T.C.
İSTANBUL UNIVERSITY
INSTITUTE OF GRADUATE STUDIES IN
SCIENCE AND ENGINEERING

M.Sc. THESIS

TISSUE WELDING WITH 1940 NM DIODE LASER:

TENSILE TEST ANALYSES

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Department of Biomedical Engineering

Biomedical Engineering Programme

M.Sc. transferred from Fatih University which has been closed

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June, 2016

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Date of Submission : 20 may 2016

Date of Defense : 3 June 2016

To the greatest man in my life …my dear father who I am proud of, and to the greatest woman in my life, my mother who dedicated her life to us…Thank you for your patience, understanding and trust in me.

ACKNOWLEDGEMENTS

I would like to express my gratitude to my supervisor Assist.Prof.Haşim Özgür TABAKOĞLU for his support, guidance, benefit advices, motivation and scientific information related to science in this thesis.

I would also like to thanks Ayşen Gürkan ÖZER for her guidance,experience,effort and assistance in the experiments, she has worked at the laboratory almost daily with me.

Special thanks and appreciation to the staff at the Boğaziçi University Life Sciences and Technologies Implementation and Research Center,particularly veterinary surgeon Arzu TEMİZYUREK ve Ersin ERUZ for the attention,patience and support as well as provision of experimental rats.

Further,special thanks and appreciation also to the staff at the Biophotonics lab, Bogaziçi University Biomedical instutite,namely Ayşe Sena SARP and her colleagues for their tolerance,assistance and attention.

I would also like to thank the laser owners Temel BİLİCİ and Adnan KURT for their contribution.

Finally,respect and love to my family members,my parents and brother for their patience as well as moral and material support at all times.

June 2016 Fatma SARI

TABLE OF CONTENTS

Page

LIST OF SYMBOLS

σ Engineering stress (Pa, N/m^2 or psi)

ε Engineering strain

P External axial tensile load (Pa or Mpa)

A_o Original cross-sectional area of the specimen (mm)

L_o Original length of the specimen (mm)

L_f Final Length of the specimen (mm)

E Elastic modulus or young modulus

ABBREVIATIONS

UTS : Ultimate Tensile Strength
Lab : Laboratory
Max : Maximum
mm : Millimeter
cm : Centimeter
nm : Nanometer
W : Watt
s : Seconds
Min : Minute
ms :Millisecond

LIST OF FIGURES

Page

LIST OF TABLES

SUMMARY

TISSUE WELDING WITH 1940 NM DIODE LASER: TENSILE TEST ANALYSES

Fatma Sarı

Biomedical Engineering Programme
MSc Thesis

Advisor: Asst. Prof. Haşim Özgür TABAKOĞLU

Progress has been made in the use of lasers in medical applications. In particular, the closure of surgical incisions by laser tissue welding has played a significant role throughout the recovery period. In the present study, surgical incisions (1 cm) were made in the dorsal skin of 9 female Wistar albino rats and the welded by a 1940 nm diode laser. Subsequently, the incisions were compared with those in the unwelded rat skin tissue. In this experiment, a period of 14 days (with examination on Day 4, Day 7 and Day 14) days was set for healing. Throughout this recovery period, from each incision a rectangular piece was excised from the dorsal skin of the rats and subjected to a mechanical tensile test. The load, time, extension, stress and tensile strength values of welded wounds were recorded by using a computer based universal testing machine. From the results, the tissue following laser tissue welding was found to be close to the healthy skin tissue. In addition, the laser welded tissue revealed strong mechanical properties, with reliable and closure of wounds immediately at set points within the healing periods.

Keywords: wound healing, skin biomechanics, 1940 nm diode laser, tensile tests

ÖZET

1940 NM DIYOT LAZER İLE CERRAHİ KESİLERİN YAPIŞTIRILMASI:

ÇEKME TESTİ ANALİZİ

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Biyomedikal Mühendisliği Programı
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Danışman: Yrd.Doç.Dr.Haşim Özgür TABAKOĞLU

Medikal uygulamalar için lazer kullanımı geleneksel yöntemlerine göre yaygınlaşmaktadır. Özellikle lazerle cerrahi dokuların yapıştırılması dokunun iyileşme süresi boyunca sağladığı faydalardan dolayı önemli rol oynamaktadır. Bu çalışmada 9 dişi wistar albino sırtı üzerine paralel açılan 1 cm cerrahi kesiler 1940 nm diyod lazer kullanılarak yapışması sağlanmış ve boş deri dokusuyla karşılaştırılmıştır. Deneyde 14 günlük (4.7.14) iyileşme periyodu belirlenmiştir. Belirlenen iyileşme günlerinde her bir kesi sırt yüzeyinden dikdörtgen ekzisyon yapılmıştır. Belirlenen bu süreçlerde deri dokusu çekme testine maruz bırakılmıştır. Kapatılan cerrahi yaraların gerilimi, kuvvet, zaman, uzama ve dayanım değerleri bilgisayar kontrollü bir çekme aleti tarafından kaydedilmiştir. Sonuç olarak, lazerle doku kapanması sağlam deriyle karşılaştırıldığında yakın bulunmuştur. Lazer kullanımın cerrahi kesiklerin 14 günlük iyileşme periyodunda mekanik olarak güçlü ve kapanmada önemli rol olduğu saptanmıştır.

Anahtar kelimeler: yara iyileşmesi, deri, biyomekanik,1940 nm diyod lazer, çekme testi

CHAPTER 1

INTRODUCTION

There have been continuous advances in medical use of lasers for different types of treatment. Laser tissue welding is one such area experiencing major progress, particularly in the field of the dermatology. Other fields in which this clinically applied include cardiothoracic and vascular surgery, dermatology, general surgery (such as gastrointestinal tract operations), gynecology and obstetrics, laparoscopic and endoscopic surgery, neurosurgery, ophthalmology, orthopedic surgery and urology [1].

1.1 Motivation

Laser tissue welding continues to develop as a laparoscopic, endoscopic and microsurgical method in surgery [17].

Conventional mechanical techniques with a long history include suturing, stapling and the use of clips. However, these difficult methods cause many problems. In addition as a traditional closure procedure, biological adhesives are available e.g. fibrin glue which is used effectively for hemostasis. However bio-adhesives exhibit tissue cytotoxicity and are associated with absorption problems during the normal wound healing process and they also cause allergic reactions and foreign body granulomas. The use of laser welding closure as an alternative to traditional methods, reduces tissue injury and foreign-body reaction and inflammation (redness and swelling),granuloma formation (development of a grain-like tissue lesion),scar formation and stenosis (abnormal narrowing or constriction of tissue lumens) and bleeding, as well as improves cosmetic appearance and hastens wound healing compared with other methods. This laser application provides immediate water absorption, early re-epithelialization, and maximum mechanical strength.However,there has been little research on the biomechanical properties of the skin when using a diode laser system. Therefore, the main aim of this study was to examine the details of the mechanical properties of the welded tissue. In particular, this study focused on comparing welded and unwelded skin tissues at the 4, 7 and 14 days in the healing period of.

The aim was to achieve wound closure in rat skin tissue using a 1940 nm diode laser and to examine the mechanical properties of the skin by comparing welded and unwelded skin tissues.

1.2 Objectives

1. To apply a 1940 nm laser for welding surgical incisions and shed light on whether a laser with a light of this wavelength is appropriate for clinical use.
2. To investigate the biomechanical properties of 1940 nm laser welded skin by tensile test analysis in terms of stress-strain relationship, tensile strength, breaking strength.

3. To examine laser welded surgical skin incisions during a recovery period of 14 days and to apply the above mentioned techniques throughout the healing periods.

1.3 Physical Properties of the Skin

The skin is the largest organ of the body and has many physiological functions [3]. It plays a major role providing mechanical strength. It consists of 3 layers, epidermis, dermis and subcutaneous tissues (hypo-dermis).The mechanical behavior of the skin includes non-homogeneous, anisotropic and non-linear visco-elasticity at the macroscopic level [2, 4].

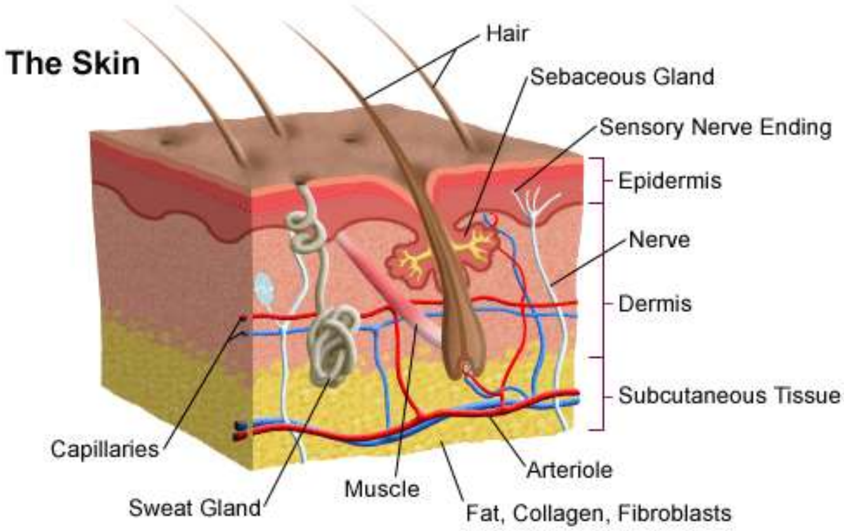


Figure 1.1 Structure of skin layers (dermis, epidermis, and subcutaneous layer [5].

The epidermis is the outermost layer of the skin. It is composed of keratinocytes, which produce keratin protein and is tens to hundreds of micrometers thick. It has no blood vessels.

The dermis is underneath the epidermis and is a few hundred micrometers to several millimeters thick. It plays an important role in maintaining the mechanical integrity of the skin. This layer also contains fibroblasts, which produces the structural proteins collagen and elastin and has larger blood vessels. These features support the absorption and scattering properties of the dermis layer.

The Subcutaneous layer (hypo-dermis) is underneath the dermis. It contains the adipose tissue, large blood vessels and connective fibrils [6].

1.4 Mechanical Properties of the Skin

Collagen and elastin are the main components of most biological connective tissues. They have different mechanical properties in terms of their strength and elasticity. Collagen is an extracellular protein that is responsible for strength and flexibility .It accounts for 75% of the dry weight of the skin, 18% -30% of the dermis volume and 25% –30% of proteins in biological tissues. Collagen forms a fibrous structure and provides mechanical support to the tissue because of the covalent crosslinks between collagen molecules. When tissues are exposed to laser irradiation, the heat-labile intramolecular crosslinks are broken, collagen denaturation occurs, fibrils shrink and the tissue itself contracts. Therefore, collagen is the main factor in welding because its mechanical behavior changes during the thermal process. The other major component of the skin, elastin, is found at a low level (0.1% of the dry weight of the skin), but it is resistant to denaturation and is thermally stable. Therefore, it cannot be addressed in the welding [7,8].

The mechanical properties of the skin are determined by the dermis. In this layer, collagen is responsible for mechanical strength and elastin is responsible for elasticity. The highest degree of elasticity is demonstrated in the epithelial region and adjoining connective tissue in the dermis. Changes in skin thickness are also important. For example, there is 16% decrease in skin thickness in the dorsal region under mechanical stress, which is related to retraction of the epithelium in the dorsal region and collagen fibers concentration. The mechanical properties of the skin are thus related to skin thickness [26].

1.5 Biomechanics of Laser Irradiated Tissue

1.5.1 Tensile Tests

Tensile tests are used in engineering applications. The uniaxial tensile test is mechanical test (Figure 1.2) a basic and universal way of the determining mechanical parameters such as ultimate strength, stress, strain, yield strength, elongation, and Young's modulus(elastic modulus)[9].Tensile properties are important for clarifying the mechanical behavior of materials under a certain load [10].

