Overview of Proton Beam Cancer Therapy

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THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER
Making Cancer History™

Acknowledgments

- Dr. Kirk for the kind invitation
- NIH/NCI through grant 1-R01-CA131463-01A1
- Many colleagues at The University Texas M. D. Anderson Cancer Center

Basic Economic Parameters (US)

- Population 286 million
- Gross Domestic Product $10 trillion
- GDP per capita $35 thousand
- Health care spending
  - 13% of GDP, highest in the world!
  - $1.3 trillion, or $4500 per capita
  - Yet ~*46 million* Americans are uninsured!

Basic Cancer Statistics (USA)

- Cancer Rates
  - No. 2 cause of death after heart disease
  - 1 of 2 men, 2 of 3 women will develop cancer
  - 1.2 million new cases per year (0.4%)
  - 550,000 deaths per year (0.2%)
- Breast, lung, and prostate most common
  - More than 50% of direct medical costs
- Survival increasing
  - 8 million American cancer survivors
  - About 3% of the total population!


Robert Wilson
Circa 1946

A Condensed History

1904 Bragg & Kleeman report ion energy loss curves

1910 Geiger reports “range-energy” relation for α’s

1913 Bohr postulates atomic nucleus

1919 *Rutherford proposes existence of the proton*

1932 Lawrence & Livingston report 1st cyclotron

1946 *Wilson proposes proton therapy*

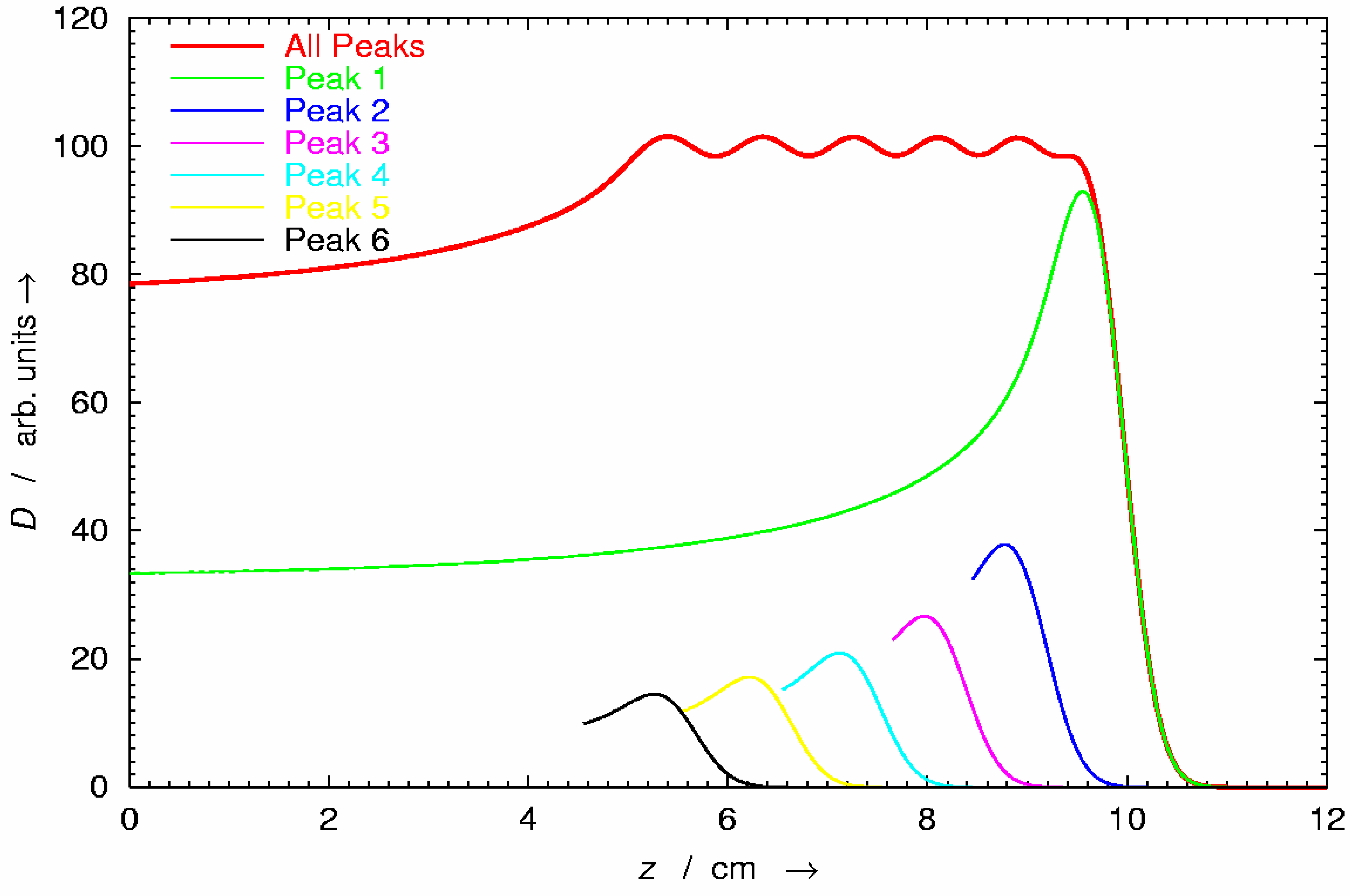
1954 *Tobias et al treat patients w/ 340 MeV p at LBL*

1961 Kjellberg et al treat w/160 MeV p at HCL

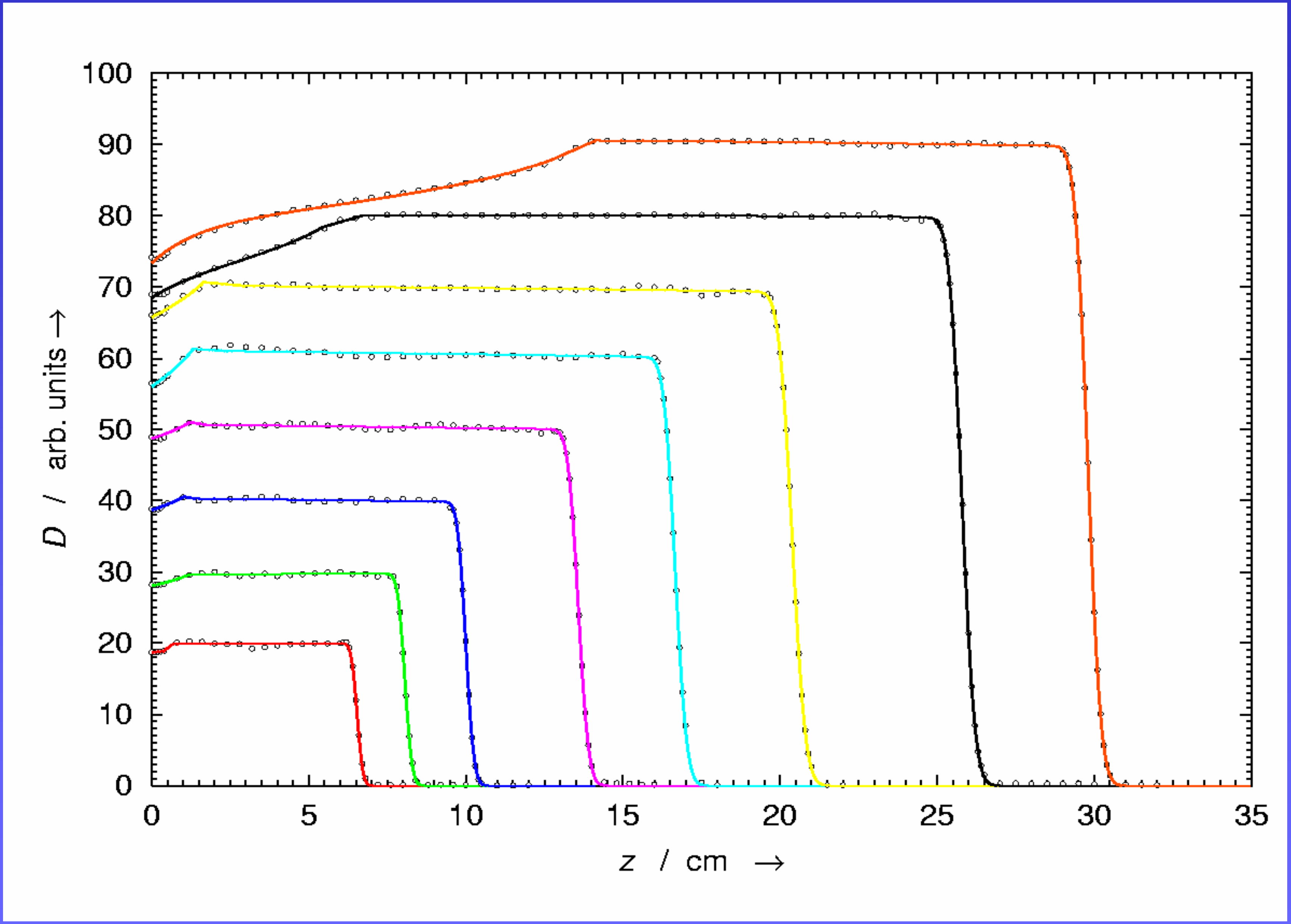
Present Status: ~25 proton centers (6 in USA)

