Hadron Beam Therapy

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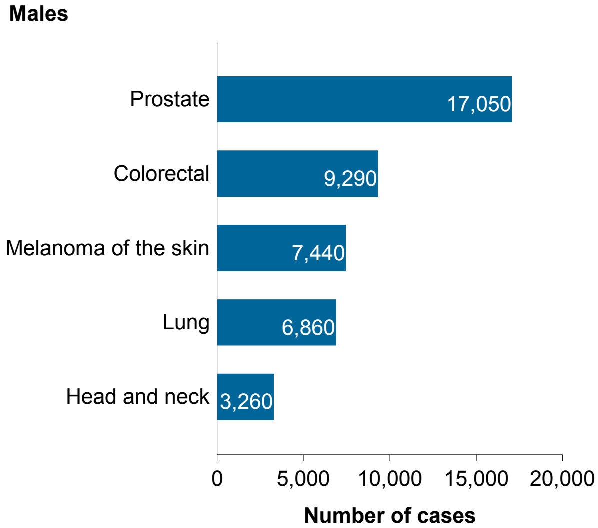
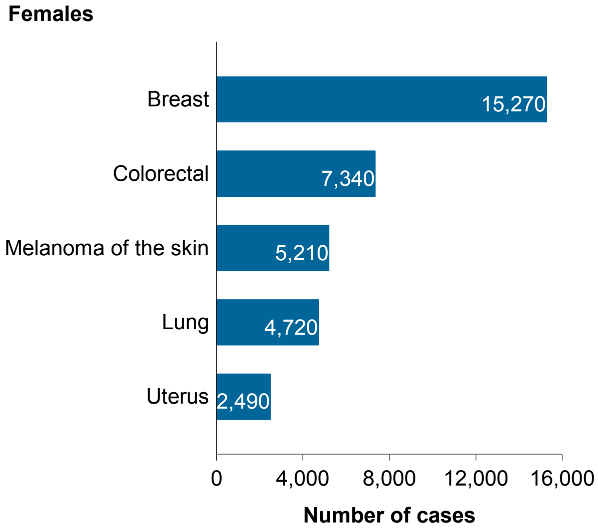
New cancer cases: cancer type

Cancer is a class of 100+ diseases characterized by out-of-control cell growth.



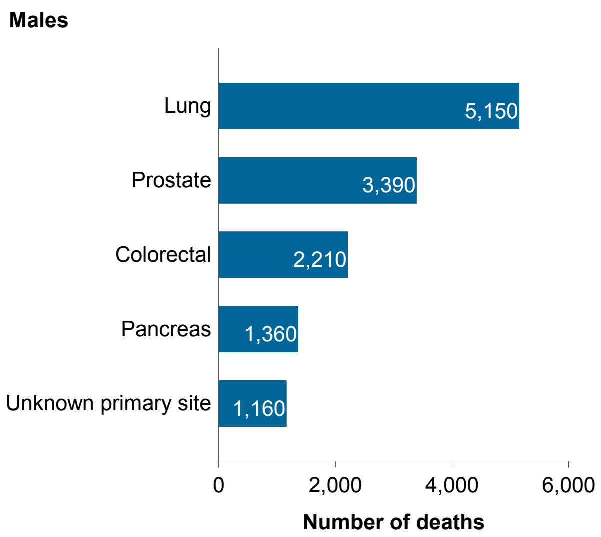


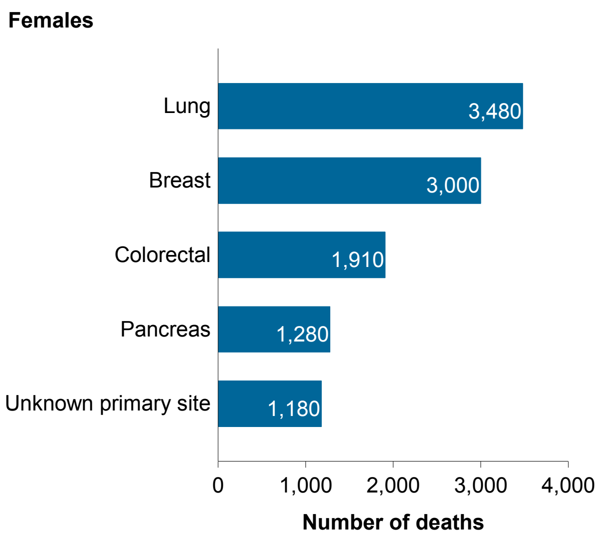
Prostate cancer is the most commonly diagnosed cancer for males.
Breast cancer is the most commonly diagnosed cancer for females.

Cancer in Australia: an overview 2014. AIHW 2014

Deaths from cancer: cancer type

Lung cancer is the most common cause of cancer deaths for both males and females.

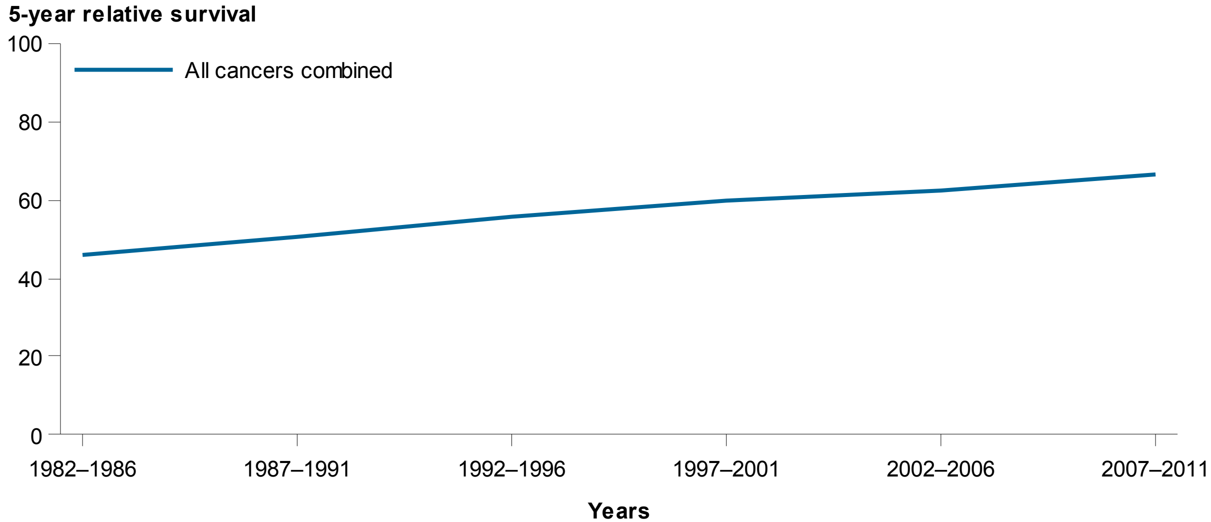




Cancer in Australia: an overview 2014. AIHW 2014

Survival: trend

Five-year relative survival for people diagnosed with cancer increased over time from 46% in 1982–1986 to 67% in 2007–2011.

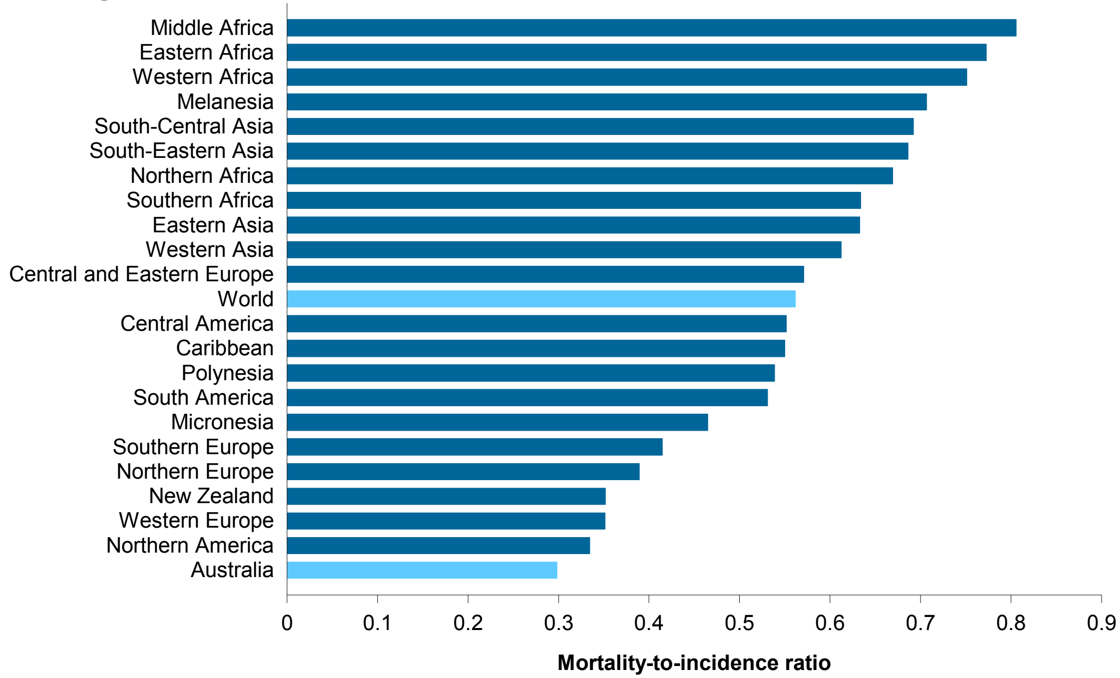


Cancer in Australia: an overview 2014. AIHW 2014

Australian Government
Australian Institute of Health and Welfare

International comparisons

The mortality-to-incidence ratio (MIR) for Australia was 0.3, suggesting that comparatively, cancer survival was high in Australia.



Cancer in Australia: an overview 2014. AIHW 2014

Australian Government
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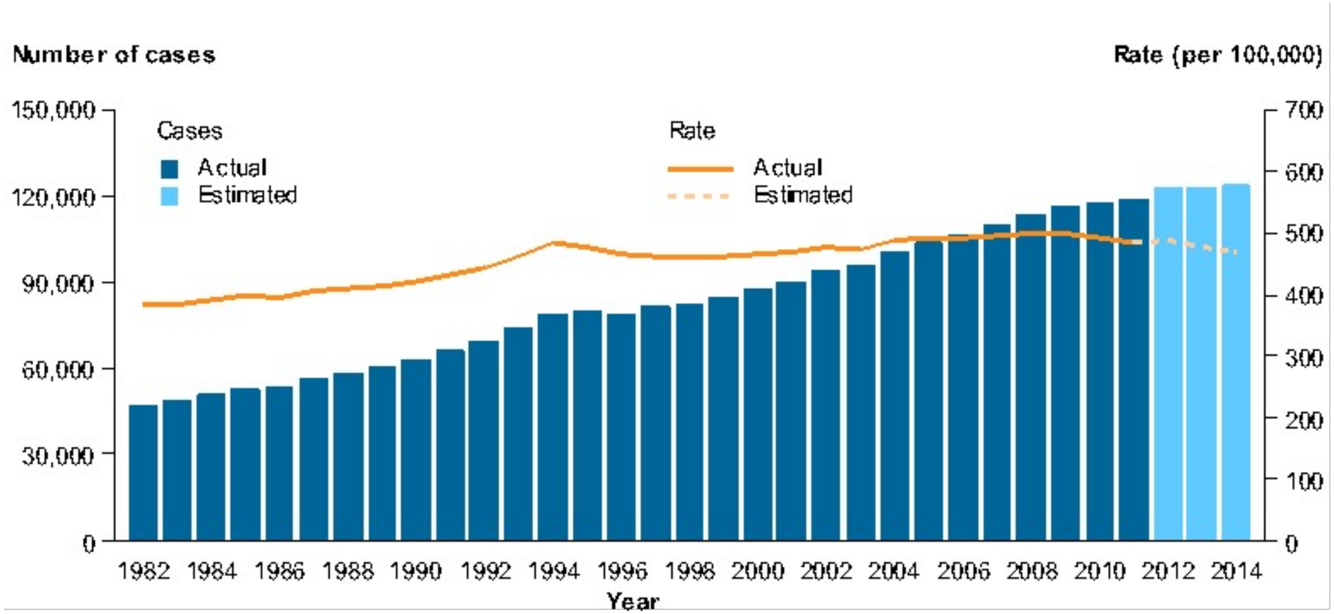
New cancer cases: trend

In 2014, it is estimated that the number of new cancer cases diagnosed will be 2.6 times as high as that in 1982.

Living longer, improved cardiovascular outcomes



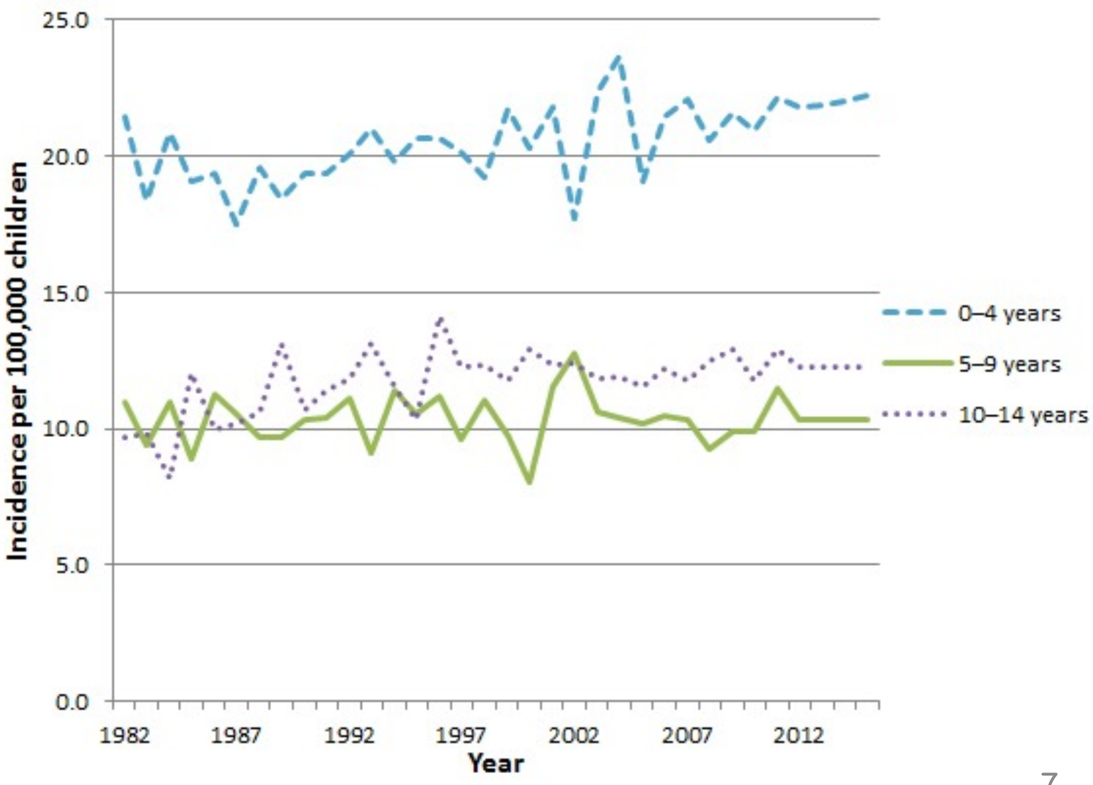
Cancer in Australia: an overview 2014. AIHW 2014

CANCER IN AUSTRALIA *in brief* 2014

Pediatric Tumors

- Over the last 30 years, the incidence rate of cancer in children aged 0-14 years increased by ~12%*

- In 2016, it is estimated that 650 children aged 0-14 years will be newly diagnosed with cancer in Australia (365 boys and 285 girls)*



*Australian Institute of Health and Welfare 2012

How cancer is treated

- 5 year survival 67% achieved for all cancer patients.

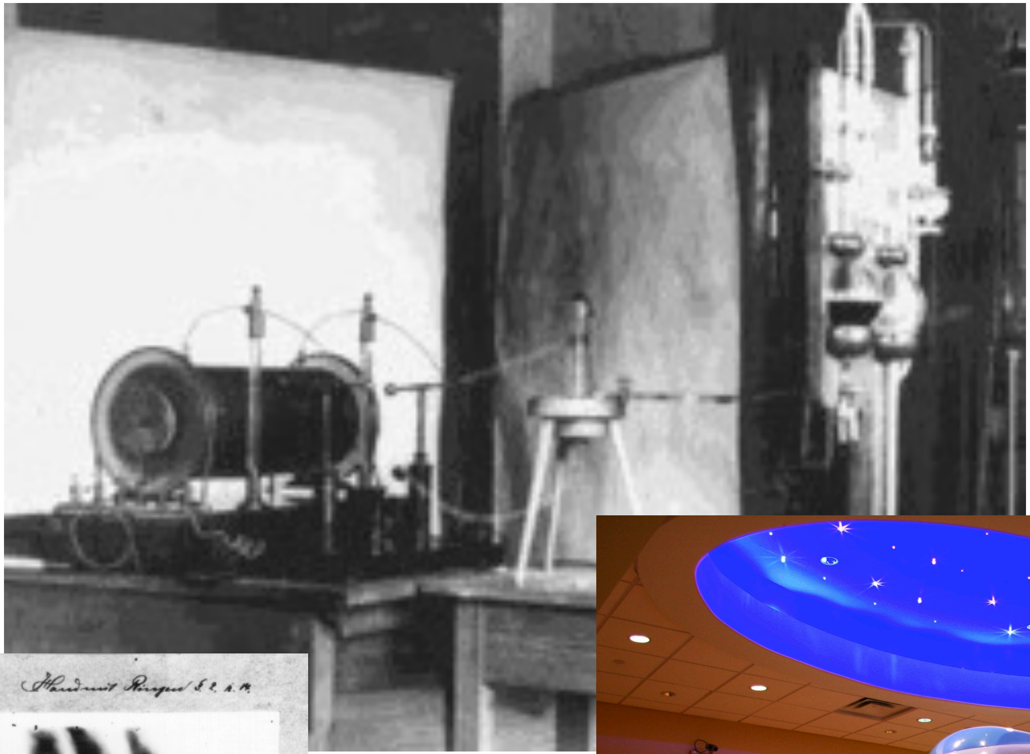
- This is achieved using available therapeutic strategies: radiotherapy, chemotherapy, surgery, immunotherapy, hormone therapy, bone marrow transplants, other….
  - *Disease type*
  - *Localized or Systemic*

- Disease is well-localized in ~2/3 of patients at time of diagnosis.

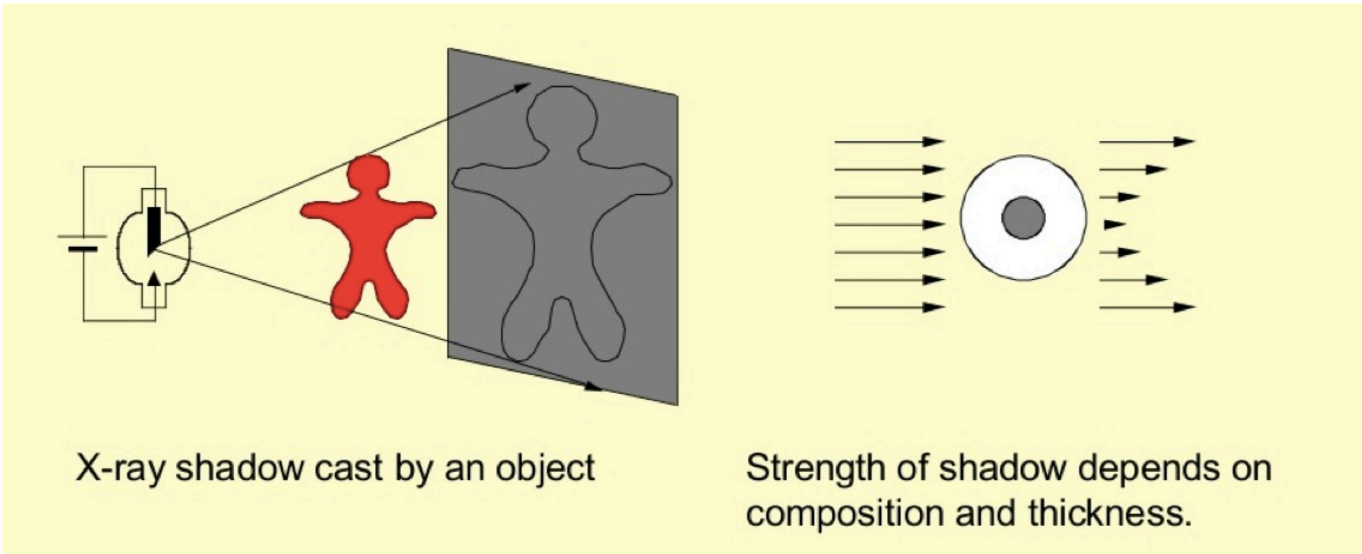
- 50% of (USA) cancer patients receive radiation treatment for localized disease sites, most with external beam.

