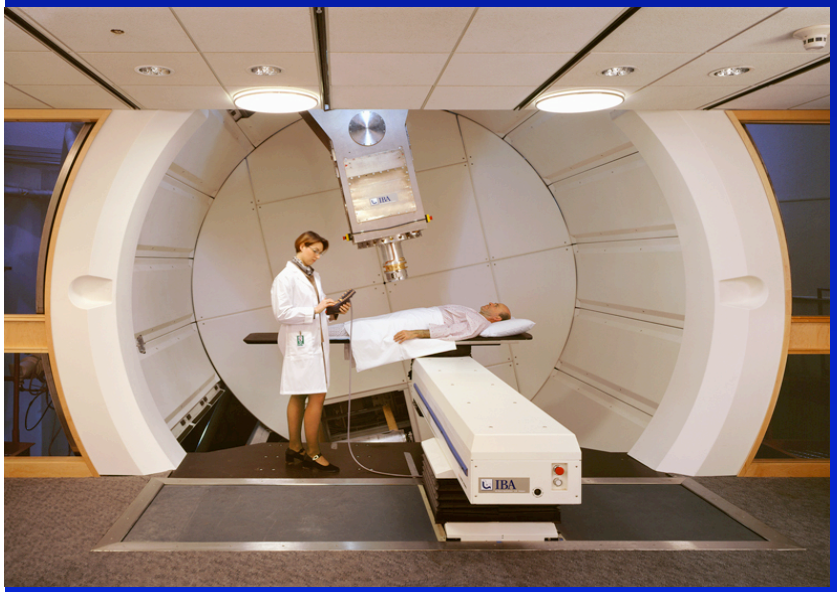
Important Clinical Issues in Charged Particle Radiation Therapy



Thomas F. DeLaney, M.D.

Medical Director
Francis H. Burr Proton Therapy Center
Massachusetts General Hospital
Boston, Massachusetts

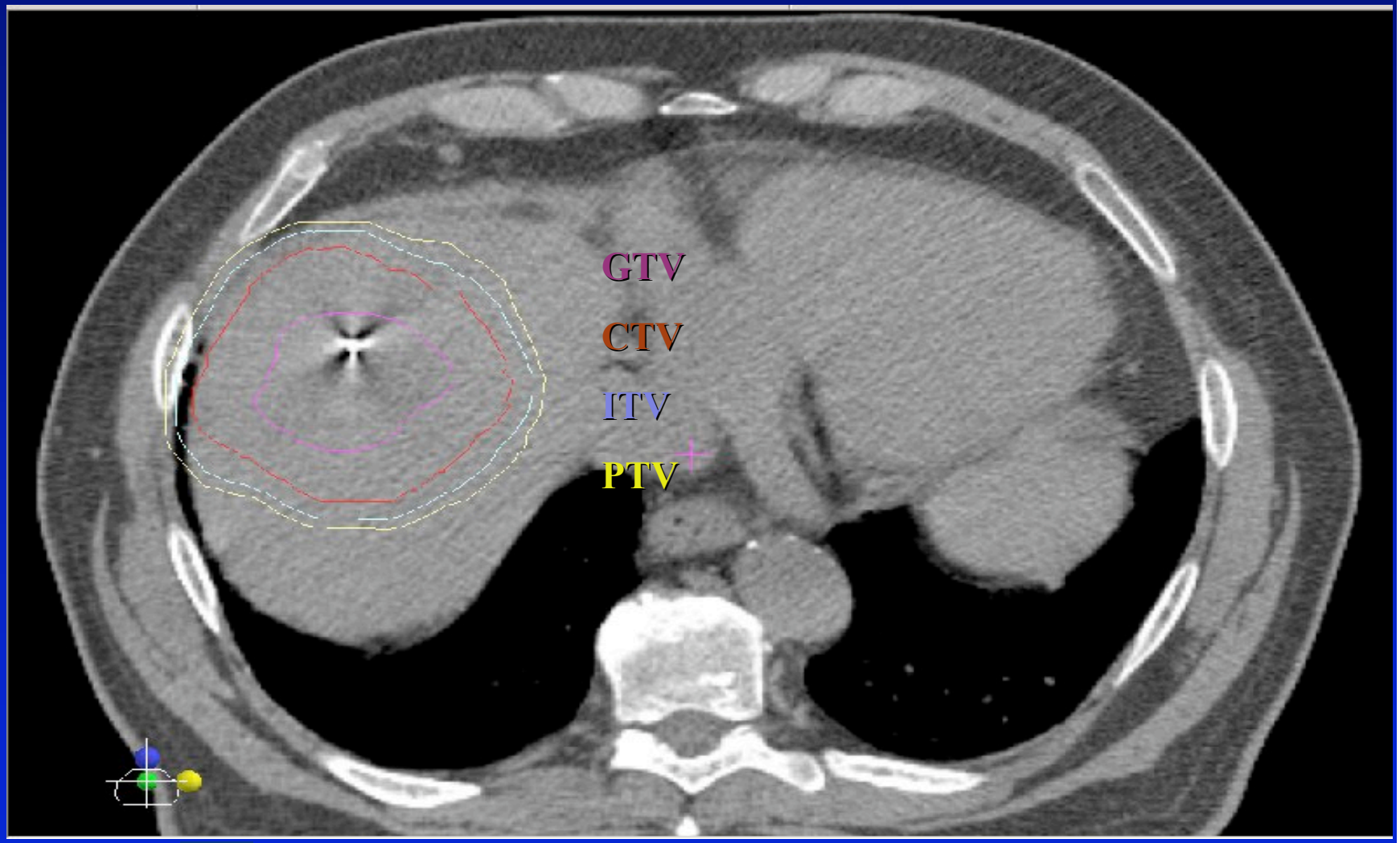
MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

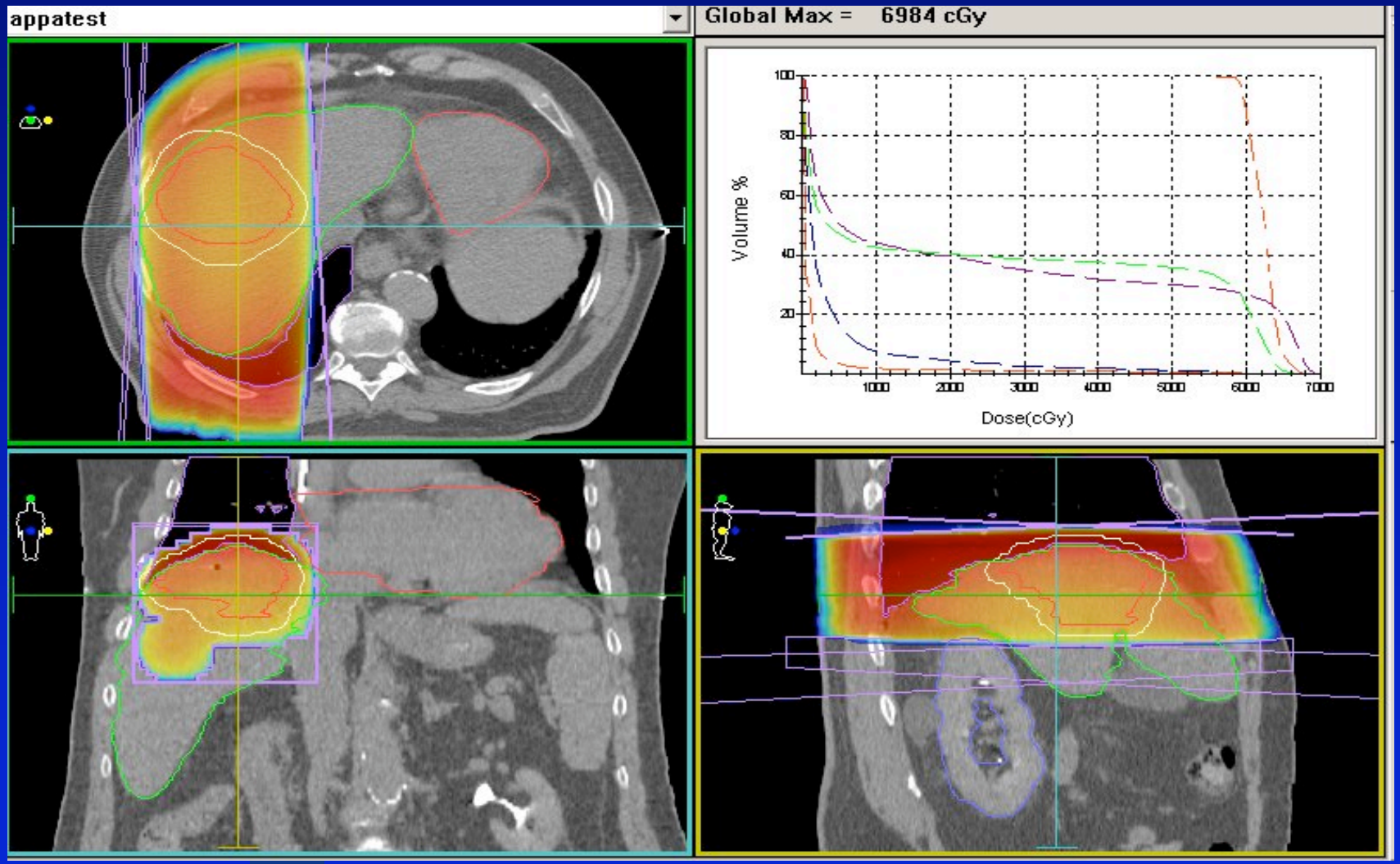
TECHNICAL ADVANCES IN RADIOTHERAPY

- Higher radiation doses to tumor increase rate of local control in animals and patients
- Higher doses to normal tissues increase the risk of normal tissue complications
  - Complications do not occur in unirradiated tissues
  - Normal tissue irradiation does not benefit patient
- Optimize the therapeutic ratio by maximizing tumor dose and minimizing normal tissue dose

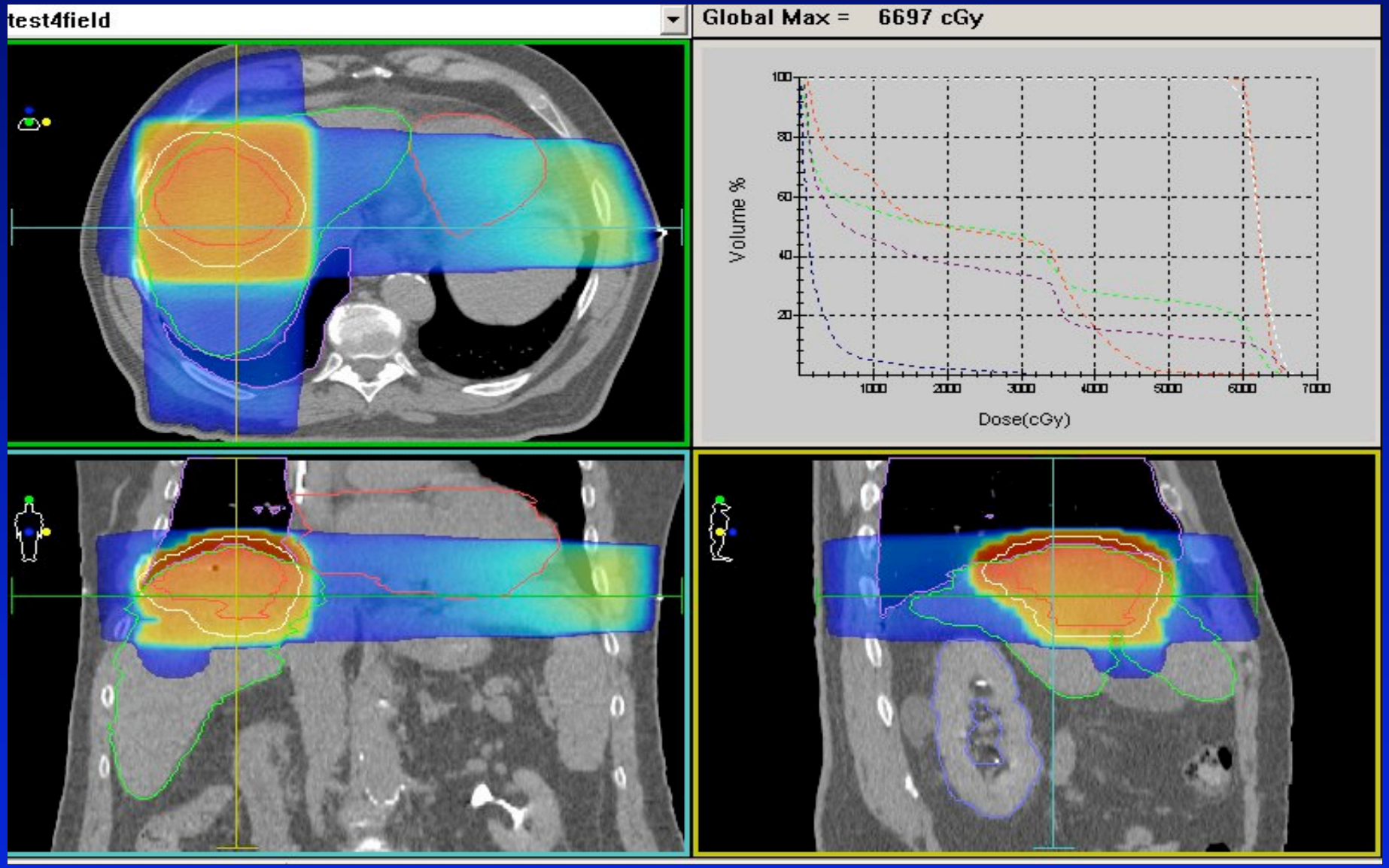
LIVER TARGET VOLUMES



AP/PA OPPOSED FIELDS



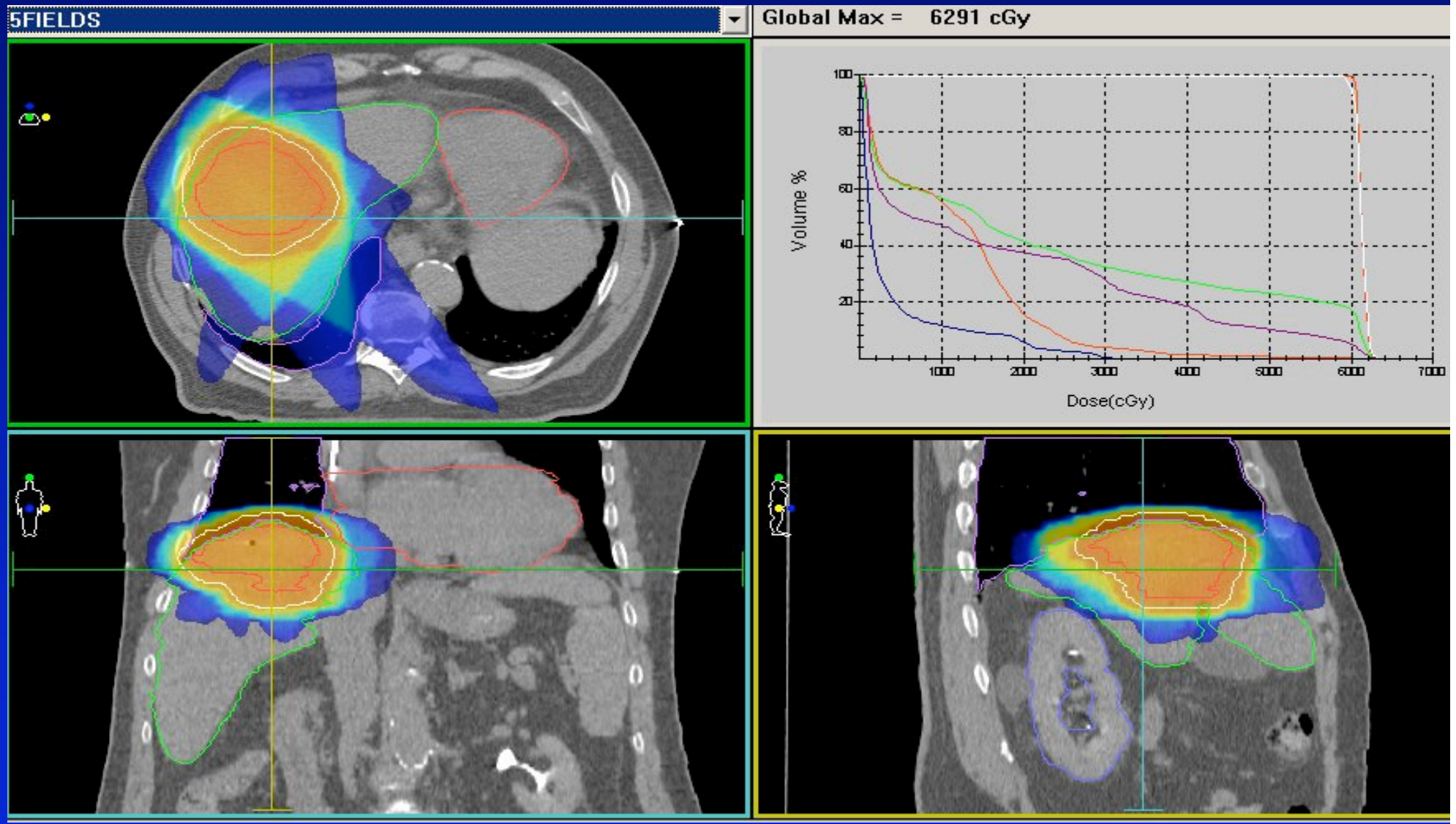
FOUR FIELD PLAN AP/PA/RLAT/LLAT



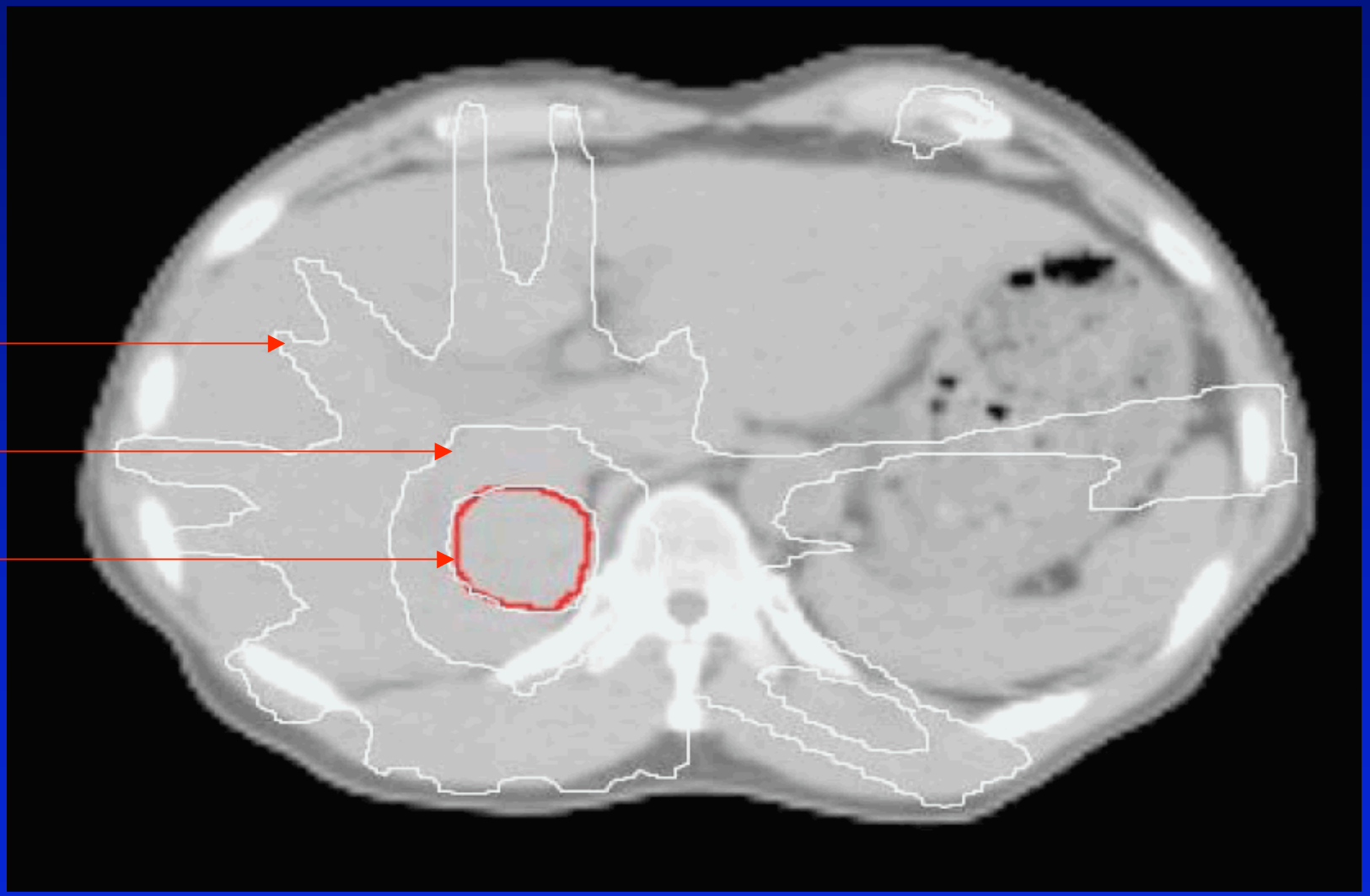
MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

5 FIELD PLAN AP/RA/RP/LP/LA



IMRT PLAN



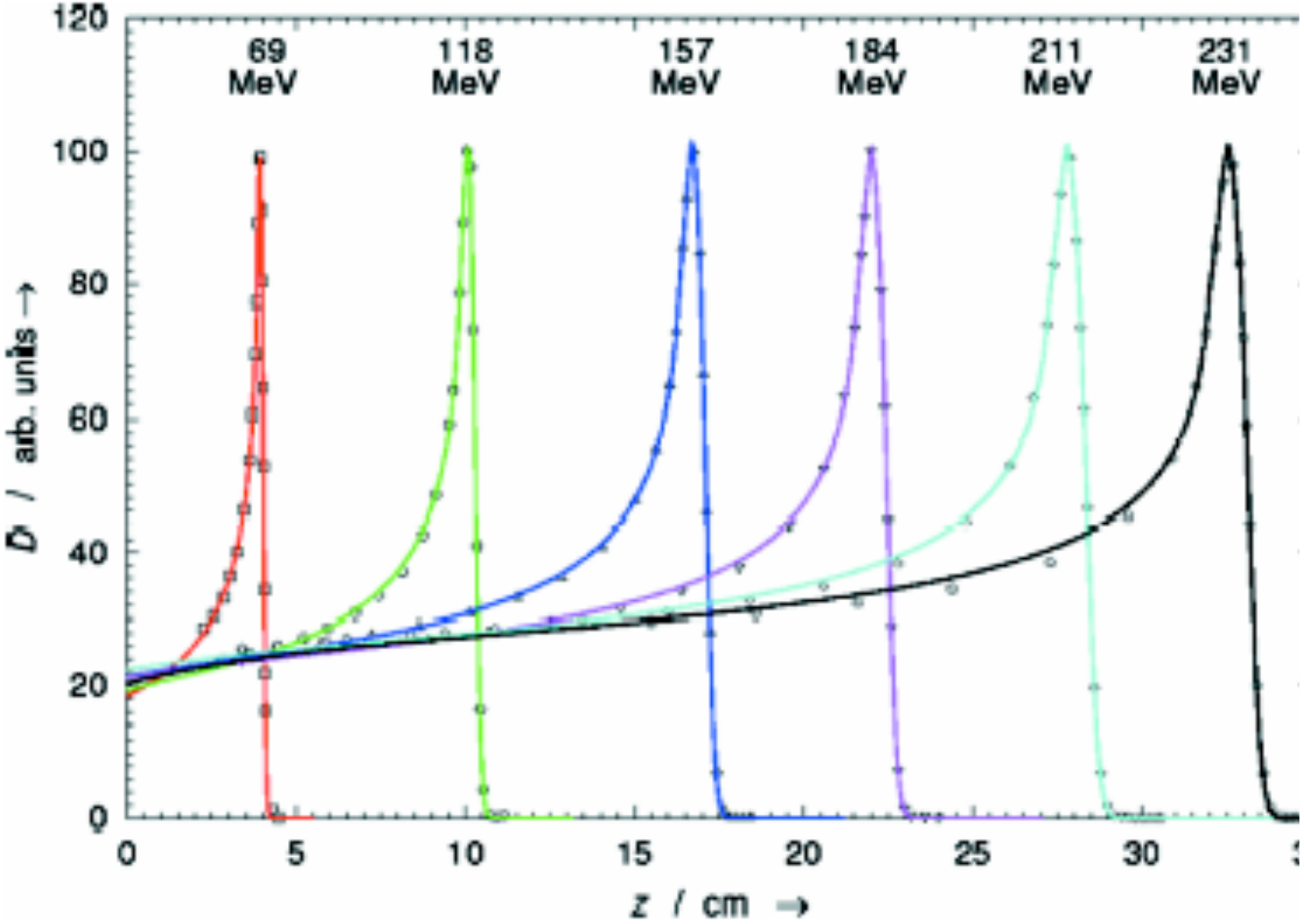
MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

PROTONS

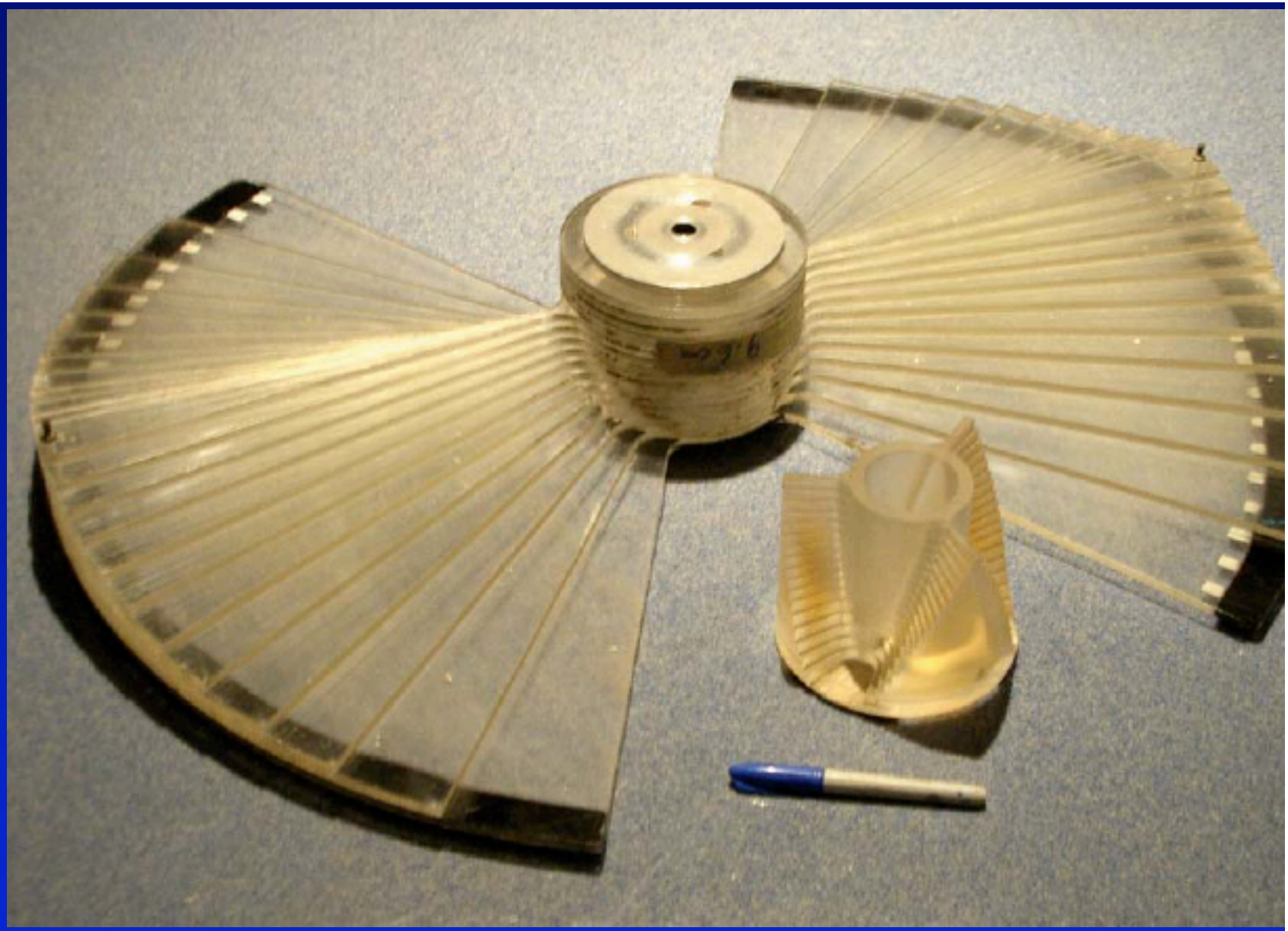
- Particles with charge and mass
  - Defined range in tissue
    - Proportional to energy
    - Unmodulated: deposit dose in sharp Bragg Peak
      - No dose delivered beyond that point
    - Bragg peak spread out toward surface to treat tumors
  - Contrast with photons (x-rays)
    - Continue to deposit dose beyond target in tissue
      - Unwanted dose to normal tissue

Pristine Bragg Peaks of Selected Energies at FHBPTC



Courtesy of H. Kooy, Ph.D.

