Introduction to Radiation Therapy

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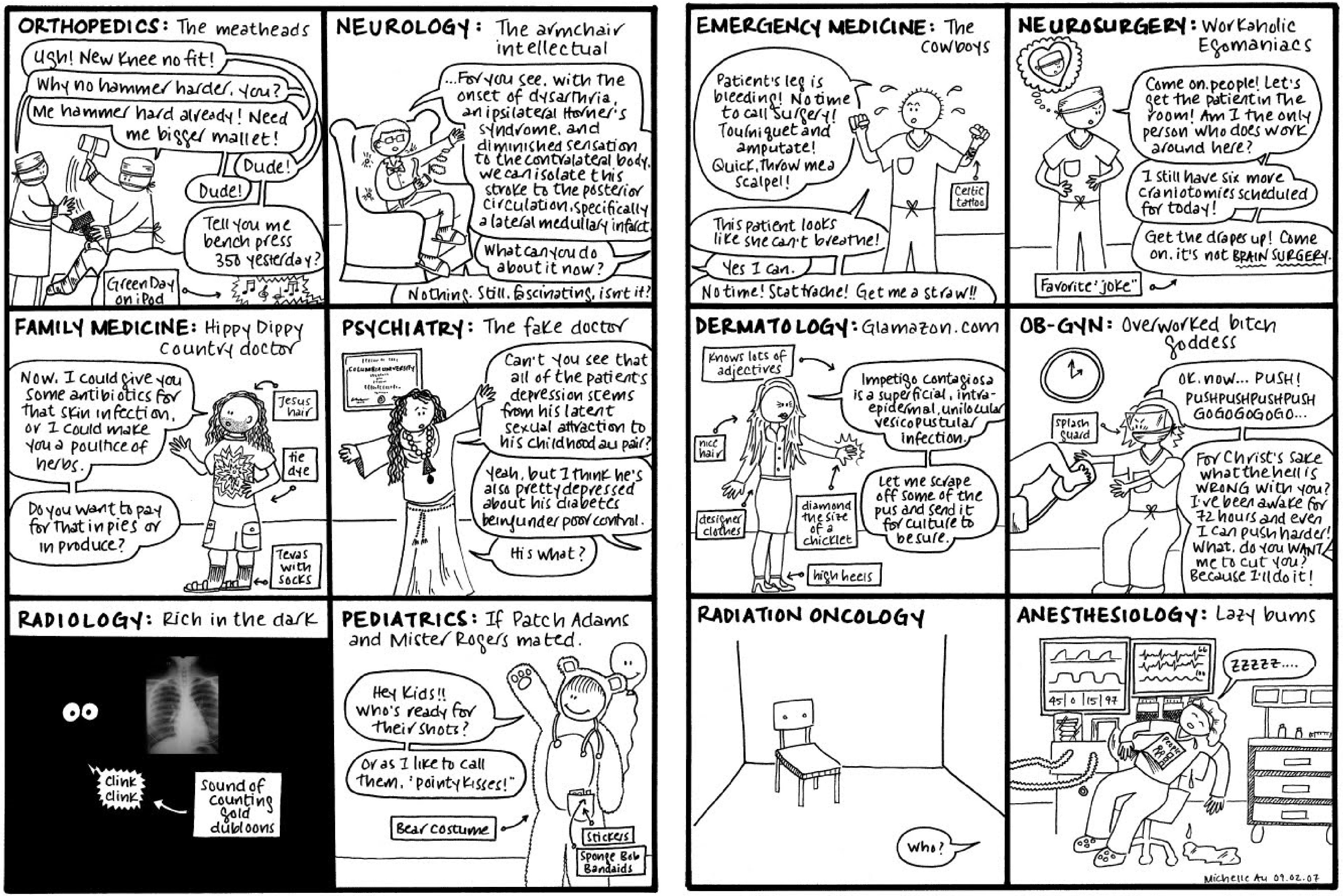
Outline

- What is Radiation Oncology/Therapy
- History of Radiation Therapy
- What is the physical and biological basis for radiation
- What are the clinical applications of radiation in the management of cancer
- What is the process for treatment
    - Simulation
    - Treatment planning
    - Delivery of radiation
- What types of radiation are available
- Summary

The 12 Medical Specialty Stereotypes



What is radiation oncology?

- Small numerically
- Usually housed in basements/bunker
- Blessing/Curse

Radiation Is Anatomic, Local Therapy

- Delineation of targets is central to improving the therapeutic ratio.

- Treatment planning is based on CT (primarily) but also MRI, PET, and physical findings.

- Treatments are focused on hitting the cancer and missing the normal stuff as best we can.

Radiation’s Role

- Unlike surgical management, radiation can treat a region without removing it (ie, organ preservation!)
- Unlike chemotherapy, radiation is spatially delineated (non-systemic)
- Unlike both, radiation therapy is simulated before delivering it

Patient interaction

- 90% or more of patients are treated as out-patients, while awake and functional.
- See patients who are actively receiving treatment at least once weekly
- Patients range broadly in age, from infancy to extreme old age.
  - Avoid radiation in pediatrics patients if possible due to risk of side effects
- Prognoses range from the excellent to the dismal (30-40% of treatment is palliative).

Radiation Treatment Team

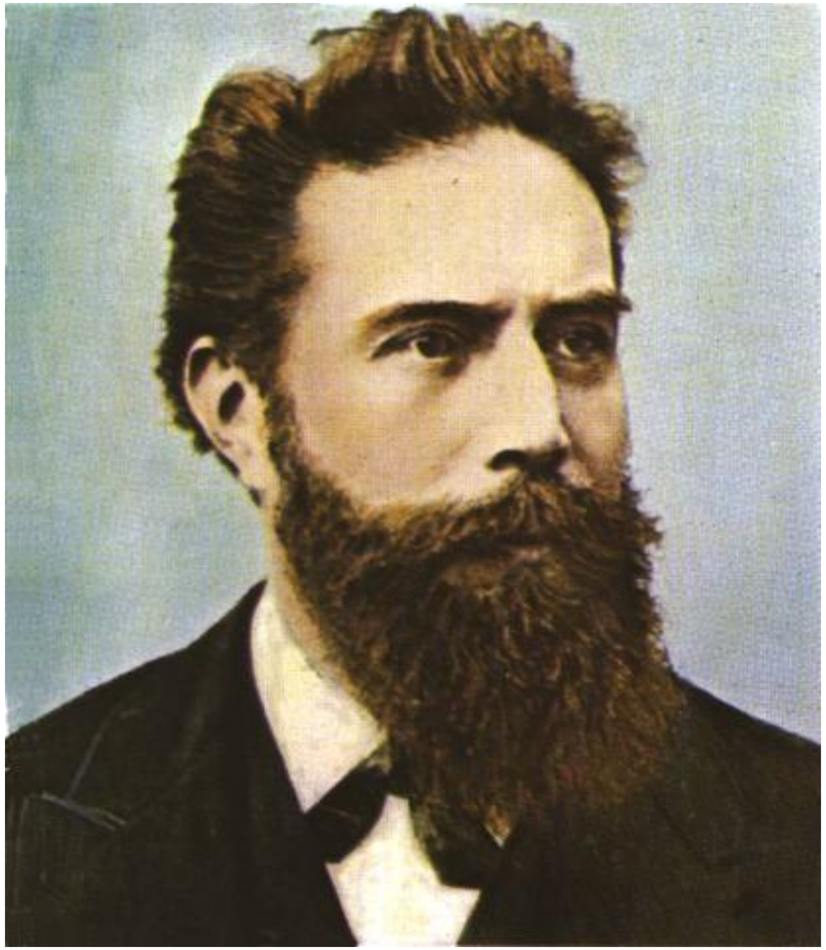
- Delivery of a quality radiation plan requires close collaboration with professional dosimetrists, physicists, and radiation therapists.
  - Medical Physicist
    - Ensures that treatment plans are properly tailored for each patient, and is responsible for the calibration and accuracy of treatment equipment
  - Dosimetrist
    - Works with the radiation oncologist and medical physicist to calculate the proper dose of radiation given to the tumor
  - Radiation Therapist
    - Administers the daily radiation under the doctor’s prescription and supervision

- Modern radiation planning is all planned in 3D (or 4D) with computer software

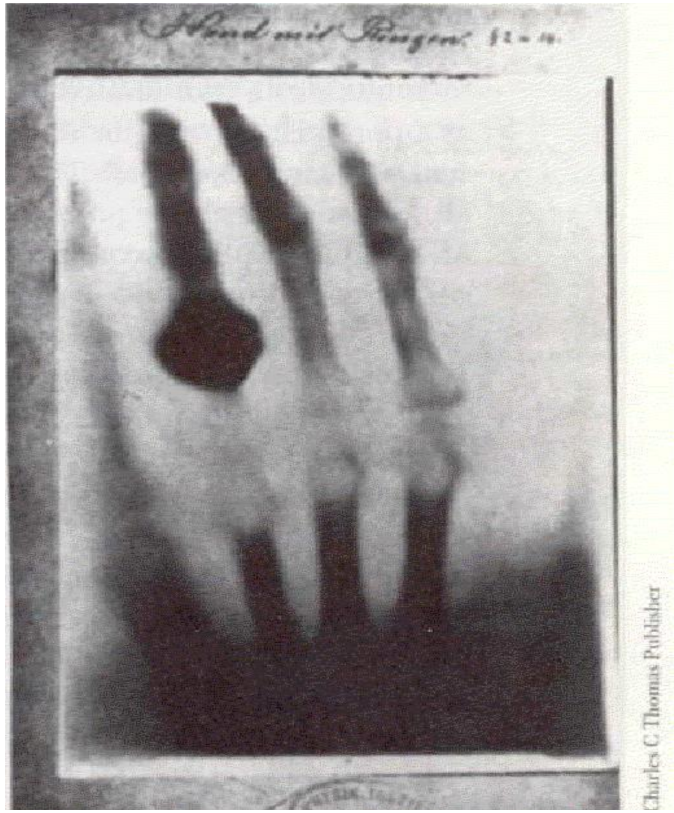
Team Outside Radiation Department

- It’s a team sport…
- Nurses, SWs, Care Coordinators
- Physicians: PCPs, surgeons, medical oncologists, radiologists, pathologists
- Dentists
- Dieticians
- ETC

