Comparison of volumetric changes in the peri-implant mucosa in horizontal defects using Connective Tissue Grafting vs. Acellular Dermal Matrix: A randomized clinical trial

INTRODUCTION

The utilization of dental implants represents the contemporary gold standard for tooth replacement therapy. However, the increasing prevalence of implant procedures has corresponded with a proportional rise in associated complications. Multiple risk factors have been identified, including periodontal disease history, inadequate plaque control, and insufficient patient compliance. The width and volume of keratinized mucosa are fundamental determinants of peri-implant tissue stability, playing crucial roles in maintaining gingival health, preventing attachment loss and ensuring optimal aesthetic outcomes (Thoma *et al*., 2009; Papi *et al*., 2020).

Evidence demonstrates that soft tissue grafting procedures enhancing peri-implant soft tissue thickness effectively prevent mucosal recession while improving the tissue-implant interface, thereby optimizing both functional and aesthetic parameters (Giannobile *et al*., 2017). Traditional approaches to volume augmentation have primarily relied on connective tissue grafts (CTG) and free gingival grafts (FGG). However, these autogenous techniques present several limitations, including extended surgical duration, palatal donor site morbidity, prolonged healing periods, and reduced patient acceptance. Furthermore, palatal harvesting procedures are associated with potential complications such as donor site hemorrhage, sensory dysfunction, and infection risk (Griffin *et al*., 2006; Zucchelli *et al*., 2019). Additional anatomical constraints, including palatal vault morphology, tissue availability, and neurovascular architecture, may preclude successful graft harvesting in certain cases (Soileau & Brannon, 2006).

Subsequently, acellular dermal matrices were developed in the 1990s as alternative grafting materials, addressing the aforementioned limitations of autogenous procedures. NovoMatrix™, a recently introduced porcine-derived dermal matrix, represents a significant advancement in this field. Its composition includes structurally essential components: fibrillar collagen and collagen VI (providing structural integrity), elastin (conferring tissue elasticity), hyaluronan (regulating tissue hydration), fibronectin (mediating cellular processes including adhesion, migration, growth, and differentiation), proteoglycans (facilitating revascularization), and preserved vascular channels (enabling initial revascularization through matrix penetration). The preservation of these biochemical properties yields a stable, resilient, and immediately available alternative to autogenous grafts. Furthermore, NovoMatrix™ demonstrates favorable clinical characteristics including rapid revascularization potential, efficient cellular repopulation, minimal inflammatory response, and superior tissue color adaptation.

In a one-year prospective case series, Stefanini *et al*. (2020) evaluated the efficacy of porcine-derived acellular dermal matrix in conjunction with coronally advanced flap for peri-implant soft tissue augmentation around single implants. The investigators reported a significant mean volumetric gain of 1.2±0.18mm in the aesthetic zone. While these findings demonstrate promising outcomes, the study's methodological limitations, including limited sample size and absence of a control group.

Furthermore, Hutton *et al*. (2018) conducted a comparative analysis of connective tissue grafts versus acellular dermal matrix, with evaluations at baseline and 16 weeks post-intervention. While their findings revealed no statistically significant differences in soft tissue volumetric outcomes between the two procedures, the acellular dermal matrix demonstrated more favorable patient-centered outcomes.

Despite the encouraging preliminary outcomes documented in the literature, current clinical investigations are constrained by limited follow-up periods. Therefore, longitudinal clinical trials are imperative to comprehensively evaluate the long-term efficacy of this biomaterial and to establish comparative effectiveness against the gold standard autogenous connective tissue graft. Such research will contribute vital evidence to inform clinical decision-making and optimize therapeutic protocols in peri-implant soft tissue management.

AIM

Primary Objective

To evaluate and compare the volumetric augmentation achieved through two distinct peri-implant soft tissue enhancement techniques: porcine dermal matrix versus connective tissue graft.

