# Contemporary optical and laser methods for therapy

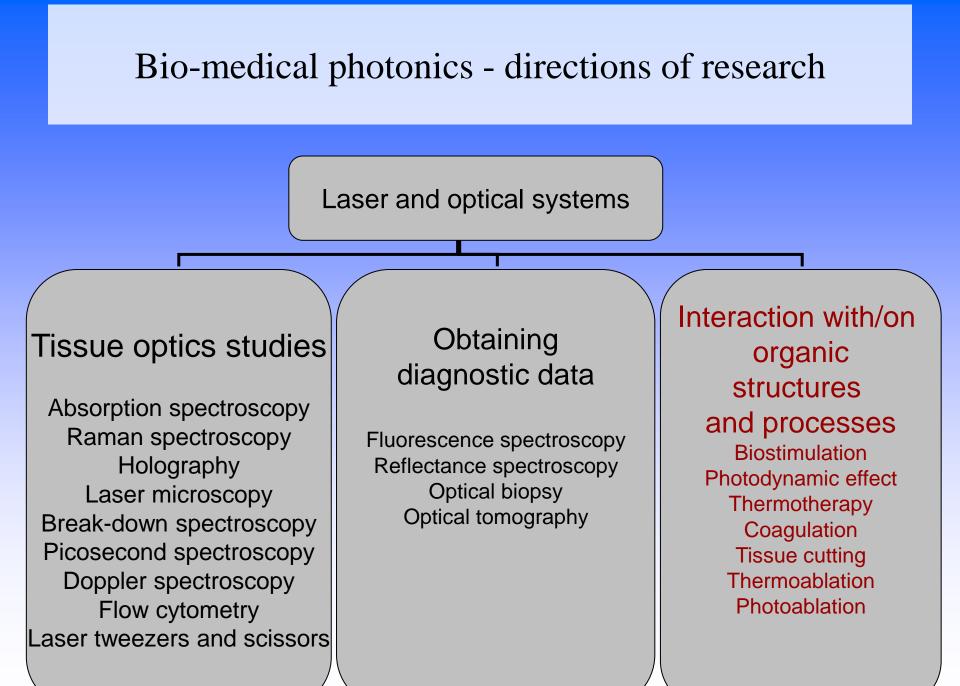
### Assoc. prof. Dr. Ekaterina Borisova Institute of Electronics, Bulgarian Academy of Sciences

# **Basic concepts**

- Tissue optics
- Laser-tissue interaction
- Optical diagnostics
- Laser therapy
- Modification of optical properties of biological tissues

# **Biomedical photonics**

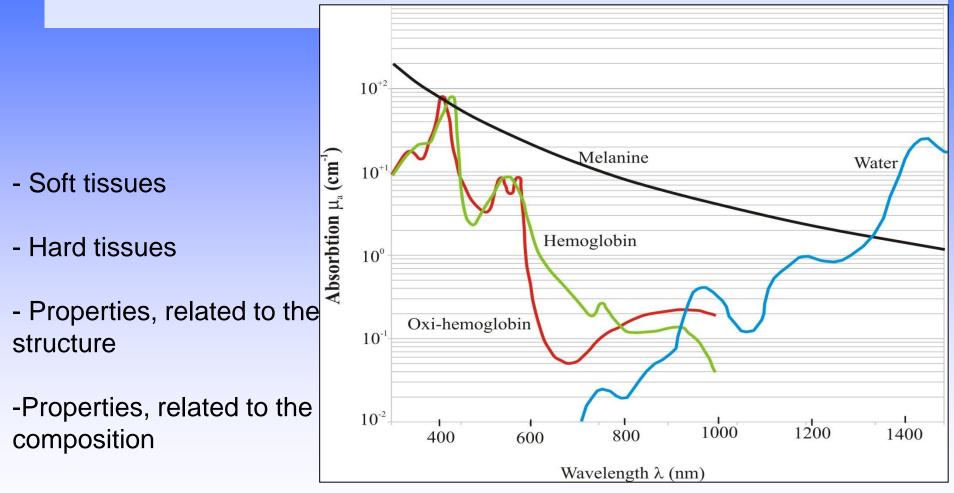
- A new scientific field that has been developing since the 1980s and has been introduced as such in scientific circles for the last decade
- Historically "lasers in medicine", "photomedicine", "phototherapy", etc.
- Biomedical Photonics Handbook, 2005? Edited by Tuan Vo-Dinh - "" Bio-Medical Photonics – "...Revolution on the Interface Science-Technology "



# **Historical reference**

- First Generation of Laser Medical Systems 1962, Leon Goldman 1963 г. Laser Laboratory at Children's Hospital Research Foundation, Cincinnati, Ohio.
- Second Generation integration of laser equipment with computer/microprocessor - 1988 MEDITEC - REINHARD GmbH - "Introducing the First Continuous Wave YAG Laser with AMR (Automatic measurement power and regulation of the output power)"
- New Generation lasers with more than one wavelength, spectral, video, endoscopic channels, telemedicine networks

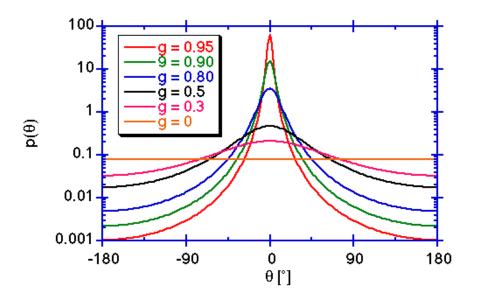
# **Optical properties of biological tissues**

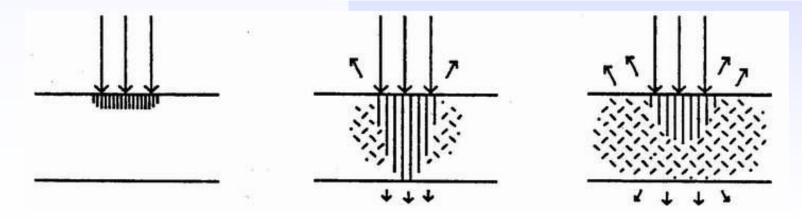


Spectra of absorption of basic tissue chromophores

# Light distribution in the tissue

- 1-predominant swallowing;
- 2 -near values for absorption and scattering coefficients;
- 3-predominant scattering





#### **Laser-tissue interactions**

#### **Non-invasive interactions**

- Laser-induced autofluorescence
- Photosensitized laser-induced fluorescence
- Reflection of light from biological tissues **Therapeutic interactions**
- Thermal effects
  - **Reversible thermal effects** 
    - Thermal biostimulation
    - Laser hyperthermia
- Irreversible thermal effects

