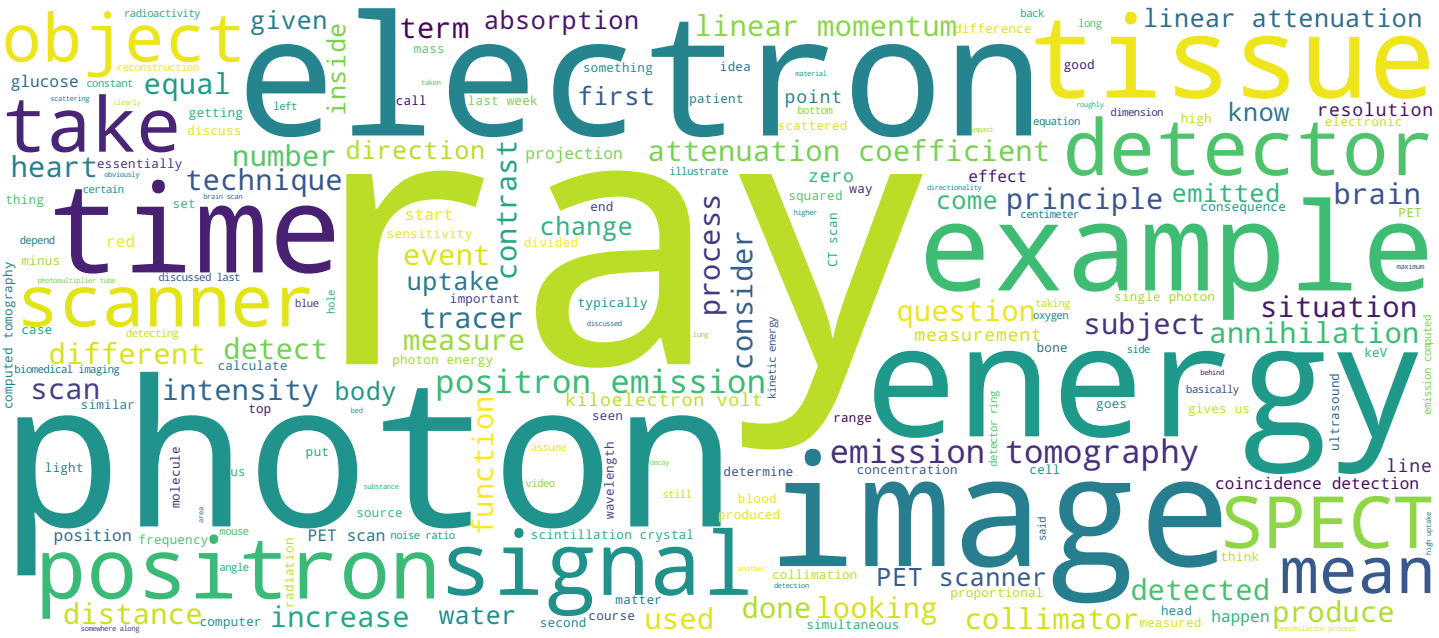
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

6.1 Introduction to PET: Coincidence detection

Fundamentals of Biomedical Imaging

Prof. Rolf Gruetter



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Video

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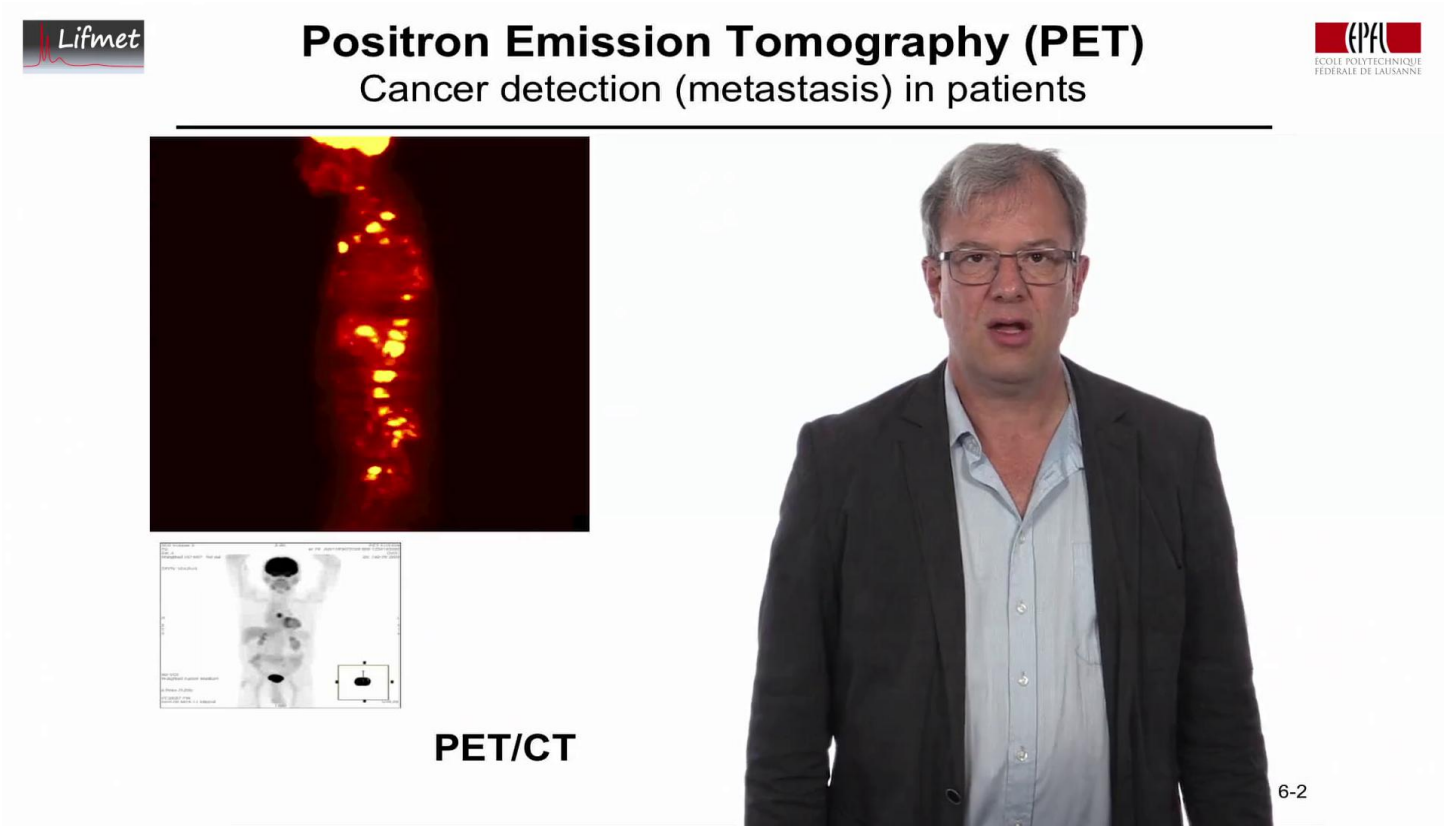


