Biophotonics
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Lecture 59
Functional Near-Infrared Spectroscopy (fNIRS) of the Brain

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Welcome back. So, in the previous class we discussed about neuroimaging, optical neuroimaging. I gave you a glimpse of it in which optical fiber tube was put inside the cranium, inside the skull of the animal. And thereby from that we were monitoring the different areas of the brain and trying to see how the animal will behave.

So, I have a question to you. That is something that we put in an animal's skull, would you be interested to volunteer yourself if we put something of that sort of optical fiber tube something of a width of a human hair, not more than that through your head we can therefore look into how the human brain behaves. Would you be willing? Think about it. How do you think we will progress? We need to get more and more complex mammals. So, jokes aside.

Today is a new topic. We are going to discuss near-infrared spectroscopy, in fact, functional near-infrared spectroscopy. And I am adding this because there was a demand from one of you, so you can blame that person. I would not take his name. When I was teaching spectroscopy, one of the students asked that they need to know near-infrared spectroscopy specially to brain

research. So, I had my work cut out. So, they gave me a specific part. And I thought that NIRS goes very well with neurophotonics. So, let us get on with it. And I think you will find it fascinating as well.

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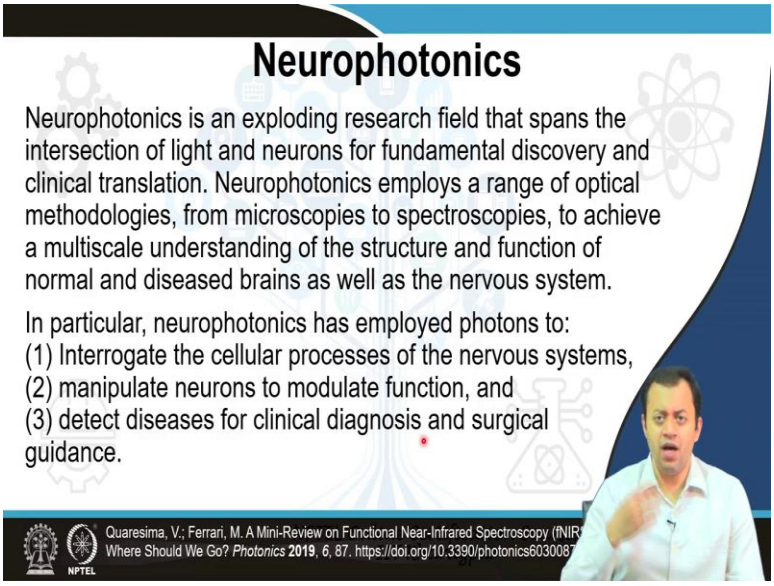

So, I keep on telling you neurophotonics, neurophotonics. So, now what is neurophotonics? So, neurophotonics is an exploding research field. Exploding, they have used the term exploding. So, Ferrari has used the term exploding. That spans the interaction of light and neurons for fundamental discovery and clinical translation. Neurophotonics employs a range of optical methodologies etc. for three main specific functions. You can read the rest at your own leisure, but A, it interrogates the cellular processes of the nervous system. It interrogates, its questions, it tries to understand.

It manipulates the neuron to modulate functions and it detect diseases. So, as you can see, several aspects of neurophotonics overlaps with optogenetics. And frankly speaking, there is no clear-cut boundary. What one person may call optogenetics can also under a certain circumstance be considered part of neurophotonics. So, interrogate the cellular processes and manipulate the neurons to modulate a function we do similar things in optogenetics as well. So, the difference, the boundary between those are unclear to me at least. I am not sure if there is a hard and fast difference.

Only thing is I think the very first experiments that was attributed to optogenetics was done by Karl Deisseroth in 2005, 2004 in Stanford, but this near-infrared spectroscopy, which is obviously a part of neurophotonics was done quite early 1979. But no one actually understood that it could be used for brain imaging. So, what exactly I am getting ahead of myself, so beg your pardon. So, what exactly is neurophotonics? Neurophotonics is these three things. It is an area which integrates neurons with photonics as compared to optics with genetics. So, you can understand. And it has the three main functions.

