

endoret[®] (prgf[®])

Endogenous Regenerative Technology

SKIN CARE



www.endoret.com



LEADER IN REGENERATIVE MEDICINE

BTI Biotechnology Institute is a Spanish biomedicine company focused on the development of translational research projects (R&D+i).

BTI is a world-level scientific leader in regenerative medicine using ENDORET in different fields of medicine.

**MORE THAN 5000 M² DEVOTED TO TRAINING,
CLINICAL PRACTICE AND RESEARCH**

TRAINING

**WE TRAIN IN ORDER TO OPTIMISE
THE CLINICAL RESULTS**

Specific training aimed at different medical specialisations.

More than 40 scientific collaboration agreements with universities and research institutes all over the world.

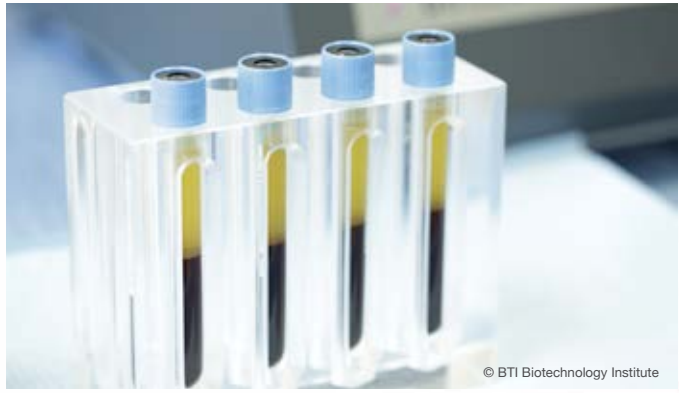
More than **1200 students** per year of all nationalities.



TRANSLATIONAL RESEARCH: KNOWLEDGE ACQUIRED IN THE LABORATORY APPLIED TO CLINICAL PRACTICE



**CLINICAL
PRACTICE**



.....

Collaboration with experts from different countries
in different fields of medicine for the development of
clinically effective protocols.



RESEARCH

MORE THAN 180 INDEXED
SCIENTIFIC PUBLICATIONS BACK THE
EFFECTIVENESS AND BIOSAFETY OF
ENDORET®

20% of the workforce dedicated to research.

.....

More than **15 years of research** in tissue regeneration.

.....

Prince Felipe Award for Technological Innovation.



ENDORET® TECHNOLOGY

1 WHAT IS IT?

ENDORET® IS A BIOMEDICAL TECHNOLOGY AIMED AT STIMULATING TISSUE REGENERATION BY APPLYING AUTOLOGOUS PROTEINS.

© BTI Biotechnology Institute

Hundreds of endogenous proteins affect the tissue repair processes, including angiogenesis, chemotaxis and cell proliferation. No exogenous agent can effectively govern all these processes. ⁽¹⁾

Endoret technology provides the necessary means for the isolation and concentration of the blood proteins involved in tissue regeneration, as well as its suitable application at the injury site. ⁽²⁾

(1) Anitua E, Sánchez M, Orive G, Andia I. Delivering growth factors for therapeutics. *Trends Pharmacol Sci.* 2008;29:37-41.

(2) Anitua E. Plasma rich in growth factors: preliminary results of use in the preparation of future sites for implants. *Int J Oral Maxillofac Implants.* 1999;14:529-535.

(3) Anitua E, Sánchez M, Zalduendo MM, de la Fuente M, Prado R, Orive G, Andia I. Fibroblastic response to treatment with different preparations rich in growth factors. *Cell Prolif.* 2009;42:162-170.

(4) Anitua E, Sánchez M, Nurden AT, Zalduendo M, de la Fuente M, Orive G, Azofra J, Andia I. Autologous fibrin matrices: a potential source of biological mediators that modulate tendon cell activities. *J Biomed Mater Res A.* 2006;77:285-293.

