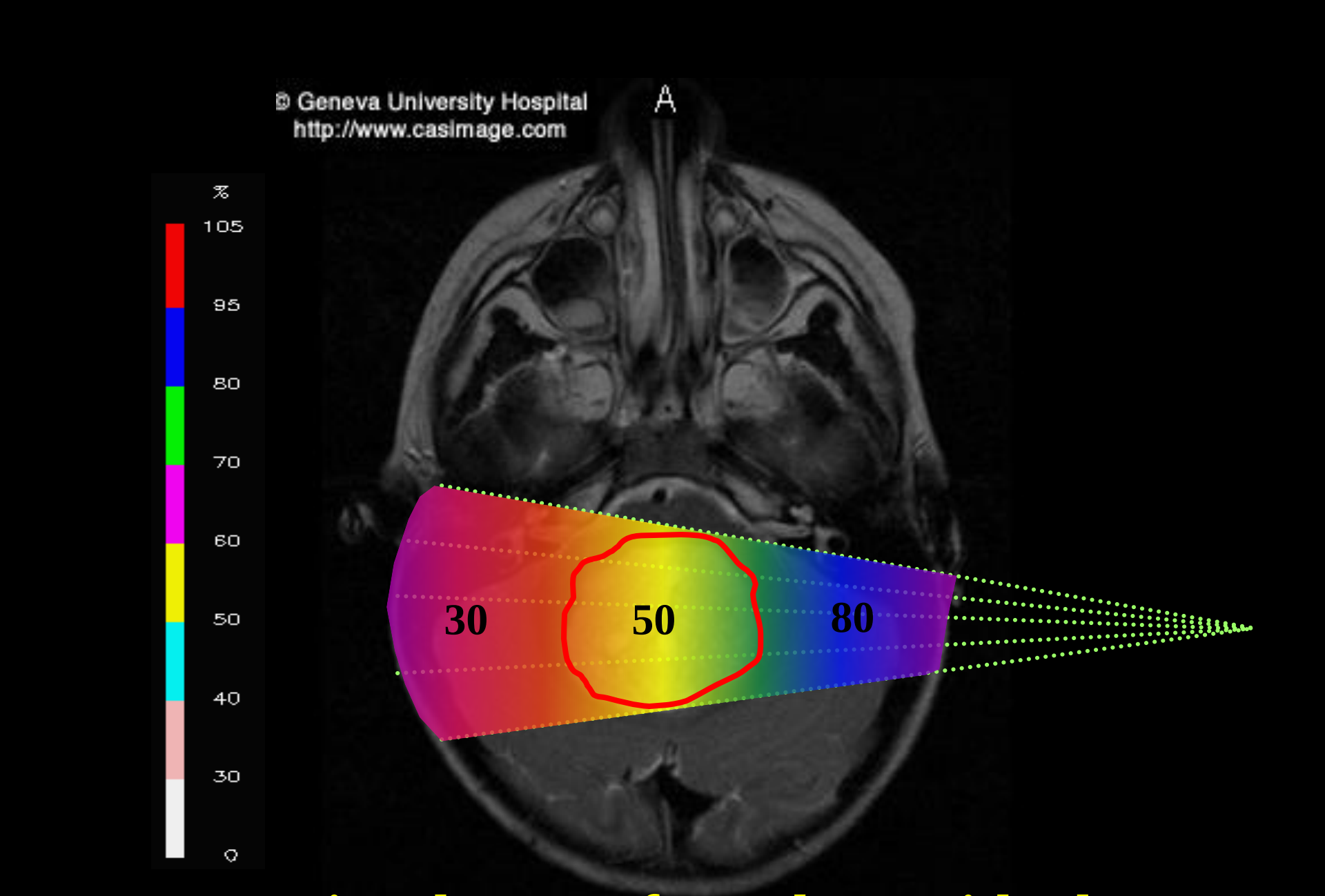
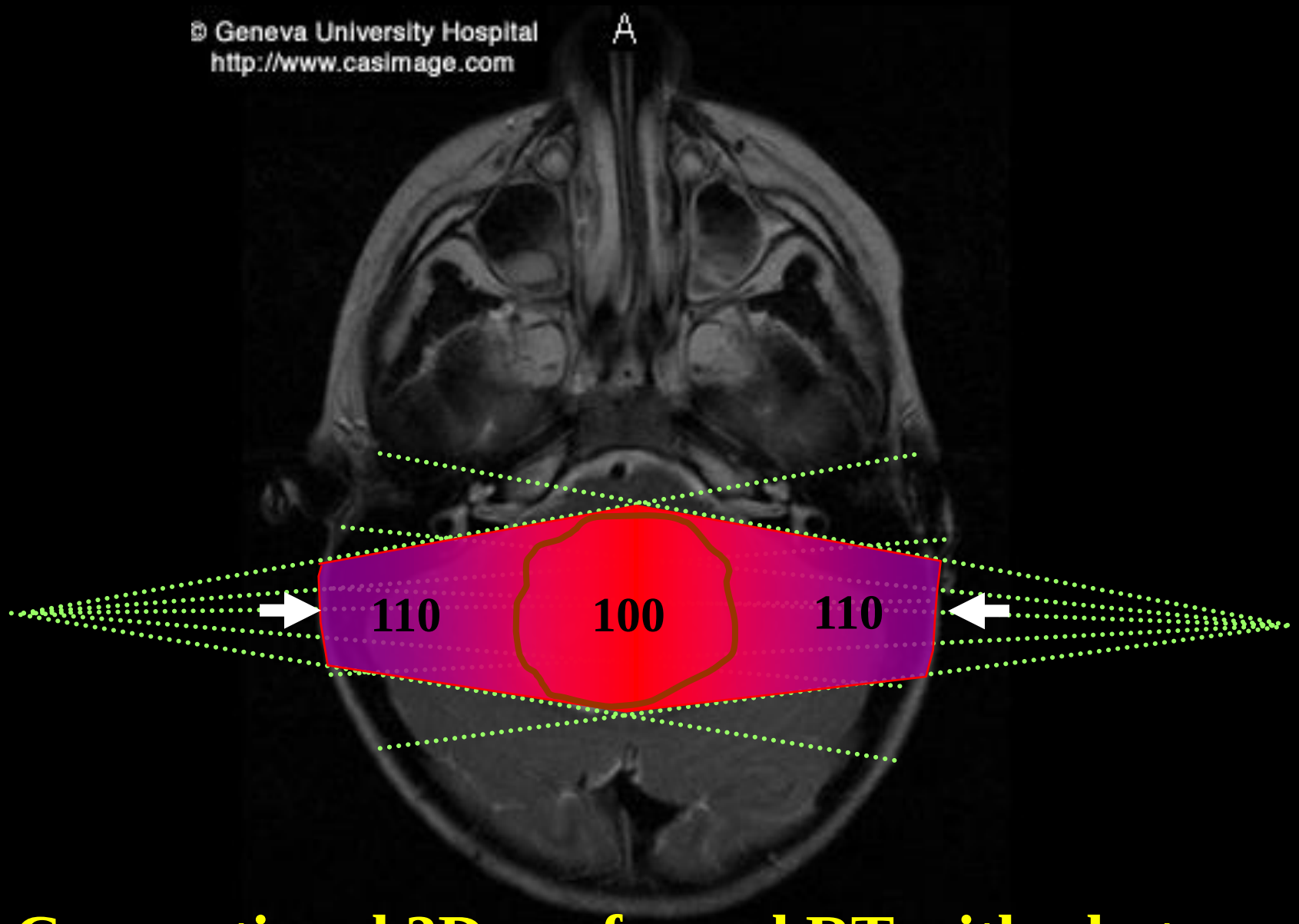


