The Promise of Protons in Cancer Therapy

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American Association of Physics Teachers
Jacksonville, Florida   January 12, 2011

A Neutron Walks Into a Bar…

A neutron walks into a bar and asks:
"Hey, how much for a beer?"

A Neutron Walks Into a Bar…

A neutron walks into a bar and asks:
"Hey, how much for a beer?"
The bartender says, "For you, no charge."

source: http://www.jokebuddha.com/Proton#ixzz1Al50LTyf

A Proton Walks Into a Bar…

A proton walks into a bar, sits down and orders a drink. After finishing the drink, the bartender says, "Would you like another drink?".

A Proton Walks Into a Bar…

A proton walks into a bar, sits down and orders a drink. After finishing the drink, the bartender says, "Would you like another drink?".

The proton says, "No, thanks."

A Proton Walks Into a Bar…

A proton walks into a bar, sits down and orders a drink. After finishing the drink, the bartender says, "Would you like another drink?".

The proton says, "No, thanks."

A few minutes later, the bartender approaches the proton again and says, "Are you sure you don't want another drink?"

A Proton Walks Into a Bar…

A proton walks into a bar, sits down and orders a drink. After finishing the drink, the bartender says, "Would you like another drink?".

The proton says, "No, thanks."

A few minutes later, the bartender approaches the proton again and says, "Are you sure you don't want another drink?"

To which the proton says, "I'm positive."
(Protons know when to stop!!)

source: http://www.jokebuddha.com/Proton#ixzz1Al50LTyf

Objectives

- Cancer
- Radiation Therapy Basics
  - Mechanism of Action
  - Non-specific Effects
  - Therapeutic Ratio
  - Dose distribution
- The Promise of Protons
- The University of Florida Project
- Clinical Applications

Cancer

The Cancer Problem

- Cancer affects 1 in every 3 to 4 Americans
- 2nd leading cause of death in US
- Affects men, women, children, all races and ages

The Nature of Cancer

- Most cancers arise from a single cell that has mutated.
- The main clinical characteristic of cancer is its aberrant growth pattern.

Cancer Growth

- Cancer grows locally, *beyond the usual normal tissue boundaries, compressing or destroying adjacent tissues.*
- In addition, most cancers can metastasize *by shedding cells into the bloodstream, lymphatic fluid, or other body fluids that can travel to and colonize a distance site*.

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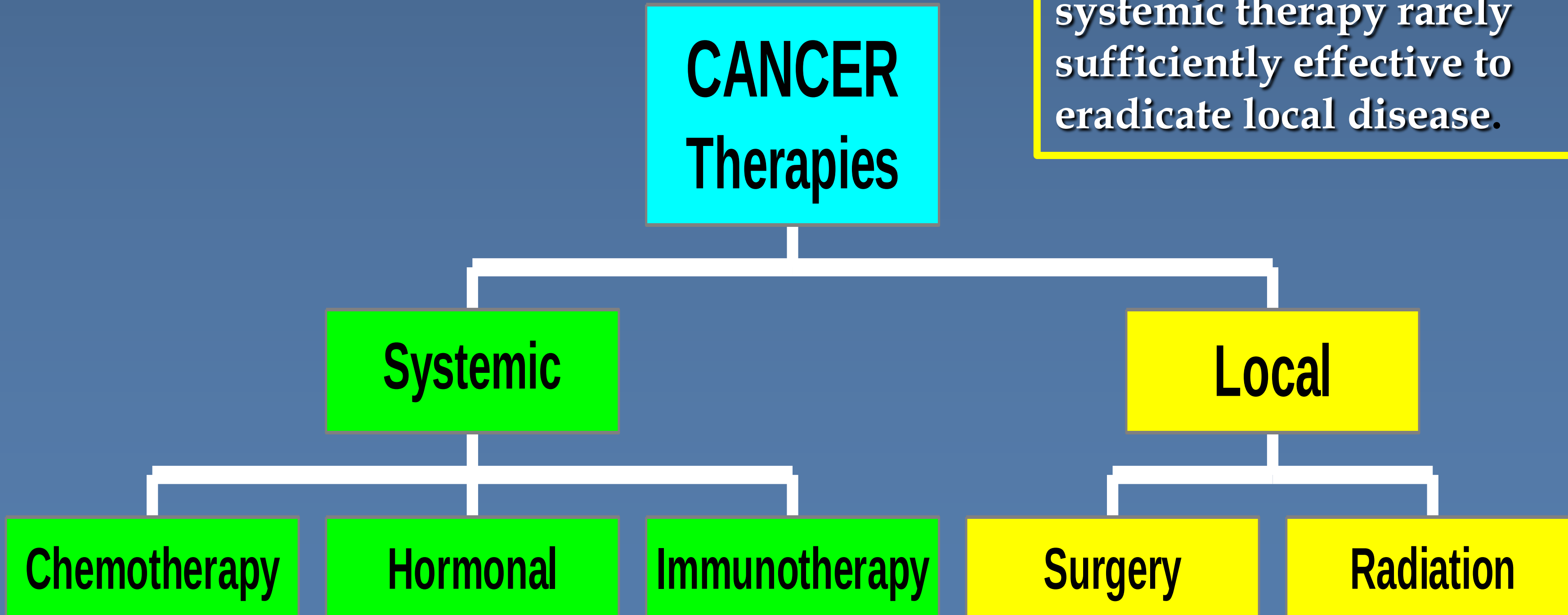
Cancer Therapies

Except in leukemia, systemic therapy rarely sufficiently effective to eradicate local disease.



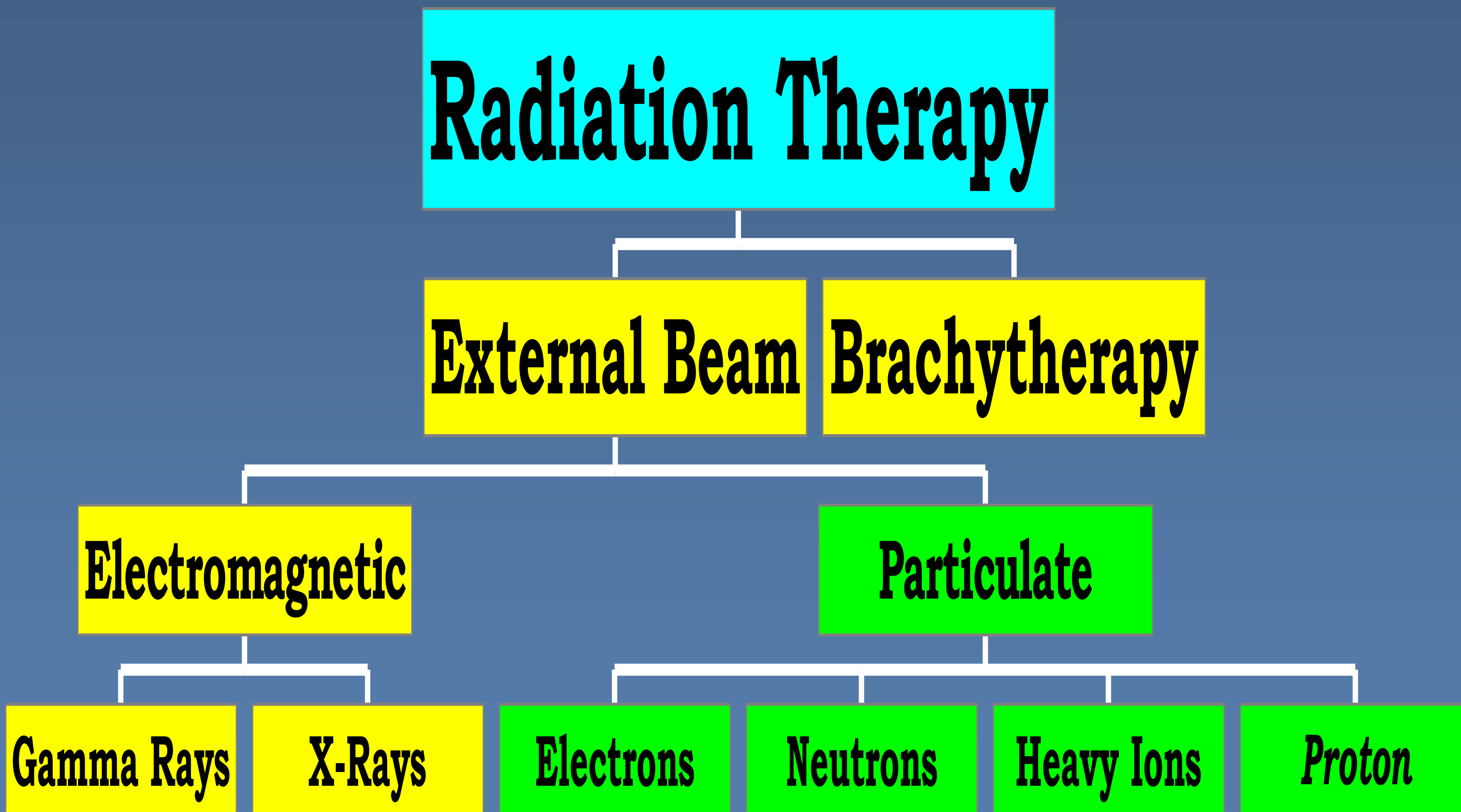
Radiation Therapy

Radiation Therapy

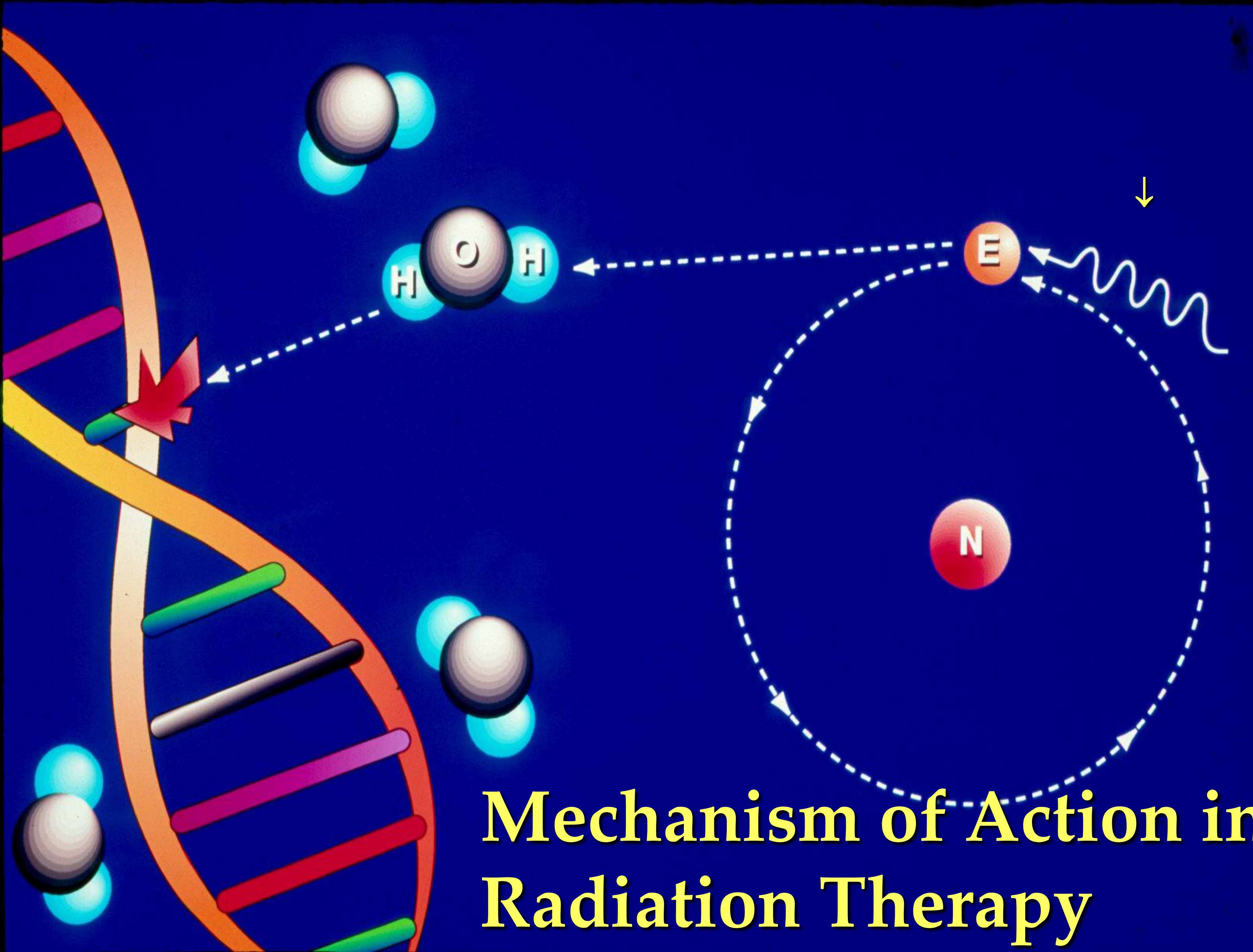
- Radiation is used
  - alone or with surgery
  - for cure or palliation
  - in most types of cancers

- ~50% all cancer patients
- ~2 m radiation treatments in Fl/yr

Types of Radiation



Mechanism of Action in Radiation Therapy



Radiation Therapy Basics

- Radiation damage is non-specific.
- Response* probability *dose-related* and *volume-related*.
- Dose distribution key to outcome.

