

BioGlue®

Surgical Adhesive

Instructions for Use



BioGlue® Syringe

 **CryoLife®**
Life Restoring Technologies®

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Sterilized Using
Irradiation



Do Not
Re-use



Do Not Use
if Package is
Damaged



Consult
Instructions
for Use



Caution



Temperature
Limit



Non-Pyrogenic

RxONLY



Not made with
natural rubber latex



**BioGlue® Surgical Adhesive
Syringe
Instructions for Use**

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BioGlue® Surgical Adhesive Syringe Instructions for Use

Caution: Federal (U.S.A.) law restricts this device to sale by or on the order of a physician.

Read *Instructions for Use* prior to using this product.

DEVICE DESCRIPTION

BioGlue® Surgical Adhesive (BioGlue) is a two-component surgical adhesive composed of solutions of purified bovine serum albumin (BSA) and glutaraldehyde. The solutions are dispensed by a controlled delivery system, composed of a double-chambered syringe, applicator tips, and optional applicator tip extenders. Once dispensed, the adhesive solutions (in a predefined ratio) are mixed within the applicator tip where cross-linking begins. The glutaraldehyde molecules covalently bond (cross-link) the BSA molecules to each other and, upon application, to the tissue proteins at the repair site, creating a flexible mechanical seal independent of the body's clotting mechanism. The delivery device-mediated application is designed to provide reproducible mixing of the components *in vitro*. BioGlue begins to polymerize within 20 to 30 seconds and reaches its bonding strength within 2 minutes. BioGlue also adheres to synthetic graft materials via mechanical interlocks within the interstices of the graft matrix.

INDICATIONS FOR USE

BioGlue is indicated for use as an adjunct to standard methods of achieving hemostasis (such as sutures and staples) in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).

CONTRAINDICATIONS

- Not for patients with a known sensitivity to materials of bovine origin.
- Not for intravascular use.
- Not for cerebrovascular repair.
- BioGlue for use in neurosurgery, including use as a dural sealant, is not an approved indication. FDA has not evaluated the safety and effectiveness in support of a neurosurgical indication; however, serious adverse events such as stroke, infection, meningitis, and cerebrospinal fluid leaks have been reported.

WARNINGS

Warning: Polymerized BioGlue has space occupying properties. When used improperly, or applied incorrectly, serious adverse events have been reported relating to compression of adjacent anatomic structures. BioGlue should be used only when complete visualization of the target application location is possible, when it is properly primed to achieve optimal viscosity, and a minimal amount is used. Please see the *Indications for Use* and *Directions for Use* sections of this label.

Warning: Animal studies have shown that direct application of BioGlue to the exposed phrenic nerve can cause acute nerve injury. BioGlue application to the surface of the heart can cause coagulation necrosis that extends into the myocardium, which could reach underlying conduction tissue and may cause acute, focal sinoatrial node degeneration.

- Use of BioGlue in pediatric patients has not been studied. BioGlue should not be applied circumferentially to tissue that needs to grow, as it bonds with the tissue and may not allow that tissue to grow or expand.
- Do not use BioGlue as a substitute for sutures or staples.
- Do not expose valve leaflets or intracardiac structures to BioGlue.
- Do not allow BioGlue in either the uncured or polymerized form to contact circulating blood. BioGlue entering the circulation can result in local or embolic vascular obstruction.
- Avoid exposing nerves to BioGlue.
- Avoid contact with skin or other tissue not intended for application.
- Minimize use of BioGlue in patients with abnormal calcium metabolism (e.g., chronic renal failure, hyperparathyroidism). Glutaraldehyde-treated tissue has an enhanced propensity for mineralization. Laboratory experiments indicate that unreacted glutaraldehyde may have mutagenic effects.
- Do not use BioGlue if staff are not adequately protected (e.g., wearing gloves, mask, protective clothing, and safety glasses). Unreacted glutaraldehyde may cause irritation to eye, nose, throat, or skin, induce respiratory distress, and cause local tissue necrosis. Prolonged exposure to unreacted glutaraldehyde may cause a central nervous system or cardiac pathology. If contact occurs, flush affected areas immediately with water and seek medical attention.
- Do not use BioGlue in the presence of infection and use with caution in contaminated areas of the body.
- Avoid repeat exposure of BioGlue in the same patient. Hypersensitivity reactions are possible upon exposure to BioGlue. Sensitization has been observed in animals.
- BioGlue contains a material of animal origin that may be capable of transmitting infectious agents.
- BioGlue, which degrades via proteolysis, can be slow to resorb dependent on the quantity of adhesive applied. The slow resorption of excessive amounts of BioGlue has been associated with sterile inflammatory response requiring explant of the material. BioGlue should be applied as a thin layer, as an adjunct to sutures or staples, and in amounts sufficient to seal the area. BioGlue should not be applied in excess.

