Review: Fibrin Sealant: Clinical Use and the Development of the University of Virginia Tissue Adhesive Center

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Abstract. The utilization of fibrin sealants to augment hemostasis, seal tissues, and facilitate targeted delivery of drugs is increasing. In 1985, a hospital-based program was established to provide autologous and allogeneic cryoprecipitate that serves as a fibrin sealant when combined with bovine thrombin. To date, more than 4,000 patients have been treated with this product at our institution, with an efficacy rate greater than 90%. Collaboration among surgical services and the blood bank fostered multispecialty expertise with this product that led, in 1997, to the establishment of the University of Virginia Tissue Adhesive Center. The Tissue Adhesive Center is a multidisciplinary center whose physician director and nursing and administrative support staff facilitate basic research, laboratory investigation, and preclinical and clinical trials with collaborators throughout the university. The Tissue Adhesive Center also provides educational programs and clinical consultation, and tracks and participates in peer review of sealant use. The licensure of a commercially produced, virally inactivated, pooled-plasma fibrin sealant in May 1998 provided an alternative source of adhesive. Utilization of the commercial product surpassed use of the blood bank product in April 1999. At present, use of the commercial product is approximately 3 times that of the blood bank–produced sealant. This report reviews the clinical uses of fibrin sealant, its regulatory history, the production of fibrin sealants, the evolution of a blood bank fibrin sealant program, the development of the Tissue Adhesive Center, and the utilization of commercial and blood bank–produced sealant at our university hospital. (received 30 June 2000; accepted 15 September 2000)

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Introduction

Fibrin sealant tissue adhesives have become an important and versatile tool in the surgical armamentarium over the past 30 years, with applications ranging from improving hemostasis and sealing tissues to targeted delivery of drugs. Composed primarily of fibrinogen and thrombin, fibrin sealant acts by mimicking the final stage of the natural clotting mechanism to form a fibrin clot that is broken down by fibrinolysis and reabsorbed naturally over the course of several days. The process by which fibrinogen and thrombin combine in the presence of Factor XIII and calcium chloride to form a fibrin clot has been well described [1-3].

Fibrin sealant has three primary applications: It can be used as a hemostat, as a sealing agent, and as a carrier mechanism for delivering drugs and other bioactive agents (such as growth factors) to targeted sites in the body. Early experiments with fibrin as a hemostat date from the beginning of the twentieth century with Bergel’s use of fibrin powder in 1909 [4] and Grey’s [5] and Harvey’s [6] use of fibrin tampons and thin fibrin plaques a few years later. In the 1940s, Young and Medawar [7] reported the use of fibrinogen to repair severed nerves in animal models. However, it was Cronkite et al [8] and Tidrick et al [9] who, in 1944, first combined fibrinogen and thrombin to form fibrin sealant for anchoring skin grafts. These early forms of fibrin sealant lacked adhesive strength due to their low fibrinogen concentrations. It was not until the 1970s that interest was rekindled, owing to the implementation of industrial plasma fractionation

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methods that allowed the production of a more concentrated form of fibrinogen [10].

Fibrin sealant applications

Currently, fibrin sealant is used in virtually every surgical specialty [11]. The primary area of usage is cardiovascular surgery, where applications include sealing of complex suture lines, vascular conduits, cannulation sites, and vascular anastomoses [12,13]. Studies have documented fibrin sealant’s effectiveness in controlling diffuse mediastinal bleeding [14], stopping pericardial serous leakage [15], and achieving hemostasis along arterial suture lines [16,17]. Fibrin sealant has been used in cardiovascular surgery in conjunction with polytetrafluoroethylene patches [17], polytetrafluoroethylene bypass grafts [16], woven Dacron grafts [18], and pericardial patches [19]. In pulmonary thoracic surgery, fibrin sealant helps to seal air leaks [20] and close bronchopleural fistulas [21,22], as well as reinforce suture or staple lines after thoracotomy or lung resection [23]. One review of clinical studies of fibrin sealant in cardiac and thoracic surgery noted that, through 1995, none of the 24 published controlled clinical studies had demonstrated a deleterious effect from use of fibrin sealant, either in terms of efficacy inferior to controls or serious adverse events [24]. However, the potential for adverse reactions, such as coagulopathy associated with the bovine thrombin present in some noncommercial fibrin sealant formulations, suggests that fibrin sealant containing human rather than bovine thrombin may be preferable.

