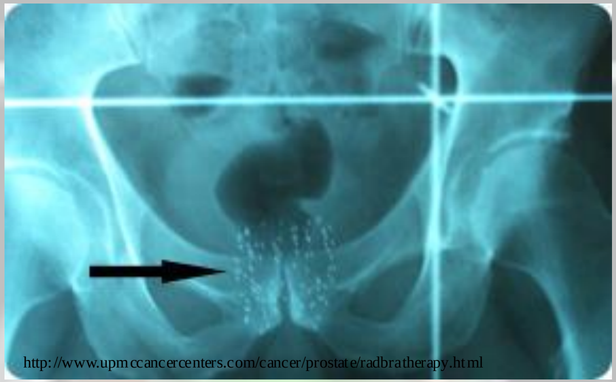
Radiation Safety, Brachytherapy & Proton Therapy for the treatment of Cancer

http://www.uos.harvard.edu/ehs/radiation/how_dosimeter.shtml



http://www.upmccancercenters.com/cancer/prostate/radbratherapy.html

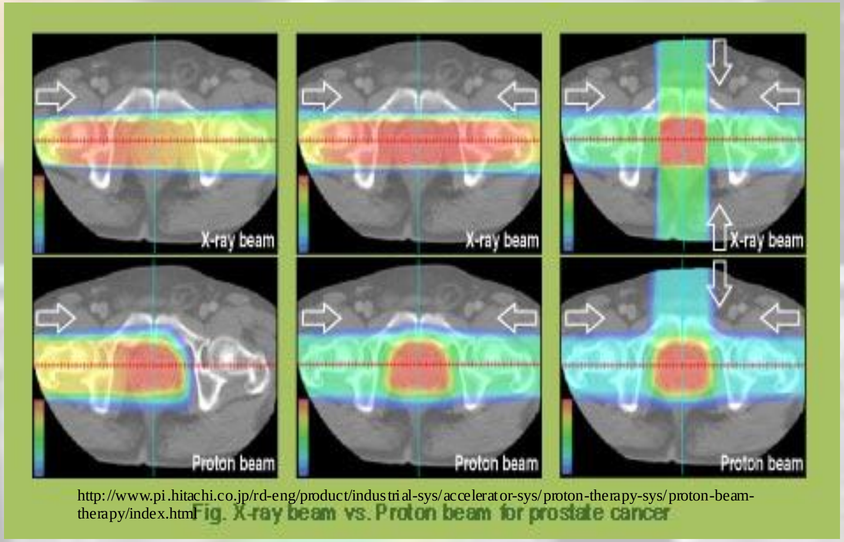
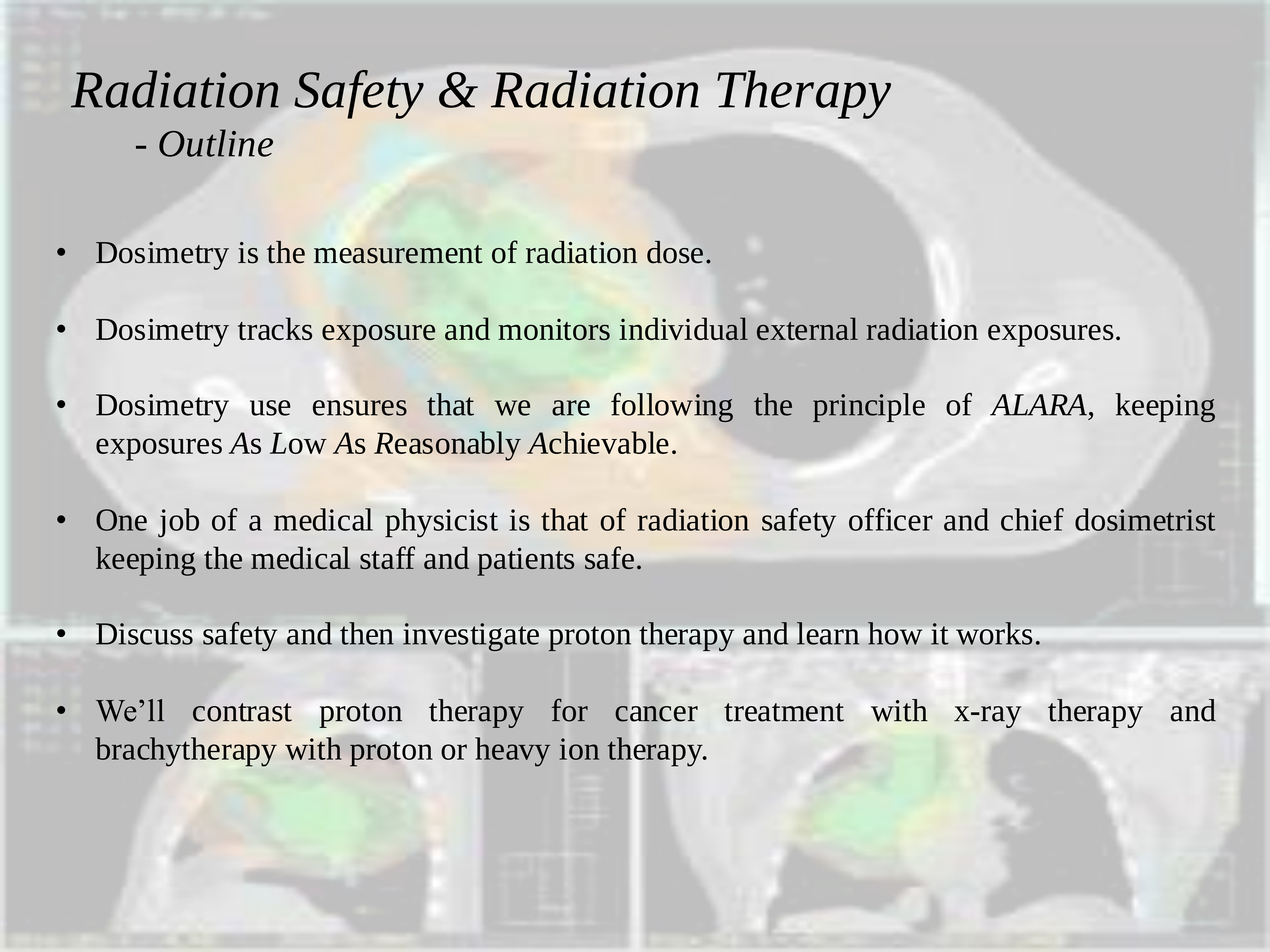


Fig. X-ray beam vs. Proton beam for prostate cancer

http://www.pi.hitachi.co.jp/rd-eng/product/industrial-sys/accelerator-sys/proton-therapy-sys/proton-beam-therapy/index.html



Radiation Safety & Radiation Therapy

- Outline

- Dosimetry is the measurement of radiation dose.

- Dosimetry tracks exposure and monitors individual external radiation exposures.

- Dosimetry use ensures that we are following the principle of *ALARA*, keeping exposures *A*s *L*ow *A*s *R*easonably *A*chievable.

- One job of a medical physicist is that of radiation safety officer and chief dosimetrist keeping the medical staff and patients safe.

- Discuss safety and then investigate proton therapy and learn how it works.

- We’ll contrast proton therapy for cancer treatment with x-ray therapy and brachytherapy with proton or heavy ion therapy.

Radiation Safety

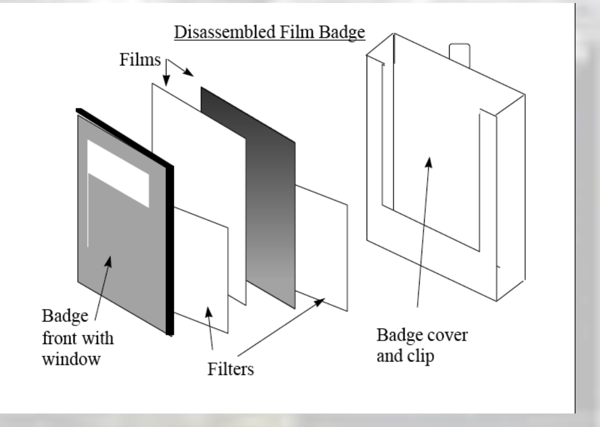
- Film Dosimeters

- Film dosimeters, or film badges, consist of layered components.

- Imagine a sandwich with the following layers starting from the top:
    - the *badge front, with a* window for exposure;
    - *filters that selectively filter* out certain types of radiation;
    - *films to detect the* radiation;
    - more *filters* perhaps;
    - *then the badge cover and clip* to attach the dosimeter to the individual's clothing.

- After a designated period of exposure, the film is taken out of the "sandwich" badge, developed, and read on a *densitometer,* which reads the amount of darkening on the film.

- The amount of darkening is proportional to the radiation exposure.



Radiation Safety

- Film Dosimeters

- The Luxel body badge contains a sheet of radiation-sensitive aluminum oxide sealed in a light and moisture proof packet. When atoms in the aluminum oxide sheet are exposed to radiation, electrons are trapped in an excited state until irradiated with a specific wavelength of laser light. The released energy of excitation, which is given off as visible light, is measured to determine radiation dose.

- The packet contains a series of filters designed so that the energy and type of radiation can be determined.

- For the radiation type and energy to be determined, the dosimeter must be worn so that the front of the dosimeter faces towards the source of radiation. Luxel Body dosimeters are among the most sensitive dosimeters available. The minimum detectable dose is 10 μGy (1 millirem) for x-rays and gamma rays and 0.1mGy (10 millirem) for energetic beta radiation.

http://www.uos.harvard.edu/ehs/radiation/how_dosimeter.shtml

Radiation Safety

- *Film Dosimeters*

- Dosimetry film badges are commonly used to measure and record radiation exposure due to gamma rays, x-rays and beta particles. The detector is, as the name implies, a piece of radiation sensitive film.

- The film is packaged in a light proof, vapor proof envelope preventing light, moisture or chemical vapors from affecting the film.

- A special film is used which is coated with two different emulsions. One side is coated with a large grain, fast emulsion that is sensitive to low levels of exposure. The other side of the film is coated with a fine grain, slow emulsion that is less sensitive to exposure. If the radiation exposure causes the fast emulsion in the processed film to be darkened to a degree that it cannot be interpreted, the fast emulsion is removed, and the dose is computed using the slow emulsion.

http://www.uos.harvard.edu/ehs/radiation/how_dosimeter.shtml

Radiation Safety

- Film Dosimeters

- The film is contained inside a film holder or badge. The badge incorporates a series of filters to determine the quality of the radiation.
- Radiation of a given energy is attenuated to a different extent by various types of absorbers. Therefore, the same quantity of radiation incident on the badge will produce a different degree of darkening under each filter. By comparing these results, the energy of the radiation can be determined, and the dose can be calculated knowing the film response for that energy.
- The badge holder also contains an open window to determine radiation exposure due to beta particles. Beta particles are effectively shielded by a thin amount of material.

http://www.uos.harvard.edu/ehs/radiation/how_dosimeter.shtml

Radiation Safety

- Film Dosimeters

Advantages

- The dose measurements for various film badges range between 0.1mGy – 15mGy (10 mrem to 1500 mrem) for gamma and x-radiation, and 0.5mGy – 10mGy (50 mrem to 1000 rem) for beta radiation.

- Film badges can distinguish between penetrating radiation (high, medium, and low photon energies) and non-penetrating radiation (beta and x-ray radiation less than 20 keV).

- Film dosimeters are practical because they are small, lightweight, and relatively inexpensive.

Disadvantages

- The response of the film to radiation is energy dependent; at energies less than 300 keV, the response tends to increase.

- The films cannot be read immediately and provide no radiation protection.

- Environmental conditions such as heat, and humidity will affect the film’s response to radiation.

- Film badges may be left or lost at a site of a radiation accident.

- They may be contaminated with radioactive materials, which will lead to a false higher result.

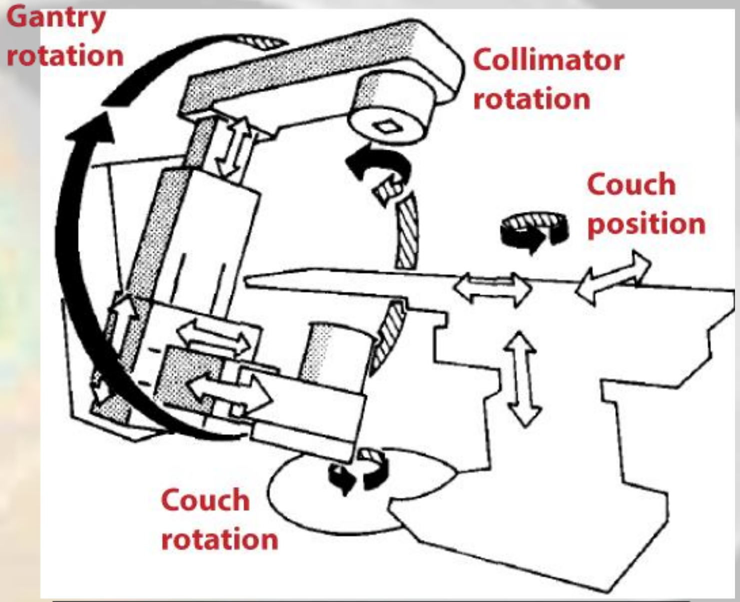
Radiation Therapy

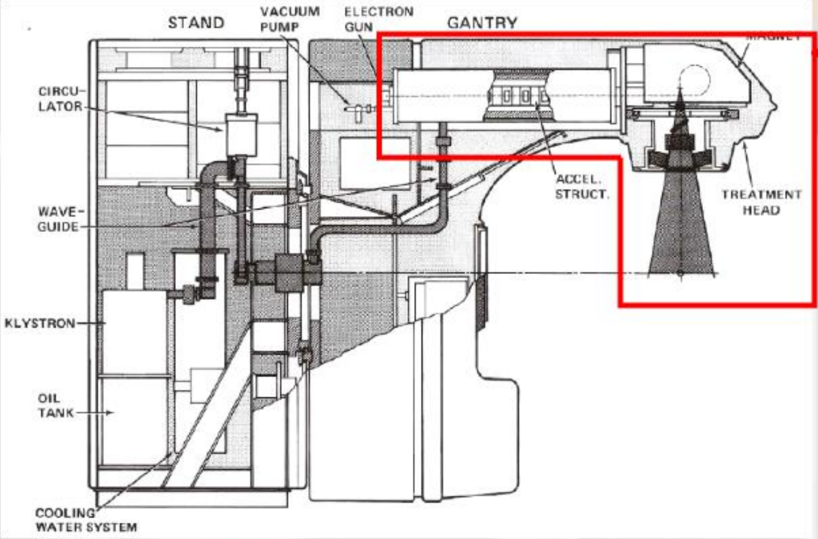
- Radiation Therapy (or Radiotherapy) is the treatment of disease (usually cancer) using very high doses of ionizing radiation in the form of x-rays or particle radiation to kill cancer cells or shrink tumors.

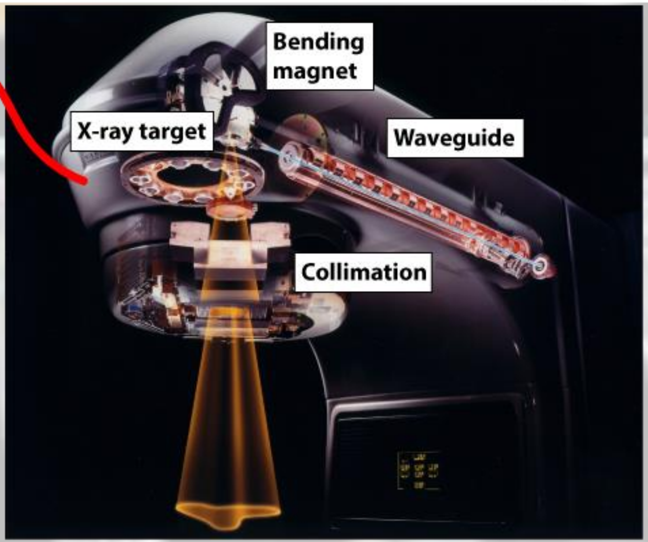
Images courtesy of Dr. Tom Mazur, PhD., DABR

Radiation Therapy

- Treatment with photons and electrons



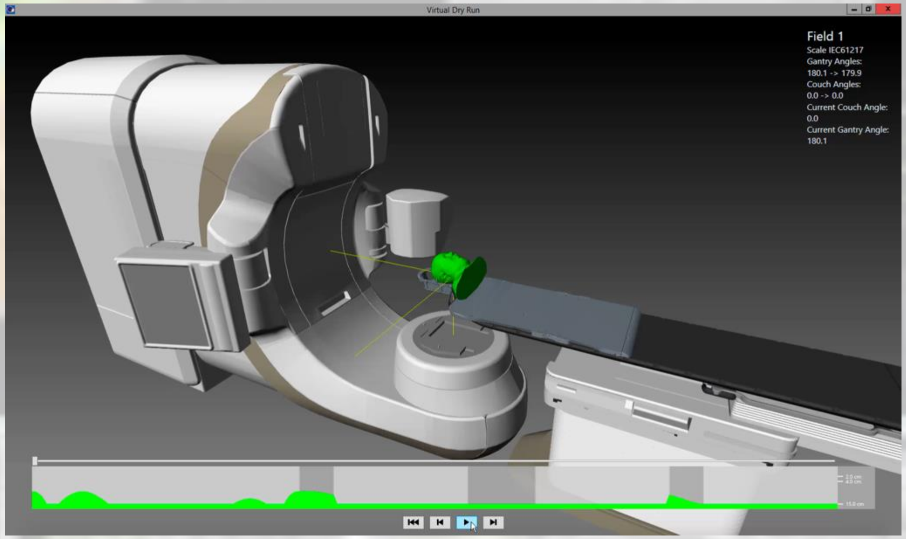




C.J. Karzmark, R.J. Morton. A Primer on Theory and Operation of Linear Accelerators in Radiation Therapy

Radiation Therapy

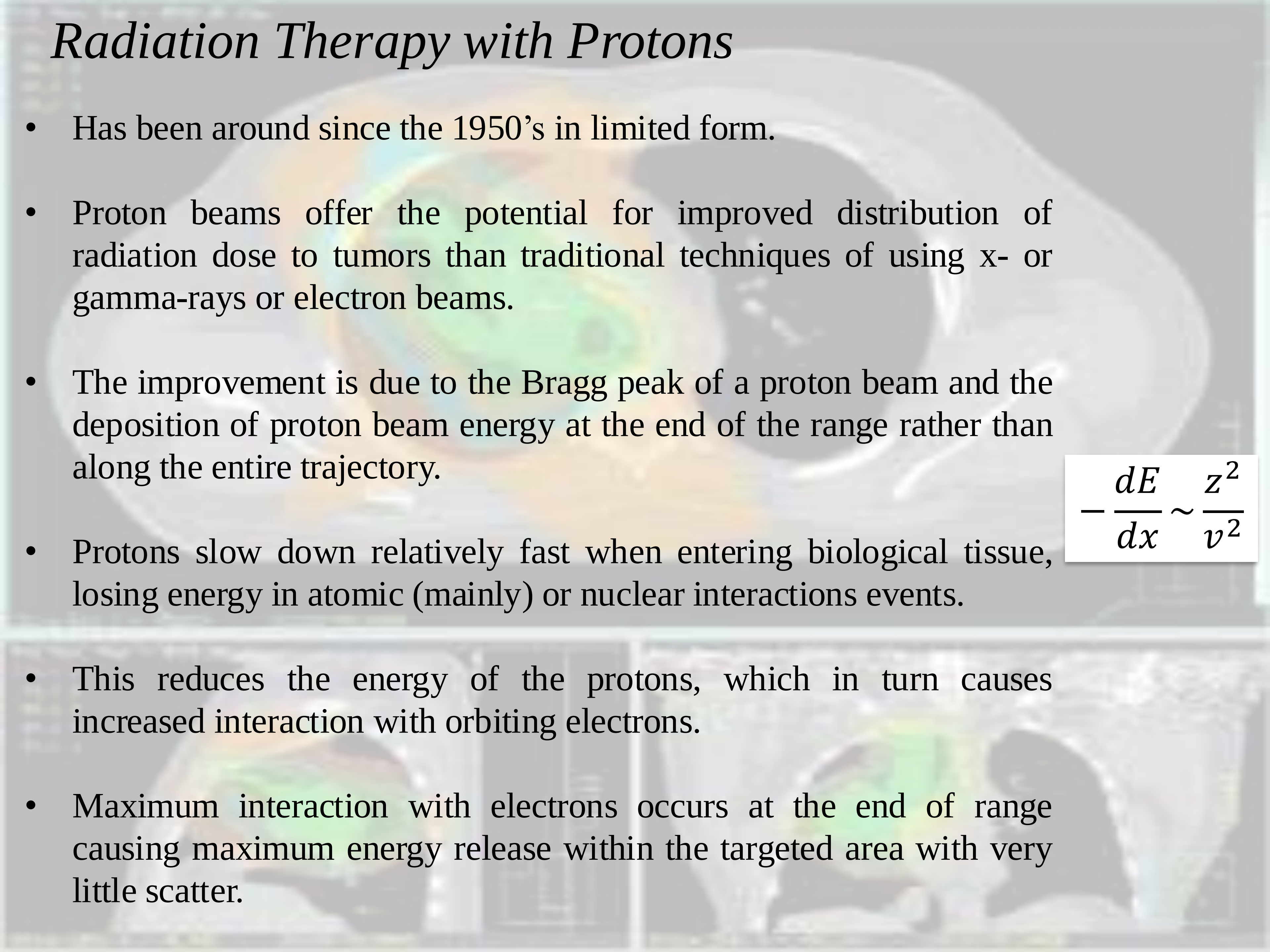
- Treatment with photons and electrons


Virtual Dry Run

Field 1
Scale IEC61217
Gantry Angles:
180.1 -> 179.9
Couch Angles:
0.0 -> 0.0
Current Couch Angle:
0.0
Current Gantry Angle:
180.1

Video simulations courtesy of Dr. Tom Mazur, Assistant Professor of Radiation Oncology, Washington University in St. Louis

Radiation Therapy with Protons

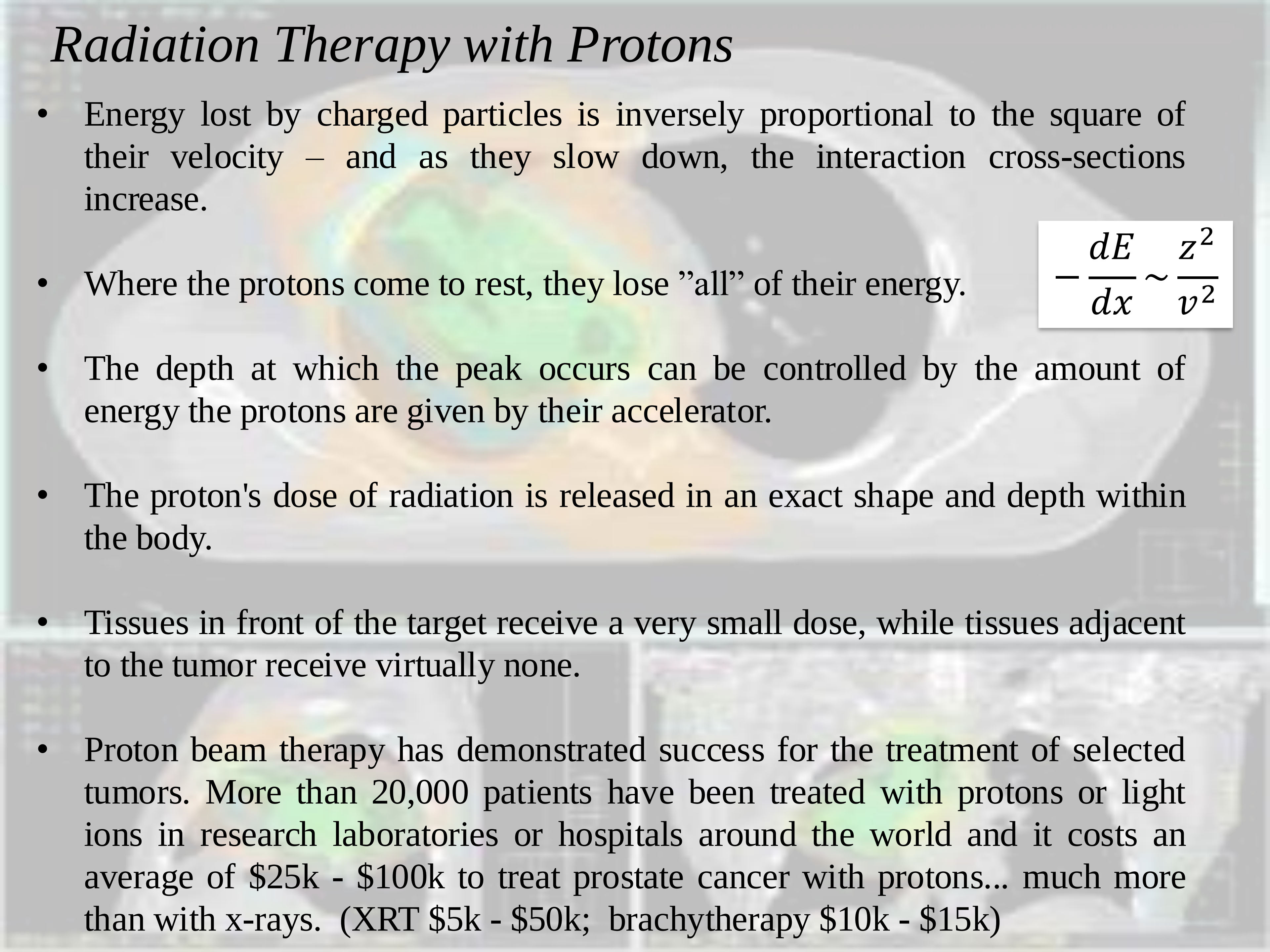


- Has been around since the 1950’s in limited form.
- Proton beams offer the potential for improved distribution of radiation dose to tumors than traditional techniques of using x- or gamma-rays or electron beams.
- The improvement is due to the Bragg peak of a proton beam and the deposition of proton beam energy at the end of the range rather than along the entire trajectory.

$$-\frac{dE}{dx} \sim \frac{z^2}{v^2}$$

- Protons slow down relatively fast when entering biological tissue, losing energy in atomic (mainly) or nuclear interactions events.
- This reduces the energy of the protons, which in turn causes increased interaction with orbiting electrons.
- Maximum interaction with electrons occurs at the end of range causing maximum energy release within the targeted area with very little scatter.

