# Thermomechanical Effect of Infrared Laser for Cartilage Regeneration

Presented by:

OSA Therapeutic Laser Applications Technical Group

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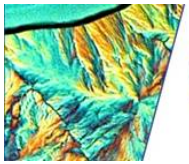

OSA Therapeutic Laser Applications Technical Group

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## Therapeutic Laser Applications (BA)

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- Public Policy
- Chapters and Sections Map
- Technical Groups
  - Bio-Medical Optics
    - Microscopy and Optical Coherence Tomography (BM)
    - Molecular Probes and Nanobio-Optics (BP)
    - Optical Biosensors (BB)
    - Optical Trapping and Manipulation in Molecular and Cellular Biology (BT)
    - Therapeutic Laser Applications (BA)
    - Tissue Imaging and Spectroscopy (BS)
    - Photobiomodulation (BL)
  - Fabrication, Design & Instrumentation
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  - Optical Interaction Science

### Therapeutic Laser Applications

This group focuses on the use of lasers in surgery or in other treatments of disease. This includes the use of lasers as surgical tools for tissue cutting, welding, and coagulation, as well as the use of optics to initiate cell-damaging photochemical reactions for the treatment of diseases such as cancer. In addition, optics, spectroscopy, and imaging provide unique tools that may allow real-time diagnostics of the efficacy of clinical procedures. For many of these applications, the development of optical tools for appropriate light delivery, especially for fiber-based or endoscopic delivery to tissues that are not directly accessible, is critical. In addition, this group emphasizes basic science studies of the mechanisms by which light can affect tissue in adverse or therapeutic ways.

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**Hosted By:** Therapeutic Laser Applications Technical Group

21 January 2020, 11:00 - 12:00

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Cartilage is avascular tissue with low metabolism and, as a consequence, with low potential for restoration.

### Announcements

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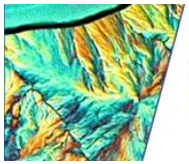

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# Welcome to today's webinar!

OSA Therapeutic Laser Applications Technical Group

## *THERMOMECHANICAL EFFECT OF INFRARED LASER FOR CARTILAGE REGENERATION*

Yulia Alexandrovskaya, PhD
Senior Researcher
*Institute of Photon Technologies,*
*Federal Scientific Research Centre "Crystallography and Photonics" of Russian Academy of Sciences*

January 21, 2020

*OSA Therapeutic Laser Applications Technical Group Webinar*

*21 January 2020*

# Thermomechanical Effect of Infrared Laser for Cartilage Regeneration


***Yulia Alexandrovskaya, PhD***
***Senior Researcher***

*Institute of Photon Technologies,*
*Federal Scientific Research Centre "Crystallography and Photonics" of Russian Academy of Sciences*

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•Dr. Obrezkova Mariya

•Medical team: Prof. Svistushkin V.M., Dr. Baskov A.V., Dr. Tokareva A.V.

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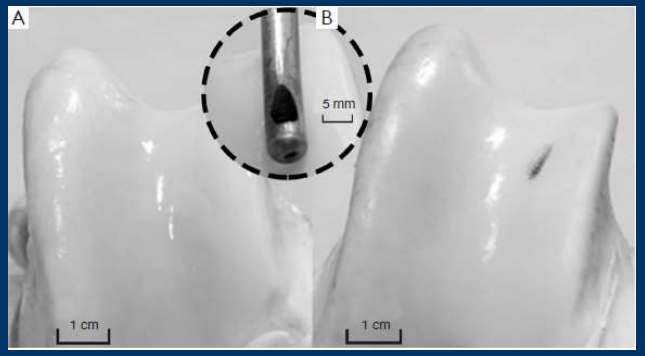
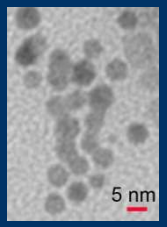
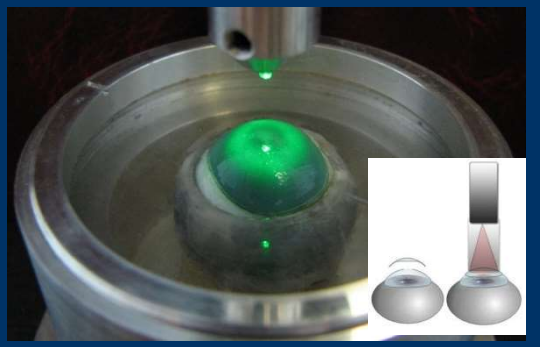
## Laser-induced regeneration of cartilage