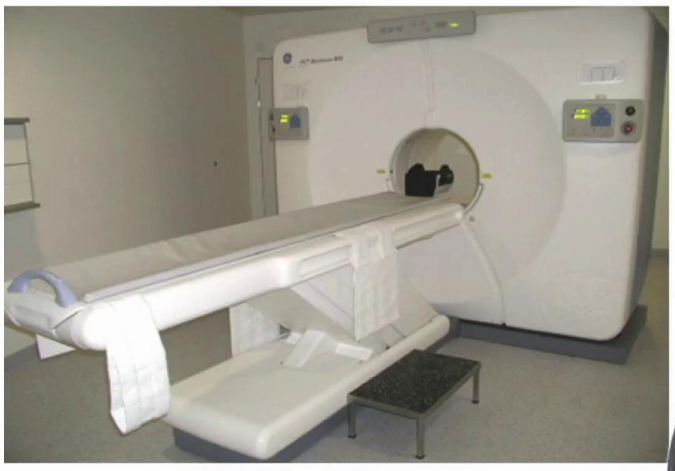
The subject of this week's lectures is positron emission tomography, which is the twin technology to emission computed tomography that we dealt with last week. First, I want to start out with some examples that illustrate what this technique does. The first we'll see here-- this is a positron emission tomography scan-- we can see the whole subject. Here you can see the arms, and you see on the top-- very bright uptake in the head, and you see a lot of spots highlighted in the body-- those are metastases. And that, actually, in the clinical application has been a major motivation for this technique-- this is the easy detection of metastases in cancer patients. Here, in this video, you see also, this is a deoxyglucose uptake scan-- you'll see on the top there-- brain, which has a lot of uptake-- in the bottom, you see the bladder-- you see in the middle the heart, and if you see, just above the heart-- this little spot there-- that spot shouldn't be there. That is a metastasis in this poor patient. We have the application, actually, is PET/CT nowadays. You can actually, nowadays, no longer buy just a pure PET scanner-- you buy a PET/CT scanner.

Notes

Summary

0m 04s

Positron Emission Tomography Scanner



Human scanner

And the reason as illustrated here in this example-- these are transaxial scans-- you can see, here, on the CT scans, you see bright-- the rib cage-- you see the heart-- dark is the lung, there are no electrons in the lung, so we don't have any absorption here. And these are-- this is the heart, here. So, the CT scan provides anatomical resolution, and the PET scan brings a functional metabolic information. And here we see in the PET scan, we see uptake here in this spot. This is not very informative to figure out what is actually going on and where-- but if it's overlaid on the grayscale image-- so, we'll take this image, we'll take this image here, and they are all fused-- color coded the PET data-- one can see very clearly where this bright spot of uptake is in the body. This is the coronal scans-- so, we are now looking as if you are looking at me. So, you see the neck is here, here are the arms, and we have the corresponding PET scan, again with the high uptake. When you fuse the CT scan, here on the left, with the PET scan, one can see where the high uptake is. That is where the new plastic lesion exactly is positioned.

Notes

Summary

1m 28s

Positron Emission Tomography Scanner

Detector ring

Human scanner

6-3

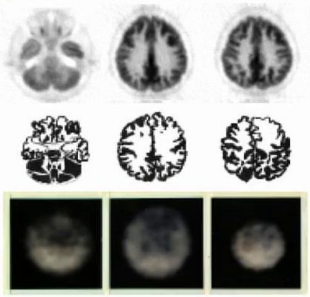
So, what does a PET scanner look like? And a PET scanner is shown here. We have a scanner with a nice white cover. We don't want to expose the patient to all the physics and engineering that's behind it, so there's a nice cover that makes it less intimidating, the patient bed, here's a hole, that this is now set up for a brain scan-- for the head, and this will go here into the hole, where the detection is being done of the head scan. Now, what is inside that scanner? What is inside that scanner is a detector ring, and this is very much the same technology that we discussed last week. It's the same principle of detection, you have scintillation crystals, photomultipliers, and then the electronics. The difference here is it's an entire detection ring that is being used for positron emission tomography-- and we'll see in a short while why this is different from SPECT. So, this goes in here-- it's actually inside the cover. So, let's look at the picture with the cover removed. And here is now such a scanner. We have a sphere here filled with some substance. And so, here you can see the cover removed, and here we can see the detector ring, this is the patient bed. So, that's what's inside a PET scanner.

Notes

Summary

2m 40s

Positron Emission Tomography Scanner



Human scanner

PET is similar to SPECT but different
(detection principle and instrumentation)

6-3

Here, I give you examples of some brain scans. On the bottom, we have the scans taken 1975-- one can see that it is a brain, but it's quite blurry, and you can appreciate the 20 years of technological development here if you look, now, at the brain scan here taken from 1995-- here, we can see very nicely the gray matter, which has higher uptake of the tracer in the brain. Now, on this video here-- what I want to show here is the start of the scan-- so, we have the patient on the bed, the bed is lifted automatically, and then moved into the gurney, and the patient is preparing for the scan-- so, to give us an idea how this scan is being done. So, these are the human scanners. The detection, as I mentioned, is very similar to SPECT, but the principle is different, and this has to do with the detection principle, and therefore, this has an impact on the instrumentation of the positron emission tomography or PET scanner.

Notes

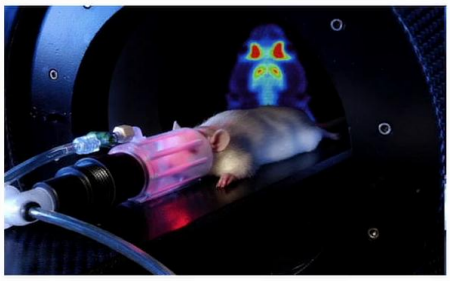
Summary

3m 59s

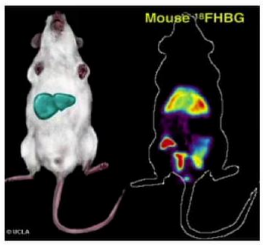
PET of animal models

transgenic mice, cancer detection

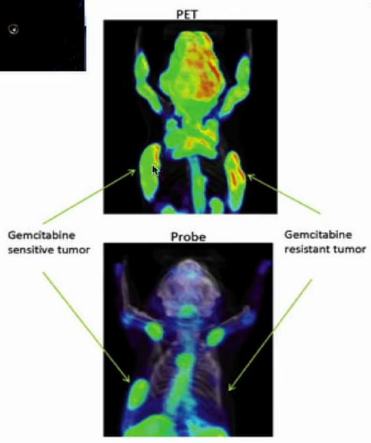
micro PET scanner



Positioning of the rodent



Imaging gene expression (HSV)



