Phenomenon of atypical vascular effects of epinephrine in rats with colon adenocarcinoma

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Using an original model of stress-induced colon adenocarcinoma (combination of chronic social stress (overpopulation during 9 months) and daily diet with toluidine (2 g/kg) in food and water with nitrites (2 g/l)), we uncover atypical vasorelaxation effects of epinephrine in colon mucosa that is associated with the high expression of mesenteric beta2-adrenoreceptors (B2-ADRs) and with the high level of beta-arrestin-1 (ARRB1) both in the blood and in the colon tissues in rats with colon cancer. Our results clearly demonstrate a high mucosal level of nitric oxide (NO), elevated sensitivity of mesenteric vessels to blocked of inducible nitric oxide synthase and an increased photodynamic diagnostics effectiveness by nitroglycerin in rats with colon adenocarcinoma vs. the control, stress and nitrosamine groups. These data shed light on mechanisms underlying stress-induced colon cancer that is characterized by hyperactivity of adrenergic and NOergic systems in gastrointestinal tissues.

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Optical imaging of glioma cells migration via the cerebral vessels: application of the beta2-adrenoreceptors blockade

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Malignant gliomas (MG) are highly invasive brain tumors that are characterized by, on the one hand, with high the blood–brain barrier (BBB) disruption and, on the other hand, drug brain delivery via the BBB is a big challenge in MG therapy. The limited information about vascular changes associated with MG growth is a reason of slow progress in prevention of MG development.

Here, we uncovered a local breach in the BBB in the main MG mass but not within the border of normal and malignant cells, where the BBB was impermeable for high weight molecules. The migration of glioma cells (GCs) were observed via the cerebral vessels with the intact BBB. The mechanisms underlying MG progression remain unknown but there is an evidence that the adrenergic nervous system via activation of vascular beta2-adrenoreceptors (B2-ADRs) can play an important role in MG metastasis. Our results clearly show an increase in the expression of vascular B2-ADRs and production of the beta-arrestin-1 - co-factor of B2-ADRs signaling pathway in rats with MG. Pharmacological blockade of B2-ADRs reduces the BBB disruption, macrophages infiltration, GCs migration and increases survival rate.

These data suggest that the blockade of B2-ADRs may be a novel adjuvant therapeutic strategy to reduce glioma progression and prevent metastasis.

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Laser Made 3D Auxetic Metamaterials for Tissue Engineering

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Multiphoton Polymerization (MPP) is a powerful ***Direct Laser Writing*** (DLW) technique capable of fabricating 3D microstructures up to a few hundreds of μm via a computer aided design (CAD). The polymerization takes place inside organic-inorganic sol/gel materials with the addition of specific photoiniciators. While the concept of architected materials is not new, recent progress in 3D printing has enabled the realization and investigation of complex mechanical metamaterials, with submicron features using a wide variety of constituent materials. In this research we fabricated a special auxetic metamaterial called reentrant honeycomb (bowtie) which has a **Negative Poison’s Ratio** and used it as scaffold for culturing **human fibroblasts**. Many tissues in the human body show auxecity, such as skin, tendon and arteries. Our experiments showed that living cells are able to deform and bend the auxetic scaffolds thus creating and shaping their own extracellular mechanical environment according to their needs without destroying them. To our knowledge, this is the first time that a well-defined 3D auxetic microstructure is used for a cell culture experiment. Our future plans include using different cell lines such as induced Pluripotent Stem Cells (iPSC), neurons and Macrophages to study deeper the association between mechanical micro- environment and signal transduction in those cell types.

Photoluminescence and Raman spectroscopic investigation of nanodiamond structures incorporating SiV centers

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Nanodiamond crystal containing optically active point defects or so called “color centers” have attracted attention of many researchers in last decades. These unique nanoobjects with excellent physical and optical properties are very promising candidates for novel photonic and biological applications, including but not limited to room temperature solid state single-photon source, extremely sensitive magnetometry, nanoscopy, biocompatible labeling or drug delivery systems [1-3]. Most of the mentioned applications are based on the superb photoemission properties of this nanosystem.