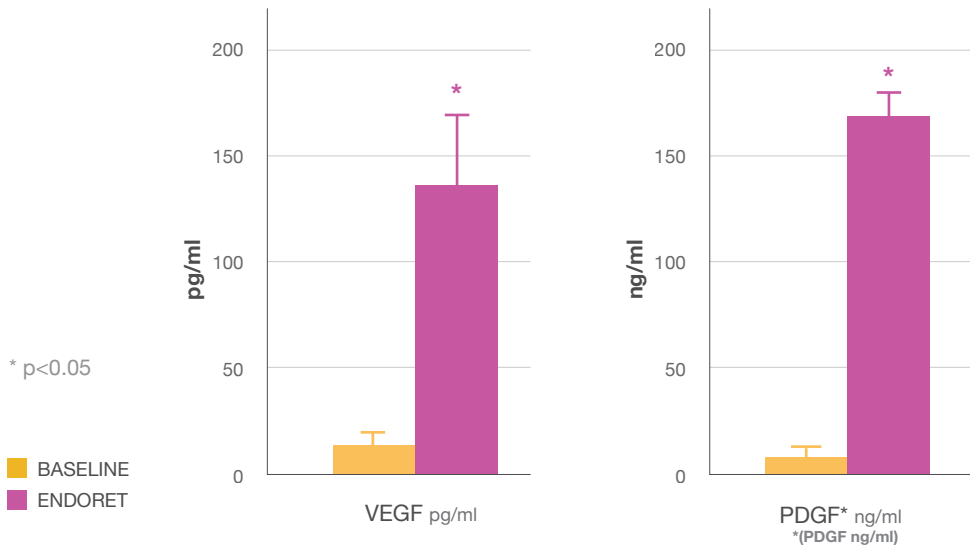
(5) Anitua E, Zalduendo MM, Alkhraisat MH, Orive G. Release kinetics of platelet-derived and plasma-derived growth factors from autologous plasma rich in growth factors. *Ann Anat.* 2013.

2 ACTIVE PRINCIPLE

A. GROWTH FACTORS

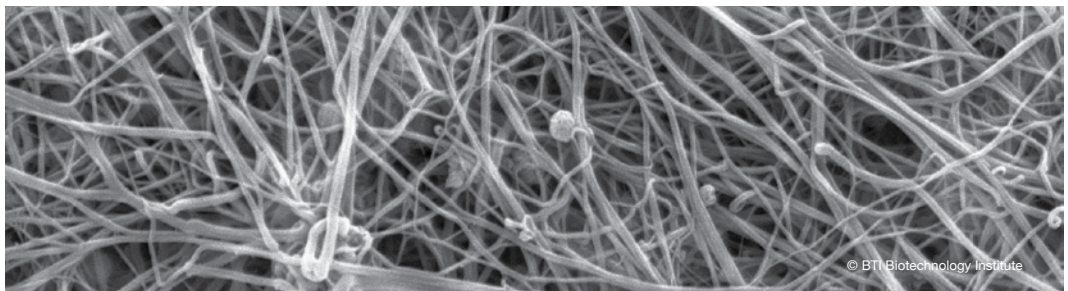
ENDORET stimulates tissue regeneration due to its content in growth factors, in greater concentrations than those of blood. ⁽³⁾

QUANTIFICATION OF THE INCREASE IN VEGF (VASCULAR ENDOTHELIAL GROWTH FACTOR) AND PDGF (PLATELET DERIVED GROWTH FACTOR)



B. FIBRIN MEMBRANE

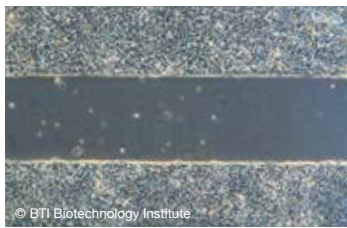
It is a temporary matrix that enables the balanced and gradual release of a large number of molecules, including growth factors and other proteins. ^{(4) (5)}



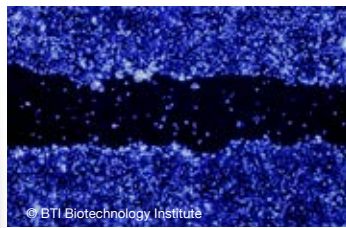
3 MECHANISMS OF ACTION

1. Promoting **angiogenesis** ⁽⁶⁾
2. Stimulating **cell migration** ⁽⁶⁾
3. Increasing **cell proliferation** ⁽⁷⁾
4. Decreasing pain and inflammation ⁽⁸⁾
5. Stimulating **autocrine and paracrine secretion** ⁽⁸⁾