Radiation Therapy with Protons



- Energy lost by charged particles is inversely proportional to the square of their velocity – and as they slow down, the interaction cross-sections increase.

- Where the protons come to rest, they lose ”all” of their energy.

$$-\frac{dE}{dx} \sim \frac{z^2}{v^2}$$

- The depth at which the peak occurs can be controlled by the amount of energy the protons are given by their accelerator.

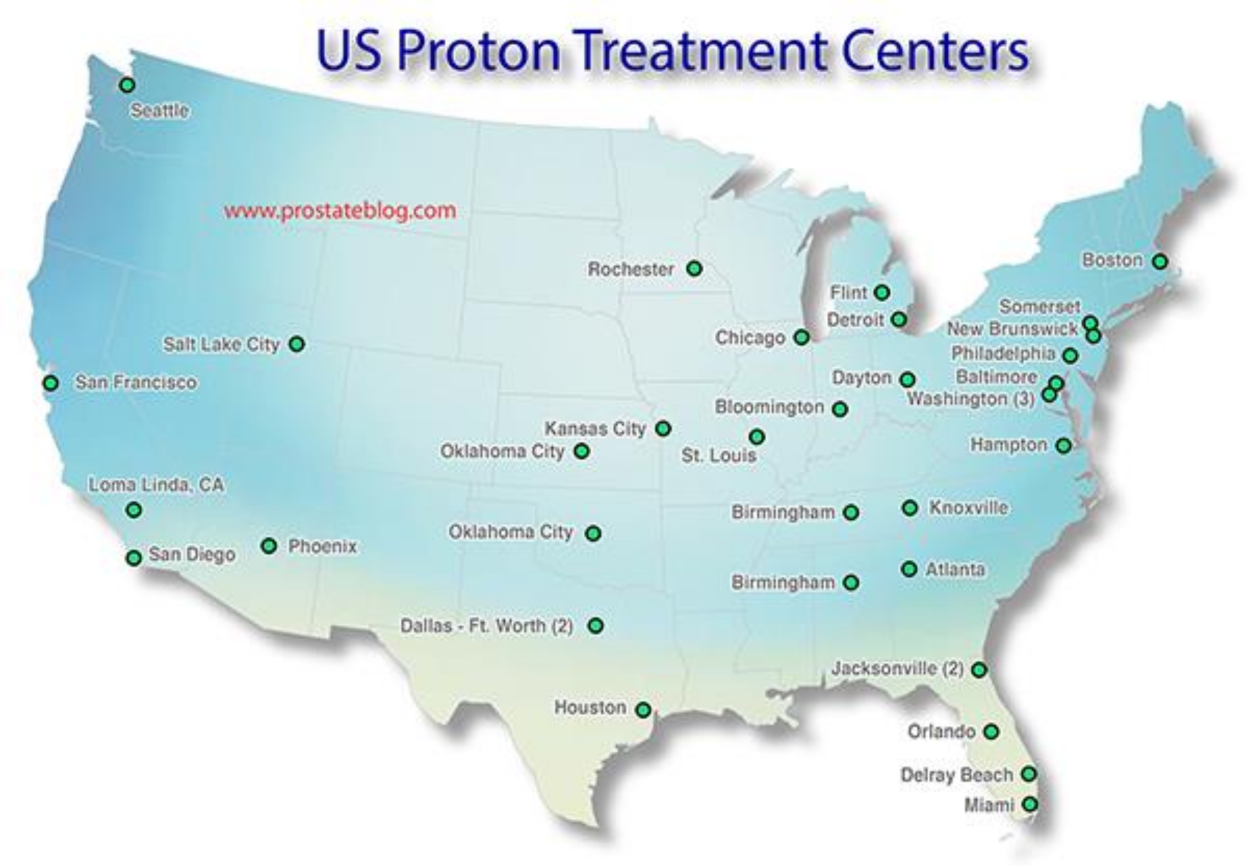
- The proton's dose of radiation is released in an exact shape and depth within the body.

- Tissues in front of the target receive a very small dose, while tissues adjacent to the tumor receive virtually none.

- Proton beam therapy has demonstrated success for the treatment of selected tumors. More than 20,000 patients have been treated with protons or light ions in research laboratories or hospitals around the world and it costs an average of $25k - $100k to treat prostate cancer with protons... much more than with x-rays. (XRT $5k - $50k; brachytherapy $10k - $15k)

Radiation Therapy with Protons

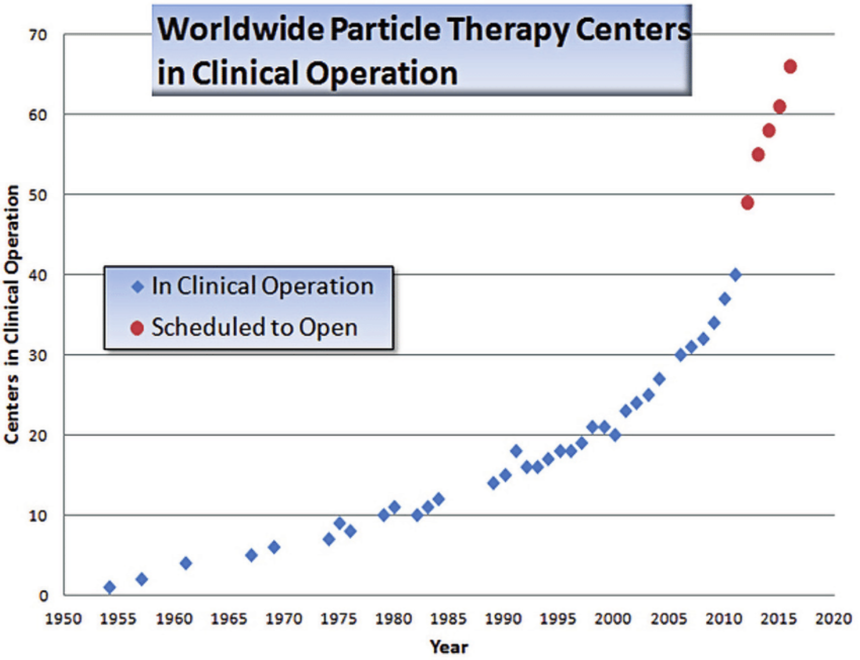
The number of proton therapy centers around the US has consistently risen over time.



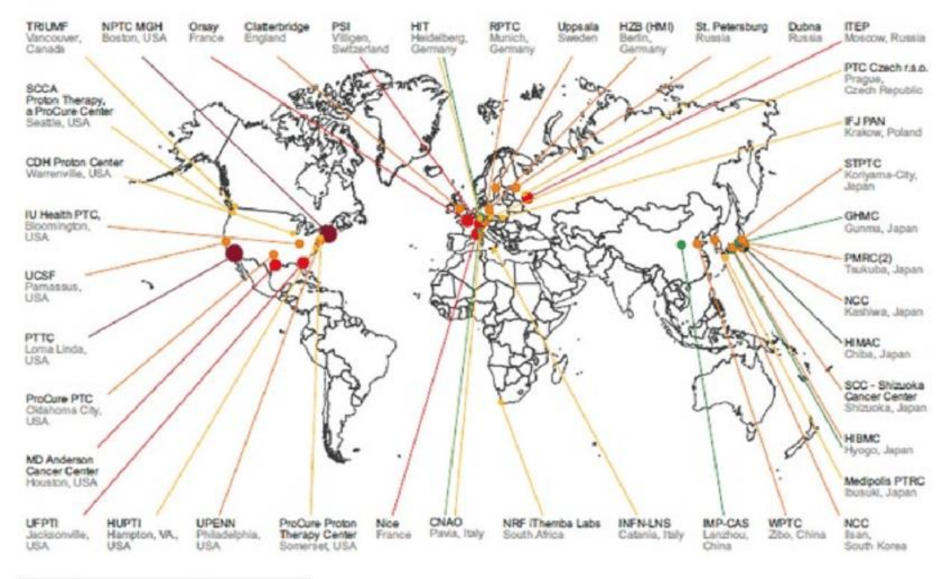
http://www.prostateblog.com/

Radiation Therapy with Protons

The number of proton therapy centers around the world has consistently risen over time.

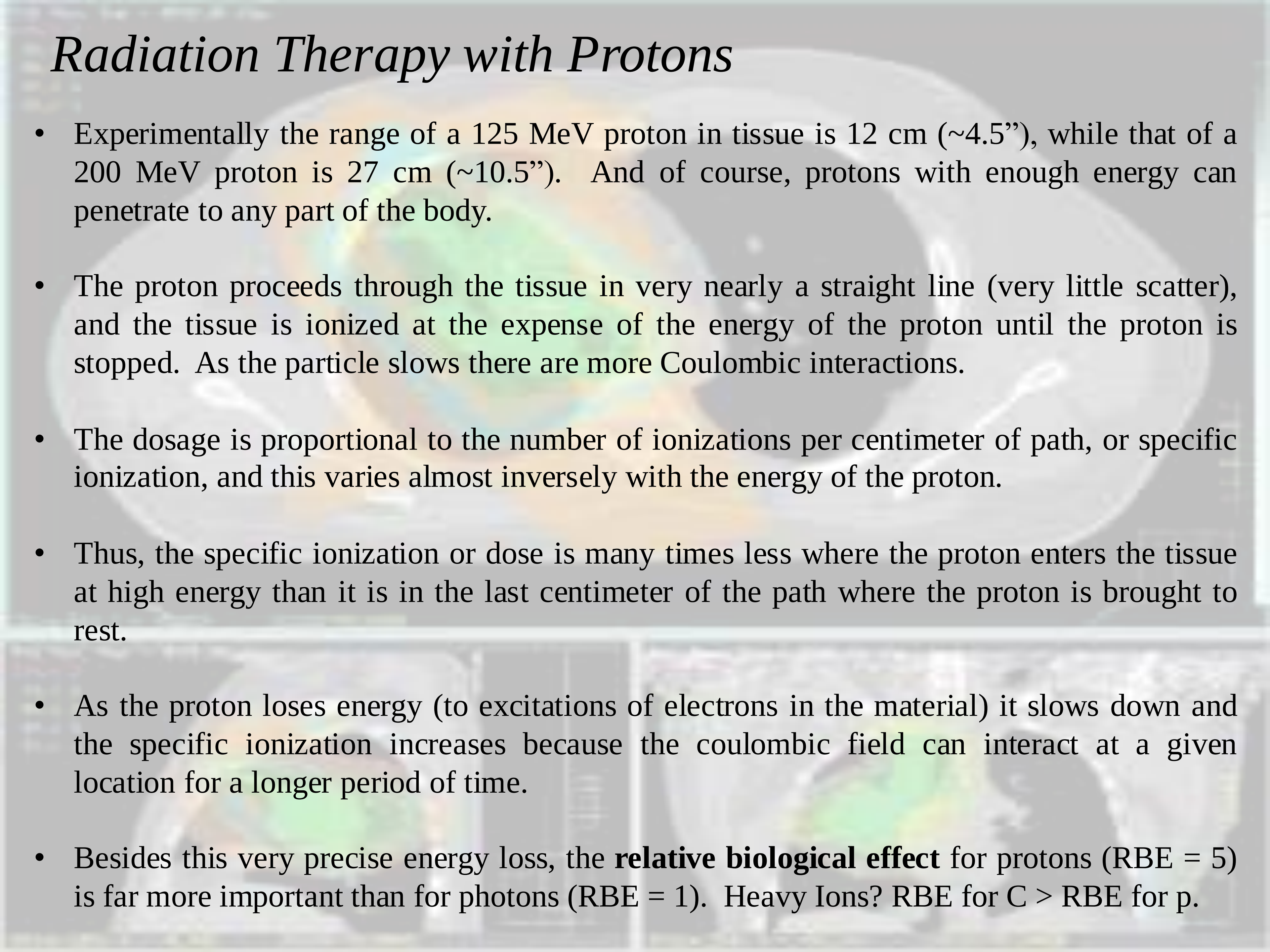


Azimi, Parisa & Movafeghi, Amir. (2016). Proton Therapy in Neurosurgery: A Historical Review and Future Perspective Based on Currently Available New Generation Systems. International Clinical Neuroscience Journal. 3. 59-80. 10.22037/icnj.v3i2.13324.



Balosso, Jacques & Baroni, Guido & Bleicher, Marcus & Brandenburg, Sytze & Burigo, Lucas & Colautti, Paolo & Combs, Univ.-Prof. Dr. Stephanie & Cuttone, Giacomo & Debus, Jürgen & De marzi, Ludovic & Dobeš, Jan & Durante, Marco & Evangelista, Laura & Fagotti, Enrico & Gales, S. & Georg, Dietmar & Graeff, Christian & Haberer, Thomas & Habrand, Jean-Louis & Wessels, Claas. (2014). Nuclear Physics for Medicine.

Radiation Therapy with Protons



- Experimentally the range of a 125 MeV proton in tissue is 12 cm (~4.5”), while that of a 200 MeV proton is 27 cm (~10.5”). And of course, protons with enough energy can penetrate to any part of the body.

- The proton proceeds through the tissue in very nearly a straight line (very little scatter), and the tissue is ionized at the expense of the energy of the proton until the proton is stopped. As the particle slows there are more Coulombic interactions.

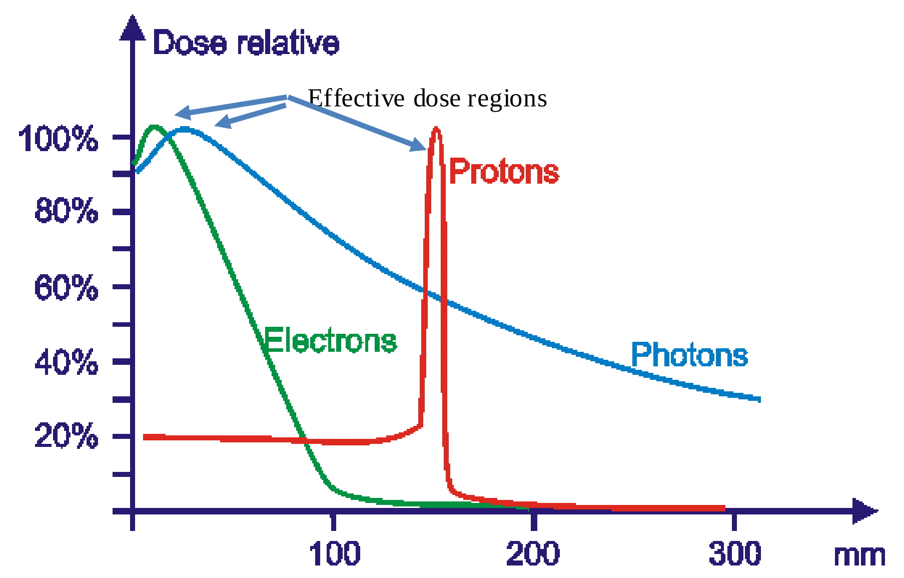
- The dosage is proportional to the number of ionizations per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton.

- Thus, the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the proton is brought to rest.

- As the proton loses energy (to excitations of electrons in the material) it slows down and the specific ionization increases because the coulombic field can interact at a given location for a longer period of time.

- Besides this very precise energy loss, the **relative biological effect** for protons (RBE = 5) is far more important than for photons (RBE = 1). Heavy Ions? RBE for C > RBE for p.

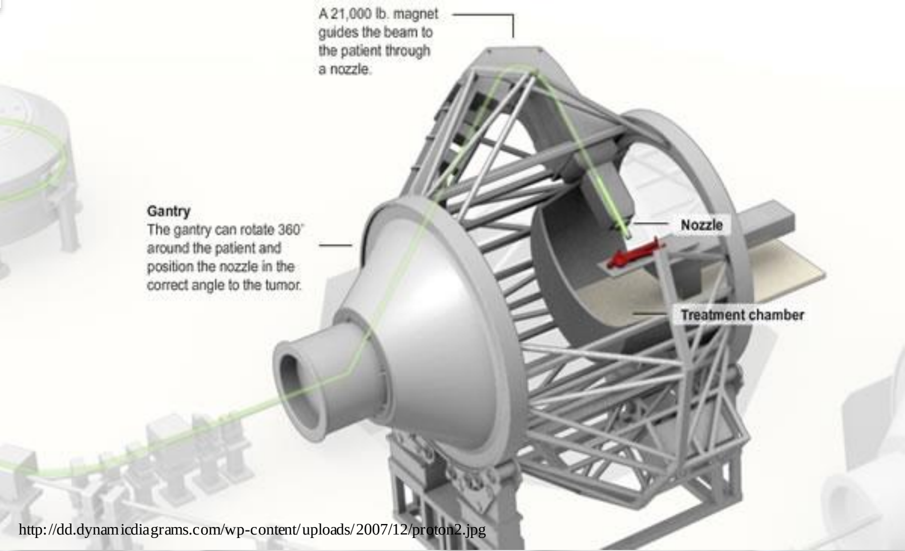
Radiation Therapy with Protons



http://www.oncoprof.net/Generale2000/g08_Radiotherapie/Images/PicBragg.gif

- The Bragg peak for electrons, protons and photons.
- By adjusting the energy of the protons, we can control the depth at which they deposit their energy.

- Protons are produced in accelerators and the accelerator ultimately determines their energy.
- The protons are steered from accelerator to patient by using large magnetic fields.



http://dd.dynamicdiagrams.com/wp-content/uploads/2007/12/proton2.jpg

Radiation Therapy with Protons

- One of the gantries at the Northeast Proton Therapy Center – a joint venture between Harvard University and Massachusetts General Hospital.
- The left picture shows the gantry structure during construction with the steel assembly being visible.
- The right picture shows the gantry treatment room during treatment.
- The beam delivery nozzle can rotate 360 degrees around the movable patient couch.

http://www.aapm.org/meetings/05AM/pdf/18-4016-65735-22.pdf

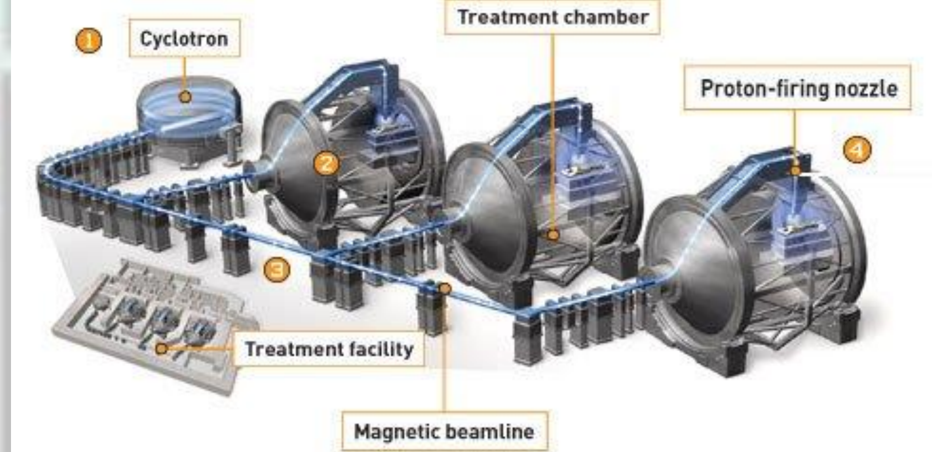
http://www.aapm.org/meetings/05AM/pdf/18-4016-65735-22.pdf

Radiation Therapy with Protons

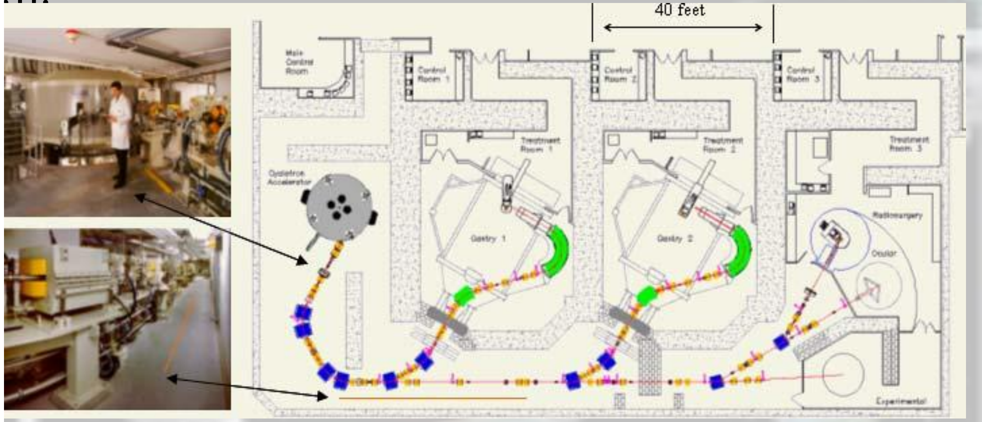
- The accelerator, which is housed in a 25,000-square-foot facility, funnels protons into a 40-foot-wide circular track known as a cyclotron. The cyclotron speeds up protons to higher energy levels.