~50,000 patients treated

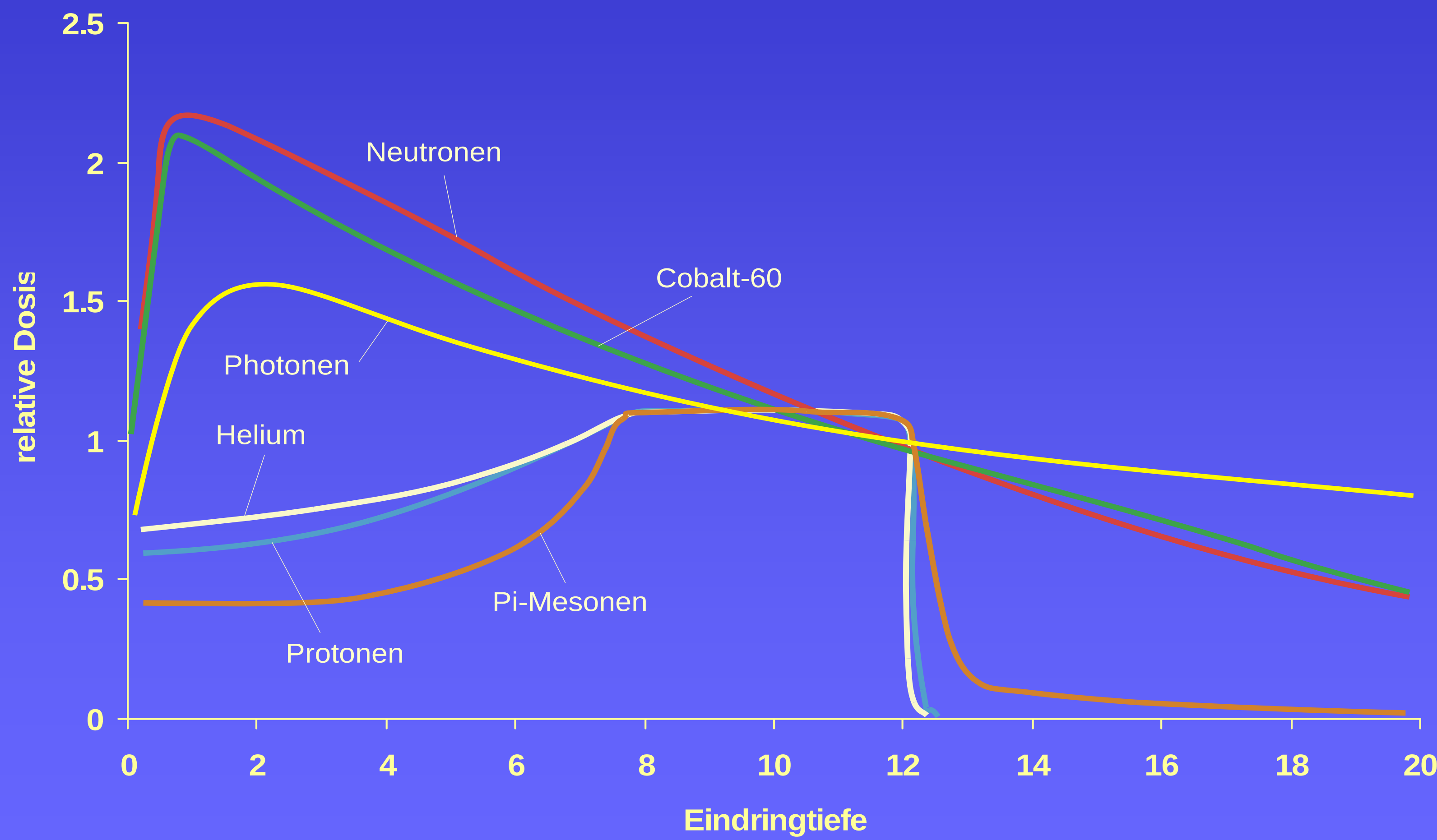
A Spread-Out Bragg Peak



SOBPs from NPTC



CAX Depth Dose Curves

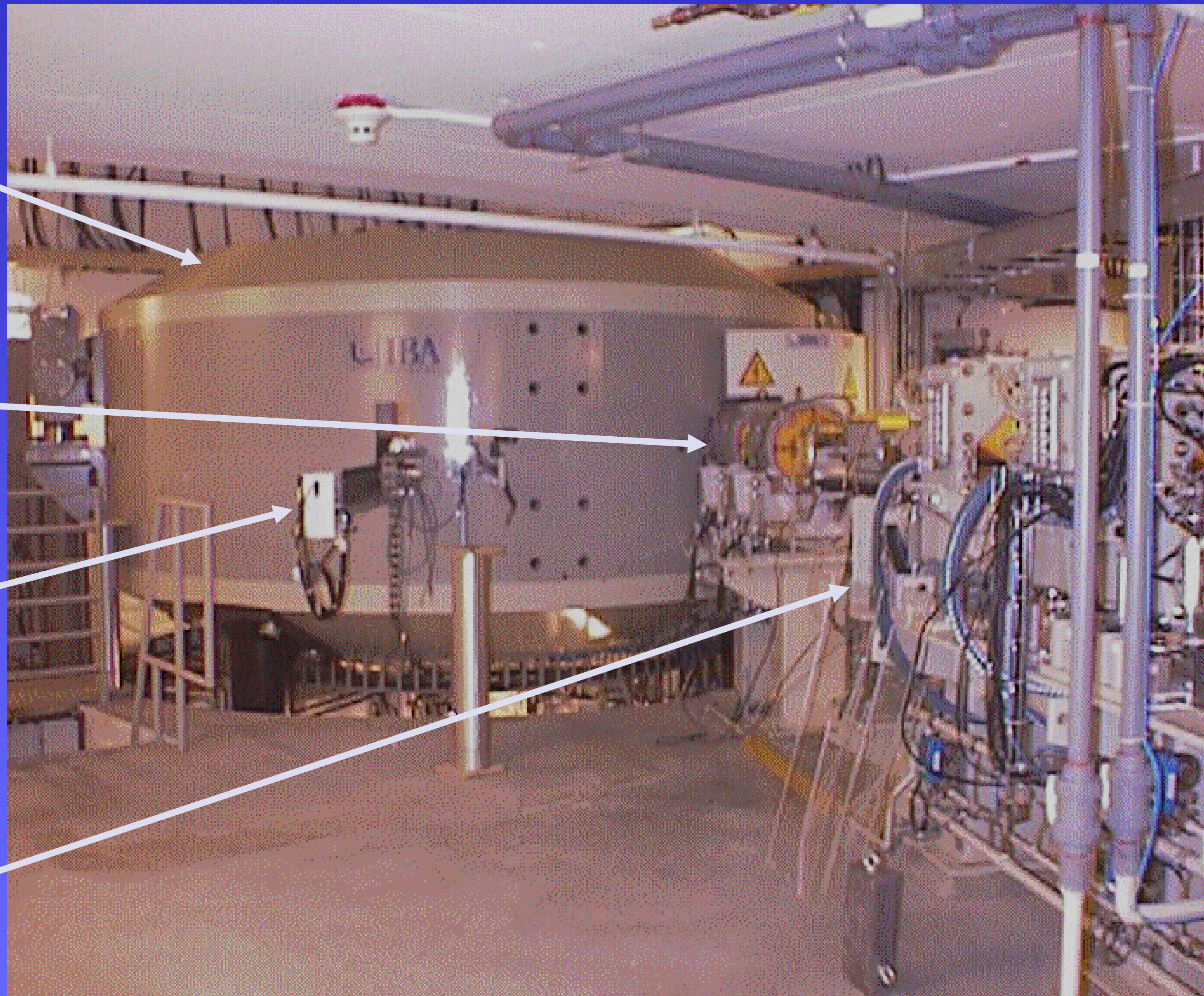


Cyclotron
235 MeV
300 nA

Extraction
Channel

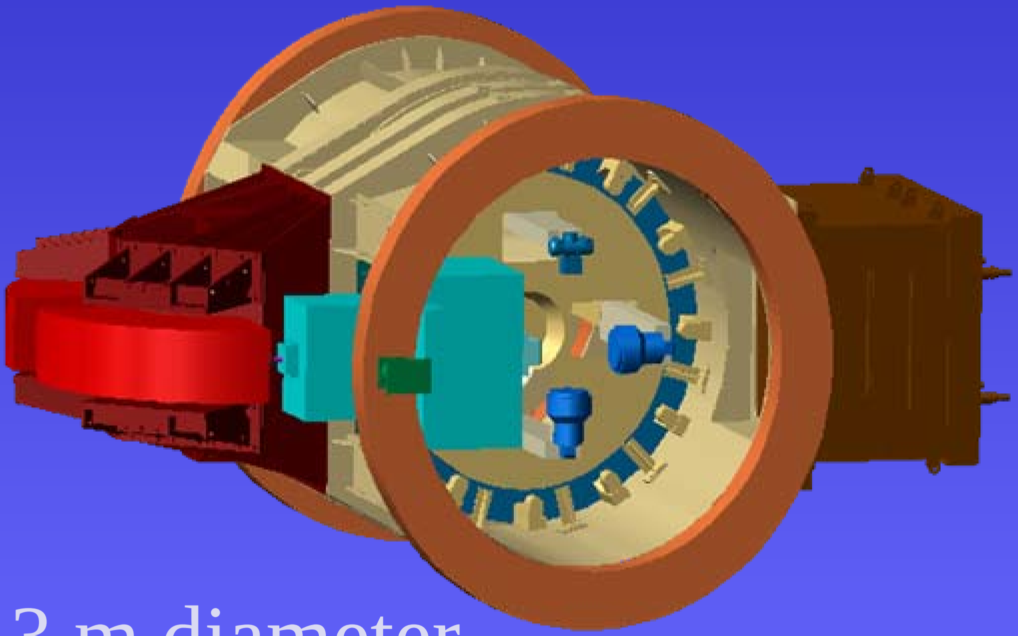
Radial
Probe

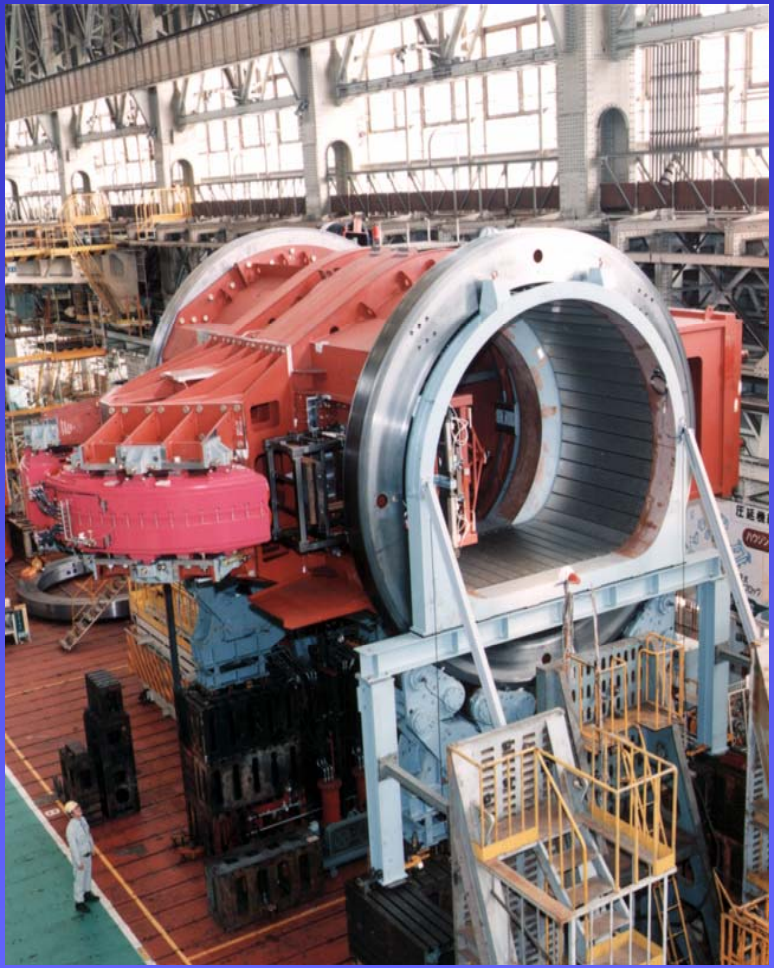
Energy
Degrader
Wheel



High-Precision Robotic Couch

Proton Gantry





13 m diameter

220 tons

SAD ≥ 2.7 m

Gantry Pit (Tsukuba University)

