# Thrombocyte

# Coagulation-induced resistance to fluid flow in small-diameter vascular grafts and graft mimics measured by purging pressure.

Authors: Nichols M.D., Choudhary R., Kodali S., Reichert W.M.

Publication Date: 2013

## Abstract:

In this study, the coagulation-induced resistance to flow in small-diameter nonpermeable Tygon tubes and permeable expanded polytetrafluoroethylene (ePTFE) vascular grafts was characterized by measuring the upstream pressure needed to purge the coagulum from the tube lumen. This purging pressure was monitored using a closed system that compressed the contents of the tubes at a constant rate. The pressure system was validated using a glycerin series with well-defined viscosities and precisely controlled reductions in cross-sectional area available for flow. This system was then used to systematically probe the upstream pressure buildup as fibrin glue, platelet-rich plasma (PRP) or whole blood coagulated in small-diameter Tygon tubing and or ePTFE grafts. The maximum purging pressures rose with increased clot maturity for fibrin glue, PRP, and whole blood in both Tygon and ePTFE tubes. Although the rapidly coagulating fibrin glue in nonpermeable Tygon tubing yielded highly consistent purging curves, the significantly longer and more variable clotting times of PRP and whole blood, and the porosity of ePTFE grafts, significantly diminished the consistency of the purging curves. © 2013 Wiley Periodicals, Inc. J Biomed Mater Res Part B: Appl Biomater, 101B: 1367-1376, 2013. 

# Patient-derived fibrin sealant: Clinical, preclinical, and biophysical aspects.

Authors: Kjoergard H.K.

Publication Date: 2003

## Abstract:

Today, there is an enormous interest in surgical sealant, not only for hemostasis, but also for binding of tissues together during surgery, and to improve wound healing. Man has imitated nature in developing fibrin sealant that is biodegradable. However, the risk of transmission of both known and unknown infectious agents can generally not be ruled out completely for plasma products from donors. In addition there is a considerable immunologic risk of using biological products of animal origin. Preclinical and clinical data has demonstrated that a safe and useable surgical fibrin sealant can be prepared from the patient's own blood using the enzyme batroxobin. Experimental data showed that patient-derived fibrin sealant provided enhanced instant adhesion strength and elasticity compared with conventional fibrin sealant due to its faster polymerisation rate. Test methods for fibrin sealant were found to be inaccurate, and we constructed and validated a new computer assisted test method to get information about elasticity and other dynamic properties of biological sealant. The method is highly reproducible and is the first validated using vital human tissue as the adhesion substrate. It takes about one half hour to prepared patient-derived fibrin sealant, which may turn a good operation into a perfect operation without any known risk.

# Significant merits of a fibrin sealant in the presence of coagulopathy following paediatric cardiac surgery: Randomised controlled trial.

Authors: Codispoti M., Mankad P.S

Publication Date: 2002

## Abstract:

Objectives: The efficacy of a fibrin sealant in paediatric cardiac surgery has been demonstrated. However, its effectiveness in the presence of significant untreated coagulopathy has not been addressed. This study was designed to investigate the role of the topical application of a fibrin sealant, Beriplast P (BP), in the presence of coagulopathy following paediatric cardiac surgery. Methods: After confirming the presence of significant post-bypass coagulopathy, patients undergoing repair of congenital heart defects using cardiopulmonary bypass were randomised to the use of BP (group BP) or no intervention (group C). BP was applied over suture lines and microvascular bleeding sites. Criteria for transfusion of blood and blood products were standardised for both groups. Outcome variables were: (1) post-operative bleeding; (2) transfusion of blood and blood products; (3) theatre time to achieve haemostasis; (4) ventilation time, intensive therapy unit (ITU) and hospital stay. Results: Fifty-two patients (n=26 in each group), aged 3 days to 17.4 years were recruited. There were no hospital deaths and no significant differences in demographic or intraoperative variables that might have affected the chosen endpoints. After protamine, all patients in both groups had significant coagulopathy (P<=0.05 versus baseline). There were fewer patients receiving transfusions of fresh frozen plasma (FPP) in the intervention group, when compared to the control group (P<=0.05). Patients receiving BP spent less time in theatre to achieve haemostasis (P<=0.05), had a lesser amount of bleeding intraoperatively (P<=0.01), at 4h (P<=0.05) and at 24h (P<=0.05), required a lower amount of transfusions of red cells (P<=0.01), FPP (P<=0.05) and platelets (P<=0.05). There were no differences in ventilation time, length of stay in ITU or in hospital.

Conclusions: Even in the presence of significant coagulopathy, intraoperative use of fibrin sealant in paediatric cardiac surgery reduces the amount of bleeding and need for transfusions of blood and blood products. The theatre time necessary to achieve haemostasis is also significantly reduced. These findings have a potential to improve clinical outcomes and enhance cost benefits. 

# Pharmacological strategies to decrease transfusion requirements in patients undergoing surgery.

Authors: Porte R.J., Leebeek F.W.G.

Publication Date: 2002

## Abstract:

Surgical procedures are inevitably associated with bleeding. The amount of blood loss may vary widely between different surgical procedures and depends on surgical as well as non-surgical factors. Whereas adequate surgical haemostasis may suffice in most patients, pro-haemostatic pharmacological agents may be of additional benefit in patients with (diffuse) surgical bleeding or in patients with a specific underlying haemostatic defect. In general, surgical haemostasis and pharmacological therapies can be complementary in controlling blood loss. The use of pharmacological therapies to reduce blood loss and blood transfusions in surgery has historically been restricted to a few drugs. Antifibrinolytic agents (aprotinin, tranexamic acid and aminocaproic acid) have the best evidence supporting their use, especially in cardiac surgery, liver transplantation and some orthopaedic surgical procedures. Meta-analyses of randomised, controlled trials in cardiac patients have suggested a slight benefit of aprotinin, compared with the other antifibrinolytics. Desmopressin is the treatment of choice in patients with mild haemophilia A and von Willebrand disease. It has also been shown to be effective in patients undergoing cardiac surgery who received aspirin up to the time of operation. However, overall evidence does not support a beneficial effect of desmopressin in patients without pre-existing coagulopathy undergoing elective surgical procedures. Topical agents, such as fibrin sealants have been successfully used in a variety of surgical procedures. However, only very few controlled clinical trials have been performed and scientific evidence supporting their use is still limited. Novel drugs, like recombinant factor VIIa (eptacog alfa), are currently under clinical investigation. Recombinant factor VIIa has been introduced for the

treatment of haemophilia patients with inhibitors, either in surgical or non-surgical situations. Preliminary data indicate that it may also be effective in surgical patients without pre-existing coagulation abnormalities. More clinical trials are warranted before definitive conclusions can be drawn about the safety and the exact role of this new drug in surgical patients. Only adequately powered and properly designed randomised, clinical trials will allow us to define the most effective and the safest pharmacological therapies for reducing blood loss and transfusion requirements in surgical patients. Future trials should also consider cost-effectiveness because of considerable differences in the costs of the available pro-haemostatic pharmacological agents.

# Efficacy of hemostatic agents in improving surgical hemostasis.

Authors: Green D., Wong C.A., Twardowski P.

Publication Date: 1996

## Abstract:

Not Available

# Bleeding hearts.

Authors: Estafanous F.G.

Publication Date: 1991

## Abstract:

Not Available

# The control of bleeding after cardiopulmonary bypass by the intrapericardial instillation of fresh frozen plasma and platelets with microfibrillar collagen.

Authors: Robicsek F., Born G.V.R.

Publication Date: 1984

## Abstract:

A technique of, and the results obtained with, the intraoperative and postoperative intrapericardial instillation of microfibrillar collagen and fresh frozen plasma and platelet mixture are presented. Intraoperatively, the mixture was instilled into the exposed mediastinum in the course of open-heart operations in 31 patients in whom diffuse oozing of blood persisted following the termination of cardiopulmonary bypass and the neutralization of circulating heparin. Immediate clot formation and decrease of blood loss were observed in all instances. This method was also found effective in 9 of 20 patients who had continuing blood loss during the hours following open-heart surgery and in whom the mixture was instilled through the mediastinal drainage tubes.

# Clinical comparison between microporrus polysaccharide hemispheres (MPH) and fibrin glue during laparoscopic partial nephrectomy.

Authors: Makiyama K., Sakata R., Sano F., Yamanaka H., Nakaigawa N., Yao M., Kubota Y.

Publication Date: 2012

## Abstract:

OBJECTIVE: Using hemostatic agents is one of the options to avoid complications during laparoscopic partial nephrectomy (LPN). Microporous polysaccharide hemispheres are made entirely from purified potato starch that activates the clotting cascade via a unique mechanism that hyperconcentrates platelets and coagulation proteins. We compare the efficacy of this new hemostatic agent, MPH and the standard hemostatic agent, fibrin glue. METHODS: Between January 2007 and October 2011, 70 LPNs with hilar clamping were completed by a single surgeon in Yokohama City University Hospital. We compare two sequential groups of patients: group A consisted of 27 patients in whom MPH was used and group B consisted of 43 patients in whom fibrin glue was used. These agents (MPH and fibrin glue) were applied to the partial nephrectomy bed before tying a suture in parenchymal suturing and after the renal hilum was unclamped. Study variables included blood loss, ischemic time and perioperative complications. RESULTS: Group A showed significantly less mean estimated blood loss (29.8 vs. 86.3 ml; p = 0.004) and less mean ischemic time (21.4 vs. 28.5 min; p = 0.002) than these of group B. Postoperative complications occurred in two patients in group B, but there were no postoperative complications in group A. CONCLUSIONS: MPH is available as an adequate hemostatic agent during LPN. There was no significant difference in the incidence of postoperative complications betweenMPHand fibrin glue.

