2024 Volume 9, Issue 2
Advances in Precision Medicine
ISSN: 2424-9106 (Online)
ISSN: 2424-8592 (Print)

A Case Report of an Unhealed Incision 4 Years After Lumbar Decompression and Internal Fixation

Yue Shen[1], Geng Chen[2], Guangda Wang[2]*
[1]The Second Clinical Medical College, Binzhou Medical University, Yantai 264000, Shandong Province, China
[2]Department of Orthopedics, Yantai Yuhuangding Hospital, Yantai 264000, Shandong Province, China

***Corresponding author:** Guangda Wang, Wgdsh123@sohu.com

Abstract:

This paper presents a case of an unhealed incision persisting for four years in a 59-year-old male farmer who underwent lumbar decompression and internal fixation surgery. Following initial treatment and discharge, the lower end of the surgical incision failed to heal, remaining open at approximately 2 centimeters. The incision site subsequently experienced recurrent rupture and exudation over four years, during which the patient did not receive consistent medical intervention. Eventually, the patient underwent debridement for soft tissue lesions, leading to satisfactory postoperative recovery. Early detection and proper management of patients at risk of poor incision healing can significantly improve healing outcomes and enhance patient quality of life.

Keywords:

Wound healing
Early diagnosis
Standardized treatment

Online publication: December 27, 2024

1. Introduction

Wound healing is a critical component of postoperative recovery, encompassing three phases: inflammation, hyperplasia, and remodeling. The effectiveness of incision healing is closely tied to postoperative complication rates and plays a substantial role in patient quality of life. An understanding of the mechanisms underlying incision healing can improve current surgical approaches, reduce postoperative complications, and lead to new clinical treatment strategies.

The inflammatory phase typically commences within 24 hours of trauma and is driven by immune cell aggregation and cytokine release to clear pathogens and necrotic tissue from the wound [1]. Initially, blood vessels at the injury site constrict and then dilate, increasing blood flow to the affected area and resulting in hematoma formation. Inflammatory cells quickly accumulate at the wound and release substances that initiate the healing process. Proper regulation of the inflammatory response is crucial for effective healing; excessive inflammation, however, may cause delayed healing, chronic wounds, and scarring [2,3].

The hyperplasia phase occurs within days to weeks after trauma, characterized by fibroblast growth and new blood vessel formation. During this stage, fibroblasts and endothelial cells proliferate to form granulation tissue. Growth factors like transforming growth factor β (TGF-β) and platelet-derived growth factor (PDGF) stimulate the formation of granulation tissue by promoting cell proliferation and migration [4]. The primary goal of the hyperplasia phase is to fill the wound defect and re-establish the local blood supply to support the upcoming remodeling phase. The quality and rate of healing depend significantly on the effectiveness of the hyperplasia stage, which can be enhanced through proper nutritional support and growth factor application [5]. These processes lay the groundwork for subsequent tissue reconstruction [6].

The remodeling phase, occurring weeks to months after trauma, enhances the strength and function of the incision through collagen reorganization and extracellular matrix remodeling. In this stage, granulation tissue is gradually replaced by collagen fibers, increasing wound strength and elasticity. Several factors influence the duration and outcome of the remodeling phase, including trauma type, individual physiological state, and environmental conditions. Effective interventions such as physical therapy and wound care can support this stage, reducing the risk of scarring [7,8].

2. Case presentation

2.1. Patient information

The patient, a 59-year-old male farmer with a BMI of 28 kg/m², was in good health. Four years prior, he underwent surgery for lumbar spinal stenosis (L3/4/5) after contraindications were ruled out. The procedure included endotracheal intubation under general anesthesia, navigation-assisted lumbar posterior laminectomy, decompression, disc removal, and bone graft fusion with internal fixation. The surgery proceeded smoothly, and the patient had a stable recovery after discharge. Before discharge, the incision on the waist, approximately 10 cm in length, was examined and showed good overall healing. However, the lower end, about 2 cm long, had not healed and exhibited slight exudation. After discharge, the patient was advised by the doctor to perform functional exercises. Despite this, the waist incision repeatedly reopened, producing a slight yellow, sticky exudate. The patient received oral antibiotics and local dressing changes, but healing did not occur, and a cutaneous sinus tract gradually formed, with slight intermittent exudation.

Three months ago, a polyp appeared at the waist incision site, measuring approximately 0.3×0.3 cm. The polyp was deeply connected to the incision base, was painless on palpation, and exhibited a white liquid exudate with white mucus attached at its base. A bacterial culture of the secretion conducted at a local hospital yielded negative results. Surgical intervention was recommended, but the specific method was not provided. Seeking further diagnosis and treatment, the patient visited the hospital. After a comprehensive medical history, physical examination, and imaging review, he was diagnosed with a “lumbar skin sinus tract” and subsequently admitted for treatment.