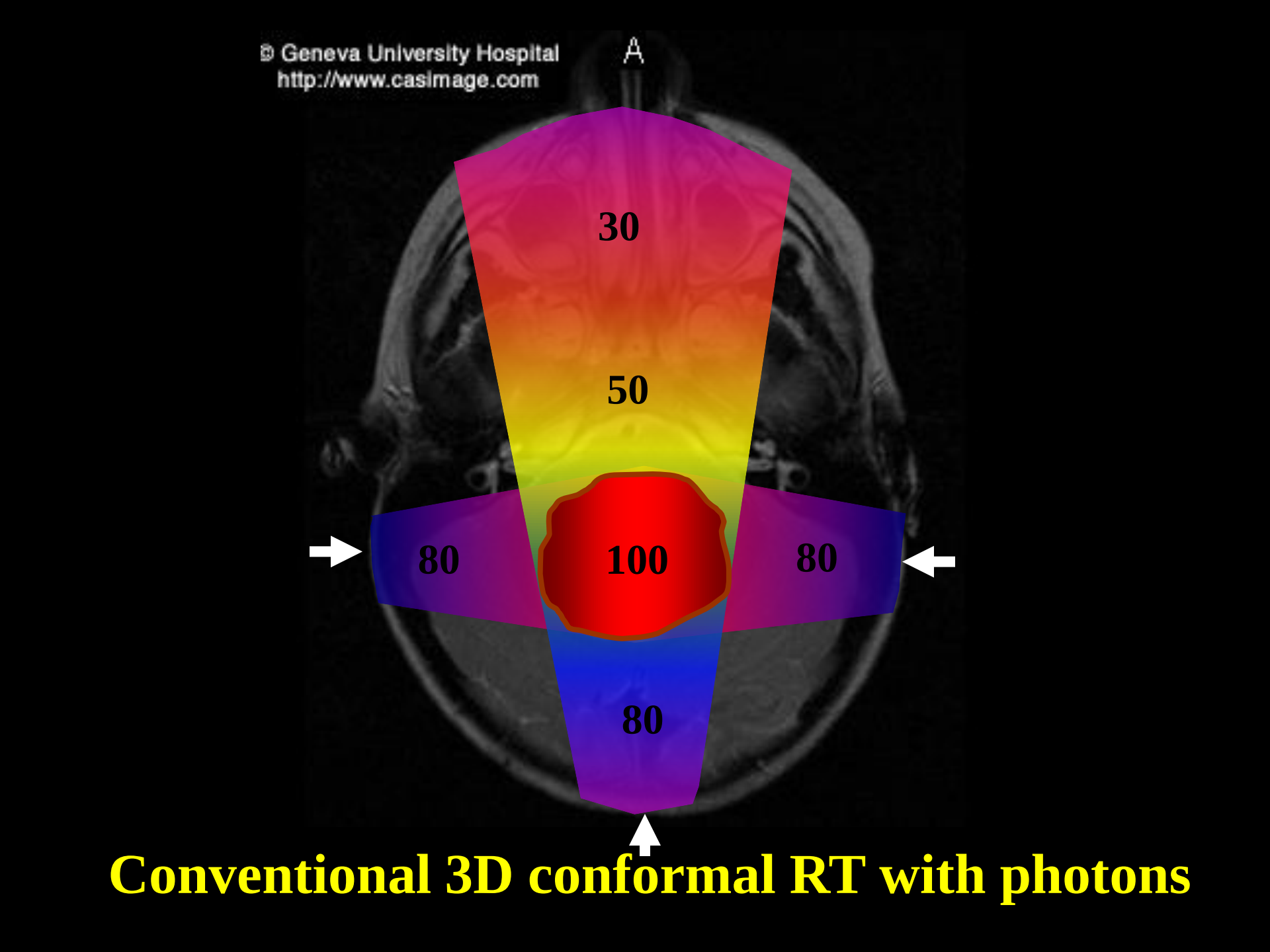
Conventional 3D conformal RT with photons



