

The dos and don'ts in the handling of PRF

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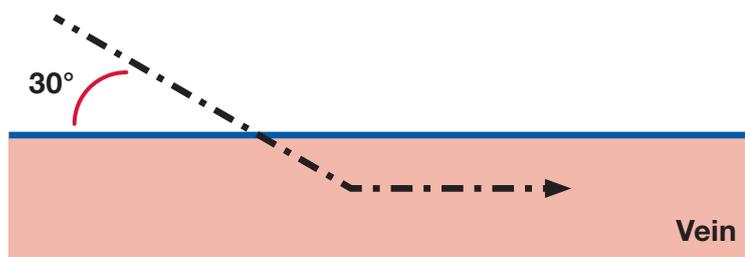


Fig. 1: Visualisation of the puncture direction during blood collection.

Autologous blood concentrates, and platelet-rich fibrin (PRF) in particular, are increasingly used today to support wound healing and regenerative processes.¹ PRF is made from the patient's own peripheral blood without the addition of anticoagulants. A solid or liquid PRF matrix can be obtained through a single centrifugation process, depending on the collection tube that is used.² Through this centrifugation process, the blood components are separated according to the centrifugal force used. The red blood cells move towards the bottom of the tube.³ The platelets and leucocytes are concentrated in the upper layer, the remaining fibrin matrix. Thus, this autologous blood concentrate, which also contains further plasma proteins, is capable of actively releasing different growth factors such as vascular endothelial growth factors (VEGF), epidermal growth factors (EGF), or platelet-derived growth factors (PDGF) over a relatively long period of time (up to fifteen days).^{4,5} These growth factors play a key role in the support of wound healing and regenerative processes, since they contribute to the formation of new vessels, epithelialisation and the stimulation of further regener-

ative cells.^{6,7} The composition and bioactivity of PRF depends primarily on the centrifugal force that is used during centrifugation.³

Several recent studies have demonstrated the influence of the centrifugal force on the composition and bioactivity of the obtained PRF.⁸⁻¹² It has been shown that the application of a low centrifugal force for accumulation leads to a significantly higher number of platelets and leukocytes in PRF compared to a medium or high centrifugal force.^{3,10} Growth factors are released in a similar way. PRF matrices that are prepared with a low centrifugal force release significantly higher concentrations of different growth factors (such as VEGF, PDGF, EGF, TGF- β 1) compared to PRF matrices that are prepared using a higher centrifugal force.⁸⁻¹² As a result, the so-called Low-Speed Centrifugation Concept (LSCC) was introduced, which aims at standardising the production of blood concentrates and enabling reproducible treatment protocols or clinical results.³ This article will particularly focus on the technical aspects of the clinical application and handling of PRF. The tubes used for the production of PRF have been specifically developed for this particular purpose. Depending on the clinical indication, two different variants of PRF matrices exist. PRF tubes with a glass surface promote coagulation. During centrifugation, a solid PRF matrix is formed. In contrast, the coagulation process can be slowed down by means of plastic-coated tubes. Accordingly, coagulation is slowed down during centrifugation. At room temperature, a PRF matrix remains liquid for about thirty minutes after centrifugation until it eventually coagulates.

Protocol	RPM (x 100)	Duration (min)	Centrifugal force (x G)
High concentration RCF	2,400	8	710
Medium concentration RCF	1,200	8	177
Low concentration RCF	600	8	44

RCF, relative centrifugal force; RPM, revolutions of the centrifuge per minute.

Table 1: Visualisation of the different LSCC protocols (Low-Speed Centrifugation Concept for a centrifuge with a radius of 110 mm).

Blood collection

For the production of PRF the patient's own venous blood is required, which is taken from the peripheral veins after the patient has been fully briefed on the procedure. This blood collection is a routine method and is particularly used in diagnostics. The blood collection should be carried out according to the guidelines of the World Health Organization (WHO).¹³ In order to find a suitable puncture site, the anatomical position of the peripheral veins should first be palpated. For this purpose, the vena mediana cubiti, which is located in the antecubital fossa (inner bend of the elbow), is ideally suited. Gloves must be worn and the tourniquet must be placed approximately 5 cm above the puncture site of the vein, which must be disinfected with a skin antiseptic according to the manufacturer's instructions. A butterfly needle is then inserted into the vein at an angle of 30° to the skin surface (Fig. 1). To avoid completely piercing through the vein, the angle should be

flattened once the vein has been hit. The vacuum system of the PRF tube then fills the tube with venous blood until an amount of 10 ml is reached and the blood supply can be stopped automatically. After loosening the tourniquet tube, the butterfly cannula can be removed. Subsequently, sufficient pressure should be exerted on the puncture site with a sterile swab in order to avoid secondary bleeding underneath the skin.

