Biophotonics
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Lecture 40
Future of PDT and Photothermal Therapy (PTT)

Welcome back. We are at the end of our discussion on Photodynamic Therapy or Light-Activated Therapy for that matter and even in this course, we are going to discuss the future of photodynamic therapy and the new therapy light-based therapy that is coming up which is called Photothermal Therapy, PTT. Let us go on with it.

So, what are the future we have thus far seen what photodynamic therapy can do what PDT can do, I am not going to repeat it once again, I have been repeating it for the past four chapters, so by this time, you should know what PDT is and how it works and so what exactly we envision as our plan in the future, where PDT can be improved, where PDT can be optimized.

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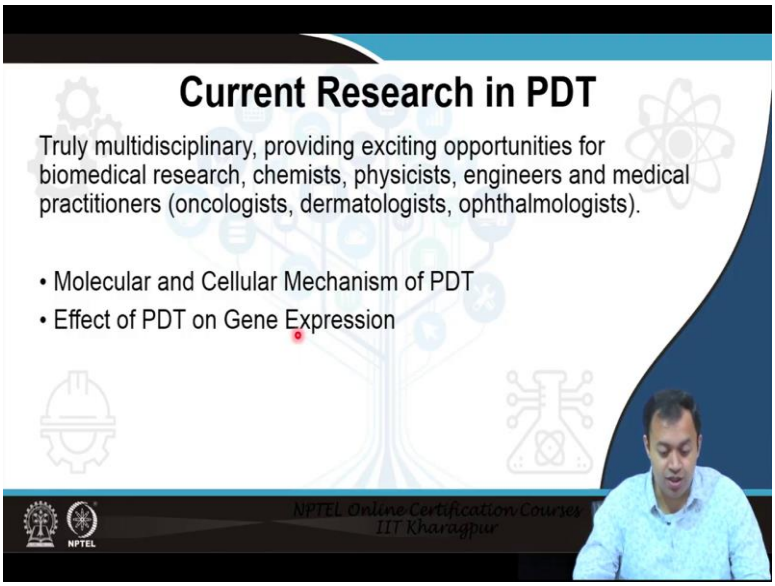

So, the present research. Well, from a normal point of view you we can understand that PDT is a truly multi-disciplinary research, it is creating a huge amount of opportunity for biomedical scientists, chemists, physicists, engineers and medical practitioners, engineers needs to know how to shine light at areas which are concealed.

Medical practitioners such as oncologist, dermatologist, ophthalmologists are directly beneficiaries of PDT, we need chemists and pharmacists to basically develop drugs that are

highly selective and upon their work being finished, they are getting quickly excreted out of the body. So, that you do not have to wait for 4 to 6 seconds.

Physicists need to know what exactly is the physics behind all of it, how the different singlet and that triplet states are forming and how are the triplet states resulting in the unpaired electrons are resulting in creation of radical species, which is causing problem and if we can create it somehow differently.

So, instead of shining light, can we have a trigger-based mechanism in which a drug is getting attached to a specific cell, an abnormal cell and say after a time period just by itself automatically, it converts, there is an inter system crossing happening and a triplet state is generated, which creates reactive oxygen species. In phosphorus or in phosphorescence you do not have to shine external light into it or do you remind me that we have discussed phosphorescence?

Do you think an external light needs to be shined to create phosphorescence maybe at the initial stage, but what happens at the late stage? Can you see phosphorescence when the light is switched off? Recall your previous lectures. So, can we have something like that where you do not need an external source of light all the time and we need to discuss the PDT's effect on different cellular mechanism, not just simply destruction, but can we manipulate?

Can we modify? And can we cause some sort of a gene expression? So, remember, CRISPR, we discussed this in the genetics that you are using genetic engineering this CRISPR based technique in which the gene mutations are removed or manipulated or changed. CRISPR is coming up very strongly and I think it has already been successful in curing, I think sickle cell anaemia or haemophilia, just check it out.

These are the genetic diseases a large section of India's population suffers from sickle cell anaemia, haemophilia, where these are genetic diseases where the blood cell cannot retain enough amount of oxygen or the blood cells have difficulty clotting. So, these are genetic diseases, but the genetic diseases form because of a particular DNA producing some sort of a protein.

