The Use of Autologous Platelet-Rich Plasma (Platelet Gel) and Autologous Platelet-Poor Plasma (Fibrin Glue) in Cosmetic Surgery

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The purpose of this study was to evaluate a new technique of harvesting and preparing autologous platelet gel and autologous fibrin glue (body glue) and to evaluate their effectiveness in stopping capillary bleeding in the surgical flaps of patients undergoing cosmetic surgery. A convenience sample of 20 patients ranging from 25 to 76 years of age undergoing cosmetic surgery involving the creation of a surgical flap were included in the study. The types of surgical procedures included face lifts, breast augmentations, breast reductions, and neck lifts. Platelet-poor and platelet-rich plasma were prepared during the procedure from autologous blood using a compact, tabletop, automated autologous platelet concentrate system (SmartPReP, Harvest Autologous Hemobiologics, Norwell, Mass.). The platelet-poor and platelet-rich plasma were combined with a thrombin-calcium chloride solution to produce autologous fibrin glue and autologous platelet gel, respectively. Capillary bed bleeding was present in all cases and effectively sealed within 3 minutes following the application of platelet gel and fibrin glue. The technique for making the solution and for evaluating its effectiveness in achieving and maintaining hemostasis during cosmetic surgical procedures is described. Autologous platelet gel and fibrin glue prepared by the automated concentrate system are compared with autotransfusor-prepared platelet gel and Tisseel (Baxter Healthcare Corp.), a commercially prepared fibrin sealant preparation. (*Plast. Reconstr. Surg.* 107: 229, 2001.)

There has been considerable interest for quite some time among plastic surgeons in some type of biologic glue that would help achieve hemostasis and seal wound surfaces. The potential advantages of the use of such substances include prevention of hematoma, reduction in surgical time, elimination of the need for drains, reduction of tension on flaps, and shorter recovery times.

Fibrin glue was originally described in 1970 and is formed by polymerizing fibrinogen with thrombin and calcium.[1] It was originally prepared using donor plasma; however, because of the low concentration of fibrinogen in plasma, the stability and quality of the fibrin glue were low.[2] The use of cryoprecipitate based fibrin glue yielded far better results. Its use, however, has been limited by concern with regard to disease transmission.[3] More recently, commercially prepared fibrin sealant products, such as Tisseel (Baxter Healthcare Corp.), have become available. These products are heat-treated, greatly reducing, but not entirely eliminating, the risk of disease transmission. Autologous fibrin glue has been well established as an excellent hemostatic agent, but its use has been limited by the need for preoperative donation and high cost.

Most recently several new approaches have surfaced. They all are based on autologous whole blood obtained in the immediate preoperative period, which is then processed immediately into autologous concentrated platelet-rich plasma. This is accomplished by the use of differential centrifugation in a conventional autotransfusion machine. When this platelet-rich plasma is combined with thrombin and calcium chloride, platelet gel is created.[4–6] This product is a rich source of growth factors and has been found to be effective in accelerating significant tissue repair and regeneration.[6–9] A benefit of this platelet gel is that upon activation, platelets release several growth factors,

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including two of which are known to promote wound healing. These two factors are platelet-derived growth factor and transforming growth factor and are present in very high concentrations in platelet gel.[7–13]

Autotransfusion machines are usually not readily available to plastic surgeons who perform the vast bulk of their cosmetic surgery in either office-based surgical facilities or ambulatory surgical centers. Therefore, to be able to avail themselves of this modality, they need to have an autotransfusion machine with a technician to operate it come to their office. This obviously represents a significant additional expense and an inconvenience. A new tabletop system (SmartPReP Autologous Platelet Concentrate System, Harvest Autologous Hemobiologics, Norwell, Mass.) has recently been introduced; it is designed to be used intraoperatively for the simple and rapid preparation of platelet-rich and platelet-poor plasma from a relatively small sample of blood[14,15] (Fig. 1). Operating room personnel, without the need for an additional technician, can easily operate the system. It requires 90 to 180 cc of blood versus the 500 cc of blood used in most autotransfusion machines. The platelet-poor plasma has a relatively high concentration of fibrinogen and can be used to prepare autologous fibrin glue. The platelet-rich plasma, as mentioned above, is useful for its high levels of growth factors and can be used to prepare autologous platelet gel.

