Biophotonics
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Lecture No. 03
Introduction to Biophotonics (Part-III)

Welcome back. Let us continue our discussion with biophotonics. And let us today now conclude the introduction to biophotonics.

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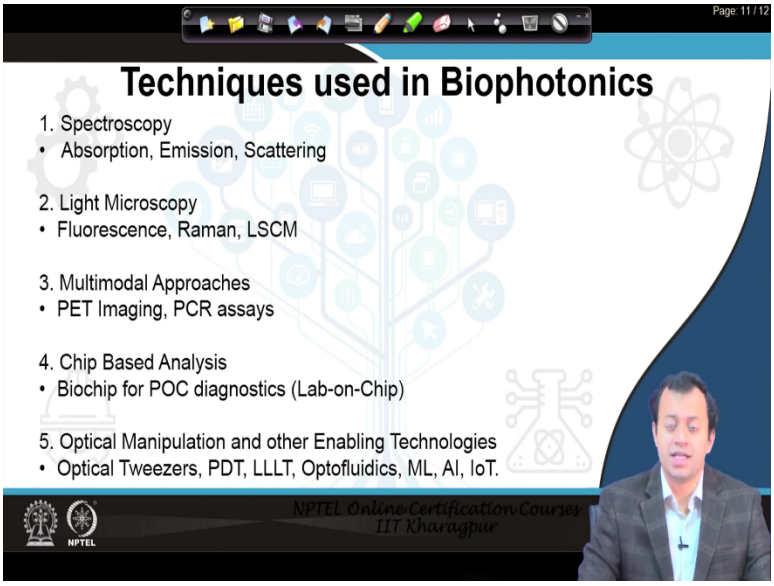

So, what are the already existing technologies that biophotonics use? I told you that biophotonics borrows ideas from vastly different fields such as nano-technology, biotechnology, chemistry, physics. So, obviously if we are looking for the interaction of light with matter, any matter, spectroscopy has to be there. Spectroscopy is by definition, where we utilize light to interact with matter and to thereby understand or observe or fully comprehend the matter.

So, in biophotonics a very large part is spectroscopy, we use FTIR, Fourier Transform Infrared Spectroscopy, we use other emission spectroscopies, Ramon spectroscopy is a very very strong part of biophotonics. Of course, microscopy has to be there, fluorescence microscopy, Ramon microscopy, laser scanning confocal microscopy is there, this is where we image at a very very high resolution and utilizing spectroscopy, we thereby try to understand the nature of the object or the biological component that we are imaging.

We have other multi-modal approaches that we also use in biophotonics, for example PET imaging; Positron Emission Tomography where a radio tracer, a radioactive material is used to tag a particular, usually a tumor, and thereby you see the emission, the positron emission and thereby see how the tumor is progressing or if the tumor has dissolved or not.

We have the biochip, the lab-on-chip. These are the small chip-based structures like a home pregnancy detection kit or a home diabetes detection kit which you can utilize at the privacy of your own home. Some amount of body fluid; blood, urine and thereby the lab-on-chip will undergo some kind of color change, color-metric change, not necessarily always a color-metric change, I am giving you an example. But a change will take place and from that change, you will be able to come to a crude and rough calculation, like in home pregnancy detection kit, you come to a calculation if you are pregnant or not, so yes-no, after that you go to the doctor.

So, these things we do regularly in biophotonics. Other enabling technologies are strongly coming up. As I said, biophotonics is a very very bourgeoning field. So optical tweezers where we use light waves to hold and place a particular component from one place to another, so like a tweezer, you can pick up objects, very small objects, microscopic objects, using light wave. We have optofluidic, where we utilize light to manipulate the flow of certain body fluid, say for example, we use laser light to manipulate the flow of blood in certain arteries.

And these days, we are seeing more and more utilization of machine learning, artificial intelligence and internet of things. You see all those images that we are taking through florescence or through spectroscopy, instead of asking a human being to analyze them, if we write some kind of a learning algorithm, some kind of a machine learning algorithm, some kind of an intelligent program, we will be saving lots of lives. So, we just take, say in a slide, some blood spatter, some smear, blood smear not blood spatter, beg your pardon, blood smear and we analyze it both chemically as well as physically.

