Review Article

Biophotonics: A Magical ray of hope in Periodontics

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Abstract: Term biophotonics denotes a combination of biology and photonics. It is a general term for all techniques that deals with the interaction between biological items and photons. It offers a great hope for early detection of diseases and for new modalities of light guided and light activated therapies. In this article the use of biophotonics has been focused for the diagnosis and therapy in the periodontics.

Keywords: Biophotonics; Laser; Light Amplification; Nanotechnology; Periodontitis; Photodynamic therapy.

INTRODUCTION

We live in era of technological revolutions that continue to impact our lives and constantly redefine the breath of our social interaction.[1] Photonics is a light based optical technology that is considered as the leading technology for the new millennium.[2] Photonics utilizes photons instead of electrons to transmit, process and store information and thus provides a tremendous gain in capacity and speed in information technology.[1]

What is Biophotonics?

A new extension of photonics is 'BIOPHOTONICS'.[1,2] Term BIOPHOTONIC is made of two greek words "bios" means life and "phos" means light. It is a multidisciplinary category and involves the fusion of photonics and biomedical sciences.[1,2] 'BIOPHOTONICS' can be defined as - the science of generating, to detect and manipulate biological materials.[2] Nature has used biophotonics as a basic principle of life from the beginning.[3] Biophotonics in dentistry is crucial for early detection of diseases, to carry out more effective minimally- invasive targeted therapies & to restore diseased tissues functionally & esthetically.[2] Biophotonics integrates 4 major technologies: Lasers, Photonics, Nanotechnology & Biotechnology.[1]

No one ever imagined that the magic beam shown in the star wars movies could someday treat our gums. In 1960, maiman introduced "Light Amplification by Stimulated Emission of Radiation" (LASER) using theories about the stimulated emission.[4] Lasers are devices that produce highly directional, monochromatic and intense beam of light. They are most commonly used light source for biophotonics. The usage of Lasers falls into 2 following categories- 1.) Utilizes laser as convenient and highly concentrated source of photons, 2.) Utilizes the highly coherent nature of the light beam.[1] An important area of biophotonics is use of light for therapy and treatment. Area of light activated therapy specially the use of light to activate a photosensitizers that eventually leads to the destruction of cancer or diseased cells. This procedure is called Photodynamic Therapy (PDT).[5] In 1904 Von Tappeiner termed a photodynamic reaction due to the phenomenon ability to excite oxygen molecules like singlet oxygen.[6]

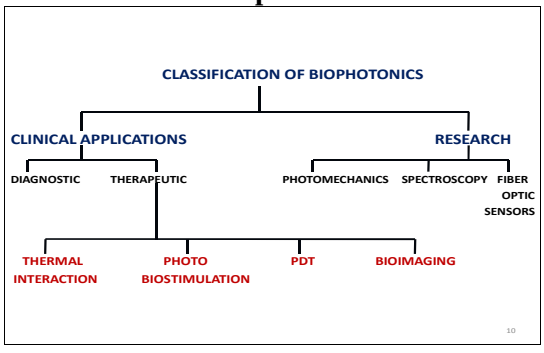
Photodynamic therapy is the light induced non thermal inactivation of cell, microorganisms or molecules.[7] A photodynamic therapy uses a laser in combination with a dye, thus utilizing the power of light and its resulting properties.[8] The association of low power laser with photosensitizers the so- called "antimicrobial photodynamic therapy", (aPDT) can also be used for reducing bacterial contamination of periodontal pocket.[7] Photonics which utilizes light- matter interaction for information processing, transmission, data storage & display, is being hailed as the dominant technology for the 21st century. Biomaterials are emerging as an important class of materials for a variety of photonics applications. The 4 types of biomaterials that hold promise for photonics applications are- Bio derived materials (naturally occurring biosystem or its chemical), Bioinspired materials (light harvesting dendrimers), Biotemplates (photonics active structure ona biological templates), Bacteria bioreactors

(use of bacteria as biosynthesizers to produce photonic polymers).[1]

K. Eric Drexler developed and popularized the concept of nanotechnology and founded the field of "Molecular Nanotechnology ".A basic definition of nanotechnology is "the engineering of functional systems at the molecular state." It is the development and use of techniques to study physical phenomena and construct structures in the physical size range of 1-100 nm, as well as the incorporation of these structures into application.[1] Biotechnology is the use of living systems and organisms to develop or make useful products. It can be defined as- "Any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use."[1] As Biophotonics is a recent treatment modality in the medical and dental field. This paper presents the use of biophotonics in the treatment of Dental problems.

