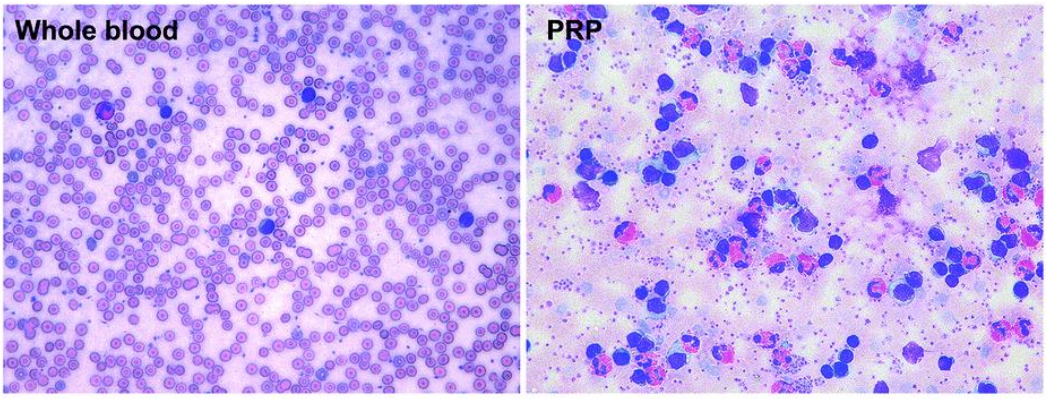
ACTIGRAFT vs. PRP

Platelet-rich plasma (PRP) is blood plasma that has been enriched with platelets. As a concentrated source of autologous platelets, PRP contains several different growth factors and other cytokines.

PRP is a product of blood separation process where a fraction of the whole blood is being extracted augmented and activated. The final product of the PRP process is a liquid extract of activated platelets which are sometimes mounted on a carrier agent such as gel.

Below are microscopic images of whole blood and PRP, containing platelets floating in plasma.



The whole blood clot by ActiGraft is a natural tissue of the human body, it is a natural tissue of a very complex and delicate process where the whole blood in its liquid form is changing into a scaffold tissue that contains all of the many elements that are essential for wound healing and are not present in PRP. Such elements include among others a rigid natural fibrin scaffold which is the optimal extra cellular replacement matrix as it contains biologic elements that magnetize macrophages and it interacts with the body to moderate the healing process.

Below is a microscopic image of the whole blood clot – containing a fibrin scaffold incorporating platelets, macrophages, neutrophils, plasma and other blood cells and clot derived materials.