6-4

Now, let's look at some examples of animal models. So, we have, first, the scanner here. So, let's look at the scanner. It's a smaller scanner. We can appreciate that. This is about body height, here. Here's the bed where the mouse will be placed or the rodent. Here's the opening, and we can see from the dimensions a human would certainly not fit in here. As we have seen with CT or SPECT, the scanner that is used for animal scanning is smaller-- it's adapted to the smaller size of the species being investigated-- and this is the standard approach here. Interestingly, they still cover up the electronics-- it's probably more for the protection of the electronics, here, rather than appeasing the volunteer, here, who is an anesthetized rodent. Rodents-- this is a rat here, they have to be anesthetized, otherwise, they start moving around. So, here's the opening of the scanner, the anesthesia mask, and here we can see a scan of the mouse's brain. Here are some examples. We have on the left-- we have the optical imaging-- this is herpes simplex virus-- mediated imaging of gene expression on the right-- we have a tracer that images where this gene has been expressed. Here's another example of optical imaging here in the bottom. And on the top, the positron emission tomography scan, and these are the two types of tumors-- one's resistant and one's sensitive to chemotherapy.

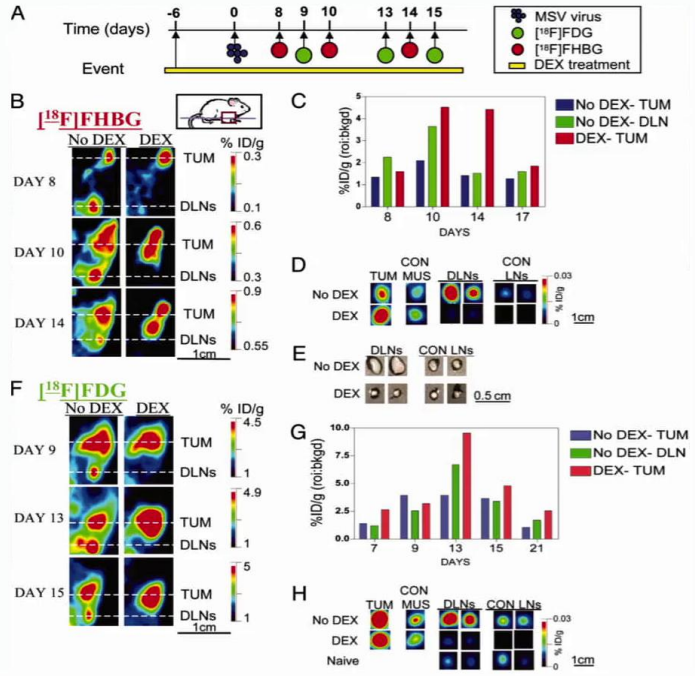
Notes

Summary

5m 07s

PET of animal models

transgenic mice, cancer detection



6-4

If we look at the atypical publication, this is a figure taken from a paper-- then we have a lot of information. We have the PET scans, here, with this FHPG tracer, and here with the FDG tracer, showing the PET images. Here are the analysis with different treatments. So, what you'll see in research is that biomedical imaging here with positron emission tomography is very often an integral part of the study.

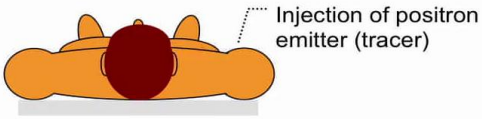
Notes

Summary

6m 51s

6-1. What is Positron Emission Tomography ?
PET

Positron Emission tomography:
measured are x-rays emitted by annihilation of positrons
emitted by exogenous substance (tracer) in body



Two issues:

1. How to determine directionality of x-rays ?

6-5

So now, let's come to the question-- what is positron emission tomography? Or PET, as we call it in shorter term. Basically, what we are measuring with positron emission tomography-- there's the word positron in there-- and what we are looking at is the annihilation of positrons with electrons-- this gives rise to x-rays that are being emitted from the annihilation process. This is the basic principle that is behind it. The positrons are emitted by a parent nucleus-- that's typically part of a tracer that's administered to the subject-- so, it's an exogenous substance that's not naturally occurring, which we desire to image. So, we'll inject the tracer here, and the days it distributes, as we can see here now, with the subject turning more and more red, and then we have the x-rays that are being emitted in all sorts of directions. And now, we have two issues. As with SPECT-- they're actually the same issues-- one is when we detect an x-ray, how do we know what it's direction was. Remember, with SPECT, we used collimation for determining direction of the x-rays-- here, the principle will be slightly different. So, we still have to deal with this question.

Notes

Summary

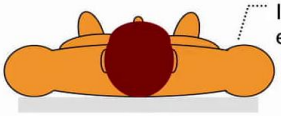
7m 19s

6-1. What is Positron Emission Tomography ?
PET

Positron Emission tomography:
measured are x-rays emitted by annihilation of positrons

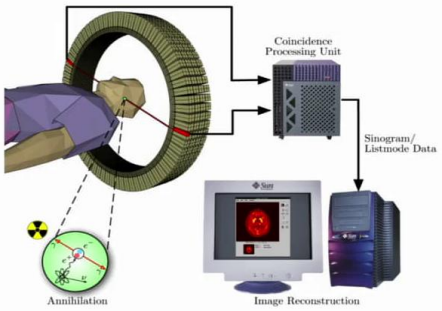
emitted by exogenous substance (tracer) in body

The principle is as emission tomography, but there is one major difference … (see later)



Two issues:

1. How to determine directionality of x-rays ?
2. Absorption is undesirable



Most widely used tracer for PET

^{18}Fluoro-deoxy-glucose

6-5

And as in SPECT, we have absorption that is undesirable. Remember, with CT scanning, absorption was the contrast generating parameter. We irradiate the subject with x-rays, and we want to see the different absorption-- that's the basis of CT scanning. With SPECT and also with PET, the absorption is, in principle, undesirable, and it would be nice if that would not happen. So, we have to consider this as a nuisance effect. So, this is the situation with PET-- very similar to SPECT or emission computed tomography. So, the principle, therefore, is similar as what we discussed last week with SPECT, but there is a major difference, and you will see, in a short while, where this difference comes from. So, if you look at the set up of a PET scanner, we have the detector ring, here is the subject, we have electronics, here is a coincidence processing unit, we have the computer for the reconstruction, and here we have the process that's at the heart of what we are detecting, and that's the annihilation of the positron. So, the most widely used tracer for PET is fluorodeoxyglucose-- it's the glucose where there's a flourine attached at the two position-- here's the example of this diagram, here.

