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Medical laser Application

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بسم الله الرحمن الرحيم

(هُوَ الَّذِي جَعَلَ الشَّمْسَ ضِيَاءً وَالْقَمَرَ نُورًا وَقَدَّرَهُ مَنَازِلَ لِتَعْلَمُوا عَدَدَ السِّنِينَ وَالْحِسَابَ مَا خَلَقَ اللَّهُ ذَلِكَ إِلَّا بِالْحَقِّ يُفَصِّلُ الْآيَاتِ لِقَوْمٍ يَعْلَمُونَ).

صدق الله العلي العظيم

سورة يونس- الآية **5**

الاهداء

إلى من علمني النجاح و الصبر... إلى من علمني
العطاء بدون انتظار... أبي حفظه الله .
إلى من علمتني و عانت الصعاب لأصل إلى ما أنا
فيه... إلى من كان دعاؤها سر نجاحي و حنانها بلسم
جراحي... أمي.
إلى جميع أفراد أسرتي العزيزة و الكبيرة كل باسمه
أينما وجدوا.
إلى أصدقائي رفقاء دربي من داخل الجامعة و
خارجها.
و إلى أساتذتي الكرام الذين أناروا دروبنا بالعلم و
المعرفة
إلى كل من يقتنع بفكرة فيدعو إليها و يعمل على
تحقيقها، لا يبغي بها إلا وجه الله و منفعة الناس.
إليكم أهدي ثمرة هذا العمل المتواضع.

الشكر والعرفان

الشكر و التقدير

اوجه شكري الى كل من ساعدني على الوقوف في دراسة هذا البحث و بالأخص اشكر اساتذتي الاعزاء و والدي و لولاهم لما تمكنت من دراسة بحثي و أهدي شكري ايضا الى كلية العلوم جامعة المثنى كما اقدم شكري و امتناني الى استاذي المحترم (**د. فراس فائق كاظم**) الذي تفضل مشكورا بالأشراف على بحثي ولا بد لنا و نحن نخطو خطواتنا الأخيرة في الحياة الجامعية من وقفة تعود الى اعوام قضيناها في رحاب الجامعة مع أساتذتنا الكرام الذين قدموا لنا الكثير من الجهود الكبيرة ببناء جيل الغد لنبعث في الأمة من جديد ...

و قبل أن أمضي تقدما بأسمى آيات الشكر والامتنان و التقدير و المحبة الى الذين حملوا اقدم رسالة في الحياة . الى الذين مهدوا الخاطر يقال علم و المعرفة . كن عالما ... فان لم تستطيع فكن متعلما فان لم تستطيع فاحب العلماء فان لم تستطيع فلا تبغضهما كما اقدم شكري و امتناني الى جميع اساتذتي الذين تلمذت على ايديهم في كافة المراحل الجامعية بارك الله فيكم جميعا أساتذتي

ومن الله التوفيق .

CONTENT:-

Abstract

Medical lasers for various clinical procedures including dermatology and plastic surgery, wound healings, nerve stimulation, dentistry, cancer therapy, and ophthalmic surgeries are reviewed. The fundamental principles behind the technologies are also presented. The laser spectra of UV (200-400) um, visible (400-700) nm, near-IR (700-2900) nm, and mid-IR (3-5) um having various penetration depths define invasive and noninvasive procedures. Diode lasers have been widely used in many surgical procedures including soft tissue cutting, coagulation and cancer thermal therapy. Various photosensitizers are presented in matching the laser absorption wavelengths. Finally, the principles and applications of photothermal therapy (PTT) and photodynamic therapy (PDT) are discussed in great details.

Chapter One

Laser Proprties

1.1 Introduction:-

Laser, a device that stimulates atoms or molecules to emit light at particular wavelengths and amplifies that light, typically producing a very narrow beam of radiation. The emission generally covers an extremely limited range of visible, infrared, or ultraviolet wavelengths. Many different types of lasers have been developed, with highly varied characteristics. Laser is an acronym for “light amplification by the stimulated emission of radiation”.

1.2 History

The laser is an outgrowth of a suggestion made by Albert Einstein in 1916 that under the proper circumstances atoms could release excess energy as light—either spontaneously or when stimulated by light. German physicist Rudolf Walther Ladenburg first observed stimulated emission in 1928, although at the time it seemed to have no practical use.[1]

In 1951 Charles H. Townes, then at Columbia University in New York City, thought of a way to generate stimulated emission at microwave frequencies. At the end of 1953, he demonstrated a working device that focused “excited” (see below Energy levels and stimulated emissions) ammonia molecules in a resonant microwave cavity, where they emitted a pure microwave frequency. Townes named the device a maser, for “microwave amplification by the stimulated emission of radiation.” Aleksandr Mikhaylovich Prokhorov and Nikolay Gennadiyevich Basov of the P.N. Lebedev Physical Institute in Moscow independently described the theory of maser operation. For their work all three shared the 1964 Nobel Prize for Physics.

An intense burst of maser research followed in the mid-1950s, but masers found only a limited range of applications as low-noise microwave amplifiers and atomic clocks. In 1957 Townes proposed to his brother-in-law and former postdoctoral student at Columbia University, Arthur L. Schawlow (then at Bell Laboratories), that they try to extend maser action to the much shorter wavelengths of infrared or visible light. Townes also had discussions with a graduate student at Columbia University, Gordon Gould, who quickly developed his own laser ideas. Townes and Schawlow published their ideas for an "optical maser" in a seminal paper in the December 15, 1958, issue of Physical Review. Meanwhile, Gould coined the word laser and wrote a patent application. Whether Townes or Gould should be credited as the "inventor" of the laser thus became a matter of intense debate and led to years of litigation. Eventually, Gould received a series of four patents starting in 1977 that earned him millions of dollars in royalties.