It understands the cellular processes, it manipulates the neuron, and it detects disease, something very, very common with the overall, in general, with the idea of biophotonics. Instead of neurons, you just put biological matter, detect disease and clinical diagnosis for brain and biological matter and optogenetics in particular. So, one of the major themes of neurophotonics, one of the fundamental themes of neurophotonics is this near-infrared spectroscopy or NIRS, Near-InfraRed Spectroscopy.

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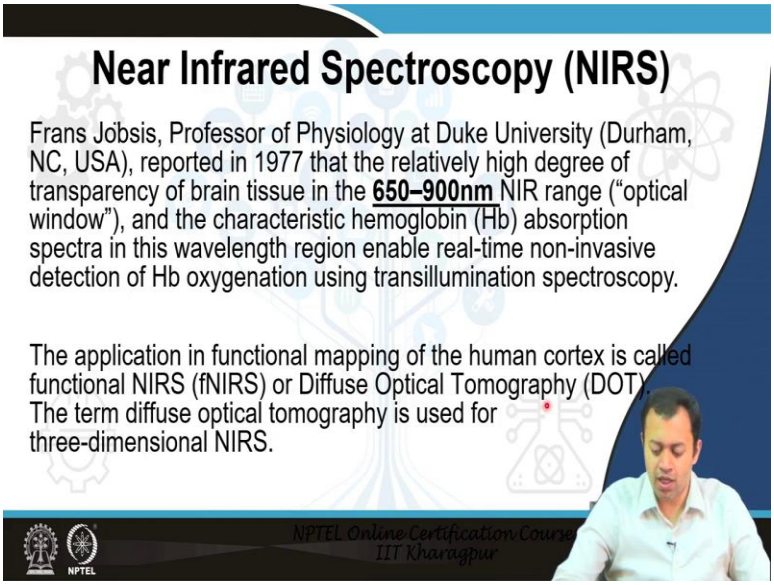

So, what happened was this gentleman, Professor Frans Jobsis of I think Duke University, Durham reported that in 1977, so quite a long time ago, that this particular frequency range 650 to 900 nanometer NIR range is something that only hemoglobin absorbs, but the brain tissue does not. This is the wavelength range which is absorbed by hemoglobin i.e. the blood, but the brain tissue is transparent at this particular frequency. Make no mistake.

Near-infrared is a slightly larger area up till 2.5 micron i.e. 2500, but 650 to 900 a little bit of this is coming in under the visible, but say 800 to 900 nanometer regions is a specific wavelength of light that is transparent when it comes to brain tissue. It simply transmits through brain tissue without touching it, without doing anything, but it is absorbed by hemoglobin both oxygenated as well as non-oxygenated.

So, people started understanding it and trying to see that if we can utilize this type of a light to illuminate different part of the brain non-invasively and try to see, try to map the, I think there is a good term hemotonic function, which means how the brain's blood bearing capacity, not blood bearing, blood bearing means getting the blood, how the, how will you call it, how will the pattern of the blood in the brain change when you are doing a particular function. So, thereby, they started calling it as functional NIRS or diffused optical tomography. So, I will make it better. Do not worry if you have not understood it yet, because I need a picture to show you.

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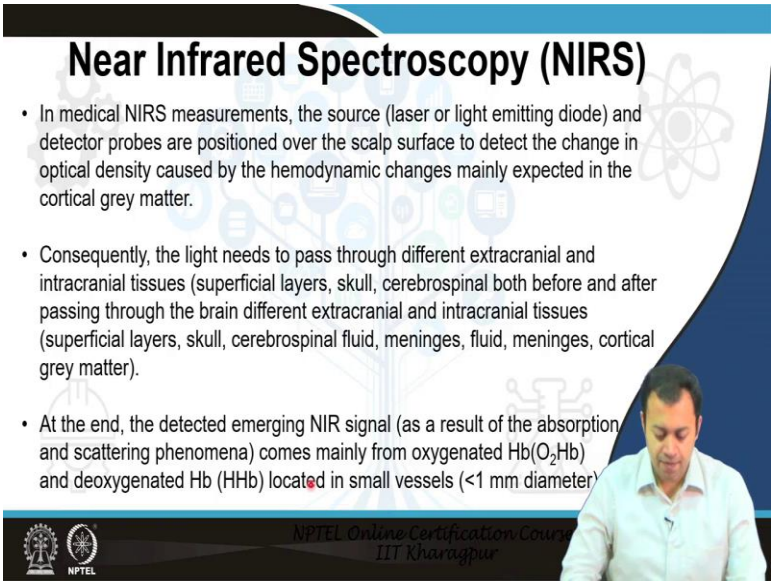

So, couple of things. In medical NIRS we go for, well, let us come to this slide later.