2.2. Specialist physical examination

The physiological curvature of the waist and the mobility of the lumbar spine were normal. A surgical scar, approximately 10 cm in length, extended along the L3–S1 spinal process. About 2 cm below the scar, an area of the incision had not healed. A smooth, ruddy spherical polyp approximately 0.8 cm in size was visible, protruding from the skin surface. It exhibited no tenderness and produced a small amount of white mucinous fluid from both the incision and the polyp surface. Sensation and muscle tone in both lower limbs were normal across all muscle groups. The skin temperature of both lower limbs was normal, the dorsal foot artery pulsation was palpable, and the toe blood circulation was adequate. Bilateral knee tendon reflexes and Achilles tendon reflexes were normal. Bilateral Babinski signs were negative.

3. The therapeutic process

3.1. Operative treatment

After completing the necessary examinations and ruling out surgical contraindications, the patient underwent resection of lumbar soft tissue lesions and debridement of necrotic skin and subcutaneous tissue under static anesthesia with endotracheal intubation. The procedure was performed as follows. The patient was placed in a supine position, and the surgical area was disinfected before a sterile drape was applied. An incision approximately 6 cm long was made behind the L3-5 vertebrae, extending from the sinus tract. Granulation tissue within the sinus tract was removed and submitted for bacterial culture. The scar tissue was dissected layer by layer, revealing that the sinus tract extended to the lamina, where the L4 lamina was missing. Granulation tissue from the L5 lamina and the muscle layer behind it, measuring about 6 cm by 4 cm, was found to contain L4 spinal canal tissue and synovial tissue. Two samples of granulation tissue were taken for pathological examination and bacterial culture. The sinus tract was excised, and granulation and synovial tissue from the spinal canal and posterior lamina were thoroughly removed. Exploration confirmed that the internal fixation devices were securely in place with no signs of loosening. Sampling was performed in accordance with the Collection Specification for Clinical Test Samples, with samples sent for inspection within 2 hours of collection.

3.2. Bacterial culture results

After 2 days of incubation in a standard culture medium, no bacterial growth was detected.

3.3. Pathological results

Figure 1 presents findings from the examination of soft tissue from the spinal canal post-lumbar surgery. The examination showed marked fibrous tissue hyperplasia, numerous acute and chronic inflammatory cell infiltrates, foam-like macrophages, granulation tissue, and focal exudative necrosis.

3.4. Imaging findings

As shown in **Figures 2** and **3**, the subcutaneous irregular signal area in the lumbosacral region showed improvement compared to the preoperative state.

3.5. Postoperative care

Following surgery, the patient received anti-inflammatory medication, treatments to reduce swelling, pain relief, and other supportive care to prevent complications. The incision was observed to heal well during dressing changes.

4. Discussion

4.1. Factors affecting wound healing

Wound healing is influenced by a range of factors, including the patient's systemic condition, environmental aspects, and surgical techniques. Properly managing these factors can significantly improve healing outcomes and reduce postoperative complications.

4.1.1. Systemic condition

The patient's overall health plays a crucial role in incision healing, as systemic factors directly impact immune function, nutritional status, and the body's ability to repair tissue. For example, poor glycemic control in diabetic patients often leads to delayed incision healing and increases the risk of infection, as high blood sugar levels can impair immune response and tissue repair [9]. Additionally, the mechanical properties of aging skin can hinder healing, making elderly patients more susceptible to slow or incomplete recovery [10]. Nutrition is also critical, as malnutrition can reduce collagen synthesis, weakening blood vessel protection and ultimately delaying the healing process [4]. Thus, preoperative

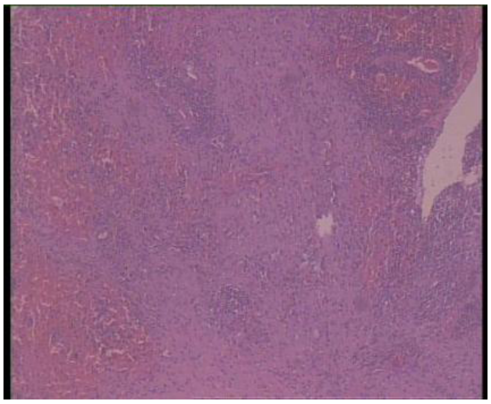

Figure 1. Pathological section

Figure 2. Preoperative

Figure 3. Postoperative

assessment and management of systemic conditions, especially chronic diseases, are essential to support optimal incision healing.

