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SCHOOL OF BIO AND CHEMICAL ENGINEERING

DEPARTMENT OF BIOMEDICAL ENGINEERING

UNIT – I – MEDICAL OPTICS AND LASER APPLICATIONS – SBM1602

OPTICAL PROPERTIES OF TISSUES

1.1 NATURE OF LIGHT

Light isnAn electromagnetic wave seen by humans. Light has the properties of a wave and a particle. Visible light wavelengths between about 400 nm-700 nm.vWavelength is the distance that light travels in one oscillation.The intensity of the light varies depending on the number of particles.

1.1.1 Light Interaction

Reflection

Refraction

Absorption

Fluorescence

Scattering

These interactions depends on constituents of tissue, Optical properties of tissue and Propagation of light

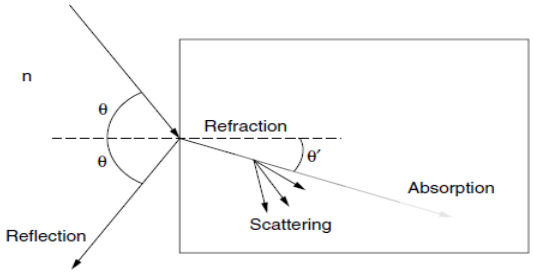

Fig 1.1 Light interaction in medium

1.2 REFRACTION

When light travels from one material to another it usually changes direction. The bending of light that occurs at the borderline of two materials is called refraction**.** Refraction is caused by the change in speed experienced by a wave when it changes medium. The amount of bending depends on the optical properties of the two materials- characterized by their index of refraction: n. The refractive index n, determines the speed of light. The refractive index of tissue is 1.35-1.55.

The relationship between the angles of incidence and refraction and the indices of refraction of the two media is known as Snell's Law. The law of refraction predicts the amount of bend.

Snell's Law:
$$n_1 \sin\theta_1 = n_2 \sin\theta_2$$

θ1 is the angle of incidence, θ2 is the angle of refraction and n1 and n2 are the speeds of light in the media

1.3 SCATTERING

Change of direction of propagation of energy of light. It is a physical process where light interacts with matter and changes direction.

Light scattering in tissue depends upon the size of the scattering particle, the wavelength of the light and the variation of the refractive indices of the various tissue components, such as cell membranes and organelles. Light scattering arises from the presence of heterogeneities within a bulk medium.

Types of Scattering

Elastic scattering: no energy change

Frequency of the scattered wave = frequency of incident wave

Gives insight into the static structure of material. The light scattered by a system has interacted with the inhomogeneities of the system. Photons are mostly scattered by the structure whose size matches the wavelength

Types are Rayleigh and Mie scattering

(a) Rayleigh Scattering

- Scattering from very small particles i.e., $\leq \lambda/10$
- Rayleigh scattering is inversely related to fourth power of the wavelength of the incident light

(b) Mie Scattering

- For scattering of particles comparable or larger than the wavelength, Mie scattering predominates. Because of the relative particle size, Mie scattering is not strongly wavelength dependent. Forward directional scattering

Inelastic scattering: energy change

Frequency of the scattered wave ≠ frequency of incident wave. Internal energy levels of atoms and molecules are excited. It gives information about vibrational bonds of the molecule.

Types are Raman and Brillouin scattering

Applications

Diagnostic applications: Scattering depends on the size, morphology, and structure of the components in tissues (e.g. lipid membrane, collagen fibers, nuclei). Variations in these components due to disease would affect scattering properties, thus providing a means for diagnostic purpose

Therapeutic applications: Scattering signals can be used to determine optimal light dosimetry and provide useful feedback during therapy

1.4 ABSORPTION

A process by which light is absorbed and converted into energy. Absorption depends on the electromagnetic frequency of the light and object's nature of atoms. Absorption of light is therefore directly proportional to the frequency. Most objects selectively absorb, transmit or reflect the light. When light is absorbed heat is generated. Absorption occurs when the photon frequency matches the frequency associated with the molecule's energy transition. Electrons absorb the energy of the light and transform it into vibrational motion.

The absorption of a photon results in: quantized change in charge separation, quantized excitation of vibrational modes. Electrons interact with neighboring atoms to convert vibrational energy into thermal energy.

Applications

Diagnostic applications: Absorption data can serve as spectral fingerprint of the molecule.

Various types of Chromophores (light absorbers) in Tissue

Tumor detection and other physiological assessments (pulse oximetry)

Therapeutic applications: Absorption of energy is the primary mechanism that allows light form a source (laser) to produce physical effects on tissue for treatment purpose Lasik Eye Surgery, Tatoo Removal.

1.5 LIGHT TRANSPORT INSIDE THE TISSUE

Tissue is a self supporting bulk medium to transport light. Scattering and absorption occur simultaneously and are wavelength dependent. Reflection and refraction also occurs. Maximum light will be delivered or penetrates the tissue when it is incident on the tissue at 90°. Scattering monotonically decreases *with* wavelength. Absorption is large in UV, near visible, and IR. Absorption is low in red and NIR. Modeling of light transport in tissues are often governed by the relative magnitudes of optical absorption and scattering.

1.6 LASER CHARACTERISTICS AS APPLIED TO MEDICINE AND BIOLOGY

- *Laser* is a narrow beam of light of a single wavelength (monochromatic) in which each wave is in phase (coherent) with other near it.
- To generate laser beam three processes must be satisfied:-
  - Population inversion.
  - Stimulated emission.
  - Pumping source – Optical and Electric

Types of Lasers

- Solid
- Liquid
- Gas

Laser characteristics include reflection,refraction, absorption and scattering.

- Monochromaticity of laser light is responsible for its selective effect on biological tissues.
- The optical effects of lasers can be applied for different medical applications like diagnosis, therapy and surgery.
- Photocoagulation of retina
- Tissue welding
- Coagulation
- Tattoo Removal
- Lithotripsy
- Dermatology

1.7 LASER TISSUE INTERACTION

Types

1. Photochemical interactions
2. Thermal interactions
3. Photoablation
4. Plasma-induced ablation
5. Photodisruption.

1.7.1 Photochemical Interactions

Lower intensities applied for longer durations. It causes a photochemical change- either by a slow transfer of energy as heat or by a specific chemical reaction as used in photodynamic therapy (PDT) and in LASIK vision correction. Laser energy can react chemically with specific molecules within tissue. Excimer lasers for modifying the shape of the cornea in LASIK procedures is based on - (UV) laser's ability to break covalent bonds in protein.

1.7.2 Photothermal Interaction

A less intense- longer pulse will cause a rapid heating- photothermal effect. When laser energy is absorbed by a chromophore - and transformed into heat which is dissipated in the target- leading to denaturation of proteins at 42-65 C. Depending on the exposure time, tissue vaporization, or coagulation, or both will take place. An example of a photothermal laser is the CO2 laser- used to cut and vaporize tissue - which mostly consists of water. Water- and thus soft tissue- vaporizes at 100 degrees C. When the laser hits soft tissue- rapid heating causes the water in the tissue to flash into steam- ablating the tissue. To minimize thermal damage- maximize the ablation- a short exposure time is necessary. This can be done by pulsed laser beam in such a way that the time it dwells over the tissue is less than its thermal relaxation time.

The thermal relaxation time- defined as the time taken by target structure to dissipate 50% of the energy absorbed- to surrounding tissue. This time is roughly equal to the square of the diameter of the target structure.

The thermal containment time- in which no heat (no thermal effect) is dissipated to surrounding tissue- and is roughly one-quarter of the thermal relaxation time.

1.7.3 Photoelectromechanical Interaction

Extremely intense- short pulse of laser light will usually cause an explosive expansion of tissue photoelectromechanical reaction. Photodisruptive . High energy- ultra short pulses of laser light cause extremely rapid heating of the target- with formation of a rapidly expanding thermal plasma. As the plasma collapses- the shock wave causes mechanical disruption of the target. This photomechanical disruption is utilized to treat tattoos- disruption of stones and certain pigmented skin lesions. When the laser fluence is very high, the electric field may attain the order of magnitude of the electric field present within the molecules. This electric field is in the range 107 to 1012 Vm−1. Breaking of chemical bonds and ionization take place, leading to the

well known electric breakdown of the medium. It Produces shock wave. This is the origin of the sound emitted during air or gas breakdown.In biological (and other) materials, the plasma (ionized gas) expands rapidly, giving rise to an electroacoustic shock wave. This is able to destroy solid grains. The plasma absorbs the incoming laser beam, hence diminishing the treated volume. This is used in ophthalmology, when one destroys some opaque elements of the vitreous humor without damaging the retina.

1.7.4 Photo Ablation

Visible and Ultraviolet laser beams are absorbed by electronic excitation. Property used to break chemical bonds without heating the material: photoablation. Condition for breaking a chemical bond by electronic excitation is that the photon energy, is equal to or larger than the bond energy. Photoablation is performed by lasers emitting ultraviolet light, i.e.excimer lasers. Along with bond breaking, there exists light energy in the form of thermal energy. This causes rapid detachment of the molecules into the gas phase, giving rise to the ablation of the material.

Advantage -Emit very short pulses (around 10−8 s), so that heat doesn't diffuse away from the irradiated zone. Photoablation is well localized to the irradiated regions. No thermal damage such as coagulation or vaporization. Another advantage is precision etching. Highly intense laser irradiation.

Photoablation is a two-step process:

- excitation
- dissociation

Interaction mechanism of photoablation is limited to the application of UV light. Pure photoablation is observed for the 193nm wavelength of the ArF excimer laser.

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UNIT – II – MEDICAL OPTICS AND LASER APPLICATIONS – SBM1602

INSTRUMENTATION IN PHOTONICS

2.1 INSTRUMENTS FOR ABSORPTION, SCATTERING AND EMISSION MEASUREMENTS

Spectrophotometers measure spectroscopic properties related to the molecular composition and structure of biochemical species in the sample of interest. There are several types of spectroscopic measurements: absorption, scattering (elastic and inelastic), and emission.

Light at a certain wavelength is used to irradiate a sample of interest. This process is called "excitation." Properties of the light that emerges from the sample are measured and analyzed. One can measure the light emitted and scattered by the sample, processes that occur at wavelengths different from the excitation wavelength; the techniques involved are fluorescence, phosphorescence, and inelastic scattering (Raman scattering).

A basic spectrophotometer generally consists of the following components:

1. An excitation light source
2. Dispersive devices (optical filters, monochromators, or polychromators)
3. A sample (usually in a compartment with a sample holder)
4. A photometric detector (equipped with a read-out device)

2.1.1 Instrument for Absorption Measurements

The collimated output of a light source is focused on the entrance slit of an excitation monochromatorfor wavelength scanning. The output of the excitation monochromator is directed to the sample inside the sample compartment. The light transmitted by the sample is collected through appropriate optics and focused onto a detector. This simple instrumental setup is often used in a single-beam absorption spectrometer.

