Introduction to Biomedical Imaging Systems

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Lecture - 28

Nuclear Med Radiotracers

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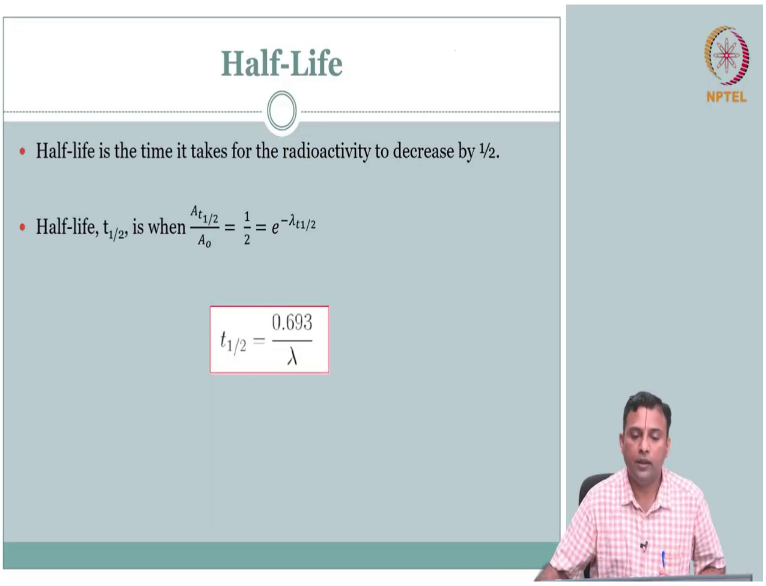

Half-Life

- Half-life is the time it takes for the radioactivity to decrease by ½.
- Half-life, $t_{1/2}$, is when $\frac{A_{t_{1/2}}}{A_0} = \frac{1}{2} = e^{-\lambda t_{1/2}}$

$$\boxed{t_{1/2} = \frac{0.693}{\lambda}}$$

So, we talked about Radioactivity and we hit upon this lambda right, the decay constant and another important idea about your half life. So, now, it is time to move on to see what are the different modes of decay that are possible ok.

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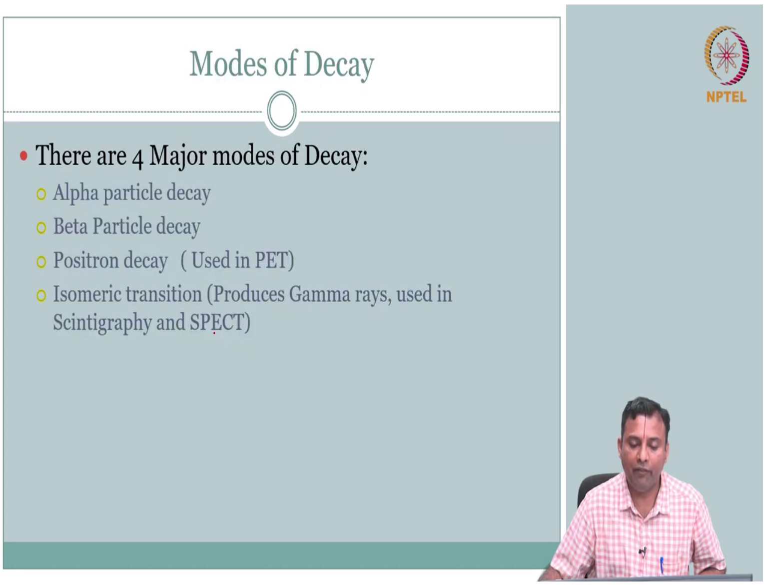

Modes of Decay

- There are 4 Major modes of Decay:
  - Alpha particle decay
  - Beta Particle decay
  - Positron decay (Used in PET)
  - Isomeric transition (Produces Gamma rays, used in Scintigraphy and SPECT)

So, we have radioactivity, we have four major modes of decay of interest right, and as you can see here some of it is these are particles; alpha particle decay, beta particle decay, we will go into each of them you know one by one.

But essentially what you see here; there are four different ways of which you could see both particulate right, similar to how we saw in our X ray. We had particulate interaction and electromagnetic interaction. Similarly, here you have alpha particle, beta particle and then this is positron decay and finally you have isomeric transition.

So, the last two in fact this is also a positron is also a particle, but you will quickly see that essentially because of the positron we still are going after, so it is used in positron emission tomography right. So, this is used in medical imaging. Isomeric transition which produces gamma rays is used also in nuclear medicine. Scintigraphy and SPECT we will see that.

So, the others, other particle interactions so we had particle interaction particulate interaction in X rays and electromagnetic a radiations right. So, here also there are particulate radiations and electro magnetical (Refer Time: 02:06) right. So, like before these are not of interest to us.

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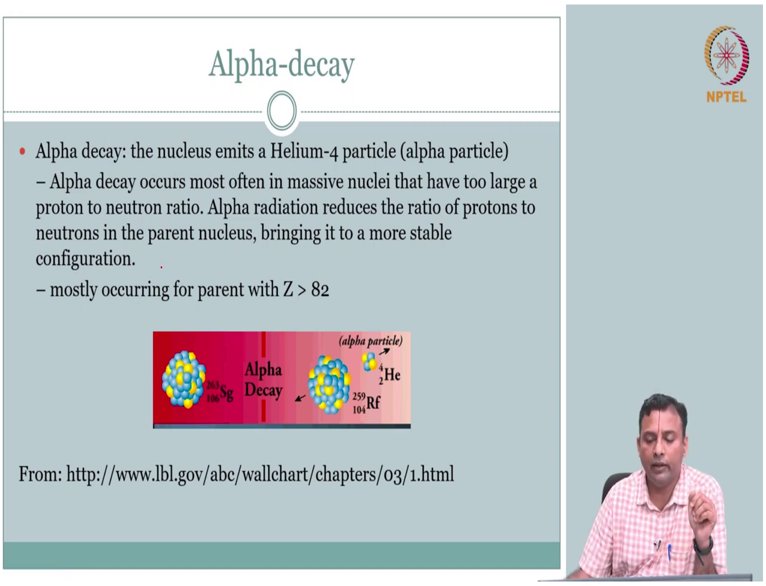

Alpha-decay

- Alpha decay: the nucleus emits a Helium-4 particle (alpha particle)
  - Alpha decay occurs most often in massive nuclei that have too large a proton to neutron ratio. Alpha radiation reduces the ratio of protons to neutrons in the parent nucleus, bringing it to a more stable configuration.
  - mostly occurring for parent with Z > 82

From: http://www.lbl.gov/abc/wallchart/chapters/03/1.html

What are these? So, alpha decay. What is alpha particle decay? So essentially, we talked about this unstable to becoming stable. The nucleus is unstable it will try to come to stability and we talked about this in terms of remember neutron and protons right. How many protons and how many neutrons are there and we talked about this line of stability.

