The Abdus Salam International Centre for Theoretical Physics

United Nations Educational, Scientific and Cultural Organization

IAEA International Atomic Energy Agency

1931-3b

Preparatory School to the Winter College on Micro and Nano Photonics for Life Sciences

4 - 8 February 2008

Fundamentals of laser-tissue interaction

Imrana ASHRAF ZAHID

Quaid-I-Azam University
Pakistan

Fundamentals of Laser-Tissue Interaction

Imrana Ashraf Zahid

Quaid-i-Azam University

Islamabad Pakistan

Layout

Introduction

Interaction of light with matter

Reflection and Refraction of light

Fresnel Equations

Absorption of Light

Lambert’s and Beer’s law

Scattering of Light

Optical Properties of Tissues

Thermal Properties of Tissues

Effect of Light on Tissue

Introduction

- Monochromaticity of laser light is responsible for its selective effect on biological tissues.
- When light hits a tissue it can be transmitted, scattered, reflected or absorbed – depending upon the type of tissue and the wavelength (color) of the light.
- Light absorption must take place for there to be any biological effect, and a given wavelength of light may be strongly absorbed by one type of tissue and be transmitted, reflected or scattered by another.

Interaction of light with matter

- When a beam of light is incident on a slice of matter three effects exist which may interfere with its undisturbed propagation:
- Reflection and refraction
- Absorption
- Scattering

Interaction of light with matter cont'd

- Reflection and refraction - strongly related to each other by Fresnel's laws
- Refraction –displacement of the transmitted beam.
- Only non-reflected and non-absorbed or forward scattered photons are transmitted by the slice and contribute to the intensity detected behind the slice

Reflection and Refraction of light

- **Reflection – is defined as the returning of electromagnetic radiation by surface upon which it is incident.**
- **Reflecting surface is the physical boundary between two materials of different indices of refraction such as air and glass or air and tissue.**

Types of Reflection

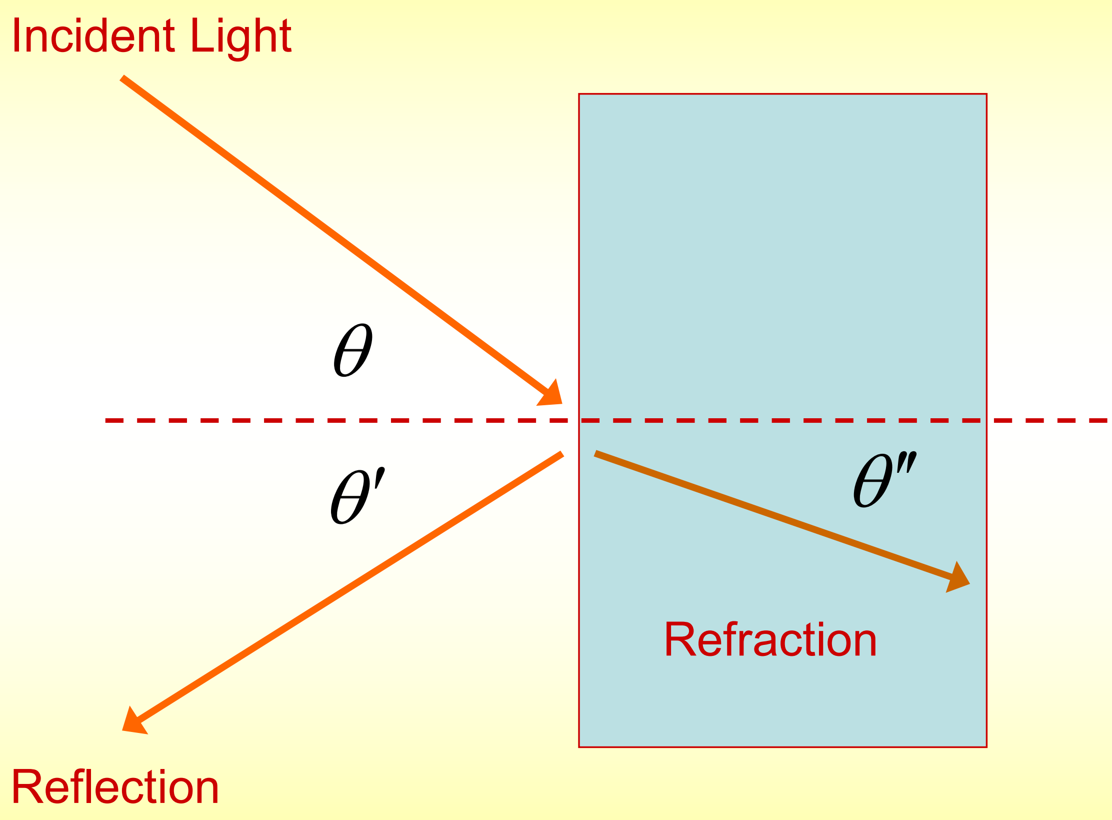
Two major types of reflection

1. **Specular Reflection**
2. **Diffuse Reflection**

Specular Reflection

- The reflection from a smooth surface – with surface irregularities being small compared to the wavelength of the radiations

$$\theta = \theta'$$



Specular Reflection cont'd

- Reflection occurs when the reflecting surface separates two media of different indices of refraction.

Snell's Law $\frac{\sin\theta}{\sin\theta''} = \frac{v}{v'}$ θ'' → Angle of refraction

v & v' → Speeds of light in the medium before and after the reflecting surface, respectively.