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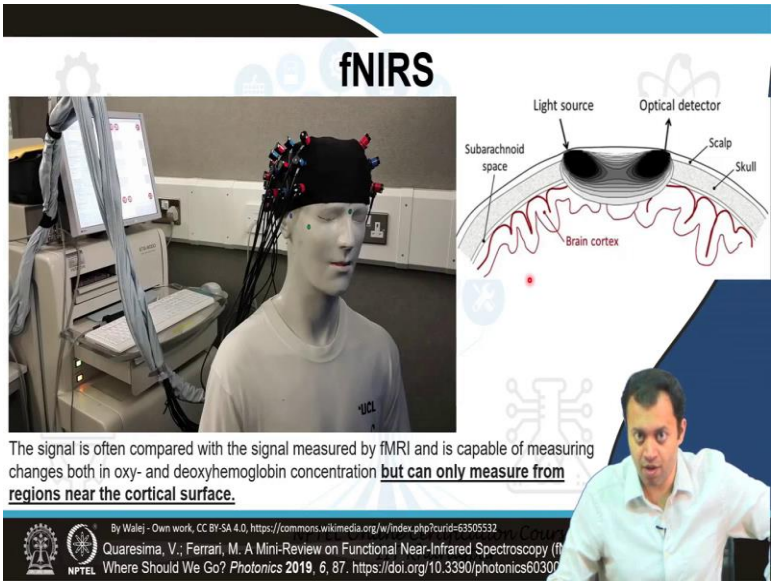

I want to show you this. This is something which I am itching to do. So, what do you do, you put some kind of a light source and an optical detector very close to the skull. In the previous case I told you that you have to penetrate not, in direct with the tissue or near about the tissue, here you are not. You are simply making the detector and the source of the light, very, very close, so this is the light source, say blue is the light source, red is the detector close on top of the skull, these are still on top of the skull, and some of the light is getting diffused through it.

If it is NIRS or near-infrared around 650 to 900, it will penetrate through your skull, through your scalp and even through your brain cortex up till a bit, but it will be absorbed by the blood that is present underneath. So, if this is your skull, this is the scalp. The scalp is the fleshy part from which hair grows and you have dandruff and whatnot scalp, shampoo, you see scalp. So, this is the scalp. This is the hardened skull. And then there is some amount of space and then the brain cortex starts.

This light source, say blue, it can penetrate through your skull, through your scalp and goes even into the brain cortex and the brain cortex is permanently transparent to it. So, it does not do anything. The light will only be absorbed by the blood that is anywhere in the brain. There are technically no blood vessels inside the brain. So, make no mistakes. There are no blood vessels, but still there is some amount of blood. You get clots of blood somewhere. If you hit your head strongly etc. blood clot does form inside brain.

So, it and there is an optical detector. So, you send the light from here and you try to measure the amount of light that has been absorbed. And thereby you form a pattern of the blood flow or I do not think blood flow or blood bearing is the term, how much the blood pattern changes when you perform a specific function.