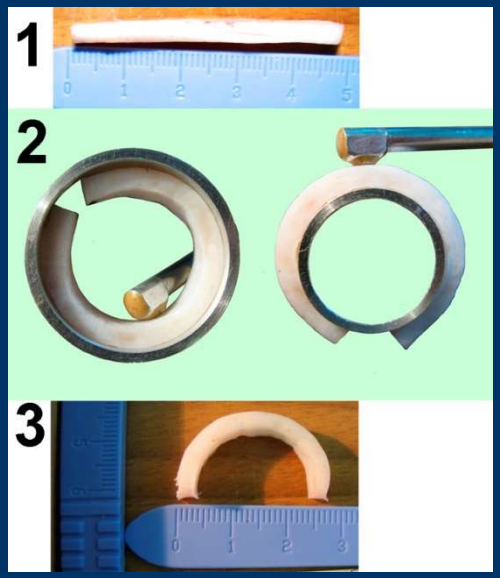



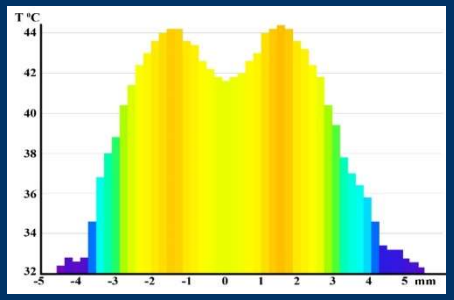

Early diagnostics of cartilage degradation using magnetic nanoparticles

## Laser correction of eye refraction and treatment of glaucoma

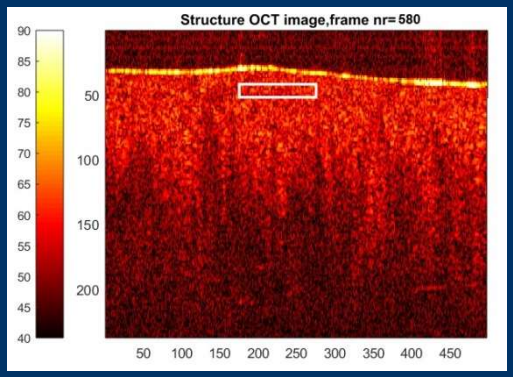


## Laser reshaping of cartilage



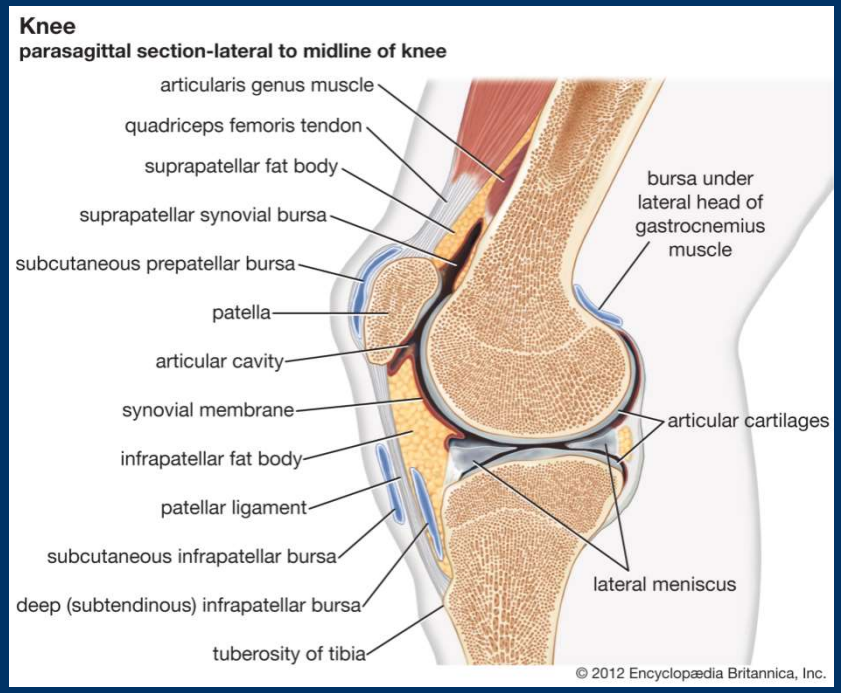




Theoretical modeling of laser-induced thermal and mechanical fields

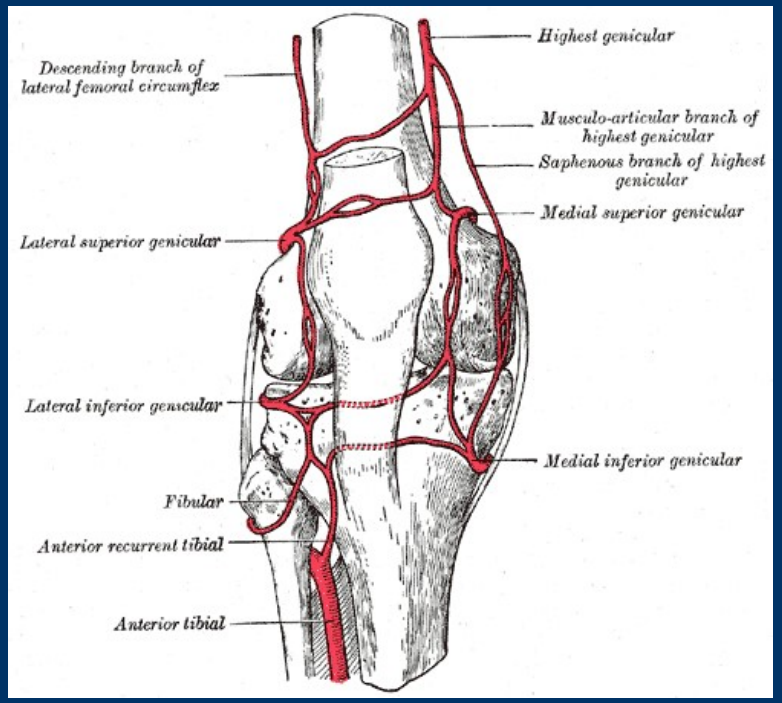



Optical coherent elastography of strains in biological tissues

# Why do we need laser stimulation of cartilage?




(c) Britannica




Arteries of knee joint,
Henry Gray (1918) Anatomy of the Human Body

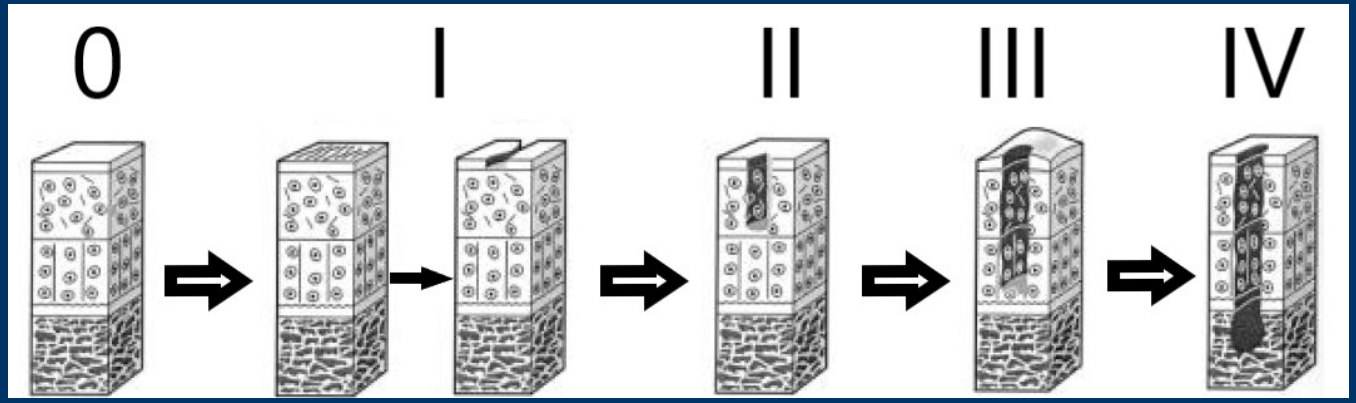
**Blood supply to cartilaginous tissue is strongly limited. Cartilage does not contain blood vessels. Oxygen and nutrients diffuse through small nanometer pores from synovial fluid.**

# Why do we need laser stimulation of cartilage?

- Cartilaginous chondrocytes have slow metabolism and lack of oxygen and nutrients

- The natural restoration potentials of cartilage are limited

- According to World Health Organization report more than 40% of population are susceptible to joint diseases. With age, every second inhabitant of the Earth suffers from arthritis and osteoarthritis of varying severity.




Osteoarthritis stages classification given by Internationa Cartilage Regenerative Society (ICRS)

**Nowadays there is no common effective approach for cartilage treatment!**

# Methods of cartilage regeneration

## Common clinical practice

### Pain relief

- *Non-steroidal anti-inflammatory drugs*
- *Corticosteroids*
- *Interstitial injections*
- *Low level light and ultrasound therapy*

### Surgical intervention

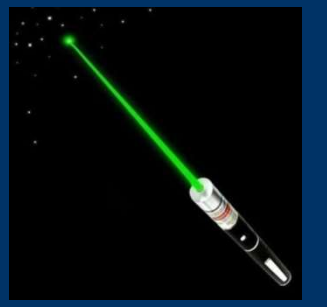
- *Bone marrow stimulation*
- *Autoimplantation of joint tissue*
- *Implantation stem cells and activated chondrocytes*
- *Joint replacement*

## Under development

### Tissue engineering

- *Natural and artificial scaffolds (frames)*
- *Scaffold seeding with activated cells*
- *Stimulation of chondrogenesis:*
  - *mechanical*
  - *hypoxia induced*
  - *biomarkers*

### Infrared Laser stimulation



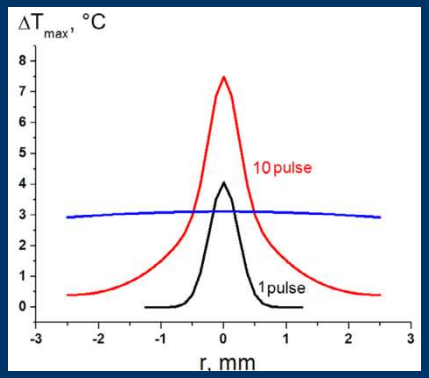
# Types of laser stimulation of cartilage regeneration

Thermomechanical (TM)

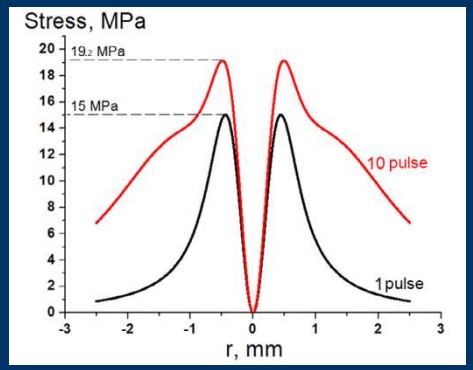
Low level light (LLL)

