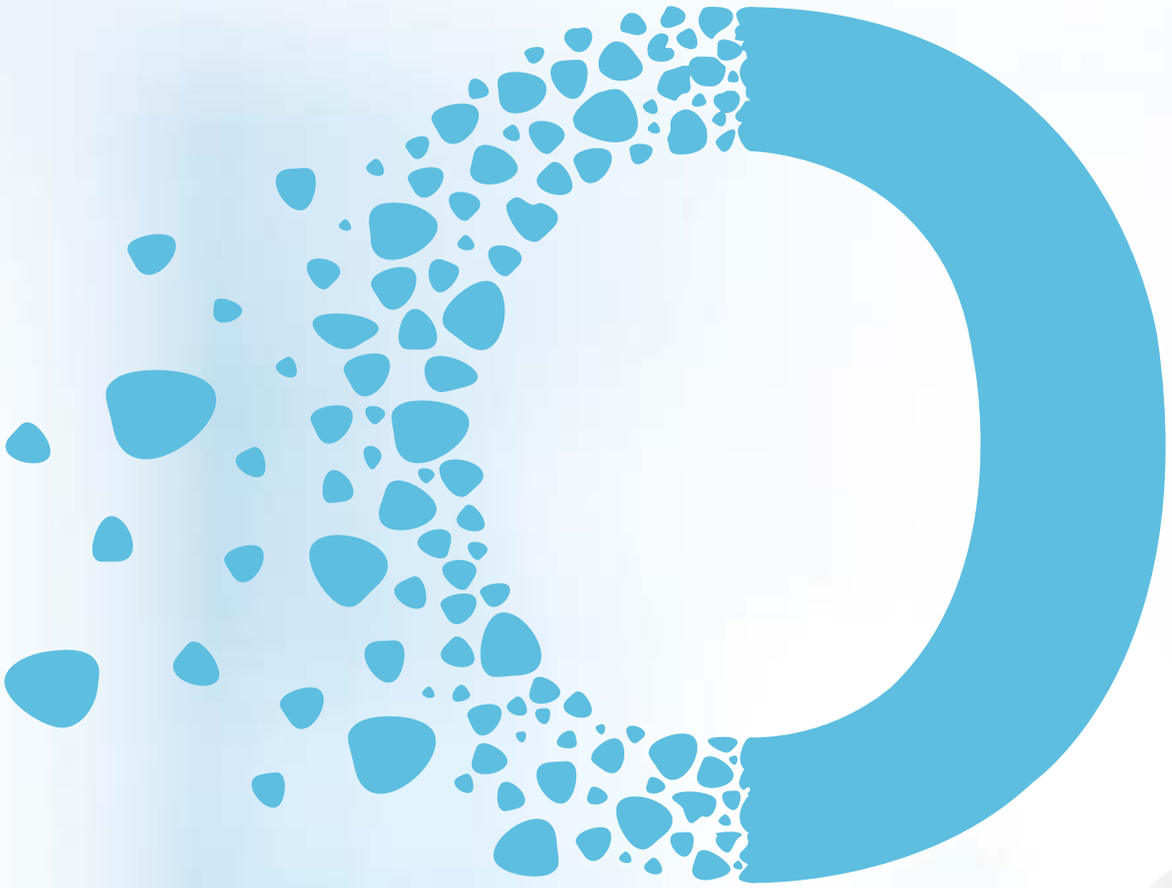
ORBONE®
CELL AND TISSUE BANK



Orbone®
Cell and Tissue Bank

Human-Derived
Allografts

cleaner grafts, safer outcomes

ORBONE®

eCOO® Technology

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explore **Orbone®**

Orbone® Tissue Bank

Orbone® tissue bank is a GMP licensed facility that processes a wide range of human-derived tissues with a focus on collecting, storing and processing bone, soft tissues and tissue components. Using licensed and proprietary eCOO® supercritical carbon dioxide technology, it provides high quality, safe, clean and innovative products to the Allograft industry.

Orbone® Tissue Bank offers a variety of surgical Allograft options from traditional bones, soft tissues to special products for transfer in GMP and ISO certificated B class laboratoires addressing Tissue Engineering expertises, with experienced employees and with using Superior production quality of eCOO® technology and unique features for cleaning tissues, sterilizating and for studies directed inoculations.

Orbone® Tissue Bank serves the medical community all over the world and is a center of excellence in the development and production of human-derived tissues.

eCOO® Technology is a proprietary platform that produces high quality human-sourced tissues, patented by Dutch Tissue Bank Leader Biomedical Europe Holding BV EMCM, and brought to Turkey by Orbone® Tissue Bank through technology transfer. Orbone® Tissue Bank Allograft continues its R&D studies with Netherlands Tissue Bank Leader Biomedical.

Orbone® Tissue Bank, which accompanies the business development platforms with the high quality licensed Tissue Banks in the world, continues to represent Turkey successfully in this sector.

