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STUDYING THE EFFECT OF SHORT PULSED LASER ON SOFT TISSUES

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المعهد القومي لعلوم الليزر
قسم علوم الليزر و تفاعــلاته

دراسة تأثير نبضات الليزر القصيرة على الأنسجة الرخوة

رسالة علمية للحصول على درجة الماجستير فى علوم الليزر

مقدمة من

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ABSTRACT

Cancer diagnosis and classification is extremely complicated and for the most part, it depends on the interpretation of biopsy materials. The early detection of cancer is of prime importance with respect to treatment and patient survival. Biopsy techniques that are currently employed for such diagnosis are invasive and time consuming. Such techniques are laborious and in some cases might results in different results depending on the histopathologist doing the examination.

Diagnosis of cancer can be done by number of procedures. These can involve: Ultrasonic, Computerized tomography (CT) scans, Magnetic resonance imaging (MRI) scans, Histopathology and Biopsy. Automated, real time diagnostic procedures would greatly facilitate cancer diagnosis and classification.

In this study Laser-induced breakdown spectroscopy (LIBS) is used for the first time to our knowledge to distinguish normal and malignant tumor cells from histological sections. Nd: YAG laser light pulses (5ns pulse duration at 1064nm wavelength and 50 mJ/pulse) have been used to generate laser-induced plasma onto samples surface under atmospheric pressure. The used echelle spectrometer permit real simultaneous multi-elemental analysis in the spectral rang of 190 - 1084 nm. This enables the user to detect qualitatively the presence of elements in normal and malignant tumor of breast cells within few minutes with good reliability and reproducibility. Quantitative measurements are also possible after having the relevant calibration curves which lead us to building a “voting” algorithm for Malignant/Normal decision making.

We found that the concentration of trace elements (Zn, Ca, Fe, and Mn) in normal and tumor cells was significantly different. For confirmation, the tissue samples were also analyzed by atomic absorption spectroscopy (AAS) system. The results from the LIBS measurements and AAS analysis were in a good agreement.

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Laser has many applications in different fields such as science, industry and medicine. In the medical field, the interactions of laser with tissues are complex phenomena influenced by both laser parameters and tissue properties. Laser can induce many effects on biological cells and tissues, such as: biostimulation, photochemical, photothermal, photo-ablation and photoelectromechanical, depending on the laser fluence and the time of exposure.

1.1 Laser Technology

A laser source is basically constituted of an active medium, where the laser radiation is generated (by energy decay of an excited species) and amplified by a process called light amplification by stimulated emission of radiation (giving origin to the acronym LASER), and an excitation source for this active medium. The active medium is placed between two dielectric coatings (mirrors), constituting the so-called laser cavity, where one of them is highly reflecting at the laser radiation wavelength (rear mirror) and the other one is partially reflecting (output mirror) so that the laser beam can be extracted. As a result, the generated radiation passes through the active medium several times, re-exciting it and, if the energy losses in this process are lower than the gain, the final emitted radiation is amplified (Figure 1.1).

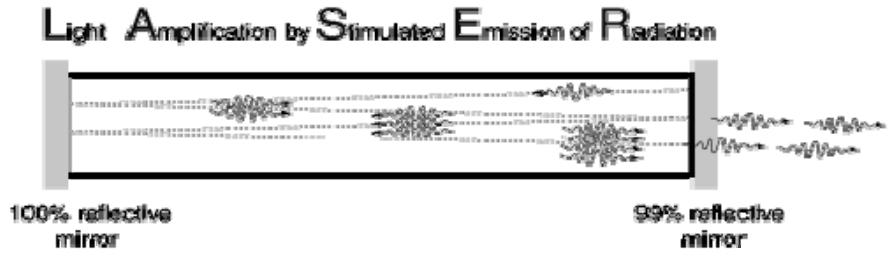

Fig. 1.1 Generation of LASER

The active medium can be a gas, such as CO_2, N_2, a combination of He/Ne, or excimers (a halogen bonded to a noble gas); a liquid, such as an organic dye solution, giving origin to dye lasers; or even a solid, such as ruby (a

Cr^{3+}-doped aluminum oxide crystal), Ti:saphire (a Ti^{3+}-doped aluminum oxide crystal), Nd:YAG (a Nd^{3+}-doped yttrium-aluminum garnet crystal), giving origin to solid state lasers. The active medium can be excited, for instance, by an electrical discharge, common for gas lasers, or the incidence of photons, more used in solid state lasers. The excitation by photons is made using flash lamps and, another laser, such as a diode laser.

Laser is characterized by some special unique properties that distinguish it from ordinary light. These properties are: 1) Monochromaticity which means that laser light consists of only one color or wavelength; 2) Directionality that is laser light travels in one direction within a narrow cone of divergence; 3) Coherence which means that the wavelengths of the laser light are in phase in space and time; 4) Focusing which means that the whole energy of the laser beam can be focused in very small area. (**Waynant., 2002**).