We want to see what are the shape, size, structures of the materials present in the blood as well as we want to understand their chemical nature. And then, this analysis is done using a machine learning tool, a machine learning algorithm, artificial intelligence algorithm. And thereby, we try to detect if there is something, however small it might be, however minute or however negligible

it might be, is there some anomaly, is there something wrong. Thereby, we would like to see or we would like to discuss if there is a disease or an infection present.

And if we have, like say, in a pandemic screening, per hour 1000 blood samples or 1000 nasopharyngeal swab, 1000 oropharyngeal swab per hour, it is impossible for a human being or even group of human beings to analyze them faithfully without any mistake, day in and day out over a large period of time. But perhaps, perhaps these machine learning tools or artificial intelligence can help us and using internet of things, we can immediately send information to the central control or to the patient or to the physician directly that this thing have been found in the patients blood, or patient's body fluid and thereby, this particular medicine needs to be prescribed or this particular cure has to be taken, needs to be present. All of these things are coming up very rapidly in biophotonics.

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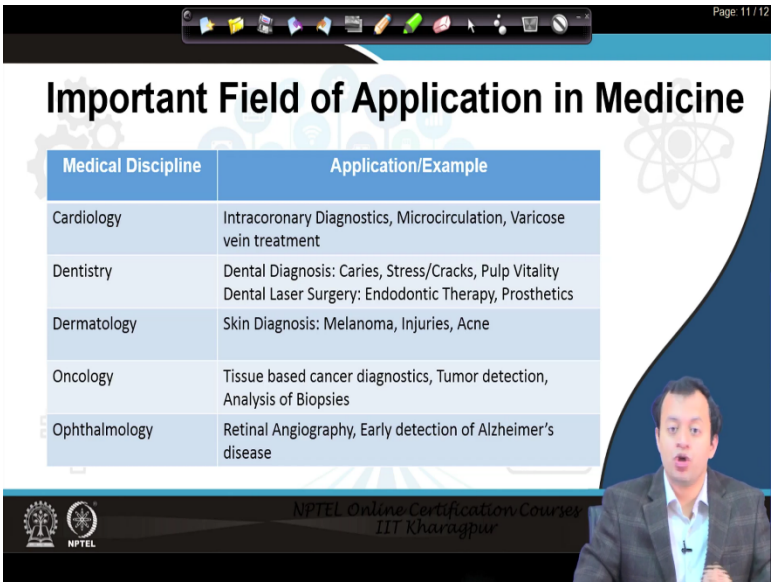

It is a very advanced field and lots and lots of exciting new topics are being generated. So, what are the important fields of application in medicine, specifically? Previously, I gave you a, you know, general idea - microscopy, photodynamic therapy, OCT. But if we are looking at the specifics from a medical discipline point of view, where we can find the potential application of biophotonics?

Well, there are several. Though this list is not exhaustive, I would like you to go through all of them side by side. Say in case of cardiology, where we are looking for thrombosis, that is, there is a blood clot, we can use laser light to break that clot and allow the blood to pass through. We can look at micro-circulations, where we would check the blood flow in very very thin and very very microscopic capillaries.

Dentistry, I know I have few dentist students listening to this talk. So, for dentistry, biophotonics can be utilized both in diagnostics as well as surgery. You are looking for very small cavity or stress or crack detection using laser light, you can look at pulp vitality, pulp is the central most part of your teeth, the soft spongy part which has all those veins and nerve endings. You can go for prosthetics using biophotonic applications. Dermatology, you can look at skin diseases, if there is an injury, internal injury, external injury, cosmetic surgery, acne.

Oncology is very strongly coming up, I myself am working at optical, oral cancer, beg your pardon, optical detection, fast optical detection of oral cancers where oral cells are being taken exfoliated and we look it under a microscope and then, using biophotonic technologies, we try to measure the progression of cancer in those oral, in those tissues. Tumor detection, as I said, and analysis or biopsies using light. Using light-based technologies, these things can be done very rapidly, very much faithfully.