*Cancer control and normal tissue damage.

Radiation Therapy

In radiation oncology, dose distribution is the main challenge. . .

> ***Oftentimes*** **radiation doses are limited to avoid toxicity.** ***Sometimes*** **the price of cure is a complication.**

Conventional Radiation in Head & Neck Cancers

Site	Dose	Local Control	Gr. 3-4 Toxicity	*Therapeutic Ratio*
Vocal Cord*	63 Gy	94%	<1	>94
Sinus**	~75 Gy	79% SX + RT 49% RT alone	27% unilateral blindness 5% bilateral blindness	1.8-15.8

***Small volume tumor with no critical structures around.**
****Large volume tumor close to visual apparatus.**

Leung, 2005; UF experience.

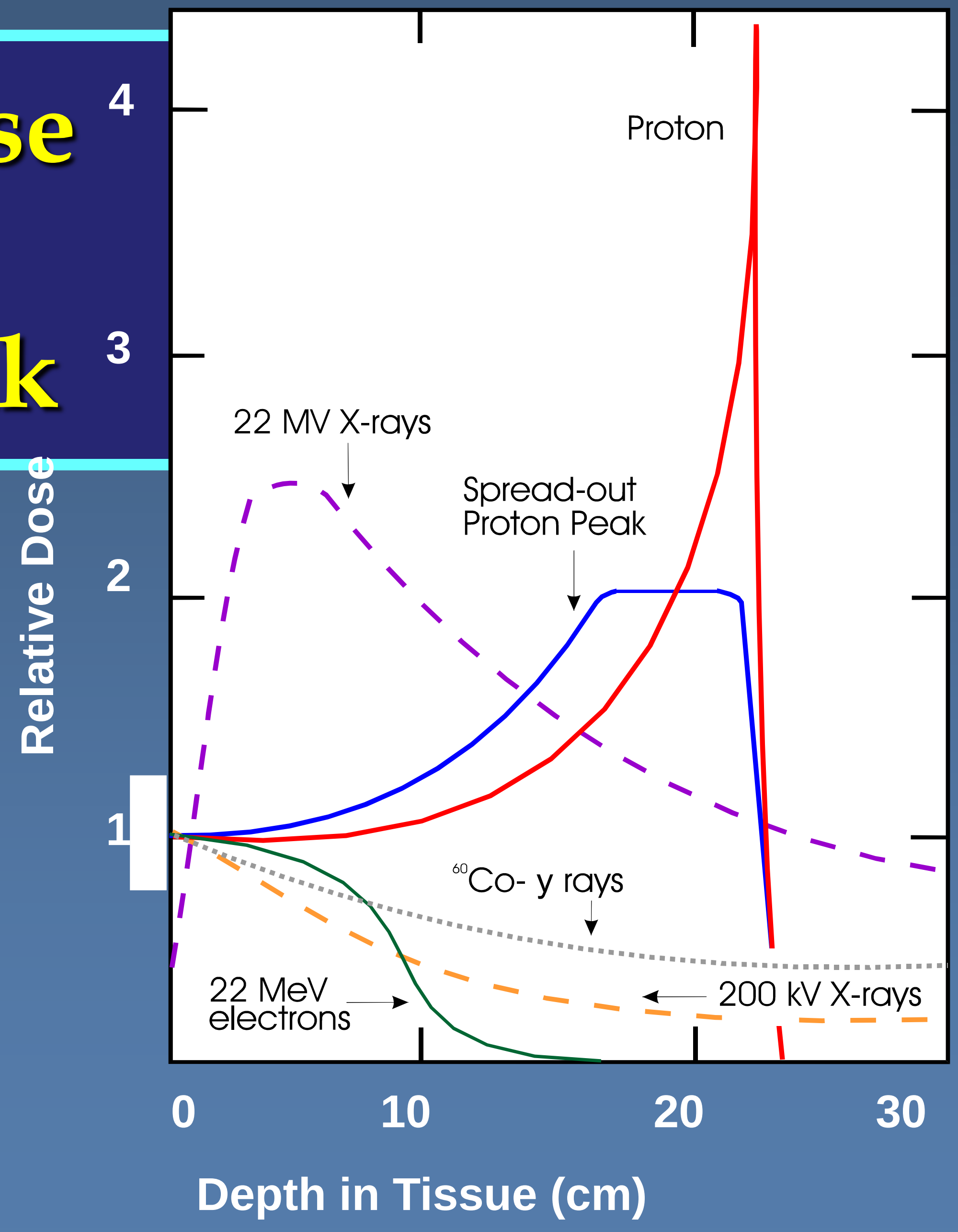
The Therapeutic Ratio

- **Radiation dose distribution is key to improving therapeutic ratio**

Promise of Protons

Radiation Dose Distribution: The Bragg Peak

- 200 KV
- 60Cobalt
- 22 MV X-rays
- 22 MEV Electrons
- Proton Bragg Peak
- Spread Out Proton Peak



The Promise of Proton Therapy

- No exit dose, less entrance dose means less normal tissue damage
- Less normal tissue damage means higher doses to tumor possible
- Higher doses to tumor means higher cure rates

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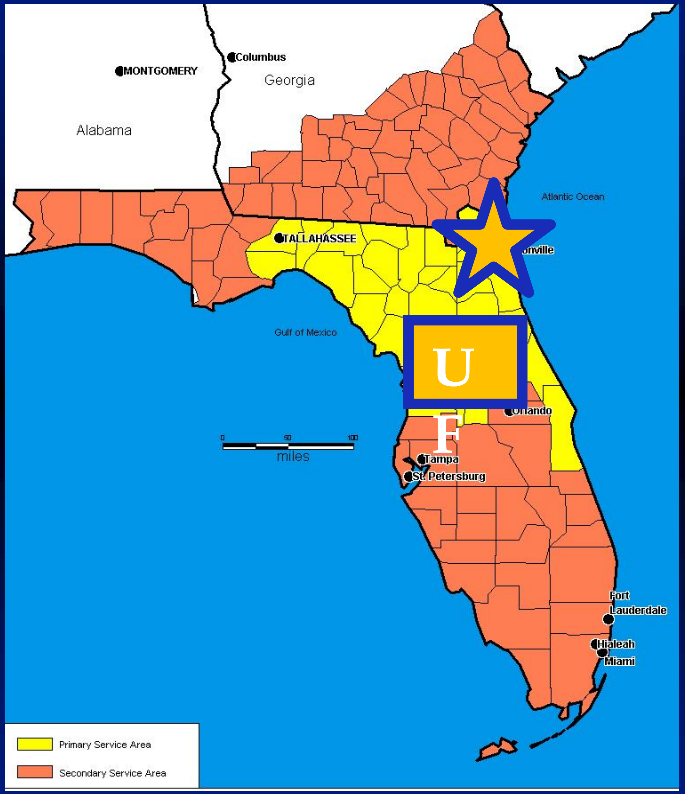
The Promise of Protons

- Less toxicity.
- Higher cure rates.
- Potential reduction in health care costs.

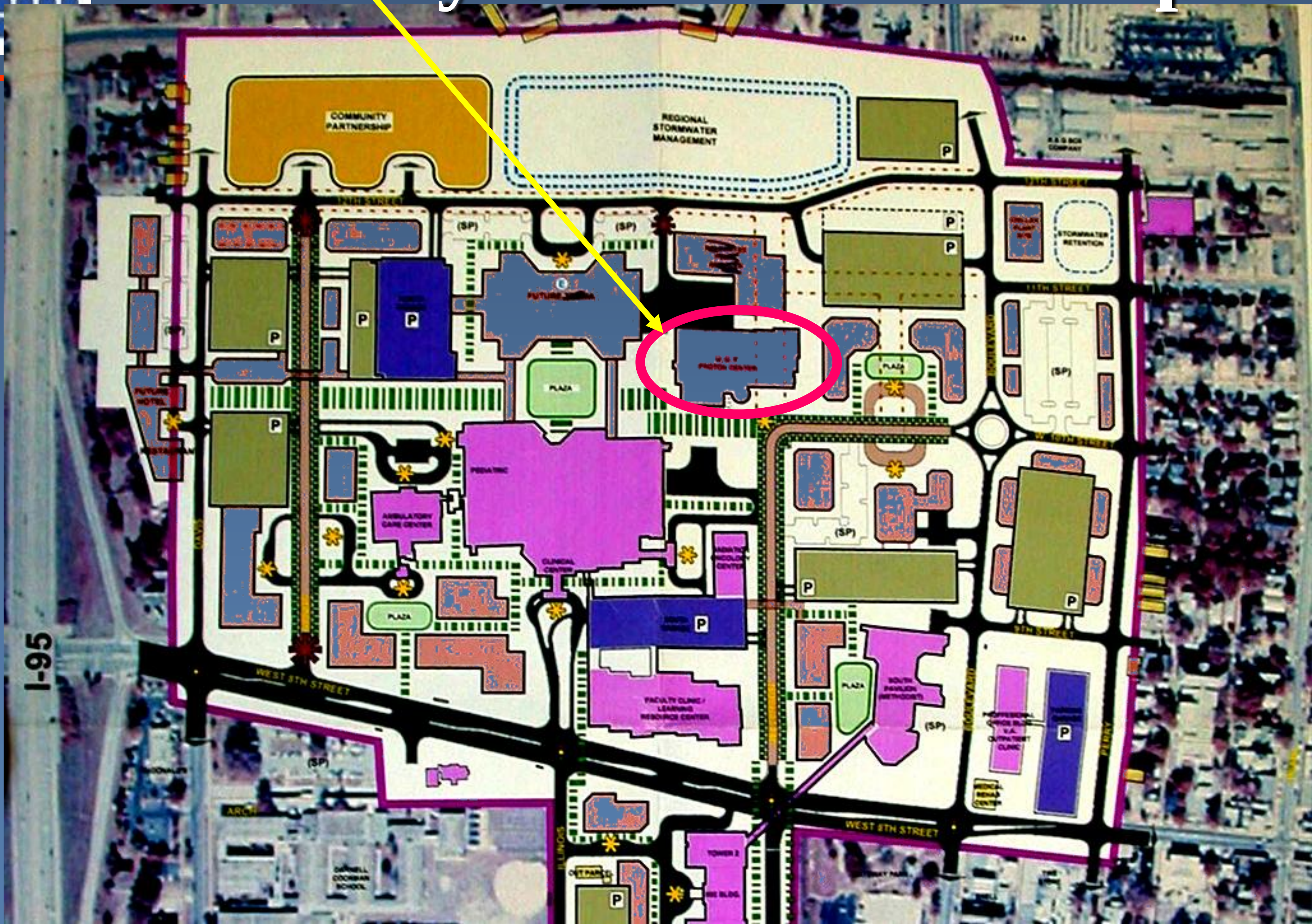
University of Florida Proton Therapy Institute

