J Surg Med. 2021;5(9):924-927.
DOI: 10.28982/josam.857885

Research article

Journal of Surgery and Medicine
e-ISSN=2602-2079

Nano-based ceramic surgical blade accelerates wound healing

Fatih Ada [1], Erkan Gumus [2], Ferit Kasimzade [3]

[1] Sivas Cumhuriyet University School of Medicine, Department of Cardiovascular Surgery, Sivas, Turkey
[2] Adnan Menderes University School of Medicine, Department of Histology and Embryology, Aydın, Turkey
[3] Ministry of Health Ankara City Hospital, Department of Cardiovascular Surgery, Ankara, Turkey

ORCID ID of the author(s)
FA: 0000-0002-6953-5906
EG: 0000-0001-6432-7457
FK: 0000-0003-3646-3181

Corresponding Author
Fatih Ada
Sivas Cumhuriyet University School of Medicine, Department of Cardiovascular Surgery, Sivas, Turkey
Kayseri - Sivas Yolu, Cumhuriyet Üniversitesi, Postal Code: 58140, Merkez, Sivas, Turkey
E-mail: drfatihada@gmail.com

Ethics Committee Approval
This study was approved with the decision of No. 65202830-050.04.04-33 by the Animal Review Board of Sivas Cumhuriyet University.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2021 September 22

Abstract

Background/Aim: Many factors affect the results of a surgical operation, one of which is the harmony of the materials used during surgery with the tissue. Zirconia is a material with antimicrobial properties, high surface sensitivity and robustness. This study was conducted to observe the acute and subacute effects of the nano-based zirconia surgical blade on living tissue.

Methods: The study was conducted after approval was granted by the Sivas Cumhuriyet University Animal Experiments Local Ethics Committee with the decision number 65202830-050.04.04-33. A total of 16 rats were used in the study. Eight were incised with classic steel surgical blade and eight, with nano-based zirconia surgical blade. A total of 4 incisions were performed to each rat and the incisions were closed with 3.0 polypropylene suture. Tissue samples were obtained from the incisions on day 0, 3, 7 and 21, and examined histologically.

Results: The epidermis layer thickness on days 7 and 21 (P=0.030, P=0.025), the dermis layer thickness on days 3 and 7 (P=0.035, P=0.030), muscle layer thickness on days 7 and 21 (P=0.030, P=0.025) were significantly increased and inflammatory cells were significantly less on days 3, 7 and 21 (P=0.030, P=0.020, P=0.025) in the nano-ceramic surgical blade compared to the other group. Collagen tissue density was significantly higher in favor of the nano-ceramic blade on the 3rd and 7th days (P=0.025, P=0.020).

Conclusion: Nano-based zirconia surgical blade has been shown to have positive effects on wound healing. The use of nano-based zirconia surgical blade should be kept in mind in patient groups with wound healing problems.

Keywords: Ceramic, Healing, Histological, Nano-based, Scalpel, Steel, Surgical blade, Wound

How to cite: Ada F, Gumus E, Kasimzade F. Nano-based ceramic surgical blade accelerates wound healing. J Surg Med. 2021;5(9):924-927.

Introduction

The final goals after a surgical operation are the rapid and scarless healing of the wound, and the absence of infection. The wound healing process depends on many factors [1]. Some of these components are interchangeable and technological advances have contributed positively to the wound healing process. One of the disciplines contributing to these positive developments is nanotechnology. With its advancement, the design of the materials changed, their effectiveness increased, and their advantageous properties have been brought to the fore. Nano-based drugs, diagnostic and therapeutic tools have begun to be used in clinical practice. It will be possible to use many nano-based instruments in surgical operations in the near future. One of the factors affecting wound healing is the features of the instruments used in surgery. Today, many methods are used to make a surgical incision, such as a conventional steel surgical blade, laser, CO_2, and electrocautery, with each having their advantages and disadvantages. Our study is the first animal experiment on nano-based zirconia surgical blade, but there are publications of material science of this issue [2-4]. This study aimed to investigate the histological changes in the surgical wound created with a nano-based zirconia surgical blade in a rat model.

