# Accelerators for Medical and Industrial Applications

**JUAS**
**Archamps, March 8th 2016**

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# Organization of the lecture

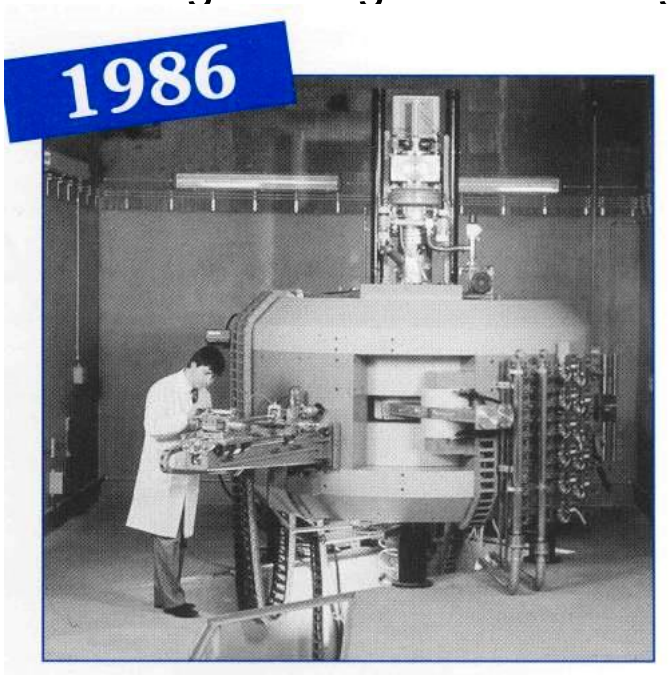
- Intro: A few words about IBA
- Part 1: Radioisotopes for medical applications
  a. Diagnosis and molecular imaging
  b. Radioisotopes for cancer therapy
- Part 2: Cyclotrons magnetic design and beam dynamics
- Part 3: Particle therapy of cancer
- Part 4: The ProteusOne and S2C2 project
- Part 5: Industrial applications of electron beam technology

# Foreword

- In this lecture, I cannot present an exhaustive overview of all accelerators and their possible applications
- I will mainly limit myself to subjects where IBA has first hand experience

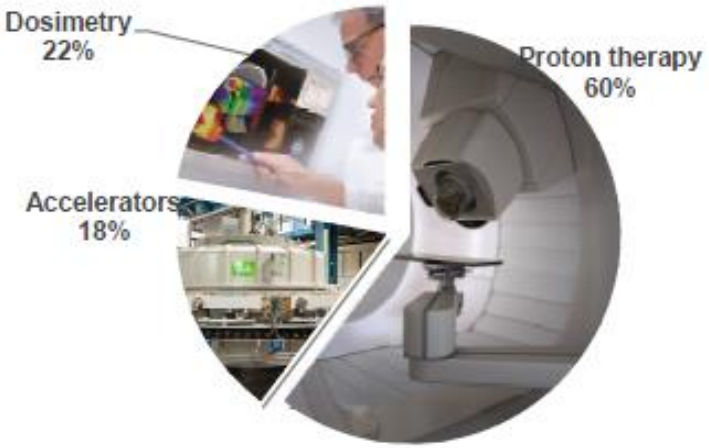
# Foundation of IBA

- 1986 => spinoff from the CRC at UCL (Catholic University of LLN)
- Start of IBA => Cyclone 30: a revolutionary cyclotron for medical isotopes => 5 x more output and 3 x less power consumption
- Founder Yves Jongen currently IBA Chief Research Officer and recognized global leading accelerator expert




# The IBA Group in 2016

- 1200 employees worlwide
- More than 300 systems (200 Cyclotrons) installed
- Not anymore just a cyclotron company, but a company focused on medical technology for the fight against cancer:
  - Cancer diagnostic: molecular imaging
  - Cancer treatment: Particle therapy & dosimetry
- More than 400 patents in use
- Listed on Euronext Brussels
- http://www.iba-worldwide.com



# IBA Today: Centering on the fight against cancer

## Accelerators

**Cyclotrons**
- To produces Radioisotopes

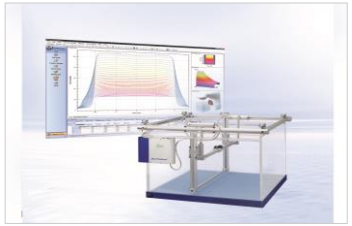
**E-beam / X-rays**
- To irradiate / treat many industrial products

## Particle Therapy

**Proton Therapy** is increasingly considered as the ultimate radiotherapy for cancer due to its superior dose distribution