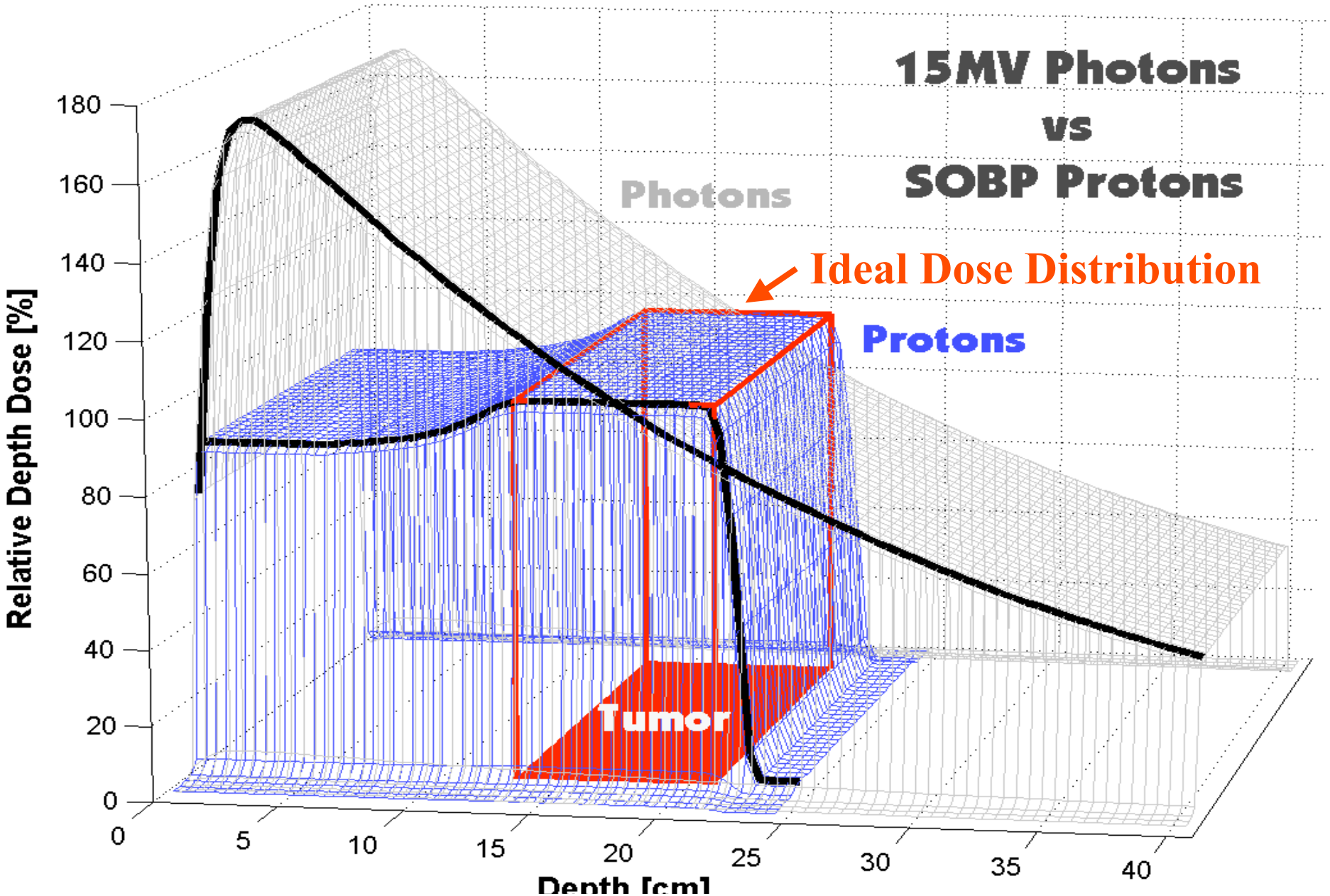
Range Modulator Wheels



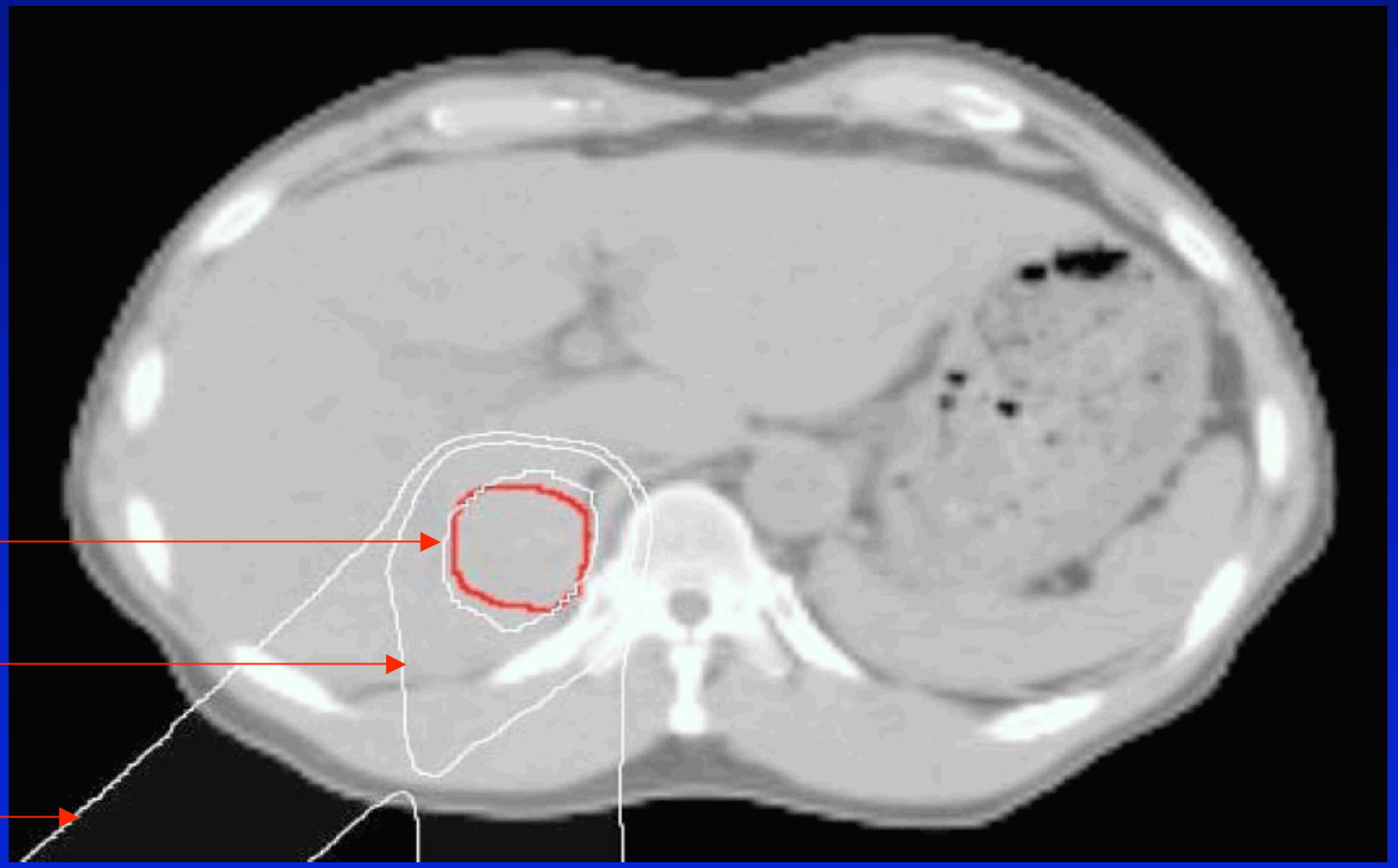
Courtesy of
B.Gottshalk, Ph.D.

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School


15MV Photons
vs
SOBP Protons
Photons
Ideal Dose Distribution
Protons
Tumor
Relative Depth Dose [%]
180
160
140
120
100
80
60
40
20
0
0
5
10
15
20
25
30
35
40
Depth [cm]

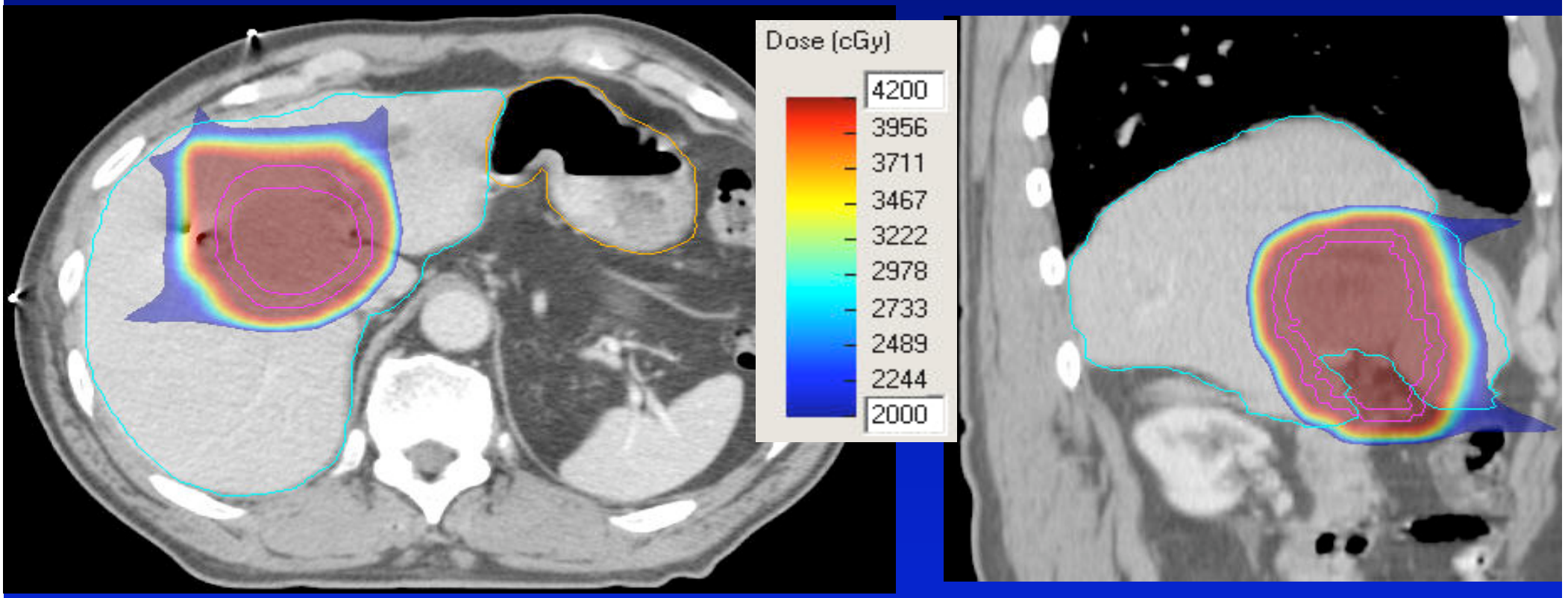
3 D CONFORMAL PROTON PLAN



MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Hepatoma – 42 CGE in 15 fractions



MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

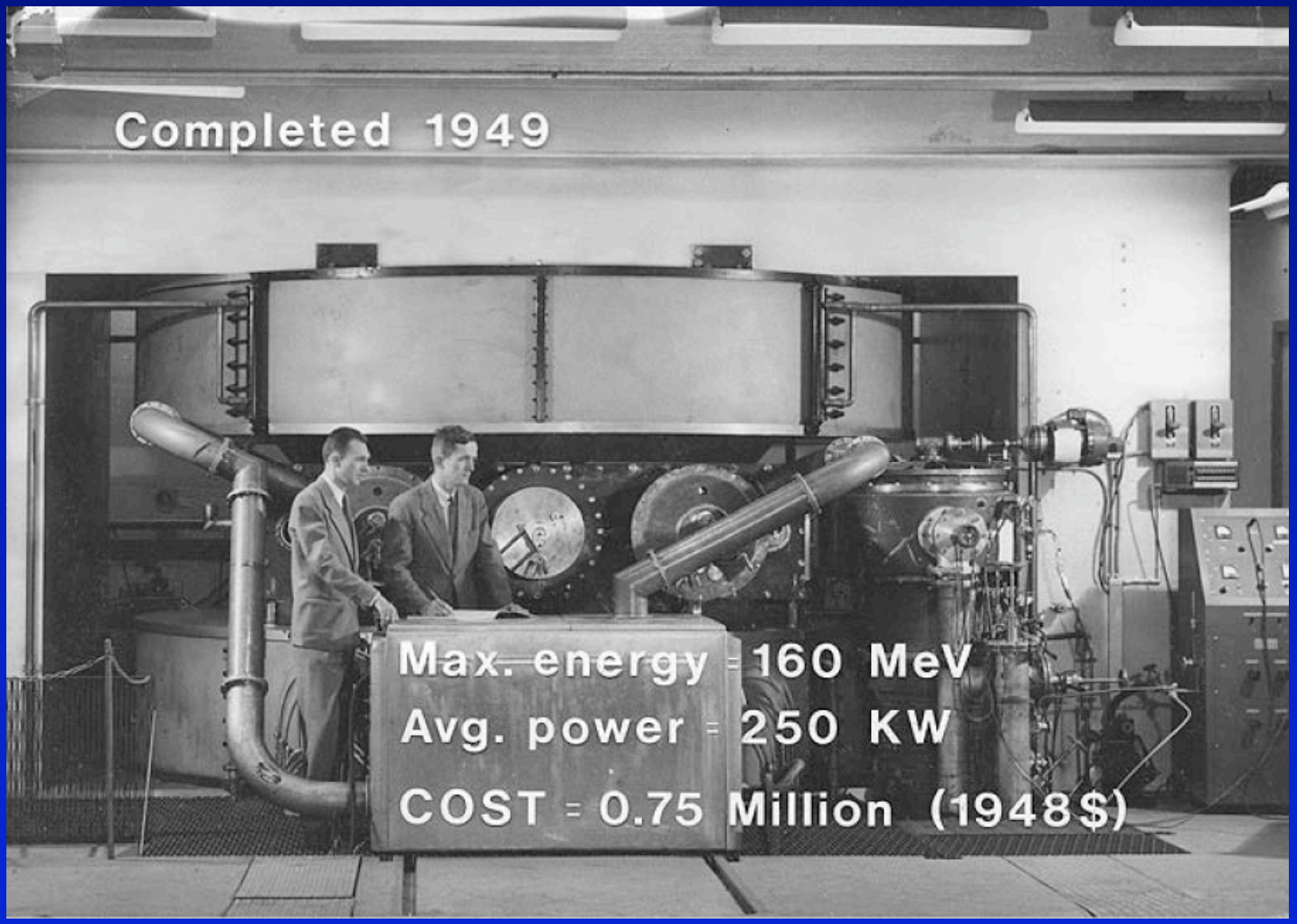
Protons: Clinical Advantages

- Clinical advantage for protons compared to photons (x-rays) is physical (vs. biologic)
- Superior dose distributions with protons
  - Less dose to normal tissue->Less toxicity
    - Improves Rx tolerance: Uninterrupted Rx
      - Allows integration with systemic chemotherapy
    - Reduces late effects (i.e. growth arrest in children)
  - **Permits dose escalation to tumor**
    - Higher tumor control

Protons: Physical Dose Advantage

- Intensity modulated radiotherapy (IMRT)
  - Target dose distributions similar to protons
    - Integral dose is ALWAYS higher that with protons
    - Although selected normal tissues can be spared with IMRT, this is at the cost of INCREASED DOSE TO OTHER NORMAL TISSUES
      - No advantage to the patient for irradiation of normal tissue
      - What is the toxicity of low-moderate dose bath with IMRT
- INTENSITY MODULATION IS APPLICABLE TO PROTONS

The Harvard Cyclotron Laboratory



MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

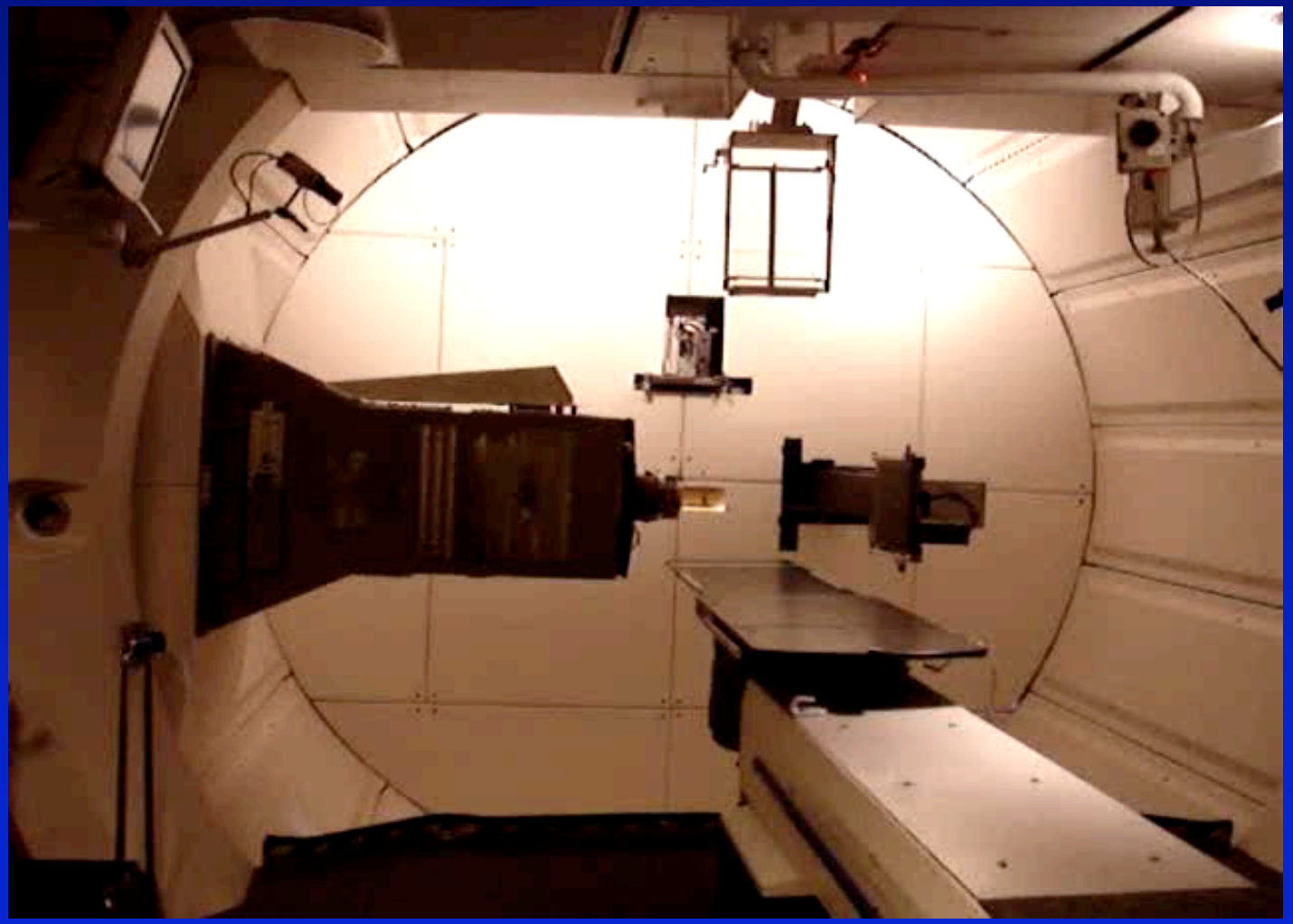
Proton Clinical Results : Local control

- **Ocular Melanoma (**70 CGE in 5 fractions)
  - 95% at 15 years (Harvard Cyclotron Lab)
- **Chondrosarcomas** (69.6 CGE in 37 fractions)
  - 95% at 10 years (Harvard Cyclotron Lab)
- **Prostate ca T1-2B** (75 GCE in 46 fractions)
  - 88% PSA disease-free 5 year survival - LLUMC

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

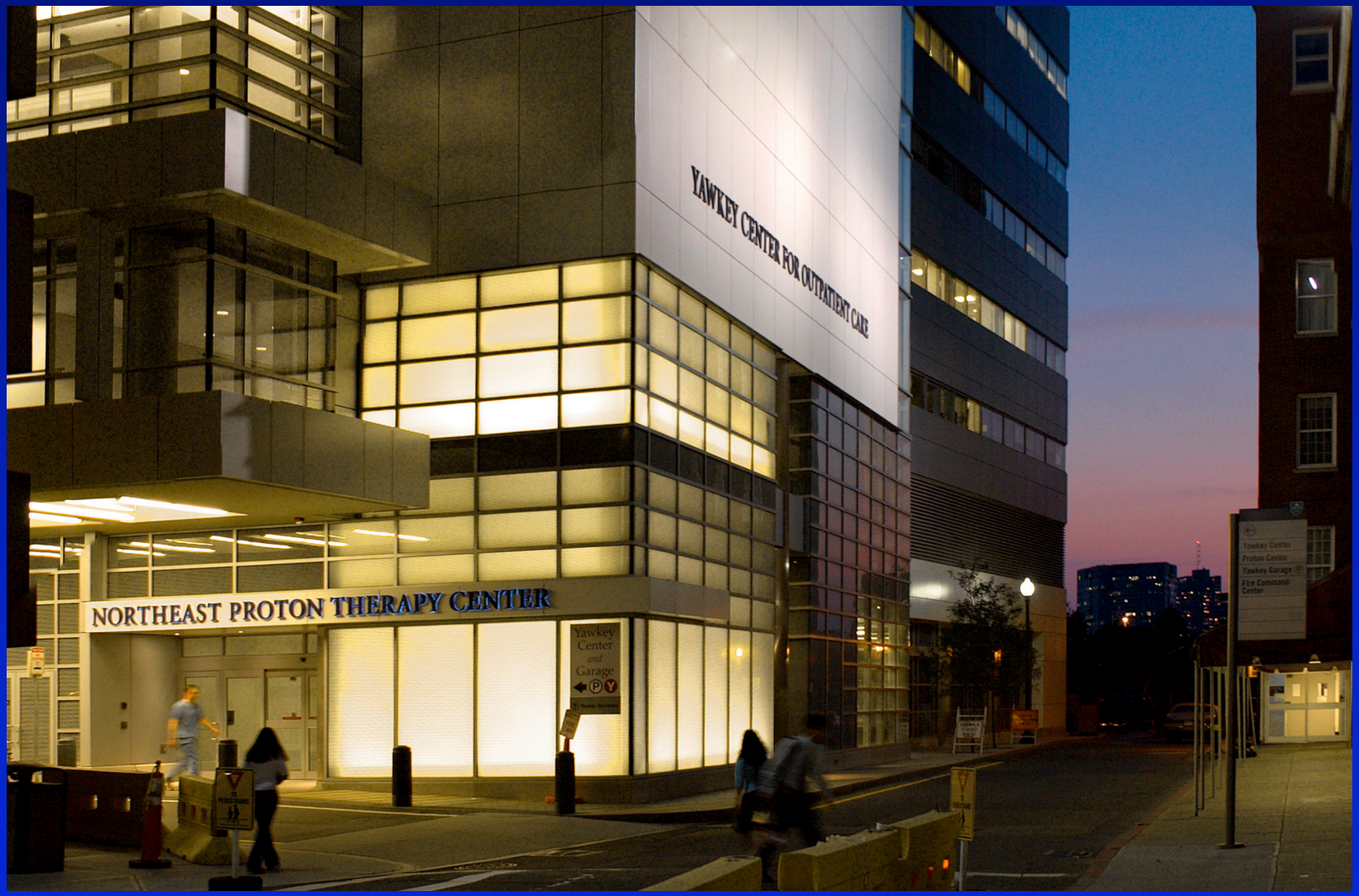
MGH Burr Proton Gantry



MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

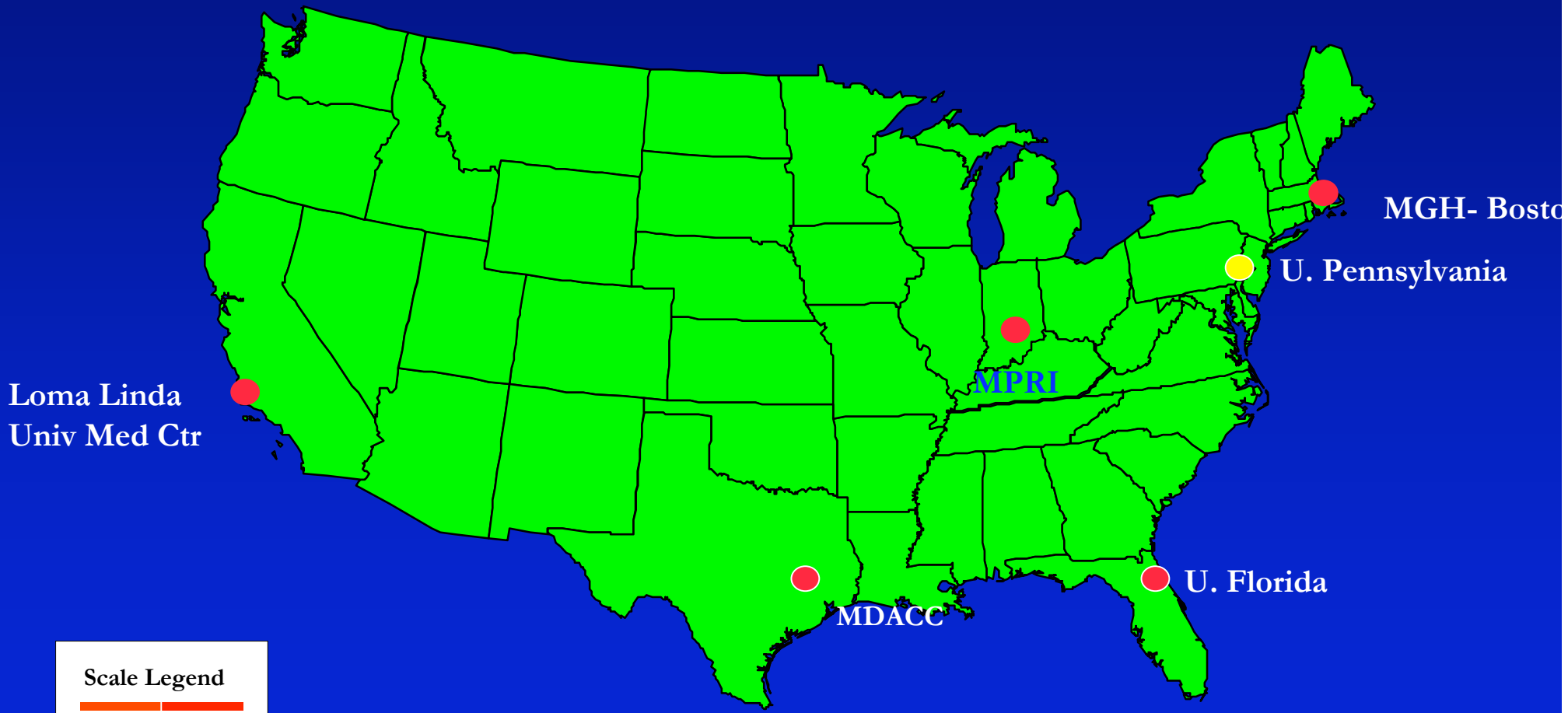
The Francis H. Burr Proton Therapy Center at MGH



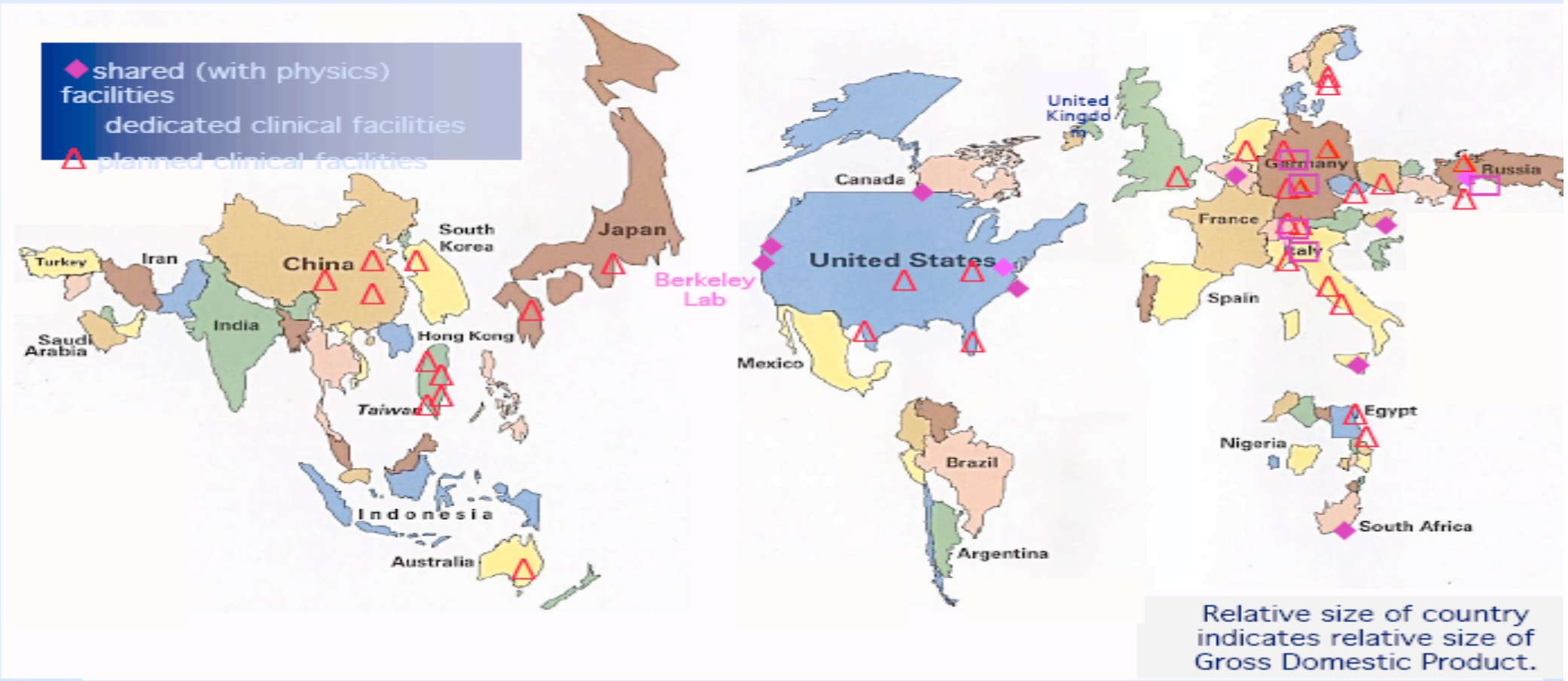
MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