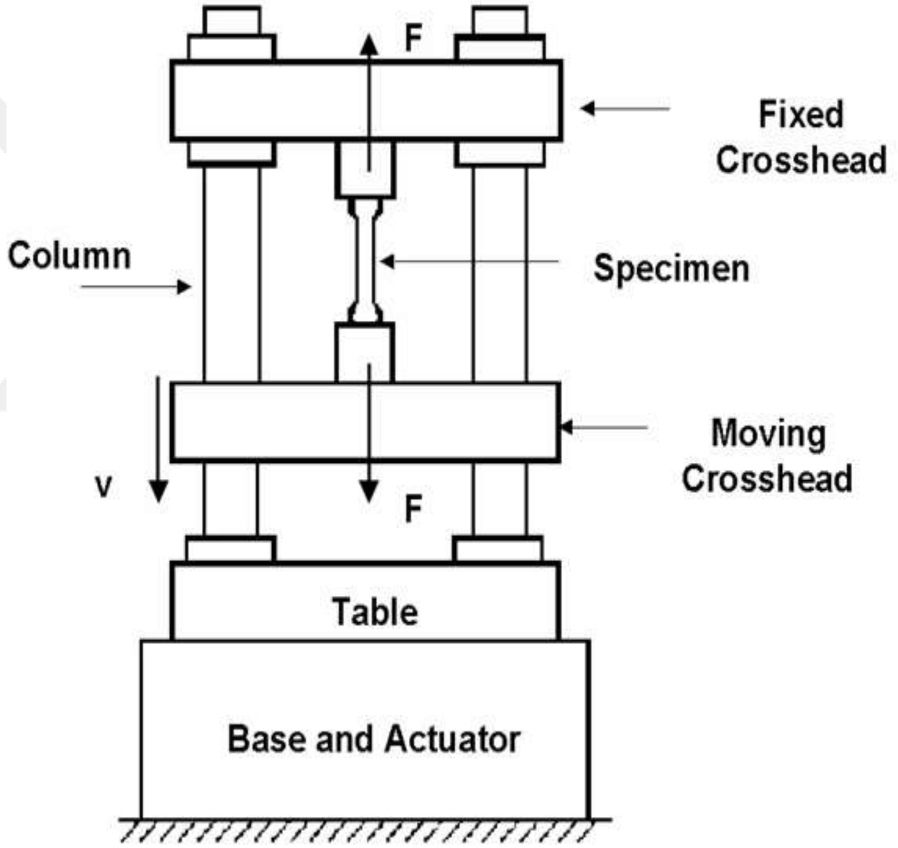


Figure 1.2 Schematics of the universal ultimate tensile test machine [11].

Deformations of the skin tissue during tensile test analysis are shown in Figure 1.3

1. The original shape of the material, when no load is applied.

2 .The materials are under uniform elongation.

3. The maximum load point and ultimate tensile strength (UTS).

4 .The necking point (plastic deformation occurs).

5 .Fracture of the material (breaking length).

6. Final length [11].

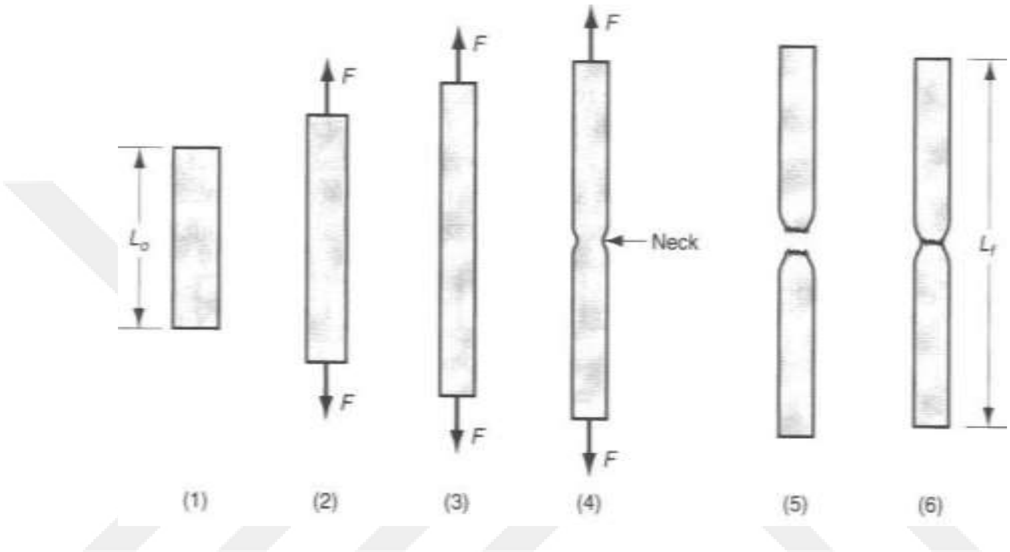


Figure 1.3 Basic principles of tensile test applications [11].

1.5.2 Stress - Strain

Tensile stress is the measurement of force per unit area. Its unit is Pascal (Pa) or N/m^2 (SI Metric Units) or (pounds per square inch (psi) (formula 1.5.2.1).

$$\sigma = \frac{P}{Ao} \qquad (1.5.2.1)$$

Tensile strain is the measurement of change per unit length due to force (formula 1.5.2.2)

$$\varepsilon = \frac{Lf - Lo}{Lo} = \frac{\Delta L}{Lo} \qquad (1.5.2.2)$$

When a material is exposed to small stresses, the bonds between the atoms are stretched (in the skin tissue the collagen fibers are stretched).If the stress is removed, the material returns to its original condition. This deformation is called the elastic deformation. In contrast, at higher stresses after which the material cannot return to its original shape, the plastic deformation occurs [12, 13].

Figure 1.4 is a stress-strain diagram showing collagen fiber elongation due to increasing stress. The behavior of the skin upon deformation is shown in parts I, II and III. In part I, in the absence of a load, the collagen fibers appear wavy and crimp. In addition, the un-welded skin behaves isotopically and can undergo large deformations of the individual collagen fibers, requiring low stress without the stretch of the fibers. Therefore, in phase I the collagen fibers play a role in stretching mechanisms. At this stage, the stress to strain relationship is linear. Here only elastic deformation occurs.

In part II, the skin is under tension .The increasing load causes collagen fibers to line up and crimped fibers elongate and resist the load. In part III, under high stress, the crimp is lost and the collagen fibers become straighter. Under even higher stresses, the tissue becomes inflexible and the straightened collagen fibers resist the load strongly, at this point UTS is exhibited. Beyond this stage, the fibers begins to rupture [14].

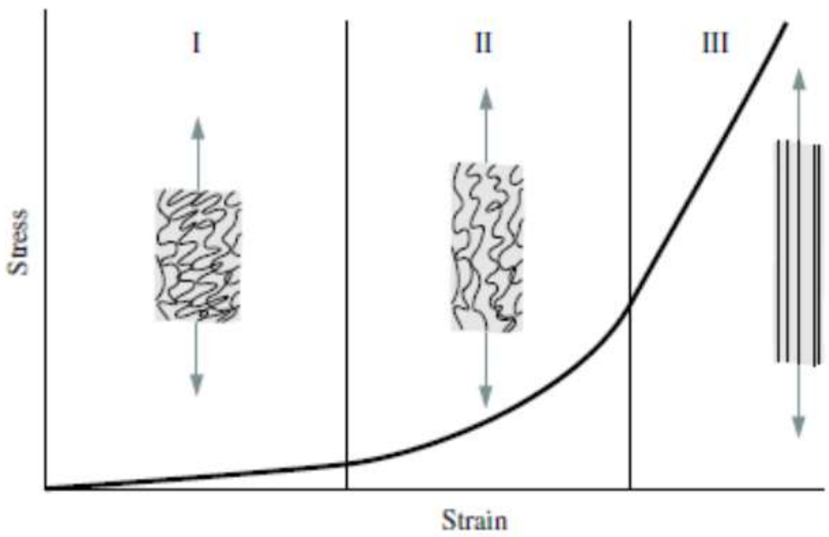


Figure 1.4 Typical stress-strain curve of skin collagen fiber morphology [14].

A stress-strain diagram and points of damage in material are presented in Figure 1.5 [13].

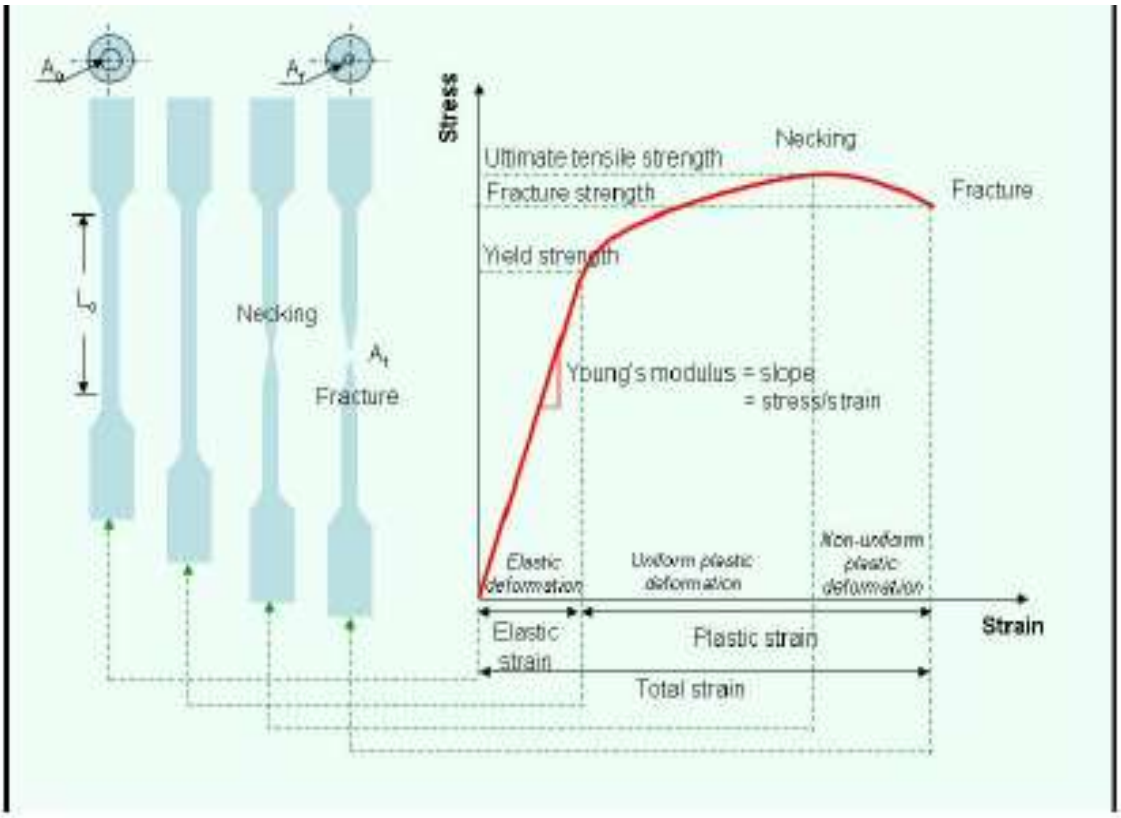


Figure 1.5 Stress-strain diagram of the material under uniaxial loading [13].

Biological materials exhibit viscoelastic behavior. When such materials are subjected to a load, the viscoelastic behavior changes e.g., the collagen of proteins and water. The slope of stress-strain increase can be observed. This behavioral characteristic is observed in various biological tissues such as tendons and ligaments (Figure 1.6) [22].

