Fig. 1

Fig. 1: Prof. Shahram Ghanaati (right) and Georg Isbaner (Editorial Manager of *implants*).

More than just PRF

Needless to say, the patient's own tissue is still the augmentation material of choice and often preferred by many clinicians to the various synthetic or xenogeneic bone replacement materials on the market. In recent years, the autologous blood concentrate known as platelet-rich fibrin (PRF) as an adjunct to surgery has established itself as a gentle and practice-oriented method of accelerating wound healing. In this interview, Frankfurt am Main-based Prof. Shahram Ghanaati discusses the significance of autologous blood concentrates in dentistry and the associated challenges. A researcher, expert and oft-invited speaker, Prof. Ghanaati has been active in the field of bone and tissue regeneration for many years.

Where does PRF come from, and how did its use come into being?

It started with the development of platelet-rich plasma (PRP), which was especially in vogue in the 1980s and 1990s. With PRP, we learned that we could work with blood products. The exclusively liquid concentrate, which was initially produced with a relatively high centrifugal force, was intended to accelerate wound healing processes. Unfortunately, however, this development was quickly followed by attempts to find a healing agent for bone healing in PRP, which heralded the demise of PRP. In the end, one simply had to admit that PRP made no contribution whatsoever to bone healing. How is a blood concentrate supposed to heal bone in the first place? The problem was that the wrong marketing concept had been pursued. In addition, PRP was seen as a product. However, blood concentrates are not products, but concentrates obtained from the patient's blood. Every human being has a different blood composition and as a result also a specific blood concentrate. This own-blood concentrate serves to accelerate and support the tissue healing of the same patient. Since blood concentrates up to the year 2000, including the PRP successor, plasma rich in growth factors (PRGF), were predominantly liquid, they had to be mixed with an anticoagulant, such as sodium citrate, in order to be centrifuged. And these concentrates were only available in injection form.

It was Dr Joseph Choukroun who finally discovered that it is possible to naturally coagulate the concentrated blood by using either glass or plastic surfaces. For example, PRF clots are made in a glass tube and liquid PRF in a silicone tube, which helps to keep the concentrate liquid for half an hour. The blood concentrates—liquid or solid—that we produce today are known as PRF. It differs from PRP and PRGF in that it does not require the addition of any anticoagulants. Personally, I believe that these concentrates shouldn't be called PRP, PRGF or PRF, but patient-specific blood concentrates, given that they are ultimately nothing more than concentrates made from blood and are produced depending on the centrifugal force. This would be an important contribution to the general understanding. In addition, we should start to move away from the "P" in "PRP", "PRGF" and "PRF". The "P" implies that only the platelets are crucial in a blood concentrate. How-

ever, there are a number of further substances and cells in the blood that make a contribution as well, such as leucocytes, which are the defence cells. It would be wrong to speak only of thrombocytes.

What is the current significance of autologous blood concentrate in dentistry?
During a surgical procedure, something is opened up which then has to be closed again. In order to heal, every wound needs some form of support. In a surgical situation, the use of patient-specific autologous blood concentrate can serve as support in that it significantly accelerates wound healing—in almost every indication and in every field of dentistry. The work is of course done by the bone substitute material or the collagen membrane used, but the communication between these two components and the rest of the tissue is done by the autologous blood concentrate. It is similar to the launch vehicle on a space shuttle that is launched on a mission into space: the launcher separates from the space shuttle after leaving the atmosphere and the actual mission is then completed by the space shuttle. We have conducted numerous studies showing that the use of PRF can complete the intended clinical indication more successfully compared with indications without the use of concentrated autologous blood.

> "We have to rethink our approach towards blood concentrate-based regeneration."

There was a time, not long ago, when people were extremely excited by stem cells, which are great cells, of course, with many functions that contribute greatly to regenerative processes in the body. However, in many countries—and that includes Germany—stem cell therapy is, for the most part, still banned from use. It is only permitted for certain exceptional indications, but not for dentistry. In addition, the use of cells or growth factors is actually not possible within the confines of a dental practice. You have to consider that you first have to remove tissue and isolate cells from it, which alone can take weeks. You then have to cultivate these cells in order to transplant them to the patient at an even later point in time. In comparison with this rather cumbersome process, autologous blood concentrates are a much more practice-oriented alternative and not as time-consuming.

