Nuclear Physics and Medical Applications: Imaging, Therapy and Innovation

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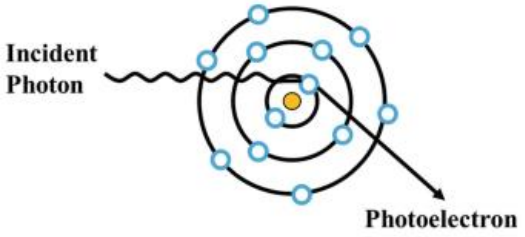
Outline

1. Basics of Nuclear Physics in Medicine
2. Accelerators in Medicine
3. Imaging Techniques
4. Radiation Therapy
5. Cutting-edge Research
6. Challenges and Opportunities

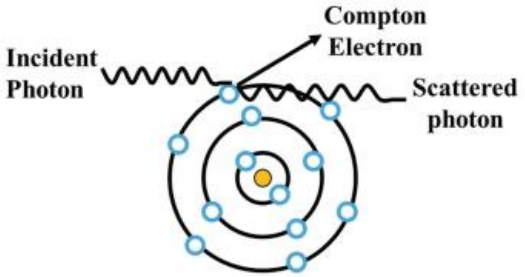
Basics of nuclear physics in medicine

Interactions of photons with matter

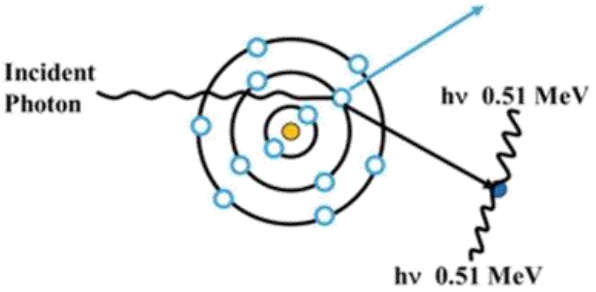
- **Photoelectric effect**
  - Dominates at low photon energies (keV range)
  - Photon is completely absorbed, ejecting an inner-shell electron
  - Strongly Z-dependent (~Z^3)
  - Important for diagnostic imaging (e.g., X-rays)
- **Compton Scattering**
  - Dominates at intermediate energies (hundreds of keV to MeV)
  - Photon transfers part of its energy to an outer electron, is scattered
  - Weakly Z-dependent, mostly depends on electron density
  - Relevant in both imaging and therapy
- **Pair Production**
  - Occurs at photon energies > 1.022 MeV
  - Photon disappears, creating an electron-positron pair
  - Occurs near the nucleus, increases with Z
  - Important in radiation therapy, especially for high-energy beams



(a) Photoelectric Effect



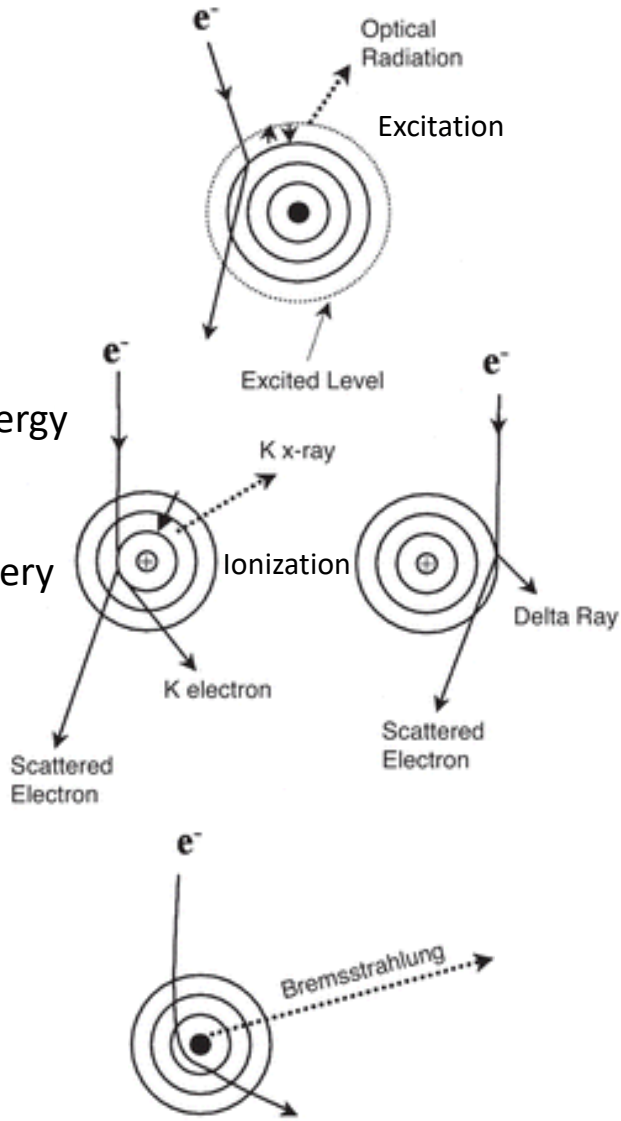
(b) Compton scattering



(c) Pair Production

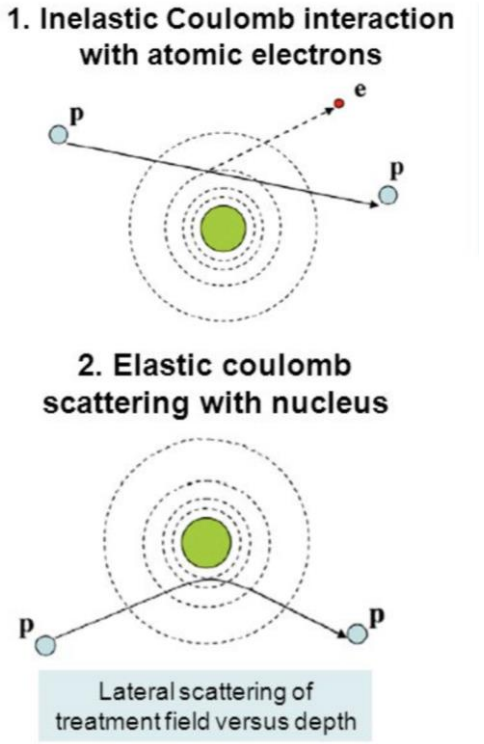
Interactions of electrons with matter

- **Elastic Scattering**
  - Electron changes direction without losing energy
  - Occurs mostly with atomic nuclei
  - Affects electron path and spatial resolution in imaging
- **Inelastic Scattering**
  - Electron loses energy by interacting with orbital electrons
  - Can cause:
    Excitation: electron raises an atomic electron to a higher energy level
    Ionization: ejects an electron, creating an ion pair
  - Leads to energy deposition in tissues → important for dose delivery
- **Secondary Electrons (Delta Rays)**
  - Knocked-out electrons from ionization
  - Can further ionize tissue
  - Contribute to lateral dose spread
- **Bremsstrahlung Radiation**
  - High-speed electrons decelerate in the electric field of nuclei
  - Energy is emitted as X-rays
  - More significant in high-Z materials and at high energies
  - Important in X-ray tube design and radiation shielding



Interaction of p, α, C-ions with matter

- **Inelastic Collisions with Electrons (Electronic Stopping)**
  - Dominant mechanism for energy loss in soft tissue
  - Leads to ionization and excitation of atoms
  - Energy loss rate described by the Bethe-Bloch formula
  - Produces delta rays (secondary electrons)
- **Elastic collisions with nuclei**
  - Particle transfers energy to atomic nuclei
  - Causes nuclear recoil and scattering
  - Important for low-energy particles and radiation damage in materials
- **Nuclear reactions**
  - Require high kinetic energy (typically MeV range)
  - Can result in:
  - Emission of neutrons, protons, or α particles
  - Transmutation of target nuclei



Why is this important in medicine?

✅ **How we image the body**

Modalities like X-rays, CT, PET, and SPECT rely on:

- Photon attenuation, scattering, and absorption
- Precise modeling of these interactions improves image quality and diagnostic accuracy

✅ **How we treat cancer with radiation**

Techniques like proton therapy, electron therapy, and external beam radiotherapy depend on:

- Energy deposition (dose) in tissue via ionization
- Controlling how radiation stops in tissue allows us to target tumors and spare healthy organs
- Example: the Bragg peak in proton therapy

✅ **How we protect patients and staff**

Knowledge of radiation absorption and secondary particle production informs:

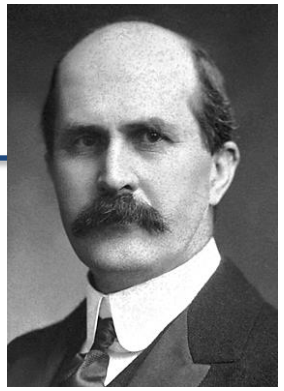
- Radiation shielding design
- Dose estimation to minimize risk
- Radiation protection protocols in hospitals and nuclear medicine units

