Radiation Oncology

Basic Principles and Updates

October 8, 2025

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Learning Objectives

By the end of this talk, you will be able to…

- Describe the fundamental concepts of radiation oncology and its role in cancer treatment.
- Recognize the different radiation therapy modalities and their clinical indications.
- Identify common acute and late side effects of radiation therapy.
- Discuss current trends and future directions in radiation oncology.

Radiation Oncology: A Brief History

1895 – Röntgen discovers x-rays (Nobel Prize 1901)

1896 – First patients with cancer treated with x-rays by Emil Grubbe in Chicago and Victor Despeignes in France

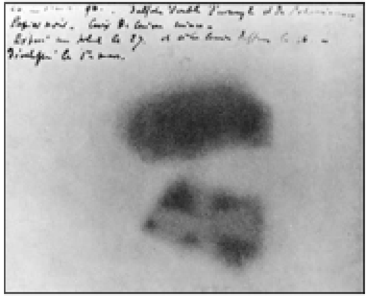
1896 – Nobel Prize in Physics awarded to Henri Becquerel, Pierre and Marie Curie for their discovery of spontaneous radioactivity

1901 – First use of brachytherapy

1952 – First "linear accelerator" used for treatment

1980s – Intensity modulated radiation treatment (IMRT), proton therapy

2000s – Image-guided RT (IGRT), MR-based RT



Marie Curie (1867-1934)

Radiation Oncology: A Brief History

- Treatment of malignant <u>and</u> non-malignant conditions
  - Tinea capitis
  - Tonsillitis
  - Enlarged thymus
  - Ankylosing spondylitis
  - Acne
  - Peptic ulcers
  - Keloids
  - Heterotopic ossification prophylaxis
  - Graves opthalmopathy
  - Orbital pseudotumor
  - Dupuytren's disease
  - Gynecomastia
  - AVMs
  - Benign tumors

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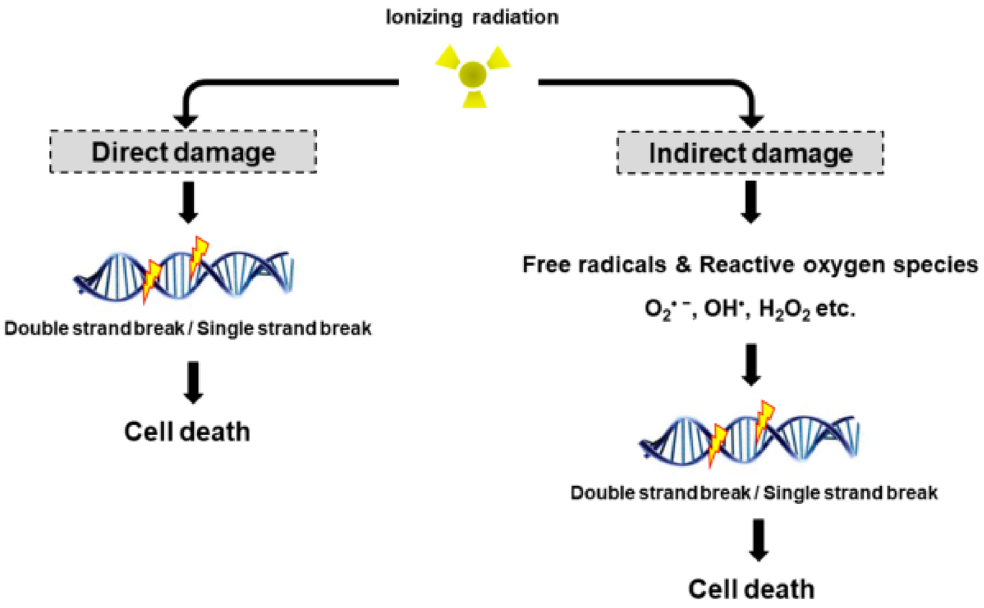
How Radiation Therapy Works

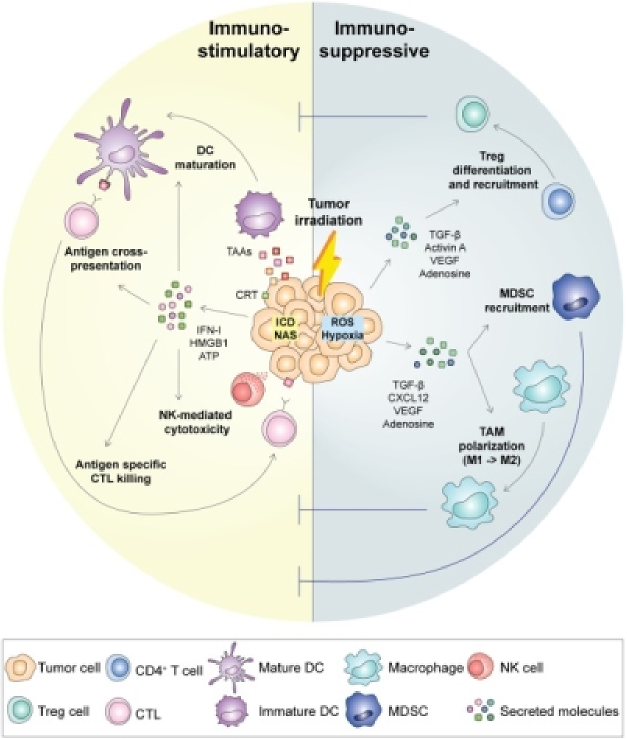
What is Radiation Therapy?

