Therapeutic Applications of Lasers

2021 Edition

Laser and Fiber Optics Educational Series

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Therapeutic Applications of Lasers

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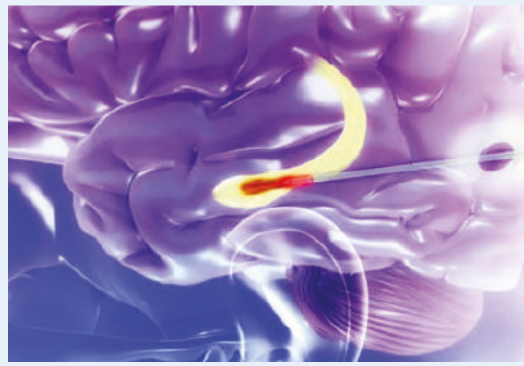

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About LASER-TEC

Laser-Tec is a not-for-profit National Center for Laser-Photonics and Fiber Optics Education. It is funded by the National Science Foundation to develop a sustainable pipeline of qualified laser and fiber optics technicians to meet the industry demand across the United States.

To learn more about LASER-TEC, visit www.laser-tec.org

About the Author of this Edition

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Preface

About the LASER-TEC Laser and Fiber Optics Educational Series

This series was created for use in engineering technology programs such as electronics, photonics, laser-electro-optics, and related programs. This series of publications has three goals in mind: 1) to create educational materials for areas of laser electro-optics technology in which no materials exist, 2) work with industry to use, adapt and enhance available industry-created material, 3) make these materials available to technicians at no cost to them making education in these areas more accessible to everyone. The Laser and Fiber Optics Educational Series is available for free online at www.laser-tec.org.

About Therapeutic Applications of Lasers

Therapeutic Applications of Lasers was created to provide a fundamental background for technicians on the theory of laser-tissue interactions, optical delivery systems, and to describe common applications of lasers in different fields of medicine. Numerous medical fields have been impacted by the use of lasers, including cosmetic dermatology, ophthalmology, gynecology, urology, dentistry, neurosurgery, and others. Lasers are used for thermal coagulation as well as ablation and vaporization of soft and hard tissues.

To the Student

This book is written at the technician level and can be used in post-secondary electronics engineering technology, or related programs. Medical laser technology is used for minimally invasive surgical applications in a variety of medical fields. The book contains all the modern pedagogy, which includes the following sections: introduction-motivation, learning outcomes, self-test questions for each section, summary, glossary, bibliography, and rich colorful illustrations.

To the Instructor

This book is intended for use in a certificate or associate degree program in electronics engineering technology. This will not only update the course content but will provide the student with the latest skills that industry expects. A Powerpoint presentation and a test bank are available by sending a request using an official college email to info@laser-tec.org.

Acknowledgments

This text is based on work contributed by Dr. Nathaniel Fried in 2021, under the direction of Dr. Chrys Panayiotou, principal investigator of LASER-TEC. It is based on work done by Dr. Fred Seeber and Dr. Tom MacGregor, under the direction of Dan Hull, principal investigator of OP-TEC in 2008. The content of this module has been reviewed for technical accuracy and pedagogical integrity by industrial and academic reviewers listed below.

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Therapeutic Applications of Lasers

Introduction

Since the discovery of the laser in 1960, lasers have become an indispensable part of many technologies, including surgical and other medical procedures. As laser technology has improved over the years, many new lasers have been discovered with extensive applications in medicine. Lasers now are available with output wavelengths ranging from the deep ultraviolet to the far infrared spectrum. Lasers whose wavelengths coincide with absorption wavelengths of human tissue components are used extensively in almost all areas of surgery.

New procedures are being developed around the unique characteristics of laser radiation. Pulsed lasers allow the laser beam to be manipulated and produce very short pulses with different energy densities. This allows surgeons to selectively perform the surgery at specific places without affecting surrounding areas. This module and the companion module *Diagnostic Applications of Lasers* provide an overview of the uses of lasers in medical and surgical diagnostic and therapeutic applications.

Prerequisites

The student should be familiar with the following before attempting to complete this module.

1. High school mathematics through intermediate algebra and the basics of trigonometry
2. LASER-TEC Optics and Photonics Series Course 1, *Fundamentals of Light and Lasers*
3. LASER-TEC Optics and Photonics Series Course 2, *Elements of Photonics*

   Module 2-1: *Operational Characteristics of Lasers*

   Module 2-2: *Specific Laser Types*

   Module 2-3: *Optical Detectors and Human Vision*

Learning Outcomes

Upon completion of this module, the student should be able to do the following:

- Describe process of reflection, absorption, scattering, and transmission of laser light in human tissue, including approximate wavelength ranges at which absorption is low and high.
- For given optical properties of tissue, understand how to calculate the optical penetration depth.
- For a laser and tissue type, determine the temperature rise resulting from a laser exposure and state whether this exposure is likely to cause tissue destruction through either vaporization or coagulation.
- Describe the use of free beams, articulated arms, optical fibers, and hollow waveguides for delivering light from the laser to the tissue.
- Understand losses of light due to reflection and attenuation in optical fibers.
- For a given value of refractive index, calculate the critical angle for total internal reflection in a fiber and the numerical aperture.
- Describe properties of laser radiation and different lasers and beam delivery methods used in medicine and surgery.
- Understand wavelength regions in which maximum absorption occurs for different tissue components or chromophores.
- Describe how lasers are used for cosmetic treatment of vascular lesions, tattoos, hair removal, and facial reconstruction in dermatology.
- Explain how *plasma-mediated*, *photothermal, photodisruptive, photoablation,* and *photochemical* laser-tissue interaction mechanisms differ and their applications in surgery.
- Understand the structure and absorptive properties of different parts of the human eye.
- Describe basic techniques involved in using lasers to treat gynecological diseases.
- Explain how lasers can be used to treat benign prostatic hyperplasia and kidney stones in urology.
- Understand how lasers treat soft dental tissues and remove hard filling materials from teeth.
- Describe how MRI-guided laser interstitial thermal therapy (LITT) is used for treatment of brain tumors and epilepsy in neurosurgery.
- Understand the roles of light, photosensitizing drugs, and oxygen in photodynamic therapy (PDT)

Note on Laboratories

Since the material and procedures covered in the module require special facilities and expensive equipment, no laboratory is provided. Instead, students should work with their instructors to find opportunities for observing the laser-assisted procedures described in the module. After the observations have been made, students should prepare reports that correlate their experiences to the material presented in the text. Completing these reports will require skills comparable to those used in a laboratory.

1. Properties of Laser Light

1.1 Introduction

It is laser light's unique characteristics that give it much of its utility. Ambient light is incoherent. Consider the average light bulb. The photons emitted cover a broad range of wavelengths from the infrared through the visible and ultraviolet. These photons spread out randomly in all directions. The light bulb is only useful for illuminating broad areas. Light from a laser is very different.

Laser light is *monochromatic, coherent,* and *directed* (Figure 1). While many laser mediums are capable of emission at several different wavelengths, generally lasers are designed to use the most efficient wavelength(s), i.e., the most intense line of emission.

While lasers can be designed to produce multiple wavelengths simultaneously, each line of fluorescence is *monochromatic*, a single narrow wavelength. Therefore, laser light can be monochromatic even when multiple lines are lasing simultaneously. Each wavelength can be separated from the others by passing the beam through a prism or a grating, separating the wavelengths by dispersion or diffraction.

Another characteristic of laser light is its *coherence*. Because of the way the emission of photons is amplified or generated within the medium, the photons are in phase, that is, in step with each other. Comparing incoherent light to coherent light would be like comparing a rain shower to an ocean wave. Raindrops fall randomly in no particular sequence, so their impact is diffused over space and time. By comparison, an ocean wave of the same volume, with all its "drops" in phase with one another, hits the same place at the same time. The impact of all of those drops is magnified by their coherence.

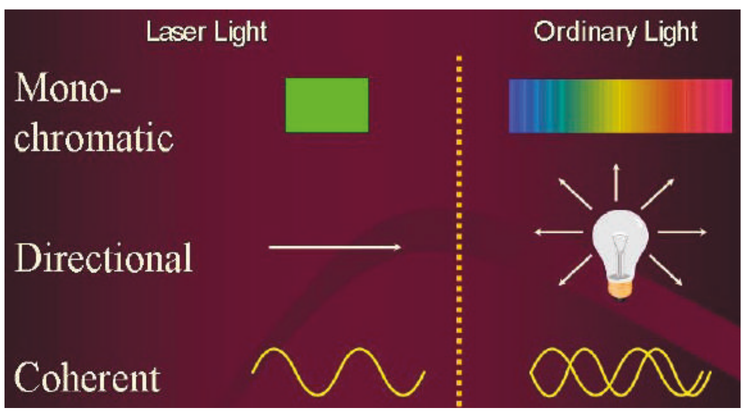


Figure 1. *Comparison of monochromatic, directional, and coherent laser light versus ordinary light which is polychromatic, incoherent, and diffuse.*

The third unique characteristic of laser light is that it is *directional*. Directed light consists of photons all traveling in the same direction with minimal divergence. Laser light is emitted in a narrow, well-defined beam that does not spread rapidly. This characteristic makes it easier to focus the laser's output to a very small, well-defined spot.

1.2 Lasers in Medicine

There are several common lasers used in medicine. Table 1 summarizes their wavelengths, laser-tissue interaction features, clinical applications, and optical delivery systems.

Table 1. Laser Types Established in Medical Applications

Laser	λ (nm)	Features	Applications	Delivery System
Excimer	193	Very high absorption in tissue for precise vaporization	Ophthalmology (LASIK eye surgery)	None
Excimer	308	High absorption in tissue	Cardiology (angioplasty) Dermatology (psoriasis)	Optical fiber
Frequency Doubled Nd:YAG	532	High absorption in blood	Ophthalmology (retina) Dermatology (tattoos) Urology (BPH)	Optical fiber
Diode	635	Wavelength matches cancer drug absorption peak	Cancer (light-based chemotherapy, PDT)	Optical fiber
Alexandrite	755	Pulsed laser with deep penetration	Dermatology (hair and tattoo removal)	Optical fiber
Diode	808, 980	Low absorption, deep penetration	Cancer (LITT) Dermatology (hair removal)	Optical fiber
Nd:YAG	1064	Low absorption, deep penetration	Cancer (LITT); Dermatology (hair and tattoo removal)	Optical fiber
Diode	1470	Similar depth to Ho:YAG	Endovenous therapy	Optical fiber
Th:YAG	2010	Intermediate penetration depth for vaporization and coagulation	Gastroenterology Urology (BPH)	Optical fiber
Ho:YAG	2120	Intermediate penetration depth for vaporization and coagulation	Gastroenterology; Urology (kidney stones and BPH)	Optical fiber
Er:YAG	2940	Very high tissue absorption for precise tissue vaporization	Dermatology (skin resurfacing) Dentistry (remove tooth decay)	Articulated arm; hollow waveguide; mid-IR fiber; scanner
CO_2	9,600 10,600	High absorption in tissue (water and mineral)	General Surgery Dentistry (remove tooth decay)	Articulated arm; hollow waveguide; scanner

Self-Test

1. Which of the following is a monochromatic light source?
(a) Sun (b) Flashlight (c) Laser (d) Light emitting diode or LED

2. Which of the following is an example of a highly divergent light source?
(a) Lightbulb (b) Flashlight (c) Laser (d) All of the above

2. Laser-Tissue Interactions Theory

2.1 Lasers in Medicine

When laser energy is incident on tissue, five things happen. Some of the light will be *reflected,* some will be *refracted* through the interface between the air and tissue surface, some will be *absorbed* at the treatment site, some will be *scattered* in different directions within the tissue, and some will be *transmitted* into tissues beyond the treatment site (Figure 2). For the laser to be effective, the light must be absorbed by the targeted tissues. The degree to which each occurs is a function of the laser wavelength and how the laser energy interacts with the tissue being irradiated. If the laser wavelength has been selected properly, the majority of energy is absorbed in the targeted tissue. Reflection of some of the laser energy reduces the laser's efficiency. Any energy not reflected, absorbed, or scattered is transmitted through and eventually dissipated in the underlying tissues.

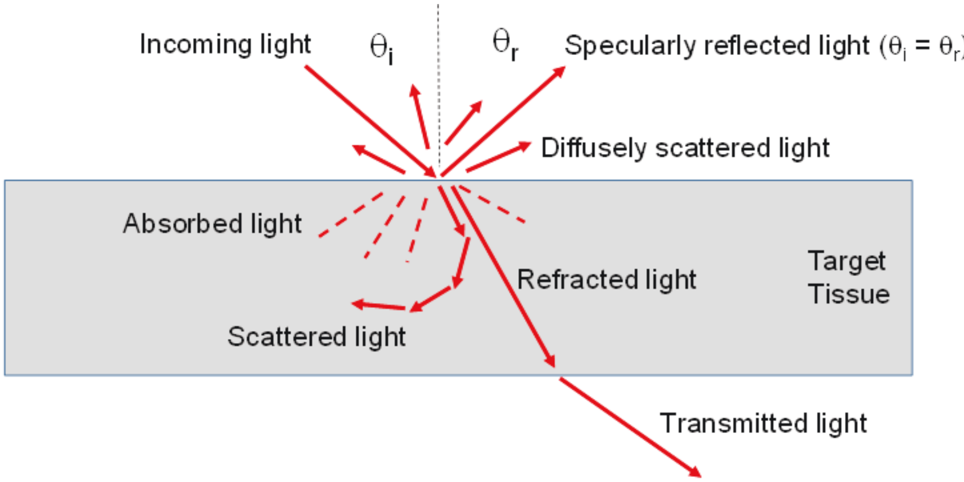


Figure 2. *Interaction of light on target tissue, showing reflected, refracted, absorbed, scattered, and transmitted light.*

Reflection can be categorized as *specular* if light is reflected from a smooth surface or *diffuse* for light scattered from a rough surface. In specular reflection, the angle of incidence is equal to the angle of reflection, while in diffuse reflection, light rays are reflected in multiple directions. This section will focus on light traveling inside the tissue in terms of both light *absorption* and *scattering*.

The optical properties of any tissue for a specific wavelength (λ) can be completely described by four parameters: *refractive index (n)*, *absorption coefficient (μ_a)*, *scattering coefficient (μ_s)*, and *anisotropy factor (g)*, or direction of scattering. If these values are all known, then it is possible to predict how deep light will travel through tissue. If the laser wavelength is changed, then these parameters will also change. Let's describe each of these parameters in more detail.

The *refractive index*, n, is defined as the ratio of the speed of light in a vacuum, c, given by 3 x 10^8 m/s, divided by the speed of light in a medium or tissue, v (Equation 1).

$$(1) \qquad n = c / v$$

The refractive indices of materials will be used to determine how much light is lost due to Fresnel reflection at the interface between two different media, as well as the refraction of light through an interface between two media, as described later.

The *absorption coefficient*, μ_a, is related to the probability that a photon (packet of light) is absorbed in the tissue per a unit path length (with units of cm^{-1}). A higher value for the absorption coefficient means that the photon has a higher probability of being absorbed over a shorter distance in the tissue, while a lower value means the opposite – that the photons will travel deeper into the tissue before being absorbed. Once the photon is absorbed, it disappears and its energy is converted into heat (a temperature rise in tissue) for therapy (for example, thermal coagulation - "cooking" of tissue or ablation – "vaporization" of tissue). The photon could alternatively be re-emitted at a different wavelength (color) which is described as fluorescence and may be used for diagnostic applications.

It is important to note that the absorption coefficient (and penetration depth of light) in tissue is strongly dependent on the wavelength (λ) of light used as well as major tissue components, such as proteins, hemoglobin, melanin, and water (Figure 3). For example, in the ultraviolet spectrum (λ < 400 nm), both absorption and scattering are very high, and hence light has shallow penetration in tissue (1-100 nm). In the blue (roughly 400-500 nm) and green (roughly 500-600 nm) parts of the visible spectrum, light is selectively absorbed by hemoglobin (blood), so light penetration is also relatively short (50-800 nm). In the red (roughly 600-700 nm) and near-IR (700-1300) part of the spectrum, referred to as the "optical window", protein, blood, and water absorption are all relatively low, so light penetrates the deepest (1-5 mm), but its penetration is ultimately limited by multiple scattering in opaque tissues (most tissues except for the eye). Intuitively, we know that water absorption must be low in the visible spectrum because we can see through the atmosphere or while swimming underwater. In the infrared spectrum, there are several major water absorption peaks in tissue (at 1440, 1940, and 2940 nm), which result in strong light absorption and correspondingly shallow penetration.

If the goal is to thermally coagulate tissue for removal of a tumor or abnormal growth, then operating in the "optical window" at near-IR laser wavelengths between 800-1300 nm provides the deepest heating and treatment volume. For precise laser tissue vaporization, an UV wavelength (e.g. 193 nm for corneal surgery) or mid-IR wavelength (2790 nm for vaporization of dental caries, tooth decay or cavities) is chosen.

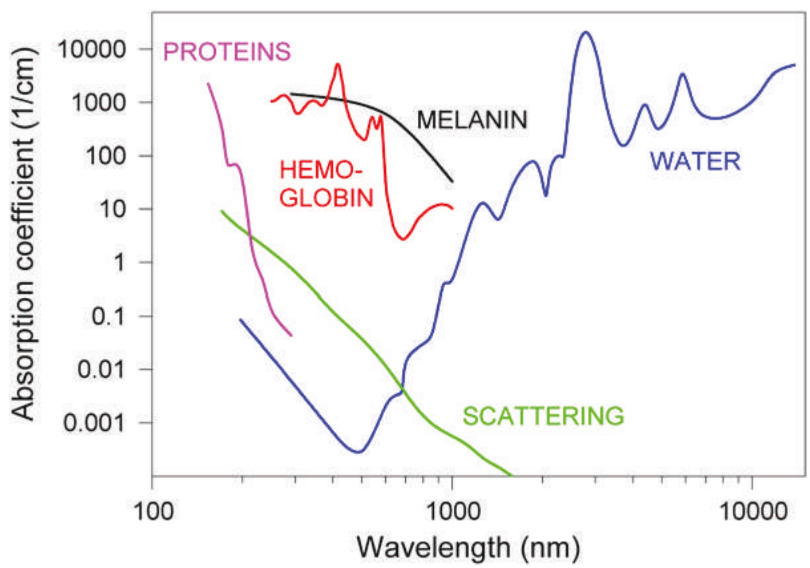


Figure 3. *Absorption coefficient values plotted on the vertical axis, as a function of laser wavelength, for several common components in soft tissues, including proteins, melanin, hemoglobin (blood), and water.*

Much of laser medicine involves choosing a laser wavelength that is either highly absorbed by a major tissue "chromophore" (e.g. water or blood), or avoiding these absorption peaks for deep penetration. Water typically makes up about 60-80% of all soft tissues and 10-30% of all hard tissues, and so it is a major component in all tissues in the body and absorbs very strongly in the UV and mid-IR spectrum.

Oxygenated and deoxygenated hemoglobin (blood) are also major absorbers of light in the visible spectrum. Vascular tissues have about 2% blood content which can increase to 5-10% for inflamed tissues, so blood absorption can also dominate laser-tissue interactions in the blue (400's nm) and green (500's nm) parts of the visible spectrum.

The *scattering coefficient*, μ_s, is related to the probability that a photon is scattered in tissue per a unit path length. A higher value for the scattering coefficient means that the photon has a higher probability of being scattered over a shorter distance in the tissue, while a lower value means the opposite – that the photons will travel deeper into the tissue before experiencing a scattering event.

Scattering in tissues originates from light interaction with biological structures, which range from cell membranes (roughly 10 nm) to whole cells (roughly 10 μm). Light is strongly scattered when the size of the biological structure matches the laser wavelength, and when the refractive index of the biological structure does not match the surrounding medium. Cell mitochondria and nuclei are on the order of 0.5 – 5 μm, and so they strongly scatter visible (0.4 – 0.7 μm) and IR light (> 0.7 μm). Multiple scattering of light ultimately limits the penetration depth of light in tissues, not absorption. Although light scattering decreases at longer laser wavelengths, increasing light absorption due to water dominates and light penetration depth is therefore still limited (Figure 3).

The *total attenuation coefficient* is the sum of the absorption and scattering coefficients. While the absorption and scattering coefficients do not have any inherent physical meaning, it is useful to think of their inverse values (units of cm), which correspond to the *mean free path* or distance that a photon is likely to travel before undergoing either an absorption or scattering event.

When a photon experiences a scattering event, it is important to know in what direction the photon is likely to be scattered. This property is quantified by the *anisotropy factor*, or direction of scattering, given by the symbol, g. The value of g is based on a cosine trigonometric function, and hence theoretically can have any value between $-1 \leq g \leq 1$. A value of -1 is interpreted as the photon being back-scattered towards where it originally came from. A value of 0 refers to isotropic scattering, meaning that the photon has an equal probability of being scattered in any direction (think of light being emitted equally in all directions from a light bulb). A value of +1 means that the photon continues exactly in the forward direction after being scattered, without any change in its route of travel (as if the photon was never scattered in the first place!). Most tissues have a high positive g value, around 0.9, meaning that the photons continue in a narrow cone in the forward direction.

The *reduced scattering coefficient*, μ_s', takes into account the scattering coefficient and anisotropy factor, g, to provide a more accurate description of the overall effect of a light scattering event. If a photon is scattered but continues to travel in the forward direction, the net effect of the scattering event is limited, and the photon appears to continue roughly along its current path. In such a case, μ_s' would be a much lower value than μ_s. The reduced scattering coefficient is given by the formula (Equation 2),

$$(2) \qquad \mu_s' = \mu_s (1-g)$$

The amount of light *reflected* off of the tissue surface can be quantified by the *albedo*. Lighter skin has a higher albedo because it reflects a higher percentage of the light, while darker skin has a lower albedo because it absorbs a higher percentage of light. Albedo (a) is calculated using the formula (Equation 3):

$$(3) \qquad a = \mu_s / (\mu_a + \mu_s)$$

Throughout the visible spectrum there are also appreciable differences in the amount of light reflected, depending on the pigmentation level of the skin. This means that, for a KTP (green) or ruby (red) laser, more light will be reflected from the skin of a fair-skinned person than from a darker-skinned person (Figure 4). Note that in the near-infrared spectrum (IR), the three curves come together. In the mid-infrared spectrum and beyond, the reflectance drops to a low value and is not strongly dependent on the pigmentation level of skin. Therefore, for the Er:YAG laser at 2940 nm or the CO_2 laser at 10,600 nm, very little radiation will be reflected, regardless of the pigmentation. This means that absorption can be high. The reflectance value is important because reflected light is lost and is not available for coagulation or vaporization of the tissue. For example, with a ruby laser incident on a fair-skinned person, 0.6 or 60% of the incident energy may be reflected. However, exposure to sufficiently high concentrations of laser energy will damage exposed tissue. Once tissue has been damaged, its characteristics are altered, and this alteration can significantly affect the ratios of reflected, absorbed, and transmitted energy.

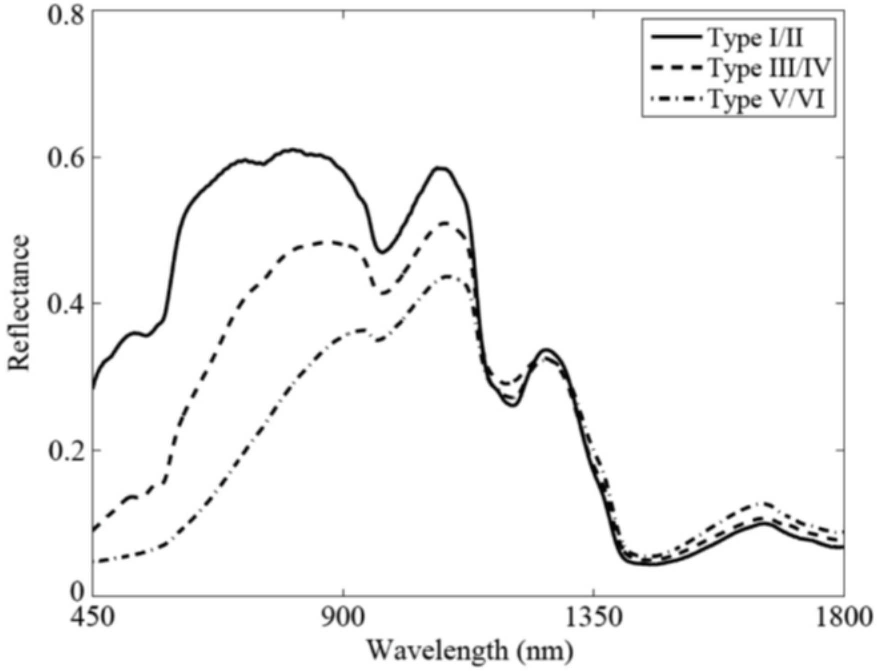


Figure 4. Reflectance of skin as a function of both wavelength and skin type. The skin types I/II are fairest, types III/IV are moderately darker, and types V/VI are the darkest or most heavily pigmented. The visible region (VIS) extends from 400 – 700 nm.

Transmitted light tends to scatter multiple times as it passes through tissue. It eventually penetrates into the surrounding tissue where it is absorbed. If enough laser energy is absorbed in the adjacent tissues, it can cause undesirable *collateral thermal damage*. Choosing the correct wavelength, where light is selectively absorbed by the target tissue, but not surrounding tissue, as well as delivering the laser energy in a pulsed mode, sufficiently short to prevent thermal conduction of the heat to surrounding tissues during the laser pulse, will minimize collateral thermal damage. Many cosmetic dermatology applications (e.g. removal of wrinkles, hair, port-wine stains, and tattoos) as well as other laser ablation procedures (e.g. LASIK eye surgery and dentistry) exploit pulsed lasers for selective laser surgery.

In certain cases, a laser wavelength may be selected so that it will transmit through surface tissues to reach underlying target tissues, where it will be absorbed. Lightly pigmented tissues will reflect or transmit visible and near-visible wavelengths that heavily pigmented tissues would absorb. Since hemoglobin and oxyhemoglobin appear as red, they will tend to reflect red light and absorb its complement, green light. For this reason, in the past, lasers emitting green wavelengths were often used to treat vascular lesions such as port wine stains. The energy is transmitted through the skin to the underlying lesion where it is absorbed by the hemoglobin, thereby destroying the vascular structure that makes up the lesion. While this is easily accomplished on a fair-skinned person, it becomes more complicated as the concentration of melanin in the skin increases. Melanin and hemoglobin have similar absorption (Figure 3). Depending on the laser wavelength being applied, the energy may be absorbed in the skin's melanin before it reaches the lesion. This can lead to a bleaching effect over the treated area. Today, newer vascular lasers operate in the near IR at 755 nm.

The total attenuation (or loss) of light in tissue is given by adding the effects of both absorption and scattering. The *effective attenuation coefficient*, μ_{eff}, is given by the formula (Equation 4):

$$(4) \qquad \mu_{eff} = [3\mu_a (\mu_a + \mu_s')]^{1/2}$$

Again, this value does not have any physical meaning. However, the *optical penetration depth*, δ, or the value for the depth that the light penetrates through tissue before the irradiance drops to 1/e, or 37% of its initial value, does have physical meaning, and is given by the inverse of μ_{eff}, or (Equation 5),

$$(5) \qquad \delta = 1 / \mu_{eff}$$

where, δ, assumes use of a “wide” collimated laser beam or large laser spot diameter (about 4 mm or greater). The optical penetration depth is an important value. For example, as mentioned earlier, laser medicine applications requiring precise vaporization of tissue typically use UV or mid-IR wavelengths which are strongly absorbed by water and/or proteins in the tissue, so the optical penetration depth is small. Near-IR wavelengths are used for deep volumetric heating and thermal coagulation of tumors and benign growths because the optical penetration depth is large. Figure 5 provides estimates of the optical penetration depth in generic vascular soft tissues for some common medical lasers.

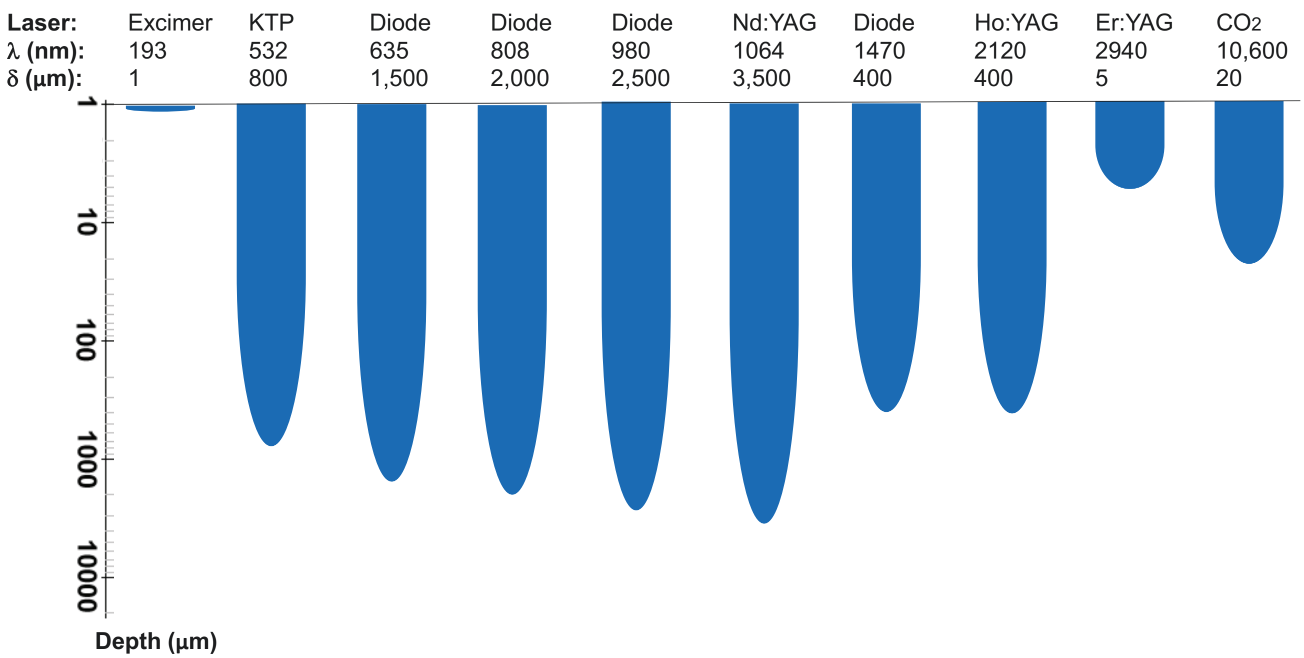


Figure 5. *Optical penetration depth (δ), plotted on a logarithmic scale in micrometers, for some common laser wavelengths (λ) used in medicine*.