✅ **How we develop new technologies**

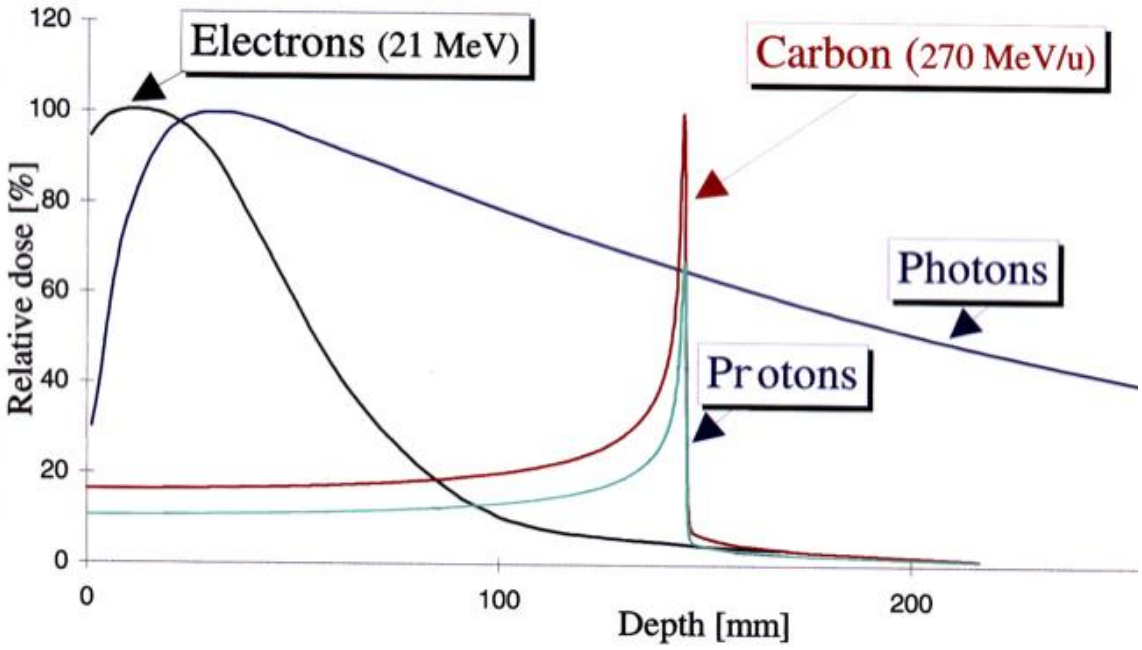
Advancements in detectors, contrast agents, and radiopharmaceuticals are based on:

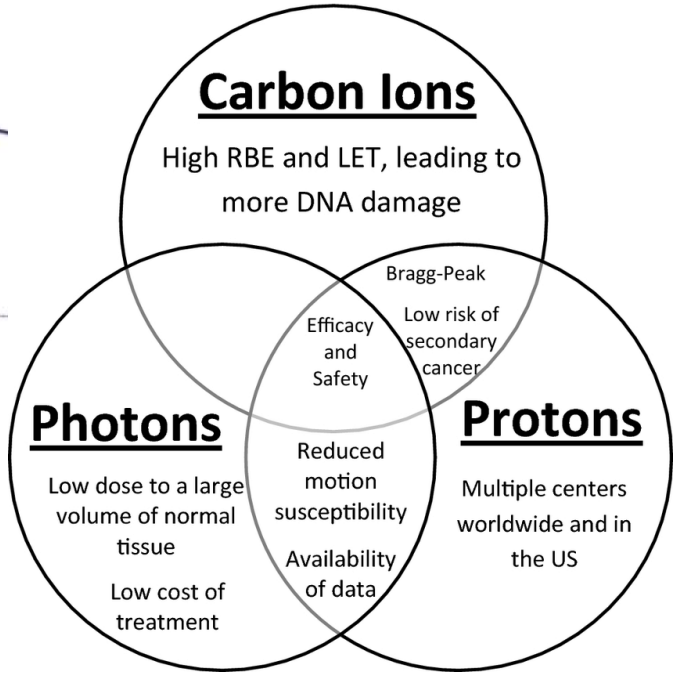
- Tailoring radiation–matter interactions for specific medical tasks
- For example, using high-Z materials in detectors to enhance X-ray absorption

Dose deposition in matter



Sir H.W. Bragg





How do we deliver radiation?
How do we know where to deliver it?
How can we maximize outcome?

Treating cancer with radiation

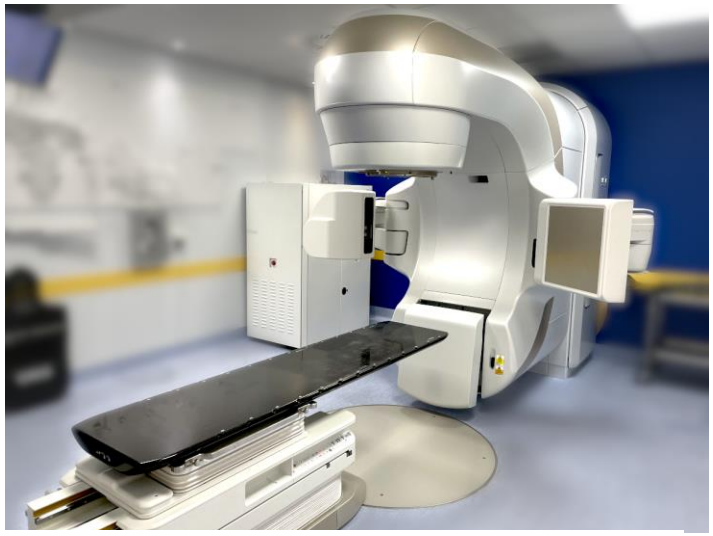
How do we deliver radiation?
How do we know where to deliver it?
How can we maximize outcome?

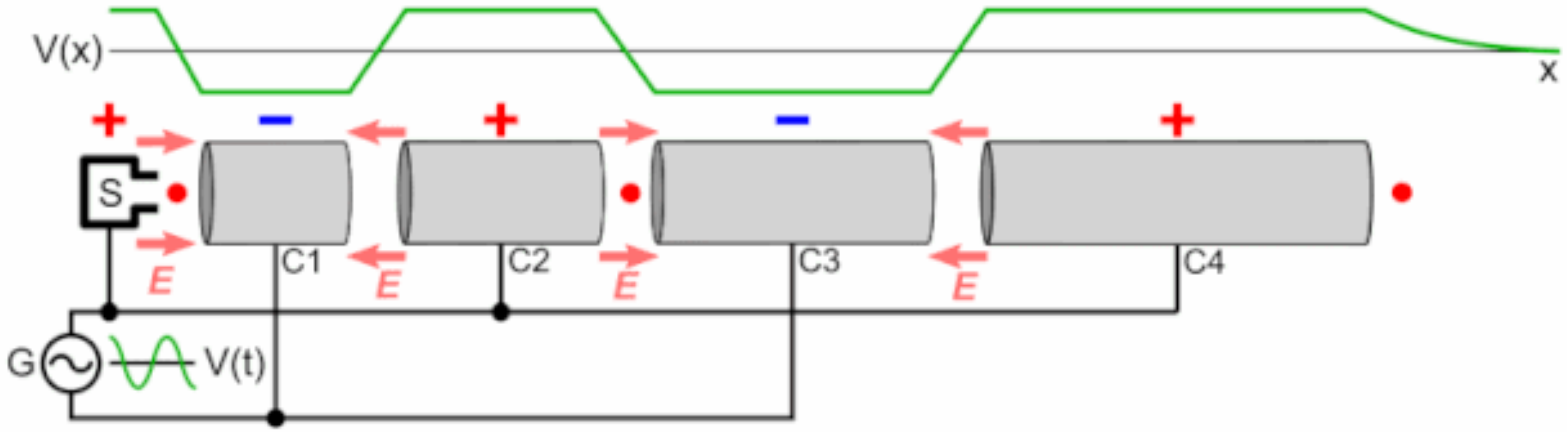
- Role of accelerators in medicine
  - Cyclotrons, synchrotrons, LINACs
  - Treatment / diagnosis
  - Facilities in hospitals and research
- Imaging modalities
  - CT (Computerized tomography)
  - MRI (Magnetic resonance imaging)
  - PET (Positron Emission Tomography)
  - SPECT (Single Photon Emission Computed Tomography)
- Radiation therapy
  - External beam therapy
  - Dosimetry and quality assurance
  - Real-time monitoring and verification

Role of accelerators in medicine

LINACS (Linear Accelerators)

- Linacs accelerate charged particles (like electrons) using oscillating electromagnetic fields.
- These particles are then directed at a target, where they produce X-rays or electrons.
- The energy and intensity of the beams can be adjusted to target specific areas and depths within the body.



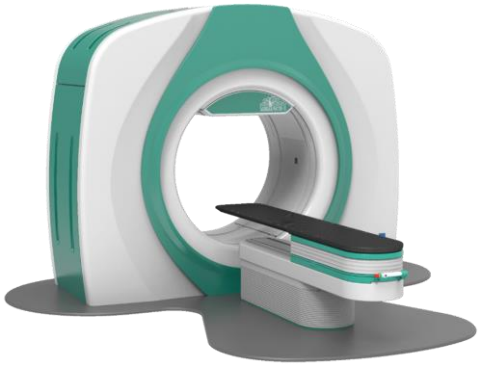


Types of LINACS in Medicine:

- **Gantry-based Linacs**: most common type, featuring a rotating gantry that allows the linac to deliver radiation from various angles around the patient. They are versatile and can be used for a wide range of treatments, including conventional radiation therapy, IMRT (Intensity-Modulated Radiation Therapy), and VMAT (Volumetric Modulated Arc Therapy).

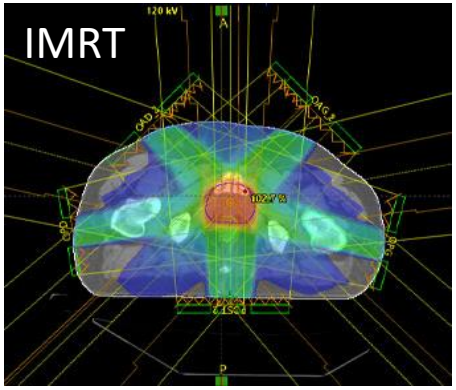
- **Ring-based Linacs:** Designed to deliver radiation in a circular arc, often used for stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT).

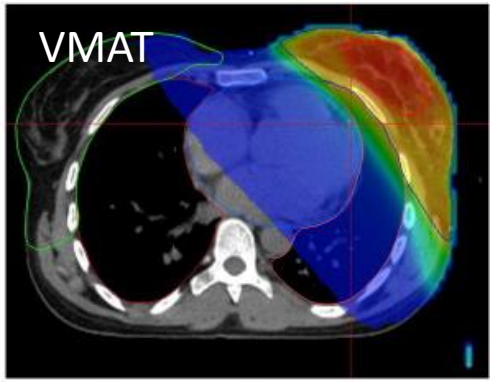
- **RAM (Robotic-Arm Mounted) Linacs:** These linacs use a robotic arm to move the radiation beam, providing greater flexibility and precision in treatment planning and delivery. They are particularly useful for treatments that require precise targeting and complex shapes, such as stereotactic radiosurgery.



