



 Vivostat[®]
Fibrin





A revolution in fibrin sealant technology

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In approx. 24 minutes the fully automated Vivostat® system prepares 5-6 ml of autologous fibrin sealant from 120 ml of the patient's own blood

Compared to conventional sealant products, Vivostat® Fibrin Sealant offers a multitude of benefits to both the patient and the surgeon:

- **Excellent safety profile and high biocompatibility**

Vivostat® Fibrin Sealant is derived from the patient's own blood and as such it demonstrates excellent biocompatibility. Unlike conventional products, which are most often based on single donor blood, pooled blood or bovine components (e.g. aprotinin), Vivostat® Fibrin Sealant does not contain any exogenous thrombin or bovine components. The autologous nature of Vivostat® efficiently eliminates the risks of bovine or human-borne contaminants. This is the only way to

protect the patient and the surgeon against viral diseases not yet identified.

- **Unique and versatile application devices**

The wide selection of application devices provide the surgeon with unparalleled freedom in the use of fibrin sealant throughout surgery. The application devices can be used intermittently during 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 allowing for pinpoint application, and rapid polymerisation ensures that the fibrin remains where it is applied.

- **Superior physical properties**

Clinical studies and comparative tests have demonstrated that Vivostat® Fibrin Sealant is superior to conventional fibrin sealants on important parameters such as time to haemostasis, elasticity, adhesion to tissue and impact on tissue^{1,2}.

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 operating theatres if required. Furthermore, the innovative Danish design makes the system easy to operate, maintain and clean.

1) Comparative kinetics of polymerisation of three fibrin sealants and influence on timing of tissue adhesion · Kjaergard H K et al. · Thrombosis Research 2000; 98: 221-228

2) The Vivostat® application system: A comparison with conventional fibrin sealant application systems · Dodd R A, Cornwell R et al. · Technology and Health Care 2002; 10: 401-411



COMPLETE
REMOVE PREP UNIT

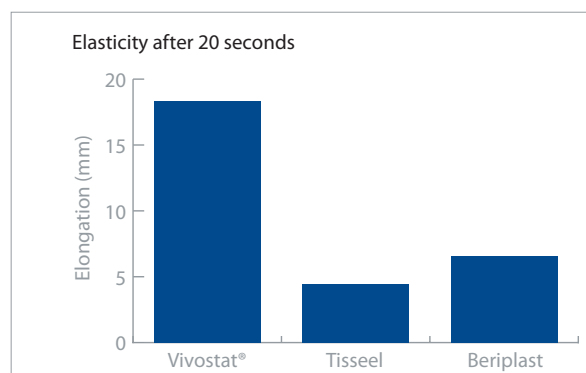
A black, cylindrical device with a digital display is mounted on a silver-colored metal stand. The display shows the word "COMPLETE" in large, white, sans-serif capital letters, with the instruction "REMOVE PREP UNIT" in smaller, white, sans-serif capital letters below it. The device has a smooth, glossy finish and a circular top surface. The background is a plain, light-colored wall.

Vivostat® Fibrin Sealant has excellent properties

Clinical studies and comparative tests have demonstrated that Vivostat® Fibrin Sealant outperforms other fibrin sealants on important parameters such as time to haemostasis, elasticity, adhesion to tissue and impact on tissue

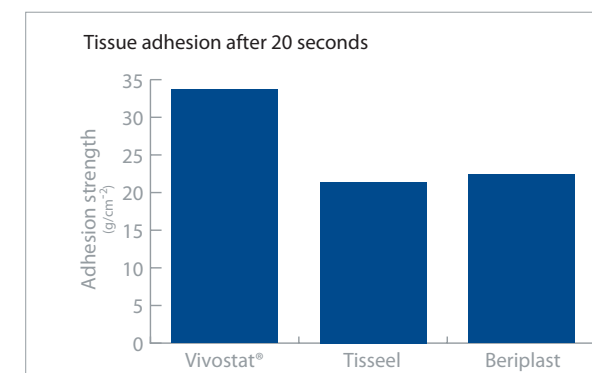
In order to evaluate and compare the clinically important physical and adhesive properties of Vivostat® Fibrin Sealant, a series of in-vitro rheologicals, tensile tests and ex-vivo tissue adhesion models were developed¹.