The irradiance (I) of a circular laser beam is given by power (P) divided by laser spot area (A). The area can be calculated as $A = \pi r^2$, where r is the radius of the laser spot (Equation 6):

$$(6) \qquad I = P / A = P / \pi r^2$$

The spot diameter is sometimes measured using a full width half maximum (FWHM) or 50% value, or more commonly the $1/e^2$ or 13.5% value from the peak (where e = 2.7).

Irradiance is dependent on power and laser spot size. Low irradiance laser settings can be used for low-level laser therapy (LLLT) such as laser acupuncture, accelerated wound healing, and infrared nerve stimulation. Medium irradiance settings can be used for thermal coagulation of tissue for removal of tumors, benign growths, retinal photocoagulation, removal of vascular birthmarks, and endovenous therapy. High irradiance settings are used for ablation of tissues in applications such as LASIK eye surgery, removal of dental caries, removal of tattoos, and fragmentation of kidney stones.

An obvious way to change irradiance is to change the laser power setting. However, surgeons also frequently keep laser power fixed, but vary laser spot size instead, by changing the working distance between the optical fiber tip and the target tissue, since the light is diverging in a cone as it exits the distal fiber tip. A short working distance increases irradiance and provides higher temperatures for tissue vaporization, while a longer working distance decreases irradiance, yielding lower tissue temperatures for thermal coagulation of tissue.

The irradiance of light at a specific depth in tissue, or through a tissue layer thickness, can be calculated using a simple formula. *Beer's Law* states that the light irradiance decays at an exponential rate in a medium, based on the tissue depth (x) and the total attenuation coefficient, which is in turn dependent on both the absorption and scattering coefficients. For the UV (< 400 nm) and mid-IR (> 1900 nm) spectrum, absorption dominates scattering ($\mu_a >> \mu_s$), and so scattering can be neglected, and Beer's Law provides an accurate measurement of light irradiance with tissue depth (Equation 7):

$$(7) \qquad I = I_0 \exp(-\mu_a x),$$

where I (W/cm^2) is final irradiance, I_0 (W/cm^2) is initial irradiance, μ_a is absorption coefficient (cm^{-1}), and x is tissue depth (cm).

If Beer's Law is re-written in terms of I / I_0, then this ratio is defined as the fraction of collimated light which is transmitted through the tissue at a given depth. If the value is multiplied by 100, then a percentage of *transmitted* light is obtained (Equation 8):

$$(8) \qquad T = I / I_0 = \exp(-\mu_a x) \times 100\%$$

There is a large matrix of laser parameters, as shown in Table 2. For a specific medical laser application, only a handful of these parameters may be relevant. Typically, the wavelength is the most important parameter because all of the tissue optical properties are dependent on wavelength. The pulse energy, power, pulse duration, pulse repetition rate, spot size, and irradiation time are also typically considered.

Table 2. Summary of important laser parameters

Parameter	Units	Definition
Wavelength (λ)	nanometers (nm)	indicates the color of light
Pulse Energy (E)	Joules (J)	energy in a single laser pulse
Average Power (P_{ave})	Watts (W)	amount of energy over 1 s time period
Peak Power (P_{peak})	Watts (W)	energy divided by pulse duration
Spot Size (d)	millimeters (mm)	diameter of laser spot
Radiant Exposure (F)	J/cm^2	energy density
Fluence	J/cm^2	total energy deposited in a spot area
Spatial Beam Profile	None	shape of single laser pulse in space
Irradiance (I)	W/cm^2	power density
Pulse Duration (t)	seconds (s)	length of single laser pulse in time
Pulse Repetition Rate (R)	Hertz (Hz) or 1/s	number of laser pulses delivered in 1 s
Temporal Beam Profile	None	shape of laser pulse in time
Duty Cycle	None	ratio laser is "on" divided by period
Irradiation Time	seconds (s)	total time that laser is on

Lasers may be operated in continuous-wave (CW) or pulsed mode. In CW mode, laser power, average power, and peak power are all equivalent. However, when a laser is operated in pulsed mode, average and peak power can be very different. The *average power* refers to amount of energy delivered over a 1 s time period and can be calculated by multiplying pulse energy, E, in Joules, times pulse repetition rate, R, in Hertz (Equation 9):

$$(9) \qquad P_{ave} = E \times R$$

The *peak power* refers to energy (J) contained in a single pulse divided by the duration of the pulse (s):

$$(10) \qquad P_{peak} = E / t$$

As Figure 6 shows, although the average power may be low, the peak power can be extremely high, since lasers are capable of emitting light with extremely short pulse durations, as short as femtoseconds (10^{-15} s).

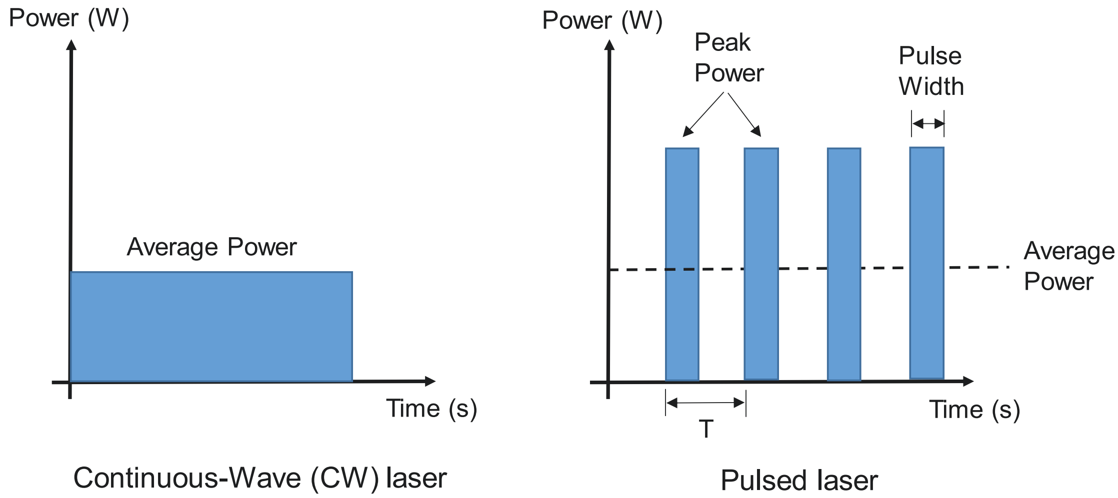


Figure 6. *Comparison of continuous-wave (CW) and pulsed operation modes for lasers.*

When a laser is operated in pulsed mode, the time duration of the laser pulses may vary considerably depending on the specific laser system and mode of operation (Table 3).

Table 3. Laser Modes of Operation

Mode	Pulse Length	Time Period
Continuous-wave (CW)	always on	seconds (s)
Modulated, chopped, or gated	milliseconds	10^{-3} s
Long-pulse (free-running)	microseconds	10^{-6} s
Short-pulse (Q-switched)	nanoseconds	10^{-9} s
Ultrashort-pulse (mode-locked)	picoseconds-femtoseconds	10^{-12} s - 10^{-15} s

When a laser is operated at a wavelength in which photons are not highly absorbed, then multiple light scattering dominates ($\mu_s >> \mu_a$). This is typical for wavelengths of 600 – 1300 nm, in the red to near-IR spectrum, referred to as the “optical window”. For this regime, the laser spot diameter is important in determining the intensity of light at a given depth in tissue. For example, the light intensity of a pencil thin beam decays much more rapidly in tissue than for a wide beam, due to higher losses from light scattering along the periphery of the laser beam. This can be observed by taking the ratio of the volume to surface area of a cylindrical shaped beam ($V = \pi r2l$ and $A = 2\pi rl$), which scales roughly as the radius of the beam. Thus, a larger beam radius (or diameter) has proportionally less surface area exposed at which photons can be scattered in the tissue and lost from the central part of the beam. The implications are widespread. For example, cosmetic laser applications (e.g. tattoo removal, skin resurfacing, hair removal, and treatment of vascular birthmarks) use a large diameter beam to provide more uniform delivery of light to the target depth.

The laser beam shape in space, or *spatial beam profile*, is also important, because it shows how uniformly the laser power is distributed. Single-mode laser beams produce a Gaussian shaped beam profile that can be focused down to a smaller spot for coupling of higher laser power into smaller optical fibers, for surgery. Multimode beams are non-uniform and cannot be focused to as small a spot.

The laser beam shape in time, or *temporal beam profile*, characterizes how energy is distributed during a single laser pulse. Flashlamp-pumped, solid-state lasers (e.g. Ho:YAG and Er:YAG), as well as CO_2 lasers, typically produce a “front-loaded” temporal beam profile, characterized by an initial spike, followed by a decay in intensity. Diode lasers and diode-pumped lasers typically produce a flat-top temporal beam profile where the laser energy is more uniformly distributed over the duration of the pulse.

2.2 Laser-Tissue Interaction Mechanisms

There are several major mechanisms of laser-tissue interactions. These interactions are usually categorized based on the laser power density or irradiance and the exposure time (Figure 7 and Table 4).

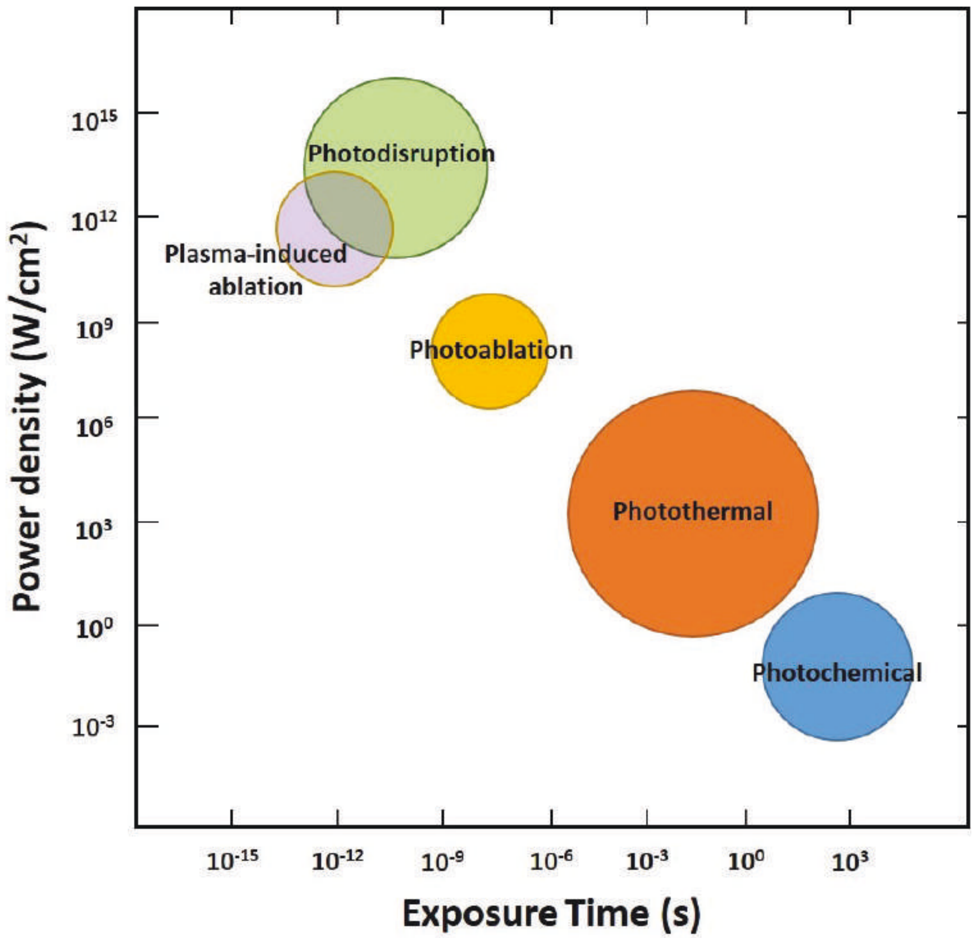


Figure 7. *Major laser-tissue interaction mechanisms.*

Photodisruption or photomechanical ablation refers to mechanical effects that occur in tissues at very high irradiances ($10^{11} – 10^{16}$ W/cm^2) and at short pulse durations (100 fs – 100 ns). Plasma sparking, generation of shockwaves, cavitation, and jet formation are typically observed in tissues. Soft tissues are cut by mechanical forces resulting in tissue holes or poration, tearing, and rough or serrated edges. Hard tissues may experience crack formation and fragmentation into pieces. There are only a few clinical laser applications utilizing a photomechanical mechanism of tissue ablation, including fragmentation of opacified or clouded lenses during removal of cataracts in ophthalmology and short-pulse laser fragmentation of kidney stones in urology.

Plasma-induced ablation refers to the use of very high irradiances ($10^{11} – 10^{13}$ W/cm^2) typically delivered in laser pulses at the picosecond or femtosecond time scales ($10^{-10} – 10^{-13}$ s) in tissue. These high irradiances and electric field strengths produce dielectric or optical breakdown of the tissue at the atomic scale, stripping electrons off of the atoms, and creating an "ion soup" or plasma in the local tissue volume. Typically, laser beams from ultrashort pulse lasers are focused down inside of tissue to produce irradiances capable of plasma formation. A unique characteristic is that the plasma may have a much higher absorption coefficient than the normal tissue, allowing non-invasive and precise tissue ablation of otherwise transparent, non-absorbing tissue structures such as the cornea or lens, in ophthalmic applications. Plasma generation and absorption is independent of the laser wavelength chosen, unlike photothermal ablation. Overall, advantages of plasma-induced ablation in laser surgery include ultra-precise vaporization of small amounts of tissues with minimal collateral thermal and mechanical damage. Disadvantages include the high cost of the short-pulse picosecond or femtosecond laser system, a very slow ablation rate preventing removal of tissues in bulk quantity, and the lack of an optical fiber delivery system that can deliver such high peak powers.

Photoablation refers to the use of high-energy (short-wavelength) photons delivered at high irradiances (10^7 – 10^9 W/cm^2) and short pulses (10-100 ns) for directly breaking chemical bonds in tissue and providing precise tissue ablation. Short, ultraviolet wavelengths (< 400 nm), such as the Excimer laser at 193 nm, produce high-energy photons sufficient for breaking carbon-carbon molecular bonds, and the short pulse length on the scale of nanoseconds (10^{-9} s) also allows tissue ablation (vaporization). The only major clinical application of photoablation is Excimer laser corneal shaping for vision correction utilized during ophthalmic procedures. However, the role of photoablation in corneal shaping is controversial, since high protein absorption as well as high light scattering in the deep UV spectrum at such short wavelengths yields precise tissue ablation through a photothermal contribution as well.

Photothermal interactions with tissue usually occur for laser irradiances of less than 1 x 10^6 W/cm^2 (1 MW/cm^2) and on time scales greater than 1 μs (1 x 10^{-6} s). This process involves absorption of photons with transformation of optical energy into thermal energy, or heat. The temperature of tissue rises above about 60 ^{o}C for thermal denaturation of proteins, resulting in tissue coagulation and necrosis, which is desirable for destroying cancerous tumors and benign growths, as well as stopping bleeding through hemostasis. As temperatures rise above 100 ^{o}C, tissue melting, carbonization, and vaporization occurs. Several hundred degrees Celsius is typically required for soft tissue ablation and several thousand degrees Celsius for hard tissue ablation. Tissue ablation is desirable for selective and precise vaporization and removal of diseased tissues without collateral heating and thermal damage to adjacent healthy tissues. The vast majority of therapeutic laser applications involve a photothermal mechanism. These specific applications are too numerous to name, but include applications in the medical fields of cosmetic dermatology, ophthalmology, gynecology, urology, dentistry, and neurosurgery.

Photochemical interactions with tissue usually occur at lower irradiances, below 1 W /cm^2, and on long time scales of minutes. In these applications, the light energy is transferred either to a photodynamic agent, known as a photosensitizer, or the tissue molecules directly, and serves as a catalyst for initiating a chemical reaction in the tissue. In photodynamic therapy (PDT), or light-based chemotherapy, red or near-infrared light matching the absorption peak of the photosensitizing agent (e.g. photofrin), results in the generation of either singlet oxygen or other reactive oxidizing species, which destroy abnormal tissues at the cellular level. The three components necessary are light, PDT drug, and oxygen. PDT has been FDA-approved for a number of clinical applications, including treatment of Barrett's esophageal cancer, late-stage lung cancer, benign skin diseases such as acne and psoriasis, as well as macular degeneration in ophthalmology. An advantage of PDT over conventional chemotherapy includes elimination of side-effects (such as fatigue, pain, nausea, hair loss, and mouth sores). Photochemical treatments also include direct application of UV laser wavelengths for treatment of skin disorders such as acne, psoriasis, fungis, and vitiligo. For example, Xenon Chloride Excimer lasers operating at a UV wavelength of 308 nm induce cell death during treatment of psoriasis.

Table 4. Summary of Laser-Tissue Interaction Mechanisms

Mechanism	**Intensity (W/cm^2)**	**Exposure Time (s)**	**Observations**	**Applications**
Photodisruption	10^{11} – 10^{16}	10^{-13} – 10^{-7}	fragments, tears, cracks	cataracts, kidney stones
Plasma-induced ablation	10^{11} – 10^{13}	10^{-10} – 10^{-13}	clean ablation, audible noise, blue plasma	corneal shaping (PRK/LASIK)
Photoablation	10^7 – 10^9	10^{-8} – 10^{-7}	clean ablation, direct breaking of chemical bonds	corneal shaping (PRK/LASIK)
Photothermal	< 10^6	> 10^{-6}	coagulation, melting, carbonization, vaporization	numerous soft and hard tissue applications
Photochemical	< 1	> 10	chemical reaction using UV light or red light and agent	chemotherapy, UV light for skin disorders

2.3 Time Constants

Thermal Time Constant and Principle of Selective Photothermolysis

The majority of successful therapeutic laser applications involve the use of pulsed lasers, in order to confine the laser-tissue interaction to the targeted absorber or chromophore in the tissue. For example, this could be an ink particle in a tattoo or the hemoglobin in an abnormal blood vessel of a port-wine stain vascular birthmark, which needs to be removed. In such cases, it is insufficient to choose the correct laser wavelength that is strongly absorbed by the tissue target. It is also necessary to operate the laser with a pulse duration shorter than the thermal time constant for the tissue, which is determined by both the optical and thermal properties of the tissue itself. If this is achieved, then optical energy that is converted into thermal energy through absorption of photons in the tissue, will be consumed by the target tissue, and will not have sufficient time to conduct out of the target tissue and cause undesirable collateral thermal damage to adjacent healthy tissue, which may otherwise lead to delayed wound healing and possibly scarring.

The thermal relaxation time, τ_{th}, is given by the formula (Equation 11),

$$(11) \qquad \tau_{th} = \delta^2 / 4\kappa$$

where τ_{th} is the calculated thermal time constant, in seconds, δ is penetration depth of light in targeted tissue structure (also usually equivalent to diameter or thickness of target), in cm, and κ is thermal diffusivity of tissue, in cm^2/s. For water-rich soft tissues, $\kappa = 1.5 \times 10^{-3}\ cm^2/s$ for water is a good approximation.

It is important to note that the light absorber and the target may not always be the same. For example, during port-wine stain therapy, a laser wavelength is chosen that is strongly absorbed by the hemoglobin, however, the goal is to destroy the blood vessel wall as well to collapse the vessel. Therefore, the value for δ would include both the lumen and wall thicknesses combined, in such a situation, so that the heat leaks out into the vessel wall, but no further.

If the thermal confinement criteria is satisfied, then,

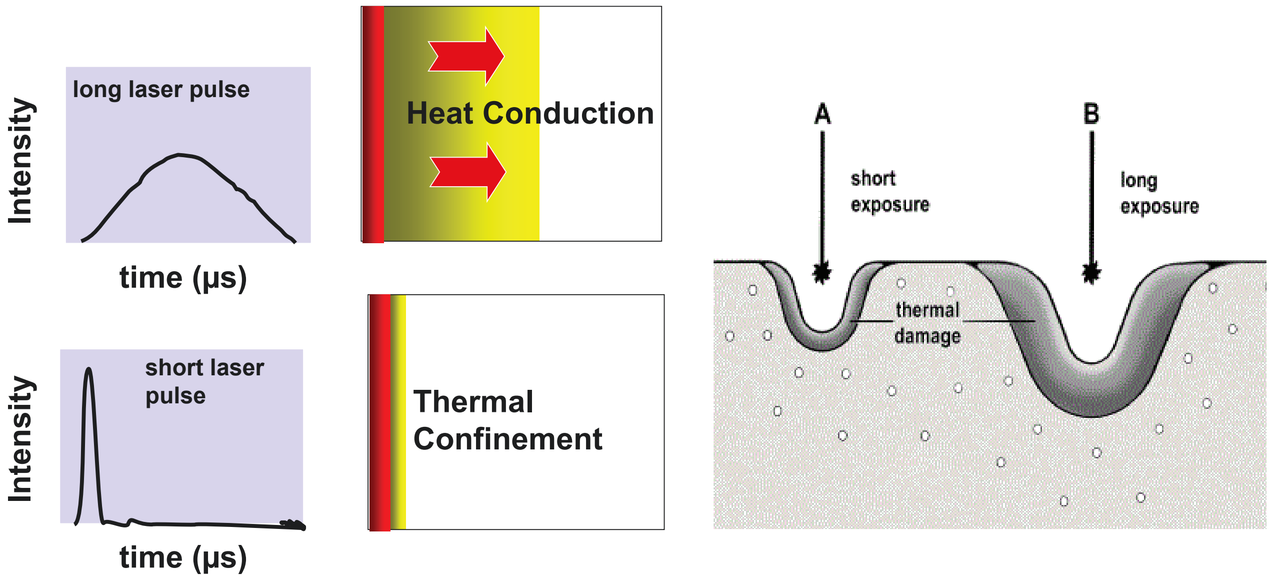
$$(12) \qquad t_p < \tau_{th}$$

where t_p is the chosen laser pulse duration, then the thermal energy is confined to the target area during the laser pulse, and the energy goes into either thermal coagulation or thermal ablation of the tissue component, rather than undesirable heat deposition and potential thermal damage in the adjacent tissue. Table 5 provides calculated thermal relaxation times for some common tissue structures.

Table 5. Thermal time constants for common laser targets

Tissue Target	Size	Thermal Relaxation Time (τ_{th})
Melanosome	1 μm	1.7 μs
Erythrocyte	10 μm	170 μs
Microvessel	100 μm	17 ms
Vessel	1 mm	1.7 s

Figure 8 provides a schematic representation of this effect for both short and long pulse lasers.



(a) (b)

Figure 8. *(a,b) Diagrams showing the difference in heat conduction between short laser pulses that are thermally confined in the tissue versus long laser pulses that are not thermally confined. Note that during photothermal tissue ablation, there is always at least a small residual zone of thermal damage.*

These formulas above (Equations 11 and 12) form the foundation of the ***Principle of Selective Photothermolysis***. If a laser wavelength is chosen that is strongly absorbed by a target tissue structure, but not the surrounding tissue, then delivery of a laser pulse shorter than the thermal relaxation time will result in light (*photo*) absorption, heating (*thermo*), and *selective* destruction (*lysis*) of the targeted tissue structure. This principle is used in the optimization of the laser parameters in many successful medical laser applications which utilize pulsed lasers, including removal of wrinkles, hair, port-wine stains, and tattoos.

Mechanical Time Constant

For very short laser pulses, typically less than a microsecond, mechanical effects in the tissue can also occur, due to a buildup in pressure in the targeted tissue structure during the laser pulse. The mechanical time constant, τ_m, describing this effect is calculated from the following formula (Equation 13):

$$(13) \qquad \tau_m = \delta / V_s$$

where V_s is the speed of sound in the tissue. For soft tissues, a good approximation is V_s = 1500 m/s, while for hard tissues, V_s = 4000 m/s. If the mechanical confinement criteria is satisfied, meaning that (Equation 14):

$$(14) \qquad t_p < \tau_m$$

then pressure builds up in the local region of the targeted tissue during the laser pulse.

There are only a few photomechanical applications in surgery. Short-pulsed (Q-switched) lasers with pulse durations of nanoseconds have been used for fragmentation of cataracts (opacified, clouded, and hardened lenses) in ophthalmology and kidney stones in urology. One limitation of using short-pulsed lasers is that the mechanical effects can cause undesirable tissue tearing in soft tissues and crack formation in hard tissues. For example, early in the development of dental lasers, Q-switched Er:YAG lasers were tested for ablation of caries, but they produced millimeter-long cracks across the entire tooth, instead of "precise" removal of tooth decay.

Some lasers can be operated in long-pulse (free-running) mode at hundreds of microseconds, or in short-pulse (Q-switched) mode in nanoseconds. In such cases, the optical penetration depth and laser pulse duration determine if the thermal and mechanical confinement criteria listed above are satisfied (Figure 9).

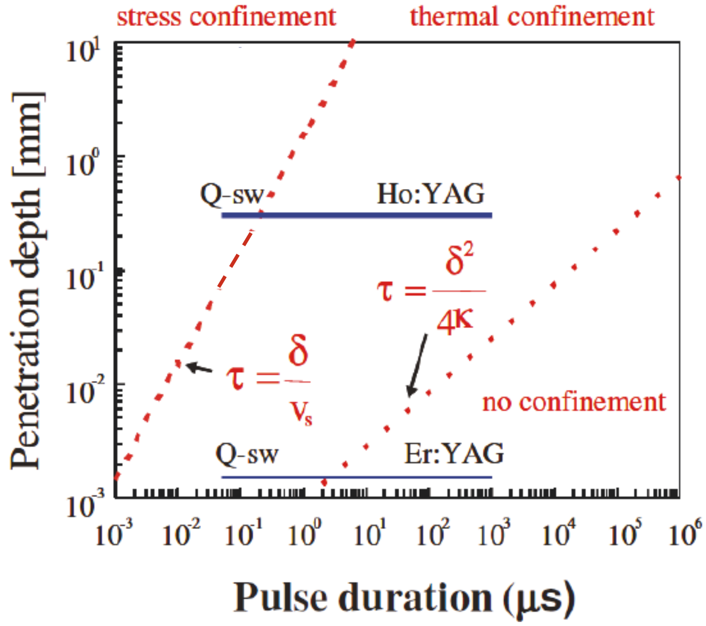


Figure 9. *Plot of mechanical (stress) and thermal confinement zones (dashed lines) as a function of optical penetration depth, which is related to wavelength, and operating mode (pulse duration). The Holmium:YAG and Erbium:YAG lasers, which can be operated in both long-pulse and q-switched mode, are provided as examples.*

If thermal confinement of the laser energy is achieved during pulsed laser delivery, then the maximum temperature reached during the laser pulse can be calculated, based on the formula (Equation 15)

$$T = T_0 + (\mu_a I_0 / \rho c)\, t = T_0 + (\mu_a F / \rho c) \qquad (15)$$

where T is the maximum temperature at the end of the laser pulse, T_0 is the initial tissue temperature (usually body temperature of approximately 37 °C, μ_a is the absorption coefficient of the tissue, I_0 is the irradiance (W/m^2), F is the radiant exposure (J/m^2), ρ is the tissue density (kg/m^3), c is the specific heat capacity (J / kg-°C), and t is the laser pulse duration. The radiant exposure is equal to the irradiance multiplied by time ($F = I_0 t$).

2.4 Photothermal Laser Ablation

Pulsed Laser Tissue Ablation

In many medical laser applications, the goal is to perform precise and selective vaporization and removal of diseased or abnormal tissue, with minimal collateral thermal damage to surrounding healthy tissue, which may otherwise result in adverse effects such as delayed wound healing and scarring. In such cases, a pulsed laser is chosen. Based on some of the theory already discussed, the optimal parameters for precise and selective laser vaporization of tissue are summarized below:

(1) The laser *wavelength* (λ) should be strongly absorbed by the target tissue (high μ_a), so the light does not penetrate deeply into surrounding tissue (low δ).

(2) The laser pulse energy density, or *radiant exposure*, should be well above the ablation threshold, to produce sufficiently high temperatures for tissue vaporization [$T = T_0 + (\mu_a I_0 / \rho c)\, t$].

(3) The laser *pulse duration* should be shorter than the calculated thermal relaxation time ($t_p < \tau_{th}$). However, a very short laser pulse duration may cause mechanical effects (e.g. tissue tearing or cracking), and ultra-short pulses may produce a plasma, which slows down the ablation rates considerably.

(4) The laser *spatial beam profile* should be a flat-top, to provide uniform intensity across the laser spot, and prevent collateral thermal damage from the wings of the beam at lower temperatures.

(5) The laser *pulse repetition rate* should be sufficiently low to allow tissue cooling between laser pulses (and prevent thermal buildup). Alternatively, scanning or rastering of the laser beam across the tissue surface may produce a similar outcome.

Example 1
The CO_2 laser (λ = 10,600 nm) is used for soft tissue surgery. The optical penetration depth (δ) in soft tissues at this wavelength is about 20 µm. Using a CO_2 laser pulse energy of 1.0 mJ, pulse duration of 200 µs, and laser spot diameter of 500 µm, calculate the maximum tissue temperature after a single laser pulse. The maximum temperature can be calculated using the formula: $T = T_0 + (\mu_a F / \rho c)$.

Solution

First, we need to calculate absorption coefficient, μ_a, assuming that at λ = 10,600 nm, $\mu_a \gg \mu_s$. (This is a good assumption because we are operating in the mid-IR spectrum where water absorption is high and light scattering is low, due to the long wavelength).

$\mu_a \sim 1 / \delta = 1 / 20\ \mu m = 1 / (2 \times 10^{-5}\ m) = 5 \times 10^4\ m^{-1}$

Next, confirm that thermal confinement during the laser pulse is achieved (assume $\kappa = 1.5 \times 10^{-7}\ m^2/s$).

$\tau_{th} = \delta^2 / 4\kappa = (2 \times 10^{-5}\ m)^2 / 4(1.5 \times 10^{-7}\ m^2/s) = 6.7 \times 10^{-4}\ s = 670\ \mu s$.

Yes, thermal confinement ($t < \tau_{th}$) is achieved because 200 µs < 670 µs.

Next, calculate the energy density or radiant exposure (F):

$F = E / \pi r^2 = (1 \times 10^{-3}\ J) / [(3.14)\ (250 \times 10^{-6}\ m)^2] = 5.1 \times 10^3\ J/m^2$

Now, calculate T:

$T = T_0 + (\mu_a F / \rho c) = 37\ ^oC + [(5 \times 10^4\ m^{-1})\ (5.1 \times 10^3\ J/m^2)] / [(1 \times 10^3\ kg/m^3)\ (4.3 \times 10^3\ J / kg\text{-}^oC)]$

$T = 37\ ^oC + 59.3\ ^oC = 96.3\ ^oC$

Continuous-wave Laser Tissue Ablation

In some laser medical applications involving highly vascular tissues, it is necessary to both vaporize tissue and produce some collateral thermal heating and coagulation, for hemostasis, to prevent excessive blood loss from the patient during the procedure. Removal of sections of highly vascular organs (e.g. liver, kidney, and prostate) provides some examples of when continuous-wave (CW) laser vaporization of tissue is used, instead of pulsed laser operation. During CW laser ablation, the goal is to vaporize the diseased or abnormal tissue, and provide a small zone of thermal coagulation for hemostasis. The process of CW laser ablation follows several steps:

(1) The laser energy is absorbed and the tissue temperature rises above 100 ^oC.

