

# SeraSeal Introduction

## What is SeraSeal?

SeraSeal is a new and innovative hemostatic agent that is designed to stop bleeding on contact, and within seconds for arterial hemorrhages. It is comprised of agar and bovine factor proteins: II, VII, IX and X and acts as a catalyst in the clot formation process. This patented single component system can tackle any bleeding situation with the potential to save many lives. When seconds count, SeraSeal can make the difference between life and death.

Have you thought of how many deaths occur every year from uncontrolled bleeding? Did you know that hemorrhage is the leading cause of death, far surpassing any disease? Have you thought about how much blood is routinely wasted? And time? The patient's time to recovery. Your time trying to stop the bleeding. Your staff's time cleaning up and attending the recovery. There is new innovation from Wortham Laboratories called SeraSeal to stop any kind of bleeding in seconds including arterial bleeds. SeraSeal can be used on all bleeding wounds.

Agar, the complex sugar in SeraSeal, when added to a bleeding wound, will cross-link with the ions of platelet phospholipids, and cations from amine groups in fibrinogen/fibrin monomers and tissue proteins, forming an  $\alpha$ -1,6-linked galactophospho and  $\alpha$ -1,6-galactoamine forming a gelatin barrier over the wound. This barrier reduces blood from escaping through the opening of the wound, allowing the patient's cascade system to form a fibrin clot sooner. The second active agent, vitamin K factors II, VII, IX, and X, function in an ancillary way, by facilitating the agar to cross-link with the platelets and fibrinogen, lending strength to the gelatin barrier, and by biologically facilitating only the blood outside of the wound, which has already been activated by tissue thromboplastin from platelets and damaged cells due to trauma, to assist in forming a clot. The clotting cascade is a biological activity system, and the clotting factors in the product are participating in this biological activity as a catalyst to form a fibrin clot. Further, platelets do an internal surface translocation, where more phospholipids are available to cross-link with agar, and covalent lysine to glutamine linkages between gamma chains of adjacent fibrin molecules and between adjacent alpha chains create clot stabilization.

## Why SeraSeal?

SeraSeal's ability to achieve hemostasis in seconds not only benefits the patient but the hospitals as well, in substantial cost savings in their overhead expenses. By controlling bleeding, the need for blood transfusions is strongly reduced. When SeraSeal is applied to a wound it captures all the bleeding blood vessels in a single motion, and achieves hemostasis in seconds for the entire wound, as compared to minutes by electric cauterization. Although cauterization does stop the bleeding upon contact, cauterization must be applied to each blood vessel in that wound, taking a minute or more to assure all the bleeding has stopped. As a result, when you add up each bleeding wound treatment, SeraSeal will reduce surgical time as much as 50% or more.

Uncontrolled bleeding is a leading cause of death, a depletion of blood product resources, and creates an intrinsically high level amount of stress. A primary hemostatic agent, SeraSeal, is now available to manage the most challenging hemorrhages.

SeraSeal is able to effectively control bleeding in Level III and Level IV type hemorrhages in seconds, and can be used in emergency and trauma cases. Clinical studies and clinical use have demonstrated SeraSeal's unique formulation to be effective in a wide range of coagulopathies.

When SeraSeal is applied to a wound, it does not create inflammation or damage to the tissues, allowing wound healing to occur sooner. A one-component hemostatic agent, SeaSeal requires no mixing or preparation, and is available in multiple delivery systems to administer any wound to any part of the body.

By controlling bleeding, the need for blood transfusions is substantially reduced, thereby, reducing risk and cost to the patient. Additional cost savings are realized through the use of SeraSeal by reducing surgical time, where in some cases the savings is as much as 50%, and shorter hospital stay.

## How To Use SeraSeal

### Overview

SeraSeal is applied topically to the bleeding site, and **NEVER** injected into the vascular system. After applying the hemostatic agent leave it undisturbed for 1 minute. Do not wipe. Work in another area during this 1 minute period while the fibrin strands cross-link to create a stronger tensile strength clot. After a minute irrigate or gently dab the fibrin clot to check for any hidden bleeding. If there is a hidden bleed, repeat the above process.

### SeraSeal on Venous Bleeding

SeraSeal is a new technical product for professional use. Physicians have been taught to deal with bleeding in traditional ways. SeraSeal is *not* traditional. It introduces new ways of controlling bleeding. Properly applied, SeraSeal reliably arrests venous bleeds in seconds.

Before applying SeraSeal to a bleeding wound it is essential to locate the point origin of the bleed. This may require the removal of any pooled blood in the wound through suction or absorption onto a surgical sponge.

***Surface bleeds:*** Apply SeraSeal drop wise to the surface of the bleeding site until bleeding stops. ***Note:*** A visual sign of hemostasis has occurred is when the blood becomes a brighter red. Adding more SeraSeal after hemostasis has occurred will wash the erythrocytes off the fibrin clot, giving the elusion of an active bleed.



***Lacerations or incisions:*** First apply SeraSeal to the base of the wound, continually applying the agent as you draw it up from the wound. This assures the arrest of hemorrhage below the surface. No local pressure is needed. **Do Not Wipe.** Wiping will remove the fibrin clot and reintroduce bleeding. Instead, wait 60 seconds to allow the fibrin strands to cross-link. This will give greater tensile strength to the fibrin clot. After 1 minute irrigate the wound to confirm no hidden bleeding.

### **SeraSeal on Arterial Bleeding**

There are two different methods used to arrest two types of an arterial hemorrhage.