Laser coagulation Laser welding Laser Evaporation (Cutting) of tissues

- Photodynamic effect photodynamic therapy
- Laser biostimulation

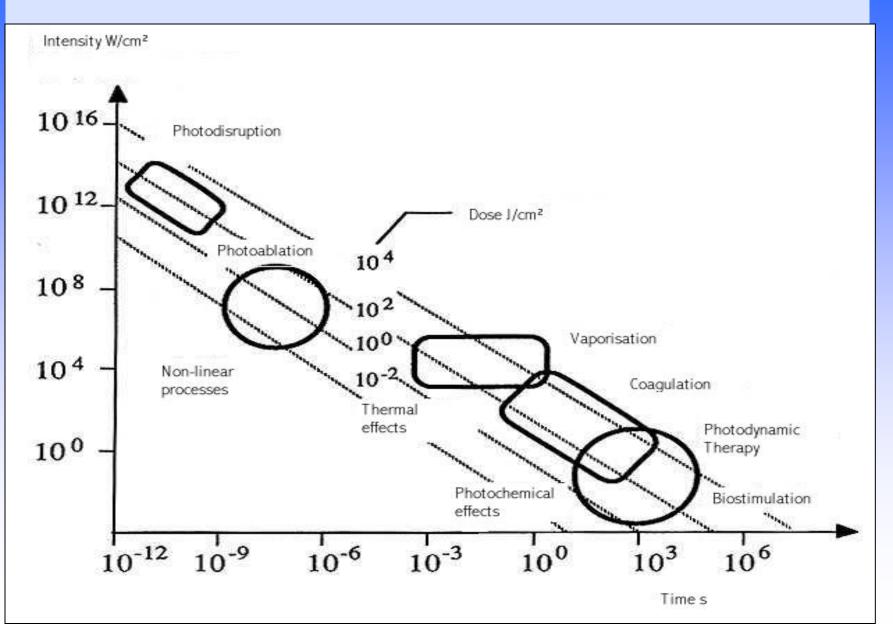
# **Types of interactions**

- properties of radiation
- Impact of irradiation / pulse time
- Influence of power / energy
- properties of the environment
- Influence of wavelength of irradiation
- Influence of radiation geometry

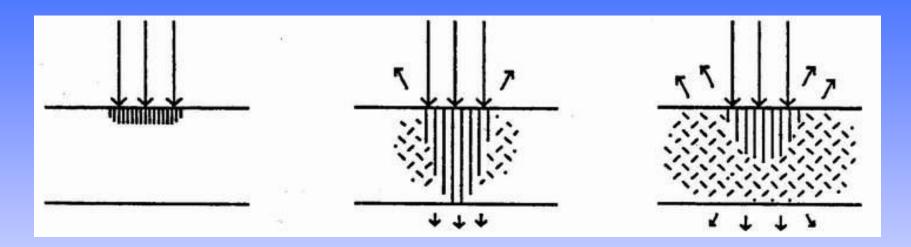
# **Types of effects**

- Photochemical effects
  - Biostimulation
  - Photodynamic effect
- Thermal effects
  - Coagulation (hyperthermia)
  - Evaporation
  - Photoablation
  - Photo breakdown (covalent links destruction)
- Non-linear processes
  - Two-photon absorption
  - Photobreakdown ( plasma formation)

#### **Laser-tissue interactions**



# **Penetration of light into the tissues**



- 1-ultraviolet and far infrared range defining by water and protein absorption;
- 2-visible spectral range 450-600 nm determined by blood absorption;
- 3- area of therapeutic window red-near infrared spectral area suitable for the introduction of contrast agents/compounds/markers

# Thermotherapy

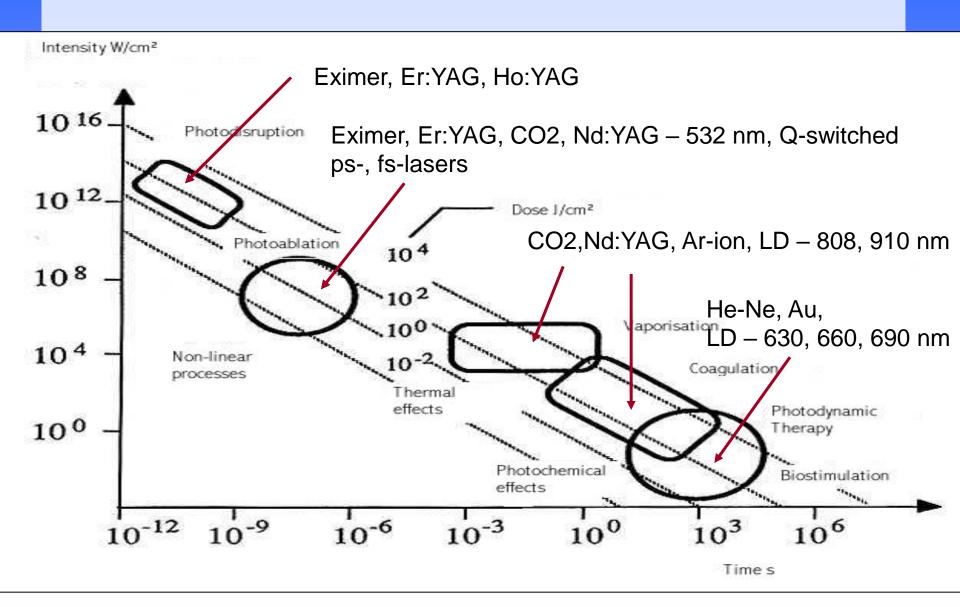
- Coagulation (hyperthermia)
- Evaporation
- Photoablation
- Photo breakdown /breakage (covalent links destruction)



"Nurse, get on the internet, go to SURGERY.COM, scroll down and click on the 'Are you totally lost?' icon."

# SUPERFICIAL BCC TREATED WITH CRYOSURGERY USING 3-4mm MARGINS

#### **Laser-tissue interactions**



# **Laser-tissue interactions**

#### **Non-invasive interactions**

- Laser-induced autofluorescence
- Photosensitized laser-induced fluorescence
- Reflection of light from biological tissues

#### Laser interactions

Thermal effects

Reversible thermal effects Thermal biostimulation

Laser hyperthermia

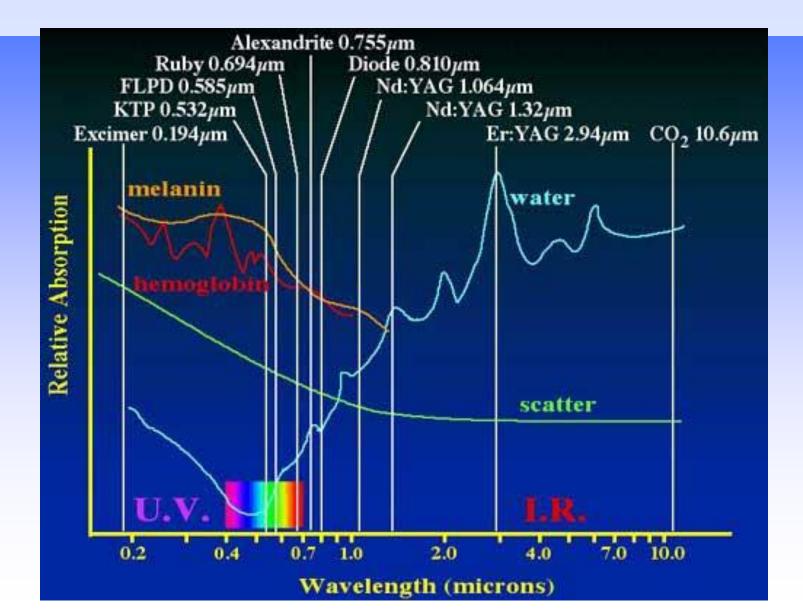
Irreversible thermal effects
Laser coagulation