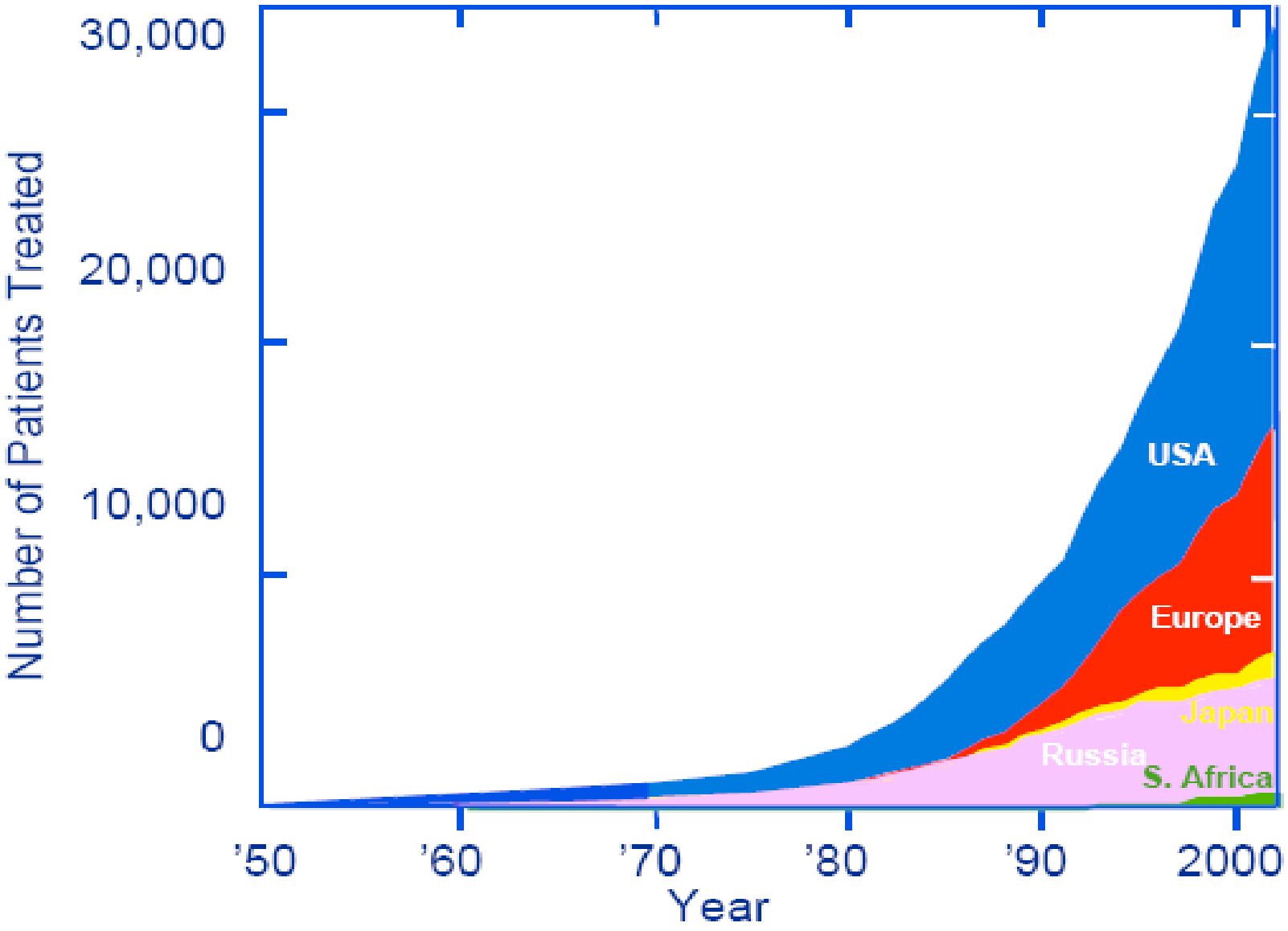
Current and Future Treatment Sites for Proton Delivery



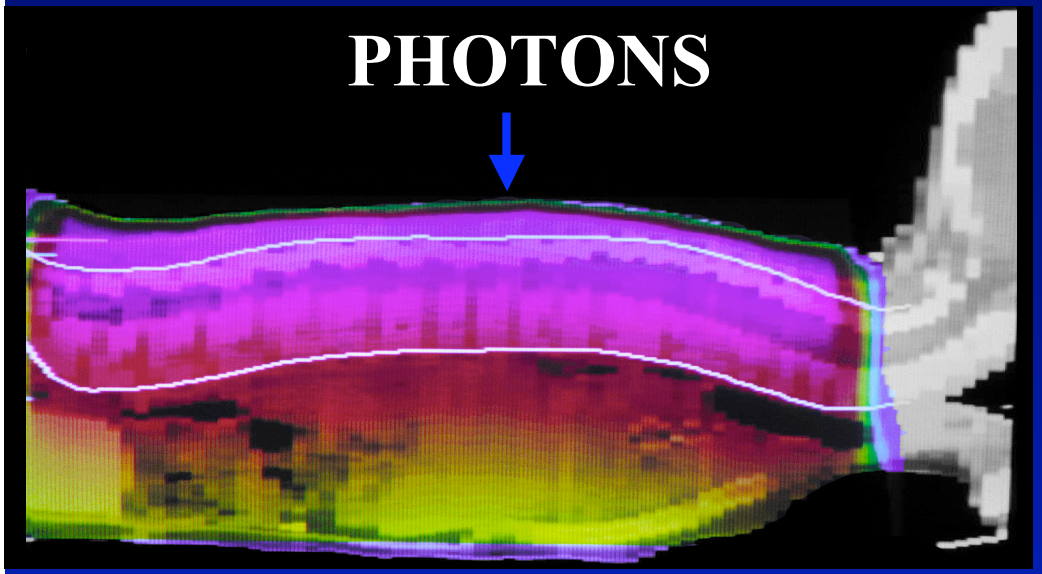
Proton Therapy Facilities Around the World (2001)

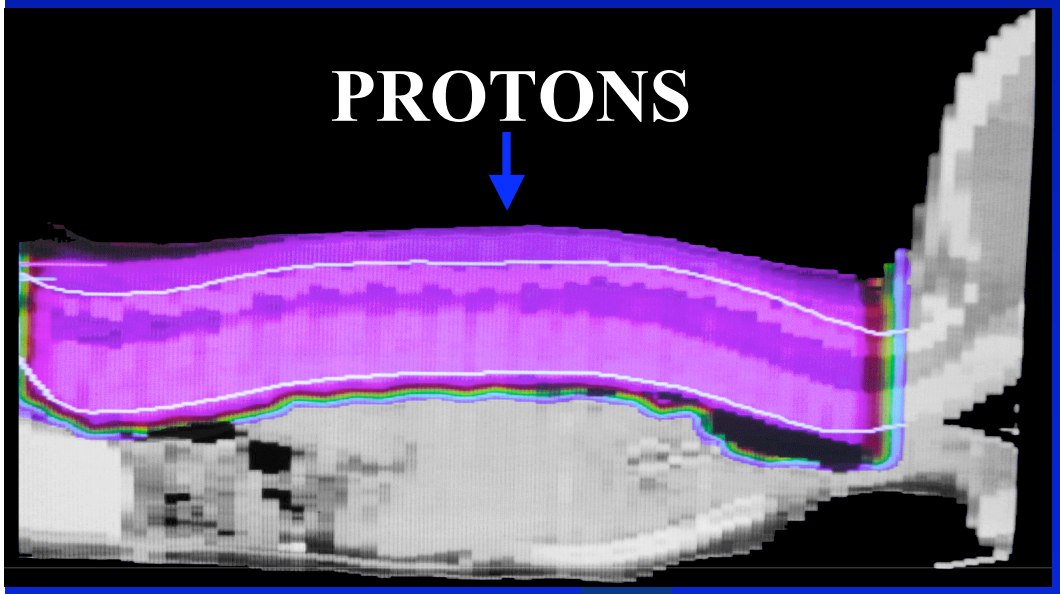


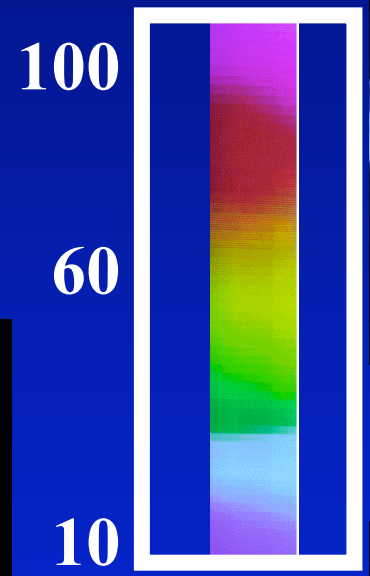
Growth of Proton Treatments

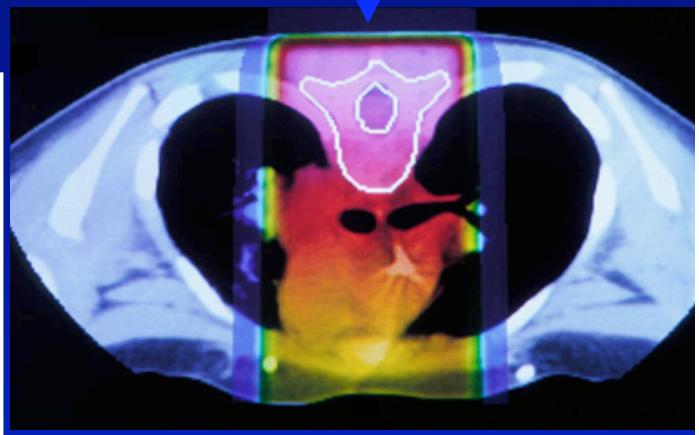


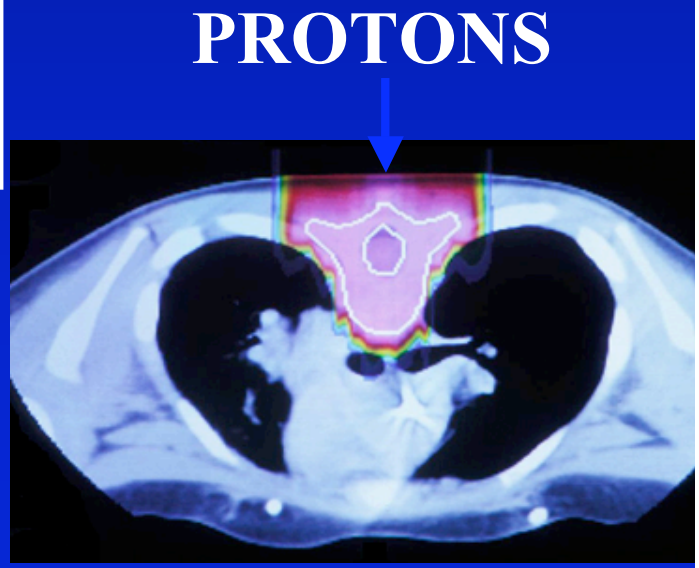
MEDULLOBLASTOMA







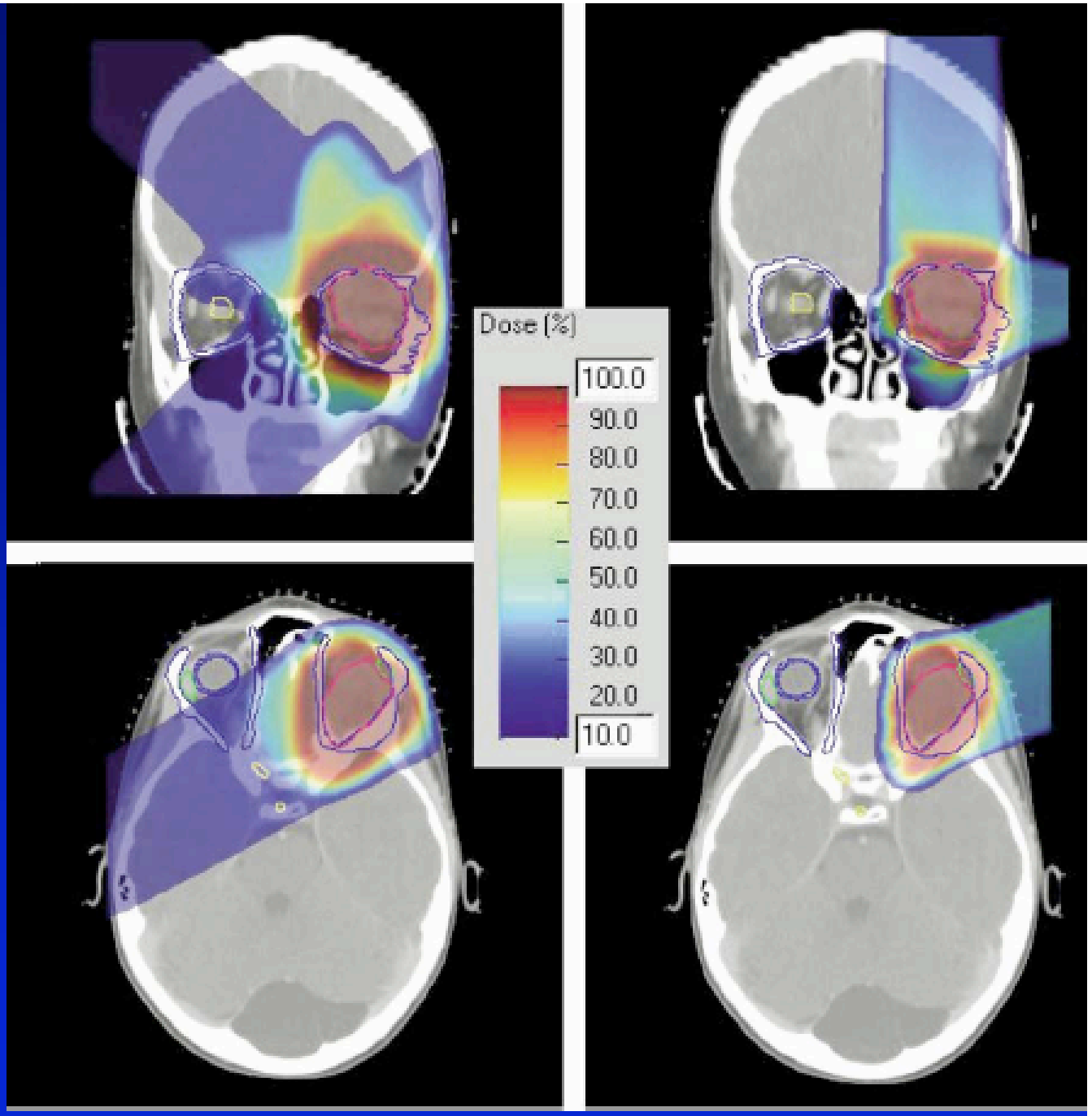




MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Orbital Rhabdomyosarcoma



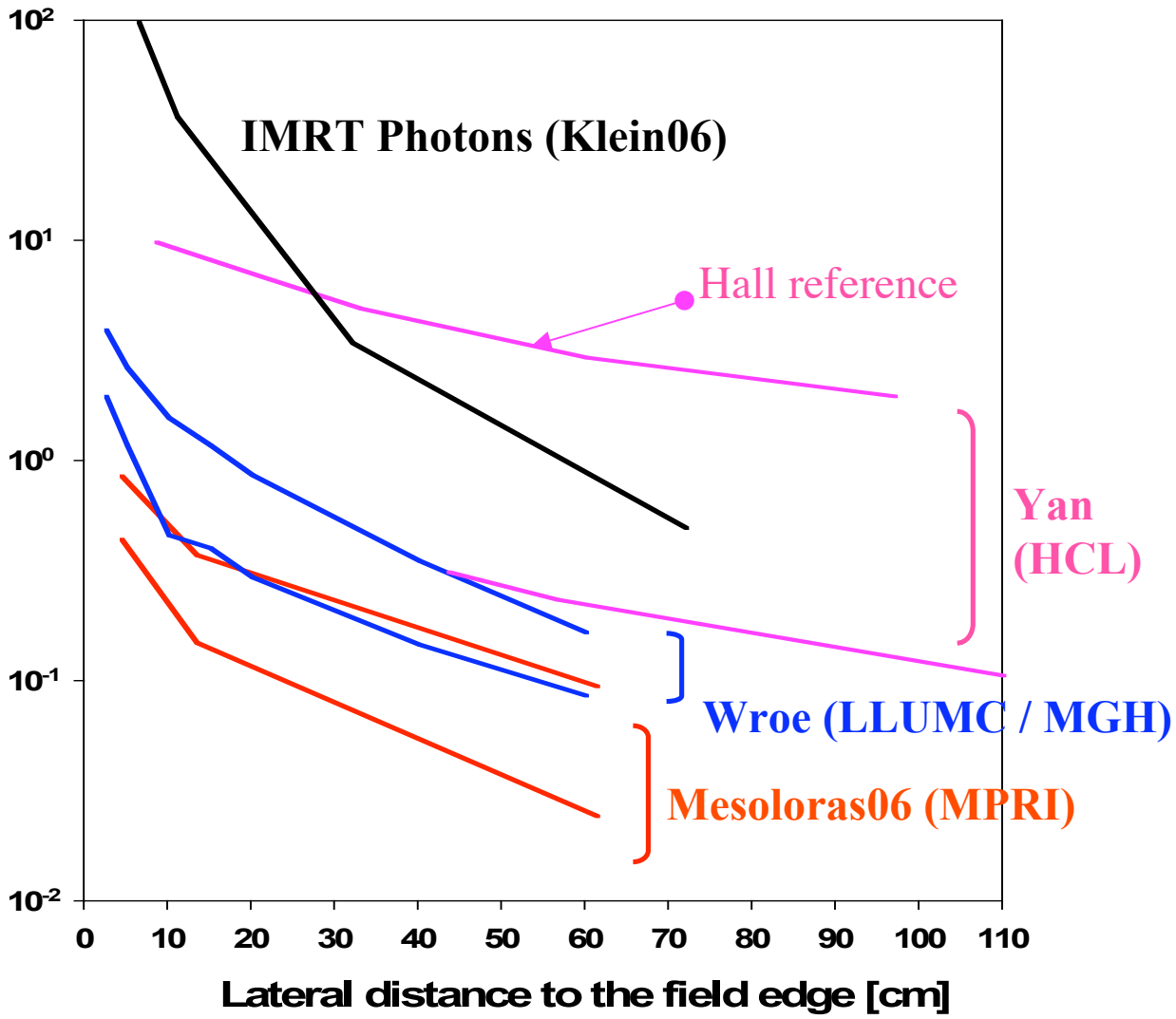
Courtesy T. Yock, N. Tarbell, J. Adams

Protons: Reduction in Second Malignancies

- Comparative Treatment Plans
  - Protons vs. Photons (Conformal or IMRT)
    - Rhabdomyosarcoma
      - Protons reduce risk of 2nd tumors by factor of $\geq$ 2
    - Medulloblastoma
      - Protons reduce risk of 2nd tumors by factor of 8-15
      - Bigger volumes: larger advantage for protons

Miralbell, Lomax et al, Int J Radiat Oncol Biol Phys. 2002;54:284-9

Neutrons: How great a problem?



Reduction in XR
associated
tumors may only
seen with
scanned protons
Hall, IJRPBP, 20

Neutrons: How Big a Problem?

- Some evidence suggests that the risk of neutrons from passively scattered protons will still be less than that associated with larger irradiation volumes from IMRT
- Nevertheless, magnetically scanned beams can further reduce neutron dose to the patient
  - Have additional advantages including eliminating need for fabrication of heavy, expensive brass apertures

Protons: Clinical Advantages

- **How do we document these with Level 1 evidence in clinical trials?**
- Pediatrics: Phase II studies are the only ones that can be conducted from ethical perspective
  - Children eligible for these should be considered for referral to appropriate center
  - Efforts should be made to expand the available centers with proton, pediatric oncology, pediatric anesthesia expertise to manage these patients
    - Scanned beams

Protons: Cost

- Goitein et al. (2003)
  - IMPT cost is 2.4 X higher than IMRT
    - Primarily related to Δ in capital (construction) cost
      - Cost difference projected to ↓ with time to 1.7
      - Might ↓ further to 1.4 with philanthropic/government support
- Lundqvist (2005)
  - Medulloblastoma (model using 5 year old child)
    - Protons associated with €23,600 in cost savings and 0.68 additional quality-adjusted life-years (QALYs) per patient.
  - Left sided breast cancer
    - Cost per QALY gained of €67,000 Euro for average patient
    - The cost per QALY gained considerably lower if a population with high-risk of developing cardiac disease was treated

Issues – Cost-Benefit

- $50,000 QALY is accepted criteria
  - Konski et al *J Clin Oncol 25:3603-3608*:
    - **Conclusion:** Even when based on the unproven assumption that protons will permit a 10-Gy escalation of prostate dose compared with IMRT photons, proton beam therapy is not cost effective for most patients with prostate cancer using the commonly accepted standard of $50,000/QALY. Consideration should be given to limiting the number of proton facilities to allow comprehensive evaluation of this modality.
    - **Assumptions**
      - Cost ratio p / IMRT = 1.6 (and maybe ~1!)
      - Prostate is not the only measure for protons
      - $50,000 is relative. What is the absolute value?

Need to meet an accepted QALY ceiling

- ***Reduced Cost***
- ***Increased Efficacy and Efficiency***
- ***Generalize p RT***

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Courtesy of H. Kooy, Ph.

Protons: Cost

- **Reduction in cost differential between proton radiation therapy and IMRT and other photon therapies should be a priority**
  - If protons/photons were = in cost, talk about need for randomized proton vs. photon studies would end
  - Less expensive facilities
  - Improved efficiency
  - Hypofractionation where appropriate
    - Early stage lung cancer, hepatocellular
  - Combined photon/proton treatment

Hypo-Fractionation

Phase I/II Study of Neoadjuvant Accelerated Short Course Radiation Therapy with Proton Beam and Capecitabine for Resectable Pancreatic Cancer

PI: T. Hong / H. Mamon – MGH / DFCI

- Phase I: To determine the feasibility and tolerability of radiation therapy delivered with proton beam in a one week accelerated schedule with concurrent capecitabine for pancreatic cancer.
- Phase II: To follow

Dose Level	Step 1	Dose/fraction	# Tx	Fractionation Schedule	Dtot	Week 1 Schedule	Week 2 Schedule	Total Days
1	1	3 CGE	10	QD	30	M T W Th Fri	M T W Th Fri	12
	Step 2	**Dose/fraction**	**# Tx**	**Fractionation Schedule**	**Dtot**	**Week 1 Schedule**	**Week 2 Schedule**	**Total Days**
2	1	5 CGE	5	QD	25	M W F	T Th	11
3	2	5 CGE	5	QD	25	M T Th Fri	M	8
4	**3**	**5 CGE**	**5**	**QD**	**25**	**M T W Th Fri**	**-**	**5**

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Hypo-fractionation

Professional Charges	CPT	3D-CRT 50.4Gy	IMRT 50.4 Gy	Proton 25 Gy
Clinical plan	77263	1	1	1
IMRT Plan	77301		1	
Simulation: simple	77280	1	1	1
Simulation: 3D	77295	1		1
Dosimetry calc	77300	7	9	2
Plan complex	77315	1		
Device simple	77332			1
Device complex	77334	6	9	4
Weekly mngmt	77427	6	6	1
Special procedure	77470		1	
Consult: comps	99245	1	1	1
Total Prof.		**$2,600**	**$3,100**	**$1,200**

Technical Charges	CPT	3D-CRT 50.4 Gy	IMRT 50.4 Gy	Prot 25 G
CT guidance	76370	1	1	1
Simulation: simp	77280	1	1	1
Simulation: 3D	77295	1		1
Dosimetry calcs	77300	7	9	2
IMRT plan	77301		1	
Plan: complex	77315	1		
Device: simple	77332			1
Device: complex	77334	6	9	4
Physics consult	77336	5	6	1
Treatment γ	77414	28		
IMRT treatment	77418		28	
Port film	77417	5	5	1
Special proc	77470		1	
Treatment:p	77523			5
Consult: comp	99245	1	1	1
Total Technical		**$7,500**	**$13,700**	**$8,00**
Overall Cost		**$10,000**	**$16,700**	**$9,20**

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Differentiate between cost to institution and cost to patient!

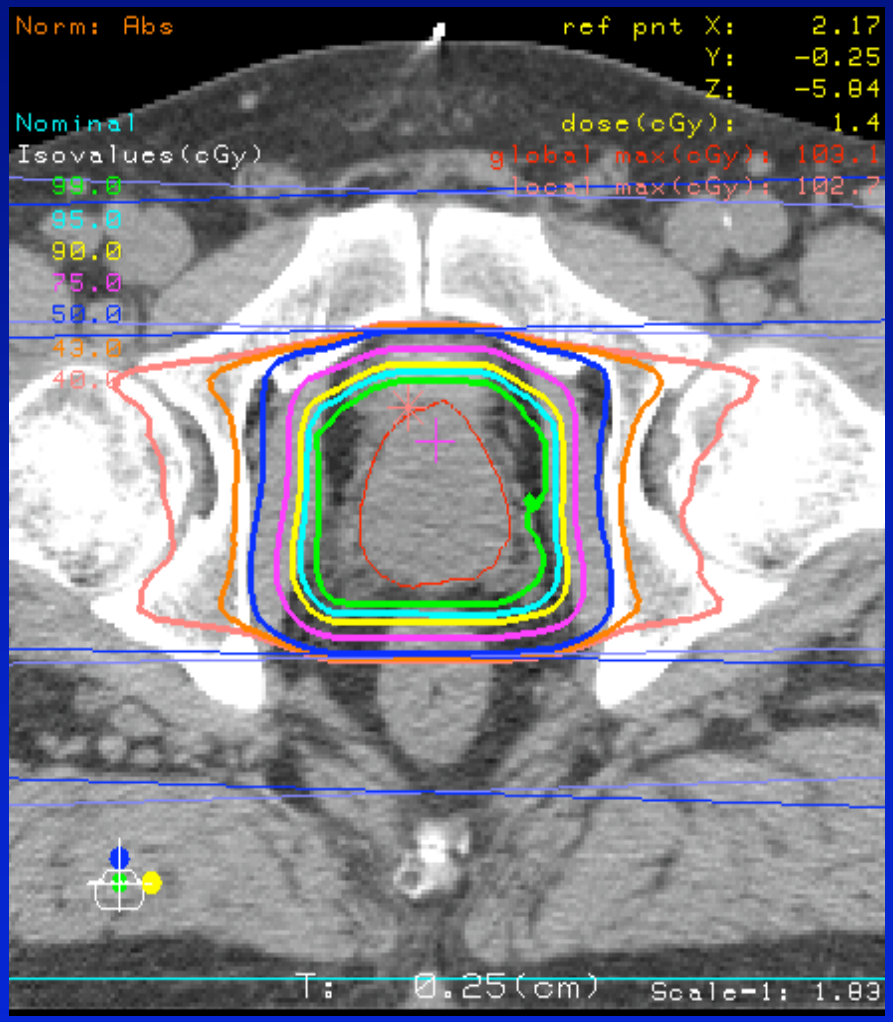
Protons: Clinical Advantages

- **ADULT MALIGNANCIES**
- Randomized studies of protons vs. photons
  - Equipoise: Clinicians and patients aware of dose advantage may refuse to participate in randomized phase III studies in some anatomic sites: i.e.: head/neck
    - ? Tissue heterogeneity (i.e. mucus in sinus), motion, changes in tumor/tissue density more critical to protons
    - Was it necessary to randomize patients between orthovoltage and megavoltage photons?
  - Prostate?