Use of LINACS in Medicine:

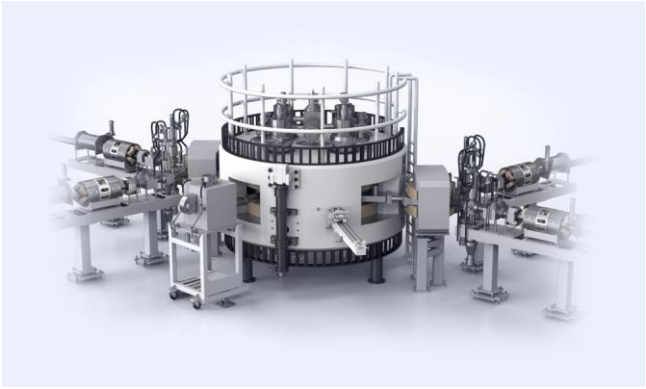
- **IMRT (Intensity-Modulated Radiation Therapy):** Uses complex beam shapes to deliver radiation with high precision, minimizing dose to surrounding healthy tissues.
- **VMAT (Volumetric Modulated Arc Therapy):** A type of IMRT that delivers radiation continuously while the linac rotates around the patient, allowing for even faster and more accurate treatment.
- **IGRT (Image-Guided Radiation Therapy):** Uses imaging techniques (as MRI) during treatment to ensure accurate positioning and delivery of radiation.
- **SRS (Stereotactic Radiosurgery):** Uses fewer high doses of radiation to target small, localized tumors to preserve healthy tissues, such as brain tumors.
- **SBRT (Stereotactic Body Radiation Therapy):** A similar technique to SRS, but used for tumors outside the brain, such as lung or liver tumors.

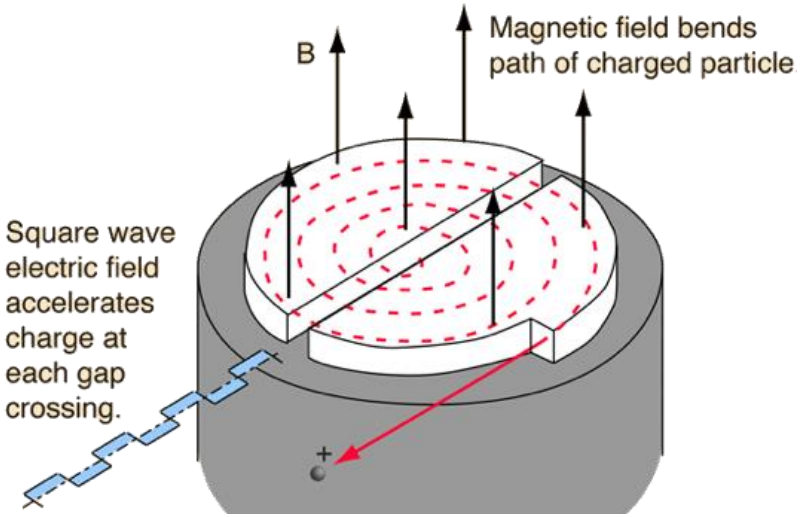




Cyclotrons

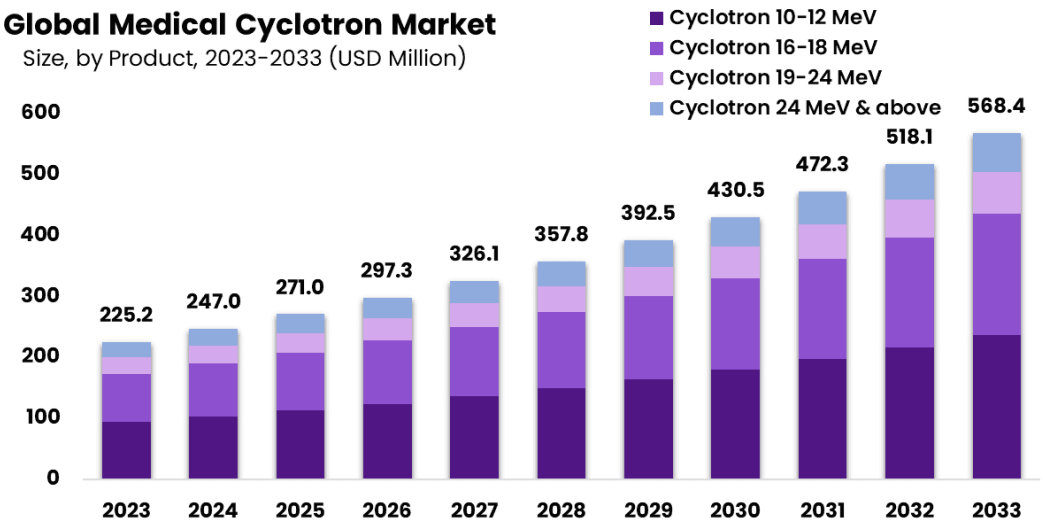
- Circular particle accelerator that uses a constant magnetic field and a radiofrequency (RF) electric field to accelerate charged particles to high energies.
- Low energy cyclotrons specifically made to produce medical isotopes for imaging or treatment (10–30 MeV)
  - Relatively cheap.
  - Can be conveniently located in hospitals or near hospitals.
- High energy cyclotrons used directly for treatment (70–250 MeV)
  - More expensive
  - Need more space.





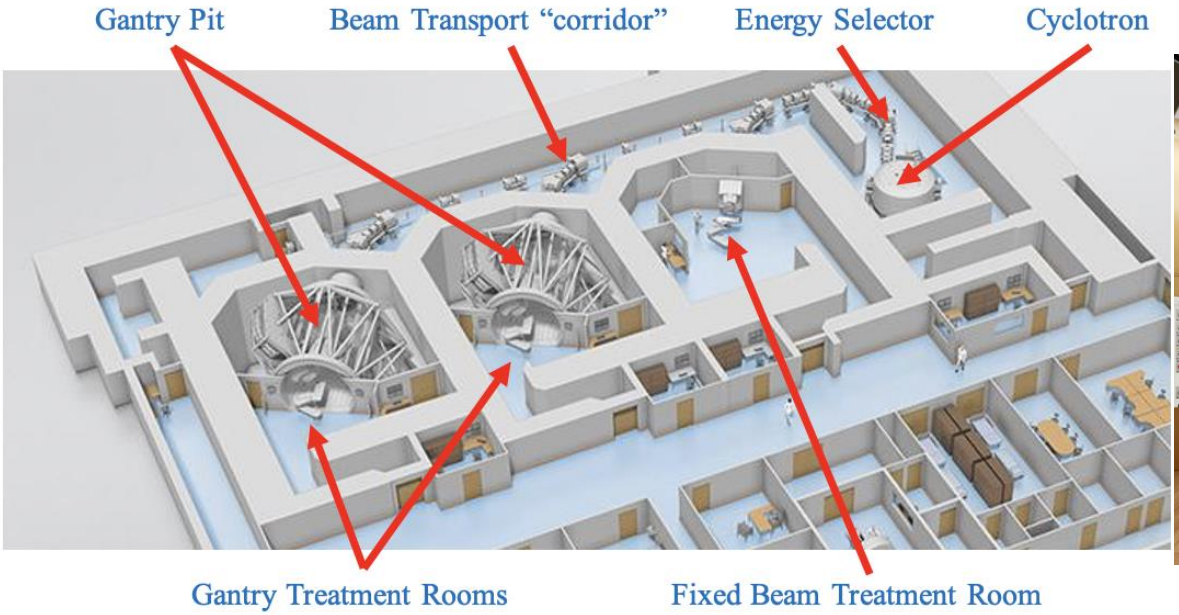
Medical uses of cyclotrons

- Production of radioisotopes.
  - Cyclotrons accelerate charged particles (like protons or alpha particles) to high energies.
  - These accelerated particles then collide with target atoms, resulting in nuclear reactions that create new, radioactive isotopes.
  - Some common isotopes produced in cyclotrons include fluorine-18 ([F-18]-FDG), used in **PET scans**, and palladium-103 (Pd), used in **internal radiation therapy**.



Medical uses of cyclotrons

- External radiation therapy.
  - Cyclotrons accelerate charged particles (like protons) to higher energies, which allows them to penetrate deep within the body to target tumors.
  - Energy of the proton beam can be adjusted to match the specific treatment needs of each patient. This is often done by passing the beam through a degrader, which reduces the beam's energy.