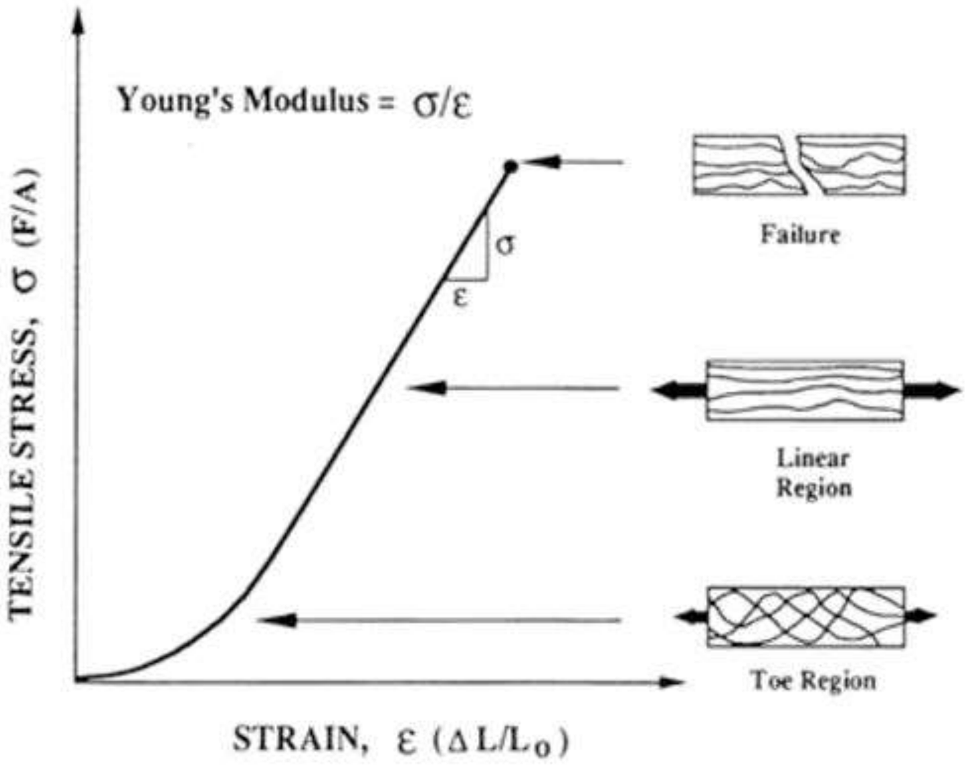


Figure 1.6   Stress-strain curve of tendon or ligament connective tissue [32].

1.5.3   (UTS): Maximum Tensile Strength

Continuous loading causes to an increase in the stress on a material and eventually causes plastic deformation, as can be seen in the stress-strain curve. With the application of continuous loading, the stress-strain diagram shows that the maximum stress occurs before necking. The highest stress at that point occurs at the time of UTS [13].In case of ductile materials, In the deformation causes forming a neck in tensile strength. Less ductile materials fracture before they exhibit necking. At this point, the fracture strength is the tensile strength [10].

1.5.4 Breaking Strength (Fracture)

The maximum level of stress occurs when materials rupture, as shown in the stress-strain curve. The breaking strength is more commonly known as the tensile strength. This is when materials break or deform under the applied load. This point is the necking region [13].

1.5.5 Elastic Modulus (Young's Modulus)

The modulus of elasticity or elastic modulus is the measurement of the stiffness of a material. In the elastic region, which is the linear region in the stress-strain curve "Hooke's Law is obeyed" and the stress to strain ratio is constant ($\frac{\sigma}{\varepsilon} = E$).The slope of the stress-strain curve is the Young's modulus which is a characteristic property of a material. When the modulus of elasticity increases, the specimen's tensile strength and yield strength can also increase [10, 13].

1.5.6 Yield Strength

If the loading continuous in the elastic region in the stress-strain curve , yielding consists at the beginning of the plastic region. The permanent deformation occurs in the materials [10].

1.6 Laser-Tissue Interactions

In biological and medical applications of lasers, the laser and tissue affect each other. The photo thermal effect occurs because of heat generation, heat transport and thermal relaxation [30].

In clinical laser treatments, photo thermal interactions are utilized. When laser light interacts with the tissue, the photo thermal reactions occur [28]. In tissue hyperthermia, coagulation, carbonization, and vaporization occur [31]. Chromophores in the skin (oxyhaemoglobin, haemoglobin, melanin and carotene) absorb irradiated light from a laser with a specific wavelength. The increment laser light is converted to heat, resulting in a local temperature increase, known as heat generation. For example, at room temperature (25°C), the tissue temperature is normally 37°C and if heat is applied, a clear color change is indicative of hyperthermia and cell injury, inflammation and macromolecule deformation occur between Van der Waal's bonds. When the temperature reaches at 60°C, coagulation occurs. In addition, the DNA and protein structures are broken and the excessive thermal heat on water at 100°C causes its vaporization, which damages cells and blood vessels. Because of this the levels of scattering and absorption of light are important for penetration depth. Thermal relaxation means that laser irradiated tissues loses heat before conduction of the heat surrounding tissues [29]. On the other hand, heat transport means that heat is conducted through biological tissues.The irradiated tissue exposed the heat loss when conduct with the unexposed tissue [30].

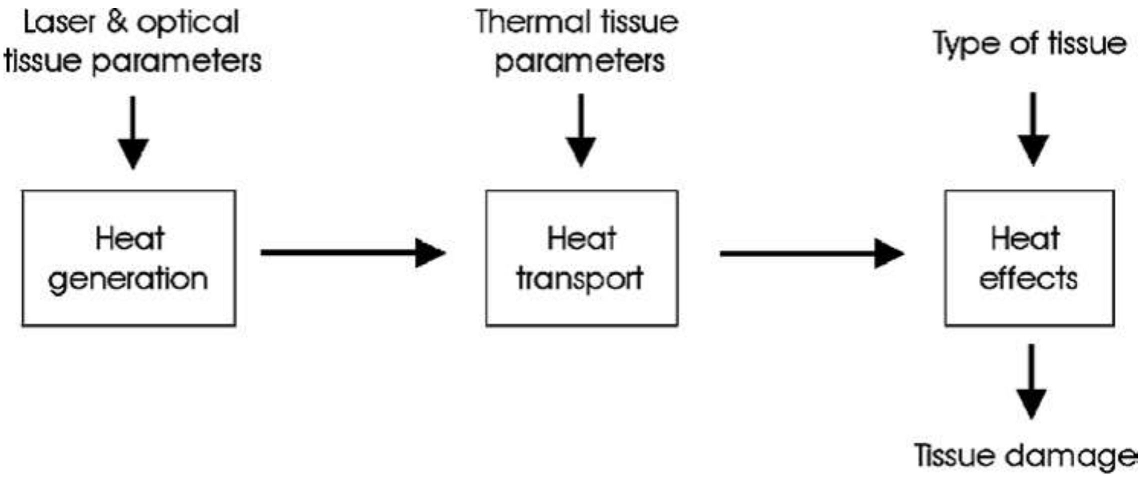


Figure 1.7 Parameters that influence the laser's thermal interaction properties with the tissue [30].

1.7 Literature Review

J.Michael Lee [38] reported that beyond the 1960s, i.e following the development of the biomedical engineering discipline ,mechanical engineering methods were used in tissue mechanics studies.

In addition, Talmor et al.[17] reported laser tissue welding as an the alternative approach that can be applied in many fields. In 1960, Geeraetes performed the first study on lasers in clinical context to research the spectral absorption characteristics of ocular fundus. Laser tissue welding was successfully performed for the first time in 1979 by Jain and Gorisch who repaired the small blood vessels of rats using an Nd:YAG laser.

Wanda et al.[18] also reported that in wound healing, one of the goals is to measure the resistance of the tissue to external forces. Most previous studied reviewed the breaking and tensile strength under tension. Therefore the models of rats, which are loose-skinned, are useful for studying elasticity associated with the skin anatomy.

F. Xu .et al.[15, 20] suggested that the tensile behavior of the skin tissue is the most studied issue in this field, as it has been focused on in many reviews. Upon the denaturation of the collagen tissue in a thermal process, the structure as well as mechanical properties of collagen change. Therefore, a stress-strain diagram can be used to show the mechanical relationships.

Fried et al.[16] investigated the strength (tensile) of welded incisions during the healing period at 6, 10, 14, 21, and 28 days postoperatively. Welding was performed by a CW Nd:YAG laser at 1.06 µm, in adult female albino guinea pigs. Welding was performed on wounds of 2 cm full thickness to parallel to the spine with a power of 10 W, velocity of 47.6 mm/s, cooling time 8 s, laser spot of 4 mm and operation time of 10 min per incision. In the control group, suture alone was applied to the wounds. The results revealed that welding is associated with a significant improvement in tensile strength compared with suturing ($p<0.01$).

Živčák et al.[19] reported that a tensile test is a suitable biomechanical test to measure tensile strength, they studied this to determine the mechanical properties of skin wounds during healing for 7 days. Forty-two female Sprague-Dawley rats were used and (7 animals were per group).Two longitudinal incisions were created (3.5 cm long, 3 cm apart) to the dorsal skin of the rats. The tensile strength versus time for healing and the tensile strength at the breaking point were investigated. The results showed that the tensile properties of the skin wounds improved at 24 h after surgery as a function of fibroblasts .Except 6th and 7th healing period, others have no significant difference.The 6th and 7th day $p<0.0001$.

Aylin Bekem et al.[21] reported on biomechanical analysis aimed at determining parameters of materials, including skin force(N),elongation(mm),tensile strength and elastic modulus (E).Using force elongation diagrams, stress-strain curves can be obtained. In addition, the elastic modulus can be determined by measuring the slope of a stress-strain curve.

Rodney et al. [22] demonstrated while stress was increasing according to applied strain. Therefore, stress was bending and decrease slowly, that means materials become stiffness to reach maximum applied strain. The characteristics of viscoelasticity were also shown to be dependent on the increment in stiffness with the strain applied to materials such as skin and tendons in biological tissues.

Chachra et al.[23] suggested that stress was increased with the increase in tensile strength. By using load-extension curves, the stress-strain curves are obtained and UTS which was defined as stress at the fracture, strain at the fracture, and elastic tissue modulus (the maximum slope of the linear part in the stress- strain curve).

In addition, Chen et al. [24] demonstrated that the skin is a non-homogeneous, anisotropic, non -linear and viscoelastic material when exposed to stress .If the stress rate is increased, UTS and fracture strain also increase .

Gulsoy et al.[25] also studied the effects of a 980 nm diode laser on the skin tissue. They used 13 healthy male Wistar rats (3 pairs incisions of 1 cm full thickness, over muscular layer ,bilateral and parallel to the spinal cord) using a laser with a power of 6 W and duration of 400 ms for welding. Analysis during the healing period was performed at 1, 4,7,14 and 21 days to compare welded tissue with the tissue subjected to suturing as a control.

Zak et al. [26] suggested that the skin thickness decreased by 12 % in the dorsal region because of the retraction of the epithelium and the high concentration of the dermis. Furthermore, when the skin stretched, collagen fibers arrange themselves parallel to each other leadings to an increment in local friction to prevent further movement. If the strength becomes excessive, the skin may tear.

DominiqueP.Pioletti[36] mentioned that when mechanical tests were performed, in stress-strain curve occurred and the stress was decreased under constant strain.

Eshel proposed [37] that the mechanical response of the skin is nonlinear, anisotropic and time dependent. The stresses to strain curves are nonlinear at the mean strain rate. In addition, elastin causes the skin to be looser. Therefore, in a mechanical test, the skin loses its elasticity and undergoes larger deformation, as shown by morphological observation.

In another study, Wong [39] demonstrated that the relationship between the structure and function of the skin is extremely important for understanding skin behavior under mechanical loading. Therefore, viscoelasticity is important for the mechanical response. In addition, viscoelasticity results in a loss of strain energy to the viscous component as the tissue deforms. The skin structure was shown to change under the mechanical stress which causing the orientation of fibers to undergo mechanical deformation.