Secundary Objectives

1. To assess and compare the gain in keratinized tissue width
2. To evaluate aesthetic outcomes utilizing the Pink Esthetic Score (PES) (Fürhauser *et al.,* 2005)
3. To analyze Patient Reported Outcome Measures (PROMs)

MATERIAL AND METHODS

This investigation will be conducted in accordance with the Helsinki Declaration principles and will be submitted for approval to the Egas Moniz Ethics Committee. The study protocol will be registered in the ISRCTN platform.

Study Population

Participant recruitment will be conducted at Egas Moniz University Clinic (Almada, Portugal). Informed written consent will be obtained from all participants. A total of 32 patients with horizontal soft tissue deficiencies around a single osseointegrated implant will be enrolled in this randomized controlled clinical trial. Participants will be randomly allocated to either:

- Test group (n= 16): Porcine dermal matrix (NovoMatrix™) intervention
- Control group (n= 16): Autogenous connective tissue graft

Eligibility Criteria

Inclusion criteria:

- Patients >18 years old
- Presence of a single osseointegrated implant with horizontal volumetric deficiency
- Full-mouth plaque score (FMPS) < 25%

Exclusion criteria:

- Presence of vertical defects
- Palate thickness < 2.5mm
- Systemic conditions affecting soft tissue healing (e.g., diabetes with HbA1c >7%)
- Current chemotherapy or radiotherapy treatment
- Immunocompromised status
- Pregnancy or lactation
- Smoking > 10 cigarettes/day
- Previous bone augmentation in the treatment area
- Active periodontal disease or local inflammation and/or infection
- Known hypersensitivity to porcine-derived materials

Surgical Protocol

A calibrated examiner (JL), who will remain blinded to treatment allocation and uninvolved in therapeutic interventions, will perform all clinical measurements to minimize assessment bias. Prior to study initiation, examiner calibration will be conducted to ensure measurement reliability.

In the first appointment a clinical examination and a intra-oral scanning (3shape, Copenhagen, Denmark) will be performed for baseline peri-implant mucosal volume documentation. A full mouth plaque index and peri-implant probing will be performed at six standardized positions: mesio-vestibular (mv), mid-vestibular (v), disto-vestibular (dv), mesio-palatine/lingual (mp/ml), mid-palatine/lingual (p/l), disto-palatine/lingual (dp/dl). Measurements obtained using a calibrated periodontal probe (CP-15), measured in millimetres from the mucosal margin to the bottom of the probable pocket. The height of keratinized tissue will be measured using a graduated periodontal probe and Lugol's solution. Tissue phenotype assessment via periodontal probe transparency method, placed in the peri-implant sulcus. Standardized radiographic examination using a film holder for baseline bone level documentation

All the surgical procedures will be performed by the same operator (MB), to ensure standardization. Following a rinse with 0,2% chlorohexidine for 30 seconds and local anesthesia administration (2% articaine with 1:100,000 epinephrine) an intrasulcular incision around the implant and adjacent teeth will be performed. A partial thickness tunnel will be prepared using a spoon microblade, overpassing the mucogingival junction. During the tunnel preparation, care

will be taken to ensure complete graft coverage. After preparing the tunnel, an opaque envelope will be opened, which will determine whether an autologous graft or a dermal matrix will be used. In the control group, a connective tissue graft is harvested from the palatal mucosa with the single incision technique (Lorenzana & Allen, 2000). The connective tissue graft is placed inside the flap and fixed with 6/0 poliamide suture. The flap will be sutured tension-free with primary closure, using the same suture material. In the test group, the dermal matrix, NovoMatrix™ will be hydrated for five minutes in sterile saline solution. The matrix will be placed in the recipient bed and the remaining surgical procedure (fixation and closure protocol) will be identical to the one described in control group. To ensure standardization of graft dimensions, the acellular dermal matrices (15x15mm) will be trimmed to precise measurements of 10mm in width and 8mm in height. These standardized dimensions were determined based on the requirement for the graft to extend 3mm both mesially and distally beyond the circumference of a regular platform implant (4mm). Autogenous connective tissue grafts will be harvested to match these predetermined dimensions, with the height specification accounting for potential anatomical constraints of the donor site. The length of the surgery will be recorded.