In neurosurgery, fibrin sealant has commonly been used as an adjunct to dural closures, to reduce postoperative cerebral spinal fluid leakage [25,26], and in the repair of dural defects [27]. Additional applications include microvascular decompression, laminectomy, tumor resection via craniotomy, myelomeningocele repair, rhizotomy, and arteriovenous malformation repair. In plastic surgery, fibrin sealant has been especially effective in controlling bleeding following burn debridement [28] and as an adjunct to maxillofacial [29] and head and neck surgery [25,30]. Used as an adjunct to mandibular reconstruction along with cancellous bone and marrow, fibrin sealant has been noted to accelerate revascularization and migration of fibroblasts, thereby stimulating healing and growth. Several articles attest to fibrin sealant’s efficacy in promoting skin graft adherence [31-33].

Fibrin sealant is effective in sealing dead spaces left after surgical excision (as in axillary dissection), where there is a potential for serous drainage leading to seroma formation [36], and has been shown to reduce seroma formation following radical neck dissection [34] or breast surgery with axillary dissection [35]. Otolaryngology, otology, and neurotology are other fields in which fibrin sealant has been widely used [25,37-39], with applications in sinus surgery [40], tonsillectomy [41,42], tympanoplasty [43], and, potentially, other forms of ear surgery [44-46].

In general surgery, fibrin sealant is used to achieve hemostasis on raw surfaces of the liver and in reconstruction of the spleen, especially following traumatic injury [47,48]. The planned introduction of a fibrin sealant bandage and dry fibrin sealant formulations may provide new treatment alternatives for trauma patients [49]. Fibrin sealant has proved valuable for sealing colon anastomoses (one of its current FDA-approved indications). There may be significant potential for reduced-suture and sutureless anastomosis using fibrin sealant [50]. There are other documented applications of fibrin sealant in orthopaedic, ophthalmologic, trauma, head and neck, gynecologic, urologic, gastrointestinal, and dental surgery [11].

Recent reviews have documented a wide variety of surgical settings in which fibrin sealant has proved valuable, such as promoting hemostasis in patients who have coagulation disorders [51] or are receiving anticoagulant therapy, or to promote the closing of rectovaginal, perirectal, and other fistulas [52]. The future of fibrin sealant extends beyond hemostasis and sealing. Its ability to act as an effective delivery medium for growth factors and antibiotics in order to promote healing is receiving growing attention [53-56]. Fibrin sealant may also prove to be an adjunct to minimally invasive surgery (eg, laparoscopic and endoscopic procedures) [57-59].

Regulatory History

Although commercial fibrin sealant made from pooled plasma–derived human fibrinogen and human thrombin has been available in Europe, Canada, and Japan for several years (since 1972 in Europe), the US
Food and Drug Administration (FDA) did not approve the commercial product for use in the USA until May 1998. Delay in availability of commercial fibrin sealant in the USA was largely due to concerns over possible viral disease transmission from blood-borne pathogens such as HIV, hepatitis B virus, and hepatitis C virus. In fact, approval for use of commercial fibrinogen derived from pooled plasma was withdrawn in the USA in 1978 due to concern over virus transmission [60].

Large-scale clinical trials that documented fibrin sealant’s efficacy and safety, and the advent of improved techniques for virus inactivation, such as nanofiltration and heat pasteurization, led the FDA to approve the clinical use of commercial fibrin sealant in May 1998. Currently, commercial fibrin sealant is approved for “on-label” use in the USA for only 3 procedures: as a hemostatic agent in cardiopulmonary bypass procedures, treating splenic injuries, and sealing anastomoses in closure of temporary colostomies. Currently, licensed commercial sealants contain fibrinogen and thrombin derived from pooled, virally inactivated human plasma. They also contain an antifibrinolytic agent, bovine aprotinin. Future generations of fibrin sealant are likely to be free of bovine products due to reported instances (albeit rare) of reactions to bovine aprotinin [61].

Commercial fibrin sealant has been used in >4 million procedures worldwide to date, with only one reported case of suspected viral disease transmission (human parvovirus transmission in Japan) [62]. As increasingly sensitive virus detection techniques become available [63], shortening or even closing the window for infectious donations, and as improved virus inactivation techniques are developed, such as solvent detergent cleansing [64], general acceptance of products derived from pooled plasma may grow. In fact, pooled, virus-inactivated blood products have been shown to be very safe [65]. Risk/benefit analyses of fibrin sealant usage should take into account the product’s potential to reduce exposures to more risky blood components. Furthermore, recombinant fibrinogen and thrombin are likely to become available, thereby eliminating the viral disease risk [66].