Notes

Summary

8m 45s

6-1. What is Positron Emission Tomography ?
PET

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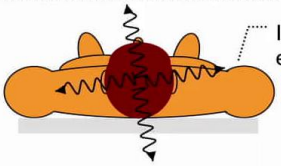
measured are x-rays emitted by annihilation of positrons

emitted by exogenous substance (tracer) in body

The principle is as emission tomography, but there is one major difference … (see later)



Two issues:

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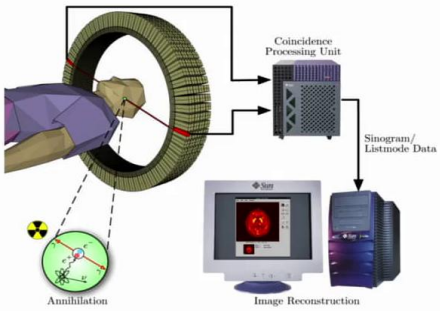
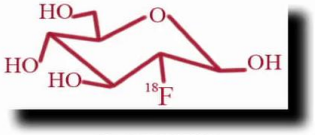
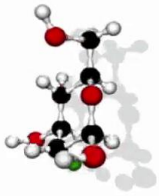


Most widely used tracer for PET

^{18}Fluoro-deoxy-glucose



F-18 FDG



6-5

This is the one position, here's the two position-- instead of an OH group, there's a flourine attached, here. And here's the three dimensional graphic-- in green, you can see the fluorine atom at this position-- fluorine 18. So, fluorine 18 is an unstable nucleus that decays, and as it decays it emits a positron.

Notes

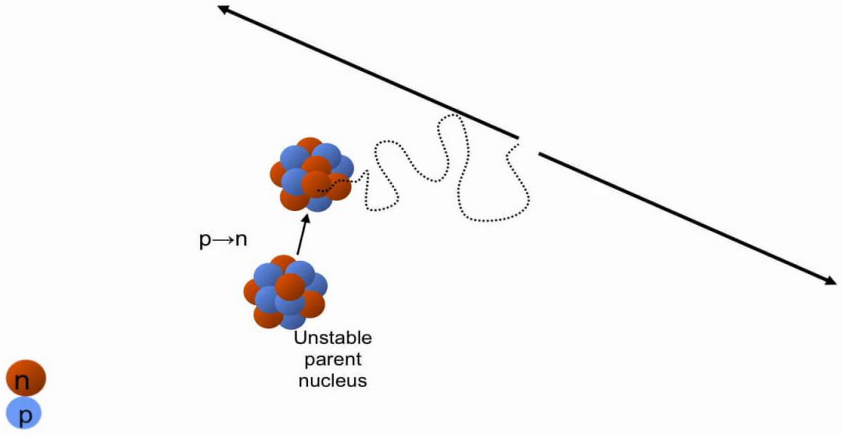
Summary

10m 08s

What does one want to measure with PET ?

Annihilation photons

Question: Why are two photons are produced?



NB. Light travels 1m in 3ns :