University of Florida Proton Therapy Institute Site Selection

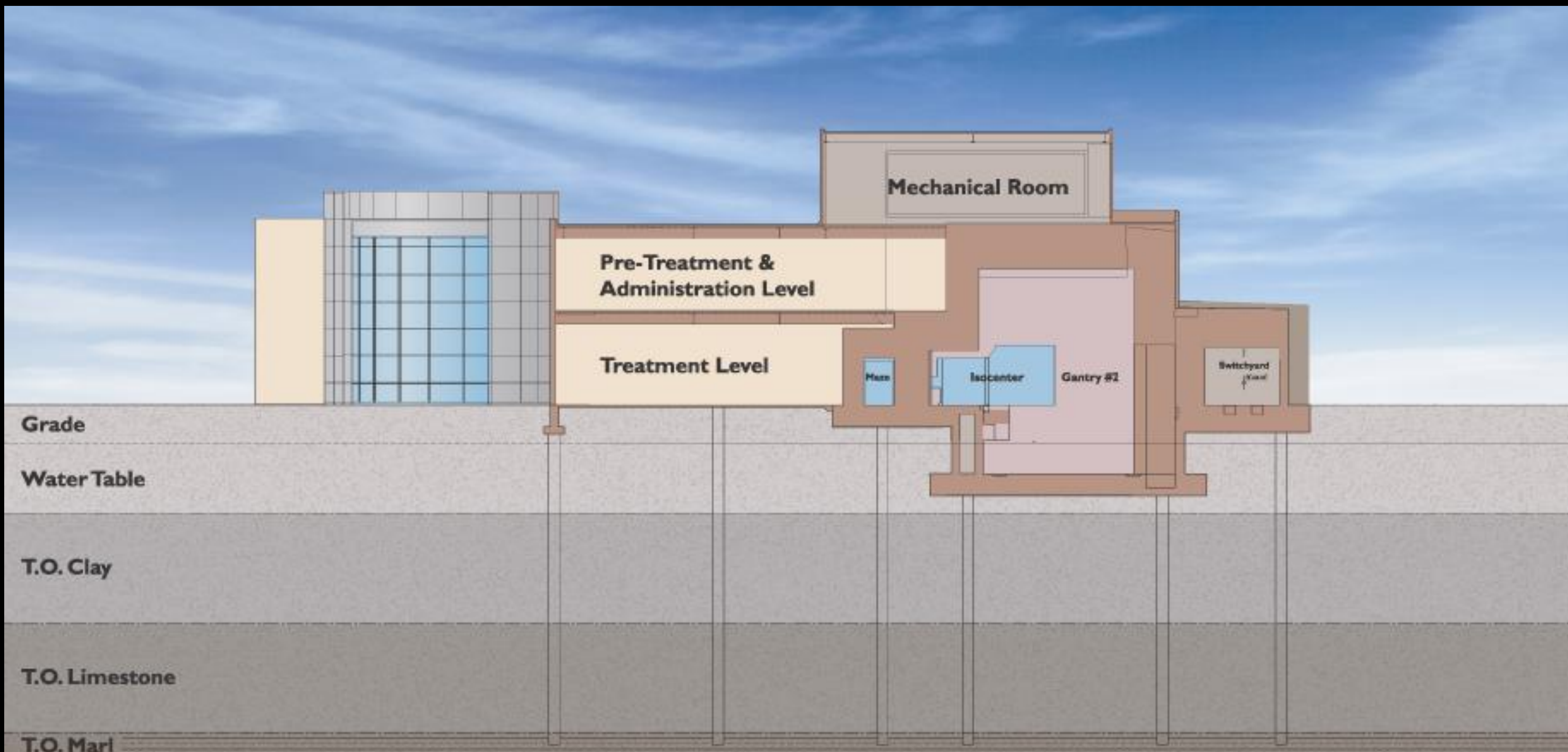
- UFPTI to serve Florida & SE US.
- UF has two healthcare campuses: Gainesville and Jacksonville.
- JAX strategically located with international air and sea ports and interstate highway.
- Strong long-visioned and principle-guided city and state legislative support for UFPTI.
- UFPTI sited adjacent to UF affiliated tertiary hospital, ambulatory diagnostic radiology, and close to pediatric hospital.



Proton Facility-Shands JAX Campus



University of Florida Cancer Center

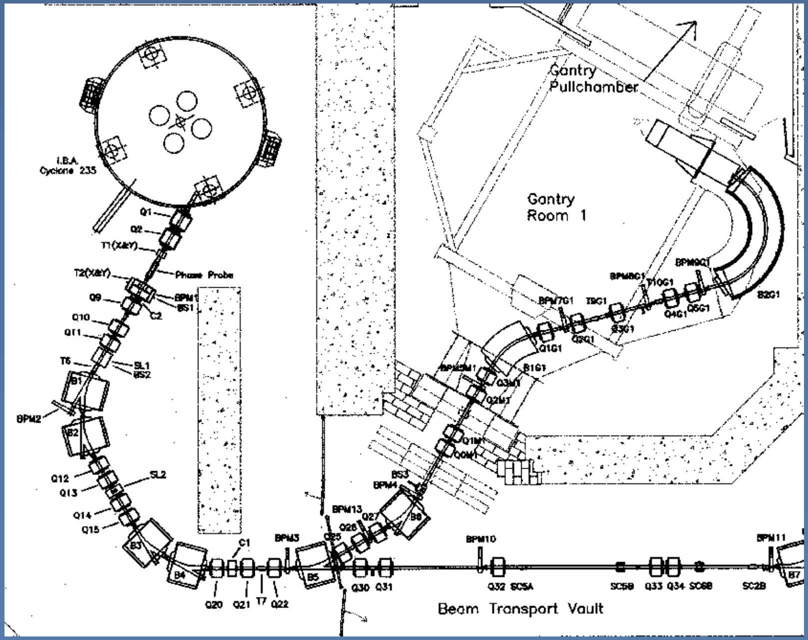


University of Florida Cancer Center

Treatment Level Plan

Production of Proton Beams

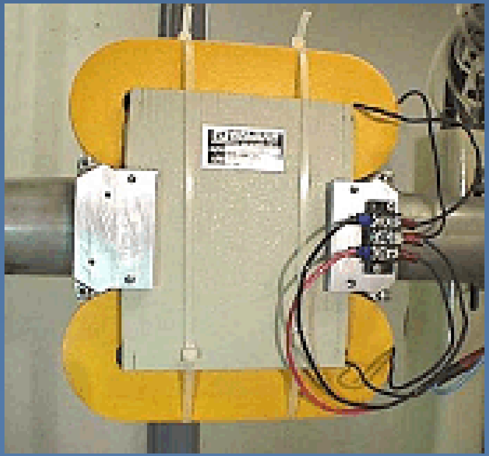
- Cyclotron: 230 MeV proton beams (~33 cm depth in water)
- Energy degrader: reduce energy to the desired value
- Beam line: guide the proton beam to the treatment room
- At the end of the beam line, the proton beam is
  - Small and narrow
  - Monoenergetic (almost)



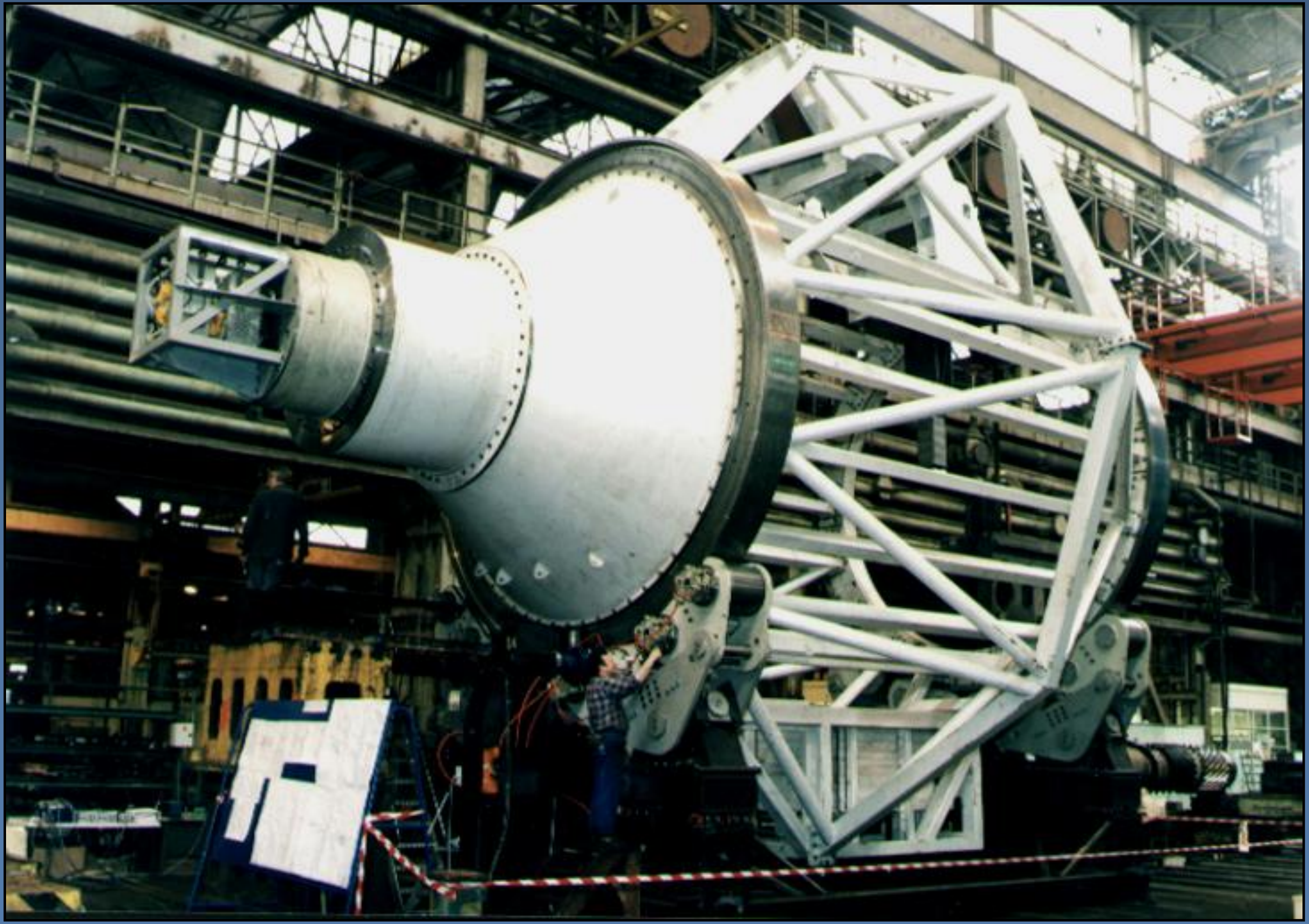
Production of Clinically-Useful Proton Beams
Proton Accelerators - CYCLOTRON

Production of Clinically-Useful Proton Beams
Beam Line

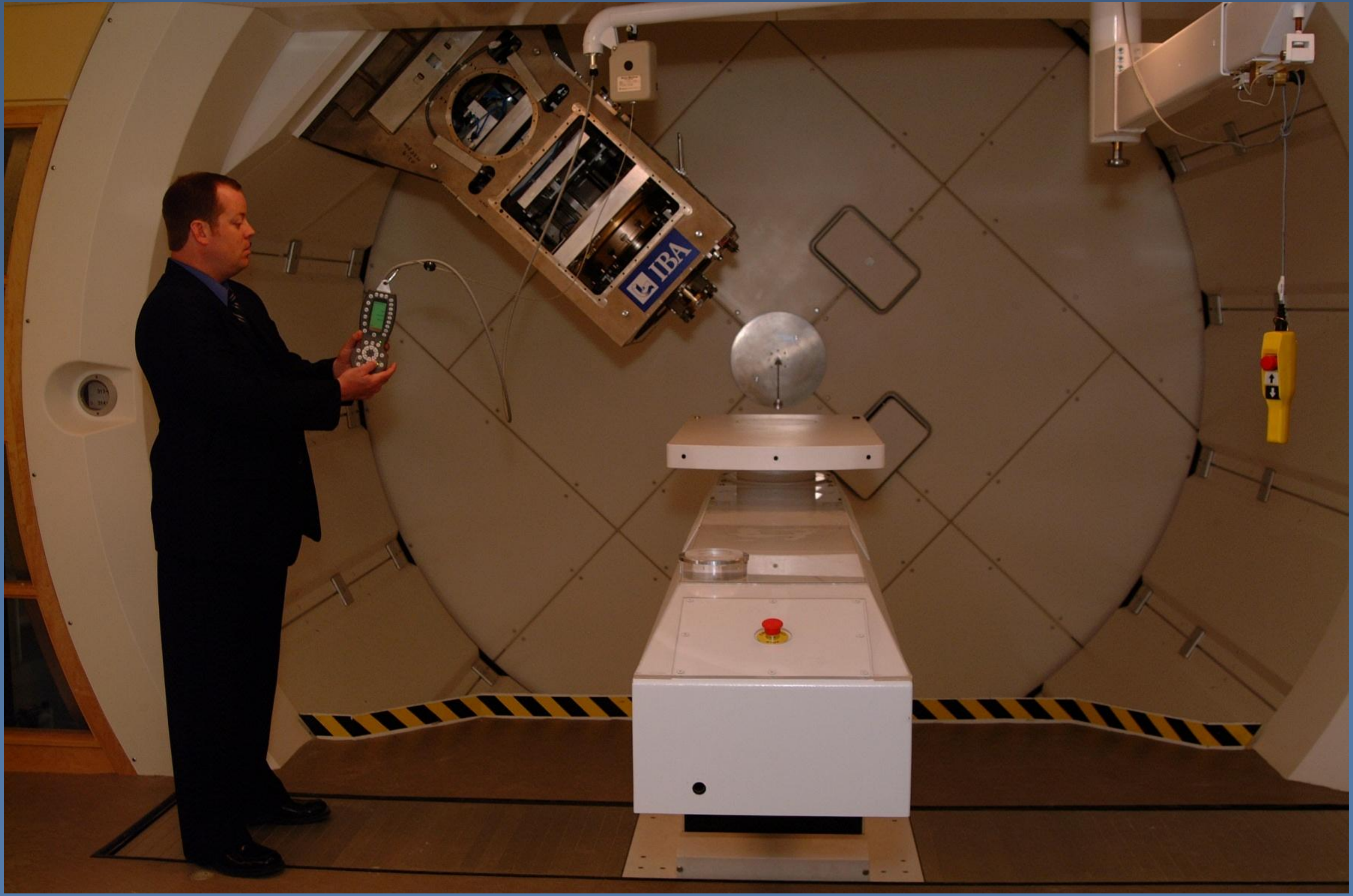
- **Protons are Charged Particles**
  - **Dipoles – Bend, guide the proton beam**
  - **Quadrupoles – Focus the proton beam**
  - **Steering Coils – Fine-tune direction of beam**



