DESIGN AND FABRICATION OF SUTURE-LESS WOUND CLOSURE DEVICE

Author

USMAN ASHRAF

Registration Number

00000206199

Supervisor

DR. NOSHEEN FATIMA RANA

DEPARTMENT OF BIOMEDICAL ENGINEERING AND SCIENCES

SCHOOL OF MECHANICAL & MANUFACTURING ENGINEERING

NATIONAL UNIVERSITY OF SCIENCES AND TECHNOLOGY

ISLAMABAD, PAKISTAN

AUGUST 2019

DESIGN AND FABRICATION OF SUTURE-LESS WOUND CLOSURE DEVICE

Author

USMAN ASHRAF

Registration Number

00000206199

A thesis submitted in partial fulfillment of the requirements for the degree of

MS Biomedical Sciences

Thesis Supervisor:

DR. NOSHEEN FATIMA RANA

Thesis Supervisor's Signature: _____

DEPARTMENT OF BIOMEDICAL ENGINEERING AND SCIENCES

SCHOOL OF MECHANICAL & MANUFACTURING ENGINEERING

NATIONAL UNIVERSITY OF SCIENCES AND TECHNOLOGY,

ISLAMABAD

AUGUST, 2017

FORM TH-4

National University of Sciences & Technology

MASTER THESIS WORK

We hereby recommend that the dissertation prepared under our supervision by **Usman Ashraf (00000206199)**

Titled: **Design and Fabrication of Suture-less Wound Closure Device** be accepted in partial fulfillment of the requirements for the award of MS Biomedical Sciences degree. Grade (_____)

Examination Committee Members

1. Name: Dr. Umar Ansar Signature: _____

2. Name: Dr. Aamir Mubashar Signature: _____

Supervisor's name: Dr. Nosheen Fatima Signature: _____

Date: _____

_____ _____

Head of Department Date

COUNTERSINGED

Date: _____

_____

Dean/Principal

THESIS ACCEPTANCE CERTIFICATE

Certified that the final copy of MS/M. Phil Thesis written by Mr. Usman Ashraf**, Registration No. (**00000206199**)**, of **School Of Mechanical And Manufacturing Engineering (SMME)** has been vetted by the undersigned, found complete in all respects as per NUST Statutes/ Regulations, is free of plagiarism, errors and mistakes and is accepted as partial fulfillment for award of MS/Mphil Degree. It is further certified that necessary amendments as pointed out by GEC members of the scholar have also been incorporated in the said thesis.

Name of supervisor: Dr. Nosheen Fatima Rana

Signature: _____

Date: _____

Signature of (HOD): _____

Date: _____

Signature (Principal): _____

Date: _____

Declaration

I certify that this research work titled "*Design and Fabrication of Suture-less Wound Closure Device"* is my own work. The work has not been presented elsewhere for assessment. The material that has been used from other sources it has been properly acknowledged/referred.

Signature of Student

USMAN ASHRAF

Proposed Certificate for Plagiarism

It is certified that MS Thesis Titled **Design and Fabrication of Suture-less Wound Closure Device** by **Usman Ashraf** has been examined by us. We undertake the follows:

a. The thesis has significant new work/knowledge as compared already published or are under consideration to be published elsewhere. No sentence, equation, diagram, table, paragraph or section has been copied verbatim from previous work unless it is placed under quotation marks and duly referenced.
b. The work presented is original and own work of the author (i.e. there is no plagiarism). No ideas, processes, results or words of others have been presented as Author own work.
c. There is no fabrication of data or results which have been compiled/analyzed.
d. There is no falsification by manipulating research materials, equipment or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
e. The thesis has been checked using TURNITIN (copy of originality report attached) and found within limits as per HEC plagiarism Policy and instructions issued from time to time.

Name & Signature of Supervisor: _Dr. Nosheen Fatima Rana _

Signature**: _ _**

Plagiarism Certificate (Turnitin Report)

This thesis has been checked for Plagiarism. Turnitin report endorsed by Supervisor is attached.

Signature of Student

Usman Ashraf

00000206199

Signature of Supervisor

Copyright Statement

Acknowledgments

I am thankful to my Creator Allah Subhana-Watala to have guided me throughout this work at every step and for every new thought which You set up in my mind to improve it. Indeed, I could have done nothing without Your priceless help and guidance. Whosoever helped me throughout the course of my thesis, whether my parents or any other individual was Your will, so indeed none be worthy of praise but You.

I am profusely thankful to my beloved parents who raised me when I was not capable of walking and continued to support me throughout every department of my life.

I would also like to express special thanks to my supervisor **Dr. Nosheen Fatima** for her help throughout my thesis and for HAP and NMDDS courses which she has taught me. I can safely say that I haven't learned any other subject in such depth than the ones which she has taught.

I would also like to pay special thanks to **Dr. Aamir Mubashar** for his tremendous support and cooperation. Each time I got stuck in something, he came up with the solution. Without his help, I wouldn’t have been able to complete my thesis. I appreciate his patience and guidance throughout the whole thesis.

I would also like to thank **Dr. Aamir Mubashar** and **Dr. Umar Ansari** for being on my thesis guidance and evaluation committee and express my special thanks to **Dr. Nosheen Fatima** for her help. I am also thankful to **Malik Naveed** and **Khizer Jan** for their support and cooperation.

Finally, I would like to express my gratitude to all the individuals who have rendered valuable assistance to my study.

Dedicated to my exceptional parents and adored siblings whose tremendous support and cooperation led me to this wonderful accomplishment.

Abstract

Injuries are among one of the leading threats to health that people especially soldiers face in daily routine. Most of the injuries that armed forces face consist of wounds in the cutaneous layer. Moreover, in daily routine people get cuts on their skin. Therefore, the search for such devices and materials that can effectively and efficiently work for the closure of superior cutaneous wounds on skin both in the battlefield and in a medical clinic setting to favor cutaneous wounds just to assist careful closure has huge importance. The methods and materials for suturing open wounds are improved during last few years but conventional needle and thread method is most practiced in normal routine. Unlike conventional suturing techniques, this study presents development of a new, painless, easy to apply and needle-free non-invasive device that does not cause extra damage to the site of injuries and requires no anesthesia infusion to wound before applying the device. This research proposes a device that features strip and lock parts that are easily 3d printable with Polymer. It attaches with microporous adhesive tape through cyanoacrylate glue. The suture-less wound closure device was applied to the edges of injury on skin and wound is closed by pulling strips through locks, strips fit into locks like zip ties and wound edges come closer to each other. The design of this device makes eversion of edges of skin which is the main purpose of skilled doctors to achieve while closing the wound. The performance of this device was tested on animal models and it performs well in comparison with conventional suturing techniques.

Key Words: Non-Invasive technique, 3d printable device, Cyanoacrylate glue, Conventional suturing techniques

Table of Contents

List of Figures

List of Tables

CHAPTER 1: INTRODUCTION

The research work in this dissertation has been presented in two parts. The first part is designing of suture-less wound closure device. The main objective of this part is to develop a design which can be manufactured with low-cost additive manufacturing technique without any supports. The second part includes the in-vivo testing of the developed patch. The objective of this part is to verify the design and check efficacy and accuracy of materials used to manufacture a suture-less wound closure device.

1.1 Motivation

Injuries are among one of the leading threats to health that soldiers face in daily routine. Most of the injuries that armed forces face consist of wounds in the cutaneous layer moreover in daily routine people get cuts on their skin. Therefore, search for devices that can effectively and efficiently perform the closure of superior cutaneous wounds on skin both in battlefield and in a medical clinic setting, is a continuous topic of battle search. The methods and materials for suturing open wounds have improved during past years but conventional needle and thread method is considered standard practice. The development of Suture-less wound closure device can fulfill the purpose of closing a cutaneous wound.

1.2 Background:

A huge amount of data is present regarding conventional wound closure techniques like sutures, adhesives, and staples. Both positive and negative aspects of these conventional techniques are demonstrated in practical experiences and past studies. One study elaborated that patients are satisfied with conventional suturing techniques and revealed that staple closure method and sutures had no noteworthy difference among them [1] however Singh et al[2] and Elson & Stockley [3] announced that staples were perpetually more painful to evacuate than sutures, this result is explained in a non-orthopedic research previously [4]

[5] [6]. Some researchers proposed that the application time of the staple closure method is less than suturing method due to this reason doctors and theater staff prefer this method after hectic and long surgeries [7, 8]. The use of glues for dermal wound closure instead of staples and sutures for wounds smaller than 100mm was reported by Gupta and Singh et al and reported increment in cost of wound closure [9]. Closure of wounds with glues needs to give patients local anesthesia as well as it may cause some severe skin allergies for weeks or longer. It is demonstrated that the sutures that passed the skin make the skin vulnerable to infection and bacterial entry into the inner layers of skin at wound site [10, 11]. It's not astonishing, that sutured wounds have been appeared to have less protection from contamination than those treated by different methods [12, 13]. A report comprising of successful manufacturing and review by clinical practices of adhesive tape used for surgeries was published in 1960s [14]. This tape was microporous hence no pore of skin was closed and remain ventilated by this tape, have strong adhesive and it was inert physiologically, so it makes no allergic reaction on skin wounds.

Due to recent advancement in the field of biomedical scientists are trying to put on the effort of making non-invasive skin closure devices. Medizip surgical zipper is a form of non-invasive wound closure device that was recently developed for closing cutaneous wounds. For wound closure zipper could be a better and safer option as compared to conventional suturing methods [15]. The zipper is pointless in high-strain or wet injuries, wounds with significant bends of 20 degrees or more and in patients who are obese [16]. Recently another non-invasive wound closure device, "DermaClip" was developed and practiced in China for closing cutaneous wounds [17].

1.3 Objective:

The subject of this study is to develop a new, painless, easy to apply and needle-free non-invasive device that does not take extra damage to the site of injuries and requires no anesthesia infusion to the wound before applying the device. The advancement of the Suture-less wound closure device tends to reduce

issues related to conventional suturing techniques, interpreting the device better than those techniques. This device is developed to be used in battle settings and in emergencies where instant action is needed if one got injured.

The device consists of two parts strip and lock that are attached with microporous adhesive tape. The design of this device is quite simple but very advanced for non-invasive wound closure. The suture-less wound closure device is applied to the edges of injury on the skin and wound is closed by pulling the strips through the locks, strips fit into the lock like zip ties and wound edges come closer to each other, pull the strip until the two edges of wounds do not meet.

You can also say, the design of this device makes eversion of the edges of the skin which is the main purpose of the skilled doctor to achieve while closing the wound as it is broadly trusted that wound eversion is fundamental for limiting scarring on the injury site that it boosts the opportunity for appropriate epidermal estimation also, keeps away from the potential for reversal. Furthermore, since the device is connected to the approximated edges of the injury, wound arrangement is kept up without forceps or other skin control.

The device is present in multiple forms from one strip to multiple strips depending on the nature and length of the wound. When the injury edges are in attractive juxtaposition and the clips are closed, the abundance strips are expelled, and dressing is connected if required.

CHAPTER 2: LITERATURE REVIEW

2.1 Dermal Wounds and Healing Process:

When we talk about the closure of cutaneous wounds then it requires a special understanding of specific closure technique, material selected closing wounds, healing mechanism as well as anatomy of the skin as shown in figure 1. There are many different types of dermal wounds which include incisions, lacerations, bite wounds, penetrating wounds, puncture wounds, hematomas, and contusions. The focus of this study was on incision, lacerations, bite wounds, penetrating and puncture wounds. The incision is wounds that are clean and clear cuts which may occur due to some sharp knife or surgical cuts as shown in figure 2a. Lacerations are irregular wounds which may occur due to rupturing of skin during accidents or as a result of fall from height described in figure 2b**.** Puncture and penetrating wounds occur when some round pointed objects enter skin and create open wounds as shown in figure 2c and 2d respectively, and bite wounds occur due to biting of some animals or humans can be seen in figure 2e. There are three different phases that are involved in wound healing mechanism on the bases of molecular and cellular level. To accomplish a better wound closure, it is necessary that cellular component interacts with growth factors present in cascade. The 1^{st} step of wound closure is inflammation which may last for three to four days. 2^{nd} step of wound healing is tissue formation which may overlap with 1^{st} step, it starts from second day and last on 14^{th} day. The last step of wound healing is wound remodeling and it is observed form 6^{th} day of injury or wound closure to 1 year or less. The timeline graph of wound healing phases is shown in figure 3. Inflammatory cells start to set up and move through the damaged veins into the injury site after initial injury. At present time these inflammatory cells make complex interactions with local mediators which is normally at the highest point of 1^{st} phase of wound healing. The epithelial cells start migrating from 12^{th} to 24^{th} hour even though formation of new tissue starts from 10^{th} to 14^{th} day.

