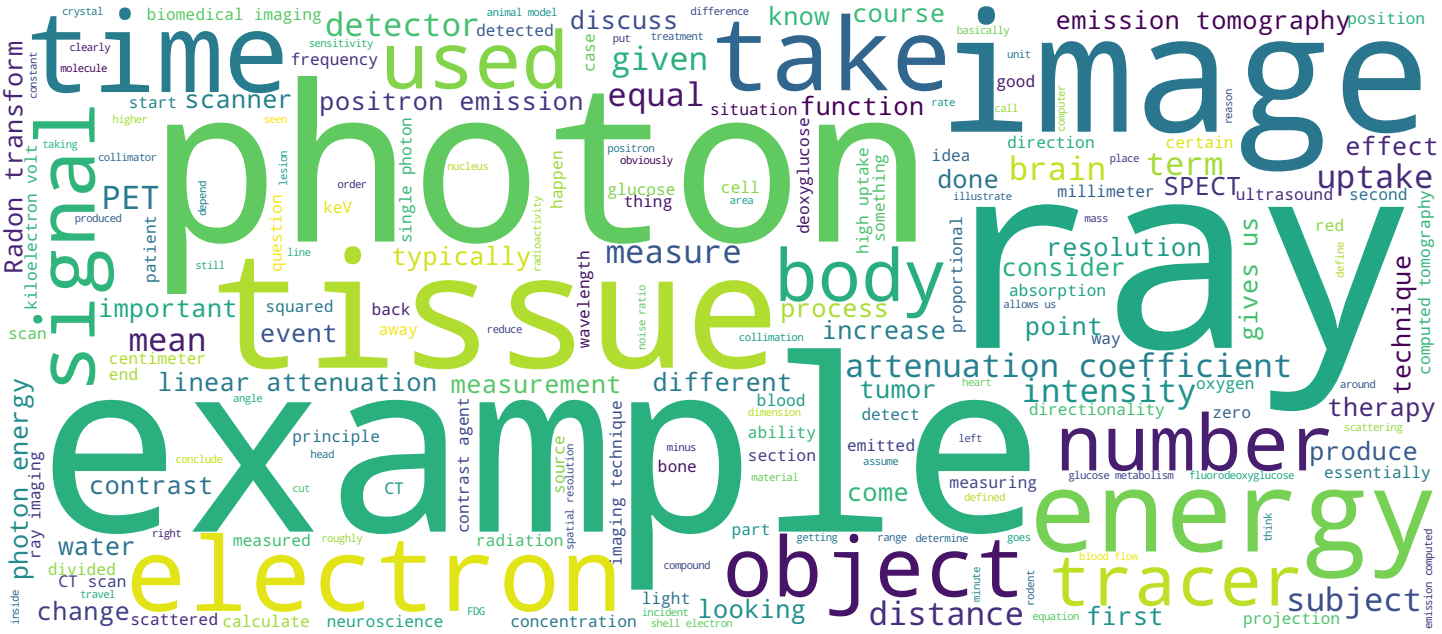
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

6.5 Examples of typical PET tracers; Overview of x-ray imaging techniques

Fundamentals of Biomedical Imaging

Prof. Rolf Gruetter



Search MOOC

Video

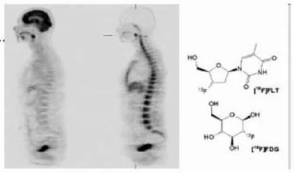
EPFL

6-5. What are typical PET tracers ?

Oncology and neuroscience

Oncology

^{18}Fluoroethyl-Tyrosine (FET)	Amino acid transport
Deoxy-^{18}fluoro-thymidine (FLT)	Proliferation
^{18}Fluoromisonidazole (FMISO)	Hypoxia
^{11}C-Methionine	Amino acid transport and metabolism
$H_2{}^{15}O$	Blood flow
^{18}Fluoro-Deoxyglucose (FDG)	Glucose metabolism



6-16

So, in this section, we want to discuss some applications, primarily oncology and neuroscience, of the positron emission tomography, but first, I want to start out with typical PET tracers. At the end of this section, I'll give a brief overview of the x-ray imaging techniques that we're treating in this course. So, let's look at cancer. We have a tracer that's fluoroethyltyrosine, fluorinating. It is used as a marker of amino acid transport. We have deoxyfluorothymidine, which is used as a marker of proliferation, that is, cell growth. We have fluoromisonidazole, FMISO, a tracer for hypoxia. Then we have C11-methionine, that is amino acid transport and metabolism, and oxygen-15, for blood flow, and finally, fluorodeoxyglucose for glucose metabolism. So these are some of the tracers that are used in oncology. Here's a comparison of two scans. We have FDG. On the left, the brain has high uptake. We have the bladder here, and here is FLT fluorothymidine proliferation. We see some spots here, so they clearly trace different mechanisms in the body. Here is the fluorothymidine molecule, fluorine is here, and the fluorodeoxyglucose, the fluorine is here.

Notes

Summary

0m 04s

6-5. What are typical PET tracers ?

