# Platelet-rich Plasma Role in Bone Tumors Defects

Systematic Review

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By

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Mohamed Gad

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# List of Abbreviations

| Abb. | Full term |
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*ADSCs* .....*Adipose Derived Stem Cells*
*BMP*.....*Bone morphogenetic proteins*
*BPBM* .....*Bovine porous bone mineral*
*CPD*..... *Citrate–phosphate–dextrose*
*DBM*..... *demineralized bone matrix*
*ECM*..... *Extracellular matrix*
*ELISA*.....*Enzyme-linked immunosorbant assay*
*FDBA*.....*Freeze-dried bone allograft*
*FGF*.....*Fibroblast growth factor*
*g* .....*Gravitational force*
*GFs*.....*Growth factors*
*HA*..... *Hydroxyapatite*
*HBV* .....*Hepatitis B virus*
*HCV* .....*Hepatitis C virus*
*HIV* ..... *Human immunodeficiency virus*
*IGF* .....*Insulin Growth Factor*
*IGF-I*.....*Insulin growth factor I*
*IL*.....*Interleukin*
*L-PRF* ..... *Leucocyte- and platelet-rich fibrin*
*L-PRP* ..... *Leucocyte- and PRP*
*L-PRP* .....*Leucocyte- and PRP*
*MGCSH* .....*Medical-grade calcium sulphate hemihydrate*
*MIS* ..... *Minimally invasive surgery*
*MMP* .....*Matrix metalloproteinase*
*MP*..... *Melting point*
*MSCs* ..... *Mesenchymal stem cells*
*PCBM* .....*Particulate cancellous bone and marrow*
*PDGF*.....*Platelet-derived growth factor*

# List of Abbreviations (Cont...)

| Abb. | Full term |
|---|---|

*PG* ..... *Proteoglycan*
*PGA*..... *Polyglycolic acid*
*PLA* ..... *Poly lactic acid*
*PLGA* .....*Poly lactic-co-glycolide*
*PPP* ..... *Platelet-poor plasma*
*PPP* .....*Platelet-poor plasma*
*P-PRF* ..... *Pure platelet-rich fibrin*
*P-PRP* ..... *Pure Platelet-Rich Plasma*
*PRC*..... *Platelet-rich concentrate*
*PRGF* .....*Preparation Rich In Growth Factors*
*PRP*.....*Platelet-rich plasma*
*RBC*.....*Red blood cells*
*RCT*.....*Randomized controlled trials*
*RhD*..... *Rhesus factor D*
*TCP*..... *Tricalcium phosphate*
*TGF* .....*Transforming Growth Factor*
*TGF-β*..... *Transforming Growth Factor β*
*TGF-β1*.....*Transforming growth factor-β1*
*Ti*.....*Titanium*
*TSS* ..... *Tissue Sparing surgery*
*VEGF* ..... *Vascular Endothelial Growth Factor*
*WB* .....*Whole blood*
β-*TCP*.....β-*tricalcium phosphate*

# ABSTRACT

***Background:*** The treatment of large bone defects represents a significant clinical Challenge for orthopaedic surgeons. The well orchestrated regenerative ability of bone to heal is hampered, in the case of complex defects, by the lack of a template for regeneration and, eventually, it requires surgical intervention.

***Aim of the Work:*** To determine the effectiveness of platelet-rich plasma in bone healing.

***Methodology:*** A Search was performed on the PubMed database considering the literature from 2000 to 2019, using the following string: ("Bone Substitutes" [Mesh] OR "Bone Transplantation" [Mesh] OR "Bone Regeneration" [Mesh] OR "Osseointegration" [Mesh]) AND ("Blood Platelets" [Mesh] OR "Platelet-Rich Plasma"[Mesh]). After abstracts screening, the full-texts of selected papers were analyzed and the papers found from the reference lists were also considered for the literature analysis of this review.

***Results:*** Systematic research showed a growing interest in this treatment approach for the integration of bone-graft, bone-graft substitutes, or bone implants, with an increasing number of published studies over time.

***Conclusion:*** However, several aspects have to be clarified, such as what biomaterials can benefit the most from PRP and what is the best protocol for PRP both for production and application. Randomized controlled trials are needed to support the potential of this treatment approach and the advantages and disadvantages of PRP as an augmentation procedure to favor implant integration.