# Laser welding

Laser Evaporation (Cutting) of tissues

- Photodynamic effect photodynamic therapy
- Laser biostimulation

# Laser spectrum



# Laser spectrum

•	Laser	Wavelength (nm)	<b>Application</b>
•	Er:YAG	2940	Skin resurfacing
•	Argon	488/514	Vascular lesions
•	KTP:YAG	532	Vascular lesions
•	Copper vapor	578	Vascular lesions
•	FLPPD	585	Vascular lesions
•	Long pulse	595-600	Leg veins
٠	Ruby, Q-switched	694	Tattoo removal
٠	Long pulse	694	Hair removal
٠	Q-switched Alexand	drite 755	Tattoo removal
٠	Nd:YAG	1064	Deep vascular
٠	Q-switched YAG	1064	Tattoo removal
٠	CO2	10600	Cut/coag/resurf

Laser media	Color	Wavelength (nm)	Typical application
Carbon dioxide	Far infrared	10.600	General, cutting
Nd: YAG	Near infrared	1.064	General, coagulation
KTP:YAG	Green	532	General, pigmented lesions
Argon	Green	514	Vascular, pigmented lesions
Xenon fluoride	Ultraviolet	351	Cornea, angioplasty

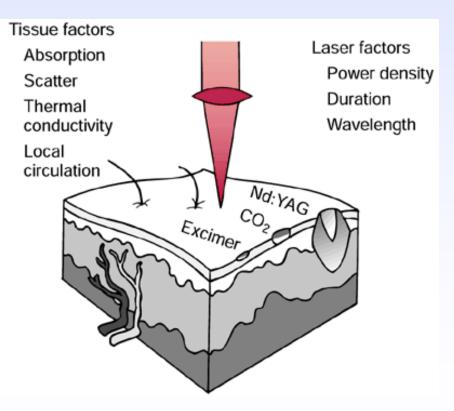
# **Effect of Laser on tissues:**

#### • Laser factors:

- <u>Wavelength</u>
- Power density
- <u>Duration</u>

#### • Tissue factors:

- Absorption
- <u>Thermal conductivity</u>
- Local circulation
- <u>Scatter</u>

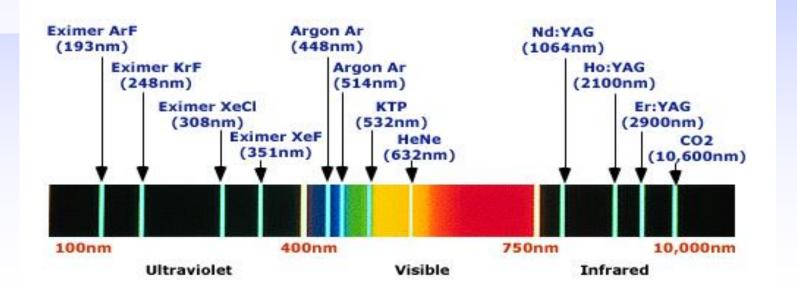


# **Laser Materials/Properties**

- Infrared light: primarily absorbed by water
- Visible and UV light are absorbed by hemoglobin and melanin
- As wavelength becomes shorter – scatter begins to dominate the penetration of light

Table 2. APPROXIMATE TISSUE PENETRATION DEPTHS FOR SEVERAL LASERS

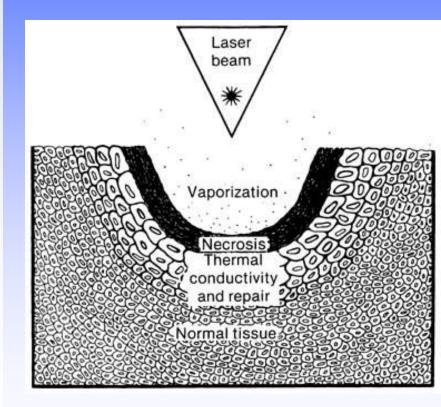
Laser	Wavelength	Penetration Distance
Argon	514 nm	0.8 mm
KTP 532	532 nm	0.9 mm
Dye Lasers (for PDT)	577 nm	0.9 mm
Nd:YAG	<b>1.</b> 06 μm	4 mm
Ho:YAG	2.1 µm	0.4 mm
Er:YAG	2.94 μm	3 μm
CO <sub>2</sub>	10.6 µm	30 µm



# **Tissue Ablation**

- 10 C 45 C: Conformation change of proteins
- 50 C: Reduction of enzyme activity
- 60 C: Denaturation
- 100 C: Water vaporizes

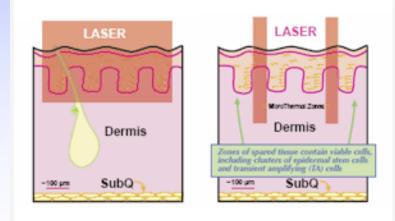
• Thermal damage



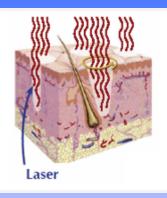
### PRINCIPLE



MTZ(Micro Thermal Zone)



#### Laser treatment Diagram



#### Skin Response From Scar

Scar repair response after Fractional laser is different with other treatment technique. Because Hulle cell which has the cell have possibility to growth containing stem cells and transient amplifying, TA cells is remained between treatment area. Matter will be damaged in direct proportion to its value.

The speed of skin rejuvenation is in direct to density and quantity of TA and stem cell.

So the side effect after treatment is very low or not occurred comparing old type of laser device like CO2 laser.

# CO<sub>2</sub> Laser

# • 10,600 nm wavelength

- Water is target chromophore
- Aiming helium-neon (HeNe) beam
- Highest power continuous-wave laser

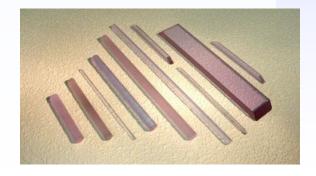
# • Cutting or ablating tool

- Focus to 200  $\mu m$
- Seals blood vessels less than 0.5 mm
- Pulsed to accommodate thermal relaxation time, less pain and less edema
- Pattern generators
- Work in distal airway in "hands off" fashion
  - Used in majority of procedures except those requiring coagulation of larger vessels
  - No current optical fiber to carry beam



# Nd: YAG Laser

- 1064 nm wavelength (neodymium-doped yttrium aluminum garnet )
  - Aiming helium-neon (HeNe) beam
  - Wavelength is between minimal absorption of water and a small amount of scatter
  - Solid state laser
  - Fiberoptic carrier
- Application
  - Deeper penetration (up to 4 mm) for ablative therapy and hemostasis
  - Preferentially absorbed by pigmented tissues
  - Vascular malformations amenable to treatment
  - Used in a multitude of pulmonary, urology and gastroenterology procedures
  - Minimally invasive percutaneous laser disk decompression
- Limitations
  - Greater scatter than CO2
  - Deep thermal injury
  - Risk for transmural injury