What does the production entail in concrete terms?
The patient comes to a dental practice and lies down on a stretcher. Under sterile conditions, blood is taken from him or her and then placed in a centrifuge, which stands chairside on an adjacent table. The blood taken from the patient is centrifuged there according to our low-speed centrifugation concept (LSCC). According to the LSCC, autologous blood concentrate can be produced with a high, medium or low centrifugal force. All you have to do is press a few different buttons to rotate the centrifuge differently. In this way, we are able to produce not only PRF but PRP and PRGF as well. The centrifugation duration is always eight minutes, no matter whether you are producing high-, medium- or low-concentrated concentrate. Using glass and silicone-based tubes, a high centrifugal force results in a large clot with a relatively high volume, but few cells and growth factors. The lower the centrifugal force, the smaller the clot, but the more growth factors and cells it contains. As a result, we are able to work with PRF based on indication. In situations where a dense fibrin matrix is required, high centrifugation is required, and in situations where concentrated autologous blood is to be mixed with bone graft substitutes, for example, a matrix is required that allows the cells to grow the tissue between the granules. In periodontal therapy, however, there are times when autologous blood concentrate with a liquid matrix is needed as an alternative to Emdogain (Straumann) or to treat the mucous membrane.

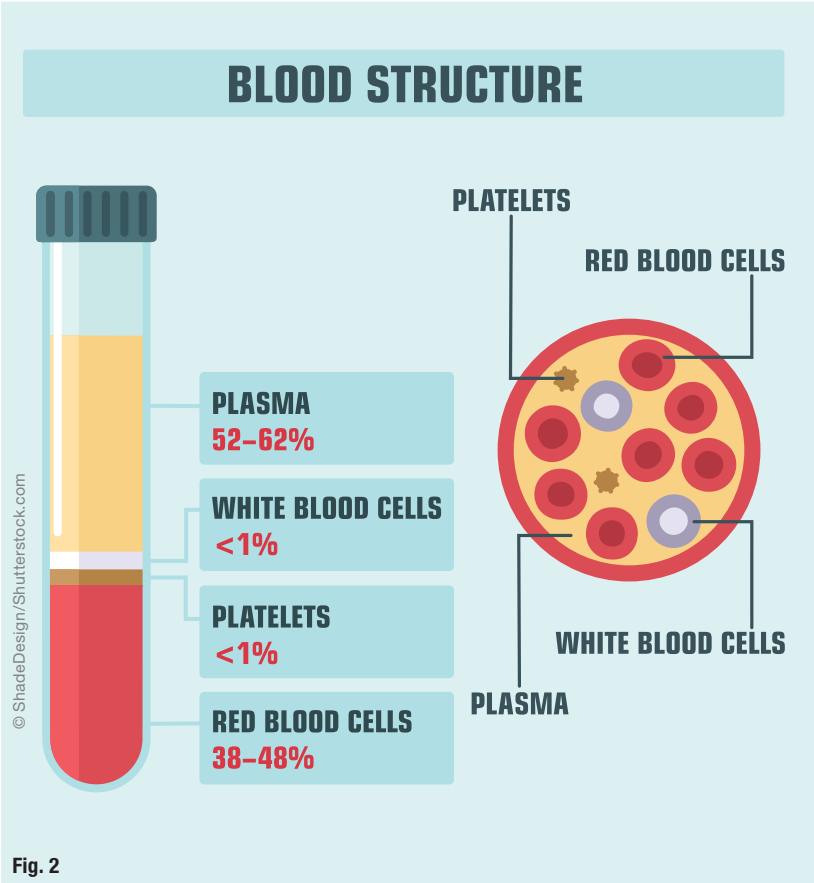

Fig. 2

Fig. 2: Graphic representation of the blood structure.