(2) Tissue at the surface is vaporized and then cooled by natural convective cooling mechanism (e.g. air or water flow), while the subsurface tissue layers continue to rise in temperature.

(3) The increasing temperatures and vaporization of water in the subsurface tissues results in thermal expansion, with steam being vented from the subsurface tissue layers.

(4) Rapid dehydration and desiccation of the tissue occurs, followed by carbonization or charring of the tissue, as temperatures reach 300-400 ^oC.

(5) Tissue ablation (vaporization) and bulk tissue removal occurs.

Figures 10 and 11 summarize the different stages of soft tissue heating during photothermal applications.

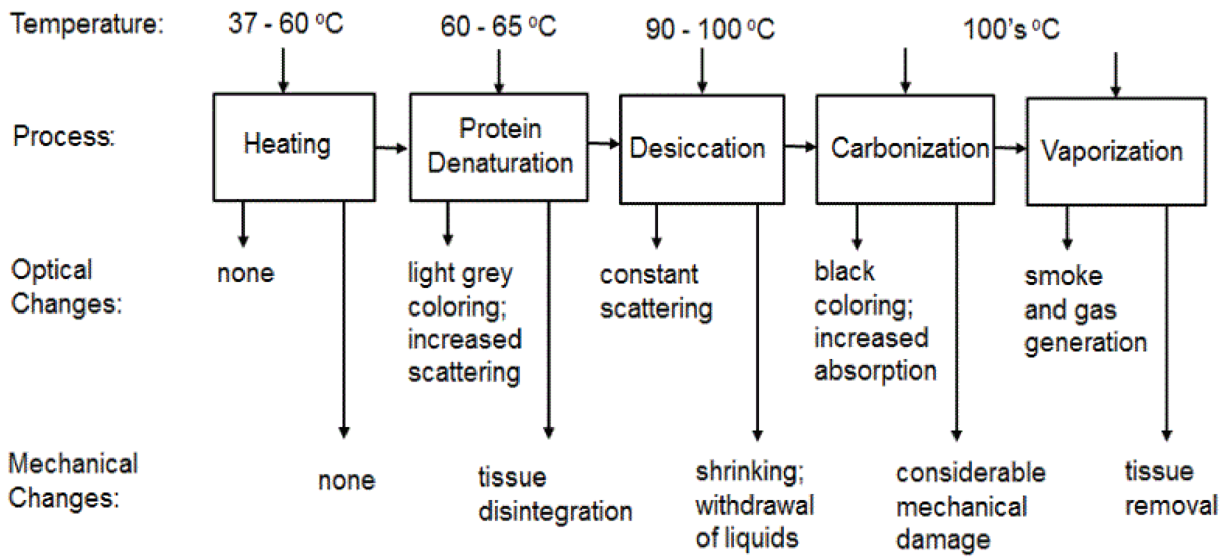


Figure 10. *Flow chart showing different stages of tissue transformation during photothermal applications.*

In surgical applications the goal is generally to destroy tissue. How that is accomplished depends on the wavelength used and how it is applied to the tissue. A major consideration when using lasers in a surgical application is the degree of collateral damage that results. With some wavelengths, the amount of transmitted light and its effect on underlying tissues is a concern. The interaction of laser radiation with tissue produces a thermal response. If the absorption of the thermal energy raises the tissue to a high enough temperature for a long enough time, cells will be destroyed. Normal body temperature is 37 °C (98.6 °F). Cell death should not occur even after six hours at 45 °C (113 °F). However, if the tissue temperature is raised to between 55 and 60 °C (130–140 °F), cell death can occur in as little as a few seconds. When underlying tissue is sufficiently heated by transmitted laser energy, it will be destroyed. As a result, a layer of necrotic (dead) tissue will remain after the targeted tissue has been destroyed. The depth of the dead tissue is called "the zone of thermal necrosis." The depth of this zone is a function of the wavelength and how it is applied. Which wavelength is chosen and how the energy will be applied often depends on the application.

It should be noted that while the initial development of new minimally invasive medical procedures commonly involves laser sources, frequently other energy-based devices replace lasers in the latter stages of product development, due in part to lower cost, ease of use, and/or improved eye safety. For example, for clinical applications requiring thermal coagulation of diseased or abnormal tissues, there are many alternative devices. These alternatives include electrocautery, electrosurgery utilizing both monopolar and bipolar radiofrequency devices, therapeutic ultrasound, microwaves, and even cryoblation for cooling tissues. However, for clinical applications requiring selective and precise ablation or vaporization of tissues (e.g. ophthalmology and dentistry), lasers continue to be most advantageous.

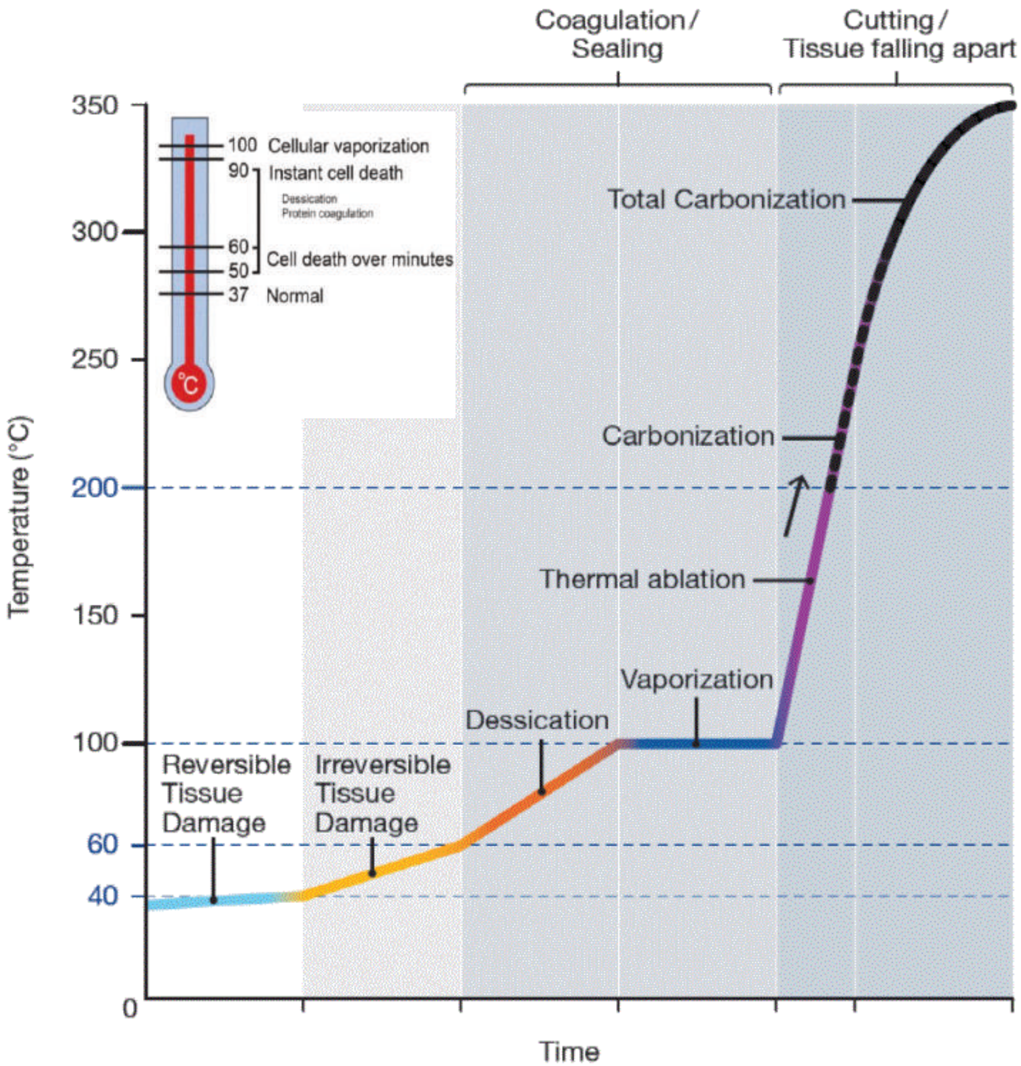


Figure 11. *Plot of tissue transformation as a function of temperature during photothermal applications.*

Example 2

The following lasers are used for tissue ablation. For each laser application listed below (given wavelength and pulse duration), name the primary mechanism (photothermal, photomechanical, or plasma-mediated) of tissue ablation and briefly explain how it works.

(a) Neodymium:YLF laser (λ = 1052 nm, t_p = 110 fs) for incision of corneal flap in LASIK.

(b) Erbium:YSGG laser (λ = 2790 nm, t_p = 300 μs) ablation of dental decay.

(c) Explain why continuous-wave (CW) laser tissue ablation may sometimes be used instead and provide one example of a clinical application.

Solution

(a) For precise incision of the cornea flap, a *plasma-mediated* ablation mechanism is used, as noted by the extremely short, femtosecond laser pulse, and the lack of a natural absorber in the cornea at 1052 nm. The laser beam is tightly focused, producing a sufficient intensity to create a plasma (ionized gas). The absorption coefficient of the plasma is greater than the normal tissue, and increases with pulse energy.

(b) This mid-IR, Er:YSGG laser wavelength utilizes a *photothermal* ablation mechanism, as noted by the long pulse duration. The laser wavelength is strongly absorbed by the water component in hard tissue. A water spray is used with the laser to further minimize collateral heating and to augment the tissue ablation rate. The goal is to selectively ablate the dental decay (caries tissue) while preventing the pulp from heating up. A germanium oxide optical fiber with sapphire tip is used clinically for delivering the laser energy to the tooth.

(c) In applications where it is desirable to both vaporize tissue and achieve sufficient collateral thermal damage for hemostasis to avoid blood loss, a high power continuous-wave laser is used for *photothermal* laser tissue ablation. One example is use of a 532 nm, frequency doubled Nd:YAG laser to couple into blood in the tissue, to vaporize the prostate gland for treatment of benign prostatic hyperplasia (BPH).

Self-Test

3. What part of the electromagnetic spectrum refers to the "optical window", in which light penetrates the deepest in tissue?
(a) Ultraviolet (b) Visible (c) Near-infrared (d) Mid-infrared

4. The approximate penetration depth of light in the "optical window" is approximately _____.
(a) 1 µm (b) 30 µm (c) 500 µm (d) 3 mm

5. In the "optical window", what tissue structure most strongly scatters light?
(a) Cell membrane (b) Cell nuclei (c) Extracellular fluid (d) Intracellular fluid

6. What tissue chromophore is the strongest absorber of light in the mid-infrared spectrum?
(a) Water (b) Collagen (c) Melanin (d) Hemoglobin

7. What skin type has the highest albedo?
(a) African (b) Mediteranean (c) White (d) Albino

8. What part of the electromagnetic spectrum is absorbed most strongly by blood or hemoglobin?
(a) Visible (b) Near-infrared (c) Mid-infrared (d) Far-infrared

9. Which laser wavelength is most strongly absorbed by soft tissues?
(a) Excimer, 193 nm (b) Diode laser, 808 nm (c) Ho:YAG, 2120 nm (d) CO_2, 10,600 nm

10. If the effective attenuation coefficient for a given tissue and laser wavelength is 1,000 cm^{-1}, then what is the optical penetration depth?
(a) 100 nm (b) 1 µm (c) 10 µm (d) 100 µm

11. If skin has a scattering coefficient of 200 cm^{-1} and an anisotropy factor of 0.9, then what is the value for the reduced scattering coefficient?
(a) 10 cm^{-1} (b) 20 cm^{-1} (c) 50 cm^{-1} (d) 100 cm^{-1}

12. If skin has an absorption coefficient of 200 cm^{-1} and an absorption coefficient of 0.5 cm^{-1}, then what is the albedo?
(a) 0.1 (b) 0.5 (c) 0.9 (d) 0.998

13. The intensity of light at a specific depth in tissue depends on what factor?
(a) Tissue depth (b) Absorption coefficient (c) Initial intensity (d) All of the above

14. Lasers are attractive light sources for tissue vaporization because they produce high _____.
(a) Peak powers (b) Average powers (c) Pulse repetition rates (d) Spot sizes

15. Q-switched mode of laser operation refers to delivery of laser pulse on what time scale?
(a) Milliseconds (b) Microseconds (c) Nanoseconds (d) Femtoseconds

16. Which laser-tissue interaction mechanism uses low power and long irradiation times?
(a) Photochemical (b) Photothermal (c) Photodisruption (d) Plasma-mediated

17. Which laser-tissue interaction mechanism is used for tissue coagulation and hemostasis?
(a) Photochemical (b) Photothermal (c) Photodisruption (d) Plasma-mediated

18. Photodynamic therapy uses which laser-tissue interaction mechanism?
(a) Photochemical (b) Photothermal (c) Photodisruption (d) Plasma-mediated

19. Which laser-tissue interaction mechanisms uses mechanical waves to break up tissue?
(a) Photochemical (b) Photothermal (c) Photodisruption (d) Plasma-mediated

20. Selective photothermolysis requires which of the following laser parameters?
(a) Highly absorbed wavelength and small laser spot size
(b) Highly absorbed wavelength and short pulse duration
(c) Small laser spot size and high pulse repetition rate
(d) Small laser spot size and uniform spatial beam profile

21. Why is it sometimes necessary to utilize selective photothermolysis to avoid heat conduction during the laser pulse?
(a) To provide sufficient hemostasis
(b) To minimize collateral thermal damage which can delay wound healing and lead to scarring
(c) To treat and destroy large volumes of tissue, for example a tumor or benign growth.
(d) All of the above

22. Which mode of operation provides the most precise laser tissue ablation?
(a) Pulsed (b) CW (c) Quasi-CW (d) It depends on other factors as well

23. Approximately what minimum temperature is needed to thermally coagulate tissues?
(a) 20 ºC (b) 37 ºC (c) 60 ºC (d) 100 ºC

3. Beam Delivery Methods

3.1 Introduction

To be useful in medical procedures, a laser beam must be delivered to a treatment site, which may be either outside or inside the body. There are four ways in which the beam of a medical laser is delivered to the body: (1) by direct output from the laser, (2) through an articulated arm, (3) through a fiber optic delivery system, or (4) through a hollow waveguide.

3.2 Free beam delivery

This is the least complicated way to deliver a beam. A laser is simply aimed at the treatment site. Optics may be used to focus the beam at the desired area. This type of system is not useful where a high degree of accuracy is required. Small CO_2 lasers and diode lasers can be used in this way. This method is mostly used in dermatology, dentistry, and hair removal. A particular drawback of this technique is the lack of a visible aiming beam. The position of the affected area must be approximated.

3.3 Articulated arms

An articulated arm consists of a series of tubes that are joined by a number of precision bearings (Figure 12) that allow the arm to move in three dimensions. At each of these bearings, front surface mirrors with multiple reflection coatings are positioned such that the beam is carried from the laser to the treatment site. At the end of the flexible arm is a focusing device. These arms are made out of aluminum alloys or carbon-fiber-reinforced composites. The weight of the arms is compensated by counterweights or spring devices. These allow arms to be very flexible and easy for the surgeon to use.

The main problem with articulated arms is alignment. Some lasers (e.g. CO_2) operate at wavelengths that do not allow beam transmission through an optical fiber. Low-power visible lasers such as He-Ne and diode lasers are used for alignment. These lasers can guide the CO_2 beam to the target spot by making them follow the same path. Most lasers with articulated arms come with alignment procedures provided by their manufacturers.

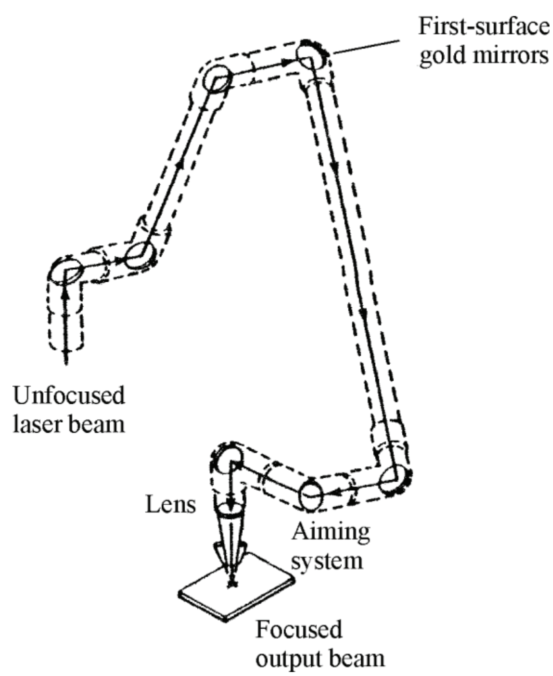


Figure 12. *A sketch of an articulated arm and its components.*

3.4 Fiber optic delivery systems

Optical fibers used for medical lasers typically have diameters ranging from 100-1000 µm. The optical fiber consists of a core, cladding, and a buffer or coating (Figure 13). The core transmits the energy. The cladding, with lower refractive index, enables total internal reflection. The coating or buffer is usually a tough plastic and acts as a cover to prevent damage to the fiber and allow bending of the fiber as well.

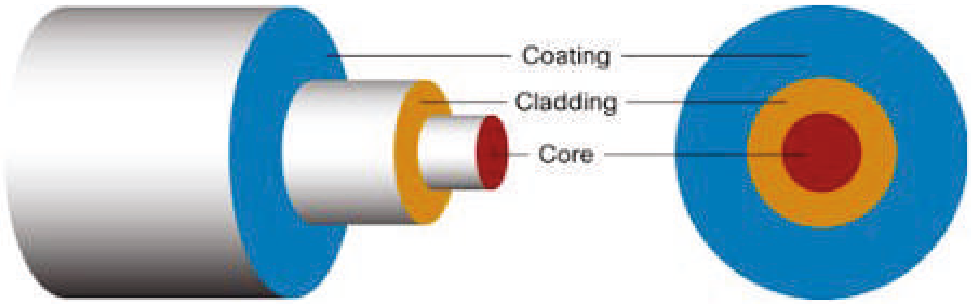


Figure 13. *Components of an optical fiber.*

Fiber optic probes used in medical applications use both straight and flexible fibers (Figure 14). In flexible fibers, the fiber is used to deliver energy to cut, coagulate, or ablate the tissue.

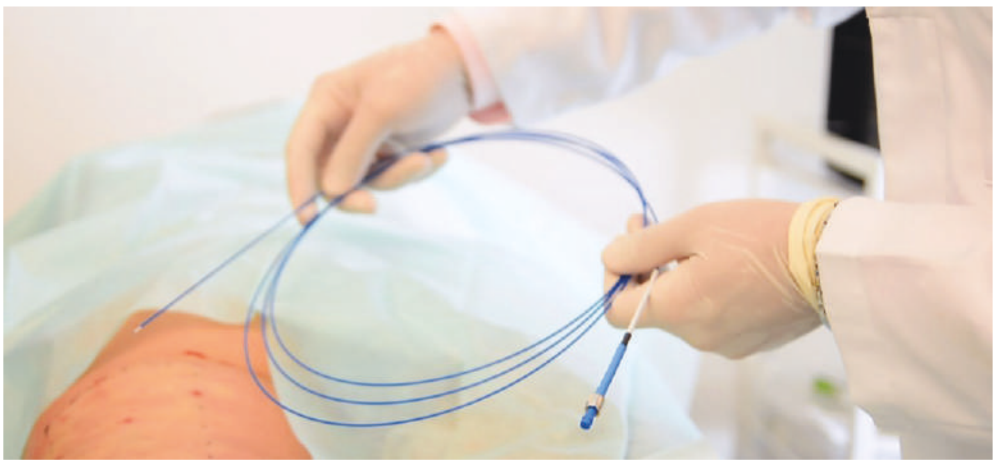


Figure 14. *Optical fibers enable flexible delivery systems.*

The fiber cladding material is selected so that it has a lower index of refraction than the core. Total internal reflection (TIR) is a function of the difference between the higher index of refraction of the core material and lower index of refraction of the cladding material. The difference in the indices of refraction creates a mirror-like surface at the core-cladding interface. At this interface, a light ray is incident at an angle θ. If θ is greater than a certain *critical angle,* θ_{crit}, *all of the incident light* is reflected back into the fiber. This reflection obeys the ordinary law of reflection, with the reflected angle equaling the incident angle. If the incident angle θ is less than the critical angle θ_{crit}, the incident ray partially penetrates the interface in accordance with Snell's law, thereby losing photons into the cladding.

The critical angle can be derived from Snell's Law of refraction ($n_1 \sin\theta_1 = n_2 \sin\theta_2$), for the case when the refracted angle, $\theta_2 = 90°$, corresponding to light rays being reflected at the core/cladding interface, instead of being refracted. Substituting $\theta_2 = 90°$ results in $\sin 90° = 1$, and then solving for θ_1 yields the definition for the critical angle. In this formula, for the specific case of optical fibers, θ_1 is renamed θ_{crit}, n_1 becomes the n_{core}, and n_2 becomes the n_{clad} (Equation 16):

$$(16) \qquad \theta_{crit} = \sin^{-1}(n_{clad} / n_{core})$$

Again, light rays traveling inside the core of the optical fiber and incident on the core-cladding interface at angles greater than the critical angle (glancing to surface) will continue to be totally internally reflected, while light rays incident at a smaller angle (steeper to surface) will not be reflected, but instead will be refracted through the interface and lost into the cladding.

Note that total internal reflection (TIR) of the light can only occur if the core material has a higher refractive index than the cladding material ($n_{core} > n_{clad}$), the primary condition for TIR.

Severe bending of the fiber will change the angle of incidence and can affect the amount of power lost. Also, the fiber material itself may result in attenuation due to both absorption and scattering losses in the glass. Losses in optical fibers are rated in *decibels per kilometer* (dB/km) in other fields such as telecommunications. Since most surgical fibers are only a few meters in length, this rating means little. The attenuation of light traveling down the fiber (dB) can be calculated from the following formula (Equation 17):

$$(17) \qquad A = -10 \log (P_{out} / P_{in})$$

Alternatively, if the attenuation (dB/m) of the material is known, then the fraction of power emitted through the fiber, or Transmission ($T = P_{out} / P_{in}$) , can also be calculated, by rearranging the equation (Equation 18):

$$(18) \qquad T = 10^{(-A/10)}$$

Losses due to reflection occur at the fiber ends, and reflections occurring at the air/core interface account for most of the normal losses. For example, Fresnel reflection losses at each fiber end can be calculated, if refractive indices of each medium are known for the interface (Equation 19):

$$(19) \qquad R = [(n_1 - n_2) / (n_1 + n_2)]^2$$

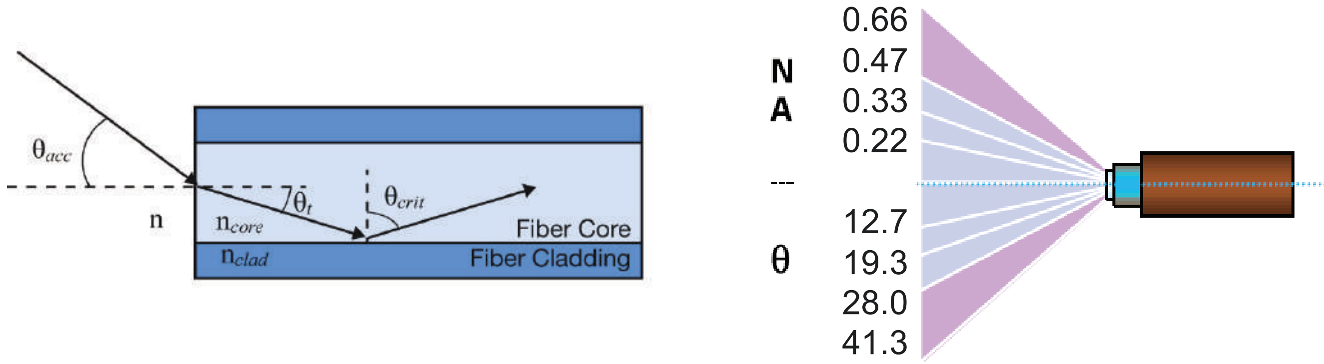
For an air-glass interface, $n_1 = 1$ and $n_2 = 1.45$, yielding reflection losses of 0.034 or 3.4%, at each of the proximal and distal fiber ends. Thus, 100% of the laser power can never be transmitted down an optical fiber even if absorption losses in the fiber are negligible. Note that the reflection losses change with laser wavelength used, since refractive index values for materials are dependent on wavelength.

There is also a phenomenon called cladding modes where light that leaks from the core becomes trapped between the core and buffer. In longer fibers this light usually leaks out of the cladding but in short surgical fibers it can be transmitted to the surgical site. This can sometimes be seen as a halo effect when viewing the transmitted energy.

Fiber optic core diameters can vary from a few micrometers to over a millimeter. Most surgical fibers are at the larger end of the scale (200-600 µm). The larger sizes are used for a number of reasons. Larger fibers, while more rigid, are also more robust and less likely to fracture when passed through a secondary device. Many fibers are used in contact with tissue and as such need to be fairly rigid. Also, most higher-power lasers have large-diameter beams. The fibers selected for use with a particular laser must be large enough to accept the spot size to which the beam can be focused and have a numerical aperture (NA), which determines the entrance "cone angle of acceptance." The entrance cone angle is shown as angle θ_{acc} in Figure 15. The minimum spot size to which a laser beam can be focused is a function of the wavelength and the angle of divergence of the unfocused beam. For the typical air medium between the laser and fiber, the numerical aperture (NA) is given by (Equation 20):

$$(20) \qquad NA = \sin\theta_{acc} = (n_{core}^2 - n_{clad}^2)^{1/2}$$

Changing the refractive index of the core or cladding is achieved by doping the glass. Typical NA values for medical optical fibers range from 0.22 – 0.66. A large value accepts a wide cone of light on the input end, but results in a wide cone of diverging light on the output end, which is important to consider when working in non-contact mode with a certain working distance and desired irradiance.



(a) (b)

Figure 15. *(a) The numerical aperture (NA) measures extent of acceptance cone of light for an optical fiber and is dependent on refractive indices of core and cladding materials. (b) Each NA value corresponds to the half angle (θ) of acceptance cone of light into the fiber.*

Once the laser energy has been transmitted through the fiber it can be used in two ways. It can be applied in either a *free-beam* or in *contact* mode. Using just the fiber in the free-beam mode, the energy can be directed onto the target tissue without making contact. The spot size applied to the tissue can be varied by adjusting the working distance from the fiber tip to the tissue. Varying the diameter of the spot size dramatically affects the irradiance, as we have already seen. Alternately, the light diverging from the fiber can be captured by a lens, or a series of lenses, to re-collimate or focus the light for use with a handpiece, microscope, slit lamp, or other secondary device.

In contact mode, the fiber itself or a special tip can be used in contact with tissue. The tip of a bare fiber can be used directly in contact with tissue for cutting or ablation. Or, a special sapphire or diamond tip can be attached to the ferrule of a jacketed fiber. In either case the tip will become coated with carbonized matter. Many tips are manufactured with a frosted or pre-carbonized surface. Generally, these tips are carbonized prior to use on a patient. The laser energy is absorbed by the carbonized matter, thereby heating the tip to a very high temperature. Once carbonized, very little of the laser wavelength escapes the tip or fiber to interact with the surrounding tissue. For this reason, when used in a contact mode, there is no appreciable difference in tissue effects between lasers of different wavelengths. There are a variety of special tip shapes available for contact applications including hemispherical, cylindrical, conical, flat and chisel shapes.

3.5 Hollow waveguides

A *hollow waveguide* is essentially a special case of the optical fiber. Used primarily with the CO_2 and Er:YAG lasers, a waveguide is basically a fiber without a core, or a core of air. Since the mid-IR wavelength of the CO_2 laser does not transmit through glass or other materials suitable for making a flexible fiber, one viable option is to use a flexible hollow tube with a reflective lining. These waveguides have fairly high losses compared to glass fibers and are limited in length—with most being under two meters. An air purge is used to help cool the waveguide, prevent damage to the coating, and prevent debris from collecting on and eventually clogging the surgical tip. Since the CO_2 laser is always used in a noncontact mode, this type of delivery system is never used in contact with tissue. The Er:YAG laser, using a hollow waveguide, may have a sapphire tip at the distal end to allow contact applications such as soft tissue cutting or cavity removal in dentistry.

3.6 Hand pieces

A hand piece is any handheld device that helps direct the beam to the treatment site. It can be as simple as a holder in which to place the end of an optical fiber or as sophisticated as a device consisting of a series of focusing and viewing mechanisms. Hand pieces are designed to be compatible with the laser wavelengths being used. In a simple hand piece, a fiber is held in a rigid tube; the fiber extends beyond the distal end and a clamping device is attached to the proximal end. This allows for adjustment of the fiber length. Hand pieces with short lengths are used in many surgical applications; those with long tips (200–400 mm) are used with rigid endoscopes and laparoscopes. More complex hand pieces contain a series of lenses for focusing the beam. Focusing a pulsed beam creates higher energy densities, which are useful in cutting and ablating tissue in noncontact situations. In the case of IR beams produced by CO_2 lasers, a single or double lens is used at the end of a hollow tube for focusing the beam. The size of the focused spot is adjusted by moving the hand piece closer to or further away from the target position. One of the main problems encountered when attempting to focus the beam is that the intense heat at the tissue surface generates a plume. This will reduce the intensity of the beam and must be removed by using a purge gas.

Self-Test

24. Which of the following components is <u>not</u> part of an articulated arm?
(a) Hollow tubes (b) Joints (c) Angled mirrors (d) Optical fibers

25. What primary advantage does an optical fiber provide over an articulated arm?
(a) Higher power delivery (b) small, flexible light delivery (c) robust (d) All of the above

26. The core and cladding layers of a standard optical fiber are composed of _____.
(a) Silica or quartz (b) Hollow for light transmission (c) Silver (d) Gold

27. Approximately what percentage of light is reflected at a single air-glass interface?
(a) 0% (b) 4% (c) 10% (d) 25%

28. A higher numerical aperture (NA) results in light exiting the fiber being _____.
(a) More divergent (b) More focused (c) More collimated (d) It depends on other factors

4. Lasers in Dermatology

4.1 Introduction

Dermatology is the science that deals with the skin, hair, nails, and sweat glands. Skin protects the inside of living beings from the potentially harmful contaminants and substances that exist in the environment all around us. Lasers are used for treating many diseases of the skin. To understand how lasers are used in medicine, one must first understand the basic structure and functions of human skin.