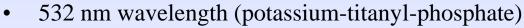


# **Argon Laser**

- 488 514 nm wavelength (ion laser)
  - Oxyhemoglobin is target chromophore
  - Small spot size (0.1 1 mm) variable in size and intensity
  - Flexible delivery system
- Applications
  - Retina or middle ear surgery
  - Facial spider veins
  - Junctional nevi
  - Cherry hemangioma
  - Vascular birthmarks
- Limitations
  - Also absorbed by epidermal and dermal tissues due to melanin
  - Continuous mode of operation
  - Higher prevalence of postoperative pigmentary alteration and fibrosis
  - <u>Pulsed Dye Laser (PDL) preferred for many roles Argon laser originally used</u> (treatment of vascular lesions, including spider veins, strawberry birthmarks and port wine stains)



# **KTP Laser**



- Frequency doubling
- Nd: YAG laser passes through a KTP crystal emission is <sup>1</sup>/<sub>2</sub> its wavelength
- Oxyhemoglobin is primary chromophore
- Fiberoptic carrier
- Continuous wave (CW) mode to cut tissue
- Pulsed mode for vascular lesions
- Q-Switched mode for red/orange tattoo pigment
- Applications
  - Granuloma excision of the respiratory tract
  - Subglottic/tracheal stenosis
  - Subglottic/supraglottic cyst excision
  - Inferior turbinate reduction
  - Nasal papilloma excision
  - Nasopharyngeal stenosis
  - Supraglottoplasty
  - Laryngeal papilloma excision
  - Middle ear surgery (Cholesteatoma excision, stapes surgery)
- Delivery
  - CW/pulsed mode: insulated fiber, fiber handpiece, scanner, or microscope
  - Q-Switched mode: articulating arm

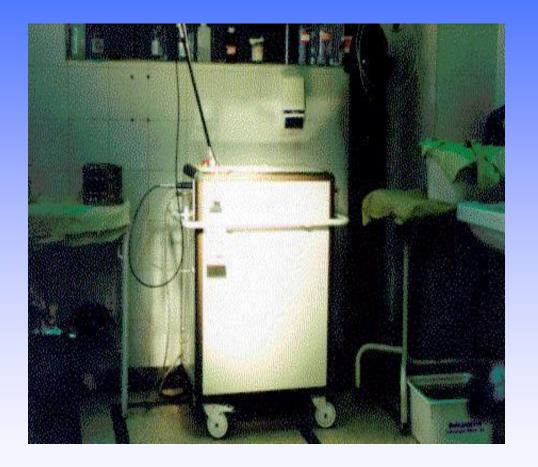




#### **Examples from the practice of IE-BAS**

- Nd: YAG Laser Systems for Surgery and Laser Coagulation at 1064 and 1320 nm
  - Introduced to Alexandrovska Hospital
  - Implemented in SBALOncology
- Applications
  - General Surgery
  - Urology
  - Trans-cutaneous rejuvenation
  - Hyperthermia, coagulation and ablation of biological tissues

#### "MedRay" - a family of laser systems



#### МИНИСТЕРСТВО НА ЗДРАВЕОПАЗВАНЕТ:0



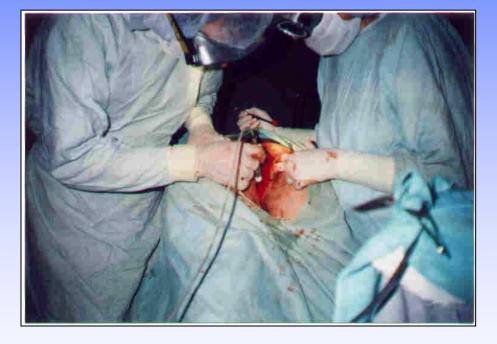
Дата: 03.02.1998 год.

началник отдел: Жегу

ныж. Т.Илиев

"MediRay 100/40" - iintroduced at "Alexandrovska Hospital".

#### "MediRay100/40" in surgery room



# Over 500 operations, including complicated surgical interventions of patients suffering from the following diseases:

Hepatic echinococcal cyst (Echinococcus hepatis); Rectal carcinoma (Ca recti); Skin cancer (Ca cutis); Malignant melanoma (Nevus, melanoma); Decubitus (Decubitus); Skin tumors (Tu cutis); Rectal polyps (Polipus recti); Condylomata; Cysta dermoidalis; Perianal fistula (Fistula perianalis); Varicose ulcers (Ulcus varicosum); External and internal haemorrhoids (Haemorroides ext et int); as well as numerous small operations of a number of predominantly dermatological pathologies:

Vulnus atonicum; Ganglioma; Clavus; Circumscisio; Unguis incarnatus; Veruces; Fissura ani; Vulnera ped.; Atheroma et fibroma; Cornu cutaneum; Panaritium.

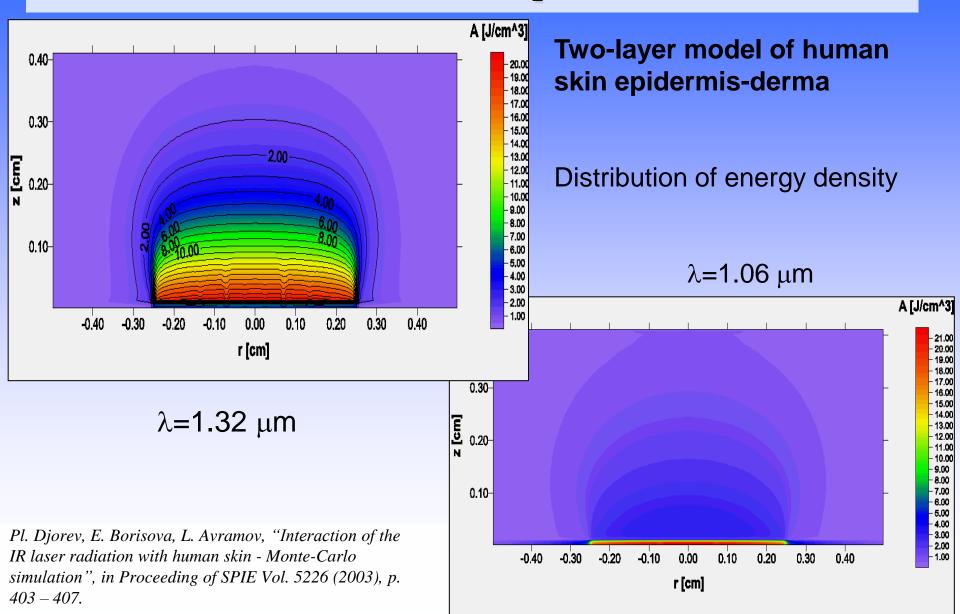
#### 1.06 µm technology





• Laser Assisted Treatment of Echinococcal Cyst in situ

# Computer Model Laser Therapy - Hyperthermia / Laser Scalpel

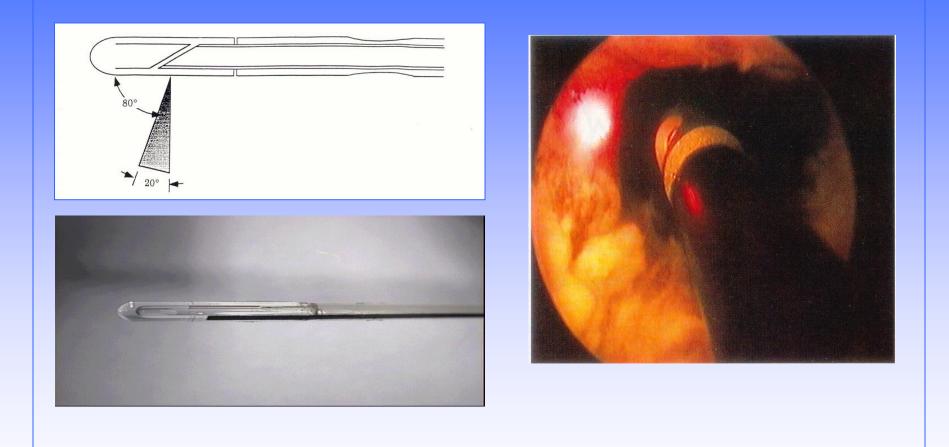


### "MediRay U" - a urological laser system



"MediRay U" - at the National Oncology Center. Performs endoscopic operations of patients with various urological diseases

