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EVALUATION OF SKIN TISSUE AFTER LASER TISSU WELDING USING RAMAN SPECTROSCOPY

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By

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T.C.
FATİH ÜNİVESİTESİ
BİYOMEDİKAL MÜHENDİSLİK ENSTİTÜSÜ

LASER İLE DOKU KAYNAĞI UYGULAMASINDAN SONRA DERİ DOKUSUNUN RAMAN SPEKTROSKOPİSİ İLE İNCELENMESİ

FARUK MUSTAPHA ABDULLAHI

YÜKSEK LİSANS TEZİ
BİYOMEDİKAL MÜHENDİSLİĞİ PROGRAMI

DANIŞMAN
YRD. DOÇ. DR. HAŞIM ÖZGUR TABAKOĞLU

İSTANBUL / TEMMUZ 2015

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FARUK MUSTAPHA ABDULLAHI, a MSc. Student of Fatih University **Institute of Biomedical Engineering** student ID 520113013, successfully defended the thesis entitled " **EVALUATION OF SKIN TISSUE AFTER LASER TISSUE WELDING USING RAMAN SPECTROSCOPY",** which he prepared after fulfilling the requirements specified in the associated legislations, before the jury whose signatures are below:

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……**Prof. Dr. Sadık KARA**
Director

Date Of Submission: 3th July 2015

Date Of Defense: 13th July 2015

To my family: Prof. Abdullahi Mustapha (my Father) and Hajiya Zainab Mustapha (my Mother) and also I'm dedicating this to my late friend Mustapha Ibrahim Hassan

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JULY 2015 FARUK .M. ABDULLAHI

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ABBREVIATIONS

AKT: Ali Kaan Tabakoglu

CUR: Current

App: Appendix

CW: Continuous Wave

DUO: Dual Wavelength mode

OfT: Off Time

OnT: On Time

Nd; YAG: Neodymium Ywittrium Aluminium Garnet

UV: Ultraviolet

PO: Post Operation

LTW: Laser Tissue Welding

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SUMMARY

EVALUATION OF SKIN TISSUE AFTER LASER TISSUE WELDING USING RAMAN SPECTROSCOPY

FARUK MUSTAPHA ABDULLAHI

Biomedical Engineering Programme

MSc Thesis

Advisor: Asst. Prof. Dr. Haşim Özgür TABAKOĞLU

Laser tissue welding of the skin is a very encouraging method of wound closure, especially when the formation of scar tissue is undesirable, such as plastic surgery. Raman measurements were taken from 10 Wistar rats. Incisions were made along vertical plane on the dorsal region of shaved Wistar rats. The incisions were closed by laser irradiation at 1W and exposure time, 10 seconds in pulsed mode to deliver a total energy of 5J per spot onto the incision respectively. Animals from each group were sacrificed at 24hr, 4, 7, 14 and 21 days and the sample were used to obtain Raman measurements of the healing process allowed in vivo investigation into the degree of collagen deposition, formation of new tissue, and conformational changes in proteins. The intensity ratio of the 1247 cm^{-1} band to the 1326 cm^{-1} band proved to be a good marker for collagen deposition and for determining the extent of the healing process. LTW skin after 21 days post-operation exhibited an appearance to that of the normal skin; the Raman spectra show that the skin was successfully healed and was identical to normal skin.

Keywords: Raman spectroscopy, pulsed mode, FT-IR spectroscopy, Dual wavelength, Collagen, laser irradiation.

ÖZET

LASER İLE DOKU KAYNAĞI UYGULAMASINDAN SONRA DERİ DOKUSUNUN RAMAN SPEKTROSKOPİSİ İLE İNCELENMESİ

FARUK MUSTAPHA ABDULLAHI

Biyomedikal Mühendisliği Programı

Yüksek Lisans

Danışman: Yrd. Doç. Dr. Haşim Özgür TABAKOĞLU

Lazer ile deri kaynağı özellikle plastik cerrahide iyileşmenin güç olduğu durumlarda yara kapama yöntemi olarak oldukça umut vericidir. Raman ölçümlerinin alındığı deneylerde 10 Wistar sıçanı kullanılmıştır. Kesiler Wistar sıçanlarının sırtında, omurgaya paralel olacak şekilde açılmıştır. Kesiler 1W lazer ışımasının darbeli modta 10 saniye süresince uygulanarak toplam 5 jullük bir enerji aktarımı ile kapatılmıştır. Her bir gruptaki denek hayvanları deneylerden 24 saat, 4 gün, 7 gün, 14 gün ve 21 gün sonra sakrifiye edilmiş, ve kesiler toplanarak yara iyileşme sürecinde kollajen miktarındaki değişim ve yeni dokunun oluşumu Raman ölçümleri ile tespit edilmeye çalışılmıştır. Raman Spektroskopisinde ölçülen 1247 cm-1 ve 1326 cm-1 bantları kollajen birikimi ve iyileşme süreci hakkında bilgi veren işaretlerdir. Lazer ile deri kaynağı yapılmış dokular 21 gün sonunda sağlıklı bir deri görüntüsü vermiştir; Raman ölçümleri derinin sağlıklı bir iyileşme sergilediğini ve pratikte normal deri ile eşdeğer olduğunu göstermiştir.

Anahtar sözcükler: Raman spektroskopi, pulslu modda, FT-IR spektroskopi, Çift dalga boyu, Kolajen, lazer ışınlama.

CHAPTER 1

INTRODUCTION

1.1 Laser Tissue Welding

The first successful medical application of laser energy to approximate tissue was reported for the repair of small arteries in 1979[1]. Laser tissue welding (LTW) had been used to repair variety of tissue types including skin, nerve, liver, urinary tract, etc. The potential advantages of these techniques are that, it reduces operation time, faster healing, and immediate watertight anastomoses.

To achieve laser tissue welding successfully, wavelength of laser light, optical and thermal properties of tissue, spot size of the laser, exposure time, laser power and pulse duration are carefully selected.

According to previous studies, laser tissue welding is a soft thermal treatment of wound edges in which laser radiation is absorbed by the tissue, either by it's principal absorbers like water, or exogenous chromosphores applied directly to the wound site[2]. At the welded site, the main components undergo thermal modifications, resulting into the fusion of the apposed flaps[1]. If the laser radiation used is in excess or the exposure time on the tissue exceeds the normal parameter, an undesired thermal damage may be prompt in the surrounding area, and the strength of the weld may be poor.

Despite advancements in this field, to successfully weld large defect the tissue edges must be approximated and kept under minimal tension[1]. Although the exact mechanism of laser welding is not completely understood, most data support the view that the absorption

of light by tissue result in it's thermal remodeling. The structural changes in collagen fibrils are involved in this process.

The disadvantages have been low strength (due to low penetration depths) and thermal damages to the surrounding tissue.

The 980nm and 1064nm lasers have shown by many researchers to be good candidates for skin wound closure. Tabakoğlu et. al. in 2006 closed the skin incisions by using the 980nm-diode laser. He suggested that diode laser could be a good candidate for skin closure. In 2014 Ibrahim UBA in his study used both 980nm and 1064nm to close skin incision.

1.2 Laser Tissue Interaction

When laser light interacts with tissue, it can be reflected, scattered, absorbed, or transmitted in to the surrounding tissue. Absorption controls a great degree to which reflection, scattering and transmission occur, and the wavelength determines the absorption rate. Most materials and tissues consistently absorb the Carbon Dioxide (CO2) laser. The factors, that determine the initial tissue effect, include the laser wavelength, laser power, laser waveform, tissue optical properties, and tissue thermal properties.

The mechanisms involved in laser tissue interaction include; thermal mechanisms, photochemical, photo-disruption, plasma-induced ablation and photo-ablation mechanisms [11].

1.2.1 Thermal mechanisms

These mechanisms are of primary importance to surgical procedures, and tissue welding is known to fall under this category. It has three distinct phenomena, starting with heat production in the tissue by absorbing the laser light and then heat transport (light absorption converted in to heat). The effect of this mechanism can produce ***coagulation, vaporization, carbonization and melting.*** (Figure 1)

1.2.2 Photochemical

In this mechanism, the laser light induces a chemical reaction initiated by the absorption of energy in the form of light. The consequence of molecules absorbing light is the creation of transient excited state. Which can occur even at low optical power density. (Figure 1)

1.2.3 Photo-disruption

These are mechanisms by which tissues are destroyed through a shockwave generation at high pulse intensity. Fragmentation and cutting of the tissue can be done by mechanical force of shockwave. When a laser beam is focused below the tissue, cavitation occurs in soft tissues and fluids produced by cavitation bubbles that consists of gaseous vapors such as water vapor and Carbon Dioxide (CO2). (Figure 1)

1.2.4 Photo-ablation mechanism

This is the highest level of interaction leading to tissue decomposition by exposing it to high intensity laser irradiation in order to destroy chemical bonds of its molecular constituents, without temperature rise in the surrounding tissues. A very useful method for tissue contouring and refractive corneal surgery. (Figure 1)