***Transected Artery:*** Apply SeraSeal at a right angle and at a superior point to the proximal artery in quick drop succession. Each drop will cascade around the peripheral opening of the artery, causing fibrin clot formation to begin at the outer edges. With each drop the opening will get smaller and smaller until the fibrin clot seals off the wound.

***Longitudinal Arterial Wound:*** Starting at the proximal end of the injured artery, apply SeraSeal at a right angle in quick drop succession, moving distally as you apply the hemostatic agent. This approach is like closing a zipper. No local pressure is needed. **Do Not Wipe.** Wiping will remove the fibrin clot and reintroduce bleeding. Instead, wait 60 seconds to allow the fibrin strands to cross-link. This will give greater tensile strength to the fibrin clot. After 1 minute irrigate the wound to confirm no hidden bleeding.

## SeraSeal Use Outside the Clinical Setting

SeraSeal's ability to control Level 3 and Level 4 type hemorrhages, such as from the iliac or femoral artery, and the agent's one component delivery system, makes it uniquely qualified to treat life-threatening wounds outside the clinical setting. Application of SeraSeal out in the field will significantly reduce the number of incidences of hypotensive cases, and lessen the need for infusion of blood products. If blood products are needed for the restoration of the blood pressure on SeraSeal treated patients, the fibrin clot will remain in situ.

Two SeraSeal delivery systems are recommended for field use: SeraSeal Battlefield Dressing and SeraSeal Foam. The battlefield dressing is recommended for all open and gapping wounds, and the foam is designed to arrest hemorrhages in a closed cavity, such as gunshot or impalement wounds.

## Application

### *SeraSeal Battlefield Dressing*

Remove the rolled dressing from the tyvek pouch. Grasp the end of the rolled dressing and toss the remaining rolled dressing over the shoulder to unfurl it. Before packing the wound, remove any pooled blood, if possible, in order to see the point of origin of the bleed. Pack the wound by first gathering the end piece of the dressing with the thumb and fingers of one hand in a pinch like fashion. Apply the pinched end of the dressing directly on to the site of the point of origin of the bleed. Create direct pressure to the wound by pushing the damaged blood vessel up against the bone or muscle in the immediate area starting with the pinched end of the dressing, and with the continuous tight packing of the wound with the rolled dressing. Transport the patient. Unpacking the wound: Remove the majority of the packed dressing. Soak the remaining dressing inside the wound with sterile water or saline to reduce the possibility of the fibrin clot adhering to the dressing, and for the clot to remain in situ.



## ***SeraSeal Foam***

SeraSeal foam can be applied to both an open or a closed type wound. Open Wound Application: An application of foam to an open wound requires it to be a cavity type wound, or the wound is surrounded by tissue in order to contain the SeraSeal foam. Remove the plastic cap. Remove any pooled blood in order to locate the point of origin of the bleed. Point the canister actuator nozzle downward, just above the point of origin, and apply the foam directly to the wound. Apply enough SeraSeal foam to completely fill the wound cavity. Place a dressing over the treated wound and secure with tape or a wrap dressing, in order to retain the foam within the wound during transport. Closed wound application: Remove plastic cap. Insert the canister actuator nozzle into the portal wound, and inject the SeraSeal foam into the cavity by pressing the actuator button. Inject all of the hemostatic foam into the cavity or until the foam begins to bubble out of the portal wound. If there is more than one portal wound, apply SeraSeal foam into each of the portal wounds. This may require more than one canister of the hemostatic agent. Transport to surgery as soon as possible.

## SeraSeal Indications

### **SeraSeal Hemostatic Sealant Indications**

SeraSeal is indicated in all surgical procedures as a primary to hemostasis when control of bleeding by cauterization, ligature, or conventional procedures is ineffective or impractical.

