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# Low-level laser therapy for inflammation control

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PhD in Technology

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<https://lazzmik.ru>





# LLLT - low-level laser therapy

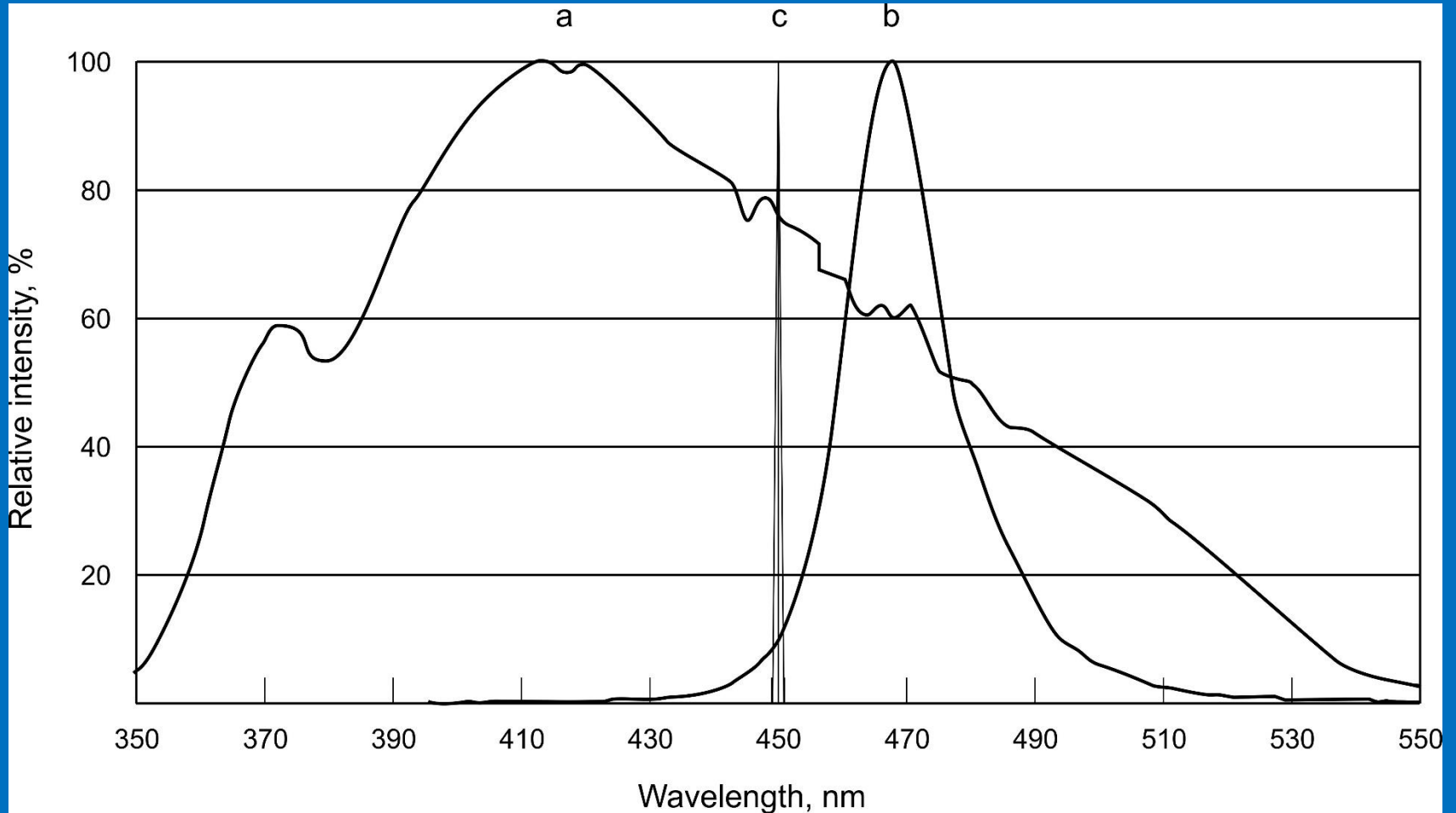
Only “laser”

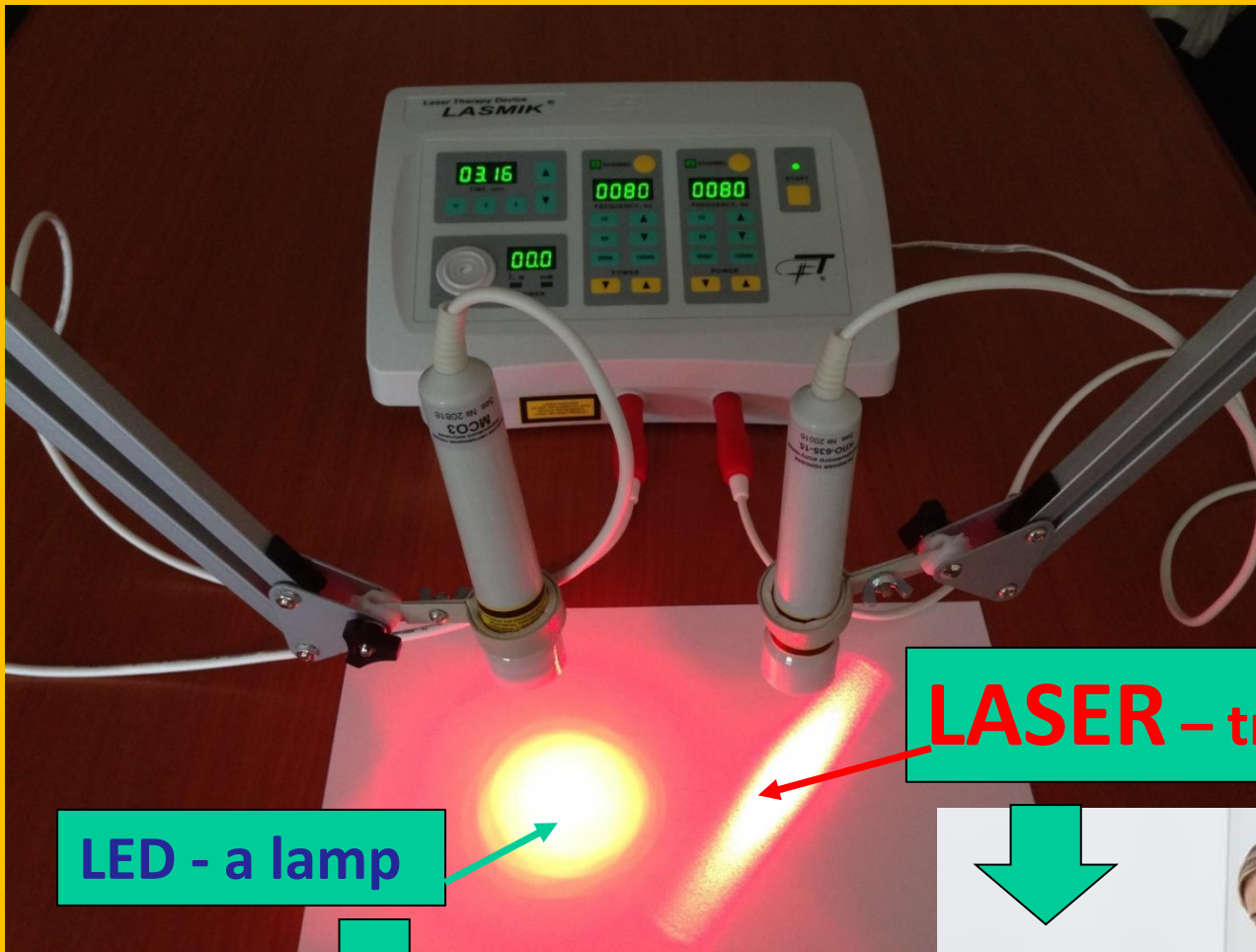
**NO!** low-level laser ~~(light)~~ therapy

LLLT  $\neq$  PBM!