Materials and methods

Animals

All experimental protocols were performed according to the guidelines for the ethical procedures of experimental animals and approved by the Sivas Cumhuriyet University local ethics committee for laboratory animal care and use. Male/female Wistar rats weighing 220-240 g were obtained from experimental animal center of Sivas Cumhuriyet University. The animals were kept under a 12-h-light-dark cycle in a room temperature of 20–22 °C and a relative humidity of 50–65% and had free access to standard laboratory food and water. After the back hair was removed by a clipper, the rats were anesthetized with intraperitoneal injection of ketamine (30 mg/kg, CEVA SanteAnimale, Brussels, Belgium) and xylazine (10 mg/kg, Rompun, Bayer Animal Health, Brussels, Belgium). For the first 3 days after surgery, each animal was administered ceftriaxone sodium intramuscularly (30 mg/kg). In all rats, euthanasia was performed under ketamine/xylazine anesthesia.

Experimental groups and treatments

The study was carried out after approval was granted by Sivas Cumhuriyet University Animal Experiments Local Ethics Committee with the decision number 65202830-050.04.04-33. The animals were cared for and housed in the experimental animal laboratory of Sivas Cumhuriyet University. A total of sixteen rats were included, among which 8 were incised with nano-based zirconia surgical blades (H2 Zir Medikal, Kütahya/Turkey) (Figures 1-2) and eight, with classic steel surgical blades (Braun, Tuttlingen/Germany), the latter comprising the control group. A total of four incisions were made on each rat, two to the right and two to the left, with 1 cm to the middle part of the dorsum. A specimen was taken from the near right side cranial incision for histological examination on postoperative day 0, at the 12th hour. Three days after the first incision, a specimen was taken from the incision near the left side. Seven days after the first incision, a specimen was taken from the right caudal incision. Finally, after 21 days, the specimen was taken from the caudal incision near the left side for histological examination. All incisions were closed with prolene sutures and daily dressings were performed with standard povidone iodine solution. The procedure was performed separately for each group and under general anesthesia. No rats died during the procedures. On the 21st day, after the last tissue samples were taken, all rats were sacrificed with high dose anesthetic agents.

Figure 1: Nano-based ceramic surgical blade

Figure 2: Appearance of the surgical model of the study

Histological examination

Wound skin tissue samples were obtained from the control and experimental groups on days 0 (12 h), 3, 7, and 21 by a scalpel for histological observation. After a 36-hour fixation in Bouin's solution, all the investigated tissues were embedded in paraffin blocks, cut into 5-μm-thick serial sections, mounted on glass slides coated with poly-L-lysine, and subjected to hematoxylin-eosin (HE; Thermo Fisher Scientific) staining for morphological assessment.

Skin sections were examined for depth of epidermis, dermis, and muscle layer at the center of each wound. Specific features were used based on location and characteristics of the layer to measure the thickness. The epidermis is the outermost layer of the skin composed of keratinized, stratified squamous epithelium. Directly lying beneath the epidermis and above the subcutaneous layer is the dermis, which consists of connective tissue, cellular elements, and ground substance. Inferior to the subcutaneous layer is the muscle layer composed of mature myocytes. In this study, dermis and subcutaneous layers were evaluated together as a single layer due to thickness differences between skin sections. The thicknesses of the layers were measured using ImageJ software (ImageJ; National Institutes of Health, Bethesda, MD). The percentage of each skin section occupied by resident mononuclear cells was measured using the

IHC Toolbox plug in for ImageJ software. Briefly, the numbers of dark purple-colored pixels were identified with "color deconvolution function" by separating the HE stains. It was quantified and represented as a percentage relative to the total number of pixels per skin section. Skin sections were also stained with Masson's trichrome to observe the site of collagen deposition per skin section. The percentage of collagen was calculated using the ImageJ software as described previously [5]. An algorithm was used to deconvolve the color information acquired with stained sections. The number of blue colored pixels was quantified and represented as a percentage relative to the total number of pixels per skin section.

