Selected case stories, Vivostat® platelet rich fibrin (PRF®) in the treatment of chronic wounds

Case Study by:

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Introduction

Platelets are considered to play an important role in the healing process of bones and wounds, as they release growth factors upon activation following application onto the wound bed[1].
Of particular importance in the wound healing process is platelet-derived growth factor[2] (PDGF), transforming growth factor-β[3] (TGF-β), and vascular endothelial growth factor[4] (VEGF). Together with other growth factors, also released from the activated platelets, they contribute to the repair of injured tissue through angiogenesis, synthesis of extracellular matrix components like collagen, granulation tissue formation, and re-epithelialisation.

Autologous platelet rich plasma and autologous platelet rich plasma gels have been used in treatment of chronic wounds, and platelet gel applications have been reported to improve soft tissue healing in chronic non-healing wounds[5,6]. Many commercially available devices for production of platelet rich gels do not concentrate viably active platelets in sufficient numbers to produce an efficient healing enhancement[7,8]. Studies suggesting lack of benefit from platelet rich plasma can often be traced to poor quality platelet concentrates produced by inadequate devices. Moreover, platelet rich plasma and platelet gels are difficult to handle and apply, and to fix on vertical and inverted wound surfaces. The growth factors from these concentrates are released from the platelets almost instantly, instead of gradually over time.

It is with these limitations in mind that the Vivostat® PRF® concept was developed, to provide a fully automated system for convenient preparation and efficient application of autologous platelet rich fibrin (PRF®) in wound treatment.

The Vivostat® PRF® System

The system consists of 3 components: An automatic Processor Unit, an Applicator Unit (Figure 1) and a single use kit providing the required consumables, including the unique Spraypen® for application of PRF® (figure 2).

Figure 1.
Vivostat Automatic Processor Unit (left) and Vivostat Automatic Applicator Unit (right)

120 ml of venous blood is drawn from the patient into a sterile Preparation Unit containing citrate buffer and the anti-fibrinolytic agent tranexamic acid (figure 2).

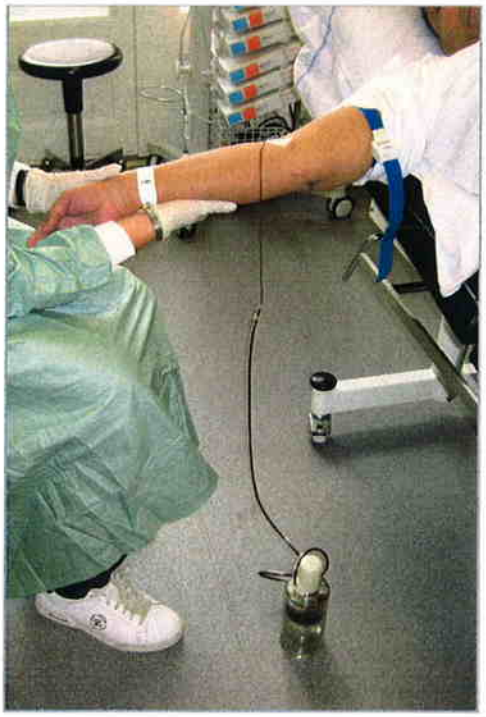


Figure 2.
Venous Blood from the patient is drawn into the Preparation Unit

The Preparation Unit is then placed in the Automatic Processor Unit and 5-6 mL of Vivostat® PRF® is prepared in approximately 23 minutes. No thrombin or bovine components are added to the Vivostat® PRF® at any time. The syringe containing the Vivostat® PRF® solution is then loaded in the Applicator Unit and is applied to the wound surface with the Spraypen® (figure 3).