Cleaner Grafts, **Safer Outcomes**

Quality and Safety

eCOO® Technology is successfully audited by the Tissue Bank UFSDA, ANVISA and other European authorities to provide products to global markets, to which it transfers technology to ensure quality compliance. The Netherlands Tissue Bank conducts these inspections one-to-one and completely at the Orbone® Tissue Bank facility.

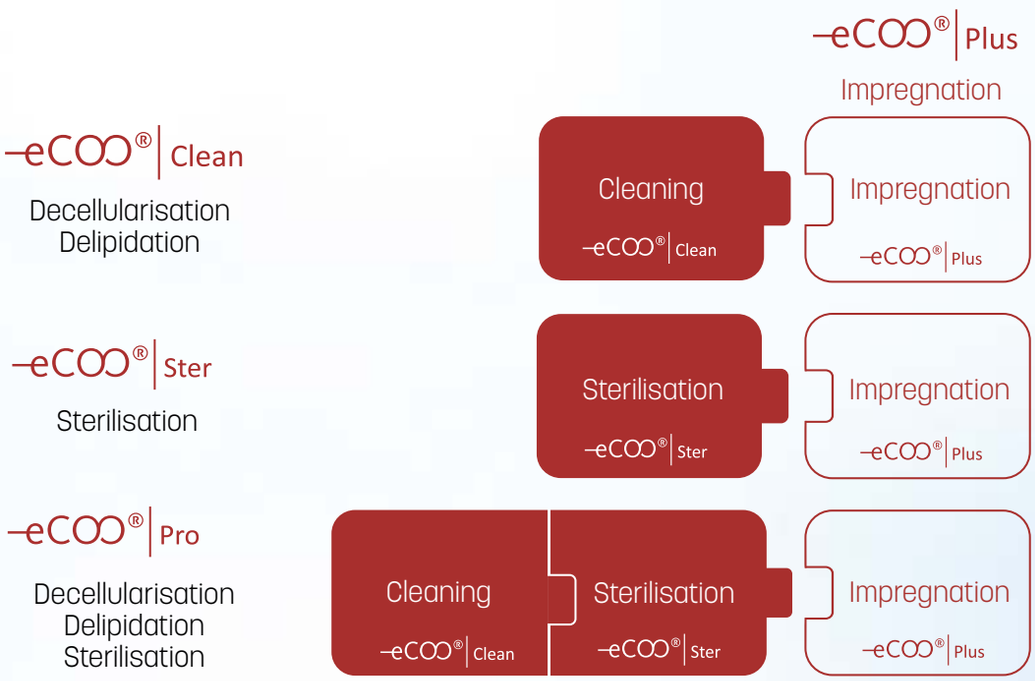
All tissue groups produced by Orbone® Tissue Bank are released after they pass the quality and safety stages and are audited by Dutch Tissue Bank Leader Biomedical.

Orbone® Tissue Bank applies European quality and safety standarts in all the tissues it collect. Tissues are sent to contracted serological testing laboratories for the possibility of contagious diseases.

These tests are performed and published by a certified laboratory. Human tissues processed in the Orbone Tissue Bank are obtained by donors, which include the results of 12 negative tests covering, among others, Hepatitis B, Hepatitis C, Syphilis and HIV, and fulfill all the requirements of the European Directives on "Quality and Safety of Human Tissues and Cells (2004/23EC, 2006/86EC and 2006/17EC)".

Orbone® Technology Platform

eCoo® technology, a production technology transferred by Orbone® Tissue Bank, is licensed by the Dutch Ministry of Health in accordance with European Directives (2004/23EC, 2006/86EC and 2006/17EC) and is a member of the European Tissue Union. Human cells and tissues processed in Orbone® Tissue Bank, licensed by the Turkish Ministry of Health for Cell and Tissue Bank, are produced by applying the quality and safety requirements of European directives.



Making a Difference

Common methods used to clean, decellularize and sterilize tissue are a combination of chemical solvents, heat and oxidizing agents. In most processes, the use of solvents such as chloroform or acetone is necessary to clean bone or decellularize tissue. The presence of fat, dermis, or cells prevents the tissue from getting wet.

Chemicals cannot penetrate deep enough into bone and soft tissue. As a result, the risk of toxic residues and immunological reactions, as well as processing efficiency, is reduced.

Depending on the structure of the raw material, Orbon ® Tissue Bank's eCOO® Technology is ideal for cleaning, decellularisation, virus inactivation, sterilization and inoculation while preserving the specific properties of the original tissues.