Lasers of Infrared range

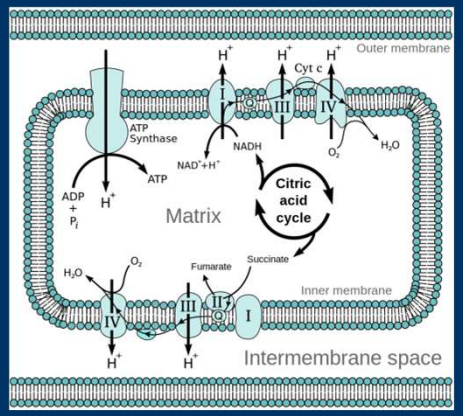
Lasers of visible and near infrared




Temperature gradient field




Mechanical stress field



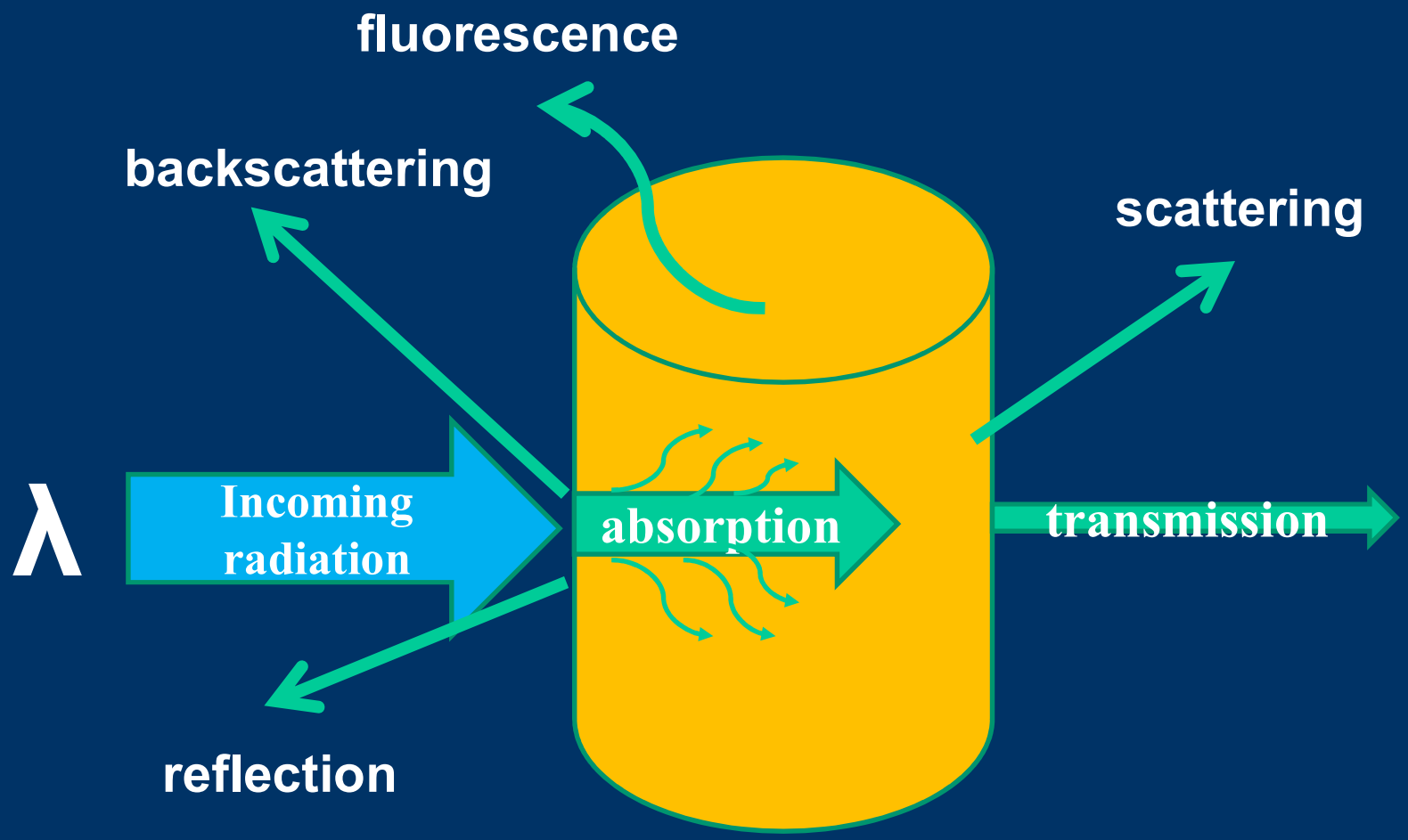

The mitochondrion electron transport chain, https://en.wikipedia.org/wiki/Electron_transport_chain

**Thermal and mechanical effect**

**Photochemical reactions?**

Laser Phys. Lett., 2018, 15, 085601

# Light-matter interaction

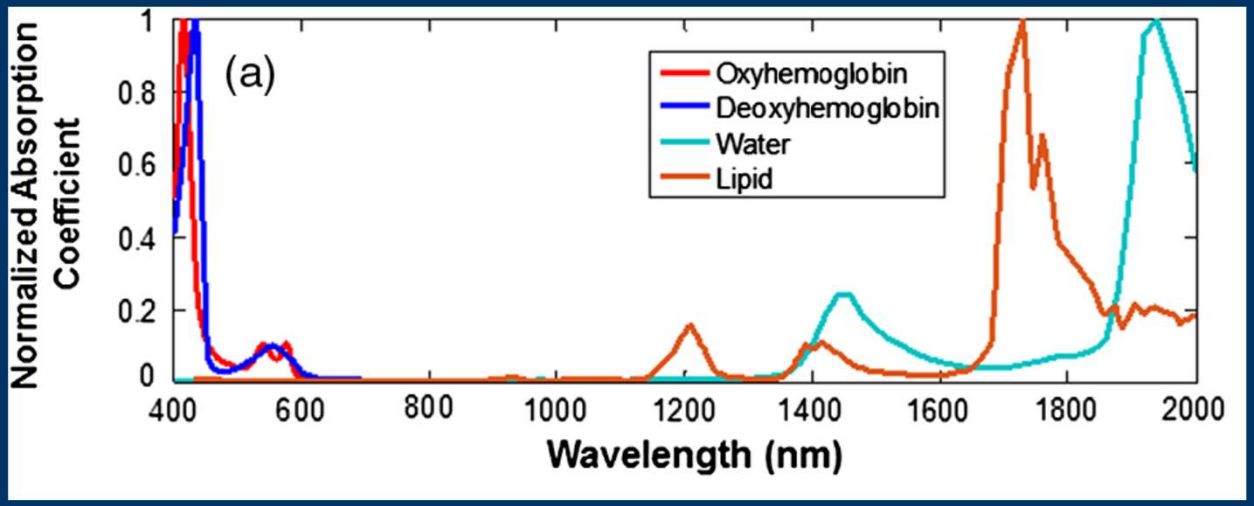



The light effect depends on which process is dominant for particular wavelength and type of material

# Biological tissues

Biological tissues are “turbid” media rich with water and different kind of scatterers, such as cells, organelles, collagen fiber, lipids, etc.

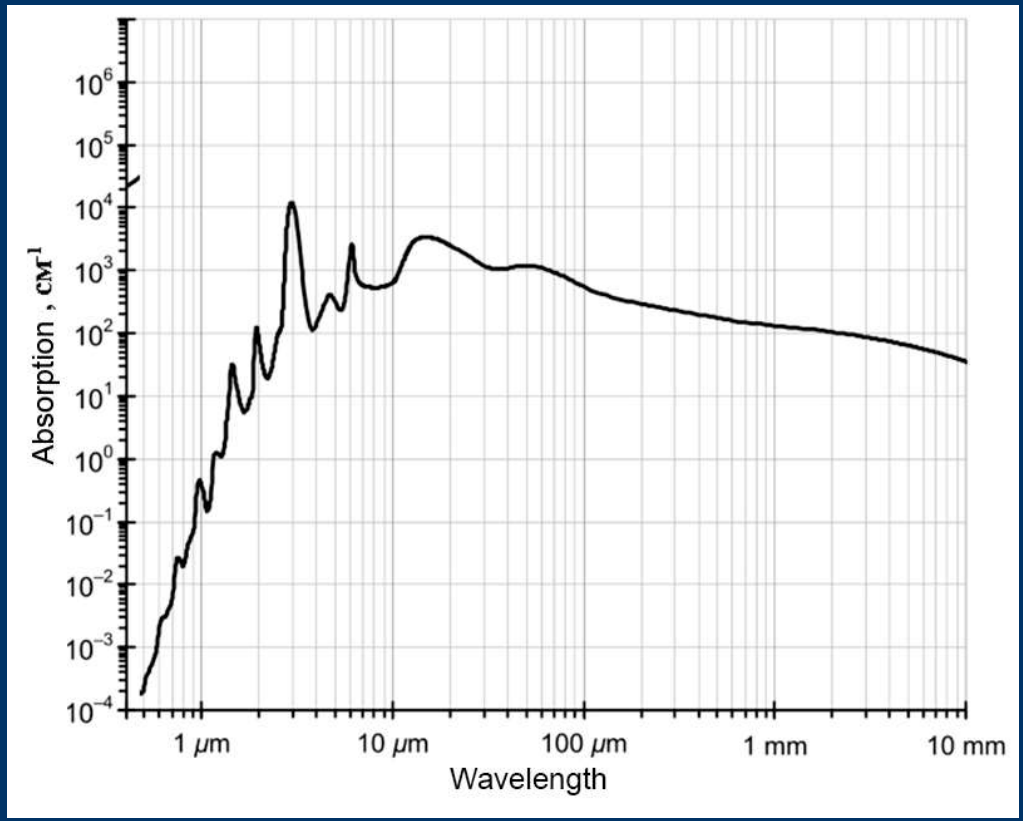
The action of light on biological tissue depends on the presence of specific absorbers and chosen wavelength




Spectra of main light absorbers in tissue

J Biomed Opt. 2015 Mar;20(3):030901.