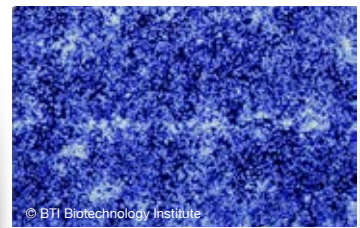
ENDORET ACCELERATES CELL MIGRATION FOR REGENERATIVE PURPOSES ⁽⁶⁾



BASELINE (0H.)



CONTROL (24H.)

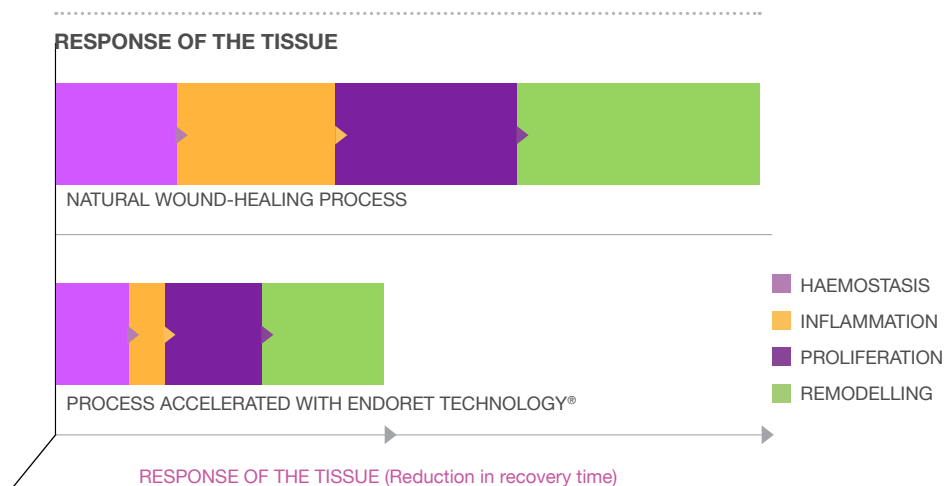


ENDORET® (24H.)



SCAN THE CODE WITH YOUR SMARTPHONE TO WATCH THIS VIDEO

ENDORET TECHNOLOGY® REDUCES THE TISSUE REPAIR TIME ^{(9) (10)}

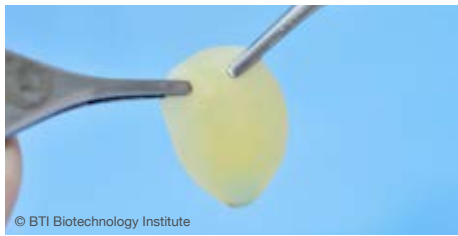


4 THERAPEUTIC FORMULATIONS

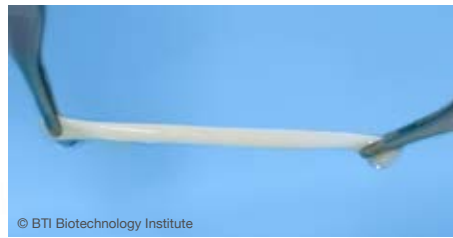
With Endoret technology we can make **3 different therapeutic formulations** and adapt them to the different clinical goals. ⁽¹¹⁾



1. LIQUID



2. CLOT



3. FIBRIN MEMBRANE

5 SAFETY

Autologous product, there are no incompatibilities nor risk of rejection.

More than 700,000 patients have been treated in more than 20 countries, **without any adverse effects being reported.**

(6) Anitua E, Troya M, Orive G. Plasma rich in growth factors promote gingival tissue regeneration by stimulating fibroblast proliferation and migration and by blocking transforming growth factor- β 1-induced myodifferentiation. *J Periodontol.* 2012 Aug;83(8):1028-37.