The gene expression is happening and that protein results in creation of mutated, mutated red blood cells. Using CRISPR, you can target that particular gene Using CRISPR you can target

that particular gene and thereby cure it and CRISPR has done that, can we do that with PDT as well?

So, you inject some amount of drug, sooner or later that drug gets attached to specific genes, inside your body, inside your cells inside your nucleus and they then destroy the bad genes, something that is causing you making you prone to, I do not know cancer or diabetes or haemophilia or any other kind of genetic disease, can we do that?

Where PDT is applied with genetic engineering, so you obviously have CRISPR technology, but can we have can we generate a parallel genetic engineering technology using PDT or can we combine PDT with CRISPR? So, these are some of the debates, some of the discussion that are, that is going on in the current research you keep on, I keep on hearing this from student what are the hot topics what I should write a paper on, a specific project my Institute has asked me to write a specific paper, a specific journal on a hot topic on biophotonics.

So, these are your hottest of the hot topics just fresh out of the oven, it cannot get any hotter than this. Look into it, you are combining genetic engineering with physics, electronics engineering, of course optoelectronics basically, photonics and biomedical research with the direct application in medicine, oncology, cancer detection, ophthalmology as well as several genetic diseases that you form, these are some of the latest topics that we are working on.

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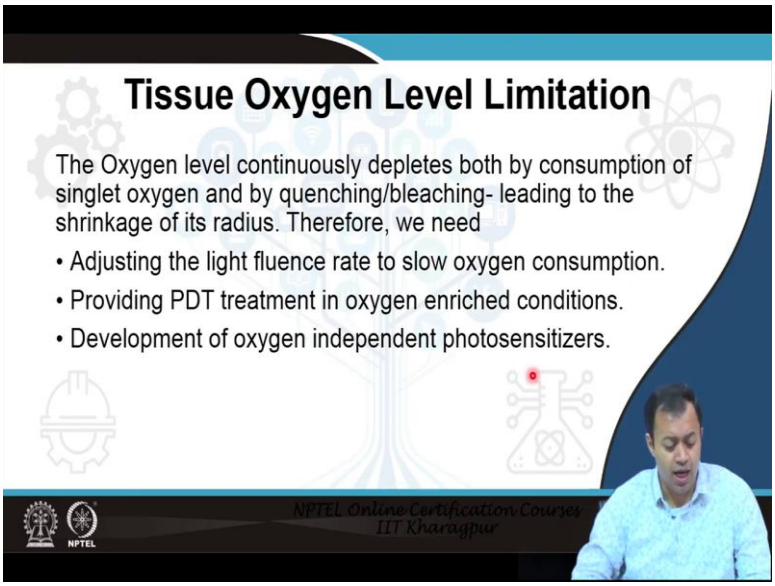

We also need to work on tissue oxygen level limitation. So remember, when we basically the idea is generation of raw species, but the Ross keep on destroying the immediate surrounding

cells and after some time, you know about this process that the singlet oxygen can go on, can get quenched or bleached because this phosphorus species or this species, they can get affected by the nearby surrounding area and the singlet oxygen species or even the triplet oxygen species, how long will they continue?

They can get exhausted leading to shrinkage of its radius. It is actually a problem of dosimetry, I understand what dose? How much amount of tumor can be, can it affect how much what size of tumor it can affect? Thereby at this present moment, we are trying to work on light fluence to slow oxygen consumption providing PDT treatment in oxygen enriched area, some areas say for example, your lung bronchiolar tract which is already oxygen enriched and development of oxygen independent photosensitizer which does not necessarily generate reactive oxygen species.

It does not generally develop or generate oxygen species you need to destroy, what is your ultimate aim, you need to destroy the nearby abnormal cells and yes, generation of raw species will destroy it. But is this the only way to destroy that area?