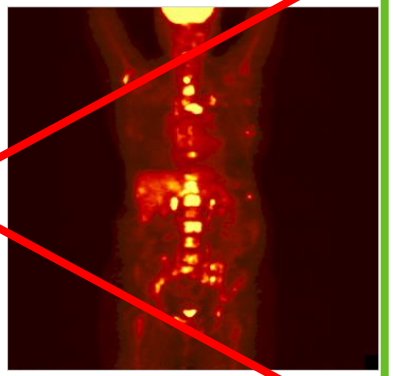
## Dosimetry

**Dosimetry equipment**
to measure and calibrate radiation dose for
- Radiotherapy
- Radiodiagnostics



## Pharmaceuticals

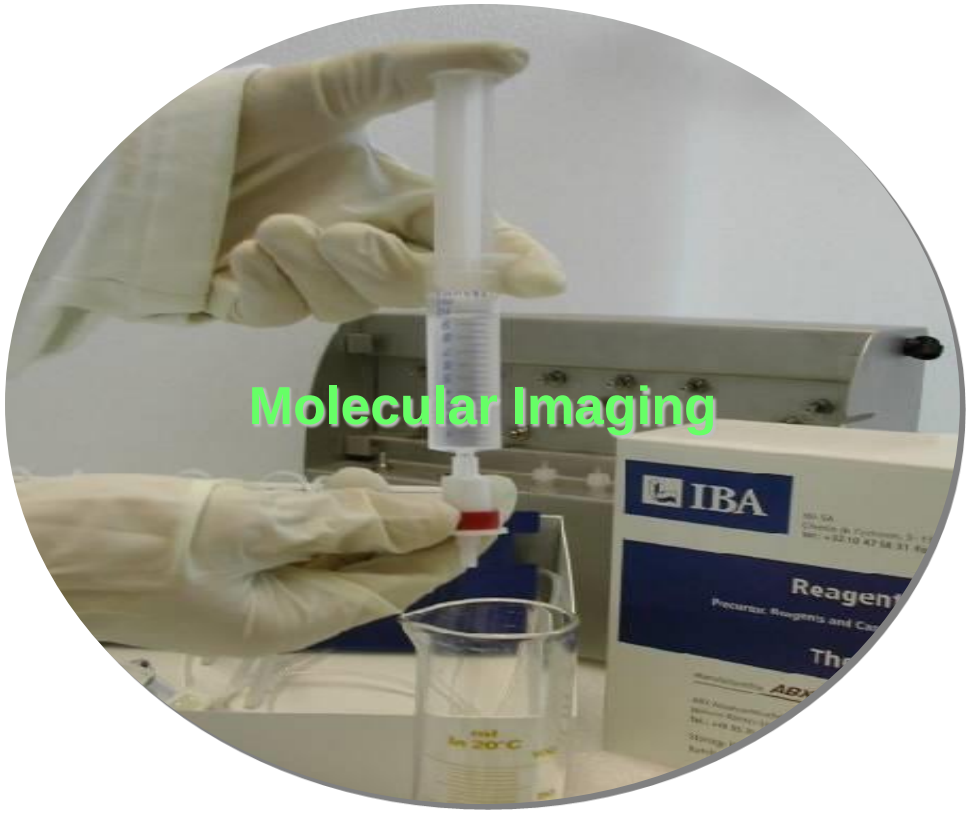
**Radiopharmaceuticals**
- Molecular Imaging
- Nuclear Medicine (diagnostics & therapy )



# Part I-A: radio-isotopes for medical diagnosis

SPECT: Single Photon Emission Computed Tomography

PET: Positron Emission Tomography






Particle Therapy

# How is imaging done with radio-tracers ?

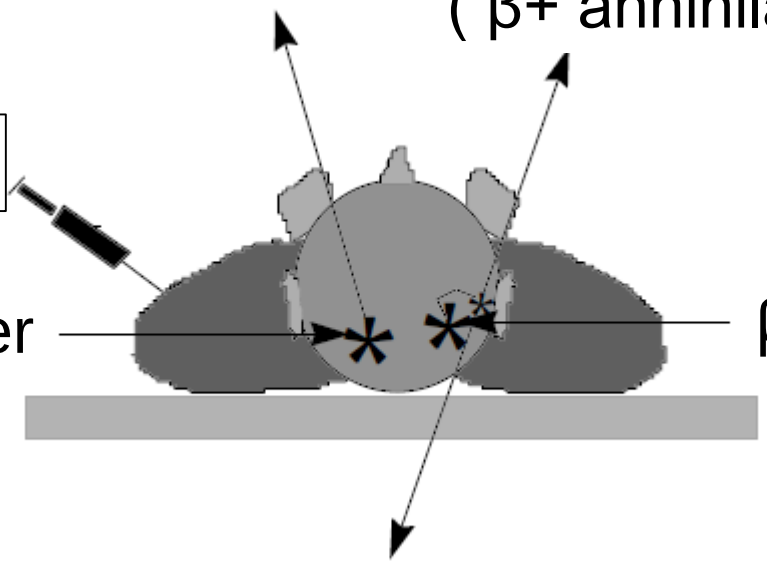
SPECT

PET

Single photon

2 photons of 511keV
( β+ annihilation )

