Biophotonics
Professor Basudev Lahiri
Department of Electronics & Electrical Communication Engineering
Indian Institute of Technology Kharagpur
Lecture 37
Application of Photodynamic Therapy (PDT)

Welcome back; let us continue our discussion on Photodynamic Therapy that is light induced therapy. We are utilizing drugs that are sensitive to light upon excitement by light specific wavelengths of light, specific sets of energies of light, these drugs produce reactive oxygen species, the reactive oxygen species burns or oxidizes the surrounding areas and these drugs are made specifically, these drugs are made specifically to attach to tumorous region to cancerous region for their treatment. So, that is photodynamic therapy.

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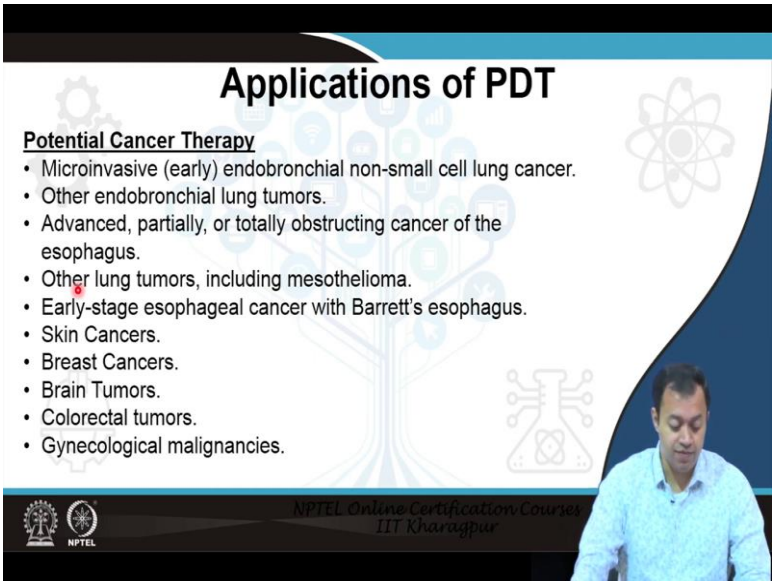

So, let us go a little bit farther, I have shown you several previous applications where PDT could be used, but these are the upcoming future. The one in the previous lecture that I showed is where PDT has already been proven and it is already standardized and different health organization different hospitals are already utilizing them mostly skin cancer, mouth cancer, and breast cancer, but these are the upcoming potential areas where PDT has shown initial very promising results. These are mostly being done in a research manner, these are not yet been standardized.

So, I am asking the oncologist or the medical professionals or anyone who is somehow attached with the hospital to try and see even if it is some kind of an in vitro analysis, even it is some kind of a petri dish-based analysis to try and see simply by buying that porphyrin

drug it is costly, I would not say it is cheap. So, if you can afford it, just buy it and shine some sort of a laser 630-700 nanometre laser, these are red lasers you get them at a specific, they are also available, nom laser pointer will not work you need something more than that.

But if you want to do a run of the mill experiment, few tissue cells, few cancerous tissue cells that you have extracted from some patient, put it in a petri dish I would like you to try, if you have access to it obviously, if you have access to any of these, just try this experiment see how much it works.

I know several of my students are faculties of very prestigious hospitals who I am talking to right now. So anyways, potential cancer therapy these are micro-invasive, I cannot pronounce this one. These are non-small cell lung cancer advanced or partially obstructing esophagus, esophagus is the food pipe.

Lung tumour, they are mostly utilizing it in lung tumor. This is coming up brain tumor, colorectal tumor and gynaecological malignancies. There are certain cancers which are very, very specific to subcontinent. Oral cancer is one of them. Oral cancer has been already standardized proved using PDT, but we do not see much more application of PDT for curing oral cancer, it could be done.

There is standardized procedure, I am not even asking you to develop the protocol, the protocol already exists. It simply that someone needs to take this initiative and do it before you ask me why I do not do it myself. Well, maybe because I am not a doctor, I cannot operate on normal human patients. I will go to jail if I do something like that.