# Use of single-donor platelet glue and fibrin glue in human cranioplasty.

Authors: Burnouf T., Chen T.M., Tsai J.-C.

Publication Date: 2010

## Abstract:

Background: Reconstruction of post-traumatic, full-thickness calvarial bone defects is needed to provide brain protection, to restore aesthetic contours, and to correct intracranial ventricular collapse. The two most widely used materials, autogenous bone graft and methyl methacrylate, are not ideal. Much effort has been directed to the development of osteoconductive materials composed of various calcium phosphate compounds. However, as an osteoinductive agent is needed to favor bone regeneration, there is interest in the use of growth factors (GF) - rich platelet materials in this indication. Aim: Evaluate a bone graft substitute obtained by combining hydroxy-apatite/s-tricalcium phosphate (HA/s-TCP) with human platelet glue rich in growth factors. Methods: The safety and efficacy of (HA/s-TCP)-platelet glue to reconstruct post-traumatic, full-thickness, calvarial bone defects was evaluated in 6 consecutive patients (5 males and 1 female; 26-66 years). Interval between injury and reconstruction ranged from 6 months to 4 years. Equal volumes of single-donor platelet-rich-plasma and cryoprecipitate were mixed with HA/s-TCP. Twice the volume of human single-donor thrombin was then added and the mixture was gently stirred for a few seconds, quickly consolidating into a firm moldable paste. The paste was applied to the bone defect and shaped using simple finger pressure. The HA/s-TCP granules were carefully compacted to prevent the formation of dead spaces. Once the desired bone contour had been achieved, a closed suction drain was placed through a separate stab incision well behind the reconstructed site. Single-donor fibrin glue was sprayed to facilitate hemostasis, the wound was closed and a pressure dressing applied. Patients were followed for 28-48 months subsequent to surgery (mean period: 30 months).

Post-operative evaluation included serial photography, repeated physical examinations, and three-dimensional computed tomography (CT) scan performed 2 years subsequent to surgery. Results: High fibrin concentration of the platelet glue allowed easy molding and sculpting of the scaffold, providing mechanical stability and avoiding spillage of the granules into the operating field. The HA/s-TCP-human platelet glue paste demonstrated good tissue biocompatibility in all 6 patients. No infection of the surgical site or extrusion of HA/s-TCP was observed. The contour of the reconstructed calvarium was esthetically acceptable during the follow-up period. No secondary depression resulting from resorption of the HA/s-TCP was noted. There was no visible thinning of the overlying skin or sharp edges at the HA/s-TCP host bone interface. Three dimensional CT scans taken 2 years subsequent to reconstruction revealed good reconstruction of the bone defect in all six patients. Visual inspection of the reconstructed calvarium 2 years after surgery in one patient evidenced conversion of the scaffold into solid new bone. Section of the biopsy demonstrated new bone formation at the expense of the scaffold. Conclusion: Combining an osteoconductive scaffold with single-donor growth factor-rich platelet glue offers an interesting alternative to autogenous bone graft or methyl methacrylate for post-traumatic calvarium bone defect reconstruction.

# Autologous fibrin glue in peripheral nerve regeneration in vivo.

Authors: Choi B.-H., Han S.-G., Kim S.-H., Zhu S.-J., Huh J.-Y., Jung J.-H., Lee S.-H., Kim B.-Y.

Publication Date: 2005

## Abstract:

The activity of several growth factors on peripheral nerve regeneration is reported. Autologous fibrin glue contains a large number of platelets, which release significant quantities of growth factors. In order to understand the role of autologous fibrin glue in peripheral nerve regeneration, a 15-mm rabbit peroneal nerve defect was repaired using a vein graft filled with autologous fibrin glue. Axonal regeneration was examined using histological and electrophysiological methods. The extent of axonal regeneration was superior when treated with autologous fibrin glue. Our data suggest that fibrin nets formed by fibrinogen, in combination with growth factors present in autologous fibrin glue, might effectively promote peripheral nerve regeneration in nerve defects. 

# Autologous fibrin sealant for treatment of persistent fistula after upper gastrointestinal resektions and bariatric surgery.

Authors: Devyatko Y., Langer F., Schoppmann S., Puspok A., Prager G., Zacherl J.

Publication Date: 2011

## Abstract:

Aims: Anastomotic leak is a potentially life-threatening complication after upper gastrointestinal resections and bariatric surgery requiring long, cost-intensive and frequently failed treatment. This study has been undertaken to evaluate, whether endoscopic sealing with autologous fibrin glue is an effective treatment for persistent postoperative fistula. Methods: During the last three years 17 patients who developed non-healing upper gastrointestinal leaks after oncologic (n = 6), non-oncologic resektions (n = 3), and bariatric surgical procedures(n = 8) were treated by endoscopic Vivostatdegree Platelet Rich Fibrin (PRFdegree) autologous fibrin sealing. Fibrin sealant was applied in patients without systemic or advanced local sings of infection with a sufficient external drainage of leakage site. Location was cervical (n = 1), intrathoracic (n = 4) and abdominal (n = 12). Previous leak treatment included surgery, external drainage or/and endoscopic stenting. Endoscopic sealing occurred in 6 patients with novel anastomotic insufficiency during the first week after manifestation of leakage and in 11 patients with persistent fistula after a median interval of 35 days (range 16-70). Results: Fourteen of seventeen patients had complete healing of the anastomotic leak or fistula after one (8 patients), two (3 patients), tree (2 patients) or five (1 patient) sealing procedures. In seven from eleven patients with persistent fistula complete wound healing was achieved during a week after the first sealing, in 2 patients during three weeks. In six procedures sealing was completed by simultaneous implantation of a stent. In three patients treatment failed and the healing of the abdominal fistula was achieved by following insertion of a stent on the leakage site. Conclusions: Autologous fibrin sealing could be successfully used for

management of persistent upper gastrointestinal fistula and promotes healing.

# Life-threatening pleural hemorrhage following intrapleural enzyme therapy and successful treatment with fibrin-thrombin sealant pleurodesis: A case report.

Authors: Vun S.V., Lance D.G.

Publication Date: 2015

## Abstract:

Introduction: Intrapleural fibrinolytic enzyme therapy is a potentially surgery-sparing treatment for poorly resolving parapneumonic effusion and empyema. It is safe in the majority of patients, however the most significant risk associated with this treatment is severe bleeding secondary to pleural hemorrhage. Contraindications for intrapleural enzyme therapy are not widely agreed upon and little is known about how to treat this difficult and potentially lethal hemorrhagic complication. Case presentation: An independent 82-year-old Caucasian man presented to hospital with an empyema complicating community-acquired pneumonia and coincidental pulmonary embolus. He was initially commenced on intravenous antibiotics, pleural drainage and anticoagulation, however failed to improve significantly and was commenced on intrapleural fibrinolytic enzyme therapy. Shortly after, he suffered severe pleural hemorrhage that was uncontrollable despite emergency thoracotomy and washout. Subsequent hemostasis was achieved after re-exploration and application of topical fibrin-thrombin sealant spray. The patient survived and was discharged home. Conclusions: Intrapleural enzyme therapy can be effective in loculated parapneumonic effusion and empyema, but massive pleural hemorrhage can complicate its use. Pleural hemorrhage appears to be associated with anticoagulation or coagulopathy, and can be difficult to manage. This case adds to the body of data on bleeding complications following intrapleural enzyme therapy, and to the best of our knowledge is the first report of fibrin-thrombin sealant use in this setting.

# Fibrin Sealants, Platelet Gels, and Spinal Fusion.

Authors: Elder B.D., Witham T.F.

Publication Date: 2016

## Abstract:

Not Available

# Protection of colonic anastomosis with platelet-rich plasma gel in the open abdomen.

Authors: Zhou B., Ren J., Ding C., Wu Y., Chen J., Wang G., Gu G., Li J.

Publication Date: 2014

## Abstract:

Background Although evidence for colonic anastomosis in the damage control abdomen continues to accumulate, anastomotic leak is common and associated with greater morbidity. The purposes of our study was to evaluate the effect of platelet-rich plasma (PRP) gel on the healing of colon anastomosis and anastomotic strength in the open abdomen. Methods PRP was prepared by enriching whole blood platelet concentration from healthy rat. In the rodent model, standard colonic anastomoses followed by closure of abdomen (Control; n = 10) and anastomoses followed by open abdomen (OA; n = 10) were compared to PRP-sealed anastomoses in open abdomen (OA + PRP; n = 10). One week after surgery, body weight, anastomotic bursting pressure, hydroxyproline concentration, and histology of anastomotic tissue were evaluated. Results All rats survived surgery and had no signs of anastomotic leakage. Compared with the control and PRP group, OA group exhibited a significant decrease in body weight, anastomotic bursting pressure, hydroxyproline concentration, and collagen deposition. No significant difference was detected in these variables between the PRP group and the control group. Conclusion PRP gel application prevented delayed anastomotic wound healing after open abdomen, which suggested that anastomotic sealing with PRP gel might improve outcome of colonic injuries in the setting of open abdomen. 