Oncology and neuroscience

Oncology

^{18}Fluoroethyl-Tyrosine (FET)	Amino acid transport
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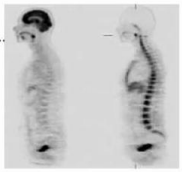
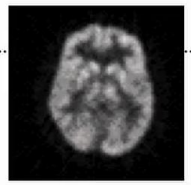
$H_2{}^{15}O$	Blood flow
^{18}Fluoro-Deoxyglucose (FDG)	Glucose metabolism
^{18}FDOPA	Presynaptic dopaminergic function
^{15}O-Butanol	Blood Flow
^{11}C-Flumazenil	Benzodiazepine-receptor mapping

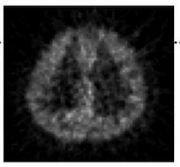


FDG FLT

Neuroscience



FDG or ^{18}F fluorodeoxyglucose



^{15}O Water

6-16

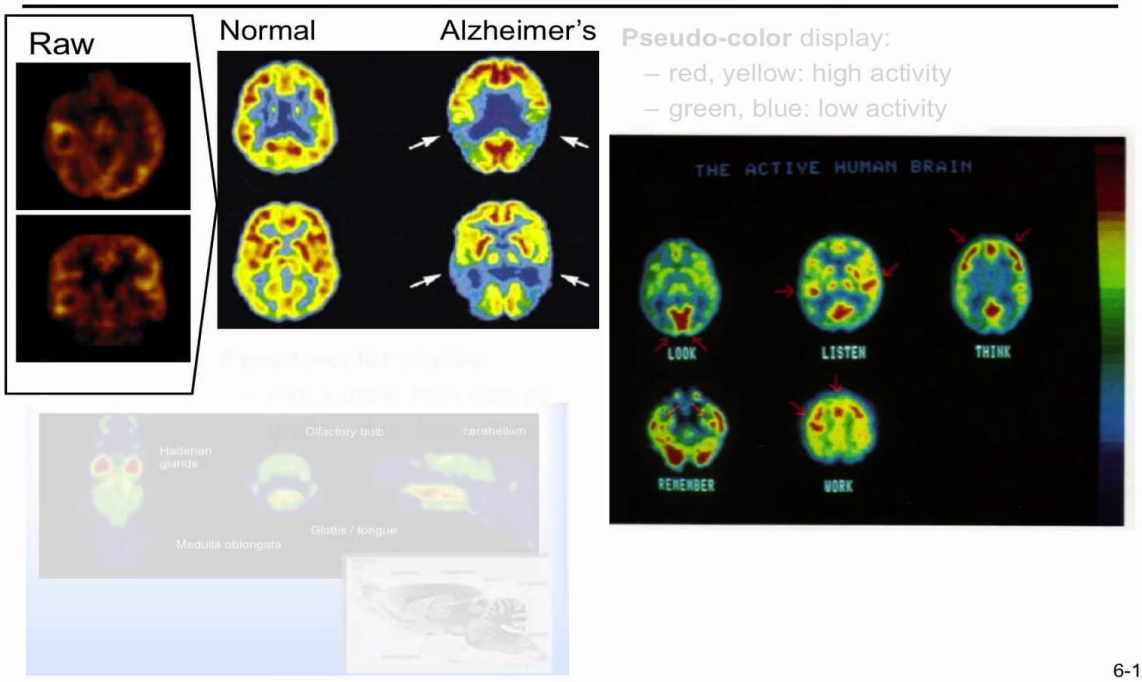
Some of the tracers are also used in neuroscience, so brain research or brain applications. These are are methionine, water, and fluorodeoxyglucose. We also have fluorodopa, that's obviously for pre-synaptic dopaminergic function. We have O15-butanol, as a blood flow marker. We have flumazenil, for benzodiazepine receptor mapping. This is C11, and here are now some examples of the brain. This is the NFDG scan, fluorodeoxyglucose, and here we have an O15 water scan. We can see that the resolution is quite better with the FDG scan than with the O15 water, and the reason is-- part of the reason has to do with the fact that the mean free path length, or the positron range of oxygen-15 positrons, is longer than those of the fluorine positrons.