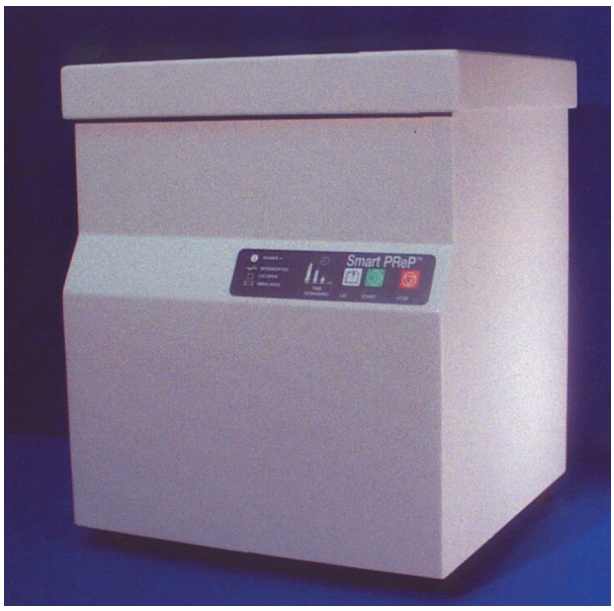

FIG. 1. The SmartPReP automated platelet concentrate system.

The purpose of this study was to evaluate the effectiveness of platelet-rich and platelet-poor plasma prepared with the SmartPReP system in achieving and maintaining hemostasis during cosmetic surgical procedures.

MATERIALS AND METHODS

Study Design

The Human Subjects Review Committee of the Institutional Review Board at Florida Atlantic University in Boca Raton, Florida, approved the study. Written informed consent assuring both anonymity and confidentiality was obtained from 20 patients scheduled to undergo a variety of cosmetic surgical procedures all involving the creation of surgical flaps. The intent of the study was to document the effectiveness of intraoperatively prepared autologous platelet gel and fibrin glue in minimizing the capillary bleeding which occurs within these flaps. Patients with any history of allergy to bovine products were excluded in that thrombin of bovine origin is used to prepare both products.

The following data were kept for each case: case number and date; type of surgical procedure; number of surgical flaps in the procedure; measured area for each flap; volume of platelet-poor plasma/calcium thrombin used in each flap; stop watch timed interval in seconds from spray to sealing of capillary bed in flap; and a timed, 3-minute observation of capillary bed to confirm cessation of bleeding. If bleeding occurred, the platelet-poor plasma solution would be reapplied and the area timed again.

Preparation of Fibrin Glue and Platelet Gel

Using the autologous platelet concentrate system, platelet-poor and platelet-rich plasma were prepared in the operating room from the patient's own blood. After the patient was placed on the operating room table and anesthesia had been induced, the anesthesiologist used two 60-cc syringes that had been prefilled by the circulating nurse with 5 cc of anticoagulant citrate dextrose in each syringe. The anesthesiologist then withdrew into each syringe 45 cc of the patient's blood from a venous puncture in the upper arm using a butterfly

catheter supplied in the kit. In more extensive surgical procedures, four syringes (180 cc) of blood were drawn. The blood must be drawn before the commencement of surgery, because surgery itself leads to platelet activation as well as activation of the coagulation system. These factors would interfere with the preparation of optimal products. The syringes were then handed to the circulating nurse and the anticoagulated whole blood was then injected into the double chambered processing vessels. The processing vessels were then placed in the concentrate system and the processing cycle initiated. The system automatically separates whole blood into (1) red blood cells, (2) platelet-poor plasma, and (3) platelet concentrate. When the 12-minute cycle was complete, the device shut off and the circulating nurse removed the double-chamber processing vessels. Red blood cells were observed in one chamber and 22 cc of platelet-poor plasma with a platelet concentrate button below it in the second chamber (Fig. 2).

