Biophotonics
Professor Basudev Lahiri
Department of Electronics & Electrical Communication Engineering
Indian Institute of Technology Kharagpur
Lecture 41
Laser Based Tissue Engineering

Hello and welcome. So, today we will start our module number 9, which happens to be Tissue Engineering with Light. And in this module, we are going to discuss the direct application of laser, laser light onto human tissues. Previously we have discussed photodynamic therapy where either a specific type of chromophore, specific type of a drug or something else like photothermal therapy you have seen, gold nanoparticles they have been used which interacted with laser and thereby created either reactive oxygen species or generated heat.

Here, instead of any of those intermediator things, we are going to apply directly laser light onto human tissue for the purpose of tissue engineering. Now, all of or at least some of you engineers not the biomedical engineers, of course, but maybe perhaps the Electrical and Electronics Engineers as well as the physics people are wondering what is tissue engineering.

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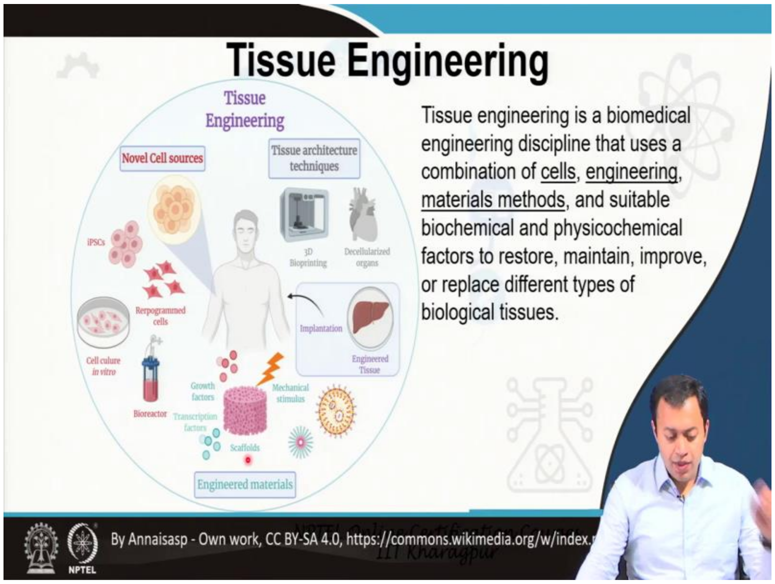

So, here is a useful chart for you. Tissue engineering it is a discipline of the biomedical engineering and it uses various methodologies, it uses cells, different types of materials, as well as engineering concepts to restore, maintain, improve or replace different types of biological tissues. Replacing or removing or restoring, maintaining of biological tissues are of, one of the primary importance for the wellbeing of a person.

Certain valves get damaged or you have known about angioplasty or retinal detachment or some wound healing or skin grafting all of those things can be, can be faithfully, reproducibly, safely done by the process of tissue engineering. Tissue engineering is very strongly coming up subject is a part of biomedical engineering and I hope to see like you these days in engineering colleges, see disciplines such as civil engineering, mechanical engineering, electronics engineering,

I hope to see tissue engineering in itself coming out of biomedical engineering as a discipline rather than a chapter or rather than a subject or rather than just a small additional topic that biomedical engineers needs to study because tissue engineering has the capacity to believe it or not convert human beings into super human beings.

So, what does tissue engineering actually do? So, I discussed a bit about stem cell therapy, it utilizes either stem cells or some kind of a culture, some kind of a growth factor, some kind of scaffolding, etc. insert them into, into human body, to, as I said, to either replace or maintain or improve, improve the quality of life, improve the health condition of the person. So again, as I said, tissue engineering needs to come out and create its own discipline by itself.

I am taking this opportunity to teach you a very common and a very interesting topic of tissue engineering, which is not directly related to biophotonics per se but by giving this example, for those of you who do not know or are hearing tissue engineering for the first time, we will come to a clear understanding what it is.

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So, we are creating artificial human hair, human ear, artificial human ear. So, this is a lab made ear. And no, this is not made up of plastic, this is made up of the same material which is cartilage, which, which our ears are made up of. We can create in a petri dish, this is a petri dish, you all know and putting it under certain sets of conditions temperature, pressure, pH, and by adding some cartilage cells, it could be stem cells, or certain similar things with proper growth conditions, proper factors, biomedical students know this under certain circumstances you can actually grow them.