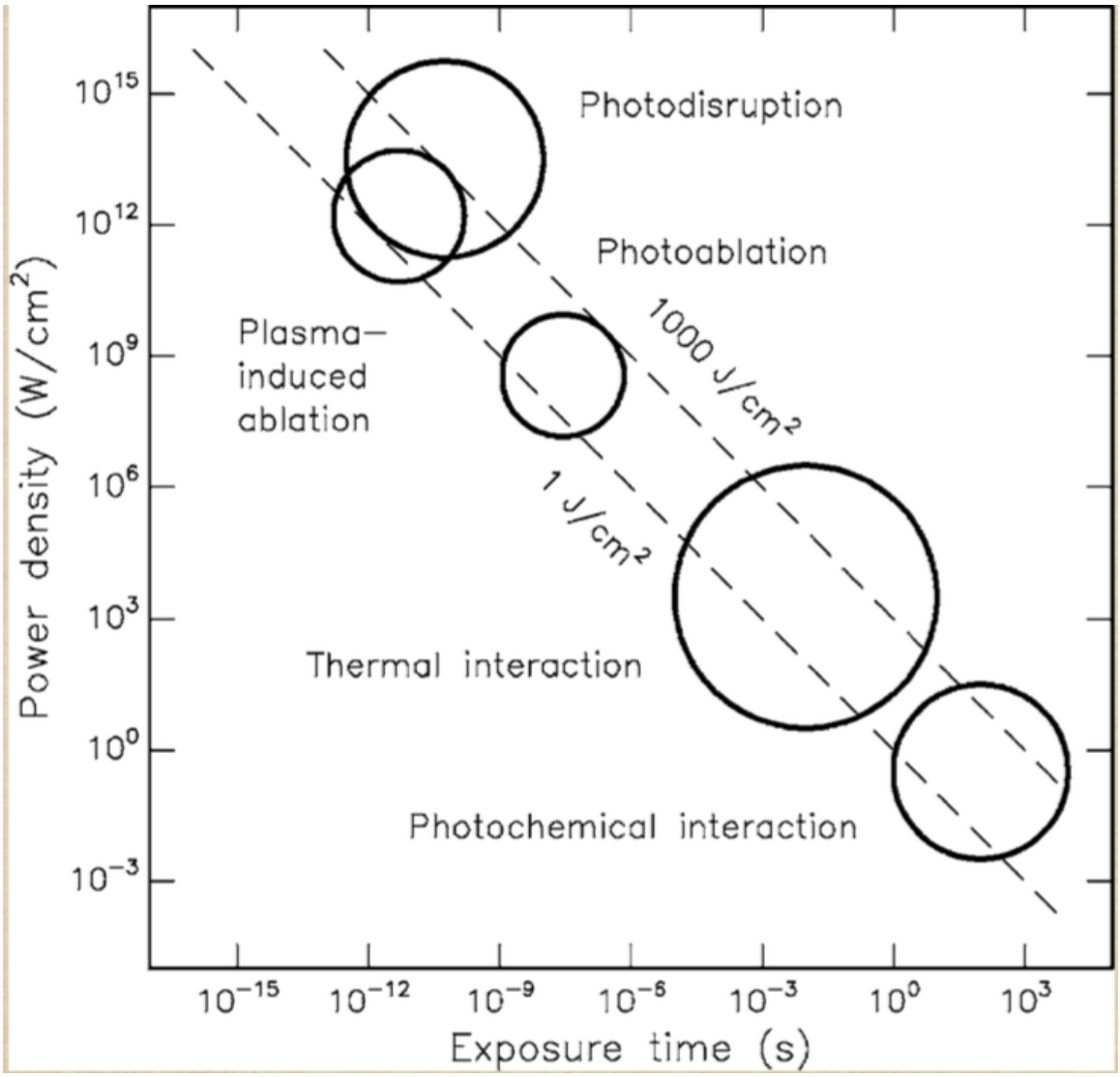

Figure 1 Showing map of laser-tissue interactions. The circles give only rough estimates of the associated laser parameters. (Picture Adapted from [25])

The interaction of laser light with biological tissue is of interest both for medical applications and for the establishment of laser safety standards. On the medical side, lasers are widely used in ophthalmology for the treatment of retinal diseases. Therapies range from established photocoagulation, to new ophthalmic laser applications such as selective retinal pigment epithelium (RPE) treatment, photodynamic therapy, and transpupillary thermotherapy.

1.3 Welding Method

When laser is turned to an overtone of water vibrational band, the absorption of laser light by the tissue results in the controlled heating of water molecules in tissue. Water in tissue exists in both free and bond states [12]. Bound water stabilizes the collagen matrix by creating a bond between fibers of the triple helix [3]. The absorbed energy is transferred from the water to the collagen matrix.

Careful control of the laser energy input can result in partial denaturation of the collagen helix, followed by renaturation. This results in the rapid formation of watertight seal at the welded site [3].

The initial formation of crosslinks between collagen molecules, when tissue is cooled it forms a matrix, which serves as the foundation for subsequent tissue rebuilding. Post-weld strength and long-term stability of laser-welded tissue can be affected as a result of the effects on existing collagen crosslinks as well as from new crosslinks synthesized as part of the wound healing process. Healing time is expected to reduce due to the laser exposure that forms the provisional matrix, compared to the conventional methods, which merely join the tissues. Several works support this theory, Gülsoy et al., performed a comparative study of epidermal thickness and granulation area of incisions on a large number of mice using sutures and laser techniques. Abdullahi Ibrahim Uba et al., performed closure of skin incision by DUAL wavelength (980 and 1064 nm) laser application.

The only disadvantage of this method is that the technique responsible for the tissue fusion can cause cell necrosis, by thermal effects. This reaction is directly proportional to the exposure time of the laser and exponential with temperature [13]. The control of heat accumulation in the tissue is the principal factor for controlling the range of this undesirable reaction.

To avoid significant thermal damage the exact laser parameters has to be followed and the tissue surface temperature is of critical importance too, but because of this being a difficult

goal to achieve, this method is now seen as a viable alternative, with the advancement of knowledge in laser-tissue interaction.

Both the radiation penetration depth and radiation absorption has to be considered deeply. Using higher wavelength results in high absorption causing undesirable tissue damages. To reduce this, lasers with lower wavelength are more suitable for this method, lasers that emit at 1064 or high power diode laser. UV lasers are excluded due to their extreme high power absorption.

Dyes or chromosphores are added to the soldering materials to reduce thermal damage in the primary and lateral tissues in the method. In this form of wound closure the absorption of the radiation occurs directly on the dyed area and regulating the extent of thermal damage. The chromophore must be compatible to the laser being used, to absorb the monochromatic radiation and the concentration predetermined to control optical penetration. Examples of such dyes used are indocyanine green for use with 808nm diode lasers and fluorescein dye for argon lasers [11].

1.3.1 980nm laser and skin welding application

Infrared lasers have shown to be good candidates for tissue welding, because of their distinct capability to bring about the thermal apposition of biological tissues [4]. The success of laser application depends on the wavelength, optical and thermal properties of tissues.

The skin-welding ability of 980nm diode laser has previously been studied by H.O Tabakoglu. A good closure of the incision was recorded for the early days (1-4 days) of the healing period. The local absorption peak (within 700-1,100 nm) for water makes the 980 nm laser preferable amongst near infrared diode laser [4].

The photo-thermal interaction of 980nm wavelength diode laser with tissue is thought to be attributed to the moderate absorption of the tissue components to that wavelength. This

wavelength is absorbed by water and also by other proteins molecules such as hemoglobin and melanin.

In 2005 Tabakoglu et al., and Murat Gulsoy in their study compared 2 distinct application methods by histological and mechanical test. Six incisions, 1cm long, were welded with 980nm diode laser by two separate applications; high power (6W-400ms) and low power (0.5W-5s). Throughout the 21 days healing period, incisions were monitored on control days (1^{st}, 4^{th}, 7^{th}, 14^{th} and 21st) for histological and mechanical tests. Closure index, epidermal thickness and granulation areas of H&E stained samples were calculated [14]. They concluded that the 980nm laser irradiation on skin tissue was very encouraging.

1.3.2 1064nm laser and skin welding application

The 1064nm laser among all non-ablative laser sources holds the most prominent position. This is so because of it's wavelength, which in terms of absorption, lies in an optical window that allows light of this wavelength to penetrate deep into the skin, while it's absorption by blood vessel or a hair follicle is strong enough to affect the target.

The 1064nm laser is also known for producing photothermal effect on the irradiated skin due to its penetrativity and it is easily absorbed by melanocyte [15].

The undesirable effects associated with their widespread use comes the increased risk of injury from their use and the need for methods to mend these injuries. Studies have shown 1064nm laser as a source to create a wound tissue environment to understand laser-tissue interactions. Yi-Ming et al., 2013 performed a study to compare 1064nm laser-induced skin burn and thermal burn by adopting 1064nm laser to induce skin damage, and to investigate photothermal effect on the irradiated skin [16]. Several studies on skin burn have been performed [17]. In these study a heated copper brass bar attached to an HQ soldering iron was used to induce thermal burns on skin, as a control to laser. The aim of the study was to understand the difference between 1064nm laser-induced burns and thermal burns. The result revealed that the laser induced burn injury intensified significantly in both horizontal dimension and vertical depth with the prolongation of exposure time. The laser is likely to

injure the deep-seated tissues. Until 10^{th} day, the laser induced thermal injuries as noted, were more severe. The above results provided us with data about the injury pattern and turnover in the skin and other tissues by the laser. It also showed the difference between the laser-induced skin burns and the normal thermal skin burns, establishing a sound foundation for treatment of laser burn [18].

1.4 Laser Modes Of Operation

A laser can either be in a continuous or pulsed mode, depending on whether the power output is continuous over time or whether its output takes the form of pulses of light on one or another time scale.

1.4.1 Continuous Wave Operation

Continuous wave (CW) emission has no interruption during the delivery of their energy. CW mode is like a light that is constantly "on". Some laser applications depend on a beam whose output power is constant over time and thus make use of such a laser known as CW. A great number of these lasers actually work in several longitudinal modes at the same time, and beats between the slightly different optical frequencies of those oscillations will in fact produce amplitude variations on time scales shorter than the round trip time (the reciprocal of the frequency that is spacing between modes), typically a few nanoseconds or less [19]. For a laser to be able to operate in continuous wave mode it is required for the population inversion of the gain medium to be constantly replenished by a steady pump source. In some laser media this is very hard to obtain. In some it would require pumping the laser uninterruptedly at a very higher power level, which seems impractical or destroy the laser by producing excessive heat. Such lasers cannot be run in CW mode [20]. (Figure 1.1)

1.4.2 Pulsed Operation

Pulsed operation lasers refers to any laser not classified as continuous wave, so that the optical power is delivered in pulses of some duration at some repeated rate producing light

that is “on” half the time and “off” half the time. The cycle is 50% due to the light being “on” and “off” half the time. Another definition of duty cycle is the duration of the pulse divided by the period, or the time from the start of one pulse to the beginning of next one.