IBA Isocentric Gantry



Gantry in Motion

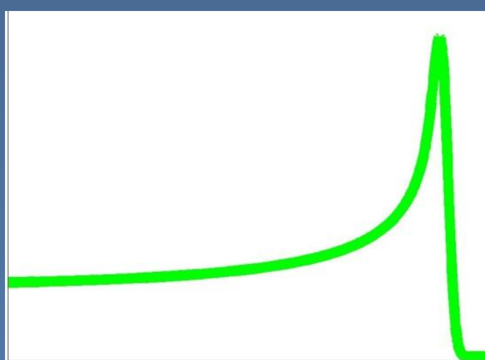


Nozzle

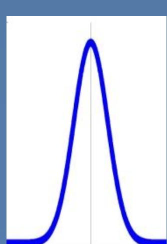
Mono-energetic pencil beam

Treatment Nozzle

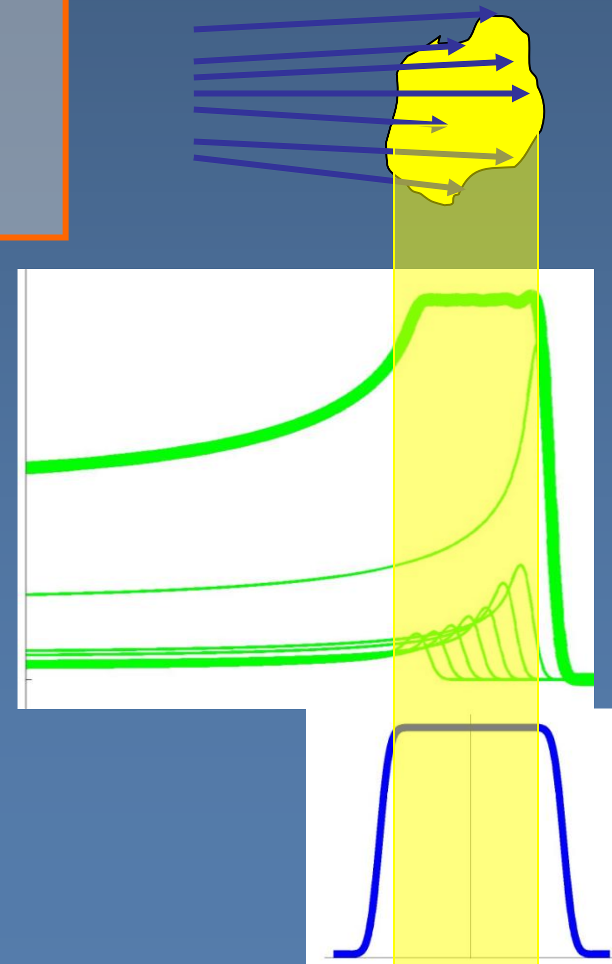
3D dose distribution



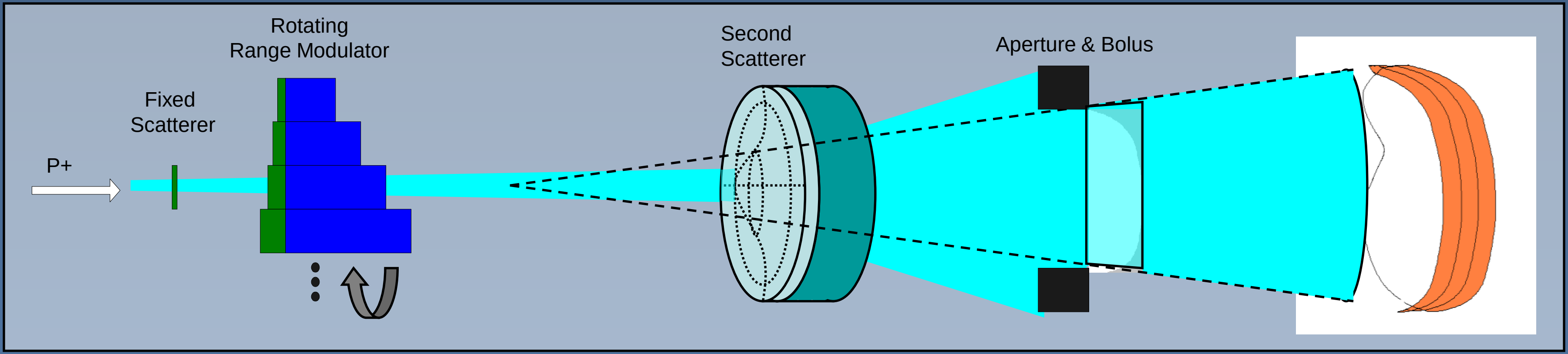
Depth Dose Distribution



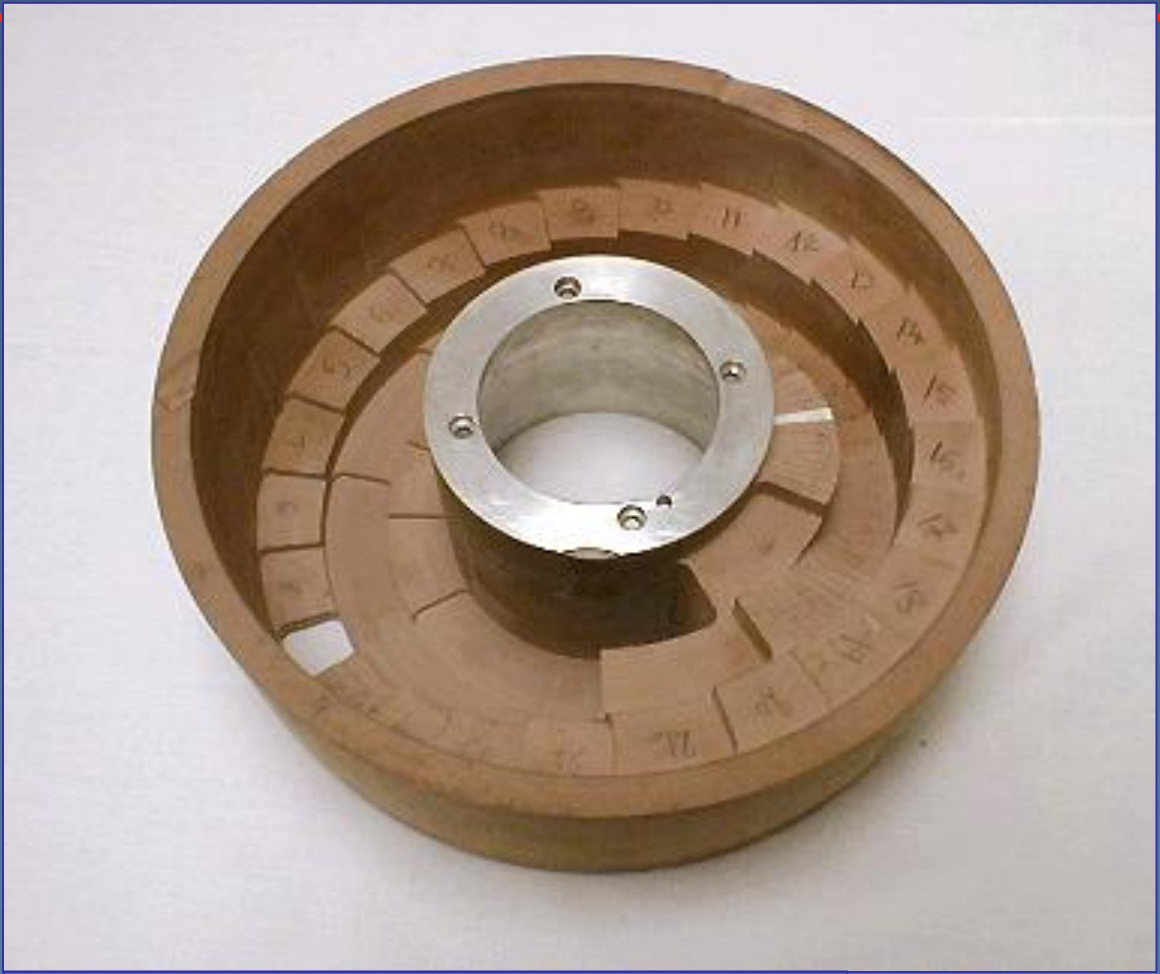
Lateral Dose Distribution



Double Scattering



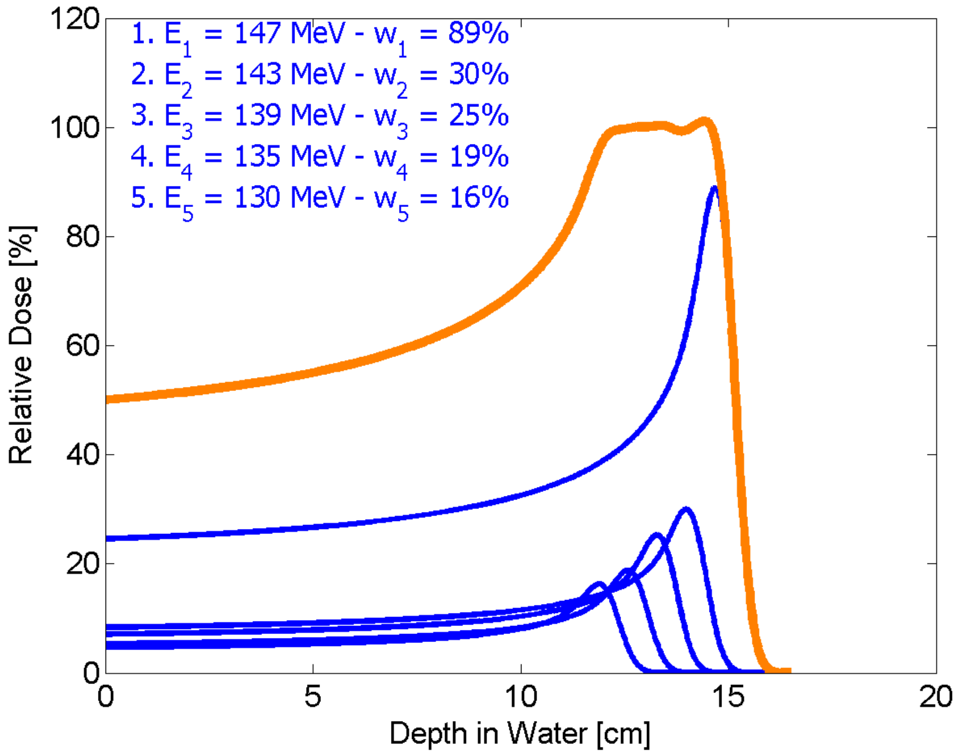
Range modulation / RM wheels

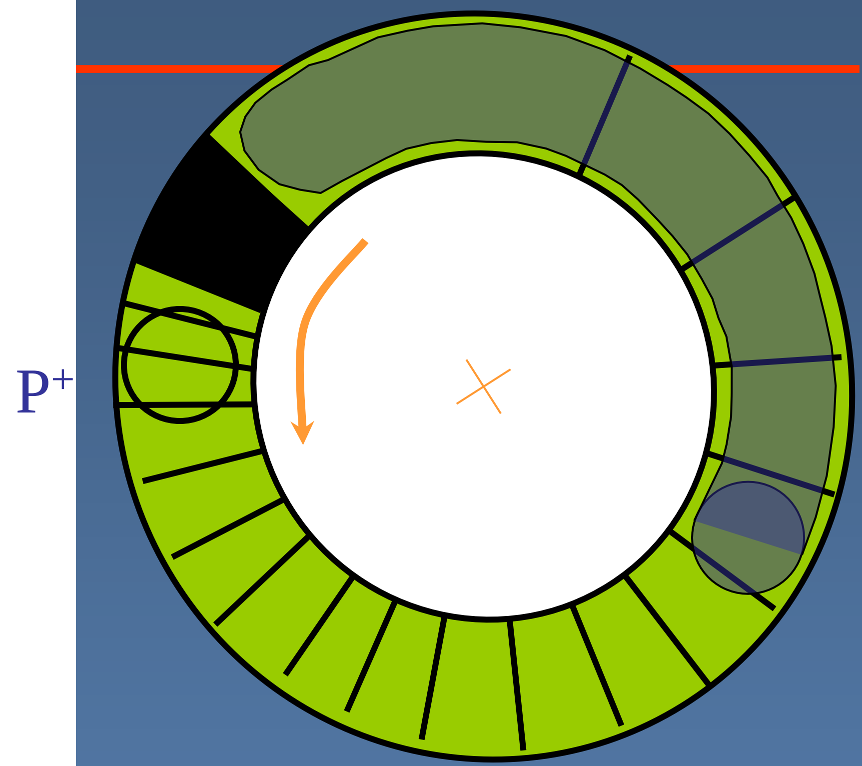


IBA design (3 tracks on single wheel, gating used to adjust modulation)

Photos courtesy MGH / IBA

Range modulation / RM wheel





Step#	thickness	angular width
1	1.8 cm.H20	76 deg
2	2.3 cm.H20	27 deg
3	2.9 cm.H20	20 deg
4	3.4 cm.H20	14 deg
5	4.0 cm.H20	11 deg

