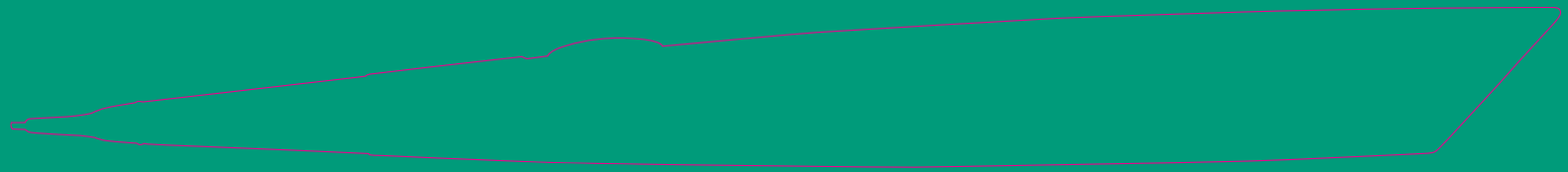


Vivostat®
PRF


A new approach to tissue regeneration

Vivostat® PRF

Vivostat PRF® – A New Approach to Tissue Regeneration

The Vivostat® system was the first on the market to offer a convenient and fully automated process for the preparation of a true Platelet Rich Fibrin (PRF®)

The presence of growth factors is essential to the process of tissue regeneration (e.g. soft tissue, connective tissue, muscle and bone). Using the Vivostat® system, you can prepare autologous platelets with multiple growth factors embedded in a fibrin sealant matrix. From 120 ml blood, 5-6 ml of Platelet Rich Fibrin (PRF®) is prepared.

By combining a platelet concentrate with a fibrin sealant solution, it is possible to have a carrier, a controlled release, and a medium for tissue ingrowth – all in one product, Vivostat PRF®. Compared to conventional PRP products, Vivostat PRF® offers a number of advantages.

- **Combining the benefits of platelets and fibrin**
  With an average 7-fold increase over baseline blood levels, the platelet concentration in Vivostat PRF® is well above the baseline platelet count of 1 million/µL, which has become a benchmark within platelet therapy. The fibrin matrix ensures a slow release of growth factors over time and effectively protects the growth factors against proteolytic degradation[1].

- **Superior application**
  The specially designed Vivostat® application devices and the unique combination of platelets and fibrin ensures easy, accurate and efficient application of Vivostat PRF®. Due to instant polymerisation and excellent adhesive properties of the fibrin component, the PRF® solution remains where it is applied – even when applied on vertical or inverted surfaces. As the fibrin component in Vivostat PRF® is based on a fibrin 1 solution, thrombin activation is not required, resulting in faster tissue repair[2].

The Vivostat® system is designed with emphasis on user-friendliness.

You will find the system straightforward and easy to use. It can easily be moved between departments or even to the outpatient department if required. Furthermore, the innovative Danish design makes the system easy to operate, maintain and clean.

1) Bioactivity and stability of endogenous fibrogenic factors in platelet-rich fibrin · Lundquist R. et al. · Wound Repair and Regeneration 2008; 16(3): 356-365
2) Nonactivated versus Thrombin-activated Platelets on Wound Healing and Fibroblast-to-Myofibroblast Differentiation · Scherer S. et al. · Plastic and Reconstructive Surgery 2012; 129(1)