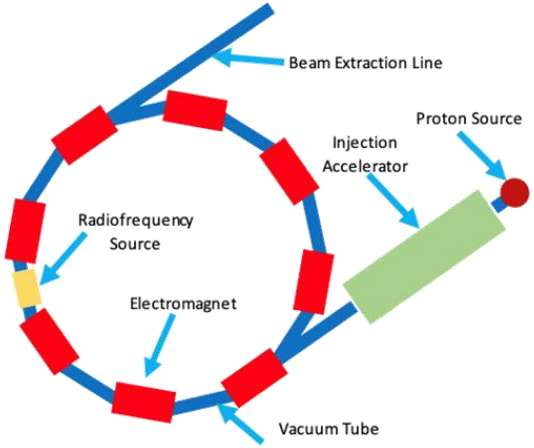


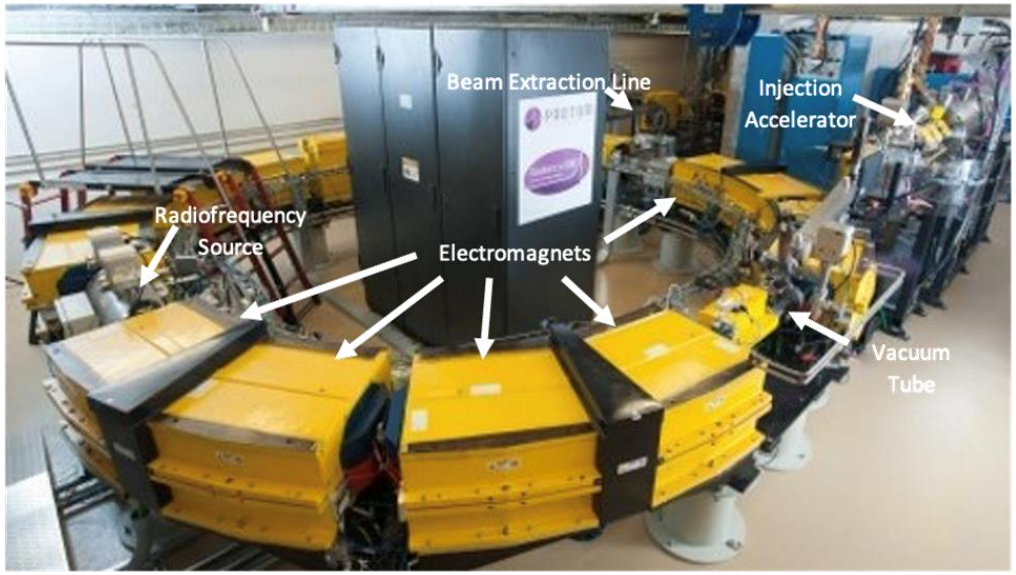
Synchrocyclotron

- Cyclotrons can be classified into two types: isochronous cyclotrons and synchrocyclotrons, which modulates the radiofrequency (RF) of the accelerating voltage to account for the relativistic increase in the particle's mass as it approaches higher speeds.
- Unlike a classical cyclotron, which uses a constant RF, the synchrocyclotron reduces the frequency over time to keep the particles in phase with the accelerating electric field.
- Suitable for accelerating protons to high energies
- Typically pulsed beam (not continuous)

Synchrotrons

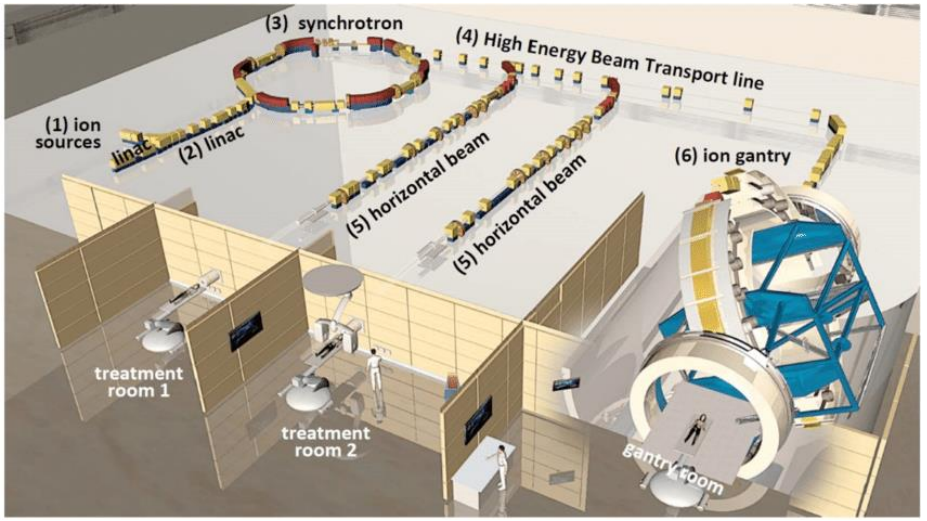
- Circular particle accelerator. Particles are typically injected into the synchrotron after being accelerated by a linac, which provides them with a starting energy.
- Particles are guided along a circular path by a series of electromagnets.
- As the particles gain energy, the magnetic field strength is increased in synchrony with their acceleration, ensuring they stay on their circular path.
- This process allows the particles to gain energy repeatedly as they circumnavigate the ring.





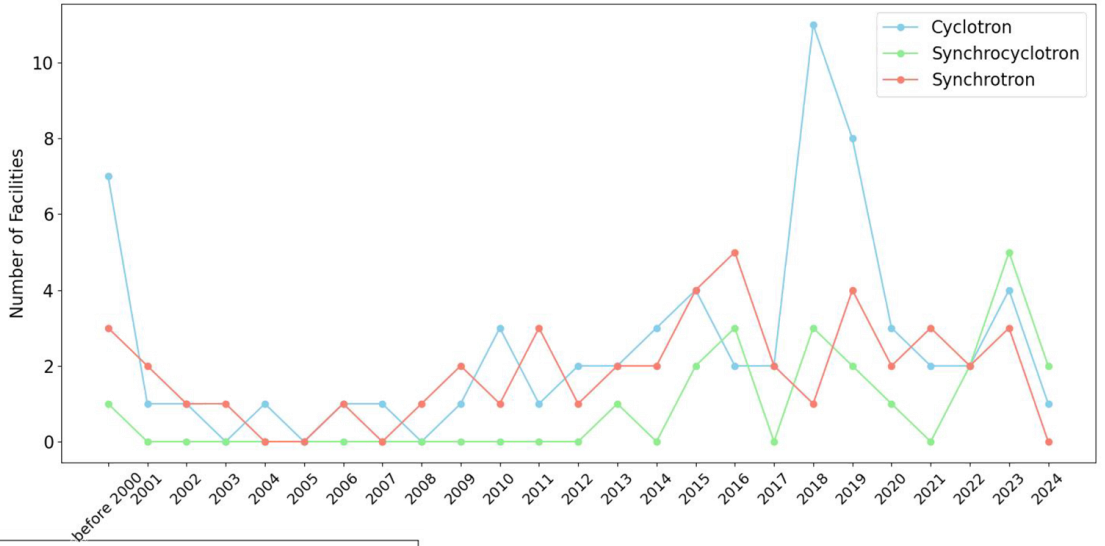
Synchrotrons for particle therapy

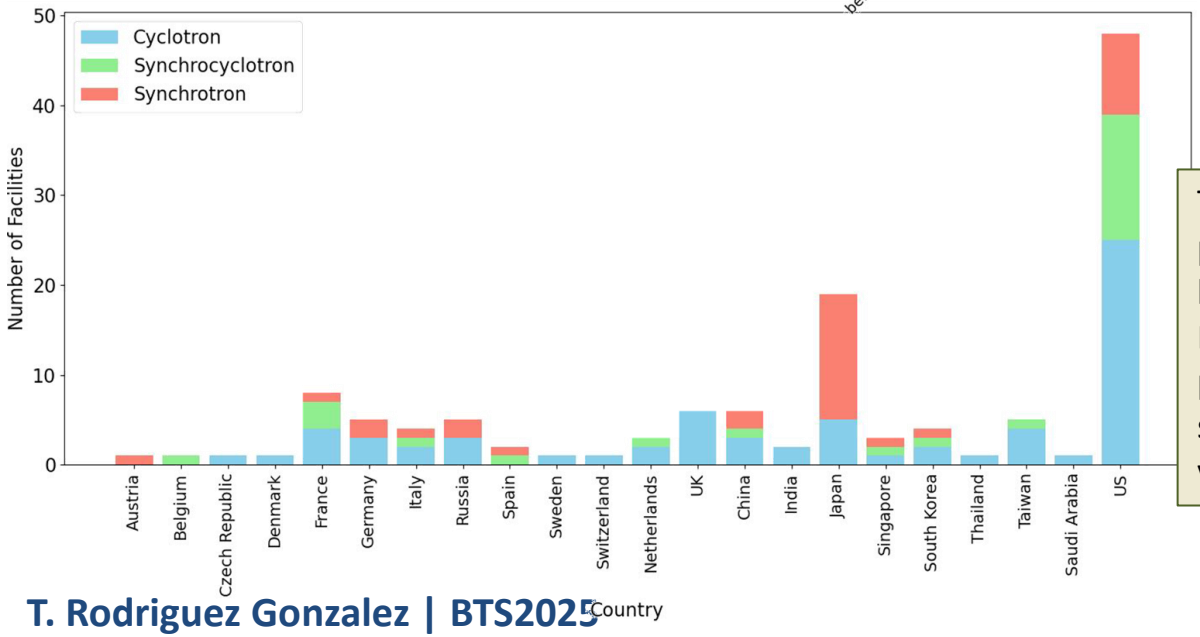
- Unlike cyclotrons that provide continuous beams at a fixed energy, synchrotrons produce pulsed beams at varying energies throughout the acceleration cycle
- Synchrotrons offer advantages in terms of beam transmission rate, and higher and easily adjustable beam energy, making them well-suited for both proton and carbon ion therapy. Cyclotrons are typically faster and more compact but have limitations in terms of energy and beam quality



