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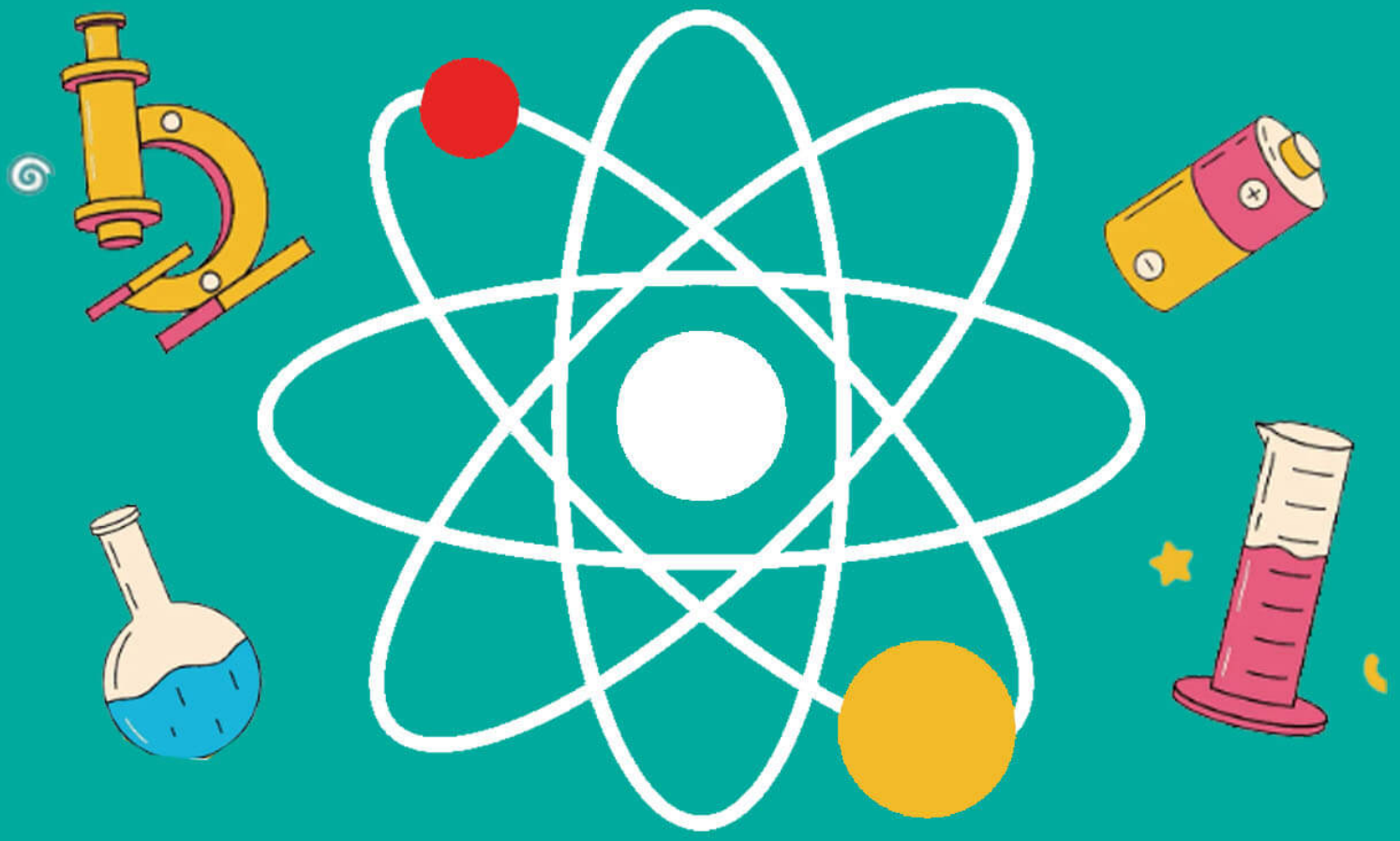
10.6 Radionuclide Imaging & Therapy



AQA A Level Physics Revision Notes

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10.6.1 Radioactive Tracers

Radioactive Tracers

- A **radioactive tracer** is defined as:

  A radioactive substance that can be absorbed by tissue in order to study the structure and function of organs in the body

- Gamma emitters make good radioactive tracers, as the gamma can **leave** the body and doesn't **ionise** tissues as much as alpha or beta radiation
- To be suitable for medicine, the radioactive isotope must be able to be bonded to molecules
  - A molecule labelled with a radioactive isotope is known as a **radiopharmaceutical** product
  - To be a good tracer, this molecule must not affect the body's regular function, but gather in tissues
  - Different molecules can be used to make the tracer accumulate in **specific** organs or tissues
- Three common radioactive tracers which emit **gamma** radiation are:
  - Technetium-99m (the m refers to a **metastable** excited state of the nucleus)
  - Iodine-131
  - Indium-111
- The radioactive tracer is injected or swallowed into the patient and flows around the body
- Once the tissues and organs have absorbed the tracer, then they appear on the screen of a gamma camera as a bright area
  - Using tracer-labelled glucose, for example, highlights areas of higher respiration (e.g. tumours) which use more glucose
  - Labelling white blood cells can show the location of an infection in the body
  - Labelling red blood cells can highlight areas with decreased blood supply (e.g. regions in the brain, for a diagnosis of Alzheimer's disease)