Roller Bearings

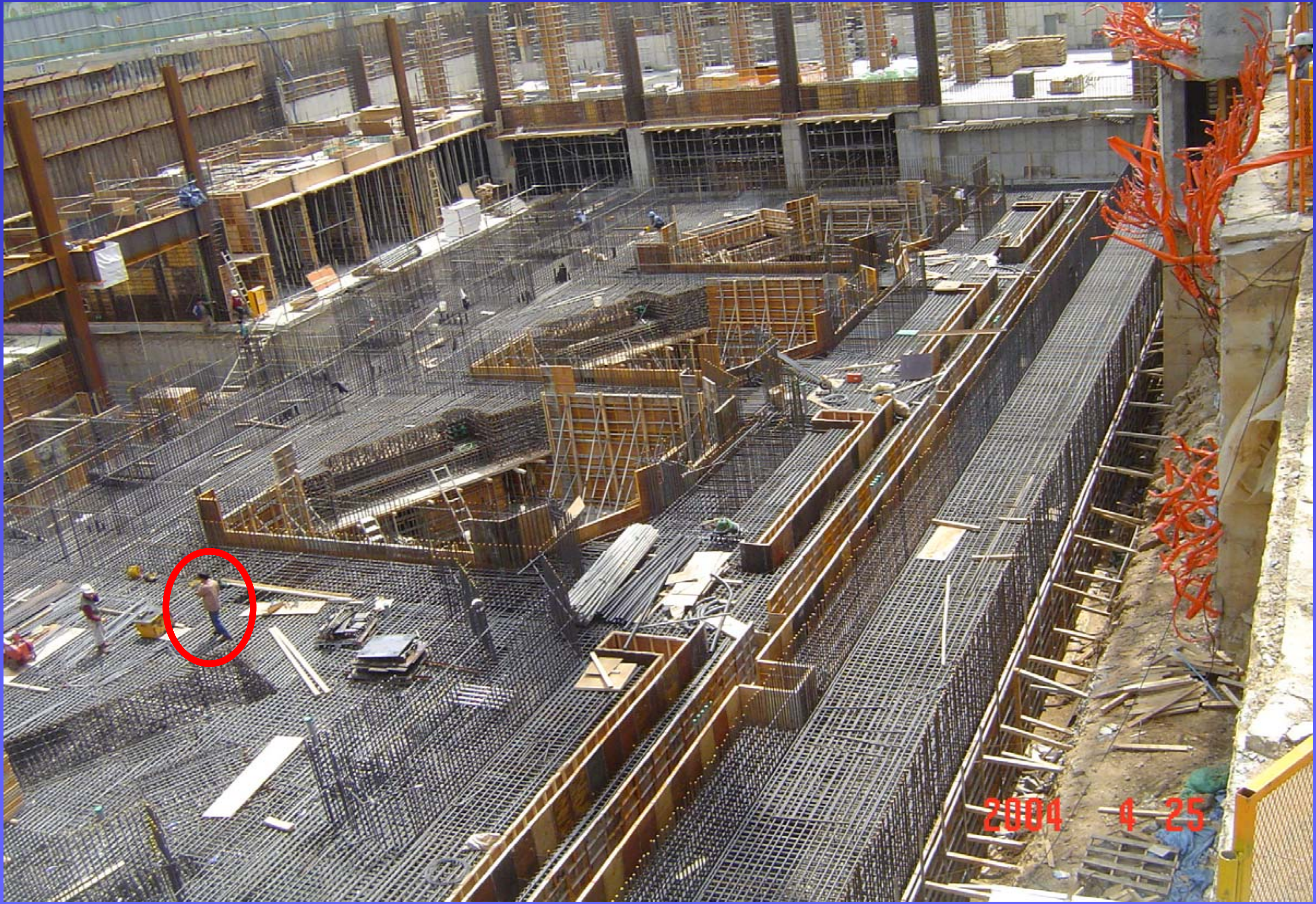
Rotating Mass

~200 T!!!

~12 m dia.

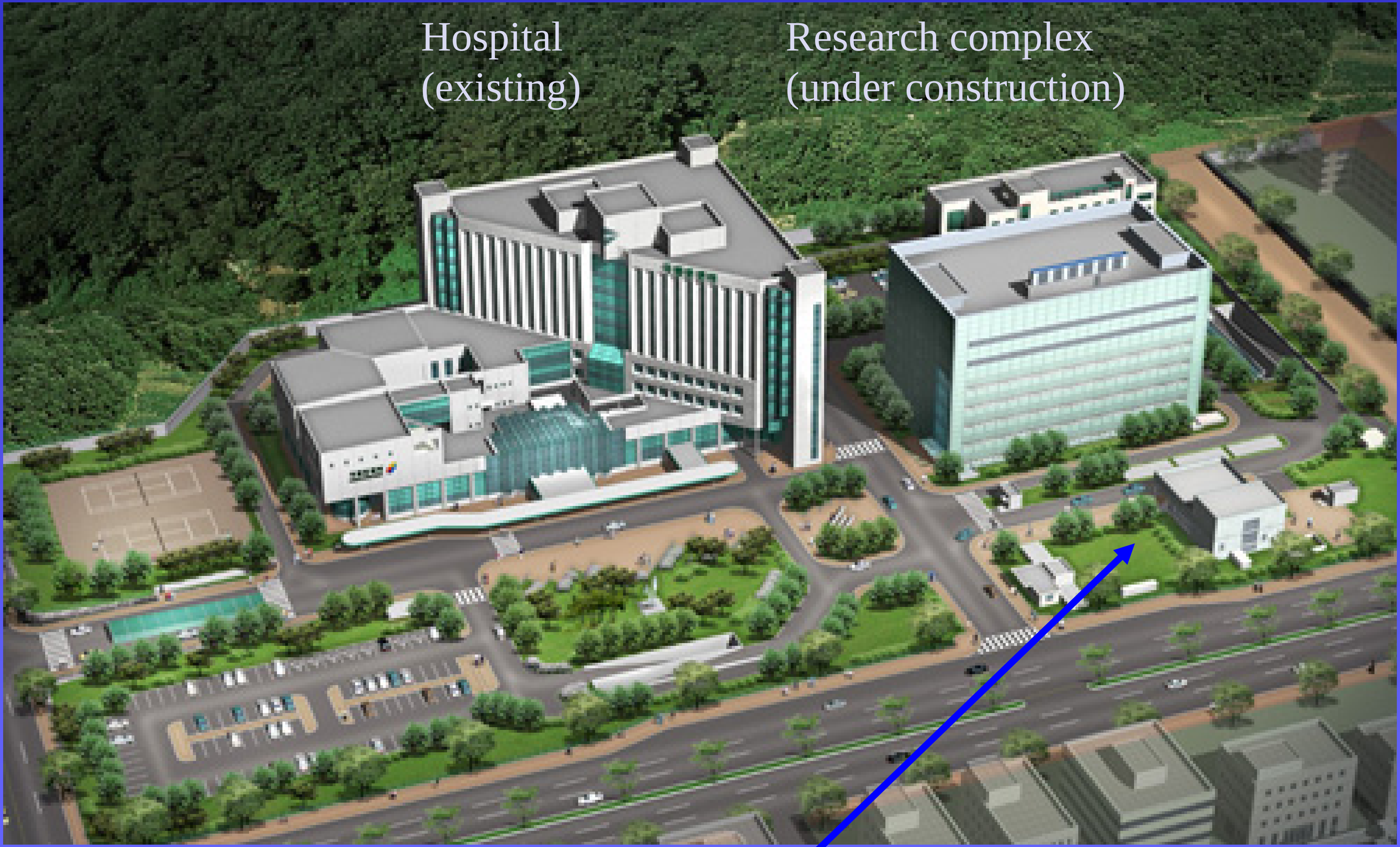
NPTC First Patient Treatment on 8 November, 2001

Proton Bldg Construction, NCC Korea



Courtesy J Kim

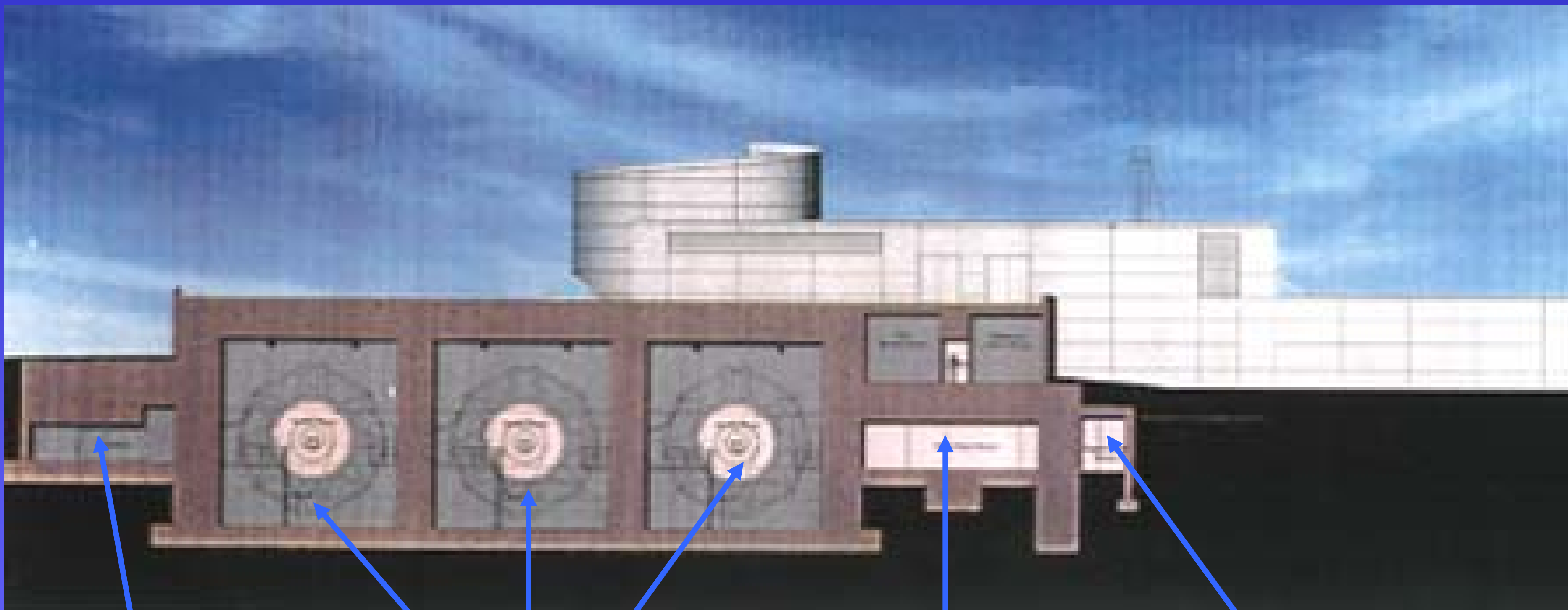
NCC, Korea



Courtesy J Kim

Proton therapy facility
(under construction)