The circulating nurse, using a long, blunt cannula supplied in the processing disposables kit, aspirated 15 cc of platelet-poor plasma into a 20cc syringe. This was done for all the processing vessels, yielding a total of 30 cc or 60 cc of plasma, depending on whether 90 cc or 180 cc of whole blood was processed. The circulating nurse transferred the total volume of plasma into a prelabeled sterile cup located on an instrument tray in the sterile field. The remaining product, approximately 7.5 cc of platelet-poor plasma and the platelet concen-

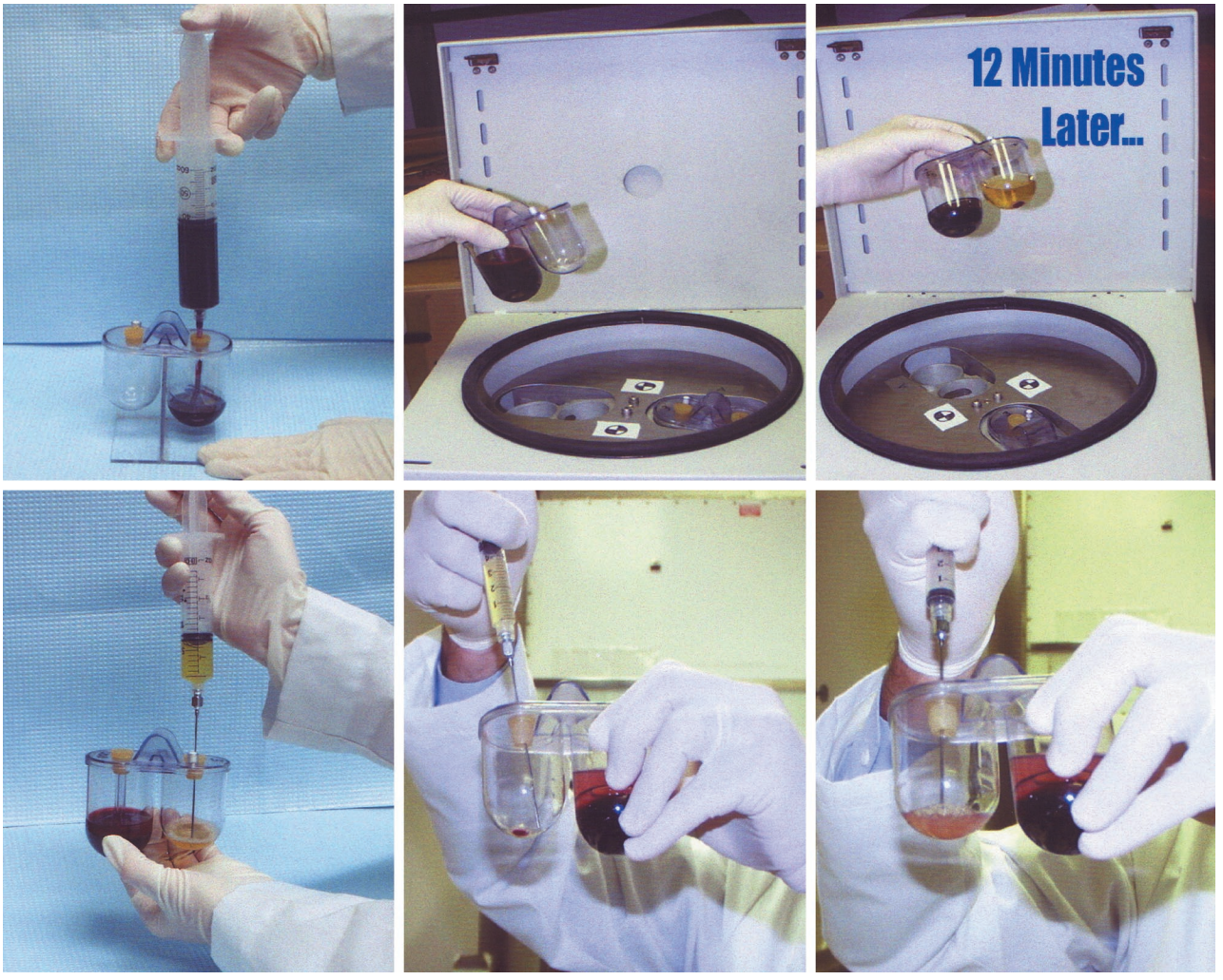

FIG. 2. (*Above, left*) Loading the processing vessel. (*Above, center*) Loading the processing vessel into the concentrate system. (*Above, right*) Removing the processing vessel from the concentrate system after a 12-minute cycle. (*Below, left*) Aspirating platelet-poor plasma from the processing vessel. (*Below, center*) Mixing platelet concentrate. (*Below, right*) Aspirating platelet-rich plasma.

trate button, was then mixed to yield platelet-rich plasma.