Imaging Respiration using Radioactive Tracers

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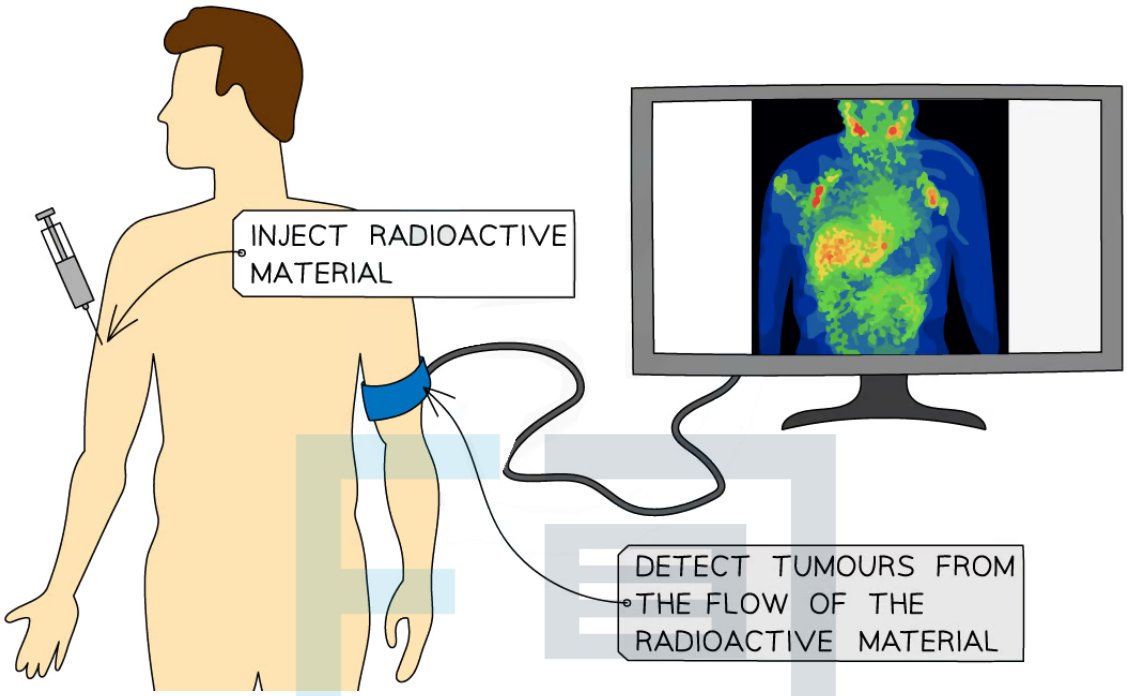

Tracers can show areas of increased respiration, if bonded to glucose.

Worked example

Discuss the advantages of using a gamma-emitting tracer in a patient rather than a beta-emitting tracer.

Answer:

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Step 1: Consider the properties of gamma and beta particles

- Gamma particles are not (very) ionising and have a long range
- Beta particles are very ionising and have a short range

Step 2: Compare the effects of the gamma and beta particles in relation to detection

- Gamma radiation will pass through the patient and hence can be easily detected
- Beta particles will be absorbed by the patient and hence cannot be detected

Step 3: Compare the effects of the gamma and beta particles in relation to patient safety

- Gamma radiation is not very ionising, hence, it does little damage to cells
- Beta particles is highly ionising, hence, it can cause a lot of damage to cells

Properties of Radioactive Tracers

- Each radioactive tracer has a unique set of properties, making them ideal for different medical uses
- The main properties of radioactive tracers are:
  - The **types of radiation** it emits
  - The **half-life** of the isotope
  - The **energy** of the gamma radiation it emits
  - Any **tissues** or **organs** it has a specific affinity for
  - Whether it can be used to **label** specific cells and compounds

Technetium-99m

- This is the most commonly used radioisotope for **diagnosis**
- Tc-99m decays to Tc-99
  - The 'm' indicates the nucleus is in an excited, but somewhat stable, state (**metastable**)
- A gamma photon with 140 keV of energy is emitted in this decay
- The half-life is 6.0 hours
  - This is short enough to avoid prolonged irradiation of the body
- The chemical properties of Tc-99m allow it to be bonded to many molecules which have specific affinities for different organs and tissues
- This means it can be used to study:
  - The skeleton
  - The flow of blood
  - The heart
  - The brain
  - The thyroid
  - Tumours

Iodine-131

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- Unlike Tc-99m, I-131 emits both beta-minus particles and gamma photons when decaying
  - The gamma photons have energies of 360 keV, whereas the beta minus particles have energies of keV
- The half-life of this decay is 8.0 days
- Iodine can bond to thyroid hormones, so it is the most commonly used tracer for **thyroid activity**
  - I-131's beta emission can be used to destroy parts of an overactive thyroid or kill remaining thyroid cells after a thyroid gland is removed (usually because it contains cancerous cells)
- In recent years, I-131 as a thyroid tracer has been replaced with I-132, as it doesn't emit beta and has a shorter half-life

Indium-111

- In-111 emits gamma photons at energies of 170 keV and 250 keV
- The half-life of this decay is 68 hours (2.8 days)

- In-111 is particularly useful for '**labelling**' certain cells, such as:
  - Red blood cells and platelets (to identify issues in the blood)
  - White blood cells, bone marrow and spinal fluid (to locate inflammation or infection)
  - Tumours (to allow precise cancer detection)
- This makes it useful for diagnosing blood diseases or rare cancers

Comparing Radioactive Tracers

- Different tracers are used for different purposes, but the essential properties of a tracer are:
  - It must be a **gamma emitter** so that the radiation can be detected outside the body
  - The gamma rays must be as **low-energy** as possible to reduce the risks of ionisation damage
  - It must have a **half-life** which is **short** enough to reduce the total dose given to the patient but produces a high enough gamma intensity to be detected

	Technetium-99m	Iodine-131	Indium-111
types of radiation emitted	γ only	β^-, γ	γ only
half-life	6 hours	8 days	68 hours
energy of gamma photons	140 keV	360 keV	170 keV & 250 keV
common uses	to investigate most organs, blood and tumours	to treat overactive thyroids or thyroid cancer	to label cells and diagnose blood disorders and rare cancers

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Exam Tip

While all these tracers emit gamma radiation, it is their **chemical** properties that make them appropriate for different scenarios. Different tracers label different radiopharmaceuticals which have an affinity for different organs.