- **Definition:** Use of high-energy radiation to kill cancer cells, primarily via damage to DNA.
- **Goals:** Broadly, to maximize damage to tumor cells while minimizing harm to normal tissue.
    - Curative/Definitive
    - Palliative



Radiation Biology 101

- Secondary effects of RT:
  - Disruptive effects on tumor vasculature
  - Very high dose or high LET radiation may affect cell membrane integrity and protein structures
  - Interplay with the immune response

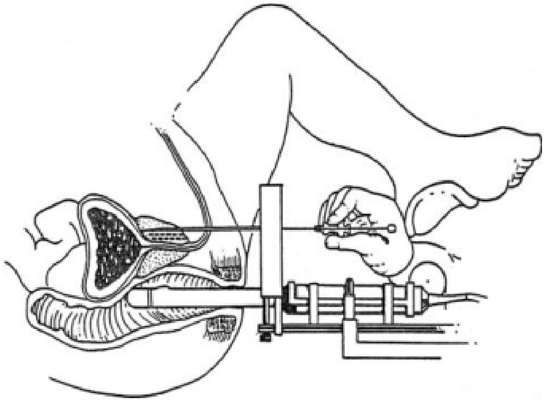


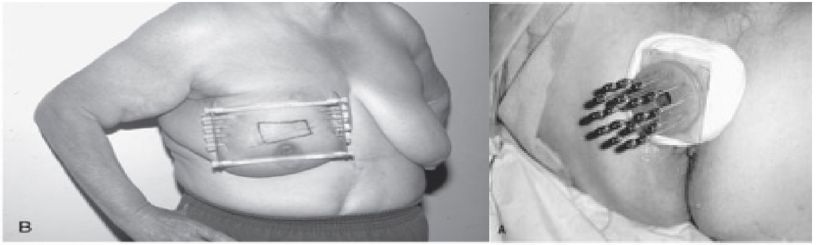
De Martino, Seminars in Immunology 2021

Types of Radiation Therapy

Brachytherapy

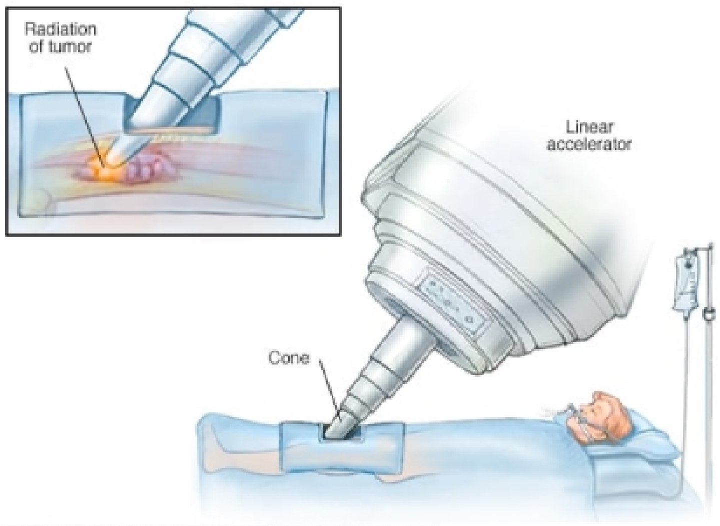
- Delivered via radioactive sources via an implant or surface application.



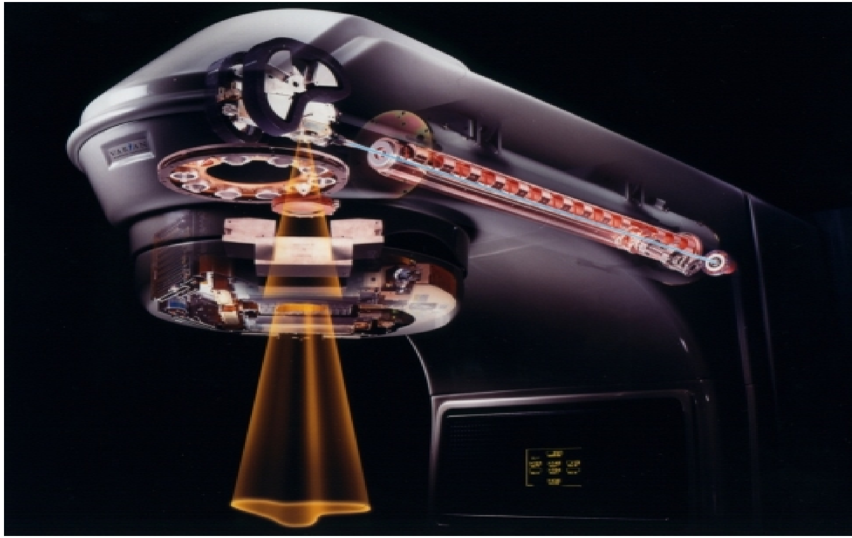


Intra-Operative Radiation Therapy

- Delivered directly to tumor bed in the operating room.



External Beam Radiation Therapy (EBRT)



EBRT Modalities

3DCRT - 3-D conformal RT

IMRT - intensity modulated RT

VMAT - volumetric modulated arc therapy

SBRT - stereotactic body RT

SABR - stereotactic ablative radiation

SRS - stereotactic radiosurgery

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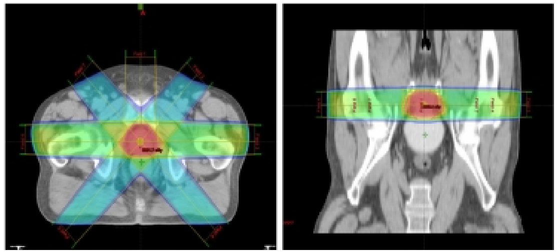

Figure 1. Axial (left) and Coronal (right) Isodose Distribution by 3DCRT of one Representative Patient were Shown

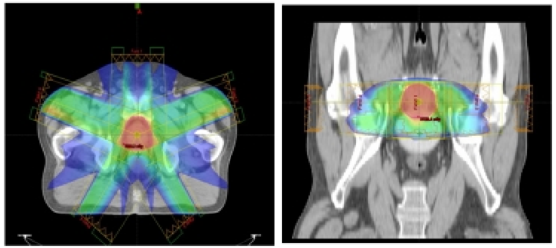

Figure 2. Axial (left) and Coronal (right) Isodose Distribution by 5 field IMRT of one Representative Patient were Shown

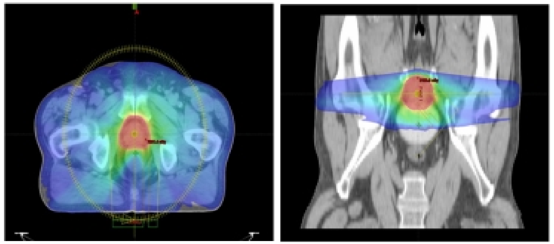

Figure 3. Axial (left) and Coronal (right) Isodose Distribution by VMAT of One Representative Patient were Shown