Range-compensated contoured scatterer

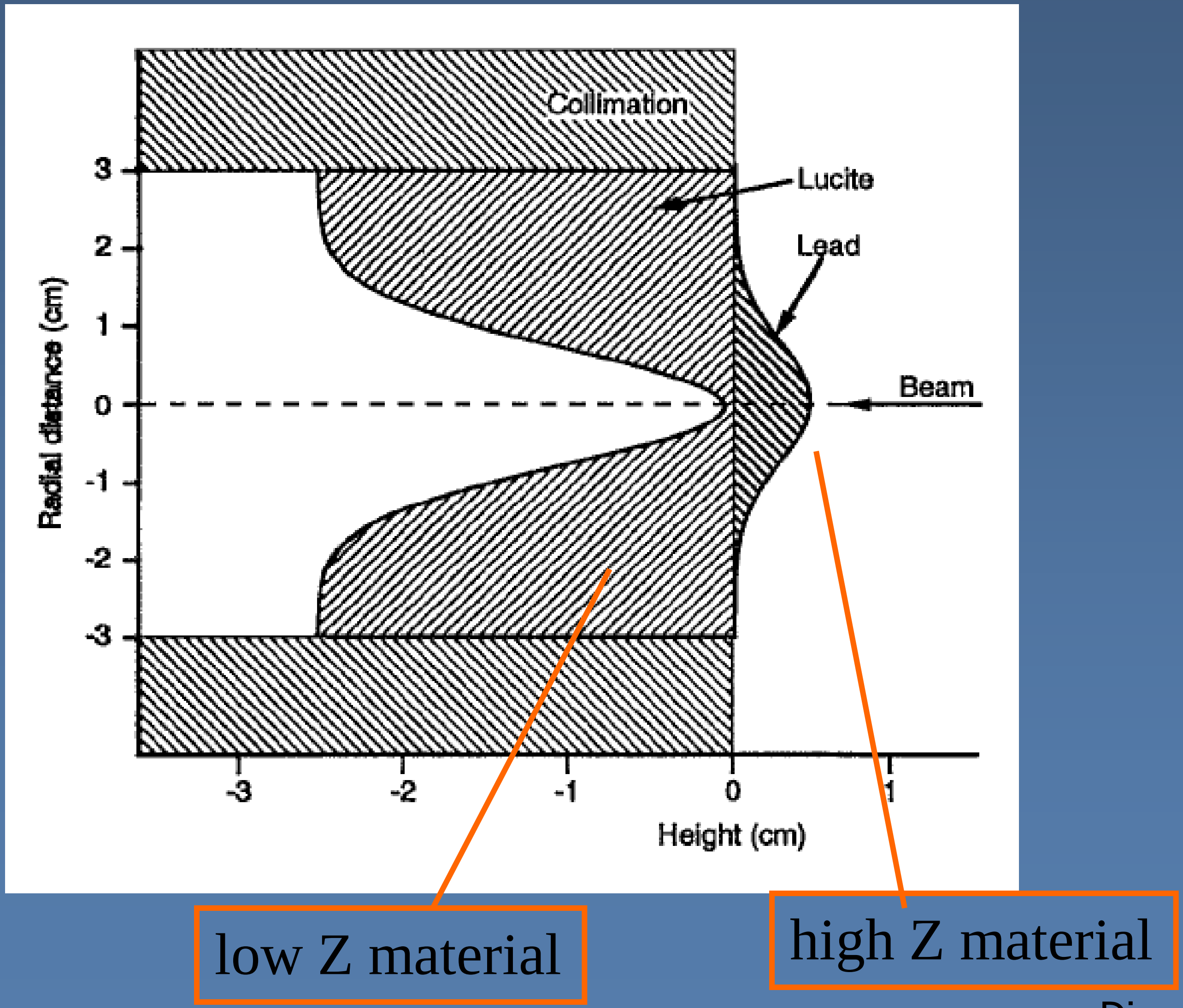
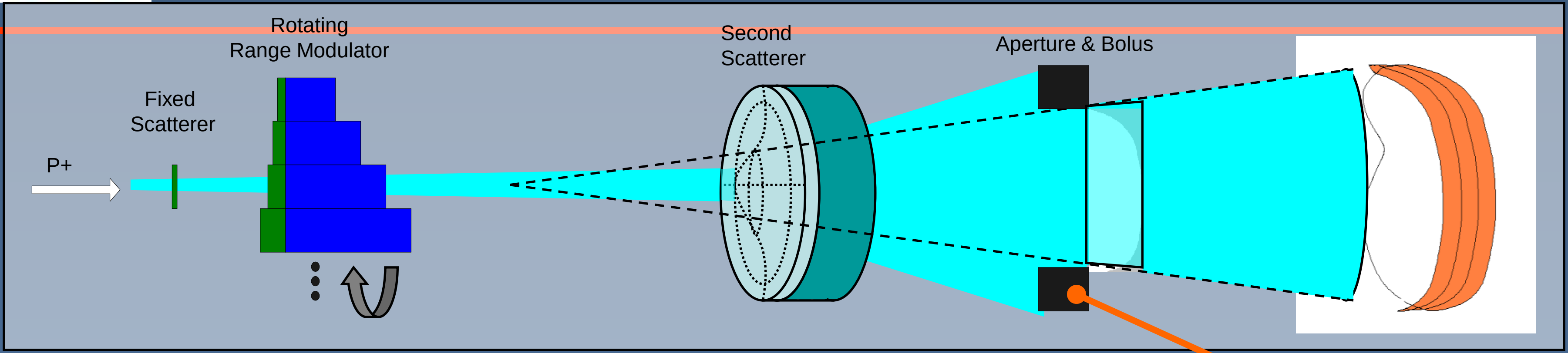


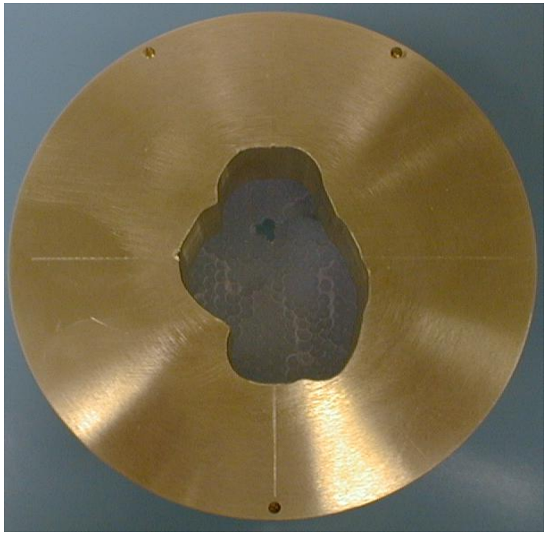
Diagram: Gottschalk

Double Scattering

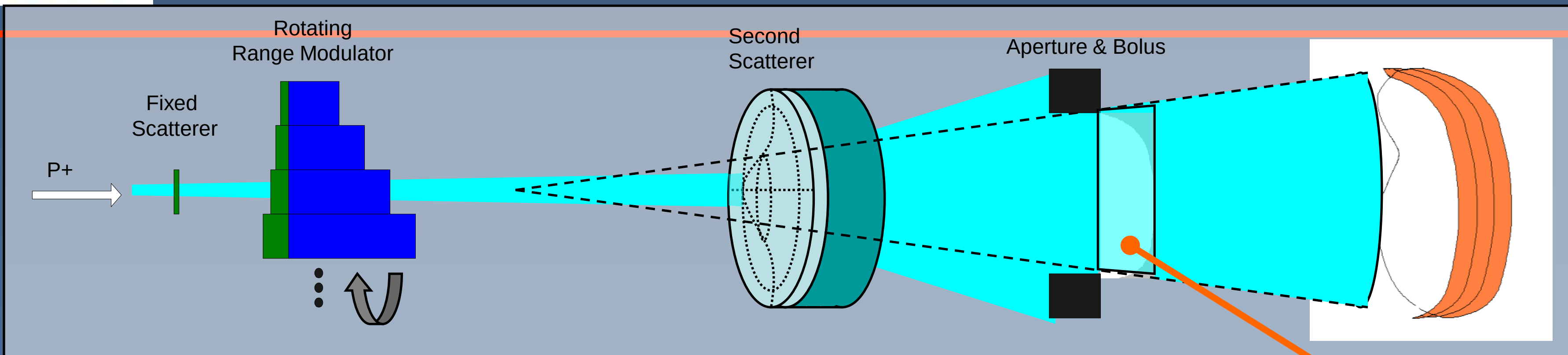


<u>Field-specific aperture:</u>

- Used to conform the dose to the lateral shape of the target
- Brass
- 2-6.5 cm thickness
- Positioned as close to the patient as possible

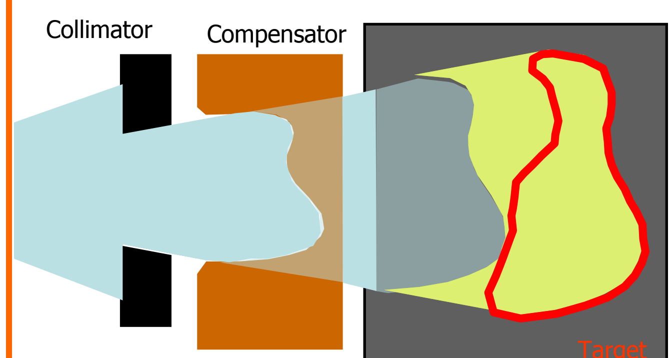


Double Scattering



<u>Field-specific range compensator</u>

- Used to conform the dose to the distal end of the target
- Lucite
- 0-15 cm thickness
- Positioned as close to the patient as possible (2 cm from skin)



Applications for Proton Therapy

Brain Tumors: Craniopharyngioma

Craniopharyngioma

Craniopharyngioma

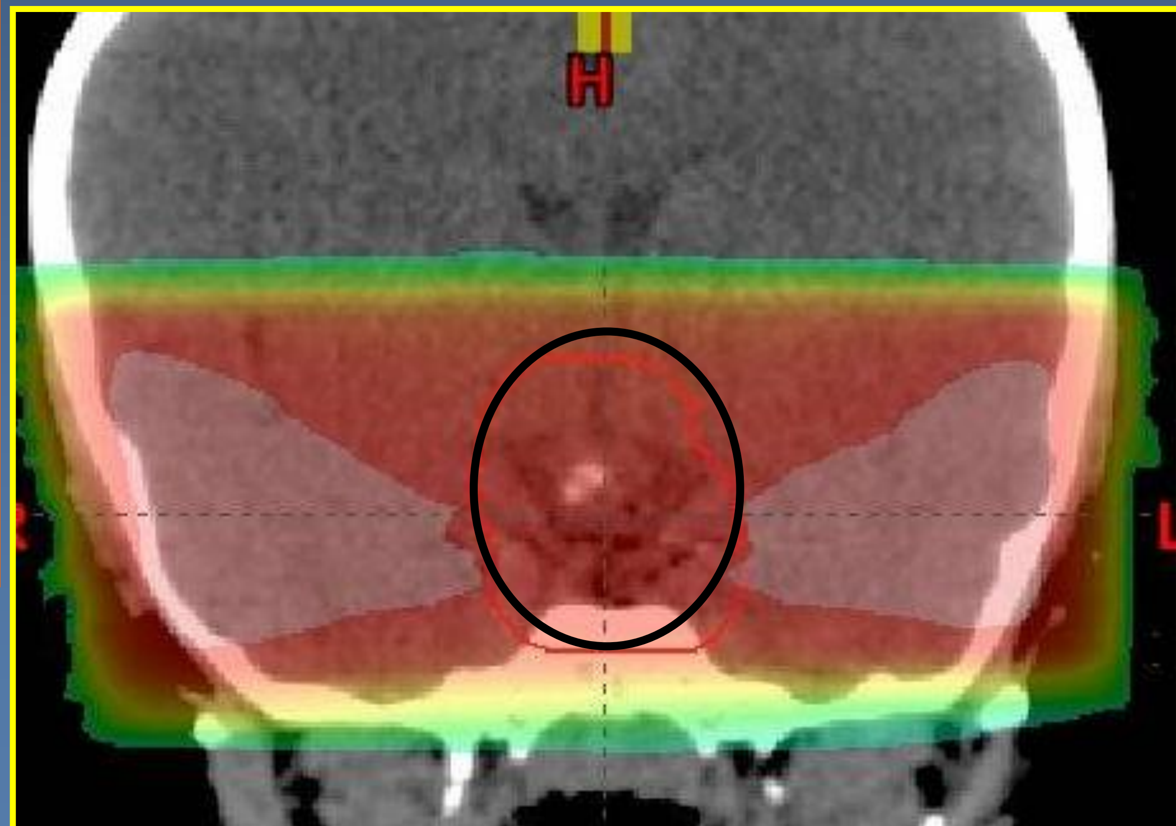
Colorwash Representation of Radiation Dose:

Range from ~105% (pink) to ~20% (aqua)

Desired target dose is 100% (red)