The five parameters that are most important for the efficacy of surgical sealants have been tested and compared with two conventional fibrin sealants, Tisseel® from Baxter and Beriplast® from CSL Behring (distributed by Takeda).



Elasticity

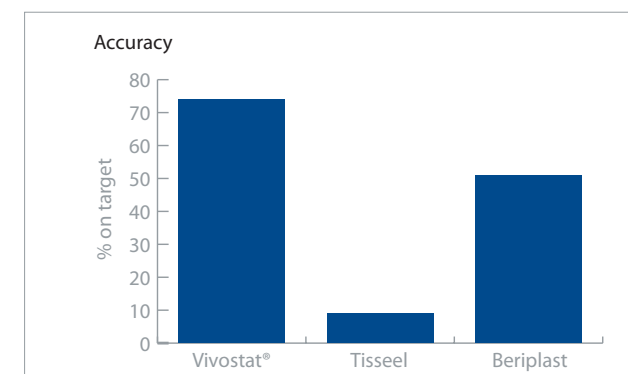
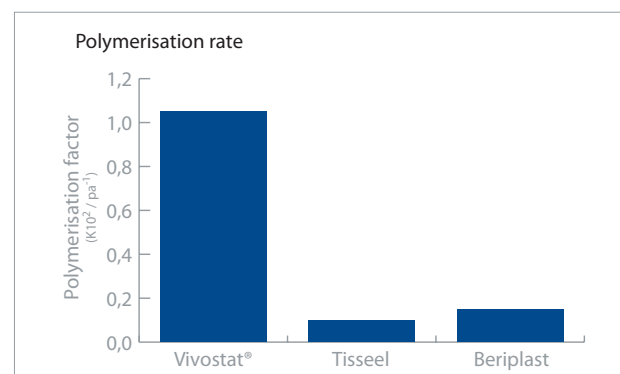
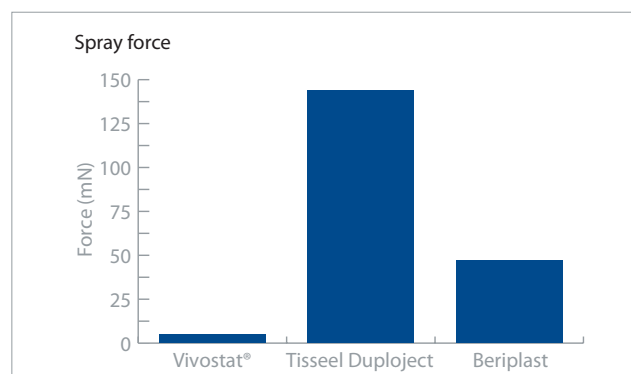
Surgical sealants must be very flexible to move with the tissue. This is especially important in thoracic procedures as the sealant is often applied when the lung is partly deflated. Most compounds have an inverse relationship between strength and elasticity. Comparative tests have, however, shown Vivostat® Fibrin Sealant to be extremely flexible², more than three times as flexible as conventional products while maintaining sufficient strength.



Adhesion

Numerous products focus on the tensile strength of the sealant, but neglect the most important parameter of adhesion to tissue. Provided that the internal strength of the sealant and the tissue itself are sufficiently high, it is the sealant:tissue adhesive strength that is the determining factor for tissue:tissue joint failure. The graph shows adhesion strength at first break and clearly demonstrates the superior performance of Vivostat® Fibrin Sealant².

1) Development of a model for measurement of adhesion strength of fibrin sealant to human tissue · Kjaergard H K et al. · European Surgical Research 1999; 31: 491-496
2) Comparative kinetics of polymerisation of three fibrin sealants and influence on timing of tissue adhesion · Kjaergard H K et al. · Thrombosis Research 2000; 98: 221-228



Impact on tissue

All designers of spray systems face a challenge as they want to minimise disruption or damage to the tissue caused by the high flow rate of the propellant. The Vivostat® system solves this problem with the unique design of the application devices and the Applicator Unit, which provides efficient mixing and imparts very low forces on the tissue. The graph shows the spray force (impact on the tissue) 5 cm from the nozzle³.