Particle therapy facilities in operation

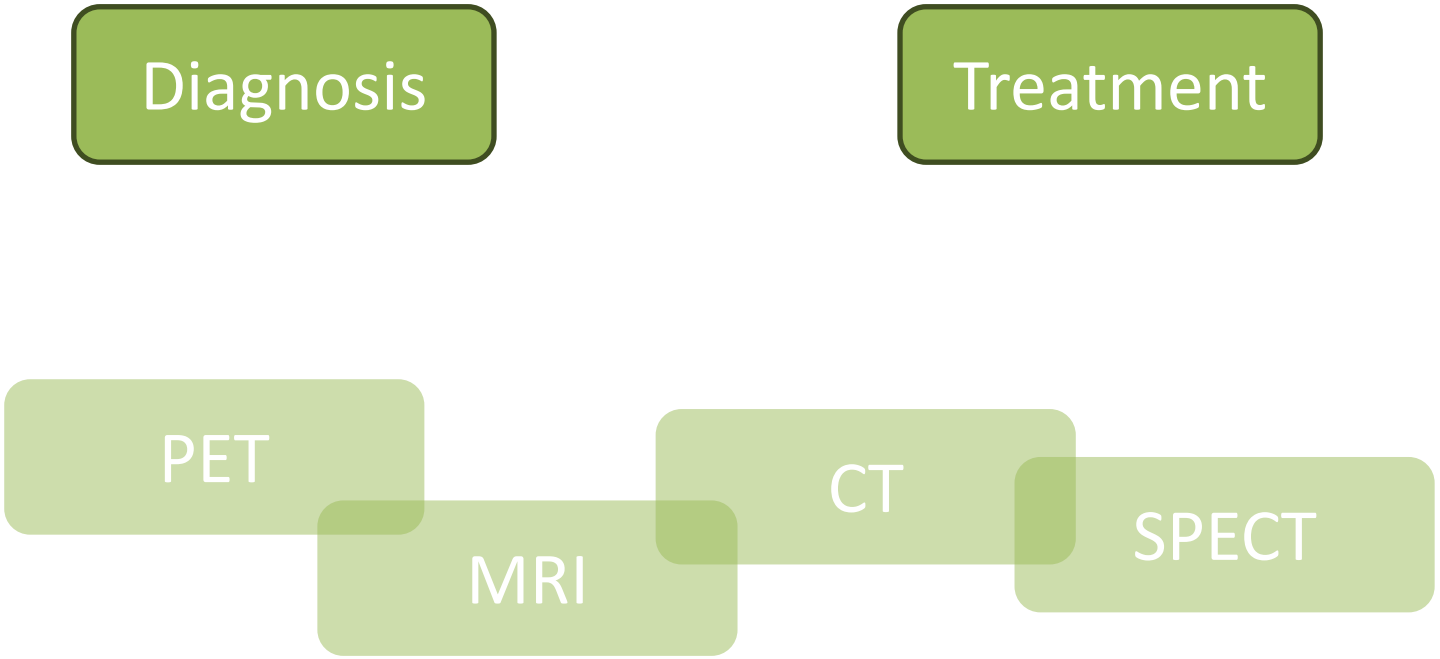
Growing interest and investment over the last 30 years. It seems there is a high increase in the number of cyclotrons built or operational in recent years → advancements in accelerator technology, such as the superconducting techniques that further reduce the cost, size, and weight of the facility





The United States focuses exclusively on proton therapy, whereas Japan provides both proton and carbon ion therapies. Europe has a diverse and well-established particle therapy infrastructure with a significant number of facilities across various countries.

Medical Imaging



PET imaging

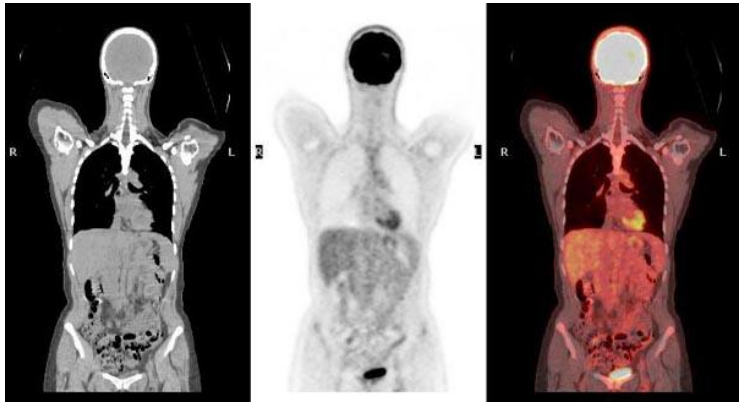
PET is a **nuclear medicine imaging technique** that provides **functional and metabolic information** by detecting **positron-emitting radiotracers**.

- **Injection of radiotracer:** A biologically active molecule (e.g., glucose) is labeled with a positron-emitting radionuclide (e.g., $^{18}F \rightarrow$ FDG)
- **Positron emission and annihilation:**
  - The radionuclide decays, emitting a positron (β^+)
  - The positron travels a short distance (~mm) before annihilating with an electron
  - This produces two 511 keV photons, emitted in opposite directions
- **Coincidence detection:**
  - A ring of detectors surrounding the patient detects these two photons simultaneously
- **Line of Response (LOR) and image reconstruction**
  - Localization of the annihilation event
  - Thousands of LORs are collected and reconstructed using tomographic algorithms (e.g., filtered back projection or iterative methods)

PET imaging

- High **sensitivity** and **quantitative capability**
- Measures **biological activity**, not just anatomy
- Common tracers:
  - ^{18}F-FDG (glucose metabolism)
  - ^{11}C, ^{13}N, ^{68}Ga, etc.

- **Applications in Medicine:**
  - Oncology: tumor detection, staging, therapy response
  - Neurology: Alzheimer's disease, epilepsy, brain metabolism
  - Cardiology: myocardial perfusion and viability
  - Theranostics: pairing diagnostics with targeted radiotherapy



SPECT imaging

SPECT (Single Photon Emission Computed Tomography) is a **functional nuclear imaging technique** that uses **gamma-emitting radiotracers** to create 3D images of physiological processes.

- **Radiotracer injection:**
  - A compound is labeled with a gamma-emitting radionuclide (e.g., ^{99m}Tc, ^{123}I, ^{111}In) and injected into the patient
- **Gamma emission:**
  - The radionuclide emits single photons as it decays (unlike PET, no positrons or annihilation)
- **Detection:**
  - Gamma cameras rotate around the patient to collect projections at multiple angles
  - Each camera uses a collimator to determine the direction of incoming photons
- **Image reconstruction:**
  - 2D projections are used to reconstruct 3D tomographic images
  - Shows distribution of the tracer in tissues or organs

SPECT imaging

- Applications in medicine:
  - Cardiology: myocardial perfusion imaging
  - Neurology: epilepsy, Parkinson's, cerebral perfusion
  - Oncology: tumor localization
  - Bone scans: detection of metastases or fractures

Isotope	Half-life	Application
^{99m}Tc	6 h	Perfusion, bone, cardiac, brain scans
^{123}I	13 h	Thyroid imaging
^{201}Tl	73 h	Cardiac imaging

- Lower cost and broader availability than PET
- Uses longer-lived isotopes
- Spatial resolution typically lower than PET (~8–10 mm)
- Imaging takes longer than PET (~20–30 min)

	PET	SPECT
Emission type	$\beta^+ \rightarrow$ 2x511 keV photons	Single gamma photon
Detectors	Coincidence detectors	Collimated cameras
Resolution	~4–6 mm	~8–10 mm
Sensitivity	Higher	Lower
Cost	Higher	Lower

MRI imaging

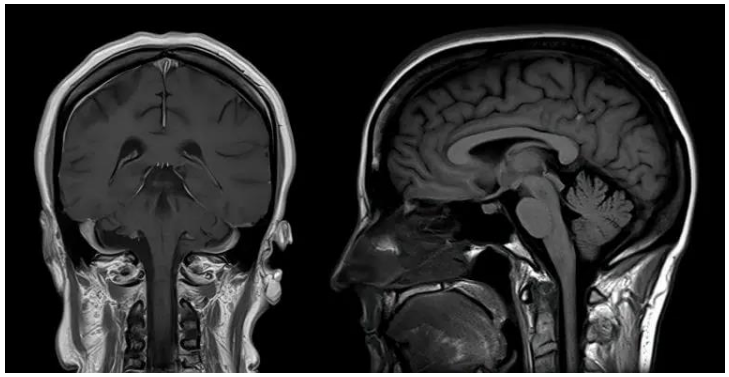
MRI (Magnetic Resonance Imaging) is a **non-ionizing imaging modality** that uses strong magnetic fields and radiofrequency pulses to generate **high-resolution images of soft tissues** based on **proton (^{1}H) behavior** in water and fat.

- **Static magnetic field (B_o):**
  - Aligns the nuclear spins (mainly hydrogen nuclei, i.e., protons) in body tissues
  - Typical field strength: 1.5T–3T (clinical), up to 7T (research)
- **Radiofrequency (RF) pulse:**
  - Applies energy to flip the aligned protons out of equilibrium
  - This excites the system, altering the spin orientation
- **Relaxation & signal detection:**
  - Protons relax back to equilibrium, emitting RF signals
  - Two relaxation times are measured:
    - T1 (longitudinal)
    - T2 (transverse)
  - Signal is detected by coils and processed to form images
- **Gradient Fields:**
  - Spatially encode the signals by altering the magnetic field across the body
  - Enables slice selection and 3D localization

MRI imaging

- No ionizing radiation (safe for repeated use)
- Excellent soft tissue contrast (e.g., brain, muscle, tumors)
- Adjustable contrast by tuning imaging parameters (T1, T2, proton density, etc.)
- Functional and spectroscopic imaging also possible (e.g., fMRI, MRS)

- Applications in Medicine
  - Neurology: brain anatomy, tumors
  - Orthopedics: muscles, joints, spine
  - Cardiology: cardiac morphology, perfusion
  - Oncology: tumor localization and monitoring
  - Obstetrics: fetal imaging without radiation



	MRI	PET/SPECT
Radiation	None	Ionizing radiation (γ, β^+)
Primary signal source	Proton spin relaxation	Radioactive decay events
Image type	Anatomical (structural)	Functional/metabolic
Spatial resolution	High (~1 mm)	Moderate (~4–10 mm)
Soft tissue contrast	Excellent	Limited

CT imaging

CT (Computed Tomography) uses **X-rays and computer reconstruction** to generate **cross-sectional images** of the body, providing detailed **anatomical information**, especially for dense tissues like **bone and lungs**.