EBRT Modalities

3DCRT - 3-D conformal RT

IMRT - intensity modulated RT

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SBRT - stereotactic body RT

SABR - stereotactic ablative radiation

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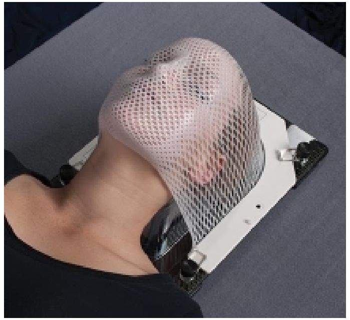
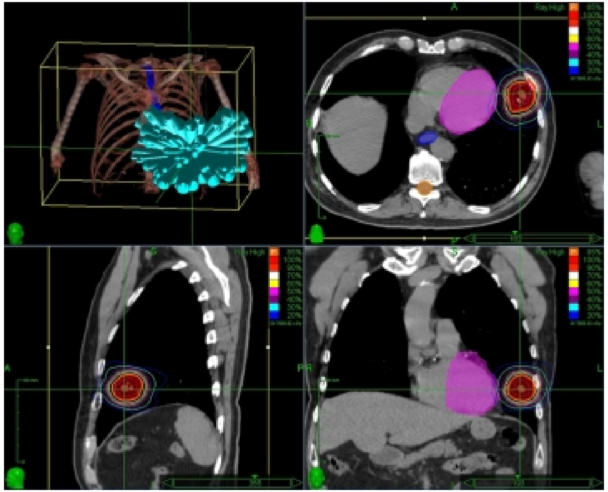


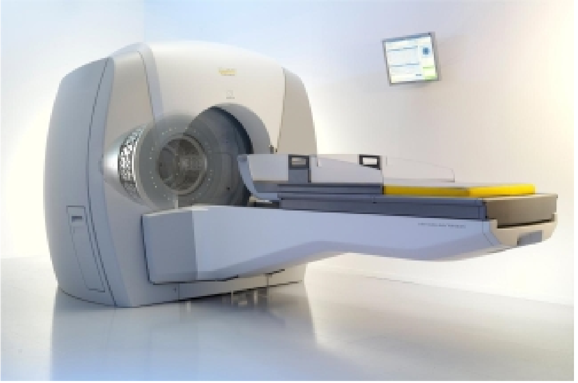


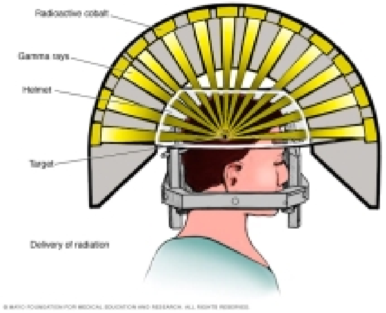
Radiation Treatment Machines: SRT

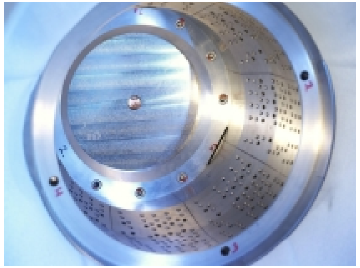
- Superficial RT (orthovoltage)
- Low energy radiation delivery machines
- Skin cancer

Radiation Treatment Machines: Gamma Knife

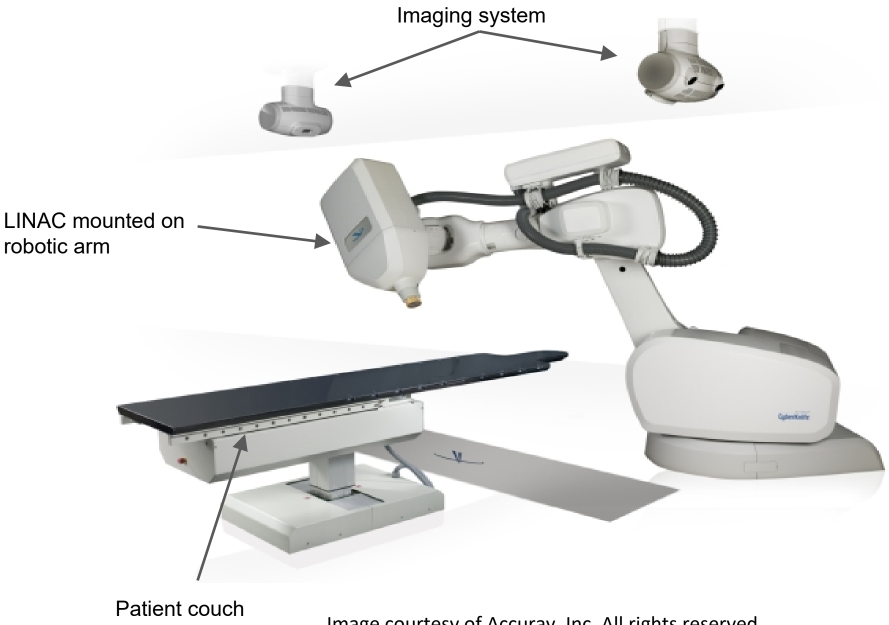
- Radiosurgery / SRS
  - Single high-dose radiation
  - Very conformal (i.e. tight margins)