History of Radiation

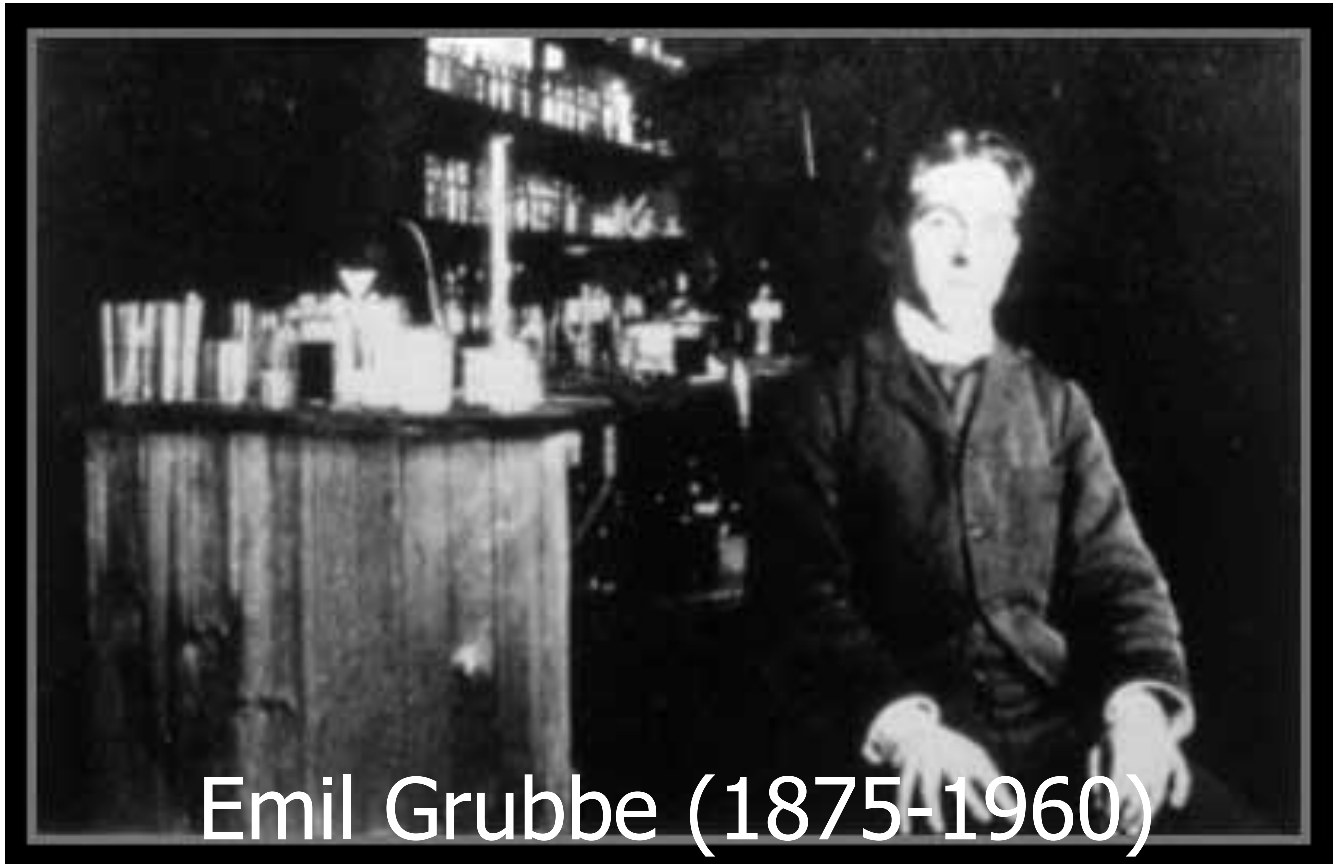


November 8, 1895



Wilhelm Conrad Roentgen
1845 - 1923

History of Radiation



Emil Grubbe (1875-1960)

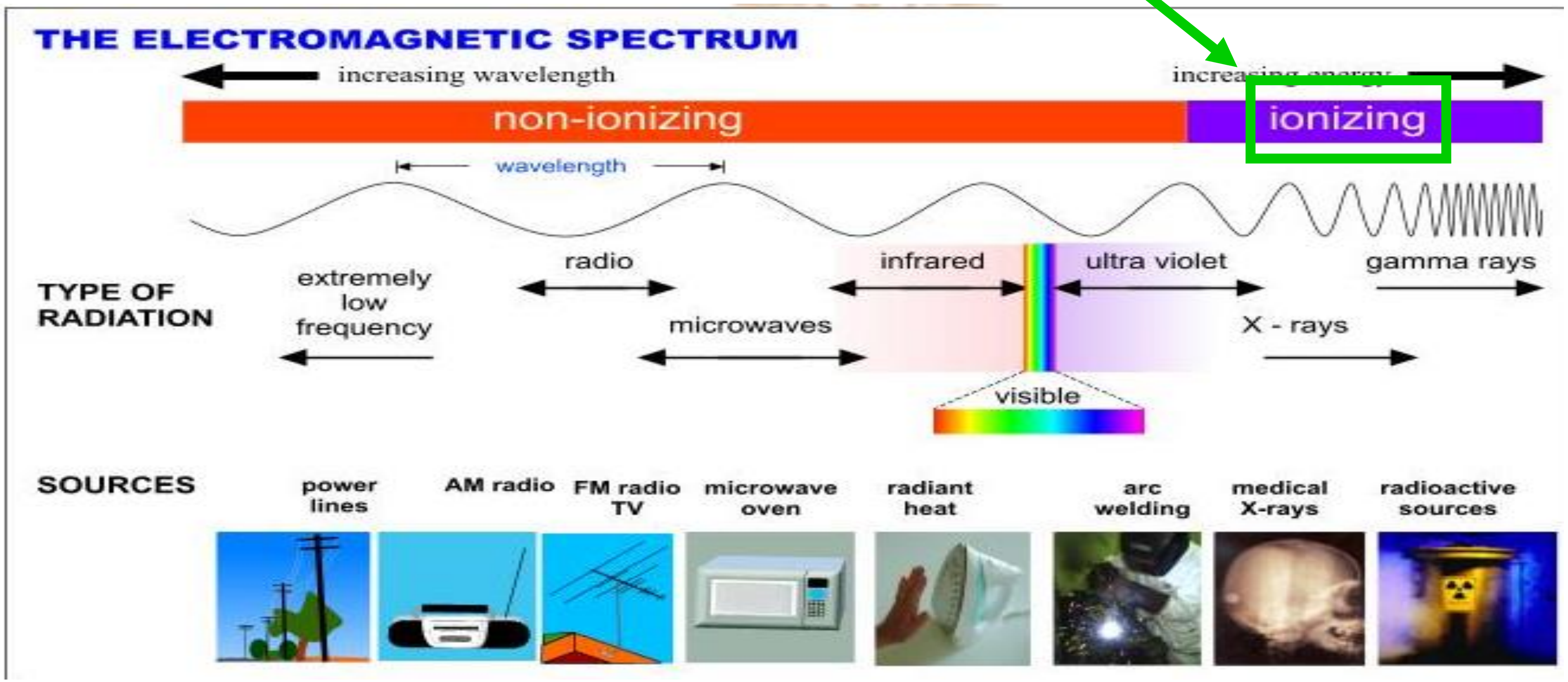
First therapeutic use of radiation. Used for recurrent breast cancer in January 1896

Why are typical courses of radiation delivered daily for several weeks?

- France 1920s-1930s
  - Spreading out dose over time prevented skin toxicity
- **Fractionation:** dividing the total dose into small daily fractions over several weeks, takes advantage of differential repair abilities of normal and malignant tissues
- Fraction = treatment (typically daily, occasionally BID)

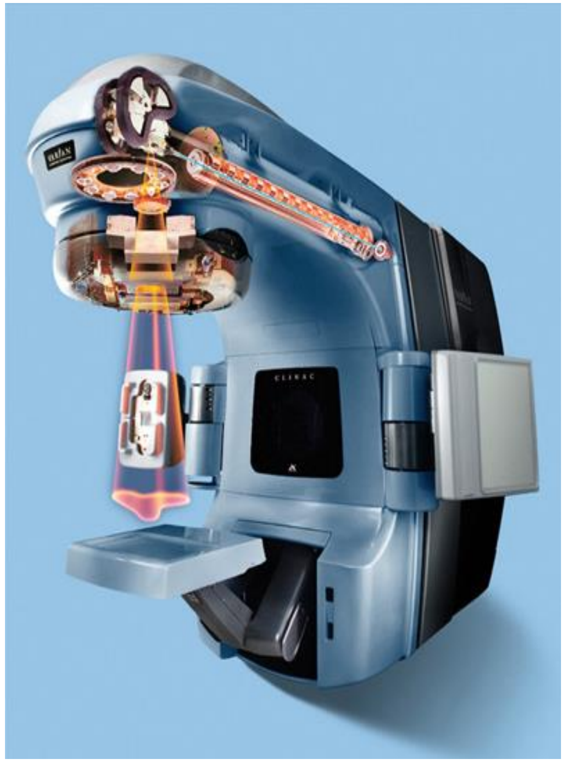
Nonionizing vs Ionizing Radiation

- Radiation: movement of energy through space



Sources of Ionizing Radiation

- Photons
  - Gamma Rays
    - Emitted from a nucleus of a radioactive atom
      - Cobalt treatment machine
      - Radioisotopes used in brachytherapy (radiation implants)
  - X-rays **90% of radiotherapy**
    - Generated by a linear accelerator when accelerated electrons hit a target
- Particle Beams
  - Protons
  - Neutrons
  - Electrons



1990s

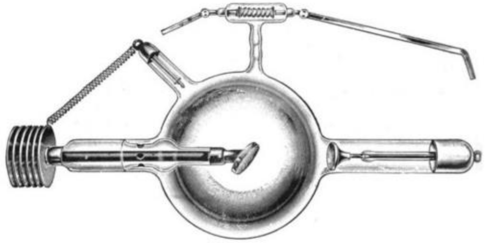
- 4 innovations radically changed radiotherapy
  - Linear Accelerators*
  - CT simulation*
  - Computer based planning*
  - Multi leaf collimators (MLC)*

- 2000s: Image-guided radiation treatment (IGRT)*

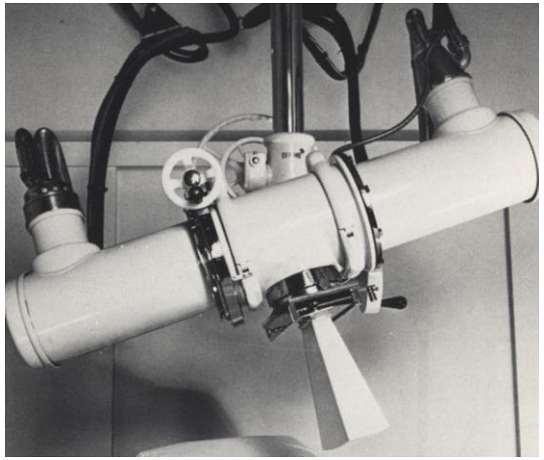
- *will denote these advances in remainder of talk