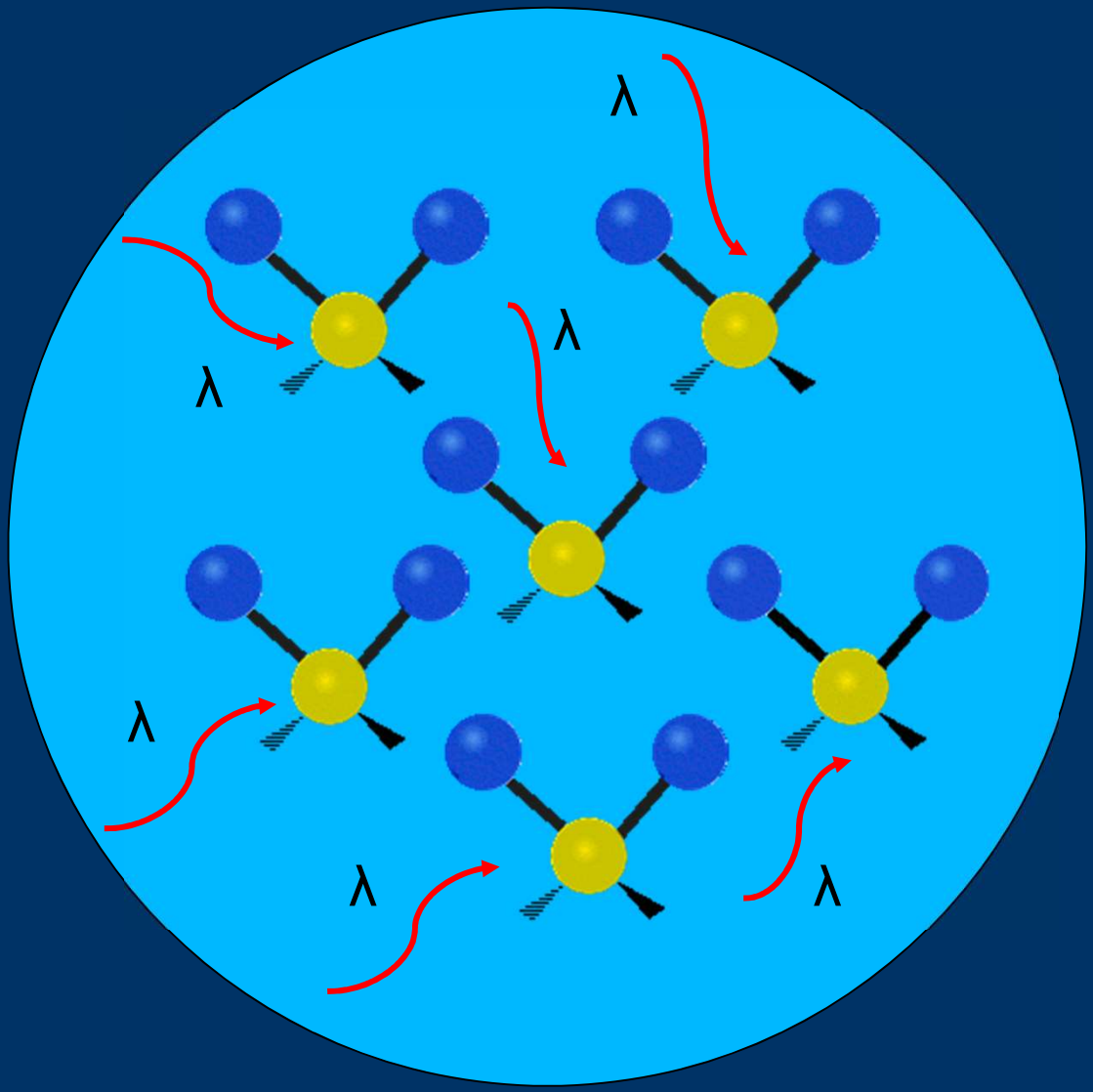
# IR light interaction with cartilage




As cartilage does not contain blood vessels, the principal absorber of infrared light is water

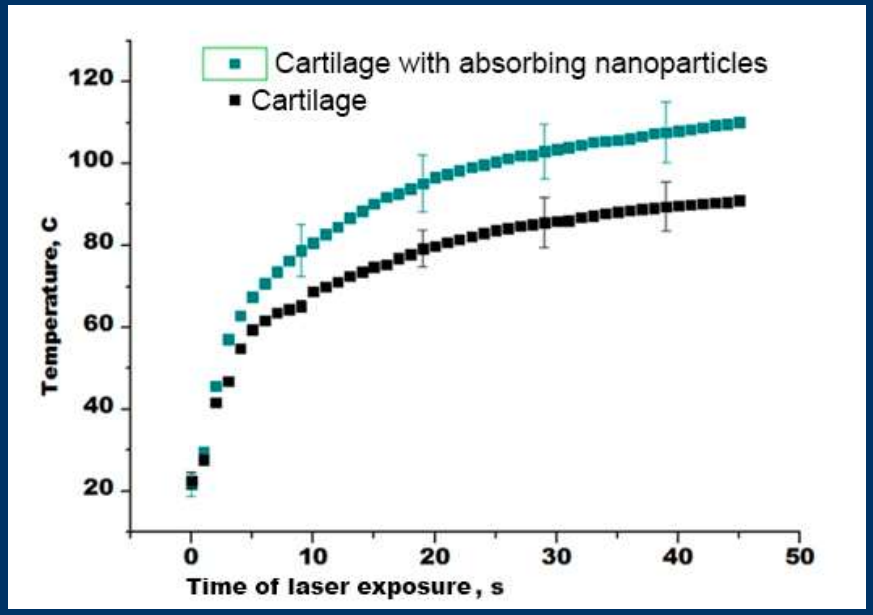
Water spectrum in infrared range.
Absorption increases in $10^{8}$ times from visible to far infrared!

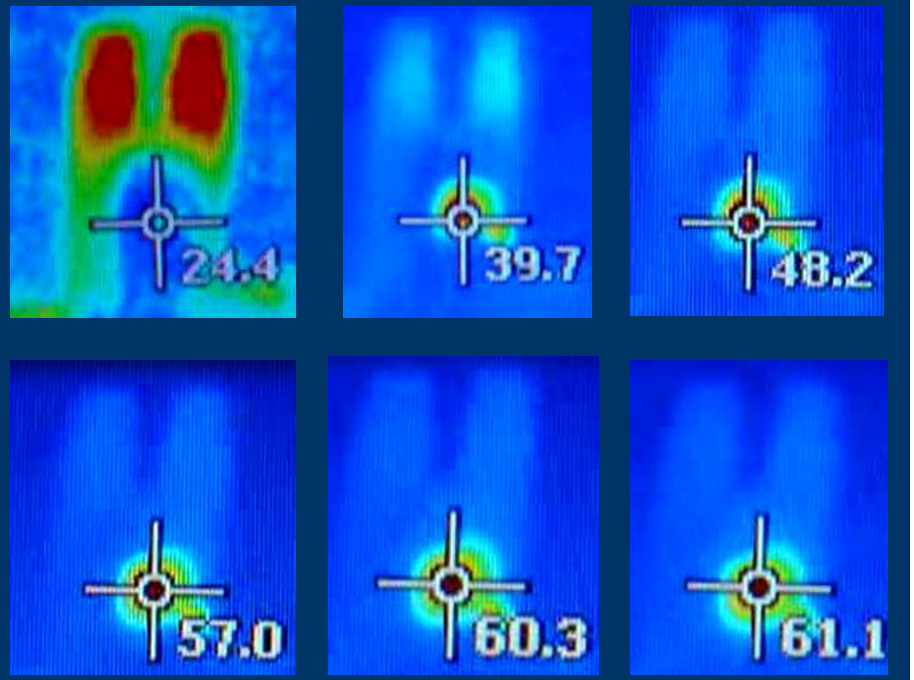
# Heat effect




Absorbed infrared light activates vibrational states of molecules, so it “promotes” the motion within the tissue, thus, the incoming LIGHT energy transforms into HEAT