So, if it turns out that it is unstable because of this proton and neutron ratio is not you know is not close to the line of stability, then what is going to happen? It is going to rearrange itself and send out a alpha particle in this case. What is an alpha particle? Here, helium right, you have H 2 4 this is your alpha particle.

So, clearly you can see from here that typically right; your alpha decay occurs typically in a massive nucleus. So, you see here 162 263, so massive nuclei where you have a large proton to neutron ratio. So, what is the objective? So, if it is not along the line of stability what is going to happen? It is going to shed out right it is going to shed out alpha radiation to reduce this ratio of protons to the neutrons. So, once that is reduced it will become little more stable ok.

So, the idea is, this is alpha particle decay, but we will not study more about this, because it is not really used for our medical imaging purpose that we are going to talk. So, this happens mostly with you know we said heavy nucleus. So atomic number greater than 82 right. So, we will not worry about this.

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Beta Decay

- Beta decay occurs when, in a nucleus with too many protons or too many neutrons, one of the protons or neutrons is transformed into the other.
- Beta minus decay (or simply Beta decay): A neutron changes into a proton, an electron (beta particle) and a antineutrino
- Mass number A does not change after decay, proton number Z increases or decreases.

From: http://www.lbl.gov/abc/wallchart/chapters/03/2.html

Then you have your beta decay. In beta decay there is something interesting. So, beta decay occurs again when in a nucleus with too many protons or too many neutrons right. You have this neutrons and protons in the nucleus when the numbers are not conducive, right there if it is not appropriately distributed then you have a problem, it is not stable.

So you can have either of this right in unstable form, it may have this imbalance. So, it can switch right one of the one of the protons or neutrons is transformed to the other so that the ratio is broughts down to your line of stability, so that it becomes more stable ok. So, you can have beta you can have when we talked about beta decay when this rearrangement take, you can have what is called as beta minus decay.

So, this beta minus decay is what is simply talked about as beta decay. Here what happens, a neutron changes into proton. So, you have neutrons and protons and neutron changes to proton here and in the process an electron and antineutrino are emitted. So, this electron is called as your beta particle. So, commonly when we say beta decay they refer to the beta particle that is coming out or the electron that is coming out ok.

So, naturally when the electron comes out with the energy right it is a particulate and then that ionizing that causes ionization. So, it is a particulate emission after that right, so we are not really interested in that. So, here you have a notice you have your carbon 614 form and you have your N 714 and that with beta particle and antineutrino ok.

So, what to be noticed? You notice the mass number is same right, mass number is same. Whereas, the element atomic number has changed or in other words your mass number is same your proton is changed right. Mass number does not change after decay, proton number increases or decreases. This is what happens in a beta decay. In beta decay, if your electrons come out right then it is your typical beta particle emission beta particle emission, beta d; this we are not going to use ok.

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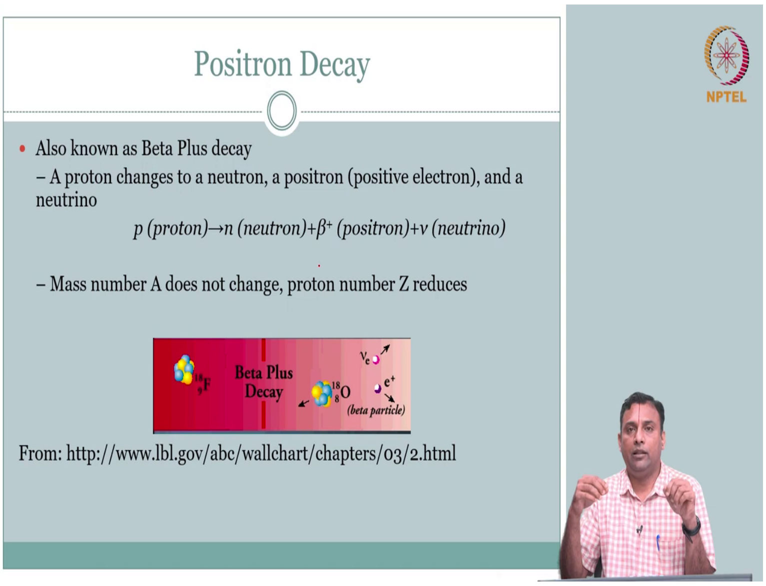

Positron Decay

- Also known as Beta Plus decay
  - A proton changes to a neutron, a positron (positive electron), and a neutrino

$$p\ (proton) \rightarrow n\ (neutron) + \beta^+\ (positron) + \nu\ (neutrino)$$

  - Mass number A does not change, proton number Z reduces

From: http://www.lbl.gov/abc/wallchart/chapters/03/2.html

What we are going to use is another type of beta decay which is also known as beta plus decay. What is beta plus decay? Here a proton changes to neutron, right a proton changes to neutron and it gives out a positron. What is a positron? Neutron, proton, electron we saw; what is a positron? Positron is a positively charged particle with a mass of an electron.

So, you can think about it as a positive charged electron ok, and a neutrino. So, proton so this rearrangement is the key for to make sure that they become along the line of stability. So, proton gets converted to neutron in the process it re sends out a positron and a neutrino ok.

So here, here also what do you notice? You notice it is a beta it is a beta decay. Beta decay can be beta plus or beta minus ok in beta plus or beta minus. The idea is there is a rearrangement of your neutrons and protons. So, you notice here in beta plus decay or was it is positron decay also your mass number is same, your atomic number has changed ok. So, mass number does not change, a proton number reduces in this case clear. So, this is your positron decay.

But we talked about, we are not interested in particle this is a particle as well right. We are not really interested in particulate interaction. We are interested in gamma rays, right or that is what we were thinking all along. So, what happens to this positron, are we using it? Yes, you see the modality name positron emission tomography. You will say positron is used, but how it is used is essentially this positron when it is created, it is not just going to be there.