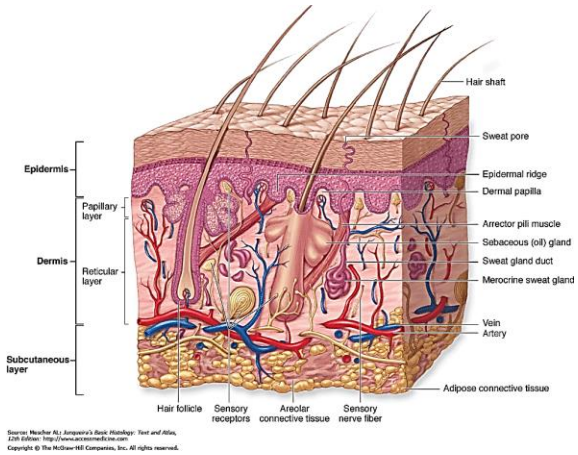

Figure 1: skin anatomy of Humans [18]

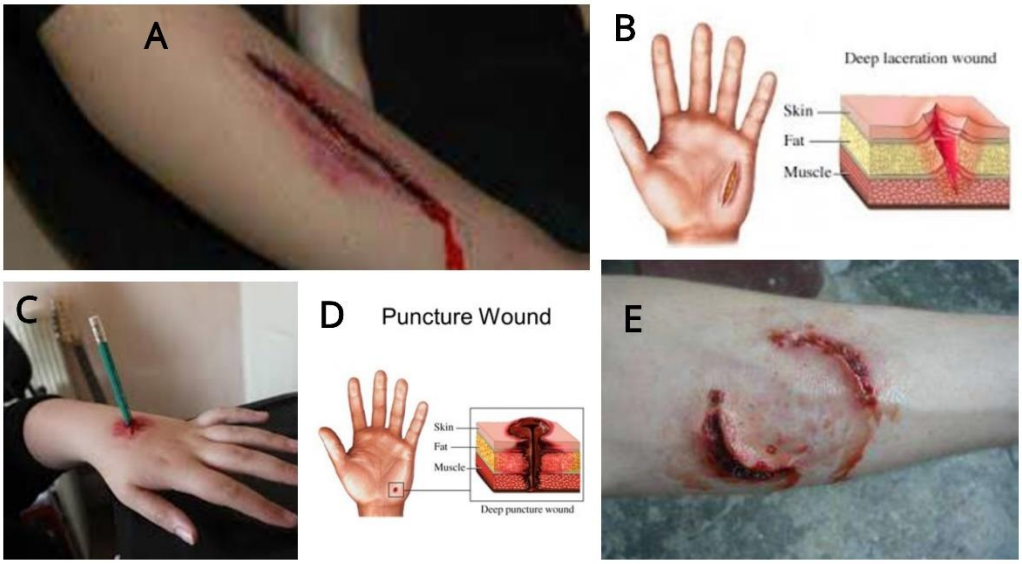

Figure 2: (a) Incisions (b) Lacerations (c) Penetrating Wounds (d) Puncturing wound (e) Bite Wounds [19]

Neovascularization and epithelialization increase the activity of cells, emittance, and organization of extracellular material starts and the formation of granulating tissue completes through specific growth factors during the process of healing. During final phase of healing due to increasing strength and wound contraction physical properties are achieved. Normal wound healing may be affected by some systematic disease or other local factors.

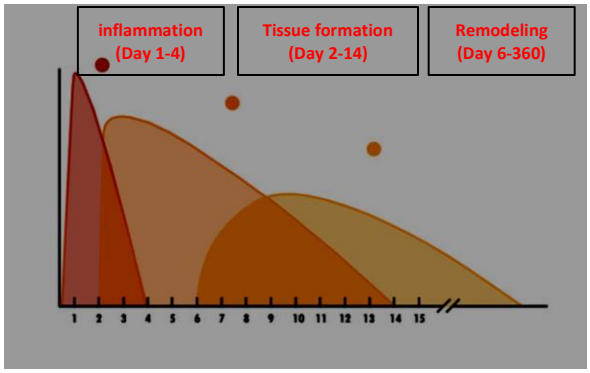

Figure 3: Schematic Diagram showing wound healing phases[18]

2.2 Mechanical Forces required for Wound Closure:

Different mechanical forces are required to close wounds of different dimensions, moreover, these mechanical forces may decrease during relaxation and increase the extension of muscles on same wound. The forces required for closing dermal wound of different dimensions are elaborated in table.

Table 1: Mechanical Forces required to close dermal wounds[20]

Number	Gender	Age (years)	BMI (kg/m^2)	Dimensions (mm)	Maximal force (N)	Force after relaxation (N)	D fo
1a	Male	54	31.3	37 × 6	1.7	1.4	1
1b	Male	38	28.7	38 × 6	1.5	1.2	2
1c	Female	48	34.2	36 × 5	1.1	0.9	1
1d	Male	62	32.3	37 × 5	1.3	1.1	1
2a	Male	53	27.6	43 × 9	2.3	2.1	
2b	Male	47	24.2	45 × 11	2.5	2.3	
2c	Female	46	23.8	44 × 10	2.6	2.2	1
2d	Male	37	27.6	42 × 8	2.4	2	1
2e	Male	41	18.1	40 × 8	2.4	2.1	1
2f	Male	66	29.5	45 × 12	2.1	1.9	
3a	Female	28	24.3	46 × 13	3.2	2.8	1
3b	Male	33	33.1	45 × 14	3.1	2.6	1

2.3 Conventional Techniques for wound Closure:

2.3.1 Suturing:

Cutaneous incisions are most common since the early times so different techniques were developed and practiced during different periods. The most common wound closure techniques that are still accepted and practiced were the use of suture which is 1st used in Egypt in 1500 B.C. Suturing was performed with linen material at that time. A lot of data is present on the use of natural materials like throne, bark of different trees and parchment as sutures. With the passage of time and advancement of science & technology suturing material and suturing application techniques had improved. Suturing techniques and procedures which are currently being used are shown in figure 4. Suturing is done with thread as suturing material and needle to apply the sutures. Suturing needle may vary in size, shape, and structure according to the need and type of wound which is to be closed. A sturdy absorbable suture was developed by Philip Syng Physick in 1806 from skin of buck basically developing a modern suturing technique [17]. Occasionally there are a lot of discussions about ideal material for suturing that are present in the literature. For repairing skin, the ideal suture material ought to be inert, does not make any foreign reaction in body, must have smooth surface and fine caliber and it should be strong enough and easy to apply. Additionally, suturing material should cause minimal trauma after its application and must possess safe knotting characters [21]. A wide range of materials for suturing is accessible to specialists today. The selection of suture for a specific procedure ought to be decided on the known properties of healing of sutured incision, technique of suturing, biological and physical properties of suturing material.

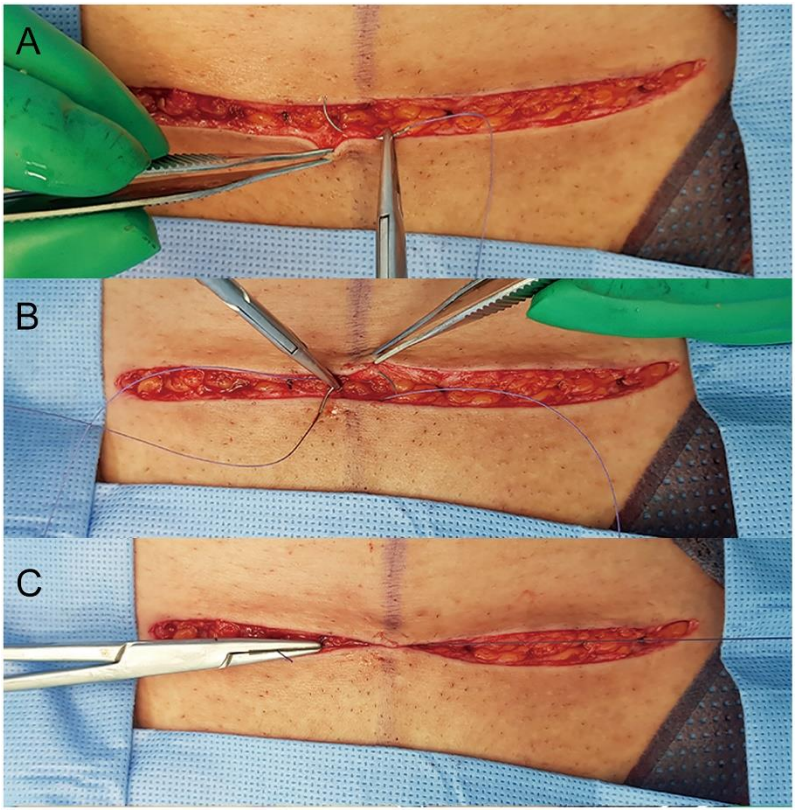

Figure 4: Suture application on surgical incisions[22]

2.3.2 Skin Closure Staples:

For closing lengthy incisions on skin mechanical disposable staplers are a fast and most efficient technique as shown in figure 5. Three to four times reduction in application time of staplers to close skin wound is observed as compared to conventional suture technique. However, it takes more time for their removal from skin postoperatively [23]. With the advancement of technology absorbable staplers were developed in contrast with sutures for closing clinical incisions. These U-shaped absorbable staplers are prepared from copolymer polyglycolic and polylactic. These copolymers maintain stapler's strength to 40% till the 14th day of their application, but it takes them months to be completely absorbed by body [24]. These staplers are applied to the subcutaneous layer of skin and did not puncture epidermis layer of skin. These absorbable staplers are structured to combine their rapid application in wound eliminating the need for their removal with improved results as compared to the sutures

[25]. There is always a risk of skin contamination due to application of external staplers because it breeches the integrity of epidermis [25]. Flick and his colleagues demonstrated better results of dermal stapler device over absorbable suture in animals which includes reduction in inflammation, better healing of incisions and clean and better appearance of closed incisions [26].

Cross at el, firstly conducted a clinical study on absorbable staplers applied on dermis which was a blinded, controlled and randomized study in human subjects. They reported that there are many advantages of closing skin incisions with dermal absorbable staplers like reduction in anesthesia and operating room time, good economically, additionally, it gives improved, effective and efficient results cosmetically [27]. Tellis at el conducted a study on subcuticular absorbable staples in renal transplantation surgery. This study demonstrated that these staples are effective and secure hence preferable over staples made of metals even when the renal transplant patients are given immunosuppressants [28].

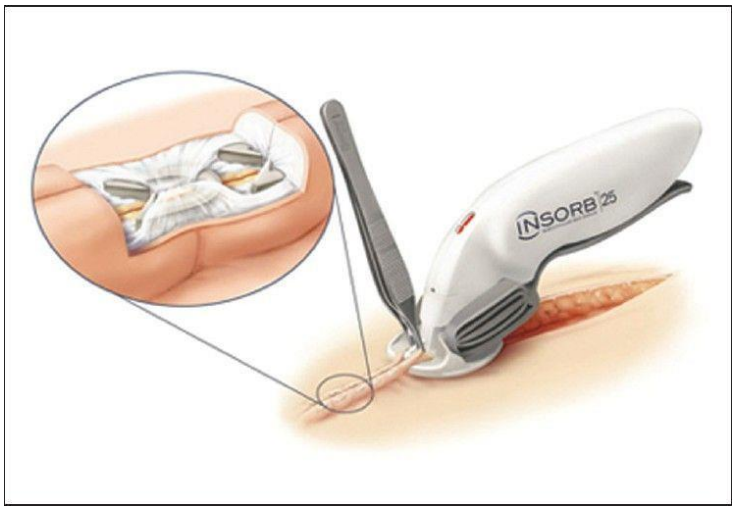

Figure 5: INSORB staplers for closing dermal incisions [16]

2.3.2.1 Challenges Associated:

Staples that are applied externally enter the epidermis on two sides to close wounds, this may cause incontinence to patients, skin irritation, involve painful removal, leave holes on the skin due

to puncturing which may cause extra damage to the skin [25]. Even though these Subcuticular absorbable staples save time in the operation room, produce better and improved results cosmetically, are easily applicable yet they are not tested for long term use and for every patient their cost is about 25$ [16].