- **X-ray Source and Detector:**
  - A rotating X-ray tube emits fan-shaped or cone-shaped beams
  - Detectors measure the attenuated X-rays after they pass through the patient
- **Multiple Projections:**
  - As the system rotates, hundreds of projections are acquired from different angles
- **Image Reconstruction:**
  - Computer algorithms (e.g., filtered back projection or iterative reconstruction) process these projections into 2D slices
  - Slices can be stacked into 3D volumes

CT imaging

- High-resolution anatomical images
- Excellent contrast for bone, lung, and blood vessels (with contrast agents)
- Fast scan times (~seconds)
- Often combined with PET or SPECT in hybrid systems (PET/CT, SPECT/CT)
- Applications in Medicine
  - Trauma: rapid assessment of internal injuries
  - Oncology: tumor localization, treatment planning
  - Pulmonology: lung imaging (e.g., COVID-19, embolism)
  - Cardiology: coronary CT angiography
  - Radiotherapy: CT is essential in dose planning

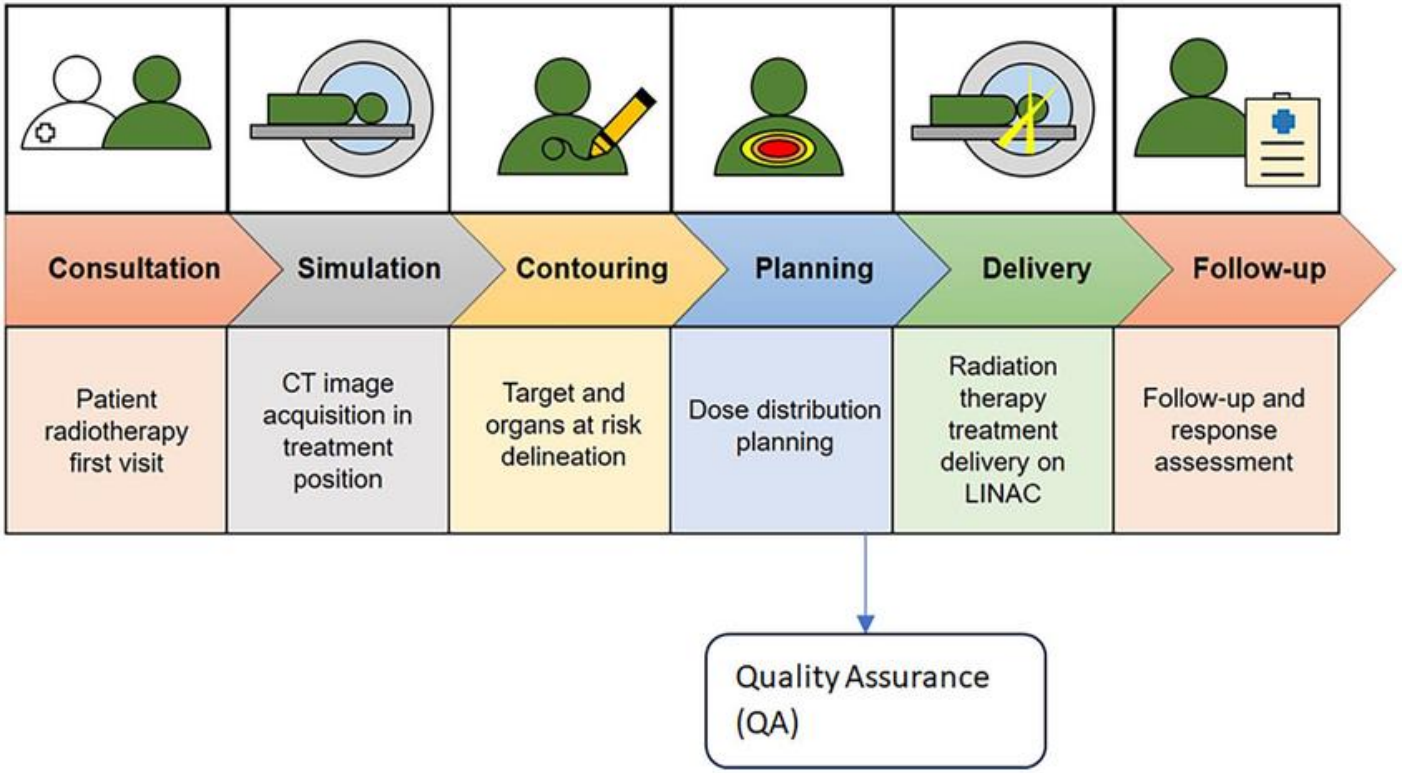
	CT	MRI
Radiation	Ionizing (X-rays)	No ionizing radiation
Best for	Bone, lung, acute imaging	Soft tissue contrast
Speed	Fast (~seconds)	Slower (~minutes)
Contrast agents	Iodine-based (radiopaque)	Gadolinium-based

Radiation therapy

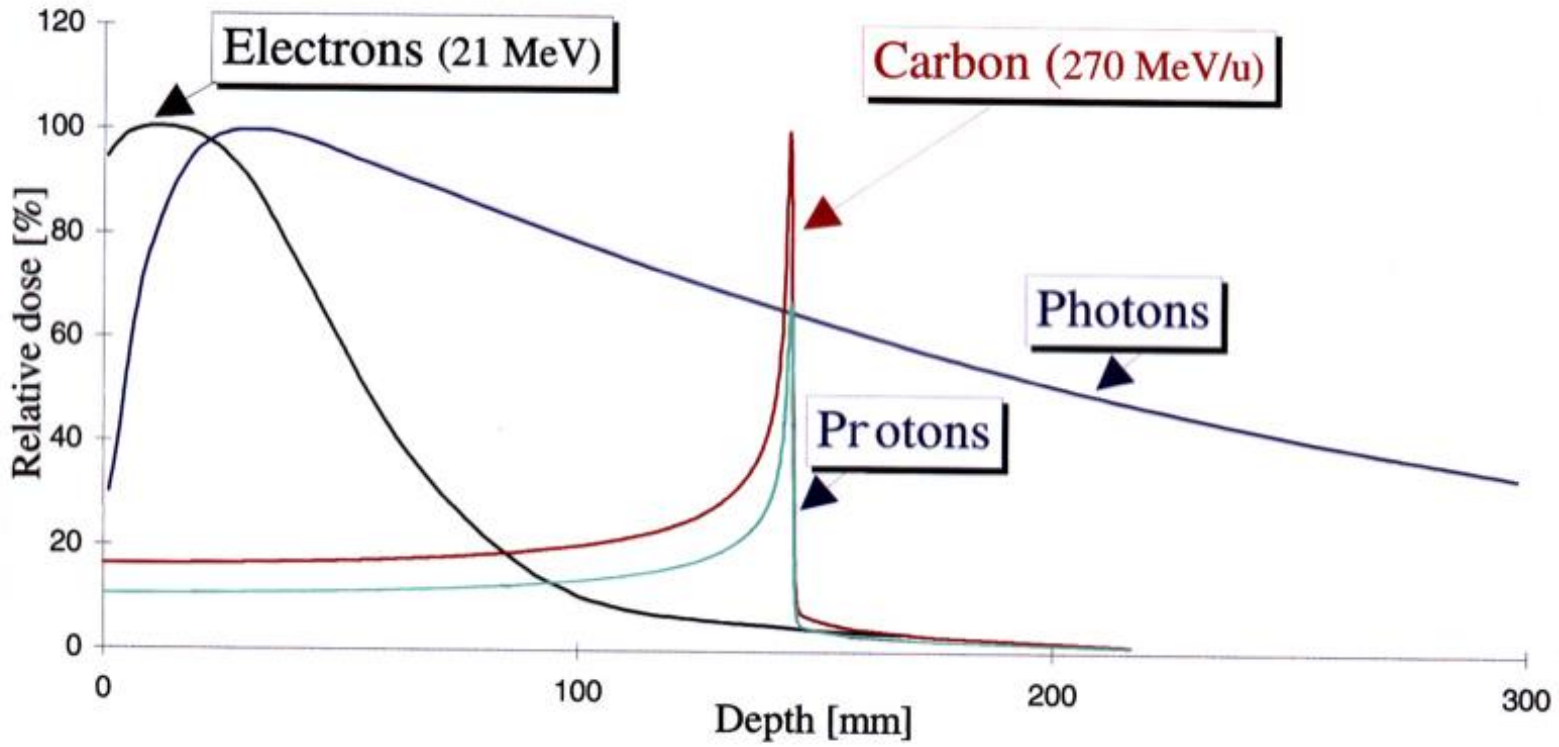
Workflow in radiation therapy

Radiation therapy (RT) uses **high-energy ionizing radiation** (photons, electrons, protons, or heavy ions) to **destroy cancer cells** while minimizing damage to healthy tissues.

The **workflow** involves several steps from diagnosis to treatment delivery and verification.



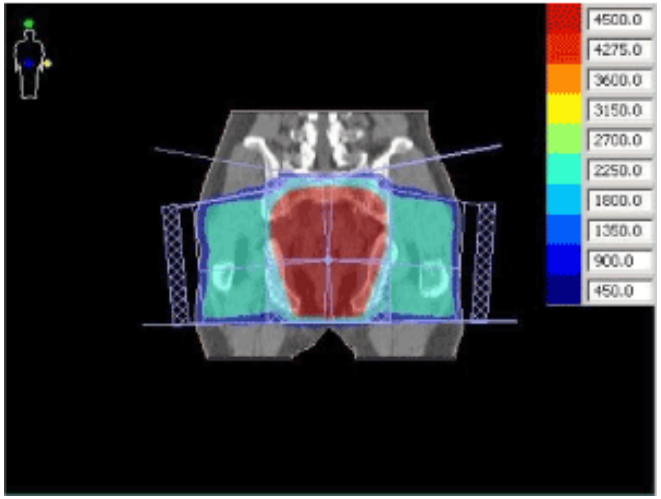
Dose deposition in matter



Conventional radiation therapy

Delivers **ionizing radiation** to the tumor from outside the body using **high-energy X-rays or electrons**, typically produced by a **linear accelerator (LINAC)**.