PTC-H Side View



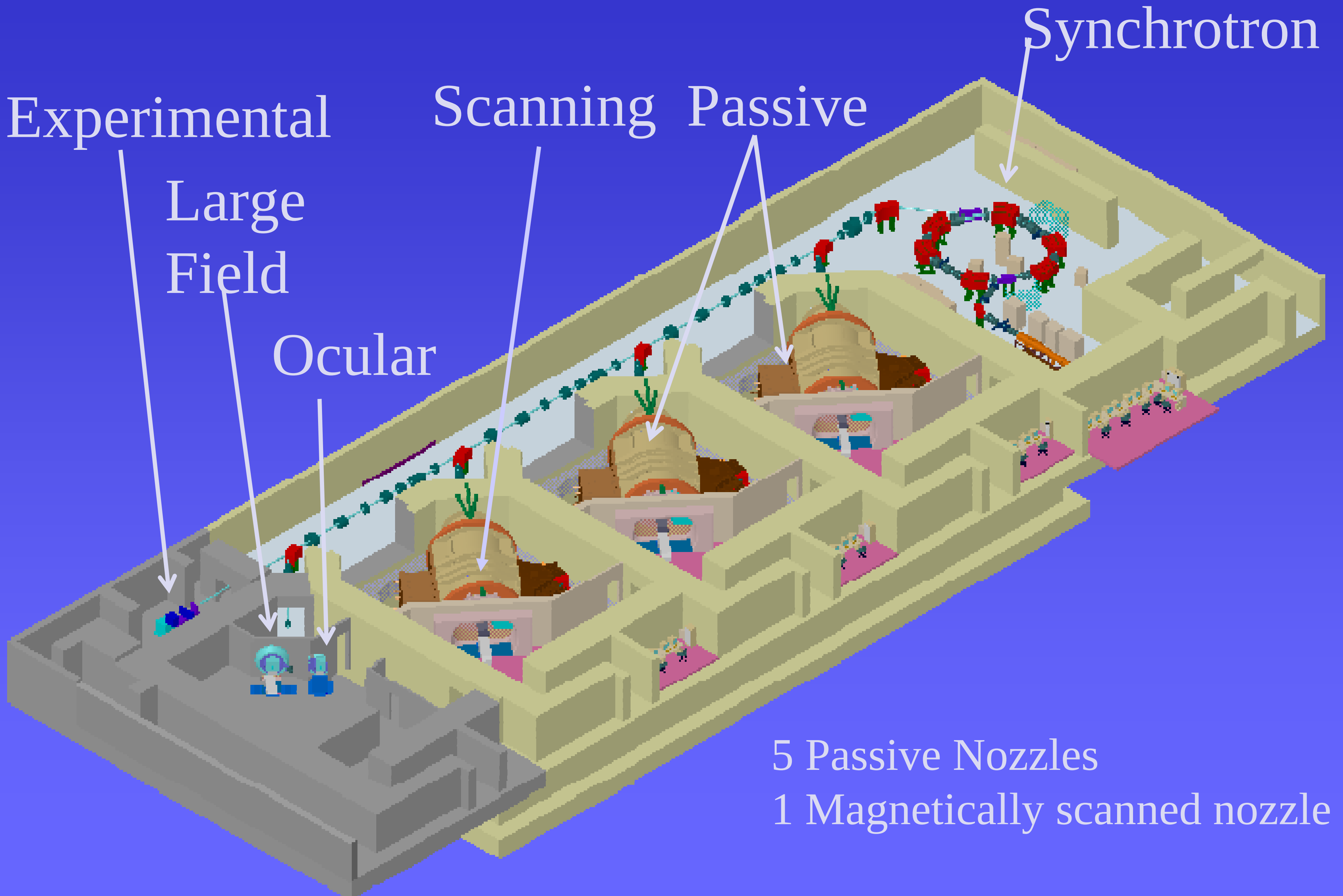
Accelerator Vault

Gantry Rooms

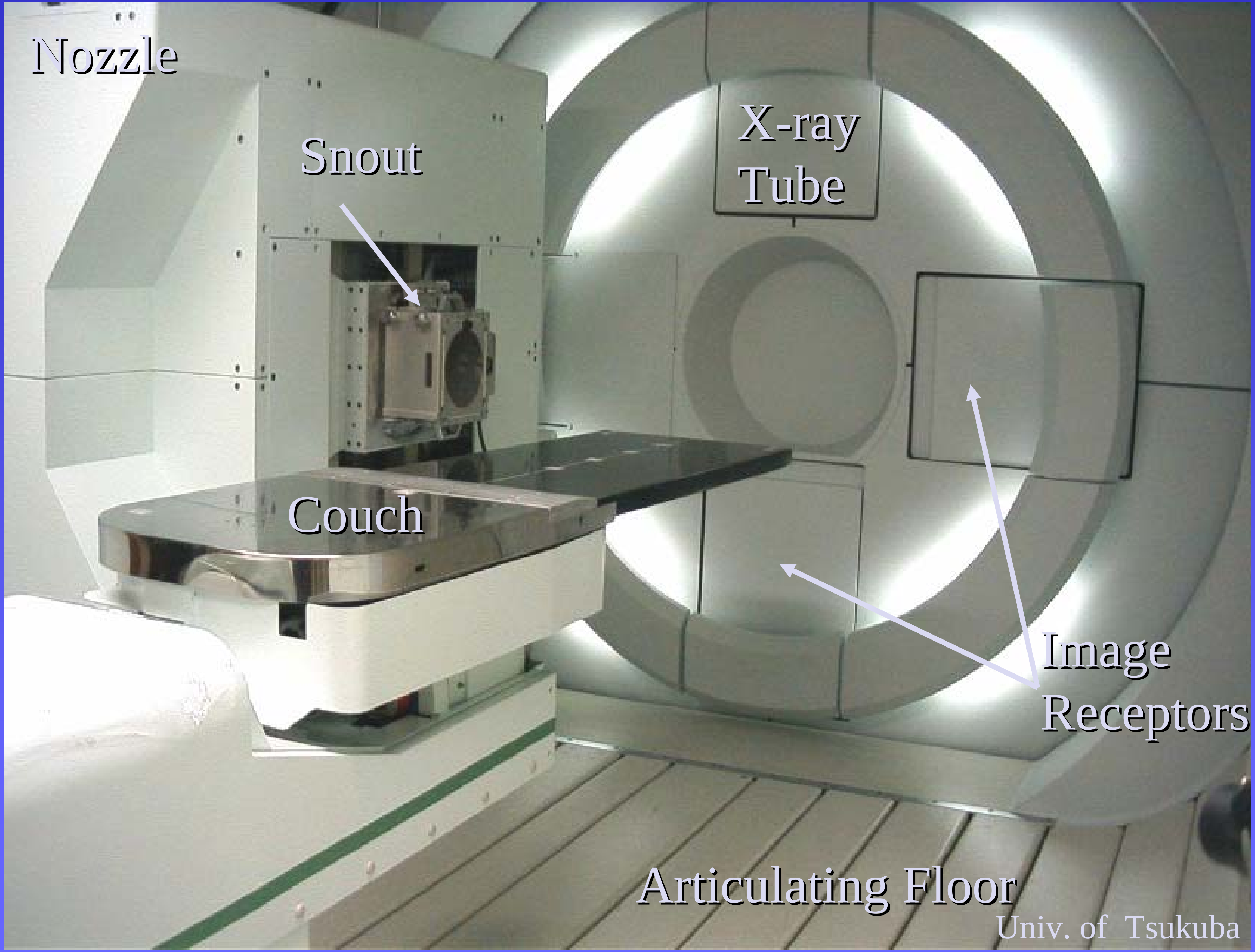
Fixed Beam Treatment Room

Experimental Room

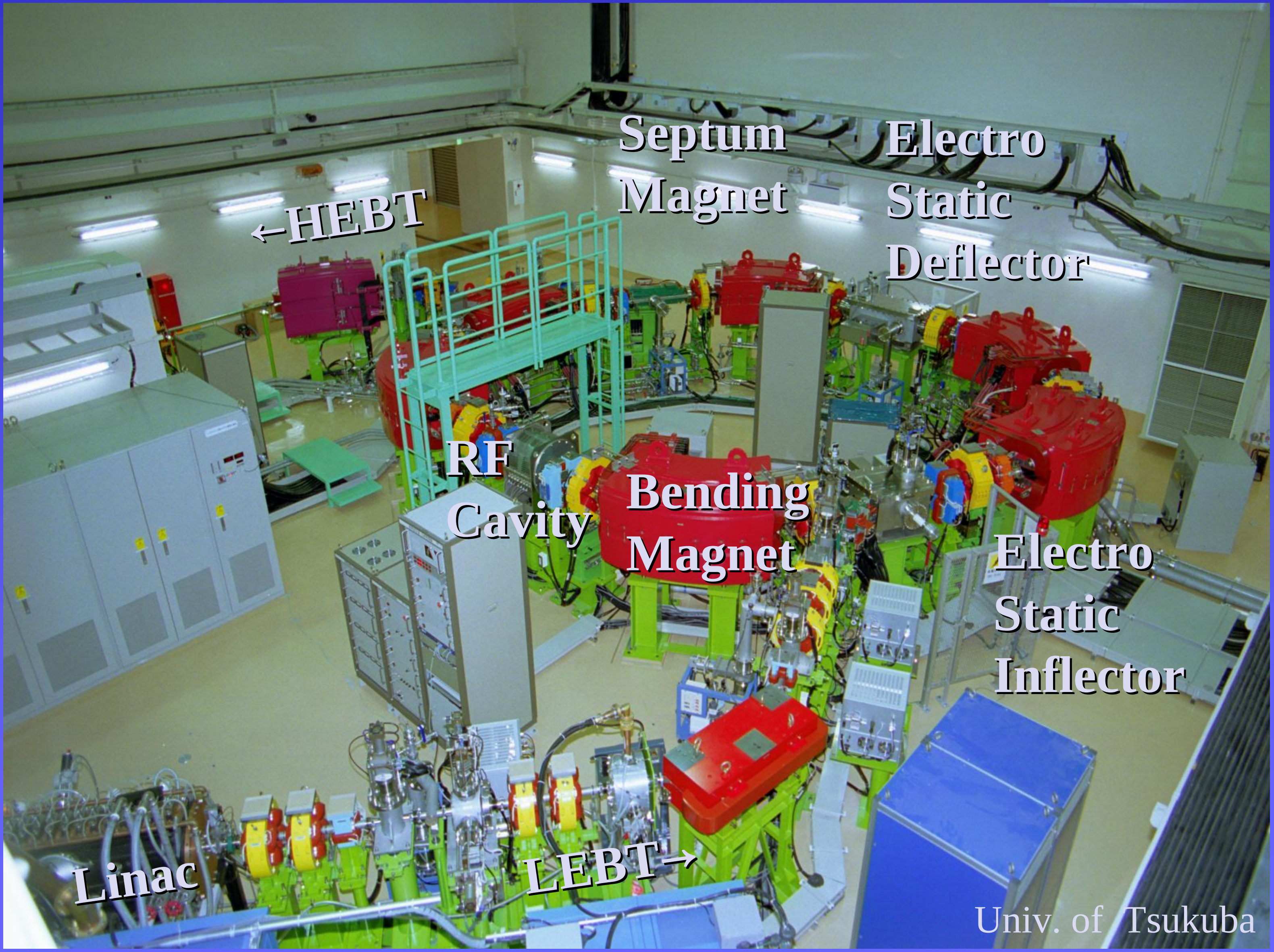
PTC-H Treatment Level



5 Passive Nozzles
1 Magnetically scanned nozzle


Nozzle
Snout
X-ray
Tube
Couch
Image
Receptors
Articulating Floor
Univ. of Tsukuba

Linac Injector and Synchrotron



70-250 MeV

8 10^{10} p/spill

2 - 6.7 s rep

0.5-5 s/spill

Stable beam properties (no feedback)

High reliability

Our Research: Reducing Treatment-Related Morbidity and Mortality

- Review the basics of stray radiation exposures
  - Guiding principles
  - Practical Methods
- Ex 1: Central nervous system cancer
- Ex 2: Prostate cancer
- Try to answer, "Are we doing enough?"