2.4 Skin Adhesives:

Newer alternative techniques for closing skin incisions are developed recently such as adhesive tapes as closing material. A German Chemist manufactured a tissue adhesive (Cyanoacrylate) in 1949, it was clinically tested for the 1st time in 1959 by a British Surgeon [29]. In 1998 Octyl-2-Cyanoacrylate got approval by the Food and Drug Administration (FDA) for use clinically. The functioning time of Octyl-2-Cyanoacrylate is 10 seconds after application. The breaking strength of Octyl-2-Cyanoacrylate is almost five times better than conventional monofilament suture made of nylon. Tissue adhesive has wide applications in the medical field like implant fixation, adhesive for tissues and closing the leaks of cerebrospinal fluids and artificial or natural formation of blood vessels [30]. Additionally, these tissue adhesives are now used for inguinal canal wounds, laparoscopic incisions, facial incisions, hand injuries, transplantation of hair, closure of lacrimal punctum and blepharoplasty [31] (Figure 6).

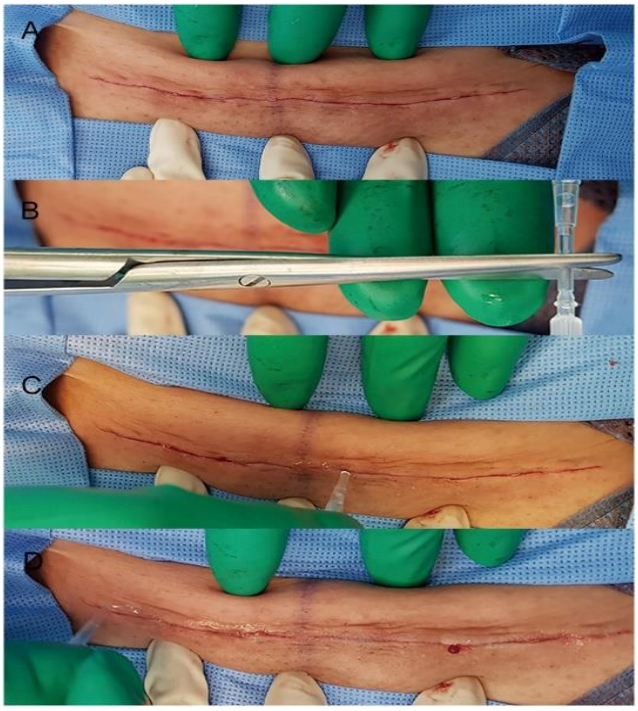

Figure 6: Surgical incision closure with Cyanoacrylate adhesive [22]

2.5 Non-invasive Suture closure devices:

2.5.1 MediZip Surgical Zipper

An innovative non-invasive cutaneous wound closure technique introduced recently which is “MediZip Surgical Zipper” shown in figure 7. A report by Rockler et al demonstrated that there is no noteworthy difference between “MediZip surgical zipper” and suture considering complications and cosmetic results [24]. The Zip in “MediZip surgical Zipper” can be open for inspecting wound conditions. Patients feel comfortable with “Medizip surgical Zipper” as compared to conventional techniques. In addition, this procedure reduces the amount of time for closing wounds in operation rooms and this does not require removal. A controlled, randomized and prospective study was conducted by Onuminya et al to check the efficacy of “MediZip Surgical Zipper”. In this study, they elaborated that Surgical Zipper is preferably good over conventional techniques considering the cosmetic outcome and other associated problems. Massone et al explained in their report that MediZip

Surgical Zipper is safe and effective as an alternative to conventional techniques because it is non-invasive, easy to apply and easy to handle and it does require any invasive removal at all [30][32].

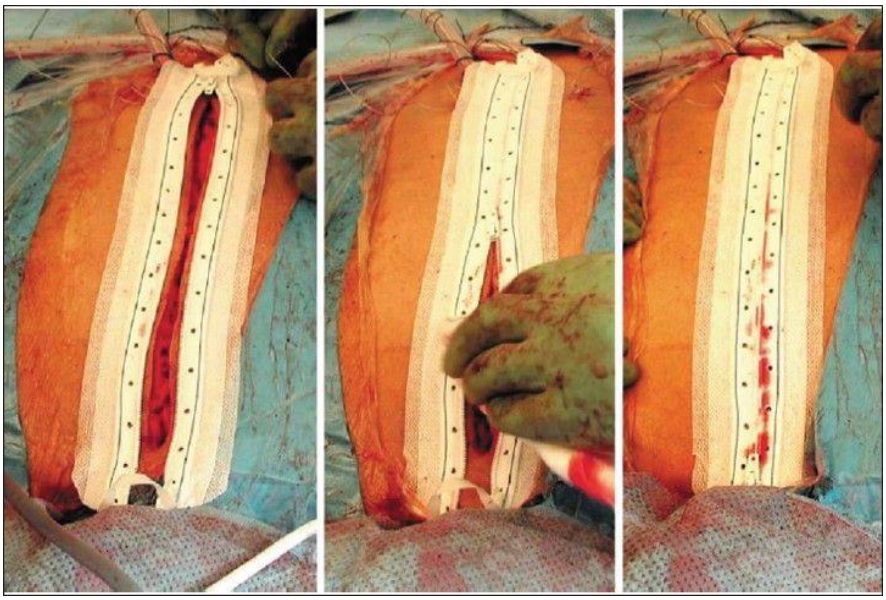

Figure 7: MediZip Surgical Zipper for closing surgical incisions [16]

2.5.1.1 Limitations:

Although, MediZip Surgical zipper is better in many ways over conventional suturing techniques, yet it has some issues like it cannot be used on a wound requiring high tension or curved wounds having an angle of 20 degrees or more. This technique does not work if the area around wound is wet and if patient is whom it is being applied is obese [17].

2.5.2 Derma Clip

The DermaClip is one of the new approaches to close dermal wounds non-invasively. This device consists of two patches that are connected through a bridge of polypropylene. These patches are applied to edges of the wound and closed by pulling the polypropylene bridge tabs in divergent track until it sounds a click. The sound of click indicates the proper closure of clips and attachment of wound edges. This

polypropylene bridge is an angled face and causes elevation of wound at closing site, so it makes natural closure of skin.

2.6 Additive Manufacturing Techniques:

Among so many different techniques to manufacture objects that are currently being used 3D printing is one of low-cost additive manufacturing techniques. This technique is used to make three dimensional solid objects from the design made in computer software. During the last few years, 3D printing technology is being used in the pharmaceutical industry to enable the rapid production of implants and for the creation of more specific tablets. This technique has changed the way of operations and procedures that doctors and surgeons plan [33]. The process has a lot of different applications and it is fastest growing in pharmaceutical and medical industry with the beginning of 3D printing [34]. There are five steps that are necessary to decide the selection of model being printed as shown in figure 8.

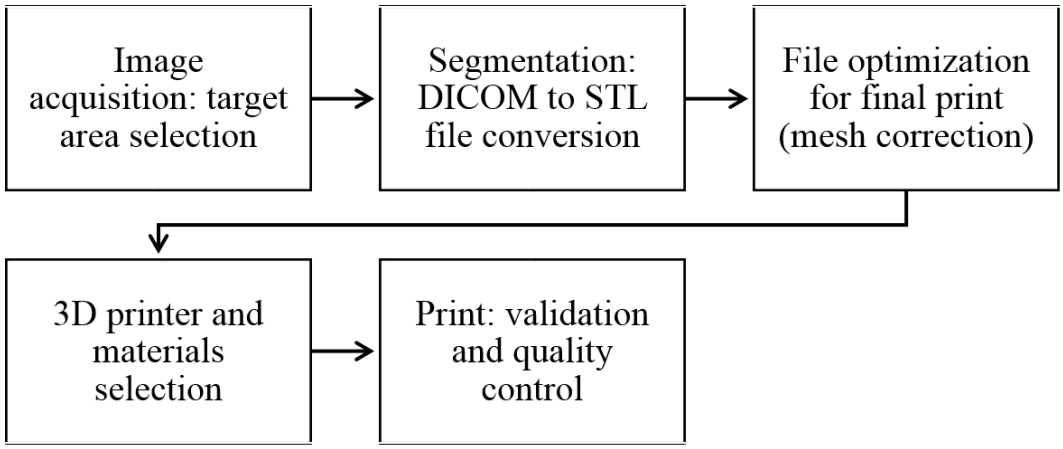

Figure 8: Workflow of 3D printing

2.6.1 Use of 3D printing in the medical field:

There are seven technical procedures of 3D printing that represent technologies commercially being used to manufacture 3D models which are elaborated in Table 2.

With the advancement of technologies more and more applications are being offered by 3D printing to improve the healthcare industry for saving the lives of patients. 3D printing has wide range of applications which includes neuro and cardio surgery [35], maxillary and oral surgery [36], orthopedic surgery [37], otolaryngology surgery [38], vascular and transplant surgery [39, 40], plastic and oncology surgery [41, 42].

3D printing is now widely used in the medical industry, there are following some examples of in which 3D printing technology is being used to help in medical field.

The 3D printing techniques provide the surgeon with a customized 3D model according to specific anatomy of patients which may help in accurately planning surgical approach. It can make prosthetic parts of body and surgical tools for specific anatomy of different patients [42-44]. 3D printing is being used to validate the results obtained by pharmacological treatment, this gives accurate and better estimation of condition of the patient's bone and helps in improving surgical treatment [45].

3D printing produces prototypes of innovative designs concepts and improvements made in already existing devices, the designs can be tested at low cost and their effectiveness and validation can be checked before installing industry [33]. 3D printing is being used in bioprinting that allows the modeling of different implantable tissues of body. Examples of bioprinting include transplanting of synthetic skin manufactured by 3D printing to patients suffering from burn injuries [46]. Heart valve stiffness can be controlled by replication of valves by combining biomaterials and cells which are manufactured using 3D printing [47], human's ears and other organs can also be replicated using bovine cartilage cells and other cells of the body [48]. Powdered drug layers are made using 3D printing so that it can faster dissolve in circulatory system than pills being used previously [49].

Table 2: Summary of Different 3D printing techniques and their uses in the medical Industry [33]

Designation additive-manufacturing process	Process description	Technologies	Materials	Medical use	Pros	Cons
Vat photo-polymerisation	Vat polymerisation uses a vat of liquid photopolymer resin, out of which the model is constructed layer by layer	Stereolithography (SLA) Digital light processing (DLP)	(i) Photopolymer resin	Bone, dental models [13], dental implant guides [14], hearing aids [15]	(i) High resolution and accuracy (ii) Complex parts (iii) Decent surface finish: smoother finish (iv) Flexible printing setup	(i) Lacking in strength and durability (ii) Still affected by UV light after print (iii) Not for heavy use
Material jetting	Material jetting creates objects in a similar method to a two-dimensional ink jet printer. Material is jetted onto a build platform using either a continuous or drop on demand (DOD) approach	Multijet modelling (MJM)	(i) Plastics (ii) Polymers: polypropylene, HDPE, PS, PMMA, PC, ABS, HIPS, EDP	Medical models [16], dental casts, dental implant guides [17]	(i) High accuracy (ii) Low waste of material (iii) Multiple material parts and colours in one process	(i) Required support material (ii) Limited materials: only polymers and waxes are supported
Binder jetting	The binder-jetting process uses two materials; a powder-based material and a binder. The binder is usually in liquid form and the build material in powder form. A print head moves horizontally along the x and y axes of the machine and deposits alternating layers of the build material and the binding material	Powder bed and inkjet head 3D printing (PDIH) Plaster-based 3D printing (PP)	(i) Stainless steel (ii) Polymers: ABS, PA, PC (iii) Ceramics: glass	Colour models especially colour coding of anatomy [18]	(i) Range of colours (ii) Multiple materials supported (iii) Faster (iv) Different binder-powder combination for various mechanical properties	(i) Not always suitable for structural parts (ii) The cleaning of the 3D-printing result needs time and increases the time of the procedure
Material extrusion	Fuse deposition modelling (FDM) is a common material extrusion process and is trademarked by the company Stratasys. Material is drawn through a nozzle, where it is heated and is then deposited layer by layer. The nozzle can move horizontally, and a platform moves up and down vertically after each new layer is deposited	Fused deposition modelling (FDM) Fused filament fabrication (FFF)	(i) Plastics; (ii) Polymers: ABS, nylon, PC, AB	Medical instruments and devices [19], rapid prototyping exoskeleton [20]	(i) Inexpensive process (ii) Widespread (iii) ABS plastic supported: good structural properties and easily accessible	(i) Dependence of quality on the noozle radius: bigger nozzle leads to less quality (ii) Low accuracy and dependence on the nozzle thickness (iii) Low speed (iv) Contact pressure needed to increase quality

