



Topical Hemostatic Agents in Minimally Invasive Surgery: A Team Approach

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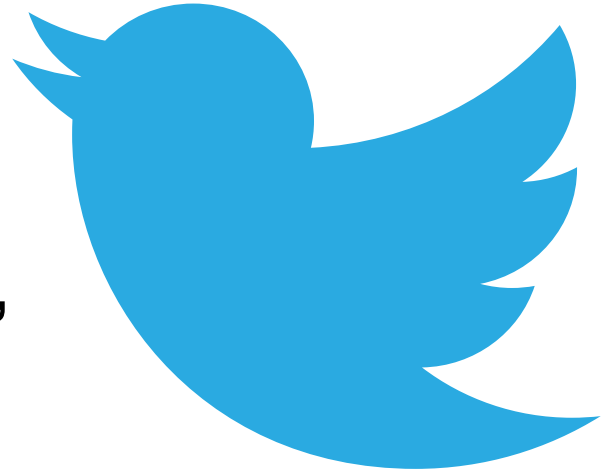
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Part 1

Topical Hemostatic Agents in MIS

Julia Park, MD



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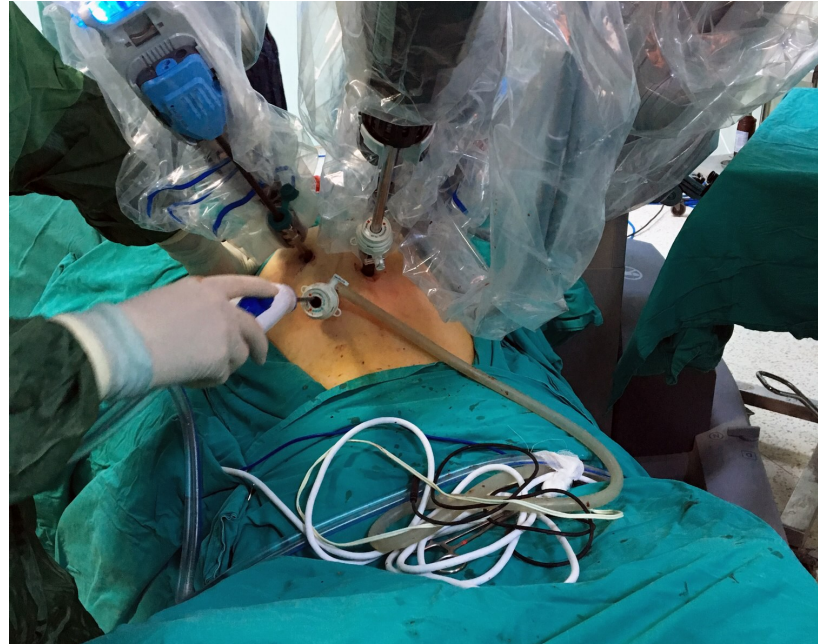
Learning Objective 1

Evaluate the role of topical hemostatic agents in minimally invasive surgical (MIS) procedures.

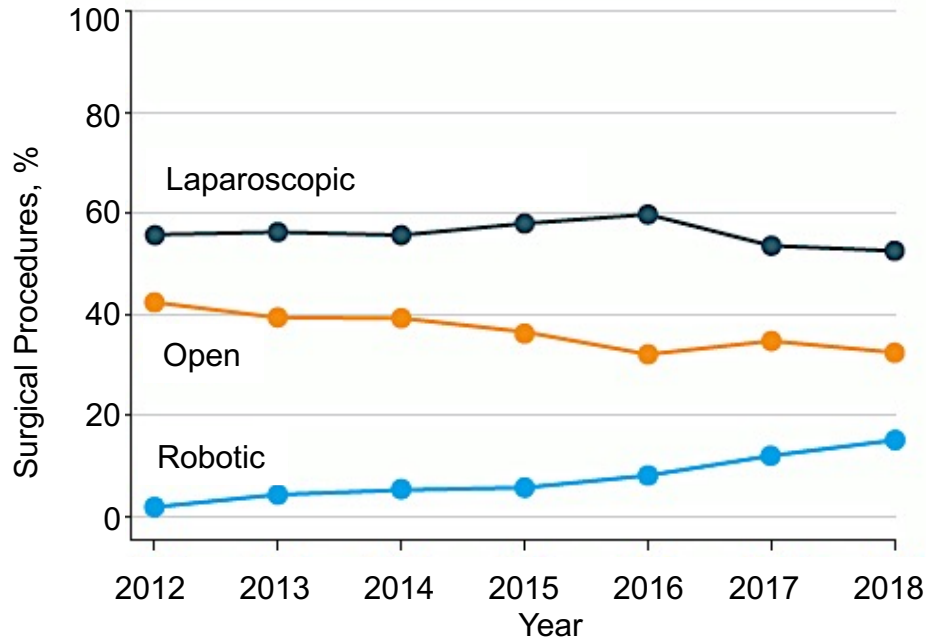


Hemostatic Modalities in Surgery

- Critical to the success of surgical interventions
- Mitigates blood loss and need for transfusions
- Has evolved to facilitate MIS, including robotic surgery



Trends in MIS and Open Surgery



No. at risk: 18527 20978 23475 16588 32050 38689 19097

- Cohort study using clinical registry data from Michigan 2012-2018
- Study determined how procedural approaches evolved with the initiation of robotic surgery
- Cohort included 169,404 patients at 73 hospitals
- Procedures included inguinal hernia repair, ventral hernia repair, colectomy, reflux surgery, proctectomy, cholecystectomy, and complex cancer resections

Methods to Achieve Hemostasis in Surgery

Method	Examples
Mechanical	Direct pressure Fabric pads/gauze sponges/sponges Sutures/staples/ligating clips
Thermal/energy-based	Electrocautery Ultrasonic device Lasers
Pharmacologic	Epinephrine, vitamin K, protamine, desmopressin, lysine analogues
Topical hemostatic agents	Mechanical (e.g., cellulose-based products, gelatin-based products) Active (e.g., thrombin-based products) Flowables Fibrin sealants