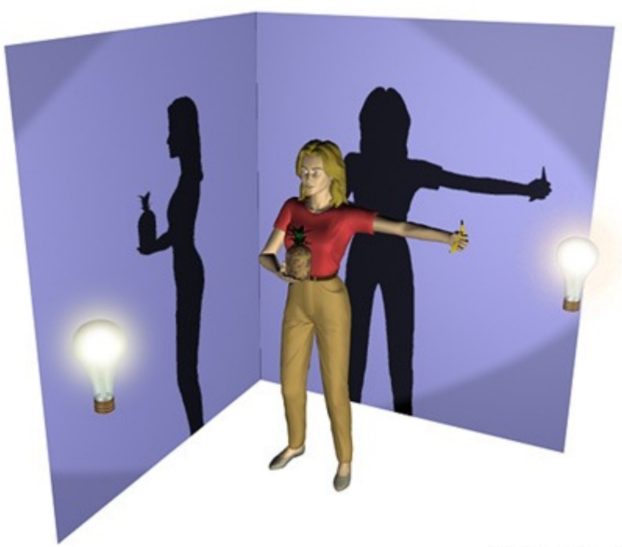
External Beam Radiation Therapy

Predominantly targeted x-rays generated by medical accelerators



Improved technology – *but the physics doesn't change*





Tumor and the healthy tissue both absorb dose

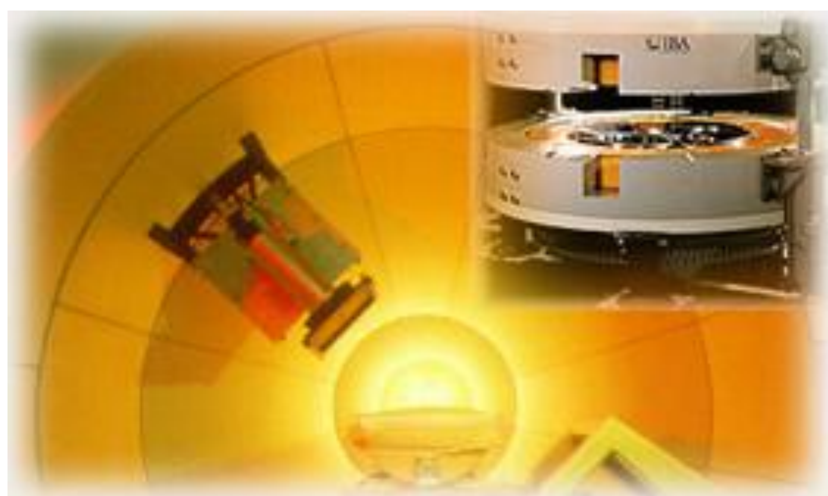
Leads to both disease control and side effects of radiotherapy

- Hadron therapy is also a type of external beam radiation therapy *– will discuss mostly proton therapy here!*

- Widely recognized as the *most* effective external beam method in the selective destruction of cancer cells.

  Because…….

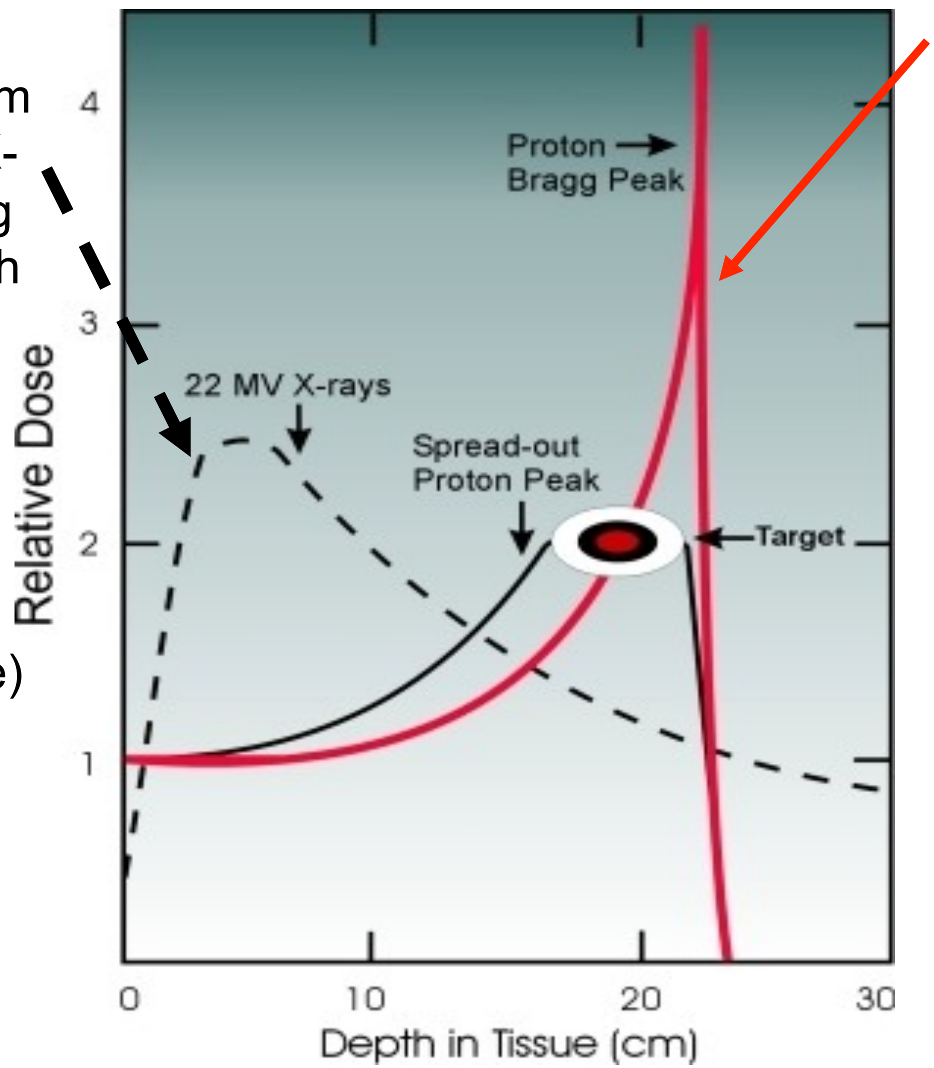
- The goal in radiation therapy is to deliver lethal doses to the tumor while minimizing or eliminating normal tissue injury.



About Proton Therapy: *Fundamental Nuclear Physics*

Conventional beam therapy delivers X-ray radiation along entire path through patient, and maximal dose in front of the tumor

Photons interact with matter (tissue) via photoelecric effect, Compton scattering, pair production



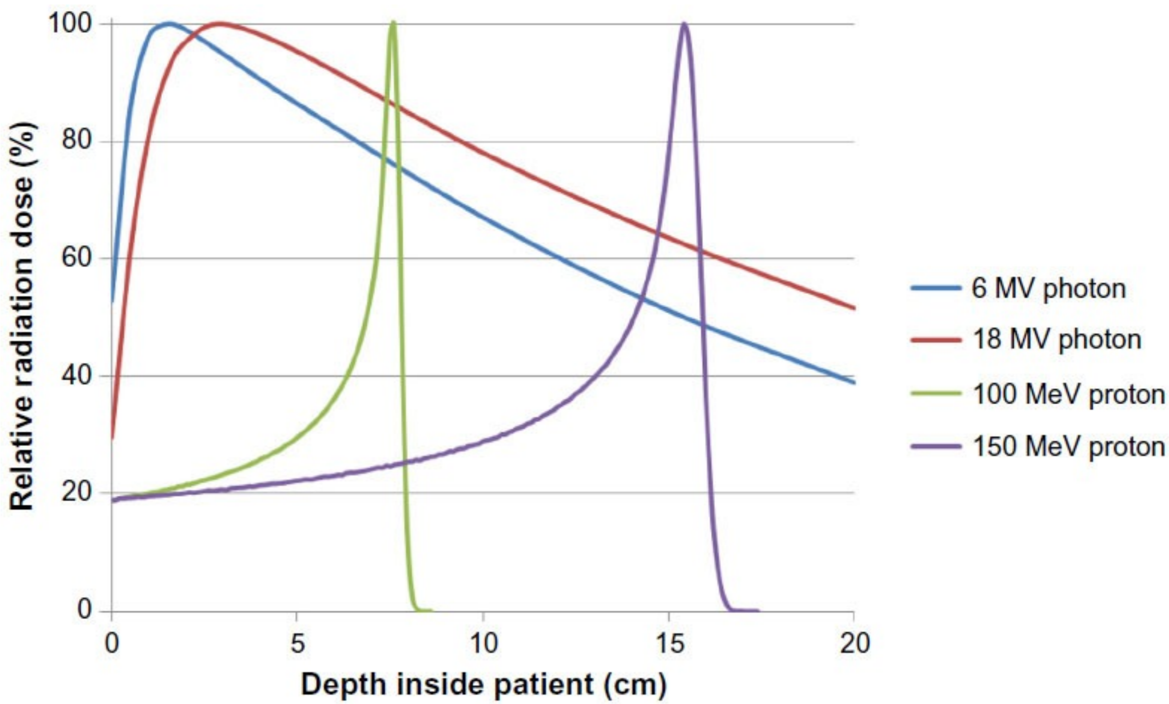
Proton beam treatments deliver minimal dose in front of of the tumor, over 4 times higher dose to the tumor region, and *no dose* behind it

Proton ionization energy deposition

$dE/dx \sim 1/(\beta c)^2$

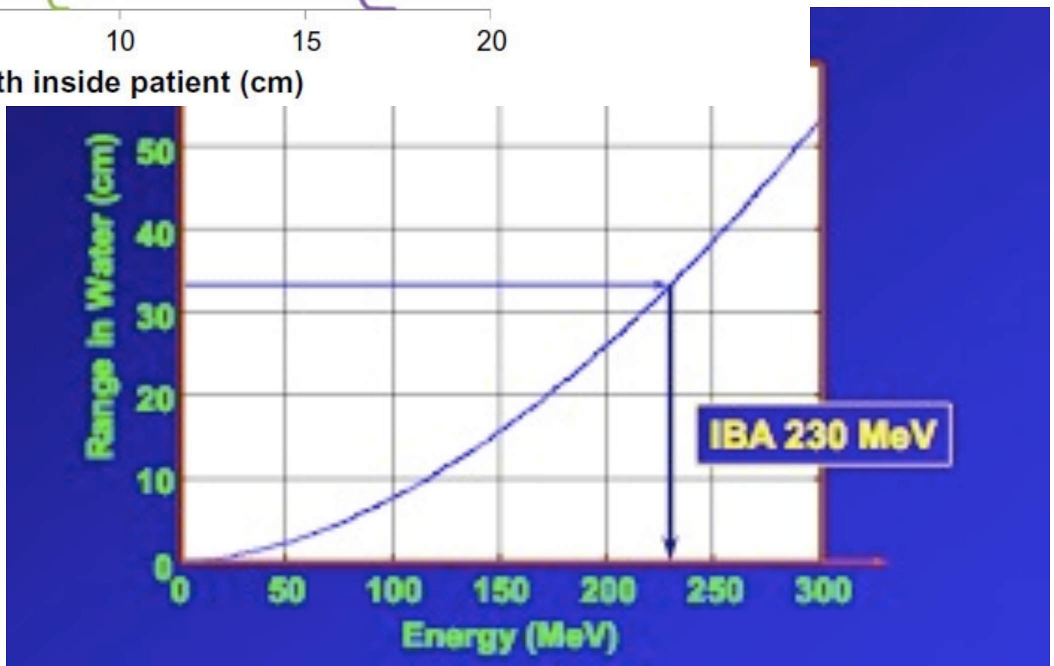
is inversely proportional to the square of the speed of the particle (Bethe-Bloch)

About Proton Therapy: Fundamental Physics



Proton treatment dose depth can be controlled by energy tuning

Higher energy = increased depth in patient

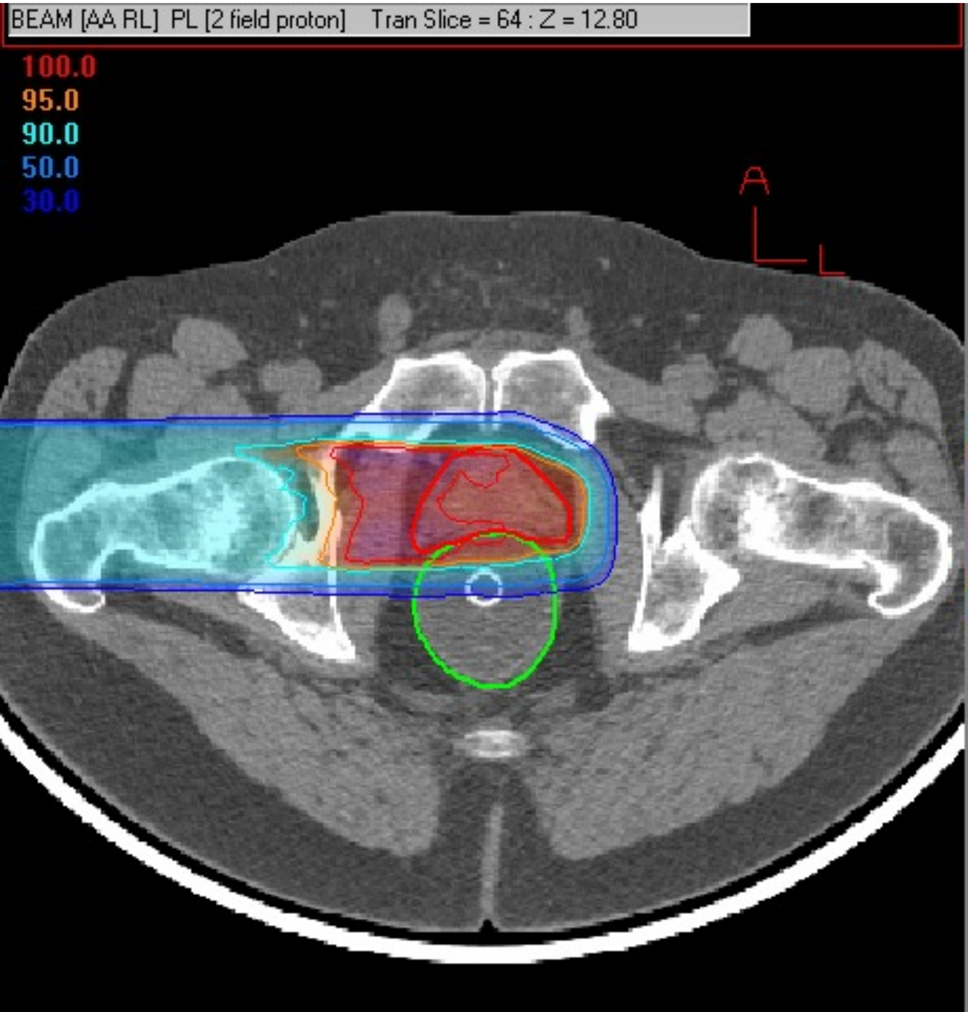


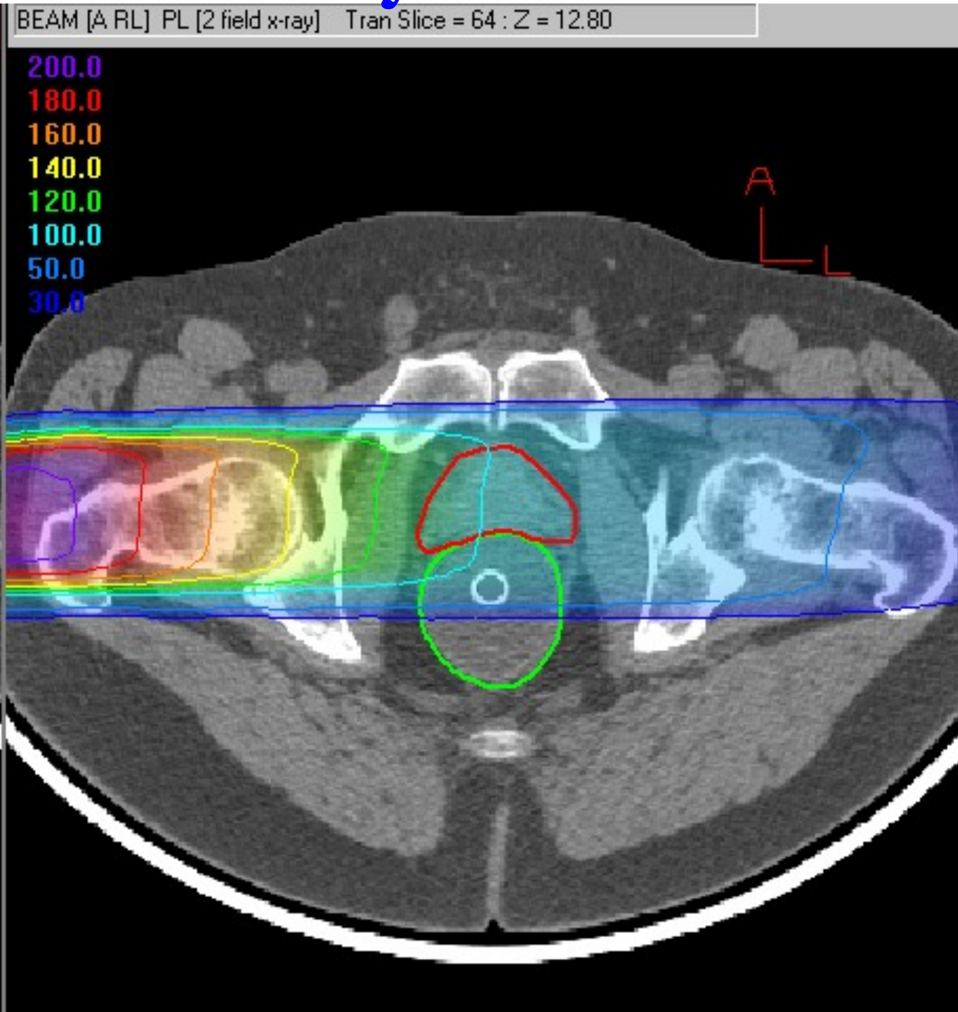
~230 MeV is highest energy needed

Bragg Peak translates to:

- Minimal proximal dose
- No distal dose
- Optimized dose to tumor

Proton Beam **X-Ray Beam**

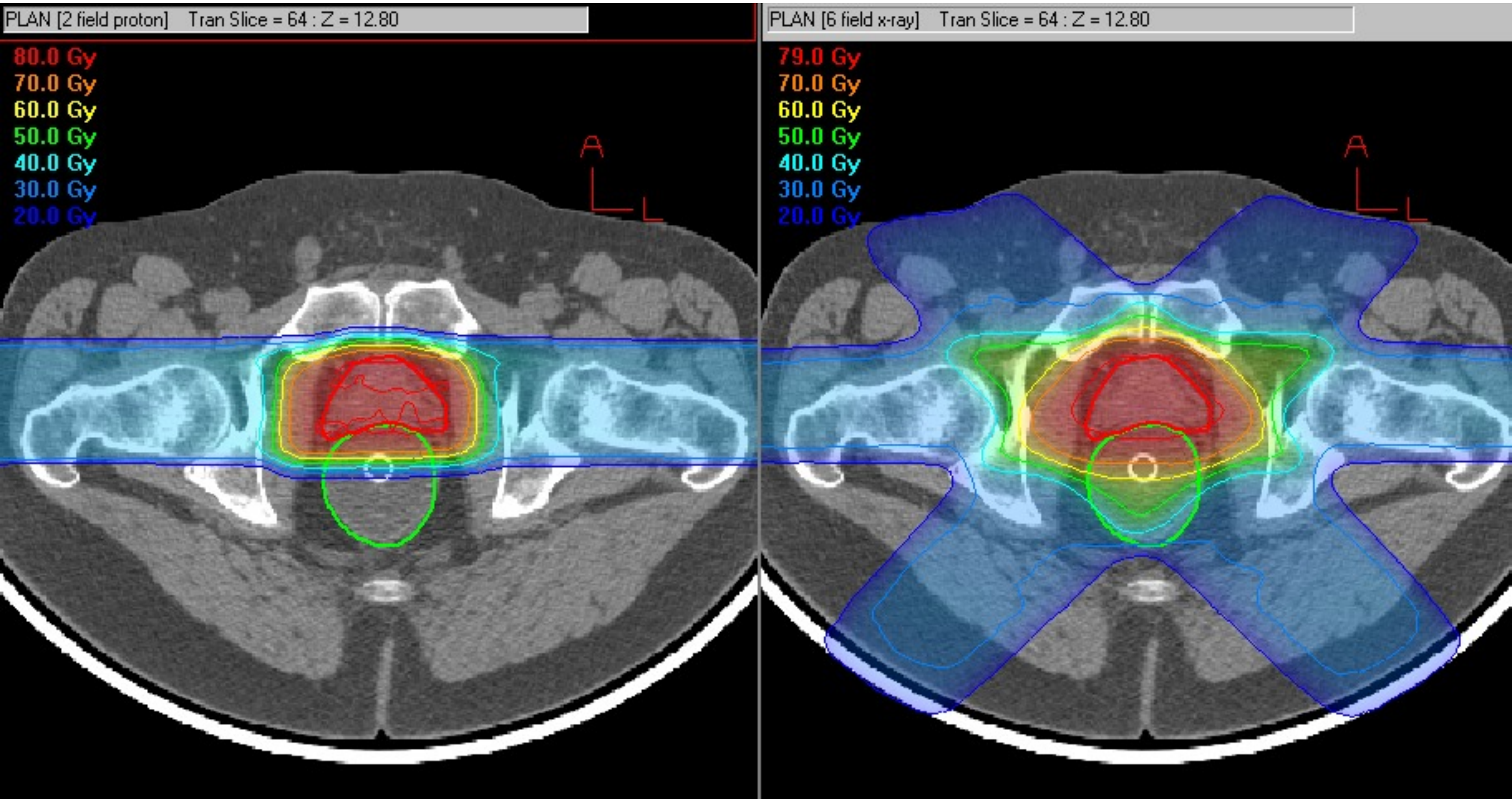




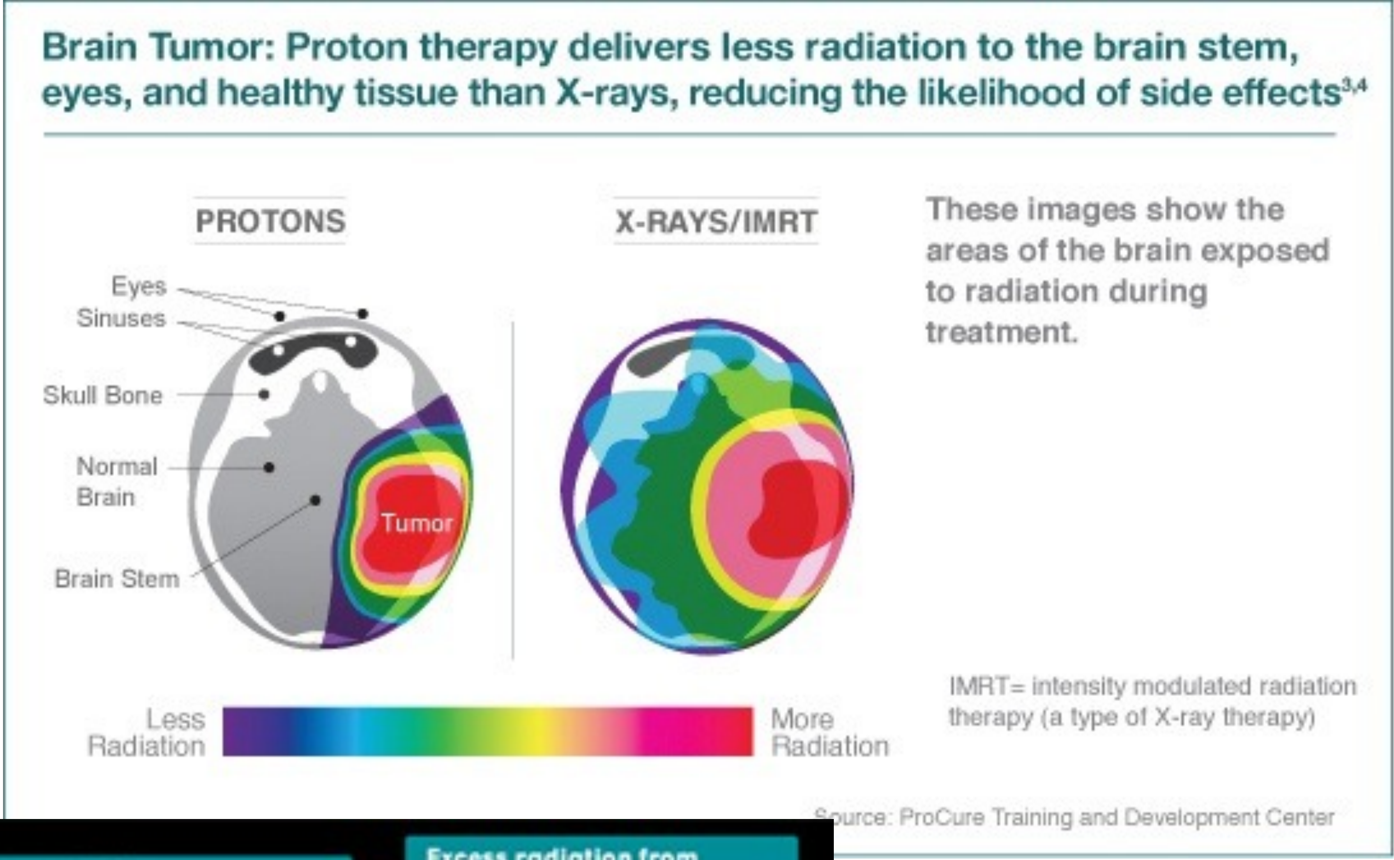
Proton Beams

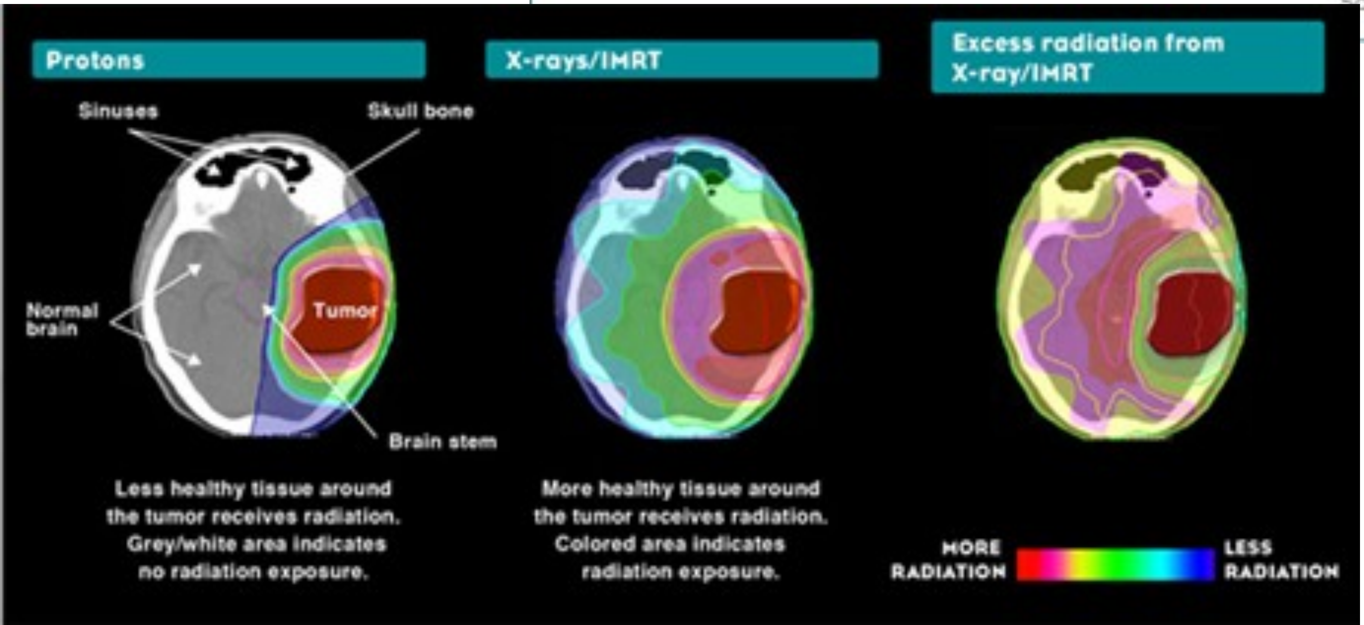
X-Ray Beams

- Lower dose, but to more healthy tissue



Proton therapy minimizes damage to healthy tissues that surround the tumor.





- Vernimmen, Harris, Wilson, Melvill, Smit, Slabbert. Int J *Radiat Oncol Biol Phys.* 2001;49(1)
- Bolsi, Fogliata, Cozzi *Radiother Oncol.* 2003;68:1-14.

Pediatric Radiotherapy Considerations

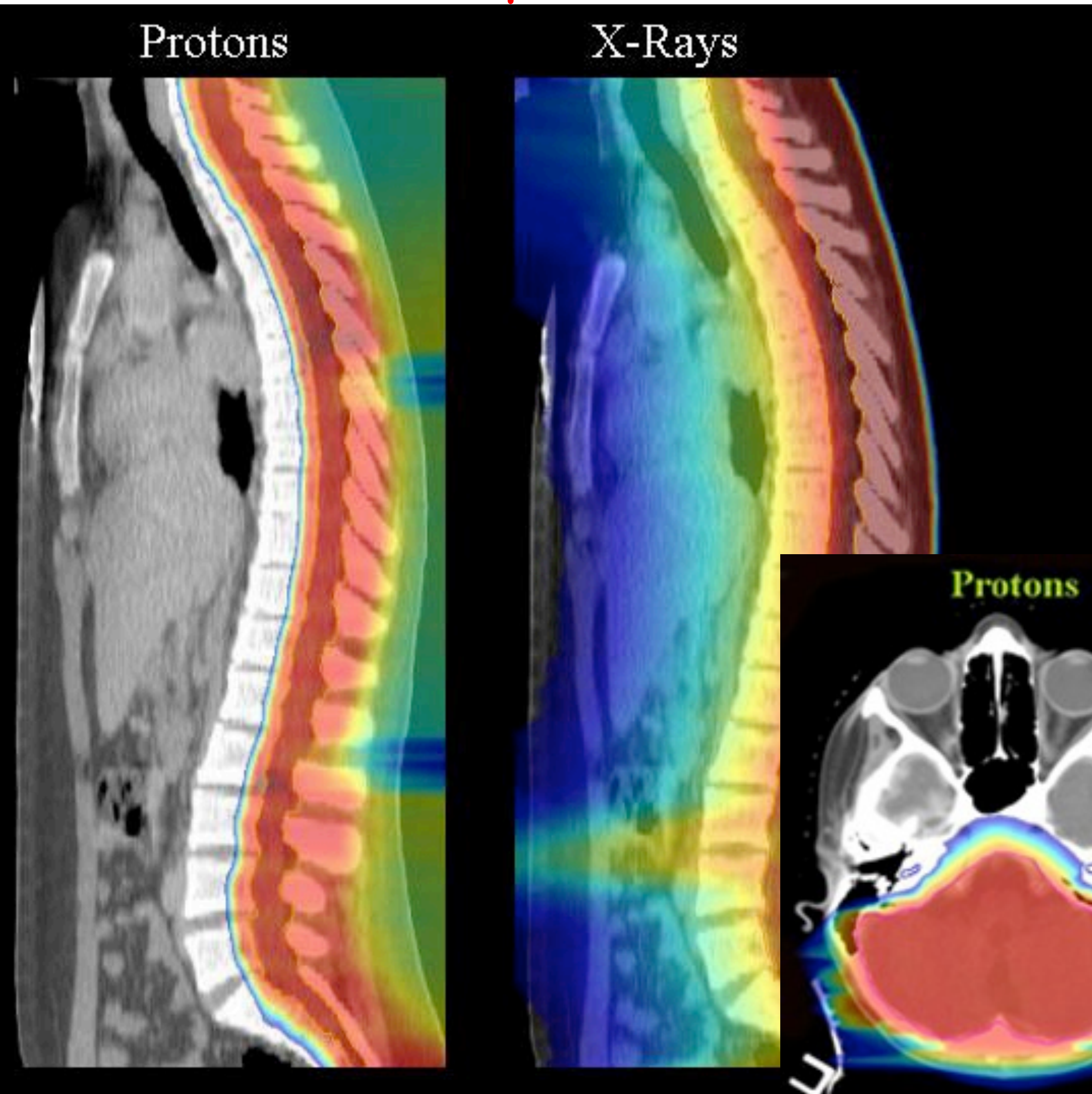
Example: Brain Tumors

- Low radiation doses can
  - produce decline in memory and intelligence
  - damage the hypothalamus and pituitary gland, effecting production of, for instance, growth hormone
  - play a major role in the development of second, radiation-induced cancers.
- Growing tissues are more likely to experience damage from radiation.

- *Proton radiation spares more normal tissue, and thus may reduce the risk of many complications*
  - *factor of 2-10 in secondary malignancy**

* Paganetti, Athar, Moteabbed, *et al. Phys Med Biol* 2012;57

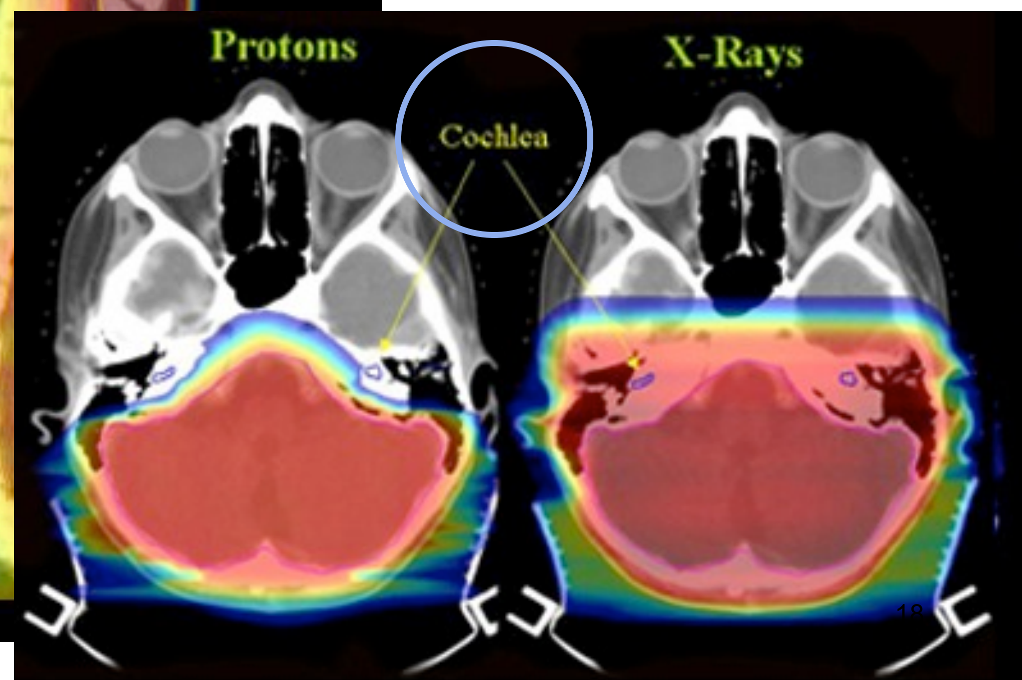
Example…..



Medulloblastoma

Most common malignant brain tumor in children

Spreads to CNS - deliver radiation to the entire neuraxis

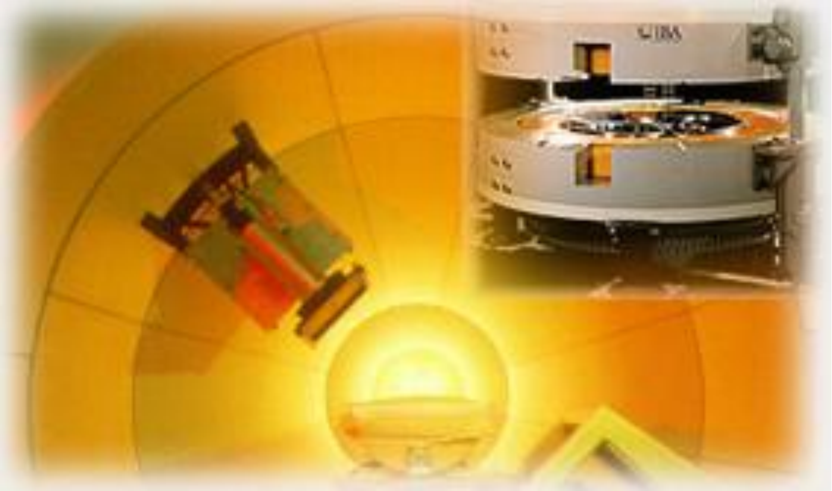


- Proton therapy is also a type of external beam radiation therapy

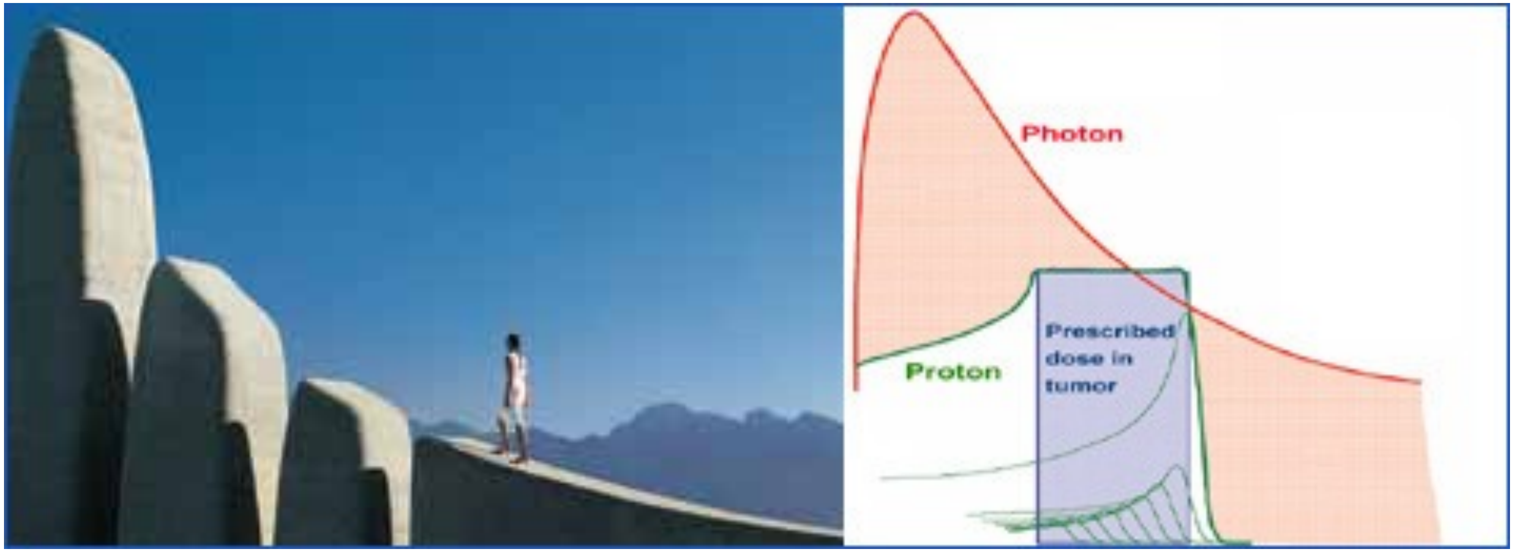
- Widely recognized as the *most* effective external beam method in the selective destruction of cancer cells.

