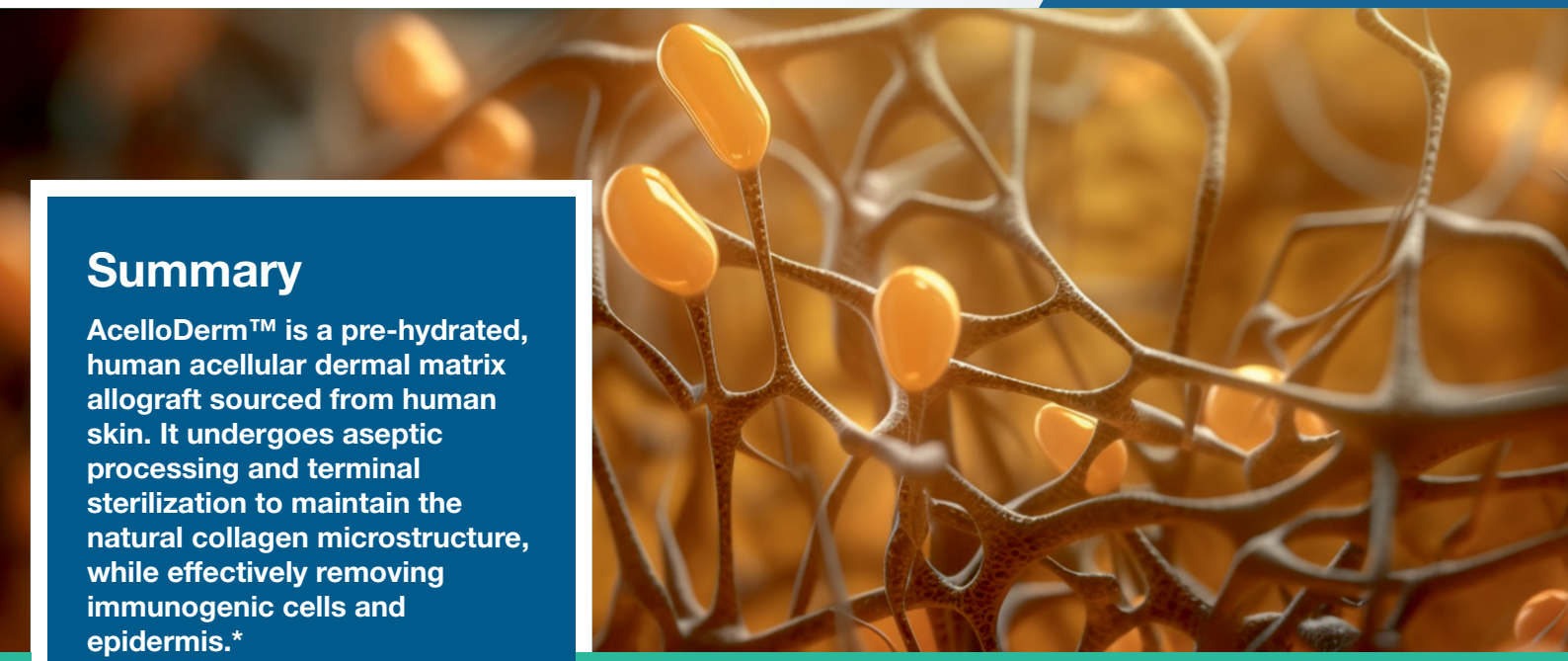
AcelloDerm | **Hydrated** Acellular Dermal Matrix



Summary

AcelloDerm™ is a pre-hydrated, human acellular dermal matrix allograft sourced from human skin. It undergoes aseptic processing and terminal sterilization to maintain the natural collagen microstructure, while effectively removing immunogenic cells and epidermis.*