Challenges in Hemostasis for MIS



- Access ports limited in diameter; restrict size of tamponade products
- Some agents friable and adhere to access ports upon insertion
- Some products may stick to adjacent tissue as the surgeon attempts to position them
- Spray-type products may disperse rather than adhere to local area
- Difficult to access and difficult to visualize operative sites

Topical Hemostatic Agents in MIS

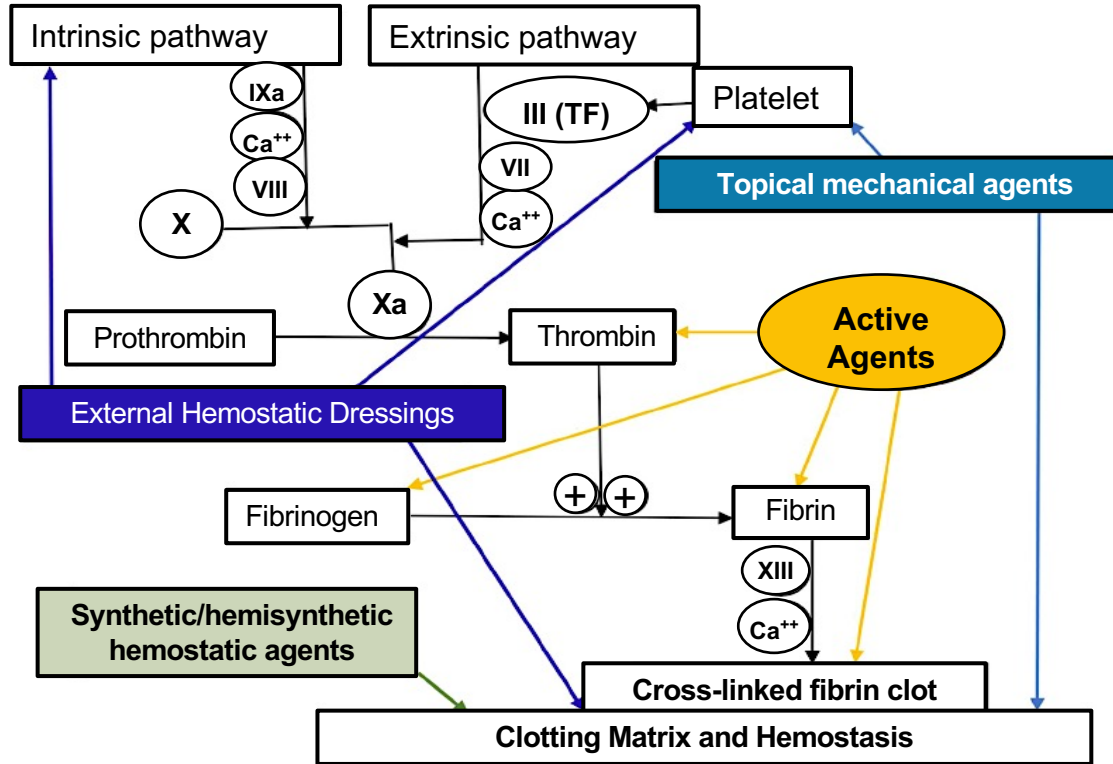
- **Topical adjuvants** (e.g., pre-rolled sponges)
- **Gelatin preparations** (sometimes with thrombin to directly act on the clotting cascade)
- **Collagen products** (multiple available, contact activation stimulates clotting cascade)
- **Cellulose-based products** (absorbable hemostats derived from wood pulp – swells when contacting liquid; provides a scaffold for platelet and clotting factor interaction)
- **Fibrin sealants** (multicomponent products with hemostatic and adhesive properties)
- **Recombinant activated factor VII** (thought to act by binding to tissue factor at site of endothelial damage, amplifying clotting cascade)

Topical Hemostatic Products by Category

Category	Product Examples
Mechanical Vary in composition and include bovine collagen, porcine gelatin, oxidized cellulose, polysaccharide spheres	Gelfoam [®] , Surgifoam [®] , Avitene [™] sheets and collagen sponges, HELISTAT [®] & HELITENE [®] , INSTAT [®] MCH, Surgicel [®] , Surgicel Fibrillar [™] , Surgicel SnOW [™] , Surgicel Nu-Knit [®] , Arista [®] AH, Hemostase MPH [®] , Vitasure [™]
Active Derived from bovine, pooled human thrombin, or recombinant thrombin	Thrombin-JMI [®] , Evithrom [®] , Recothrom [®]
Flowable Gelatin granules crosslinked into a matrix for use with or without thrombin	Floseal [®] , Surgiflo [®] GEL-FLOW [™] NT
Fibrin sealant Combination of thrombin, fibrinogen, and sometimes other components	Beriplast [®] , TachoSil [®] , Tisseel [™] , Artiss, Vistaseal [™] , Vitagel [™] , Vivostat [®]

Adapted from Corral M, et al. *Clinicoecon Outcomes Res.* 2015;7:409-421.; UpToDate. Wolters Kluwer Website. 2021. www.uptodate.com. Accessed December 5, 2021.
Product Information: U.S. Food and Drug Administration (FDA): Vaccines, Blood, and Biologics. FDA Website. 2021. <https://www.fda.gov/vaccines-blood-biologics>. Accessed December 5, 2021.; U.S. Food and Drug Administration (FDA): Production Information: Devices. FDA Website. 2021. <http://www.fda.gov/medical-devices>. Accessed December 5, 2021.

Effects of Topical Hemostatic Agents on the Coagulation Cascade



Note: external hemostatic dressings (e.g., QuickClot[®]) and synthetic hemostatic agents (e.g., Dermabond[®]) are largely for trauma-induced and open-wound bonding and not within purview of MIS discussion.