# Temperature dynamics under IR laser exposure

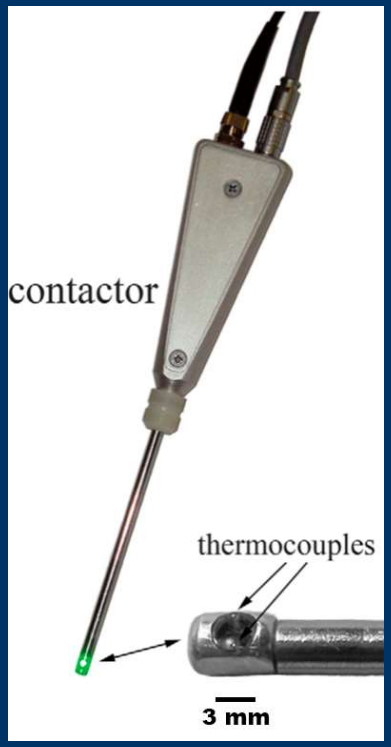



J Biophotonics, 2017, doi: 10.1002/jbio.201700105

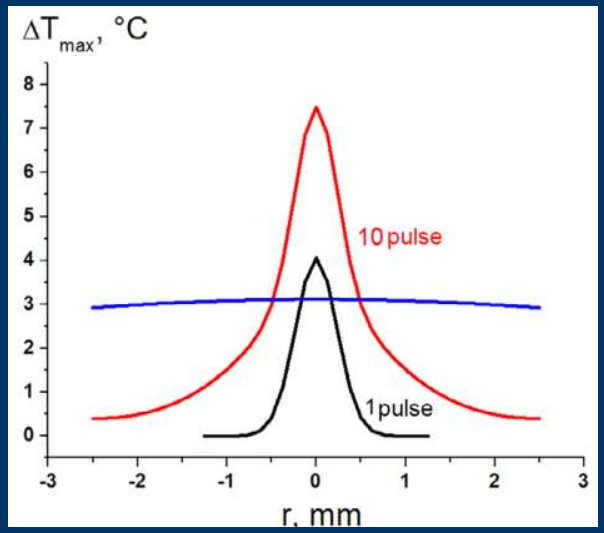
Careful optimization of laser wavelength, power and exposure time is needed not to overheat the tissue

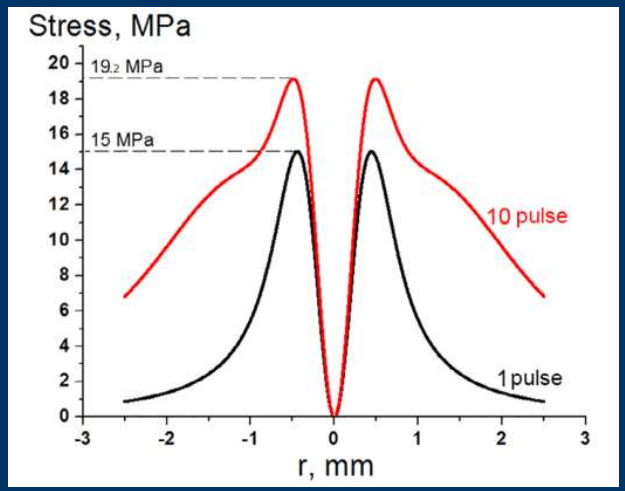
# Mechanical effect of IR laser exposure




Laser irradiation can be applied locally using optical fiber or emitter of arbitrary shape and size developed for certain medical purpose.

The resulted temperature field is non-uniform



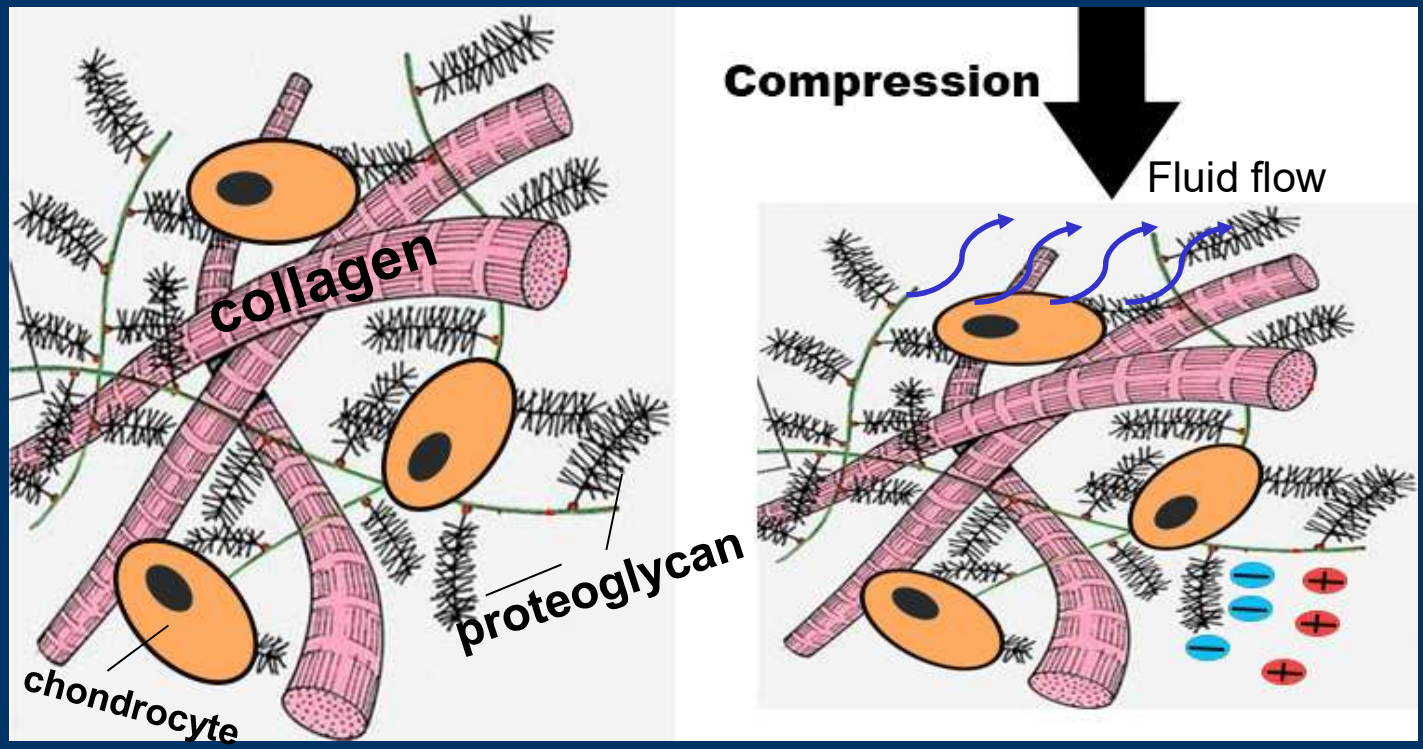




Non-uniform temperature field causes the non-uniform field of mechanical stress

Laser Phys. Lett., 2018, 15, 085601

# Mechanical stimulation of cartilage regeneration

Mechanical load bearing is a natural function of articular cartilage

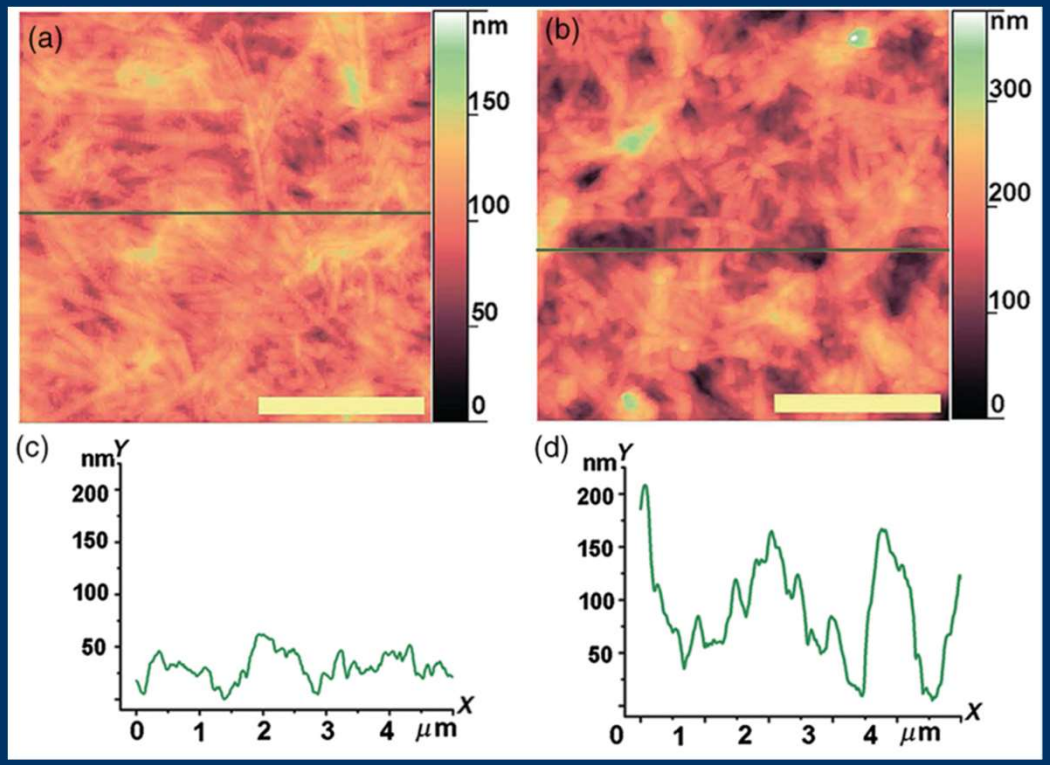



Dynamic mechanical compression activates many processes such as fluid flow, deformation of cells, hydrostatic gradients, electrical streams, convective transport.