And of course, ophthalmology, OCT is a prime example of photonic technologies, biophotonic technologies and recently, these days, we are looking for early detection of Alzheimer diseases. These are the protein misfolding diseases, we try to image proteins and try to look at its confirmation. Proteins have a morphology as well as, they are chemical entities. So, a particular protein has to have to have a particular shape to perform a specific function.

If the shape is somehow changed, the protein is unable to do this particular function. We still do not know what causes, or we still do not know what are the main, absolute reason that, that occurs inside a protein misfolding and thereby, what effect is causes, but all those protein misfolding diseases; Alzheimer's, Parkinson's etc, we see large amount of misfolded proteins, we do not even know whether they are the cause or the symptom.

It is envisioned that biophotonics will be able to give some amount of information regarding protein misfolding and thereby, come to, say, I will not use the term cure but I would say, some

kind of a treatment for, or detection, early detection of Alzheimer's or Parkinson's diseases. So, these are some of the specific where biophotonics can contribute significantly, they are either contributing already or they have great potential in their contribution.

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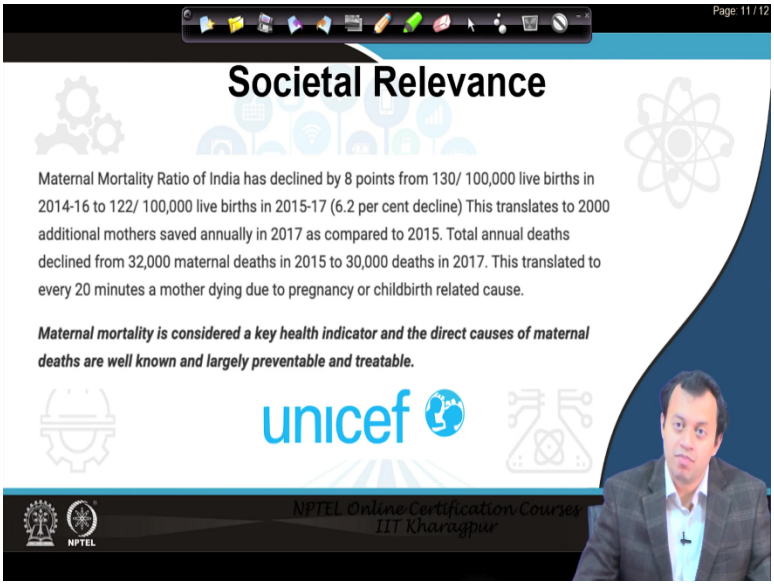

So, why do any of this? Why go for developing new technologies that can be used to detect diseases or cure them. Well, apart from the obvious reason that this is a moral obligation, health is a right and we should be working on providing healthcare facilities to every single human being on to this planet. There are other such important applications or other such reasons why we need to develop newer and better healthcare technologies.

Let me give you certain specific examples to let you know why I think is this important. So, this is the UNICEF data from I think 2019 which talks about maternal mortality rate, i.e, the total number of women who died during the period of their pregnancy, either while they were pregnant or while giving birth to a child or within few days after giving birth to their child. That is basically maternal mortality rate.

So, if you look at the last few lines, that every 20 minutes, a mother is dying due to pregnancy or childbirth related causes in India. Women in my country are dying every 20 minute for pregnancy or childbirth related causes. Though our maternal mortality have declined, but we are

still behind some of our neighbors. Believe it not, the more number of women in India die during pregnancy or childbirth related causes than Pakistan, than Venezuela.

Though the average rate has quite declined in India, this maternal mortality rate, some of the states of India, shows the maternal mortality rate worse than that of sub-Saharan Africa. The maternal mortality rate in the state of Assam is worse than I think Rawanda or Namibia. The maternal mortality rate of Uttar Pradesh and Madhya Pradesh are equally bad. And most of the time, they are, if you look at the bold line, they are the causes of death are both well-known and they are largely preventable and treatable. It is not that it is corona virus, no one knows how to treat it or it is a new thing, the maternal mortality rate could be prevented. These women are dying for something that we already know the cause as well as they are largely preventable and the cost for the cure is also quite affordable.

