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Revolutionizing Wound Healing: Integrating 4D Bioprinting with Adaptive Bioactive Coatings for Dynamic Tissue Regeneration

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INTRODUCTION & AIM

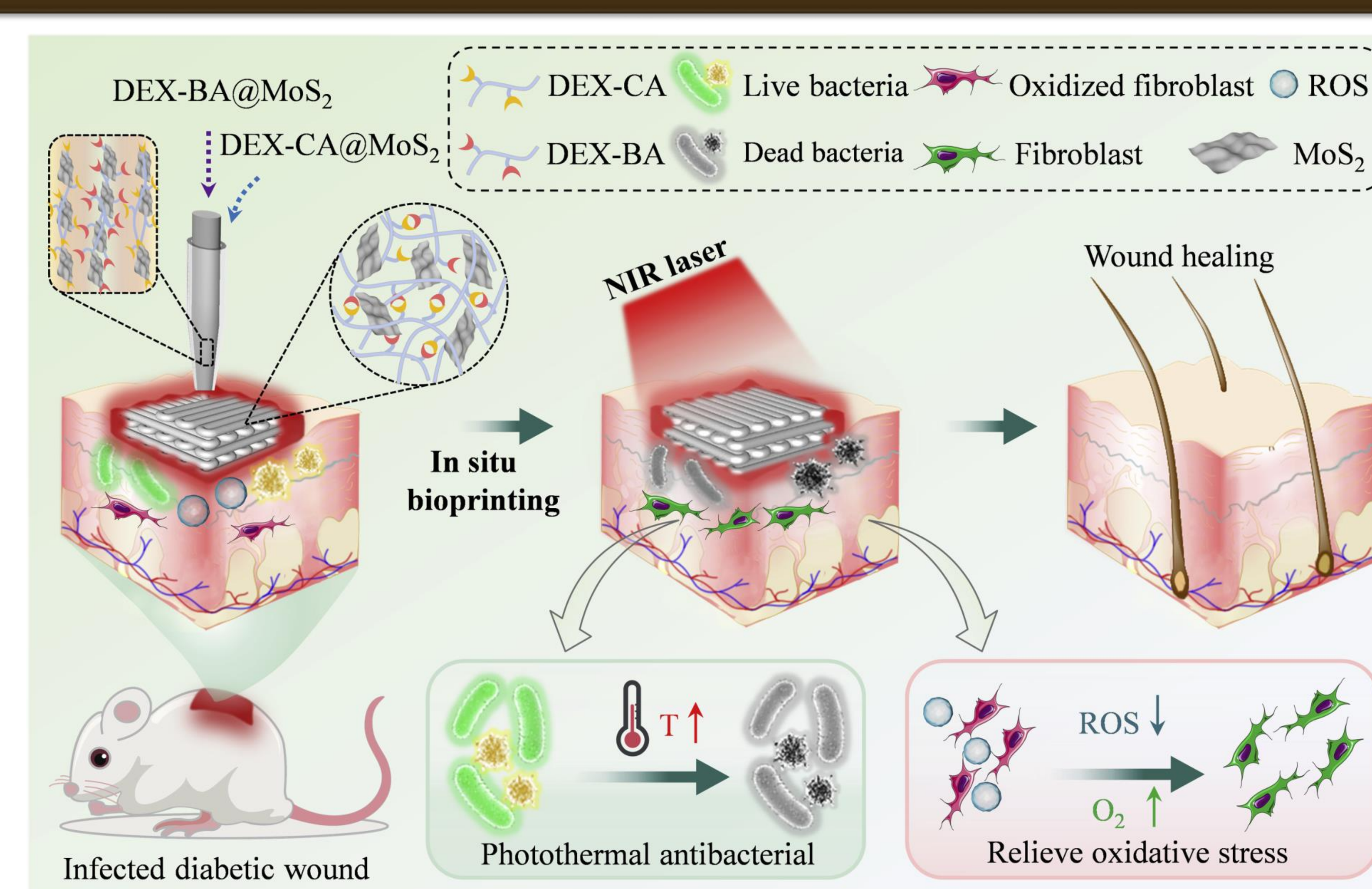
The integration of 4D bioprinting with advanced bioactive coatings is one of the most significant advances in the field of wound healing in recent years. As an emerging technology that introduces the time dimension to 3D printing, 4D bioprinting enables the creation of dynamic, adaptive, and self-regenerating tissue constructs.
In this technology, biocompatible materials are engineered to respond to environmental stimuli (such as temperature, pH, or mechanical forces), making them ideal for enhancing tissue regeneration.