LLLT is not PBM!

# The spectrum width of Finsen's lamp with a filter (a), LEDs (b), lasers (c)





**LASER – treatment & health**

**LED - a lamp**



# The parameters of effective Low-Level Laser Therapy

The main rule – all the parameters of laser action must be specified in the following sequence:

- wavelength and mode of operation of the laser;
- average or pulsed power of illumination;
- frequency for pulsed or modulated mode;
- localization and area of impact;
- zone of exposure and total time of a treatment;
- number and frequency of treatments.

Area of illumination is distinguished by special nozzles.

# Energy and spatial-temporal organization of LLLT effects on the body

## Energy component of the impact

$$\text{Energy} = P_{\text{av.}} \times T \text{ (J)}; \text{ED} = (P_{\text{av.}} \times T) / S \text{ (J/cm}^2\text{)}$$

$$\text{For pulse mode} - P_{\text{av.}} = P_{\text{p.}} \times \tau_{\text{p.}} \times F \text{ (mW)}$$

$P_{\text{av.}}$  – average output power (1-200 mW)

$P_{\text{av.}}$  – very strongly depends on the wavelength ( $\lambda$ , nm)

$P_{\text{av.}}$  – proportional to frequency for pulse mode

$P_{\text{p.}}$  – pulsed power (5-100 W)

$\tau_{\text{p.}}$  – pulse duration (100-200 ns)

$F$  – frequency (10 – 10 000 Hz)

$T$  – exposure time (30, 100 or 300 s – local; 3-15 min - ILBI)

$S$  – impact area (1 cm<sup>2</sup>)

\*ED – energy density; ILBI - intravenous laser blood illumination

## Spatial-temporal component of the impact

- exposure time (biorhythms)
- modulation frequency (biorhythms)
- periodicity of exposure (biorhythms)
- light spot area
- localization of exposure

# The parameters of effective Low-Level Laser Therapy

In Low-Level Laser Therapy, there is **no** such parameter as “dose” or “dosage”!

There are “energy” = power  $\times$  time (W  $\times$  s) [J] and  
“energy density” = Energy / area [J/cm<sup>2</sup>].

Mathematical calculations make no sense!

**1  $\neq$  1  $\neq$  1 !**

The calculation only hinder the effectiveness  
of LLLT!



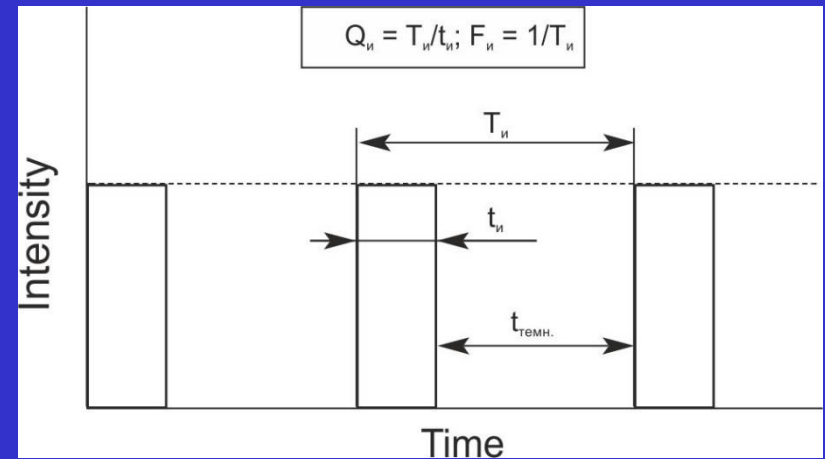
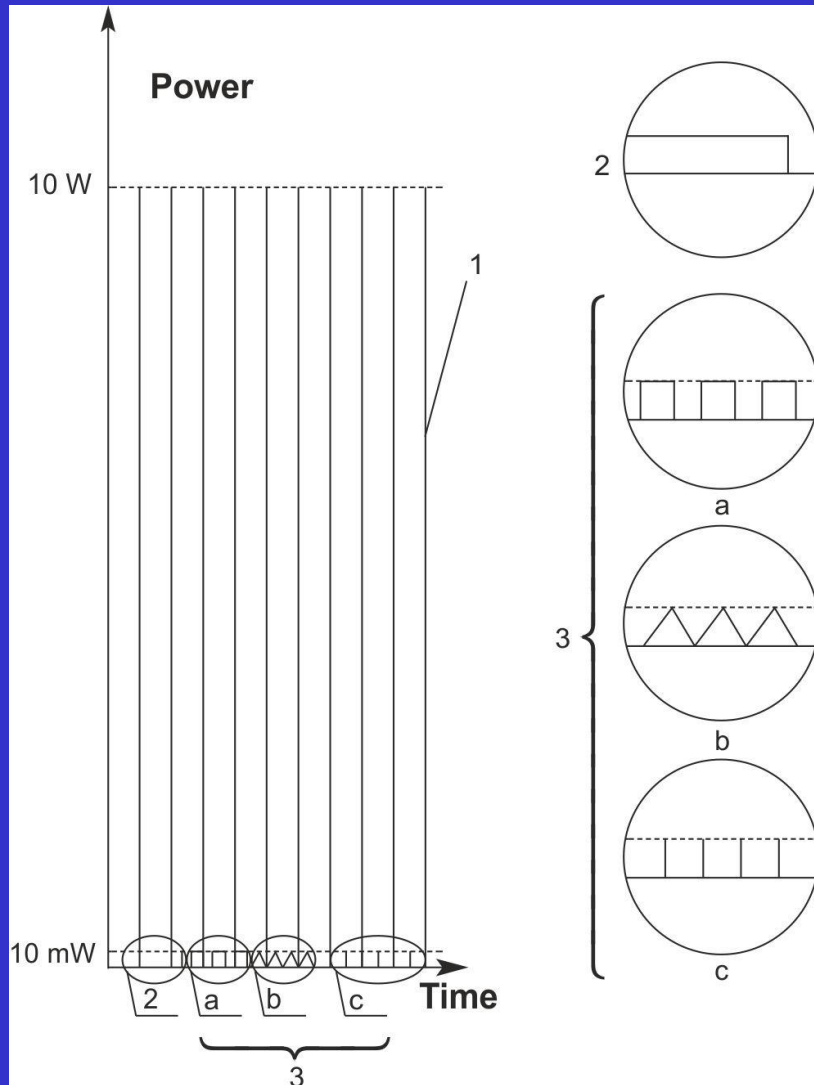
# The parameters of effective low-level laser therapy

The ED may be the same (most often the optimal  $1\text{J}/\text{cm}^2$ ) with a wavelength of  $635\text{nm}$  (red spectrum).