Radio-isotope



γ emitter

β+ emitter

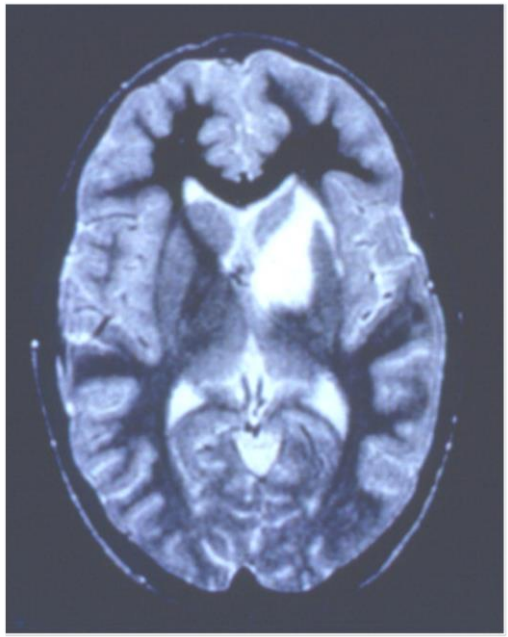
A camera (Gamma or PET) detects the photons emitted from the body and computes 3D distributions of the radio-activity

# The use of Radio Isotopes for medical imaging

- Radio tracers can be used to label a specific bio-chemical molecule.
- They allow to see metabolism
  - X-ray (CT-) scan or MRI are better to see the anatomy (structure)
- Nuclear medicine (imaging of metabolism using molecules labeled with an appropriate radioisotope) is therefore not in competition, but in complement of imaging techniques such as X-ray, X-ray CT-scan or MRI.

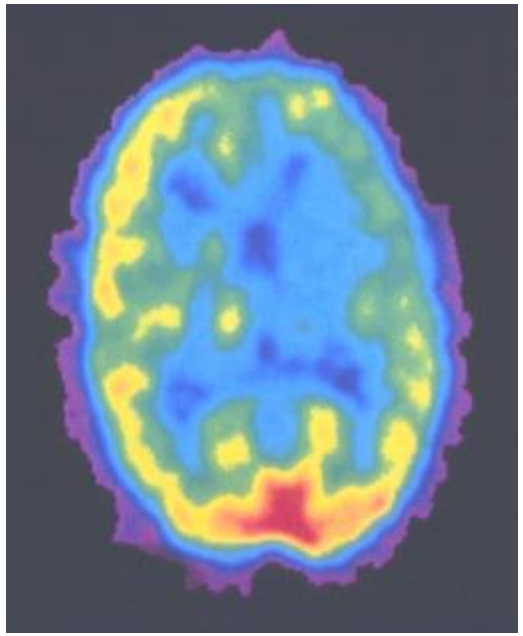
# Metabolic versus anatomic imaging

MRI



Anatomic View
(Tissue-structure)

PET



Metabolic imaging
(Biological-function)

# Combination of two imaging techniques in one




Particle Therapy

# How is imaging done with radio-tracers ?

**Single photon isotopes (SPECT)**

- The imaging of single photons emitters requires:
  - a collimator (causes a loss of efficiency !).
  - a position-sensitive detector (with good detection efficiency): the Gamma (or Anger) camera.

- The image obtained is a projection.
- Multiple (perpendicular) projections can be mathematically correlated to produce a 3D representation.
- SPECT (Single Photon Emission Computed Tomography).

# How is imaging done with radio-tracers ?

## Positron emitting radio-isotopes (PET)

- The emitted positron travels a few millimeters, then meets an electron and annihilates, emitting two anti-parallel photons of 511keV.
- These two photons can be detected in **coincidence** by a ring of detectors surrounding the region of interest.
- One knows then that the origin of the photons is on the line connecting the two detectors => no collimator needed
- Several detections allow to locate the source.
- By mathematical reconstruction, a 3D representation of the activity can be obtained.
- PET (Positron Emission Tomography).

# How to select a good single-photon radio-tracer?

1. The energy of the emitted photon
   - Low enough to keep a good detector efficiency
   - Low enough in order to achieve good collimation
   - High enough to cross the body tissue
   - 100 keV $\leq$ E $\leq$ 300 keV is generally the optimum

# How to select a good single-photon radio-tracer ?

2. The half-life:
   - Short enough to minimize the patient's exposure
   - Long enough to allow industrial production and distribution to the hospitals
   - Practically 10h $\leq T_{1/2} \leq$ 100h is roughly best
   - Generators are great too !

$^{99}Mo$ (66 hours) = $^{99}Tc_m$ (6 hours)