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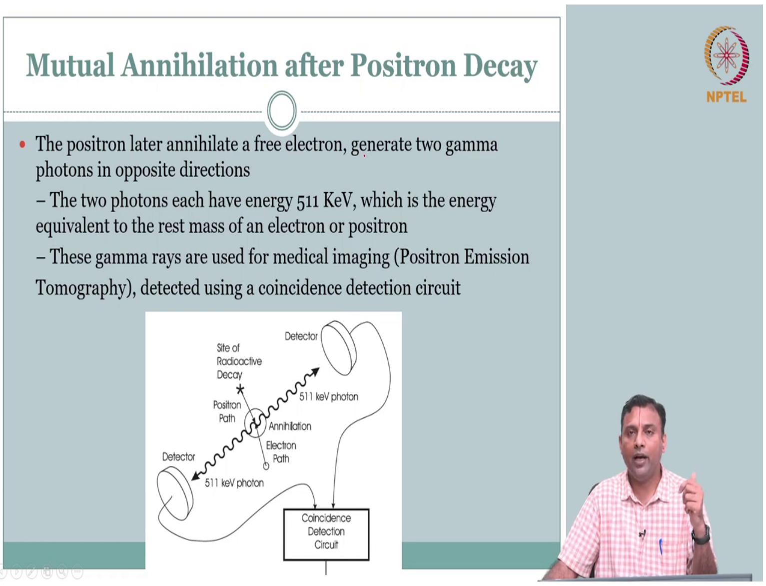

Mutual Annihilation after Positron Decay

- The positron later annihilate a free electron, generate two gamma photons in opposite directions
  - The two photons each have energy 511 KeV, which is the energy equivalent to the rest mass of an electron or positron
  - These gamma rays are used for medical imaging (Positron Emission Tomography), detected using a coincidence detection circuit

It is going to move and you, usually what happens is, it hits a electron, there is a free electron that is there. So this positron, after it is created right after this beta decay positron is created it finds a free electron. When it finds a free electron it gets annihilated. We talked about this term annihilation before as well, remember. In the charge particle bremsstrahlung right it can get annihilated by the nucleus.

So we have seen this term annihilation before. So, here what happens? This positively charged the electron, when it moves around, there is a free electron that is there, so they collide and they get annihilated. When it is annihilated what happens is, you generate two photons that energy gives raise to two photons which is a gamma photons and then they go in the opposite direction, that is the key.

Gamma photons they go in the opposite direction. What is the energy of these two photons? You are talking about electrons right, either it is positively charged mass or electron. The mass is same. Mass is electron mass. So, what is the relationship between mass and energy?

Half MC square. So, essentially this when this annihilation takes place, the photon that comes out has an energy of 511 kilo electron volt which is the energy equivalent of the rest mass of electron or positron. Because positron mass is same as electron, so right equivalent of the rest mass.

So, this is the so the good news about this is, you know the exactly there is a energy particular energy that you are looking at, that is one aspect. The other is, there are two of them which are exactly going opposite because the you know conservation of momentum. So, it will go in the exact opposite direction; 180 degrees apart. See that is a another powerful information right.

So, these gamma rays essentially what we do is, even though it is called positron emission tomography, this positron quickly degenerates right and gets annihilated and creates to gamma rays of 511 kilo electron volt. So, what do you do is in medical imaging, this gamma rays that are coming at 511 kilo electro volt 180 degrees apart, if you can detect right which we call coincident detection.

Will talk little more about this when we get to PET instrumentation, but you get the idea. So, this is used, even though this is a particle right positively charged electron, it is actually the gamma the energy that comes out because of the annihilation that we are detecting ok.

So in some sense, once you are able to detect that you know it is coming along a line, so coincidental. So, you can then get an idea on where this decay is happening, where this radioactivity is happening. Which is our main idea right? We going to send some radioactivity in based on the measure from outside, we are going to say where that radioactive is source is located in the body, that is the big picture right ok. So that is for positron decay.

So we have alpha, the beta. We saw beta minus beta plus. Beta plus is called as your positron and then you have isomeric ok.

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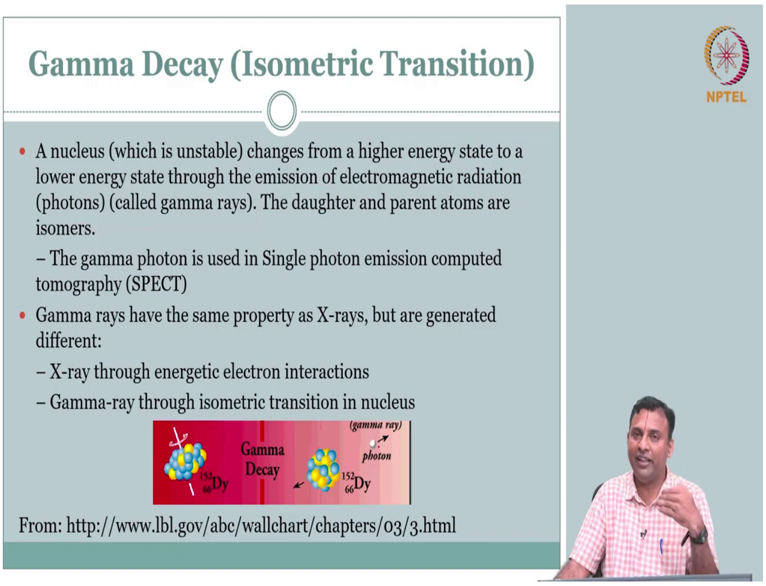

Gamma Decay (Isometric Transition)

- A nucleus (which is unstable) changes from a higher energy state to a lower energy state through the emission of electromagnetic radiation (photons) (called gamma rays). The daughter and parent atoms are isomers.
  - The gamma photon is used in Single photon emission computed tomography (SPECT)
- Gamma rays have the same property as X-rays, but are generated different:
  - X-ray through energetic electron interactions
  - Gamma-ray through isometric transition in nucleus

From: http://www.lbl.gov/abc/wallchart/chapters/03/3.html

Isomeric transition is another way to get gamma decay. So here again, the logic is same, you have unstable, but here the mass number of atomic number does not change. It is just so that look at here. Your mass number and atomic number does not change after the decay. What happens is, this is in a excited state. So, it has in a higher energy state what we call as meta state ok.

So, a nucleus is unstable. It has a higher energy state so it has to come to its lower energy state, it will give out the energy and that energy happens to be in gamma ray gamma band so it is called as gamma rays. So, here both the parent and daughter are called as isomers, meaning they have right you look at here. So, it is a same atomic number, same mass number, but you have some energy that is coming out in the gamma range.

