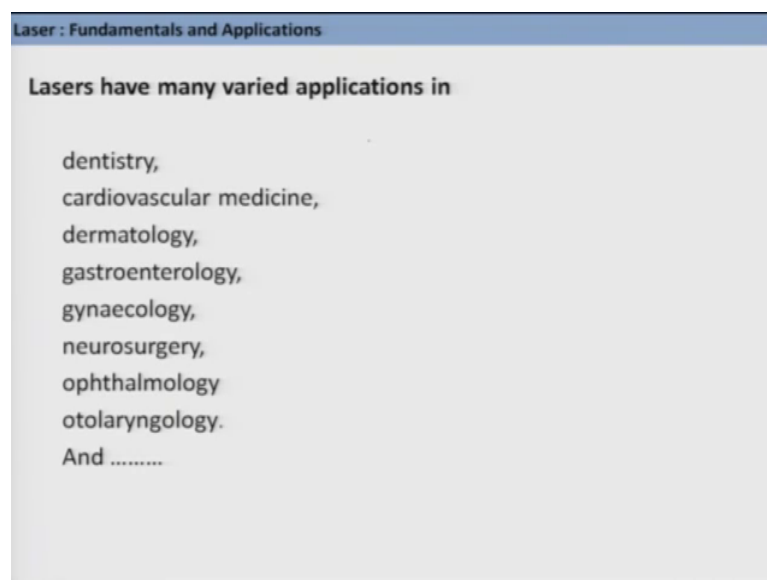


Laser: Fundamentals and Applications
Prof. Manabendra Chandra
Department of Chemistry
Indian Institute of Technology, Kanpur

Lecture – 38
Lasers in Medical Sciences

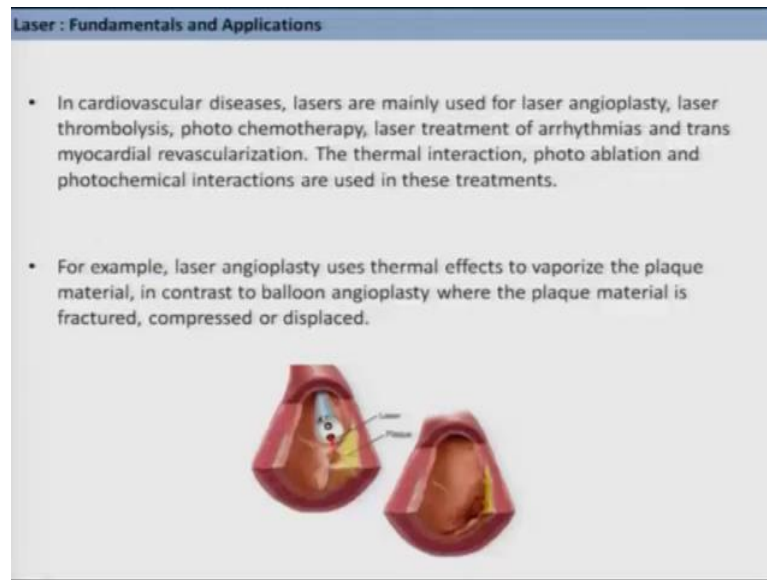
Hello and welcome we were discussing different applications of laser. So, today we will be talking about applications of lasers in medical science and related areas. So, lasers can have you know different types of applications in the medical field.

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So, it can have application in dentistry cardiovascular medicine dermatology related to skin gastroenterology which deals with you know treatment or diagnosis in the gastrointestinal tract gynecology, neurosurgery, ophthalmology and otolaryngology and many other things. It may not be possible for us to you know go through all the different areas in medical sciences where laser can be application applied, but some of them we will definitely look at.

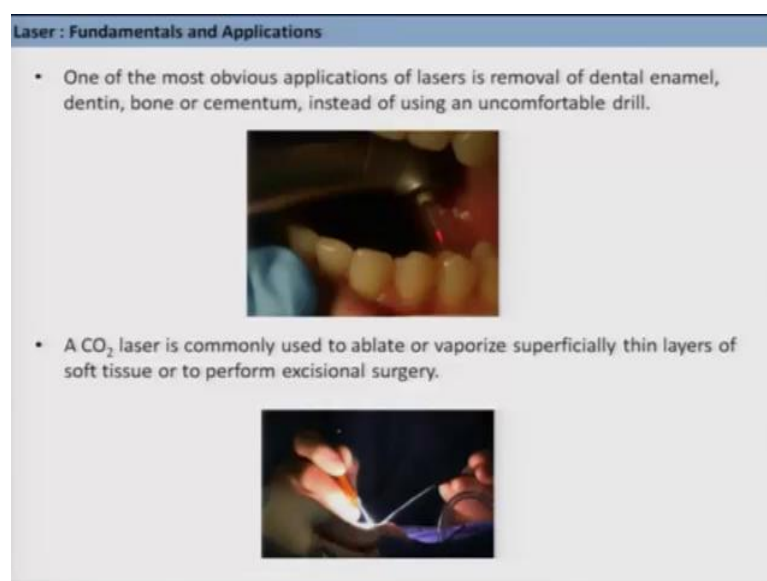
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So, we will start with the cardiovascular diseases. So, in cardiovascular diseases lasers are mainly used for laser angioplasty. Laser thrombolysis photo chemotherapy, laser treatment of arrhythmias and trans myocardial revascularization. The thermal interaction photo ablation and photochemical interactions are 3 different modes of the laser treatment used in this particular segment. So for example, the laser angioplasty uses thermal effects. So, on your screen you can see that the image is given for you know part of artery where you send in your laser through fiber optic cable. And in the affected region where so, it is written in you know given by this yellow color. So, in this region you have kind of blockage in the you know artery and this laser you know is sent by 5 fiber optic cable. So, focus laser beam is you know used to remove those blockages that is created in the artery in case of angioplasty.

