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Effect of A-PRF Application on Palatal Wound Healing after Free Gingival Graft Harvesting:
A Prospective Randomized Study

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Abstract

This study aimed to investigate the healing effect of advanced platelet-rich fibrin (A-PRF) clot membranes in the reduction of palatal wounds resulting from free gingival graft (FGG) harvesting, in the re-epithelization rate and in the pain experience after surgery. Twenty-five patients requiring soft tissue augmentation (gingival recession coverage or keratinized gingiva augmentation) participated in this prospective randomized clinical study. After FGG harvesting, the test group (n=14) received A-PRF clot membranes at the palatal wound and the control group (n=11) a gelatin sponge. Epithelialization rate of the palatal wound, wound healing area, correspondent percentage of reduction and post-surgical pain experience were assessed. The follow-up period was 90 days. There was a significantly higher reduction of the palatal wound area in the A-PRF group vs. the control group, at 7 ($p<0.001$), 14 ($p=0.009$) and 30 days ($p<0.001$) follow-up. The maximum difference between groups was attained at 30 days (91.5% for A-PRF vs. 59.0% for the control group). At 14 days a significant difference in the proportion of patients showing total epithelization was found: 64.3% for A-PRF vs. 9.1% for the control group ($p=0.012$). At 90 days, both groups showed total recovery. Overall, the control group experienced a higher level of pain and discomfort until the 14th day, being significantly higher on the second day ($p=0.013$). The results suggest that A-PRF membranes haste the healing process by promoting a greater reduction along the recovery period and an apparent less painful postoperative period.

Keywords: Platelet-rich fibrin, A-PRF, Gingival graft harvesting, Healing, Periodontal plastic surgery.

1 | Introduction

The hard palate is a usual source of soft-tissue grafts for both periodontal and peri-implant plastic surgery procedures (7,17). Despite the advantages against more conservative methods (1), free soft-tissue grafts involve a secondary intervention and demand an appropriate donor site, which, after the harvest, cures through secondary intention, and is more uncomfortable and painful requiring a more extended healing period (19).

Leukocyte- and platelet-rich fibrin (L-PRF) has a similar appearance to an autologous cicatricial matrix (6). L-PRF is a very dense fibrinogenic biomaterial with winning biomechanical and biological properties (Ehrenfest 2009) and broad application in several areas of Medicine (2,3,5,10,18). In this way, it serves as a biological healing matrix and acts as an immune regulation node with inflammation control abilities, supporting the cell migration and cytokines (6). Recently, it has emerged an advanced protocol with the decrease of rotations per minute (rpm) and increase of the centrifugation time, the so-called advanced platelet-rich fibrin (A-PRF), which results in the enhanced presence of neutrophilic granulocytes in the distal part of the clot (12). Also, literature points out that A-PRF is not only a scaffold *per se* but also a growth factors reservoir, with a continuous release action (11,15).

Thereupon, two randomized clinical trials have investigated the therapeutic potential of L-PRF on palatal wounds after free gingival graft harvesting (9,16). Whereas in (9) quadruple PRF membrane layers were placed over the wound and held with multiple sutures, in (16) the wound was spatially filled with the required and undefined amount of L-PRF and stabilized with cyanoacrylate adhesive on all borders and surfaces. Both trials have concluded that L-PRF stimulates palatal wound healing and improves patients' postoperative morbidity. However, there is a lack of studies that have investigated the influence of A-PRF on the wound area reduction nor the re-epithelization.

Therefore, this study aimed to assess the healing effect of A-PRF clot membranes in the reduction of palatal wounds after free gingival graft harvesting and to compare the post-surgical pain experience and complications with a conventional procedure.

2 | Materials and Methods

Study design

This was a prospective case-control study, assessor-blinded, with flipping coin randomization. To participate in the study, the following inclusion and exclusion criteria needed to be satisfied.

2.1.1 | Inclusion criteria

Inclusion criteria were (i) patient at least 18 years old, (ii) without systemic and periodontal diseases, (iii) no medical contraindications for periodontal surgery, (iv) adequate level of plaque control (plaque index <15%).

