Minimizing Intra-Operative Bleeding in Orthopedics: ARISTA™

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DAV/ARS1/1217/0180(1)

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BARD provides unique hemostat solutions to address certain forms of intraoperative bleeding. While this document describes all types and degrees of bleeding, it is important to keep in mind that the specific BARD products described herein may not be indicated and appropriate for every bleeding situation. For complete information regarding the use of any BARD product discussed in this document, please refer to the Instructions for Use included with the respective product(s) or refer to the electronic Instructions for Use on C. R. Bard's website at www.davol.com.

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All figures and charts contained within this document have been adapted from their original formats. Source data is cited within the text.

Disclosures

Consultant

- DePuy Synthes
- Zimmer Biomet
- Arthrex
- Smith & Nephew
- Trice Medical
- Exactech
- BD/Bard

Surgeon Advisory Boards

- Mitek Sports Medicine
- Rotation Medical
- Trice Medical

About Me

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Sean Mc Millan, DO

- Chief of Orthopedics:
  - Lourdes Medical Center
- Director of Orthopedic Sports Medicine & Arthroscopy
  - Burlington, NJ
- Fellowship-trained in arthroscopic surgery of the shoulder, hip, and knee.
- Assistant professor of orthopedic surgery at Rowan University- School of Osteopathic Medicine (RU-SOM)

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Why ARISTA™ Matters to Me

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1000 Cases Yearly

- 80 - 100 Shoulder Replacements
- 80 - 100 Knee Replacements
- Community Trauma/ Military Injuries

Teaching Orthopedic Residents

Chief or Orthopedics / Products Committee

- Co-Management Agreement with Hospital

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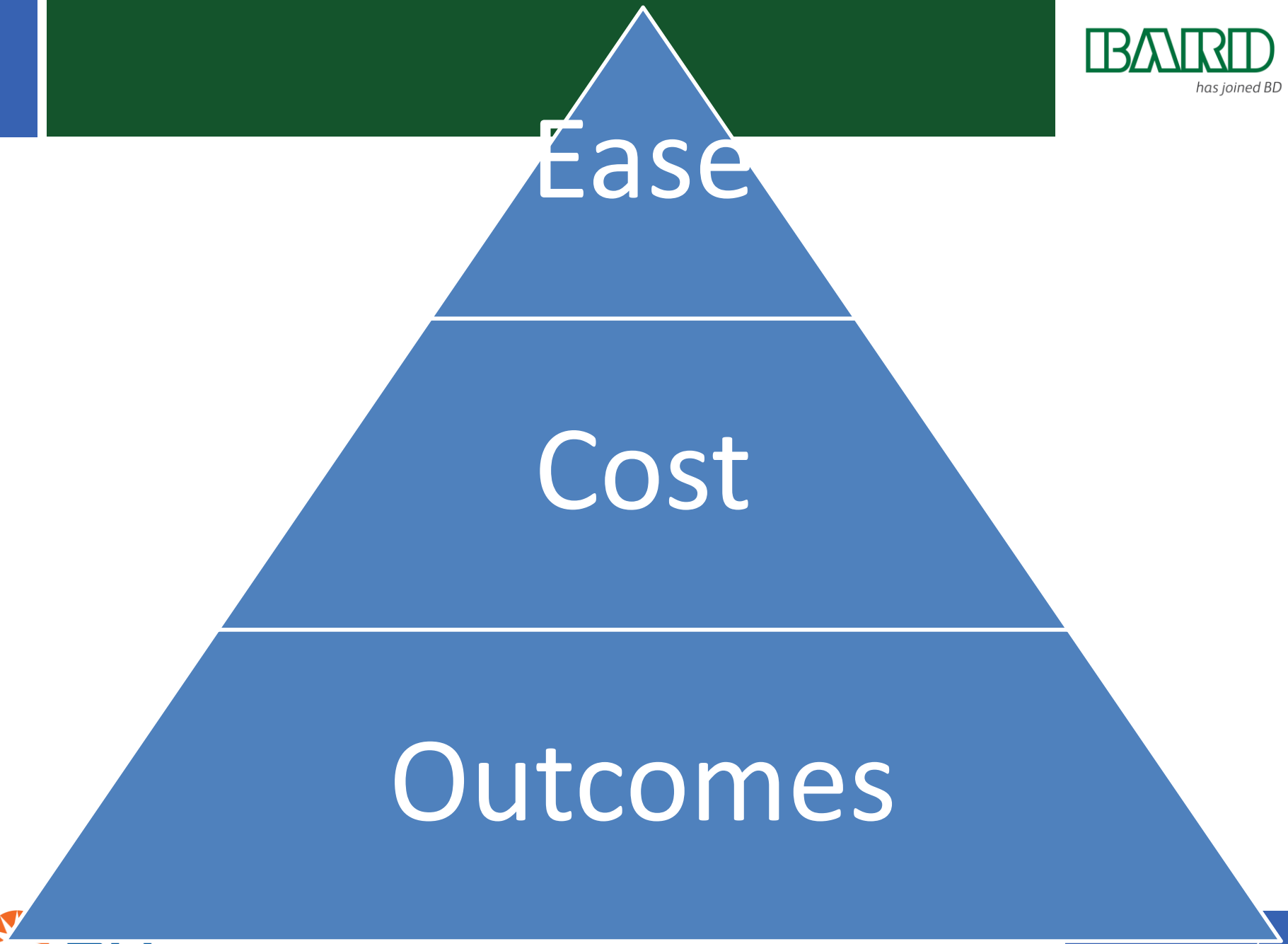