Notes

Summary

1m 42s

PET: Neuroscience



6-17

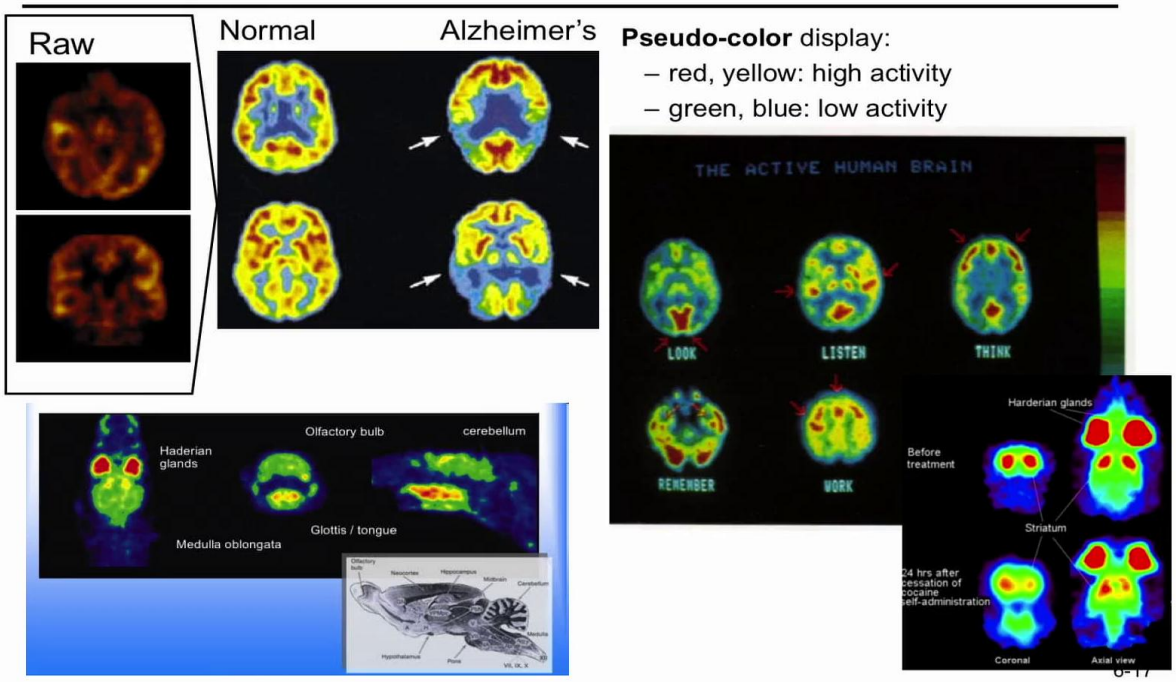
Now, some examples from neuroscience. If we take the color-coded raw image of the brain here, this is what it looks like, and then typically it's pseudo-colored, so we have the red and yellow provides high activity; green, blue, low activity. In a normal subject, here, the uptake would look like this. This is deoxyglucose, it's glucose metabolism in the brain, and here, in a patient with Alzheimer's, one can see that in the back of the head, there is reduced glucose metabolism, consistent with the degeneration of the nervous system. Until the early '90s, positron emission tomography was pretty much-- not the only, but it was the major technique by which one was able to look at how the brain responds to certain mental tasks. So, what is done here is measuring the uptake of glucose, when you look, listen, think, remember or use your working memory, and you can clearly see the uptake of the glucose is different in the different brain regions, depending on the task. This has-- since the early '90s, has been replaced by functional MRI, which we will discuss as part of the MRI techniques in the second part of this course. Here's an example of a rodent brain.