PRECAUTIONS

- Safety and effectiveness of BioGlue in minimally invasive procedures have not been established.
- Safety and effectiveness of BioGlue in coronary artery bypass grafting (CABG) and other use on small diameter vessels have not been established.
- Do not use blood saving devices when suctioning excess BioGlue from the surgical field.
- Clamp and depressurize vessels prior to applying BioGlue to targeted anastomoses.
- To prevent the entrance of BioGlue into the cardiovascular system, avoid any negative pressure during application and polymerization of BioGlue. For example, left ventricular vents should be turned off prior to the application of BioGlue. There have been reports of BioGlue being suctioned into the aorta and impeding heart valve function when used in conjunction with an active left ventricular vent.
- It is recommended that surgical gloves, sterile gauze pads/towels, and surgical instruments be maintained moist to minimize the potential for BioGlue inadvertently adhering to these surfaces.
- BioGlue syringe, applicator tips, and applicator tip extenders are for single patient use only. Do not re-sterilize.

- Do not use if packages have been opened or damaged.
- Take care not to spill contents of the syringe.
- Do not compress the syringe plunger while attaching it to the syringe.
- Do not apply BioGlue in a surgical field that is too wet. This may result in poor adherence.
- Avoid tissue contact with material expelled from applicator during priming.
- BioGlue polymerizes rapidly. Priming must occur quickly, followed immediately by the application of BioGlue. Pausing between priming and application can cause polymerization within the applicator tip.
- Do not peel away BioGlue from an unintended site, as this could result in tissue damage.

ADVERSE EVENTS – OBSERVED AND POTENTIAL

Observed Adverse Events

Adverse events observed during the clinical studies included the following (see Table 3 for more detail):

- | | |
|---|-----------------------------------|
| • BioGlue applied to nontargeted tissue | • Neurological deficit |
| • Failure of BioGlue to adhere | • Organ system failure |
| • Death | • Paraplegia |
| • Hemorrhage | • Pleural effusion |
| • Infection | • Renal dysfunction/failure |
| • Inflammatory, immune systemic allergic reaction | • Respiratory dysfunction/failure |
| • Irreversible morbidity | • Stroke or cerebral infarction |
| • Ischemia | • Thromboembolism |
| • Myocardial infarction | • Thrombosis |

Potential Adverse Events That May Occur From the Use of BioGlue

- A hypersensitivity reaction such as swelling or edema at the application site
- Application of adhesive to tissue not targeted for procedure
- Failure of BioGlue to adhere to tissue
- Local tissue necrosis
- Mineralization of tissue
- Possible transmission of infectious agents from material of animal origin
- Thrombosis and thromboembolism

Potential Adverse Events Related to Cardiac and Vascular Procedures

Adverse events associated with cardiac and vascular repair procedures may include but are not limited to:

- | | |
|--------------------------------------|------------------------------------|
| • Adhesions | • Neurological deficits |
| • Anastomotic pseudoaneurysm | • Organ system dysfunction/failure |
| • Aortic insufficiency | • Paraplegia |
| • Cardiac tamponade | • Pleural effusion |
| • Cerebral emboli | • Pulmonary emboli |
| • Death or irreversible morbidity | • Renal dysfunction/failure |
| • Dissection | • Respiratory dysfunction/failure |
| • Hemorrhage | • Stroke or cerebral infarction |
| • Infection | • Thrombosis |
| • Injury to normal vessels or tissue | • Vasospasm |
| • Ischemia | • Vessel rupture and hemorrhage |
| • Myocardial infarction | |

CLINICAL STUDIES

In June 1998, CryoLife, Inc. began a clinical trial investigating the use of BioGlue as an adjunct in the surgical repair of acute, Stanford Type A aortic dissections. A total of 175 patients were enrolled in this study. This included 54 nonrandomized (lead-in) patients, 60 patients randomized to standard surgery plus BioGlue, and 61 patients randomized to standard surgery only. An interim analysis was performed after the 100th patient was enrolled into the randomized portion of the trial and had completed the 30-day follow-up period. There was no statistically significant difference in early mortality (primary endpoint) between the two groups; however, BioGlue-treated patients required fewer pledgets, hemostatic agents, and make-up stitches than the patients in the control group. There were no confirmed unanticipated adverse device effects, and no differences in adverse events between the two groups.

Based on data from the lead-in patients, CryoLife filed a Humanitarian Device Exemption (HDE) for the use of BioGlue in the surgical repair of acute thoracic aortic dissections, which was approved by FDA in December 1999 (H990007). CryoLife gained approval in May 2000 to investigate the use of BioGlue for sealing anastomotic sites in cardiac and vascular repairs. During this investigation, the HDE remained active, allowing for the use of BioGlue in the surgical repair of acute thoracic aortic dissections. CryoLife gained approval to market BioGlue in December 2001 for sealing anastomotic sites in cardiac and vascular repairs, which included the use of BioGlue as an adjunct in the surgical repair of acute thoracic aortic dissections. The HDE close-out report was submitted to FDA in February 2002.

The following information is from the cardiac and vascular repair investigation:

Study Design

The BioGlue Effectiveness and Safety Trial as a Surgical Adjunct in Cardiac and Vascular Surgical Repairs was a prospective, multi-center, randomized, controlled trial. Patients were randomized to receive standard surgical repair with BioGlue applied to the anastomotic site prior to clamp removal (BioGlue group, n = 76) or standard surgical anastomotic repair alone (control group, n = 75). One patient crossed over from the control group to the BioGlue group due to uncontrolled bleeding. Data from this patient are included in the safety table, but omitted in the effectiveness table below. The overall objective was to collect clinical data concerning the safety and effectiveness of BioGlue used as an anastomotic sealant to provide hemostasis. The hypothesis was that hemostasis would be achieved in a higher percentage of the BioGlue-treated patients than in the control patients.

Patient Assessment

Safety and Effectiveness Evaluations

The BioGlue group and the control group were compared to evaluate the following endpoints:

Primary Evaluation

- Anastomotic hemostasis (yes or no) of each of the repaired sites
Anastomotic hemostasis was defined as an anastomosis that did not require additional agents (pledgets, sutures, hemostatic devices, antifibrinolytic agents, thrombin glues, fibrin glues) at the treated site(s) to control bleeding at any point during the course of the original operation.
- Anastomotic hemostasis (yes or no) on a per patient basis
Patients with hemostasis at all anastomotic sites were considered successful.

Secondary Evaluations

- Quantity, type, and number of donor exposures of blood replacement products administered
- Type of additional agents used (pledgets, sutures, hemostatic devices, antifibrinolytic agents, thrombin glues, fibrin glues)
- Re-operation due to anastomotic site bleeding
- Major complications/adverse events through final follow-up
- Minor complications/adverse events through final follow-up
- Early hospital discharge mortality and mortality through last follow-up

Safety Evaluations

- Unanticipated Adverse Device Effects (UADE)
- Device complications
- Surgical procedure complications

Demographic Data

A total of 151 patients (76 in the BioGlue test group, and 75 in the control group) were treated at 6 investigational sites in the cardiac and vascular repair arm of the U.S. IDE clinical trial. Surgical procedures performed are shown in Table 1.