So, we could we also call this that high energy state as a metastate right. So, it comes down to ground state and gives. So this is something that is commonly used ok we will talk about this. So, where it is used? This is used in your SPECT right which we will which is single photon emission.

The name is very suggestive right; single photon you see single photon that is coming, emission, radioactivity is emitting, single photon emission, computed tomography computed tomography. We should know by now, we did X ray computed tomography that is you catch from outside and then project and say where it came from right. So, you can get an idea.

So here, the wherever the sources it is going to decay, if it is going to send gamma rays, the outside you have detector collect the gamma rays and then you use your algorithms to reconstruct and say where this single photon is coming from. That is your source of your radioactivity. So, source of your radioactivity and how much of radioactivity, those are the key things that we are going to exploit in nuclear medicine ok.

So, the difference I mean just to make sure because we do this comparison all the time right, because we covered X ray first and now we are covering gamma rays, just a alert we did alert you before as well. So, gamma and X rays the; these are a just photons having gamma, having slightly higher energy than your X rays. So, their interaction with tissue will be right same physics that we covered before.

But what is key here is, the origin is different, right the gamma rays are generation is different. X ray we talked about energetic electrons; whereas, in gamma rays it is generated using isomeric decay or isomeric transition. So, the origin is different but apart from that the photon, when the photon comes out how does it interact with the tissue is going to be similar to what we did for X ray.

Even though here, we are not interested in; see is subtle, but very important, here we are not actually interested in the gamma photon interacting with the tissue. Whereas in X rays, we were very interested in X ray interacting with the tissue photoelectric effect we wanted to maximize. Whereas here, the objective is not that right. Hopefully you get that subtle point. We will reiterate this as we go forward.

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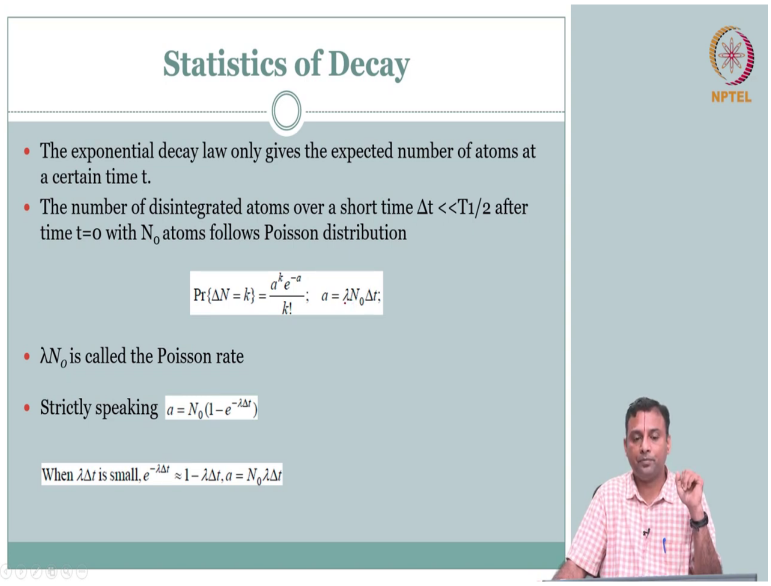

Statistics of Decay

- The exponential decay law only gives the expected number of atoms at a certain time t.
- The number of disintegrated atoms over a short time Δt <<T1/2 after time t=0 with N_0 atoms follows Poisson distribution

$$\Pr\{\Delta N = k\} = \frac{a^k e^{-a}}{k!}; \quad a = \lambda N_0 \Delta t;$$

- λN_o is called the Poisson rate
- Strictly speaking $a = N_0(1 - e^{-\lambda \Delta t})$

When $\lambda \Delta t$ is small, $e^{-\lambda \Delta t} \approx 1 - \lambda \Delta t, a = N_0 \lambda \Delta t$

So, now the question is ok. We have this radioactivity and there is a radioactive decay, we talked about half life, we talked about this radioactivity and we talked about the modes of decay. How all this radioactive atom decays are right.

So now, the question is, ok since we have a formulation is the decay deterministic that can I say, ok if I give this much gram right you talked about half life. So, I know the lambda for the material, so can I say that it is deterministic? Not, what you did here exponential law that we did right, that gives you what is theoretically expected.

However, if you are to do this experiment take some x grams x milligrams of a radioactive material and you know you observe it over time some delta t, so it has its half life right. So, you observe over some short time, see how many photons have disintegrated right, how many atoms are disintegrated.

And, you take the same material, same everything, same time duration, another time and do it and do it multiple times. What will you notice? You will notice that you will not get the same expected value every time. This theoretically this is what you expect using your exponential model right exponential decay law. But you will not get every time the same value, you will be in and around that, but when you average several of them statistically the mean will tend to the ground truth or what is expected theoretically.

So, each time you even though it is a same material, same lambda, you start observe it over the small time interval, there is a random process right the decay is a random process. So, the number of disintegrated atoms over a small time delta t. What do we mean by small time? We have some time benchmark which is your half life.

So, when you are observing your t over a small time in relation to your half life of that material of the radioactive atom right, then it turns out that this the radioactivity will follow a Poisson distribution, N o atoms right. The number of disintegration over short duration when you start with some N naught of the material at t equal to 0 will follow a Poisson distribution.

What is Poisson distribution we know. Probability of the disintegrations right number of atoms disintegration equal to some k is equal to a power k e power minus a by k factorial. So, this a is your mean. What is the mean here in this case? I do radioactivity, every time I do the experiment I get the number of disintegrations.

So, mean is lambda N naught delta t, but this is not straight forward right. This is the value of the mean, this is the Poisson distribution, but this one let us see if we can agree to this how did we get a equal to lambda N naught delta t. So, we talked about this guy already. Delta t is far far less than t half life. So, if that is the case this distribution is valid and therefore, this mean is obtained right. So, let us think about what happens, lambda N naught is called as your Poisson rate that is of interest rate or Poisson rate, how fast the decay.

But, really speaking what do we know? From our previous module we know lambda is your decay rate t half, we know as when you have half right half life. So, the point is, we know in some sense what is a number of atoms that are have disintegrated. If you know number of atoms that have disintegrated, so you start with some quantity some have disintegrated in some time, so you have the remaining.

And what did we know about this radioactivity? Radioactivity is proportional to the amount of atoms that are radioactive atoms that are there, that is what we saw right. So, here in that sense we know your radioactivity is going to be what you started with minus whatever is disintegrated in the time delta t.