Non-Commercial Fibrin Sealant

Despite the lack of approved commercial fibrin sealant, surgeons in the USA explored applications of this adhesive throughout the 1980s and 1990s, using fibrin sealants produced locally from autologous or allogeneic single-donor blood. Even with the current availability of commercial fibrin sealant, some institutions, including the University of Virginia, continue to make their own fibrin sealant, particularly for autologous use, due to continued concerns over the cost, and, to a lesser extent, safety of commercial preparations. Numerous “recipes” for making concentrated fibrinogen from autologous blood donated pre-operatively, or fresh frozen plasma, have been described. The concentrated fibrinogen produced by these various methods, or from standard cryoprecipitate, is then combined with topical bovine thrombin, and occasionally an antifibrinolytic agent such as aprotinin, tranexamic acid, or epsilon aminocaproic acid to slow fibrinolysis of the fibrin clot [67]. Because thrombin concentration is directly related to the rate of polymerization of fibrin, studies have been conducted to determine the ideal ratios and concentrations of thrombin and fibrinogen [68,69]. It has been found that high concentrations of thrombin (2000 U/ml) in a 3:1 ratio result in very rapid polymerization of fibrin sealant [69].

Concerns about safety of bovine thrombin have been raised due to reports of adverse reactions, which include hypotension, anaphylactic shock, and coagulopathy [70]. About 10% of patients exposed to bovine thrombin develop antibodies, although only a small percentage of these patients have clinically significant complications due to these antibodies, which may be directed against both thrombin and other clotting factors, eg, Factor V [71]. Although infrequent, the occurrence of adverse reactions to bovine thrombin underscores the need for vigilance in the use of topical bovine thrombin and the importance of identifying patients with previous exposure to this product. Such patients appear 8-times more likely to develop antibodies than patients exposed for the first time [71]. While safety concerns have occasionally been raised about commercial fibrin sealant, due to its pooled-plasma origin, the fact that the commercial product contains human rather than bovine thrombin makes it relatively safer than blood-bank fibrin sealant for patients with previous exposure to bovine thrombin. However, as noted above, the licensed commercial preparations contain bovine aprotinin, which may produce adverse reactions in rare instances.
Preparing Non-Commercial Fibrin Sealant

When the fibrin sealant program at the University of Virginia (UVA) was begun in 1985, the standard method of preparing blood bank fibrin sealant, both in the USA and abroad, had been to combine fibrinogen-rich “cryoprecipitate” made from autologous or allogeneic single-donor units of plasma with topical bovine thrombin. The term cryoprecipitate is used loosely in the literature and may refer to (a) the FDA-licensed product Cryoprecipitated AHF (anti-hemophilic factor), used to treat Factor VIII deficiency and deficiencies of von Willebrand Factor, fibrinogen, and Factor XIII, or (b) cryoprecipitated plasma made by individual institutions by approximately the same methods, with institutional variations. Whole plasma has also been used as a source of fibrinogen in fibrin sealant [72]. Since it appears that the bonding strength of the adhesive is directly related to the fibrinogen concentration, cryoprecipitate is considered a more desirable source of the fibrinogen component of fibrin sealant than whole plasma. Consequently, adhesives made with whole plasma and thrombin are sometimes referred to as fibrin “gels” rather than fibrin sealant [72,73]. These autologous fibrin “gels” differ from autologous platelet gels, which use platelet-poor plasma rather than the platelet-poor plasma obtained with standard fractionation techniques [74].

Plasma Sources for the Fibrinogen Component

Although the most common source of fibrinogen in locally produced fibrin sealant is cryoprecipitate prepared from fresh frozen plasma [75], methods have also been described using plasma obtained (a) from pericardial blood [76], (b) via plasmapheresis [77], (c) from platelet-poor plasma obtained intraoperatively from the Cell Saver® apparatus (Haemonetics Corp., Braintree, MA) [78] or (d) from platelet-rich plasma obtained from the Plasma Saver® apparatus (Haemonetics) [79,80]. These methods have the advantage of not requiring advance planning; however, as with fresh frozen plasma, unless the plasma collected is subjected to further processing in order to increase fibrinogen concentrations, it tends to be less viscous and to have a lower bonding strength than cryoprecipitated plasma [79]. It has been argued, however, that whole, fresh, citrated plasma fractionated from autologous blood is as effective as cryoprecipitate as a hemostatic agent [72]. Methods for making concentrated fibrinogen for use in fibrin sealant from small volumes of blood drawn peri-operatively have also been described [81,82], which allow rapid production and volume customization for applications that only require small amounts of fibrin sealant.