Conditions Treated With MIS/Robotic Surgery and Topical Hemostatic Agents (Partial List)

Specialty	Conditions
General	Hernias, liver tumors, gallbladder cancer, severe GERD, obesity (gastric bypass, bariatric surgery, gastric banding), GI/rectal conditions, pancreatic cancer and benign lesions
Cardiac	Mitral valve prolapse and repair, atrial septal defect, atrial fibrillation, aortic regurgitation, aortic insufficiency, aortic stenosis
Gynecologic	Endometriosis, gynecologic cancers (ovarian/cervical), heavy uterine bleeding, uterine fibroids, uterine prolapse and repair, ovarian cysts, benign cervical disorders
Head and neck	Skull base brain tumors, anterior cranial fossa tumors, posterior cranial fossa tumors, oropharyngeal cancer, thyroid cancer
Neurosurgery/ spine	Spine conditions, cervical disc hernias, lumbar disc hernias, degenerative disc disease, spinal trauma
Urologic conditions	Bladder cancer, kidney stones, kidney cysts, kidney cancer, kidney removal, prostate cancer, incontinence, vaginal prolapse

GERD = Gastroesophageal reflux disease. GI = Gastrointestinal.

Johns Hopkins Medicine Website. https://www.hopkinsmedicine.org/minimally_invasive_robotic_surgery/types.html. Accessed December 1, 2021.

Types of Bleeding Manageable With Various Topical Hemostatic Agents



- From diffuse raw surfaces with a multitude of bleeding points
- Close to the bone
- Cancellous (spongy) bone bleeding
- Around delicate structures, including nerves
- In inaccessible locations
- Needle-hole bleeding

Indications for Topical Hemostatic Agents

Mechanical Topical Hemostats (representative list)

	Hemostatic or adjunctive hemostatic device in surgical procedures	When control of capillary, venous, and/or arteriolar bleeding by pressure, ligature, or other conventional procedures is ineffective or impractical	Includes procedures with cancellous bone bleeding	Although not necessary, can be used either with or without thrombin	Excludes neurologic surgical procedures	Excludes ophthalmic surgical procedures	Saturate with sterile sodium chloride solution
ARISTA™ AH	✓	✓			✓	✓	
AVITENE™	✓	✓					
GELFOAM®	✓	✓	✓	✓			✓
SURGICEL®	✓	✓					
SURGIFOAM®	✓	✓		✓		✓	✓

U.S. Food and Drug Administration (FDA): Vaccines, Blood, and Biologics. FDA Website. 2021. <https://www.fda.gov/vaccines-blood-biologics>. Accessed December 5, 2021.;

U.S. Food and Drug Administration (FDA): Production Information: Devices. FDA Website. 2021. <http://www.fda.gov/medical-devices>. Accessed December 5, 2021.

Indications for Topical Hemostatic Agents

Active Topical Thrombin (representative list)

	As an aid to hemostasis whenever oozing blood and minor bleeding from capillaries and small vessels is accessible and control of bleeding by standard surgical techniques (suture, ligature, cautery) is ineffective or impractical	May be used in conjunction with an absorbable gelatin sponge
EVITHROM®	✓	✓
RECOTHROM®	✓	✓
THROMBIN-JMI®	✓	✓

Indications for Topical Hemostatic Agents

Flowables (representative list)

	For surgical procedures (other than ophthalmic) as an adjunct to hemostasis when control of bleeding by ligature or other conventional methods is ineffective or impractical	Mix with sterile saline or thrombin solution	Including surgical procedures involving cancellous bone bleeding
FLOSEAL®	✓	✓	
SURGIFLO®	✓	✓	
GEL-FLOW™ NT	✓	✓	✓

Indications for Topical Hemostatic Agents

Fibrin Sealants (representative list)

	As an adjunct to hemostasis for mild to moderate bleeding in adults undergoing surgery when control of bleeding by standard surgical techniques (such as suture, ligature, and cautery) is ineffective or impractical. Effective in heparinized patients.	Hemostasis: For use as an adjunct to hemostasis in adult and pediatric patients (> 1 month of age) undergoing surgery when control of bleeding by conventional surgical techniques (such as suture, ligature, and cautery) is ineffective or impractical. Effective in heparinized patients	Sealing: For use as an adjunct to standard surgical techniques (such as suture and ligature) to prevent leakage from colonic anastomoses following the reversal of temporary colostomies
VISTASEAL™	✓		
TISSEEL™		✓	✓


Approximate Absorption Times for Topical Hemostatic Agents

Agent	Source	Form	Absorption Time
Oxidized regenerated cellulose (e.g., Surgicel)	Plant	Woven mesh or powder	1-2 weeks
Microfibrillar collagen (e.g., Avitene)	Bovine	Sponge or powder	8-12 weeks
Microporous polysaccharide hemospheres (e.g., Arista)	Plant	Powder	48 hours
Gelatin matrix (e.g., Gelfoam, Surgifoam)	Porcine	Sponge or powder	4-6 weeks
Thrombin (e.g., Thrombin-JMI, Evithrom, Recothrom)	Various	Reconstituted powder, frozen liquid	Immediate
Thrombin + Gelatin granules [flowables] (e.g., Surgiflo, Floseal)	Bovine-derived gelatin matrix; thrombin	Liquid	4-6 weeks
Fibrin sealant (e.g., Tisseel, Vistaseal)	Human	Frozen liquid (spray)	Immediate

Pennington KP, Dunivan G. *Obstet Gynecol.* 2020;136(4):e81-e89. U.S. Food and Drug Administration (FDA): Vaccines, Blood, and Biologics. FDA Website. 2021. <https://www.fda.gov/vaccines-blood-biologics>. Accessed December 5, 2021.; U.S. Food and Drug Administration (FDA): Production Information: Devices. FDA Website. 2021. <http://www.fda.gov/medical-devices>. Accessed December 5, 2021.