This unique process overcomes the shortcomings of tissues produced by conventional techniques, increasing sterilization, safety and regenerative properties, keeping the patient and patient safety as the highest priority. It returns the patient to their normal life in a very short time.

eCOO®
Technology Approach

One of the most distinctive features of Orbone® eCOO® Technology is that it can penetrate solid materials with its gas structure and dissolve materials by acting like a liquid. By controlling or regulating the pressure and temperature, the density or solvent strength of scCO2 can be varied to simulate a wide variety of organic solvents. This dissolving power is applied to obtain, extract and sterilize a wide variety of sensitive materials. The low temperature of the process and the stability of CO2 also allow compounds to be removed without damaging and denaturation of allograft tissues.

Due to these properties, eCOO® Technology can greatly reduce the presence of microorganisms, thereby thoroughly cleansing the tissues. It also meets the sterility assurance level of 10-6 (SAL6) for all types of microorganisms.

• Viral Inactivation and Safety:

A viral inactivation study conducted by Institute Pasteur Texcell in Paris in 1995 demonstrated the effectiveness of this process over viral inactivation. The results obtained are superior to the safety level recommended by the European recommendations (6 log reduction versus 14 log reduction). The results have been confirmed by a study by Sanquin Pharmautical Services on behalf of eCOO technology.

• Sterilization:

When using eCOO® Technology to introduce and extract bactericidal sterilizers like peri-acetate acid into tissue, the process renders tissue sterile by inactivating a wide range of bacteria, including Bacillus.

• Biogenesis and Osseointegration:

Allografts treated with Orbone® eCOO® Technology lead to a much faster osseointegration compared to unprocessed allografts. Treatments based on Orbone eCOO Technology do not alter the biomechanical properties of the tissue.

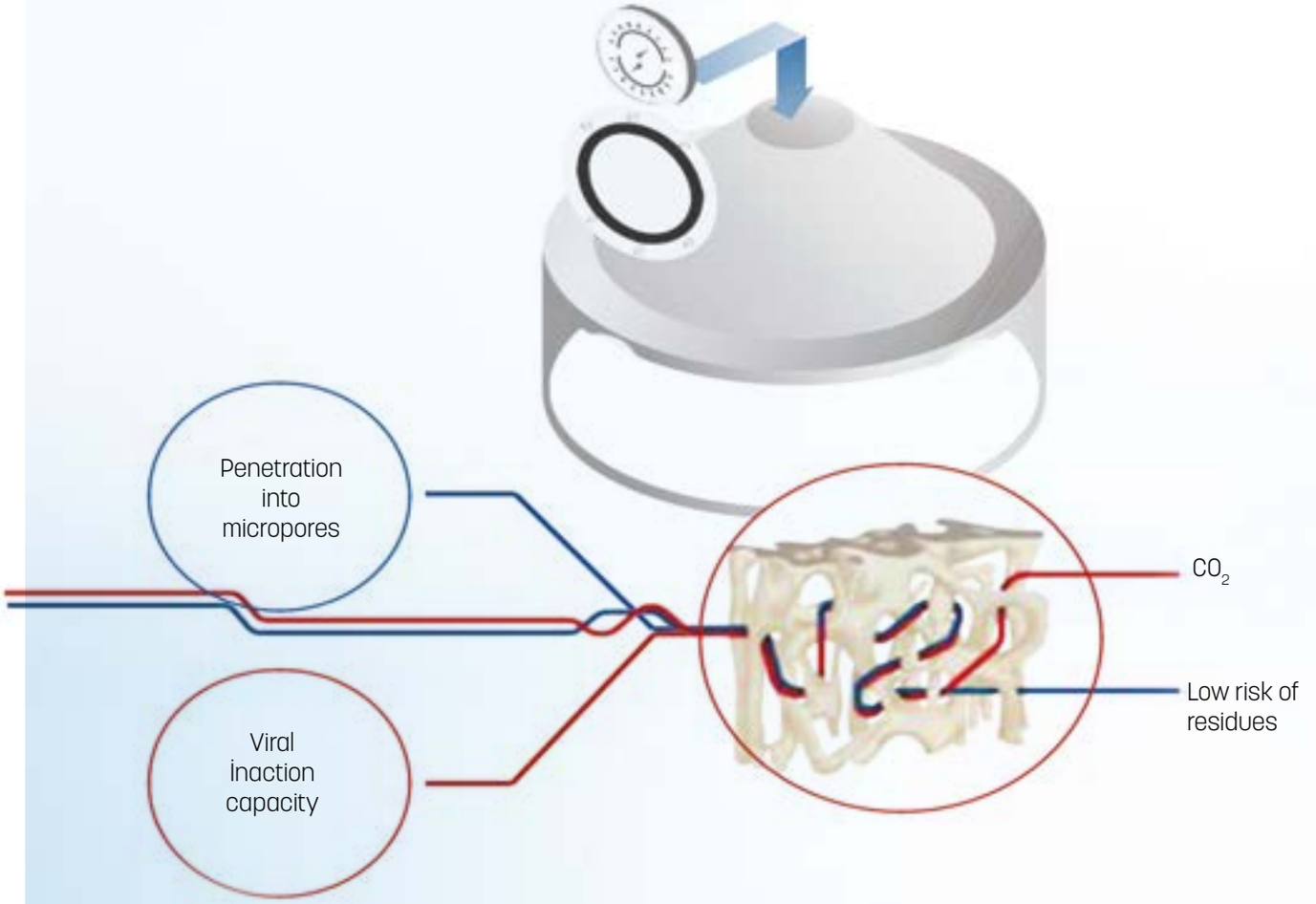
• Clinical Evidences:

Processed Orbone® eCOO® grafts have proven to have superior biochemical composition, biocompatibility, tolerance and biofunctional properties compared to grafts processed by conventional methods.

