



Review

Platelet-Rich Fibrin and Its Emerging Therapeutic Benefits for Musculoskeletal Injury Treatment

Alexandru Florian Grecu ¹, Lucien Reclaru ², Lavinia Cosmina Ardelean ³, Oliviu Nica ^{1,*}, Eduard Mihai Ciucă ^{4,*} and Marius Eugen Ciurea ⁵

¹ University of Medicine and Pharmacy Craiova, 200349 Craiova, Romania; alexandrugrecu@yahoo.com

² Varinor Matériaux SA, CH 2800 Delémont, Switzerland; lucien.reclaru@varinor.ch

³ Department of Technology of Materials and 9 Devices in Dental Medicine, “Victor Babes” University of Medicine and Pharmacy from Timisoara, 300041 Timisoara, Romania; lavinia_ardelean@umft.ro

⁴ Department of Oro-Maxilo-Facial Surgery, University of Medicine and Pharmacy Craiova, 200349 Craiova, Romania

⁵ Department of Plastic Surgery, University of Medicine and Pharmacy of Craiova, 200349 Craiova, Romania; meciurea@gmail.com

* Correspondence: oliviu.nica@gmail.com (O.N.); Ciuca.md@gmail.com (E.M.C.); Tel.: +40-746020496 (O.N.); +40-745158317 (E.M.C.)

Received: 19 February 2019; Accepted: 23 April 2019; Published: 15 May 2019



Abstract: New therapies that accelerate musculoskeletal tissue recovery are highly desirable. Platelet-rich fibrin (PRF) is a leukocyte- and platelet-rich fibrin biomaterial that acts as a binding site for both platelets and growth factors. Through increasing the local concentration of growth factors at specific tissues, PRF promotes tissue regeneration. PRF has been frequently used in combination with bone graft materials to reduce healing times and promote bone regeneration during maxillofacial surgery. However, its benefits during muscle repair and recovery are less well-documented. Here, we perform a narrative review on PRF therapies and muscle injuries to ascertain its beneficial effects. We reviewed the factors that contribute to the biological activity of PRF and the published pre-clinical and clinical evidence to support its emerging use in musculoskeletal therapy. We include in vitro studies, in vivo animal studies and clinical articles highlighting both the success and failures of PRF treatment. PRF can promote the healing process when used in a range of orthopaedic and sports-related injuries. These include cartilage repair, rotator cuff surgery and anterior cruciate ligament surgery. However, conflicting data for these benefits have been reported, most likely due to inconsistencies in both PRF preparation protocols and dosing regimens. Despite this, the literature generally supports the use of PRF as a beneficial adjuvant for a range of chronic muscle, tendon, bone or other soft tissue injuries. Further clinical trials to confirm these benefits require consistency in PRF preparation and the classification of a successful clinical outcome to fully harness its potential.

Keywords: platelet-rich fibrin; musculoskeletal system; biological therapy; bone regeneration; platelet activation

1. Introduction

Autologous platelet concentrates are simple and cost-effective methods that allow high local concentrations of growth factors at a target tissue [1]. Platelet-rich fibrin (PRF) is a second-generation platelet concentrate developed by Choukroun et al. because of legal restrictions on blood handling. PRF contains platelets, leukocytes, cytokines and adhesive proteins including fibrinogen, fibronectin, vitronectin, and thrombospondin-1 [2,3]. The presence of white blood cells (WBCs), that secrete a large quantity of growth factors, is a key feature of PRF which is named for this reason leukocyte-PRF (L-PRF).

The polymerization of the fibrin produces a 3-dimensional cross-linked fibrin matrix [4–8]. This serves as a binding site for both platelets and growth factors [9,10]. By increasing the local concentration of growth factors at a specific tissue location, PRF promotes tissue regeneration by closely mimicking the wound repair process over a prolonged period of time [2,3,11–14]. The ultimate result is a healing matrix that possesses unique mechanical properties, making it distinct from platelet-rich plasma (PRP) and other platelet concentrates [15–17]. Herein we discuss the promising clinical benefits of PRF with a focus on its ability to promote wound and muscle healing.

1.1. Muscle Injury and Repair

Muscle repair is an evolutionarily conserved multicellular process requiring the synchronized activity of infiltrating macrophages, resident myogenic and non-myogenic stem cells, and connective tissue fibroblasts [18]. Despite the effectiveness of this intrinsic repair mechanism, severe injuries that result in a significant loss of muscle tissue and/or a loss of tissue function overwhelm the repair process and require therapeutic intervention. Musculoskeletal disorders are classed as any injury, damage or disorder of the joints or tissues in the upper/lower limbs or the back [19]. The World Health Organization (WHO) reports that musculoskeletal injuries affect the lives of hundreds of millions globally, and are the major worldwide cause of long-term pain, trauma and physical disability [20–22]. Soft tissue injuries comprise 40–50% of musculoskeletal problems and are typically the result of cartilage, ligament and tendon damage. Severe impact injuries, arthritis and osteoporosis are examples of chronic and degenerative musculoskeletal conditions that pose severe challenges for clinicians [23]. Chronic injuries, including those resulting from sports- and overuse-related injuries, often require surgery leading to prolonged recovery times. In addition, a successful outcome and complete recovery following surgery are often not guaranteed and current adjuvant therapies that aid the healing process remain limited [19,20].

Hope has been offered through the discovery of orthobiologics. These refer to the use of biological substances that improve the healing of injured muscles, tendons and ligaments [24]. Orthobiologics are derived from substances naturally found in the body. They include bone grafts, autologous blood, PRP, autologous conditioned serum and stem cells [24–28]. The benefits of using orthobiologics are the reduced need for surgery when treating musculoskeletal injuries and to augment the effectiveness of existing surgical techniques [28]. Autologous blood, PRP and conditioned serum work by delivering growth factors to the injured area, stimulating the repair process [24,25]. Autologous blood products have surpassed the use of recombinant growth factors for this purpose due to their lower cost, longer life span, and more efficient delivery to the target tissue [24].

1.2. Orthobiologics

Autologous blood injections were first used to deliver blood-derived growth factors to injured tissue. This involved drawing blood from a patient and injecting it into the desired area. This procedure delivers growth factors contained in platelets. This method has been questioned, with both positive [29–31] and negative results reported [32]. The knowledge of growth factors being primarily contained in the alpha granules of platelets led researchers to focus on more effective growth factor delivery methods [33]. These have evolved from the use of autologous whole blood to the use of concentrated platelets, otherwise known as PRP. PRP is defined as a plasma fraction of autologous blood with a platelet concentration above baseline levels [34]. Despite some clear benefits, solid evidence in favor of its clinical application to trauma and orthopaedic surgery is still lacking [25]. PRP has been commercialized, yet it contains products that are unnatural and, in some instances, can inhibit wound healing. By removing these anti-coagulants and modifying the blood collection protocols, PRF was introduced some years later, with the exciting potential to markedly improve surgical performance.