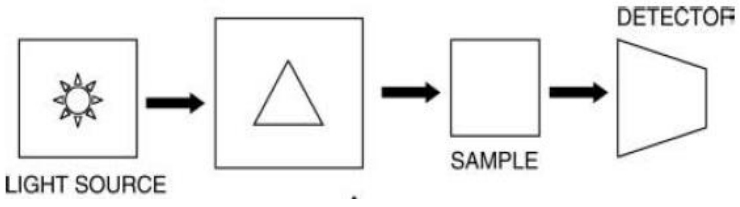

Fig 2.1 Absorption Measurement

2.1.2 Instrument for Scattering Measurements

The elastic scattering (ES) technique involves detection of the backscattering of a broadband light source irradiating the sample of interest. A spectrometer records the backscattered light at

various wavelengths and produces a spectrum that is dependent on sample structure, as well as chromophore constituents. In general, the sample is illuminated with the excitation light, which is selected with a dispersive element and then directed to a specific point location (e.g., via an optical fiber) of the sample. The scattered light is measured at the same wavelength as the excitation wavelength. With inelastic scattering measurements, one measures the scattered light from the sample in a spectral region different from the excitation wavelength. In this case, the basic setup is similar to the ES setup but has an additional dispersive element to analyze the scattering emission from the samples .

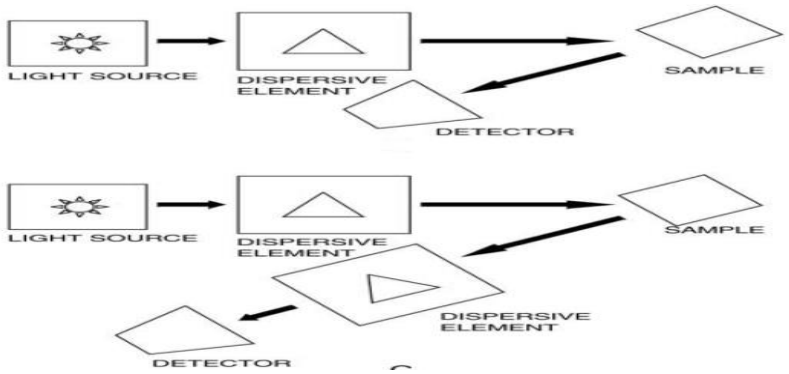

Fig 2.2 Scattering Measurement

2.1.3 Instrument for Emission Measurements

The excitation light source is usually a laser or high-intensity xenon arc lamp. The collimated output of the light source is focused on the entrance slit of an excitation monochromator whose output is directed to the sample. When a laser is used as the excitation source, the excitation monochromator is not required. The emission from the sample is collected through appropriate optics and focused onto the entrance slit of an emission monochromator. The excitation beam and the emission beam are usually focused at right angles for minimum interference from scattered light.

There are three basic classes of spectrophotometers: filter instruments, monochromator instruments, and multichannel devices. The first type of device uses optical filters, whereas the latter two systems use prisms or gratings as dispersive elements. The three major features to consider are the intensity of the excitation light source, the resolution and throughput of the monochromators, and the sensitivity of the detector.

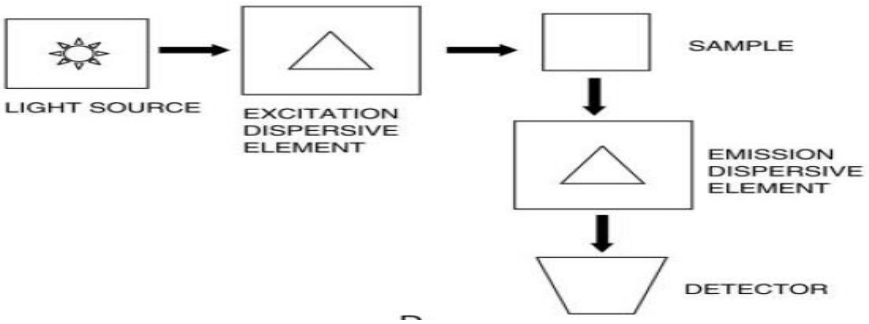

Fig 2.3 Emission Measurement

2.2 EXCITATION LIGHT SOURCES

Light sources utilized in laser optics are high pressure mercury and sodium lamps, Lasers and LEDs.

2.2.1 High-Pressure Arc Lamps

High-pressure arc lamps are the most commonly used radiation sources. These lamps produce an intense quasi-continuum radiation ranging from the UV (<200 nm) to the near-infrared (NIR) (>1000 nm) with only a few broad bands at approximately 450 to 500 nm. The lamps consist of two tungsten electrodes in a quartz envelope containing gases under high pressure, for example, xenon (Xe), mercury, an Xe–mercury mixture. Lamps of this type are commercially available in a wide range of input power from a few watts to several kilowatts. If excitation can be carried out at only one wavelength or a few fixed wavelengths of the mercury emission lines, the mercury lamp is probably the most effective radiation source. The Xe lamp, however, is more commonly used because it provides a smoother spectral profile more suitable for conducting excitation spectra measurements.

The Xe arc lamp is the most versatile light source for steady-state spectrometers. Xenon arc lamps typically have a lifetime between 400 and 600 hours. Three categories: continuous-output xenon short-arc lamps, continuous-output xenon long-arc lamps, and xenon flash lamps. Xenon arc lamps of smaller sizes, down to 10 watts, are used in optics and in precision illumination

for microscopes.

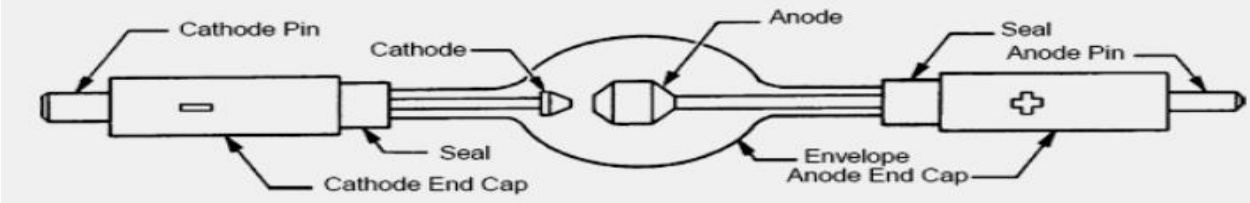

Fig 2.4 High Pressure Arc Lamp

2.2.2 LED

Light-emitting diodes (LEDs) are solid-state light sources that provide output over a wide range of wavelengths. These devices require little power and generate little heat. PN junction opto-semiconductor that emits a monochromatic (single color) light when operated in a forward biased direction. Emits light when activated by a suitable voltage is applied to the leads.

When a suitable voltage is applied to the leads, electrons recombine with electron holes within the device, releasing energy in the form of photons. exotic semiconductor compounds such as Gallium Arsenide (GaAs), Gallium Phosphide (GaP), Gallium Arsenide Phosphide (GaAsP), Silicon Carbide (SiC) or Gallium Indium Nitride (GaInN) all mixed together at different ratios to produce a distinct wavelength of colour.

Table 2.1 LED Materials asnd Colors

Typical LED Characteristics			
Semiconductor Material	Wavelength	Colour	V_F @ 20mA
GaAs	850-940nm	Infra-Red	1.2v
GaAsP	630-660nm	Red	1.8v
GaAsP	605-620nm	Amber	2.0v
GaAsP:N	585-595nm	Yellow	2.2v
AlGaP	550-570nm	Green	3.5v
SiC	430-505nm	Blue	3.6v
GaInN	450nm	White	4.0v

Types of LED

1. Surface Emitting Diode

SLED is a five layered double hetrojunction on device consisting of a GaAs and GaAlAs layers. A massive electron injection into a thin active layer for recombination of electron and holes and enhanced focus of emitted light into the optical fiber. Plane of the active light emitting region is oriented perpendicularly to the axis of the fiber. From the substrate of the device, a well is

etched. Fibers are connected in the well to accept the emitted light. The circular active area in practical surface emitters in normally 50μm in diameter and up to 2.5μm thick SLED. Only active region near the surface will emit the significant amount of light while absorbing from the other parts. Hence it is known as surface emitting LED.

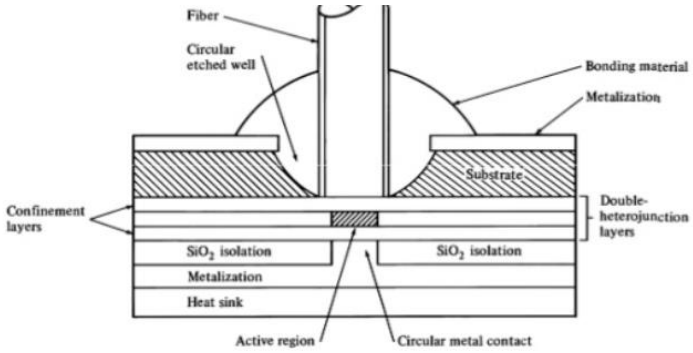

Fig 2.5 SLED

2. Edge Emitting Diode

Primary active region of the ELED is a narrow stripe, which lies below the surface of the semiconductor substrate. The semiconductor substrate is cut or polished (facets) so that the stripe runs between the front and back of the device. Rear facet is highly reflective and the front facet is antireflection-coated. The rear facet reflects the light propagating toward the rear end-face back toward the front facet. By coating the front facet with antireflection material, the front facet reduces optical feedback and allows light emission. ELEDs emit light only through the front facet.

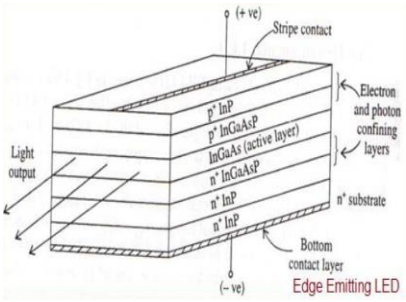

Fig 2.6 ELED

3. Superluminiscent Diode

A semiconductor device that emits low-coherence light of a broad spectrum like LED but high brightness like Laser Diode. Emission occurs by flowing forward current to a p-n junction. When a power supply is connected to the p-layer positive and the n-layer negative, electrons

enter from the n-side and holes from the p-side. When the two meet at the junction, an electron drops into a hole and light is emitted. Light is reflected at the end surface of the active layer.

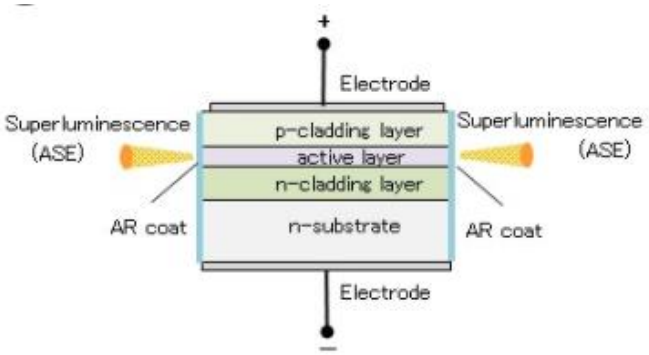

Fig 2.7 SuperLuminiscent LED

2.2.3 Laser/Laser Diode

LASER — Light Amplification by Stimulated Emission of Radiation

A Source of highly directional, monochromatic, coherent light. It Operates under a "stimulated emission" process. The semiconductor laser differs from other lasers (solid, gas, and liquid lasers)

Principle

The principle of laser is based on the stimulated emission of light.

Components of a typical laser are:-

1.Gain Medium for Population energy

2. Laser Pumping energy

3. Cavity

4.Reflector

5.Laser Beam

Semiconductor Laser

A semiconductor laser diode is a device capable of producing a lasing action by applying a potential difference across a modified p-n junction. This modified pn-junction is heavily doped and contained within a cavity thus providing the gain medium for the laser. A feedback circuit is also implemented in order to control the amount of current sent to the laser diode.