Faculty Discussion





Part 2

Preparing Topical Hemostatic Agents for Use

Michelle Olivo, BSN, RN, CNOR

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Learning
Objective **2**

Prepare topical hemostatic agents in the operating room environment for use in MIS.



Collaborative Planning and Coordination



- Interprofessional team: surgeons, anesthesiologists, nurses, technologists (varies depending upon type of surgery, clinical condition of patient)
- Responsibilities in OR include:
 - Maintenance of sterile environment
 - Coordination of patient care
 - Anticipation of equipment needs

Preparing Topical Hemostatic Agents: General Considerations

- Ensure safe management of the sterile field
- Follow manufacturer's instructions for specific storage, preparation, application instructions, safety considerations
- Before providing agent to the sterile field, check expiration date, inspect product for sterility compromise, transfer to the sterile field using aseptic technique



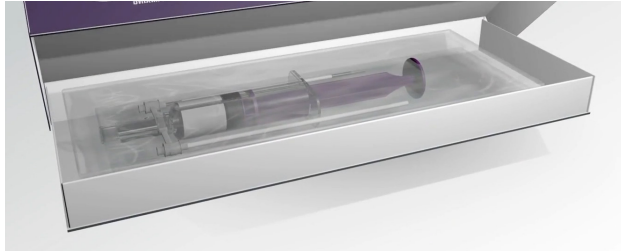
Preparing Mechanical “Out of the Box” Hemostatic Agents for Surgery

- Surgicel
 - Original
 - Fibrillar
 - SNoW
 - Nu-Knit
- Provides a physical matrix for clot initiation
- These topical hemostats can be cut to size for use in MIS procedures

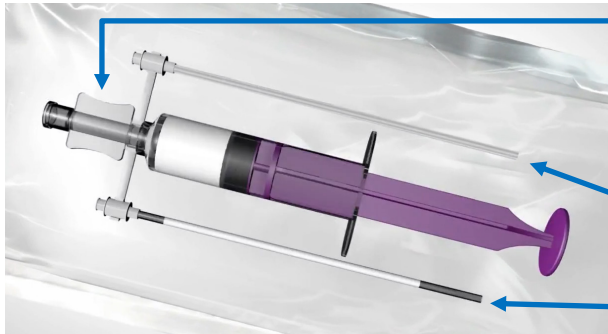


U.S. Food and Drug Administration (FDA): Vaccines, Blood, and Biologics. FDA Website. 2021. <https://www.fda.gov/vaccines-blood-biologics>. Accessed December 5, 2021.; U.S. Food and Drug Administration (FDA): Production Information: Devices. FDA Website. 2021. <http://www.fda.gov/medical-devices>. Accessed December 5, 2021.

Preparing a Flowable Hemostatic Agent



- GEL-FLOW NT sterile prefilled syringe in an inner sterile pouch
- Syringe contains 550 milligrams of prefilled sterile absorbable gelatin powder



- Pre-attached connector port
- Two applicator tips for delivery of the flowable mixture to deep and narrow administrative sites
 - Clear rigid tip
 - White malleable tip

Also needed (not included): 5 mL of sterile saline or thrombin solution and one 10 mL sterile syringe with luer lock.

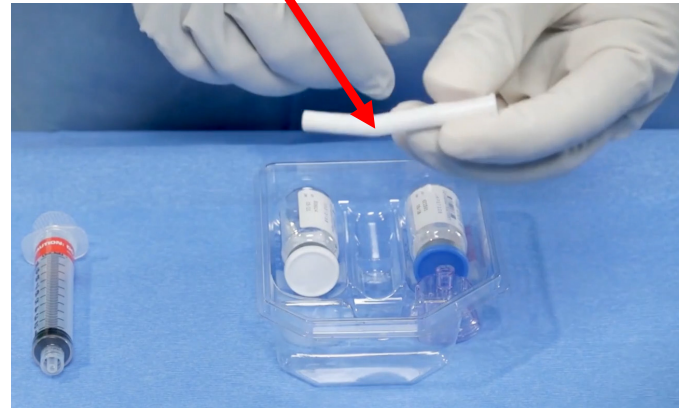
mL = milliliter.

GEL-FLOW™ NT (absorbable gelatin powder hemostatic matrix for flowable applications). New York, NY: Pfizer Inc.; 2021. <https://labeling.pfizer.com/ShowLabeling.aspx?id=10493>. Accessed December 5, 2021. Images: GEL-FLOW NT Preparation Video. Pfizer Website. <https://gelflow.pfizerpro.com/dosing-administration/gel-flow-nt-preparation-video>. Accessed December 5, 2021.

GEL-FLOW NT with Thrombin-JMI 5000 IU Syringe Spray Kit



- One vial Thrombin-JMI 5000 IU
- 5 mL sterile saline diluent
- 10 mL sterile syringe with luer lock and a transfer device
- Spray tip (Note: discard: not for use with GEL-FLOW NT)



IU = International units.

Images: GEL-FLOW NT Preparation Video. Pfizer Website. <https://gelflow.pfizerpro.com/dosing-administration/gel-flow-nt-preparation-video>. Accessed December 5, 2021.

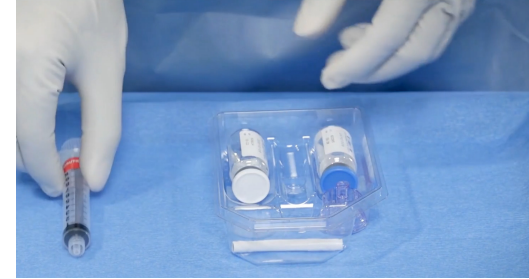
Preparing GEL-FLOW NT With Thrombin-JMI 5000 IU Syringe



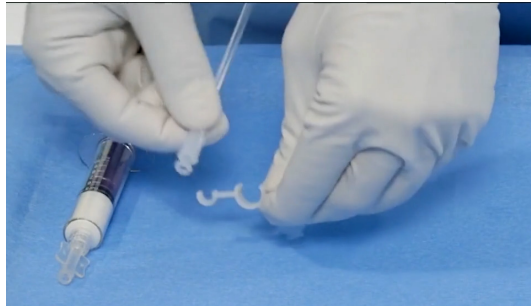
1. Open box, remove contents.