Notes

Summary

2m 44s

PET: Neuroscience

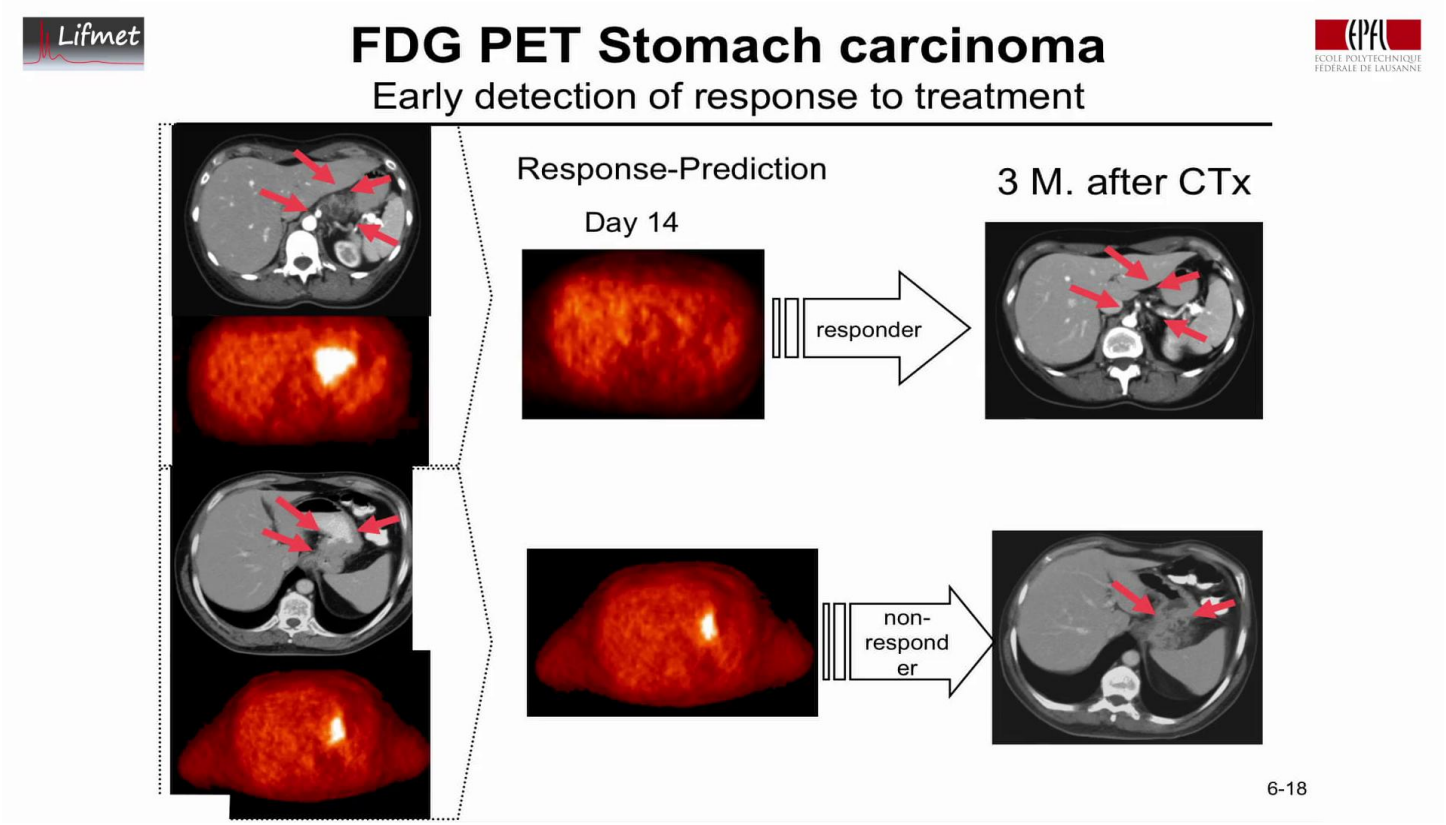


We have the rodent brain; at the front, we have the olfactory bulb, so this is cut through the olfactory bulb. We have the cerebellum and the cerebrum here, and one particular feature of rodents is the Harderian glands, which take up glucose very highly, and they produce an uptake that's very strong. They're not part of the brain, but they have a strong uptake. Here's an example of a measurement of metabolism using PET, and this is an animal model of administration of cocaine-- self-administration. These are some examples of PET in neuroscience.

Notes

Summary

4m 09s

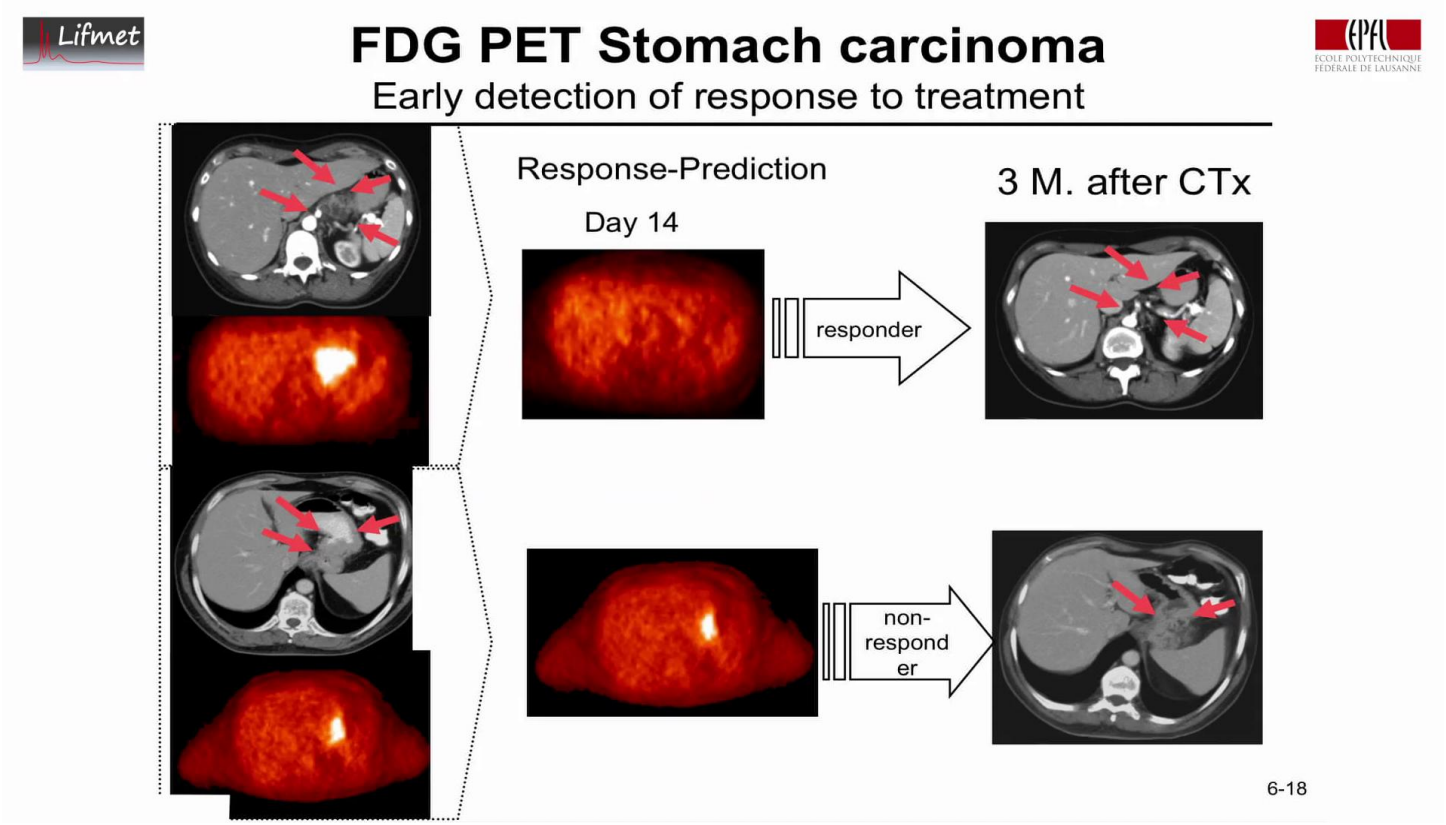


Now, here I want to take a clinical example, and this is a stomach carcinoma. We have the CT scan here, before chemotherapy treatment. The arrows delineate where the lesion is-- the tumor is, and the PET scan gives us here a high uptake indicative of neoplastic cancerous tissue. The subject is then subjected to chemotherapy, and on day 14, the subject here is measured again with PET, and this high-uptake region is gone. So, in this study, one has classified the subject as a responder, and what one finds three months after the chemotherapy-- that the lesion is gone and the treatment was successful. Conversely, here we have another subject, again, with a stomach carcinoma. High uptake of deoxyglucose, and 14 days after the therapy started, the uptake is still there. Prediction was that this subject is a non-responder, and indeed, the carcinoma has stayed in place and not responded to the therapy. Now, ideally, this is-- and I like this example a lot, because it illustrates one of the hopes and dreams of biomedical imaging. Chemotherapy, as you may know, is not a nice treatment. It has a lot of side effects and it is very unpleasant.