- Clean and sterile state-of-the-art tissue products without compromising on structural integrity
- Excellent biocompatibility and advanced regenerative properties
- It can be adapted to meet tissue specific demands.
- It does not leave hazardous material residues.

Orbone® eCOO®
Supercritical Extraction

The Orbone® Tissue Bank Technology platform encompasses several technology handles for cleaning, sterilising, and impregnating biological and synthetic grafts. These processes are generic processing protocols and production methodologies that can be combined, opti-mized, and then applied to a variety of tissues.



eCOO® Supercritical Extraction

scCO2 extraction is the ideal first step of any bone processing cascade because microporosity of bone tissue becomes much more accessible, which may enhance osteoconduction once implanted.

Applying of **eCOO®** Technology

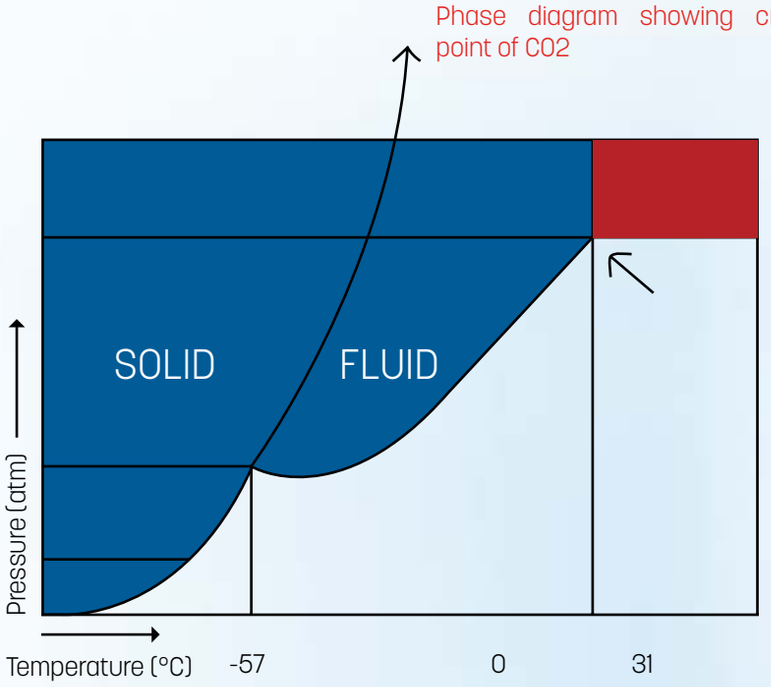
Various applications have been developed to date to devitalize bone tissues. These usually contain solvents for oxidative treatment of oils. In traditional methods, solvent (chloroform or acetone) is the main ingredient to dissolve the fat in the marrow cavity containing adiposity fat cells. The presence of large amounts of lipids increases the moisturizing property of the tissues by inhibiting aqueous oxidants.

Diffusion in bone tissue is limited, the volume of bone fragments can be treated less effectively. In addition, the use of degreasing solvents can cause unwanted toxic residues.

In addition to viral inactivation, Orbone® ecOO® Technology also perfectly preserves the organo-mineral structure of the bone tissue, which consists of carburized apatite in the bone, by removing fats, cell debris and marrow proteins.

Regardless of the volume of the femoral head, after it turns into Supercritical state, it shows solvent character, and exclusive power diffusion takes place by guaranteeing unification. Being a natural substance, scCO2 leaves no toxic residue.

CO2 enters a supercritical state when both the temperature and pressure simultaneously exceed the critical point of 31°C and 73 atm, respectively. In this state CO2 has both gas- and liquid-like properties, providing the ideal conditions for cleaning a wide variety of tissues from human origins. scCO2 can penetrate tissue like a gas and dissolve materials like a liquid.



By regulating pressure and temperature, the solvent strength can be adjusted to simulate a wide range of organic solvents.

This dissolving power can be applied to purify and sterilise different types of tissues.

- **Protection of structural and mechanical features**
- **Viral inactivation**
- **Modular and adaptable**
- **Eco-friendly**

eCOO®
Technology Advantage

Conventional tissue processing techniques rely heavily on chemical and biological agents. These agents affect the inherent structural and mechanical properties of the grafts.

