





### ANTHEC | ACADEMY OF NON TRANSFUSIONAL HEMO-COMPONENTS

ANTHEC Associazione medici, Accademia emocomponenti

### Milano - 25 Marzo 2023

# Aggiornamento sugli Emocomponenti a Uso Non Trasfusionale (EunT)







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### Gli emocomponenti ad uso non trasfusionale:



dalla letteratura alla clinica

Massimo Del Fabbro & Tiziano Testori

Università degli Studi di Milano



Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico

IRCCS Ospedale Galeazzi-Sant'Ambrogio





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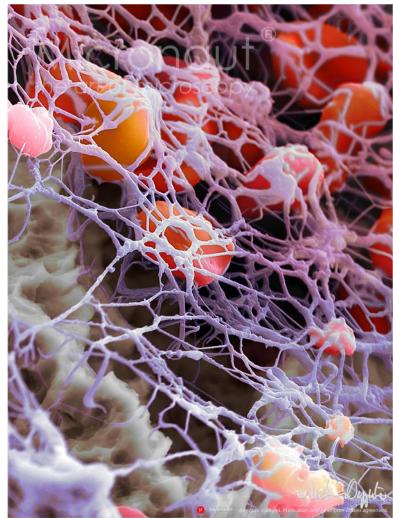
Università degli Studi di Milano

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### **Platelet concentrates:**

- release large amounts of growth factors
- Trigger tissue healing and recall progenitor cells
- promote the formation of a 3D fibrin mesh



#### **Journey of Platelet Concentrates: A Review**

#### Komal Saini, Priyanka Chopra and Vidushi Sheokand

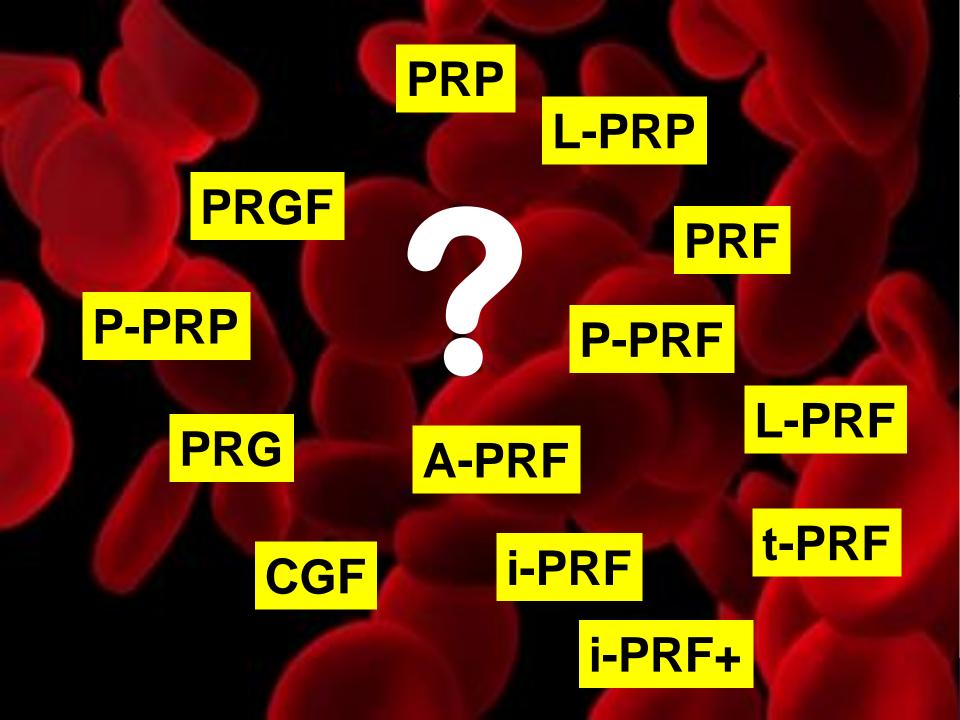
Department of Periodontology, SGT University, Gurugram, India. \*Corresponding Author E-mail: drpriyankachopra79@gmail.com

http://dx.doi.org/10.13005/bpj/1875

(Received: 29 May 2019; accepted: 17 January 2020)

One of the important action of platelets is their role in haemostasis and healing of wound. Now they are gaining popularity in Dentistry in periodontal regeneration. Earlier fibrin glue was introduced as sealant, later the platelet-rich plasma (PRP); first generation of platelet concentrates was utilized in various fields of Dermatology from chronic ulcer management to trichology and also in aesthetics. Choukroun et al. in Francein 2000's introduced the second generation of platelet concentrates (PRF)Platelet Rich Fibrin. PRF have comparatively several advantages over traditionally prepared PRP. In this review we are focusing on why Platelet Concentrates are so important in Healing and Regeneration and we will also discuss the journey of fibrin glue from PRP to PRF, i-PRF, L-PRF etc.

Keywords: Platelet concentrates, PRP, PRF, and Wound Healing.



### Recent evolution of platelet concentrates

|                 | Year | N. CF | tubes    | Anticoag | rpm                     | min     | RCF   |
|-----------------|------|-------|----------|----------|-------------------------|---------|-------|
| PRP (L-PRP)     | 1997 | 2     | glass    | Y        | 1300x10'+2000x10'       |         |       |
| /PRG            |      |       |          |          | >20 different protocols |         |       |
| PRGF (P-PRP)    | 1999 | 1     | glass    | Y        | 1800                    | 8'      | 580g  |
| PRF (L-PRF)     | 2000 | 1     | glass    | Ν        | 2700/3000               | 12'/10' | 400g  |
| CGF             | 2006 | 1     | glass    | Ν        | Alternate speed tot 12' |         |       |
| A-PRF           | 2013 | 1     | glass    | Ν        | 1500                    | 14'     | 208g  |
| T-PRF           | 2013 | 1     | titanium | Ν        | 2800                    | 12'     | ~400g |
| i-PRF / i-PRF M | 2014 | 1     | plastic  | Ν        | 700                     | 3'      | 100g  |
| A-PRF+          | 2016 | 1     | glass    | Ν        | 1300                    | 8'      | 180g  |
| i-PRF+          | 2015 | 1     | plastic  | Ν        | 700                     | 3'      | 100g  |
| S-PRF           | 2017 | 1     | plastic  | Ν        | 1300                    | 14'     | 180g  |
| C-PRF           | 2020 | 1     | plastic  | Ν        | 2000                    | 8′      |       |
| E-PRF           | 2020 | 1     | plastic  | Ν        | 700                     | 8'      |       |

# Research topics (for laboratory)

### VARIABLES

- centrifugation protocol (time, speed, RCF, acceleration/deceleration)
- tube material (glass, plastic, titanium)
- inclination during centrifugation
- centrifuge features (vibration)

### <u>OUTCOMES</u>

- Cell (platelet/WBC) concentration
- Cell distribution
- Growth factor concentration
- Pattern of growth factor release
- Growth factors activity cell cultures
- Mechanical/biophysical properties of the final product

#### The impact of the centrifuge characteristics and centrifugation protocols on the cells, growth factors, and fibrin architecture of a leukocyte- and platelet-rich fibrin (L-PRF) clot and membrane

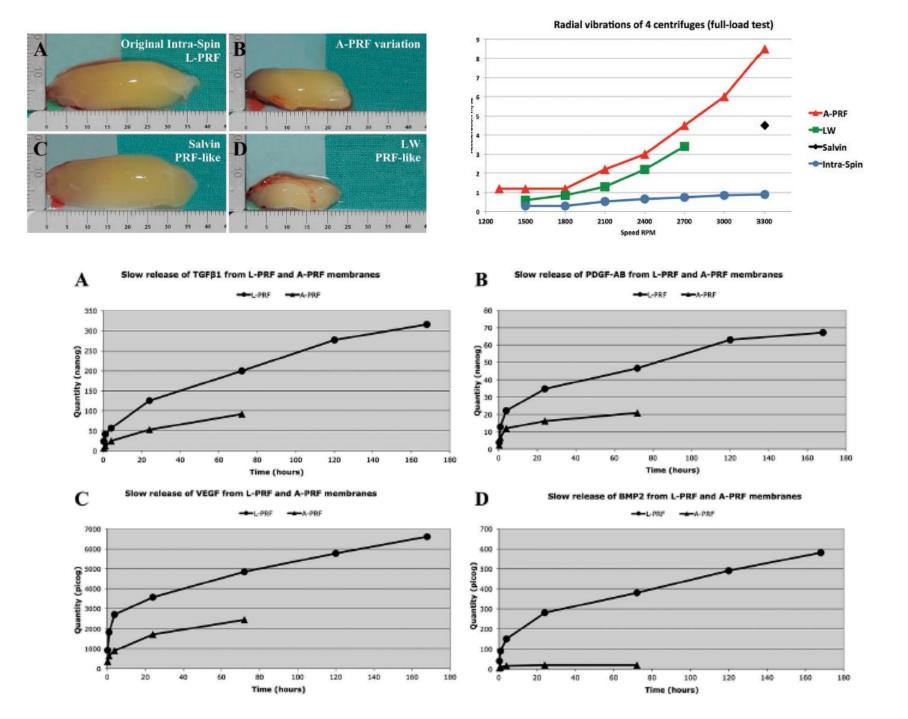
2018

David M. Dohan Ehrenfest<sup>1,2</sup>, Nelson R. Pinto<sup>3,4</sup>, Andrea Pereda<sup>3</sup>, Paula Jiménez<sup>3</sup>, Marco Del Corso<sup>5</sup>, Byung-Soo Kang<sup>6</sup>, Mauricio Nally<sup>3</sup>, Nicole Lanata<sup>7</sup>, Hom-Lay Wang<sup>8</sup>, & Marc Quirynen<sup>4</sup>