# Mechanical stimulation of cartilage regeneration

As a result of mechanical stimulation of physiological amplitude 5 – 20 MPa and frequency 1 Hz the pronounced synthetic activity of chondrocytes can be achieved.

IR laser effect  is capable of generating the same mechanical fields and additionally promote liquid flow caused by heating and formation of pores

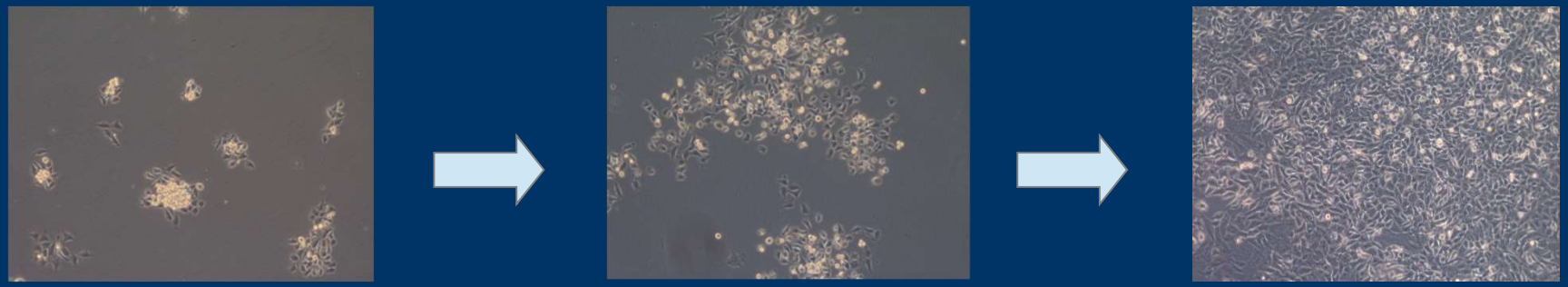



Atomic force microscopy visualization of laser-induced micropores in cartilage (a-before irradiation, b – after irradiation) and their distribution along green line (below, c-d)

J Biomed Opt, 2017, №22, 9, 91515

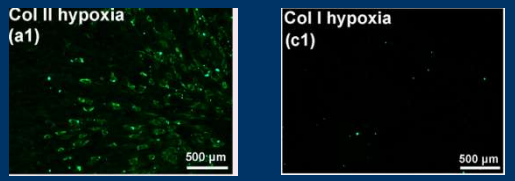
# Thermomechanical laser effect on isolated cells

## Chondrocyte cultures

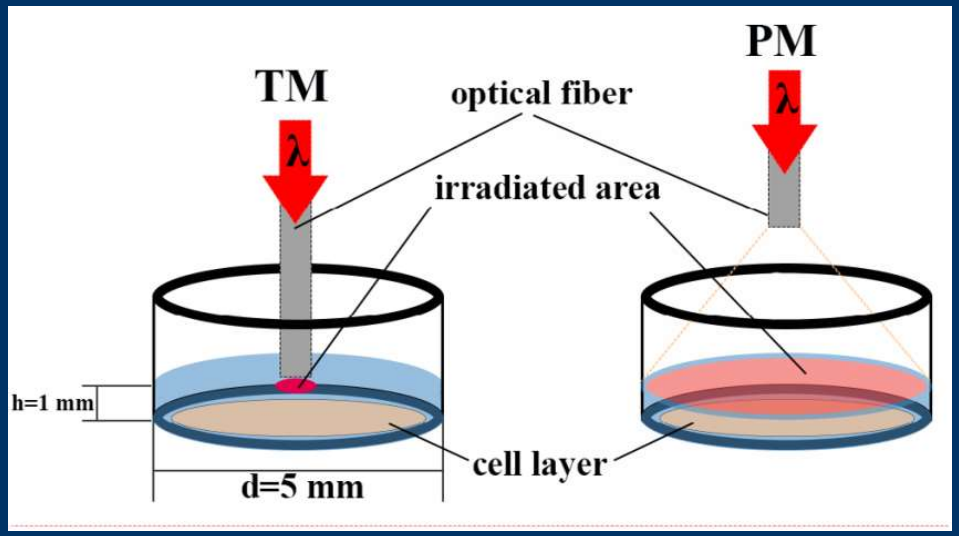


3 days 5 days 10 days

The increase in cell size immediately after exposure


Collagen II and I antibodies (phenotype validation)

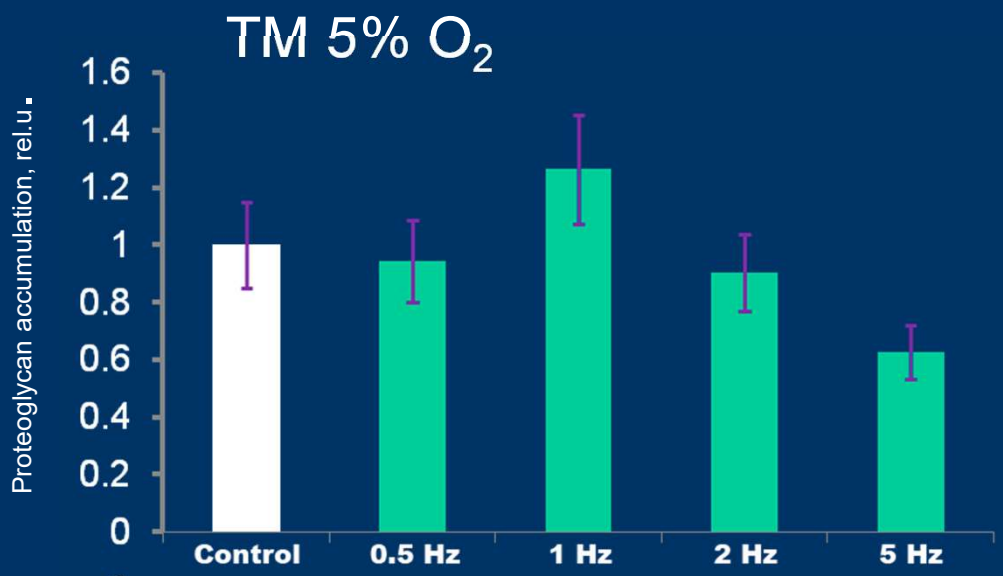



Thermomechanical: λ=1,56 µm, Power density 300 W/cm$^2$, irradiation is localized on 0,3 mm$^2$

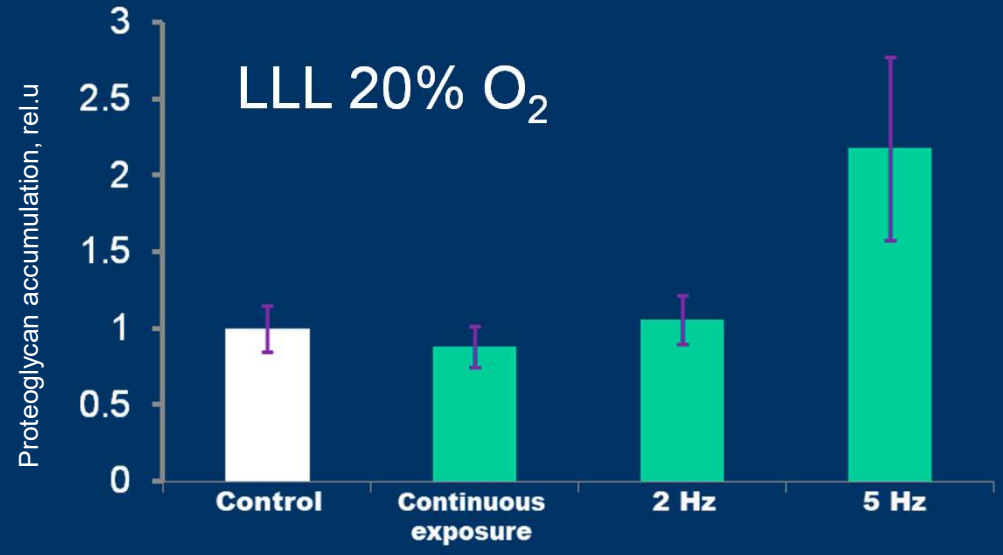
Low level light: λ=1,56 µm, Power density 0,3 W/cm$^2$, total cell population is irradiated