So, this is strictly your a. This is what you have, radioactivity after delta t. However, you notice, we made this assumption, delta t is far far less than t half. So, if your lambda delta t is much small right, if this is quantity is very small then when lambda delta t small then you can approximate the exponential to 1 minus lambda a t.

In this case, you can get your a to be lambda naught delta t clear. So, all this is valid for a short time interval of observation. So, you give the radioactivity and the radioactivity starts to disintegrate right, atom starts to, this the radioactive atom is disintegrating. At what rate? That is characterized by its lambda. All you know is t half is 0.693 by lambda.

So, if you are taking observation over a short duration delta t, short in the context of delta t far far less than your t half life then the photons that are the disintegrations are coming right, so you are capturing the number of counting the disintegrations. That is going to be a Poisson random variable. So, this whole process is a Poisson random process and you have a mean value ok.

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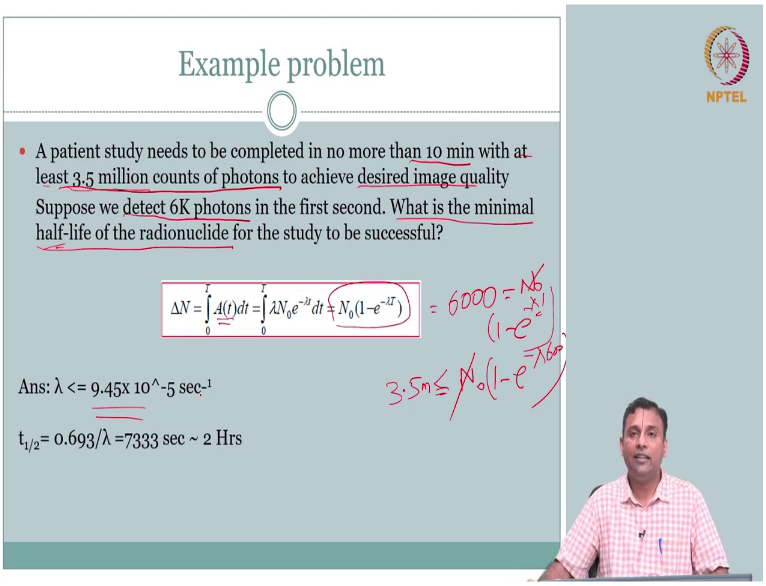

Example problem

- A patient study needs to be completed in no more than 10 min with at least 3.5 million counts of photons to achieve desired image quality Suppose we detect 6K photons in the first second. What is the minimal half-life of the radionuclide for the study to be successful?

$$\Delta N = \int_0^T A(t)dt = \int_0^T \lambda N_0 e^{-\lambda t} dt = N_0(1-e^{-\lambda T})$$

$= 6000 = N_0(1-e^{-\lambda 1})$

$3.5m \leq N_0(1-e^{-\lambda 600})$

Ans: λ <= 9.45x 10^-5 sec-¹

$t_{1/2}$= 0.693/λ =7333 sec ~ 2 Hrs

So, how do we get a hang of this concept? Just some numbers let us throw in the context of a typical imaging right. What is a number that we are talking about?

So, you have a patient. So, key information; patient study needs to be completed in no more than 10 minutes right. This is a practical constraint. I want to do the imaging in 10 minutes, but I need to have at least so many counts of photon. Because, we will talk about the signal to noise ratio, but you know already number of photons have a influence on image quality. We say X ray photon we did that. So, here it is going to be gamma photon. So, you can the detail may be slightly different how you capture it, but then the concept is going to be similar right.

So, you need maximum more number of photons to have good quality. So, what is that? At least 3.5 million counts of photons to get the desired image quality. So now, the question is, you cannot do it with more than 10 minutes you have given that upper bound. You are given a partial information, you are able to count 6000 photons in the first second right. So, we are able to count we are able to detect 6000 photons in the first second. So, these are the constraints that are given. What is the minimum half life of the radionuclide?

So, in order to achieve these constraints, what should be my radionuclides or at least I could have potential different radionuclides. What is the half life? What is the minimum half life that I should have to satisfy this condition? So, what do we do? Well, looking at it you know you are given some information. Here, within first second I have 6000 right, so this is 6000 photons after radioactivity accumulated over 1 second right. So, you can get your delta N accumulated over 1 second, this is your radioactivity right.

So, you have your lambda N naught e power minus lambda T from your previous slide right. So, what is this? This is your 6000 right. This is the number of photons; detected number of photons. So, delta N is this guy. Here, I am given some N naught times 1 minus e power minus lambda, T is given to be 1 right. So, this is from first information. What is required or 10 minutes I want 3.5 million counts ok at least 3.5 million counts.

So, this is going to be again your delta N is again 3.5 million right equal to can be equal to no, it says at least 3.5 million counts right. So, will have to have some this quantity should be at least means less than equal to N naught into 1 minus e power minus lambda T is 10 minutes ok, so 1 minute you have 60 seconds 10 minutes you have 600 seconds clear.

So now, what do you need? You need to find lambda. I can find right. If I take the ratio between these two I can cancel my N naught, so I will be left with only one unknown right. So, if you calculate that you will get lambda to be 9.45 10 power minus 5 second inverse. Just punch it in the calculator you should get this. But I hope you understand the logic ok.

So, if this is the case then you can look at what is the minimum half life. This is lambda from this, what is asked this your half life you know the relationship between half life and lambda right. 0.693 divided by, so if you do that you are getting approximately about two hours. I mean, I hope you get the sense of numbers here. So, the idea is, the half life is in the order of

2 hours right and your lambda, because we made this assumption lambda T right is much smaller than your 2 hours right.

So, look at the constraints. You can get still thousands of photons, but they are saying at least millions of photons are required to have a reasonable image quality. So, you see the constraint between, if the radioactivity is small then you will have to acquire for longer duration right, because it will take so much more time to give out so many number of photons. If the radioactivity is high, then you will have to quickly catch the data, right quickly catch the photons ok. So, there is going to be some constraints.