(7) Anitua E, Prado R, Orive G. Bilateral sinus elevation evaluating plasma rich in growth factors technology: a report of five cases. *Clin Implant Dent Relat Res.* 2012;14:51-60.

(8) Bendinelli P, Matteucci E, Dogliotti G, Corsi MM, Banfi G, Maroni P, Desiderio MA. Molecular basis of anti-inflammatory action of platelet-rich plasma on human chondrocytes: mechanisms of NF- κ B inhibition via HGF. *J Cell Physiol.* 2012;225:757-766.

(9) Sánchez M, Anitua E, Azofra J, Andía I, Padilla S, Mujika I. Comparison of surgically repaired Achilles tendon tears using platelet-rich fibrin matrices. *Am J Sports Med.* 2007;35:245-251.

(10) Anitua E. Plasma rich in growth factors: preliminary results of use in the preparation of future sites for implants. *Int J Oral Maxillofac Implants.* 1999;14:529-535.

(11) Anitua E, Sánchez M, Orive G, Andía I. The potential impact of the preparation rich in growth factors (PRGF) in different medical fields. *Biomaterials.* 2007;28:4551-4560.

APPLICATIONS

OF ENDORET TECHNOLOGY®

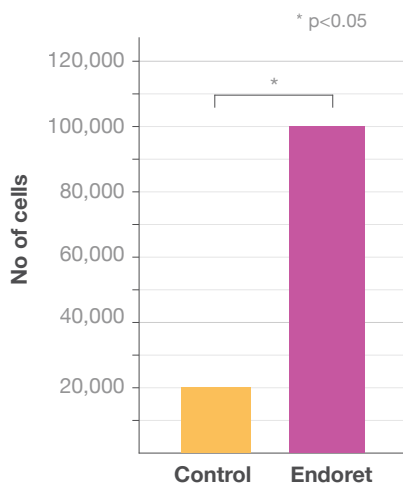
COSMETIC DERMATOLOGY

The infiltration of ENDORET promotes tissue remodelling in older skin **affecting the hydration, angiogenesis and overall health** of the skin. ^{(12) (13)}

IMPROVED SKIN CONSISTENCY

ENDORET increases the proliferation of the cells and improves the secretion of procollagen. ^(14,15)

PROLIFERATIVE EFFECT ON THE FIBROBLASTS OF THE SKIN



DERMIS REMODELATION

In photoaged skin, Endoret has a collagen remodelling effect and also reduces the solar elastosis.

(12) Anitua E, Sánchez M, Sarabia R, Sanz J, Aguirre JJ, Orive G. Eficacia y seguridad del PRGF (Plasma Rico en Factores de Crecimiento) en la regeneración cutánea facial. Effectiveness and safety of PRGF® (plasma rich in growth factors) in facial cutaneous regeneration. Clinical, randomised and controlled trial with hyaluronic acid. Revista de la AECEP.2011;Feb;23-33.

(13) Dae Hun Kim, M.D. et al. Can Platelet-rich Plasma Be Used for Skin Rejuvenation? Evaluation of Effects of Platelet-rich Plasma on Human Dermal Fibroblast. Ann Dermatol Vol. 23, No. 4, 2011

(14) Anitua E, Sánchez M, Zaldueño MM, de la Fuente M, Prado R, Orive G, Andía I. Fibroblastic response to treatment with different preparations rich in growth factors. Cell Prolif. 2009 Apr;42(2):162-170.

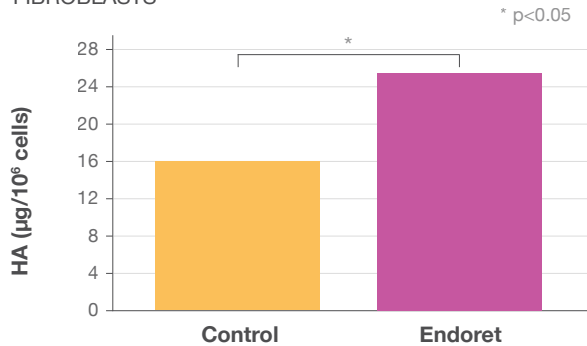
(15) Blanca Díaz Ley. Efectos del PRGF en el tratamiento del envejecimiento cutáneo. Comunicación oral de la XXV reunión GEDET. Alicante 29-30 Noviembre 2013.