Corresponding index of refraction are

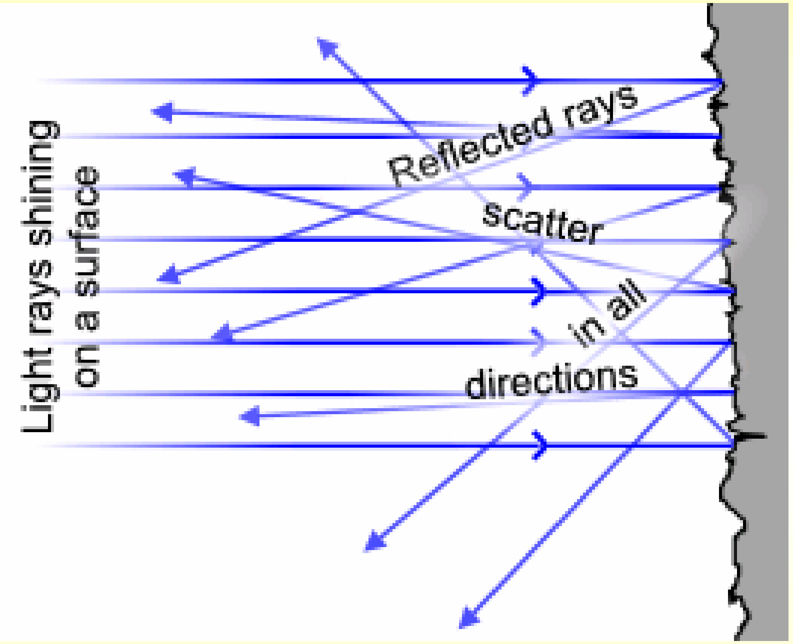
$$n = \frac{c}{v} \quad n' = \frac{c}{v'} \quad \Rightarrow \quad n\sin\theta = n'\sin\theta''$$

c – Speed of light

For $\sin\theta > \frac{n'}{n}$ Total reflection

Diffuse Reflection

- When the roughness of the reflecting surface is comparable or even larger then the wavelength of radiation- diffuse reflection occurs.
- Several beams are reflected which do not necessarily lie with in the plane of incident and θ=θ' no longer applies.



Reflectivity

- The reflectivity of a surface is a measure of the amount of reflected radiation- the ratio of reflected and incident electric field amplitudes.
- Reflectance – ratio of the corresponding intensities

  = Square of reflectivity

Reflectivity and Reflectance

•Depend on the angle of incidence, the polarization of radiation, and the indices of refraction of the materials forming the boundary surface.

• Relations b/w reflectivity and refraction are given by Fresnel's Equations.

Fresnel's Equations

$$\frac{E'_s}{E_s} = -\frac{\sin(\theta-\theta'')}{\sin(\theta+\theta'')} \qquad \frac{E'_p}{E_p} = \frac{\tan(\theta-\theta'')}{\tan(\theta+\theta'')}$$

$$\frac{E''_s}{E_s} = \frac{2\sin\theta''\cos\theta}{\sin(\theta+\theta'')} \qquad \frac{E''_p}{E_p} = \frac{2\sin\theta''\cos\theta}{\sin(\theta+\theta'')\cos(\theta-\theta'')}$$

$E \rightarrow$ Electric field of incident wave

$E' \rightarrow$ Reflected

$E'' \rightarrow$ Refractive

The subscripts "s" and "p" two planes of oscillations

s – perpendicular and p – parallel to plane of incidence

Fresnel's Equations cont'd

The reflectance in either plane are given by

$$R_s = \left(\frac{E'_s}{E_s} \right)^2 \qquad R_p = \left(\frac{E'_p}{E_p} \right)^2$$

The angle at which R_p=0 is called the Brewster angle.

For $\theta = \theta'' = 0$ $\quad R_p = \frac{0}{0}$ indeterminate

For small θ tangents equal to sines.

$$R_p \approx R_s = \frac{\sin^2(\theta - \theta'')}{\sin^2(\theta + \theta'')} \simeq \left(\frac{n' - 1}{n' + 1} \right)^2$$

Brewster's Angle

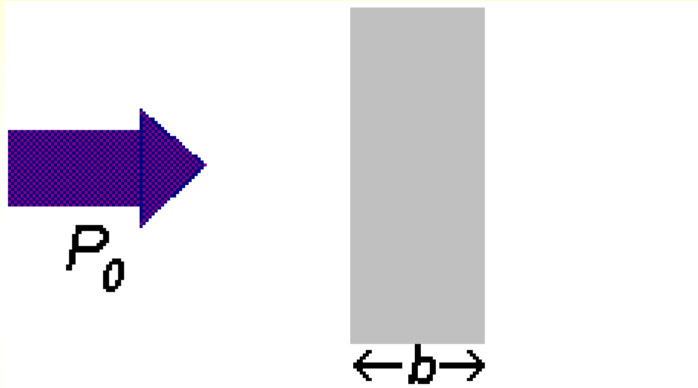
- The angle of incidence at which light with one particular polarization cannot be reflected -is called Brewster's angle.
- The polarization for which the electric field of the light waves lies in the same plane as the incident ray and the surface normal – cannot be reflected.
- Light with this polarization is said to be *p-polarized*-it is parallel to the plane.

Absorption of Light

- **The intensity of an incident electromagnetic wave is attenuated in passing through a medium.**
- **The absorption of a medium is defined as the ratio of absorbed and incident intensity.**
- **Absorption is due to partial conservation of light energy into heat or certain vibrations of the molecules of the absorbing material.**

Absorption of Light cont'd

- A perfectly transparent medium permits the passage of light without any absorption i.e., the total radiant energy entering into and emerging from such a medium is the same.
- In contrast, media in which incident radiation is reduced practically to zero are called opaque.
- The terms transparent and opaque are relative, since they certainly are wavelength dependant.



Absorption of Light cont'd

- The ability of a medium to absorb electromagnetic radiation depends on:

1. The electronic constitution of its atoms and molecules
2. The wavelength of radiation
3. The thickness of absorbing layer
4. The temperature or concentration of absorbing agents

- Two laws are applied to describe the effect of either thickness or concentration on absorption:

Lambert's law and Beer's law

Lambert's and Beer's law

Lambert's law

$$I(z) = I_o \exp(-\alpha z)$$

Beer's Law

$$I(z) = I_o \exp(-k^{'} c z)$$

z- optical axis
I (z) – Intensity at a distance z
Io – Incident intensity
α – Absorption coefficient of the media
c – is the concentration of the absorbing agent
$k^{'}$ - Depends on internal parameter other than concentration

Lambert's and Beer's law cont'd

- Both laws describe same behavior of absorption – known as Lambert-Beer Law.

$$z = \frac{1}{\alpha} \ln \frac{I_0}{I(z)}$$

The inverse of absorption coefficient α is also referred to as absorption length L

$$L = \frac{1}{\alpha}$$

L – measures the distance z in which I(z) has droped to 1/e of incident value I_0.