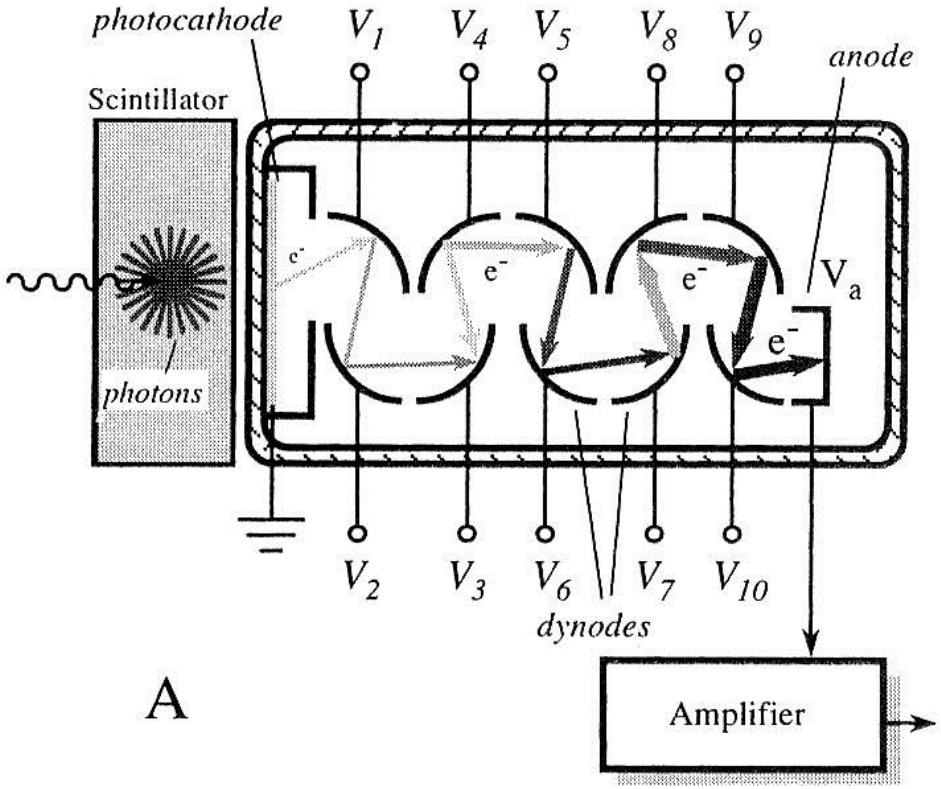
$^{81}Rb$ (4.6 hours) => $^{81}K_r$ (13sec)

# How to select a good single-photon radio-tracer

3. The chemistry
   - The radio-tracer should bind easily to organic bio-molecules of interest
   - Essential bio-chemical behavior of the molecule should remain intact after labeling
     - Halogens (Fluor, Iodine), Technetium ⇒good;
     - Noble metals (Gold) ⇒ difficult

# Detecting the radiation

## Scintillator with photomultiplier tube

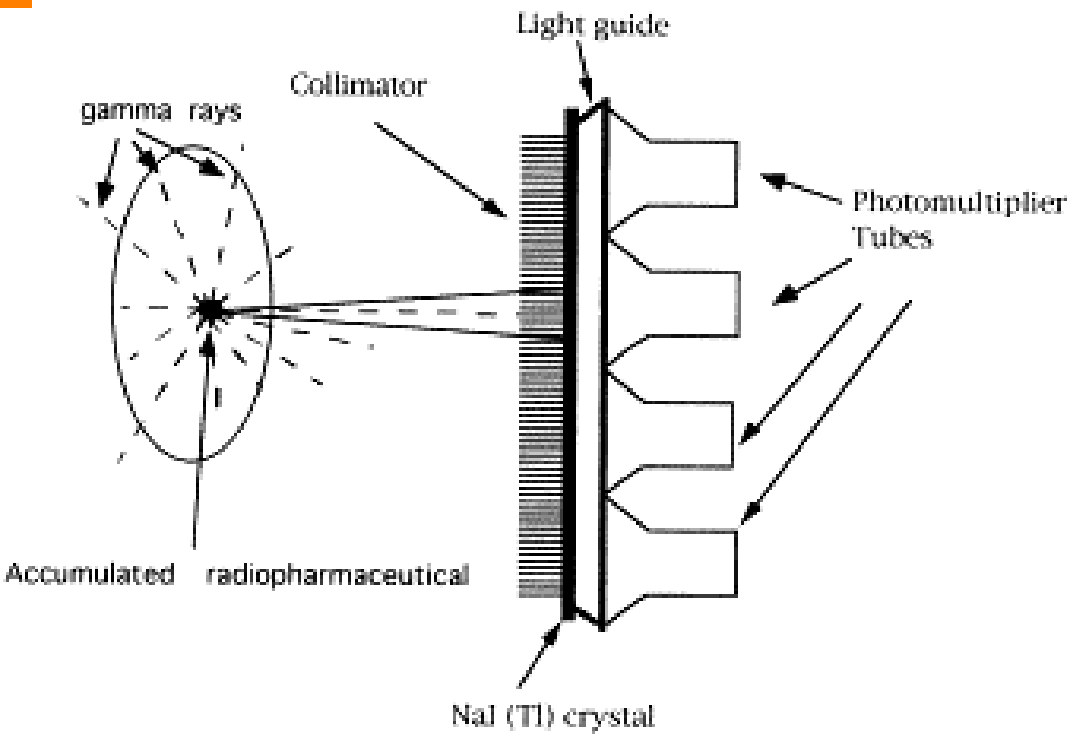



The incoming gamma ray interacts with the scintillator to produce photons. These photons dislodge electrons from the photocathode in the photomultiplier tube. These electrons are accelerated to the first nearest dynode where they dislodge further electrons. This process continues down the tube, resulting in a cascade of electrons. Multiplication factor can be up to $10^8$

# The SPECT gamma camera (Anger camera)

**Anger camera**

The collimator prevents photons that are not approximately perpendicular to the collimator holes from interacting with the detector.