Three different situations (assuming a contact-mirror technique and an effective area of  $1\text{cm}^2$ )

Power, mW	Time, s	Energy, J	Effect
1	1000	1	No
10	100	1	Yes!!!
1000	1	1	No

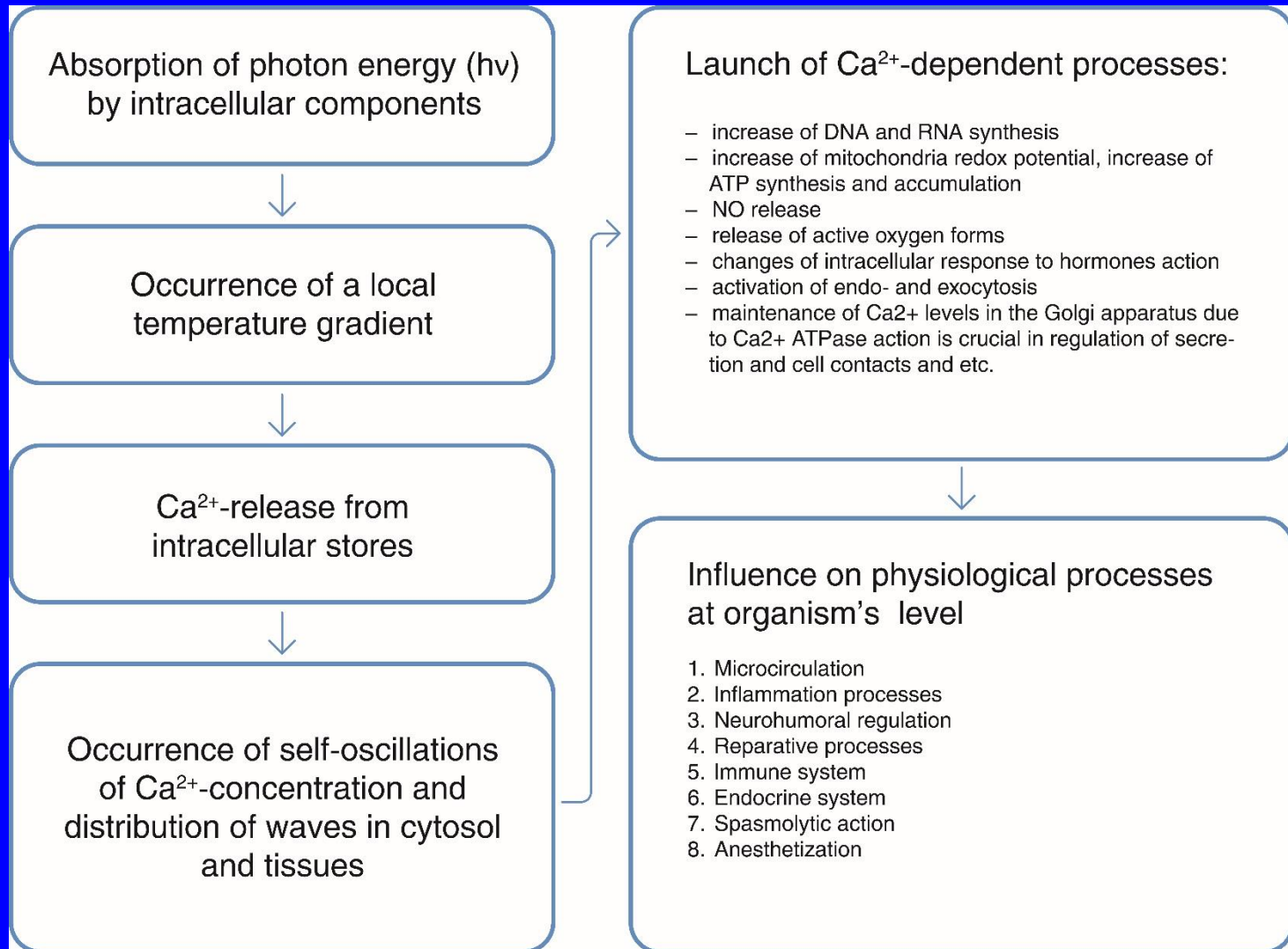
# Different illumination modes

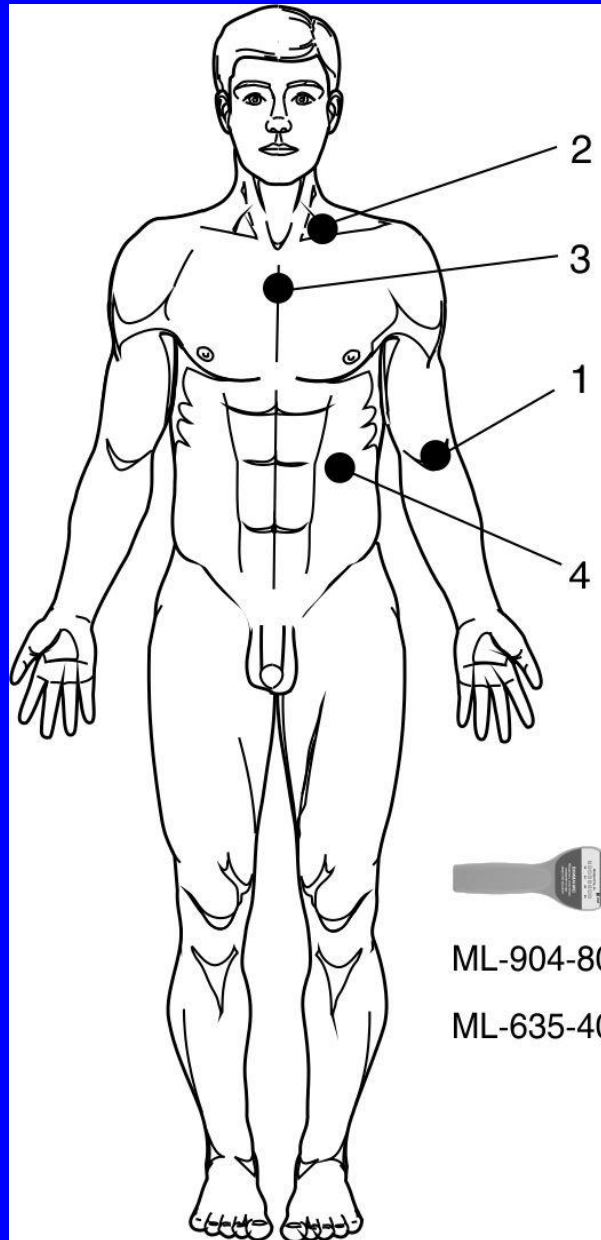


$$P_{av.} = P_p \times \tau_p \times F$$

During modulated illumination, average power does not change in the modulation frequency, and in the pulsed mode, laser light is directly proportional to pulse repetition rate!