In some cases the application requires the production of pulses having as large energy as possible. Since the pulse energy is equal to the average power divided by the repetition rate. Some lasers are in pulsed mode because they cannot be used in continuous mode. (Figure 1.1)

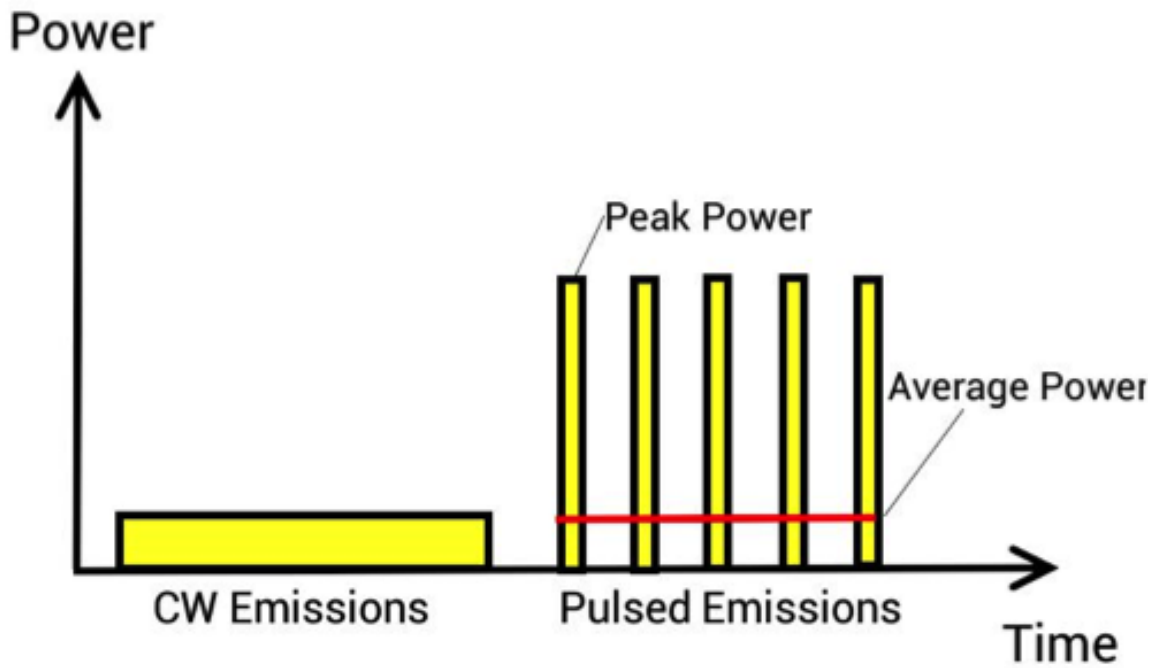

Figure 1.1 Continuous Wave laser emission compared to Pulsed laser emissions (picture adapted from [21].)

1.5 Physiology Of Wound Healing

Wounds can occur as part of a disease process or have an accidental or intentional aetiology. Damage to any tissue triggers a cascade of events that leads to rapid repair of the wound-if the tissue is skin, then repair involves re-epithelialization, formation of granulation tissue and contraction of underlying wound connective tissues[5]. This process of healing is divided into four distinct phases.

- ***Haemostasis;*** process which causes bleeding to stop. First stage of wound healing, changing blood from liquid to gel. Through contraction process, vessels up to a diameter of 5 mm can be closed, although this can only occur if the injury is in transverse plane[6]. Within minutes, the reduced blood flow mediated by arteriole constriction leads to tissue hypoxia and acidosis.
- ***Inflammation;*** the main objective of this stage of wound healing is to prevent infection. "Neutrophils, the 'first responders', are highly motile cells, which infiltrate the wound within an hour of the insult and migrate in sustained levels for the first 48 hours[6]. Neutrophils have three main mechanisms for destroying debris and bacteria. Firstly they directly ingest and destroy foreign particles, a process termed **phagocytosis**. Secondly, neutrophils degranulate, releasing a variety of toxic substances (lactoferrin, proteases, neutrophil, elastase and cathepsin), which will eliminate bacteria and dead host cells from the tissue". Lastly, neutrophils can also produce chromatin and protease 'traps' which capture and kill bacteria in the extracellular space.
- ***Proliferation;*** process by which an organism produces others of its kind; procreation, reproductions. "This complex process leads to angiogenesis, the formation of granulation tissue, collagen deposition, epithelialization and wound retraction, which occurs simultaneously".
- ***Tissue remodeling;*** the final stage of wound healing can take up to 2 years and results in the development of normal epithelium and maturation of the scar tissue[6]. "It involves a balance between synthesis and degradation, as the collagen and other proteins

deposited in the wound become well organized. They will eventually recoup to a structure similar to that seen in normal tissue".

1.5.1 Wound Healing Process

Disruption of the integrity of skin, mucosal surface or organ tissue results in the formation of a wound. "The healing process includes a series of overlapping stages. Immediately after incision, platelet aggregation and blood coagulation form the dense cross-linked network (provisional matrix), which prevents blood loss[3]. The matrix provides the main structural support. The main components are fibrin and fibronectin proteins. Twenty-four hours after insult, the polymorpho-nuclear neutrophils (PMNs) arrive becoming the main type of cell at the wound area. The PMNs fight bacteria and release the proteases, which break down damaged tissues[6]. Approximately 48 hours after insult, fibroblasts begin to enter the wound site, replacing the provisional matrix with granulation tissue composed of fibronectin and collagen. The number of fibroblast reaches a maximum in the first or second week post-wound[3]. Fibronectin rich granulation tissue provides a vascularized network for the deposition of collagen. Scar tissue is created from the bundled and cross-linked collagen fibrils". The most rapid change in the extent of collagen deposition and tensile strength on the wounded skin occur at week 6 or 7 post-injury, after which the rate of change flattens[3].

1.5.2 Collagen

The most abundant glycoprotein in the extracellular matrix (ECM) of most animal cells is collagen. It forms strong fibers outside the cells. Collagen accounts for about 40% of the total protein in the human body. The collagen fibers are embedded in a network woven from proteoglycans. A proteoglycan molecule consists of small core protein with many carbohydrate chains covalently attached, so that it may be up to 95% carbohydrate.

The primary roles for collagen fibers in tissues are to prevent premature mechanical failure and help store or transmit and dissipate energy imparted either by the musculoskeleton or as a result of externally applied forces[7]. Collagen fibers are required for effective

locomotion, and for tissue regeneration and repair through mechanochemical transduction processes[8].

The major collagens present in the skin are Type I and Type III. “The mass of Type I collagen is about 290 Kda, accounting for approximately 80% of the total amount of collagen in the dermis, collagen Type I is abundant in the skin, tendon, ligament, bone, teeth, and between organs. Collagen Type II is abundant in the cartilage and eyes. Type III collagen makes up 10% of dermal collagen, mostly found in the muscle, blood vessels, and skin. It is also called fetal collagen because it is noted first in embryonic dermis where it serves as a framework on which Type I collagen is subsequently manufactured.

Type IV collagen is a constituent of basement membrane, usually found in the lamina densa. Type V collagen accounts for less than 5% of all collagen in the dermis. Type VI collagen may be found in a variety of tissues, including skin where it is assembled into thin microfibrils which form a network that acts as an anchor for stabilizing the broad assembly of collagen fibers, the same time serving as a basement membrane. Type VII collagen is produced mostly by keratocytes, from which it is transported across the basement membrane at the dermoepithelial junction to its final destination, where it anchors fibrils in the papillary dermis”. (Figure 1.2)

Collagen can be used in some biomedical application, such as drug delivery system. The use of collagen as a drug delivery system is very comprehensive and diverse. Collagen can be extracted into an aqueous solution and molded into various forms of delivery systems[7]. The main applications of collagen as drug delivery systems are collagen shields in ophthalmology (Kaufman et al., 1994), sponges for burns/wounds (Rao, 1995) gel formulation in combination with liposomes for sustained drug delivery (Fonseca et al.,) and nanoparticles for gene delivery (Rossler, 1995)

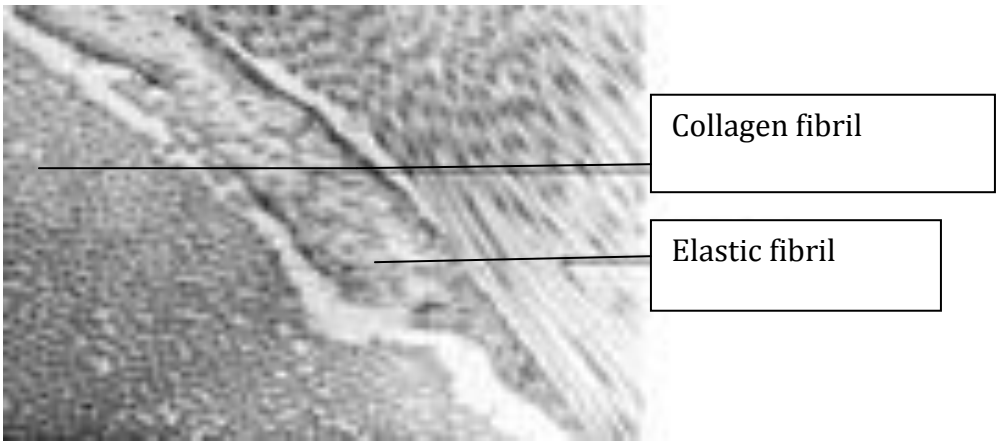

Figure 1.2 Collagen fibrils cut longitudinally have a structure distinctly different from that of the elastic fibril, the latter consisting of non-collagenous micro-fibrils embedded in homogenous elastin. (x 55,000)(Picture adapted from [23]).