Protons: Clinical Advantages

- **ADULT MALIGNANCIES**
- Randomized studies of protons vs. photons
  - Prostate?
    - When/where protons are a limited resource, protons should ideally be used for patients not well or not able to be treated by protons
    - Prostate cancer treatment options
      - Protons
      - IMRT
      - Prostate brachytherapy
      - Watchful waiting

Prostate Proton Treatment Plan



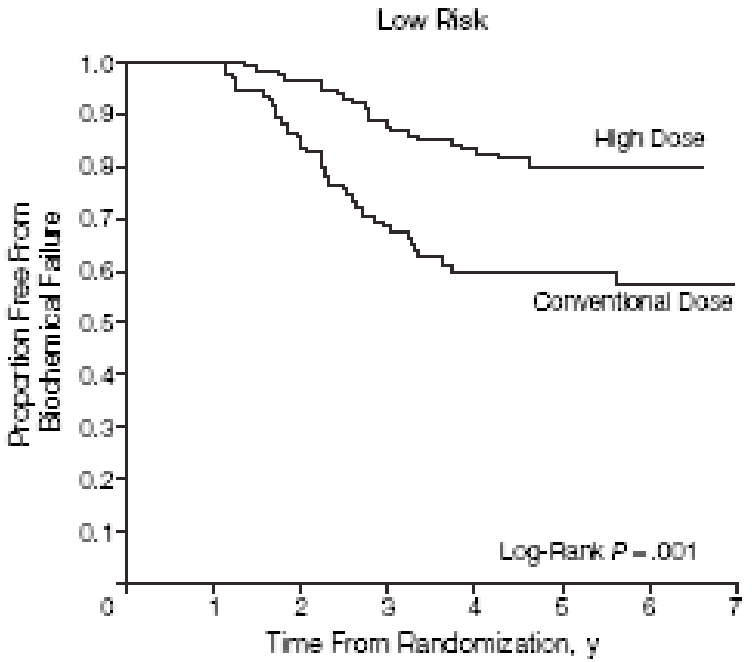
MASSACHUSETTS GENERAL HOSPITAL

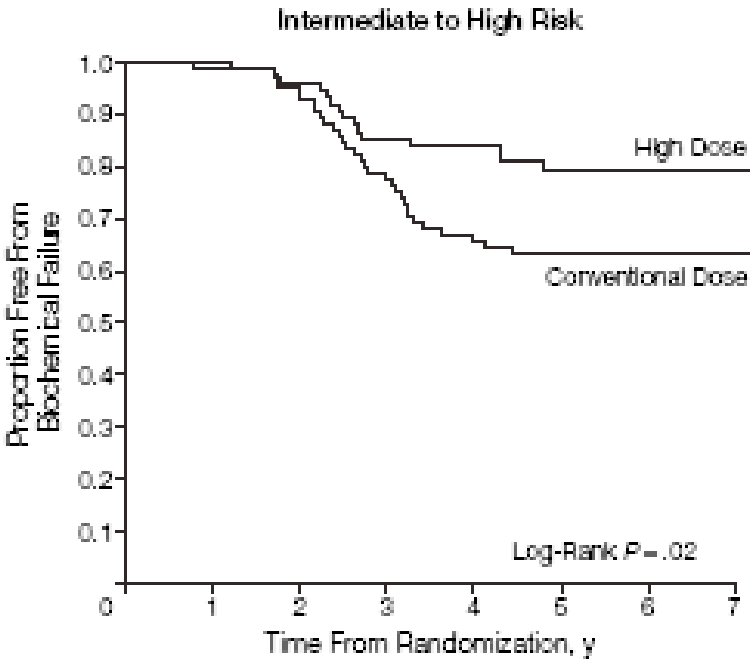
Harvard Medical School

Zietman A, Shipley W

Dose Escalation for Prostate Cancer with Protons

Figure 3. Freedom From Biochemical Failure (ASTRO Definition) Following Either Conventional-Dose (70.2 GyE) or High-Dose (79.2 GyE) Conformal Radiation Therapy



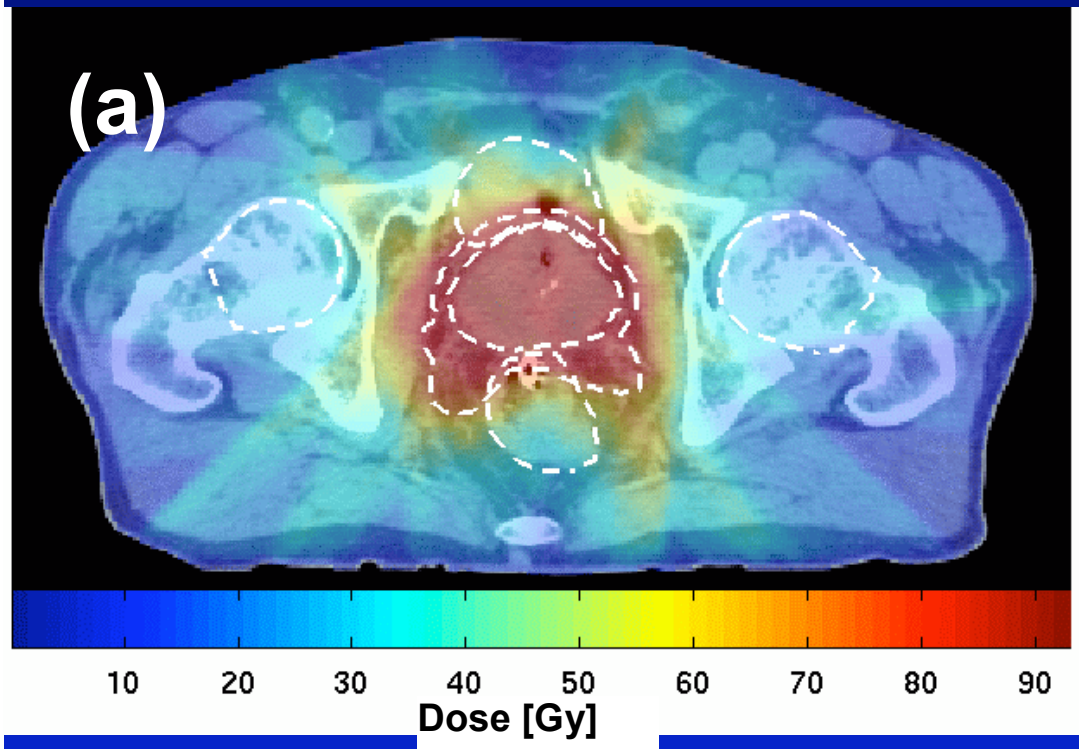


No. at Risk								
High Dose	111	111	92	74	64	39	14	4
Conventional Dose	116	116	111	99	69	56	24	12

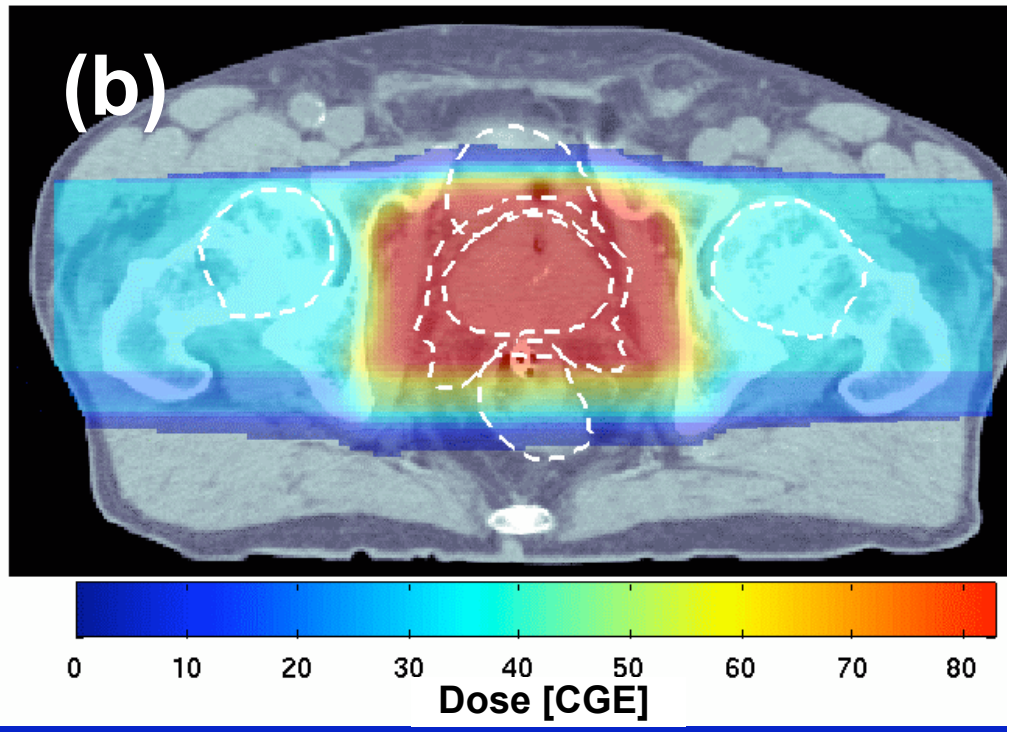
No. at Risk								
High Dose	96	95	79	65	54	38	17	6
Conventional Dose	76	75	70	61	57	40	19	8

Analysis of these early cases is by risk subgroup. Low-risk patients have prostate-specific antigen level <10 ng/mL, stage ≤T2a tumors, and Gleason scores ≤6. ASTRO indicates American Society for Therapeutic Radiology and Oncology; GyE, gray equivalents (see "Methods" section).

Prostate IMRT and Proton Treatment Plans



IMRT



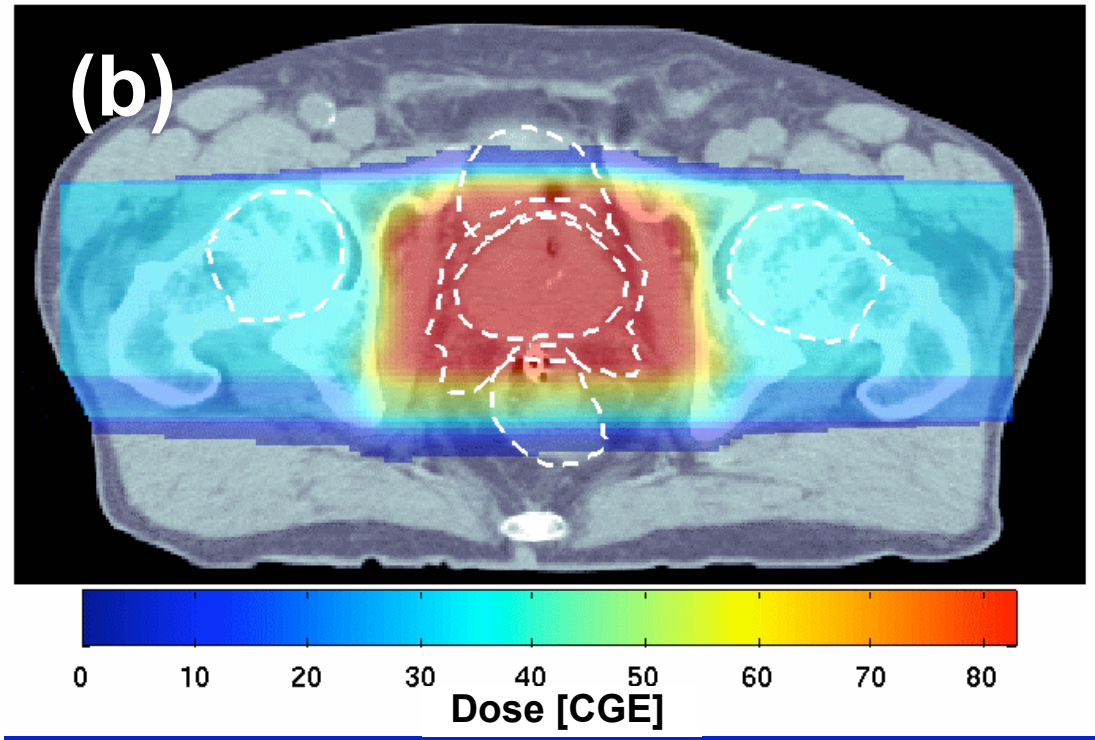
3D Conformal Protons

MASSACHUSETTS GENERAL HOSPITAL

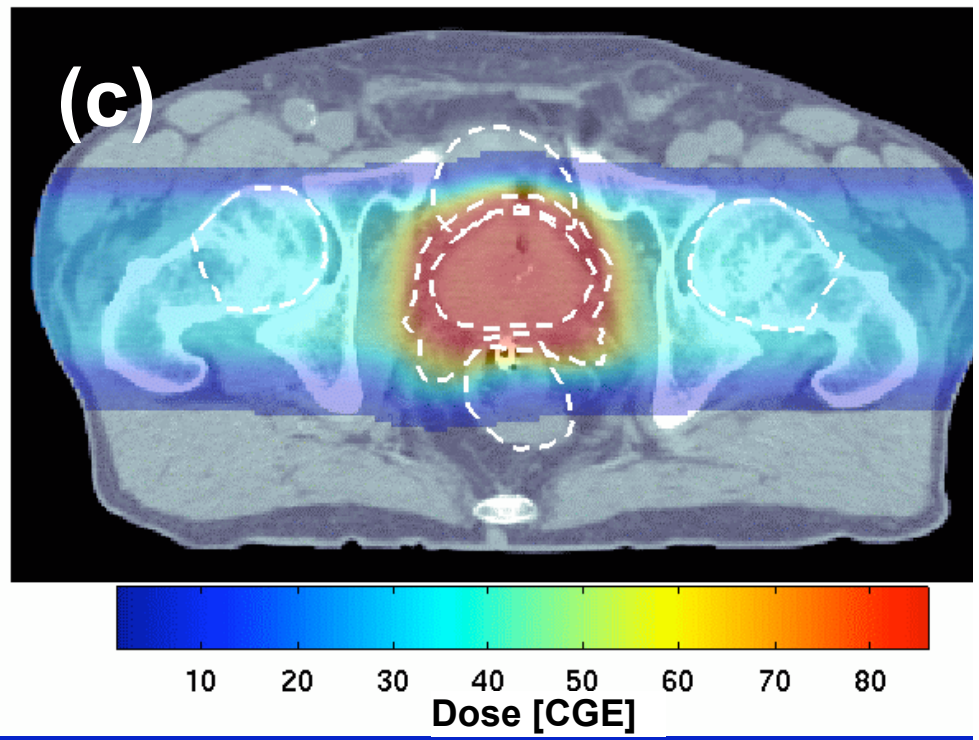
Harvard Medical School

Trofimov et al, 2007

Prostate IMRT and Proton Treatment Plans



3D Conformal Protons



Intensity Modulated Protons**

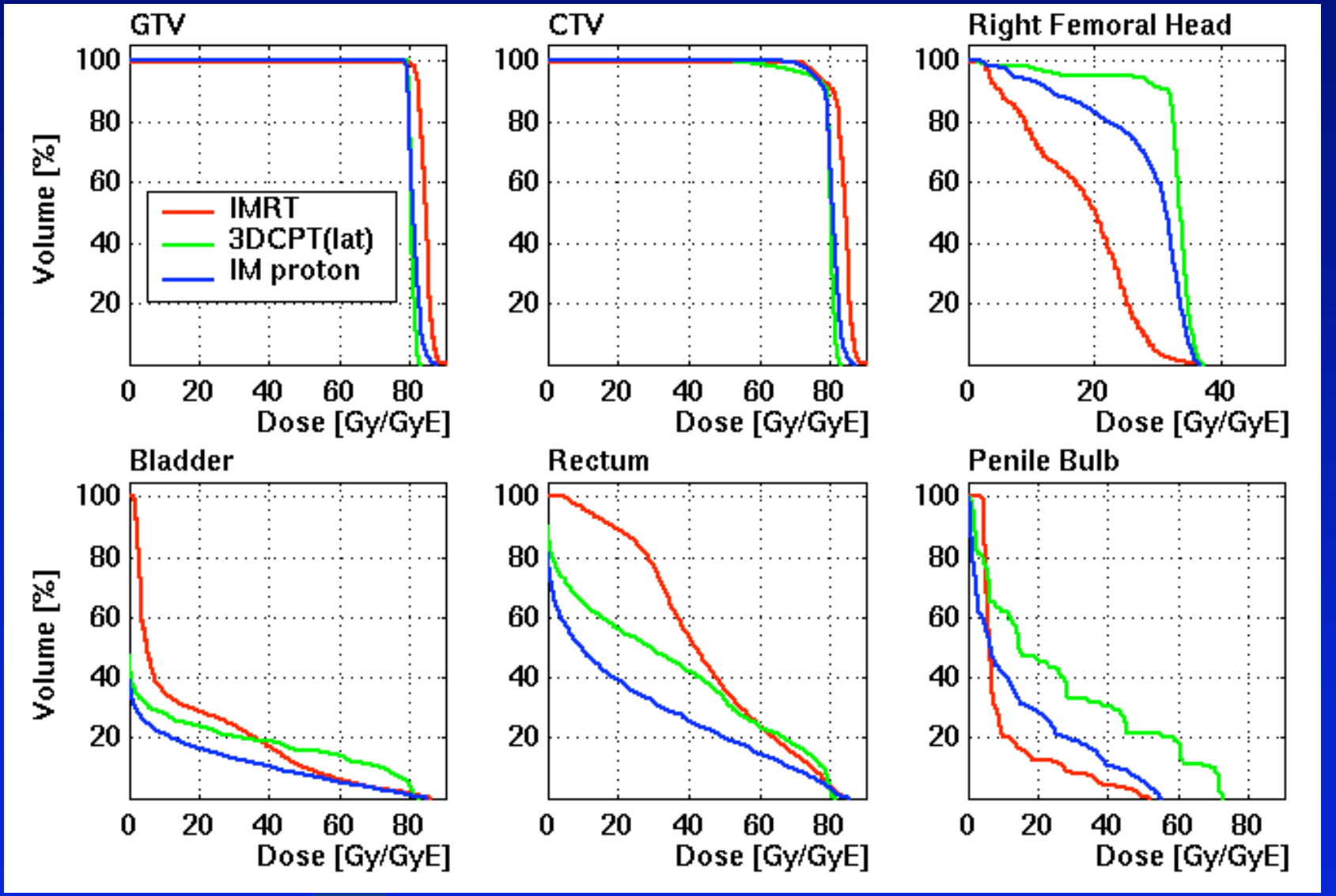
Optimal IMPT will need to account for range uncertainty→Rectal probe dosimeter→NCI X

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Trofimov et al, 2007

Prostate IMRT and Proton Treatment Plans



MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Trofimov et al, 2007

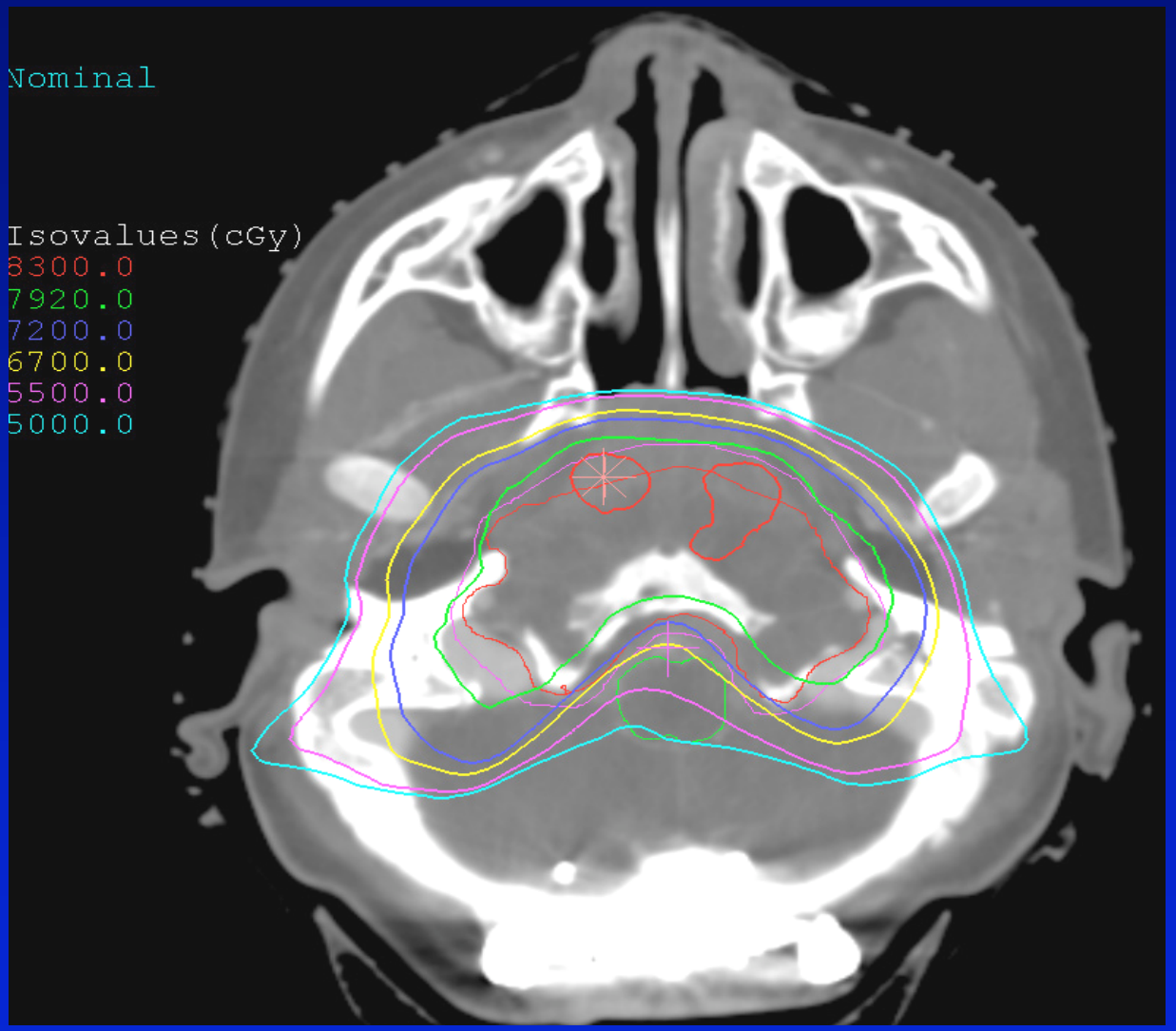
Clinical Use of Protons

- **There are certain to be clinical gains at a number of anatomic sites**
- **Societal question:**
  - How to provide access to the benefits of this technology for the greatest gain for the maximum number of patients?
    - Protons for patients not well treated by photons
    - Combined photons and protons in adult patients
    - Hypofractionation: Hepatocellular, lung cancer
    - Technological improvements to reduce cost

Base of Skull Chordoma

8 year-old boy with
Clivus chordoma

Prescription dose 79.2 CGE



MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

N Liebsch MD, J Adams CMD

Sacral Chordoma

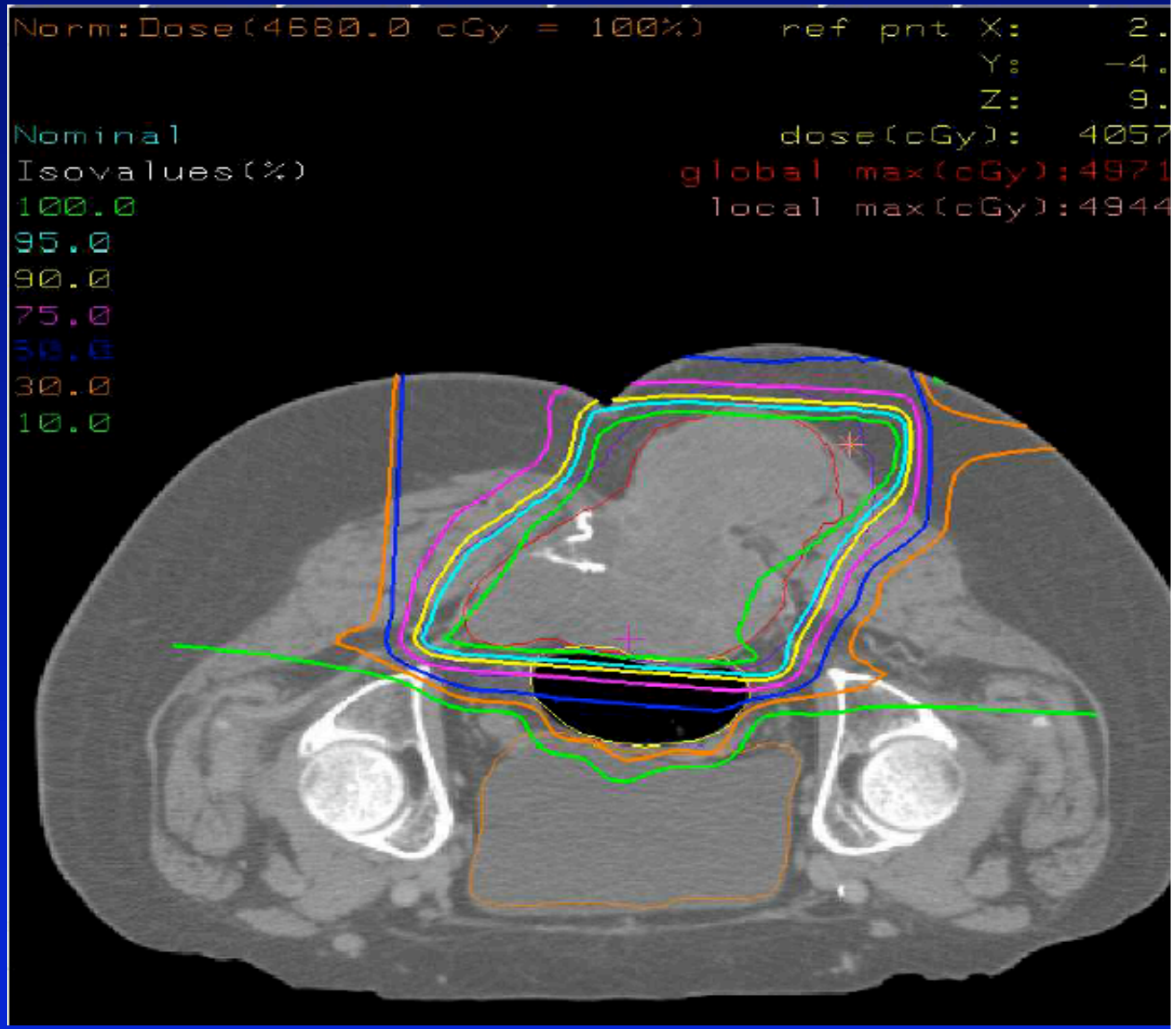
Treatment plan

S2-5 chordoma

Biopsy only

77.4 GyE (photons 30.6 Gy
protons 46.8 GyE)

No evidence of progressive disease 51 months after start of proton treatment



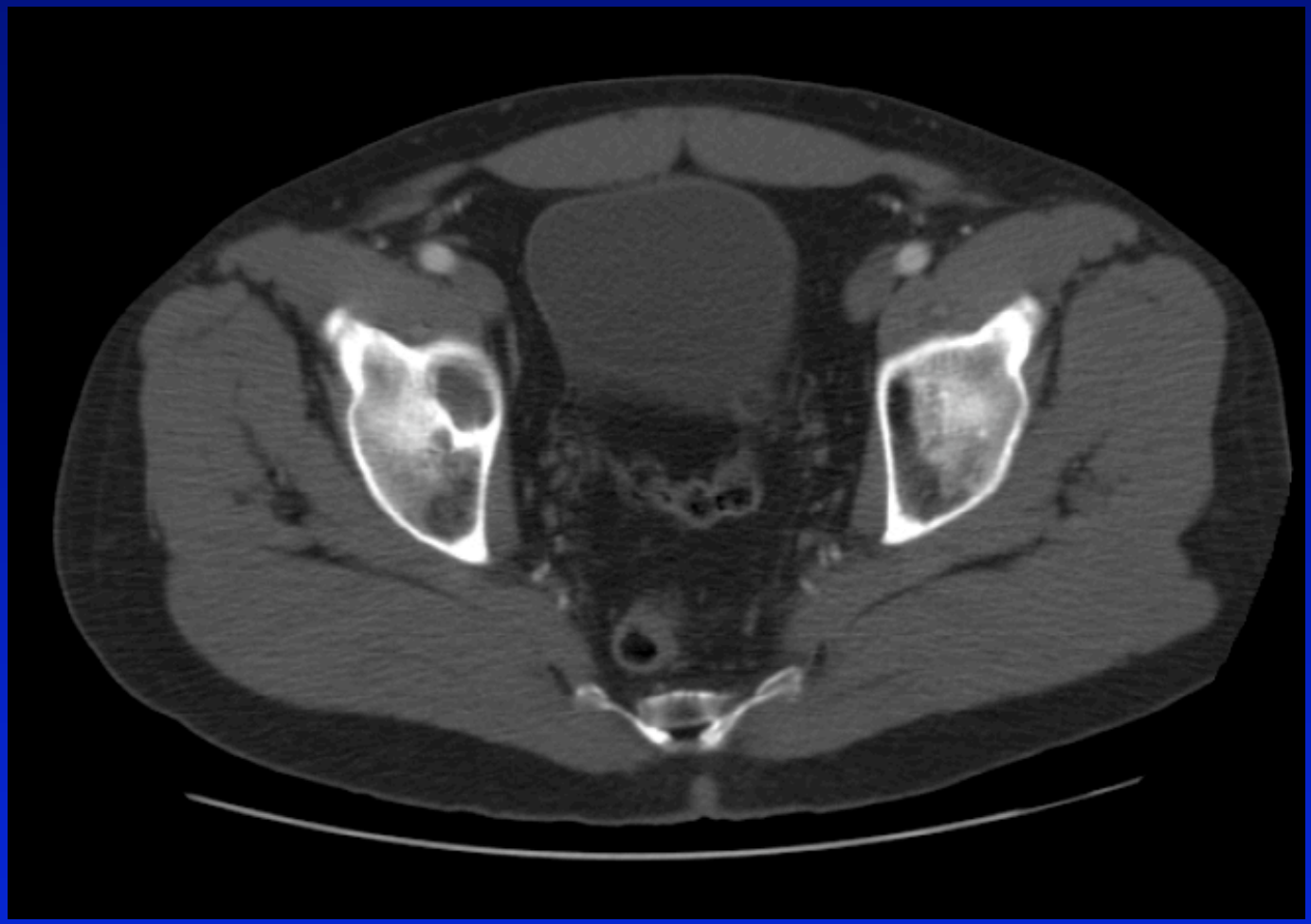
Protons: How User Friendly?

