6 Light dosimetry in tissues

Medical Laser Treatments

- **Laser surgery**
  - **Eye (Ar-ion , Nd:YAG, Excimer lasers)**
  - **Dermatological (CO_2, Dye, Ruby, Ar-ion lasers)**
  - **General surgery (Nd:YAG, diode, CO_2 lasers)**
  - …
- **Thermotherapy**
- **Photodynamic therapy**
- **…**

Dosimetry is essential !!

An understanding and control of the therapeutic effect requires knowing the energy quantity delivered to the tissue during treatment by the laser beam

Light dosimetry in tissues allows answering the following question:

If a given tissue is irradiated by a laser/light beam:

- **with a power P**
- **at a wavelength λ**
- **on a spot section S**
- **…**

how many photons per second and per unit area will reach a target at a given depth below the tissue surface ?

Many parameters have an impact on the light dosimetry

Light dose / fluence

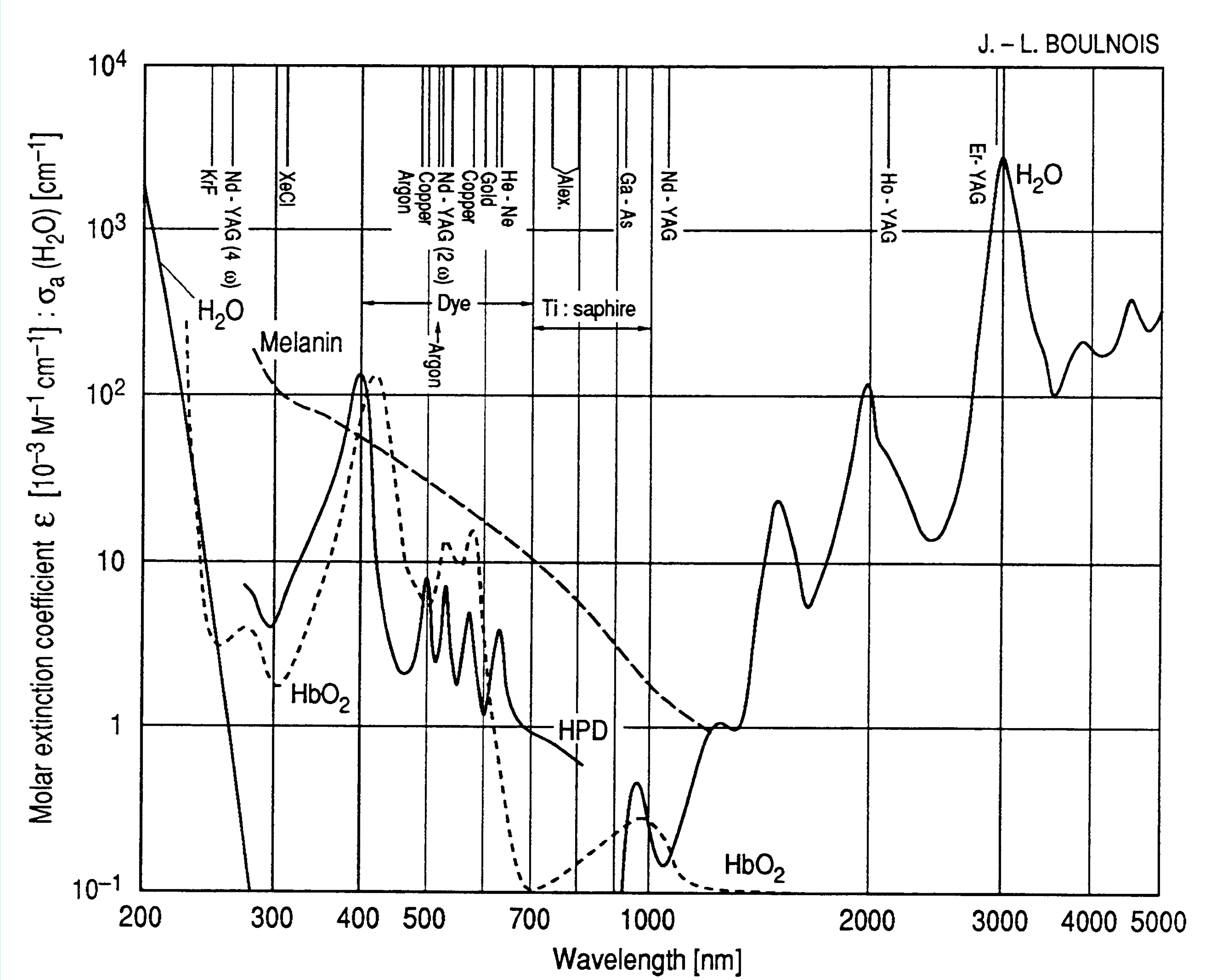
Light dose rate / fluence rate

Geometry

Wavelength / tissue optical properties

…

Molar extinction coefficients of tissue absorbers with selected laser lines

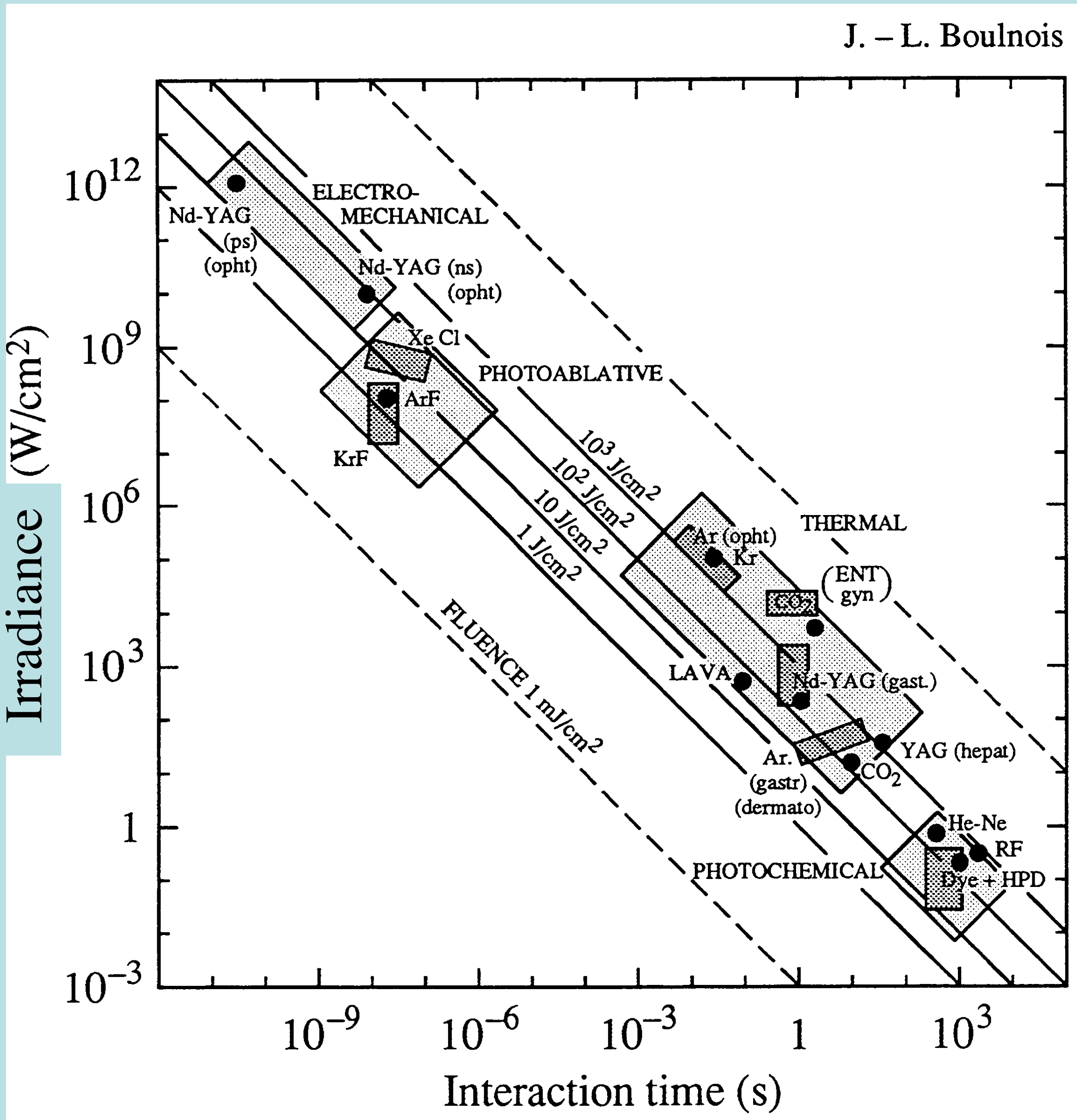


Light/Laser therapy uses four mechanisms depending on the fluence and fluence rate

Electromechanical effect	**plasma creation**
Photoablative effect	**rupture molecular bonds**
Thermal effect	**heat**
Photochemical effect	**chemical agent activation**

**Whatever the desired therapeutic effect,
the action mechanism always starts by an
energy transfer from the light beam to the tissue**

Classification of the medical lasers



The 4 large rectangles correspond to the types of tissue interactions: Photochemical, Thermal, Photoablative and Electro-mechanical. The circles correspond to more than several hundreds of publications Abbreviations: Nd-YAG, "neodymium-dopped yttrium aluminium garnet laser"; XeCl, "xenon chloride laser"; ArF, "argon fluoride laser"; KrF, "krypton fluoride laser"; Ar, "argon laser"; Kr, "krypton laser"; CO_2, "carbon dioxide laser"; LAVA, "laser-assisted vascular anastomosis"; He-Ne, "helium-néon laser"; Hpd, "hematoporphyrin derivative"; RF, "radio frequency"; ps, "picosecond"; ns, "nanosecond"; opht, "ophtamology"; ent, "otorhinolaryngology"; gyn, "gynaecology"; gastro, "gastrology"; dermato, "dermatology"; hepat, "hepatology".

3-D classification of the light-tissue interaction:
the time course of the tissue response must be considered

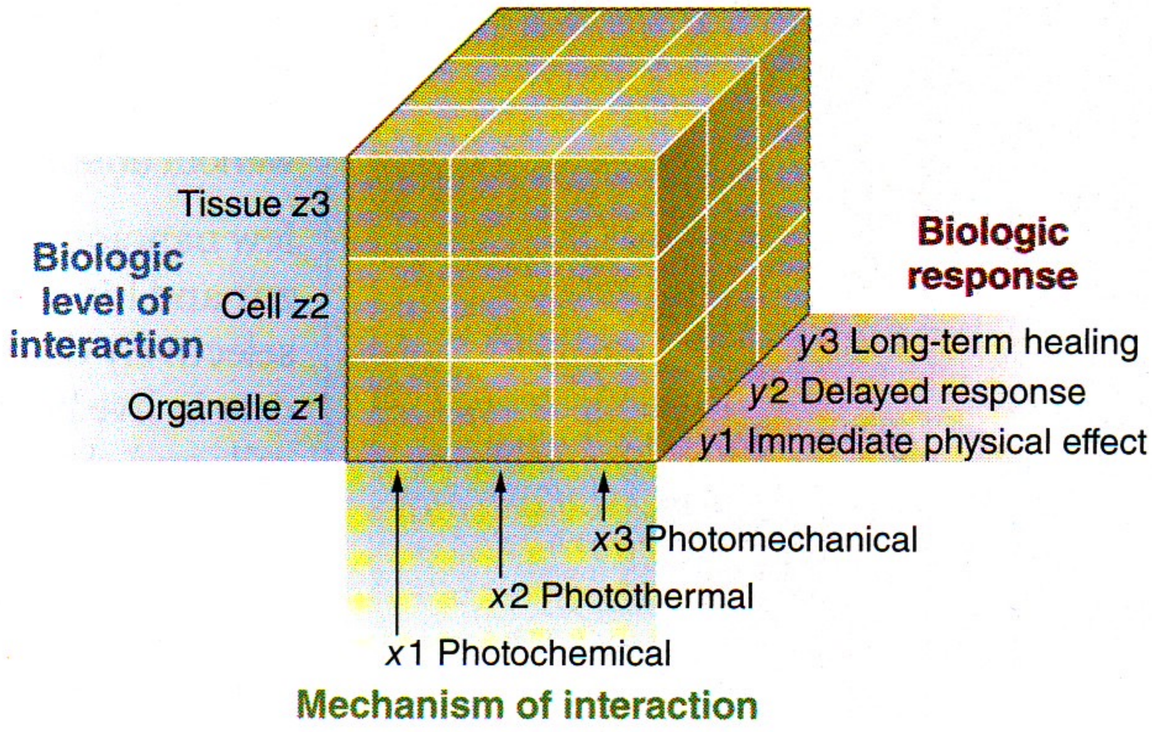


FIGURE 1. The laser-tissue interaction cube comprises three axes: (*x*) the mechanisms of interaction, (*y*) the time course of the tissue response, and (*z*) the level of biologic structures. When laser energy irradiates tissue and something happens, the resulting event will map somewhere in this cube.