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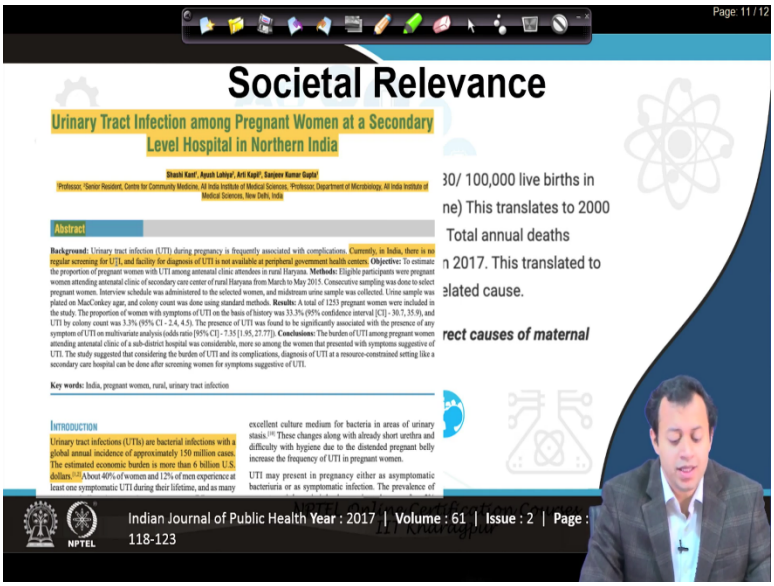

This is another information because a large number of deaths happen because of urinary tract infection and in this journal of public health, professor Shashikant and team, figured out that urinary tract infection, one of the primary causes of, well, death or other complications in pregnant women, and look at the area that I have highlighted. Currently, in India, there is no regular screening for UTI and facility for diagnosis of UTI, urinary tract information, is not available at peripheral government health centres.

Let that sink in, that we do not have a UTI detection facility in peripheral government health centers. Urinary tract infection causes maternal mortality rate, it can cause maternal mortality rate, there are other factors for women dying during pregnancy as well, but UTI is quite significant. We very well know what causes UTI, it is basically the E. coli bacteria, one of the most common bacteria. We know everything about E. coli bacteria.

In fact, students of microbiology will back me up when I say that, students of microbiology go to laboratory, undergraduate students go to laboratory, it is probably E. coli, this is the first bacteria they are being given to work with. So, we know everything or almost everything that is there to know about E. coli bacteria and we know the cure. Antibiotics are available for 5200 Indian Rupees and it, if you consume it, the UTI can go, it could be cured.

The problem is not neither the cost nor difficulty in detection, not it is something new. Yet, as a society, not government, as a society, we have completely failed in reducing the maternal mortality rate as much as we would have liked to be.

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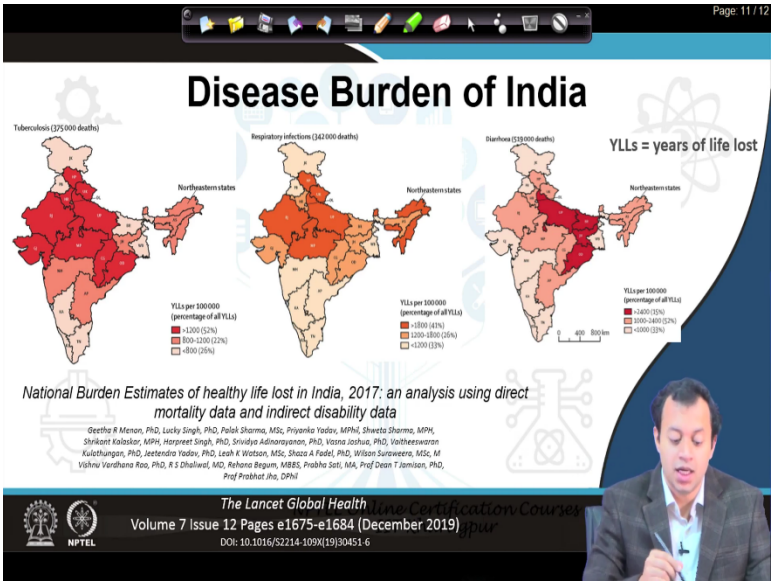

Next, what is the disease burden of India? These are some of the shocking statistics that I found out from papers from the Lancet. We are not discussing about tremendously complicated diseases like brain tumor or say, cardiac disease or corona virus per se, we are discussing normal diseases such as tuberculosis, respiratory infection and diarrhoea. And see the total number of

deaths that are depicted. This is the data from 2017, this is a compilation of all the data from 2017.