Table I. Results of the macroscopic analysis of the clots and membranes produced with the four tested centrifuges. Values expressed in Mean and Standard Deviation (SD).

| Variable                                | IntraSpin<br>Mean (SD) | A-PRF<br>Mean (SD) | Salvin<br>Mean (SD) | LW<br>Mean (SD) |
|---|------------------------|--------------------|---------------------|-----------------|
| Final T° of tube (°C)                   | 27.5 (0.66)            | 28.83 (0.67)       | 28.8 (0.66)         | 27.88 (0.57)    |
| Clot weight (g)                         | 2.09 (0.19)            | 1.38 (0.24)        | 1.73 (0.27)         | 0.74 (0.15)     |
| Membrane weight (g)                     | 0.62 (0.15)            | 0.48 (0.17)        | 0.6 (0.19)          | 0.3 (0.25)      |
| Exudate weight (g)                      | 1.47 (0.13)            | 0.9 (0.21)         | 1.12 (0.27)         | 0.44 (0.26)     |
| Clot length (mm)                        | 35.69 (3.43)           | 26.56 (4.25)       | 35.25 (4.1)         | 20.12 (4.29)    |
| Clot width (mm)                         | 12.81 (0.75)           | 10.93 (1.08)       | 13.06 (0.94)        | 9.12 (1.13)     |
| Membrane length (mm)                    | 34.81 (2.95)           | 26.81 (3.38)       | 34.43 (2.87)        | 21.5 (2.39)     |
| Membrane width (mm)                     | 12.25 (0.71)           | 10.37 (0.92)       | 11.93 (0.78)        | 9.12 (0.64)     |
| Weight ratio(%) clot/blood sample 10 ml | 20.94 (2.4)            | 13.98 (2.6)        | 17.42 (2.63)        | 7.41 (1.45)     |

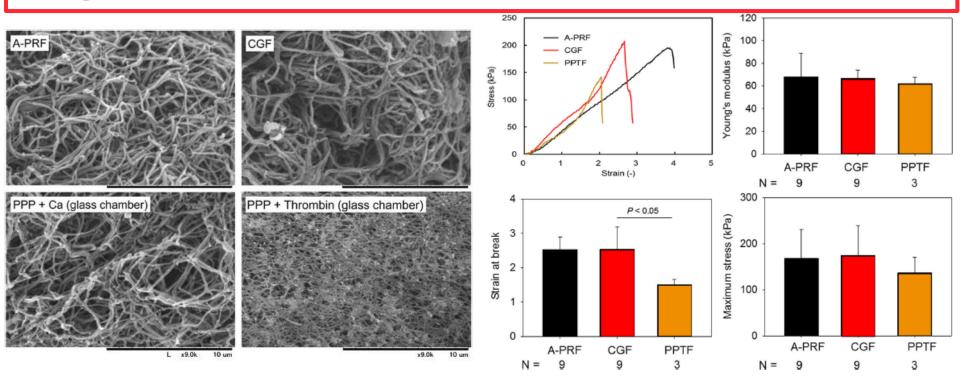


#### Mechanical and degradation properties of advanced platelet-rich fibrin (A-PRF), concentrated growth factors (CGF), and platelet-poor plasma-derived fibrin (PPTF)



Kazushige Isobe<sup>1</sup>, Taisuke Watanebe<sup>1</sup>, Hideo Kawabata<sup>1</sup>, Yutaka Kitamura<sup>1</sup>, Toshimitsu Okudera<sup>1</sup>, Hajime Okudera<sup>1</sup>, Kohya Uematsu<sup>2</sup>, Kazuhiro Okuda<sup>3</sup>, Koh Nakata<sup>4</sup>, Takaaki Tanaka<sup>5</sup> and Tomoyuki Kawase<sup>6\*</sup>

**Conclusions:** Although the centrifugal conditions are different, A-PRF and CGF are prepared by essentially identical mechanisms. Therefore, it is conceivable that both membranes have similar mechanical and chemical properties. Only PPTF, which was prepared by a different mechanism, was characterized as mechanically weaker and enzymatically more degradable.

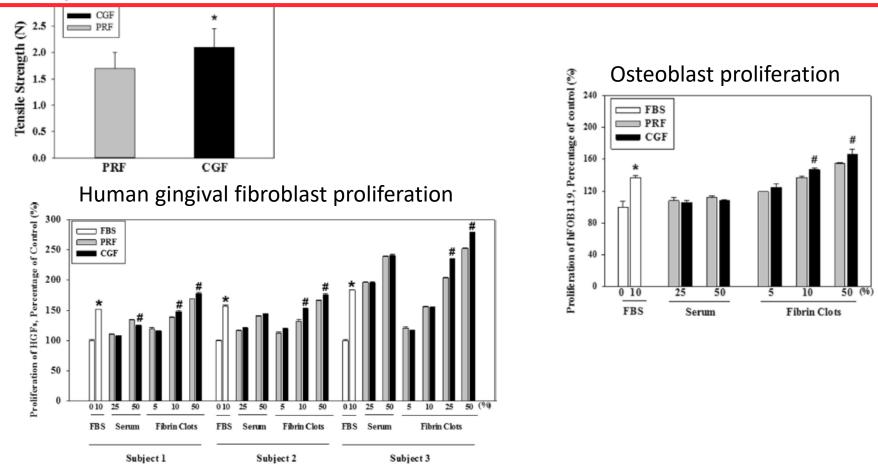


#### Tensile strength, growth factor content and proliferation activities for two platelet concentrates of platelet-rich fibrin and concentrated growth factor



Hung-Maan Lee <sup>a,b</sup>, E-Chin Shen <sup>c,d</sup>, John T. Shen <sup>e</sup>, Earl Fu <sup>c,d</sup>, Hsien-Chung Chiu <sup>c,d</sup>, Yi-Jan Hsia <sup>c,d</sup>\*

Conclusion: Varying centrifugation speeds can modify the tensile strength and biological activities of platelet fibrin clots.



# Comparison of platelet-rich fibrin (PRF) produced using 3 commercially available centrifuges at both high (~ 700 g) and low (~ 200 g) relative centrifugation forces



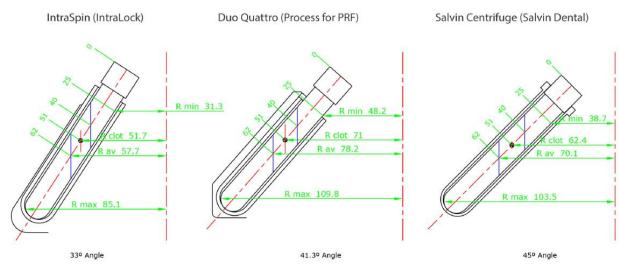
Richard J. Miron<sup>1,2</sup> • Hudi Xu<sup>1</sup> • Jihua Chai<sup>1</sup> • Jiaolong Wang<sup>1</sup> • Shihang Zheng<sup>1</sup> • Mengge Feng<sup>1</sup> • Xia Yan Wei<sup>1</sup> • Yan Chen<sup>1</sup> • Carlos Fernando de Almeida Barros Mourão<sup>3</sup> • Anton Sculean<sup>2</sup> • Yufeng Zhang

PRF produced at <u>low RCF</u> (200g), respect to <u>high RCF</u> (700g):

- contained higher conc. of evenly distributed platelets
- secreted higher conc. GFs over 10 days
- were smaller in size

independent of the centrifuge used.