Photomechanical
Stands for:
- Electromechanical
AND
- Photoablative effects

Accuracy of the laser/light therapy

Electromechanical effect

Photoablative effect

Thermal effect

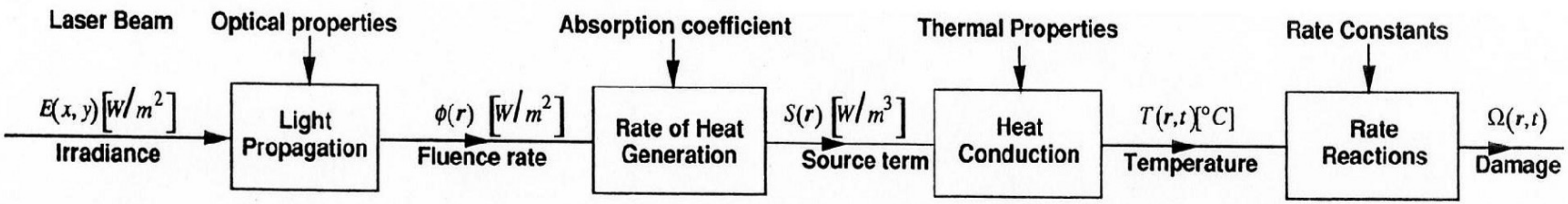
Photochemical effect

ACCURACY OF THE MODELS / THEORY / MEASUREMENTS

The calculation of the light dosimetry is more difficult when the fluence rate is large due to the changes of the optical properties during the treatment.

⇒ Empirical approaches are used for the electromechanical and photoablative effects

Optical and Thermal Laser-Tissue Interactions



Transport Equation for Diffuse Light

$$\frac{dL(r,\hat{s})}{ds} = \mu_t L(r,\hat{s}) + \mu_s \int_{4\pi} p(\hat{s},\hat{s}')L(r,\hat{s}')d\omega$$

Source Term

$$S(r) = \mu_a(r)\phi(r)$$

Heat Conduction Equation

$$\rho c\frac{\partial T(r,t)}{\partial t} = \nabla k \nabla T(r,t) + S(r)$$

Damage Integral

$$\Omega(r,t) = A\int_0^t \exp\left[-\frac{\Delta E}{RT(r,t')}\right]dt'$$

Beer's Law for Collimated Light

$$E(x,y,z) = E_0(x,y)e^{-\mu_t z} = L(r,\hat{s})\delta(\hat{s},-\hat{z})$$

$r = x,y,z \qquad \mu_t = \mu_a + \mu_s \qquad \phi(r) = \int_{4\pi} L(r)d\omega$

$d\omega$: infinitesimal solid angle in direction $\hat{s}$

$\mu_a[1/m]$: absorption coefficient

$\mu_s[1/m]$: scattering coefficient

$\mu_t[1/m]$: attenuation coefficient

p : scattering phase function

$L\left[W/m^2 \cdot sr\right]$: radiance

$\rho\left[kg/m^3\right]$: density

$c[J/kg \cdot °C]$: specific heat

$k[W/m \cdot °C]$: conductivity

$A[1/s]$: frequency factor

$\Delta E[J/mole]$: activation energy

$R[J/mole \cdot °C]$: gas constant

Thermal Relaxation Time: τ_R

- **<u>Time needed to get heat transfer out of the target</u>**

$\Updownarrow$

- Time it would take to reduce the maximum temperature reached at the center of the target by a factor of two

- cell: 10 μs – 100 μs
  vessel 30 – 300 μm diameter: 1 ms - 100 ms
  vessel 0.3 mm - 1 mm diameter: 0.1 s – 1 s

One key Parameter

Laser pulse duration τ_P

- Selected according to the target thermal relaxation time τ_R
- Determines the action mode:
  thermomechanical or **thermal**

Influence of Laser Pulse Duration

$\tau_P \ll \tau_R$ = thermomechanical effect

- no heat diffusion
- heat accumulation in the target tissue
- thermal confinement + high fluence ➡ explosion

$\tau_P \approx \tau_R$ = thermal effect

- diffusion of heat within tissue
- affected area 2 - 3 x target size
- according to fluence rate ➚ coagulation ➘ vaporization

One key Parameter

Wavelength

- Enables selective thermal action

Selected according to the target

- water → infrared
- hemoglobine → blue - green
- melanine → visible - near IR

Temperature increase following light absorption

If the pulse of light is « short* » (if $\tau_P \ll \tau_R$)

$$\Delta T = \mu_a H / \rho c$$

where μ_a is the absorption coefficient (typical units, cm^{-1}), H is the radiant exposure (typical units, J cm^{-2}), ρ is the density (gm cm^{-3}), and c is the heat capacity (J °C^{-1} gm^{-1}). For tissue, a reasonable estimate is that $\rho c \approx 4.2$ J cm^{-3} °C^{-1};

* Such is the case if the duration of the pulse is shorter than the thermal relaxation time ($\tau_R \approx r^2/4\alpha$, where r is the characteristic dimension of the absorbing target, and α is the thermal diffusivity of the material (for tissue a reasonable estimate is $\alpha \approx 1.3 \times 10^{-3}$ cm^2 s^{-1}).

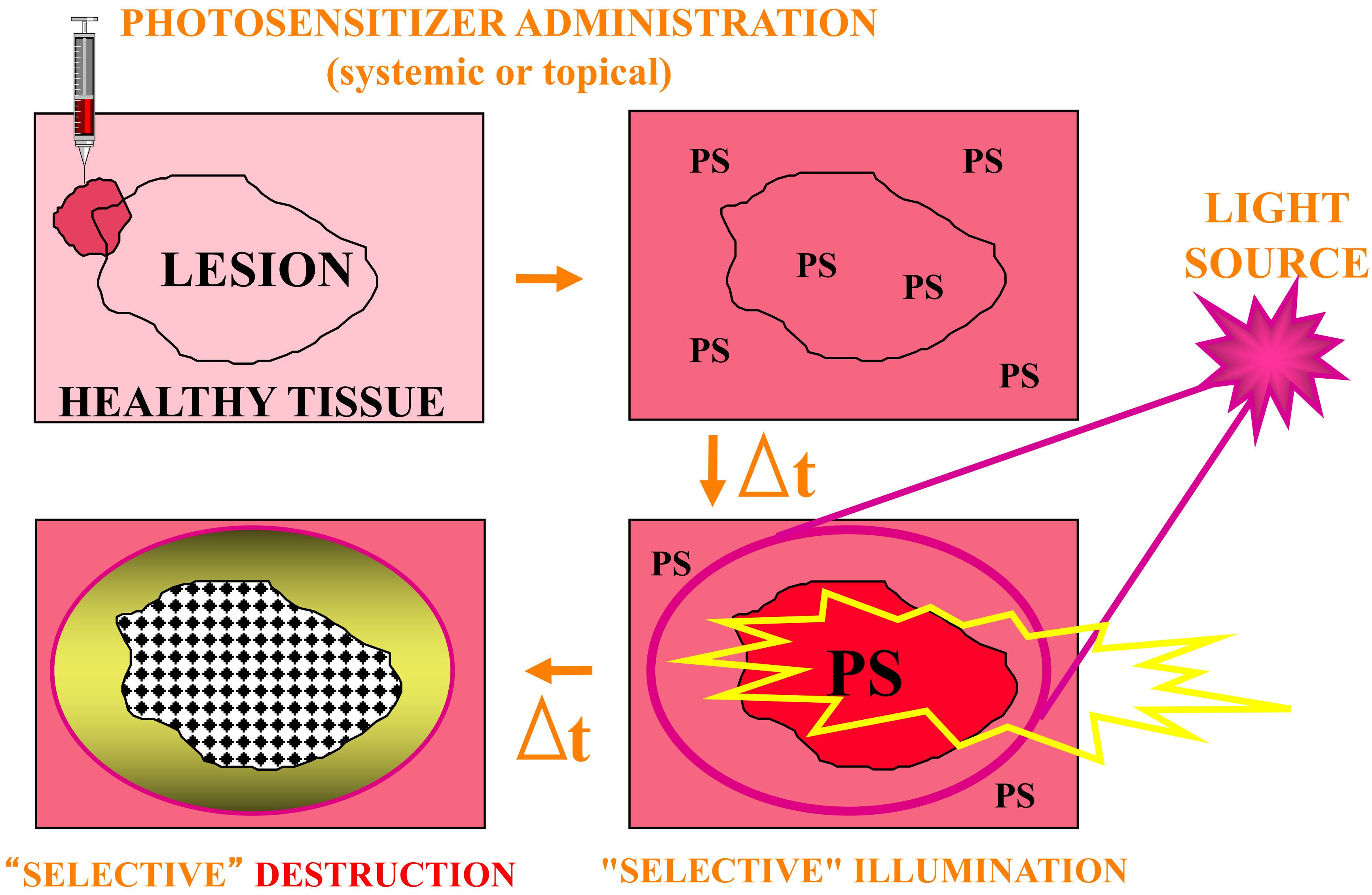
If r = 100 μm → τ_R= 20 ms

Optical-Thermal Response of Laser-Irradiated Tissue: Ashley J. Welch, Martin van Gemert, Springer, 2010.

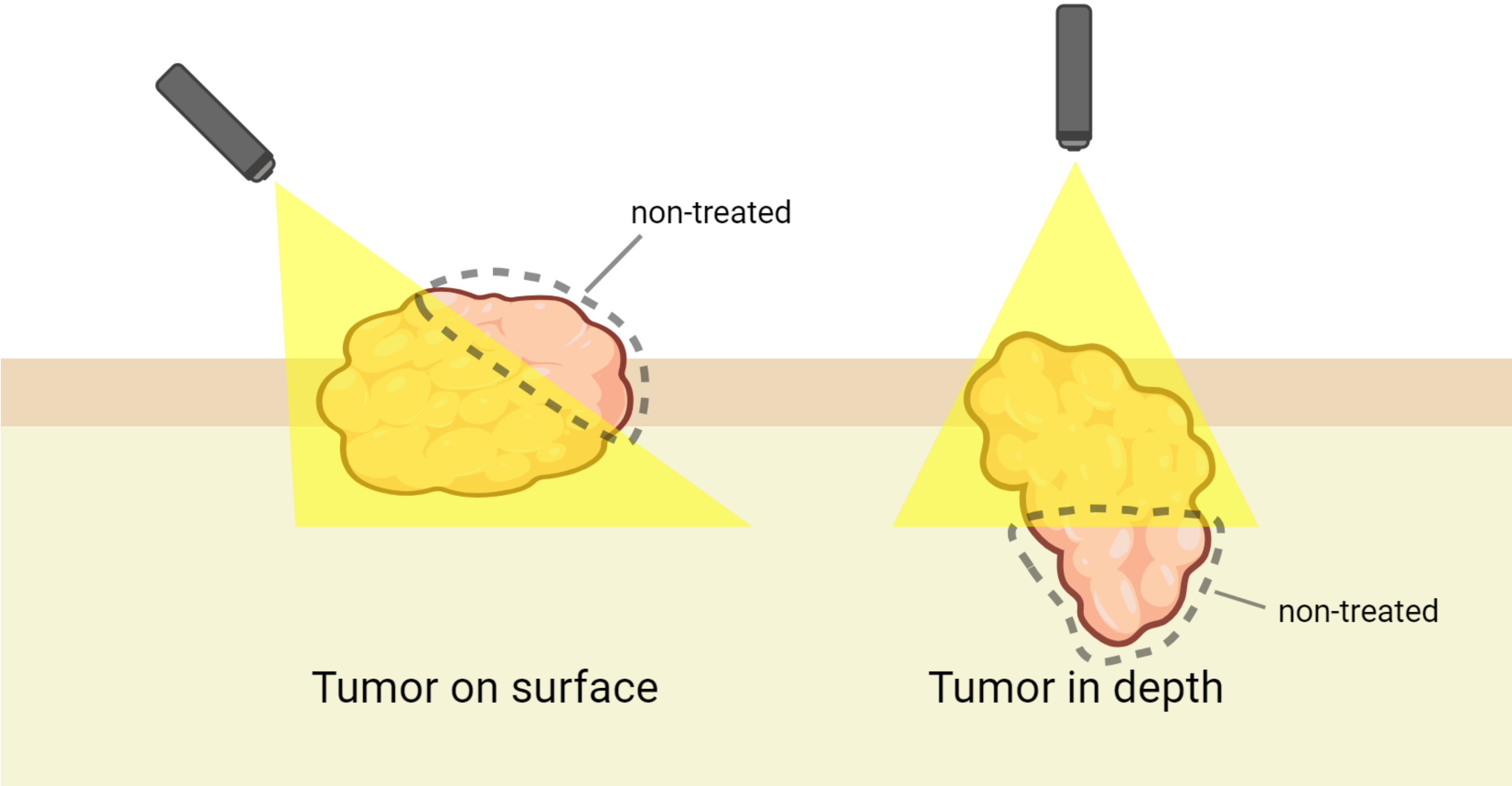
Light dosimetry in Photodynamic therapy

(Photochemical effect induced by a CW illumination during several minutes)