The Townes-Schawlow proposal led several groups to try building a laser. The Gould proposal became the basis of a classified military contract. Success came first to Theodore H. Maiman, who took a different approach at Hughes Research Laboratories in Malibu, California. He fired bright pulses from a photographer's flash lamp to excite chromium atoms in a crystal of synthetic ruby, a material he chose because he had studied carefully how it absorbed and emitted light and calculated that it should work as a laser. On May 16, 1960, he produced red pulses from a ruby rod about the size of a fingertip. In December 1960 Ali Javan, William Bennett, Jr., and Donald Herriott at Bell Labs built the first gas laser, which generated a continuous infrared beam from a mixture of helium and neon. In 1962 Robert N. Hall and coworkers at the General Electric Research and Development Center in Schenectady, New York, made the first semiconductor laser [2].

1.3 Fundamental principles

1.3.1 Energy levels and stimulated emissions

Laser emission is shaped by the rules of quantum mechanics, which limit atoms and molecules to having discrete amounts of stored energy that depend on the nature of the atom or molecule. The lowest energy level for an individual atom occurs when its electrons are all in the nearest possible orbits to its nucleus (see electronic configuration). This condition is called the ground state. When one or more of an atom's electrons have absorbed energy, they can move to outer orbits, and the atom is then referred to as being "excited." Excited states are generally not stable; as electrons drop from higher-energy to lower-energy levels, they emit the extra energy as light [3].

Einstein recognized that this emission could be produced in two ways. Usually, discrete packets of light known as photons are emitted spontaneously, without outside intervention. Alternatively, a passing photon could stimulate an atom or molecule to emit light—if the passing photon's energy exactly matched the energy that an electron would release spontaneously when dropping to a lower-energy configuration. Which process dominates depends on the ratio of lower-energy to higher-energy configurations. Ordinarily, lower-energy configurations predominate. This means that a spontaneously emitted photon is more likely to be absorbed and raise an electron from a lower-energy configuration to a higher-energy configuration than to stimulate a higher-energy configuration to drop to a lower-energy configuration by emitting a second photon. As long as lower-energy states are more common, stimulated emission will die out.

However, if higher-energy configurations predominate (a condition known as population inversion), spontaneously emitted photons are more likely to stimulate further emissions, generating a cascade of photons.

Heat alone does not produce a population inversion; some process must selectively excite the atoms or molecules. Typically, this is done by illuminating the laser material with bright light or by passing an electric current through it [4].

The simplest conceivable system, such as the ammonia maser built by Townes, has only two energy levels. More useful laser systems involve three or four energy levels. In a three-level laser, the material is first excited to a short-lived high-energy state that spontaneously drops to a somewhat lower-energy state with an unusually long lifetime, called a metastable state. The metastable state is important because it traps and holds the excitation energy, building up a population inversion that can be further stimulated to emit radiation, dropping the species back to the ground state. The ruby laser developed by Theodore Maiman is an example of a three-level laser.

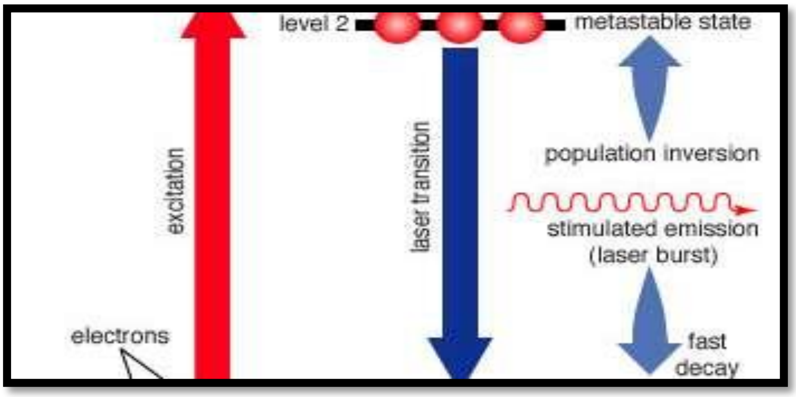

Figure (1.1): shows the two-level system [3].

Unfortunately, the three-level laser works only if the ground state is depopulated. As atoms or molecules emit light, they accumulate in the ground state, where they can absorb the stimulated emission and shut down laser action, so most three-level lasers can only generate pulses. This difficulty is overcome in the four-level laser, where an extra transition state is located between metastable and ground states. This allows many four-level lasers to emit a steady beam for days on end.

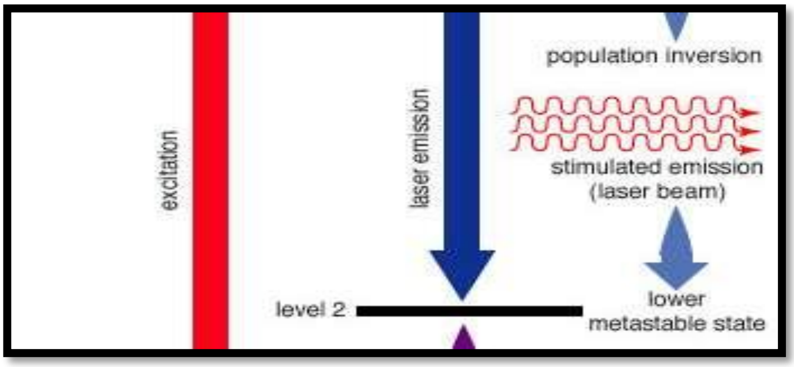

Figure (1.2): Shows the three-level laser [4].

1.4 Laser elements

Population inversions can be produced in a gas, liquid, or solid, but most laser media are gases or solids. Typically, laser gases are contained in cylindrical tubes and excited by an electric current or external light source, which is said to "pump" the laser. Similarly, solid-state lasers may use semiconductors or transparent crystals with small concentrations of light-emitting atoms.[5].