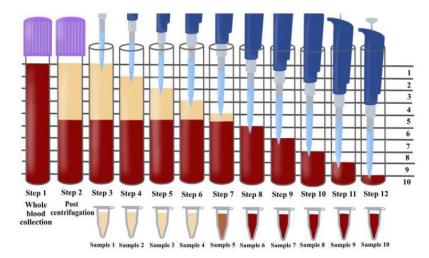
The type of <u>tube</u> also has a significant impact on the size and quality of the PRF clot

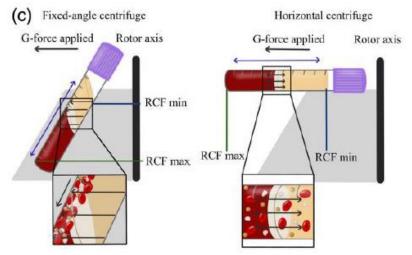


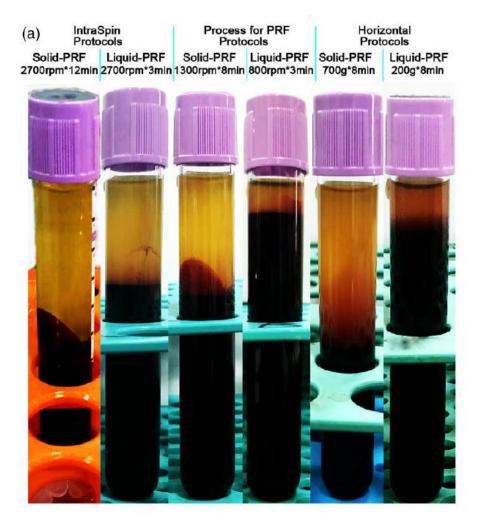
#### A novel method for evaluating and quantifying cell types in platelet rich fibrin and an introduction to horizontal centrifugation

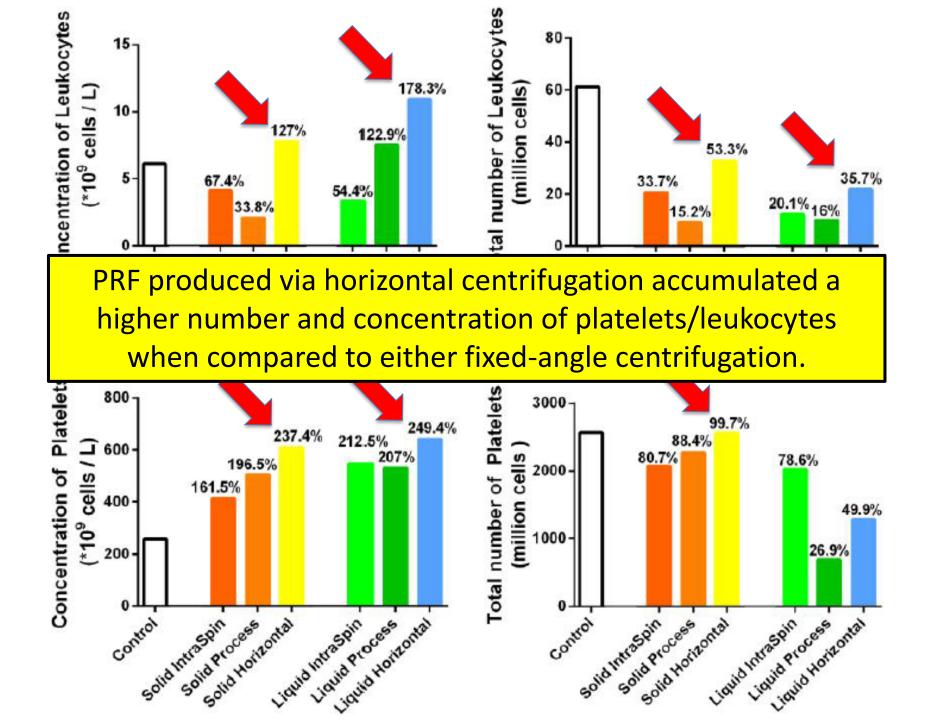
2019

Richard J. Miron<sup>1,2</sup> | Jihua Chai<sup>1</sup> | Shihang Zheng<sup>1</sup> | Mengge Feng<sup>1</sup> | Anton Sculean<sup>2</sup> | Yufeng Zhang<sup>1,3</sup> <sup>1</sup>









# Research question (for clinics)

### Which is the best protocol?

### How to know? What to measure?



# Research question (for clinics)

## Which is the best protocol?

### How to know? What to measure?

### MAIN OUTCOMES

- Hard tissue healing
- Soft tissue healing
- Incidence of complications/adverse events
- Control of infection
- Patient's quality of life/satisfaction for esthetics/function
- Facilitation of operative procedures

Focused questions (for clinics)

**Do platelet concentrates work?** 

### Which is the «most effective» product?

## We need clinically relevant QUESTIONS

and evidence-based ANSWERS !

### **WELL-BUILT CLINICAL QUESTION**

## **PICO(S) question**:

- 1. Patient or Population
- 2. Intervention
- 3. Comparison
- 4. Outcome
- 5. (**S**tudy design)





#### Absolute effect

"In patients suffering from XX bone defects is the adjunct of platelet concentrates beneficial respect to standard treatment in terms of defect reduction? "

#### **Relative effect**

"In patients with XX defect, is the use of PRP or PRGF as effective as PRF in terms of tissue healing (any healing parameter)?"

### How to answer to the focused questions ?





### Two ways:

**Literature Review** 

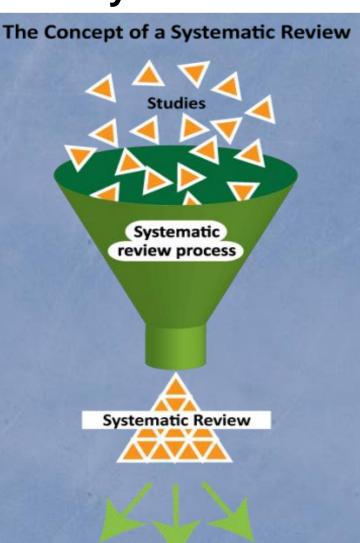
### **1. Perform evidence-based studies**

### **2. Scan the literature**



# The best evidence from the literature: systematic reviews & meta-analyses

- transparent methods (search, selection, evaluation)
- objective evaluation
- quality assessment of the studies
- results based on "filtered" evidence
- identification of the certainness and of the limits of the current available evidence
- recommendations for the clinical practice
- indications for future research
- upgradable as new evidence appears
  - THE OUTCOME OF SYSTEMATIC REVIEWS DEPENDS ON THE QUALITY OF THE AVAILABLE STUDIES





## **Overview of the recent literature**

What is the popularity of platelet concentrates in the different fields of medicine?

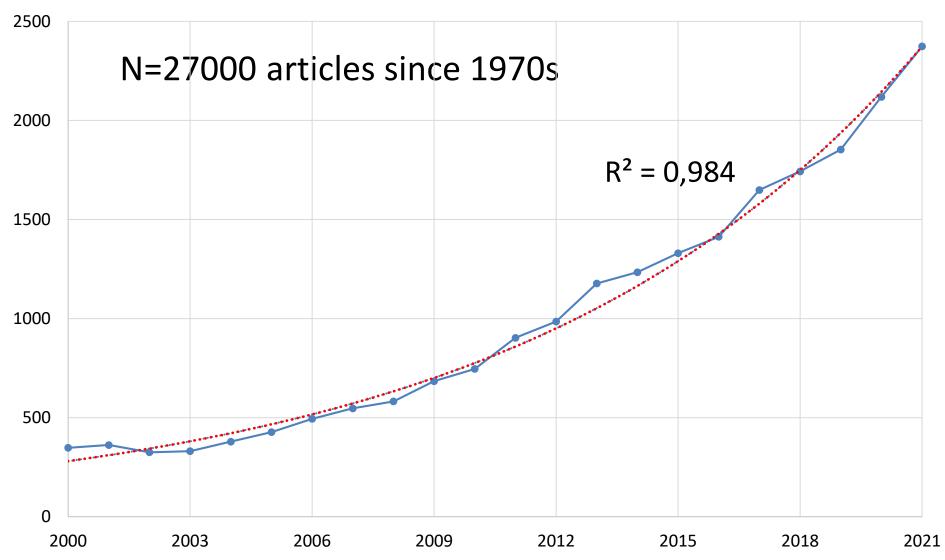
What is the strength of evidence?

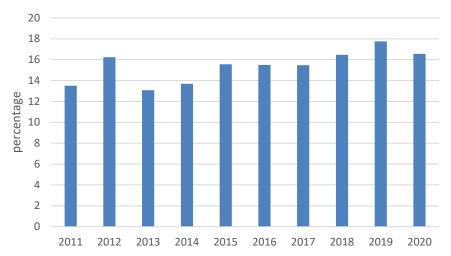


### Exponential growth

publications on platelet concentrates

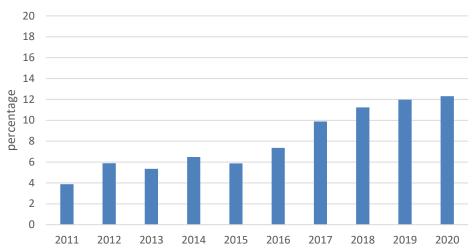




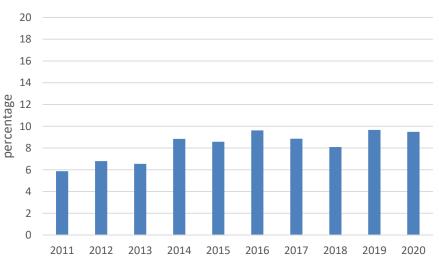


#### Oral and craniofacial surgery

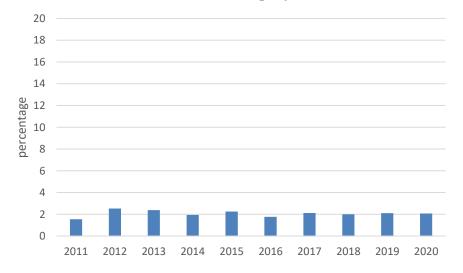
#### Dermatology- Plastic surgery



**Orthopedics & Traumatology** 



Vascular Surgery





Traditionally, PCs in dentistry have been used for

- maxillary sinus augmentation
- intrabony periodontal defects
- post-extraction ridge preservation

