rti surgical®

A HIGHER STANDARD®

Why Choose RTI Surgical® Tendons?

Sterilization is just one part of the BioCleanse® Tissue Sterilization Process

RTI employee performs laboratory testing.

RTI Surgical's primary goal is to address graft safety. Donor screening, the BioCleanse Tissue Sterilization Process and aseptic packaging provide three levels of safety for BioCleanse processed tendons. These safeguards provide the highest level of confidence that patients will receive safe, high quality tissue.

DONOR SCREENING/ELIGIBILITY

After authorization for donation is obtained, potential donors are screened for risk factors associated with infectious diseases and medical conditions that would rule out donation.

RTI donors meet U.S. FDA, AATB and applicable international and state requirements.

Screening includes, but is not limited to:

- Donor risk assessment interview
- Medical/hospital record review
- Medical examiner/coroner's report (when provided)
- Laboratory, pathology and radiology reports (when provided)

Final determination of donor eligibility is made an RTI medical director, who is a licensed physician.

Historically, fewer than four percent of donors referred make it through the screening process and are accepted as eligible donors.

The BioCleanse® Tissue Sterilization Process

HOW THE BIOCLEANSE PROCESS WORKS

- After donor screening, tissue is prepared into the desired final shapes and allografts from a single donor are placed into one of the BioCleanse processing chambers.
- In the initial phase of the process, mild detergents and sterilants fill the BioCleanse processing chamber.
- A series of mechanical oscillations consisting of alternating pressure and vacuum cycles are then applied.
- Studies have shown that the specific pressure and vacuum forces applied during the BioCleanse Process do not adversely affect the biomechanical properties of allograft tissue.[1]
- During the pressure cycle of the mechanical oscillations, detergents and sterilants completely penetrate the entire collagen matrix of the tissue.
- These sterilants are validated to inactivate or remove a panel of viruses including HIV and hepatitis, as well as bacteria, fungi and spores.
- During the vacuum cycle of the mechanical oscillations, blood, lipids and marrow are removed from the tissue and are drained away with the detergents and sterilants at the end of each phase.
- Over the course of several hours, tissue is subjected to multiple phases, each consisting of numerous pressure and vacuum oscillations.
- While some phases are performed with fresh detergents and sterilants, other intervening phases are conducted with pharmaceutical grade water, known as water for injection, to remove debris.
- The final phases of pressure and vacuum oscillations are performed with pharmaceutical grade water to remove residual detergents and sterilants, ensuring biocompatibility and complete sterilization.

BioCleanse processing operator placing tissue from a single donor in a BioCleanse processing chamber.

The BioCleanse Process is a validated, fully-automated chemical and mechanical sterilization process that achieves a 12 log reduction of bacteria, fungi and spores, and inactivates viruses for allograft tendons without augmentation of irradiation.

A key component of the BioCleanse Process is not the detergents and sterilants, but rather the mechanical pressure and vacuum oscillations that allow these chemicals to penetrate the entire collagen matrix. Without the mechanical oscillations, the detergents and sterilants might only address viruses, bacteria, fungi and spores on the surface of allograft tissue.

The BioCleanse Process uses isopropyl alcohol, hydrogen peroxide and detergents. These chemicals are mild detergents and sterilants common to the tissue banking industry. Studies have shown that the specific concentration levels and contact times of these mild detergents and sterilants used in the BioCleanse Process do not adversely affect the biomechanical properties of allograft tissue.[1,2]

The BioCleanse Process Validation

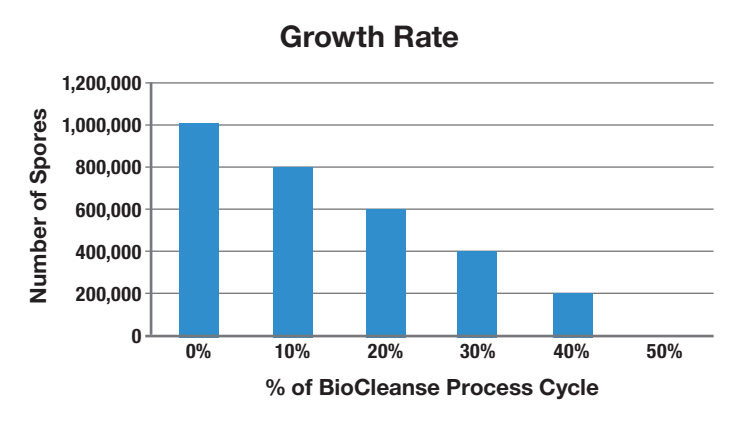
The tendon on the left has been aseptically processed. The tendon on the right has been processed through the BioCleanse Tissue Sterilization Process, which removes blood, lipids and marrow.