CHAPTER 2

MATERIALS & METHODS

2.1 1940 nm Diode Laser System

A projected and manufactured 1940 nm diode laser system was used for the irradiation experiments. The laser system was designed and developed (Figure 2.1) by Omnibil Technologies Ltd. and controlled by the Computer Lab View interface (Figure 2.2). During the experiments, the following laser parameters were used:

Applied current: 1500 mA,

Laser maximum output: 600 mW

Spot size of laser beam: 2.5 mm

Duration of application: 3000 ms

Operation Mode: continuous wave (CW)

Figure 2.1 The 1940 Diode laser system. The Laser connector to the power supply, the power supply, the pilot beam point and the laser beam output are shown. The laser optical parameters are determined inside the laser

Figure 2.2 Computer based 1940 nm diode laser lab view interface.

2.2 Animal Preparation

The experiments were performed following a protocol approved by the Institutional Animal Research and Care Ethics Committee at Bogazici University (coded reference:2013-05-08).The research was performed at the Bogaziçi University Life Sciences and Technologies Implementation and Research Center, in the experimental animal care and production unit (vivarium).In the experiments,9 randomly selected female wistar albino rats were used (5-6 months, 170-200 g). They were housed in plastic cages under 12 hour light-12 hour dark cycle in a temperature-controlled medium (22±2°C). Sufficient food (pellet feed) and water were provided to them. The rats were divided into 3 groups (n=3 in each group).The rats were anesthetized with ketamine (alfamine %10,1 ml, 100 mg ketamine HCL) + 2 cc xylazine (alfazyne %2) by intraperitoneal injection at a level depending on their weight.

2.3 Operation

The dorsal hairs of rats were cleaned. Four pairs of full-thickness 1 cm long incisions were created in parallel to the spinal cord until the muscle visible. The incisions were performed in sterile conditions with no.12 surgical blades to limit bleeding. To prevent possible light absorption in the skin rather than the tissue, the remnant blood was cleaned away. The incisions were irradiated using the 1940 nm diode laser system (Figure 2.3) (600 mW, laser beam spot size: 2.5 mm, 4 continuous shots per 3 incisions).During the laser treatment and surgery, a water pocket was put on the tails of the rats.The unwelded skin tissue was used as a control group [33].

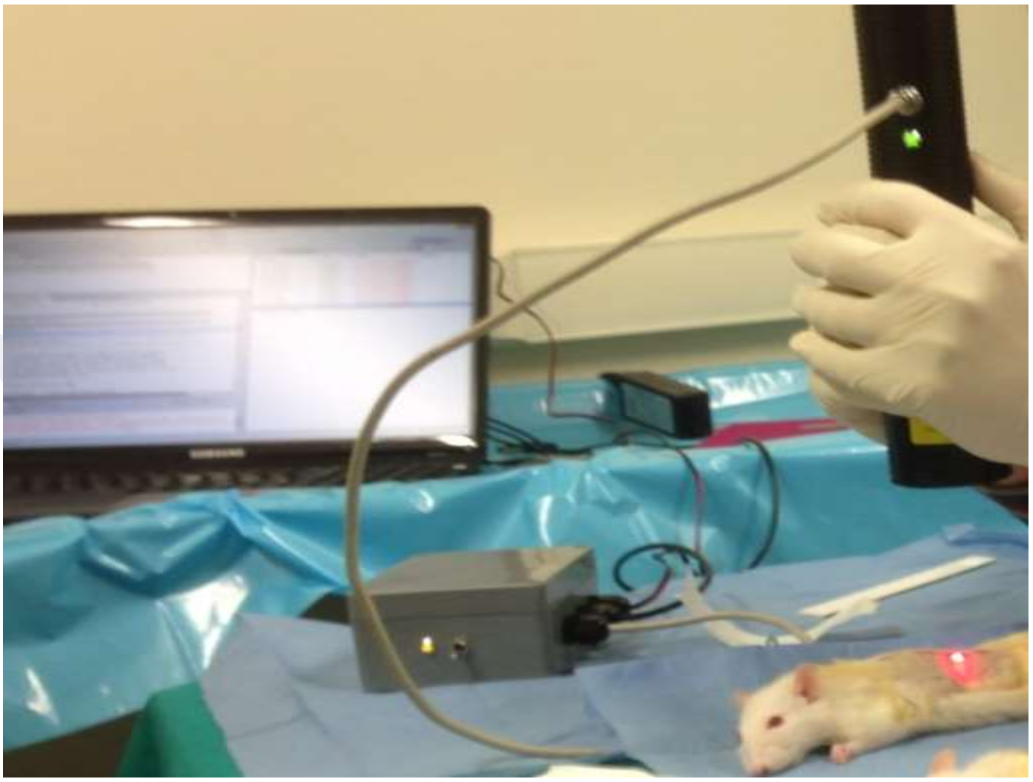
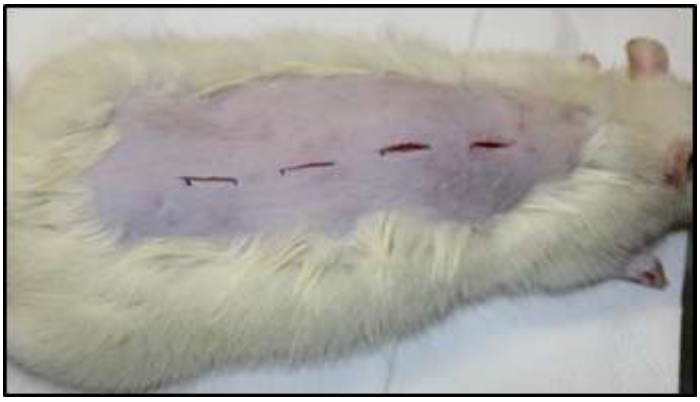


Figure 2.3 1940 nm diode laser applications and laser system apparatus



(a)

(b)

Figure 2.4 (a) incisions before laser applications on Day 14, (b) incisions after the laser application

2.4 Post-operative Analysis

After wound closure, no food or water was given for 24 h. The thickness of the length was measured by digital caliper (Digital Mitutoyo).During the recovery period, the wound infection; hair formation and wound closure were examined and photographed. The healing period set as 14 days(with examination Day 4,Day 7 and Day 14).The rats were sacrificed with CO_2 on these particular days and a rectangular piece of their skin was excised from the dorsum for tensile testing (Figure 2.5).The excised skin was immersed in saline solution at room temperature.

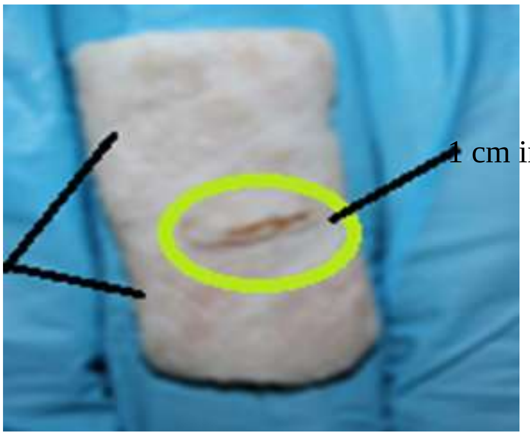


Figure 2.5 Excised rectangular skin tissues on Day 7 before tensile analysis. The 1 cm incision and grips holding the tissue in place 3 mm above and below the incision.

2.5 Tensile Analysis

Tensile analysis was performed Bogazici University at the Bio photonics lab. Biomedical institute. The rectangular excised skin tissue was placed between the grips at a distance of 3-4 cm (Universal testing machine LF plus Lloyd Instruments, UK) for tensile testing and controlled using a computer based program with Nexygene Plus software.To avoid slippage of the skin tissue through the jigs in the grips, a large grained rubber was used to fix it in place. The loading capacity of the machine was 250 N and each the skin tissue sample was tested at a speed of 0.02 mm/s .The load(N) andtime (s) at the breaking point were recorded with NexygenPlus software (the breaking point was when the 1 cm incision first open)(Figure 2.5).

2.6 Statistical Analysis

Statistical analysis was performed using t-test to show the significance of differences between the groups. $P< 0.05$ was considered to represent a statistically significant difference

CHAPTER 3

RESULTS

3.1 Tensile Tests

Mechanical properties of 1940 nm diode laser welded rat skin tissue have been investigated by using Universal Testing Machine. Tensile test has been performed and results were recorded by Nexygen plus Software.

Load (N), Tensile Strength (Mpa), Load at maximum load (N), Breaking point(N), Extension and Stress (Mpa) to Strain (mm) was measured.

Analysis was performed comparatively throughout 14^{th} days healing periods on the determined specific control days (4, 7, 14). Below Load (N) to healing period was presented in figure (3.1).The load performed the skin tissue change with Day-4 4.5 ± 2.1 N ,Day-7 3.7±2.0 N and Day-14 10.01 ±2.0 at healing periods. The 14^{th} days were the highest value in the mechanical testing. The significantly differences was seen $p<0.05$ (table 3.1).

Table 3.1 Load t-test measurement in the healing periods

Comparison	Load T-test
Day-4 - Day-7	0.977899035
Day-7 - Day 14	0.035455405
Day-4 - Day-14	0.000862744

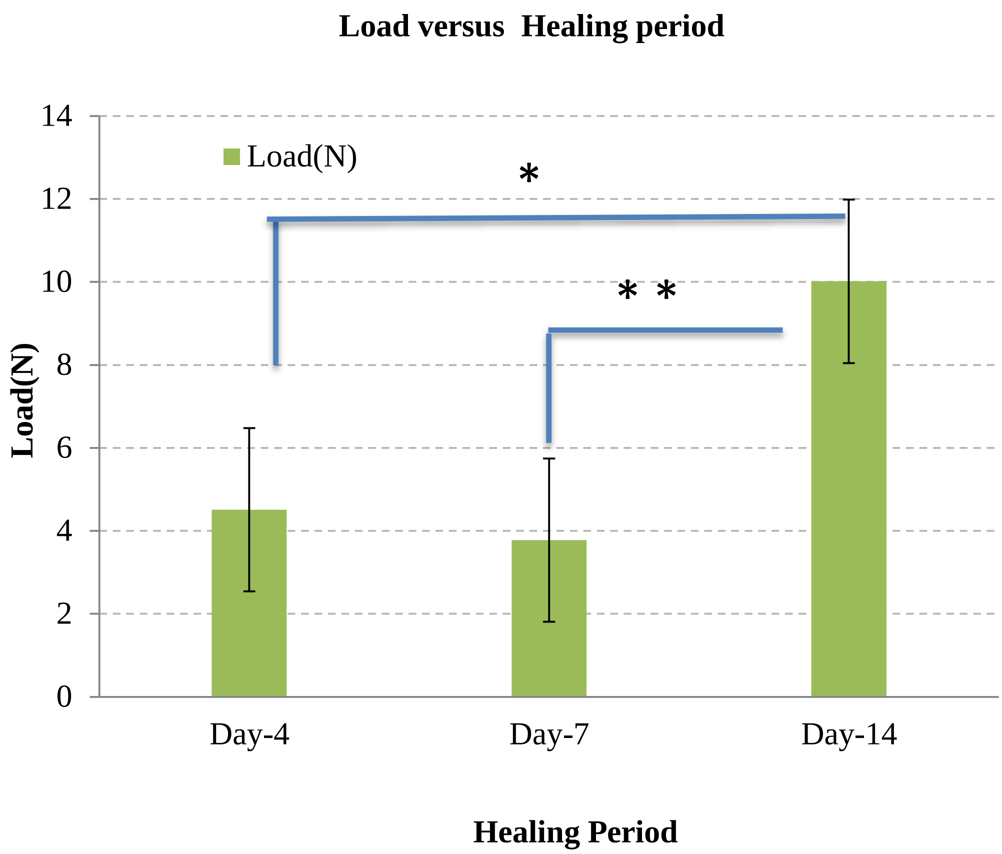


Figure 3.1 Load (N) in the healing period is shown. The load was increased at 4, 7 and 14 day's postoperatively.*A significant difference was observed between Day-4 and Day-14 groups. **A significant difference was observed between Day-7 and Day-14 groups.(t-test: $p<0.05$)

Below Tensile strength (Mpa) versus to healing period.The tensile strength were increasing significantly Day-4 0.05 ± 0.02 Mpa.Day-7 0.05±0.01 N and Day-14 0.08 ±0.01 due to recuperation days. In Day 4-Day 7 p>0.05 no significant differences was seen. However, Day7-Day14 and Day4-Day14 was statistically different p<0.05(figure 3.2)[16,27]. T-test results were shown in table 3.2.

