Medicinal Chemistry

Positron Emission Tomography (PET)

CHB 331
Jens Frigell, Prof. Elena Dubikovskaya
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Molecular Imaging

• **Molecular imaging** is the visualization, characterization, and measurement of biological processes at the molecular and cellular levels in humans and other living systems.

• Typically includes two- or three- dimensional **imaging** as well as **quantification** over time.

• The **techniques** used include radiotracer imaging/nuclear medicine, MRI, microscopy, optical imaging, ultrasound and others.

• **Molecular imaging agents** are probes used to visualize, characterize, and measure biological processes in living systems.

By Sanjiv Sam Gambhir MD, PhD
(Reprinted from *MI Gateway*, the MCoE newsletter, 2007-1)
Molecular Imaging

- **Molecular imaging** is a new biomedical research discipline

- Enables the visualization, characterization, and quantification of **biological processes** taking place at the cellular and subcellular levels within living subjects including patients.

- The field **originated from radiopharmacy** but has since then encompassed several imaging modalities

- Non-invasive

Imaging Modalities

• What techniques do we have to perform molecular imaging?

• For this we need a source and a detector
  • The source is usually injected into the subject and is then called the probe or the tracer.
  • The detector is usually outside the subject reading the emitted signal (photon, gamma rays etc)
Examples of Imaging Modalities

- **MRI** – Magnetic Resonance Imaging
  - High resolution
  - Low sensitivity

- **Optical**
  - Safe
  - Cheap
  - Sensitive
  - Tissue penetration problem

- **SPECT** – Single Photon Emission Computed Tomography
  - Expensive

- **PET** – Positron Emission Tomography
  - Expensive
  - Very sensitive
  - No tissue penetration limits

http://www.alnmag.com/article/small-animal-imaging-center-design
Table 1 – In vivo imaging techniques currently used in the context of biomedical research and/or medical diagnosis.

<table>
<thead>
<tr>
<th>Technique</th>
<th>Clinical imaging</th>
<th>Resolution</th>
<th>Animal imaging</th>
<th>Resolution and time scale</th>
<th>Application</th>
<th>Main characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPECT (low energy γ-rays)</td>
<td>yes</td>
<td>6-8 mm; s</td>
<td>yes</td>
<td>1-2 mm; min</td>
<td>Functional</td>
<td>radioisotopes have longer half-lives than those used in PET; sensitivity 10 to 100 times smaller than PET</td>
</tr>
<tr>
<td>PET (high energy γ-rays)</td>
<td>yes</td>
<td>4 mm; s</td>
<td>yes</td>
<td>1-2 mm; min</td>
<td>Metabolic, functional, molecular</td>
<td>High sensitivity (picomolar concentrations); cyclotron needed</td>
</tr>
<tr>
<td>CT</td>
<td>yes</td>
<td>0.5 mm; s</td>
<td>yes</td>
<td>50-100 μm; min</td>
<td>Anatomical, functional</td>
<td>Poor soft tissue contrast</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>yes</td>
<td>300-500 μm; s</td>
<td>yes</td>
<td>50 μm; min</td>
<td>Anatomical, functional</td>
<td>Difficulties to image through bone or lungs; microbubbles used for contrast enhancement</td>
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<tr>
<td>MRI</td>
<td>yes</td>
<td>1 mm; s to min</td>
<td>yes</td>
<td>80-100 μm; s to h</td>
<td>Anatomical, functional</td>
<td>High spatial resolution and soft tissue contrast</td>
</tr>
<tr>
<td>Bioluminescence</td>
<td>no</td>
<td>–</td>
<td>yes</td>
<td>1-10 mm; s to min</td>
<td>Molecular</td>
<td>High sensitivity; transgene-based approach; light emission prone to attenuation with increased tissue depth</td>
</tr>
<tr>
<td>Optical imaging</td>
<td>no</td>
<td>–</td>
<td>yes</td>
<td>1-3 mm; s to min</td>
<td>Molecular</td>
<td>Excitation and emission light prone to attenuation with increased tissue depth</td>
</tr>
</tbody>
</table>

**Abbreviations:**

ADMET absorption, distribution, metabolism, excretion and toxicology; CT computerized tomography; FDA Food and Drug Administration; GLP Good Laboratory Practice; HTS high-throughput screening; MR magnetic resonance; MRI magnetic resonance imaging; MRS magnetic resonance spectroscopy; PET positron emission tomography; SPECT single photon emission computed tomography
What is Positron Emission Tomography (PET)?