Designation additive-manufacturing process	Process description	Technologies	Materials	Medical use	Pros	Cons
Powder bed fusion	The powder bed fusion process includes the following commonly used printing techniques: direct metal laser sintering (DMLS), electron beam melting (EBM), selective heat sintering (SHS), selective laser melting (SLM) and selective laser sintering (SLS)	Selective laser sintering (SLS) Direct metal laser sintering (DMLS) Selective heat sintering (SHS) Selective laser melting (SLM) Electron beam melting (EBM)	Powder-based materials. Common metals and polymers used are (i) SHS: nylon (ii) DMLS, SLS, SLM: stainless steel, titanium, aluminium, cobalt chrome, steel (iii) EBM: titanium, cobalt chrome, stainless steel material, aluminium and copper	Models that require a lattice, medical devices such as implants and fixations [21]	(i) Inexpensive (ii) Small technology: office size machine (iii) Large range of material options	(i) Low speed; lack of structural properties in materials (ii) Limited sizes (iii) Dependence on powder grain size
Sheet lamination	Sheet lamination processes include ultrasonic additive manufacturing (UAM) and laminated object manufacturing (LOM). The ultrasonic additive manufacturing process uses sheets or ribbons of metal, which are bound together using ultrasonic welding	Laminated object manufacturing (LOM) Ultrasonic consolidation (UC)	Paper, plastic and sheet metals	Orthopaedic modelling of bone surfaces [22]	(i) Speed (ii) Inexpensive (iii) Ease of materials handling	(i) Dependence on paper or plastic material (ii) Need of postprocessing (iii) Limited material range
Direct energy deposition	Directed energy deposition (DED) covers a range of terminology: "Laser engineered net shaping, directed light fabrication, direct metal deposition, 3D laser cladding" it is a more complex printing process commonly used to repair or add additional material to existing components	Laser metal deposition (LMD)	Metals: cobalt chrome, titanium	Limited. Commonly used to repair existing parts and build very large parts	(i) High control of grain structure (ii) High-quality-dependent on speed (iii) High-accuracy-dependent on accuracy (iv) Fast built with rapid material deposition (v) Fully dense parts; no need for supports (vi) Best process for part repair	(i) Limited range of materials; (ii) Poor surface quality; (iii) Wire process is less accurate

2.7 Summary:

During the last few years, skin adhesives and staple closure have widely accepted techniques for dermal wound closure. Despite all widely made advancements in this field no one had found a proper solution that can improve wound closure speed, ease of application, safety and efficient results. All conventional techniques have some limitations like suturing involves additional marks on the body, it needs very high-level skills to apply and very slow speed of application. Staplers penetrate the skin and cause scarring tracks post-surgically, more painful and disconformable to remove. Adhesives are somewhat messy, not useful for lengthy wounds, cause premature failure and can result in adverse allergic reactions.

The aim of this study is to find the best material and procedure for closing dermal wounds that make a better understanding of complications resulting from closure of wounds. The satisfaction of patients reported keeping in view the cosmetic outcomes while closing dermal wounds and reported discomfort during the removal of material post-treatment.

CHAPTER 3: METHODOLOGY

3.1 Designing of Patch:

The design of strips and locks for non-invasive wound closure is made using commercial modeling software Pro-Engineer. Pro-Engineer is a parametric computer-aided design (CAD) software where parts are made by characterizing features such as extrusion, cut, warp, round, hole, slot, etc. Pro-Engineer is a powerful design and assembly tool due to its parametric capability and dimension-based 3D modeling.

3.1.1 Preliminary design:

The preliminary design was based on the concept of two locks and one strap. This design was not possible through a single tool in Pro-Engineer, so multiple extrusion and other features were used to develop this design. In the 1st extrusion, the strap of this design was 4mm wide and 80mm in length, and 1 mm thick. This strap was flat on base and had multiple saw-like elevations of 1mm height on upper side of the strap which was made using 2nd extrusion command explained in figure 9A.

The locking clip was made using extrusion command, its base was 2mm in height and 10mm in length and 10mm in width. 2nd extrusion solid was made on one end of 1st extrusion which was 10mm in height, 10mm in width and 4mm thick. A cut command was used to make a square hole in 2nd extrusion whose dimensions were 3mm in height and 4.3mm width. An inclined extrusion was made on the upper surface in the hole so it may fit into elevations on the strap and act as a lock to hold the strip. A flat surface of 20 by 20mm was made using 4th extrusion command that may increase surface area at base to attach with microporous tape that can be seen in figure 9b and 9c.

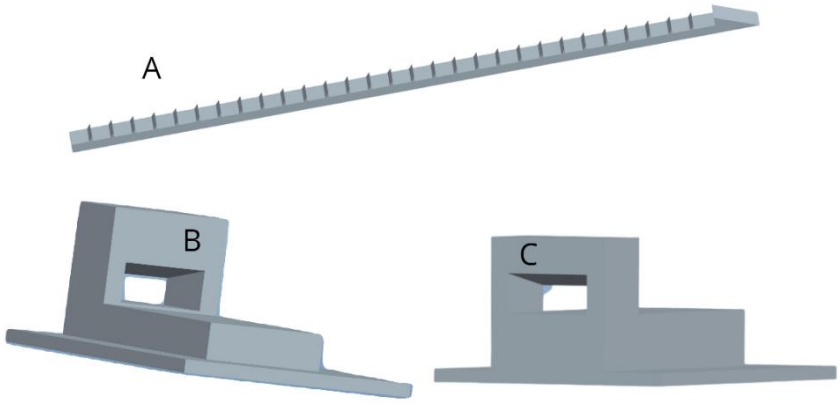

Figure 9: (A) Show Strap with elevations, (B, C) Locking Clips having an inclined surface to lock

This design was printed using a fused deposition modeling 3D printer with ABS filament material. Although ABS is not biocompatible it was used in printing design to validate the functioning. This printed model is shown in figure 10. The problem with this prototype was that ABS is quite hard material and the clips and strap were printed cannot bend around the curved parts of human body. Moreover, ABS is not a biocompatible product, it is a carcinogenic material so keeping these problems in mind the design was revised and searched other materials which are softer and biocompatible.

Figure 10: Printed Strap and Lock Clips with ABS

3.1.2 PLA Based Design:

To resolve problems associated with preliminary design 1st revision of design was made using Pro-Engineer CAD software. In this design, only two clips were made and instead of strap zip ties were used to close these clips due to its flexibility and economic benefit. For making the clip design extrusion solid command was used to make its base, which

is 15mm in length, 10mm in width and 1.5mm in height. 2nd extrusion solid was made on one end of base which is 4mm in length, 10mm in width and 5 mm in height. 3rd extrusion cut command was used to make a square hole in 2nd extrusion solid which is 4.5mm wide and 3mm in height. Both these designs are shown in Figures 11a and 11b respectively.

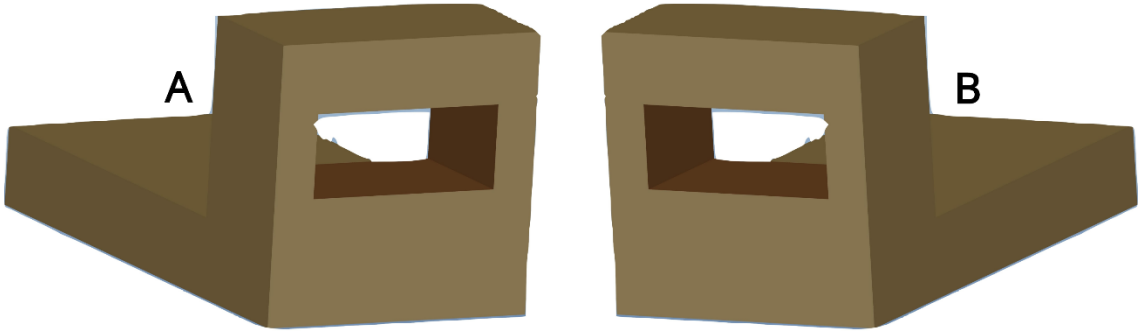

Figure 11: Two Clips having Space to pass Zip-ties

This design was printed using additive manufacturing 3D printing techniques which is Fused Deposition Modeling (FDM). The material used for printing this prototype was PLA filament. Printed clips and zip-tie to close these clips are shown in figure 12. The main problem associated with this printed prototype was that this material was also very hard to make suture-less wound closure strips and locks as well as it deforms at 50 to 60-degree temperature [50]. So, this material was not suitable for making suture-less wound closure stirps and lock to close dermal wounds.

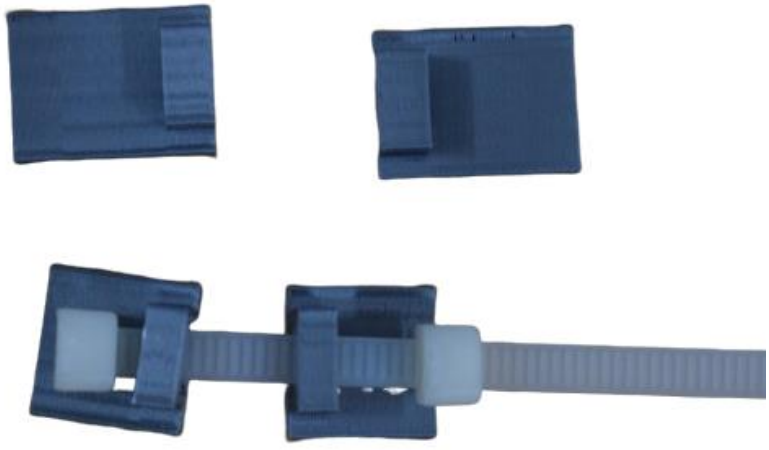

Figure 12: Two Clips printed with PLA and zip-tie

3.1.3 TPU Based Design:

To eliminate the problems faced during the first revision of the design, second revision of design was made using Pro-Engineer CAD software. This improvised design consists of a strap and a locking clip. Extrusion solid command was used to make base of strap, which is 50mm in length, 4mm in width and 1.5mm in height. One end of strip is pointed, and other ends of this strap contain a flat and wide part, which is 13mm in width, 12mm in length and 2.5 in height. 2nd extrusion solid was used to make fourteen saw-like triangle shape inclined elevation on the strap. The base of is triangle was 2.5mm, height of this triangle was 3mm and inclined surface makes an angle of 50 degrees angle with base as shown in figure 13a.

To make lock clip extrusion solid tool was used to design base of lock clip, which is 12mm in length, 13mm in width and 1.5mm in height. 2nd extrusion model was made on 1st extrusion using extrusion solid tool, which is 4mm in length, 13mm in width and 5mm in height. A square hole was made on the 2nd extrusion model using an extrusion cut tool of 4.5mm length and 4mm width as shown in figure 13 b.

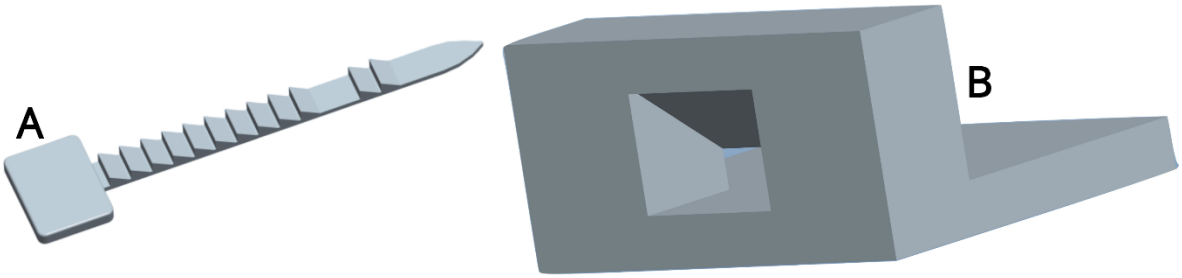

Figure 13: (a) TPU Based Strap (b) Locking Clip

Multiple designs of variable straps and locks was made using pattern tool. Design of five straps for wound of 65mm length, two straps for medium-sized wounds having length of 26mm and one strap for curved or irregular wounds (Figure 14).