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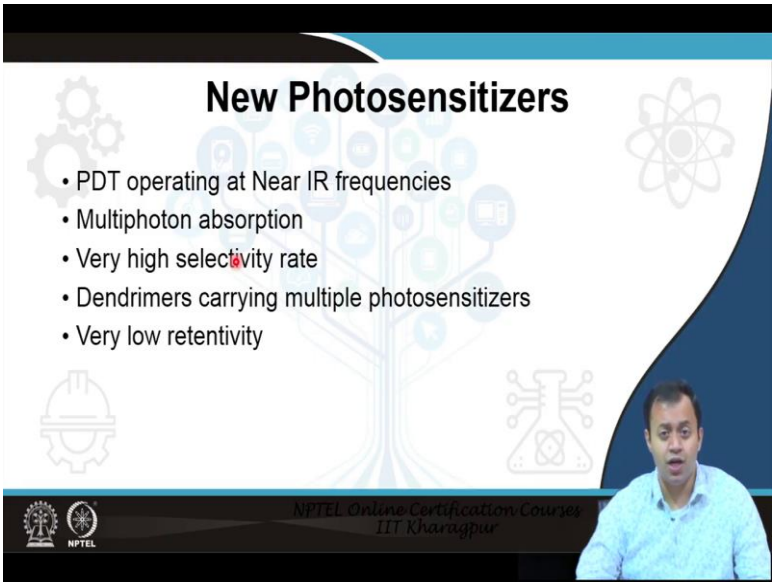

We have therefore, developing various new sets of photosensitizers, which are operating at near infrared frequency, thereby less harmful several one PD one photosensitizer can take multiple photons, they have highly selective rate and they have very low retentivity these are the topics. But what I want to actually discuss is if we do not generate reactive oxygen species what do we do.

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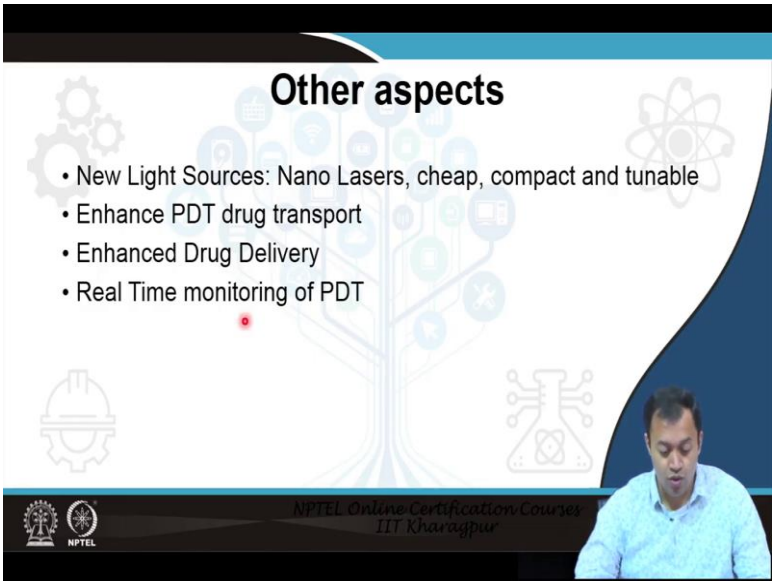

Well, there are other new light sources nano lasers which are cheap compact and real time monitoring this you can read at your own leisure.

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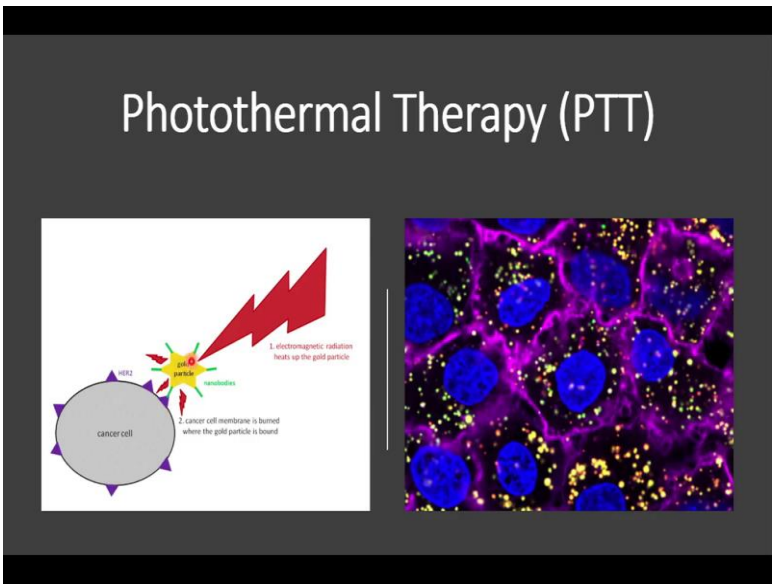