Table 3.2 Tensile strength t-test measurement in the healing period

Comparison	Tensile strength (Mpa)
Day-4 - Day-7	0.969364064
Day-7 - Day-14	0.006804566
Day-4 - Day-14	0.025670722

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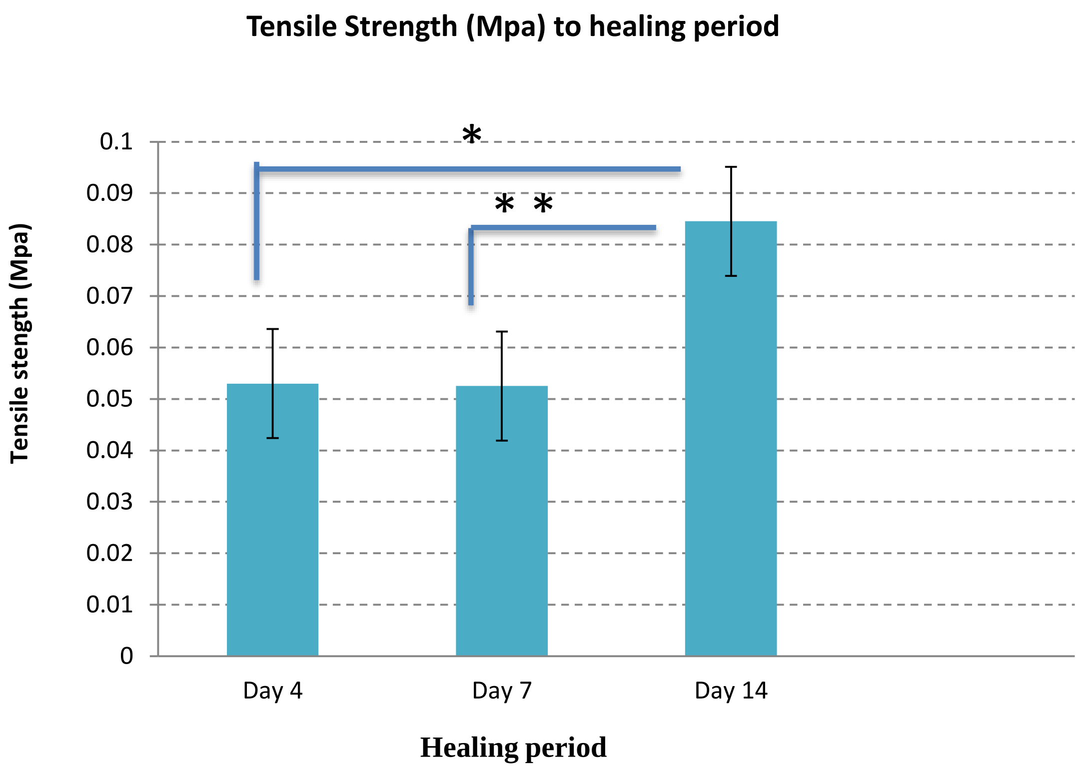

Figure 3.2 Mean tensile strength of wound during healing period of rat skin and standard deviations for 14th days. A significant difference was observed between Day-4 and Day-14 groups. **A significant difference was observed between Day-7 and Day-14 groups.(t-test: $p<0.05$)

The max stress (Mpa) of the healing periods was represented in Figure 3.3.In Day-4 0.04 ± 0.012 Mpa.Day-7 0.04 ± 0.011 N and Day-14 0.05 ± 0.008 at recovery days. The max stress was highly in Day 14 compare with the other days. Also, 4th day result is higher than 7th day. The standart deviations were also showed in the figure (3.3).

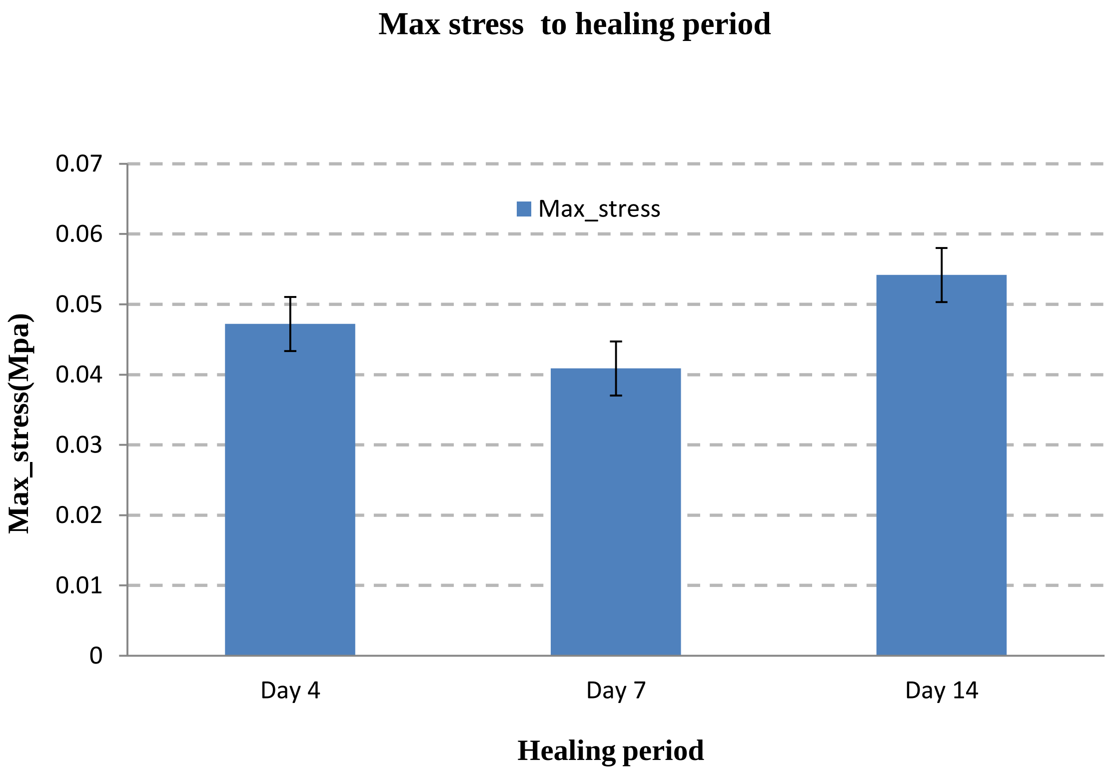

Figure 3.3 Maximum stress on particular reopening 4, 7 and 14 days. The highest maximum stress was observed on Day 14 of the healing period.

Below The load versus time curve was given in figure 3.4. The mechanical behavior under the load was shown in the particular welded and unwelded skin tissue. Increment of the load can be seen in 4,7,14 days.14th days of load was the highest compare with other days 10.01±6.5 N ,the 4th day was 4.5 ± 3.07 N and 7th day was 3.7±2.1 N. In Day 4-Day 7 $p>0.05$ has no meaningful differences. On the other hand,Day7-Day14 and Day4-Day14 was statistically different $p<0.05$.Load T-test results were exhibited in table 3.3.

Table 3.3 Load t-test measurement in the healing periods

Comparison	Total Load T- test
Day-4 - Day-7	0.060305551
Day-7 - Day-14	1.21108E-11
Day-4 - Day-14	1.56986E-09

Total Load versus time mechanical behaviours in 60 seconds

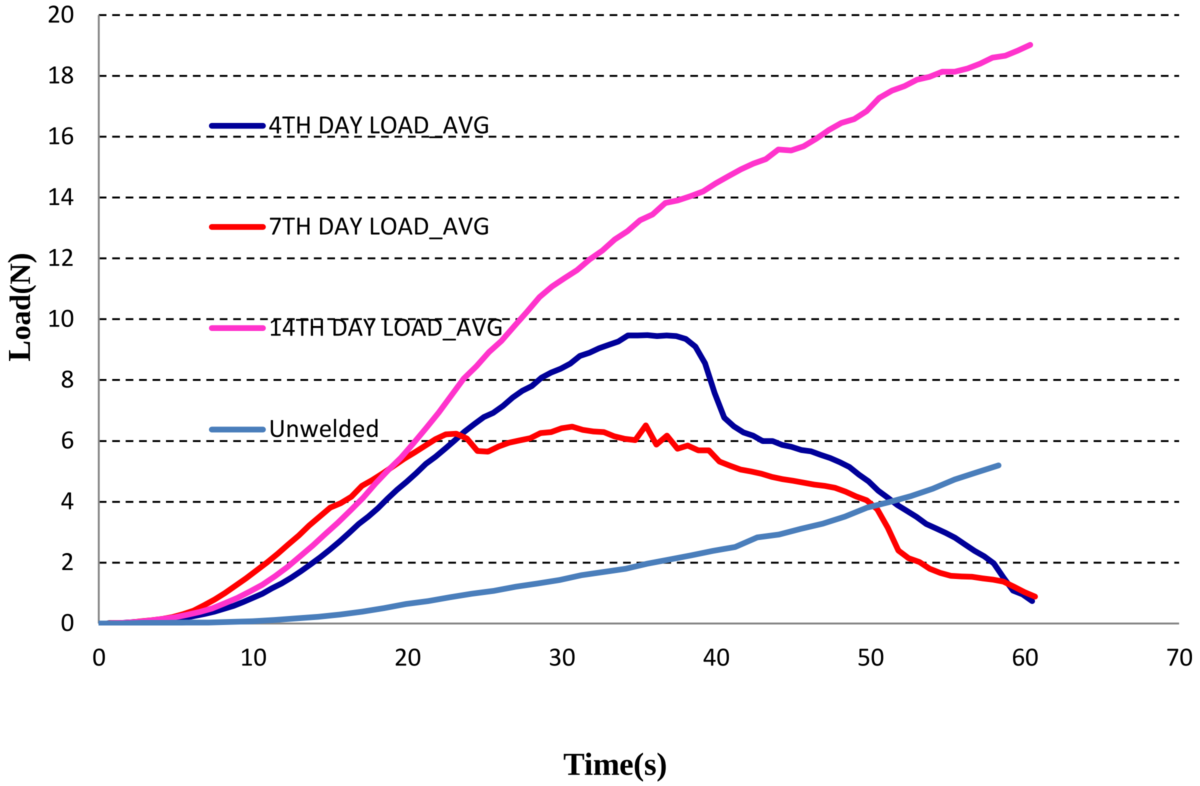

Figure 3.4. Total load versus time in the postoperative days in welded skin tissue and control unwelded skin tissue within 1 minute. Statistically significant differences were demonstrated at $p<0.05$.The unwelded skin tissue exhibited linearity.

The maximum stress (Mpa) comparison to the Tensile strength(Mpa) was represented in the figure 3.6.When the max stress was increased, the tensile strength increase. The max stress Day-4 0.04 ± 0.012 Mpa. Day-7 0.04 ± 0.011 N and Day-14 0.05 ± 0.008. Tensile strength Day-4 0.05 ± 0.02 Mpa.Day-7 0.05±0.01 N and Day-14 0.08 ±0.01.The significantly meaningful differences obtained in tensile strength p<0.05 was shown Table 3.2.