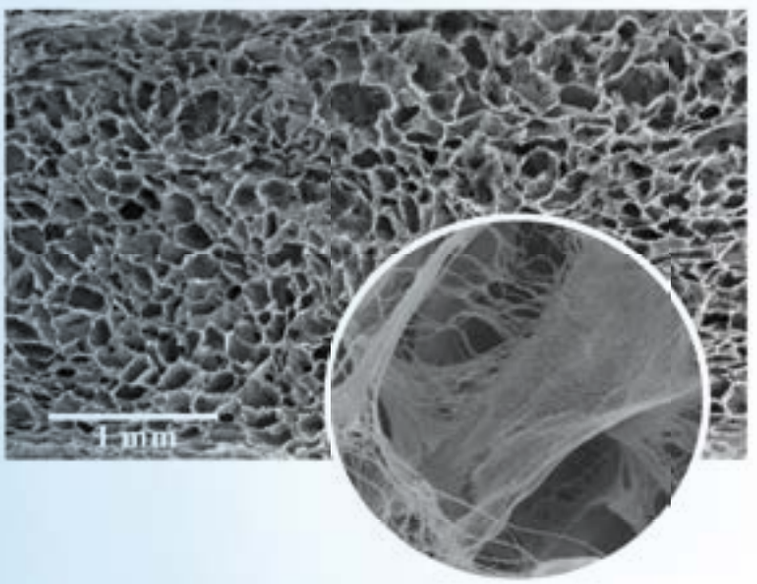
Orbone ® eCOO® Technology provides a mild and effcient platform to clean and sterilise tissue with limited use of chemicals. Research has shown that the use of scCO2 minimally affects the structural integrity of tissue grafts when compared to conventional processing techniques. scCO2 treatment also removes medullary tissues responsible for adverse immune response. In addition to the scCO2 treatment step, the eCOO® Clean process includes a viral inactivation step.

The combination of these two techniques has been shown to achieve a 12-fold reduction in the microbial load in the processed grafts . The successful removal of cellular and medullary materials, and inactivation of viruses is the most crucial step in ensuring cleaner grafts for better patient outcomes. Once cleaned of the cell and lipid debris, the non-sterile acellular tissues can also be sterilised using the eCOO® Ster process of the technology platform. The resulting sterile tissue can either be freeze-dried or fresh frozen. Alternatively, the non-sterile acellular tissue material can be first freeze-dried before terminal sterilisation with irradiation technologies.

eCOO® | Technology

Bone cleaned with scCO2

SEM imagery confirms that scCO2 minimally impacts the extracellular matrix.



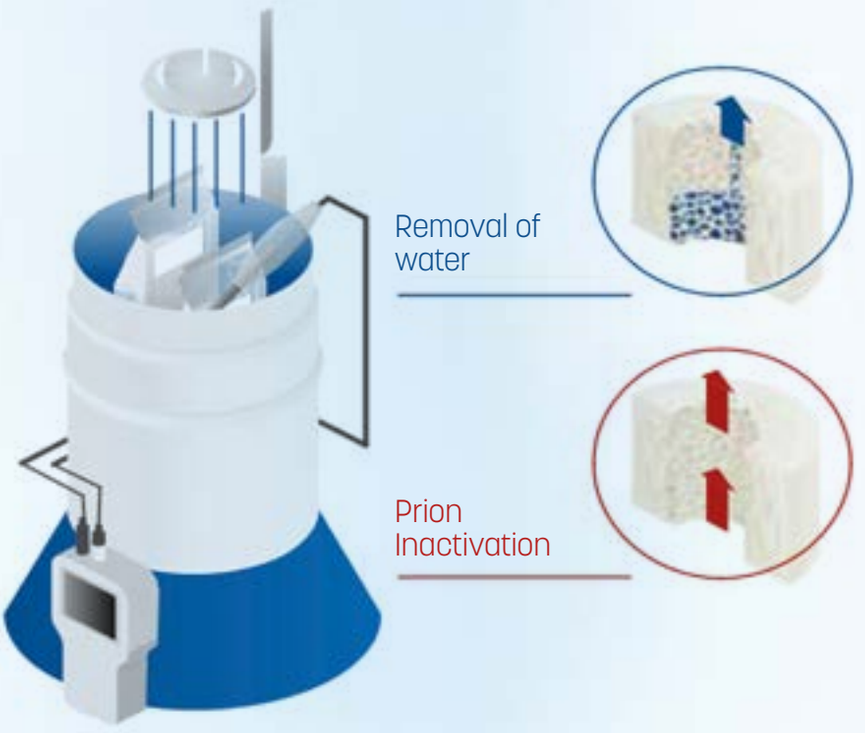
Orbone® Tissue Bank eCOO® Technology Platform encompasses cutting-edge handles for cleaning, sterilizing and grafting biological grafts using a breakthrough solution based on supercritical carbon dioxide. The scCO2 extraction process is highly effective at inactivating viruses and provides superior inactivation compared to tissues obtained by conventional methods.

