Recent Advances in Acellular Regenerative Tissue Scaffolds

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KEYWORDS

• Acellular • Chronic wounds • Dermis • Foot ulcers • Lower extremity
• Regenerative scaffold • Wound care • Wound healing

KEY POINTS

- Regenerative scaffolds reestablish a favorable wound environment by providing a matrix to facilitate cell migration, chemoattraction, angiogenesis, wound bed granulation, and expedited wound closure.
- Research has confirmed the safety and efficacy of acellular matrices in wound healing, demonstrated their capacity to accelerate epithelialization, and validated their ability to significantly increase the proportion of healed lower extremity wounds.
- When selecting an acellular regenerative tissue matrix, the clinician must consider patient- and wound-specific characteristics and have a thorough understanding of the differences between acellular matrices.
- To maximize wound healing, multimodal treatments should be employed.

INTRODUCTION

Originally, acellular biologic tissue scaffolds were used for rotator cuff repair, but with advancements in the field of orthobiologics, the versatile nature of these grafts was realized and exploited across a variety of fields and applications. Similar to the shoulder, when first introduced to the lower extremity, the regenerative tissue matrix was most commonly used for tendon repair.[1] Over time, however, clinical and scientific interest increased, indications expanded, and these scaffolds established a promising role in the continuum of wound care.[2,3]

Chronic wounds occur owing to an imbalance in the normal phases of wound healing, often secondary to diabetes, infection, ischemia, and trauma.[4,5] In the presence of

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a nonhealing wound, the wound environment often demonstrates deficits in the extracellular matrix, alterations in cellular concentrations, and increased bacterial bioburden.[6,7] Biochemical impairments can include elevated concentrations of proinflammatory cytokines, increased levels of matrix metalloproteinases, diminished activity of growth factors, failure of fibroblasts, and degradation of receptor sites.[6] Moreover, bacterial biofilm can prevent eradication of infection and impair migration of keratinocytes, thereby compromising epithelialization.[7] Consequently, many complex, chronic, full-thickness wounds are unresponsive to traditional management therapies. With advances in tissue engineering, however, acellular matrices have emerged as a viable alternative treatment.[8–11]

Acellular tissue scaffolds are classified as allogeneic, derived from adult human cadaveric tissue; xenogenic, derived from animals; or synthetic, derived from synthetic materials.[3] Human and animal tissues are processed to remove the cellular components while preserving the native collagen matrix and retaining the biochemical components. In doing so, an immune response is eliminated, an inflammatory response is avoided, and the appropriate signals are provided to guide revascularization and cellular repopulation throughout the 3-dimensional structure, after transplantation (**Fig. 1**). Biomechanically, suture retention is supported and the surrounding soft tissues are reinforced.[5] Thus, acellular matrices are primed for intrinsic regeneration and with the assistance of mesenchymal stem cells drive reparative processes to produce normal, physiologic tissue and wound closure.[8–11] Herein, recent advances in acellular biologic tissue scaffolds as they relate to wound care are highlighted and discussed, and the surgical techniques for applying regenerative tissue scaffolds to a variety of wound types are also reviewed.

Acellular Biologic Tissue Scaffolds in Wound Care

The majority of chronic wounds fall into 3 primary categories: diabetic ulcers, venous ulcers, and decubitus ulcers.[12] Consequently, these patient populations have been

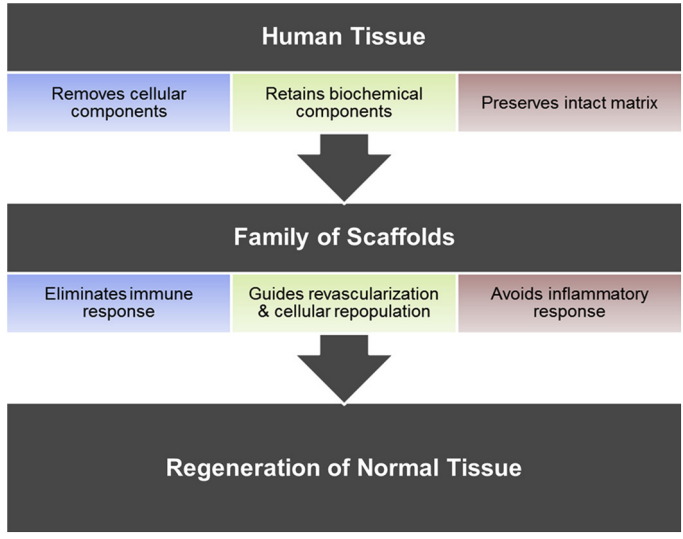

Fig. 1. Processing of human tissue to create an acellular dermal regenerative matrix that is devoid of an immune and inflammatory response. After transplantation, the scaffold guides revascularization and cellular repopulation to regenerate normal, physiologic tissue.