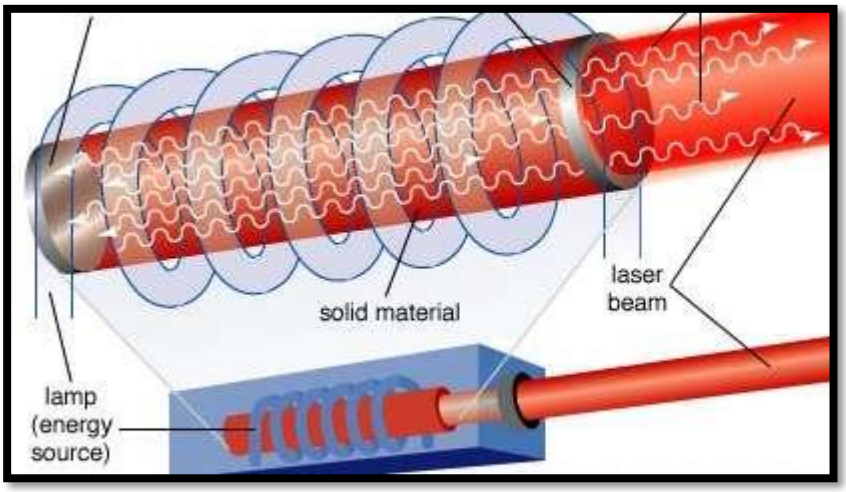

Figure (1.3): Shows the laser pumping process [5].

An optical resonator is needed to build up the light energy in the beam. The resonator is formed by placing a pair of mirrors facing each other so that light emitted along the line between the mirrors is reflected back and forth. When a population inversion is created in the medium, light reflected back and forth increases in intensity with each pass through the laser medium. Other light leaks around the mirrors without being amplified. In an actual laser cavity, one or both mirrors transmit a fraction of the incident light. The fraction of light transmitted—that is, the laser beam—depends on the type of laser.

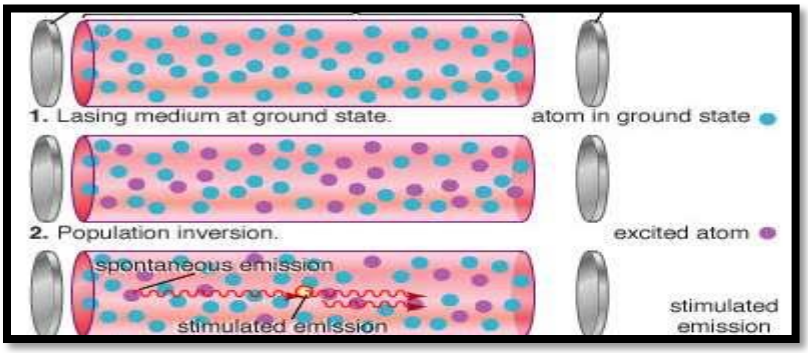

Figure (1.4): shows the emission process in the laser [5].

If the laser generates a continuous beam, the amount of light added by stimulated emission on each round trip between the mirrors equals the light emerging in the beam plus losses within the optical resonator.

The combination of laser medium and resonant cavity forms what often is called simply a laser but technically is a laser oscillator. Oscillation determines many laser properties, and it means that the device generates light internally. Without mirrors and a resonant cavity, a laser would just be an optical amplifier, which can amplify light from an external source but not generate a beam internally. Elias Snitzer, a researcher at American Optical, demonstrated the first optical amplifier in 1961, but such devices were little used until the spread of communications based on fibre optics [6].

1.5 Laser beam characteristics

Laser light generally differs from other light in being focused in a narrow beam, limited to a narrow range of wavelengths (often called “monochromatic”), and consisting of waves that are in phase with each other. These properties arise from interactions between the process of stimulated emission, the resonant cavity, and the laser medium.

Stimulated emission produces a second photon identical to the one that stimulated the emission, so the new photon has the same phase, wavelength, and direction—that is, the two are coherent with respect to each other, with peaks and valleys in phase. Both the original and the new photon can then stimulate the emission of other identical photons. Passing the light back and forth through a resonant cavity enhances this uniformity, with the degree of coherence and the narrowness of the beam depending on the laser design.

Although a visible laser produces what looks like a point of light on the opposite wall of a room, the alignment, or collimation, of the beam is not perfect. The extent of beam spreading depends on both the distance between the laser mirrors and diffraction, which scatters light at the edge of an aperture. Diffraction is proportional to the laser wavelength divided by the size of the emitting aperture; the larger the aperture is, the more slowly the beam spreads. A red helium-neon laser emits from a one-millimetre aperture at a wavelength of 0.633 micrometre, generating a beam that diverges at an angle of about 0.057 degree, or one milliradian. Such a small angle of divergence will produce a one-metre spot at a distance of one kilometre. In contrast, a typical flashlight beam produces a similar one-metre spot within a few metres. Not all lasers produce tight beams, however. Semiconductor lasers emit light near one micrometre wavelength from an aperture of comparable size, so their divergence is 20 degrees or more, and external optics are needed to focus their beams.[7].

The output wavelength depends on the laser material, the process of stimulated emission, and the optics of the laser resonator. For each transition between energy levels, a material can support stimulated emission over a limited range of wavelengths; the extent of that range varies with the nature of the material and the transition. The probability of stimulated emission varies with wavelength, and the process concentrates emission at wavelengths where that probability is the highest.

Resonant cavities support laser oscillation at wavelengths that meet a resonant condition—an integral number N of wavelengths λ must equal the distance light travels during a round trip between the mirrors. If the cavity length is L and the refractive index of the material in the laser cavity is n, the round-trip distance 2L must equal $N\lambda/n$, or $2L = N\lambda/n$. Each resonance is called a longitudinal mode. Except in semiconductor lasers, cavities are thousands of wavelengths long, so the wavelengths of adjacent modes are closely spaced—and usually the laser simultaneously emits light on two or more wavelengths within 0.1 percent of each other. These beams are monochromatic for most practical applications; other optics can be added to limit laser oscillation to a single longitudinal mode and an even narrower range of wavelengths. The best laboratory lasers emit a range of wavelengths that differ by less than 0.0000001 percent [8].

The narrower the range of wavelengths, the more coherent the beam—meaning the more precisely every light wave in the beam is in exact synchronization with every other one. This is measured by a quantity called coherence length. If the centre of the range of wavelengths emitted is λ and the range of wavelengths emitted is $\Delta\lambda$, this coherence length equals $\lambda 2/2\Delta\lambda$. Typical coherence lengths range from millimetres to metres. Such long coherence lengths are essential, for instance, to record holograms of three-dimensional objects.