Time to haemostasis

An efficient sealant needs to polymerise quickly in order to build up its internal strength and provide a rapidly effective barrier. The polymerisation of Vivostat® Fibrin Sealant is activated by a simple pH change and does not require an enzymic reaction. Polymerisation rates are therefore much faster than conventional sealants based on fibrinogen/thrombin². Vivostat® Fibrin Sealant obtains 80% of its full strength within only 1 minute.

Accuracy

The ability to accurately place the fibrin sealant increases the efficiency (faster haemostasis, rapid sealing etc.) and enables the surgeon to make better use of the fibrin that is available. Accuracy is most important in pinpoint application, in difficult to reach areas and small anastomoses. The graph shows the relative amount of fibrin that reaches a target area of 2 cm² at the manufacturer's recommended spray distance³.

3) The Vivostat® application system: A comparison with conventional fibrin sealant application systems · Dodd R A, Cornwell R et al. · Technology and Health Care 2002; 10: 401-411

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 fibrin sealant without using cryoprecipitation and without the need for a separate thrombin component.

The fully automated Vivostat[®] system consists of three components:

- **Disposable Set**

The single-use set contains all components needed for preparation and application of Vivostat[®] Fibrin Sealant. It is available with a range of application devices each optimised for different surgical procedures.

- **Processor Unit**

The Processor Unit is used to process the patient's blood and prepare the fibrin solution.

- **Applicator Unit**

The Applicator Unit controls the delivery of fibrin sealant to the surgical site and offers a number of different spray modes. The Co-Delivery Applicator, furthermore, allows drugs or cells to be co-delivered with Vivostat[®] Fibrin Sealant.

The Processor Unit can be placed in any room or corridor in the surgical department. It is often placed centrally in the department to supply multiple operating theatres. It can, however, easily be moved between operating theatres if required.

The Applicator Unit is positioned outside the sterile field in the operating theatre. The integrated microprocessor technology automatically primes the application device and the large display informs the surgeon of the remaining volume of fibrin sealant at all times.



The Vivostat[®] Applicator Unit
and Processor Unit

Three easy steps to prepare Vivostat® Fibrin Sealant



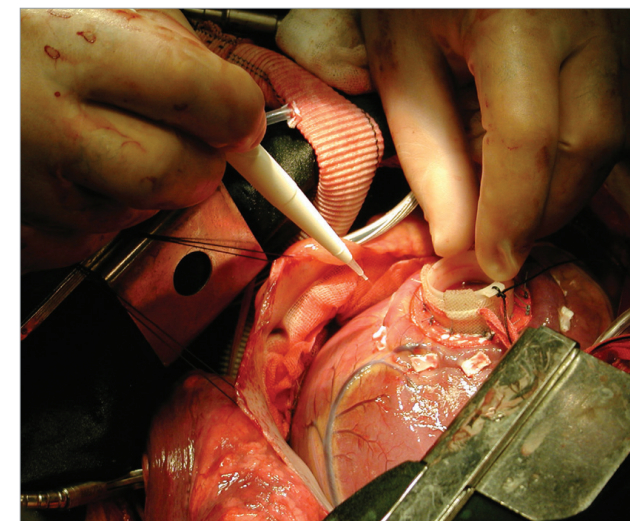
1. Draw blood from the patient

At the time of surgery or up to 24 hours before, 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. 24 minutes, an autologous fibrin solution is ready for use. No thrombin or bovine components are added to the blood or fibrin sealant at any time.



3. Load the Applicator Unit and spray

The fibrin solution is easily loaded into the Applicator Unit and applied to the surgical site using one of the unique application devices (e.g. the Spraypen).

Application devices for all situations

The Vivostat® system offers a variety of different disposable application devices. They are designed for the delivery of fibrin sealant to the surgical site in a precise and targeted manner, without experiencing the blockage that is common in conventional sealant systems

Each application device has been developed using the knowledge of specialised surgeons to improve product performance. The application devices are used in conjunction with the Applicator Unit and are all based upon the well-known Vivostat® micro-spray technology. The Applicator Unit continually displays the volume of fibrin sealant available and allows the surgeon to choose from a number of different spray modes to carefully control the delivery of fibrin to the surgical site.