10.6.2 The Molybdenum-Technetium Generator

The Molybdenum-Technetium Generator

- A molybdenum-technetium generator is a device that produces technetium from molybdenum
- Technetium-99m (Tc-99) has a half-life of 6.0 hours
  - This allows it to be used as a tracer with low irradiation of the patient, thanks to the short half-life
  - The short half-life, however, means it must be **produced** in the hospital when needed, as it cannot maintain the required levels of radioactivity for long periods of time
- Molybdenum-99 (Mo-99) has a half-life of **66 hours** (2.8 days)
  - It is produced in nuclear reactors, and due to its slightly longer half-life, it can be transported to hospitals every week
- Once Mo-99 arrives at a hospital, it can be placed in a molybdenum-technetium generator to produce Tc-99m
- In the generator, Mo-99 decays over the course of a few days, producing Tc-99m for up to a week
  - Tc-99m is extracted from the generator every few days by passing a saline solution over the radioactive materials
  - Tc-99m enters the solution, which can then be extracted and injected into patients ready for scanning

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Worked example

A medic suggests that the molybdenum-technetium generator should be kept at the nuclear power station and Tc-99m should just be shipped into the hospital.

It is a 12 hour journey for a truck from the nearest nuclear power station.

Calculate the percentage of Tc-99m lost in the process of supplying the hospital with 1 kg of Tc-99m.

The half-life of Tc-99m is 6.0 hours.

Answer:

Step 1: Determine the number of half-lives that pass during the journey

- The journey is 12 hours long
- Two half-lives pass over the course of the journey

Step 2: Determine the initial mass of Tc-99m

- Mass has halved twice to reach 1 kg
- Initial mass was 4 kg

Step 3: Determine the percentage of Tc-99m lost

- 3 kg of Tc-99m was lost
- This is 75% of the initial mass

Exam Tip

You don't need to know the ins-and-outs of the molybdenum-technetium generator, but expect to come across questions regarding the half-lives of each radioisotope and why the generator is required.

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10.6.3 The PET Scanner

Positron Emission Tomography

- Positron Emission Tomography (PET) is defined as:

  A type of nuclear medical procedure that images tissues and organs by measuring the metabolic activity **of the cells of body tissues**

- In PET scanning, a beta-plus emitting radioactive tracer is used in order to stimulate positron-electron annihilation to produce gamma photons
  - These are then detected using a ring of gamma cameras

Principles of PET Scanning

Before the scan

- The patient is injected with a beta-plus emitting isotope, usually fluorine-18 (F-18)

During the scan

- The part of the body being studied is surrounded by a ring of gamma cameras
- The positrons from the F-18 nuclei **annihilate** with electrons in the patient
- The annihilation of a positron and an electron produces two identical gamma photons travelling in opposite directions
- The **delay time** between these two gamma-ray photons is used to determine the location of the annihilation due to the F-18 tracer
- Photons that do not arrive within a nanosecond of each other are ignored since they cannot have come from the same point

After the scan

- The signals from the gamma camera detectors are sent to a computer which builds up an image

A PET Scanner

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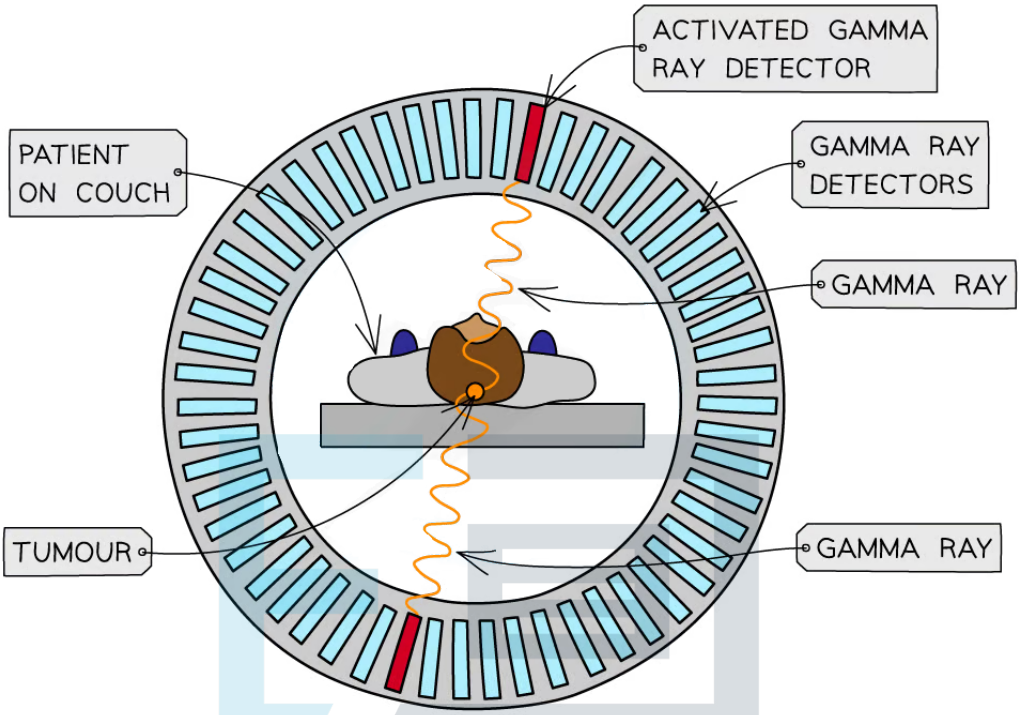

Detecting gamma rays with a PET scanner

Annihilation

- Annihilation can happen between any particle and antimatter counterpart, but in PET scanning, only the electron and positron interaction is considered
- When a positron is emitted from a tracer in the body, it travels less than a millimetre before annihilating with an atomic electron
- As with all collisions, mass, energy and momentum are always **conserved**