- Reliability of most proton equipment is lower than linear accelerators
  - Downtime higher
  - Back-up not available if cyclotron down
  - Maintenance requires more time
    - Hampered by lack of back-up proton facility
- Training for personnel in the multiple new centers under construction or in development

Increasing Importance of Target Definition

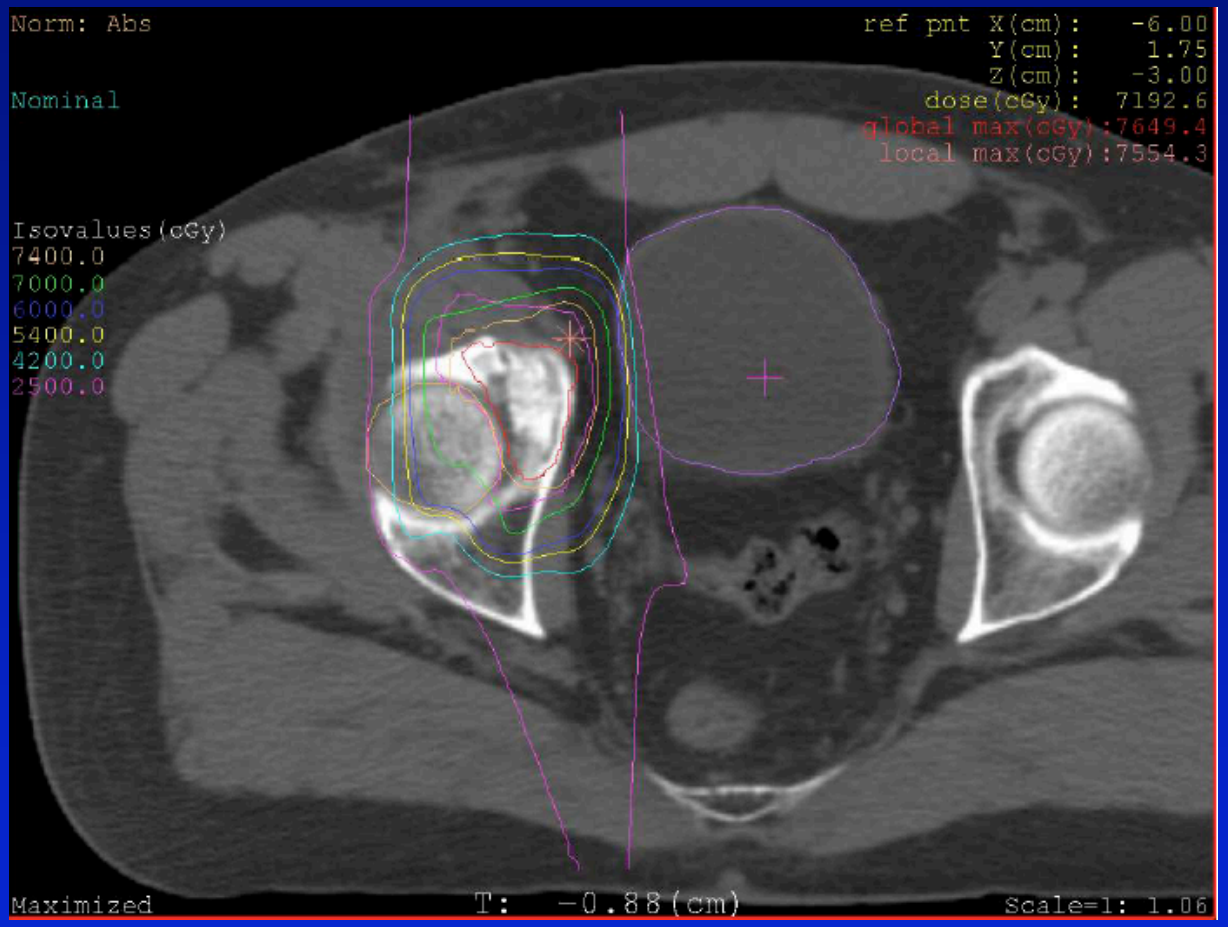
- For static target, dose can be delivered with protons with more precision and certainty than our knowledge of where the tumor cells are

Pelvic Chondrosarcoma



Low grade chonsrosarcoma, managed by curettage, cement packing

Pelvic Chondrosarcoma

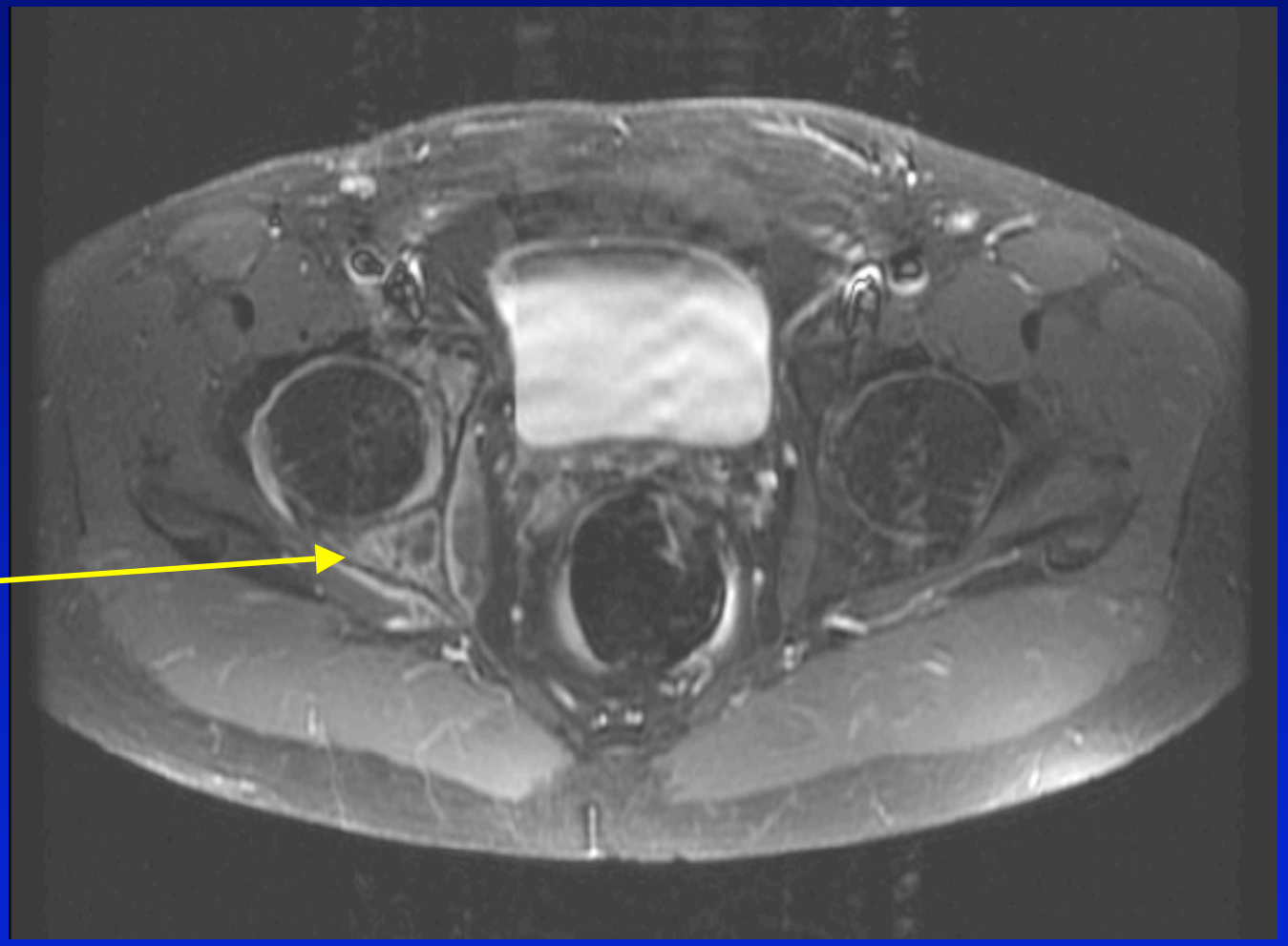


Managed by curettage, cement packing, and protons 74 GyE in 37 fx

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Pelvic Chondrosarcoma



Marginal Miss

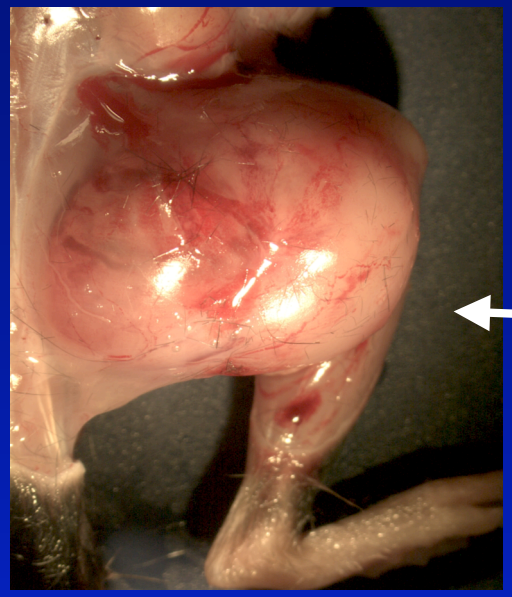
3 years after end of treatment

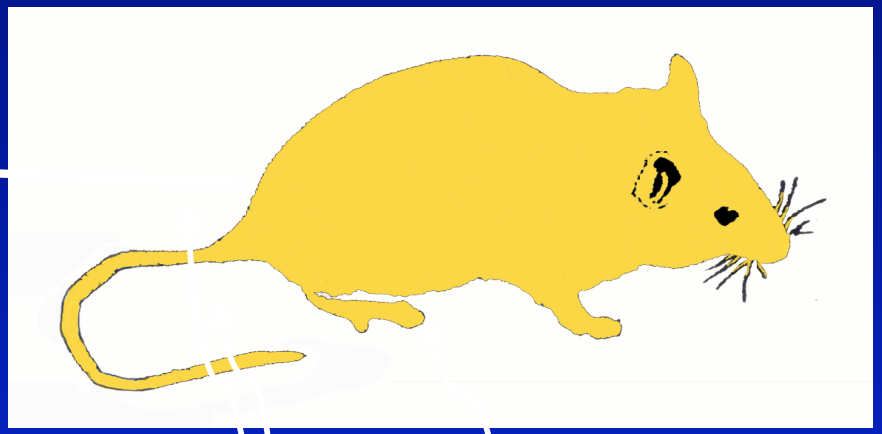
Managed by curettage, cement packing, and protons 74 GyE in 37 fx

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

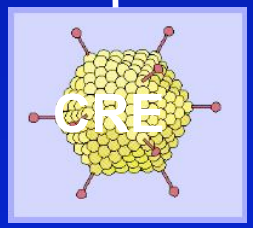
Intramuscular injection of Adeno-Cre

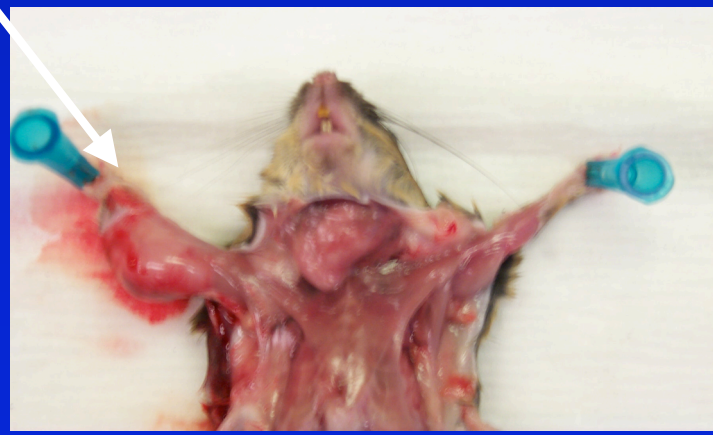




K-ras$^{LSL.G12D}$; p53$^{LSL.R172H/Flox}$

High grade spindle cell sarcomas

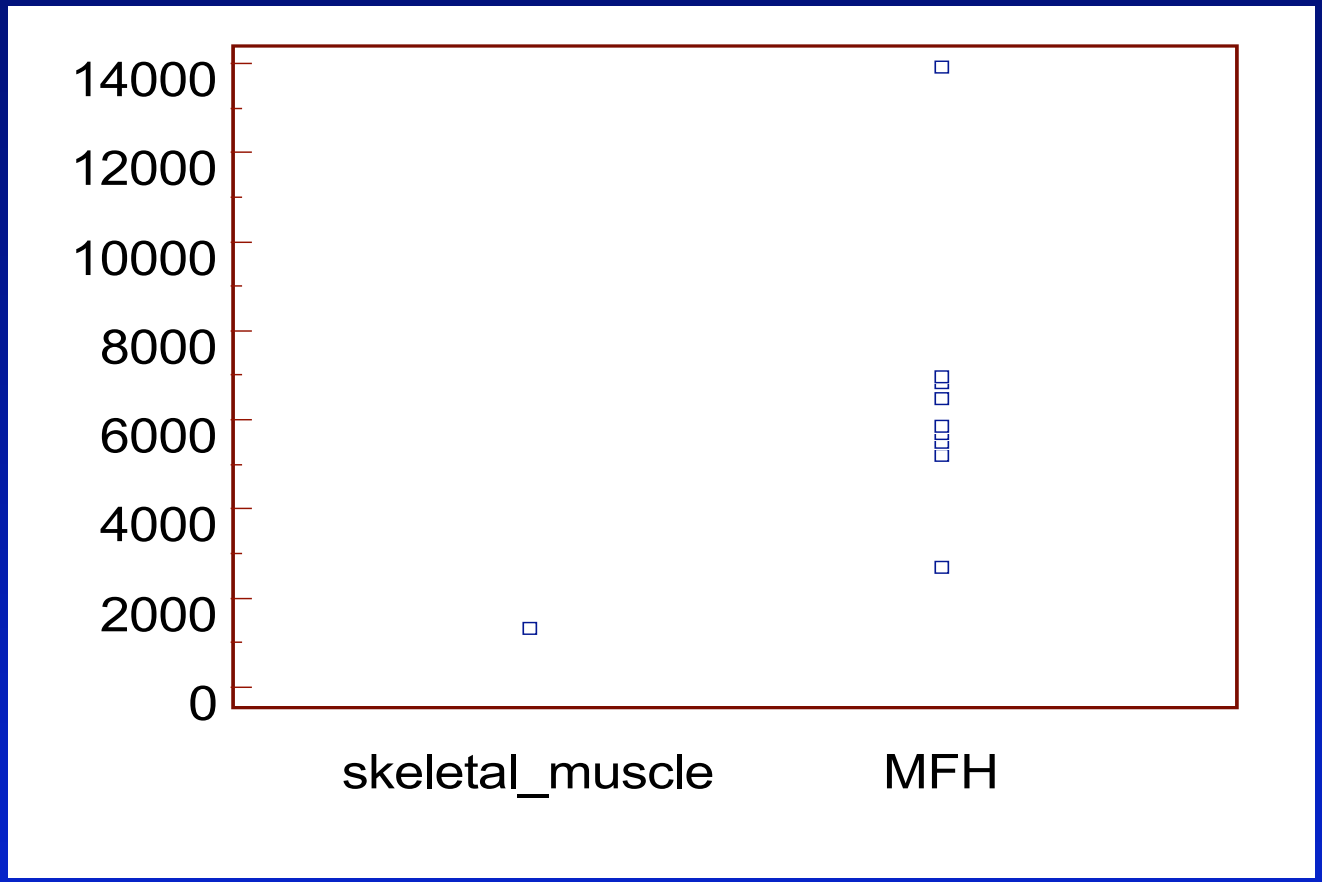




MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Cathepsin B in Human Sarcomas



Intra-operative imaging of human sarcomas may be feasible with a probe activated by cathepsin B or another enzyme expressed in human sarcomas

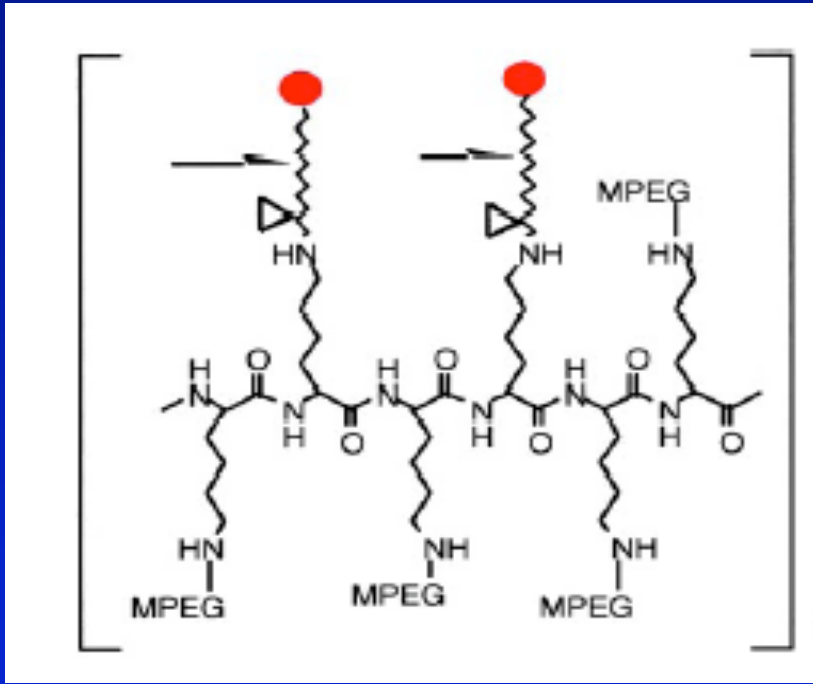
Sam Yoon

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Molecular Imaging of Tumors with Optical Probe for Cathepsin B

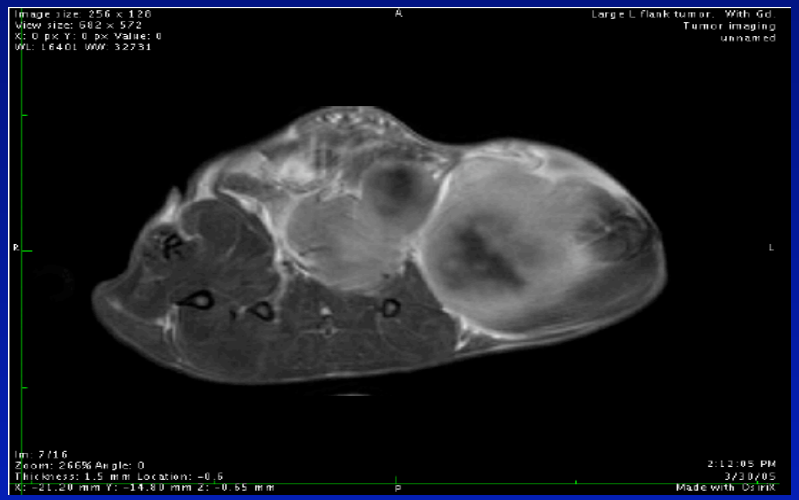
- Near infra-red fluorochromes quenched due to FRET
- Probes taken up into lysosomes
- Cathepsin B cleavage releases fluorochromes
- Signal amplification of several hundred fold

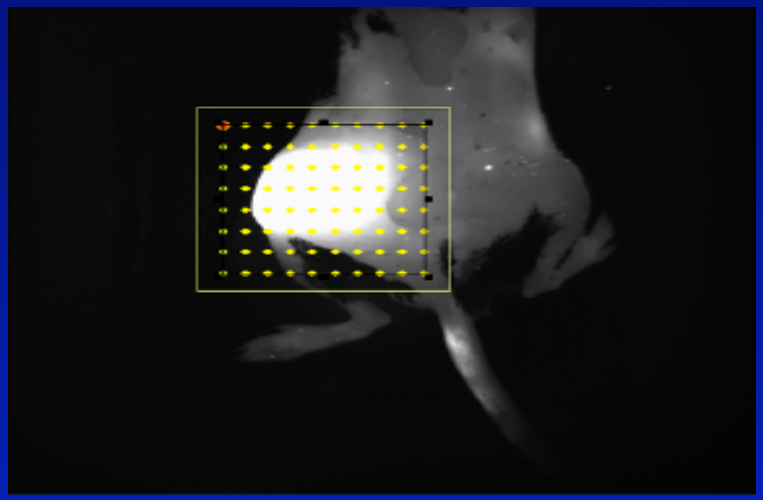


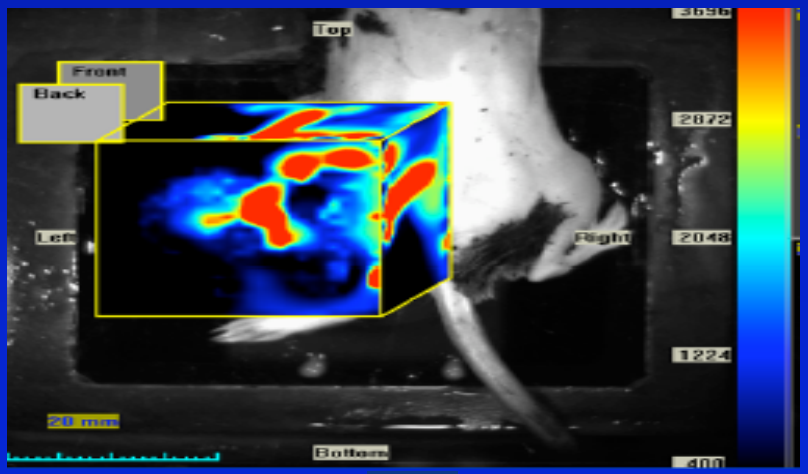
MASSACHUSETTS GENERAL HOSPITAL

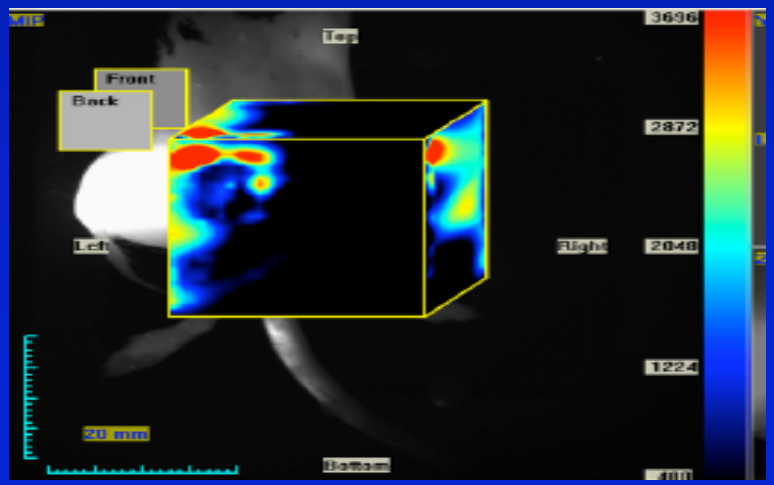
Harvard Medical School

Imaging Sarcoma with Fluorescence Molecular Tomography





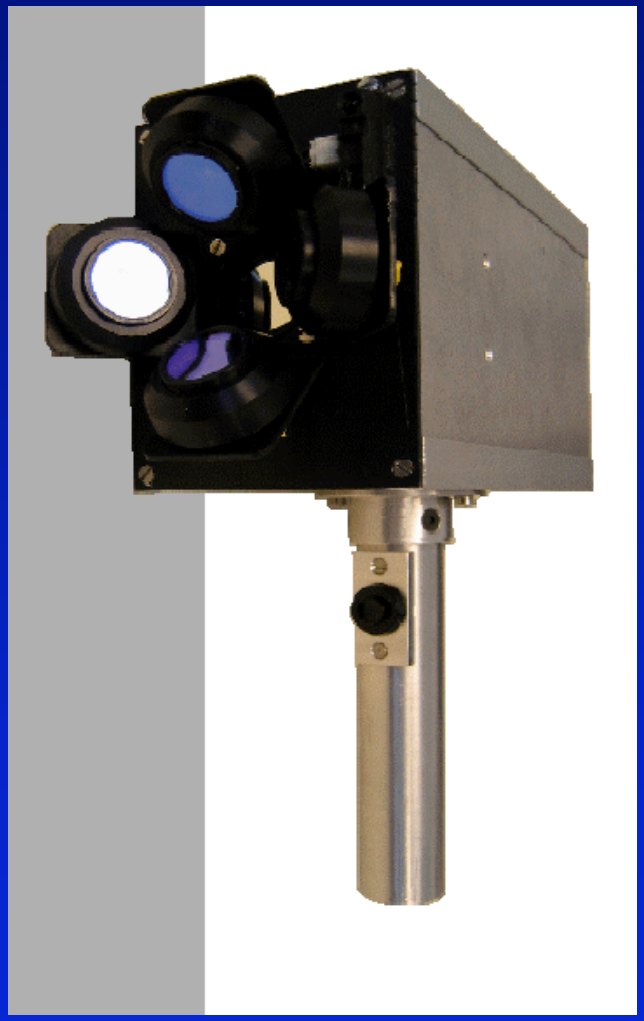


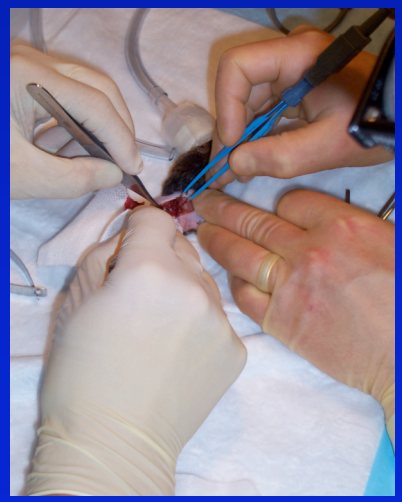


MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Intra-operative Imaging

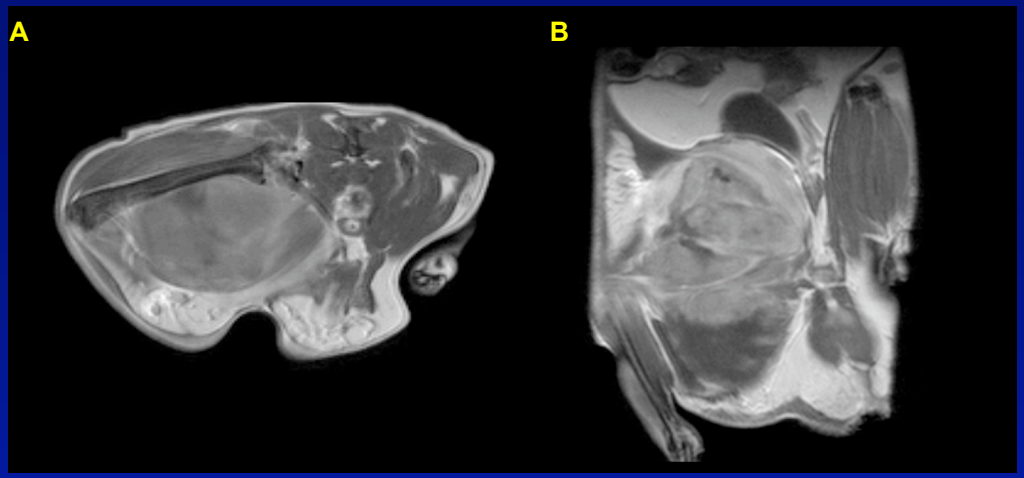




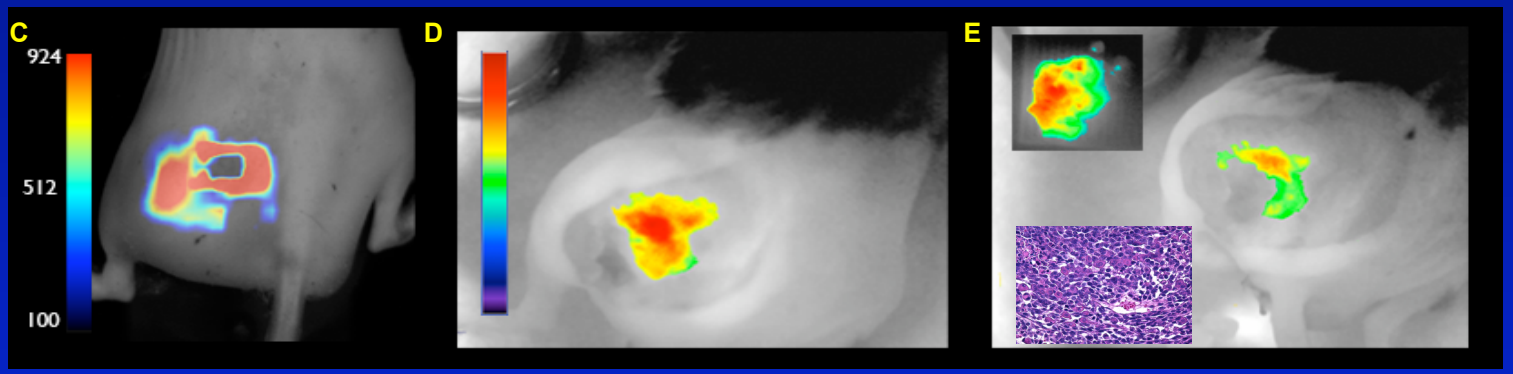
MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

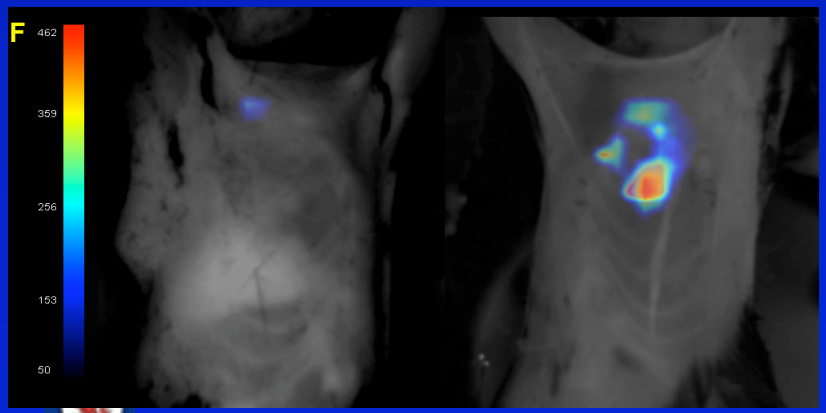
MRI



C:FMT/
HHD: before (D) and after (E) surgical resection



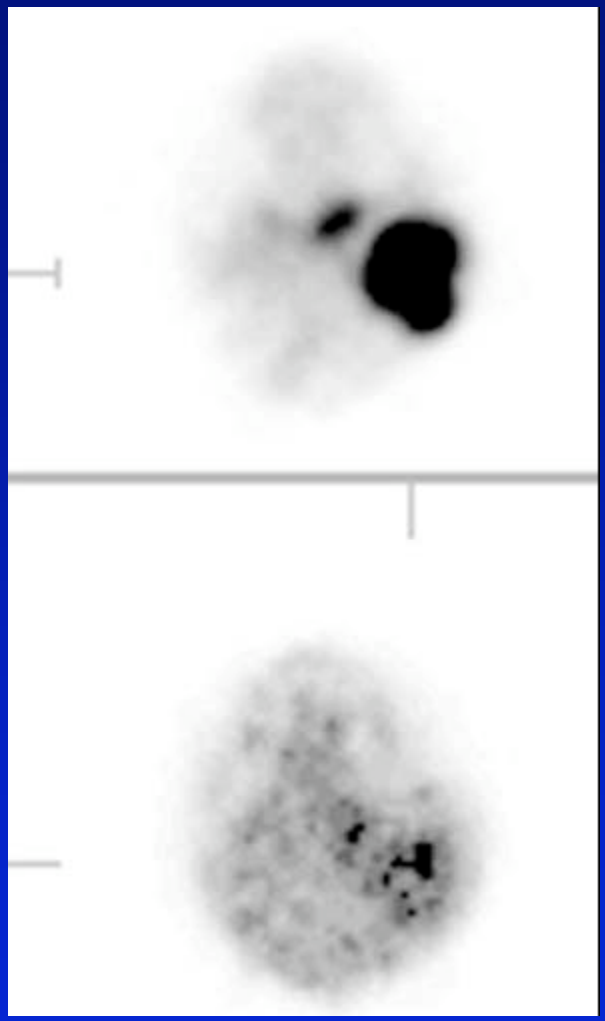
FMT of mouse without and with Lung mets.