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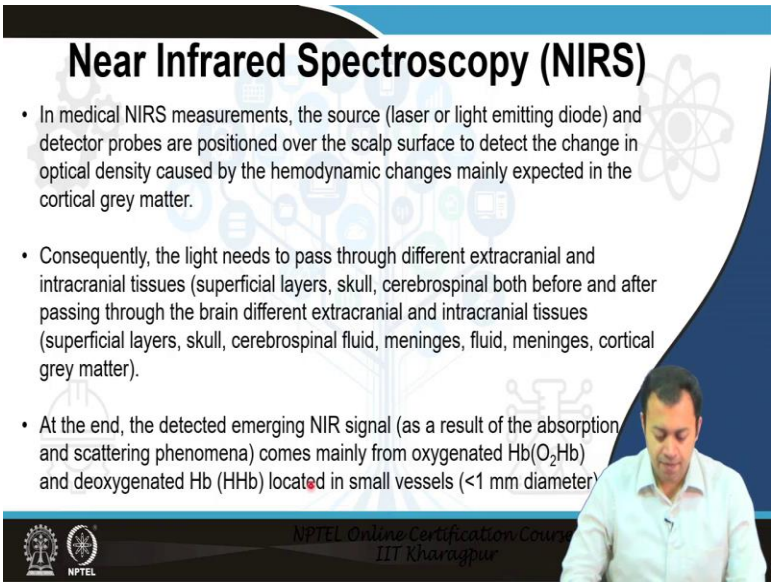

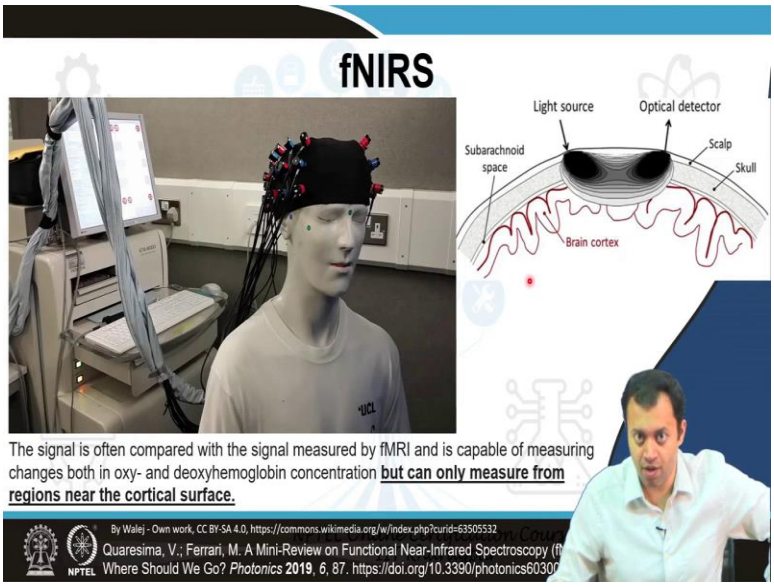

So, now, returning back to it. The source, laser or light emitting diode and detector probes are positioned over the scalp surface, its position over the scalp surface, to detect the change in the optical density, this is the term I was looking for, hemodynamic changes in the cortical grey matter. So, the blood changes hemodynamic, hem is blood, well, actually from the iron, hematite

or something, but us in this medical term is blood, hemodynamic changes happening in the cortical grey matter.

So, this is that cortical gray matter. This is the brain cortex. This is the one which is just beneath our skull. This is the brain matter just beneath our skull. So, the source, the laser and detector probes are position over the scalp surface to detect the change in optical density. So, how much blood pattern changes. Thereby, the source like the, input light and output light pattern changes. Consequently, the light needs to pass through different extracranial and intracranial tissue. Cranium is the overall head, superficial layer, skull, cerebrospinal fluid etc, etc. cortical grey matter.

And at the end, the detected NIR signal comes mainly from oxygenated and deoxygenated blood located in small vessels. It is coming from the amount of blood or the blood pattern, hemodynamic pattern coming from oxygenated and deoxygenated blood. Your blood is constantly churn, some amount of oxygenated then CO2 forms. So, the pattern that is forming, basically the formation of oxygen near the skull, because of a particular activity being done, hence functional NIRS is something that this equipment measures.

The disadvantage, it can only measure from regions near the cortical surface. It cannot go deeper inside the brain. It cannot get, the light will diffuse simply. The light will simply diffuse. And if you use very strong light, you might damage the skull. You can obviously penetrate the skull, make a drill hole, but then it goes back to the original thing is it safe.