4.1.2. Environmental factors

Environmental factors such as incision cleanliness, blood supply, tissue oxygenation, and infection control are pivotal to successful wound healing. A sterile surgical environment and adequate blood flow are essential to promote proper healing, while the presence of infection can disrupt it [5]. Infected wounds can trigger an inflammatory response, leading to local tissue necrosis and a prolonged healing process [8]. Temperature and humidity at the wound site are also influential; maintaining an optimal humidity level can enhance cell migration and proliferation, thereby accelerating healing [11]. Ensuring a favorable local environment throughout surgery and postoperative care is thus crucial for effective incision recovery.

4.1.3. Surgical technique and incision type

The surgeon's technique and the type of incision used also play a significant role in determining how well an incision will heal. Prolonged exposure to mechanical actions such as clamping and ligation can cause aseptic tissue inflammation, liquefaction of fatty tissue, and the formation of dead spaces, all of which may hinder healing if not managed carefully. Furthermore, improper drainage can prevent blood absorption, complicating the healing process to varying extents [12]. Different incision types also heal at different rates; more complex incisions can cause greater tissue damage and therefore require longer recovery times [13]. Surgeons should consider how their chosen techniques and incision types will impact healing and make adjustments to ensure optimal outcomes [14].

4.2. Assessment and evaluation methods for incision healing

Identifying patients at risk of poor incision healing early in the recovery process allows for timely interventions that can enhance healing and improve clinical outcomes [15,16]. Continuous research into the mechanisms of incision healing is leading to the development of new treatments and techniques, broadening the options available to improve healing outcomes [17,18].

4.2.1. Visual assessment criteria

Visual assessment is one of the most commonly used clinical observation tools, relying on the observer's experience for accuracy. However, existing visual assessment tools and scoring systems sometimes lack sufficient sensitivity and specificity, making it challenging to capture the complexities of incision healing thoroughly [19]. This limitation emphasizes the need for more objective and standardized methods to enhance the precision and reliability of visual evaluations.

4.2.2. Scoring systems

Scoring systems convert clinical observations into quantifiable data, aiding in the analysis and comparison of incision healing progress. The National Pressure Ulcer Advisory Panel (NPUAP) scoring system, for instance, assesses ulcer severity based on depth, color, and surrounding skin condition [20]. Another widely used system is the Bates-Jensen scoring system, which evaluates wound healing objectively and minimizes observer bias [21]. While scoring systems improve the reliability of clinical observations, their effectiveness depends on rigorous scientific validation and clinical applicability, underscoring the need for ongoing refinement and verification.

4.2.3. Imaging techniques

Imaging plays a pivotal role in incision assessment, though ongoing optimization is essential to ensure these methods are feasible and safe for clinical use.

(1) Ultrasonography: Ultrasound is a non-invasive, real-time imaging technique that provides detailed images of the tissue surrounding incisions, aiding in procedures like guided puncture and drainage while minimizing pain and complications [22]. Studies show that low-frequency ultrasound can inhibit IL-6 and TNF-α expression while increasing VEGF and TGF-β1 levels, thus promoting healing in diabetic rat models [23]. However, ultrasound's effectiveness depends on the operator's skill, which can lead to subjective variations in results.

(2) Magnetic resonance imaging (MRI): MRI is particularly useful for visualizing soft tissues, as it provides detailed images of structures

surrounding incisions and highlights pathological changes such as edema, inflammation, and scar formation [24,25]. Given these advantages, 3D MRI is highly valuable for evaluating wound healing. However, the high cost and lengthy examination times limit MRI's utility in emergency settings, where quicker diagnostic tools are often required.

(3) Computed tomography (CT): CT scans are beneficial for assessing gas distribution, abdominal incision healing, and injuries from blunt trauma [26]. They have also been used in rare case reports of infections following hernia repairs associated with methicillin-resistant staphylococci [27]. Advances in CT technology, such as photon-counting detector CT (PCD CT), enable low-dose examinations with improved image quality, particularly for pediatric patients [28]. The development of targeted CT contrast agents holds promise for enhancing imaging contrast and utility in clinical settings [29].

4.2.4. Biomarkers in incision assessment

Biomarkers have gained recognition for their role in early diagnosis, prognosis, and treatment monitoring in wound healing. Biomarkers reflect physiological and pathological processes and offer insights into factors affecting healing, particularly in cases of chronic or complex wounds.

(1) Diabetic wound healing: Chronic wounds in diabetic patients are influenced by inflammation, cell proliferation, angiogenesis, and extracellular matrix (ECM) remodeling. Elevated levels of hydrogen peroxide (H_2O_2) and reactive oxygen species (ROS) are associated with delayed healing in diabetic foot ulcers (DFUs), and biomarkers like CXCL12 and neutrophil extracellular traps (NETs) have been linked to impaired healing in diabetic wounds [30-32]. Additionally, high levels of citrullinated histone 3 (citH3) are associated with poor healing and an increased risk of amputation [33].