Lasers can generate pulsed or continuous beams, with average powers ranging from microwatts to over a million watts in the most powerful experimental lasers. A laser is called continuous-wave if its output is nominally constant over an interval of seconds or longer; one example is the steady red beam from a laser pointer. Pulsed lasers concentrate their output energy into brief high-power bursts. These lasers can fire single pulses or a series of pulses at regular intervals. Instantaneous power can be extremely high at the peak of a very short pulse. Laboratory lasers have generated peak power exceeding 1015 watts for intervals of about 10−12 second [9].

Pulses can be compressed to extremely short duration, about 5 femtoseconds (5 × 10−15 second) in laboratory experiments, in order to "freeze" the action during events that occur very rapidly, such as stages in chemical reactions. Laser pulses also can be focused to concentrate high powers on small spots, much as a magnifier focuses sunlight onto a small spot to ignite a piece of paper.

1.6 Types of lasers

Crystals, glasses, semiconductors, gases, liquids, beams of high-energy electrons, and even gelatin doped with suitable materials can generate laser beams. In nature, hot gases near bright stars can generate strong stimulated emission at microwave frequencies, although these gas clouds lack resonant cavities, so they do not produce beams.

In crystal and glass lasers, such as Maiman's first ruby laser, light from an external source excites atoms, known as dopants, that have been added to a host material at low concentrations. Important examples include glasses and crystals doped with the rare-earth element neodymium and glasses doped with erbium or ytterbium, which can be drawn into fibres for use as fibre-optic lasers or amplifiers. Titanium atoms doped into synthetic sapphire can generate stimulated emission across an exceptionally broad range and are used in wavelength-tunable lasers.

Many different gases can function as laser media. The common helium-neon laser contains a small amount of neon and a much larger amount of helium. The helium atoms capture energy from electrons passing through the gas and transfer it to the neon atoms, which emit light. The best-known helium-neon lasers emit red light, but they also can be made to emit yellow, orange, green, or infrared light; typical powers are in the milliwatt range. Argon and krypton atoms that have been stripped of one or two electrons can generate milliwatts to watts of laser light at visible and ultraviolet wavelengths. The most powerful commercial gas laser is the carbon-dioxide laser, which can generate kilowatts of continuous power [10]

The most widely used lasers today are semiconductor diode lasers, which emit visible or infrared light when an electric current passes through them. The emission occurs at the interface (see p-n junction) between two regions doped with different materials. The p-n junction can act as a laser medium, generating stimulated emission and providing lasing action if it is inside a suitable cavity. Conventional edge-emitting semiconductor lasers have mirrors on opposite edges of the p-n junction, so light oscillates in the junction plane. Vertical-cavity surface-emitting lasers (VCSELs) have mirrors above and below the p-n junction, so light resonates perpendicular to the junction. The wavelength depends on the semiconductor compound.

A few other types of lasers are used in research. In dye lasers the laser medium is a liquid containing organic dye molecules that can emit light over a range of wavelengths; adjusting the laser cavity changes, or tunes, the output wavelength. Chemical lasers are gas lasers in which a chemical reaction generates the excited molecules that produce stimulated emission. In free-electron lasers stimulated emission comes from electrons passing through a magnetic field that periodically varies in direction and intensity, causing the electrons to accelerate and release light energy. Because the electrons do not transition between well-defined energy levels, some specialists question whether a free-electron laser should be called a laser, but the label has stuck. Depending on the energy of the electron beam and variations in the magnetic field, free-electron lasers can be tuned across a wide range of wavelengths. Both free-electron and chemical lasers can emit high powers.[11].

1.7 Properties of Laser

The laser light exhibits some peculiar properties compared with the conventional light which make it unique. Let us study the factors that make laser light stand out. These are

1- Monochromatic
2- Coherence
3- Directionality
4- Highly Intense or Brightness

1- Monochromatic

Monochromatic light is a light containing a single colour or wavelength. The light emitted from ordinary light sources have different energies, frequencies, wavelengths, or colors. But laser light has a single wavelength or colour [12].

Laser light covers a very narrow range of frequencies or wavelengths. This can be due to the stimulated characteristics of laser light. The bandwidth of the conventional monochromatic light source is 1000 Å.

But the bandwidth of an ordinary light source is 10 Å. For a highly sensitive laser source it is 10-8 Å.

2- Coherence

A predictable correlation of the amplitude and phase at any one point with another point is called coherence.That means if two or more waves of same frequency are in the same phase or have constant phase difference then these waves are said to be coherent in nature.

In the case of conventional light, the property of coherence exhibits between a source and its virtual source whereas in the case of laser the property coherence exists between any two or more light waves.There are two types of coherence. Temporal coherence and Spatial coherence.

3- Directionality

The light ray coming from an ordinary light source travels in all directions, but laser light travels in a single direction. For example, the light emitted from torchlight spreads 1km distance it spreads 1 km distance. But the laser light spreads a few centimeters distance even it travels lacks kilometer distance [13].

4- Highly Intense or Brightness

Laser light is highly intense than conventional light. We know that the intensity of a wave is the energy per unit time flowing through a specific area. A one mill watt He-Ne laser is more intense than the sun intensity. This is because of the coherence and directionality of the laser .

Suppose when two photons each of amplitude a are in phase with another, then young's principle of superposition, the resultant amplitude of two photons is 2a and the intensity is 4a2. Since in laser many numbers of photons are in phase with each other, the amplitude of the resulting wave becomes na and hence the intensity of the laser is proportional to n2a2. So the 1mW He-Ne laser is more intense than the sun [14].

Chapter Two

Laser Applications

2.1 Introduction

Lasers deliver coherent, monochromatic, well-controlled, and precisely directed light beams. Although lasers make poor choices for general-purpose illumination, they are ideal for concentrating light in space, time, or particular wavelengths. For example, many people were first introduced to lasers by concerts in the early 1970s that incorporated laser light shows, in which moving laser beams of different colours projected changing patterns on planetarium domes, concert-hall ceilings, or outdoor clouds.