### 1.06 µm technologies



• Laser transurethral contactless coagulation of prostate adenoma

#### **Example - cost – benefit analysis**

"Open prostatectomy" and its alternative "transurethral laser coagulation of prostate hyperplasia "- category" average "

	prostatectomy	Laser coagulation
Days in hospital	6-8	1
Days for recovery	60-90	30

"Bladder tumor electroresection of up to 20 mm" (TER) and "laser coagulation" of the same tumor - category "small"

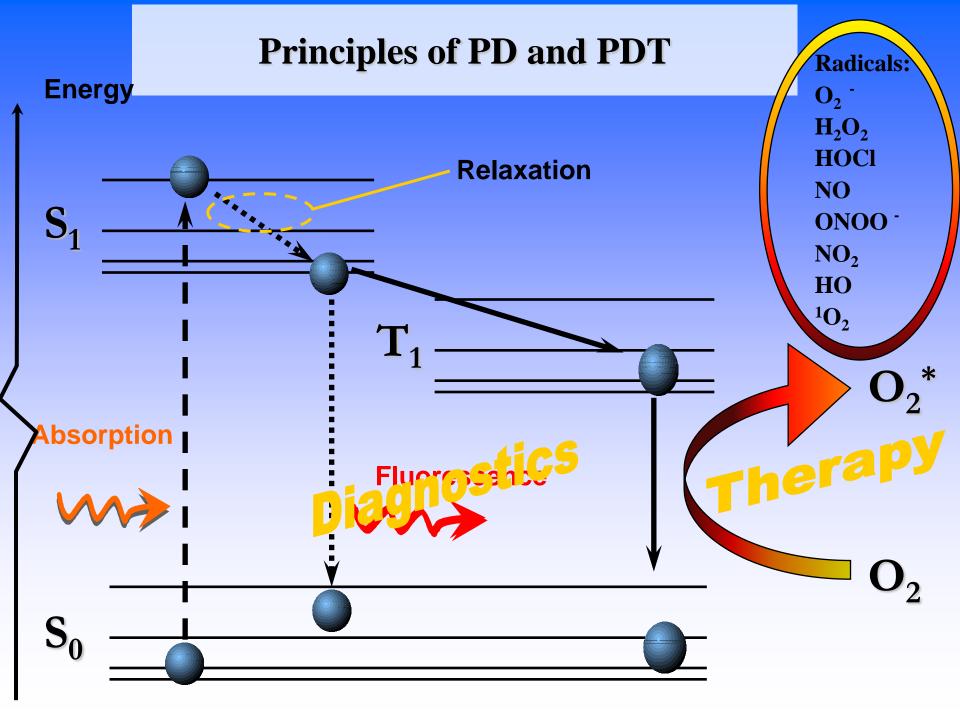
	TER	Laser coagulation
Days in hospital	3-4	1
Days for recovery	30-60	20

## **Cost - benefit analysis**

- Savings from postoperative bed days reductions total savings for 600 patients: ≈ 500,000 BGN per year
- Savings from postoperative disability reduction overall economy:
- ≈ 300 000 BGN per year
- Savings on medication and materials
- ≈ 30 000 BGN per year
- •
- Economic effect of lower cost of equipment:
- $\approx 30\ 000\ \mathrm{BGN}$
- Total economic effect: 1 100 000 BGN for one year or 8.8 million BGN (minimum) per unit during its lifetime (8 years). ≈ 4,5 MEuro

# **Types of applications - photodynamic therapy**

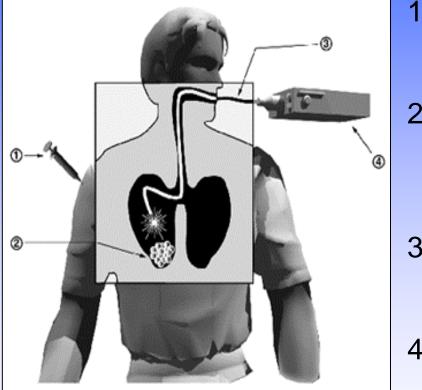
- Photodynamic therapy
  - Tumor therapy
  - Photodynamic inactivation
  - AMD (age macular degeneration) for retinal therapy
  - Diabetic retinopathy
  - Inflammatory processes arthritis, tonsillitis, etc.



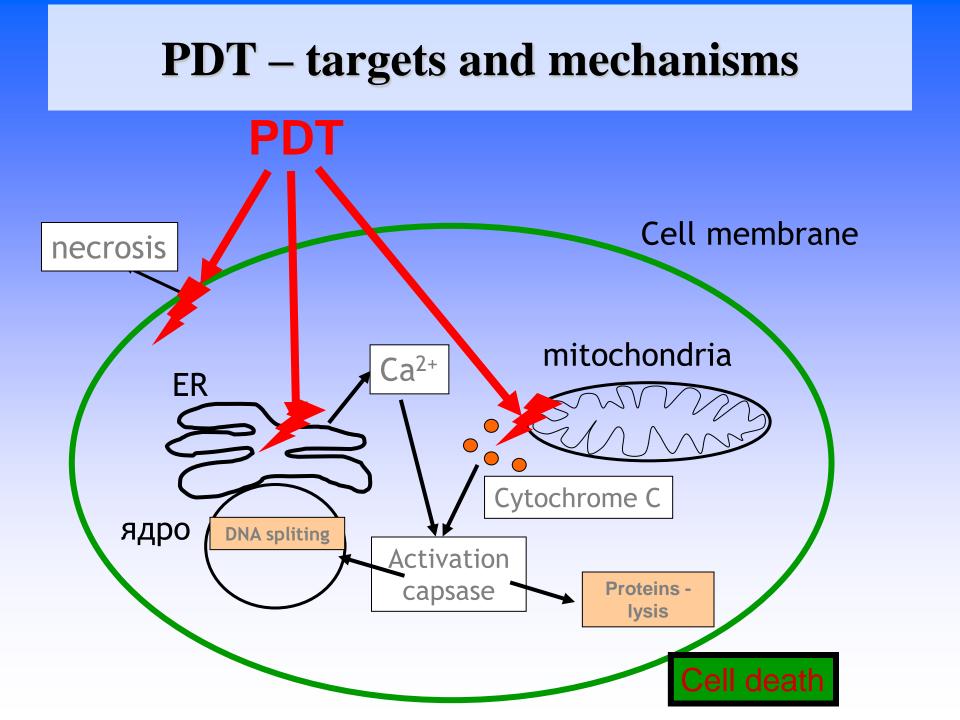
## **Effectiveness of photosensitizers**

- low dark toxicity of practically used doses;
- good selectivity in accumulation in tumor tissue;
- a high degree of cleansing of the PS by the body;
- high quantum yield of singlet oxygen;
- the wavelength of the radiation must fall into the therapeutic window of the tissue;
- acceptable price of the substance.