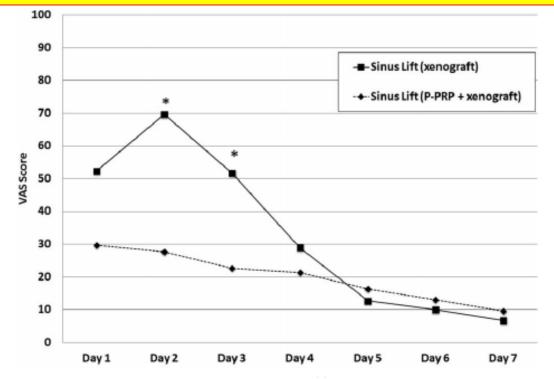
# Maxillary Sinus augmentation

#### Plasma Rich in Growth Factors Improves Patients' Postoperative Quality of Life in Maxillary Sinus Floor Augmentation: Preliminary Results of a Randomized Clinical Study

# Clin Impl Dent Rel Res 2015;17:708-716

Massimo Del Fabbro, BSc, PhD;\* Stefano Corbella, DDS, PhD;<sup>†</sup> Valentina Ceresoli, MSc;<sup>‡</sup> 1 Caterina Ceci, MSc;<sup>§</sup> Silvio Taschieri, MD, DDS<sup>§</sup>

# The adjunct of PRGF reduces pain, swelling and other symptoms during the first week after maxillary sinus floor augmentation



### Platelet-Rich Plasma and Deproteinized Bovine Bone Matrix in Maxillary Sinus Lift Surgery: A Split-Mouth Histomorphometric Evaluation

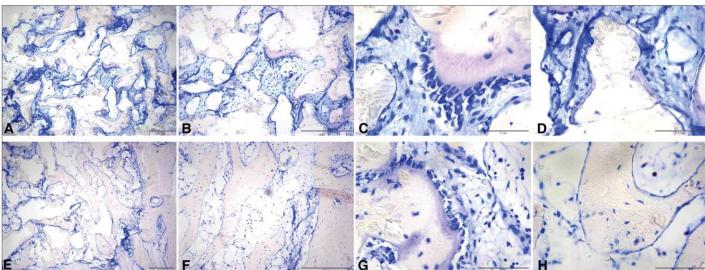
Silvio Taschieri, MD, DDS,\* Tiziano Testori, MD, DDS,† Stefano Corbella, DDS, PhD,‡ Roberto Weinstein, MD, DDS,§ Luca Francetti, MD, DDS,¶ Alessia Di Giancamillo, VD, PhD,|| and Massimo Del Fabbro, BSc, PhD#

### **Implant Dentistry 2015**

### 6 split-mouth patients 6 months CTR (DBBM alone)

Vital bone %: 22.72 : 9.21%

TEST(DBBM+PRGF) Vital bone %: 30.70 ±7.89%



#### Effect of Autologous Growth Factors in Maxillary Sinus Augmentation. A Systematic Review

Massimo Del Fabbro, BSc, PhD; Monica Bortolin, BMT; Silvio Taschieri, MD, I Roberto L. Weinstein, MD, DDS

**CIDRR 2013** 

#### Effects of Platelet-Rich Plasma on Sinus Bone Graft: Meta-Analysis **JOP 2011**

Ji-Hyun Bae,\* Young-Kyun Kim,<sup>†</sup> and Seung-Kwon Myung<sup>†</sup>

Effects of platelet-rich plasma in association with hone grafts in

C. A. A. Lemos, C. C. Mello, D. M. dos Santos, F. R. Verri, M. C. Goiato, E. P. Pellizzer Department of Dental Materials and Effectiveness of platelet-rich plasma as an adjunctive material to bone graft: a systematic review and

A. Pocaterra<sup>1</sup>, S. Caruso<sup>2</sup> S. Bernardi<sup>2</sup>, L. Scagnoli<sup>3</sup>, M. A. Continenza<sup>2</sup>, R. Gatto<sup>2</sup> <sup>1</sup>School of Dentistry, University of L'Aquila, L'Aquila, Italy; <sup>2</sup>Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy; <sup>3</sup>Private Practice, Rome, Italy

ON/C

201

Systematic reviews could not find a clear advantage of platelet concentrates for improving bone healing.

Advantages in graft handling, perforation management, pain and symptoms reduction, and shortening graft maturation time were reported. Standardization of the experimental design and procedures is necessary to

#### understand the true effect of platelet concentrates

bone and growin laciors of (solely) bone substitutes. A systematic review

nds; demic ningen 2012

review

#### **Review** Article

Review Sinus Lift Associated with Leucocyte-Platelet-Rich Fibrin (Second Generation) for Bone Gain: A Systematic Review

Ada Isis Pelaez Otero <sup>1</sup>, Juliana Campos Hasse Fernandes <sup>2</sup>, Tiago Borges <sup>1,3</sup>, Leo **JCM 2022** Rogerio de Moraes Castilho <sup>5</sup> and Gustavo Vicentis de Oliveira Fernandes <sup>3,5,\*</sup>

The Effect of Autologous Platelet Concentrates on Maxillary Sinus Augmentation: A Meta-Analysis of Randomized Controlled Trials and Systematic Review **BMR Int 2020** 

Suárez-López del Amo & Monje Efficacy of Biologics for Alveolar Ridge Preservation/Reconstruction and Implant Site JOP 2022 in press Development: An American Academy of Periodontology Best Evidence Systematic Review

"Histomorphometric outcomes were positively influenced by the use of biologics.»

implant therapy. A systematic

Do osteoconductive bone substitutes result in similar bone regeneration for maxillary sinus augmentation when compared to osteogenic and osteoinductive bone grafts? A systematic review and frequentist network meta-analysis

International Journal of Oral & Maxillofacial Surgery

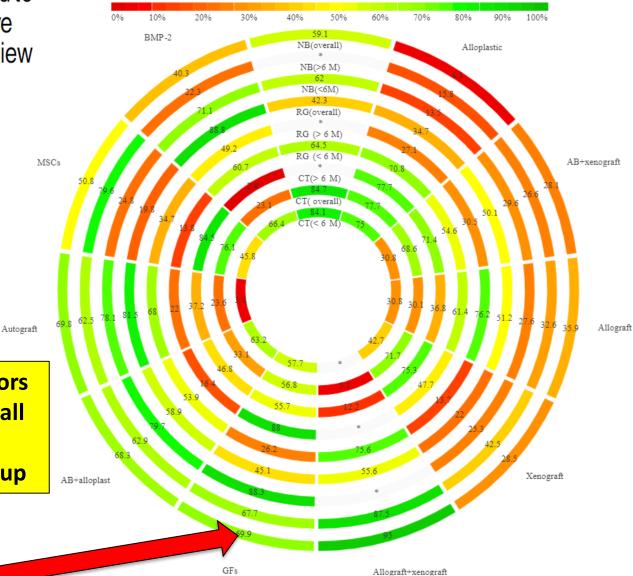
The adjunct of growth factors had the best effect among all biomaterials on new bone formation in a <6m follow-up

E. A. Al-Moraissi<sup>1</sup>, A. S. Alkhutari<sup>1</sup>, B. Abotaleb<sup>2</sup>, N. H. Altairi<sup>1</sup>, M. Del Fabbro<sup>3,4</sup> <sup>1</sup>Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Thamar University, Thamar, Yemen; <sup>2</sup>Department of Oral and Maxillofacial Surgery, Faculty of

Dentistry, Ibb University, Ibb, Yemen; <sup>3</sup>Department of Biomedical, Surgical and Dental Sciences, Università degli Studi di

Milano, Milan, Italy; <sup>4</sup>IRCCS Orthopedic Institute Galeazzi, Milan, Italy

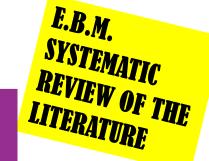




# Periodontal defects







#### Autologous platelet concentrates for treating periodontal infrabony defects (Review)

Del Fabbro M, Karanxha L, Panda S, Bucchi C, Nadathur Doraiswamy J, Sankari M, Ramamoorthi S, Varghese S, Taschieri S. Autologous platelet concentrates for treating periodontal infrabony defects. Cochrane Database of Systematic Reviews 2018, Issue 11. Art. No.: CD011423.

- 38 RCTs included, 1016 pts, 1402 teeth(defects)
- (22 sp

Outcome

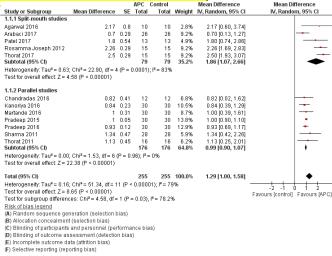
24 further RCTs (and 19 SRs/MAs) published since publication of this Cochrane review Is an update required?