So, normally angioplasty is done using something called balloon surgery where you sent one small device with which has like a propeller kind of features. So, it goes and open you know inside artery and then it starts you know moving. And that you know takes out those blockages and those you know derisions are actually comes into the blood. So, using laser you can you know do it in much better way compared to the balloon surgery, because here you just you know completely you know destroy that you know region which is creating this blockage within artery.

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Another very obvious application of laser is the removal of dental enamel. So, in many cases we have cavities formed in the teeth. So, they are affected areas in particular teeth one can use a laser beam to totally remove that infected region. And this is not only done to remove the dental element enamel, but also dentine or it is also used in case of bone or cementum. And this technique is much superior than the conventional technique where you use a drilling machine and you clean your teeth or say some effective region of bones, here the use of laser is much less painful in many cases it is almost painless compared to the conventional method.

And the commonly used laser for this purpose is a carbon dioxide laser, which essentially ablates some region of that teeth wherever it is required or it can vaporize that one also. So, you can remove a very thin layer of that portion or a plaque on the teeth or bone or even in the soft tissues. So, this is also much better than in a conventional surgery where you go through really painful methods of removing the affected parts of teeth skin bone etcetera.


So, in terms of like in the case of dermatology the most common imperfections of the skin such as pigmented lesions.

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- The most common imperfections of the skin, such as pigmented lesions (port wine stains, haemangioma, lentigines) and tattoos, are usually treated with visible lasers including dye, argon, diode and ruby lasers.



- Laser are applied in gastroenterology to treat gastrointestinal haemorrhage from peptic ulcers (Nd:YAG) lithotripsy to fragment common duct stones in humans (tuneable dye, Q-switched Nd:NAG, pulsed Nd:YAG) and many other applications.



So, like you know you have many cases on the skin there are like you know either white or you know dark spots appear. So, also you know one can to you know get tattoos on the skin and later on you want to remove that. So, this things are turn essentially using lasers and the kind of laser that is used here are likely eye laser organ laser diode laser ruby laser etcetera. Now a days you know the use of diode laser for this purposes are very very common in the you know area of gastroenterology different type of diseases like gastrointestinal hemorrhage where you know the blood comes out due to peptic ulcer.

India is used India laser is used to treat that. Lithotripsy to fragment common duct stones in human is also done by using laser such as Q-switched Nd:YAG or dye lasers and many applications also you know the pulsed lasers are also used in many of the applications.

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So, here in this page you can see image where this skin treatment is being done using a laser. Then one of the very important in our is very common surgery involving laser which is known as laser assisted in situ keratomileusis or in short lasik. Many of you must be must have heard about this term lasik at least. So, this lasik surgery it involves sachsenring that holds the I study, while you know performing the this microkeratome which is essentially cutting instrument and this is you know put in proper place as you can see in this image also. So, something is holding this you know eye. So, that you know it is opened and then you come with this microkeratome which is kind of microtome which is used to cut very thin slices. And afterwards you bring in your laser to do the operation surgery.

So, this microkeratome which you know cuts a very thin slice and then it is just you know removed such that there is an end part still attached to the eye surface. So, that it acts like a chinch, and once this is done then you bring your laser and you use the laser beam to you know correct the curvature of the surface of you know the retina using laser ablation and you correct your power.

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Laser : Fundamentals and Applications

A few important points

- In surgery, femtosecond pulses allow for much more precise cutting than do nanosecond lasers.
- The biggest advantage of ultrashort pulsed lasers in surgical applications is limiting biological tissue damage. The pulse interacts with the tissue faster than thermal energy can diffuse to surrounding tissues. It simply means less, if any, burning and destruction of neighbouring tissue.
- The radiation–biological tissue interaction is determined mainly by the laser irradiance [W/cm^2], which depends on the pulse energy, pulse duration, and the spectral range of the laser light. The interaction depends also on thermal properties of tissue – such as heat conduction, heat capacity and the coefficients of reflection, scattering and absorption.
- The main components of biological tissue that contribute to the absorption are melanin, haemoglobin, water and proteins.