Table 1 – Cardiac and Vascular Procedures Included (*All Randomized*)

System	Treatment Group		Cross-over	Total
	Surgical Repair with BioGlue	Conventional Surgical Repair		
Cardiac Procedures**	24	25	0	49
Aortic Procedures†	57	47	1	105
Peripheral Vascular Procedures***	25	23	0	48
Total	106	95	1	202

**Cardiac repairs include: aortic root replacement (4), aortoplasty (1), aortic valve annuloplasty (5), aortic valve resuspension (1), aortic valve replacement (23), Bentall procedure (2), composite valved conduit procedure (8), mitral valve replacement (2), Ross procedure (2), coronary artery bypass grafting (1).

†Aortic aneurysm repairs include: abdominal aortic aneurysm (21), ascending aortic aneurysm (21), ascending/ transverse aortic arch aneurysm (9), ascending/ transverse arch/ descending aortic aneurysm (1), descending aortic aneurysm (8), thoracoabdominal aortic aneurysm (32), transverse aortic arch aneurysm (12), Type B aortic dissection (1).

***Peripheral vascular repairs include: aorto-femoral bypass (5), aorto-iliac bypass (2), aorto-innominate bypass (1), carotid bypass (1), carotid endarterectomy (19), femoral-distal bypass (3), femoral-femoral bypass (2), femoral-popliteal bypass (5), hepatic-renal bypass (1), popliteal-dorsalis pedis bypass (1), profunda endarterectomy (1), renal bypass (6), renal endarterectomy (1).

Data Analysis and Results

The tables and figures in this section present information from the cardiac and vascular repair arm of the U.S. IDE clinical trial.

Table 2 – Effectiveness Endpoints

Parameter of Interest	BioGlue Group (n = 76)	Control Group (n = 74)	Comments/p value
Hemostasis Success per Patient ¹	61% (46/76)	39% (29/74)	0.014
Hemostasis Success per Repair Site ²	81% (164/202)	57% (105/184)	<0.003
RBC Used	2.3 ± 3.6	1.9 ± 2.4	NS ⁴
0 units	37	33	
1-5 units	29	34	
>5 units	10	7	
Platelets Used	5.1 ± 10.1	5.2 ± 10.0	NS
0 units	47	42	
1-10 units	21	27	
>10 units	8	5	
Fresh Frozen Plasma Used	3.8 ± 6.6	3.3 ± 5.0	NS
0 units	43	41	
1-10 units	24	23	
>10 units	8	9	
Cryoprecipitate Used	4.3 ± 11.9	2.0 ± 8.3	NS
0 units	63	67	
1-10 units	3	1	
>10 units	9	4	
Donor Exposures			NS
0 donors	26	23	
1-20 donors	11	15	
>20 donors	11	13	
Pledgets Used on Primary Repair	26% (53/202)	36% (66/184)	0.047
Make Up Stitches Used	82% (31/38) ³	81% (64/79) ³	1.00
Hemostatic Agent Used	8% (3/38) ³	10% (8/79) ³	1.00
Additional BioGlue	55% (21/38) ³	N/A	N/A
Other	8% (3/38) ³	19% (15/79) ³	0.17
Re-operation for Bleeding	0	1 (1.4%)	One-sided 95% CI [-∞, 0.9]
Bypass Time (min)	168.1 ± 67.6 (54 - 358) n = 34	144.2 ± 60.6 (54 - 387) n = 35	NS
Cross-clamp Time (min)	74.0 ± 46.1 (10 - 196) n = 54	69.1 ± 41.3 (19 - 196) n = 55	NS
Total Operative Time (min)	228.7 ± 100.8 (60 - 515) n = 73	228.7 ± 100.8 (60 - 515) n = 73	NS
ICU Time (days)	3.9 ± 5.6 (0 - 32) n = 70	4.8 ± 7.1 (0 - 36) n = 72	NS
Hospitalization Time (days)	9.5 ± 10.6 (1 - 81) n = 72	10.9 ± 9.7 (1 - 55) n = 73	NS

¹ Defined as hemostasis of 100% of the anastomotic repair sites.