# Fibrin glue therapy for severe hemorrhagic cystitis after allogeneic hematopoietic stem cell transplantation.

Authors: Tirindelli M.C., Flammia G.P., Bove P., Cerretti R., Cudillo L., de Angelis G., Picardi A., Annibali O., Nobile C., Cerchiara E., Dentamaro T., de Fabritiis P., Lanti A., Ferraro A.S., Sergi F., di Piazza F., Avvisati G., Arcese W.

Publication Date: 2014

## Abstract:

Hemorrhagic cystitis (HC) occurring after allogeneic transplantation significantly affects quality of life and, in some cases, becomes intractable, increasing the risk of death. To date, its therapy is not established. We used the hemostatic agent fibrin glue (FG) to treat 35 patients with refractory post-transplantation HC. Of 322 adult patients undergoing an allogeneic transplantation for hematological malignancy, 35 developed grade >= 2 HC refractory to conventional therapy and were treated with FG, diffusely sprayed on bleeding mucosa by an endoscopic applicator. The cumulative incidence of pain discontinuation and complete remission, defined as regression of all symptoms and absence of hematuria, was 100% at 7days and 83% +/- 7%, respectively, at 50 days from FG application. The 6-month probability of overall survival for all 35 patients and for the 29 in complete remission was 49% +/- 8% and 59% +/- 9%, respectively. In the matched-pair analysis, the 5-year probability of overall survival for the 35 patients with HC and treated with FG was not statistically different from that of the comparative cohort of 35 patients who did not develop HC (32% +/- 9% versus 37% +/- 11%, P = not significant). FG therapy is a feasible, effective, repeatable, and affordable procedure for treating grade >=2 HC after allogeneic transplantation.

# Fibrin sealant patch for repair of acute type a aortic dissection.

Authors: Lisy M., Kahlil M., Stock U.A., Wildhirt S.M.

Publication Date: 2013

## Abstract:

Introduction The use of glues to repair disrupted tissue during acute type-A aortic dissection (TAD) surgery may be discontinuous, and cause embolization and cell necrosis. We report a method of fibrin sealant patch (FSP) to reinforce dissected aortic tissue with a collagen double layer coated with fibrinogen/thrombin on either side (TachoSil; Takeda, Konstanz, Germany). Methods In 12 patients (seven male, 66.9 +/- 11.7 years) with acute TAD we performed FSP of the intima-media disruption at the proximal and distal anastomosis of the aorta. We analyzed the perioperative course and echocardiographical, radiological, and clinical outcomes up to one year. Additionally, we investigated the adhesive potential of the FSP in vitro. Results In vitro, the adhesive strength of the FSP was 60 N/cm<sup>2</sup>. In-hospital mortality was 8.3% (n = 1), recovery was satisfactory with no major neurologic events, mean ICU stay was 13.6 +/- 6.0 days, mean hospital stay was 20.7 +/- 4.4 days. A total of 7.0 +/- 2.6 RBC, 3.4 +/- 1.5 platelets, and 8.0 +/- 4.3 FFP were transfused. One-year survival was 83.3%. In 6/6 DeBakey II dissections the intimal tear was completely resected, in 2/6 DeBakey I dissections the false lumen in the descending aorta completely collapsed. No redissections and no relevant aortic valve insufficiencies were seen during follow-up. Conclusion This analysis shows that FSP using a collagen matrix double layer coated with fibrinogen/thrombin is feasible, safe, and effective in repairing the dissected aortic tissue. It results in continuous reinforcement of aortic tissue and completely avoids the need for conventional glues. 

# Single-donor allogeneic platelet fibrin glue and osteoconductive scaffold in orbital floor fracture reconstruction.

Authors: Chen T.M., Tzeng Y.S., Tsai J.C., Burnouf T.

Publication Date: 2013

## Abstract:

Commonly used materials for orbital floor fracture reconstruction include autologous cranial bone graft and titanium mesh. We have evaluated here a biomaterial combining biphasic calcium phosphate (hydroxyapatite [HA]/beta-tricalcium phosphate [TCP]) osteoconductive scaffold with single-donor allogeneic platelet fibrin glue. The study was conducted on 10 consecutive patients with a follow-up of up to 4 years. Platelet fibrin glue was prepared by mixing equal volumes of single-donor platelet-rich plasma and cryoprecipitate with HA/beta-TCP followed by activation with human thrombin prepared by plasma activation. Postoperative evaluations included serial photographs, repeated physical examination, and 3-dimensional computed tomography scan performed 2 years after surgery. The fibrin-rich platelet biomaterial was easy to mold and to apply on the surgical site allowing the surgeon to sculpt accurately the bone defect, providing mechanical stability while avoiding spillage of the scaffold. No infection of the orbit or extrusion of HA/beta-TCP was observed. Ocular motility was normal, and no diplopia or enophthalmos of the injured orbit was noted. Coronal computed tomography scans of the reconstructed orbits revealed good restoration of the orbital floor defect in all 10 patients. The use of single-donor platelet fibrin glue combined with an osteoconductive scaffold offers a valuable alternative to autologous cranial bone graft or titanium mesh in the reconstruction of orbital floor bone defect.

# Fibrin glue for treatment of severe haemorrhagic cystitis following allogeneic haematopoietic stem cell transplantation.

Authors: Tirindelli M.C., Flammia G., Sergi F., Cerretti R., Cudillo L., Picardi A., De Angelis G., Bove P., Cefalo M.G., Cerchiara E., Altomare L., Allori G., Lanti A., Avvisati G., Arcese W.

Publication Date: 2013

## Abstract:

Background: Patients undergoing hematopoietic stem cell transplant (HSCT) are particularly exposed to the risk of developing haemorrhagic cystitis (HC), which is characterized by symptoms ranging from macroscopic haematuria to renal failure. HC signifi- cantly affects quality of life and in some cases becomes intractable leading to patient death. Its therapeutic management has not been established. In this prospective study, we used Fibrin Glue (FG), an haemostatic agent derived from human plasma, to treat 34 patients with refractory post-transplant HC. Materials and methods: Between January 2006 and October 2012, 1116 (249 children and 867 adults) underwent an HSCT at the Rome Transplant Network. Among adults, 554 received an autologous HSCT and no patient developed HC. Of 313 patients undergoing an allogeneic HSCT (HLA sib. n=140, MUD n=71, UCB n=28, Haplo n=74) 45 (14%) developed HC, which was of grade >=II in 34 patients ( grade: II n=10, III n=21, IV n=3). All these patients refractory to conventional therapy for HC were treated with FG. During cystoscopy bladder distension was maintained at a constant pressure of 12 mmHg by a carbon dioxide insufflator and FG was diffusely sprayed on bleeding and raw surfaces of bladder mucosa by an endoscopic applicator. The response was evaluated at 10, 30 and 60 days from first FG application. Results: The number of FG application was 1 in 21 patients, 2 in 10 and 3 in 3 with a median FG volume of 10.8 ml (range, 6.3-16). The pelvic pain disappeared within the first 24 hours from FG application in all patients and the complete remission, defined as regression of all symptoms and absence of haematuria, evaluated at 10, 30 and 60 days was achieved in 18%, 61%

and 83% of patients, respectively. The response was independent from platelets recovery and BK viruria and its treatment. Conclusions: FG therapy is an effective, feasible, and reproducible procedure to treat grade >= II refractory HC.

# L-PRP/L-PRF in esthetic plastic surgery, regenerative medicine of the skin and chronic wounds.

Authors: Cieslik-Bieleck A., Choukroun J., Odin G., Dohan Ehrenfest D.M.

Publication Date: 2012

## Abstract:

The use of platelet concentrates for topical use is of particular interest for the promotion of skin wound healing. Fibrin-based surgical adjuvants are indeed widely used in plastic surgery since many years in order to improve scar healing and wound closure. However, the addition of platelets and their associated growth factors opened a new range of possibilities, particularly for the treatment of chronic skin ulcers and other applications of regenerative medicine on the covering tissues. In the 4 families of platelet concentrates available, 2 families were particularly used and tested in this clinical field: L-PRP (Leukocyte- and Platelet-rich Plasma) and L-PRF (Leukocyte- and Platelet-Rich Fibrin). These 2 families have in common the presence of significant concentrations of leukocytes, and these cells are important in the local cleaning and immune regulation of the wound healing process. The main difference between them is the fibrin architecture, and this parameter considerably influences the healing potential and the therapeutical protocol associated to each platelet concentrate technology. In this article, we describe the historical evolutions of these techniques from the fibrin glues to the current L-PRP and L-PRF, and discuss the important functions of the platelet growth factors, the leukocyte content and the fibrin architecture in order to optimize the numerous potential applications of these products in regenerative medicine of the skin. Many outstanding perspectives are appearing in this field and require further research. 

# A retrospective review of the use of autologous platelet gels for rhytidectomy.

Authors: Farrior E., Ladner K.

Publication Date: 2012

## Abstract:

Not Available

# Effect on Blood Loss and Cost-Effectiveness of Pain Cocktails, Platelet-Rich Plasma, or Fibrin Sealant After Total Knee Arthroplasty.