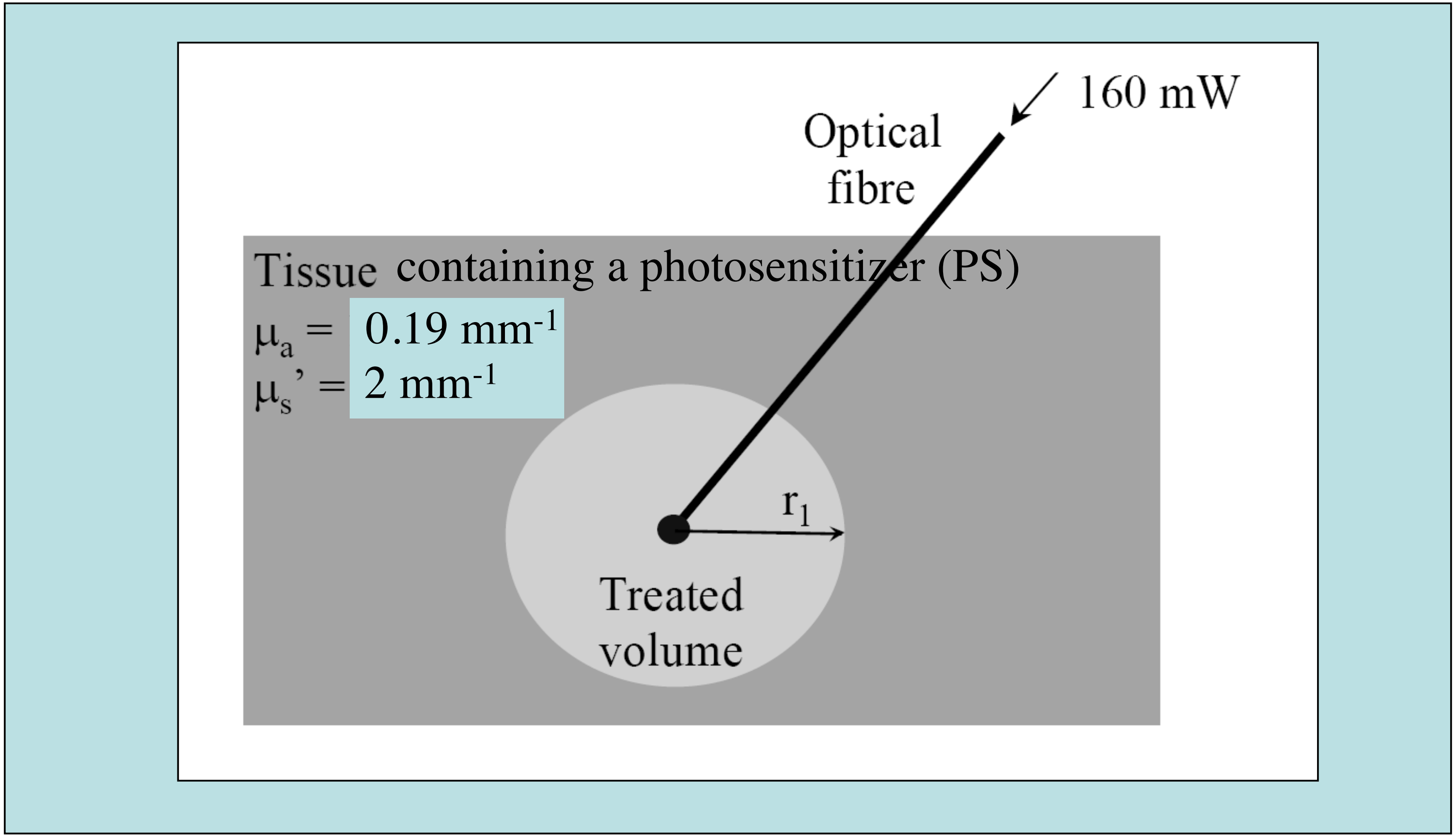
Principle of photodynamic therapy
(Based on photochemical effects)



Problems of photodynamics treatments
Irradiation inhomogeneity



Interstitial PDT geometry



PDT dosimetry

During PDT, assume that 10 J/cm^3 need to be absorbed by the photosensitizer to kill the tissue. Calculate the volume killed for a 15 minutes treatment from an isotropic interstitial fiber-tip emitting 160 mW. Assume the optical properties to be (μ_a^{tissue} = 0.19 mm^{-1}, μ_a^{PS} = 0.01 mm^{-1}, μ_s' = 2 mm^{-1}).

Guidelines

First considerer the solution to the steady-state diffusion equation as valid for this problem:

F = fluence rate

$$F(r) = \frac{P\mu^2{}_{eff}}{4\pi\mu_a}\frac{1}{|r|}e^{(-\mu_{eff}\cdot|r|)}$$

with $$\mu_{eff} = \sqrt{3\mu_a(\mu_a + \mu'_s)}$$

Guidelines cont'd (II)

Secondly, consider the absorbed power density $a(\mathbf{r})$ (mW/mm^3) to be: $a(r) = \mu_a^{PS} F(r)$

Thirdly, the absorbed energy density $\mathrm{U}(r)$ depends on the treatment time t as $\mathrm{U}(r) = \mathrm{t} \cdot \mu_a^{PS} F(r)$

Insert all values in the equation:

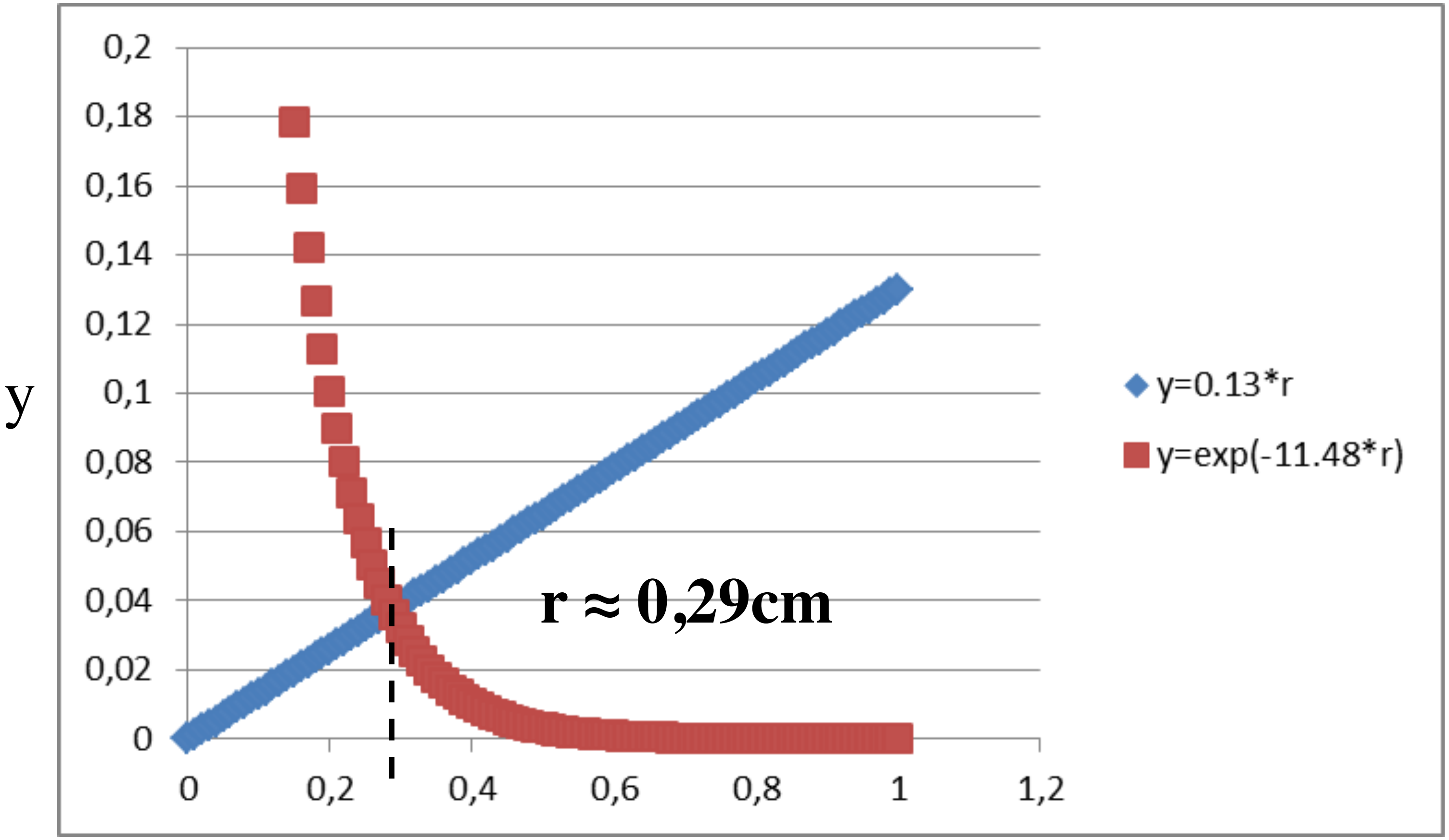
Guidelines cont'd (III)

This will result in an equation of the form:

$$\frac{1}{r} e^{-\mu_{eff} r} = C$$

where C is a value calculated from all parameters given. It is difficult to find an expression for r from this equation, and it is easier to solve the problem graphically or iteratively.