Photon Technology Improvements

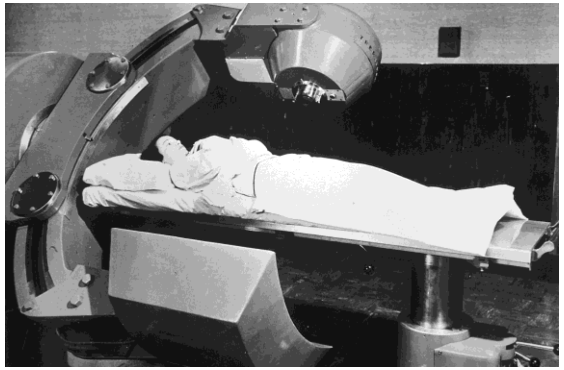
Early X-ray Tube



Orthovoltage



Cobalt-60 Unit

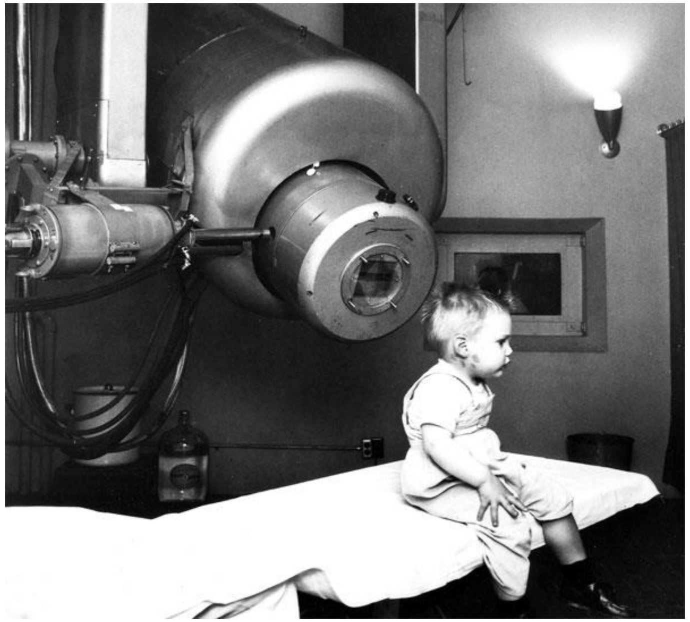


More Skin Dose
Lower Energy

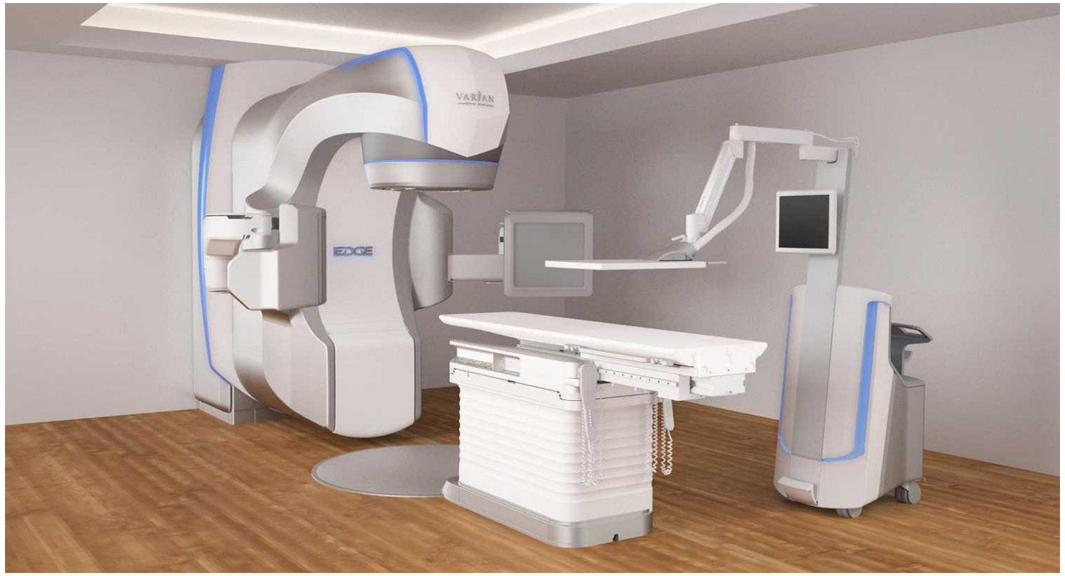
Less Skin Dose
Higher Energy

Photon Technology Improvements

Early LINAC* (1956)



Modern Linear Accelerator*



More Skin Dose
Lower Energy

Less Skin Dose
Higher Energy

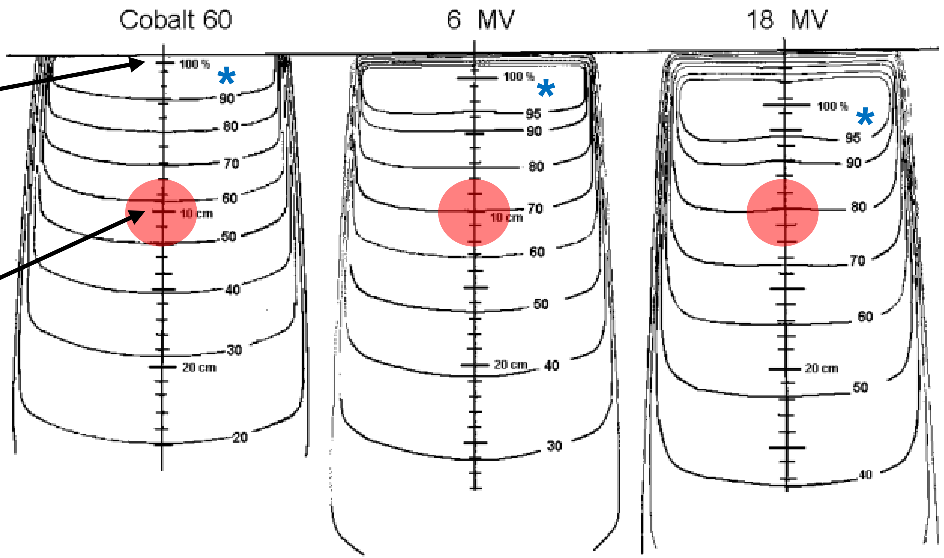
What type of radiation is used therapeutically?

- >90% of modern radiotherapy uses <u>photons</u>
  - Electrons used for treatments close to skin surface
  - Protons used in special occasions

The figures below compare the isodose distributions for Cobalt-60, 6 MV, and 18 MV X rays.

…it gets really hot here.

To get enough dose here…



Higher beam energy improves the ratio of dose at depth vs. surface some, but not enough

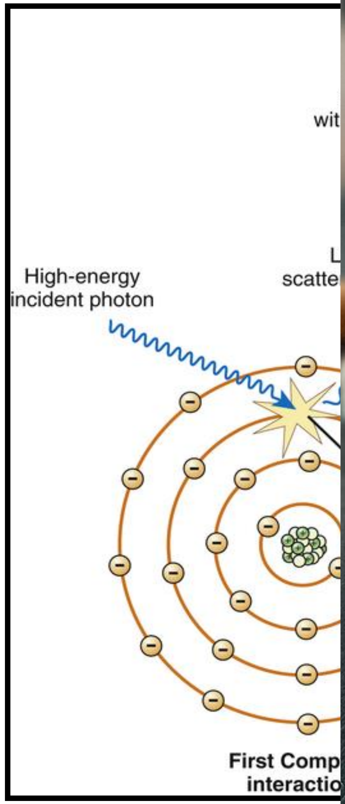
What Is the Biologic Basis for Radiation Therapy?

- Radiation therapy works by damaging the DNA of cells and destroys their ability to reproduce

- Both normal and cancer cells can be affected by radiation, but cancer cells have generally impaired ability to repair this damage, leading to cell death

- All tissues have a tolerance level, or maximum dose, at which point damage may occur

How Does Radiation Work?



ncer Cell Dies

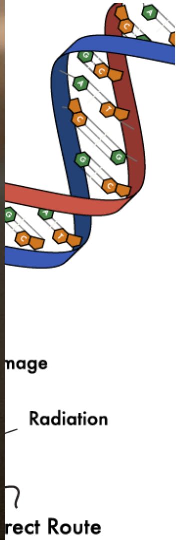


Image Credits: https://radiologykey.com and https://sites.duke.edu/

What’s the radiobiological basis behind fractionated radiation treatment?

- Four major factors are believed to affect tissue’s response to fractionated radiation:
  - **Repair** of sublethal damage to cells between fractions caused by radiation
    - Cancer cells less capable of repair
  - **Repopulation** or regrowth of cells between fractions
    - If radiation treatment not completed in timely manner, the most radioresistant cancer cells proliferate (ie, avoid prolonged treatment breaks!)
  - **Redistribution** of cells into radiosensitive phases of cell cycle
    - E.g. cells in late G2 or mitosis phase of cell growth more sensitive than those in S-phase
  - **Reoxygenation** of hypoxic cells to make them more sensitive to radiation
    - Tumors have poor oxygenation, fractionating treatment allows new oxygen to enter tumor between treatments

Clinical Uses for Radiation Therapy

- Therapeutic radiation serves two major functions
  - To cure cancer (local treatment for local control)
    - Destroy tumors that have not spread
    - Kill residual microscopic disease left after surgery or chemotherapy
    - Avoid morbidity of surgery to preserve organs/function
  - To reduce or palliate symptoms (maintain or improve QoL)
    - Shrink tumors affecting quality of life, e.g., a lung tumor causing shortness of breath
    - Alleviate pain or neurologic symptoms by reducing the size of a tumor
- More than 50 percent of patients diagnosed with cancer will receive radiation therapy as part of their treatment
- Radiation also used for some benign conditions (eg, keloids, heterotopic ossification, or dupuytren’s disease)

Radiation Therapy Basics

- The delivery of external beam radiation treatments is painless and usually scheduled five days a week for one to ten weeks
- The effects of radiation therapy are cumulative with most significant side effects occurring near the end of the treatment course.
    - Acute side effects usually resolve a few weeks after radiation ends
    - There is a slight risk that radiation may cause a secondary cancer many years/decades after treatment

Example of radiation dermatitis after several weeks of radiotherapy with moist desquamation

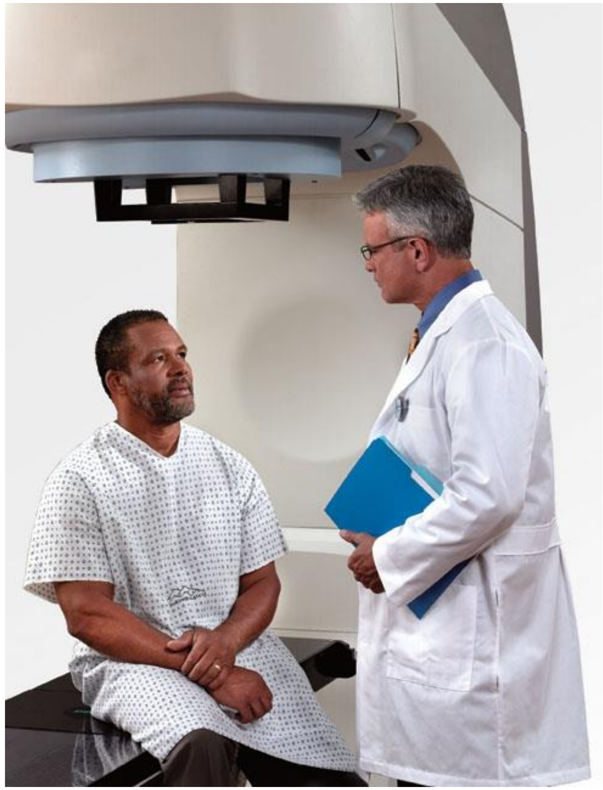
Source: sarahscancerjourney.blogspot.com

Common Radiation Side Effects

Side effects during the treatment vary **depending on site** of the treatment and affect the tissues in radiation field:

- Breast – swelling, skin redness
- Abdomen – nausea, vomiting, diarrhea
- Chest – cough, shortness of breath, esophageal irritation
- Head and neck – taste alterations, dry mouth, mucositis, skin redness
- Brain – hair loss, scalp redness
- Pelvis – diarrhea, cramping, urinary frequency, vaginal irritation
- Prostate – impotence, urinary symptoms, diarrhea
- Fatigue is often seen when large areas are irradiated

Modern radiation therapy techniques have decreased these side effects significantly



Unlike the systemic side effects from chemotherapy, radiation therapy usually only impacts the area that received radiation

Palliative Radiation Therapy

- Commonly used to relieve pain from bone metastases/tumors
  - ~30-50 percent of patients receive total relief from their pain
  - ~80 percent of patients will derive some relief
- Other palliative uses:
  - Spinal cord compression
  - Vascular compression, e.g., superior vena cava syndrome
  - Bronchial obstruction
  - Bleeding from gastrointestinal or gynecologic tumors
  - Esophageal obstruction
- Any effect from radiation is unfortunately not immediate, takes at least a few days
  - cancer cells must try to divide after DNA damage to die
- 8-30 Gy in 1-10 fractions are standard palliative doses

Advantages of RT over Narcotics for cancer related pain

- No sedation or clouding of sensorium
- No constipation
- No tolerance
- Targeted to location needing palliation
- Kills cancer cells
  - Durable response, peaking 2-4 weeks after RT
  - Decreases risk of pathologic fracture for bone mets
- Can maintain QOL and function (may improve OS)