”A positron emission tomography (PET) scan is an imaging test that can help reveal how your tissues and organs are functioning. A small amount of radioactive material is necessary to show this activity. The radioactive material may be injected into a vein, inhaled or swallowed.

More radioactive material accumulates in areas that have higher levels of chemical activity. This often corresponds to areas of disease and shows up as brighter spots on the PET scan. A PET scan is useful in evaluating a variety of conditions — including neurological problems, heart disease and cancer.”

(Information from a hospital to patients)
What is Positron Emission Tomography (PET)?

**PET scans** are becoming more and more frequent in the clinic and more and more people have heard about it or even been diagnosed by one.

A single PET or PET/CT exam can provide information that once would have required several medical studies and possibly surgery. PET scans are most often used to help the physician detect cancer and monitor response to treatment. PET scans are also used to evaluate heart disease, neurological conditions and other physiological problems.

*Information collected from information sites for the public*
What is Positron Emission Tomography (PET)?

- *Originally* was used only in research.

- PET procedures were performed only in dedicated imaging facilities that had ready access to a cyclotron and a radiochemistry lab to make the radiopharmaceutical.

- *Now, private companies* are producing radiopharmaceuticals for distribution to imaging facilities increasing availability.

- The risks associated with a PET scan are minimal. The quantity of radiation is low.
In research we say that PET is:

- An analytical imaging technology developed to use compounds labeled with **positron-emitting radioisotopes** as molecular probes to image and measure biochemical processes of mammalian biology *in vivo*.

- Typical isotopes include $^{11}$C, $^{13}$N, $^{15}$O, $^{18}$F, $^{64}$Cu, $^{62}$Cu, $^{124}$I, $^{76}$Br, $^{82}$Rb and $^{68}$Ga, with $^{18}$F being the most clinically utilized.

- There is **no positron emitter of hydrogen**, so fluorine-18 is used as a hydrogen substitute.

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Halflife</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}$C</td>
<td>20.3 min</td>
</tr>
<tr>
<td>$^{13}$N</td>
<td>9.97 min</td>
</tr>
<tr>
<td>$^{15}$O</td>
<td>124 sec</td>
</tr>
<tr>
<td>$^{18}$F</td>
<td>110 min</td>
</tr>
</tbody>
</table>
Research Field of PET

The research field of *in vivo* PET is how to *introduce, detect and quantify a radioisotope in a living system.*

A radioisotope is a single atom, of an element. What we need to master is to:

1) obtain the isotope (cyclotron)
2) incorporate the isotope into a molecule/carrier (lab work of chemists)
3) Detect and quantify the isotope in a living system (development and use of camera and software as well as biological knowledge)

→ It is an exciting research field bordering onto many disciplines, from organic and analytical chemistry to animal handling and anatomical knowledge, to physics and mathematics and engineering.
Cyclotron

The cyclotron was one of the earliest types of particle accelerators, and is still used as the first stage of some large multi-stage particle accelerators. It makes use of the magnetic force on a moving charge to bend moving charges into a semicircular path between accelerations by an applied electric field.

Due to the short half-life of many radioisotopes, a radiolab usually needs to have access to a cyclotron.
PET

• PET imaging relies on the nature of the positron and positron decay. The positron was first conceived by P.A.M. Dirac in the late 1920s. It was experimentally discovered in 1932, the same year as the neutron.

• The positron is the antimatter counterpart to the electron, and therefore has the same mass as the electron but the opposite charge.
Spatial Resolution of PET

Spatial resolution is an important factor in PET image quality. Several factors impact the spatial resolution:

1. **Positron path.** The positron travels some distance from the decay to the point where it annihilates, based on its initial energy.

2. **Noncollinearity.** The annihilation photons are not emitted exactly 180° apart.

3. **Detector.** The size of the detector is related directly to spatial resolution. Generally, the smaller the detectors are, the better the spatial resolution.
The life of an isotope..