Types of Absorption

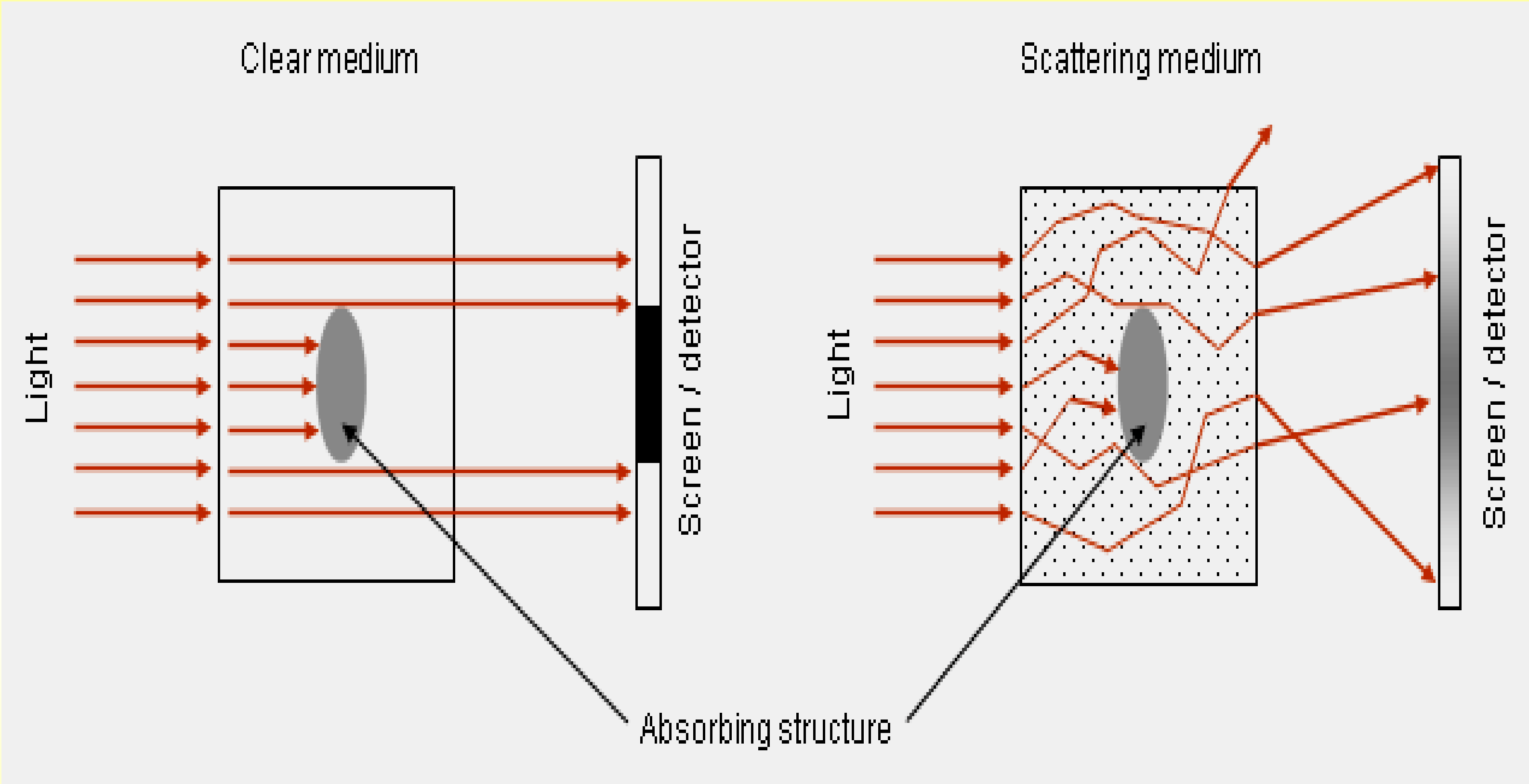
1. **General Absorption**: It reduces the intensity of all wavelengths in the considered spectrum by a similar fraction.
2. **Selective Absorption**: It absorbs certain wavelengths in the presence of others. The existence of colors originates from selective absorption.

Scattering of Light

- **Scattering:**
- A physical process whereby some forms of radiation- light , sound or moving particles- are forced to deviate from a straight trajectory by one or more localized non-uniformities in the medium through which it passes.
- The types of non-uniformities that can cause scattering, sometimes known as *scatterer* or *scattering centers.*

$$I(z) = I_o \exp(-\alpha_s z)$$

Where α_s Scattering coefficient


Clear medium
Scattering medium
Light
Screen / detector
Light
Screen / detector
Absorbing structure

