Examining the Effects of Collagen Coating on the Mechanical and Biocompatibility Properties of Surgical Sutures

Hasan DALOO[1], Kübra ÇETİNER[1], Barış GÜÇLÜ[1], Mehmet Özgür SEYDİBEYOĞLU[2], Şenay MİHÇİN[1]
[1]Biyomedical Engineering, [2]Material Science and Engineering,
Izmir Katip Çelebi University, İzmir, Turkey

hassan.daloo.gl@gmail.com, kubracet05@gmail.com
barisguclu249@gmail.com, seydibey@gmail.com,
senay.mihcin@ikc.edu.tr

***Abstract*—Surgical suture is a medical device used to hold and approximate body tissues together after an injury or surgery. Application generally involves using a needle with an attached length of thread. Quite various shapes, sizes, and thread materials are being used currently. Surgical sutures need to be continuously enhanced and must measure up to certain standards in order to be safely used. In this review study, we looked into the scientific literature that involves the effects of coating the threads with a protein called collagen. The main considerations were regarding the biocompatibility properties, and mechanical properties. Promising results were marked regarding using collagen-coated surgical sutures, providing future perspectives in this field.**

Keywords — Surgical Sutures, Coating, Collagen.

I. INTRODUCTION

Post-operation complications, like surgical site infections (SSIs) are major concern for doctors. In spite of the remarkable improvements that happened in infection control procedures, such as sterilization methods and surgical techniques, the majority of postoperative morbidity and mortality increase among patients is still caused by SSIs. [1]

Properties of used sutures are key factors that contribute to how likely SSIs will happen. For instance, braided sutures (multifilament) and the sites of suture knots are typical sites for SSIs to occur. Those sites can provide suitable conditions to initialize microbial colonization and bacterial proliferation in wound area, which lead to the formation of biofilm, which, in turn, increases risk of SSIs. [2-3] In order to minimize the suture-associated SSIs, different methods of treating and coating the threads have emerged. For instance, non-absorbable sutures can be coated with poly(tetrafluoroethylene), paraffin, or silicone.

The aim of this study is to review the scientific literature researching the effects of natural collagen on the characteristics of the surgical sutures, overcoming the suture-associated SSIs. Multiple types of sutures coated with collagen have been examined. Collagen is the main structural insoluble fibrous protein that is found in the extracellular space in the connective tissue. Mechanical properties of those sutures, such as straight-pull and knot-pull strength, have also been investigated.

II. BACKGROUND

A. Surgical Sutures

i. Overview

Surgical sutures are medical devices that are basically threads with or without needles. They are used to fix and close body tissues after an injury or after a surgery [4]. Current sutures can be classified based on the origin of the material used in the thread (natural or synthetic), absorbability (absorbable or non-absorbable), and their structure (monofilament or multifilament).

Tensile strength, tension upon the knot, knot security, dynamic and static fatigue alongside constant friction are all factors that affect the sutures, which makes observing and foretelling how the sutures are going to behave and interact within the living tissue quite a big challenge [5]. This obligate the surgeons to have the knowledge to predict the mechanical deformation and its consequences on the performance of the suture they are going to use, so that they (the surgeons) can make the right decision in terms of choosing the appropriate suture for the surgery [6].

The tensile characteristics, which are closely related to the size, structure, and the material of the thread, directly affect the repairing capabilities of the sutures. For instance, multifilament sutures, when compared with monofilament sutures, generally have higher mechanical properties with higher endurance tensile stress and better flexibility and pliability. Moreover, non-absorbable sutures can maintain their mechanical properties, such as tensile strength, for a longer time, because they show little to no degradation within the tissues of the body [6-7].