(2) Infection markers: Infected chronic wounds delay healing significantly. C-reactive protein, procalcitonin, prolactin, and bacterial protease activities serve as valuable indicators of infection and can aid in timely diagnosis and intervention [34]. For burn patients, biomarkers such as hsa-miR-21 and hsa-miR-31 are involved in regulating the fibroproliferative response, providing additional insights for treatment [35].

(3) Matrix metalloproteinases (MMPs): MMPs are critical to wound healing, with changes in their levels corresponding to various stages of the process [36]. Monitoring MMP levels is particularly useful for evaluating prolonged healing in dense connective tissues, such as the Achilles tendon, and managing chronic wounds [37,38].

Advances in omics and DNA origami technology are paving the way for rapid and sensitive biomarker detection in clinical settings, enhancing precision medicine [39]. The integration of biomarkers with digital technology to create digital biomarkers enables real-time monitoring and personalized care, which represents a promising direction for future research [40]. The exploration of biomarkers specific to different disease states holds the potential for improving early diagnosis and treatment efficacy across various conditions [41,42].

4.3. Advances in incision healing treatments

Significant progress has been made in treating incisions to enhance healing rates, reduce complications, and improve patient outcomes. Innovations in suture techniques, wound therapy, biomaterials, molecular biology, and tissue engineering offer promising solutions to the challenges associated with wound healing.

4.3.1. Suture techniques

The primary purpose of suture techniques is to align wound edges precisely, facilitating healing and minimizing scarring. Recent technological advances have introduced new suture methods that reduce postoperative complications and promote faster recovery [43]. Additionally, the development of more biocompatible suture materials has improved suture efficacy by lowering the risk of infection and further supporting healing [44].

4.3.2. Negative pressure wound therapy

Negative pressure wound therapy (NPWT) applies localized negative pressure to the wound surface, which enhances blood flow, decreases tissue edema, and aids in the removal of exudates [45,46]. Moreover, a cost-effective version known as "Turtle VAC" has demonstrated favorable clinical outcomes, expanding NPWT's applications in healthcare [47].

4.3.3. Advanced wound dressings

The selection of appropriate wound dressings is essential for incision healing. Modern dressings come in diverse types tailored to specific needs, such as high-exudate foam dressings for heavy drainage and hydrogel dressings for dry or necrotic tissues. Transparent film dressings are another option that can protect the wound while allowing for observation [48,49]. Technological innovations have also led to novel dressings, such as hydrogel combined with phototherapy, which enhances the healing process [50,51]. Clinicians are encouraged to select dressings based on wound type and patient condition for optimal healing outcomes.

4.3.4. Biomaterials in tissue regeneration

Biomaterials have proven effective in tissue repair, with advances in polymers, ceramics, and composites offering high biocompatibility that fosters cell growth and tissue regeneration [52]. Collagen-based biomaterials, particularly useful in skin and soft tissue engineering, show promise for promoting healing [53]. Additionally, genetic engineering now allows researchers to design biomaterials with targeted biological functions, enhancing the regenerative effects of tissue repair interventions [54].

4.3.5. Molecular biology and gene therapy

Molecular biology research has led to important advancements in chronic and diabetic wound healing. Growth factor gene therapy, for example, has shown efficacy in accelerating wound healing and enhancing clinical outcomes. Combining hepatocyte growth factor with insulin-like growth factor-1, for instance, mitigates oxidative stress and aids cellular repair [55,56]. Researchers are exploring combinations of multiple growth factors, including engineered proteins that boost the effectiveness of certain receptor tyrosine kinase inhibitors [57]. In addition to growth factors, exosome products have been studied for their regenerative potential. Clinical-grade platelet exosome products (PEP), combined with fibrin sealants, have been shown to promote wound healing and complete skin regeneration in chronic wounds [58].

Ongoing RNA-based research is providing insights into incision management, especially for diabetic patients. Hypoxia-pretreated ADSC exosomes containing Circ-Snhg11, for example, activate the miR-144-3p/HIF-1α/VEGF signaling pathway to support vascular differentiation and healing in diabetic wounds. Other RNA-based therapies, such as LncRNA FAM83A-AS1 and LncRNA-H19, have also demonstrated potential for promoting fibroblast proliferation and wound healing in diabetic foot ulcers (DFUs) [30].

4.3.6. Advances in tissue engineering and bioprinting

Tissue engineering innovations, particularly in bioprinting, have created new opportunities in regenerative medicine. Recent developments in 3D bioprinting technology have enabled the creation of complex tissue structures that offer an optimal environment for cell growth [59]. Additionally, organoid technology is showing potential in simulating organ function, facilitating more accurate drug testing, and developing disease models [60].