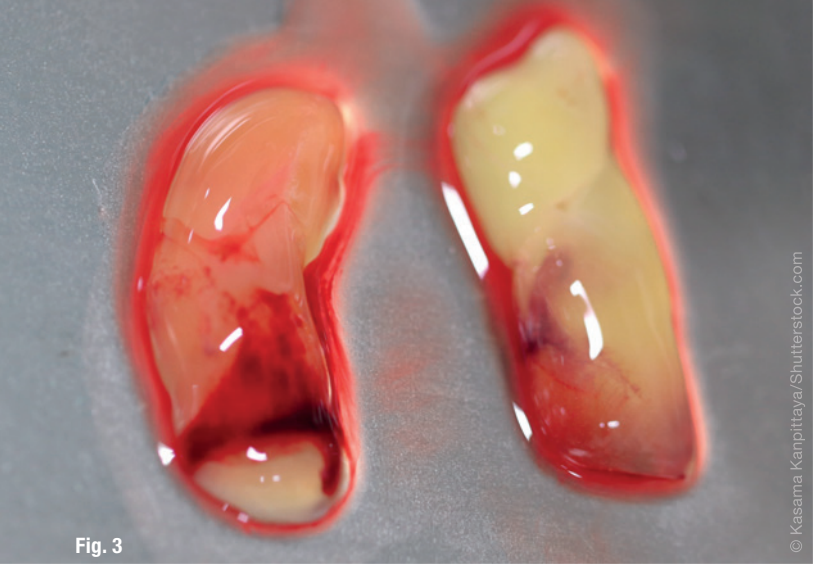

Fig. 3: Platelet-rich fibrin is used to accelerate wound healing processes and enhance the effectiveness of bone grafting material.

Is autologous blood concentrate already used in other clinical areas?
Concentrated autologous blood has a significant and elegant effect on patients suffering from temporomandibular joint problems and on patients with refractory fractures. In orthopaedics, PRP, which is nothing other than PRF in a different concentration, is used in the field of joint regeneration. In aesthetic treatment, it is used to treat a range of scar formations, acne and various other skin diseases, and as a hyaluronic acid replacement. Furthermore, we use the patient's own blood concentrate for chronic pain patients. There, we do exclusively autologous blood therapy indicated as pain therapy. Hence, dentistry is rather a niche area. I would like to draw attention to another problem, which will increasingly come up in the future: the number of cases of bisphosphonate-associated bone necrosis and osteogenic and radiogenic bone necrosis is progressively increasing, as bisphosphonates are often administered to ageing patients as part of cancer therapy. The resulting bone necrosis can have serious consequences, such as partial resection of the jaw. In fact, the number of carcinoma patients is generally increasing. Here in Frankfurt am Main, we have already established treatment concepts that achieve great revitalisation with autologous blood concentrates.

The main focus of dentistry is mostly on implantology, although this discipline is a secondary one. Periodontics, for example, is much more important because the focus is on saving the tooth. We have developed treatment concepts to regeneratively support periodontal therapy. However, it is essential that patients assume as much responsibility as possible on a metabolic level. This concerns vitamin D3, proper nutrition, water balance management, etc. One can, for example, enable kidney illnesses to develop, simply by drinking too little water. This is exactly what is meant by "biological dentistry", namely the promotion of the regenerative powers of the patient through a holistic therapy approach. The understanding of this, however, should be conveyed in effective ways in the media, and the media should be committed to doing so because patients are simply unaware of many of these things.

What are the major challenges associated with establishing autologous blood concentrates?
In order to establish something successfully, it always requires pioneers to drive development forward. But this, of course, also has its downside: something can become excessively used as soon as everyone starts doing it. At present, there are certain things that we simply don't have. For example, we do not yet have a manual on how to use autologous blood concentrates for certain indications in dentistry. There is no such thing—or at least not yet. There are also no online education platforms with full-high-definition videos demonstrating the correct use of certain protocols step by step. We urgently need to make this information publicly available. In addition, we need a systematic series of articles on the respective indications from the perspective of a practice-oriented scientist. There is currently no understanding of what can or cannot be done with autologous blood concentrates. In addition to which, Henry Schein has been causing confusion for several months with so-called L-PRF. This was established around 2007 and was originally obtained by a very high centrifugal force. After the break with Dr Choukroun, Intra-Lock declared the term "L-PRF" and trademarked it for marketing reasons.