–eCOO® Pro		–eCOO® Plus
–eCOO® Clean	–eCOO® Ster	
ADVANTAGES	**ADVANTAGES**	**ADVANTAGES**
•Maintains natural crosslinking of extracellular matrix (ECM) •Promotes cell attachment • Fewer time-consuming rinsing steps • Deep microstructural penetration • Low immunogenic risk	• ECM not damaged by radiation • Milder operating temperatures • Quicker runtime	• Greater control over release of compound • Deep microstructural penetration

Studies have shown that the use of eCOO® technology minimally affects the structural integrity of bone and tissue grafts compared to conventional processing techniques. eCOO® technology also eliminates the medullary tissues responsible for adverse immune responses.

Decontamination and Lyophilisation

By using scCO2 as the cleaning solvent, excessive incubation in detergents becomes unnecessary, thus reducing the risk of residuals of processing and extracellular matrix denaturation. scCO2 treatment, along with prion inactivation rinses, also contributes to the overall viral load reduction.



eCOO® | Clean

Clinical Case Studies

Treatment of infected nonunion with eCOO® Clean cancellous chips

The patient had three surgeries after he had a car accident, but these were unsuccessful and he had femoral nonunion.

Before surgery x-ray

After surgery x-ray

After surgery x-ray

Diagnosis and Treatment	Results	Reference
The surgeon inserted an intramedullary nail into the femur with four fixation screws and treated the infection and fracture with antibiotic-grafted cancellous chips that were cleared with eCOO® Technology (eCOO® Clean).	The patient was able to walk again without crutches within two months after surgery. A year later, he's dying to have it to save two screws. Afterwards, the patient did not experience any movement disorder. He was also able to actively participate in running, cycling and sports.	Winkler H. One Stage Treatment of Infected Non-Union using Osteomycin I. Courtesy of the Ostetitis Center Privatklinik Döbling

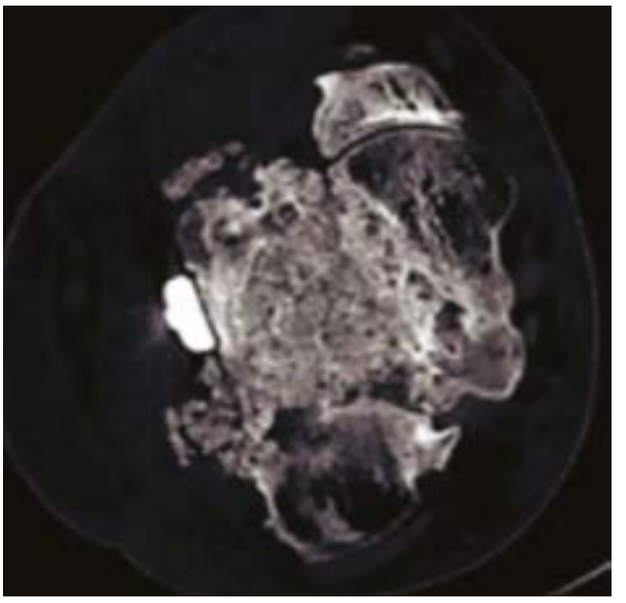
eCOO® | Clean

Clinical Case Studies

Treatment of chronic osteomyelitis after heel bone fracture with eCOO® Clean cancellous chips

Developed both malleolus and chronic osteomyelitis after multiple surgeries after heel bone fracture

Before surgery x-ray



After surgery x-ray

Diagnosis and Treatment	Results	Reference
After basic debridement, the fracture was stabilized with locking plates and screws. The surgeon inserted antibiotic-infused cancellous chips cleaned with eCOO® Technology (eCOO® Clean) to provide an antibiotic-laden scaffold.	The patient was given bed rest for two weeks and partial weight for three months. After one year, the graft was completely resorbed and no recurrent osteomyelitis was observed.	Winkler H. One Stage Treatment of Infected Non-Union using Osteomycin II. Courtesy of the Ostetitis Center Privatklinik Döbling

Excellent Bone Regeneration

Orbone® Tissue Bank has the knowledge of collecting, storing and processing all human tissue groups and achieves international success with the high technology it works with.

From trauma and spine surgeries to hip and knee arthroplasty, there is a great need for biocompatible grafts with osteoconductive properties. While autografts have historically been the gold standard, their use is associated with availability, safety concerns, and higher morbidity.

Orbone® Tissue Bank products reduce the patient's hospital stay and do not require a second surgery, which increases the time spent in the operating room. Our Tissue Bank produces high quality human-sourced tissues.