An Electron-Positron Annihilation

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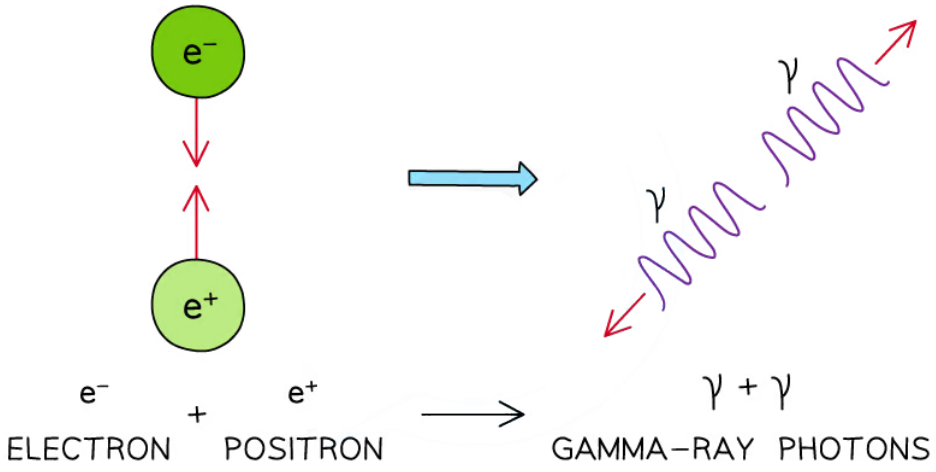

Annihilation of a positron and electron to form two gamma-ray photons

- The gamma-ray photons produced each have an energy of 512 keV
  - This is the same each time as determined by the mass-energy equivalence of the positron-electron pair
- The energy of each photon is given by

$$E = hf = m_e c^2$$

- Where:
  - m_e = mass of the electron or positron (kg)
  - h = Planck's constant (J s)
  - f = frequency of the photon (Hz)
  - c = the speed of light in a vacuum (m s^{-1})

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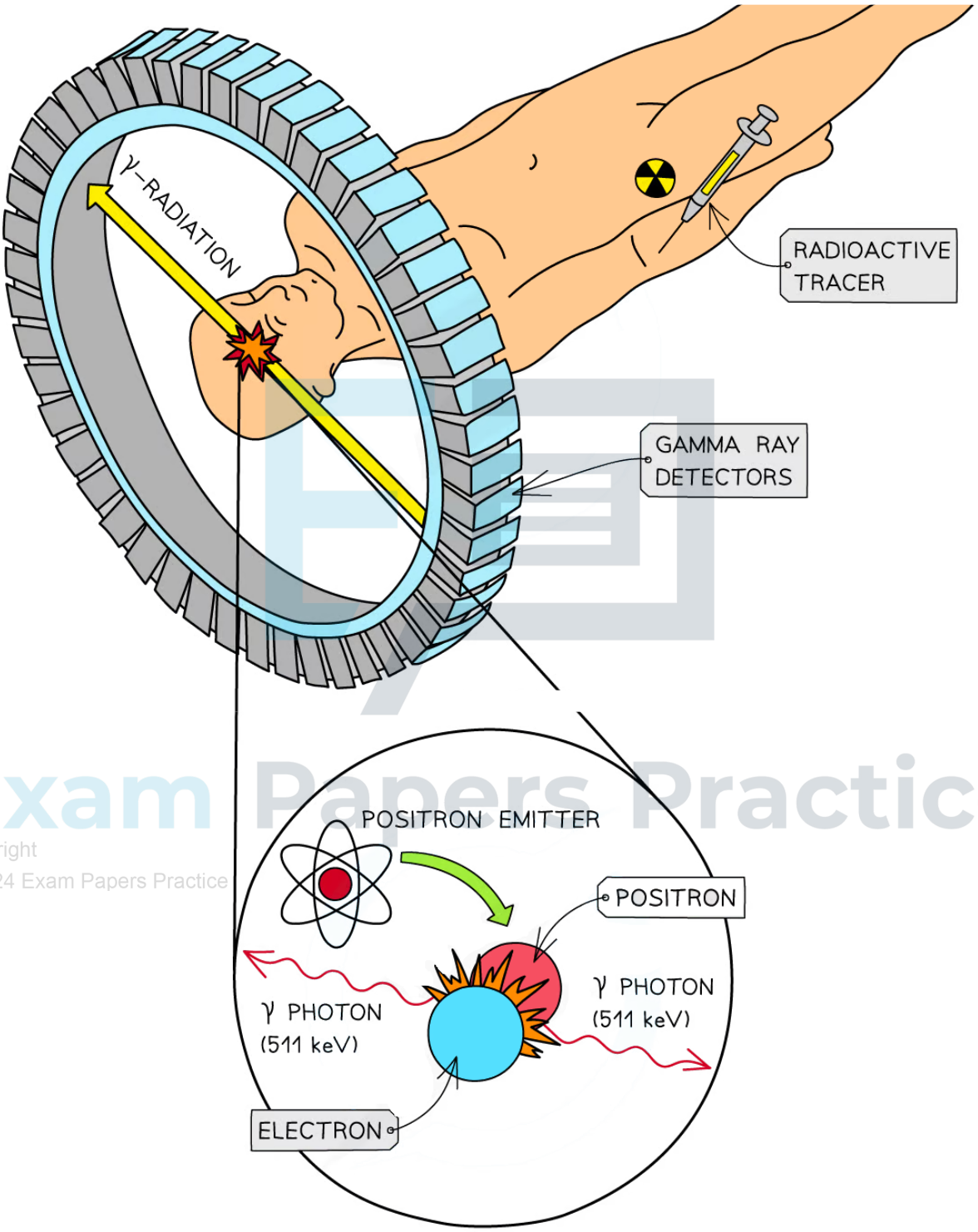
Diagnosis Using PET Scanning

- The signals produced by the photomultiplier tubes are used to produce an **image**
- The *y* rays travel in straight lines in opposite directions when formed from the annihilation of the positron and electron
  - This happens in order to **conserve momentum**
- They hit the detectors in a line – known as the **line of response**
- The tracers will emit lots of *y* rays simultaneously, and the computers will use this information to create an image
- The more photons from a particular point, the more tracer that is present in the tissue being studied, and this will appear as a bright point on the image
- An image of the **tracer concentration** in the tissue can be created by **processing the arrival times** of the gamma-ray photons

Annihilation in the PET Scanner



Annihilation of a positron and an electron is the basis of PET Scanning

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- Once the tracer is introduced to the body it has a **short** half-life, so, it begins emitting positrons (β^+) immediately
  - This allows for a short exposure time to the radiation
  - A short half-life does mean the patient needs to be scanned quickly and not all hospitals have access to expensive PET scanners

Worked example

Fluorine-18 decays by β+ emission. The positron emitted collides with an electron and annihilates producing two γ-rays.