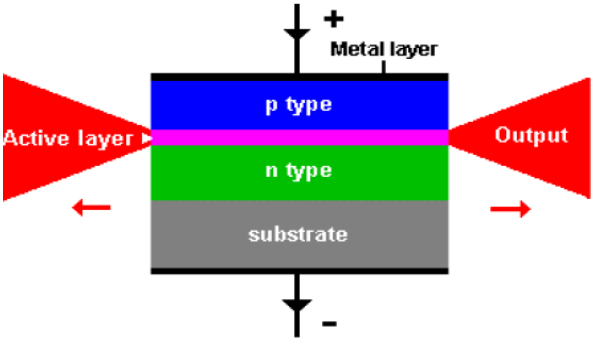

Fig 2.8 Semiconductor Laser Diode

Components of laser diode- Metal contact, P-type material , Active region (n-type material) , N-type material , Metal contact

Materials include: GaAlAs,AlGaInP, InGaAsP

Semiconductor laser diodes are cheap and easy to use compared to other types of lasers.

Precisely controlled current source is needed to regulate the amount of current to the laser diode.

2.3 OPTICAL FILTERS

Filters transmits only the desired wavelengths and either absorb or reflect light of unwanted wavelengths. It utilized to select a portion of the incoming light for use as an input for an optical system. It is used to select a portion of the light to be used as an output. It is used to split light into multiple components with differing wavelengths. Filter out background noise from the rest of the optical spectrum

Properties

- Long pass filters transmit wavelengths above a cut-on wavelength
- Short pass filters transmit wavelengths below a cut-off wavelength
- Band pass filters transmit wavelengths in a narrow range around a specified wavelength

2.3.1 Types

Absorbance filters -Color glass filters -absorb the unwanted wavelengths\ Light is blocked based on the absorption properties of the glass substrate used. Light that is blocked does not reflect off the filter; rather, it is absorbed and contained within the filter. Consist of dye molecules uniformly suspended in glass or plastic. Will often fluoresce

Interference filters -Dichroic, Dielectric, reflective filters - Reflect the unwanted wavelengths. Composed of transparent glass or quartz substrate on which multiple thin layers of dielectric material, sometimes separated by spacer layers . They are wavelength-selective.

Dichroic Filters- They used to direct light in different spectral region to different detectors. They are interference filters , long pass or short pass. Angle Sensitive. Reflects unwanted wavelengths, and transmits the desired portion of the spectrum.

2.4 OPTICAL DETECTORS

An optical detector converts the optical signal into an electrical signal, which can then be further processed. Generates an electrical current proportional to the intensity of incident optical radiation.

2.4.1 Classification

Diodes

PN-diodes - The photo- generated electron hole pairs in the depletion region of the diode contribute to the overall photocurrent. Operated under short circuit conditions or under reverse bias voltage.

PIN diodes - The depletion region is extended across the intrinsic or lightly doped layer and therefore more photo-generated carriers contribute to the photocurrent. All three layers (p-,i- and n-region) have the same optical bandgap. The thicker the i-layer the further the sensitivity.

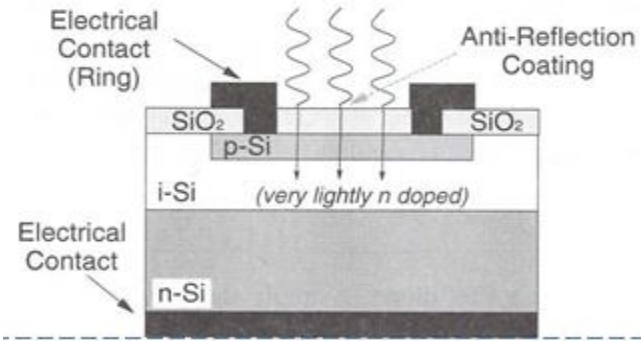

Fig 2.9 PIN diode

Avalanche photodiodes - APDs amplify the signal during the detection process. The operating principle of a APD is based on the avalanche effect, where a highly accelerated electron excites another electron due to "impact ionization". However, in the first step a photon has to be absorbed and a electron-hole pair has to be generated. The device consists of two regions. In region 1 of the device the electron hole pairs are generated and separated. In region 2 of the device the carriers are accelerated and impact ionized.

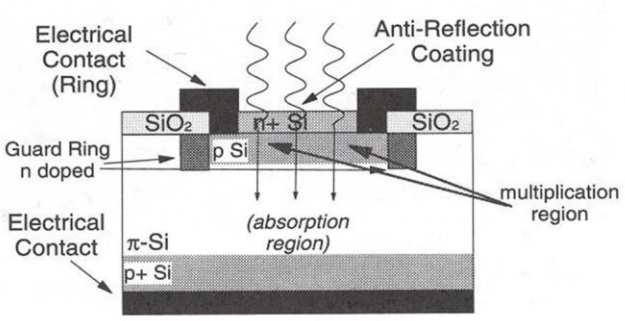

Fig 2.10 Avalanche Diode

Arriving photons pass through thin n^+p- junction. The carriers are absorbed in a p- region. The absorption leads to the generation of electron-hole pairs in this region. The electric field in the p-region is high enough to separate the carriers. The electric field across the p-region is not high enough for the charge carriers to gain enough energy for multiplication to take place. The electric field, however, in the n^+p-region the electric field is significantly higher, so that the charge carriers (in this case electrons only) are strongly accelerated and pick up energy. The electrons collide with other atoms in the lattice, which leads to the production of new electron-hole pairs ("impact ionization"). The newly released charge carriers again will collide with the lattice to produce more electron-hole pairs.

Schottky diodes - A thin metal layer replaces either the p- or the n-region of the diode. Depending on the semiconductor and the metal being involved a barrier is formed at the interface of the two materials. This barrier leads to a bending of the bands. Due to the applied voltage the bands can be bended more or less. In the region of the band bending electron hole pairs can be separated.

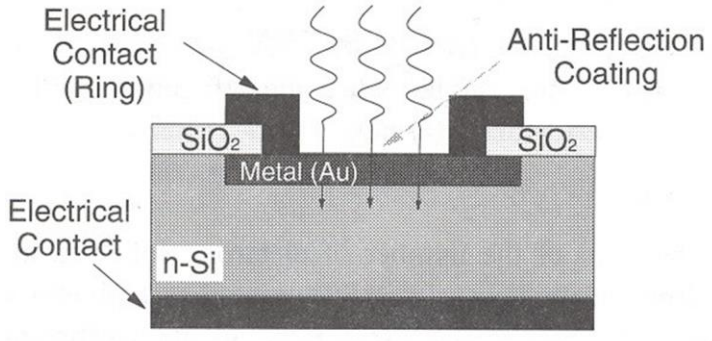

Fig 2.11 Schottky Diode

Photo conductors

In the case of a photoconductor the resistivity of the device is changed as a function of the intensity and not photocurrent. A voltage is applied to the detector to measure the change in current flow. The photoconductive detector is formed by two adjacent finger contact which are placed on a semiconducting material. The photoconductive detector is an unipolar device, which means that the current flow is either completely dominated by electrons or by holes.

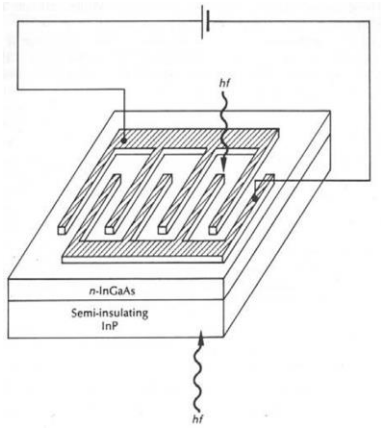

Fig 2.12 Photo conductive detectors

Time resolved detectors

Pulse excitation source is used. Width of the excitation is generally much shorter than the emission process of interest, i.e., much shorter than the lifetime (decay time) of the samples. To measure the lifetime, the time-dependent intensity is measured following the excitation pulse, and the decay time is calculated from the slope of a plot of log I (t) vs. t, or from the time at which the intensity decreases to 1/e of the initial intensity value I (t = 0).

Phase resolved detectors

It is also called frequency domain techniques.Sample is excited with intensity-modulated light. The intensity of the incident light changes with a very high frequency compared with the reciprocal of the decay time . Following excitation with a modulated signal, the emission is also intensity-modulated at the same modulation frequency. Because the emission from the sample follows a decay profile, there is a certain delay in the emission relative to the excitation . This delay is measured as a phase-shift , which can be used to calculate the decay time. The shape of the frequency response is determined by the number of decay times displayed by the sample. If the decay is a single exponential, the frequency is simple.

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UNIT – III – MEDICAL OPTICS AND LASER APPLICATIONS – SBM1602

SURGICAL APPLICATIONS OF LASERS

3.1 LASERS IN OPTHALMOLOGY

Ophthalmology is a branch of medicine and surgery which deals with the diagnosis and treatment of eye disorders. Ophthalmologists are allowed to use medications to treat eye diseases, implement laser therapy, and perform surgery when needed. Laser has particular use in ophthalmology because the eye can be used as an optical device. The transparency of the front part of the eye, the cornea, allows light such as LASER to reach almost all the tissues of the eye.

Lasers Used

Argon blue-green laser (70% blue (488 nm) and 30% green (514nm))

Frequency-doubled Nd-YAG Laser (532 nm) -treatment of many retinal conditions proliferative diabetic retinopathy, diabetic macular edema, vein occlusions

Krypton red (647 nm) - treatment of subretinal neovascular membrane.

Diode laser (805-810 nm) -treatment of Retinopathy of Prematurity (ROP) .

Nd:YAG LASER (1064 nm)-produce photodisruption in the eye for the treatment of acute angle closure glaucoma

Absorption Spectrum

- Melanin absorption in 400-700nm
- Deoxyhemoglobin 555nm
- Oxyhemoglobin 542nm, 577nm
- Xanthophyll <500nm

Effects of Laser Effects Eye

- Laser coagulation- Thermal effect of the laser radiation is used, therapeutic effect in vascular pathology of the eye: laser coagulation of vessels of iris, cornea, retina, trabeculoplasty, and the effects on the cornea with infrared radiation (1,54-2,9 m), which is absorbed by the stroma of the cornea, to change the refraction.Commonly used is an argon laser.
- Photodestruction (photodiscision) -Dissection of tissues using high peak power of Laser . Based on an electro "breakdown" of tissue that occurs due to the release of large amounts of energy in a limited volume. In this case, at the point the laser plasma is formed, and

this leads to the creation of a shock wave and of microscopic tearing of tissue. Infrared YAG-laser utilised.

- Photoevaporation and photoincision - Effect is based on prolonged heat exposure to the evaporation of tissue. Used for this purpose infrared CO2 laser (10.6 m) to remove surface formations of the conjunctiva and eyelids.
- Photoablation (photodecomposition) - Based on the removal of biological tissue. It is an excimer laser operating in the hard UV range (193 nm). Application: refractive surgery, treatment of degenerative changes in corneal opacities, inflammatory disease of the cornea, and glaucoma
- Laser stimulation - Low-intensity red light He-Ne-laser. Found that the interaction of radiation with various tissues from complex photochemical processes are shown anti-inflammatory, desensitizing, resolving effects

3.1.1 Photorefractive Keratomy

It corrects refractive vision errors by changing the shape of the cornea. It alters the contours of the cornea so that it bends light correctly. It is an effective treatment myopia (nearsightedness), hyperopia (farsightedness) and/or astigmatism. PRK completely removes the epithelium to access the cornea, and then the epithelium grows back. It utilizes a type of laser called an excimer laser(Cold UV).

3.1.2 Radial Keratomy

A surgical procedure used to decrease nearsightedness. During the procedure, radial incisions are made in the cornea of the eye with a highly precise diamond blade set to a particular depth. The number of incisions and their location is determined by the degree of nearsightedness. These incisions allow the sides of the cornea to bugle outward and thereby flatten the central portion of the cornea. This brings the focal point of the eye closer to the retina and improves one's distance vision.