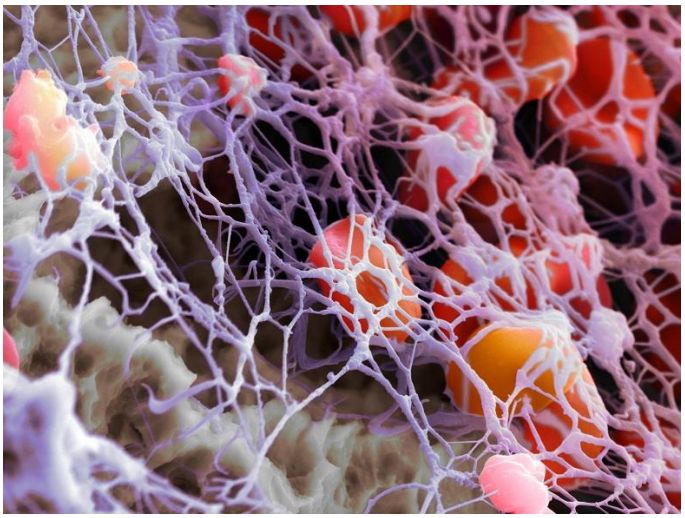
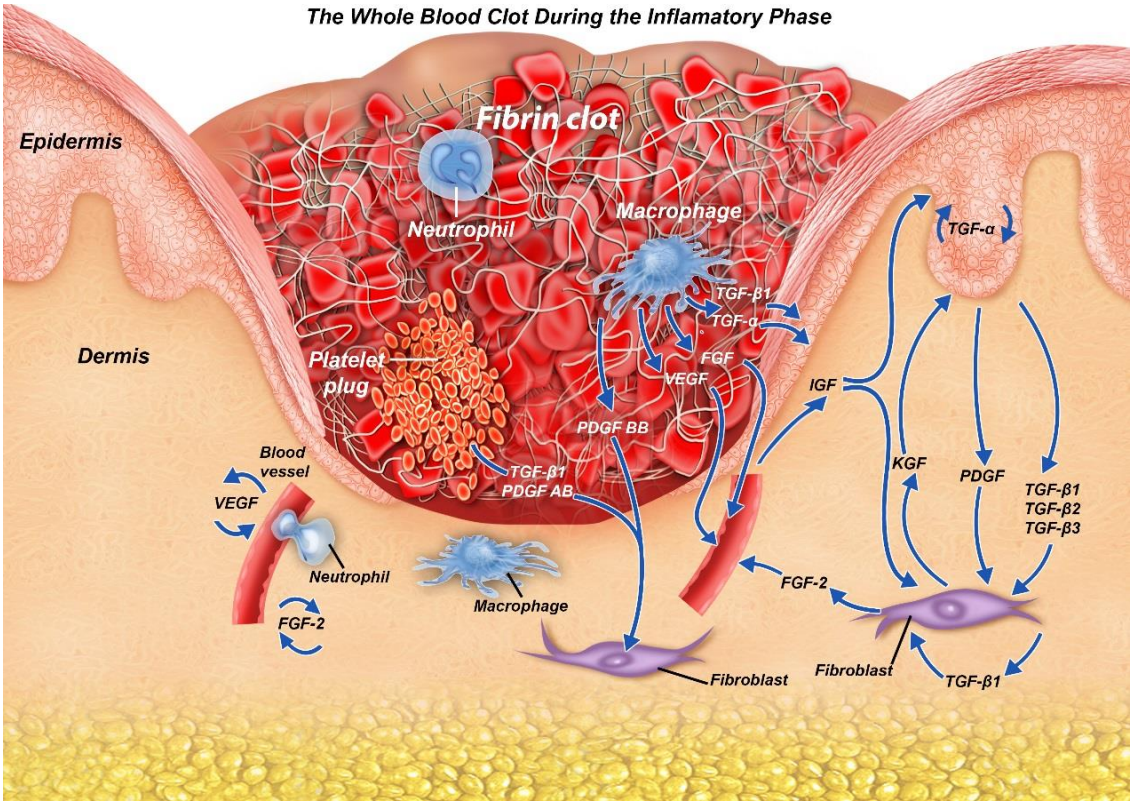


Photo by Martin Oeggerli, supported by School of Life Sciences, FHNW

The attempt to isolate a single or several selected elements from the blood and augment them will always be significantly inferior to the use of the whole tissue that was designed by evolution to perfection. Beyond PRP there were also failed attempts to use activated macrophages for wound healing.

The interactions that the whole blood clot has with the body and with the wound are many and complex. Even clot elements that until recently were considered redundant in the wound healing process are known today to play a significant role. As an example, red blood cells were considered to be inert bystanders in wound healing, however it was found that they actively participate in the dynamic process of ECM modulation in the wound healing process.

Below is a drawing of some of the interactions the whole blood clot has with the wound, taking out even one element of this delicate tissue will reduce the natural effectiveness of this tissue.



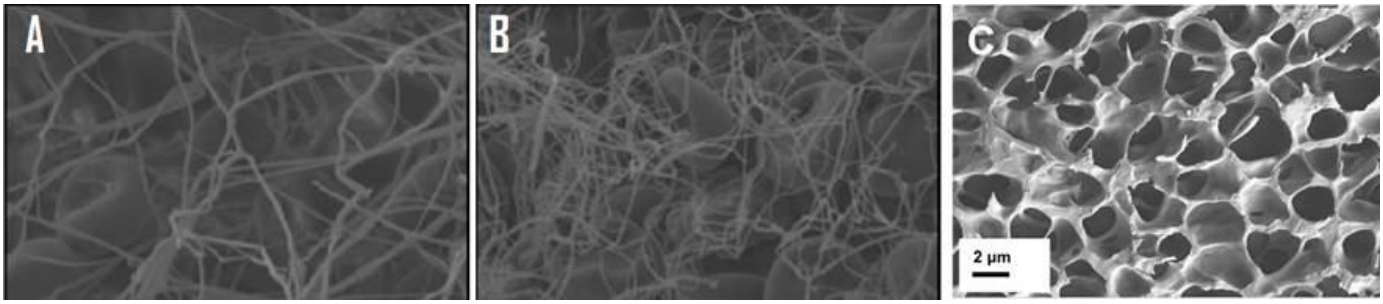
ActiGraft vs Platelet Rich Fibrin (PRF)