Review: Deterministic Effects

- Severity increases with dose, above a threshold
- Effect usually occurs after large doses
- Occurs hours, days, months or years after exposure
- Examples
  - Reduction in fertility
  - Cataracts

National Eye Institute

Review: Stochastic Effects

- Probability increases with dose
- Severity independent of dose (all or nothing)
- Principal effect after exposure to low doses
- Examples
  - Lung Cancer
  - Genetic effects

www.nlm.nih.gov

“Houston, we have a problem”

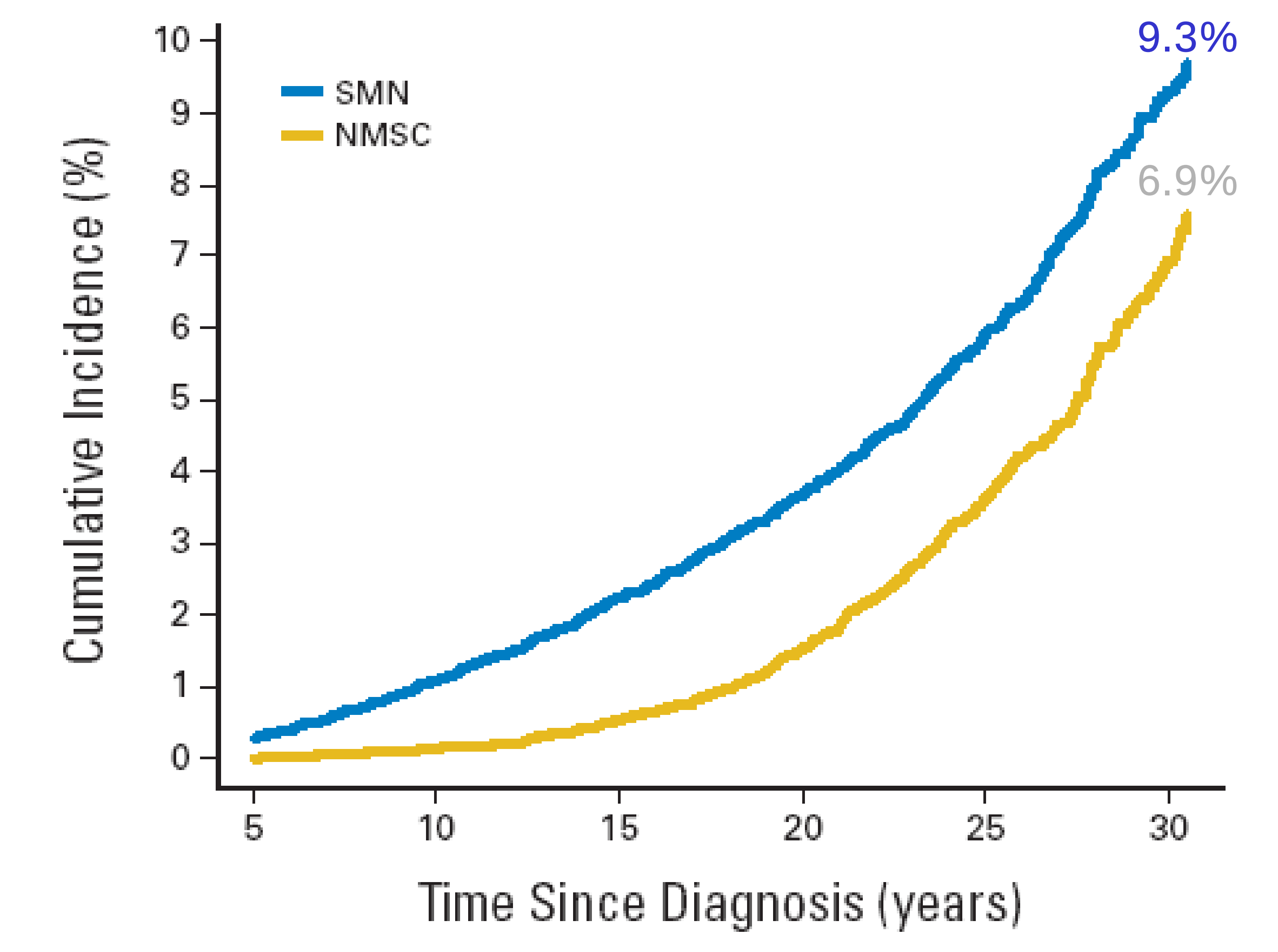
In a study published in the New England Journal of Medicine in 2006, which looked at outcomes in more than 10,000 survivors, CCSS researchers found that almost two-thirds of patients reported at least one chronic health problem, one-quarter had a severe condition, and almost one-quarter had three or more chronic health problems. Late effects reported most frequently in this study were second cancers, cardiovascular disease, kidney disease, musculoskeletal conditions, and endocrine abnormalities. The risk of developing a health problem related to cancer treatment in childhood increased over time.

Women face higher risks than men for late effects including breast cancer, cognitive dysfunction, heart disease, and hypothyroidism. Other factors influencing late effects include age at diagnosis, type of cancer, and types of treatment received. Radiation treatment, especially to the brain - and, in women, the chest - carries a high risk of long-term effects.

"Both the magnitude and the diversity of the long-term health effects have been striking," says CCSS principal investigator Dr. Les Robison of St. Jude Children's Research Hospital in Memphis. "At 30 years after their diagnosis, more than 70 percent of childhood cancer survivors have a late-effect chronic health condition."

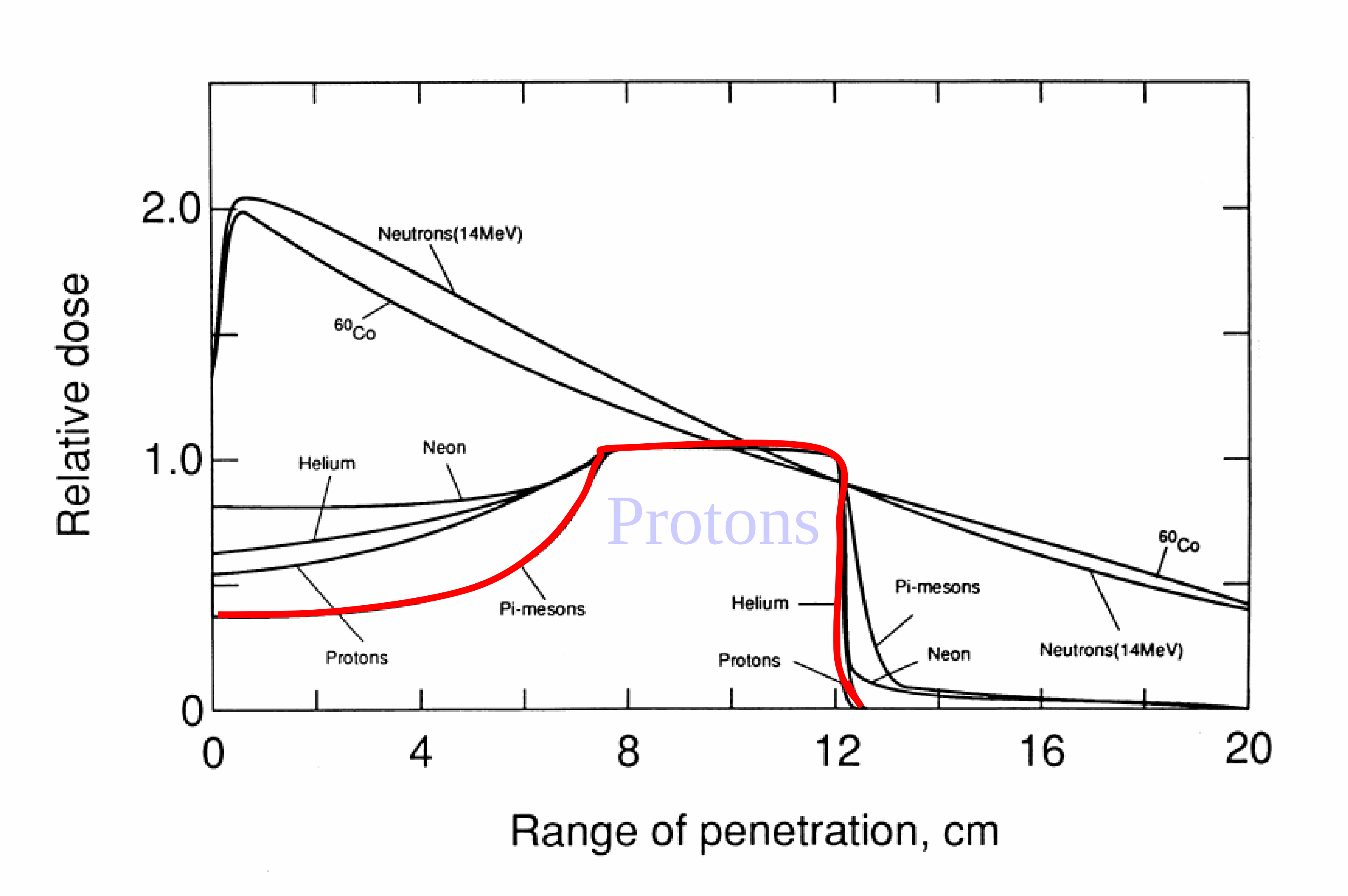
From NCI Ca Bul, March 18, 2008 • Volume 5 / Number 6

Incidence of Second Malignant Neoplasms and Non-malignant Skin Cancer (CCSS)



Meadows et al. J Clin Oncol (eprint ahead of print, 2009)

Solution: Charged Particle Beams Reduce Dose to Healthy Tissue



Background

- Radiation increases risk of second malignant neoplasms (SMN)

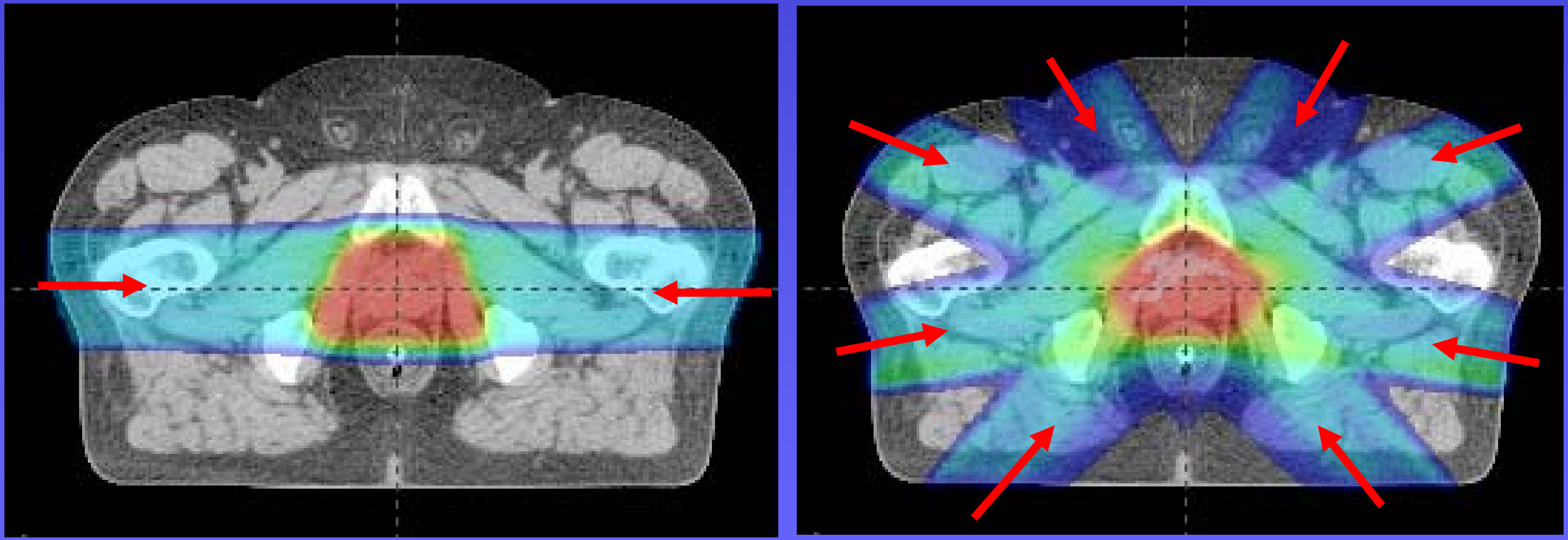
- Increasing concern about SMN
  - Escalation therapeutic dose
  - Earlier detection/intervention of first cancer
  - Increasing life expectancies
  - Evolution of radiotherapy treatments

Proton Therapy: the Problem?