- The patient enters one of three chambers, depending on the type of treatment, and lies on a gurney-like bed. A computer-controlled proton-firing nozzle positions itself over the target area.

- Meanwhile, magnets guide a beam of protons along the center of a long, narrow tube. The beam races toward a gantry, which rotates around the patient as its nozzle fires protons at the tumor.



http://www.popsci.com/files/imagecache/article_image_large/articles/tumor_485.jpg

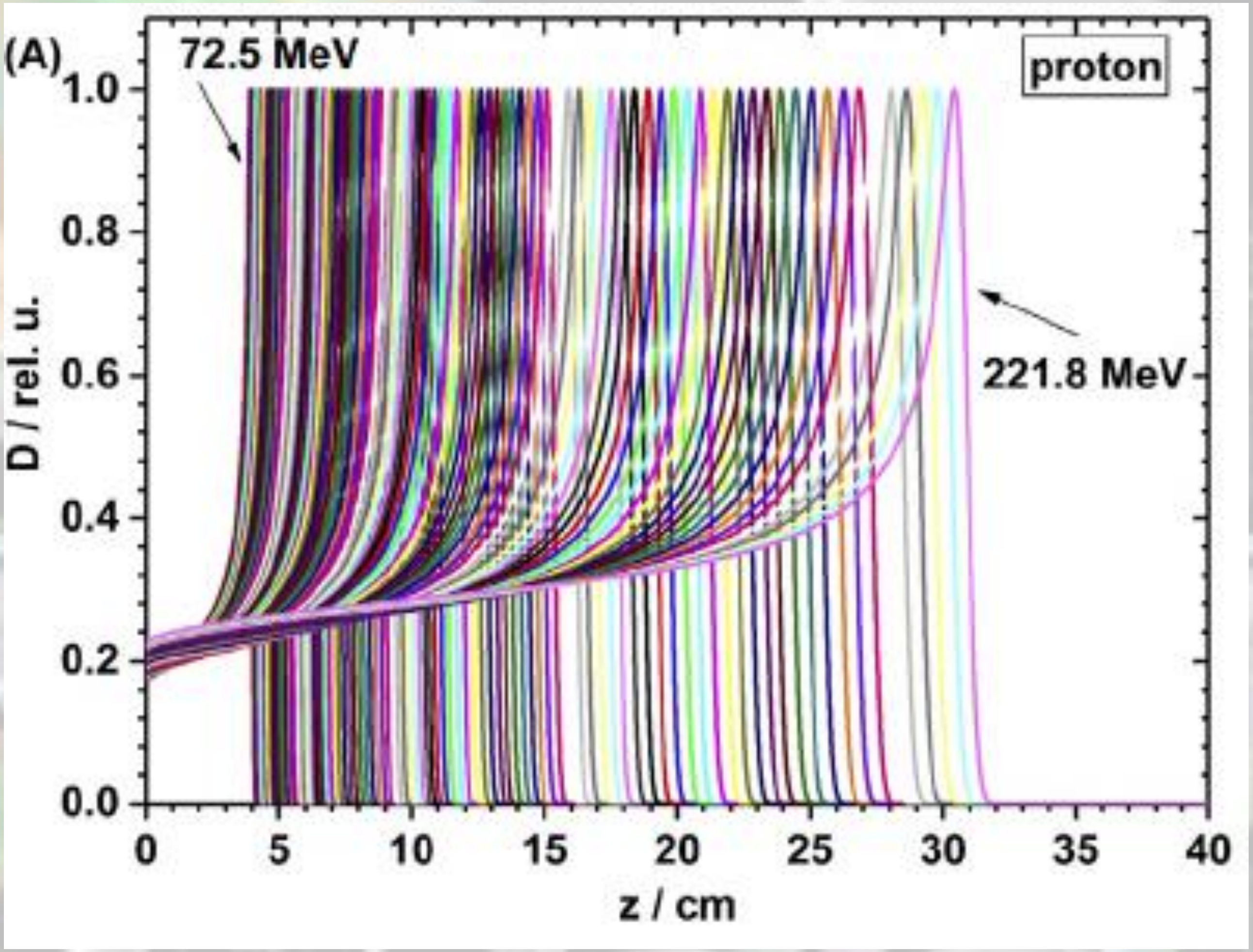


Radiation Therapy with Protons

- Depth dose curves for protons in water as a function of the incident proton energy

- As the proton's energy increases, they penetrate farther into the target material.

- By knowing the depth of the tumor, you can control the dosage delivered by selecting a proton (or a range of protons) of sufficient energy to reach the treatment spot.



Changran, Geng & Gates, Drake & Bronk, Lawrence & Ma, Duo & Guan, Fada. (2018). Physical parameter optimization scheme for radiobiological studies of charged particle therapy. Physica Medica. 51. 13-21. 10.1016/j.ejmp.2018.06.001.

Radiation Therapy with Protons

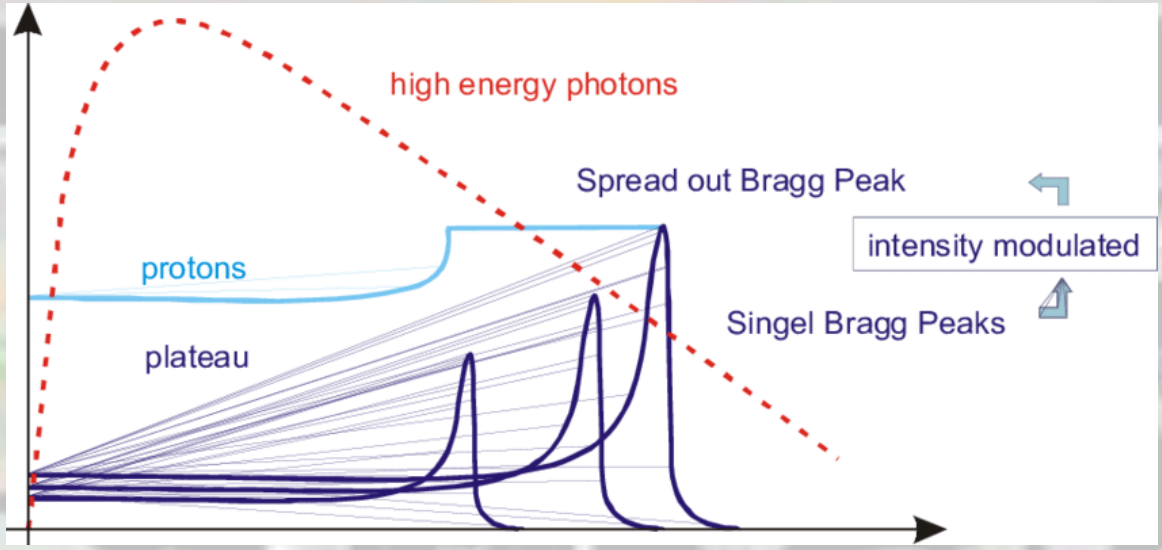
- You can use proton beams with different energies to cover the tumor by depositing the energy at various depths in the tumor.

- This is called the *Spread-Out Bragg Peak*, or *SOBP*.

- Here you can deposit a homogenous dose in the target region using only a single proton beam direction

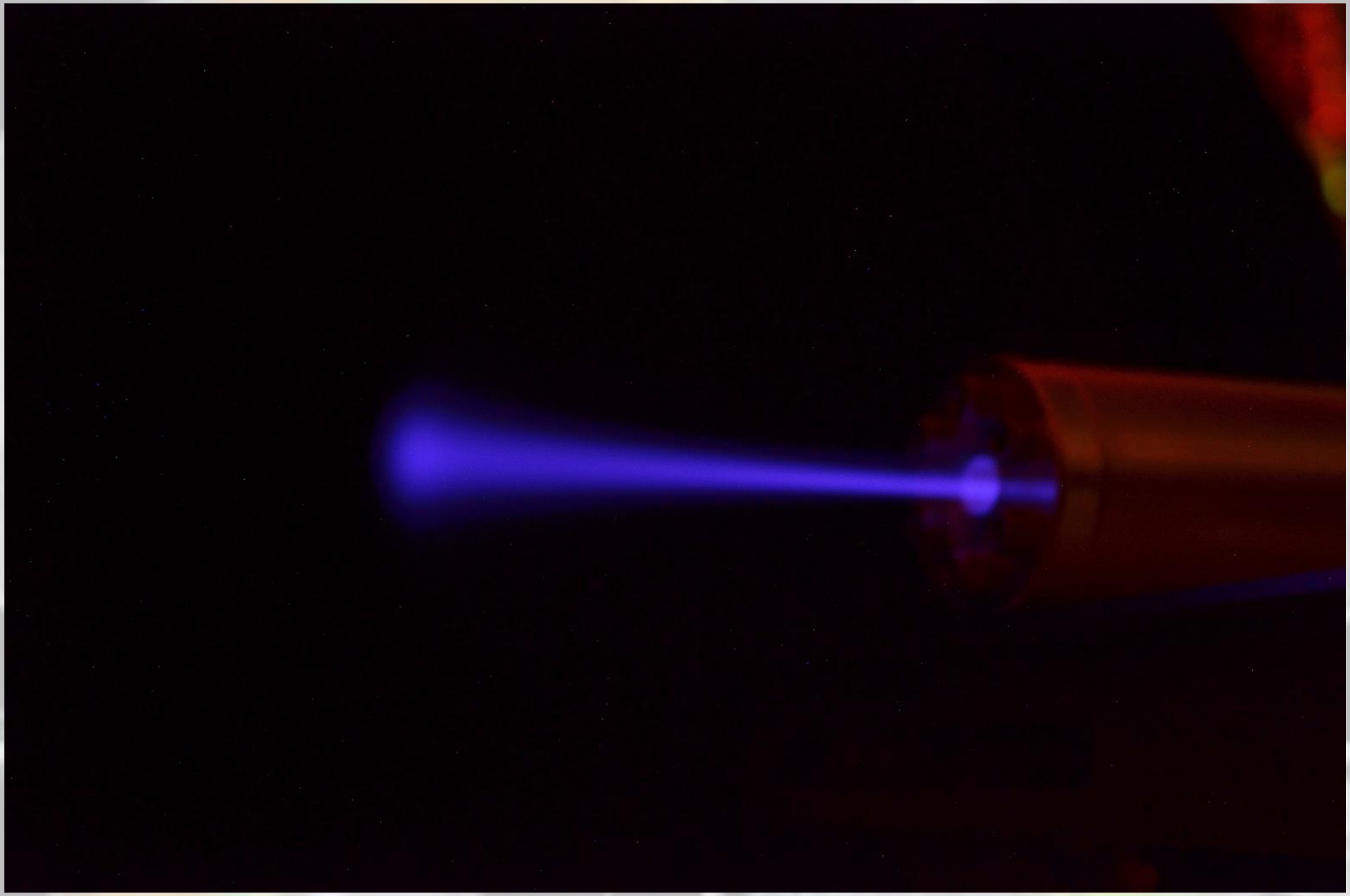
- Thus, you can provide an effective treatment to irradiate the entire tumor.

- However, in practice usually multiple proton beams are used all incident from different directions.



Regler, M. & Benedikt, Michael & Poljanc, Karin. (2023). Medical Accelerators for Hadrontherapy with Protons and Carbon Ions (With an Introduction to the Physical Advantage of Heavy Charged - Particle Radiation).

External Proton Beam

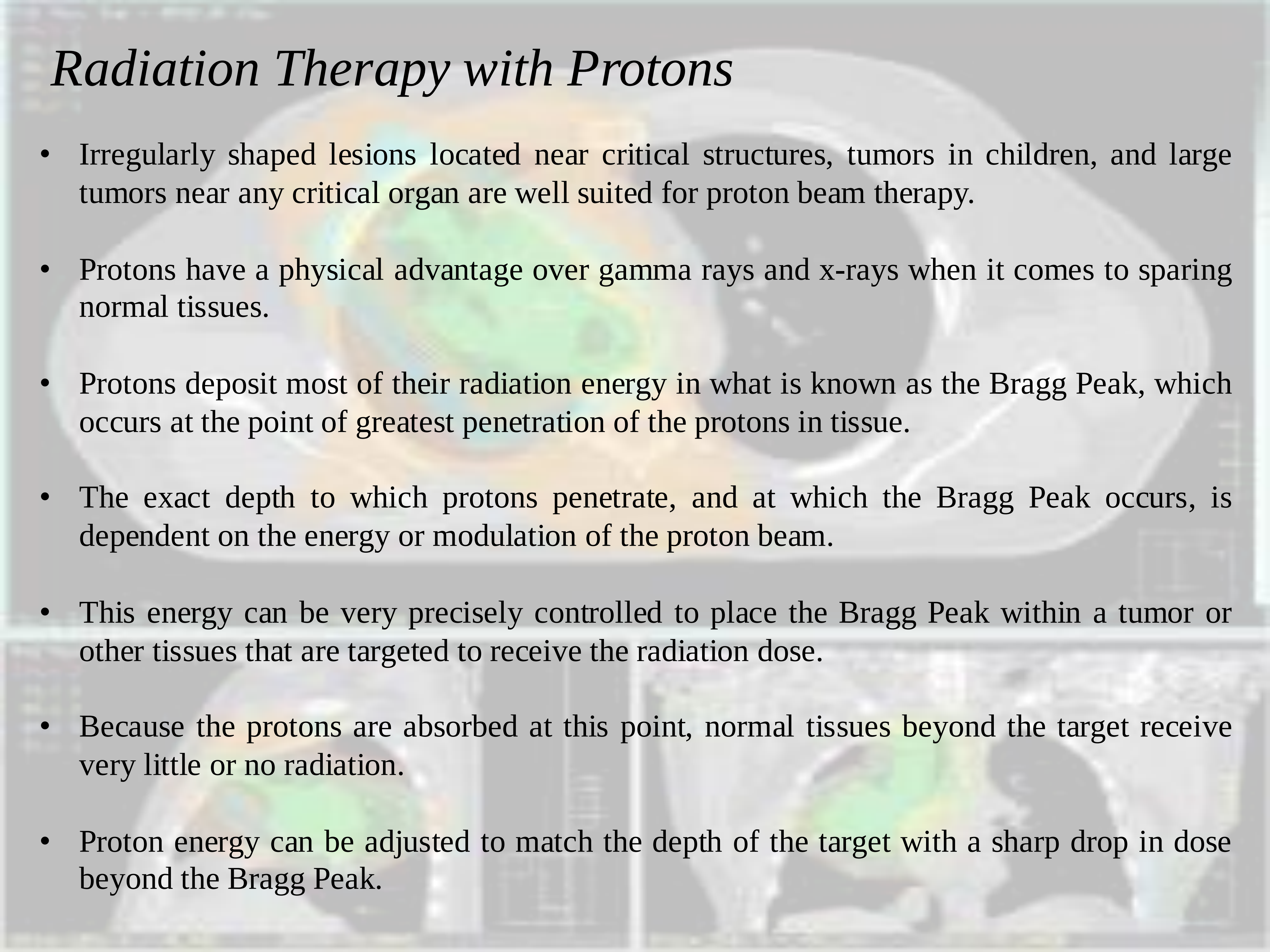


2.2 MeV proton beam in air from our accelerator.

Length is about $8cm$, and the color is from excitations in nitrogen in the air

Beam gets brighter at the end – Bragg Peak

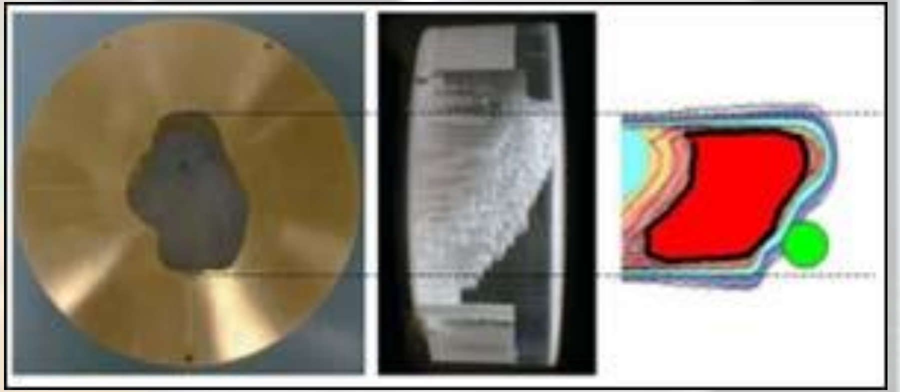
Radiation Therapy with Protons



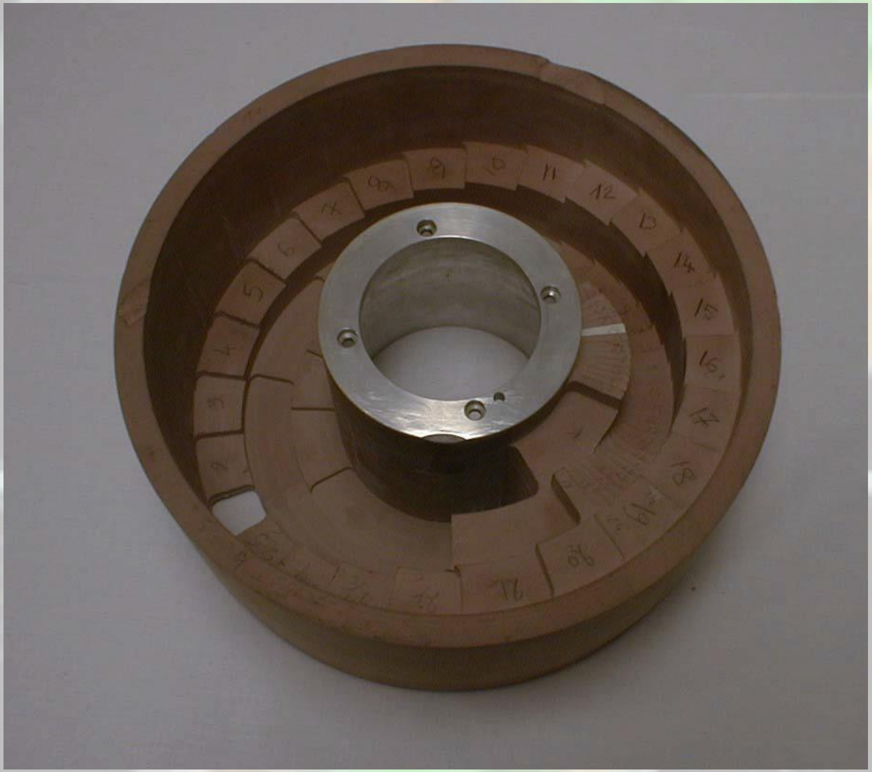
- Irregularly shaped lesions located near critical structures, tumors in children, and large tumors near any critical organ are well suited for proton beam therapy.
- Protons have a physical advantage over gamma rays and x-rays when it comes to sparing normal tissues.
- Protons deposit most of their radiation energy in what is known as the Bragg Peak, which occurs at the point of greatest penetration of the protons in tissue.
- The exact depth to which protons penetrate, and at which the Bragg Peak occurs, is dependent on the energy or modulation of the proton beam.
- This energy can be very precisely controlled to place the Bragg Peak within a tumor or other tissues that are targeted to receive the radiation dose.
- Because the protons are absorbed at this point, normal tissues beyond the target receive very little or no radiation.
- Proton energy can be adjusted to match the depth of the target with a sharp drop in dose beyond the Bragg Peak.

Radiation Therapy with Protons

- Filter block used to select out various proton energies.
- Mask used to contour the proton beam to the patient’s tumor.



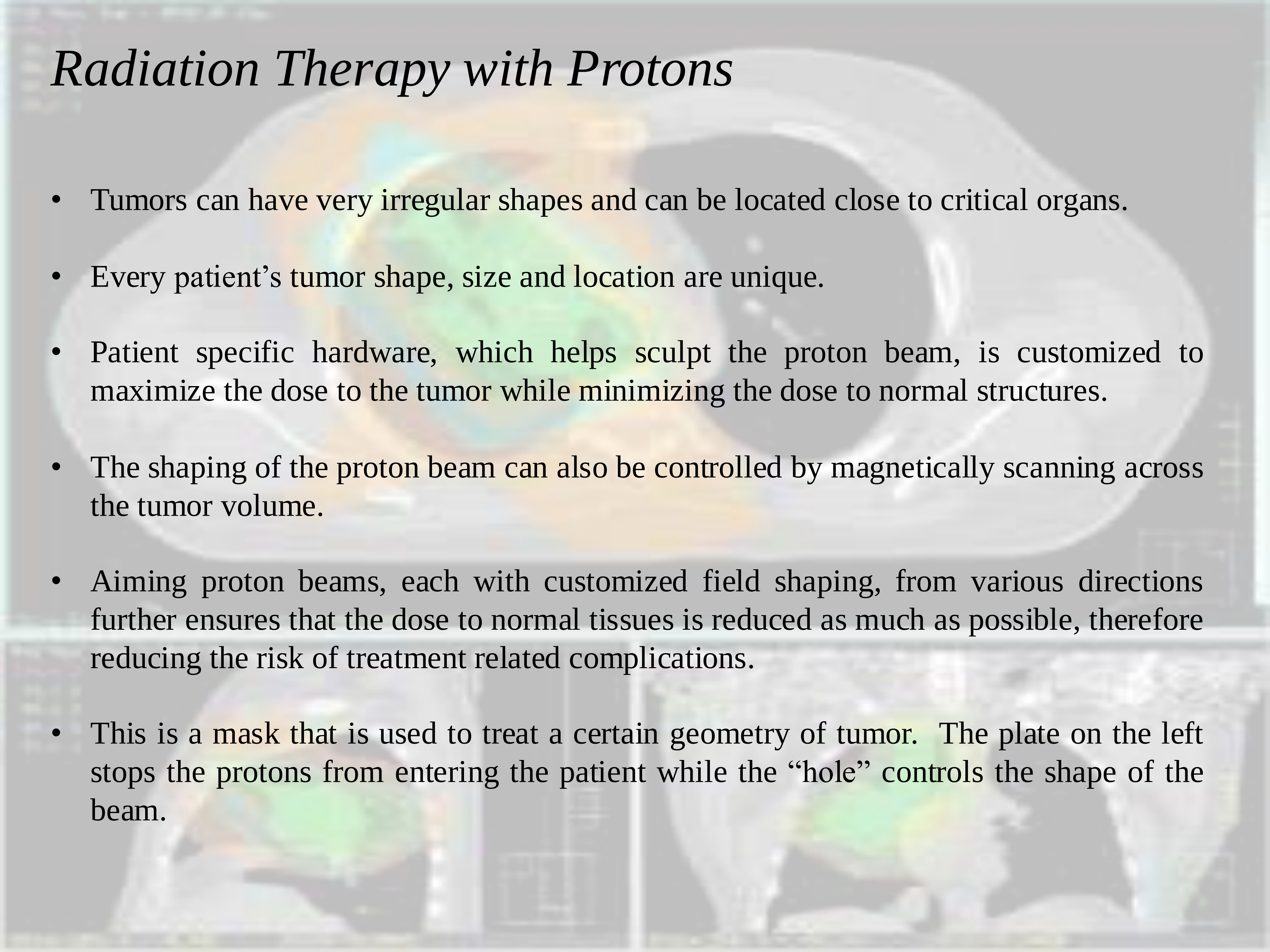
http://www.massgeneral.org/radiationoncology/assets/ProtonTreatment/principlesProtonTh_1.jpg



http://www.aapm.org/meetings/05AM/pdf/18-4016-65735-22.pdf

Morel, Paul. (2014). MSPT : Motion Simulator for Proton Therapy. 10.13140/RG.2.1.1802.0006.

