Review Article

Biophotonics: A Novel Approach Biomedical Diagnosis

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ABSTRACT

Biophotonics is a multidisciplinary category under photonics, which involves the fusion of photonics and biomedical sciences. *Biophotonics* defined as the science of generating and harnessing light *(photons)* to image, detect and manipulate biological materials. It is applied in Medicine and Dentistry to understand, diagnosis and treatment of diseases. Biophotonics mainly involves the interaction between light with biological tissues, and is used to study biological tissues and biological processes at different scales that ranges from micro to nano-levels. Biophotonics integrates Lasers, Photonics, Nanotechnology and Biotechnology. This integrated approach provides new dimension for diagnostics and therapeutics. This rapidly growing new discipline will have a major impact on health care.

Keywords: Biophotonic, medical therapy, laser.

INTRODUCTION

Photonics is a light based optical technology that is considered as the leading technology. Most applications of photonics in health care are based on various types of light and different types of photon-tissue interactions.[1]

A biophoton *(from the Greek βιο meaning "life" and φωτο meaning "light")* is a photon of light emitted in some fashion from a biological system. From a scientific point of view, there is no difference between such a photon and a photon emitted by any other physical process. Biophotons are light waves that exist in the living cells of plants, animals, and human beings. Cells emit biophotons, which cannot be seen by the naked eye, but can be measured by special equipment. The quest for understanding the biochemical basis of human disease is the most important area in the development of modern medicine. Biochemical changes within tissue may either initiate disease or occur as a result of disease process. In physiological systems, molecular changes often precede the onset of disease. These changes, if detected and interpreted properly, could provide vital information regarding the stages of disease progression and the effect of therapy. Malignant tumor causes clinical symptoms when it is usually large enough and can be detected by various conventional methods such as X-ray, Computerized tomography, Magnetic resonance imaging, Ultrasound, and Mammography. These techniques have their own advantages and limitations. Most of the advanced stage cancers are difficult to treat effectively, and, therefore, it is important to detect cancers at an early stage.[2-3]

SCOPES OF BIOPHOTONICS

- New laser technology Imaging and image analysis.
- Non imaging sensors and systems.
- Holography and coherent optics.
- Components for optical systems and devices.
- Designer metamaterials and applications.
- Integrated optics.
- Fiber optics.
- Optical engineering
- Optical computing and logic.
- Non destructive testing.
- Laser cutting, welding, heat treatment, etc.
- Interferometry.
- Display technologies.
- Analysis and applications of optically derived data.
- Particle characterization and manipulation.
- Biomimetic optics.
- Bio inspired systems and components.

APPLICATION OF BIOPHOTONICS IN MEDICAL SCIENCE

Biophotonics has a pervasive effect on medical methods for diagnosis and therapy. Biophotonics can be applied to the field of life science, microbiology (viral and bacterial analysis), pharmaceutical and drug analysis, medicine and clinical diagnosis. The distinctive characteristics of photons offer a non-contact, effective, fast and painless way for sensing, monitoring and treatment of various diseases. The six most significant characteristics of photons are

- Ultra-sensitive detection (by which a single molecule can be detected)
- Ultra-high selectivity (related to the features of spectroscopy)

- Advanced visual degree (which visualizes nano-sized objects)
- Noninvasiveness (no damage to biomedical tissues)
- Ultra-high special resolution
- Non-coherency and safety.