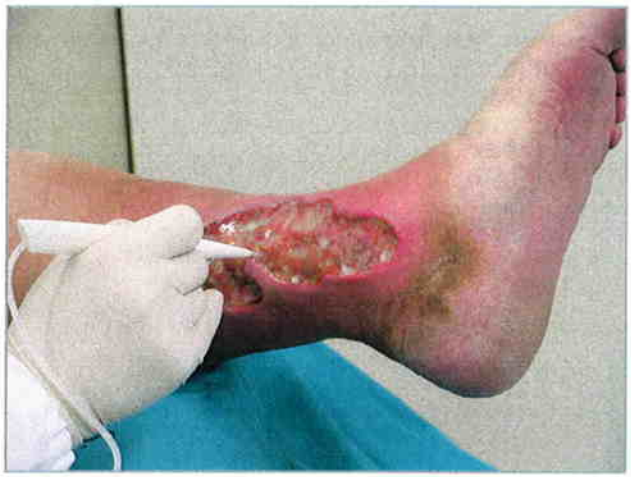


Figure 3.
Application of Vivostat® PRF® using the Spraypen®

Following application, a non-absorbent bandage is applied. Application of Vivostat® PRF® is repeated with one week's intervals in conjunction with normal change of dressings. Usually, granulation is initiated within the first two to three applications, but it is recommended to continue treatment for altogether 5-6 weeks.

When sprayed onto the wound the fibrin will immediately polymerise and crosslink to form an opaque, elastic,- yet strong fibrin mesh in which platelets are embedded. In this way the fibrin acts as a carrier for platelets, and promotes the gradual release of growth factors to the tissue. The instant polymerisation of fibrin ensures that the PRF® will remain at the location where it was applied. The concentration of platelets in 5-6 mL Vivostat® PRF® is usually 7-10 times the baseline level of the patient's blood, corresponding to some 1,7-2,0 million platelets per 1 µL . This is a significantly higher concentration of platelets than seen in e.g. most platelet rich plasma concentrations and gels and is well above the required therapeutic level.

Clinical Data

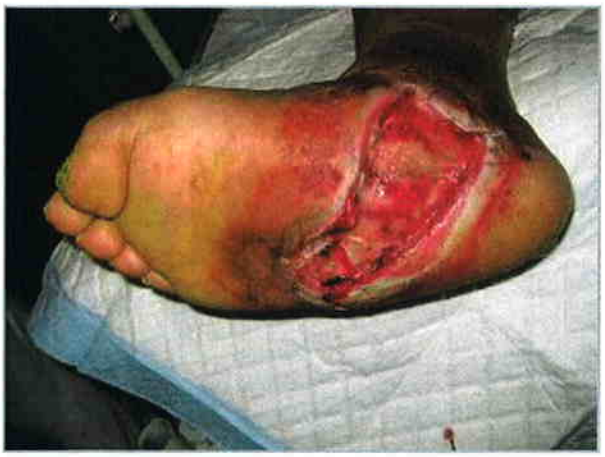
So far no controlled studies have been conducted to document the efficacy of Vivostat® PRF® in the treatment of chronic wounds. However, several cases have been published indicating an effect of Vivostat® PRF® in different types of chronic wounds[9,10]. This has encouraged the manufacturer of the Vivostat® System to initiate an European multicentre cohort trial to provide final proof of effect of Vivostat® PRF® in diabetic foot ulcers.

Case Studies

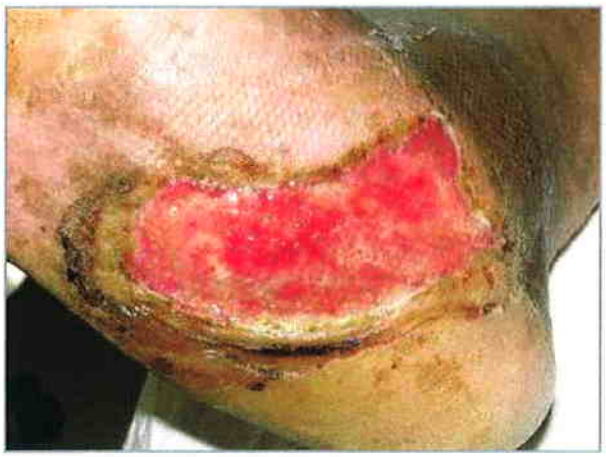
Case study 1

A 57-year old, type II diabetic male was admitted to the Copenhagen Wound Healing Centre at Bispebjerg Hospital suffering from a 1,3 cm deep, 12 cm x 6 cm, slow–healing, non-ischemic, wound on the right foot (Charcot foot) following surgical removal of a plantar abscess. Debridement was undertaken and Vivostat® PRF® treatment was initiated in an attempt to prepare the wound for later skin transplantation. Vivostat® PRF® was applied consecutively at one week's intervals for 4 weeks, resulting in gradual reduction of wound depth and area and formation of granulation tissue. Upon readmission for skin transplantation 4 weeks later, the wound was almost fully covered with epithelium and only a very small, superficial healing wound remained. Skin transplantation was then found to be unnecessary.