INTRAOPERATIVE BLEEDING ACROSS SURGICAL SPECIALTIES AND PROCEDURE

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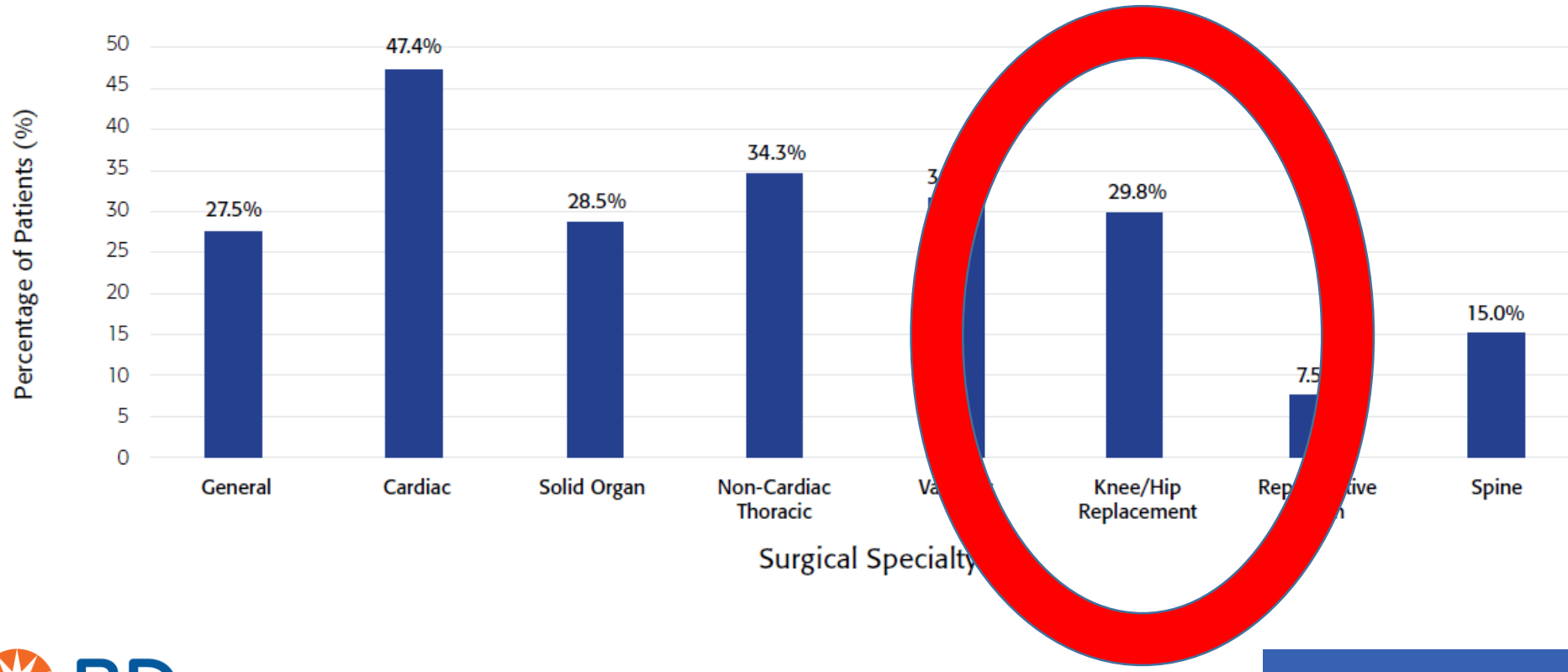
- **Intraoperative bleeding is common**
  - 27.5% in general surgery to 47.4% in cardiac surgery.[3]

Prevalence of Bleeding Related Complications by Specialty[3]



Bleeding-related complications were identified if the hospital record contained ICD-9-CM diagnosis codes for hemorrhages or hematomas complicating procedures, interventions (return to operating room to control for bleeding), or blood product transfusions.