2. Open outer package and deliver sterile inner pouch to the sterile field.



3. Remove outer lid of thrombin JMI kit and transfer inner tray to sterile field; remove contents. (Discard spray tip.)



4. Open the GEL FLOW NT sterile inner pouch and remove the contents.

Images: GEL-FLOW NT Preparation Video. Pfizer Website. <https://gelflow.pfizerpro.com/dosing-administration/gel-flow-nt-preparation-video>. Accessed December 5, 2021.

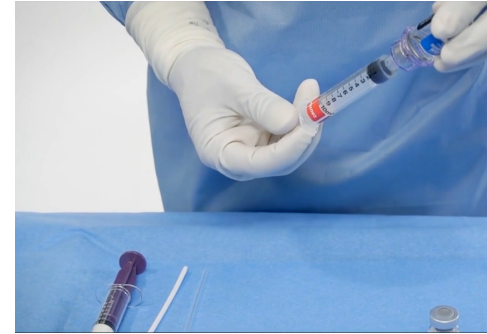
Both Products Within Sterile Field



Image: GEL-FLOW NT Preparation Video. Pfizer Website. <https://gelflow.pfizerpro.com/dosing-administration/gel-flow-nt-preparation-video>. Accessed December 5, 2021.

First, Prepare Thrombin-JMI

5. Use GEL-FLOW NT sterile syringe with transfer device to draw 5 mL of saline diluent from the vial into the syringe.



6. Inject all 5 mL of saline diluent into the Thrombin-JMI vial from the syringe to reconstitute the thrombin powder.



Preparing Thrombin-JMI (cont'd)

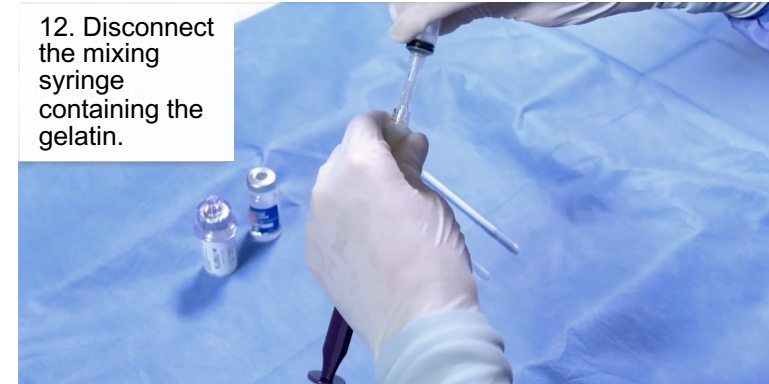
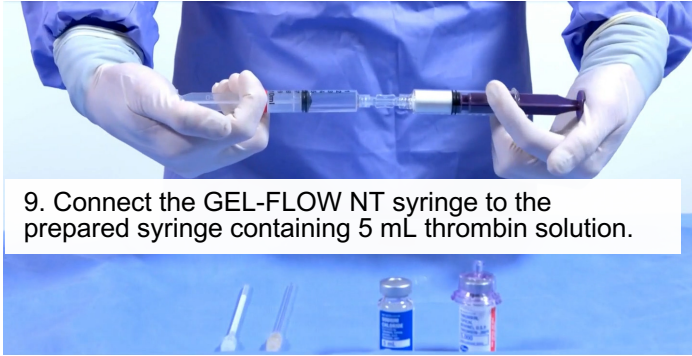
7. When the thrombin powder is completely dissolved, draw the thrombin solution back into the syringe.



8. Then, remove syringe from the transfer device by turning the syringe counterclockwise.



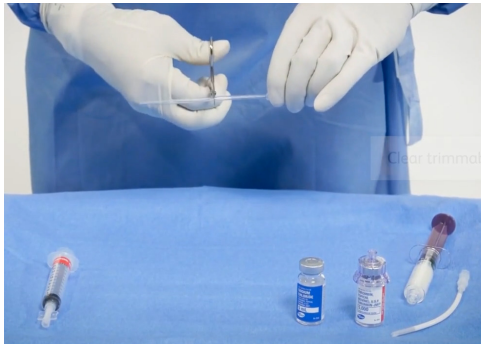
Next, Connect the Gelatin Syringe to the Thrombin Syringe



Attach Either the Malleable Tip or the Clear Rigid Tip



Malleable tip
(white)



Clear, rigid tip
(cut to size, if
needed with
square angle to
avoid creating
sharp tip)

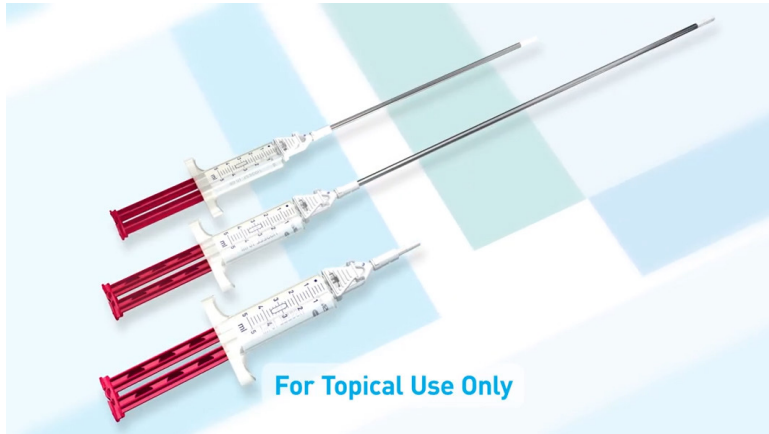
- Product is now ready for immediate use
- Remains usable for up to 3 hours
- Intended for single use only
- Resulting mixture may be smeared, filled, or pressed against the bleeding surface