  Because…….

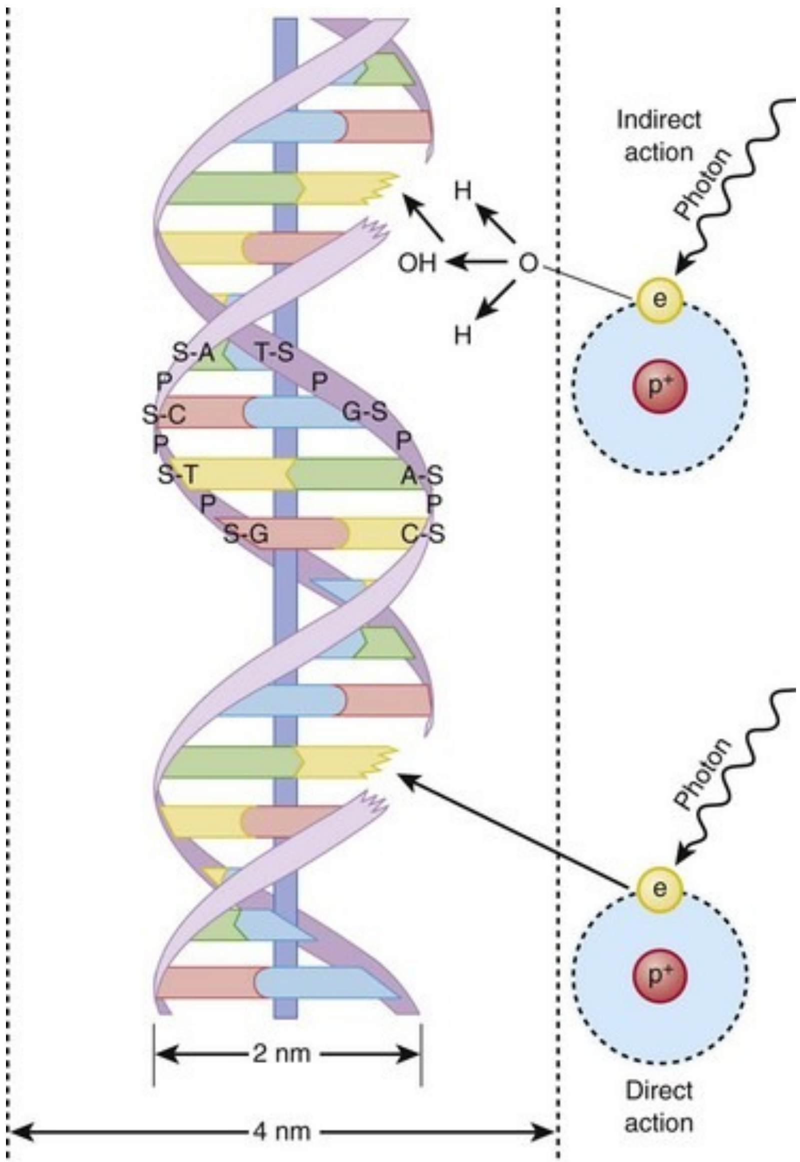
- The goal in radiation therapy is to deliver lethal doses to the tumor while minimizing or eliminating normal tissue injury.



- The goal in radiation therapy is to deliver lethal doses to the tumor while minimizing or eliminating normal tissue injury.
  - *- Higher relative biological effectiveness*
  - *- Increased dose*

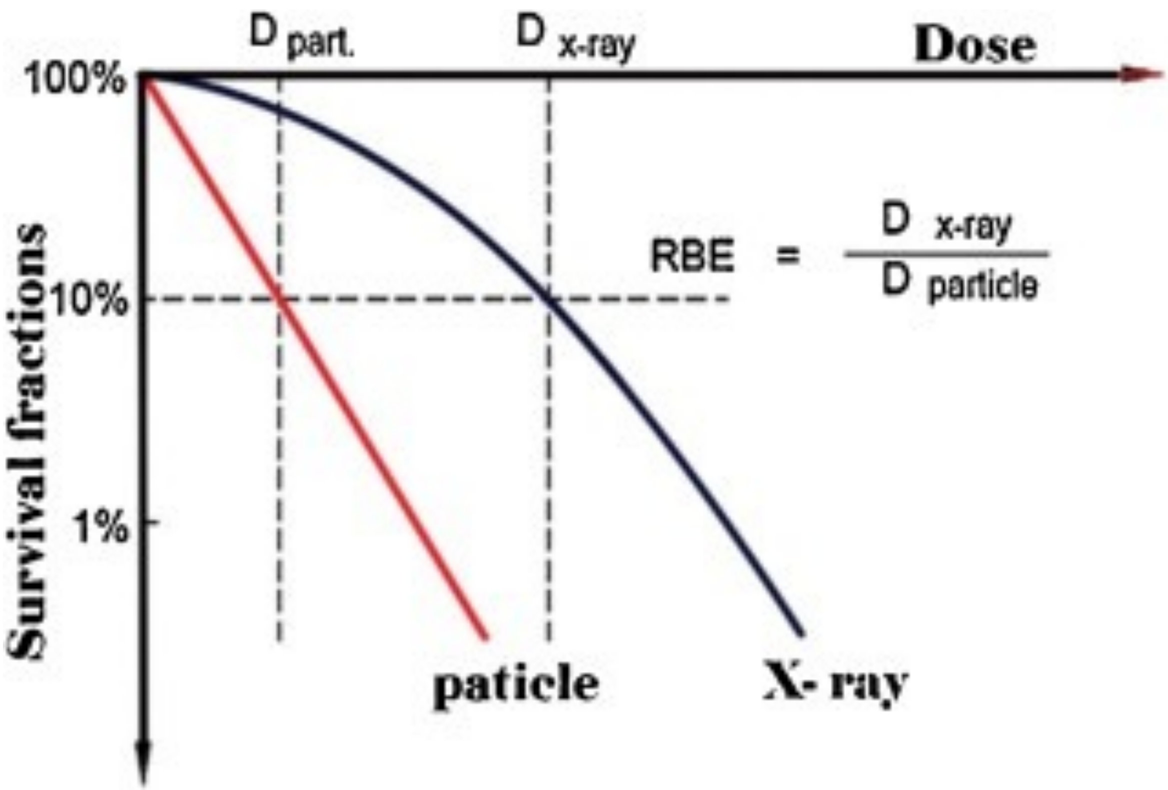


Radiobiology



- Radiation therapy works by damaging the DNA of cells.
- Double and single strand DNA breaks in sugar-phosphate backbone
- Ionizing radiation ejects an electron from a target molecule - *directly or indirectly*
- Indirect ionization happens as a result of the ionization of water, forming free (hydroxyl) radicals which then damage the DNA - dominant mechanism in x-ray treatments
- Direct (protons) vs. Indirect (photons) injury - different *relative biological effectiveness* (RBE - protons higher)

Particles have enhanced tumor killing power - even for SAME dose



Particles could be protons or other ions

Proton RBE = 1.1: 10% higher than X-rays

Heavier ions have even higher RBE

Advantages of Irradiation with Protons

- Deliver *minimal* dose *in front* of the tumor

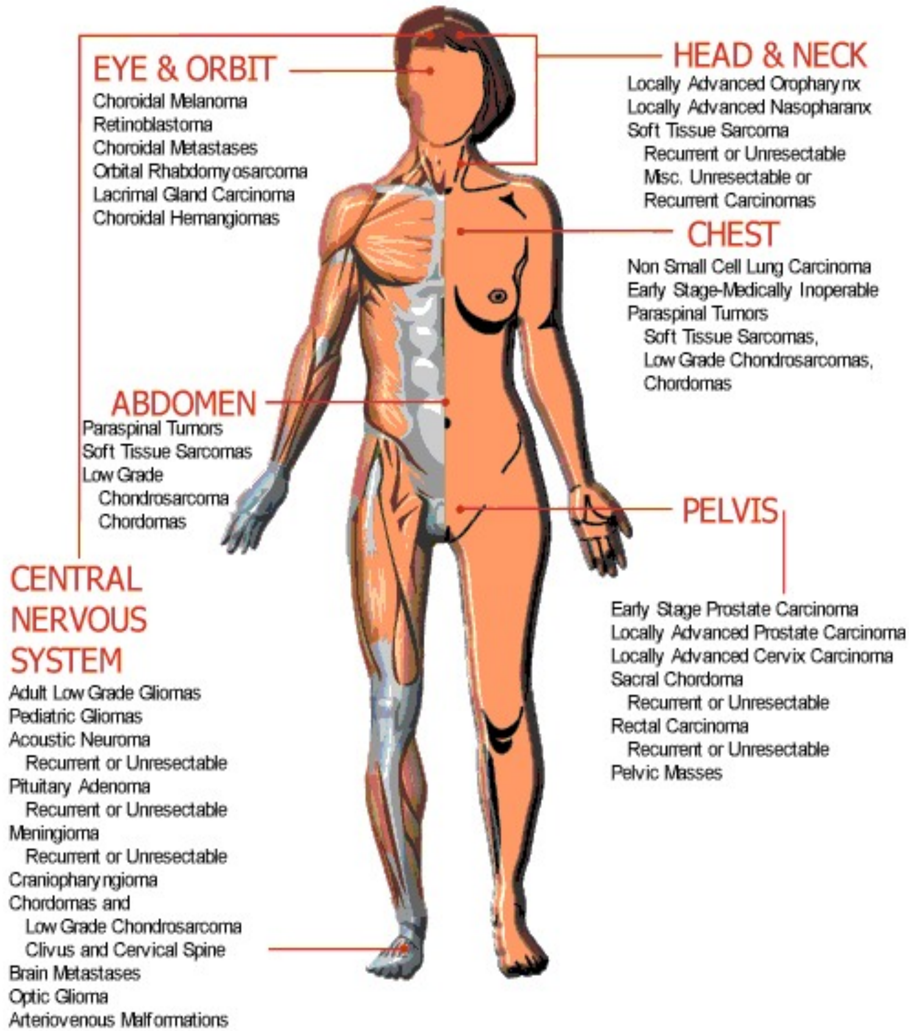
- *Deliver maximum dose* to the *tumor region*

- *NO DOSE behind* the tumor

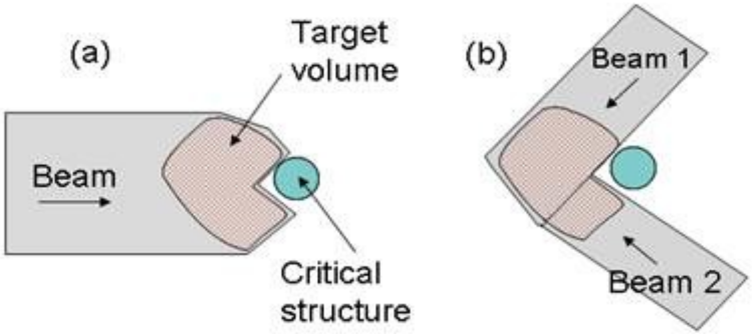
- **Protons destroy tumor more effectively** - higher RBE

Many cancers treatable

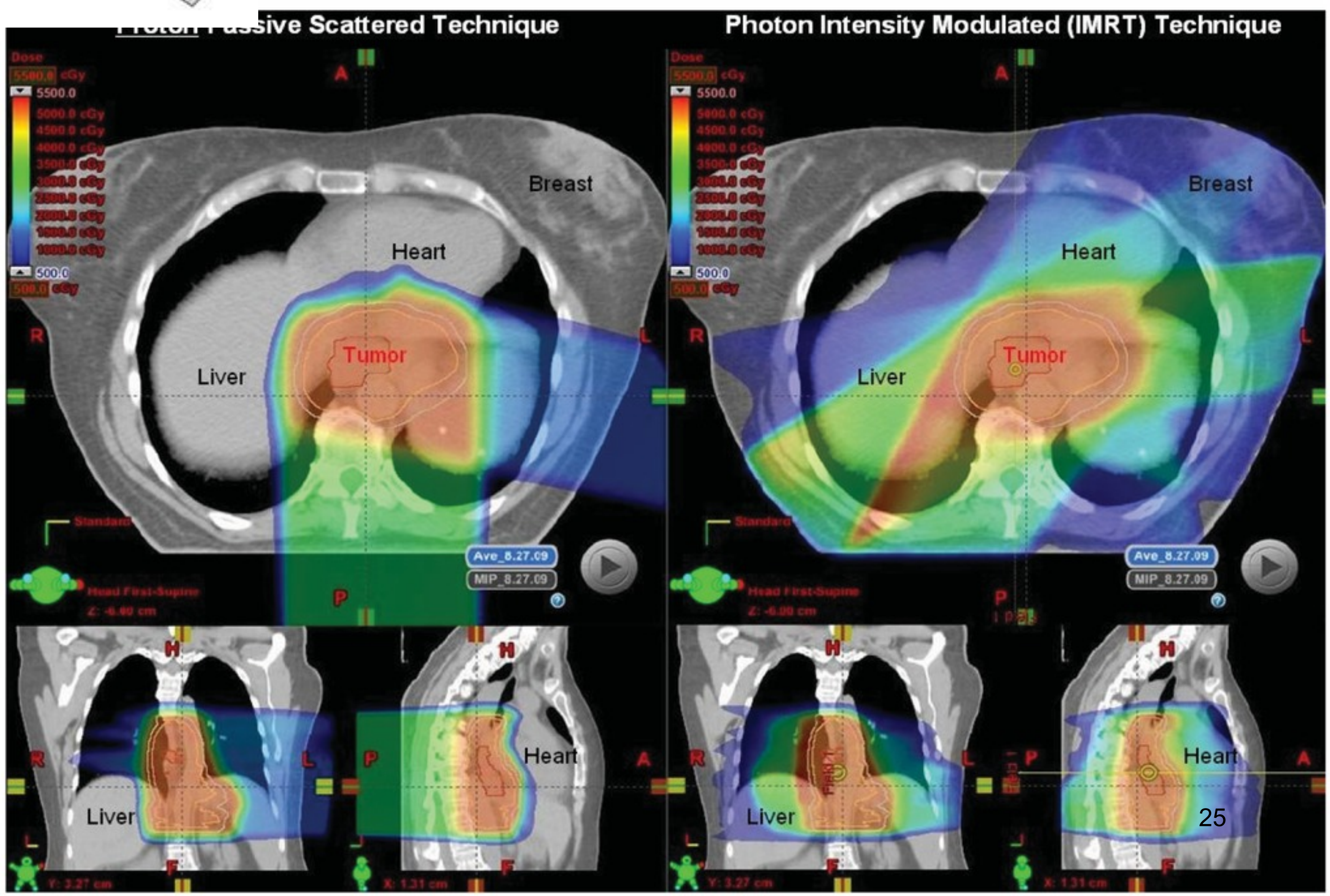
- More than 137,000 (175,000+) patients were been treated with particle therapy worldwide from 1954 to 2014 (2016).
- 86% were treated with protons and 14% with carbon ions and other particles.
- About 10% of patients are pediatric.



Combinations of Proton Beams



– Can avoid aiming beam at critical structures adjacent to tumors

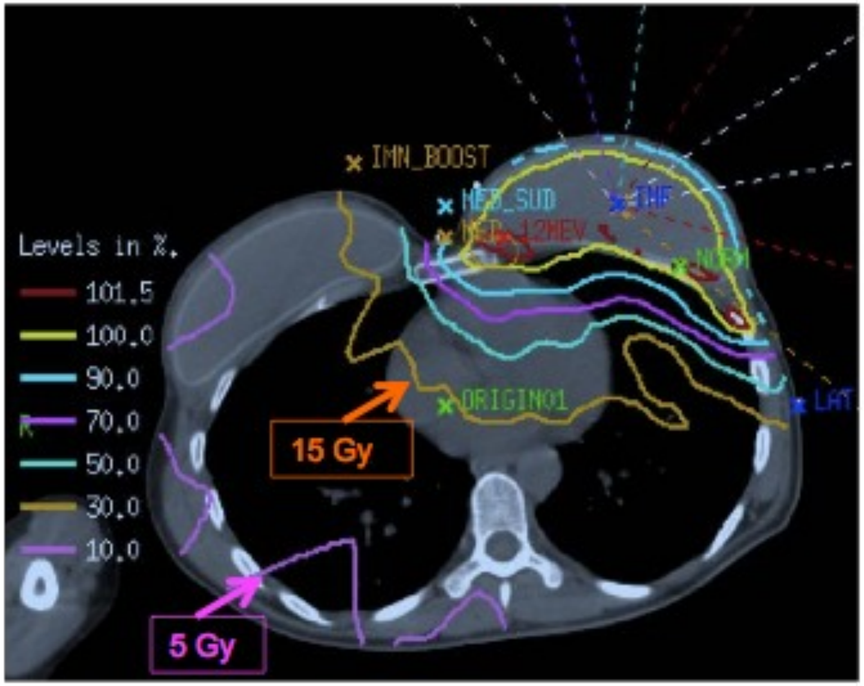


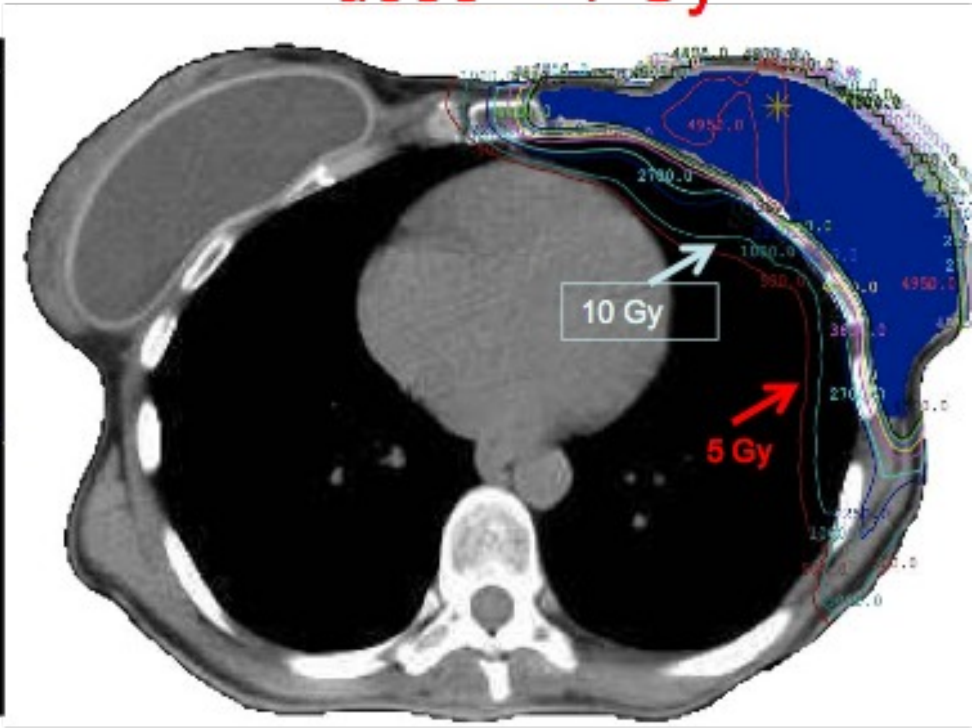
Example:
esophogeal cancer, 5 field x-ray vs. 2 field proton