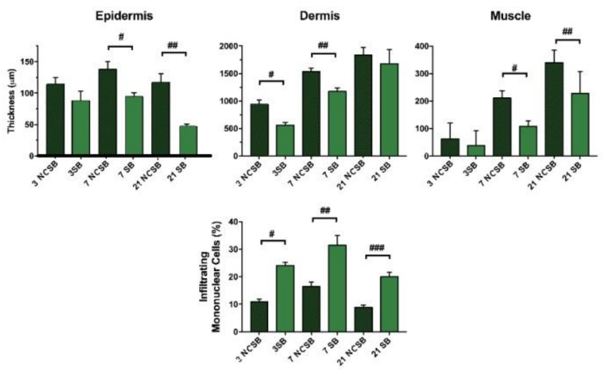
Statistical analysis

Statistical analysis was performed using the SPSS (version 24.0, StataCorp LP, College Station, TX, USA) software package. The Kruskal Wallis test was used to compare the differences between the groups in the histopathological examination of the data obtained semi-quantitatively. The differing groups were identified by the Mann Whitney U test. A *P*-value of <0.05 was considered statistically significant.

Results

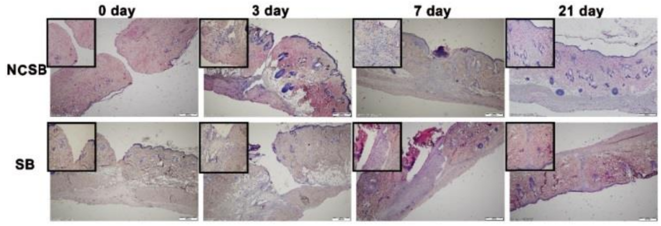
The epidermis, dermis, muscle tissue, collagen tissue and inflammatory cells were similar in the samples taken at the 12th hour of the first incision. The epidermis layer thickness on days 7 (140µm vs 100µm) (P=0.030), and 21 (110µm vs 40µm) (P=0.025), the dermis layer thickness on days 3 (900µm vs 500µm) (P=0.030), and 7 (1500µm vs 1100µm) (P=0.035), muscle layer thickness on days 7 (200µm vs 100µm) (P=0.025), and 21 (320µm vs 210µm) (P=0.030) were significantly increased and inflammatory cells were significantly less on days 3 (10% vs 25%)(P=0.030), 7 (15% vs 30%)(P=0.020), and 21 (8% vs 20%) (P=0.025) in the nano-ceramic surgical blade compared to the steel blade group (Figure 3, 4). Collagen tissue density was significantly higher in favor of the nano-ceramic blade on the 3rd (38% vs 30%) (P=0.025) and 7th (30% vs 15%) days (P=0.020) (Figures 5, 6).

Figure 3: Epidermis: $^{\#, \#\#}P$=0.030 vs. NSCB 7d, SB 7d, NSCB 21d, and SB 21d.
Dermis: $^{\#, \#\#}P$=0.035 vs. NSCB 3d, SB 3d, NSCB 7d, and SB 7d.
Muscle: $^{\#, \#\#}P$=0.030 vs. NSCB 7d, SB 7d, NSCB 21d, and SB 21d.
Infiltrating Mononuclear Cells: $^{\#, \#\#, \#\#\#}P$=0.020 vs. NSCB 3d, SB 3d, NSCB 7d, SB 7d, NSCB 21d, and SB 21d.