# The sequence of the development of biological effects of laser exposure (low-level laser light)



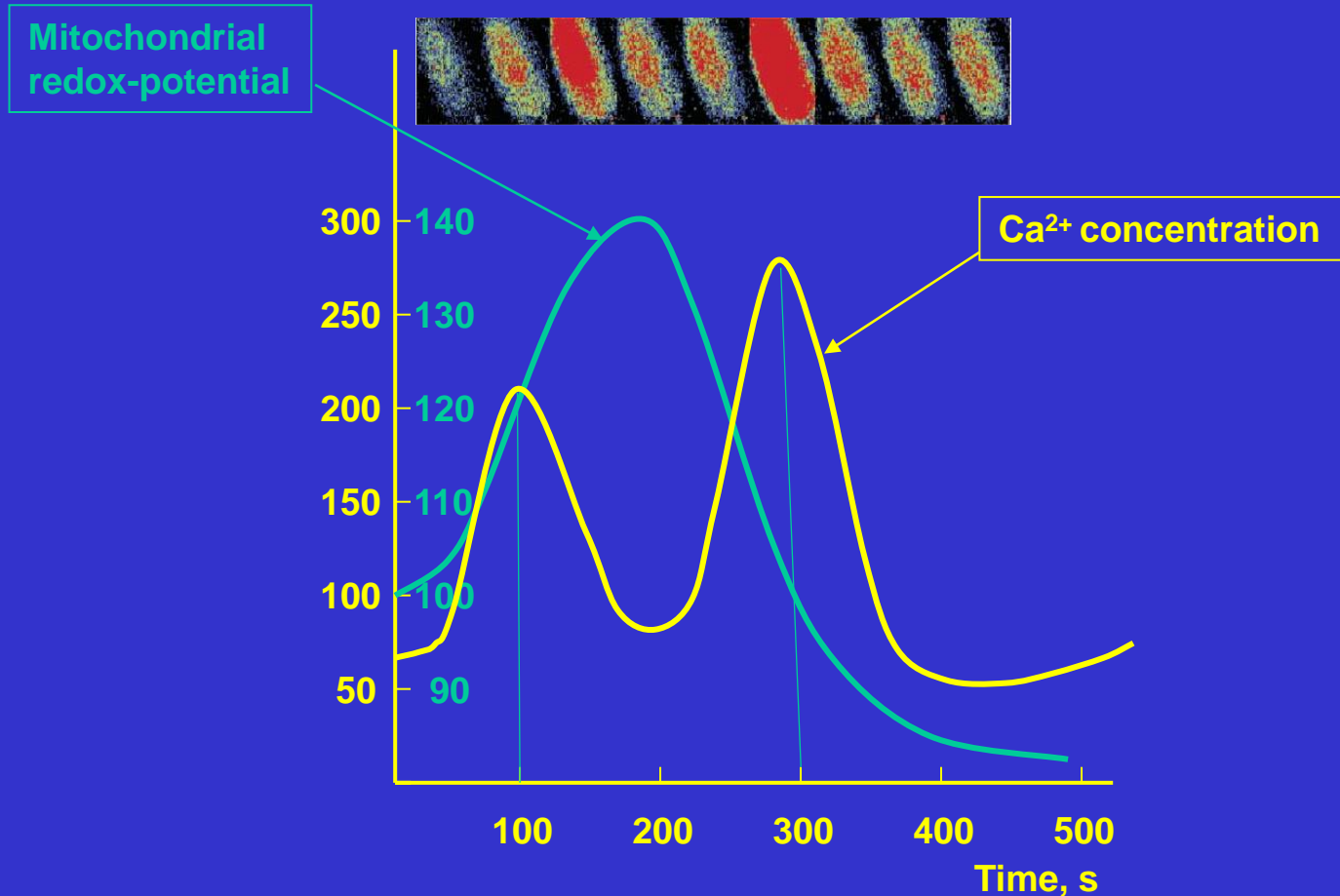


ML-904-80

ML-635-40

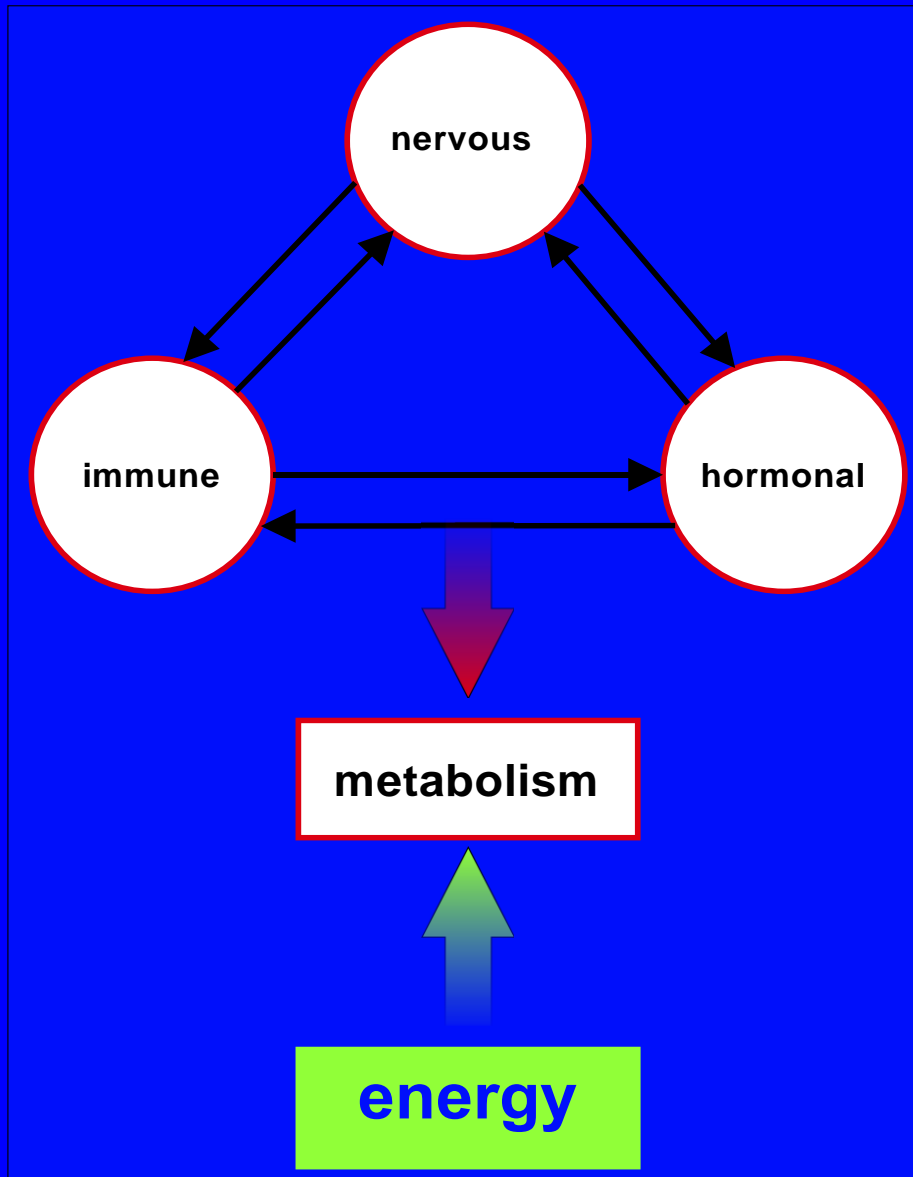
# Intracellular $\text{Ca}^{2+}$ oscillations evoked by low-level laser light

(Alexandratou E., Yova D., Handris P. et al. Human fibroblast alterations induced by low power laser irradiation at the single cell level using confocal microscopy // Photoch. & Photob. Sciences. – 2002, 1 (8): 547-552.)