Biophotonics in Medical Diagnosis

- Laser optical, photonic and biophotonic principles revolutionize diagnostic investigational and clinical medicine. Light-based technologies are often contact-free, have little impact on the integrity of living matter and can therefore easily be applied in situ. Many old examples of the introduction of optical sensors in medicine exist, for example in recirculation of indicator substances and flow measurements in vivo and a multitude of in-vitro applications for analytical purposes.
- Advanced optical technologies in medicine now help to detect and monitor cellular biochemistry and function, tissue characteristics and integrity of organs. They do so by the application of lasers (including femtosecond lasers), photonic and biophotonic metrology and imaging in diagnostic and analytical medicine.
- Tissue, cells, proteins and DNA are labeled with optical tags and their fluorescence or incandescence is measured and modifications interpreted according to the physiological or pathological (functional) situation.
- Fluorescence spectroscopy, light absorption and scattering analysis, angle-resolved low coherence interferometer and spontaneous biophotonic activity also offer opportunities for non-invasive tissue or blood/body fluid analysis.
- Sophisticated laser technology has allowed the visualisation of vasculature and other structures of the retina and the optic nerve head to diagnose ocular diseases precisely. Visualization of changes in ocular capillaries also allows the diagnosis of general vascular disorders. Examples for such diagnostic tools are laser scanning systems, laser polarimetry, optical coherence tomography, all of which allow to obtain precise information about the retinal vessels, the retina, the retinal pigment epithelium and the choroid.
- Furthermore metabolic products like lipofuscin can be used to judge disease processes in the retina and help to determine the dignity of tumors of the choroid. Further improvement of the resolution of imaging techniques allow progress into the cellular or molecular level.
- The combination of optical with endoscopical methods allows the evaluation of dysfunction of swallowing and phonation. The simulation and analysis of deglutition and phonation is performed as a basis to optimize reconstructive surgery in tumor patients.

Biophotonics in Medical Therapy

- In the field of therapy, sensor controlled laser systems have the potential to optimize the outcome of surgery and to minimize complications especially when bone has to be cut.
- Osteotomies performed with laser systems promise improved results. The effect of lasers is based on photoablation.
- However, when using a laser system it is hard to control the depth of the cut. Therefore it is desirable to develop closed-loop control systems that allow performing safe laser osteotomy without damaging internal and surrounding tissues.
- The aim of the control mechanism is to detect different tissue structures during the application of laser energy. Emissions caused by the interaction of laser light and tissue surfaces are registered to stop laser tissue ablation as soon as the characteristics change, i.e. when the bone has been cut through, so as not to destroy the surrounding soft tissues. The interaction of laser and tissue cause's optical and acoustic emissions such as burn- or pyrolysis lights, thermal radiation, air- and structure-borne sounds. Photodiodes, pyrometers, microphones and piezoelectric accelerometers are suitable for detecting such emissions.
- Sensor controlled laser systems are a focus in the field of therapy. They have been already applied in experimental trials with living tissues as well as in humans. Another focus is the destruction of tumor tissue and intraluminal calculi by medical lasers. Tumors are nowadays destroyed by photodynamic therapy and by vaporization using various laser sources.
- The development of sensors for malignant tissue in combination with laser sources for specific, efficient and safe tissue destruction is investigated. New materials, laser sources and application devices need to be developed for more cost-efficient use and wider distribution in medical therapy.
- Calculi, in various clinical settings, are efficiently fragmented also using tissue-stone discriminating technology. Pancreatic stones are particularly difficult to sense and to destroy, and their spectroscopic and mechanical characteristics need to be reinvestigated.
- Refractive corneal surgery uses advanced wave-front analysis techniques to provide algorithms, which are used for treatment of refractive errors with excimer and femtosecond lasers. The further development of laser techniques will enable the reliable treatment of myopia as well as hyperopic and astigmatism.
- One of the great dream s of mankind is artificial vision, which through opto-mechanical stimulation allows the provision of sight for ocular blindness. The

implantation of chips in the sub retinal or epiretinal space could allow for supplementation of the visual pathway with useful information in diseases which normally would cause blindness. In the future, direct stimulation of the visual cortex with electrical signals from video systems might even bypass the eye and allow for a new era of artificial vision.

APPLICATIONS OF BIOPHOTON LASER PROCESSING OF TISSUE

The use of the different laser tissue interaction mechanisms for cutting, coagulating or removal of tissue is being used for surgical procedures in most of the clinical specialties - ophthalmology, gynecology, urology, dentistry, and surgery of ear, nose and throat, to name a few. This is motivated by the fact that the exquisite control on laser parameters allows ultra-precise surgical procedures without any adverse effect on surrounding normal tissue.