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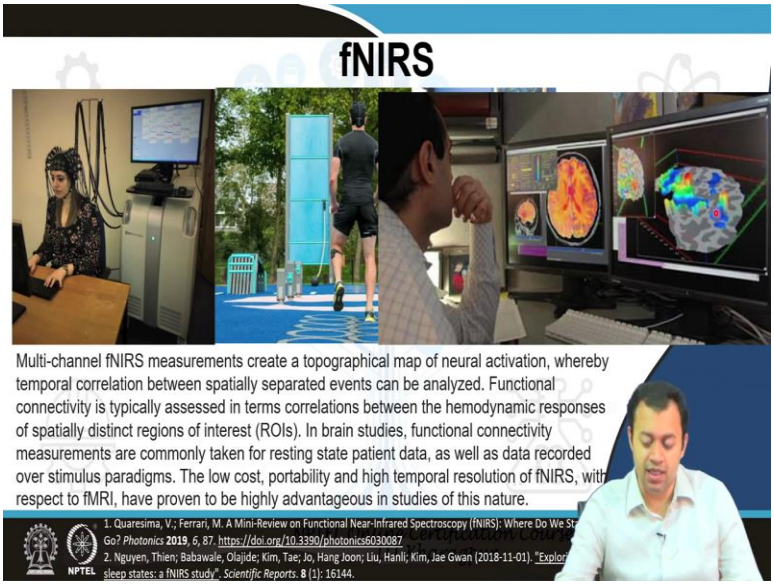

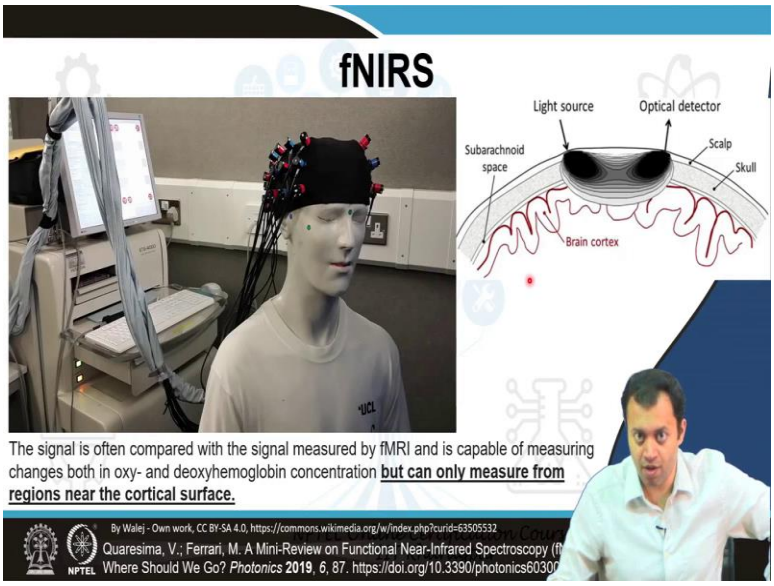

This fNIRS, functional near-infrared spectroscopy is very safe. So, this is something that they were performing. So, you have this cap like thing where blue is the source. I am just guessing blue is the source, red is the detector very close to one another and trying to see the diffusion of blood, the blood pattern, hemodynamic pattern inside the blood and you see it is so safe that even babies are wearing it.

And it correlates the hemodynamic response at different regions of interests with respect to different activities like this person is, she is doing the computer, she is doing something mundane or static, which requires some amount of concentration, whereas this person is doing performing some sort of an exercise going through this hoop running where some sort of directional capacity, some sort of hand to muscle coordination is, brain to muscle coordination is required.

I have heard people do wear these kinds of caps for athletes. Sports person try to ascertain that kind of thing. And here you see this was an interesting phenomenon. The mother and the baby, the mother and the child are wearing similar cortex and try to see if there is a connection in the neural activity between mother and the baby. And no please do not go into bunkum theories like telepathy and extrasensory perception etc. If it exists, this is not eaten. It might exist and that would be news to me. This is scientific. We try to analyze pattern of the baby and pattern of the mother and try to see if there are any similarities through it.

So, functional connectivity measurements are common. And this is comparatively cheaper and easier to use as compared to functional MRI. MRI can also be functionalized, but it is costly and

there is difficulty with magnetic resonance imaging. So, with all these, with the person jumping or saying static, doing some kind of concentrated work on a computer or a mother and baby finally generates this blood flow pattern, this overall hemodynamic pattern, this blood pattern, oxygenation and deoxygenation. Maybe different parts of the brain will require different amount of oxygen to perform different functions. But the only problem is we are unable to go deeper inside.