Centrifugation

In order to avoid early physiological coagulation of the blood, the PRF tubes must be centrifuged quickly after blood collection in a dedicated centrifuge that stands on a table nearby in the same treatment room. Through centrifugation, a separation process is triggered, which sediments cells and/or biomolecules from a suspension (i.e. blood), depending on the relative centrifugal force and the size, shape and density of the vari-

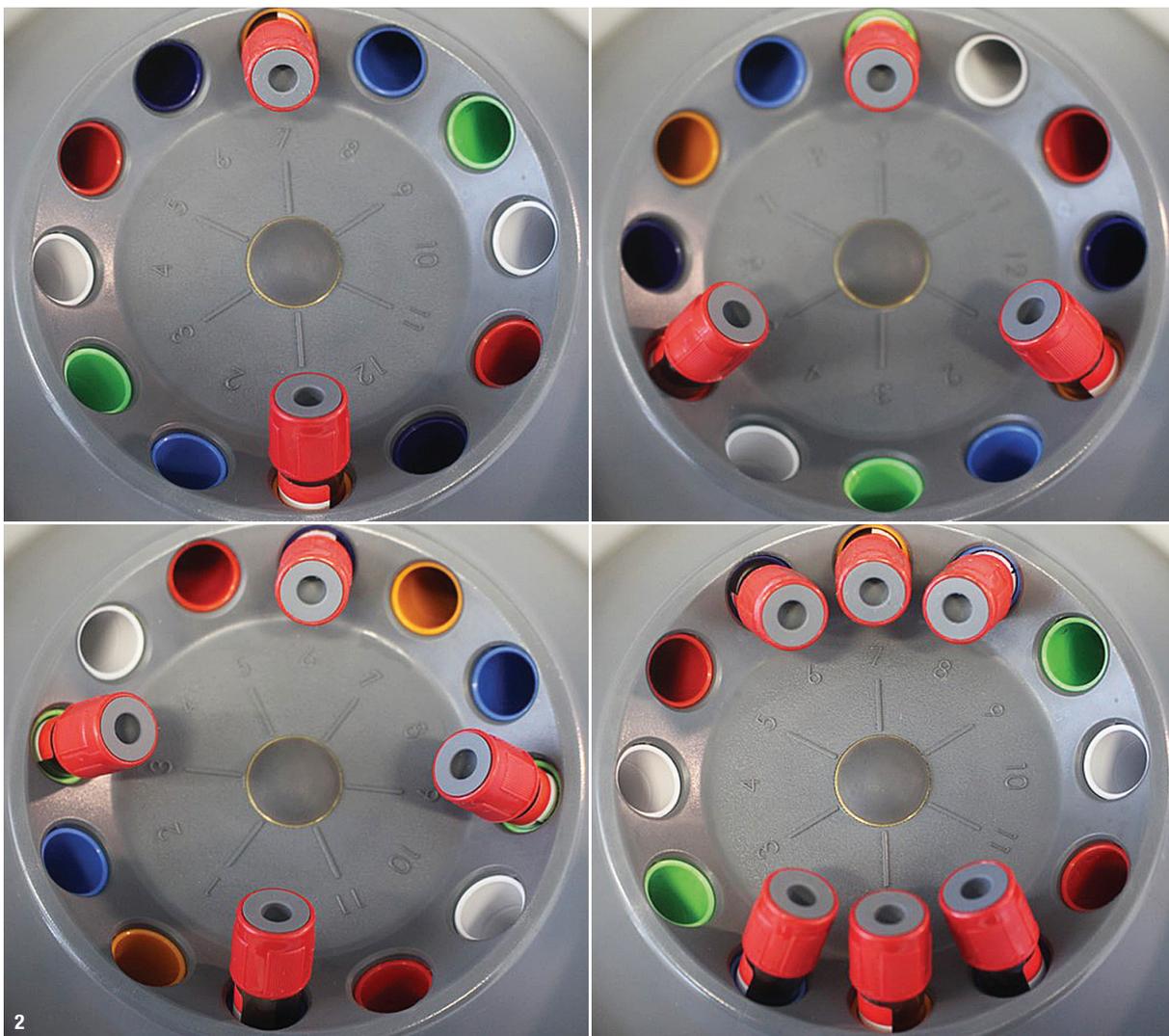


Fig. 2: Balance pattern of the centrifuge when loading two, three, four and six tubes. Centrifugation of five, seven, nine or eleven tubes is not possible. For this purpose, an additional tube filled with water must be used.