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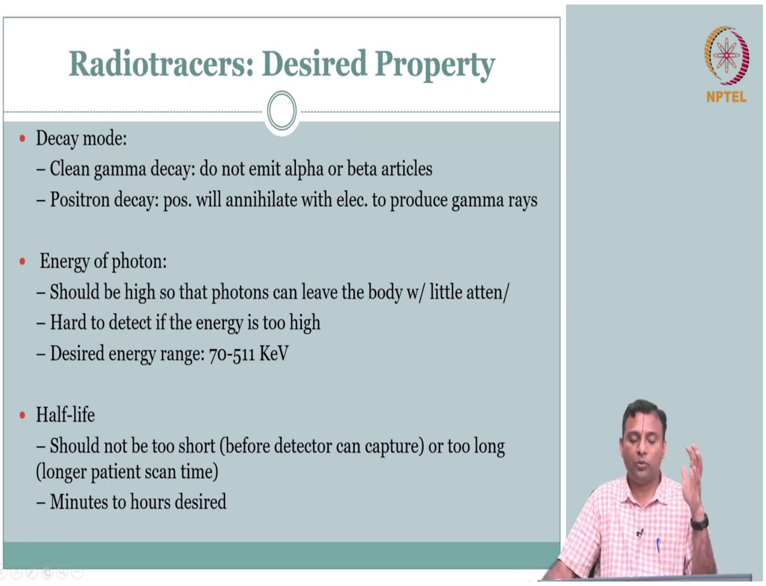

Radiotracers: Desired Property

- Decay mode:
  - Clean gamma decay: do not emit alpha or beta articles
  - Positron decay: pos. will annihilate with elec. to produce gamma rays
- Energy of photon:
  - Should be high so that photons can leave the body w/ little atten/
  - Hard to detect if the energy is too high
  - Desired energy range: 70-511 KeV
- Half-life
  - Should not be too short (before detector can capture) or too long (longer patient scan time)
  - Minutes to hours desired

So, what are the, I mean we talked about constraints, but the more ideas ok. So now, we understand this idea of sending the radio tracer and there is this photons that are coming out modes of decay, we talked about that. And, so is there and we just had an example where we talked about lambda right or half life of the radio tracer. So, is there what are the desired property? So, some of the aspects that we covered we will have to just put it more formally; one is decay mode.

What do you think about the decay mode? The radio tracer should undergo decay which is good for medical imaging. I do not want particulate right, I do not want alpha, I do not want beta, what do I want? I want gamma or positron right. So clean gamma decay, so I do not want these two.

So, I want to have a radio tracer that can be engineered so that it will have a clean decay producing only gamma, no alpha or beta, otherwise you will end up dosing the patient right. Positron decay will annihilate and again produce gamma rays. So, you want only these two ok. Energy of the photon; what is your energy of the photon? What is your energy of the photon? We talked about X ray interacting with the tissue and there we said if it is too low it will get absorbed, if it is too high it will not interact with the tissue.

In our case, what do we need? The photons should be, should it interact with the tissue or not? Well, we already you should not right. We want the photon wherever the radioactivity is inside the body, if it decays and sends the photon gamma photon out we should be able to catch the photon and say, it came from this location and this is how much it is coming. So, we are not really interested if it is going to get attenuated along the path right that is not good for us.

So, the idea is, if you have high energy, we know from X ray also high energy you do not interact with the tissue. So, you should choose a energy right energy of the photon so that it does not interact with the tissue. So, it should be high so that the photons can leave the body without or with little attenuation.

Because, if it is too high what is going to happen? You have to detect it right. So, then your detector has to be carefully done. We talked about this earlier. If the body is not detecting your detector has to detect the energy. So, again your thickness of your detector all those things what we talked about in X ray, similar issues will start to come here.

So, the idea is you have to have high energy so that it does not interact with the body, but if it is too high it would have difficulty in stopping it on the detector as well. So, you have to make sure it is not too high. So roughly this is the range that is operated ok.

Clearly; that means, there is some detector material is going to be engineered for this purpose right, because in X ray we did not really deal with so much of energy we beam hardened it and so that was not you know, we did not really talk about worry about that. Whereas here, we have too high is also a problem and therefore, a desired range is this one.

Then comes half life, what do you mean by half life? You think oh I need to have a high half life meaning radioactivity happens faster. So, what will happen? I can have a within a short duration I can have many photons. So, we may be tempted to think that I you need a half life that is high or in the other words, half life that is low right. Lower the half life more the disintegrations. So, you want ok so that logic seems ok, because you want more number of radioactivity be detector in short time.

But what will be the problem if it is too short, if the half life is too short? You have to give the radio tracer to the body, it has to allow it to go right, it has to distribute and then the radioactivity you have to detect the radioactivity. If it is too short what will happen is, by the time you prepare the patient and you set it up your detector may not be able you know your detector will not be good it has to be such faster. So, it puts lot of requirements.

And, the radioactivity, we talked about the t observation should be less, like delta t should be less compared to your half life you do, right that is the idea. So, if it is already small half life, you have to acquire even shorter duration. So that becomes a difficulty with respect to logistics ok.

So, you do not want really low, at the same time you do not want the half life to be too high. Safe right, half life is no problem this half life is 1 year right, no problem correct it takes 1 year to get, but then what is going to be the problem? I want to do imaging, I want to see these activities come out, I want to see where it is coming out differentially.

So, if it is too large a half life then also it is not useful for me from my imaging perspective. So, it should not be too short or too long. If it is too long then like I said patient scan time will be increased. I have to wait there for a long time before I can catch sufficient photons. The previous example we said right some million photons have to be captured. If the half life is so large, then I have to wait there to you know forever to get the million photons.

So, there is a sweet spot somewhere in the minutes to hours is kind of desired. So, you are engineering these radio tracers, you have radio chemists who do this. So, you engineer this radio tracers, these are some of the desired property, is that all? No.

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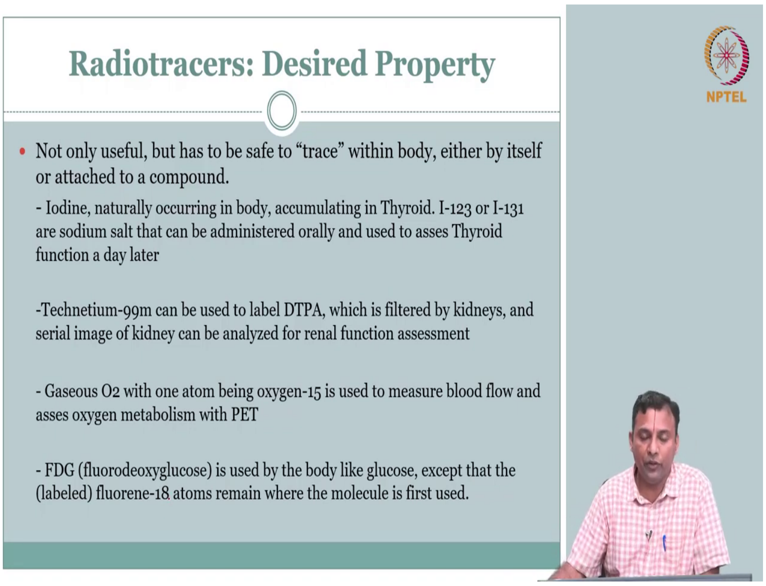

Radiotracers: Desired Property

- Not only useful, but has to be safe to "trace" within body, either by itself or attached to a compound.