### **Important Risk Information for SeraSeal**

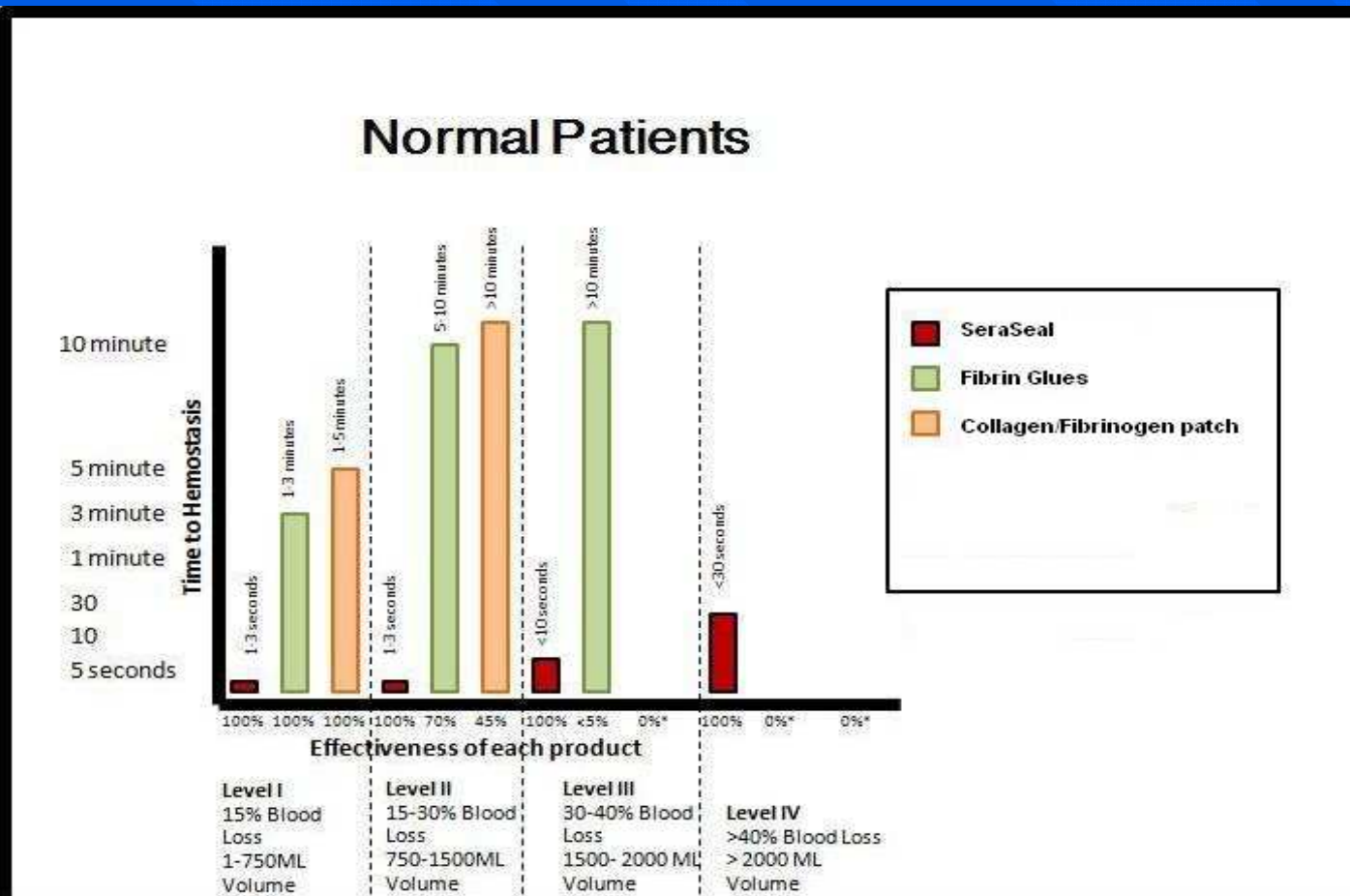
Do not use SeraSeal in patients with known allergies to materials of bovine origin.

SeraSeal must not be injected into blood vessels, or allowed to enter blood vessels. This may lead to extensive intravascular clotting or even death.

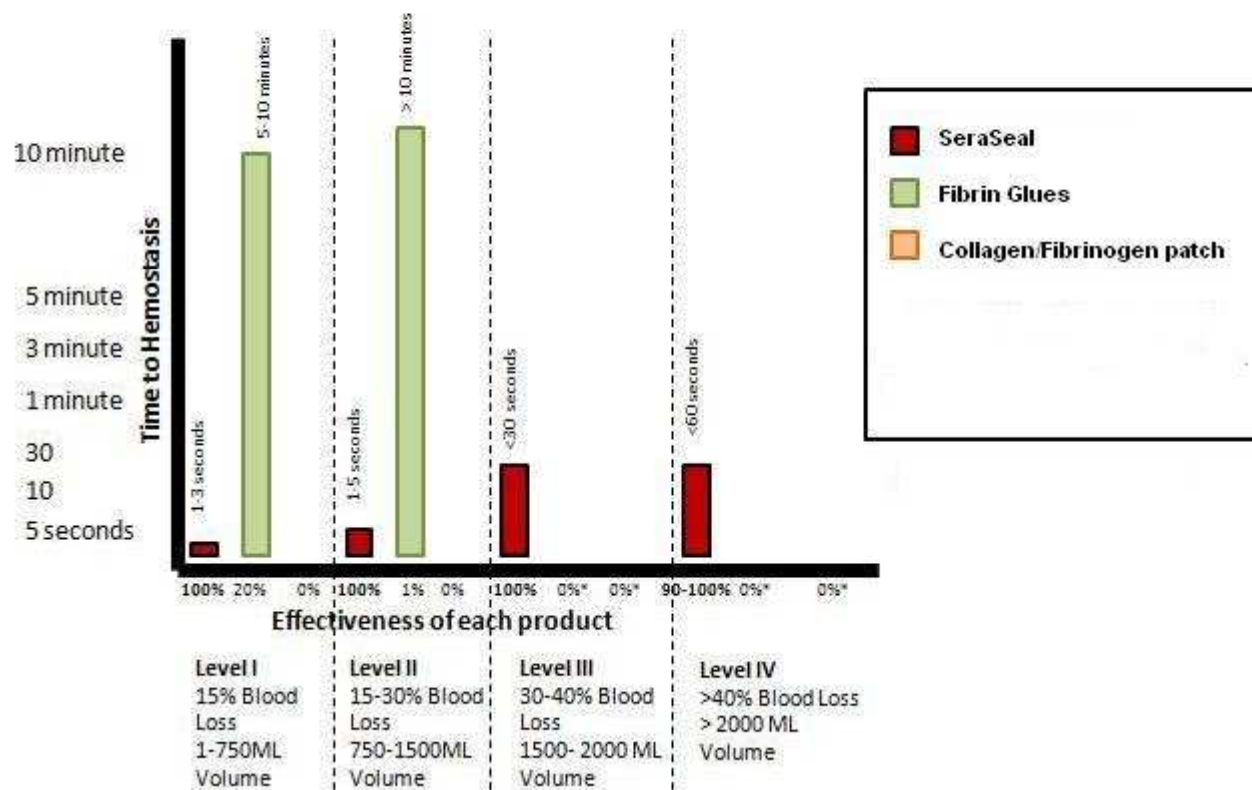
# SeraSeal Compared To Competitive Hemostatic Agents