In muscle tissue engineering, advancements in biomaterial-based scaffolding and optimized cell sourcing have improved muscle regeneration efficiency [61]. Research is also focused on vascular tissue engineering, developing innovative approaches to address the shortage of vascular transplantation options in clinical practice [62]. Although these biomedical advances hold substantial promise for clinical application, challenges related to safety, effectiveness, cost, and patient acceptance remain key considerations for successful implementation [63].

Interdisciplinary research in nanotechnology, biomaterials, and regenerative medicine continues to inspire novel healing-promoting treatments [64]. The integration of genomics and proteomics is also expected to aid in identifying healing-associated biomarkers, enabling early intervention and personalized treatment approaches [42]. Future research should focus on fostering collaboration across disciplines to bridge the gap between basic research and clinical applications, ultimately addressing the complexities of wound healing and its associated clinical challenges.

5. Conclusion

Incision healing is a complex process influenced by multiple factors. A thorough investigation of the mechanisms underlying incision healing will enhance understanding of its biological basis and aid in developing personalized assessment criteria and interventions for various types and locations of incisions. Despite ongoing research, poor incision healing continues to affect clinical outcomes. Future studies should focus on optimizing current treatment options, and systematically evaluating the effects of different strategies by combining clinical trials with foundational research. Additionally, emphasis should be placed on multidisciplinary collaboration to integrate advancements in surgery, regenerative medicine, and materials science, thereby promoting progress in incision healing technology.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Niederstätter IM, Schiefer JL, Fuchs PC, 2021, Surgical Strategies to Promote Cutaneous Healing. Med Sci (Basel), 9(2): 45. https://doi.org/10.3390/medsci9020045

[2] Rossaint J, Margraf A, Zarbock A, 2019, Perioperative Inflammation. Anaesthesist, 68(7): 421–427. https://doi.org/10.1007/s00101-019-0596-9

[3] Maruyama M, Rhee C, Utsunomiya T, et al., 2020, Modulation of the Inflammatory Response and Bone Healing. Front Endocrinol (Lausanne), 11: 386. https://doi.org/10.3389/fendo.2020.00386

[4] Lin YA, Chu PY, Ma WL, et al., 2021, Enzyme-Digested Peptides Derived from *Lates calcarifer* Enhance Wound Healing after Surgical Incision in a Murine Model. Mar Drugs, 19(3): 154. https://doi.org/10.3390/md19030154

[5] Singh D, Chopra K, Sabino J, et al., 2020, Practical Things You Should Know about Wound Healing and Vacuum-Assisted Closure Management. Plast Reconstr Surg, 145(4): 839e–854e. https://doi.org/10.1097/PRS.0000000000006652

[6] Grada A, Phillips TJ, 2022, Nutrition and Cutaneous Wound Healing. Clin Dermatol, 40(2): 103–113. https://doi.org/10.1016/j.clindermatol.2021.10.002

[7] Widodo A, Rahajoe PS, Astuti RT, 2020, TGF-β Expression and Wound Tensile Strength After Simple Interrupted Suturing and Zip Surgical Skin Closure (IN VIVO Study). Ann Med Surg (Lond), 58: 187–193. https://doi.org/10.1016/j.amsu.2020.08.009

[8] Goto T, Sapio MR, Maric D, et al., 2021, Longitudinal Peripheral Tissue RNA-Seq Transcriptomic Profiling, Hyperalgesia, and Wound Healing in the Rat Plantar Surgical Incision Model. FASEB J, 35(10): e21852. https://doi.org/10.1096/fj.202100347R

[9] Zhou SC, Liang JW, Zhou HT, et al., 2020, Risk Factor Analysis for Perineal Incision Complications After Abdominoperineal Resection in Elderly Patients with Rectal Cancer. Zhonghua Zhong Liu Za Zhi, 42(1): 65–69. https://doi.org/10.3760/cma.j.issn.0253-3766.2020.01.010

[10] Blair MJ, Jones JD, Woessner AE, et al., 2020, Skin Structure-Function Relationships and the Wound Healing Response to Intrinsic Aging. Adv Wound Care (New Rochelle), 9(3): 127–143. https://doi.org/10.1089/wound.2019.1021

[11] Wang J, Xing H, Chang Z, 2023, Effects of Different Sponge Implantation Methods of Negative Pressure Wound Therapy on Wound Healing of Deep Surgical Site Infection After Spinal Surgery. PLoS One, 18(9): e0291858. https://doi.org/10.1371/journal.pone.0291858

[12] Gotlin MJ, Catalano W, Levine JP, et al., 2022, Wound Closure Following Intervention for Closed Orthopedic Trauma. Injury, 53(2): 313–322. https://doi.org/10.1016/j.injury.2021.11.062

[13] Dalci K, Gumus S, Saritas AG, et al., 2022, Modified Techniques Versus Hadfield's Procedure in Patients with Periductal Mastitis. BMC Surg, 22(1): 40. https://doi.org/10.1186/s12893-022-01496-0

