APPLICATIONS OF RADIATION IN MEDICINE

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CONTENTS

• Principles of Radiation Therapy
• Radiobiology
• Radiotherapy Treatment Modalities
• Special Techniques
• Nuclear Medicine
X-RAYS

• **1895** Professor Wilhelm Conrad Roentgen discovered x-rays by accident

• Experimented with x-rays using vacuum tubes and saw the could pass through wood, paper, skin etc.

• Took 1\textsuperscript{st} x-ray of his wife’s hand using photographic plate

• **1896** Henri Becquerel discovered radioactivity

• **1898** Marie Curie discovered radium

• X-rays widely used as essential diagnostic tool in medicine, but also in cancer treatment
WHAT IS CANCER?

- Cancer describes disease characterised by uncontrolled and unregulated cell division that invades healthy tissues and affects their function.
- Cancer can be malignant or benign (do not spread to distant parts).
- Malignant cells can spread locally or to distant parts of the body via the bloodstream or lymphatic system.
- Treated with surgery, chemotherapy, radiotherapy, hormone treatments (conventional medicine) or in combination e.g., Pre or post surgery.
PRINCIPLES OF RADIOTHERAPY

- Deliver maximum radiation dose to tumour to achieve cell death whilst minimising dose to neighbouring healthy tissues
- Approximately 50% cancer patients treated with radiotherapy
- Royal College of Radiologists estimates that 40% of all long term cancer survivors owe their cure to radiotherapy
- High doses of radiation needed for tumour control
- Sensitivity of tumour vs. sensitivity of normal tissue = Therapeutic Ratio
Oncologist will prescribe a dose to the tumour volume (Gray)

1 Gy = 1J/kg

Named after the British physicist Louis Harold Gray

Treatment is delivered in sessions or fractions

The time over which the dose is delivered is very important

Patients may attend treatment for 1 day to up to 7 weeks, depending on the Intent of the treatment

Radiotherapy given radically (cure) or palliative (symptom relief)
A photon is \( E = hv \)

- \( h \) is Planck’s constant \((6.62 \times 10^{-34} \text{ J-sec})\)
- \( v \) is the frequency of the photon
- Frequency is equivalent to the quotient of the speed of light \((3 \times 10^8 \text{ m/sec})\) divided by the wavelength
- High-energy radiations have a short wavelength and a high frequency
- The interaction of a photon beam with matter results in the attenuation of the beam
- Four major interactions occur:
  - Compton Scattering
  - Thompson Scattering
  - Photoelectric Absorption
  - Pair Production
RADIATION INTERACTIONS

Radiation:Matter Interaction

Photoelectric Effect

Compton Scattering
• High energy particles collide into a living cell with enough energy they knock electrons free from molecules that make up the cell

• Most damage occurs when DNA (deoxyribonucleic acid) is injured. DNA contains all the instructions for producing new cells.

• Ionizing radiation causes damage in two ways: 1. **Indirectly** – H2O in our bodies absorbs radiation, produces free radicals which react with and damage DNA strand 2. **Directly** – radiation collides with DNA molecule, ionizing it and damaging it directly.
• Unless repair occurs, the cumulative breaks in the DNA strand will lead to cell death

• Factors affecting cells response to radiation: (4 R’s)
  – Reoxygenation
  – Repopulation
  – Repair
  – Redistribution
Oxygen stabilizes free radicals

Hypoxic (low O2 content) cells require more radiation to kill

Hypoxic tumor areas
- Temporary vessel constriction from mass
- Outgrow blood supply, capillary collapse

Tumor shrinkage decreases hypoxic areas

Reinforces fractionated dosing
REPOPULATION

• Rapidly proliferating tumors regenerate faster e.g., mucosa cells
• Determines length and timing of therapy course
• Regeneration (tumor) vs. Recuperation (normal)
• Reason for accelerated treatment schedules
REPAIR

• Sub lethal injury – cells exposed to sparse ionization fields, can be repaired

• Cell death requires greater total dose when given in several fractions

• Most tissue repair in 3 hours, up to 24 hours

• Allows repair of injured normal tissue, potential therapeutic advantage over tumor cells
CELL CYCLE

- Cell cycle position sensitive cells
- S phase – radio resistant
- $G_2$ phase delay = increased radio resistance
- Fractionated XRT redistributes cells
- Rapid cycling cells more sensitive (mucosa, skin)
- Slow cyclers (connective tissue, brain) spared
RADIOTHERAPY TREATMENT MODALITIES

- **Teletherapy**: use of sealed radiation sources at an extended distance i.e. x-rays, electrons (ionized particles), beta or gamma radiation