The number of known optically active centers in diamond exceeds one hundred, but only a few of them shows optical or physical properties useful for real applications. Among them nitrogen-vacancy (NV) and silicon-vacancy (SiV) centers are the most widely studied ones. In aspect of biological applications, the SiV center has more beneficial light emission properties than NV center. The zero-phono line (ZPL) of the SiV is located in the near-infrared transmission window of live tissues at 738 nm. Moreover, most part of photoluminescence (PL) is concentrated in this narrow ZPL and its contribution usually exceeds 70% of the overall PL intensity (for NV it is 4%).

The SiV center can be created in nanodiamond structures by ion implantation and in situ doping of the growing crystal as well. Despite of the well-controlled character of both techniques, the emission and spectral properties of the created centers are distributed in a wide range [4], which is a serious limitation for mass production.

In this study we report about the systematic study of spectral parameters and emission intensities of SiV center ensembles embedded in single diamond nanocrystals, nanodiamond films and nanopillars prepared by chemical vapor deposition (CVD), photolithography and reactive ion etching of CVD nanodiamond films. Using multi-wavelengths PL and Raman investigations, correlation between the structure and SiV spectral parameters was found and discussed in terms of residual internal stress – acting in the vicinity of the SiV centers – and morphology of the host nanodiamond structures, determined by scanning electron microscopy.

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In-situ Raman spectroscopic studies of laser transformations of cage-like As-S molecules

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Remarkable structural, electronic and optical properties of chalcogenide based media have attracted significant attention and their controlled modification is representing an important scientific and technological challenge. Thanks to the advantageous combination of infrared properties, optical activity, structural photosensitivity and high third-order optical non-linearity these materials offer wide possibilities in domains such as photonics, modern information and renewable energy technologies, medicine, thermal imaging, sensing and biosensing *etc.* In addition, recent studies have indicated that arsenic sulphide (realgar) has an anticancer effect, especially on hematological cancer, which can be related to the realgar to pararealgar transformation under light illumination. The possibility of post fabrication material processing using coherent light irradiation (*i.e.* relief formation, surface activation *etc.*) can further increase their functionality allowing several applications based on this phenomenon to be developed [1].

We report on the light induced transformation of the structure of As-S nanocrystallites synthesized by nano-gold catalyzed thermal deposition of As_2S_3 glass. For film preparation the Si substrates were covered with a layer of 5, 20, 40 and 60 nm spherical gold nanoparticles and placed downstream in a tube furnace flowed with As_2S_3 vapor. The vapor was obtained by sublimation of As_2S_3 glass powder at temperature elevated up to ~300°C and was forced to downstream by H_2/As carrier gas. The synthesis was done with elevated (~100° C) and room temperatures of the substrates.

The photo-induced transformations of realgar (r) type As_4S_4 cage-like molecules were investigated *in-situ* by using the surface enhanced Raman spectroscopy. A diode laser operating at 785 nm was used as excitation source. The Raman spectra of fresh prepared film contain the narrow bands at 134, 144, 165, 185, 219, 231, 341 and 360 cm^{-1} characteristics of r-As_4S_4. Essential spectral transformation is taking place under focused 785 nm laser irradiation of the sample. The changes in the Raman spectra of As-S sample during laser irradiation were monitored *in-situ*. Density functional theory calculations of different cage-like As-S molecules were performed in order to assist the spectral interpretation and elucidate the structural origin of the transformations. The intermediate state and the structural changes during the transformation is discussed in details and some applications of the observed phenomena were proposed.