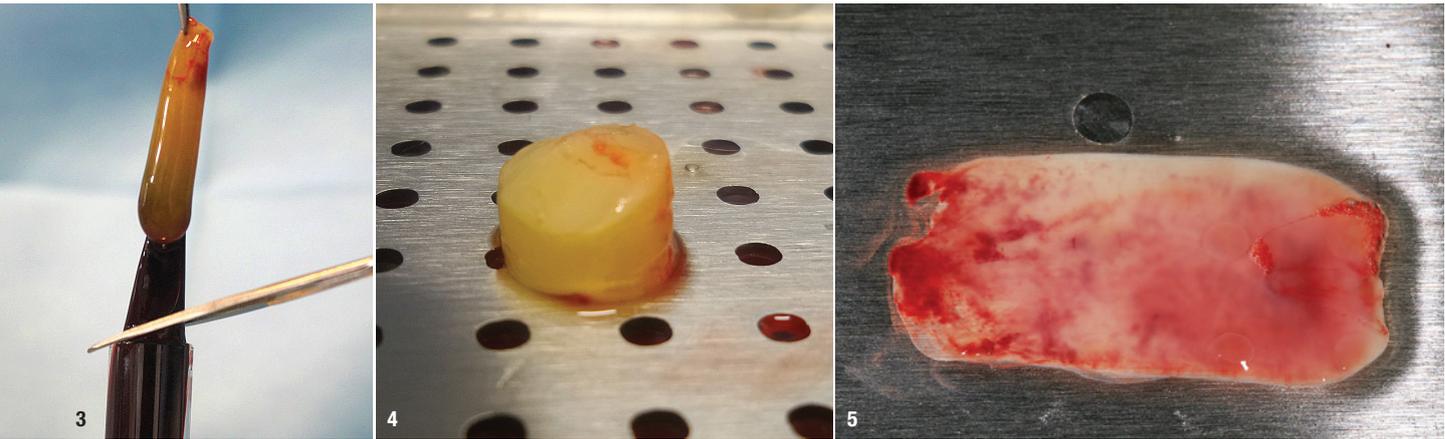


Fig. 3: Separating the red phase from the solid PRF phase. **Fig. 4:** A PRF plug. **Fig. 5:** A thinly pressed PRF matrix.

ous suspension components. The relative centrifugal force (RCF) represents the centrifugal force as a multiple of the Earth's gravity and is often expressed as the value G. Moreover, it is a decisive factor for the resulting concentration of the sedimented cells and biomolecules in PRF. The value G indicates exactly the force required for an optimal centrifugation of a corresponding suspension (in this case blood) to obtain the desired sediment (in this case PRF) as final product, and allows the calculation of the necessary speed of the centrifuge rotor for a corresponding tube and centrifuge.

For centrifuges where only the rotational speed (revolutions of the centrifuge per minute, RPM) can be set, the RCF or the necessary G-value must first be calculated by means of a fixed formula. The relation between rotational speed (RPM) and RCF depends on the size of the rotor (r = radius of rotation = distance between the axis of rotation and the bottom of the tube). Here, the following formula is used for conversion:¹⁴ $RCF = 1.12 \times \text{radius} \times (\text{RPM}/1,000)^2$. The relative centrifugal force required for PRF production using the established LSCC

is given in Table 1 and should be set on the centrifuge according to the clinical indication ($r = 110\text{mm}$). In general, the centrifuge should be placed on a stable and even fundament. When loading the centrifuge with the blood-filled tubes, it is imperative to ensure that any imbalance is eliminated. This means that the tubes must be placed inside of the rotor in such a way that the weight of the tube placed exactly opposite the other is identical (Fig. 2). If the number of tubes is uneven, a tube filled with the equivalent volume (such as sodium chloride, for example) must be added to compensate for the weight.