- 1. APC+OFD alone vs OFD alone (7 KCIS) evidence of advantage using APC
- 2. APC+OFD+BG vs OFD+BG (17 RCTs) evidence of advantage using APC
- 3. APC+GTR vs GTR alone (5 RCTs) NO evidence of advantage using APC
- APC+EMD+OFD vs EMD+OFD (2 RCTs) 4. NO evidence of advantage using APC











Mean Difference

IV. Random, 95% C

Risk of Bias





**ORIGINAL ARTICLE** 



### Effect of injectable platelet-rich fibrin (i-PRF) in accelerating orthodontic tooth movement

#### A randomized split-mouth-controlled trial

Talar S. Zeitounlouian<sup>1</sup> · Kinan G. Zeno<sup>2</sup> · Bassel A. Brad<sup>3</sup> · Rania A. Haddad<sup>1</sup>

Received: 9 April 2020 / Accepted: 27 November 2020 © Springer Medizin Verlag GmbH, ein Teil von Springer Nature 2021

#### Abstract

**Background** The role of platelet-rich fibrin (PRF) in accelerating orthodontic tooth movement has been controversially discussed in available clinical studies.

**Objective** To investigate the effectiveness of i-PRF in accelerating maxillary canine retraction.

Advisible and mathade A sulit month design was smalled in 21 nontisiumets (6 man 15 warman, mass san 2005 ;





#### **Platelet-Rich Fibrin in Bone Regenerative Strategies in Orthodontics: A Systematic Review**

Inês Francisco<sup>1</sup>, Maria Helena Fernandes<sup>2,3,\*</sup> and Francisco Vale<sup>1,\*</sup>

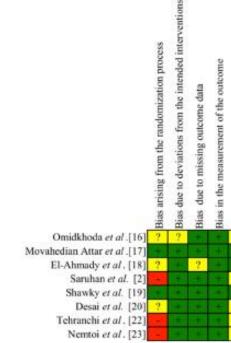
- <sup>1</sup> Institute of Orthodontics, Faculty of Medicine of the University of Coimbra, 3000-075 Coimbra, Portugal; ines70.francisco@gmail.com
- <sup>2</sup> Faculty of Dental Medicine, University of Porto, 4200-393 Porto, Portugal
- <sup>3</sup> LAQV/REQUIMTE, U. Porto, 4160-007 Porto, Portugal
- \* Correspondence: mhfernandes@fmd.up.pt (M.H.F.); fvale@fmed.uc.pt (F.V.)

Received: 5 April 2020; Accepted: 13 April 2020; Published: 16 April 2020

Abstract: Preservation of the alveolar bone is a determinant in the outcome of orthodontic treatment. Alveolar bone defects or a decrease of their height and width may occur due to common reasons such as inflammation, tooth extraction, or cleft lip and palate. The aim of this systematic review was to investigate and appraise the quality of the most up to date available evidence regarding the applications and effects of platelet-rich fibrin (PRF) in orthodontics. This study was carried out according to preferred reporting items for systematic reviews and meta-analyses guidelines using the following databases: Medline via PubMed, Cochrane Library, Web of Science Core Collection and EMBASE. The qualitative assessment of the included studies was performed using Cochrane Risk of Bias tool and ROBINS-I guidelines. Results: From a total of 489 studies, nine studies were selected. The majority of the included studies demonstrate that autogenous anterior iliac graft with PRF had a higher amount of newly formed bone. Furthermore, this review also suggests that the application of platelet derivatives in the extraction socket can accelerate orthodontic tooth movement. Despite the limitations in the included studies, this systematic review suggested that PRF can improve alveolar cleft reconstruction and orthodontic tooth movement.

9 studies included

- (6 cleft palate reconstr.)
- **MDPI** Greater amount of bone formation
  - improved alveolar cleft reconstruction
  - Accelerated orthodontic tooth movement



in selection of the reported result

Bias

2

2

check for

updates

# TMJ disorders

## Platelet-rich plasma for the therapeutic management of temporomandibular joint disorders: a systematic review

M. Bousnaki, P. Koidis: Platelet-rich plasma for the therapeutic management of temporomandibular joint disorders: a systematic review. Int. J. Oral Maxillofac. Surg. 2017; xxx: xxx-xxx. © 2017 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Abstract. This systematic review aimed to investigate whether intra-articular injections of platelet-rich plasma (PRP) are beneficial for the treatment of degenerative temporomandibular disorders, such as temporomandibular joint osteoarthritis (TMJ-OA) and disc displacement with osteoarthritic lesions, when compared to other treatments, such as injections of hyaluronic acid (HA) or saline. An electronic search of the MEDLINE and Scopus databases was performed using combinations of the terms "temporomandibular" and "platelet rich plasma", to identify studies reported in English and published up until May 2017. A hand-search of relevant journals and the reference lists of selected articles was also performed. The initial screening identified 153 records, of which only six fulfilled the inclusion criteria and were included in this review. Of these studies, three compared PRP with HA, while three compared PRP with Ringer's lactate or saline. Four of the studies found PRP injections to be superior in terms of improvements in mandibular range of motion and pain intensity up to 12 months after treatment, while the remaining two studies found similar results for the different treatments. There is slight evidence for the potential benefits of intra-articular injections of PRP in patients with TMJ-OA. However, a standardized protocol for PRP preparation and application needs to be established.



#### Systematic Review TMJ Disorders

#### M. Bousnaki, P. Koidis

Department of Prosthodontics, Faculty of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece



Key words: temporomandibular disorders; platelet-rich plasma; intra-articular injections; temporomandibular joint osteoarthritis.

Accepted for publication 25 September 2017





# Endodontic surgery





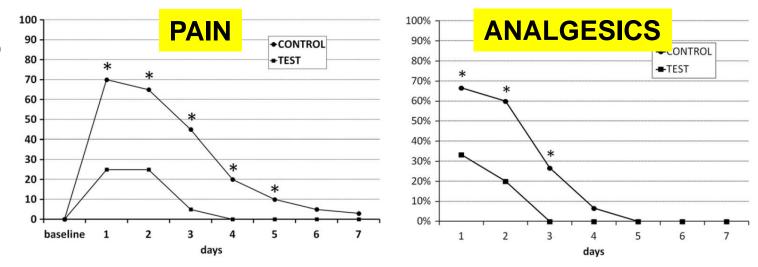
#### Effect of Platelet Concentrate on Quality of Life after Periradicular Surgery: A Randomized Clinical Study

Massimo Del Fabbro, BSc, PbD, Valentina Ceresoli, BMT, Alessandra Lolato, BMT, and Silvio Taschieri, MD, DDS



#### RANDOMIZED TRIAL: 18 test patients (+PRGF) 18 control patients endodontic surgery questionnaires first 7 days post-op

- symptoms
- function
- daily activities



#### J Endod 2012

## Endodontic procedures for retreatment of periapical lesions (Review)



**Cochrane** Database of Systematic Reviews

Del Fabbro M, Corbella S, Sequeira-Byron P, Tsesis I, Rosen E, Lolato A, Taschieri S

There was evidence that adjunctive use of a gel of plasma rich in growth factors reduced postoperative pain compared with no grafting (measured on visual analogue scale: one day postoperative MD -51.60 mm, 95% CI -63.43 to -39.77; one RCT, 36 participants; low quality evidence).

#### Analysis 8.3. Comparison 8 Grafting versus no grafting, Outcome 3 PRGF versus no grafting - pain (VAS).

Review: Endodontic procedures for retreatment of periapical lesions

Comparison: 8 Grafting versus no grafting

Outcome: 3 PRGF versus no grafting - pain (VAS)

| Study or subgroup           | PRGF |             | No grafting |             | ۱<br>Differ  | 1ean<br>ence       | Mean<br>Difference        |
|-----------------------------|------|-------------|-------------|-------------|--------------|--------------------|---------------------------|
|                             | Ν    | Mean(SD)    | N           | Mean(SD)    | IV,Fixed     | ,95% CI            | IV,Fixed,95% CI           |
| I I day<br>Del Fabbro 2012  | 18   | 21.7 (18.6) | 18          | 73.3 (17.6) |              |                    | -51.60 [ -63.43, -39.77 ] |
| 2 2 days<br>Del Fabbro 2012 | 18   | 25 (16.4)   | 18          | 66.7 (15.4) |              |                    | -41.70 [ -52.09, -31.31 ] |
| 3 3 days<br>Del Fabbro 2012 | 18   | 3.3 (8.8)   | 18          | 48.3 (30.6) | - <b>-</b>   |                    | -45.00 [ -59.71, -30.29 ] |
|                             |      |             |             |             | -100 -50 0   | 50 100             |                           |
|                             |      |             |             |             | Favours PRGF | Favours no graftir | ng                        |

#### CONSORT RANDOMIZED CLINICAL TRIAL

Impact of Platelet-rich Plasma in the Healing of Through-andthrough Periapical Lesions Using 2-dimensional and 3-dimensional Evaluation: A Randomized Controlled Trial