The BioCleanse Process was validated using most difficult case testing. According to the U.S. Centers for Disease Control and Prevention, "biological indicators are.....closest to the ideal monitors of the sterilization process because they measure the sterilization process directly by using the most resistant organisms (i.e. Bacillus spores)."[3] During the BioCleanse Process validation, a spore suspension of *Bacillus stearothermophilus* was used as the "most difficult case" biological indicator. Internal studies conducted prior to the validation concluded that *Bacillus stearothermophilus* is more resistant to the BioCleanse Process than *Clostridium sporogenes.**

Achilles tendons were tested as the "most difficult" tissue because Achilles tendons are the largest tendon grafts available by RTI and present the most difficult case configuration for germicidal penetration.

THE VALIDATION PROTOCOL

- Achilles tendons were spiked with one million Bacillus spores and run through the BioCleanse Process in one of several fractional cycles (i.e. ¼ cycle, ½ cycle, ¾ cycle).
- Spiked Achilles tendons were cultured using conditions designed to promote spore growth.
- The positive growth rate for each fractional cycle was used to determine the fraction of a cycle needed to achieve 1 log reduction.



» The results of the validation concluded the BioCleanse Process inactivates a panel of viruses per ICH Q5A and confirms a 12 log reduction of bacteria, fungi and spores to achieve a Sterility Assurance Level (SAL) 10^{-6} in one full BioCleanse Process cycle per ISO 14161.*

» RTI validated the BioCleanse Process using most difficult case testing. How did your tissue bank validate their sterilization process?

Sports operator preparing documentation for donor processing.

Aseptic Packaging is RTI's Soft Tissue Advantage

Numerous published studies suggest allograft tendons are negatively impacted by terminal sterilization.[1,2,6]

RTI, in consultation with a surgeon advisory panel, made the conscious decision not to terminally sterilize tendons. RTI decided to sterilize tendons through the BioCleanse Process and then aseptically package them to preserve the biomechanical properties and clinical performance of our tendon implants.

- BioCleanse processed tendons are packaged using aseptic technique in an ISO certified class 5 clean environment, which has more stringent criteria than an ISO certified class 6 or class 7 clean room (typical of an operating room environment).
- Microbial swab cultures are taken from each graft and the inside of each package.
- One tissue sample from each donor is used for destructive culture testing. This sample is processed alongside all the other tendons from the same donor.
- This sampling method employed by RTI is a highly effective detection system. It exaggerates potential contamination by physically contacting the sample with every piece of equipment used during the packaging episode.
- This sampling system was designed as a “most difficult case” assessment of the environment and equipment to which the final grafts are exposed in the final inspection and packaging step.
- Grafts are quarantined for 14 days per USP <71> sterility tests to await results of cultures.
- If cultures are positive, all associated tissue is rejected and destroyed.

Stringent Inspection Criteria

Literature suggests donor age has no effect on biomechanical properties or clinical performance of allograft tendons.[4] However, some surgeons prefer implants from a younger patient population due to the occasional tendinopathy seen in the older patient population. Because RTI uses a stringent inspection process post-sterilization during aseptic packaging, bead-like inconsistencies that are indicative of tendinopathy and fiber separation are identified and rejected.

- During the packaging step, tissue is evaluated with a magnification light to assess graft quality.
  - » Because blood and lipids are removed from tissue inside the BioCleanse processing chamber, it is easier for processors to identify issues such as fiber separation and tendinopathy.
  - » Only tissues that meet RTI's strict inspection criteria are released for implantation.
- A study conducted with 550 BioCleanse processed tendons by Swank et al.[4] concluded that donor age has only a minor, if any, influence on the structural and mechanical properties of allograft posterior tibialis tendons.
  - » The conclusions of this study apply to BioCleanse processed tendons because of the rigorous inspection during aseptic packaging to assess graft quality.
  - » Other tissue banks may not be able to assess graft quality because their grafts are terminally sterilized in their final packaging.
    - › We are not certain the conclusions of this study can be applied to these grafts.

» If terminal sterilization leaves residual blood, lipids, and marrow in the tendons, how can your tissue bank screen for issues related to tissue quality?

Sports packaging operator performing final trimming and inspection of tendons.

Why doesn’t RTI irradiate BioCleanse processed tendons?

It's simple. We don't have to.

Advancing Beyond Aseptic Processing

Some tissue banks only aseptically process tissue. Aseptic processing does not fully address existing organisms or completely remove cellular elements from donor tissue.

Despite HIV, Hepatitis C and Clostridium infections associated with unsterilized allograft tissue, sterilization is not required, and not all tissue banks sterilize allograft tissue.[5]

While risk of disease transmission remains for all donated human tissue, sterilization adds a measure of added safety above screening and testing alone.

At RTI, allograft tendons are sterilized through the BioCleanse Tissue Sterilization Process.

RTI operator performing tissue processing activities.

Why We Don't Irradiate

The BioCleanse Process is a stand-alone sterilization process that does not require augmentation with irradiation or peracetic acid. Other tissue banks commonly augment their process to achieve SAL 10^{-6}.

If the disinfection and rinse steps used by other tissue banks are effective, why is augmentation with irradiation or peracetic acid necessary?