3.1.3 Astigmatism Coorrection

Excimer laser can be used to reduce astigmatism when performing LASIK or PRK surgery. The degree of astigmatism currently approved for correction is 0.75 D to 4.0 D. Astigmatism measurements describe to what degree the cornea is non-spherical. The excimer laser reduces the degree of astigmatism by removing corneal tissue in an asymetric manner. This is accomplished by utilizing an oval-shaped laser beam.

3.1.4 Laser Iridotmy

The technique creates a bypassing hole in the iris to allow fluid trapped behind it to flow to the AC. Fluid blockage occurs due to closure of the ACA or to pupillary block. Argon and Nd:YAG lasers can be used — separately or in combination. Laser parameters for the argon laser are energy = 800 to 1000 mW, diameter = 50 μm, and exposure time = 0.1 sec. A total of 40 to 80 applications are used. For the Nd:YAG laser, energy = 3 to 7 mJ, and four to ten applications are used.

3.1.5 LASIK

LASIK stands for "LAser in SItu Keratomileusis". Excimer laser and the microkeratome are used to alter the degree of near-sightedness in an eye. After anesthetic eyedrops are put on the eye, a suction ring is centered. The suction ring stabilizes the position of the eye and increases the pressure to a level that is needed for proper functioning of the microkeratome. The microkeratome is a mechanical shaver(device) that contains a sharp blade that moves back and forth at high speed. This shaver is placed in the guide tracks of the suction ring and is advanced across the cornea using gears at a controlled speed. This process creates a partial flap in the cornea of uniform thickness. The flap is created with a portion of the cornea left uncut to provide a hinge. After the suction ring and microkeratome have been removed, the corneal flap is folded back on the hinge exposing the middle portion of the cornea. The excimer laser is then used to remove tissue and reshape the center of the cornea. The amount of tissue removed is dependent upon the degree of near-sightedness that is being corrected.In the final step, the hinged flap is folded back into its original position. The front surface of the eye is now flatter since the flap conforms to the underlying surface. In effect, the change made in the middle of the cornea is translated to the front surface of the cornea.

3.2 LASERS IN DERMATOLOGY

Lasers have been used to treat skin conditions occurred over 40 years ago . Recent past major advances in laser technology has revolutionized their use in the treatment of many skin conditions and congenital defects.

In pigmented epidermis, melanin absorption is in the optical spectrum (200– 1000 nm). In the dermis, there is strong, wavelength-dependent scattering by collagen fibres. In general, between 280 and 1300 nm, the depth of penetration increases with wavelength. Above 1300 nm, penetration decreases due to the absorption of light by water. The most deeply penetrating

wavelengths are 650–1200 nm, while the least penetrating wavelengths are within the far-UV and far-IR regions

Penetration of laser depends upon

1. Absorption and scattering
2. Dept of penetration increases with wavelength
3. Amount of scattering is inversely proportional to wavelength

The ablative laser treatments work mainly on the epidermis (surface skin cells) . Non-ablative treatments work solely on dermal collagen (mid-layer of skin) only. Fractional laser treatment works at both the epidermal and dermal layers of the skin.

3.2.1 Applications

- Ablative (Vaporizing) Skin Resurfacing
- Treatment of Vascular Lesions
- Interactions During Treatment of Pigmented Lesions and Tattoos
- Interactions During Hair Removal
- Interactions During Non-ablative Skin Rejuvenation
- Fractional Photothermolysis
- Laser-Based Diagnostics

3.3 LASERS IN DENTISTRY

The rapid development of laser technology has seen its introduction into various fields of dentistry.

The laser is directed on the rotten area, which contains more water molecules than rest of the tooth. Water molecules in the decay are heated rapidly. The pressure increases and the rotten area “explodes” making a popping sound. The laser kills bacteria in the area leaving the tooth surface sterile

3.3.1 Classification

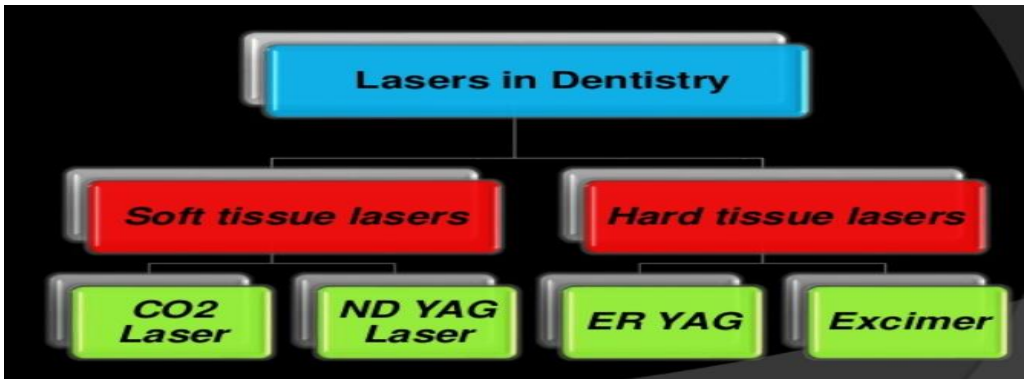

Fig 3.1 Laser classification in dentistry

3.3.2Applications

Diagnosis

- •Detection of pulp vitality
- •Doppler flowmetry
- •Laser fluorescence- Detection of caries, bacteria and dysplastic changes in the diagnosis of cancer

Hard tissue applications

- •Caries removal and cavity preparation
- •Re-contouring of bone (crown lengthening)
- •Endodontic (root canal preparation , sterilization and Apicectomy)
- •Laser etching
- •Caries resistance

Soft tissue applications

- •Laser-assisted soft tissue curettage and peri-apical surgery
- • Bacterial decontamination
- • Gingivectomy and Gingivoplasty
- • Gingival retraction for impressions
- • Implant exposure

3.3.3Lasers used

CO2 Laser

- Mode : vaporisation, cutting (>100˚C)
- Specification : 10.6 micron wavelength
- Used effectively in treating patients with oral lesions with blood dyscrasias.
- Oral indication: sealing of pits and fissures, welding of ceramic material to enamel , prevention of dental caries
- Disadvantages : -Cornea at risk -Haemostasis may not be adequate on very vascular area (posterior tongue)

Nd YAG Laser

- Mode: coagulation (>60˚c), central vaporisation
- Specification : 1.06 micron wavelength Can be combined with CO2 (combo laser) or KTP
- Oral indications: Coagulation of very vascular lesions or near major blood vessel, Excision in vascular areas such as posterior tongue, Gingivectomy
- Disadvantages: - Retina at risk - Penetration could cause inadvertent spread - Oedema more than CO2 laser

Diode Lasers

- Compact size and relatively affordable pricing. It is used in both contact and non-contact mode and can function with continuous wave or gated pulse modes. Diode lasers are invisible near infrared wavelengths and current machines range from 805–1064 nm.
- Effective for a host of intraoral soft tissue-gingivectomy, biopsy, impression troughing, and frenectomy. Diode lasers also exhibit bactericidal capabilities and can be used for adjunctive periodontal procedures. They also are used for laser assisted tooth whitening. Diode lasers have excellent photobiomodulation

3.3.4 Advantages

Less pain in some instances (reducing the need for anesthesia)

Reduce anxiety in patients uncomfortable with the use of the dental drill.

Minimize bleeding (high-energy beam photocoagulation) and swelling.

Reduce bacterial infections (sterilizes the area being worked on)

Preserve more healthy tooth during cavity treatment.

3.3.5 Disadvantages

Lasers can’t be used on teeth with fillings that are already in place.

Lasers can't be used in many commonly performed dental procedures. Eg. lasers can't be used to fill cavities located between teeth, cavities around old fillings, and large cavities.

Traditional drills may still be needed to shape the filling, adjust the bite, and polish the filling even when a laser is used.

Do not eliminate the need for anesthesia.

More expensive since the cost of the laser is much higher.

3.4 LASERS IN UROLOGY

Lasers represent one aspect of the continued development and application of light technology in urology. The photothermal, photochemical, and photomechanical properties of lasers are used for both the diagnosis and treatment of urologic disease.

3.4.1 Applications

- Urologic disorders
- Stones, (holmium laser)
- Benign prostatic enlargement (BPE)
- Bladder cancer
- Kidney cancer
- Urothelial tumours
- Strictures

3.4.2 Urinary Lithiasis

Lithiasis goes by the name Laser lithotripsy also. Pulsed-dye laser (504 nm, 1 μsec) is coupled to a 250-μm quartz fiber for endoscopic stone fragmentation. Concentrically propagating cavitation bubble created at the laser–stone interface, collapsing and producing a photoacoustic shockwave and causing the calculus to fragment. (Nd:YAG) and alexandrite lasers are also effective in fragmenting calculi. Ho:YAG laser has moved to the forefront of laser lithotripsy technology. Laser in combination with miniaturized actively deflectable ureteroscopes to reach the proximal ureter and even intrarenal calculi are also utilized.

3.4.3 Benign Prostatic Hyperplasia

Urinary frequency, incomplete bladder emptying, and nocturia due to enlargement of prostrate gland causes hyperplasia.

Laser prostatectomy has 2 main tissue effects - 1.coagulation 2. vaporization .

Coagulation occurs when somewhat diffusely focused laser energy heats tissue to 100°C. Proteins denature, and necrosis ensues . This results in subsequent sloughing of necrotic tissue. This process often initially results in edema. Vaporization occurs when greater laser energy is focused (increased power density) and tissue temperatures reach as high as 300°C. This causes tissue water to vaporize and results in an instantaneous debulking of prostatic tissue.

The transurethral ultrasound-guided laser-induced prostatectomy (TULIP) incorporated a side-firing Nd:YAG laser that used real-time ultrasound monitoring during treatment. It is Expensive and complex. Visual laser ablation of the prostate (VLAP) incorporates endoscopic for the direct application of laser energy (Nd:YAG) to the obstructing prostatic tissue. Technique incorporates a gold alloy tip at the end of the laser-delivery fiber, which allowed right-angle delivery of laser energy directly into the obstructing prostate tissue.Coagulation of treated prostatic tissue created the desired therapeutic effect. Ho:YAG laser has been used to remove obstructing prostate by a combination of the cutting and ablative effects of the laser. The procedure has been associated with little blood loss.

3.4.4 Urological Oncology

Prostrate Cancer- Nd-YAG Laser and CO2 laser

Bladder Cancer- Nd:YAG, argon, and Ho:YAG lasers have all been used in the treatment of bladder tumors.

Nd:YAG laser is the most widely used laser for the treatment of bladder neoplasms.

Ho:YAG in the treatment of superficial bladder cancer

Ureteral and Renal Pelvis Carcinoma-Nd-YAG Laser with endoscopy.

3.4.5 Advantages

Immediate relief of symptoms – Rapid evacuation during recovery.

Fewer symptoms of irritation and side effects.

The patient usually leaves either the same or the next day. Workable even in outpatients.

Rapid recovery

3.5 LASERS IN OTOLARYNGOLOGY

A medical specialty which is focused on the problems of ears, nose, and throat. It is also called otolaryngology-head and neck surgery because specialists are trained in both medicine and surgery. An otolaryngologist is often called an ear, nose, and throat doctor, or an ENT.

Lasers are tools that are adaptable to certain of the necessary surgical procedures in these regions. The energy in the laser beam exists as focused light and may be used for diagnostic and therapeutic interventions.