"Does it make any sense to spend over $100 million on a proton facility, with the aim to reduce doses to normal tissues, and then to bathe the patient with a total body dose of neutrons …"

Hall, Technol in Ca Res Treat 2007;6:31-34

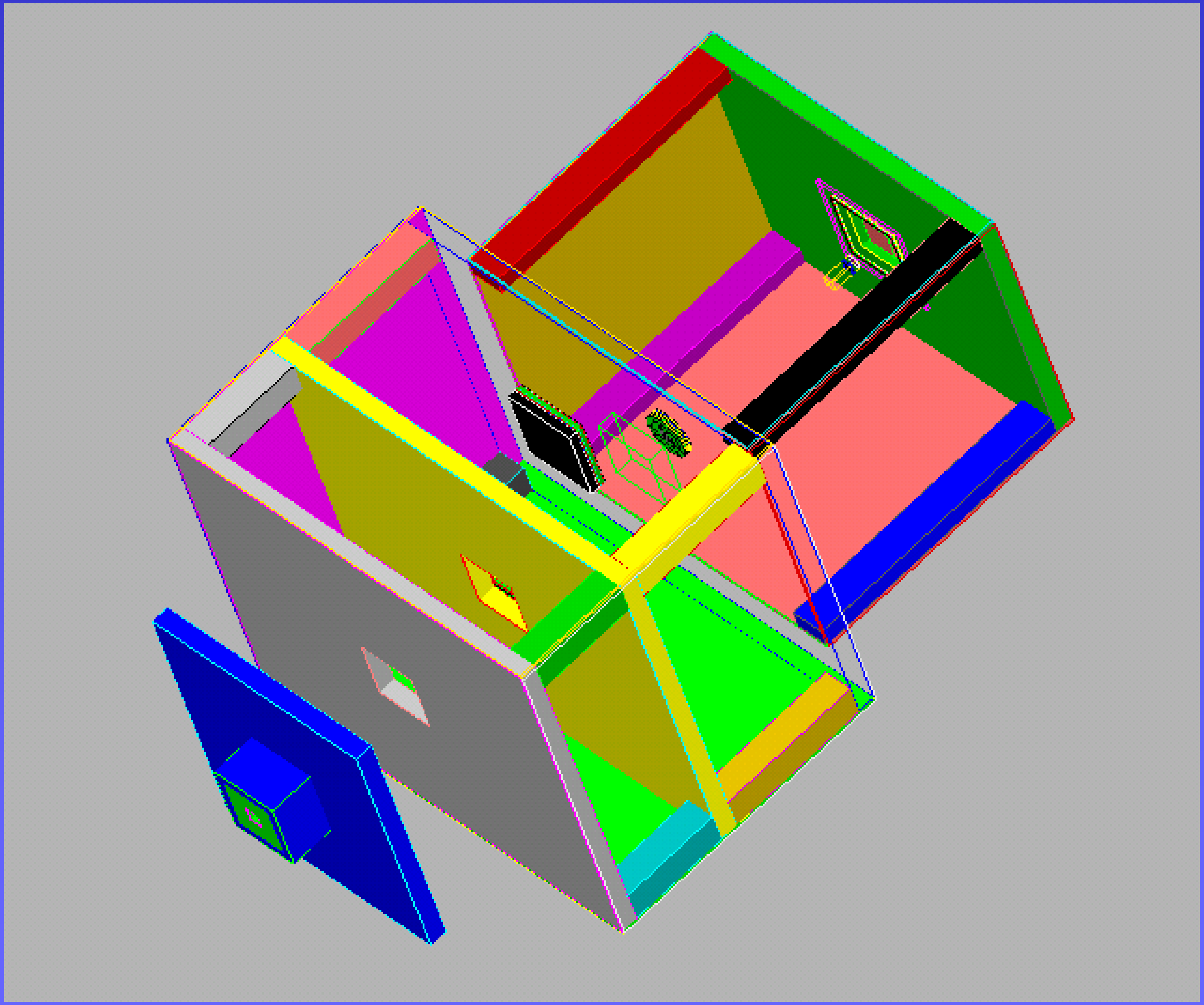
Comparative Risk for SMN Following Proton RT v IMRT for Prostate Cancer



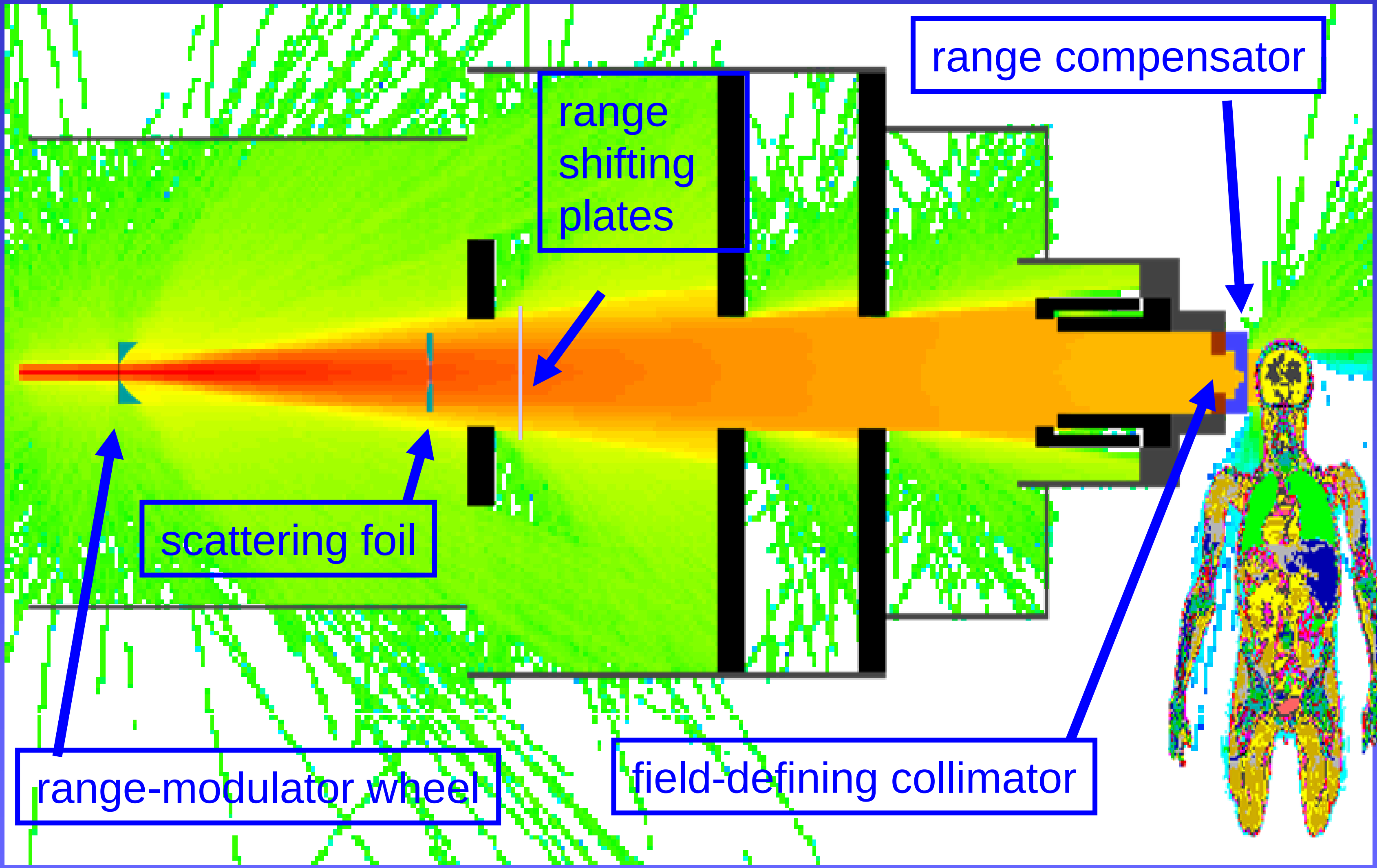
Passively scattered protons   6-MV IMRT with photons

Fontenot et al, IJROBP 74 616-622 (2009)