Conventional 3D conformal RT with photons

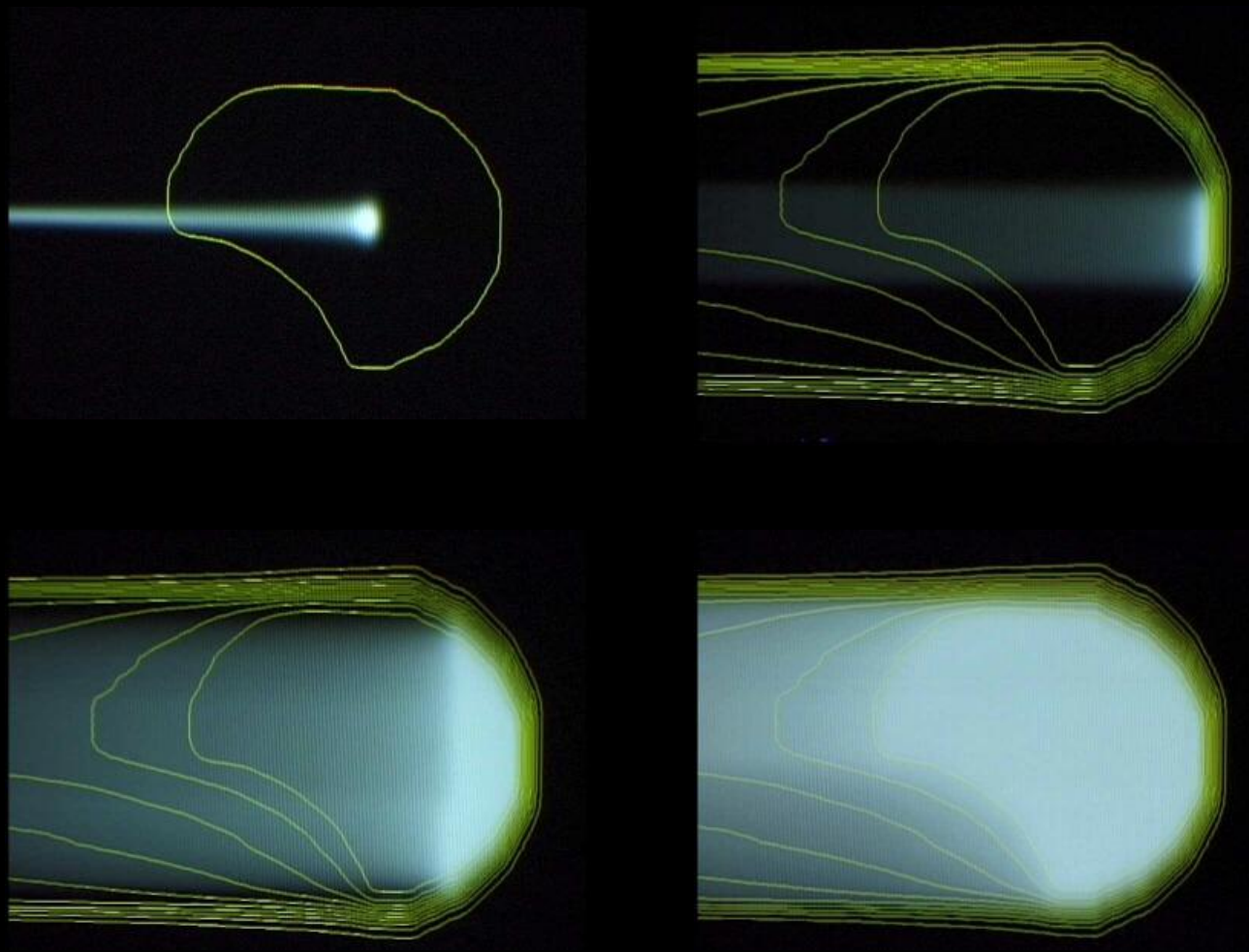


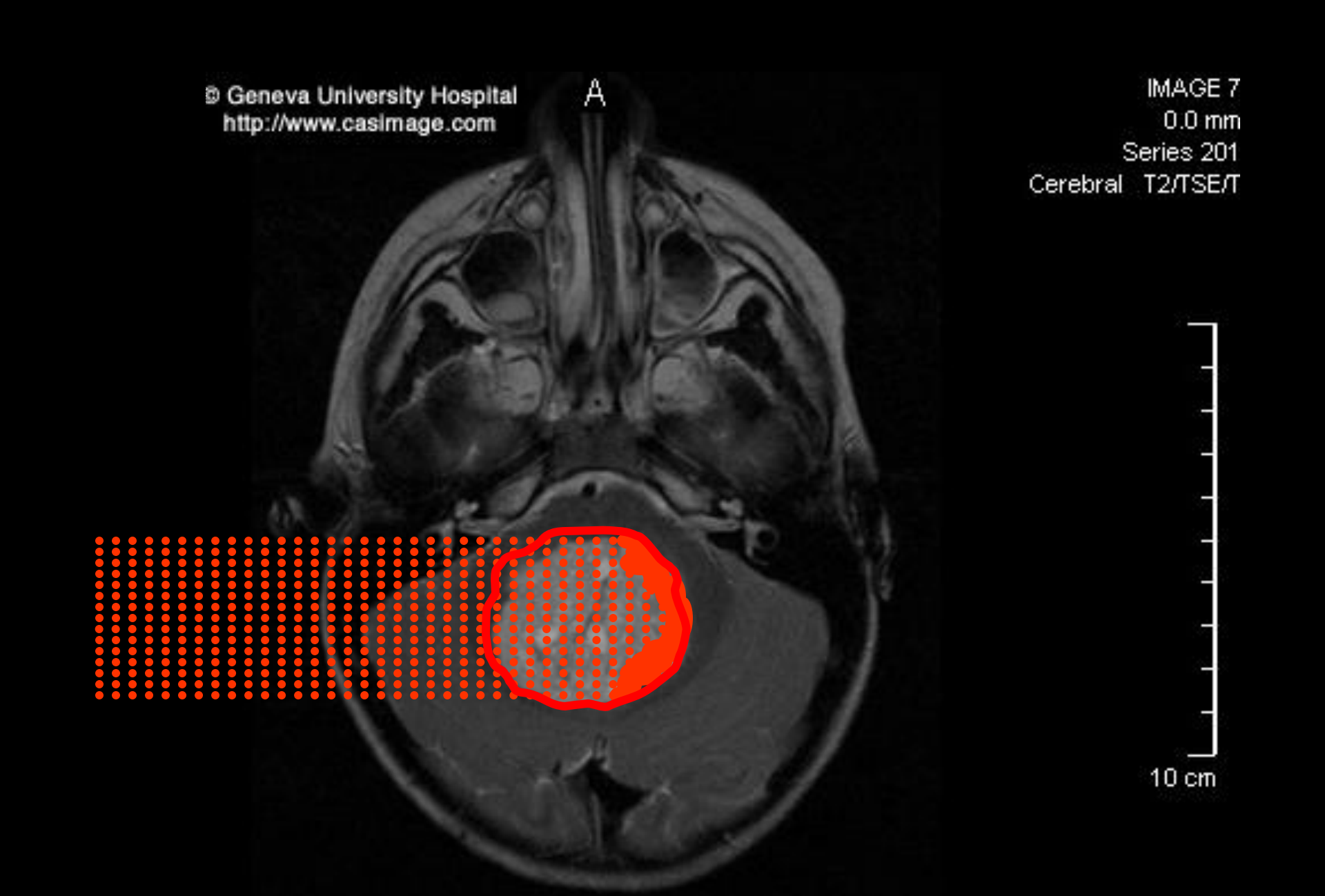
Conventional 3D conformal RT with photons