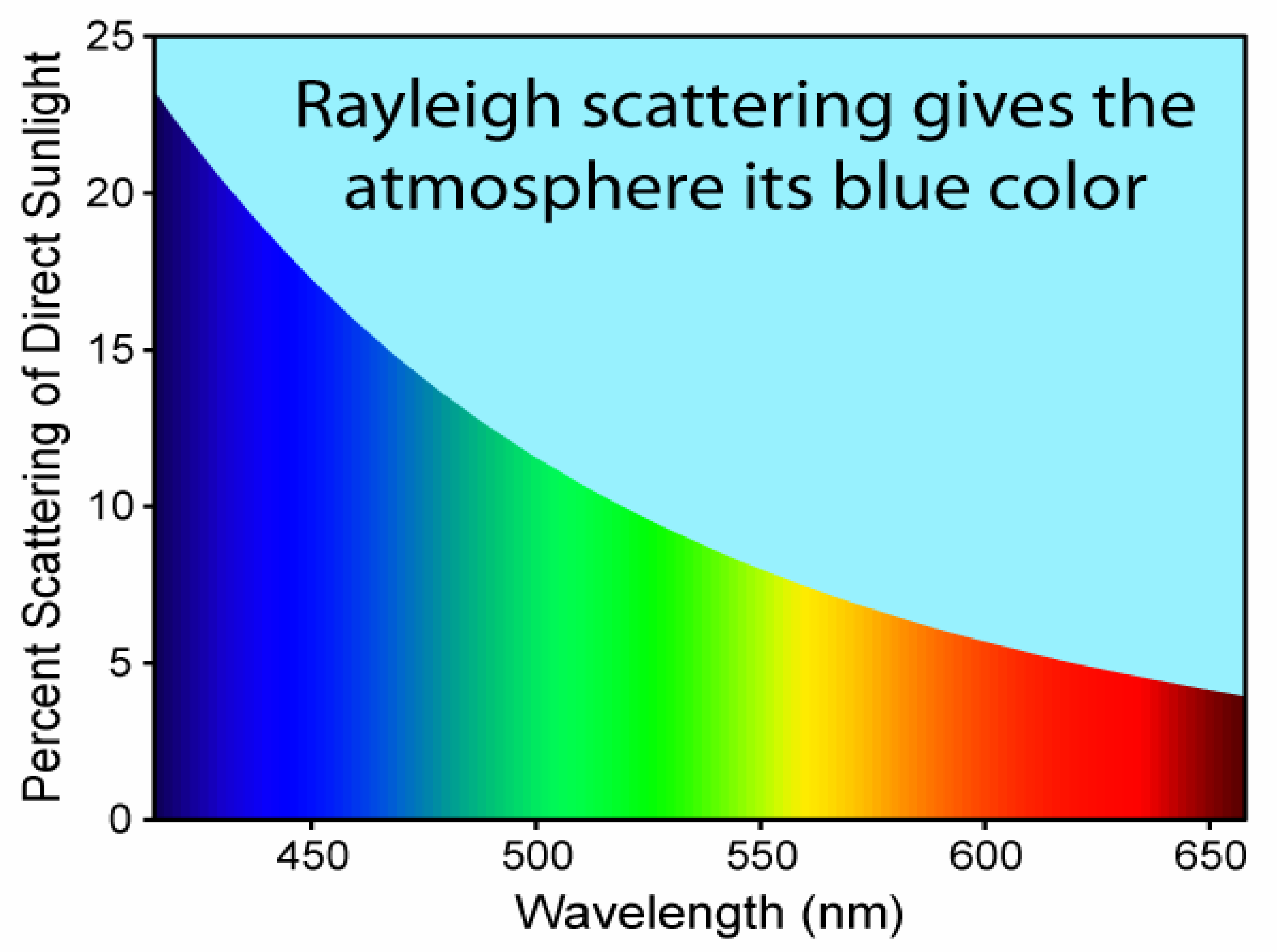
Scattering of Light cont'd.

- **Elastic Scattering**: Involves no (or a very small) loss or gain of energy of the radiation.
- **In-elastic Scattering**: Involves some change in the energy of the radiation.
- **Single Scattering**: Radiation is only scattered by one localized scattering center.
- **Multiple Scattering**: Scattering centers are grouped together, and the radiation may scatter many times.

Rayleigh Scattering

Rayleigh scattering:

- is the scattering of light or other electromagnetic radiation by particles much smaller than the wavelength of the light.
- It can occur when light travels in transparent solids and liquids, but is most prominently seen in gases.
- Rayleigh scattering of sunlight in clear atmosphere is the main reason why the sky is blue.


Rayleigh scattering gives the atmosphere its blue color
Percent Scattering of Direct Sunlight
25
20
15
10
5
0
450
500
550
600
650
Wavelength (nm)

Rayleigh Scattering cont'd

- The size of a scattering particle is defined by the ratio (x) of its characteristic dimension (r) and wavelength (λ):

$$x = \frac{2\pi r}{\lambda}$$

- Rayleigh scattering can be defined as scattering in small size parameter regime $x << 1$.
- The amount of Rayleigh scattering that occurs to a beam of light is dependent upon the size of the particles and the wavelength of the light.
- The intensity of the scattered light varies inversely with the fourth power of the wavelength.

Rayleigh Scattering cont'd

- The intensity ***I*** of light scattered by a single small particle from a beam of unpolarized light of wavelength **λ** and intensity is given by:

$$I = I_0 \frac{1+\cos^2\theta}{2R^2}\left(\frac{2\pi}{\lambda}\right)^4\left(\frac{n^2-1}{n^2+2}\right)^2\left(\frac{d}{2}\right)^6$$

- where ***R*** is the distance to the particle, **θ** is the scattering angle, ***n*** is the refractive index of the particle, and ***d*** is the diameter of the particle.

Rayleigh Scattering cont'd

- The angular distribution of Rayleigh scattering, governed by the $(1+\cos^2 \theta)$ term- symmetric in the plane normal to the incident direction of the light, and so the forward scatter equals the backwards scatter. Integrating over the sphere surrounding the particle gives the Rayleigh scattering cross section σs:

$$\sigma_s = \frac{2\pi^5}{3}\frac{d^6}{\lambda^4}\left(\frac{n^2-1}{n^2+2}\right)^2$$

Mie Scattering

- If the size of the scatterer becomes comparable to the incident radiation- Mie scattering occurs.
- Mie scattering and Rayleigh scattering differ in two important aspects.