# **Main secondary mechanisms of the biological action of LLLT at the organismal level**

- 1. Activation of central blood flow and microcirculation**
- 2. Increased lymph flow**
- 3. Anti-inflammatory effect**
- 4. Restoring the immune system**
- 5. Stimulation of reparative processes**
- 6. Hormonal system activation**
- 7. Activation of the nervous system (central and peripheral)**
- 8. Analgesia**
- 9. ...**



The concept of neuro-immune-endocrine-metabolic interactions of various systems as the basis of laser therapy modern methodology

Inflammation is a protective and adaptive process, the first stage of the immune system activation in response to a damage. Inflammation is classified as acute or chronic. It is also classified by the type of cytokines and T helper cells involved

Autoimmune diseases\*:

- ✓ autoimmune (Hashimoto's) thyroiditis;
- ✓ bronchial asthma;
- ✓ diabetes mellitus;
- ✓ rheumatoid arthritis;
- ✓ multiple sclerosis, etc.

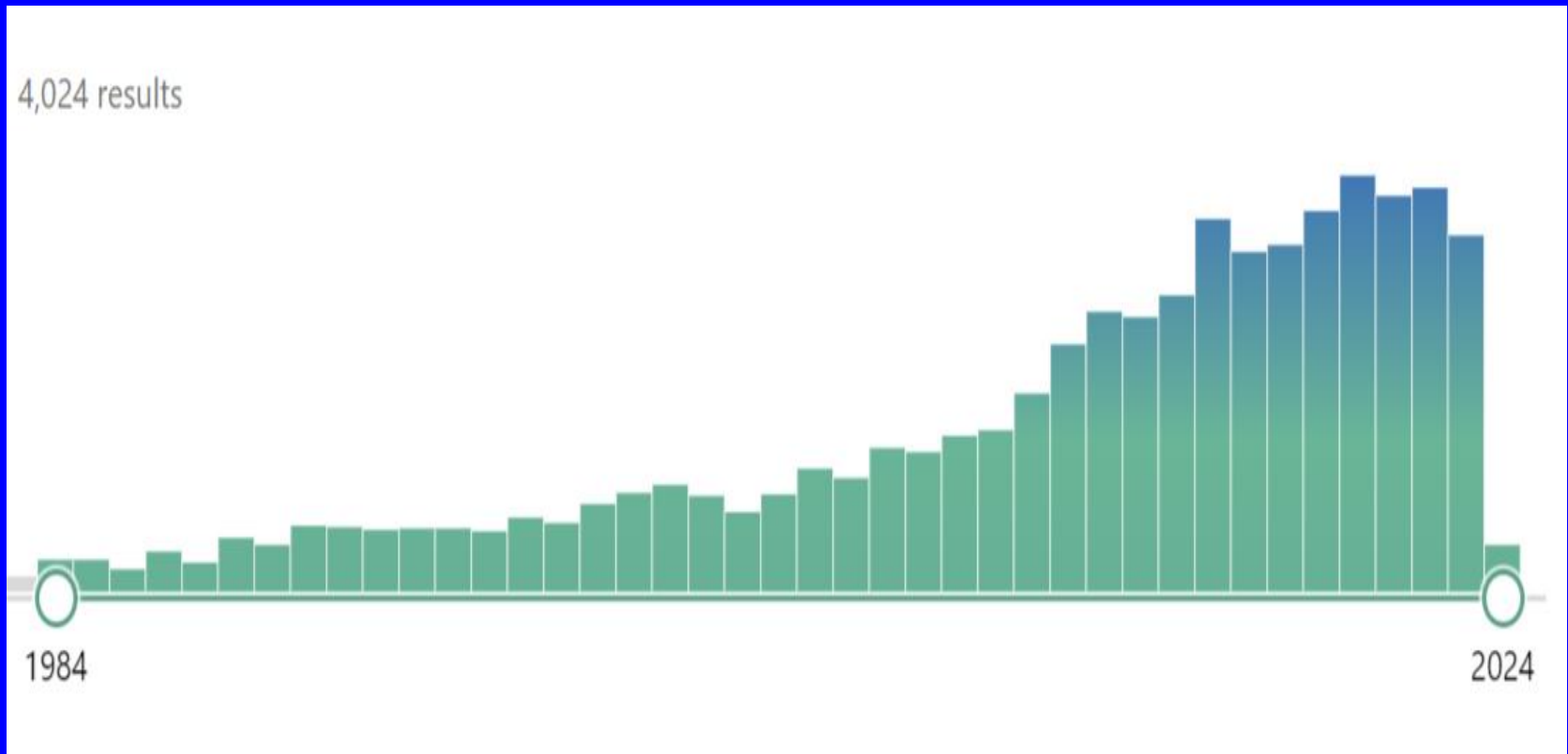
...

\* - more than 30 years of work allows us to confidently speak about clinical effectiveness at the level of 90% with a remission duration of up to 3 years



# PubMed

«Inflammation laser therapy»  
4.024 results



Google Scholar  
1 180 000 results

# The impact of LILI on various components of the immune system

Cytokines	In vitro		In vivo		Clinic	
	Cells type	Reference	Animals	Reference	Disease	Reference
IL-1 $\alpha$	Keratinocytes	Yu H.-S. et al.,				
	Stromal cells of mice bone marrow		Mice BALB/c, allergic pneumonia	Silva V.R. et al., 2014		
IL-5			Mice BALB/c, asthma	Rigonato-Oliveira N.C. et al., 2019		
IL-1 $\beta$	Human gum fibroblasts	Basso F.G. et al., 2016	Mice C57BL/6, induced arthritis	Dos Anjos L.M.J. et al., 2019	premolars, orthodontic treatment	Jose J.A. et al., 2018
	Skin fibroblasts (HFF-1)	Maldaner D.R. et al., 2019	Rats Wistar, joint inflammation	Alves A.C.A. et al., 2013	Orthodontic movement of teeth	Varella A.M. et al., 2018
			Rats Wistar, muscle injury	Mantineo M.E. et al., 2014		
IL-2			Mice NMRI	Novoselova E.G. et al., 2005	Type 2 diabetes mellitus and periodontitis	Bunjaku V. et al., 2018
			Rats Wistar, muscle injury	Mantineo M.E. et al., 2014		
IL-4			Mice BALB/c, allergic pneumonia	Silva V.R. et al., 2014		
			Rats Wistar, asthma	Wang X.-Y. et al., 2014		
			Rats Sprague-Dawley, spinal cord injury	Song J.W. et al., 2017		

IL-5			Mice BALB/c, allergic pneumonia	Silva V.R. et al., 2014		
			Mice BALB/c, asthma	Rigonato-Oliveira N.C. et al., 2019		
IL-6	Human skin fibroblasts (HSFs)	Esmaeelinejad M., Bayat M., 2013	Mice C57BL/6, induced arthritis	Dos Anjos L.M.J. et al., 2019	Obese women, LI combined with workout, helps to lose weight	da Silveira Campos R.M. et al., 2018
	See above	Basso F.G. et al., 2015, 2016	Rats Wistar, joint inflammation	Alves A.C.A. et al., 2013	Peritonitis in cancer patients in the early postsurgical period	Khvostuntsev S.M., 2007
	Stromal cells of mice bone marrow	Amaroli A., et al., 2018	Rats Wistar, muscle injury	Mantineo M.E. et al., 2014	Chronic obstructive pulmonary disease (COPD)	Mehani S.H.M., 2017
	Skin fibroblasts(HFF-1)	Maldaner D.R. et al., 2019			Stomatitis related to the use of dentures	Simunović-Soskić M. et al., 2010
IL-8	Human gum fibroblasts	Basso F.G. et al., 2015, 2016			Free gingival graft	Keskiner I. et al., 2016
	Alveolar macrophages	Souza N.H. et al., 2014				
	Keratinocytes	Yu H.-S. et al., 1996				
IL-10	Stromal cells of mice bone marrow	Amaroli A., et al., 2018	Mice C57BL/6, induced arthritis	Dos Anjos L.M.J. et al., 2019		
	Skin fibroblasts (HFF-1)	Maldaner D.R. et al., 2019	Мыши C57BL/6, COPD	Alves C. et al., 2017		