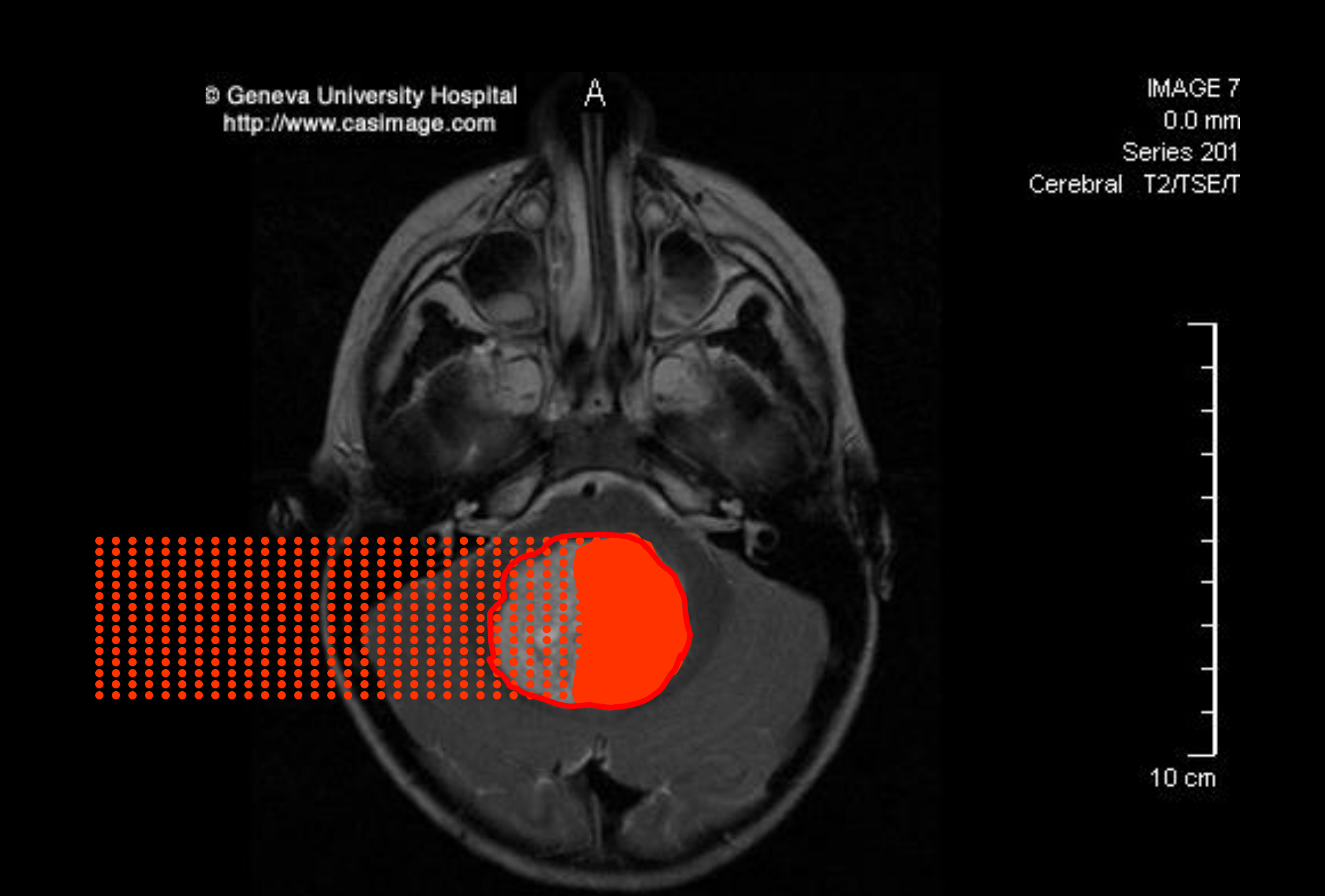
Conventional 3D conformal RT with photons