Exclusion criteria

Exclusion criteria were (i) smokers, (ii) patients with removable upper denture, (iii) patients taking medication that could interpose the healing process, (iv) patients undergoing bisphosphonate therapy, (v) patients with history of radiation therapy of the jaws, and (vi) patients who dropped follow-up consults.

Patients who met these criteria were invited to participate in the study after being thoroughly informed about the purpose of the clinical research. All patients that agreed to participate in the study were invited to sign the informed consent form. The study was approved by a Portuguese state recognized Ethics Committee (Ethics Committee of Egas Moniz - Cooperativa de Ensino Superior, C.R.L. - Process Ref. nº 601) and a written consent was obtained from all participants. This study was conducted following the obligations of the Helsinki Declaration of 1975 and revised in 2013. After the beginning of the study, there were no changes in the protocol nor the inclusion/exclusion criteria.

This protocol followed the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines (8).

Participants and randomization

The study took place between March and June 2018, involving patients referred to the Periodontology Department of Egas Moniz Dental Clinic (Almada, Portugal).

At the beginning of the study, and according to the sample size calculation (section 2.6), 30 patients in need of soft tissue augmentation (gingival recession coverage or augmentation of keratinized gingiva), which met the inclusion criteria, were enrolled to participate. They were, *a priori*, randomly 1:1 allocated to control (n=15) or A-PRF (n=15) groups, via coin toss, carried out by an assistant not involved in the study. Five of the patients refused to participate, resulting in a final sample of 25 individuals (n=11 control, n=14 A-PRF). During the 90 days' follow-up period, there were no subjects withdrawing the study.

Interventions

Prior to surgery, to ensure levels of plaque index below 15%, all participants received oral hygiene instructions and scaling, root planing and polishing. Alginate impressions were made for a palate protective splint production, to be used within two days after the surgery.

All interventions were performed under strict sterile conditions and local anesthesia (articaine 72 mg + epinephrine 0.009 mg / 1.8 mL). A free gingival graft with about 1.5 mm thickness was removed from the palatal area from first premolar to first molar, as described in (23). All surgeries were supervised by the same periodontist (RA). The treatment at the test site was performed as follows:

1. Preparation of A-PRF: It was performed a standard venipuncture (median basilica vein, median cubital vein, median cephalic vein). Ten mL of blood was drawn into a tube without anticoagulant (VACUETTE®; PRF Process™, Nice, France). A-PRF was prepared following (11). The tubes were immediately centrifuged according to the manufacturer instructions at 1,500 rpm for 8 minutes (DUO Quattro®; A-PRF Process™, Nice, France). After centrifugation, A-PRF clot from was removed from the tube and separated from the red element phase at the base with pliers. Then, A-PRF was delicately squeezed between a sterile metal plate and a metal box (gravity, no loading).
2. Palatal wound, as a result of free gingival graft harvesting, was occupied by two A-PRF clot membrane after careful positioning, and criss-cross sutures were done to hold it in position (Figure 1).

For the control group, the surgical wound as a result of the graft collecting was filled with lyophilized hydrolyzed collagen sponge (Technew™, Rio de Janeiro, Brazil) (Figure 1).