[14] Ibrahiem SMS, 2023, Concha-Type Microtia: New Surgical Incision. Aesthet Surg J, 43(11): NP815–NP822. https://doi.org/10.1093/asj/sjad191

[15] Sun J, Yang G, Yang C, 2024, Influence of Postoperative Hypoalbuminemia and Human Serum Albumin Supplementation on Incision Healing Following Total Knee Arthroplasty for Knee Osteoarthritis: A Retrospective Study. Sci Rep, 14(1): 17354. https://doi.org/10.1038/s41598-024-68482-9

[16] Srivastava GK, Martinez-Rodriguez S, Md Fadilah NI, et al., 2024, Progress in Wound-Healing Products Based on Natural Compounds, Stem Cells, and MicroRNA-Based Biopolymers in the European, USA, and Asian Markets: Opportunities, Barriers, and Regulatory Issues. Polymers (Basel), 16(9): 1280. https://doi.org/10.3390/polym16091280

[17] Krishnaswami V, Raju NS, Alagarsamy S, et al., 2020, Novel Nanocarriers for the Treatment of Wound Healing. Curr Pharm Des, 26(36): 4591–4600. https://doi.org/10.2174/1381612826666200701203432

[18] Xi J, Li W, Li T, et al., 2024, Effects of Loose Combined Cutting Seton Surgery on Wound Healing and Pain in Patients with High Anal Fistula: A Meta-Analysis. Int Wound J, 21(3): e14675. https://doi.org/10.1111/iwj.14675

[19] Lin YH, Chen YC, Cheng KS, et al., 2021, Higher Periwound Temperature Associated with Wound Healing of Pressure Ulcers Detected by Infrared Thermography. J Clin Med, 10(13): 2883. https://doi.org/10.3390/jcm10132883

[20] Gu Q, Liu Q, Wang X, Xia Y, Hu J. Clinical effects of Special Pressure Ulcer Intervention Combined with Gel Positioning Pad Intervention on Preventing Acute Stress Injury in Patients Undergoing Long-Term Lateral Position Spinal Surgery. Altern Ther Health Med, 30(8): 282–289

[21] Gupta S, Srivastava A, Malhotra R, et al., 2023, Wound Assessment Using Bates Jensen Wound Assessment Tool in Acute Musculoskeletal Injury Following Low-Cost Wall-Mounted Negative-Pressure Wound Therapy Application. Indian J Orthop, 57(6): 948–956. https://doi.org/10.1007/s43465-023-00861-2

[22] Chen C, Luo LB, Gao D, et al., 2019, Surgical Drainage of Lactational Breast Abscess with Ultrasound-Guided Encor Vacuum-Assisted Breast Biopsy System. Breast J, 25(5): 889–897. https://doi.org/10.1111/tbj.13350

[23] Chen L, Zheng Q, Chen X, et al., 2019, Low-Frequency Ultrasound Enhances Vascular Endothelial Growth Factor Expression, Thereby Promoting the Wound Healing in Diabetic Rats. Exp Ther Med, 18(5): 4040–4048. https://doi.org/10.3892/etm.2019.8051

[24] Ashikyan O, Wells J, Chhabra A, 2021, 3D MRI of the Hip Joint: Technical Considerations, Advantages, Applications, and Current Perspectives. Semin Musculoskelet Radiol, 25(3): 488–500. https://doi.org/10.1055/s-0041-1730910

[25] Altahawi F, Pierce J, Aslan M, et al., 2021, 3D MRI of the Knee. Semin Musculoskelet Radiol, 25(3): 455–467. https://doi.org/10.1055/s-0041-1730400

[26] Lansier A, Bourillon C, Cuénod CA, et al., 2023, CT-Based Diagnostic Algorithm to Identify Bowel and/or Mesenteric Injury in Patients with Blunt Abdominal Trauma. Eur Radiol, 33(3): 1918–1927. https://doi.org/10.1007/s00330-022-09200-9

[27] Du Y, Han S, Zhou Y, et al., 2023, Severe Wound Infection by MRCNS Following Bilateral Inguinal Herniorrhaphy. BMC Infect Dis, 23(1): 85. https://doi.org/10.1186/s12879-023-08039-9

[28] Siegel MJ, Bugenhagen SM, Sanchez A, et al., 2023, Comparison of Radiation Dose and Image Quality of Pediatric High-Resolution Chest CT Between Photon-Counting Detector CT and Energy-Integrated Detector CT: A Matched Study. AJR Am J Roentgenol, 221(3): 363–371. https://doi.org/10.2214/AJR.23.29077

[29] Jiang Z, Zhang M, Li P, et al., 2023, Nanomaterial-Based CT Contrast Agents and Their Applications in Image-Guided Therapy. Theranostics, 13(2): 483–509. https://doi.org/10.7150/thno.79625