What are qualifications of an ideal bone graft?	What are features of an ideal bone graft?	How do Orbone Tissue Bank bone grafts achieve these properties?
• Safe: It is designed and manufactured in accordance with safety standards. • Biocompatative: Ensuring graft acceptance • Biodegradable: Gradual biodegradation and bioresorption	• Osteoconductive: Stimulating bone growth • Osteogenic: Contributing to new bone growth • Osteoinductive: Enabling cell differentiation	• Macroporous: Stimulate cell colonization and osteoconduction • Microporous: To allow biological fluids to pass through the structure • Bioactive: To ensure the interaction of the tissue graft with the patient's body

Orbone® Allograft Products

eCOO® | Technology

Human bone has the right mineral composition to break down easily, and the natural micro and macroporosity of allografts is highly osteoconductive. For this reason, allografts are the preferred option for many surgeons.

However, traditional tissue processing techniques rely heavily on chemical and biological agents. These agents affect the natural structural and mechanical properties of grafts.

All Orbone® allografts use proprietary eCOO® Technology, a lightweight and efficient platform for cleaning, sterilizing and grafting bone and tissue of human and animal origin. Unlike traditional methods, it offers tissues as quality as autogenous tissues the medicine society.

Orbone® Tissue Bank offers its wide portfolio in Orthopedics and Traumatology, Brain Surgery, Maxillofacial and Dental Surgery as a finished product to either tissue banks or hospitals. It provides special tissue needs according to difficult surgical areas.

Orbone®

Void Fillers

The cancellous bone processed with eCOO® technology creates excellent osteoconductive capacity and a stable complex with the patient's adjacent bone. It finds solutions to various bone defects in different shapes and forms. Special blocks and extra chips are available for dental applications. Cavity fillings can be used for a wide variety of orthopedic and dental applications.

- Cancellous Chips Group
- Cortical Chips Group
- Cancellous/Cortical Chips
- Crushed
- Cube
- Block
- Wedge

Structural Grafts

Bone tissue has the most use in orthopedic, plastic, maxillofacial and neurosurgery. Pre-cut bone allografts are used to fix trauma, tumor removal, and osteoporosis or bone deformities. These bone allografts are cleaned and sterilized with eCOO® Technology. Various sizes of structural grafts are available. Structural grafts: used in the treatment of lumbar fusion, cervical spinal fusion and fracture.

- Iliac crest wedge
- Femur Shafts
- Tibial Shafts
- Cervical Separators
- Femoral Cortical Supports
- Femur Grafts (left/right)
- Tibia Grafts (left/right)
- Humerus Grefts (left/right)

Femoral Heads

Femoral heads are obtained from donors who have undergone hip replacement surgery. In order to meet the needs of the patient, the femoral heads are completely cleaned and sterilized after the bone has been optimally shaped surgically. Femoral heads can be used in hip replacement surgery and general orthopedic reconstruction.

- Full Femoral Head
- Half Femoral Head

Demineralized Bone Matrix

Demineralized Bone Matrix is formed by demineralization of cortical bones processed with eCOO Technology by encapsulating growth factors such as bone morphogenetic proteins. These growth factors appear to significantly induce osteoinduction, which improves the bone regeneration process. These growth factors appear to significantly induce osteoinduction, which improves the bone regeneration process. They are ready-to-use forms. It is used in trauma, periodontology and spinal surgery.

- DBM Powder
- DBM Gel
- DBM Putty
- DBM Crunch
- DBM Block
- DBM Cube

Soft Tissues

Tendon allografts play an important role in tendon and ligament reconstruction, especially when there is a shortage of suitable autologous tissue. All tendon tissues are frequently used in sports-related injuries.

- Anterior Tibialis
- Posterior Tibialis
- Achilles Tendon
- Preshaped Achilles
- Semitendinosus
- Gracilis
- Peroneus Longus
- Semitendinosus
- Patellar Tendon/Hemi BTB

Orbone®
Dental Allografts

After tooth extraction, bone resorption begins in the Maxilla and Mandible. In order for dental implants, which have been used for many years in the treatment of partially and totally edentulous individuals, to be successful, the hard tissues must be in ideal volume. In cases with advanced jawbone atrophy, guided bone regeneration and augmentation procedures with allografts may be required before implant treatment.

Allografts are indispensable for the reconstruction of oral maxillofacial defects.

For guided bone regeneration with allografts;

Orbone® 100% Cancellous Chips Group

Orbone® 100% Cortical Chips Group

Orbone® 100% Demineralized Bone Matrix Group

And combined in certain proportions according to the desired bone structure;

The use of our Orbone® Cortico Cancellous Chips Group grafts is indispensable.

It is made in all sizes and dimensions.

Orbone allograft indication in implant surgery

Orbone allograft is used to increase bone volume/quality without implant placement due to the existing insufficient alveolar contour, by providing the mechanisms of osteoconduction, osteoinduction and osteogenesis, respectively.

Orbone® allograft indication in open sinus lift cases

It is accepted that dental implant placement without sinus floor elevation is contraindicated in cases of atrophic edentulous maxilla with wide sinuses. Allograft application for augmentation of the maxillary sinus base is a common method in oral and maxillofacial surgery.