² The average number of sites (anastomoses) per patient were 2.6 (range 1 to 8).

³ Denominator reflects number of patients in whom immediate hemostasis was not achieved.

⁴ Not statistically significant.

Table 3 - Safety Endpoints

Adverse Event Description	BioGlue Group N = 77			Control Group N = 74			p value
	n	%	#events	n	%	#events	
Pleural Effusion	20	26.0%	25	21	28.4%	22	0.855
Respiratory Dysfunction/Failure	13	16.9%	18	12	16.2%	15	1.000
Infection	13	16.9%	15	10	13.5%	13	0.653
Renal Dysfunction/Failure	13	16.9%	13	9	12.2%	10	0.492
Neurological Deficits	5	6.5%	6	16	21.6%	18	0.009
Death	5	6.5%	5	5	6.8%	5	0.999
Hemorrhage	3	3.9%	3	3	4.1%	3	1.000
Ischemia	3	3.9%	3	2	2.7%	2	1.000
Organ System Dysfunction/Failure	3	3.9%	4	2	2.7%	2	1.000
Myocardial Infarction	3	3.9%	3	1	1.4%	1	0.620
Inflammatory, Immune Systemic Allergic Reaction ¹	2	2.6%	2	0	0%	0	0.497
Stroke or Cerebral Infarction	1	1.3%	1	3	4.1%	5	0.360
Paraplegia	1	1.3%	3	2	2.7%	3	0.615
Thromboembolism	1	1.3%	1	1	1.4%	4	1.000
Application of Adhesive to Nontargeted Tissue ²	1	1.3%	1	0	0%	0	1.000
Failure of Products to Adhere to Tissue ²	1	1.3%	1	0	0%	0	1.000
Irreversible Morbidity	0	0%	0	1	1.4%	1	0.490
Thrombosis	0	0%	0	1	1.4%	1	0.490
Other ^{3,4}	46	59.7%	108	40	54.1%	100	0.514

¹ These adverse events were not device related. One patient had an allergic reaction to a preoperative antibiotic and the other patient had an allergic reaction to protamine sulfate.

² These adverse events were device related, see Warnings and Precautions Sections of this Instructions for Use.

³ Other adverse events observed in the BioGlue group were as follows: acidosis (1%), acute shortness of breath (1%), altered mental status (3%), anemia (5%), atelectasis (8%), cardiac arrhythmia (22%), cerebral hemorrhage (1%), colecystitis (1%), coagulopathy (1%), congestive heart failure (4%), decreased femoral pulse (1%), deep vein thrombosis (1%), depression (4%), diarrhea (3%), dysphagia (5%), edema (3%), fever (3%), heart enlargement (4%), hematuria (1%), hemoptysis (1%), hernia (4%), hoarseness (1%), hypotension (1%), ileus (4%), incisional pain (3%), lymphatic fistula (1%), malnutrition (5%), nausea (3%), perforated viscus (1%), pericardial effusion (1%), pneumothorax (3%), rectal bleeding (1%), seizure (1%), thigh and back pain (3%), thrombocytopenia (1%), urinary retention (4%), vocal cord paralysis (3%).