Protons: scanning the beam

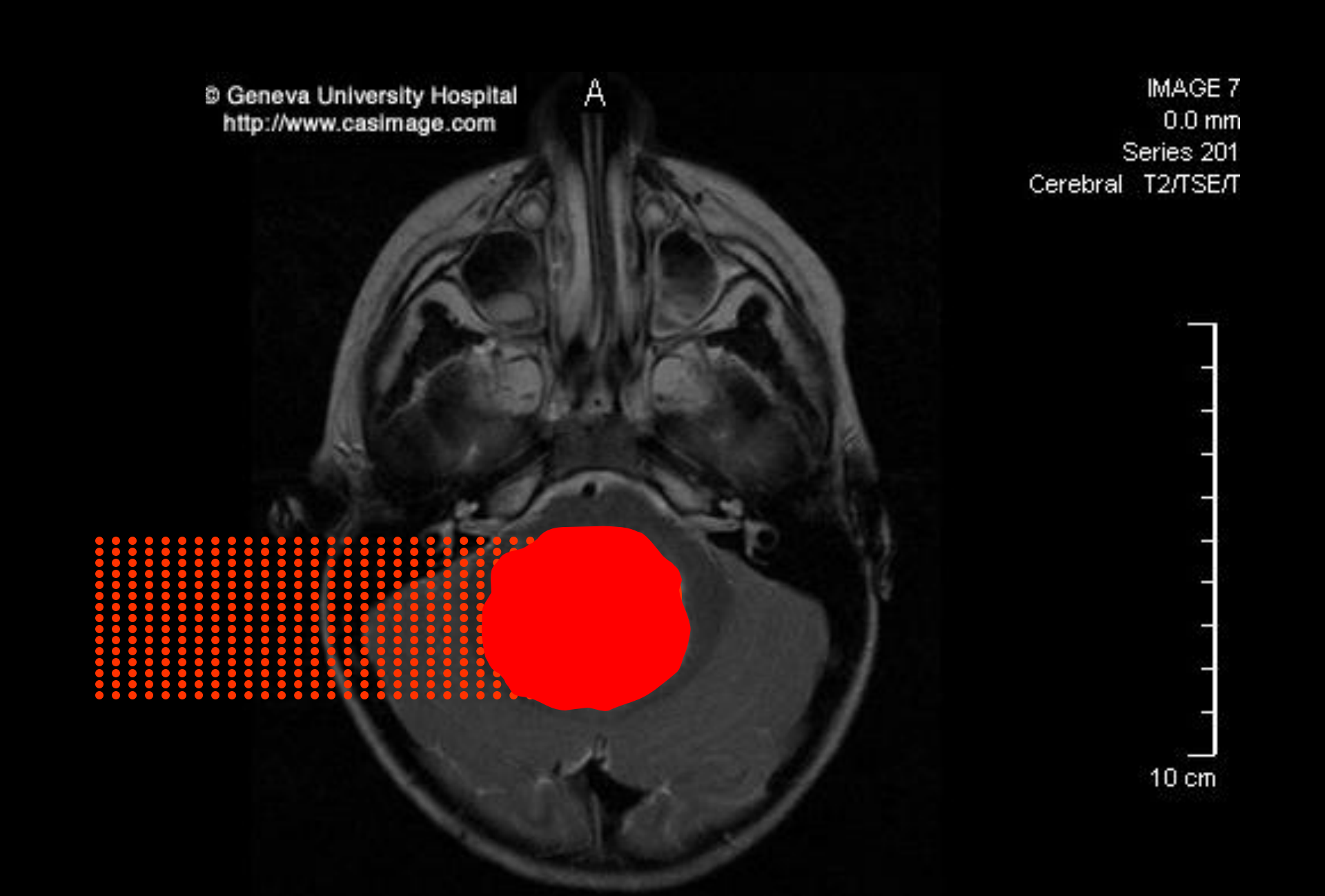




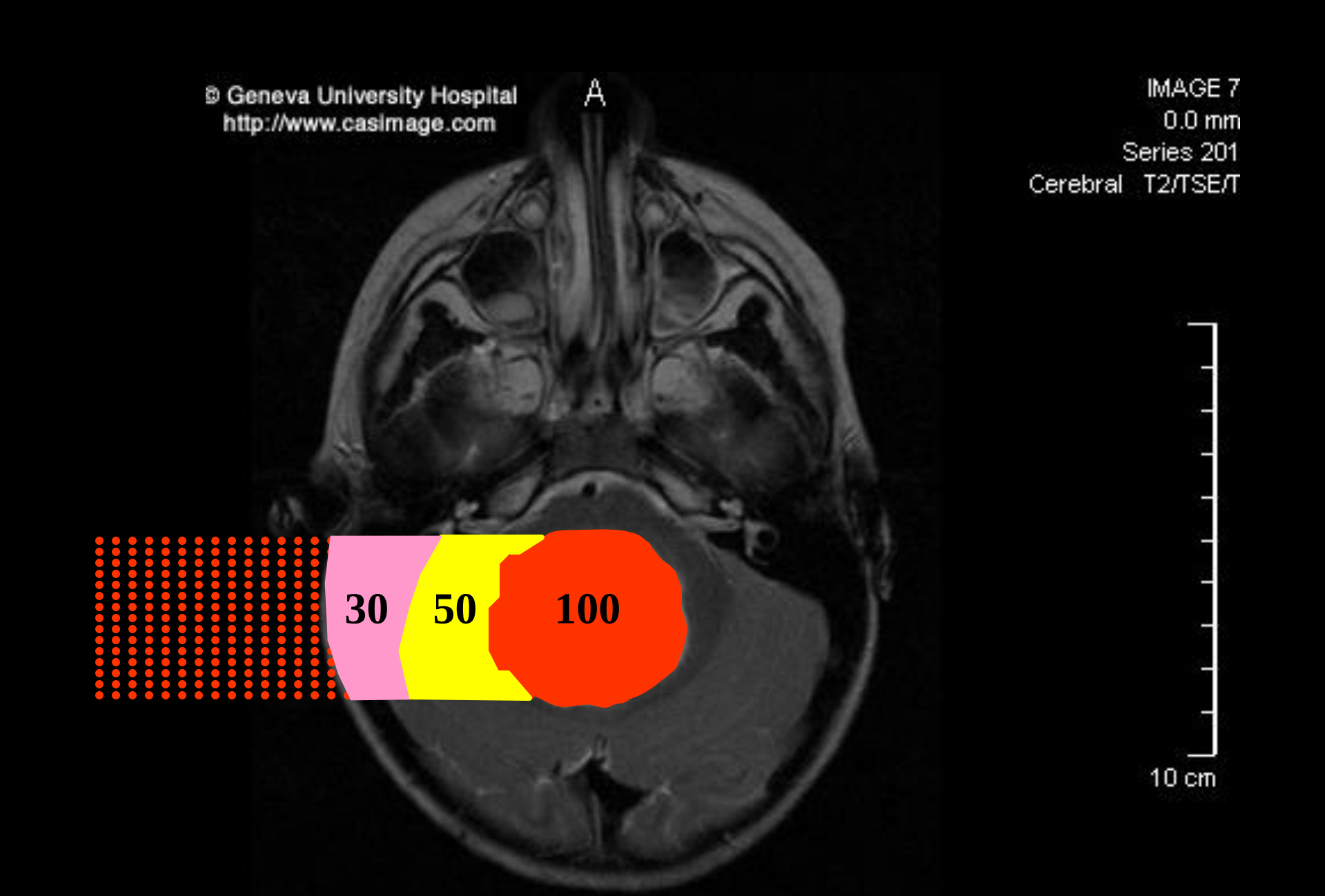
High precision RT with proton beams



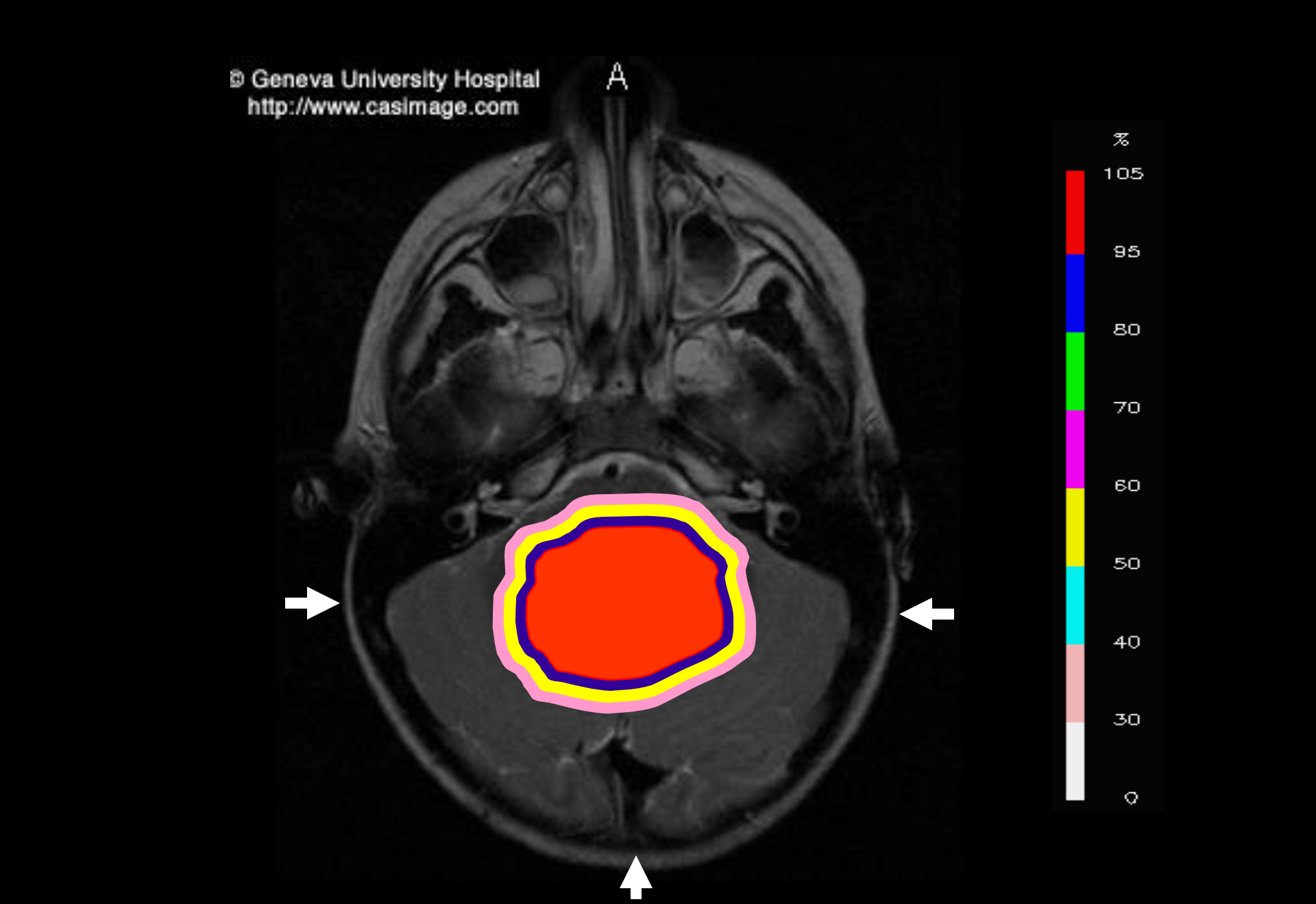
High precision RT with proton beams



High precision RT with proton beams



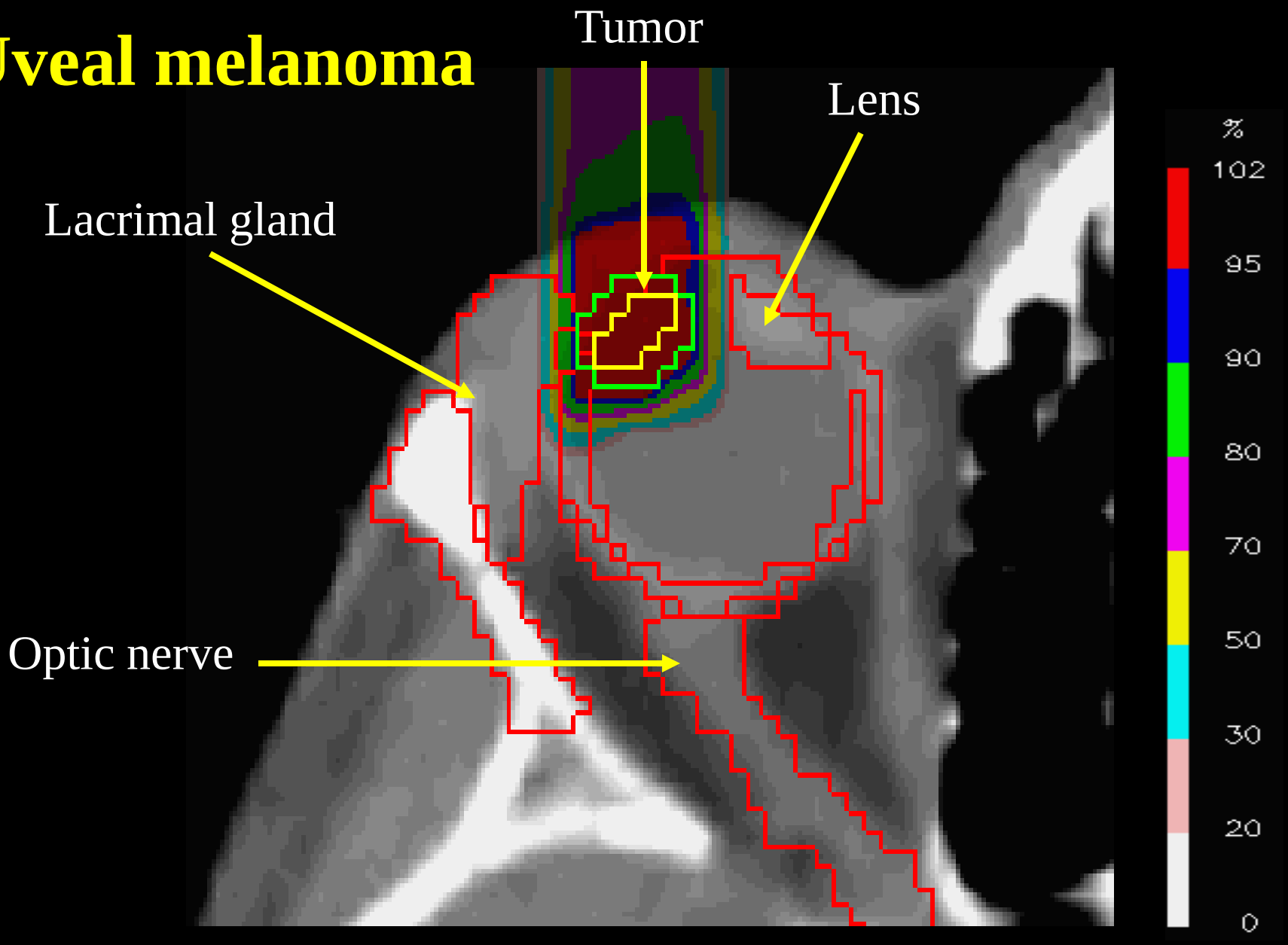
High precision RT with proton beams