Developing surgical sutures with optimal quality is very critical, which means that surgical sutures need to be enhanced continuously. Surgical sutures must measure up to certain standards in order to be safely used. The properties of the ideal suture can be listed and summarised as follows [8-14]:

1. Provide convenient handling experience

978-1-7281-2420-9/19/$31.00 ©2019 IEEE

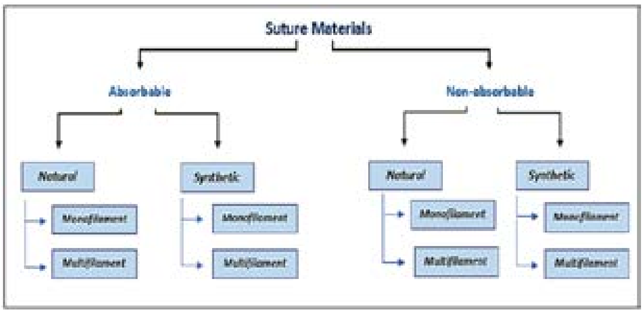

Figure 1: Classification of the suture materials.

2. Provide appropriate mechanical properties, which include:
    a. Provide sufficient tensile strength
    b. Provide good knot security and convenient tying experience
    c. Provide suitable range of intended degradation periods.
3. Be conveniently sterilisable.
4. Provide appropriate biocompatibility properties, which include:
    a. Cause no or minimal tissue irritation and/or allergic reaction
    b. Does not maintain a suitable medium for bacterial growth
    c. Does not induce carcinogenic actions.

ii. Classifications

Surgical sutures can be classified either based on their material or their structure. As for the material-based classification, surgical sutures can be divided into absorbable or non-absorbable sutures, with each class further divided into natural or synthetic (see Fig. 1). Each one of the previous four sub-classes can be yet further divided based on their structure into monofilament or multifilament. [9-13]

United States Pharmacopeia (USP) is a non-profit agency that provides guidelines for the process and tests of suture manufacturing. The USP measuring and testing system was first introduced in 1937 to reach international comparison and standardization of the suturing materials. Surgeons use different sutures with different diameters depending on demand of the wound. According to the USP system, the diameters of the sutures are described in numbers like: (starting from the thinnest diameter) 10/0, 9/0, 8/0, …, 2/0, 0 (or 1/0), 1, 2,3, … etc. for standardization purposes. This enables regulations to take place more effectively related to manufacturing and IS0 13485 medical device standards.

B. Collagen

Collagen is the most copious protein in the animal kingdom. It is the most abundant fibrous protein in the extracellular matrix (ECM) and in the connective tissues of animals. In humans, for instance, collagen constitutes 1/3 of the total protein in the body as well as 3/4 of the dry weight of the skin. Collagen has numerous types, with between 80% and 90% of the collagen found in the body constitutes of collagen type I, II and III [15-16]. These collagen molecules are packed together, forming long thin molecules, called *fibrils*, that have similar structural features. The unusual abundance of three amino acids, glycine, proline, and hydroxyproline, is what gives rise to the triple-helical structure of the aforementioned collagens. These three amino acids are what makes the distinct repeating pattern Gly-Pro-X, where X can be any amino acid [15].

Denaturing of the type I collagen molecule involves unwinding the triple helix, thus exposing arginine, glycine, and aspartate (or RGD) peptides. This may contribute in the increase in adhesion, proliferation, and differentiation that was observed in an experiment in primary HOB cultures. [17]

III. Collagen-Coated Surgical Sutures

Although there are currently no commercially available collagen-coated surgical sutures, scientists are studying the effect of collagen-coating sutures on the human body. Coating surgical sutures is not something new, but coating with collagen has been thoroughly tested only quite recently. In this part, we will examine, in a concise manner, the three most prominent studies that involve collagen-coated surgical sutures as follows:

A. Experimentation of Augustus D. Mazzocca et al., 2007

Study proposal	To study the effects of coating with collagen on the performance of commercially-available surgical sutures.
Study environment	*in vitro*
Cells/animals used	primary human osteoblasts (HOBs) & Tenocytes
Suture material(s)	Polyester & Polyethylene.
Collagen source	Bovine Achilles tendon.
Tests conducted	• Adhesion • Proliferation ([3H]-thymidine test) • Differentiation Rate (Alk. Phos. Act.) • Tensile Strength • Multiple Coatings