THE BURDEN OF INTRAOPERATIVE BLEEDING

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- Uncontrolled bleeding can often **prolong, interrupt, or complicate surgical procedures**, reduce visualization of the surgical field, and increase morbidity and mortality rates (from 0.5% to 20%).[4,8-10,20,29,30]

- ***13.3 – 37.6 minutes lost to Uncontrolled Bleeding***[a]

[A] In a retrospective database analysis, operating time was anywhere from 13.3 to 37.6 minutes longer for procedures with uncontrolled vs. controlled bleeding.[2]

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BLEEDING IS NEVER GOOD…

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- **Clinical complications** associated with intraoperative bleeding may include:[4]
  - Anemia
  - Hemodynamic instability
  - Hypothermia
  - Hypovolemia
  - Reduced oxygen delivery to tissues
  - Transfusion-related complications

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Costs of Blood Transfusions

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- Transfusion costs[17]

Cost per unit of blood	$190-300
Cost to run tests	$170
Storage cost	$100
Cost to transfuse (over 2 hours)	$50
Cost of disposables	$10

$700-$800

- There are additional costs associated with any transfusion reactions (e.g. fever, antibiotics, CXR, cultures, etc.)

- Increased hospital costs[18]

- ***LOS was extended on average by 3.1 - 6.4 days in patients that received transfusions*** compared to those who did not receive a transfusion[18]

THE BURDEN OF INTRAOPERATIVE BLEEDING

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- Uncontrolled surgical bleeding is associated with economic burden due to **increased use of costly resources**.[2,3,10]

Costs of Health Care Resources Impacted by Uncontrolled Bleeding (USD), as compiled from a number of articles

Health Care Resource	Year	Unit Cost*
Repeat cardiac surgery for bleeding[35]	2007	$30,000
Treatment of infection[35]	2007	$20,000
Bleeding-related complications[†3]	2011	Up to $17,279
Intensive care unit stay (per day)[39]	2005	$3,180 - $10,794
Operating room time (per hour)[38]	2005	$1,260 - $7,980
Length of hospital stay (per day)[35]	2007	$1,280
Blood transfusion (per unit RBC)[40]	2010	$761

*Unit costs may be greater due to inflation

[†]Including bleeding event, intervention to control for bleeding, or blood product transfusion.

THE BURDEN OF INTRAOPERATIVE BLEEDING

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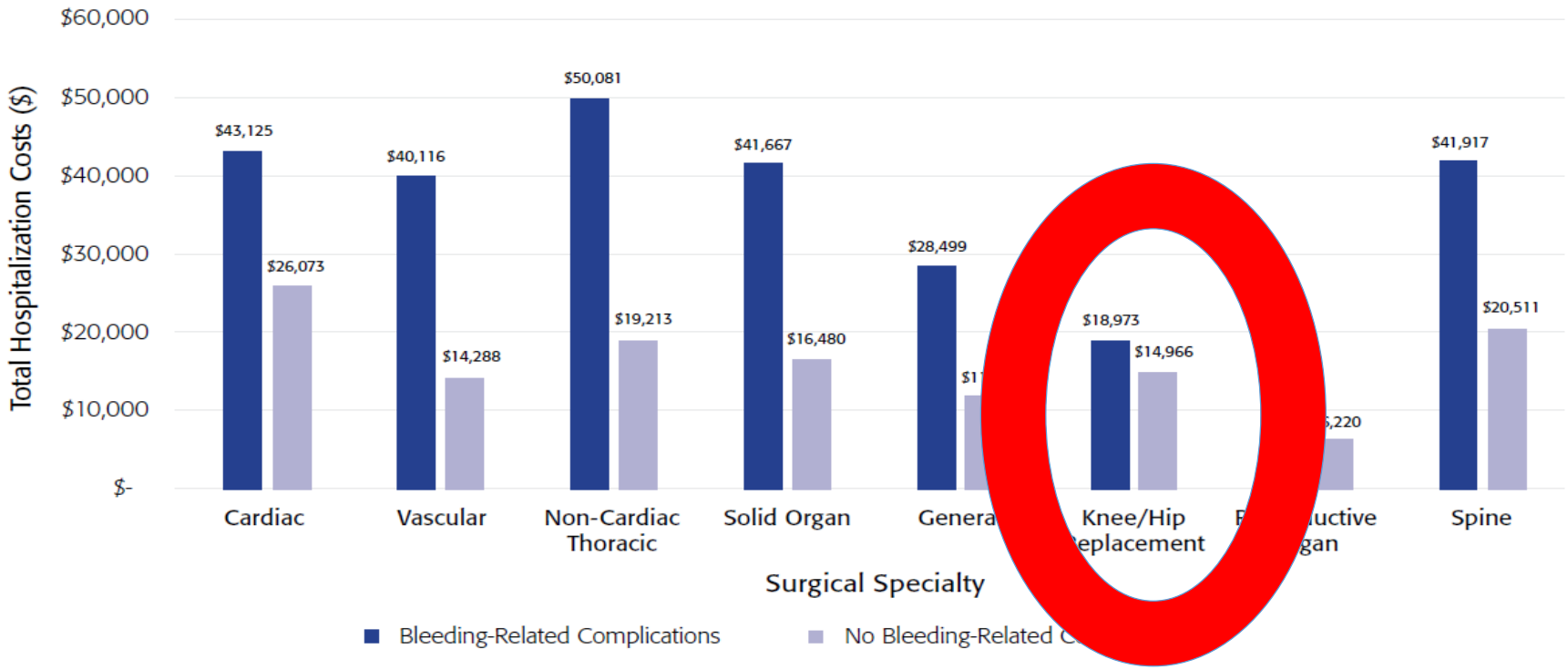
- In a U.S. retrospective database analysis in 2012, uncontrolled bleeding costs in USD ($24,203-$61,323) were significantly greater than those for controlled bleeding ($14,420-$45,593).[2]