Notes

Summary

4m 53s

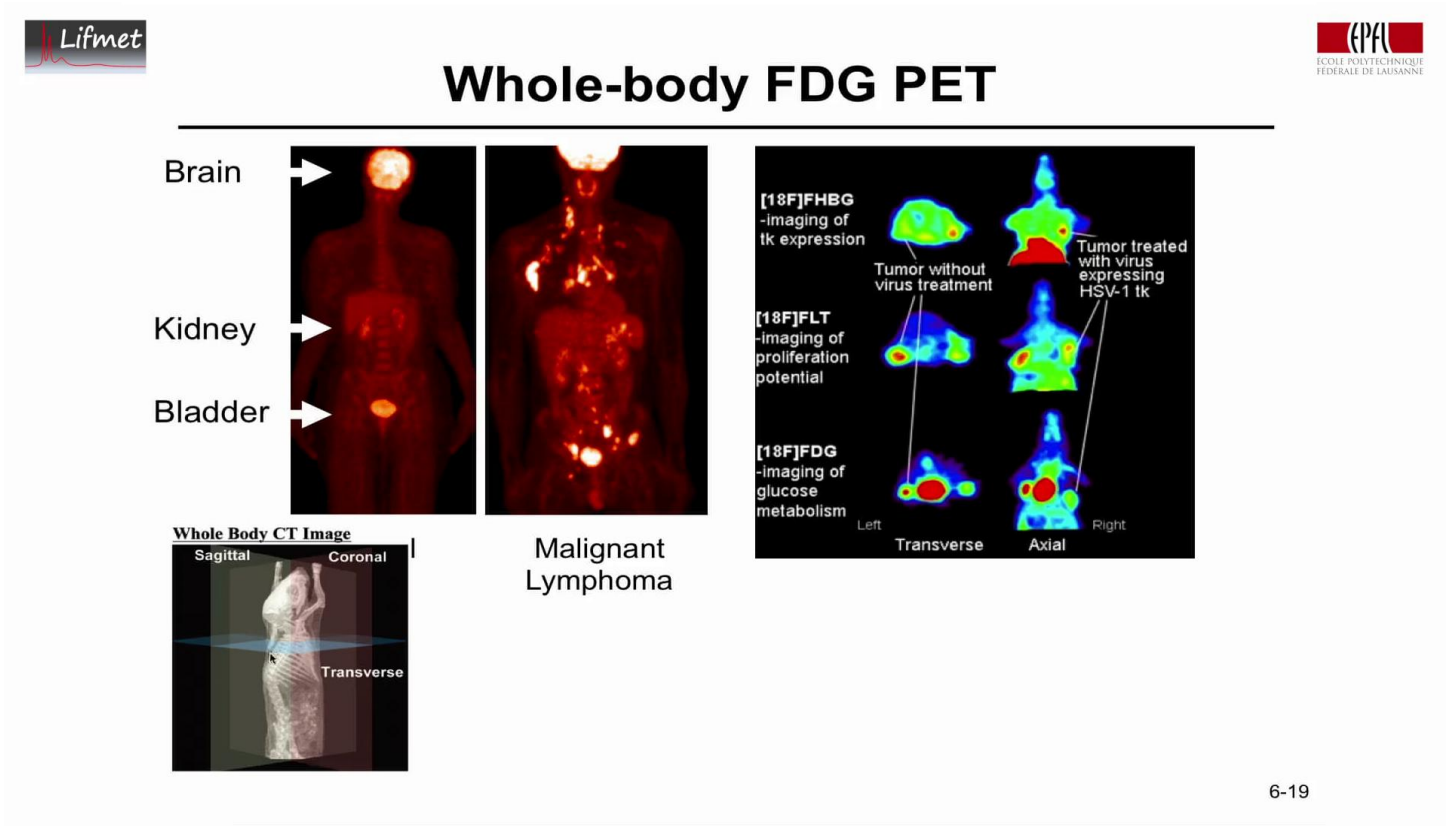


Ideally, we don't want to a few months later find out that we have been undergoing this harsh treatment and our tumor has not responded to the therapy. If indeed we can very early determine, with an imaging technique, "Yes, this therapy is... The tumor is most likely responding to the therapy," and will go away with the therapy, then we can basically, here, for this patient make the decision after two weeks, we'll have to take another approach to therapy if one is available, be it another chemotherapeutic agent, be it another way of treatment, to get this tumor to go away.