Rationale for Proton Therapy for Breast Cancer
x-rays (IMRT) vs protons

MSK IMRT:
Mean heart dose 6 – 10 Gy

Protons:
Mean heart dose < 1 Gy



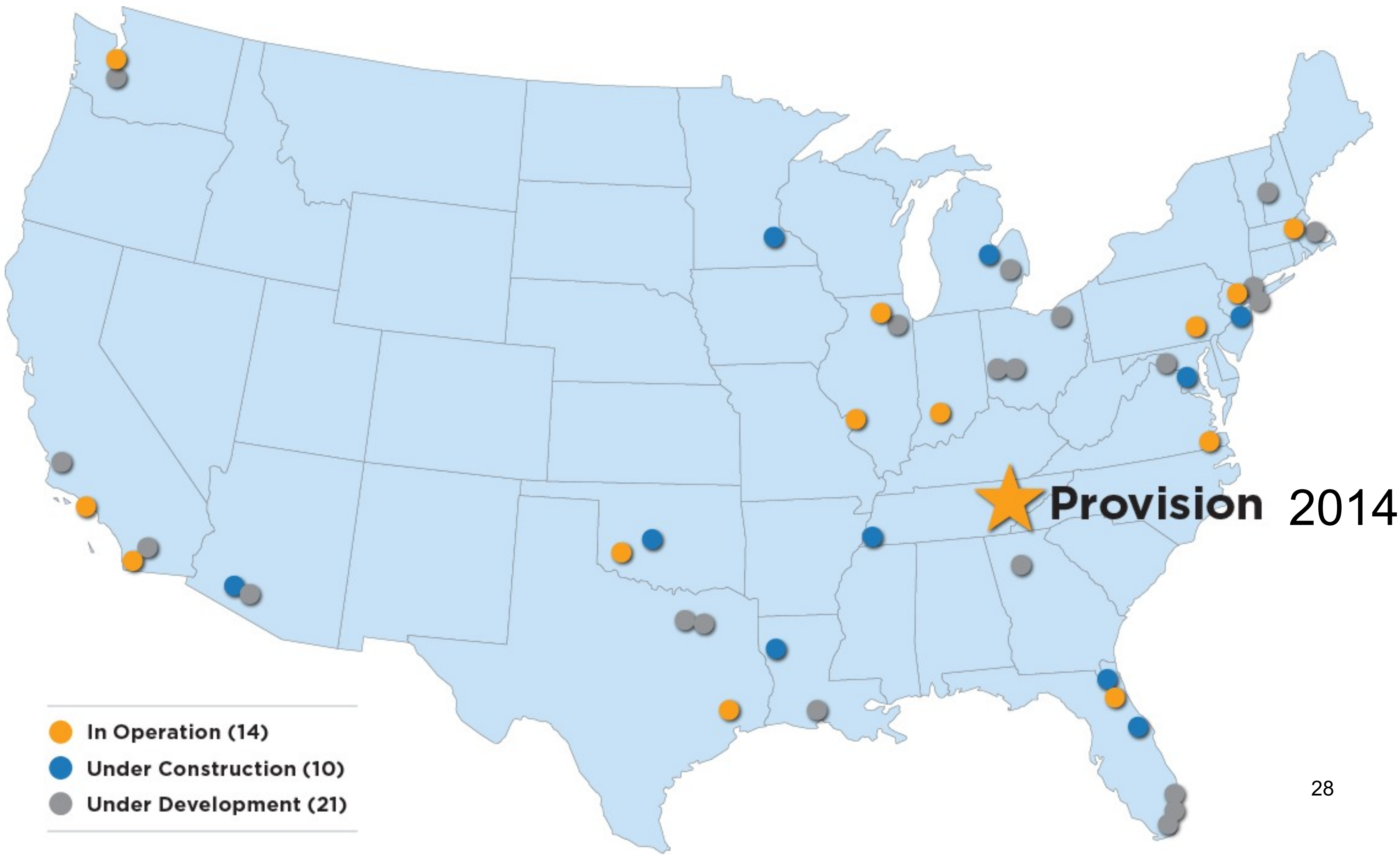


Proton and Particle Therapy in the World

48 particle therapy facilities worldwide

Proton Therapy in the USA – 16 centers,

- compare to 1 X-ray center for every ~250,000 people, ~1,500 treatment rooms



The global proton therapy market eclipsed the billion-dollar mark for sales orders in 2015

- more than double the 2014 total*

11 new centers started construction in 2016

- eight in the United States
- three in Hong Kong, Belgium and the Netherlands

Introduction of compact proton therapy systems

- can be order of magnitude less expensive

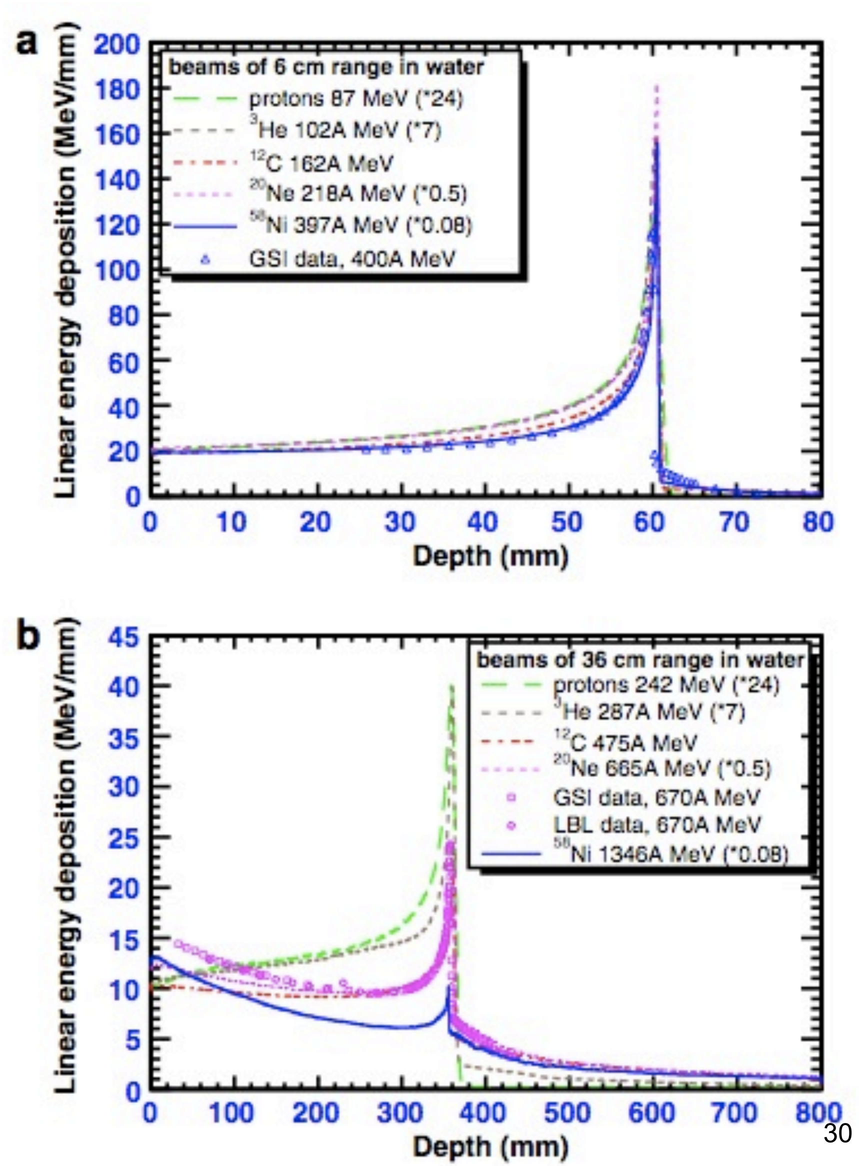
* Data from market intelligence firm Medraysintell

(Carbon) Ion Therapy

- Heavier particles have a higher RBE, making them more effective at treating tumors with an anoxic core
- Example: renal-cell carcinoma - a notoriously radioresistant tumour for which there had been few reports of curative radiotherapy
- Few carbon-beam facilities in the world, two in Japan (HIMAC and HIBMC) and two in Germany (GSI and Heidelberg) - more to come?

But….

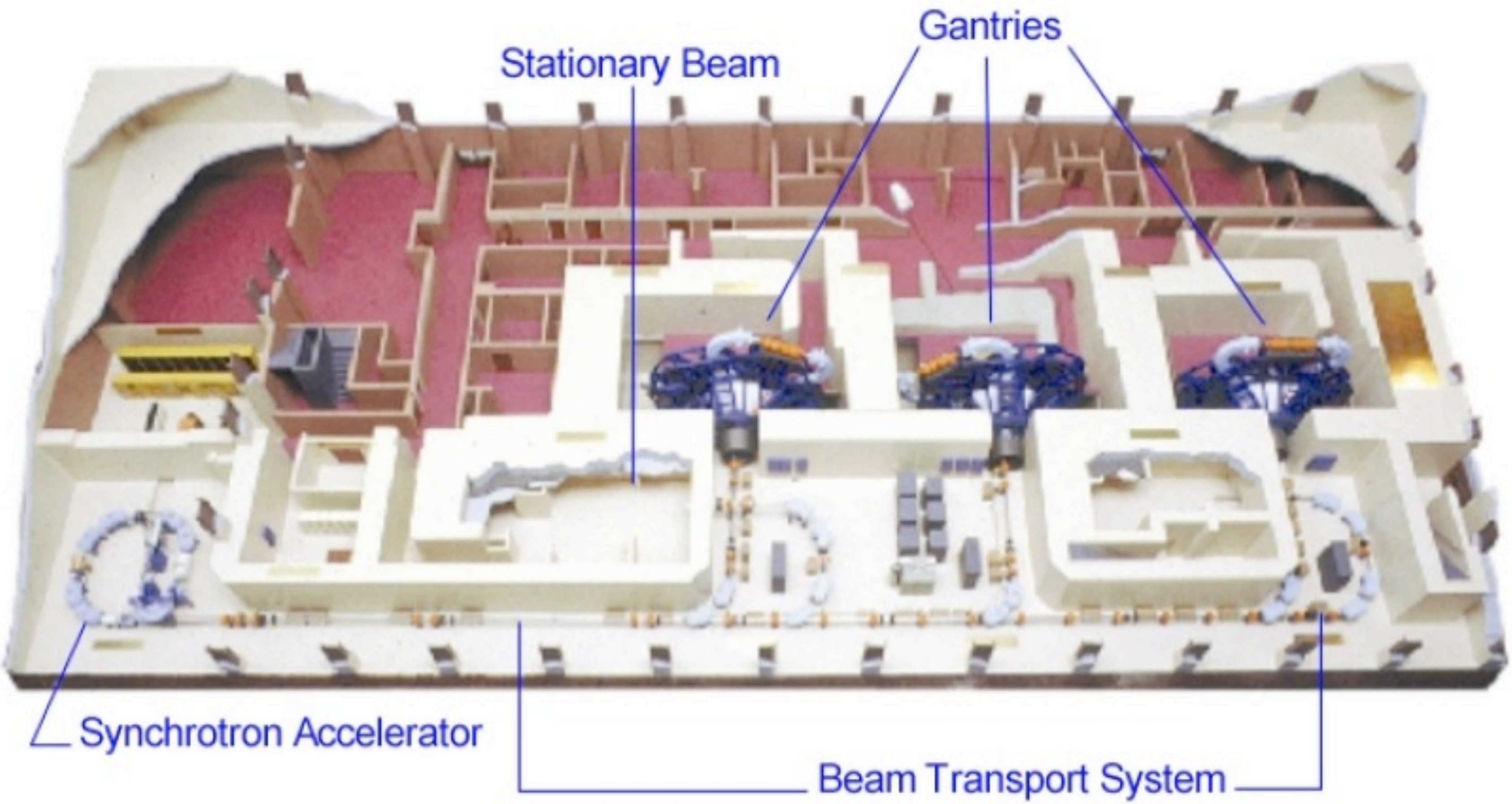
- At high energies, nuclear fragmentation plays increasing role with heavier ions - secondary particle tail
- RBE higher for proximal dose as well



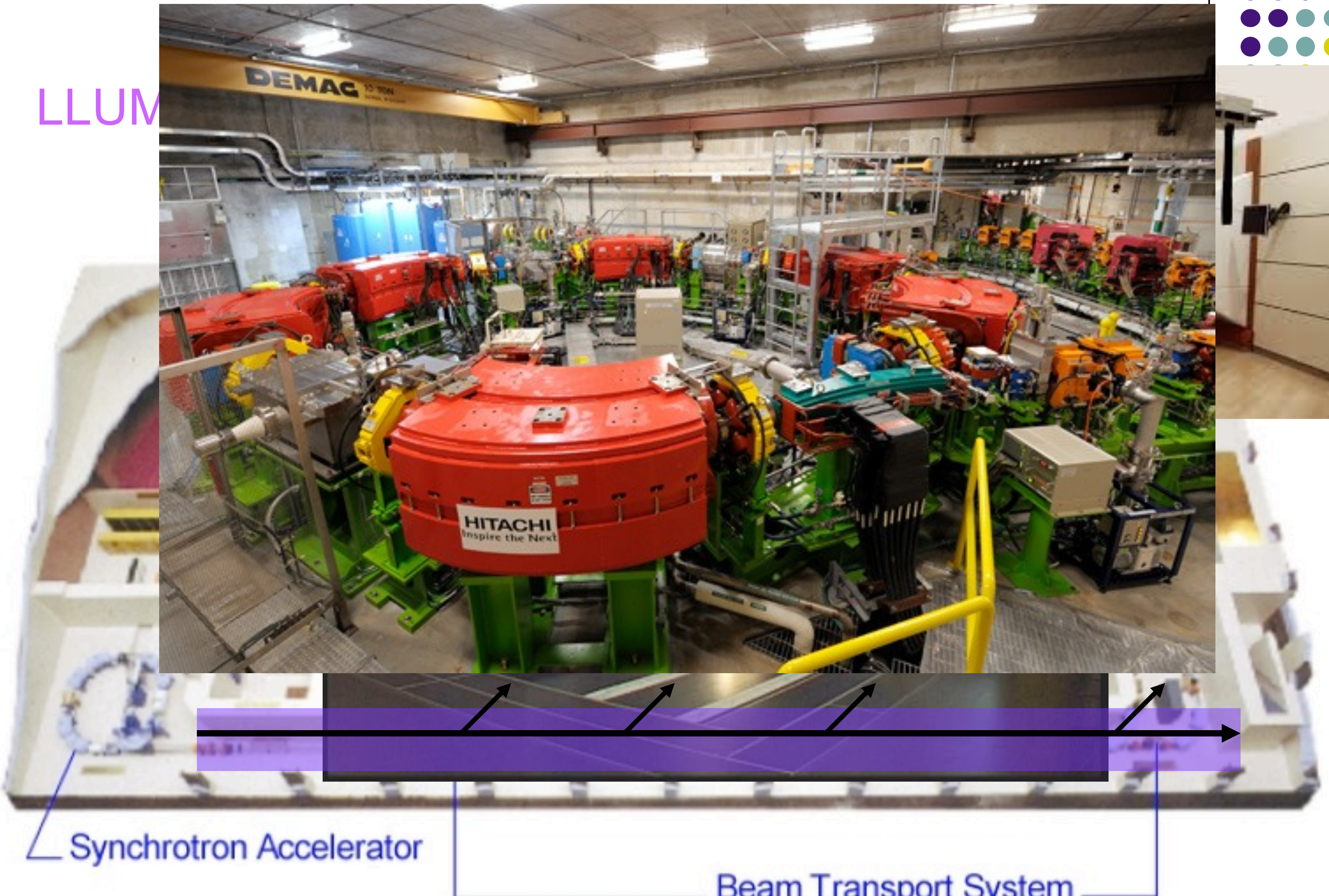
I. Pshenichnov et al. / Nucl. Instr. and Meth. in Phys. Res. B 266 (2008) 1094–1098

Typical Center Design

LLUMC

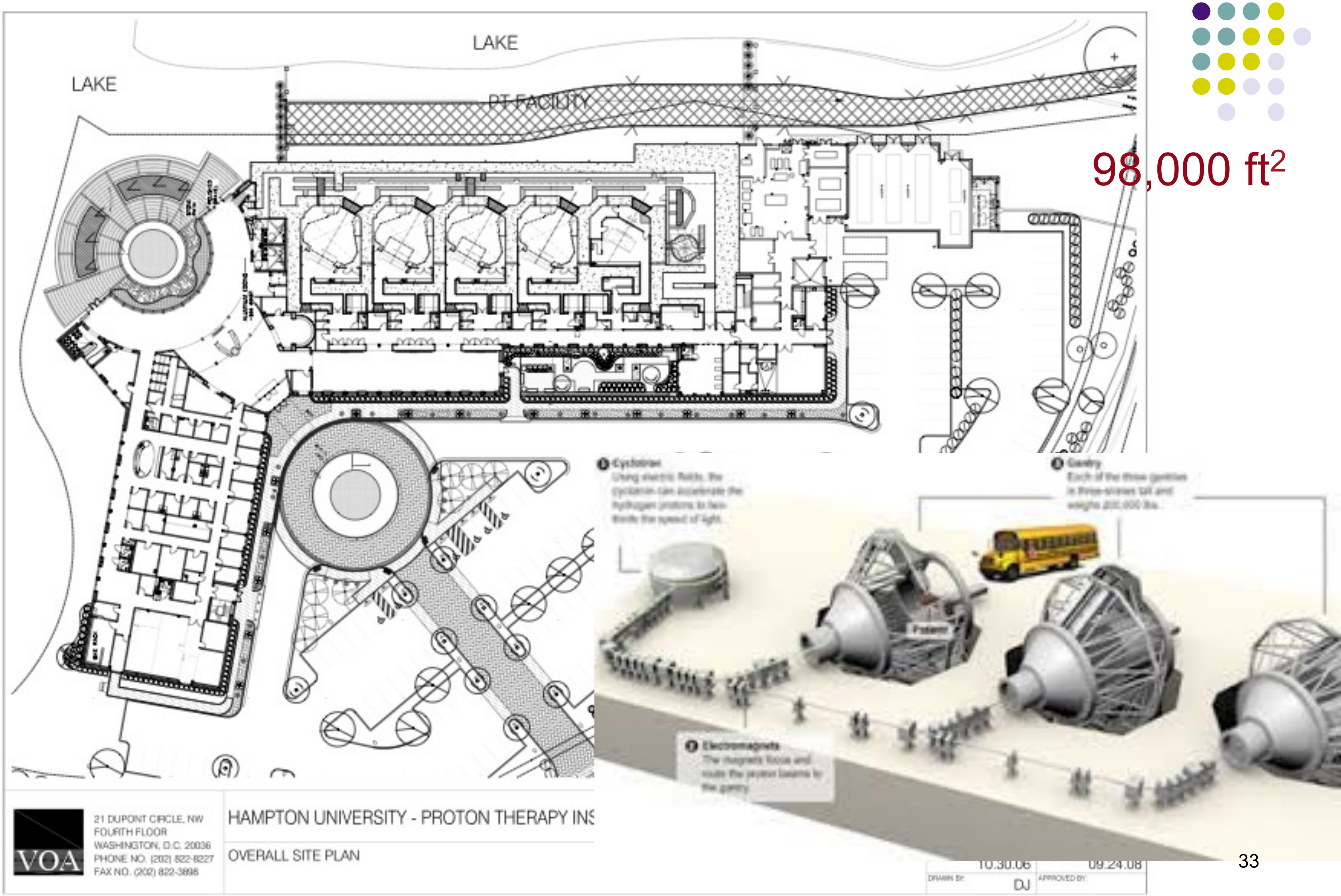


LLUM


DEMAG
HITACHI
Inspire the Next
Synchrotron Accelerator
Beam Transport System

Hampton University Proton Therapy Institute

98,000 ft^2



A Brief Tour....