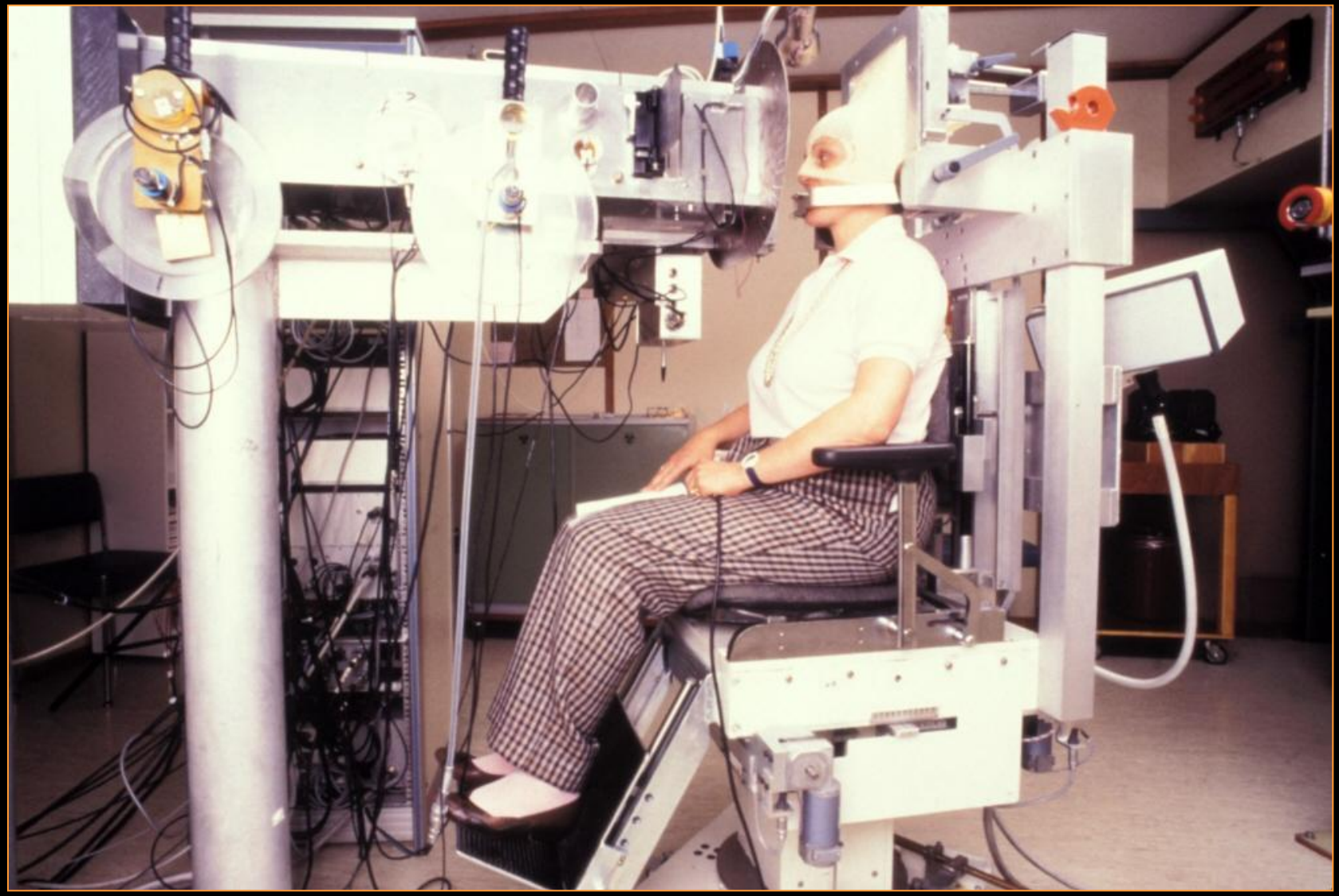


High precision RT with proton beams

Ocular melanomas

Uveal melanoma





Uveal melanoma

- Since 1974, at *Harvard Cyclotron, Cambridge, Massachusetts*

- Since 1984, at *Paul Scherrer Institut, Villigen, Switzerland*

More than 10000 patients treated so far

Proton Therapy Program

OPTIS – Programa de tractament de tumors oculars al PSI