3.5.1 Delivery system

Articulated arm - The emerging beam is transferred from the laser aperture in a hollow metal tube, usually known as an articulated arm

Micromanipulator delivery -Device consisting of a system of lenses and a mirror with a joystick attachment. It is attached to the microscope

Handpiece delivery - The beam is focused by the system of lenses and mirrors onto the handpiece at a fixed point some 2 cm from its emergence at the distal end. A guide probe extends from the end of the handpiece

3.5.2 Lasers used

Ho YAG Lasers

Wavelength: 2,100 nm; Near to mid Infrared wavelength (invisible)
Penetration: 3-5 mm; deeper penetration allows for improved tissue coagulation
Otolaryngologic Uses:

Lithotripsy (via sialendoscopy), Tonsillectomy, Endonasal and sinus surgery, Laryngeal surgery

KTP *Lasers*

Wavelength:b532 nm; visible wavelength

Penetration: 0.9-1 mm

Absorbtion: skin pigmentation and hemoglobin absortion

Otolaryngologic Uses:

Stapedectomy and middle ear surgery, Laryngeal/tracheal surgery, Sinus surgery

ARGON lasers

Wavelength: 485-515 nm; Infrared wavelength (invisible)

Penetration: 0.8-1 mm

Absorbtion: -absorbed by pigmented tissues and hemoglobin; reflected by tissues white in color

Otolaryngologic Uses:

Treatment of skin lesions, stapedectomy

3.5.3 Benefits

Minimally invasive surgery

Minimal bleeding

Minimal postoperative oedema and crusting

Revision surgery

Ambulatory surgery

Cost benefit

3.6 LASER TISSUE WELDING

Laser energy is used to induce thermal changes in connective tissue proteins for joining tissues.

It aims to seal wounds and openings in a surgery using laser. Denaturation of tissue proteins occurs as a result of temperature raise due to absorption of laser light by water molecules and collagen present in the tissue. A new stronger connecting structure is formed by proteins when the temperature is brought down.

Types: Photo thermal TW (non covalent bonding), Photochemical TW (covalent bonding)

Coagulation is one of the key processes in tissue welding, and lasers are used to induce this in tissues. Coagulation is the heating of tissues above 50 C and below 100 C to bring about denaturing of biological compounds. Proteins can break away from their quaternary structure and become long tangled fibrous substances.

3.6.1 Lasers used

Infrared : Co2 , THC:YAG , Ho:YAG, Tm:YAG, Nd:YAG, GaAlAs => Water absorption

Visible : KTP, Nd:YAG, Argon => Hemoglobin absorption

Depending on the body tissue being soldered, there are various temperature limitations.

Optimal temperature for collagen bonding is within 60-80 ^{o}C.

Diode lasers used for vascular welding operate at around 80 ^{o}C.

Argon lasers used for arterial vein anastomosis heat the tissue to approximately 70 ^{o}C.

Conventional closure methods • Sutures • Staples • Clips • Fibrin glue

3.6.2 Soldering

High tensile strength is needed so that the welded tissues do not break apart. Soldering biomaterial is used for this purpose. Albumen is used as a soldering material while performing anastomosis. After the laser heats the tissues in the junction to bring about denaturation along with the soldering biomaterial, the substructure is allowed to cool down. During this step, renaturation through covalent and electrostatic bond formation among the tissues takes place to hold the whole junction.

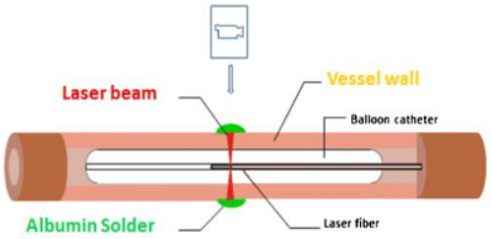

Fig 3.2 Albumen Soldering

3.6.3 Applications

Cardiovascular surgery: Vascular anastomosis – seals to reduce blood loss during surgeries

Thoracic surgery: Seal air leakage after lung surgery, bronchial stump

Dermatology: Skin closure – improved cosmoses , faster healing

Gynecology : Repair of fallopian tube

Neurology: Welding of peripheral nerves

Ophthalmology: Laser solder closure of cornea & sclera

Urology: Urinary tract closure to prevent water leakage & infection

3.6.4 Advantages

Reduced operation time

Reduce skill requirement

Reduced suture & needles trauma

Reduced foreign body reaction

Reduced bleeding

Faster healing

Grow back ability and better cosmetic appearance

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SCHOOL OF BIO AND CHEMICAL ENGINEERING

DEPARTMENT OF BIOMEDICAL ENGINEERING

UNIT – IV – MEDICAL OPTICS AND LASER APPLICATIONS – SBM1602

NON THERMAL DIAGNOSTIC APPLICATIONS

4.1 Optical Coherence Tomography

Optical coherence tomography (OCT) is a non- invasive imaging test. OCT uses light waves to take cross-section pictures of your retina. Each of the retina's distinctive layers is visible. It can map and measure their thickness. These measurements help with diagnosis. Provide treatment guidance for glaucoma and diseases of the retina. These retinal diseases include age-related macular degeneration (AMD) and diabetic eye disease. It obtain high resolution cross-sectional images of the retina. The layers within the retina can be differentiated and retinal thickness can be measured to aid in the early detection and diagnosis of retinal diseases and conditions.OCT uses rays of light to measure retinal thickness. No radiation or X-rays are used in this test, anOCT scan does not hurt and it is not uncomfortable. Optical Coherence Tomography uses technology that is best compared to ultrasound, except that it employs light rather than sound and thereby achieves clearer, sharper resolution. Employs near-infrared light (1.3 μM) to probe micrometer-scale structures inside biological tissues. It shows real time image for intravascular structure. It gives high resolution and good tissue characterization.

Principle

OCT images are obtained by measuring -echo time and intensity of reflected light. It is also called optical ultrasound. It gives Optical properties of ocular tissues, not histological section. Laser output from OCT is low, using a near- infra-red broadband light source. It measures backscattered or back-reflected light. The source of light: 830nm diode laser.

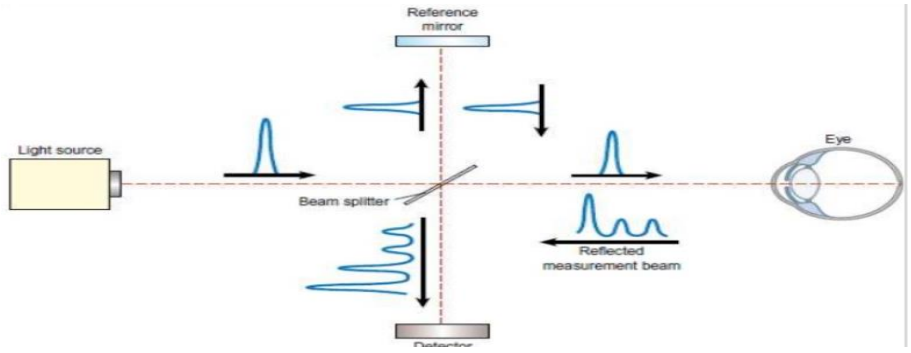

Fig 4.1 Measuring set up

Technique is called Low coherence interferometry or Michelson Interferometer

A beam of light passes through semitransparent mirror that splits the beam into two. These two beams are then thrown on two equidistant mirrors; reflected light from these mirrors is then picked up and summed up by a detector. The equidistant mirrors reflect the light wave in same phase; however, if one of the mirrors is moved by a distance less than the wavelength of the incident light, the reflected lights from the two mirrors will then possess a phase difference. This phase difference then produces an interference pattern at the level of the detector. The resulting interference patterns are used to reconstruct an axial A-scan, which represents the scattering properties of the tissue along the beam path. A moving beam of light along the tissue in a line results in a compilation of A-scans with each A-scan having a different incidence point. From all these A-scans, a two-dimensional cross-sectional image of the target tissue can be reconstructed and this is known as a B- scan.

Technique

Quality images can be taken even with a 3 mm pupil; otherwise dilatation is recommended. The patient is seated comfortably in front of the OCT machine with chin positioned on the chin rest. He is asked to fixate on the fixation target. The internal fixation (green color light) target is the commonly used fixation target. After fixation the operator selects the desired scan and aligns the instrument so that fundus image and scan beam is displayed on the screen.

Scan Protocols

Line -scan simply scans in a single, straight line. The length of the line can be changed as well as the scan angle.

Raster – Scans in parallel straight lines

Circle- scans in a circle instead of a line.

Radial - scans 6 consecutive line scans in a star pattern

Types

Time Domain OCT - Image resolution and acquisition speed are inversely related

Spectral Domain OCT - Simultaneous increase in imaging speed and resolution can be brought about by spectral domain OCT

Advantages

Broad dynamic range
High resolution
Rapid data acquisition rate
Compact portable structure
Acquisition of 4-8 frames /second.

4. 2 ELASTOGRAPHY

Elastography is a non-invasive medical imaging technique that helps determine the stiffness of organs and other structures in your body. It maps the elastic properties and stiffness of soft tissue. Also gives information if the tissue is hard or soft will give diagnostic information about the presence or status of disease. It measures movement or transformation of tissue in response to a small applied pressure. Elastography techniques have been developed for both ultrasound and MR imaging.

Basic method of elastography involves applying a mechanical force to the tissue, internally or externally, and imaging the stiffness by analyzing the spatial deformation caused by the stimulation over a period of time. Palpation is the most common and primitive method for understanding the changes in the stiffness of the tissue.

Principle

Elastogarphy is a tissue elasticity imaging, important to understand the general principles which govern the behaviour of an elastic material when acted upon by an external force.When external forces are applied to objects made up of elastic materials, they undergo a change in shape and size.

STRAIN is a relative change in shape or size of anobject due to externally applied forces.

STRESS is the internal force (per unit area) associated with strain

HOOK'S LAW states that strain is directly proportional to stress for a linearly isotropic elastic material

Ultrasonic Elastography

It is based on high frequency compressional waves or ultrasound waves, morphological images of organs can be re-constructed.

The technique computes the difference between pre-compressed and postcompressed ultrasound signals to calculate the axial displacement occurring in the tissue. It is classified into quasi-static method and dynamic method on the basis of application of the external force.

a)Quasi-static method involves application of constant stress on the required region. The two-dimensional cross-correlation of the ultrasound images yield the displacement and the strain generated by the applied load. Drawback associated with this method is that it is difficult to find the Young's Modulus since the stress distribution is unknown. Technique is hence considered qualitative.

(b)Dynamic method involves application of time varying force which can either be a short transient mechanical force or an oscillatory force of fixed frequency. The shear waves which are basically low frequency (10Hz to 2000Hz) mechanical waves are directly proportional to the shear modulus of the medium. The dynamic method can yield quantitative and higher resolution Young's Modulus mapping when compared to the quasi- static method.

Magnetic Resonance Elastography

A special Magnetic Resonance Imaging (MRI) technique to assess the propagation of mechanical waves through a medium thus, deducing the stiffness of the medium. Magnetic Resonance Elastography (MRE) uses mechanical shear waves of a single frequency which are synchronized with the magnetic resonance pulse sequence. A magnetic resonance imaging technique called phase contrast MRI is used to image the tissue motion due to the propagation of the shear waves. This technique is based on conventional MRI.