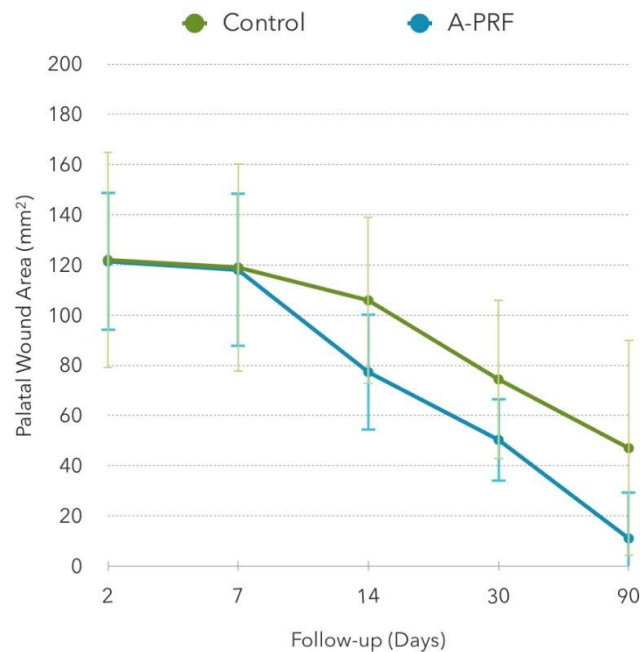


Figure 1. Surgical technique for application of advanced platelet-rich fibrin (A-PRF), and evaluation of postoperative epithelialization in the PRF and test groups at baseline, 14 days and 30 days after surgery.

All patients were advised to take paracetamol (1 g), three times a day, to use the protective splint for two days, avoid heat sources and opt for a cold and soft foods diet. To prevent results' bias, no type of disinfectant was indicated for use in the following days, due to difficulty in monitoring the frequency and duration of its use. Patients were scheduled for controls visit at 2, 7, 14, 30 and 90 days.

Two days after surgery, all patients returned the protective splint to prevent continued usage. Palatal sutures were removed at seven days after surgery, and receiving zone sutures at 14 days. The control protocol consisted in the assessment of the palatal wound healing area and evaluation of postoperative pain and discomfort sensation.

Primary outcomes: epithelialization of the palatal wound, wound healing area and percentage of reduction

Follow-up control protocol included palatal wound measuring, using a CP-12 probe, and photography of the wound healing area. Additionally, post-surgery, postoperative complications (hemorrhage, suppuration, edema and necrosis) were searched and properly recorded. For the epithelialization clinical appraisal, it was used the wound closure visual criteria of (17).

Secondary outcomes: postoperative pain and discomfort- sensation

Patient's pain and discomfort perceptions were rated using the visual analogue scale (VAS) score (0-10), and registered during the follow-up period.

Sample size and statistical analysis

The sample size was calculated to provide a power $1-\beta = 90\%$, with $\alpha = 5\%$, to detect the difference in the proportion of patients who exhibited epithelialization after three weeks among patients whose palatal wounds were treated with L-PRF (test group) and with an absorbable gelatin sponge (control group), as reported in (9). Under this principle a minimum of 7 patients per group (14 in total) would have been required. To avoid a loss of statistical power, as a consequence of patient drop-out, a total of 30 patients, who met the inclusion criteria, were enrolled to participate.

Data analysis was performed using IBM SPSS Statistics version 24.0 for Windows (Armonk, NY: IBM Corp.). Descriptive and inferential statistics methodologies were applied. Descriptive statistics such as mean and standard deviation (SD) or median and interquartile range (IQR) were calculated for the clinical scale and ordinal variables, respectively. Population means were estimated by calculating 95% confidence intervals (95% CI). In the inferential analysis, since the assumptions for valid parametric inference were not met, Mann-Whitney test was used to compare the primary clinical outcome (percentage decrease of palatal wound area) and the postoperative pain and discomfort sensation (VAS) between groups. Correlation between percentage decrease of wound area and postoperative pain and discomfort sensation with depth of the palate was assessed by Spearman's rank-order correlation coefficient. Fisher's exact test was used to compare total epithelialization proportion between groups. The level of statistical significance was set at 5% in all inferential analysis.

Results

Demographic data

Twenty-five patients participated in this prospective randomized case-control study. The mean age was 36.4 ± 14.9 years (range 19-65 years) and the female/male ratio was 16/9.

Palatal surgical wound area decrease, percentage of reduction and epithelialization

Results for the palatal wound area, as a function of the follow-up period, are displayed in Table 1 and represented in Figure 2. On the second day sutures were intact, and in the test group all A-PRF membranes were adherent to the palate.