Further, due to the fact that tissue cutting and removal occurs at high temperatures in laser surgery, small blood vessels and nerve-endings cut during surgery get coagulated resulting in reduced blood loss and the sensation of pain. Another important advantage with lasers is that their radiation can be transported via thin, flexible optical fibers to internal organs endoscopically, through natural body orifices or minor incisions. Thus, major incisions required in conventional surgery, can be avoided using laser endoscopic surgery and some of the potentially major operations are even reduced to an outpatient treatment. This considerably reduces patient trauma and hospitalization time.

In the given table some lasers used for medical applications and their important characteristics have been enlisted.

Medical imaging

Photonic semiconductor imagers are now starting to beam introduced, though these devices are primarily based on photographic film technology. Use of photonic semiconductor imagers can be expected to grow. Laser Scanning Confocal Microscopy (LSCM - also referred to as CSLM), is now established as a valuable tool for obtaining high-resolution images and 3-D reconstructions of a variety of biological specimens. LSCM uses a laser to irradiate a biological sample dyed with a fluorescent chemical. An optical system using lenses, a pinhole device and a photo-detector can then be used to obtain 3-D images of the structure of the biological sample. Standard LSCM systems are limited to small samples. Because of this, non-X-ray light-based imaging techniques using optical or infrared frequencies and laser light sources are being developed to image larger structures such as organs. These techniques are based on the concept of photon scattering in human tissue, which is an area of intense investigation. As these techniques improve they can be expected produce photonics based diagnostic devices.

Use of Biophotonics in Endoscopes

The optical fiber is also used in medical applications to allow for minimally intrusive viewing and surgery of internal structures. An endoscope consists of a lens and a light source at the end of an optical fiber. The fiber is passed into the body and a view of the internal structure of the body is obtained. This allows a diagnosis to be made without intrusive surgery. An optical fiber can also be used to deliver high intensity laser light to an internal region in the body, for example, to remove tumors.

Photodynamic therapy (PDT)

One of the most useful applications of biophotonics in medicine is photodynamic therapy, or PDT. PDT involves three parts: a photosensitizer (a chemical compound that can be excited by a light of a particular wavelength), light, and tissue oxygen. The treatment is used for cancer, but can also be used on acne and psoriasis. In order for PDT to work, a photosensitizer must be administered to the patient. The surgeon will then shine a light of a particular wavelength (whichever energy level acts on the photosensitizer being utilized). There are a number of diseases which can be cured by PDT are described below.

A. Non-Malignant Diseases

1. Ophthalmic Disease
2. Cardiovascular Disease
3. Dermatological Disease
4. Urological Disease

B. Malignant Diseases

1. Brain Tumor
2. Head and Neck Cancer
3. Ophthalmic Tumor
4. Pulmonary and Pleural Mesothelial Cancer
5. Breast Cancer
6. Gastroenterological Cancer
7. Urological Cancer
8. Gynecological Cancer
9. Skin Premalignant and Malignant Diseases

C. Biophotonics in Dentistry

D. Miscellaneous

Key areas

- **Laser microsurgery**

Some years ago we developed cell ablation system for use with embryos, in particular *C. elegans*. Derivatives of this system are now widely used in many laboratories to study inductive cell-cell interactions in developing embryos. It was found that the optimum strategy for a cell ablation system that has high precision yet produces a minimum amount of collateral damage was to use a pulsed source of around 1ns duration and a wavelength around 440nm. A nitrogen laser pumping a dye laser is currently the most favored irradiation source.[4]

- **Optical Trapping**

Small particles (0.5m - 10m) may be trapped by radiation pressure in the focal volume of a high-intensity, focused beam of light. This technique may be used to move small cells or sub-cellular organelles around at will by the use of a guided, focussed beam. Ingenious systems, using optical trapping in conjunction with interferometry to measure small displacements, have been used to measure the force exerted by individual motor proteins Optical trapping offers a variety of experimental possibilities. For example, a bead coated with an immobilized caged bioactive probe could be inserted into a tissue or even a cell and moved around to a strategic location by an optical trapping system. The cage could then be photolyzed by multiphoton uncaging. This would provide a non-diffusable localization of the bioactive probe at a time and place determined by the experimenter. The optimal wavelengths for optical trapping are in the 800nm -1100nm range. Typically powers of around 100mw are used.[5]