1.6 Optical Evaluation Method

1.6.1 Raman History

In 1928, sir C.V. Raman and his colleague K.S. Krishnan made their discovery of what came to be called Raman scattering while searching for an optical analog to the

Compton effect. Their discovery was concurrent with G.S. Landsberg and L.I. Mandelstam, two Russian physicists, during the course of their studies on specific heats

of solids. "Raman and Krishnan observed the inelastic scattering of light first by focusing filtered sunlight, and later by focusing a quartz mercury arc lamp through a photographic filter to remove all lines of greater wavelength than 4356 Å, and directing it into samples

of common solvents [22]. The resultant spectra were collected on photographic plates, and showed modified lines that indicated a change of wavelength in the outgoing light. In

total, Raman and Krishnan observed scattered secondary radiation in 60 liquids and vapors.

Due to the inefficient nature of the scattering, several technological advances were necessary before Raman spectroscopy became a common laboratory technique. Only 1 in 10^6 to 10^8 incident photons are returned shifted by the interaction with the molecules. The development of the laser then, permitted much more effective measurements because of the dramatic increase in the amount of incident light. Improvements in monochromatic systems, both to resolve the Raman spectrum and limit the amount of Rayleigh scattering present in spectral data, also encouraged the use of Raman spectroscopy to study molecular structure and chemical systems".

Further, narrow notch filters are also available for the removal of the excitation light in the spectra and sophisticated software solutions exist for background elimination and in support of end-user purpose. Today, many researchers in various fields' focuses on the Raman spectroscopy due the following reasons;

- Increasing of light transmission by developments of optical component, such as lens, mirror, and especially optical filters for stray light remover.
- Improvements of stability by developments of spectrometer.
- Increasing of light detection sensitivity by evolutions of detectors such as CCD enables.

1.6.2 The Theory of Raman Spectroscopy

When monochromatic radiation passes through a sample, and then this light will interact with the sample, in a way it may be reflected, absorbed or scattered in some manner. "It is the scattering of the radiation that occurs which can tell the Raman spectroscopy something of the samples molecular structure. (Figure 1.3)

If the frequency (wavelength) of the scattered radiation is analyzed, not only is the incident radiation wavelength seen (Rayleigh scattering) but also, a small amount of radiation that is scattered at some different wavelength (Stokes and Anti-Stokes Raman scattering) [22]. It

is the change in frequency of the scattered photon, which provides the chemical and structural information.

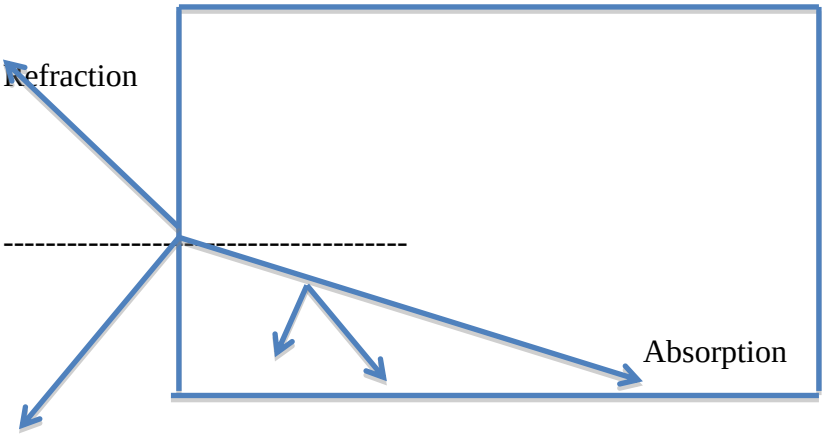

Figure 1.3 Interaction of light with a bulk Matter

Light scattered from a molecule has several components – the Rayleigh scatter and the Stokes and Anti-Stokes Raman scatter.

In molecular systems, these frequencies are principally in the ranges associated with rotational, vibrational and electronic level transitions. The scattered radiation occurs over all directions and may also have observable changes in its polarization along with its wavelength.

- The scattering process without a change of frequency is called Rayleigh scattering, and is the same process described by Lord Rayleigh and which accounts for the blue color of the sky.
- A change in the frequency (wavelength) of the light is called Raman scattering. Raman shifted photons of light can be either of higher or lower energy, depending on the vibrational state of the molecule".

The Raman scattering technique is a vibrational molecular spectroscopy, which derives from an inelastic light scattering process[9]. With Raman spectroscopy, a laser photon is

scattered by a sample molecule and losses (or gains) energy during the process. The amount of energy lost is seen as a change in energy (wavelength) of the irradiation photon. This energy loss is a characteristic for a particular bond in the molecule. Raman can be thought of as producing a precise spectral fingerprint, unique to a molecule and individual molecular structure[9].

1.6.3 Raman Instrumentation

The correct selection of the laser wavelength can be an important consideration for the Raman spectroscopy. With advance equipment, often several laser wavelengths may be used as to achieve the best and accurate detection of the Raman signal.

For instance, many samples, especially those of an ‘organic’ or ‘biological’ nature have the tendency to fluorescence upon excitation. “Exciting these samples with a laser in the green (532 nm) may promote this fluorescence, and may swamp any underling Raman spectrum to such an extent that it is no longer detectable.

The use of a laser in the red (633 nm) or NIR (785 nm) may offer a better solution. With the lower photon energy, a red or NIR laser may not promote the electronic transition (and hence the fluorescence) and so the Raman scatter may be far easier to detect.

If there is an increase in the wavelength, from green to red to NIR, the scattering efficiency will decrease; so longer integration times or higher power lasers may be needed. Thus, it is often most practical to have a number of laser wavelengths available to assign to the various sample properties one may encounter, be it resonance enhancements, penetration depth of fluorescence”.

1.6.4 FT-IR SPECTROSCOPY

Fourier Transform Infrared (FTIR) is a vibrational spectroscopic technique that can be used in biological studies, can also be used in clinical investigations related to malignancy and

cancer detection. “FTIR spectroscopy, is potential tool for noninvasive optical tissue diagnosis[10].

Research had been carried out on a number of natural tissues using spectroscopic techniques, including FTIR spectroscopy. These vibrational spectroscopic techniques are comparatively simple, reproducible, non-destructive to the tissue, and only small amounts of material with a simple sample preparation are required[10]. These techniques also provide molecular-level information enabling investigation of functional groups, bonding types, and molecular conformations.

The spectral bands in vibrational spectra are molecule specific and provide information about the biochemical composition. FTIR peaks are relatively narrow and can be associated with the vibration of a particular chemical bond in the molecule. Although Raman and FTIR spectroscopy are relevant techniques, with their spectra complementary to one another, the two actually have some differences between them. The most important difference is the type of samples that can be used by each of these methods. FTIR mainly deals with non-aqueous samples, while Raman is as effective with both aqueous and non-aqueous samples. The limitation of the use of FT-IR in aqueous solution is due to the formation of strong absorption bands of water. Another important difference is that, Raman requires minimal sample preparation and can perform confocal imaging, whereas FTIR requires delicate sample preparation and does not have ability of confocal imaging”. FTIR spectroscopy is due to changes in dipole moment during molecular vibration, whereas Raman spectroscopy involves a change in polarizability.

1.7 Motivation

There has been very little information in the literature about the application of Raman and FT-IR spectroscopic techniques in the study of biological tissues welding. This has not been shown to be practical with current technology for commercial use in daily clinical usage. The benefits of such a technology would be to change the conventional suturing, clipping, stapling with laser tissue welding to repair tissue damage. The ultimate goal of

such a technique is to replace suture materials, which are most often are sources of wound infection if not thoroughly sterilized. In addition, the technique would shorten the wound healing time.

1.7.1 Purpose of The Thesis (Background and Objectives of The Study)

This study is aimed at evaluating the thermal effects of DUAL wavelength, 980 nm and 1064 nm lasers used in laser tissue welding.

The main objectives are:

1. To evaluate collagen deposition at the wound (incision site) using Raman spectroscopy.
2. To evaluate the status of skin healing using Raman spectroscopy.

1.8 Hypothesis

After laser tissue welding, the healing process of the skin was evaluated by Raman spectroscopy. DUAL method could be or is a better application, showing minimal collagen deposition, near-normal surface contour and minimal loss of dermal appendages.

CHAPTER 2

MATERIALS AND METHOD

2.1 AKT-Epidermis Dual wavelength Laser System

AKT Dual Wavelength Laser System for skin application is a laser system with two wavelengths, 980nm, 1064nm, designed to produce radiation with maximum output power of 2Watts. Optical apparatus, two wavelengths laser light by combining co-axis, the optical lens, and focusing on fiber optomechanical mechanism that sends transmission. In the metal box, the laser power supplies electronic microprocessor and control cards, power measuring unit is all located in the user interface. These wavelengths can be used individually and in a combined beam form. Laser modules and optical apparatus, are housed in a separate box, which are mounted on an optical table.