The Treatment Process

- Referral
- Consultation
- Simulation
- Treatment Planning
- Quality Assurance

Referral

- Tissue diagnosis has typically has been established

- Referring physician reviews potential treatment options with patient

- Treatment options may include radiation therapy, surgery, chemotherapy or a combination

>95% of new patient visits to radiation oncology come from referrals from other physicians

Consultation

- Radiation oncologist determines whether radiation therapy is appropriate

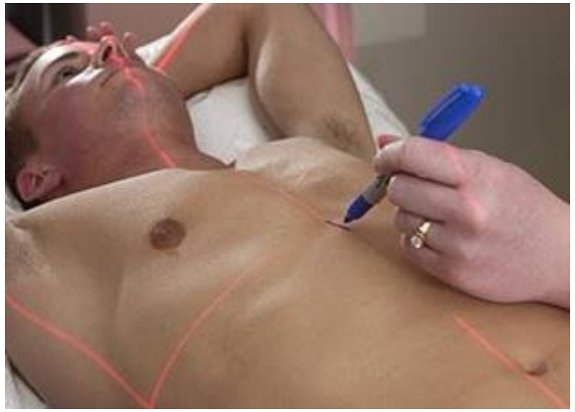
- A treatment plan is developed

- Care is coordinated with other members of patient's oncology team

The radiation oncologist will discuss with the patient which type of radiation therapy treatment may be indicated

Simulation (ie, treatment planning appt)

- Patient is set up in treatment position on a dedicated CT scanner*
  - Immobilization devices may be created to assure patient comfort and daily reproducibility
  - Reference marks or “tattoos” may be placed on patient
- CT simulation images are often fused with PET or MRI scans for treatment planning



Treatment Planning

- Physician outlines the target and organs at risk
  - Sophisticated software is used to carefully derive an appropriate treatment plan
    - Computerized algorithms enable the treatment plan to spare as much healthy tissue as possible

- Medical physicist checks the chart and dose calculations (ie, QA process)

- Radiation oncologist reviews and approves final plan

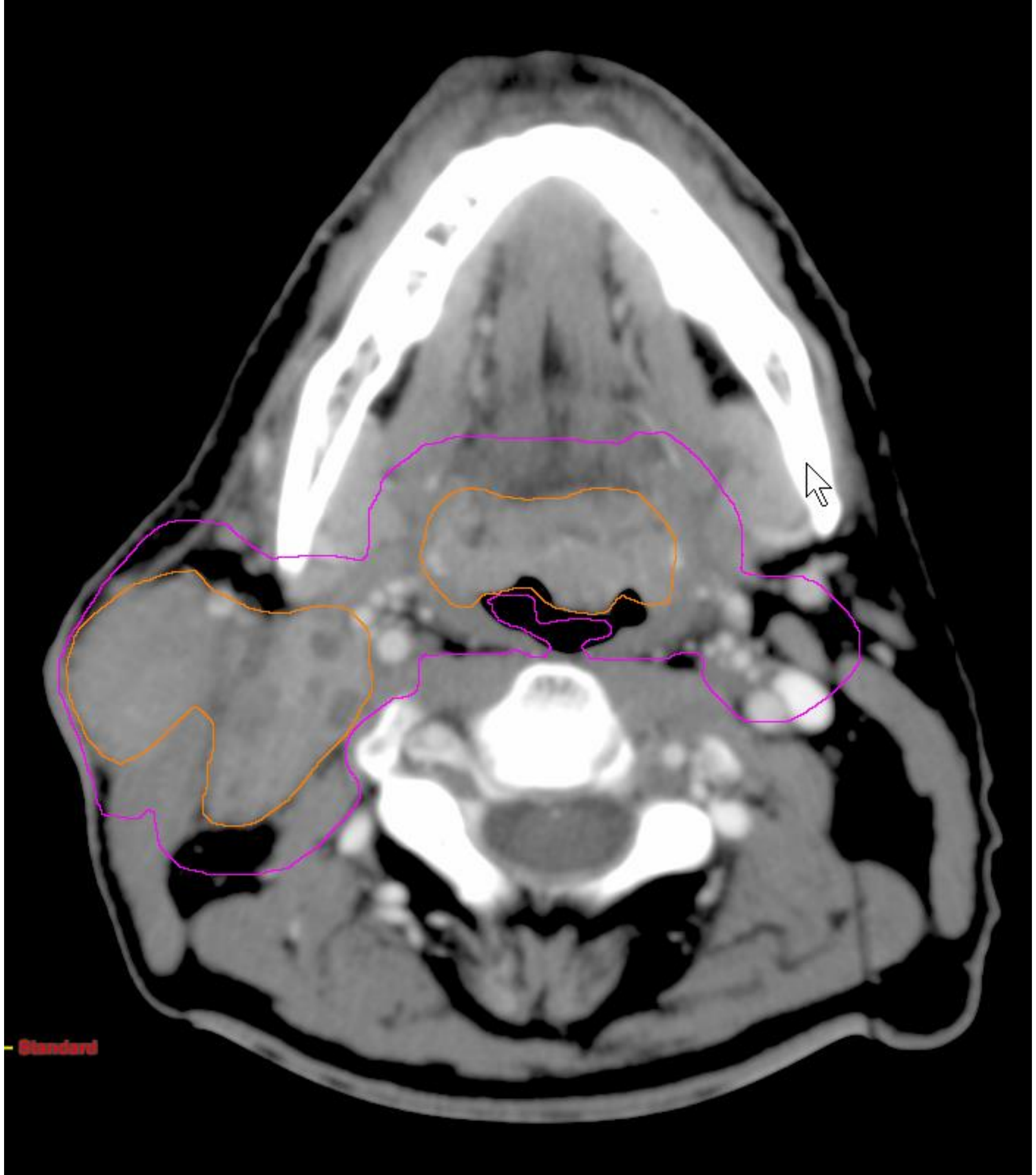
Radiation oncologists work with medical physicists and dosimetrists to create the optimal treatment plan for each individualized patient

-59M nonsmoker presented with right neck mass. Admits to 3-mo history of difficuly eating/swallowing meats and dull right ear pain.
-CT Neck showed thickened tissue in the base of tongue and right cervical neck adenopathy.
-Referred to ENT who performs direct layngoscopy and biopsy of base of tongue mass/oropharyngeal mass.
-Pathology: Squamous cell carcinoma, p16+.
-Curative chemoradiation recommended.

Orange = Tumor Seen on Scan

Orange = Tumor Seen on Scan

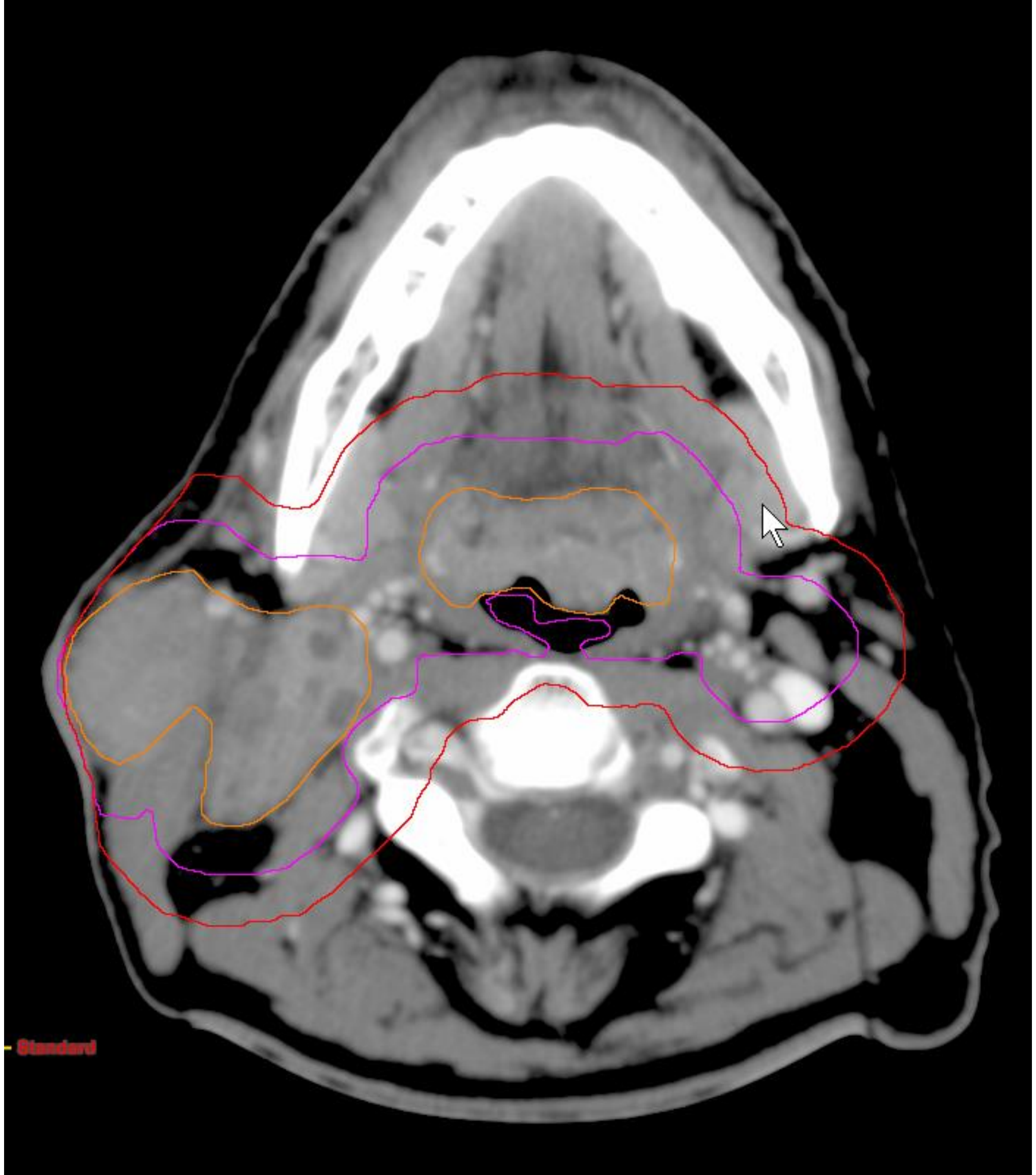
Purple = Where Tumor Could Be Microscopically