- **Bioelectromagnetic Healing – Biophotons & DNA**

DNA and living organisms emit biophotons, which radiation is coherent and blackbody, i.e. not thermal. DNA's biophotonic emissions provide a holographic biofield for the generation of physical structures. A seed, for instance, changes itself from a particle state into the tree's biofield for the purpose of self-reproduction. From the systems point of view a seed or genotype constitutes the phenotype tree system's input and output

The phenomenon of ultraweak photon emission from living systems was further investigated in order to elucidate the physical properties of this radiation and its possible source. We obtained evidence that the light has a high degree of coherence because of

(1) Its photon count statistics

(2) Its spectral distribution

(3) Its decay behavior after exposure to light illumination

(4) Its transparency through optically thick materials.

- **Photoactivation of caged compounds**

Several fluorophores (fluorescein, rhodamine green) and bioactive agents (calcium, ATP, neurotransmitters, calmodulin inhibitors) can be rendered inert by the addition of a molecular cage. The cage is designed such that it can be photolyzed by short-wavelength irradiation thereby releasing the fluorophore or bioactive agent. Irradiation by a focused, transient beam of light allows the bioactive agent (e.g. a signaling molecule) to be released within a cell with high spatial and temporal precision. This technique is becoming a very powerful experimental tool for the cell and neuro biologist, particularly as more caged molecules are becoming available. Most currently favored caging techniques require irradiation at around 320nm for photolysis of the cage. There is considerable interest in the possibilities for multiphoton uncaging. As in the case of multiphoton excitation fluorescence imaging, multiphoton events only occur in significant abundance within the focal volume of an objective which is directing light derived from a high-peak power laser source into the sample. This gives the technique exquisite spatial localization as photolysis (and hence the release of a bioactive agent) will only occur in the focal volume of the objective.[6-7]

- **Fluorescent recovery after photo bleaching**

This technique has been used to measure intracellular movements such as the diffusion of proteins in membranes and the movements of microtubules during mitosis. Fluorescently-labeled target structures are illuminated by a high-intensity patterned source for a short time in order to produce a bleached pattern. The structures are then imaged using low levels of irradiation to visualize the dynamic changes in the bleached pattern. From these data diffusion rates or movement velocities can be calculated**.**[8-9]

CONCLUSION

biophotonics" is the science, research and application of photons in their interactions within and on biological systems. Topics of research pertain more generally to basic questions of biophysics and related subjects (for example, the regulation of biological functions, cell growth and differentiation, connections to so-called delayed luminescence, and spectral emissions in super molecular processes in living tissues, etc.) The term *biophoton* is used more specifically to denote those photons that are detected by biological probes as part of the general weak electromagnetic radiation of living biological cells. The promise of increased sensitivity and speed and reduced cost and labor makes Biophotonics an appealing alternative to current diagnostic techniques for clinical. The potential diagnostic uses of Biophotonics are numerous, with the most promising applications being in the areas of Tumor detection, Tissue imaging, Intracellular imaging, Immunohistochemistry, Infectious agent detection, Multiplexed diagnostics, and Fluoroimmunoassays. Biophotonics also have considerable potential for in vivo imaging, but there are concerns over their toxicity, both to patients and the environment. In time biophotonics may become very cost-effective, as is currently the case with some magnetic nanoparticles. This should allow better clinical diagnostic services, particularly in economically deprived regions. These technologies can also be applied to point-of-care testing and lab-on-a-chip technologies. Whether biophotonics will replace current diagnostic methods remains to be seen. Many aspects of these biophotonic techniques need to be evaluated further, especially the safety issues.[10, 11]

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