## Overview

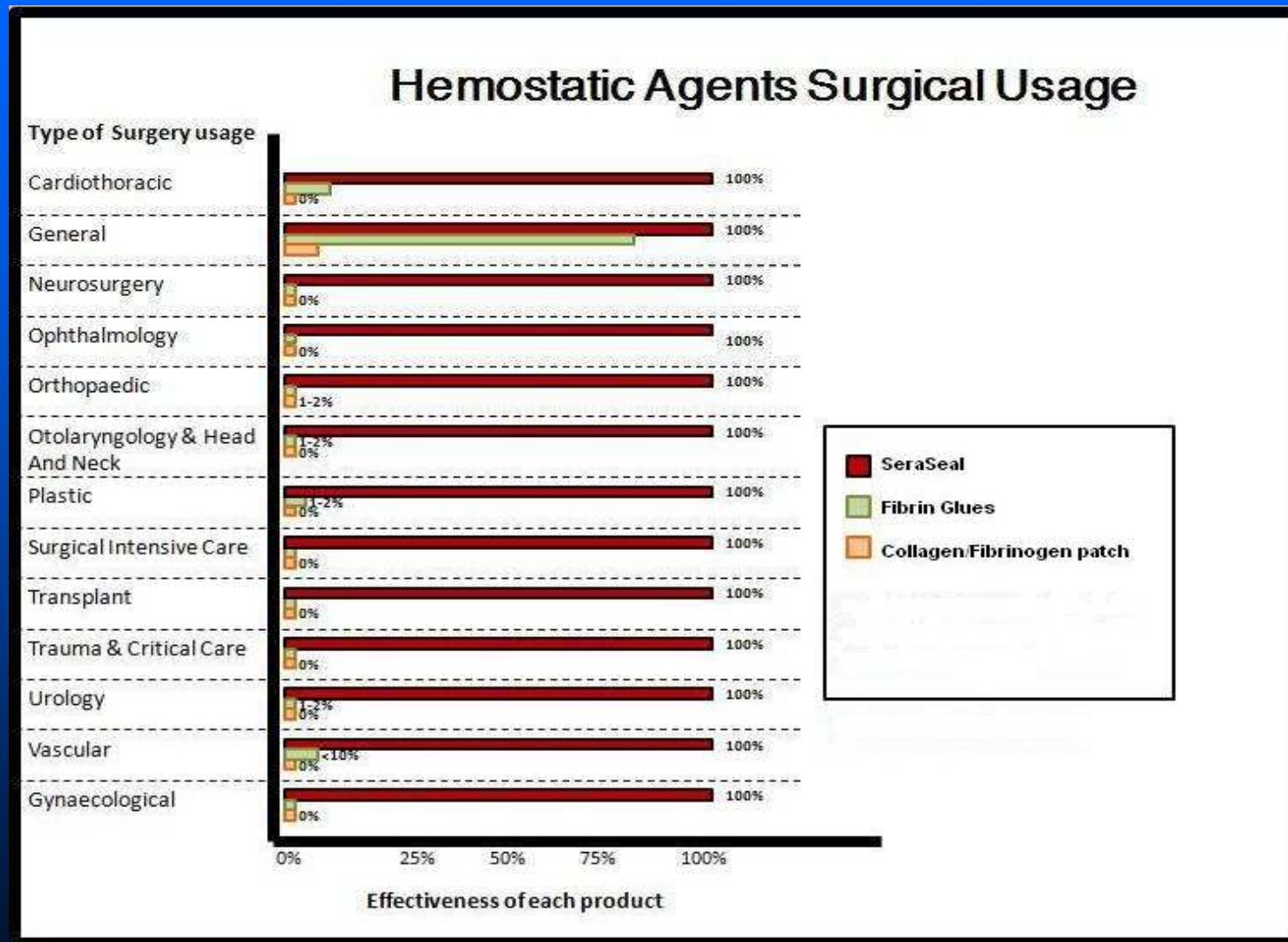
The effectiveness of SeraSeal compared to fibrin glues and collagen/fibrin patches in 4 levels of intensity of hemorrhage in normal and anticoagulant patients:



## Heparin & Coumadin Patients



## The effectiveness of SeraSeal in 13 surgical categories:







## SeraSeal Technical

In a clinical study, SeraSeal was compared to cauterization in Level II - Level IV type hemorrhages. Two hundred and thirty patients were enrolled, 214 adults and 24 children, ages 20 days - 92 years (mean 50.1 years). Out of the 238 patients enrolled, 26 were on heparin therapy (mean 279 U/Kg).

SeraSeal was significantly more effective to control bleeding in a wide range of tissues and intensity of hemorrhages, with a mean total individual bleeds of 1.59 minutes, compared to 31.22 minutes in the cauterization group ( $P=0.0001$ ). This same effectiveness was also observed in the sub-study group, anticoagulant patients, with a mean hemostatic time of 0.69 minutes compared to 10.20 minutes for the cauterized heparin patients ( $P=0.0001$ ).

Determining the magnitude of the observed effects, hemostasis and blood loss, the d type of effect of SeraSeal compared to cauterization to control bleeding was  $d=1.45$ , a large effect, which was also observed in the two subgroups studied, pediatric  $d=2.00$  and heparinized patients  $d=1.19$ . A large effect was also seen with the measurement of blood loss, with d values of 0.74, 1.35, and 1.59, respectively, for the three studied groups.