Solution

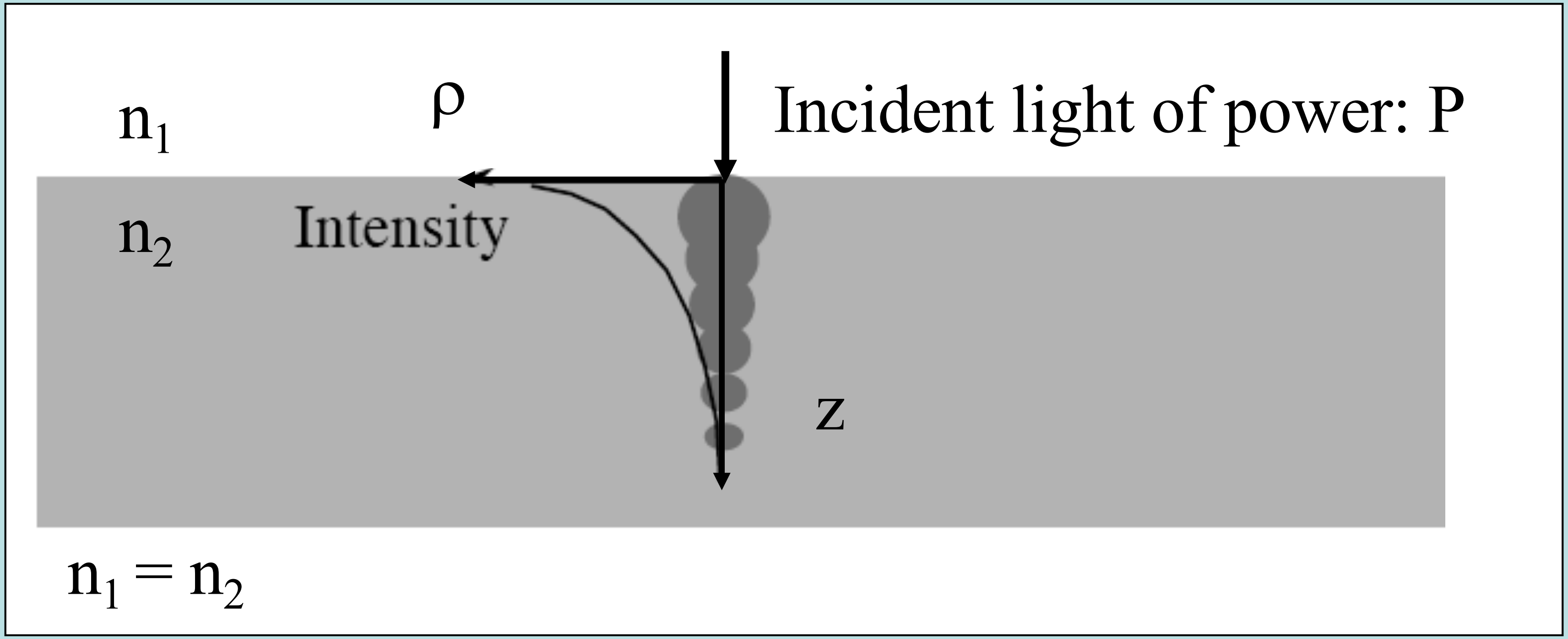


$$V_{killed} = \frac{4\pi r^3}{3} \approx 0.098\left[cm^3\right] \approx 98mm^3$$

Point source solution

Tissue / water interface

If we consider a pencil beam incident perpendicular on a semi-infinite volume of tissue



The Time-independent Fluence Rate

This solution would yield the following fluence inside a semi-infinite homogeneous medium:

$$F(p,z) = \frac{1}{4\pi D}\left\{\frac{e^{-\mu_{eff}[(z-z_0)^2+\rho^2]^{\frac{1}{2}}}}{[(z-z_0)^2+\rho^2]^{\frac{1}{2}}} - \frac{e^{-\mu_{eff}[(z+z_0)^2+\rho^2]^{\frac{1}{2}}}}{[(z+z_0)^2+\rho^2]^{\frac{1}{2}}}\right\}$$

with $\quad z_0 = \frac{1}{\mu'_s}$

"Frontal" Light distributor for PDT in the oral cavity and the bronchi

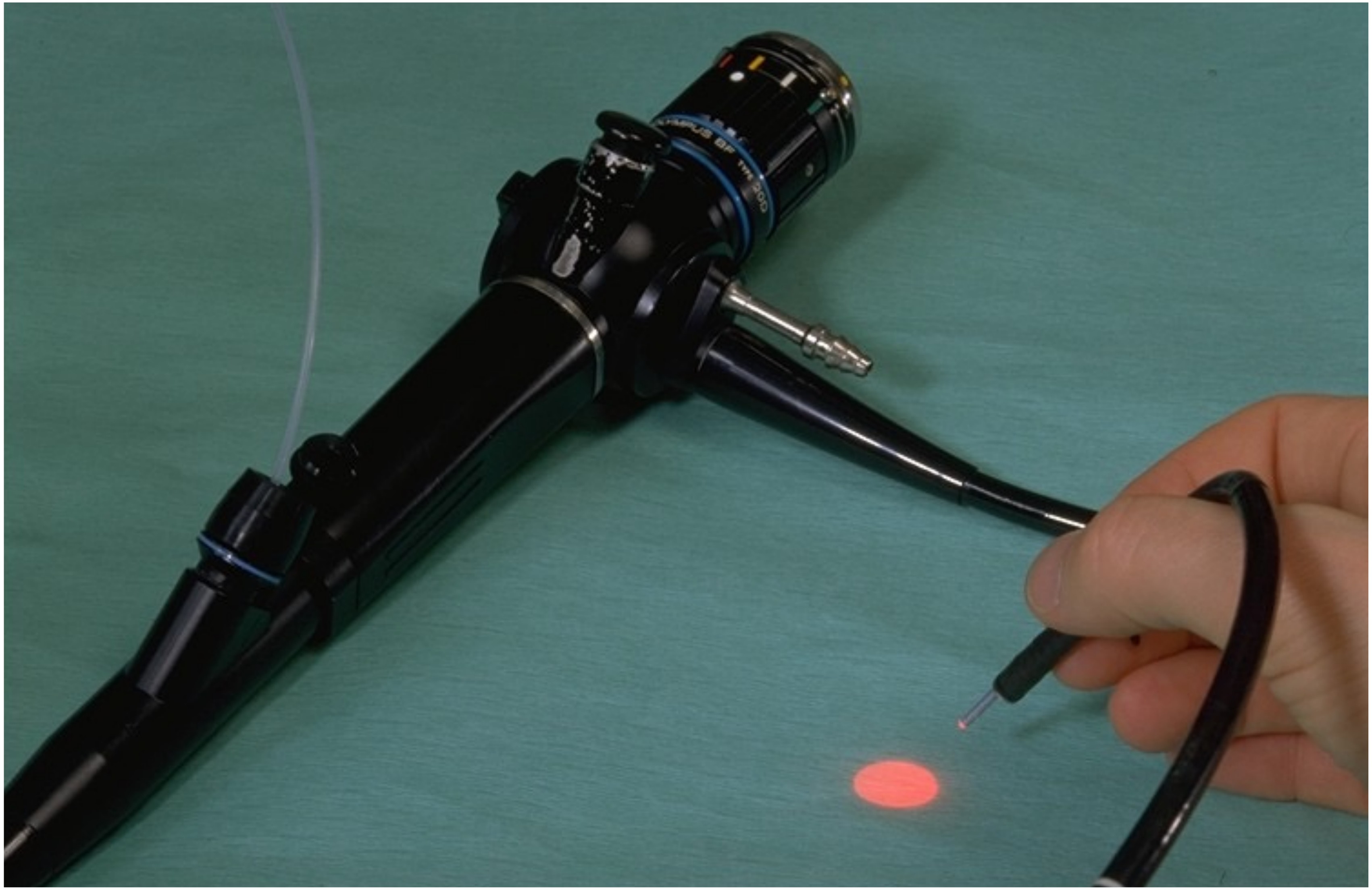
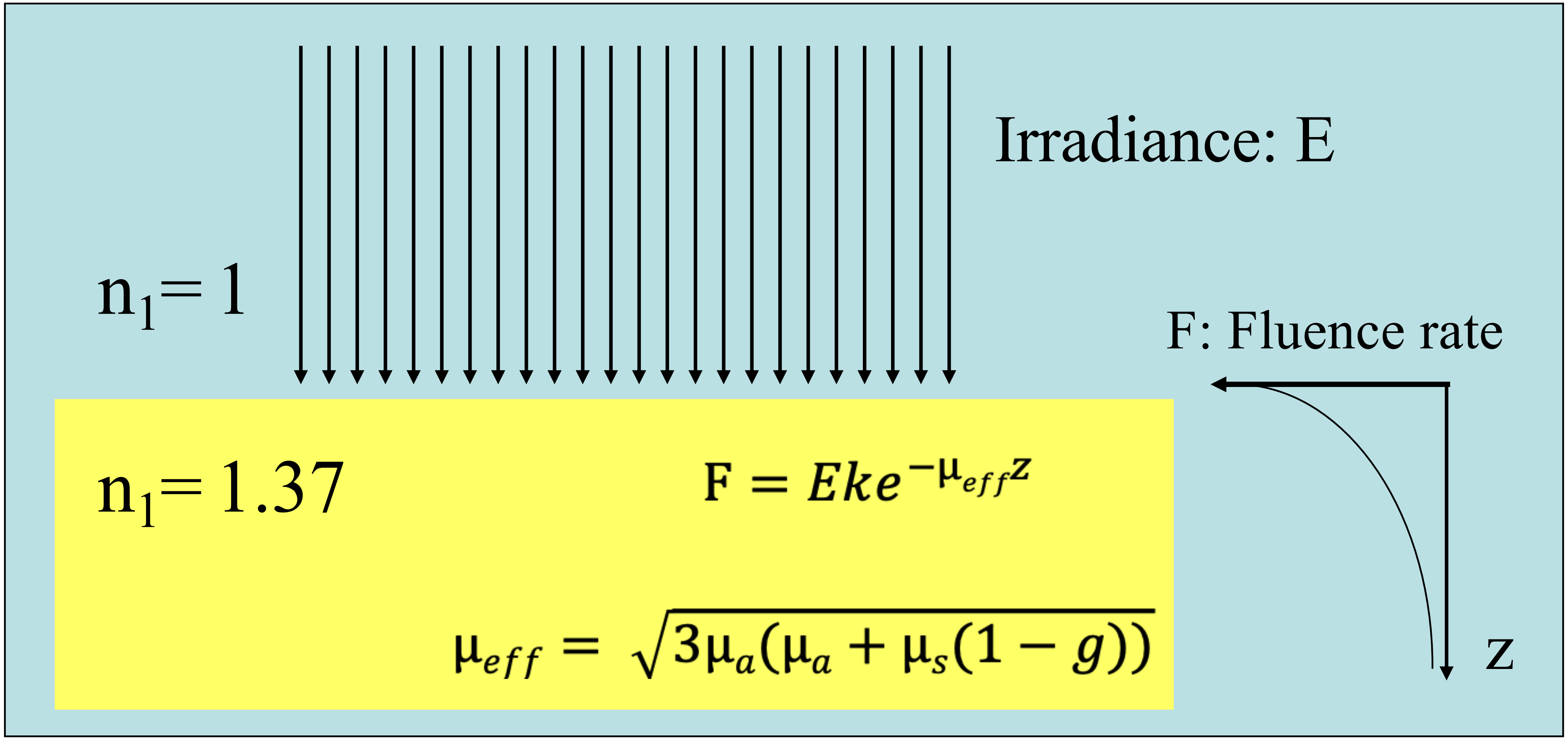


Photo courtesy of Medlight SA

Collimated “Broad” illumination perpendicular to the air-tissue interface

Semi-infinite volume of tissue



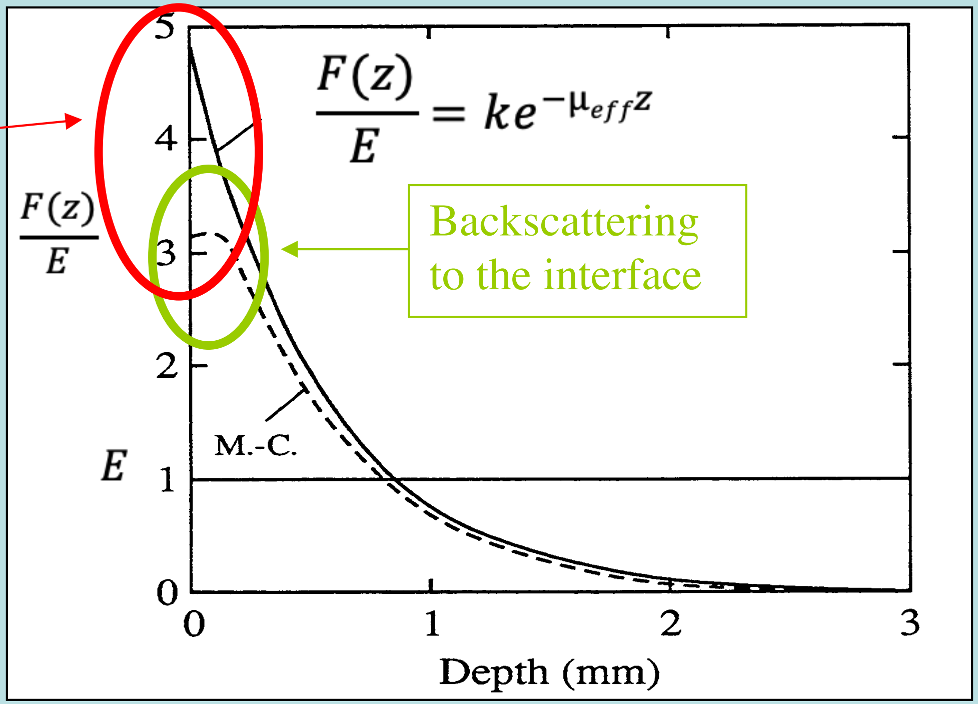
Collimated “broad” illumination perpendicular to the air-tissue interface