Most laser applications fall into one of a few broad categories:

1- Transmission and processing of information.
2- Precise delivery of energy.
3- Alignment, measurement, and imaging.

These categories cover diverse applications, from pinpoint energy delivery for delicate surgery to heavy-duty welding and from the mundane alignment of suspended ceilings to laboratory measurements of atomic properties [15].

2.2 Transmission and Processing of Information

2.2.1 Laser Scanners

Figure (2.5): shows the laser scanner [16].

The ability to focus laser beams onto very small spots and to switch them on and off billions of times per second makes lasers important tools in telecommunications and information processing. In laser supermarket scanners, a rotating mirror scans a red beam while clerks move packages across the beam. Optical sensors detect light reflected from striped bar codes on packages, decode the symbol, and relay the

Tiny, inexpensive semiconductor lasers read data from a growing variety of optical compact disc formats to play music, display video recordings, and read computer software. Audio compact discs, using infrared lasers, were introduced around 1980; CD-ROMs (compact disc read-only memory) for computer data soon followed. Newer optical drives use more powerful lasers to record data on light-sensitive discs called CD-R (recordable) or CD-RW (read/write), which can be played in ordinary CD-ROM drives. DVDs (digital video, or versatile, discs) work similarly, but they use a shorter-wavelength red laser to read smaller spots, so the discs can hold enough information to play a digitized motion picture. A new generation of discs called Blu-ray uses blue-light lasers to read and store data at an even higher density [16].

2.2.2 Fiber-Optic Communication Systems

Fibre-optic communication systems that transmit signals more than a few kilometres also use semiconductor laser beams. The optical signals are sent at infrared wavelengths of 1.3 to 1.6 micrometres, where glass fibres are most transparent. This technology has become the backbone of the global telecommunications network, and most telephone calls traveling beyond the confines of a single town go part of the way through optical fibres.

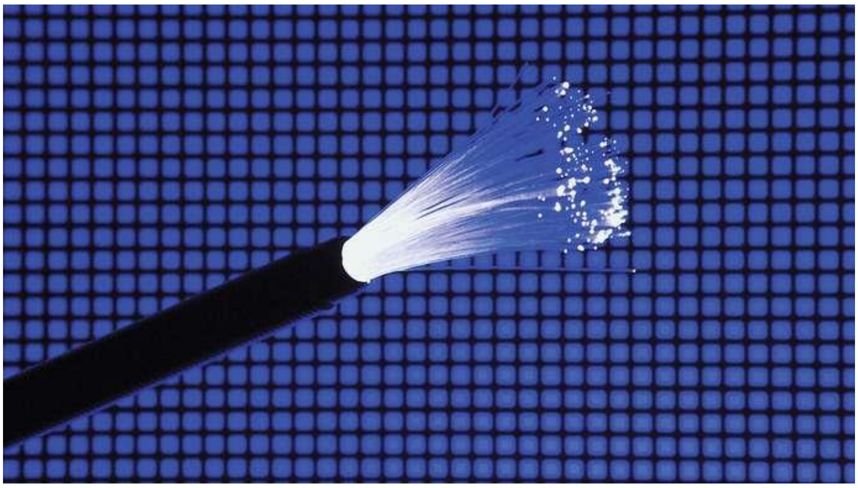

Figure (2.2): The commercial optical fiber [17].

2.2.3 Precise delivery of energy

1) Industrial uses

Laser energy can be focused in space and concentrated in time so that it heats, burns away, or vaporizes many materials. Although the total energy in a laser beam may be small, the concentrated power on small spots or during short intervals can be enormous. Although lasers cost much more than mechanical drills or blades, their different properties allow them to perform otherwise difficult tasks. A laser beam does not deform flexible materials as a mechanical drill would, so it can drill holes in materials such as soft rubber nipples for baby bottles. Likewise, laser beams can drill or cut into extremely hard materials without dulling bits or blades. For example, lasers have drilled holes in diamond dies used for drawing wire [17].

2.3 Medical laser application

Medical laser application is a broad area armed with advanced technologies to meet challenges in clinical diagnostics and therapy and to address health care issues that impact broad populations. Recent research and emerging developments provide the vision of improving clinical therapeutic procedures or extending the use of lasers to new fields of medicine. Novel biomedical laser applications and new types of lasers widen the possible spectrum of laser-tissue interactions to improve target-oriented, precise application of laser radiation in clinical practice [18].

Lasers have been used for various medical procedures including dermatology, plastic surgery, wound healings, nerve stimulation, dentistry, ophthalmology and many other therapeutic and surgical procedures. Combining the nanoparticles and photosensitizers, diode lasers have been also used for cancer diagnosis and therapy. Selected medical laser systems (devices) which have been commercialized or used for research are shown in Table 2.1 for both photodynamic and photothermal and applications, where pulsed lasers are in energy per pulse (mJ) and CW lasers are in power (W).

Table (2.1): Laser candidates for various medical applications [18].

Laser type	Wavelength (pulse width)	Energy/power
Ti:sapphire	780 nm (p.s. and f.s.)	(0.01 – 0.1) mJ
Nd:YAG/YLF	1064/1053 nm (n.s. and p.s.)	(1.0 – 20) mJ
Ho:YAG	2100 nm (µs)	(10 – 20) mJ
Er:YAG	2940 nm (µs)	(10 – 20) mJ
Fiber-laser	0.5-3.2 microns (n.s-p.s)	(0.05 – 0.1) mJ
UV excimer laser	193, 308 nm (ns)	(5 -20) mJ
Solid state laser	213, 266, 532 nm (ns)	(2-10) mJ
Solid state laser	430-1064 (cw)	0.5 – 10 W
Gas lasers	413, 488, 580,647 nm (cw)	0.5-10W
Diode laser	360 -2100 nm (cw)	0.1 – 50 W

Interaction of light (coherent or non-coherent) with cells may be categorized to:

(a) Endogeneous: direct absorbing by the constituents of the cells or tissue, and

(b) Exogeneous: light absorbed via the added photosensitizer, a process called photodynamics therapy (PDT) can be used to destroy cancerous or diseased cells and/or unwanted abnormal tissues.[19].