1. Mie scattering shows a weaker dependence on wavelength $(\sim \lambda^{-x} \text{ with } 0.4 \leq x \leq 0.5)$ compared to the Rayleigh scattering $(\sim \lambda^{-4})$
2. Mie scattering preferably takes place in the forward direction whereas Rayleigh scattering is proportional to $1 + \cos^2 \theta$ i.e., forward and backward scattered intensities are the same
3. In contrast to Rayleigh scattering, the Mie solution results in numerical summation of infinite sums.

Optical Properties of Tissues

- Biological tissues- optically inhomogeneous and absorbing media- average refractive index is higher than that of air.
- This is responsible for partial reflection of the radiation at the tissue/air interface- while the remaining part penetrates the tissue.
- Multiple scattering and absorption are responsible for laser beam broadening and eventual decay as it travels through a tissue.
- Bulk scattering is a major cause of the dispersion of a large fraction of the radiation in the backward direction.

Optical Properties of Tissue cont'd

- **Most important among optical tissue properties are:**
- **The coefficient of reflection**
- **The coefficient of absorption.**
- **The coefficient of scattering.**
- **Together they determine the total transmission of the tissue at a certain wavelength.**

Reflection & Refraction of light by tissue

- Diffuse reflection is a common phenomenon of all tissues, since none of them is provided with highly polished surfaces such as optical mirrors.
- Only in special cases such as wet tissue surfaces might specular reflection surpass.
- In medical laser applications- refraction plays a significant role- irradiating transparent media like corneal tissue.
- In opaque media- the effect of refraction is difficult to measure due to absorption and scattering.

Absorption of light by Tissue

- Each type of tissue has specific absorption characteristics depending on its specific components.
- The main absorbing components-chromophores of tissue are:

Hemoglobin - in blood

Melanin -skin, hair, moles etc.

Water – all biological tissue

Protein - Scatter

Absorption of light by Tissue Cont'd

Chromophore:

- A part of a molecule responsible for its color.
- Absorbs certain wavelengths of visible light and transmits or reflects others- giving the molecule a color.
- In biological molecules that serve to capture or detect light energy.
- The chromophore is the moiety that causes a conformational change of the molecule when hit by light.

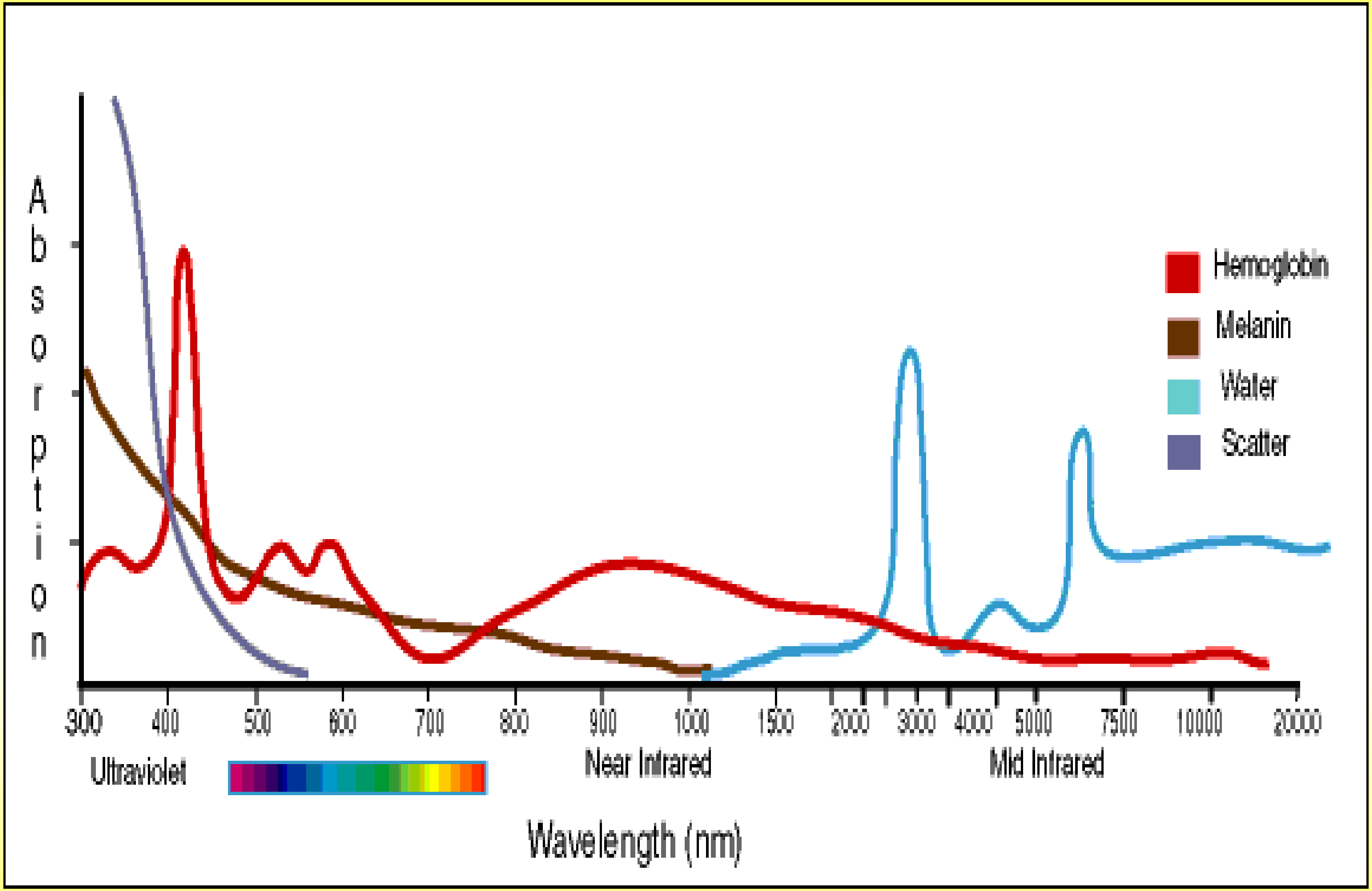
Absorption of light by Tissue Cont’d

Hemoglobin

- Hemoglobin is predominant in vascularized tissue.
- Visible and ultraviolet light are absorbed mainly by hemoglobin (HbO_2) - translucent to light beyond this range.
- It has relative absorption peaks around 280nm, 420nm, 540nm, and 580nm and then exhibits a cut-off at approximately 600nm.