But if you are a doctor, if you have a medical license, if you are an oncologist and I know several of my students are, try to see, try to convince if PDT could be utilized, these are non-invasive techniques and if it could save some lives, why not? These are the potential areas where PDT could, I mean we have seen earlier results, we have seen several exciting scientific peer reviewed papers coming up which has shown that they work.

Maybe it is time for us to take it to the next level. We can develop the drug ourselves at our institute. So, if you are thinking about developing the drug that could be managed and lasers could be bought as well.

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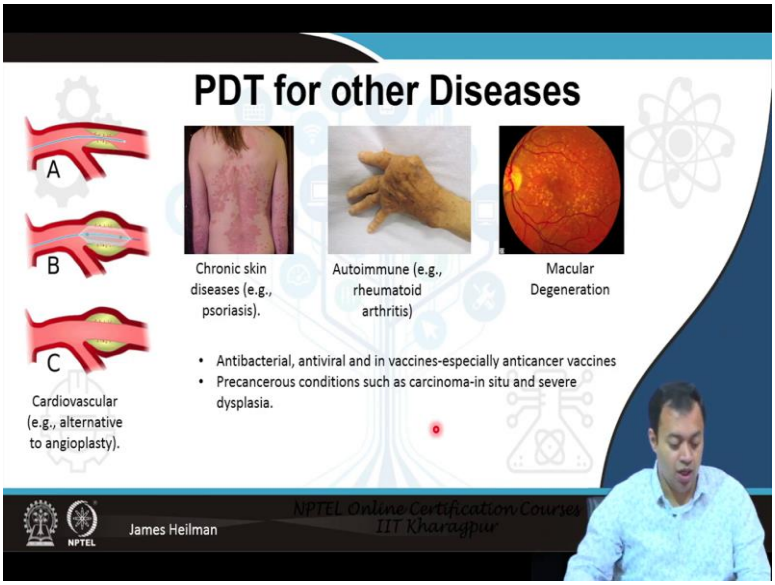

Anyways, what are the other type of diseases, where PDT is mostly used or PDT could be used? Well, the number one I find quite interesting is alternative to angioplasty, cardiovascular. You know, what angioplasty is? This is recently in news. Sourav Ganguly went through angioplasty recently, if you do not know who Sourav Ganguly is, well do not bother. That gentleman used to be our hero when we were teenagers. You have to figure out your own heroes.

But anyways, angioplasty is a procedure by which you open up blocked arteries or veins. So, what happens is that arteries or veins that carry blood, that carry blood vessels basically that transport blood and thereby oxygen throughout our body, sometimes get choked due to the position of lipid or other kinds of fats.

Now, it is common knowledge that cholesterol causes it, but that is not the only thing that can cause it. Yes, cholesterol heavily contribute towards choking of arteries by these kinds of fat or lipid deposition. But there are several other mechanisms, other things that can cause lipids or fats to generate inside your blood vessel, thereby resulting in restricted blood flow, thereby causing heart attack.

Several of it is genetic, several of it is your lifestyle-based smoking, it does cause apart from cancer, it has been proved to show some kind of effect on the heart. Obviously, alcohol and fatty, fat-based food, heavily fatty high cholesterol food also causes problem. So, in

angioplasty, you basically insert a catheter, a catheter a small tube type thing might have seen a catheter, it is a small incision tube type thing and that contains a balloon.

And upon reaching that constricted area, the balloon just inflates, the balloon is inflating and that is, you know, the balloon is inflating and opening up the artery. So, more amount of blood can flow. That is simply balloon based angioplasty. So, this is the constricted part you insert a catheter, the catheter contains balloon once it is inserted and put into the place of the choke point, the bottle neck, you inflate the balloon, the balloon simply opens up the blood vessel, the blood vein and now obviously the question came, what after removal of this catheter it gets constricts. Well, that can happen just do not tell it to Sourav Ganguly.

So, well we obviously give drugs and other kinds of things, so that the lipid gets dissolved or destroyed. But instead of doing this, instead of doing this, what if we attached our photo dynamic drugs PDTs, onto these fat deposits, onto this lipid deposits, we can do that, because the surrounding area is non-fat. This is the blood vessel. This is blood and this is the lipid area. So, once a specific area of lipid has certain molecules, certain functional groups that will be completely different from the nearby surrounding area.