⁴ Other adverse events observed in the control group were as follows: abdominal pain (1%), abnormal lab value (5%), acidosis (1%), altered mental status (3%), anemia (3%), angina (1%), aphasia (1%), atelectasis (4%), back pain (1%), cardiac arrhythmia (19%), cerebral hemorrhage (3%), congestive heart failure (1%), diarrhea (3%), dizziness (1%), duodenal ulcer (1%), dysphagia (1%), edema (1%), emphysema (1%), encephalopathy (1%), failed extubation (1%), fever (3%), heart block (2%), hematuria (1%), hemothorax (1%), hernia (1%), hoarseness (4%), hypotension (4%), ileus (3%), incisional pain (5%), lower extremity weakness (1%), nausea (4%), near syncope (1%), neck deformity (1%), pericardial effusion (3%), pneumothorax (3%), post-kidney collection (3%), reintubation (1%), seizure (1%), sexual dysfunction (1%), shortness of breath (1%), thrombocytopenia (4%), thrombophlebitis (1%), transfusion reaction (3%), urinary retention (1%), valve surgery (1%), vocal cord paralysis (3%).

Adverse events were equal in severity in both the BioGlue group and the standard surgical repair group. There were no unanticipated adverse device effects (UADE) in this investigation.

Conclusion

The BioGlue group was noted to have a higher rate of successful intra-operative hemostasis when compared to the control group on both a “per patient” and a “per anastomotic site” basis, this was statistically significant. BioGlue-treated patients demonstrated a lower incidence of adjunctive pledgets use on their primary repairs to achieve hemostasis. There were no statistically significant differences in adverse events between BioGlue and control patients.

HOW SUPPLIED

The BioGlue syringe and applicator tips are supplied sterile for single-patient use only. Discard any unused material from opened or damaged product.

The BioGlue solutions are contained within a capped, double-chambered, sterile syringe. Polymerized BioGlue is nonpyrogenic. Store below 25°C, but do not freeze.

PATIENT COUNSELING INFORMATION

Exposure to BioGlue may cause a hypersensitivity reaction such as swelling or edema at the application site. Development of immune complex disease, with various manifestations, as the device undergoes resorption is also a possibility.

Patients should be counseled to inform surgeons that they have been previously exposed to BioGlue and may be sensitized.

BioGlue contains a material of animal origin, which may be capable of transmitting infectious agents.

DIRECTIONS FOR USE

Apply BioGlue Surgical Adhesive prior to clamp release or after a leak is detected to seal the cardiac or vascular repair site.

Device Preparation

The BioGlue Surgical Adhesive Syringe delivery system consists of: syringe, syringe plunger, and applicator tips.

Inside the BioGlue Syringe box there are two separate pouches. One contains the syringe and the syringe plunger, and one contains four applicator tips.

The 10mL BioGlue Syringe box includes an additional pouch containing three, 12mm Spreader Tips.

1. Remove the syringe, syringe plunger, and applicator tips from their packaging. While holding the syringe upright, tap the syringe until the air bubbles in the solutions rise to the top of the syringe.



Figure 1

NOTE: Continue to hold the syringe upright during the entire assembly of the delivery system to keep the bubbles toward the top of the syringe.

2. Remove an applicator tip from its packaging and inspect the collar portion of the tip to ensure that the pointer portion is directly over the larger port. If not, rotate the locking collar on the shaft until the pointer is over the larger port.

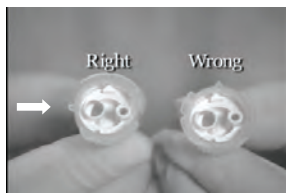


Figure 2

3. While firmly grasping the syringe, nose upward, turn the cartridge cap 90° counterclockwise and remove the cap by rocking it from side-to-side. Align the tip with the cartridge using the corresponding notches on each and place the tip on the syringe.



Figure 3

CAUTION: Take care not to spill solution from the syringe during assembly.

4. Lock the applicator tip in place by pushing the tip firmly toward the syringe and rotating the tip collar 90° clockwise.



Figure 4

5. While keeping the syringe upright, align the small and large barrels of the syringe with the corresponding syringe plunger heads and slide the plunger into the back of the syringe until resistance is felt. The syringe delivery device is now assembled.