Next, the circulating nurse prepared a thrombin-calcium chloride solution using 5000 units of thrombin dissolved in 5 cc of 10% calcium chloride. The solution was then transferred by syringe into a sterile cup on the instrument tray in the sterile field. The platelet-poor plasma and calcium thrombin solution was then available for the scrub nurse to use in preparing autologous fibrin glue when needed during the procedure. The preparation of the fibrin glue requires a 10:1 ratio of platelet-poor plasma to thrombin-calcium chloride solution. The easiest method to deliver the plasma and thrombin product is by dual syringe with the platelet-poor plasma drawn into a 10-cc syringe and the thrombin-calcium solution into a 1-cc syringe. The two syringes are then connected to a dual spray applicator tip and then sprayed onto the surgical bed. The platelet-poor plasma and thrombin-calcium cannot be combined before being applied in that they gel almost instantaneously, and their application is very difficult once they have gelled. The dual syringe method allows both solutions to be mixed as they are administered into the surgical bed (Fig. 3). This same dual syringe method is also used for the application of autologous platelet gel, simply substituting platelet-rich plasma for platelet-poor plasma.

For each patient the type of surgical procedure, the average area of the capillary bed under the flap in each case, and the volume of platelet-poor and platelet-rich plasma prepared were recorded. Once adequate hemostasis had been obtained, and just before closure, each surgical bed was sprayed with platelet-poor plasma/calcium-thrombin. The area was observed to determine time required for a seal to form and all capillary bleeding to cease. After the bleeding was determined to have stopped, the area was observed for an additional 3 minutes before it was judged to be effectively sealed by the platelet-poor plasma/calcium thrombin solution. Just before closure, a layer of platelet gel was applied creating a "carpeted bed" effect (Fig. 4) so as to take advantage of the wound healing properties and the quicker healing time associated with the use of platelet gel. Using gentle pressure on the operative area, any surplus fibrin glue and platelet gel was pressed out. No drains were used in any of the patients.

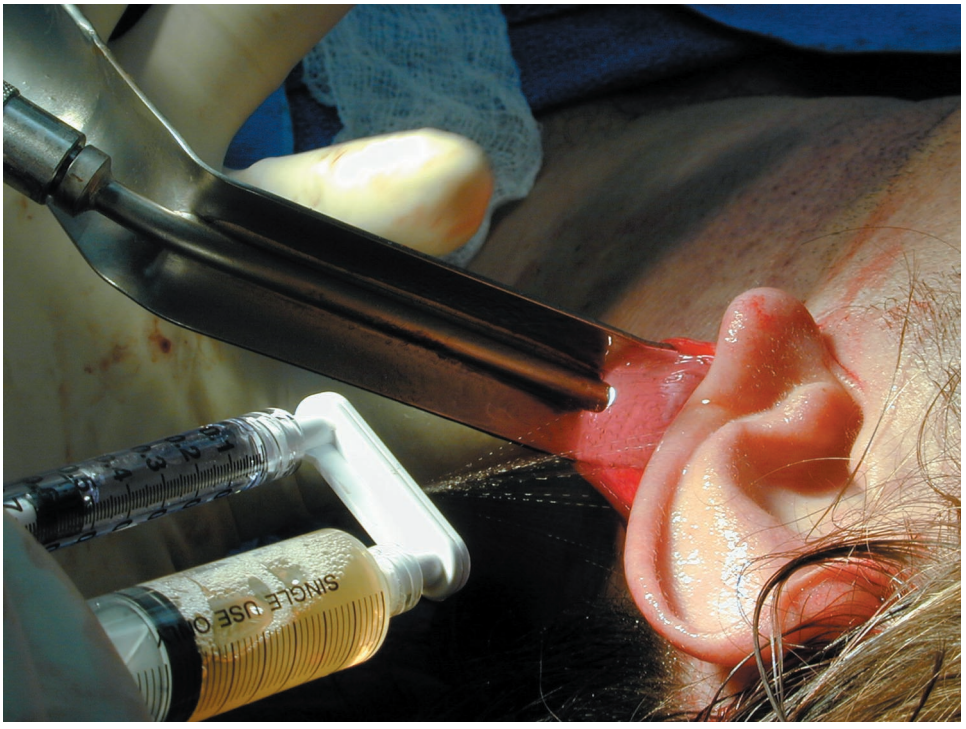

FIG. 3. Fibrin glue being applied to the surgical field by a dual syringe method.