YLL stands for years of life lost or potential years of life lost, what does that mean? So, it basically depicts the premature death. Meaning, if the life expectancy of a particular area, particular region is say, 75 years, meaning, on an average, a person lives up to 75 years, and if a person in that area dies at say 5 years of age, so the year of life, years of life lost is 75 minus 5, is 70. i.e, that person should have been alive for 70 more years but died 70 years too young.

So, years of life lost basically gives you an information instead of the death rate per se, years of life lost gives you how much young people are dying, how much premature death is happening and we have 375000 premature deaths due to tuberculosis, tuberculosis has been completely eradicated in several European and north American countries. It longer exists. Diarrhoea, have long ceased to exist in not just Europe or America, but other east Asian countries like Japan and Singapore and Korea. Yet we are failing behind and look at the total number of years of life lost.

So, it is a societal responsibility that we need to come together, to not only develop strategies and you know, distribute free medicine and free healthcare facilities but also make all of that accessible. Say for example, urinary tract infection, we know what the disease is, we also know what the cure is. Yet, pregnant women are dying. So, I ask you, is it possible for us to develop some kind of point of care diagnostic device, a chip; a chip such as a pH detection strip, you know, all of you must have used this pH detection paper. Those pH papers that, in high school you used to put in acids or bases, the color would change and thereby you can say whether the solution that you are using is acidic or basic.

If we make a some kind of a material, some kind of a bio material, some kind of a biophotonic material, as such, cheaply made, distribute it among pregnant women where they can, at the privacy of their own home, put some amount of urine in it and see if the color is changing or not. And the color change will depict whether a particular pathogen is present or not. See, you are already doing it with home pregnancy detection kit. In home pregnancy detection kit, the hormone, the pregnancy hormone present in urine is detected, the amount give you how long you are pregnant, 3 weeks, 1 month, couple of months and thereby you come to a conclusion, you come to an information that yes, pregnancy have had occurred and I need to go to the physician.

If we are able to provide these kinds of kits to, for not just pregnancy but for urinary tract infection, tuberculosis, where at the privacy of your own home, you will put some amount of your body fluid, it could blood, it could be urine, it could be something else and see, is there a change in color. This is just an example. And based on that, you go to the nearest physician or you go to the nearest pharmacy to buy an antibiotic and thereby try to get cured. Several of these things are already available, that, it is not that this technology is impossible to make. This technology or technology further advance that this is already available.

The responsibility lies with all of us as students, as professors, as industrial partners, as physicians, all of us to come together to solve these societal problem. And it is my opinion that biophotonics can play a very very important part in solving several of these already existing problems. See, tuberculosis, diarrhea are not as complicated or as new as corona virus infection. Yet, we are still seeing large number of deaths which could be prevented very easily.

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So, what are the disadvantage that we find in biophotonics? As I said, biophotonics deals with both people from a physics background, engineering background, as well as people from a medicine background or biology background. So, there exists a significant communication gap between these two groups and that gap is reflected strongly in the field of biophotonics. We do not know which particular disease to focus on. What are the most prevalent diseases which we could simply focus on to eliminate? I gave you example of tuberculosis, I gave you example of

urinary tract infection. Shall we look for them or we look for Alzheimer, Parkinson's, blood cholesterol etcetera.

Some of biophotonics research is too much technology driven. We need something very very user friendly so that minimally trained person, like I said, the home pregnancy detection kit as an example; anybody can utilize at the privacy of their own home, you do not need to, what is the point of having a technology that requires, 5 different people to interpret the results.

Biophotonics research sometimes tends to get too much technology driven, where more than 4-5 people are required to analyze different aspects of it and then come to a conclusion. Whereas, easier and cheaper though not so efficient methods are already available. So, cost or the overall circumstances prevents biophotonics technologies from taking form. It might be better, it might be more efficient, more accurate but simply it is too much technology driven, too difficult for people to understand or to use or require so many different skill sets that people simply give up.