AcelloDerm™ is engineered to preserve the structural integrity of extracellular matrix components, including collagen, elastin, and glycosaminoglycan (GAG). These components create an ideal microenvironment for tissue remodeling in regenerative medicine applications, providing mechanical strength, collagen integrity, and bioactive elements akin to unprocessed dermis.[1] Additionally, it maintains the basement membrane to prevent adhesion formation and a basement membrane complex of blood vessels to promote angiogenesis.[2]

Our proprietary methodology for processing and sterilizing grafts utilizes low-dose precision gamma irradiation to achieve a Sterility Assurance Level (SAL) of 10^{-6}. As a sterile graft, AcelloDerm™ offers an additional layer of safety critical for successful surgical procedures by reducing the risk of adverse immune responses and capsular formation. Our unique processing technique preserves the essential characteristics of the natural dermal matrix, ensuring AcelloDerm™ closely resembles unprocessed dermis. The matrix properties of AcelloDerm™ are rigorously evaluated through both in vitro and in vivo studies.*†

Preservation of the Extracellular Matrix (ECM)

The extracellular matrix components and their natural structure in unprocessed dermal tissue are crucial for facilitating proper cell-cell interactions and overall tissue function. To ensure robust tissue remodeling and regeneration following surgical procedures using acellular dermal matrix allografts, it is essential that the acellular dermal matrix maintains the intact extracellular matrix structure. AcelloDerm™ is produced using proprietary methods that avoid harsh chemicals, which could compromise the microstructure by weakening the collagen network or cross-linking the tissue. The matrix component and structure of AcelloDerm™ were evaluated against unprocessed skin tissue using histology, immunohistochemistry, transmission electron microscopy, and gel electrophoresis to assess the preservation of the extracellular matrix.†

The collagen structures in unprocessed human skin and AcelloDerm™ were compared and evaluated using histology. Hematoxylin and eosin (H&E) stained sections of both unprocessed human skin and AcelloDerm™ (Figure 1A) reveal a similar collagen structure in terms of density and orientation (depicted in pink). AcelloDerm™ also effectively preserves the dermal papillae. In contrast, cellular components (blue punctate nuclear staining) and the epidermis layer (purple layer on top of papillae) visible in unprocessed human skin are absent in AcelloDerm™, demonstrating the effectiveness of the proprietary process in removing potential immunogenic cellular components while preserving the extracellular matrix.†

Verhoeff-Van Gieson (VVG) stained sections in Figure 1B show the elastin fibers present in both unprocessed human skin and AcelloDerm™. Elastin, another key component of the human dermis, contributes to its natural flexibility and compliance. No differences were observed between the unprocessed human skin and AcelloDerm™.

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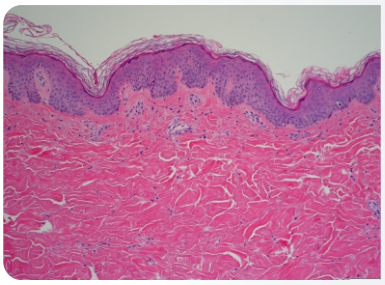
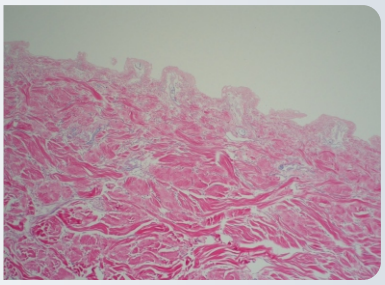
H&E Staining† Fig. 1A

Both unprocessed dermis and AcelloDerm™ show similar collagen structure and papillae.