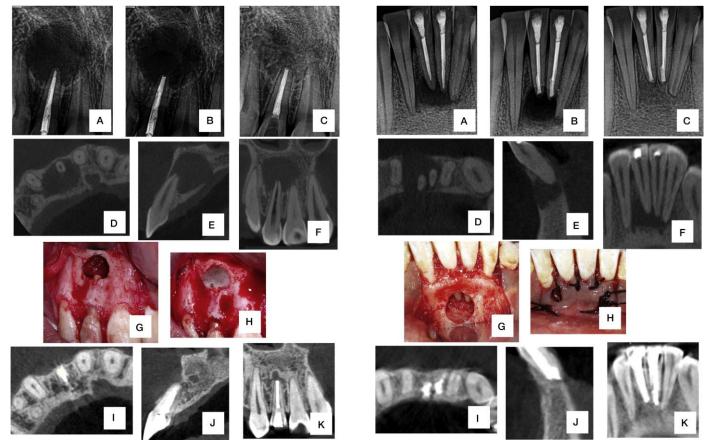
Ritika Dhamija, MDS, Sanjay Tewari, MDS, Pankaj Sangwan, MDS, Jigyasa Duhan, MDS and Shweta Mittal, MDS



34 patients treated, 32 evaluated 2D success: 93.7% PRP, 93.7% control 3D success: 87,5% PRP, 50% control

A significantly higher percentage reduction in the lesion volume was documented in the PRP group

than the control group. Resected plane, apical area, and cortical plate indexes revealed a significantly higher scoring at the resected plane and cortical plate parameter **in the PRP group**.



Tooth extraction ridge preservation

#### CLINICAL APPLICATIONS IN ORAL SURGERY

#### **Post-extraction sites**



**IJOMS 2011** 

M. Del Fabbro, M. Bortolin, S. Taschieri Del Fabbro et al. EJOI 2014

Massimo Del Fabbro, Stefano Corbella, Silvio Taschieri, Luca Francetti, Roberto Weinstein

Is autologous platelet concentrate beneficial for postextraction socket healing? A systematic review

Autologous platelet concentrate for post-extraction socket healing: A systematic review



## Healing of Postextraction Sockets Preserved With Autologous Platelet Concentrates. A Systematic Review and Meta-Analysis JOMS 2017

Massimo Del Fabbro, BSc, PbD, \* Cristina Bucchi, MD, DDS, † Alessandra Lolato, BSc, ‡ Stefano Corbella, MD, DDS, § Tiziano Testori, MD, DDS, || and Silvio Taschieri, MD, DDS ¶

- This updated review on one side <u>confirmed the benefits of</u> <u>autogenous platelet concentrates in many aspects</u>, on the other side, emphasized the <u>wide range of outcome variables</u> used to assess the efficacy of such bioproducts and the <u>wide differences</u> <u>among protocols</u> (PRPs, PRFs, PRGF)
- PRGF<sup>®</sup> is the only technology that underwent minimal changes since its introduction, which guarantees repeatability and comparability among studies using this product

ADJUNCTIVE USE OF PLASMA RICH IN GROWTH FACTORS FOR IMPROVING ALVEOLAR SOCKET HEALING. A SYSTEMATIC REVIEW *JEBDP 2018* (PRGF only)

MASSIMO DEL FABBRO, MSc, PhD<sup>a,b</sup>, SOURAV PANDA, MDS<sup>a,c</sup>, AND

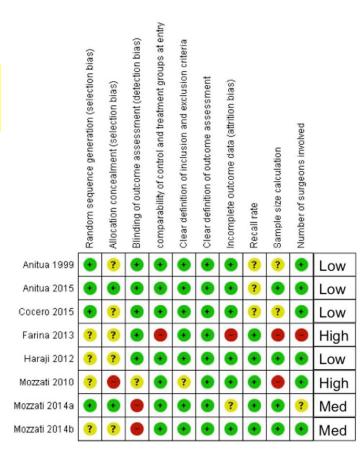
Records Excluded (N = 570)

Full text articles excluded with

reasons (n = 7)

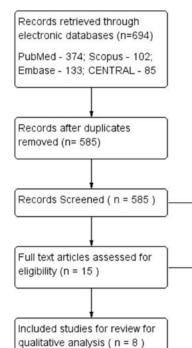
8 studies (5 RCTs) included 338 patients, 614 extractions Outcome variables:

- Post-op pain
- Complications
- Hard tissue healing
- Soft tissue healing



## **CONCLUSIONS**:

PRGF may bring advantages in some relevant clinical and radiographic outcomes, eg bone density, soft tissue healing. It could also represent a useful tool for reducing adverse events, complications and patients' discomfort







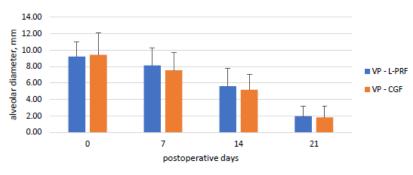


# One of the few clinical studies comparing 2 APCs

Article Concentrated Growth Factors vs Leukocyte-and-Platelet-Rich Fibrin for Enhancing Postextraction Socket Healing. A Longitudinal Comparative Study

Marco Mozzati 1, Giorgia Gallesio 1, Margherita Tumedei 2 and Massimo Del Fabbro 3,4,\*

- Split-mouth study
- L-PRF Vs. CGF
- 45 patients with bilateral extraction
- Pain, socket closure, healing index
- There was no clinically relevant difference in outcomes between CGF and L-PRF groups



(a)

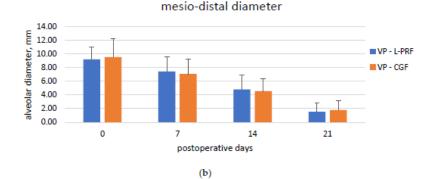
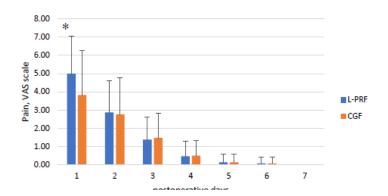


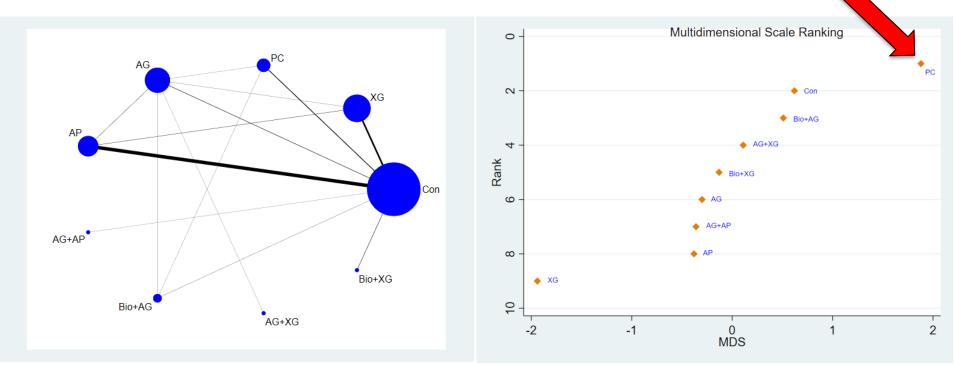
Figure 2. (a) Alveolar diameter in the vestibular-palatal dimension; (b) Alveolar diameter size in the mesio-distal dimension.



#### Dimensional and histomorphometric evaluation of biomaterials used for alveolar ridge preservation: a systematic review and network meta-analysis *COI 2022 - NMA*

L. Canullo<sup>1</sup> · M. Del Fabbro<sup>2,3</sup> · S. Khijmatgar<sup>2</sup> · S. Panda<sup>2,4</sup> · A. Ravidà<sup>5</sup> · G. Tommasato<sup>3</sup> · A. Sculean<sup>1</sup> · P. Pesce<sup>6</sup>

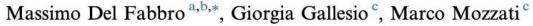
- 74 RCTs included for dimension change, 45 for NBF
- Platelet concentrates resulted the best material for promoting new bone formation in studies with histomorphometric data 2-4 months after extraction

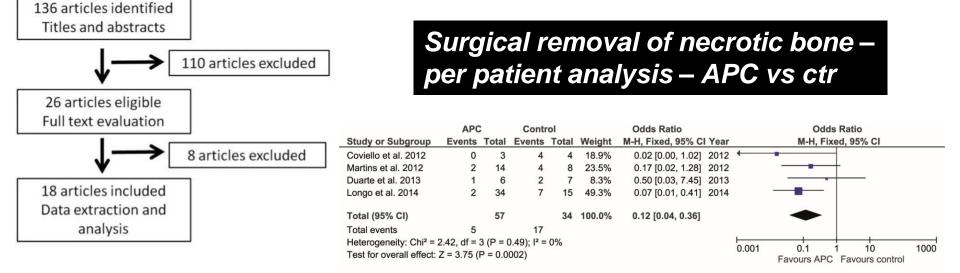


# Patients with systemic conditions

Autologous platelet concentrates for bisphosphonate-related osteonecrosis of the jaw treatment and prevention. A systematic review of the literature

the results of this review, though based on low-evidence level studies, suggest that the use of platelet concentrates as an adjunct to oral surgery procedures may have a beneficial effect for preventing the postsurgical occurrence or recurrence of BRONJ in patients under bisphosphonate therapy.