Well, lack of knowledge on unmet medical needs, we do not know not just the diseases but the manifestation of diseases. We do not know the symptoms, we do not understand, or we understand the symptoms, we do not talk with the people who understand these symptoms and what needs to be done to cure them. There is a missing knowledge for technical potential. This is where the missing knowledge of medical practioners comes up. Several of them do not even know that a technology already exist and that could immediately be put into utilization of their day to day practice to get a more efficient diagnosis.

This knowledge gap between both physicist as well as physician is something that is plugging this field. And finally, my favorite, the great chasm between physicians and physicists. I jokingly tell my students that they are like vampires. Vampire is a very strong supernatural entity but as soon as it sees sunlight, it weakens. Or Superman, the fictional superhero, Superman is man of steel, tremendously powerful, but as soon as Superman sees kryptonite, he becomes weak. So, that is the thing with physicians and physicists. You talk about DNA to people from physics background, they start getting weak kneed. At the same time, you talk about mathematics of Schrödinger wave equation to people from a medical background, they start getting bored.

So, obviously I am not talking about you particularly, I am not talking about a vast majority of physicians and physicists, I am talking about a tiny but significant percentage, but you have to

understand, if we as a society need to come together to solve these healthcare challenges, we cannot simply stay in our silos and say that I am software, you are hardware, I am physics, you are mathematics, I am biology, you are chemistry. We need to come together as a society from different discipline to find you know, multi-disciplinary solutions to multi-disciplinary problems. So, the communication gap exists in biophotonics, it is my intention to reach out to you from different backgrounds to help breach this communication gap.

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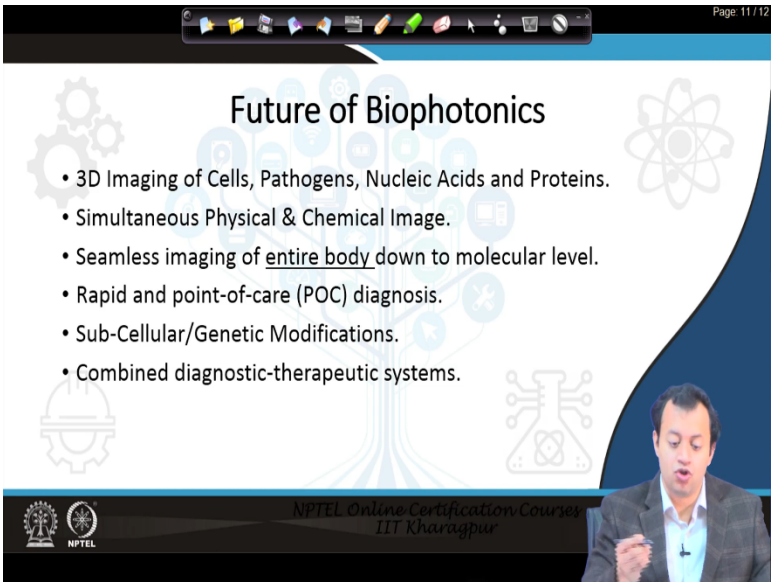

So what is the future of biophotonics? I thus far have discussed where biophotonics already exist or it has the potential. But as a technology, what exactly are we looking for from biophotonics in the coming say, near foresee-able future; 10 to 20 years, where biophotonics is going. Well, firstly, we would very much like to utilize biophotonic technologies for a 3-dimensional image. Maybe you have seen already some 3-dimensional image of viruses. Several of them are illustration and not real images.

But with biophotonics technologies, we can actually see 3-dimensional images of cells, pathogens, nucleic acids. We want to get simultaneous physical and chemical information. And this is the most important thing - we need to seamlessly image the entire body, the entire body needs to be image from your body, from organism to organs to tissues to cell and down to the molecular level in one go. In one go, like you pass things through conveyor belts, you know in

airport security or even other places, you put a package and it completely gets passed through and you can see what is inside.

