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 53,820 SQUARE FEET DEVOTED TO TRAINING, CLINICAL PRACTICE AND RESEARCH

WE TRAIN IN ORDER TO OPTIMIZE THE CLINICAL RESULTS

Specific training aimed at different medical specializations.

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

More than 1200 international students per year.
TRANSLATIONAL RESEARCH: KNOWLEDGE ACQUIRED IN THE LABORATORY APPLIED TO CLINICAL PRACTICE

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

MORE THAN 100 INDEXED SCIENTIFIC PUBLICATIONS SUPPORT 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.
Hundreds of endogenous proteins affect the tissue repair processes, including angiogenesis, chemotaxis and cell proliferation. No exogenic agent can effectively govern all these processes. (1)

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

2 ACTIVE SUBSTANCES

A. GROWTH FACTORS

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

\[ \text{QUANTIFICATION OF THE INCREASE IN VEGF (VASCULAR ENDOTHELIAL GROWTH FACTOR) AND PDGF (PLATELET DERIVED GROWTH FACTOR)} \]

<table>
<thead>
<tr>
<th>BASELINE</th>
<th>ENDORET®</th>
</tr>
</thead>
<tbody>
<tr>
<td>VEGF pg/ml</td>
<td>0</td>
</tr>
<tr>
<td>PDGF ng/ml</td>
<td>0</td>
</tr>
</tbody>
</table>

\* p<0.05

B. FIBRIN MEMBRANE

Enables the balanced and gradual release of a large number of molecules, including growth factors and other proteins. (4) (6)
MECHANISMS OF ACTION

1. Promoting angiogenesis (6)
2. Stimulating cell migration (7)
3. Increasing the proliferation (8) (9) (10)
4. Decreasing inflammation and pain (11)
5. Stimulating autocrine and paracrine secretion of growth factors (8) (9) (10)

ENDORET® ACCELERATES CELL MIGRATION FOR REGENERATIVE PURPOSES (6)

INITIAL STATUS (0H.)

CONTROL (24H.)

ENDORET® (24H.)

ENDORET TECHNOLOGY® REDUCES THE TISSUE REPAIR TIME (12) (13)

RESPONSE OF THE TISSUE

NATURAL WOUND-HEALING PROCESS

PROCESS ACCELERATED WITH ENDORET TECHNOLOGY®

RESPONSE OF THE TISSUE (Reduction in recovery time)

With ENDORET® technology we can make **4 different therapeutic formulations** and adapt them to the different clinical goals. (14)

1. LIQUID

2. CLOT

3. AGGLUTINATING AUTOLOGOUS / HETEROLOGOUS GRAFT

4. FIBRIN MEMBRANE

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**SAFETY**

100% Autologous product, there are no incompatibilities **nor risk of rejection**.

All the formulations of ENDORET® have a **bacteriostatic effect**, especially during the 4 hours after application. (15)

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

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APPLICATIoNS OF ENDORET TECHNOLOGY® IN IMPLANTOLOGY

THE USE OF ENDORET® SIGNIFICANTLY INCREASES THE SUCCESS RATE IN TREATMENTS WITH DENTAL IMPLANTS. (16)(17)(18)

When the surface of the implants is wet with ENDORET® liquid a fibrin membrane is formed that adheres to the surface of the implant and releases growth factors and improves the osseointegration.

The nano-rough surface of BTI implants is specially designed to boost the biological effects of ENDORET®.

WETTING WITH ENDORET® INCREASED THE TRABECULAR THICKNESS AND MATURITY OF THE BONE

SURVIVAL RATES REPORTED IN PROSPECTIVE TRIALS:

- **5-year follow-up study**
  - 5787 implants. 99.2% (16)
- **5-year follow-up study**
  - 1139 immediate load implants. 99.3% (17)
- **8-year follow-up study**
  - 1287 short implants. 99.3% (18)
- **10-12-year follow-up study**
  - 111 short implants. 98.9% (19)

(18) Anitua E, Orive G. Short implants in maxillae and mandibles: a retrospective study with 1 to 8 years of follow-up. J Periodontol. 2010;81:819-826.
The application of ENDORET® in the treatment of post-extraction sockets reduces inflammation and pain, accelerates the epithelization of soft tissues and promotes bone regeneration. (20) (21) (22)

The survival rate of an implant placed in an alveolus post-extraction immediately is 98%, and is a safe, effective and predictable treatment. (23)

Treatment with ENDORET® after resecting the necrotic bone increases the activity of the osteoclasts and causes angiogenesis, which can be used as an adjuvant for patients with BRONJ. (24)

The results of various studies suggest that treatment with ENDORET® can lessen the risk of developing BRONJ after a dental extraction in high-risk patients in treatment with bisphosphonates. (25) (26)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of extractions</th>
<th>Osteonecrosis of the maxilla</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>267</td>
<td>5</td>
</tr>
<tr>
<td>Endoret® (PRGF®)</td>
<td>542</td>
<td>0</td>
</tr>
</tbody>
</table>

**CLINICAL TRIAL OF THE PREVENTION OF BISPHOSPHONATE-ASSOCIATED OSTEONECROSIS OF THE JAW (BRONJ)**

**ENDORET® (PRGF®)**

1

2

3

CONTROL
ENDORET® TECHNOLOGY

4 ENDORET® IN THE TREATMENT OF BRONJ

ENDORET was effective in the surgical treatment of bisphosphonate-associated osteonecrosis of the jaw, achieving closure of the defect in 32 patients in a prospective study. (27)