Figure 5

CAUTION: Do not lay the assembled device on its side until all air has been purged (see next paragraph).

CAUTION: Before using BioGlue in the procedure, the syringe must be purged of the residual air space and the applicator tip must be primed. Refer to [Site Preparation, Syringe Air Space Removal and Applicator Tip Priming](#).

6. If using an applicator tip with a flexible extension, a desired angle may be created by bending the extension at the appropriate location to the desired angle and holding for 3-5 seconds. The angle created should be maintained for up to 5 minutes.
7. To remove occluded applicator tips, grasp the applicator tip collar, rotate the tip collar counterclockwise, and lift the tip off the syringe by rocking it side-to-side.

Site Preparation, Syringe Air Space Removal and Applicator Tip Priming

1. The target surgical field must be properly prepared prior to either removal of the residual air space, priming, or applying BioGlue. BioGlue works best when the target surgical field is dry. A dry surgical field can be described as a field that does not restrain with blood within 4-5 seconds after wiping dry with a surgical sponge.

CAUTION: Do not attempt to apply BioGlue to a field that is too wet. Application of BioGlue into a wet field may result in the failure of BioGlue to adhere.

2. The residual syringe air space must be removed prior to BioGlue application. Again, it is important to hold the assembled syringe upright to ensure that the air bubbles in the solutions are located at the top of the syringe. Purging of the air space can now be accomplished using two different methods:
 - a. Compress the plunger only until the solutions are even with the top of the syringe body. Once the residual air space has been removed the syringe is ready for priming (refer to Step 3) and immediate use.
 - b. Compress the plunger until both solutions can be visibly seen in the base of tip. The airspace has now been removed, but this tip is now occluded with polymerized BioGlue and will need to be changed prior to priming (refer to Step 3) and application to the target site.



Figure 6

NOTE: Each syringe only needs to be purged of residual airspace upon its initial use.

3. Each applicator tip must be primed prior to BioGlue application. Priming ensures the BioGlue solutions are properly mixed. The surgeon should compress the plunger and expel a narrow ribbon of BioGlue approximately 3 cm long onto a sterile disposable surface (e.g., sponge, gauze, or towel).
4. The surgeon should examine the material expelled during priming and ensure that it is of uniform light yellow to amber color and that it is free from air bubbles. If this material looks colorless or contains bubbles, repeat the prime as outlined in Step 2 until the device delivers a uniform liquid with no bubbles.

CAUTION: Avoid direct contact with material expelled during priming.

5. When the applicator tip has been properly primed, proceed immediately to application.

CAUTION: BioGlue polymerizes very quickly. The surgeon must apply BioGlue immediately after priming. Pausing between priming and application can cause polymerization of BioGlue within the applicator tip. Should this occur, replace the obstructed tip with a new tip and repeat the steps for applicator tip priming. Do not continue to apply pressure to the plunger once the tip has occluded.

General Techniques for the Use of BioGlue in Surgery

1. BioGlue works best when the target surgical field is dry. A dry surgical field can be described as a field that does not restrain with blood within 4-5 seconds after wiping dry with a surgical sponge.
2. Tissues surrounding the target surgical site should be protected from the unintentional application of BioGlue. The most effective method of protection is to cover any nontarget tissues with moist sterile gauze pads. These protective pads should be removed before complete polymerization occurs.

Warning: Animal studies have shown that direct application of BioGlue to the exposed phrenic nerve can cause acute nerve injury. BioGlue application to the surface of the heart can cause coagulation necrosis that extends into the myocardium, which could reach underlying conduction tissue and may cause acute, focal sinoatrial node degeneration.

3. Apply an even coating of BioGlue to the target area. In general, use an approximately 1.0 – 3.0 mm thick coating for vessels that are greater than 2.5 cm in diameter or an approximately 0.5 – 1.0 mm thick coating for vessels that are less than 2.5 cm in diameter.

