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ADVANCES IN TISSUE ENGINEERING AND 3D BIOPRINTING FOR SKIN RECONSTRUCTION

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Abstract: Skin reconstruction represents a significant challenge in clinical practice, especially in patients with large skin losses resulting from extensive burns, trauma, chronic wounds, and oncological resections. In recent decades, tissue engineering and 3D bioprinting have emerged as promising strategies to overcome the limitations of traditional skin grafts and conventional skin substitutes. These advances enable the development of bioengineered tissues that are closer to native skin, with potential for vascularization, tissue integration, and functional restoration. This article reviews the main advances in tissue engineering and 3D bioprinting applied to skin reconstruction, addressing fundamental concepts, biomaterials, cell types, technical challenges, clinical applications, and future perspectives.

Keywords: Tissue engineering; 3D bioprinting; Skin reconstruction; Skin substitutes; Regenerative medicine.

Introduction

The skin is the largest organ in the human body and performs essential functions such as mechanical protection, thermal regulation, immune defense, and sensory perception. Extensive skin lesions compromise these functions and are associated with high morbidity, infectious risk, and a significant impact on quality of life.

Traditional methods of skin reconstruction, such as skin grafts and flaps, although effective, have important limitations, including restricted availability of donor areas, additional morbidity, and variable aesthetic and functional results. In this context, tissue engineering and, more recently, 3D bioprinting have emerged as innovative alternatives with the potential to create personalized and biologically active skin substitutes.

Fundamentals of tissue engineering applied to skin

Tissue engineering is based on the interaction between three main components: cells, biomaterials (scaffolds), and bioactive factors. The appropriate combination of these elements aims to promote functional tissue regeneration.

Cell types

The main cell types used in skin reconstruction include:

- Keratinocytes: essential for the formation of the epidermis;
- Fibroblasts: responsible for the production of the dermal extracellular matrix;
- Endothelial cells: essential for neovascularization;
- Mesenchymal stem cells: notable for their differentiation potential and immunomodulatory effect.

The use of autologous cells reduces the risk of immune rejection and improves graft integration.

Biomaterials and scaffolds

Scaffolds provide structural support for cell adhesion, proliferation, and differentiation. Natural biomaterials, such as collagen, fibrin, chitosan, and hyaluronic acid, have good biocompatibility, while synthetic biomaterials, such as polyurethanes and polylactides, allow for greater mechanical control and predictable degradation. The choice of scaffold is a central challenge in skin tissue engineering.

3D bioprinting: concepts and technologies

3D bioprinting consists of the controlled deposition of bioinks—composed of living cells, biomaterials, and growth factors—layer by layer, forming complex three-dimensional structures that mimic the architecture of the skin.

Types of bioprinting

- Extrusion bioprinting: widely used, allows high cell density printing;
- Inkjet bioprinting: offers high resolution, but is limited to low-viscosity bioinks;
- Laser bioprinting: provides high precision, but is costly and technically complex.

Bioinks

Bioinks must have adequate rheological properties, biocompatibility, and the ability to maintain cell viability. Hydrogels based on collagen, alginate, and methacrylated gelatin (GelMA) are widely used in skin bioprinting.

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Applications in skin reconstruction

Extensive burns

3D bioprinting enables the production of customized skin substitutes, reducing wound coverage time and the risk of infection. Experimental models demonstrate better tissue integration and less hypertrophic scarring.

Chronic wounds

In diabetic ulcers and pressure injuries, bioengineered tissues promote healing by stimulating angiogenesis and extracellular matrix remodeling.

Post-oncological reconstruction

After extensive tumor resections, tissue engineering allows for more precise reconstruction, with the potential for reduced scar retraction and better aesthetic results.

Current challenges

Vascularization

The absence of a functional vascular network is one of the main limitations of bioprinted tissues. Strategies such as vascular channel printing and endothelial cell incorporation are under development.

Tissue maturation and integration

Obtaining functional bioengineered skin with a stratified epidermis, organized dermis, and skin appendages (hair follicles and glands) still represents a major scientific challenge.

Scalability and cost

Large-scale production of bioprinted tissues and their routine clinical application are limited by high costs, production time, and regulatory requirements.

Ethical and regulatory aspects

The clinical use of bioengineered tissues involves ethical issues related to cell manipulation, especially when stem cells are used. In addition, the regulation of these products varies between countries, requiring rigorous clinical trials to prove safety and efficacy before widespread clinical adoption.

Future prospects

The continuous advancement of 3D bioprinting, coupled with the development of more sophisticated bioinks and vascularization strategies, points to the possibility of creating fully functional skin. The customization of tissue according to individual patient characteristics and integration with artificial intelligence to optimize printed models represent promising avenues.

Conclusion

Tissue engineering and 3D bioprinting represent a milestone in skin reconstruction, offering innovative alternatives to traditional methods. Despite the technical and regulatory challenges that still exist, recent advances point to a promising future, with the potential to transform the management of large skin losses and significantly improve the functional and aesthetic outcomes for patients.

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