• An unstable isotope has a parent isotope and a daughter isotope:

An example:  

Germanium-68 ➔ Gallium-68 ➔ Zinc-68  

Half-life 271 days  
Half-life 68 min  
Stable  

X-ray (Electron capture) ➔ Positron  

Parent  
Daughter of Ge-68  
Daughter of Ga-68  

Electron capture: Nucleus absorbs an electron and forms a neutron from a proton increasing the number of neutrons in the nucleus by 1 and decreases the number of protons by 1. The nuclide now technically has transformed to another element but is in an excited state and releases a gamma ray (or equivalent).

* This is a slightly simplified explanation. Unstable isotopes usually have a statistical distribution of different modes of decay.
Exponential growth of PET. Number of year-limited publication hits for ‘positron emission tomography’ using the Scopus abstract and citation database.
Evolution of Technology

CT

1973

2000

PET

PET/CT

2001

PET : Positron Emission Tomography
CT: Computed Tomography
PET and brain function

- PET studies of glucose metabolism to map human brain’s response in performing different tasks.

- Tasks: Working, looking, thinking, remembering, listening.

- Highest metabolic rates are in red, with lower values from yellow to blue.
• **visual scene** activated visual cortex (arrow),
• **listening** to a mystery story with language and music activated left and right auditory cortices (arrows)
• **counting** backwards from 100 by sevens activated frontal cortex (arrows)
• **recalling** previously learned objects activated hippocampus bilaterally (arrows)
• **touching** thumb to fingers of right hand activated left motor cortex and supplementary motor system (arrows).
PET and brain function

- PET study of glucose metabolism in Alzheimer’s disease.

- In “late Alzheimer’s,” metabolic deficit has spread

- At late stage disease, metabolic function in Alzheimer’s is similar to that of newborn, shown to the far right, which underlies their similar behavior and functional capacity
PET and cancer

PET images of **glucose metabolism in various types of cancers**.

Study illustrates that **increased glycolysis** is a **common property of cancer**. Arrows point to some tumors.
PET scans are commonly used to investigate the following conditions:

- **Epilepsy** – PET can reveal what parts of the brain are causing epileptic seizures. This helps the doctors to determine the best course of treatment.

- **Alzheimer’s disease (AD)** – Sugar uptake (activity) and plaque formation can be measured with PET. It help the doctors distinguishing AD from dementia.

- **Cancer** – PET scans show presence of cancer, stage of cancer and spread of cancer in the body. The scan helps the doctor to come up with the best treatment for the patient. Ongoing chemotherapy and a patient’s reponse to radiation treatment can be evaluated during or after treatment of cancer.

- **Heart disease** – Damages or scars in the heart can be visualized as well as other irregularities in the heart.

- **Medicinal research** – every day, all around the world, reserachers use PET to learn more about our bodies and the biological pathways and their functions and regulatory effects.
Combination of PET with CT or MRI

- **PET** scans are increasingly read alongside **CT** or magnetic resonance imaging (MRI) scans, with the combination (called "co-registration")

- Gives both **anatomic and metabolic information** (i.e., what the structure is, and what it is doing biochemically).

- Because PET imaging is most useful in combination with anatomical imaging, such as CT, modern PET scanners are now available with integrated CT scanners (so-called "PET/CT").
Abnormal PET - CT Body Scan

PET: Positron Emission Tomography
CT: Computed Tomography
III. Radiolabeling – Synthetic methods

• Due to the decaying nature of the isotope, radiolabeling must be fast and high-yielding.

• Purification must be easy (filtering/washing and/or HPLC)

• The choice of tracer dictates the chemistry needed. Two types of labeling:
  – Covalent ($^{11}$C, $^{18}$F, $^{13}$N etc)
  – Chelation (mostly metals)
Ideal Biological Characteristics of Radiopharmaceuticals

• High target:non-target ratio
  – rapid blood clearance
  – rapid localization in target tissue
  – rapid clearance from non-target tissues (liver, kidney, intestines)

• Ideal biological half-life
  – long enough to complete the study (i.e. localize to target tissue while minimizing background)
  – short enough to reduce overall radiation dose to the patient
Radiolabeling – GMP and safety

• **GMP**: Good manufacturing practice (necessary for clinical use)
• All members of a lab working with radioactive are trained for this purpose and wear **suitable protection**. They also carry two **dosimeters**, one for the finger (hands are more in contact with the work space) and one on the chest.
Covalent Radiolabeling – $^{11}$C