Total Hospitalization Costs for Bleeding-Related Complications by Surgical Specialty[3]



Current Intra-Operative Considerations

MANAGEMENT OF INTRAOPERATIVE BLEEDING

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- When conventional methods of hemostasis are ineffective or impractical, **hemostatic agents and surgical sealants may be required to provide a useful adjunctive therapy**.[7]

- **Local hemostatic agents demonstrate various advantages, including:[1,7]**
  - Direct application to bleeding site
  - Reduced adverse effects
  - Flexibility
  - Ease of use/preparation
  - Application to both localized and diffuse bleeding
  - Lower costs

- **The need for effective hemostatic agents is increasing,** in one study from 2000-2010, **a third of procedures** utilized hemostatic agents.[42,43,44]

THE NEED FOR HEMOSTAT OPTIONS

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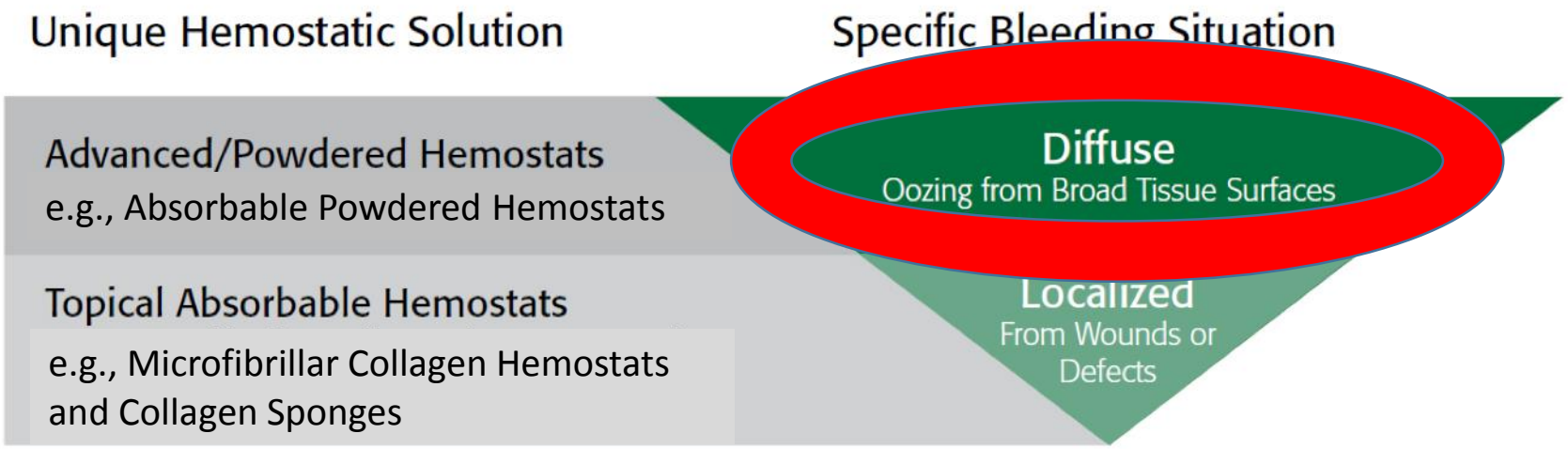
Unique hemostatic solutions are needed to control different bleeding situations.[4,7]

- **Advanced/Powdered Hemostats** (e.g., Absorbable Powdered Hemostats) are designed to achieve broad tissue coverage, conforming to irregular surfaces.[1]
- **Topical Absorbable Hemostats** (e.g., Microfibrillar Collagen Hemostat) are available in unique forms such as sponges, foam, or sheets, which offer ease-of-use for packing, wrapping, and adherence to complex surfaces.[7]