**Table: SeraSeal Technical Data Sheet**

		Hemostasis (min)		Blood Loss (ml)	
Surgery	Dosage (IU)	SeraSeal	Caut	SeraSeal	Caut
<b>Cardio-Vascular</b>					
<b>n</b>	36	36	36	36	36
<b>mean</b>	5000	1.05	9.31	350.97	747.22
<b>SD(+)</b>	2236	1.72	7.04	161.37	286.34
Aortic valve replacement					
Mitral valve replacement					
Aortocoronary bypass					
Heart transplant					
Carotid endarterectomy					
Femoro-popliteal					
Lobectomy					
Aneurismectomy					
Iliac artery replacement					
<b>Neurosurgery</b>					
<b>n</b>	11	11	11	11	11
<b>mean</b>	3818	1.00	45.91	234.54	709.09
<b>SD(+)</b>	1401	0.00	14.29	163.79	262.51
Laminectomy					
Craniotomy					

Surgery	Dosage (IU)	Hemostasis (min)		Blood Loss (ml)	
		SeraSeal	Caut	SeraSeal	Caut
Head & Neck					
n	15	15	15	15	15
mean	4456	2.00	47.67	10.20	183.33
SD(+)	2222	2.30	23.21	12.08	85.91
Thyroidectomy					
Parotidectomy					
Radical cervical resection					
Parieto-occipital resection					
Oral mucosa					
Maxillary sinus cancer					
Orthopedics					
n	7	7	7	7	7
mean	9643	4.43	54.29	77.00	1183.33
SD(+)	6053	4.04	28.78	80.04	14.09.14
Amputation					
Femoral osteomyelitis					
Hip disarticulation					
Subcondillar Hemimandibulectomy					

Surgery	Dosage (IU)	Hemostasis (min)		Blood Loss (ml)	
		SeraSeal	Caut	SeraSeal	Caut
General Surgery					
n	48	48	48	48	48
mean	3833	1.71	34.48	189.64	578.57
SD(+)	1356	2.54	15.20	294.10	547.63
Liver					
Spleen					
Pancreas					
Gastrectomy					
Cholesystectomy					
Potocaval shunt/PTFE graft					
Mesenteric-caval bypass/PTFE graft					
Appendectomy					
Whipple					
Gynecology					
n	2	2	2	2	2
mean	3000	0.66	32.50	85.00	275.00
SD(+)	0.00	0.47	17.68	91.92	106.07
Mastectomy					
Ruptured ovarian cyst					



## Normal Patient

	SeraSeal		Cauterization	
Hemostasis (min)	Adult	Pediatric	Adult	Pediatric
n	107	12	107	12
mean	1.56	1.74	28.74	51.45
SD(+)	2.42	1.08	17.72	24.70

## Blood Loss (ml)

n	107	12	107	12
mean	200.60	72.92	600.08	329.16
SD(+)	241.73	48.48	553.77	189.68

## Heparin Patients (62-400 U/Kg)

	SeraSeal	Cauterization
Hemostasis (min)		
n	24	24
mean	0.73	10.42
SD(+)	0.29	8.13

## Blood Loss (ml)

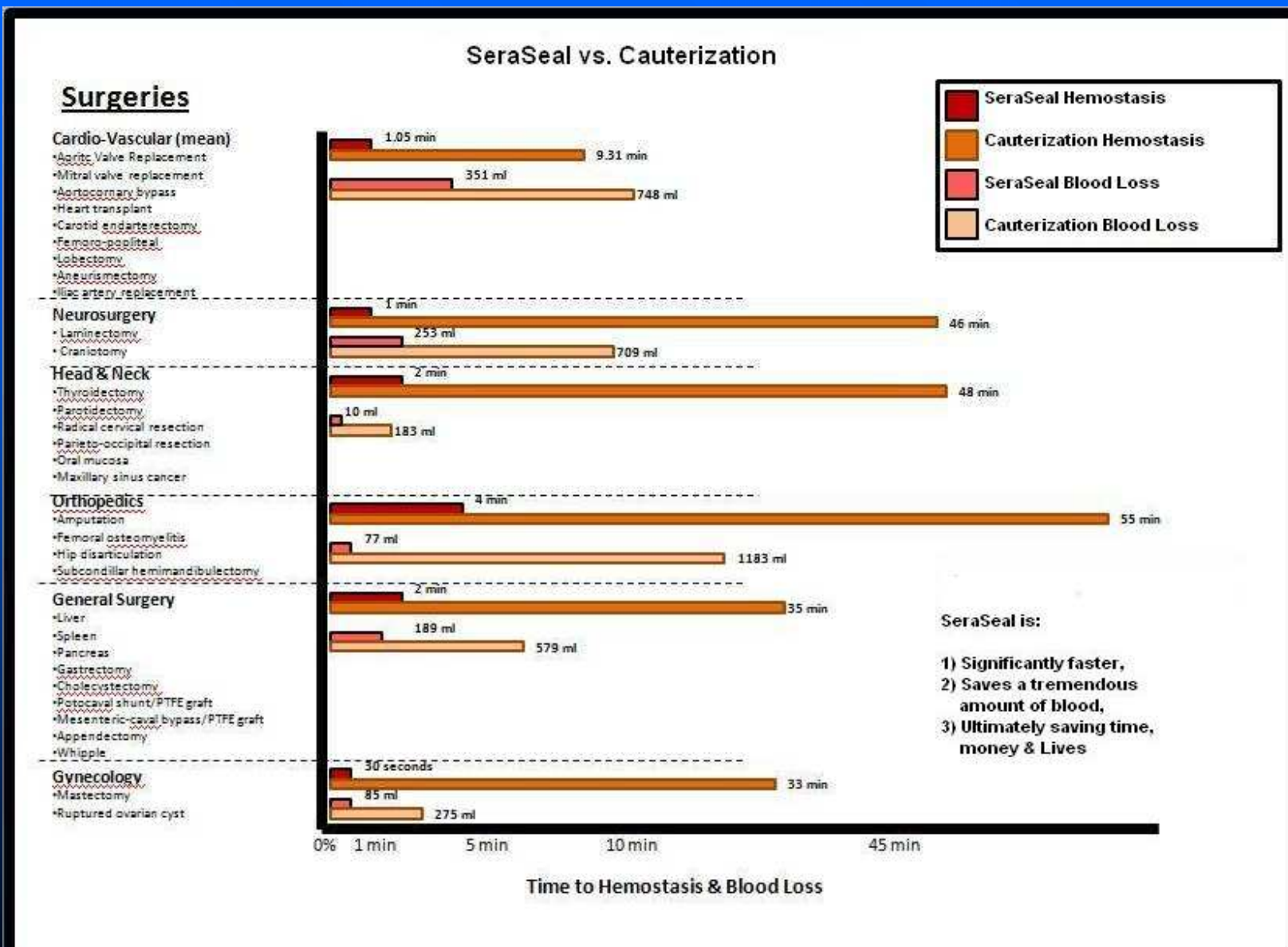
n	24	24
mean	370.00	766.67
SD(+)	133.97	251.37