MORE HYDRATED SKIN

An increase in hyaluronic acid is linked to better hydration of the skin.

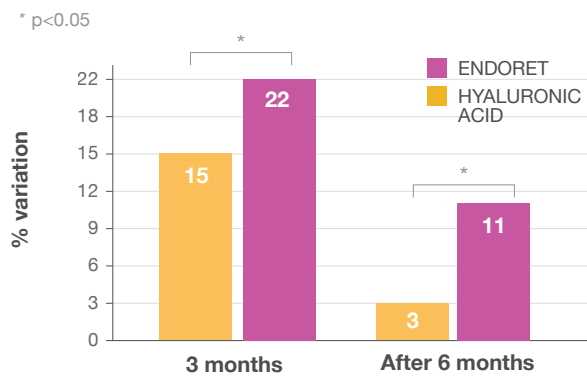
ENDORET significantly increases the production of endogenous hyaluronic ACID. ^{(14) (16)}

HYALURONIC ACID PRODUCTION FROM SKIN FIBROBLASTS ⁽¹⁶⁾



The skin is significantly more hydrated compared to treatment with hyaluronic acid, up to 3 and 6 months after treatment ⁽¹²⁾

COMPARATIVE TEST WITH HYALURONIC ACID. % EVOLUTION OF THE CORNEOMETRY COMPARED TO THE BASELINE FOR BOTH TREATMENT GROUPS



MAINTAINED EFFECTS

The activation of product enables the formation of a matrix in situ after the infiltration in the dermal area ⁽¹⁶⁾. Thus, **the release of the Growth Factors is gradual** prolonging the biological response. ⁽¹⁷⁾

⁽¹⁶⁾ Anitua E, Troya M, Orive G. Plasma rich in growth factors promote gingival tissue regeneration by stimulating fibroblast proliferation and migration and by blocking transforming growth factor-β1- induced myodifferentiation. J Periodontol. 2012 Aug;83(8):1028-1037.

⁽¹⁷⁾ Anitua E., Zalduendo M. et al; Release kinetics of platelet-derived and plasma-derived growth factors from autologous plasma rich in growth factors. Ann Anat. 2013.

WOUND HEALING

The application technique of ENDORET on chronic skin ulcers **significantly accelerates the healing process** compared to conventional treatment. ^{(18) (19) (20)}

TREATMENT OF AN ULCER WITH ENDORET.



LONG-TERM VASCULAR ULCER



STATE OF THE WOUND AFTER ONE TREATMENT (1 WEEK AFTER)



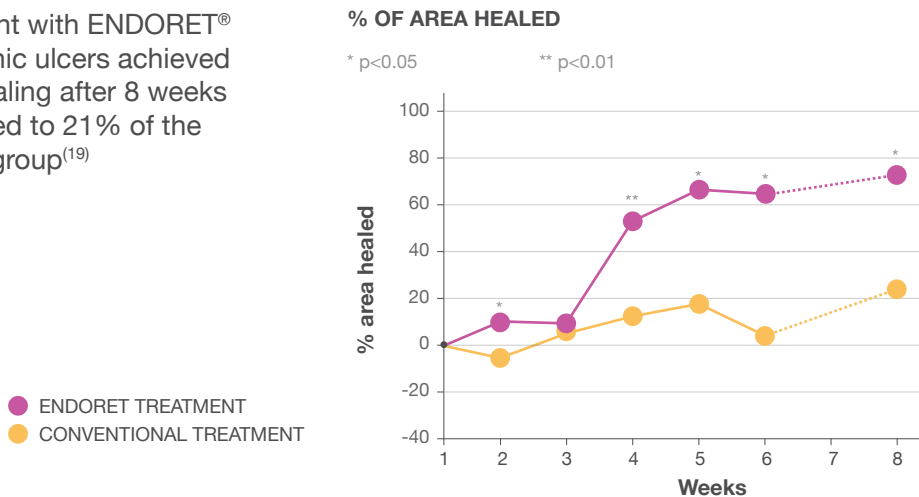
WOUND CLOSURE IN 8 WEEKS.