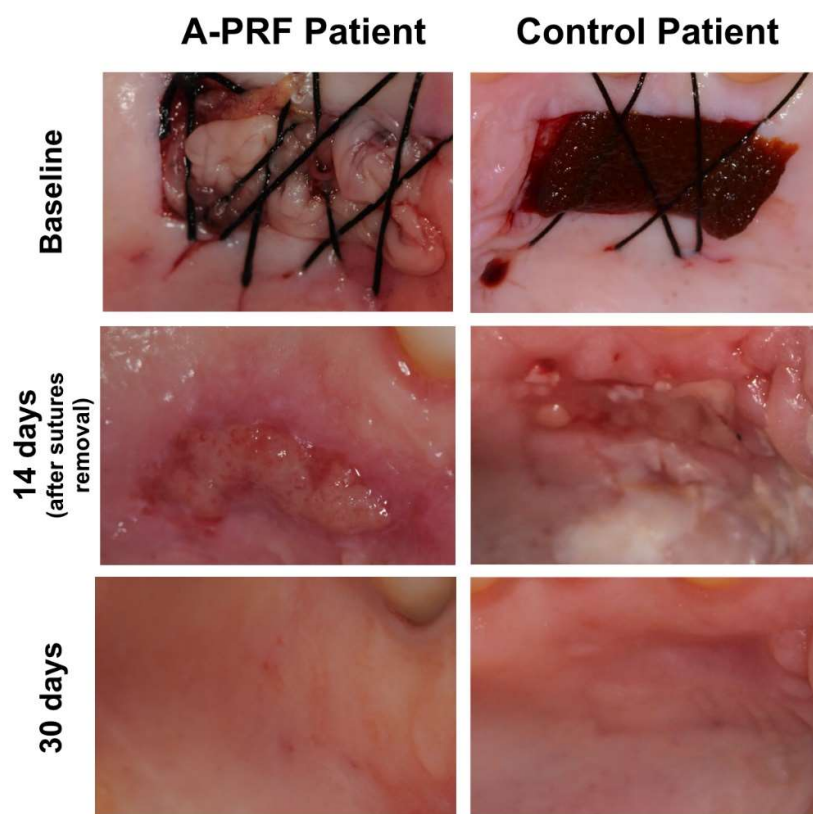


Figure 2. Palatal wound area (mm^2), evaluated along the follow-up visits, for the control ($n=11$) and A-PRF ($n=14$) groups.

Table 1. Palatal wound area (mm²), presented as mean (standard deviation - SD) and estimated mean (95% CI), evaluated at surgery and along the follow-up visits, for the control (n=11) and A-PRF (n=14) groups.

	Palatal wound area (mm ²)			
	Control Group		A-PRF Group	
Follow-up (days)	Mean (SD)	95% CI	Mean (SD)	95% CI
0 (surgery)	122.0 (43.1)	93.0-151.0	121.4 (27.8)	105.4-137.5
2	119.0 (41.6)	91.0-146.9	118.0 (30.8)	100.2-135.8
7	105.1 (33.4)	82.7-127.5	77.3 (23.3)	63.8-90.7
14	74.5 (31.9)	53.0-95.9	50.3 (16.6)	40.7-59.9
30	47.0 (17.2)	35.4-58.6	11.0 (18.8)	0.16-21.8
90	0 (0)	-	0 (0)	-

Table 2 presents the mean percentage reduction area of the palatal wound during the follow-up visits. A-PRF group shows a significant larger decrease percentage than the control group, at 7 ($p < 0.001$), 14 ($p = 0.009$) and 30 days ($p < 0.001$), conversely to the first two days after surgery, where no statistical significant difference was found ($p = 0.687$). Maximum difference between groups was attained at 30 days (91.5% for A-PRF vs. 59.0% for the control group). At 90 days, both groups showed total recovery.

Table 2. Percentage decrease of the palatal wound area, presented as mean (standard deviation - SD), along the follow-up visits, for the control (n=11) and A-PRF (n=14) groups.