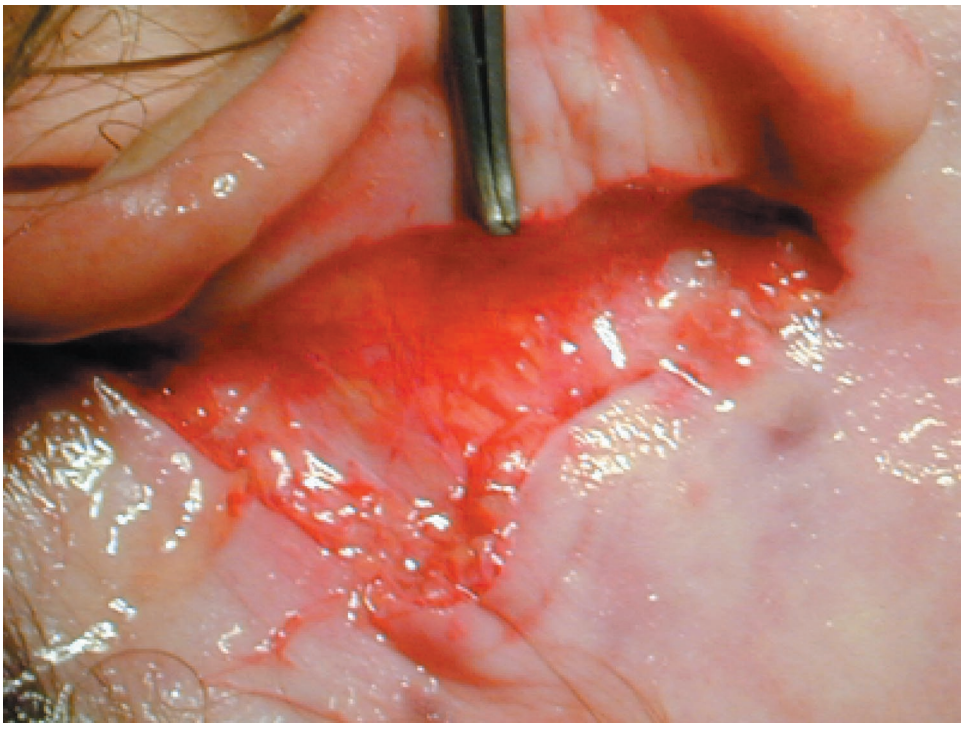

FIG. 4. Surgical field with a layer of platelet gel applied. Note the "carpeted bed" appearance.

RESULTS

A total of 20 patients (18 female and 2 male) ranging from 25 to 76 years of age were enrolled in the study. The procedures they underwent, the volume of blood withdrawn, and the volume of platelet-poor and platelet-rich plasma prepared are shown in Table I. The blood volume withdrawn was 90 cc in 10 of 20 cases and 180 cc in the remaining 10 cases. This blood volume yielded a volume of platelet-poor and platelet-rich plasma that ranged from 30 cc to 60 cc, respectively. For each patient an approximate area of the capillary bed under the skin flap was documented along with the volume of platelet-poor plasma/calcium thrombin solution dispensed over this area. Even after obtaining hemostasis by conventional means, all patients showed some evidence of oozing from the capillary beds on the surfaces below the skin flaps before the application of the autologous fibrin glue. The times to observed sealing by the application of the fibrin glue varied from 15 to 45 seconds. In no case did the application of fibrin glue and calcium thrombin fail to develop a seal and stop capillary bleeding. One patient who had undergone a face lift required the re-exploration for bleeding of one side immediately following closure of that side, which upon exploration was found to be caused by a bleeding vein.

DISCUSSION

This study demonstrated that the use of autologous fibrin glue and platelet gel (body glue) in cosmetic surgical procedures involving the creation of flaps, such as face lifts, reduction mammaplasties, abdominoplasties, resulted in many advantages. These included shorter operating times, the elimination of the need for drains, a reduction in the need for compressive dressings, a reduction in pain and postoperative swelling, and improved wound healing with a resultant shorter recovery time. Despite these numerous advantages, fibrin glue has been underutilized in the past because of fear of disease transmission with donor products and because of the lack of a simple, cost-effective method of preparing this product in a standardized fashion. An important consideration in cosmetic surgery is the occurrence of bleeding postoperatively once the vasoconstrictive effect of the epinephrine used in the local anesthetic solutions has worn