- $^{[11]}$C-methyl iodide can be prepared in 70%-95% radiochemical yield from $^{[11]}$C carbon dioxide within 3-5 min after its generation. This reagent can then be used in the preparation of L-[methyl-$^{11}$C]methionine. $^{11}$C has a half-life of 20 mins.
$^{13}$N is a relatively short-lived isotope (half-life: 9.97 min) that is used in PET studies. It is generated in the form of $[^{13}$N]$\text{NH}_4^+$ by bombarding mixtures of water/ethanol ($\text{H}_2\text{O}$) with high energy protons.
Covalent Radiolabeling - $^{18}$F

**F-18** labeling is a **common** way to label small molecules. The fluoride is viewed as the equivalent of a proton here since hydrogen does not have positron-emitting isotope. **Half-life ca 2 hours.**
F-18 labeling is a common way to label small molecules. The fluoride is viewed as the equivalent of a proton here since hydrogen does not have positron-emitting isotope. Half-life ca 2 hours.
Radiolabeling via chelation

- Many tracers are not suitable for covalent labeling and here a chelator is used.
- Common tracers are $^{64}\text{Cu}$, $^{68}\text{Ga}$, $^{89}\text{Zr}$, $^{57}\text{Co}$, $^{111}\text{In}$
Metal chelation

• Below is an example how chelation usually is depicted. X here indicates possible sites for linkers.
• These chelant are also frequently used in other modalities such as MRI.

DOTA: \(1,4,7,10\)-tetraazacyclododecane-\(1,4,7,10\)-tetraacetic acid
NOTA: \(1,4,7\)-triazacyclononanetriacetic acid
Metal chelation

• Chelation is done just by mixing the chelant with the tracer at an appropriate pH and temperature in aqueous media.

• Purification consists of washing (and/or filtering and/or HPLC) the reaction mixture.

• Typically, a series of stability and selectivity tests for the labeled compound must be made to ensure its quality.
Metal chelation

- Chelation can be done just by mixing the chelant with the tracer at an appropriate pH and temperature. Purification consists of washing and filtering the reaction mixture.

- Typically, a series of stability and selectivity tests for the labeled compound must be made to ensure its quality.

Half-life of Ga-68 is approx. 1 h

- We inject 0.6 N HCl
- We elute Ga-68 in 0.6 N HCl (6 mL)

Buffer pH 3-4

Reaction
70°C
30 min

Washing repeated 3-7 times

Washing to remove free Ga-68 (false positives)
IV. Examples of PET probes - FDG

- **FDG**: Fludeoxyglucose (or 2-[fluorine-18]fluoro-2-deoxy-D-glucose)

...Glucose is the *ubiquitous energy source* in biology and FDG is therefore quickly taken up by cells.
FDG - Fludeoxyglucose

- FDG is the most important PET probe today, not least for detection of tumors.

- All cells take up glucose, but cancer cells with high metabolism and overexpression of receptors on the cell surface have an increased uptake.

- FDG crosses the BBB which is helpful for detecting brain tumors.
FDG - Fludeoxyglucose

- $^{18}$F-FDG can be used for the assessment of glucose metabolism in the heart, lungs, and the brain.

- $^{18}$F-FDG is taken up by cells, **phosphorylated by hexokinase** (whose mitochondrial form is greatly elevated in rapidly growing malignant tumours).

- A dose of $^{18}$F-FDG in solution is injected into a vein, in a patient who has been fasting for at least 6 hours, and who has a suitably low blood sugar.

- Wait one hour before PET scan in order to let the FDG distribute properly.

- After $^{18}$F-FDG decays radioactively, however, its 2'-**fluorine is converted to** $^{18}\text{O}^-$, and after picking up a proton, the molecule becomes glucose with harmless nonradioactive "heavy oxygen" in the hydroxyl at the 2' position.
Metabolic Trapping of FDG

- FDG-6-P unable to undergo glycolysis/glycogen formation
- FDG-6-P too polar to diffuse out of cell
- Thus becomes “metabolically trapped”
FDG uptake in Normal Tissues

- Brain
- Heart
- Skeletal muscle
- Larynx
- GI tract:
  - Stomach, Colon, Liver
- GU tract:
  - Kidneys, Ureter, Bladder
  - Uterus during menstruation
- Bone marrow
- Thyroid
- Spleen
- Salivary gland
- Brown fat