MASSACHUSETTS GENERAL HOSPITAL

Medical School

[F^{18}] Fluoromisonidazole for Imaging of Hypoxia



FDG-PET showing primary tumor, large nodal metastasis

FMiso-PET demonstrating focal areas of hypoxia

Opportunity for dose paintin

MASSACHUSETTS GENERAL HOSPITAL

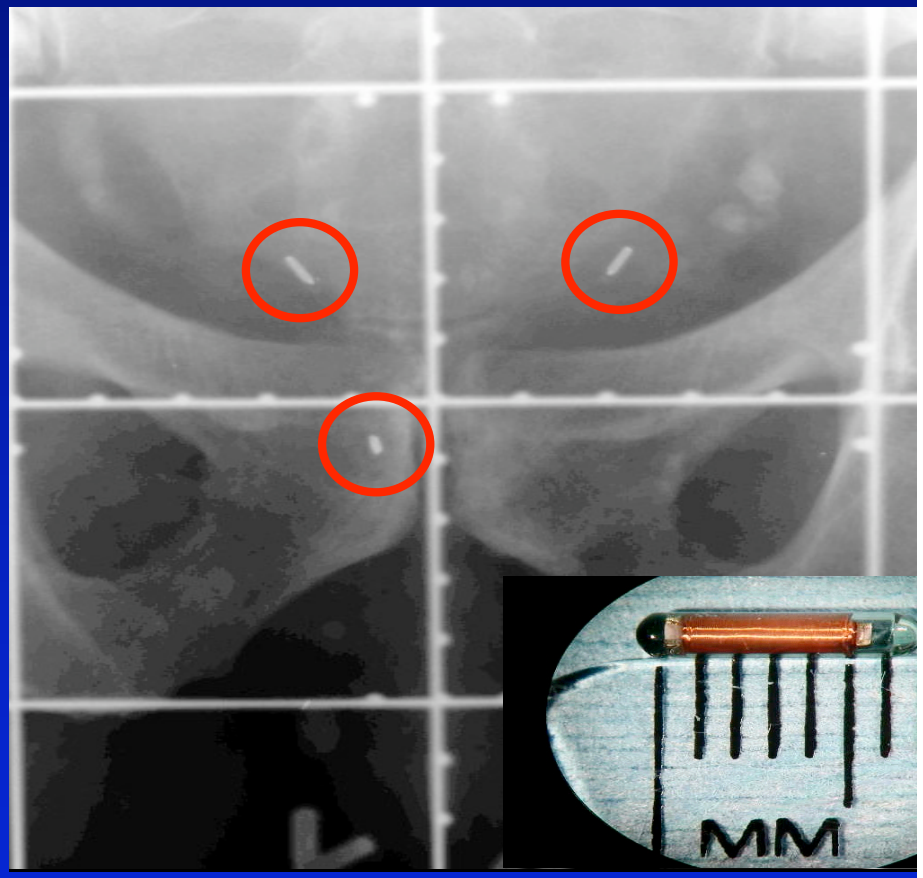
Harvard Medical School

Image Guidance

- Orthogonal orthovoltage digital imaging panels
  - Cone beam becoming standard for photons
- Patient positioners
  - Couches with 6 degrees of freedom interfaced with imaging system
  - Robotic patient positioners
- Tracking

Implanted Transponders

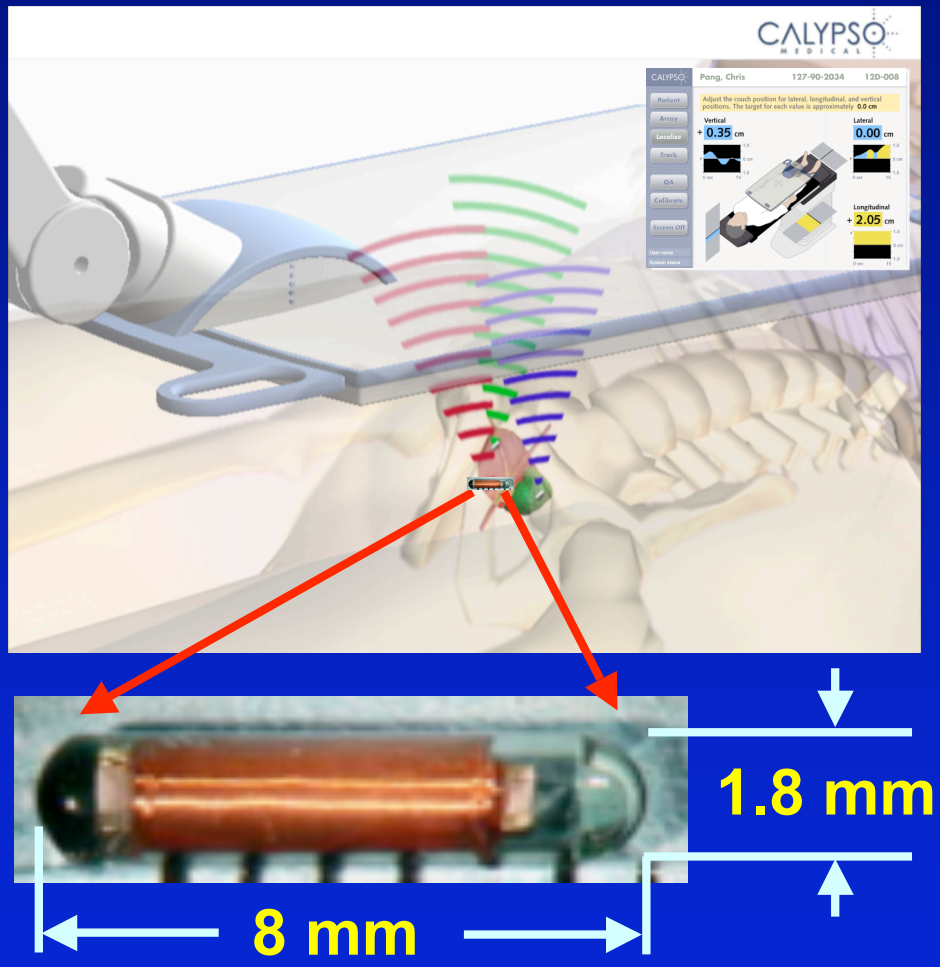
- 3 transponders
- Implanted transrectally under ultrasound guidance
- 10 minute procedure
- Consistent with gold marker implant effects
- Good positional stability over 8 weeks (s_{ave} = 0.8 mm)



MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

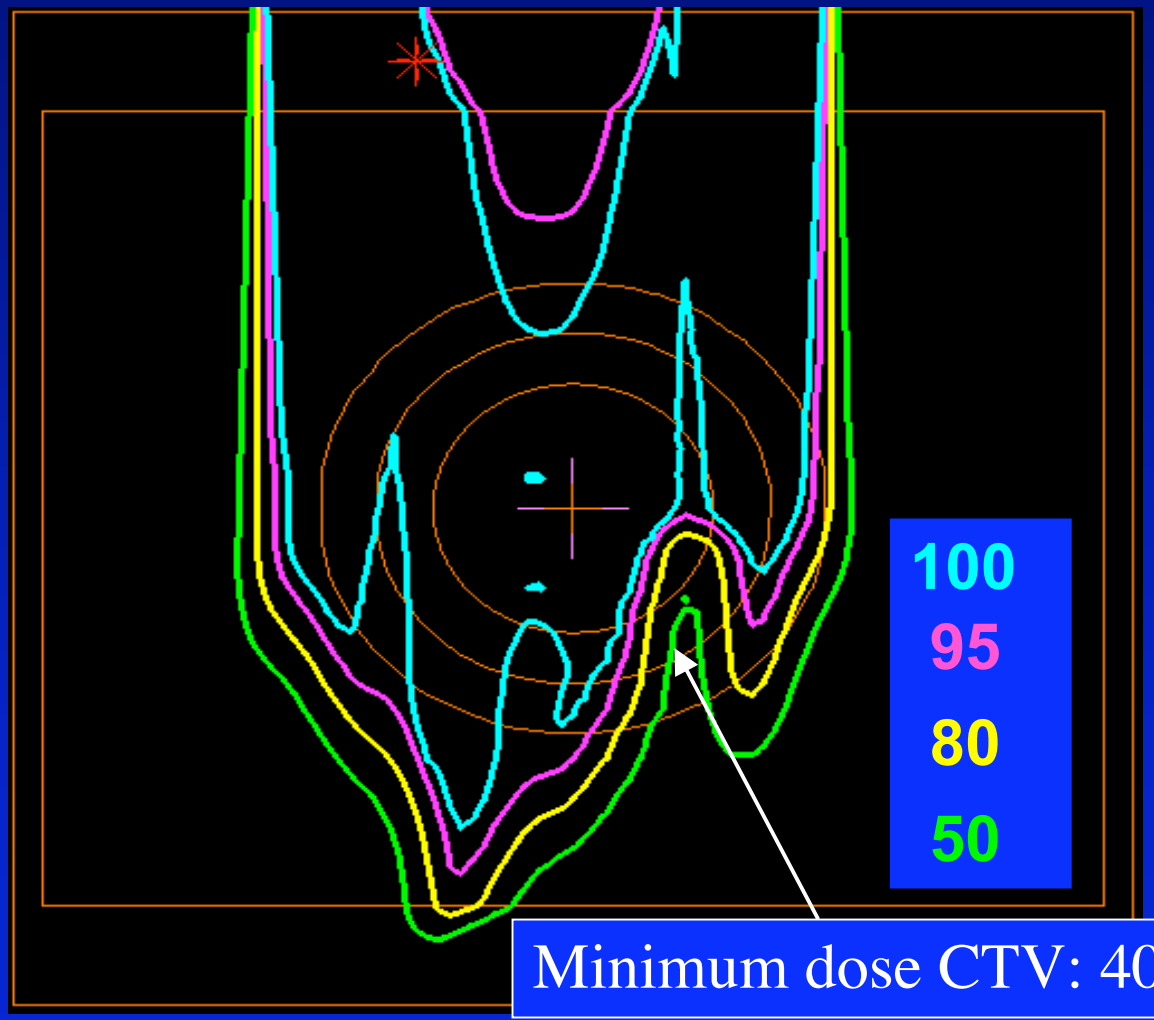
AC Wireless Magnetic Tracking



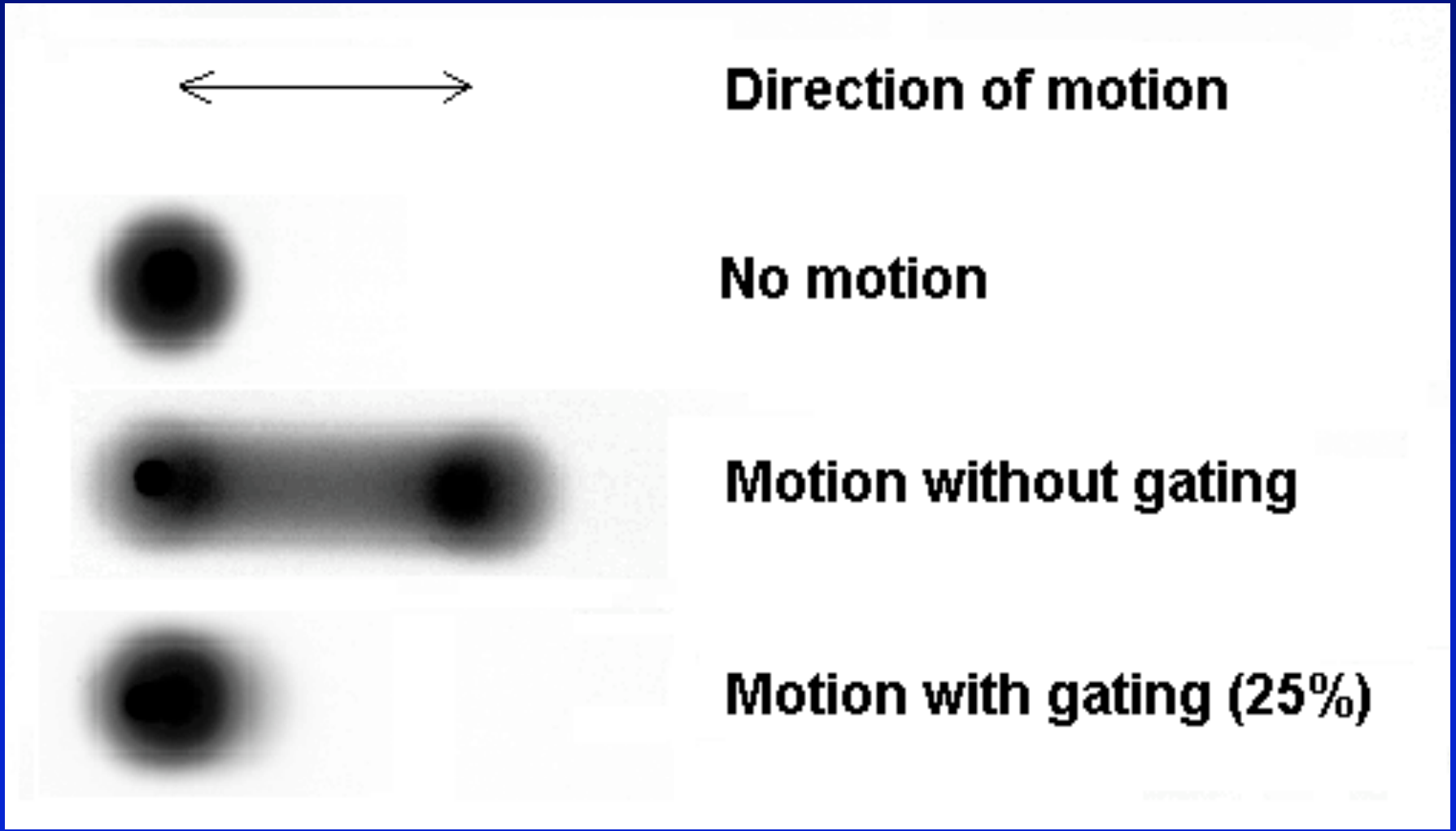
MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

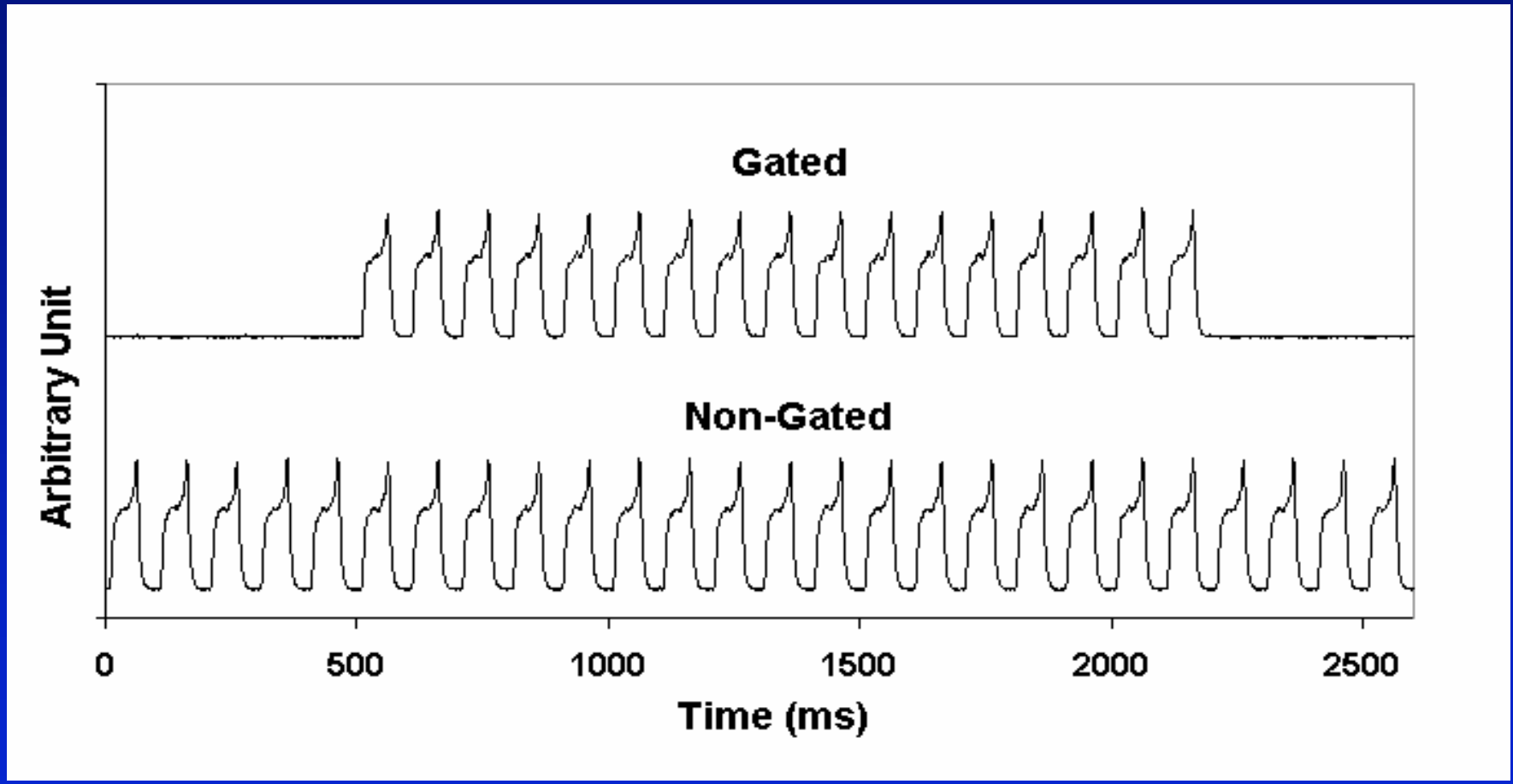
Dose deformation protons, tumor 5 mm off



Respiratory Gating



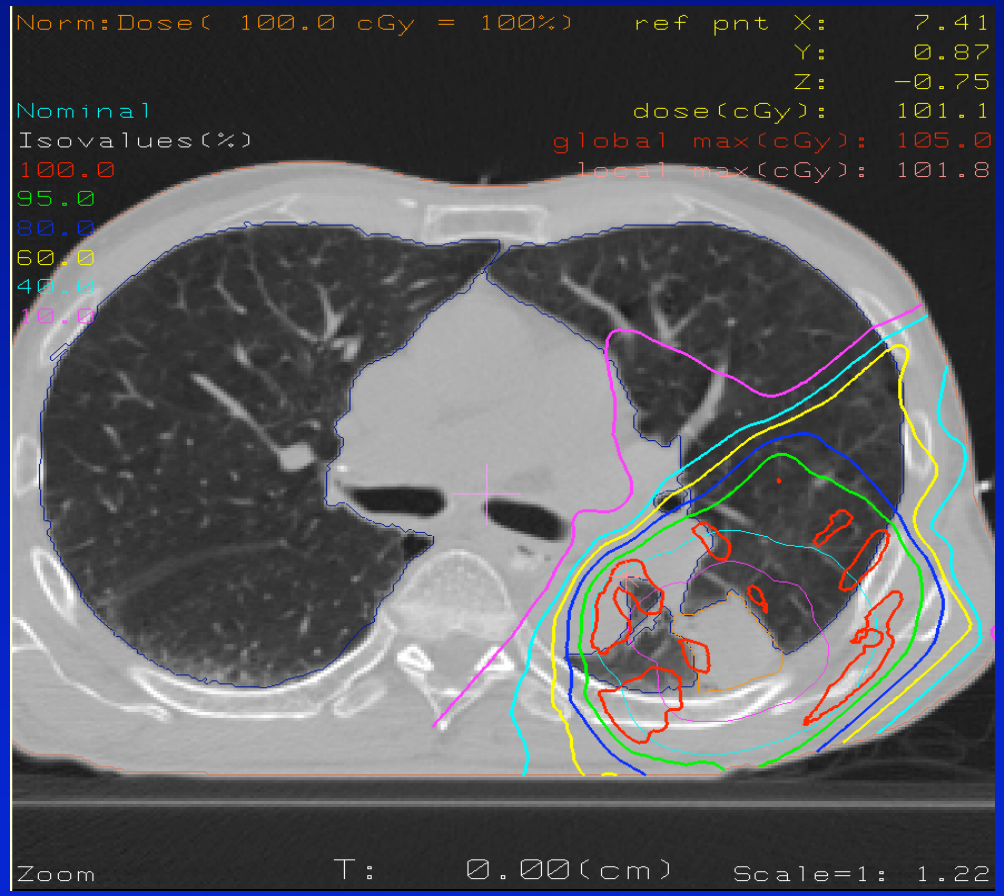
Respiratory Gating

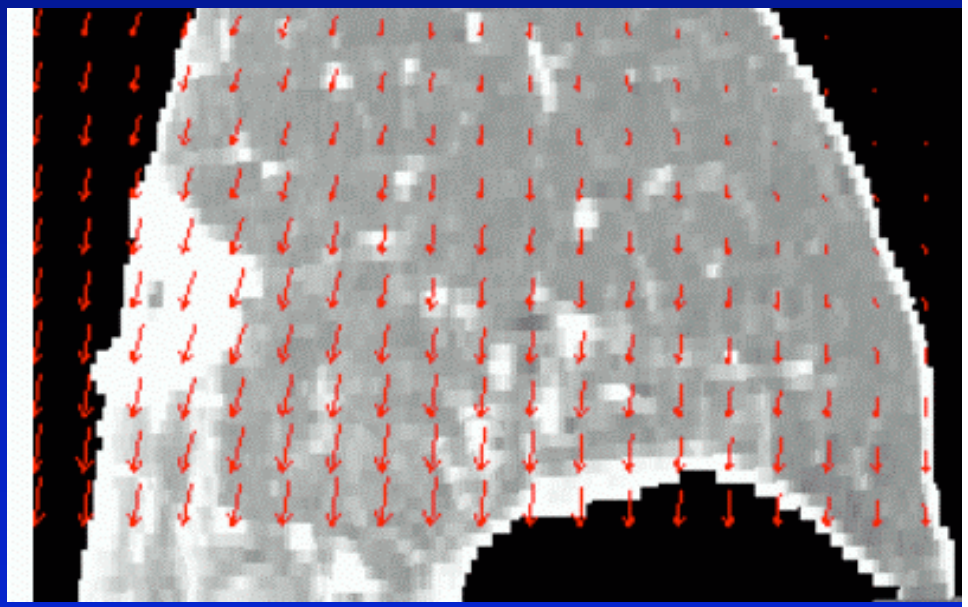


MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

4D CT and Motion Effects





MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

TREATMENT IMPLICATIONS

Need to evaluate the dosimetric implications of motion

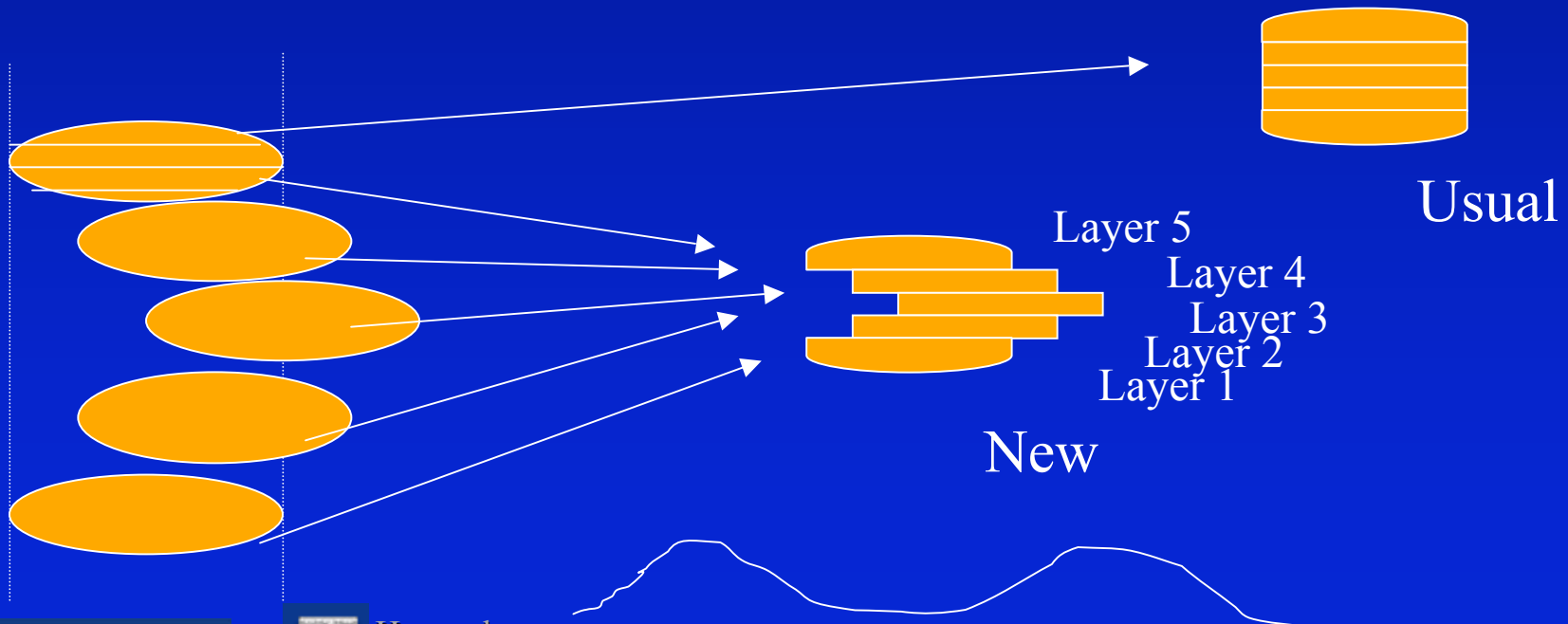
Adjustment Strategies

- Margins
- Manual gating
- Intrafraction position adjustment with specific thresholds
- Real time tracking and treatment delivery modifications (4D DELIVERY)
  - Rectal probe dosimeter
  - Automatic couch motion
  - Automatic beam motion

Scanning with Respiration Compensation
(Not just gating)

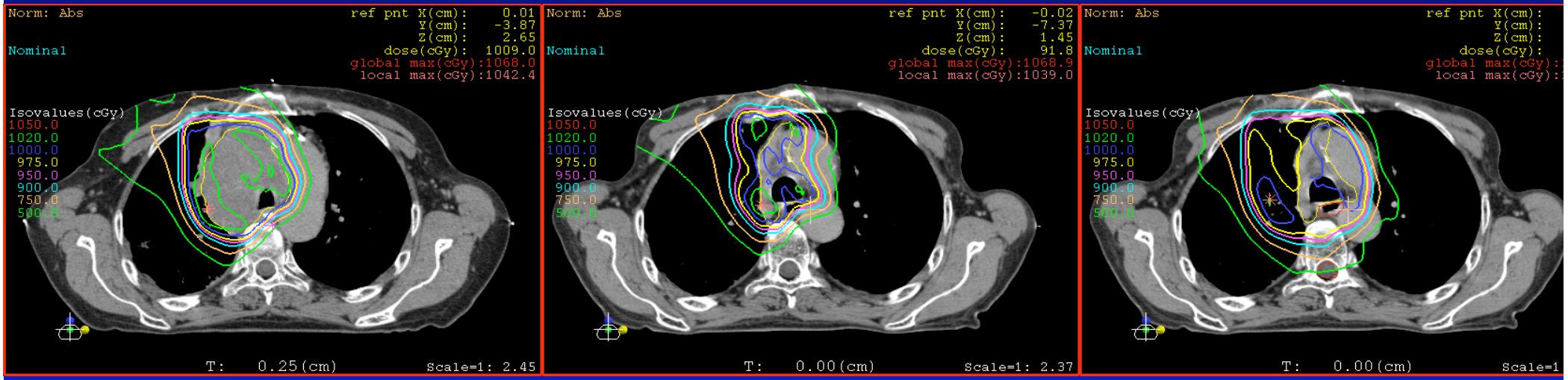
Jay Flanz Ph.