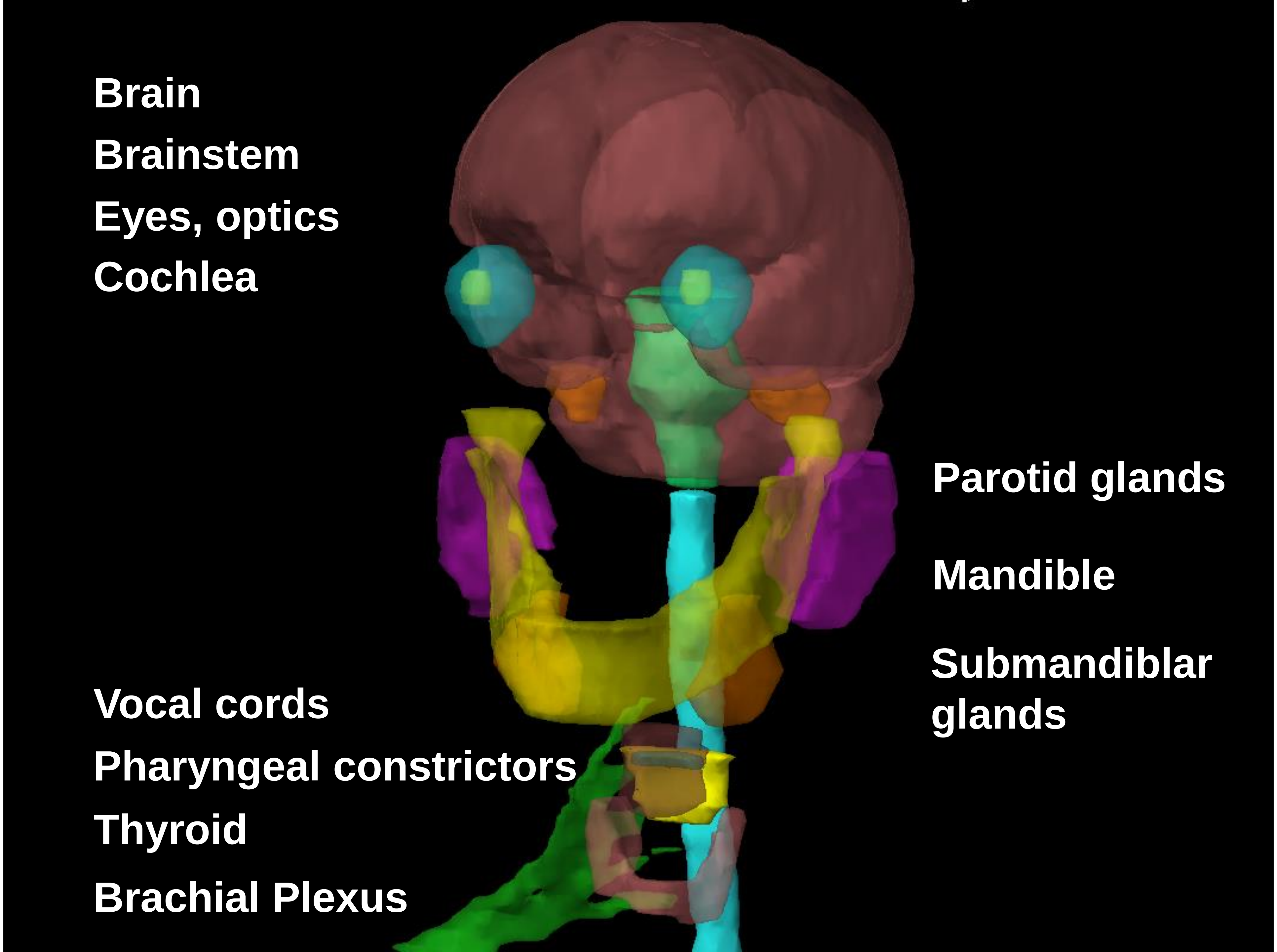


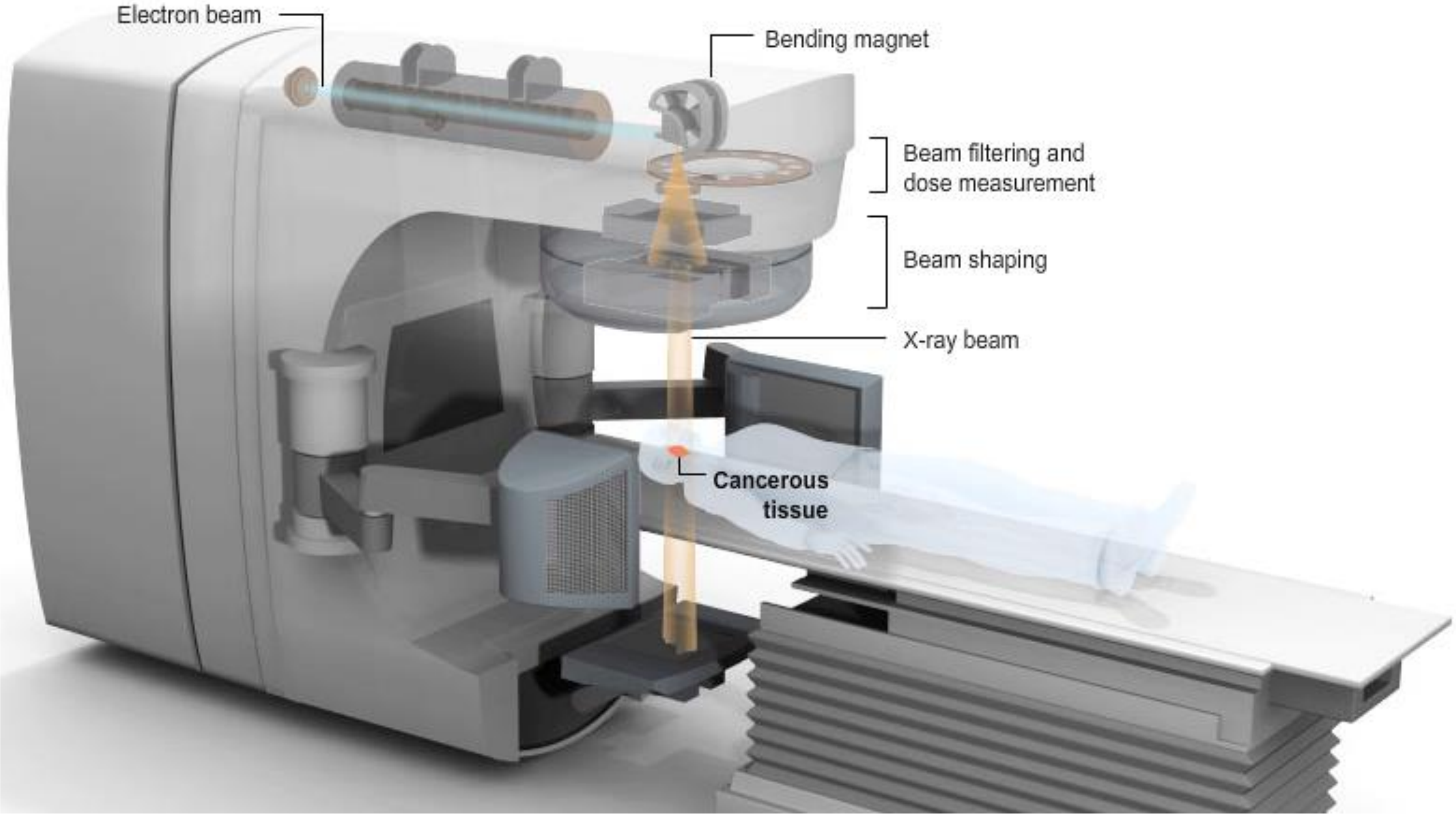
Orange = Tumor Seen on Scan

Purple = Where Tumor Could Be Microscopically

Red = Margin for Uncertainty

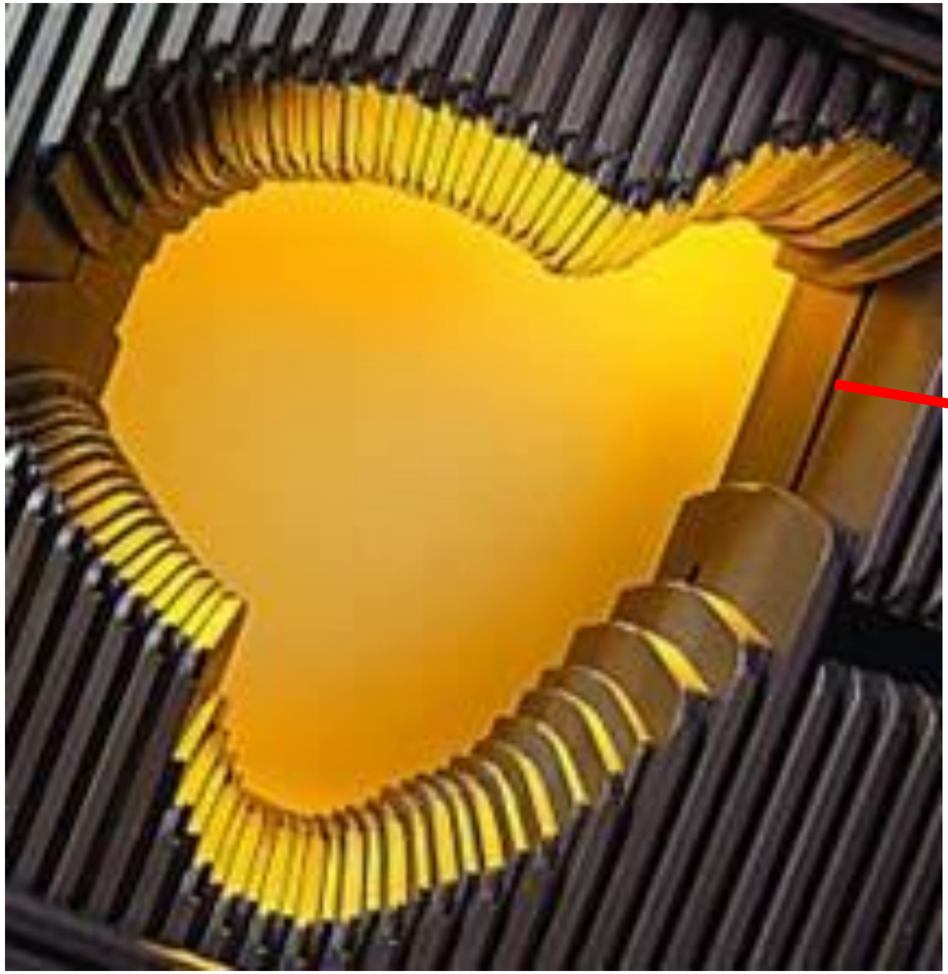


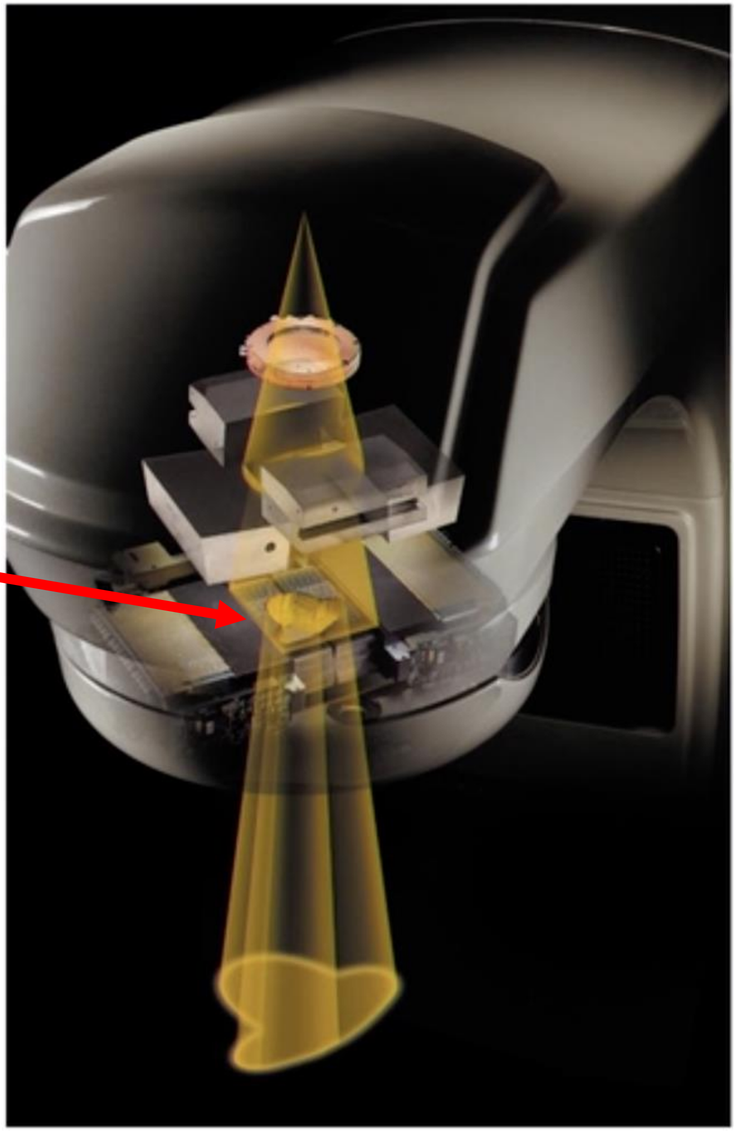

Brain
Brainstem
Eyes, optics
Cochlea
Parotid glands
Mandible
Submandiblar glands
Vocal cords
Pharyngeal constrictors
Thyroid
Brachial Plexus