B. Experimentation of Ying Yang et al., 2017

Study proposal	Reducing the adverse side-effects of antibacterial coating (triclosan) by coating with collagen and chitosan.
Study environment	Both *in vitro* and *in vivo*.
Cells/animals used	•Cells used during *in vitro* tests: •Human fibroblasts cells •*Staphylococcus epidermidis*

	• Methicillin-resistant *Staphylococcus aureus* • Animals used during *in vivo* tests: Sprague-Dawley rats
Suture material(s)	Vicryl™ (Polyglactin)
Collagen source	Calf skin
Tests conducted	• Adhesion (on bacterial strains) • Proliferation inhibition (on bacterial strains) • Cytotoxicity (on human fibroblasts cells) • Histology and immunohistochemistry (*in vivo*)

C. *Experimentation of Christopher Uggen et al., 2010*

Study proposal	Coating surgical sutures with collagen and recombinant human platelet-derived growth factor BB (rhPDGF-BB) in order to enhance the histological properties as well as the mechanical integrity of the sutures
Study environment	*in vivo*
Cells/animals used	Sheep
Suture material(s)	FiberWire™ (Ultra-high molecular weight polyethylene (UHMWPE))
Collagen source	Bovine Achilles tendon
Tests conducted	• Stability of the coating after passing through tissue (scanning electron microscope (SEM)) • Histological analysis • Biomechanical tests

IV. Results and Discussion

What we can conclude from these studies is that there are multiple factors that are related to the use of sutures in surgeries. Surgeons are supposed to make the right decisions when they decide which suture material and technique to use. Those sutures have to possess some certain properties like [18]:

- Durable against mechanical stresses,
- Ability to withstand the sterilization process without getting weaker mechanically or being less biocompatible,
- Possess consistent degradation time profile,
- Provide optimal shelf-life,
- Techniques used by surgeons, like shuttling sutures and knot tying, along with the continuous exposure to the moist environment during surgeries must not cause adverse side-effects and/or interfere with bio-active coating that is applied onto the sutures.

According to the aforementioned studies, coating surgical sutures with collagen proved to be a promising approach in improving the properties of surgical sutures. For instance, Mazzocca's experimentations showed significantly enhanced cell adhesion, proliferation, and differentiation rates without compromising the mechanical properties of the sutures. The study conducted by Ying Yang *et al.* also showed better biocompatibility properties with reduced SSIs and lower occurrences of inflammation and irritation. Moreover, the study of Christopher Uggen *et al.* also showed promising results regarding coating surgical sutures with collagen. They have successfully and consistently coated surgical sutures with collagen without compromises in the mechanical properties as well as enhanced healing process with less inflammations and irritations. Those studies were conducted in various mediums with using collagen from different sources and suture materials with various chemical compositions.

V. Conclusion

Coating surgical sutures with collagen proved to be viable option for enhancing the performance of surgical sutures in terms of stimulating faster healing with better biocompatibility without sacrificing the structural and mechanical integrity of the sutures. Yet there is still a need for further investigation for the effects and the possibilities of collagen-coatings for surgical sutures. That is because those studies conducted experiments only *in vitro* or on small groups of animals. Even though these studies were conducted and planned thoroughly to mimic the real-life conditions, results obtained from *in vitro* experiments may not reflect the accurate results that would have been obtained from *in vivo* experiments.

Furthermore, current research still lacks the knowledge of optimal parameters, like the optimal mixture, concentrations, collagen adsorbing techniques, and the optimal release time of growth factors to enhance the improvement and healing after an orthopedic surgery. It is proved that coating surgical sutures with healing-improvement agents, like collagen, growth factors, and antimicrobial loads is in fact feasible and reproducible, and *in vitro* data showed hopeful results that promises lower SSIs [19].