We ensure that our drug our PDT drug is targeting that specific lipid molecule, getting attached to these lipid parts and then using the same catheter, it is a tube instead of blowing a balloon up, inflating a balloon up, you just from here shine laser light, the laser light will burn the facts, which will then be you know from your blood, the blood vessels will carry the residue forward residue, you get some amount of energy by burning the fat oxidizing the fat and that is it.

So, as an alternative to angioplasty, you have completely removed to the fact the position inside your inside your blood vessel. So, that could be done. There are several auto immune diseases like psoriasis as well as rheumatoid arthritis, auto immune systems are basically where the immunity of your own body turns against a specific organ.

You have an immune system the immune system is keeping you healthy trying to prevent infection destroying pathogens that is attacking your body, but sometimes it is so happened that your immune system attacks your own body, your soldiers instead of defending starts offending, they start attacking your own body.

There are several different diseases, autoimmune diseases, psoriasis is a skin disease as you can see, there will be red patches, scaly and itchy skin and they can barn and they can sometimes fall off, this this this can be quite chronic. Similarly, rheumatoid arthritis where there is a huge pain in your joints, because some part of your immune system has turned against your own joints. These are the areas where PDT is finding incredible application.

The PDT is selectively affecting the immune cells. Selectivity is the question, I told you there are different types of immune cells IGG and IGA and IGD, they might be there are, they might have some basic components, but their paratopes are all slightly different, we can target those paratope and thereby, the drug can get attached to a specific paratope of a specific antibody that is attacking your own body, skin or joints and destroy them living other types of paratope containing antibodies intact. That could be done.

You have macular degeneration, in the previous section I told you about macular degeneration, the internal or the central part of your retina gets destroyed, degenerated. So, we can or some sort of debris is forming. We can prevent that by sending certain molecules which will destroy the debris causing region antibacterial, antiviral and vaccines especially anti-cancer vaccines.

So, there are certain viruses that does induce cancer human papilloma virus causes as a significant well, I would not say cause but it does induce oral cancer. So, you can obviously have antibacterial and antiviral properties using PDT, so think about it, a virus has infected and spread or all around your lung.

Coronavirus for example, you are sending drugs that are getting attached only to the viruses, we can do that, antibody antigen complexes, it is only targeting the spike protein of the corona viruses even if it is inside the cell, it gets cell you stand in front of a lamp which shines light, the light gets penetrated or we put some kind of catheter some kind of a tube inside your lung, we can do that and by shining that light, the drugs that get, that are attached.

Drug molecules which are attached with the virus generates oxygen species which oxidizes the viruses. So, we can go for communicable diseases as well antiviral diseases using PDT and obviously precancerous conditions such as carcinoma-in situ and severe dysplasia. So again, I do not know how much of a knowledge on cancer you have. So, there are several different stages very, very rudimentary.

If a normal cell starts abnormally multiplying, keeping the overall shape structure of the cell as it is, but the multiplication rate has increased tremendously. We call it hyperplasia. Just the rate has multiplied tremendously, so blood cells say multiplies say one every second, now you have 10 every second, but it is still blood cells RBCs, red blood cells, we call it hyperplasia.

However, if the multiplication has increased and the shape is no longer retained, i.e. the cell has mutated and it is showing metastasized cell, a cell which are multiplying at a very rapid rate but it is no longer blood cells, it is something which is, which has a different structure different nucleus it has mutated growth but a rapid growth we call it dysplasia, we call it dysplasia.

A rapid growth of bad cells, rapid growth of mutated cell, metastasized cells and when this severe dysplasia has you know rapidly spread is and is almost ready to breach the different sections of the tissue there are different layers of tissues from one layer it is trying to invade into another layer that boundary is carcinoma in-situ cancer inside, carcinoma-in situ is inside.

There is obviously controversy regarding what is the boundary between dysplasia carcinoma-in situ and actual cancer. These are all the precancerous stage dysplasia carcinoma-in situ these are all precancerous stage and in certain section, if you are caught at a dysplasia stage or even to a point in carcinoma-in situ it can somewhat be reversed to a non-cancerous stage.