Authors: Bernasek T.L., Burris R.B., Fujii H., Levering M.F., Polikandriotis J.A., Patterson J.J.

Publication Date: 2012

## Abstract:

This study evaluated the effect of periarticular pain cocktail, platelet-rich plasma, or fibrin sealant injections on blood loss, transfusion rate, and hospital costs after total knee arthroplasty. A retrospective review of 400 patients undergoing primary total knee arthroplasty with one of the different periarticular treatments as stated above was performed. Postoperative blood loss, hemoglobin levels, allogenic blood transfusion rates, and per-case hospital injection cost were reported. Although platelet-rich plasma and fibrin sealant decreased blood loss compared with the control group ($P < .001$), there was no significant difference in blood loss in the pain-cocktail group or in postoperative hemoglobin levels or transfusion rates between all groups. Significant efficacy and cost-effectiveness for these modalities could not be identified and have, therefore, been discontinued at our practice. Level of evidence: level III. 

# Use of autologous fibrin glue (platelet-poor plasma) in abdominal dermolipectomies.

Authors: Schettino A.M., Franco D., Franco T., Filho J.M., Vendramin F.S.

Publication Date: 2012

## Abstract:

Autologous plasma is endowed with properties that speed up healing, hemostasis, and adhesiveness, in addition to growth factors. Through an established protocol, it was possible to isolate thrombin, as well as the platelet-rich plasma (PRP) and platelet-poor plasma (PPP) fractions. The purpose of this study was to analyze autologous use of thrombin and PPP to foster adhesion between an abdominal dermoadipose flap and the aponeurotic surface in abdominal dermolipectomies. The data from 40 patients who underwent abdominal dermolipectomies were analyzed, with 20 patients using thrombin and autologous PPP (Plasma group) and 20 patients with no intervention (Control group). An attempt was made to assess adhesive power by quantifying the serohematic liquid volume gauged during the postoperative days (POD), and also noting the incidence of seroma. Other variables such as age and body mass index (BMI) were also analyzed. The reduction in the aspiration drain debit was statistically relevant only on the first POD in the Plasma group. There was no reduction in the incidence of seroma in these patients. Similarly, age and BMI did not influence these outcomes. The PPP fostered adhesion between the abdominal dermoadipose flap and the aponeurotic surface only on the first POD and had no influence whatsoever on the incidence of seroma. There are few reports on the use of PPP for plastic surgery, particularly the autologous type, opening up possibilities for further research projects to expand its use. LEVEL OF EVIDENCE III: This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the table of contents or the online instructions to authors www.springer.com/00266.

# Effect of preoperative subcutaneous platelet-rich plasma and fibrin glue application on skin flap survival.

Authors: Findikcioglu F., Findikcioglu K., Yavuzer R., Lortlar N., Atabay K.

Publication Date: 2012

## Abstract:

The aim of this study was to compare the effects of preoperative subcutaneous platelet-rich plasma and fibrin glue administration on skin flap survival. One week before surgery; saline, platelet-rich plasma, fibrin glue, and thrombin solutions were applied under rat skin flap areas in Groups I, II, III, and IV, respectively. Unipedicled epigastric flaps were elevated in the first three groups but could not be elevated in Group IV because of preoperative abdominal skin necrosis. Necrotic area measurements, microangiography, and histological and immunohistochemical evaluations were performed. Platelet-rich plasma reduced the percentage of necrotic area when compared to other groups. Histologically and microangiographically an increased number of arterioles were observed in the platelet-rich plasma group. Thrombin (when used alone) caused abdominal skin necrosis. Increased expression of VEGF and PDGF was found in all platelet-rich plasma-treated flaps. There was no significant difference between groups with respect to TGF-beta3 staining intensity. In this study preoperative administration of platelet-rich plasma mimicked the pharmacological delay effect and enhanced flap survival. Individual use of thrombin was found to be unsuitable in flap surgery. LEVEL OF EVIDENCE I: This journal requires that authors assign a level of evidence to each article.

# Effect of intraoperative platelet-rich plasma and fibrin glue application on skin flap survival.

Authors: Findikcioglu F., Findikcioglu K., Yavuzer R., Lortlar N., Atabay K.

Publication Date: 2012

## Abstract:

The experiment was designed to compare the effect of intraoperative platelet-rich plasma (PRP) and fibrin glue application on skin flap survival. In this study, bilateral epigastric flaps were elevated in 24 rats. The right-side flaps were used as the control of the left-side flaps. Platelet-rich plasma, fibrin glue, and thrombin had been applied under the flap sites in groups 1, 2, and 3, respectively. Five days later, all flap pedicles were ligated. Necrotic area measurements, microangiography, and histologic and immunohistochemical evaluations were performed to compare the groups. Platelet-rich plasma reduced necrotic area percentages as compared with other groups. Histologically and microangiographically increased number of arterioles were observed in PRP groups. Thrombin when used alone increased flap necrosis. Vascular endothelial growth factor, platelet-derived growth factor, and transforming growth factor A3 primary antibody staining showed increased neovascularization and reepithelialization in all PRP-applied flaps. This study demonstrated that PRP, when applied intraoperatively under the skin flap, may enhance flap survival. Thrombin used alone was found to be unsuitable in flap surgery. 

# Platelet gels and hemostasis in facial plastic surgery.

Authors: Farrior E., Ladner K.

Publication Date: 2011

## Abstract:

Over the last decade, the availability of autologous and homogenous platelet-rich and fibrin-rich gels has increased. Due to their more widespread availability and the potential benefits of improved hemostasis and wound healing, their use during facial plastic and reconstructive surgery procedures has also grown. These gels, when applied topically, attract inflammatory cells and fibroblasts and stimulate collagen deposition. Various studies have investigated the potential surgical applications and benefits of these gels. What follows is an in-depth review of the various fibrin and platelet gels available. Furthermore, it clarifies the current applications and proven benefits in facial plastic surgery. 

# Tension-free primary closure with autologous platelet gel versus vivostatTM for the definitive treatment of chronic sacrococcygeal pilonidal disease.

Authors: Gipponi M., Reboa G., Testa T., Giannini G., Strada P.

Publication Date: 2010

## Abstract:

Objective: A randomized clinical trial was performed in patients with chronic or recurrent pilonidal sinus (PS) comparing primary closure coupled with random application of in house autologous platelet gel or produced by means of VivostatTM in order to assess whether a standardized product had an impact on the wound healing process. Patients and Methods: Between June 2006 and June 2009, 100 patients (82 males, 18 females: median age 30 years; range, 16-51 years) underwent wide excision of the pilonidal area with midline tension-free closure and were randomly given either the in house autologous platelet gel (Group 1) or the VivostatTM gel (Group 2). Results: Group 2 patients had shorter wound healing time (8 vs. 10 days; $p<0.0001$), time to return to full activity (11 vs. 16 days: $p<0.0001$), less uncomplicated fluid collections (120 vs. 190 ml: $p<0.0001$), and fewer postoperative wound complications (1/50=2% vs. 5/50=10%, $p<0.001$). After a median follow-up of 21 months (range: 4-40 months), two recurrences were detected in Group 1. Conclusion: The standardized production of platelet gel by means of the VivostatTM system guarantees the reproducibility of the procedure and its use was correlated with an improved outcome, with a high degree of patient satisfaction and better cosmetic results.

# A novel technique combining single-donor platelet gel and fibrin glue with skin graft to heal recalcitrant lower extremity ulcers.

Authors: Burnouf T., Chen T.M., Tsai J.-C.

Publication Date: 2010

## Abstract:

Background: There is no ideal procedure for the treatment of chronic skin ulcers. Recently, the use of platelet gel (PG) in this indication has generated great interest. Aim: Evaluate the safety and efficacy of a new procedure combining allogeneic single-donor (S-D) PG and S-D fibrin glue (FG) to enhance skin graft take for treating recalcitrant ulcers. Methods: This study was approved by the Institutional Review Board of Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan. Protocol 096-05-042. The protocol conformed to ethical guidelines of the 1975 Declaration of Helsinki. 15 patients (17 ulcers) who provided their informed consent and presenting various etiology were enrolled. Skin ulcer was debrided and the wound covered with moist saline dressing. 3-14 days later, the wound bed was sprayed with PG that was obtained by activating S-D platelet concentrate by S-D thrombin (obtained by activation of S-D plasma by calcium chloride). Thin-split-thickness skin graft with multiple slits was then put on the wound bed, and finally S-D FG was sprayed on the skin graft. Short leg P-P splint was used to immobilize the skin graft. Results: Most skin grafts took well. The interval between skin graft and complete wound healing ranged from 3 weeks to 2 months. No recurrence of ulcers was noted during the 3-18 months follow-up period. No adverse reactions were observed. Conclusion: The procedure provides dual advantages in skin grafting for recalcitrant ulcers because PG functions as a delivery system of powerful mitogenic and chemostatic growth factors, and FG as a hemostatic tissue sealant that avoids the use of staple or sutures.

# Applications of platelet-rich fibrin matrix in facial plastic surgery.

Authors: Sclafani A.P.