Follow-up (days)	Palatal wound reduction area (%)		p^*
	Control Group Mean (SD)	A-PRF Group Mean (SD)	
2	2.0 (5.1)	2.9 (10.7)	0.687
7	12.9 (12.2)	36.4 (12.2)	< 0.001
14	36.6 (20.4)	58.0 (14.2)	0.009
30	59.0 (14.3)	91.5 (14.6)	< 0.001
90	100.0 (0.0)	100 (0.0)	-

* Mann-Whitney test

The baseline palatal depth ranged from 3 to 5 mm (control group) and 2 to 6 mm (A-PRF group), with an average of 3.8 (0.6) and 3.6 (1.1) mm, respectively. Moreover, when assessing the healing rate, via the the percentage reduction of wound area, as a function of the depth of the palate, a significant negative correlation occurred for the A-PRF group, at 30 days' follow-up (Spearman's correlation coefficient = -0.61, $p = 0.021$), indicating that in palates with greater baseline thickness, A-PRF accelerated the recovery. Additionally, correlation of palatal depth with the postoperative pain sensation was not found to be significant in either of the groups.

Table 3 displays the epithelization rate for both groups, along with the follow-up period (Figure 1). At 14 days a significant difference in the proportion of patients showing total epithelization was found: 64.3% for A-PRF vs. 9.1% for the control group ($p=0.012$). At 30 days, total epithelization was observed in more than 90% of the patients (92.9% for A-PRF vs. 90.9% for the control group), the difference being not statistically significant ($p=1.000$).

Table 3 Total epithelization, presented as n (%), along the follow-up visits, for the control (n=11) and A-PRF (n=14) groups

Follow-up (days)	Total epithelization, n (%)		p^*
	Control Group	A-PRF Group	
2	0 (0.0)	0 (0.0)	-
7	0 (0.0)	0 (0.0)	-
14	1 (9.1)	9 (64.3)	0.012
30	10 (90.9)	13 (92.9)	1.000
90	11 (100.0)	14 (100.0)	-

* Fisher's exact test

Postoperative complications

Postoperative complications were identified at the second day (hemorrhage: one patient in the control group and two patients in the A-PRF group) and at the seventh day, in the control group, one patient exhibited necrosis of donor site margins.

Postoperative pain experience

Overall, the control group experienced a higher level of pain and discomfort until the 14th day being significantly higher at the second day ($p=0.013$). Subjects in the A-PRF group felt pain only until the second day after surgery. At 30 and 90 days no pain was detected in either of the groups (Table 4).

Table 4. Postoperative pain experience, recorded through a VAS and presented as median (interquartile range - IQR), along the follow-up visits, for the control (n=11) and A-PRF (n=14) groups.

	Postoperative pain experience (VAS)				
	Control Group		A-PRF Group		<i>p</i> *
Follow-up (days)	Median (IQR)	Min.-Max.	Median (IQR)	Min.-Max.	
2	2.0 (2)	0-9	0.0 (1)	0-7	0.013
7	1.0 (2)	0-9	0.0 (0)	0-0	-
14	0.0 (0)	0-5	0.0 (0)	0-0	-
30	0.0 (0)	0-0	0.0 (0)	0-0	-
90	0.0 (0)	0-0	0.0 (0)	0-0	-

* Mann-Whitney test

Discussion

In this prospective randomized clinical study, we used A-PRF to accelerate palatal wound healing, as a result of free gingival graft. The main results demonstrate that A-PRF benefits palatal tissue recovery up to 30 days after surgery, and, as expected, from there up to 90 days this difference vanishes. Thus, we can state that A-PRF as a palatal dressing enhances the patient's surgery experience by improving healing of the donor site. These outcomes are in accordance with previous studies that have investigated other types of PRF for the same purpose (9,13,16,20).

Nevertheless, although from the short-term view A-PRF significantly promotes the re-epithelialization of the wound (on day 14), from a long-term perspective it was not shown to be significant, as observed at 30 days after surgery. In fact, being the first time A-PRF is used in this palatal bandage procedure, there are no forms of comparison other than other types of PRF. Plausibly, this difference may be due to the smaller thickness / quantity of the PRF membranes used in our study, since similar results have been found using single membranes of PRF and T-PRF (13,20), and are different described in Femminella et al. (9), that used quadruple layer clots. Therefore, apparently the thicker the PRF the lower its degradation and the faster the re-epithelialization process. However, this should be confirmed with a more comprehensive and dedicated randomized clinical trial.