Optical Coherence Tomography

OCE is a non-invasive imaging method can gives more details than ultrasound or MRI. Using light source to image biological tissue, OCE is considered generally safe compared to CT scan and other radiographic imaging modalities which involve with ionizing radiation. More affordable and time efficient compared to MRI. Tissue exhibits varying degrees of viscoelasticity (time-dependent response to a load), poroelasticity (presence of fluid-filled pores or channels), and anisotropy, as well as a nonlinear relationship between elasticity and the applied load.

Laser speckle technique used for the mechanical characterization of tissue has many advantages of being non-contact, non-invasive as well as in providing high resolution . This method is aimed at computing relative strain in tissue by tracking the laser speckle pattern obtained by illumination of coherent light on the deformed tissue.Optical elastography has a disadvantage of lesser penetration depth compared to other modalities.

Optical elastography is done by tracking the speckle pattern obtained by illuminating the region of interest during the application of deformation. A reference image of the speckle pattern before deformation is acquired and then the movement in the speckle pattern due to deformation is tracked by acquiring subsequent images for each stage of deformation. The tracking of the speckle pattern is done by image processing algorithm which gives the corresponding relative strain that occurred in the region of interest due to deformation. High speed sampling of the speckle pattern is required to track the movement during deformation and hence, the system requires to acquire speckle images at a high frame rate.

Applications

Dermatology
Oncology
Opthalmology
Cardiology

4.3 LASER INDUCED FLUORESCENCE IMAGING

Laser Induced Fluorescence (LIF) is an optical spectroscopic technique where a sample is excited with a laser, and the fluorescence emitted by the sample is subsequently captured by a photodetector. Usual lamp excitation is replaced by a laser source. LIF spectroscopy was first developed by Richard Zare in 1968 for the detection of atoms and molecules in the gas phase.

Principle

LIF is a two step process: absorption of a laser photon followed by emission of a fluorescence photon from the excited state. For absorption the laser wavelength λL must match an allowed energy transition of the LIF-active molecule (atom). Only a fraction of these excited molecules fluoresces, the rest relaxes without light emission. An optical filter selects the usually red-shifted fluorescence light at the emission wavelength λ. Only the fraction η of all emitted LIF-photons is detected and converted to the camera signal SF.

Imaging

A laser beam is formed to a light sheet (or volume) and intersects the fluid area of interest, e.g. in flames, sprays or thermal flows. The resulting fluorescence light from excited molecules in the light sheet is imaged through a selective filter onto a time-gated digital camera. For pulsed UV LIF applications usually an image intensifier amplifies the LIF signal. The conversion of LIF images into meaningful concentration or temperature fields is based on calibration measurements.

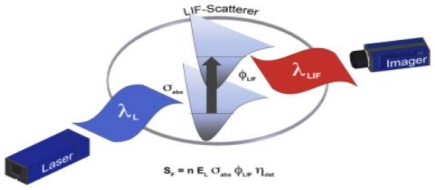

Fig 4.2 Set up

Light Sources

Light sources of LIF are range from ultraviolet ray, visible ray, to infrared ray. Ultraviolet range is usually built up as the pulse laser, which cannot supply the stable output as the continuous-

wave (CW) exciting light source for LIF. The mostly utilized light sources for LIF are visible lasers from red ray to blue ray, even purple ray. Red diode laser, its main irradiation wavelength is at 635 nm and was used for the detection of Cy-5-labeled anti-ovalbumin microfluidics capillary electrophoresis (CE). The gas laser, solid-state laser, dye laser, and diode laser have been utilized as exciting light source for LIF integration with microfluidics/nanofluidics for the detection of molecules, particles, as well as cells

Types

Depends on the laser and detection system used.

(a)Excitation LIF spectroscopy

Laser is employed to excite molecules from their ground state into an electronically excited state. As the molecules relax back into the ground state, fluorescence is detected by a photomultiplier tube (PMT).

The excitation wavelength is varied using a tunable laser which allows one to resolve the vibrational structure of the excited state. In a liquid sample, the molecules will fluoresce from the lowest vibrational level of their excited singlet state, decaying to a series of vibrational levels in the ground state, however the emission spectrum is not resolved by the detection system.A bandpass filter is placed between the sample and PMT to detect all the emission from the sample whilst removing any scattered laser light.

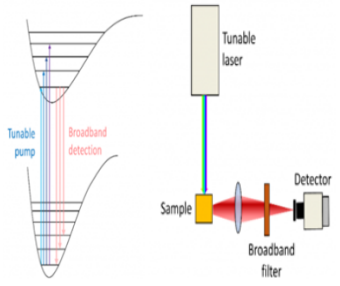

Fig 4.3 Excitation Spectroscopy bands and set up

(b)Emission LIF - A fixed pump wavelength is used to excite the sample and the sample's emission spectrum is analysed utilising a monochromator to select the detection wavelength. Figure shows single-point detection with a PMT, but it is also possible to employ an array detector (CCD or CMOS) to capture the full spectrum in one shot.

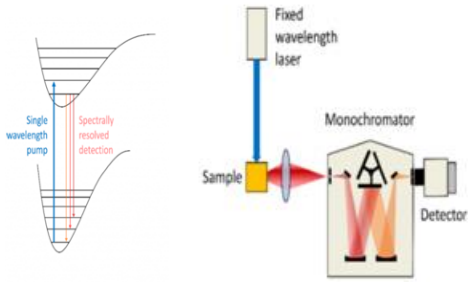

Fig 4.4 Emission Spectroscopy bands and set up

(c)Continuous wave or time-resolved LIF – This utilizes a continuous laser for excitation and is employed when only spectral information is required.

(d)Time-resolved LIF- a pulsed laser is used to excite the sample and its emission (either a single wavelength or the full spectrum) is detected as a function of time. It provides valuable time-resolved information such as the lifetimes of chemical intermediates and their associated time-gated spectral evolution.

Applications

Detection of purity
Optical tumor diagnosis
Imaging of paleontological specimens
Detection and quantification of biomolecules and biological processes (e.g DNA sequencing)

4.4 HOLOGRAPHY

Holography –(whole+ write) is the science of producing holograms. It is an advanced form of photography that allows an image to be recorded in three dimensions. A method of producing a visual three-dimensional (3-D) image of an object by means of light wave patterns recorded on a photographic plate. The measured three dimensions are height, width, and depth. It is also known as Lensless Photography. It produces life like images.

Hologram is a photograph of interference pattern which, when suitably illuminated by laser light, produces a three-dimensional image. These images can be seen through naked eye. The image floats in free space

Properties

Objects are visible from different perspectives

Divisible property i.e If you cut one in half, each half contains whole views of the entire holographic image.

Components

Laser light… usually helium-neon (HeNe) laser is used

Beam splitter…device that use mirrors and prisms to split laser beam into two beams - Object beam and Reference beam

Mirrors…Direct the beams of light to correct locations

Holographic Film…to record image very high resolution

Hologram Construction

To create a hologram, a laser beam (coherent light) is split in two beams :

Reference beam: that stays undisturbed

Object beam: strikes the object and then bounces onto the plate

Working of holography is divided into two phases:

Recording

Reconstruction

Recording

The first step is the recording of the interference pattern formed between the sample beam, which diffusely reflects from the object and the reference beam which is sent directly to the film. These two beams must be coherent and are normally obtained from a single laser by splitting its beam. The reflected, or scattered light, is directly mixed with the reference beam. When the film is developed (the developed film is called the hologram) and examined directly by eye, it does not look at all like a normal photograph, but is simply a complex interference pattern of light and dark bands in complex shapes and bears no direct resemblance to the original objects.

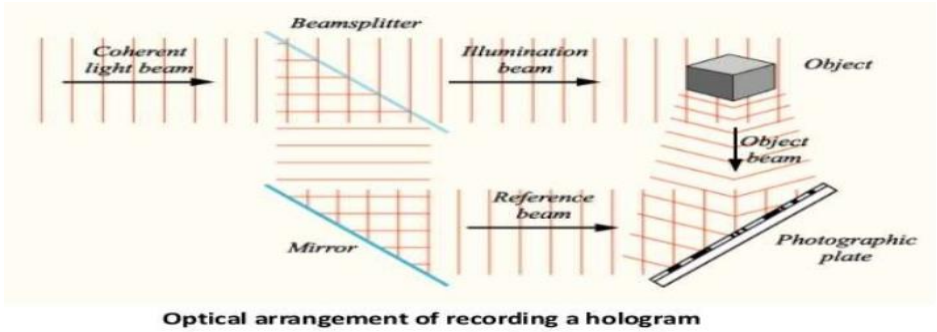

Fig 4.5 Recording of Hologram

Reconstruction

When a hologram is later illuminated with coherent light of the same frequency that created it, a three-dimensional image of the subject appears. Reconstruction is done by "playing back" the reference beam with the same orientation to the developed hologram as it had when the hologram was made and viewing the image as shown below. The interference pattern on the film diffracts the reference beam - known as the reconstruction beam now - to produce a light wave that duplicates the original beam that was scattered from the real object, complete with all amplitude and phase information. Further, the developed hologram acts like a window glass so that if you move your eye around and examine different portions of the diffracted light you will see different views of the virtual image of the object, all in 3D.

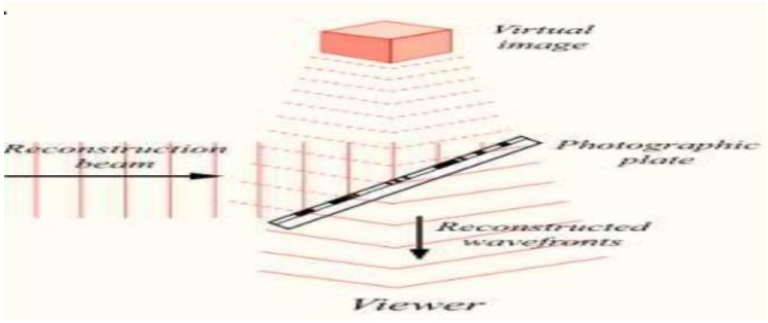

Fig 4.6 Reconstruction of Hologram

Applications

Endoscopy

X Ray Hologrpahy

Cardiac

Dentistry

Orthopedics

Opthalomology

Advantages

Cost effective

Higher storage capacity

Increased feasibility of objects(depth)

Enables the achievement of multiple images on a single plate and give 3-D images
Ability to combine with other technologies.

4.5 SPECKLE APPLICATION OF LASER IN BIOLOGY AND MEDICINE

Speckle pattern is a pattern made up of irregularly spaced dots (specs). In optics, the speckle pattern is created by interference between a great number of wavelets with random phase values. These wavelets are formed when coherent light is reflected from a rough surface or transmitted through a diffusing media. Speckle is generally considered to be "optical noise". Speckle actually describes the microscopic details the surface structure of the object. Optical interference effect can be observed when objects are illuminated with laser light. Effect is grainy in appearance, with light and dark "speckles" caused by constructive and destructive interference, respectively, of scattered laser light. Interference of elementary coherent beams of radiation from many secondary light point sources is located on the rough surface of the object. Laser speckle offers the possibility of developing a full-field technique for velocity map imaging which produces an instantaneous map of velocities in real time: blood flow measurement in assessing condition such as inflammation, healing process, burn assessment, intra-operative measurement, dermatology (psoriasis, skin flap failure, skin irritation.

Imaging

Fast, full-field, cheap, and relatively simple imaging method that gives 2-D perfusion maps of large surfaces.

Principle is that the backscattered light from a tissue that is illuminated with coherent laser light forms a random interference pattern at the detector, the so-called speckle pattern. Movement of particles inside the tissue causes fluctuations in this speckle pattern resulting in blurring of speckle images when obtained with an exposure time equal to or longer than the speckle fluctuation time scale. This blurring can be related to blood flow if the fluctuations are caused by the movement of red blood cells.