Notes

Summary

6m 20s

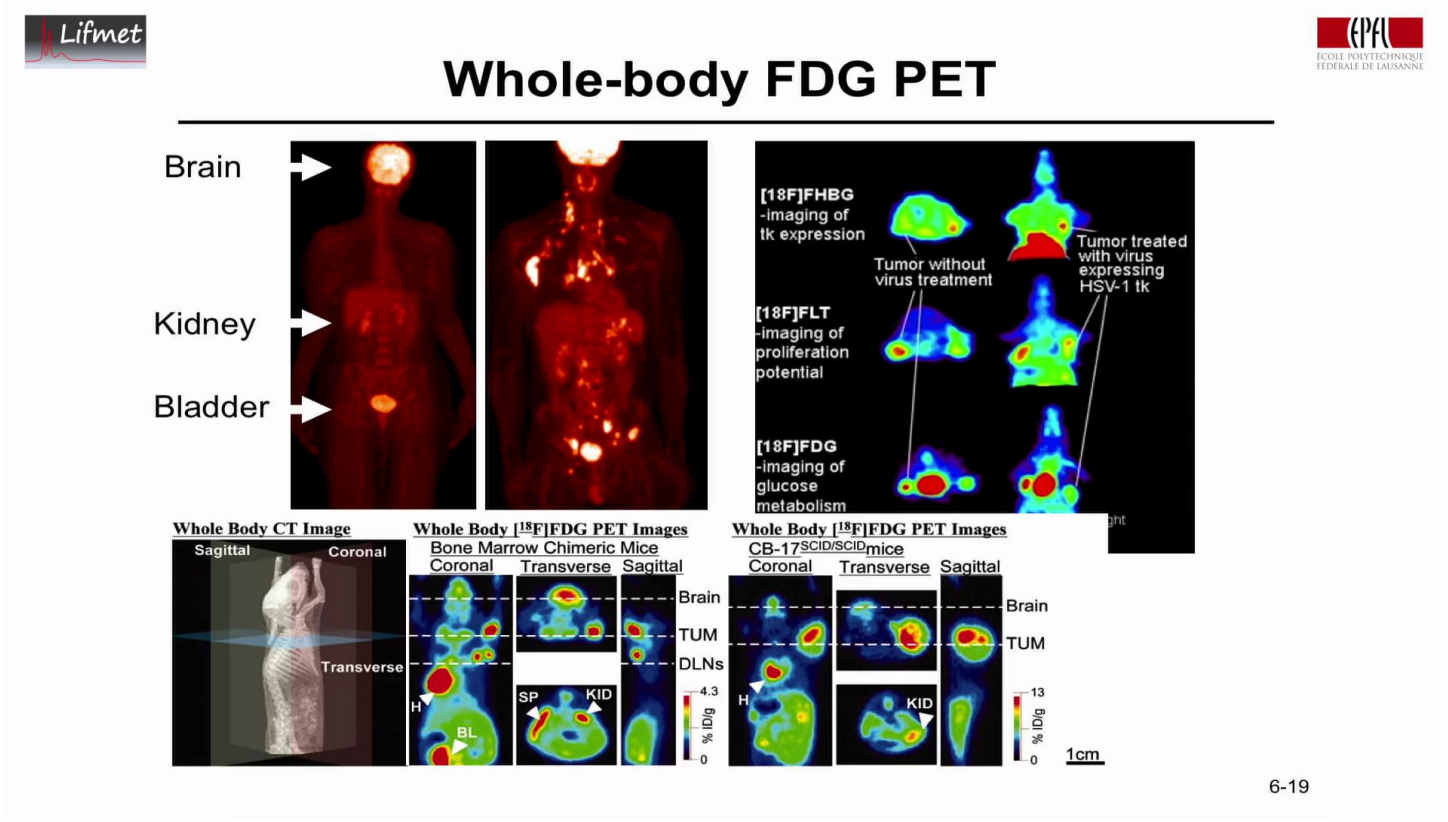


Now, I mentioned that FDG PET is the most ubiquitous clinical use of positron emission tomography. And so, I want to give some examples where FDG PET was used. This is a whole-body image of deoxyglucose uptake. We have the brain here. We have the kidneys, they're lighting up, and we have the bladder, obviously the deoxyglucose is at some point being secreted into the bladder. This is a normal subject, and if you look at a malignant lymphoma, this unfortunate subject has uptake of FDG all over the body, consistent with multiple metastases in his or her body. So, this ability to detect cancer in the body, to determine how many metastases the primary tumor has formed, is among the many reasons, but is a major reason, why PET has become such an important clinical modality in practice. Here's an example of an animal model. We have FHBG. This is imaging of gene expression. We have proliferation with FLT, and we have FDG glucose uptake. This is a tumor without treatment here, and here we have a tumor with treatment, with, actually, gene therapy. An example here is a CT scan, again of a rodent. We have the CT scan, and then, the cut through the body here gives us the uptake of the FDG into the body in these chimeric mice, and these are another set of mice, also, here.