Hemostasis: Total collective time of all bleeding wounds.

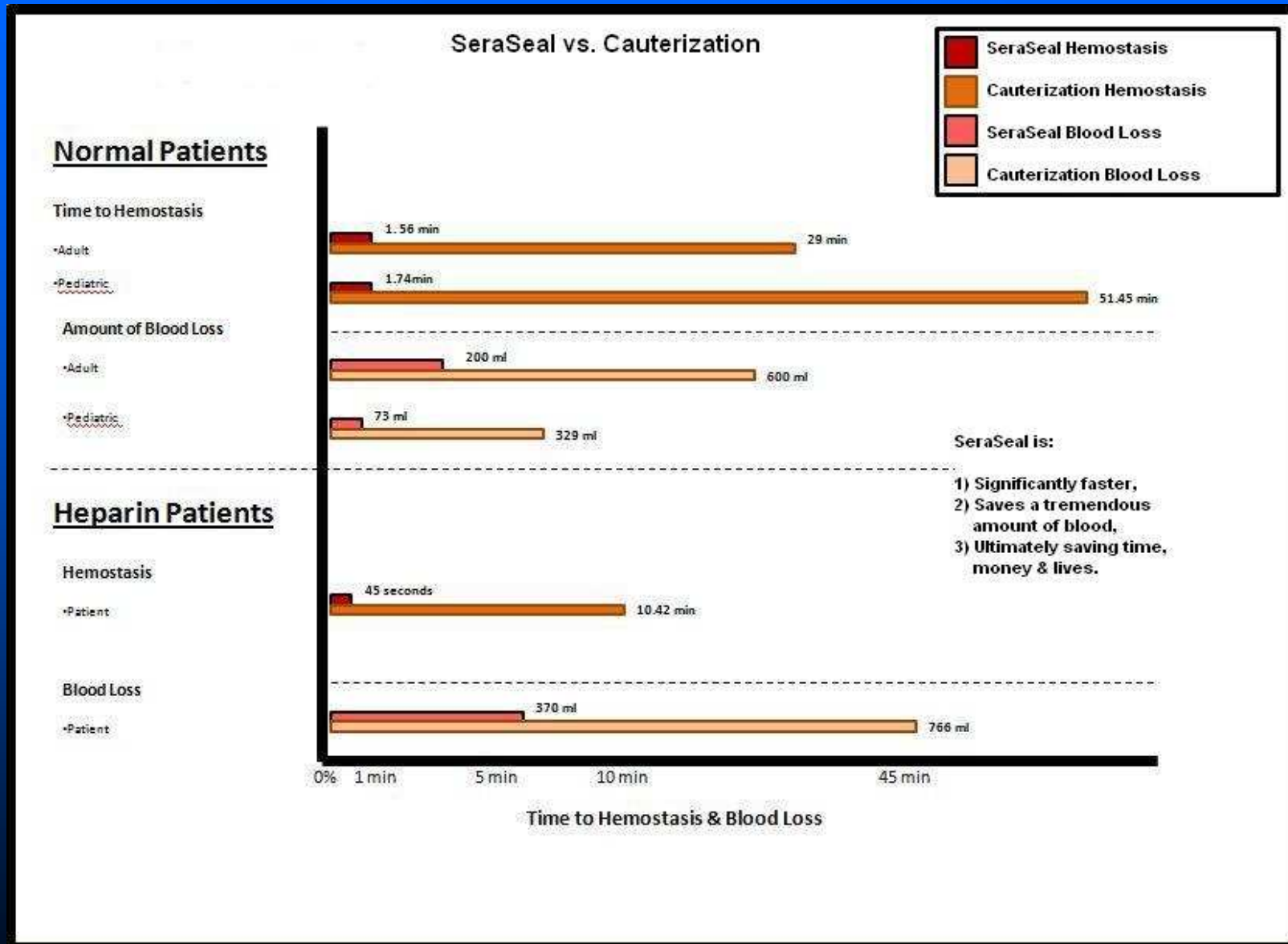
Blood Loss: Total amount of blood loss.