Semi-infinite volume of tissue (n=1.37)

Model and Monte-Carlo simulation (S.L Jacques)

$\mu_a = 0.27mm^{-1}, \mu_s = 18.7mm^{-1}, \mu_{\text{eff}} = 1.76mm^{-1}$
$g = 0.81, k = 4.87$

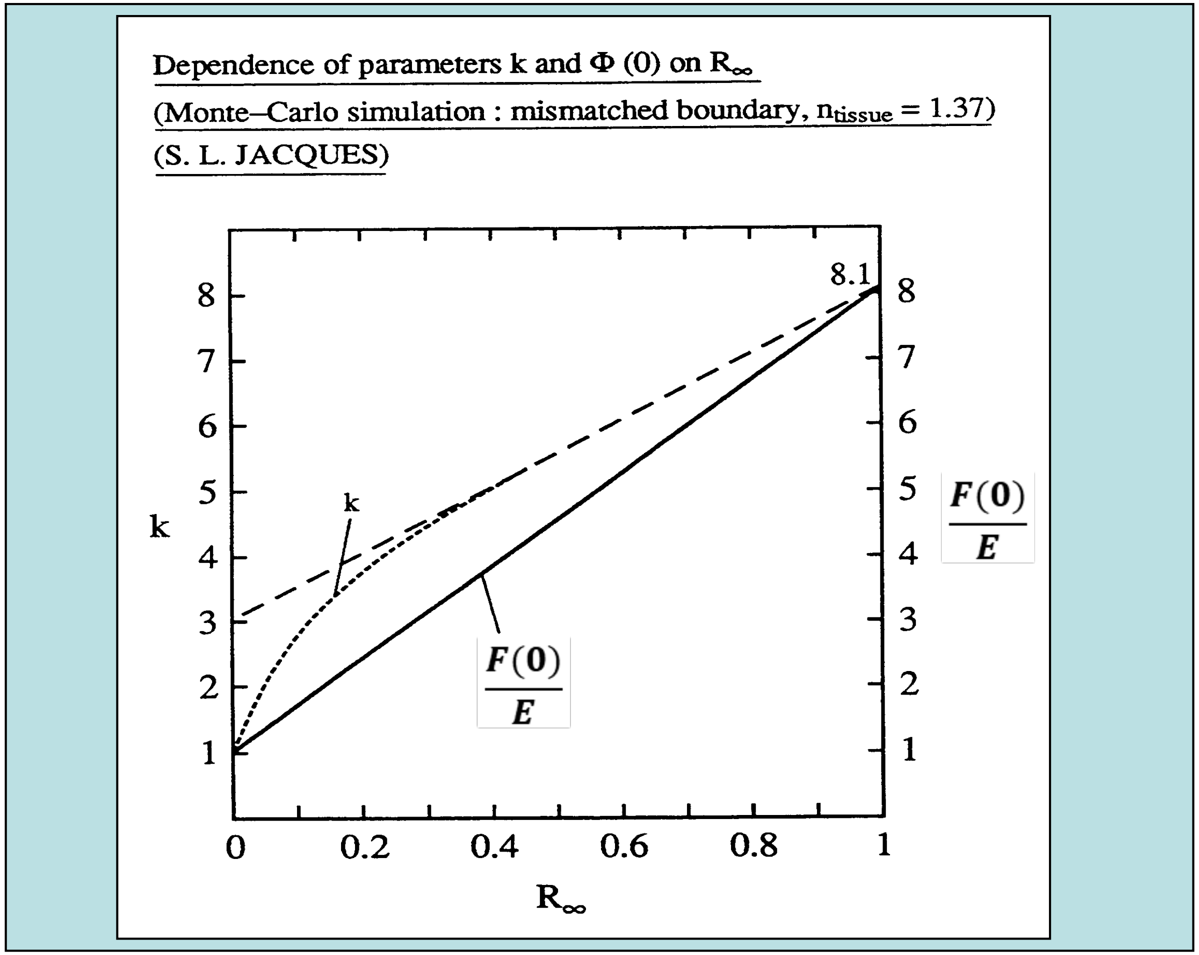
Diffusion approximation is not valid anymore



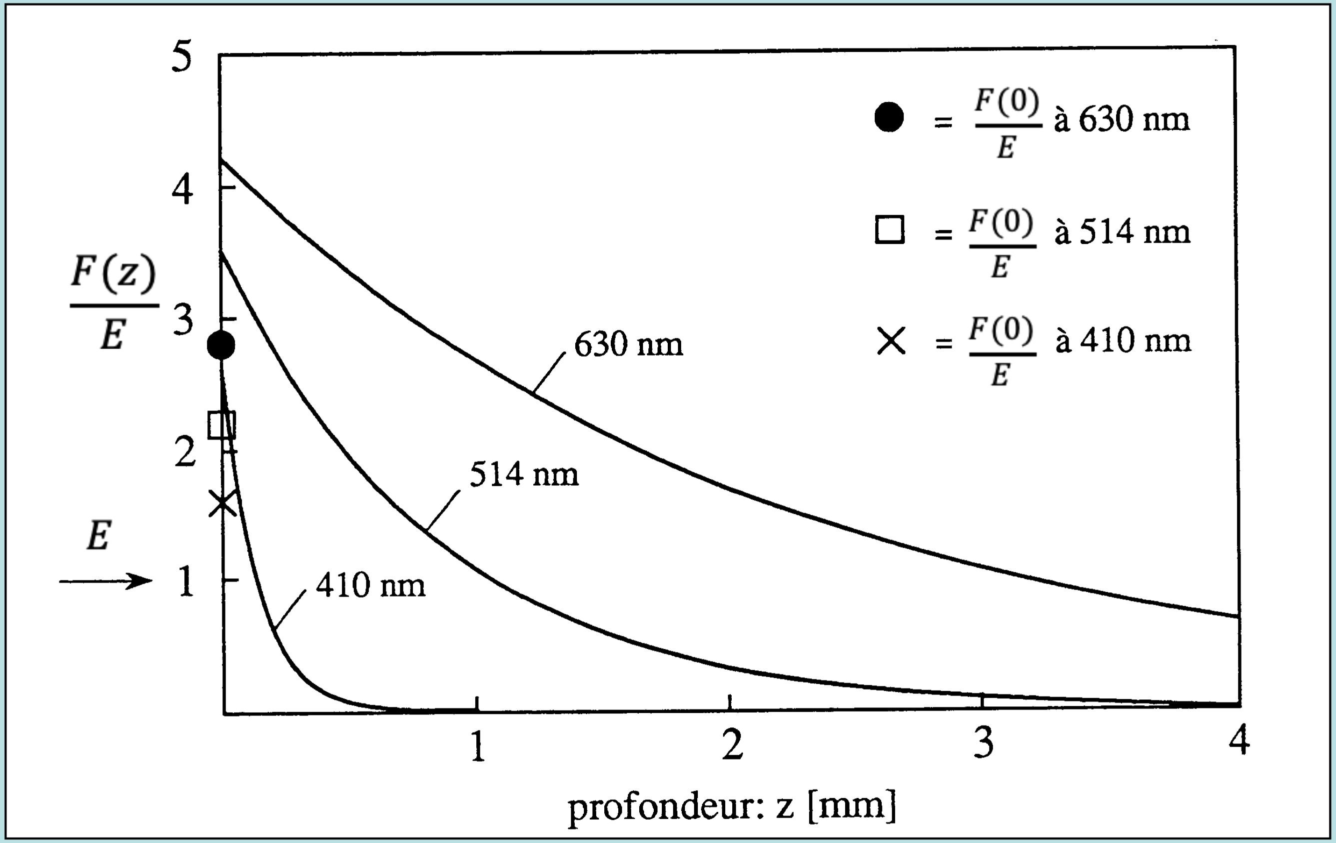
Backscattering to the interface

Collimated "Broad" illumination perpendicular to the air-tissue interface

Semi-infinite volume of tissue

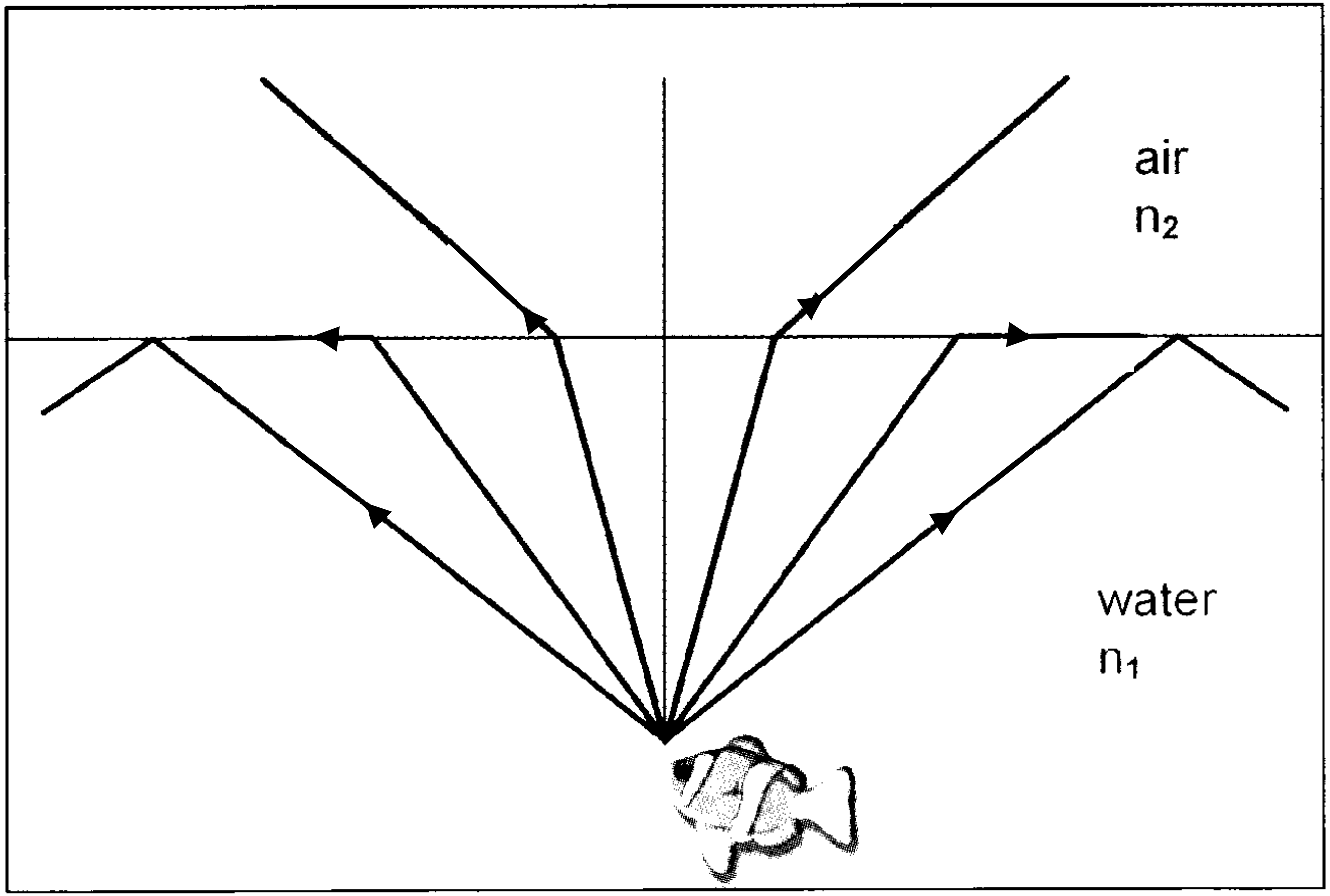


Fluence rate in the wall of an excised human esophagus for a collimated “broad" illumination perpendicular to the air-tissue interface