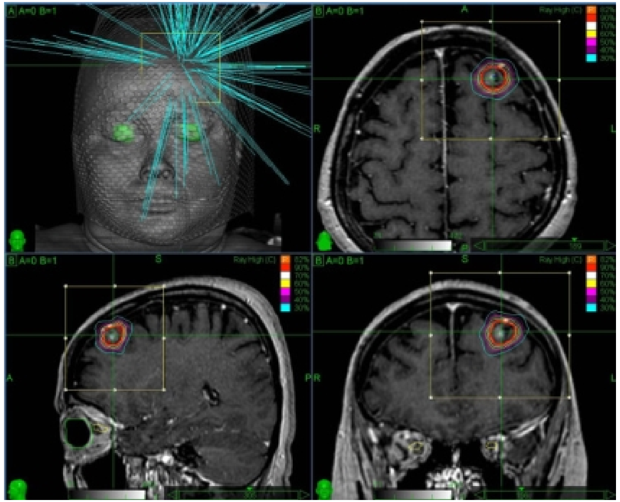






Radiation Treatment Machines: CyberKnife





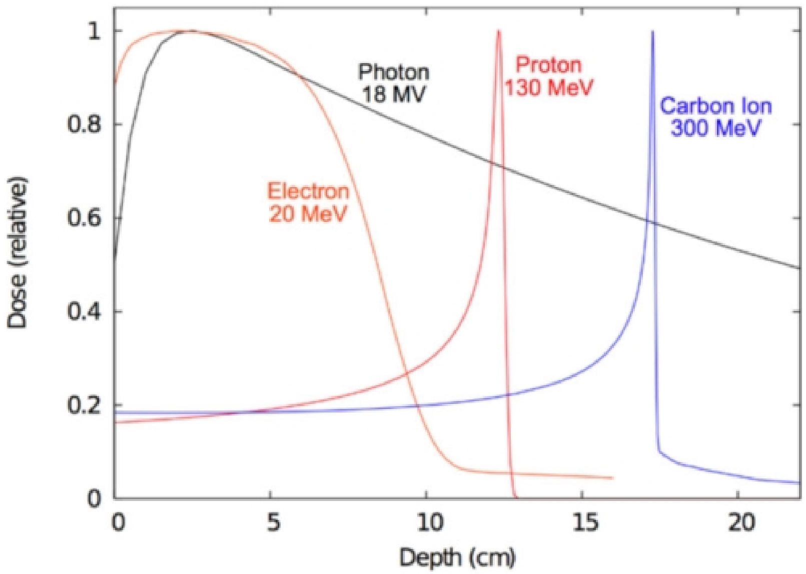
Radiation Treatment Machines: MR-LINACs

- The best soft-tissue resolution
- Real-time imaging
- Automated gating
- First system launched commercially in 2014