[30] Shi S, Gong Y, Hu H, et al., 2023, Topical Dihydroartemisinin Improves Wound Healing in Diabetic Mice. J Plast Surg Hand Surg, 58: 26–32. https://doi.org/10.2340/jphs.v58.5775

[31] Luo X, Cheng S, Zhang W, et al., 2024, Near-Infrared Fluorescence Probe for Indication of the Pathological Stages of

Wound Healing Process and Its Clinical Application. ACS Sens, 9(2): 810–819. https://doi.org/10.1021/acssensors.3c02147

[32] Yang S, Gu Z, Lu C, et al., 2020, Neutrophil Extracellular Traps Are Markers of Wound Healing Impairment in Patients with Diabetic Foot Ulcers Treated in a Multidisciplinary Setting. Adv Wound Care (New Rochelle), 9(1): 16–27. https://doi.org/10.1089/wound.2019.0943

[33] Peddibhotla S, Caples K, Mehta A, et al., 2023, Triazolothiadiazine Derivative Positively Modulates CXCR4 Signaling and Improves Diabetic Wound Healing. Biochem Pharmacol, 216: 115764. https://doi.org/10.1016/j.bcp.2023.115764

[34] Li S, Renick P, Senkowsky J, et al., 2021, Diagnostics for Wound Infections. Adv Wound Care (New Rochelle), 10(6): 317–327. https://doi.org/10.1089/wound.2019.1103

[35] Siu MC, Voisey J, Zang T, et al., 2023, MicroRNAs Involved in Human Skin Burns, Wound Healing and Scarring. Wound Repair Regen, 31(4): 439–453. https://doi.org/10.1111/wrr.13100

[36] Yadav JP, 2023, Based on Clinical Research Matrix Metalloprotease (MMP) Inhibitors to Promote Diabetic Wound Healing. Horm Metab Res, 55(11): 752–757. https://doi.org/10.1055/a-2171-5879

[37] Chen H, Wang J, Hart DA, et al., 2022, Complement Factor D as a Predictor of Achilles Tendon Healing and Long-Term Patient Outcomes. The FASEB Journal, 36(6): e22365. https://doi.org/10.1096/fj.202200200RR

[38] Mota FAR, Passos MLC, Santos JLM, et al., 2024, Comparative Analysis of Electrochemical and Optical Sensors for Detection of Chronic Wounds Biomarkers: A Review. Biosens Bioelectron, 251: 116095. https://doi.org/10.1016/j.bios.2024.116095

[39] Yuan C, Zhou F, Xu Z, et al., 2024, Functionalized DNA Origami-Enabled Detection of Biomarkers. Chembiochem, 25(13): e202400227. https://doi.org/10.1002/cbic.202400227

[40] Montag C, Elhai JD, Dagum P, 2021, On Blurry Boundaries When Defining Digital Biomarkers: How Much Biology Needs to Be in a Digital Biomarker? Front Psychiatry, 12: 740292. https://doi.org/10.3389/fpsyt.2021.740292

[41] Fang B, 2020, Introduction to this Special Issue: “Biomarker Discovery and Precision Medicine”. J Cancer Metastasis Treat, 6:1. https://doi.org/10.20517/2394-4722.2019.42

[42] Li J, Xu M, Peng J, et al., 2021, Novel Technologies in cfDNA Analysis and Potential Utility in Clinic. Chin J Cancer Res, 33(6): 708–718. https://doi.org/10.21147/j.issn.1000-9604.2021.06.07

[43] Zhang W, Xie J, Zeng A, 2022, The Origin and Development of Interrupted Subcuticular Suture: An Important Technique for Achieving Optimum Wound Closure. Dermatol Surg, 48(6): 619–624. https://doi.org/10.1097/DSS.0000000000003437

[44] Suthar P, Shah S, Waknis P, et al., 2020, Comparing Intra-Oral Wound Healing After Alveoloplasty Using Silk Sutures and N-Butyl-2-Cyanoacrylate. J Korean Assoc Oral Maxillofac Surg, 46(1): 28–35. https://doi.org/10.5125/jkaoms.2020.46.1.28

[45] Bhardwaj H, Joshi R, Gupta A, 2024, Updated Scenario on Negative Pressure Wound Therapy. Int J Low Extrem Wounds, 2024: 15347346241228788. https://doi.org/10.1177/15347346241228788

[46] Marouf A, Mortada H, Khedr B, et al., 2022, Effectiveness and Safety of Immediate Application of Negative Pressure Wound Therapy in Head and Neck Free Flap Reconstruction: A Systematic Review. Br J Oral Maxillofac Surg, 60(8): 1005–1011. https://doi.org/10.1016/j.bjoms.2022.04.003