Of course, the question then arises: should blood products be allowed to be legally protected through trademarks at all? Intra-Lock's idea was to exclusively establish their own brand along the lines of the name "iPhone", which has come to be used synonymously for smartphones. Intra-Lock also wanted to achieve this with its L-PRF, that is, that the term L-PRF would eventually be used synonymously for blood concentrates. However, this approach contradicts mine. I would like to teach dentists that it is not about a specific product, but only about blood concentrates—pure contributions to wound healing. It would be fatal if companies tried to create even more confusion with more pseudo-product names. There's L-PRF, there's A-PRF, there's I-PRF—and everything has a trademark. We have to rethink our approach towards blood concentrate-based regeneration. Research and clinical application should be at the forefront. I look at this increasing commercialisation and the tendency to plunge obsessively into a product with great concern. There is still a lot of educational work to be done.

How do you meet these challenges?
We can't generate long-term data with one protocol if new protocols are added every other month. It would be like the film *Groundhog Day*, where the process is constantly repeated anew. There is no scientific evidence because everyone has only pursued their own agendas so far. Dentists work a little with this PRF, a little with that PRGF, a little with this PRP, and when you then look back over ten years, private health insurance companies say: "Yes, there is available data—but it doesn't fit together

at all." And that's why they don't pay. For each of these protocols—be it PRP, PRGF or PRF—you would have to systematically show whether it works or not. Therefore, my goal is to summarise all existing data in one review. This is where our LSCC comes into play—it was developed with the idea that dentists around the world would use the same protocol, so that in ten years' time, we'd be able to say what the survival rate of certain implants placed with which specific protocol is. At our academy for autologous blood concentrates, which I set up in cooperation with Goethe University in Frankfurt am Main, over 20 clinical trials using the LSCC are currently being conducted. We hope that we will soon be able to describe the corresponding indications for the LSCC and clarify the questions of what can be done with it and how it can be done. None of this is done for fame or to demonstrate greatness. To me, it is just very important that the work that has already been done is not nullified by an uncoordinated series of cases from dentists who are uninformed. My vision is to bring medicine into dentistry and to move away from this pure case observation that we've primarily been doing so far. Cases are good for showing what something looks like. However, it would be dangerous to make assessments on what is good and what is bad based on one case.

Lastly, I would not assume to explain to my fellow dentists why PRGF or PRP is bad. What I reject is this dogged attachment to a particular product and the view that everything can be cured with it. One should not get carried away. I successfully use autologous blood concentrates to treat chronic or diabetic wounds. We are even able to accelerate hair growth by means of concentrated autologous blood. Before I proclaim this publicly at a congress, however, I must have at least one study that proves that, after autologous blood treatment, the hair is significantly longer than after treatment with, for example, sodium chloride—and not only in one patient, but in 20 others too. This scientific standard should apply to everyone. If Dr Eduardo Anitua thinks that his concept is the best, then he must prove it and point out the indications for which this applies. He has to show for what it works and for what it doesn't. Talking about problems is important. At the congresses at which I give lectures, I like to encourage the audience to reflect on what can and cannot be done with blood concentrates. As a matter of fact, there are also complications when using autologous blood concentrates. One must not succumb to the mistaken belief that life would be completely carefree because of concentrated autologous blood. I would like also to be able to address these things in the future—openly and together with other experts in this area.

contact

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Blood Concentrate Day to be held in September 2020

On 11 September 2020, the first Blood Concentrate Day will be held at Goethe University Frankfurt am Main in Germany. The objective of the conference, hosted by the Blood Concentration Academy (BCA) under the scientific direction of Prof. Shahram Ghanaati and Prof. Robert Sader, will be to further the understanding of autologous blood concentrates and to discuss the numerous application possibilities within the scope of regenerative and general dentistry. Produced from the peripheral blood of patients, today's autologous blood concentrates are commonly used to improve wound healing and relieve pain in a wide variety of clinical indications. The success of dental implants can also be optimised with the aid of bioactive blood concentrates rich in platelets, fibrin and growth factors. In addition, blood concentrates are successfully used as an aid for tooth preservation, making them an effective tool in periodontology. At the first Blood Concentrate Day, it will be discussed in what ways autologous blood concentrates as adjuncts to dental surgery contribute to the current trend towards a biologisation of bone and soft tissue within the context of modern dentistry. For more information on the event visit **www.abc-day.com** or contact **event@oemus-media.de**.

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