Melanin

- Melanin is the basic pigment of skin and is by far the most important epidermal chromophore.
- Its absorption coefficient monotonically increases across the visible spectrum toward the UV.



Absorption
Hemoglobin
Melanin
Water
Scatter
300
400
500
600
700
800
900
1000
1500
2000
3000
4000
5000
7500
10000
20000
Ultraviolet
Near Infrared
Mid Infrared
Wavelength (nm)

Absorption of light by Tissue cont'd

Water

- In biological tissues- absorption is mainly caused by water molecules – the main constituent of most tissues.
- Infrared light is absorbed primarily by water- beginning with a small amount of absorption from 300-2000nm- a point at which the degree of absorption increases rapidly and continuous for several thousand nanometers.
- The CO_2 lasers produces light in the far infrared spectrum (10,600 nm). This is heavily absorbed by water contained in tissue and- does not penetrate deeply.

Absorption of light by Tissue cont'd

Protein

- Macromolecules such as proteins are second main absorber in biological tissue.
- Proteins mainly absorbs in the UV and visible range of the spectrum- in particular have an absorption peak at approximately 280nm
- As the wavelength decreases toward the blue-violet, and ultraviolet, ***scatter*** - which limits the depth that light may penetrate into tissue- becomes more significant.
- Cellular organelles such as mitochondria are the main scatterers in various tissues.

Scattering of Light by Tissues

- The interaction of light with tissue is composed of multiple internal reflections and redirections of incident light.
- In biological media scattering is typically highly forward directed (anisotropic) for visible wavelength
- This phenomenon cannot be explained by Rayleigh scattering.
- On the other hand- the observed wavelength-dependence is somewhat stronger than predicted by Mie scattering.
- Thus neither Rayleigh scattering nor Mie scattering completed describe scattering in amorphous biological shapes.

Scattering of Light by Tissues cont’d

- With a few exceptions (e.g., cornea)- light propagation in tissues thicker than tens of microns- characterized by multiple scattering.
- Multiple scattering wash out any detailed structure associated with individual scattering events.
- Scattering in optically thick media can be characterized by two parameters:

1. The scattering coefficient
2. The scattering anisotropy

Scattering of Light by Tissues cont'd

- **It is very convenient to define a probability function $p(\theta)$ of a photon to be scattered by an angle ɵ which can be fitted to experimental data**
- **Isotropic scattering: Probability function does not depend on ɵ.**
- **Anisotropic scattering: Probability function depends on ɵ.**

Anisotropy of Scattering

Anisotropy of Scattering

Coefficient of Anisotropy:

- A measure of the anisotropy of scattering is given by the coefficient of anisotropy g.
- If **g=1** - purely forward scattering.
- If **g=-1** - purely backward scattering
- If **g= 0** – isotropic scattering

$$g = \frac{\int_{4\pi} p(\theta)\cos\theta \, d\omega}{\int_{4\pi} p(\theta) d\omega}$$

$p(\theta)$ -Probability function

$$d\omega = \sin\theta \, d\theta \, d\phi$$

Elemental Solid Angle

Anisotropy of Scattering cont'd

- The coefficient of anisotropy g represents the average value of the cosine of the scattering angle ɵ.
- As a good approximation- g ranges from 0.7 to 0.99 for most biological tissues.
- The probability function p(ɵ) is also called phase function and is usually normalized by

$$\frac{1}{4\pi}\int_{4\pi} p(\theta)\,d\omega = 1$$

$$p(\theta) = \sum_{i=0}^{\infty}(2i+1)g^{i}P_{i}(\cos\theta)$$ Henyey-Greenstein

Turbid Media

The media in which both absorption and scattering are present- called Turbid media

$$\alpha_t = \alpha + \alpha_s$$

Mean free optical path of incident photon is

$$L_t = \frac{1}{\alpha_t} = \frac{1}{\alpha + \alpha_s}$$

It is convenient do define an additional parameter- the optical albedo **a**

$$a = \frac{\alpha_s}{\alpha_t} = \frac{\alpha_s}{\alpha + \alpha_s}$$

For **a=o** – attenuation due to absorption only

For **a=1** – attenuation due to scattering only

Thermal Properties of Tissues

- Local tissue properties combined with the wavelength of laser light used- affect the quality of laser-tissue interaction.
- The more dense or opaque a tissue is – greater the degree of absorption of light energy and the greater the transformation to heat.
- Local blood circulation affects the degree of laser energy absorption in two mechanisms.

1. The absorptive properties of individual blood components differ and interact with light in specific wavelength ranges.
2. The circulating blood acts as heat sink or radiator by transporting absorbed thermal energy away from the site of delivery.

Effect of Light on Tissue

- The wavelength of laser light can be proportional to the depth of penetration into specific tissues.
- The longer the wavelength-the deeper the expected penetration.
- Tissue composition and molecular absorption-play into laser end effect.
- The Nd:YAG - near infrared (1060nm)- penetrates approximately 5-10mm in most tissues- not absorbed by water and hemoglobin in significant quantity.
- The CO^2 – 10,600nm- penetrates to 0.1mm-absorbed by tissue water

Effect of Light on Tissue cont'd

- **When light is absorbed- it delivers energy to tissue- and the tissue's reaction depends on the intensity and exposure time of the light.**
- **Three major categories of interaction**:

1. **Photomechanical**
2. **Photo thermal**
3. **Photochemical**

- **In actual practice, all of these interactions coexist, although by selecting the proper wavelength, intensity, and pulse duration, the desired effect can be maximized.**

Photomechanical Reactions

- Extremely intense- short pulse of laser light will usually cause an explosive expansion of tissue- **photomechanical** reaction.