COMPLETE
REMOVE PREP UNIT

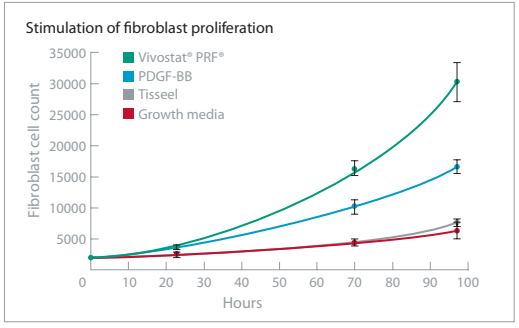
Vivostat® PRF

The ideal combination of platelets and fibrin

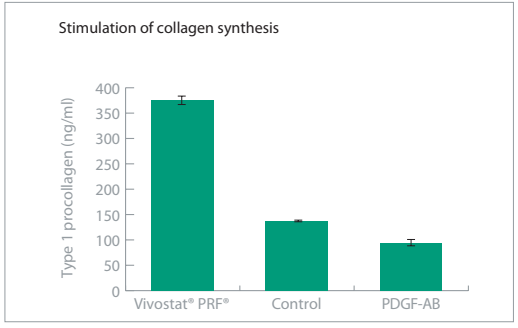
Clinical studies have demonstrated the beneficial effect of combining a platelet concentrate with a high concentration of fibrin[1]

Vivostat PRF® provides a unique combination of platelets and fibrin unobtainable by conventional PRP systems or homemade platelet gels. The fibrin component serves as a scaffold for cell migration and provides structure during tissue regeneration. Platelets in the PRF® solution contain a large variety of growth factors among others TGF-β, PDGF-AB, PDGF-BB, FGF-2 and VEGF[2]. These growth factors serve different purposes in the complex process of tissue regeneration, and their presence in volume and variety is thus key to successful tissue repair.

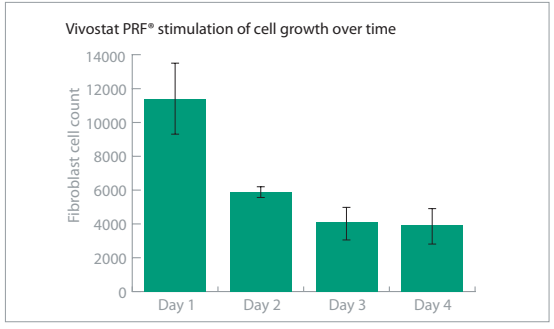
Several in-vitro investigations confirm the unique characteristics of Vivostat PRF® and its ability to stimulate cell growth.

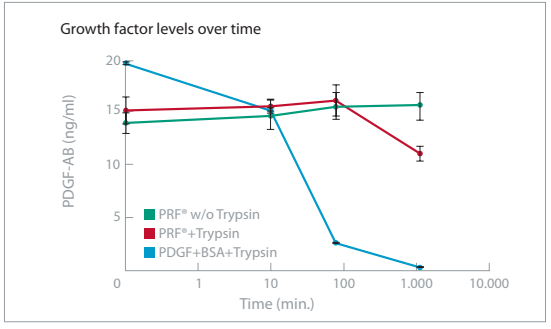


Stimulation of fibroblast proliferation[3]
Fibroblasts are fundamentally important in the process of tissue regeneration. Apart from producing structural proteins such as collagen, they stimulate both angiogenesis and epithelialisation. In-vitro studies have proven the positive effect of Vivostat PRF® on fibroblast proliferation. As illustrated, Vivostat PRF® increases the growth of normal human skin fibro blasts compared to control and performs significantly better than PDGF-BB (commercial growth factor)[4].



Stimulation of fibroblast collagen synthesis[3]
Collagen deposition is an essential component in the wound healing cascade. In-vitro studies have illustrated the positive effect of Vivostat PRF® on the ability of fibroblasts to synthesise collagen. Vivostat PRF® performs better than PDGF-AB, the major PDGF isoform in human platelets[5]. The reason for this may be that Vivostat PRF® contains multiple growth factors and not just PDGF-AB.





Release of growth factors over time[6]

Vivostat PRF® delivers a concentrate of growth factors embedded in a fibrin matrix. Following application of the Vivostat PRF® solution, the fibrin matrix will naturally be broken down by fibrinolytic processes (fibrinolysis), and during this process the growth factors contained in the platelets are gradually released to the site of treatment over a period of 4 days or more. In effect, the fibrin matrix is a delivery media that slowly releases growth factors over time[7].

Protection against proteolytic degradation[3]

The use of Vivostat PRF® in tissue repair is largely dependent on the effect and stability of the PRF®-derived growth factors. Controlling the release of platelet contents over several days requires not only a delivery media but also protection of the platelets against degradation. The autologous fibrin matrix in Vivostat PRF® has shown to protect endogenous growth factors against proteolytic degradation and thereby preserve their biological activity.