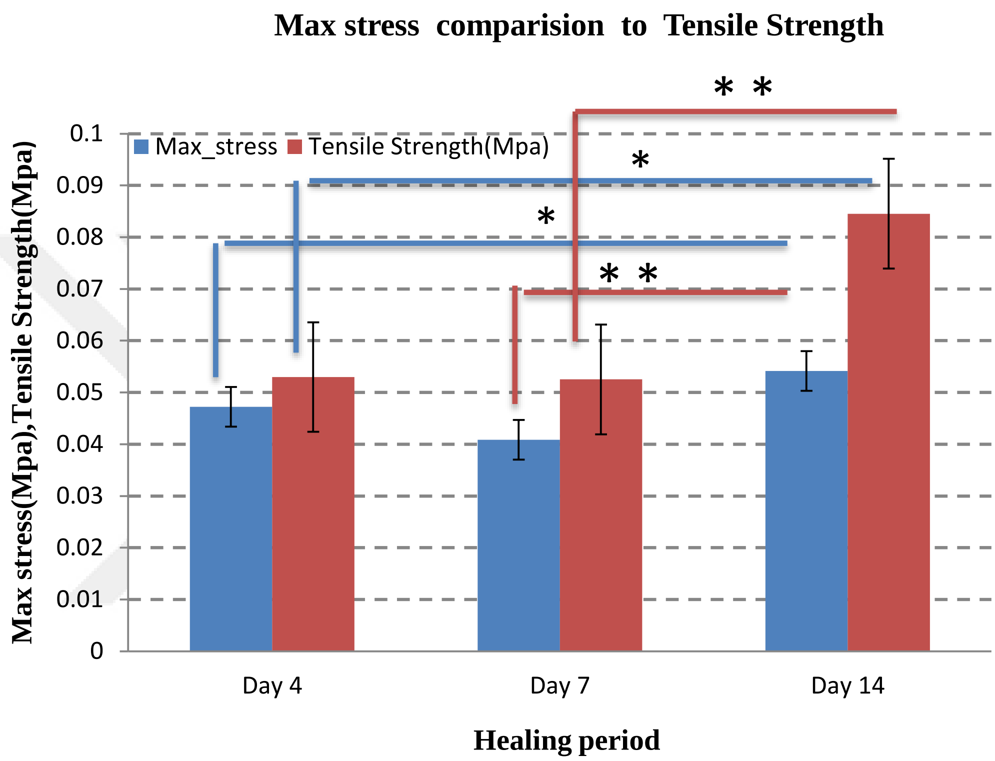

Figure 3.5 Average tensile strength versus average maximum stress .For the tensile strength and maximum stress ,* a significant difference was observed between Day-4 and Day- 14 groups. ** Significant differences were observed in (Day-7 and Day-14) groups(t-test: p<0.05).

The stress to strain until fracture time for unwelded tissue representing (figure 3.6) when the stress (Mpa) rise, also the strain proportionally increase.The rupture point was the 88.2 s at 0.44 Mpa stress at the 0.2 mm strain. The unwelded skin tissue resists this point.

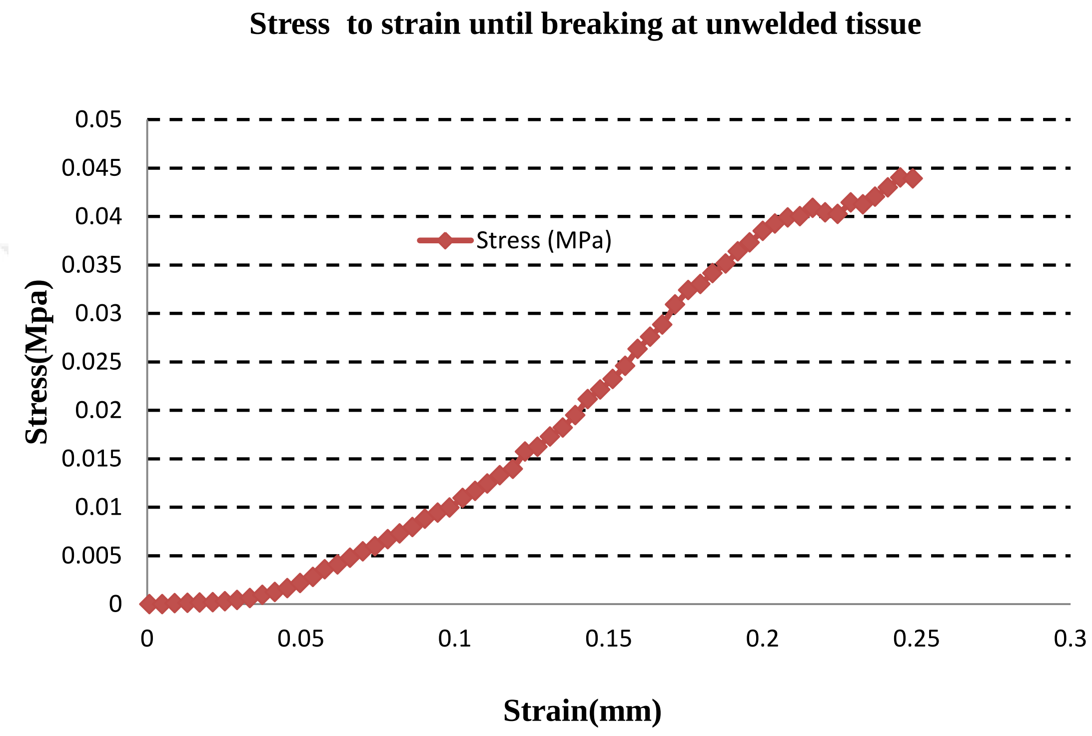

Figure 3.6 Stress-strain relationship until breakage in unwelded rat skin tissue.The rupture time was 88.2 s until 0.44 MPa stress.

Figure 3.7 represented the stress (Mpa) rate increased systematically with strain (mm) at unwelded rat skin tissue at 1 minute. The Stress to strain 0.028 Mpa at 0.16 mm strain in 59.72 s that time the skin tissue had no deformation. In the linearity is almost constant.

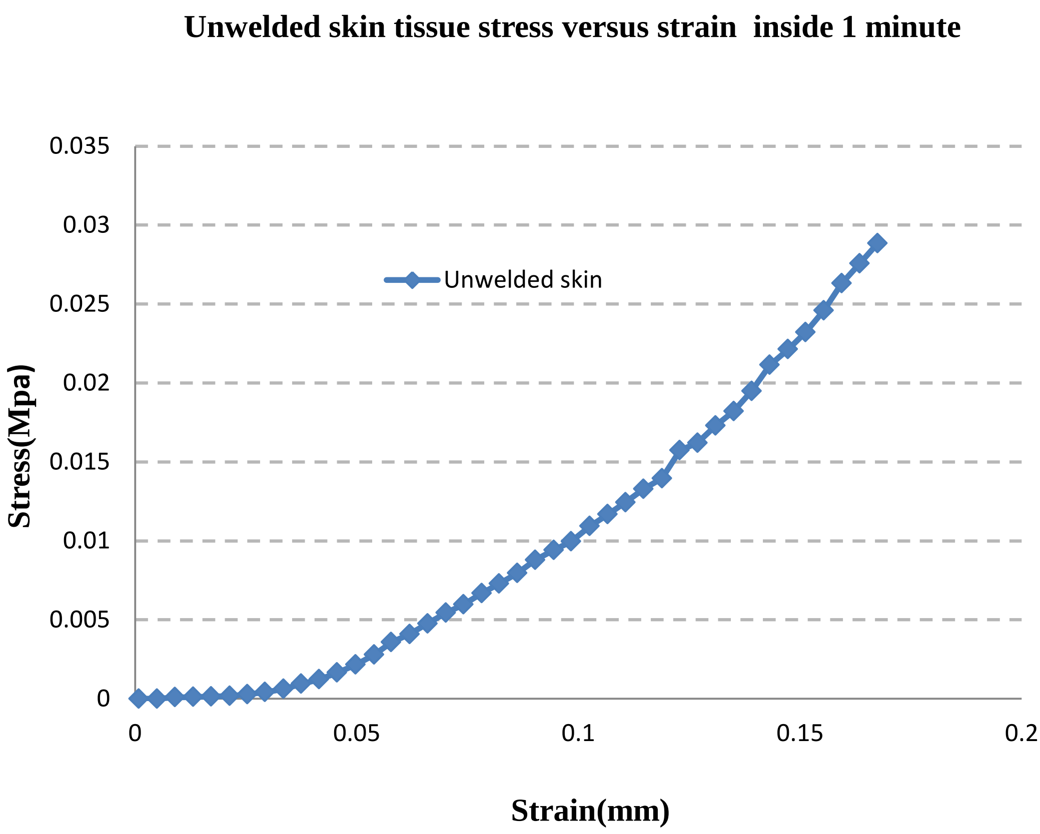

Figure 3.7 Stress-strain curve for non-irradiated rat skin tissue in 1 min.

The figure 3.8 shows comparison of Load at maximum load (N) and the breaking point of the skin tissue. When the load at max load increases, breaking point increase and vice versa. The load at maximum load amounted Day 4 11.8 ±5.14 N, Day 7 9,45±3.02 N and 20.15 ±4.87 N. On the other hand the breaking point was Day 4 9.03 ± 4.92 N ,Day 7 8.13 ± 2.72 N and 13.8 ± 2.79 N. There was a statistically significantly difference between the load at maximum load and breaking point until laser irradiation inside 1 minute. Table 3.4 shows the significantly difference between the days($p<0.05$).

Table 3.4 Load at max load and Breaking point t-test measurement in the healing periods

Comparison	Load at max load(N)	Breaking point(N)
Day-4 - Day-7	0.318395	0.684664
Day-7 -Day-14	0.00031	0.002766
Day-4 - Day-14	0.007433	0.048169

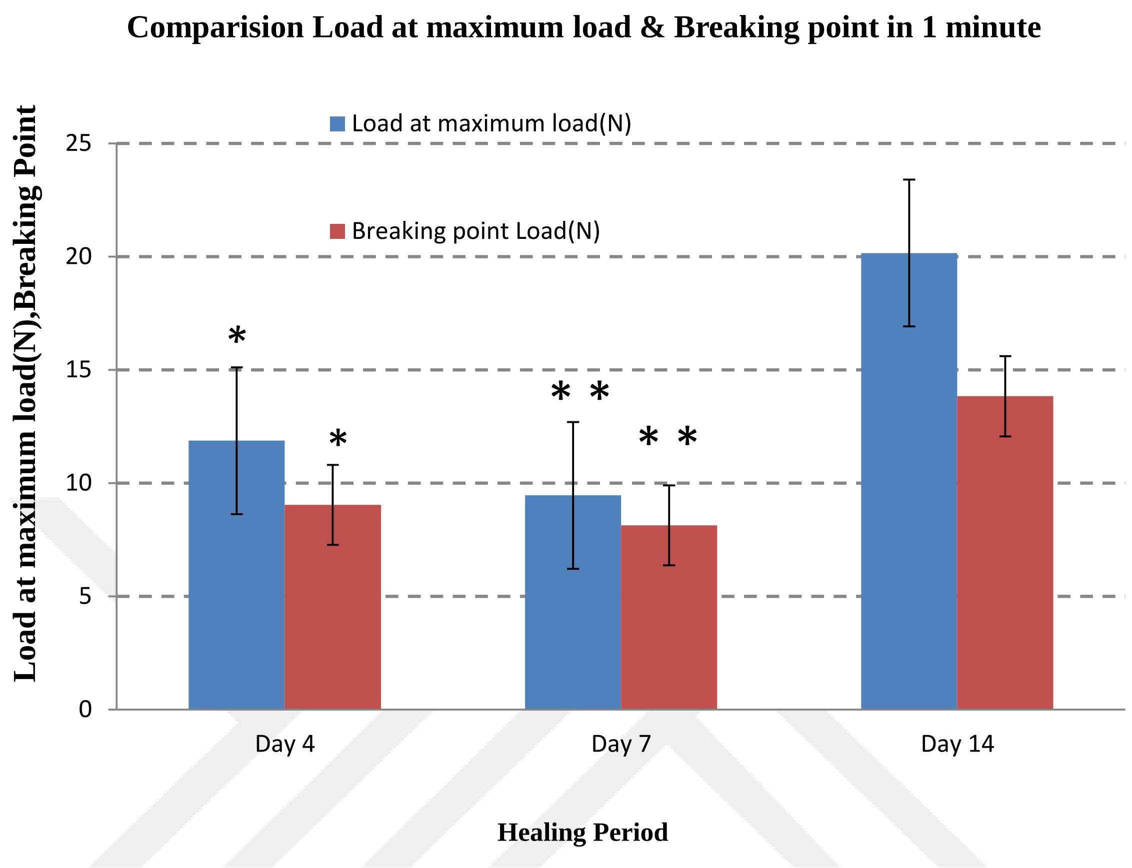

Figure 3.8 Comparison of loads in terms of maximum load versus breaking point load. The increase and decrease were proportional.* A significant difference was observed between Day-4 and Day- 14 groups. ** Significant differences were observed in (Day-7 and Day-14) groups (t-test: $p<0.05$).