Source: G. Wagnières EPFL Thesis Nr. 1024

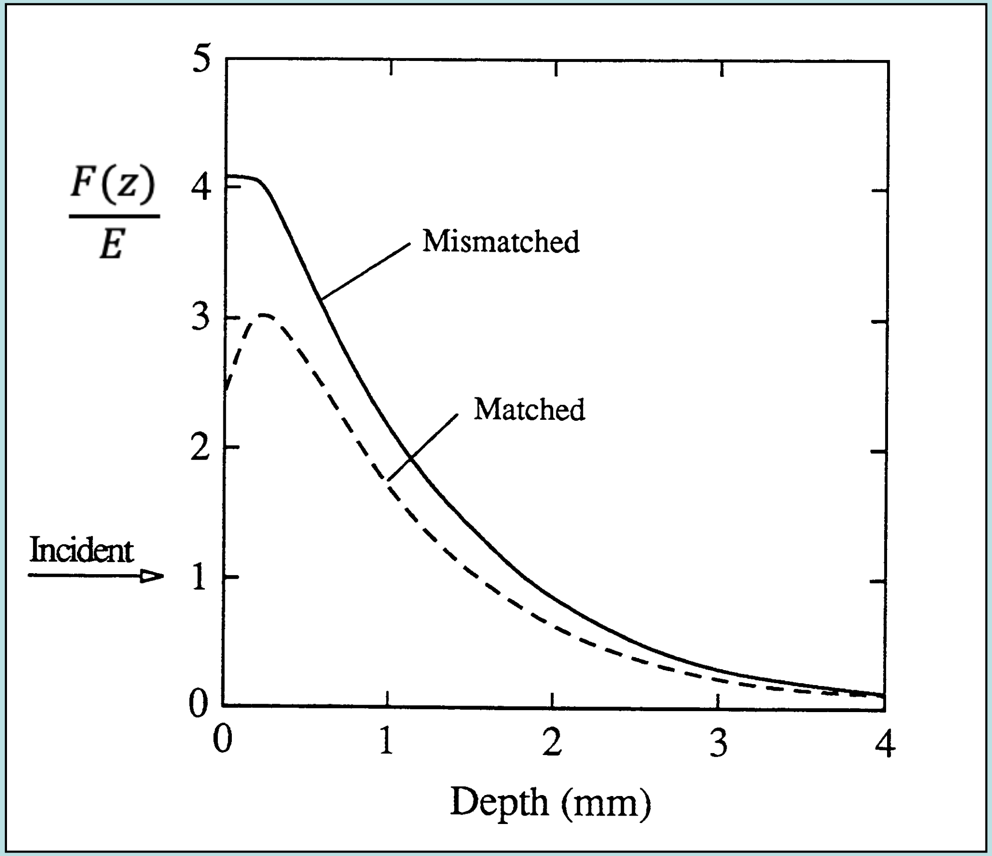
Effect of a refractive index mismatch



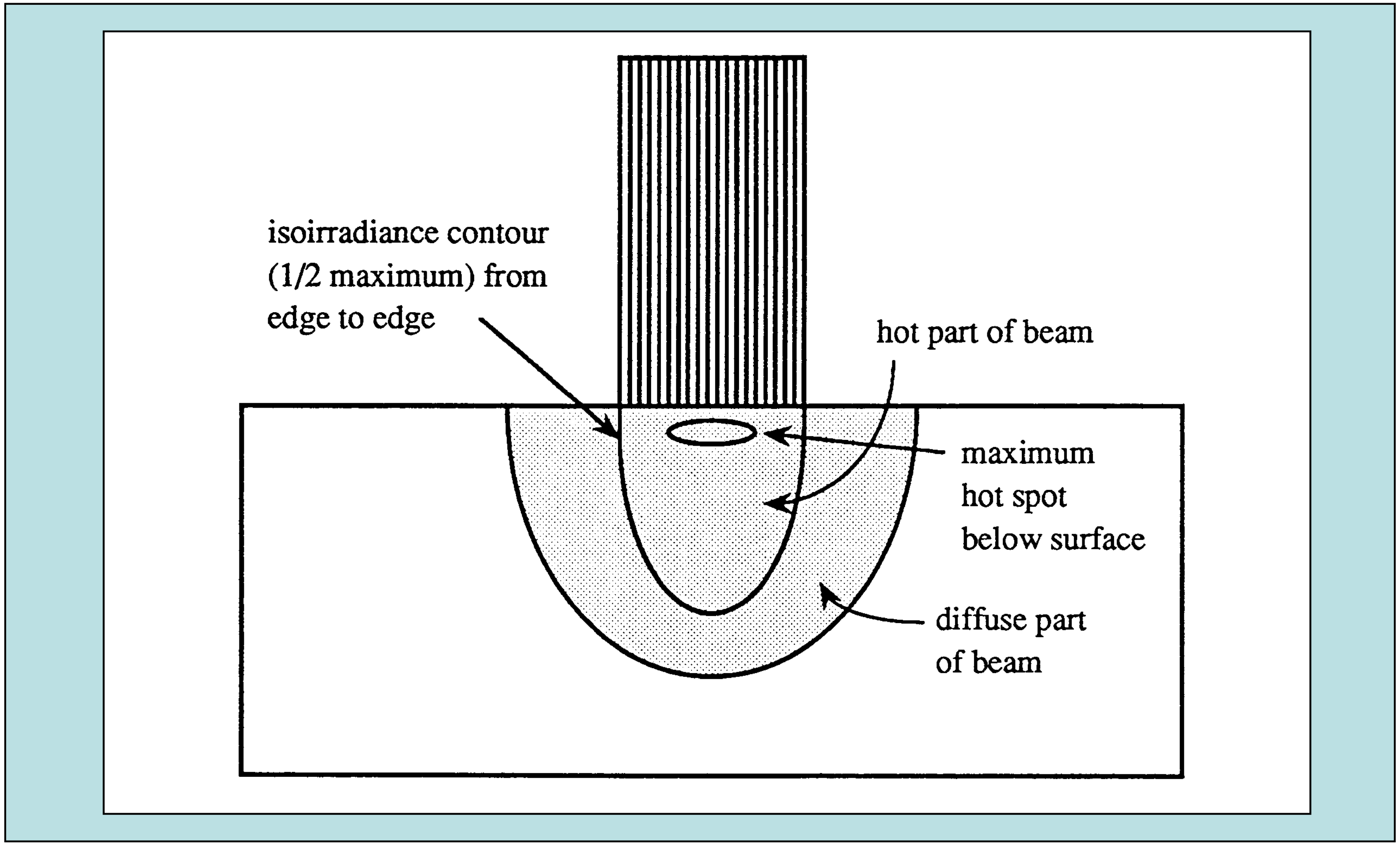
Sketch of fisheye vision.

Influence of the refractive index matching condition for a collimated “broad" illumination perpendicular to the interface (air-tissue; water-tissue)

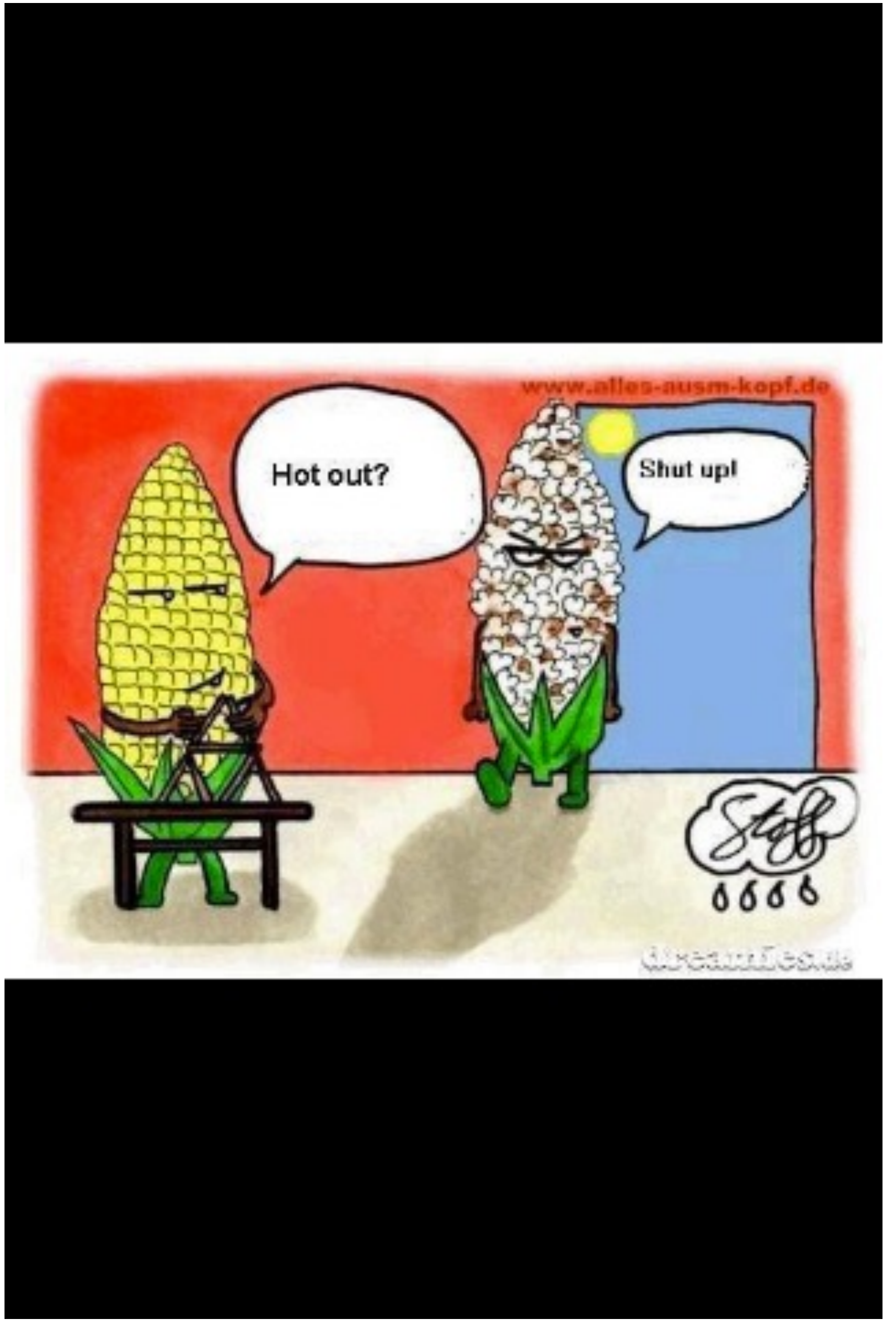
(Monte-Carlo simulation: $\mu_a = 0.1\ mm^{-1}$; $\mu_s = 10\ mm^{-1}$; $g = 0.7$; S. L. Jacques)



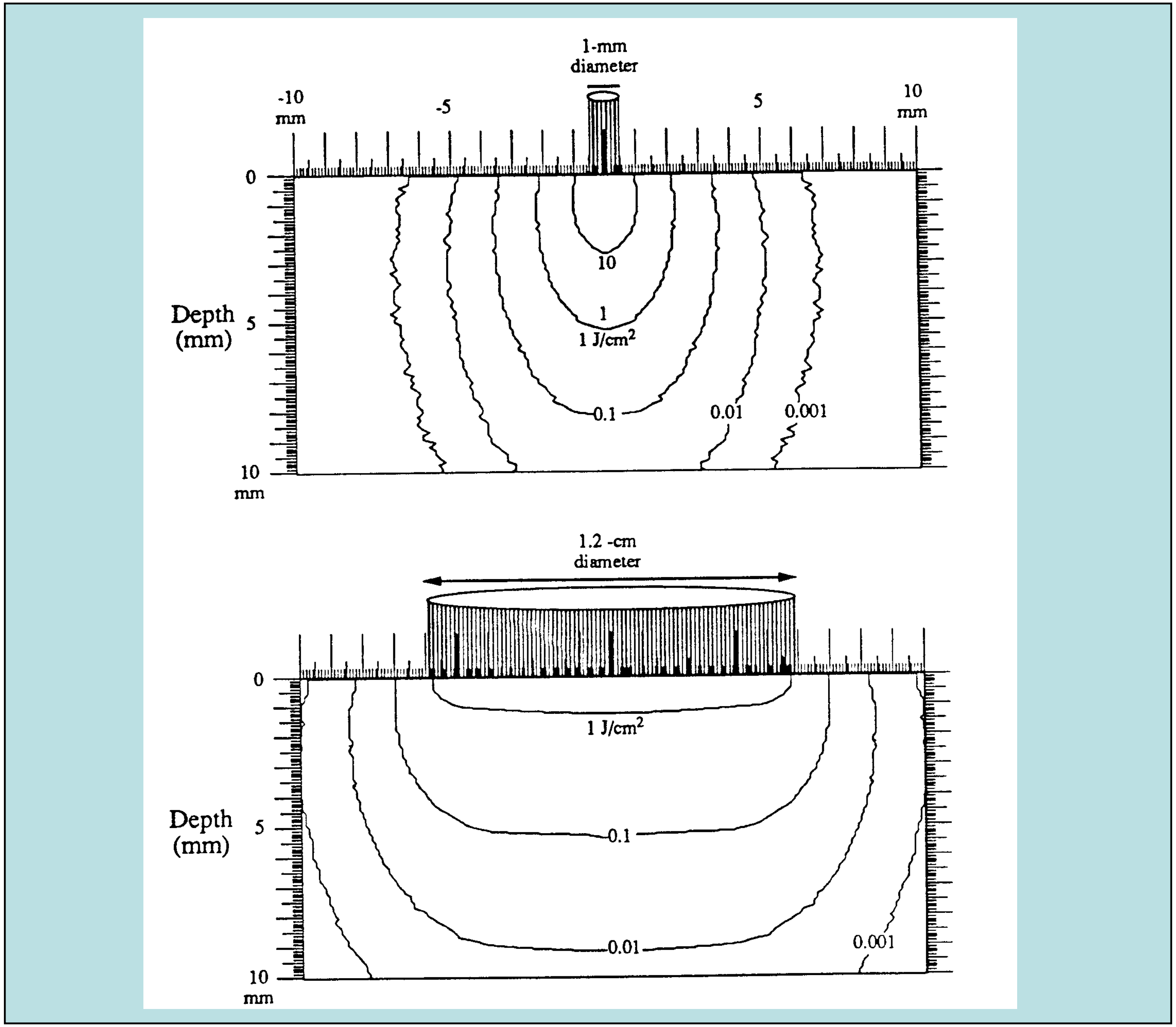
Influence of the refractive index matching condition