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A full Mueller matrix measurement of ex vivo colon samples with Stokes polarimeter

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Any turbid media can be described by means of its own Mueller matrix, containing significant information about polarization/depolarization properties. Measuring the full Mueller matrix of a desired sample is not a trivial task at all and may require quite expensive optical set-up to build, not to mention a huge rise in the price with regard to a commercially available Mueller matrix polarimeters. Additionally, any Mueller matrix can be decomposed to three matrices of depolarization $\mathbf{M}_{\Delta}$, diattenuation $\mathbf{M}_{\mathbf{D}}$ and retardance $\mathbf{M}_{\mathbf{R}}$. These processes occur simultaneously, when light travels into biological tissues and inevitably lead to light depolarization. By applying the symmetrical decomposition, the final form of the experimental Mueller matrix can be acquired $\mathbf{M}_{\mathbf{sample}} = \mathbf{M}_{\mathbf{R}}\mathbf{M}_{\mathbf{D}}\mathbf{M}_{\Delta}\mathbf{M}_{\mathbf{D}}\mathbf{M}_{\mathbf{R}}$ (valid for reflection geometry). In this work, we present practical approach how to obtain indirectly a full Mueller matrix of *ex vivo* colon samples, only by knowing the input and output Stokes vectors $\mathbf{S}_{\mathbf{i}}$ and $\mathbf{S}_{\mathbf{o}}$ respectively. This method requires illuminating independently a sample of interest with four different input polarization states (H, V, M, C) and known input Stokes vectors. Then, after conducting several simple but necessary, algebraic operations with regard to the output measured Stokes vectors, the full Mueller matrix can be derived. Although this method could be time consuming, on the other hand it can be budget-saving and, therefore, is worth paying attention. The results from the experiments show high sensitivity to any tissue alterations, resulting from tumor sections in the samples, which can change both the optical properties and the tissue structure. Furthermore, all measured Stokes parameters can be represented via the Poincare sphere, in order to track their evolution, according to the histological origin of the measurements.

Keywords: Tissue polarimetry, Stokes polarimetry, Mueller matrix, Symmetrical decomposition, Poincare sphere representation, *ex vivo* colon samples.

Local and systemic effects after 1270 nm laser irradiation of BALB/c Nude mice skin

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Study of new wavelength ranges of laser radiation is among the priorities of modern laser medicine to enhance the laser prospects in treatment of cancer diseases frequently associated with disturbances in the antioxidant system of a body. Photobiomodulation (PBM) effects on a model organism at 1265-1270 nm are of particular interest for preclinical research due to the fact that this spectrum range corresponds to the maximum oxygen absorption band.

We report comprehensive biomolecular studies of the changes in the BALB/c Nude mice skin after an exposure to the continuous laser radiation at the 1270 nm wavelength and energy densities of 0.12 and 1.2 J/cm2. Our study has demonstrated biostimulating effects of laser exposure, presumably due to the short-duration increase of ROS levels.

In the BALB/c Nude mouse model, PBM has induced a photo-stimulating effect at the dose of 1.2 J/cm2 in both an irradiated skin spot and peripheral blood cells. This irradiation regime decreases the synthesis of pro-inflammatory cytokines in blood plasma, mainly IL-6. In the skin region of laser exposure, the proliferation intensifies without inflammation signs. Thus, in the BALB/c Nude mouse model the laser at the wavelength of 1270 nm and dose of 1.2 J/cm2 produces local and systemic stimulation effect highly likely due to an increase in the ROS levels which activates the cell antioxidative system.

The further studies should be done with higher radiation doses for revealing whether 1270 nm laser irradiation can treat the melanoma planted on BALB/c Nude mouse model.

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Observation of laser resonances at 1265 nm in eukaryotic cells

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In our work we suggest that the surface plasmon-polariton phenomenon which it is well described in metallic nanostructures could also be used for explanation of the unexpectedly strong oxidative effects of the low-intensity laser irradiation in living matters (cells, tissues, organisms). Here, we reveal the singlet oxygen generation induced by the laser radiation in individual HCT116 cells (with the size of about 10 μm), which demonstrated narrow-band resonant sensitivity in the range of 1265-1268 nm. Therefore, we assume that the observed narrow band resonance could be explained through the generation of the localized slow waves plasmon resonance in the cells characterized by a high effective refractive index (>25). The mitochondrial membrane surfaces being highly electrically conductive are the most probable object, where such plasmon polaritons can be generated. The conditions for phase-synchronization could be founded in the periodic organic structures such as the lipid bilayer or mitochondrial cristae. In this context, the observed light-oxygen effect of low-intensity laser irradiation can be explained by the formation of highly localized plasmon-polariton wave packs which enable the generation of singlet-oxygen in the strong field localization points. Our experimental conditions, the low-intensity irradiation, the narrow spectrum band (< 4 nm) of the laser and comparably small size bio-structures (~10 μm) are shown to be sufficient for the plasmon-polariton generation and strong laser field confinement enabling the oxidative stress observed. This plasmon-polariton explanation of the LLL-induced cellular ROS effect is in agreement with the reported experimental data. Besides, in our recent experiments we have directly compared the effects induced by a low-intensity narrowband (highly coherent) and relatively high-intensity wideband lasers exploring specific features of two processes. These new observations are also consistent with plasmon-polariton interpretation of the effect proposed here.