Publication Date: 2009

## Abstract:

Platelet concentrates enjoyed some clinical popularity in facial plastic surgery several years ago. However, interest waned due to expense, amount of blood required, equipment, space, and staff needed, and lack of clinically significant benefit. A novel, simple method of preparing an autologous platelet derivative (Selphyl; Aesthetic Factors, Princeton, NJ) allows rapid and inexpensive generation of a platelet-rich fibrin matrix (PRFM) that can be used to enhance healing after facial procedures as well as to rejuvenate the face without tissue manipulation. PRFM provides autologous, natural, but concentrated platelet growth factor release and stimulation of surrounding tissue. This article describes its use for cosmetic facial applications. 

# Use of autologous platelet-rich fibrin on hard-to-heal wounds.

Authors: Steenvoorde P., van Doorn L.P., Naves C., Oskam J.

Publication Date: 2008

## Abstract:

This retrospective study found that use of autologous platelet-rich fibrin on a range of hard-to-heal wounds achieved full healing or a significant reduction in wound diameter with no adverse effects. Prospective studies are now needed

# Vertical alveolar ridge augmentation using autogenous bone grafts and platelet-enriched fibrin glue with simultaneous implant placement.

Authors: Lee H.-J., Choi B.-H., Jung J.-H., Zhu S.-J., Lee S.-H., Huh J.-Y., You T.-M., Li J.

Publication Date: 2008

## Abstract:

Objective: The aim of this study was to evaluate the combined use of autogenous bone and platelet-enriched fibrin glue as grafting material for vertical alveolar ridge augmentation with simultaneous implant placement in a canine alveolar ridge defect model. Study design: In 6 mongrel dogs, bilateral vertical alveolar ridge defects were created in the mandible. After 3 months of healing, 2 dental implants were placed in each defect of the mandible, creating 6-mm supra-alveolar peri-implant defects. The 2 implants per defect were subjected to surgical treatments involving either a combination of autogenous bone grafts and platelet-enriched fibrin glue, or a conventional flap procedure only (control). After a healing period of 6 months, the dogs were humanely killed for histological and histometric analyses. Results: Implant placement alone produced limited vertical alveolar height (0.6 +/- 0.4 mm). However, alveolar augmentation including a combination of autogenous bone grafts and platelet-enriched fibrin glue with simultaneous implant placement resulted in alveolar ridge augmentation amounting to 4.2 +/- 1.0 mm, comprising 63% of the defect height. New bone-implant contact was 40.5% in the defects treated with combined autogenous bone grafts and platelet-enriched fibrin glue, and was 48.4% in the resident bone; this difference was not statistically significant. Conclusion: The present study demonstrates that vertical alveolar ridge augmentation using autogenous bone grafts and platelet-enriched fibrin glue with simultaneous implant placement might effectively increase vertical alveolar ridge height and allow for an acceptable level of osseointegration. 

# Treatment of experimental peri-implantitis using autogenous bone grafts and platelet-enriched fibrin glue in dogs.

Authors: You T.-M., Choi B.-H., Zhu S.-J., Jung J.-H., Lee S.-H., Huh J.-Y., Lee H.-J., Li J.

Publication Date: 2007

## Abstract:

Objective: The purpose of this study was to evaluate the effects of autogenous bone grafts and platelet-enriched fibrin glue in the treatment of peri-implantitis. Study design: Thirty-six screw-type commercially pure titanium implants with rough acid-etched surfaces were inserted into 6 mongrel dogs 3 months after extraction of mandibular premolars. After 3 months of healing, peri-implantitis was induced by placing gauze and wire around the implants. Once peri-implantitis was created, surgical treatments involving a combination of autogenous bone grafts and platelet-enriched fibrin glue, autogenous bone grafts alone, or a conventional flap procedure only (control) were carried out. Six months later, biopsies of the implant sites were taken and prepared for ground sectioning and analysis. Results: The amount of reosseointegration was significantly higher in peri-implantitis defects treated with combined autogenous bone grafts and platelet-enriched fibrin glue as compared with the other 2 treatment procedures. A mean bone-to-implant contact of 50.1% was obtained in the peri-implantitis lesions treated with combined autogenous bone grafts and platelet-enriched fibrin glue. The corresponding values for the autogenous bone grafts and control groups were 19.3% and 6.5%, respectively. Conclusion: The present study demonstrates that surgical treatment involving the combined use of autogenous bone grafts and platelet-enriched fibrin glue might effectively promote reosseointegration in lesions resulting from peri-implantitis. 

# Autologous platelet gel and fibrin sealant enhance the efficacy of total knee arthroplasty: Improved range of motion, decreased length of stay and a reduced incidence of arthrofibrosis.

Authors: Everts P.A.M., Devilee R.J.J., Oosterbos C.J.M., Mahoney C.B., Schattenkerk M.E., Knape J.T.A., Van Zundert A.

Publication Date: 2007

## Abstract:

In this study we describe the potential role of autologous platelet gel and fibrin sealant in unilateral total knee arthroplasty to improve the postoperative range of motion and to reduce the incidence of arthrofibrosis. Total knee arthroplasty is often associated with a considerable amount of post-operative blood loss. Persistent limited motion directly after surgery may ultimately result in arthrofibrosis. To counteract these effects we investigated whether the use of autologous derived platelet gel and fibrin sealant would reduce postoperative blood loss, decrease the impaired range of motion and the incidence of arthrofibrosis. All patients were consecutively operated and assigned to the study or control groups. Study group patients (n = 85) were treated with the application of autologous platelet gel and fibrin sealant at the end of surgery. Eighty patients were operated without the use of platelet gel and fibrin sealant, and served as the control group. The postoperative hemoglobin decrease, range of motion and length of hospitalization were recorded. During a 5-month postoperative period patients were followed to observe the incidence of arthrofibrosis. In patients in the treatment group the hemoglobin concentration in blood decreased significantly less when compared to the control group. They also showed a superior postoperative range of motion when compared to those of the control group ($P < 0.001$). The incidence of arthrofibrosis and subsequent forced manipulation was significantly less ($P < 0.001$) in patients managed with platelet gel and fibrin sealant. We conclude that peri-operatively applied platelet gel and fibrin sealant may

improve the range of motion after total knee arthroplasty, decreases the length of stay and may reduce the incidence of arthrofibrosis. 

# Maxillary sinus floor augmentation using autogenous bone grafts and platelet-enriched fibrin glue with simultaneous implant placement.

Authors: Lee H.-J., Choi B.-H., Jung J.-H., Zhu S.-J., Lee S.-H., Huh J.-Y., You T.-M., Li J.

Publication Date: 2007

## Abstract:

Objective: The aim of this study was to evaluate the use of autogenous bone in combination with platelet-enriched fibrin glue as a grafting material for maxillary sinus augmentation with simultaneous implant placement in dogs. Study design: The mucous membranes of 12 sinuses in 6 dogs were elevated bilaterally. In the right sinus, autogenous bone mixed with platelet-enriched fibrin glue was grafted into the space between the membrane and the sinus wall. In the left sinus, autogenous bone alone was grafted as a control. At the same time, 2 dental implants were inserted into the grafting material through the maxillary sinus floor. The animals were killed 6 months after surgery. Results: The mean bone-implant contact was 40.5% on the fibrin glue side and 32.3% on the control side ($P < .05$). The mean height of newly formed bone in the augmented area was 12.2 mm on the fibrin glue side and 10.7 mm on the control side ($P < .05$). Conclusion: The results indicate that the use of autogenous bone mixed with platelet-enriched fibrin glue can achieve results superior to those for grafts of autogenous bone alone. The specific improvements of this technique include enhanced osseointegration of dental implants and increased height of new bone. 

# A comparative histologic analysis of tissue-engineered bone using platelet-rich plasma and platelet-enriched fibrin glue.

Authors: Zhu S.-J., Choi B.-H., Jung J.-H., Lee S.-H., Huh J.-Y., You T.-M., Lee H.-J., Li J.

Publication Date: 2006

## Abstract:

Objective: The aim of this study was to compare the effects of platelet-rich plasma (PRP) and platelet-enriched fibrin glue on bone formation in bone tissue engineering. Study design: PRP was mixed with bone marrow mesenchymal stem cells and bone morphogenetic protein-2 (BMP-2), and the composites were injected into the subcutaneous space on the dorsum of nude mice. On the contralateral side of the dorsum, platelet-enriched fibrin glue/bone marrow mesenchymal stem cells/BMP-2 composites were injected. Bone formation was evaluated after 12 weeks. Results: The volumes of subcutaneous nodules formed in nude mice were 55 +/- 18 muL at the PRP/bone marrow mesenchymal stem cells/BMP-2 sites and 135 +/- 27 muL at the platelet-enriched fibrin glue/bone marrow mesenchymal stem cells/BMP-2 sites. Histomorphometric analysis demonstrated that the nodules contained 14.9 +/- 4.1% newly formed bone when using PRP and 19.8 +/- 3.6% newly formed bone when using platelet-enriched fibrin glue. Conclusion: The results indicated that the osteogenic characteristics of platelet-enriched fibrin glue are superior to PRP in bone tissue engineering. 

# Simultaneous implant placement and bone regeneration around dental implants using tissue-engineered bone with fibrin glue, mesenchymal stem cells and platelet-rich plasma.

Authors: Ito K., Yamada Y., Naiki T., Ueda M.