Though I know oncologist will say that there is much more nuance to it and it is not that simple that straightforward, but these are precancerous state, pre-cancer is the overall definition was precancerous means that full blown cancer has not happened under certain circumstances they can be reversed but not always, not always it is possible meaning there are still chances, there is still hope left.

And if you are able to catch a cell which started mutate just initially or there is cancer in a specific section of this tissue, but it has not completely spread out, you can send PDT drugs which will target only those mutated cellular regions, mutated cells mutated tissues and do its thing I oxidize the area and thereby destroy the cell. So, that is what it is able to do.

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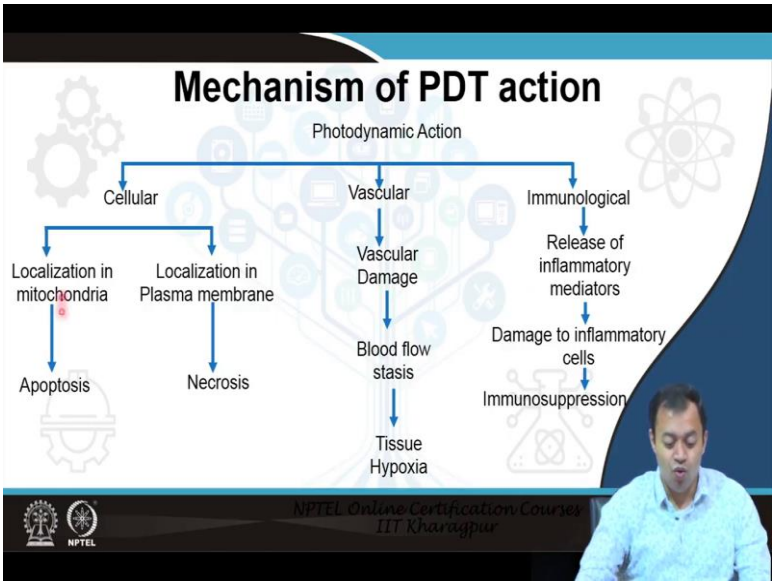

So, what are the different areas or the different regions or what is basically the mechanism of PDT, when I say that the oxidation takes place the surrounding area the cancerous cell or the cancerous tissue is vaporized or oxidized or burned or destroyed or any related what exactly does that mean. Well, there are three major categories in which photodynamic action happens. Cellular, vascular and immunological.

Cellular in which the PDT drug localized in mitochondria or in the plasma membrane. The mitochondria localization, thereby destroying the mitochondria. Plasma membrane localizing in plasma membrane thereby oxidizing burning melting the plasma membrane. Their results are apoptosis and necrosis, what are they wait next slide I am coming to that, I have a very cool thing to show you.

Vascular, the vascular is so cancerous cells are cancerous tissue probably you know that they require constant blood supply to survive and grow I mean they are growing at a rapid and abnormal rate, but they need to get nutrients, they need to get oxygen from some areas and though they basically formed their own network they basically formed their own mutated network of blood vessels blood flows et cetera, that keeps the tumor alive the tumor is very much alive and growing and it requires constant supply of blood constant supply of food.

So, that blood flow that blood circulation that bad blood flow, bad circulation that is keeping the cancerous cell alive that could be damaged, that simply network can be targeted and that

entire blood network, the vascular network can be simply damaged, the platelets can be removed, the thrombosis can come up.

The arteries that are feeding the veins that are feeding can simply be destroyed resulting in tissue hypoxia, hypoxia means less amount of oxygen, i.e. something that happens when you when you travel very high up into the mountain and your basically breathlessness, basically lack of oxygen, hypoxia simply means lack of oxygen, i.e. you destroy the vesicles you destroy the arteries, you destroy the veins, that is providing blood to the tumor from which the tumor is generating energy, generating sustenance and growing and that vesicles or vesicles, the arteries, the veins are basically destroyed, they are targeted and thereby they are destroyed.

Then I told you about the autoimmune immune system, how we target immune cells, the release of inflammatory mediators basically damages the inflammatory cells the inflammation basically inflammation means swelling up, this is one of the main defence mechanisms you see several times when you get a hit somewhere it swells up there is an inflammation, things swell up, that is one of the defence mechanisms of your body.