2. Methods—Literature Review

We searched several databases including Pubmed and MEDLINE as well as reference lists of relevant articles to compile a consensus for the role of PRF and its therapeutic effectiveness. A Pubmed search of “platelet-rich fibrin” yielded 783 peer-reviewed articles that were filtered for relevance. The criteria for inclusion were (1) *in vitro* studies that report the effects of PRF on cell lines or cultures of primary cell lines *in vitro*, (2) *in vivo* animal studies evaluating the effect of PRF on muscle repair, (3) Clinical articles highlighting both successes and failures of PRF treatments. Through MEDLINE, the number of PRF clinical trails to date are recorded as 114 (clinicaltrials.gov). The selected studies were reviewed and their reference lists checked for all other eligible articles. Keywords used in this review include PRF and: maxillofacial surgery, muscle, cartilage, rotator cuff surgery, hamstring injury.

2.1. Platelet Rich Fibrin

PRF represents a significant advance in the evolution of platelet concentrates. In its simplest form, PRF is a fibrin membrane with trapped platelets ± leukocytes [22,25,33,35–42]. These solid membranes display excellent handling characteristics, and can be firmly sutured in an anatomically desired location during open surgery [43–53]. PRF has generated much excitement through its potential benefits to wound healing and tissue injury, which will be discussed herein. Ease of preparation, low cost, minimal risks for the patients, and possible outpatient use make PRF an optimal scaffold for tissue healing processes [54].

2.2. Preparation of PRF

A major advantage of PRF is the simplicity of preparation. PRF is drawn from the blood of a patient using a sterile 10 mL vacutainer either before, during or after surgery [2,3,11–13]. Blood is collected into a vacuum-sealed tube without anticoagulants and centrifuged for 12 minutes at 2700 rpm to separate red blood cells and plasma from platelets [55,56]. The fibrin clot containing the platelets is located in the center of the tube, between the lower layer of RBCs and the plasma acellular on the top. The PRF produced is free of anticoagulants and/or other artificial biochemical modifications [2,3,11–13,57]. Changing the PRF centrifugation protocol can influence both the structure and density of PRF clots [58,59]. The clinical efficacy of centrifugation protocols still requires validation, as open access methods have led to many variations of the original PRF protocol that have confused the literature [54,60]. This presents a problem as the material produced from each protocol differs from that of the original PRF [54,55,61,62]. These include differences in the size and weight of the clots/membranes leading to varying biological signatures and clinical outcomes [54]. To date, the differences between the methods of PRF production and the biological characteristics of final PRF product have not been clearly characterized. Standardization of centrifugation protocols to control growth factor content and fibrin architecture are now required, and the effects of modifications of the original production protocol on PRF activity require clarification [54].

2.3. Handling and Application of PRF

PRF membranes can be easily departed over a surgical or augmented site. Due to its elastic consistency, a clinician can puncture a hole in the membrane which can be draped over a healing area. PRF is blood-derived living tissue, so it must be handled accordingly. As PRF lacks anticoagulants, blood samples will coagulate upon contact with the tube glass. Quick handling ensures a clinically usable PRF matrix. If the duration between blood collection and centrifugation is too long, PRF samples become inconsistent. By driving out the fluids trapped in the fibrin matrix, very resistant autologous fibrin membranes can be obtained. Advanced platelet-rich fibrin (A-PRF) defines a new set of centrifugation speeds/times that prevent cell loss within the PRF matrix [63]. A-PRF is richer in WBCs compared to PRF and displays improved collagen matrix synthesis and enhanced recruitment of progenitor cells [62,64]. Injectable platelet-rich fibrin (i-PRF) was developed to act as a regenerative

agent that could be delivered in liquid formulation [65,66]. To achieve this, blood is drawn rapidly in a specific centrifugation tube at a low speed (approximately 700 rpm for 3 minutes). I-PRF can be mixed with bone grafts to form a stable fibrin-graft that also improves wound healing [64,65].

2.4. PRF Growth Factors

Kobayashi et al. performed a comparison of growth factor release for PRP, PRF, and A-PRF over time [67]. The various platelet concentrates were shown to have differing growth factor release kinetics. PRP released significantly higher levels of growth factors at earlier time points, whilst PRF displayed continual and steady release over a 10-day period. A-PRF released significantly higher quantities of growth factors when compared to traditional PRF [66]. From the same samples of peripheral blood, Qiao et al. compared the levels of five important growth factors in activated PRP and PRF by ELISA (enzyme-linked immunosorbent assay) [68]. The results revealed that the levels of basic fibroblast growth factor (bFGF) in PRF were significantly higher than that in activated PRP. For the other growth factors tested, namely platelet-derived growth factor-BB (PDGF-BB), transforming growth factor β -1 (TGF- β 1), insulin-like growth factor-1 (IGF-1), and vascular endothelial growth factor (VEGF), no significant differences between the two platelet concentrates were observed [67]. PRP is thus recommended for the fast delivery of growth factors whilst PRF and A-PRF are better suited for long-term growth factor release.

2.5. Uses of PRF

2.5.1. Oral and Maxillofacial Surgery

Before discussing muscle injury, we first discuss other widely accepted benefits of PRF, particularly during oral and maxillofacial surgery. PRF membranes are frequently used in combination with bone graft materials to reduce healing times and promote bone regeneration. Choukroun et al. showed that PRF with freeze-dried bone allograft increased bone formation during sinus lift procedures [2]. These findings were confirmed and more efficient methods to alleviate the postoperative complications of this procedure using PRF evolved [69,70]. PRF was also used with success during the treatment of Intrabony periodontal defects [71–73]. Greater attachment levels and bone-fill were notable findings. Similar improvements in patient outcomes were observed for mandibular Grade II furcation defects [74] and gingival recession defects [75–81]. Its ability to relieve pain and post-operative swelling during tooth extractions and in the treatment of tooth lesions, are also widely documented [82–92]. PRF was also used in the treatment of medication-related osteonecrosis of the jaw (MRONJ), with promising results for the healing and quality of life improvement of patients with MRONJ [93].

2.5.2. Orthopaedics and Sports Injuries

Although skeletal muscle can respond to a range of environmental changes, the appropriate treatment for chronic muscle injuries remains a clinical challenge. Healing with conventional therapies is frequently insufficient, leading to substantial interest in the potential of platelet concentrates to aid muscle recovery. The process of muscle healing and the contribution of growth factors to the healing process is an intensively studied field and is reviewed in [21,22]. By concentrating these growth factors, PRF can promote the cellular events required for muscle repair and regeneration [94]. Some of the first studies to reveal this were performed by Wright-Carpenter and co-workers who assessed the effects of PRF on muscle strain injuries in humans. Subjects were treated with PRF two days after injury and every two days thereafter [21]. The study revealed that the recovery time of the PRF-treated subjects was reduced to 16.6 days compared to 22.3 days in subjects treated with anti-inflammatory treatments. This supported the use of PRF during muscle therapy, validating previous observations from animal models and in vitro studies.