Now few important points that I would like to discuss at this point that in surgery femtosecond pulses allow much more precise cutting than do nanosecond lasers, because they have you know much higher peak power compared to nanosecond lasers and one of the biggest advantage of this ultra short pulses coming from femtosecond lasers in surgical applications is that they limit the you know damage of the biological tissue. So, most of this medical applications they involved you know the laser contact with you know different parts of you know living body.

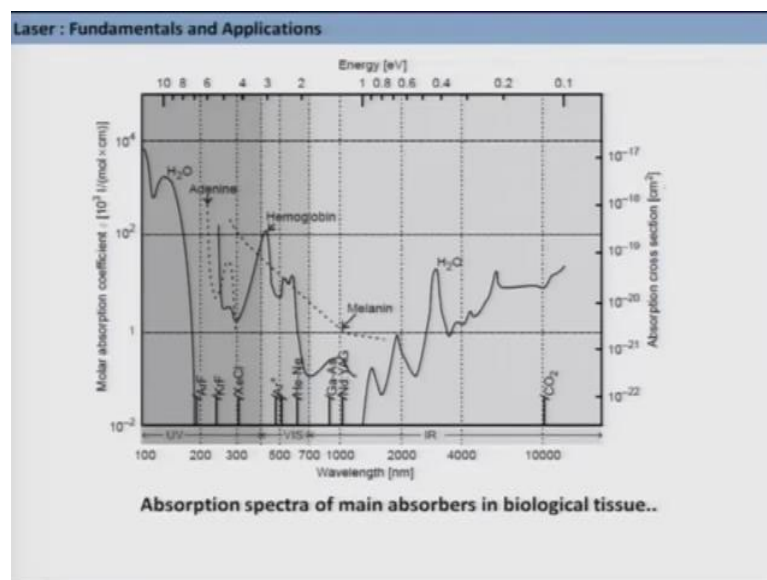
So, if the light is very you know strong then if the body part absorbs lot of light then that can be detrimental. Know usage of this ultra short pulse avoids this kind of problems; because they are you know the skin is exposed for a very short period of time. So, the you know the amount damage is very very limited. So, the radiation and you know biological tissue interaction is determined mainly by the laser irradiance which depends on the pulse energy pulse duration and the spectral range of the laser light the interaction depends also on the thermal properties of the tissues such as heat conduction like once a heat is generated at a place if the heat is you know quickly dissipated then the chances of damages are less.

And you know also it depends on the heat capacity of the particular region or particular tissue that we are talking about and how much light is reflected from that particular surface or you know scattered or absorbed that also determines how much interaction

will take place between light and that particular you know said tissue and with that there is a chance of damage or not. And these biological tissues which are of our interest when we try to do laser surgery they have several components and the most you know the important you know the components for us which actually contribute to the light absorption includes melanin hemoglobin and of course, you know several a minor proteins and water. So, they absorb lights of various different wavelengths. So, this are few things that we should you know keep in mind.

And spectra the spectra of several absorption spectra of several structure components are you know showed here.

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And you can see that they have several absorption band in the different regions of the light spectrums starting from ultra violet to infrared. And the corresponding laser lines are also displayed here. So, if one wants to use the absorption property of this components within the biological tissue than one can selectively choose the wavelength by selectively choosing a particular laser. And you know some other properties are also given here in this slide

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Laser : Fundamentals and Applications

- The absorption properties of the main biological absorbers determine the depth of penetration of a laser beam.

Comparison of penetration depths in biological tissue for different types of lasers

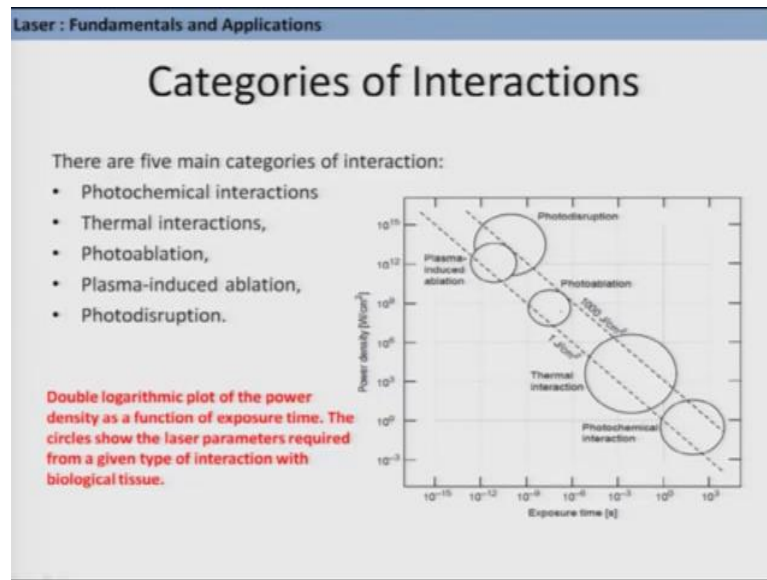
Laser type	Wavelength [μm]	Penetration depth [mm]
CO ₂	10.60	0.10
Nd:YAG	1.064	6.00
Ar ⁺	0.4880, 0.5145	2.00
Excimer	0.193–0.351	0.01

- For example, the Nd:YAG laser can penetrate deeper and a cut made with the Nd:YAG laser will not bleed due to tissue coagulation, in contrast to the CO₂ laser which is a better “scalpel” for precise thermal cutting of tissue due to vaporization by focusing on the tissue along a short optical path.