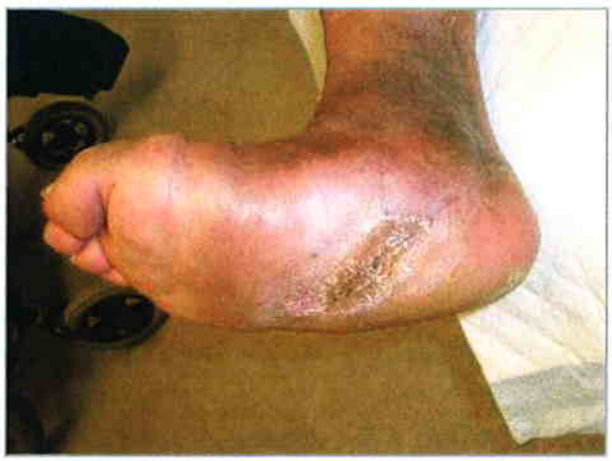
Case 1.



Before 1st Vivostat® PRF® treatment



After 4 weeks treatment



Wound 11 weeks after 1st treatment

Case study 2

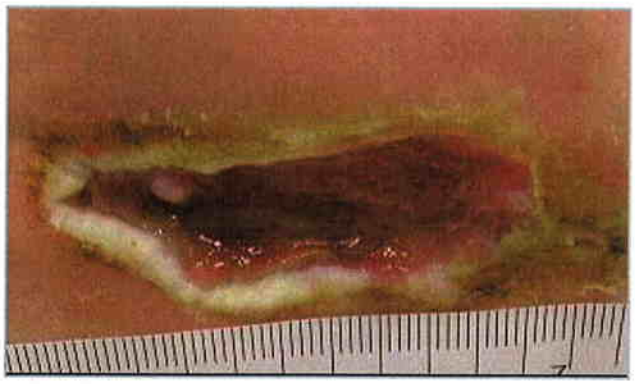
A 58-year old woman with diabetes mellitus type 1 since 1969 was admitted to the University Hospital in Lund. Sweden in August 2006 due to coronary ischemia. She had a coronary-by-pass surgery done. During the first days of her hospitalization a pressure ulcer developed under her right heel as she was bedridden without any kind of off-loading. When she was admitted to the Diabetes Foot Clinic in October the ulcer measured 60x55 mm and was covered by a dry necrosis. Her foot pulses was not present at clinical examination, she had severe neuropathy and a rocker-bottom deformity, due to an acute Charcot foot ten years earlier.

She was initially treated with antibiotics, diuretics and off-loaded with a Botexa® offloading device. Her systolic toe blood pressure was only 55 mm Hg and she was referred to MRI. A tibialis posterior and fibularis were occluded, but as she had opened vessels from a iliaca to the foot arcade no vascular surgery was possible. Debridement was regularly done when needed.