- We can Scan Fast Enough!!
- Create a Temporal slice composite and use as the treatment plan/beam delivery plan



MASSACHUSETTS GENERAL HOSPITAL
Harvard Medical School

Adaptive Radiotherapy



Original scan & plan

New scan with adaptive plan

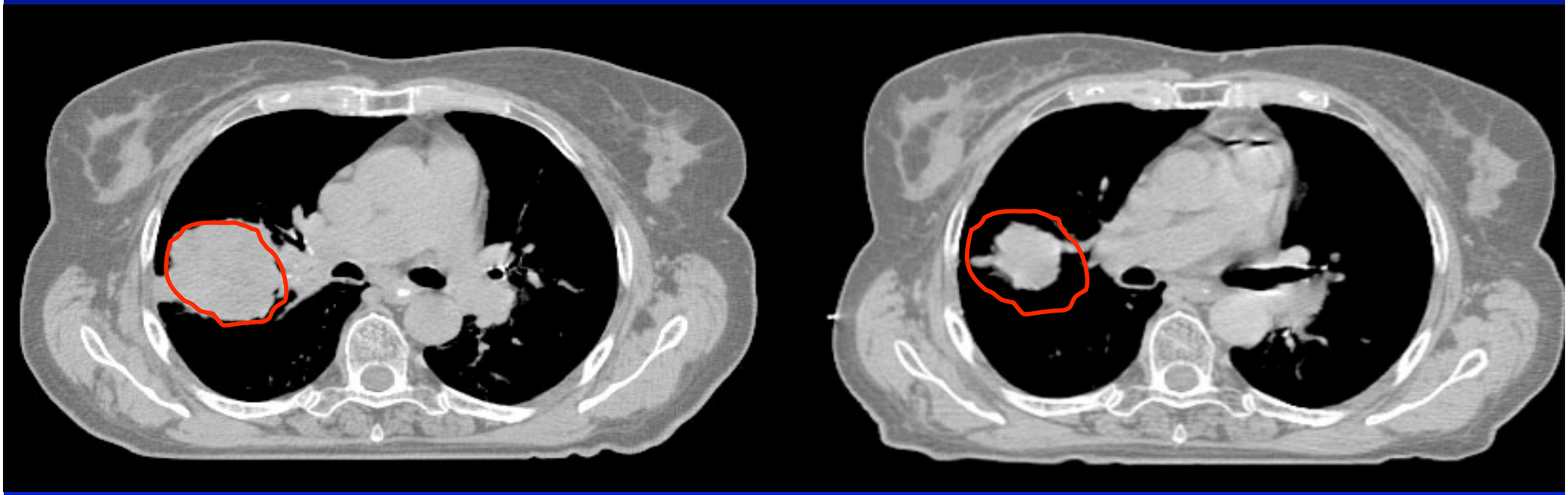
New scan, non-adaptive pl

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Initial Planning CT
GTV 115 cc

5 weeks later
GTV 39 cc



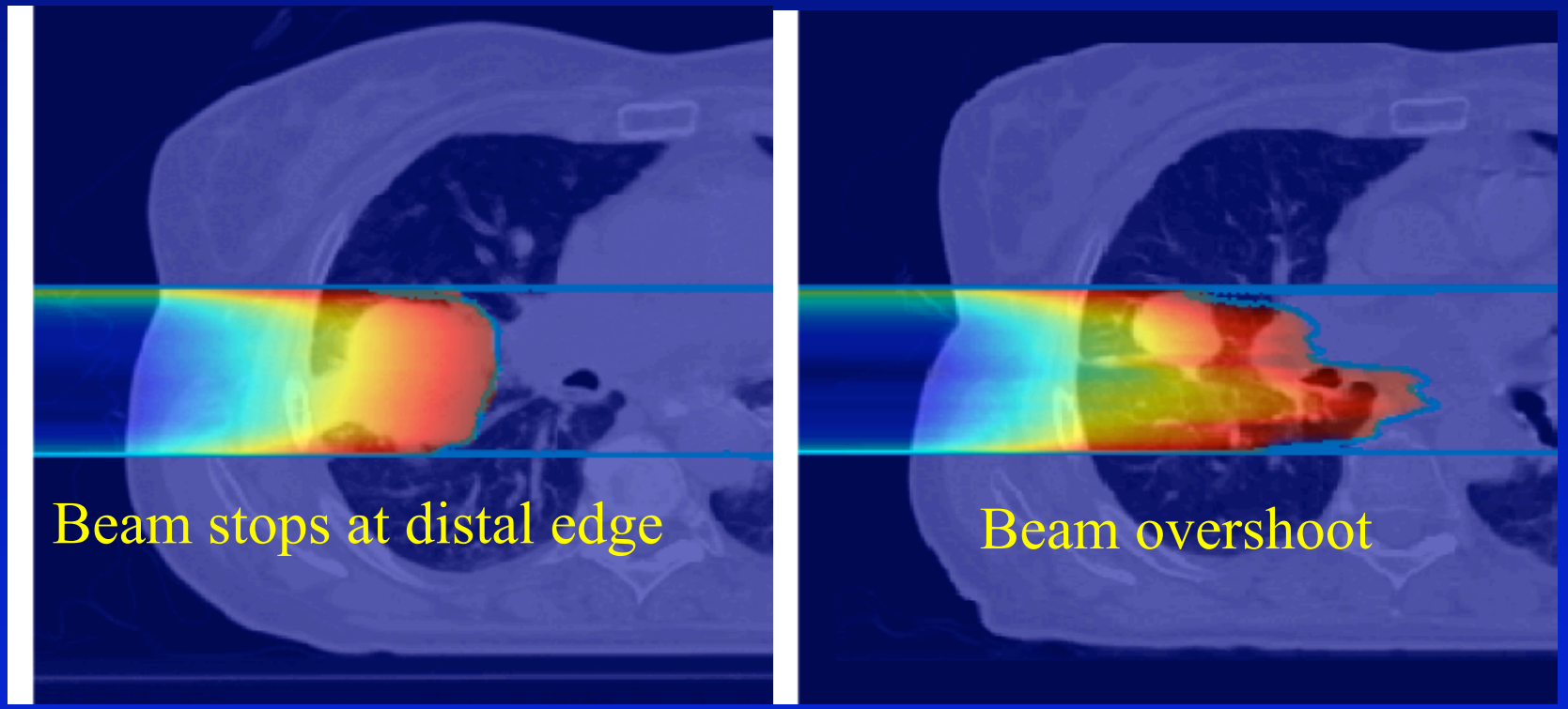
S. Mori, G. Chen

MASSACHUSETTS GENERAL HOSPITAL

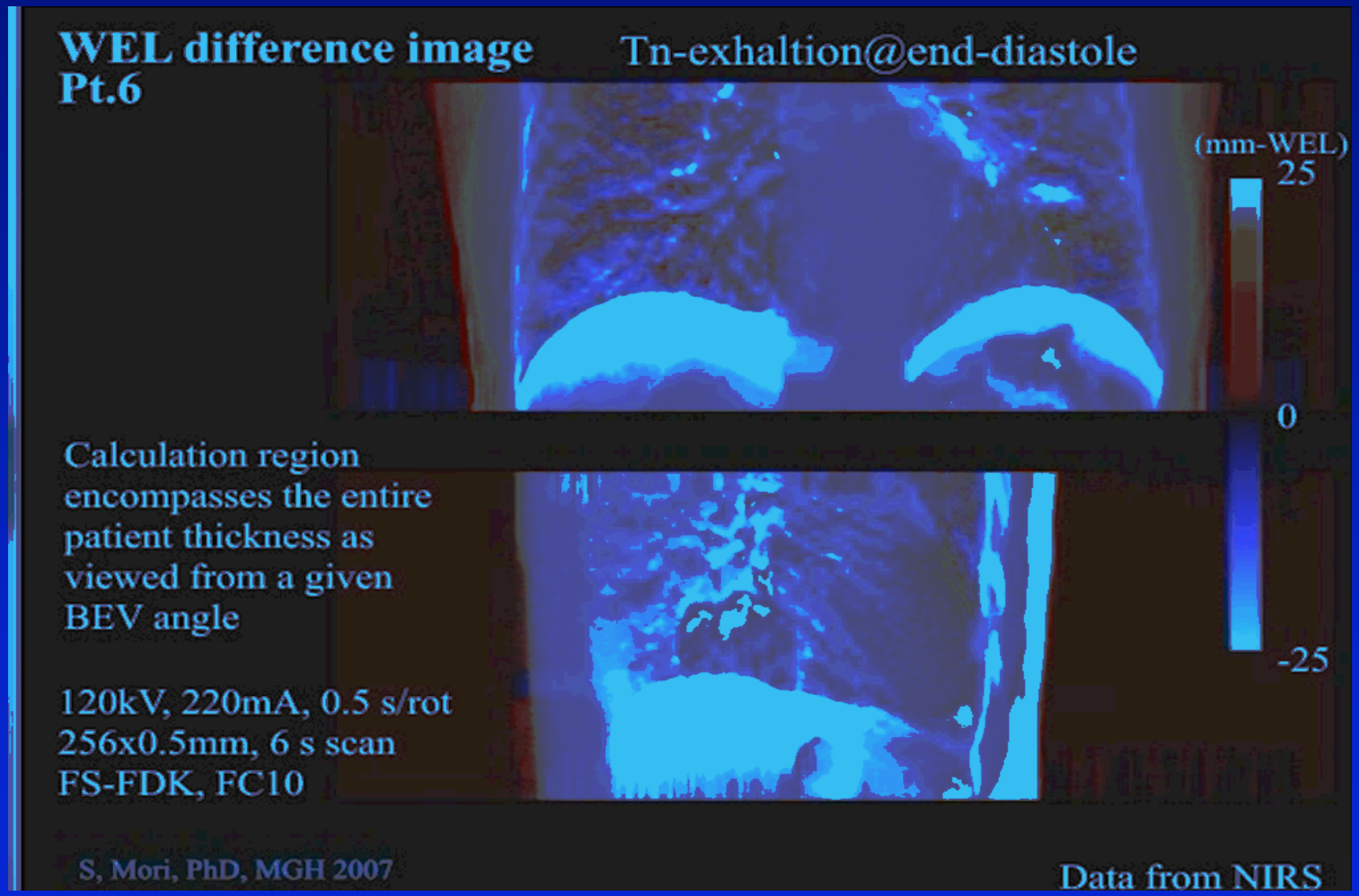
Harvard Medical School

Planning CT (T40%)

CT after 5 weeks (T40%)



S. Mori, G. Chen

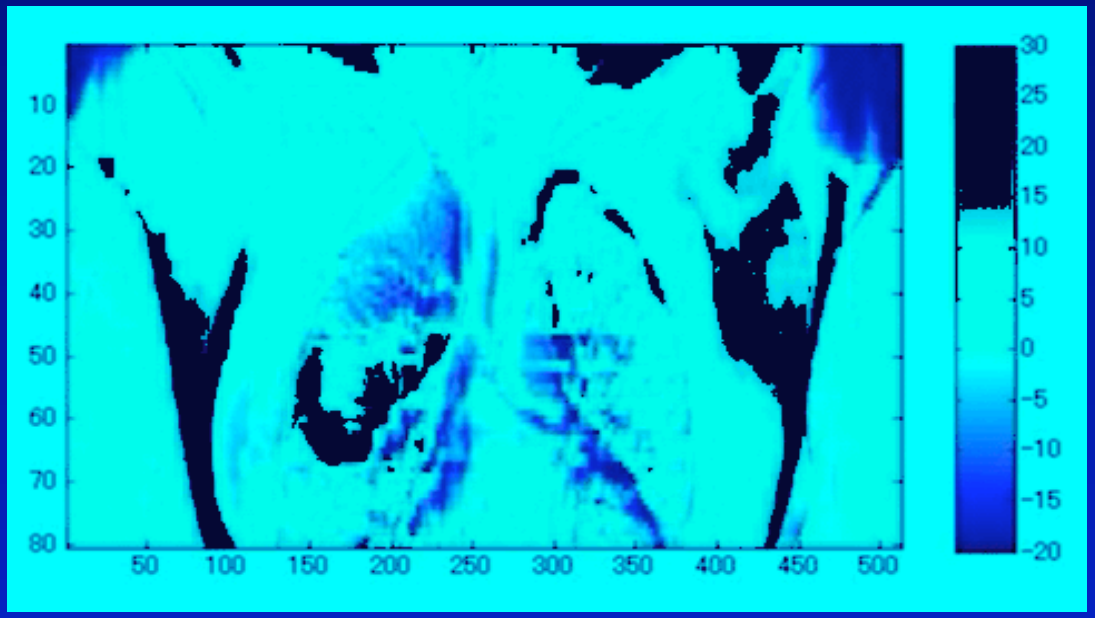


MASSACHUSETTS GENERAL HOSPITAL

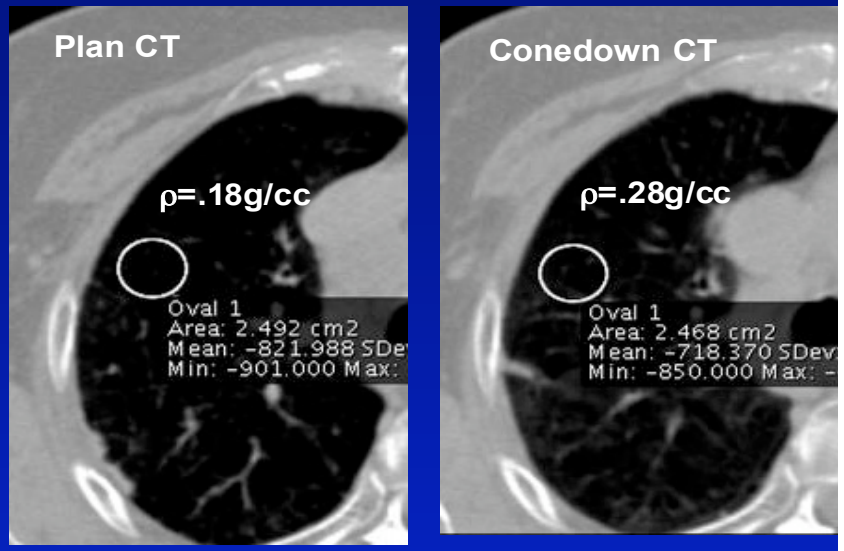
Harvard Medical School

Effects of anatomical change on range

a



b



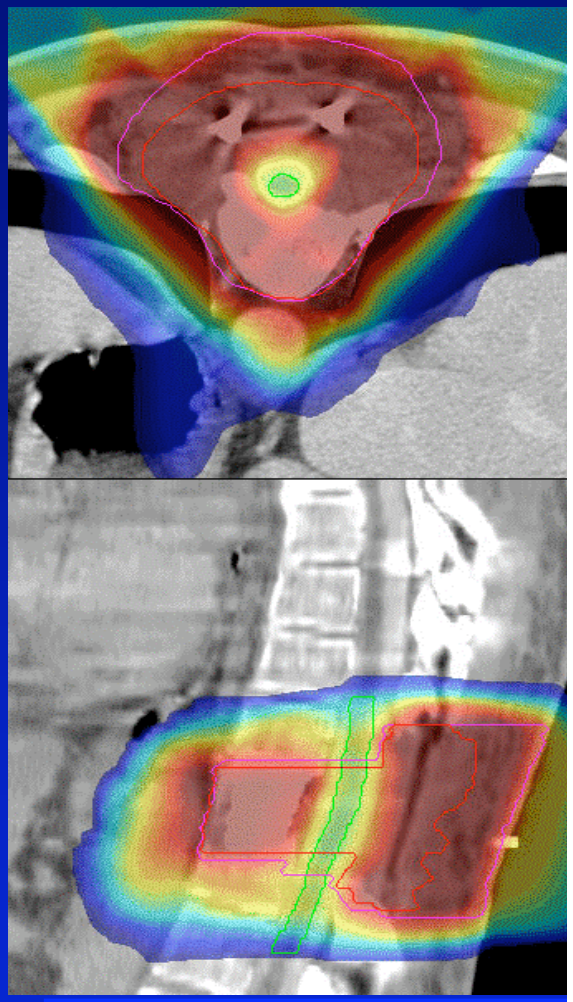
a) Path length (range) difference map (values in mm) from initial planning CT and conedown CT for respiratory phase T=0%. Note range perturbations due to tumor shrinkage, and the blue region above the tumor. b) Hounsfield unit analysis of planning and conedown CT scans at same respiratory phase show significant change in blue region above tumor.

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Current Operation

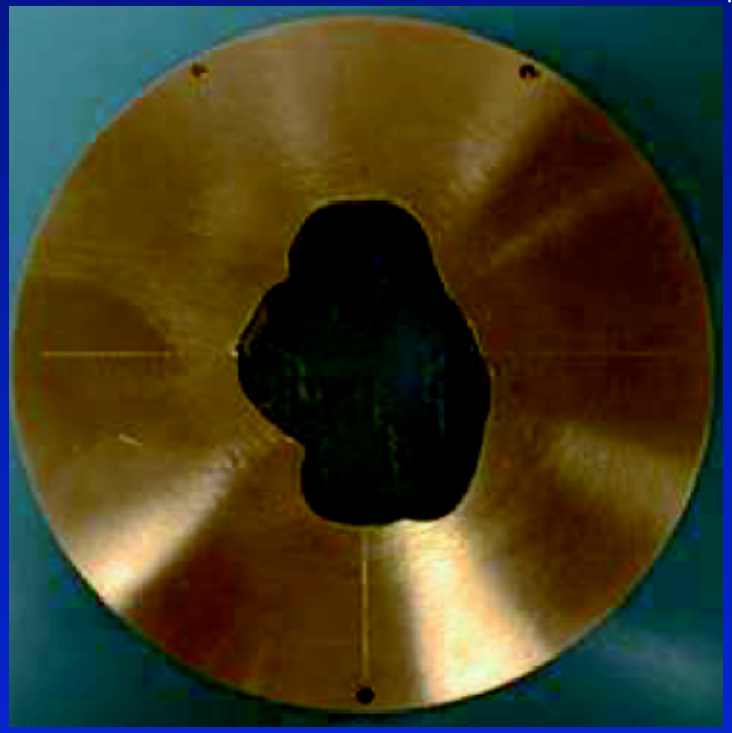
- Scattered field delivery is very clumsy
  - Especially for large(r) volumes
    - Apertures > 25 (18?) cm are simply not manageable
    - Multi-isocenter setups are extremely painful
  - Patching is the only technique for “complex” shapes
    - Sole reliance on penumbral edge
    - Insufficient knowledge of distal edge
      - General BIG problem
  - Brass apertures are very expensive
    - FHBPTC produces ~5,000 apertures+range-compensators / year (~$500,000 / yr)
  - MLC is not the solution (H. Kooy PhD)
    - Pencil Beam Scanning



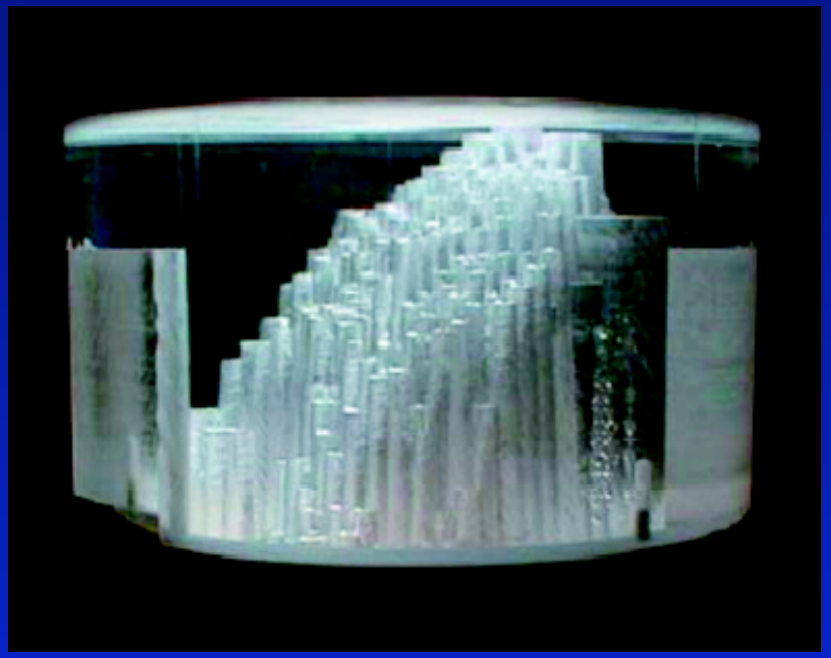
3 PA/PO Fields

Aperture and Compensating Bolus

~$800 / field



Lateral Field Edge Shaping



Distal Field Edge Shaping

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

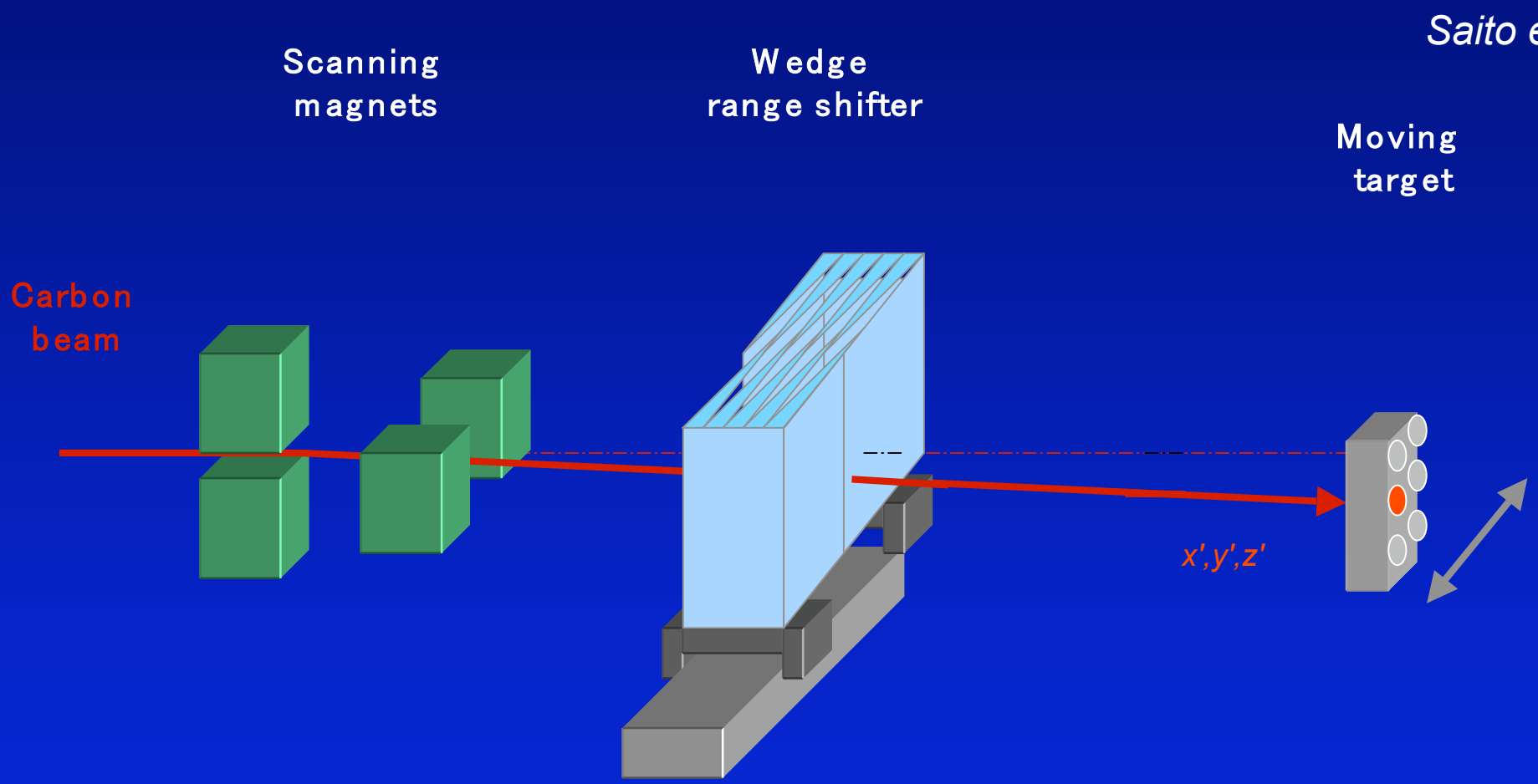
Computer Controlled Milling Machines (~5)

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Beam tracking system

Saito et al.

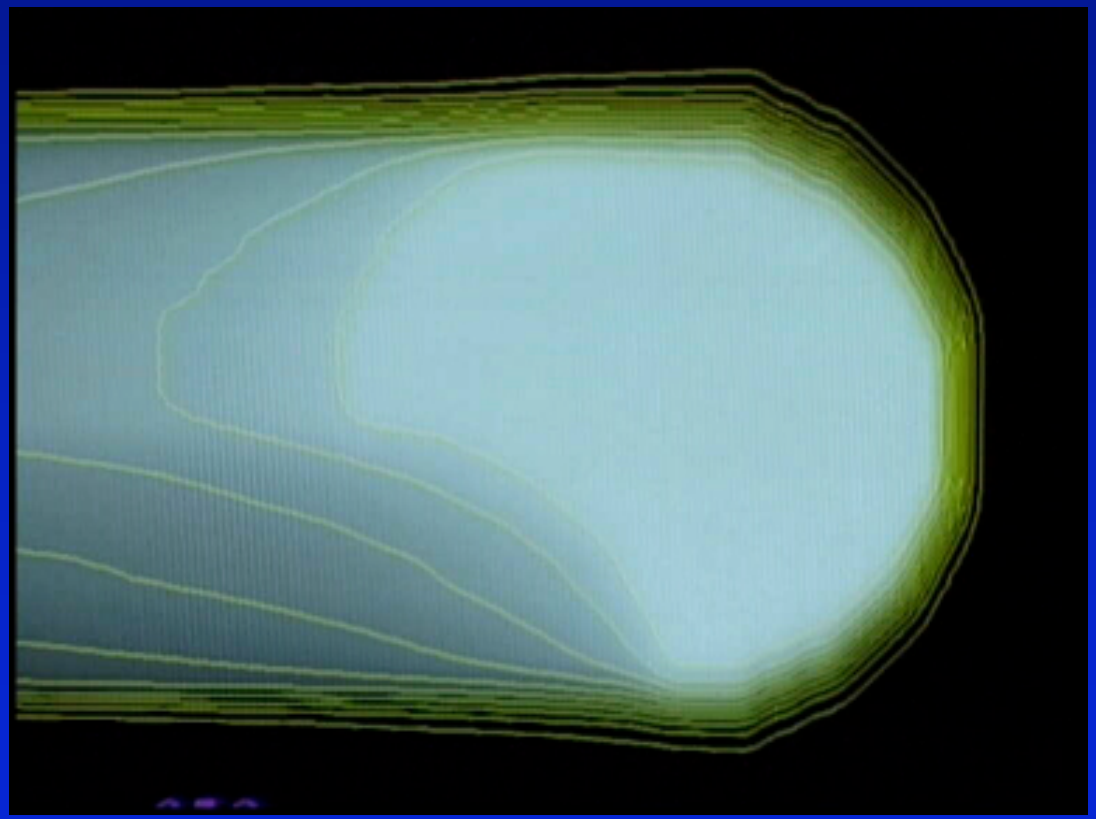


Alex Schmidt GSI
MASSACHUSETTS GENERAL HOSPITAL
Harvard Medical School

Intensity Modulated Proton Therapy (IMPT)

Spot Scanning - Principle

The dynamic application of scanned
and modulated proton pencil beams



A full set, with a homogenous dose conformed distally *and* proximally

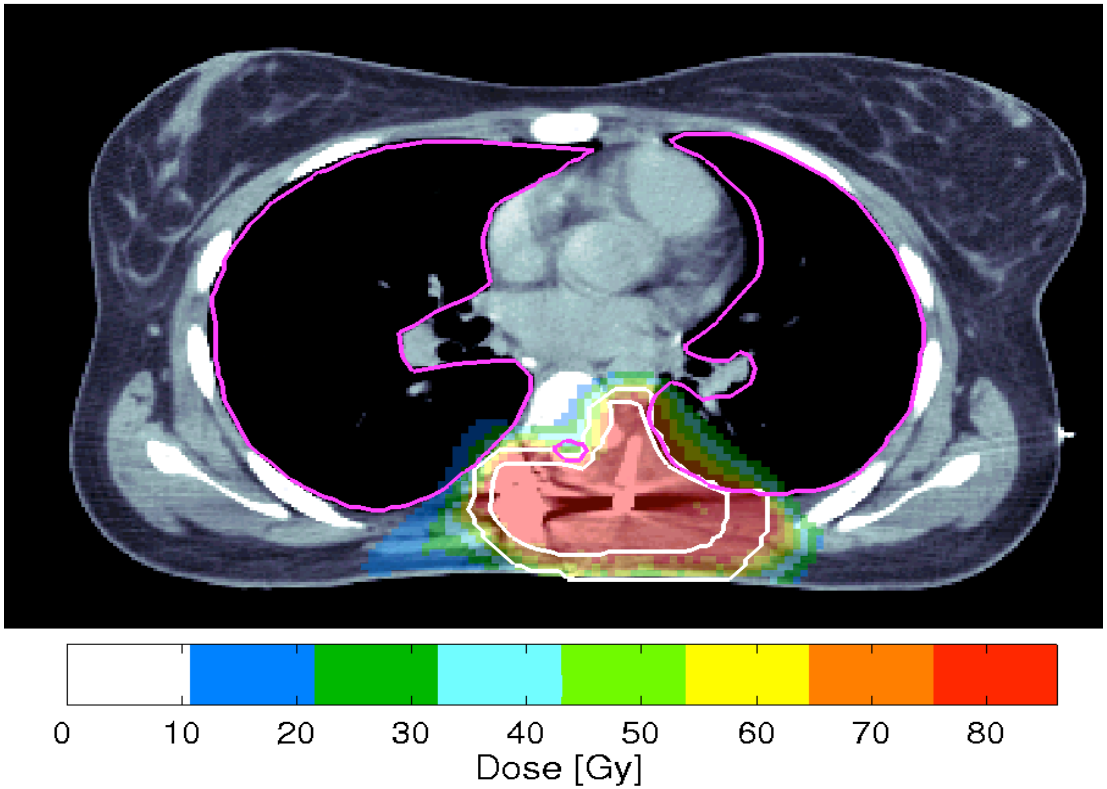
MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

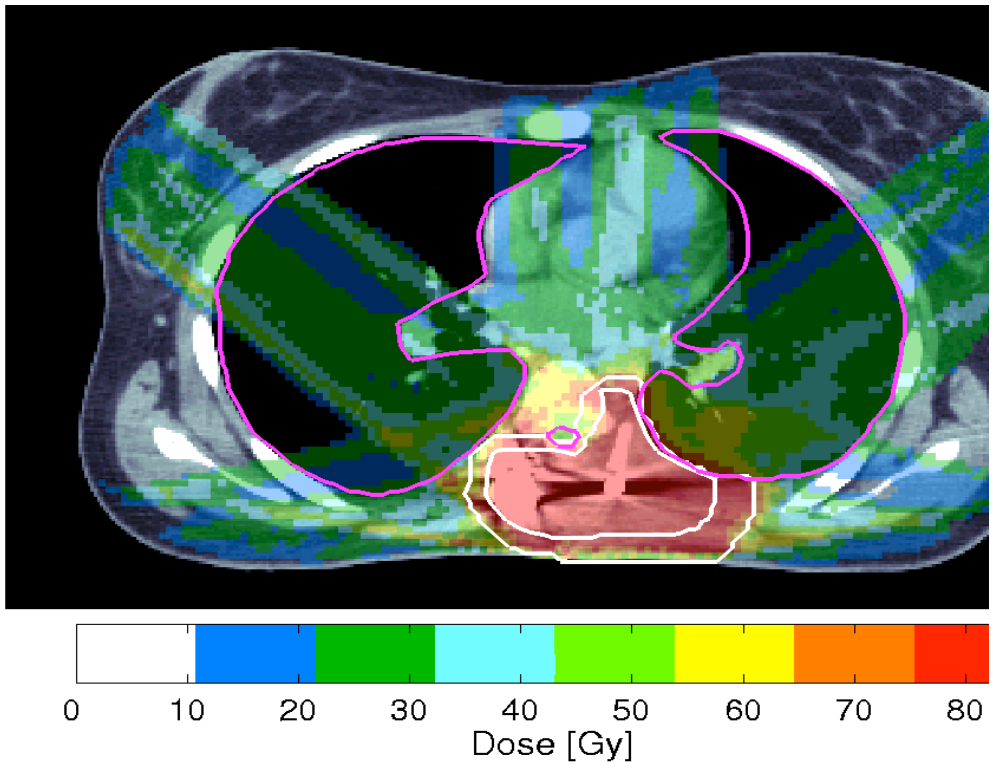
Images courtesy of Eros Pedroni

Paravertebral Epithelioid Sarcoma
Intensity Modulated Protons (IMPT) vs. Intensity Modulated Photons (IMRT) (7 field)