We want to see that up to a molecular level, importantly, not damaging the body per say. X-rays have harmful effect, so we are trying to avoid that in this particular case. Rapid and point of care diagnostics, I discussed this quite a lot. We want to see what kind of genetic modifications we can get using photonic technologies and this is a very very murky and this is a very very controversial area. This is potential mine field. Whether you want to change, genetically, something inside a human being or even an organism, that is quite controversial.

We will be slightly touching upon this subject at the very end of this course in, where I will discuss optic, optogenetics or neuro-photonics. And combined diagnostic-therapeutic systems, where not only you detect but at the same time, as soon as you immediately detect an infection is, has occurred, you eliminate the source as well as the cause of the infection, thereby curing the entire ailment per say. So, these are the, these are some of the topics that we can expect from future of biophotonics and we can expect it more if all of you join me together and we try to see how many of this we can faithfully replicate.

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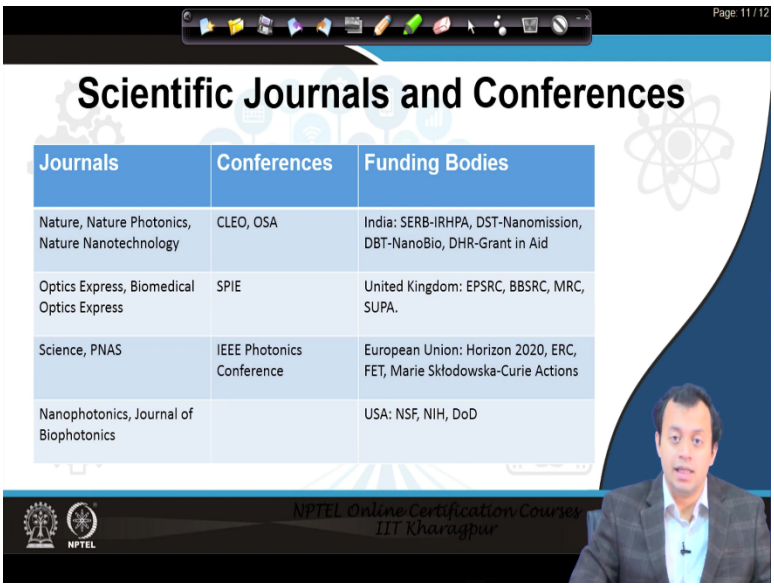

There are several scientific journals, conferences as well as funding bodies these days which are invested in the topic of biophotonics. If you are working in the research of biophotonics, you can

publish your work in Nature, Nature Photonics, Nature Nanotechnology, Optics Express. Proceeding of the national academy of science, there is a bio journal of biophotonics per se. There are several international conferences, we have IEEE conferences, SPIE, CLEO, Optical Society of America that regularly convenes at international location and discuss about the latest progresses that has happened in the field of biophotonics.

And then, there are several governmental funding bodies both in India as well as abroad, which gives you enormous amount of money to pursue your research in biophotonics. In India, we obviously have Department of Science and Technologies Nanomission, we have Department of Health Research - Grant in it, we have Indian Council of Medical research ICMR's extramural grant. Science and education research board, so and so forth in United States, United Kingdom and the European Union. The horizon 2020 is very very popular among them.

At the same, there are several private entities which are coming together in the areas of biophotonics. Novartis is one such company. There are other companies, vaccine development companies. They are also working rapidly, the areas of biophotonics. And let us see, with a combination of all of us, industrial partners, government, students, medical practioners, physicists, physicians, researches, professors, we need to utilize, we need to invest in this particular technology if we want to reduce the healthcare cost and provide quality healthcare, not just healthcare, quality healthcare to every human being on this planet. It is an ambitious goal but perhaps, we can try to start somewhere. And biophotonics may be a route, a path to go there.

So, that basically ends my module on introduction to biophotonics. From next class onwards, we will start working on the basics, that is basic of light, matter interaction, basic of biology and slowly, as we progress, we will go into the heart of the matter where we will see how biophotonics have been specifically utilized for imaging or biophotonics have been specifically used for therapeutic purposes.

So, I hope you are understanding some of what, some of the topics that I am discussing here. Please leave me a comment on what more you want to see and I will try to incorporate all of those, if possible, into my lectures. Thank you, thank you very much.