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Transcranial photobiomodulation of lymphatic clearance of beta-amyloid from the mouse brain

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Here we propose a novel non-invasive method of transcranial photobiomodulation (tPBM, 1267 nm, 32 J/cm^2) for stimulation of clearance of β-amyloid from the brain via the meningeal lymphatic vessels.

We used an model of Alzheimer’s disease based on intrahippocampal injection of Aβ(1-42) peptide. To test effectiveness of AD development, we studied neurobehavioral status of mice obtained by the neurological severity score.

The immunohistochemical and confocal data clearly demonstrate the significant reduction of deposition of Aβ plaques in mice after tPBM vs. untreated animals. The behavior tests showed that tPBM improved the cognitive, memory and neurological status of mice with AD. Using of our original method based on optical coherence tomography (OCT) analysis of clearance of gold nanorods from the brain, we proposed possible mechanism underlying tPBM-stimulating effects on clearance of Aβ via the lymphatic system of the brain and the neck.

These results open breakthrough strategies for a non-pharmacological therapy of AD and clearly demonstrate that tPBM might be a promising therapeutic target for preventing or delaying AD.

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Age Differences in Photodynamic Opening of the Blood-Brain Barrier Through the Optical Clearing Skull Window in Mice

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Photodynamic therapy (PDT), a minimally invasive therapeutic tool, has been an important option for post-surgical treatment of malignant gliomas (MGs). In our recent studies we discovered that PDT can also open the blood-brain barrier (BBB) that might be an important therapy of MGs that is different between ages.

Here we aimed to answer question, whether age differences in PDT-opening of the BBB that to optimize PDT usage for therapy of MGs.

With this aim, we studied PDT-induced BBB opening through the optical clearing skull window in healthy 4- and 8-week-old mice. PDT used in different radiant exposures (635 nm, 10–20–30–40 J/ cm^2) and with 5-aminole-vulinic acid (5-ALA, 20 mg/kg). The BBB permeability was evaluated by: (i) spectrofluorimetric assay of Evans Blue dye (EBd) leakage; (ii) confocal imaging of 70 kDa FITC-dextran extravasation and the BBB integrity; and (iii) histological analysis of brain tissues.

Our results demonstrated that dose of PDT 20 J/ cm^2 is more effective for the BBB opening with high BBB permeability for tested tracers and minimal morphological changes (perivascular edema) in the brain. The PDT-opening of BBB for high weight molecules (EBd and FITC-dextran) and solutes (vasogenic edema) was more pronounced in 4-week-old mice than in 8-week-old mice.

The more pronounced PDT-induced BBB disruption in juvenile mice compared with adult mice suggests age differences in PDT-related BBB opening. This might be an important informative platform for a new application of PDT as a method for brain drug delivery, especially for post-surgical treatment of MGs.

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Acrylated epoxidized soybean oil as a plant-based resin for three-dimensional photostructuring

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Optical manufacturing technology have emerged as one of the most precise additive fabrication ways to create free-form three-dimensional (3D) objects. There are two main types of such techniques. One of them is optical 3D printing (O3DP). It is based on linear light absorption and allows fabrication of macroscale objects out of photosensitive resins in a layer-by-layer manner. On the contrary, there exists other technique for 3D objects production employing nonlinear light absorption and is known as nonlinear laser lithography (NLL). Using ultrashort pulsed laser irradiation, conditions to fabricate microscale objects with nanometer resolution out of transparent materials can be achieved. Both methods have limits due to technical, fundamental and material selection issues. In this work, we concentrate on the material case, as most of the photosensitive resins are petroleum-derived even though alternative materials obtained from renewable resources can be used instead.