Cauterization: primary modality

# Graph 1: SeraSeal vs Cauterization for Hemostasis and Blood Loss in Different Surgical Categories



## Graph 2: SeraSeal vs Cauterization for Hemostasis and Blood Loss in Normal and Heparin Patients



## SeraSeal Cost Savings

The rise of health care cost has been steadily rising. Stemming this growth has become a major policy priority, as the government, employers, and consumers increasingly struggle to keep up with health care costs.

SeraSeal, unlike other hemostatic agents, does not deplete the budgetary funds but adds back other expenditures, allowing more patients to be treated on the same budget.

### Examples

Cost Savings Examples:

Assume the following:

Operating theater	\$10 / minute
Anesthesia	\$5 / minute
Blood	\$100 / minute
Pain Medication	\$2 / pill
Hospital room	\$50 / day

# Example I - Mastectomy:

STANDARD		SAVINGS	
OR	60 minutes	15 minutes	\$150.00
Anesthesia	60 minutes	15 minutes	\$75.00
Units	0	0 Units	0
Medication	15 pills	3 pills	\$6.00
Hospital Room	4 days	1 day	\$50.00
		<b>Sub Total</b>	<b>\$281.00</b>
		<b>SeraSeal Cost</b>	<b>\$65 [ 1 ml ]</b>
		<b>Total Savings</b>	<b>\$216.00</b>

Numbers presented are quite conservative. Nevertheless, they represent substantial savings to the patient, hospital or government for each surgical case.



# Example II – Hip Replacement:

STANDARD		SAVINGS	
OR	120 minutes	30 minutes	\$300.00
Anesthesia	120 minutes	30 minutes	\$150.00
Units	2-3	1 Unit	\$100.00
Medication	21 pills	3 pills	\$6.00
Hospital Room	21 days	1 day	\$50.00
		<b>Sub Total</b>	<b>\$606.00</b>
		<b>SeraSeal Cost</b>	<b>\$130 [ 2 ml ]</b>
		<b>Total Savings</b>	<b>\$476.00</b>

Numbers presented are quite conservative. Nevertheless, they represent substantial savings to the patient, hospital or government for each surgical case.

# Example III – Femoral-Popliteal Bypass:

STANDARD		SAVINGS	
OR	180 minutes	60 minutes	\$600.00
Anesthesia	180 minutes	60 minutes	\$300.00
Units	2-3	2 units	\$200.00
Medication	15 pills	3 pills	\$6.00
Hospital Room	5 days	1 day	\$50.00
		<b>Sub Total</b>	<b>\$1156.00</b>
		<b>SeraSeal Cost</b>	<b>\$130 [ 2 ml ]</b>
		<b>Total Savings</b>	<b>\$1026.00</b>

Numbers presented are quite conservative. Nevertheless, they represent substantial savings to the patient, hospital or government for each surgical case.

## SeraSeal Product Line

SeraSeal's patented one component system offers a variety of delivery systems to treat a wide range of bleeding episodes, and to provide the surgeon another tool to overcome limitations in current surgical techniques. Listed here are the different delivery systems of the product:

### ***SeraSeal*/Delivery System and Use**

All *SeraSeal* products contain the same hemostatic agent irrespective of the delivery system. Although every *SeraSeal* product can be used in the clinical setting, the rolled gauze and the foam are also available for the battlefield or areas outside the clinical setting.

*SeraSeal* will maintain >90% activity at ambient temperatures for approximately 5 days, and 30 days at refrigeration temperatures. However, to maintain long-term maximum viability we recommend storing the products at -10°C when not operational. *\*Wortham Laboratories, Inc. now has a lightweight insulated container for the SeraSeal foam that will allow it to maintain maximum activity in environments of 42°C for 15 days without refrigeration.*

### Liquid (3,000 IU/ml)

**Used for treatment of the visceral organs, particularly the spleen. Also used for lacerations, incisions, dissections, biopsies, resections, and fiber optic and catheter delivery.**

- Most surgical cases - Spleen laceration - Anastomosis - Endoscopy
- Root canals - Spinal, neurosurgery - Liver resection - Bladder tumor
- C-section - Cranio-spinal - Ophthalmology - Orthopedic surgery
- Bowel resection - Trauma - Gastric ulcers - Esophageal varices
- Diverticulitis - Colon-ovarian-prostate cancers

Lacerations or incisions: Apply *SeraSeal* to the base of the wound and work upwards. This will assure of capturing of the bleeds below the surface of the wound.

*Arterial bleeds:* apply drops in quick succession at a right angle and superiorly to the severed vessel. Each drop will cascade around the wound allowing *SeraSeal* to clot the outer diameter working inward. With each drop the opening of the wound becomes smaller until it is sealed; which in most cases occurs within 10 seconds.

*Note:* using an excess amount of *SeraSeal* will not harm the patient, but only waste of the product. When too much *SeraSeal* is applied after the clot is formed it will wash the erythrocytes off the clot giving an illusion that blood is still oozing. Hemostasis can be observed when the blood becomes a brighter red in appearance.