(a) Calculate the total energy released when a positron and an electron annihilate.
(b) Show that each gamma ray has an energy of 512 keV.
(c) Calculate the frequency of the gamma rays.

Answer:

Part (a)

Step 1: Write down the known quantities

- Mass of an electron = mass of a positron, $m_e = 9.11 \times 10^{-31}$ kg
- Total mass = mass of the electron and positron = $2m_e$
- Speed of light, $c = 3.00 \times 10^8$ m s^{-1}

Step 2: Write out the equation for mass-energy equivalence

$$E = m_e c^2$$

Step 3: Substitute in values and calculate energy *E*

$$E = 2 \times (9.11 \times 10^{-31}) \times (3.00 \times 10^8)^2 = 1.64 \times 10^{-13} \text{ J}$$

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Part (b)

Step 1: Determine the energy of one photon

- Planck's constant, $h = 6.63 \times 10^{-34}$ J s
- Two photons are produced, so, the energy of one photon is equal to half of the total energy from part (a):

$$E = \frac{1.64 \times 10^{-13}}{2} = 8.2 \times 10^{-14} \text{ J}$$

- **Note:** if you keep the exact value for energy in your calculator, you would have E = 8.199 × 10^{-14} J

Step 2: Convert the energy in J into eV:

- 1 eV = 1.6 × 10^{-19} J

$$E = \frac{8.199 \times 10^{-14}}{1.6 \times 10^{-19}} = 512\,438 \text{ eV} = 512 \text{ keV}$$

Part (c)

Step 1: Write out the equation for the energy of a photon

$$E = hf$$

Step 2: Rearrange for frequency *f* and calculate

$$f = \frac{E}{h} = \frac{8.2 \times 10^{-14}}{6.63 \times 10^{-34}} = 1.2 \times 10^{20} \text{ Hz}$$

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10.6.4 Physical, Biological & Effective Half Life

Physical, Biological & Effective Half Life

- In a medical context, multiple half-life definitions must be considered
  - The radionuclides introduced have a half-life, but the radiopharmaceuticals (molecules with radionuclides attached) are also removed from the body by natural processes over time
- The physical half-life T_P of a radioisotope is defined as

  The time taken for the number of radioactive nuclei to halve

- This is the same as the half-life of a radioactive nuclide, which is a constant quantity for a given nuclide
- The biological half-life T_B of a substance is defined as:

  The time taken for the concentration of a substance in the body to decrease by half

- This accounts for the processes of removing drugs from the system through excretion and respiration
  - This depends on many factors, such as the health and metabolism of the patient
- Effective half-life T_E is the **combined** half-life of physical and biological half-life
  - This accounts for radioactive processes and biological excretion
- Effective half-life is given by the equation:

$$\frac{1}{T_E} = \frac{1}{T_P} + \frac{1}{T_B}$$

- Effective half-life T_E is **always shorter** than the shortest half-life out of T_P and T_B
- If the physical half-life is short, the effective half-life is even shorter
  - This is because the body is also **excreting** the chemical to which the radionuclide is attached
- If the biological half-life is short, the effective half-life is even shorter
  - This is because the radionuclide is also **decaying** while the body is excreting the radiopharmaceutical at this fast rate

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Worked example

A medical physicist is reading up on her health and safety documentation for iodine-131 before administering it for thyroid treatment.

According to the document, I-131 has a biological half-life of 138 days and a physical half-life of 8.05 days.

Calculate the effective half-life.

Answer:

Step 1: Find the equation for effective half-life on the data sheet

$$\frac{1}{T_E} = \frac{1}{T_P} + \frac{1}{T_B}$$

Step 2: Substitute the known half-lives into this equation

$$\frac{1}{T_E} = \frac{1}{8.05} + \frac{1}{138} = 0.1315$$

Step 3: Rearrange for the effective half-life

$$T_E = \frac{1}{0.1315} = 7.60 \text{ days}$$

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Exam Tip

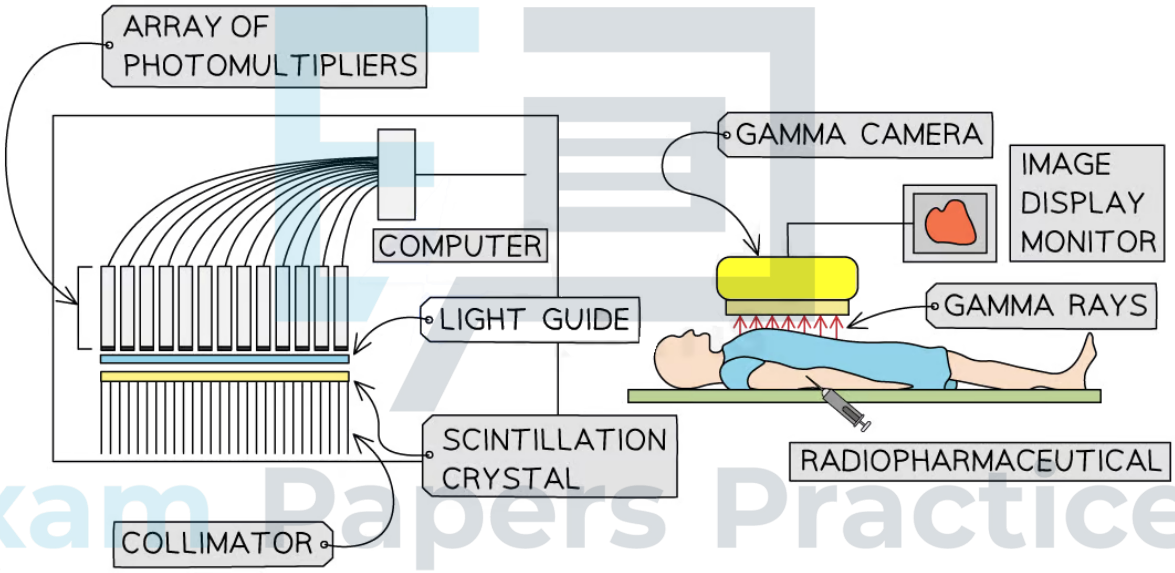
Remember when checking your answer: the effective half-life should always be the **shortest** of the three half-lives. If it isn't then you need to repeat the calculation.