Laser Phys. Lett., 2018, 15, 085601

# Synthetic activity of the cells after irradiation



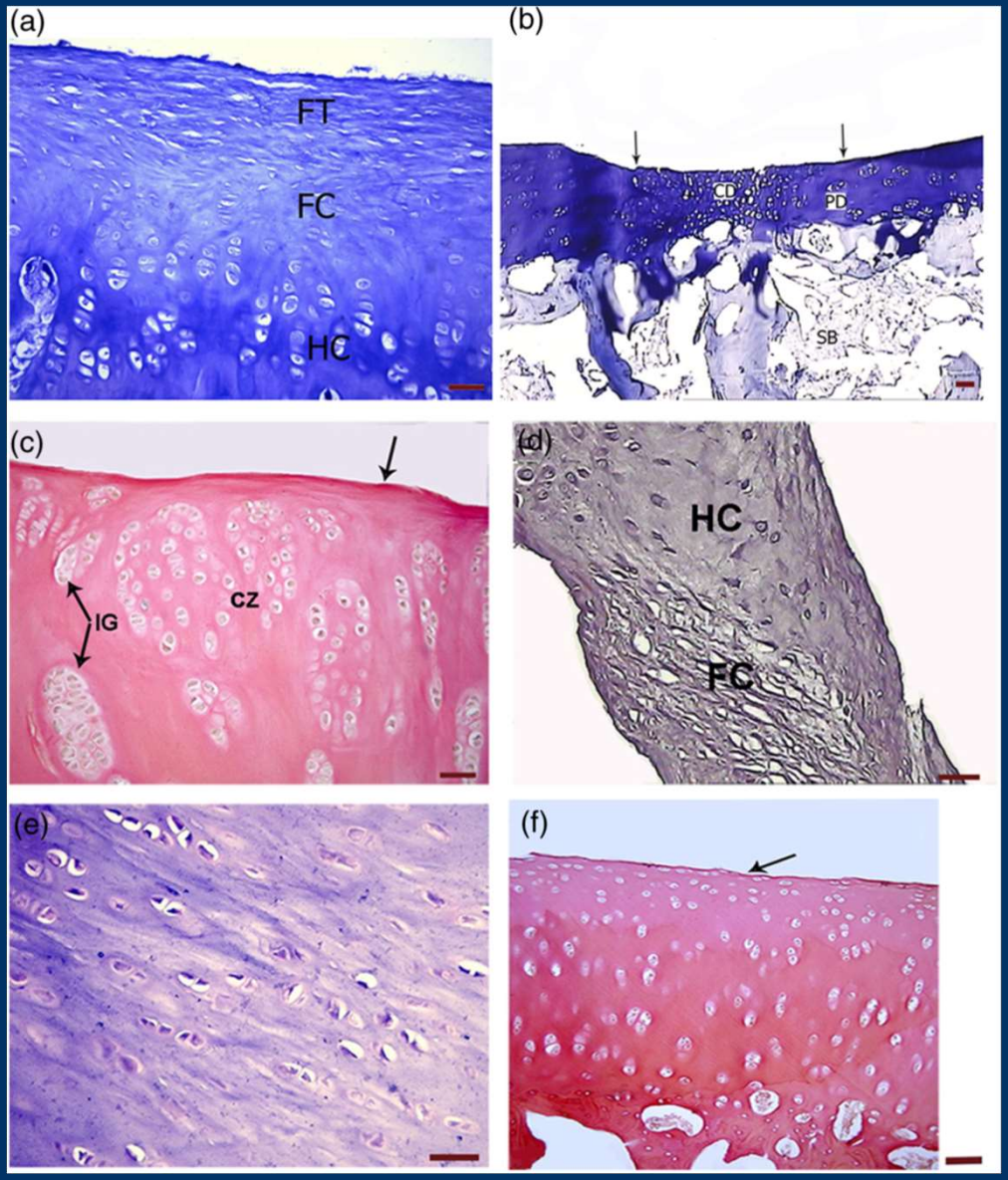

Thermomechanical laser has a stimulating effect in hypoxia.
The optimal frequency of TM exposure is 1 Hz




Low level laser has a stimulating effect in the conditions of normoxia.
The accumulation of proteoglycan increases with increasing frequency of exposure

Laser Phys. Lett., 2018, 15, 085601

# Thermomechanical laser effect on living tissue




(a) Non-irradiated defect. filled with fibrous tissue (FT )and fibrous cartilage (FC); residuary hyaline cartilage HC is below;

(b) The common view of the laser-irradiated defect (between the arrows) after 2 months. In the center of the defect, there is a noticeable chondrocyte proliferation., 100×.

(c)–(e) The images taken 2 months after the laser treatment. (c) Transformation of chondrocytes: isogenous groups IG (multicellular clones)

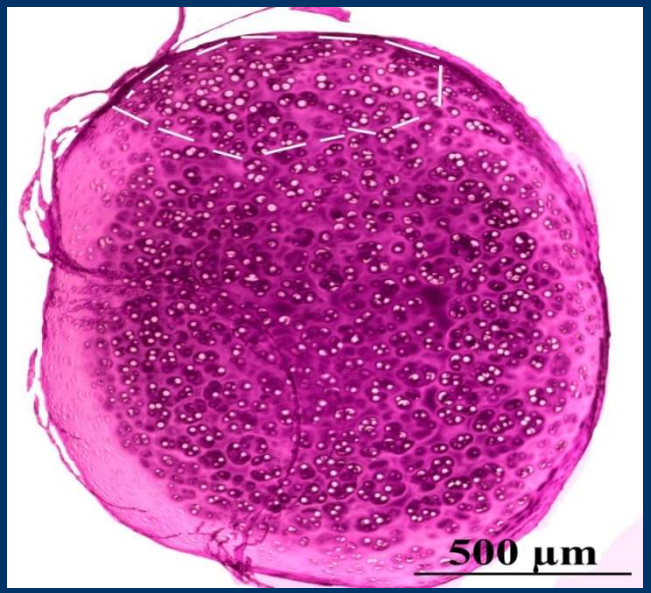
(d) Growing HC substitutes FC, 400×

(e) Intermediate fibro-HC (in the centrum), 400×,

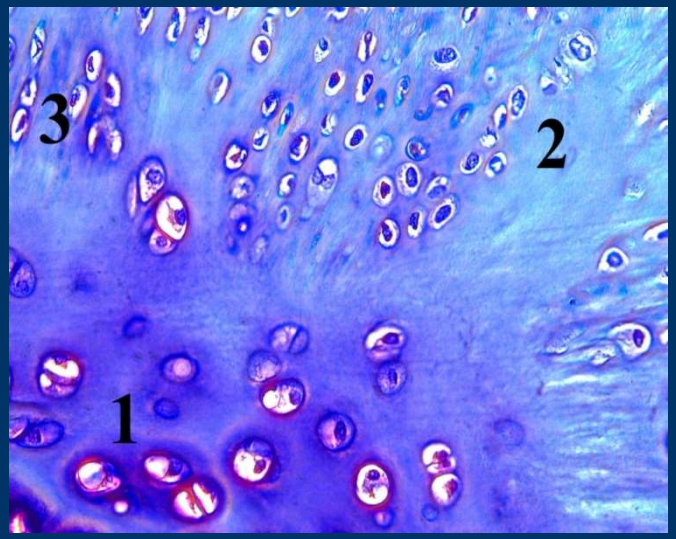
(f) Completely recovered HC and lamina splendid (marked with the arrow) in 3 months after laser treatment of articular cartilage defect, 200×

J Biomed Opt, 2017, №22, 9, 91515

# Histology of the laser irradiated costal cartilage implants




**Crosscut of laser irradiated implant**, H&E,x100. Hyaline cartilage and pronounced manifestations of regeneration processes are seen. The structure of implant contains the increased number of isogenous groups of chondrocytes in an area (marked with the dashed line) which was adhered to the native cartilage.




**Phase contrast image**.
1- hyaline cartilage with the homogenous matrix and large chondrocytes;
2 – fibrous cartilage;
3 – fibro-hyaline cartilage with the smaller chondrocytes in discrete lacunas and the typical fibrous structure of matrix.