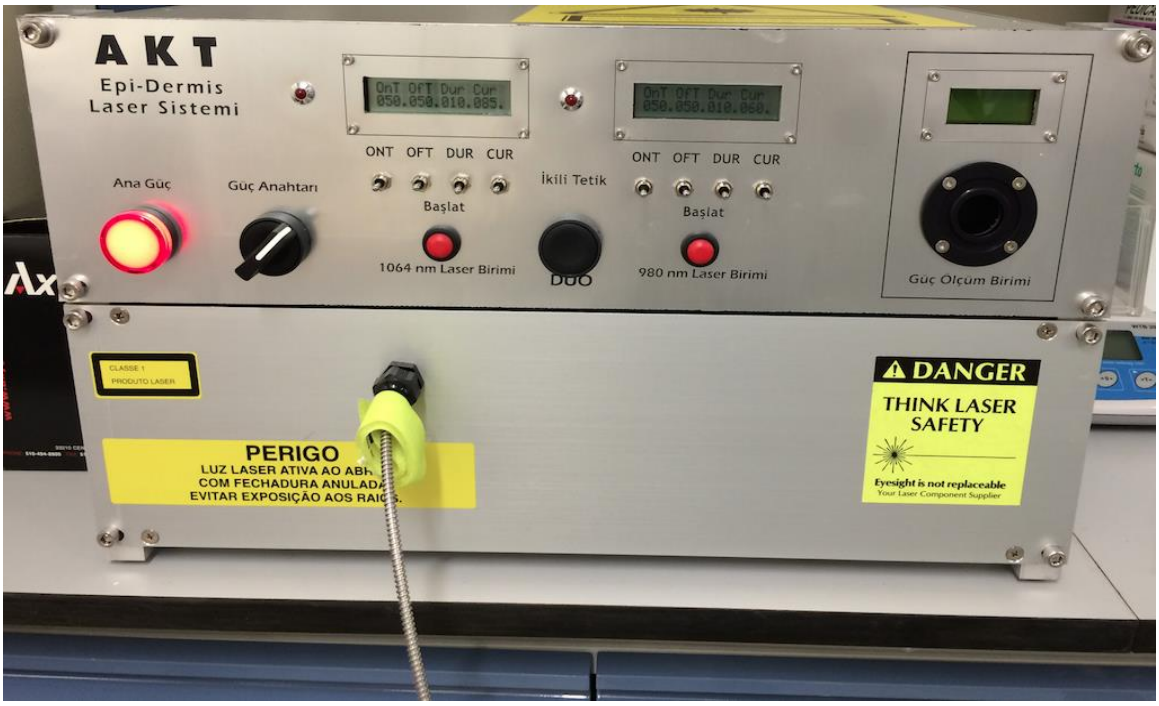

Figure 2. AKT-Epidermis Dual Wavelength System

Figure 2.1 Using the AKT-Epidermis System To Close Skin Incision

Table 2. Optimized measurement values for the connection of fiber optic lasers with collimator

980 nm			
Current (A)	Fiber Input (W)	Fiber output (W)	Coupling efficiency
1.5	1.05	0.940	90%
1.5		0.900	OK
1064 nm			
Current (A)	Fiber Input (W)	Fiber output (W)	Coupling efficiency
2.5	1.27	1.09	86%
2.5		1.10	OK

2.2 Methodology

2.2.1 Study site and subjects

The experiments were conducted under an approved protocol of Institutional Ethics Committee for the Local Use of Animals in Experiments at Boğaziçi University (No: 2013-05-08). Wistar rats between the ages of 7 and 8 weeks and weighing approximately 200-220g were taken prior to the experiment. The animals were housed at the vivarium section of Boğaziçi University Istanbul, Main Campus and therefore the laser irradiation; post-irradiation animal care and wound excision were carried out there with the approved permission of the university.

2.2.2 Animal preparation (Anesthesia and incision)

Ten female Wistar rats were divided into five groups (24hr, 4days, 7days, 14days, and 21days). The animals were anesthetized with anesthesia containing ALFAZYNE %2 and ALFAZYNE %10 by intraperitoneal injection. Their back (dorsal region) was shaved and a total of twelve incisions were made with a No. 3 scalpel. Each incision was 1 cm long and 2mm deep (skin deep). One of the incision was allowed to heal on its own without laser or sutures, served as a control.

2.2.3 Laser Irradiation

Four incisions at the left side of the Wistar rats were laser-welded with a 980nm pulsed fiber laser. Four incisions at the right side of the Wistar rats were laser-welded with a 1064 nm pulsed fiber laser. Dual wavelength was used to weld the four incisions at the middle/spine region of the Wistar rats**. Laser power of 1W for 10s exposure time to deliver a total energy of 5.0J and power density of 31.83 per spot on the skin incision in Pulse mode (980nm: On Time=050 Off Time=050 Duration=010 Current=060) (1064nm: On Time=050 Off Time=050 Duration=010 Current=085).** The method employed was based on previous studies carried out [24].

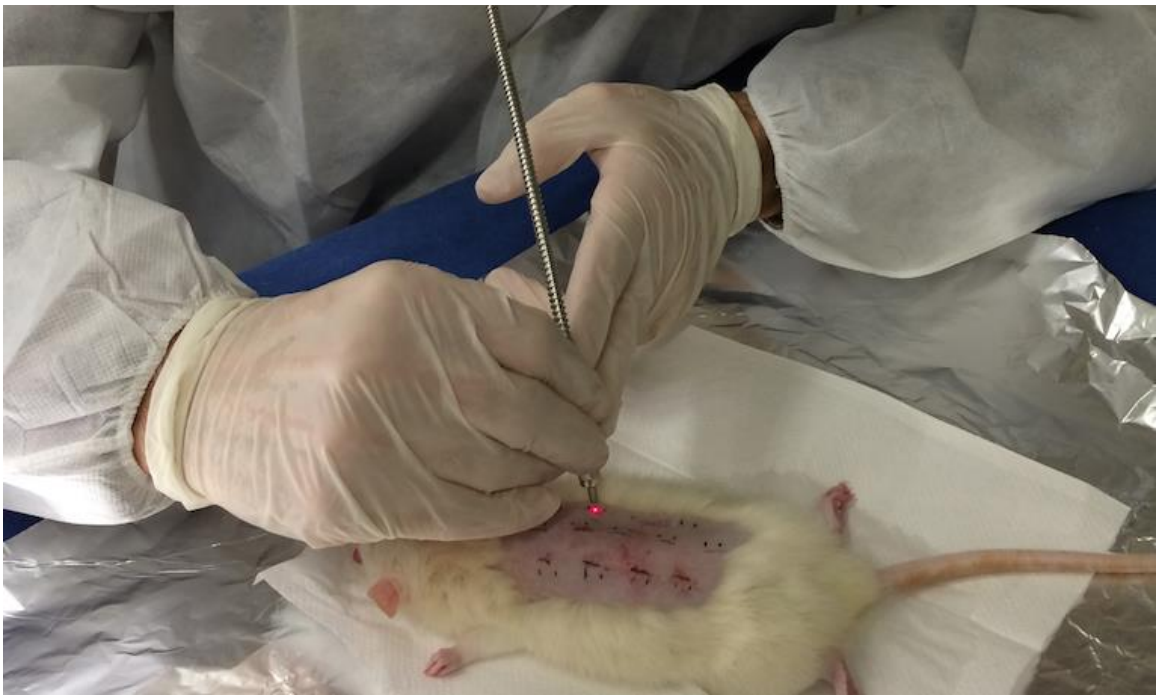

Figure 2.2 Incision Irradiation.

Figure 2.3 Weld Incisions Post-irradiation.

Dual Wavelength 1064nm 1864nm

Wistar rats were sacrificed 24hr, 4, 7, 14 and 21 days after the laser tissue welding. Two Wistar rats for each time period were sacrificed. Raman spectras were measured using Raman spectroscopy, connected to a personnel computer. The Raman spectras were measured at different locations directly on the welded line. Raman spectra were also acquired at a distance of 2-3 cm away from the incision for each group, which served as control skin (CS). The Raman spectra and FT-IR spectra were measured for the incisions on the dry skin for histological purpose.

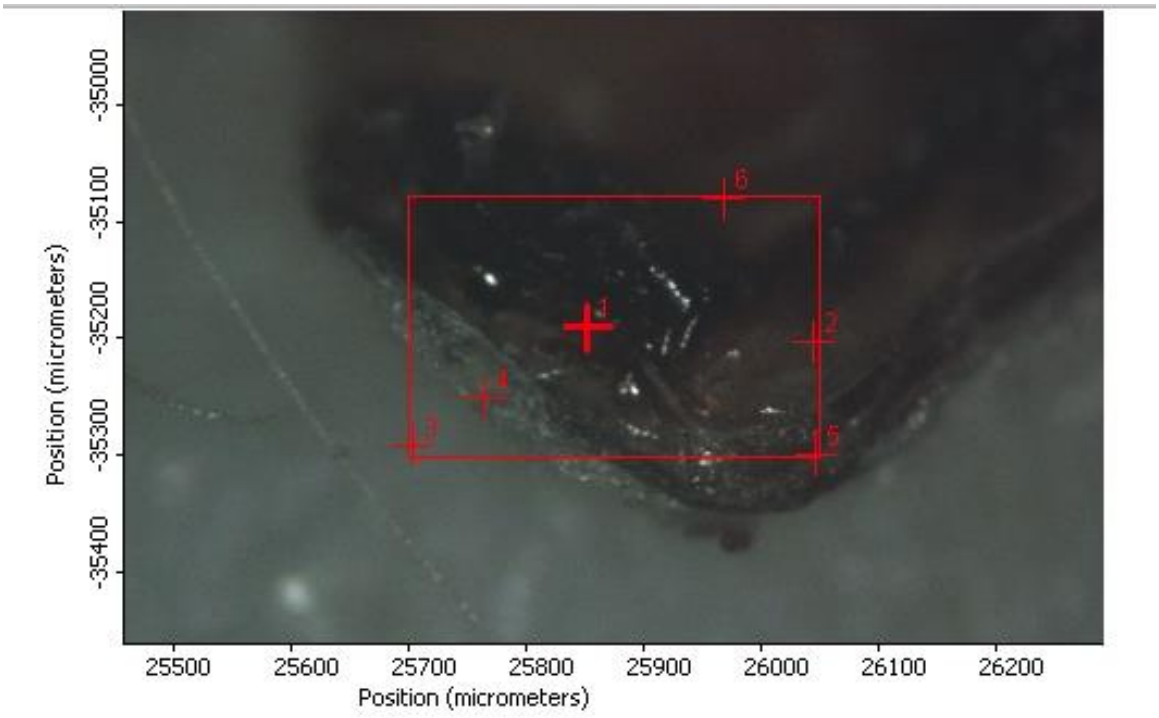

Figure 2.4 Raman Spectra Measurements at different locations.