1[m]/3 10^8 [m/s]=3ns

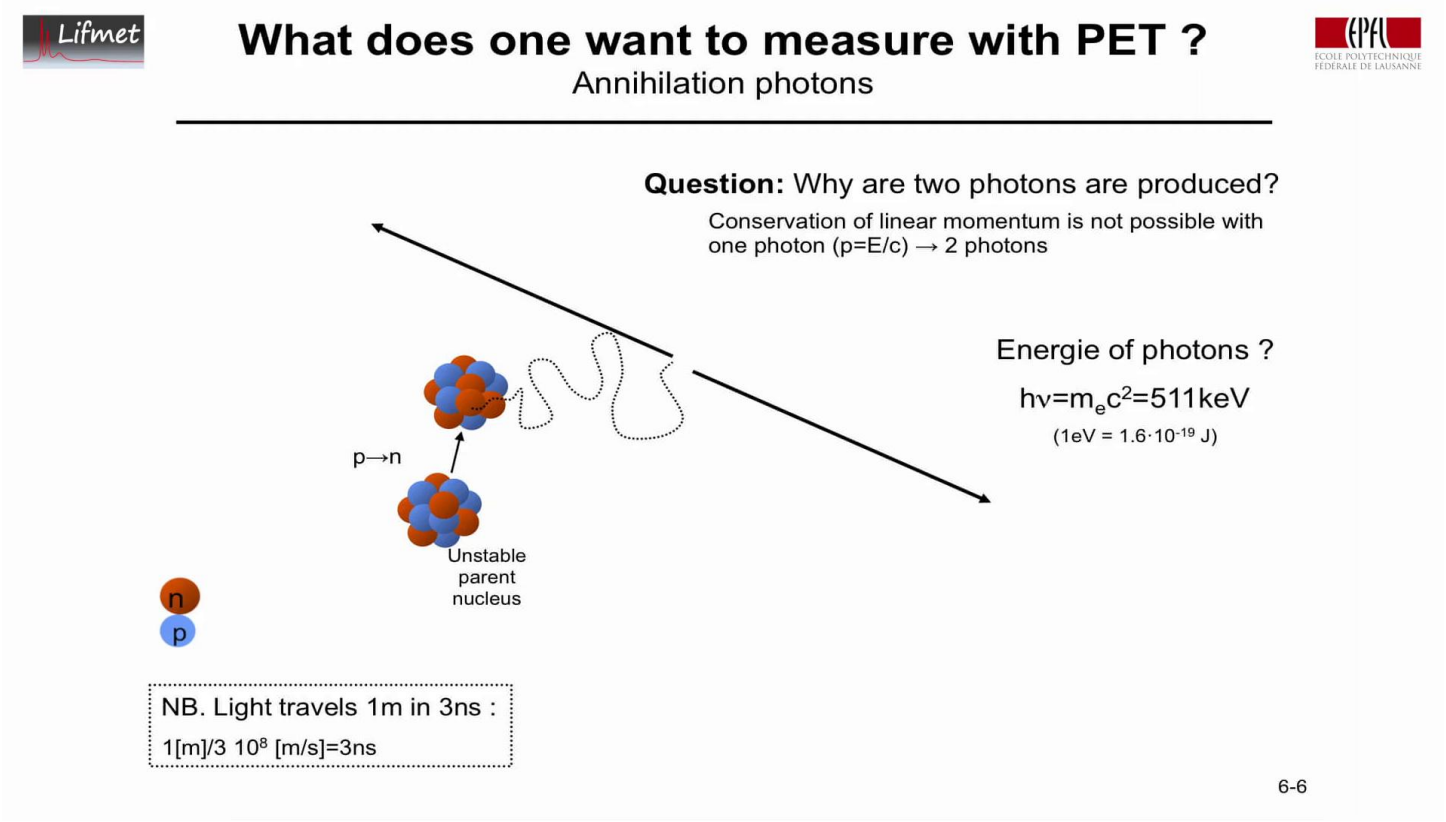
6-6

So, we are looking at imaging antimatter-- that is the annihilation of antimatter-- with matter. So, what is going on here? So, we have the unstable parent nucleus, here. We have in red the neutrons, and in blue, the positrons. And now, when this unstable nucleus decays, there is a conversion of a positron to a neutron. So, we're changing the charge by minus one. We'll have a different charge. We have charge conservation. So, we will have this positive charge emitted from the nucleus in the form of a positron. And this positron diffuses through the tissue, undergoes different interactions, akin to the electrostatic Coulomb interaction, just like we've seen with bremsstrahlung. And after this positron has lost most of its kinetic energy, at some point, it will be attracted by a nearby electron-- the two get together-- they combine, it's matter and antimatter, and when matter and antimatter come together, they are annihilated, so, there is the emission of two x-rays. To give you an idea, these x-rays travel at 3 times 10^8 meters per second, so, in 3 nanoseconds, the x-ray will have traversed 1 meter in the scanner. So, now, question: Why are two photons being produced? Why not just one?

Notes

Summary

10m 30s

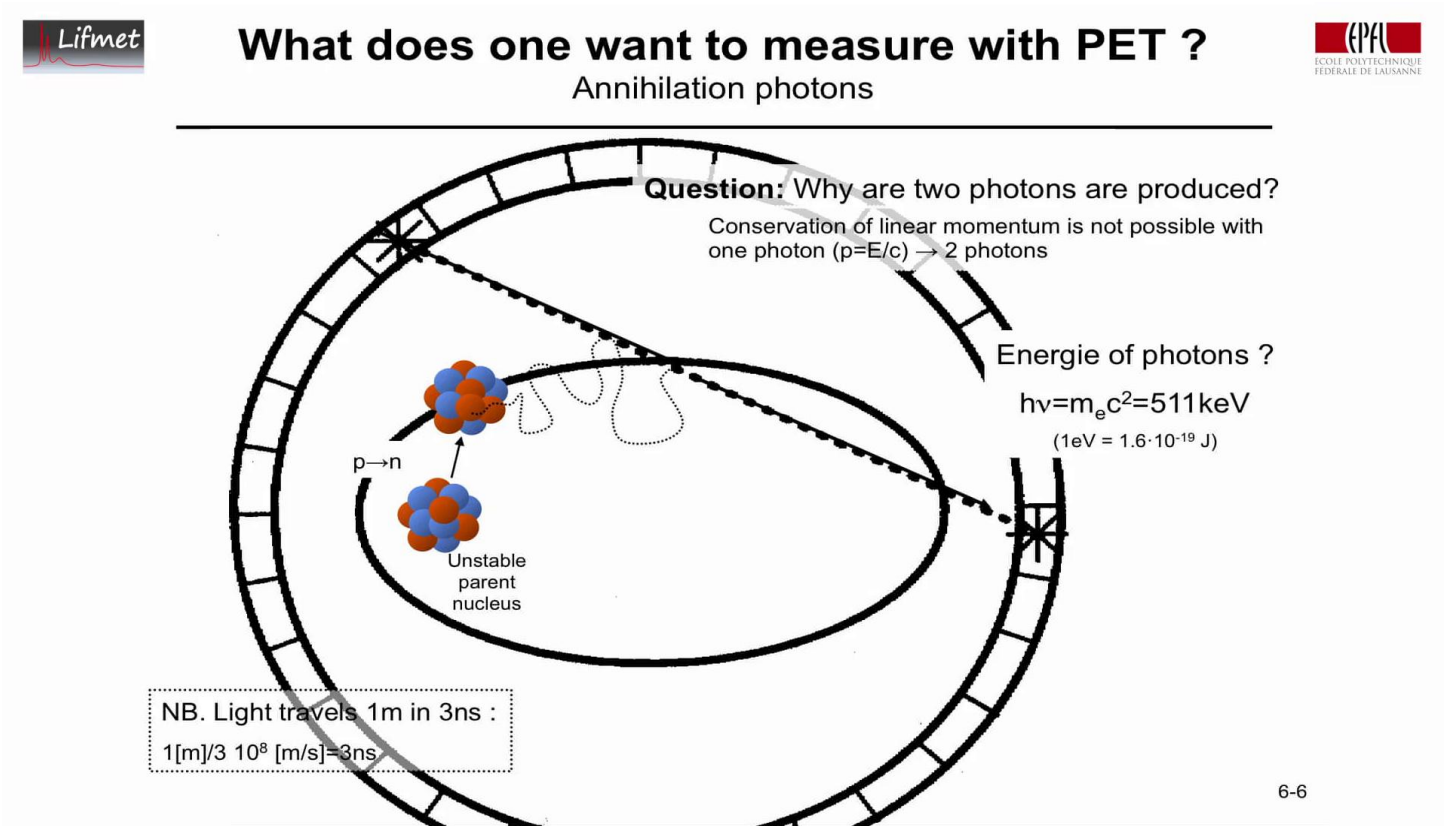


We could, in principle, have the electron and the positron combine. From an objective standpoint, we could produce a single photon. Remember, that we said that the positron and electron-- the positron loses most of its kinetic energy. So, let's consider the situation, idealized-- that the positron and the electron, at the time of annihilation, have zero kinetic energy. So, the total linear momentum of the positron-electron pair is zero. If we had a single photon that's emitted, that photon would have energy. And if it has energy, as we've discussed two weeks ago-- three weeks ago, the photon carries a linear momentum. So, if we have a single photon, we would have, suddenly, a net linear momentum-- and this would violate conservation of linear momentum. If we have two photons that go in opposite directions, those two photons, with equal energy, would produce a situation with zero net linear momentum. So, this is a consequence of the conservation of linear momentum-- that we need to have two photons. What is the energy of the photons? Well, the energy of the photons, at rest-- there's two electrons-- masses of electrons-- the electron and positron-- that convert into energy.