IL-12	Dendritic cells obtained from the mice bone marrow	Chen A.C.-H. et al., 2011				
IL-13			Mice BALB/c, allergic pneumonia	Silva V.R. et al., 2014		
			Rats Sprague-Dawley, spinal cord injury	Song J.W. et al., 2017		
IL-17	Stromal cells of mice bone marrow	Amaroli A., et al., 2018	Mice C57BL/6, COPD	Alves C. et al., 2017		
IFN- $\gamma$	Skin fibroblasts (HFF-1)	Maldaner D.R. et al., 2019	Rats Wistar, asthma	Wang X.-Y. et al., 2014		
			Rats Wistar, wounds on the gum	Safavi S.M. et al., 2008		
HIF-1 $\alpha$			Rats Sprague-Dawley, burns	Gupta A. et al., 2015		
COX-2			Rats Wistar, plantar muscle	Albertini R. et al., 2007		
PGE <sub>2</sub>	Alveolar macrophages	Souza N.H. et al., 2014			Removal of premolars, orthodontic treatment	Jose J.A. et al., 2018
	Human gum fibroblasts	Sakurai Y. et al., 2000			Pain, orthopedic patients	Mizutani K. et al., 2004

TNF- $\alpha$	See above	Basso F.G. et al., 2015, 2016	Rats Sprague-Dawley with suppressed immunity	Keshri G.K. et al., 2016	See above	Khvostuntsev S.M., 2007
	See above	Souza N.H. et al., 2014	Mice NMRI	Novoselova E.G. et al., 2005	Stomatitis related to the use of dentures	Simunović-Soskić M. et al., 2010
	Stromal cells of mice bone marrow	Amaroli A. et al., 2018	Mice C57BL/6, induced arthritis	Dos Anjos L.M.J. et al., 2019		
	Skin fibroblasts (HFF-1)	Maldaner D.R. et al., 2019	Rats Wistar, muscle injury	Mantineo M.E. et al., 2014		
			Rats Sprague-Dawley, burns	Gupta A. et al., 2015		
TNF- $\beta$			Mice NMRI	Novoselova E.G. et al., 2005		
NF- $\kappa$ B	Mice embryonic fibroblasts	Chen A.C. et al., 2011	Rats Sprague-Dawley with suppressed immunity	Keshri G.K. et al., 2016		
	Human periodontal ligament cells	Lee J.H. et al., 2018	Rats Sprague-Dawley, burns	Gupta A. et al., 2015		
HSP-60			See above	Gupta A. et al., 2015		
HSP-70			Mice NMRI	Novoselova E.G. et al., 2005		
HSP-90			Rats Sprague-Dawley with suppressed immunity	Keshri G.K. et al., 2016		
			Rats Sprague-Dawley, burns	Gupta A. et al., 2015		

MMP-2 and MMP-9	MC3T3-E1 cells	Oliveira F.A. et al., 2017	Diabetic rats	Aparecida Da Silva A. et al., 2018		
			Rats Wistar, osteoarthritis	Alves A.C. et al., 2014		
Fibronectin			Rats Sprague-Dawley with suppressed immunity	Keshri G.K. et al., 2016		
			See above	Gupta A. et al., 2015		
$\beta$ -actin			See above	Gupta A. et al., 2015		

Anti-inflammatory cytokines : IL-2, IL-4, IL-8, IL-10.

Proinflammatory cytokines : IL-1 $\alpha$ , IL-1 $\alpha$ , IL-1 $\beta$ , IL-6, COX2, PGE<sub>2</sub>, TNF- $\alpha$ .

# The influence of LIL on differentiation clusters

CD	In vitro		In vivo		Clinic	
	Cells	Source	Animals, model	Source	Disease	Source
CD3	Human blood samples	Al Musawi M.S. et al., 2017			Hematopathology in children	Kartelisev A.V. et al., 1994
CD4	K562	Belan O.S., 2009	Rats, sarcoma 45	Belan O.S., 2009	Stage I Uterine cancer	Kosenko I.A. et al., 2006
	Human blood samples	Al Musawi M.S. et al., 2017	Mice, COPD	Vitoretta L. et al., 2015	Tooth extraction, patients with HIV	Halon A. et al., 2015
					Chronic obstructive pulmonary disease (COPD)	Mehani S.H.M., 2017
CD5					Hematopathology in children	Kartelisev A.V. et al., 1994
CD7					Hematopathology in children	Kartelisev A.V. et al., 1994
CD8	K562	Belan O.S., 2009	Rats, sarcoma 45	Belan O.S., 2009	Stage I Uterine cancer	Kosenko I.A. et al., 2006
	Human blood samples	Al Musawi M.S. et al., 2017	Mice, COPD	Vitoretta L. et al., 2015	Chronic obstructive pulmonary disease (COPD)	Mehani S.H.M., 2017
					Hematopathology in children	Kartelisev A.V. et al., 1994
CD8 $\alpha$			Mice C57BL/6J, before vaccination	Kimizuka Y. et al., 2018		

CD11b			Mice C57BL/6J, before vaccination	Kimizuka Y. et al., 2018		
CD11c	Dendritic cells obtained from the mice bone marrow	Chen A.C.-H. et al., 2011	Mice C57BL/6J, before vaccination	Kimizuka Y. et al., 2018		
CD16	K562	Belan O.S., 2009	Rats, sarcoma 45	Belan O.S., 2009	Stage I Uterine cancer	Kosenko I.A. et al., 2006
	Human blood samples	Al Musawi M.S. et al., 2017				
CD19	Human blood samples	Al Musawi M.S. et al., 2017				
CD22					Stage I Uterine cancer	Kosenko I.A. et al., 2006
CD25			Mice C57BL/6, induced arthritis	Dos Anjos L.M.J. et al., 2019	Stage I Uterine cancer	Kosenko I.A. et al., 2006
CD29			Rats Wistar, spinal cord injury	Sarveazad A. et al., 2019		
CD34			Rats, LI of abdominal muscle flap after nicotine exposure, increased vitality	das Neves L.M.S. et al., 2017		
			Rats Wistar, spinal cord injury	Sarveazad A. et al., 2019		