The most basic fundamental clinical/scientific difference is that ActiGraft is a live tissue while PRF is processed blood product. The whole idea behind ActiGraft is that while all blood-based products (PRP, PRF, growth factors, etc.) are destroying the natural balance of the natural wound environment created in a blood clot, ActiGraft maintains it with no disturbance.

Following are several examples illustrating this difference.

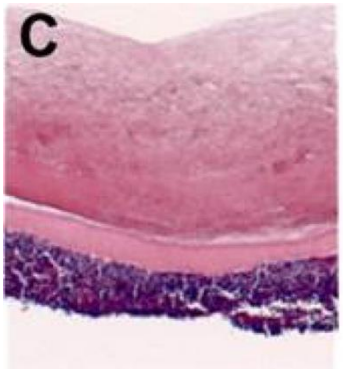
- Comparison of the Fibrin scaffold:
    - PRF– by centrifuge, the PRF results in a very dense and rigid fibrin product.
    - ActiGraft – allows the fibrin network to be created as in the natural clot, allowing various attributes- such as allowing migration of cells, capturing of fluids, optimal distance between cells, ingrowth of blood vessels.

Below are 3 microscopic pictures: **A.** natural clot, **B.** ActiGraft clot, **C.** PRF; One can see that the fibrin in the PRF clot has no resemblance to how a natural fibrin scaffold should look.



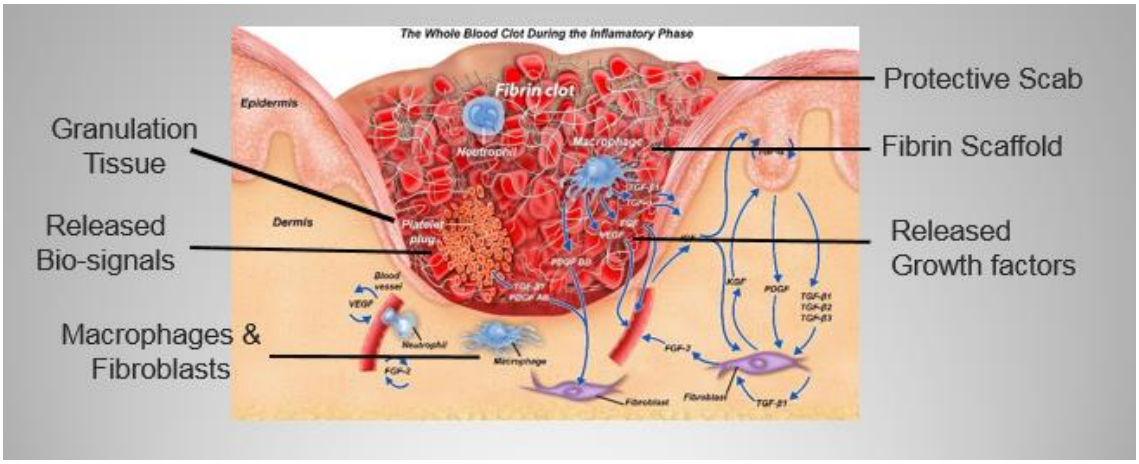
*ACTIGRAFT and whole blood clot photos by Prof Alisa Wolberg Univ North Carolina, PRF photo by Reapplix.

- Comparison of the Product structure:
    - PRF is engineered to be 3-layer product –the lower layer is in contact with the wound, while the next 2 layers do not contact and cannot directly interact with the wound (PLT and Fibrin -as shown below (Reapplix)).



    - ACTIGRAFT is a homogenic distributed tissue- same as the natural clot with full direct contact of all essential elements including a complete set of cells, proteins, and biologic attributes.