4.2 Structure of the Skin

The skin consists of two layers (Figure 16), the surface layer called *epidermis* and the inner layer called *dermis*. The epidermis is approximately 0.1 mm thick while the dermis is several millimeters thick. The outermost layer of the epidermis is the *stratum corneum*. It consists mainly of dead cells. It gives protection against water loss, abrasion, dust, air, and radiant energy. This layer is 8 to 20 μm thick. Immediately below the stratum corneum there are special cells that produce melanin pigment granules. These granules migrate throughout the epidermis. They help to protect the dermis against UV radiation and become dark when exposed to it. The change of skin color after sun tanning is due to this process. The dermis is typically several millimeters thick and consists of many specialized cells and glands. It also contains connective tissue that gives elasticity and support to the skin. The dermis consists of numerous blood vessels, nerve cells, sweat glands, and hair follicles. The sweat glands regulate temperature through evaporation and cooling of the body. The nerve cells contain heat sensors, pain sensors, and touch sensors (*tactile*). The blood vessels contribute to the maintenance of healthy tissue and heat regulation.

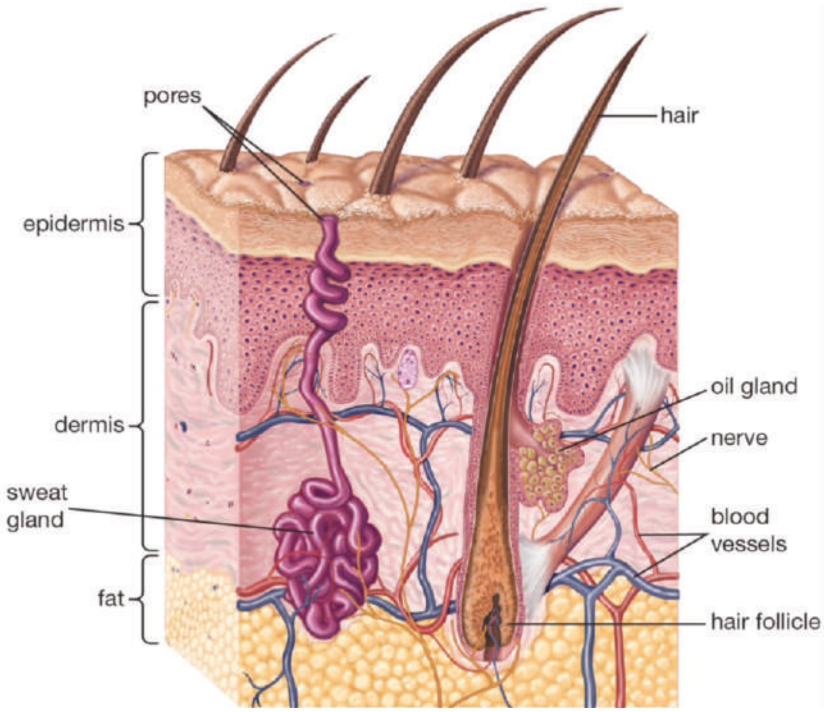


Figure 16. *Anatomy of human skin.*

The skin absorbs and reflects the visible portion of the electromagnetic spectrum. It reflects most infrared radiation. The epidermis absorbs most ultraviolet light (100 nm to 315 nm) as well as the 1400 nm to 1 mm range of the infrared region. The skin is less sensitive in the 315–400 nm region. The *melanin granules* of the epidermis absorb most of the ultraviolet light incident upon them and protect the dermis from harmful radiation effects. However, with sufficient intensity, any wavelength of visible, near infrared, or near ultraviolet radiation can penetrate the skin and cause damage.

Laser-induced thermal change to the skin is the most important laser-tissue interaction. When light is incident on a tissue, part of the light will be transmitted, part will be absorbed, and part will be reflected. Table 6 provides a list of lasers used in dermatology, along with information on wavelengths, output modes, absorption characteristics, and applications.

Table 6. Lasers Used in Dermatology

Laser	Wavelength (nm)	Mode	Absorber	Application
Argon	488, 514	CW	Melanin, hemoglobin	Malformations
Dye	500–585	Pulsed	Melanin, hemoglobin	PWS, Nevus flemmus, fine veins
Nd:YAG	532, 1064	Q-switched	Melanin, hemoglobin	Tattoos, brown lesions, freckles
Krypton	568	CW	Melanin, hemoglobin	Fine veins, spider veins
Ruby	694	Q-switched	Melanin	Tattoos, freckles, blue veins
Alexandrite	700–818	Q-switched	Melanin	Tattoos, pigmented lesions
GaAlAs	810	Pulsed	Melanin	Hair removal, leg veins, tattoos
Er:glass	1,540	Q-switched	Melanin, hemoglobin	Wrinkles, scars
Er:YAG	2,940	Q-switched	Water	Wrinkles, scars
CO_2	10,600	Pulsed	Water	Acne, chicken pox, wrinkles, skin tags, warts, dermatosis, papulosa

4.3 Treatment of Vascular Lesions

Lasers are successfully used to treat a variety of vascular lesions. Many types of lasers have been tried, including pulsed dye, argon, krypton, frequency doubled Nd:YAG, and copper vapor. However, the pulsed dye laser with a wavelength of 585 nm is the laser of choice for treating most vascular lesions because of its clinical efficacy and low risk. Vascular lesions contain endogenous *chromophores*, hemoglobin, and *deoxyhemoglobin*. The pulsed dye laser with 450 μsec pulse width and 5–10 kW power can be used to treat them.

Visible, individual vessels and skin defects can be treated with almost any pulsed laser with a wavelength range of 500–600 nm (Figure 17). Where individual vessels within the defect require treatment, the beam can be focused to the size of the vessel. In treating these skin defects, the laser is slowly scanned over the lesion. In the case of diffuse erythema, the laser beam is defocused to a 5–10 mm diameter and used with a single pulse. The pulsed dye laser with short pulse duration produces short impact damage to the skin without scabbing or blistering. Repeated application of the treatment is often necessary. The laser treatment is more effective in younger people than in older people because the stains in older people tend to become thick and develop nodules. Techniques using multiple wavelengths and longer pulse duration have been successfully used to remove the nodules and the thickness of the stains. The long-pulsed laser beam also results in more uniform blood vessel damage. This reduces postoperative *purpura* (bruising). Dynamic cooling of the skin surface using a pulsed cryogen spray also increases the patient's comfort during the procedure and prevents skin reddening or erythema. Vascular malformations associated with smaller, more superficial blood vessels respond better to treatment than deeper, larger vessels. The fading of the stain usually takes 8 to 10 treatments.

Before After

Figure 17. *Laser removal of vascular birthmarks such as port wine stains.*

Example 3

During port-wine stain (PWS) therapy, the laser energy is selectively absorbed by abnormal blood vessels in the dermis of the skin. For a blood absorption coefficient of $\mu_a = 50\ cm^{-1}$, describe the effects of a 600-μs-long laser pulse on dermal blood vessels with diameters of 5 μm? 25 μm? 100 μm?

Solution

Assume that for dermis, $\mu_s >> \mu_a$, the radiant exposure per laser pulse within the dermis is given by $F = 5\ J/cm^2$, density of tissue, $\rho = 1\ g/cm^3$, and heat capacity of tissue is $c = 4.2\ J / g\text{-}^oC$.

First, calculate the temperature rise ($\Delta T = \mu_a F / \rho c$) and the maximum temperature in the blood vessel.

$\Delta T = \mu_a F / \rho c = (50\ cm^{-1})\ (5\ J/cm^2) / (1\ g/cm^3)\ (4.2\ J / g\text{-}^oC) = 60\ ^oC$

Since normal body temperature is 37 ^oC, the maximum temperature is given by:

$T_{max} = T_o + \Delta T = 37\ ^oC + 60\ ^oC = 97\ ^oC$.

Now calculate the thermal relaxation times ($\tau_{th} = \delta^2 / 4\kappa$) for each different blood vessel diameter, assuming a thermal diffusivity of $\kappa = 1.5 \times 10^{-3}$ cm^2/s.
$\tau_{th} = \delta^2 / 4\kappa$, where $\kappa = 1.5 \times 10^{-3}$ cm^2/s.
For a 5 µm blood vessel, $\tau_{th} = (5 \times 10^{-4}\ \text{cm})^2 / [4\ (1.5 \times 10^{-3}\ \text{cm}^2/\text{s})] = 42\ \mu\text{s}$
For a 25 µm blood vessel, $\tau_{th} = (25 \times 10^{-4}\ \text{cm})^2 / [4\ (1.5 \times 10^{-3}\ \text{cm}^2/\text{s})] = 1\ \text{ms}$
For a 100 µm blood vessel, $\tau_{th} = (100 \times 10^{-4}\ \text{cm})^2 / [4\ (1.5 \times 10^{-3}\ \text{cm}^2/\text{s})] = 17\ \text{ms}$

Now, interpret the results above and compare the above answers for each blood vessel diameter in the context of PWS therapy, where abnormal blood vessels are larger than normal vessels.
If the laser pulse is 600 µs long, thermal confinement is only achieved for medium and large blood vessels ($t_{pulse} < \tau_{thermal}$). This is desirable because large abnormal blood vessels that are targeted during PWS reach much higher temperatures and are thermally coagulated. The normal smaller blood vessels do not experience thermal confinement (heat leaks out), so the temperature is lower and they are preserved.

4.4 Treatment of Pigmented Lesions and Tattoos

High-energy, Q-switched, short-pulsed lasers with pulse durations shorter than the thermal relaxation time of the pigment granules (< 5 nsec) are most effective in lightening or eradicating tattoos, birthmarks, freckles, and other pigmented lesions. The *melanosomes* are tiny granules containing melanin inside the pigment cells. These can be removed by Q-switched, short-pulsed lasers. In tattoo removal, different lasers are used to remove pigments of different colors to prevent excessive damage to the surrounding skin (Table 7 and Figure 18).

Before After

Figure 18. *Laser application in removal of tattoos after multiple treatments.*

Superficially located pigments are treatable by shorter-wavelength lasers, while removal of deeper pigment requires longer-wavelength lasers. It is more difficult to remove tattoos from darker skin than lighter skin because permanent *hypopigmentation* and *depigmentation* can occur in darker skin. A pigmented lesion should always be tested for malignancy before subjecting it to laser treatment. Single-color tattoos are easier to remove than tattoos with multiple, deeply concentrated colors. Some amount of scarring is inevitable in any tattoo removal, but this will heal in time.

Table 7. Lasers for Tattoo Removal

Characteristics	Q-switched Ruby	Q-switched Nd:YAG	Q-switched Alexandrite
Wavelength (nm)	694	532 and 1064	755
Spot diameter (mm)	3.5-5	5	4
Operation mode	pulsed	pulsed	pulsed
Pulse duration (ns)	15-40	40-80	50
Removable colors	Black, Blue, Green	Black, Red, Orange, Yellow	Black
Optical penetration depth (mm)	1	3-5	2
Recommended skin tone	Light / Fair	Any	Dark
Sessions required	4-6	Up to 10	4-10

Example 4
Laser tattoo removal is a successful cosmetic dermatology procedure. Assume a black ink particle of approximately 200 nm (2×10^{-7} m) diameter, located about 1 mm below the skin surface in the upper or papillary dermis. A short pulse, Q-switched, Nd:YAG laser with a wavelength of 1064 nm and a pulse duration of 50 ns (5×10^{-8} s) is commonly used for tattoo removal. Using your basic knowledge of the interaction of different laser parameters with tissues, answer the following questions:

(a) Explain why the Nd:YAG laser wavelength of 1064 nm is good choice for this procedure

(b) Explain why a pulsed laser is used for this procedure.

(c) Calculate the thermal relaxation time ($\tau = \delta^2 / 4\kappa$) for a black ink particle and answer whether thermal confinement is achieved during the laser pulse. Assume $\kappa = 1.5 \times 10^{-3}$ cm^2/s.

(d) Which beam diameter is best for tattoo removal (500 nm, 5 μm, 50 μm, 500 μm, 5 mm)? Why?

(e) Undesirable heating of skin surface may occur during laser tattoo removal. What simple approaches could be taken to reduce or eliminate skin reddening?

Solution
(a) The Nd:YAG laser (λ=1064 nm) operates in the optical window (600-1300 nm) where light penetrates the deepest in soft tissues. This is necessary for laser tattoo removal because ink particles can be located deep underneath the skin surface (500-2000 μm).

(b) A pulsed laser prevents heat from leaking out of the treatment area (ink particle diameter), and causing collateral thermal damage to healthy tissue, based on principle of selective photothermolysis.

(c) The ink particle diameter determines the target dimensions, δ = 200 nm = 2×10^{-5} cm. Therefore, $\tau = \delta^2 / 4\kappa = (2 \times 10^{-5}\ \text{cm})^2 / [4(1.5 \times 10^{-3}\ \text{cm}^2/\text{s})] = 6.7 \times 10^{-8}$ s = 67 ns. The laser pulse duration is 50 ns, less than the thermal confinement time constant of 67 ns, so, yes, thermal confinement achieved.

(d) A diameter of 5 mm. A wide laser beam provides higher radiant exposure at a given tissue depth than a thin laser beam, for the same initial radiant exposure at surface (normalized). Loss of fluence due to scattering of photons is less for a wider beam. For a cylindrical beam, compare ratio of volume to surface area: $\pi r^2 l / 2\pi r l$, which simplifies to an r/2 dependence. A larger radius beam provides greater ratio of volume to surface area ratio, and relative leakage of photons from surface area is diminished.

(e) Applied cooling of the skin surface (epidermis) using contact (e.g. cooled sapphire window or gel) or non-contact (cold air or cryogen) methods may prevent skin reddening.

4.5 Hair Removal

Lasers are used to remove excessive and cosmetically disabling hair. The removal is not permanent; the hair will grow back in three or four months. Laser treatments are less painful and much quicker than electrolysis. Superficial burns, pigment changes, and scarring may occur during a laser procedure. Figure 19 illustrates the effects of laser hair removal.

Among the lasers used for hair removal are pulsed Nd:YAG, ruby, alexandrite, and GaAlAs diode lasers with 810 nm wavelength. The Nd:YAG laser is often the best choice, as it has the best safety profile and is capable of removing 100 percent of the hair at the treatment site. Also, the replacement hair, which may appear in 3 to 4 months, is much lighter and thinner. Ruby lasers with long pulses can also be effective and create minimal damage to the surrounding collagen. Transient pigment changes without scarring may occur. The use of the alexandrite laser for hair removal is a recent occurrence. Its 755 nm wavelength is effective in removing hair and creates minimal risk to the patient.

More recently, filtered intense pulsed light (IPL's) sources, which are broadband incoherent light sources, have replaced many laser systems with eye safe characteristics for use in low cost home hair removal systems.

Before After

Figure 19. *Removal of unwanted hair using a laser.*

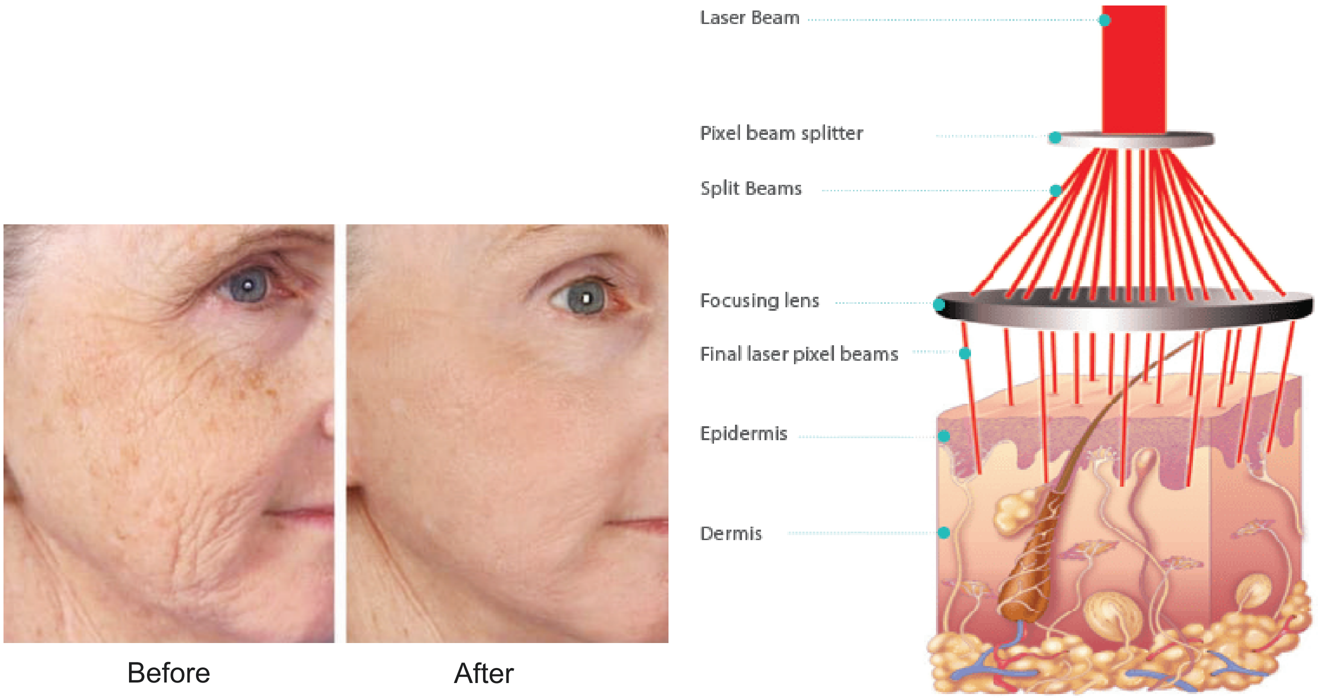
4.6 Treatment of Wrinkles, Scars, and Sun Damage

Pulsed CO_2 and Er:YAG lasers are used to remove facial wrinkles, acne scars, and sun-damaged skin. High-energy pulsed and scanned CO_2 lasers are most often used for this purpose (Figure 20). Side effects reported include postoperative tenderness, redness, swelling, and scarring. However, these side effects are temporary and are mitigated by the replacement skin in a few weeks.

Treatment of darker skin with lasers is not as successful as treatment of lighter skin as permanent loss or variable pigmentation may occur. The Er:YAG laser has the same results and side effects as the CO_2 laser but is easier to maintain and control. Lasers also are used to vaporize viral warts and destroy dermal blood vessels.

Skin resurfacing can be performed using both ablative and non-ablative approaches, to remove wrinkles and stimulate new collagen growth and healthy, younger looking skin. With ablative skin resurfacing, the epidermis and papillary (upper) dermis are vaporized to a depth of 10-200 μm, creating channels of treated tissue. In non-ablative skin resurfacing, deeper zones of 600-1000 μm are thermal coagulated. The treatment depth can be controlled not only with choice of laser wavelength, but also by changing laser pulse duration to allow variable amounts of thermal conduction and leakage of heat from the absorbed tissue volume during the procedure.

Fractional skin resurfacing has also been implemented, where a single laser beam is split into multiple laser beams to provide a grid of superficial thermal coagulation zones in the skin (Figure 20). The advantage of fractional skin resurfacing is that the skin remodeling process is accelerated and there are fewer side-effects if there is a contiguous region of healthy tissue surrounding the thermal treatment zone. Besides the CO_2 lasers, both Erbium doped fiber and Thulium doped fiber lasers have also been used due in part to their superior spatial beam profile which lends itself to a fractional approach.



(a) (b)

Figure 20. (a) *Laser removal of wrinkles for skin rejuvenation; (b) Fractional skin resurfacing, producing a grid of small thermal coagulation zones surrounded by healthy tissue, for accelerated wound remodeling.*

4.7 Body Contouring and Removal of Fat

Body contouring and fat reduction liposuction is common within the field of cosmetic surgery. Liposuction is a surgical procedure that involves the use of a cannula to suction unwanted fat. However, it requires anesthesia and involves risks associated with any major surgery including uneven results, blood loss, fluid accumulation, numbness, and infection.

Laser lipolysis has been introduced as a noninvasive alternative to liposuction and surgery. A deeply penetrating near-infrared laser wavelength, typically between 900-1300 nm (Figure 5), consisting of either an Nd;YAG laser or laser diodes, delivers energy through the skin to the underlying fat or adipose tissue layers (Figure 16) to destroy fat cells. The laser may operate in continuous-wave mode, and deliver laser energy with irradiances of about 2 W/cm^2 for approximately 25 minutes, with the goal of heating up the subcutaneous adipose tissue layers to between roughly 42-47 ^{o}C, well above normal body temperature of 37 ^{o}C. A very large laser spot size measured in several centimeters by centimeters, is used with each of the multiple laser treatment arms both to treat large surface areas and provide deeper penetration of the laser energy (Figure 21). Multiple sessions are typically required to provide acceptable cosmetic results.

During laser lipolysis, the laser energy heats up and liquefies fat cells, coagulates small blood vessels, induces collagenesis with associated tissue remodeling, and provides tissue tightening. Fat reduction usually appears over a period of weeks to months after the procedure. Continuous contact cooling of the skin using a thermally conductive and optical transparent sapphire window is used to prevent skin irritation and burns during the procedure. However, due to the absence of major absorption peaks by adipose tissue in the near-infrared spectrum, strong selective absorption of the laser energy by the adipose tissue is not possible.

A major limitation of laser lipolysis is that patients may experience in some cases an intolerable amount of pain during the procedures. Other energy-based devices, including radiofrequency electrosurgical techniques and cryolipolysis are also widely used alternative to laser lipolysis. Cryolipolysis, in particular, appears to provide a more attractive approach, since cooling not only destroys the fat cells, but also acts as a natural anesthetic, to numb the skin and treatment area and minimize the pain experience by the patient.

(a) (b) (c)

Figure 21. *(a) An example of a laser lipolysis system consisting of near-infrared laser energy delivery and contact cooling of the skin, integrated into multiple large applicators, strapped around the patient's body. (b,c) Photographs of the patient's treatment area before and after laser lipolysis treatment.*

4.8 Reshaping of Cartilage

Cartilage is a dense connective tissue composed of 60-80% water and a small proportion of chondrocyte cells within an extracellular matrix. Lasers have been used to reshape cartilage in several facial tissues for cosmetic surgery (e.g. ears and nose). Originally, Nd:YAG and CO_2 lasers were used, but more recently 1540 nm Er:glass lasers and 1450 nm diode lasers have been adopted for cartilage reshaping, due in part to their intermediate penetration depths in tissues. The method utilizes mechanical pressure in the form of a mold or fixture on the tissue in combination with laser energy delivered in long pulse mode, to heat, soften, and reshape the cartilage in the ears and nose (Figure 22). Radiofrequency energy has also been used as a less expensive alternative to lasers for cartilage reshaping.

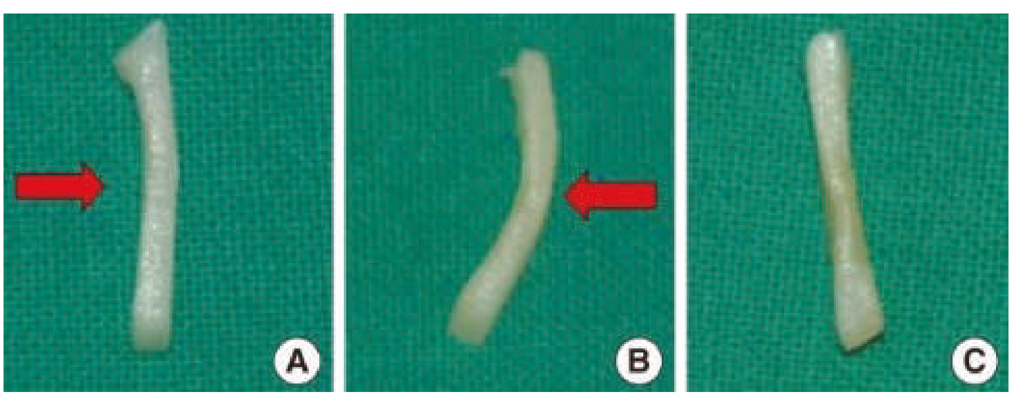


Figure 22. *Shape change of human septal cartilage before (A) and immediately after (B) diode laser irradiation. Reshaped cartilage was then recovered into flat shape after re-irradiation by laser to the convex side (C). The red arrow indicates the direction of laser irradiation.*

4.9 Endovenous Laser Therapy

Endovenous laser therapy (EVLT) is used for minimally invasive thermal treatment of swollen legs, varicose veins, and chronic venous insufficiency. During the procedure, a small cut is made in the skin, the vein is numbed with local anesthetic, and a catheter is placed inside the lumen of the vein. Then an optical fiber with a diffusing distal tip is inserted through the catheter and the vein. Laser energy is applied circumferentially, heating up the abnormal vessel wall, until the vessel collapses and is permanently sealed. The laser fiber is continuously pulled back and then eventually withdrawn from the closing vein (Figure 23). Cosmetic improvements after EVLT can be significant (Figure 24).

Although several near-IR diode lasers have been used for EVLT, the 1470 nm diode laser provides some desirable characteristics, including 5-10 W of average power in a compact design, long-pulse operation, and an intermediate optical penetration depth in water of about 400 µm, so the entire vessel wall (which is mostly water) is heated, but the light does not penetrate too deeply into surrounding healthy tissue. The blood inside the vessel lumen is displaced during insertion of the fiber, so blood is not a major light absorber. A diffusing fiber tip provides uniform, 360° irradiation of the vessel wall.

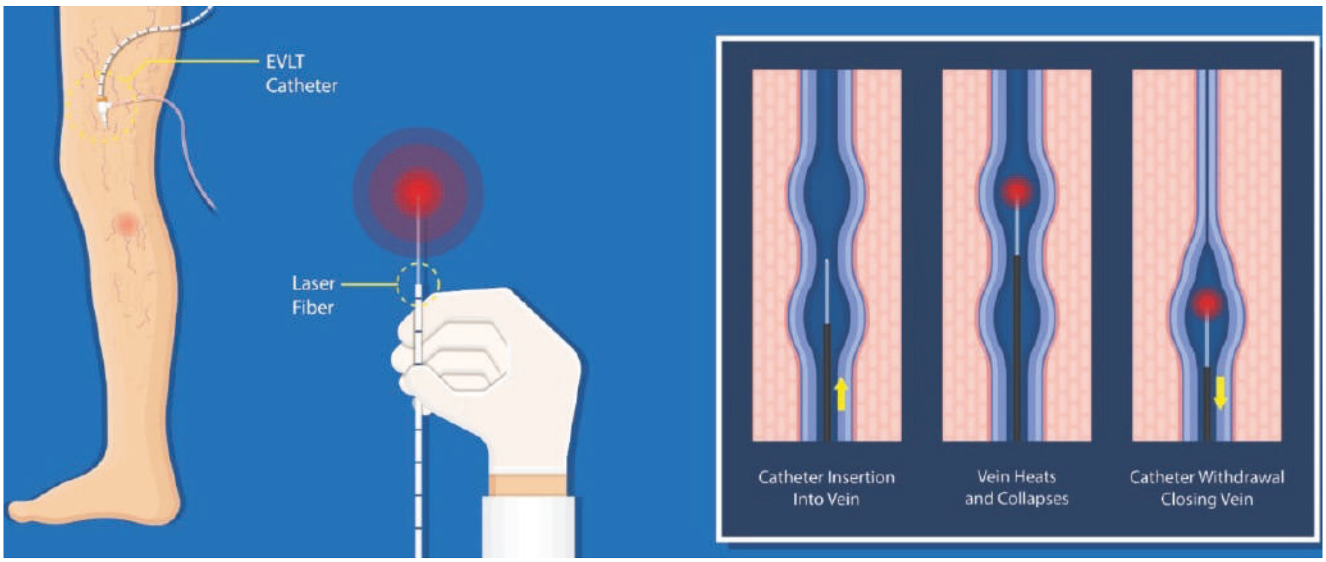


Figure 23. *Endovenous laser treatment of varicose veins.*

Before After

Figure 24. *Before and after photographs for endovenous laser therapy.*

Self-Test

29. What is the approximate thickness of the epidermis layer in skin?
(a) 1 µm (b) 100 µm (c) 1 mm (d) 10 mm

30. What is the approximate thickness of the dermis layer in the skin?
(a) 1 µm (b) 25 µm (c) 700 µm (d) 3 mm

31. Which of the following parameters is required for successful treatment of port-wine stains?
(a) Wavelength strongly absorbed by blood but not skin (b) Short laser pulse duration
(c) Large laser spot (d) All of the above

32. Which cosmetic dermatology application utilizes the principle of selective photothermolysis?
(a) Tattoo removal (b) Hair removal (c) Port wine stain removal (d) All of the above

33. Which laser application utilizes a diffusing fiber optic tip for thermal tissue coagulation?
(a) Cartilage reshaping (b) Endovenous therapy (c) Wrinkle removal (d) All of the above

5. Lasers in Ophthalmology

5.1 Introduction

Lasers are used extensively in ophthalmology. In the past, argon, krypton, dye, and Nd:YAG lasers were used. More recently, frequency doubled Nd:YAG, diode, excimer lasers, and ultrashort pulse lasers have been employed. In this section, laser applications in ophthalmology will be discussed.

5.2 Structure of the Eye

The main parts of the human eye are shown in Figure 25. The human eye is approximately spherical in shape and measures 24 mm long and 22 mm across. The front portion includes the cornea, which is optically transparent, and the lens, which can adjust its shape to change its focal length. The adjustable iris in front of the lens restricts the amount of light that enters the eye. These components are connected to the tough sclera, which protects the eye and muscles that move the eye. The eye is filled with two main fluids. The watery fluid between the cornea and the lens is the *aqueous humor.* It is derived from blood plasma. The liquid that fills the body of the eye is the *vitreous humor*. It is a gel with electrolyte composition and contains protein fibers. The lens is biconvex and contains a transparent gel. Its shape is altered (to change the focal length) by a group of muscles in the ciliary body.

When light strikes the eye, part is reflected and part is transmitted. This is due to the differences between the refractive indexes of the air and the cornea. The iris controls the amount of light that goes through the vitreous liquid and is focused on the retina. Interestingly, the eye lens can change its focal length instantaneously and does not normally have either spherical or chromatic aberrations. (Spherical aberration occurs when non-paraxial rays come to a focus at different points. Chromatic aberration occurs when images of different colors do not come to a focus at the same point.)

The absorptive properties of different portions of the eye depend upon the wavelength of light. The retina contains three major pigments, *melanin, hemoglobin,* and *macular xanthophyll*. These absorb visible light from 400 to 700 nm. The retina has numerous layers. One layer consists of a number of rods and cones. The other layers consist of four types of neurons, *bipolar, ganglion, horizontal,* and *amacrine cells.* The rods and cones, coupled with the neurons, act as the receptors, converting the light energy into electro-mechanical pulses and passing it on to the optic nerve.