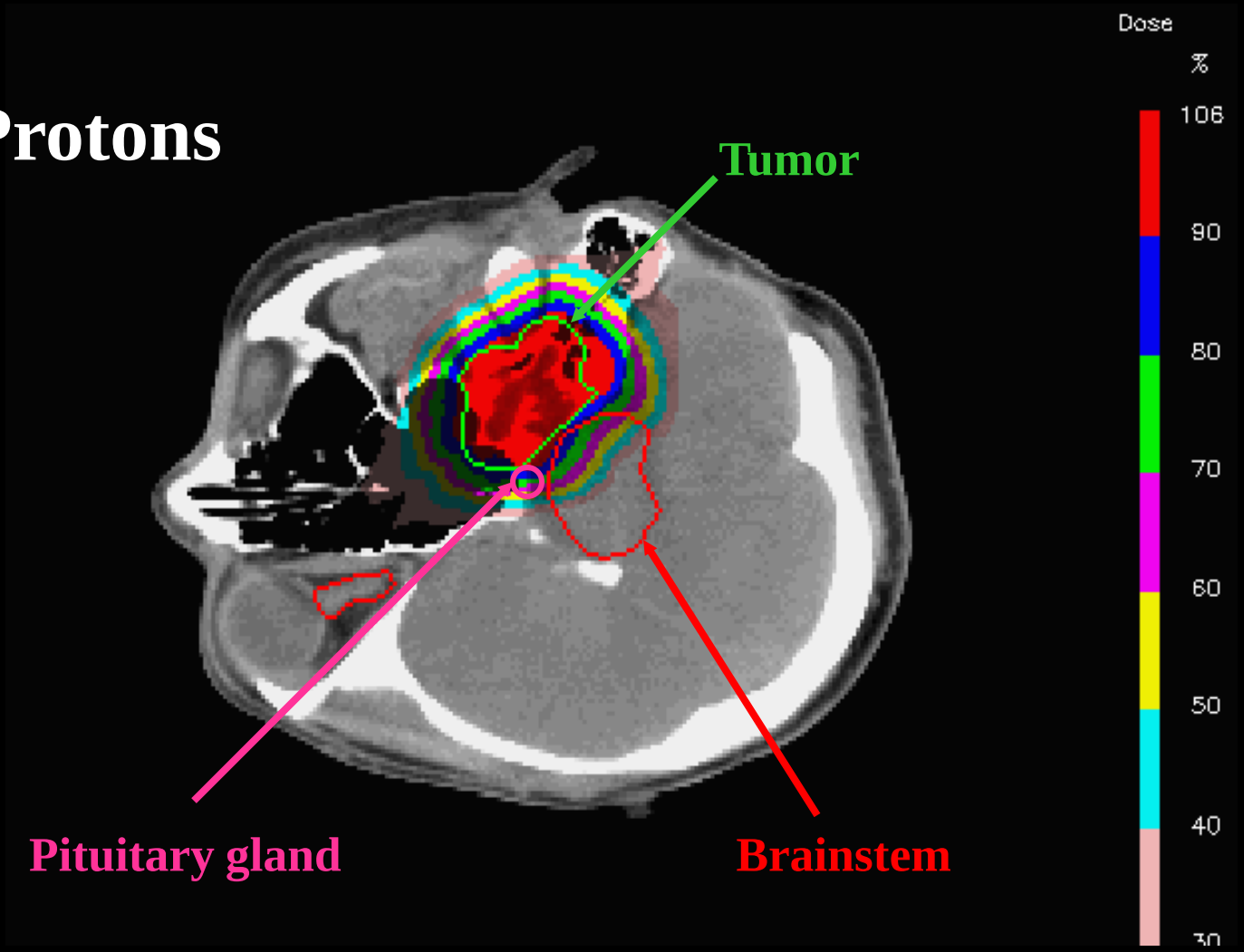
1. **Outcome** — 98% of overall local control

2. **Eye retention** — 100% for small tumors, 90% for large tumors

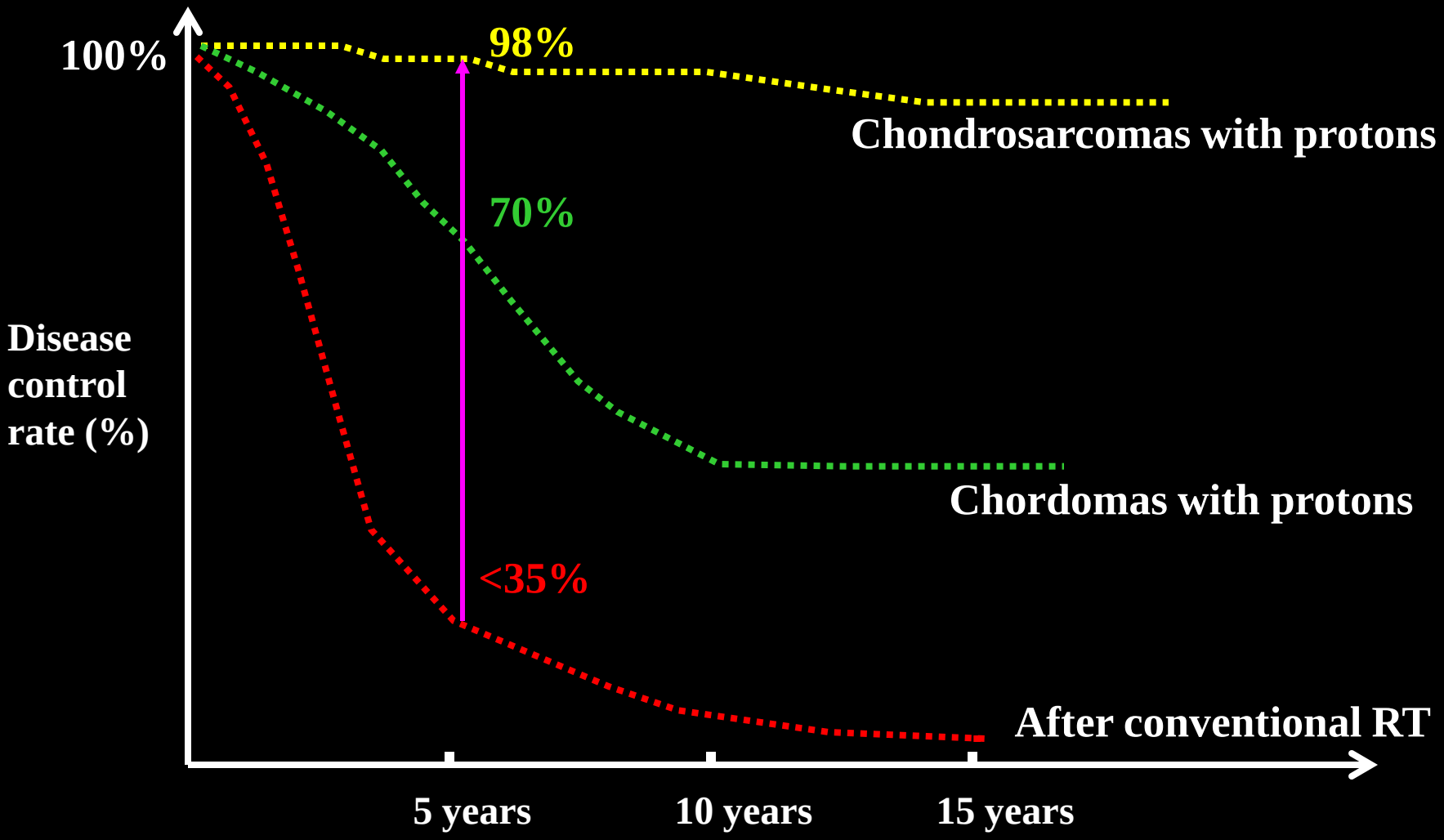
3. **Vision** — Preserved in 50% of patients

Base of skull tumors

Base of skull chondrosarcoma in a 22 year-old female



Base of skull tumors



Summary

- High quality RT will likely continue to play an important role in the curative treatment of cancer in years to come.

- Better imaging and 3-D treatment planning have helped to safely escalate the dose to the tumor (by simultaneosuly reducing the dose to surrounding normal tissues).

- Thus, IM X-ray and proton beams may greatly improve local control rates, simultaneously reducing morbidity.