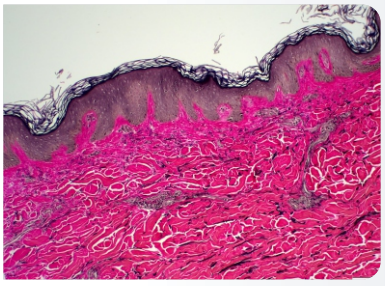
Unprocessed Dermis



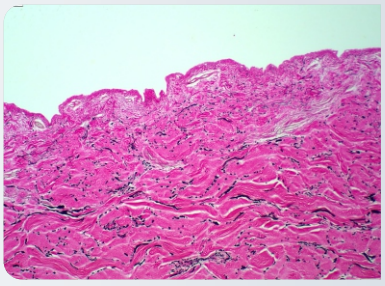
AcelloDerm™

Verhoeff-Van Gieson Staining† Fig. 1B

Both unprocessed dermis and AcelloDerm™ show similar elastin fiber structure (dark grey/ black stains)



Unprocessed Dermis



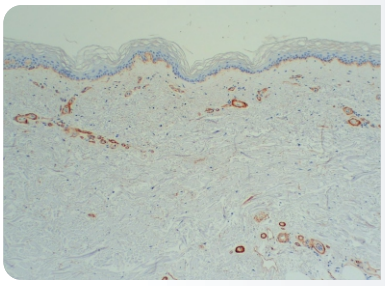
AcelloDerm™

The immunohistochemistry staining for collagen type IV in unprocessed human skin and AcelloDerm™ **(Figure 2)** demonstrates that AcelloDerm™ retains significant levels of collagen type IV found in unprocessed dermis. Collagen type IV is particularly present in the basement membrane complex at the epidermis-dermis junction and around blood vessels.[1,2] This basement membrane complex supports angiogenesis, or the formation of new blood vessels.†

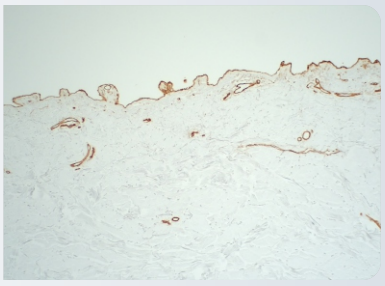
Transmission Electron Microscopy (TEM) images in **Figure 3** show the ultrastructural features of collagen fibrils in both unprocessed human skin and AcelloDerm™. Intact collagen fibrils were observed in both samples, indicating that the proprietary process effectively preserves the ultrastructural architecture of the collagen matrix.†

Immunohistochemistry Staining Against Collagen Type IV† Fig. 2

Collagen type IV is significantly present in the basement membrane at the epidermis-dermis junction and around blood vessels.



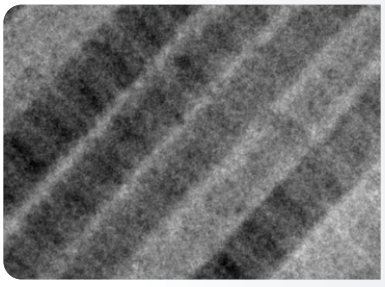
Unprocessed Dermis



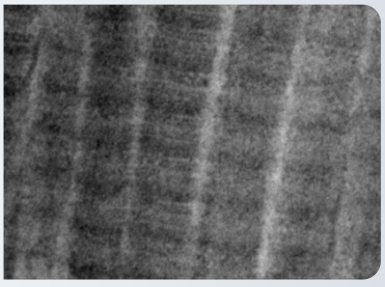
AcelloDerm™

Transmission Electron Microscopy† Fig. 3

Similar collagen fibril structures are evident in unprocessed human skin and AcelloDerm™.