CD45			Rats Wistar, spinal cord injury	Sarveazad A. et al., 2019		
CD56	K562	Belan O.S., 2009	Rats, sarcoma 45	Белан О.С., 2009	Stage I Uterine cancer	Kosenko I.A. et al., 2006
	Human blood samples	Al Musawi M.S. et al., 2017				
CD71					Hematopathology in children	Kartelishev A.V. et al., 1994
CD73			Rats Wistar, spinal cord injury	Sarveazad A. et al., 2019		
CD80	Dendritic cells obtained from the mice bone marrow	Chen A.C.-H. et al., 2011	Mice C57BL/6, induced arthritis	Dos Anjos L.M.J. et al., 2019		
CD81	See above	Chen A.C.-H. et al., 2011				
CD86	See above	Chen A.C.-H. et al., 2011	Mice C57BL/6, induced arthritis	Dos Anjos L.M.J. et al., 2019		
			Mice C57BL/6J, before vaccination	Kimizuka Y. et al., 2018		
CD103			Mice C57BL/6J, before vaccination	Kimizuka Y. et al., 2018		
CD105			Rats Wistar, spinal cord injury	Sarveazad A. et al., 2019		
CD207			Mice C57BL/6J, before vaccination	Kimizuka Y. et al., 2018		

# Main low-level laser therapy techniques

## 1. External, local:

- locally (percutaneously) stably or labile
- locally (percutaneously) laser acupuncture
- paravertebrally
- on the projection of internal organs
- transcranial
- on the projection of immune organs

## 2. Intracavitary illumination

## 3. Intravenous laser blood illumination (ILBI)

## 4. Laser ultraviolet blood illumination (LUVBI®)

## 5. Non-invasive laser blood illumination (NLBI)

## 6. Combined techniques:

- magnetic-laser therapy
- vibro-magnetic-laser therapy
- laser-vacuum therapy
- laser-phoresis

# Basic principles for choosing a laser therapy technique to eliminate inflammation

1 – to use systemic methods of exposure (laser blood illumination and laser acupuncture) combined with the local methods, on the focus of inflammation

2 – to use either Intravenous Laser Blood Illumination (ILBI) or non-invasive (NLBI) one; simultaneous use of both methods is unacceptable

3 – it is necessary to additionally expose the projection of immunocompetent organs (thymus, spleen, etc.) while using Noninvasive Laser Blood Illumination (NLBI)

4 – for ILBI use a combination of methods: every other day\* use LILI with a wavelength of 525 nm (green spectrum) or 635 nm (red spectrum), which allows to improve tissue trophism and metabolism. This technique must be combined with LUVBI® (ultraviolet spectrum,  $\lambda = 365$  nm, laser blood illumination), which has the best impact on immunity

\* for example, use ILBI-525 (power 2 mW, exposure 7 min) on Monday and ILBI-365 (2 mW, 7 min) (LUVBI) on Wednesday

5 – use only minimum powers, frequencies and exposures



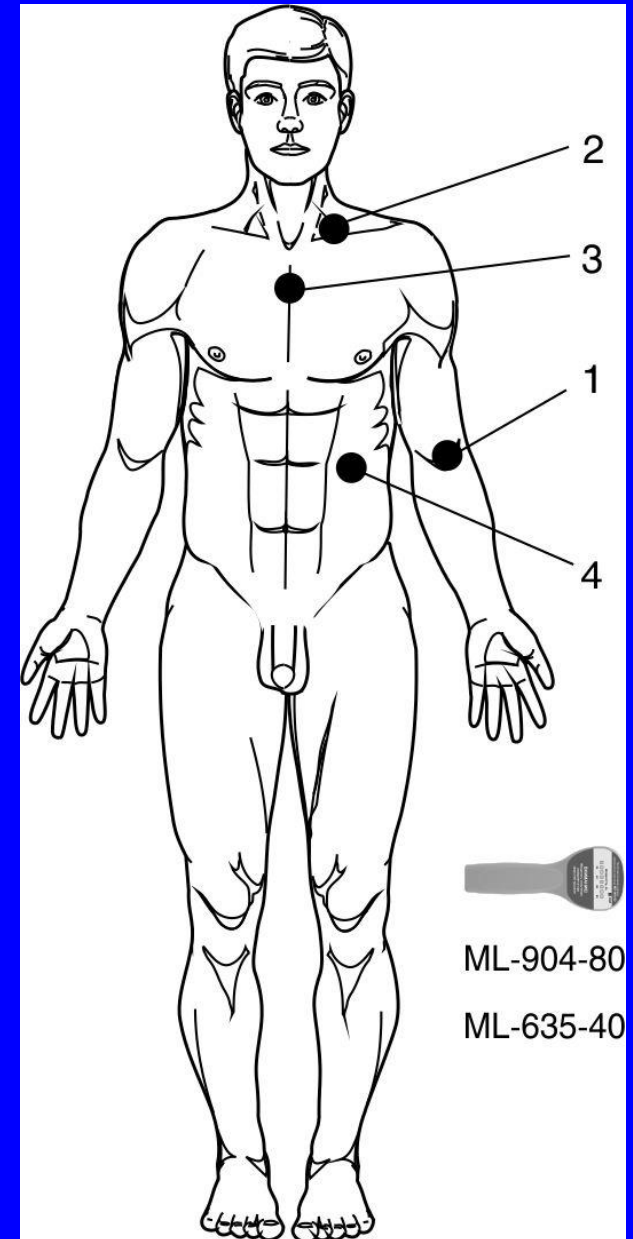
# Laser therapy device Lasmik®

Block concept of laser therapeutic devices:  
basic block + laser heads + nozzles

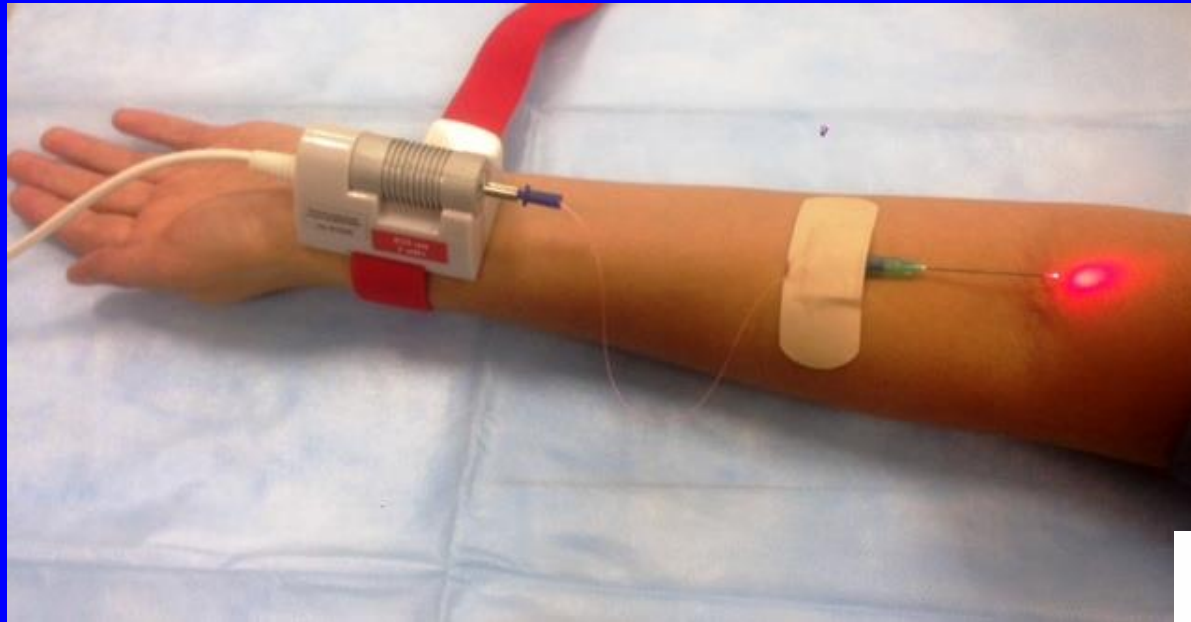


## Intravenous laser blood illumination (ILBI)

<b>ILBI-635:</b> $\lambda$ , nm	635 (red)
Power, mW	2-3
Time, min	10-20
Localization	1 ( <i>v. mediana cubiti</i> )
<b>ILBI-525:</b> $\lambda$ , nm	525 (green)
Power, mW	2-3
Time, min	5-10
Localization	1 ( <i>v. mediana cubiti</i> )
<b>LUVBI®:</b> $\lambda$ , nm	365 (UV)
Power, mW	2-3
Time, min	2-5
Localization	1 ( <i>v. mediana cubiti</i> )



