HRT® Human Regenerative Technologies

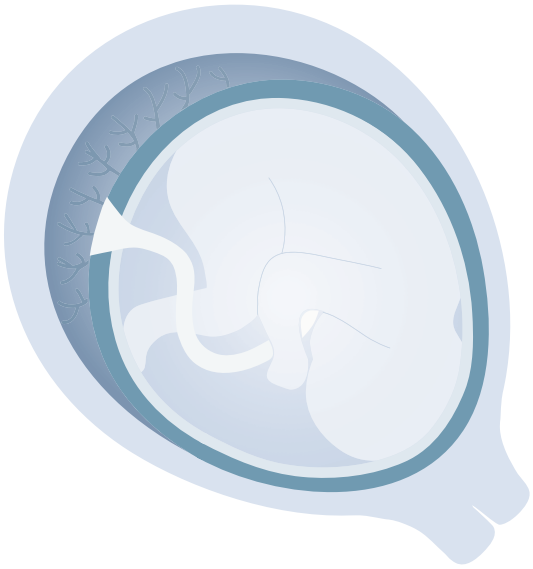
humantissue.com

Next Generation Amniotic & Placental Allografts

HydraTek® Process Innovation, Quality & Safety

PROCESSED WITH HydraTek®
HUMAN REGENERATIVE TECHNOLOGIES®

Why all amniotic & placental tissues are not equal.



HydraTek® is an industry-leading process with scientifically validated quality and safety.

Amniotic membrane tissues have been used clinically throughout the 20th century to successfully treat various chronic and acute wounds.

Over the last decade tissue banks have made a variety of amniotic membrane-based products commercially available in the U.S. Most of these processors have focused on creating limited product forms using only the basic amniotic membranes available from the placenta.

The HydraTek® Process has made numerous advancements in the field of placental processing, maximizing the rich biologic potential that the entire placenta has to offer. HydraTek® is designed to utilize all of the key biologic components available from the placenta, preserve them in their most natural form, and deliver the ultimate range of product forms and formulations for every indication.

While various tissue processors may use a similar donated placental tissue source, the resulting quality and performance of a human tissue allograft varies greatly depending on the processing methods that it undergoes.

The HydraTek® Process uses new revolutionary technology and sophisticated processing methods to extract and utilize the full potential of the placenta like no other company, producing biologically rich product forms and improved delivery methods. HydraTek® Process has proven safety and quality, surpassing FDA and AATB standards to provide the utmost in patient safety and biologic potential.

References on file.

Rich Biologic
Connective Tissue Matrix Flowables

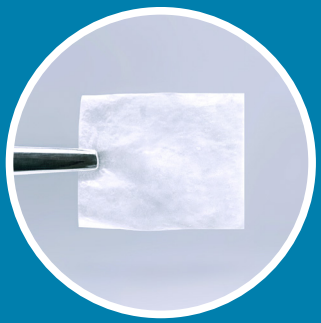
HRT **placental tissue matrix products** provide an easy to use human Connective Tissue Matrix biologic, rich in connective tissue components including BioActive® Fluid, ExtraCellular Matrix (ECM) components, Collagens, Growth Factors, and BioActive® molecules.

Indication I HRT flowable products are intended to supplement or replace damaged or inadequate connective tissue.

Native Biologic
ECM Covering Membranes

HRT **amniotic & placental membrane products** provide a versatile native human ExtraCellular Matrix (ECM) biologic membrane, rich in integral ECM components, Collagens, Growth Factors, and BioActive® molecules.

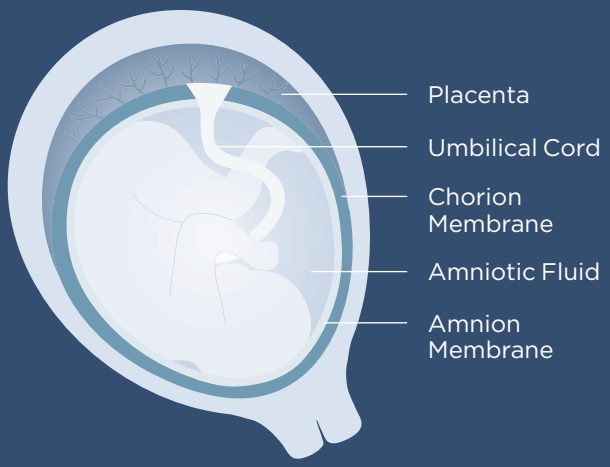
Indication I HRT membrane products are intended to cover and protect the intended site, and provide natural gliding capabilities between tissues.



References on file.

Where are **HydraTek®** tissues derived from?

