

**Public title**

Patient perception and clinical effectiveness of an allogeneic cortical sheet versus an autologous laminated bone graft for the treatment of horizontal bone defects: a randomized multicenter clinical trial

**Scientific title**

Patient perception and clinical effectiveness of an allogeneic cortical sheet versus an autologous laminated bone graft for the treatment of horizontal bone defects: a randomized multicenter clinical trial

**Background and aims:**

The loss of one or more teeth carries a series of dimensional changes in the alveolar process, both at the level of hard tissues and at the level of soft tissues that could sometimes compromise or hinder the placement of the implant in the appropriate three-dimensional position (Schropp and cols 2003, Chappuis et al 2015). Therefore, it is not surprising that there are numerous systematic reviews that aim to analyze the efficacy of different horizontal and vertical guided bone regeneration procedures, simultaneously or prior to implant placement (Sanz-Sanchez et al 2015, Naenni et al 2019, Thoma et al 2019, Urban et al 2019). The available scientific evidence considers autologous bone graft to be the gold standard for lateral / horizontal and / or vertical reconstruction of bone defects (Cordaro et al 2002). The main advantage of this type of bone graft is its biological properties (osteoconductivity, osteoinduction and osteogenesis). However, autologous grafts are associated with a series of disadvantages such as limited intraoral availability (Cremonini et al 2010), an increase in morbidity due to having to go to a second surgical area to obtain the bone graft (Nkenke et al 2014 , Cordaro et al 2011) and even the risk of sensory disturbances (Von Arx et al 2005). Consequently, in recent decades the number of scientific studies that analyze the efficacy of grafts of non-autologous origin has increased exponentially (Di Raimondo et al 2020, Sanz & Vignoletti 2015). Probably the non-autologous bone grafts with the greatest scientific support are those of xenogenic origin (Ortiz-Vigón et al 2017), however they lack osteogenic capacity.

Another of the bone substitutes used to reduce the drawbacks of autologous grafts are allografts. Bone grafts of allogeneic origin have properties such as osteoinduction and osteoconduction, and for this reason recent research has proposed it as a valid alternative to autologous grafts (Park et al. 2017, Spin -net et al. 2015, Silva et al. 2017, Tunkel et al. 2020). However, these types of grafts do not have osteogenic capacity and therefore bone formation will require a longer healing time and will result in a lesser amount of newly formed bone (Chiapasco et al 2015). Therefore, the objective of this work is to analyze the clinical efficacy of bone allografts in the three-dimensional reconstruction of atrophic maxillae prior to implant placement

**Study hypothesis**

Allograft Bone Sheet (OraGRAFT Cortical Plate®) provides results similar to autologous sheet graft in terms of horizontal bone gain but with higher overall patient satisfaction with treatment due to lower morbidity.

**Ethics approval**

Approved 19/06/2017, Ethical Committee of the Basque Country (CEIm de Euskadi [Comité de Ética de la Investigación Clínica con medicamentos] Farmaziako Zuzendaritza / Dirección de Farmacia. Osasun saila / Departamento de Salud. Eusko Jaurlaritza / Gobierno Vasco C/ Donostia-San Sebastián, 1 – 01010 Vitoria-Gasteiz; +34 (0)945 01 64 59; ceic.eeaa@euskadi.eus), ref: PS2017017

**Study design**

Multicenter randomized controlled clinical trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

Interventions

**Randomization:**
The randomization will be done in blocks according to a randomization list generated by computer using the SPSS program. Treatment allocation will be hidden in sealed, opaque envelopes until the time of surgery. In this study, neither the patient nor the operator nor the examiner can be blinded. The statistician will be blinded.