Taking into consideration the patient's pain experience perspective, A-PRF group participants apparently had a minimal but significant less sense of pain. However, there is insufficient data to associate this less experience with the placement of A-PRF membranes, since we cannot dissociate the possible effect of the extent and time of the periodontal surgery performed. Furthermore, it is difficult to isolate the pain originating from donor and recipient site, particularly if they are on the same quadrant. Therefore, in the future, this matter must be broadly and deeply investigated.

Noteworthy, deeper palates showed better healing results using A-PRF, which can be explained by the wealth of growth factors present in this type of platelet-concentrated biomaterial. Yet, according to Wyrębek et al. (22) pain had no association with the free gingival graft length and width, although they did not consider the initial thickness of the palate, and in our investigation the thickness of the graft was not measured, which may explain the powerlessness with post-surgery pain.

Since its introduction, A-PRF has been extensively studied in its composition, biocompatibility and performance in vitro (11,12,15,21). Clinically, A-PRF exhibited promising characteristics as biomaterial for ridge preservation (4) and regenerative periodontal therapy (14), although its limits are little explored. Regarding the limitations of this study, A-PRF maintains some major disadvantages of the PRF technique. PRFs require blood collection and careful handling, there is vague knowledge on the leukocytes, platelets and growth factors concentration on the clots, and the established protocols are highly variable. Additionally, while these results are encouraging, we can't forget the fact that this study design lacks RCT methodology, such as random sequence generation and allocation concealment, since the remaining aspects were covered. Also, patient-centered outcome measures, like oral health-related quality of life, and thorough medication dosage should be pondered in future investigations, since these surgical adjunct healing procedures aim to improve patient experience periodontal surgeries.

Conclusion

Despite the limitations of this study, the results suggest that A-PRF membranes accelerate the healing process by promoting a higher reduction along the recovery period and an apparent less painful postoperative period.

Ethics statement/confirmation of patients' permission

This study was approved by the Ethics Committee of Egas Moniz. All participants gave their signed informed consent.

Conflicts of interest

All authors declare no personal, commercial and financial relationships.

Funding information

The materials were kindly provided on a temporary basis by PRF Process™, France. This research was initiated by the investigators who independently performed all phases of the study including protocol development, experimental procedures, data analysis, result interpretation and reporting.

Clinical Relevance

The use of A-PRF dressings may be a simple and effective method of accelerating the healing process and reducing post-operative discomfort associated with free gingival graft harvesting.

References

1. Bennani, V, Ibrahim H, Al-Harathi L LK. The periodontal restorative interface : esthetic considerations. *Perio 2000* 2017; 74: 74–101.
2. Castro AB, Meschi N, Temmerman A, *et al.* Regenerative potential of leucocyte- and platelet-rich fibrin. Part A: intra-bony defects, furcation defects and periodontal plastic surgery. A systematic review and meta-analysis *J Clin Periodontol* 2017; 44: 67–82.
3. Castro AB, Meschi N, Temmerman A, *et al.* Regenerative potential of leucocyte- and platelet-rich fibrin. Part B: sinus floor elevation, alveolar ridge preservation and implant therapy. A systematic review. *J Clin Periodontol* 2017; 44: 225–234.
4. Clark D, Rajendran Y, Paydar S, *et al.* Advanced platelet-rich fibrin and freeze-dried bone allograft for ridge preservation: A randomized controlled clinical trial. *J Periodontol* 2018; 89: 379–387.
5. Ding H, Yuan JQ, Zhou JH, *et al.* Systematic review and meta-analysis of application of fibrin sealant after liver resection. *Curr Med Res Opin* 2013; 29: 387–394.
6. Dohan DM, Choukroun J, Diss A, *et al.* Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part III: Leucocyte activation: A new feature for platelet concentrates? *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology* 2006; 101.
7. Dragan IF, Ms DDS, Paterno L, *et al.* Clinical Outcomes of Comparing Soft Tissue Alternatives to Free Gingival Graft: A Systematic Review and Meta-Analysis. *J Evid Based Dent Pract* 2017; 17: 370–380.e3.
8. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Int J Surg* 2014; 12: 1495–1499.
9. Femminella B, Iaconi MC, Di Tullio M, *et al.* Clinical Comparison of Platelet-Rich Fibrin and a Gelatin Sponge in the Management of Palatal Wounds After Epithelialized Free Gingival Graft Harvest: A Randomized Clinical Trial. *J Periodontol* 2016; 87: 103–113.
10. Fredes F, Pinto J, Pinto N, *et al.* Potential Effect of Leukocyte-Platelet-Rich Fibrin in Bone Healing of Skull Base: A Pilot Study. 2017 Epub.
11. Fujioka-Kobayashi M, Miron RJ, Hernandez M, Kandalam U, Zhang Y, Choukroun J. Optimized Platelet-Rich Fibrin With the Low-Speed Concept: Growth Factor Release, Biocompatibility, and Cellular Response. *J Periodontol* 2017; 88: 112–121.
12. Ghanaati S, Booms P, Orlowska A, *et al.* Advanced Platelet-Rich Fibrin: A New Concept for Cell-Based Tissue Engineering by Means of Inflammatory Cells. *J Oral Implantol* 2014; 40: 679–689.