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THE NEED FOR HEMOSTAT OPTIONS

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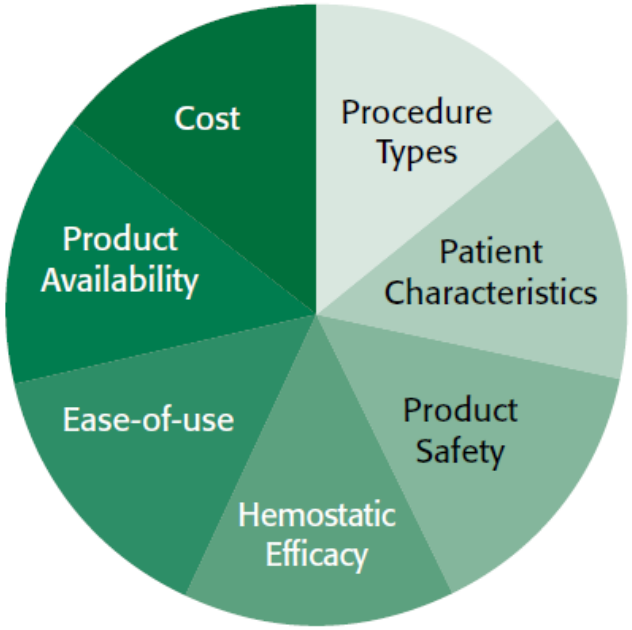
- The **selection of the hemostatic agent** and delivery method is highly dependent on the source and magnitude of the bleeding, and the anatomy and coagulation profile of the patient. [7,45]
- **An ideal hemostat across all situations does not exist** and individual operative experience remains an important factor in selecting a hemostat for each clinical scenario.[45]

Considerations for Optimal Selection of a Hemostatic Solution



Example of Blood Loss That May Require Transfusion

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- **TOTAL KNEE ARTHROPLASTY:**

- Approximately **700,000** TKA performed in US Yearly
  - ***18-35%* require transfusion**
  - ***20%* have adverse Reaction to Transfusion**

- Increased use of hemostats **has reduced** number of transfusions over time[8]

7. Prasad N, et al. Blood loss in total knee athroplasty: an analysis of risk factors. Int Orthop. 2007 Feb;31(1):39-44
8. Wright JD, Ananth CV et al. Patterns of use of hemostatic agents in patients undergoing major surgery. J Surg Res. 2014 Jan; 186(1): 458–466

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Use of Hemostatic Agent and Transfusion Requirements

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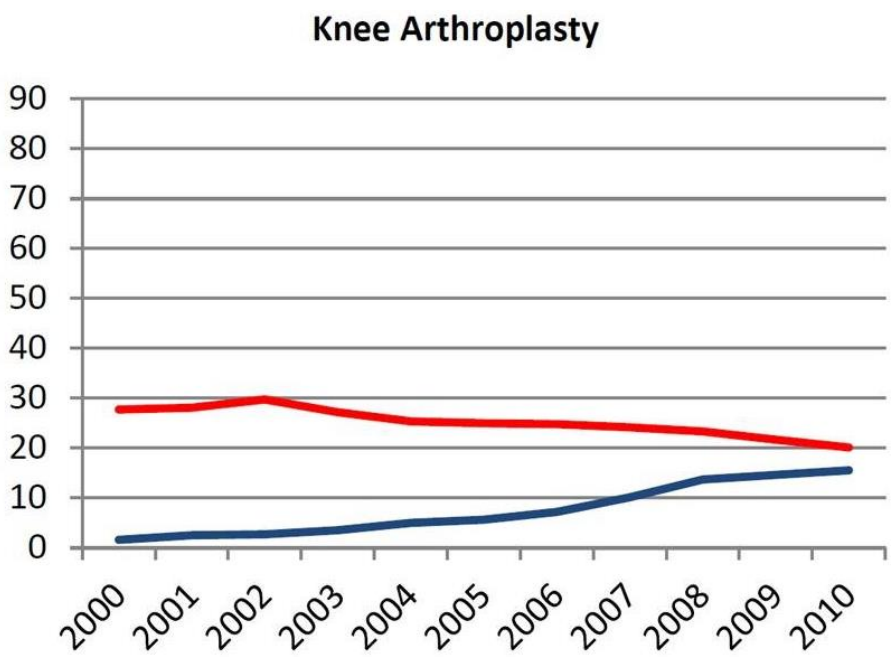