10.6.5 Gamma Camera

Gamma Camera

- The progress of a medical tracer around the body can be detected using a **gamma camera**
- Images obtained by a gamma camera can be used for diagnosing issues in specific organs
- A gamma camera is comprised of **four** major components:
  - Collimator
  - Scintillator
  - Photomultiplier tubes
  - Computer and display

Structure of the Gamma Camera



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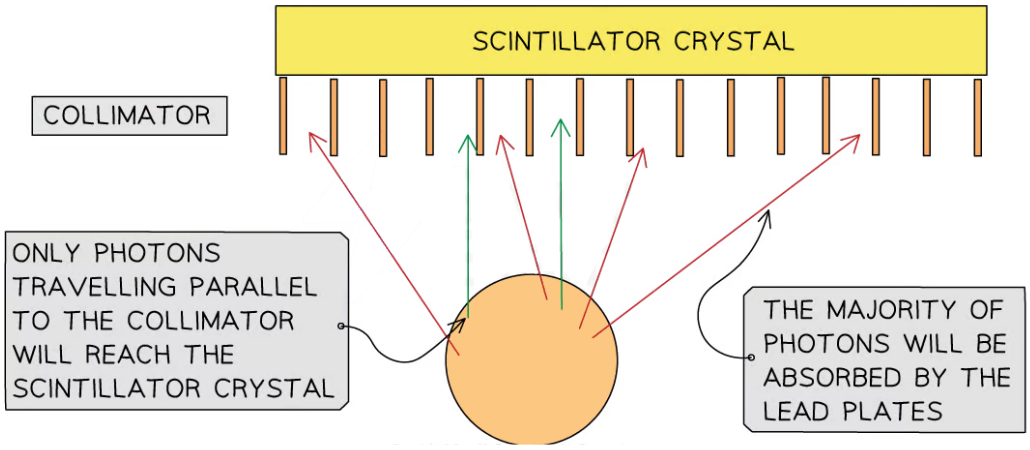
A gamma camera detects the gamma rays emitted by a radioactive tracer in the body using a large scintillator crystal connected to an array of photomultipliers

Collimator

- Images of slices of the body can be taken to show the position of the gamma-emitting **radioactive tracers**
- Once injected with a tracer, the patient lays stationary in a tube surrounded by a ring of detectors
- When gamma rays are emitted, they are absorbed by thin lead tubes known as **collimators**
- Collimators are the key to producing the **sharpest** and **highest resolution** images
  - Only photons moving **parallel** to the collimator will be absorbed, this improves the sharpness of the image as scattered photons are excluded
  - The **narrower** and **longer** the collimators, the more gamma rays that are absorbed and hence, the more electrons that will be produced
  - This improves the image quality as more electrons contributing to the electrical pulse output will increase the **resolution** of the image

The Collimator

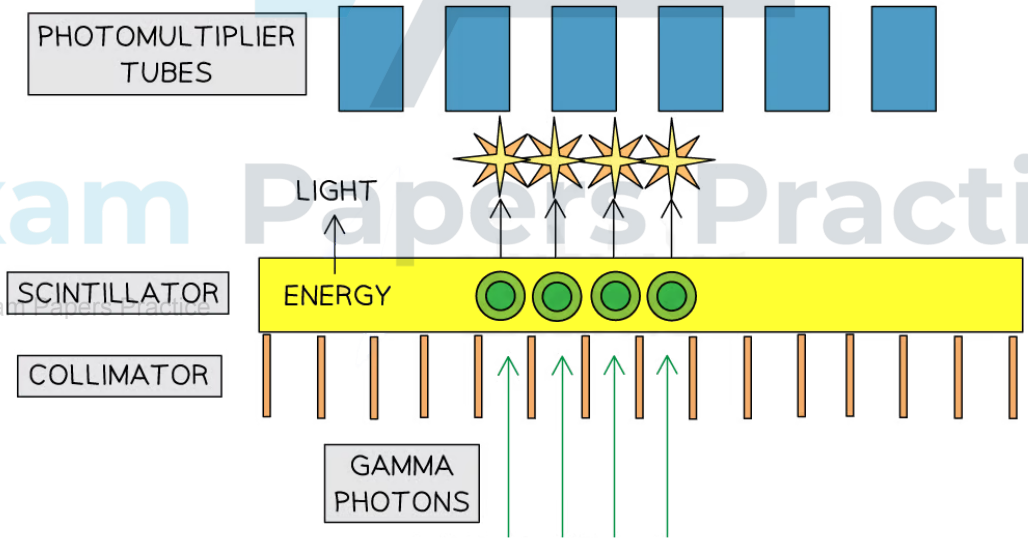


The collimator ensures high resolution images are produced by only allowing photons travelling parallel to the lead plates to pass through

Scintillator

- When the gamma-ray (γ-ray) photon is incident on a crystal scintillator, an electron in the crystal is excited to a higher energy state
  - As the excited electron travels through the crystal, it excites more electrons
  - When the excited electrons move back down to their original state, the lost energy is transmitted as visible light photons