So, one of the defence mechanisms of your body to prevent further damage to the area underneath. So, but in autoimmune, the same thing is happening to your body some kind of inflammation has taken place, which is thereby preventing some other function to take place in your skin, the rashes, itching, skin becoming red and inflamed. Similarly, certain areas of your joints are becoming inflamed. As a result, you have pain and you cannot move these joints and these are all auto immune systems, auto immune disorders.

So, we target specific immune cells, specific immune cells, that is targeting your own body, leaving other type of immune cells intact without touching them and we go into immunosuppression. That is the main mechanism. Photodynamic therapy either targets certain cellular components or it targets the immune cells, which are causing autoimmune disorder or it targets the blood flow, something that is bringing oxygen or something which is bringing blood into the into your tumor system.

Again, I am not an expert in cancer. So, if you want to know more about the overall mechanism of cancer, I suggest you go at a different place than here. This is not the right place to learn about cancer biology. But I am tackling cancer from an electronics engineering point of view and nanotechnology point of view.

So, if I have made any mistake, please, please point them out into the comment section or write it into the forum. Medical students I am looking into you, especially oncology or those clinical practitioners who work in medicine. So, what is apoptosis and necrosis?

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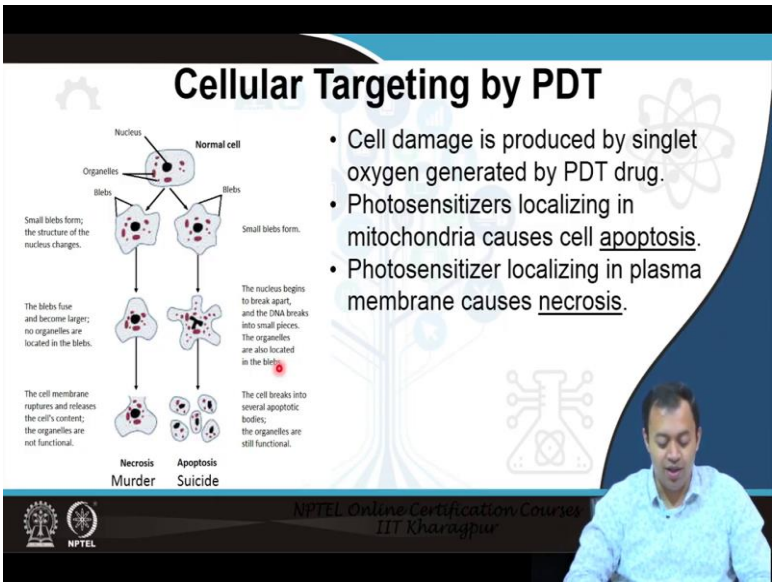

This is apoptosis and necrosis. Cell damage is caused by PDT and if the mitochondria is damaged, it caused apoptosis and if the localized cell membrane is destroyed, you have necrosis, I have figured out or I tried to understand it from this point of view, necrosis is murder apoptosis is suicide. I know medical students are having this incredible urge to do either of this on me, because I have probably reduced it to this, but you will accept that this is pretty much close.

Apoptosis is programmed cell death. This is where the cell dies by itself, you trigger something, you trigger a specific mechanism into the cell and the cell simply destroys. It is a programmed cell death. Necrosis on the other hand is because of some external factor. Necrosis is when the cell has undergone some kind of a huge injury.

Some sort of injury has taken place either simply by cutting, simply by tearing or you have heated it up or some sort of pathogenesis has occurred something external. So, necrosis, where you will find the cell or the tissue becoming char, becoming black, I call it murder. Externally, the cell has been killed and apoptosis where cell fragments into different parts is suicide. Is where a mechanism is triggered like you destroy the mitochondria.

The mitochondria are the area where energy is produced the battery of the cell, you destroy the battery most important energy centre of the cell and it starts itself today the enzymes that are produced basically eats itself up, the enzymes simply eats itself up, the nucleus begin to break apart, the DNA breaks into small pieces. The organelles are also located in the blebs, the cell breaks into several apoptotic bodies and the organelles however, the organelles are still functional, and they usually either get consumed or removed.