2.3 Raman Examinations

2.3.1 Raman spectra processing

Raman spectra are acquired by irradiating a sample with a powerful laser source of usually visible or near-infrared monochromatic radiation and measuring the scattered radiation with a suitable spectrometer.

Knowing the frequency of the incident light and measuring the frequency of the Raman scattered light, it is possible to calculate the vibrational energy difference. This energy is known as the Raman shift and is usually expressed in wavenumbers (cm^{-1}) in a plot known as the Raman spectrum. The Raman spectral features can be used to identify a particular substance because complex molecules have several specific vibrational energy modes allowing the Raman spectrum of each substance to be highly specific and distinctive[9].

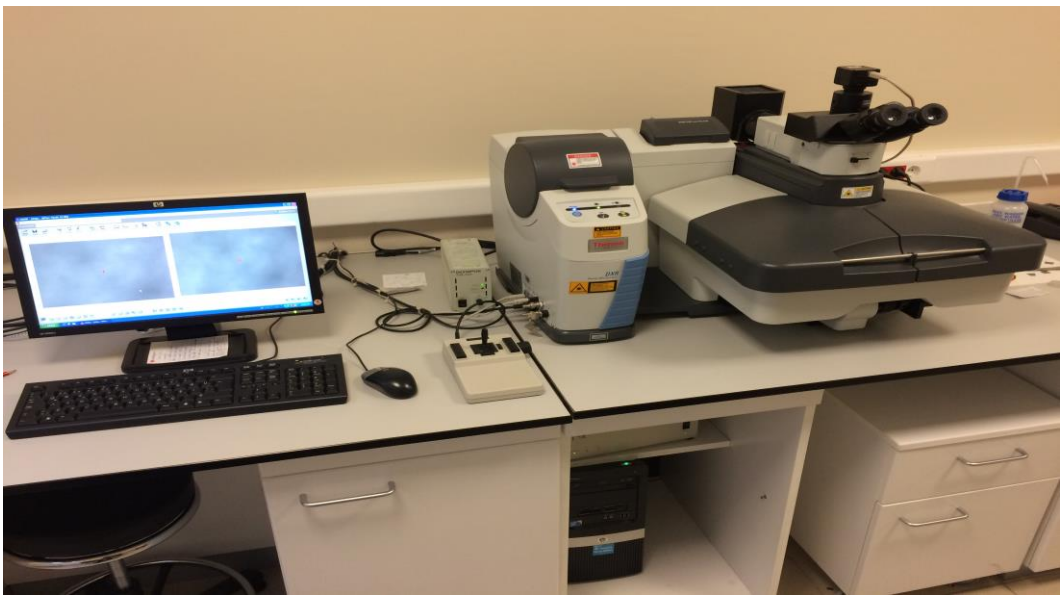

Figure 2.5 A DXR Raman spectroscopy connected to a personnel computer

In other to obtain a Raman spectra the following steps must be followed.

- Start the personnel computer
- Switch on the power source to the Raman
- Switch on the laser power source
- Switch on the Raman spectroscopy
- Open the OMINIC application software
- Click on Exp. Setup
- Click on open – desktop – open the existing folder
- Clink on bench
- Switch on the laser and wait for 5 minutes
- Click on collect
- Click on ok
- Click on Atlus to show window
- Place your sample to analyze
- Click on sample point
- Collect map
- Click on Atlus
- Click on split map
- Select path
- Rename; save as SPA & CSV

The major drawback to Raman measurements in tissue is the presence of a strong fluorescence wing. At the time we take the Raman signals, due to the property of the laser light we expected some of the signals to be fluorescence signals, therefore baseline corrections were made to correct the fluorescence signals.

Statistical Analysis: Analysis of Mean, Standard deviation and paired comparison analysis by T-test were employed to test for statistical differences in the set of data at p= 0.05 level of significance among laser groups and daily comparison between lasers.

CHAPTER 3

3.1 RESULTS

The combination of 980nm and 1064nm wavelength pulse mode laser, showed incisions were almost at near-normal surface contour. In the Dual mode we observed carbonization in some cases. On day-4 and day-7, the incisions at the back of the Wistar rats were almost not visible due to almost complete healing from the 980nm with control incision. The Dual wavelengths, the incisions were almost completely healed but still visible to the eye, it might be because for the 980nm and 1064nm hair was present at the incision site, so it was difficult to collect their spectroscopy (Figure 3).

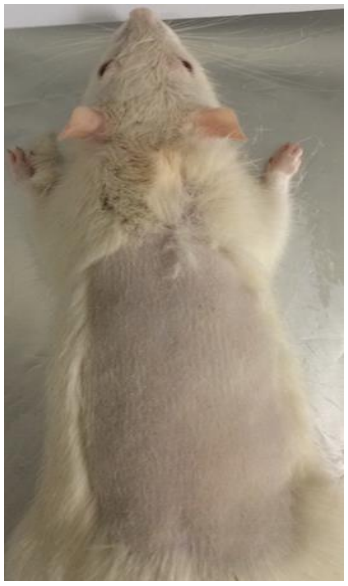

Figure 3 Showing the back of a wistar rat after laser irradiation.
(Day-21, with Control incision).

In order to characterize the degree of tissue repair at the incision site, the intensity of the amide III band at 1247 cm^{-1} relative to the intensity at 1326 cm^{-1} was used. The intensity at 1247 cm^{-1} and 1326 cm^{-1} band which are mostly from the collagen, provides information about collagen deposition and hence, the status of wound healing [3]. The 1326 cm^{-1} consists of a superposition of the desmosine and iso-desmosine bands at 1335 cm^{-1} (components of elastin) and keratin band at 1320 cm^{-1}. Both elastin and keratin are indicators of the status of tissue repair [3].

The intensity ratio at 1247 cm^{-1} and 1326 cm^{-1} calculated for all laser groups was plotted in Figure 3.1 and Figure 3.2 respectively.

DAY-4					
	980 nm	DUAL	1064 nm	CS	CI
	9.91	25.57	24.6	16.5	17.6
	27.24	14.03	41.7	7.51	18.5
	17.7	19.7	23.5		20.3
	20.6	14.5			
	18.29				
MEAN	18.748	18.45	29.93333333	12.005	18.8
STD	6.22419232	5.39740061	10.25050641	6.356889963	1.37477271

Table 3 Raman Spectroscopy Intensity Ratio at 1247 cm^{-1} on DAY-4.

DAY-4					
	980 nm	DUAL	1064 nm	CS	CI
	1.41	10.9	6.24	3.84	5.94
	1.7	8.64	4.14	3.84	7.47
	8.07	10.8	5.46	3.84	
	9.13	11.1	7.37	3.84	
	2.41	5.79	12.6	384	
	3.44	9.37		3.84	
	6.94	8.46		3.84	
	2.93	8.07		3.84	
	2.94	9.6		3.84	
MEAN	4.33	9.192222222	7.162	3.84	6.705
STD	2.90804058	1.696118936	3.259389513	3.84	1.08187338

Table 3.1 Raman Spectroscopy Intensity at 1326 cm^{-1} on DAY-4.

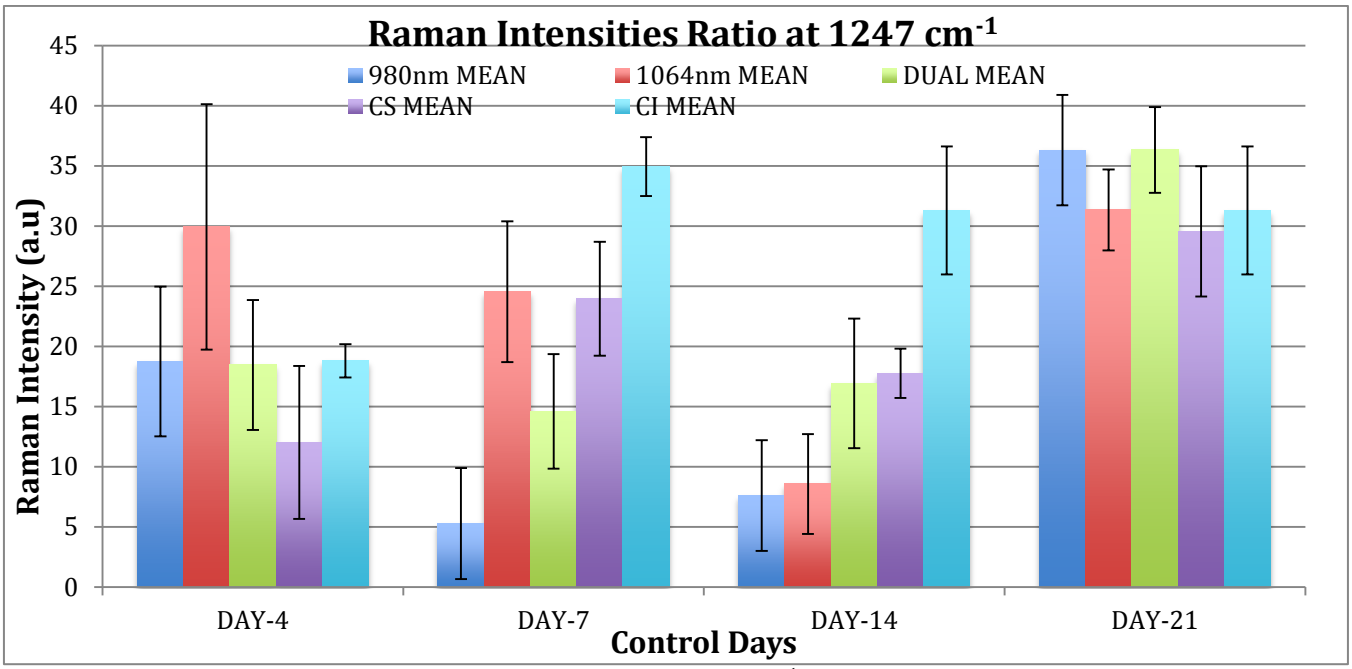

Figure 3.1 Raman Spectroscopy Intensity ratios at 1247 cm^{-1} of skin samples collected on different healing days.