Pop-corn effect



Importance of the light beam diameter



Importance of the light beam diameter, cont.

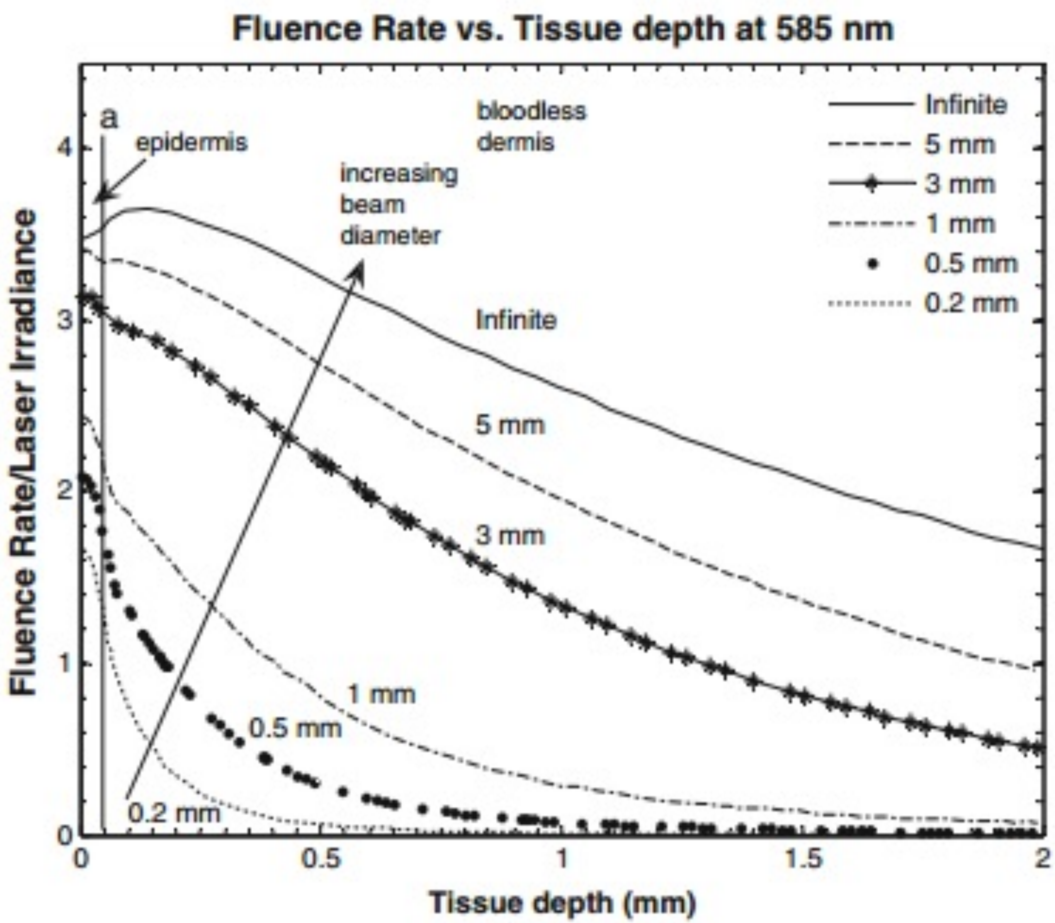


Fig. 3.15 The fluence rate within the skin below the beam center is fluenced (due to scattering) by the beam diameter. For the same incident irradiance (1 W/cm^2), the larger the beam (spot) diameter, the greater is the fluence rate. These Monte Carlo calculations were made for a flat top beam profile at 585 nm using optical properties summarized in Table 3.2

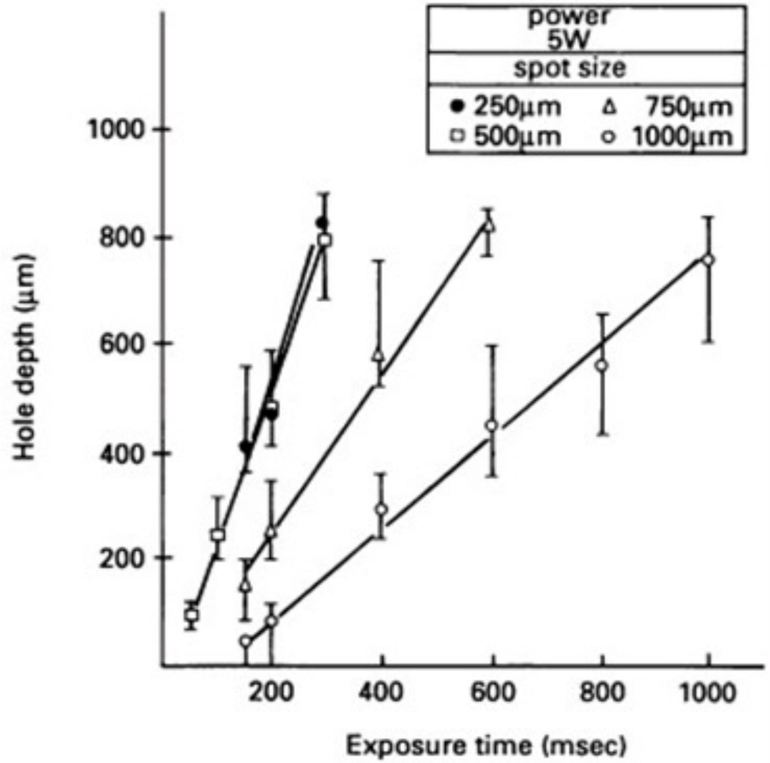


Fig. 10 Ablation depth as a function of spotsize.

(From Cothren RM, et al,[2] with permission from IEEE J Quantum Electronics.)

Aortic tissue

514 nm

A power of 5 watts was used. Vaporization depth as a function of irradiation time was measures for spot sizes of 1000, 750, 500 and 250 µm. Because of constant power and variable spot size each curve represent a different irradiance (W/cm^2). Between the 250 and 1000 µm spot sizes there is a factor of 4 increase in diameter or a factor 16 increase in irradiance (W/cm^2). Therefore, it takes longer to achieve the same hole depth when the irradiance is decreased by increasing the spot size. As the spot size became smaller and smaller some other interaction must be happening in the tissue.