We investigated an acrylated epoxidized soybean oil (AESO). It has high amount of various functional groups such as the acrylic, epoxy and hydroxy groups, thus can be cross-linked. The aim was to assess if AESO as a plant-based renewable resin can be suitable for both technologies: O3DP, employing non-laser UV and visible light (385 nm and 405 nm wavelengths) digital light processing (DLP), and NLL using 515 nm wavelength (fundamental 1030 nm), 300 fs pulsed laser irradiation with high pulse repetition rate (200 kHz). There were used photoinitiator (PI) BAPO to absorb aforementioned irradiation and induce efficient radical photopolymerization. Two diluents (ethyllactate, Genomer 1122) were applied to dilute PI and reduce monomers viscosity. In DLP case, penetration depth h_a to the resin and critical duration T_c, required to reach critical does to fully polymerize the resin, were assessed using Beer-Lamber law. In NLL case, irradiation power P, beam scanning velocity v and distance between adjacent beam scans d_{xy} were modified. It allowed finding the fabrication window and highest spatial resolution in the AESO based resins.

It was shown, that AESO monomers can be selectively polymerized employing 385 nm and 405 nm wavelengths light. Measured h_a and T_c were: 260 µm and 0.4 s for the 385 nm light; 400 µm and 0.8 s for the 405 nm light. It was assessed, that pure AESO monomers can be photostructurized employing NLL. Evaluated fabrication parameters were: P = 0.4-1.2 mW (1.3-4 TW/cm^2), v = 2.5-10 mm/s and d_{xy} = 0.25-1 µm. Achieved spatial resolution was 1.2 µm in lateral and 2 µm in longitudinal scanning direction. Evaluated parameters showed great perspectives for applications of AESO in O3DP and NLL technologies as a resin derived from natural resources.

Strong coupling and transfer of information between distant $FePS_3$ nanodrums

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Two-dimensional nanoelectromechanical systems (NEMS) are ubiquitous systems in modern technology. With 2D-materials suspended on top of a wafer with pre-patterned cavities, one could study a mechanical motion of the membrane using laser interferometry. Despite having thickness down to an atomic level, those structures have large spatial area and strong motion transduction with optical and electrical actuation. The low mass of such resonators and exceptional mechanical properties, combined with high coupling to external actuation, have made them interesting candidates for perspective sensing applications. Among other applications, mechanical resonators hold an interesting alternative to conventional systems for data management when these operate in a strongly coupled regime.

In this work, we demonstrate that nanodrums made of $FePS_3$ can exchange energy and support motion of each other, thus exhibiting a strong coupling. This effect causes a splitting in resonance frequencies of the first vibrational modes up to $2\pi\times 9.2$ kHz, which corresponds to cooperativity of 11. The coupling strength is shown to be dependent on electrostatic stiffening of the membrane introduced by a local potential applied between the flake and the bottom electrode. The strong coupling was found to occur both in the presence of the channel connecting two drums as well as in its absence. Although the exact coupling-mediating mechanism remains to be unclear, we illustrate that these systems are capable of transfer of information bit-to-bit using amplitude modulation.

These experiments demonstrate a new, smaller system for transferring sound at the micro/nanoscale, which can become useful for sensing and communication applications. In particular, the results suggest that data networks created from 2D-material resonators are fundamentally possible and could be capable of data manipulation and transfer in strong coupling regime.