1) Basic Studies on the Clinical Applications of Platelet-Rich Plasma · Yazawa M, Ogata H, Nakajima T, Mori T, Watanabe N, Handa M · Cell Transplantation 2003; 12: 509–518

2) Growth factor and proteinase profile of Vivostat platelet-rich fibrin linked to tissue repair · Ågren M. et al. · Vox Sanguinis 2013; 107(1), 37-43

3) Bioactivity and stability of endogenous fibrogenic factors in platelet-rich fibrin · Lundquist R. et al. · Wound Repair and Regeneration 2008; 16(3): 356-63

4) Fibroblast proliferation, measured by ViaLight Plus (Cambrex), shows exponential growth over a 96-hour treatment period. Data are presented as mean ± SEM (n = 8). The recombinant human PDGF-BB (Sigma-Aldrich) was used at 10 ng/ml.

5) Synthesis of collagen by confluent and quiescent normal human dermal fibroblasts over a 24-hour treatment period. Data are presented as mean ± SEM (n = 6). Recombinant human PDGF-AB (Chemicon) was used at 10 ng/ml.

6) Vivostat Technical Report No. 1005 · Data on file at Vivostat A/S.

7) PRF® clots were incubated in culture medium at 37°C for the indicated time periods and then assessed for proliferative bioactivity using the ViaLight Plus method.

The Vivostat® system

The Vivostat® process is fully automated, and because of the straightforward and intuitive handling it is easy to operate by the healthcare personnel

The uniqueness of the Vivostat® system is a novel patented biotechnological process that enables reliable and reproducible preparation of autologous Platelet Rich Fibrin (PRF®) without using cryoprecipitation and without the need for a separate thrombin component. The fully automated Vivostat® system consists of three components:

- **The Disposable Set**
  The single-use set contains all components needed for preparation and application of Vivostat PRF®. It is available with a range of application devices each optimised for different types of applications.

- **The Processor Unit**
  The Processor Unit is used to process the patient's blood and prepare the PRF® solution. The display keeps the user informed at all times about the process and the time remaining.

- **The Applicator Unit**
  The Applicator Unit controls the delivery of PRF® to the site of treatment. The Co-Delivery Applicator, furthermore, allows drugs or cells to be co-delivered with the PRF® solution.

During the procedure, the Applicator Unit informs about the volume of PRF® available and allows the healthcare specialist to choose from a number of different spray modes that carefully control the delivery of PRF® to the site of treatment.

The spray modes have been developed with focus on optimal application in open and minimally invasive surgery.

The Vivostat® Applicator Unit and Processor Unit

Vivostat® PRF

Three easy steps to prepare Vivostat PRF®

1. Draw blood from the patient

Prior to treatment, citrate supplied with the kit is added to the Preparation Unit. 120 ml of the patient's own blood is then drawn into the same unit.

2. Process the patient's blood

The Preparation Unit is placed in the Processor Unit. At the touch of a button the process starts; after approx. 26 minutes, an autologous PRF® solution is ready for use. No thrombin or bovine components are added to the blood or PRF® solution at any time.

3. Load the Applicator Unit and spray

The PRF® solution is easily loaded into the Applicator Unit and is applied to the site of treatment using one of the different application devices. Due to the instant polymerisation of the fibrin component, the PRF® solution remains where it is applied.

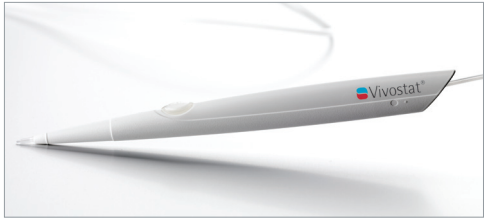
Vivostat® PRF

Application devices for all situations

The Vivostat® system offers a range of unique application devices, designed for the delivery of PRF® to the site of treatment in a precise and targeted manner, with minimum waste and without blockage

Each application device has been developed using the knowledge of healthcare professionals to improve product performance. Vivostat can therefore offer application devices adapted to each surgical setting. Whether you are performing open surgery, work in an endoscopic setting, need to treat fistulas or cavity wounds Vivostat has the solution. In the right column examples of Vivostat® application devices are listed.