Processing of PRF

Immediately after centrifugation, the tubes are carefully removed from the centrifuge and transferred to an appropriate tube holder. Owing to the applied RCF and depending on the size, shape and density of the blood components, only two phases can now be visually identified: a red phase at the bottom of the tube, which contains mainly erythrocytes and a PRF phase on top of it, filling up the upper part of the tube. In the case of solid PRF, which is obtained by centrifuging the blood in the red PRF tubes, these two phases coagulate very quickly. In order to separate the solid PRF matrix from the red lower phase, it is recommended to first separate the two phases roughly by cutting them with scissors. In concrete terms, this means carefully lifting up the upper phase of solid PRF with sterile tweezers (the lower red phase is lifted as well) and then roughly separate the two phases in the upper part of the red phase (Fig. 3). The PRF phase (with remains of the red phase) is then transferred into a dedicated PRF box provided for this particular purpose. This PRF box, which has been specially developed for various PRF indications, consists of a stainless-steel container with a self-weighted lid and a large and small stamp. In this box, the remaining parts of the red phase can now be removed from the PRF phase by carefully wiping it off with a blunt object (such as a closed pair of scissors). Thereafter, solid PRF matrices can be further

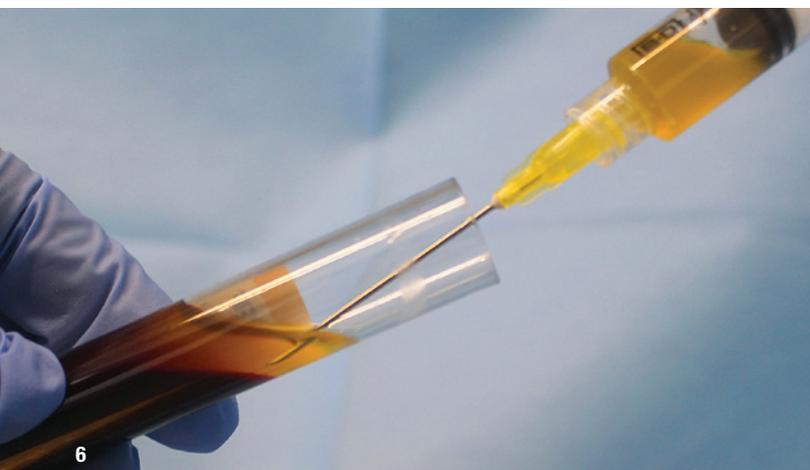


Fig. 6: Separating liquid PRF from the red phase by means of a syringe.

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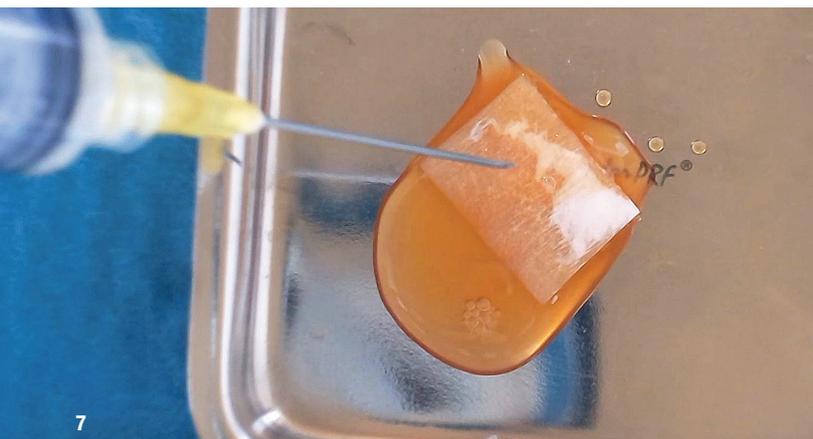


Fig. 7: Biologising a collagen-based matrix with liquid PRF.

processed either into a PRF plug (Fig. 4) or into a thinly pressed PRF matrix (Fig. 5), depending on the clinical indication. For PRF application in the extraction sockets of wisdom teeth, the fibrin clot is placed in the containers in the box, which are specifically provided for this very indication, and carefully compressed with the small stamp until the appropriate size of the PRF plug is reached.