2.5.3. Cartilage Injuries

In the past decade, PRF has emerged as a promising non-operative procedure for the treatment of cartilage injuries. Chien and colleagues were amongst the first to assess the incorporation of PRF into biodegradable fibrin (FB) scaffolds as a regeneration matrix for promoting chondrocyte proliferation and re-differentiation [95]. Chondrocytes are the only cells found in healthy cartilage and are responsible for the production of the cartilaginous matrix. It was concluded that FB scaffolds promoted proliferation and re-differentiation that was enhanced by PRF, offering promise for cartilage tissue engineering. PRF also aids the healing of knee cartilage defects in animal models [96,97]. Defects in the left hind limbs of dogs receiving PRF implantation were found to display improved articular cartilage repair [16,98,99]. Studies in rabbits also demonstrated the ability of PRF to enhance the viability of diced cartilage grafts, promoting its use as an appropriate biological wrapping material to aid cartilage grafting [100,101]. More recent studies reveal that cartilage regeneration improves more significantly using i-PRF as opposed to autologous PRF [58]. Complicated procedures requiring in vitro chondrocyte expansion prior to cartilage repair were also shown to be avoidable through the development of a culture-free, single-stage approach that combines PRF with autologous cartilage grafts [96].

2.5.4. Rotator Cuff Repair

Rotator cuff tears are a common cause of shoulder pain and disability and can be caused by traumatic and degenerative elements. This frequently makes surgical repair challenging as the original tendon-bone insertion is difficult to recreate. Accordingly, non-healing rates are reported to be as high as 94% [36]. Zumstein and colleagues showed that l-PRF delivered in a standard/gelatinous-type matrix could locally deliver healing growth factors for up to 28 days, aiding rotator cuff repair [36]. In later pilot trials, when l-PRF was added in between tendon and bone during arthroscopic rotator cuff repair, the vascularization index improved in contralateral healthy shoulders at 6 and 12 weeks, with no post-operative complications reported [102]. Thus, arthroscopic rotator cuff repair using l-PRF appeared technically feasible, supporting earlier in vitro studies that demonstrated its ability to enhance tenocyte proliferation and promote extracellular matrix synthesis. Despite this progress, later studies questioned the clinical benefits of PRF for more severe muscle rotator cuff injuries. When PRF was applied to massive rotator cuff tears, two independent studies revealed no changes to anatomic healing rates, mean postoperative defect sizes and tendon quality [103,104]. Hasan and colleagues also showed that PRF induces a disordered healing response characterized by fibrovascular scar tissue in rat models of severe rotator cuff repair [105]. Further studies are therefore required to clarify the benefits of PRF during this procedure.

2.5.5. Other Sports-Related Injuries

The success of PRF augmentation was noted by Alviti and colleagues who assessed its effects on ankle stiffness and the mechanical work of the ankle in patients who had undergone Achilles tendon surgery [106]. The findings suggested that treatment with a suture and PRF resulted in a significant functional improvement in terms of the efficiency of motion, improving patient recovery. Similar benefits were reported for operations involving the replacement of torn anterior cruciate ligaments (ACL) [107]. Most of the patients had normal knee scores and returned to normal levels of sporting activity when PRF was used. In other studies, PRF augmentation did not appear to have an effect on gluteus medius tendon repair in terms of pain or clinical evidence, but was shown to improve hip-specific physical functioning following surgical repair [108]. The potential benefits of PRF to elite-level athletes were also highlighted in randomized control trials that assessed its effects on ankle sprains. Ultrasound-guided injections of PRF into the injured antero-inferior, tibio-fibular ligaments, led to benefits that included a shorter recovery, re-stabilization of the syndesmosis joint and reduced long-term pain [109]. Beneficial effects of PRF have also been reported in cases of

patellar tendinopathy [110], partial ulnar collateral ligament tears [111], elbow ulnar collateral ligament insufficiency in high-level throwers [112], and in the treatment of meniscal lesions [113]. The promise of PRF is not limited to muscle injuries, and recent studies reveal its ability to promote bone healing and regeneration when applied with several grafting materials in animal and human calvarial defects [114–116]. Thus, iPRF offers hope to aid both bone and muscle regeneration following serious trauma-induced injuries.

3. Conclusions

The articles included and presented in this review were chosen due to the clarity of proof, concise and clear results. The articles that were disregarded either presented inadequate information about the topic or they were considered as lacking clarity.

Despite the vast majority of articles proving the benefits of PRF to promote tissue regeneration and speed up recovery, there is still some controversy in the literature regarding this. Recent controlled clinical trial data provides hope that PRF benefits cartilage injury, whilst its use is supported for partial ulnar collateral ligament tears, elbow ulnar collateral ligament insufficiency and in the treatment of meniscal lesions. The literature for other muscle interventions has been conflicting as well (exemplified by rotator cuff injuries), most likely due to the fact that not all PRFs are the same and those with higher leukocyte levels may be detrimental to tendon healing. To date, the clinical data do not conclusively prove the benefits of PRF treatment to aid muscle injury.

Consistent dosing and reproducible measures of success outcomes are now required to definitively prove effectiveness. Whether our scientific ability to fully harness its potential is still lacking remains an important question to consider during future investigations.

Author Contributions: Conceptualization, A.F.G. and M.E.C.; methodology, L.R.; software, O.N.; validation, E.M.C., L.C.A. and L.R.; formal analysis, L.R.; investigation, A.F.G.; writing—original draft preparation, A.F.G.; writing—review and editing, O.N.; visualization, E.M.C. and L.C.A.; supervision, M.E.C.; project administration, O.N.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Prakash, S.; Thakur, A. Platelet concentrates: Past, present and future. *J. Maxillofac. Oral Surg.* **2011**, *10*, 45–49. [[CrossRef](#)]
2. Choukroun, J.; Diss, A.; Simonpieri, A.; Girard, M.O.; Schoeffler, C.; Dohan, S.L.; Dohan, A.J.; Mouhyi, J.; Dohan, D.M. Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part V: Histologic evaluations of PRF effects on bone allograft maturation in sinus lift. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **2006**, *101*, 299–303. [[CrossRef](#)] [[PubMed](#)]
3. Choukroun, J.; Diss, A.; Simonpieri, A.; Girard, M.O.; Schoeffler, C.; Dohan, S.L.; Dohan, A.J.; Mouhyi, J.; Dohan, D.M. Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part IV: Clinical effects on tissue healing. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **2006**, *101*, e56–e60. [[CrossRef](#)] [[PubMed](#)]
4. Gigante, A.; Del Torto, M.; Manzotti, S.; Cianforlini, M.; Busilacchi, A.; Davidson, P.A.; Greco, F.; Mattioli-Belmonte, M. Platelet rich fibrin matrix effects on skeletal muscle lesions: An experimental study. *J. Biol. Regul. Homeost. Agents* **2012**, *26*, 475–484.
5. Rudagi, K.B.; Rudagi, B. One-step apexification in immature tooth using grey mineral trioxide aggregate as an apical barrier and autologous platelet rich fibrin membrane as an internal matrix. *J. Conserv. Dent.* **2012**, *15*, 196–199. [[CrossRef](#)] [[PubMed](#)]
6. Kumar, A.; Yadav, A.; Shetty, N. One-step apexification using platelet rich fibrin matrix and mineral trioxide aggregate apical barrier. *Indian J. Dent. Res.* **2014**, *25*, 809–812. [[CrossRef](#)]
7. Del Torto, M.; Enea, D.; Panfoli, N.; Filardo, G.; Pace, N.; Chiusaroli, M. Hamstrings anterior cruciate ligament reconstruction with and without platelet rich fibrin matrix. *Knee Surg. Sports Traumatol. Arthrosc.* **2015**, *23*, 3614–3622. [[CrossRef](#)] [[PubMed](#)]