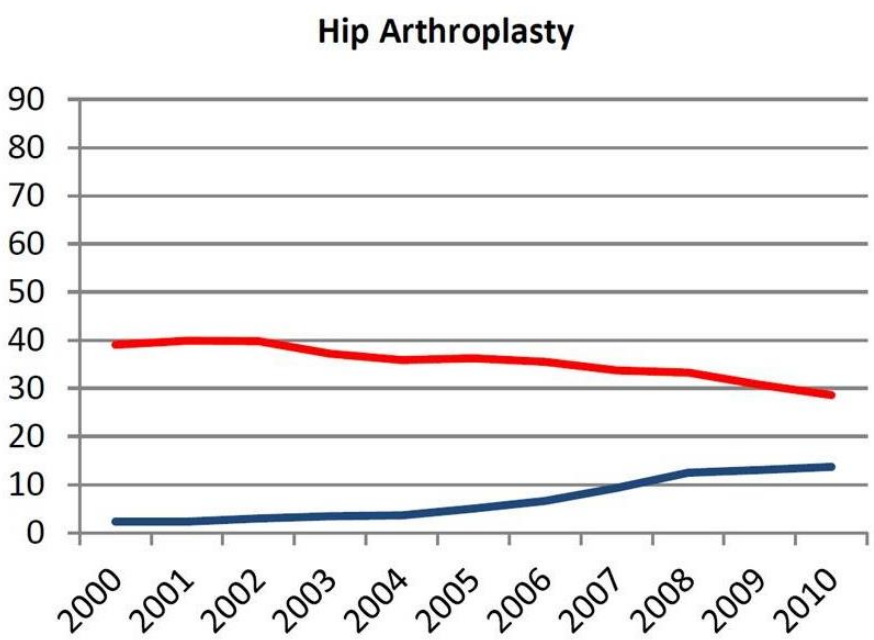

--- Hemostatic agents

--- Transfusion requirements

JD, Ananth CV et al. Patterns of use of hemostatic agents in patients undergoing major surgery. J Surg Res. 2014 Jan; 186(1): 458–466

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THE MANAGEMENT OF INTRAOPERATIVE BLEEDING

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- **Mechanical interventions**
- **Thermal techniques**
- **Pharmacologic strategies**

- **Selection Process:**
  - Origin of Bleeding
  - Nature of Bleeding
  - Severity of Bleeding.[4,45]

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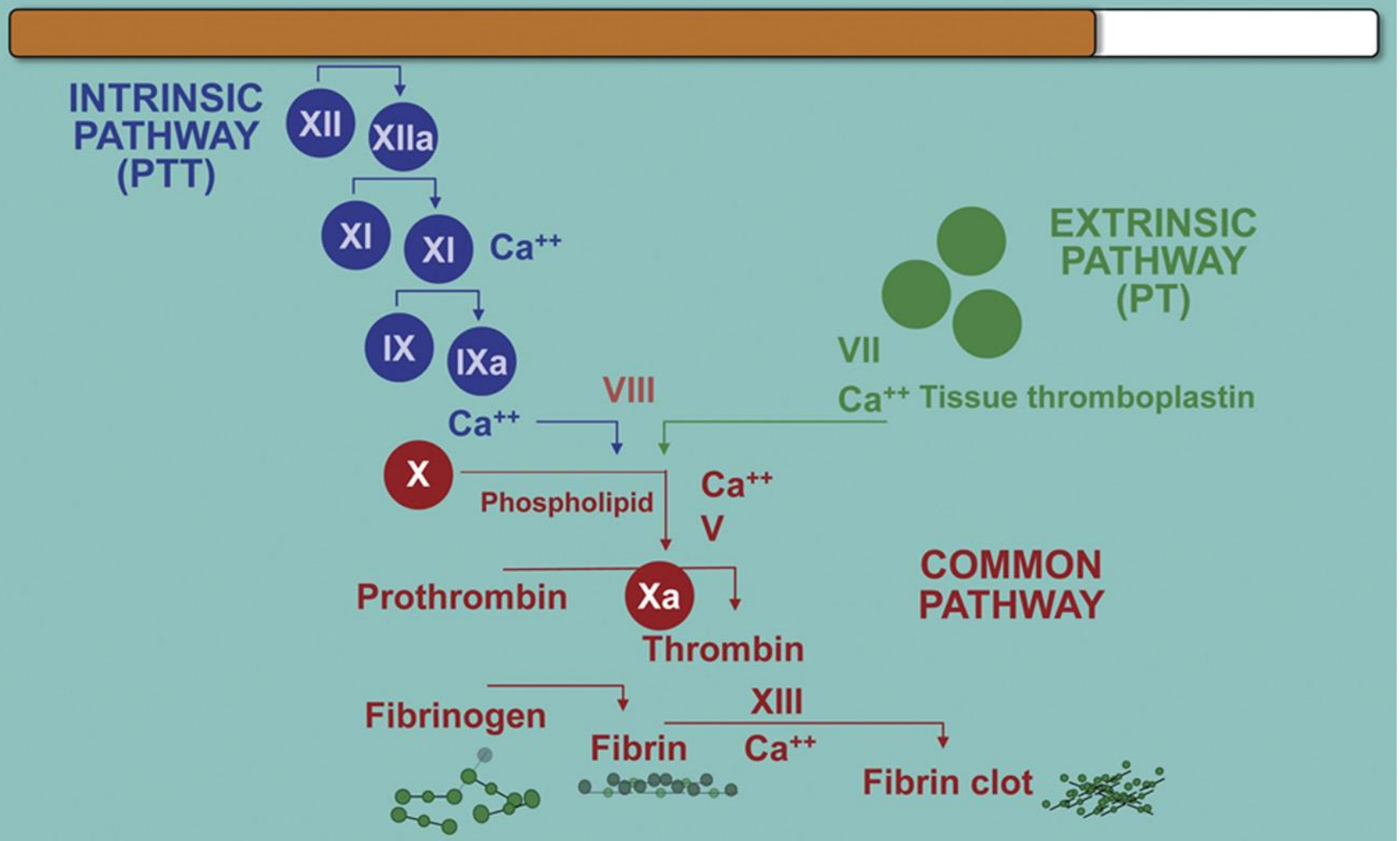
Figure 1. Coagulation Cascade