All donated placental tissues are obtained from healthy mothers who are under the care of a licensed OB/GYN physician at a partner facility. Both donor and tissues are highly screened, and only those that pass all safety tests are cleared for processing. All donations are sourced from U.S.-based donors, and only after live, healthy, successful cesarean birth delivery. No maternal or fetal tissues are collected during the process.



Why **HydraTek®** uses Placental Tissues

HydraTek® uses placental tissues as they are the ideal natural and intact biologic source for human tissue allografts, providing distinct advantages over cadaver-based allograft (human) or xenograft (non-human) sources. Placental tissues are incredibly rich with biologic potential, as they played a role in developing all of the body's various tissues during gestation. They contain highly viable, un-aged biologic components versus aged cadaver tissues. Placental tissues are naturally anti-inflammatory, antifibrotic, anti-microbial, and promote tissue regeneration versus scar tissue formation. They also provide a safer tissue source, as both the donor and the donated tissues are screened before product release. Not all tissue processing systems are the same or have the ability to preserve these natural and robust attributes. HydraTek® uses this unparalleled native human tissue and preserves it with unequaled processing quality to provide the industries most innovative product line.

References on file.

Biologic ECM Components of Placental Tissues

Factor	Role in the Extracellular Matrix
Angiogenin	Antimicrobial, plays important roles in various physiological and pathological processes through regulating cell proliferation, survival, migration, invasion, and/or differentiation. Stimulates growth of blood vessels.
Chondroitin	Major component of cartilage. Plays a role in cushioning the joints.
Collagens I, III, IV, V, VI, VII	Provide scaffold for biomechanical structure and strength. Supports proliferation, migration and adherence.
b-defensins	Anti-microbial peptides, part of the innate immune system.
EGF	Enhances epidermal and keratinocyte proliferation. Stimulates extracellular matrix (ECM) remodeling.
Elafin	Protease inhibitor, modulates inflammation.
Elastin	Provides elasticity properties within tissues for proper biomechanical function.
Fibronectin	Mediates a wide variety of cellular interactions with the ECM and plays important roles in cell adhesion, migration, growth and differentiation.
Heparin Sulfate	Binds many ligands, modulate numerous cellular activities, and aid in tissue architecture and physiology.
Hyaluronic Acid	One of key components of the ECM. Contributes significantly to cell proliferation and migration.
FGF	Roles in regulating cell proliferation, migration and differentiation. Function in ECM repair and response to injury.
HGF	Plays a role in angiogenesis, tumorogenesis, and tissue regeneration.
IFNy	Performs important antiviral and immunoregulatory functions.
IGF-I	Involved in mediating growth and development.
IL-4	Stimulates ECM repair. Modulates immune response, anti-in ammatory properties. Promotes ligament healing.
KGF	Enhances migration and proliferation of keratinocytes and epithelial cells. Plays role in wound healing.
Laminin	Performs a significant strengthening role in the ECM. May have role in adhesion, migration and differentiation.
MMPs & TIMPs	Regulate ECM degredation and support ECM remodeling.
Nidogen	May play a role in cell interactions within the ECM.
PDGF	Regulate cell growth and division. Plays significant role in blood vessel formation (angiogenesis). Has important mitogenic effects for bone cells.
PIGF	Promotes angiogenesis. Augments bone repair. Stimulates cartilage remodeling. Increases fibroblast migration.
SLPI	Antimicrobial, anti-inflammatory protein. Contributes the immune response, has antibacterial, antifungal and antiviral activity.
TGF-a	Induces epithelial development. Believed to promote angiogenesis.
TGF-B	Stimulates angiogenesis. Stimulates broblast proliferation. Increases collagen synthesis and deposition and remodeling of the new ECM. Modulates immune response, anti-inflammatory properties.
TNF	Regulation of a wide spectrum of biological processes including cell proliferation, differentiation, apoptosis, lipid metabolism, and coagulation.
VEGF	Stimulates angiogenesis. Stimulates endothelial cell proliferation. Promotes ossification during bone repair.
Vitronectin	Promotes cell adhesion and migration.

Bryant-Greenwood, G. D. (1998). Bankowski et al. (1996). Sobolewski et al. (2015). Koizumi et al. (2000). Warrier et al. (2012). Insaust et al. (2010). Niknejad et al. (2008). Hadjizadeh et al. (2010).