Proton Therapy: When to Use It

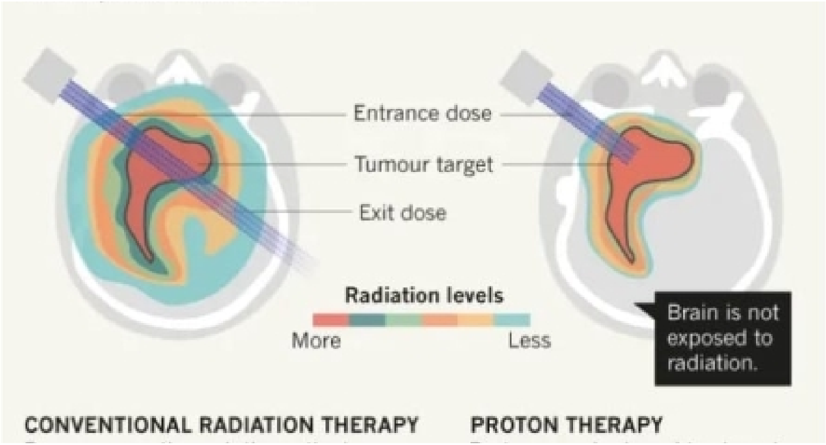
Particle Therapy Types

- Photons
- Electrons
- **Protons**
- Neutrons
- Carbon Ions

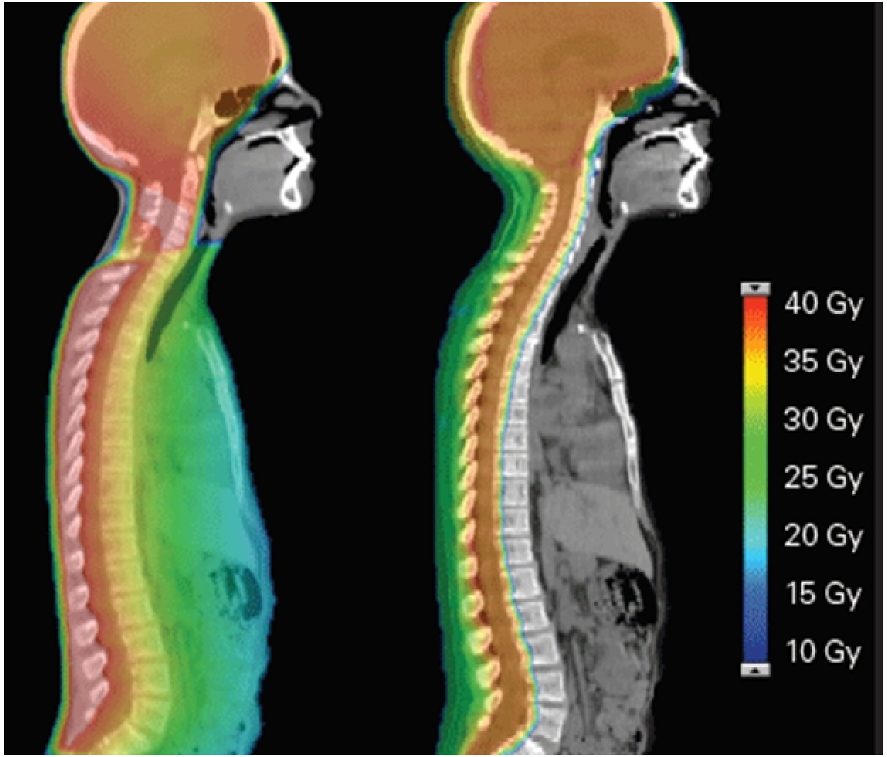


Proton Therapy

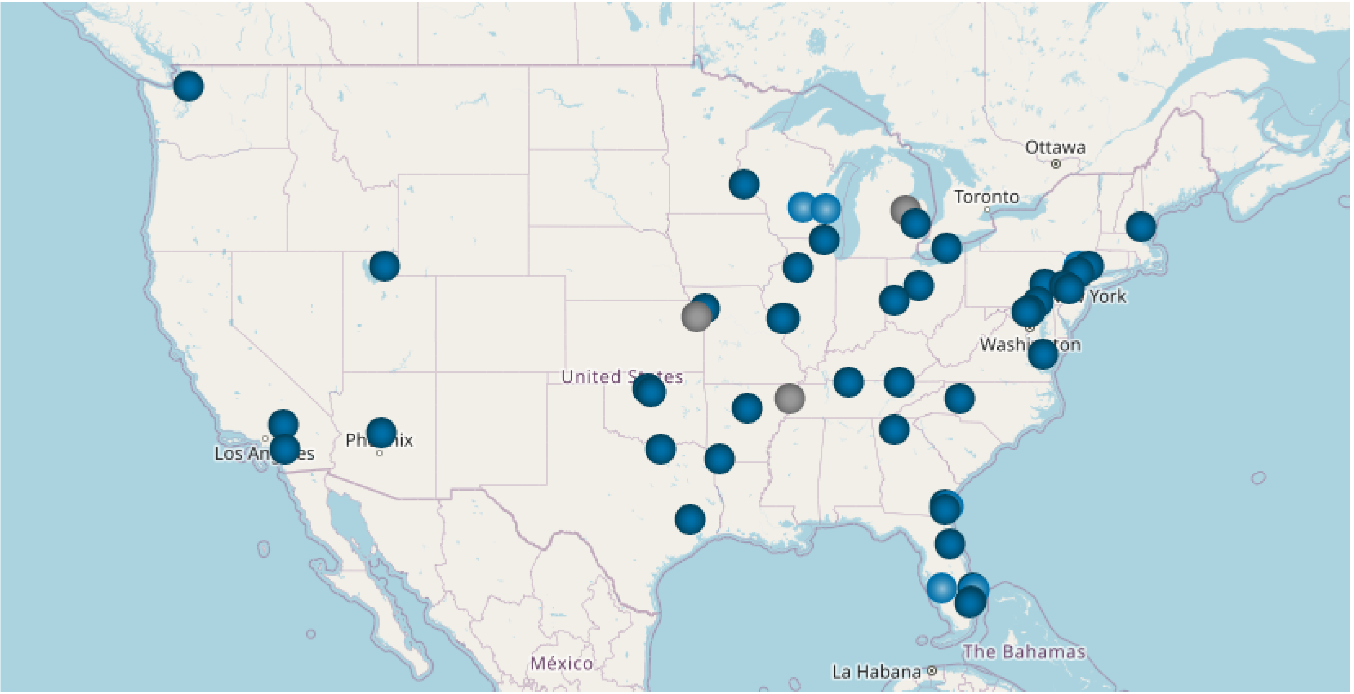
- Proton radiation is a type of external beam radiation
- FDA approved in 1988
- Travels a specific depth into tissue, and then stops (**no exit dose**).



Proton Therapy



Proton Therapy Centers



Photons vs. Protons

- **No difference in efficacy**
- Due to the lack of exit dose, using protons can result in reduced radiation dose to normal tissues.
- Protons take longer to plan (2 weeks vs. a few days)
- Sometimes we can shape the photon dose distribution better
- Some biological effects questions

Proton Therapy: ASTRO Guidelines

ASTRO Group 1

- Ocular tumors
- Base of skull tumors
- Bone tumors
- CNS tumors, including spinal tumors near the cord
- CSI
- Many H&N cancers
- Esophageal cancer
- Mediastinal tumors
- Mesothelioma
- HCC and biliary cancers
- Pediatric tumors
- Patients with genetic syndromes with RT hypersensitivity (e.g. NF-1, Rb, BRCA1/2)
- RP sarcomas
- Re-RT

ASTRO Group 2

- Other H&N cancers
- Lung cancers
- Other GI malignancies
- Prostate cancer
- Breast cancer

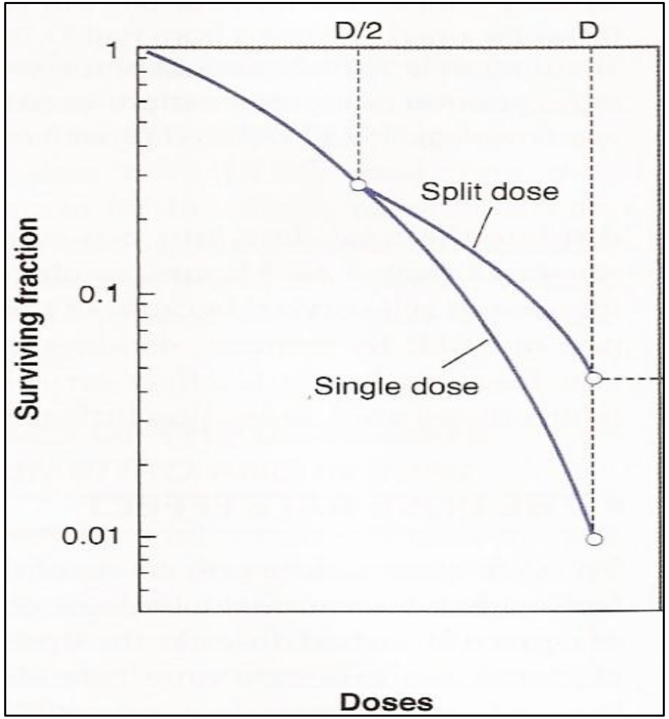
Determining Radiation Dose and Fractionation

Radiation Oncology: Dose

1. Dose needed to kill a particular type of cancer has typically been established by prospective dose-finding studies
2. Consider the alpha/beta of the tumor
3. Consider patient safety
4. Consider patient convenience

Radiation Oncology: Fractionation

- Radiation therapy has traditionally been a “fractionated” treatment course spread over several weeks.
- Takes advantage of differential repair abilities of normal and malignant tissues.