8. Matz, E.L.; Pearlman, A.M.; Terlecki, R.P. Safety and feasibility of platelet rich fibrin matrix injections for treatment of common urologic conditions. *Investig. Clin. Urol.* **2018**, *59*, 61–65. [[CrossRef](#)]
9. Soyer, T.; Ayva, S.; Boybeyi, O.; Aslan, M.K.; Cakmak, M. The effect of platelet rich fibrin on growth factor levels in urethral repair. *J. Pediat. Surg.* **2013**, *48*, 2545–2549. [[CrossRef](#)]
10. Nishimoto, S.; Fujita, K.; Sotsuka, Y.; Kinoshita, M.; Fujiwara, T.; Kawai, K.; Kakibuchi, M. Growth Factor Measurement and Histological Analysis in Platelet Rich Fibrin: A Pilot Study. *J. Maxillofac. Oral Surg.* **2015**, *14*, 907–913. [[CrossRef](#)] [[PubMed](#)]
11. Dohan, D.M.; Choukroun, J.; Diss, A.; Dohan, S.L.; Dohan, A.J.; Mouhyi, J.; Gogly, B. Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part III: Leucocyte activation: A new feature for platelet concentrates. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **2006**, *101*, e51–e55. [[CrossRef](#)]
12. Dohan, D.M.; Choukroun, J.; Diss, A.; Dohan, S.L.; Dohan, A.J.; Mouhyi, J.; Gogly, B. Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part II: Platelet-related biologic features. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **2006**, *101*, e45–e50. [[CrossRef](#)]
13. Dohan, D.M.; Choukroun, J.; Diss, A.; Dohan, S.L.; Dohan, A.J.; Mouhyi, J.; Gogly, B. Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part I: Technological concepts and evolution. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **2006**, *101*, e37–e44. [[CrossRef](#)]
14. Ito, K.; Yamada, Y.; Naiki, T.; Ueda, M. Simultaneous implant placement and bone regeneration around dental implants using tissue-engineered bone with fibrin glue, mesenchymal stem cells and platelet-rich plasma. *Clin. Oral Implants Res.* **2006**, *17*, 579–586. [[CrossRef](#)]
15. Schwartz-Arad, D.; Levin, L.; Aba, M. The use of platelet rich plasma (PRP) and platelet rich fibrin (PRF) extracts in dental implantology and oral surgery. *Refuat Hapeh Vehashinayim* **2007**, *24*, 51–55.
16. Kazemi, D.; Fakhrjou, A. Leukocyte and Platelet Rich Plasma (L-PRP) Versus Leukocyte and Platelet Rich Fibrin (L-PRF) For Articular Cartilage Repair of the Knee: A Comparative Evaluation in an Animal Model. *Iran. Red Crescent Med. J.* **2015**, *17*, e19594. [[CrossRef](#)]
17. Papalia, R.; Diaz Balzani, L.; Torre, G.; Tirindelli, M.C.; Nobile, C.; Maffulli, N.; Denaro, V. Intraoperative application Platelet rich fibrin, postoperative injections OF PRP or microfracture only for osteochondral lesions of the knee: A five-year retrospective evaluation. *J. Biol. Regul. Homeost. Agents* **2016**, *30*, 41–49.
18. Milner, D.J.; Cameron, J.A. Muscle repair and regeneration: Stem cells, scaffolds, and the contributions of skeletal muscle to amphibian limb regeneration. *Curr. Top. Microbiol. Immunol.* **2013**, *367*, 133–159. [[CrossRef](#)]
19. De Albornoz, P.M.; Aicale, R.; Forriol, F.; Maffulli, N. Cell Therapies in Tendon, Ligament, and Musculoskeletal System Repair. *Sports Med. Arthrosc. Rev.* **2018**, *26*, 48–58. [[CrossRef](#)]
20. Woolf, A.D.; Pfleger, B. Burden of major musculoskeletal conditions. *Bull. World Health Organ.* **2003**, *81*, 646–656.
21. Wright-Carpenter, T.; Klein, P.; Schäferhoff, P.; Appell, H.J.; Mir, L.M.; Wehling, P. Treatment of muscle injuries by local administration of autologous conditioned serum: A pilot study on sportsmen with muscle strains. *Int. J. Sports Med.* **2004**, *25*, 588–593. [[CrossRef](#)]
22. Baoge, L.; Van Den Steen, E.; Rimbaut, S.; Philips, N.; Witvrouw, E.; Almqvist, K.F.; Vanderstraeten, G.; Vanden Bossche, L.C. Treatment of skeletal muscle injury: A review. *ISRN Orthop.* **2012**. [[CrossRef](#)]
23. Maffulli, N.; Del Buono, A.; Oliva, F.; Giai Via, A.; Frizziero, A.; Barazzuol, M.; Brancaccio, P.; Freschi, M.; Galletti, S.; Lisitano, G.; et al. Muscle Injuries: A Brief Guide to Classification and Management. *Transl. Med. UniSa* **2015**, *12*, 14–18.
24. Dhillon, M.S.; Behera, P.; Patel, S.; Shetty, V. Orthobiologics and platelet rich plasma. *Indian J. Orthop.* **2014**, *48*, 1–9. [[CrossRef](#)]
25. Alsousou, J.; Thompson, M.; Hulley, P.; Noble, A.; Willett, K. The biology of platelet-rich plasma and its application in trauma and orthopaedic surgery: A review of the literature. *J. Bone Joint Surg. Br.* **2009**, *91*, 987–996. [[CrossRef](#)]
26. Dohan Ehrenfest, D.M.; Andia, I.; Zumstein, M.A.; Zhang, C.Q.; Pinto, N.R.; Bielecki, T. Classification of platelet concentrates (Platelet-Rich Plasma-PRP, Platelet-Rich Fibrin-PRF) for topical and infiltrative use in orthopedic and sports medicine: Current consensus, clinical implications and perspectives. *Muscles Ligaments Tendons J.* **2014**, *4*, 3–9. [[CrossRef](#)]