The Scintillator



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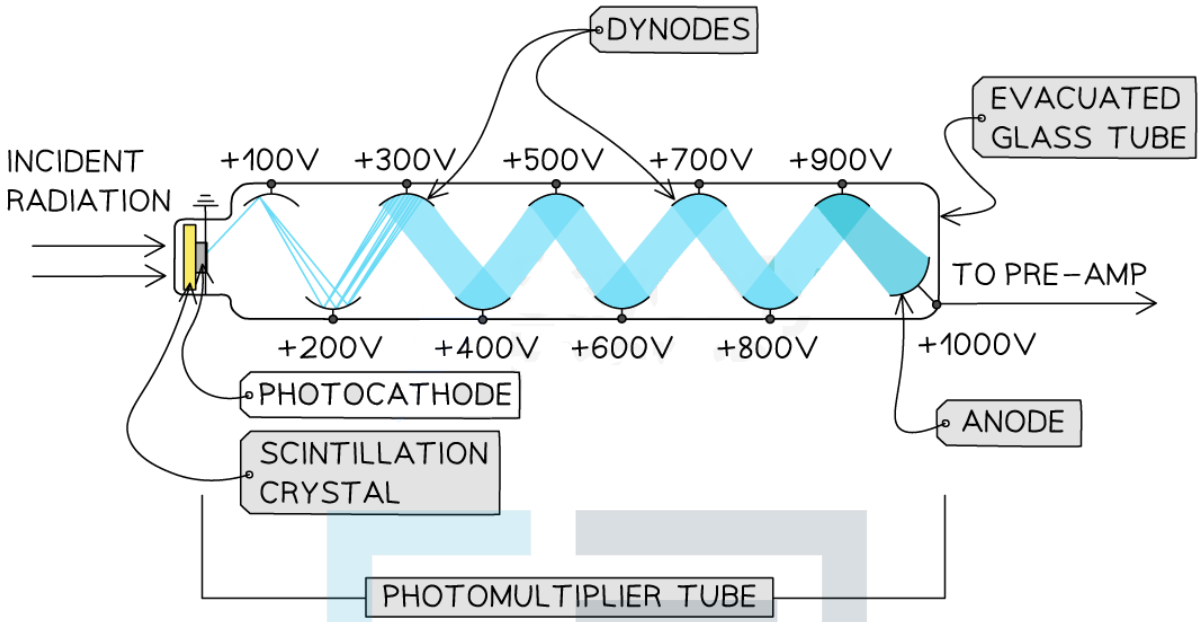
The scintillator crystal converts the energy from gamma photons into visible light photons

Photomultiplier Tubes

- The photons produced by the scintillator are very faint
- Hence, they need to be converted to an electrical signal and **amplified** by a photomultiplier tube
- When photons from the scintillator reach the photomultiplier, electrons are released from a **photocathode**
- The liberated electrons **accelerate** through a series of dynodes, each at a progressively higher potential difference, before reaching an **anode** at the end of the tube
- Energy gained by the acceleration of the electrons triggers the release of **more electrons** at each dynode, resulting in a stronger electrical signal

A photomultiplier tube



A photomultiplier detects the faint flashes of light from the scintillator, converts them into voltage pulses and amplifies the signals

Image Formation on a Computer

- The signals produced by the photomultiplier tubes are used to produce an **image** using the electrical signals from the detectors
- The tracers will emit lots of *γ* rays simultaneously, and the computers will use this information to create an image
- The more photons from a particular point, the more tracer that is present in the tissue being studied, and this will appear as a bright point on the image
- An image of the **tracer concentration** in the tissue can be created by **processing the arrival times** of the gamma-ray photons

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10.6.6 Radiotherapy

Use of High Energy X-rays

- Cancerous cells divide more frequently than healthy cells
  - As a result of this, X-rays destroy cancer cells at a **greater rate** than they destroy healthy cells
- Different energies of X-rays are used for treating cancer in different areas of the body
  - Lower-energy X-rays are used for treating skin cancer
  - Higher energy X-rays are used for targeting tumours deeper in the body

External treatment using low-energy X-rays

- Low-energy X-rays can be used to treat skin cancer
- These X-rays can be directed at surface tumours, but they do not penetrate deep into the body
  - Therefore, the risk of damage to deeper tissues is reduced

External treatment using high-energy X-rays

- To treat a tumour deep inside the body, high-energy X-rays can be directed at the tumour from an external source
  - This is known as **external beam radiotherapy** (EBRT)
- When cells divide, they are sensitive to X-ray radiation
  - In EBRT, X-rays from an **external** source destroy cancer cells during division

Limiting Exposure to Healthy Cells

- During high-energy X-ray radiotherapy, the risk to healthy tissue is reduced by:
  - Using **metal filters** to remove low-energy X-rays
  - Directing the X-rays from **different directions**

Using metal filters limits exposure because...

- During the EBRT process, which lasts a few minutes, the patient is held in a made-to-fit mould made from aluminium to ensure they do not move
  - This ensures that only the target tissue receives the radiation dose
- When X-rays are produced, they are emitted with a wide range of energies
- Filtering the beam through an aluminium sheet ensures that the low-energy X-rays are removed
  - The **less energetic** X-rays are likely to damage tissues close to the surface
  - This means that only the **more energetic** X-rays reach the tumour deep inside the body

Using X-rays from different directions limits exposure because...

- The beam of X-rays can be precisely controlled to minimise damage to healthy tissue
  - The beam of X-rays is shaped to match the exact dimensions of the tumour (called **conformal** radiotherapy)
- X-rays are produced in a linear accelerator (LINAC) by accelerating electrons towards a heavy metal target

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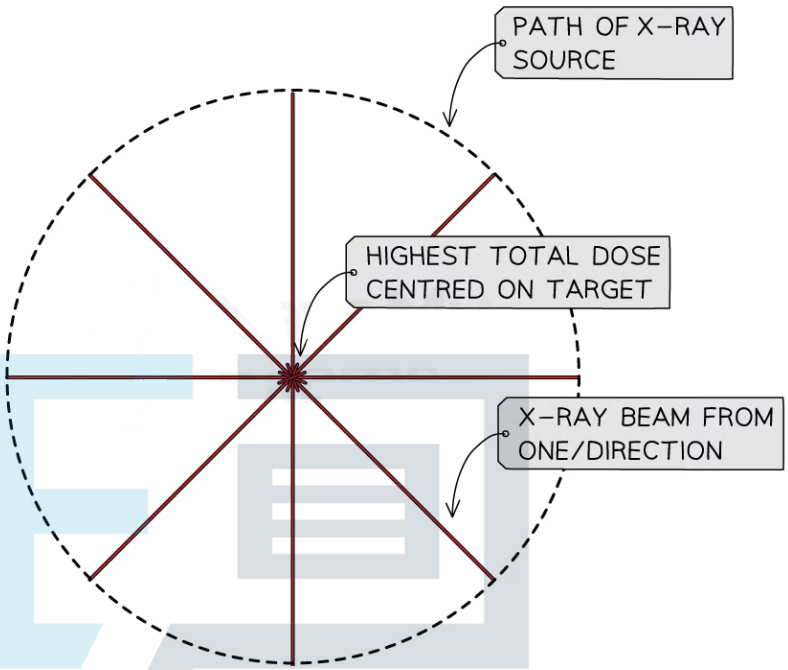
- This LINAC source can be rotated around the patient
- The target tissue is placed at the centre of rotation and therefore receives a much greater dose of radiation than the surrounding healthy tissue