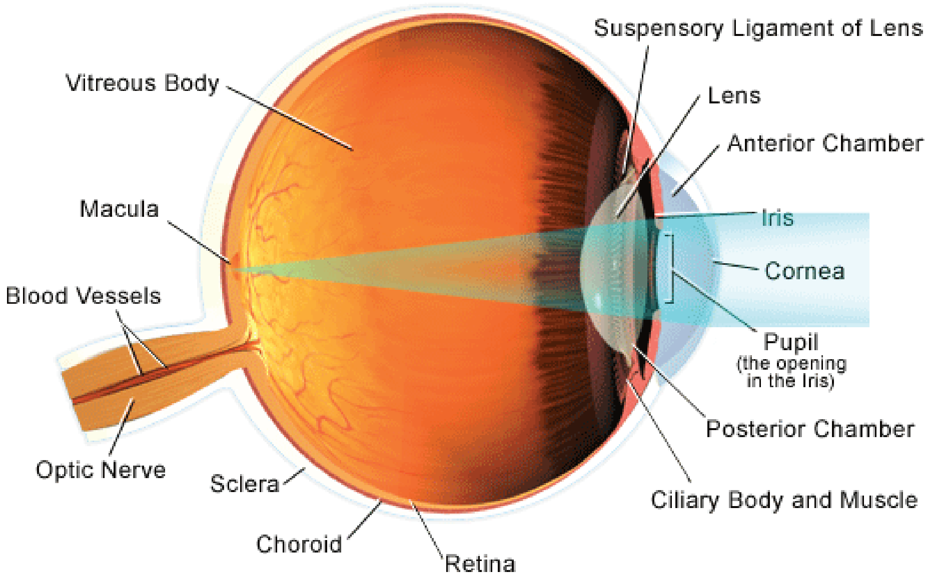


Figure 25. *Schematic diagram of the human eye.*

The cornea consists of several layers of different thicknesses (Table 8 and Figure 26). Most of the cells in all the layers are renewable except those in the endothelium. Surgical procedures require extreme care to ensure that these cells are not destroyed.

Table 8. Layers of the cornea.

Layers	Thickness (μm)	Composition
Epithelium	50	Stratified squamous epithelium
Bowman's membrane	8-14	Compact layer of collagen fibers
Stroma	500	Orderly arrangement of collagen lamellae with keratocytes
Descemet's membrane	10-12	Consists of collagen and glycoprotein
Endothelium	5	Single layer of simple squamous

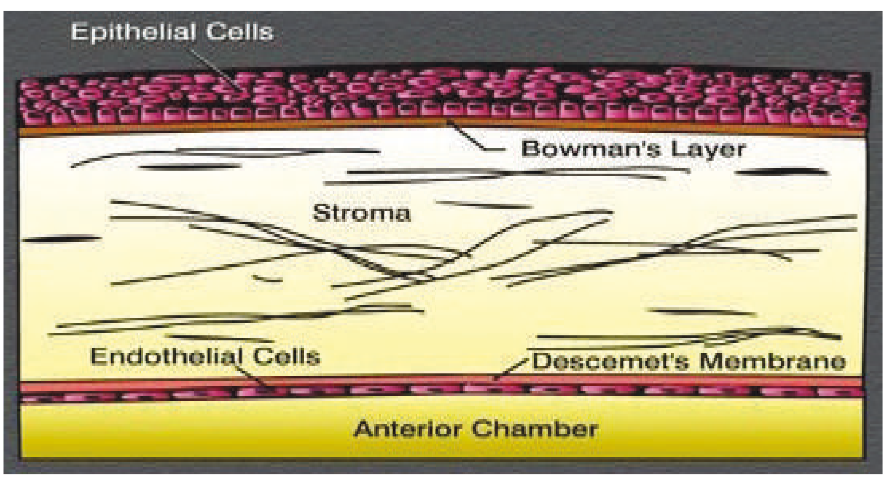


Figure 26 *Schematic diagram of the fiver layers that make up the cornea of the eye.*

The transmission characteristics of different portions of the eye are shown in Figure 27. The transmission of the eye lens decreases at lower wavelengths (400–600 nm) as a person becomes older.

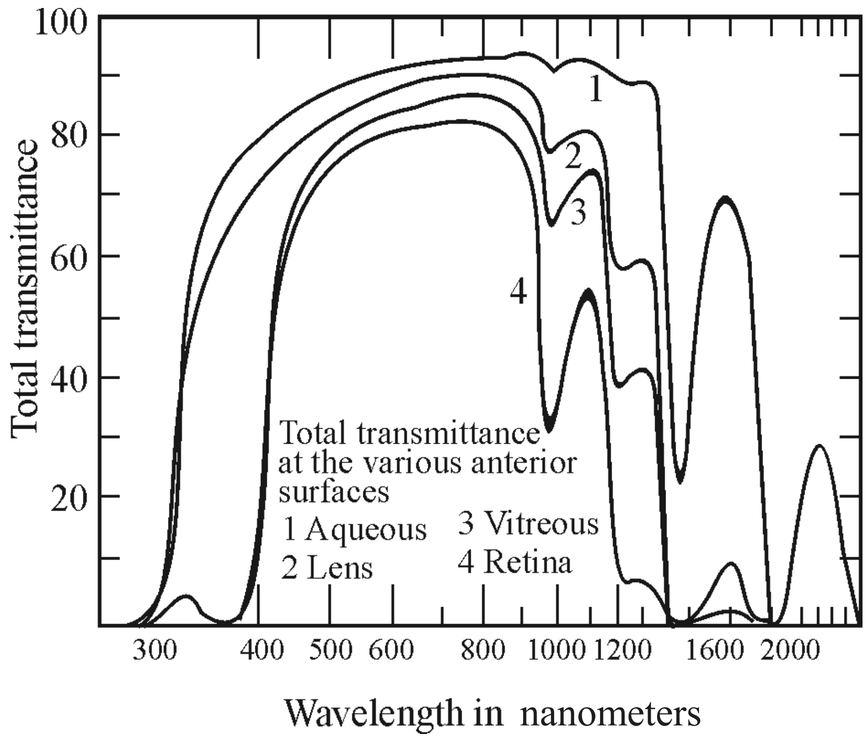


Figure 27. *Transmission characteristics of the human eye.*

The optic nerve carries information from the eye to the brain. The retinal layers are tightly sealed and do not allow leakage of blood or protein fluid into the surrounding retina. However, in persons with diabetes and other vascular diseases, the blood vessels become brittle and allow fluid leakage into the posterior region. This causes retinal dysfunction and loss of vision. Also, sometimes fragile blood vessels grow on the surface of the retina and cause leakage of fluid into the eye.

When viewed through a fundus camera, the central optic disc and the connecting blood vessels can be seen (Figure 28). A fundus camera is a low-power microscope designed to photograph the interior of the eye. The size of this disc depends on the individual's sex and race. The area called the *fovea* (near the optic disc) contains the maximum number of photoreceptors. In any laser application to the eye, this is the area that requires the most protection. Destruction of the fovea can lead to loss of vision or blindness. The blood vessel network and the fovea are called the *arcades*.

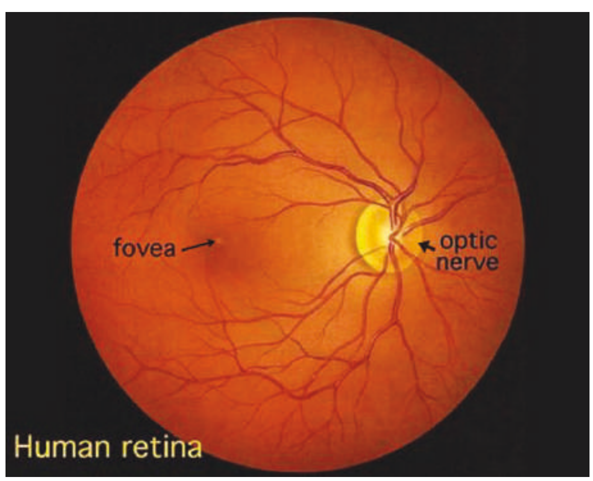


Figure 28. *The visible retinal surface and blood vessels.*

5.3 Optical Properties of the Eye

The focal length of the eye is about 16.7 mm. Measured in diopters (1/*f*), where *f* is in meters), this corresponds to 59.88 diopters. About two thirds of this (44 diopters) is due to the curvature of the cornea, and one third is due to the lens. The eye behaves like a double lens combination. A small change in the curvature of the cornea can result in a large change in focal length. When people are less than 50 years old, focusing on nearby objects is not difficult. The lens can adjust its shape to provide the required focal length. At later ages, this becomes more difficult. For people with perfect vision, the combination of cornea and lens focuses the object exactly on the fovea, which has the highest density of receptors. However, for nearsighted (*myopic*) eyes, the focal length of the combination is too short (optical power in terms of diopters becomes large) and the image is focused in front of the fovea. For farsighted (*hyperopic*) eyes, the image is formed behind the retina (Figure 29).

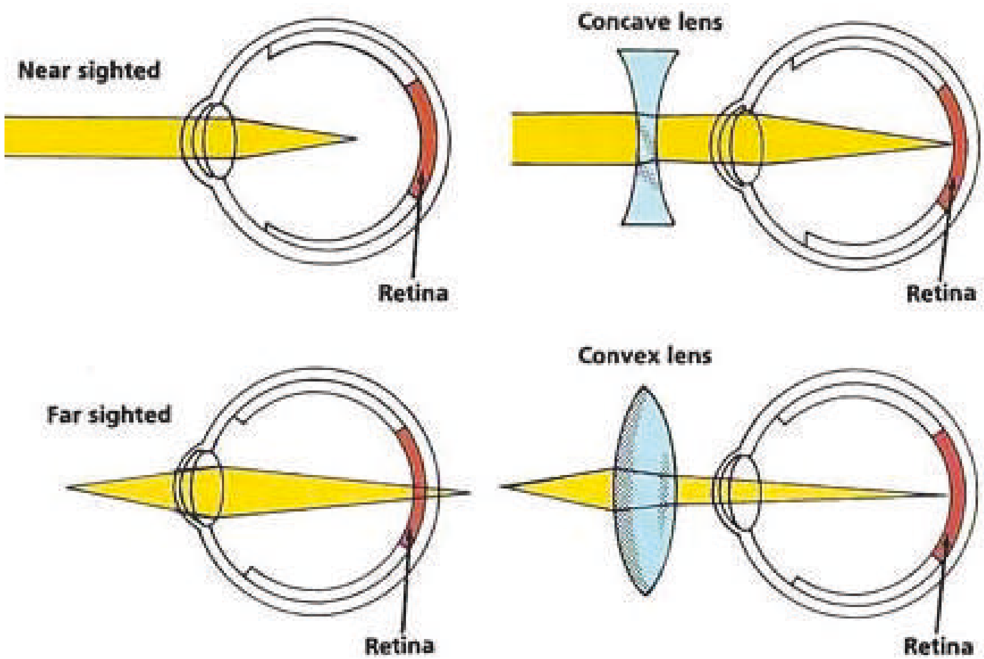


Figure 29. *Diagram showing near-sighted (myopic) and far-sighted (hyperopic) eyes and their corrections.*

5.4 Laser Therapeutic Applications

Photocoagulation of Retinal Tissue

Photocoagulation is the technique used by surgeons to cauterize blood vessels. Cauterization results from the heat generated by a laser beam. This is the most widely used technique in the treatment of diabetic macular edema (leakage of blood into the retina). In the early years, ruby and krypton lasers were used with some degree of success. More recently, frequency doubled Nd:YAG lasers (532 nm) are successfully used. Macular degeneration of subretinal neovascular membranes, a condition associated with aging, can also be treated with the photocoagulation technique. In most applications, powers of 100 W/cm^2 with pulse duration ranging from 0.1 to 1.0 s are used. Some side effects in this kind of therapy are noticed. For example, coagulation of peripheral tissues may cause loss of night vision. In most cases, the advantages outweigh the side effects. Laser photocoagulation is also used for repairing severe retinal detachment.

Photothermal Treatment of Glaucoma

Glaucoma is a group of eye diseases that damage the optic nerve. The damage occurs as a result of elevated pressure of the fluid (aqueous humor) in the eye. This results in gradual visual changes and loss of vision. In the laser treatment of glaucoma, continuous-wave frequency doubled Nd:YAG lasers with a wavelength of 532 nm are used to drill a small hole in the peripheral iris. This creates an alternative pathway for the aqueous humor. The major pigment in the iris is melanin, which absorbs the 532 nm laser wavelength. A typical arrangement of glaucoma treatment with a laser is shown in Figure 30. The patient sits with his/her eye illuminated by a halogen illuminator and the laser beam is directed toward the eye. A CCD (charge coupled device) camera and bio-microscope allow the administering of the surgery.

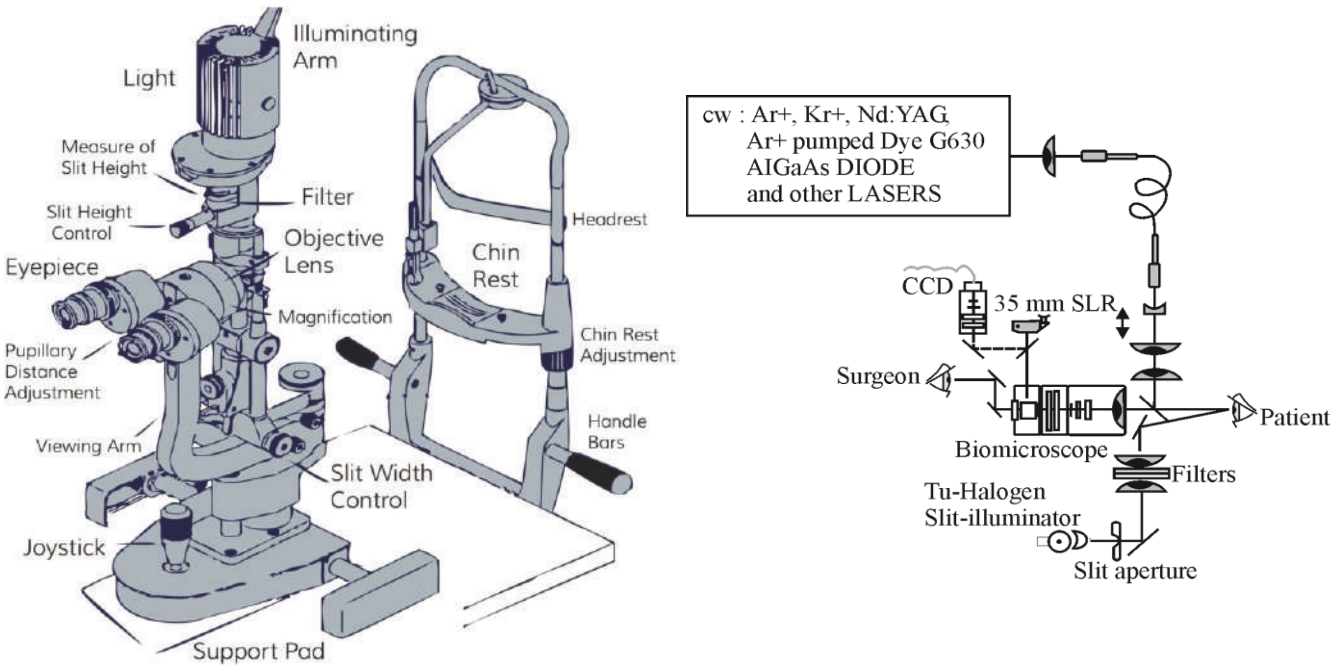


Figure 30. *A drawing and schematic diagram of a slit lamp and laser-assisted delivery system.*

Laser Cataract Surgery

With aging, some portion of the intraocular lens becomes clouded. This is called a cataract. The clouded areas reduce vision and can be treated by removing the clouded portion and replacing it with a plastic lens. Figure 31 shows the procedure used in cataract surgery. The cataract is removed through a small incision with a laser shown in (a). The capsular bag is filled with a fluid with the same refractive index as the original lens which is shown in (c) and (d). The XeCl excimer laser at 308 nm and ultrashort pulsed lasers have been successfully used to remove cataracts. However, the fluorescence produced by these pulses causes significant retinal damage.

Figure 31. *Schematic diagram of a cataract surgery.*

During photodisruptive applications, a laser beam is used to ionize the molecules at the target. The radiation beam from a Q-switched Nd:YAG laser (10 ns) is focused to give a 20–40° cone angle and extremely high irradiance of 10^{10} W/cm^2. This beam is then focused on the target. The beam will ionize the molecules at the target, thereby creating a plasma. The shock waves caused by the plasma produce mechanical breakdown of structures adjacent to the target site. One of the most successful applications of photodisruptive techniques is to reduce the opacity of the lens. People who have had cataract surgery often experience fading vision after a few years because the epithelial cells proliferate over time. These cells can be destroyed using a Q-switched Nd:YAG laser.

Laser Surgery of the Cornea

An ArFl Excimer laser (193 nm) can produce *photoablation*. This takes place when short laser pulses from an Excimer laser are focused on a small area of the target tissue. The extremely rapid heating caused by the absorption of radiation by tissue leads to vaporization. When the laser wavelength is carefully matched to the absorption wavelength of the tissue, precise control of the depth of interaction can be attained. The cornea has extremely high absorption at 193 nm. The energy from the laser at this wavelength is much higher than the bonds linking carbon atoms in the cornea. Because of this, the laser can vaporize bonds. Precisely controlled volumes of corneal tissue can be removed. Typical laser parameters used are depth of ablation (0.1–0.5 μm) and pulse intensity (50–250 mJ/cm^2).

The most common application of photoablation using an Excimer laser is the sculpting and reshaping of the outer surface of the cornea to correct for refractive errors during Photorefractive Keratectomy (PRK) and Laser-Assisted In Situ Keratomileusis (LASIK). A primary difference between PRK and LASIK is that the former procedure involves application of the laser beam directly to the cornea surface, while the latter procedure uses a microtome (fine knife) or ultrashort pulse laser for creating a cornea flap and then applying the Excimer laser beam to the central section of the cornea (stroma). One disadvantage of the Excimer laser is the low pulse repetition rate (10–20 Hz) and rectangular beam shape (25 mm × 7 mm). Beam focusing to very small areas is also difficult. Recently, a third option for laser corneal surgery, Small Incision Lenticule Extraction (SMILE), has been developed, using a femtosecond laser to noninvasively carve out a lenticule in the cornea, which is then removed through a small incision, resulting in a shape change of the cornea for vision correction (Figure 32).

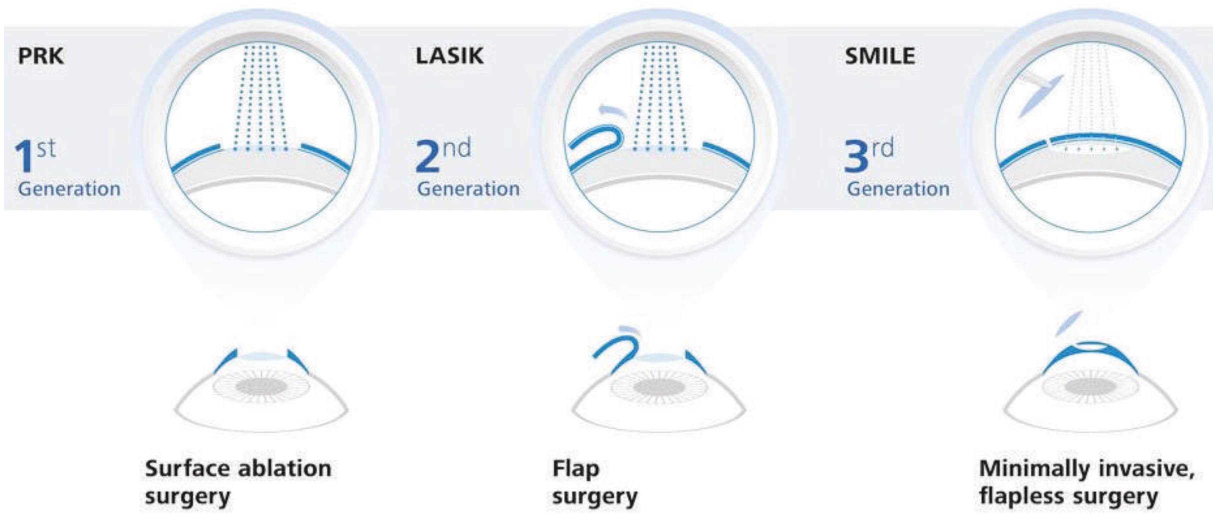


Figure 32. *Diagram comparing PRK, LASIK, and SMILE approaches to corneal shaping and vision correction.*

Table 9. Laser Parameters for Excimer Laser Ablation of the Cornea.

Parameter	Value
Wavelength, λ	193 nm (1.93 x 10^{-7} m)
Radiant exposure, F	0.2 J/cm^2 (2000 J/m^2)
Pulse Duration, t_p	10 ns (1 x 10^{-8} s)
Energy of a photon, E	hc/λ
Speed of light, c	3 x 10^8 m/s
Planck's constant, h	6.63 x 10^{-34} J-s
Carbon-Carbon molecule radius, r_{bond}	0.154 nm (1.54 x 10^{-10} m)
Body temperature, T_0	37 ^{o}C
Boiling temperature of water, T_f	100 ^{o}C
Density of water, ρ	1 x 10^3 kg/m^3
Specific heat capacity of water, C	4.3 x 10^3 J/kg-K
Latent heat of vaporization, L_v	2.3 x 10^6 J/kg

Example 5
Excimer UV laser ablation of the cornea during LASIK procedures has been attributed to both photoablation and photothermal mechanisms. Using real values for laser parameters in Table 9 above, solve for tissue ablation depth per laser pulse, with photoablation and photothermal approaches, and compare the results. Assume that cornea (~ 80% water), has a similar density and heat capacity as water.

Part (a) If we assume that the LASIK mechanism is photoablation, then:

(i) Calculate the energy of a single UV photon at λ = 193 nm.

(ii) Calculate number of UV photons per unit area (N) in laser beam if radiant exposure F = 2000 J/m^2.

(iii) Assume that each photon breaks a single chemical bond in the cornea, and that bond radius of C-C molecule is $r_{bond} = 1.54 \times 10^{-10}$ m, with molecules evenly distributed in spherical volume of $V = 4/3\ \pi r^3_{bond}$. Use formula to find laser cut depth per pulse: $d_{cut} = N\ [4/3\ \pi r^3_{bond}]$

Part (b) If instead we assume mechanism is photothermal, then calculate:

(i) Energy per unit volume to raise temperature to boiling point (E_c) from: $E_c = \rho C \Delta T$

(ii) Latent energy for vaporization per unit volume (E_v), from: $E_v = \rho L_v$

(iii) Laser cut depth per pulse from: $d_{cut} = F / (E_v + E_c)$

Part (c) If experiments suggest that a single Excimer laser pulse removes about 300 nm of cornea tissue, then is the LASIK mechanism primarily photoablation or photothermal in nature?

Solution

Part (a)

(i) $E = hc / \lambda = (6.63 \times 10^{-34}$ J-s) $(3 \times 10^8$ m/s) / $(1.93 \times 10^{-7}$ m) $= 1.03 \times 10^{-18}$ J

(ii) $N = F / E$ = (2000 J/m^2) / $(1.03 \times 10^{-18}$ J) $= 1.94 \times 10^{21}$ photons/m^2

(iii) $d_{cut} = N\ [4/3\ \pi r^3_{bond}] = [1.94 \times 10^{21}$ ph/m^2] [4/3 (3.14) $(1.54 \times 10^{-10}$ m)^3] $= 2.97 \times 10^{-8}$ m = 30 nm

Part (b)

(i) $\Delta T = 100\ ^oC - 37\ ^oC = 63\ ^oC = 63$ K

$E_c = \rho C \Delta T = (1 \times 10^3$ kg/m^3) $(4.3 \times 10^3$ J/kg-K) (63 K) $= 2.7 \times 10^8$ J/m^3

(ii) $E_v = \rho L_v = (1 \times 10^3$ kg/m^3) $(2.3 \times 10^6$ J/kg) $= 2.3 \times 10^9$ J/m^3

(iii) $d_{cut} = F / (E_v + E_c)$ = (2000 J/m^2) / $(2.3 \times 10^9$ J/m^3 + 0.27×10^9 J/m^3) $= 7.8 \times 10^{-7}$ m = 780 nm

Part (c) From part (a), our calculations suggest that photoablation removes about 30 nm of tissue per laser pulse while photothermal ablation removes about 780 nm per laser pulse. The photothermal value is the same order of magnitude as the experimental value of 300 nm, but the photoablation value is an order of magnitude smaller. Therefore, the photothermal contribution to LASIK appears to be the dominant mechanism. The short optical penetration depth in cornea tissue at 193 nm can be explained by high absorption from tissue proteins and water, as well as high scattering at the short wavelength.

Self-Test

34. Approximately how thick is the cornea of the eye?
(a) 1 µm (b) 50 µm (c) 500 µm (d) 2 mm

35. In terms of optical properties of the eye, why can we see well?

(a) Low absorption and scattering of light (b) Low absorption, high scattering of light
(c) High absorption and low scattering of light (d) High absorption and scattering of light

36. What type of laser is used for LASIK/PRK procedures on the cornea for vision correction?
(a) Excimer, 193 nm (b) Nd:YAG, 1064 nm (c) Ho:YAG, 2120 nm (d) CO_2, 10,600 nm

6. Lasers in Cardiology

6.1 Introduction

The human cardiovascular system consists of the heart and a vast network of veins and arteries. The anatomy of the heart is shown in Figure 33. It is divided into four compartments. Blood enters the heart through the right artery. It enters the right ventricle through a one-way valve called the *tricuspid valve*. From here, it is pumped into the left lung through pulmonary arteries for oxygenation. The oxygenated blood from the lungs enters the left atrium through pulmonary veins. The blood then passes through the *mitral valve* into the left ventricle. The left ventricle pumps blood through the aortic valve into the arteries of the entire body. The deoxygenated blood returns to the right atrium and the cycle repeats. A variety of causes can prevent the flow of blood through the heart. Congenital diseases can cause abnormal thickening (*hypertrophy*) of any part of the heart muscle. In those cases, no external inorganic substance is responsible for the condition. Aging can cause deterioration of the cardiovascular system. In those cases, inorganic crystals mixed with organic tissue material are usually present. Lasers are used in treating both hypertrophy and age-related deterioration.

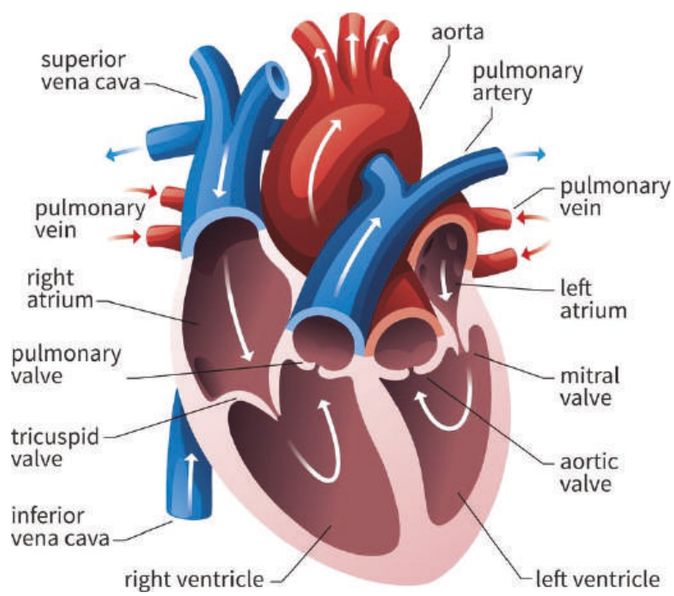


Figure 33. *Schematic diagram of the human heart.*

6.2 Angioplasty

The technique of removal of plaque deposited in the arteries is called *angioplasty*. This usually takes the form of complete removal of the plaque by using short pulses of an Excimer laser or partial removal of the plaque (using the laser) followed by insertion of a tiny balloon. A thin, flexible catheter consisting of a bundle of optical fibers is introduced into the artery in the groin and then manipulated into the coronary artery where the plaque buildup is located. The fiber bundle is connected to a XeCl Excimer laser (308 nm) with microsecond pulses and power outputs on the order of 100 J/cm^2. These laser pulses are delivered through the fiber to ablate the plaque. Despite much hype over laser angioplasty, results have been disappointing, with plaque frequently coming back and creating a stenosis. There is also risk of arterial perforation during the laser ablative procedure.

6.3 Thrombolysis

A *thrombus* is a blood clot in the artery; the disease associated with this condition is called *thrombosis*. Lasers can be used to selectively ablate these organic arterial lumps. A thrombus consists of hemoglobin, which is much more laser-energy-absorbent than an artery for the visible region of the spectrum (400–600 nm). As a result, a thrombus can be vaporized through laser ablation. Frequency-doubled Nd:YAG lasers with millisecond pulses have been successfully used in this treatment.

The process involves a catheter consisting of an optical fiber surrounded by a clear liquid that has a higher refractive index than the hollow tube surrounding it. The output of the Nd:YAG laser is directed through the optical fiber, which is directed towards the thrombosis. As the clot absorbs the laser energy, a portion of it is vaporized. A vapor bubble is formed; the bubble expands and collapses, causing the clot to further disintegrate. The tip of the catheter is open toward the clot so that blood can flow out through the catheter. Laser thrombolysis is another disappointing application of lasers in cardiology that never really became adopted on a wide scale, due in part to safety concerns as well.

6.4 Vascular Anastomosis

Vascular anastomosis is the welding together and re-attachment of blood vessels. Over the past few decades, there has been significant interest in laser welding of blood vessels and other fluid-carrying organs (e.g. ureter, urethra, vas deferens, and bladder), small tissue structures (e.g. nerves), and tissues in general (e.g. skin). The potential advantages of laser welding versus conventional use of sutures, staples, and clips in surgery include improved fluid-tight closure, more rapid repair, less skill and labor needed, and improved cosmetic outcome. There are at least three different approaches to laser re-anastomosis and welding. The first approach is direct laser welding of collagen-rich tissues which produces weak, non-covalent bonds from the thermal coagulation of the tissue and “protein soup” is created. The second approach involves the use of an 808 nm diode laser, whose wavelength closely matches an absorption peak of a biocompatible dye such as indocyanine green (ICG). This dye is mixed with a natural tissue protein, such as albumen or fibrinogen, to create a “solder”. The solder is applied to the closed edges of the tissue, and upon laser heating, it is melted to the tissue surface and acts as a “thermal band-aid” to keep the tissue incision closed long enough for it to gain strength during the wound healing process. The third approach does not involve heat at all. Photochemical tissue welding uses a photoactivated agent to provide strong covalent bonds and tissue closure without any collateral thermal damage. Unfortunately, laser welding is still limited to experimental use, due in part to the large number of laser parameters, inconsistent welds, and a poor understanding of the mechanism. It is also difficult to compete with the familiarity, ease of use, low cost, and high mechanical strengths provided by sutures, staples, and clips. Table 10 summarizes the laser tissue welding approaches discussed above.