Notes

Summary

7m 01s

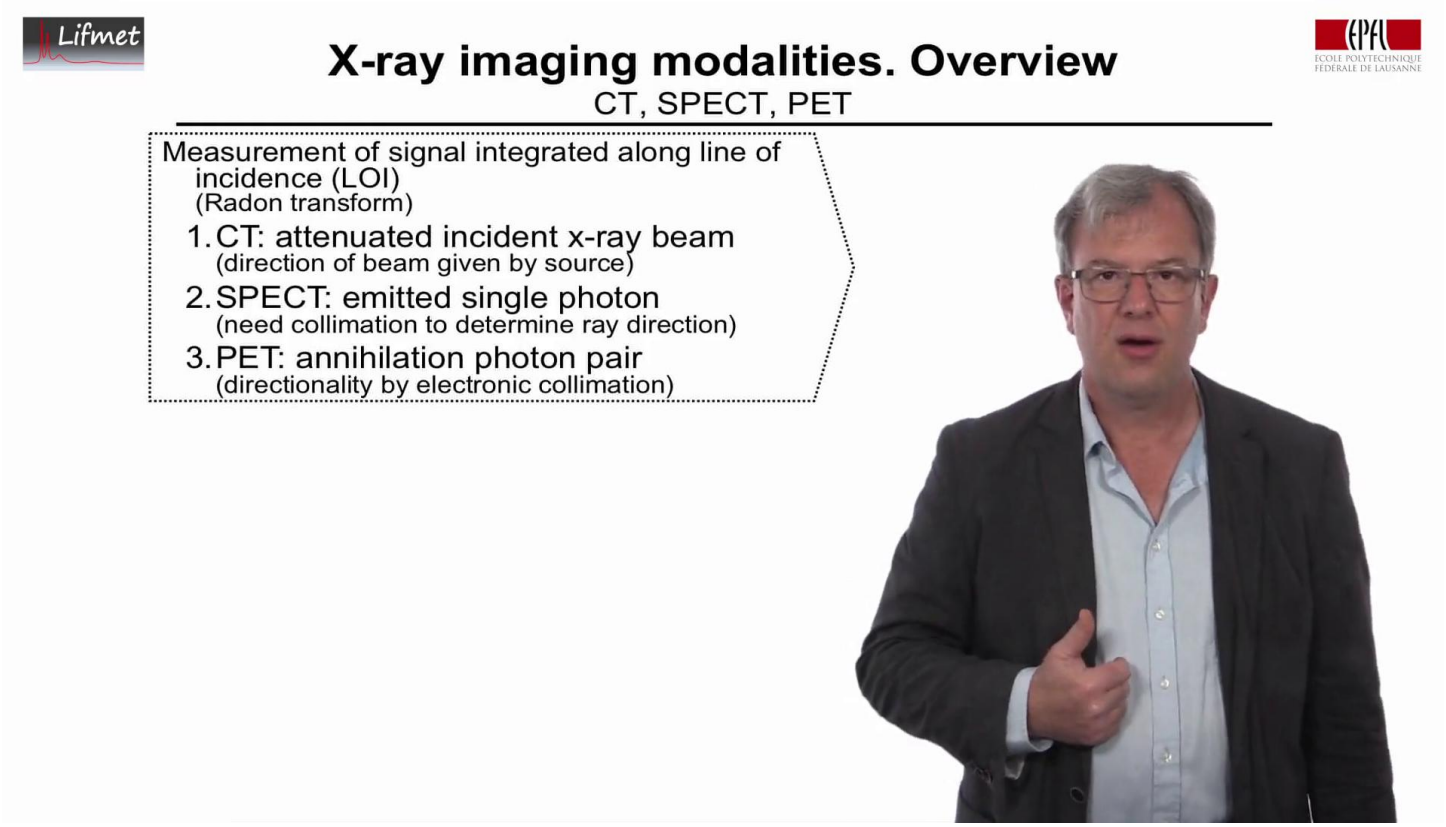


The ability of biomedical imaging to provide us with information of what is happening with the animal with the gene therapy, or with the therapy, et cetera-- and one has to consider that the generation of genetic animal models is relatively costly-- so the ability to take an animal, subject it to biomedical imaging repetitively, and thereby obtain good measures of the evolution of the disease or whatever we are looking at, allows us to reduce the number of animals that need to be produced, and also reduce the number of animals for animal research. This concludes the examples for positron emission tomography.

Notes

Summary

8m 46s



Now, in this section, at the last, I want to provide a rough overview of the x-ray imaging modalities that we've discussed. We have primarily discussed CT, SPECT, and PET, and they share a few things in common. They do a measurement of a signal integrated along the line of incidence. This provides us mathematically with a Radon transform. They are a bit different in how they do it. In computed tomography, it's the attenuated incident x-ray beam. What is important to define the Radon transform is that we have the directionality of the x-ray, so, the direction of the beam is given by the x-ray source. Source and detector location, that defines the directionality of the photon. For SPECT, single photon emission computed tomography, we're measuring a single photon that's being emitted from a nucleus, and here, to determine the x-ray direction, one needs to use collimation, brute force collimation. For positron emission tomography, one measures the annihilation photon pair, so, the directionality of the photons is given by electronic collimation; that is, the coincidence-- simultaneous-- detection of two photons in two different detectors.

Notes

Summary

9m 29s

X-ray imaging modalities. Overview

CT, SPECT, PET

Measurement of signal integrated along line of incidence (LOI)
(Radon transform)

1. CT: attenuated incident x-ray beam
   (direction of beam given by source)
2. SPECT: emitted single photon
   (need collimation to determine ray direction)
3. PET: annihilation photon pair
   (directionality by electronic collimation)

Apply correction to measured Radon transform
(attenuation, scatter, etc.)
Backprojection or central slice theorem:

Finally an image!