But I want to quickly go into the process of photo thermotherapy, photo thermotherapy where you are simply generating heat. You are simply generating heat and the heat is destroying the nearby cancerous cell. There is no requirement of generating oxygen species.

So, most of the photo thermotherapy these days are being done with gold nanoparticles, I have heard or I have read work on two dimensional materials especially graphene, graphene oxide may be black phosphorus has also been used, if you do not know two dimensional

materials do not worry, I think in the 11th chapter, where nano bio photonics is coming up I will discuss two dimensional materials, two dimensional material just it has length and breadth one atom thick and hence we call it two dimension. The thickness is very, very small one atom, large surface area. So, it is but what we basically do in photothermal therapy, we use gold nanoparticles.

These gold nanoparticles are very small in size, much, much smaller than the wavelength of light. These gold nanoparticles get attached to specific areas of the cancer cell again, I told you how it can be done, thiolation, antibody, several mechanisms are available in which a part of gold nanoparticle or sulphur-based part especially is the thiol part attached with the gold, another part gets attached, octadecathiol or these kind of chain molecules they can attach with biological component.

And once so these are the cancer cells, these are a huge nucleus and these are the cancer cells and you have infiltrated it with gold nanoparticles. So, these are nanoparticles, these are gold nano bodies are nanoparticles and their size are ultra-small as compared to ultra-small as compared to the entire cellular structure.

So, these are the cancer cell which has been infiltrated with gold nanoparticles, you are shining light on two gold nanoparticles, the electrons the plasmas the conductive electrons inside the gold nanoparticles agitate and they relax, they relax resulting in creation of heat, basically, non-radiative transition or non-radiative relaxation, they generate phonons or vibrations or heat as I have been telling you.

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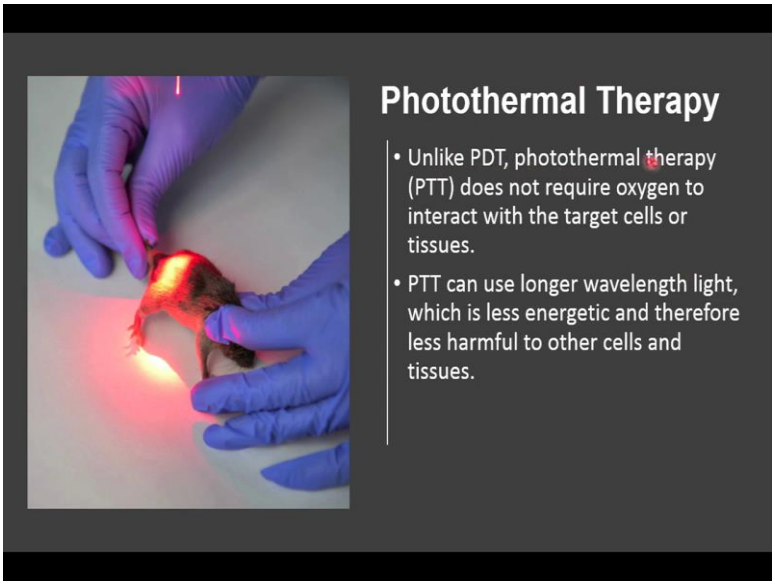