Where we give the particular wavelength of the laser that you know are normally used say for example, carbon dioxide laser ND laser organ laser and excimer laser. And one very important parameter which is known as penetration depth like if you shine laser on any particular surface then how much below that surface laser light is present that is you know determined by this penetration depth ok.

So, if one needs to you know use laser much successfully you know and particularly in a non lasik we then much more penetration depth is required. So, here in this table certain some you know values of the penetration depths for those laser lights are given.

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Now, we talked about interaction of biological tissues and laser light, now what are the different types of interactions that are possible. So, basically we can categorized this interaction into the in this following in you know 5 parts. One is photochemical interaction, then thermal interaction, then plasma induced ablation photo ablation and photo disruption. So, in the you know adjacent plot it is shown like you know what are the you know what are the what are the chances of having one of this type of interactions as a function of the exposure time of laser.

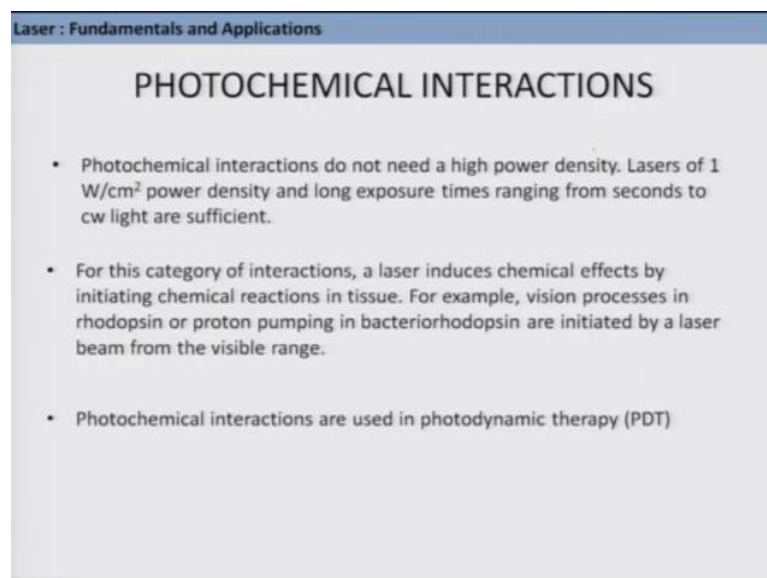
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- Laser : Fundamentals and Applications
- With cw lasers or exposure time >1 s, only photochemical interaction can be induced. Powers of only a few mW can be used for these purposes.
 - For thermal interactions shorter exposure times (1 min–1 μ s) and higher energies must be used. Thermal effects can be induced both by cw or pulsed lasers of 15–25 W power.
 - Photoablation occurs at exposure time between 1 μ s and 1 ns. In practice, nanosecond pulses of 10^6 – 10^9 W/cm² irradiance should be employed.
 - Plasma-induced ablation and photodisruption occur for pulses shorter than nanoseconds. In practice, pico- and femtosecond lasers with an irradiance of 10^{12} W/cm² should be used.
 - Both phenomena occur at a similar time exposure and irradiance, they differ according to the energy densities that are significantly lower for plasma-induced ablation.

Now, using continuous wave laser or exposure time greater than one second, only photo chemical interaction can be induced. And you know if you use a very you know few millivolt of power you know you can use for this purposes. And for thermal interaction you need to have a shorter exposure time that is you know in the order of microsecond, and one must use very high power and it can be this thermal effects can be induced both by continuous as well as pulsed laser which has you know moderately moderate power that is 15 to 20 watt 20 5 watt of power next the photo ablation thing it occurs at exposure time between one microsecond and one nanosecond. So, you can easily figure out that this happens at a very short time scale and normally a nanosecond pulse is of 10 power you know 6 to 10 to power 9 watt percent centimeter square irradiance are employed for this purposes and the plasma in this tabulation and photo disruption this you know takes place for pulses which are shorter than nanosecond. So, picosecond and femtosecond lasers are normally used and irradiance used is approximately terawatt percent meter square.

Now, both this plasma induced adulation and photo desertion they occur at kind of similar exposure time and similar amount of irradiance and, but they differ according to the energy densities that are significantly lower for plasma induce ablation.

