MTF Musculoskeletal Transplant Foundation
THE ALLOGRAFT LEADER™

FlexHD Acellular Dermal Matrix

HISTOLOGY: IN VITRO and IN VIVO STUDIES

Currently, numerous materials are available for surgeons requiring allograft dermis, each material having its own set of advantages and disadvantages. Allograft dermis has been demonstrated to be an effective biomaterial for the use in the repair of abdominal wall defects[1], dental applications[2], full-thickness burns[3] and breast reconstructions post-mastectomy[4]. Among the materials that have been available, the biologic prosthetics have shown distinct histological advantages, with the distinct disadvantage of requiring time-consuming rehydration to a traditionally freeze-dried graft material.

FlexHD acellular dermal matrix was created to answer the need for a dermal graft that does not require rehydration, yet provides all the histological advantages of a biologic prosthetic.

Biomaterials for the repair and replacement of damaged tissue should provide a scaffold that allows for cell attachment and proliferation for tissue regeneration while being functionally and structurally appropriate in the environment for its intended use[5]. Materials currently used in applications for soft tissue defect repair are derived from synthetic materials, such as polypropylene and polytetrafluoroethylene and from naturally occurring biological sources, including porcine small intestine submucosa and human cadaveric dermis and fascia.

FlexHD acellular dermal matrix is derived from allograft human skin that is processed using proprietary procedures developed by MTF[†]. Allograft skin is decellularized, removing the epidermal layer and cells, leaving an acellular dermis that is disinfected and packaged.

Acellular dermal matrix is packaged hydrated in 70% ethanol solution. It does not require rehydration or rinsing prior to use. Testing has shown that Acellular dermal matrix in this packaging configuration is stable up to 18 months at ambient conditions and does not require refrigerated storage.

HISTOLOGICAL PROFILE

Acellular dermal matrix has been processed to remove cells while maintaining histomorphological integrity. Standard histology and immunohistochemical methods have been used to assess dermal matrix structure and its components. Hematoxylin and eosin staining of normal human skin and acellular dermal matrix show that the matrix is preserved during processing and demonstrates an absence of the epidermis and cells in the resulting matrix.

Hematoxylin and eosin staining of normal skin (left) and acellular dermal matrix (right) from the same donor. Note absence of cells and preservation of matrix structure after processing.

Using immunohistochemical staining methods, collagen, elastin, and other extracellular matrix components were evaluated in acellular dermal matrix. The collagen components are not affected during processing, demonstrated by consistent brown staining throughout the matrix. Elastin fibers also remain

[†] U.S. and international patents pending

present after processing, as seen by darkly stained strands throughout the dermal matrix. Alcian blue staining reveals that hyaluronan, a major glycosaminoglycan, is present in the tissue.

Elastin, in conjunction with collagen, contributes to the strength and structure of the dermal matrix scaffold. Glycosaminoglycans and glycoproteins, such as hyaluranon and vitronectin, are integral components of the extracellular matrix and play an important role in cell-cell and cell-matrix interactions[6,7,8]. Hyaluranon is present in all living organisms and provides matrix structure, osmotic balance, and assists with cell migration, and differentiation.[9,10] Vitronectin, an adhesive glycoprotein, binds to collagen, and promotes cell attachment, proliferation, and differentiation[11].

Immunohistochemical staining shows Type I collagen in normal skin (left) and staining in acellular dermal matrix (right).

Immunohistochemical staining shows Type III collagen in normal skin (left) and staining in acellular dermal matrix (right).

Immunohistochemical staining shows elastin in normal skin (left) and in acellular dermal matrix (right) as darkly stained fibers.

Immunohistochemical staining using Alcian Blue/PAS shows the presence of hyaluronan in normal skin (left) and in acellular dermal matrix (right) as indicated by indigo staining.

Immunohistochemical staining shows vitronectin in normal skin (left) and in acellular dermal matrix (right) as indicated by brown staining. All histology courtesy of Premier Laboratory, LLC.

Immunochemical evaluation of acellular dermal matrix confirms that the major components of the extracellular matrix, including collagen, elastin, and major matrix components responsible for promoting cell attachment and growth are preserved such that the histomorphological integrity of the dermal matrix is maintained after processing. Cells are effectively removed, leaving the original dermal matrix architecture intact.

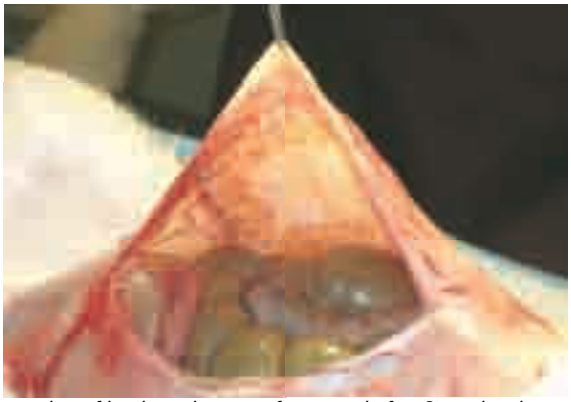
ULTRASTRUCTURAL ANALYSIS

TEM analysis shows amorphic elastin and fibrous collagen structures in normal skin (left) and acellular dermis (right). Microscopy courtesy of Structure Probe, Inc.