Figure 3.9 denoted the relations between the tensile strength (Mpa) and strain (mm) at particularly healing periods of 4,7,14 and both of them comparison to the unwelded skin tissue. Tensile strength Day-4 0.05 ± 0.02 Mpa.Day-7 0.05±0.01 N and Day-14 0.08 ±0.01.Strain on Day-4 0.08±0.04 mm,Day-7 0.08±0.05 mm and Day 14 0.06±0.04 mm.Tensile strength increase and strain decrease can be shown. The unwelded skin was tissue T.S 0.045 Mpa and strain 0.16 ±0.07.The unwelded skin tissue the Tensile strength was smaller than the welded tissue because of the structure and morphological properties of the skin and the strain rate increased. The significantly differences were observed on Day 7-Day 14 and Day 4-Day 14 ($p<0.05$).

Table 3.5 Tensile strength and strain t-test measurement in the postoperative healing periods.

Comparison	Tensile strength (Mpa)	Strain(mm)
Day 4-Day7	0.969364064	0.66112498
Day 7 -Day-14	0.006804566	0.014785078
Day 4 -Day-14	0.025670722	0.030396438

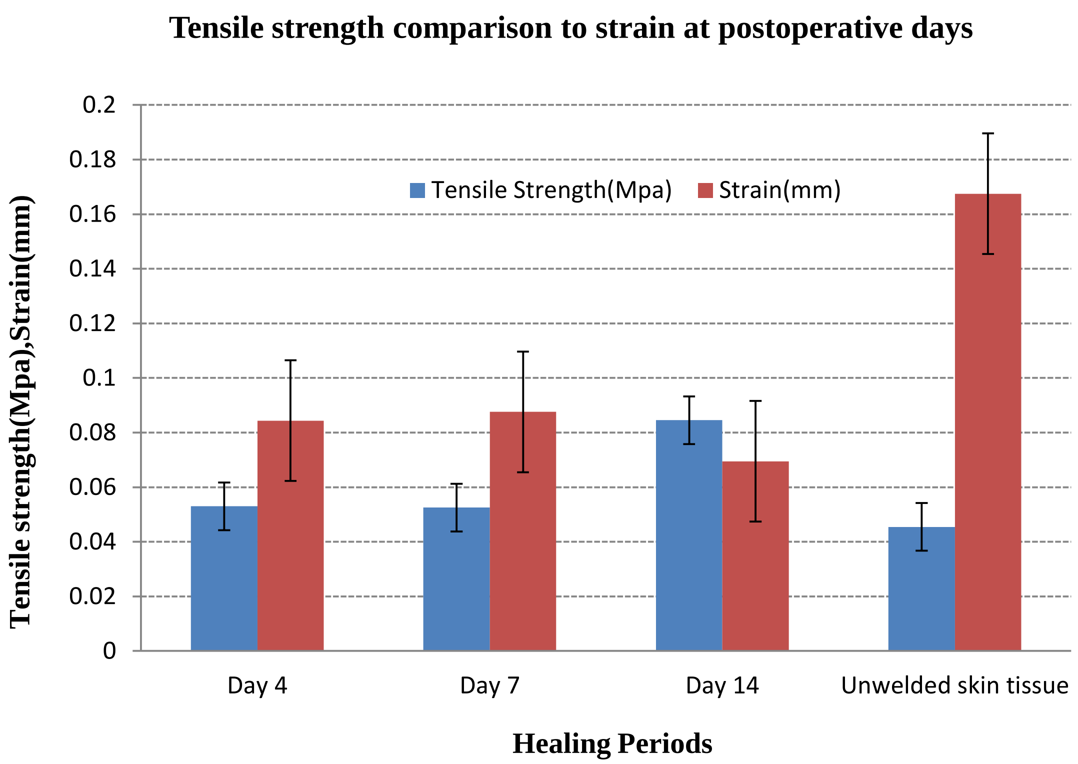

Figure 3.9 Mean tensile strength of wounds and strain(mm) in the postoperative healing period in welded skin tissue compared with that in unwelded skin tissue. Standard deviations are shown. A significant differences were observed (Day-7 and Day-14) and (Day4 and Day 14) groups (t-test: $p<0.05$).

Figure 3.10 demonstrated the average extension of the wounds at healing periods and the extension of unwelded skin tissue. Day-4, 7.13± 4.32 mm, Day-7 ,6.20±3.68 mm and Day-14, 4.85 ± 2.91 mm.Day-4 was the higher average extension according to others. The average extension was 7.31± 4.85 mm and Day 4-Day 7 no significantly difference. Other was meaningful $p<0.01$.

Table 3.6 Extension t-test measurement in the postoperative healing period

Comparison	T-test extension
Day4-Day7	0.060830755
Day 7-Day14	0.009702473
Day 4-Day 14	1.62587E-05

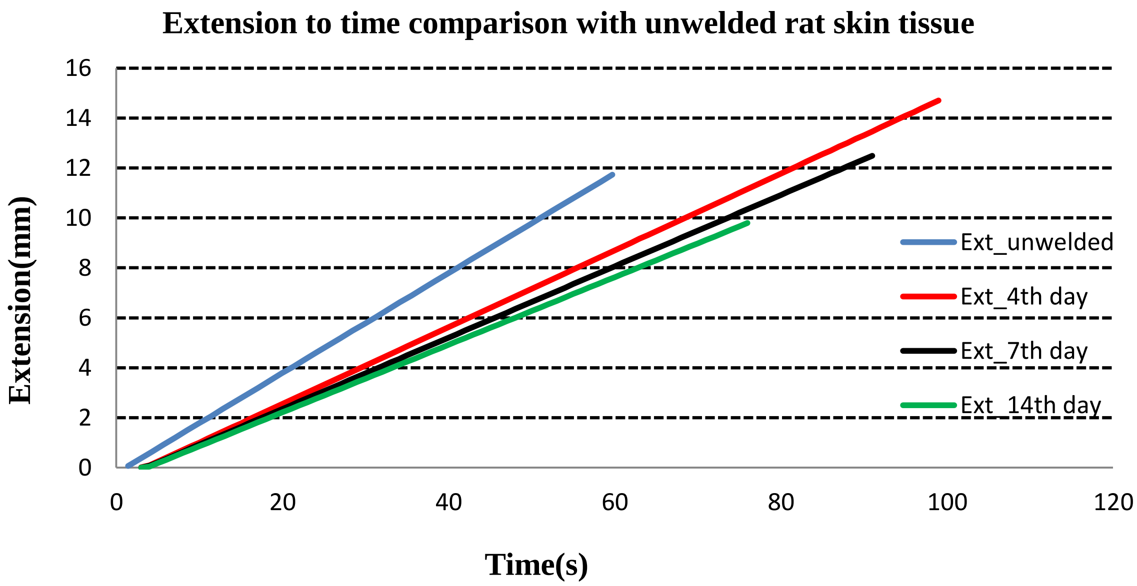

Figure 3.10 Comparison of mean extension of wounds with time in welded skin tissue with that in unwelded skin tissue during particular healing periods. ** A significant differences were observed between in (Day 7 and Day 14) and (Day 4 and Day 14) groups (t-test: $p<0.05$).

Figure 3.11 presented the higher and lower stress and strain rates compare with the unwelded skin tissue. The strain Day-4, 0.08± 0.01 mm, Day-7, 0.07±0.019 mm and Day-14 ,0.07 ± 0.014 mm. For the stress Day-4, 0.05± 0.02 Mpa, Day-7, 0.045±0.015 Mpa and Day-14, 0.059 ± 0.011 Mpa The stress was higher at Day 14 according to Day 4 and Day 7.The strain rate decreased as time. The unwelded skin tissue the strain rate was the higher when compare with the healing days. The stress and strain significantly different ($p<0.01$).

Table 3.7 T-test for measurement of Stress to strain at the breaking point in the welding skin compared with that in the unwelded skin

Comparison	Stress(Mpa)	Strain(mm)
Day4-Day7	0.68463492	0.156704563
Day 7-Day14	0.094449837	0.730898414
Day 4-Day 14	0.448159327	0.123544041

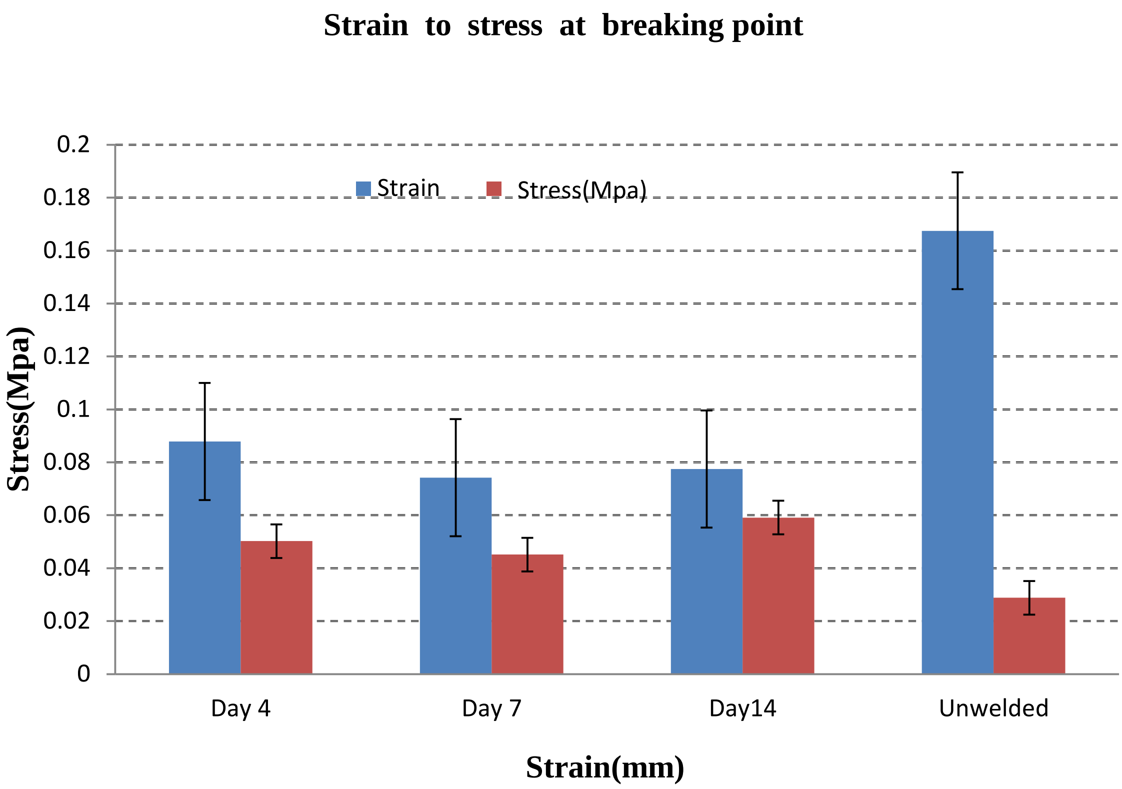

Figure 3.11 The stress value for all strains .The initial and maximum stress and strain are shown. Comparison with unwelded skin tissue is also shown. Standard deviations is omitted for the error bars.A significant difference were observed between (Day-7-Day-14) and (Day4-Day 14) groups (t-test: $p<0.05$).