Radiation Therapy with Protons



- Tumors can have very irregular shapes and can be located close to critical organs.

- Every patient’s tumor shape, size and location are unique.

- Patient specific hardware, which helps sculpt the proton beam, is customized to maximize the dose to the tumor while minimizing the dose to normal structures.

- The shaping of the proton beam can also be controlled by magnetically scanning across the tumor volume.

- Aiming proton beams, each with customized field shaping, from various directions further ensures that the dose to normal tissues is reduced as much as possible, therefore reducing the risk of treatment related complications.

- This is a mask that is used to treat a certain geometry of tumor. The plate on the left stops the protons from entering the patient while the “hole” controls the shape of the beam.

Prostate Cancer

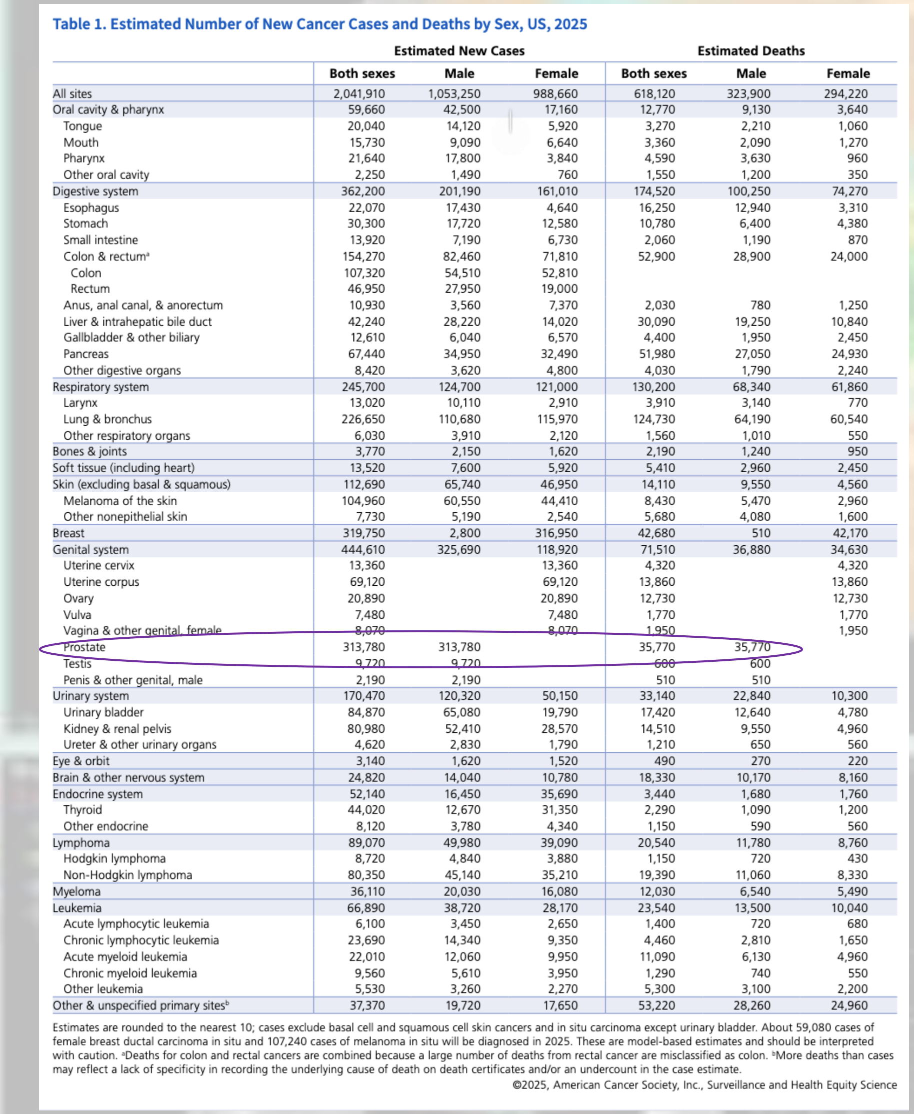


Table 1. Estimated Number of New Cancer Cases and Deaths by Sex, US, 2025

	Estimated New Cases			Estimated Deaths		
	Both sexes	**Male**	**Female**	**Both sexes**	**Male**	**Female**
All sites	2,041,910	1,053,250	988,660	618,120	323,900	294,220
Oral cavity & pharynx	59,660	42,500	17,160	12,770	9,130	3,640
Tongue	20,040	14,120	5,920	3,270	2,210	1,060
Mouth	15,730	9,090	6,640	3,360	2,090	1,270
Pharynx	21,640	17,800	3,840	4,590	3,630	960
Other oral cavity	2,250	1,490	760	1,550	1,200	350
Digestive system	362,200	201,190	161,010	174,520	100,250	74,270
Esophagus	22,070	17,430	4,640	16,250	12,940	3,310
Stomach	30,300	17,720	12,580	10,780	6,400	4,380
Small intestine	13,920	7,190	6,730	2,060	1,190	870
Colon & rectum[a]	154,270	82,460	71,810	52,900	28,900	24,000
Colon	107,320	54,510	52,810			
Rectum	46,950	27,950	19,000			
Anus, anal canal, & anorectum	10,930	3,560	7,370	2,030	780	1,250
Liver & intrahepatic bile duct	42,240	28,220	14,020	30,090	19,250	10,840
Gallbladder & other biliary	12,610	6,040	6,570	4,400	1,950	2,450
Pancreas	67,440	34,950	32,490	51,980	27,050	24,930
Other digestive organs	8,420	3,620	4,800	4,030	1,790	2,240
Respiratory system	245,700	124,700	121,000	130,200	68,340	61,860
Larynx	13,020	10,110	2,910	3,910	3,140	770
Lung & bronchus	226,650	110,680	115,970	124,730	64,190	60,540
Other respiratory organs	6,030	3,910	2,120	1,560	1,010	550
Bones & joints	3,770	2,150	1,620	2,190	1,240	950
Soft tissue (including heart)	13,520	7,600	5,920	5,410	2,960	2,450
Skin (excluding basal & squamous)	112,690	65,740	46,950	14,110	9,550	4,560
Melanoma of the skin	104,960	60,550	44,410	8,430	5,470	2,960
Other nonepithelial skin	7,730	5,190	2,540	5,680	4,080	1,600
Breast	319,750	2,800	316,950	42,680	510	42,170
Genital system	444,610	325,690	118,920	71,510	36,880	34,630
Uterine cervix	13,360		13,360	4,320		4,320
Uterine corpus	69,120		69,120	13,860		13,860
Ovary	20,890		20,890	12,730		12,730
Vulva	7,480		7,480	1,770		1,770
Vagina & other genital, female	8,070		8,070	1,950		1,950
Prostate	313,780	313,780		35,770	35,770	
Testis	9,720	9,720		600	600	
Penis & other genital, male	2,190	2,190		510	510	
Urinary system	170,470	120,320	50,150	33,140	22,840	10,300
Urinary bladder	84,870	65,080	19,790	17,420	12,640	4,780
Kidney & renal pelvis	80,980	52,410	28,570	14,510	9,550	4,960
Ureter & other urinary organs	4,620	2,830	1,790	1,210	650	560
Eye & orbit	3,140	1,620	1,520	490	270	220
Brain & other nervous system	24,820	14,040	10,780	18,330	10,170	8,160
Endocrine system	52,140	16,450	35,690	3,440	1,680	1,760
Thyroid	44,020	12,670	31,350	2,290	1,090	1,200
Other endocrine	8,120	3,780	4,340	1,150	590	560
Lymphoma	89,070	49,980	39,090	20,540	11,780	8,760
Hodgkin lymphoma	8,720	4,840	3,880	1,150	720	430
Non-Hodgkin lymphoma	80,350	45,140	35,210	19,390	11,060	8,330
Myeloma	36,110	20,030	16,080	12,030	6,540	5,490
Leukemia	66,890	38,720	28,170	23,540	13,500	10,040
Acute lymphocytic leukemia	6,100	3,450	2,650	1,400	720	680
Chronic lymphocytic leukemia	23,690	14,340	9,350	4,460	2,810	1,650
Acute myeloid leukemia	22,010	12,060	9,950	11,090	6,130	4,960
Chronic myeloid leukemia	9,560	5,610	3,950	1,290	740	550
Other leukemia	5,530	3,260	2,270	5,300	3,100	2,200
Other & unspecified primary sites[b]	37,370	19,720	17,650	53,220	28,260	24,960

Estimates are rounded to the nearest 10; cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. About 59,080 cases of female breast ductal carcinoma in situ and 107,240 cases of melanoma in situ will be diagnosed in 2025. These are model-based estimates and should be interpreted with caution. [a]Deaths for colon and rectal cancers are combined because a large number of deaths from rectal cancer are misclassified as colon. [b]More deaths than cases may reflect a lack of specificity in recording the underlying cause of death on death certificates and/or an undercount in the case estimate.

https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2025/2025-cancer-facts-and-figures.pdf

- Other than lung cancer, prostate cancer is the most common cancer in American men. The American Cancer Society's estimates for prostate cancer in the United States for 2025 are:

  About 313,000 new cases of prostate cancer.
  About 36,000 deaths from prostate cancer.

- About 1 in 7 men (about 13%) will be diagnosed with prostate cancer during their lifetime.

- Prostate cancer occurs mainly in older men. About 6 cases in 10 are diagnosed in men aged 65 or older, and it is rare before age 40. The average age at the time of diagnosis is about 66.

- Prostate cancer is the second leading cause of cancer death in American men, behind only lung cancer. About 1 in 38 (about 3%) will die of prostate cancer.

- Prostate cancer can be a serious disease, but most men diagnosed with prostate cancer do not die from it. More than 2.9 million men in the United States who have been diagnosed with prostate cancer at some point are still alive today.

Prostate Cancer

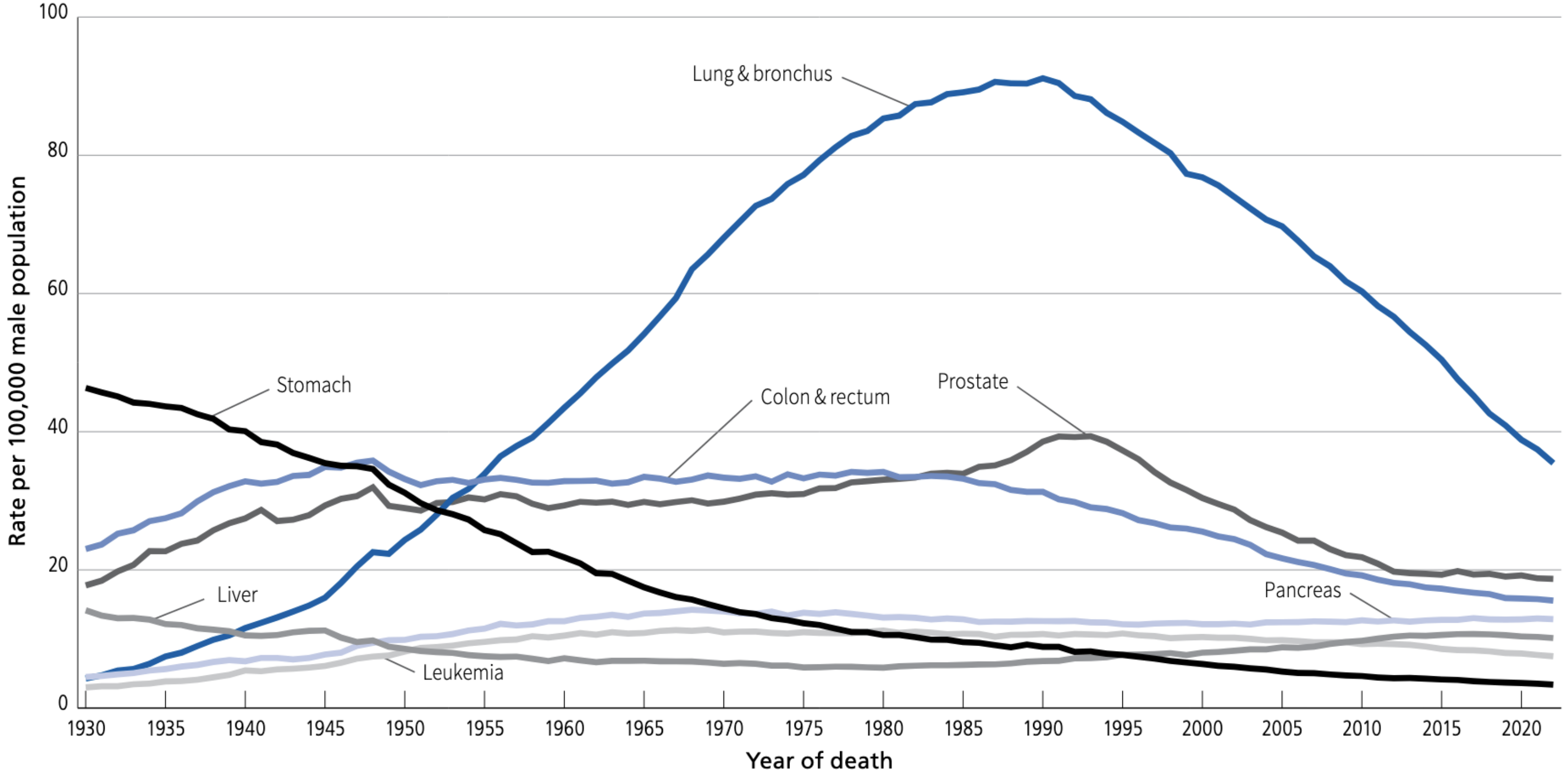


Figure 1. Trends in Age-adjusted Cancer Death Rates by Site, Males, US, 1930-2022

Rates are age adjusted to the 2000 US standard population and exclude deaths in Puerto Rico and other US territories. Due to improvements in classification, site-specific information differs from contemporary data for cancers of the liver, lung and bronchus, and colon and rectum.

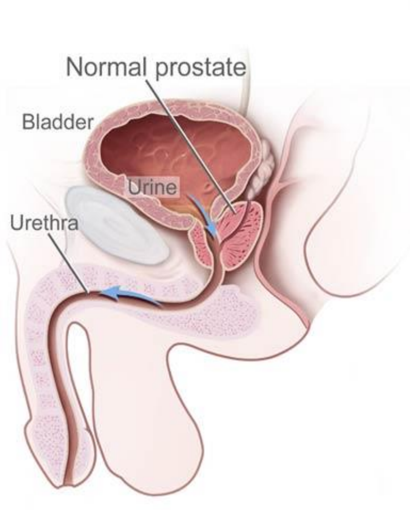
Data source: US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2022, National Center for Health Statistics, Centers for Disease Control and Prevention.

https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2025/2025-cancer-facts-and-figures.pdf

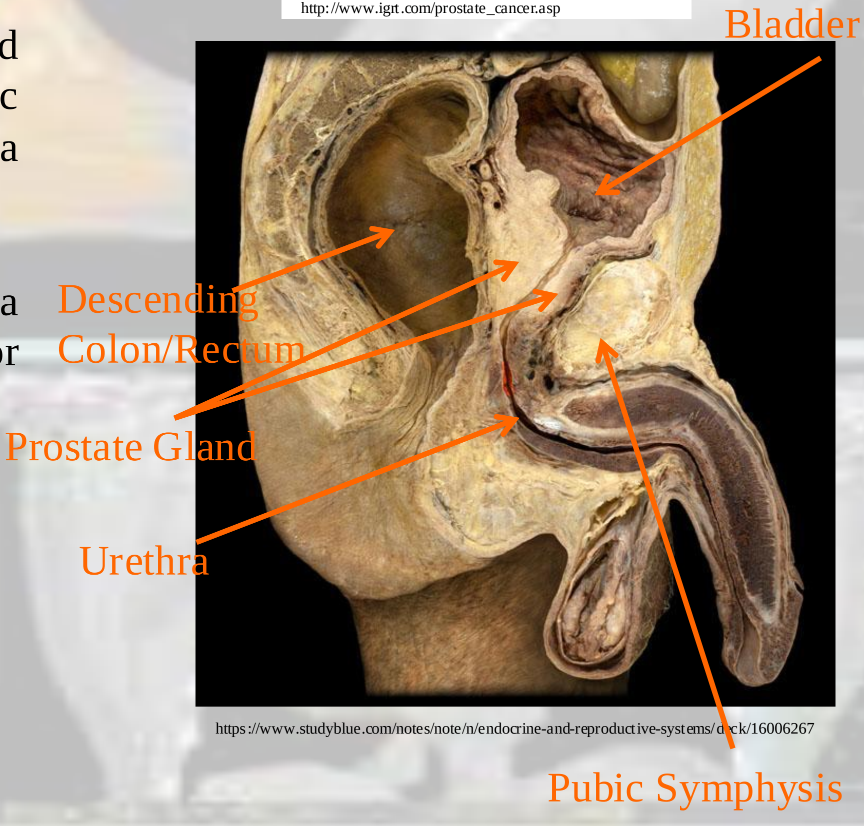
Prostate Cancer

- Prostate function

- The prostate is a small walnut shaped gland that wraps around a tube called the urethra, which carries urine and semen out of the penis.
- The prostate produces the white fluid found in semen, or the white fluid that contains sperm.
- Prostate cancer is usually diagnosed with a blood test measuring the amount of prostate specific antigens (PSA) in the body by your PCP or a urologist.
- Can also be found by a physician conducting a rectal exam and manually examining the prostate or can be diagnosed using a CT/PET scan.
- Symptoms can include:
  - Changes in urinary flow: frequency, urgency, hesitancy
  - Frequent night-time urination
  - Painful urination
  - Blood in urine



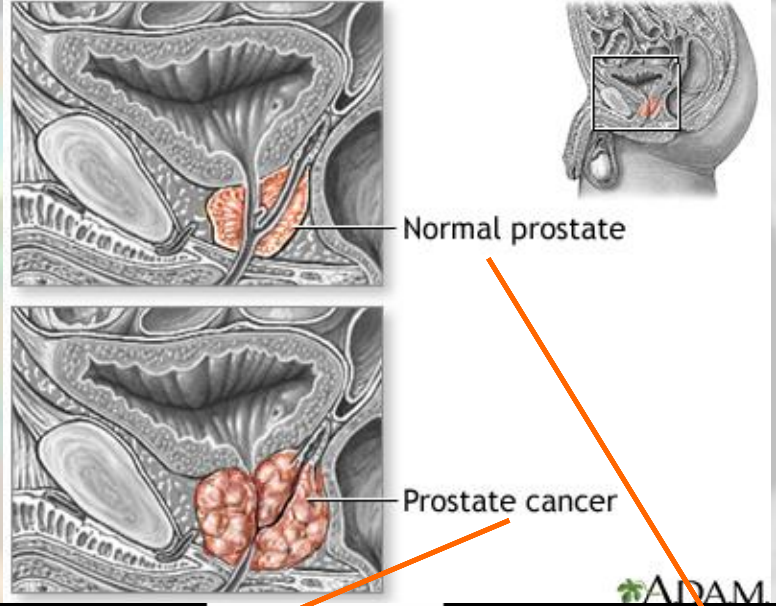
http://www.igrt.com/prostate_cancer.asp

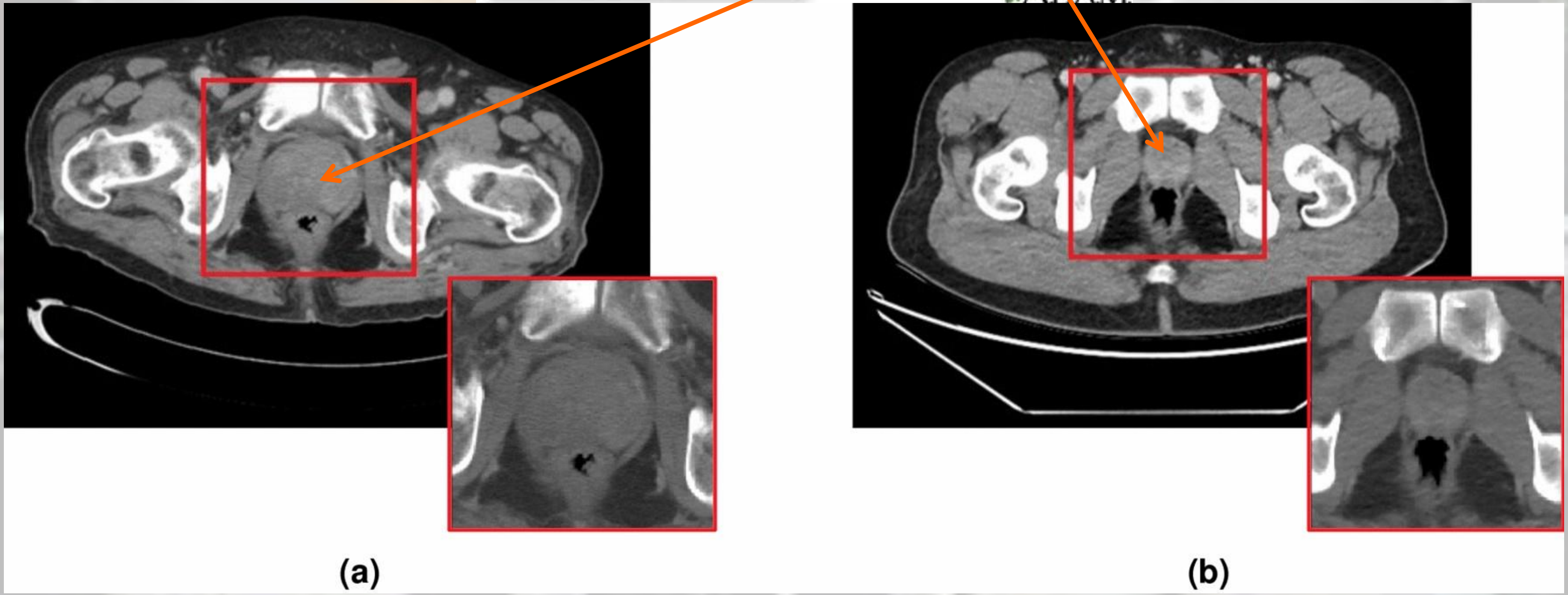


https://www.studyblue.com/notes/note/n/endocrine-and-reproductive-systems/deck/16006267

Prostate Cancer

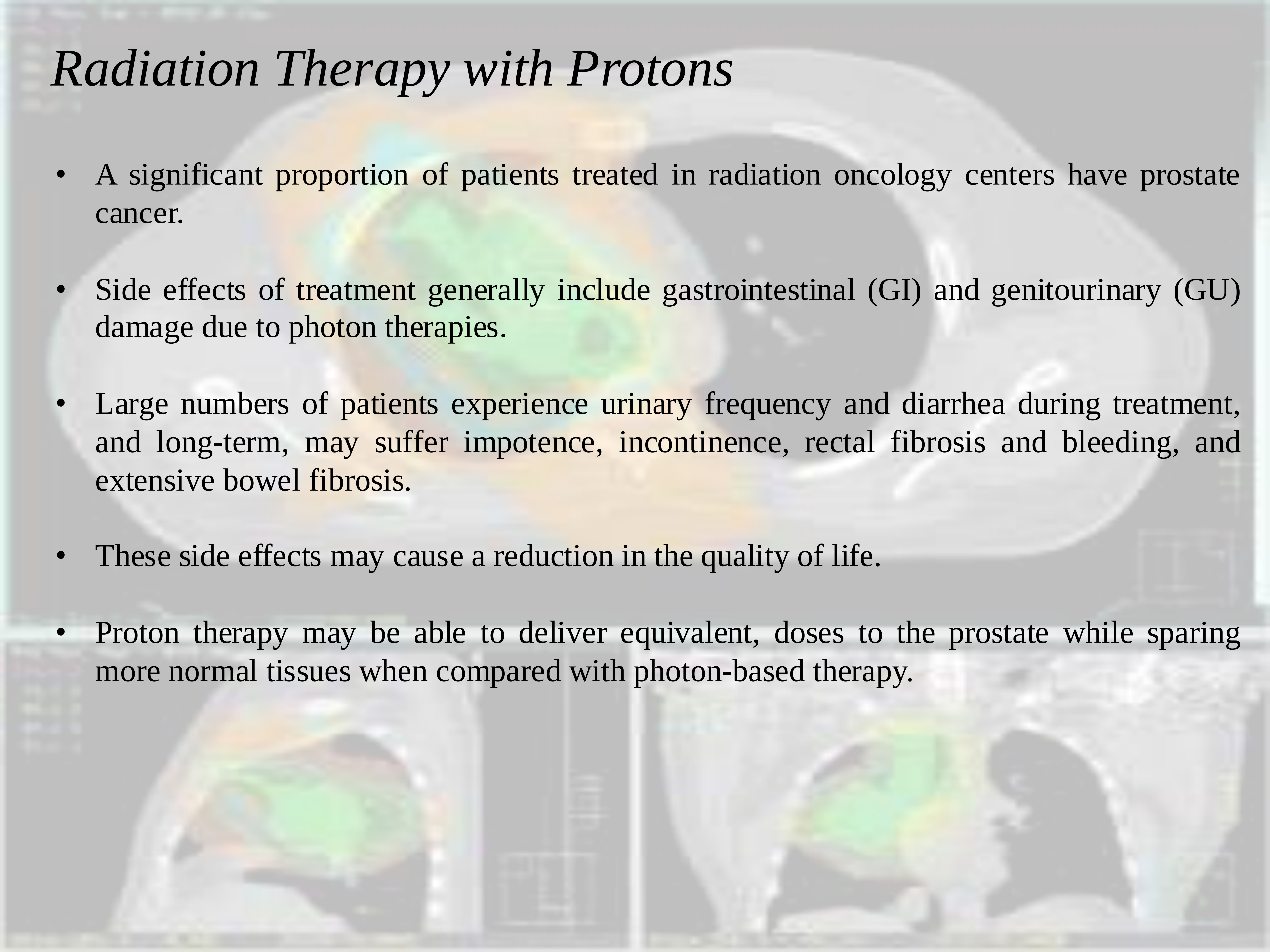
https://www.nlm.nih.gov/medlineplus/ency/article/000380.htm





https://www.nature.com/articles/s41598-021-86972-y/figures/1

Radiation Therapy with Protons



- A significant proportion of patients treated in radiation oncology centers have prostate cancer.