Radiation validation for allograft tissue is not designed to address viruses. AAMI TIR37:2013, Sterilization of health care products – Radiation,[6] states "This TIR does not address validation requirements for eliminating and/or inactivating viruses..."

In addition, Nguyen et al (2011) states "gamma irradiation at low, or standard doses is directed towards achieving a SAL of 10^{-6} with respect to the bacterial bioburden rather than the viral bioburden."[7]

Therefore, tissue banks that only irradiate allograft tissue may be addressing viral contamination only through serology testing, which may give false results.

Per the International Atomic Energy Agency's (IAEA's) Code of Practice for Radiation Sterilization of Tissue Allografts,[8] "The approach as described here is not applicable if viral contamination is identified. Thus, it is emphasized that the human donors of the tissues must be medically and serologically screened...This adaptation of established ISO methods can thus only be applied to sterilization of tissue allografts if the radiation sterilization described here is the terminal stage of a careful, detailed, documented sequence of procedures involving: donor selection; tissue retrieval; tissue banking general procedures; specific processing procedures; labeling; and distribution."

Without a validated viral inactivation process, allograft tissue that is only irradiated to achieve SAL 10^{-6} and labeled "STERILE R" may harbor viruses such as HIV and hepatitis since viruses are highly resistant to irradiation.

RTI's BioCleanse Process addresses both bacteria and viruses. What does your tissue bank's process address?

At RTI, high levels of quality are not just set, they're constantly maintained.

Ensuring Quality Through Manufacturing

RTI goes above and beyond the BioCleanse Process validation.

- Data Report Review
  - » A data report generated for each BioCleanse Process cycle contains the processing specifics that occurred inside the BioCleanse processing chamber during the sterilization process:
    - › Detergent and sterilant concentration
    - › Pharmaceutical grade water, detergent and sterilant contact time
    - › Temperature
    - › Mechanical oscillations
    - › Chemical and air filter test results
  - » The data report is reviewed and verified by a trained BioCleanse processing operator.
  - » A second verification of the data report is performed by a trained auditor.
- Steam-in-Place (SIP) Sterilization Cycle
  - » After the tissues from a single donor are removed from the BioCleanse processing chamber, a validated steam-in-place (SIP) sterilization cycle is performed to sterilize the chamber in between BioCleanse processing cycles.
  - » The BioCleanse processing software program will not allow a BioCleanse Tissue Sterilization cycle to be initiated in a chamber until a SIP sterilization cycle has been completed.
- Filter Integrity Tests
  - » Chemical and air filters, which are critical components of the BioCleanse Process, are tested for integrity after each BioCleanse Process cycle.
  - » The filters ensure the chemicals and air entering the BioCleanse processing chamber are of the highest quality.

Monitoring the processing environment

Environmental monitoring is an essential component of manufacturing. Consistent and effective monitoring of the processing environment is performed during tissue processing activities to ensure the utmost quality and safety of our implants.

- All post-BioCleanse processed tissue is packaged in an ISO certified class 5 clean environment.
- Routine germicidal and sporicidal disinfection of the clean room environment is performed to ensure prevention of contamination or cross contamination between donor processing episodes.
- Samples that are taken in the clean room environment include, but are not limited to:
  - » Bacterial monitoring of surfaces, personnel, and equipment used in tissue processing
  - » Bioburden and endotoxin monitoring of pharmaceutical grade water used in tissue processing
  - » Viable and non-viable air sampling to monitor air quality
- Routine environmental monitoring of the clean rooms is performed in order to show the effectiveness of the cleaning and disinfection processes.

BioCleanse Process operator monitoring BioCleanse processing software during donor processing.

Clinically Proven Safety & Performance

Safety

Our track record speaks for itself: More than five million biologic implants have been processed through RTI's proprietary sterilization processes with zero confirmed incidence of implant associated infection.

Retention of Biomechanics

The *American Journal of Sports Medicine* published an article that investigated the effects of the BioCleanse Process on biomechanical properties of soft tissue allografts.[1]

- The study concludes that data for "time zero" physiological stiffness and failure loads indicate that the BioCleanse Process does not adversely affect the biomechanical properties of the allograft material.

Clinical Performance

Knee Surgery Sports Traumatology Arthroscopy published a prospective clinical study[2] with controls for surgical technique that compared the clinical outcomes of BioCleanse processed BTB allografts with aseptically-processed BTB allografts for ACL reconstruction.

- The results indicate that BioCleanse processed tendons compared favorably with aseptically-processed tendons.

"The BioCleanse Process may provide surgeons with allografts clinically similar to aseptically processed allograft tissue with the benefit of addressing donor-to-recipient disease."

» Does your tissue bank rely on biomechanical studies alone or retrospective clinical studies that don't account for surgical technique and rehabilitation protocol?

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rti surgical®

Not all companies can match the level of allograft tendon safety offered by RTI. When choosing a tendon implant, be sure to ask for RTI Surgical.

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Distributed by: RTI Surgical, Inc.
11621 Research Circle
Alachua, FL 32615 USA
t: 877.343.6832

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