This is the scientist who is analyzing which areas are showing greater activity. And they are trying to map it chemically. And then sometimes maybe they will corroborate with it with functional MRI as well. But this is an exploding area. I am unable to give you much more information because of two main reasons. First, I myself do not understand. Let us be absolutely honest here. There is no shame in saying that I do not understand. There is obviously shame in saying I understand but then not being able to teach you. And thirdly, there is no standardized value as of yet.

With photodynamic therapy, photothermal therapy there is somewhat tissue engineering. There is a standardized formula. Here there is not, everything is a new discovery. And what was discovered today may come into question the very next day. So, I can only point you in the right direction. I cannot tell you that this is the finalized version.

So, these are the two papers. My supervisor used to say that if a topic has a textbook available, then most of the things on that topic has already been covered, already been discovered, already been researched. If it only scientific journals and scientific papers on that particular area you are finding then there is still some hope for you to do research.

Well, not always true, I semi-agree with him, but you get the point. So, these are so called hot topic. I get this question always in the forum which topic I should look on to. So, optogenetics, neurophotonics, brain imaging, functional brain spectroscopy is something that is incredibly challenging, incredibly complicated and equally rewarding. Not many institutes have the capacity to perform this. Remember, you will get into several different kinds of ethical and moral trouble.

Is it okay whatever you are seeing is frustrating because you are only understanding a tiny, tiny percentage, only the areas which are closer to the brain, you can, closer to the scalp, closer to the

surface you can measure, not every brain function is because of change of oxygen or change of blood pattern, what is happening to the cortex inside we can only understand when you have inserted something and that brings in whole new type of trouble. So, this is an exploding area. Those of you who are interested, I strongly suggest you to do a thorough literature search on neurophotonics, optogenetics and neurophotonics and you will see huge amount of convergence between this.

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So, that more or less brings me at the end of this specific module and with that into the biophotonics there is only one lecture left which I will dedicate to mostly discussing revisions or summarizing the entire topic. This is from an exam point of view, from your course, syllabus point of view, this is where I draw the line.

This is all that I had to teach you in this particular course. I hope some of you have understood, some of you are excited, some of you are curious, wants to go further, wants to know more, you are more than welcome. I am here to answer any of your questions. We meet every four weeks live. So, you can ask me question there or you can drop me an email. But this overall completes your course.

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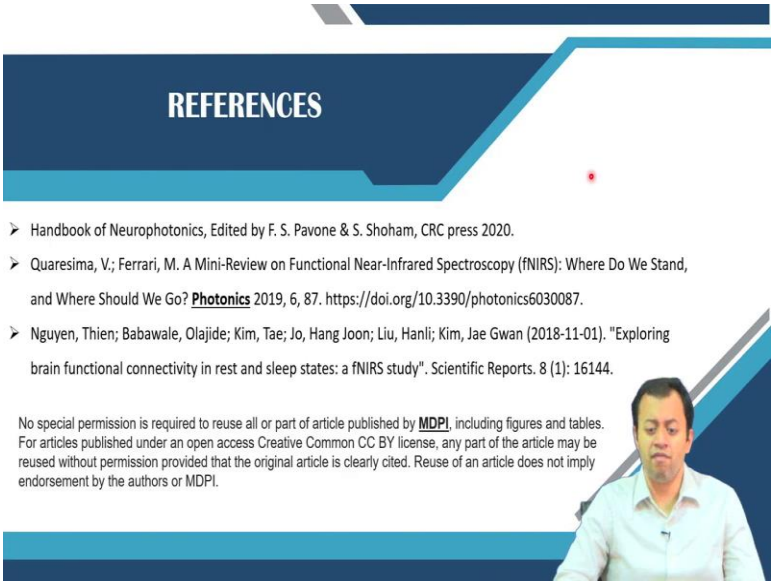

So, just please go through some of my references. And there is only one chapter remaining. One lecture remaining, beg your pardon, one lecture remaining. All the chapters are finished. And the course for all intent and purpose is finished with this.