4-D Model of Proton Nozzle

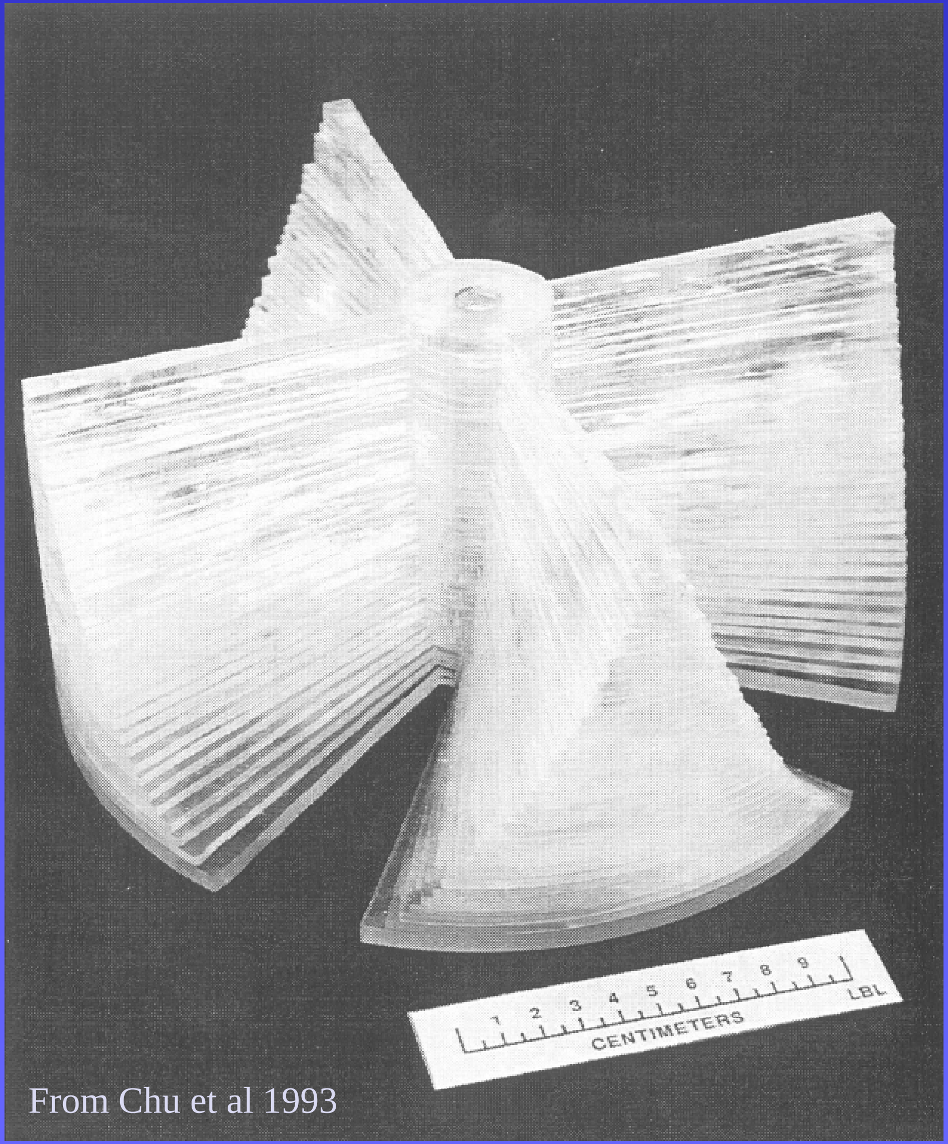


Monte Carlo Simulation of Treatment

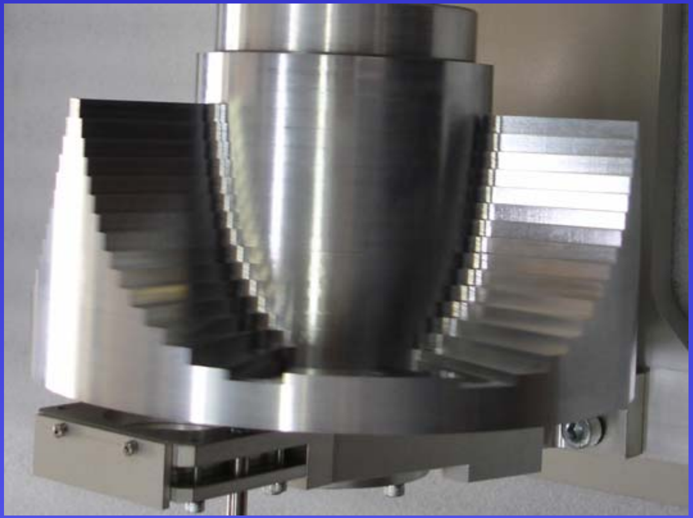


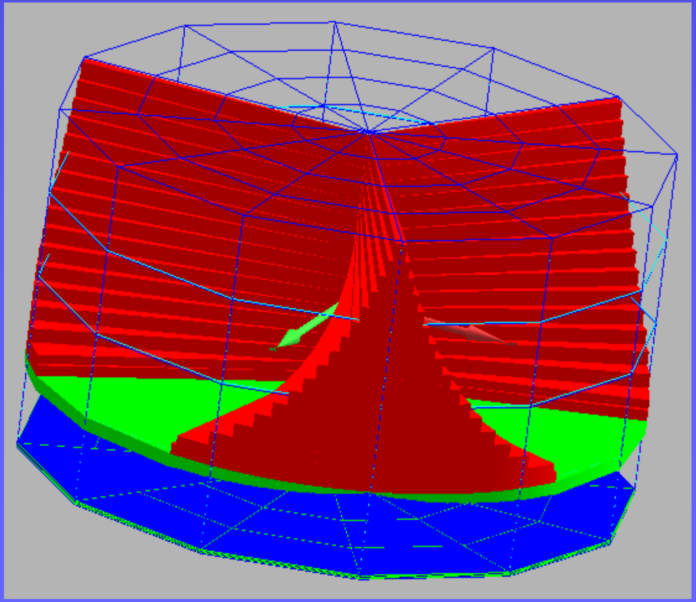
(log scale)

Range Modulation



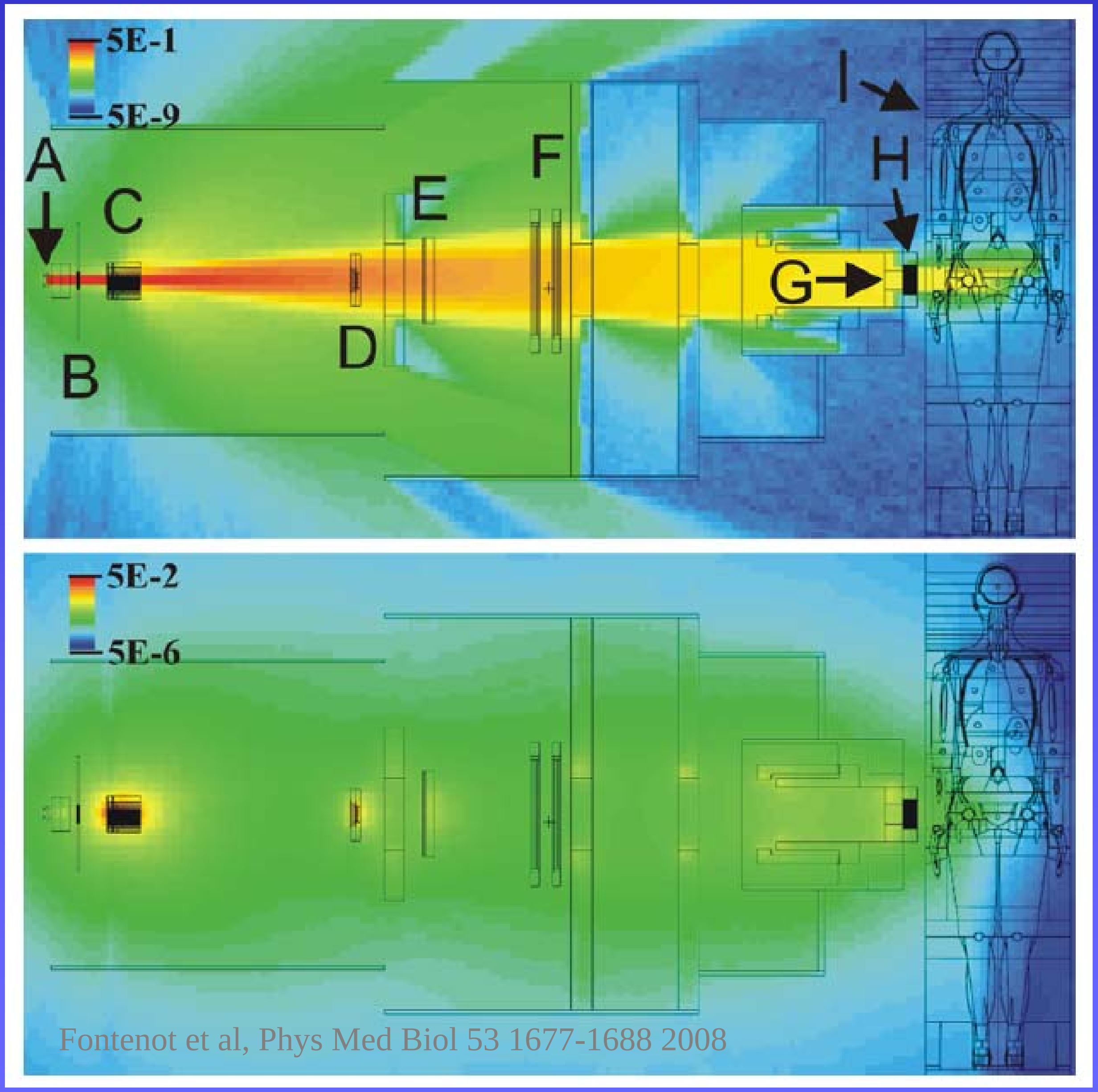
From Chu et al 1993





From Y. Zheng, UTMDACC

Monte Carlo Simulation of Proton Treatment



Fontenot et al, Phys Med Biol 53 1677-1688 2008

Log Proton Fluence

Log Neutron Fluence

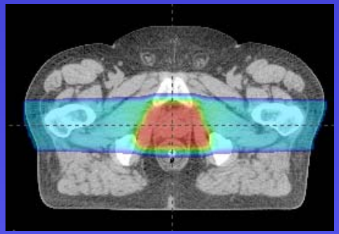
MDA's HPC Cluster

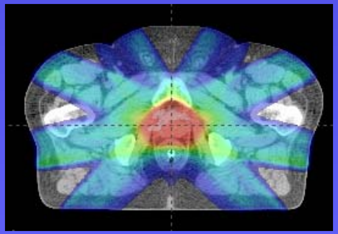
- 1072 processor computer cluster
  - Linux (Red Hat derivative)
  - 268 nodes
  - Node: 2 Dual-Core AMD Opterons
  - 10 TB data storage
  - Infiniband interconnect: sustained bandwidth of 625 GB/s
- Biggest high performance computing environment within any Cancer Center in the United States dedicated exclusively to cancer research
- Smaller testbed clusters available

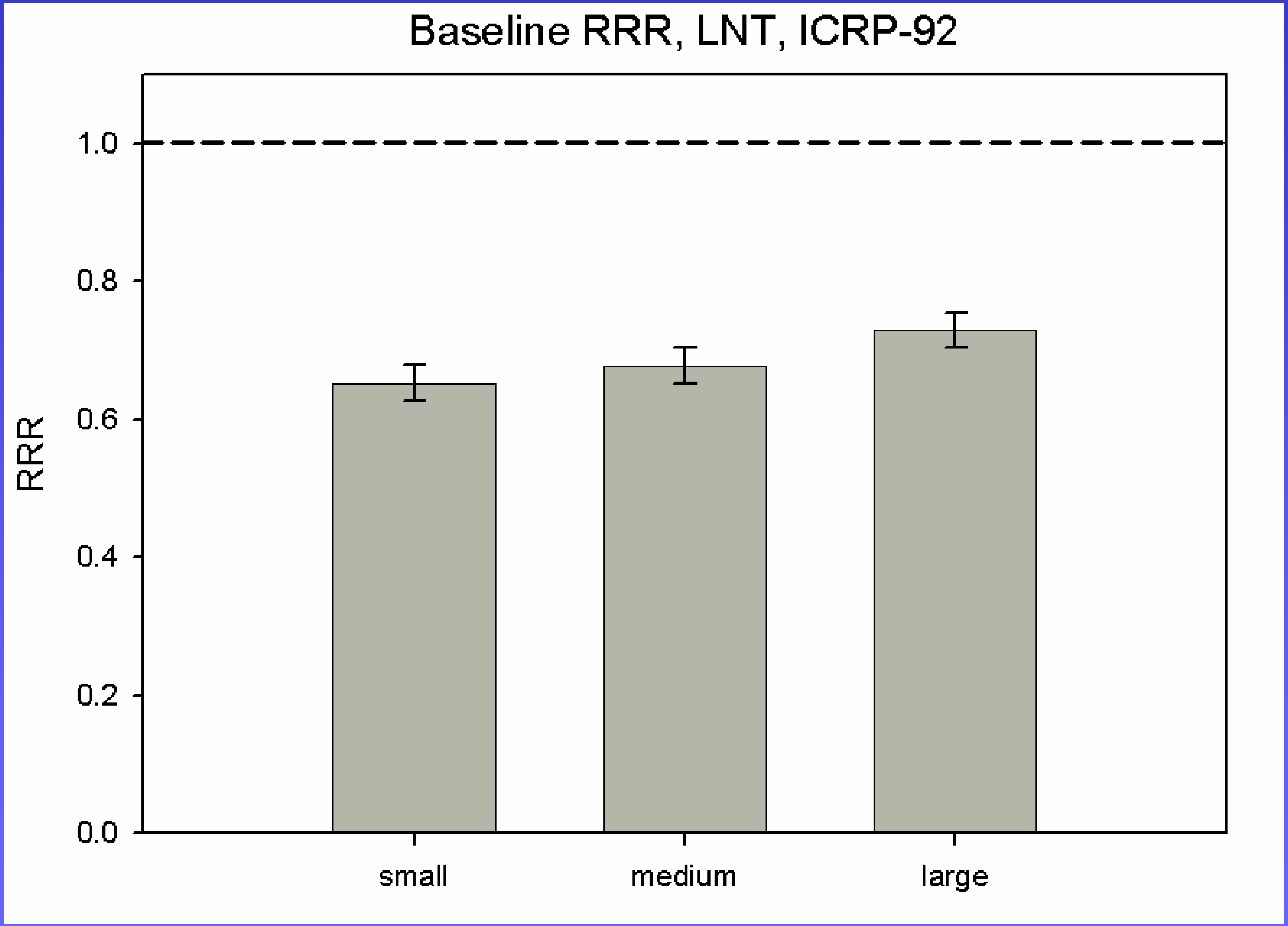
Photo Courtesy of Dan Jackson

Ratio of Relative Risk

$RRR=RR_{PSPT}/RR_{IMRT}$ (Includes Neutrons)