- Side effects of treatment generally include gastrointestinal (GI) and genitourinary (GU) damage due to photon therapies.

- Large numbers of patients experience urinary frequency and diarrhea during treatment, and long-term, may suffer impotence, incontinence, rectal fibrosis and bleeding, and extensive bowel fibrosis.

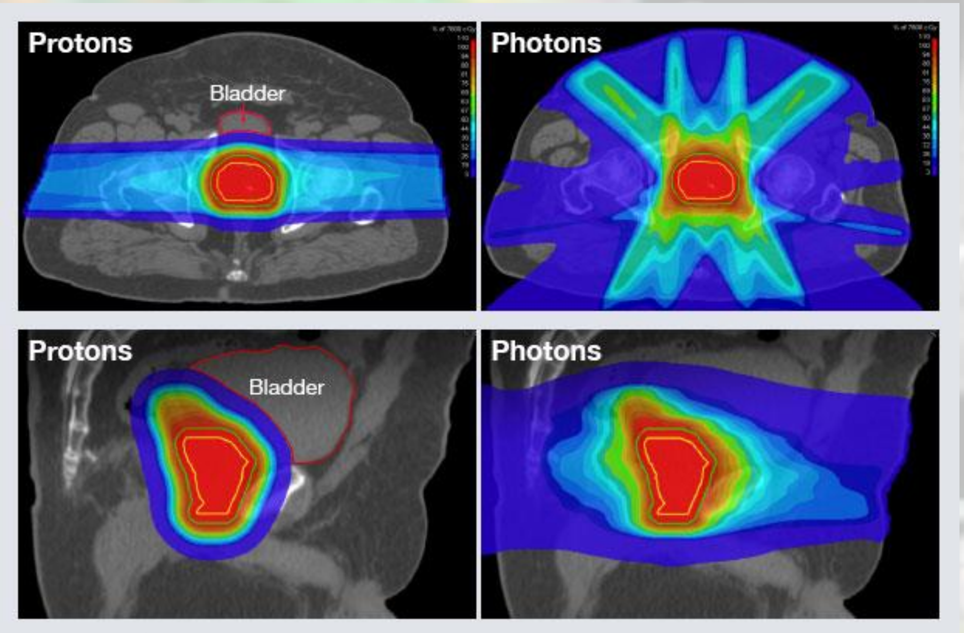
- These side effects may cause a reduction in the quality of life.

- Proton therapy may be able to deliver equivalent, doses to the prostate while sparing more normal tissues when compared with photon-based therapy.

Radiation Therapy with Protons vs. Photons

Conventional treatment:

- Tumors are generally irradiated with 2Gy dose per fraction delivered almost daily to a homogeneous field over a 4-to-6-week period to a specified total dose.

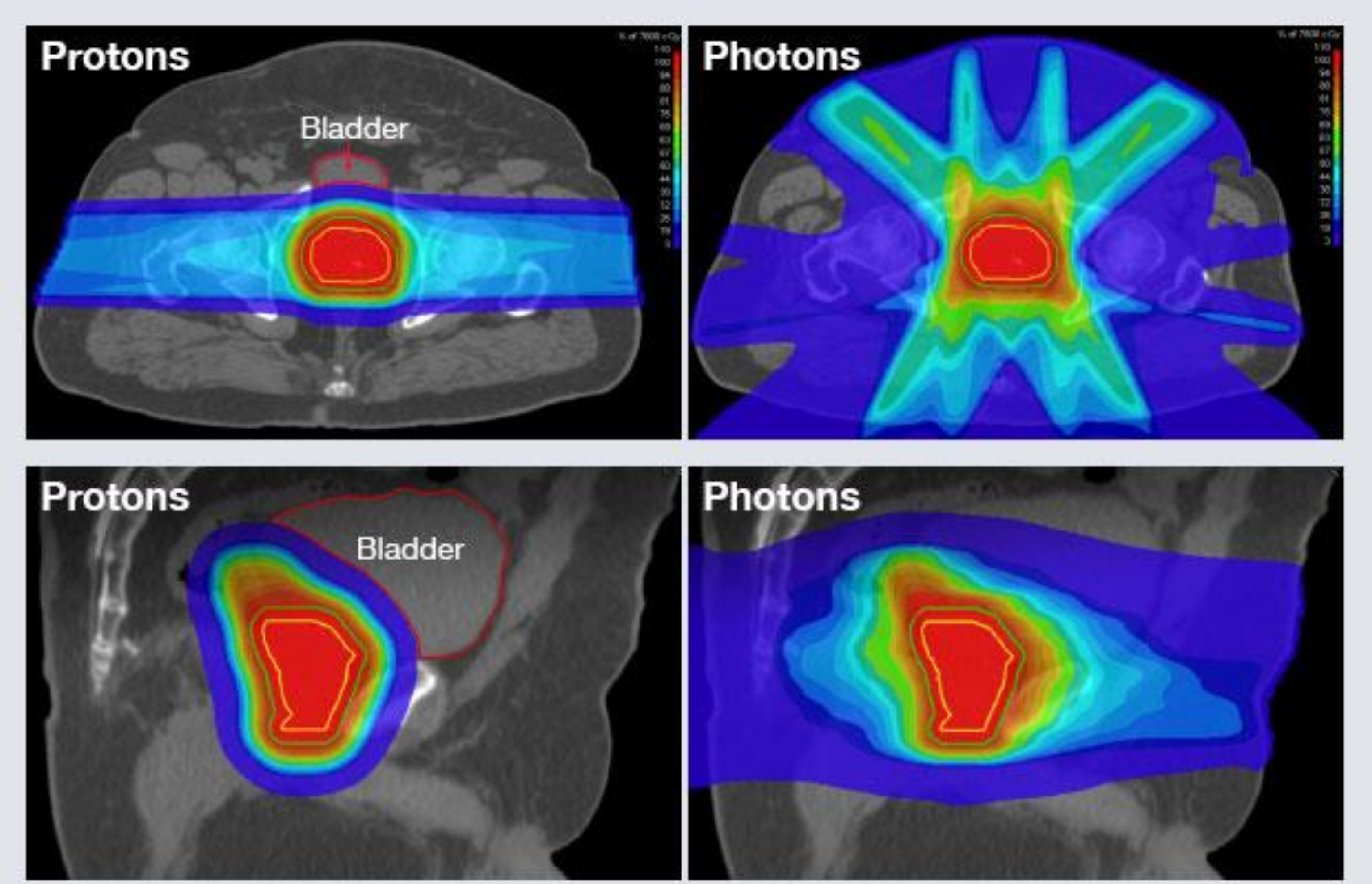


https://www.floridaproton.org/cancers-treated/prostate-cancer

- Preserves healthy tissue

- Suppose that you wanted to give a total of 60Gy as a treatment. This would be done as say 30 fractions (of 2 Gy each) and you'd have treatment about 4 times a week for 4 weeks.

Radiation Therapy with Protons vs. Photons

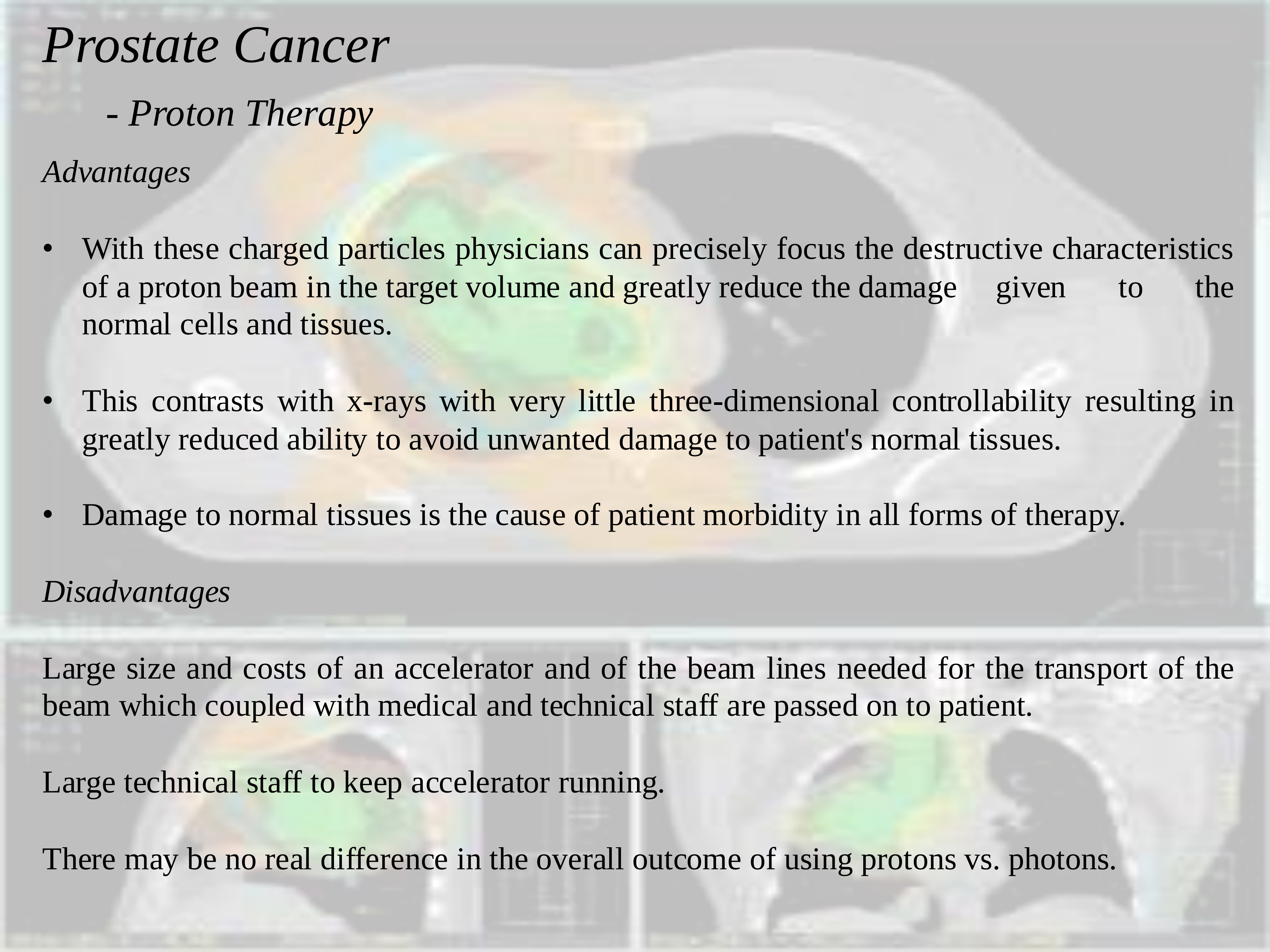


https://www.floridaproton.org/cancers-treated/prostate-cancer

- A tumor of the prostate gland appears in each MRI/CT image. The various colors indicate the intensity of the dose deposited in the tissue. Red is the maximum dose, followed by orange, yellow, green, blue, and purple, the minimum.

Prostate Cancer

- Proton Therapy



Advantages

- With these charged particles physicians can precisely focus the destructive characteristics of a proton beam in the target volume and greatly reduce the damage given to the normal cells and tissues.
- This contrasts with x-rays with very little three-dimensional controllability resulting in greatly reduced ability to avoid unwanted damage to patient's normal tissues.
- Damage to normal tissues is the cause of patient morbidity in all forms of therapy.

Disadvantages

Large size and costs of an accelerator and of the beam lines needed for the transport of the beam which coupled with medical and technical staff are passed on to patient.

Large technical staff to keep accelerator running.

There may be no real difference in the overall outcome of using protons vs. photons.

Brachytherapy

- Brachytherapy is a type of radiation therapy used to treat cancer.

- Brachytherapy involves placing a radioactive material directly inside or next to the tumor.

- Brachytherapy, also called internal radiation therapy, allows a physician to use a higher total dose of radiation to treat a smaller area and in a shorter time than is possible with external beam radiation treatment.

- Brachytherapy is used to treat cancers throughout the body, including the:
  - prostate
  - cervix/uterus/vagina
  - head and neck
  - skin
  - breast
  - gallbladder
  - lung
  - rectum
  - eye

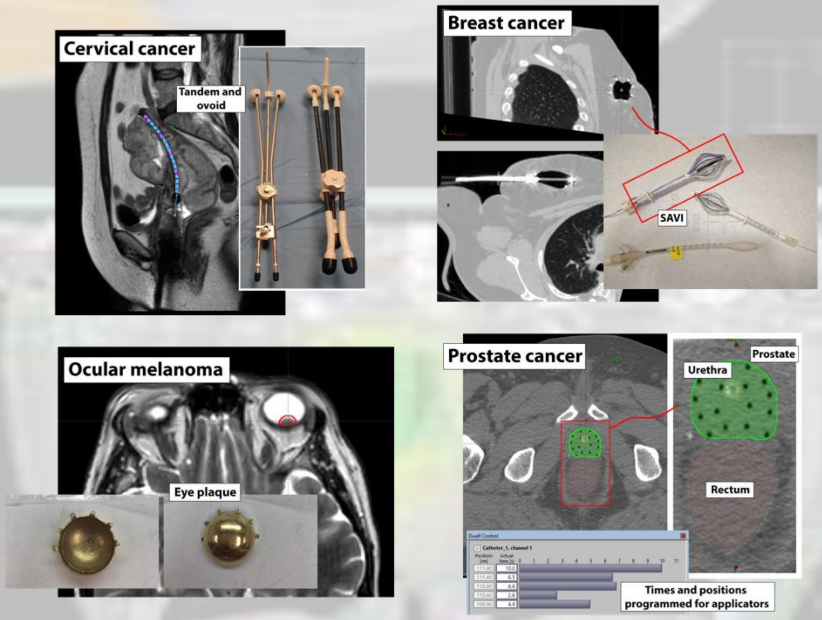
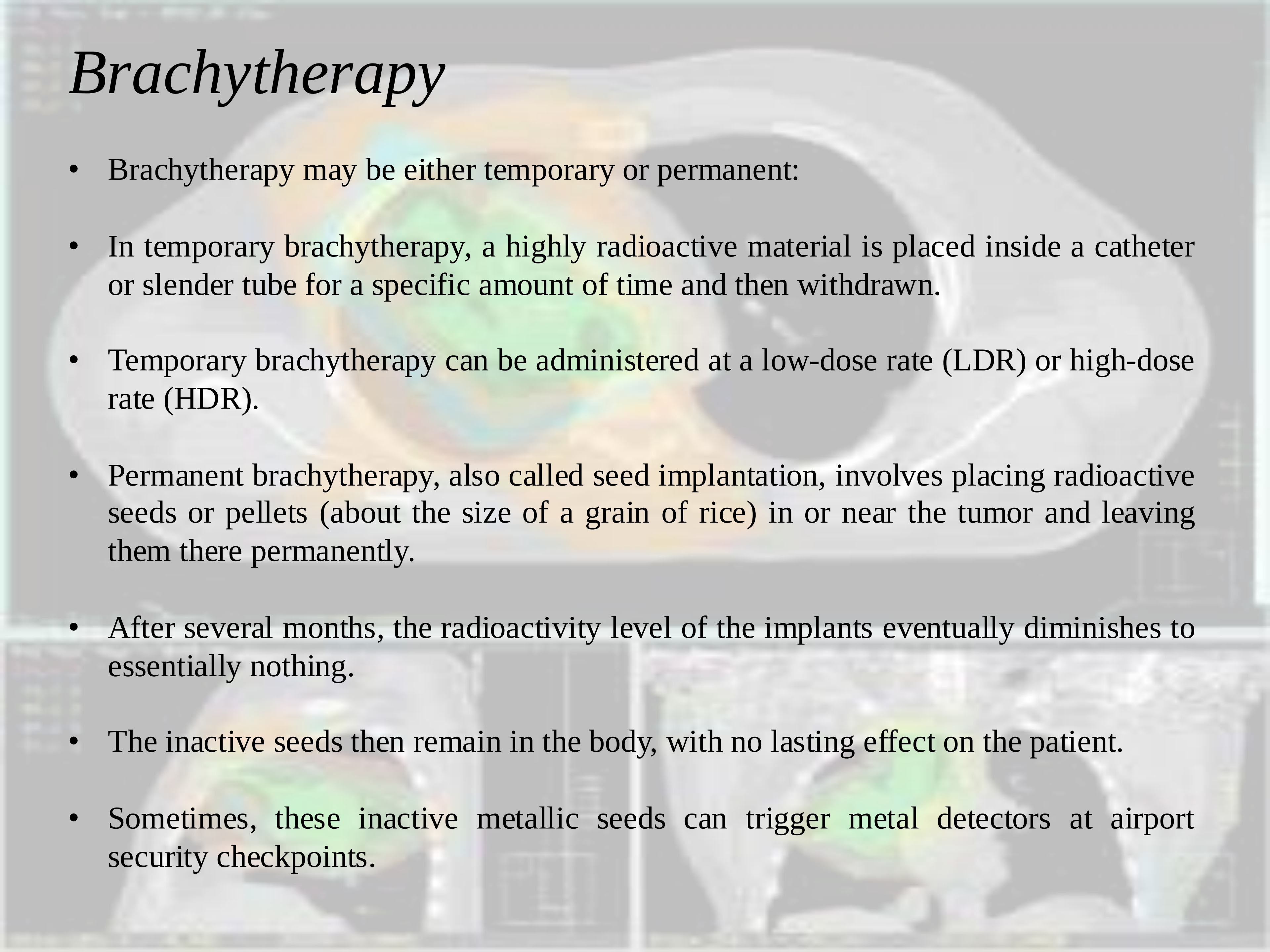


Image courtesy of Dr. Tom Mazur, PhD., DABR

Brachytherapy

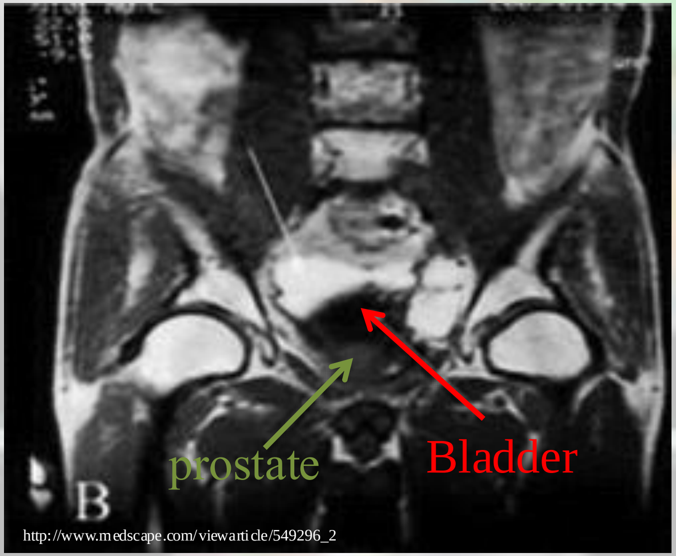


- Brachytherapy may be either temporary or permanent:
- In temporary brachytherapy, a highly radioactive material is placed inside a catheter or slender tube for a specific amount of time and then withdrawn.
- Temporary brachytherapy can be administered at a low-dose rate (LDR) or high-dose rate (HDR).
- Permanent brachytherapy, also called seed implantation, involves placing radioactive seeds or pellets (about the size of a grain of rice) in or near the tumor and leaving them there permanently.
- After several months, the radioactivity level of the implants eventually diminishes to essentially nothing.
- The inactive seeds then remain in the body, with no lasting effect on the patient.
- Sometimes, these inactive metallic seeds can trigger metal detectors at airport security checkpoints.