Target outlined in thin black line

X rays~1980

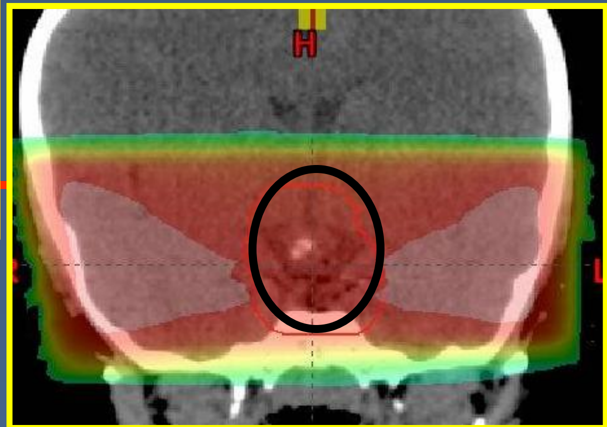


Courtesy:
D Louis,
D Yeung,
Z Li, C Li

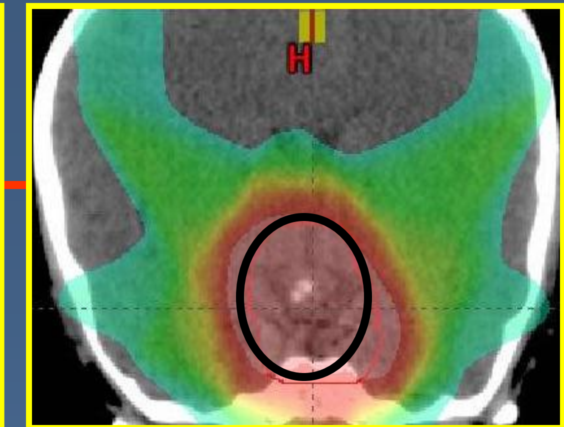
Radiation Therapy Progress

Pink = 105%
Red = 100%
Yellow = 90%
Green = 50%
Aqua = 20%

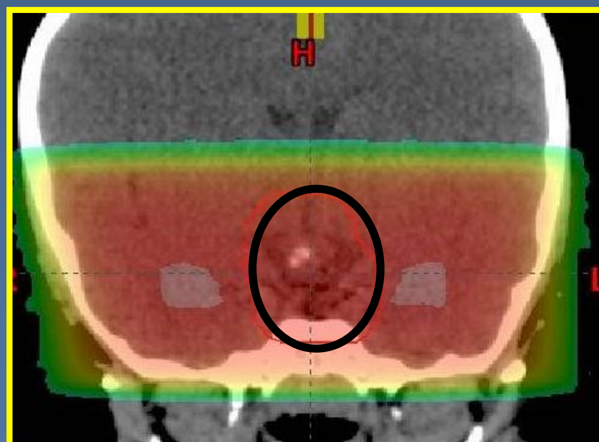
Opp 6X ~1980



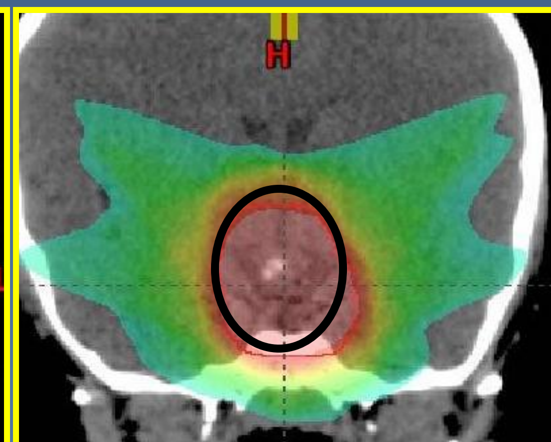
3D-C ~1995



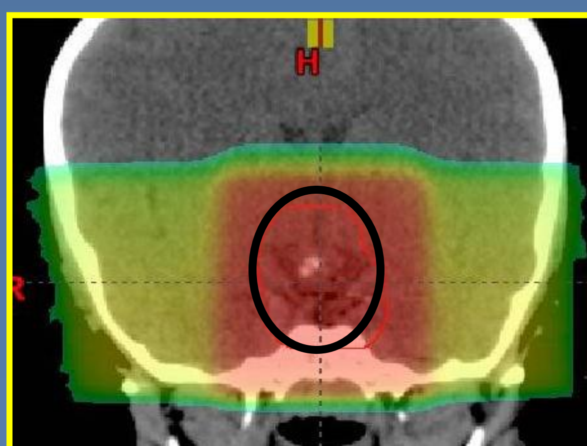
Opp 15X ~1985



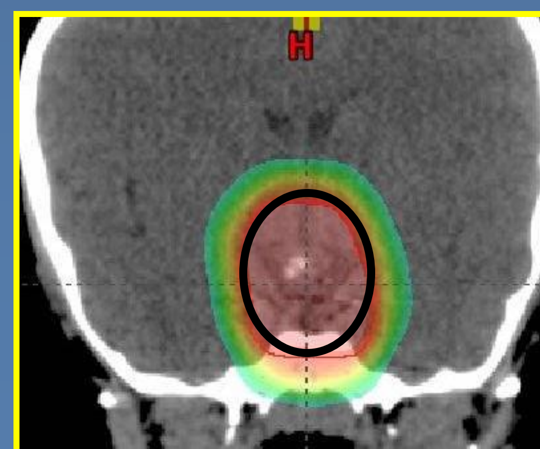
IMRT ~2005



3 Field ~1990



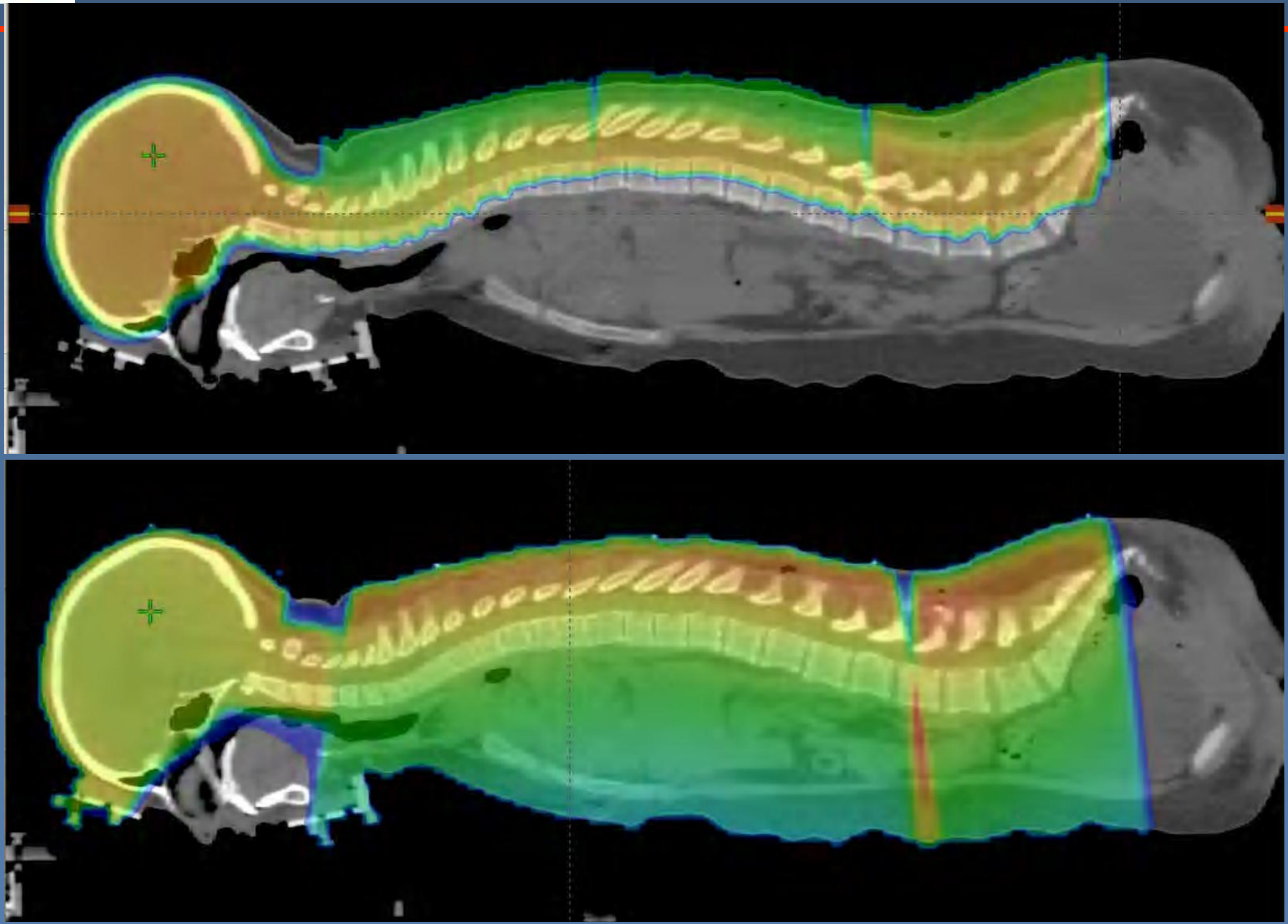
Proton ~2009



V20 = 22% for IMRT vs 5.6% for protons

Courtesy:
D Louis, D Yeung,
Z Li, C Li
N Mendenhall

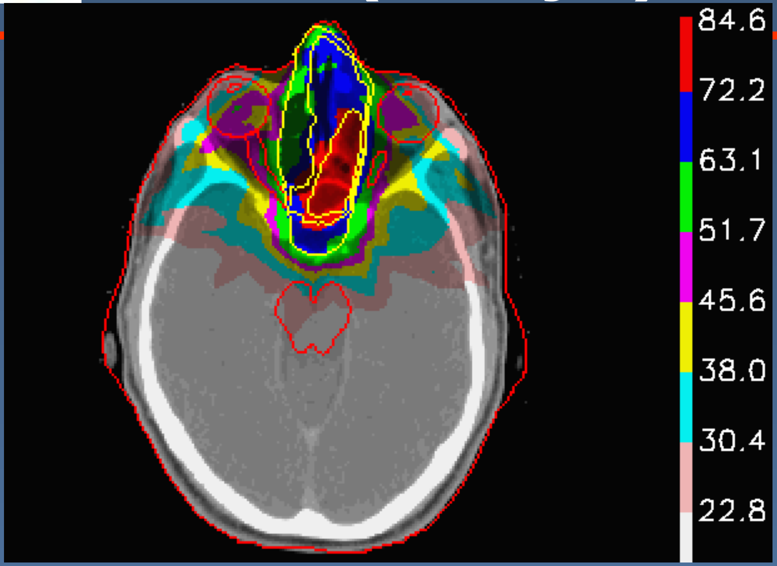
Craniospinal Axis Irradiation for CNS Tumors



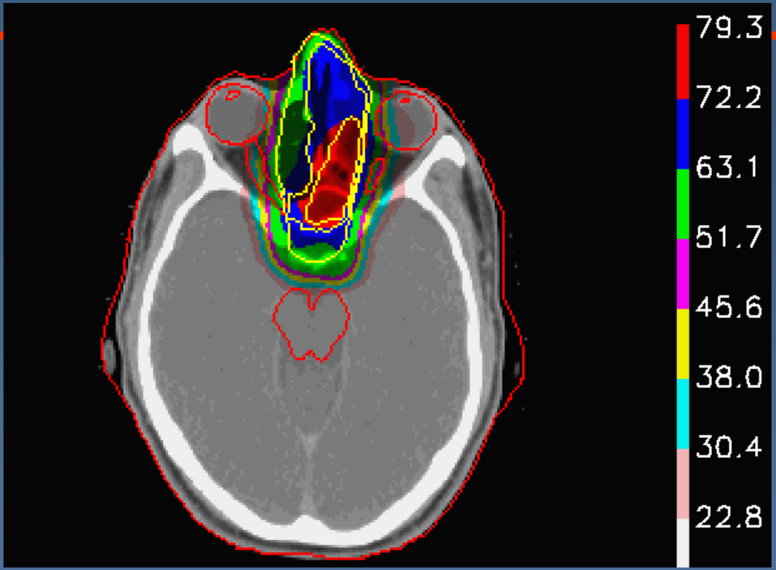
Paranasal Sinus Tumor

Paranasal Sinus

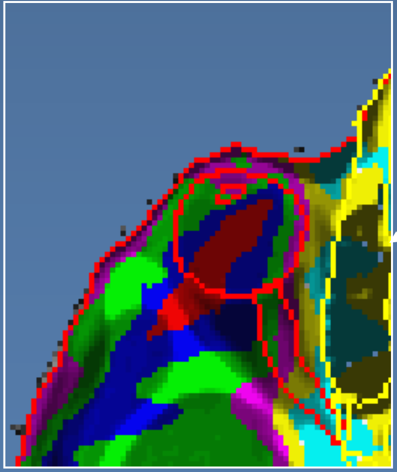
IMXT (X rays)

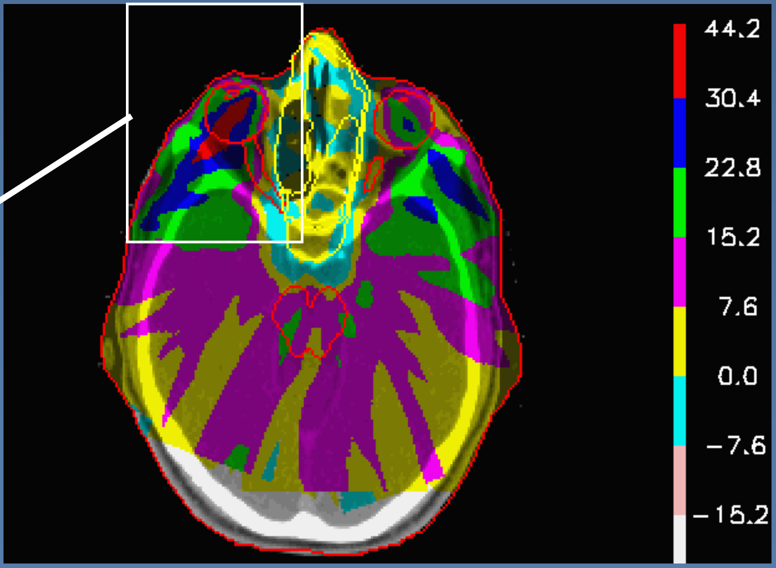


Protons



Dose Difference →





PSI

Prostate Cancer

Prostate Cancer: bPFS and Grade 3+ GI Toxicity in Dose Escalation Studies

	Dose	d/Fx	bPFS	Gr 3+GI
Dutch[1]	78	2	66	5
MRC[2]	74	2	71	6
MDA[3]	78	2	73	7
PROG[4]	79.2	1.8	91[4]	1
UFPTI*	78-82	2	--	<0.5

[1]Peeters et al, 2006; [2]Dearnaley et al, 2007; [3]Kuban et al, 2008; [4] Zeitman et al, 2010, for low risk disease bPFS was 97%; UFPTI PR010203 2 Y.