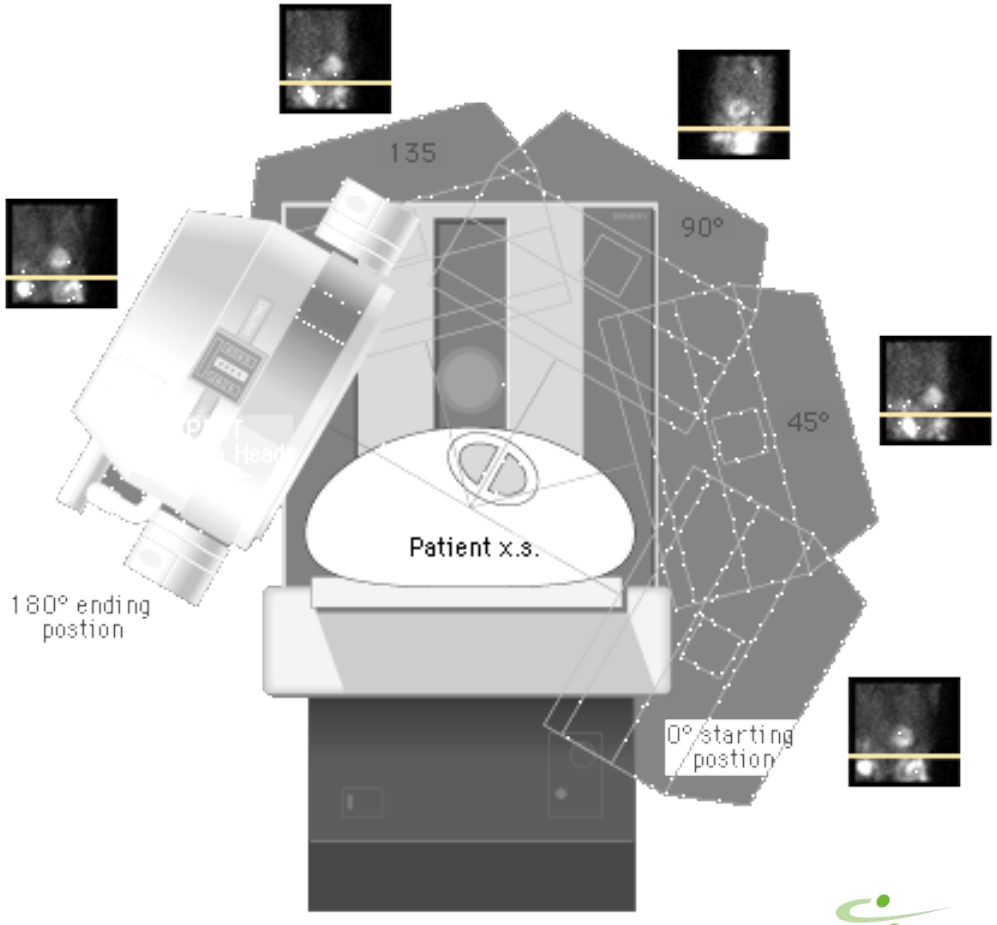



The field of view for the detector element behind each hole of the collimator is divergent, so that in a gamma camera, spatial resolution degrades as the distance to the object is increased. Collimators are usually made of lead.

Typical dimensions: holes 3mm, walls 1mm, depth 40mm.

# The SPECT gamma camera

Projections from different angles are taken by rotating the camera around the patient



# Nuclear reactions used for the production of medical isotopes

1. Nuclear Reactors $\Rightarrow$ neutrons
   - Neutron capture, as well as fission is performed in nuclear reactors (famous example: Mo-Tc generator)
2. Accelerators (often cyclotrons) $\Rightarrow$ charged particles
   - To bring a positive charged particle into a nucleus requires to overcome the Coulomb barrier and requires therefore the use of accelerators
   - The compound nucleus formed is unstable, and immediately cools off by emitting neutrons or alpha particles (more rarely protons)
   - Typical reactions are: (p, xn) , (p, $\alpha$) , (d, xn)….

# Nuclear reactions for Radio-Isotopes production

| Radioisotope | Half-life | Reaction | Energy (MeV) |
|---|---|---|---|
| $^{201}$Tl | 73.1 h | $^{203}$Tl (p,3n) => $^{201}$Pb => $^{201}$Tl | 17~28 |
| $^{67}$Ga | 78.3 h | $^{68}$Zn (p,2n) => $^{67}$Ga | 12~28 |
| $^{111}$In | 67.4 h | $^{112}$Cd (p,2n) => $^{111}$In | 12~28 |
| $^{123}$I | 13.2 h | $^{124}$Te (p,2n) => $^{123}$I | 20~25 |
| | | $^{124}$Xe (p,2n) => $^{123}$Cs => $^{123}$I | 20~30 |
| | | $^{124}$Xe (p,pn) => $^{123}$I | |
| | | $^{127}$I (p,5n) => $^{123}$Xe => $^{123}$I | 45~68 |