Significance of Biophotonics: It is applied in medicine and dentistry to understand, diagnosis and treatment of diseases. It is used to study biological tissues and biological processes at different scales that ranges from micro to nano levels.[2] As an increasingly aging world population presents unique health problems. Biophotonics offers great hope for the early detection of diseases and for new modalities of light guided and light activated therapies.[1] In dentistry, the soft lasers have been used for acceleration of wound healing, enhanced remodeling and repair of bone, restoration of normal neural function following injury, normalization of abnormal hormonal function and modulation of immune system.[2]

Classification of Biophotonics:



1. Clinical Applications

a.) *Diagnostic*

- The most important benefit of light based diagnostic methods is their capability to detect clinically relevant information much early before actual clinical signs and symptoms appear in patients.[2]
- An emerging area of biophotonics is invivo imaging and spectroscopy for optical diagnosis.[1]

b.) *Therapeutic*

I. Thermal Interaction:

- In this process heat generated by the high energy laser light is used to disrupt tissues.[2]
- The main effect of laser energy is 'Photothermal'. The final response of the target tissues depends on the degree of temperature increase and the tissue water content.[4]

II. Laser tissue welding is a developing biotechnology that looks promising for application in practically all surgeries. Laser tissues welding utilizes the energy from the laser beam to join or bond tissues instead of using sutures.[1, 2]

III. Photobiostimulation:

- Activation of life processes under laser radiation, often called "biostimulation". Radiation by low intensity laser (LIL) and light emitting diode (LED) is widely used by physical therapist, dentists, surgeons, dermatologists etc.
- The low powered laser producers does not produce heat and therefore does not damage biological tissues, and promotes healing by penetrating deep into the tissues initializing the process of photochemical effect.[2]

IV. **Photodynamic Therapy:** The effectiveness of a light source for photodynamic treatment depends on spectral irradiance, tissue transmission & photosensitizer absorption.[6] PDT is defined as a photochemical reaction used to selectively destroy tissue. It is a two-stage therapeutic technique in which the use of a topical or systemic sensitizing drug is followed by visible light radiation. The photosensitizers, administered exogenously or formed endogenously, are activated by the light and transfer energy to molecular oxygen, thereby generating

reactive oxygen species to induce cell death.[9]

V. **Bioimaging:** It is a method that non-invasively visualizes biological processes in real time. It aims to interfere as little as possible with life processes. In cell body, bioimaging can be used to follow cellular processes quantify ion or metabolite levels. Recent development includes two photons fluorescence excitation microscopy, fluorescence resonance energy transfer (FRET).[10] Reconstruction of images in both two and three dimensions has allowed better visualization of models and disease processes.[2]

2. Research

a. ***Photomechanics:*** In dentistry it is used to examine relationship between macroscopic mechanical stress and strain gradients within root dentin structure.[11] In this polymer solutions and solids that contain light sensitive molecules can undergo photo-contraction, whereby light energy is converted into mechanical energy.[11] Photo-mechanical experiments are optics based used to study the material property gradients in biological materials.[2]

b. ***Spectroscopy:*** A spectrum is a representation of the electromagnetic radiation which is absorbed or emitted by a sample.[2] Spectroscopy is the study of the interaction between matter and radiated energy. There are different types of spectroscopy. They are- Absorption, Fluorescence, UV/VIS, Mass, Infrared and nuclear magnetic resonance spectroscopy. Raman spectroscopy is based on Raman scattering.[2] In Raman scattering the difference in energy generates a vibrational excitation in the molecule.[1]

c. ***Fibre optic sensors:*** Optical fibers can be used for remote sensing of chemical and physical parameters. Light is focussed into the core and guided to a sample to produce analytical information. The optical signals return through the same fibers and its intensity is measured. It is widely accepted in sensing clinically and biochemically important analytes such as serum electrolytes, a metabolites, enzymes and immunoproteins. Sensors responding to these parameters are frequently called 'biosensors'.[13]

Fundamental Basis of Biophotonics[1]

- The total energy can be divided into 4 parts: electrical, vibrational, rotational and translational. Only electronic and vibrational energy levels are of significance to biophotonics, because they are an integral part of spectroscopy, bioimaging, biosensing, flow cytometry, photodynamic therapy and biomaterials for photonics.
- Properties of light and matter form the very fundamental basis to create an insight and biological systems.
- Light as waves exhibit properties such as interference and diffraction and light as a photons carries energy.
- The biological application of spectroscopy and fluorescence microscopy utilize the photons while the interference feature of the wave is used in a number of biophotonics applications such as phase contrast microscopy and optical coherence tomography as well as in biosensing.