Lung Cancer

Proton Beam Results in Lung Cancer

Stage I/II

***87% Local Control**

***63 % Disease Free**

Bush et al, CHEST, 1999.

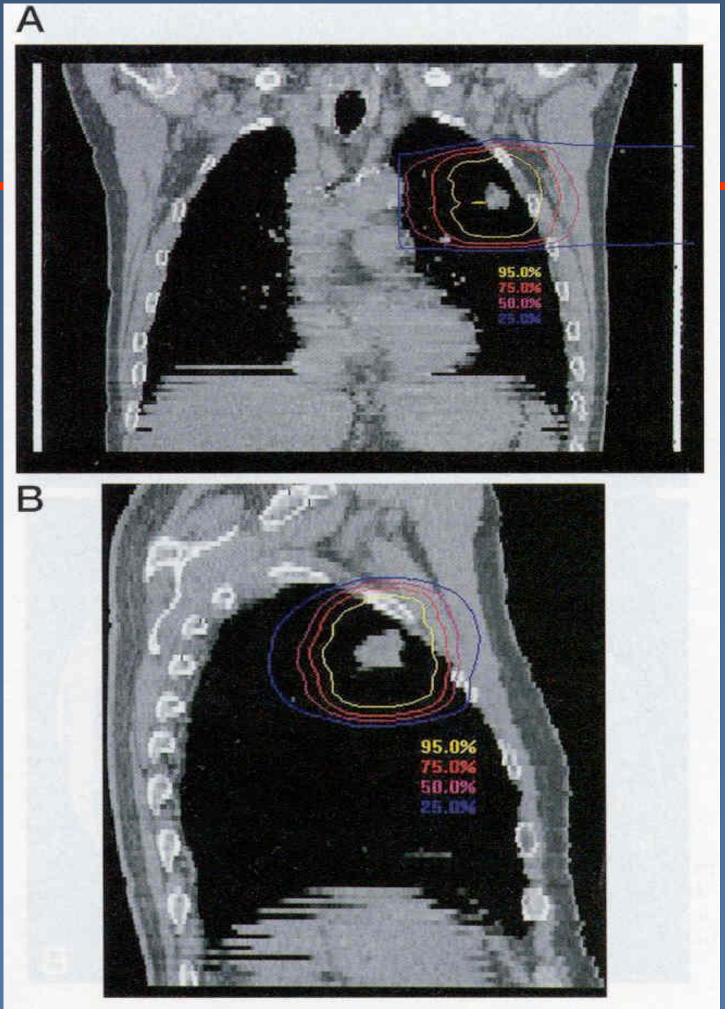


FIGURE 1. Proton dose distribution. *Top, A*: coronal plane. *Bottom, B*: sagittal plane. The colored contours represent the area receiving the indicated percentage of the total dose given.

Treatment given intensely over 2 weeks rather than traditional 8 weeks, increasing effectiveness and reducing costs.

Hodgkin's Lymphoma

Background- General

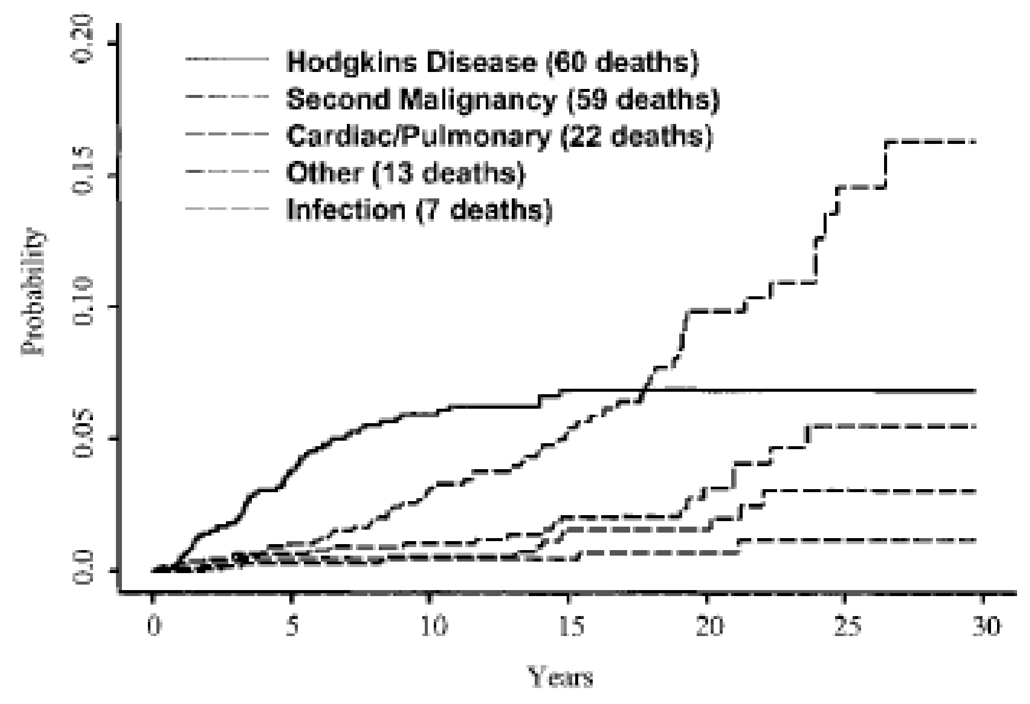


Fig 2. Competing causes of death.

Ng JCO 2002

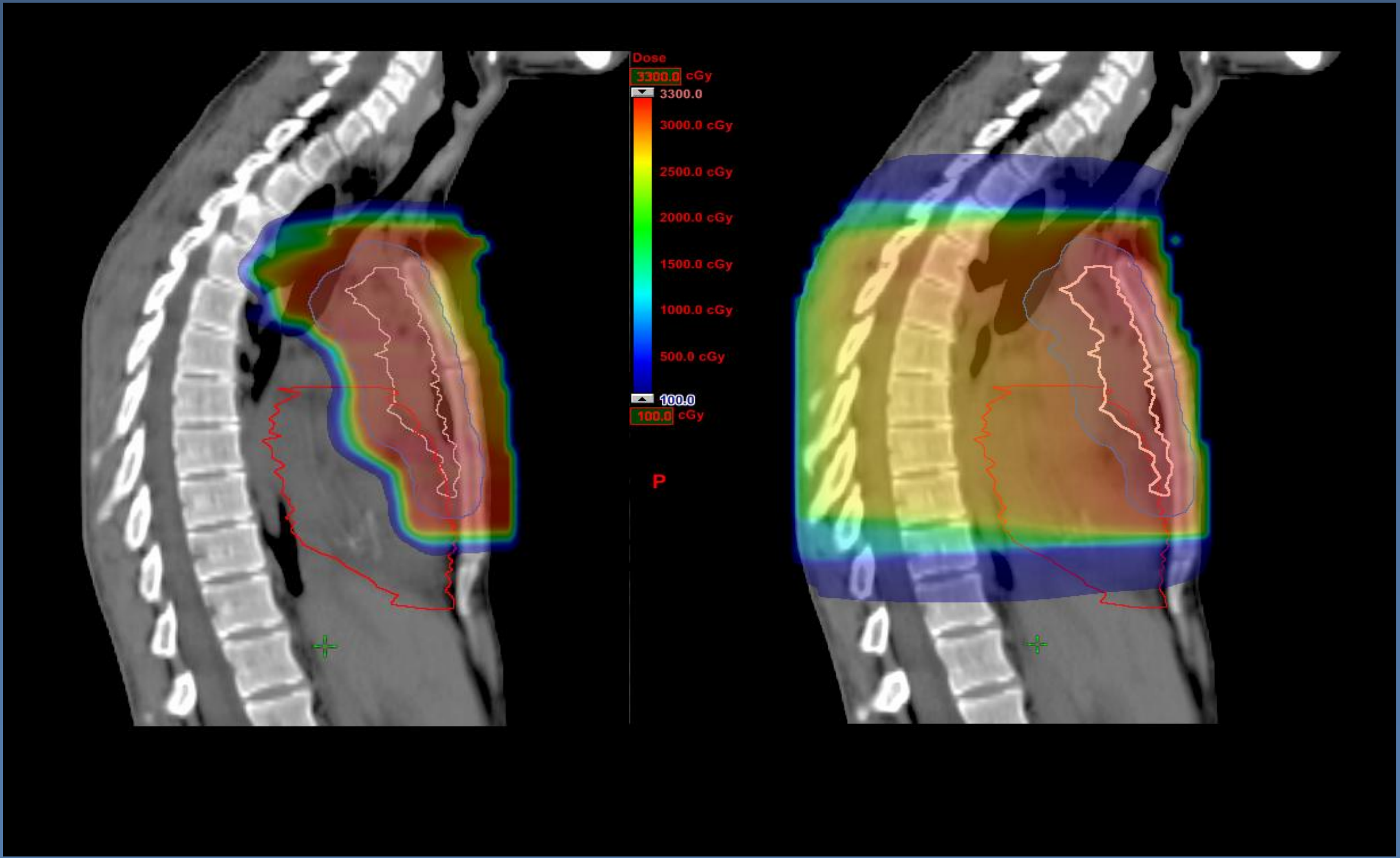
Childhood Cancer Survivor Study- Oeffinger et al NEJM 2006

HL survivors (as a group) were: highest risk of severe or life threatening chronic health conditions (highest risk of second cancer and heart disease)