- Iodine, naturally occurring in body, accumulating in Thyroid. I-123 or I-131 are sodium salt that can be administered orally and used to asses Thyroid function a day later

-Technetium-99m can be used to label DTPA, which is filtered by kidneys, and serial image of kidney can be analyzed for renal function assessment

- Gaseous O2 with one atom being oxygen-15 is used to measure blood flow and asses oxygen metabolism with PET

- FDG (fluorodeoxyglucose) is used by the body like glucose, except that the (labeled) fluorene-18 atoms remain where the molecule is first used.

We have some more right; more importantly ok all this is engineered nicely, so with respect to our timelines half life all those things are good. That is not sufficient alone. It has to be safe biologically because you are going to give it to the body right. So, the trace quantity should be safer right. You want to attach that to some compound that you take and it goes. So, it has to be safe that is a another important requirement ok.

So, therefore, you have some natural candidate for this. Say for example, iodine which is naturally available in the body. So, you can start to right, in the thyroid it starts to accumulate in the thyroid. So, you can start to have some compounds, you can label some iodines right I-123 or I-131 are all sodium salt, so you can label that and administer it orally.

So, what happens here? These have a half life that are in the order of days ok and therefore, this is since its safe right, since this is mimicking your natural iodine, you can allow it will take its own time to go right, you can do thyroid imaging a day later. So, you have had enough time, so that the body by itself thyroid will accumulate right take all the iodine. So, iodine whatever you gave in the labeled radio labeled tracer, it will go and you can do thyroid imaging after a day. So, you can assess the functionality of the thyroid using this radio.

So even though this is in the order of days right, the half life of this is the order of days it is safe and it is you know kind of labeled using a naturally available compound and therefore, it is safe to use. Likewise, you have a technetium-99 which is typically used right. So, it can label DTPA. So, where this happens is actually filtered by the kidneys. So that means, I can monitor the functioning of the kidney right. Serial image of kidney can be analyzed to do renal function assessment.

So, what is the idea of kidney? It is doing the filtration. So, if I give a technetium based radio tracer, it goes through the filtering, so in the kidney and so you can essentially start to image that and see how the filtering is happening right. So, this is one another, so the idea is you have to have a radio tracer that can naturally be labeled to find some processes, some functionality, some physiology ok, that is also an important aspect.

You can use gaseous oxygen, only thing is you can knock being oxygen 15. So, when you do this what can you do? It will go wherever blood goes right, so you could assure measure the blood flow using this tracer. And of course, you can also assess the oxygen metabolism. So, the idea is the radio tracers not only should be useful right all of these are all safe ok.

Another commonly used safe one is your glucose right; FDG, fluorodeoxyglucose. Here again, the idea is it is very similar to your glucose, it is just that labeled with fluorine. What happens? It will go wherever glucose is going, it gets used glucose gives you energy right, so it gets a participated in the metabolic activity.

So, when that happens, the glucose it does its job. Your the labeling right, a fluorine 18 that goes and it goes along with the a glucose, once the glucose is consumed a fluorine stays there. So essentially, the more the glucose activity the more radioactivity from there because fluorine gets accumulated. So, in that sense this can be used as a functional imaging for metabolic activity.

So, you know typically you would have seen some brain scans right. We want to know when you think hard which part of your brain is active. When you are moving your right arm which part of your brain is active. So, brain is using energy right. So, it is so the idea is even for routine activities of course, if you have a cancer like we showed in one of the images earlier for pet, if you have cancer, cancer is aggressive right, it is going to be metabolically more active.

So, it is going to use up more glucose and therefore, radioactivity will start to accumulate there and contrast it out. So, either so these are very routine; so, it is going after the functional aspect ok. So, not only should it be useful, it should be safe and it should be able to participate in the functional aspect without affecting the function.

So, it cannot change the function, so it has to participate there. So, here for example, fluorine. Fluorine does not participate in anything; glucose does its job. Fluorine goes there and sends here is where the radio you know glucose is getting used up. It will send that information right or at least you can infer that. It does not alter the metabolic activity per se ok. So, those are the desired properties that you would want for your radio tracers.

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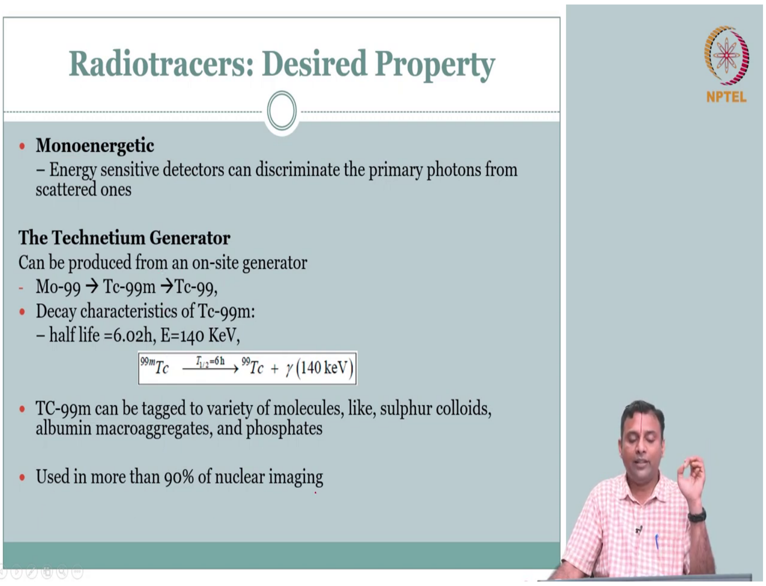

Radiotracers: Desired Property

- **Monoenergetic**
  - Energy sensitive detectors can discriminate the primary photons from scattered ones

The Technetium Generator

Can be produced from an on-site generator

- Mo-99 → Tc-99m →Tc-99,
- Decay characteristics of Tc-99m:
  - half life =6.02h, E=140 KeV,

$$\boxed{{}^{99m}Tc \xrightarrow{T_{1/2}=6\,\mathrm{h}} {}^{99}Tc + \gamma\,(140\,\mathrm{keV})}$$

- TC-99m can be tagged to variety of molecules, like, sulphur colloids, albumin macroaggregates, and phosphates
- Used in more than 90% of nuclear imaging

Of course not, but last, but not the least, we would like it to be mono energetic. We had this wishful thinking even for our X ray right. Why? Because, see if it is mono energetic, if I know I am going to get only one energy then any other energy I know is coming from some scattered gamma right. You have your Compton scattering.