**In the experimental groups with laser irradiation in more than 1/3 of the cases regeneration was more pronounced and manifested as the formation of multicellular clones — isogenic groups.**

# Clinical application of laser-induced regeneration

## Thermomechanical

*Proc. SPIE 2009, 7179, 71790B*

Tissue irradiation with a fiber laser

- Intervertebral disc regeneration: more than 3000 operations in Russia, the beginning of clinical trials in the USA
- Regeneration of the knee: clinical trials in Russia, more than 20 operations on patients

## Low level light

Non-invasive high-repititive pulsed laser

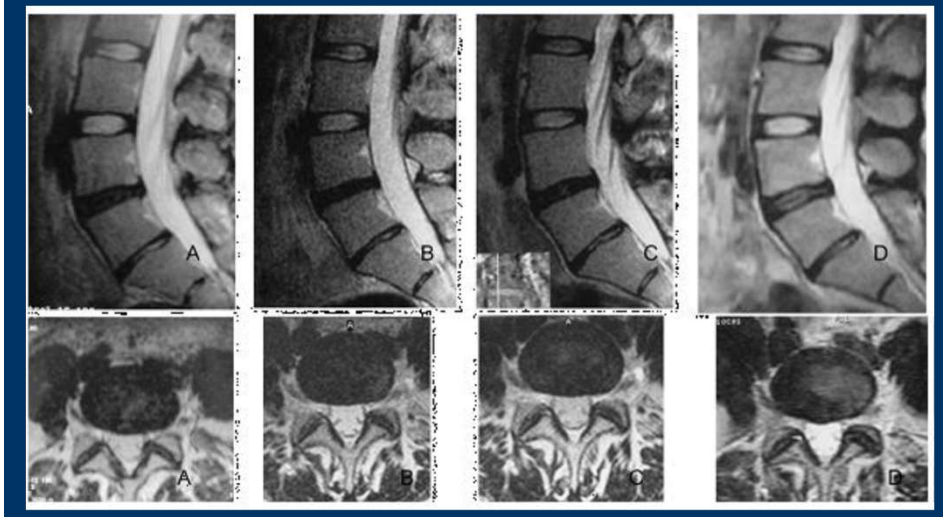
Physiotherapy to reduce inflammation, pain, support basic therapy

# Laser reconstruction of interverbal disc (LRD)

*Proc. SPIE 2009, 7179, 71790B*

Low-invasive fiber-assisted procedure;

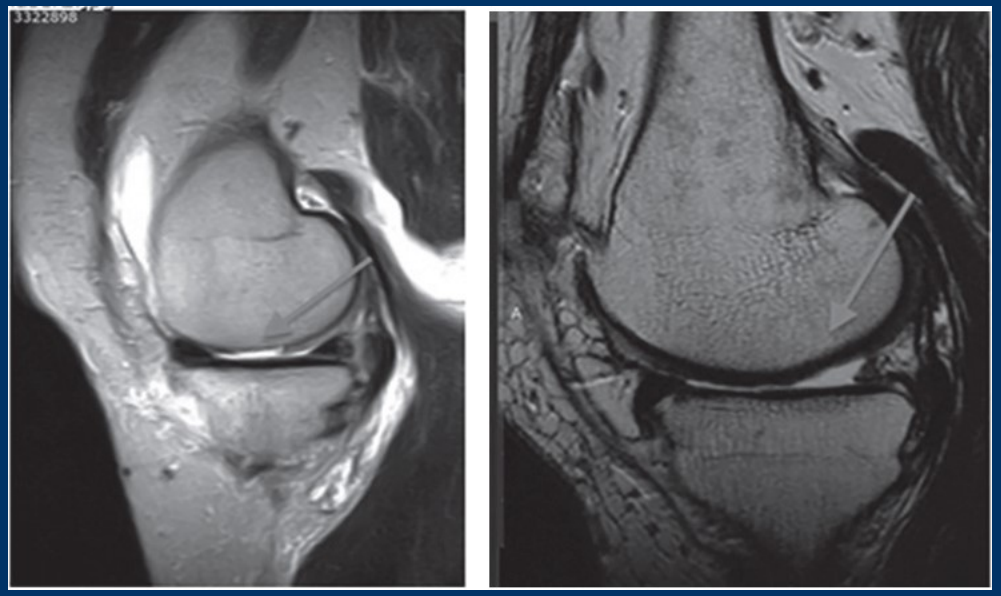
General view of the equipment




Baskov, et al., J Spine 2015, 4:1

Dynamics of MRI examination results for a patient before and after LRD.
A – Before LRD. Degenerative structure of the L4-L5 disc is visible.
B - One year after LRD. There are no visible changes at MRI image, whereas the patient has demonstrated significant pain relief.
C – Two years and three months after LRD. Note increase of T2 signal.
D - Five and a half years after LRD.
Evident signs of reparation of the disc are visible: note increase of the disc height and reparation areas in the disc.

# Laser reconstruction of articular cartilage



In six month after laser irradiation of femoral joint defect (left) the cartilage layer became smoother and increased in 1 mm (right)

Irradiation of joint cartilage can be performed with 3 mm laser contactor during arthroscopy or through 400-600 μm optical fiber under ultrasound visualization control


Laser contactor for cartilage irradiation

Quantum Electron., 47:10 (2017), 935–941

# Conclusions

Thermomechanical laser stimulation of cartilage is a new perspective tool for repair of degraded tissue

It has completely different mechanism from well-known low level light stimulation and is based mainly on physical principles of interaction of infrared light with water-rich tissue

Laser technique of thermomechanical stimulation of cartilage is minimally invasive, which makes it very promising for hard-to-reach joint cartilages, like knee, femoral and facet joints

Better understanding of biophysical mechanisms of stimulation will contribute to extension of possible applications of this technique to other types of tissues and cells.

# Bibliography


1. Yu M Alexandrovskaya, OI Baum, AB Shekhter, EV Petersen, OA Tiflova, AK Dmitriev, VA Ulyanov, VM Svistushkin, LV Selezneva and EN Sobol, Mechanisms of laser activation of chondrocytes in osteoarthritis healing, 2018, Laser Phys. Lett., 15, 085601.
2. Alexandrovskaya Yu.M., Sadovnikov K., Sharov A., Sherstneva A., Evtushenko E., Omelchenko A., Obrezkova M., Tuchin V., Lunin V., Sobol E., Controlling the near infrared transparency of costal cartilage by impregnation with clearing agents and magnetite nanoparticles, Journal of Biophotonics, 2017, doi: 10.1002/jbio.201700105.
3. Sobol E, Baum O, Shekhter A, Wachsmann-Hogiu S, Shnirelman A, Alexandrovskaya Y, Sadovskyy I, Vinokur V. Laser-induced micropore formation and modification of cartilage structure in osteoarthritis healing, Journal of Biomedical Optics, 2017, №22, 9, 91515.
4. Baskov, Andrei & I.A., Borshchenko & Shekhter, Anatoly & V.A., Baskov & Guller, Anna & Sobol, Emil. (2015). Long Term Clinical Results in Laser Reconstruction of Spine Discs. Journal of Spine. 04. 10.4172/2165-7939.1000210.
5. Sobol E, Shekhter A, Guller A, Baum O, Baskov A. Laser-induced regeneration of cartilage. J Biomed Opt. 2011 Aug;16(8):080902.
6. AI Omelchenko, VN Bagratashvili, EN Sobol, AA Karabutov. Control of Tissue Mechanics upon the Repetitive-Pulse Laser Heating of Cartilage. Laser Physics, 2006, 16(12):1681–1688.

# Bibliography. Some related works and reviews


1. Jacques SL. Optical properties of biological tissues: a review. Phys Med Biol. 2013 Jun 7;58(11):R37-61.
2. Natenstedt J., Kok A.C., Dankelman J., Tuijthof G.J.M., What quantitative mechanical loading stimulates in vitro cultivation best?, J of Experimental Orthopaedics, 2015 , 2:15.
3. G. M. Hale, and M. R. Querry, Optical constants of water in the 200 nm to 200 µm wavelength region, Appl. Opt., 12, 555-563, 1973.
4. MV Padalkar, RG Spencer, and N Pleshko. Near Infrared Spectroscopic Evaluation Of Water In Hyaline Cartilage. Ann Biomed Eng. 2013 November ; 41(11): . doi:10.1007/s10439-013-0844-0.
5. Iolascon G, Gimigliano F, et al. Early osteoarthritis: How to define, diagnose, and manage. A systematic review. European Geriatric Medicine 2017; 8 (5–6), 383-396.