Ultrastructural analysis of acellular dermis using high power transmission electron microscopy reveals that the collagen and elastin components of the extracellular matrix are preserved after processing. Collagen in normal skin is observed in the cross-section while in acellular dermis, the fibers are observed oriented in the transverse direction. Elastin appears as an amorphic structure in both sections.

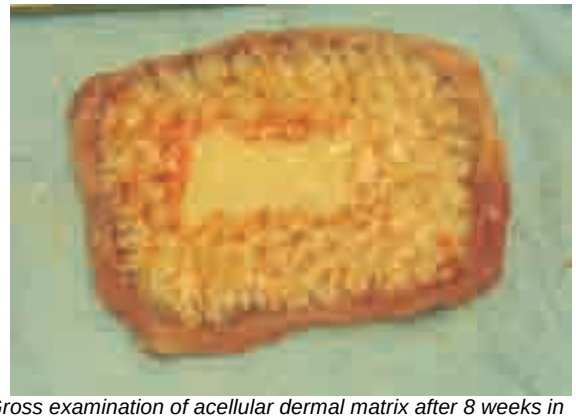
PRECLINICAL EVALUATION

Preliminary results in a study evaluating acellular dermal matrix in a rabbit model for the repair of an abdominal wall defect after 8 weeks demonstrates an absence of visceral attachment to the dermis with vascularization occurring around the perimeter of the implant. Acellular dermis was compared to polypropylene mesh, a prosthetic commonly used in the open repair of abdominal wall defects[††].



Inspection of implant site at graft removal after 8 weeks shows an absence of adhesion to acellular dermal matrix

Inspection of Implant site at graft removal after 8 weeks revealed erythema and extensive visceral attachments to polypropylene mesh



Gross examination of acellular dermal matrix after 8 weeks in vivo reveals neovascularization around graft perimeter

[††] Study conducted at the Institute of Regenerative Medicine, Wake Forest University

Implanted graft region facing bottom left with vessels (arrows) and some inflammatory infiltrate. Center region showing mixed inflammatory cells, fibroblasts, blood vessels, and fatty vacuoles surrounded with more organized collagen network. Skeletal muscle region intact with some mixed cellular infiltrate. (100x)

Collagen network showing some organization at graft implant site with mixed cellular infiltrate with fibroblasts and some inflammatory cells, and blood vessels. (200x)

Histology sections of acellular dermis after 8 weeks in vivo reveal a mixture of cellular infiltrate in layers. The outermost section of tissue shows the formation of new blood vessels along with inflammatory infiltrate and fibroblasts. Deeper in the section, more fibroblasts are present mixed with inflammatory cells as the collagen network shows signs of organization and remodeling. The skeletal muscle region is intact with normal fibroblast infiltrate. Inspection of another section at higher magnification reveals the formation of an organized collagen network with a mixture of fibroblasts and inflammatory cells in the early stages of tissue remodeling.

These preliminary results showing vascularization and resistance to adhesions suggest that acellular dermal matrix possesses the desired biomaterial properties required for the repair of abdominal wall defects.

TISSUE SAFETY AND BIOMECHANICAL PROPERTIES

Testing illustrates that FlexHD's strength and flexibility are greater than its top competitor, creating a strong and reliable biologic matrix for patient recovery. Its acellular properties and proprietary processing technique further ensure tissue safety. Please refer to the separate white papers "Biomechanical Properties," and "Tissue Safety" for further information.

CONCLUSION

In conclusion, Flex HD acellular dermal matrix shows great promise, offering the advantages of a biologic allograft that lends itself to superior tissue integration, remodeling and vascularization. FlexHD also offers the strategic advantage of an allograft that does not require time-consuming rehydration.

FlexHD is made available through the Musculoskeletal Transplant Foundation, a non-profit organization that is a national consortium of medical schools, academic institutions and recovery organizations involved in the recovery, processing and distribution of bone and related soft tissue for use in transplant surgery. Our quality and safety standards have been developed by leading physicians, transplant surgeons, and specialists in the fields of science and medicine.

MTF's quality and safety standards consistently meet or exceed the requirements of the American Association of Tissue Banks and the current regulations published by the federal Food and Drug Administration. MTF is also in compliance with established Good Tissue Practices and the International Standards Organization. MTF uses the most complete and technically advanced testing available, including Nucleic Acid Testing (NAT), for detection of transmittable diseases such as HIV, and Hepatitis to assure the safety of every allograft we supply.

Visit our website at mtf.org, or contact MTF at 1-800-433-6576, for further information.

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