Processing Plasma to Produce Fibrinogen

Not only have multiple sources of plasma been used in making fibrin sealant, but various methods have been employed to process the plasma obtained by these sources to enhance the concentration and yield of fibrinogen beyond those achieved by standard cryoprecipitation methods, and to shorten processing time [83]. Successful methods for precipitation of plasma with ammonium sulfate [84,85], ethanol [86], and polyethylene glycol [87,88] have been described, as well as subjecting plasma to multiple freeze/thaw and centrifugation cycles [77].

While the foregoing methods all appear to enhance fibrinogen yield and concentration, there is no consensus about which one gives the highest fibrinogen concentration. Several studies have identified ammonium sulfate precipitation as yielding a higher fibrinogen concentration (and therefore greater bonding strength) than standard cryoprecipitation or precipitation with ethanol or polyethylene glycol [89-91], but other studies have failed to confirm these findings [92,93]. Variations in yields and concentrations of fibrinogen obtained by these various methods are not surprising, given the variations in (a) donor blood fibrinogen levels, (b) concentrations and volumes of precipitating agent used (87), and (c) methods and parameters used to measure bonding power (91,92). Regardless of the processing method, the final fibrinogen concentrations are directly related to fibrinogen concentrations in the donated blood (67). Fibrinogen concentrations in cryoprecipitated fresh frozen plasma are reported as low as 20 mg/ml [75], and in plasma cryoprecipitated using the ammonium sulfate, ethanol, or polyethylene glycol method, they range from 13-57 mg/ml [1,67,94,95]. Although precipitation with exogenous agents may shorten the time required for obtaining fibrinogen
concentrate from plasma, the potential risks involved with use of such agents in the cryoprecipitation process have not been fully elucidated. For instance, the ethanol method can lead to elevated alcohol concentrations in the product, which may cause premature clotting of fibrinogen [96] and reduced Factor XIII activity [1]. Casali et al [77] found a fibrinogen concentration of 78 mg/ml in plasma collected by plasmapheresis and subjected to a double cryoprecipitation cycle without additives [77]. The University of Virginia blood bank product is typically manufactured by cryoprecipitation of plasma followed by resuspension in fibrinogen-depleted cryosupernatant to yield fibrinogen concentrations of 25-30 mg/ml in approximately 15 ml. By varying the amount of supernatant, the blood bank can customize the volume and fibrinogen concentration. When the plasma is initially frozen at -80°C for one month and then frozen at -30°C for one month, the fibrinogen yield is greater than from plasma frozen at -30°C for two months [97].

The FDA-approved commercial preparation of fibrin sealant contains equivalent volumes of fibrinogen (75-115 mg/ml) and thrombin, in a total of 2, 4, or 10 ml of sealant. Commercial fibrin sealant preparations with high fibrinogen concentrations produce sealant with increased strength, but in locally-produced products, thrombin concentrations can be adjusted to manipulate the rate of sealant formation. In plastic surgery procedures this may be especially advantageous, as reduced thrombin concentrations in the sealant give the surgeon more time to manipulate the tissues.

Evolution of the UVA Tissue Adhesive Center

Until 1998, investigations in the USA of potential uses for fibrin sealant depended largely upon collaboration with hospital clinical laboratories and local blood banks. Such a program was developed in 1985 at the University of Virginia (UVA); the surgical services and the blood bank collaborated to make fibrin sealant for clinical use within the University of Virginia Health System [98]. This effort fostered multispecialty expertise with fibrin sealant, and eventually led in 1997 to the creation of a research center, the “University of Virginia Tissue Adhesive Center.” This is a unique, multidisciplinary research center authorized by the Dean of the UVA School of Medicine in order to foster research, development, and education in the field of tissue adhesives and improve the clinical care of patients. The Center has a core staff of nurses, a physician director, and administrative staff. Relationships among the UVA Blood Bank, the Center, and the surgical services have provided unique opportunities for collaboration and have resulted in tracking and peer review of fibrin sealant use at UVA, identification of educational needs and development of in-service programs, and preclinical and clinical fibrin sealant trials [41,99,100]. This effort has been so successful that a new Tissue Adhesive Center, modeled on the UVA program, has been established at Temple University in Philadelphia. The evolution of fibrin sealant experience and use at UVA shows how blood bank–produced and commercial fibrin sealant can enhance and promote each other.