After the surgery, patients from both groups will be instructed to rinse twice daily with 0.2% chlorhexidine for 60 seconds for 10 days, mantain a soft diet, regular oral hygiene measures avoiding surgical site and anti-inflammatory medication (Ibuprofen 600mg) will be prescribed. Sutures removal will be scheduled at 14 days post-operative and patients will be instructed to use a soft post-surgical toothbrush. Furthermore, a range of patient-reported outcomes (PROMs) will be evaluated, including postoperative pain using a Visual Analogue Scale (VAS), the need of rescue medication (to be evaluated twice daily for the first five days, followed by once daily until 14 days postoperatively), oral health-related quality of life using the OHIP-14 questionnaire, and postoperative bleeding on the seventh day.

Standardized evaluations will be conducted at baseline, 3 months, 6 months, and 1 year post-intervention, comprising: plaque index, peri-implant probing dephts, height of keratinized tissue, tissue phenotype assessment, maginal bone level measurments and the Pink Esthetic Score (PES) (Fürhauser et al., 2005). For volumetric assessment, digital scan acquisitioned filles will be superimposed and compared in the different stages of healing. Volume differences will be calculated using a specific software program (Medit 2D).

Patient-centered outcomes will be evaluated through a standardized questionnaire assessing three primary domains. First, participants will complete a comprehensive treatment satisfaction assessment regarding aesthetics. Subsequently, they will be queried regarding their willingness to undergo the same procedure again if necessary. Finally, participants will indicate their likelihood of recommending the intervention to others requiring similar treatment.

Statistical Analysis

Based on volumetric outcome data from Schmitt *et al.* (2020), considering the volumetric changes at the 6-month follow-up assessment, sample size calculation was performed using an effect size of d=1.116, with statistical power set at 80% and significance level at α=0.05. The analysis indicated a minimum requirement of 28 participants, with equal allocation of 14 subjects per intervention group. To account for an anticipated dropout rate of 20%, the final sample size was adjusted to 32 participants, with 16 subjects allocated to each intervention group.

Data management and analysis will be conducted using a secure, password-protected electronic database (Microsoft Excel, Microsoft Corporation, Redmond, WA, USA). Subsequently, relevant variables will be coded and transferred to IBM SPSS Statistics software (Version 30, IBM Corporation, Armonk, NY, USA) for inferencial comparative analysis.