Preparing a Fibrin Sealant

Tisseel Pre-Filled Syringe

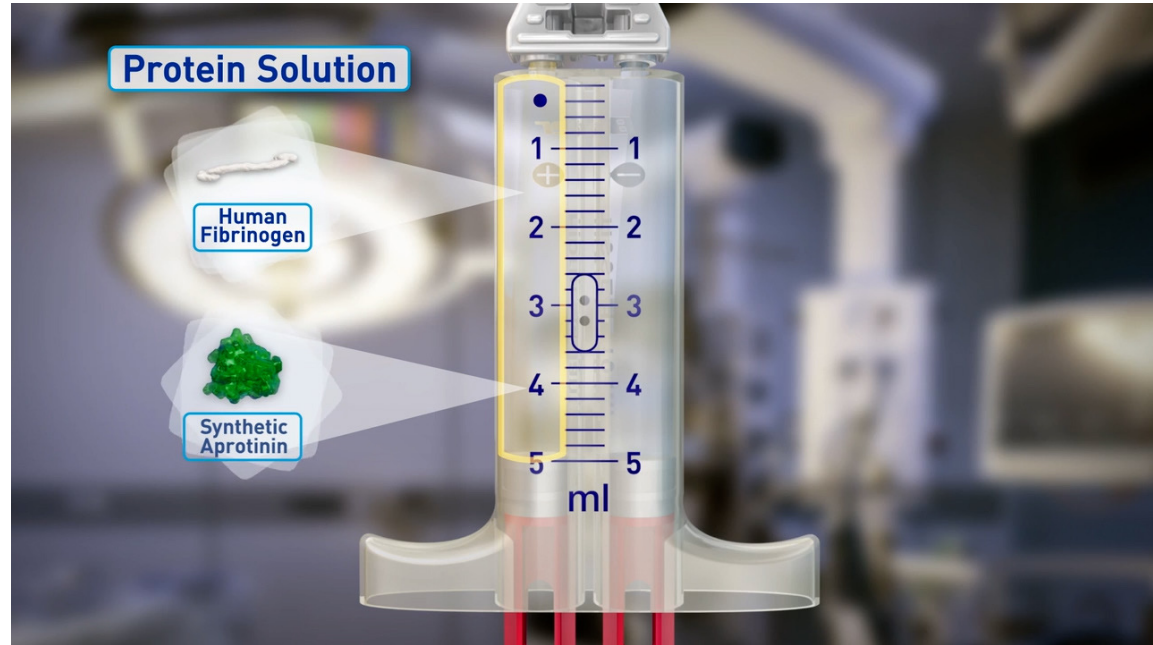
- 2 component fibrin sealant
- Gasless tip applicator propels spray through grip force alone, eliminating need for pressurized gas source
 - Broad spray or drip



Preparing a Fibrin Sealant (cont'd)

2-component fibrin sealant:

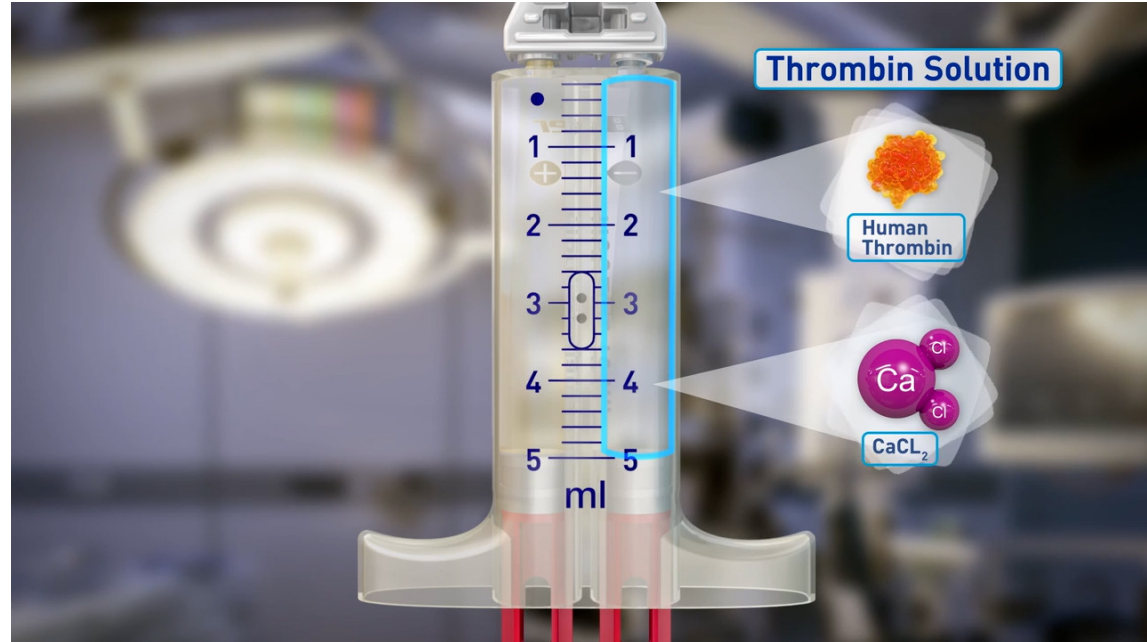
1. Protein solution contains human fibrinogen and synthetic aprotinin



Preparing a Fibrin Sealant (cont'd)

2-component fibrin sealant:

2. Thrombin solution includes human thrombin in calcium chloride



Preparing a Fibrin Sealant (cont'd)



- Prefilled product comes frozen in 2 mL, 4 mL, and 10 mL syringes (there is also a freeze-dried kit version that requires reconstitution)
- Thaw to body temperature in a sterile water bath (5 minutes for 2 mL and 4 mL product; 10 minutes for 10 mL)

Preparing a Fibrin Sealant (cont'd)



- Snap and lock together syringe and gasless tip

Preparing a Fibrin Sealant (cont'd)

Various tips
accommodate
MIS and
endoscopy




Preparing a Fibrin Sealant (cont'd)

Also available:
Tisseel gas-assisted
spray



Faculty Discussion





Part 3

Applying Topical Hemostatic Agents in MIS

Patricia C. Chui, MD, PhD

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Learning
Objective **3**

Implement strategies to control bleeding in MIS using topical hemostatic agents.