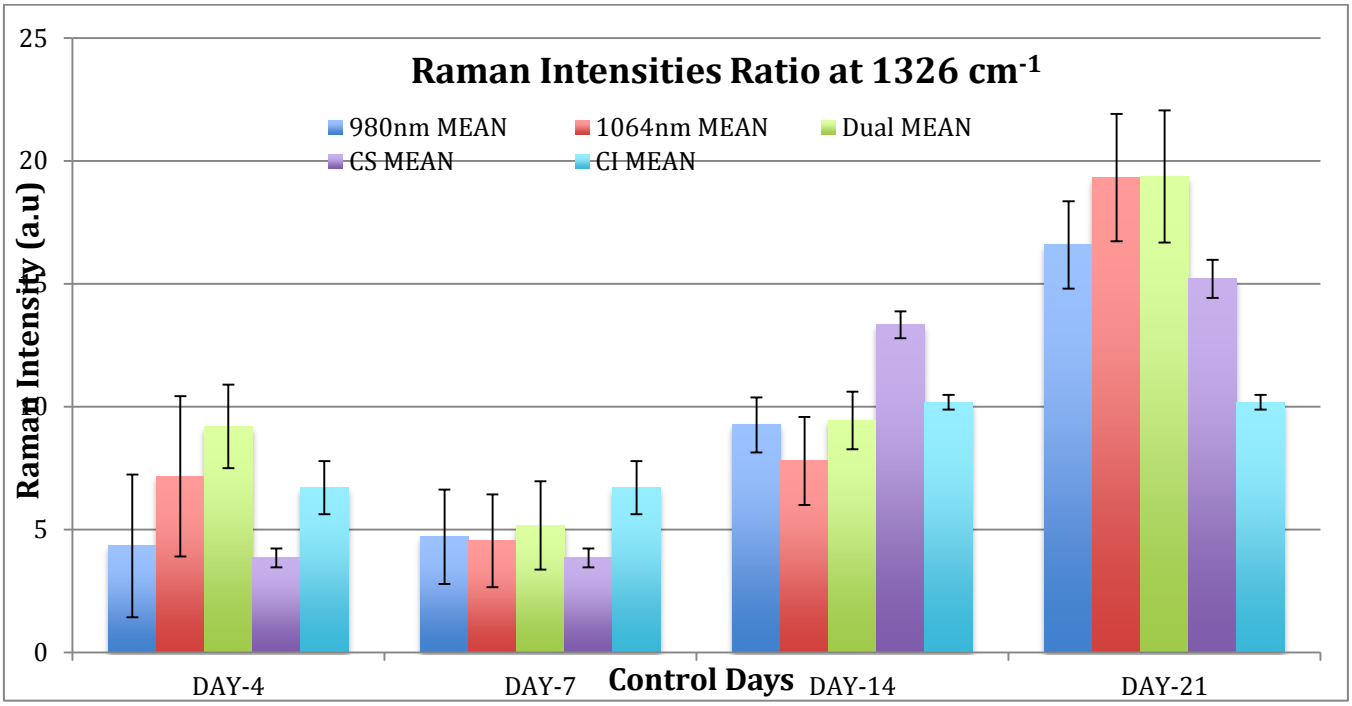

Figure 3.2 Raman Spectroscopy Intensity ratios at 1326 cm^{-1} of skin samples collected on different healing days of the period.

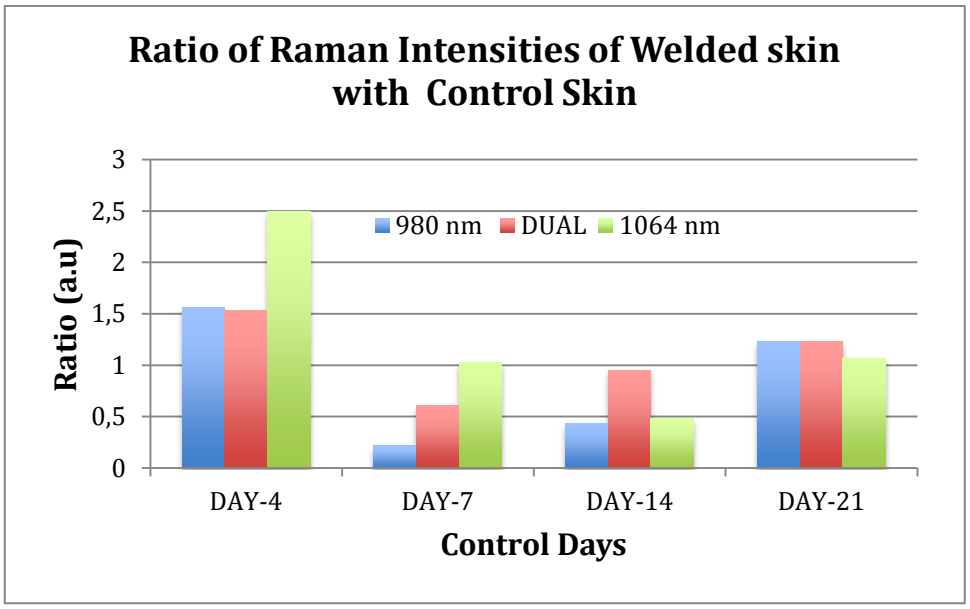

Figure 3.3 Ratio of Raman Intensities of Welded skin with CS.

Controlled laser energy delivery to the skin tissue can result in partial denaturation of collagen helix, accompanied by renaturation and any unwanted effects such as carbonization can be avoided. "This results in the formation of a watertight seal at the welding skin. The ratio of the intensity of the amide III band (1247 cm^{-1}), which are mostly from collagen, to the intensity of the 1326 cm^{-1} band provides information about collagen deposition and hence, the status of wound healing. The 1326 cm^{-1} is a superposition of Raman signals from elastin and keratins [3]. The measurements were taken at day 4, day 7, day 14, and day 21 after operation, times corresponding to major phases in the skin repair process".

T-TEST	1064 nm	DUAL	CS	CI
980 nm	0.18708092	0.94090966	0.339239548	0.986417023
1064 nm	X	0.17953931	0.094695895	0.197528848
DUAL	0.17953931	X	0.357206785	0.907788151
CS	0.0946959	0.35720679	X	0.366141596

Table 3.2 T-Test Among Laser Groups On DAY-4.

T-TEST	1064 nm	DUAL	CS	CI
980 nm	0.00010684	0.04902453	0.054387046	1.00621
1064 nm	X	0.04097091	0.896513111	0.005588654
DUAL	0.04097091	X	0.147777652	0.00926166
CS	0.89651311	0.14777765	X	0.16005577

Table 3.3 T-Test Among Laser Groups On DAY-7

T-TEST	DAY-7	DAY-14	DAY-21
DAY4	0.00472019	0.0121158	0.001076051
DAY7	X	0.40071369	3.75946
DAY14	0.40071369	X	7.67589

Table 3.4 T-Test On 980 nm Laser Daily Comparison.

T-TEST	DAY-7	DAY-14	DAY-21
DAY4	0.36580106	0.67239165	0.00234829
DAY7	X	0.54326497	0.00380807
DAY14	0.54326497	X	0.00013139

Table 3.5 T-Test on Dual Wavelength Daily Comparison.

T-TEST	DAY-7	DAY-14	DAY-21
DAY4	0.4659542	0.05841317	0.836329556
DAY7	X	0.00039601	0.042295441
DAY14	0.00039601	X	3.40542

Table 3.6 T-Test on 1064 nm Laser Daily Comparison.

CHAPTER 4

4.1 DISCUSSION

Immediately after laser tissue welding (LTW), the incision skin experienced thermal exposure due to laser irradiation. Therefore denaturation of collagen fibers was expected, making polymorpho-nuclear neutrophils (PMNs) arrive at the incision site. PMNs are cells that help in developing inflammatory response. The Control Incision (CI) experienced no thermal exposure.

On day 4 post-operation, a significant decrease in the 1247 cm^{-1} to 1326 cm^{-1} ratio for both welded and CS. They exhibited a higher ratio compared to that of the Control Skin (CS). "At this stage of the tissue repair process, the damaged tissue was being removed by the action of macrophages and was being replaced by provisional matrix". The removal of the damaged tissue go hand in hand with tissue denaturation, which caused conformational changes in proteins, such as α-helical transitions to β-sheet and /or to random coils [3].

On day 7 post-operation, the 1247 cm^{-1} to 1326 cm^{-1} intensity for LTW skin continue to decrease, but for CI the ratio was higher than both the CS and welded skin. "The decrease in Raman intensity of the amide III band at this stage is related to the removal of damaged tissue and formation of granulation tissue. LTW at the 7^{th} day showed almost complete wound healing of the epidermis, the presence of granulation tissue in the dermis, and significant inflammatory cell infiltration. The CI exhibited minimal healing of the epidermis, minimal granulation tissue in the dermis".

On day 14 post-operation, an increase in the 1247 cm^{-1} to 1326 cm^{-1} was observed. The ratio was still lower than that of CS. For CI the ratio decreased, which was not significantly different to the 7^{th} day ration. At this point we observed that the incised tissues were

beginning to return to a normal state. Shift to the higher energy indicates the formation of more ordered structural proteins.

On day 21 post-operation, the ratio of amide III band at 1247 cm^{-1}, 1326 cm^{-1} continue to increase, for the 1064 nm laser it's ratio of the amide III band at 1247 cm^{-1} were almost similar to that of the CS. While collagen deposition, as evidence by an increase in the 1247 cm^{-1}, 1326 cm^{-1} ratio started at an early time and progressed more excessively for the CI. The intensity of the amide band III for the CI at 1247 cm^{-1} was higher than that of the CS, reflecting the excessive collagen formation.