Planning Time: 0.5-2 weeks after CT simulation to treatment start

Multileaf Collimators* (MLCs)





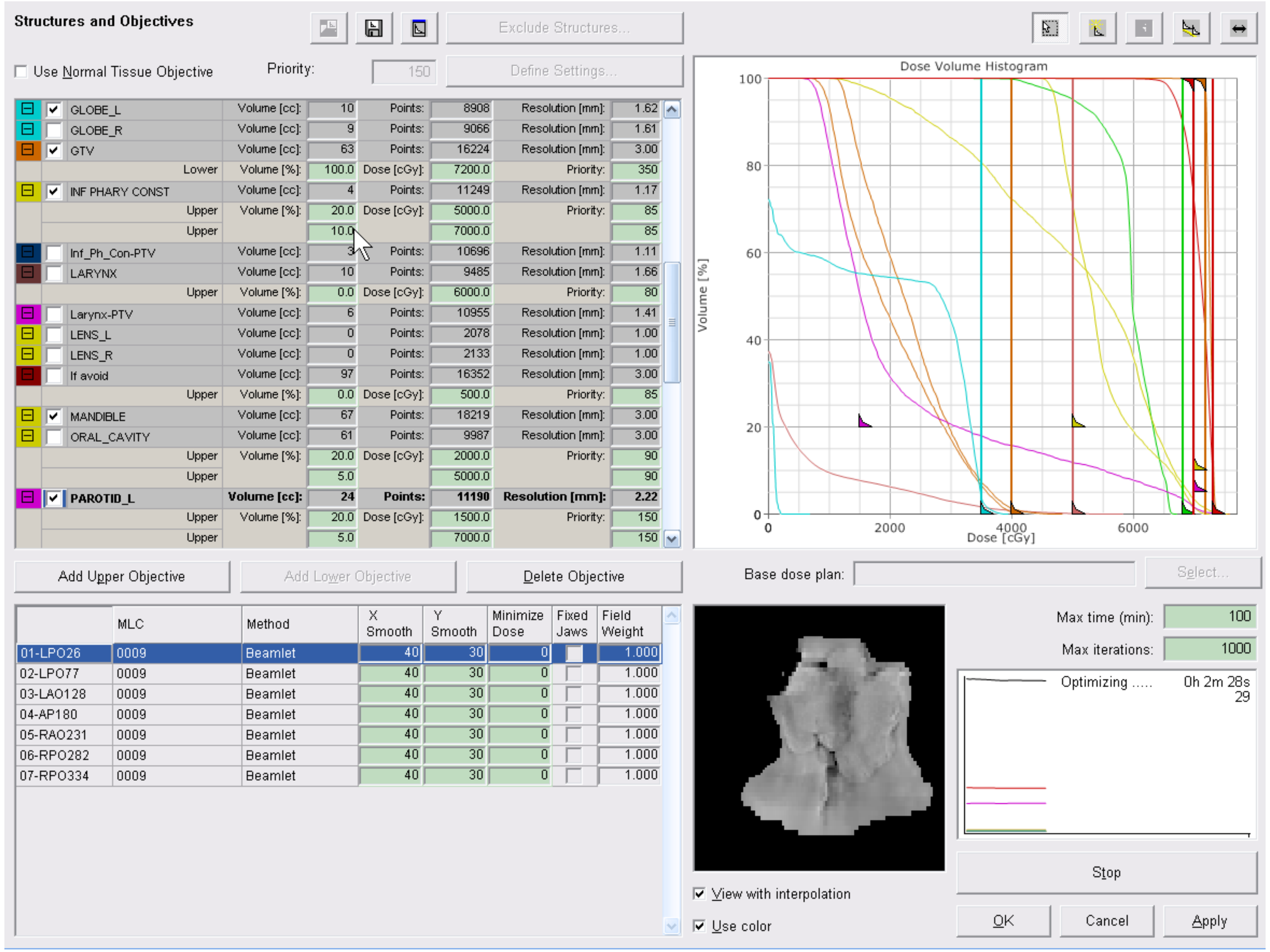
Two Main Types of External Beam Radiation Treatment Delivery

- 3D Conformal RT
  - Using CT/PET/MRI to create a target in 3D space
  - Conforming MLCs to the shape of the 3D target
    - Rather than planning using bony anatomy (oldschool 2D approach)
  - ~1-5 beams, chosen to avoid normal tissues
  - Trial and Error process

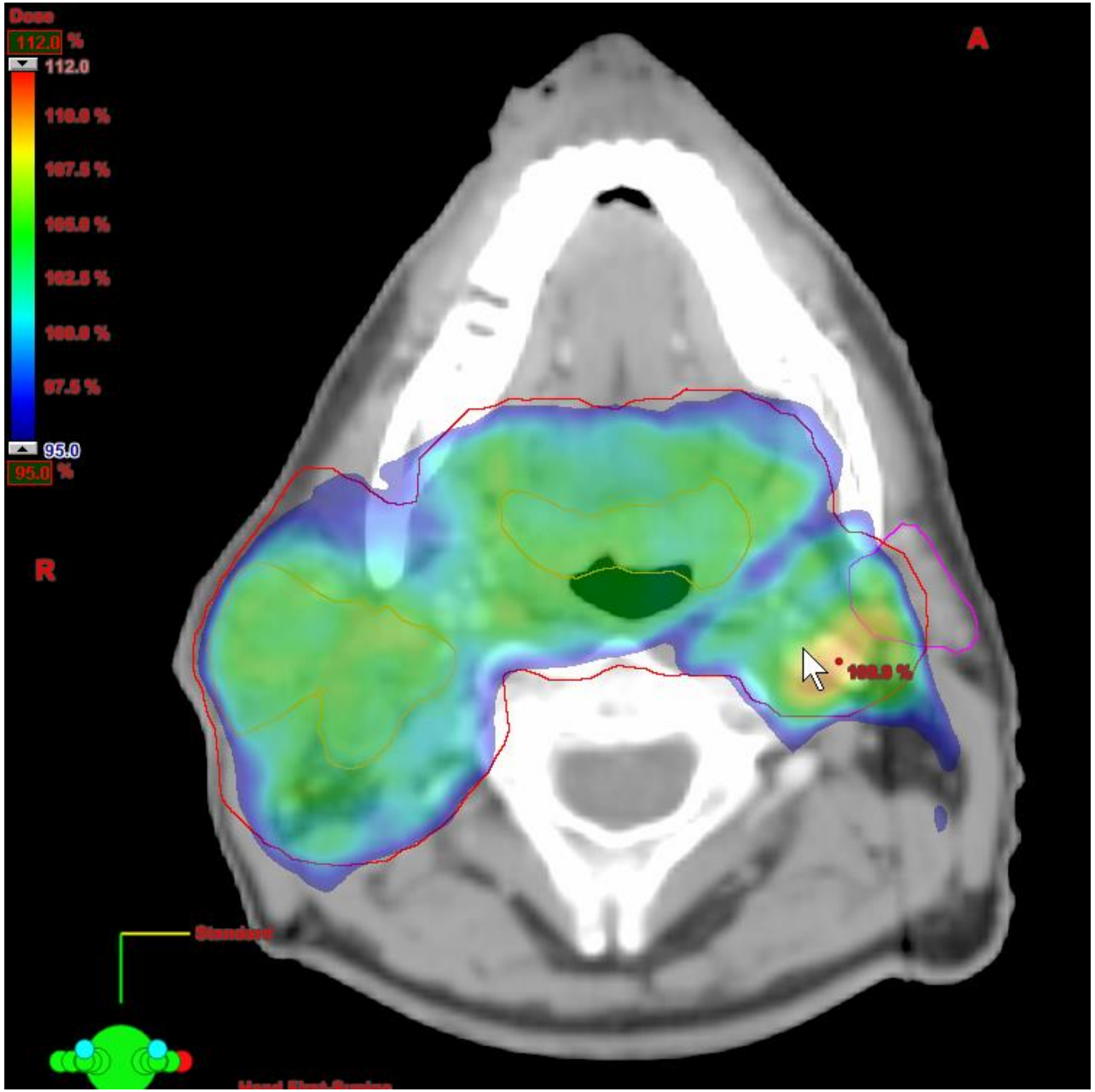
- Intensity-Modulated Radiotherapy (IMRT)
  - MLCs move across the field at different speeds to modulate the dose while the beam is on
  - Requires computer-aided optimization
  - Allows higher doses of radiation to be delivered to the tumor while sparing more healthy surrounding tissue

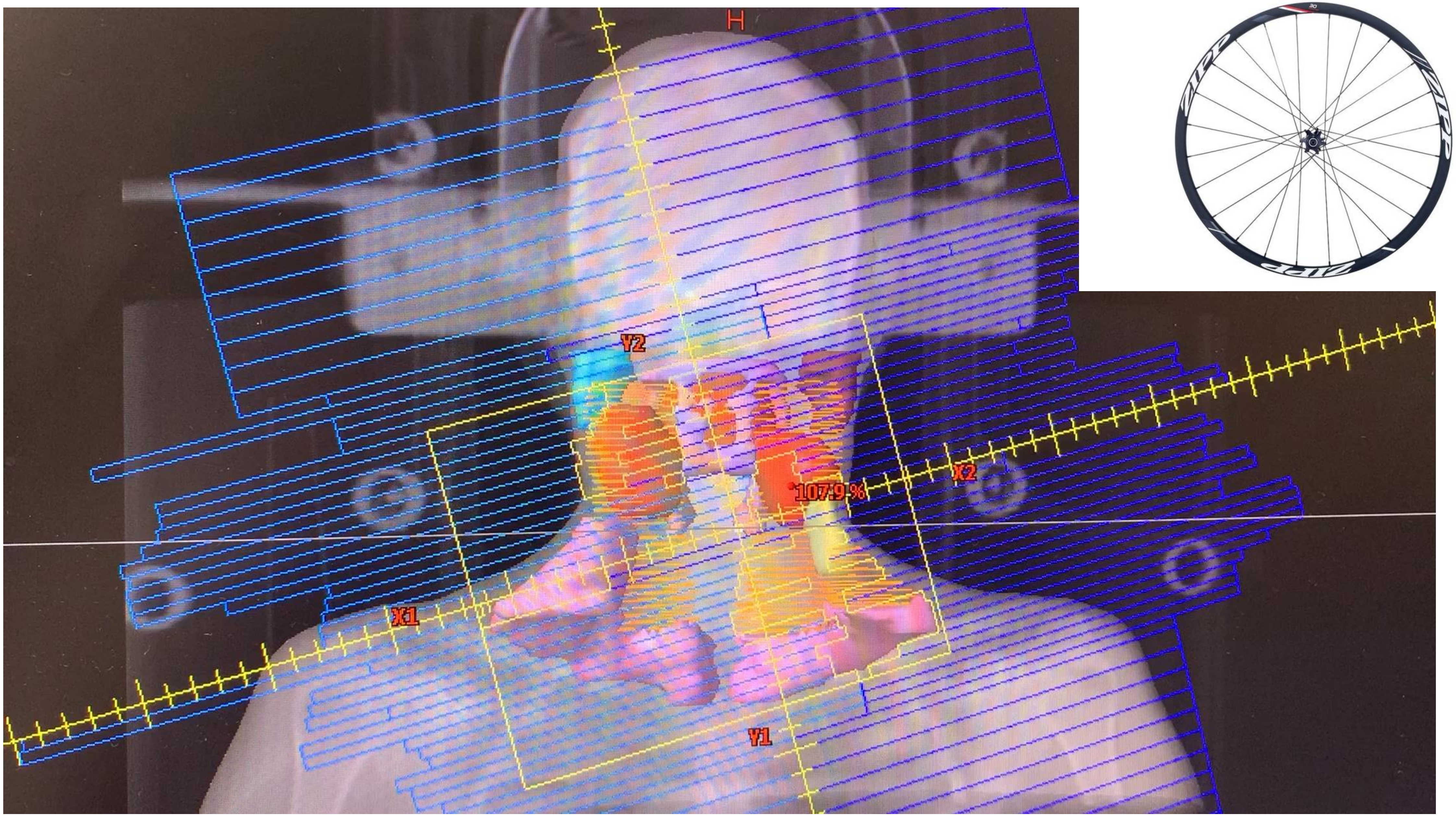
IMRT preferred for H&N Cancers

- Computer optimization process*
- Tell the computer your priorities for which targets and organs should receive prespecified doses or exposure to irradiation