27. Munoz, F.; Jiménez, C.; Espinoza, D.; Vervelle, A.; Beugnet, J.; Haidar, Z. Use of leukocyte and platelet-rich fibrin (L-PRF) in periodontally accelerated osteogenic orthodontics (PAOO): Clinical effects on edema and pain. *J. Clin. Exp. Dent.* **2016**, *8*, e119–e124. [[CrossRef](#)]
28. Wee, J.; Thevendran, G. The role of orthobiologics in foot and ankle surgery: Allogenic bone grafts and bone graft substitutes. *EFORT Open Rev.* **2017**, *2*, 272–280. [[CrossRef](#)]
29. Edwards, S.G.; Calandrucchio, J.H. Autologous blood injections for refractory lateral epicondylitis. *J. Handb. Surg. Am.* **2003**, *28*, 272–278. [[CrossRef](#)]
30. Connell, D.A.; Ali, K.E.; Ahmad, M.; Lambert, S.; Corbett, S.; Curtis, M. Ultrasound-guided autologous blood injection for tennis elbow. *Skeletal Radiol.* **2006**, *35*, 371–377. [[CrossRef](#)]
31. James, S.L.; Ali, K.; Pocock, C.; Robertson, C.; Walter, J.; Bell, J.; Connell, D. Ultrasound guided dry needling and autologous blood injection for patellar tendinosis. *Br. J. Sports Med.* **2007**, *41*, 518–521, discussion 522. [[CrossRef](#)]
32. Kazemi, M.; Azma, K.; Tavana, B.; Rezaiee Moghaddam, F.; Panahi, A. Autologous blood versus corticosteroid local injection in the short-term treatment of lateral elbow tendinopathy: A randomized clinical trial of efficacy. *Am. J. Phys. Med. Rehabil.* **2010**, *89*, 660–667. [[CrossRef](#)]
33. Sánchez, A.R.; Sheridan, P.J.; Kupp, L.I. Is platelet-rich plasma the perfect enhancement factor? A current review. *Int. J. Oral Maxillofac. Implants* **2003**, *18*, 93–103.
34. Marx, R.E.; Carlson, E.R.; Eichstaedt, R.M.; Schimmele, S.R.; Strauss, J.E.; Georgeff, K.R. Platelet-rich plasma: Growth factor enhancement for bone grafts. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **1998**, *85*, 638–646. [[CrossRef](#)]
35. Eshghpour, M.; Majidi, M.R.; Nejat, A.H. Platelet-rich fibrin: An autologous fibrin matrix in surgical procedures: A case report and review of literature. *Iran. J. Otorhinolaryngol.* **2012**, *24*, 197–202.
36. Zumstein, M.A.; Berger, S.; Schober, M.; Boileau, P.; Nyffeler, R.W.; Horn, M.; Dahinden, C.A. Leukocyte- and platelet-rich fibrin (L-PRF) for long-term delivery of growth factor in rotator cuff repair: Review, preliminary results and future directions. *Curr. Pharm. Biotechnol.* **2012**, *13*, 1196–1206. [[CrossRef](#)]
37. Naik, B.; Karunakar, P.; Jayadev, M.; Marshal, V.R. Role of Platelet rich fibrin in wound healing: A critical review. *J. Conserv. Dent.* **2013**, *16*, 284–293. [[CrossRef](#)]
38. Asadi, M.; Alamdari, D.H.; Rahimi, H.R.; Aliakbarian, M.; Jangjoo, A.; Abdollahi, A.; Bahar, M.M.; Azadmand, A.; Forghani, N.; Sadegh, M.N.; et al. Treatment of life-threatening wounds with a combination of allogenic platelet-rich plasma, fibrin glue and collagen matrix, and a literature review. *Exp. Ther. Med.* **2014**, *8*, 423–429. [[CrossRef](#)]
39. Liao, H.T.; Marra, K.G.; Rubin, J.P. Application of platelet-rich plasma and platelet-rich fibrin in fat grafting: Basic science and literature review. *Tissue Eng. Part B Rev.* **2014**, *20*, 267–276. [[CrossRef](#)]
40. Shah, M.; Deshpande, N.; Bharwani, A.; Nadig, P.; Doshi, V.; Dave, D. Effectiveness of autologous platelet-rich fibrin in the treatment of intra-bony defects: A systematic review and meta-analysis. *J. Indian Soc. Periodontol.* **2014**, *18*, 698–704. [[CrossRef](#)]
41. Ali, S.; Bakry, S.A.; Abd-Elhakam, H. Platelet-Rich Fibrin in Maxillary Sinus Augmentation: A Systematic Review. *J. Oral. Implantol.* **2015**, *41*, 746–753. [[CrossRef](#)]
42. Borie, E.; Oliví, D.G.; Orsi, I.A.; Garlet, K.; Weber, B.; Beltrán, V.; Fuentes, R. Platelet-rich fibrin application in dentistry: A literature review. *Int. J. Clin. Exp. Med.* **2015**, *8*, 7922–7929.
43. Asutay, F.; Yolcu, Ü.; Geçör, O.; Acar, A.H.; Öztürk, S.A.; Malkoç, S. An evaluation of effects of platelet-rich-fibrin on postoperative morbidities after lower third molar surgery. *Niger. J. Clin. Pract.* **2017**, *20*, 1531–1536. [[CrossRef](#)]
44. Du Toit, J.; Siebold, A.; Dreyer, A.; Gluckman, H. Choukroun Platelet-Rich Fibrin as an Autogenous Graft Biomaterial in Preimplant Surgery: Results of a Preliminary Randomized, Human Histomorphometric, Split-Mouth Study. *Int. J. Periodontics Restorative Dent.* **2016**, *36*, s75–s86. [[CrossRef](#)]
45. Bilginaylar, K.; Uyanik, L.O. Evaluation of the effects of platelet-rich fibrin and piezosurgery on outcomes after removal of impacted mandibular third molars. *Br. J. Oral Maxillofac. Surg.* **2016**, *54*, 629–633. [[CrossRef](#)]
46. Uyanik, L.O.; Bilginaylar, K.; Etikan, İ. Effects of platelet-rich fibrin and piezosurgery on impacted mandibular third molar surgery outcomes. *Head Face Med.* **2015**, *11*, 25. [[CrossRef](#)]
47. Ozgul, O.; Senses, F.; Er, N.; Tekin, U.; Tuz, H.H.; Alkan, A.; Kocyigit, I.D.; Atil, F. Efficacy of platelet rich fibrin in the reduction of the pain and swelling after impacted third molar surgery: Randomized multicenter split-mouth clinical trial. *Head Face Med.* **2015**, *11*, 37. [[CrossRef](#)]