Unprocessed Dermis



AcelloDerm™

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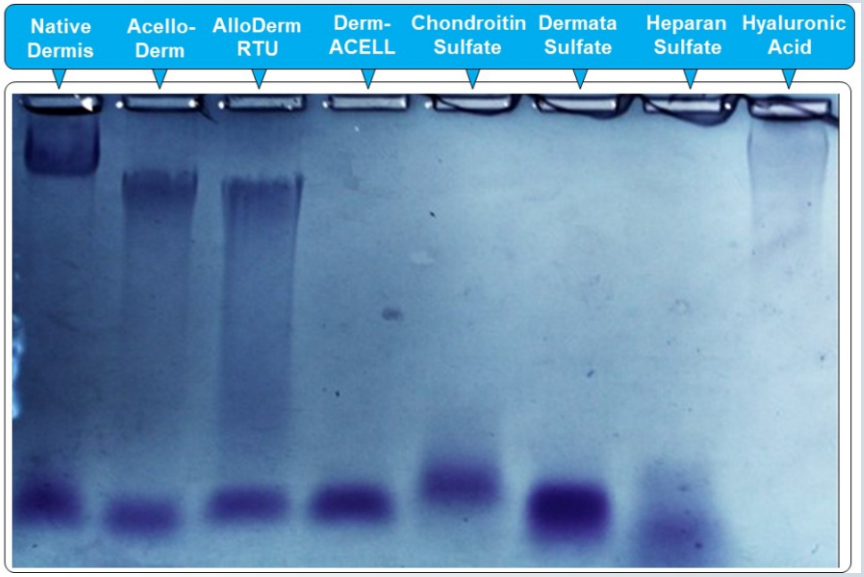
Glycosaminoglycans (GAGs) are key structural components of the extracellular matrix in skin tissue.[1] They interact with other extracellular matrix proteins, including the collagen network, and regulate the mechanical properties of the tissue, such as stiffness.[6] GAGs also play a crucial role in various biological functions, including cell growth and proliferation, adhesion, stem cell niche formation, and tissue hydration.[7] GAGs are classified into four groups: 1) chondroitin sulfate/dermatan sulfate, 2) heparan sulfate, 3) keratan sulfate, and 4) hyaluronic acid.

GAGs present in unprocessed human skin, AcelloDerm™, and two other commercial products (AlloDerm® RTU and DermACELL®), were isolated, separated by agarose gel electrophoresis, and evaluated (Figure 4). The results show that AcelloDerm™ closely matches the profile of unprocessed dermis. AcelloDerm™ is highly comparable to AlloDerm® RTU, and both AcelloDerm™ and AlloDerm® RTU preserve the hyaluronic acid component of the dermis, which is absent in DermACELL®.

Fig. 4



Agarose gel electrophoresis separation of GAGs isolated from the Native Dermis, SimpliDerm™, AlloDerm® RTU and DermACELL® shown in comparison to the four GAG standards (Chondroitin Sulfate, Dermatan Sulfate, Heparan Sulfate, and Hyaluronic Acid).

Preservation of MATRIX INTEGRITY

Preserving the intact structure of the extracellular matrix is essential for maintaining the functionality of biological materials. This is particularly important for proteins, whose three-dimensional structure is crucial for their function and interaction with other biological macromolecules.

AcelloDerm™, along with two other commercial products (AlloDerm® RTU and DermACELL®), were subjected to various test methods designed to denature collagen protein structures. These tests were conducted to evaluate whether each product's matrix integrity remained intact and functional after processing.†

Collagen Stability

Collagen type I is a major component of the extracellular matrix in human dermis. The matrix stability of AcelloDerm™ was assessed by evaluating its susceptibility to collagenase type I. The results show that AcelloDerm™ most closely resembles the unprocessed dermis, with an average difference of 4.18% in enzymatic digestion profiles among the three Hydrated Acellular Dermal Matrix products. AlloDerm® RTU exhibited an average of 9.61% less digestion than the unprocessed dermis at all time points, possibly due to higher collagen crosslinking following processing. DermACELL® displayed a gradual digestion trend, but the digestion amount after 24 hours was 10.67% lower than that of the unprocessed dermis, likely due to changes in collagen structure during processing that allow for more rapid digestion.†

The matrix stability of AcelloDerm™ compared to the unprocessed dermis was also evaluated by measuring the percentage of acid-soluble collagen content **(Figure 5).** Damage to the collagen matrix during processing increases the presence of denatured or unraveled collagen, which can be easily hydrolyzed by strong acids like hydrochloric acid. Thus, a higher acid-soluble collagen content compared to the unprocessed dermis indicates altered collagen integrity. The results show that AcelloDerm™ has the lowest acid-soluble collagen content among the three commercially available acellular matrix products, closely matching the values of the unprocessed dermis **(Figure 6).**