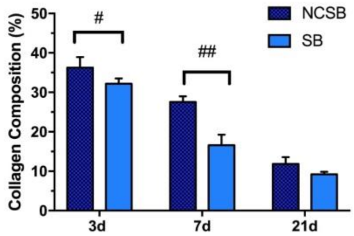
NCSB: nano-ceramic surgical blade, SB: surgical blade

Figure 4: Representative images of skin sections stained with hematoxylin and eosin. Infiltrating mononuclear cells were assessed by color deconvolution followed by quantification of dark purple stain. Thickness of the epidermis, dermis, and muscle layers of skin (mean with SD).



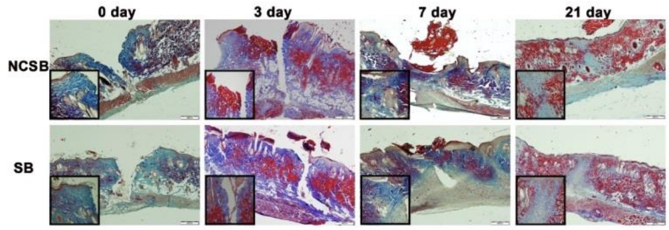
#, ##, ### P<0.05 between nano ceramic surgical blade and steel surgical blade group. NCSB: nano-ceramic surgical blade, SB: surgical blade

Figure 5: Collagen Composition: $^{\#, \#\#}P$=0.025 vs. NSCB 3d, SB 3d, NSCB 7d, and SB 7d.



NCSB: nano-ceramic surgical blade, SB: surgical blade

Figure 6: Representative images of skin sections stained with Masson's trichrome. Collagen composition was assessed by color deconvolution followed by quantification of blue stain (mean with SD). #, ## P=0.025 P<between nano ceramic surgical blade and steel surgical blade group.



NCSB: nano-ceramic surgical blade, SB: surgical blade

Discussion

Wound healing is a complex process involving cytokines, as well as matrix and components. This process is divided into three phases, namely, the inflammation, proliferation, and maturation phases [6, 7]. The inflammation phase includes the first 5-day period, when fibrin formation and angiogenesis are highest for the stabilization of the wound. The cellular elements that dominate the wound tissue are neutrophils and monocytes. The proliferation phase covers days 5 to 14, and collagen production from fibroblasts is highest. In this phase, wound contraction is achieved by the action of myofibroblasts, and the wound size begins to decrease [8]. Maturation phase refers to the process after the 14th day and sometimes takes years. In this phase, type 3 collagen is transformed into to the more robust type 1 collagen, helping to restore tissue to its original strength. It is observed that the tissue regains approximately 95% strength after about 6 weeks of wound is formed [7, 9]. Local and systemic factors play a major role in wound healing. Local factors include tissue blood flow (oxygenation), hematoma or seroma development in the wound site, infection, over-pressure wound dressing, surgical technique, foreign bodies, necrotic tissue, local steroid use, tissue edema, and radiotherapy. Systemic factors include advanced age, anemia, lack of nutrition, systemic steroid use, cytotoxic drug use, sepsis, diabetes, uremia, severe pain, and connective tissue diseases [1, 10, 11]. Although there are a number of studies on the various components of wound healing, studies on the effects of the materials used in the surgical incisions on wound healing are limited.

Studies show that methods such as CO_2 assisted incision, ultrasound-assisted incision, and laser incision are superior to conventional steel surgical blades. Ryu et al. conducted a study on wound healing in the oral mucosa of the Guinea pig and showed that Er, Cr: YSGG laser incision group had less TNF-α and TGF-ß1 expression in the wound tissue compared to CO_2 scalpel, indicating better wound healing [12]. Carreira and colleagues showed that the CO_2 laser surgical blade had a better healing process than the conventional surgical blade, resulting in fewer leukocytes, minor tissue trauma, and reduced albumin extravasation in the skin incision. It was also noted that postoperative patient comfort was increased due to less pain and, better cosmetic results were obtained in CO_2 laser group [13]. Jawad and colleagues studied wound healing on the rabbit model with the steel scalpel. They found that the best wound healing occurred after the 14^{th} day of surgery [14].