HydraTek®

Innovation

HRT is a biotech processor specialized in human amniotic and placental tissue products. Our HydraTek® Process is a scientifically advanced technology, with numerous innovations in amniotic and placental tissue processing, and has been independently validated to preserve the biologic properties of its tissues. HydraTek® is **leading the industry** by producing the broadest line of products in market **with improved tissue forms, delivery options and the broadest indications.** HydraTek® has developed a series of scientific methods to provide a distinct advantage in handling, safety, quality and performance of its products.

1

Unique
Cryo and Ambient Formulations

2

Industry-First
Room Temp Flowable

3

ExCellerate®
Flowable Technology

4

BioAware®
Membrane Technology

5

Fast-Acting®
Membrane Performance

Innovation

1. Unique Flowable Formulations

HydraTek® is the **only process** designed to harvest, extract and encapsulate The Complete Placental Connective Tissue Matrix® in an ideal native flowable form.

2. Industry First Room Temperature Flowable

HydraTek® invented a revolutionary way to preserve this connective tissue matrix in ambient (room temp) form – an **industry first** that gives surgeons ideal delivery options and unparalleled ease of use.

The Triple Advantage of HydraTek®

Richest Source

Only HydraTek® extracts the raw connective tissue components from within all of the beneficial areas of the placental organ, providing the richest flowable placental biologic on the market.

Most Concentrated

HydraTek® not only contains the richest source, but also provides the most biologic content (by volume) of any known processor. Our formulations contain up to 600mg of placental connective tissue matrix per vial.

On Indication

Only HydraTek® flowables are indicated for use in all areas of connective tissue within the body. Others are limited to wounds & integumentary tissue.

3. ExCellerate® Flowable Technology

HydraTek® flowable products are a rich biologic Connective Tissue Matrix (CTM) including BioActive® Fluid, ExtraCellular Matrix (ECM) components, Collagens, Growth Factors, and BioActive® molecules. This CTM creates the cellular environment and supports the migration, proliferation and remodeling processes. This flowable tissue matrix can be precisely applied to the areas of damaged connective tissue, and provides **improved resorption and incorporation** for the ideal biologic response.

References on file.

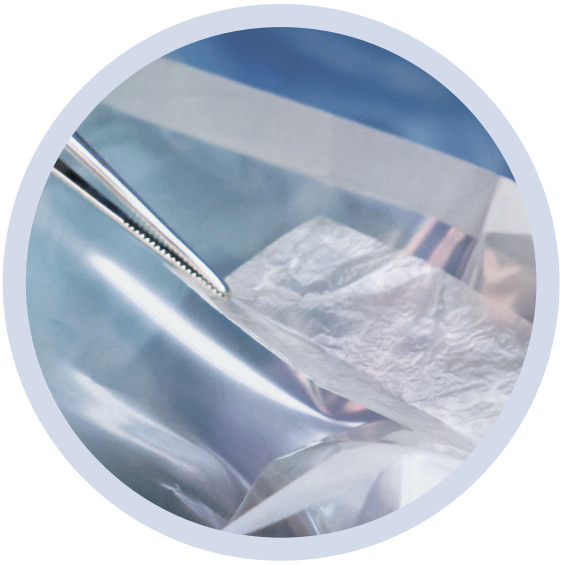
4.

BioAware®

Membrane Preservation System

HydraTek® has designed the **unique BioAware® preservation system** to optimize the structural tissue integrity, biologic viability, handling and performance of its membrane-based allografts. This system scientifically controls the moisture levels in both dehydrated and non-dehydrated membrane products, and carefully preserves the natural tissue structure without compromising it through traditional lyophilization (freeze drying), heat-baking, chemical cross-linking or other disadvantageous methods.

The result is a lineup of membrane products that maintain ideal structure and integrity when used dry or hydrated. These products are omni directional, meaning they can be applied up or down, without orientation issues. The dehydrated membranes adhere extremely well naturally, but are also strong enough to allow for suture fixation as needed. In addition, a non-dehydrated option is available, with load-bearing strength and added thickness for additional support. HydraTek® membranes are also biologically viable, and FastActing®, meaning they resorb faster to go to work quicker.



5.

Fast-Acting®

Membrane Performance

HydraTek® BioAware® Technology is designed to protect the biomechanical structure of its membrane tissues versus other membranes which may be cross-linked or collapsed due to their inferior processing methods. This produces Fast-Acting® membrane products that provide an immediate covering with ideal gliding capabilities at the site, then resorbs quickly allowing the beneficial biologic properties to incorporate into the patient's tissues sooner and go to work faster.