In conclusion, the collagen stability of AcelloDerm™ is the closest to that of the unprocessed dermis when compared to other commercial products AlloDerm® RTU and DermACELL®.†

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Fig. 5
Enzymatic Degradation Profile

Enzymatic Degradation Profile Evaluated by measuring the matrix digestion over time through remaining percentage of dry mass

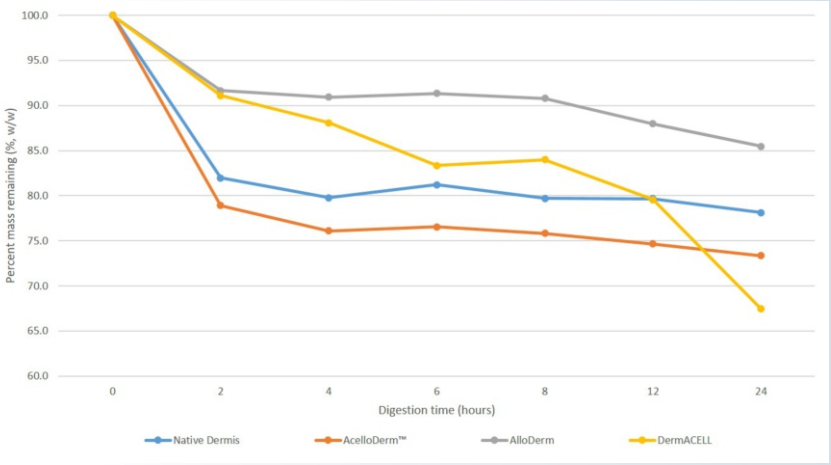
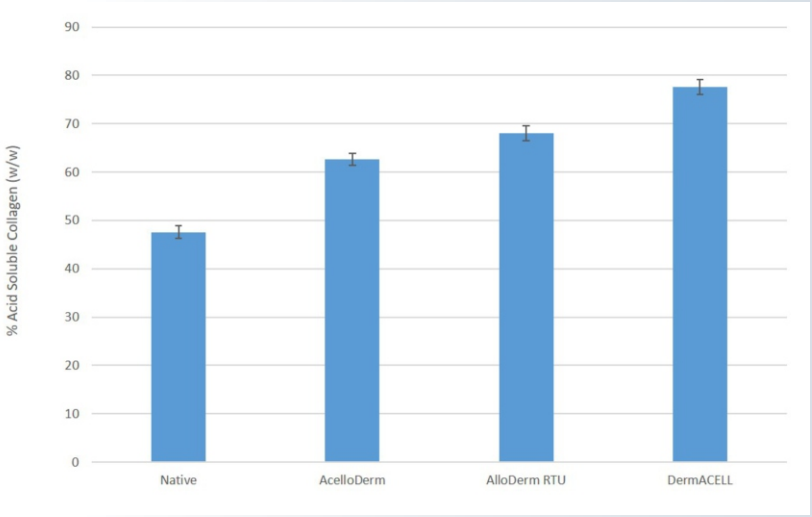


Fig. 6
Acid Soluble Collagen Content

Acid Soluble Collagen Content Indirectly obtained by measuring the hydroxyproline content