48. Kumar, N.; Prasad, K.; Ramanujam, L.K.R.; Dexith, J.; Chauhan, A. Evaluation of treatment outcome after impacted mandibular third molar surgery with the use of autologous platelet-rich fibrin: A randomized controlled clinical study. *J. Oral Maxillofac. Surg.* **2015**, *73*, 1042–1049. [[CrossRef](#)]
49. Guinot, A.; Arnaud, A.; Azzis, O.; Habonimana, E.; Jasienski, S.; Frémond, B. Preliminary experience with the use of an autologous platelet-rich fibrin membrane for urethroplasty coverage in distal hypospadias surgery. *J. Pediatr. Urol.* **2014**, *10*, 300–305. [[CrossRef](#)]
50. Garin, P.; Mullier, F.; Gheldof, D.; Dogne, J.M.; Putz, L.; Van Damme, J.P. Platelet-rich fibrin (PRF): An autologous packing material for middle ear microsurgery. *B-ENT* **2014**, *10*, 27–34.
51. Eshghpour, M.; Dastmalchi, P.; Nekooei, A.H.; Nejat, A. Effect of platelet-rich fibrin on frequency of alveolar osteitis following mandibular third molar surgery: A double-blinded randomized clinical trial. *J. Oral Maxillofac. Surg.* **2014**, *72*, 1463–1467. [[CrossRef](#)]
52. Tashnizi, M.A.; Alamdari, D.H.; Khayami, M.E.; Rahimi, H.R.; Moeinipour, A.; Amouzeshi, A.; Seifalian, A.M. Treatment of non-healing sternum wound after open-heart surgery with allogenic platelet-rich plasma and fibrin glue-preliminary outcomes. *Indian J. Plast. Surg.* **2013**, *46*, 538–542. [[CrossRef](#)]
53. Tatullo, M.; Marrelli, M.; Cassetta, M.; Pacifici, A.; Stefanelli, L.V.; Scacco, S.; Dipalma, G.; Pacifici, L.; Inchingolo, F. Platelet Rich Fibrin (P.R.F.) in reconstructive surgery of atrophied maxillary bones: Clinical and histological evaluations. *Int. J. Med. Sci.* **2012**, *9*, 872–880. [[CrossRef](#)]
54. Fortunato, L.; Barone, S.; Bennardo, F.; Giudice, A. Management of Facial Pyoderma Gangrenosum Using Platelet-Rich Fibrin: A Technical Report. *J. Oral Maxillofac. Surg.* **2018**, *76*, 1460–1463. [[CrossRef](#)]
55. Dohan Ehrenfest, D.M.; Pinto, N.R.; Pereda, A.; Jiménez, P.; Corso, M.D.; Kang, B.S.; Nally, M.; Lanata, N.; Wang, H.L.; Quirynen, M. 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. *Platelets* **2018**, *29*, 171–184. [[CrossRef](#)]
56. Jiménez-Aristizabal, R.F.; López, C.; Álvarez, M.E.; Giraldo, C.; Prades, M.; Carmona, J.U. Long-term cytokine and growth factor release from equine platelet-rich fibrin clots obtained with two different centrifugation protocols. *Cytokine* **2017**, *97*, 149–155. [[CrossRef](#)]
57. Anitua, E.; Sánchez, M.; Nurden, A.T.; Nurden, P.; Orive, G.; Andía, I. New insights into and novel applications for platelet-rich fibrin therapies. *Trends Biotechnol.* **2006**, *24*, 227–234. [[CrossRef](#)]
58. Man, D.; Plosker, H.; Winland-Brown, J.E. The use of autologous platelet-rich plasma (platelet gel) and autologous platelet-poor plasma (fibrin glue) in cosmetic surgery. *Plast. Reconstr. Surg.* **2001**, *107*, 229–237. [[CrossRef](#)]
59. Abd El Raouf, M.; Wang, X.; Miusi, S.; Chai, J.; Mohamed AbdEl-Aal, A.B.; Nefissa Helmy, M.M.; Ghanaati, S.; Choukroun, J.; Choukroun, E.; Zhang, Y.; Miron, R.J. Injectable-platelet rich fibrin using the low speed centrifugation concept improves cartilage regeneration when compared to platelet-rich plasma. *Platelets* **2017**, *14*, 1–9. [[CrossRef](#)]
60. Kawase, T.; Okuda, K.; Wolff, L.F.; Yoshie, H. Platelet-rich plasma-derived fibrin clot formation stimulates collagen synthesis in periodontal ligament and osteoblastic cells in vitro. *J. Periodontol.* **2003**, *74*, 858–864. [[CrossRef](#)]
61. Simonpieri, A.; Del Corso, M.; Sammartino, G.; Dohan Ehrenfest, D.M. The relevance of Choukroun's platelet-rich fibrin and metronidazole during complex maxillary rehabilitations using bone allograft. Part I: A new grafting protocol. *Implant Dent.* **2009**, *18*, 102–111. [[CrossRef](#)]
62. Shah, R.; M G, T.; Thomas, R.; Mehta, D.S. An Update on the Protocols and Biologic Actions of Platelet Rich Fibrin in Dentistry. *Eur. J. Prosthodont. Restor. Dent.* **2017**, *25*, 64–72. [[CrossRef](#)]
63. Ghanaati, S.; Booms, P.; Orłowska, A.; Kubesch, A.; Lorenz, J.; Rutkowski, J.; Landes, C.; Sader, R.; Kirkpatrick, C.; Choukroun, J. Advanced platelet-rich fibrin: A new concept for cell-based tissue engineering by means of inflammatory cells. *J. Oral. Implantol.* **2014**, *40*, 679–689. [[CrossRef](#)]
64. Clark, D.; Rajendran, Y.; Paydar, S.; Ho, S.; Cox, D.; Ryder, M.; Dollard, J.; Kao, R.T. Advanced platelet-rich fibrin and freeze-dried bone allograft for ridge preservation: A randomized controlled clinical trial. *J. Periodontol.* **2018**, *89*, 379–387. [[CrossRef](#)]
65. Mourão, C.F.; Valiense, H.; Melo, E.R.; Mourão, N.B.; Maia, M.D. Obtention of injectable platelets rich-fibrin (i-PRF) and its polymerization with bone graft: Technical note. *Revista do Colégio Brasileiro de Cirurgiões* **2015**, *42*, 421–423. [[CrossRef](#)]