In this article, we would discuss the two major applications of light in biophotonics, i.e.-

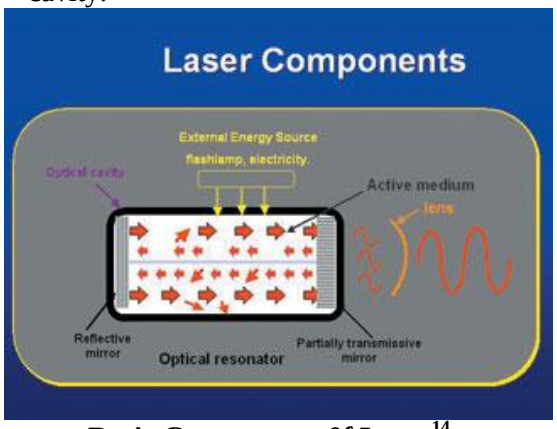
Lasers: Lasers are devices that produce highly directional, monochromatic and intense beam of light.[1] Lasers, an acronym for 'Light Amplification by Stimulated Emission of Radiation' was first developed by Maiman (1960).[5]

Basic Structure:[14]

- An optical cavity is at centre of the device. The core of the cavity is comprised of chemical elements, molecules or compounds and is called the Active medium.
- Lasers are generally named for the material of Active medium. There are two gaseous active medium lasers used in dentistry are- Argon and CO_2.
- There are two mirrors, one at each end of the optical cavity, placed parallel to each other. Surrounding this core is an excitation source, either a flash lamp device or an electrical coil, which provides the energy into the active medium. There is some heat generated in the process, and the optical cavity must be cooled. A cooling system, focusing lenses and other

controls complete the mechanical components.

- The parallelism of mirrors ensures that the light is collimated. One of the mirror is selectively transmissive, allowing light of sufficient energy to exit the optical cavity.



Basic Components 0f Laser[14]

Risk and Precautions in Clinical use of Laser[15]

There are some risks for the operator, patient and the assistant during the use of laser for which following precautions should be taken-

1. Caution before and during irradiation
   - Use of glasses for eye protection (patient, operator and assistants)
   - Precautions for inadvertent irradiation and reflection from shiny metal surfaces.
   - Protection of patients throat and oral tissues outside the target site.
   - Accurate foot pedal control.
   - Adequate high speed evacuation to capture the laser plume.
2. Risk of thermal injury during interaction with the tissues
   - Understanding of the penetration depth of each laser.
   - Thermal injury to the root surface, gingival tissue, pulp and bone tissues.
   - Effective use of water spray to minimize heat generation.
3. Risk of excessive tissue destruction by direct ablation and thermal side effects
   - Excessive ablation of root surfaces and gingival tissues during pocket irradiation.
   - Destruction of the attachment apparatus at the bottom of pockets during pocket irradiation.
   - Damage of the tooth enamel by inadvertent irradiation.

Uses of Laser in Periodontics:[14]

There are many uses of laser in the medical and dental field. Here few uses of Laser in Periodontics are explained:

1. Mobility Assessment: Laser Doppler Vibrometry is used to assess even small amount of tooth mobility.

2. In Prevention of plaque: Laser toothbrush is designed to provide an antibacterial effect in oral cavity. It does not need toothpaste but directly radiates laser on teeth. It is shown that that the ability of the Er: YAG laser to remove lipopolysaccharides, smear layer & calculus from the root surface.

3. In Hypersensitivity: Low level laser therapy (LLLT) has anti-inflammatory, analgesic and cellular effects in both hyperemia and inflammation of dental pulp. The effects of laser therapy on hypersensitive teeth are: 1.) Primary or immediate effect: remission of painful symptoms; 2.) Secondary or late effect: intense cellular metabolic activity; proliferation of odontoblasts; and production of dentine. LLLT causes sealing of dentinal tubules by the coagulation of hydroxyapatite crystals as well as formation of reparative dentine.