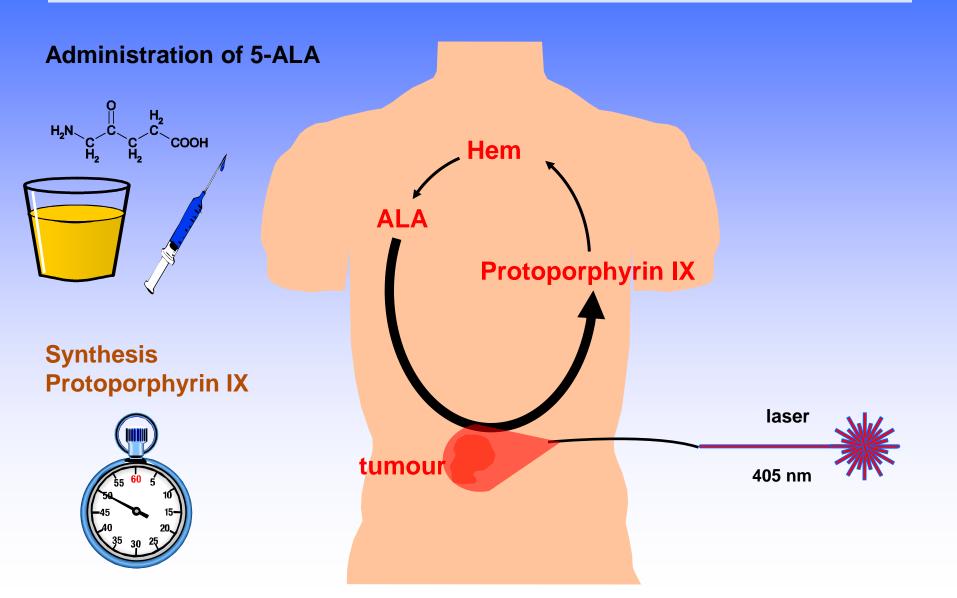
### **Photodynamic therapy of tumors - basic steps**



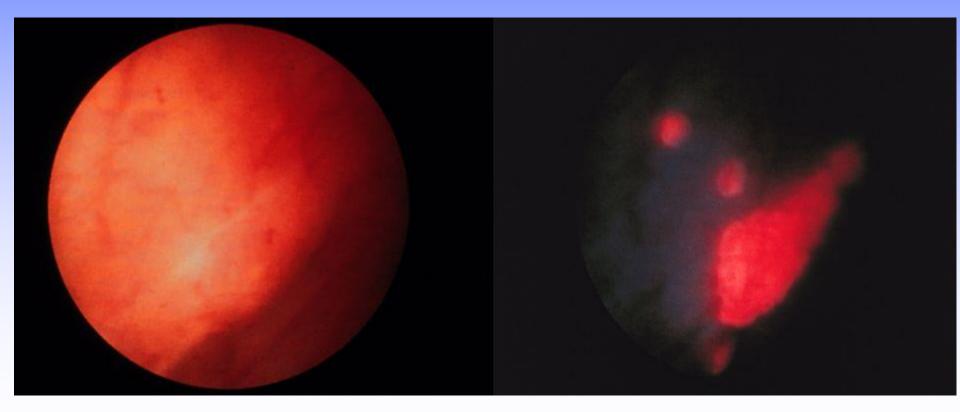
- 1. In the body is introduced lightsensitive chemical compound (photosensitizer)
- 2. The drug selectively accumulates in the tumor tissue where it is irradiated with a laser of appropriate wavelength
- 3. The photosensitizer transmits the laser energy and creates a toxic form of oxygen and free radicals
- Tumor cells are destroyed with a minimal damage to surrounding healthy cells



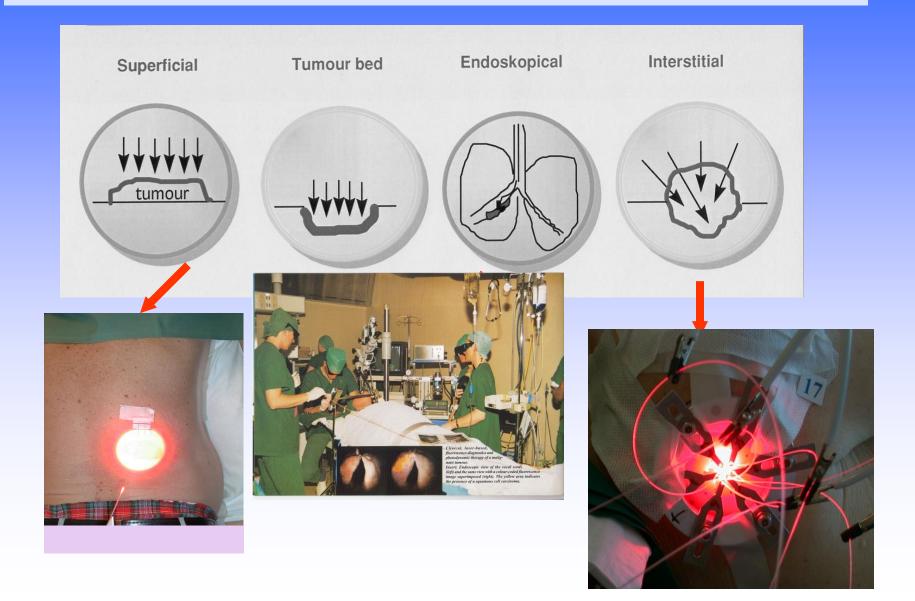
## ALA - PDT



## **2-D visualization**



## **Main types of PDT**



## **PDT - advantages and disadvantages**

## **Superficial PDT**

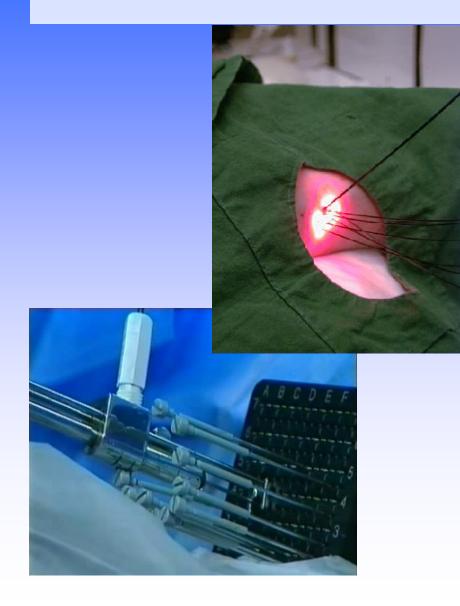
+Selectivity

- + Good cosmetic results
- + Fast recovery
- + multiple application possibility
- + Outpatient procedure
- + "Simple" method (water cooling or local anesthesia)