# Intravenous laser blood illumination (ILBI)



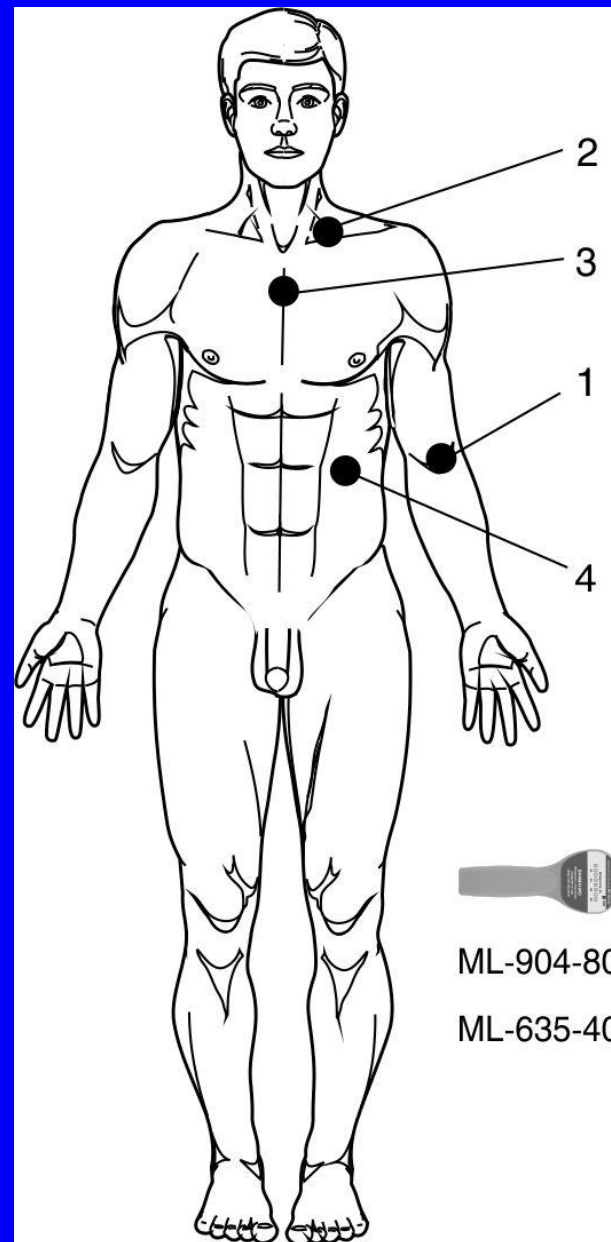
## Intravenous laser blood illumination (ILBI)

Day	Method
1-st (Monday, for example)	LUVBI®
2-nd (Tuesday)	ILBI-635 or ILBI-525
3-rd (Wednesday)	LUVBI®
...	ILBI-635 or ILBI-525
...	LUVBI®
...	ILBI-635 or ILBI-525
...	LUVBI®
...	ILBI-635 or ILBI-525
...	LUVBI®
...	ILBI-635 or ILBI-525

# Non-invasive laser blood illumination (NLBI) #1

Parameters	Laser head	
	ML-904-80	ML-635-40
$\lambda$ , nm	904	635
Mode of operation	Pulse	Pulse
Pulse duration, ns	100-200	100-200
Power, W	80	40
Surface area, cm <sup>2</sup>	10	10
Number of laser diodes	8	8
Power density, mW/cm <sup>2</sup>	8	8

Laser head	Frequency, Hz	Time, min	Localization
ML-635-40	80	5	2 (above the collarbone on the left)
ML-904-80	80	1,5	3 (thymus)
ML-904-80	80	1,5	4 (spleen)

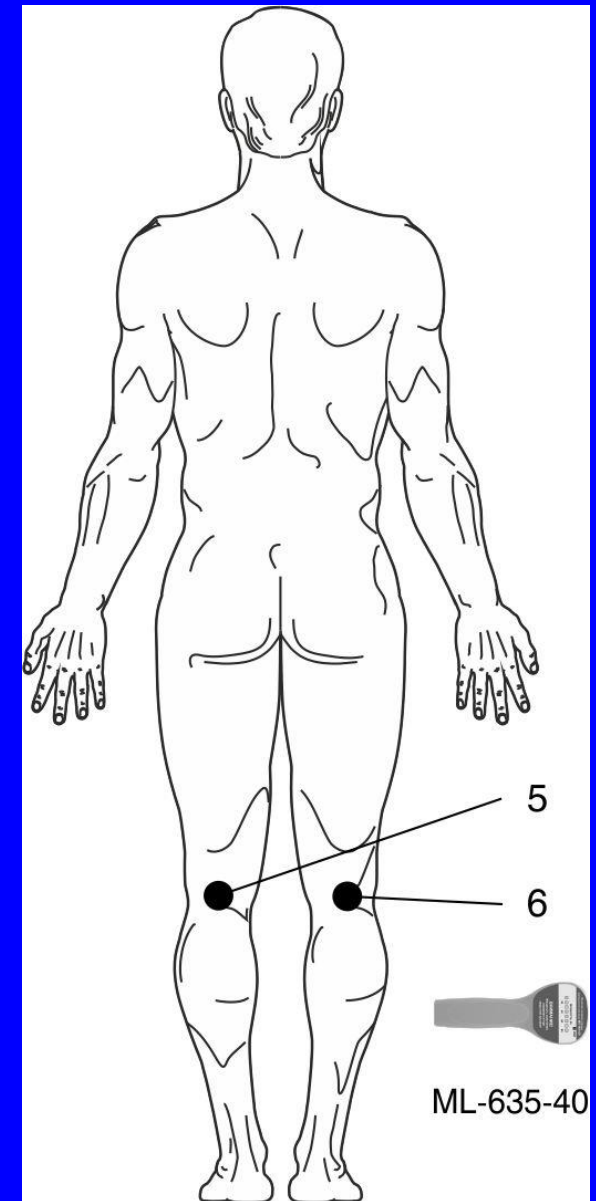




# Non-invasive laser blood illumination (NLBI) #2

Parameters	Laser head	
	ML-904-80	ML-635-40
$\lambda$ , nm	904	635
Mode of operation	Pulse	Pulse
Pulse duration, ns	100-200	100-200
Power, W	80	40
Surface area, cm <sup>2</sup>	10	10
Number of laser diodes	8	8
Power density, mW/cm <sup>2</sup>	8	8

Laser head	Frequency, Hz	Time, min	Localization
ML-635-40	80	2	5
ML-635-40	80	2	6
ML-635-40	80	1,5	3 (thymus)
ML-635-40	80	1,5	4 (spleen)





**Thank you!**

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