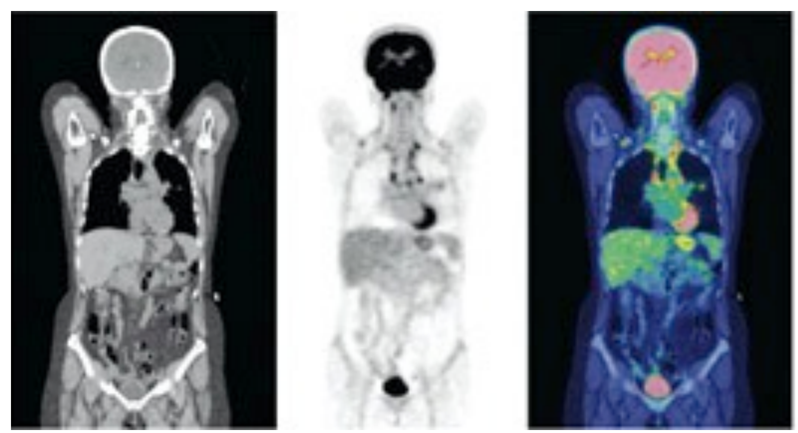
- To assure both treatment and simulation imaging in same position, with no motion, the patient must be immobilized during imaging and treatment.
- The patient lies in a mold lined with plastic and insulating material to have foam placed, in a conformable form, or in an evacuable beanbag.
- Patients who will be treated in the head or neck area are immobilized using lightweight plastic masks which, upon heating, mold to the patient's face, head, and neck.

A Brief Tour...

- (MRI or PET)/CT scans are performed.
- The patient lies in the custom immobilization device.
- The CT scan creates several high-resolution images to provide accurate information about the patient's anatomy, tumor location and geometry, and tissue density.
- CT images of the tumor and surrounding areas are used to:

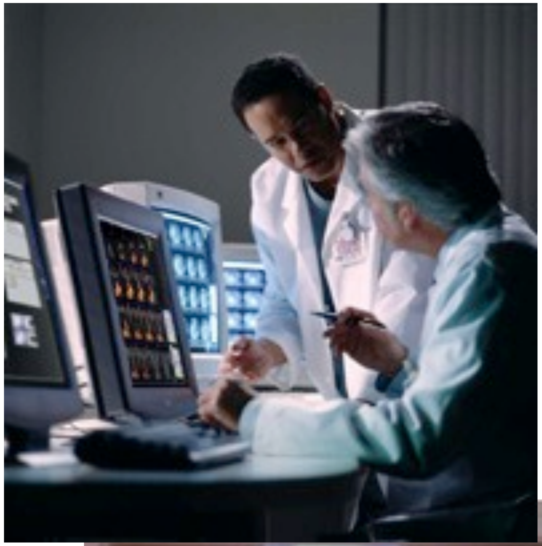
    -design the radiation therapy plan

    -align the patient during each treatment

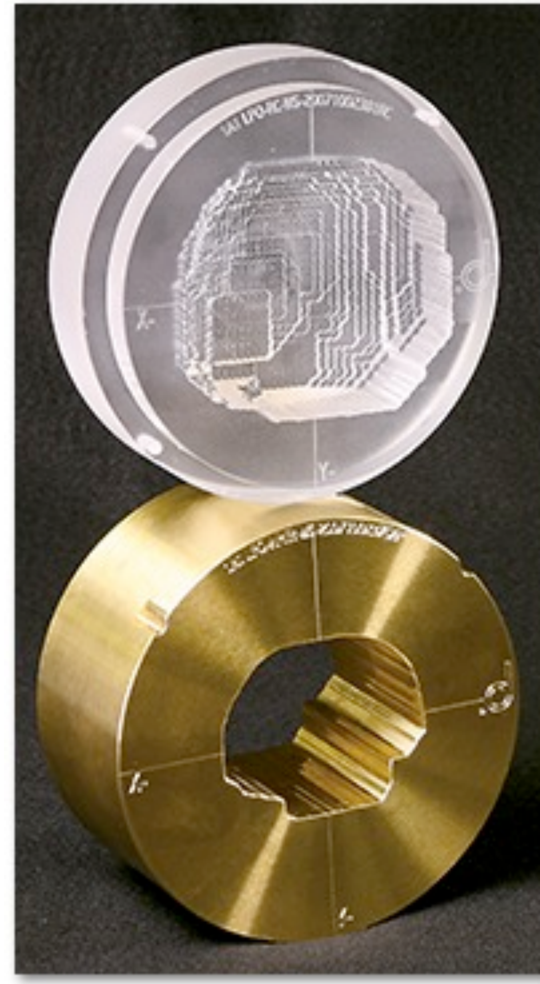


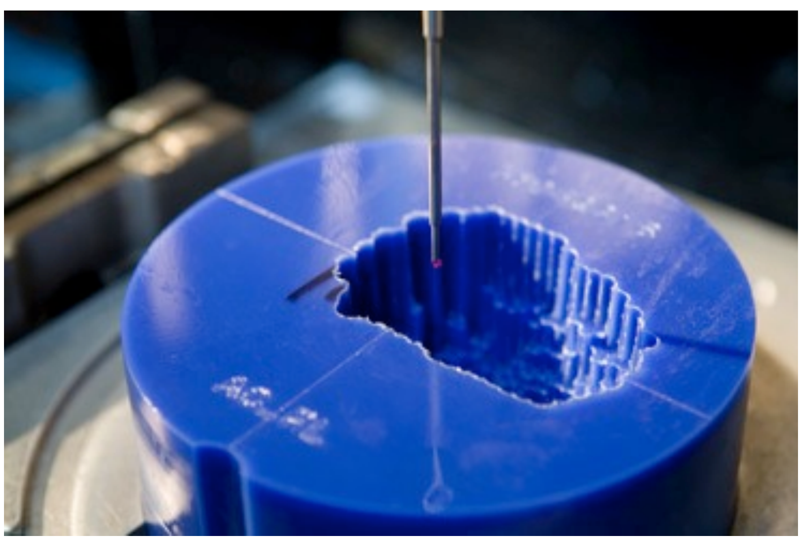
A Brief Tour

- The CT images are studied by a physician, a medical physicist, and a dosimetrist on a treatment planning computer workstation.
- The tumor and critical structures are outlined using the computer, and the physician selects radiation fields which will minimize the dose to critical structures and normal tissue and maximize the dose to the target.
- The completed and approved plan is used to generate the treatment prescription (target angle, proton beam energy, dose per treatment, etc.)

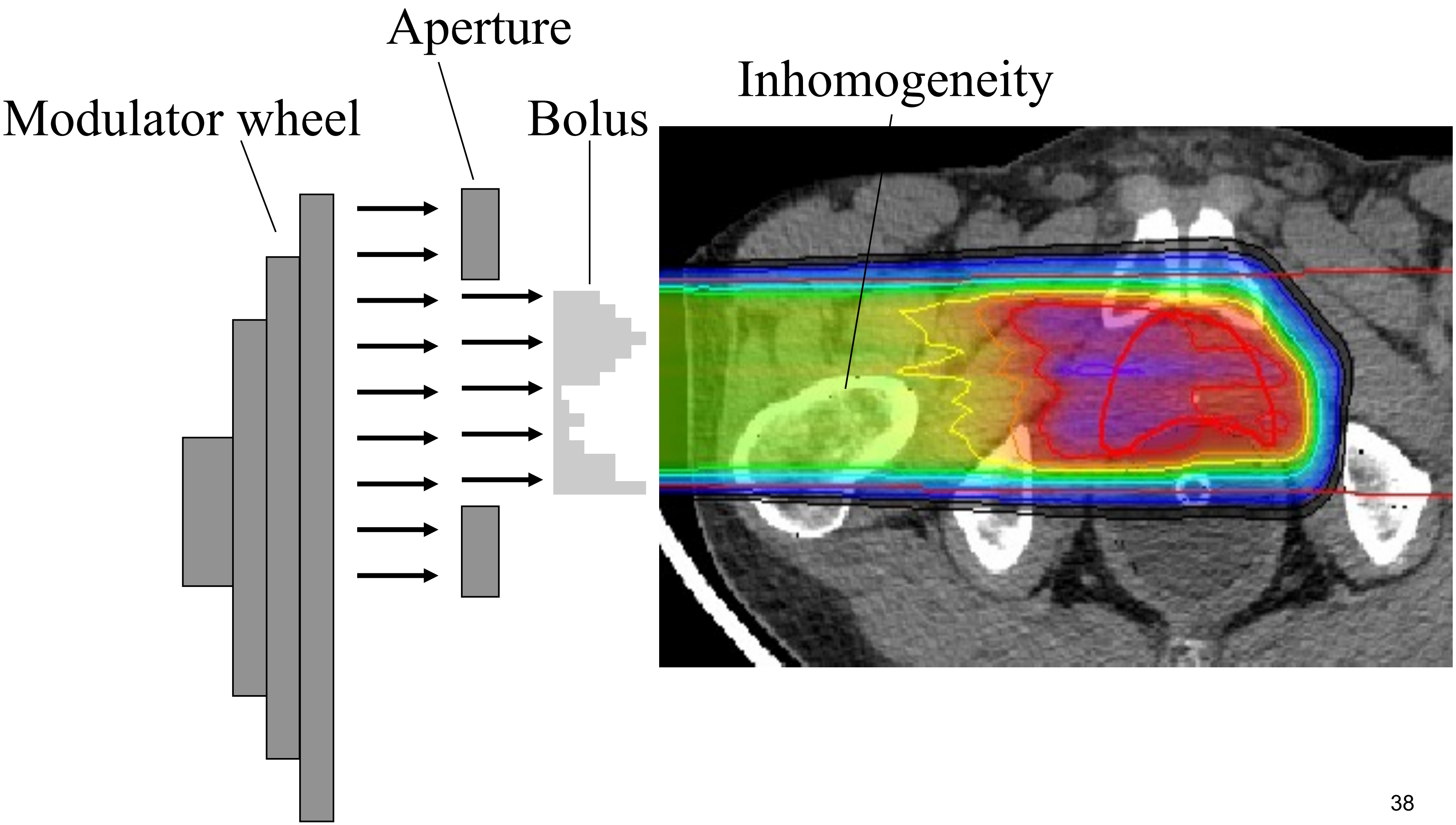


- In the treatment planning process, digital files representing three-dimensional images of the tumor are generated
- The digitized three-dimensional images are sent to specialized machinery to mill customized boluses from high-grade wax or plastic and customized apertures from brass
- The aperture and bolus are placed in the beam line to help conform the proton beam to the shape of the tumor.

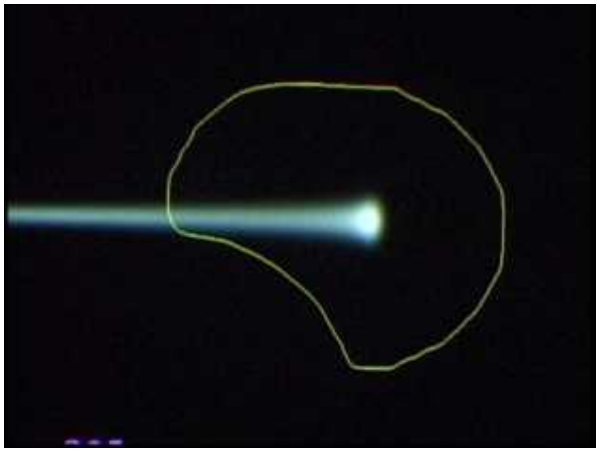




Proton Beam Design

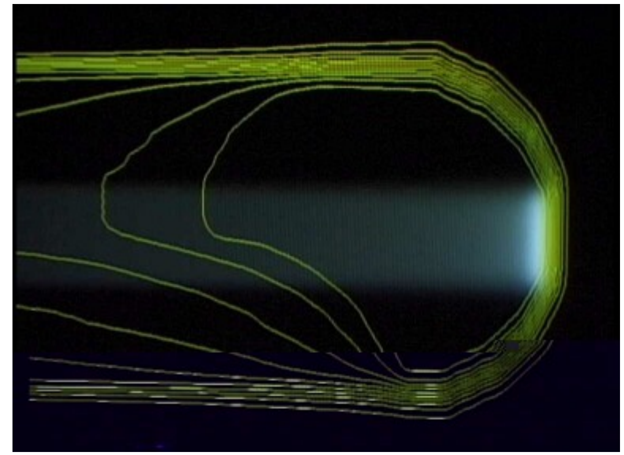


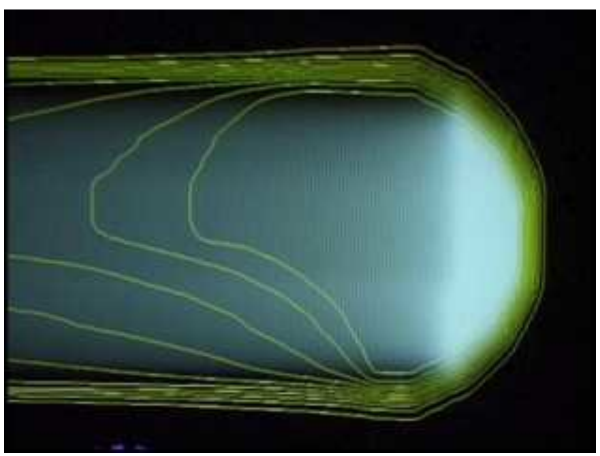
Alternatively…. Spot Scanning



One spot

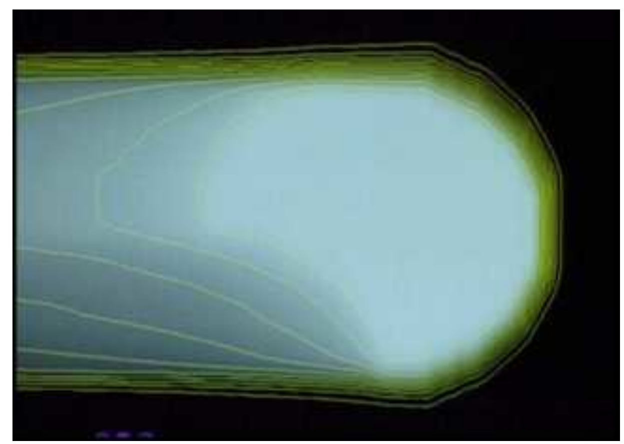
... a few spots



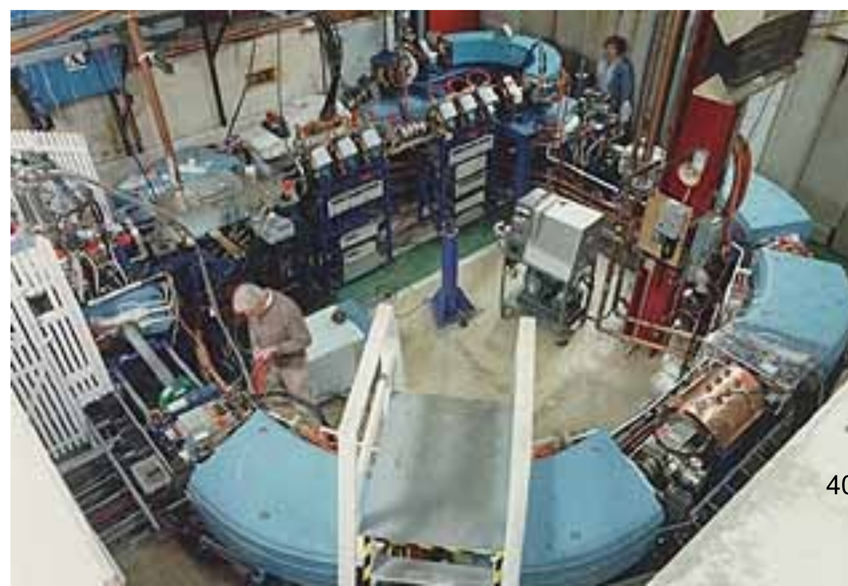


... more

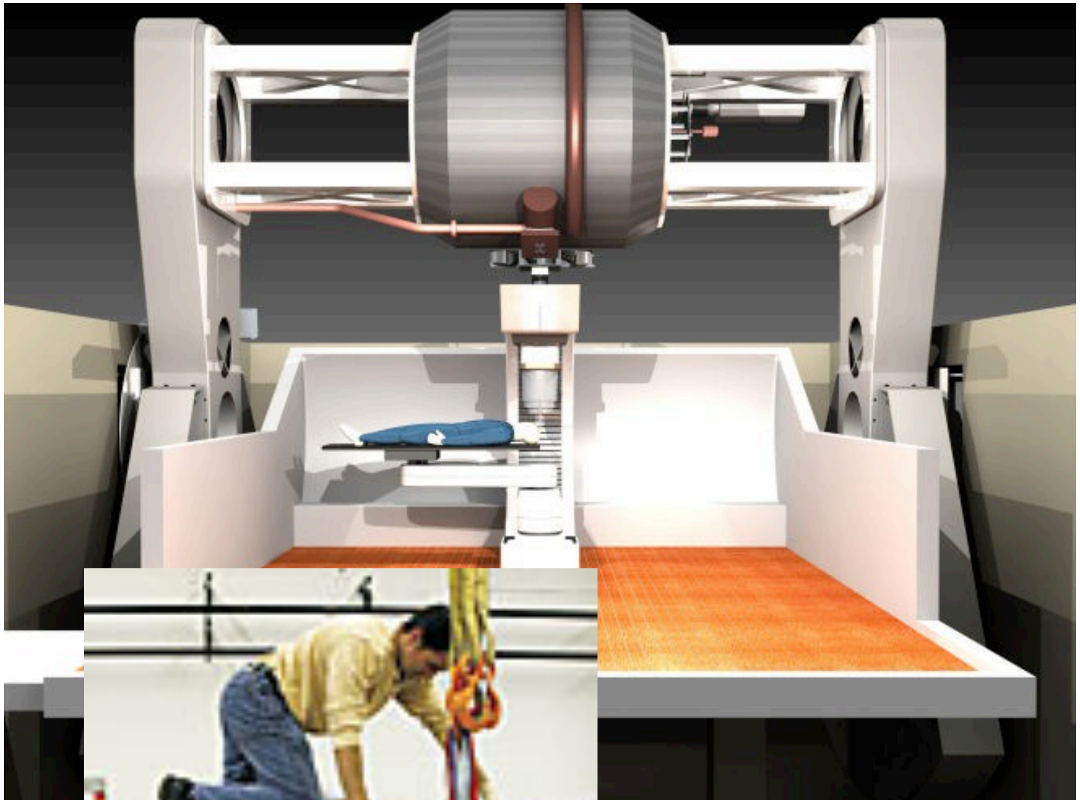
... until it is complete



The Accelerator



Single Room Units



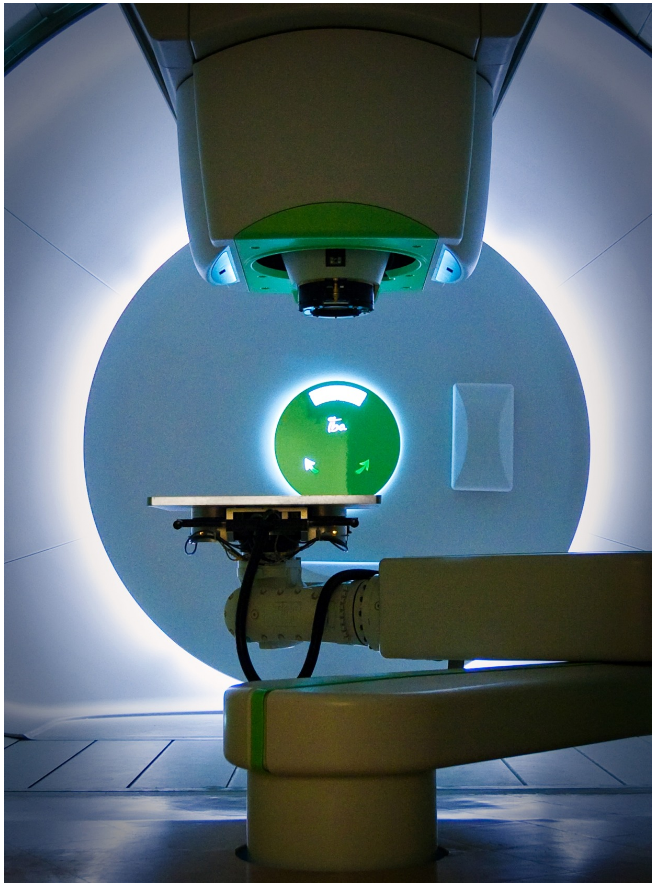
- Mevion S250

  One of the world's highest magnetic field cyclotron, operating at 10 T

- IBA ProteusONE

Back, again, to the tour….