Table 10. Experimental Laser Tissue Welding Approaches

	Photothermal Soldering	Photothermal Welding	Photochemical Welding
Objective	Thermal band-aid	Full thickness weld	Heat free weld
Interface	Solder-tissue	Tissue-tissue	Tissue-dye-tissue
Wavelength	808 nm	450-1300 nm	470 nm
Mode	CW	CW or pulsed	CW
Irradiance	High power	High power	Low power
Irradiation time	Short (15 s – 10 min)	Short (15 s – 10 min)	Long (> 10 min)
Dye	Indocyanine green (ICG)	None	Naphthalimides / Riboflavin
Adhesive	Albumin, fibrinogen, chitosan	None	None
Advantages	Fluid-tight seals	Strong welds	No thermal damage
Limitations	Poor solder-tissue adhesion	Thermal damage, inconsistent welds	Variable tissue apposition, long irradiation times

6.5 Transmyocardial Laser Revascularization (TMLR)

The heart requires a constant supply of oxygen-rich blood for survival. The heart receives the blood from the coronary arteries. In patients with *coronary artery disease* (CAD), the arteries are clogged and can no longer deliver enough blood to the heart. *Ischemia* is a general term that refers to an insufficient supply of oxygen to an organ. When the heart muscle does not receive adequate oxygen, the result is the condition called *angina*. Most often, the treatment for angina is *coronary artery bypass surgery*. However, for patients with serious heart disease or those who have already had multiple bypass surgeries, this can be dangerous. TMLR has been tested for these patients. TMLR cannot cure coronary artery disease, but it may reduce the pain due to angina.

In TMLR, a laser cuts tiny channels through heart muscle and into the lower left chamber (left ventricle), which is the strongest and is the heart's main pumping chamber (Figure 33). These channels stimulate growth of small blood vessels in the heart muscle wall (*angiogenesis*), which bring more blood into the heart muscle. TMLR lasers also destroy nerves that cause pain in the heart muscle.

Both Holmium:YAG and CO_2 lasers have been tested for TMLR. The advantage of the Ho:YAG laser is that its energy can be delivered through a small, flexible silica optical fiber, so the procedure can be performed endoscopically, with the fiber physically advanced through the channel as it is created. The advantage of the high-power, 850 Watt, CO_2 laser is that a single laser pulse can be applied between heart beats to drill each channel (with a total of 15-30 one-millimeter channels), and reduce angina, so heart motion does not affect the procedure. TMLR can be done while the heart is still beating and full of blood. The heart does not need to be cut open as in open heart surgery, and a heart-lung machine is not required. Unfortunately, TMLR represents another application of lasers in cardiology that has not been widely adopted due in part to a lack of understanding of the mechanism, a placebo effect among patients, and generally inconsistent results.

6.6 Treatment of Atrial Fibrillation

Atrial fibrillation (AF) is a common abnormal heart rhythm affecting millions of Americans. It is a very fast, uncontrolled heart rhythm that occurs when the upper chambers of the heart (atria) beat too fast (350-600 beats per minute versus normal heart rhythm of 60-100 beats per minute) that they can only quiver, due to abnormal electrical signals on the heart wall (Figure 34). The heart's pumping function is not working properly, so blood is not completely emptied from the heart's chambers, causing it to pool and clot. Clotted blood may dislodge from the atria, causing a stroke.

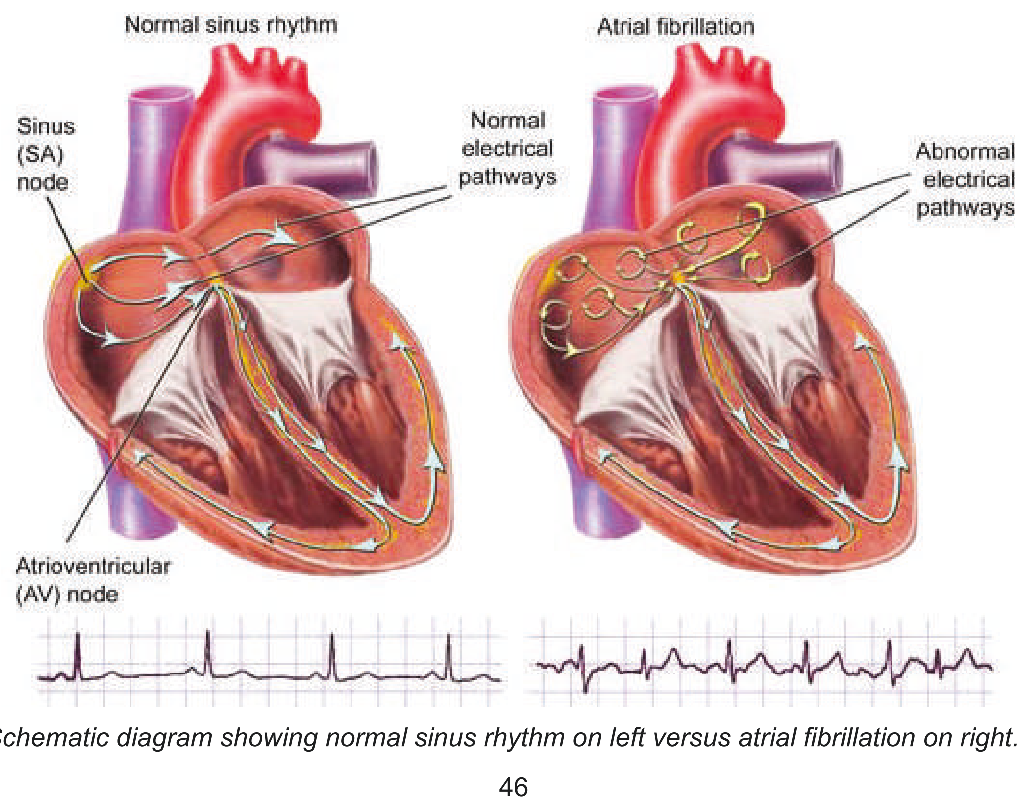
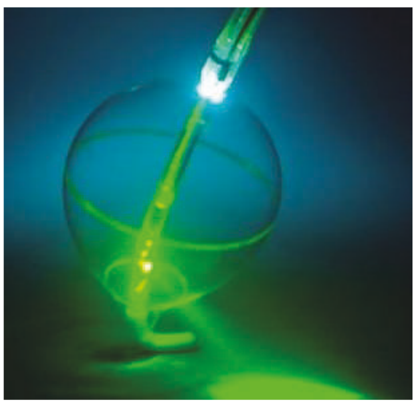


Figure 34. *Schematic diagram showing normal sinus rhythm on left versus atrial fibrillation on right.*

Some patients do not respond well to drug therapy and need alternative minimally invasive methods of treatment. One minimally invasive approach is to insert an energy-based device (e.g. radiofrequency, ultrasound, microwave, cryoablation, or laser) on a catheter into the left atrium under guidance from x-ray fluoroscopy. The catheter then delivers energy to intentionally destroy cardiac tissue along the atrial walls and create scar tissue, which is not electrically conductive and therefore creates electrical conduction blocks. If this scar tissue is strategically created in specific anatomical locations, then the procedure may result in elimination of the stray electrical currents and abnormal electrical pathways, and restore the heart's normal rhythm.

Although use of RF ablation catheters is the conventional approach, there is concern that the RF energy does not consistently penetrate sufficiently deep into the atrial wall to provide a full-thickness thermal lesion, scar tissue, and electrical conduction block. Furthermore, the catheter is immersed in an environment full of blood inside the heart, and the moving blood may carry away much of the heat before it has a chance to create a thermal lesion.

Other energy-based devices which provide deeper penetration of energy, including near-infrared (980 nm) diode lasers, have been used for treatment of AF. Initially, it was believed that a series of linear thermal lesions on the atrial wall would be most effective, however, further anatomical and physiological studies also revealed sleeves of cardiac tissue extending from the left atrium into the pulmonary veins (PV) as well, which also served as sources and pathways for the abnormal electrical signals. Therefore, some ablation catheters utilize a balloon (for anchoring of catheter inside PV) and radial delivery of the energy (e.g. diffusing or side-firing fiber optic tip) to provide a circular or circumferential thermal lesion at 360^o around the entire PV wall (Figure 35).



(a)

(b)

Figure 35. *(a) Flexible balloon catheter used with a rotating side-firing optical fiber to deliver near-IR laser energy to the atrial wall. The green aiming beam is shown as well. (b) Diagram of catheter used in procedure.*

Self-Test

37. Lasers have <u>not</u> been very successful in cardiology in part because of ______.

(a) Safety risk of perforation to arteries (b) Risk of restenosis
(c) Poor understanding of interaction mechanism (d) All of the above

7. Lasers in Gynecology

7.1 Introduction

Lasers are used in a number of procedures in gynecology. While a surgical knife loop electrical excision procedure (LEEP) continues to be used extensively, the use of laser treatments for vaginal and vulvar diseases has grown steadily over the last several years. The CO_2 laser is most often used because of its reduced risk of thermal injury. Since the beam is in the mid-infrared (10.6 μm), fiber optic transmission poses a problem. The beam must be used along with a low-powered, visible laser so diseased tissue can be targeted. In recent years, waveguide delivery systems have been developed, making it easier to reach targeted tissues. Nd:YAG and frequency-doubled Nd:YAG lasers are also used, but less extensively. Nd:YAG lasers are mostly used for deep coagulation.

The CO_2 laser has the further advantage of creating maximum vaporization, minimum lateral scatter, and minimum coagulation. When focused, the beam can be used as a vaporizing tool; when defocused, it can be used for cutting. Typical required power densities are 700–1000 W/cm^2 for cutting and 1000–1200 W/cm^2 for vaporization. The laser can be used both in continuous-wave and pulsed modes. However, the continuous-wave mode is preferred for gynecological procedures.

7.2 Treatment of CIN and CIS Lesions

Cervical intraepithelial neoplasia (CIN) is a disorder of the *uterine cervix* (the entrance to the womb). This results in a change of the surface cells that can lead to malignancy if left untreated. The CIN lesions consist of abnormal cells that actively divide and grow. When a virus called HPV (*human papilloma virus*) infects normal cells, abnormal cells begin to be produced in the transformation zone and a lesion develops. The CIS lesion (*carcinoma in situ*) occurs in the urinary bladder and can be the precursor to bladder cancer. Both types of lesions are treated with CO_2 lasers. The depth of vaporization required varies from 3 to 7 mm. Higher-power densities (> 1000 W/cm^2) and smaller spot sizes are used in treatment of these lesions. Complications from bleeding or *cervical stenosis* are less frequent when the laser is used in cutting mode. To achieve good results with a laser, the entire transformation zone should be treated rather than individual lesions.

7.3 Laparoscopy

Endometriosis is a condition that normally occurs in young women. When endometriosis occurs, tissue that looks like the lining of the uterus grows outside of the uterus in the form of tumors, lesions, and nodules. This condition causes severe pain. Most endometriosis is found on or under the ovaries, behind the uterus, or on the bowels or bladder. Laparoscopy is the preferred surgical technique for removing endometriosis (Figure 36). Doctors remove the growths or destroy them with intense heat. Nd:YAG and frequency doubled Nd:YAG lasers have been successfully used in laparoscopy. They are able to treat the condition without harming healthy tissue around it.

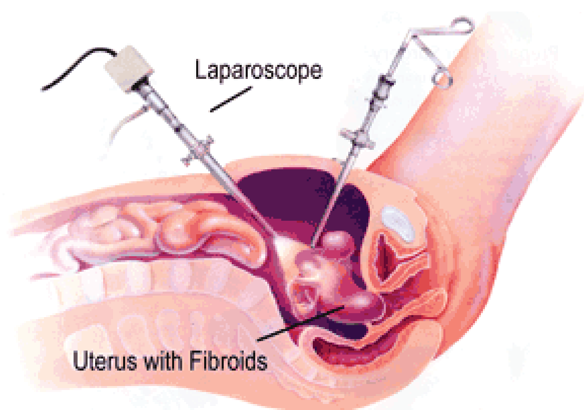


Figure 36. *Diagram showing removal of fibroids attached to the outside of uterus by a stalk using a laparoscope.*

7.4 Myomectomy, Myolysis, and Hysterectomy

Uterine fibroids are growths or tumors that develop in the muscular walls of the uterus. Surgical removal of fibroids is called *myomectomy*. Unlike conventional myomectomy, laparoscopic myomectomy uses several small incisions rather than one large incision.

In *laparoscopic myolysis*, multiple punctures are created on the fibroid using an Nd:YAG laser. In both cases, a laser with 30 to 50 watts of continuous wave power is used. Laser-induced thermal therapy has also been performed with Nd:YAG and frequency doubled Nd:YAG lasers.

Hysterectomy is surgical removal of the uterus. Laser-assisted vaginal hysterectomy (LAVH) is a common type of hysterectomy. It is preferable to conventional electrocautery because the laser cauterizes during the surgery, causing blood loss to be considerably less.

7.5 Treatment of Tubal Disease

One of the causes for infertility in women is *tubal disease*. Tubal infertility includes inflammation of the *fallopian tube* and its connection to the *ovary* in a way that affects the transport of the egg, sperm, or embryo. X-rays and laparoscopy provide a way of categorizing different forms of the condition (Figure 37). These categories can be described as (1) *peritubal* or *periovarian* adhesion, (2) distal tubal obstruction, (3) *isthmo-cornual* block, and (4) reversal of sterilization.

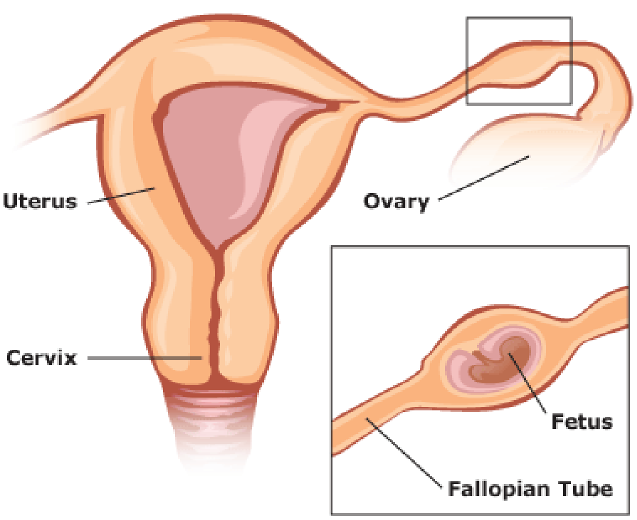


Figure 37. *Schematic diagram showing ectopic pregnancy which can be surgically destroyed using a laser.*

In distal tube obstruction, the tube connecting to the ovary is constricted as a result of inflammation or lesions. A laser can vaporize adhesions between the *fimbria* to create a pathway. This technique is laser-assisted laparoscopy. CO_2 and Nd:YAG lasers have been successfully used in this procedure.

In *ectopic pregnancy*, a fertilized egg is implanted outside the uterus. The egg settles in the *fallopian tubes*, ovary, or abdomen. None of these areas is suitable for fetal development. As the fetus grows, it can burst the organ that contains it and cause severe bleeding, endangering the mother's life. CO_2, Nd:YAG, frequency doubled Nd:YAG, and diode lasers are used to provide *hemostasis* (stoppage of bleeding) by cutting along the length of the tube. After incision of the tube, the products of conception are removed and the incision left to heal by itself. The laser has the advantage that it enables precise incision and hemostasis to occur at the same time. Fiber optic delivery of the beam is used (except for CO_2) because of the ease of reaching the target. In the cases of *isthmo-cornual* blocks as well as reversal of sterilization, CO_2-assisted laparoscopy is employed. The success of laparoscopic techniques using CO_2 lasers is comparable to that of microsurgical techniques.

7.6 Treatment of Vaginal Atrophy

During menopause, women suffer from a lack of estrogen, which can lead to changes in vulva, vagina, and lower urinary tract (Figure 38). Post-menopausal women may experience a variety of symptoms, including vaginal dryness, burning sensations, irritation, absence of lubrication, and painful sexual intercourse. Local estrogen treatment may be effective in treating some of these vaginal changes, the safety data for this type of treatment is still lacking.

Laser therapy or vaginal rejuvenation has recently been introduced for vaginal atrophy. The approach for laser vaginal rejuvenation is very similar to that of fractional laser skin resurfacing and wrinkle removal in cosmetic dermatology. Both CO_2 and Erbium:YAG lasers are used for creating fractional micro-thermal lesions in the tissue to stimulate the production of new collagen growth. The affect is to reorganize the components of the vaginal mucosa. These mid-infrared laser wavelengths are used because the light penetration is superficial, on the order of tens of micrometers. Unlike skin resurfacing, due to the different anatomic location, a side-firing laser probe is used, and is rotated and pulled back in the vaginal canal during the procedure (Figure 39). Laser treatment triggers a tissue regeneration process which lasts several weeks. The vaginal mucosa is more hydrated and has more blood flow, and the epithelium, or outer layer, is thicker, more toned, and elastic. The vaginal wall is in effect rejuvenated, providing a more effective barrier to infection and improved sexual function.

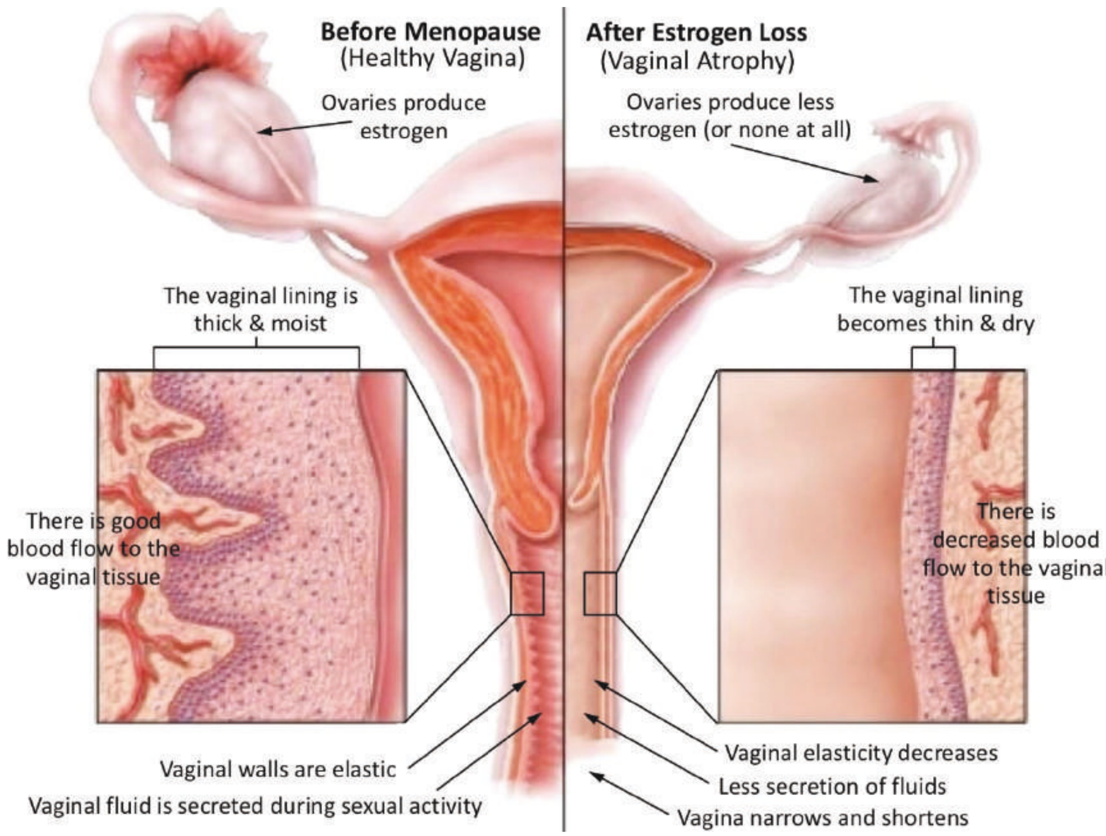


Figure 38. *Schematic diagram comparing healthy vagina before menopause with vaginal atrophy afterwards.*

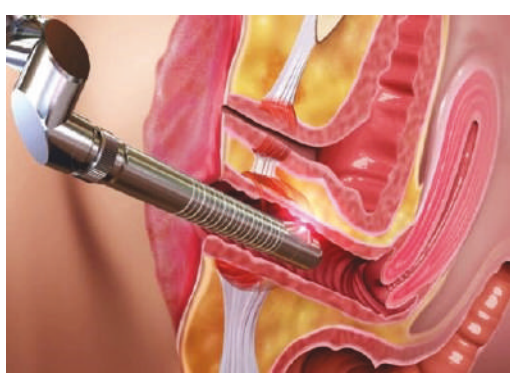


Figure 39. *Diagram showing articulated arm and fractional laser scanning system for vaginal rejuvenation.*

7.7 Treatment of Female Stress Urinary Incontinence

Lasers may also be used to treat female stress urinary incontinence (SUI), although data is still lacking. SUI occurs in women after menopause or childbirth. This condition results in leakage of urine when there is sudden pressure on the bladder and urethra (during forces exerted from exercise, sneezing, laughing, or coughing), causing the sphincter muscles to open temporarily (Figure 40).

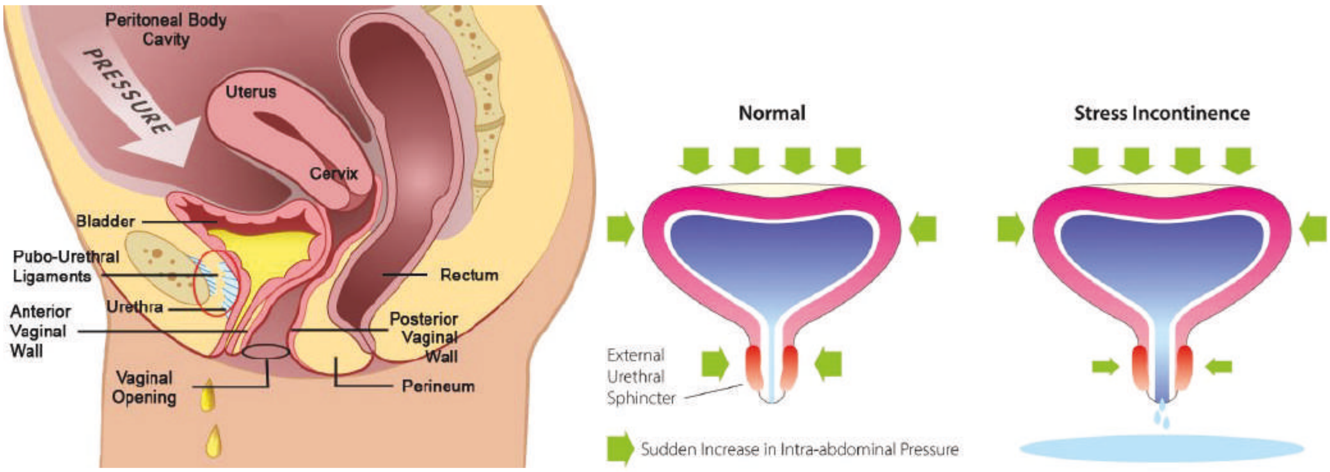


Figure 40. *(a) Anatomy of female lower urinary tract. (b) Changes during female stress urinary incontinence.*

Treatment of SUI in women includes behavioral or non-pharmacologic treatments (e.g. bladder training and Kegel exercises, medication, biofeedback, neuromodulation, surgery, catheterization, or a combination of these therapies). Non-surgical treatments (e.g. Kegel exercises, biofeedback, pelvic floor stimulation) are limited by burdensome compliance and treatment requirements and issues of efficacy and durability. While surgery involving insertion of a synthetic mesh material provides a permanent solution, the need for general anesthesia, long recovery time, incisions, potential treatment failures with future pregnancy, and procedural morbidity lead to patient hesitation to have surgery.

Other energy-based devices (e.g. radiofrequency energy), have been used for transurethral thermal shrinkage and micro-remodeling of submucosal collagen in the bladder neck and proximal urethra for treatment of SUI, but with mixed results. Laser vaginal rejuvenation has reportedly also produced improvement in female continence as well, although long-term data is still lacking. These laser procedures, utilizing Erbium:YAG and CO_2 mid-infrared lasers for treatment of vaginal atrophy and SUI, are performed by surgeons in several different disciplines, in this case, cosmetic dermatologists, female urologists, and gynecologists.

Self-Test

38. Potential applications of lasers in gynecology include treatment of ______.
(a) Uterine fibroids (b) Vaginal atrophy (c) Stress urinary incontinence (d) All of the above

8. Lasers in Urology

8.1 Introduction

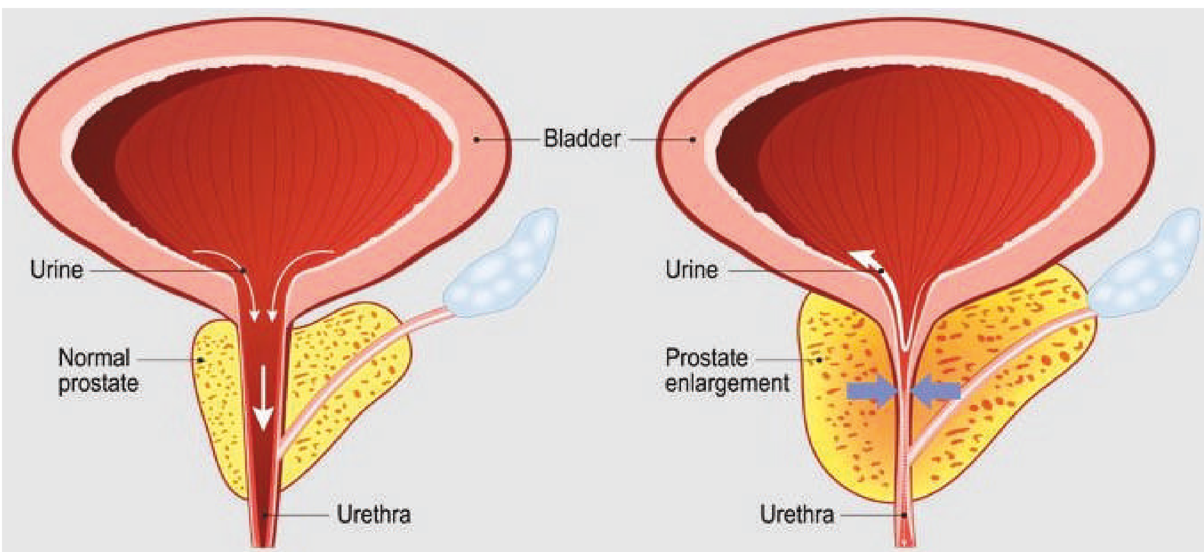
Lasers are used in urology for a variety of procedures, including photothermal coagulation of tumors, incision of ureteral and urethral strictures, and photochemotherapy of bladder cancer. However, the most common laser urology procedures are treatment of benign prostatic hyperplasia (BPH) and kidney stone disease (Table 11).

Table 11. Common Lasers Used in Urology

Laser	Wavelength (nm)	Delivery system	Applications
Frequency doubled Nd:YAG	532	Side-firing, 600-μm-core fiber	Prostate vaporization for BPH
Thulium fiber	1940	≥ 150 μm core fiber	Kidney stones
Th:YAG	2010	Side-firing, 600-μm-core fiber	Prostate incision for BPH
Ho:YAG	2120	200-1000 μm core fiber	Kidney stones; urethral and ureteral strictures; incision of prostate for BPH

8.2 Treatment of Benign Prostatic Hyperplasia (BPH)

Benign prostatic hyperplasia (BPH) in men is a swelling of the prostate gland, resulting in increased pressure on the urethra and inability to properly urinate (Figure 41). This condition may cause severe discomfort. For years, transurethral resection of the prostate (TURP) was the clinical standard, which involves use of an electrosurgical loop to shave off parts of the prostate gland and relieve the pressure. Initially, Nd:YAG lasers were tested as an alternative to TURP for treatment of BPH, however, the Nd:YAG laser energy penetrated too deep through tissues, resulting in undesirable side-effects (e.g. urethral strictures). Over the past few decades, two different laser approaches have become popular for photothermal laser ablation of the prostate gland.



(a) (b)

Figure 41. *(a) Normal prostate gland; (b) Swollen prostate gland observed in benign prostatic hyperplasia, resulting in difficulty in urination.*

The first method uses a frequency doubled Nd:YAG laser, also known as a Greenlight laser, due to its emission of visible green light at a wavelength of 532 nm. This wavelength is desirable because it not strongly absorbed by fluids (urine and water) in the urinary tract, but is strongly absorbed by hemoglobin (blood). The prostate gland is highly vascular and blood loss during treatment of BPH is a concern. The high power (up to 180 W) Greenlight laser light is operated in CW mode and is strongly absorbed by blood in the tissue, resulting in ablation or vaporization, while also providing a sufficient thermal coagulation zone (a few millimeters) for hemostasis. The Greenlight laser is used with a large, 600-μm core side-firing optical fiber, placed in the urethra, and the light is re-directed sideways to vaporize the prostate gland. One advantage of this procedure is that it is easy to learn, but limitations include potential carbonization of the tissue and the smoke that results from it. Also, while the high power Greenlight laser can be used for BPH and other soft tissue procedures, it cannot be used for treating kidney stones, the other main application of lasers in urology.

The second method for treatment of BPH uses a pulsed, infrared Holmium:YAG laser at a wavelength of 2120 nm and average powers up to 140 W for incision and enucleation of the prostate, with a large, 550-μm-core optical fiber. This wavelength is strongly absorbed by water in the prostatic tissue. Unlike the Greenlight vaporization of the prostate, the goal of the Ho:YAG laser is to incise or cut the prostate lobes into chunks, and then push the chunks of tissue up into the bladder. A mechanical morcellator is used to churn up these large chunks into smaller pieces that can then be more easily removed from the urinary tract. One limitation of Ho:YAG laser enucleation of the prostate is that the learning curve is much longer for urologists. However, an advantage of the high power Ho:YAG laser is that it can be used as a single platform for both soft and hard tissue applications, including treatment of kidney stones.

8.3 Treatment of Kidney Stones (Laser Lithotripsy)

Kidney stone disease affects about 10% of the United States population and is becoming more common due to increasing rates of obesity, diabetes, and even climate change. There is no cure for kidney stone disease. Instead, medical and surgical options are considered. Extracorporeal shockwave lithotripsy (ESWL) has long been used for non-invasive ultrasonic fragmentation of kidney stones. However, with recent improvements in laser, fiber optic, and endoscope technologies, minimally invasive laser lithotripsy has overcome ESWL, as a more successful approach to treating small to moderate size (up to 2 cm) kidney stones, with higher postoperative stone-free rates. During this procedure, a small optical fiber is inserted through a flexible ureteroscope inside the urinary tract, and the distal fiber optic tip is placed either in contact with or in close proximity with the stone (Figure 42). A pulsed infrared laser is activated and fragments the stone into smaller pieces through primarily a photothermal mechanism. The stone fragments are then either removed using a stone basket or are spontaneously passed out of the urinary tract.