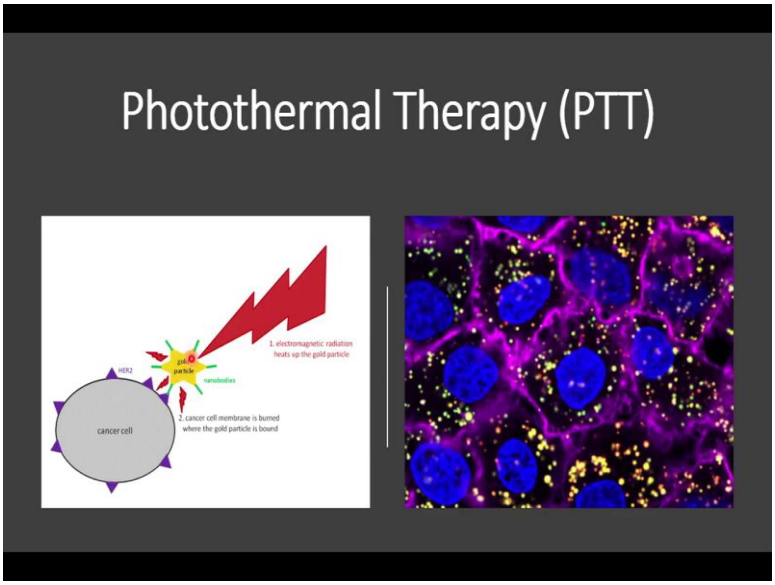

So, this is the mouse who have been injected with gold nanoparticles, they have accumulated inside their, inside itself and you are then shining light onto it externally. So, this is the laser source which is shining light onto it and unlike PDT photothermal therapy does not require oxygen to interact, it can use longer wavelength light which is less energetic and therefore less harmful to other cells and tissues.

All it is doing all the light is doing is simply exciting the electrons that are available, conducting electrons that are available in the gold particle to get excited, the electrons are jumping at different energy levels and we can depend on the nanoparticle size depending on the nanoparticle size of the gold particles, we can generate them too, we can we can send them at different energy level.

So, whenever these electrons are returning back to its original position, they return back by phononic vibration, by phononic vibration they do not generate everything does not fluoresce, everything does not fluoresce, remember there are non-radiative relaxation as well, these are the gold particles were non-radiative relaxation will happen non-radiative relaxation, meaningful phononic vibration, which in other words can be considered as heat.

So, basically you put a metal particle into the cell, the metal particle upon getting excited by light, generates heat, light is getting converted. So, you are heating up the metal, simply you are heating up the metal, the metal is eating up and it is dissipating the heat in the surrounding regions.

It is dissipating the heat in the surrounding region, the heat dissipated is strong enough to destroy either completely or partially some part of the bad cell either mitochondria or cell membrane, thereby resulting in apoptosis or necrosis. Your work is done, your work is done. It can use longer wavelength of light, it does not require oxygen species to create because oxygen species can destroy other areas as well. It simply needs oxygen rich radical it needs to eat something. So, it might attack the other areas.

So, photothermal therapy is strongly, strongly coming up where you have cut out the middleman which is the, it does not require the oxygen to interact with target cells or tissues, it simply generates heat a very, very localized heat, a very, very localized heat that destroys certain cellular components, all you need is to target certain areas to destroy a cell membrane is good enough mitochondria is good enough, nucleus is good enough and your work is done.

So, this is another hot of the hot topic, literally photothermal, so light is generating heat, so hot topic light based hot topic, that is very strongly coming up I myself personally invested or would like to be more personally invested in working on photothermal and photodynamic therapy PTT and PDT using two dimensional materials, this is something which I would strongly be looking forward to doing research in my future.

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So, that basically brings me to the end of this entire module of light based therapy, I hope some amount of this is clear, remember this is an entire field in itself and very strongly merging and maybe it will become standardized pretty soon, where several cancer treatment instead of doing chemotherapy, where a drug is being induced to attack the cancerous cell, light will be sent to generate either localized heat or localized oxygen species and thereby treat the cancer.

So, an alternative to chemotherapy, an alternative to chemotherapy and obviously an alternative to surgery. So, hope some of the topics were clear, please send me your feedback, please send me your comments, please ask me questions on the forum, I will try to answer them as soon as possible and I will see you next week for a different module thank you, thank you very much.