Notes

Summary

12m 08s

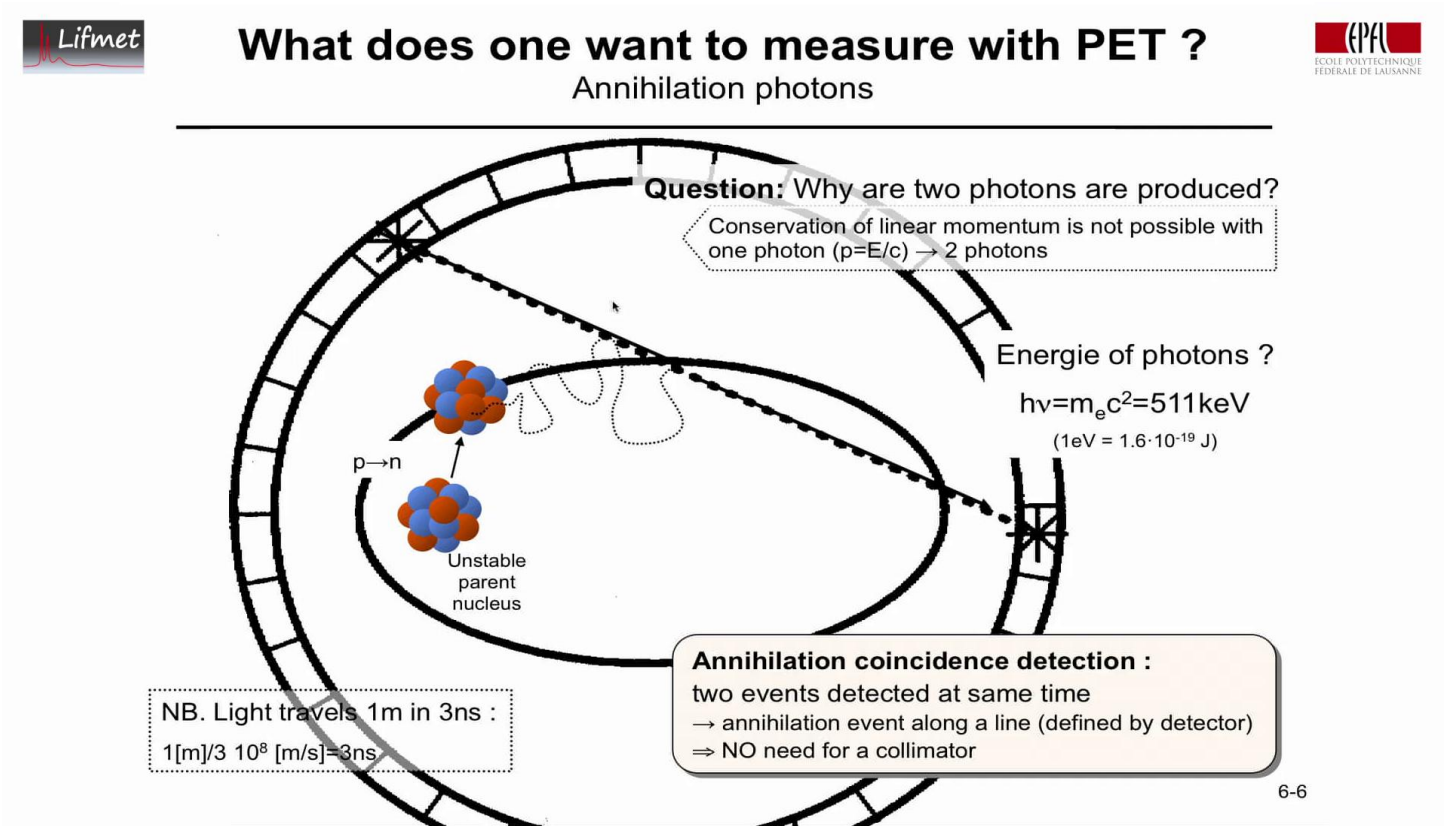


So, we have a total energy of [mec^2]-- we have 2 times [mec^2]-- but we have two photons-- so, one of those photons has an energy of [mec^2], and that is, in kiloelectron volts, that's around 510 kiloelectron volts. I'm giving here, also, the conversion of electronvolt into joules, if you ever wish to verify this calculation with SI units, using c^2 and the mass of the electron. So, now, what does this mean? This basically means-- in order to determine the location of an annihilation event, what we need to do is we need in the detector-- we need to select two events that happened simultaneously-- that is, two x-rays that we detect simultaneously, at the same time. And then, we will know, that if we have a detection here and a detection here, then we will know somewhere along this line, there has been an annihilation of an electron and a positron. And this is the basic detection principle. As a side note, here, notice here that the light travels around the meter in 3 nano-seconds-- that's an awfully short time. This, in general, does not allow us to determine the exact location of the electron-positron annihilation process.

Notes

Summary

13m 28s



It is too imprecise, as we will see later, the time resolution of the scanner being below 3 nanoseconds is not the typical time resolution that the detection materials provide us. So, what we have here, then--the principle is annihilation coincidence detection. The basic principle is we detect two photons at the same time, we attribute a location--somewhere along the line that connects the two detectors. And somewhere along this line, we had an annihilation of a positron and an electron. So, what does this mean? Well, it means we detect two events at the same time, and this defines the event along a line.

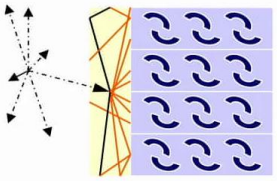
Notes

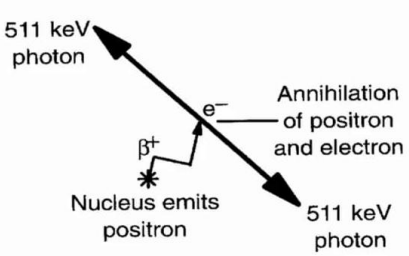
Summary

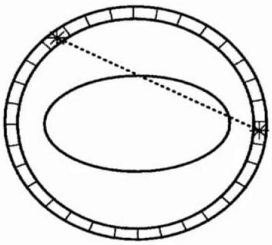
14m 46s

What is coincidence detection ?

electronic collimation (i.e. w/o physical collimators)







6-7

Moreover, we do not need a collimator. So, for positron emission tomography, there's the difference between SPECT and positron emission tomography, due to the fact of annihilation coincidence detection on the two sides, we do not need to have a collimator to establish the directionality of the x-ray. This is done by the coincidence detection process. So, what is coincidence detection? What do we do when we do coincidence detection? Just as a reminder, we'll start out here when you have the positron that's emitted by nucleus, diffuses, annihilates with the electron, and produces two 510 kiloelectron volts x-rays that are going in opposite directions. We detect them simultaneously, and this establishes lines of incidence-- along this line has been the event. This simultaneous detection provides the collimation-- it's electronic collimation, and this gives us the directionality of the x-rays. So, let's look at the situation in the detector. We have an x-ray that hits our scintillation crystal. Here, the detection principle is the same as the principle used for SPECT. This produces, as we've discussed last week, visible light.