Investigations on mechanical stability of laser machined optical fibre tips for medical application

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Light delivery is a challenging task, when it comes to medical applications. The light is guided through optical fibers from the light source towards the treatment region. In case of interstitial light application, the light has to be decoupled from the fibre and spread to the surrounding tissue. To reach larger tissue volumes, this can be either obtained by adding a scattering volume to the tip of the fibre, or by directly modifying the optical fibre itself in order to break the total reflection within the fibre core. Such modifications can be either on the fibre surface itself or internally in the fibre core. One approach to obtain the fibre structuring could be laser induced surface roughening using an ultrafast laser source. While using volume scattering as diffusor at the fibre tip is currently the gold standard for non-thermal applications (< 0.3W/cm), the decoupling of high power laser intensities for thermal treatment options is still challenging. Structuring the fibre core itself usually is related with a loss of mechanical stability. As fibre breakage and potential loss within the human body can have serious consequences, the mechanical stability is one of the quality criterion in diffuser manufacturing. Therefore, investigations about the mechanical stability of laser manufactured optical fibre diffusers are needed.

In order to evaluate the mechanical stability, a 4-point as well as a 2-point breaking test were developed. Different fibre diffusers, based on volume or surface scattering, were manufactured using fs-laser ablation techniques and its breaking strengths were investigated.

It could be shown that for surface fibre modifications, the mechanical stability reduces with increasing defect depth. The stability significantly drops when the laser ablation was performed in the thermal energy range. Volume scattering modified fibres only showed a slight reduction in stability compared to un-machined fibres.

In conclusion, internal fibre modification seems to be the most promising method to establish optical fibre diffusers, which are capable of several watts of emission power, while preserving its mechanical strength.

Photodynamic opening of the blood-brain barrier through an optical clearing skull window

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The aim of research was to study noninvasive photodynamic (PD) opening of BBB in mice for high weight molecules and liposomes (100 nm) using a newly developed technique of optical clearing skull window.

In the first step, we selected optimal PD dose (10-20-30-40 J/cm^2) for BBB opening in experiments using a spectrofluorometric assay of BBB permeability to Evans Blue dye (EBd). Our results showed that 20 J/cm^2 is more favorable for BBB opening due to high EBd with less morphological changes in the brain.

In the second step, we evaluated BBB permeability to rhodamine -dextran 70 kDa and liposomes (100 nm) using confocal and two-photon laser scanning microscopy. Our results clearly demonstrate the effectiveness of PD (20 J/cm^2) for opening of the BBB through an intact and optically cleared skull in mice. Indeed, we observed distribution of tested tracers among the astrocytes and outside of the cerebrovascular endothelium and the basal membrane.

These results suggest that PD with optical skull clearing window is effective method for non-invasive opening of the BBB and brain drug delivery that might be important for development of new therapy of brain tumors.

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Functional interrelationship between opening of the blood-brain barrier and lymphatic clearance

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The peripheral lymphatics is a part of the vascular system that is opened in the extracellular space providing fluid drainage. The understanding of functions of recently re-discovered meningeal lymphatic vessels (MLVs) and the anatomical pathways of the lymphatic drainage of the brain fluids is a topic issue due to the blood-brain barrier (BBB) restriction of fluid filtration. Physiological relationship between MLVs and BBB is also remained unknown.

Recently it has been shown that MLVs play an important role in clearance of beta-amyloid. Other studies demonstrate therapeutic effect of BBB opening for patients with Alzheimer's disease. It allows us to assume about the functional interrelationship between BBB and MLVs that gives an opportunity to activate clearance of beta-amyloid via the meningeal lymphatics after BBB opening.

To test our hypothesis, in this study on healthy male mice, we analyzed the interaction between BBB opening and functional changes in MLVs localized in the pia mater. We clearly reveal an increase in size of some MLVs and an accumulation of the brain fluids in the cisterna manga after BBB opening compared with intact mice from the control group. Using two methods for mild and strong BBB opening by repeated sound (RS) and photodynamic treatment respectively, we found more pronounced changes in MLVs and in the brain fluids accumulation in the cisterna manga in the PDT-group vs. the RS-group.

We first uncover phenomenon of clearance of molecules crossing the opened BBB via MLV. So, using of confocal microscopy, we demonstrate clearance of dextran 70 kDa via MLV after its crossing the opened BBB. Using optical coherent tomography, we observed gradual accumulation of gold nanorods in the deep cervical lymph nodes during 1h after its crossing the opened BBB.