Publication Date: 2006

## Abstract:

This study was undertaken to evaluate the use of tissue-engineered bone as grafting material for alveolar augmentation with simultaneous implant placement. Twelve adult hybrid dogs were used in this study. One month after the extraction of teeth in the mandible region, bone defects on both sides of the mandible were induced using a trephine bar with a diameter of 10 mm. Dog mesenchymal stem cells (dMSCs) were obtained via iliac bone biopsy and cultured for 4 weeks before implantation. After installing the dental implants, the defects were simultaneously implanted with the following graft materials: (i) fibrin, (ii) dMSCs and fibrin (dMSCs/fibrin), (iii) dMSCs, platelet-rich plasma (PRP) and fibrin (dMSCs/PRP/fibrin) and (iv) control (defect only). The implants were assessed by histological and histomorphometric analysis, 2, 4 and 8 weeks after implantation. The implants exhibited varying degrees of bone-implant contact (BIC). The BIC was 17%, 19% and 29% (control), 20%, 22% and 25% (fibrin), 22%, 32% and 42% (dMSCs/fibrin) and 25%, 49% and 53% (dMSCs/PRP/fibrin) after 2, 4 and 8 weeks, respectively. This study suggests that tissue-engineered bone may be of sufficient quality for predictable enhancement of bone regeneration around dental implants when used simultaneous by with implant placement. 

# The effect of platelet-enriched fibrin glue on bone regeneration in autogenous bone grafts.

Authors: Huh J.-Y., Choi B.-H., Zhu S.-J., Jung J.-H., Kim B.-Y., Lee S.-H.

Publication Date: 2006

## Abstract:

Objective. The aim of this study was to examine the ability of platelet-enriched fibrin glue to enhance bone formation in critically sized defects in the dog mandible. Study design. Seven adult female mongrel dogs underwent continuity resections on both sides of the mandible; 1 defect was reconstructed with the original particulate bone mixed with platelet-enriched fibrin glue, and as a control the contralateral defect was reconstructed with the original particulate bone alone. Results. Biopsies after 6 weeks showed that the addition of platelet-enriched fibrin glue enhanced new bone formation in the autogenous bone grafts. Conclusion. Our data suggest that fibrin nets formed by fibrinogen, in combination with growth factors present in platelet-enriched fibrin glue, might effectively promote bone healing at bone graft sites. 

# Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part IV: Clinical effects on tissue healing.

Authors: Choukroun J., Diss A., Simonpieri A., Girard M.-O., Schoeffler C., Dohan S.L., Dohan A.J.J., Mouhyi J., Dohan D.M.

Publication Date: 2006

## Abstract:

Platelet-rich fibrin (PRF) belongs to a new generation of platelet concentrates, with simplified processing and without biochemical blood handling. In this fourth article, investigation is made into the previously evaluated biology of PRF with the first established clinical results, to determine the potential fields of application for this biomaterial. The reasoning is structured around 4 fundamental events of cicatrization, namely, angiogenesis, immune control, circulating stem cells trapping, and wound-covering epithelialization. All of the known clinical applications of PRF highlight an accelerated tissue cicatrization due to the development of effective neovascularization, accelerated wound closing with fast cicatricial tissue remodelling, and nearly total absence of infectious events. This initial research therefore makes it possible to plan several future PRF applications, including plastic and bone surgery, provided that the real effects are evaluated both impartially and rigorously.

# Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part I: Technological concepts and evolution.

Authors: Dohan D.M., Choukroun J., Diss A., Dohan S.L., Dohan A.J.J., Mouhyi J., Gogly B.

Publication Date: 2006

## Abstract:

Platelet-rich fibrin (PRF) belongs to a new generation of platelet concentrates geared to simplified preparation without biochemical blood handling. In this initial article, we describe the conceptual and technical evolution from fibrin glues to platelet concentrates. This retrospective analysis is necessary for the understanding of fibrin technologies and the evaluation of the biochemical properties of 3 generations of surgical additives, respectively fibrin adhesives, concentrated platelet-rich plasma (cPRP) and PRF. Indeed, the 3-dimensional fibrin architecture is deeply dependent on artificial clinical polymerization processes, such as massive bovine thrombin addition. Currently, the slow polymerization during PRF preparation seems to generate a fibrin network very similar to the natural one. Such a network leads to a more efficient cell migration and proliferation and thus cicatrization.

# Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part V: Histologic evaluations of PRF effects on bone allograft maturation in sinus lift.

Authors: Choukroun J., Diss A., Simonpieri A., Girard M.-O., Schoeffler C., Dohan S.L., Dohan A.J.J., Mouhyi J., Dohan D.M.

Publication Date: 2006

## Abstract:

Objective. Platelet-rich fibrin (PRF) belongs to a new generation of platelet concentrates, with simplified processing and without biochemical blood handling. The use of platelet gel to improve bone regeneration is a recent technique in implantology. However, the biologic properties and real effects of such products remain controversial. In this article, we therefore attempt to evaluate the potential of PRF in combination with freeze-dried bone allograft (FDBA) (Phoenix; TBF, France) to enhance bone regeneration in sinus floor elevation. Study design. Nine sinus floor augmentations were performed. In 6 sites, PRF was added to FDBA particles (test group), and in 3 sites FDBA without PRF was used (control group). Four months later for the test group and 8 months later for the control group, bone specimens were harvested from the augmented region during the implant insertion procedure. These specimens were treated for histologic analysis. Results. Histologic evaluations reveal the presence of residual bone surrounded by newly formed bone and connective tissue. After 4 months of healing time, histologic maturation of the test group appears to be identical to that of the control group after a period of 8 months. Moreover, the quantities of newly formed bone were equivalent between the 2 protocols. Conclusions. Sinus floor augmentation with FDBA and PRF leads to a reduction of healing time prior to implant placement. From a histologic point of view, this healing time could be reduced to 4 months, but large-scale studies are still necessary to validate these first results. 

# Assessment of the thrombogenic effect of fibrin sealant dressing in a vascular surgery model in rabbits.

Authors: Kheirabadi B.S., Sieber J., Holcomb J.B.

Publication Date: 2006

## Abstract:

This study's objective was to investigate the potential thrombogenic effects of thrombin-containing fibrin sealant dressings (FSD) in a vascular repair model. Oval-shaped pieces of the rabbit abdominal aorta and vena cava were excised, the injuries were repaired with FSD, and animals were allowed to recover. Thrombus formation was examined by (1) an infusion of indium-labeled platelets into the rabbits following FSD application and estimation of total number of platelets attached to the wounds at 2, 4, and 6 h later (short-term effect, n = 12); and by (2) morphological and histological examinations of the vessels and dressings on days 1, 3, and 7 after repair operation in another group of rabbits (long-term effect, n = 12). Application of FSD sealed the vascular injures and produced immediate hemostasis that was stable up to 1 week. The highest numbers of platelets (both native and labeled) adhered to the arterial and venous repair sites were 6.5 x 10<sup>6</sup> and 4.4 x 10<sup>7</sup>, respectively, 6 h after operation. The adhered platelets, however, did not form a visible and clinically significant thrombus. In long-term experiments, no evidence of thrombus was found in the lumens of the repaired vessels or on the dressings, and no microthrombi were detected histologically in other tissues at any time point. Although vena caval injuries showed signs of healing at day 7 postoperatively, the aortic wounds expanded progressively (pseudoaneurysm) and were prone to rupture at later times. Thus, direct exposure of FSD does not cause intravascular thrombosis or thrombotic events in rabbits. The dressing appears to be safe and effective for short-term repair of vascular injuries. It may also allow healing of minor venous defects, but cannot replace conventional surgical techniques (suturing) for permanent repair of arterial

damages.

# Prevention of bleeding after islet transplantation: Lessons learned from a multivariate analysis of 132 cases at a single institution.

Authors: Villiger P., Ryan E.A., Owen R., O'Kelly K., Oberholzer J., Saif F.A., Kin T., Wang H., Larsen I., Blitz S.L., Menon V., Senior P., Bigam D.L., Paty B., Kneteman N.M., Lakey J.R.T., Shapiro A.M.J.

Publication Date: 2005

## Abstract:

Islet transplantation is being offered increasingly for selected patients with unstable type 1 diabetes. Percutaneous transhepatic portal access avoids a need for surgery, but is associated with potential risk of bleeding. Between 1999 and 2005, we performed 132 percutaneous transhepatic islet transplants in 67 patients. We encountered bleeding in 18/132 cases (13.6%). In univariate analysis, the risk of bleeding in the absence of effective track ablation was associated with an increasing number of procedures (2nd and 3rd procedures with an odds ratio (OR) of 9.5 and 20.9, respectively), platelets count <150 000 (OR 4.4), elevated portal pressure (OR 1.1 per mm Hg rise), heparin dose >=45 U/kg (OR 9.8) and pre-transplant aspirin (81 mg per day) (OR 2.6, p = 0.05). A multivariate analysis further confirmed the cumulative transplant procedure number (p < 0.001) and heparin dose >=45 U/kg (p = 0.02) as independent risk factors for bleeding. Effective mechanical sealing of the intrahepatic portal catheter tract with thrombostatic coils and tissue fibrin glue completely prevented bleeding in all subsequent procedures (n = 26, p = 0.02). We conclude that bleeding after percutaneous islet implantation is an avoidable complication provided the intraparenchymal liver tract is sealed effectively. 

# Autologous fibrin glue with growth factors in reconstructive maxillofacial surgery.

Authors: Thorn J.J., Sorensen H., Weis-Fogh U., Andersen M.