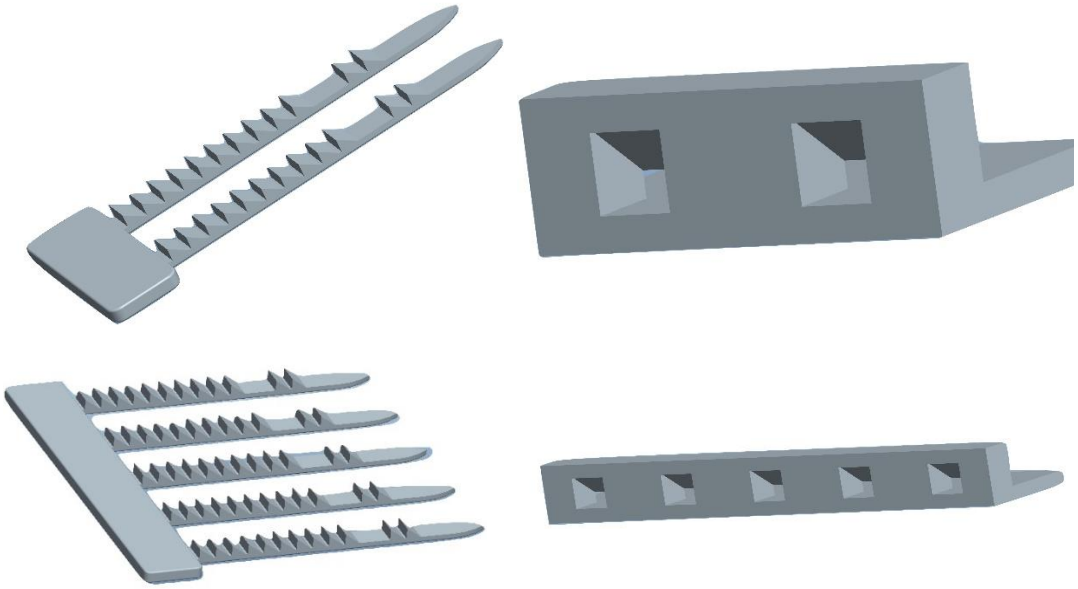

Figure 14: Multi-designs for strips and locks

3.2 Selection of Material:

The selection of material for fabrication of non-invasive dermal wound closure patch is a crucial step. The material for suture-less non-invasive wound closure patch should have following properties.

- The material should be soft and flexible.
- It should have low shore hardness on the durometer scale.
- This should be 3D printable to be easily handled in additive low-cost manufacturing.
- This should be biocompatible so it may not evoke any adverse or allergic reaction on wounds.

Three different materials i.e Polylactic Acid (PLA), Thermoplastic Polyurethane (TPU) and Acrylonitrile Butadiene Styrene (ABS) were compared keeping in mind above attributes of materials. All the above-mentioned properties comparison is shown in table 3.

Table 3: Comparison of differnt 3D printable materials [51, 52]

Subject	TPU	PLA	ABS
Soft and Flexible	✓	**X**	**X**
3D printable	✓	✓	✓
Biocompatible	✓	✓	**X**
Resistance against Oils and Chemicals	✓	**X**	✓
Shore Hardness	20D	80D	100D

So, Thermoplastic Polyurethane (TPU) found to be the most suitable material for making a suture-less wound closure device due to its high resistance against oils and chemicals, biocompatibility and soft and flexible nature.

3.3 Fabrication of Patch:

One of the additive manufacturing techniques, Fused Deposition Modeling (FDM) shown in figure 15, was used to make designed CAD models. During last few years this technique gained a lot of interest in making prototypes because it is a quickest and most affordable way to create 3D things. The objects that are to made using FDM firstly designed on CAD software and before printing this design are converted into STL file using.STL format which 3D printer can read and understand. The FDM used to fabricate design is Tronxy p802ma. The infill percentage was adjusted to 100% on parameter 3. The layer length of printer was adjusted to 0.1 mm.

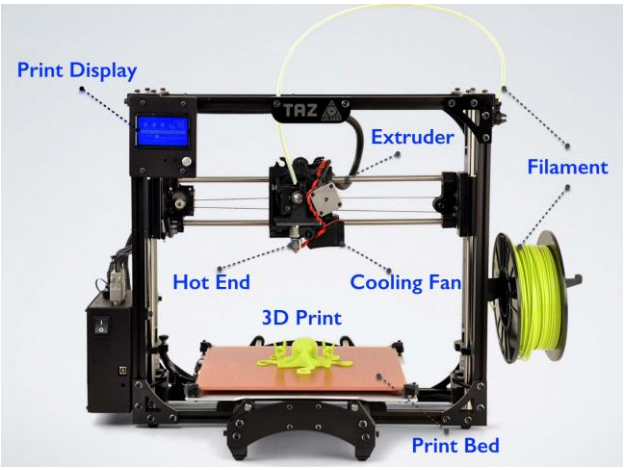

Figure 15: Fused Deposition Modeling 3D printer (Tronxy p802ma)

The role of TPU filament was loaded on the printer and one end of the filament was adjusted in the nozzle of FDM printer extruder. The TPU filament was melted in the nozzle, this melted material extruded on the printed bed layer by layer. Computer control both extrusion nozzle and print bed to translate perfect dimensions of the model following directions of design prepared during printing. The extruder moved overprint bed vertically and horizontally making a specific section of design. Once a layer was printed, it became hard and cooled down by a fan in printer. After completion of one layer, the print bed moved down by one-sixth of an inch to make new layer on previous layer. In this way design was completely printed layer by layer and support material was removed by hand or by using heat gun. Figure 16 shows different straps and locks were printed with FDM additive manufacturing technique.

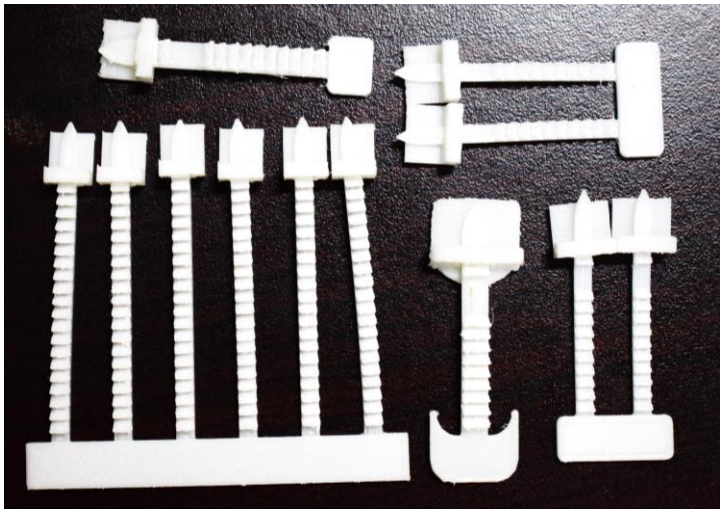

Figure 16: Multiple stirps and locks of Suture-less wound closure device (TPU Based)

3.4 Assembly of Patch:

These printed straps and locks were attached with microporous tape using cyanoacrylate adhesives. Figure 17 shows assembled strips and locks attached to the microporous tape. The microporous tape was cut in pieces of different sizes and lengths i.e 25mm of width and 15mm, 26mm and 65mm of lengths. The tape edges were cut in round shape to remove sharp edges. The strap part was attached on one end of a piece of tape and locks were attached on one end of another piece of tape according to the strip orientation.

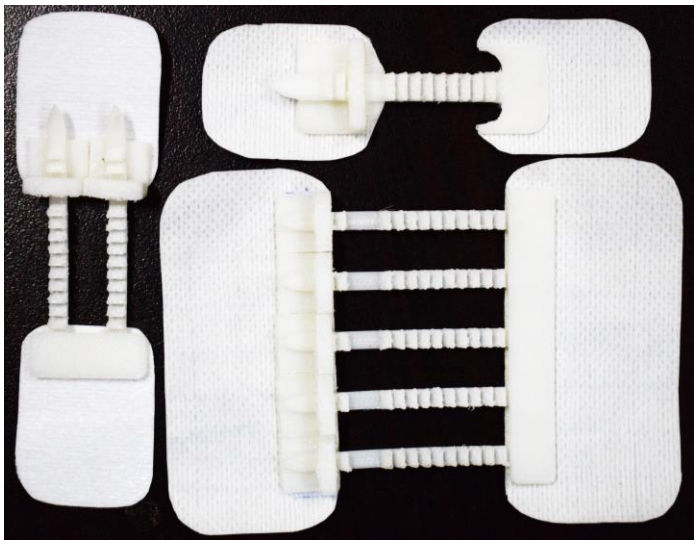

Figure 17: Strips and locks of different sizes attached with microporous tape

3.5 Mechanical Testing of Patch:

3.5.1 Mechanical Testing of TPU Strap:

Mechanical testing of the TPU strap was done using Shimadzu AG-XPlus Universal Testing Machine (UTM) to check the strength of designed strap. This machine had a strain rate ranging from 0.0005 to 1000mm/min. The machine had a 20KN load cell and grip section had maximum thickness of 7mm and width of 24mm for flat samples, and maximum diameter of 4-9mm for round samples. The applied displacement rare was 5mm/min. The stress, strain, ultimate strength, fracture point, and elongation were obtained after testing.

3.5.2 Mechanical Testing of Microporous Tape:

Mechanical testing of Microporous tape was done on UTM to check the shear strength of adhesive applied between microporous tape and skin. To perform the test a piece of goatskin was cut into two equal pieces of 40mm by 24mm. Figure 18 shows the goatskin and patch assembly. The assembled patch was attached to skin pieces and was locked by passing straps through locks, as shown in figure 18. The skin portions were adjusted into grip of UTM and displacement rate of 5mm/min was adjusted. The resulting stress and strain provided the shear strength of the adhesive joint. Three samples were tested in this test.

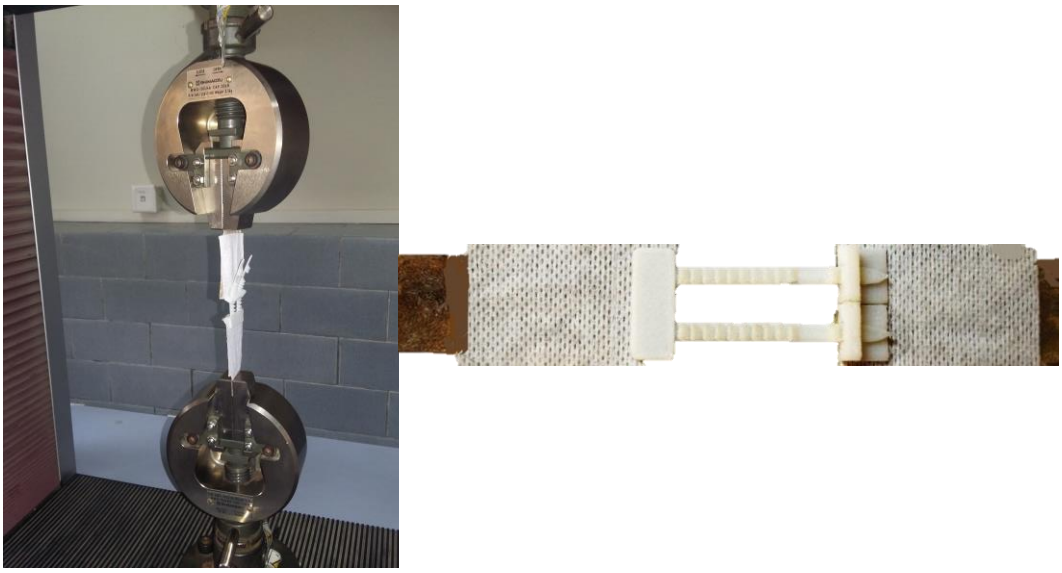

Figure 18: Patch assembled on goatskin (Right side image) Testing on UTM machine (Left side Image)

3.6 In vivo studies:

Newly developed suture-free strip bond patch and conventional suture available in the market were used in this study. Eight native rabbits were used in the study to compare non-invasive wound closure strip bond patch and conventional suturing techniques according to the institutional guidelines. The animals selected were 11 months to 13 months old having weights from 500g to 600g. Hair of rabbits from their back was removed by shaver or trimer to make incision and to apply sutures and Suture free strip bond patch. The general description of the subjects used in this study is given in table 4.

Table 4: General Description of Subjects

Subject	Description	Experimental Group	Comparison Group
Age	Male	3 (1 year)	3 (1 Year)
	Female	2 (1 Year)	
Weight	Male	3 (570 g)	3 (594 g)
	Female	2 (553 g)	
Allergy History	No	5 (100%)	3 (100%)
	Yes	5 (0%)	3 (0)
Previous History	No	5 (100%)	3 (100%)
	Yes	5 (0%)	3 (0%)
Wound Length	Male	3 (26 × 5 mm)	3 (20 × 5 mm)
	Female	2 (25 × 5 mm)	

Each rabbit was given 0.8ml anesthesia injection intramuscular with Xylazine (0.75mL) & Ketamine (0.25mL) solution on the day to procedure. After 10 minutes of anesthesia injection, the skin of rabbit was wiped with a cotton swab soaked in 70% alcohol solution. Under the observation of licensed veterinarian 20mm to 26mm long incision was made on the back of each rabbit as shown in figure 19. The incision made on 5 rabbits was closed with Non-invasive Suture-less wound closure device which is our experimental group.