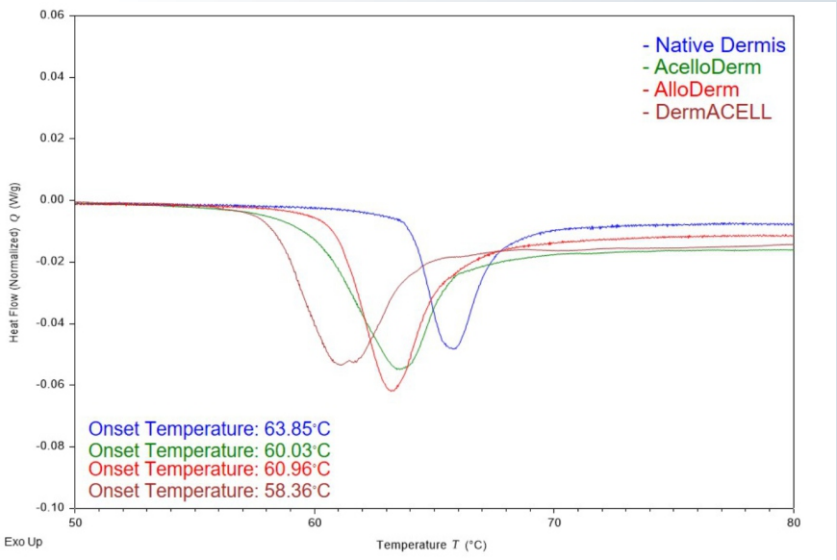


Thermal Stability

Differential Scanning Calorimetry (DSC) is a thermal analysis method commonly used to study the thermal transitions of a material and evaluate the factors that contribute to the stability of biomolecules.9 DSC was employed to measure the onset melting temperature of the dermal matrix, assessing the thermal stability of unprocessed human skin, AcelloDerm™, and other commercial products (AlloDerm® RTU and DermACELL®).†

The DSC analysis revealed that the onset melting temperature of AcelloDerm™ was closer to that of the unprocessed dermis compared to DermACELL® and was similar to AlloDerm® RTU **(Figure 7).**†

Fig. 7
Differential Scanning Calorimetry†



Thermal curve showing the onset collagen melting temperature of unprocessed dermis, AcelloDerm™, AlloDerm® RTU, and DermACELL

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Biomechanical Properties

To evaluate the mechanical properties of AcelloDerm™, samples were subjected to suture retention testing using an Instron testing system. The suture retention strength of the unprocessed dermis, AcelloDerm™, AlloDerm® RTU, and DermACELL® is shown in **Figure 8**.†

The suture retention strength of AcelloDerm™ was measured at 61.14 ± 12.22 N/mm. This value was not significantly different from that of the unprocessed dermis (61.02 ± 4.12 N/mm) and DermACELL® (57.93 ± 3.97 N/mm). † However, the suture retention strength of AlloDerm® RTU (32.02 ± 3.25 N/mm) was significantly lower compared to the unprocessed dermis, AcelloDerm™, and DermACELL®.†

Suture Retention Strength

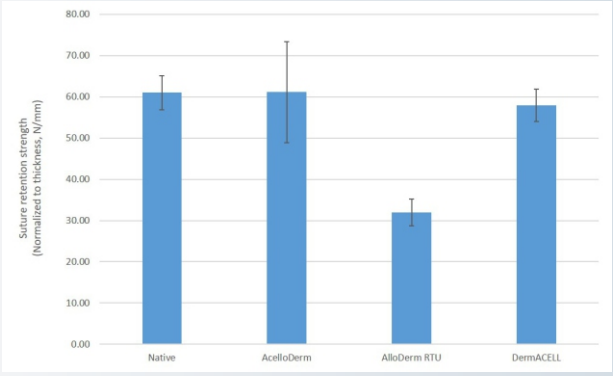

Fig. 8 Suture Retention Strength †

AcelloDerm retained mechanical properties measured by suture retention strength closest to that of unprocessed dermis.

In Vivo Study

To investigate the tissue remodeling and regeneration process of AcelloDerm™ following surgical implantation, an animal study was conducted. AcelloDerm™ was implanted into a full-thickness abdominal wall defect and evaluated at 2-week, 4-week, and 3-month intervals.†

Immunohistochemistry staining for CD68, a macrophage marker, on samples obtained at the 4-week time point indicated that AcelloDerm™ elicited a lower inflammatory response compared to the commercial product AlloDerm® RTU **(Figure 9)**.