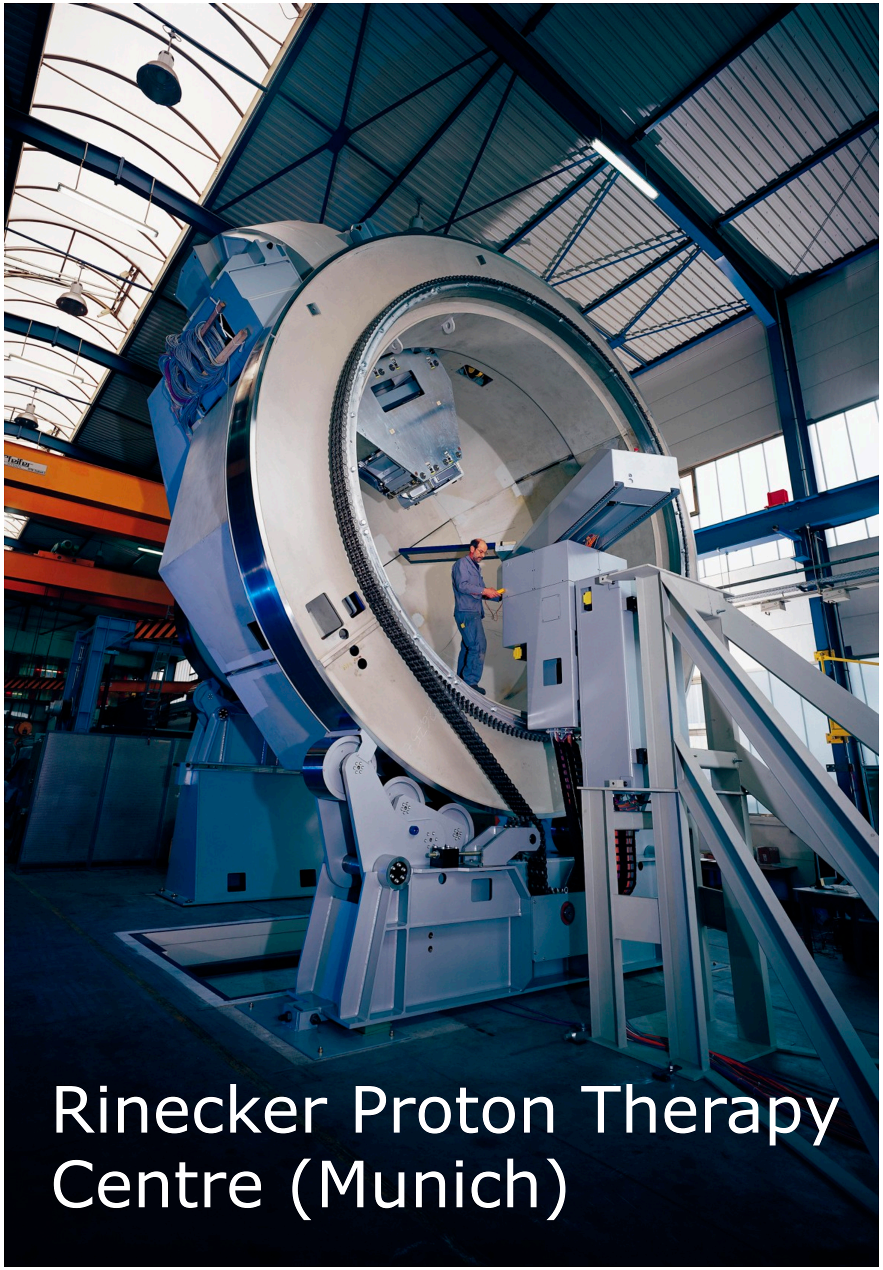
- Treatment rooms use gantries to deliver the proton beam. The gantries can be rotated 360 degrees to deliver the beam at the angles prescribed by the physician, *within a few mm isocenter.*



Gantries

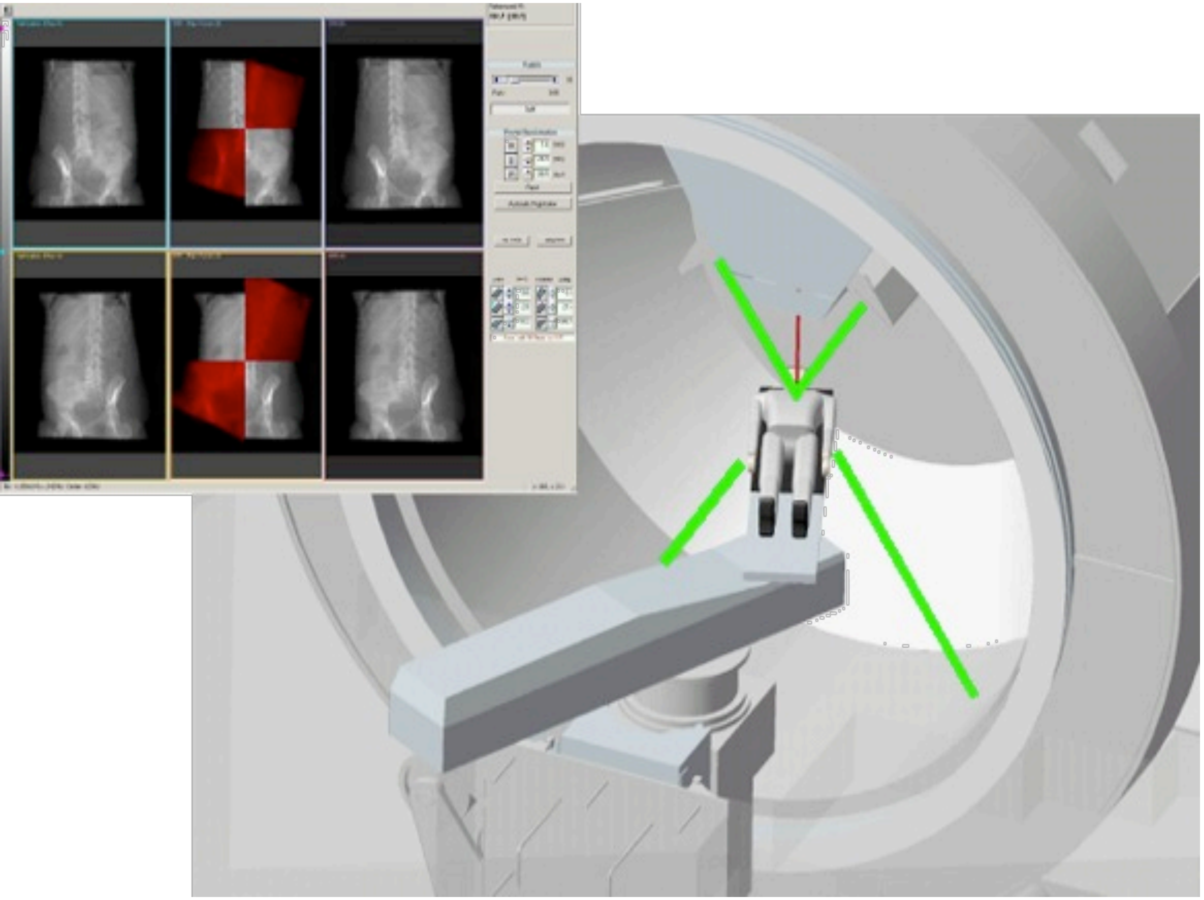
- Most of the ~40 ft. tall, 90 ton, gantry is concealed by the walls and floor of the treatment room--the patient only sees the front of the proton nozzle rotating prior to treatment

- The gantry supports the bending and focusing magnets, vacuum system, and all equipment necessary for controlling and monitoring patient treatment.



- Or, a horizontal beam line (HBL) may be used.
- In the HBL room the patient is adjusted relative to the fixed beam to achieve proper delivery angle.
- Or, ProCure, Mevion make an “inclined beam”….

Position Verification



- 30 × 40 cm² amorphous silicon panels
- Semi-automated image matching and position correction procedure
- Only 2 X-ray axes needed
- Position correction possible for any treatment position
- **Total accuracy: ± 0.5 mm**

Lasers also standard, 4D gating technologies being implemented, plus on-board CT,….

Hampton University Proton Therapy Institute

~\$200M project

Construction started 7/2007, First patient 8/2010

One of two largest in the nation / world

At maximum capacity, can treat >150 patients / day

4 gantries, fixed beam room, *dedicated research line*

We've come a long way!

Patient Treatments 1974-2002

Patient Treatments 2016

Thank You!

Daily Press | ARTICLE COLLECTIONS

Hampton University Proton Therapy center treats its first pediatric patient January 05, 2011

"Reagyn was admitted to the hospital…..the tumor was inoperable because of its location — in the part of the brain that controls balance, heart rate, swallowing and breathing…."

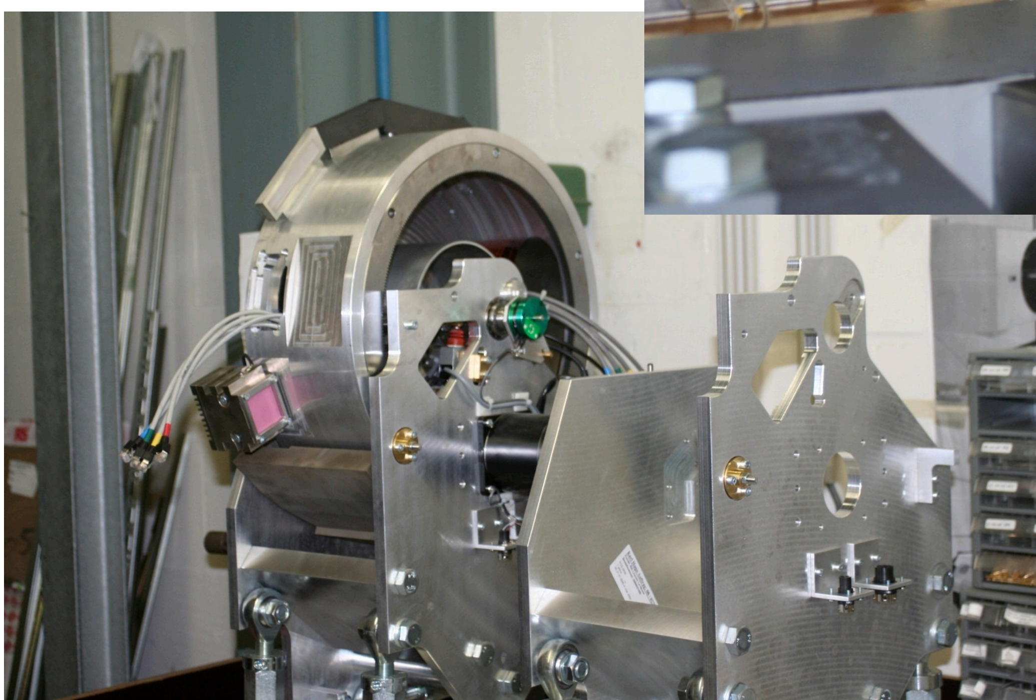
Hampton University Proton Therapy Institute

95% equipment on site for all 5 treatment rooms

Beam line installation complete

Gantry superstructures complete

Beam delivered of cyclotron March 2009

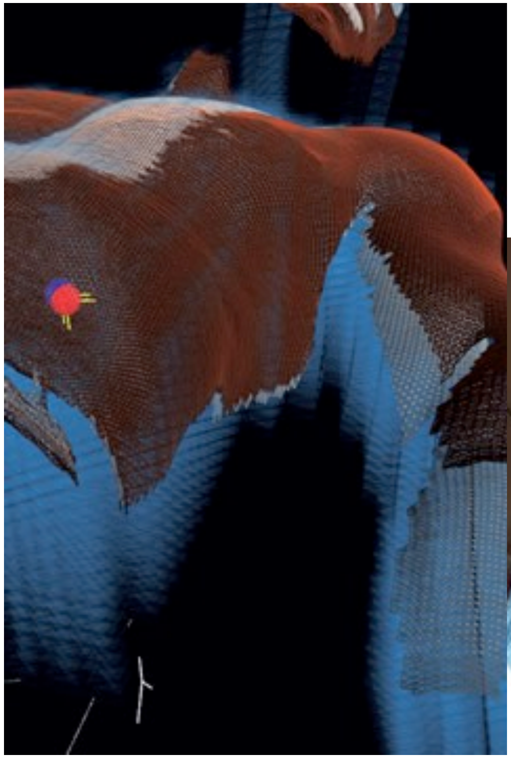


Medulloblastoma

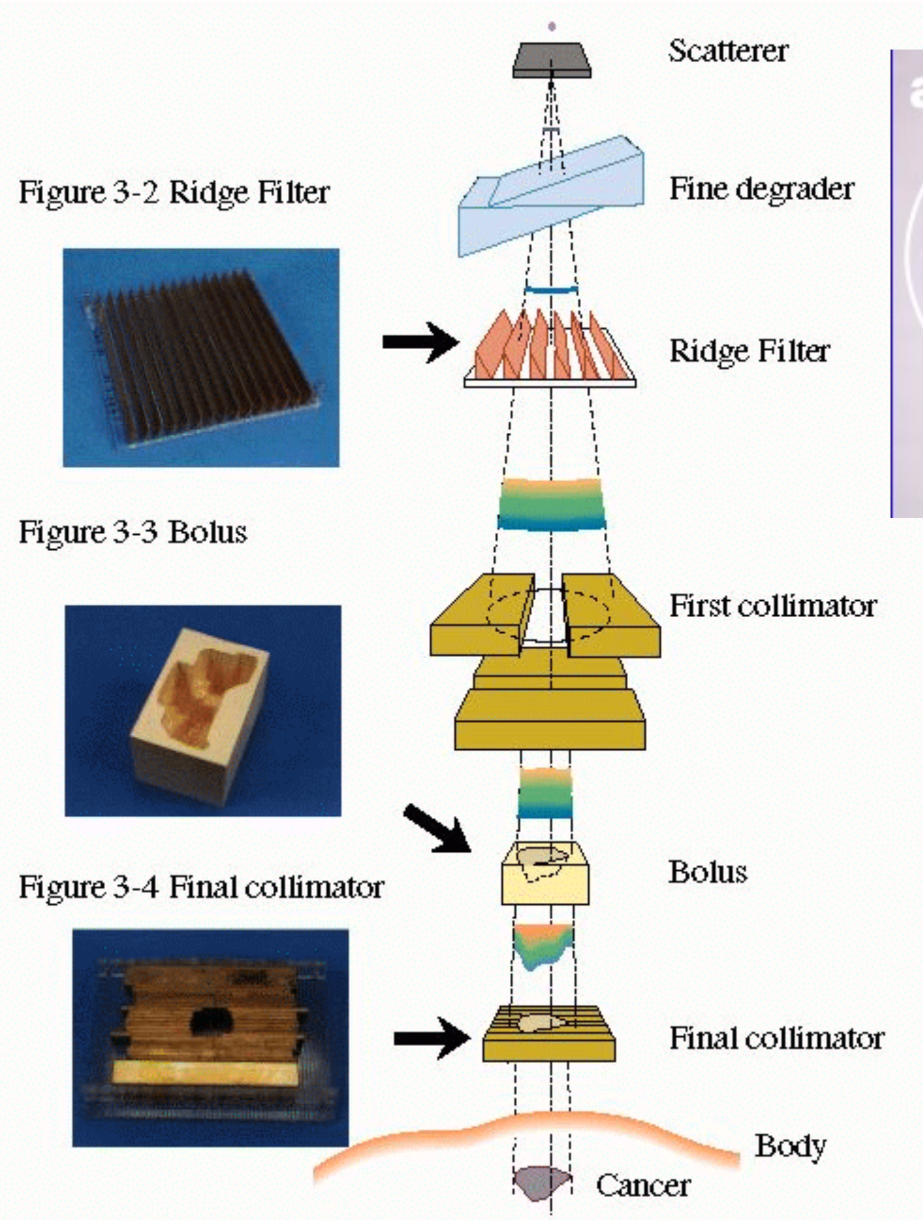
Most common malignant brain tumor in children under 20
•3350 new cases in the United States each year
•IDevelops in the part of the brain that controls balance and coordination
•IA fast-growing cancer that often spreads to the central nervous system
•44% of medulloblastoma patients are diagnosed before the age of 5
•TConventional treatment begins with maximal resection of the tumor and the addition of radiation to the entire neuraxis. Chemotherapy may increase the disease-free survival.
•5 5 year survival in more than 80% of cases

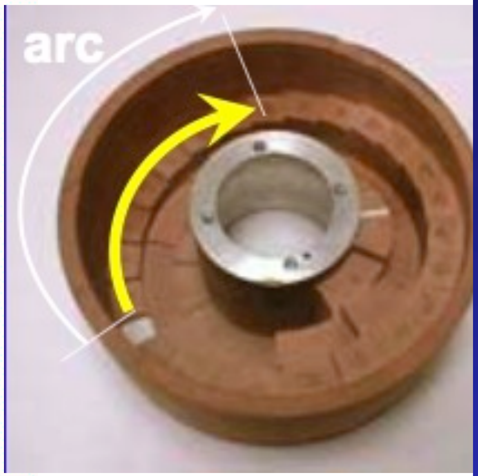
Treatment Planning

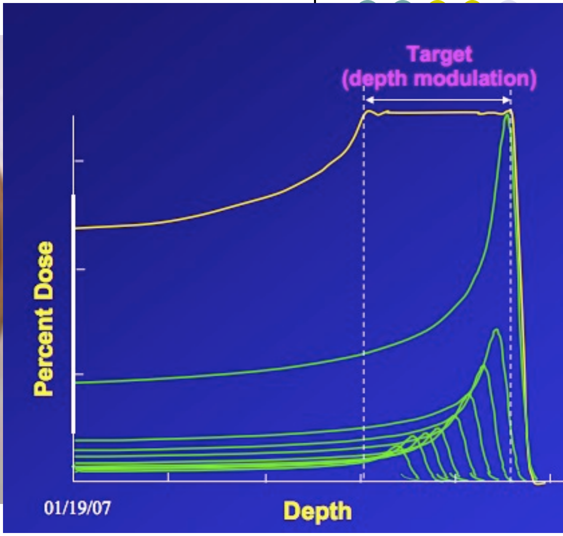
- Proton rounds (weekly)
  - Physician discussion, decision, and prescription
  - Patient position
  - Immobilization
  - Testing or technical hurdles
  - "Interesting" issues (AVM glue, pacemaker / defibrillator in field, prostheses,…!…)
  - Patient-specific concerns



Beam Delivery - Many Options







Range modulator, provides spread out Bragg peak (uniform 3D dose)

Alternative: "Pencil Beam Scanning (PBS)" - rastering, removes degraders, minimizes neutron dose….