Endoret restored the function of the inferior dental nerve affected by the BRONJ lesion. (27)

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5 PREPARATION OF GRAFTS

ENDORET® can be used to agglutinate biomaterial, making it easier to handle and improving its osteoconductive and biological properties, in both heterologous and autologous grafts. (28) (29) (30)

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(25) Mozzati M, Arata V, Gallesio G. Tooth extraction in patients on zoledronic acid therapy. Oral Oncol. 2012 Sep;48(9):817-21


ENDORET® improves tissue regeneration, and because of its versatility, it can be used in various surgical techniques.

A. LATERAL BONE INCREASE

The crestal expansion and crestal split techniques in two stages combined with ENDORET treatment can achieve an average bone expansion of 3.35 mm.\(^{(31)}\)

The use of ENDORET®, in combination with the block graft, improves the healing of the flap, avoids exposure of the graft, and improves the post-operative outlook of the patient.

TWO-STAGE CRESTAL SPLIT TREATMENT

A) LONGITUDINAL CORTICOTOMY WITH ULTRASOUND B) USE OF BONE GRAFTS AND FIBRIN MEMBRANES C) EPITHELIZATION AFTER 3 MONTHS D) REOPENING AFTER 3 MONTHS
B. SINUS ELEVATION

ENDORET® reduces inflammation and pain. It increases the bone formed and maintains the survival of the bone cells.(29)

ENDORET® is effective in the treatment of perforations in the Schneider membrane (33)

ENDORET® INCREASES THE REVASCULARIZATION OF THE BONE GRAFT AND THE FORMATION OF MATURE BONE

C. VERTICAL BONE REGENERATION

The combination of ENDORET® treatment with short and extra-short implants makes restorations in atrophic crests possible without needing to resort to more aggressive techniques. \(34\)(35)(36)(37)

7 PERIODONTAL REGENERATION

ENDORET® may be an alternative to the use of dermal material used in the field of mucogingival surgery.

ENDORET® achieves favourable results in terms of radicular cover and gain in clinical insertion. In addition, it increases the width of keratinized tissue and corrects recession. \(38\)(39)

COMPONENTS OF ENDORET TECHNOLOGY®

1 ENDORET® EQUIPMENT

START EQUIPMENT

- BTI ENDORET® Centrifuge
- Plasmaterm H Warming Oven
- Work rack
- Activation glass bowls

THE APPLICATION OF ENDORET TECHNOLOGY COMPLIES WITH ALL THE REGULATIONS REQUIRED BY THE SPANISH AGENCY OF MEDICINES AND MEDICAL DEVICES, FOOD AND DRUG ADMINISTRATION AGENCY (FDA) AND EUROPEAN UNION. FOR EUROPEAN UNION OUR MEDICAL DEVICES ARE IDENTIFIED WITH CE MARK.
THE APPLICATION OF ENDORET TECHNOLOGY COMPLIES WITH ALL THE REGULATIONS REQUIRED BY THE SPANISH AGENCY OF MEDICINES AND MEDICAL DEVICES, FOOD AND DRUG ADMINISTRATION AGENCY (FDA) AND EUROPEAN UNION. FOR EUROPEAN UNION OUR MEDICAL DEVICES ARE IDENTIFIED WITH CE MARK.

**KMU15 - US KIT**

- 6 extraction tubes (TE9)
- 4 fractioning tubes (TF9)
- 1 activation syringe
- 1 PTD 2
- 1 winged blood collection set
- 5 identification labels
- 1 tourniquet
- 1 single use Activator

**EXTRACTION TUBES**

**FRACTIONING TUBE**

**ACTIVATION SYRINGE**

**EXTRACTION SYSTEM**

**PLASMA TRANSFER DEVICE (PTD2)**
3 ENDORET® TRAINING

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

4 ENDORET® CERTIFICATION

We certify the clinical qualification and experience of our customers with our training certificates.
ENDORET® technology is the market leader 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.\(^{41}\)

FORMULATION FREE OF LEUKOCYTES
The inclusion of leukocytes increases pain and inflammation\(^{42}\) and accelerates the deterioration of the fibrin.

CONTROLLED ACTIVATION
Enables the formation of the fibrin matrix in situ and the gradual release of growth factors, maintaining its efficacy over time.\(^{43}\)

AUTOLOGOUS
It is made from the patient’s own blood, so there are no known adverse effects.\(^{44}\)

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

VERSATILE
4 therapeutic formulations obtained in the same process means we can adapt the product to the patient's clinical needs.\(^{45, 46}\)

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The application of Endoret® technology complies with all the regulations required by the Spanish Agency of Medicines and Medical Devices, Food and Drug Administration Agency (FDA) and European Union.

QUALITY ASSURANCE

· The ENDORET® closed-technique system complies with the highest standards of quality.

· Both the system and the materials have the CE health certificate awarded by TÜV for specific application to oral surgery.

GUARANTEES OF EFFICACY

· BTI has the greatest clinical support in the world published in this field; its effectiveness is proven in more than 100 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.