PDT involves selective light (often low-power laser light or LED) absorption by the external chemical agent, or a PDT drug. As shown in Table 2.2, various dyes (drugs) have been developed at specific laser absorption wavelengths from visible to near-IR. The PDT drugs may be administered either intravenously or topically depending on applications. Three principal mechanisms have been proposed for the destruction of cells and tissues by PDT: localized cell damage by targeting on a specific organelle by a particular drugs, including apoptosis (localized in mitochondiria) and necrosis (localized in plasma membrane); vascular damage induced by PDT action. For example, the porphyrin-induced PDT produces a rapid onset of vascular blood flow stasis (stopping) and hemorrhage causing tumor cell death; and immunological response of PDT results a strong inflammatory reaction which contributes to tumor destruction.

Table (2.2): Applications of photodynamic therapy (PDT) [19].

Dermatology & Cancers
Early stage (micro-invasive) lung cancer
Lung tumors (endobronchial, mesothelioma)
Skin and breast cancer
Brain, colorectal tumors
Cardiovascular
Chronic skin diseases (psoriasis, vitiligo)
Wound healing, oral cavity (anti-bacterial)
Ophthalmology
Age-related macular degeneration (AMD) induced CNV
Pathologic myopia induced CNV
Coagulation of retina

The photochemical process of PDT for cell damage further involves 2 chemical processes: photoaddition reaction (type-I) in which the light-excited photosensitizer convalently bonds to a constituent molecule of the cell, where type I is the major path for crosslinking process; and photoxidation reaction (type-II) in which the excited state of the photosensitizer produces a highly reactive oxygen specie such as an excited singlet oxygen, a superoxide anion, or a free radical of H* and it often involves a chain reaction, where type II is the major path for cancer cell damage.[20].

As shown in Table 2.2, PDT offers many applications in dermatology, ophthalmology and cancer treatments in various parts of human body.

As shown in Table 2.3, various photosensitizers are available for the absorption of lasers in visible (630-700) nm, and near-IR (700-1000) nm. These lasers are commercially available; dye lasers (at about 665 nm) pumped by a green laser; Nd:YAG (at 1064 nm); diode lasers (630-1100) nm; tunable Ti:sapphire laser (690-1100) nm; Alexandrite laser (720-800) nm. Tunable near-IR source may be also generated from an optical parametric oscillation (OPO) or amplification (OPA), where a green laser (at about 532 nm) may be used as a pump to produce tunable (900-1300) nm near-IR output (see Figure 3). In addition, high-brightness LED in visible (550-680) nm are also available for PDT using 5-ALA as the photosensitizer.

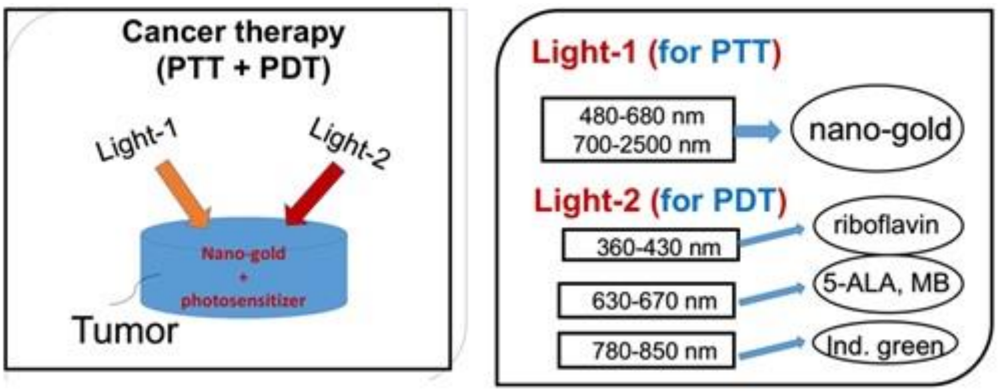

Figure (2.3): Combining PDT and PTT uisng nanogold and various photosensitizers [20].

Table (2.3): Summary of photosensitizers.[21].

Absorbing Extinction		
	wavelength (nm)	Coeff. (1/M/cm)
Name of PDT drug	-	-
Riboflavin (B2)	365	-
Photofrin (porfimer sodium)	630	3,000
5-ALA	635	5,000
Meta-THPC	652	22,400
Methylene blue	660	-
pyropheophorbides (HPPH)	665	-
Verteporfin	680-690	-
Lu-Tex	732	42.000
Phthalocyanines (PTC), na-PTC	670-780	100,000
Indocyanin green (ICG)	805	-
Si(IV)-naphthalocyanines	770-790	240000

High intensity ultra-short pulse lasers have been used in PDT using a 2-photon absorption. These include: mode-locked Ti:sapphire laser (at 800 nm), peak power about 5MW/cm^2, pulse duration 70 fsec and energy of 4 nJ/pulse; mode-lock Alexandrite laser (at about 780 nm) and a near IR-laser called Cr:forsterite (at 1230 nm). These near-IR lasers at longer wavelength offers deeper penetration than that of visible lasers, in addition to the minimal thermal effects and spatial selectivity which may be important in certain treatments such as brain cancers.

Laser penetration of tissues is limited by its absorption in melanin and oxyhomoglobin and it is a decreasing function of laser wavelength. Therefore near-IR lasers have deep penetration than visible lasers and have been used in various therapies which require deep penetrations, such as laser for hair removal and laser for acupunctures.

For ophthalmic application, retinal photocoagulation has been reported by using various visible and IR lasers such as argon blue-green laser (488/514 nm), double-YAG green laser (at 532 nm), krypton laser (at 647 nm) and diode lasers (at 806-810 nm). Photocoagulation process was also used to seal leak blood vessels for the treatment of age-related macular degeneration (AMD) which has two types, the choroidal neovascular ("CNV", wet) and non-neovascular (dry). In the wet AMD, the vascular ingrowth causes photoreceptor destruction, or bleeding with extensive loss of vision. The major drawback of photocoagulation to destroy the vascular growth beneath the retina is the nonselective necrotic damage to the adjacent normal retina and the thermal damage in the subfocal area which can cause the recurrence of the neovascular tissue. However, a short-pulse (about 3 ns) green laser has been successfully used for the treatment of open-angle glaucoma, a procedure called selective laser trabeculoplasty (SLT) which shows advantages over the conventional system using an argon CW laser [22].