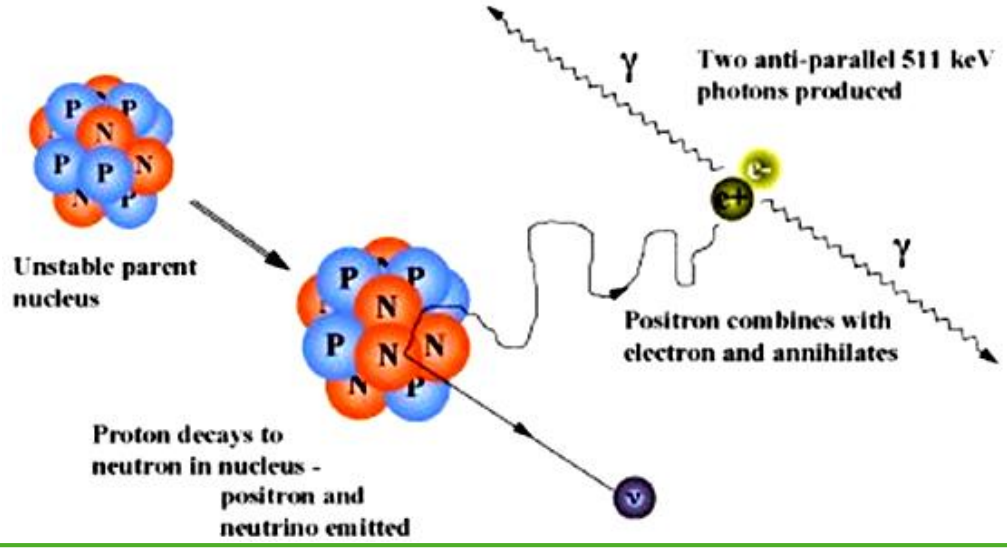
A 30 MeV cyclotron can often do the job

# “Traditional” nuclear medicine

- Technetium 99m, the most commonly used radio-isotopes in nuclear medicine is produced in reactors.
  - 90% of diagnostic studies in hospitals is done with $^{99m}Tc$ !
- But a number of other, very important nuclear medicine radio-isotopes are produced with cyclotrons of higher energy.
  - $^{201}Tl$ (Cardiac studies).
  - $^{123}I$ (Thyroid, Various examinations).
- For these longer life isotopes, international distribution is possible.
- Large, very powerful cyclotrons are owned by radiopharmaceutical companies.

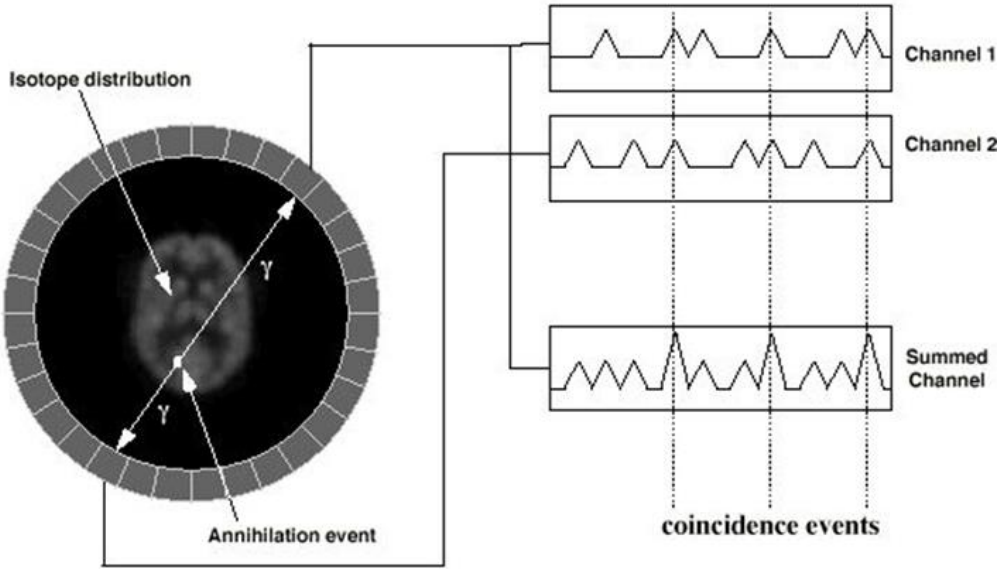
# The positron (anti-electron)

- Proton rich nucleus decays: proton → positron + neutrino.
- Positron cools off by Coulomb interaction with electrons.
- At thermal energy: positron annihilates producing two anti-parallel 511keV photons. (within 4mrad due to momentum conservation)
- The finite positron range and the non-collinearity of the annihilation photons give rise to positional inaccuracy (±5mm).