To date, over 4,000 patients have been treated with fibrin sealant produced at UVA with an efficacy rate of over 90%, as evaluated by the surgeons who applied the sealant [98]. Concerns about cost containment and effective blood product usage have led to the development of a method for preparing fibrin sealant from novel sources, such as outdated fresh frozen plasma and plasma that has been thawed but not used within the time stipulated by blood bank policies [101]. The use of “stored” plasma is cost-effective, as it utilizes blood components that might otherwise be discarded. The standard method used at UVA in preparing cryoprecipitate for concentrating fibrinogen meets the standards of the American Association of Blood Banks (AABB) for a “closed” system, unlike methods that use a precipitating agent to process fresh frozen plasma [102].

Although use of single-donor units of plasma that have been tested for viral disease markers can greatly reduce the risk of virus transmission, the only way to eliminate this risk is to use autologous blood for preparing the fibrinogen component of fibrin sealant. To date, one instance of HIV-1 transmission and one instance of “non-A, non-B hepatitis” have been reported following the use of topical cryoprecipitate in patients undergoing pyelolithotomy [103,104]. The only other risk that has been associated with topical application of fibrinogen concentrate from allogeneic blood is the occurrence of a systemic allergic reaction caused by antibodies to IgA [105].
In order to meet the demand for a safe, effective, and inexpensive fibrin sealant made with fibrinogen concentrate from autologous blood, in the early 1990s the UVA surgical services in conjunction with the University’s blood bank developed a program to facilitate preoperative collection of autologous blood. The challenges in implementing this program included addressing different time frames established for collecting blood for various surgical procedures, coordinating regional donations at outlying centers for patients, facilitating red blood cell reinfusion where necessary, accommodating variations in the volume of product required, and maintaining sterility. Implementing the UVA’s autologous program required a preoperative collection schedule that allows for transporting the blood and preparing fibrinogen in the blood bank, while ensuring safe storage of red blood cells for perioperative reinfusion, if it became necessary.

Development of a rapid method for preparing fibrinogen from a small volume of blood collected prior to surgery avoided delays in producing autologous fibrinogen from whole blood and facilitated the production of fibrin sealant for selected applications, eg, closing bleb leaks after glaucoma filtration surgery [81]. However, care must be taken that such blood is carefully handled to maintain sterility and safety of the product.

The common practice has been to collect autologous whole blood in the weeks prior to surgery. This has facilitated the production of an additional safe and effective patient care product—autologous fibrinogen concentrate—that can be used to make fibrin sealant at little additional cost, without compromising the autologous red blood cell component. Patients have been receptive to the concept of enhancing their care by participation in the autologous fibrinogen program. Patients have participated even when sealant was the only autologous component needed for their surgery.

**Fibrin Sealant Costs**

The autologous fibrinogen program, while more labor intensive and time-consuming than the stored plasma method, results in a relatively cost-effective product. An institution’s costs for preparing autologous fibrinogen concentrate depend on (a) whether blood is collected within the institution or by a blood center, (b) whether the patient will require other blood components, (c) the blood center’s policies on handling and charges for autologous blood, (d) whether fibrinogen concentrate is prepared in batches, and (e) the institution’s labor and supply costs. Use of fibrin sealant may result in reduced need for post-operative transfusions of allogeneic blood [106], and the costs of preparing the adhesive may be offset by the savings in this regard.

At UVA, autologous fibrinogen concentrate is prepared in the blood bank from whole blood collected by our blood supplier. The blood center collects and provides whole blood whether or not the physician anticipates a need for autologous red blood cells. The current UVA cost for autologous whole blood is $205 per unit. The recordkeeping, separation and freezing of plasma, and preparation of autologous fibrinogen concentrate, usually performed individually and not batchwise, requires ~75 min of technologist labor. In addition, ~$21 is incurred in supply costs in making fibrinogen concentrate. In addition, bovine thrombin used with fibrinogen concentrate costs ~$30, and the cannula and syringe needed to withdraw and apply the product cost ~$3.

For allogeneic fibrinogen concentrate, fresh frozen plasma (current cost $34) that was thawed but unused, and subsequently refrozen, is typically employed. The blood bank does not have other requests for this plasma. A batch of 12 concentrates is typically prepared, with a total labor time of ~70 min. Unlike autologous concentrate, the allogeneic product does not require separation from whole blood and subsequent freezing and requires less recordkeeping than preparing autologous concentrate. The supply costs of ~$21 to prepare concentrate, $3 to withdraw and apply it, and ~$30 for bovine thrombin are also incurred for preparation of allogeneic concentrate. As with the autologous concentrate, the institution’s cost is variable and depends on the cost of plasma, whether or not concentrate is prepared in batches, and the applicable labor and supply costs.