- **Brachytherapy**: use of small sealed radiation sources over a short distance i.e. caesium or iridium

- **Internal Isotope Treatment**: administration of radioactive isotope systemically (around body, via bloodstream)

- **Particle Therapy**: radiation treatment with Neutrons or Protons
TELEThERAPY

• External beam radiotherapy the most common form of treatment in clinical use

• Range of energies available:
  - Superficial Machines (50-150 kV); 1 cm depth
  - Orthovoltage Machines (200-300 kV), 3 cm depth
  - Megavoltage Machines (4-20 MV), deep seated tumours e.g. Linear Accelerator
TELEThERAPY

- Linear Accelerator is large stationary x-ray tube
- Contains microwave technology that accelerates electrons through a wave guide
- When electrons hit a heavy metal target, x-rays are produced
- Various collimator systems in the gantry (head of the machine) shape the beam on its way out
- Change collimator systems to the shape of the tumour volume
TELETherapy

- Patient lies on a moveable couch beneath the machine and lasers in the room used to align the patient into the correct position.
- Gantry is able to move 360 degrees around the patient delivering beams of radiation from different angles.
- Kilovoltage arms (Kv source + Image intensifier) on Varian Linac for Image Guided Radiotherapy: Verification of treatment e.g. IMRT.
MULTI-LEAF COLLIMATORS

- 40 pairs of tungsten leaves mounted external to the treatment head
- Each leaf transmits 1% of the beam
- Additional attenuation achieved with back up collimators
- These together reduces beam transmission of 0.5% of the primary beam
IMRT

• A form on conformal RT where the intensity of the radiation field varies across the treatment field: achieved by varying the position of the leaves during treatment

• Require multiple non uniform beams to achieve desired plan

• 2 Methods: Step and Shoot or Dynamic

• 3D treatment requires online imaging

• Reliable Immobilisation
CONVENTIONAL RT VS. IMRT
BRACHYTHERAPY

• Brachytherapy is the use of sealed radioactive sources placed either on or within a site involved with a tumour.

• 3 Types: Mould Treatment- superficial tumours

• Intracavitary Treatment e.g.. Cervical treatment using Iridium-192/Caesium-137

• Interstitial Treatment e.g. radioactive gold seeds/ grains for prostate cancer
## BRACHYTHERAPY

<table>
<thead>
<tr>
<th>Radio isotope</th>
<th>No. of Isotopes</th>
<th>E of Gamma Rays</th>
<th>Half-life</th>
<th>Other Emissions</th>
<th>Cost</th>
<th>Physical State</th>
<th>Stability of daughter product</th>
<th>Specific Activity</th>
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</thead>
<tbody>
<tr>
<td>Cobalt60</td>
<td>Two Photons</td>
<td>1.17 MeV</td>
<td>5.27 years</td>
<td>Beta Particles</td>
<td>Relatively Cheap</td>
<td>Flaky Solid</td>
<td>Nickel-Stable</td>
<td>High</td>
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<tr>
<td></td>
<td></td>
<td>1.33 MeV</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Iridium-192</td>
<td>Range</td>
<td>0.296 to 0.605 MeV</td>
<td>74 years</td>
<td>Beta Particles</td>
<td>Relatively cheap</td>
<td>Solid</td>
<td>Platinum-Stable</td>
<td>High</td>
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<tr>
<td>Caesium</td>
<td>Single Photon</td>
<td>0.662 MeV</td>
<td>30 years</td>
<td>Beta Particles</td>
<td>Relatively Cheap</td>
<td>Solid</td>
<td>Barium-Stable</td>
<td>Moderate</td>
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<tr>
<td></td>
<td>Range</td>
<td>0.118-2.43 MeV</td>
<td>1620 years</td>
<td>Beta + Alpha particles</td>
<td>High</td>
<td>Putty-like Solid</td>
<td>Long line of radioactive daughter products</td>
<td>High</td>
</tr>
</tbody>
</table>

BRACHYTHERAPY
BRACHYTHERAPY

• Aferloading Machine
• Designed to reduce dose to staff
• Method whereby empty source containers are placed into a body tissue/cavity and the radioactive sources are loaded at a later time
• More time ensuring accurate position
• Radiograph /CT of inert sources
• Sources are delivered remotely with the patient in the theatre room and staff at console area
• Treatment complete, retracted
• Patient does not remain radioactive
• Short hospital visits/ outpatient appointments
BRACHYTHERAPY

- Very steep dose rates around source
- High dose rate to the tumour and adjacent tissue and low dose further out to normal tissue
- Fewer side effects
PARTICLE THERAPY

• High LET i.e. higher biological damage along its track or highly focused deposit of radiation (Bragg Peak)