4.2 Conclusion and Recommendations

Laser tissue welding showed to be an encouraging method of wound closure, especially when scar formation is undesirable. The intensity ratio of the 1247 cm^{-1} band to the 1326 cm^{-1} band showed to be a positive marker for collagen deposition and for measuring the extent of the healing process. Among the laser used to weld the incised skin, the 1064 nm laser showed to be more effective in pulsed mode at power; 1W, energy; 5J per spot and exposure time; 10 seconds. (Figure 3.3)

The Ratio of the lasers showed that, the 1064 nm laser application was higher than DUAL and 980 nm wavelengths on Day4 and Day7. On Day14 when the tissue began to return to normal state, the 1064 nm showed to be at near-normal surface contour. The 1064 nm showed that it has the ability to produce greater clinical useful effects.

For the future studies, the FT-IR Spectroscopy could be used to evaluate laser tissue welding of the skin and compared with the Raman results.

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APPENDICES

APPENDIX A

Calculation of Mean and Standard deviation of Raman spectroscopy intensity ratio at 1247 cm^{-1}.

DAY-4					
	980 nm	DUAL	1064 nm	CS	CI
	9.91	25.57	24.6	16.5	17.6
	27.24	14.03	41.7	7.51	18.5
	17.7	19.7	23.5		20.3
	20.6	14.5			
	18.29				
MEAN	18.748	18.45	29.93333333	12.005	18.8
STD	6.22419232	5.39740061	10.25050641	6.356889963	1.37477271

DAY-7					
	980 nm	DUAL	1064 nm	CS	CI
	14	14.91	30.7	27.3	37.9
	1.8	9.7	20.7	20.6	33.4
	2.9	19.2	28.6		36.8
	2.5		14.8		31.9
	3.6		25.5		34.7
	6.8		27		
MEAN	5.26666667	14.6033333	24.55	23.95	34.94
STD	4.61894649	4.75741877	5.848333096	4.737615434	2.44397218

DAY-14					
	980 nm	DUAL	1064 nm	CS	CI
	16.6	27.3	9.85	16.3	32.6
	7.37	15.5	14.1	19.2	24.2
	5.19	16.56	12		26.9
	5.93	12.4	4.6		36.7
	3.62	16.6	7.1		37.5
	6.91	13.1	3.7		29.9
MEAN	7.6033333	16.91	8.55833333	17.75	31.3
STD	4.60361452	5.38544334	4.13816586	2.050609665	5.31074383

DAY-21					
	980 nm	DUAL	1064 nm	CS	CI
	29.5	35.7	28.1	22.4	32.6
	39.9	31.7	34.3	34.4	24.2
	34.2	37.8	34.4	33	26.9
	40.7	40.1	27.4	28.4	36.7
	33.5		32.5		37.5
	40.1				29.9
MEAN	36.316667	36.325	31.34	29.55	31.3
STD	4.58799157	3.56872993	3.37238788	5.412023651	5.31074383

Paired comparison among laser groups at Day4.

T-test	1064 nm	DUAL	CS	CI
980 nm	0.18708092	0.94090966	0.339230548	0.986417023
1064 nm	X	0.17953931	0.094695895	0.197528848
DUAL	0.17953931	X	0.357206785	0.907788151
CS	0.0946959	0.35720679	X	0.366141596

Paired comparison among laser groups at Day7.

T-test	1064 nm	DUAL	CS	CI
980 nm	0.00010684	0.04902453	0.054387046	1.00621
1064 nm	X	0.04097091	0.896513111	0.005588654
DUAL	0.04097091	X	0.147777652	0.00926166
CS	0.89651311	0.14777765	X	0.16005577

Paired comparison among laser groups at Day14.

T-test	1064 nm	DUAL	CS	CI
980 nm	0.71348846	0.00949261	0.00955462	1.00955
1064 nm	X	0.01401393	0.01406519	1.26141
DUAL	0.01401393	X	0.7619792	0.000894402
CS	0.01406519	0.7619792	X	0.003042341

Paired comparison among laser groups at Day21.

T-test	1064 nm	DUAL	CS	CI
980 nm	0.06874545	0.99751199	0.08739775	0.111151756
1064 nm	X	0.07411507	0.58940726	0.988265034
DUAL	0.07411507	X	0.08879465	0.111447515
CS	0.58940726	0.08879462	X	0.630464852

APPENDIX B

Calculation of Mean and Standard deviation of Raman spectroscopy intensity ratio at 1326 cm^{-1}.

DAY-4					
	980 nm	DUAL	1064 nm	CS	CI
	1.41	10.9	6.24	3.84	5.94
	1.7	8.64	4.14	3.84	7.47
	8.07	10.8	5.46	3.84	
	9.13	11.1	7.37	3.84	
	2.41	5.79	12.6	3.84	
	3.44	9.37		3.84	
	6.94	8.46		3.84	
	2.93	8.07		3.84	
	2.94	9.6		3.84	
MEAN	4.33	9.1922222	7.162	3.84	6.705
STD	2.90804058	1.696118936	3.259389513	3.84	1.08187338

DAY-7					
	980 nm	DUAL	1064 nm	CS	CI
	3.08	3.39	3.33	3.84	5.94
	4.03	4.64	6.54	3.84	7.47
	6.24	7.67	2.86	3.84	
	3.56	4.96	2.57	3.84	
	3.41		5.11	3.84	
	7.87		6.83	3.84	
MEAN	4.6983333	5.165	4.54	3.84	6.705
STD	1.9213268	1.802156116	1.883422417	3.84	1.08187338

DAY-14					
	980 nm	DUAL	1064 nm	CS	CI
	10.8	10.3	10.7	9.46	9.84
	8.57	9.86	9.84	17.2	10.2
	9.17	8.21	6.01		10.6
	10.7	10.3	6.59		10.3
	8.1	7.8	7.6		9.96
	7.88	10.3	7.28		
	8.86	10.6	6.51		
	9.96	8.15			
MEAN	9.255	9.44	7.79	13.33	10.18
STD	1.12308249	1.17153135	1.78948782	5.47300649	0.29799329

DAY-21					
	980 nm	DUAL	1064 nm	CS	CI
	15.8	24.3	19.5	17.25	9.84
	13.9	17.2	20.1	21.7	10.2
	17.9	17.9	15.1	6.63	10.6
	17.0	17.8	19.7		10.3
	18.3	18.4	22.2		9.96
		20.6			
MEAN	16.58	19.3666667	19.32	15.1933333	10.18
STD	1.7796067	2.68675765	2.59268201	7.74265028	0.29799329

Paired comparison among laser groups at Day4.

T-test	1064 nm	DUAL	CS	CI
980 nm	0.14646145	0.000829717	0.626841362	0.11093681
1064 nm	X	0.248357811	0.084878164	0.79244116
DUAL	0.24835781	X	1.27598	0.10417796
CS	0.08487816	1.27598	X	0.16611207

Paired comparison among laser groups at Day7.

T-test	1064 nm	DUAL	CS	CI
980 nm	0.88824661	0.70786036	0.323722513	0.15240015
1064 nm	X	0.614535613	0.404369417	0.1300836
DUAL	0.61453561	X	0.237795199	0.27230569
CS	0.40436942	0.237795199	X	0.16611207

Paired comparison among laser groups at Day14.

T-test	1064 nm	DUAL	CS	CI
980 nm	0.09178602	0.75190553	0.48237639	0.05636865
1064 nm	X	0.06381702	0.38270621	0.01186619
DUAL	0.06381702	X	0.49717391	0.12575483
CS	0.38270621	0.49717391	X	0.56499095

Paired comparison among laser groups at Day21.

T-test	1064 nm	DUAL	CS	CI
980 nm	0.09190284	0.07114268	0.78737179	0.00108686
1064 nm	X	0.9773304	0.45592034	0.00128847
DUAL	0.9773304	X	0.45115353	0.00035712
CS	0.45592034	0.45115353	X	0.37864029

CURRICULUM VITAE

PERSONAL SUMMARY

Possessing a comprehensive knowledge of Biomedical Engineering projects to required specifications, focusing on business, safety, reliability, quality and sustainability. Also seeking an academic career that will lead me towards the pursuit of knowledge to the highest possible level,

PERSONAL INFORMATION

Name: FARUK MUSTAPHA ABDULLAHI Date of birth: 02/11/1991
Nationality: Nigerian Gender: Male
Email: faruk_abdullahi@gmail.com

Address: No.1 Hayin Mallam Zango Zaria, Kaduna Nigeria

ACADEMIC QUALIFICATIONS

Primary School: A.B.U Staff School Zaria (1994-2002)

Demonstration Secondary School Zaria (2002-2003)

Nigerian Turkish International College (2003-2008)

BSc Genetics and Bioengineering

Fatih University 2008-2013

MSc Biomedical Engineering

Fatih University 2013-2015

WORK EXPERIENCE

Worked as an intern at a Biotechnology Research Institute A.B.U Zaria Nigeria, performed DNA extraction experiments. Also worked at Fatih University genetic laboratory on PCR with some MSc students.

Master's Thesis

Title: Molecular evaluation of skin after Laser Tissue Welding (LTW) using Raman Spectroscopy in vivo.
Supervisor: Asst. Prof. Dr. HASIM OZGUR TABAKOGULU
Description: Laser Tissue Welding using 980nm and 1064nm laser, to evaluate collagen deposition and thermal effect on the skin using Raman and FT-IR spectroscopy.

KEY SKILLS AND COMPETENCIES

- Able to explain technical ideas clearly.
- Experience of preparing projects reports.
- Knowledge of Microsoft word
- Excellent working with a computer windows/OS X.
- Knowledge of Raman and FT-IR spectroscopy.
- Self-motivated with a positive and friendly attitude.
- Providing expert technical advice.
- Giving PowerPoint presentations.
- Management skills

LANGUAGES

- English
- Hausa
- Turkish

HOBBIES AND INTEREST

- Playing Football
- Running
- Reading Newspapers