Interstitial illumination with a cylindrical light distributor

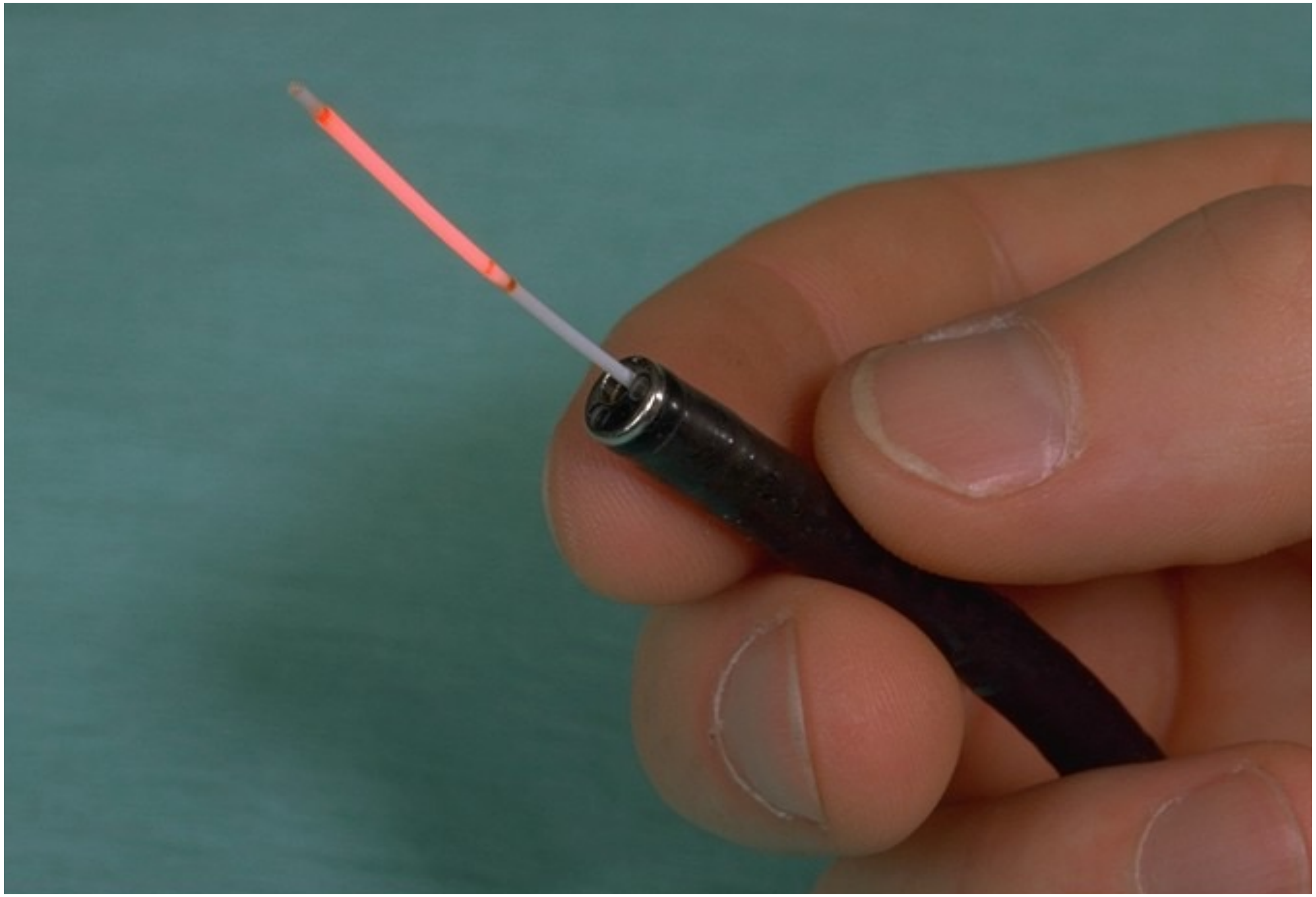


Photo courtesy: Medlight SA

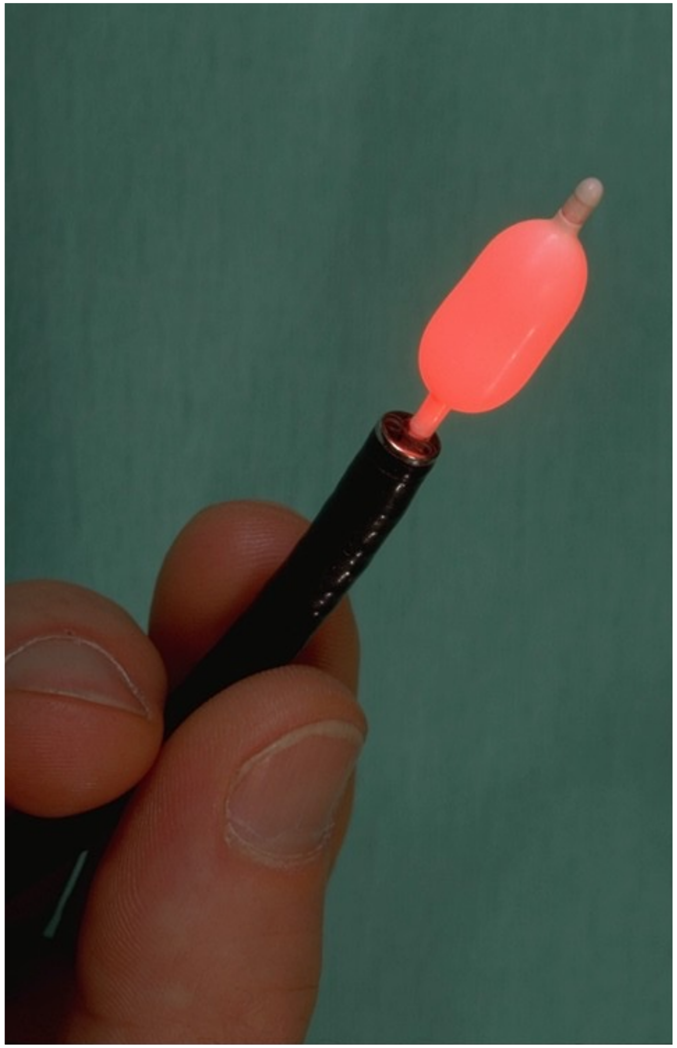
Interstitial illumination with an infinitely long cylindrical light distributor

J_c [W/cm]: Output power per unit length of fiber
r [cm]: Radial distance from the fiber axis
a_c [cm]: Fiber radius

$$F(r) = \frac{2J_c/\pi a_c}{K_0(a_c\mu_{eff}) + 2D\mu_{eff}K_1(a_c\mu_{eff})} K_0(r\mu_{eff})$$

K_0 and K_1 are modified Bessel functions of the second kind (see next slide)

"Backscattering-balloon-based" Light distributor for PDT in the bronchi (Ranges; Length: 15-40 mm. Diameter: 2-15 mm)



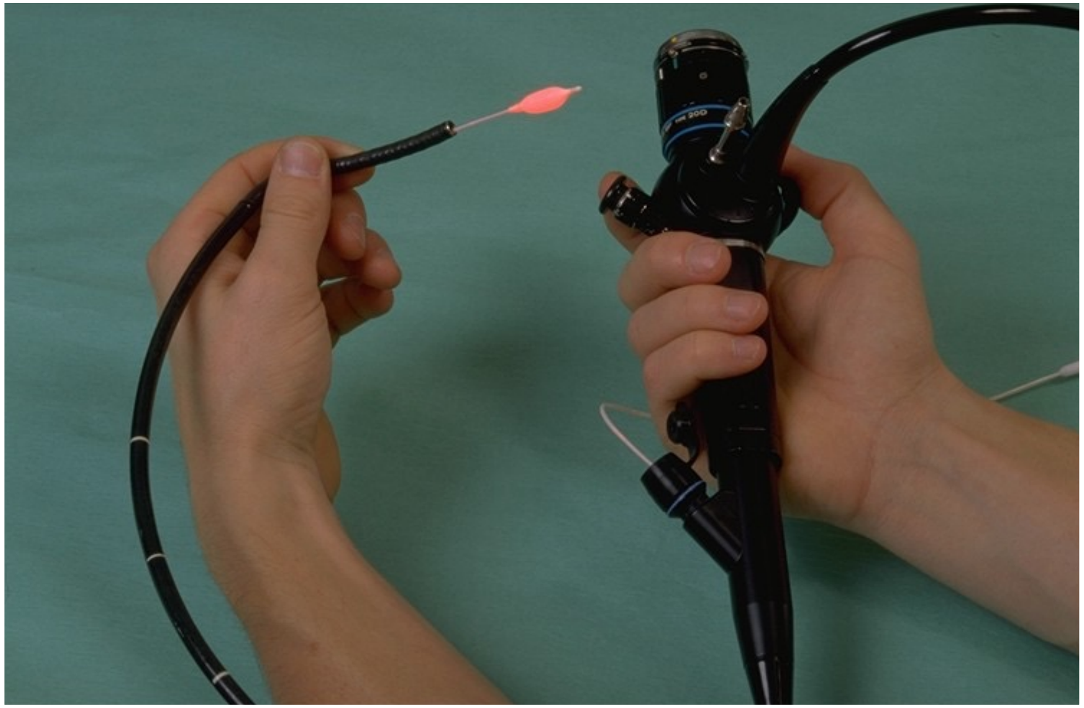


Photo courtesy: Medlight SA

"Backscattering-balloon-based" Light distributor for PDT in the bronchi

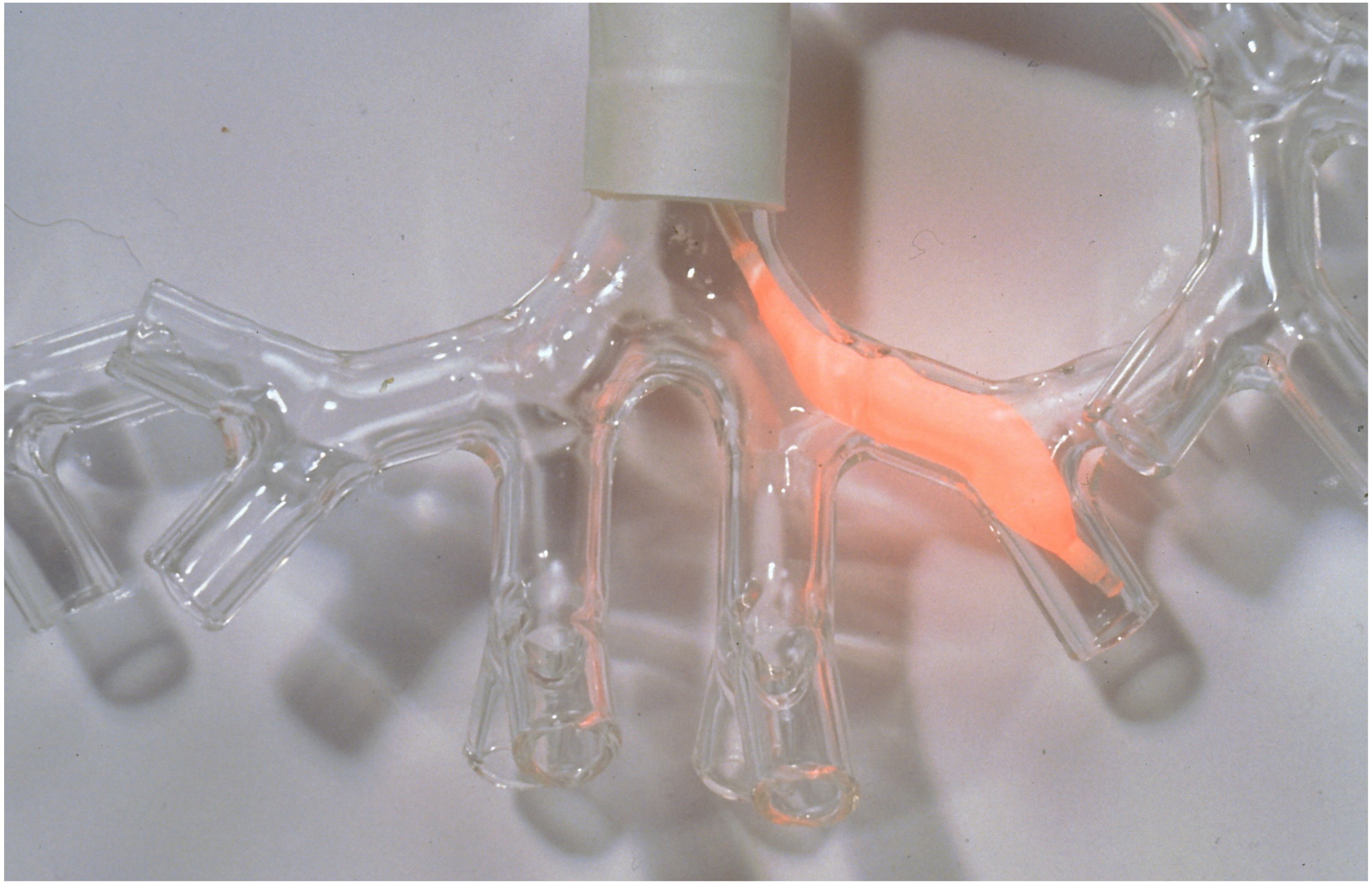
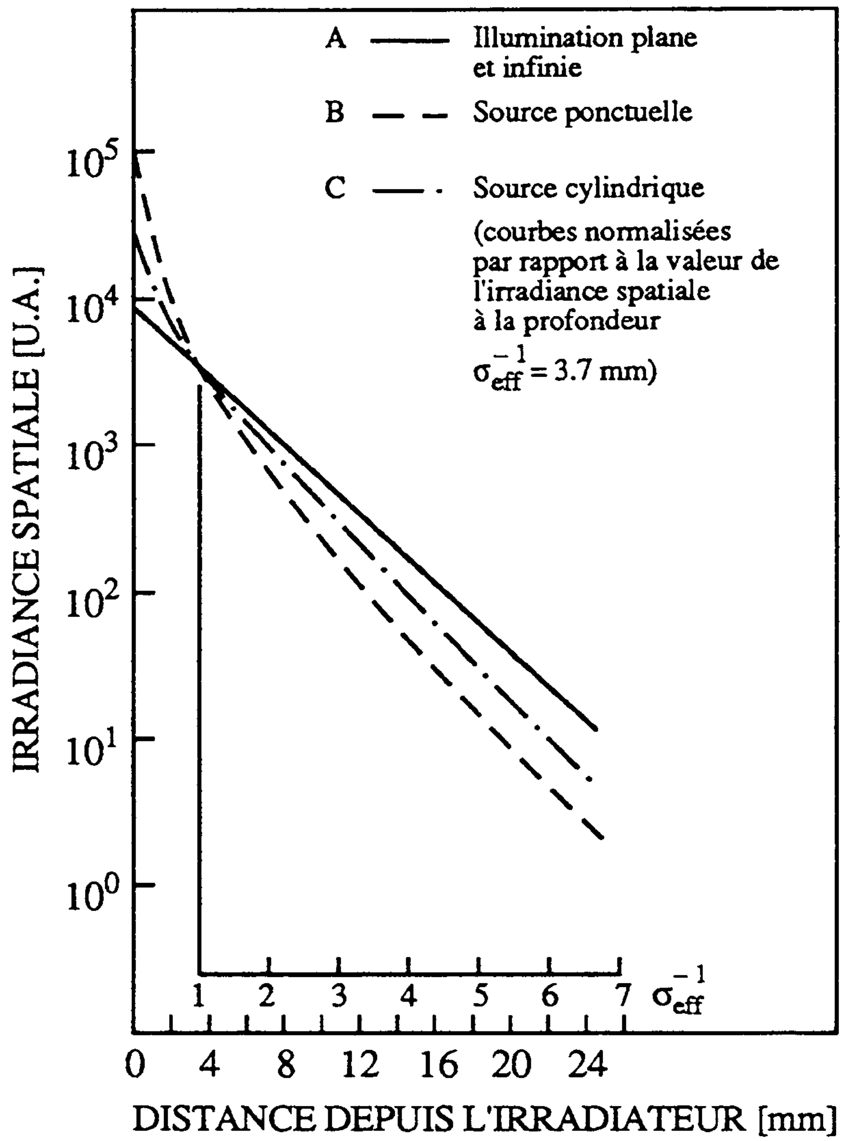


Photo courtesy: Medlight SA

Light distribution for different types of illumination geometries



σ stands for μ

Distribution de la lumière dans les tissus pour divers types d'éclairements.