Demir and colleagues studies the rabbit oral mucosa and demonstrated that Neodymium-Doped Yttrium Aluminium Garnet (Nd-YAG) laser facilitates soft tissue operations and provides faster wound healing [15]. Tuncer et al. compared the conventional surgical blade and CO_2 laser surgical blade in terms of postoperative pain relief need and showed that CO_2 laser surgical blade group needed less painkillers [16]. In the study conducted by Kara et al. Nd-YAG laser was shown to cause less pain and fewer postoperative side effects compared to the conventional surgical blade [17]. Pearce and colleagues compared the microscalpel with the conventional surgical blade in a rat model and found similar results among the two surgical blades in terms of all surgical outcomes, including inflammation [18].

The elevated cost of the mentioned methods, the lack usability in every surgical field and the unique structure of each tissue are the main obstacles against the widespread use of these devices. For this reason, the classic steel surgical blade is still widely used and seems indispensable for practical surgical life. There are also studies on changing the structure of the classical surgical blade. As reported by Tsai et al., the sharpness of the surgical blade increased with coating. Coating of the traditional surgical blades with ZrCuAlAgSi in the form of thin glass film may render them more useful in surgery [19]. Kelley et al. reported that the classical steel double-blade tissue cutters for microtomes yielded much better results in tissue sampling [20]. Mftah et al. investigated the properties, cytotoxicity, and antimicrobial properties of sulphated nano-zirconia. Sulphated nano-zirconia was found to have strong antibacterial properties against gram-positive and gram-negative bacteria, and its wide use was proposed in biomedical applications [2]. There are many methods to increase the sharpness of surgical blades. Sharpness is an important aspect of ceramic scalpels. To provide this sharpness, Kuai and colleagues used ELID grinding technology and demonstrated that more feasible results were achieved compared to traditional methods [3]. Kuai and his colleagues reported that a sharper surface was obtained in the nano ceramic scalpel along with ELID grinding technology [4].

According to our quantitative comparison of the histomorphological data, nano-based zirconia surgical blade has positive effects on wound healing. Increased collagen composition and epidermis, dermis, and muscle layer thickness, along with reduced levels of inflammatory cell infiltration indicate that the nano-based zirconia surgical blade results in better wound healing compared to the traditional steel scalpel.

Limitations

There are several limitations to our study. First, only two types of the surgical blade were compared. Second, conducting an animal experiment limited the chance of a long-term follow-up.

Conclusion

The nano-based zirconia surgical blade has been shown to accelerate wound healing process compared to the conventional steel surgical blade. It seems likely in the near future that the nano-based zirconia surgical blade will be preferred for surgical interventions in selected patients with wound healing problems.

Acknowledgements

We would like to thanks the Professor Hilmi Yurdakul and Professor Hasan Göçmez for their support in the nano surgical blade part of the study.