Choosing a Topical Hemostatic Agent

- Factors to consider
 - Type of surgery
 - Amount and location of bleeding
 - Availability of agent
 - Cost considerations
 - Surgeon preference

Choices in Surgical Scenarios

- **Pulsatile needle hole bleeding in vessel adventitia or vascular graft material**
 - Apply microporous polysaccharide spheres (Arista)
 - Apply thrombin-soaked gelatin foam (Gelfoam, Surgifoam) or oxidized regenerated cellulose (Surgicel)
 - Apply gelatin matrix-thrombin combination (FloSeal, Surgiflo, Gel-Flow NT)
 - Spray a fibrin sealant (Tisseel, Vistaseal)

Choices in Surgical Scenarios (cont'd)

- **Spleen, liver, kidney parenchymal surface post-trauma or partial resection**
 - Wrap with oxidized regenerated cellulose (e.g., Surgicel) or microfibrillar collagen (Avitene Ultrawrap) with or without suture fixation
 - Apply microporous polysaccharide spheres (e.g., Arista) and hold sponge pressure for several minutes
 - Spray with thrombin
 - Apply gelatin matrix-thrombin combination (e.g., FloSeal, Surgiflo, Gel-Flow NT)
 - Spray fibrin sealant (e.g., Tisseel, Vistaseal)

Choices in Surgical Scenarios (cont'd)

- **Venous or capillary oozing from area of dissection or deserosalization**
 - Apply oxidized regenerated cellulose (e.g., Surgicel Nu-Knit, Surgicel Fibrillar)
 - Apply microporous polysaccharide spheres (e.g., Arista) and hold sponge pressure for several minutes
 - Spray with thrombin
 - Spray with a fibrin sealant (e.g., Tisseel, Vistaseal)
- **Cancellous bone bleeding**
 - Apply Gelfoam
 - Apply GEL-FLOW NT

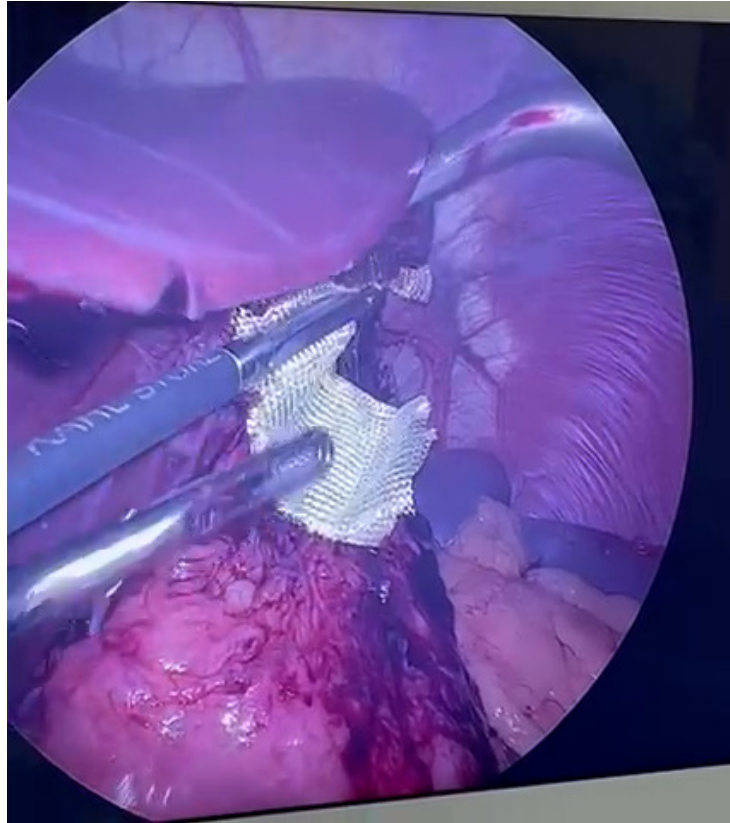
Potential Adverse Effects Associated With Topical Hemostatic Agents

Agent	Brand Name(s)	Adverse Effect
Absorbable gelatin (gelatin matrix)	Gelfilm, Gelfoam, Surgifoam, Gelfoam hemostasis kit (also contains human thrombin)	Infection, abscess or granuloma formation, fibrosis, clot disruption if sponge is removed
Oxidized regenerated cellulose	Actifoam, Avitene (Ultrafoam), Endo Avitene, Instat MCH, Helistat & Helitene, Syringe Avitene	Granuloma formation, allergenic
Microporous polysaccharide spheres (MPH)	Arista AH	Use of > 50g can alter glucose load in patients with diabetes
Topical thrombin (bovine, human, recombinant human)	Thrombin-JMI, Evithrom, Recothrom	Intravascular application leads to thrombosis; antibody formation against bovine thrombin can inhibit coagulation and prolong prothrombin time/INR
Fibrin sealant (human fibrinogen and human thrombin)	Artiss, Tisseel (also contains synthetic aprotinin), TachoSil, Evarrest, CryoSeal Fibrin Sealant System Vitagel (autologous fibrinogen and bovine thrombin), Raplixa	Potential exposure to blood-borne viruses
Combination thrombin gelatin	Floseal (bovine), Surgiflo (porcine), Gel-Flow NT (bovine)	Antibody formation against bovine thrombin can inhibit coagulation and prolong prothrombin time/INR

G = Grams. INR = International normalized ratio.