- Most widely used form of radiation therapy
- Typically uses 6–25 MeV photons or electrons
- Delivered in daily fractions over several weeks

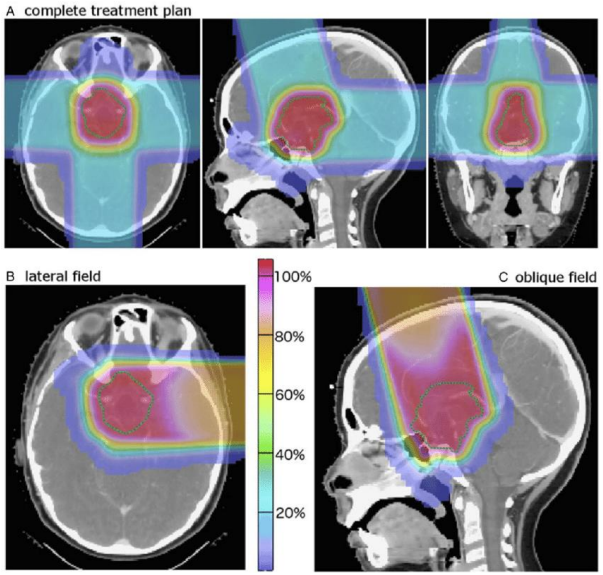


- **3D Conformal Radiation Therapy (3D-CRT):**
  - Uses CT-based planning
  - Beams shaped to match tumor geometry
  - Better sparing of healthy tissue
- **Intensity-Modulated Radiation Therapy (IMRT):**
  - Advanced form of 3D-CRT
  - Uses modulated beam intensities
  - Enables complex dose distributions
- **Volumetric Modulated Arc Therapy (VMAT):**
  - Beam is delivered in arcs with continuously changing intensity
  - Fast and highly conformal

Proton therapy

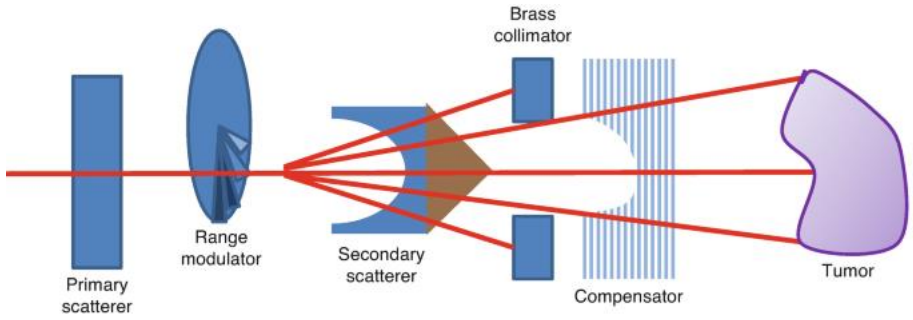
Proton therapy is an advanced form of **external beam radiation therapy** that uses **protons**—positively charged particles—to **precisely target tumors**, minimizing radiation dose to healthy tissues.

- Protons deposit most of their energy at a specific depth (the Bragg peak)
- Beyond this peak, the dose drops sharply to zero
- Enables high conformality and normal tissue sparing. In contrast, X-rays deposit energy along the entire path, affecting healthy tissues before and after the tumor.
- Ideal for tumors near sensitive structures (brain, spine, eye)
- Reduced long-term side effects, especially in pediatric patients
- Lower risk of secondary cancers due to reduced integral dose

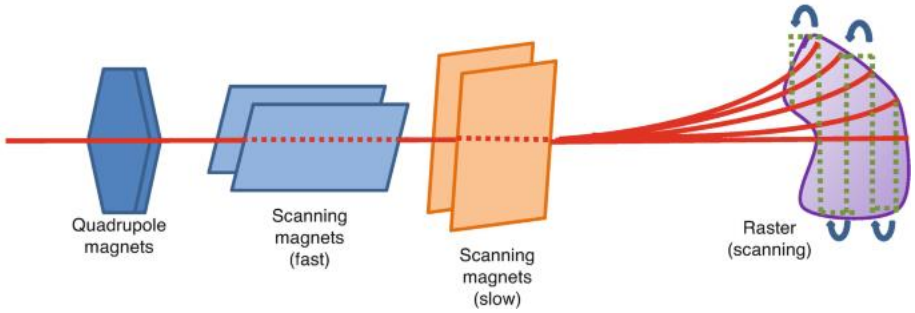


Proton therapy

- **Passive Scattering:**
  - Uniform dose over tumor volume
  - Uses scatterers, collimators, compensators



- **Pencil Beam Scanning (PBS):**
  - Narrow proton beam "paints" the tumor layer by layer
  - Enables IMPT (Intensity-Modulated Proton Therapy)
  - Higher precision and dose conformity



Cost and size: Facilities are large and expensive
Sensitivity to motion and tissue heterogeneity
Requires precise imaging and robust planning algorithms
Range uncertainty: small errors in stopping power can shift dose

Heavy ions therapy

Cutting-edge form of radiation therapy that uses **charged particles heavier than protons**, such as **carbon ions**, to treat cancer with **unmatched precision and biological effectiveness**.

- Commonly used: Carbon ions (^{12}C)
- Also under used/research: alpha particles, Oxygen (^{16}O), Neon (^{20}Ne)
- Require higher energies to reach deep-seated tumors (e.g., ~400 MeV/u for 30 cm penetration)
- Exhibit a Bragg peak, like protons, but with sharper dose fall-off
- Lower lateral scattering ⇒ very sharp beam edges
- Precise dose delivery with high conformity
- Dense ionization tracks cause complex DNA damage
- More effective at killing radioresistant or hypoxic tumors
- Higher Relative Biological Effectiveness (RBE). Less repairable DNA damage in cancer cells
- Uncertainties in range and biological effect need advanced modeling
- Facility is complex and expensive, often part of research centers

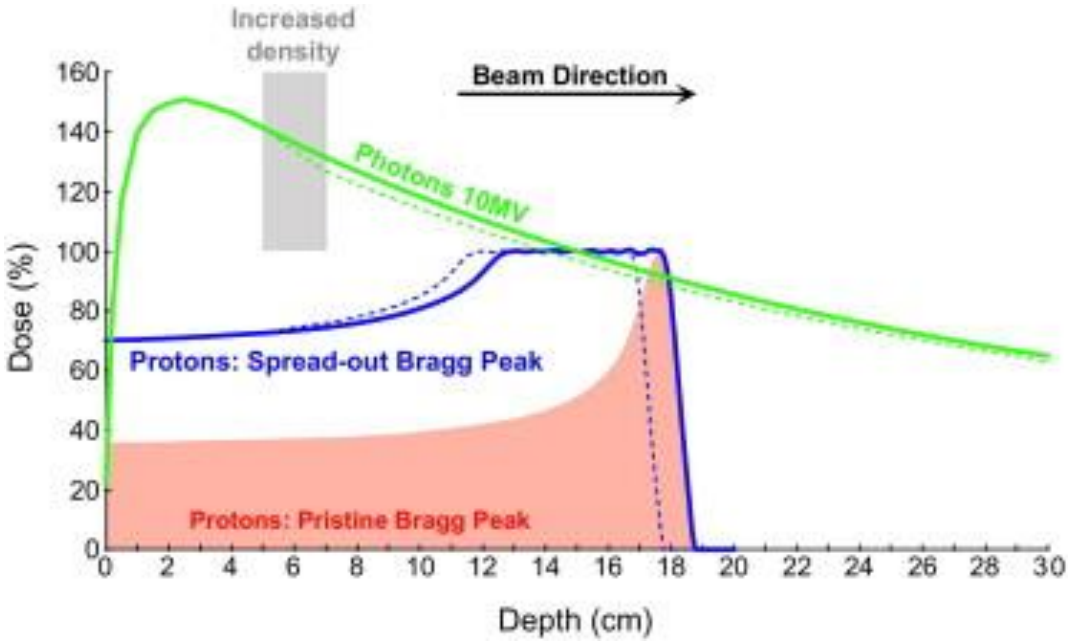
Dosimetry and quality assurance

Accurate **dosimetry** and rigorous **quality assurance (QA)** are essential for the **safety, efficacy, and reproducibility** of all radiation-based medical applications, especially in imaging and therapy

- **Reference Dosimetry**
  - Absolute dose measurement (e.g., in water phantom)
  - Ionization chambers (e.g., Farmer chamber) are standard tools
- **Relative Dosimetry**
  - Used for beam profiles, depth dose, output factors
  - Performed with diode arrays, film, 2D/3D detectors
- **In Vivo Dosimetry**
  - Measures dose inside the patient
  - Used for real-time verification and patient-specific QA

Real-time monitoring and verification

- High precision treatments (e.g. proton/carbon therapy) demand **millimetric accuracy**
- Patient motion (breathing, organ shifts) introduces **uncertainties**
- Real-time data allows **adaptive corrections** or beam interruption



Real-time monitoring and verification

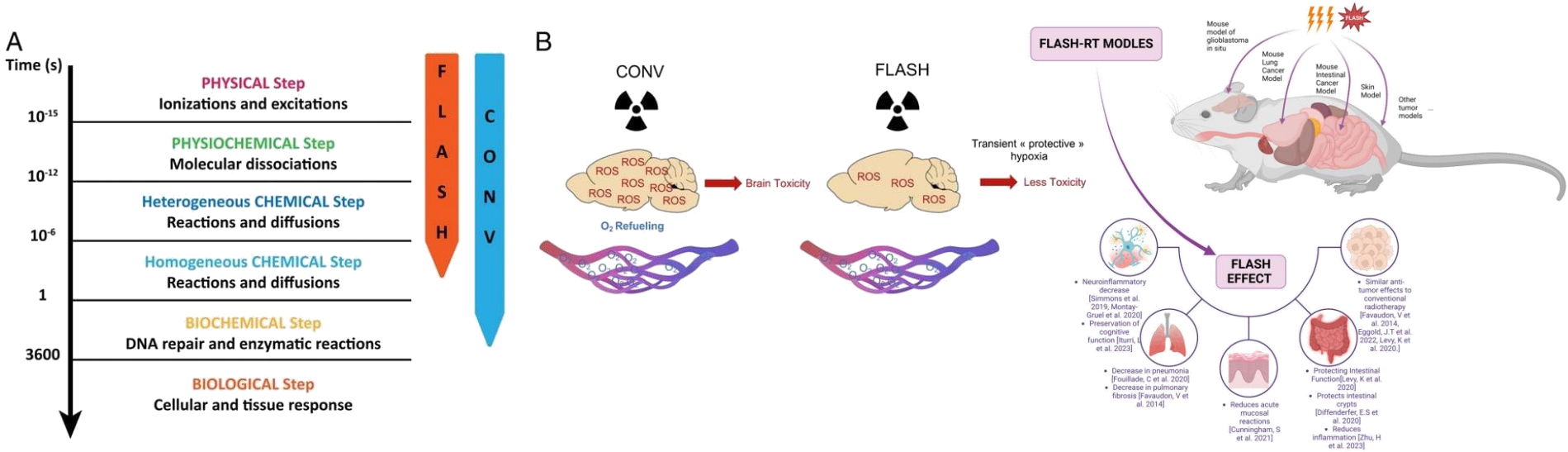
Prompt Gamma Detection	• Emitted during nuclear interactions in tissue • Provides info on beam range and stopping point • Detectors: slit cameras, Compton cameras, time-of-flight systems
PET Imaging (in-beam or offline)	• Detects β^+ emitters generated by nuclear interactions • Good for range estimation, though limited in real-time use
Ionization Chambers & Detectors	• Measure beam fluence or current continuously • Often used for QA and delivery monitoring
Scintillators and Cherenkov Detectors	• Capture light emission from charged particle interactions • Fast, real-time readout options for surface dose or beam monitoring
Surface Imaging and Tracking Systems	• Optical tracking of patient surface during beam delivery • Ensures alignment with treatment plan (especially with motion)
Ionoacoustics	• Acoustic signal generated by thermoelastic expansion • Detected using ultrasound transducers • Direct measurement of beam range and promising mm precision