TABLE I
Breakdown of Procedures

Patient No.	Sex	Surgical Procedure	Amount of Blood Drawn (cc)	Volume of Platelet-Poor/Platelet-Rich Plasma Prepared	Coagulation Time (sec)
1	F	Mastopexy	90	23/7	45
2	F	Bilateral breast augmentation	90	23/7	40
3	F	Face and neck lift	180	45/15	30
4	F	Face and neck lift	180	45/15	45
5	F	Face, neck, and endoscopic forehead lift	180	45/15	15
6	F	Neck lift	90	23/7	15
7	F	Bilateral breast augmentation	90	23/7	45
8	M	Neck lift	90	23/7	45
9	F	Bilateral breast augmentation	90	23/7	45
10	F	Face and neck lift	180	45/15	45
11	F	Capsulotomy, capsulectomy, and exchange of implants	90	23/7	45
12	F	Face and neck lift	180	45/15	45
13	F	Face and neck lift	180	45/15	10
14	F	Face and neck lift	180	45/15	15
15	F	Neck lift	90	23/7	15
16	F	Face and neck lift	180	45/15	15
17	F	Face and neck lift	180	45/15	15
18	M	Neck lift	90	23/7	15
19	F	Neck lift	90	23/7	15
20	F	Face and neck lift	180	45/15	15

off. In addition, while operating in the vicinity of nerves, it is advantageous to minimize the use of electrocautery so as to minimize the chance of causing any damage to the adjacent nerves. The use of autologous fibrin glue and platelet gel allows the achievement of excellent stable hemostasis while addressing these two concerns.

Autologous fibrin glue mimics the last steps in the coagulation cascade with the conversion of fibrinogen to fibrin with the help of thrombin and calcium, helping cross-link the fibrin into a stable clot.[10] Therefore, autologous fibrin glue will help achieve hemostasis even in the presence of coagulation defects, inherited coagulation deficits, or coagulopathies. The tensile strength and adhesive properties of autologous fibrin glue are proportional to the concentration of fibrinogen. Although the fibrin glue sealant prepared in this study has only a moderate concentration of fibrinogen, it is quite effective, because high concentrations of fibrinogen are not required as the result is more of a sealant than a glue. In fact, preparations containing high concentrations of fibrinogen yield a more viscous product. However, the more dense fibrin clot may in fact interfere with wound healing by impeding access to platelets with their wound healing factors.[11]

The role of autologous fibrin glue is primarily to obtain hemostasis and "glue down" the flaps.[4] Autologous platelet gel, on the other hand, offers the significant additional hypothetical benefit of accelerated postoperative wound healing, which is bestowed by the presence of high concentrations of growth factors and cytokines present in platelets.[7–9,11] A complete list of these factors that are released by platelets is beyond the scope of this article. The most important of these factors are platelet-derived growth factor and transforming growth factor-β1. Both of these factors potentiate wound healing as they promote granulation tissue formation.[16] These factors working synergistically have been documented to increase the rate of collagen laydown, angiogenesis, fibroblast proliferation, extracellular matrix synthesis, and overall wound healing.

Plastic surgeons have been reluctant to adopt the use of fibrin glue into their practices largely because of the lack of FDA approval, the fear of disease transmission, the high cost of the product, and the withdrawal of 500 cc of blood. Autologous fibrin glue offered a significant step forward in that it eliminated the fear of disease transmission and it has FDA approval. Although autologous fibrin glue addressed the above concerns, it continued to be plagued by certain disadvantages including its high cost, the need for a relatively large piece of equipment (the plasma saver) and its accompanying technician, requiring a rather

TABLE II
Comparison of Products

	Autologous Platelet Gel and Fibrin Glue Prepared by Concentrate System	Autologous Platelet Gel Prepared by Autotransfusor	Tisseel Fibrin Sealant
Risk of disease transmission	None	None	Low
Platelet-associated growth factors	Present	Present	Absent
Fibrinogen concentration	Moderate	Moderate	High
Cost	~$350	~$500	~$850
Amount of blood necessary	90 to 180 cc	500 cc	0
Convenience/ease of use	Easy	Complex	Very easy

large amount of space (10 feet × 10 feet), and that it is usually contracted from an outside firm creating the potential for scheduling difficulties. These concerns have been addressed by the introduction of the autologous platelet concentrate system. This small, tabletop, automated machine requires only 2 feet × 2 feet of countertop space, requires only 90 to 180 cc of blood and can be operated by any member of the operating room staff with essentially the push of a button and no specialized training.