CAUTION: Avoid contact of BioGlue with blood-saving devices, such as cell savers and pumps.

CAUTION: Clamp and depressurize vessels prior to applying BioGlue to targeted anastomoses.

CAUTION: Avoid suctioning BioGlue into the vessels when applying it to targeted anastomoses.

4. If BioGlue is inadvertently applied to nontarget tissues, allow the adhesive to polymerize completely. Then, using forceps and scissors, carefully dissect the polymerized BioGlue from the unintended area.

CAUTION: Do not peel BioGlue away from an unintended site, as this could result in tissue damage.

CAUTION: Polymerized BioGlue has space occupying properties. Caution should be used in the application of BioGlue to avoid compression of adjacent structures.

5. Do not compress the area of application or subject it to any extra pressure. BioGlue does not require any clamping or compression in order to polymerize. BioGlue works optimally when it is allowed to polymerize without any manipulation for a full two minutes.
6. When BioGlue has completely polymerized, the surgeon may trim away any excess material or irregular edges with scissors and forceps.

Specific Techniques for the Use of BioGlue in Aortic Dissection Surgery

1. The dissected layers of the aorta should be initially cleared of blood and thrombus material and should be dried, to the extent possible, with surgical sponges.
2. For the distal end of the dissection repair, insert a balloon catheter into the true lumen to define the distal terminus for the application of BioGlue. In addition, the dissected layers of

the aorta should be closely approximated by inserting a dilator, sponge, or catheter into the true lumen to preserve the natural architecture of the vessel.

BioGlue should then be dispensed into the false lumen as far distally as the distal balloon catheter will allow. Filling the false lumen should proceed from distal to proximal with a spiraling out motion for smooth application. Completely fill the false lumen with BioGlue; avoid overfilling the false lumen and spilling BioGlue into the true lumen or surrounding tissue.

3. For the proximal end of the dissection repair, the dissected layers of the aorta should also be closely approximated by using a dilator, sponge, or catheter. If necessary, moist gauze pads should be placed over the aortic valve leaflets to protect them from inadvertent application of BioGlue. BioGlue should then be dispensed to fill the false lumen.

Graft material may be sutured directly onto the tissues adhered and reinforced with BioGlue at both the proximal and distal aspects of the dissection repair. Allow BioGlue to completely polymerize without any manipulations for a full two minutes prior to suturing through the adhered tissue layers.

PRODUCT INFORMATION DISCLOSURE

Handling and storage of this device by the user, as well as factors related to the patient, the patient's diagnosis, treatment, surgical procedures, and other matters beyond manufacturer's control, may directly or indirectly affect this device and the results obtained from its use. This device should not be used except on the order of a physician.

DISCLAIMER OF WARRANTIES; LIMITS OF LIABILITY

CRYOLIFE DISCLAIMS ALL EXPRESS AND IMPLIED WARRANTIES WITH RESPECT TO THIS SURGICAL ADHESIVE, INCLUDING BUT NOT LIMITED TO THE EXPRESS AND IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. IN NO EVENT SHALL CRYOLIFE BE LIABLE FOR INCIDENTAL OR CONSEQUENTIAL DAMAGES. In the event that such disclaimer is found invalid or unenforceable for any reason: (i) any action for breach of warranty must be commenced within one year after any such claim or cause of action accrued and (ii) the remedy for any such breach is limited to the replacement of the product. Prices, specifications, and availability are subject to change without notice.

RxONLY



= Not made with natural rubber latex



= Sterilized Using Irradiation



= Do Not Re-use



= Do Not Use if Package is Damaged



= Use-by Date



= Consult Instructions for Use



= Caution



= Temperature Limit



= Non-Pyrogenic



= Catalogue Number



= Batch Code

In the United States of America Federal law restricts a prescription device to sale by or on the order of a physician.

In all other regions of the world, this device should not be used except on the order of a physician.



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