Below the Figure 3.12 presented the stress (Mpa) to strain (mm) values with the unwelded skin tissue. For 14th day the stress to strain was the highest. While the applied stress, the strain value decrease. The statistically t-test shown stress and strain (Day 7 and Day 14) and (Day 4 and Day 14) were the discrepancy ($p<0.05$) in the table 3.7.

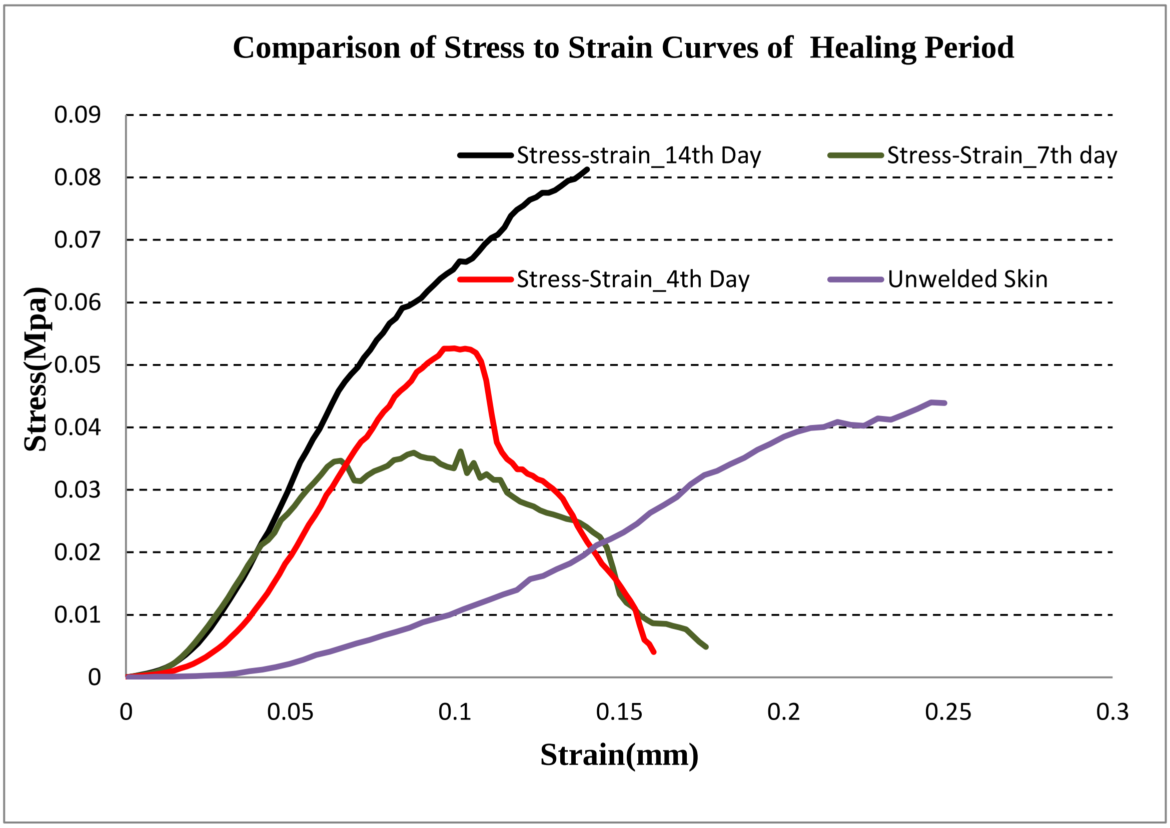

Figure 3.12 Mean stress-strain response in welded rat dorsal skin tissue compared with that in unwelded skin tissue.The unwelded tissue exhibited linearity.Significant difference were observed (Day-7 and Day-14) and (Day 4 and Day 14) groups (t-test: $p<0.05$).

CHAPTER 4

4.1 DISCUSSION

The mechanical properties of the skin are important. However, few studies have focused on the biomechanical properties of the skin tissue under the influence of a laser [3].In laser tissue welding, it is important to determine the optimal laser tissue parameters in order to decrease thermal damage and increase tissue healing. In the welding procedure important factor include the optimal laser wavelength, power density, pulse duration, operation time and spot size [35].In this study, the laser was 1940 nm CW diode laser, with a power of 600 W and duration of 3000 ms per incisions, with 4 spots per incision. The aim of this study was to investigate the biomechanical properties of laser welded tissues by measuring parameters such as load, time, elongation ,stress, tensile strength, stress to strain and fracture point on the stress-strain curve in tensile test analysis. Wound healing and closure without thermal damage were most important points with regard to this 1940 nm diode laser. A 14 day recovery period (with examinations on Day 4, Day 7 and Day 14) set. On a daily basis the wound on the dorsal skin of rats were photographed and subjected to a mechanical tensile test. There was no infection in the skin tissue. In the initial days of healing, opening of the incisions was observed because of scratching by the rats.

4.1.1 Tensile Test

According to result, in the tensile test ,there were a significant differences on various days (Day 4 and Day 14) and (day 7 and day 14) between the welded incisions and the unwelded ones. At 24 h, thermal injury was observed in some of the incision. However this is normal in the initial days after an incision. There was no full closure on the first days; therefore the results from this day were eliminated. Figure 3.1 shows the load during the healing period .By comparing (Day-7 and Day-14) groups and (Day 4 and Day 14) groups the load could be seen to be increasing over time. However, on Day 4 and Day 7,the load was smaller than that on the other days. Significant

Differences were observed in (Day-7 and Day-14) and (Day4 and Day 14) groups(t-test: $p<0.05$).The maximum load occurred on Day 14.

In terms of welding mechanisms, a temperature increment causes denaturation of structural proteins and dehydration of proteins fusion of collagen and noncovalent bonding the collagen [34].Collagen plays an important role in the mechanical test because it provides mechanical support and constitutes the principal structure of the skin [8].For ductile materials, the tensile strength refers the maximum load or stress at which point deformation starts to occur(necking).However, the less ductile materials rupture before they exhibit necking [10].Figure 3.2 presents the mean tensile strength of a wound versus the healing periods of rat skin. The standard deviations show that there was a significant difference between the tensile strength values. From Day 4 to Day 7, minimal increment was observed. The results of morphological studies correlate with those of mechanical tensile test. The reason for the initial increase in tensile strength from Day 4 to Day 7 is the function of the fibroblasts. The result of this study after Day 7 match those of other studies [19, 34].In addition, the skin tissue resisted stress for 14 days.

The maximum stress was the maximum point of average stress in particular, on reopening days 4,7 and 14.Figure 3.3 shows that the highest maximum stress occurred on Day 14 of the healing period, which was shown to be significant by statistical analysis. In addition, the ductile materials tensile strength values are as close as to max stress values.

The total load versus time in welded and unwelded skin tissues in 1 min on the postoperative days is shown in Figure 3.4 The skin exhibited increases in loading (Day 7 and Day 14) and (Day 4 and Day 14).However, the unwelded tissue demonstrate linearity means that the load applied the healthy tissue constant.There was a significant difference between the recovery days ($p<0.05$).

The tensile stress and maximum stress value were close to each other because of the properties of ductile materials [10]. Figure 3.5 shows average tensile strength was comparable to the average maximum stress. At the same time, when the tensile strength (MPa) increased,the maximum stress also increased. This confirms that the tensile strength and maximum stress values of the skin tissue were close to eachother because of the properties of ductile materials [10].The student’s t-test measurement showed that (Day 4 to Day 14) and (Day 7 to Day 14) were the meaningful.

Figure 3.6 presents the relationship between stress and strain until breakage of the unwelded rat skin tissue. The stress-strain relationship was non-linear and non-homogenous [2,4,37,39] .Figure 3.7 shows the stress-strain curve for no irradiated rat skin tissue in 1 min. In addition, rupture was not observed inside 1 minute.

It is difficult to control soft biological tissues, particularly skin during tensile tests. The point when breakage or fracture occurs is the maximum stress or load of materials. When the skin stretches, collagen fibers arrange themselves parallel to each other and local friction inhibits the movement of the skin. However, if the stretching becomes excessive, the skin tissue tears Rupture usually occurred in the center of a sample far from the grips, during the mechanical tensile test. Collagen fibers as well as elastic fibers and proteins were efficient in preventing the tearing of skin tissues under load and stress and changed the mechanical properties of the skin under tension [26,40].Figure 3.8 shows a comparison of the loads in terms of maximum load versus breaking point load. There was a significant differences the load at maximum load and Breaking point ($p<0.05$).The load at maximum load and breaking point values are close to eachother.

Collagen fibers straighten when exposed to a load. This behavior of collagenous tissue and the difference in viscoelastic strain rate properties are expressed the mechanical properties of biological tissues such as the skin and tendon [22]. Figure 3.9 represents the result of the mean tensile strength of wounds and strain(mm) in the postoperative healing periods in the welded skin tissue and enables comparison with those in the unwelded skin tissue. The results showed that the tensile strength of the skin tissue increased and the strain rate decreased. Compared with the unwelded skin tissue, the strain rate was the higher and the tensile strength was the lower. There were significant differences in this regard in (Day 7 and Day 14) and (Day 4 and Day 14) groups (t-test: $p<0.05$).With regard to the skin viscoelastic properties of the skin in the mechanical tensile test, the strain decreased when the tensile strength was the highest [35].In addition, Figure 3.10 shows extension amount versus time during mechanical stress. The results of the welded skin during the healing period can be compared with those of the unwelded skin. On Day 14 ,the extension was the smallest ,while on Day 4,it was highest. Unwelded tissues showed no deformation because the extension as was higher than that on. Day 14,the highest extension indicates that the collagen fibers are deformed and offer no resistance to the load. This is related to the viscous and elastic properties of skin tissues [22, 35].Stress and strain rates are influenced by the extent of collagen crosslinking. Biomechanical research has reported that the stress-strain curve of the skin indicates viscous dispersion during collagen fiber arrangement [23, 35].Figure 3.11 represent stress values for all strains at the breaking point in the welded skin tissue in comparison with those in the unwelded rat skin tissue.In addition, when Day 14 stress at the fracture point was the highest, the strain value was decreasing. There were significant differences in this regard in (Day-7 and Day-14) and (Day 4 and Day 14).The mean stress-strain response in the welded rat dorsal skin tissue compared with to unwelded skin tissue is shown in Figure 3.12.The results for unwelded tissue exhibited the linearity because no mechanical test was performed. When the stress increased monotonically, the collagen fibers (and not elastic fibers) beared yielding, plastic strain started to occur and strain at the fracture collagen strength and rupture were observed. The strain rate decreased on the days when the wound reopened.On Day 14 strain was minimum and stress was the maximum. The value of unwelded skin tissue strain was also the highest. These phenomena occurred because of the viscoelastic behavior of the skin tissue under mechanical stress and the structural properties of elastin fibers [2,4,37,39].Therefore ,the shape of the stress-strain curve for the skin in this study from that for tissues such as tendons and ligaments[32]. Significant differences were observed in (Day-7 and Day-14) and (Day 4 and Day 14) group (t-test: $p<0.05$).

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1940 nm diode laser skin welding of surgical incision: Tensile test analysis

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Medical Technologies National Conference (TIPTEKNO), Conferance publications

15-18 October 2015, Bodrum,Turkey