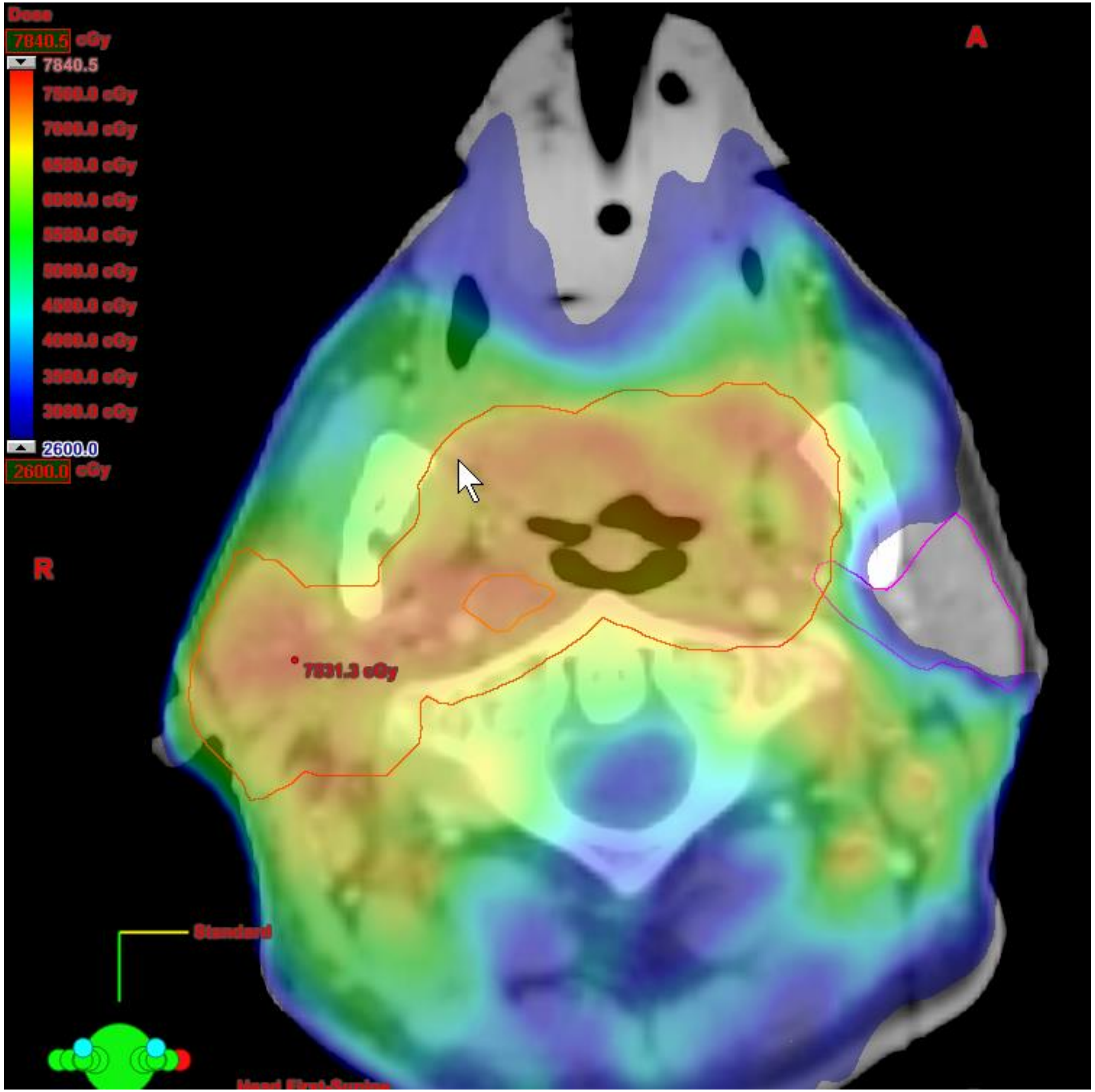


IMRT


Dose
112.0 %
112.0
110.0 %
107.5 %
105.0 %
102.5 %
100.0 %
97.5 %
95.0
95.0 %
A
R
Standard

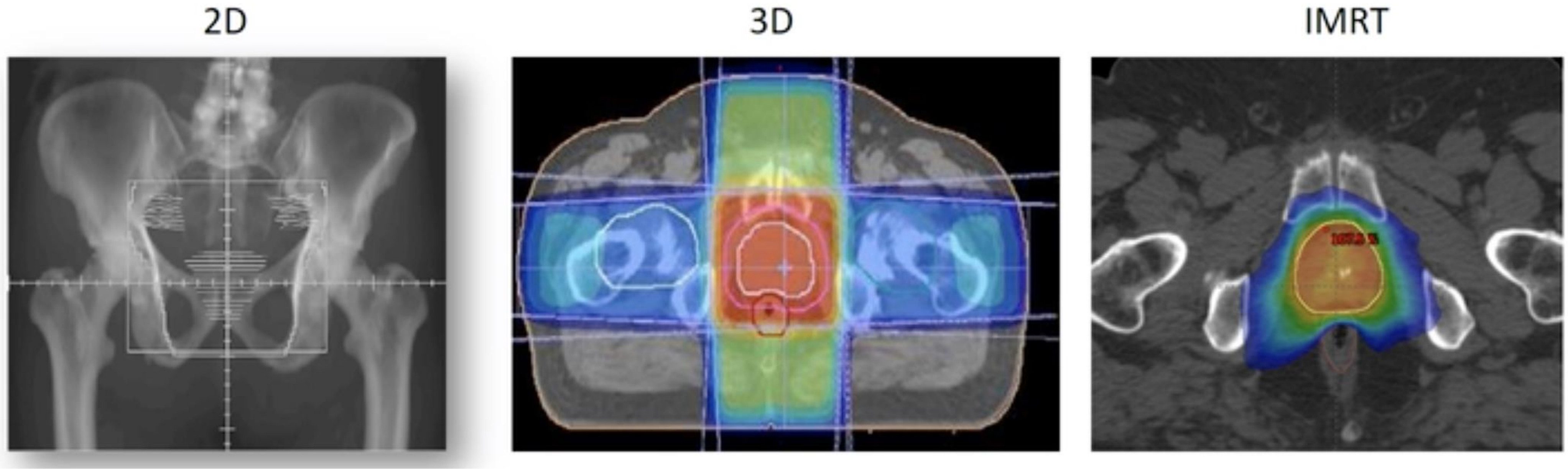

H
Y2
X2
107.9 %
X1
Y1
ZIPP
ZIPP
ZIPP
ZIPP

IMRT


Dose
7840.5 cGy
7840.5
7500.0 cGy
7000.0 cGy
6500.0 cGy
6000.0 cGy
5500.0 cGy
5000.0 cGy
4500.0 cGy
4000.0 cGy
3500.0 cGy
3000.0 cGy
2600.0
2600.0 cGy
A
R
7531.3 cGy
Standard

Evolution of Treatment for Prostate Cancer

- Advances in Radiation Therapy in One Slide:



Spratt, Dan. U Michigan.

Safety and Quality Assurance

- Each radiation therapy treatment plan goes through many safety checks
  - The medical physicist checks the calibration of the linear accelerator on a regular basis to assure the correct dose is being delivered
  - The radiation oncologist, along with the dosimetrist and medical physicist go through a rigorous multi-step QA process to be sure the plan can be safely delivered
  - QA checks are done by the radiation therapist daily to ensure that each patient is receiving the treatment that was prescribed for them

Delivery of Radiation Therapy

- *External beam* radiation therapy typically delivers radiation using a linear accelerator

- Internal radiation therapy, called *brachytherapy*, involves placing radioactive sources into or near the tumor

- The modern unit of radiation is the *Gray (Gy)*, traditionally called the *rad*
  - 1Gy = 100 centigray (cGy)
  - Defined as joules/kg

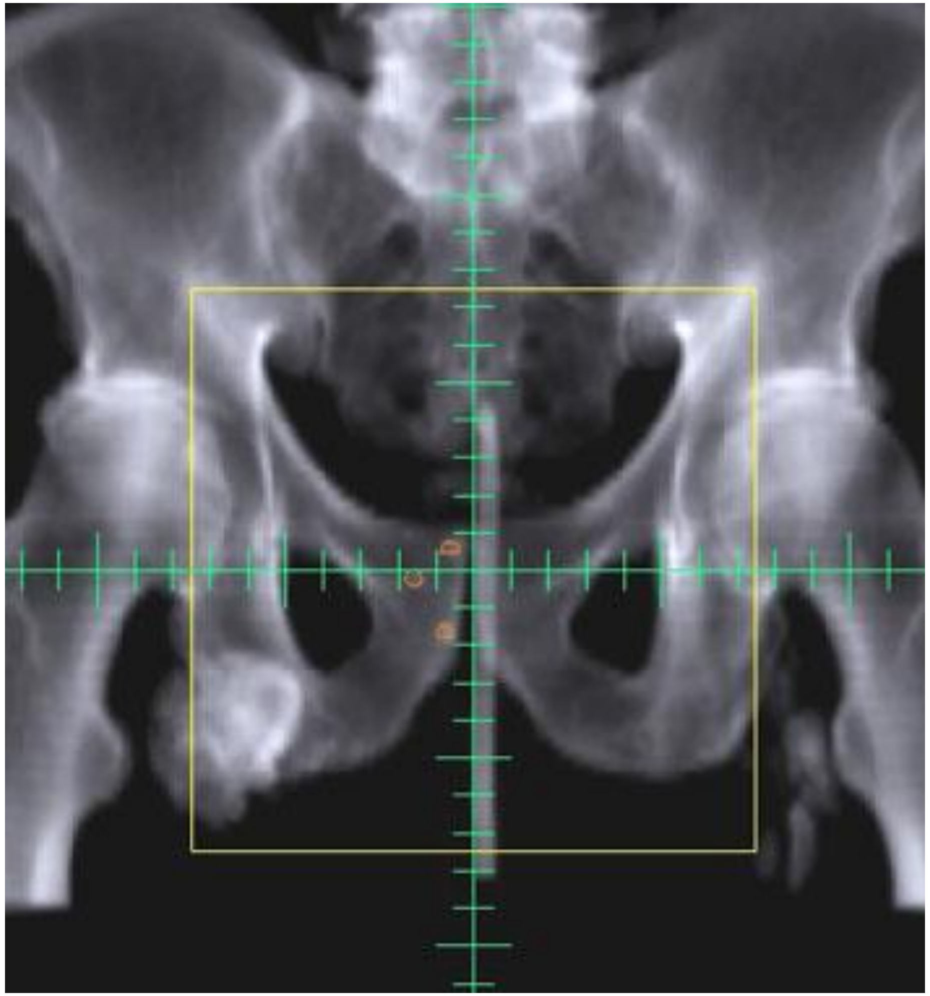
- Curative courses of radiation now range from 1-8 weeks