– "thin"/superficial tumours

...compared to conventional methods (surgery, cryosurgery, radiotherapy)

### **PDT - advantages and drawbacks**



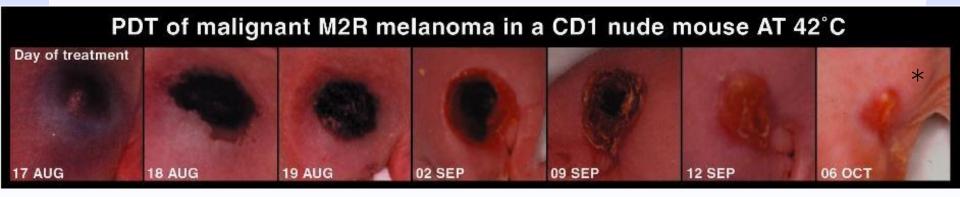
### **Intersticial PDT**

+ Large and deep situated tumours+Minimally invasive procedure

positioning of the light fibers/guidesDosymetry

## **PDT** applications

- Bladder cancer
- Brain cancer
- Uterine and cervical cancer
- Gastrointestinal tract infections
- Lung cancer
- Skin cancer
- Other Apps: Atherosclerosis, restenosis, AMD, rheumatoid arthritis, and others.

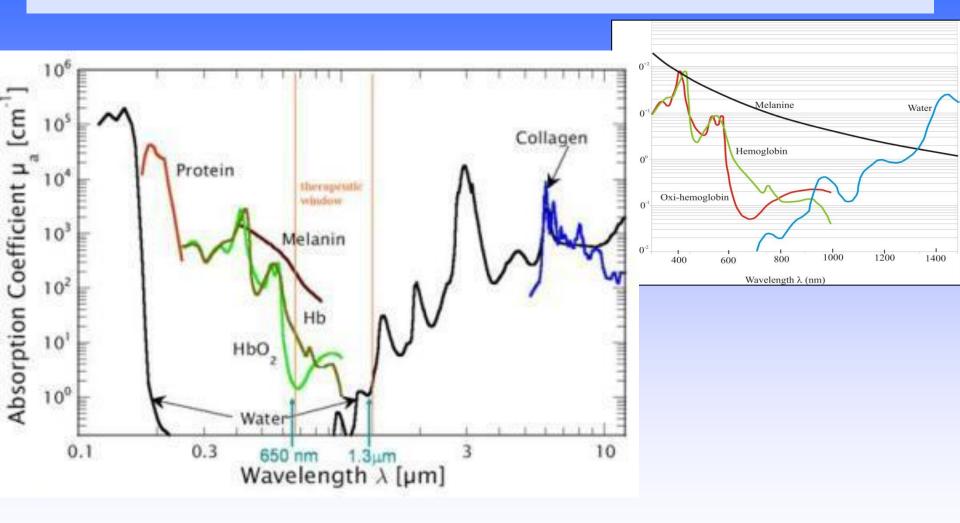


\* Y. Salomon, A. Scherz, "Binary cancer therapies", The Departments of Biological Regulation and Chemical Services, MIT, 2003

# **Types of applications - biostimulation**

- Biostimulation
- (low-level laser therapy (LLLT), "cold laser")
- Wound healing
- Anti-inflammatory action
- Pain reduction

# "Therapeutic window"



# **Therapeutic window - example**

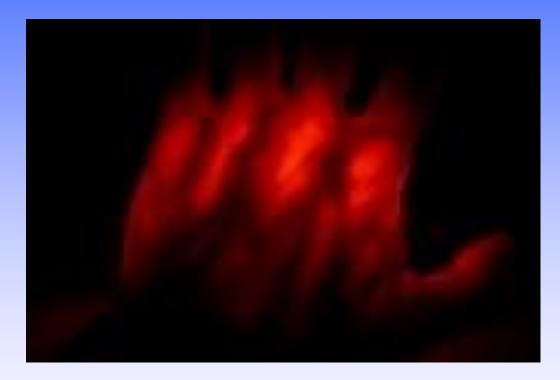
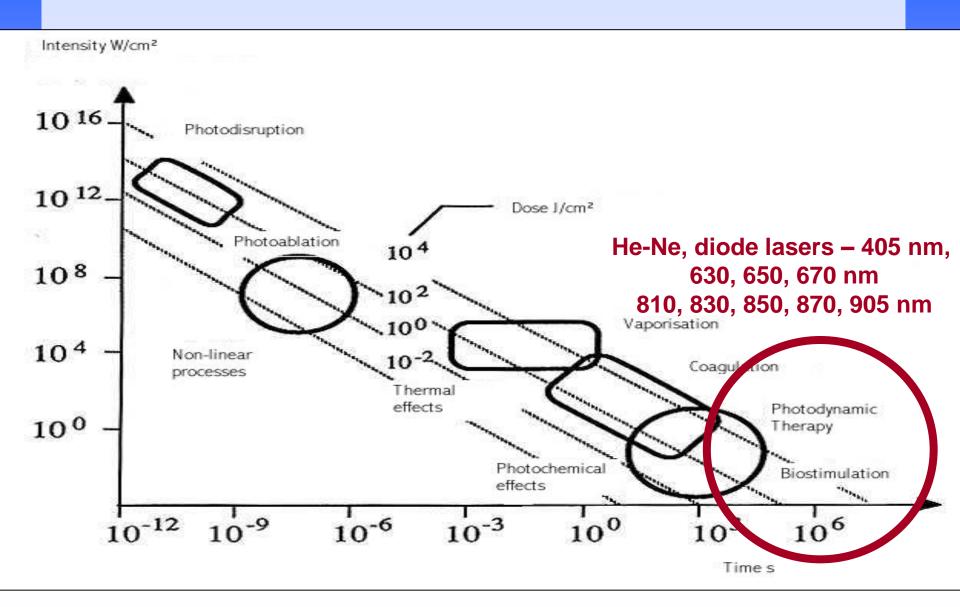


Photo of a hand - Only the red light is visible due to low absorption and high scattering in the 600-900 nm area, the blood absorbs more strongly in the range 700-800 nm

### **Laser-tissue interactions**



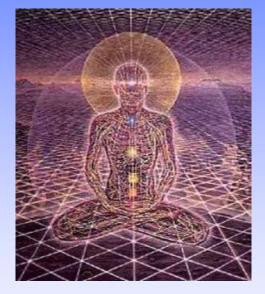
#### Light Treatment is an OLD concept in multiple cultures