4. In Non- Surgical Pocket therapy: It is a used to eliminate or to reduce the number of viable bacteria in the gingival sulcus.

Photodynamic Therapy (PDT)

History: The use of light as a therapy in human diseases has a very long history. The term 'Photodynamic Therapy' was coined by Von Tappeiner in 1904 to describe to describe the phenomenon of oxygen-dependent photosensitization.[16] Daughtery et al in 1978 sucessfully applied this novel technique for the treatment of different cancers.[16] Wilson first proposed the use of lethal photosensitization as a tool for the treatment of periodontal diseases.[9]

Mechanism of Action

PDT involves three components: Photosensitizers, light and oxygen.[16] It is

based on the dye- sensitized photooxidation of biological matter in the target tissue. This requires the presence of a dye (sensitizer) in the tissue to be treated.[9]

By irradiation with light in the visible range of the spectrum the dye (photosensitizer) is excited to its triplet state, the energy of which is transferred to molecular oxygen. The product formed is the highly reactive singlet oxygen capable of reacting with biological systems and destroying them. Only the first excited state with energy of 94 KJ/mol (22Kcal/mol) above the ground state is important, the second excited state does not react.[17]

Photochemical reactions[6]

All photochemical reactions first start with the generation of high energy triplet state photosensitizers (PS). Photoexcitation chemistry can potentially go one of three pathways and are classified as – Type I, Type II, & Type III reactions.

TYPE I: Photooxidation by radicals: Photooxidation of a substrate generates radicals and then reactive oxygen species (ROS) like hydrogen peroxide & superoxide anions.

TYPE II: Photooxidation by singlet oxygen: It involves the transfer of energy of the triplet state PS to ground triplet state oxygen ($^3O_2$) generating singlet oxygen ($^1O_2$).

TYPE III: Photoreaction not involving oxygen: These require either high concentration of the PS or a de-aerated system, in order to bypass the reaction with oxygen.

Applications of Photodynamic Therapy in Periodontics:

It is an emerging field for the treatment of periodontitis. Applications of photodynamic therapy in Periodontics are:

1. IN PERIODONTITIS
   - An effective approach of periodontal therapy is to change the local environment to suppress the growth of periodontal pathogens.
   - There are 2 basic mechanisms that have been proposed to account for the lethal damage caused to bacteria by PDT
     - DNA damage
     - Damage to cytoplasmic membrane, allowing leakage of cellular contents or inactivation of membrane transport systems & enzymes.[16]

2. IN PERIODONTAL BONE LOSS AND FURCATIONS
   - The use of PDT in furcation involvement in periodontitis shows advantages over the use of conventional antimicrobials; such as reduced need for flap procedures and shorter treatment time.[17]

3. IN IMPLANTOLOGY
   - PDT can be used in implantology to promote osseointegration and to prevent peri-implantitis.
   - Use of this can preserve tissue, with almost no adverse effects at the light microscopic level. Intraoperativly used PDT with the CO_2 laser seems to be more of value than the conventional method.[7]

4. IN WOUND HEALING
   - PDT has a bio-stimulatory effect on human osteoblast like cells during the first 72 hours after irradiation. It can promote an increase in collagen fibre deposition, as well as in the amount of well organized bone trabeculae after 30 days of induced bone defect healing, by affecting calcium transport during new bone formation.[7]
   - Hence, it may be beneficial in enhancing periodontal healing after gingivectomy, scaling, root planning, and intrabony defect surgery.[7]

BIO-NANOPHOTONICS

- Bionanophotonics is the science dealing with the interface between biomedical science and technology and nanophotonics.[1]
- Nanotechnology exploits specific phenomena and direct manipulation of materials on the nanoscale.[25]
- 'Nano' is derived from the Greek word "dwarf". Nanotechnology is the science of manipulating matter

measured in the nanometer, roughly the size of 2 or 3 atoms. [18]

- It can be defined as – " the science and technology of diagnosing, treating and preventing disease and traumatic injury of relieving pain, and of preserving and improving human health, through the use of nanoscale structured materials, biotechnology and genetic engineering and eventually complex molecular machine systems and nanorobots."
- Nanomaterials are those materials with components less than 100 nm in atleast one dimension, including clusters of atom, grains less than 100 nm diameter, films less than 100 nm in thickness & nanoholes.[3]

TYPES OF NANOTECHNOLOGY:[19]

Broadly, nano technologies consists of three mutually overlapping and progressively more powerful molecular technologies:

a. Nanoscale: Structured materials and devices that can be fabricated for advanced diagnostics and biosensors, targeted drug delivery and smart drugs.
b. Molecular Medicine: via– genomics, proteomics, artificial biobotics (microbial robots)
c. Molecular Machine Systems and Medical Nanorobots: Allow instant pathogen diagnosis and extermination and efficient augmentation and improvement of natural physiological function.