In the end, sutures that are coated with biological agents are still not widely applied despite the benefits they might provide. There are several questions that need to be answered, like the optimal concentrations, best coating technique, releasing mechanisms, tissue reactions, etc. Moreover, high production costs of such materials should also be considered. In another words, better planned research is required to provide an optimum solution finally to demonstrate and provide better understanding of the efficacy of coated surgical sutures in the surgeries and to drive a wide clinical approval of these novel products enabling its use over wider populations.

REFERENCES

[1] Mangram, A.J., et al., Guideline for prevention of surgical site infection, 1999. American journal of infection control, 1999. 27(2): p. 97-134.

[2] Chang, W.K., et al., Triclosan-impregnated sutures to decrease surgical site infections: systematic review and meta-analysis of randomized trials. Annals of surgery, 2012. 255(5): p. 854-859.

[3] Edmiston, C.E., et al., Bacterial adherence to surgical sutures: can antibacterialcoated sutures reduce the risk of microbial contamination? Journal of the American College of Surgeons, 2006. 203(4): p. 481-489.

[4] Chu, C.-C., J.A. Von Fraunhofer, and H.P. Greisler, Wound closure biomaterials and devices. 1996: CRC Press.

[5] Bayraktar, E. and A. Hockenberger. 22. Time Dependent Behaviour of Some Suture Materials. in Medical Textiles: Proceedings of the 2nd international Conference, 24th and 25th August 1999, Bolton Institute, UK. 2001. Elsevier.

[6] Dunn, D. and J. Phillips, Wound closure manual. Ethicon, Somerville, New Jersey, 2007.

[7] Ratner, B.D., et al., Biomaterials science: an introduction to materials in medicine. 2004: Elsevier.

[8] Hochberg, J., K.M. Meyer, and M.D. Marion, Suture choice and other methods of skin closure. Surgical Clinics of North America, 2009. 89(3): p. 627-641.

[9] Moy, R.L., B. Waldman, and D.W. Hein, A review of sutures and suturing techniques. The Journal of dermatologic surgery and oncology, 1992. 18(9): p. 785-795.

[10] Hon, L.-Q., et al., Vascular closure devices: a comparative overview. Current problems in diagnostic radiology, 2009. 38(1): p. 33-43.

[11] Kudur, M.H., et al., Sutures and suturing techniques in skin closure. Indian Journal of Dermatology, Venereology, and Leprology, 2009. 75(4): p. 425.

[12] Naleway, S.E., et al., Mechanical properties of suture materials in general and cutaneous surgery. Journal of Biomedical Materials Research Part B: Applied Biomaterials, 2015. 103(4): p. 735-742.

[13] Singhal, J.P., H. Singh, and A.R. Ray, Absorbable suture materials: preparation and properties. Polymer Reviews, 1988. 28(3-4): p. 475-502.

[14] Yu, G. and R. Cavaliere, Suture materials. Properties and uses. Journal of the American Podiatric Medical Association, 1983. 73(2): p. 57-64.

[15] Lodish H, Berk A, Zipursky SL, et al. Molecular Cell Biology. 4th edition. New York: W. H. Freeman; 2000. Section 22.3, Collagen: The Fibrous Proteins of the Matrix.

[16] Shoulders MD, Raines RT. Collagen structure and stability. Annu Rev Biochem. 2009; 78:929–958. doi: 10.1146/annurev.biochem.77.032207.120833

[17] Mazzocca, Augustus D., et al. "Tendon and bone responses to a collagen-coated suture material." Journal of shoulder and elbow surgery 16.5 (2007): S222-S230.

[18] Beitzel, Knut, et al. "Coated sutures." Sports medicine and arthroscopy review 23.3 (2015): e25-e30.

[19] Wang ZX, Jiang CP, Cao Y, et al. Systematic review and metaanalysis of triclosan-coated sutures for the prevention of surgical-site infection. Br J Surg. 2013; 100:465–473.