Nowadays there is 3d bioprinting, must have heard of 3d printing, it is coming up very strongly 3d printing is coming to be used in tissue engineering. We are able to generate, we are able to generate tissues in a petri dish. We are able to generate tissues of specific shape, size, colour and texture in a petri dish using either stem cells that is easier thing or normal cells we reprogram it back or just any cell taken from any other part of the body converting it into. And there is a very nice example of utilizing these kinds of tissue engineering to regrow, yes, you have heard the term regrow human ear.

So, I asked you, this is my reference here, I asked you to go through this paper and read through the fascinating surgical as well as the medical procedures these doctors were able to do. So, this child was born with this congenital ear defect where the ear was not formed, you must have seen these kinds of disability or defects, defect is a bad word in this case, disabilities coming up this is a congenital, congenital problem.

And they have regrown an ear made up of cartilage, it is not made up of plastic or any artificial material, it is not those artificial limbs or artificial leg that sometimes people who have, who have either gone through the process of amputation or some kind of accident (())(6:53), this is not artificial per se in that regard, this is not made up of plastic or metal or wood or any such thing, this is actually, actually cartilage, the cartilage is the soft tissue that, that covers the bone or that forms part of our ear and some part of our eye and several portions of our body.

These are not as hard as bone at the same time not as flexible as muscle or skin they are somewhere in between, you know what cartilage are. So, they created it with a cartilage put it surgically, put it inside the child's ear and giving sufficient growth factor the body actually accepted the ear of as its own, meaning as the child will grow the size shape characteristics of the ear will grow as well. In artificial limb or those kinds of things crutches or similar thing they are, they are fixed they are made up of plastic or metal or wood and they do not grow.

Jaipur foot for example, fantastic as it is it is not the real thing. Here, the body has accepted it and after a few years, few months as you can see that the body will start growing blood vessels onto it so that after certain time if this ear, this, this so-called artificial ear that has been implanted on the person's body get injured it will bleed, it will bleed. So, this is what tissue engineering is, this is what tissue engineering is. Now, obviously you will understand that cartilage one type of tissue and it is somewhat easier to make though easier in relative terms.

But this is just a start, this is merely the beginning think of the possibilities that we could do, we could replace a limb, we could replace maybe even torso, any other part which has been injured or which has been lost due to some sort of accident or birth defect can be replaced, tissue engineering is showing this potential, tissue engineering is showing this potential that a lost body part can be regrown in a lab and then surgically inserted into the person and it could be an external limb, external organ, external appendage or it could be an organ.

Why not, if you can grow ears can we not grow kidney, instead of good waiting for some kind of transplant let us grow a kidney into the laboratory made up of the stem cell or made up of the cells that the person him, herself or himself possess, create something like this and insert it into the person's body there will be complete acceptance that needs to be accepted, the complete acceptance or that chances of acceptance from the person's body is much more to, to a lab grown stem cells grown kidney rather than something transplanted from another person.

I know, I am simplifying it tremendously and medical students are scoffing that there is a huge amount to unpack. And obviously that is what I am saying, tissue engineering needs to be disciplined like civil engineering and I under no circumstances am trying to pretend that I can explain it to you within 2 or 3 minutes but I am abreasting you to the possibilities that tissue engineering produces.

And this is not necessarily directly related to Biophotonics, but I want you to know this because this is fascinating. So where is biophotonics coming up in this, that is what we are going to discuss, we are going to discuss laser induced tissue engineering or laser based tissue engineering that is the course module number 9, that is what we are going to discuss and it is, this module is quite not that intense, I know several of my modules have been 1 hour instead of 30 minutes, I will try to finish them these are mostly examples because you know overall, I assume you know the overall theory whatsoever beforehand. So, I think my work will be easy.