The relatively recent introduction into the U.S. marketplace of a commercially prepared fibrin sealant preparation (Tisseel, Baxter Healthcare Corp., Deerfield, Ill.) raises the possibility of having the convenience of an "off-the-shelf" product available for the production of fibrin glue. When comparing this product to the autologous fibrin glue and platelet gel produced by the concentrate system, a number of factors need to be taken into account.(Table II) Although the risk of disease transmission has been greatly reduced with this 'off the shelf' preparation, it has not been entirely eliminated. Secondly, the concentrate system, in addition to producing autologous fibrin glue, also produces autologous platelet gel, which might be the more important product of the two because of its platelet-associated growth factors contributing to improved wound healing and hemostasis. These platelet-associated growth factors are not present in Tisseel. Thirdly, as mentioned above, preparations with very high concentrations of fibrinogen, such as Tisseel, produce dense fibrin clots, which can in fact may interfere with wound healing by impeding access to platelets with their associated wound healing factors. By comparison, the concentration of fibrinogen in autologous fibrin glue prepared by the Smart-PReP system is more moderate. Lastly, the average cost to the surgeon of preparing fibrin glue and platelet gel using the autologous platelet concentrate system is approximately $350 to $400, depending on the volume of blood being processed, versus approximately $850 for 5 cc of Tisseel. Even when taking into account the initial capital cost of approximately $6000 for the purchase of the concentrate system, if one assumes two uses per week and a useful life expectancy for this device of only 2 years, the cost per procedure works out to only approximately $30 (this $30 is included in the above cost of $350 to $400). In our practice we do in fact use Tisseel, reserving its use for two sets of circumstances. The first situation in which we use it is when obtaining the blood necessary for the concentrate system is difficult because of poor venous access or other technical difficulties. The second situation is in patients in whom we unexpectedly decide that fibrin glue would be helpful once we have begun surgery, because for the preparation of platelet gel and fibrin glue, blood must be withdrawn before the initiation of surgery, as discussed above.

These 20 cosmetic surgery cases involving the creation of skin flaps demonstrate that autologous fibrin glue is effective in sealing capillary beds during the surgery and thereby easily controlling bleeding. The control of such bleeding improves the outcome of such surgery as it reduces the amount of postsurgical swelling. Additionally, there are cost benefits that can be achieved from the reduction or elimination in the use of drains and dressings, as well as decreased postoperative complications. The most common of these complications following cosmetic surgical procedures involving the creation of surgical flaps is hematoma formation, often requiring surgical re-exploration. Apart from the increased risk, inconvenience, and distress which it engenders to the patient, re-exploration is extremely costly to all parties involved. The use of autologous fibrin glue and platelet gel should reduce the incidence of this complication significantly, which in and of itself should lead to

significant cost savings. Furthermore, the improvement in wound healing can help lead to shorter recovery with earlier discharge for patients undergoing procedures on an inpatient basis. Based on the simplicity of the autologous platelet concentrate system, we have been able to incorporate the use of autologous fibrin glue and platelet get routinely in surgical procedures.

As we have gained experience with the use of autologous platelet gel, we have found it to be an extremely useful adjunct in a number of other procedures. When performing liposculpture, the addition of platelet gel to the fat can enhance the longevity of the fat when it is re-injected as a building material in various areas of the body. After laser resurfacing, we use it directly on the skin surface as a wound dressing. Based on the presence of growth factors in autologous platelet gel, we have found it to result in faster healing with much less redness. We believe that as our experience with this material continues to grow, we will find a number of additional applications where its use proves to be advantageous.

CONCLUSIONS

This new technique for the harvesting of autologous fibrin glue and autologous platelet gel, with their promise of decreased bleeding and improved wound healing combined with ease of use, moderate cost, and patient safety should pique the interest of plastic surgeons and help this technique spread to encompass a large number and variety of plastic surgical procedures. The risks are small and the potential benefits large. The technique offers immediate theoretical and practical benefits. It opens a new emerging field of "wound pharmacology"[17] and offers the exciting prospect of a revolutionary advance in plastic surgical ther-apeutics. This study has demonstrated that the use of autologous fibrin glue as a hemostatic agent and platelet gel as a tissue repair and regeneration agent has resulted in improved surgical outcomes.

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