Courtesy of Maryellen Sun, MD

Mabel Djang, HMS III
Gillian Lieberman, MD

May 2006

Patient #1

Coronal PET scan
FDG Localizes Tumors

- Increased uptake FDG in tumor
  - Elevated levels of GLUT
  - Elevated levels of hexokinase
  - Increased rates glycolysis

- Area of hypermetabolism - “hot spot”

- Useful for cancer staging
  - lung, colorectal, esophageal, stomach, head and neck, cervical, breast, melanoma, lymphoma

Patient #1

Coronal PET scan
Limitations of PET

- Not all malignancies are FDG avid
  - Prostate cancer
- Not all FDG avid tissue is malignant
  - Normal tissue uptake can vary
  - Inflammation → infection, post-rad/surg, granulomas, arthritis
- Poor resolution of images
- Lack of anatomic landmarks
Tumor growing fast give rise to hypoxic (oxygen-poor) regions in the tumor. The reason for this is insufficient blood vessel formation (angiogenesis) to the new cancer cells. FDG does not image hypoxia and the probe 18F-FAZA was developed for imaging of hypoxia. (GBM = glioblastoma multiforme, stage IV brain tumour)
Targeting Molecules

• What is a targeting molecule?

\[ \text{targeting molecule} \rightarrow \text{Fluorophore} \]

“clickable” NIR fluorescent dye

Conjugation via “click chemistry”

\[ \text{PROBE for imaging} \]

\[ \text{targeting molecule} \rightarrow \text{Fluorophore} \]
Targeting Molecules

• What is a **targeting molecule**?

• For cancer: antibodies, peptides, folic acid

• For infection: vancomycin and oligosaccharides
Examples of Targeting Molecules

RGD = arginine-glycine-aspartic acid

Folic acid with linker and azide functionality

RGD peptide with linker and azide functionality

Vancomycin with a linker

Maltodextrin with linker and azide
**Going Deeper: Dual imaging/Dual modality**

- An imaging probe that can be used in **two different modalities**, sometimes simultaneously.

- For example, we can envision a probe that carries a fluorophore and a PET tracer.

Work from Prof Dubikovskaya’s lab
V. PET and the drug industry

Molecular imaging can help companies save money!
Molecular imaging should be used to evaluate candidates as early as possible.

<table>
<thead>
<tr>
<th>Stage:</th>
<th>Target Discovery</th>
<th>Lead Discovery</th>
<th>Candidate Discovery</th>
<th>Preclinical Evaluation</th>
<th>Proof of Concept</th>
<th>Full Development</th>
<th>Registration and Launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gate:</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

Fewer risks in a project mean greater probability of success (POS).

As the project team works to **reduce risk**, the total project cost increases, but because the POS increases, the **value of the project** and corporate commitment increases.

At each stage, **work** is performed to **reduce risk and increase value**.

The latter stages of work are far more costly than earlier stages.
Opportunities for PET imaging in this process

**Early Development**

1) Biodistribution studies confirming that a drug candidate / lead reaches the target tissue (e.g. brain) & does not accumulate in non-target sites of potential toxicity.
   - Easy to accomplish in multiple species.
   - Pros/Cons versus traditional biodistribution?

2) Pharmacokinetics & occupancy measures to guide dose selection for early *in vivo* studies.

3) Use of PET as a biomarker for proof of pharmacology studies and/or to differentiate between drug-candidate efficacy data / behavior & toxicity.
How can Molecular imaging help drug discovery?

Company X has found a promising drug candidate that is able to inhibit an enzyme. The company has set up experiments in the lab in test tubes that have been successful:

In test tube (in vitro)

- Drug target (here: Enzyme)
- Lead drug (here: peptide sequence)
- Drug shows promising effects

In test tube

The company knows that the enzyme is active inside the cell in living systems.

The company then wants to evaluate if their drug candidate (peptide) can enter cells.

In cells (in vitro)

In animals (in vivo)
**Cell experiments:**

Probes can be fluorescent, bioluminescent, PET, optoacoustic, MRI etc.

Labeled drug is added to cells and incubated. The cells are then washed and analyzed for detection of the probe (PET, fluorescent microscope etc).