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® Fibrin Sealant accurately and intermittently throughout the entire procedure.



Endoscopic Kit-Straight


The Vivostat® Endoscopic Kit-Straight allows the application of Vivostat® Fibrin Sealant in multiple different endoscopic solutions e.g. Colonoscopes, Bronchoscopes, Laparoscopes or Gastrosopes and it can be used to treat fistulas.



Endoscopic Kit (also in a Co-Delivery version)

The Vivostat® Endoscopic Kit 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.

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, cells etc.) with Vivostat® Fibrin Sealant

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 system¹.

Options for Co-Delivery include:

Drugs

- Antimicrobials
- Chemotherapeutics
- Pain medications

Cells

- Stem cells
- Skin cells

Co-delivering drugs, stem cells etc. with the Vivostat® Fibrin Sealant 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® Fibrin Sealant (unlike most other sealants). 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® Fibrin Sealant 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 effect².

How does it work

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

Vivostat® Fibrin Sealant is used for the preparation and application of autologous fibrin sealant from only 120 ml of the patient's own blood. The sealant does not contain any exogenous thrombin or bovine components.

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Frequently asked questions

Can I draw less than 120 ml blood

The system and the preparation process are designed based on this specific volume. A reduction in blood volume will reduce the amount of fibrin sealant. The Preparation Unit should therefore always be completely filled with 120 ml of blood.

Can I use plasma if I cannot draw blood

Yes, this is a viable option for paediatric or anaemic patients. We recommend patients should weigh more than 20 kg to draw 120 ml blood. The Vivostat® system operates in exactly the same way with plasma. There are just a few important things to remember:

- It must be fresh frozen plasma
- You cannot use products such as SAG M or other erythrocyte products. They will not produce any fibrin as the plasma has been removed.

Can I use blood from the heart-lung machine

Yes, you can take blood from the heart-lung machine. To make sure that the priming fluid and blood is fully mixed, we recommend to wait 10 minutes after the patient has been connected to the heart-lung machine before drawing the blood.

When should I draw the 120 ml blood from the patient

We recommend to draw blood when the patient is anaesthetised or up to four hours before the operation. However, there is nothing in the design or process of the Vivostat® system that prevents you from drawing blood earlier. You can fill the Preparation Unit up to 24 hours before you place it in the Processor Unit. If the blood is drawn more than four hours before use in the Processor Unit, the Preparation Unit should be kept in the refrigerator at 5 degrees C (do not freeze).

In addition, labelling and storage procedures must be established.

For how long can I use Vivostat® Fibrin Sealant

Vivostat® Fibrin Sealant can be prepared and used intermittently throughout a lengthy operation without loss of effectiveness. Studies have shown that storage of Vivostat® fibrin solution for eight hours at room temperature after preparation has no significant effect on the physical properties of the derived sealant.

Can I use Vivostat® fibrin sealant when the patient is fully heparinised

Vivostat® Fibrin Sealant will perform very well on fully heparinised patients and on patients on aspirin and warfarin therapy.

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, onsite 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® Fibrin Sealant product was launched by the Danish company Vivolution A/S (now Vivostat A/S).

Today, the Vivostat® technology comprises more than autologous fibrin sealant. The advanced blood processing technology has been further developed and 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 PRF®

Vivostat PRF® (Platelet Rich Fibrin) solves the problems of conventional PRP systems (platelet rich plasma) by leveraging the revolutionary Vivostat® Fibrin Sealant blood processing technology.

By combining a platelet concentrate with a fibrin sealant solution, it is possible to have a carrier, a controlled release and a medium for vascular in-growth – all in one product, Vivostat PRF®.

From 120 ml blood, 5-6 ml of Vivostat PRF® can be prepared, with 7 times the platelet level of the donor's blood – corresponding to a platelet level above 1 million platelets/ μ l. Unlike conventional PRP systems, the instant polymerisation of the fibrin ensures that the growth factors remain precisely where they are applied.

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



 Vivostat®
Fibrin

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