66. Miron, R.J.; Fujioka-Kobayashi, M.; Hernandez, M.; Kandalam, U.; Zhang, Y.; Ghanaati, S.; Choukroun, J. Injectable platelet rich fibrin (i-PRF): Opportunities in regenerative dentistry. *Clin. Oral. Investig.* **2017**, *21*, 2619–2627. [[CrossRef](#)]
67. Kobayashi, E.; Flückiger, L.; Fujioka-Kobayashi, M.; Sawada, K.; Sculean, A.; Schaller, B.; Miron, R.J. Comparative release of growth factors from PRP, PRF, and advanced-PRF. *Clin. Oral. Investig.* **2016**, *20*, 2353–2360. [[CrossRef](#)]
68. Qiao, J.; An, N.; Ouyang, X. Quantification of growth factors in different platelet concentrates. *Platelets* **2017**, *28*, 774–778. [[CrossRef](#)]
69. Jeong, S.M.; Lee, C.U.; Son, J.S.; Oh, J.H.; Fang, Y.; Choi, B.H. Simultaneous sinus lift and implantation using platelet-rich fibrin as sole grafting material. *J. Craniomaxillofac. Surg.* **2014**, *42*, 990–994. [[CrossRef](#)]
70. Gurler, G.; Delilbasi, C. Effects of leukocyte-platelet rich fibrin on postoperative complications of direct sinus lifting. *Minerva Stomatol.* **2016**, *65*, 207–212.
71. Rastogi, P.; Saini, H.; Singhal, R.; Dixit, J. Periodontal regeneration in deep intrabony periodontal defect using hydroxyapatite particles with platelet rich fibrin membrane—a case report. *J. Oral. Biol. Craniofac. Res.* **2011**, *1*, 41–43. [[CrossRef](#)]
72. Lekovic, V.; Milinkovic, I.; Aleksic, Z.; Jankovic, S.; Stankovic, P.; Kenney, E.B.; Camargo, P.M. Platelet-rich fibrin and bovine porous bone mineral vs. platelet-rich fibrin in the treatment of intrabony periodontal defects. *J. Periodont. Res.* **2012**, *47*, 409–417. [[CrossRef](#)]
73. Agarwal, A.; Gupta, N.D.; Jain, A. Platelet rich fibrin combined with decalcified freeze-dried bone allograft for the treatment of human intrabony periodontal defects: A randomized split mouth clinical trial. *Acta Odontol. Scand.* **2016**, *74*, 36–43. [[CrossRef](#)] [[PubMed](#)]
74. Sharma, P.; Grover, H.S.; Masamatti, S.S.; Saksena, N. A clinicoradiographic assessment of 1% metformin gel with platelet-rich fibrin in the treatment of mandibular grade II furcation defects. *J. Indian Soc. Periodontol.* **2017**, *21*, 303–308. [[CrossRef](#)]
75. Rehan, M.; Khatri, M.; Bansal, M.; Puri, K.; Kumar, A. Comparative Evaluation of Coronally Advanced Flap Using Amniotic Membrane and Platelet-rich Fibrin Membrane in Gingival Recession: An 18-Month Clinical Study. *Contemp. Clin. Dent.* **2018**, *9*, 188–194. [[CrossRef](#)]
76. Rajaram, V.; Thyegarajan, R.; Balachandran, A.; Aari, G.; Kanakamedala, A. Platelet Rich Fibrin in double lateral sliding bridge flap procedure for gingival recession coverage: An original study. *J. Indian Soc. Periodontol.* **2015**, *19*, 665–670. [[CrossRef](#)]
77. Tunali, M.; Özdemir, H.; Arabacı, T.; Gürbüzler, B.; Pıkdöken, L.; Firatlı, E. Clinical evaluation of autologous platelet-rich fibrin in the treatment of multiple adjacent gingival recession defects: A 12-month study. *Int. J. Periodontics Restor. Dent.* **2015**, *35*, 105–114. [[CrossRef](#)]
78. Agarwal, S.K.; Jhingran, R.; Bains, V.K.; Srivastava, R.; Madan, R.; Rizvi, I. Patient-centered evaluation of microsurgical management of gingival recession using coronally advanced flap with platelet-rich fibrin or amnion membrane: A comparative analysis. *Eur. J. Dent.* **2016**, *10*, 121–133. [[CrossRef](#)]
79. Eren, G.; Kantarcı, A.; Sculean, A.; Atilla, G. Vascularization after treatment of gingival recession defects with platelet-rich fibrin or connective tissue graft. *Clin. Oral. Investig.* **2016**, *20*, 2045–2053. [[CrossRef](#)]
80. Garg, S.; Arora, S.A.; Chhina, S.; Singh, P. Multiple Gingival Recession Coverage Treated with Vestibular Incision Subperiosteal Tunnel Access Approach with or without Platelet-Rich Fibrin—A Case Series. *Contemp. Clin. Dent.* **2017**, *8*, 464–468. [[CrossRef](#)]
81. Kumar, A.; Bains, V.K.; Jhingran, R.; Srivastava, R.; Madan, R.; Rizvi, I. Patient-centered Microsurgical Management of Gingival Recession using Coronally Advanced Flap with Either Platelet-rich Fibrin or Connective Tissue Graft: A Comparative Analysis. *Contemp. Clin. Dent.* **2017**, *8*, 293–304. [[CrossRef](#)] [[PubMed](#)]
82. Yang, K.C.; Wang, C.H.; Chang, H.H.; Chan, W.P.; Chi, C.H.; Kuo, T.F. Fibrin glue mixed with platelet-rich fibrin as a scaffold seeded with dental bud cells for tooth regeneration. *J. Tissue Eng. Regen. Med.* **2012**, *6*, 777–785. [[CrossRef](#)]
83. Keswani, D.; Pandey, R.K. Revascularization of an immature tooth with a necrotic pulp using platelet-rich fibrin: A case report. *Int. Endod. J.* **2013**, *46*, 1096–1104. [[CrossRef](#)]
84. Mishra, N.; Narang, I.; Mittal, N. Platelet-rich fibrin-mediated revitalization of immature necrotic tooth. *Contemp. Clin. Dent.* **2013**, *4*, 412–415. [[CrossRef](#)]

85. Zhao, Y.H.; Zhang, M.; Liu, N.X.; Lv, X.; Zhang, J.; Chen, F.M.; Chen, Y.J. The combined use of cell sheet fragments of periodontal ligament stem cells and platelet-rich fibrin granules for avulsed tooth reimplantation. *Biomaterials* **2013**, *34*, 5506–5520. [[CrossRef](#)]
86. Sam, G.; Shivashankar, V.Y. Management of a pathologically migrated upper anterior tooth using platelet-rich fibrin and a modified crown preparation technique. *J. Indian Soc. Periodontol.* **2014**, *18*, 786–788. [[CrossRef](#)]
87. Faizuddin, U.; Solomon, R.V.; Mattapathi, J.; Guniganti, S.S. Revitalization of traumatized immature tooth with platelet-rich fibrin. *Contemp. Clin. Dent.* **2015**, *6*, 574–576. [[CrossRef](#)] [[PubMed](#)]
88. Jadhav, G.R.; Shah, D.; Raghvendra, S.S. Autologous Platelet Rich Fibrin aided Revascularization of an immature, non-vital permanent tooth with apical periodontitis: A case report. *J. Nat. Sci. Biol. Med.* **2015**, *6*, 224–225. [[CrossRef](#)] [[PubMed](#)]
89. Ji, B.; Sheng, L.; Chen, G.; Guo, S.; Xie, L.; Yang, B.; Guo, W.; Tian, W. The combination use of platelet-rich fibrin and treated dentin matrix for tooth root regeneration by cell homing. *Tissue Eng. Part A* **2015**, *21*, 26–34. [[CrossRef](#)]
90. Nagaveni, N.B.; Kumari, K.N.; Poornima, P.; Reddy, V. Management of an endo-perio lesion in an immature tooth using autologous platelet-rich fibrin: A case report. *J. Indian Soc. Pedod. Prev. Dent.* **2015**, *33*, 69–73. [[CrossRef](#)]
91. Nagaveni, N.B.; Poornima, P.; Joshi, J.S.; Pathak, S.; Nandini, D.B. Revascularization of immature, nonvital permanent tooth using platelet-rich fibrin in children. *Pediat. Dent.* **2015**, *37*, 1–6.
92. Solomon, R.V.; Faizuddin, U.; Guniganti, S.S.; Waghray, S. Analysis of the rate of maturogenesis of a traumatized Cvek's stage 3 anterior tooth treated with platelet-rich fibrin as a regenerative tool using three-dimensional cone-beam computed tomography: An original case report. *Indian J. Dent. Res.* **2015**, *26*, 90–95. [[CrossRef](#)]
93. Giudice, A.; Barone, S.; Giudice, C.; Bennardo, F.; Fortunato, L. Can platelet-rich fibrin improve healing after surgical treatment of medication-related osteonecrosis of the jaw? A pilot study. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **2018**, *126*, 390–403. [[CrossRef](#)]
94. Mosca, M.J.; Rodeo, S.A. Platelet-rich plasma for muscle injuries: Game over or time out. *Curr. Rev. Musculoskelet. Med.* **2015**, *8*, 145–153. [[CrossRef](#)]
95. Chien, C.S.; Ho, H.O.; Liang, Y.C.; Ko, P.H.; Sheu, M.T.; Chen, C.H. Incorporation of exudates of human platelet-rich fibrin gel in biodegradable fibrin scaffolds for tissue engineering of cartilage. *J. Biomed. Mater. Res. Part B Appl. Biomater.* **2012**, *100*, 948–955. [[CrossRef](#)]
96. Wong, C.C.; Kuo, T.F.; Yang, T.L.; Tsuang, Y.H.; Lin, M.F.; Chang, C.H.; Lin, Y.H.; Chan, W.P. Platelet-Rich Fibrin Facilitates Rabbit Meniscal Repair by Promoting Meniscocytes Proliferation, Migration, and Extracellular Matrix Synthesis. *Int. J. Mol. Sci.* **2017**, *18*, 1722. [[CrossRef](#)]
97. Kuo, T.F.; Lin, M.F.; Lin, Y.H.; Lin, Y.C.; Su, R.J.; Lin, H.W.; Chan, W.P. Implantation of platelet-rich fibrin and cartilage granules facilitates cartilage repair in the injured rabbit knee: Preliminary report. *Clinics* **2011**, *66*, 1835–1838. [[CrossRef](#)]
98. Kazemi, D.; Fakhrou, A.; Dizaji, V.M.; Alishahi, M.K. Effect of autologous platelet rich fibrin on the healing of experimental articular cartilage defects of the knee in an animal model. *Biomed. Res. Int.* **2014**. [[CrossRef](#)]
99. Kazemi, D.; Shams Asenjan, K.; Dehdilani, N.; Parsa, H. Canine articular cartilage regeneration using mesenchymal stem cells seeded on platelet rich fibrin: Macroscopic and histological assessments. *Bone Joint Res.* **2017**, *6*, 98–107. [[CrossRef](#)]
100. Güler, İ.; Billur, D.; Aydin, S.; Kocatürk, S. Efficacy of platelet-rich fibrin matrix on viability of diced cartilage grafts in a rabbit model. *Laryngoscope* **2015**, *125*, E104–E111. [[CrossRef](#)]
101. Göral, A.; Aslan, C.; Bolat Küçükzeybek, B.; Işık, D.; Hoşnuter, M.; Durgun, M. Platelet-Rich Fibrin Improves the Viability of Diced Cartilage Grafts in a Rabbit Model. *Aesthet. Surg. J.* **2016**, *36*, NP153–NP162. [[CrossRef](#)]
102. Zumstein, M.A.; Rumian, A.; Lesbats, V.; Schaer, M.; Boileau, P. Increased vascularization during early healing after biologic augmentation in repair of chronic rotator cuff tears using autologous leukocyte- and platelet-rich fibrin (L-PRF): A prospective randomized controlled pilot trial. *J. Shoulder Elbow Surg.* **2014**, *23*, 3–12. [[CrossRef](#)]
103. Zumstein, M.A.; Rumian, A.; Thélu, C.É.; Lesbats, V.; O'Shea, K.; Schaer, M.; Boileau, P. SECEC Research Grant 2008 II: Use of platelet- and leucocyte-rich fibrin (L-PRF) does not affect late rotator cuff tendon healing: A prospective randomized controlled study. *J. Shoulder Elbow Surg.* **2016**, *25*, 2–11. [[CrossRef](#)]