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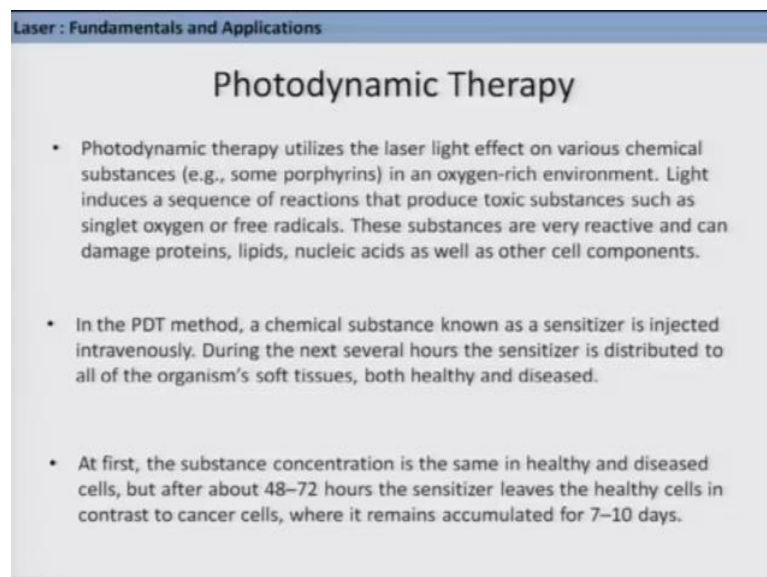
The slide is titled "PHOTOCHEMICAL INTERACTIONS" and is part of a presentation on "Laser: Fundamentals and Applications". It contains three bullet points:

- Photochemical interactions do not need a high power density. Lasers of 1 W/cm² power density and long exposure times ranging from seconds to cw light are sufficient.
- For this category of interactions, a laser induces chemical effects by initiating chemical reactions in tissue. For example, vision processes in rhodopsin or proton pumping in bacteriorhodopsin are initiated by a laser beam from the visible range.
- Photochemical interactions are used in photodynamic therapy (PDT)

Now, we will talk about each one of this type of interactions in little bit more detail. So, the photochemical interactions they do not require a very high power density we already

mentioned, that one and approximately one watt percent per meter square power density and longer exposure time is just required and you can use a continuous wave laser successfully for this purpose and for this category of interaction laser induces a chemical effects by initiating chemical reaction in tissue just as an example the vision processes in rosin or protein pumping in bacteria rosin these are proteins are initiated by a laser beam from the visible range and photo chemical interactions are used in photodynamic therapy so many of you probably have heard about this term photodynamic therapy or P D T in short that is used in various you now medical treatment particularly related to tumor or cancer treatment. So, let us little bit let us have an idea about this photo dynamic therapy.

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The slide is titled "Photodynamic Therapy" and is part of a presentation on "Laser: Fundamentals and Applications". It contains three bullet points:

- Photodynamic therapy utilizes the laser light effect on various chemical substances (e.g., some porphyrins) in an oxygen-rich environment. Light induces a sequence of reactions that produce toxic substances such as singlet oxygen or free radicals. These substances are very reactive and can damage proteins, lipids, nucleic acids as well as other cell components.
- In the PDT method, a chemical substance known as a sensitizer is injected intravenously. During the next several hours the sensitizer is distributed to all of the organism's soft tissues, both healthy and diseased.
- At first, the substance concentration is the same in healthy and diseased cells, but after about 48–72 hours the sensitizer leaves the healthy cells in contrast to cancer cells, where it remains accumulated for 7–10 days.

So, essentially the photo dynamic therapy utilizes the laser light effect on various chemical substances for example, porphyries is you know present in various is in you know important components of you know something like you know hemoglobin or myoglobin this preference are you know present. So, this photodynamic therapy it will utilizes the laser light effect on various chemical substances in an oxygen rich environment we will see why light induces a sequence of reactions that produce toxic substances such as singlet oxygen or some free radicals. Now these substances are very reactive both single singlet oxygen species as well as free radical and contain it is proteins lipase nucleic acid as well as other cell components ok.

So, all it does is that you now laser light in general singlet oxygen or periodic which in turn damages some protein leaked or anything you know present nearby. Now in photodynamic therapy a chemical substance known as sensitizer is injected intravenously during the next several hours this sensitizer is distributed to the whole you know organisms soft tissues and that includes both you know healthy tissue as well as effective tissues. Now initially the substance concentration is pretty much same in healthy tissues as well as affective tissues, but after long period of time like after 2 to 3 days the sensitizer leaves the healthy tissues, but in cancer cells they remain. So, they remain accumulated for 7 to 10 days. Now after 3 days when the healthy tissues have no more sensitizers.

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Laser: Fundamentals and Applications