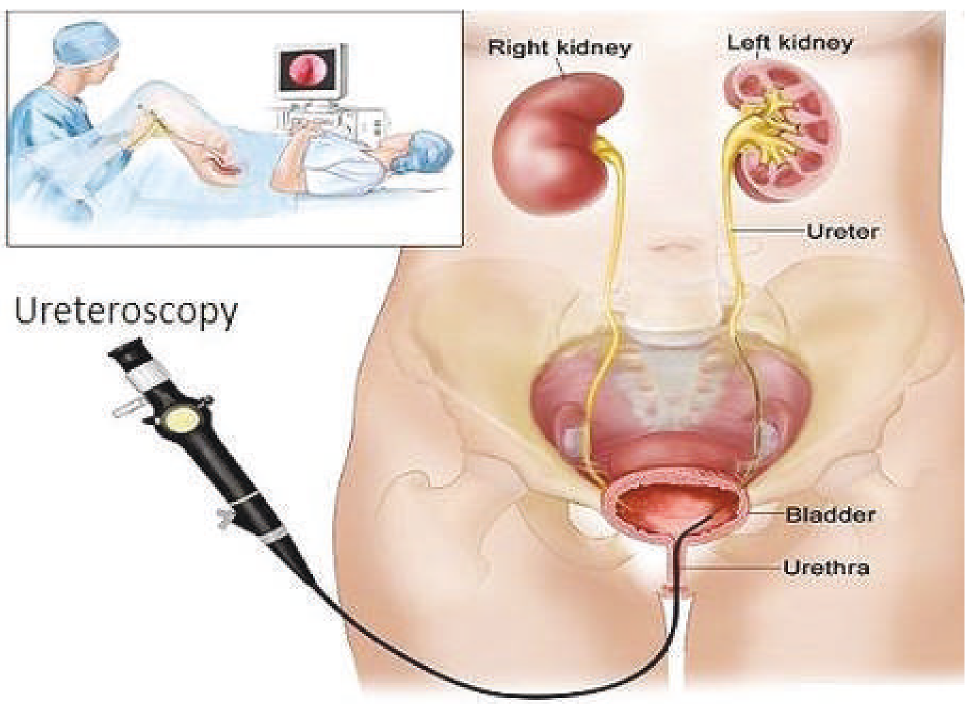


Figure 42. *Laser treatment of kidney stones using an optical fiber inserted through the working channel of a flexible ureteroscope.*

The pulsed, infrared Holmium:YAG laser with a wavelength of 2120 nm has replaced the old, short-pulse, dye lasers for lithotripsy. The Ho:YAG laser is operated in long-pulse mode, with pulse durations of 200-1500 μs. Both low power (20-30 W) and high-power (100-140 W) Ho:YAG lasers are used. The low-power version is limited to use at relatively low pulse rates (10-30 Hz) and cannot be used for treatment of BPH as well. The laser is used primarily at high pulse energies and low pulse rates for "fragmentation" of kidney stones into large pieces. The high-power versions consist of multiple laser cavities that allow high pulse rate operation (up to 100 Hz) for rapid "dusting" of kidney stones into smaller particles, more likely to be spontaneously flushed out of the urinary tract without the need for a stone basket. The higher power lasers also can be used for treatment of BPH. Figure 43 compares stone dusting and fragmentation techniques.

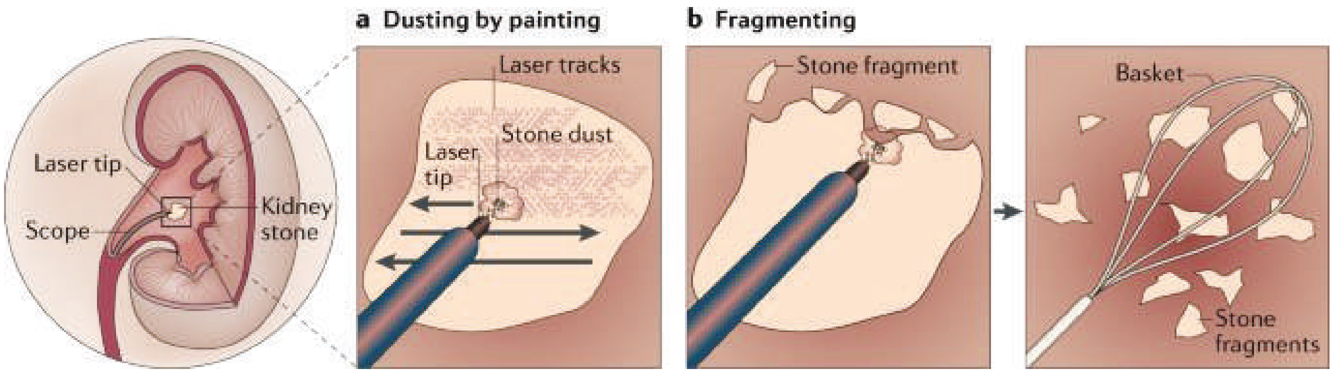


Figure 43. *Comparison of "dusting" and "fragmentation" methods of laser lithotripsy. Dusting uses low laser pulse energy (0.2-0.4 J) and high pulse rates (50-100 Hz) to create small stone particles. Fragmentation uses high pulse energies (0.5-1.0 J) and low pulse rates (5-30 Hz) to create large stone pieces, which are then removed by a stone basket.*

Standard low-hydroxyl silica optical fibers are used with the Ho:YAG laser during lithotripsy. Typical fiber core diameters are 200, 365, 550, and 940 μm, with the smallest, most flexible fibers used to treat kidney stones in the upper urinary tract through flexible ureteroscopes, and the larger sizes used to treat more accessible urinary stones located in the lower ureter or bladder through a rigid ureteroscope.

One challenge of laser lithotripsy is that the stone is free to move during the procedure. When the laser pulses impact the stone surface, it tends to move away from the fiber tip. This effect is referred to as stone "retropulsion". This is undesirable because the surgeon has to chase a moving target, and the stone may inadvertently be pushed from a relatively easy location to access (e.g. the ureter) to a less accessible location (e.g. the lower pole of the kidney). Stone retropulsion may be reduced by using a smaller optical fiber, a lower laser pulse energy, and/or a longer laser pulse duration.

The Thulium fiber laser (TFL) has recently been introduced as a potential alternative to the Ho:YAG laser for lithotripsy. The TFL operates at a wavelength of 1940 nm, more closely matching a water absorption peak in tissues, resulting in a 4-5 times lower stone ablation threshold and higher stone ablation rates than the Ho:YAG laser. Unlike the solid-state, flashlamp-pumped, Ho:YAG laser, which is limited to low pulse rates, the TFL is diode-pumped, making it more efficient and capable of operating at much higher pulse rates (up to 2000 Hz), ideal for stone dusting.

Self-Test

39. Successful laser treatment of benign prostatic hyperplasia (BPH) involves use of ______.
(a) Photothermal coagulation (b) Photodynamic therapy
(c) Photothermal ablation (d) Plasma-mediated ablation

40. Laser "dusting of kidney stones involves the use of _____.
(a) Low pulse energy (b) High pulse rates (c) Long pulse durations (d) All of the above

41. Laser "fragmentation of kidney stones involves the use of _____.
(a) High pulse energy (b) Low pulse rates (c) Short pulse durations (d) All of the above

9. Lasers in Dentistry

9.1 Introduction

Although the potential for lasers to be used in drilling teeth exists, no laser currently available can completely replace the dental drill. However, lasers *are* used in treatment of soft and hard tissues and in welding of dental bridges and dentures. A number of lasers are used in dental procedures, summarized in Table 12.

Table 12. Lasers Used in Dentistry

Laser	Wavelength (nm)	Delivery system	Applications
Diode	980	Optical fiber	Soft tissues, frenectomy, biopsy, pain therapy, teeth whitening
Nd:YAG	1064	Optical fiber	Soft tissues; endodontics, welding appliances
Er:YSGG	2790	Mid-IR specialty fibers	Hard tissues (caries)
Er:YAG	2940	Mid-IR specialty fibers	Hard tissues (caries)
CO_2	9600 10,600	Articulated arm; hollow waveguide; mid-IR specialty fibers	Soft and hard tissues (carries)

9.2 Structure of Human Teeth

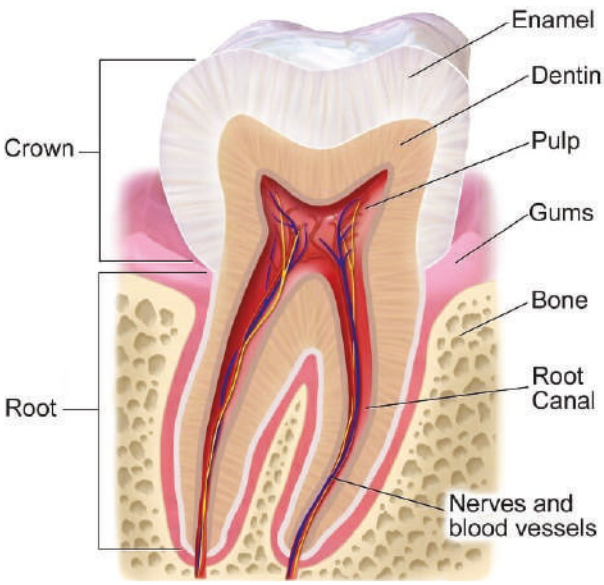
The structure of the human tooth is shown in Figure 44a. The part that is visible above the gum is called the *crown*. The unseen part that anchors the tooth is called the *root*. Some teeth have only one root (*incisors* and *canine teeth*), but others have four roots each (*molars* and *premolars*). The middle portion, the gum, is the *gingiva*. The crown of the tooth is covered by *enamel,* the hardest substance in the human body. Enamel is composed of 95% hydroxyapatite crystals, 4% water, and 1% organic matter. It is not considered a living tissue. The inner layer of the tooth is called *dentin*. It is less hard than enamel and is elastic and compressible. It contains tiny tubules that connect to the central nerve of the tooth, which is located in the next inner layer, the pulp. Below the gum, the dentin is covered with a thin layer of *cementum*. It is a hard, bone-like substance to which the *periodontal membrane* is attached. The membrane bonds the root of the tooth to the jaw bone. The pulp is made of soft tissue and contains blood vessels that supply nutrients to the tooth and nerves, which act as thermal sensors. It also contains small *lymph vessels* that carry white blood cells to the tooth and fight bacteria. The extension of the pulp into the root is called the *root canal*. The root canal is open at the end and connects to surrounding tissue. The tooth's nerves and blood enter the pulp through this opening.

9.3 Tooth Decay

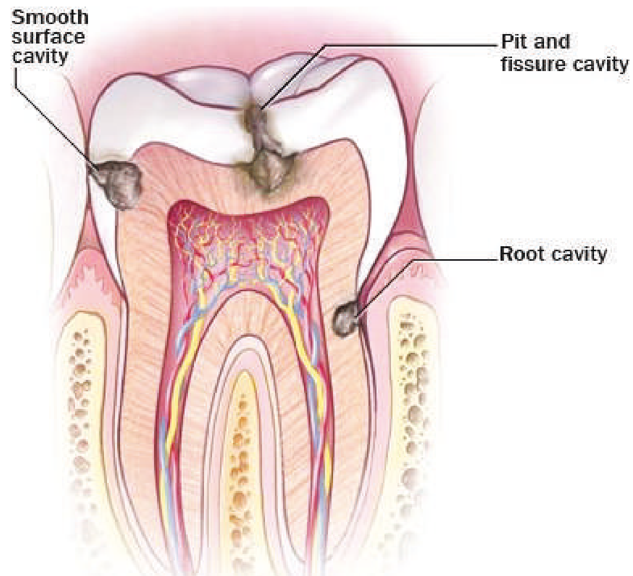
Tooth decay (*caries*) can be caused by malnourishment and lack of proper oral hygiene. Foods containing carbohydrates such as starches and sugars are major causes of tooth decay. Microorganisms will develop and multiply at the tooth surface to form *plaque*. The plaque interacts with food deposits on the teeth. When enough calcium dissolves from the tooth, the tooth's surface breaks down and forms a hole or *cavity* (Figure 44b). This decay can develop over several years. The microorganism can also infect the pulp and its interior, inducing severe pain. In such cases, the infected substance must be removed and the cavity filled by suitable alloys such as ceramics or composites.

The removal of infected substances from teeth is mostly done with a vibrating mechanical drill, which may cause significant discomfort and pain. Tooth nerves are sensitive to the vibration and increases in temperature caused by the drill. If temperature in the pulp of the tooth increases by only 5 ^{o}C, permanent damage to the pulp can occur and the entire tooth may die.

Pulsed IR lasers (e.g. Er:YAG, Er:YSGG, and CO_2) provide several advantages over the conventional dental drill. First, the laser energy may be delivered in non-contact mode, reducing the pain experienced from the vibration of the drill (a major reason why many people are hesitant to see their dentist). Second, if the proper laser parameters (namely a highly absorbing wavelength and a sufficiently short laser pulse duration) are chosen, then selective and precise removal of dental decay can be achieved. Third, the laser is quiet and eliminates concerns over loss of hearing by dentists from the high-frequency noise generated by the dental drill. Fourth, unlike the dental drill, lasers are capable of producing a high aspect ratio (depth/width), thus removing dental decay without the need to also remove large amounts of adjacent healthy tissue. Fifth, lasers can thermally modify the chemical composition of the mineral phase, increasing the resistance to acid dissolution and caries.



(a)



(b)

Figure 44. *(a) Structure of human tooth; (b) Schematic diagram showing tooth decay.*

9.4 Treatment of Soft Dental Tissue

Lesions on the soft dental tissues inside the mouth are common. Some can be malignant, some benign. Removal usually requires surgery. CO_2 lasers can be used to remove these lesions by vaporization. Since the lesions are moist and contain water, the absorption of 10.6 μm laser radiation is very high. Because of this high absorptivity, a 5 to 10 W pulsed or CW laser will vaporize the lesion in non-contact mode to provide a sterile approach. The laser also focuses on a small area and therefore interacts very little with the surrounding tissue. Since small vessels in the lesion are coagulated, no bleeding occurs and no suturing is needed. A defocused beam can be used to smooth the wound's edges.

Recently, diode lasers operating at 980 nm have been utilized as an alternative for ablation and coagulation with hemostasis during soft tissue procedures. Operation in "superpulsed" mode with high peak powers enables higher temperature for non-contact soft tissue ablation, while simultaneously minimizing collateral thermal damage zones. Specialty fiber optic tips incorporating fused carbon and titanium dioxide particles are also used to achieve a hot tip for soft tissue contact applications, where optical energy is efficiently converted to thermal energy at the distal fiber optic tip. Sophisticated temperature monitoring and feedback systems enable automated control of the fiber tip temperature for more consistent and reproducible surgical results.

9.5 Removal of Filling Materials

Sometimes it is necessary to remove older dental fillings when tooth decay occurs below the fillings. Er:YAG lasers have been used for this procedure, as well as for removal of dental enamel, dentin, and caries (Figure 45). Using lasers minimizes damage to adjacent hard surfaces. Lasers should never be used to remove amalgam. The mercury vapor released can be dangerous to the patient and the dentist.

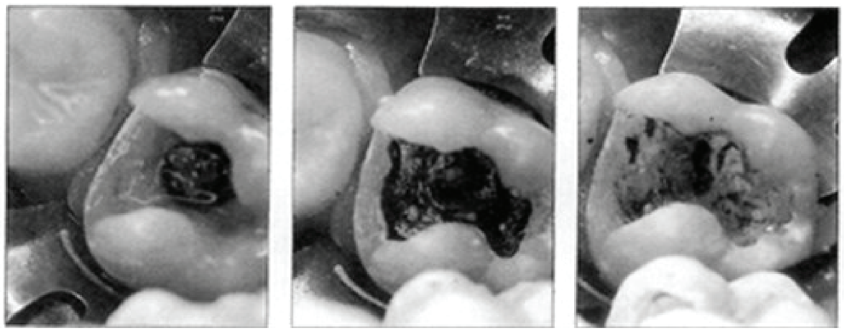


Figure 45. *Use of lasers to remove carbonized material from a tooth.*

CO_2 and Nd:YAG lasers have been used to weld dental bridges and dentures. Lasers eliminate the need for an additional substance for soldering. They fuse the two welded substances by transferring them to a fluid state. Laser-welded fixtures have a higher tear threshold than soldered samples. Laser-welded bridges have a higher resistance to corrosion. Lasers also have the advantage of being able to weld different metals and coated alloys.

Table 13. Lasers for Hard Tissue Removal

Laser	Wavelength (nm)	Pulse Duration (μs)	Radiant Exposure (J/cm^2)	Residual Heat (%)
Er:YSGG	2,790	0.150 150	80 100-200	39 58
Er:YAG	2,940	0.150 150	80 260	45 61
CO_2	9,600	5 20-30 100	15 50 57	24 33 56
CO_2	10,600	5	40	33

Example 6

Temperature rise and percent residual heat left in teeth (ratio of peak temperature of ablative pulse to peak temperature of sub-ablative pulse) was measured for laser removal of dental caries. Using Table 13 above, choose the best laser wavelength and pulse duration for this procedure and explain why.

Solution

The laser wavelength and pulse duration providing the lowest percentage of residual heat in tissue during laser vaporization of dental decay is 9,600 nm (CO_2 laser) and 5 μs. As pulse duration is increased for all wavelengths, % residual heat also increases because thermal confinement is not satisfied at longer pulse durations. More heat leaks out of the treatment zone during the pulse. However, using short, Q-switched pulse durations (< 1 μs) is less efficient and cause unwanted photomechanical effects in hard tissue (e.g. cracks).

Self-Test

42. The most precise laser wavelength used for removal hard tissues in treatment of caries is ___.
(a) Diode, 908 nm (b) Nd:YAG, 1064 nm (c) Er:YAG, 2940 nm (d) CO_2, 9600 nm

43. The most appropriate laser for soft tissue removal and hemostasis is the ____.
(a) Diode, 980 nm (b) Ho:YAG, 2120 nm (c) Er:YSGG, 2940 nm (d) Er:YAG, 2940 nm

44. What advantages over the dental drill do lasers have?
(a) More precise removal of decayed tissue (b) Less pain experienced by patient
(c) Less hearing loss by dentist (d) All of the above

10. Lasers in Neurosurgery

10.1 Introduction

Lasers have not been used on a widespread basis in the field of neurosurgery. Experimental applications such as micro-anastomosis of nerves have not proven successful. However, recently, laser interstitial thermal therapy (LITT) has gained popularity in neurosurgery for magnetic resonance image (MRI) guided laser ablation of both inoperable brain tumors and epileptic centers.

10.2 MRI-Guided Laser Ablation for Brain Tumors and Epilepsy

MRI has long been used as a reliable, high resolution, non-ionizing, non-invasive, diagnostic method for whole brain imaging and diagnosis of neurological diseases. However, MRI can also be used for real-time measurement of temperatures deep inside the body (e.g. inside the brain). Most recently, these diagnostic capabilities of MRI have been combined with therapeutic thermal coagulation of brain tumors that are resistant to conventional drug and radiation therapy and focal centers of epilepsy. There are numerous different energy-based devices that can be used for destruction of tissue, including electrocautery, radiofrequency electrosurgery, therapeutic ultrasound, microwaves, and cryoablation. However, lasers have one major advantage over all of these other energy-based devices, in that the energy delivery system, a glass optical fiber, is completely compatible with MRI systems (no RF interference and no forces on metallic components.)

During MRI-guided laser ablation in neurosurgery, a low-power (10-15 W) near-infrared diode laser (980 or 1064 nm) is placed outside the MRI suite, in a separate shielded room, containing the computers and other equipment (Figure 46). Then a long (400- or 600-μm core diameter) optical fiber is connected to the laser on its proximal end, and inserted through an applicator into the brain, on its distal end. Sometimes a robotic arm is used for precision placement of the fiber optic applicator. The optical fiber has either a side-firing tip or a diffusing tip for radial delivery of the laser energy. The fiber optic applicator also contains water or gas cooling for preventing fiber overheating and tissue carbonization near the tissue surface during the procedure. As the laser is activated and the diseased tissue volume is irradiated, an MRI temperature map is superimposed over the anatomical MRI image, to provide real-time temperature data and confirm a sufficient thermal dose to coagulate and destroy the abnormal tissue, while also preventing collateral thermal damage to surrounding healthy tissue.

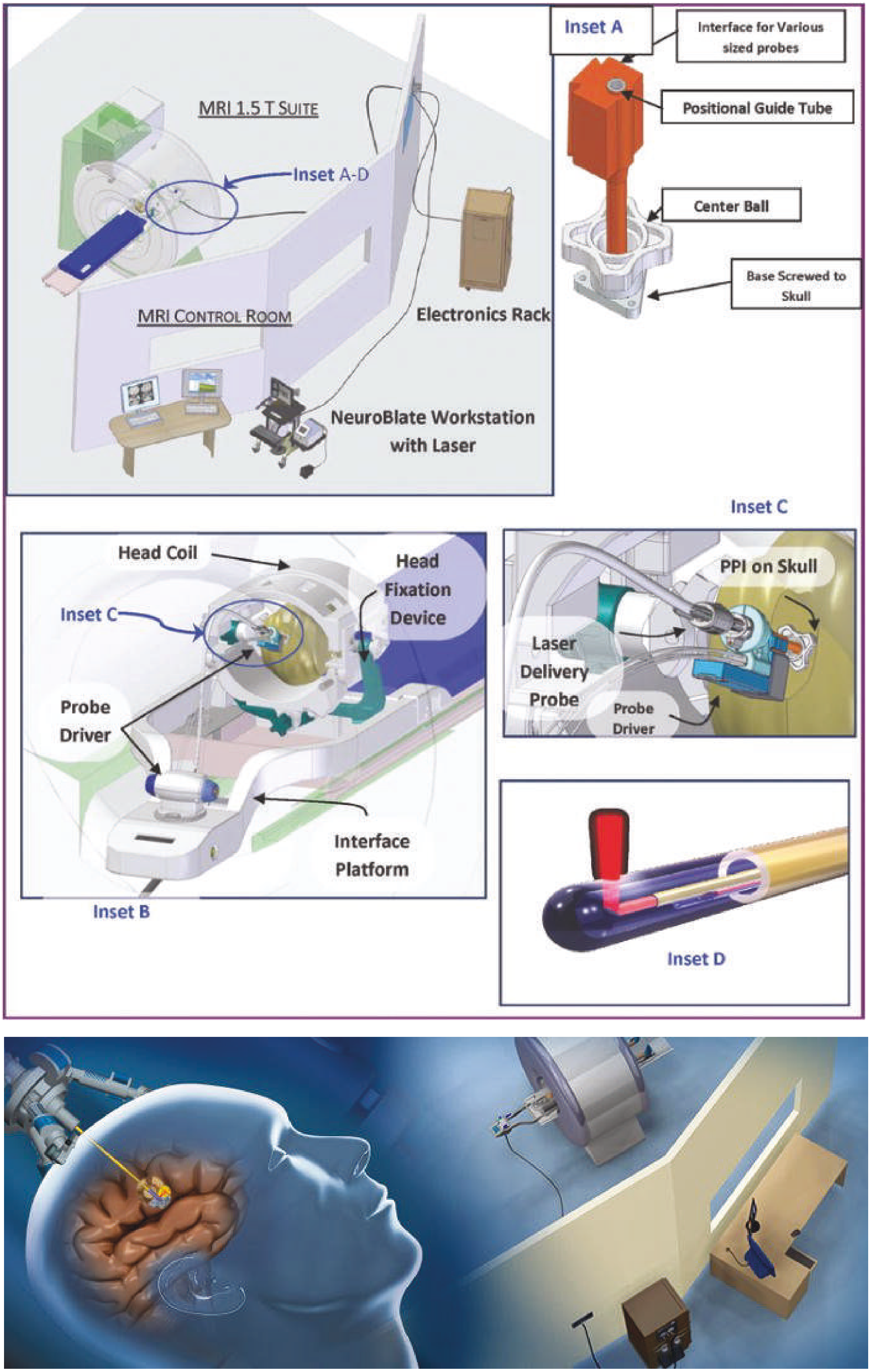


Figure 46. *Layout for the MRI suite, laser, and fiber delivery system.*

10.3 Infrared Nerve Stimulation (INS)

Electrical current is typically used to activate nerves during electrophysiology measurements and medical devices inside the body, such as pacemakers for heart pacing, cochlear implants for hearing aids, nerve stimulators for bladder function, and detection of the cavernous nerves responsible for erectile function on the surface of the prostate gland, to name a just few medical applications. However, electrical nerve stimulation (ENS) has several limitations, including the need to be in contact with the nerves, poor spatial selectivity due to electrical current spreading in tissues, and presence of electrical stimulation artifacts due to use of the same mode of electrical current for both stimulation and detection. Recently, low power (tens of milliwatts) near-infrared, pulsed laser energy has been introduced as a potential alternative method of nerve activation. Infrared nerve stimulation (INS) has several potential advantages over conventional ENS, including the capability of non-contact stimulation using light, improved spatial selectivity with the ability to activate individual nerve branches or fascicles, and the elimination of artifacts due to stimulation with light but detection with electrical current.

Initial experimental INS studies used infrared Holmium:YAG lasers with a wavelength of 2120 nm, to provide an intermediate optical penetration depth of about 400 μm in water, roughly matching the diameter of peripheral nerves for uniform irradiation. The long pulse duration of the Ho:YAG laser, a few hundred microseconds, provides a temporal temperature gradient in the nerve, believed to open temperature-dependent ion channels at the molecular level. Spatial temperature gradients provided by the laser spatial beam profile also contribute to the photothermal mechanism of INS. The range of nerve temperatures for safe and efficient INS is relatively small, from about 42 ^{o}C for threshold nerve activation to about 47 ^{o}C for onset of undesirable thermal damage to the nerve. This corresponds to a radiant exposure of about 0.3 J/cm^2 and damage threshold of about 0.7 J/cm^2.

Experimental studies have examined the combination of electrical pulses for "priming" the nerve prior to infrared stimulation to attempt to increase the effective window of laser parameters for successful stimulation. Closed-loop temperature feedback systems have also been tested with INS systems to provide real-time feedback and adjustment of the laser parameters for safe and effective INS.

For potential clinical applications, the relatively large and expensive flashlamp-pumped, solid-state Ho:YAG laser has been replaced with compact diode laser sources at wavelengths near 1440 and 1870 nm, where water absorption peaks in tissue provide approximately the same 400 μm penetration depth in tissue as at 2120 nm. All of these laser wavelengths can easily be delivered through standard silica optical fibers for flexible delivery.

Despite the presence of these more smaller diode laser sources, one of the primary challenges preventing widespread integration of INS techniques into implantable medical devices is still the lack of extremely compact laser sources with sufficient energy output to be integrated into pacemakers or cochlear implants. The safety of INS and concern over potential thermal damage to nerves is also a continued concern preventing clinical use.

Self-Test

45. What laser wavelength is used for creation of large thermal lesions during MRI-guided laser interstitial thermal therapy (LITT) of brain tumors and epileptic centers?

(a) Excimer, 193 nm (b) Frequency-doubled Nd:YAG, 532 nm
(c) Nd:YAG, 1064 nm (d) CO_2 laser, 10,600 nm

46. Why does MRI-guided LITT of brain tumors use lasers instead of radiofrequency (RF), ultrasonic (US), or microwave devices?

(a) Laser energy penetrates deeper than microwaves (b) Lasers are less expensive than RF
(c) Laser fibers are compatible with MRI systems (d) All of the above

47. What advantage(s) does infrared nerve stimulation provide over conventional electrical nerve stimulation for activation of nerves?

(a) Elimination of electrical stimulation artifacts (b) Non-contact stimulation of nerves
(c) Better spatial selectivity for stimulating nerve branches (d) All of the above

11. Photodynamic Therapy (PDT) and Ultraviolet Therapy

11.1 Introduction

Although the vast majority of successful therapeutic applications of lasers involve a photothermal mechanism, as noted in the numerous applications described above, there are also photochemical applications as well. As previously noted, photochemical interactions with tissue usually occur at lower irradiances, below 1 W /cm^2, and on long time scales of minutes. In these applications, the light energy is transferred either to a photodynamic agent, known as a *photosensitizer*, or to the tissue molecules directly, and serves as a catalyst for initiating a chemical reaction in the tissue.

11.2 Photodynamic Therapy (PDT)

Photodynamic therapy (PDT), also known as light-based chemotherapy, uses red or near-infrared wavelengths matching the absorption peak of an administered photosensitizing agent, to generate either singlet oxygen or other reactive oxidizing species, which are toxic at the cellular level and destroy cancer cells and abnormal tissues. The three components necessary for photodynamic therapy are light, a PDT drug, and oxygen. PDT is FDA-approved for a number of clinical applications, including treatment of Barrett's esophageal cancer, late-stage lung cancer, benign skin diseases such as acne and psoriasis, as well as macular degeneration in ophthalmology. An advantage of PDT over conventional chemotherapy treatment includes elimination of side-effects (e.g. fatigue, pain, nausea, hair loss, and mouth sores). PDT treatment steps are shown in Figure 47.

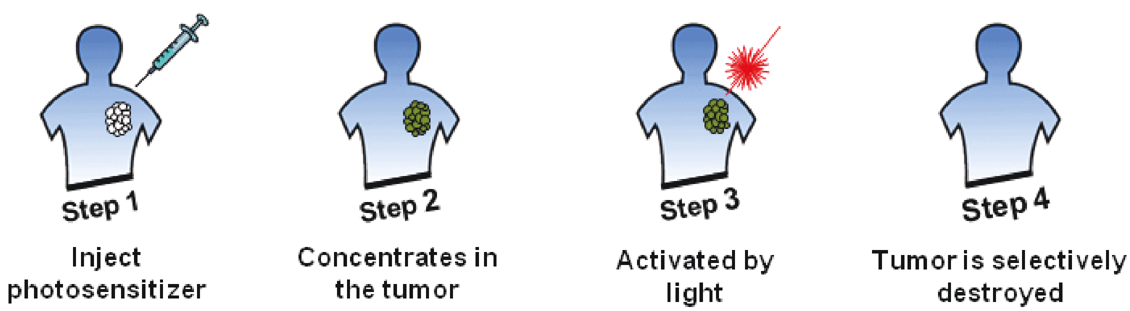


Figure 47 *Steps taken during photodynamic therapy (PDT) treatment.*

There are three major mechanisms involved in PDT treatment. The first mechanism is direct targeting of cancer cells. For cellular targeting, there are two pathways. In the first pathway, the photosensitizer concentrates in the mitochondria of the cell, leading to photodamage by apoptosis, otherwise known as programmed cell death or cell suicide. The second pathway involves photosensitizer localization in the plasma membrane, or cell membrane, resulting in necrosis through loss of cell membrane integrity, rupture, and permeability. The second mechanism is injury to the blood vessels that feed the tumor, resulting in indirect destruction of cancer cells. In this mechanism, vascular damage occurs through platelet activation, thrombosis, vasoconstriction, or increased permeability, leading to a stoppage in blood flow and cell hypoxia, or cell death due to lack of oxygen. The third mechanism is immunological in nature, where a strong inflammatory response provides an additive effect in tumor cell destruction.