	CT	SPECT	PET
Projection Encoding	Defined by incident x-ray (collimation to reduce scatter)	Collimator essential	Coincidence detection (electronic collimation)
Spatial Resolution (rodent)	100μm-mm (μm)	Typical 10mm (Variable and complex) (1.5-3 mm)	4.5-5mm at center (1mm)

6-20

We have to apply to the measure Radon transform corrections-- either corrections for scatter, for attenuation, et cetera. And then, one can use, since we have the Radon transform, one can use back-projection or central slice theorem, and finally, obtain an image. And here, what's important is, the minute we can write the process of detecting the signal as a Radon transform, we know we have the algorithm in place-- that is, back-projection-- that allows us to reconstruct an image. So, let's summarize here. The projection encoding is defined by the incident x-ray. One does use collimation to reduce scatter. For SPECT, we need a collimate, that's essential, there's no other way we can establish the directionality of the x-ray, and for PET, it is coincidence detection that does the projection encoding, or as it's also called, electronic collimation. To give you an idea what the spatial resolution is, spatial resolution is on the order of hundreds of microns in humans to millimeters for CT. For SPECT, we have around a centimeter, and around four to five millimeters for PET at the center.

Notes

Summary

10m 51s

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Attenuation	= measurement variable (Varies with energy)	Complex correction (Varies with photon energy)	Accurate correction (transmission method)
Radionuclides	None (contrast agents)	Any with hν= 60-200keV	Positron emitters only

6-20

If we are looking at a micro-CT, micro-SPECT or micro-PET, small animal scanner, we're on the order of micrometers for CT, a few millimeters for SPECT, and we can get down to a millimeter-- that is the theoretical positron range for PET. Attenuation in CT is the measurement variable. What here is important that the attenuation varies with photon energy. In SPECT, the attenuation requires a complex correction, which also varies with photon energy, and for PET, we can do an accurate correction with, for example, the transmission method. What are the radionuclides in CT? We do not use radionuclides that we administer, so, it is the absorption of the x-ray in the body that we are measuring, but we can administer so-called contrast agents. Those are compounds that modify the linear attenuation coefficient of the tissue where they are, so they are... but they are not strictly-sense radionuclides, although they have similar properties as the tracers that are being used for the other techniques. For SPECT, essentially any single-photon emitter that are typically between 60 and 200 kiloelectron-volts can be used, and for positron emission tomography, we are obviously limited to nuclei that emit the positrons, so we are only able to image positron emitters.

Notes

Summary

12m 09s

X-ray imaging modalities. Overview

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6-20

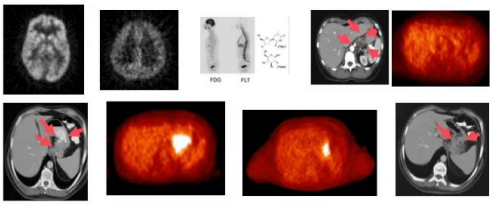
So, we have a wider choice of radionuclides with SPECT than with PET, but with PET we have a higher sensitivity, as we have coincidence detection. In terms of cost of the techniques, the cost increases to the right, for the instrumentation-- for pure purchase of the scanner, increases to the right. In particular, since PET nowadays is only sold as PET-CT.

Notes

Summary

13m 43s

Credits



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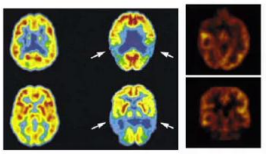
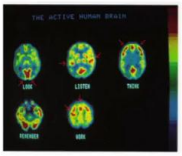
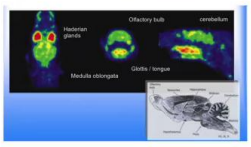


Positron Emission Tomography
http://www.diag1.com/pet.html



FDG PET
https://quizlet.com/15672574/lecture-6-brain-coverings-vessels-and-ventricles-flash-cards/



PET scan of the brain from above rat, CCC Jülich Germany
https://lhc-machine-outreach.web.cern.ch/lhc-machine-outreach/faq/mammography.htm

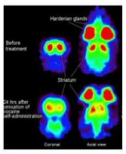
So, this concludes the section on x-ray imaging techniques. These are the major techniques that we have discussed. Next week, we will discuss how we analyze radio tracer data that we've obtained with either contrast agents or with x-ray emitting tracers in the body.

Notes

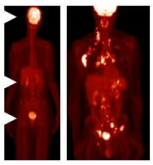
Summary

14m 11s

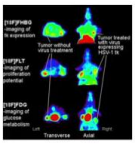
Credits



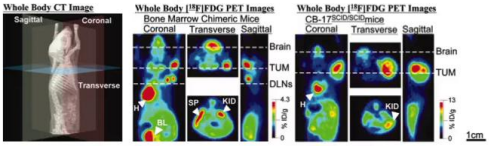
Pharmacokinetic analysis of plasma curvesobtained after i.v. injection of the PET radioligand
http://meddic.jp/raclopride



Medizintechnik, Der gläserne Patient M.Schwaiger,S.Nekolla,E Rummeny Klinikum rechets der Isar
http://www.muenchner-wissenschaftstage.de/mwt2004/content/e160/e707/e728/e779/filetitle/Medizintechnik_ger.pdf



PET Imaging
Chad Hanney 31 Juillet 2013



Chengyi J. Shu et al., Proc. Natl. Acad. Sci USA 2005; 102, 17412.

Notes

Summary

14m 36s