The figure below presents on a fraction of the multiple, complex interactions the blood clot has with a wound. The vast majority of these attributes are lost when the blood is centrifuged.



For these reasons above, the PRF and ACTIGRAFT healing results are very different, as presented in the table below – comparing ACTIGRAFT clinical results to those of an FDA-cleared PRF (Leucopatch/3C patch by Reapplix).

Table 1 – Comparison of the Leucopatch pilot study to the ACTIGRAFT pilot study

Studies #1	**LeucoPatch[1]**	**ACTIGRAFT[2]**
Design	prospective, open-label, and uncontrolled	prospective, open-label, and uncontrolled
Study Location	Denmark	Israel
Wound Type	Various etiology	Various etiology
Sample	16 wounds	9 wounds
Treatment	3C patch weekly applications for 6 weeks or until complete healing	ACTIGRAFT weekly applications until complete healing
Efficacy Results	5 wounds completely healed within 10 weeks (33%)	7 wounds completely healed within 8 weeks (77%)
Safety Results	2 AEs – 1 ulcer infection - withdraw, 1 non-compliance - withdraw	1 AE of ulcer external trauma - withdraw

Table 2 – Comparison of the Leucopatch DFU study to the ACTIGRAFT DFU study

Study #2	LeucoPatch[3]	ACTIGRAFT[4]
Design	Multi-center, prospective, open-label, and uncontrolled	Multi-center, prospective, open-label, and uncontrolled
Study Location	Europe	USA
Wound Type	Diabetic foot ulcer, Wagner grade 1 or 2.	Diabetic foot ulcer, Wagner grade 1 or 2.
Sample	44 wounds	20 wounds
Treatment	3C patch weekly applications for 19 weeks or until complete healing	ACTIGRAFT weekly applications for 12 weeks
Efficacy Results	14 wounds completely healed within 12 weeks (32%)	14 wounds completely healed within 12 weeks (68%)
Safety Results	33 AEs and 12 SAEs (45 AEs), including 3 infections in target ulcer. 2 cases of device failure, 3 cases of blood draw failure	29 AEs and 2 SAEs (31 AEs), including 1 infection in target ulcer. No case of device failure and no blood draw failure.

References:

1. Jørgensen, B., Karlsmark, T., Vogensen, H., Haase, L. & Lundquist, R. A pilot study to evaluate the safety and clinical performance of Leucopatch, an autologous, additive-free, platelet-rich fibrin for the treatment of recalcitrant chronic wounds. The International Journal of Lower Extremity Wounds 10, 218–23 (2011).

2. I Kushnir, A Kushnir, T E. Serena, D Garfinkel. Efficacy and Safety of a Novel Autologous Wound Matrix in the Management of Complicated, Chronic Wounds: A Pilot Study. Wounds 2016;28(9):317-327

3. Löndahl, M., Tarnow, L., Karlsmark, T., Lundquist, R., Nielsen, A. M., Michelsen, M., Zakrzewski, M. (2015). Use of an autologous leucocyte and platelet-rich fibrin patch on hard-to-heal DFUs: a pilot study. Journal of Wound Care, 24(4), 172–178.

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4. Robert J. Snyder, Maria A. Kasper, Keyur Patel, Marissa J. Carter, Igal Kushnir, Alon Kushnir, Thomas E. Serena. Efficacy and Safety of a Novel Safety and Efficacy of an Autologous Blood Clot Product in the Management of Texas 1A or 2A Neuropathic Diabetic Foot Ulcers: A Prospective, Multicenter, Open Label Pilot Study. Wounds 2018;30(7):205–212

Practical differences

Aside from the substantially different (2x) healing rate of ACTIGRAFT, there are other considerations:

- PRP and PRF procedures requires capital equipment, ACTIGRAFT is short and is a single use kit.
- ACTIGRAFT should stay on the wound for 1 week and can stay on a wound in some cases up to 4 weeks, we do recommend weekly change but only while the wound is exudative. Most importantly while ACTIGRAFT is on the wound there is no other care procedure.

- A 16ml blood draw provides a PRF of 2.5cm diameter of ranging in thickness between 0.1cm – 0.2 cm, but same amount of blood results in a substantially larger ACTIGRAFT clot: 6 cm in diameter and 0.8 cm thick.