Unfortunately, the field of PDT has advanced rather slowly due to several major limitations. One challenge is the need to develop better photosensitizers that absorb light at longer wavelengths in the near-infrared spectrum, where light penetrates deeper into the body, so that larger tumors and thickness tissues can be more effectively treated. Some progress has been made in this respect, as shown in Table 14.

Table 14. Photosensitizers for Photodynamic Therapy

Photosensitizer	Structure	Peak Absorption Wavelength (nm)	Approved	Trials	Cancer Types
Porfimer sodium (Photofrin) (HPD)	Porphyrin	630	Worldwide		Lung, esophagus, bile duct, bladder, brain
ALA	Porphyrin	635	Worldwide		Skin, bladder, brain, esophagus
ALA esters	Porphyrin	635	Europe		Skin, bladder
Temoporfin (Foscan) (mTHPC)	Chlorine	652	Europe	USA	Head and neck, lung, brain, skin, bile duct
Verteporfin	Chlorine	690	Worldwide	UK	Ophthalmic, pancreatic, skin
HPPH	Chlorine	665		USA	Head and neck, esophagus, lung
SnEt2 (Purlytin)	Chlorine	660		USA	Skin, breast
Talaporfin (LS11, MACE, NPe6)	Chlorine	660		USA	Liver, colon, brain
Ce6-PVP (Fotolon), Ce6 derivatives (Radachlorin, Photodithazine)	Chlorine	660		Belarus, Russia	Nasopharyngeal, sarcoma, brain
Silicon phthalocyanine (Pc4)	Phthalocyanin	675		USA	Cutaneous T-cell lymphoma
Padoporfin (TOOKAD)	Bacteriochlorin	762		USA	Prostate
Motexafin lutetium (Lutex)	Texaphyrin	732		USA	Breast

A second challenge involves developing photosensitizers that are not only biocompatible, but also do not result in residual photosensitization of the body after the treatment is completed, which has been a common side-effect of early, first generation photosensitizers, such as photofrin. It is inconvenient for patients to have to wear make-up, cover their skin, or in general avoid exposure to sunlight for days or weeks after treatment.

Finally, another challenge involves development of real-time diagnostic feedback (e.g. fluorescence, imaging, or both) to confirm that sufficient light, drug, and oxygen are all present at the local treatment site in tissue to completely destroy the tumor. The dosimetry of PDT is difficult. For example, too little drug or light will not produce a sufficient therapeutic effect. Too much drug can result in *dark toxicity*, or the drug concentration producing a toxic effect throughout the body in the absence of light. Too much light delivered to the tissue may result in *photobleaching* of the drug, changing its absorption properties, making the drug ineffective. Figure 48 shows the challenges of PDT dosimetry.

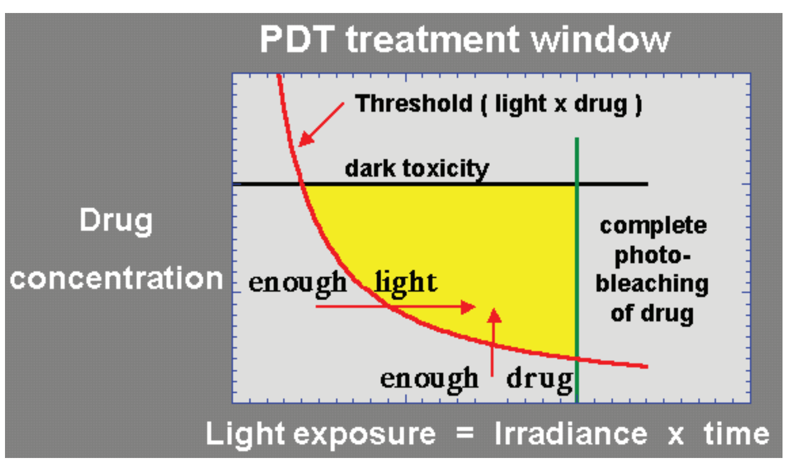
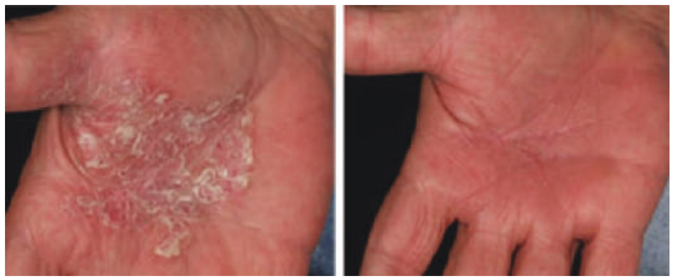


Figure 48. *Dosimetry during photodynamic therapy treatment.*

11.3 Ultraviolet (UV) Light Therapy

Photochemical treatments also include direct application of UV laser wavelengths for treatment of skin disorders such as acne, psoriasis, fungis, and vitiligo. One successful example is the use of a Xenon Chloride Excimer laser operating at a UV-B wavelength of 308 nm to induce cell death through apoptosis during treatment of psoriasis, a skin disease that results in thick, scaly, dry, and itchy skin (Figure 49).



Before After

Figure 49. *The Xenon Chloride excimer laser operating at a UV wavelength can treat psorisias.*

Self-Test

48. What needs to be present at the tissue treatment site for photodynamic therapy?
(a) Oxygen (b) Light (c) Photosensitizer (d) All of the above.

49. What wavelength is most commonly used with a photosensitizer in photodynamic therapy?
(a) Ultraviolet (b) Visible (c) Near-infrared (d) Mid-infrared

50. What wavelength is most commonly used for light-based chemotherapy in tissue directly, without the presence of a photosensitizer?
(a) Ultraviolet (b) Visible (c) Near-infrared (d) Mid-infrared

51. An advantage of photodynamic therapy over conventional chemotherapy is elimination of _____.
(a) All drugs from body (b) Dosage calculations (c) Systemic side-effects (d) All of the above

Answers to Self-Tests

1. c	2. a	3. c	4. d	5. b	6. a	7. d
8. a	9. a	10. c	11. b	12. d	13. d	14. a
15. c	16. a	17. b	18. a	19. c	20. b	21. d
22. a	23. c	24. d	25. b	26. a	27. b	28. a
29. b	30. d	31. d	32. d	33. b	34. c	35. a
36. a	37. d	38. d	39. c	40. d	41. d	42. d
43. a	44. d	45. c	46. c	47. d	48. d	49. b
50. a	51. c					

Module Review Questions

1. Which parameter dominates laser-tissue interactions in the mid-infrared spectrum?
   a. Absorption coefficient
   b. Refractive index
   c. Scattering coefficient
   d. Anisotropy factor

2. Which parameter dominates laser-tissue interactions in the near-infrared spectrum?
   a. Absorption coefficient
   b. Refractive index
   c. Scattering coefficient
   d. Anisotropy factor

3. The frequency doubled Nd:YAG laser wavelength of 532 nm is strongly absorbed by what major tissue chromophore?
   a. Water
   b. Blood
   c. Collagen
   d. Elastin

4. Which of the following lasers provides the deepest penetration depth in soft tissues?
   a. Excimer
   b. Frequency doubled Nd:YAG
   c. Nd:YAG
   d. CO_2

5. Why is the 193 nm wavelength of the Excimer laser strongly attenuated in soft tissues?
   a. Strong absorption by tissue proteins
   b. Strong absorption by water
   c. High scattering of light
   d. All of the above

6. The vast majority of successful laser applications in medicine rely on which mechanism?
   a. Plasma-induced ablation
   b. Photoablation
   c. Photothermal
   d. Photochemical

7. Which is <u>not</u> an advantage of plasma-mediated tissue ablation?
   a. Rapid ablation of large tissue volumes
   b. Precise tissue ablation
   c. Ablation mechanism is independent of laser wavelength
   d. Noncontact ablation of transparent tissues

8. Which of the following is an example of photomechanical tissue ablation?
   a. Skin resurfacing for removal of wrinkles
   b. Fragmentation of hardened lenses or cataracts
   c. Removal of port-wine stains
   d. MRI-guided laser ablation of brain tumors

9. The principle of selective photothermolysis is used in which of the following clinical procedures?
   a. Tattoo removal
   b. Hair removal
   c. Removal of vascular birthmarks and port-wine stains

   d. All of the above

10. Selective photothermolysis requires which of the following laser parameters?
    a. A laser wavelength strongly absorbed by the target tissue structure but not adjacent healthy tissue
    b. A laser pulse duration shorter than the calculated thermal time constant
    c. Sufficient cooling between laser pulses to prevent thermal buildup in the tissue
    d. All of the above

11. Collateral thermal damage to adjacent tissue in laser surgery may be undesirable because
    a. It can result in damage to sensitive tissues (e.g. nerves)
    b. It can delay wound healing
    c. It can result in more scarring
    d. All of the above

12. Precise photothermal tissue ablation requires which of the following criteria?
    a. A high absorption coefficient and low optical penetration depth in the targeted tissue structure
    b. A laser pulse energy much higher than the threshold for tissue ablation
    c. A laser pulse duration shorter than the thermal time constant but not too short
    d. All of the above

13. The approximate tissue temperature needed to thermally coagulate tissue is approximately ____.
    a. 0 ^{o}C
    b. 37 ^{o}C
    c. 60 ^{o}C
    d. 100 ^{o}C

14. Human body temperature is approximately ___.
    a. 0 ^{o}C
    b. 37 ^{o}C
    c. 60 ^{o}C
    d. 100 ^{o}C

15. Water in tissue starts to boil and vaporize at a temperature of ___.
    a. 0 ^{o}C
    b. 37 ^{o}C
    c. 60 ^{o}C
    d. 100 ^{o}C

16. Why is continuous-wave mode laser ablation of soft tissue sometimes desirable?
    a. To provide both tissue vaporization and thermal coagulation for hemostasis
    b. To provide ultra-precise removal of tissues
    c. To prevent scarring of the tissues during wound healing
    d. All of the above

17. An example of photochemical tissue application in laser medicine is ___.
    a. Laser interstitial thermal therapy for treatment of a tumor
    b. Photodynamic therapy for treatment of esophageal cancer
    c. Pulsed laser tissue ablation of dental caries
    d. None of the above

18. Which of the following mechanisms of laser tissue interaction uses the lowest intensity lasers and the longest exposure times?
    a. Plasma-induced ablation
    b. Photodisruption
    c. Photochemical
    d. Photothermal

19. During plasma-induced laser tissue ablation, a plasma consisting of ____ is formed in the tissue.
    a. High density of electrons and nuclei that are separated
    b. Water
    c. Blood
    d. Collegen

20. For total internal reflection of light to occur within the optical fiber core, what needs to be satisfied?
    a. The refractive index of the core has to equal that of the cladding
    b. The refractive index of the core has to be greater than that of the cladding
    c. The refractive index of the core has to be less than that of the cladding
    d. The fiber has to have a thick buffer or coating on the outside of the fiber

21. When are articulated arms used instead of optical fibers in laser medicine applications?
    a. At laser wavelengths deep in the ultraviolet or in the mid-infrared spectrum
    b. When laser scanning of large surface areas of tissues is needed
    c. When very high power lasers are used
    d. All of the above

22. As the numerical aperture of an optical fiber is increased, what happens at the output end of the fiber?
    a. The light has greater divergence or spreads out more
    b. The light is collimated
    c. The is better focused to a smaller spot
    d. None of the above

23. As an optical fiber is bent into a tighter circle, what happens to light rays traveling down the fiber?
    a. The light will become more concentrated within the core of the fiber
    b. More of the light will leak through the core and enter the cladding of the fiber
    c. The optical fiber transmits a higher percentage of light down the fiber
    d. There is no significant change in the properties of the fiber

24. Light traveling down an optical fiber can be lost due to ____.
    a. Absorption by impurities in the fiber
    b. Scattering of light by impurities in the fiber
    c. Leakage of light through fiber under tight bending conditions
    d. All of the above

25. Standard silica optical fibers are commonly used in laser medicine because ____.
    a. They efficiently transmit light across the visible and near-infrared spectrum
    b. They are flexible for use in endoscope applications inside the body
    c. They are inexpensive and biocompatible
    d. All of the above

26. The major limitation of standard silica optical fibers is that ____.
    a. They are too small and delicate to be used in medicine and surgery
    b. They are too expensive to manufacture
    c. They cannot transmit light in the deep ultraviolet and mid-infrared spectrum
    d. All of the above

27. The percentage of light lost due to back-reflections at each endface of a silica optical fiber is about ____.
    a. 0%
    b. 1%
    c. 4%
    d. 10%

28. The percentage of light lost due to back-reflections at each endface of a hollow waveguide measures ____.

a. 0%
b. 1%
c. 4%
d. 10%

29. What is the approximate thickness of the epidermis in the skin?
    a. 1 μm
    b. 10 μm
    c. 100 μm
    d. 1000 μm

30. What is the approximate thickness of the dermis in the skin?
    a. 0.1 mm
    b. 0.5 mm
    c. 3 mm
    d. 10 mm

31. Diode laser for hair removal have been replaced by less expensive optical systems, including ____.
    a. Ultrashort pulse laser systems
    b. Fiber lasers
    c. Intense pulsed light (IPL) sources
    d. All of the above

32. Which of the following lasers is used for tattoo removal?
    a. Nd:YAG (1064 nm) and frequency doubled Nd:YAG (532 nm)
    b. Ruby (694 nm)
    c. Alexandrite (755 nm)
    d. All of the above

33. If a large laser spot size is used for laser tattoo removal, how can ink particles be targeted for removal?
    a. Using the principle of selective photothermolysis
    b. The laser beam is eventually focused down to a small spot within the tissue
    c. The ink particles are large enough to align the laser beam on them
    d. None of the above

34. What is the approximate diameter of the human eye?
    a. 5 mm
    b. 10 mm
    c. 25 mm
    d. 50 mm

35. What is the approximate thickness of a healthy human cornea?
    a. 50 μm
    b. 100 μm
    c. 500 μm
    d. 5000 μm

36. The cornea and most soft tissues are primarily composed of ___.
    a. Water
    b. Collagen
    c. Hemoglobin
    d. Melanin

37. What part of the electromagnetic spectrum transmits the highest percentage of light in the eye?
    a. Ultraviolet
    b. Visible and near-infrared

c. Mid-infrared
d. Far-infrared

38. The Excimer laser operates in which part of the spectrum for precise corneal shaping?
    a. Ultraviolet
    b. Visible
    c. Near-infrared
    d. Mid-infrared

39. What type of laser is used for photocoagulation of the retina?
    a. Excimer
    b. Frequency doubled Nd:YAG
    c. Holmium:YAG
    d. Erbium:YAG

40. LASIK corneal shaping is based on what primary mechanism?
    a. Plasma-induced ablation
    b. Photodisruption
    c. Photochemical
    d. Photothermal

41. During PRK/LASIK corneal shaping procedures, the laser beam delivered to the cornea using a
    a. Standard low-hydroxyl silica optical fiber
    b. Hollow waveguide
    c. Free beam in air
    d. Articulated arm

42. Which laser wavelength provides the most precise removal of dental hard tissue decay or caries?
    a. 1064 nm
    b. 2790 nm
    c. 9,600 nm
    d. 10,600 nm

43. The pulp of the tooth is extremely sensitive to small temperature increases, so how is laser removal of caries achieved without destroying the tooth?
    a. Through deep, uniform heating
    b. By selective photothermolysis using pulsed lasers with shallow penetration depths
    c. By photomechanical ablation
    d. None of the above

44. Which of the following is a successful application of lasers in cardiology?
    a. Angioplasty
    b. Atrial fibrillation
    c. Thrombolysis
    d. Vascular re-anastomosis

45. The primary interest in laser re-anastomosis of blood vessels has been ___.
    a. Sealing of large blood vessels
    b. Less expensive alternatives to sutures and clips
    c. Fluid-tight closure of small vessels
    d. All of the above

46. Laser tissue welding has for the most part been a failed application due in part to ___.
    a. Low tensile strengths of laser welds
    b. Inconsistent tissue welds
    c. Complexity in performing the procedure

   d. All of the above

47. Which energy-based device provides an alternative to lasers for thermal coagulation of tissue?
    a. Radiofrequency electrosurgical systems
    b. Microwaves
    c. Therapeutic ultrasound
    d. All of the above

48. The major advantage of lasers versus other energy-based devices is that lasers can provide ____.
    a. Selective and precise removal of tissue
    b. Deeper heating of tissues
    c. Less expensive treatment options
    d. All of the above

49. What type of fiber optic tip is used during endovenous laser therapy?
    a. Diffusing tip
    b. Straight tip
    c. Side-firing tip
    d. Tapered tip

50. Laser cartilage shaping is used in medicine for surgical reconstruction. What tissues and organs have large amounts of collagen?
    a. Ears
    b. Nose
    c. Trachea
    d. All of the above

51. Why is MRI used during laser ablation of brain tumors and epileptic centers during neurosurgery?
    a. To provide high resolution images of the brain tumor before surgery
    b. To noninvasively measure temperatures during laser interstitial thermal therapy
    c. To avoid the use of ionizing radiation when imaging the brain
    d. All of the above

52. The laser technology and treatment method for treatment of vaginal atrophy most closely resembles what other procedure in laser medicine?
    a. Skin resurfacing for wrinkle removal
    b. Corneal shaping
    c. Cartilage reshaping
    d. Hair removal

53. What color light source does photodynamic therapy typically utilize with the photosensitizer, Photofrin?
    a. Blue
    b. Green
    c. Red
    d. Yellow

54. Typically photodynamic therapy laser parameters are ____.
    a. Low power
    b Continuous-wave light source
    c. Irradiation time on the scale of minutes
    d. All of the above

Solutions

1. a
2. c
3. b
4. c
5. d
6. c
7. a
8. b
9. d
10. d
11. d
12. d
13. c
14. b
15. d
16. a
17. b
18. c
19. a
20. b
21. d
22. a
23. b
24. d
25. d
26. c
27. c
28. a
29. c
30. c
31. c
32. d
33. a
34. c
35. c
36. a
37. b
38. a
39. b
40. d
41. c
42. c
43. b
44. b
45. c
46. d
47. d
48. a
49. a
50. d
51. d
52. a
53. c
54. d

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Glossary

(listed in Alphabetical Order)

Aberration: Optical aberrations are properties of optical systems such as lenses, in which abnormal deviations of light paths in the eye result in light rays spreading out rather than being focused.

Ablation: The removal of tissue through vaporization.

Absorption coefficient: A measure of how strongly tissue absorbs light.

Anastomosis: A surgical procedure to connect two tissue structures, usually tubal structures, such as blood vessels or intestines.

Angina: A condition of severe chest pain due to inadequate blood flow to the heart.

Angiogenesis: The development of new blood vessels.

Angioplasty: Procedure to clear a blocked blood vessel, typically an artery, to restore blood flow.

Anisotropy factor: The average cosine of the angle providing the direction at which a photon is scattered.

Articulated arm: A series of hollow tubes, joints, and mirrors used to reflect light.

Aqueous humor: The clear fluid filling the space in front of the eyeball between the cornea and the lens.

Attenuation: The loss of light through either absorption and/or scattering.

Benign Prostatic Hyperplasia: BPH is a benign condition with an enlarged prostate gland.

Biocompatible: Not harmful to living biological tissues.

Buffer: The outermost layer of an optical fiber, also sometimes referred to as the jacket, which provides protection and mechanical support for glass fibers under ending conditions, as well as insulation from the surrounding environment. The layer is commonly made of a polymer material.

Carbonization: The formation of a charred surface layer on the tissue with continued heating after the tissue has become completely dried out, or desiccated.

Caries: Formation of cavities in teeth caused by bacteria.

Cataract: the opacification or clouding of the lens in the eye, which leads to a loss of vision.

Catheter: A flexible tube inserted through a narrow opening into a body cavity to perform a clinical procedure or remove fluid from an organ, for example, the bladder.

Chromophore: A part of a molecule that absorbs light at a specific wavelength and is responsible for its color.

Cladding: The outer layer of an optical fiber that reflects light during total internal reflection.

Coagulation: The removal of tissue through heating and necrosis or cell death, where the connective tissue proteins undergo thermal denaturation.

Coherence: A property of light when the photons travel in phase.

Collagen: The main structural protein found in large amounts in skin and other connective tissues.

Continuous-wave: The property in which light is emitted continuously without interruption.

Core: The innermost layer of an optical fiber in which the light travels.

Cornea: A transparent layer forming front of the eye, which also acts as the outermost lens for focusing light

Coronary artery disease: A conditions when the arteries that supply blood to the heart muscle becomes hardened and narrowed.

Critical angle: Light rays traveling at a greater angle than the critical angle will be totally internally reflected, while light rays traveling at a lesser angle will be refracted through the interface.

Cystoscope: An endoscope used to access the lower urinary tract, including the urethra and bladder.

Dark toxicity: The toxic effects of a photosensitizer drug use din photodynamic therapy, on the body in the absence of light activation.

Dentin: Hard, bony tissue forming the bulk of the tooth, below the enamel.

Denaturation: The breaking of bonds in a protein macromolecule, resulting in a loss of its structure.

Depigmentation: Lightening of the skin due to loss of pigment.

Dermis: The thick layer of living tissue below the epidermis, in the skin, containing blood vessels, nerves, hair follicles, sweat glands, and other structures.

Diopter: A unit of measurement of the optical power of a lens or curved mirror, which is equal to the reciprocal of the focal length. Diopters are measured in inverse meters.

Distal: The far end or output end of a system, for example of an optical fiber or endoscope.

Ectopic pregnancy: A pregnancy in which the fetus develops outside the uterus, typically in a fallopian tube.

Enamel: Hard calcified tissue covering the dentin in the crown of the tooth.

Endovenous: Inside the vein.

Endoscope: A telescope used to see inside a natural opening in the body.

Endothelium: A cell layer that covers the inner surface of a tissue.

Epidermis: The surface outer layer of the skin, overlying the dermis.

Epithelium: A cell layer that covers the outer surface of a tissue.

Extracorporeal shockwave lithotripsy: ESWL uses focused ultrasonic waves emitted from outside the body to fragment kidney stones into smaller pieces for spontaneous removal from the urinary tract.

Fallopian tubes: The pair of tubes in a woman along which eggs travel from the ovary to the uterus.

Fluoroscopy: A medical imaging technique that uses continuous x-rays, or an x-ray movie, to track motion within the body, for example the insertion of medical instruments such as catheters with radiopaque markers.

Fovea: A small depression in the retina of the eye, where visual acuity is highest. The center of the field of vision is focused in this region.

Fundus camera: A specialized low power microscope designed to photograph the interior surface of the eye, including the retina. The fundus is the part of the eyeball opposite the pupil.

Gaussian: A bell shaped curve.

Hemoglobin: A red protein responsible for transporting oxygen in the blood.

Hemostasis: A stop in the flow of blood.

Hygroscopic: Tending to absorb water or moisture.

Hyperopic: Farsightedness, or not able to see objects that are near.

Hypopigmentation: A condition in which the skin is lighter than normal due to the insufficient production of melanin.

Hysterectomy: A surgical operation to remove all or part of the uterus.

Insufflation: The act of blowing CO2 gas into body cavities to separate tissues and provide improved workspace, visibility, and safety during laparoscopic surgery.

Irradiance: The power density.

Ischemia: Inadequate blood supply to an organ or part of the body, especially the heart muscles.

Laparoscope: A telescope inserted through a small incision in the skin to see inside the body.

Laser-Assisted In situ Keratomileusis: LASIK uses an ultraviolet laser to vaporize corneal tissue for vision correction, after the top flap of the cornea has been removed.

Laser Interstitial Thermal Therapy: LITT typically involves the use of a near-infrared laser with deeply penetrating laser energy, delivered through an optical fiber, and placed inside a tumor, for thermal coagulation and destruction of the tumor.

Lenticule: A precise, lens-shaped disk of tissue within the cornea.

Lumen: The hollow inside of an object, for example a blood vessel or working channel of endoscope. A lumen is also a quantity giving the power of a light source.

Macular degeneration: A degenerative condition affecting the central part of the retina, or macula, resulting in loss of vision, typically in older adults.

Mean free path: The distance that a photon is likely to travel before being either absorbed or scattered.

Melanin: A dark brown or black pigment found in hair, skin, and the iris of the eye. It is responsible for the tanning of skin exposed to sunlight.

Mid-infrared spectrum: Part of the electromagnetic spectrum referring to light with wavelengths longer than about 3000 nm, as defined by the medical field.

Mode-locked: Delivery of light in very short pulses on the order of picoseconds to femtoseconds.

Monochromatic: Light that has a single narrow wavelength.

Morcellator: A surgical instrument that minces or cuts bigger chunks of tissue into smaller ones during laparoscopic surgery, for easier removal from the body.

Multimode: For an optical fiber, multiple or many modes of light propagation, or different paths, are supported by the fiber core.

Myopic: Nearsightedness, or not able to see objects far away.

Near-infrared spectrum: Part of the electromagnetic spectrum referring to light with wavelengths greater than 700 nm, but less than approximately 3000 nm, as defined by the medical field.

Necrosis: Cell death

Numerical aperture: Sine of the half angle for light either entering or leaving an optical fiber.

Optical penetration depth: The depth at which light penetrates a tissue before being attenuated or lost (due to absorption and scattering), where the irradiance decays to 1/e or 37% of its initial value at the tissue surface.

Optic nerve: Pair of cranial nerves, transmitting electrical impulses from the retina to the brain.

Percutaneous: The medical device is delivered through the skin (e.g. a needle biopsy) typically in a minimally invasive manner.

Percutaneous nephrolithotomy: PCNL uses a small incision made in the back or abdomen to remove kidney stones that are too large to be removed using endoscopic methods or shockwave lithotripsy.

Photoablation: A specific term used to describe high energy, short pulse delivery of ultraviolet light capable of directly breaking chemical bonds in tissue.

Photobleaching: Loss of color or absorption properties of a photosensitizer drug during photodynamic therapy, due to excessive light irradiation of the drug.

Photochemical: The process in which light is absorbed by the tissue and contributes to a chemical reaction at the molecular level.

Photodisruption: The process by which photomechanical processes lead to tissue tearing, poration, and/or fragmentation through the production of mechanical waves.

Photodynamic therapy: PDT is a minimally invasive, light based chemotherapy treatment involving delivery of red light to a photosensitive drug which has selectively accumulated at a tumor site. The presence of light, drug, and oxygen produces a chemical reaction and singlet oxygen, which is toxic to cancer cells.

Photomechanical: The process in which light is absorbed by the tissue, resulting in rapid thermal expansion and buildup in pressure within the tissue target, leading to mechanical effects in the tissue.

Photorefractive Keratectomy: PRK uses an ultraviolet laser to vaporize corneal tissue for vision correction, unlike LASIK, the top part of the cornea is not removed during the procedure.

Photofrin: The trade name for the first FDA-approved photosensitizer used in photodynamic therapy. It absorbs red light and produces singlet oxygen, toxic to cells.

Photosensitizer: A photodynamic therapy drug applied topically to the skin or injected into the bloodstream, that is selectively accumulates in tissues, and produces singlet oxygen toxic to cells, when exposed to light.

Photothermal: The process by which light is converted into heat, resulting in a temperature rise in the tissue.

Plasma: an ionized gas composed of charged particles.

Polychromatic: Light that consists of a broad band of multiple wavelengths.

Port-wine stains: Birthmark involving the development of abnormal small blood vessels with a dark red color similar to the color of port wine.

Potassium Titanyl Phosphate: A KTP crystal used with the Neodymium:YAG laser to double the frequency and half the wavelength, from 1064 nm in the infrared spectrum to 532 nm in the visible (green) spectrum.

Protein: A large molecule that is an essential structural component of tissues.

Proximal: The near end or input end of a system, for example an optical fiber or endoscope.

Q-switched: Delivery of light in short pulses on the order of nanoseconds.

Reduced scattering coefficient: This parameters takes into account the directional scattering or anisotropy factor, g, in providing a more accurate representation of the effects of light scattering.

Refractive index: The ratio of the speed of light in vacuum divided by the speed of light in a medium.

Retina: A layer at the back of the eye containing cells that are sensitive to light and that trigger nerve impulses that pass via the optic nerve to the brain, where a visual image is formed.

Retropulsion: Movement of a kidney stone away from the fiber optic tip.

Scattering coefficient: A measure of how strongly tissue scatters light.

Sclera: The white outer layer of the eyeball.

Selective photothermolysis: The principle behind many photothermal laser applications, in which a pulsed laser emitting light with a sufficiently short laser pulse duration and a wavelength strongly absorbed by the tissue target, but not the surrounding tissue, is capable of selectively destroying the tissue target while minimizing collateral thermal damage to adjacent healthy tissues.

Single mode: For an optical fiber, only one mode of light propagation, or path, is supported by the fiber core.

Slit lamp: A lamp that emits a narrow but intense beam of light, used for examining the interior of the eye.

Spatial beam profile: The shape or structure of the laser beam, providing information on how the energy is distributed in space across the laser spot.

Stratum corneum: The outermost layer of the epidermis and primary barrier between the skin and environment.

Temporal beam profile: The shape or structure of the laser pulse, providing information on how the energy is distributed during the duration of a single laser pulse.

Total attenuation coefficient: This parameter takes into account both the absorption and scattering coefficients.

Total internal reflection: The process of light traveling down the core of an optical fiber and being reflected multiple times at the core/cladding interface.

Transmyocardial laser revascularization: TMLR is a procedure that uses a laser to make small channels in heart tissue to relieve heart pain and restore vascularization of the tissue.

Transurethral resection of the prostate: TURP is a procedure in which an instrument is inserted through the urethra to cut away a section of an enlarged prostate gland in men that is preventing normal urination.

Trocar: An access port to internal organs during laparoscopic surgery. It may consist of a sharp cutting point for piercing the skin, hollow tube for introducing laparoscopic instruments, and air- and fluid-tight seal for preventing CO_2 gas and bodily fluids from escaping. Insufflation, the delivery of CO_2 gas into a body cavity is common during laparoscopic surgery to separate tissues for improved workspace, visibility and safety

Ultraviolet spectrum: Part of the electromagnetic spectrum referring to light with wavelengths shorter than 400 nm.

Umbilicus: The hollow opening of a tube.

Ureteroscope: a rigid or flexible endoscope used to access the upper urinary tract, including the ureter and kidneys.

Uterine fibroids: Noncancerous abnormal growth in or on a woman’s uterus that may cause severe abdominal pain and heavy periods.

Varicose veins: Swollen, twisted veins caused by weakened or damaged vein walls, and located underneath the skin usually in the legs.

Visible spectrum: Part of the electromagnetic spectrum referring to light with wavelengths in the range of 400-700 nm.

Vitreous humor: The transparent gelatin like medium filling the eyeball behind the lens.

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Figure 5. Professor Nathaniel Fried, Introduction to Biomedical Optics lecture, University of North Carolina at Charlotte.

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