The application devices are used in conjunction with the Applicator Unit and are all based upon the well-known Vivostat® micro-spray technology.



Spraypen Kit (also in a Co-Delivery version)
The Vivostat® Spraypen is a central and unique component of the Vivostat® system. It enables the surgeon to apply Vivostat PRF® accurately and intermittently throughout the entire procedure.

Endoscopic Kit (also in a Co-Delivery version)
The Vivostat® Endoscopic Applicator is used in various types of Minimally Invasive Surgery. The single-use endoscopic application catheter is easily loaded into the endoscopic handle, which is inserted via a 5 mm trocar. The pre-bent spraytip enables the surgeon to manipulate the tip and spray in multiple directions.

Endoscopic Kit-Straight
The Vivostat® Endoscopic Kit-Straight is developed for the application of Vivostat PRF® in deep wounds and fistulas. More over, it can be used in different endoscopic solutions e.g. Colonoscopes, Bronchoscopes, Laparoscopes or Gastroscopes.


5.3 ml
HIGH
Vivostat®

Vivostat® Co-Delivery

Vivostat has developed the revolutionary Co-Delivery system that makes it possible to co-deliver a desired substance (drugs, stem cells, skin cells etc.) with Vivostat PRF® (Platelet Rich Fibrin)

The opportunities with the Vivostat® Co-Delivery system are vast and the system allows the surgeon to apply a selected substance easily and effectively. Furthermore, it may be possible to reduce the total cost of a procedure by using the Vivostat® Co-Delivery system[1].

Options for Co-Delivery include:

Drugs
- Antimicrobials
- Chemotherapeutics
- Pain medications

Cells
- Stem cells
- Skin cells

Co-delivering drugs, stem cells, skin cells etc. with the Vivostat PRF® solution offers the surgeon and the patient a number of benefits:

- Topical application
- Targeting affected/desired area
- Possible higher local dose
- Possible lower systemic impact
- Improved compliance

Moreover, no thrombin is added to Vivostat PRF® (unlike most other PRP products). This is beneficial to the Co-Delivery system as thrombin activation has been shown to have a negative effect on cell survival.

The fibrin membrane found in Vivostat PRF® has, furthermore, been shown to postpone the degradation process of the substance. This means that the fibrin membrane ensures a slow and sustained release of the substance offering a prolonged effect[2].

How does it work

It is possible to co-deliver more than 5 ml of substance together with the Vivostat PRF® solution. The substance is applied using one of the different Vivostat® Co-Delivery application devices, which enable the surgeon to apply the substance accurately and intermittently throughout the entire procedure.

The substance and the Vivostat PRF® solution is mixed as it leaves the tip of the application device and polymerises immediately upon application - this way the substance stays where it is intended to act.

1) Use of autologous bone marrow cells concentrate enriched with platelet-rich fibrin on cortico-cancellous bone allograft for posterolateral multilevel cervical fusion Vadalà et al. · Journal of Tissue Engineering and Regenerative Medicine 2008; 2: 515–520.

2) Intrapleural topical application of cisplatin with the surgical carrier Vivostat increases the local drug concentration in an immune-competent rat model with malignant pleuromesothelioma · Lardinois et al. · Journal of Thoracic and Cardiovascular Surgery.2006;131:697-703


Vivostat® PRF®
Vivostat® PRF® (Platelet Rich Fibrin) is used for the preparation and application of autologous platelets with multiple growth factors embedded in a fibrin matrix. The fibrin matrix ensures a slow release of growth factors over time
Vivostat® PRF
Vivostat® PRF

Vivostat® PRF

Frequently asked questions

What is the difference between PRF® and PRP

PRP (Platelet Rich Plasma) is a conventional platelet concentrate product and, as such, only contains a very low concentration of fibrin. PRF® is a 2. generation platelet product that combines a high concentration of platelets with a high concentration of fibrin – all in one solution. The fibrin matrix present in PRF® provides a number of unique product features, including protection and slow release of the growth factors over time. Furthermore, as the fibrin component in the PRF® solution polymerises immediately upon application, the platelets remain precisely where they are applied.