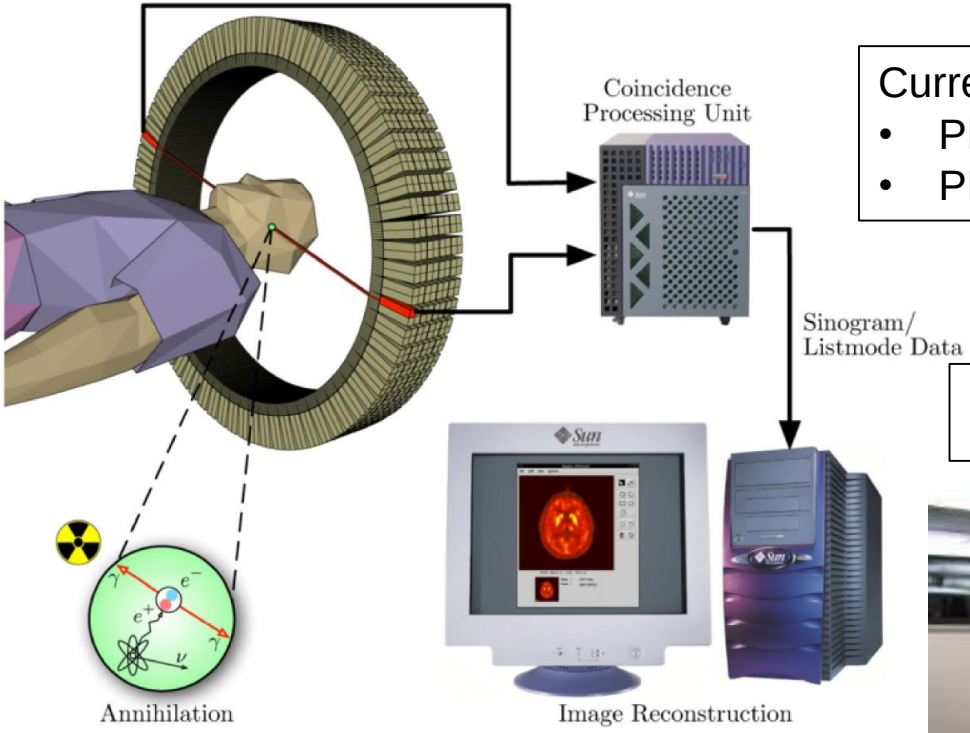


# Coincidence detection in a PET scanner

In a PET camera, each detector generates a timed pulse when it registers an incident photon. These pulses are then combined in coincidence circuitry, and if the pulses fall within a short time-window, they are deemed to be coincident. A coincidence event is assigned to a line of response joining the two relevant detectors. In this way, positional information is gained from the detected radiation without the need for a physical collimator.



# The PET scanner




Currently available are
- PET scanners integrated with CT: PET-CT
- PET scanners integrated with MRI: PET-MRI

PET scanner in a hospital

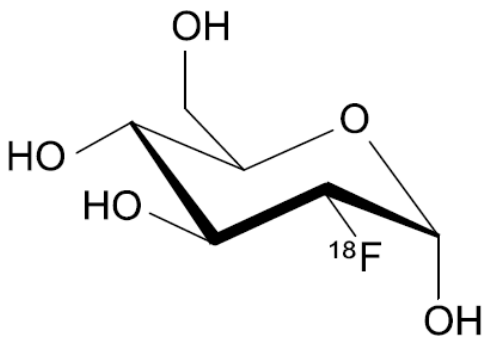
- Coincidents events are grouped into projected images (sinograms) and sorted by the angle of view
- Analogous to the projections obtained with Computed Tomography (CT) scanners
- 3D image re-construction is similar

# Common positron emitting radioisotopes for PET

| Radioisotope | Half-life (min) | Positron energy (MeV) | Reaction | Energy (MeV) |
|---|---|---|---|---|
| $^{11}C$ | 20.4 | 1.0 | $^{14}N$ (p,$\alpha$)=> $^{11}C$ | 5=>16 |
| $^{13}N$ | 9.96 | 1.2 | $^{16}O$ (p,$\alpha$)=> $^{13}N$ | 8=>16 |
| | | | $^{12}C$ (d,n)=> $^{13}N$ | 3=>8 |
| $^{15}O$ | 2.07 | 1.7 | $^{15}N$ (p,n)=> $^{15}O$ | 5=>14 |
| | | | $^{14}N$ (d,n)=> $^{15}O$ | 3=>8 |
| $^{18}F$ | 109.8 | 0.6 | $^{18}O$ (p,n)=> $^{18}F$ | 5=>14 |

# FDG = Fluoro-Deoxy-Glucose

- Most commonly made PET scan (90% of cases) is done with 18F-FDG (Fluoro-Deoxy-Glucose)
- Metabolic activity by virtue of glucose uptake in tissue
- This tracer is mainly used to explore the possibility of cancer metastasis and the response to treatment