The autologous fibrin provides an excellent vehicle for the local release of **growth factors**, functioning as a matrix to support the new blood cells and helping the migration of cells to the injured area. ⁽¹⁷⁾

ACCELERATION OF HEALING

The application of ENDORET to chronic skin ulcers significantly accelerates the healing process compared to conventional treatment. ⁽²⁰⁾

Treatment with ENDORET® on chronic ulcers achieved 73% healing after 8 weeks compared to 21% of the control group ⁽¹⁹⁾



(18) Molina-Miñano F, López-Jornet P, Camacho-Alonso F, Vicente-Ortega V. The use of plasma rich in growth factors on wound healing in the skin: experimental study in rabbits. *Int Wound J.* 2009 Apr;6(2):145-148.

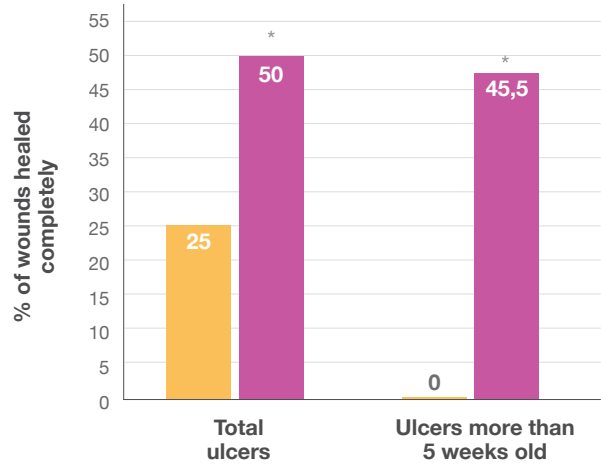
(19) Orcajo B, Muruzabal F, Isasmendi MC, Gutierrez N, Sánchez M, Orive G, Anitua E. The use of plasma rich in growth factors (PRGF-Endoret) in the treatment of a severe mal perforant ulcer in the foot of a person with diabetes. *Diabetes Res Clin Pract.* 2011 Aug;93(2):e65-67.

(20) Anitua E, Aguirre JJ, Algorta J, Ayerdi E, Cabezas AI, Orive G, Andia I. Effectiveness of autologous preparation rich in growth factors for the treatment of chronic cutaneous ulcers. *J Biomed Mater Res B Appl Biomater.* 2008 Feb;84(2):415-421.