New research lines and developments

🔬 **FLASH Radiotherapy**

- Ultra-high dose rate (>40 Gy/s) delivery in milliseconds
- Promising for reducing normal tissue toxicity
- Requires new accelerators, dosimetry, and real-time monitoring
- Proton and electron FLASH studies ongoing

🚀 *Physics challenge*: dosimetry, beam control, and understanding of FLASH effect

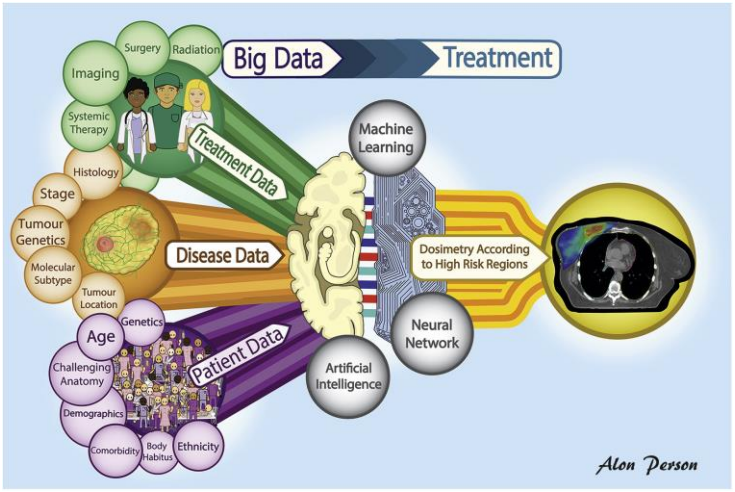


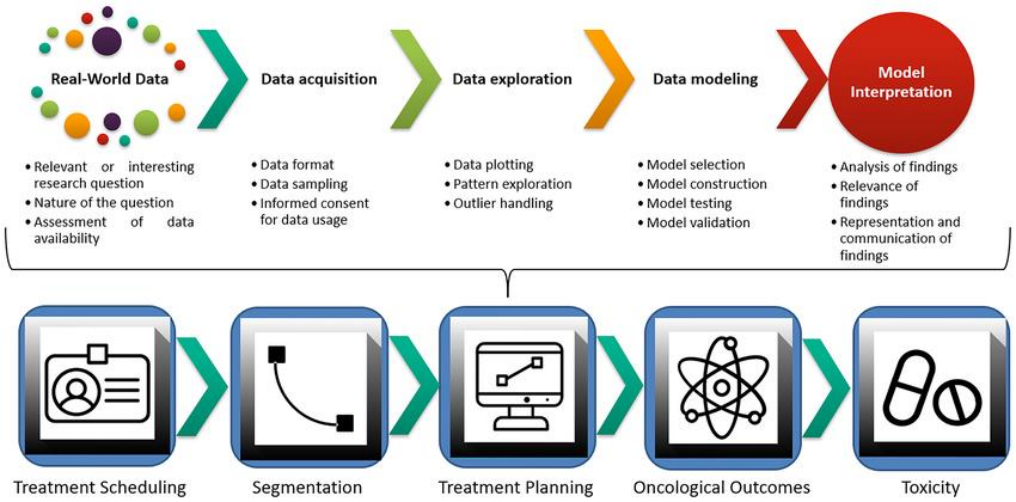
New research lines and developments

AI and Machine Learning in Radiation Oncology

- Treatment planning automation
- Image segmentation (CT, MRI, PET)
- Predictive models for patient outcome and toxicity
- Online adaptive therapy using real-time data streams

Physics challenge: integrating real-time beam monitoring + AI for adaptive control



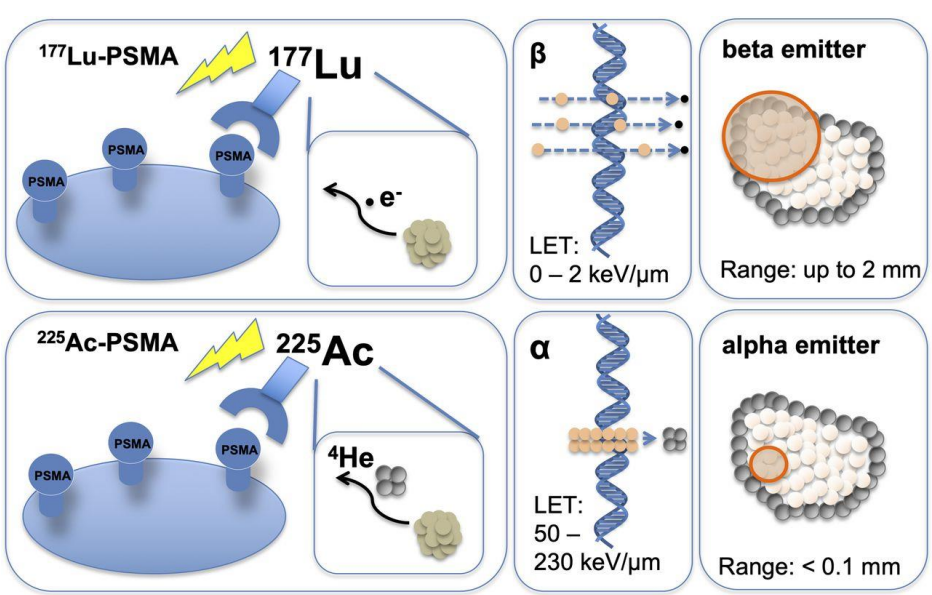


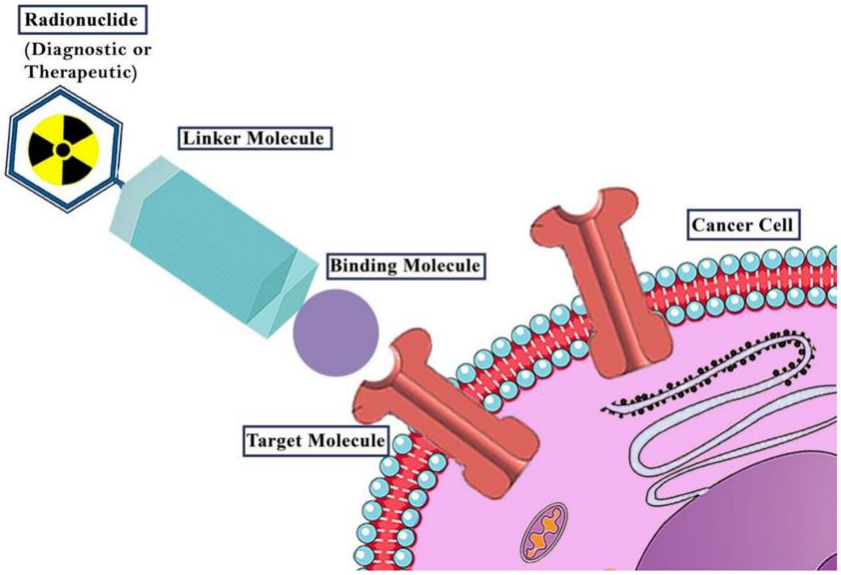
New research lines and developments

🧪 **Theranostics and Targeted Radionuclide Therapy**

- Combining diagnosis and therapy in a single radiopharmaceutical
- Examples: ^{68}Ga/^{177}Lu-labeled peptides, α-emitters (^{213}Bi, ^{225}Ac)
- Growth in α-particle therapies (high-LET, short range)

🚀 *Physics challenge*: isotope production, delivery, dosimetry at micro-scale





Multidisciplinary research and careers

… where physics meets medicine, biology, engineering, and data science

🌍 **A Collaborative Ecosystem.** Medical applications of nuclear physics are built on collaboration between:

- Physicists → Nuclear, particle, medical, accelerator physics
- Engineers → Electronics, biomedical, software, instrumentation
- Medical professionals → Radiation oncologists, radiologists, medical physicists
- Biologists → Radiobiology, pharmacokinetics, DNA damage research
- Computer scientists → AI, machine learning, image processing, big data
- Regulatory experts → Dosimetry, safety, clinical protocols

🎓 **Career Paths for Physicists**

- Academia → Research in nuclear/medical physics, radiobiology, AI in medicine
- Hospitals → Clinical medical physicist (diagnostic or therapeutic)
- Industry → Accelerator companies, imaging technologies, dosimetry systems
- Agencies → IAEA, CERN medical applications, national labs
- Startups & Innovation → AI health tech, theranostics, compact accelerators

"Bridging disciplines means opening doors — the most impactful innovations happen at the intersections."

Thank you! 😀