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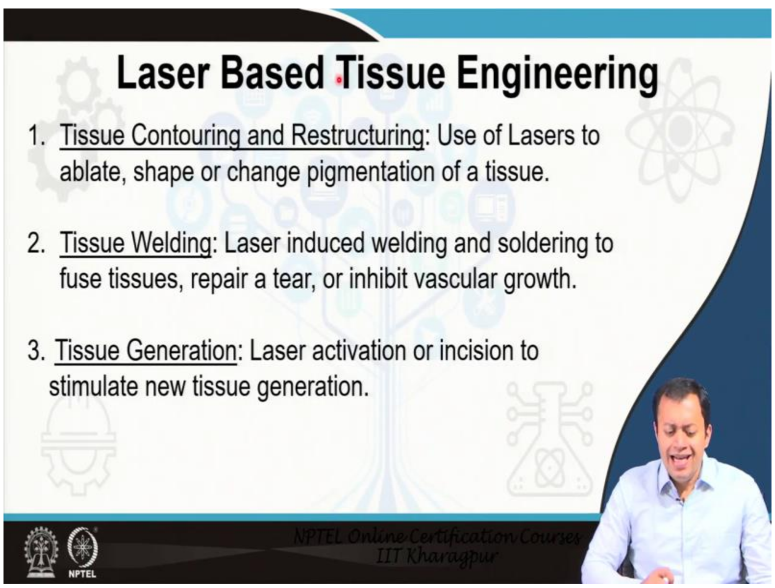

So, laser-based tissue engineering mostly fall into three categories; first is the tissue contouring and restructuring. Here tissues are mostly used to ablate, basically made some kind of incision, make some kind of, it is a destructive process overall, it is basically localized heating and then removal ablation simply means destruction or cutting. It, it changes the shape or changes the pigmentation of the tissue, this is the coloration of the tissue.

Then there is tissue welding it is just like metal welding, two metal plates are in a joint together and you have a welder with a high-power heat source or a laser source whatsoever converts the junction between the two plates into molten state and these molten two metals this the junction fuses and upon cooling they become one single plate.

So, tissue welding is very, very similar thing, welding or shouldering to fuse, fuse tissue and this is used in some kind of a wound healing or repair a tear some, some kind of blood vessels have ruptured or in your retina, retina has got detached something similar, something that, that has broken needs to be fused, needs to be connected.

And then, this is slightly controversial and we are going to take it head on as well. Tissue generation, where supposedly under with underlining the mark, supposedly laser activation stimulates new tissue generation, so by sending laser light you are creating the tissue to grow or the tissue or the cells to proliferate and thereby form it is a growth, so it is just the opposite process of restructuring, here you are you are purposefully damaging the tissue, here you are re-growing the tissue.

And this is, this is coming up very strongly but, but the jury is still out, we are still not sure about the science, so whatever we are going to discuss I have dedicated almost a separate chapter for this and we are going to discuss this at, at detail but overall laser-based tissue engineering more or less falls into these three categories.

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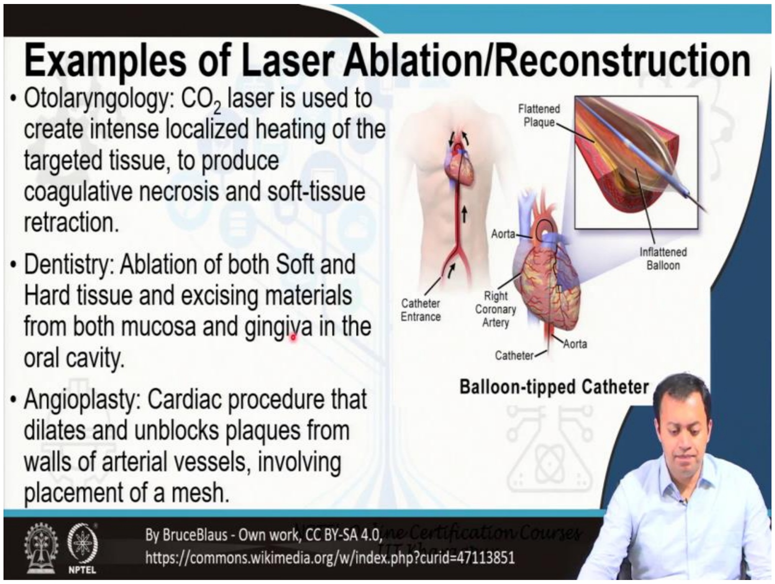

So, where, where exactly do you want to use them, like for example laser ablation or reconstruction. So, I will pretend to pronounce it like I know Otolaryngology, medical students come to my help this is well carbon dioxide laser is used to create intense localized heating and basically it produces necrosis, you burn the tissue out tumour or something like that.