Publication Date: 2004

## Abstract:

The aim of this paper was to describe a method for the preparation of autologous fibrin glue with platelet growth factors and to report its use with particulate cancellous bone in reconstructive maxillofacial surgery. The fibrin glue is a two-component glue, where the one component is a concentrated fibrinogen solution with platelet growth factors and the other component is a thrombin solution. Both components were produced from the patients own blood, thus making the glue entirely autologous. The glue was prepared from platelet rich plasma separated from 200 ml of the patient's blood prior to the operation. The fibrinogen in the glue was precipitated from the platelet rich plasma by ethanol precipitation at low temperature and separated together with the platelets by centrifugation. Raising the temperature to 37degreeC redissolved the precipitate. The thrombin solution in the glue was produced from prothrombin precipitated from 10 ml of the platelet rich plasma by lowering the pH and the ionic strength. The precipitate was separated by centrifugation and dissolved in a calcium ion solution. Increasing the pH to neutral value induced activation to thrombin. Preparation of the fibrin glue was performed in the blood bank within 60 to 90 min with the use of standard equipment. The outcome from 200 ml of blood was approximately 8 ml of fibrin glue: 6 ml fibrinogen to be coagulated with 2 ml of thrombin. The glue had a fibrinogen concentration of approximately 12 times the value in platelet rich plasma and the concentration of growth factors was approximately eight times the value in platelet rich plasma. We have used this glue successfully with particulate bone grafts for reconstructive purposes within the oral and maxillofacial field. It might as well be applied to other surgical areas. Whenever larger amount of the glue will be needed, a whole

unit of blood may be taken from the patient, and the red cells re-transfused to the patient during or after the operation.

# Perivenous application of fibrin glue reduces early injury of the human saphenous vein graft wall in an ex vivo model [3] (multiple letters).

Authors: Wilhelmi M., Stooker W., Niessen H.W.M.

Publication Date: 2002

## Abstract:

Not Available

# Usefulness of fibrin sealant (TS-DUO) in cardiovascular surgery: Multi- institutional clinical study. [Japanese]

Authors: Matsuda H.

Publication Date: 2000

## Abstract:

Not Available

# Effects of fibrin glue and growth factors released from platelets on abdominal hernia repair with a resorbable PGA mesh: Experimental study.

Authors: Zieren J., Castenholz E., Baumgart E., Muller J.M.

Publication Date: 1999

## Abstract:

Introduction. The purpose of this study was to investigate if the strength and quality of an abdominal wall repair with a resorbable PGA (polyglycolic acid) mesh can be improved by fibrin glue or releasates from platelets. Materials and methods. An abdominal wall defect in the rat was repaired using a PGA mesh in a sublay technique (CG) alone and either with additional fibrin glue (FG) or with platelet releasates (REL). Endpoints were clinical herniation pressure and hydroxyproline concentration (HP) as well as number of fibroblasts and collagen fibers at 7, 14, and 90 days after implantation. Results. In both experimental groups (REL and FG) higher herniation pressures, hydroxyproline contents, and number of fibroblasts/collagen fibers were found at all times of measurement compared to the CG. The PGA mesh alone showed a significant lack of stability after 14 days which can be compensated for by the investigated components. Significant differences ($P < 0.05$) were observed regarding the herniation pressure (REL vs CG at 7 and 14 days; FG vs CG at 14 days) and the number of collagen fibers (REL vs CG at 14 days). Conclusions. These results suggest that the quality of a PGA mesh repair can be improved by application of fibrin glue or platelet releasates in the described experimental setting.

# Comparative study of different biological glues in an experimental model of surgical bleeding in anesthetized rats: Platelet-rich and -poor plasma- based glue with and without aprotinin versus commercial fibrinogen-based glue.

Authors: Sirieix D., Chemla E., Castier Y., Massonnet-Castel S., Fabiani J.-N., Baron J.-F.

Publication Date: 1998

## Abstract:

The use of fibrin glue in cardiovascular surgery has been associated with decreased operative time, effective control of localized bleeding, and reduced postoperative blood loss. All preparations of fibrin glue mimic the final common pathway of the coagulation cascade in which fibrinogen is converted to fibrin in the presence of thrombin and calcium. The goal of the study was to compare five different types of fibrin glue, with or without aprotinin, on a surgical bleeding model in the rat. In 70 anesthetized Wistar rats, after laparotomy, a 3 cm liver incision was performed. After randomization, seven groups were studied. In the first group, Biocol was used as a pinpoint application to the bleeding site. Four groups received a fibrin glue obtained from a single human donor plasma using Cell Saver V (Haemonetics). The sealant was applied as a two-component system. The first component of the glue was either platelet-rich-plasma (PRP) or platelet-poor-plasma (PPP). The second component consisted of a mixture of 0.5 ml CaCl 10% with 1000 U of human thrombin, with or without 400KUI of aprotinin (AP). The last two groups, control and aprotinin were treated using saline solution or topical aprotinin respectively. Hemoglobin and hematocrit were measured before surgery and 30 min after application of the glue. The decrease in hemoglobin (Hb) and hematocrit (Hct) was the primary efficacy variable. Before surgery, there was no difference regarding Hb and Hct values between groups. Thirty min after the application of the glue, the decrease in hemoglobin expressed as percent of the control values is only significantly

lower in the Biocol group when compared to control. No significant difference was observed with the other groups in comparison to control. The commercial fibrin glue (Biocol) is more efficient than other preparations. This efficacy is likely due to a higher fibrinogen concentration.

# Platelet deposition on ePTFE grafts coated with fibrin glue with or without FGF-1 and heparin.

Authors: Zarge J.I., Gosselin C., Huang P., Greisler H.P.

Publication Date: 1997

## Abstract:

Introduction. The disappointing long-term patency of small-caliber prosthetic grafts may be due in part to early thromhogenicity of the prosthetic surface. We previously reported that the coating of expanded polytetrafluoroethylene (ePTFE) with fibrin glue (FG) containing fibroblast growth factor type 1 (FGF-1) and heparin accelerated spontaneous endothelial coverage of ePTFE grafts in an animal model; however, FG's effect on platelets remains unclear. This study was done to evaluate platelet deposition onto FG/FGF-1/heparin-coated vs FG-coated vs whole-blood- preclotted ePTFE surfaces. Methods. Twelve 5-cm ePTFE grafts were treated either with FG (thrombin, 0.32 U/ml, and fibrinogen, 32.1 mg/ml, n = 8) or with FG containing FGF-1 (11 ng/ml) plus heparin (250U/ml, n = 4). Twelve control ePTFE grafts were preclotted with canine (n = 8) or human (n = 4) whole blood. These treated grafts were placed onto a loop pulsatile perfusion system in pairs (preclotted with either FG or FG/FGF-1/heparin) and perfused with a M-199/10% FBS/<sup>111</sup>indium-labeled platelet suspension. After 60 min the grafts were gamma counted and CPM/mm<sup>2</sup> were determined. Results. In both trials, the preclotted ePTFE grafts demonstrated similarly increased platelet deposition when compared to grafts treated with FG/FGF-1/heparin or FG alone ($P < 0.001$ for each). Conclusion. The decrease in platelet deposition on the FG/FGF-1/heparin-coated grafts vs preclotted grafts is not due to heparin and is not specific to canine or human platelets. FG-coated grafts may induce a decrease in early graft thrombogenicity when compared to whole blood preclotting.

# Platelet gel: An autologous alternative to fibrin glue with applications in oral and maxillofacial surgery.

Authors: Whitman D.H., Berry R.L., Green D.M.

Publication Date: 1997

## Abstract:

The preparation and use of platelet gel, an autologous formulation of fibrin glue, are described. The unique features of this biologic sealant are that it is derived from autologous blood collected in the immediate preoperative period by the anesthesiologist, it contains a high concentration of platelets, and it can be used in patients who are not candidates for blood bank donation. Platelet gel has been used successfully in the area of reconstructive oral and maxillofacial surgery in conjunction with ablative surgery of the maxillofacial region, mandibular reconstruction, surgical repair of alveolar clefts and associated oral-antral/oral-nasal fistulas, and adjunctive procedures related to the placement of osseointegrated implants.

# Fibrin glue containing fibroblast growth factor type 1 and heparin decreases platelet deposition.

Authors: Zarge J.I., Husak V., Huang P., Greisler H.P.

Publication Date: 1997

## Abstract:

BACKGROUND: The early success rates of endarterectomy and angioplasty are influenced by the thrombogenicity of the deendothelialized surface. We previously reported decreased platelet deposition after 30 and 120 minutes and after 28 days on expanded polytetrafluoroethylene (ePTFE) grafts coated with fibrin glue (FG) containing fibroblast growth factor type 1 (FGF-1) and heparin in canine aortoiliac bypass grafts when compared with control uncoated grafts. The FG/FGF-1/heparin coating has been shown to enhance spontaneous endothelialization at 28 days in canine ePTFE bypass grafts. The current study evaluates the thrombogenicity of this FG/FGF-1/heparin suspension applied to a balloon de-endothelialization model of endarterectomy in canine carotid arteries. METHODS: Nine dogs underwent bilateral, deendothelialization balloon injury to 6-cm segments of their carotid arteries. Fibrin glue (fibrinogen 32.1 mg/mL + thrombin 0.32 U/mL) containing FGF-1 (11 ng/mL) and heparin (250 U/mL) was applied to the luminal surface of one carotid artery in each dog. Both femoral arteries were circumferentially dissected but not balloon injured; one femoral artery was clamped for the same period as the carotid arteries. In the 6 acute dogs, 10 minutes prior to the restitution of flow in both carotid arteries and one femoral artery, 4 to 8 x 10<sup>9</sup> <sup>111</sup>In-labelled autologous platelets were injected intravenously. Four-cm segments of both carotid and femoral arteries were excised after 15 or 120 minutes of circulation (n = 3/time/artery, 24 arteries). In the 3 chronic dogs, the radiolabelled platelets were injected 30 days after carotid injury. The carotid and femoral vessels were then excised after 120 minutes of perfusion. Radioactive platelet deposition was quantitated by gamma counting.