On day 0 the first surgical procedure will be performed, which will include the following phases: 1. Pre-surgical measurement of the width of the buccal mucosa with a probe millimeter CP15 and impression of the area to be treated
2. Pre-surgical and post-surgical periapical x-ray of the area to be intervened
3. The stopwatch is activated to measure the intervention time
4. Local anesthesia and elevation of a full-thickness flap to expose the area bone that will receive the bone graft
5. Measurement of the width of the alveolar process using a millimeter gauge 2 mm apically to the alveolar ridge in each of the positions to receive an implant
6. The flap is released by cutting the deep periosteum and a superficial release of the flap muscle attachments
7. Randomization of the type of graft to receive: bone allograft sheet (LifeNet Health OraGRAFT Cortical Plate®) versus autologous bone graft sheet. In case of receiving an autologous bone graft, the posterior retromandibular area (oblique line) will be anesthetized and a graft will be taken that has the length and width of the treated area between 1 and 2 mm in diameter thickness (Barbieri et al. 2017).

**Primary outcome measure**

The horizontal bone gain measured clinically 2 mm from the ridge

**Secondary outcome measures**

1. The general satisfaction of the patient with the treatment as well as the pre-surgical expectations, measured by the VAS scale calibrated from 1 to 100 points immediately after surgery and at 2, 4, 12, 26, and 52 weeks
2. Horizontal bone gain measured radiographically by CBCT

3. Horizontal bone gain measured with a volumetric study using digital impressions (3Shape®) and stone models
4. The peri-implant indices around the implants (bleeding on probing, plaque index, recession of the peri-implant mucosa, probing depth and clinical attachment level and radiographic bone level ) during the period of observation up to 52 weeks

5. Time spent in peri-implant bone augmentation treatment
6. Change the depth of the vestibule in the treatment area using digital impressions (3Shape®) at 12 o'clock, 26 and 52 weeks after the intervention
7. Follow-up of patients and peri-implant health Straumann BLT at 3 and 5 years

**Participant inclusion criteria**

1. Informed consent after detailed information
2. Adults at least 18 years of age
3. Candidates to receive a bone augmentation for implant placement
4. Presence of a bone defect (≥2 teeth) with at least 2 mm of mucosa
5. Keratinized remnant whose bone width is insufficient (<4 mm) measured on a CBCT-type scanner
6. The patient must be periodontally treated at least 1 month before the surgical intervention and in addition to all those oral factors that may affect the treatment

**Participant exclusion criteria**

1. General contraindications for dental/surgical treatment
2. Inflammatory or autoimmune disease of the oral cavity
3. Smokers of more than 10 cigarettes a day
4. Allergy to collagen and analgesics/anti-inflammatory NSAIDs
5. History of cancer in different parts of the body that has required radiotherapy or chemotherapy in the last 5 years

6. Radiation therapy to the head or neck in the last 5 years
7. Current medication with immunosuppressants, bisphosphonates or high doses of corticosteroids
8. Pregnant women or nursing
9. Women of childbearing age who are not using a method effective contraceptive
10. Participants in other biomedical research studies in the 24 weeks prior to the start of the study

**Trial Centre**

***Trial Centre Name***

Periocentrum Bilbao

Address

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48008

**Trial Centre**

***Trial Centre Name***

Periocentrum Madrid

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**Patient information and consent.**
Each researcher must obtain the written informed consent of each patient at least 24 hours before the start of the measures related to the clinical investigation, so that he has the possibility to change his mind. For these purposes, patients will be informed verbally and in writing by the investigator about the nature, importance, implications, and risks of clinical research prior to enrollment. All items will be explained in language and terms that are easy for patients to understand.

Each patient will receive oral and written information about clinical research, their next treatment, and that they should only participate if they really want to. Additionally, patients should be aware of the fact that they can withdraw from clinical research at any time and for any reason, without jeopardizing their future treatment.
In addition, the patient will be informed that the data of his treatment will be registered in a computer database, but that he will only be registered through a code system. Patients will be assigned a unique sequential patient identification number when enrolling in clinical research. Each patient should retain that number throughout the clinical investigation. The treatment number of any patient who discontinues or withdraws from clinical research cannot be reassigned to any other patient and cannot be reused for any reason. The investigator will maintain a patient registry that links the patient's number to the patient's name. The researcher will follow all applicable privacy laws in order to protect patient privacy and confidentiality. Information that could identify the patient will be masked in the material received by the sponsor. Each patient has the right to take part of the information stored about him / her treatment. This information will be provided by the treating physician.