***Keywords:*** *Platelet-rich Plasma - Mesenchymal Stem Cells - Bone Tumors Defects*

# Introduction

The treatment of large bone defects represents a significant clinical Challenge for orthopaedic surgeons. [1, 2] The well orchestrated regenerative ability of bone to heal is hampered, in the case of complex defects, by the lack of a template for regeneration and, eventually, it requires surgical intervention. [3]

Auto grafts and allograft are considered to be the major bone substitutes; however they each have their own limitations regarding availability, donor site morbidity and chronic pain, leading to not be always optimal results. [4]

In order to overcome these issues, several bone substitute materials have been developed and applied in the clinical practice. [5, 6]

To further improve the success rates, co-adjuvant agents have also been proposed, which may enhance implant osseointegration potential and restore bone tissue function. [7]

Among these, growth factors (GFs) are expressed during different phases of tissue healing and may represent a key element in promoting tissue regeneration. [8]

In fact, GFs delivered through orthopaedic devices have been reported to enhance osteoblastic activity and favour implant integration. [9, 10]

Platelet-rich plasma (PRP) is emerging as a powerful tool for tissue healing, thanks to the many GFs contained in platelet alpha-granules. PRP is defined as a blood derivative, where the platelets concentration is above the baseline levels, thus providing a large number of bioactive molecules in physiologic proportions. [11]

Activated platelets can release more than 300 molecules that are responsible for the coordination of numerous cell-cell and cell-extracellular matrix (ECM) interactions. [12]

The evidence for PRP osteogenic potential has been suggested by several in vitro studies, i.e. PRP addition in culture medium promoted the proliferation and differentiation of human mesenchymal stem cells (MSCs), [13, 14] and the effect of PRP on osteogenic differentiation was also seen on human adipose derived stem cells (ADSCs). [15]

Furthermore, PRP can improve cell chemokinesis and chemotaxis through cytoskeleton reorganization and accelerate cell migration, thus influencing osteoblast like cell mobility. [16]

Finally, anti-microbial effects have been suggested, [17, 18] which are highly desirable in relation to a surgical bone application. However, besides the beneficial role in terms of proliferation and differentiation, as well as cell migration and protection towards microbial contamination, in-vitro studies have also shown controversial results on PRP potential to favour bone healing. [19–21]

# Aim of the Work

In this study systematic review for platelet-rich plasma role in bone healing after removal of tumors:

- To determine the effectiveness of platelet-rich plasma in bone healing.
- To clarify the difference between platelet-rich plasma and bone grafts.

# Bone Substitutes

## 1. Bone graft:

It is the second most common transplantation tissue, with blood being by far the commonest. [22]

More than 500,000 bone grafting procedures are happening annually in the United States and 2.2 million worldwide in order to repair bone defects in orthopaedics, neurosurgery and dentistry. [23]

Furthermore, the treatment of post-traumatic skeletal complications, such as delayed unions, nonunions, malunions, are challenging. Bone-grafting is usually required to stimulate bone-healing. [24]

In addition, spinal fusions, filling defects following removal of bone tumors and several congenital diseases may require bone grafting.

Several methods of reconstructing bone defects are available namely using autograft, allograft,demineralised bone matrix (DBM), hydroxyapatitecalcium phosphate (CP, TCP), autologous bone marrow aspirates, bone morphogenetic proteins, and several other related growth factors (VEGF, PDGF, etc.).

The gold standard of bone-grafting is harvesting autologous cortical and cancellous bone from the iliac crest.

Technological evolution along with better understanding of bone-healing biology, however, have lead to the development of several bone graft substitutes that are currently available to the orthopaedic surgeons. [25]

## ***Bone graft characteristics***

Osteogenesis, osteoinduction, and osteoconduction are the three essential elements of bone regeneration along with the final bonding between host bone and grafting material which is called osteointegration.

**Osteoprogenitor** cells living within the donor graft, may survive during transplantation, could potentially proliferate and differentiate to osteblasts and eventually to osteocytes. These cells represent the ‘‘osteogenic’’ potential of the graft. [26]

**‘‘Osteoinduction’’** on the other hand is the stimulation and activation of host mesenchymal stem cells from the surrounding tissue, which differentiate into bone-forming osteoblasts. This process is mediated by a cascade of signals and the activations of several extra and intracellular receptors the most important of which belong to the TGF-beta superfamily. [26]

**Osteoconduction** describes the facilitation and orientation of blood-vessel and the creation of the new Haversian systems into the bone scaphold. [27]

Finally **‘‘osteointegration’’** describes the surface bonding between the host bone and the grafting material. [27]

## A. Autograft

**Autologous bone**, the golden standard of bone grafting, provides optimal osteoconductive, osteoconductive, and osteogenic properties. Iliac crest is the most frequently chosen donor site as it provides easy access to good quality and quantity cancellous autograft. [26]

Harvesting autologous bone from the iliac crest has, however, several downsides as it lengthens the overall surgical procedure and is usually complicated by residual pain and cosmetic disadvantages. [28]

Furthermore, it may fail in clinical practice as most of the cellular (osteogenic) elements do not survive transplantion. [29]

Other limitations include elderly or paediatric patients and patients with malignant disease. [30]

In addition autograft harvesting is associated with a 8.5-20% of complications including; haematoma formation, blood loss, nerve injury, hernia formation, infection, arterial injury, ureteral injury, fracture, pelvic instability, cosmetic defects, tumour transplantation, and sometimes chronic pain at the donor site. [28]

## B. Allograft

Allograft is the most frequently chosen bone substitute and is regarded as the surgeon's second option. [31]