13. Kulkarni MR, Thomas BS, Varghese JM, Bhat GS. Platelet-rich fibrin as an adjunct to palatal wound healing after harvesting a free gingival graft: A case series. *J Indian Soc Periodontol* 2014; 18: 399.
14. Lei L, Yu Y, Ke T, Sun W, Chen L. The application of three-dimensional printing model and platelet-rich fibrin (PRF) technology in guided tissue regeneration surgery for severe bone defects. 2018 Epub.
15. Masuki H, Okudera T, Watanebe T, *et al.* Growth factor and pro-inflammatory cytokine contents in platelet-rich plasma (PRP), plasma rich in growth factors (PRGF), advanced platelet-rich fibrin (A-PRF), and concentrated growth factors (CGF). *Int J Implant Dent* 2016; 2: 19.
16. Ozcan M, Ucak O, Alkaya B, Keceli S, Seydaoglu G, Haytac M. Effects of Platelet-Rich Fibrin on Palatal Wound Healing After Free Gingival Graft Harvesting: A Comparative Randomized Controlled Clinical Trial. *Int J Periodontics Restorative Dent* 2017; 37: e270–e278.
17. Silva CO, Ribeiro ÉDP, Sallum AW, Tatakis DN. Free Gingival Grafts: Graft Shrinkage and Donor-Site Healing in Smokers and Non-Smokers. *J Periodontol* 2010; 81: 692–701.
18. Theys T, Hoylandt A Van, Broeckx C, *et al.* Plasma-rich fibrin in neurosurgery : a feasibility study 2018 Epub.
19. Tomar N, Singh R, Jain G, Kaushik M, Dureja D. Enhancement of healing of donor hard palate site using platelet-rich fibrin. *J Curr Res Sci Med* 2016; 2: 132.
20. Ustaoglu G, Ercan E, Tunali M. The role of titanium-prepared platelet-rich fibrin in palatal mucosal wound healing and histoconduction. *Acta Odontol Scand* 2016; 74: 558–564.
21. Watanabe T, Isobe K, Suzuki T, *et al.* An Evaluation of the Accuracy of the Subtraction Method Used for Determining Platelet Counts in Advanced Platelet-Rich Fibrin and Concentrated Growth Factor Preparations. *Dent J* 2017; 5: 7.
22. Wyrebek B, Gorski B, Gorska R. Patient morbidity at the palatal donor site depending on gingival graft dimension. *Dent Med Probl* 2018; 55: 153–159.
23. Zuhr O, Bäumer D, Hürzeler M. The addition of soft tissue replacement grafts in plastic periodontal and implant surgery: Critical elements in design and execution. *J Clin Periodontol* 2014; 41: S123-S142.