Photodisruptive

- High energy- ultra short pulses of laser light cause extremely rapid heating of the target- with formation of a rapidly expanding thermal plasma.
- As the plasma collapses- the shock wave causes mechanical disruption of the target.
- This photomechanical disruption is utilized to treat tattoos- disruption of stones and certain pigmented skin lesions.

Photo-thermal Reactions

- A less intense- longer pulse will cause a rapid heating- ***photothermal*** effect.
- When laser energy is absorbed by a chromophore - and transformed into heat which is dissipated in the target- leading to denaturation of proteins at 42-65 C.
- Depending on the exposure time, tissue vaporization, or coagulation, or both will take place.

Photo-thermal Reactions cont'd

- The best example of a photothermal laser is the CO^2 laser- used to cut and vaporize tissue - which mostly consists of water.
- Water- and thus soft tissue- vaporizes at 100 degrees C.
- When the laser hits soft tissue- rapid heating causes the water in the tissue to flash into steam- ***ablating*** the tissue.

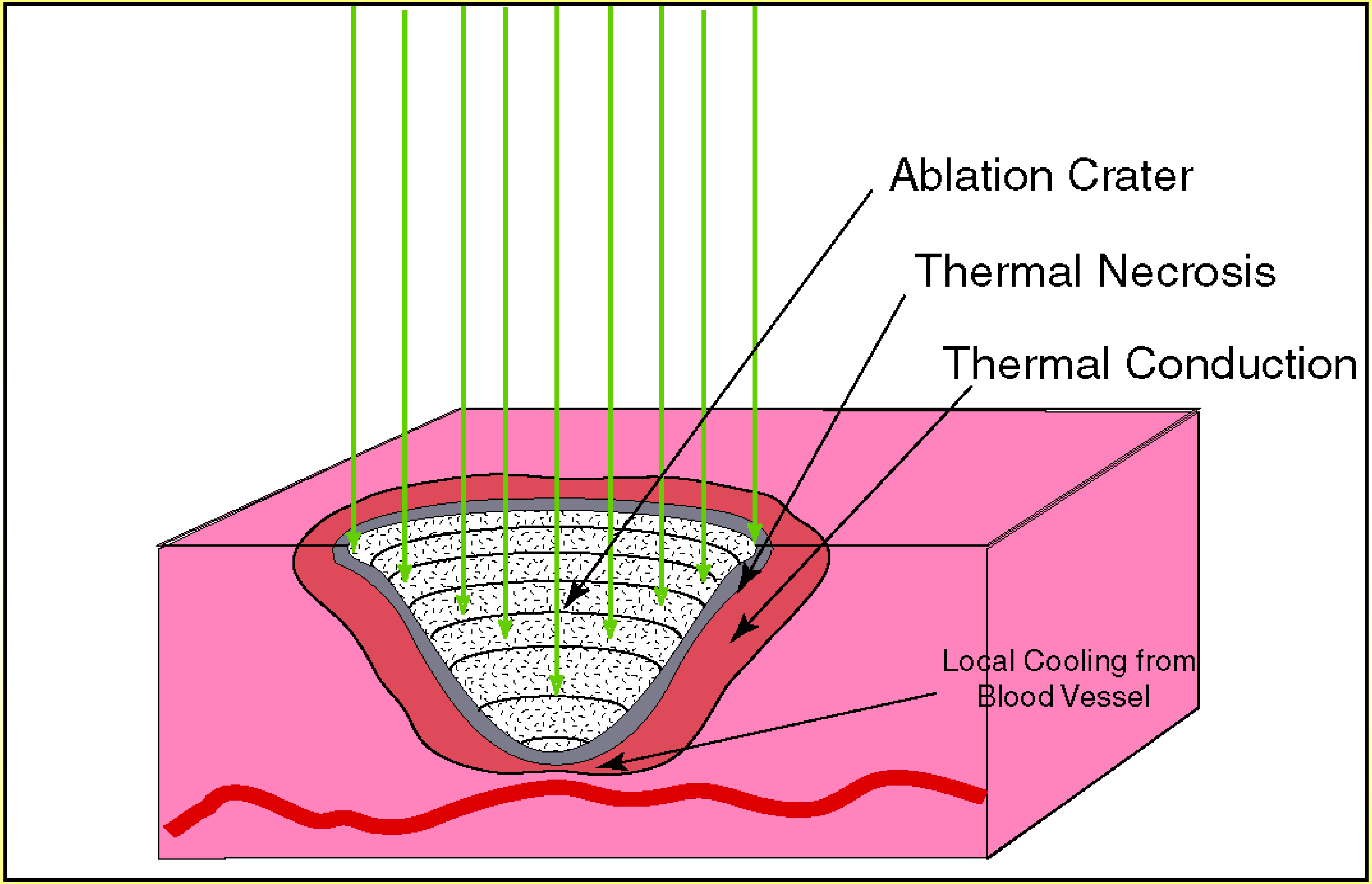

Ablation Crater
Thermal Necrosis
Thermal Conduction
Local Cooling from Blood Vessel

Photo-thermal Reactions cont'd

- To minimize thermal damage- maximize the ablation- a short exposure time is necessary.
- This can be done by ***pulsed*** laser beam in such a way that the time it dwells over the tissue is less than its ***thermal relaxation time***.
- This type of photothermal reaction is utilized in surgical laser applications -laser resurfacing, laser hair removal, and treatment of vascular lesions.

Photochemical Reactions

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

Photochemical Reactions cont'd

Photodynamic Therapy (PDT):

- A photosensitizing drug **(prophyrin)** is administered- which is selectively absorbed by tumor cells.
- When irradiated with the appropriate wavelength of laser light- a chemical reaction takes place- releasing a toxic substance (usually the highly reactive singlet oxygen) which selectively destroys the tumor.
- The use of PDT is limited by the lack of easily administered, sufficiently selective photosensitizing drugs- and difficulties with laser delivery.
- PDT techniques are used for the treatment of some skin cancers, precancerous lesions, obstructing tumors in the esophagus and bronchi.