Wells with cells

*Development of protocols to quantify the amount of drug in each cell line or at each concentration can then help the company to understand if the drug goes inside cells.*

**In test tube** (in vitro)

**In cells** (in vitro)

**In animals** (in vivo)
**In Vivo study:**

The company knows that the enzyme is over-expressed in certain unhealthy tissue, for example in the lungs.

The labeled drug can then be injected into a living animal and via molecular imaging traced within the animal.

*If the lungs can be visualized by the introduction of the probe then it strongly suggests that the drug finds the target in living systems.*
Current & recently completed trials

Positron Emission Tomography (PET) Study With (11C)Flumazenil to Determine Central GABAA Receptor Occupancy of AZD7325

Positron Emission Tomography (PET) Study With (11C) Flumazenil to Determine Central GABAA Receptor Occupancy of AZD6280

AstraZeneca also has a large ‘fleet’ of PET ligands in development: [11C]AZD2184, [11C]AZD2184, [18F]AZD4694 (β-amyloid); 2-[18F]-F-A85380 (α4β2);

Positron Emission Tomography (PET) Study With [11C]Raclopride to Determine Central D2 Dopamine Occupancy of SEROQUEL

[18F] FACBC and [18F] FLT PET Imaging in Central Nervous System Tumors

Pair of AstraZeneca Studies likely to differentiate lead compounds for GABA_A

Memorial Sloan-Kettering Cancer Center
Current & recently completed trials

Practice Effects and Amyloid Imaging Using 18F-PIB or Flutemetamol PET and FDG-PET

The most widely studied positron emission tomography ligand or in vivo amyloid imaging is 11C-Pittsburgh compound B (11C-PIB). Its availability, however, is limited by the need for an on-site cyclotron. Validation of the 18F-labeled PIB derivative 18F-flutemetamol could significantly enhance access to this novel technology.
Radiopeptides

- Desirable pharmacokinetics
- Proteases
- $^{68}$Ga, $^{64}$Cu, $^{18}$F
- “Kit-like” labeling
- Developed Targets:
  - Integrin
  - Melanocortin
  - Somatosensin
  - Bombesin


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*Peptides* (from Greek "digested") are short chains of amino acid monomers linked by peptide (amide) bonds between a carboxylic moiety and an amino moiety. Peptides are distinguished from proteins on basis of size and usually contained less than 50 aminoacids.
$\alpha_v\beta_3$ Integrin

- Cellular adhesion
- Recognizes RGD sequence
- Tumor angiogenesis
- Not expressed on normal endothelial cells

Crystal structure of the extracellular segment of integrin alphavbeta3 (Wikipedia)
Multivalent Cyclic RGD Peptides

- Increase effective concentration
- Linker region to tune pharmacokinetics

Attaching more than one targeting ligand, here the cyclic peptide RGD, gives a stronger binding to cells expressing integrins.
$^{68}$Ga-labeled multimeric RGD peptides for microPET imaging of integrin $\alpha_v\beta_3$ expression
Labeling of larger structures

- Nanoparticles
- Dendromers
- Virus-based

Above: Schematic structure of a radiolabeled nanoparticle design for molecular imaging
To summarize PET:

- **A PET scan** uses radiation, or nuclear medicine imaging, to produce 3D, color images of the functional processes within the human body.

- **PET** stands for *positron emission tomography*.

- The machine detects pairs of gamma rays which are emitted indirectly by a tracer (positron-emitting radionuclide) which is placed in the body on a biologically active molecule.

- The images are reconstructed by computer analysis.

- Modern machines often use a CT X-ray scan which is performed on the patient at the same time in the same machine.
To summarize PET:

- **Radiotracer** - the radioactive isotope is produced in a cyclotron. The isotope is then tagged to a carrier. This is called *labeling*. The carrier could be glucose, water, or ammonia or any other carrier with or without targeting properties, depending on the biological question. The labeled carrier is known as a *radiotracer*. The radiotracer is then inserted into the human body.

- When it is inside the radiotracer will go to areas inside the body that the tracer targets. For example, FDG (fludeoxyglucose) goes into those parts of the body that use Glucose for energy. Cancers, for example, use Glucose differently from normal tissue, so FDG can ”trace” cancer cells.

- PET is routinely used to investigate
  - Epilepsy
  - Alzheimer’s disease
  - Cancer
  - Heart disease
  - Medical research in general
End of lecture

- If you have any questions you are welcome to email me at:
  jens.frigell@epfl.ch