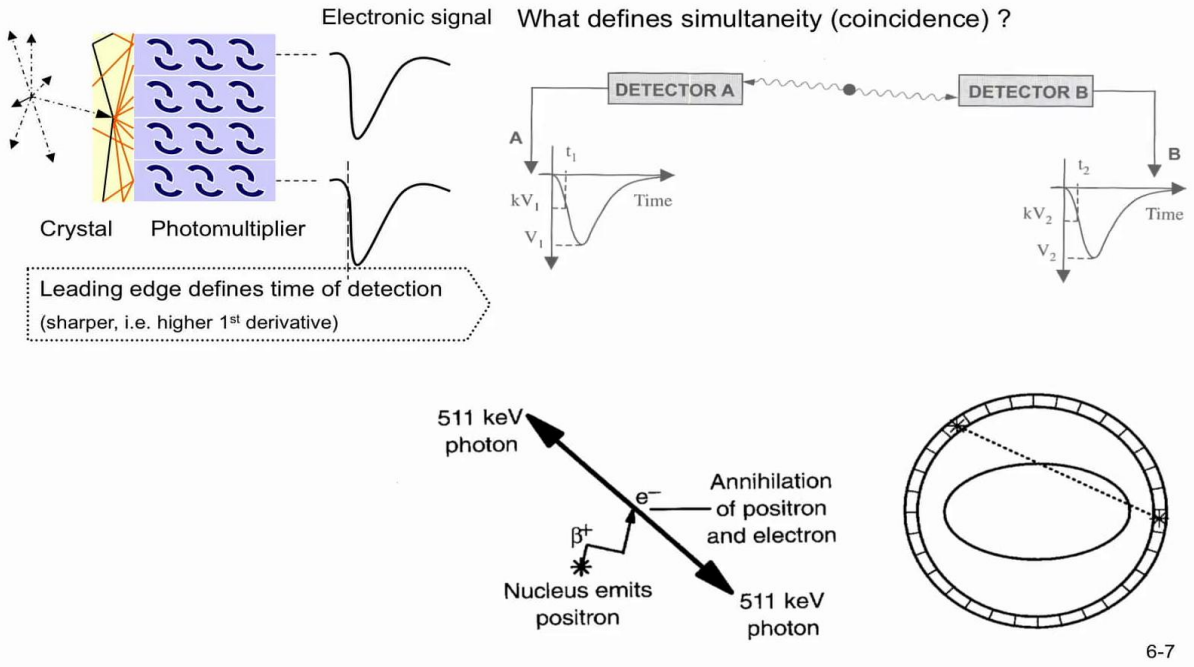
Notes

Summary

15m 36s

What is coincidence detection ?

electronic collimation (i.e. w/o physical collimators)



This visible light produced is amplified by the photomultiplier tubes, and in the end, we've produced an electronic signal that looks like something like this. This is what the signal that's being detected. And let's say, we take these two detectors, here-- we have these two signals, here. To determine the precise time-- because we want to determine simultaneity for coincidence detection-- one wants to have a precise measure of the time, and this is done on the leading edge of the amplified signal. This is steeper, so it is sharper, and it has a higher first derivative. So, now, question: how do we define simultaneity? That is, coincidence? Well, the answer could be, let's just say, they have to be at the same time. But what does it mean to be at the same time? In an ideal world, on a piece of paper, in theory, same time means at the same time, precisely-- down to attosecond precision. But we're dealing with an instrument-- we're dealing with imperfections-- and so defining simultaneity requires a certain uncertainty that one allows. Within which time interval do we consider two events that are being detected as being simultaneous? So, the situation here is in this graphic here.

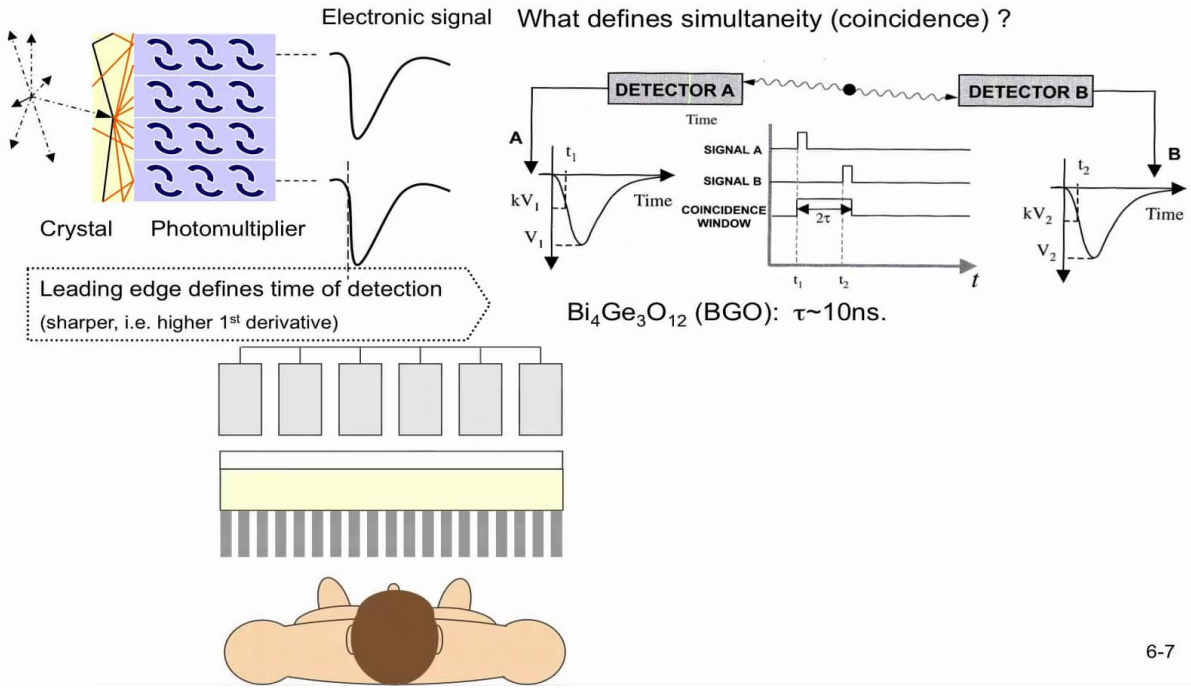
Notes

Summary

16m 58s

What is coincidence detection ?

electronic collimation (i.e. w/o physical collimators)