Whereas in necrosis that is the murder, the cell membrane ruptures and releases the cell contents, the organism not function some so it is an accident, it is some kind of a hit, you are destroying the cell externally by something. So, you just open up the cell membrane, the plasma membrane, you just tear it apart and internal material the cytoplasm et cetera, just comes out and thereby I call it murder and medical students, please take it as a joke.

I, under no circumstances wanted to belittle your years of study and I know people make their PhDs in necrosis and apoptosis studies like what mechanism what is triggering, so under no circumstances, I am belittling there, hard work, it is just my way of understanding it thing, it might not necessarily be the real deal, but overall, I tried to understand it and I think some electronics engineer, some physics students who have little idea on the biological part, will also try to see the joke.

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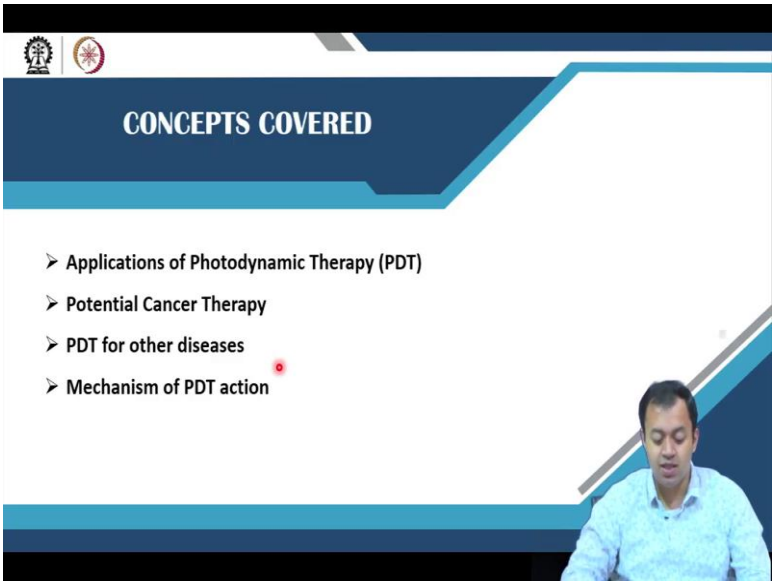

So, these are basically the concepts covered. In today's lecture, I told where are the potential areas where PDT could be used not necessarily about cancer, but antiviral, antibacterial, these are the areas the auto immune system. I also discussed about the mechanism of PDT action.

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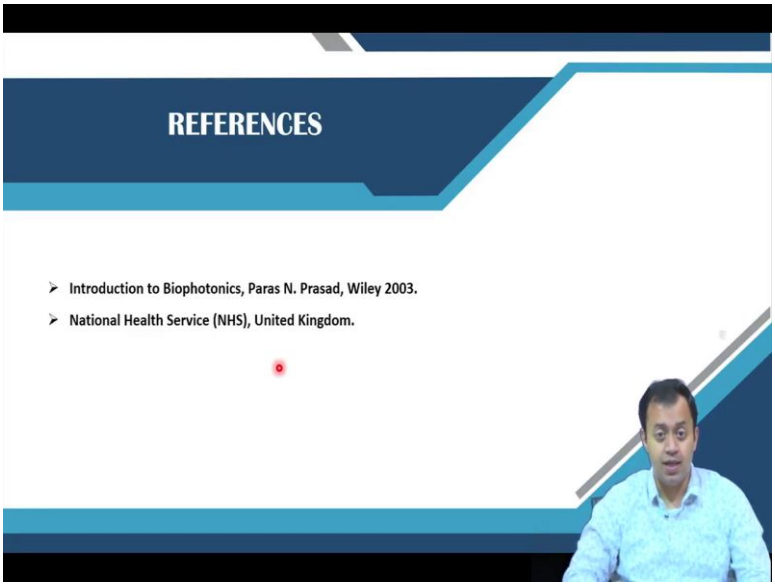

So, this is again, the reference, please visit the website of National Health Service United Kingdom as well as National Institute of Health United States and you can have a comprehensive knowledge on what cancer is how different cancers are, what are the types what are their available treatments, how far we have come in understanding and destroying and targeting and manipulating and controlling cancer and how much is still remaining. So, that is something that we can look into it. So, thank you very much. I will see you in the next class. Thank you.