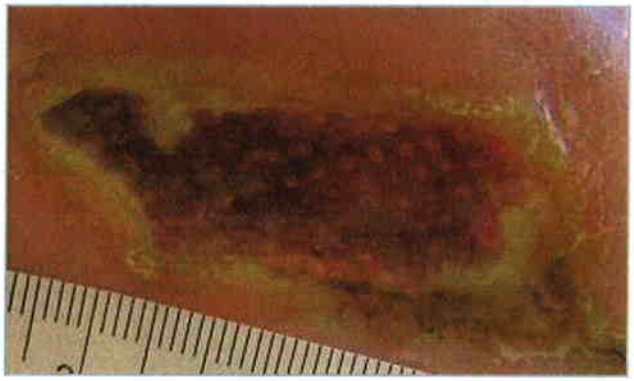
As the ulcer did not improve the off-loading was changed to a non-removable plaster. In early spring she was hospitalized due to a foot infection and later on treatment with larvae was given. As no signs of heeling were seen it was decided to treat with Vivostat® PRF®. Before the first treatment was given in the end of June 2007 her ulcer measured 56x18 mm and was approximately 4-5 mm deep. Treatment was given once weekly for five consecutive weeks. At the fifth week the ulcer size had decreased to 34x12 mm and the depth was only 1-2 mm. The ulcer was covered to 80% with granulation tissue. A month after the last treatment the ulcer worsened due to an infection, and the ulcer area increased. At her latest visit to the clinic in January her ulcer was covered with nice granulation tissue and measured 22x10 mm.

This is a case describing the horrible and long-standing consequences of neglecting appropriate off-loading of bed-ridden neuropathic diabetic patients. In this case of a longstanding ulcer it is believed that Vivostat® PRF® contributed to the initiation of the ulcer healing process.

Case 2.



Before 1st treatment



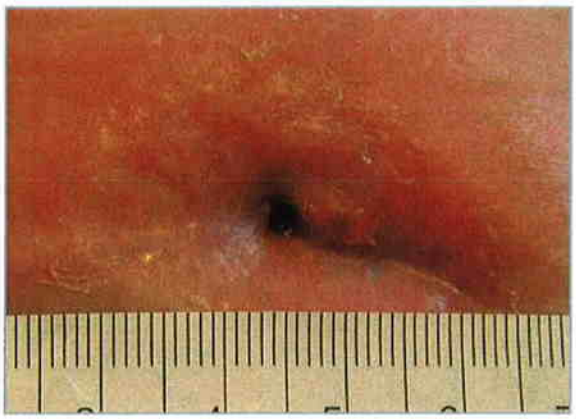
6 weeks after the first treatment

Case study 3

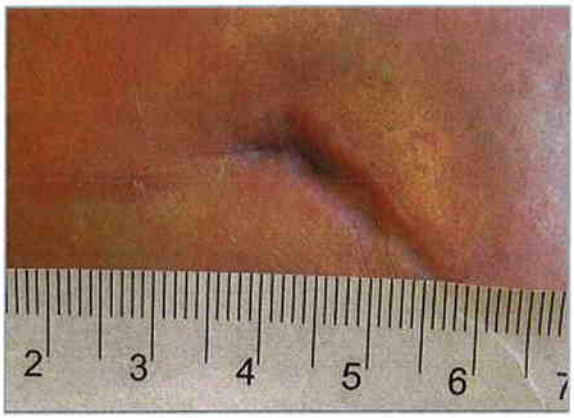
This is a 66 year-old man who has been treated at the Diabetic Foot Clinic, University Hospital in Lund, Sweden for many years due to bilaterally neuro-ischemic foot ulcers. His left leg was transtibial amputated in February 2007 due to progressive gangrene and pain on the basis of insufficient circulation. The amputation ulcer healed nicely with the exception of a persisting fistula.

The ulcer on the right foot and the fistula was treated with PRF® using a thinner catheter the 60 mm deep fistula was filled with PRF® using the Applicator's no air application mode. Treatment was given once weekly for six consecutive weeks. After four treatments the fistula had heeled and the patient was able to use his prosthesis two weeks later. The fistula is still healed, whereas the ulcer on his right foot is not.

Case 3.



Before treatment



6 weeks after the first treatment

Conclusion

The use of Vivostat® autologous platelet rich fibrin enables local application of growth factors from platelets in a fibrin matrix shown to be involved in the healing of wounds, angiogenesis and tissue remodelling. The preparation of PRF® is simple and fully automatic and the application of Vivostat® PRF® is convenient and easy to perform.

Case studies to date indicate that Vivostat® PRF® is effective and safe in the treatment of chronic and hard-to-heal wounds by a.o. initiating the granulation process. However, a prospective, controlled, multi-centre study is under way to provide final documentation for its positive therapeutic impact in wound healing.

References

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