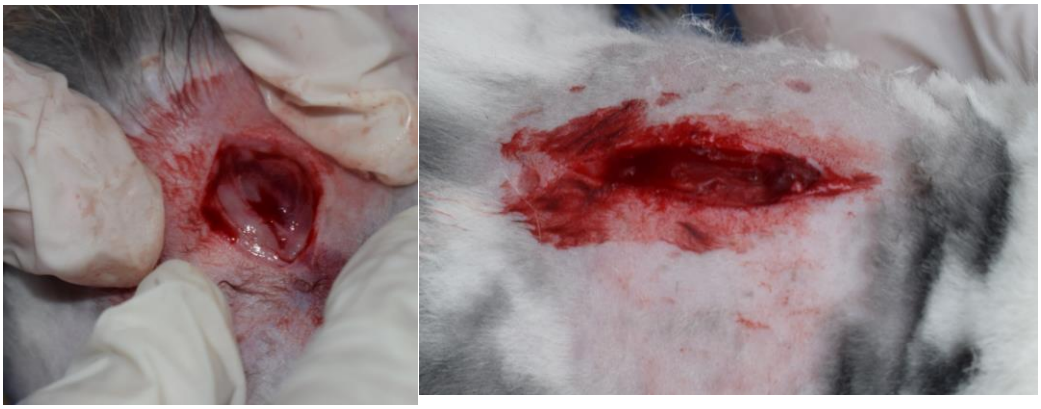

Figure 19: Incisions made on both comparison and experimental groups

Device having two straps was applied for closure of 20mm to 26 mm long incisions. The incision made on rest of 3 rabbits was closed using a conventional suturing technique (thread and needle suturing). For closing wounds of 20 to 26 mm lengths, 3 intradermal sutures were used as shown in figure 20. Wounds were cleaned with Pyodine (povidone-iodine USP) solution was applied post-treatment. Each rabbit was given 0.2mL intramuscular Traumanil injection to reduce pain and infections for two days after treatment. Rabbits were kept under care and observed regularly.

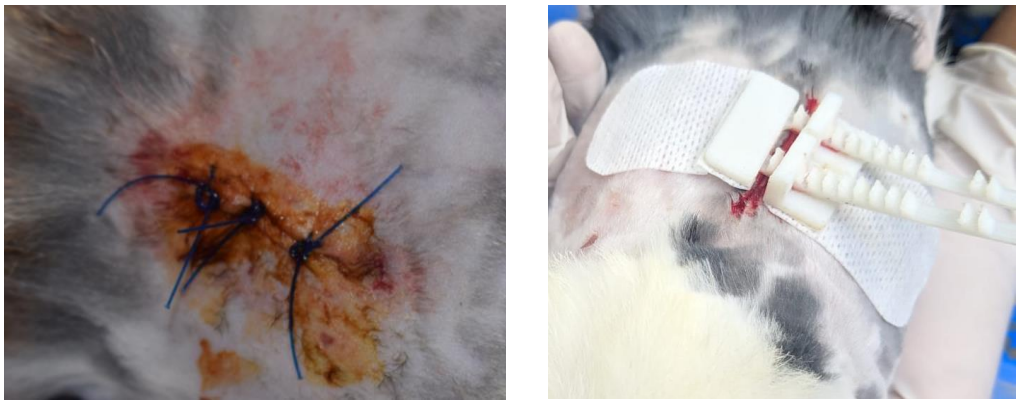

Figure 20: Incisions closed with suture and strip patch device

3.7 Bacterial quantification:

Bacterial growth was checked on the surface of the wounds through microbial culturing techniques. For that broth culture media was prepared in a petri dish and stored. Equipment is sterilized in autoclave. The autoclaved loop was rub on the surface of wound and this loop was dipped in sterilized water.

Then this bottle of water containing microbes is mixed on vortex mixer, so this solution is homogenized. After mixing water is poured onto culture media and spread water totally over culturing media through cotton swap as shown in figure 21 A. Then Petri plate was covered so there would be no contamination on culturing media as seen in figure in figure 21 B. The Petri plate was observed after 24 hours and bacterial colonies was counted on culture media.

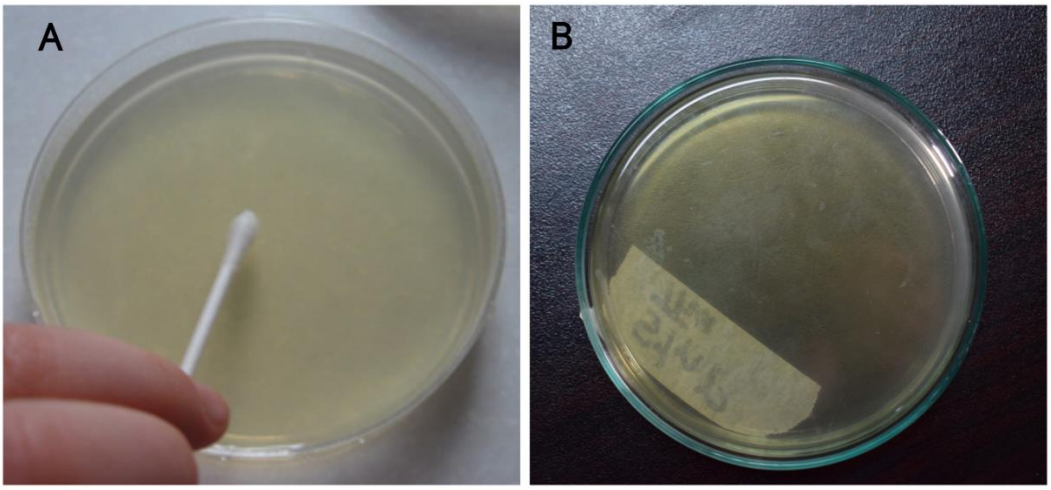

Figure 21: Culturing Technique Method

3.8 Histology:

After seven days of treatment, the section of skin was cut and stored in 10% formalin solution. This skin section which is stained with hematoxylin and eosin (H and E) stain was evaluated for bacterial infection and inflammation on the wound. The expert pathologist and mark his observation on the industrial scale.

CHAPTER 4: RESULTS AND DISCUSSIONS

4.1 Mechanical Testing of Patch:

4.1.1 Mechanical Testing of TPU Strap:

Mechanical testing results of TPU showed that a single strip of TPU patch is strong enough to hold a maximum force of 66.4 N force. Maximum stress that this strip bond patch can hold 2.6 N/mm^2. The maximum elongation of single strip was 63.1mm. The stress-strain graph of TPU based strap is shown in figure 22.

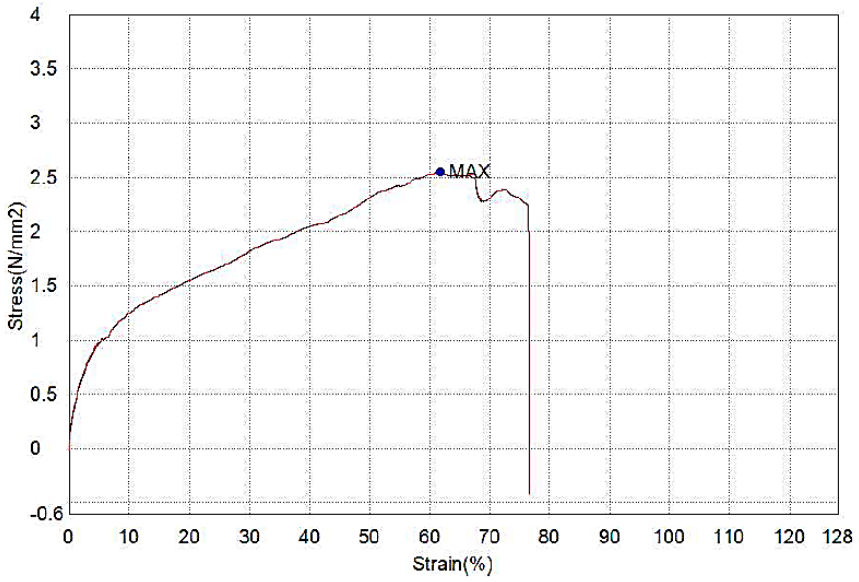

Figure 22: Stress-Strain curve of TPU Strap

4.1.2 Mechanical Testing of Microporous Tape:

Mechanical testing of the adhesiveness of microporous tape showed that this tape can hold up to 9.5 N force. It can bear a maximum stress of 0.37 N/mm^2. The maximum elongation of microporous tape was 5.2mm. The force calculated show that it can hold wounds of 26 × 13mm, which is 3 times greater than the maximum force to close 45 × 13mm wounds. So manufactured device has safety factor of 3 or more with

almost same dimensions. The stress-strain graph of microporous tape adhesiveness can be seen in figure 23.

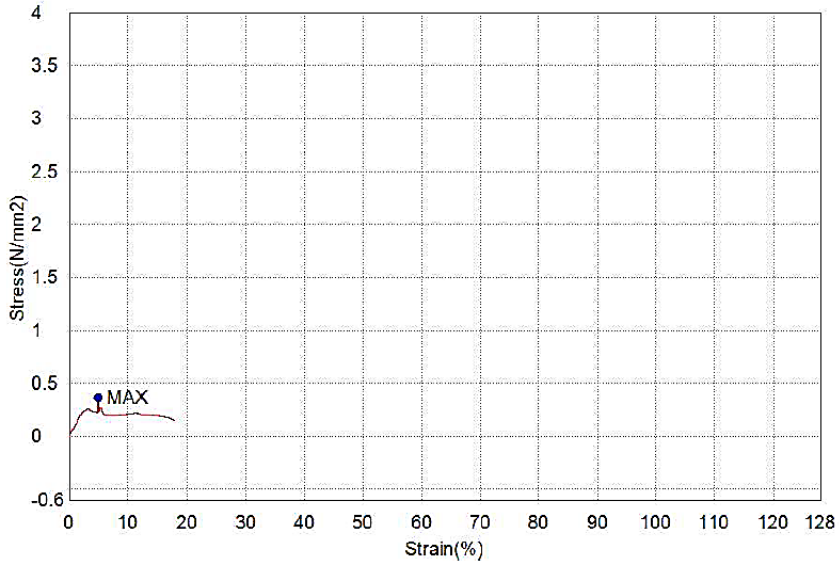

Figure 23: Stress-Strain graph of Microporous Tape's Adhesiveness

4.2 Visual observation of Wounds:

The strip patch and sutures were removed after 7 days of treatment and the area around wound was cleaned properly to visually observe the closure of wound. Visually the wound closed with strip patch was clean as compared to suture closure where wound was irregularly closed as shown in figure 24. There were no extra marks on skin of rabbits whose wound was closed with strip patch as compared to the rabbits whose wound was closed with suture. All the wounds were completely closed after 7 days of treatment.

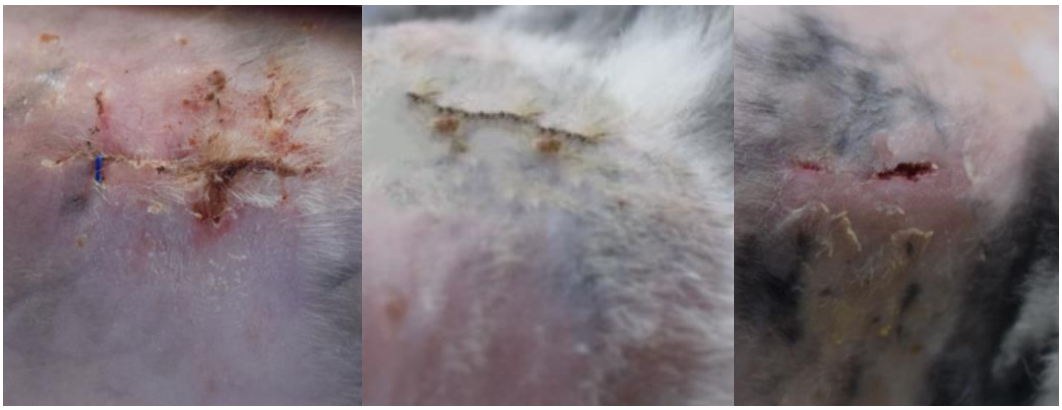

Figure 24: Wound condition after 1 week of treatment

4.3 Safety evaluation:

There was no allergic reaction, or any other inflammation observed on any of the wounds of rabbits in both experimental as well as comparison group. By the end of test period, the wound in all test animals had scabbed over both in experimental and comparison group subjects. Safety evaluation comparison of both experimental and comparison groups can be seen in table 5.