1.2 Interaction of laser with Tissue

It is important to recognize that interactions of laser with tissues are complex phenomena influenced not only by laser parameters, such as wavelength, intensity and time of exposure but also by tissue properties. When laser beam incident on a tissue it may be reflected, scattered, absorbed or transmitted. In general biological tissues are optically inhomogeneous and absorbing media. Each type of tissue has specific reflective, scattering and absorption characteristics, depending on its components. Diffuse reflection is a common property for all tissues and multiple internal reflections and redirection may be occurred for incident laser beams. Absorption is the key for laser interaction with tissue. The absorbing molecules in the tissue are generally referred to as chromophores. The main absorbing component chromophores of tissues are hemoglobin, melanin, water and protein. The absorbed laser energy can induced several

effects in tissue, such as Photomechanical, Photo ablation, Photo thermal, Photochemical, Fluorescence, Ionization and Plasma formation (figure 1.2). By selecting the proper wavelength, intensity, and pulse duration of laser beam, a desired effect can be maximized to be clinically useful.

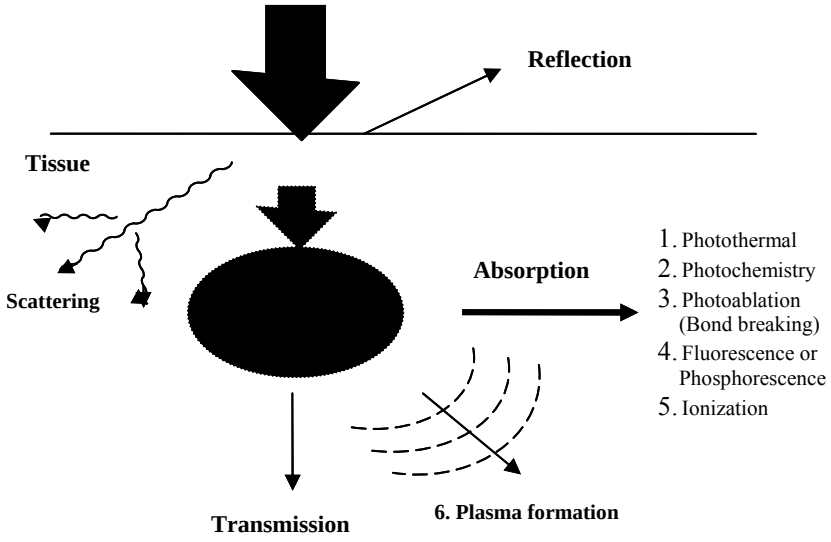

Figure 1.2: Types of laser-tissue interaction

While therapeutic aspects of lasers in medicine have been very dominant, tissue diagnostic techniques using laser spectroscopic methods have proven to be extremely useful in many areas of disease diagnosis, including cancer. Optical diagnostics for medical purposes is based on the interaction of light with tissue. These interactions may be resonant or non-resonant in nature. Resonant which includes: molecular absorption of laser, laser induced tissue heating, laser induced photochemistry and laser induced fluorescence. Non-Resonant includes; Elastic scattering and Raman scattering [**Waynant., 2002**].

Several factors contribute to the increasing interest in laser tissue diagnostics:

- Optical monitoring is non invasive in nature.
- Non-ionizing radiation is employed.

- Real-time data representation is possible.
- Spectroscopy allows molecular specificity in analysis.
- Point monitoring or imaging capability can be employed.
- Integration of laser diagnostics and therapy is possible.

Applications include cancer detection using laser such as laser induced auto fluorescence (LIAF), laser induced breakdown spectroscopy (LIBS) and others. So in this study we choose LIBS technique to demonstrate the laser interaction with tissue to diagnose cancer also the trace elements are considered due to their assay in tissue as diagnostic in patients with cancer.

1.3 Characteristic of Cancer Cell

Worldwide, there are more than 10 million new cancer cases each year, and cancer is the cause of approximately 12% of all deaths. Given this, a large number of epidemiologic studies have been undertaken to identify potential risk factors for cancer. It is difficult to say when a normal cell would be transformed into a cancer cell, for the distinctions between a normal and cancerous cell are very minute. Clear-cut differences can be observed only after a tumor growth shows up. A number of structural and functional differences have been detected by studying the cells transformed by oncogenic viruses. Analysis of cancer cells has revealed that they lack intercellular adhesion and their surfaces become convoluted. In normal cells, vinculin, a protein forms a link between the plasma membrane and the cytoskeleton. Disruption of this connection makes the plasma membrane free from the cytoskeleton and the cell assumes a spherical shape, which is a common feature of cancer cells. The morphological feature of a cancer cell is used as a marker to distinguish abnormal cells from the normal ones. The nucleus of a cancerous cell is enlarged and irregular, showing increase in the nucleo-cytoplasmic ratio. The chromosomes swell up and the number of chromosome sets increase owing to the growth of transformed cells. This