Speckle image - static and dynamic speckles.

Static speckles are speckles that do not change over time, whereas dynamic speckles do change over time due to the optical Doppler effect.

Dynamic speckles contain information about movement of the object or motion of particles within the object.

Components

Low-powered laser diode

Diffuser

Digital camera

Processing software

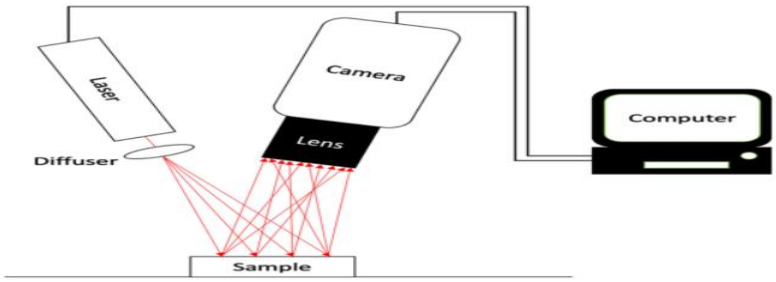

Fig 4.7 Speckle Imaging Model

Speckle Size

To ensure proper sampling of the speckle pattern, the size of a single speckle should be approximately equal to the size of a single pixel in the image.

F-stop: the size of the aperture in a lens. Larger the F-stops give smaller lens openings. i.e. f2.8 gives a larger aperture (and more exposure) than f11.

$$\sigma \approx 1.2(1+M)\lambda F$$

Single speckle size — Magnification of lens — Wavelength of laser — Camera F-stop

Applications

Rheumatology

Burns

Dermatology

Dentistry

Gastro Intestinal Tract Surgery

Neurology

Opthalmology

Limitations

Bound to qualitative measurements

Limited inter-patient comparability

Unwanted movement of tissues is the pitfall of the clinical application of laser speckle.

Needs Highly controlled environment.

4.6 RAMAN SPECTROSCOPY AND IMAGING

Raman spectroscopy was discovered by C. V. Raman in 1928

A spectroscopic technique used to observe vibration, rotational, and other low-frequency modes in a system. It is commonly used in chemistry to provide a fingerprint by which molecules can be identified.

When the radiation passes through the transparent medium the species present scatter a fraction of the beam in all direction. The difference in wavelength is between the incident and scattered visible radiation correspond to wave length in mid IR region.

Principle

When monochromatic radiation is incident upon a sample then this light may get reflected, absorbed or scattered. Scattering gives information about molecular structure. When light is scattered from a molecule most photons are elastically scattered (Rayleigh). The scattered photons have the same energy (frequency/wavelength) as the incident photons. A small fraction of light (approximately 1 in 107photons) is scattered at optical frequencies usually lower than, the frequency of the incident photons. The process leading to this inelastic scattering is the termed the Raman effect. Raman scattering can occur with a change in vibration, rotational or electronic energy of a molecule. The difference in energy between the incident photon and the Raman scattered photon is equal to the energy of a vibration of the scattering molecule. A plot of intensity of scattered light versus energy difference is a Raman spectrum. The spectrum is measured with the laser line as a reference. The peaks are measured as the shift from the laser line. Peak positions are determined by the vibrational energies associated with the bonds in the molecule(s) of which the sample is composed.

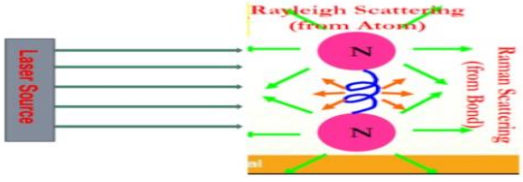

Fig 4.8 Scattering Mode

Classification

Stokes- When the change in energy of the scattered photon is less than the incident photon, the scattering is called Stokes scatter.

Anti- Stokes- Some molecules may begin in a vibrationally excited state and when they are advanced to the higher energy virtual state, they may relax to a final energy state that is lower than that of the initial excited state. This scattering is called anti-Stokes.

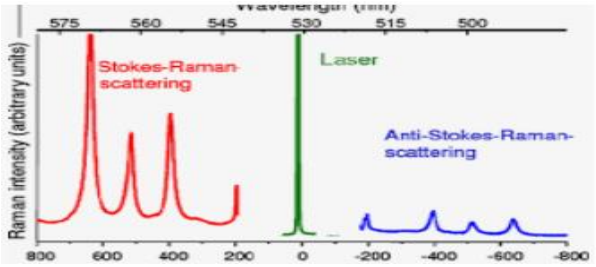

Fig 4.9 Types of Raman waveform

Working

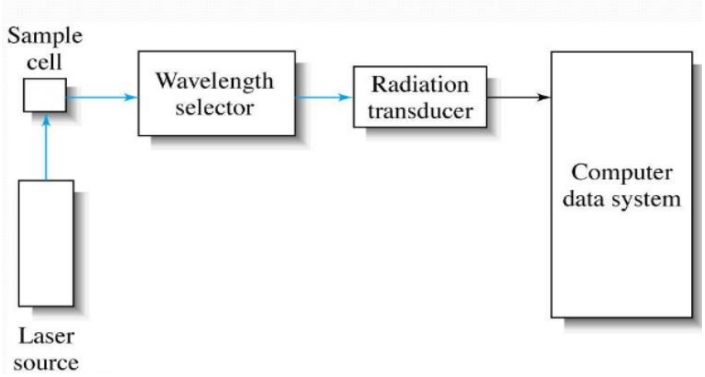

Fig 4.10 Spectrophotometer Block Diagram

Components

Instrumentation consists of three components:

Laser source

Sample illumination system

Spectrometer.

Source:

Lasers are used because their high intensity is necessary to produce Raman

Because the intensity of Raman scattering varies as the fourth power of the frequency, argon and krypton ion sources that emit in the blue and green region of the spectrum have and advantage over the other sources. Nd-YAG, Argon ion, Krypton ion, Diode and He-Ne are used.

Sample Illumination System

Liquid Samples: Aqueous solutions can be studied by Raman spectroscopy but not by infrared. This advantage is particularly important for biological and inorganic systems and in studies dealing with water pollution problems.

Solid Samples: Raman spectra of solid samples are often acquired by filling a small cavity with the sample after it has been ground to a fine powder. Polymers can usually be examined directly with no sample pretreatment.

Gas samples: Gas are normally contained in glass tubes, 1-2 cm in diameter and about 1mm thick. Gases can also be sealed in small capillary tubes .

Raman spectrometers are either Fourier transform instruments equipped with cooled germanium transducers or multichannel instruments based upon charge- coupled devices.

Raman Imaging

Raman imaging is a powerful technique for generating detailed chemical images based on a sample's Raman spectrum.

A complete spectrum is acquired at each and every pixel of the image, and then interrogated to generate false colour images based on material composition, phase, crystallinity and strain.

Standard point-by-point mapping affords the ultimate sensitivity for materials with extremely low Raman scattering properties, and additionally allows high resolution, large spectral range capability.

Typical acquisition times for such maps can be in the order of 1s-10s per point

Applications

Bio-compatibility

DNA/RNA analysis

Drug/cell interactions

Photodynamic therapy (PDT)

Disease diagnosis

Single cell analysis

Characterisation of bio-molecules

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DEPARTMENT OF BIOMEDICAL ENGINEERING

UNIT – V – MEDICAL OPTICS AND LASER APPLICATIONS – SBM1602

THERAPEUTIC APPLICATIONS

5.1 PHOTOTHERPAY

Phototherapy (light treatment) is the process of using light to eliminate bilirubin in the blood. Baby's skin and blood absorb these light waves. Light waves absorbed convert bilirubin into products, which can pass through their system. Lamps emitting light between the wavelengths of 400 - 500 nanometres (peak at 460nm) are specifically used for administering phototherapy as bilirubin absorbs this wavelength of light. Visible blue light is used.

Mechanism

Bilirubin, are present in the interstitial spaces and superficial capillaries of the skin, subcutaneous tissues. During the phototherapy, these molecules are exposed to light. Photons of energy are absorbed by the pigment, bilirubin. Leads to a sequence of photochemical reactions; configurational isomerisation, structural isomerisation and photo-oxidation.

Energy converts bilirubin into its nontoxic isomers such as photobilirubin ,lumilirubin which are more polar and thus water soluble. Photo-isomers are eliminated from the body more easily without undergoing the process of conjugation in the liver. As formation of lumirubin is the rate limiting step, less amount of lumirubin is formed.

Lights

1.White Halogen lights -Positioned above the infant and can deliver 10 to 30 µ W/cm2 /nm.
Quartz halogen bulb
Tendency to become hot
It is positioned at 52cm away from baby.
2. 2 Blue and 2 White Fluorescent lights -Blue light is the most effective light for reducing the bilirubin.
It delivers 12µW/cm2 /nm.
Light should not be delivered from the side of the infant.
3. Biliblanket - Blue Halogen light -Uses a halogen bulb directed into a fiberoptic mat.
Filter removes the ultraviolet and infrared components and the eventual light is a blue-green colour.

Blanket to give double phototherapy and increases the surface area exposed.

4. Bilibed – Blue Fluorescent light -Blue fluorescent tube is fitted into a plastic crib with a stretched plastic cover over the top for the baby to lie on.

Baby is dressed in the Bilicombi baby suit and nursed on the soft plastic cover.

Suit attaches to the crib by Velcro attachments.

Irradiance delivered is up to 40 µ W/cm2 /nm.

Risks

Progressive and gradual damage to your skin on a molecular level

Risk of developing skin cancer

Lead to immunosuppression.

Eyes become more sensitive to light

5.2 PHOTODYNAMIC THERAPY

A treatment that uses a drug, called a photosensitizer or photosensitizing agent, and a particular type of light. When photosensitizers are exposed to a specific wavelength of light, photoactivation causes the formation of singlet oxygen, which produces peroxidative reactions that can cause cell damage and death. Each photosensitizer is activated by light of a specific wavelength. This wavelength determines how far the light can travel into the body.

Steps

Three steps : –

1.Application of photosensitizer drug

2. Incubation

3. Light activation

In the first step of PDT for cancer treatment, a photosensitizing agent is injected into the bloodstream. Agent is absorbed by cells all over the body but stays in cancer cells longer than it does in normal cells. Approximately 24 to 72 hours after injection, when most of the agent has left normal cells but remains in cancer cells, the tumor is exposed to light. Photosensitizer in the tumor absorbs the light and produces an active form of oxygen that destroys nearby cancer cells

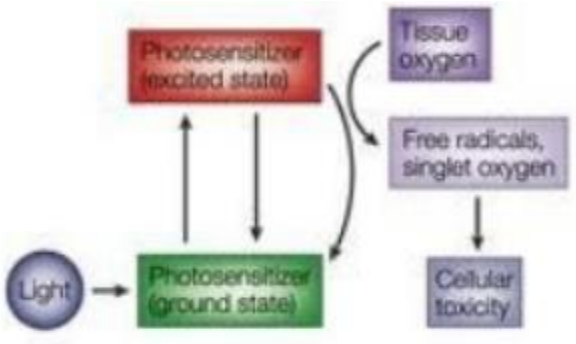

Fig 5.1 PDT Mechanism

In addition to directly killing cancer cells, PDT appears to shrink or destroy tumors in two other ways. The photosensitizer can damage blood vessels in the tumor, thereby preventing the cancer from receiving necessary nutrients. PDT also may activate the immune system to attack the tumor cells. Light used for PDT include laser, intense pulsed light, light-emitting diodes (LEDs), blue light, red light, and many other visible lights (including natural sunlight). Laser light can be directed through fiber optic cables (thin fibers that transmit light) to deliver light to areas inside the body. A fiber optic cable can be inserted through an endoscope (a thin, lighted tube used to look at tissues inside the body) into the lungs or esophagus to treat cancer in these organs. Other light sources include light-emitting diodes (LEDs), which may be used for surface tumors, such as skin cancer

Mechanism

Type I Reaction:-

Direct reaction with substrate (cell membrane or molecule)

Transfer of H atom to form radicals

Radical react either O2 to form oxygenated products

Type II reaction:-

Transfer of oxygen to form singlet oxygen

Drugs Used

Porfimer sodium

Benzoporphyrin derivative & Aminolevulinic acid

Methyl ester of ALA-

Advantages

No long term side effects when used properly.