Table 5: Safety evaluation of subjects seven days post treatment

Subject	**Description**	**Experimental Group**	**Comparison Group**
Allergy Reaction	No	5 (100%)	3 (100%)
	Yes	5 (0%)	0 (0%)
Wound Infection	No	5 (100%)	3 (100%)
	Yes	5 (0%)	0 (0%)
Other Adverse Reaction	No	5 (100%)	3 (100%)
	Yes	5 (0%)	0 (0%)

4.4 Bacterial quantification:

All wound surfaces closed with strip patch devices showed lesser bacterial growth as compared to wounds closed with sutures. Most probably during the suturing procedure when suture material enters the body it may take in some microbes in body of subjects but there is not insertion or puncturing of skin when strip patch device is applied so there are fewer chances of microbial entry. Bacterial colonies counted from the incisions closed with strip patch device and sutures from 3rd to 6th days from the Petri-plates after 24 hours of streaking that can be seen in figure 26. The result showed mean bacterial count on surface of wounds closed with strip bond patch was 45.5 colonies and, on the wounds,

closed with suture was 188 colonies. A comparison of bacterial quantification on both strips and patch is seen in figure 25.

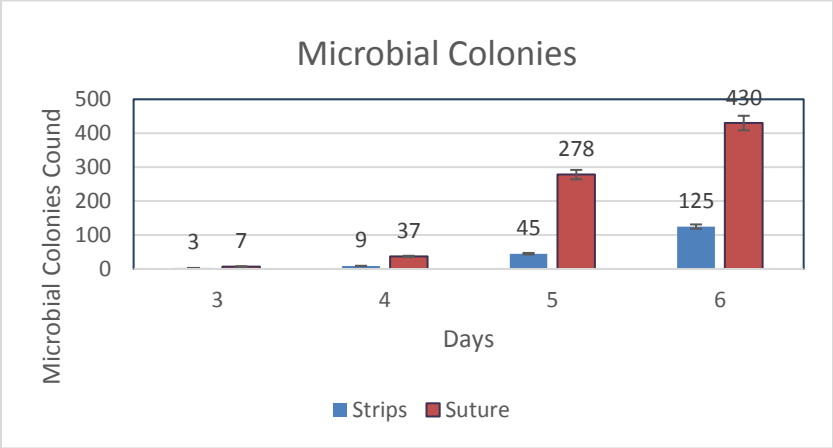

Figure 25: Comparison of bacterial count on surface of suture and strip patch closed wounds

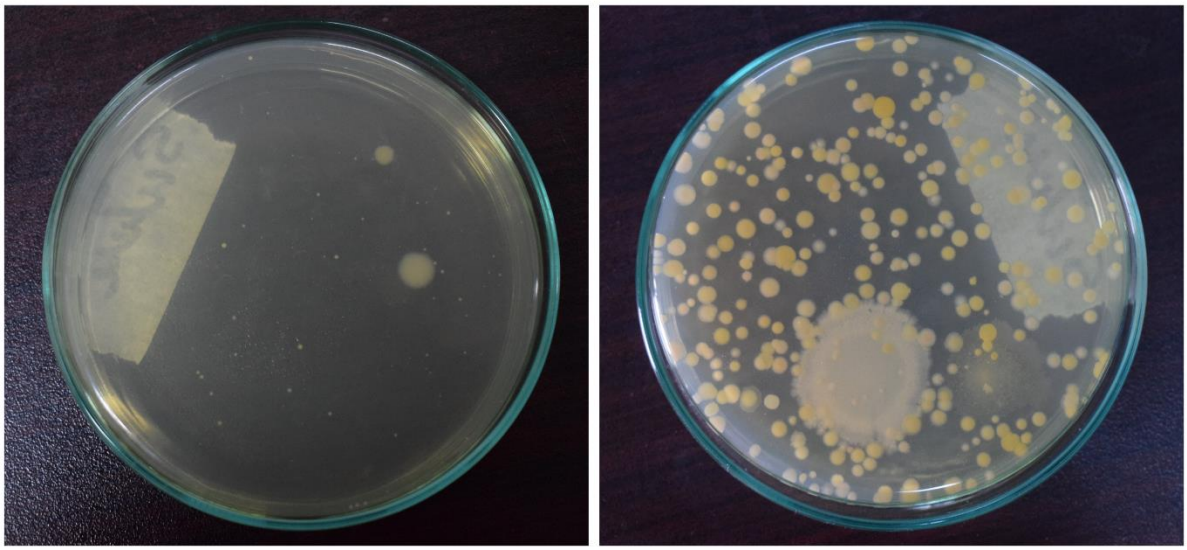

Figure 26: Bacterial growth on culture nourishing media

4.5 Histology Sample:

The epidermis of wounds closed with a suture-less wound closure device was intact in all the animals in the experimental group. There was only residual inflammation with formation of some new collagen was seen on all the samples. Incisions closed with suture-less wound closure patch showed lack of inflammation which is indication of lower scar tissue formation in all samples of skin that can be seen in figure 27. A contrary to suture-less strip patch incisions

closed with sutures had some areas containing debris, a huge number of bacteria and some suture material. High magnified photos of dermis indicate there is foreign body inflammation in the which surrounds the cross-section of suture thread. Bacterial colonies are associated with thread of suture that can be seen in figure 28.

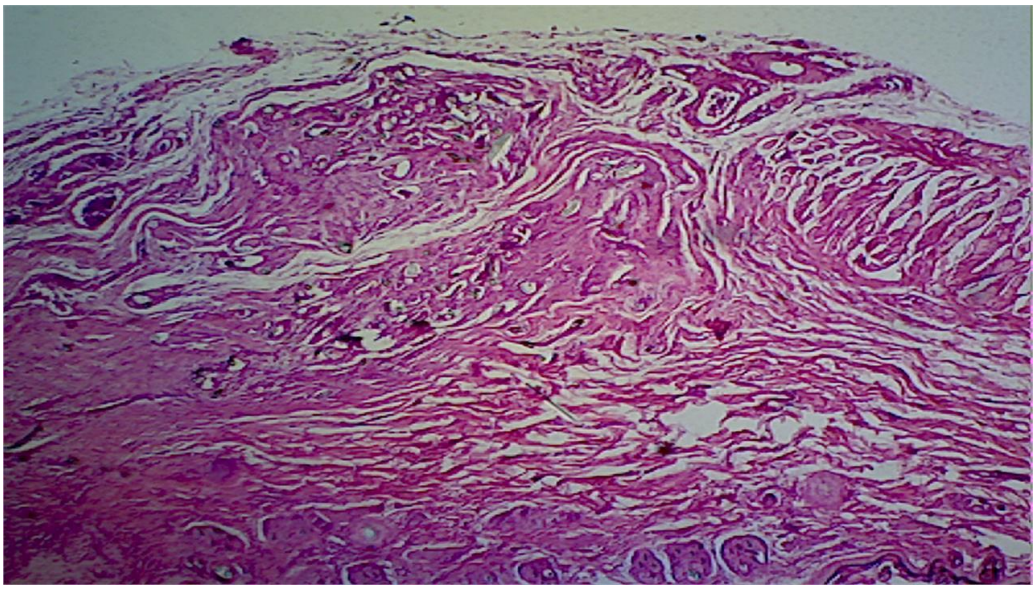

Figure 27: H&E stained Skin and bacterial infection in strip patch closure

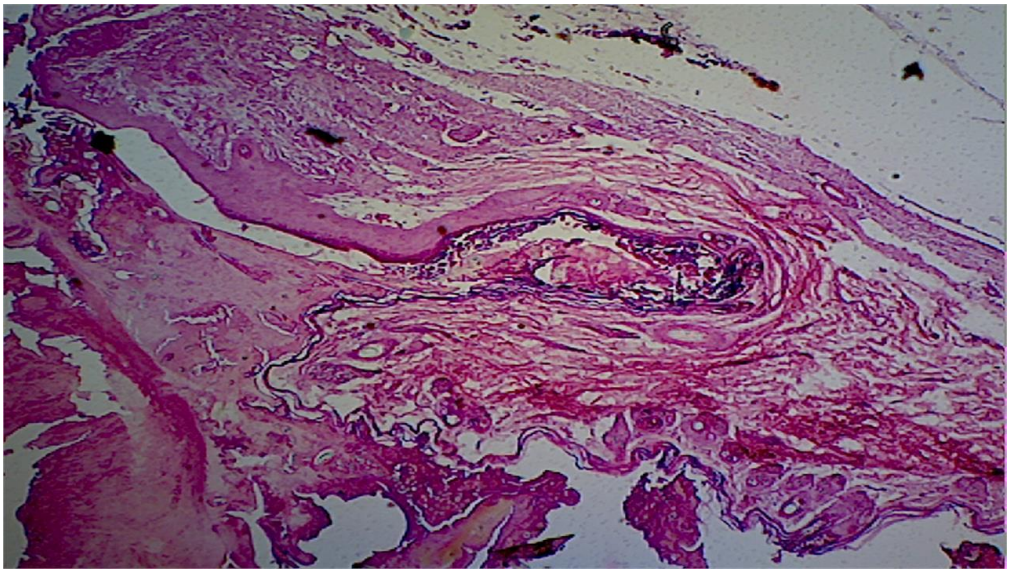

Figure 28: H&E stained Skin and bacterial infection in suture closure

4.6 Comparison of Sutures and Strip patch:

Results of both stirps and sutures were compared, wounds closed with strip patches show much better results as shown in table 6.

Table 6: Comparison of Suture and Strip Patch

Subject	Strip Patch	Sutures
Additional Marks on body	X	✓
Introduction of Foreign material in body	X	✓
Time of Application	3-5 minutes	15-20 minutes
Bleeding after application	2 minutes	2 minutes
Wound visible for surveillance	✓	X
Need a skilled physician to apply and remove	X	✓
Susceptible to microbial attach	X	✓
Anesthesia Required	X	✓

CHAPTER 5: CONCLUSIONS AND FUTURE PERSPECTIVES

5.1 Conclusions:

As a result of this research, a low-cost 3D printable design for a suture-less wound closure device for open wounds was successfully designed. This design was printed and validated accurately with TPU material, which is found to be the most suitable, economical, biocompatible and compliant for manufacturing non-invasive wound closure. Microporous tape along with mechanical fastening provided enough force for closing open dermal wounds until incision was completely healed. The device did not induce infection or adverse reaction during pre-clinical tests and these incisions healed in less time than suture closure without any inflammations or microbial infections to these incisions. Cultural growth tests and histology study of section of skin at the site of incision one-week post-treatment proved less microbial growth on incisions closed with device as compared to incisions closed with conventional suture technique.

5.2 Future Perspective:

For the last few years due to the advancement of modern technologies and their use in medical field suture procedures had changed enormously. Conventional suturing techniques has been changed to non-invasive innovative device for closure of open skin incisions. A better understanding of wound healing and components required to heal open incisions is needed and will help in manufacturing non-invasive wound closure devices which will stop microbial growth completely.

Targeting the manufacturing of microporous tape or adhesive through which TPU material can better attach with skin or with microporous tape.

Manufacturing stirps that has week point so the extra strap may cut off, after successful closure of wounds, by hand as shown in figure 29.

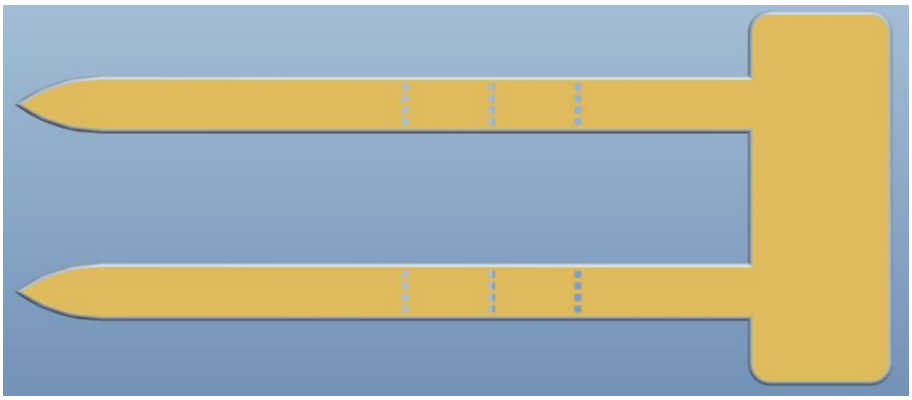

Figure 29: Strips with Week points

Designing different other designs for strap and lock that can improvise skin closure and its application as shown in figure 30.

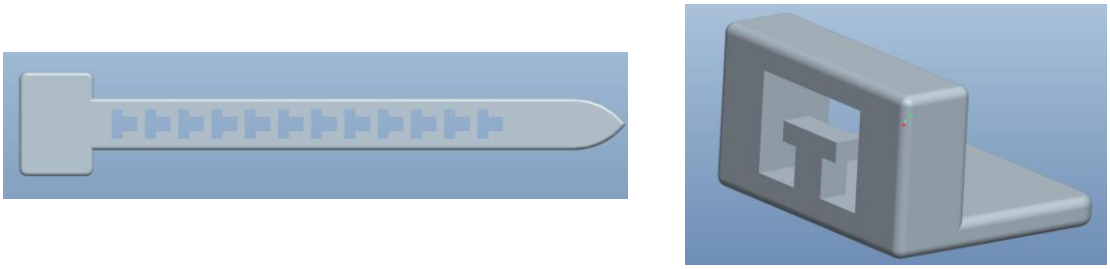

Figure 30: New Design for lock and strips

In vivo studies in human patients, for determination of closing time in incisions with different lengths and depths.