Hall Figure 5.6a

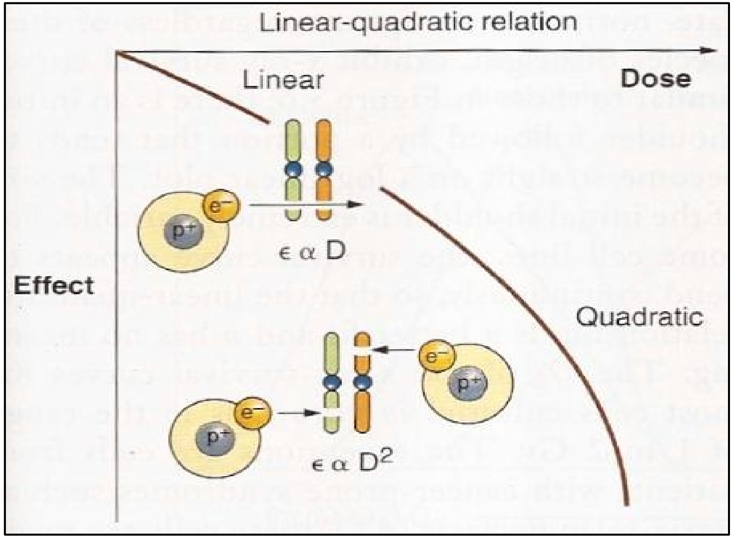
Radiation Oncology: Fractionation

- Regaud and The French Ram
  - A single dose of radiation that is sufficient to sterilize a ram also causes significant skin toxicity
  - If the same dose is delivered in several fractions, the ram is sterilized, but there is no skin toxicity
- 1920's – 1930's
  - Regaud – extended treatment time for uterine cancer improved outcomes
  - Coutard – fractionated treatment for head and neck cancer reduced toxicity with better outcomes

Hall Figure 23.1

Radiation Oncology: Fractionation

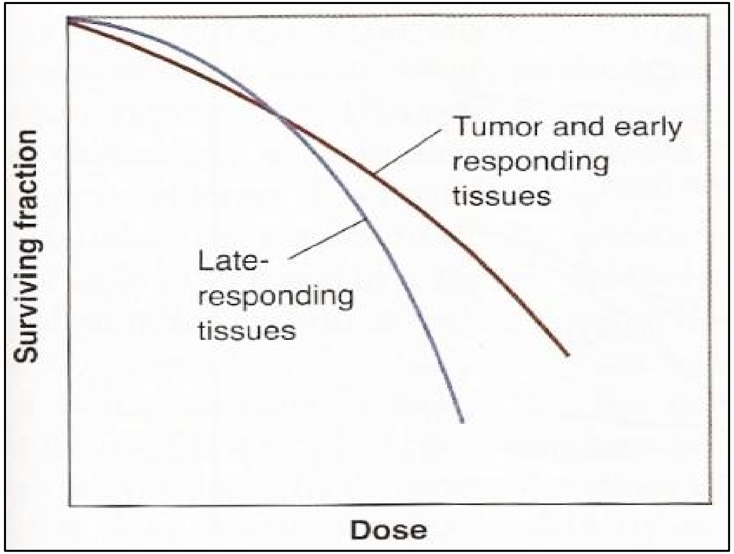
- Linear quadratic (α/β) model
  - Alpha = single hit kills
  - Beta = double hit kills



Hall Fig 3.5

Radiation Oncology: Fractionation

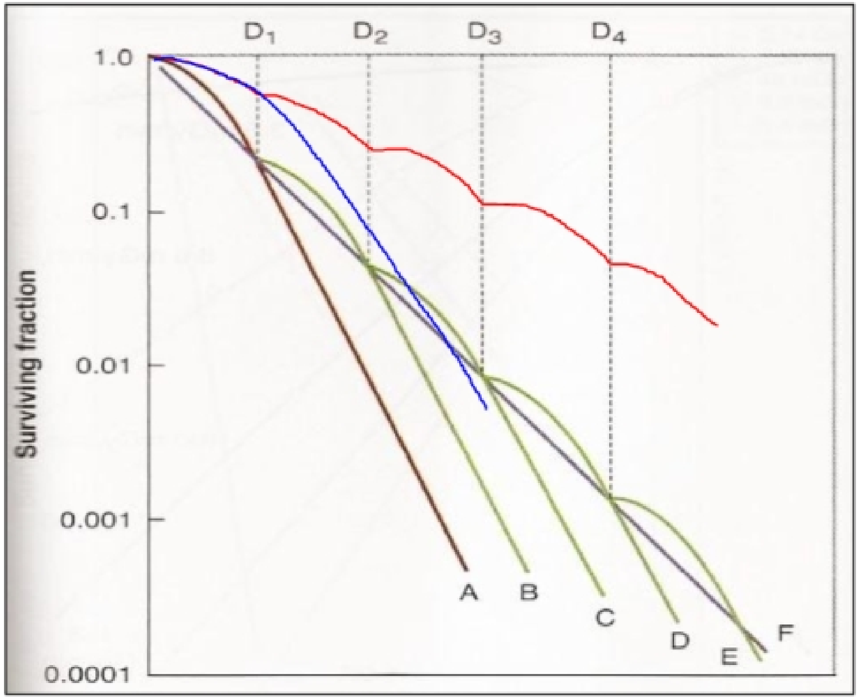
- Different cell lines, tissues, and tumors have different α/β ratios
  - α/β defines the dose of radiation at which the number of cells killed by a single hit equals the number killed by two hits
  - High α/β = most tumors, early responding normal tissues
  - Low α/β = late responding tissues, some tumors (e.g. prostate)



Hall Figure 23.6

Radiation Oncology: Fractionation

- Radiation prescription can be modified to take advantage of different dose response curves.
  - Change number of fractions, keep same “biologically effective dose” (BED).

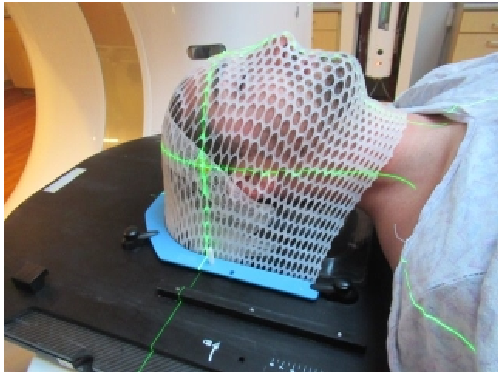


Hall Figure 5.8

A Day in Radiation Oncology Clinic

Radiation Therapy Timeline

- **Consultation**: Review history, exam, counsel patient.
- **Simulation**: CT scan in the exact treatment position, with treatment devices in place.
- **Contouring**: Define tumor/targets and normal tissues.
- **Planning**: Calculate, evaluate, approve, and QA the RT plan.
- **Delivery**: Daily treatments (fractions) over days to weeks.