So the gamma photon could get hit, get scattered. Similar to your X ray right I mean, so Compton scattering can happen. So, if you have a range of energy that is coming out then you do not know some is from the signal some is from the Compton. Whereas, if you get only one energy then you know anything apart from this energy is probably from Compton scattering.

So, energy sensitive detectors can discriminate primary photons from scattered ones. So, you if you have mono energetic right, the radioactivity, the tracer that you have, if the radioactive decay happens such that it gives one energy only right then that is preferred.

So, for this reason example is a technetium right; technetium is a we did see that earlier as well. So, here it can be prepared on site ok. And, like you said this metastate right is usually intermediate state, so you have this molybdenum that gets when you do this preparation it gets to your technetium-99 which is in the higher energy state which we call as the metastate, but it cannot state stay in that metastate for right because it is a high energy unstable state.

So, immediately what it will do is, it will give out gamma rays and come down to more stable technetium-99. So, the idea is, you can prepare you can prepare this right at the site before administering. And so the characteristics if you see for this, half life is about 6 hours energy is 140 kilo electron volts. So now, you see the thing half life in the order of hours. So, it is neither too short nor too long and also you get only one energy ok. So, this is very desirable.

So, we are talking about desirable conditions right. So, you have gamma decay ok, modes of decay gamma decay; good, then mono energetic; good, half life neither too long nor too short; good, safe it can be labeled with several things right. So, it can be tagged with variety of molecules like sulphur, colloids, albumin, phosphates. So, you see already that because of all the it takes right checks out most of the desirable properties and therefore, more than 90 percent of nuclear imaging studies use technetium ok.

So, this is a we talked about some of the desired property and this is a routinely used one because it satisfies several of this. By the way there are maybe 1000, 1200, 1500 radio tracers that have been you know developed. Maybe about 10 20 are also available in the market right, as a compound that can be used.

Each one has you know if depending on the functionality that you are imaging some have some requirement, so you have those, but 90 percent of them you have technetium right. So, you look at where you started out you have say 1000, 1500, but then when you start to put all the desirable features you come to a handful ok and then maybe you have to still custom make it for certain disease certain physiology that they want to understand. Maybe you will have to create a new compound. So, this is what know the active areas that people pursue in radio chemist for example.

How do you prepare, how do you synthesize this, how do you know, there is process, there is several levels of understanding and finally, of course, how do you use this for a can you label it, does it really uptake in the body, then is there as is it safe to take that. All this is a very you know involved skill sets.

Of course, from biomedical engineering perspective our interest is ok we understand all this, so when I say I want better image quality I know the complexity involved in the signal origin, these are all signal origin right I give the radioactivity after that I get the signal. So, this is signal source. So, there is a lot of engineering for that.

But, typically when you are looking at a imaging systems perspective you are imaging engineer, you have to understand appreciate this problem and therefore we can you know we will have to do the best we can with respect to the other components that are in our at least we think that we have some more control. Say for example, your detector, your setup right ok.

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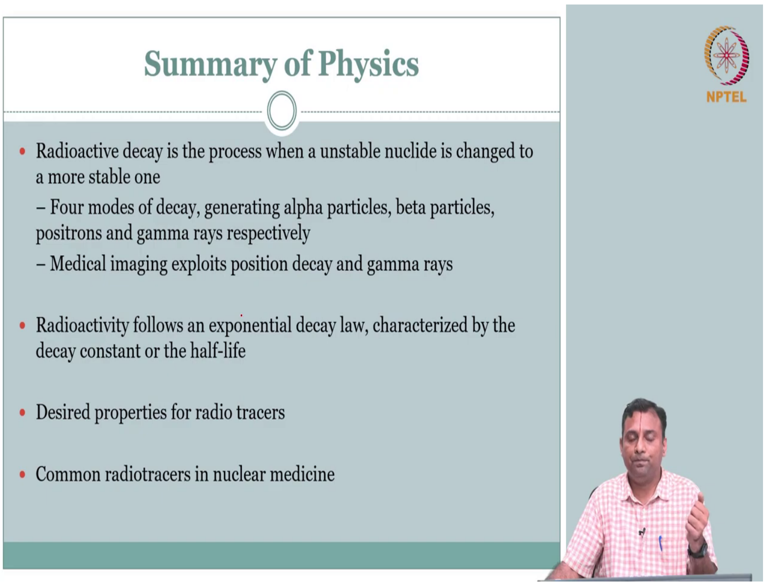

Summary of Physics

- Radioactive decay is the process when a unstable nuclide is changed to a more stable one
  - Four modes of decay, generating alpha particles, beta particles, positrons and gamma rays respectively
  - Medical imaging exploits position decay and gamma rays
- Radioactivity follows an exponential decay law, characterized by the decay constant or the half-life
- Desired properties for radio tracers
- Common radiotracers in nuclear medicine

So, to summarize radioactive decay is a process where you have your unstable nuclide changed to more stable one. In that we talked about the different modes of decay you have particulate decay and also you have gamma. Only the gamma is used in gamma rays is used in your medical imaging. So, we also talk talked about this radioactivity right.

You can model that using exponential decay law and when we talked about that law, we talked about the half life as well. So, you have a exponential model and then you have a half life that is usually characteristic. And, we went on to talk about some of the desired property of radio tracers and also few of the radio tracers that are commonly used or routinely used.

So, this is a good time to stop the physics of radioactivity. Then we will the nuclear medicine remember we will now move on to the different modalities that exploit the gamma rays ok, your SPECT right. So, if you really think about it, SPECT is having a t tomography. When we did X ray, we did X ray physics we started with projection radiography right chest X ray right projection radiography. So, like that we have a equivalent here, analogous here, which is scintigraphy.

So, we will start with scintigraphy and then we will go to the tomography. So, SPECT would be single photon emission tomography and then we will have positron emission tomography ok. So, with this physics we should be able to cover the instrumentation and the imaging equations and image quality for the three modalities scintigraphy, planar scintigraphy, SPECT and PET ok.

Thank you.