Selective Photothermolysis

Selective Photothermolysis:

- A process in which transfer of laser energy is restricted to a particular site because of the selective absorption of a chromophore at that site.
- In other words, ***proper selection of the wavelength and exposure time damages only the desired target tissue***. This principal is what distinguishes lasers from many other tools in medicine
- **Selective photothermolysis occurs with :**
- The appropriate **Wavelength-** selectively absorbed by the target tissue
- The appropriate **Exposure time-** should be less than the thermal relaxation time of the target tissue
- The appropriate **Energy density** , or ***Fluence-*** to produce the desired effect, such as vaporization, coagulation, or photodisruption.

Thermal Relaxation time

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

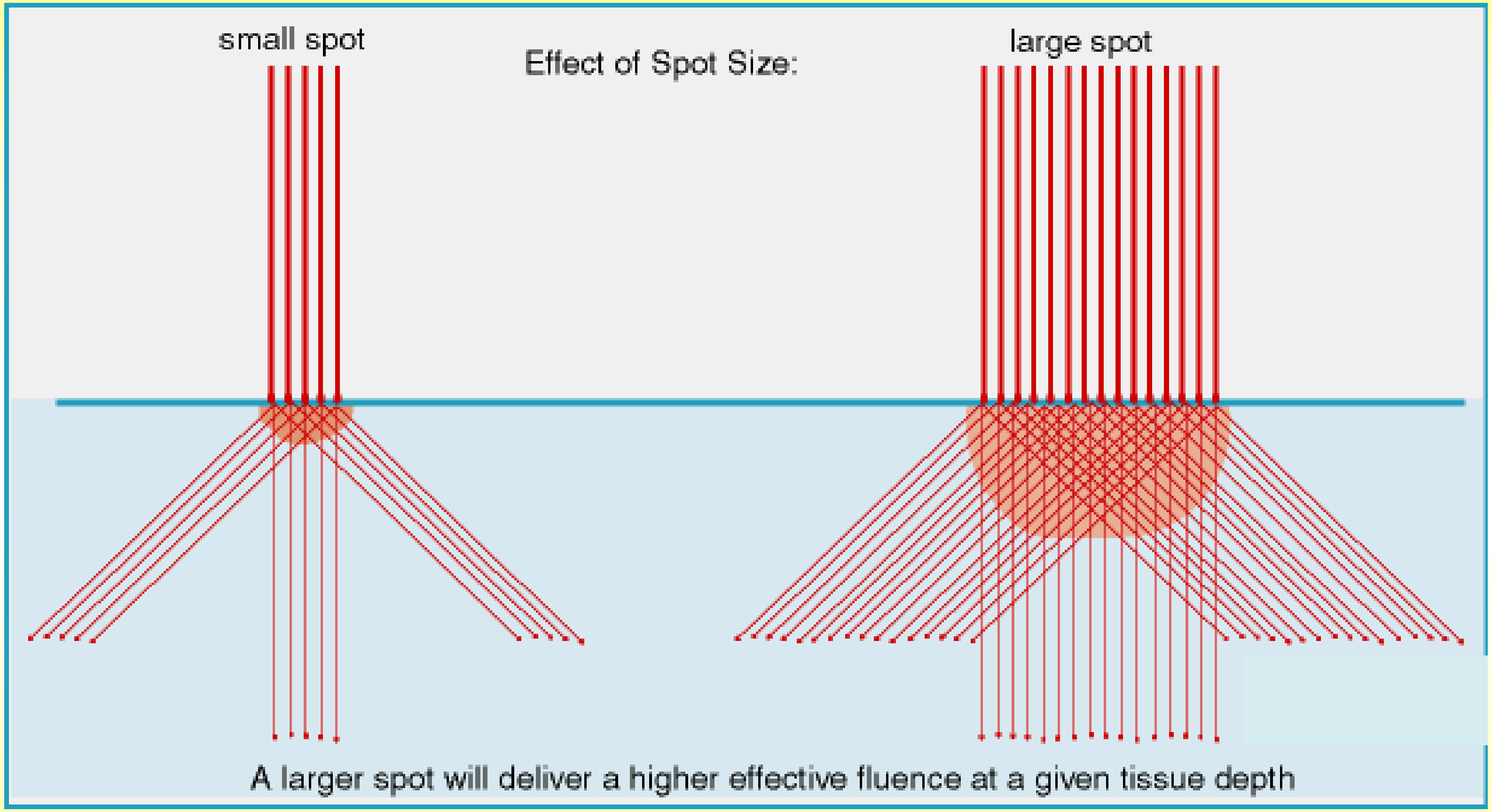
$$t_r \approx d^2$$

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

Laser Spot Size on Tissue

Effect of Laser Spot Size on Tissue Distribution of Light energy:

- A beam of light incident on tissue may be reflected, absorbed, or ***scattered.***
- ***Scattering -*** broadens the incident beam - decreasing the effective fluence in the intended target area. Doubling the spot size will increase the effective volume by a factor of eight.
- A larger spot size usually enables faster and more effective treatment in dermatologic applications.
- It needs - more photons must be supplied by more complex and expensive power supplies, components, and delivery devices.
- As a general rule, doubling the spot size and halving the fluence will yield an equivalent <u>effective</u> fluence at a given depth. This effect become more pronounced with increasing depth.


small spot
Effect of Spot Size:
large spot
A larger spot will deliver a higher effective fluence at a given tissue depth

Conclusion

To perform a laser procedure properly, the surgeon must uses the laser with the right wavelength- then selects the appropriate Fluence and Exposure time to achieve a selective photothermal, photomechanical, or photochemical effect on the target.

References

- LASER-TISSUE INTERACTIONS: Fundamentals and Applications

  By Markolf H. Niemz

- TISSUE OPTICS: Light Scattering Methods and Instruments for medical Diagnosis

  By Valey Tuchin

THANK YOU