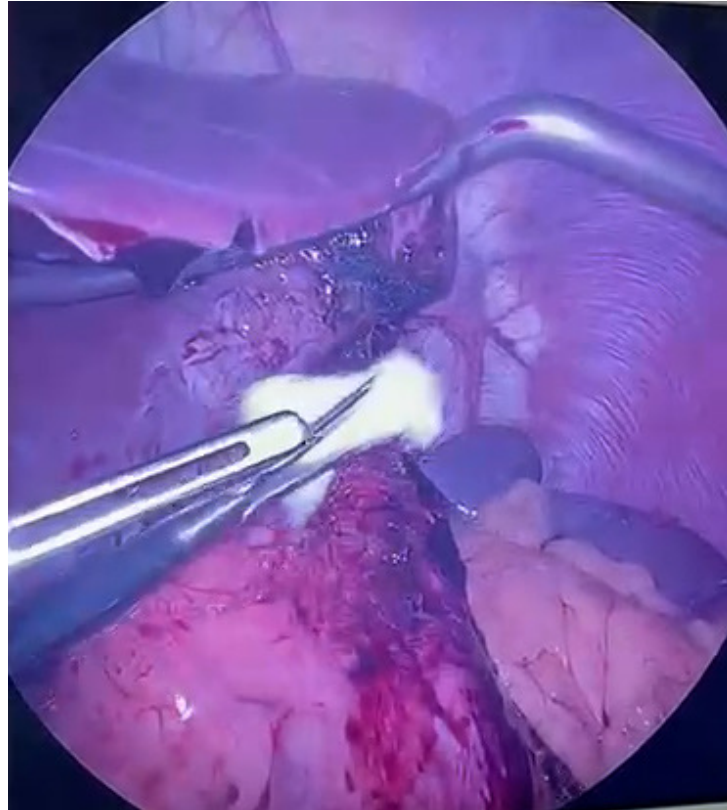
UpToDate. 2021. Topical hemostatic agents and tissue adhesives. www.uptodate.com Accessed December 5, 2021. U.S. Food and Drug Administration (FDA): Vaccines, Blood, and Biologics. FDA Website. 2021. <https://www.fda.gov/vaccines-blood-biologics>. Accessed December 5, 2021.; U.S. Food and Drug Administration (FDA): Production Information: Devices. FDA Website. 2021. <http://www.fda.gov/medical-devices>. Accessed December 5, 2021.

Case Example 1



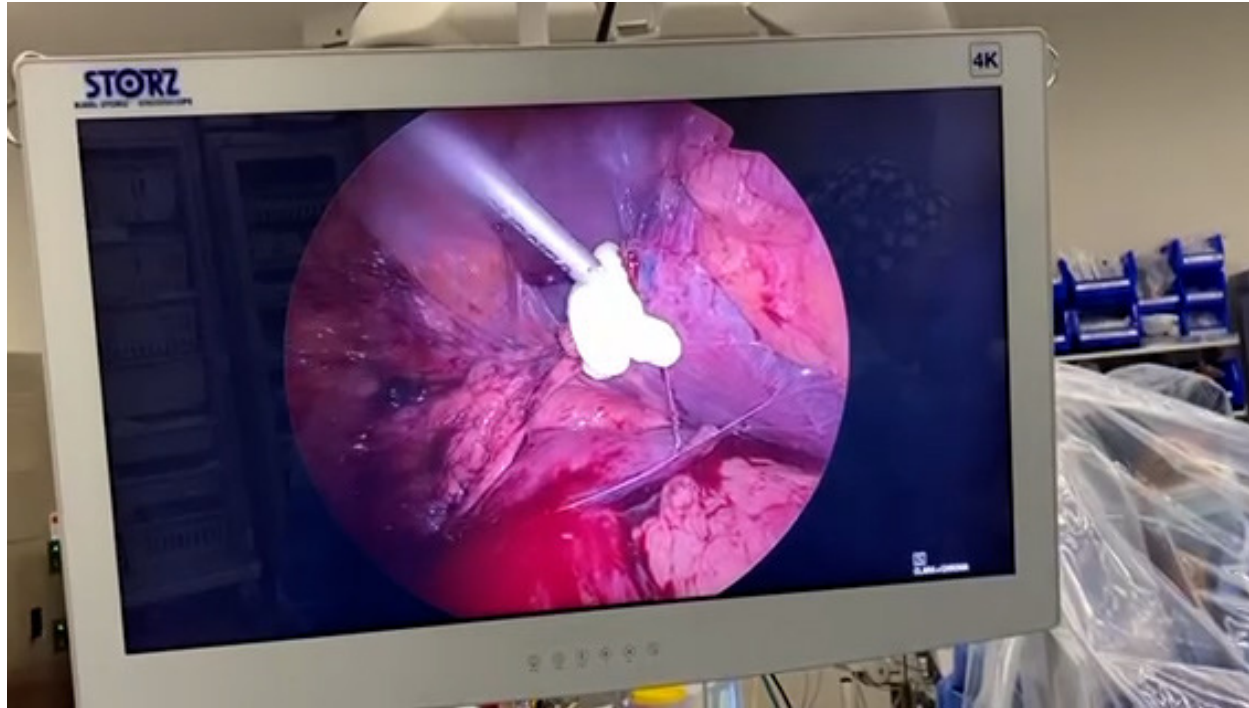
Video courtesy of Julia Park, MD

Case Example 2



Video courtesy of Julia Park, MD

Case Example 3



Video courtesy of Julia Park, MD

Faculty Discussion



SMART GOALS

- Involve the interprofessional team when planning for perioperative hemostasis
- Follow manufacturer instructions for safe storage and sterile preparation of topical hemostatic agents
- Choose topical hemostatic agents based on type of surgery, amount/location of bleeding, and surgeon preference

To Ask a Question

To ask a question, select the *Ask Question* tab below the slide viewer. Please include the faculty member's name if the question is specifically for them.

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AFTER
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Questions & Answers





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