<u>Product No.</u>	<u>Description</u>	<u>Packaged</u>
4003-1-1	SeraSeal, 1 ml vial	each
4003-1-2	SeraSeal, 2.5 ml vial	each
4003-1-3	SeraSeal, 5 ml vial	each



## **Atomizer Spray (3,000 IU/ml)**

*SeraSeal* spray delivery system utilizes an atomizer to create a nebulizing effect. The atomizers are malleable and they retain their shape. The atomizer is offered in four lengths: 4 cm, 11 cm, 22 cm, and 35 cm for laparoscopy procedures. Examples of applications for the different length atomizers are provided below.

### **4 cm Atomizer**

- Burn debridement
- Abrasions
- Plastic surgery
- Mastectomies
- Amputations
- Epistaxia
- Polyps
- Deviated septum
- Nose fractures
- Scalp
- Spinal/Neurosurgery

### **11 cm Atomizer**

- Tonsillectomy
- Thyroidectomy
- Lingual tumors
- Periodontal
- Prostheodontial
- Extractions
- Oral surgery
- Hard to reach areas

### **22 cm Atomizer**

- Post partum hemorrhage
- Larynx
- Esophagus
- Fibroid tumors
- Ectopic pregnancy
- D & C
- TURPS
- Lyposuction
- Hard to reach areas

### **35 cm Atomizer**

- Laparoscopy



**Product No.   Description**

**Packaged**

4003-2-1   SeraSeal, 1 ml vial/4 cm atomizer/syringe   each  
4003-2-2   SeraSeal, 2.5 ml vial/4 cm atomizer/syringe   each  
4003-2-3   SeraSeal, 5 ml vial/4 cm atomizer/syringe   each



4003-3-1   SeraSeal, 1 ml vial/11 cm atomizer/syringe   each  
4003-3-2   SeraSeal, 2.5 ml vial/11 cm atomizer/syringe   each  
4003-3-3   SeraSeal, 5 ml vial/11 cm atomizer/syringe   each



4003-4-1   SeraSeal, 1 ml vial/22 cm atomizer/syringe   each  
4003-4-2   SeraSeal, 2.5 ml vial/22 cm atomizer/syringe   each  
4003-4-3   SeraSeal, 5 ml vial/22 cm atomizer/syringe   each



4003-7-1   SeraSeal, 1 ml vial/35 cm atomizer/syringe   each  
4003-7-2   SeraSeal, 2.5 ml vial/35 cm atomizer/syringe   each  
4003-7-3   SeraSeal, 5 ml vial/35 cm atomizer/syringe   each



## Foam (8,000 IU/ml)

**Used for closed cavity hemorrhages or pockets of tissue that can contain the foam.**

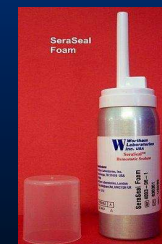
- Gun shot wounds
- Stabbings
- Deep lacerations
- Impalements
- Eviscerations

The foam comes in a 30 ml canister with a 1" or 2" nozzle. **Note: apply the foam into a cavity or pocket where the foam can be contained. Do not apply the foam onto a flat surface. This will cause the foam to be sluffed off.** When sprayed into a closed cavity or pocket the foam begins to turn into a liquid within 10 seconds and "trickles" down throughout the tissue. The foam is designed to do this for approximately 10 minutes, which enables it to achieve hemostasis on follow-on bleeders, which typically occur during vigorous patient manipulation and transportation. Ideally, when applying the foam into a pocket start at the base of the wound and work upwards.

**Product No.**  
4003-8-1

**Description**  
SeraSeal, foam

**Packaged**  
each



## **Battlefield Dressing (5,000 IU, 50 IU/cm<sup>2</sup>)**

**Used for packing wounds, deep lacerations and amputations.**

The entire rolled gauze is impregnated with *SeraSeal* and comes in 1 m, 2 m, and 3 m. rolls. Packets can be vacuum-sealed upon request. The material is identical in look and feel to Kerlix® rolled gauze.

Visualize the point of bleeding origin, if possible. Pack the dressing at the point of origin, tightly against a bone or muscle, to assure pressure is being applied to the blood vessel. If dressing is applied outside the clinical setting, do not remove dressing. Transport immediately. To remove dressing, apply water or saline to avoid removing clot.

<b><u>Product No.</u></b>	<b><u>Description</u></b>	<b><u>Packaged</u></b>
4003-10-1	SeraSeal, 10 x 99 cm battlefield dressing	each
4003-10-2	SeraSeal, 10 x 198 cm battlefield dressing	each
4003-10-3	SeraSeal, 10 x 297 cm battlefield dressing	each



**Trauma Dressing (5,000 IU, 50 IU/cm<sup>2</sup>)**  
**(Available Soon)**

Used for all forms of trauma to include amputations and deep lacerations. Press dressing to the wound for 60 seconds. If bleeding should continue, reapply with a fresh or unused portion of the dressing and apply pressure for another 60 seconds. To avoid removing the clot, wet dressing with water or saline, if necessary.

**Surgical Sponge (1,000 IU, 10 IU/cm<sup>2</sup>)**  
**(Available Soon)**

Used for minor to moderate hemorrhages in lacerations, incisions and dialysis. Press dressing to the wound for 10-30 seconds for minor wounds, and 30-60 seconds for moderate wounds. Avoid removing the clot by wetting the dressing with water or saline.

**Swab (100 IU)**  
**(Available Soon)**

Used for minor bleeds and distal applications to include tympanic surgery. Press the cotton tip to the wound for 10-30 seconds. Avoid removing the clot.

**Bandage Strip (100 IU)**  
**(Available Soon)**

Used for minor cuts and abrasions.  
Wash the wound and dry the area before covering it with the bandage strip.