References

1. Parsak CK, Sakman G, Çelik, Ü. Yara iyileşmesi, yara bakımı ve komplikasyonları. Arşiv Kaynak Tarama Dergisi. 2007;16(2):145-59.
2. Mftah A, Alhassan FH, Al-Qubaisi MS, El Zowalaty ME, Webster TJ, Sh-eldin M, et al. Physicochemical properties, cytotoxicity, and antimicrobial activity of sulphated zirconia nanoparticles. International Journal of Nanomedicine. 2015;10: 765.
3. Kuai JC, Zhang FH, Liu YZ. ELID Grinding Technology of Nano-Material Cutting Tool. In Applied Mechanics and Materials. 2012;155:960-4.
4. Kuai JC, Zhang FH, Liu YZ. ELID Grinding Technology of Nano-Ceramic Scalpel. In Advanced Materials Research. 2012;468:1560-3.
5. Strong AL, Bowles AC, MacCrimmon CP, Frazier TP, Lee SJ, Wu X, et al. Adipose stromal cells repair pressure ulcers in both young and elderly mice: potential role of adipogenesis in skin repair. Stem Cells Translational Medicine. 2015;4(6):632-42.
6. Barbul A. Wound healing. Schwartz's Principles of Surgery. Mc Graw Hill Eight edition. 2005;223.
7. Sherris DA, Kern EB. The Wound. In Basic Surgical Skills, Mayo Foundation for medical Education and research, Rochester, 1999:8-12.
8. Pakyari M, Farokhi A, Jalili RB, Kilani RT, Brown E, Ghahary, A. Local Expression of Indoleamine 2, 3, Dioxygenase Prolongs Allogenic Skin Graft Take in a Mouse Model. Advances in Wound Care. 2018;8(2):58-70.
9. Özpolat B, Gürpınar Aylin Ö, Ayva Şebnem E, Gazyağcı S, Niyaz M. The effect of basic fibroblast growth factor and adipose tissue-derived mesenchymal stem cells on wound healing, epithelization and angiogenesis in a tracheal resection and end-to-end anastomosis rat model. Turkish Journal of Thoracic and Cardiovascular Surgery. 2013;21:1010-9.
10. Gupta A, Kumar P. Assessment of the histological state of the healing wound. Plastic and Aesthetic Research. 2015;2(5):239.
11. Durgun M, Durgun Öğücü S, Özakpınar Rıfat H, Eryılmaz Tolga A, Öktem Fatih H, İnözü E, et al. Approach to of infected sternotomy wounds in the management of mediastinitis. Turkish Journal of Thoracic and Cardiovascular Surgery. 2012;20:820-5.
12. Ryu SW, Lee SH, Yoon HJ. A comparative histological and immunohistochemical study of wound healing following incision with a scalpel, CO2 laser or Er, Cr: YSGG laser in the Guinea pig oral mucosa. Acta Odontologica Scandinavica. 2012;70(6):448-54.
13. Carreira LM, Azevedo P. Comparison of the Influence of CO2-laser and Scalpel Skin Incisions on the Surgical Wound Healing Process. ARC Journal of Anesthesiology. 2016;1(3):1-8.
14. Jawad MM, Alam MK, AbdulQader ST, Al-Azzawi LM, Husein A, Mahmood AS. Histological evaluation of incision healing response made by metallic scalpel on rabbits skin: preliminary study. International Medical Journal. 2013;20(4):496-8.
15. Demir T, Kara C, Özbek E, Kalkan Y. Evaluation of neodymium-doped yttrium aluminium garnet laser, scalpel incision wounds, and low-level laser therapy for wound healing in rabbit oral mucosa: a pilot study. Photomedicine and laser surgery. 2010;28(1):31-7.
16. Tuncer I, Özçakır-Tomruk C, Şencift K, Çöloğlu S. Comparison of conventional surgery and CO2 laser on intraoral soft tissue pathologies and evaluation of the collateral thermal damage. Photomedicine and laser surgery. 2010;28(1):75-9.
17. Kara C, Süleyman H, Tezel A, Orbak R, Cadirci E, Polat B, Kara I. Evaluation of pain levels after Nd: YAG laser and scalpel incisions: an experimental study in rats. Photomedicine and laser surgery. 2010;28(5):635-8.
18. Pearce EC, Hall JE, Boyd KL, Rousseau B, Ries WR. The Ophthalmology Microscalpel versus Standard Scalpels and Wound Healing in a Rat Model. Otolaryngology-Head and Neck Surgery. 2014;151(3):424-30.
19. Tsai PH, Lin YZ, Li JB, Jian SR, Jang JSC, Li C, et al. Sharpness improvement of surgical blade by means of ZrCuAlAgSi metallic glass and metallic glass thin film coating. Intermetallics. 2012;31:127-31.
20. Kelley DB, Abt AB. Uniform Tissue Sections Cut with a Double-Bladed Scalpel. Journal of Histotechnology.2013;16(4):363-4.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.