Can I freeze Vivostat PRF®

Vivostat A/S has developed the PRF® Split Kit. The PRF® Split Kit offers the possibility to freeze an unused part of the PRF® solution. This may be an advantage if a second application is deemed beneficial.

When should I draw the 120 ml blood from the patient

As soon as the patient is incised, the platelets will start to aggregate and this will prevent proper preparation of the PRF® solution. Therefore, it is very important that you draw blood directly from the patient before any surgical procedure is started. The PRF® Preparation Unit containing the blood must be processed within 1 hour after drawing the blood.

Can I use plasma if I cannot draw blood

No, it is not possible to use plasma as this does not contain any platelets.

Is 5-6 ml of PRF® enough

Yes, the revolutionary design of both the Spraypen and the delivery system enables the healthcare specialist to cover an area of up to 200 cm^2, depending upon the thickness of the Vivostat PRF® layer.

What is the concentration of platelets and fibrin in Vivostat PRF®

The concentration of platelets in Vivostat PRF® is approximately 7 times the base level of the donor's blood. In addition, Vivostat PRF® offers a very high concentration of fibrin – it contains an average of 18.1 mg/ml[1]. This combination of platelets and fibrin is unobtainable from conventional platelet concentrate systems.

For how long can I use Vivostat PRF®

In the majority of cases, the PRF® solution will be used immediately after preparation. Should the procedure require postponement of the treatment, you can store the PRF® syringe at room temperature for up to 8 hours. It is very important that you invert the PRF® syringe approximately 10 times immediately before inserting it in the Applicator Unit to avoid sedimentation of the platelets.

1) Bioactivity and stability of endogenous fibrogenic factors in platelet-rich fibrin · Lundquist R. et al. · Wound Repair and Regeneration 2008; 16(3): 356-63

Vivostat® PRF

Ideas have come to life

The Vivostat® idea was conceived in 1992 by a group of Danish researchers searching for a simple and fully automated way of preparing fibrin sealant, on-site and from the patient's own blood

Following the initial development phase, the idea was further matured in co-operation with specialists from across the world, and in 2001, the first generation of the Vivostat® products – Vivostat® Fibrin Sealant – was launched by the Danish company Vivolution A/S (now Vivostat A/S).

Today, the Vivostat® technology comprises more than fibrin sealant. The advanced blood processing and application technology has been further developed and now a wide range of Vivostat® products are used on a daily basis in numerous surgical departments and wound care centres across Europe and Asia. The idea has come to life!

Vivostat® Fibrin Sealant

Vivostat® Fibrin Sealant offers a safe and effective alternative to conventional fibrin sealants. The fully automated system prepares approximately 5-6 ml of autologous fibrin sealant from only 120 ml of the patient's own blood in approx. 24 minutes. The autologous nature of the product efficiently eliminates the risks of viral infection and unlike conventional fibrin sealants, Vivostat® Fibrin Sealant does not contain any exogenous thrombin or bovine components.

The unique application devices (e.g. the Spraypen) offer the surgeon unparalleled freedom to apply Vivostat® Fibrin Sealant intermittently throughout the entire surgical procedure without experiencing the blockage that is common in conventional systems. Furthermore, Vivostat® Fibrin Sealant can be applied at very close range for pinpoint application, and rapid polymerisation ensures that the fibrin sealant remains where it is applied.

For more information about Vivostat® Fibrin Sealant or Vivostat PRF® and their areas of use please visit **www.vivostat.com** or call +45 8880 8400

Vivostat®
PRF

Vivostat A/S
Borupvang 2
DK-3450 Alleroed
Denmark

Tel. +45 8880 8400
Fax +45 4582 4800

info@vivostat.com
www.vivostat.com