PDT for the treatment of subfocal choroidal neovascularization (CNV) using verteporfin as the phtosensitizer has been proven for subfoveal. CNV in both AMD and in pathologic myopia (or non-AMD) patients. CNV may be also treated by a procedure called transpupillary thermotherapy (TTT) using diode laser at 810 nm, where PDT drug is not needed.

In contrast to the PDT without too much heat involved, photothermal therapy (PTT) is a thermal process with heat generated by the thermal lasers. Examples of PTT for various applications in cancer therapy, cosmetic and dermatology are presented as follows [23].

2.4 Cancer Therapy Lasers

Combining the nanoparticles, diode lasers have been also used for cancer therapy, bio-sensing, bio-imaging, drug delivery and diagnostics of cancer. Various nanoparticles (gold, polymers, silica etc) have been explored for the use of surface plasmon resonance (SPR) including shapes in spheres, rods, boxes, cages and shells. For example, by changing the shape of nanogold from sphere to nanorod, the absorption and scattering peaks change from visible (about 530 nm) to the near-infrared (NIR) regime (about 750 to 980 nm) . Comparing to the visible light, light in the NIR regime offers the advantages of larger absorption and scattering cross sections and much deeper penetration depth in tissues [21]. The in vivo studies in animal and/or human cancer therapy shall include the non-uniform gold nanorod (NGR) concentration in the tumor, the multi-layer normal-cancer tissue medium with multiple thermal parameters, and the blood flowing of the laser-targeted areas. The design of multiple-wavelengths laser system shall partially overcome the issues of GNRs non-uniform and multiple thermal medium for a 3-dimensional-therapy, in which various absorption penetration depths are available via the fiber-coupled multiple-wavelength laser simultaneously targeting the cancer tumors [24].

Combining PDT and PTT using nanogold and various photosensitizers for cancer therapy is shown in Figure 2.4. The critical factors of the synergistic therapy efficiency to be discussed include: the concentration of the initiator (nanogold or photosensitizers) in the treated medium, the wavelength, energy and the irradiation period of the light applied to the medium.

2.5 Cosmetic and Dermatology Lasers

Figure 4 shows various cosmetic lasers and their applications for invasive and non-invasive uses defined by their tissue penetration depth (d). Lasers with small depth (d<0.1 mm) suitable for invasive wrinkle or tattoo removal, whereas large depth (with d> 2 mm) suitable for non-invasive simulation or hair removal. Figure 2.4 can be compared with Figure 2 for the penetration depth. Figure 2.4 shows the commercial laser for hair removal (using a diode laser at 810 nm with large penetration depth about 4 mm) and hair growth device (using a red, 635 -690 nm, LED or laser with smaller penetration depth and low power for surface stimulation). Figure 2.5 shows a UV (308 nm) light device for the treatment of psoriasis; and a pen-type blue laser (at 405 nm) combined with a red laser (at 660 nm) for the treatment of acne [25].

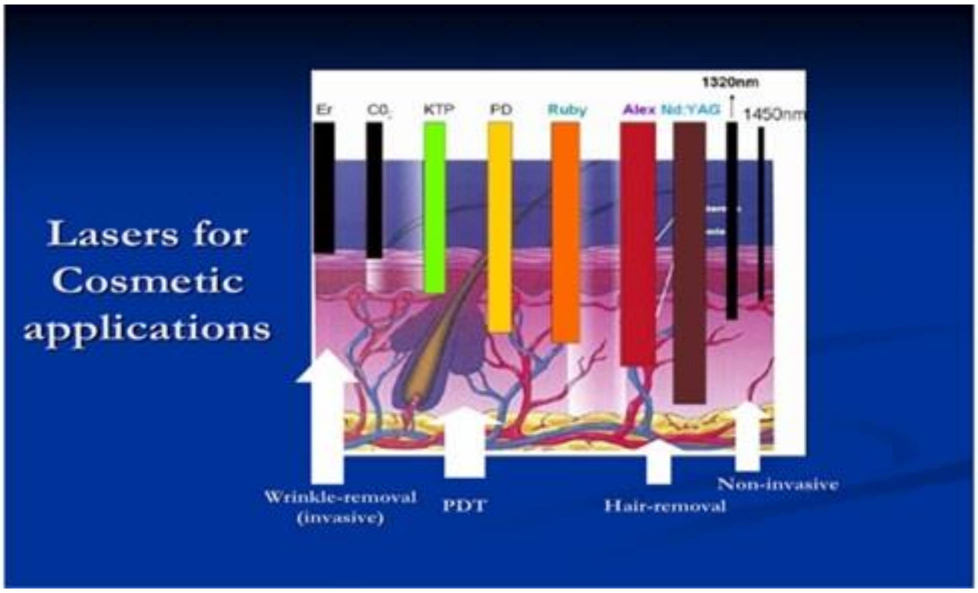

Figure (2.4): Cosmetic lasers and their tissue penetration depth which defined their applications in both invasive and non-invasive uses [25].

Figure (2.5): The commercial laser for hair removal (using a diode laser at 810 nm) and hair growth device (using a red, 635 - 690 nm LED or laser) [25]

2.6 Dental Lasers

Lasers (or LEDs) currently commercialized for dental applications include: (1) low power red laser (or LED, see Figure 2.6) activating methylene blue for antimicrobial photodynamic therapy (aPDT) to treat periodontal deceases; (2) diode laser (at 808 or 980 nm) for soft tissue cutting and stimulation; (3) Er:YAG laser, also called as "water-laser" (made by Biolase, US) for hard tissue cutting; (4) low power UV-blue laser (at 405 nm) for caries and cancer detection via light stimulated fluorescence.[26].

Figure (2.6): (Left) a UV (308 nm) light for the treatment of psoriasis; (Right) a pen-type blue laser (at 405 nm) for the treatment of acne (made by New Vision Inc.) [26].