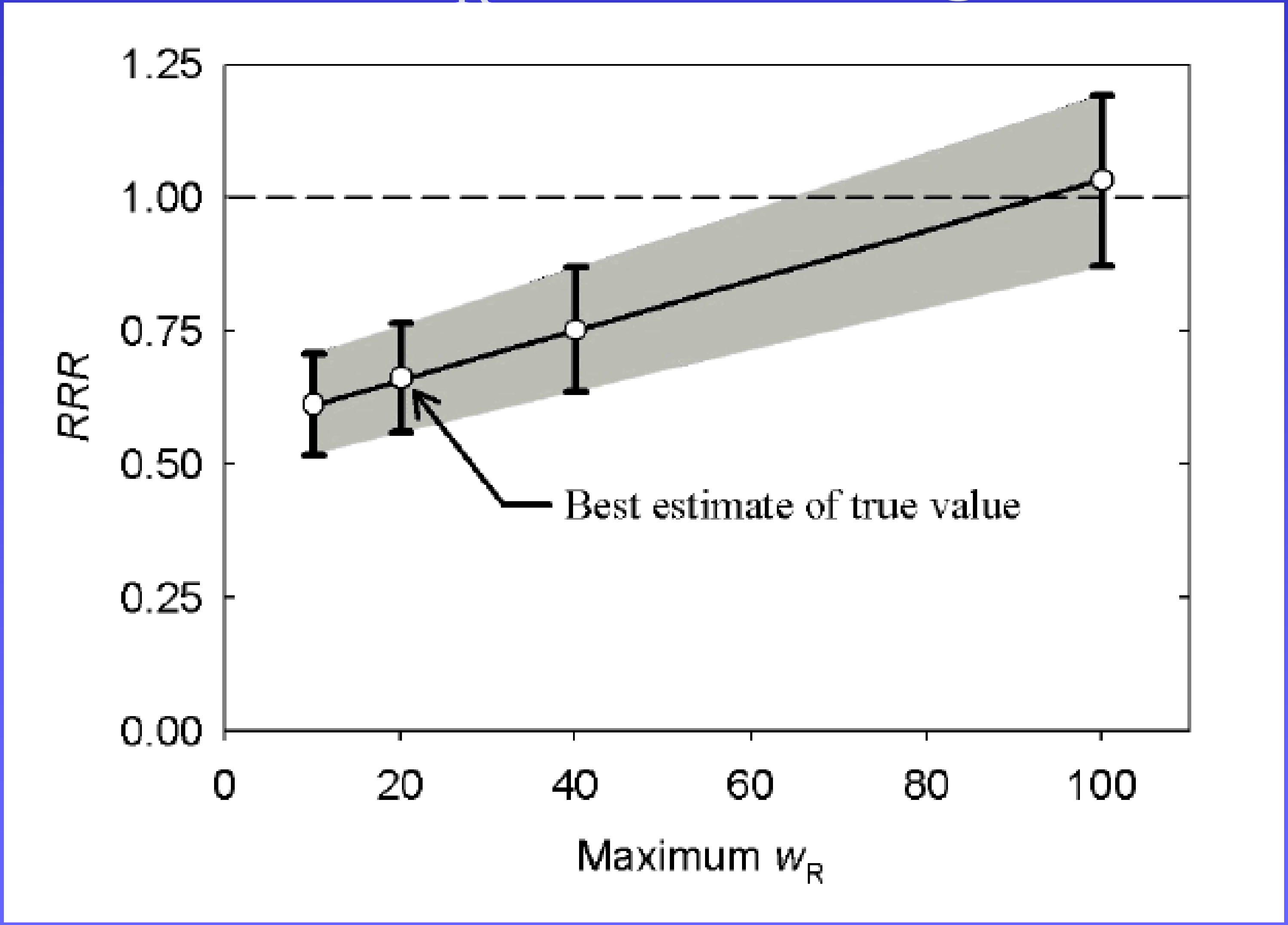




Results: Fontenot et al, IJROBP 74 616-622 (2009)

Uncertainties: Fontenot et al, in preparation

RRR Dependence on Neutron w_R for Carcinogenesis



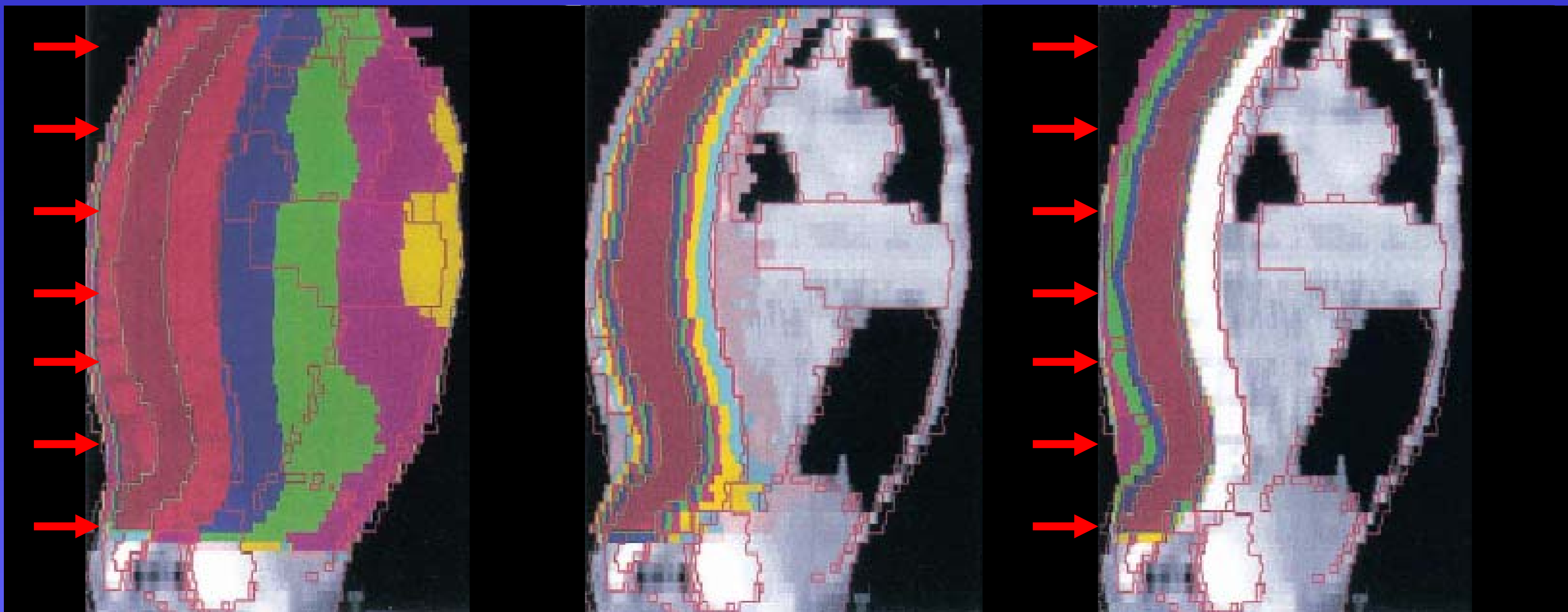
Newhauser et al, Proc of CAARI, AIP, 450-455 (2009)

Prospective Randomized Clinical Trial of SMN Following Proton Therapy *v* IMRT

- 2000 pts/y for 5 y
- 80% power to detect an *RRR* of 0.67 for developing SMN with 2-sided t-test at significance level of 0.05
- Obstacles
  - Duration of study: 12.1 years
  - Ethical issues associated with equipoise

Calculations courtesy of Mark Munsell, personal communication, 2009

Comparative Risk for SMN Following Photon CRT and IMRT *versus* Proton Therapy for Craniospinal Irradiation



	Photon CRT (6 MV, 1 field)	Photon IMRT (15 MV, 9 field)	Protons (SOBP, 1 field)
Risk:	55%	31%	4-5%
Rel. risk:	**12**	**7**	**1**

From Newhauser et al, PMB, 2009; Miralbell et al., IJROBP 2002

Methods Include Supercomputing Monte Carlo Dose Calculations

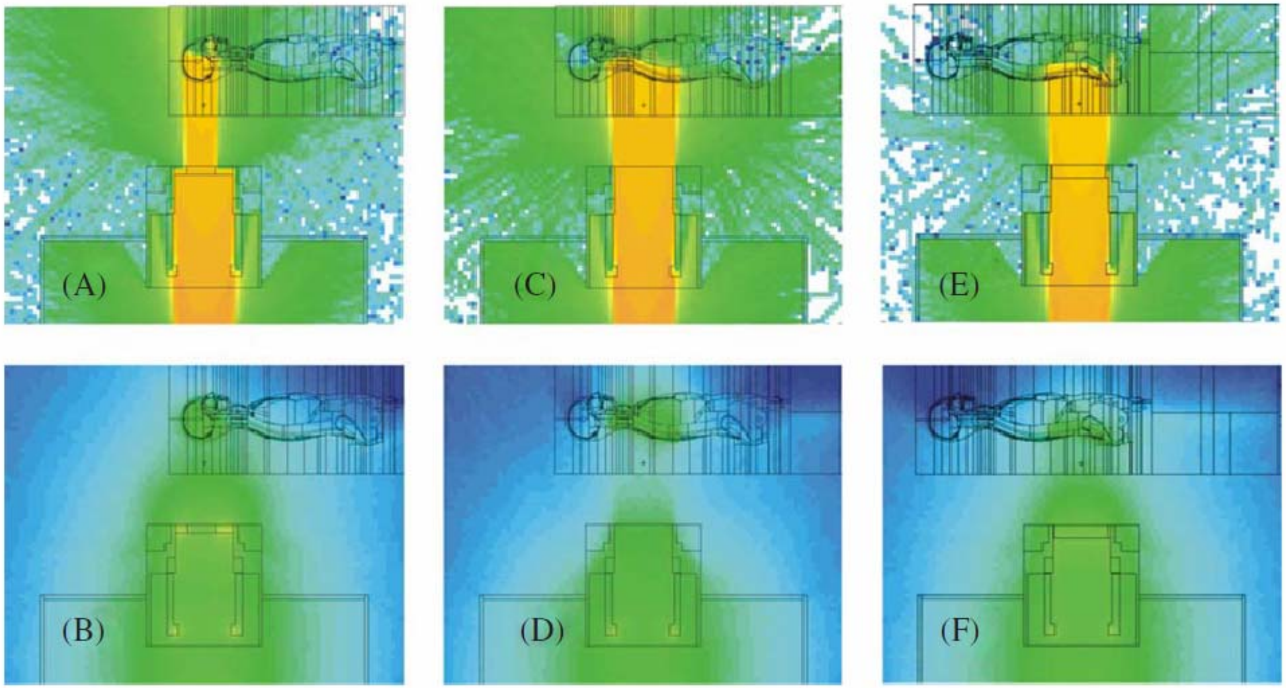


Figure 1. Monte Carlo simulation of particle fluences for the three craniospinal treatment fields. The upper plots represent the logarithm of the proton fluence, including primary protons and secondary protons generated via (n, *x*p) reactions in the treatment unit and in the phantom. The corresponding lower plots represent the logarithm of neutron fluence, including neutrons generated internally and externally to the phantom. Note that the fluence in each plot was scaled to maximize the visibility of the shape of the distributions, not their magnitude. (A), (B) Cranial field. (C), (D) Superior spinal field. (E), (F) Inferior spinal field.

Newhauser et al, PMB, 54 2277-2291 (2009)

Newhauser et al, Trans Am Nucl Soc 99 63-64 (2008)

Conclusions on 2nd Cancer Risk

RCT data unavailable for advanced RT modalities

In-silico RCTs can provide rigorous evidence for selecting treatment modality

In-silico case studies revealed lower risk following proton *v* photon therapies

More evidence needed with increased rigor

End of Lecture