霐

2015



## **2018**

#### Platelet Concentrates as an Adjunctive Therapy for Medication-Related Osteonecrosis of the Jaw: A Systematic Review and Meta-Analysis

Massimo Del Fabbro<sup>1,2</sup>, Silvio Taschieri<sup>1,2,3</sup>, Funda Goker<sup>1,2</sup>

<sup>1</sup>Department of Biomedical, Surgical and Dental Sciences, University of Milan, <sup>2</sup>Dental Clinic, IRCCS Galeazzi Orthopedic Institute, Milan, Italy, <sup>3</sup>Faculty of Dental Surgery, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

# MRONJ prevention & treatment 18 studies included

INTERNATIONAL JOURNAL OF GROWTH FACTORS AND STEM CELLS IN DENTISTRY Volume 1 · Issue 2 · May - August 2018



|                                     | PRP        |          | Contr                   | lo    |        | Odds Ratio           |      |          | Odd            | s Ratio                 |     |
|-------------------------------------|------------|----------|-------------------------|-------|--------|----------------------|------|----------|----------------|-------------------------|-----|
| Study or Subgroup                   | Events     | Total    | Events                  | Total | Weight | M-H, Fixed, 95% CI Y | fear |          | M-H, Fb        | ced, 95% Cl             |     |
| Martins et al. 2012                 | 2          | 16       | 4                       | 8     | 26.7%  | 0.14 [0.02, 1.09] 2  | 012  |          | -              | -                       |     |
| Coviello et al. 2012                | Ō          | 4        | 5                       | 5     | 25.8%  | 0.01 [0.00, 0.62] 2  | 012  | +        |                |                         |     |
| Duarte et al. 2013                  | 1          | 7        | 2                       | 7     | 9.8%   | 0.42 [0.03, 6.06] 2  | 013  | <u> </u> |                |                         |     |
| Longo et al. 2014                   | 2          | 34       | 7                       | 34    | 37.7%  | 0.24 [0.05, 1.26] 2  | 2014 | -        | -              | +                       |     |
| Total (95% CI)                      |            | 61       |                         | 54    | 100.0% | 0.17 [0.06, 0.50]    |      | 9        | •              |                         |     |
| Total events                        | 5          |          | 18                      |       |        |                      |      |          |                |                         |     |
| Heterogeneity: Chi <sup>2</sup> = 2 | 2.44, df = | 3 (P = ( | ).49); l <sup>2</sup> = | 0%    |        |                      |      | -        | +              | 1 10                    | 400 |
| Test for overall effect:            | Z = 3.21 ( | P = 0.0  | 01)                     |       |        |                      |      |          | 0.1<br>urs PRP | 1 10<br>Favours control | 100 |

#### TREATMENT

|                                   | PRP          | •        | Contr                   | lo  |        | Odds Ratio         | Odds Ratio   |  |  |
|-----------------------------------|--------------|----------|-------------------------|-----|--------|--------------------|--|--|--|
| Study or Subgroup                 | Events Total |          | Events Total            |     | Weight | M-H, Fixed, 95% Cl | M-H, Fixed, 95% Cl                                   |  |  |
| Asaka 2017                        | 0            | 52       | 12                      | 166 | 51.7%  | 0.12 [0.01, 2.02]  |  |  |  |
| Mozzati et al. 2012               | 0            | 275      | 5                       | 267 | 48.3%  | 0.09 [0.00, 1.57]  |  |  |  |
| Total (95% CI)                    |              | 327      |                         | 433 | 100.0% | 0.10 [0.01, 0.80]  | -  |  |  |
| Total events                      | 0            |          | 17                      |     |        |                    |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = | 0.02, df =   | 1 (P = ( | ).88); l <sup>2</sup> = | 0%  |        |                    | 0.001 01 1 10 1000                                   |  |  |
| Test for overall effect:          | Z = 2.18 (   | P = 0.0  | 3)                      |     |        |                    | 0.001 0.1 1 10 1000<br>Favours PRP Favours [control] |  |  |

#### PREVENTION

## recent studies on PRF, PRP, PRGF / oral field

| Authors                    | Country     | Type of Study      | Systemic<br>Condition/drug | PRF Result          | Conclusion  |
|----------------------------|-------------|--------------------|----------------------------|---------------------|---|
| Shahram Ghanaati<br>(2018) | Germany     | Systematic Review  | -dentistry, OMFS           | Favours PRF         | Significantly improves bone and soft tissue regeneration. |
| Srinivas B (2018)          | India       | Split mouth        | -(Socket Healing)          | Favours PRF         | Better healing index and increase in bone density         |
| Yuce E (2019)              | Turkey      | RCT                | -alveolar osteitis         | Favours PRF         | Better hard and soft tissue healing and in reducing pain. |
| Sarkar S (2019)            | India       | Not Mentioned      | Antiplatelet<br>Therapy    | Favours PRF         | Shortens the clotting time                                |
| Del Fabbro M (2019)        | Italy       | Systematic Review  | (Socket Healing)           | Favours PRGF        | Bone and soft tissue healing is<br>improved               |
| Giudice A (2019)           | Italy       | RCT                | Antiplatelet<br>Therapy    | Favours PRF, A-PRF+ | Bleeding management is good                               |
| Asaka T (2017)             | Japan       | RCT                | Bisphosphonates            | Favours PRF         | Useful in MRONJ   |
| Simonpeiri A (2012)        | South Korea | Review             | Reconstructive<br>Surgery  | Favours PRF         | Positive outcome  |
| Mauceri R (2018)           | Italy       | Longitudinal Study | BRONJ                      | Favours PRP         | Positive outcome  |
| Stellar D (2019)           | Germany     | InVitro            | Bisphosphonate             | Favour PRF and PRP  | Positive outcome  |
| Cardoso CL (2019)          | Brazil      | -                  | Bisphosphonate             | Favours PRP         | Positive Outcome  |
| Stellar D (2019)           | Germany     | -                  | Bispheephonate             | Favours PRF/PRP     | Positive Outcome  |
| Valente NA (2019)          | Italy       | Retrospective      | MRONJ                      | Favours L-PRF       | Positive Outcome  |
| Mahajan M (2018)           | India       | RCT (              | Oral Mucosal<br>Lesions    | Favours PRF         | Positive Outcome  |
| Pathak H (2015)            | India       | Case-series        | Oral Mucosal               | Favours PRF         | Positive Outcome  |
| Maluf G (2018)             | Brazil      | Case-Series        | MRONJ                      | Favours L-PRF       | Positive Outcome  |
| Nørholt SE (2016)          | Denmark     | Prospective        | ONJ                        | Favours PRF         | Positive Outcome  |
| EL-Komy MH (2015)          | Egypt       | Pilot Study        | Pemphigus<br>Vulgaris      | Favours PRF         | Accelerates Healing                                       |
| Asmael HM (2018)           | Iraq        | Controlled study   | Smokers                    | Favours PRF         | Accelerates Healing                                       |





Article

Dental Implants with a Calcium Ions-Modified Surface and Platelet Concentrates for the Rehabilitation of Medically Compromised Patients: A Retrospective Study with 5-Year F<u>ollow-Up</u>

Using P-PRP and implants with Ca-modified

surface, outcomes in medically compromised

- patient are comparable to those of healthy ones
- Diabetes, osteoporosis, rheumatoid arthritis, LES
- 224 dental implants
- 5-year survival = 94.6%
- Mean MBL change = 0.45mm
- Only transient complications, no adverse effect

# Orthopedics «musculoskeletal medicine»

Dermatology

Difficult ulcers

Esthetic medicine

Ophtalmology

Reproductive apparatus Obstetrics and Gynecology

## A Systematic Review Evaluating the Efficacy of Intra-Ovarian Infusion of Autologous Platelet-Rich Plasma in Patients With Poor Ovarian Reserve or Ovarian Insufficiency

Soumya R. Panda $^1$ , Shikha Sachan $^2$ , Smrutismita Hota $^3$ 

1. Obstetrics and Gynaecology, All India Institute of Medical Sciences, Mangalagiri, Guntur, IND 2. Obstetrics and Gynaecology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, IND 3. Radiodiagnosis and Imaging, All India Institute of Medical Sciences, Mangalagiri, Guntur, IND

Corresponding author: Soumya R. Panda, drsome4141@gmail.com



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#### Journal of Reproductive Immunology

journal homepage: www.elsevier.com/locate/jri

Review article





Intrauterine infusion of autologous platelet-rich plasma in women undergoing assisted reproduction: A systematic review and meta-analysis

Arezoo Maleki-Hajiagha<sup>a</sup>, Maryam Razavi<sup>b</sup>, Safoura Rouholamin<sup>c</sup>, Mahroo Rezaeinejad<sup>d</sup>, Saman Maroufizadeh<sup>e</sup>, Mahdi Sepidarkish<sup>f,\*</sup>

<sup>a</sup> Research Development Center, Arash Women's Hospital, Tehran University of Medical Sciences, Tehran, Iran

<sup>b</sup> Pregnancy Health Research Center, Department of Obstetrics and Gynecology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

<sup>d</sup> Department of Obstetrics and Gynecology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

<sup>e</sup> School of Nursing and Midwifery, Guilan University of Medical Sciences, Rasht, Iran

intrauterine administration of PRP, irrespective of study design and study population, increases the clinical pregnancy rate in women experienced frozen-thawed ET cycle.