ENDORET achieves healing in 8 weeks for 45% of long-term ulcers ⁽²¹⁾

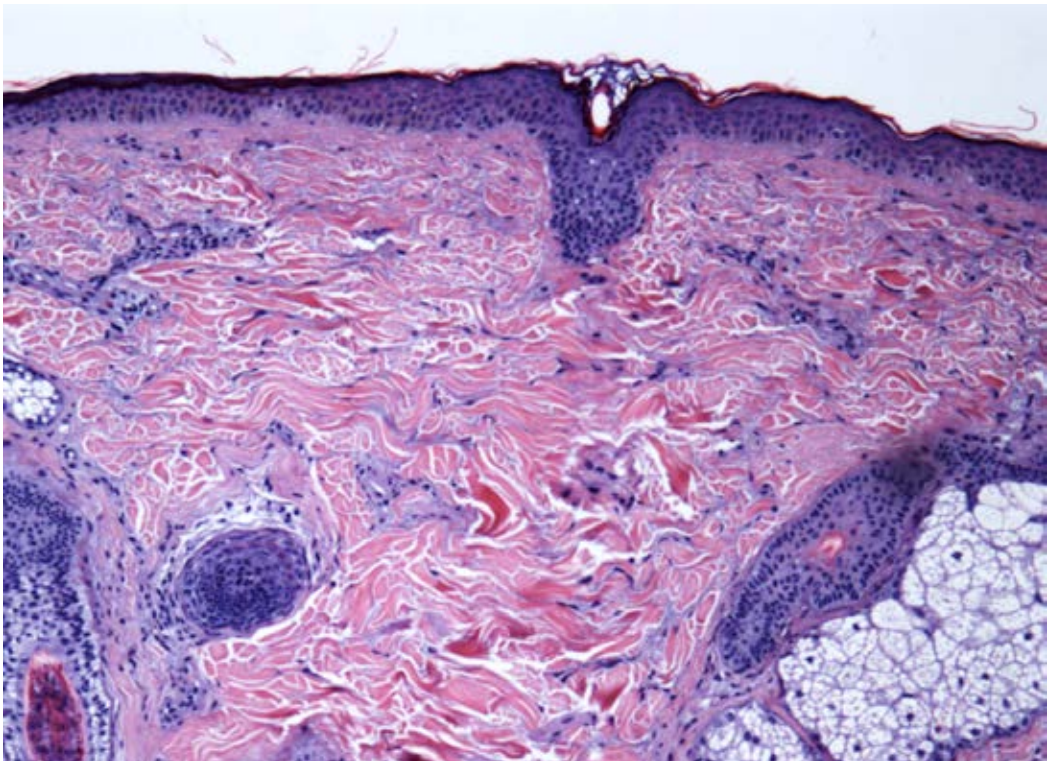
■ CONTROL
■ ENDORET

* $p < 0.05$



REDUCTION OF INFLAMMATION

The application of ENDORET accelerates the inflammatory process, decreases pain and increases the reepithelised area in wounds. ^{(16) (18)}



(21) Aguirre JJ et al. Eficacia del PRGF-ENDORET en el tratamiento de las úlceras cutáneas secundarias a insuficiencia venosa: Ensayo clínico aleatorizado controlado con tratamiento convencional. Sent for publication.

COMPONENTS OF ENDORET TECHNOLOGY®

1 ENDORET® DISPOSABLE KIT SINGLE-USE KIT*

* MEDICAL DEVICES CERTIFIED FOR APPLICATION IN DERMATOLOGY

COSMETIC KITS

KMU 10

The amount of product obtained with ENDORET technology is:

- 8ml for skin infiltration.
- 8ml to make a facial mask post-treatment.
- It includes infiltration material.

WOUND HEALING KIT

KMU HE

BTI innovation to get the Endoret membranes quicker and easier, with all ENDORET regenerative properties.



2 ENDORET® EQUIPMENT*

- System V Centrifuge
- Work rack
- Activation containers



* MEDICAL DEVICES CERTIFIED FOR APPLICATION IN DERMATOLOGY

3 ENDORET® TRAINING

Exclusive training adapted to medical needs. We share our new clinical research and provide training for innovative, top-quality healthcare.



© BTI Biotechnology Institute

4 ENDORET® CERTIFICATION

We certify the clinical qualification and experience of our customers with our training certificates.



ADVANTAGES

OF ENDORET TECHNOLOGY®

Endoret is the most experienced technology of the market in the development of specific protocols for tissue regeneration, a pioneering technology manufactured exclusively by BTI Biotechnology Institute.

OPTIMUM CONCENTRATION OF PLATELETS

The **right concentration of platelets** affects the final efficacy. ⁽²²⁾

LEUKOCYTE - FREE FORMULATION

The inclusion of **leukocytes** increases the pain and inflammation. ⁽²³⁾

CONTROLLED ACTIVATION

Enables the formation of the fibrin matrix in situ **and the gradual release of growth factors**, maintaining its efficacy over time. ⁽²⁴⁾

AUTOLOGOUS

It is made from the patient's own blood, so **there are no known adverse effects**. ⁽²⁵⁾

REPRODUCIBLE

The protocol for the preparation process and its clinical application is strictly defined and tested.

VERSATILE

Three therapeutic formulations obtained in the same process means we can adapt the product to the patient's clinical needs. ^{(26) (27)}

⁽²²⁾ Anitua E, Sanchez M, Prado R, Orive G. The type of platelet-rich plasma may influence the safety of the approach. *Knee Surg Sports Traumatol Arthrosc.* 2012.