104. Antuña, S.; Barco, R.; Martínez Diez, J.M.; Sánchez Márquez, J.M. Platelet-rich fibrin in arthroscopic repair of massive rotator cuff tears: A prospective randomized pilot clinical trial. *Acta Orthop. Belg.* **2013**, *79*, 25–30.
105. Hasan, S.; Weinberg, M.; Khatib, O.; Jazrawi, L.; Strauss, E.J. The Effect of Platelet-rich Fibrin Matrix on Rotator Cuff Healing in a Rat Model. *Int. J. Sports Med.* **2016**, *37*, 36–42. [[CrossRef](#)]
106. Alviti, F.; Gurzi, M.; Santilli, V.; Paoloni, M.; Padua, R.; Bernetti, A.; Bernardi, M.; Mangone, M. Achilles Tendon Open Surgical Treatment With Platelet-Rich Fibrin Matrix Augmentation: Biomechanical Evaluation. *J. Foot Ankle Surg.* **2017**, *56*, 581–585. [[CrossRef](#)]
107. Eggli, S.; Kohlhof, H.; Zumstein, M.; Henle, P.; Hartel, M.; Evangelopoulos, D.S.; Bonel, H.; Kohl, S. Dynamic intraligamentary stabilization: Novel technique for preserving the ruptured ACL. *Knee Surg. Sports Traumatol. Arthrosc.* **2015**, *23*, 1215–1221. [[CrossRef](#)]
108. Saltzman, B.M.; Ukwuani, G.; Makhni, E.C.; Stephens, J.P.; Nho, S.J. The Effect of Platelet-Rich Fibrin Matrix at the Time of Gluteus Medius Repair: A Retrospective Comparative Study. *Arthroscopy* **2018**, *34*, 832–841. [[CrossRef](#)]
109. Laver, L.; Carmont, M.R.; McConkey, M.O.; Palmanovich, E.; Yaacobi, E.; Mann, G.; Nyska, M.; Kots, E.; Mei-Dan, O. Plasma rich in growth factors (PRGF) as a treatment for high ankle sprain in elite athletes: A randomized control trial. *Knee Surg. Sports Traumatol. Arthrosc.* **2015**, *23*, 3383–3392. [[CrossRef](#)]
110. Rowan, T.L.; Drouin, J.L. A multidisciplinary approach including the use of platelet-rich plasma to treat an elite athlete with patellar tendinopathy—A case report. *J. Can. Chiropr. Assoc.* **2013**, *57*, 301–330.
111. Deal, J.B.; Smith, E.; Heard, W.; O'Brien, M.J.; Savoie, F.H. Platelet-Rich Plasma for Primary Treatment of Partial Ulnar Collateral Ligament Tears: MRI Correlation With Results. *Orthop. J. Sports Med.* **2017**, *5*, 2325967117738238. [[CrossRef](#)]
112. Dines, J.S.; Williams, P.N.; El Attrache, N.; Conte, S.; Tomczyk, T.; Osbahr, D.C.; Dines, D.M.; Bradley, J.; Ahmad, C.S. Platelet-Rich Plasma Can Be Used to Successfully Treat Elbow Ulnar Collateral Ligament Insufficiency in High-Level Throwers. *Am. J. Orthop.* **2016**, *45*, 296–300.
113. Blanke, F.; Vavken, P.; Haenle, M.; von Wehren, L.; Pagenstert, G.; Majewski, M. Percutaneous injections of Platelet rich plasma for treatment of intrasubstance meniscal lesions. *Muscles Ligaments Tendons J.* **2015**, *5*, 162–166. [[CrossRef](#)]
114. Knapen, M.; Gheldof, D.; Drion, P.; Layrolle, P.; Rompen, E.; Lambert, F. Effect of leukocyte- and platelet-rich fibrin (L-PRF) on bone regeneration: A study in rabbits. *Clin. Implant. Dent. Relat. Res.* **2015**, *17*, e143–e152. [[CrossRef](#)]
115. Jeon, Y.R.; Kim, M.J.; Kim, Y.O.; Roh, T.S.; Lee, W.J.; Kang, E.H.; Yun, I.S. Scaffold Free Bone Regeneration Using Platelet-Rich Fibrin in Calvarial Defect Model. *J. Craniofac. Surg.* **2018**, *29*, 251–254. [[CrossRef](#)]
116. Abdullah, W.A. Evaluation of bone regenerative capacity in rats claverial bone defect using platelet rich fibrin with and without beta tri calcium phosphate bone graft material. *Saudi. Dent. J.* **2016**, *28*, 109–117. [[CrossRef](#)]