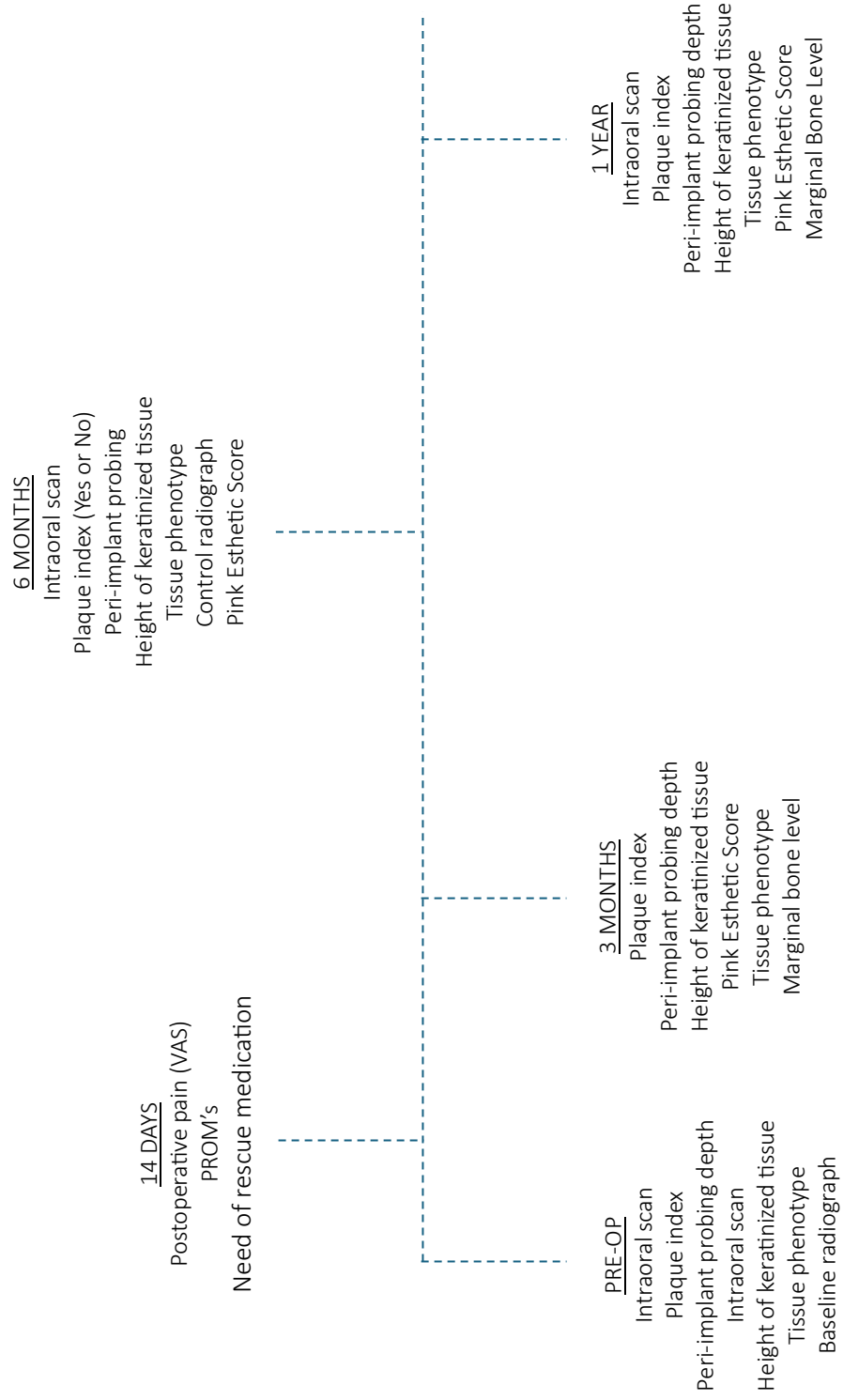
STUDY PLAN

Group	Intervention
Control Connective tissue graft harvested from the palate	Procedure: Soft tissue augmentation around single implants After a partial thickness tunnel, the connective tissue graft is fixed inside the flap and stabilized with 6/0 poliamide suture
Test Acellular dermal matrix of porcine origin, NovoMatrix™	Procedure: Soft tissue augmentation around single implants After a partial thickness tunnel, Novomatrix is fixed inside the flap and stabilized with 6/0 poliamide suture

Primary outcome variable: Compare peri-implant soft tissue volume augmentation between dermal matrix and connective tissue graft

Secondary outcome: Compare keratinized tissue gain, Pink Esthetic Score (PES) and PROMs.

Measurements throughout the study timeline are described above:



PROJECT SCHEDULE

ASSIGNMENTS	MONTH/YEAR
Submission to the ethics committee	07/25
Patient Recruitment	09/25
End of the recruitment phase	01/27
Start 1 year follow-up appointments	09/26
End 1 year follow-up appointments	01/28
Analysis of results	02/28
Results publication	04/28
EXPECTED DATE FOR CONCLUSION OF THE STUDY	April 2028

RELEVANCE OF THE PROJECT

This investigation aims to contribute significant advances to the field of implant dentistry by evaluating alternative approaches for peri-implant soft tissue management, potentially establishing protocols that reduce patient morbidity, enhancing treatment predictability and patient acceptance and providing evidence-based recommendations for clinical practice.

SUMMARY FOR PUBLIC INFORMATION

Peri-implant soft tissue deficiencies present significant challenges to both aesthetic outcomes and long-term implant health maintenance. While autologous grafting procedures demonstrate established efficacy, they are associated with increased morbidity and potential complications. The emergence of dermal matrices as therapeutic alternatives offers the potential for simplified treatment protocols, reduced surgical time, and enhanced patient acceptance. This investigation seeks to provide comparative data regarding clinical outcomes between dermal matrix applications and traditional connective tissue grafting in the management of horizontal volume deficiencies.