In order to process PRF into a thinly pressed matrix, the fibrin clot is carefully placed on the grid of the PRF box and processed into a pressed PRF matrix using the self-weighted lid of the PRF box. This pressed PRF matrix can then, for example, be placed as a wound cover on the surgical sites where autologous palatal soft-tissue transplants have been removed to support the wound healing process. In addition, it can be used during implant surgeries as a support of the mucosal flap. As opposed to the earlier-described solid PRF, which is produced through centrifugation in glass tubes, the two phases of the blood remain liquid at first for a few minutes if centrifugation is done with plastic tubes. The production of liquid PRF opens up the possibility of further PRF applications in the field of regenerative medicine, such as the combination of PRF with bone grafting materials and collagen membranes. The upper, still liquid PRF phase is carefully removed from the remaining lower red phase using a syringe. A 5 ml syringe with a long and wide 21-gauge cannula is best suited for this purpose (Fig. 6). It is recommended that the tube is slightly tilted so that the boundary between the two phases can be seen more easily. In this way as much liquid PRF as possible can be extracted from the tube, without extracting too much of the red phase. With a liquid matrix, the wetting of the biomaterial surface can be carried out in a reproducible fashion. In contrast, based on the preliminary results of the ongoing clinical studies, it is no longer recommended to cut up a solid PRF matrix and mix the obtained pieces with bone grafting material in order to create so-called sticky bone. Current research findings indicate that this can lead to a loss of volume, since the fibrin is resorbed

after 10 to 15 days, facilitating the formation of cavities in the augmentation sites as a result.

In order to biologise biomaterials of different classes and origin, such as bone grafting materials and collagen-based membranes (allogeneic, xenogeneic, synthetic), they can be combined with solid or liquid PRF. Here, biomaterials that do not trigger a foreign body reaction should ideally be used. With the help of PRF it is possible to biologise or functionalise these biomaterials, since they themselves do not have any bioactive components, but serve only as a mere scaffold. The functionalisation of biomaterials with endogenous cells, plasma and growth factors that are found in great concentration in PRF should lead to an improved integration of the biomaterial in certain defects and, as a consequence, to an increased regenerative capacity. When combining PRF with bone grafting material and collagen-based membranes, PRF in liquid form should be used. In order to biologise and stabilise these bone grafting materials or membranes, liquid PRF collected in the syringe is drizzled onto them, which also simplifies clinical handling (Fig. 7).

A comprehensive list of references can be obtained from the authors.



about the author



Frankfurt am Main-based **Prof. Shahram Ghanaati** is a specialist in maxillofacial surgery and oncology. In 2013, he was appointed Director of the University Cancer Center of the Frankfurt University Hospital. He is the Senior Physician and Deputy Director of the Department of Oral and Maxillofacial Plastic Surgery of the Frankfurt University Hospital. In addition, he is the Director of the research laboratory FORM-Lab (Frankfurt Orofacial Regenerative Medicine).

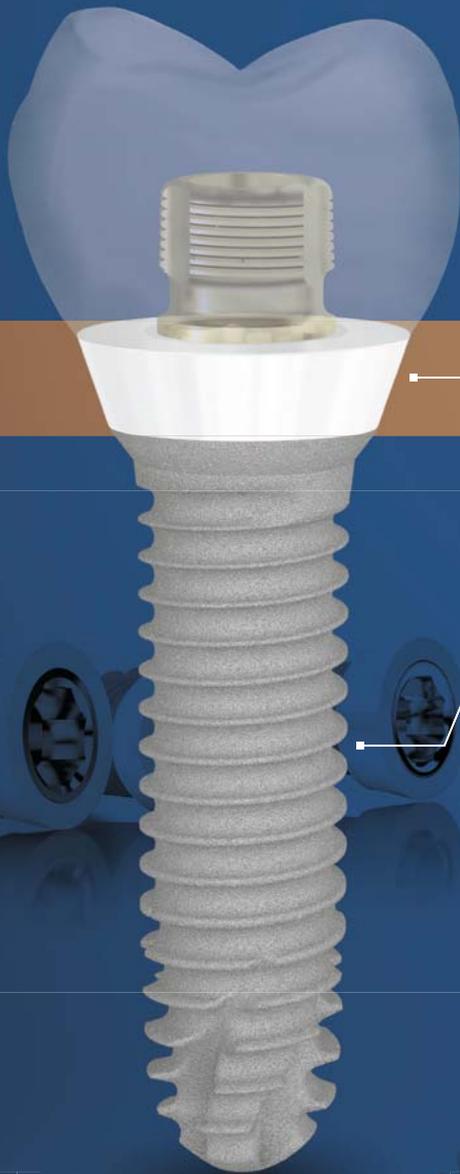
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