Orbone® allograft indication in closed sinus lift cases

After the extraction of the maxillary posterior teeth, the pneumatization of the maxillary sinus and alveolar bone resorption results in horizontal and vertical bone resorption, the sinus floor is broken with osteotomes and the sinus is elevated, and the Orbone allograft is added to the resulting cavity.

Orbone® allograft indication after tooth extraction

Bone resorption that occurs after tooth extraction causes a ridge structure that is not suitable for implant placement. Orbone allograft provides alveoal crest volume by providing osteoconduction, osteoinduction and osteogenesis mechanisms, respectively.

Orbone allograft has a very high success rate in the use of oral maxillofacial surgical operation defects.

Plastic Surgery with Orbone® Allografts

By using Orbone block, Cube and other bone grafts, you can safely meet aesthetic needs with remodeling in oral maxifacial surgery.

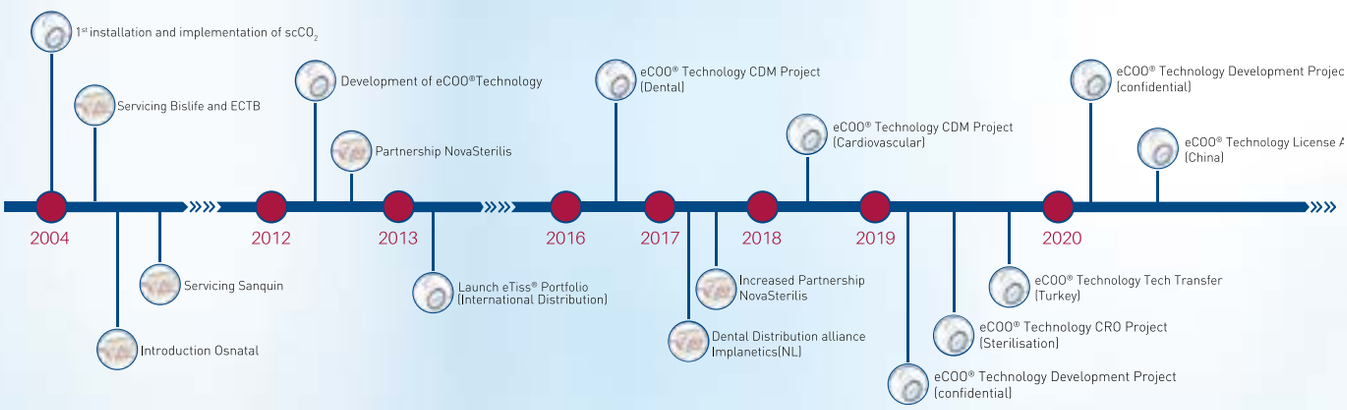
Due to rapid tissue fusion in operations performed with Orbone allografts, the comfort you will experience during the healing process provides an advantage to both our physicians and our patients.

Why Orbone® Tissue Bank?

Traditional cleaning and sterilization methods are mostly used in hard bone treatments that affect the mechanical or structural properties of tissue grafts. Many studies show that these methods have detrimental effects on protein structure, adsorption rate, cell adhesion and tensile strength.

Conversely, cleaning of tissues with the Orbone Tissue Bank's eCOO® Clean Technology and eCOO Ster sterilization minimally affects the structural integrity of the tissue. So far the sterile level and virus inactivation SAL6 have been reached. Biomolecular properties (e.g. protein degradation and cell adherence) and mechanical properties (i.e. tensile strength and extreme torque) are retained to support the weight-bearing and/or sensitive application stress of tissue grafts required for tissue-dependent processing/sterilization using eCOO® Technology. In addition, the system has been adapted to meet the specific requirements of the tissue and to leave a minimal carbon footprint.

In the case of product development, experience of decellularization techniques, virus inactivation procedures using eCOO technology, and an additional USP add to the product.



// A world brand in

allograft

is in Turkey //

References

E-catalogue

orbone.com.tr

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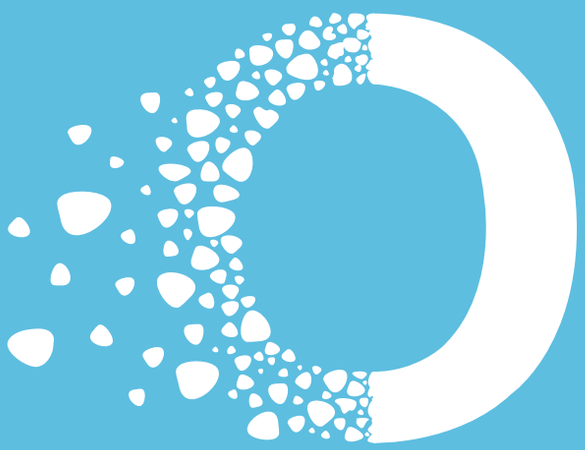

High quality
human allograft

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