Integrating 4D Bioprinting with Adaptive Bioactive Coatings

Using advanced coatings on 4D bioprinted scaffolds offers a promising new approach to wound care. These coatings, made of either plant-derived compounds or nanomaterials, are designed as thin, porous layers that work with the 4D structure to release drugs in a controlled manner, triggered by changes in the scaffold's shape or porosity as it evolves over time. The innovation lies in merging these responsive 4D structures with bioactive coatings to improve biocompatibility, fight bacteria, and boost cell growth and activity crucial for healing. This combination creates a dynamic environment that adapts to the changing needs of the wound, leading to faster healing and a lower chance of chronic wound development.

Key Features and Applications

Integration of 4D bioprinting with adaptive bioactive coatings presents a range of innovative features that altogether improve the wound healing process in different tissues, such as skin and bone (Zhou, Dong et al. 2022). One of the most important aspects of this system is its time responsiveness, meaning that bioprinted structures can dynamically change their shape or physical properties in response to external stimuli such as temperature changes, pH changes, or mechanical forces (Kalogeropoulou, Díaz-Payno et al. 2024). This responsiveness allows the construct to interact actively with the wound environment, mimicking the behavior of natural tissues. Complementing this are smart bioactive coatings, composed of natural compounds like polyphenols or nanomaterials such as silver nanoparticles embedded in hydrogels. These coatings form thin, porous layers on the surface of the construct and are designed to release therapeutic agents in a controlled and localized manner, based on the changing conditions of the wound site. This synchronized interaction between the construct and coating leads to improved tissue regeneration, improved biocompatibility, and antibacterial protection. The system's ability to facilitate cell migration, proliferation, and extracellular matrix formation further supports its role in accelerating tissue repair. By creating an adaptive microenvironment, this hybrid technology addresses both immediate and long-term wound healing needs, providing a highly responsive and efficient therapeutic platform (Kalogeropoulou, Díaz-Payno et al. 2024)(Sadraei and Naghib 2024).
This method is especially useful for long-lasting wounds like pressure sores or venous leg ulcers, which frequently don't heal properly with standard therapies. This system significantly helps heal diabetic foot ulcers by combating infection and promoting tissue regeneration (Ding, Yu et al. 2023). Additionally, it aids in burn recovery by encouraging skin regrowth, keeping the area moist, and protecting against infection. Post-surgical wounds and bone defects can also benefit from this technology, as they close more quickly and the risk of infection is reduced (Zhou, Dong et al. 2022) (Naghib, Hosseini et al. 2024). Moreover, the platform's versatility and customizability pave the way for personalized medicine, enabling treatment strategies tailored to individual wound characteristics and patient-specific healing profiles (Zhou, Dong et al. 2022) (Shen and Shen 2025).



Schematic diagram of the fabrication of an accelerated gelling MoS2 hydrogel scaffold via microfluidic-assisted in situ printing technique and its application to facilitate the healing of chronic infected wounds. (Ding, Yu et al. 2023)

FUTURE WORK

Further studies will aim to improve smart biomaterials and create coatings that react to multiple stimuli, enhancing the accuracy of drug delivery. The main objectives involve testing these materials in living organisms, combining them with wearable sensors for continuous monitoring, and improving production methods to make them more efficient and cost-effective. Also, incorporating individual patient information will allow for the creation of customized wound treatments that adjust to changing conditions, bringing us nearer to treatments that are both effective and suitable for

CONCLUSION

The integration of 4D bioprinting with adaptive bioactive coatings marks a paradigm shift in the field of wound healing and regenerative medicine. This approach moves beyond traditional static scaffolds by introducing dynamic systems that evolve over time, closely mimicking the behavior and adaptability of native tissues. These 4D-printed constructs can modulate their structure and function in response to physiological cues, such as changes in the wound microenvironment, thus allowing for more precise and efficient interaction with surrounding biological tissues. When combined with smart coatings capable of releasing therapeutic agents in a spatially and temporally controlled manner, these systems become intelligent wound care platforms. This synergistic strategy offers several key benefits, including customized healing responses tailored to the patient's wound characteristics, reduction in healing time through improved cellular activation and extracellular matrix remodeling, minimized infection risks due to the incorporation of antimicrobial agents, and decreased dependency on external interventions, as the scaffold-coating system autonomously adapts to wound progression. Furthermore, this innovation also lays the foundation for next-generation precision medicine. In the future of medicine, it is predicted that treatment will not only be targeted and efficient but also sustainable and responsive over time. Meanwhile, the convergence of materials science, bioengineering, and nanotechnology promises to redefine clinical approaches to managing complex and chronic wounds. Ultimately, this technology could significantly improve treatment outcomes, reduce healthcare burdens, and set new standards in personalized restorative therapies.

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