Trends in Five-year Relative Survival (%)* Rates, US, 1975-2004

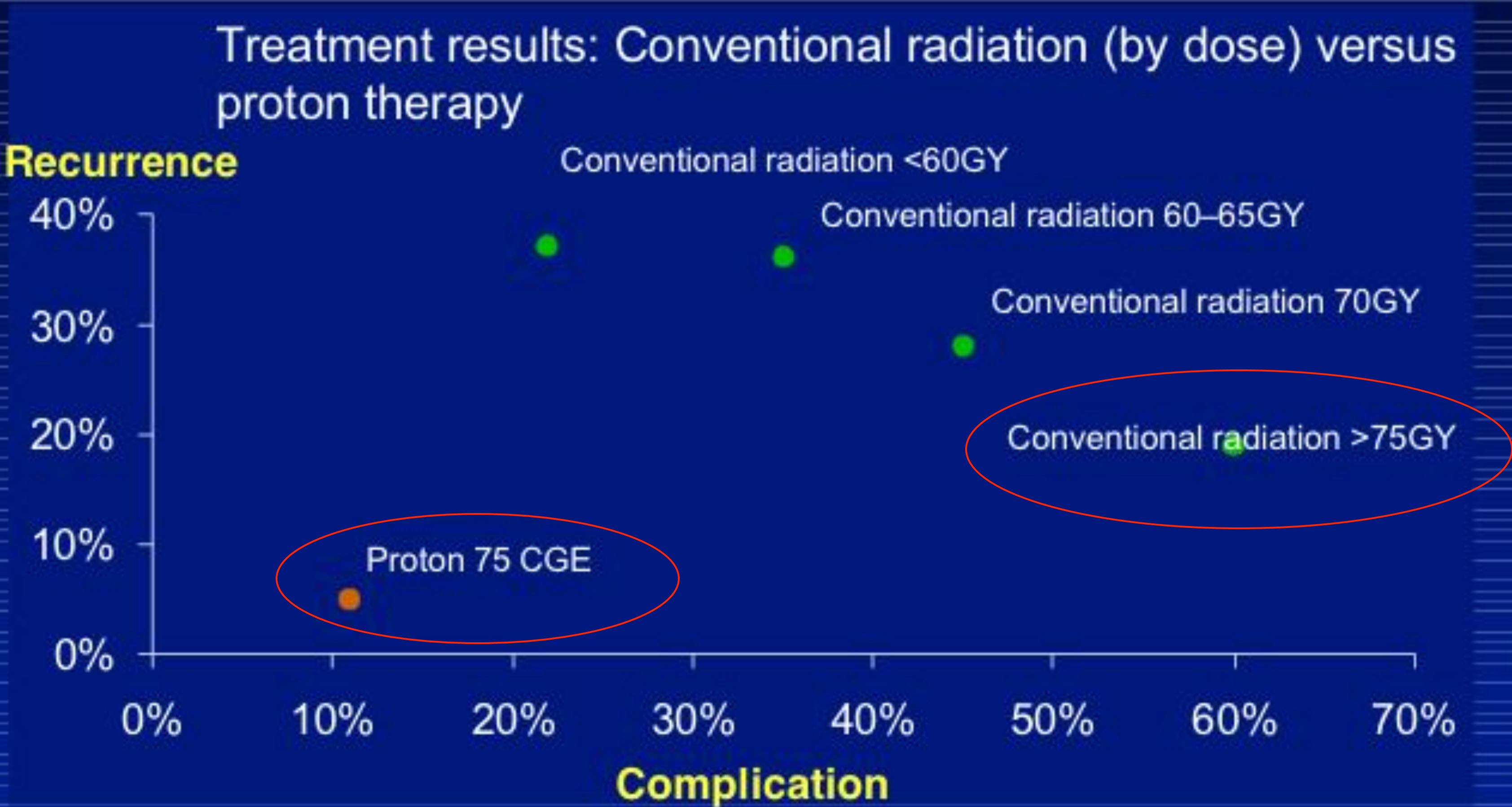
Site	1975-1977	1984-1986	1996-2004
• All sites	50	54	66
• Breast (female)	75	79	89
• Colon	52	59	65
• Leukemia	35	42	51
• Lung and bronchus	13	13	16
• Melanoma	82	87	92
• Non-Hodgkin lymphoma	48	53	65
• Ovary	37	40	46
• Pancreas	3	3	5
• Prostate	69	76	99
• Rectum	49	57	67
• Urinary bladder	74	78	81

Technological advancements are making an impact!

***5-year relative survival rates based on follow up of patients through 2005.**
Source: Surveillance, Epidemiology, and End Results Program, 1975-2005, Division of Cancer Control and Population Sciences, National Cancer Institute, 2008.

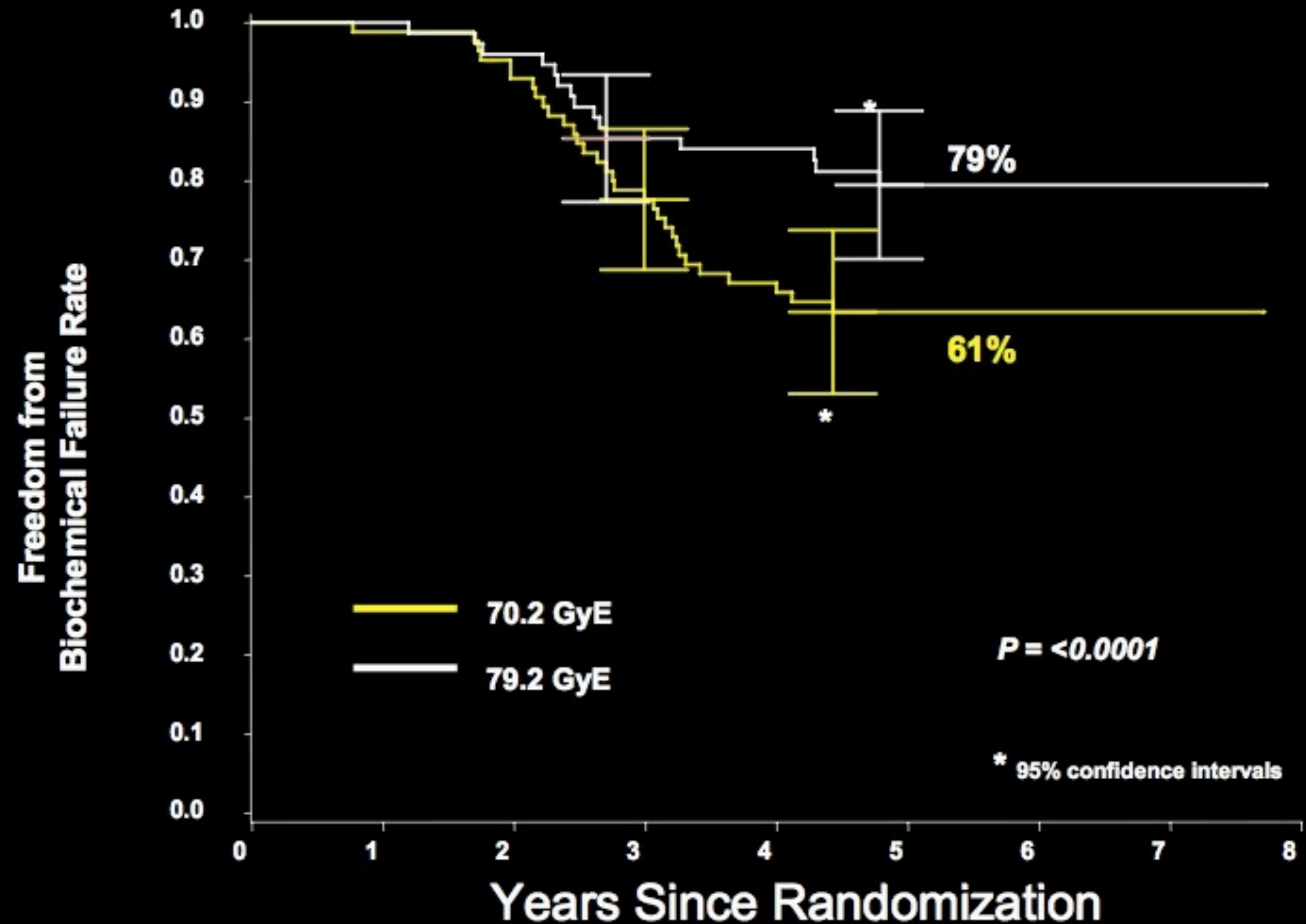
Proton results: Locally advanced prostate cancer

Loma Linda University Medical Center clinical results



f. presentation Dr. N. Mendenhall, University of Florida

Improved Freedom from Biochemical Failure (PSA)

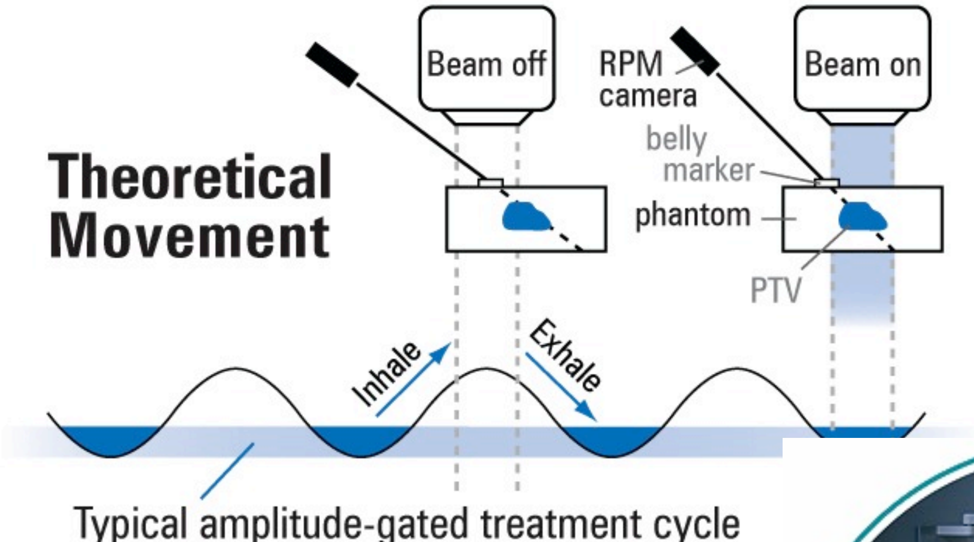


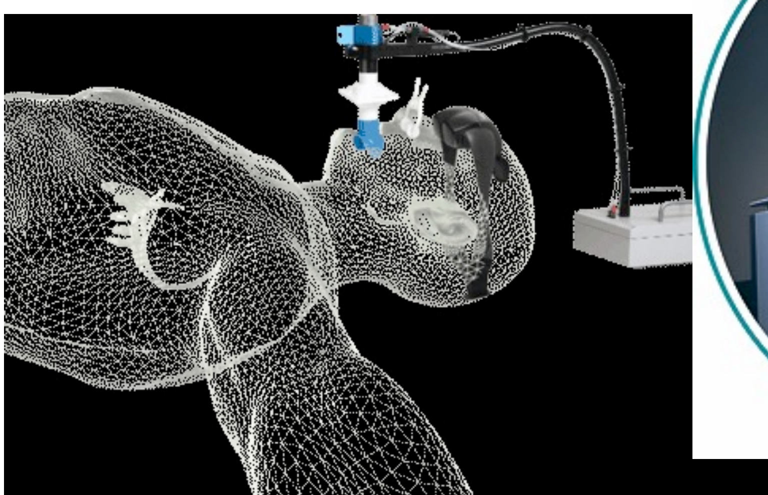
# at risk									
70.2 GyE	197	196	171	139	118	76	31	10	10
79.2 GyE	195	194	184	163	148	99	46	20	2

Zietman et al 2005

Respiration Gating

Many options in development to account for tumor and organ motion – lung, breast, liver,…





Breath hold

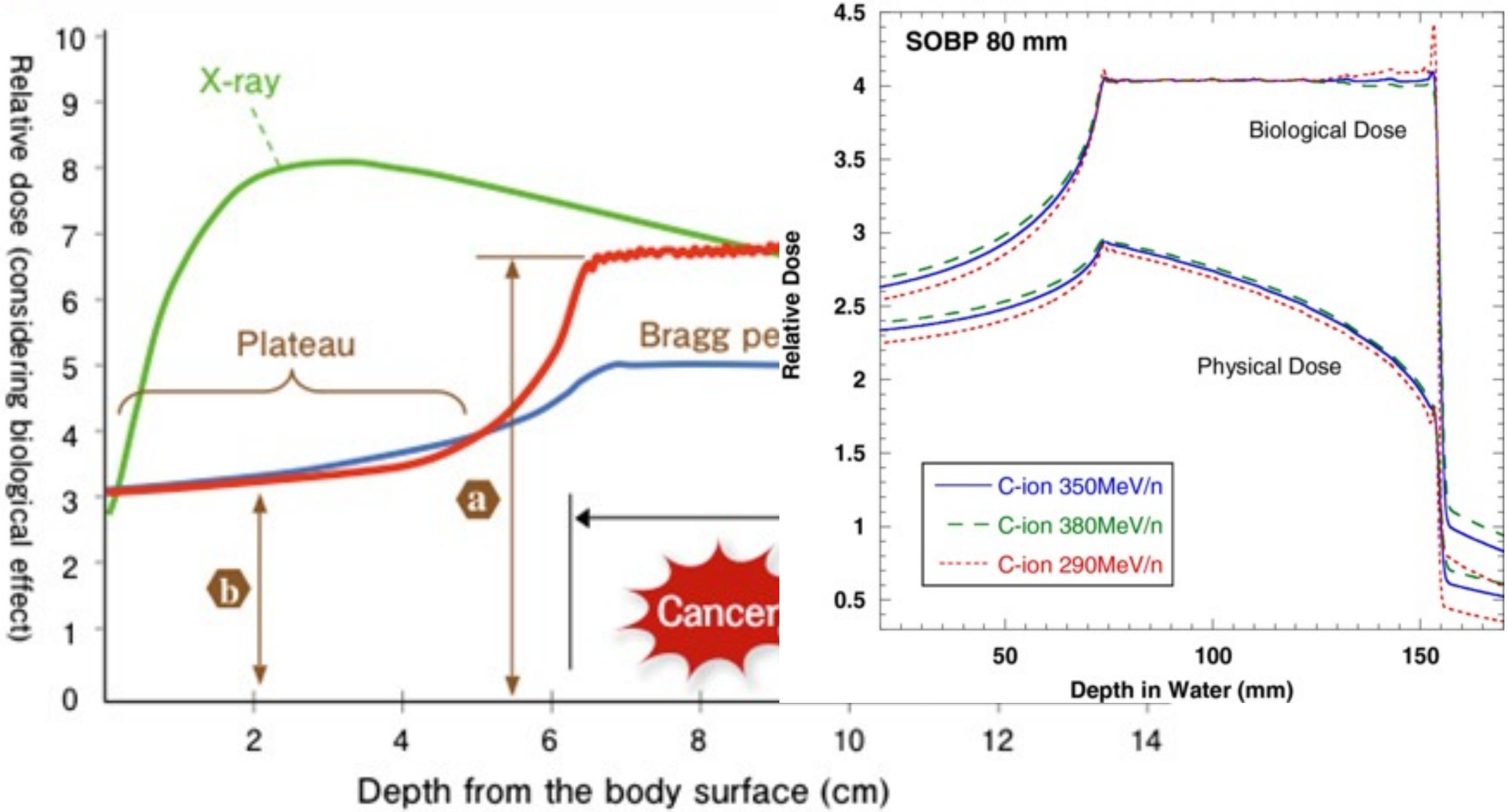
Video capture

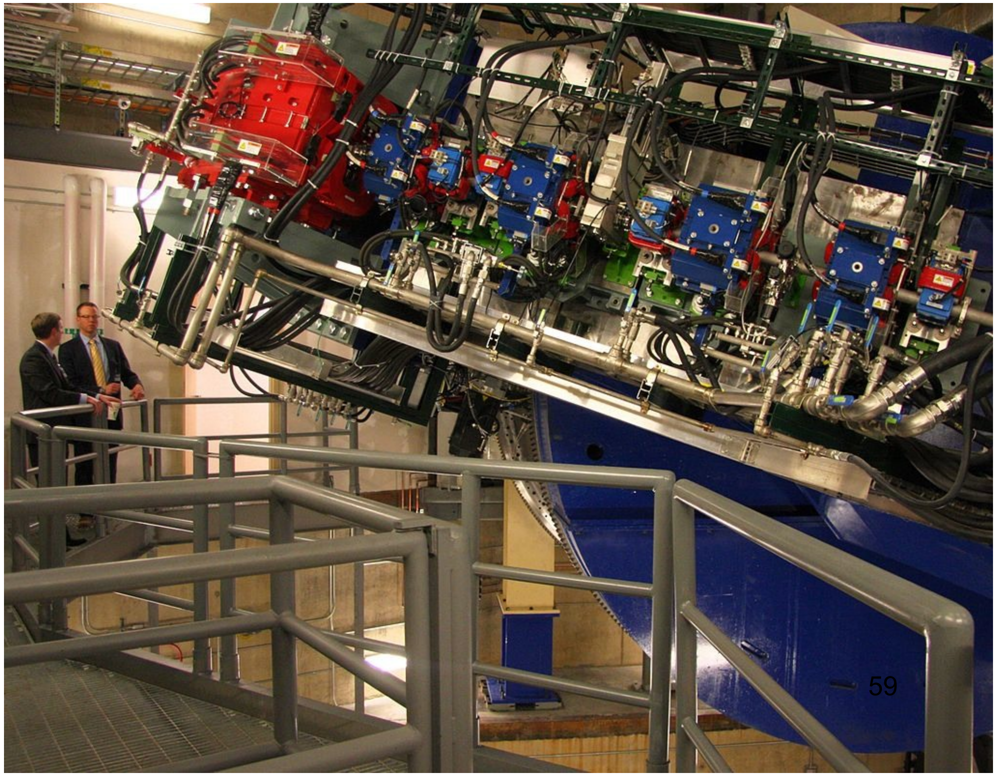
Spirometry

Laser interferometry

Other sites / technologies!

When the ratios of peak to plateau (a/b) are compared while considering biological effect, the carbon beam has the largest value.





PET Image Beam Path Through Patient

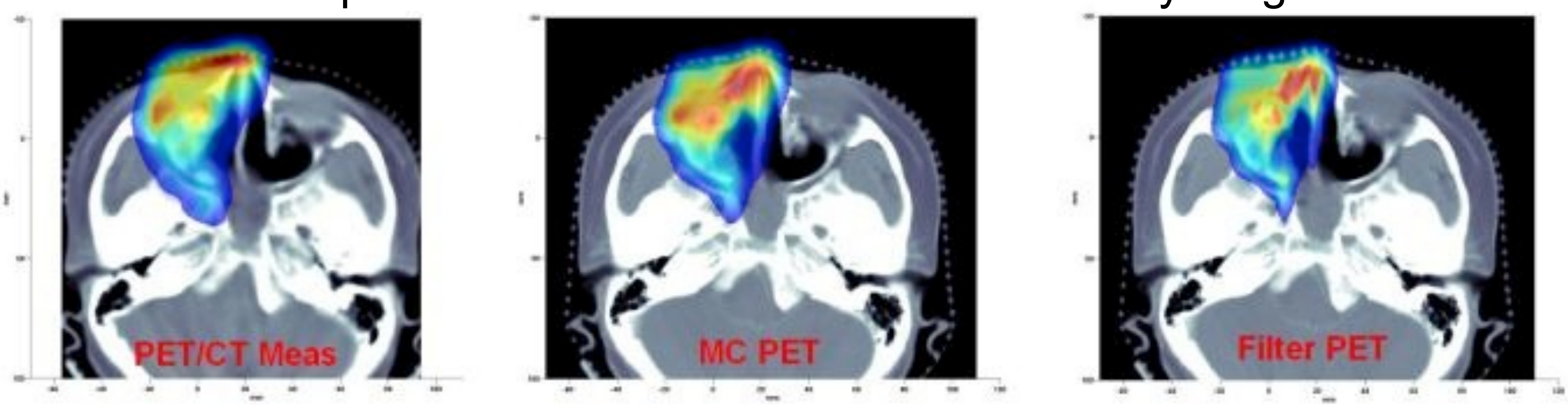
No Injection! Detect annihilation gamma-rays following the decay of positron emitting nuclei (^{11}C and ^{15}O), produced via nuclear reactions between tissue and the impinging ions

Dose verification - difficult:

- No unique correlation between dose and activity distribution
- Patient and tissue specific activity
- Wash-out

Range verification - promising:

- Unique correlation between dose and activity range



Parodi K, et al; Int J Radiat Oncol Biol Phys. 2007 Jul 1;68(3):920-34, Medical Physics 2007: 34, 419-435, Phys Med Biol. 2006 Apr 21;51(8):1991-2009