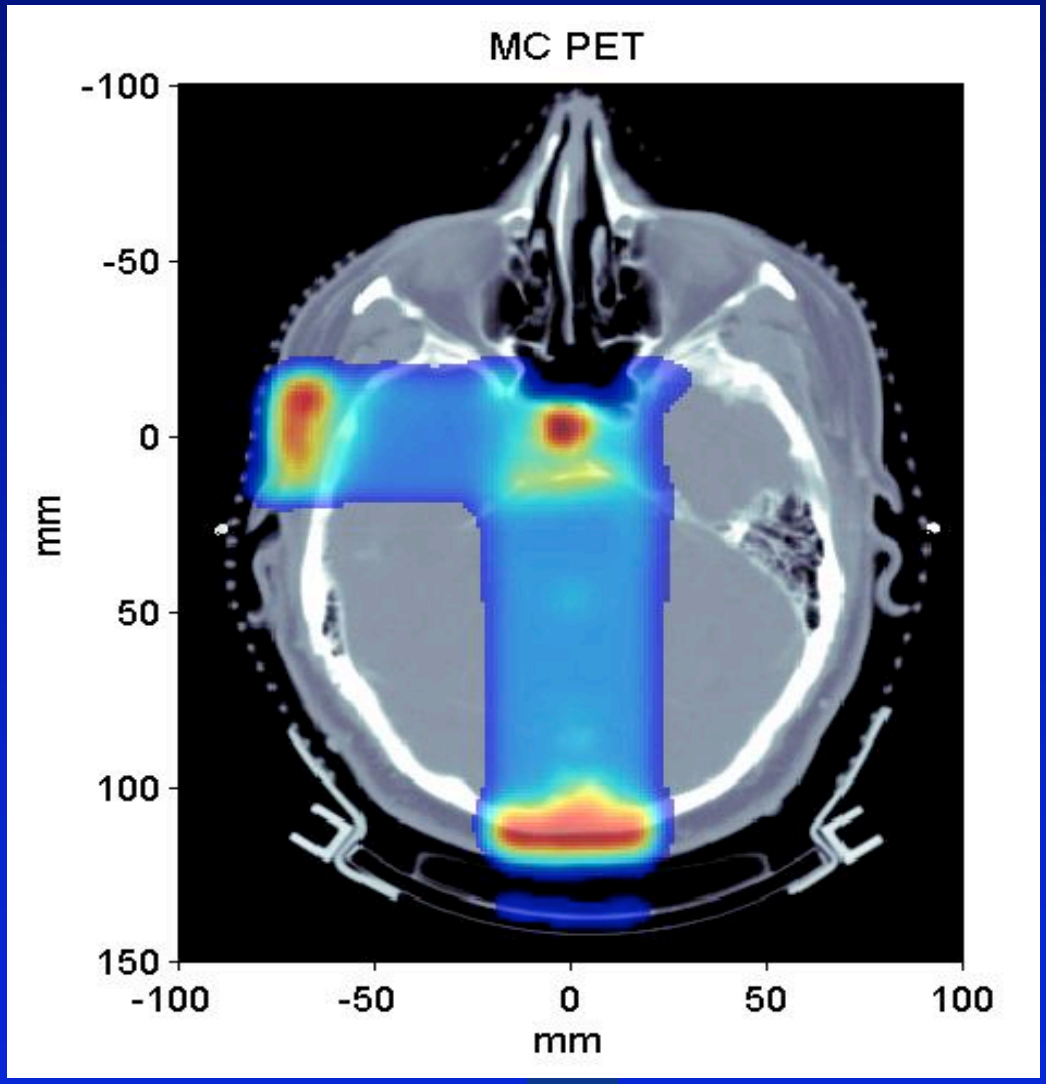
IMPT

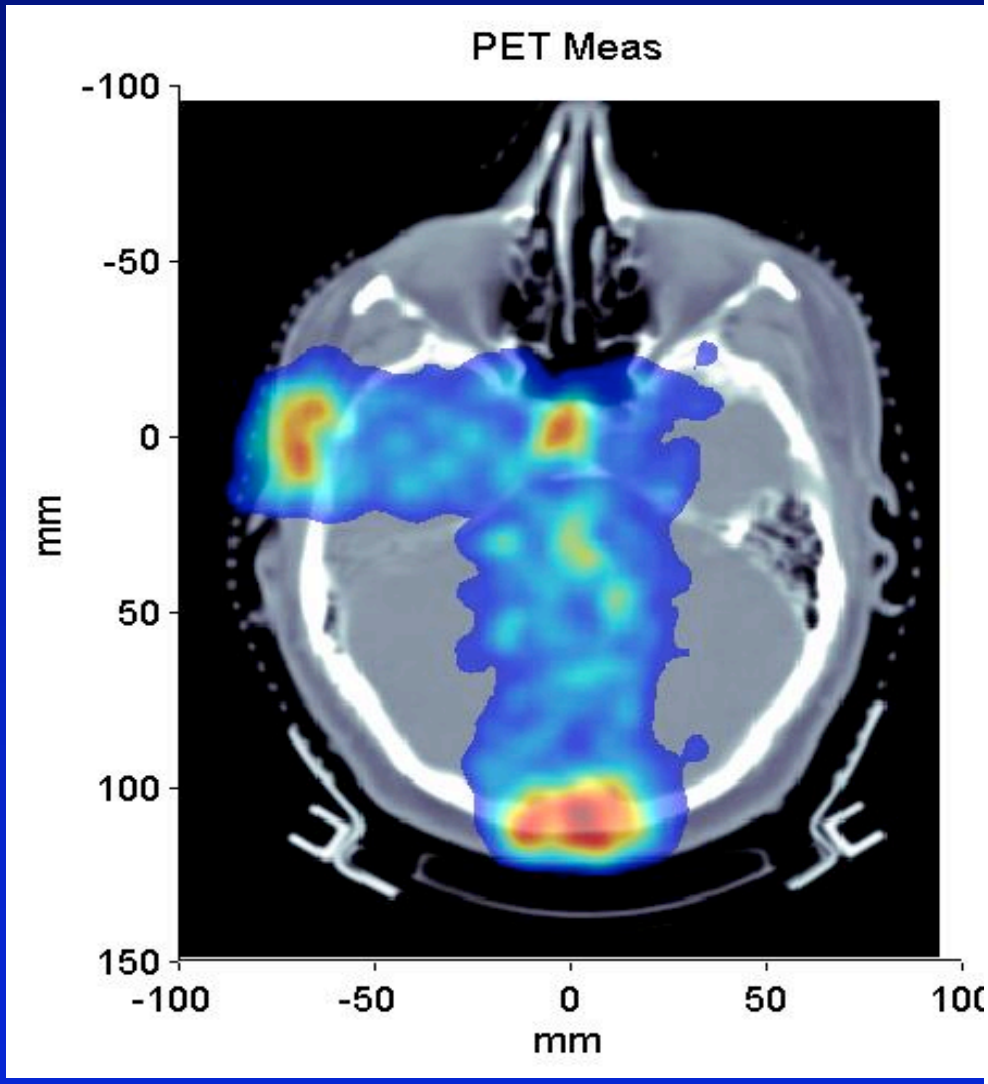


IMXT



In vivo range prediction with PET/CT





Protons: Radiation Biology

- **Low LET(linear energy transfer) radiation**
  - Ionization with similar biologic effect to photons
  - Relative Biologic Effect (RBE) is ~1.1 vs. ^{60}Co
  - Proton doses: cobalt gray equivalents (CGE)
    - CGE= physical dose in Gray x 1.1 (RBE correction)
  - Protons have been successfully combined with photons in reasonably straight forward manner
    - Many reported results are combined photon-proton results

Relative Biologic Effect

- Generic RBE of 1.1 has been applied at most centers for all tumor types, all normal tissues

- ? Any differences in interactions of protons with chemotherapy and/targeted biologic agents (anti-EGFR, anti-angiogenesis, kinase inhibitors, etc.)

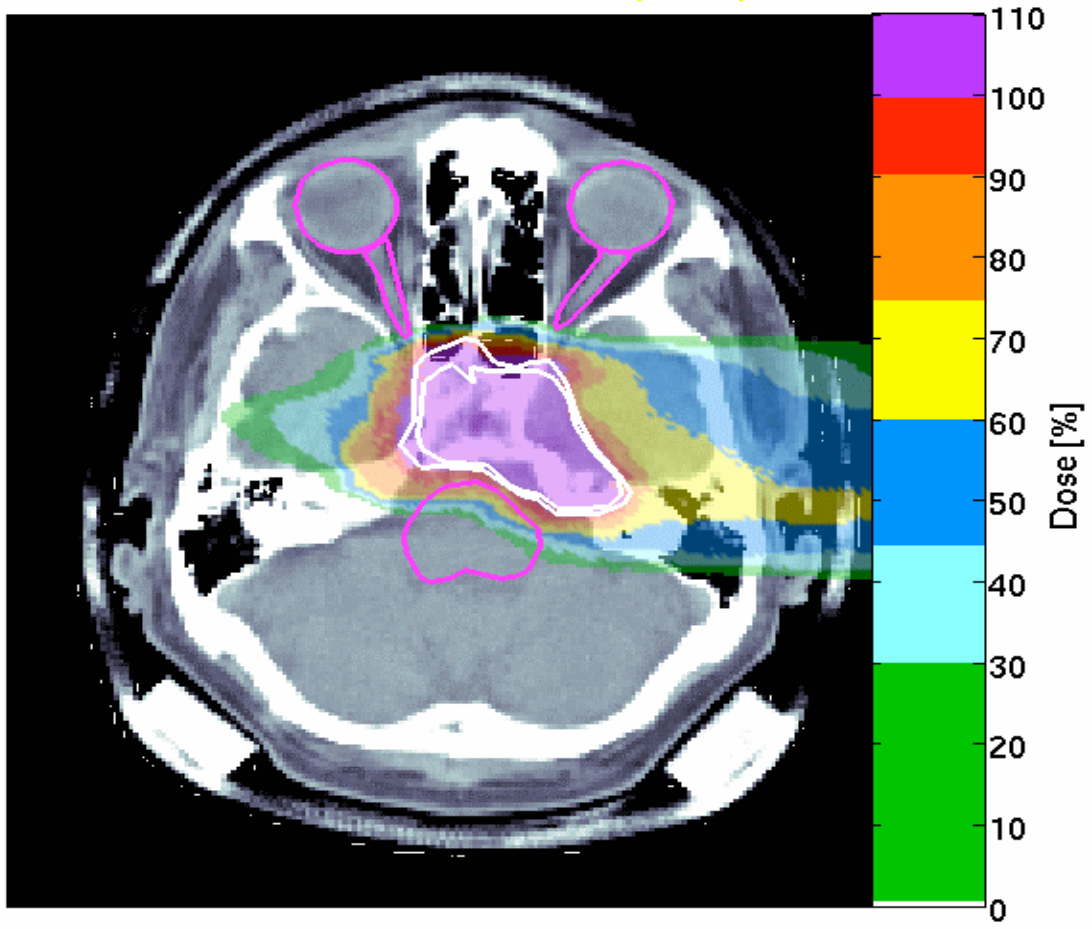
Carbon Ion Therapy

- Carbon ions are under study in Japan and Germany
- Less lateral diffusion and sharper Bragg peak
- Higher RBE (~3) that may be even higher in tumor vs. normal tissue because of
- Lower oxygen enhancement ratio (OER)
  - ? Relatively more effective vs photons against hypoxic tumor
- ↓ capacity for sublethal/potentially lethal damage repair
  - ? More effective against slowly proliferating tumors
- Cost is higher than protons
  - Hyogo (2001: 28 B ¥/ $ 230 million) vs. ~ $100 million proton
  - Will be important to define indications for carbon ions

DKFZ case 1

Carbon

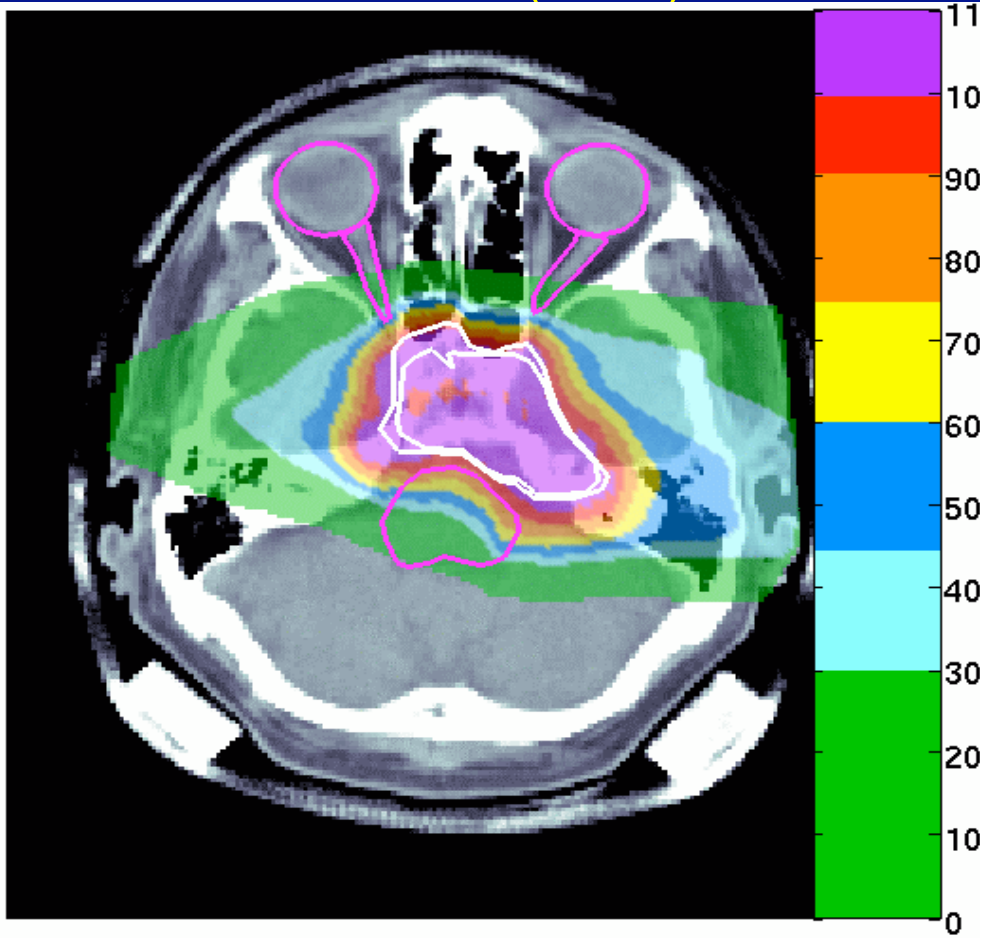
Jaeckel (GSI)



Proton (IMPT)

Plan: O.

Plan: A.Trofimov (MGH)



Carbon Ion Therapy

- Carbon ions are under study in Japan and Germany
- Less lateral diffusion and sharper Bragg peak
- Higher RBE (~3) that may be even higher in tumor vs. normal tissue because of
- Lower oxygen enhancement ratio (OER)
  - ? Relatively more effective vs photons against hypoxic tumor
- ↓ capacity for sublethal/potentially lethal damage repair
  - ? More effective against slowly proliferating tumors
- Cost is higher than protons
  - Hyogo (2001: 28 B ¥/ $ 230 million) vs. ~ $100 million proton
  - Will be important to define indications for carbon ions

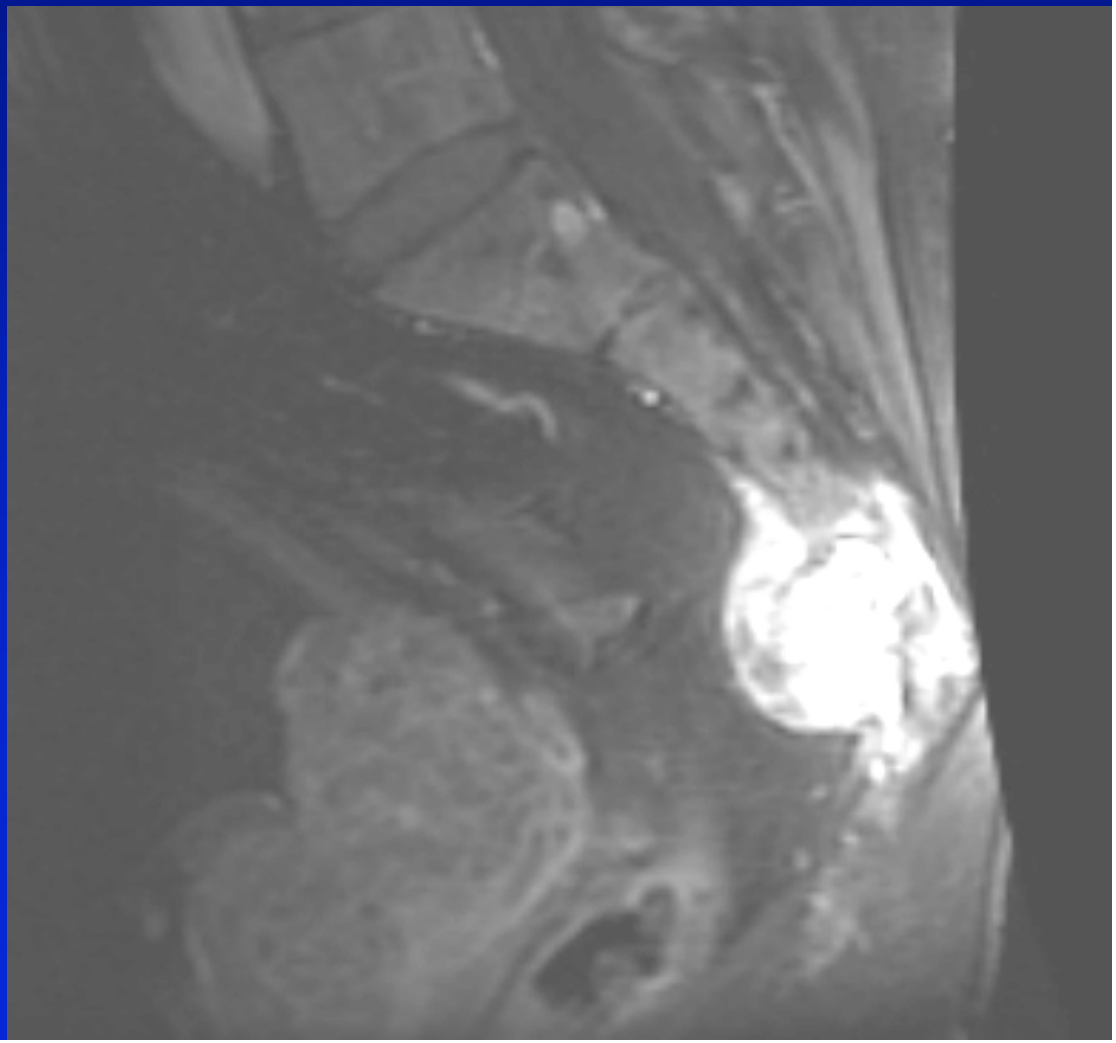
Sacral Chordoma

T1 post-gadolinium sagittal MRI

Pre-treatment

S3-4 chordoma

77.4 GyE (photons 30.6 Gy
protons 46.8 GyE)



MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Spine and Paraspinal Sarcoma

- Local Failure Chordoma (n=3/29)
  - Primary 0/23 Locally recurrent 3/6

	Number	5-year Actuarial %
– R0	0/7	0%
– R1	1/10	13%
– R2	1/3	33%
– Biopsy only	1/9	13%

- R0 vs. R1,2 p= 0.258 (2-sided)

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

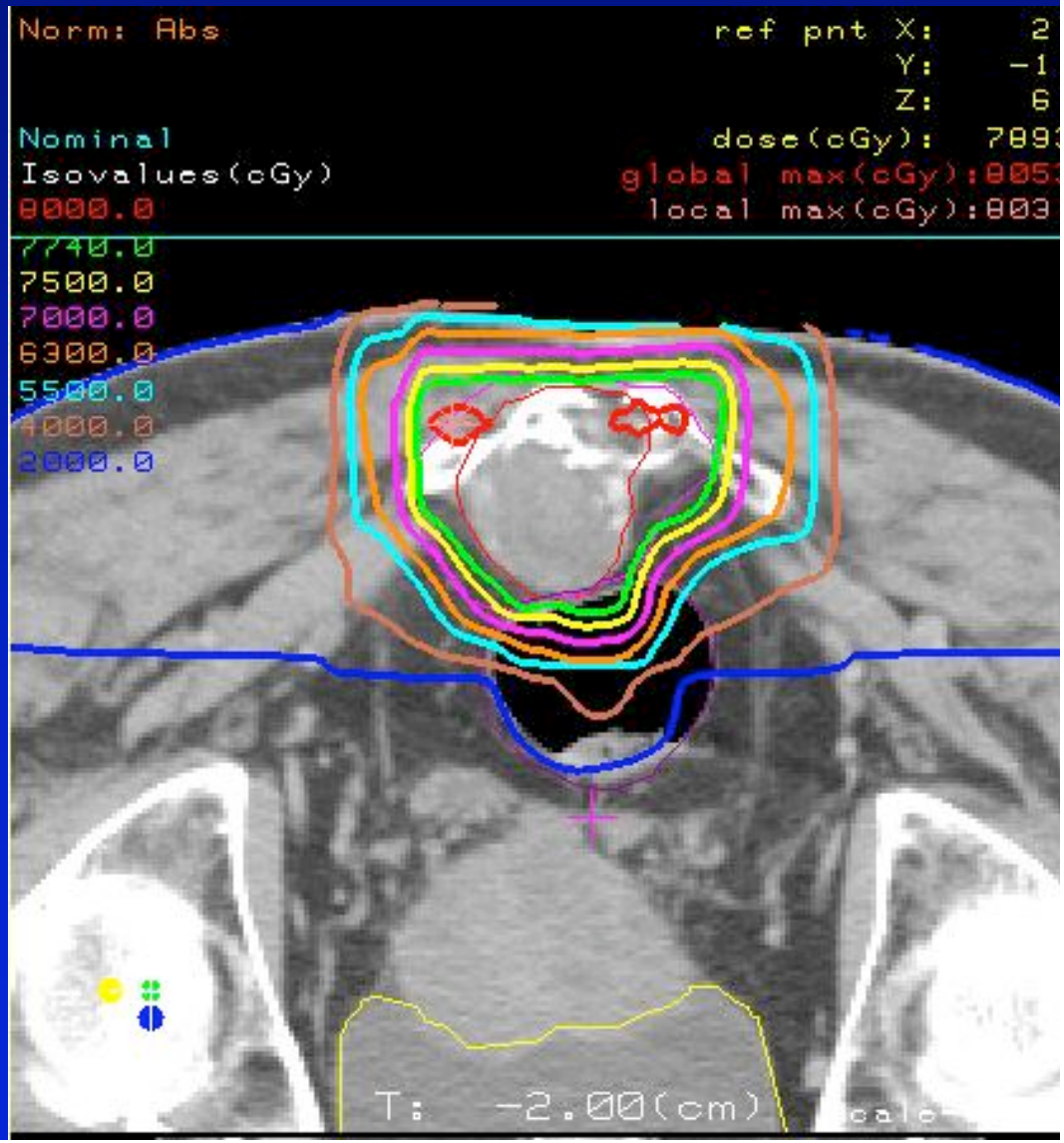
Sacral Chordoma

Treatment Plan

S3-4 chordoma

Biopsy only

77.4 GyE (photons 30.6 Gy
protons 46.8 GyE)



MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Sacral Chordoma

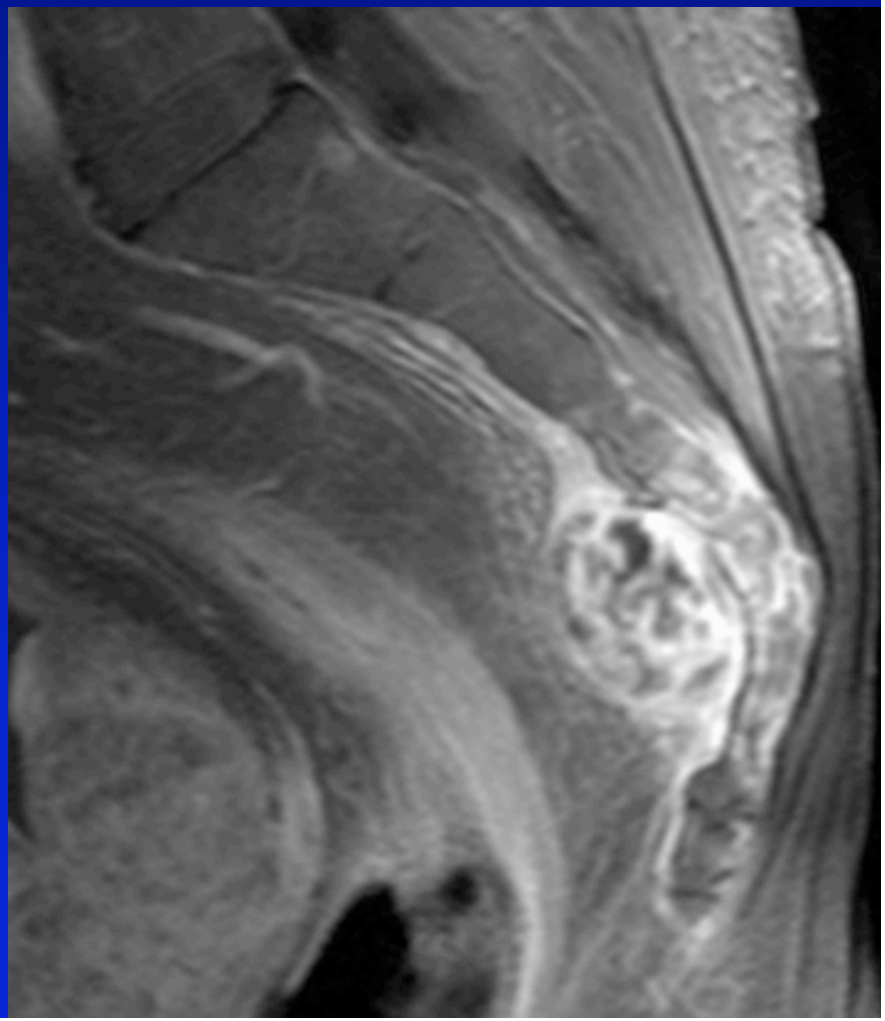
T1 post-gadolinium sagittal MRI

S3-4 chordoma

Biopsy only

77.4 GyE (photons 30.6 Gy
protons 46.8 GyE)

No evidence of progressive disease at 36 months



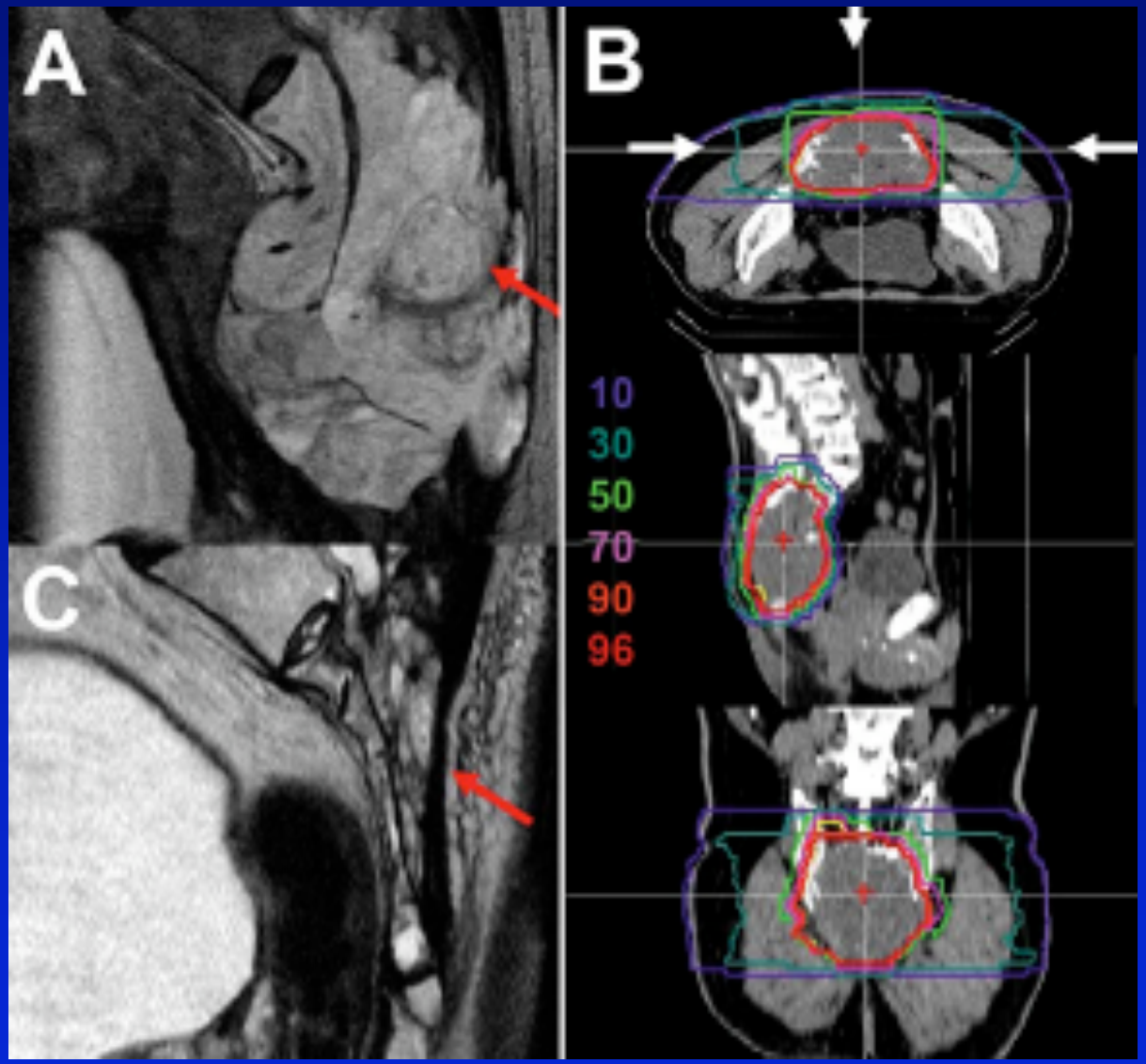
MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Sacral chordoma treated with carbon ion 70.4 GyE/16 Fx

Pre-Rx

3 years Post-Rx



Courtesy of Tadashi Kamada, M.D., Ph.D.

MASSACHUSETTS GENERAL HOSPITAL

Harvard Medical School

Chordomas of the Sacrum

- Imai *et al.* (NIRS, Chiba, Japan)
  - 30 patients with unresectable sacral chordomas
    - 23 primary 7 local recurrent after resection
      - **Clinical target volume 546 cm^3**
    - 52.8-73.6 GyE (median 70.4) in 16 fx over 4 weeks
  - Local control rate at 5 years: 96%
    - 26 patients alive
    - 24 disease-free at median f/u of 30 months (range, 9-87 mos)
  - Two skin/soft tissue complications requiring skin grafts.
  - No other treatment-related surgical interventions, including colostomy or urinary diversion, were carried out.
  - All patients ambulatory at home after carbon ion RT

Heavier Charged Particles

- Will need to compare carbon ions vs. protons
  - ? More late effects related to the higher RBE
    - Neutron experience-Poor physical dose distribution
  - Protons for CTV and carbon for GTV (H. Suit)
  - Comparative studies
    - Unresected sacral chordomas
      - IRB approved Carbon (NIRS, Chiba) vs protons (Boston)
      - Matched pair analysis
    - ? Potential for other centers and anatomic sites
    - Heidelberg Ion Therapy Center
      - Carbon and protons in a single facility