Our data suggest that BBB opening is accompanied by functional changes in MLVs, which gives completely new ideas about the physiology of the lymphatic system of the brain. These novel findings may call for a reassessment of basic assumptions on mechanisms underlying the brain recovery after events associated with BBB disruption, such as stroke, traumatic brain injuries, tumor, diabetes, neurodegenerative disorders.

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Novel design of an ATRF-TIR fiber probe for measurements of hard tissues

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Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy is a well-established fast high-throughput technique for biomedical applications such as investigation of body fluids and pathological changes in tissues, cell line classification and discrimination [1]. The guidance of an IR beam via an ATR-crystal by a series of internal total reflections is accompanied by the emission of an evanescent field through the crystal’s surface. The ATR-FTIR relies on the absorption of the evanescent field by the adjacent adsorbing sample tissue [1]. The absorbance of this evanescent field depends on the number and angle of internal reflections inside the ATR crystal as well as on the refractive index *n* of the ATR crystal [2].

Here, we introduce a novel design of the ATR fiber probe to investigate hard bio-tissues. Thin ATR probe with diameter of 3 mm includes 2 polycrystalline (PIR) fibers (700 μm) and frustum-shaped diamond (Di) ATR crystal flushed with the probe tip. Using wet chicken cartilage, liver, and muscles tissues, we compared the performance of the flat ATR probe with a standard probe with a conical silicon (Si) ATR crystal. Whereas the standard probe allows for 2 internal reflections, the flat Di-probe facilitates only one total reflection bounce. These probes are tested with respect to the intensity of the absorbance spectra depending on the loading pressure. In particular, we focus ourselves on the pronouncement of the principal protein markers Amide I, Amide II, the methyl (CH_3) group, and glycogen bands [cf. 3]. Independent from the tissue, the Di-probe causes much less mechanical damage to the tissue than the Si-probe which is thanks to the flat surface of its frustum crystal. The absorbance spectra taken with this probe show less dependence on the loading pressure making it more suitable for, for instance, measurements of cartilage tissues. Further, we observe that Amide I marker is better pronounced for the Di-probe than in the case of the Si-probe. As for the liver and muscle tissues, the Di-probe allows for a better-resolved spectroscopy of the methyl (CH3) group. However, we also observe a decrease of sensitivity to glycogen bands, especially in case of the cartilage tissue. This drawback will be overcome by the further coupling of the probe with a quantum cascade laser as a light source, which is the next step of the development. We acknowledge the funding from the following H2020 projects: ProDelSys and MIRACLE (Grant agreement IDs 792421 and 780598, respectively). Further, the project is an initiative of the Photonics Public Private Partnership.

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Evaluation of microhaemodynamics regulation types using wearable laser Doppler flowmetry devices

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Microcirculation is subject to significant structural and functional changes in the development of various pathological processes, for example, in diabetes mellitus (DM). It can be assessed using laser Doppler flowmetry (LDF). This work aimed to assess the violations in the mechanisms of regulating microcirculation that occur in DM using the novel wearable blood perfusion sensor system.

The study involved healthy volunteers and patients diagnosed with type 2 diabetes. A novel wearable distributed multipoint LDF system consisting of four “AMT-LAZMA 1” devices (Aston Medical Technologies Ltd., UK) was used to analyse microcirculatory blood flow. Volunteers rested supine with the analyzers located on the volar surface of big toes and middle fingers. Each study consisted of a 10-minute recording of the LDF signal simultaneously from 4 points and subsequent data processing.

During the study, the following parameters were calculated and analysed: average microcirculation index, nutritive and shunt blood flow, microcirculation oscillations in the endothelial, neurogenic, myogenic, respiratory and cardiac frequency ranges. The results of the study revealed that despite the similar parameters of average perfusion, patients with DM have significantly reduced levels of nutritive blood flow, indicating disorders in the work of precapillary sphincters. Oscillations in the endothelial and myogenic ranges have also been considerably reduced in patients. These differences are more pronounced in the LDF signals recorded in the toes.

Thus, the study has shown that the proposed approach allows one to identify differences in the microhaemodynamics parameters in normal conditions and diabetes. The use of a wireless wearable fibre-free LDF device is a very convenient solution for use in a point-of-care diagnostics.

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