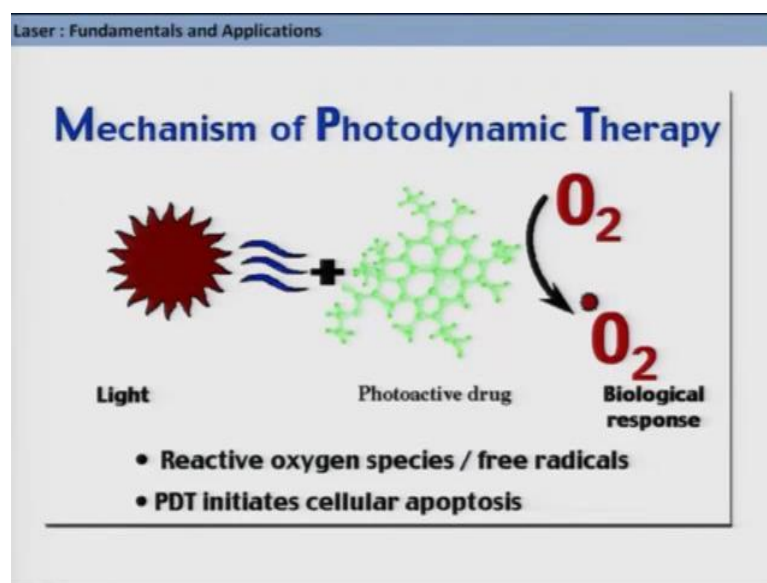
- After about 3 days post injection, the concentration of the sensitizers is about 30 times higher in diseased cells than in healthy ones.
- About 3 days after the sensitizer injection, a patient is irradiated by a laser light. The laser light induces a sequence of reactions with the excited singlet state of oxygen $^1\text{O}_2^*$ as a final product.
- The singlet oxygen $^1\text{O}_2^*$ is very reactive, which makes it extremely toxic as it reacts with components of biological cells and destroys them.
- To protect healthy cells carotene is injected. Carotene reacts with $^1\text{O}_2^*$ causing oxygen transfer to the harmless triplet oxygen state $^3\text{O}_2$.
- The advantage of photodynamic therapy in cancer treatment over commonly used radio- and chemotherapy is selective destruction of diseased cells while saving healthy cells to a large extent.
- In most clinical applications haematoporphyrin derivatives (HPD) as well as dihaematoporphyrinethers (DHE) are used. The commercial name for DHE is sodium porfimer.

You essentially can have nearly 30 times higher concentration of the sensitizers in the effected cells. And at that time that is after 3 days a patient is irradiated with laser light. And the laser light induces sequence of reactions with the excited singlet state of oxygen as a final product. And then singlet oxygen being very reactive it acts as very toxic material and it reacts with components of biological cells and kills then. So, after 3 or 4 days when the laser is irradiated it is made sure that they have left that healthy issues because we do not want to kill the healthy tissue we want to kill the affected tissues that issues which are cancers ok.

So, this time period is given. So, that all the healthy tissues are free from the sensitizer and only the effect tissues are targeted by laser which create single oxygen and the singlet oxygen kills everything within the cell. So, the advantage of photodynamic therapy in cancer treatment over commonly used radio and chemo therapy is that this is selective in chemo therapy the you know the organs or regions are exposed to this you know in many cases the whole body is exposed to you know radioactive chemicals and this is totally unselective. So, it affects everything healthy and un healthy or here we utilize you know a selection of healthy and unhealthy that is affected tissues by the sensitizer them self, which decides that these are not healthy issues. So, they just you know get out of that you know. So, they find out these are the health tissues. So, let us not be here then they just come out while the cancers tissues gets more and more accumulated.

So, after certain time this is totally you know concentrate the sensitizer concentrated only into the affected areas. So, there when we shine laser it kills only those cells which are affects. So, these are very very you know selective, it also does not have those you know hazardous consequences of chemotherapy which many of you are aware that it causes several other side effects which are really really hazards. And so, what is the sensitizer that is used mostly haematoporphyrin derivatives as well as dye haematoporphyrinether are as sensitizer for this purpose.

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So, in this picture the mechanism of the photodynamic therapy is given. So, light falls on the sensitizer sensitizer it helps the oxygen to be converted into single oxygen. And then it singlet oxygen it goes and kills the surrounding you know protein leaped basically whatever is there in that cell.

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Laser : Fundamentals and Applications

Photochemistry of Sensitizers

- There are two main mechanisms of photochemical reactions in sensitizers- I and II type photooxidation.
- In type I photooxidation, the sensitizer reacts directly with another chemical entity by hydrogen or electron transfer to yield transient radicals, which react further with oxygen.
- In type II photooxidation, the sensitizer triplet interacts with oxygen, most commonly by energy transfer, to produce an electronically excited singlet state of oxygen, which can react further with a chemical entity susceptible to oxidation.

So, this sensitizer they have their own photo chemistry and you know one needs to know quite a bit of detail about the photo chemistry of this sensitizer in order to understand or in order to be able to make a much better way to treat cancers using laser. We are not going to the detail of this photo chemistry of the sensitizers next will move into another type of interaction which is thermal interaction.

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Laser : Fundamentals and Applications

Thermal Interaction

- Thermal interactions are induced in a tissue by the increase in local temperature caused by a laser beam.
- In contrast to photochemical interactions, thermal interaction may occur without only specific reaction path and is highly non-selective and non-specific.