Prostate Cancer

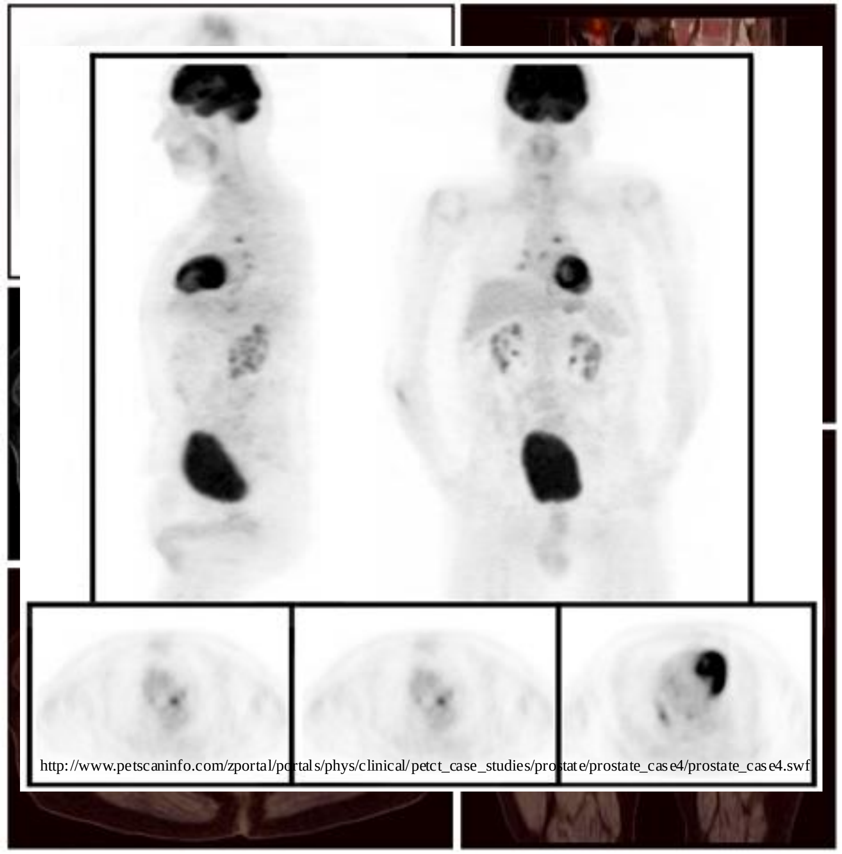
- *Case Study*

An 82-year-old male with prostate cancer diagnosed 17 years ago, status post TURP (Transurethral Resection of the Prostate), radiation therapy, orchiectomy in 1995. He has recent rising PSA.



http://www.medscape.com/viewarticle/549296_2

Normal MRI image of the lower abdomen showing the bladder and prostate.



http://www.petscaninfo.com/zportal/portals/phys/clinical/petct_case_studies/prostate/prostate_case4/prostate_case4.swf

PET scan using 11.1mCi ^{18}F FDG administered left arm IV with CT and fused CT/PET scan showing possible recurrence of prostate cancer.

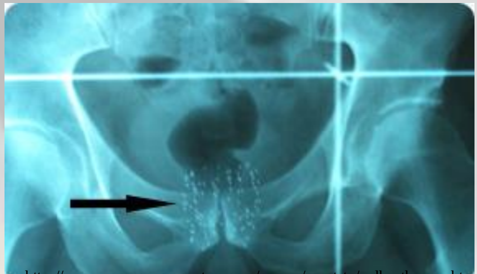
Prostate Cancer

- Brachytherapy treatment

- *Prostate Brachytherapy*, also known as a seed implantation, is often done in the operating room. It delivers a very high dose of radiation to your tumor by inserting radioactive seeds directly into your prostate gland under US and/or CT guidance while you are asleep.

- Iodine or palladium are most used. The seeds are about four millimeters long and less than a millimeter in diameter.

- Sometimes both prostate brachytherapy and external radiation may be used to combat your tumor.



http://www.upmccancercenters.com/cancer/prostate/radbratherapy.html

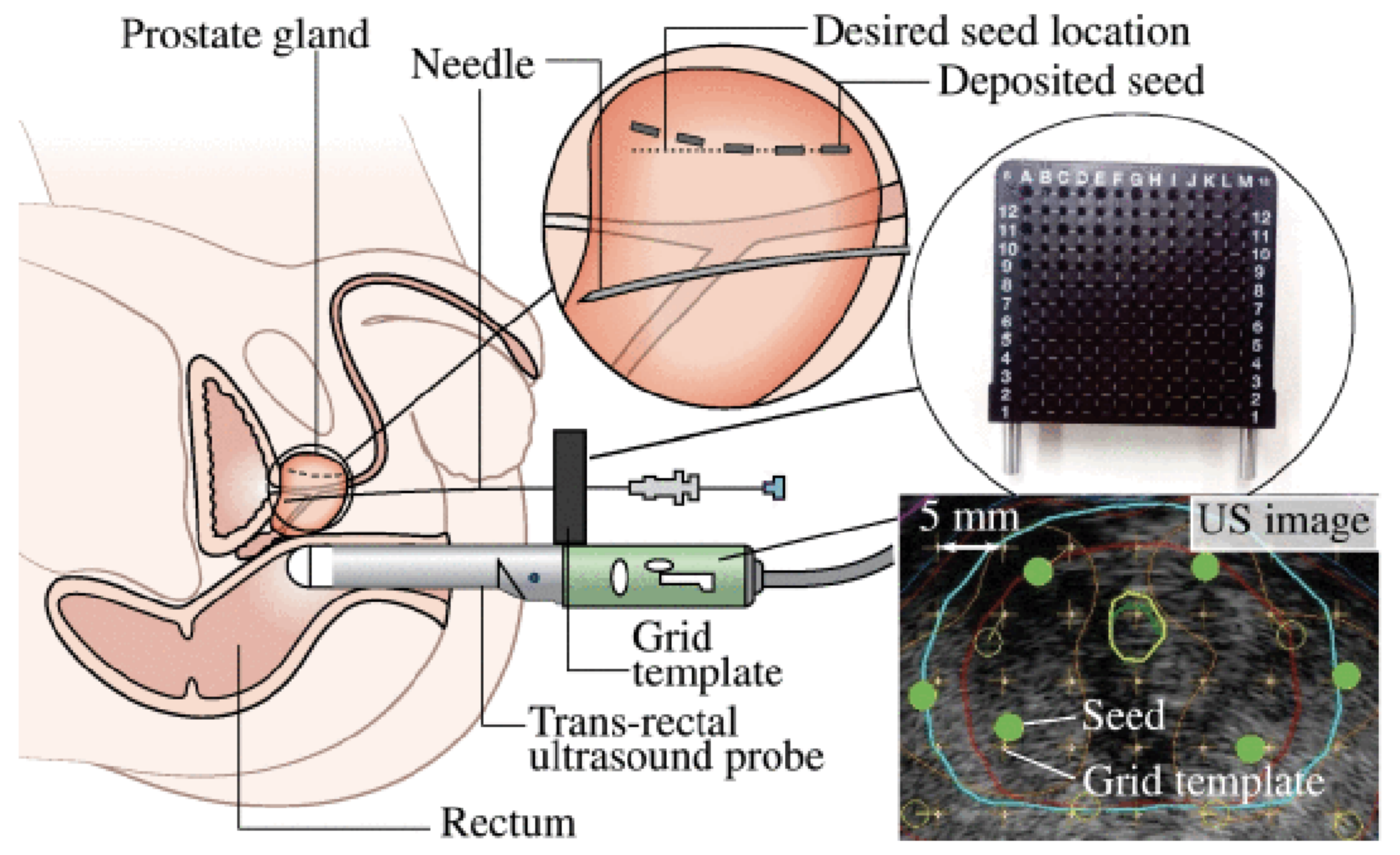
http://www.igrt.com/prostate_cancer.asp#

Dr. Stephen J. Amadon Jr., DABR, Therapeutic Medical Physicist

- Depending on the stage of your disease, you often have more than one treatment option to consider. Several factors should be considered when choosing these options, including potential benefits and risks.

Prostate Cancer

- Brachytherapy treatment



The Use of Biomaterials in Internal Radiation Therapy, Ben Milborne, Abul Arafat, Rob Layfield, Alexander Thompson, Ifty Ahmed, Recent Progress in Materials, 2020, volume 2, issue 2 doi:10.21926/rpm.2002012

LDR: Prostate Seed Implant – Iodine 125

Prostate Brachytherapy

- The placement of the seeds is planned by a physician and the seeds are “built” by a medical physicist who ensures that the delivery and dose are correct for the procedure.

- A grid is placed over the area of the prostate and needles which contain the seeds are inserted into the treatment area.

- The seeds are released and implanted into the prostate for treatment of prostate cancer.

- A transrectal US probe is used to see where the seeds are going to be implanted.

- CT imaging is done to see that the seeds are placed in the desired location.

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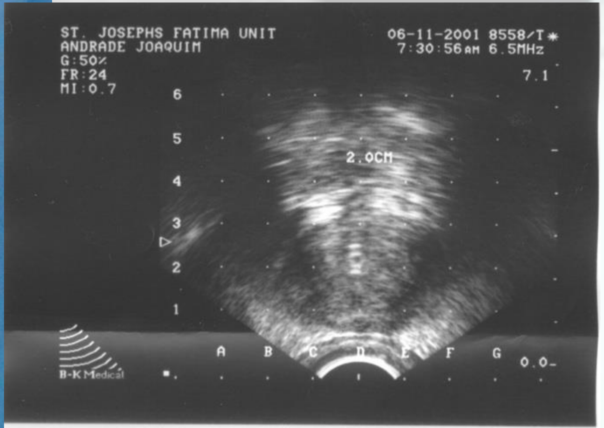

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LDR: Prostate Seed Implant – Iodine 125

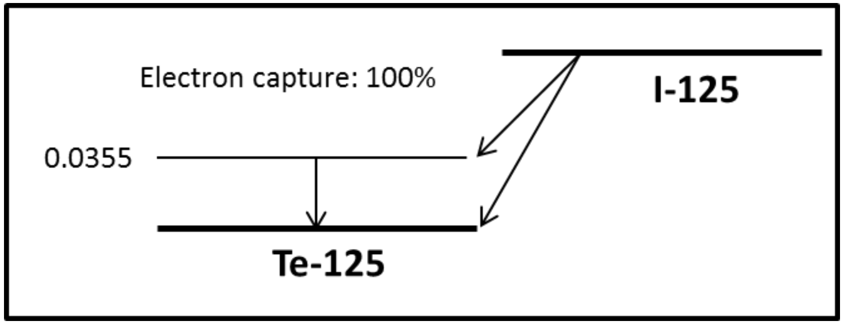
- Iodine 125 decays by electron capture with a half-life of about 60days.

- This is different than the other decays we've seen where things come out of the nucleus.

- In EC processes, the nucleus absorbs one of the inner shell electrons and when higher orbital electrons de-excite to fill the vacancies in the orbitals, x-rays of decreasing energies are released. In the nucleus a gamma ray is emitted as a result of exciting the proton to a higher energy state. In this case gamma rays of energy 35.5 keV are produced. These are the ones that are used for treatment.

$$ {}^{125}_{53}I + {}^{0}_{-1}e = {}^{125}_{52}Te + g $$

$$ \rightarrow \ {}^{0}_{-1}e + {}^{1}_{1}p \rightarrow {}^{1}_{0}n $$



http://www.ehs.utoronto.ca/services/radiation/radtraining/nuclideinformation.htm

Prostate Cancer

- Brachytherapy treatment

- Side effects are generally caused by the radiation emitted by the seeds in the prostate. The effects may last for 2 to 12 months after the implant and will decrease gradually as the seeds lose their radioactivity.
- Frequent urination, burning with urination and urinary urgency occur in 75 percent of men, six weeks to three months after seed implant. These side effects generally last for a few weeks. Dietary changes and bladder medications can control symptoms.
- Urinary obstruction occurs occasionally, due to an initial swelling of the prostate caused by the seeds. Obstruction is a higher risk for patients who had obstructive symptoms prior to surgery.
- Diarrhea or a change in bowel habits occurs very rarely.
- Erectile dysfunction, with brachytherapy as the sole treatment, occurs when radiation thickens the walls of blood vessels, limiting the blood supply to the nerves responsible for erections. It is seen in 30-35 percent of men five years after seed implantation. Vascular problems caused by smoking, arteriosclerosis, or diabetes can significantly increase the chances of erectile dysfunction after radiation.

Breast Cancer

- Brachytherapy treatment

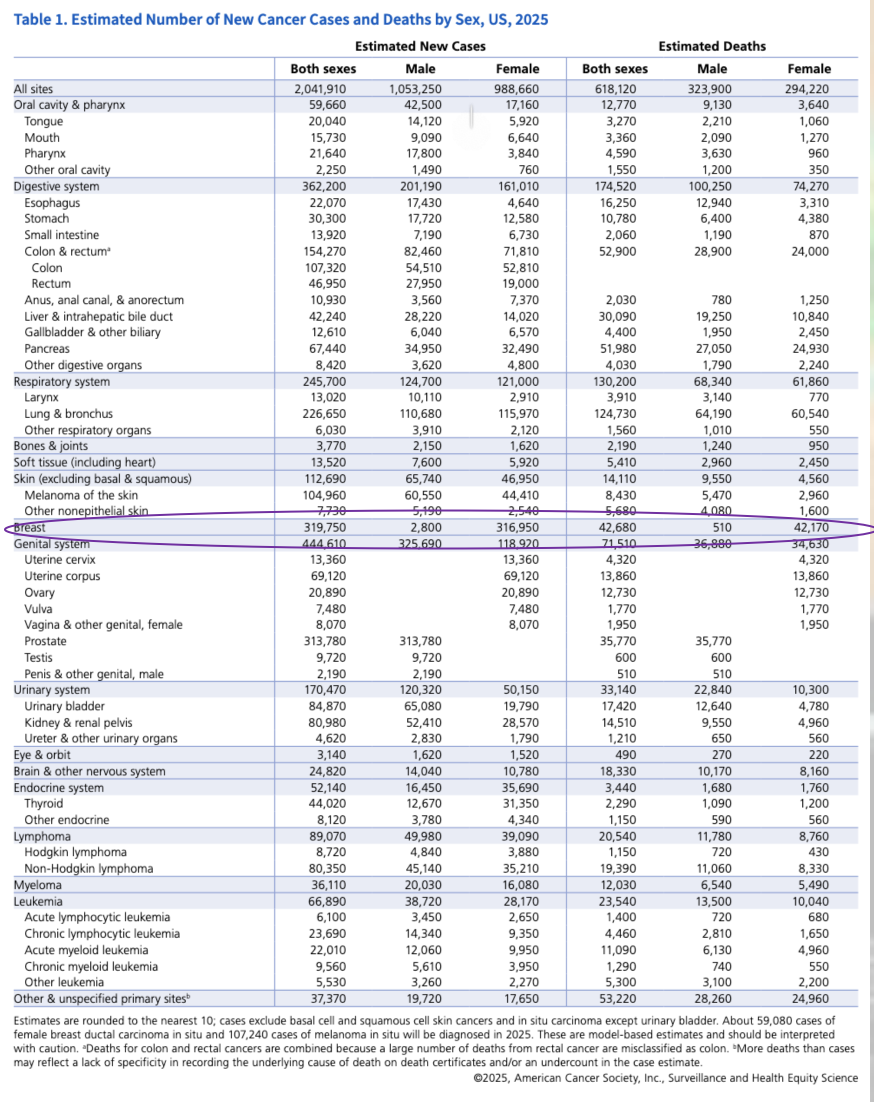


Table 1. Estimated Number of New Cancer Cases and Deaths by Sex, US, 2025

	Estimated New Cases			Estimated Deaths		
	Both sexes	**Male**	**Female**	**Both sexes**	**Male**	**Female**
All sites	2,041,910	1,053,250	988,660	618,120	323,900	294,220
Oral cavity & pharynx	59,660	42,500	17,160	12,770	9,130	3,640
Tongue	20,040	14,120	5,920	3,270	2,210	1,060
Mouth	15,730	9,090	6,640	3,360	2,090	1,270
Pharynx	21,640	17,800	3,840	4,590	3,630	960
Other oral cavity	2,250	1,490	760	1,550	1,200	350
Digestive system	362,200	201,190	161,010	174,520	100,250	74,270
Esophagus	22,070	17,430	4,640	16,250	12,940	3,310
Stomach	30,300	17,720	12,580	10,780	6,400	4,380
Small intestine	13,920	7,190	6,730	2,060	1,190	870
Colon & rectum[a]	154,270	82,460	71,810	52,900	28,900	24,000
Colon	107,320	54,510	52,810			
Rectum	46,950	27,950	19,000			
Anus, anal canal, & anorectum	10,930	3,560	7,370	2,030	780	1,250
Liver & intrahepatic bile duct	42,240	28,220	14,020	30,090	19,250	10,840
Gallbladder & other biliary	12,610	6,040	6,570	4,400	1,950	2,450
Pancreas	67,440	34,950	32,490	51,980	27,050	24,930
Other digestive organs	8,420	3,620	4,800	4,030	1,790	2,240
Respiratory system	245,700	124,700	121,000	130,200	68,340	61,860
Larynx	13,020	10,110	2,910	3,910	3,140	770
Lung & bronchus	226,650	110,680	115,970	124,730	64,190	60,540
Other respiratory organs	6,030	3,910	2,120	1,560	1,010	550
Bones & joints	3,770	2,150	1,620	2,190	1,240	950
Soft tissue (including heart)	13,520	7,600	5,920	5,410	2,960	2,450
Skin (excluding basal & squamous)	112,690	65,740	46,950	14,110	9,550	4,560
Melanoma of the skin	104,960	60,550	44,410	8,430	5,470	2,960
Other nonepithelial skin	7,730	5,190	2,540	5,680	4,080	1,600
Breast	319,750	2,800	316,950	42,680	510	42,170
Genital system	444,610	325,690	118,920	71,510	36,880	34,630
Uterine cervix	13,360		13,360	4,320		4,320
Uterine corpus	69,120		69,120	13,860		13,860
Ovary	20,890		20,890	12,730		12,730
Vulva	7,480		7,480	1,770		1,770
Vagina & other genital, female	8,070		8,070	1,950		1,950
Prostate	313,780	313,780		35,770	35,770	
Testis	9,720	9,720		600	600	
Penis & other genital, male	2,190	2,190		510	510	
Urinary system	170,470	120,320	50,150	33,140	22,840	10,300
Urinary bladder	84,870	65,080	19,790	17,420	12,640	4,780
Kidney & renal pelvis	80,980	52,410	28,570	14,510	9,550	4,960
Ureter & other urinary organs	4,620	2,830	1,790	1,210	650	560
Eye & orbit	3,140	1,620	1,520	490	270	220
Brain & other nervous system	24,820	14,040	10,780	18,330	10,170	8,160
Endocrine system	52,140	16,450	35,690	3,440	1,680	1,760
Thyroid	44,020	12,670	31,350	2,290	1,090	1,200
Other endocrine	8,120	3,780	4,340	1,150	590	560
Lymphoma	89,070	49,980	39,090	20,540	11,780	8,760
Hodgkin lymphoma	8,720	4,840	3,880	1,150	720	430
Non-Hodgkin lymphoma	80,350	45,140	35,210	19,390	11,060	8,330
Myeloma	36,110	20,030	16,080	12,030	6,540	5,490
Leukemia	66,890	38,720	28,170	23,540	13,500	10,040
Acute lymphocytic leukemia	6,100	3,450	2,650	1,400	720	680
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Estimates are rounded to the nearest 10; cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. About 59,080 cases of female breast ductal carcinoma in situ and 107,240 cases of melanoma in situ will be diagnosed in 2025. These are model-based estimates and should be interpreted with caution. [a] Deaths for colon and rectal cancers are combined because a large number of deaths from rectal cancer are misclassified as colon. [b] More deaths than cases may reflect a lack of specificity in recording the underlying cause of death on death certificates and/or an undercount in the case estimate.

https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2025/2025-cancer-facts-and-figures.pdf

- Other than lung cancer, breast cancer is the most common cancer in American women. The American Cancer Society's estimates for breast cancer in the United States for 2023 are:

  About 320,000 new cases of breast cancer.
  About 42,000 deaths from breast cancer.

- About 1 in 7 women (about 17%) will be diagnosed with breast cancer during her lifetime.

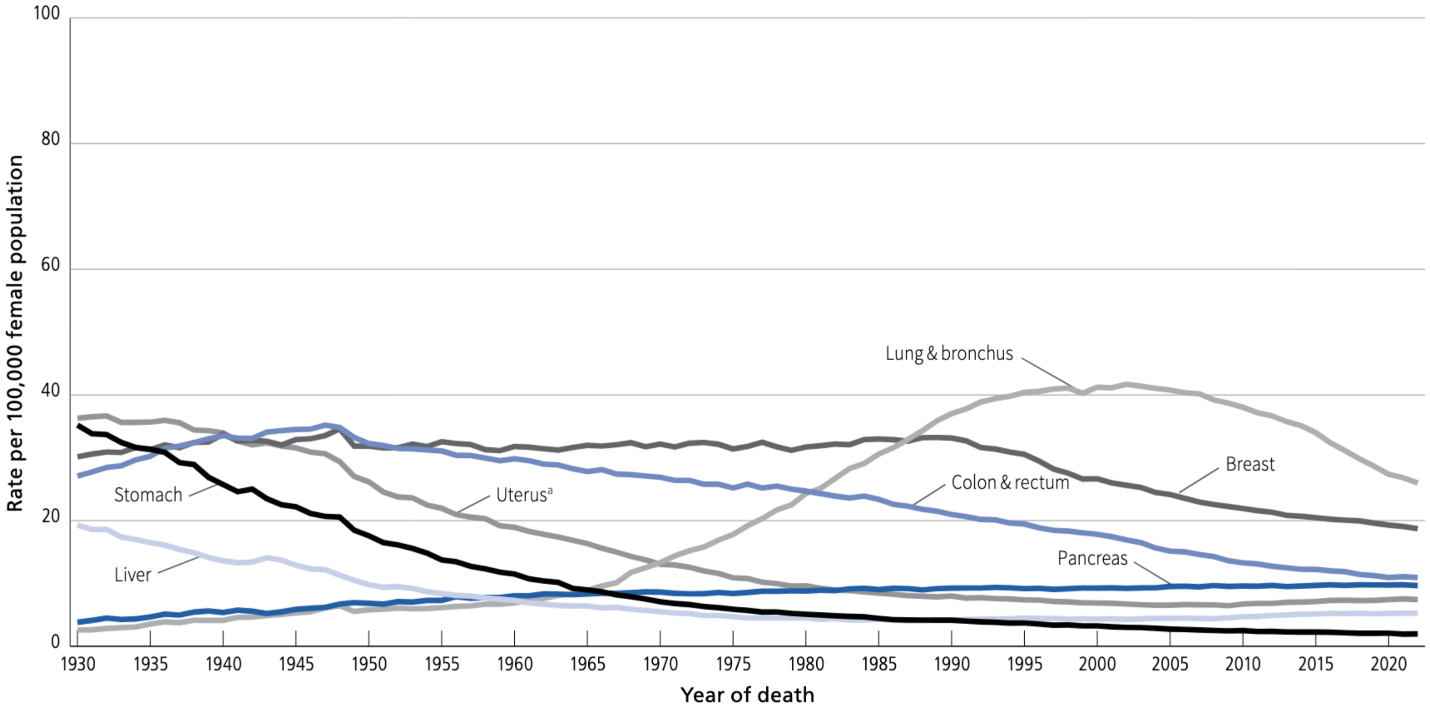
- Although breast cancer in men is rare, an estimated 2,800 men will be diagnosed with breast cancer and approximately 500 will die each year.

- Over 3.5 million breast cancer survivors are alive in the United States today.