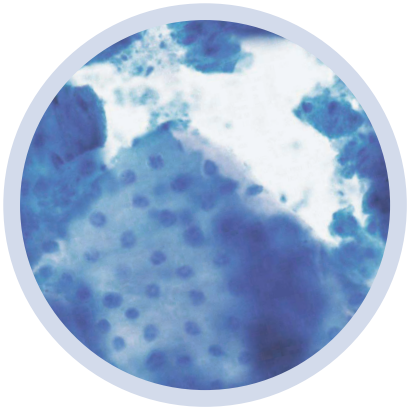
References on file.

HydraTek®

Quality

Proven

HydraTek® is leading the industry with validated preservation of tissue integrity, biologic content, and safety, giving surgeons and patients best in class biologics.



Tissue Integrity

Collagen Content

Growth Factor Content

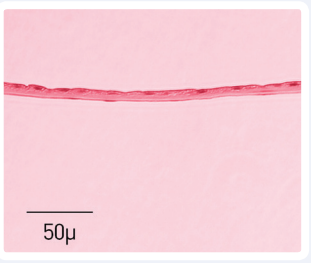
Immuno-Suppressive

The HydraTek® Difference

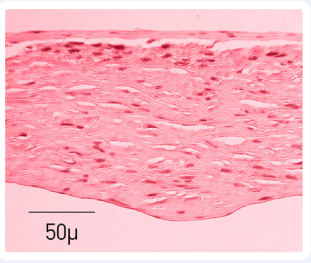
In another industry first, HydraTek® products are scientifically proven to be immunosuppressive,[10] proactively modulating the inflammatory response for improved results. HydraTek® is the first process to document immunosuppressive capabilities of its amniotic membrane and placental tissue matrix products post-processing, setting a new standard for patient safety. Other processors claim that their products are immune-privileged, meaning that they do not induce an immune response. However, they typically cite generic literature that is unrelated to their products, and reports on the placenta's natural ability to avoid an immune response.

References on file.

Quality



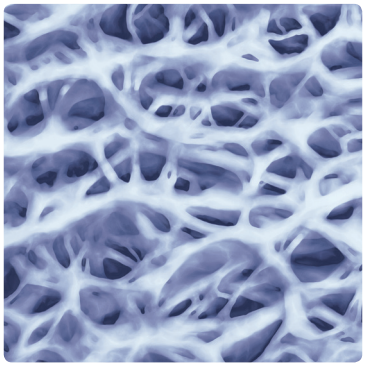
HydraTek® Thin Membrane



HydraTek® Thick Membrane

Improved Tissue Integrity

HydraTek® BioAware® membrane products are shown to better preserve the tissues natural biomechanical structure versus other membrane products.



Collagen Content

HydraTek® is proven to retain the majority of collagen found in unprocessed placental tissues.*

Growth Factor Content

HydraTek® is proven to contain the growth factors found in natural placental tissues.*

ImmunoSuppressive

HydraTek® products are proven to be immunosuppressive, modulating the inflammatory response which can lead to rejection and failure.

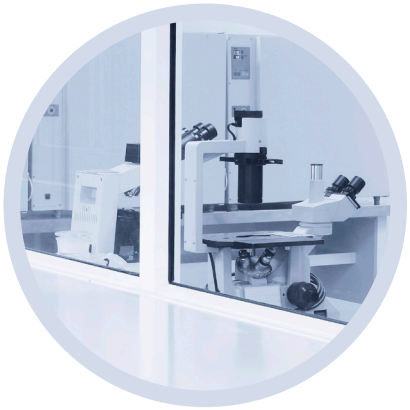
Proven Anti-Microbial

HydraTek® products are proven to be bacteriostatic, with the ability to stop bacteria from growing. This has the potential to reduce the risk of infection, and create a healthier healing environment, providing an added level of safety.

References on file.

HydraTek®

Safety



Utmost in Patient Safety

HydraTek® provides an outstanding standard of safety, through its stringent donor screening, tissue testing, and strict quality and safety standards.

1 AATB **Tissue Bank**

2 Quality **Tissue Source**

3 Stringent **Donor Screening**

4 Safe **Tissue Recovery**

5 Aseptic **Collection**

6 Validated **Sterility**

Safety

1. Tissue Bank

HRT is an **FDA registered** and **AATB accredited** tissue bank since 2014, and is one of the nation's leading tissue banks specializing in regenerative human tissues. Along with its quality advantages, HRT's stringent safety standards are setting a new standard in the industry for tissue processing.

2. Tissue Source

All of HRT's donated placental tissues are obtained from **healthy mothers** who are under the care of a licensed OB/GYN physician at a partner facility. All donations are sourced from U.S.-based donors, and only after **live, healthy, successful cesarean birth delivery.** No maternal or fetal tissues are collected during the process.