# Light is even depicted as a "healing power"







#### Heliotherapy - history





#### **Biological Photo acceptors - Molecules**

## Plants

- Chlorophyll
- Carotenoids

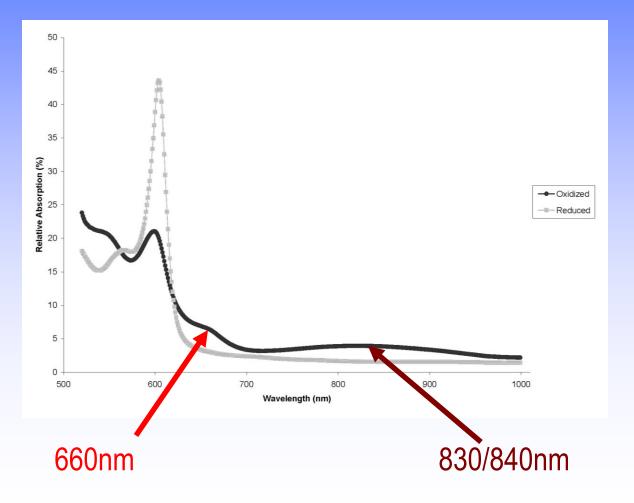


### Humans

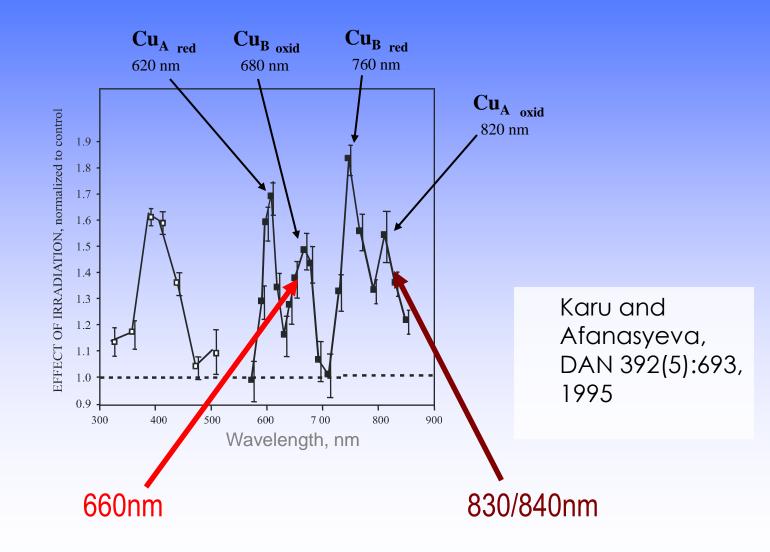
- Rhodopsin (eye, vision)
- Hemoglobin (blood)
- Myoglobin (muscles)
- Cytochrome (all cells)



#### Cytochrome C oxidase - absorption



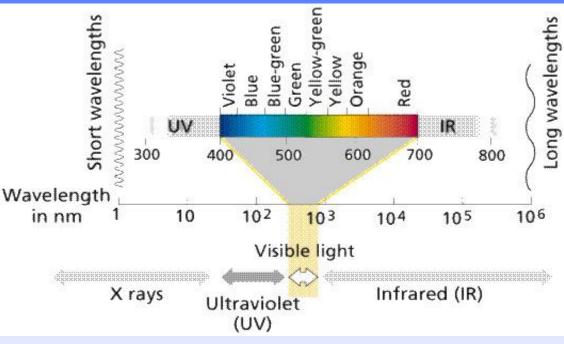
#### Action spectrum



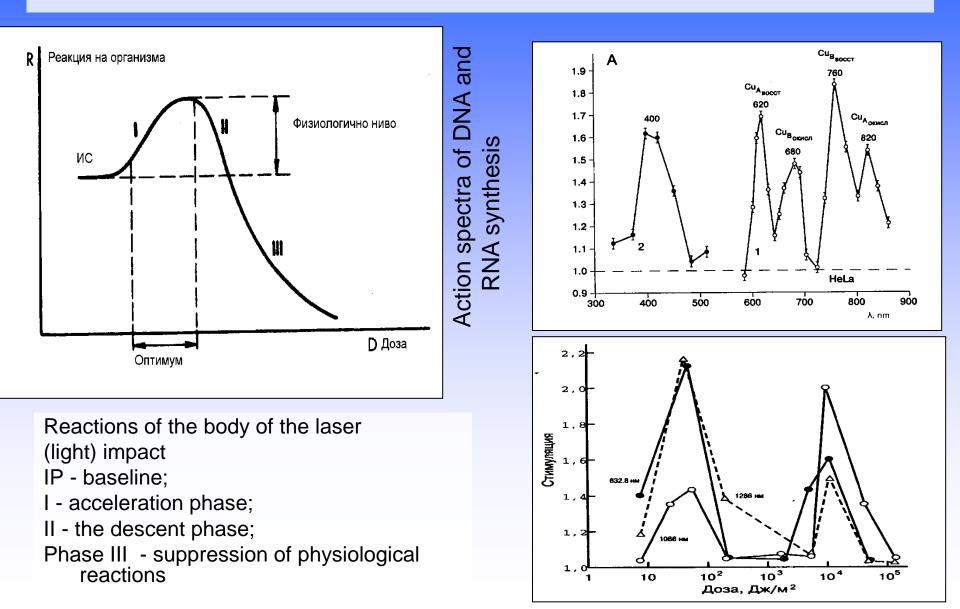
(780 NM) - bones, inflamations, pain, joints, teeth

(660 NM) – soft tissue, pain, skin, muscles, gums, inflammation, scarring, wounds, burns, wrinkles, acne

(405 NM) – DNA, RNA, antiacne, acne, wrinkles, muscles, nerves, blood



## Laser (light) biostimulation



# **LLLT** -effects

Primary effects:

## ENERGY!!!

Secondary effects:

**1.Anti-inflammatory** 

**2.**Tissue regeneration

**3.Reduce pain** 

**4.Increased microcirculation** 

# Anti-inflammatory effect

- •Laser gives energy
- Energy leads to reactive oxygen species (ROS)
- ROSs induce inflammatory proteins
- The body responds with an anti-inflammatory response
- •Restoration of the tissue

**Drugs** Non-steroidal anti-inflammatory drugs Indomethacin, meloxicam, and others.



- allergies
- cardiovascular
- -gastrointestinal
- -hematologic
- -renal reactions, etc..





#### no side effects

# Effect of pain reduction

## **1.** Stimulation of nerves

**2.** Nerve inhibition

## **3.** Regeneration of the nerves

# Tissue regeneration

The process of wound healing is a series of events from the time of injury and can last months and even years ...... The healing process can be divided into three steps:

- 1) Phase of inflammation
- 2) Phase of proliferation
- 3) Phase of maturity and remodeling of the tissue (scar)

#### LLLT can affect each of these stages

Improving circulation

Poor blood circulation is one of the main causes of multiple chronic conditions

LLLT increases the microcirculation IMMEDIATELY after irradiation of the tissue

Vasodilatation is modulated by photobiostimulation of NO production

#### Effect of light on the biotissues

- Increased ATP production
- Circulation
  - Relaxation of smooth muscles
  - angiogenesis
- Increased production of :
  - fibroblasts
  - Macrophages
  - Collagen
- Changed nerve conduction

- Increased metabolism:
  - endorphins
  - acetylcholine
  - serotonin
  - Increased synthesis of:
  - DNA
  - Proteins
- Stimulating the immune response of the body

# **Application examples**

### Diabetes Mellitus: gangrene



After 6 1-hour irradiation procedures

### Diabetes Mellitus





#### Post traumatic hematoma

#### begining



#### After 4 treatments



#### After 5 treatments









#### burns

#### 5 treatments for 8 days



#### Fracture - 66 years patient

#### start

#### intermediate





10/29/2006



11/04/2006



11/29/2006







10/25/2006

12/06/2006

# Thank you very much for your attention!