Breast Cancer

- Brachytherapy treatment

Figure 2. Trends in Age-adjusted Cancer Death Rates by Site, Females, US, 1930-2022



Rates are age adjusted to the 2000 US standard population and exclude deaths in Puerto Rico and other US territories. Due to improvements in classification, site-specific information differs from contemporary data for cancers of the liver, lung and bronchus, colon and rectum, and uterus. [a]Uterus refers to uterine cervix and uterine corpus combined.

Data source: US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2022, National Center for Health Statistics, Centers for Disease Control and Prevention.

https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2025/2025-cancer-facts-and-figures.pdf

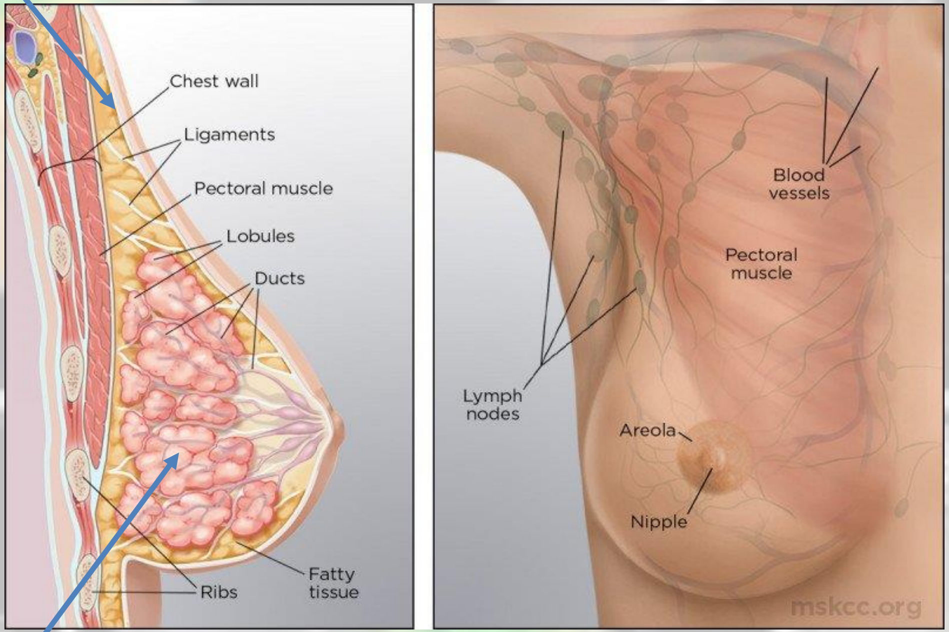
Breast Cancer

- Brachytherapy treatment

Female Beast Anatomy

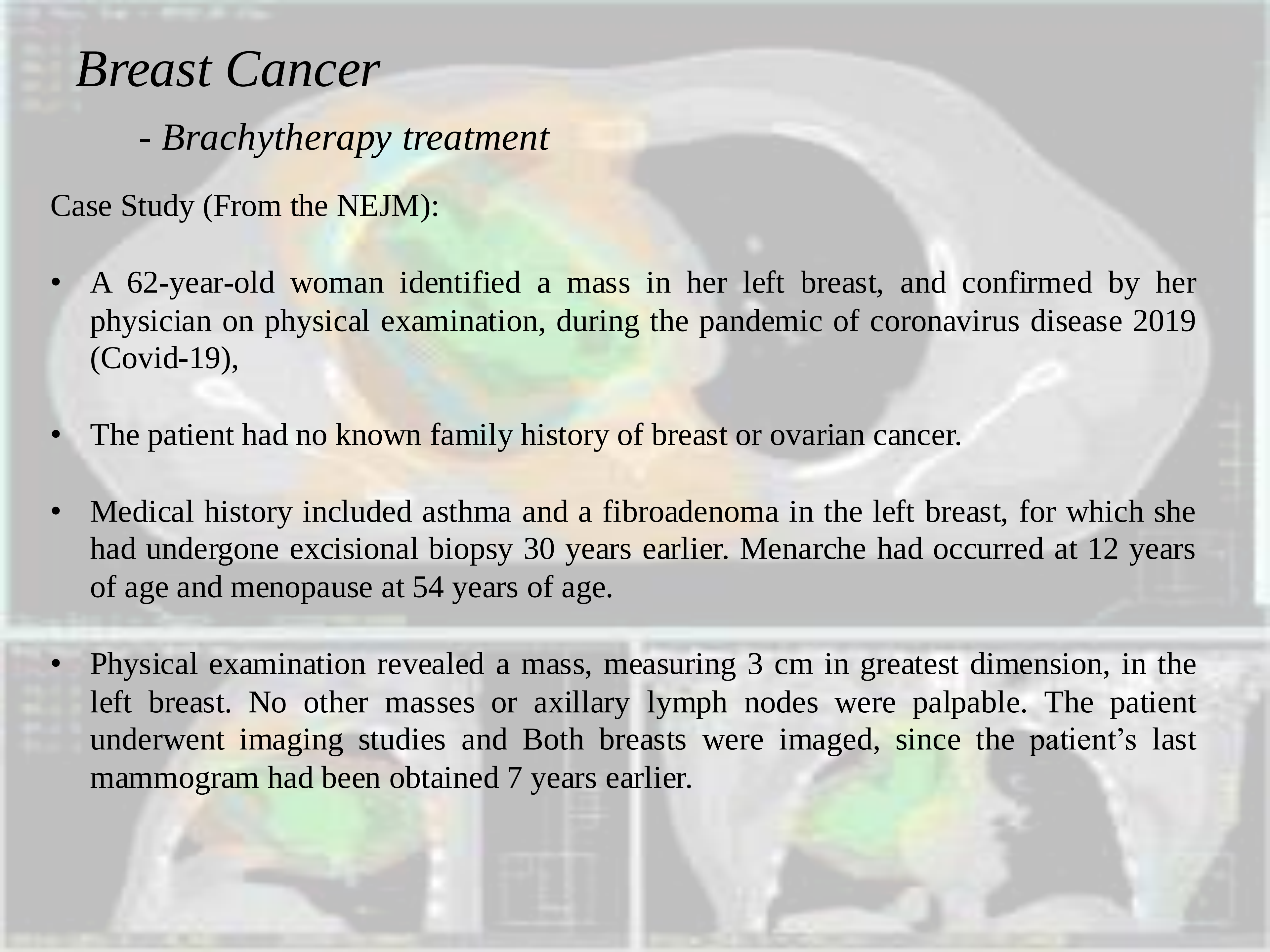
Subcutaneous layer

https://webmedia.unmc.edu/eLearning/CAHP/RST/Anatomy_of_the_Breast_Mobile/story_html5.html?lms=1



https://www.mskcc.org/cancer-care/types/breast/anatomy-breast

Mammary layer



Breast Cancer

- Brachytherapy treatment

Case Study (From the NEJM):

- A 62-year-old woman identified a mass in her left breast, and confirmed by her physician on physical examination, during the pandemic of coronavirus disease 2019 (Covid-19),

- The patient had no known family history of breast or ovarian cancer.

- Medical history included asthma and a fibroadenoma in the left breast, for which she had undergone excisional biopsy 30 years earlier. Menarche had occurred at 12 years of age and menopause at 54 years of age.

- Physical examination revealed a mass, measuring 3 cm in greatest dimension, in the left breast. No other masses or axillary lymph nodes were palpable. The patient underwent imaging studies and Both breasts were imaged, since the patient’s last mammogram had been obtained 7 years earlier.

Breast Cancer

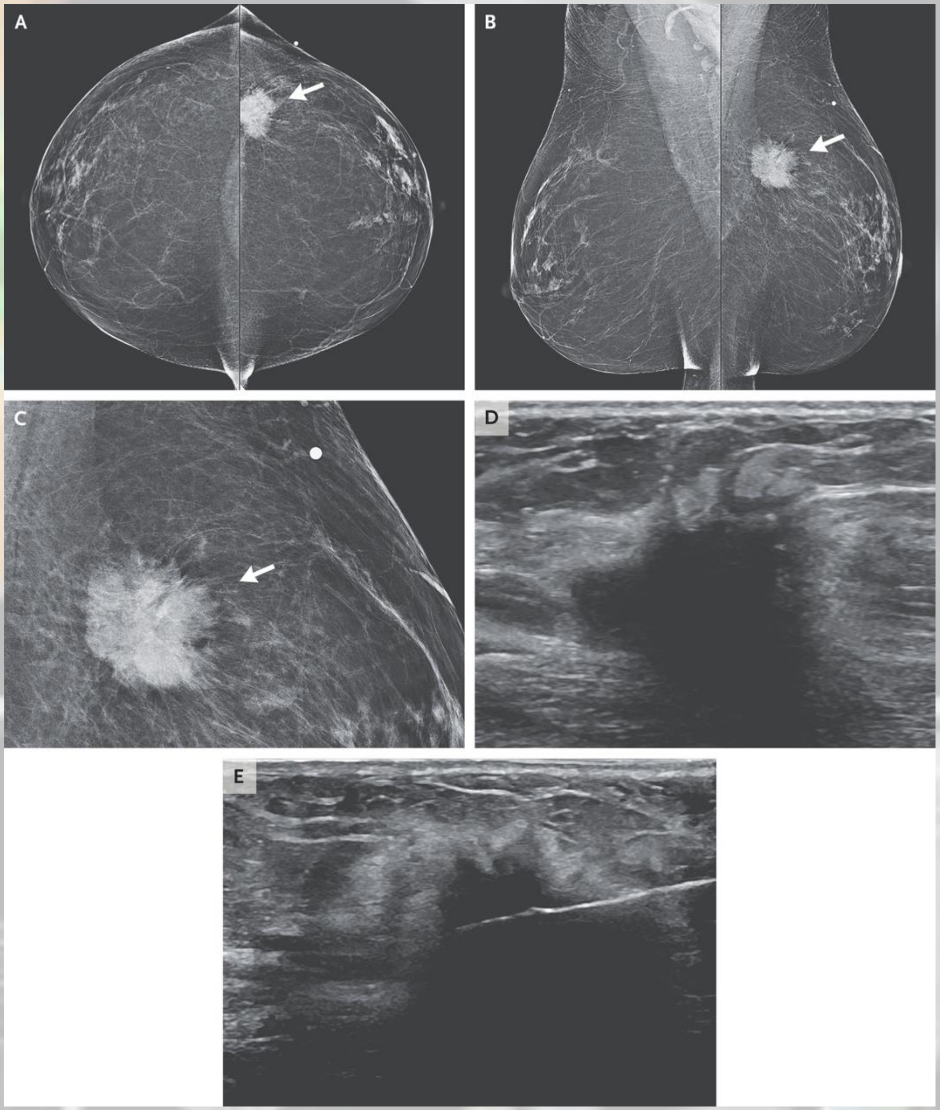
- Brachytherapy treatment

Clinical Findings

- Mammography revealed an irregular mass with spiculated margins underlying the skin marker in the left breast, with imaging characteristics highly suggestive of cancer

- Subsequent ultrasound examination revealed a solid, irregular mass in the left breast that measured 3.1 cm by 1.5 cm by 1.2 cm and normal left axillary lymph nodes.

- Tissue sampling with core-needle biopsy under ultrasonographic guidance was performed



https://www.nejm.org/doi/full/10.1056/NEJMcpc2002422

Breast Cancer

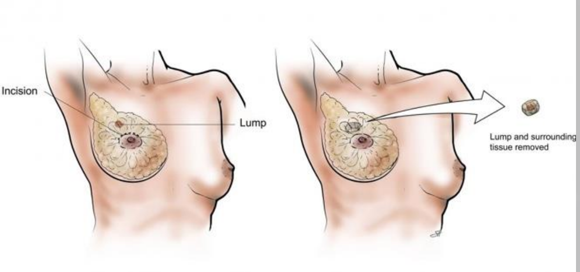
- Brachytherapy treatment

Breast Cancer treatment options:

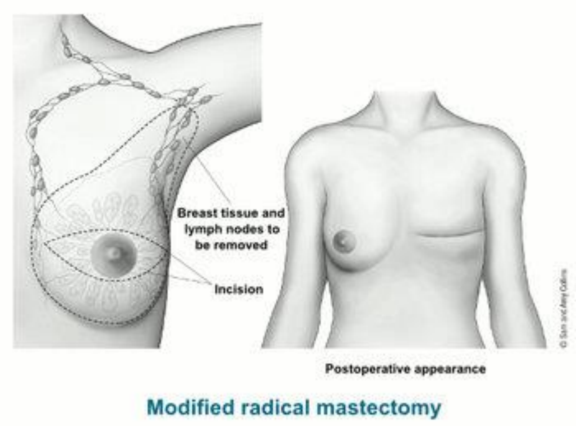
- Surgery to remove the cancerous lump (lumpectomy) or complete removal of the breast (mastectomy).

- External Beam Radiation therapy (XRT) – targeted dose of x-rays to the tumor site and surrounding margins (of some healthy and potentially diseased tissue.) This may be done in addition to the lumpectomy or the mastectomy.

- Brachytherapy – implantation of permanent or temporary radioactive material into the lumpectomy site.



https://www.bcm.edu/healthcare/specialties/oncology/cancer-types/breast-cancer/breast-cancer-surgery/lumpectomy



https://www.cancer.org/cancer/breast-cancer/treatment/surgery-for-breast-cancer/mastectomy.html

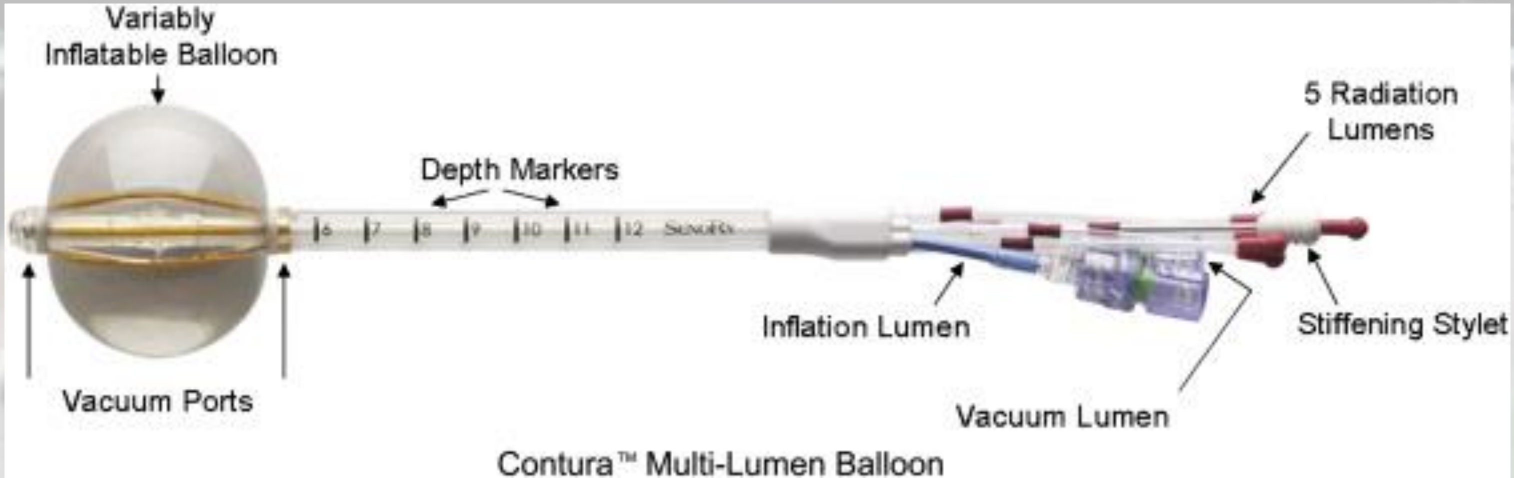
Breast Cancer

- Brachytherapy treatment

- SenoRx Inc. launched the Contura Multi-Lumen Balloon (MLB) Catheter for delivering brachytherapy to the surgical margins following lumpectomy for breast cancer.

- Contura is one of a new class of devices designed to reduce radiation treatment time from six to eight weeks to five days in patients eligible for the treatment.

https://content.time.com/time/specials/packages/article/0,28804,1852976_1852971_1852953,00.html



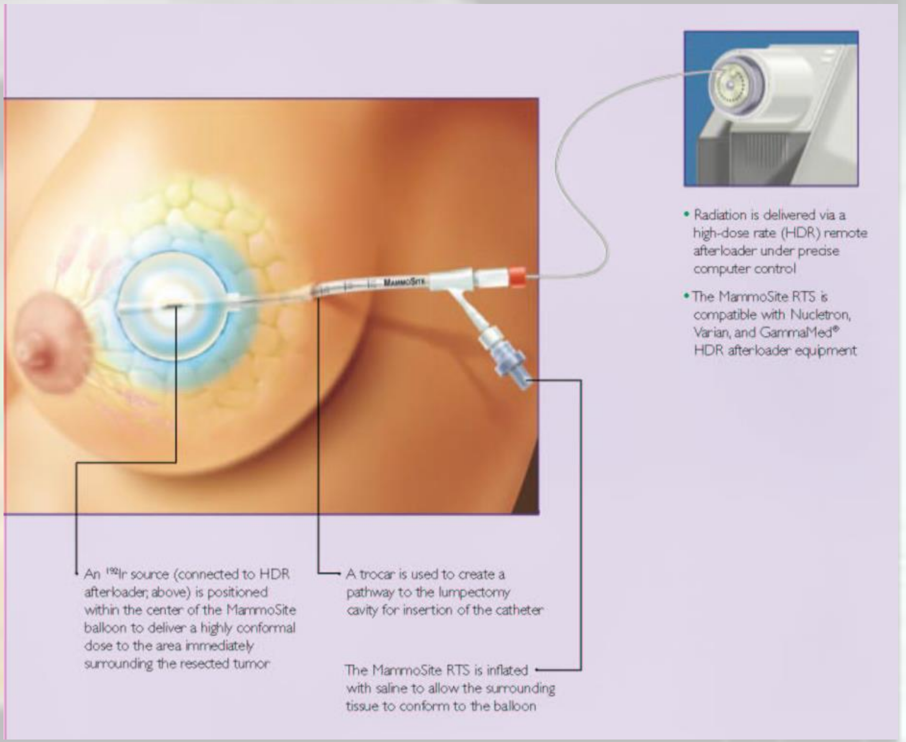
Contura™ Multi-Lumen Balloon

Sheree Brown, Mark McLaughlin, Keith Pope, Kenneth Haile, Laurie Hughes, Philip Z. Israel, Initial radiation experience evaluating early tolerance and toxicities in patients undergoing accelerated partial breast irradiation using the Contura Multi-Lumen Balloon breast brachytherapy catheter, Brachytherapy, Volume 8, Issue 2, 2009, Pages 227-233, ISSN 1538-4721, https://doi.org/10.1016/j.brachy.2008.11.013.

Breast Cancer

- Brachytherapy treatment

Image courtesy of Dr. Stephen Amadon, PhD., DABR



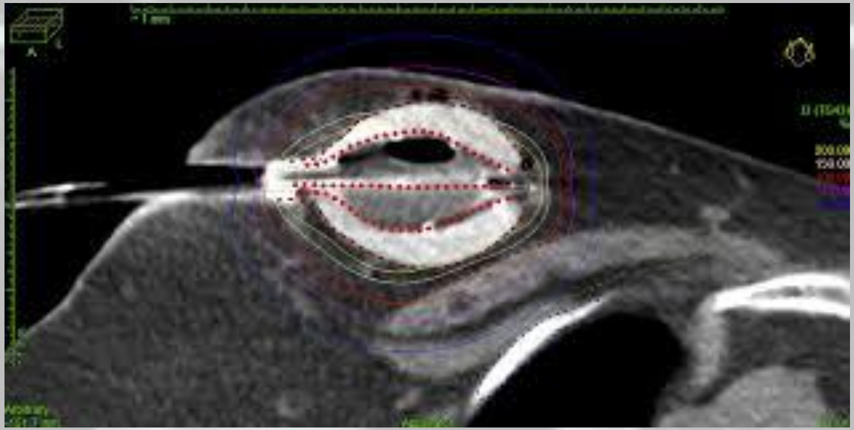
- Radiation is delivered via a high-dose rate (HDR) remote afterloader under precise computer control
- The MammoSite RTS is compatible with Nucletron, Varian, and GammaMed® HDR afterloader equipment

An ^{192}Ir source (connected to HDR afterloader, above) is positioned within the center of the MammoSite balloon to deliver a highly conformal dose to the area immediately surrounding the resected tumor

A trocar is used to create a pathway to the lumpectomy cavity for insertion of the catheter

The MammoSite RTS is inflated with saline to allow the surrounding tissue to conform to the balloon

https://www.semanticscholar.org/paper/Early-experience-with-balloon-brachytherapy-for-Dowlatshahi-Snider/a23f16256967b3be5fd2f4f013431e9d2baac5dd



https://www.brachyjournal.com/article/S1538-4721%2817%2930420-8/pdf

- Treatment with 34Gy (10 fractions at 3.4Gy each) for 1 week.
- Radioactive source: $^{192}_{77}Ir$

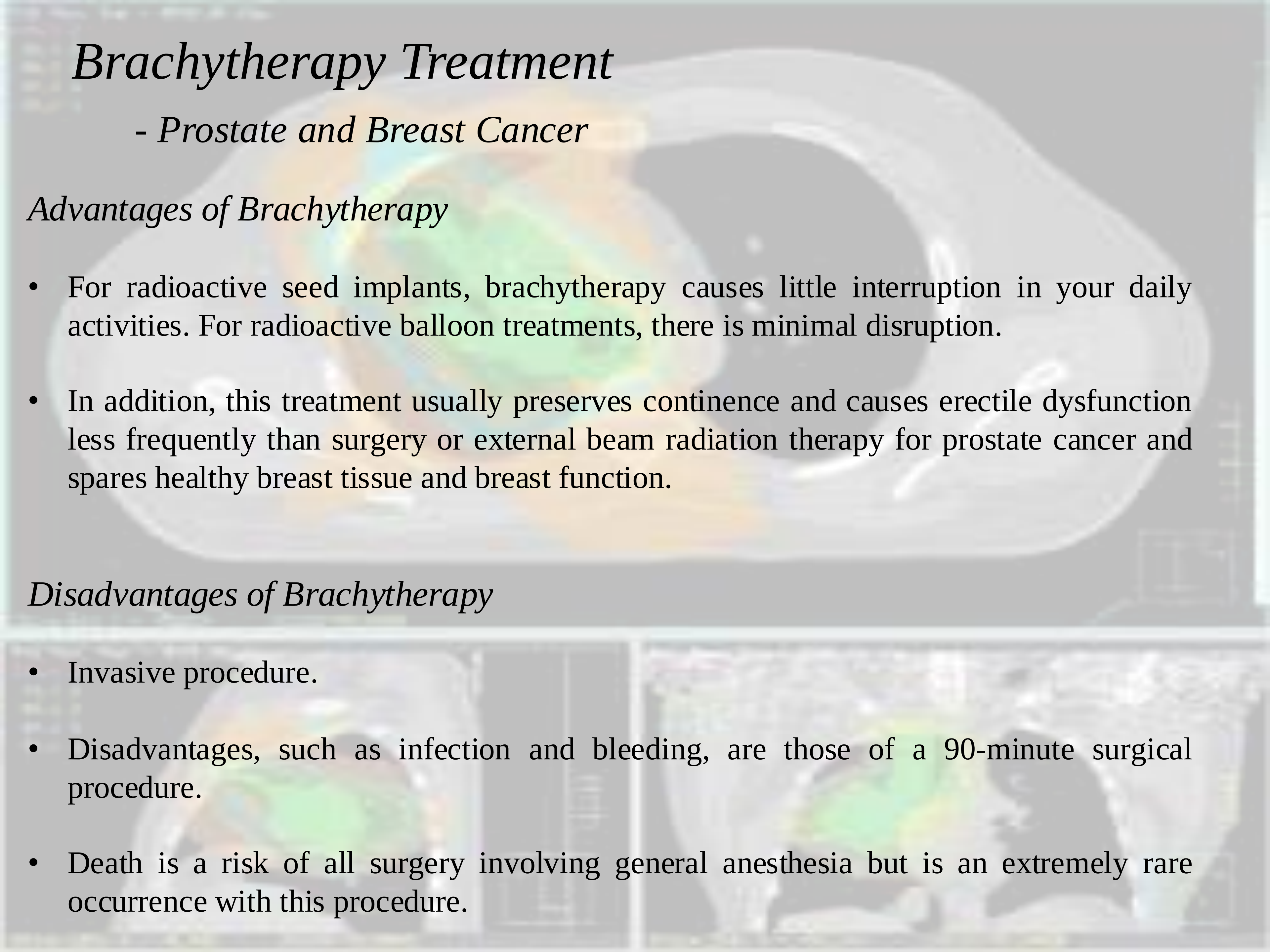
$$^{192}_{77}Ir \rightarrow {}^{0}_{-1}e + {}^{192}_{78}Pt + \bar{\upsilon}$$

Breast Cancer

- Brachytherapy treatment

Image courtesy of Dr. Stephen Amadon, PhD., DABR

Image courtesy of Dr. Stephen Amadon, PhD., DABR



Brachytherapy Treatment

- Prostate and Breast Cancer

Advantages of Brachytherapy

- For radioactive seed implants, brachytherapy causes little interruption in your daily activities. For radioactive balloon treatments, there is minimal disruption.