Typical RT Treatment Day

- Typically 30-45 minutes “car door to car door”.
- 2 hours if anesthesia (patients age 0-5 years, maybe 6-9 years).
- Most of time spent checking in, changing into gown, getting position correct (verified by lasers).
- Radiation beam on for only a few minutes (Except TBI). Patients do not feel the radiation happening, and are not radioactive afterward.

RT Side Effects: Acute

- All short-term side effects slowly accumulate over course of radiation treatment
- Except for fatigue, effects are local to radiation beam (entry and exit)
- Most site-specific side effects improve in the weeks to months after radiation therapy

Examples:

- **CNS:** Nausea/vomiting, headaches, hair loss
- **H&N:** Mucositis, xerostomia, dehydration, dermatitis
- **Thoracic:** Esophagitis, chest wall pain
- **GI/GU:** Nausea/vomiting, diarrhea, proctitis, dysuria
- **Extremities:** Dermatitis, edema

RT Side Effects: Long Term

- Develop weeks, months, or years after RT.
- May be permanent.

Examples:

- **CNS:** Radiation necrosis, cognitive changes, cataracts, hearing loss
- **H&N:** Fibrosis, dysgeusia, xerostomia
- **Thoracic:** Pneumonitis/lung fibrosis, cardiac disease, scoliosis/kyphosis
- **GI/GU:** Infertility, bowel obstruction, ulcers
- **Extremities:** Decreased bone growth, joint fibrosis
- Secondary malignancy

Recent Trends and Future Directions in Radiation Oncology

Current Trends in Radiation Oncology

- Hypofractionation for definitive treatment
- Expanding role of RT in metastatic patients
- Precision radiation oncology

Hypofractionation: Fewer Treatments

- Traditionally, definitive RT courses were ≥5 weeks long.
- More recently, prospective trials across disease sites demonstrated comparable outcomes and toxicities with shorter treatment courses.
- Shorter courses are associated with lower costs and greater patient convenience.

Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial

Adrian Murray Brunt*, Joanne S Haviland*, Duncan A Wheatley, Mark A Sydenham, Abdulla Alhasso, David J Bloomfield, Charlie Chan, Mark Churn, Susan Cleator, Charlotte E Coles, Andrew Goodman, Adrian Harnett, Penelope Hopwood, Anna M Kirby, Cliona C Kirwan, Carolyn Morris, Zohal Nabi, Elinor Sawyer, Navita Somaiah, Liba Stones, Isabel Syndikus, Judith M Bliss†, John R Yarnold†, on behalf of the FAST

Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial

David Dearnaley, Isabel Syndikus, Helen Mossop, Vincent Khoo, Alison Birtle, David Bloomfield, John Graham, Peter Kirkbride, John Logue, Zafar Malik, Julian Money-Kyrle, Joe M O'Sullivan, Miguel Panades, Chris Parker, Helen Patterson*, Christopher Scrase, John Staffurth, Andrew Stockdale, Jean Tremlett, Margaret Bidmead, Helen Mayles, Olivia Naismith, Chris South, Annie Gao, Clare Cruickshank, Shama Hassan, Julia Pugh, Clare Griffin, Emma Hall, on behalf of the CHHiP Investigators

Radiation Therapy in Metastatic Cancer

- Traditionally, RT was used for palliative purposes.

- Recent studies are changing this paradigm.

OPEN ACCESS | RAPID COMMUNICATIONS | June 02, 2020

Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastatic Cancers: Long-Term Results of the SABR-COMET Phase II Randomized Trial

Authors: David A. Palma, MD, PhD, Robert Olson, MD, MSc, Stephen Harrow, MBChB, PhD, Stewart Gaede, PhD, Alexander V. Louie, MD, PhD, Cornelis Haasbeek, MD, PhD, Liam Mulroy, MD, ... SHOW ALL ..., and Suresh Senan, MBBS, PhD | AUTHORS INFO & AFFILIATIONS

Publication: Journal of Clinical Oncology • Volume 38, Number 25

FREE ACCESS | ORIGINAL REPORTS | September 25, 2023

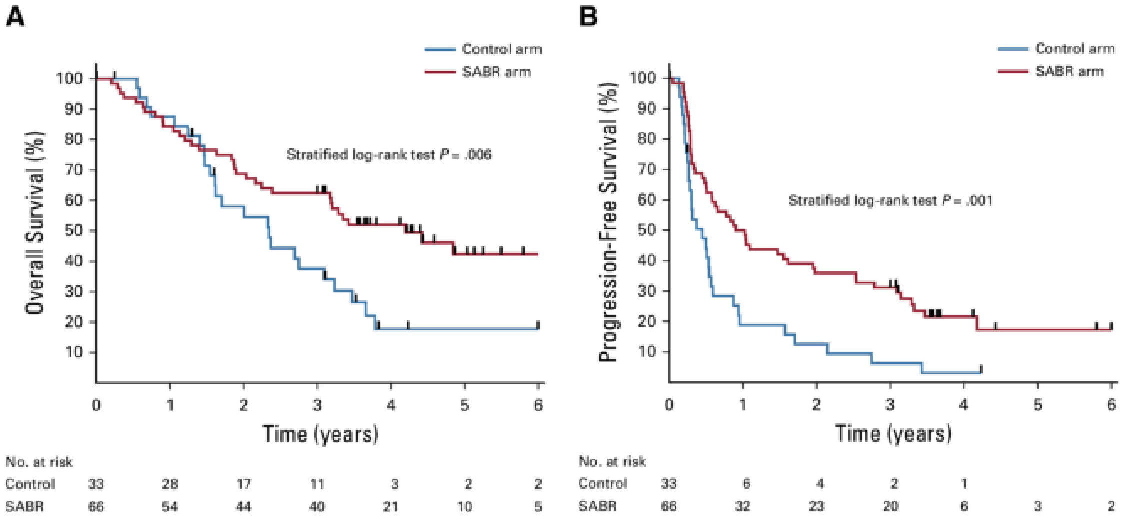
Prophylactic Radiation Therapy Versus Standard of Care for Patients With High-Risk Asymptomatic Bone Metastases: A Multicenter, Randomized Phase II Clinical Trial