⁽²³⁾ Filardo G, Kon E, Pereira Ruiz MT, Vaccaro F, Guitaldi R, Di Martino A, Cenacchi A, Fornasari PM, Marcacci M. Platelet-rich plasma intra-articular injections for cartilage degeneration and osteoarthritis: single- versus double-spinning approach. *Knee Surg Sports Traumatol Arthrosc.* 2012.

⁽²⁴⁾ Anitua E, Sanchez M, Nurdén AT, Zalduendo M, de la Fuente M, Orive G, Azofra J, Andía I. Autologous fibrin matrices: a potential source of biological mediators that modulate tendon cell activities. *J Biomed Mater Res A.* 2006;77:285-293.

⁽²⁵⁾ Anitua E, Sánchez M, Nurdén AT, Nurdén P, Orive G, Andía I. New insights into and novel applications for platelet-rich fibrin therapies. *Trends Biotechnol.* 2006;24:227-234.

⁽²⁶⁾ Anitua E, Sánchez M, Orive G. Potential of endogenous regenerative technology for in situ regenerative medicine. *Adv Drug Deliv Rev.* 2010 Jun 15;62(7-8):741-52.

⁽²⁷⁾ Anitua E, Sánchez M, Orive G, Andía I. The potential impact of the preparation rich in growth factors (PRGF) in different medical fields. *Biomaterials.* 2007 Nov;28(31):4551-60.

SAFETY AND REGULATORY ASSURANCE

QUALITY ASSURANCE

- The ENDORET system complies with the **highest standards of quality**. The protocol for the preparation of Endoret is described in detail in the Manual for Use contained in each Endoret PRGF Kit.
- Both the technology and the materials related to it have the **CE health certificate** for their specific application in: Soft tissue regeneration for treating skin ulcers and treatment of skin aging.

GUARANTEES OF EFFICACY

- BTI has the greatest clinical support in the world published in this field; its effectiveness is proven in **more than 150 international scientific publications**.

ADDITIONAL GUARANTEES

- BTI **certifies its customers' specific training** in the use of this technology.
- In addition, BTI guarantees the **traceability of its materials**, and helps transfer all necessary information to its patients.





BTI Commercial
San Antonio, 15 · 5º
01005 Vitoria-Gasteiz
(Álava) · España
Tél : +34 945 140 024
Fax : +34 945 135 203
pedidos@bticomercial.com

B.T.I. Biotechnology Institute S.L.
Parque Tecnológico de Álava
Leonardo da Vinci ,14
01510 Miñano (Álava) España
bti.implantes@bti-implant.es

GERMANY
Mannheimer Str. 17
75179 Pforzheim · Alemania
Tel. +49 (0) 7231 428060
Fax +49 (0) 7231 4280615
info@bti-implant.de

FRANCE
6 Avenue Neil Armstrong
Immeuble Le Lindbergh
33692 Merignac CEDEX · Francia
Tel: (33) 06 45 07 36 78
info@bti-implant.fr

ITALY
Piazzale Piola, 1
20131 Milano · Italia
Tel: (39) 02 7060 5067
Fax: (39) 02 7063 9876
bti.italia@bti-implant.it

MEXICO
Ejercito Nacional Mexicano 351, 3A
Col. Granada Delegación Miguel Hidalgo
Messico DF · CP 11520 · Mexico
Tel: (52) 55 52502964
Fax: (52) 55 55319327
bti.mexico@bti-implant.com

PORTUGAL
Praça Mouzinho de Albuquerque, 113, 5º
4100-359 Porto · Portugal
Tel: (351) 22 120 1373
Fax: (351) 22 120 1311
bti.portugal@bticomercial.com

UK
870 The Crescent
Colchester Business Park · Colchester
Essex CO49YQ · UK
Tel: (44) 01206580160
Fax: (44) 01206580161
info@bti-implant.co.uk

USA
1730 Walton Road
Suite 110
Blue Bell, PA 19422-1802 · USA
Tel: (1) 215 646 4067
Fax: (1) 215 646 4066
info@bti-implant.us

www.bti-biotechnologyinstitute.com



BTI APP
ENDORET® (PRGF®)

iPhone / smartphone version
iPad / Tablets version (**Customer Area**)