Dentistry, ablation of both soft and hard tissues and excising materials from both mucosa and gingiva in the oral cavity, what does gingiva, I just learned this new term what does gingiva means, I know many dental students are giggling it means gums, gums where your teeth are connected, mucosa is the upper line.

So, in dentistry you are going to destroy some part of the soft and hard tissue for oral or mucosal surgery if you have some sort of a tumour or some sort of incision, some sort of a wound something needs to be done. This is basically burning of, of a soft tissue something that has damaged maybe cancer. And angioplasty, I discussed about angioplasty beforehand. Here the laser-based angioplasty instead of PDT you are directly putting the laser and destroying the plaque, destroying the plaque here.

This is the balloon tip catheter, I discussed about the balloon tip, the balloon opens up the artery and see how it has gone you insert your catheter which is which could be at optical fibre tube and it goes inside the heart and then it put goes through the ventricles or the smaller, smaller capillaries which when is zoomed you can see that the balloon tip catheter or balloon tipped angioplasty have had happened.

This is, so how, how small this is the zoomed in version, so how small this area might be what would be the diameter, is this thinner than the width of your hair, what do you think, this capillary inside your blood, inside your heart do you think this is thicker or thinner than a strand of your hair.

I also asked what happens when the balloon is removed it might fall back, so we usually put a mesh, some sort of a strong and sturdy material permanently being put involving placement of a mesh, mesh is basically a net which supposedly does not, it basically keeps it is like a scaffold thing it keeps the artery open and does not let it collapse it is made up of either steel or any other kind of implantable material and the idea of this mesh is it should not be interfering with either the blood flow per se, well obviously it will open up but it will not have any adverse allergic reaction to the plaques, so that is the idea we put a permanent mesh.

So, laser destroys these plaques or heats it up, melts it down and the balloon opens it up and then you put some kind of a mesh behind. So, these are all tremendous surgical procedures that could be either done directly or with the help of laser. So, what basically laser does, laser burn or produce localized heating at a specific, specific area without damaging the surrounding places that's the overall idea.

Here, however unlike PDT, since it is a direct laser connecting with the tissue you have to bring the laser light pretty close to the area, pretty close to the area of your operation that is the requirement. So, usually it has found application in either dentistry, I have dedicated lecture for laser-based tissue engineering in dentistry or in dermatology skin basically where you can directly bring or in ophthalmology eye, so these are the three major, major areas however the other areas there. Today in this module I am just giving you the introduction.

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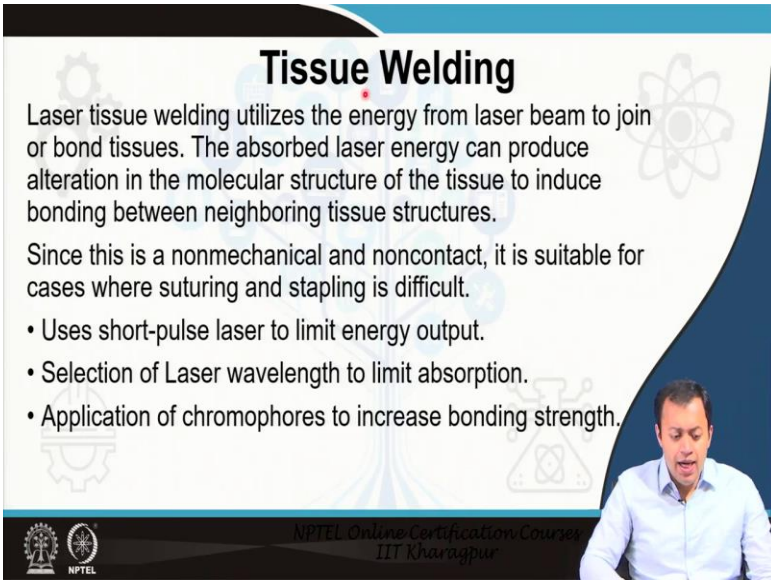

So, tissue welding on the other hand it utilizes the energy of the laser beam to join or bond tissues, as I said what does welding actually means. The absorbed laser energy can produce alteration in the molecular structure of the tissue to induce bonding between neighbouring tissue structures, it is the same thing two metal plates by heat you are fusing them together, they are liquefying.

But the liquification is with the help of a laser is only at the periphery or at the junction or at a specific area which is helping them which are, which is basically altering their molecular structure previously they were solid now they have, they got more energy they are liquefied so the molecule or structure has changed and this molecular structure is used to fuse two different types of tissues, to different types and then upon cooling they combine together.