REFERENCES

[1] R. Khan, D. Fick, F. Yao, K. Tang, M. Hurworth, B. Nivbrant, *et al.*, "A comparison of three methods of wound closure following arthroplasty: a prospective, randomized, controlled trial," *The Journal of bone and joint surgery. British volume,* vol. 88, pp. 238-242, 2006.

[2] I. Stockley and R. Elson, "Skin closure using staples and nylon sutures: a comparison of results," *Annals of The Royal College of Surgeons of England,* vol. 69, p. 76, 1987.

[3] B. Singh, M. Mowbray, G. Nunn, and S. Mearns, "Closure of hip wound, clips or subcuticular sutures: does it make a difference? " *European Journal of Orthopaedic Surgery & Traumatology,* vol. 16, pp. 124-129, 2006.

[4] G. Frishman, T. Schwartz, and J. Hogan, "Closure of Pfannenstiel skin incisions. Staples vs. subcuticular suture," *The Journal of reproductive medicine,* vol. 42, pp. 627-630, 1997.

[5] M. Reed and T. Lennard, "Prospective randomized trial of clips versus subcuticular polydioxanone for neck wound closure," *British journal of surgery,* vol. 84, pp. 118-118, 1997.

[6] D. Selvadurai, C. Wildin, G. Treharne, S. Choksy, M. Heywood, and M. Nicholson, "Randomised trial of subcuticular suture versus metal clips for wound closure after thyroid and parathyroid surgery," *Annals of the Royal College of Surgeons of England,* vol. 79, p. 303, 1997.

[7] M. Murphy, P. Prendergast, and J. Rice, "Comparison of clips versus sutures in orthopedic wound closure," *European Journal of Orthopaedic Surgery & Traumatology,* vol. 14, pp. 16-18, 2004.

[8] D. Gatt, C. Quick, and M. Owen-Smith, "Staples for wound closure: a controlled trial," *Annals of the Royal College of Surgeons of England,* vol. 67, p. 318, 1985.

[9] A. K. Gupta, R. R. Singh, A. Gupta, and A. S. Shah, "Skin closure with 2-octyl cyanoacrylate glue versus skin stapler: a comparative study," *International Surgery Journal,* vol. 3, pp. 1954-1958, 2016.

[10] T. Gillman and J. Penn, "Studies on the repair of cutaneous wounds," in *Med. Proc,* 1956, p. 121.

[11] T. Gillman, "Healing of cutaneous abrasions and of incisions closed with sutures or plastic adhesive tape," in *Med Proc,* 1958, pp. 751-755.

[12] S. D. Elek and P. Conen, "The virulence of Staphylococcus pyogenes for man. A study of the problems of wound infection," *British Journal of experimental pathology,* vol. 38, p. 573, 1957.

[13] G. Taylor, R. Shooter, P. Frandsen, W. Fielder, and W. Kerth, "Staphylococcal wound infection an experimental study in guinea-pigs," *British Journal of Surgery,* vol. 49, pp. 569-571, 1962.

[14] T. Golden, "Non-irritating, multipurpose surgical adhesive tape," *The American Journal of Surgery,* vol. 100, pp. 789-796, 1960.

[15] R. P. Luck, R. Flood, D. Eyal, J. Saludades, C. Hayes, and J. Gaughan, "Cosmetic outcomes of absorbable versus nonabsorbable sutures in pediatric facial lacerations," *Pediatric emergency care,* vol. 24, pp. 137-142, 2008.

[16] L. Al-Mubarak and M. Al-Haddab, "Cutaneous wound closure materials: an overview and update," *Journal of cutaneous and aesthetic surgery,* vol. 6, p. 178, 2013.

[17] J. S. Freed and J. Ko, "An innovative advance in non-invasive wound closure: a new paradigm," *Military medicine,* vol. 183, pp. 472-480, 2018.

[18] A. Saalabian, J. Covi, and R. Horch, "A review on wound closure techniques," *Journal of Wound Technology,* 2011.

[19] R. D. Wolcott, K. F. Cutting, S. E. Dowd, and S. L. Percival, "Types of wounds and infections," in *Microbiology of Wounds*, ed: CRC Press, 2010, pp. 232-245.

[20] L. Capek, E. Jacquet, L. Dzan, and A. Simunek, "The analysis of forces needed for the suturing of elliptical skin wounds," *Medical & biological engineering & computing,* vol. 50, pp. 193-198, 2012.

[21] K. H. Katz, E. B. Desciak, and M. E. Maloney, "The optimal application of surgical adhesive tape strips," *Dermatologic Surgery,* vol. 25, pp. 686-688, 1999.

[22] J. Y. Kwon, H. G. Yun, and I. Y. Park, "n-Butyl-2-cyanoacrylate tissue adhesive (Histoacryl) vs. subcuticular sutures for skin closure of Pfannenstiel incisions following cesarean delivery," *PloS one,* vol. 13, p. e0202074, 2018.

[23] D. Lubowski and D. Hunt, "Abdominal wound closure comparing the proximate stapler with sutures," *Australian and New Zealand Journal of Surgery,* vol. 55, pp. 405-406, 1985.

[24] W. Roolker, E. Kraaneveld, H. Been, and R. Marti, "Results of a prospective randomized study comparing a non-invasive surgical zipper versus intracutaneous sutures for wound closure," *Archives of orthopedic and trauma surgery,* vol. 122, pp. 2-4, 2002.

[25] G. J. Parell and G. D. Becker, "Comparison of absorbable with nonabsorbable sutures in closure of facial skin wounds," *Archives of facial plastic surgery,* vol. 5, pp. 488-490, 2003.

[26] J. L. Fick, R. E. Novo, and N. Kirchhof, "Comparison of gross and histologic tissue responses of skin incisions closed by use of absorbable subcuticular staples, cutaneous metal staples, and polyglactin 910 suture in pigs," *American Journal of veterinary research,* vol. 66, pp. 1975-1984, 2005.

[27] K. J. Cross, E. H. Teo, S. L. Wong, J. S. Lambe, C. H. Rohde, R. T. Grant, *et al.*, "The absorbable dermal staple device: A faster, more cost-effective method for incisional closure," *Plastic and reconstructive surgery,* vol. 124, pp. 156-162, 2009.

[28] V. A. Tellis, "Renal transplant incision closure using new absorbable subcuticular staple device," *Clinical transplantation,* vol. 21, pp. 410-412, 2007.

[29] C. Carleo, A. J. Singer, and H. C. Thode Jr, "Effect of frequent water immersion on the rate of tissue adhesive sloughing: A randomized study," *Canadian Journal of Emergency Medicine,* vol. 7, pp. 391-396, 2005.
[30] D. M. Toriumi, K. O'Grady, D. Desai, and A. Bagal, "Use of octyl-2-cyanoacrylate for skin closure in facial plastic surgery," *Plastic and reconstructive surgery,* vol. 102, pp. 2209-2219, 1998.
[31] J. B. Sterling and J. W. Skouge, "Surgical glue to secure small split-thickness skin grafts: A cost-effective and time-saving technique," *Dermatologic Surgery,* vol. 34, pp. 246-248, 2008.
[32] C. C. Dowson, A. D. Gilliam, W. J. Speake, D. N. Lobo, and I. J. Beckingham, "A prospective, randomized controlled trial comparing n-butyl cyanoacrylate tissue adhesive (LiquiBand) with sutures for skin closure after laparoscopic general surgical procedures," *Surgical Laparoscopy Endoscopy & Percutaneous Techniques,* vol. 16, pp. 146-150, 2006.
[33] A. Aimar, A. Palermo, and B. Innocenti, "The Role of 3D Printing in Medical Applications: A State of the Art," *Journal of healthcare engineering,* vol. 2019, 2019.
[34] C. L. Ventola, "Medical applications for 3D printing: current and projected uses," *Pharmacy and Therapeutics,* vol. 39, p. 704, 2014.
[35] S. N. Kurenov, C. Ionita, D. Sammons, and T. L. Demmy, "Three-dimensional printing to facilitate anatomic study, device development, simulation, and planning in thoracic surgery," *The Journal of thoracic and cardiovascular surgery,* vol. 149, pp. 973-979. e1, 2015.
[36] H. Saijo, K. Igawa, Y. Kanno, Y. Mori, K. Kondo, K. Shimizu, *et al.*, "Maxillofacial reconstruction using custom-made artificial bones fabricated by inkjet printing technology," *Journal of Artificial Organs,* vol. 12, pp. 200-205, 2009.
[37] F. Auricchio and S. Marconi, "3D printing: clinical applications in orthopedics and traumatology," *EFORT open reviews,* vol. 1, pp. 121-127, 2016.
[38] T. D. Crafts, S. E. Ellsperman, T. J. Wannemuehler, T. D. Bellicchi, T. Z. Shipchandler, and A. V. Mantravadi, "Three-dimensional printing and its applications in otorhinolaryngology–head and neck surgery," *Otolaryngology-Head and Neck Surgery,* vol. 156, pp. 999-1010, 2017.
[39] N. N. Zein, I. A. Hanouneh, P. D. Bishop, M. Samaan, B. Eghtesad, C. Quintini, *et al.*, "Three-dimensional print of a liver for preoperative planning in living donor liver transplantation," *Liver transplantation,* vol. 19, pp. 1304-1310, 2013.
[40] P. Hangge, Y. Pershad, A. A. Witting, H. Albadawi, and R. Oklu, "Three-dimensional (3D) printing and its applications for aortic diseases," *Cardiovascular diagnosis and therapy,* vol. 8, p. S19, 2018.
[41] M. P. Chae, W. M. Rozen, P. G. McMenamin, M. W. Findlay, R. T. Spychal, and D. J. Hunter-Smith, "Emerging applications of bedside 3D printing in plastic surgery," *Frontiers in surgery,* vol. 2, p. 25, 2015.

[42] S. Su, K. Moran, and J. L. Robar, "Design and production of 3D printed bolus for electron radiation therapy," *Journal of applied clinical medical physics,* vol. 15, pp. 194-211, 2014.
[43] J. P. Costello, L. J. Olivieri, L. Su, A. Krieger, F. Alfares, O. Thabit, *et al.*, "Incorporating three-dimensional printing into a simulation-based congenital heart disease and critical care training curriculum for resident physicians," *Congenital heart disease,* vol. 10, pp. 185-190, 2015.
[44] M. Frame and J. S. Huntley, "Rapid prototyping in orthopedic surgery: a user's guide," *The Scientific World Journal,* vol. 2012, 2012.
[45] H. Dodziuk, "Applications of 3D printing in healthcare," *Kardiochirurgia I torakochirurgia polska= Polish journal of cardio-thoracic surgery,* vol. 13, p. 283, 2016.
[46] P. He, J. Zhao, J. Zhang, B. Li, Z. Gou, M. Gou, *et al.*, "Bioprinting of skin constructs for wound healing," *Burns & trauma,* vol. 6, p. 5, 2018.
[47] M. Vukicevic, B. Mosadegh, J. K. Min, and S. H. Little, "Cardiac 3D printing and its future directions," *JACC: Cardiovascular Imaging,* vol. 10, pp. 171-184, 2017.
[48] G. Zhou, H. Jiang, Z. Yin, Y. Liu, Q. Zhang, C. Zhang, *et al.*, "In vitro regeneration of patient-specific ear-shaped cartilage and its first clinical application for auricular reconstruction," *EBioMedicine,* vol. 28, pp. 287-302, 2018.
[49] A. Konta, M. García-Piña, and D. Serrano, "Personalised 3D printed medicines: which techniques and polymers are more successful?," *Bioengineering,* vol. 4, p. 79, 2017.
[50] J. Krotký, J. Honzíková, and P. Moc, "Deformation of print PLA material depending on the temperature of reheating printing pad," *Published by Manufacturing Technology, ISSN,* pp. 1213-2489, 2016.
[51] R. R. Vogels, A. Lambertz, P. Schuster, S. Jockenhoevel, N. D. Bouvy, C. Disselhorst-Klug, *et al.*, "Biocompatibility and biomechanical analysis of elastic TPU threads as new suture material," *Journal of Biomedical Materials Research Part B: Applied Biomaterials,* vol. 105, pp. 99-106, 2017.
[52] E. Svensson, "Material characterization of 3D-printed energy-absorbent polymers inspired by nature," *CHALMERS University of Technology,* 2017.