Nanotechnology in Periodontics

Functions may be controlled by an onboard nanocomputer executing programmed instructions in response to local sensor stimuli. Alternatively, the dentists may issue strategic instructions by transmitting his orders directly to invivo nanorobots via acoustic signals (eg. ultrasound) or by other means.[18]

Applications:

Uses of nanotechnology in Periodontics are:

1. Perioprotect: It is a comprehensive method that is customized for individual patients to help manage biofilms, growing in the spaces or pockets between teeth and gums tissues. The overall goal is to manage oral biofilm with minimally invasive dentistry for lasting oral health.[18]

2. Local Anesthesia: A colloidal suspension containing millions of active analgesics, micron- size dental robots which will be instilled on the patients gingival, resulting in anesthesia.[19]

3. Photosensitizers and carriers: "Quantum dot" nanocrystals are tiny particles measuring only a few nanometers across, about the same size as a protein molecules or a short sequence of DNA. Quantum dots can be used as photosensitizers and carriers.[19]

4. Nanorobotics Dentifrice (Dentifrobots): Subocclusal dwelling nano-robotics dentifrice delivered by mouthwash or toothpaste could patrol all supragingival & subgingival surfaces atleast once a day, metabolizing trapped organic matter into harmless, and odorless vapours and performing continuous calculus debridement.[19]

CURRENT TRENDS IN PERIODONTICS:[20]

New researches for Biophotonics in the department of Periodontics is going on day to day. Here are few current researches in the field of Periodontics are:

A. DIAGNOSIS

1. Advances in traditional diagnostics
   a.) Controlled- force, electronic probes.
   b.) Computer- assisted, digitalized substraction radiography.
   c.) Mobility measuring devices
2. Detection of periodontopathic organisms
   a.) Bacteriologic DNA analysis
   b.) Immunologic- based tests for putative pathogens.
   c.) Microbiologic enzymes assay
   d.) PCR
3. Indicators of local physical/ metabolic changes
   a.) Subgingival temperature
   b.) Nuclear medicine techniques (bone scanning)

B. THERAPEUTIC

1. Waterlace[18]

Combination of laser energy and water by a process called Hydrophotonics.

Uses:

- Full/ Partial/ Split thickness flap

- Laser soft tissue curettage
- Laser removal of diseased, inflamed & necrosed soft tissue within periodontal pocket.
- Removal of granulation tissue from bony defects.

2. RNA interference (RNAI)[18]

- A conserved biological response to double stranded RNA known as RNAI or post transcriptional gene silencing.
- Helps in periodontal regeneration – through the silencing of gene that negatively controlled cell proliferation and cell differentiation or genes that induce inflammation and/ apoptosis, & favour tissue regeneration.

2. Laser Periodontal Therapy (LPT)[21]

Vaccines using cross reactive immunodominant epitopes as antigenic molecules in an attempt to stimulate antigen-specific regulatory T- cells, secreting IL- 10 & TGF-β, may provide new clues for periodontal disease prevention.

FUTURE TRENDS

Researches are still going in the respective field which can be used in the treatment of Periodontics in future.

1. Second harmonic generation (SHG) microscopy[22]
   a. Probing collagen organization
2. Nanorobots[18]
3. Computer controlled robotic devices constructed of nanometer scale components to molecular precision, usually microscopic in size.
4. Dentifrobots can identify and destroy pathogenic bacteria residing in plaque.
5. DETEC Tar[23]
   a. Detection of plaque and calculus subgingivally and in deep pockets.
6. Nanocoated implant surfaces [24]
   a. New coatings are being developed at a nanolevel which will greatly improve the wear characteristics, fixation and biocompatibility of implants.
7. Bone replacement materials [24]
   a. Hydroxyapatite nanoparticles used as bone replacement materials, sized & shaoed like native bone crystals with strength of stainless steel.

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