- In addition, this treatment usually preserves continence and causes erectile dysfunction less frequently than surgery or external beam radiation therapy for prostate cancer and spares healthy breast tissue and breast function.

Disadvantages of Brachytherapy

- Invasive procedure.

- Disadvantages, such as infection and bleeding, are those of a 90-minute surgical procedure.

- Death is a risk of all surgery involving general anesthesia but is an extremely rare occurrence with this procedure.

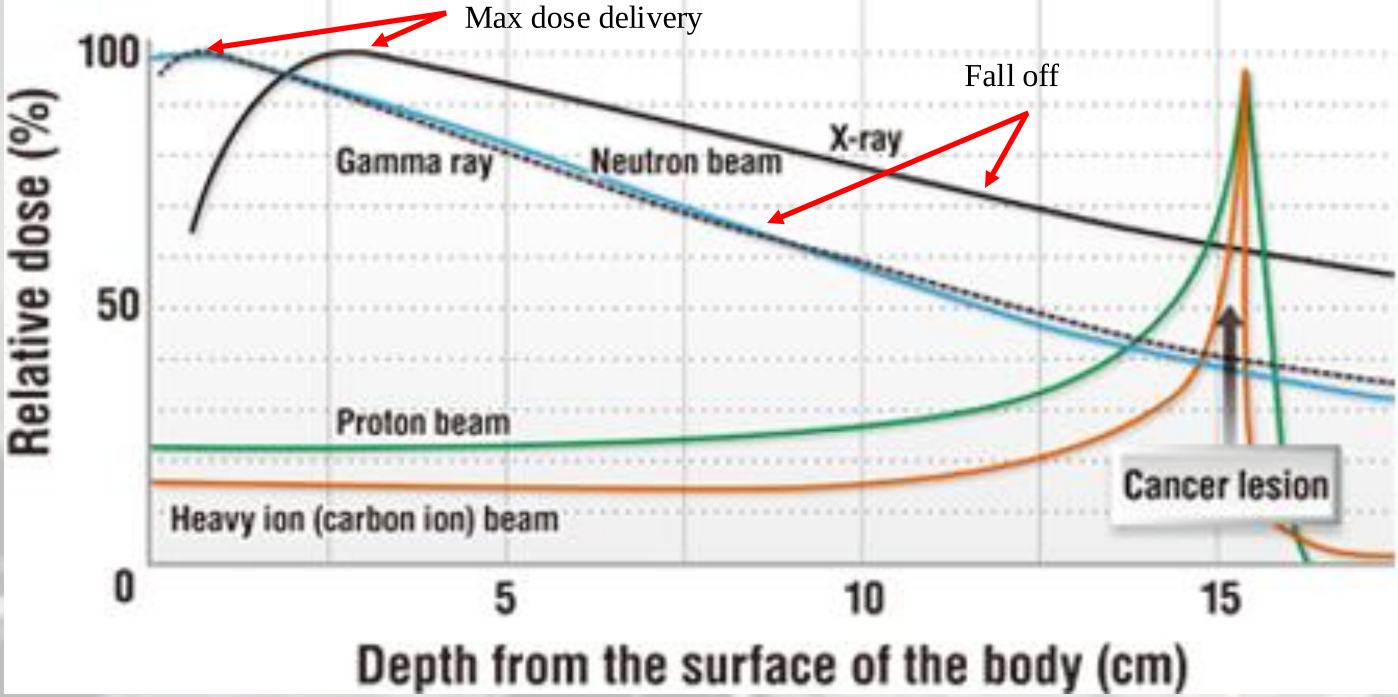
Heavy Ion Radiotherapy

- Carbon Ions

- Heavy ion radiotherapy is the treatment of disease by using ions heavier than protons.
- The ions are produced in particle accelerators.
- The major disadvantage with conventional radiotherapy (external beam therapy) is the dose is highest just below the surface of the body and gradually decreases with depth.
- It has less effect on cancers deep in the body and causes damage to the surrounding normal tissue.
- Heavy ion beams are used, due to their high physical dose distribution, we can concentrate the high dose to a targeted cancer lesion deep in the body, with little effect on the surrounding normal tissue, by adjusting the dose peak.
- Heavy ion beams have an advantage in cancer therapy in that their relative biological effectiveness increases with the depth from the surface of the body, and thus heavy ion radiotherapy is effective against cancers deep in the body.

Heavy Ion Radiotherapy
- *Carbon Ions*

So, are carbon ions a better choice than protons?



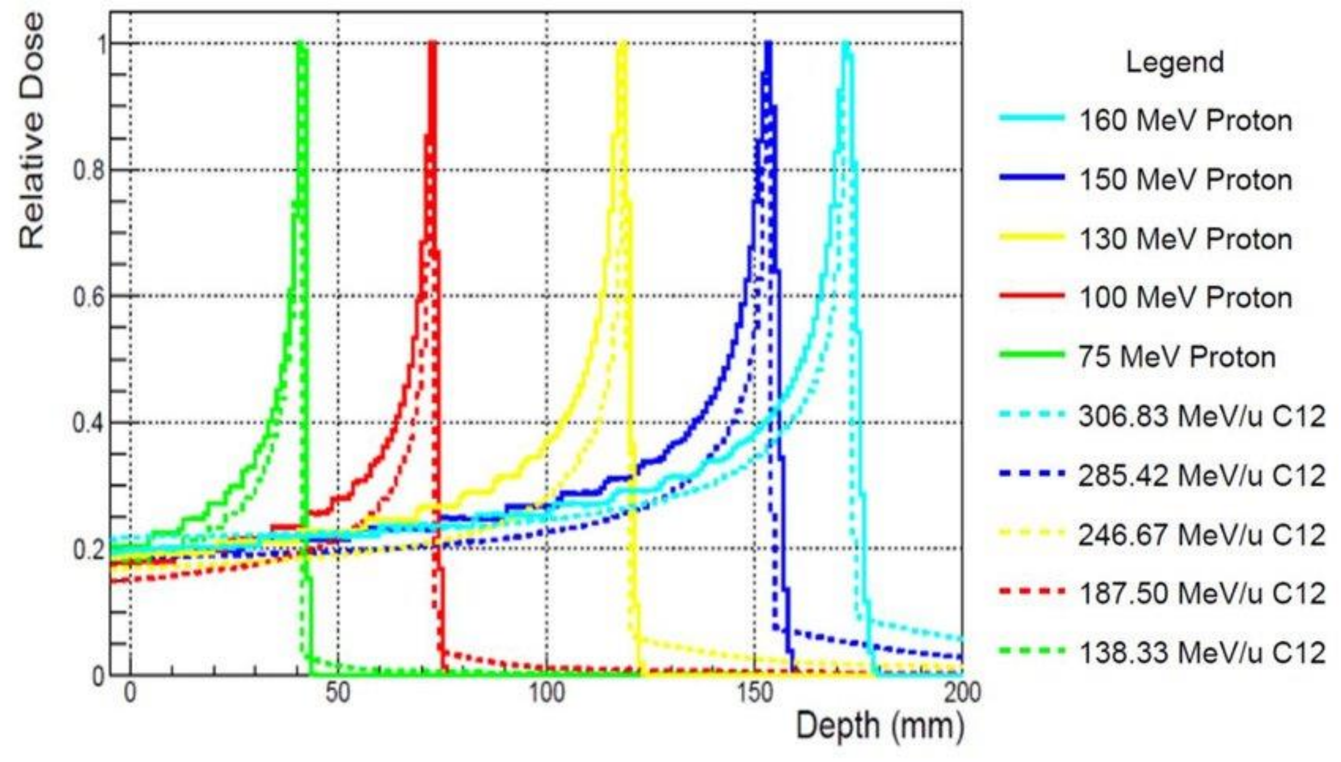
http://www.hirt-japan.info/en/medical/about/merit.html

It would seem that ions heavier than protons would be better because their Bragg peak is much narrower than for protons leading to a greater dose delivery at the target site.

Heavy ions are also less prone to scatter, unlike protons.

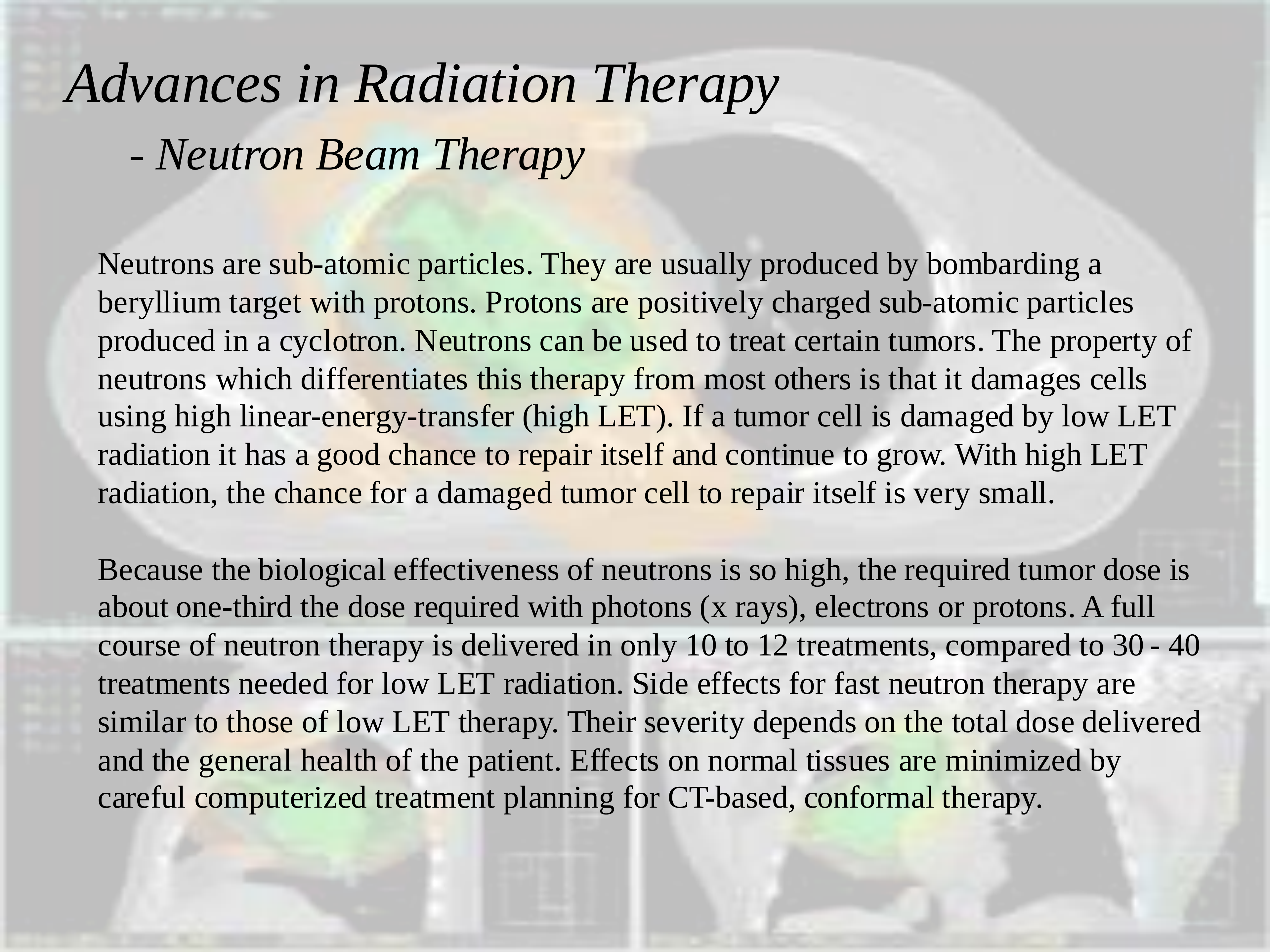
Heavy Ion Radiotherapy

- *Carbon Ions*



Pamisa, Dainna Recel & Convicto, Vernie & Lintasan, Abdurajan & Quiñones, C. (2020). Monte Carlo Investigation of the Depth-dose Profile of Proton Beams and Carbon Ions in Water, Skeletal Muscle, Adipose Tissue, and Cortical Bone for Hadron Therapy Applications. Journal of Physics: Conference Series. 1505. 012010. 10.1088/1742-6596/1505/1/012010.

- Dose depth curves for carbon ions in water compared to protons in water.
- Carbon ions have a much narrower Bragg peak



Advances in Radiation Therapy

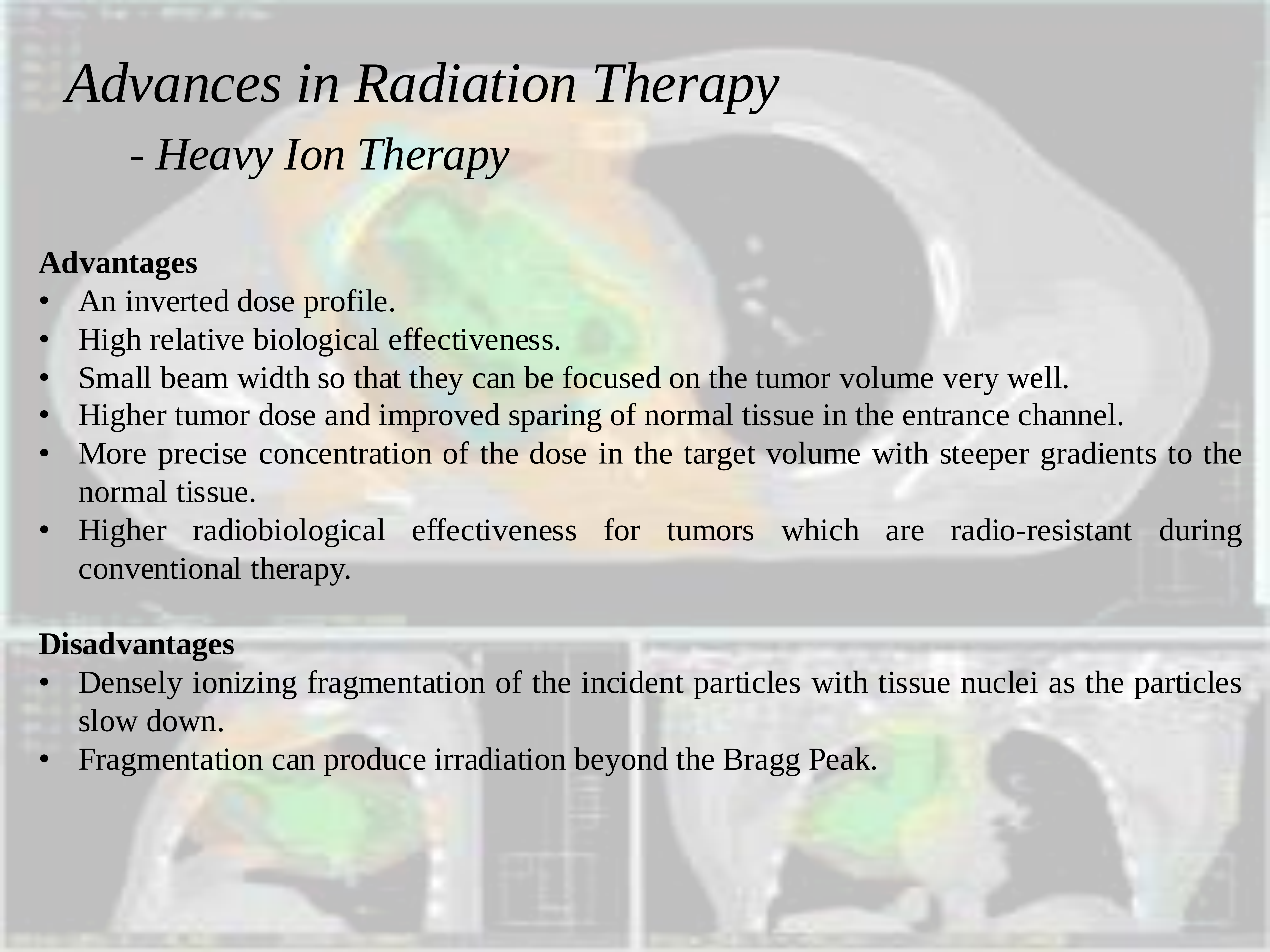
- Neutron Beam Therapy

Neutrons are sub-atomic particles. They are usually produced by bombarding a beryllium target with protons. Protons are positively charged sub-atomic particles produced in a cyclotron. Neutrons can be used to treat certain tumors. The property of neutrons which differentiates this therapy from most others is that it damages cells using high linear-energy-transfer (high LET). If a tumor cell is damaged by low LET radiation it has a good chance to repair itself and continue to grow. With high LET radiation, the chance for a damaged tumor cell to repair itself is very small.

Because the biological effectiveness of neutrons is so high, the required tumor dose is about one-third the dose required with photons (x rays), electrons or protons. A full course of neutron therapy is delivered in only 10 to 12 treatments, compared to 30 - 40 treatments needed for low LET radiation. Side effects for fast neutron therapy are similar to those of low LET therapy. Their severity depends on the total dose delivered and the general health of the patient. Effects on normal tissues are minimized by careful computerized treatment planning for CT-based, conformal therapy.

Advances in Radiation Therapy

- Heavy Ion Therapy



Advantages

- An inverted dose profile.
- High relative biological effectiveness.
- Small beam width so that they can be focused on the tumor volume very well.
- Higher tumor dose and improved sparing of normal tissue in the entrance channel.
- More precise concentration of the dose in the target volume with steeper gradients to the normal tissue.
- Higher radiobiological effectiveness for tumors which are radio-resistant during conventional therapy.

Disadvantages

- Densely ionizing fragmentation of the incident particles with tissue nuclei as the particles slow down.
- Fragmentation can produce irradiation beyond the Bragg Peak.

Proton & Heavy Ion Facilities

In the US & Canada (All proton facilities):
Loma Linda (Fermilab), Mass General (IBA), Crocker (Davis)
Jacksonville, Texas (Hitachi), Indiana (NSF), TRIUMF (Canada)

In Asia:
HIMAC, Chiba (carbon), Tsukuba (Hitachi), Wanje (China)
Almost completed: Hyogo (Near Kobe)(carbon)
Planned facilities: (all carbon)Sendei, Tokyo, Nagoya, Hiroshima and Kyushu, Seoul, Austron (Australia).

In Europe:
Nice (protons) (and plans to go to higher energy), PSI (protons),
Orsay (France), ITEP (Moscow), Svedbog (Sweden), Dubna and St. Petersburg (Russia),

Almost completed:Heidelberg (carbon)
Under construction:Munich, Lyon, Wiener Neustadt, Pave, etc.

Proton & Heavy Ion Facilities

WHO, WHERE	COUNTRY	PARTICLE	MAX. CLINICAL ENERGY (MeV)	BEAM DIRECTION
ITEP, Moscow	Russia	p	250	horiz.
St.Petersburg	Russia	p	1000	horiz.
PSI, Villigen	Switzerland	p	72	horiz.
Dubna	Russia	p	200***	horiz.
Uppsala	Sweden	p	200	horiz.
Clatterbridge	England	p	62	horiz.
Loma Linda	CA.,USA	p	250	gantry,horiz.
Nice	France	p	65	horiz.
Orsay	France	p	200	horiz.
iThemba Labs	South Africa	p	200	horiz.
MPRI(2)	IN.,USA	p	200	horiz.
UCSF	CA.,USA	p	60	horiz.
HIMAC, Chiba	Japan	ion	800/u	horiz.,vertical
TRIUMF, Vancouver	Canada	p	72	horiz.
PSI, Villigen	Switzerland	p**	250*	gantry
G.S.I. Darmstadt	Germany	ion**	430/u	horiz.
HMI, Berlin	Germany	p	72	horiz.

Proton & Heavy Ion Facilities

WHO, WHERE	**COUNTRY**	**PARTICLE**	**MAX. CLINICAL ENERGY (MeV)**	**BEAM DIRECTION**
NCC, Kashiwa	Japan	p	235	gantry
HIBMC,Hyogo	Japan	p	230	gantry
HIBMC,Hyogo	Japan	ion	320	horiz.,vertical
PMRC(2), Tsukuba	Japan	p	250	gantry
NPTC, MGH Boston	USA	p	235	gantry,horiz.
INFN-LNS, Catania	Italy	p	60	horiz.
Shizuoka	Japan	p	235	gantry, horiz.
Wakasa WERC,Tsuruga	Japan	p	200	horiz.,vertical
WPTC, Zibo	China	p	230	gantry, horiz.
MD Anderson Cancer Center, Houston, TX	USA	p	250	gantry, horiz.
FPTI, Jacksonville, FL	USA	p	230	gantry, horiz.

Proton & Heavy Ion Facilities

WHO, WHERE	COUNTRY	PARTICLE	MAX. CLINICAL ENERGY (MeV)	START OF TREATMENT PLANNED
RPTC, Munich*	Germany	p	250 SC cyclotron	2007
PSI, Villigen*	Switzerland	p	250 SC cyclotron	2007/08 (OPTIS2/ Gantry2)
NCC, Seoul*	Korea	p	230 cyclotron	End of 2007
UPenn*	USA	p	230 cyclotron	2009
Med-AUSTRON	Austria	p, ion	synchrotron	2011?
Trento	Italy	p	? cyclotron	2010?
CNAO, Pavia*	Italy	p, ion	430/u synchrotron	2009?
Heidelberg/GSI Darmstadt*	Germany	p, ion	430/u synchrotron	2008
iThemba Labs	South Africa	p	230 cyclotron	2009?
RPTC, Koeln	Germany	p	250 SC cyclotron	?
WPE, Essen*	Germany	p	230 cyclotron	2009
CPO, Orsay*	France	p	230 cyclotron	2010
PTC, Marburg*	Germany	p, ion	430/u synchrotron	2010
Northern Illinois PT Res.Institute, W. Chicago, IL	USA	p	250 accelerator	2011