**Fibrin Sealant Utilization at UVA**

Tracking fibrin sealant utilization at UVA (from autologous and single-donor units of blood) over the period 1996-1998 showed that demand grew from 316
units in 1996 to 418 units in 1998. Autologous fibrinogen units represented ~6% (27 units) of total usage in 1998. There were wide fluctuations in monthly unit use (Fig. 1). From January 1998 to June 1998, the thoracic cardiovascular service was the primary user of blood bank fibrin sealant (70%), followed by ear, nose, and throat (10%), neurosurgery (8%), general surgery (4%), and orthopaedic surgery (2%), and non-surgical use (6%).

In June 1998, commercial fibrin sealant was first used at UVA, and in September 1998, commercial fibrin sealant became routinely available, with significant inservicing efforts to educate surgeons, operating room personnel, and other clinicians about fibrin sealant properties, reconstitution, and use. Since that time, the Tissue Adhesive Center has tracked levels of both commercial and blood bank fibrin sealant use.

In 6 months after the introduction of commercial fibrin sealant, 3 surgical services began using fibrin sealant: urology, plastic surgery, and pediatric surgery. Fibrin sealant utilization by service in the 6 months following commercial fibrin sealant introduction was dominated by the thoracic cardiovascular service (54%), followed by neurosurgery (16%), pediatric surgery (7%), ear, nose, and throat (6%), pediatric surgery (7%), orthopaedics (4%), general surgery (3%), plastic surgery (2%), urology (1%), and non-surgical services (7%). The number of surgeons using fibrin sealant increased; 29 surgeons used fibrin sealant following introduction of commercial fibrin sealant, vs 16 surgeons in the prior period (Table 1).

From August 1998 to January 1999 (the initial period of commercial fibrin sealant availability), blood bank fibrin sealant use was ~3 times greater than commercial sealant use (225 units vs 80 kits), although expenditures for the two products were comparable ($25,730 for blood bank sealant vs $27,650 for commercial). In 1999, the first full year in which commercial and blood bank fibrin sealant were both available, utilization of commercial product steadily increased, surpassing blood bank product in April 1999. From January to June 1999, 194 kits of commercial fibrin sealant were used, compared to 157 units of blood bank fibrin sealant. During July to December 1999, 269 kits of commercial product were used, vs 74 units of blood bank fibrin sealant. Compared with the first half of 1999, commercial fibrin sealant use increased 39%, and blood bank fibrin sealant use declined 53% during the second half of 1999. Overall in 1999, the average use was 19 units/mo of blood bank fibrin sealant and 39 kits/mo of commercial fibrin sealant. For the first 6 months of 2000, average monthly use was 10 units/mo of blood bank and 30 kits/mo of commercial fibrin sealant.

Thus, even in an institution with a strong tradition of local blood bank production of fibrin sealant, the new commercial product surpassed the use of the blood bank material within a year of its introduction. These trends in sealant utilization suggest that the well-established blood bank fibrin sealant program helped to facilitate introduction of the commercial product.
Of surgeons already using fibrin sealant, some elected to switch to the commercial product, especially those for whom the higher concentration of commercial product gave it a great advantage. Other surgeons continue to use the blood bank product, some because of cost (commercial fibrin sealant cost during this period was ~$220 for the kit with 2 ml of fibrinogen concentrate) or concern about using a pooled plasma–derived product. Other surgeons began using commercial fibrin sealant without ever having used blood bank fibrin sealant. Concerns such as ease of availability, cost, and safety have continued to dictate not only the decision to use fibrin sealant or not, but which form to use.

The market for fibrin sealant in the United States is changing rapidly. New commercial products are being developed and second generation fibrin sealants as well as specialized delivery systems and applicators are becoming available. The current role of blood bank-produced products is not clearly defined. Because of its low cost, high volume, clinical effectiveness, and patient participation, the blood bank sealant program may continue to be important. Prior to availability of the commercial product, the blood bank fibrin sealant program enabled safe and effective fibrin sealant preparation and use at UVA. The UVA program continues to serve as a model for clinical collaboration between surgical services and clinical laboratories.

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