So, and this is a nonmechanical and noncontact, so where suturing or stapling is difficult. Suturing is basically stitching, when you have wound or some kind of a deep wound doctor stitch that area many of you might have got stitches as child, I surely got several because I used to run quite a lot and fall down more than that. So, suturing in my knees and places where the stitches are done. So, where it is difficult to suture, say for an internal injury or even stapling, perhaps, we do staple as well for a proper procedure for wound healing.

Now, tissue welding is being used more and more and it is non-mechanical and noncontact there, I would not say it is been painless though some people claim it is, definitely, definitely not painless, trust me in this one, but it is suitable for cases where these are difficult. If it is a normal surface wound doctors are still doing suturing, stitching, but tissue welding is coming up, this is very strongly coming up in wound healing.

So, basically, you use short pulse lasers to limit energy output, you do not want to melt the entire area, you want to melt specific tissue, specific cells and then they need to get coagulated and fused together. If you have completely killed of the cell, if you have completely cause necrosis, remember from last class what does necrosis actually means, if you have carbonated the cell or carbonated the tissue charred the tissue then obviously, it is not going to work you have to make it with a specific, specific power with limited energy.

And obviously, you have to select the laser wavelength that is only absorbed by the target itself. Say for example, you are targeting epidermis or dermis part of you of your, of your skin. So, you have to ensure that, that needs to be selective and specific. And then, you can add some kind of a chromophore beforehand to increase the bonding strength, but that comes at a later stage that is that is important, but not so important, these two things are important.

So, basically, you are generating heat directly onto the tissue by laser light. Laser is getting absorbed, certain photons of the lasers are getting absorbed by certain, certain organelles, certain cellular components certain part of the issue and upon absorption of heat, either, either the emit heat or emit light or the basically dissipate heat, their molecules structure change and that this molecular structure change and their dissipation of heat is being utilized to engineer, to mould, to restore something that has gone bad, very, very simply put.

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So, as I said, this is going to be a very small and very easy chapter, mostly examples, I will show you pictures and that is it. So, these are again the most of the topics that I, that I discuss tissue engineering and laser tissue engineering. Biomedical students or those of you who are non-biomedical, but have strong interest in this regard, I strongly suggest you to look into tissue engineering very, very seriously.

This is a fascinating topic. And though it does not directly come under the realm of bioengineering, it is it is coming up very strongly as something of middle ground between engineering and medicine directly.

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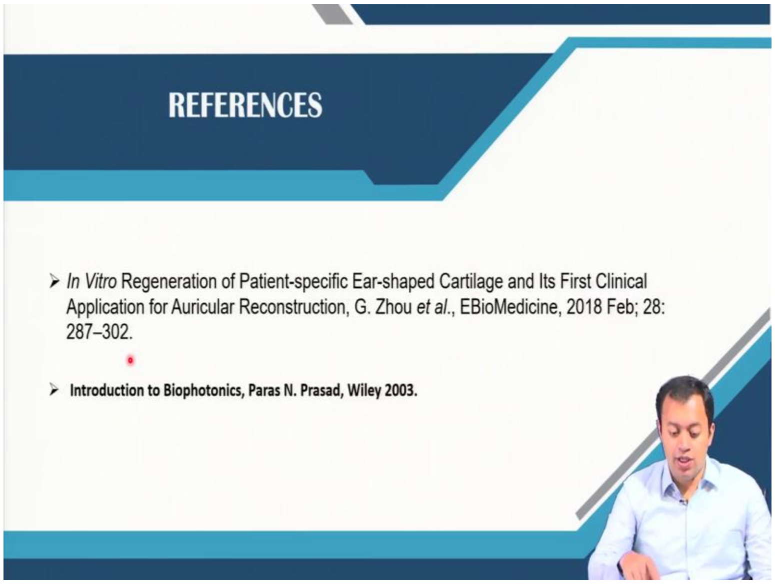

So, this is the paper that actually discuss how the ear was grown and then it was fused into the patients and this is patient's specific ear shape, so it is not just a random ear of any xyz shape that you have grown into the lab and fixed to the child it has to be of a specific shape. And it is a very interesting paper. Please, please go through it. And I will see you in the next class. Thank you very much.