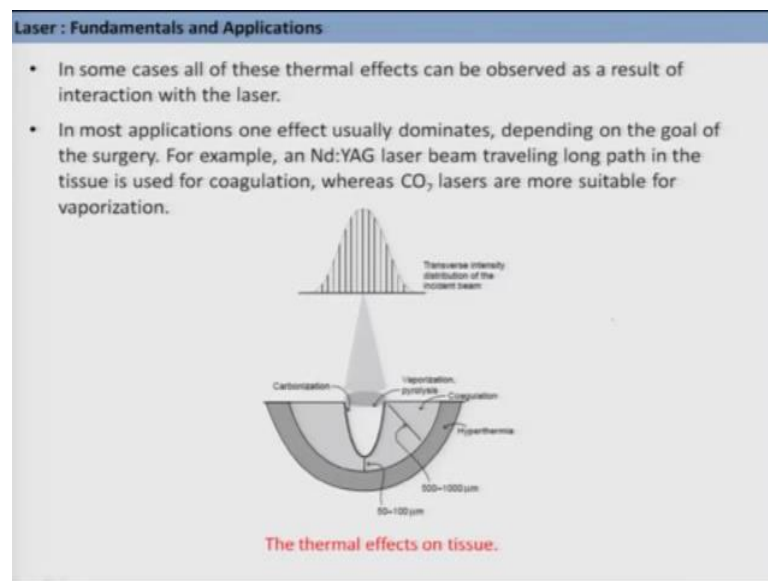
Depending on the temperature achieved, the thermal effect on the tissue can be classified as:

- Reversible hyperthermia ($T > 31^{\circ}\text{C}$) – some functions of the tissue can be perturbed but the effect is reversible.
- Irreversible hyperthermia ($T > 42^{\circ}\text{C}$) – some fundamental functions of the tissue can be destroyed irreversibly
- Coagulation ($T > 60^{\circ}\text{C}$) – the tissue becomes necrotic,
- Vaporization ($T \geq 100^{\circ}\text{C}$),
- Carbonization ($T > 150^{\circ}\text{C}$),
- Pyrolysis ($T > 300^{\circ}\text{C}$).

So, this thermal interactions are induced in a tissue by the increase in local temperature which immediately clear from the name itself and this increase in temperature is caused by the laser beam that we are shining. It in contrast to the photo chemical interaction method the thermal interaction can occur without you know a specific reaction part and is highly non selective and also non specific which is a bit disadvantage.

Now, depending on the temperature achieve the thermal effect on the tissue can be classified as a reversible hyperthermia which is. So, for temperature greater than one degree centigrade which in the in that case some function of the tissue can be perfect, but effect is reversible. So, we withdraw the laser you know the things that is this tissue condition will revert back. Next you can have at a compatibly high temperature that is greater than 42 degree centigrade you have irreversible hyperthermia. So, here continue to the previous 1 it is the conditions of the tissue after the laser exposure will not be reversible, with a larger temperatures like you know greater than 60 degree or greater than 100 degrees or 150 degrees or even 300 degrees there several other processes like a coagulation or vaporization carbonization or even pyrolysis you know is possible.

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Now in certain cases all of these thermal effects can be observed as a result of interaction with laser light. And most applications one effect will dominate others will be kind of subsume, but you may see most of them. Now one effect can dominate depending on the goal of the surgery for example, and Nd:YAG laser beam travelling along path in the tissue is used to achieve coagulation why does a carbon dioxide laser are more suitable for vaporization. So, this is also used for the treatment of you know tumors where you want to you know get rid of that whole effective tissue, but you know the problem it remains that this is highly non specific and non selective contrast to the photo chemical interaction which apparently seems much better than thermal, but never the less the thermal interaction is another method of you know treating cancers patients using laser.

Next we will talk about photo ablation. So, what happens in case of photo ablation.

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Laser : Fundamentals and Applications

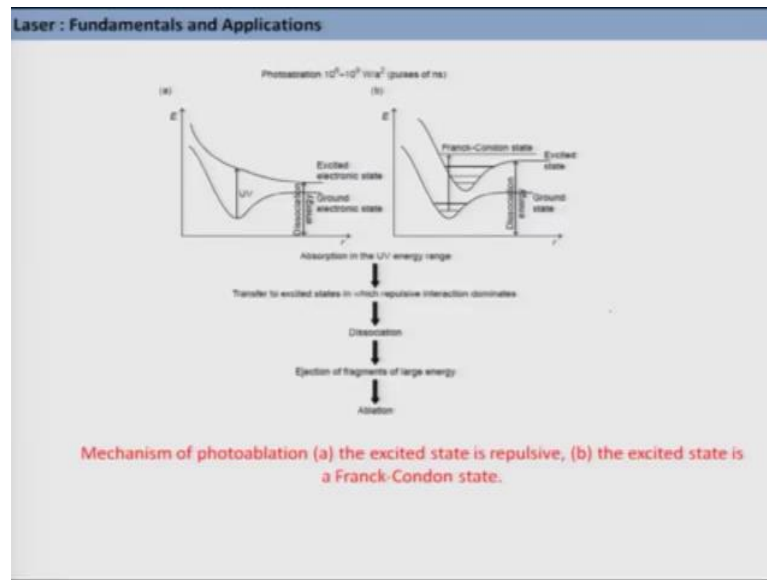
PHOTOABLATION

- A molecule is promoted to the repulsive excited state (or to the Franck-Condon vibrationally hot state) followed by dissociation.
- The chemical bond is broken, leading to the destruction of biological tissue.
- As electronic transitions occur usually in the UV range, the photoablation process is usually limited to UV lasers. Therefore, excimer lasers (ArF, KrF, XeCl, XeF) are mainly employed but higher harmonics of other lasers can also be applied.