At 3 months, AcelloDerm™ exhibited prominent new collagen deposition, cellular infiltration by fibroblasts, and mild vasculature formation **(Figure 10A/B)**, all indicative of a robust tissue regeneration process.†

At all time points, there were no significant adverse reactions such as fibrin, necrosis, mineralization, osseous metaplasia, or cavity/pocket formation (e.g., seroma).†

Overall, AcelloDerm™ demonstrated effective tissue repair and regeneration in vivo, as evidenced by low host immune response, neovascularization, and new collagen formation.†

AcelloDerm™ **AlloDerm® RTU**

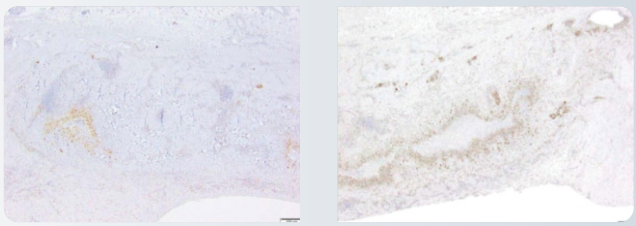

Fig. 9

Immunohistochemistry staining against CD68: AcelloDerm shows pockets of inflammatory cell concentration, while AlloDerm RTU shows significant confluent bands of inflammatory cell infusion.†

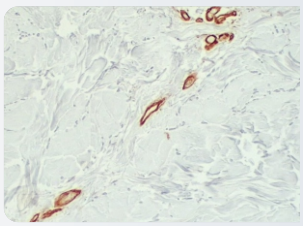

Fig. 10A

Immunohistochemistry staining against collagen IV Showing blood vessels complex in Pre-implant Accello Dream

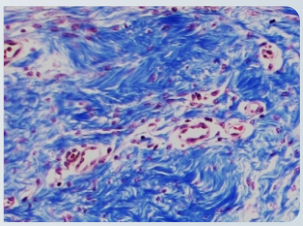

Fig. 10B

Masson's Trichrome staining: new collagen formation (light blue stains) and neovascularization (dark red stains) are evident.†

Conclusion

The preclinical studies on AcelloDerm™, including matrix characterization and in vivo animal studies, demonstrate that AcelloDerm™ is designed and processed to preserve the natural matrix as closely as possible to unprocessed dermis for optimal tissue repair and regeneration.† The proprietary processing of AcelloDerm™ allografts achieves a Sterility Assurance Level (SAL) of 10^{-6} while maintaining a structurally intact matrix that retains similar collagen integrity, mechanical strength, and bioactive components as the unprocessed dermis.† These properties collectively indicate that AcelloDerm™ is the closest to unprocessed dermis and supports a lower inflammatory response and superior tissue regeneration compared to other commercially available acellular dermal matrices, including AlloDerm® RTU and DermACELL®.†

AcelloDerm | **Hydrated** Acellular Dermal Matrix

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Product Ordering Information

THICKNESS: 0.90mm – 1.99mm		THICKNESS: 0.40mm – 0.80mm	
AD.090.0404	4cm x 4cm	AD.040.0404	4cm x 4cm
AD.090.0407	4cm x 7cm	AD.040.0404M	4cm x 4cm Meshed
AD.090.0510	5cm x 10cm	AD.040.0408	4cm x 8cm
AD.090.1020ELP	10cm x 20cm Ellipse	AD.040.0408M	4cm x 8cm Meshed
AD.090.1616P	16cm x 16cm Perforated	**THICKNESS: 2.80mm - 3.50mm**	
AD.090.1620P	16cm x 20cm Perforated	AD.280.0407	4cm x 7cm
AD.090.2020P	20cm x 20cm Perforated	AD.280.0408	4cm x 8cm

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