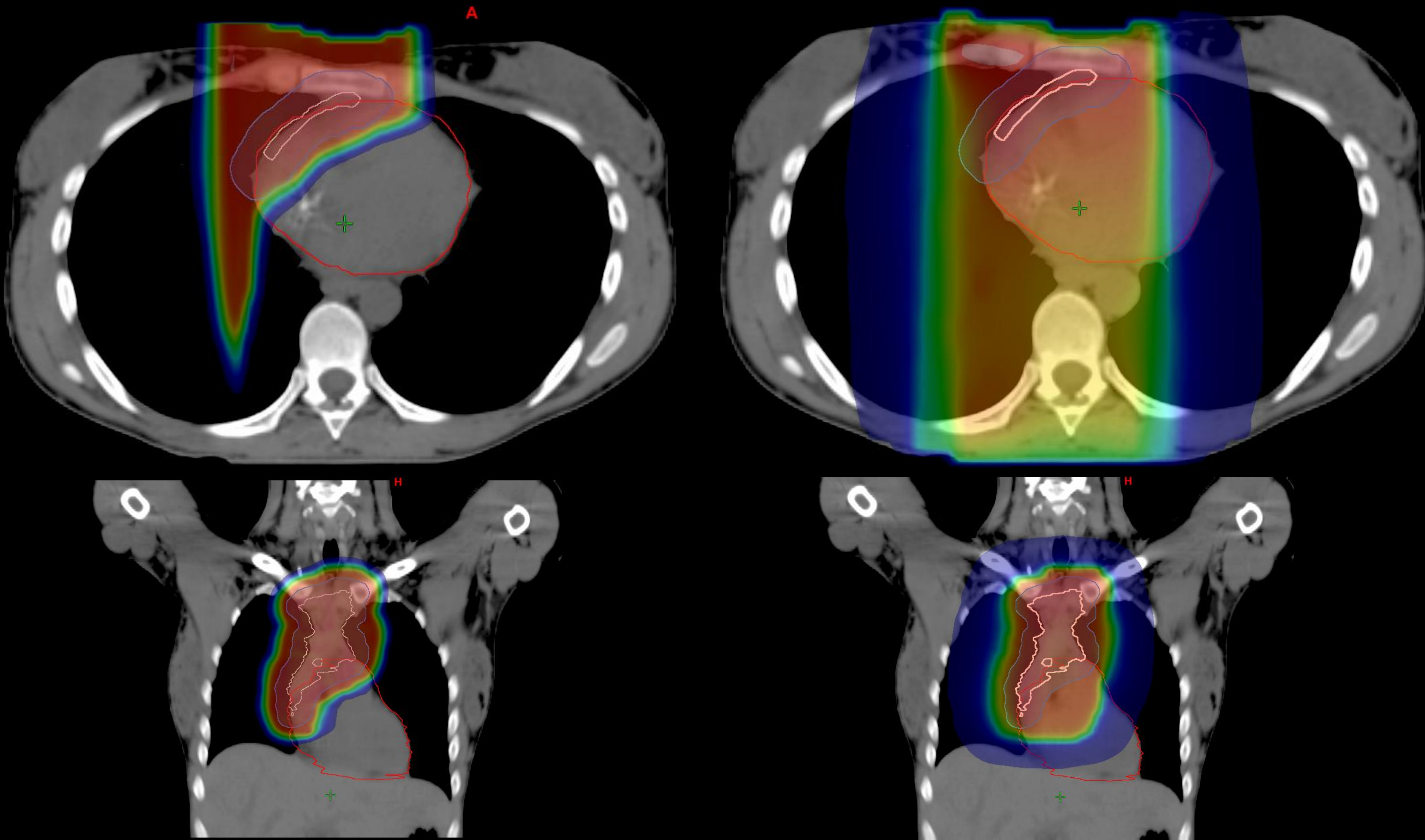
RT dose & late effects HL survivors

Author	Disease	Dose	RR
Travis et al 2002	Breast Cancer	≥ 4 Gy	3.2
Travis et al 2003	Lung Cancer	≥ 5 Gy	5.9
Van Den Belt-Dusebout 2009	Gastric Cancer	≥ 11 Gy	3
Mulrooney et al 2009	CHF	≥ 15 Gy	2.2
	MI	≥ 15 Gy	2.4
	Pericardial	≥ 15 Gy	2.2
	Valvular	≥ 15 Gy	3.3

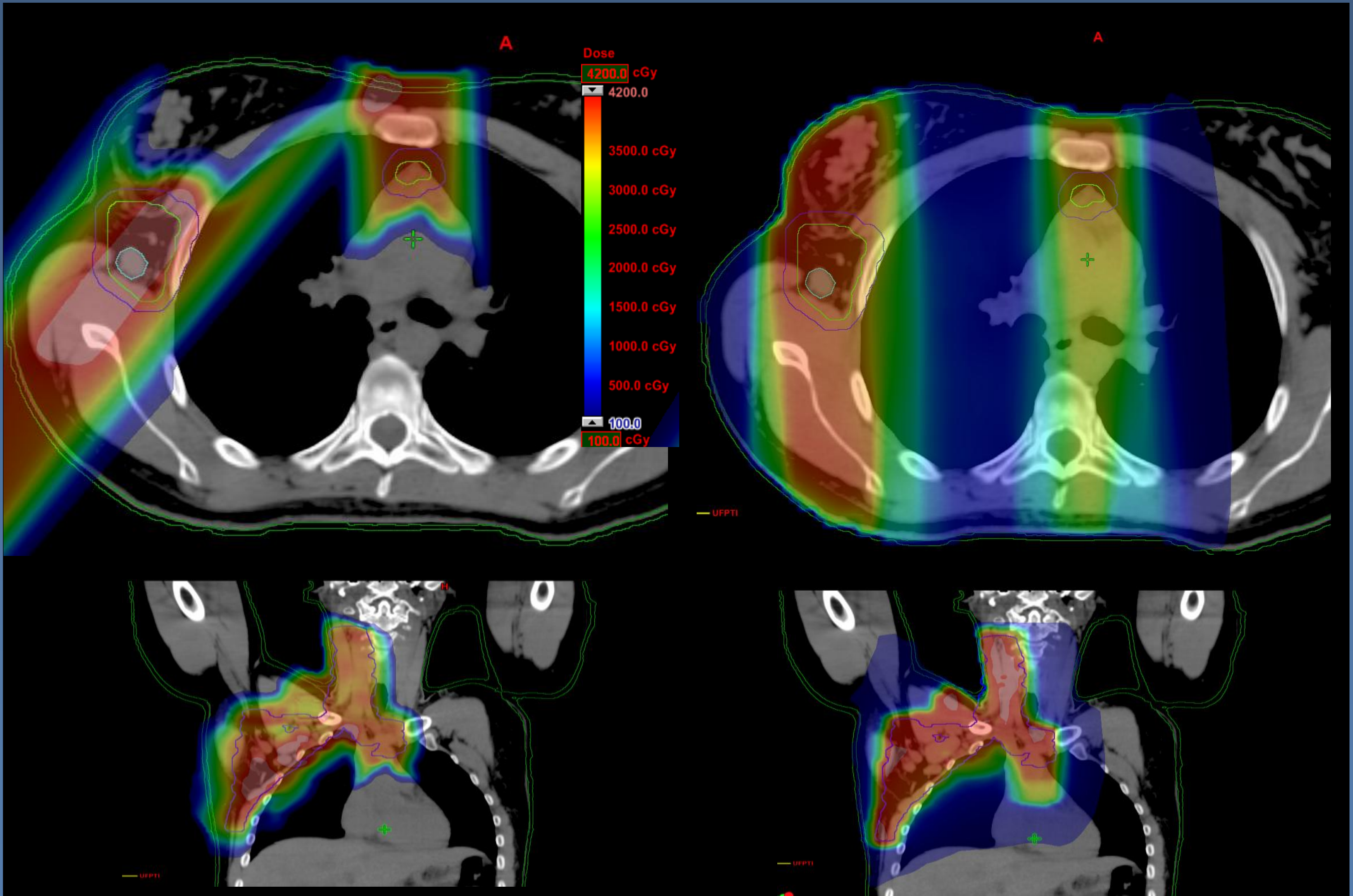
1 field- AP- Cardiac Sparing



1 field- AP- Cardiac Sparing



Cardiac & Breast Sparing



UFPTI Clinical Research Protocols

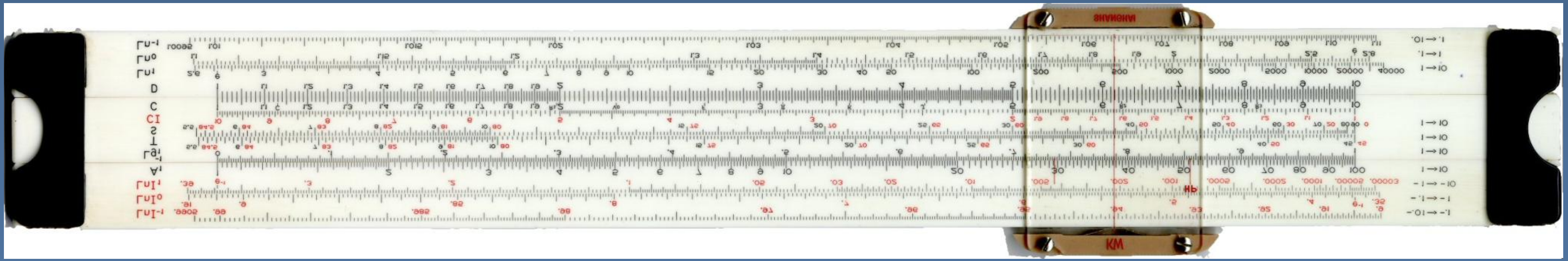
PROSTATE	HEAD&NECK	LYMPHOMA
Prostate PR01	NX 01	HL01
Prostate PR02	PS 01	LUNG
Prostate PR03	OX 01	LG01
Prostate PR04	SK01	LG02
Prostate PR05	SARCOMA	CENTRAL
Prostate PR06	CH01	NERVOUS
Prostate PR08	SA01	SYSTEM
PANCREAS	SA02	PI01
PC01	GENERAL	CN01
PC02	OT01	SJEP(SJCP)

~95% on protocol

Promise of Proton Therapy

- **Reduced toxicity** (brain function, vision preservation, gastrointestinal damage, pulmonary damage, thyroid and reproductive organ function, cardiovascular disease and second malignancy)
- **Increased cure rates** through dose escalation and or intensification.
- **Reduced health care costs** through lowering costs of recurrence and toxicity and reducing overall treatment time.
- **Main barrier** to proliferation of proton facilities for treatment is cost.

The Slide Rule

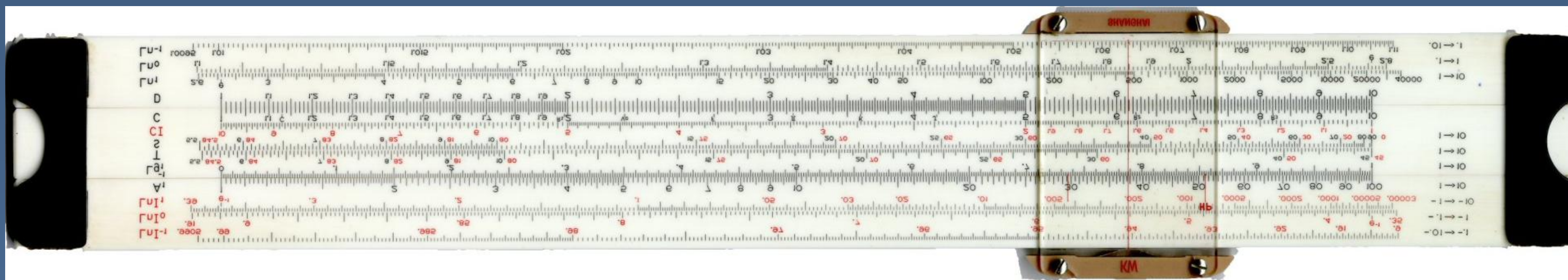


1980: ~$12.50

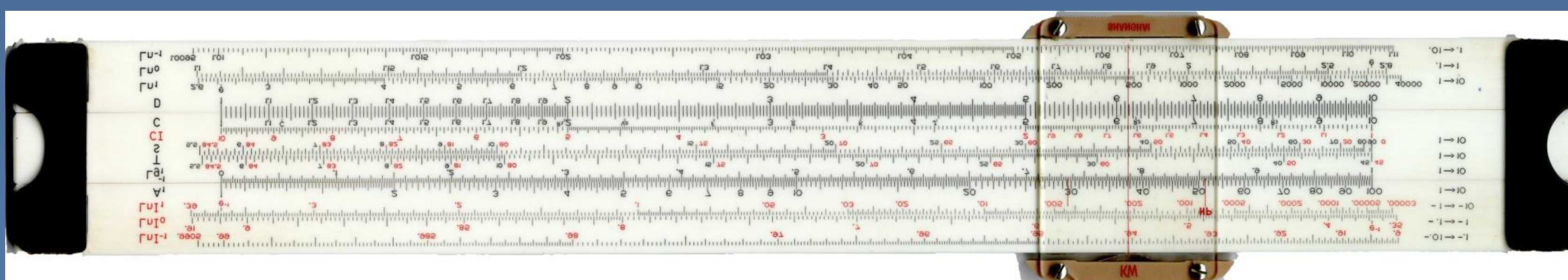
The Hewlett-Packard HP-35

1980: ~$399.00

The Slide Rule



1980: ~$12.50



2011: ~$33.00

The Slide Rule and The HP-35

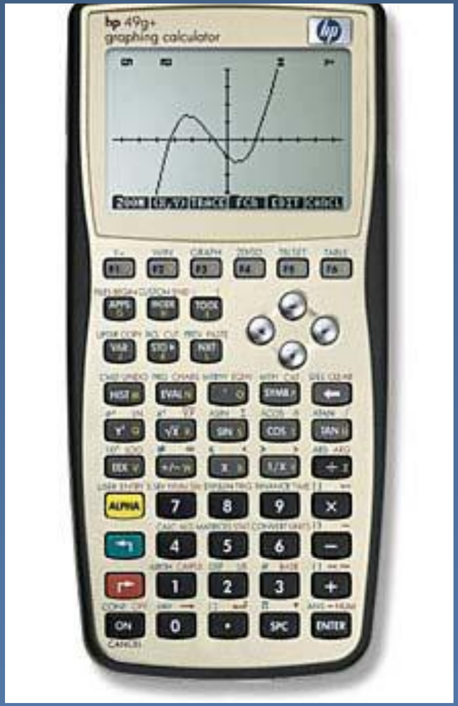
Accuracy

Efficiency

Increased potential for good

The Hewlett-Packard HP-35

1980:
$399.00



2010:
~$79.99

Walmart Price
2010: ~$7.99

Acknowledgements

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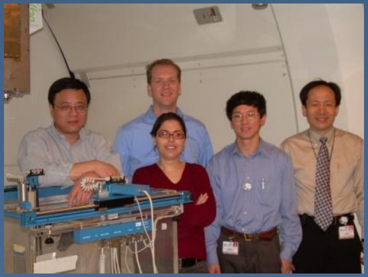

Gainesville Team
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