Rotating X-Ray Source



The source of high energy X-rays rotates around the target, ensuring the targeted area receives a much larger dose of radiation than the surrounding healthy tissues

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Use of Radioactive Implants

- Internal radiotherapy is when a **radioactive implant** is placed next to, or into the tumour itself
  - This implant consists of metal 'seeds' containing radioisotopes which irradiate the tumour and a small radius of tissue around it
- The main **advantage** of internal radiotherapy is that the source of radiation can be placed as close to the cancer as possible
- However, the main **disadvantage** is that a small amount of healthy tissue is likely to be exposed to ionising radiation

What type of radioisotope should be used in an implant?

- The radioisotope used in an implant should:
  - Have a short half-life (as long as the activity is also high)
  - Have a short range (as long as it can pass through the implant casing)
  - Be highly ionising
- The radiation must not penetrate far from the implant site to avoid irradiating healthy tissue further from the tumour
  - This is why **beta radiation** is the most common choice, as it can penetrate the seed's metal casing, but does not penetrate further than a few mm beyond the implant site
  - Alternatively, **low-energy gamma** rays can be used, as they are less penetrating than high-energy gamma
- Alpha radiation is **not appropriate** for this form of radiotherapy
  - The alpha particles would be unable to penetrate the metal casing of the seeds
  - Even if they were able to, they would only heavily ionise the tissue near the seed
  - As a result, the seeds would be harming healthy tissue rather than irradiating cancerous tissue
  - Additionally, the alpha particles could not penetrate the whole way through the tumour

Worked example

Suggest why EBRT is more appropriate for treating a tumour in the brain than using a radioactive implant.

Answer:

Step 1: Consider the downsides of the implant

- Radioactive implants must be mechanically placed inside the body
- The skull and fragile structure of the brain would make this highly challenging
- Any radiation affecting healthy tissue could impair brain function

Step 2: Consider the benefits of EBRT

- The largest dose of radiation is localised to the tumour
- No surgery is required to irradiate the tumour
- The beam can be shaped to fit the exact dimensions of the tumour

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Exam Tip

The reason there are so many methods for removing cancerous tissue is that it can appear in almost any part of the body, and different methods work better for different situations.

It's your job to know each method well enough to be able to suggest an appropriate one, if presented with a new situation in your exam.

10.6.7 Comparing Imaging Techniques

Comparing Imaging Techniques

- All imaging techniques are beneficial in their own context, but often the positive outcomes of the scan must be balanced against the potential risks
- The scan must have a level of resolution high enough to image the target clearly, while minimising risk
  - Performing an X-ray scan on a foetus is too risky, when other types of scans provide a good enough resolution
  - However, when identifying a potential tumour, resolution must be high and the risks associated with the scan are much smaller than the risks associated with not catching cancer in its early stages

A table of advantage, disadvantage and resolution of each method

Imaging Method	Advantage	Disadvantage	Resolution (mm)
CT Scan	Show different tissue types High resolution	Expensive Large radiation dose	0.5
External X-rays	Cheap, fast and easy operation High resolution	Cannot distinguish different tissues Cannot image some organs	0.5
MRI	Distinguish types of tissue No radiation risk	Expensive and time-consuming Uncomfortable for some patients	1
PET	Shows the function of organs Good for imaging the brain	Expensive and time-consuming Does not work for every organ	1
Ultrasound	No radiation danger Safe for use on a foetus	Cannot show certain organs (e.g. brain) Lower resolution, hard to operate	2
Ingested gamma source	Shows function of organs Relatively simple to use	Lowest resolution Radiation risk associated	6

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Worked example

Three patients visit a hospital. Patient 1 has a lower-body injury, patient 2 has a suspected tumour in their lung and patient 3 is suspected to have a hyperactive thyroid.

The hospital has the following facilities:

- Ultrasound imaging
- Gamma sources for ingestion
- External X-ray imaging
- CT scanner

For each patient, select an appropriate imaging method, explaining why this method is appropriate while the others are not.

Answer:

Patient 1 (lower body injury)

Step 1: Select an appropriate imaging method, explaining your answer

- External X-ray imaging is most appropriate

Step 2: Compare this method to alternative imaging methods

- This is quick and easy and shows potential bone damage in the injury
- Whereas a CT scan has a higher radiation dose and an image that detailed is unnecessary
- Real-time scanning is not needed, so an ultrasound would be inappropriate
- The function of organs is not needed, so gamma imaging would be inappropriate

Patient 2 (lung tumour)

Step 1: Select an appropriate imaging method

- A CT scan is best for this patient

Step 2: Compare this method to alternative imaging methods

- This highlights cancer tissue against healthy tissue
- Cross sections throughout the lungs can show all potential tumour locations
- Ultrasound is absorbed by air in the lungs and the detail is not great enough
- X-ray scanning may not differentiate tissues and the ribcage may obscure the view of a tumour
- An ingested gamma source may not provide a detailed enough image

Patient 3 (hyperactive thyroid)

Step 1: Select an appropriate imaging method

- An ingested gamma source

Step 2: Compare this method to alternative imaging methods

- This shows the function of tissues and therefore if the thyroid is performing at a higher than normal rate
- Ultrasound, X-ray and CT scans show structures and tissues but not the level of their function

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Exam Tip

You will only be asked to compare image resolution, convenience and safety issues. Make sure you use clear comparative language in these answers.