3. Donor Screening

HRT employs stringent donor screening criteria in compliance with FDA HCT/P regulations and American Association of Tissue Banks (AATB) standards. See attached abbreviated Donor Screening Criteria.

As an integral part of donor screening, HRT screens the living donor for communicable disease (serologic and nucleic acid amplification) test markers for human immunodeficiency virus 1 & 2, hepatitis B virus, hepatitis C virus, human T cell lymphotrophic virus I/II and causative agent of syphilis in accordance to FDA regulations and AATB standards. The employed testing laboratory is FDA registered and CLIA certified to perform such tests. All test kits are FDA approved and cleared for living donor testing.

4. Tissue Recovery

HRT strictly controls the entire tissue process and does not rely on outside recovery agencies that may not operate at HRT's level of strict process control. HRT runs its own placental donation program, PlacentaDonor.org, to connect donors with partner donation sites. All donated tissues are recovered aseptically in an operating room environment of a Joint Commission accredited hospital. For sanitary reasons, donated tissues are not obtained from birth deliveries performed at birthing centers. Each recovered tissue is placed on wet ice and maintained at wet ice temperature range within the hour of recovery to prevent growth of microorganisms (maintain the low bioburden of the tissue) and preserve the biologic properties of the tissue.

5. Collection and Processing

Tissues are processed aseptically and subjected to minimal processing to maintain the biologic properties and biomechanical integrity of the tissue. HRT HydraTek® technology is a proprietary preservation system which encapsulates the biologic components and preserve the natural fluid consistency of the connective tissue. Other processing methods utilize harsh chemicals, high-heat baking or lyophilization which have been shown to denature proteins, cause collagen collapse, and/or disrupt the delicate tissue matrix and protein structure of the tissues.*

6. Sterility

HydraTek® Process utilizes a cutting edge sterility system which enables our grafts to be preserved throughout the entire process and acheive sterility without harming the integrity of our grafts. We are leading the industry by testing our products post-processing to ensure effective preservation of the biologic viability and biomechanical integrity.

HRT sets the new standard in biologic safety through its ability to offer its finished products in a terminally sterilized form by a validated precise and low-dose E-Beam derived Technological method (in compliance to ANSI/AAMI/ISO11137-2: 2013 Method VDmax15 Dose Substantiation), and are "Sterile" with a 10-6 Sterility Assurance Level (SAL).

Donor Screening Criteria	HRT	FDA
Hepatitis B Virus	•	•
Hepatitis C Virus	•	•
HIV 1/2	•	•
Malaria	•	•
Sepsis	•	•
Syphilis	•	•
Transmission Spongiform Encephalopathy (TSE)*	•	•
Vaccinia	•	•
West Nile Virus (WNV)	•	•
Ebola Virus	•	
Zika Virus	•	
Clinically significant metabolic bone disease	•	
Illicit drug use, injected drugs	•	
Leprosy (Hansen's disease)	•	
Polyarteritis nodosa	•	
Rabies	•	
Rheumatoid arthritis	•	
Sarcoidosis	•	
Systemic lupus erythematosus	•	
Systemic mycosis	•	
Tuberculosis (clinically active)	•	
Active genital herpes	•	
Acute infection / septic illness	•	
Alzheimers Disease	•	•
Ankylosing spondylitis	•	
Autoimmune hemolytic anemia	•	
Autoimmune thrombocytopenia purpura	•	
Autoimmune vasculitis	•	
Cancer (MDD)	•	
Chagas Disease	•	
Degenerative Disease of CNS	•	•
Dementia	•	•
End stage renal disease / chronic dialysis	•	
Epstein Barr Virus (clinically symptomatic mononucleosis)	•	
Gonorrhea (clinically active)	•	
Encephalitis (clinically active)	•	
Endocarditis (clinically active)	•	
Guillain-Barre syndrome (clinically active)	•	
High risk behavior	•	
Illicit drug use, non-injected drugs	•	
Meningitis (clinically active)	•	
Mixed connective tissue disease	•	
Multiple sclerosis	•	
Myasthenia gravis	•	
Neurological Diseases	•	•
Peritonitis	•	
Poliomyelitis	•	
Pyelonephritis	•	
Reactive arthritis (Reiter's syndrome)	•	
Rheumatic fever	•	
Steroid use / Treatment Chronic	•	
HTLV I/II Virus	•	
Vaginal delivery	•	
Human Papilloma Virus (HPV)	•	

*Including CJD & VCJD

Safety

HRT strives to provide the highest quality, safest amniotic and placental tissues available, and maintains an **outstanding safety record**.

Our stringent donor screening criteria surpasses AATB standards, for improved tissue safety.