Agents Used in TJS

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- **Hemostatic Agents/Topical Agents**

  ARISTA®

  FloSeal Tisseel
  SURGIFLO® Thrombin

- **Platelet Rich Plasma (PRP)**

  Hypothesis: growth factors released from platelets may induce a healing effect

- **TXA (Tranexamic acid)**
  - inhibits fibrinolysis
  - prevents clot breakdown rather than promoting new clot formation.

- Carter MJ, Fylling CP, Parnell LKS. Use of Platelet Rich Plasma Gel on Wound Healing: A Systematic Review and Meta- Analysis. *Eplasty*. 2011;11:e38.
- Gandhi R, Evans HM, Mahomed SR, Mahomed NN. Tranexamic acid and the reduction of blood loss in total knee and hip arthroplasty: a meta-analysis. *BMC Research Notes*. 2013;6:184. doi:10.1186/1756-0500-6-184.

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Mechanical Hemostatic Agents

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- **Porcine gelatin**
  - (Gelfoam®, Gelfoam® Plus, Surgifoam®)
- **Cellulose**
  - (Surgicel®, Surgicel Nu-Knit®)
- **Bovine collagen**
  - (Avitene® sheets, UltrafoamTM collagen sponges)
- **Polysaccharide Spheres (Arista®)**

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What is Arista™ AH MPH Technology?

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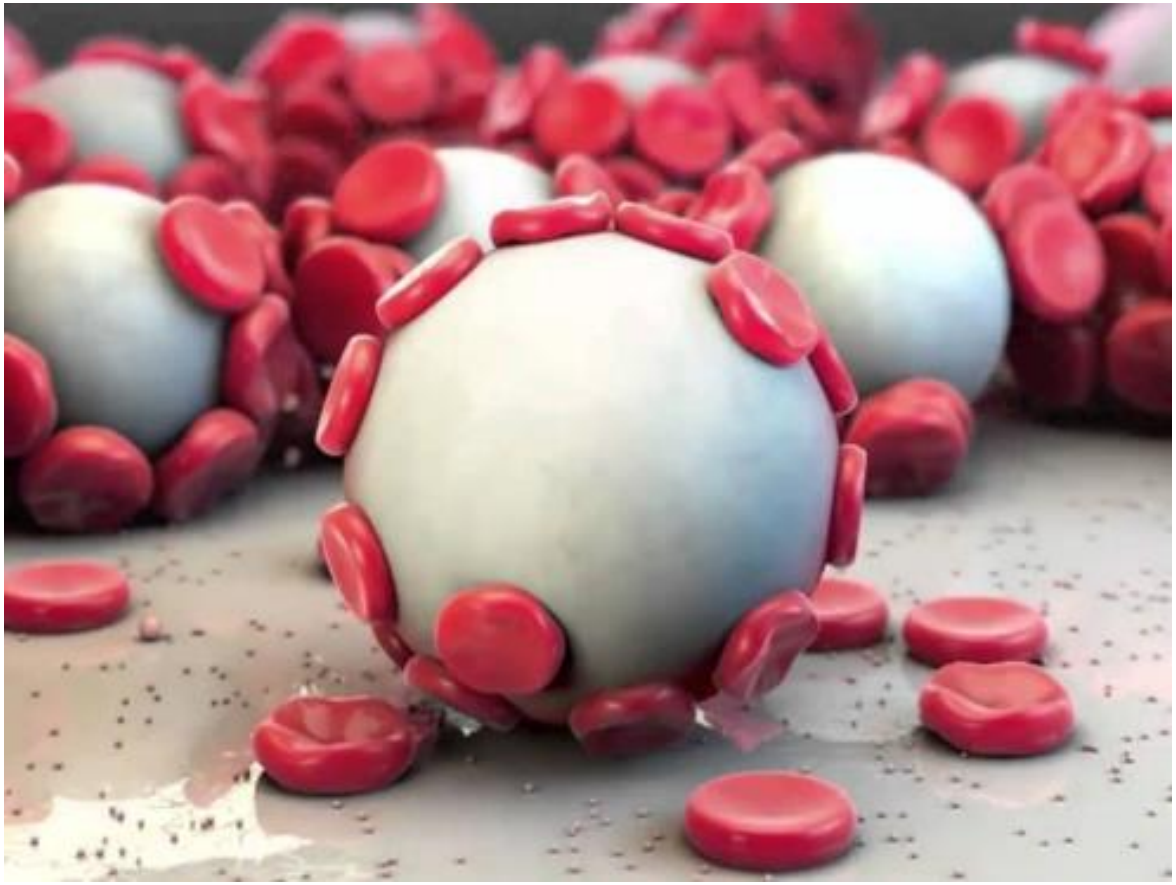