[47] Barau Dejean JMC, Pean JTM, Ottesen TD, et al., 2021, Advantages of a New Low-Cost Negative Pressure Wound Therapy Using the “Turtle VAC”: A Case Series. JBJS Case Connect, 11(2). https://doi.org/10.2106/JBJS.CC.20.00056

[48] Orlov A, Gefen A, 2022, The Fluid Handling Performance of the Curea P1 Multipurpose Dressing Against Superabsorbent and Foam Dressing Technologies. Int Wound J, 19(4): 945–956. https://doi.org/10.1111/iwj.13774

[49] Ahmad N, 2022, In Vitro and In Vivo Characterization Methods for Evaluation of Modern Wound Dressings. Pharmaceutics, 15(1): 42. https://doi.org/10.3390/pharmaceutics15010042

[50] Xu Y, Chen H, Fang Y, et al., 2022, Hydrogel Combined with Phototherapy in Wound Healing. Adv Healthc Mater, 11(16):

e2200494. https://doi.org/10.1002/adhm.202200494

[51] Zhao X, Zhou Y, Li J, et al., 2022, Opportunities and Challenges of Hydrogel Microspheres for Tendon-Bone Healing After Anterior Cruciate Ligament Reconstruction. J Biomed Mater Res B Appl Biomater, 110(2): 289–301. https://doi.org/10.1002/jbm.b.34925

[52] Golba B, Benetti EM, De Geest BG, 2021, Biomaterials Applications of Cyclic Polymers. Biomaterials, 267: 120468. https://doi.org/10.1016/j.biomaterials.2020.120468

[53] Wang Y, Wang Z, Dong Y, 2023, Collagen-Based Biomaterials for Tissue Engineering. ACS Biomater Sci Eng, 9(3): 1132–1150. https://doi.org/10.1021/acsbiomaterials.2c00730

[54] Xiao M, Tang Q, Zeng S, et al., 2023, Emerging Biomaterials for Tumor Immunotherapy. Biomater Res, 27(1): 47. https://doi.org/10.1186/s40824-023-00369-8

[55] Mullin JA, Rahmani E, Kiick KL, et al., 2023, Growth Factors and Growth Factor Gene Therapies for Treating Chronic Wounds. Bioeng Transl Med, 9(3): e10642. https://doi.org/10.1002/btm2.10642

[56] Sahan OB, Gunel-Ozcan A, 2021, Hepatocyte Growth Factor and Insulin-like Growth Factor-1 based Cellular Therapies for Oxidative Stress Injury. Curr Stem Cell Res Ther, 16(7): 771–791. https://doi.org/10.2174/1574888X16999201124153753

[57] Wang EA, Chen WY, Wong CH, 2020, Multiple Growth Factor Targeting by Engineered Insulin-like Growth Factor Binding Protein-3 Augments EGF Receptor Tyrosine Kinase Inhibitor Efficacy. Sci Rep, 10(1): 2735. https://doi.org/10.1038/s41598-020-59466-6

[58] Shi A, Li J, Qiu X, et al., 2021, TGF-β Loaded Exosome Enhances Ischemic Wound Healing In Vitro and In Vivo. Theranostics, 11(13): 6616–6631. https://doi.org/10.7150/thno.57701

[59] Yilmaz B, Tahmasebifar A, Baran ET, 2020, Bioprinting Technologies in Tissue Engineering. Adv Biochem Eng Biotechnol, 171: 279–319. https://doi.org/10.1007/10_2019_108

[60] He J, Zhang X, Xia X, et al., 2020, Organoid Technology for Tissue Engineering. J Mol Cell Biol, 12(8): 569–579. https://doi.org/10.1093/jmcb/mjaa012

[61] Luo W, Zhang H, Wan R, et al., 2024, Biomaterials-Based Technologies in Skeletal Muscle Tissue Engineering. Adv Healthc Mater, 13(18): e2304196. https://doi.org/10.1002/adhm.202304196

[62] Iwaki R, Shoji T, Matsuzaki Y, et al., 2022, Current Status of Developing Tissue Engineering Vascular Technologies. Expert Opin Biol Ther, 22(3): 433–440. https://doi.org/10.1080/14712598.2021.1960976

[63] Eck BL, Yim M, Hamilton JI, et al., 2023, Cardiac Magnetic Resonance Fingerprinting: Potential Clinical Applications. Curr Cardiol Rep, 25(3): 119–131. https://doi.org/10.1007/s11886-022-01836-9

[64] Zhang YL, Wang C, Yuan XQ, et al., 2023, Multifunctional Xyloglucan-Containing Electrospun Nanofibrous Dressings for Accelerating Infected Wound Healing. Int J Biol Macromol, 247: 125504. https://doi.org/10.1016/j.ijbiomac.2023.125504