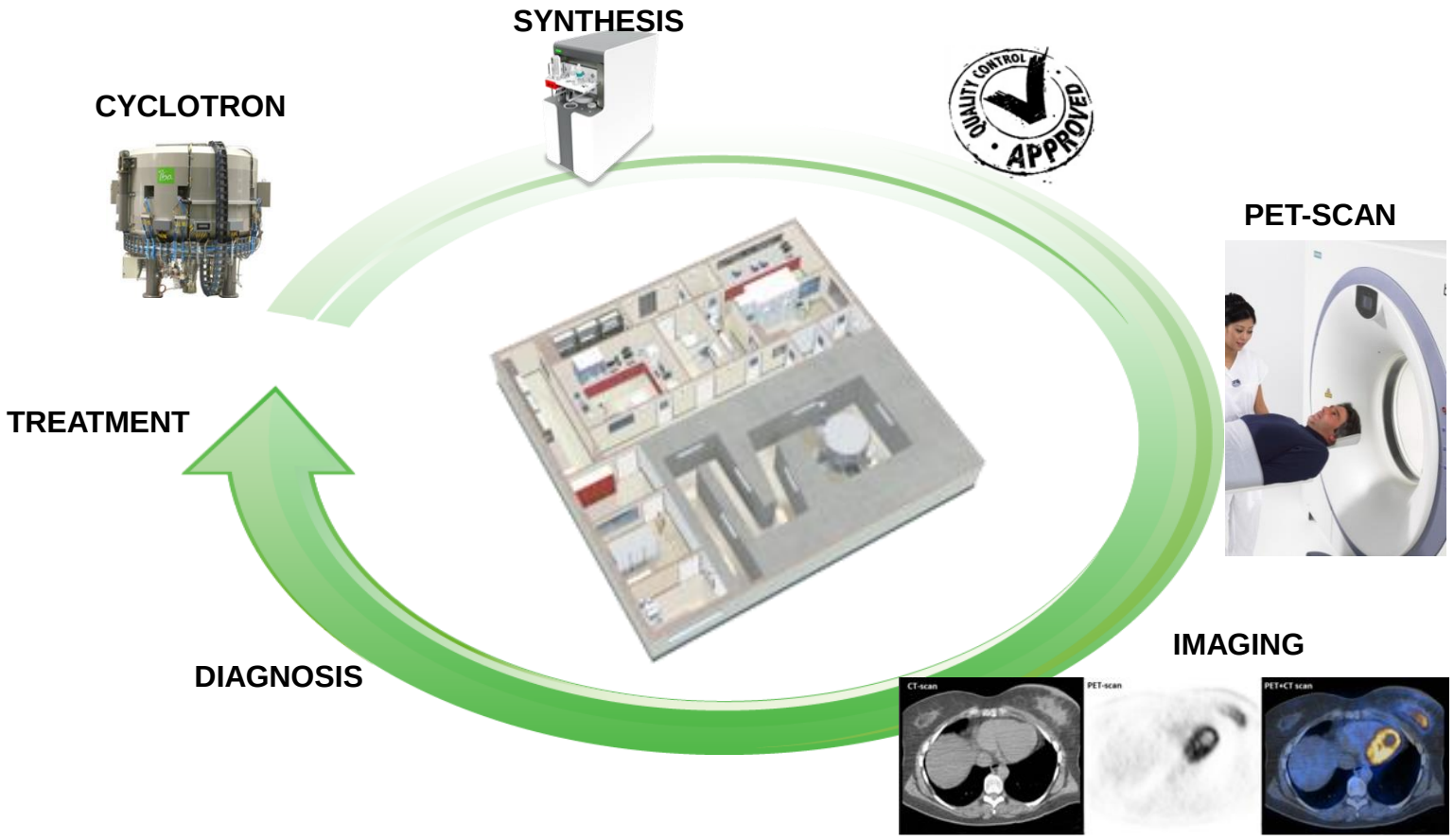



- In glucose one OH-group is replaced by a 18-F atom
- Both atoms have about the same size =>
- Bio-chemical behaviour almost not altered



iba Particle Therapy

# Production and Application of PET radio-isotopes






iba Particle Therapy

# Four different types of radiation therapy

1. External beam radiation therapy (teletherapy)
   - Radiation source is external (like proton therapy)
2. Brachy therapy:
   - Sealed radioactive sources placed precisely in the tumor
   - Can use temporary or permanent placement of radioactive sources
3. Systemic radiation therapy
   - Radioistopes are given by infusion or by oral ingestion. Example: iodine => thyroid gland
4. BNCT: Boron Neutron Capture Therapy
   - mixture of 1 and 3.

# Radioisotopes

- Radiation types

In a radioisotope, the nucleus decays spontaneously, giving off particles and energy.

$\beta^+$ $\gamma$ — diagnosis

$\alpha$ $\beta^-$ — therapy

PET - $T_{1/2}$:
- F-18- 2h
- Ga-68- 1h
- Zr-89-3 d
- I-124-4 d
- O-15- 2min

SPECT- $T_{1/2}$ :
- I-123-13d
- Tc-99m-6h
- Ga-67
- In-111
- Tl-201

- I-131
- Y-90
- Re-188
- Lu-177
- At-211*

# Pairs of radioisotopes for systemic therapy

| Diagnostic (PET) RI | Therapy RI |
|---|---|
| $^{124}I$ | $^{131}I$ |
| $^{86}Y$ | $^{90}Y$ |
| $^{64}Cu$ | $^{67}Cu$ |
| Etc! | |

Problem of dosimetry and treatment planning: how to assess the radiation dose received by the tumor and by the healthy organs at risk.

- Biochemical properties of pairs are exactly the same
- PET-study allows quantitative diagnostics of distribution and uptake of the labelled molecule
- With this information the actual delivered dose of therapeutic treatment can be predicted

# Brachy therapy

- Dose is delivered by placing the radiation source directly inside the area requiring treatment
- Commonly used for cervical (uterus), prostate, breast and skin cancer
- Irradiation affects only a very localized area => healthy tissues are spared
- Much higher doses can be delivered. For comparison:
  - Proton therapy: about 40 Gray
  - Prostate brachytherapy: about 100 to 150 Gray
- Brachytherapy can often be completed in less time
  - Reduce the possibility of recovery of cancer cells between treatment intervals

# Prostate brachytherapy with Pd-103 or I-125

Seeds placed with 3D precission verified with ultrasound probe
Seeds are not harmfull and can stay in place after treatment