Authors: Erin F. Gillespie, MD, MPH, Joanna C. Yang, MD, MPH, Noah J. Mathis, BA, Catherine B. Marine, BA, Charlie White, MS, Zhigang Zhang, PhD, Christopher A. Barker, MD, ... SHOW ALL ..., and Jonathan T. Yang, MD, PhD | AUTHORS INFO & AFFILIATIONS

Publication: Journal of Clinical Oncology • Volume 42, Number 1

SABR-COMET: Ablative Radiation for Oligometastases

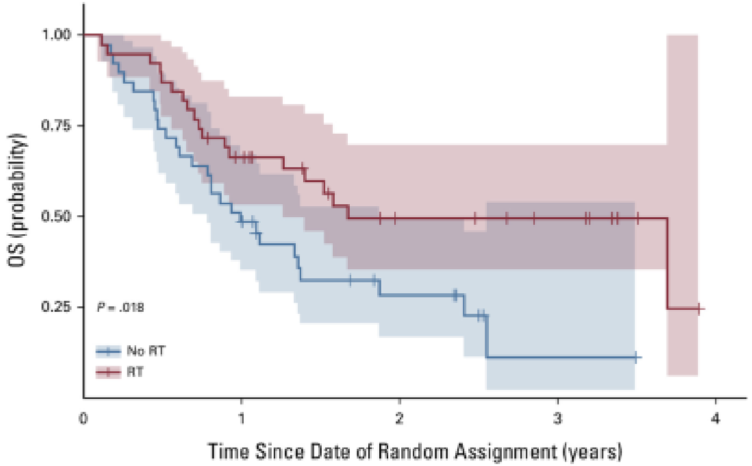
- Recent large prospective trials have indicated improvement in outcomes with ablative therapies for patients with oligometastatic disease.



Palma, JCO 2020

Prophylactic Radiation for Asymptomatic Bone Mets

- This prospective trial suggested that prophylactic RT for asymptomatic bone mets can improve outcomes, including overall survival.



No. at risk:

	0	1	2	3	4
No RT	39	18	7	1	0
RT	39	24	11	7	0

Events

	0	1	2	3	4
No RT	0	20	26	28	28
RT	0	13	18	18	19

Gillespie, JCO 2024

Precision Radiation Oncology

- Tailoring radiation treatment based on a patient's clinical and biologic factors
  - Treatment de-escalation based on HPV status in H&N SCC
  - Genetic/molecular tumor testing
  - Response to neoadjuvant treatment

OPEN ACCESS | ORIGINAL REPORTS | January 28, 2021

Reduced-Dose Radiation Therapy for HPV-Associated Oropharyngeal Carcinoma (NRG Oncology HN002)

Authors: Sue S. Yom, MD, Pedro Torres-Saavedra, PhD, Jimmy J. Caudell, MD, John N. Waldron, MD, Maura L. Gillison, MD, Ping Xia, PhD, Minh T. Truong, MD ... SHOW ALL ..., and Quynh-Thu Le, MD AUTHORS INFO & AFFILIATIONS

Publica

CLINICAL INVESTIGATION

Genomic Classifier Performance in Intermediate-Risk Prostate Cancer: Results From NRG Oncology/RTOG 0126 Randomized Phase 3 Trial

Daniel E. Spratt, MD,[a] Vinnie Y.T. Liu, MSc,[b] Jeff Michalski, MD, MBA, FASTRO,[c] Elai Davicioni, PhD,[b] Alejandro Berlin, MD, MSc,[d] Jeffry P. Simko, MD, PhD,[e] Jason A. Efstathiou, MD, DPhil,[f] Phuoc T. Tran, MD, PhD,[g] Howard M. Sandler, MD,[h] William A. Hall, MD,[i] Darby J.S. Thompson, PhD,[b] Matthew B. Parliament, MD, FRCPC,[j]

ORIGINAL ARTICLE

Omitting Regional Nodal Irradiation after Response to Neoadjuvant Chemotherapy

Authors: Eleftherios P. Mamounas, M.D., Hanna Bandos, Ph.D., Julia R. White, M.D., Thomas B. Julian, M.D., Atif J. Khan, M.D., Simona F. Shaitelman, M.D., Mylin A. Torres, M.D., +20 , and Norman Wolmark, M.D. Author Info & Affiliations

Published June 4, 2025 | N Engl J Med 2025;392:2113-2124 | DOI: 10.1056/NEJMoa2414859 | VOL. 392 NO. 21

Thank you for your attention!

- Questions? LisaNi@UW.edu

Post-Presentation Questions

Question #1: By what mechanism does radiation therapy treat malignancy?

A. Direct cytotoxicity via DNA damage
B. Disruption of tumor vasculature
C. Impairing cell membrane integrity and denaturing proteins
D. Release of neo-antigens facilitating immune recognition
E. All of the above

Answer: E

Question #2: What characteristic of a cell indicates its sensitivity to radiation damage, and for cancers determines the optimal fractionation?

A. Oxygen enhancement ratio
B. The alpha/Beta ratio
C. Dose-depth profile
D. The Bragg peak
E. Nucleus:cytoplasm ratio

Answer: B

Post-Presentation Questions

Question #3: Why might a shorter radiation therapy treatment course be more beneficial than a longer one?

A. Patient convenience
B. Better local control based on tumor's alpha/Beta ratio
C. Widening the therapeutic window
D. Reduced cost
E. All of the above

Answer: E

Question #4: What is the most common particle used in radiation therapy?

A. Electrons
B. Protons
C. Photons
D. Neutrons
E. Carbon ions

Answer: C