Figure (2.7): (Right) power red laser (or LED) for antimicrobial photodynamic therapy (aPDT) and (Left) diode laser (at 808 or 980 nm) for soft tissue cutting [26].

2.7 Ophthalmology Lasers

As shown by Table 3, various lasers have been used for various ophthalmic applications including retinal photocoagulation using argon blue-green laser (488/514 nm), double-YAG green laser (at 532 nm), krypton laser (at 647 nm) and diode lasers (at 806-810 nm). Photocoagulation process was also used to seal leak blood vessels for the treatment of age-related macular degeneration (AMD).

Figure 8 shows a surgical procedure called LASIK for vision corrections (myopia, hypeopia and astignism) using a UV excimer laser to reshape the corneal surface. Femto-second (f.s.) lasers combined with excimer laser are alo commercialized for the so-called bladeless LASIK procedure, in addition to the fetom-second laser cataracts treatment .[27].

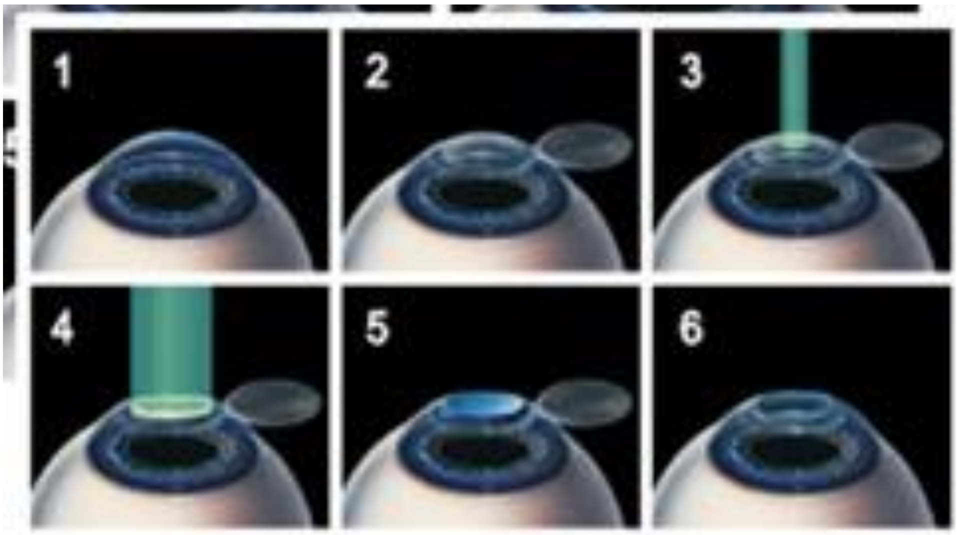

Figure (2.8): Surgical procedure called LASIK for vision corrections, where the corneal flap is prepare (either by microkeratom or a femtosecond laser), then an excimer UV laser (at 193 nm) is applied to cut a thin surface layer of the central part of the stroma tissue to reshape its curvature (for myopic correction); the corneal flat is placed back for healing [27].

Figure 2.9 shows a patented system using a solid-state (213 nm) laser for PRK and LASIK in replacing the gas excimer laser, where nonlinear crystals are sued to convert the 1064 nm laser to its fifth harmonics at 213 nm. Figure 2.10 shows a scanning Lasik system using a small flying spot for customized vision corrections.

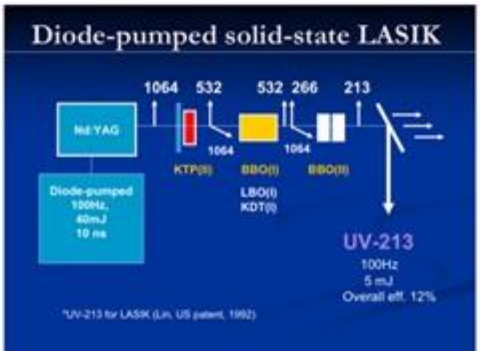

Figure (2.9): shows a patented system using a solid-state (213 nm) laser for PRK and LASIK (JT Lin, US 1992 patent) [27] .

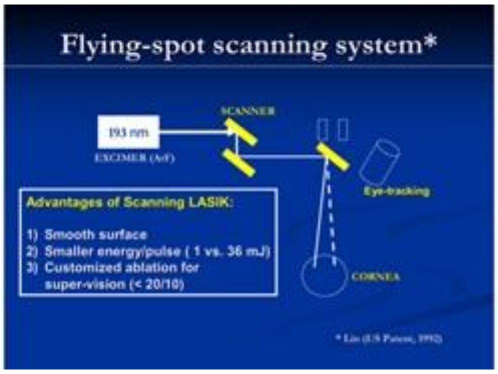

Figure (2.10): Shows a scanning Lasik system using a small flying spot for customized vision corrections (JT Lin, US patent, 1993) [27].

Figure 2.11 shows a diode laser (at 808 or 980 nm) for photocoagulation of the corneal tissue for glaucoma treatment. Figure 12 shows two systems (made by New vision Inc. and MLase AG) using UV LED (at 365 nm) for corneal collagen crosslinking (CXL) for the treatment of keratoconus and other corneal deceases.

Figure (2.11): Shows a diode laser (at 808 or 980 nm) for photocoagulation of the corneal tissue for glaucoma treatment, where a probe tip connected to the fiber is used to deliver the laser energy [27].

Figure (2.12): Shows two systems (made by MLase AG, Germany, top; and New vision Inc., Taiwan, low) using UV LED (at 365 nm) for corneal collagen crosslinking (CXL). Also shown is a pen-type CXL specially designed for VET uses [28].

Chapter Three

Conclusion

1) Applications of medical lasers are characterized by the properties of the tissues and the matching absorption wavelengths.
2) For PDT procedures, the properties of the activated photosensitizers also play an important role.
3) Synergistic therapy efficiency may be improved by combining PDT and PTT using nanogold and various photosensitizers.
4) Recent new technology also combines the nanomateirials for improved clinical outcomes.

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