Less invasive than surgery.

Takes only a short time and is most often done as an outpatient.

Targeted very precisely.

PDT can be repeated many times at the same site if needed.

Little or no scarring after the site heals.

Costs less than other cancer treatments.

Limitations

Light needed to activate most photosensitizers cannot pass through more than about one-third of an inch of tissue (1 centimeter).

PDT is usually used to treat tumors on or just under the skin or on the lining of internal organs or cavities.

PDT is also less effective in treating other tumors, because the light cannot pass far into these tumors.

PDT is a local treatment and generally cannot be used to treat cancer that has spread

Side Effects

Skin and eyes sensitive to light for approximately 6 weeks after treatment

Photosensitizers tend to build up in tumors and the activating light is focused on the tumor. As a result, damage to healthy tissue is minimal.

PDT can cause burns, swelling, pain, and scarring in nearby healthy tissue.

Other side effects include coughing, painful breathing, trouble swallowing, stomach pain, or shortness of breath; these side effects are usually temporary.

5.3 ONCOLOGICAL APPLICATIONS

1.Obstructive Esophageal Cancer-

Palliation of partially or totally obstructing tumors in the esophagus

Photofrin powder, is dissolved in 5% dextrose for injection.

48 h post injection the photosensitizer localized to the tumor is activated by light at 630 nm (laser) that is directed via a single-quartz fiber optic and delivered to the tumor through the biopsy channel of an endoscope. Light is scattered laterally to the tumor on the wall of the esophagus or the fiber may be inserted directly into the tumor. Experience mild to severe chest pain

2.Early Stage Endobronchial Tumors –

Treatment of microinvasive, nonsmall cell endobronchial tumors using Photofrin-PDT

Patients received 2 mg/kg Photofrin and 2 d later were treated endoscopically using a diffuser fiber (usually 1 to 2.5 cm) delivering 200 J/cm of diffuser length at 630 nm.

Because these lesions are very thin, the fiber was held in the lumen adjacent to the lesion.

Patients were rescoped 2 days following treatment,and treated area was debrided.

3.Obstructing Endobronchial Tumors (Nonsmall Cell Lung Cancer)-

Palliative treatment of obstructive endobronchial tumors.

Photofrin, 630 nm light treatment 48 h later

2 days following treatment patients are re-endoscoped, and all necrotic tumor debris and exudate must be removed because they can further obstruct the airway.

Adverse reactions included photosensitivity reaction hemoptysis, cough, dyspnea, chest pain, and fever

4.Early Stage Esophageal Cancer-

Barrett's esophagus

Endoscopic PDT was applied using a specially designed balloon light applicator.

Balloon is inserted, deflated and then inflated in place to an appropriate pressure to allow "unfolding" of the esophageal wall without shutting down the blood flow.

5.Cholangiocarcinoma- Bile duct cancer

6.Head and Neck Cancer- adjuvant to surgery in an attempt to "clean up" the remaining cancer cells in the operative bed.

7.Brain Tumors- glioblastoma or astrocytoma.

8.Mesothelioma - asbestos-induced disease

5.4 BIOSTIMULATION EFFECTS

Biostimulation, also known as LILT or LLLT Low Intensity(Level) Laser Therapy, improves post operative healing and yields excellent antalgic effects. It also called photobiology. Biostimulation is obtained using a defocalised beam with low energy density. Light energy is absorbed by tissues, and stimulates the metabolic processes inducing tissue regeneration. It emits no heat, sound, or vibration. Another name is cold laser therapy. Low levels of light does not heat the body tissue. Level of light is low when compared to other forms of laser therapy, such as those used to destroy tumors and coagulate tissue. Superficial tissue is commonly treated with

wavelengths between 600 and 700 nanometers (nm). For deeper penetration, wavelengths between 780 and 950 nm are used. It generates light of a single wavelength. No temperature elevation within the tissue, but rather produce their effects from photobiostimulation effect within the tissues. Low-level lasers do not cut or ablate the tissue.

LLLT devices include the gallium arsenide, gallium aluminum arsenide infrared semiconductor (gallium-aluminum-arsenide), and helium-neon lasers. Output powers range from 50 to 500 mW with wavelengths in the red and near infrared of the electromagnetic spectrum, from 630 to 980 nm with pulsed or continuous-wave emission.

Mechanism

Biostimulatory and inhibitory effects of LLLT are governed by the Arndt-Schulz law.

The law states that low-dose will increase physiologic processes, and strong stimuli will inhibit physiological activity. It represents a set of structural, biochemical and functional changes in living microorganisms. It acts directly on stimulating components of the so-called antenna pigments of the respiratory chain and manifest as an immediate effect cell vitalization by adenosine triphosphate (ATP) mitochondrial production increase. It Induces intracellular metabolic changes, resulting in faster cell division, proliferation rate, migration of fibroblasts and rapid matrix production.

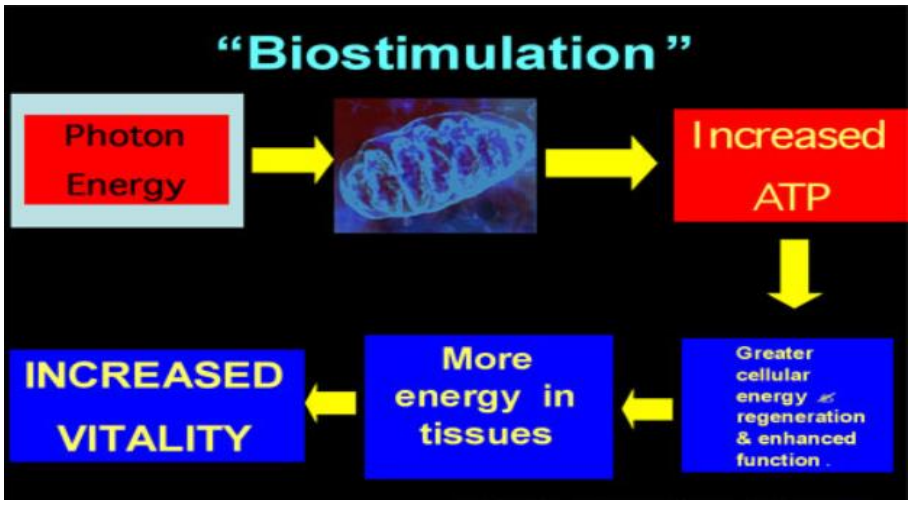

Fig 5.2 Mechanism of Biostimulation

Benefits

Increases ATP synthesis

Stimulates cell growth

Increases cell metabolism

Improves cell regeneration

Invokes an anti-inflammatory response

Promotes edema reduction

Reduces fibrous tissue formation

Stimulates nerve function

Laser used

Previously helium-neon (HeNe) laser of <1 mW was used.

Limited by the need for an optic fiber, the size of the machine and the still rather low power option

Replaced by the indium-gallium-aluminum-phosphide laser, a diode producing red laser in the range 600-700 nm and able to deliver as much as 500 mW.

Frequently used in dentistry is the gallium-aluminum-arsenide laser.

Operates in the spectrum between 780 and 830 nm. The output is typically between 10 and 500 mW.

Advantage of the diode lasers is the small size and option for battery operation, making them rather handy and portable. T

Work in continuous mode, but can be mechanically or electronically pulsed.

Effects

Reduction of inflammation: It can occur within hours to days.

Pain relief

Accelerated tissue regeneration: LLLT stimulates cell proliferation of fibroblasts , keratinocytes , endothelial cells and lymphocytes.

Wound healing in a range of sites, like surgical wounds, extraction sites, recurrent aphthous ulcerations - Dental

Applications

Minor injuries and sprains

Inflammation

Aches and Pain

Skin rejuvenation

Wound healing

Acupuncture

5.5 LASER SAFETY PROCEDURES

Laser treatment increases the potential for laser accidents also increases.

Beam Hazards

Hazardous effects related to unintentional direct contact with the laser beam

- Eye related
- Interaction hazards (Plume and Fire)
- Skin related

1.Eye Related

- Corneal/Sclera Injury:caused by wavelengths that do not pass through fluid (roughly above 1400 nm and below 400 nm)
- Retinal Burns Injury: caused by wavelengths that do pass through fluid from (roughly 400-1400nm)
- Injury can result from exposure to:
  - direct beam
  - mirror reflection (surgical instruments)
  - diffuse beam (tissue reflection)
- Damage dependent on:
  - intensity - lens of eye can focus beam onto the retina
  - wavelength - absorbed by different parts of the eye
  - duration - fraction of second, before you can blink

2.Interaction Hazards

- Plume - Smoke from vaporization
  Creates a visibility problem
  Can cause nausea
- Can be Carbon, Aerosolized blood, Gases – including benzene, toluene and formaldehyde with particle size - 0.1 microns. Smoke evacuators is the preferred control method
- Fire and explosion

- Can occur if the laser beam comes into contact with combustible or volatile materials, such as: gauge pads ,surgical drapes ,gowns ,alcohol ,anesthetic gases

3.Skin related

- Thermal burn
  - Laser effects on tissue are dependent on 4 factors: power density of laser beam ,wavelength ,duration of exposure ,effects of circulation and conduction

Non beam hazards

- Hazards associated with the generation of the laser beam
  - Electrical - High voltage – many lasers require high voltage to generate the laser beam.
  - Accidental exposure can result in electrical shock or death
  - Chemical
  - Dye lasers use hazardous dyes to generate the laser beam (hazardous waste)

Control Measure

- Engineering- control measures that are built into the laser system, such as: enclosing the electrical system, within a cabinet , enclosing the beam within fiber optics or mechanical arms
- Administrative Control

  a. Controlled Entry- Closing doors and covering windows (when required) ,Posting of the PROPER "Laser in Use" signs outside all entries.
- b.Education-All personnel that may be exposed to the laser shall be required to attend regular "in-services" on operating the laser and laser safety.
- c.Standards- Each medical facility should develop their own set of operating standards

Personal Protection

- Eyewear - Each laser requires specific eyewear that is capable of absorbing laser light of that specific wavelength. Everyone in the laser OR must wear eye protection including the patient. Patient eye's can be protected by covering with moist towels, goggles, intra-ocular shields . The surgeon must have eye protection, even during microscopic and endoscopic procedures. Lens filters that fit over the eyepiece can be used.

- Skin Protection- Clothing , Gloves , Fire resistant gowns , Fire resistant surgical drapes , Moist gauze and drapes around surgical area . All gauze and drapes around the surgical area should be moistened with sterile saline. Smoke evacuators filter out the smallest particles (0.1 μ) found in the laser plume. Smoke evacuator suction tube must be placed as near to the site of laser ablation as possible

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