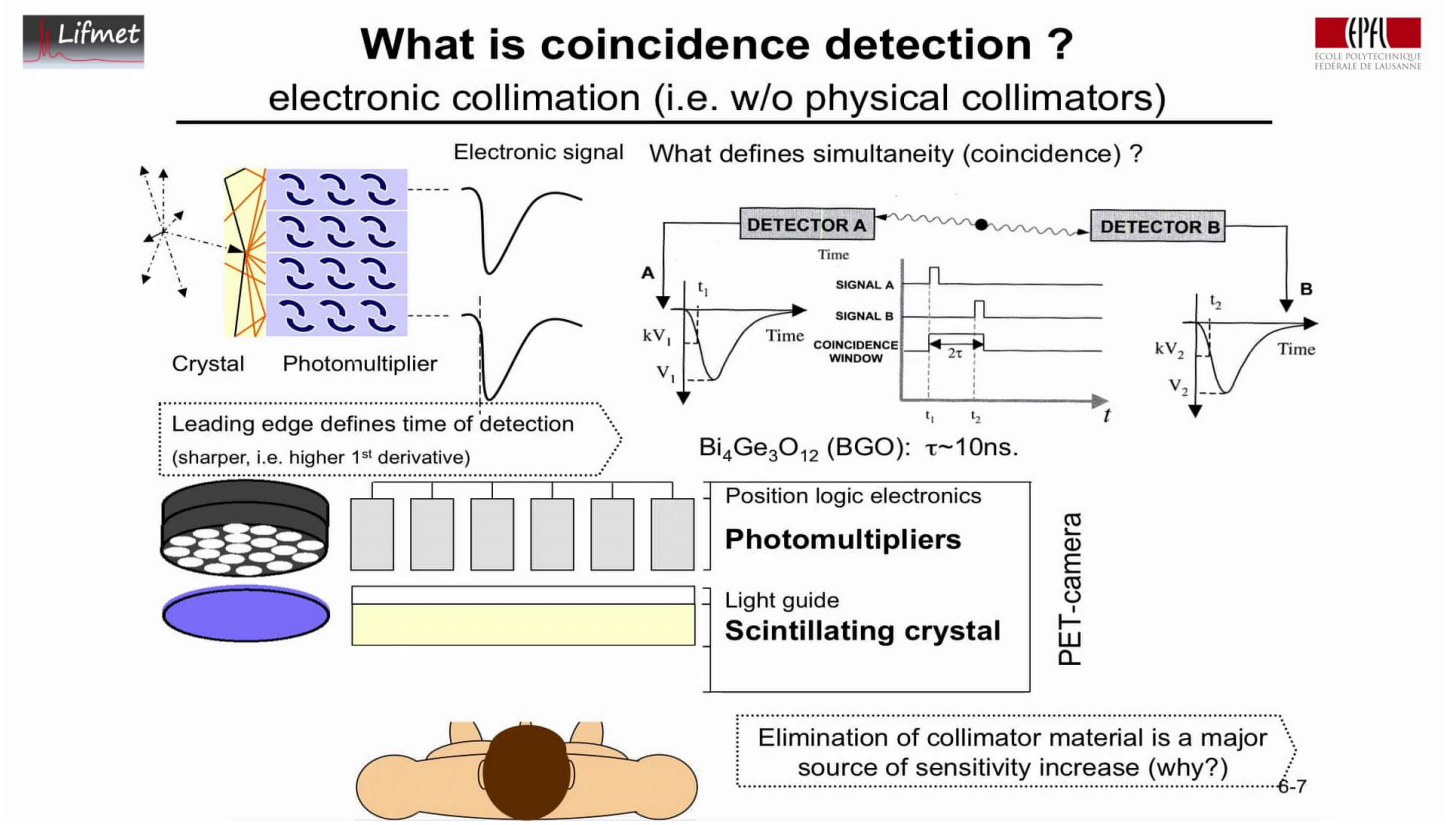
6-7

We have a detector A, a detector B, we detect a signal in detector A-- this could be this one-- detector B could be this one, for example, and we get two signals. And now, we want to say-- determine if these two signals are simultaneous or not. So, we're getting a signal A-- we're detecting the leading edge of signal A-- the leading edge of signal B-- and then, what is-- in practice, is being done, we define a coincidence interval-- tau-- which has a certain value in here-- for the BGO crystal it is, typically, 10 nanoseconds. So, anything that's within this interval-- 2 times tau-- is considered as being simultaneous. So, these events, if they happen within 20 nanoseconds, we would say this has happened simultaneously, and we'll consider them as being due to the annihilation process. If we now recap what the detector is made of-- you see the graphic here-- and you'll say, "Wait, this is the same as in SPECT." And what I'm drawing you here is actually the same situation as what we have in the SPECT scanner.

Notes

Summary

18m 19s



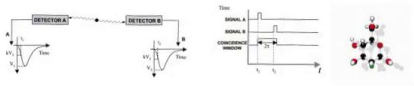
So, we're looking at the gamma camera, the basic elements, here-- now, it's the PET camera, we have the scintillating crystal-- this is unchanged-- we have the photomultipliers-- it is the same thing-- so, we have the scintillation crystal, the photomultipliers, we have, also, position logic electronics, and the light guide-- this is all the same, and here, I have drawn the collimator. But wait, didn't I just say we don't need a collimator? Well, this is the situation-- what you have with the SPECT scanner. And with the PET scanner, we have said we do not need the collimator, so we can forget about this. Here's a piece of the instrumentation of the detection process that we don't need in PET scanning, because we have the simultaneity of events that establishes-- with which we can establish the direction of the x-rays that are being detected. So, what is the consequence of not having the need for collimators? One consequence is that this is an increase in sensitivity that comes from that. Now, why is this so?

Notes

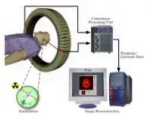
Summary

19m 30s

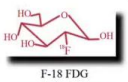
Credits



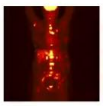
Unidentifiable source *(from the Internet)*



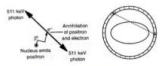
Creative Commons Picture
http://psychology.wikia.com/wiki/Positron_emission_tomography



Cyclotron
https://mnr.mcmaster.ca/index.php/research/additional-facilities/cyclotron

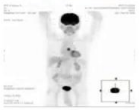


Fundamental chemistry, Ken Costello
http://www.chemistryland.com/CHM130W/05-EarlyAtom/EarlyAtomAssignment.html



“The Essential Physics of Medical Imaging”
Fig. 22-14, from Jerrold T. Bushberg, J. Anthony Seibert, Edwin M. Leidholt, John M. Boone

What is a PET scan? Positron Emission Tomography
https://youtu.be/QZQq7chGoO4



Positron Emission Tomography
https://youtu.be/pOejGHnvSV0

Let's think about it. Why are we getting an increase in sensitivity if we do not need collimators? Remember, the process of collimation is brute force. We just basically say we put the material in place that blocks the x-rays that do not satisfy our geometric condition of collinearity. So, what we're doing is we're taking x-rays, and we're eliminating the bad guys with the wrong geometrical arrangement. So, this collimation is the process of establishing directionality by eliminating all the x-rays that are not coming in perpendicular to the scintillation crystal. Whereas, with positron emission tomography, due to the detection of simultaneous events, we don't do that. So, we can, essentially, accept all x-rays that are being detected, as long as they are simultaneous, that is, as long as they are x-ray pairs. So, this is a major source of sensitivity increase for positron emission tomography compared to SPECT.

Notes

Summary

20m 45s