Type of External Beam Radiation Treatment

- Three-dimensional conformal radiation therapy (3-D CRT)
- Intensity modulated radiation therapy (IMRT)
- Image Guided Radiation Therapy (IGRT)
- Stereotactic Radiotherapy (SRS/SBRT)
- Particle Beam Therapy

Image Guidance

- Developed in 2000s
- For patients treated with 3-D or IMRT
- Physicians use frequent imaging of the tumor, bony anatomy or implanted fiducial markers for daily set-up accuracy
  - Imaging performed using CT scans, high quality X-rays, MRI or ultrasound
  - Motion of tumors can be tracked to maximize tumor coverage and minimize dose to normal tissues

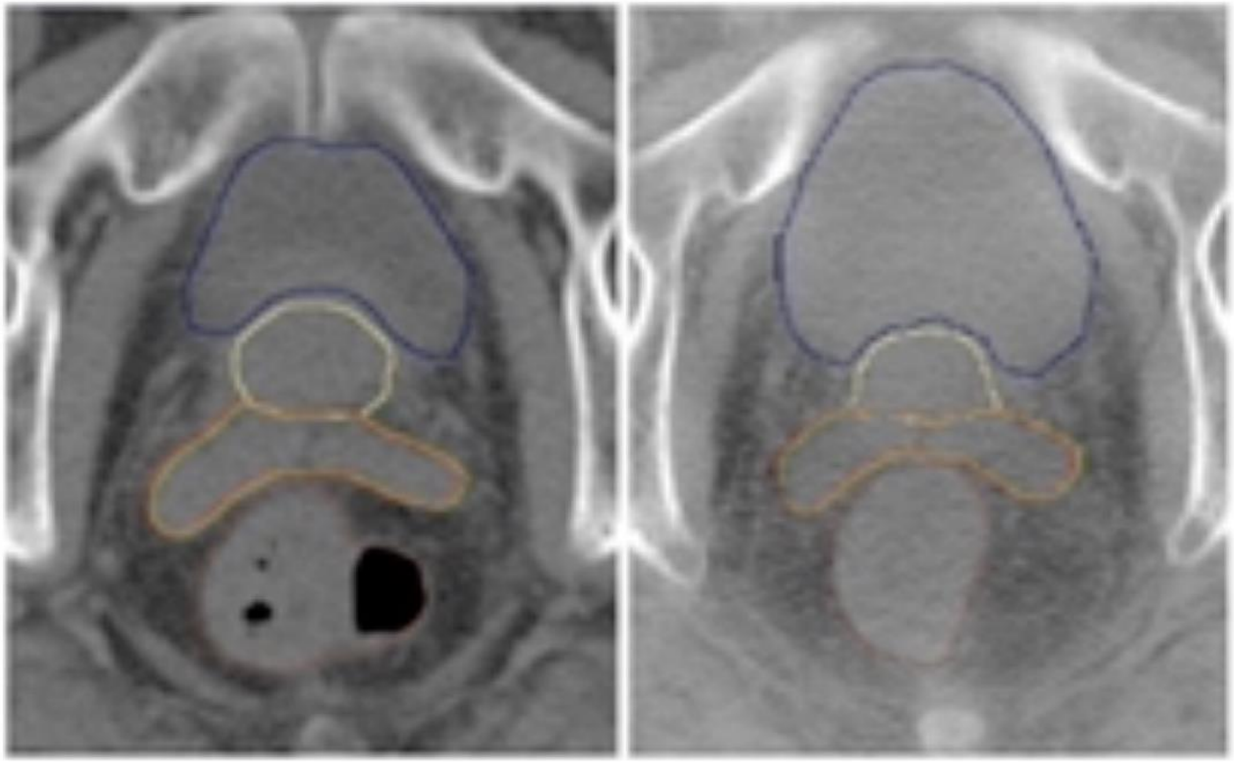


Fiducial markers in prostate visualized and aligned

Modern Image Guided Radiation Treatment*

- Cone Beam CT Scan (CBCT)
- Taken immediately prior to treatment delivery

Simulation CT for RT planning | CBCT (prior to tx)



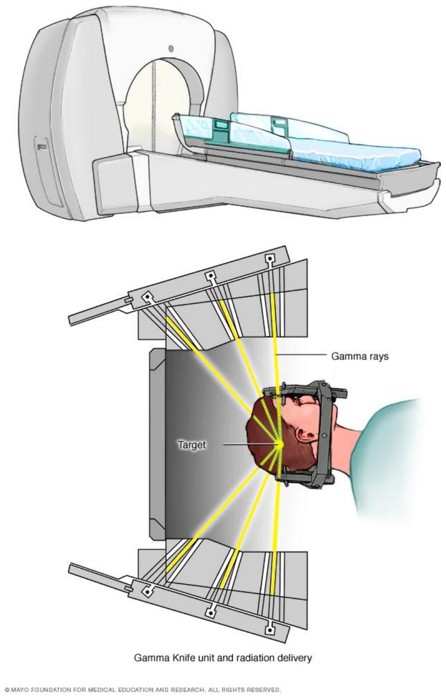
Spratt, Dan. U Michigan

Stereotactic Radiosurgery (SRS) or Body Radiation Treatment (SBRT)

- SRS/SBRT is a specialized type of external beam radiation that uses high dose, focused radiation in 1-5 treatments
    - Overcomes radioresistant tumors to deliver ~100 Gy equiv
- SRS relies on detailed imaging, 3-D treatment planning and complex immobilization for precise treatment set-up to deliver the dose with extreme accuracy
- SRS/SBRT is used for a number of sites: spine, lung, liver, brain, adrenals, pancreas, pancreas

“Truebeam”

“Cyberknife”



“Gamma Knife”

Proton Beam Therapy

- Protons are charged particles that deposit most of their energy at a given depth
  - Potential to minimizing risk to tissues beyond that point
  - More inherent uncertainty than traditional photon radiation (less forgiving)
- Allows for highly specific targeting of tumors located near critical structures
- Increasingly available in the U.S.
- Most commonly used in treatment of pediatric, CNS, and intraocular malignancies
  - Data needed for use in other tumor sites
- Costly

Emory Proton Therapy Center

Types of Internal Radiation Therapy (Brachytherapy)

- Brachy=short

- Intracavitary implants
  - Radioactive sources are placed in a cavity near the tumor (breast, cervix, uterine)

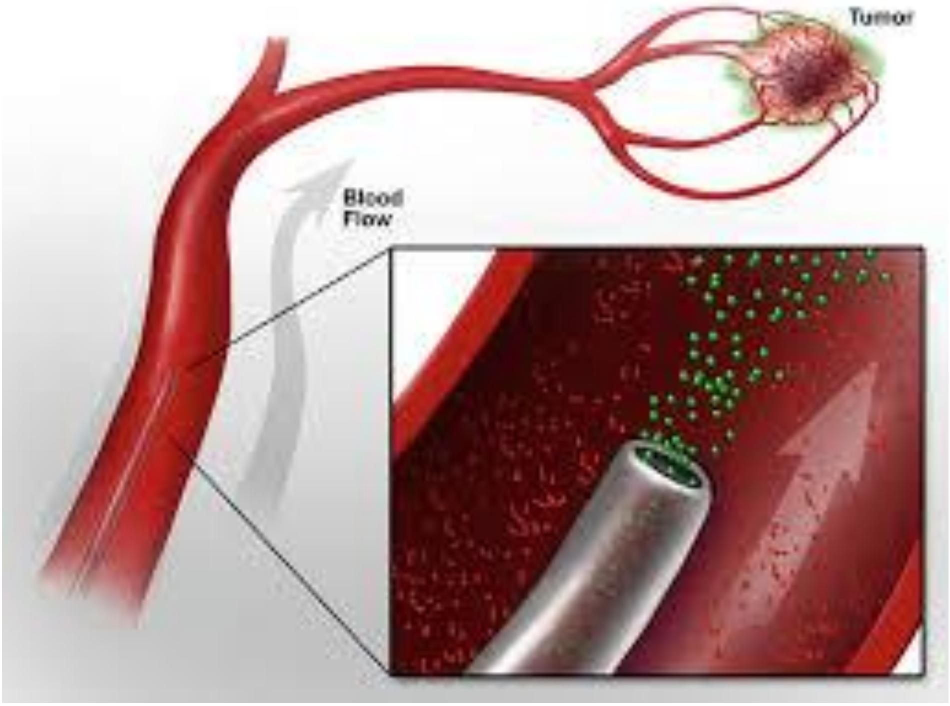
- Interstitial implants
  - Sources placed directly into the tissue (prostate, vagina)

- Intra-operative implants
  - Surface applicator is in direct contact with the surgical tumor bed

Radioactive seeds for a permanent prostate implant, an example of low-dose-rate brachytherapy.

Systemic Radiation Therapy (exception)

- Radiation can also be delivered by an injection.
  - Xofigo (^{223}Radium) are radioactive isotopes absorbed primarily by cancer cells
    - Used for treating bone metastases
  - Radioactive isotopes may be absorbed by thyroid cells (the original targeted therapy)
    - I-131 for hyperthyroid and thyroid cancers
  - Radioactive "beads" may be used to treat primary or metastatic liver cancer
    - Y^{90}-Microspheres



Y^{90}-Microspheres

Summary

- Radiation therapy is a well established modality for the treatment of numerous cancers

- Radiation therapy effectiveness and side effects are limited to local, anatomic region where treatment is delivered
  - Fundamentally different from systemic drug/chemo therapy

- Advances in radiation technology have made radiation treatment delivery safe, quick, painless, precise, and with ever-decreasing side effects to adjacent organs

Resources for Patients

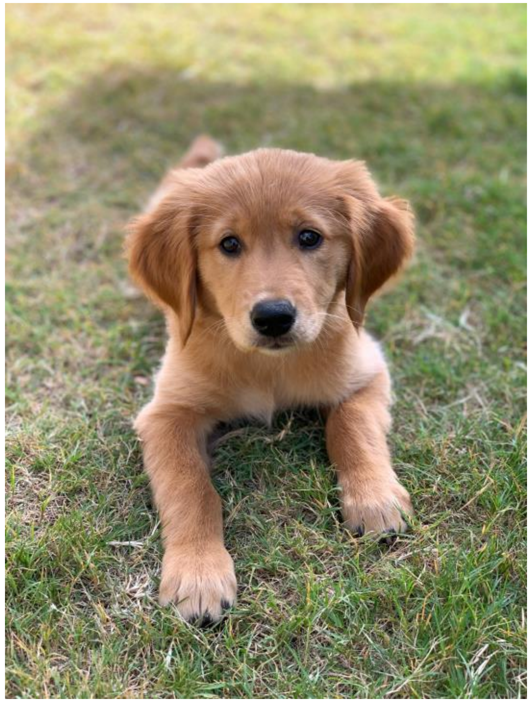
- NCCN.org (National Comprehensive Cancer Network)
- RTanswers.org

Thank you for coming

kirkland.spencer@gmail.com

205-838-3660

Contact anytime with questions



Sources

- ASTRO – Intro to Radiation Therapy for Health Care Professionals
- Sam Marcrom, MD
- Others cited herein