So, a molecule is promoted to repulsive excited state which is like dissociative state which we have seen during this class many times and then it undergoes dissociation, now this chemical bond is broken due to dissociation which also causes the destruction of the biological tissue because I am exciting the molecules within this biological system and this is eating it. So, this is sitting molecule within the biological system means the biological total exception of the biological system itself.

Now, as electronic transitions occur in the ultra violet range the photo ablation process is uses limited to UV lasers therefore, aximer laser is used quite a lot within aximer laser you can think of you know organ fluoride or krypton fluoride or you know xenon fluoride xenon fluoride type of lasers. And not only the fundamental of those which hole in the evolution, but also we can generate the higher harmonic of those laser to get into the deep UV to you know be able to do the photo ablation. And here on the you know screen we are showing the pictorial depiction of this photo ablation process Where dissociate state is shown on your left while the excitation is taking place.

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And then from there is dissociating completely whereas, you can have an excitation above the dissociation level for a bound excited state as well and achieve the dissociation. So, this is summarized here also like absorption in the UV range followed by transport of the excited state you know in which that decal civil interaction dominates then it undergo dissuasion and then you achieve the condition of ablation.

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Laser: Fundamentals and Applications

PLASMA-INDUCED ABLATION

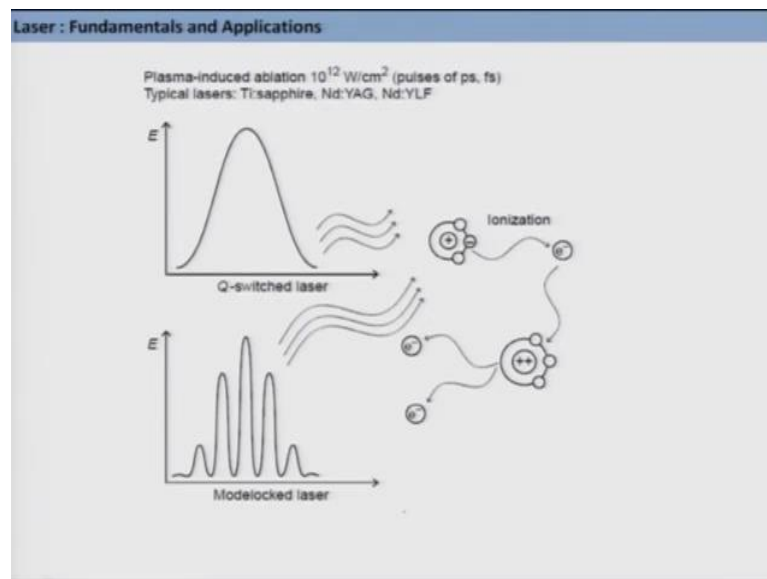
- Typical lasers used for plasma-induced ablation are Nd:YAG, Nd:YLF, Ti:sapphire with pico- or femtosecond pulses generating irradiance at about 10^{12} W/cm².
- Therefore, the Q-switched or modelocked lasers can ionize molecules in biological tissue.
- An ultrashort pulse from a Q-switched or mode-locked laser ionizes biological tissue and generates a very large density of free electrons in a very short period of time with typical values of 10^{18} cm⁻³ due to an avalanche effect.
- Free electrons from ionization accelerate to high energies and collide with molecules, leading to further ionization.
- Light electrons and heavy ions move at different velocities, leading to the effect similar to that in the acoustic wave with areas of compression and dilation.

The next part will be plasma induced ablation, where typical lasers used for plasma induced ablation Nd YAG or Nd YLF type of lasers and ND s that is used approximately

at tetra per centimeter square, and you can you can imagine these are all basically q switched laser because that can give you that much of you know energy irradiance also and all the shots from q switch mod lock laser it ionizes the biological tissue and generates very large density of free electrons in a very short period of time with typical values of 10 to the power 18 cc per cc due to an avalanche effect. So, one you know periodical creates another periodical. So, if you generate 10 periodical those 10 periodicals themselves will generate a 100 periodicals then you know it will keep going. So, it is like a chain reaction or an avalanche effect.

So, this free electrons from this ionization process they accelerate to high energy and they go and collide with the molecules which leads further. And as I said this light there may be light electron there may be heavy electrons and heavy ions produced in this process and they move at different velocities which lead to they effect.

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Similar to that in the acoustic wave where areas of you know compression and dilation take place here we have we have showing that in a schematic way. So, you have you know laser generating this ions and electrons and they do that job in the next step, these are the few applications of lasers in biology we which we should cover many more such applications, but due to the shortest of time we have to stop here. So, in the next day we will come with some more applications of lasers in the field of material science and engineering and also in optical communication.

Thank you very much for your attention.