• **Neutrons**:  
  - Downside: not selective for cancer cells, therefore more damaging to normal tissue  
  - Severe late side effects  
  - EU + USA

• **Protons**: highly localised, high peak in their beam, use of absorbing materials and manipulation of the beam=
  - Similar action to x-rays  
  - Useful for inaccessible tumours i.e. of the eye, pituitary,  
  - Limitation: cost and technology required  
  - Use EU, USA and 1 centre in Clatterbridge in UK
PROTON TREATMENT
PROTON RADIOTHERAPY

Disadvantages
• Set up proton facility
• Cost (1 1/2 times more than LA)
• Training
• Problems with breakdown: 1 accelerating structure
• Demands on immobilisation
SIDE EFFECTS OF RADIOTHERAPY

• Acute Effects: Those which occur early (within the first few weeks to 3 months of treatment)
• Non-permanent/ Reversible
• Long term side effects are those that occur months after completion of a course of treatment
• Permanent/ Irreversible
• Most patients will experience a skin reaction and fatigue
• Side effects depend on the what area is being treated
• Management requires skills of Multi-disciplinary Team
Respiratory Gating

- Lung and Gastrointestinal tumours
- Track breathing and location of tumour
- Used with IMRT
SPECIAL TECHNIQUES

- Gamma Knife Radiosurgery
- Malignant and benign conditions of the brain
- Patient fitted with an aluminium head frame with approximately 200 apertures through which radioactive cobalt-60 sources are focused at the target
- Area to be treated mapped out using MRI, CT, PET and angiography
- High dose can be delivered to the exact shape of the tumour with highly focused radiation beams, accurate to 0.5mm
SPECIAL TECHNIQUES

Total Body Irradiation

- Blood related cancers e.g. Leukaemia
- Part of a preparative regime for bone marrow transplant
- Used in conjunction with chemotherapy to destroy the patient's immune system and prevent rejection by the donor bone marrow cells
- Total body irradiation, shielding of lung to prevent lung damage
- Using a standard Linear Accelerator with extended distance to encompass entire patient in radiation field
Tomotherapy

- Combination of two technology systems: Spiral CT scanner and Intensity Modulated Radiotherapy
- Treatment delivered slice by slice therefore the entire volume can be treated at once (rather than multiple beams)
- Cone beam capacity to take CT image prior to treatment for treatment matching to exact location of tumour
- Typical prostate treatment takes 3-5 minutes vs. 12-15 Linac
- 6 centres in UK
NUCLEAR MEDICINE

• Nuclear Medicine is the clinical application of unsealed radiation source
• Diagnostic, Localisation, Treatment
• Radiopharmaceutical: pharmaceutical is chemical substance that will selectively seek out the tumour cells that you want to locate. A radionuclide is added that will not interfere with the uptake
• Administered in-vitro or in-vivo (ingestion, inhalation, intravenous)
• Diagnostic: a gamma camera will show up hot spots (areas appear dark due to higher uptake of radiopharmaceutical, i.e., With good blood supply or greater metabolic activity or appear as a cold spot=less activity
TECHNETIUM-99MM

- Half life is the time it takes for half the nuclei in an atom to decay
- Effective half life
  - \( \frac{1}{\text{T}_{\text{eff}}} = \frac{1}{\text{T}_{\text{physical}}} + \frac{1}{\text{T}_{\text{biological}}} \)
- \( \text{Tc} \ 99\text{M} = \text{T} \ 1/2 = 6 \text{ hours} \)
- Short half life = scanning procedure data collected quickly low dose to patient
- Extracted by kidneys in Urine
- Unit of measurement in mCi
- 1 mCi = 37 MBq
BONE SCAN TC-99M
NUCLEAR MEDICINE

• **Treatment:**
  - Hyperthyroidism- **Iodine-131**
  - Ablation therapy for carcinoma of the thyroid- **Iodine-131**
  - Bone pain palliation- **Stontium-89**
  - Treatment for Polycythaemia Ruba Vera - **32P Sodium phosphate**
  - Non-Hogkins Lymphoma- **Radioactive Monoclonal Antibodies**-
Disadvantages:

• Radiopharmaceuticals used in treatment have a longer half life
• Longer in-patient stays in isolation
• Radiation exposure to staff
• Minimal family visits
• Expensive
• Long term effects - leukaemia
Physics continues to play a vital role in advancing radiotherapy

Installation and commissioning of new equipment

Maintenance and Quality Assurance checks of equipment – safe and fit for purpose

Dosimetry and planning

Radiation Protection and safety

Work closely with the oncologists and radiation therapists in designing, planning and executing accurate and safe delivery of radiation treatments for our patients