RESULTS: After 2 hours, the injured carotid arteries demonstrated significantly more platelet deposition than either uninjured femoral artery controls ($P < 0.001$). There was also a significant 45.2% decrease ($P = 0.008$) in platelet deposition on the balloon injured carotid arteries treated with FG/FGF-1/heparin when compared with balloon injured carotid arteries alone. At 30 days there was an insignificant trend toward decreased thrombogenicity in the FG/FGF-1/heparin treated injured carotids. CONCLUSION: Surface coating with FG/FGF-1/heparin significantly decreases platelet deposition on balloon injured canine carotid arteries after 2 hours of perfusion and may be clinically applicable in endarterectomy and angioplasty procedures. The long- term induction of reendothelialization of arterial surfaces by this technique is under investigation.

# In vitro-lined endothelium: Initial integrity and ultrastructural events.

Authors: Zilla P., Preiss P., Groscurth P., Rosemeier F., Deutsch M., Odell J., Heidinger C., Fasol R., Von Oppell U.

Publication Date: 1994

## Abstract:

Background. The early fate of in vitro-endothelialized prosthetic vascular grafts was assessed in the nonhuman primate. Methods. Each of 17 male chacma baboons received a control and a confluently endothelialized 4 mm polytetrafluoroethylene graft in femoro-femoral positions (8.2 +/- 0.8 cm). All experimental grafts were precoated with fibrinolytically inhibited fibrin glue and lined with cultured autologous endothelial cells (EC) from the external jugular vein. The average time period needed to obtain first- passage mass-cultures sufficient for preconfluent graft endothelialization was 19.8 +/- 5.2 days. Before implantation in vitro-lined grafts were kept in culture for another 16.1 +/- 4.3 days to achieve complete confluence and maturation of the EC cytoskeleton. Results. After 9 days of implantation, endothelial-lined grafts still showed a confluent endothelium that was free of any fibrin deposits. However, the EC density was significantly lower than at implantation (39.7 +/- 7.6 x 10<sup>3</sup> versus 59.9 +/- 8.5 x 10<sup>3</sup> EC/cm<sup>2</sup>; $p < 0.05$), and occasional 10-mum-wide intercellular gaps with adherent platelets and leukocytes were visible. Transmission electron microscopy showed leukocytes and cell debris in the underlying fibrin glue. After 4 weeks of implantation, the endothelium of experimental prostheses had regained a high cell density (72.7 +/- 10.5 x 10<sup>3</sup> EC/cm<sup>2</sup>) with a mature and well-differentiated morphologic appearance. At both observation periods, the surface of control grafts showed a wide range from fibrin deposits to an amorphous protein coverage containing spread platelets. Conclusions. The endothelium of in vitro-endothelialized vascular prostheses remains confluent after implantation and is nonthrombogenic in spite of a moderate initial cell loss.

# Inhibition of intra-abdominal adhesions: Fibrin glue in a long term model.

Authors: Sheppard B.B., De Virgilio C., Bleiweis M., Milliken J.C., Robertson J.M.

Publication Date: 1993

## Abstract:

Fibrin glue is being used more frequently to assist in the control of surgical bleeding in the abdominal and thoracic cavities. Prior investigation at this institution has indicated that fibrin glue actually inhibits adhesion formation in the peritoneal cavity of rats up to the first week postoperatively. To ascertain whether this protective effect is borne out in the long term, a randomized study was performed in 42 rats. As in the initial study, bilateral circular peritoneal-muscular defects were created to induce adhesion formation. The right-sided defects were closed linearly with interrupted sutures, thus closing the peritoneum, and the left-sided defects were closed with a continuous suture placed circumferentially, leaving the peritoneal defect open. The rats were randomized to two groups. In 21 animals, the abdomen was closed with no further treatment. In the other 21 animals the defects were covered with fibrin glue made from 0.2 mL of human fibrinogen (31.5 g/L) from cryoprecipitate and 0.2 mL of bovine thrombin and calcium. All rats were killed at 30 days, and adhesions were graded on a scale of 0 to 4 by a blinded observer. In the control group, 15 of 21 rats had high grade adhesions to the closed defect compared with 3 of 21 in the experimental (fibrin glue) group (P = 0.0003). For the left-sided lesions, 16 of 21 animals in the control group had high grade adhesions compared with 2 of 21 animals in the experimental group (P = 0.0004). In addition, the liver was firmly adhesed to 10 of the 42 defects created in the control models compared with only 3 of the 42 defects in the experimental group (P = 0.035). We conclude that fibrin glue serves as a biological dressing that protects against adhesion formation in the abdomen during the initial healing process and that through this inhibition, there is a marked

decrease in the amount of adhesions, even at long term follow-up.

# Use of fibrin glue for partial nephrectomy.

Authors: Scott R., Meddings R.N., Buckley J.F., Johnson D.E.

Publication Date: 1992

## Abstract:

Not Available

# Autologous fibrin glue from intraoperatively collected platelet-rich plasma.

Authors: Oz M.C., Jeevanandam V., Smith C.R., Williams M.R., Kaynar A.M., Frank R.A., Mosca R., Reiss R.F., Rose E.A.

Publication Date: 1992

## Abstract:

A simple and inexpensive means of creating autologous fibrin glue is described that avoids the potential disadvantages of conventionally obtained material. This improvement may allow more widespread use of fibrin glue for operative bleeding.

# The use of autologous platelet and plasma products in salvage neck dissections: a prospective clinical study evaluating early and late wound healing.

Authors: Yoo J., Chandarana S., Fung K., Franklin J.H., Nichols A.C., Doyle P.C.

Publication Date: 2012

## Abstract:

To evaluate the effect of autologous platelet and plasma adhesives (APA) on postoperative drainage and soft-tissue fibrosis following neck dissections. This was a blinded comparative prospective cohort study done as two parts: part one evaluated early post-surgical outcomes and part two evaluated late tissue fibrosis. Salvage neck dissections were stratified into two groups based on severity of prior treatment. High risk patients were defined as those who had previously undergone chemoradiation therapy and autologous platelet adhesives were administered to the surgical wound intraoperatively. The low risk group consisted of patients undergoing salvage neck dissections following radiation only and acted as controls. Part one evaluated postsurgical wound drainage as the primary outcome as well as length of hospital stay and complications. Part two evaluated late postoperative tissue fibrosis by comparing neck skin using the Cutometer. R2 and F0 were the specific Cutometer parameters for quantifying the viscoelastic properties of the skin. Postoperative wound drainage was significantly less (253.7 vs. 345.8) in the autologous platelet adhesive group as compared to the control group (p less than 0.03). Length of stay in the APA group versus the control group was 3.13 and 3.86 days respectively (p less than 0.004). Both R2 and F0 measurements showed improved viscoelastic properties of the skin in the APA group (R2 p less than 0.05, F0 p less than 0.05). APA application following salvage neck dissections may reduce early postperative wound drainage and improve long-term skin quality.

# Life-threatening pleural hemorrhage following intrapleural enzyme therapy and successful treatment with fibrin-thrombin sealant pleurodesis: A case report.

Authors: Vun S.V., Lance D.G.

Publication Date: 2015

## Abstract:

Introduction: Intrapleural fibrinolytic enzyme therapy is a potentially surgery-sparing treatment for poorly resolving parapneumonic effusion and empyema. It is safe in the majority of patients, however the most significant risk associated with this treatment is severe bleeding secondary to pleural hemorrhage. Contraindications for intrapleural enzyme therapy are not widely agreed upon and little is known about how to treat this difficult and potentially lethal hemorrhagic complication. Case presentation: An independent 82-year-old Caucasian man presented to hospital with an empyema complicating community-acquired pneumonia and coincidental pulmonary embolus. He was initially commenced on intravenous antibiotics, pleural drainage and anticoagulation, however failed to improve significantly and was commenced on intrapleural fibrinolytic enzyme therapy. Shortly after, he suffered severe pleural hemorrhage that was uncontrollable despite emergency thoracotomy and washout. Subsequent hemostasis was achieved after re-exploration and application of topical fibrin-thrombin sealant spray. The patient survived and was discharged home. Conclusions: Intrapleural enzyme therapy can be effective in loculated parapneumonic effusion and empyema, but massive pleural hemorrhage can complicate its use. Pleural hemorrhage appears to be associated with anticoagulation or coagulopathy, and can be difficult to manage. This case adds to the body of data on bleeding complications following intrapleural enzyme therapy, and to the best of our knowledge is the first report of fibrin-thrombin sealant use in this setting.