Further prospective, large, and high quality randomized controlled trials (RCTs) are needed to identify the sub- population that would most benefit from PRP.

<sup>&</sup>lt;sup>c</sup> Department of Obstetrics and Gynecology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>&</sup>lt;sup>f</sup> Department of Biostatistics and Epidemiology, Babol University of Medical Sciences, Babol, Iran





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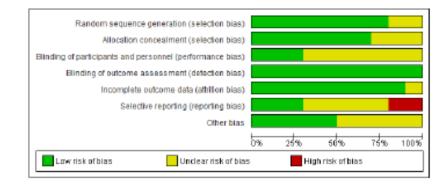
#### Systematic Review

Efficacy of Platelet-Rich Plasma in Women with a History of Embryo Transfer Failure: A Systematic Review and Meta-Analysis with Trial Sequential Analysis

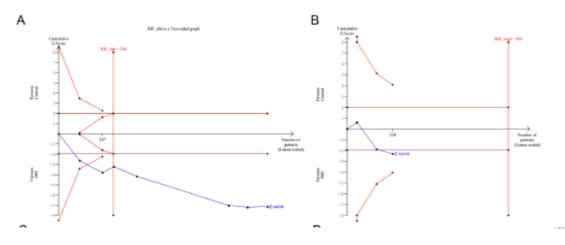
Eduardo Anitua <sup>1,2,\*</sup>, Mikel Allende <sup>1,2</sup>, María de la Fuente <sup>1,2</sup>, Massimo Del Fabbro <sup>3,4</sup> and Mohammad Hamdan Alkhraisat <sup>1,2</sup>

- Assisted reproductive technology (ART) is used to enhance pregnancy in infertile women.
- Only RCTs
- Outcomes: Clinical pregnancy rate,
- Implantation rate, biochemical pregnancy rate, live birth rate and miscarriage rate

### PRP therapies might be an effective treatment in cases of poor responsiveness to conventional ART.



|  | PRP          |           | Control    |           | Risk Ratio               |   | Risk Ratio   |
|--|--------------|-----------|------------|-----------|--------------------------|---|--|
| Study or Subgroup                      | Events       | Total     | Events     | Total     | Weight                   | M-H, Fixed, 95% CI                      | M-H, Fixed, 95% Cl                                 |
| 1.3.1 Repeated Implanta                | ation Failt  | нe        |            |           |                          |   |  |
| Allahveisi et al 2020                  | 7            | 25        | i (9       | 25        | 9.5%                     | 0.78 [0.34, 1.76]                       |  |
| Ershadi et al. 2022                    | 13           | 40        | 11         | 45        | 11.0%                    | 1.33 0.67, 2.63                         |  |
| Nazari et al.2020                      | 22           | 49        | 8          | 48        | 8.5%                     | 2.69 [1.33, 5.45]                       |  |
| Nazari et al.2021                      | 96           | 196       | 38         | 197       | 40.2%                    | 2.54 [1.84, 3.49]                       |  |
| Obidniak et al. 2017                   | 24           | 45        | 11         | 45        | 11.7%                    | 2.18 [1.22, 3.90]                       |  |
| Zamaniyan et al. 2020                  | 29           | 55        | 10         | 43        | 11.9%                    | 2.27 [1.25, 4.12]                       |  |
| Zargar et al.2021<br>Subtotal (95% CI) | 5            | 40<br>450 | 1          | 40<br>443 | 1.1%                     | 5.00 (0.61, 40.91)<br>2.18 [1.76, 2.70] | •  |
| Total events                           | 196          |           | 88         |           |                          |   |  |
| Heterogeneity: Chi# = 9.9              | 97. df = 6   | (P=0.1    | 13); P= 4  | 0%        |                          |   |  |
| Test for overall effect Z =            | = 7.16 (P    | < 0.000   | 01)        |           |                          |   |  |
| 1.3.2 Thin Endometrium                 |              |           |            |           |                          |   |  |
| Eftekhar et al.2018                    | 13           | 40        | 16         | 43        | 6.1%                     | 2.33 (0.98, 5.54)                       |  |
| Subbotal (95% CI)                      |              | 40        |            | 43        | 6.1%                     | 2.33 [0.98, 5.54]                       |  |
| Total events                           | 13           |           | 16         |           |                          |   |  |
| Heterogeneity: Not appli               | cable        |           |            |           |                          |   |  |
| Test for overall effect Z =            | = 1.91 (P =  | = 0.06)   |            |           |                          |   |  |
| Total (95% CI)                         |              | 490       |            | 486       | 100.0%                   | 2.19 [1.78, 2.70]                       | •  |
| Total events                           | 209          |           | 94         |           |                          |   |  |
| Heterogeneity: Chi# = 10               | 1.01, df = 7 | (P=0      | 19); P=    | 30%       |                          |   | 01 02 05 2 5 1                                     |
| Testfor overall effect Z =             | : 7.41 (P    | 0.000     | 01)        |           |                          |   | 0.1 0.2 0.5 1 2 5 1<br>Favours Control Favours PRP |
| Test for subgroup differe              | ences: Ch    | P= 0.0    | 2. df = 1. | P = 0.8   | 19), I <sup>#</sup> = 01 | 86                                      | Failure Control Failours Fifth                     |



|   | PRF         |                | Contr      | ol           |             | Risk Ratio                          | R                           | isk Ratio                   |
|---|-------------|----------------|------------|--------------|-------------|-------------------------------------|-----------------------------|-----------------------------|
| r Subgroup  | Events      | Events Total   |            | Events Total |             | M-H, Fixed, 95% CI                  | M-H, I                      | Fixed, 95% CI               |
| epeated implant   | ation Faik  | # e            |            |              |             |                                     |                             |                             |
| i et al. 2022   | 16          | 40             | 12         | 45           | 12.2%       | 1.50 [0.81, 2.78]                   |                             |                             |
| et al.2020  | 26          | 49             | 13         | 48           | 14.2%       | 1.96 [1.15, 3.34]                   |                             |                             |
| et al. 2021   | 101         | 196            | 49         | 197          | 53.0%       | 2.07 [1.57, 2.74]                   |                             |                             |
| hran et al. 2020<br>al (95% CI)                             | 20          | 55<br>340      | 10         | 43<br>333    | 12.2% 91.6% | 1.56 [0.82, 2.98] 1.91 [1.54, 2.37] |                             | •                           |
| onts  | 163         |                | 84         |              |             |                                     |                             | 1.000                       |
| geneity: Chi# = 1.<br>roverall effect Z:<br>hin Endometrium | = 5.89 (P   |                |            |              |             |                                     |                             |                             |
| r et al 2018  | 14          | 40             | 8          | 43           | 8.4%        | 1.88 (0.88, 4.00)                   |                             |                             |
| at (95% Cl)   | 27          | 40             |            | 43           | 8.4%        | 1.88 [0.88, 4.00]                   |                             |                             |
| ents  | 14          |                | 8          |              |             |                                     |                             |                             |
| peneity: Not appl   | icable      |                |            |              |             |                                     |                             |                             |
| overall effect Z  | = 1.64 (P : | 0.10)          |            |              |             |                                     |                             |                             |
| 95% CI)   |             | 380            |            | 376          | 100.0%      | 1.91 [1.55, 2.35]                   |                             | •                           |
| rents   | 177         |                | 92         |              |             |                                     |                             |                             |
| geneity: Chi#= 1.   | 30, df = 4  | P=0.8          | (6); P=0   | 6            |             |                                     | 0.1 0.2 0.5                 | 1 1 1 1                     |
| overall effect Z:   | = 6.11 (P   | 0.000          | 01)        |              |             |                                     | 0.1 0.2 0.5<br>Favours Cont | 1 2 5 10<br>rol Favours PRP |
| subaroup differ   | ancas Ch    | $\theta = 0.0$ | 0.4t - 1.t | P = 0.0      | 25 H = 04   | 1. · · ·                            | r avours com                | rol randura r'Pit"          |

Platelets concentrates can be helpful for patients and clinicians! However, they are not magic!



## Conclusions

- Platelet concentrates represent a useful tool in oral surgery and many fields of medicine
- Acceleration of soft tissue closure/wound healing and epithelization, which may also protect and promote healing of underlying hard tissues
- Better control of post-op symptoms (pain, swelling)
- Help in post-op infection control
- Improved handling of grafts due to adhesive/cohesive properties
- Helpful to promote healing in medically compromised patients
- Unclear if one product is better than others
- The clinical impact of newest protocols needs evidence
- Bureucracy in Italy still needs improvement in order to facilitate the use of such valuable tools

## THANK YOU FOR YOUR KIND ATTENTION !

## massimo.delfabbro@unimi.it

Ken Scott

## **GRAZIE PER L'ATTENZIONE**