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Arista™ AH History

- In 1999, James F. Drake, PhD conceived of a particle with “molecular sieve” properties as a hemostat
- Over ensuing years many attempts were made to develop the product
- 2006 – Arista™ AH received PMA Class III approval
- October 1, 2013 – Acquired by C. R. BARD

Arista™ AH Works

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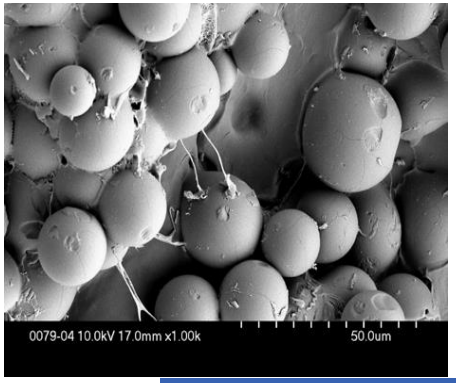
- Proprietary MPH™ (Microporous Polysaccharide Hemospheres) technology -
  - microporous particles with a controlled pore size
  - Multi-Chain Glucose / Plant Based

- Initiates clotting process on contact with blood = Gelled Matrix

- Normal clotting process enhanced by providing barrier to further blood loss, ***regardless of the patient's coagulation status***[19]
  - ***-Primarily PTT Pathway***



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Microporous Polysaccharide Hemospheres (MPH™)

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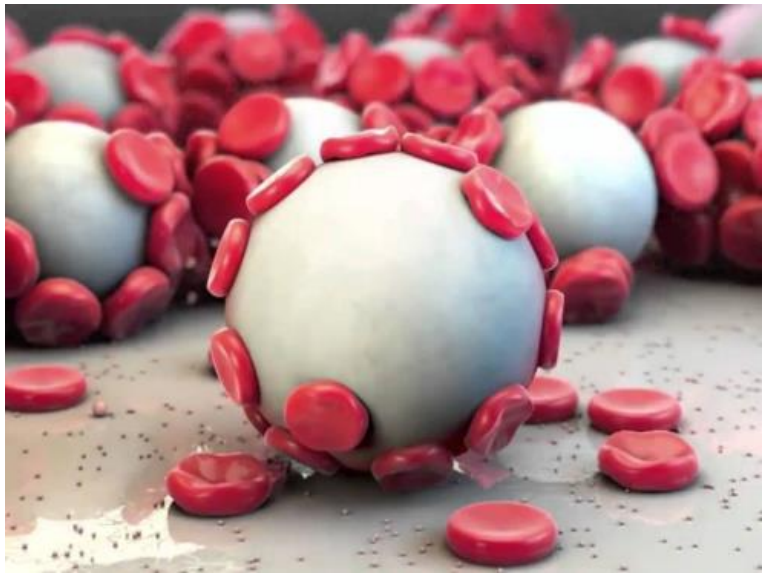
- An absorbable powdered HEMOSTATIC AGENT
- ***Hydrophilic = DEHYDTRATES THE BLOOD!***
- Concentrating blood solids such as platelets, red blood cells & blood proteins on the particle surfaces - gelled matrix
  - provides a barrier to further reduce blood loss
- Suited for control of capillary, venous, and small arterial bleeding
- **Absorbs in 24-48 hours**



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ARISTA EASE OF USE

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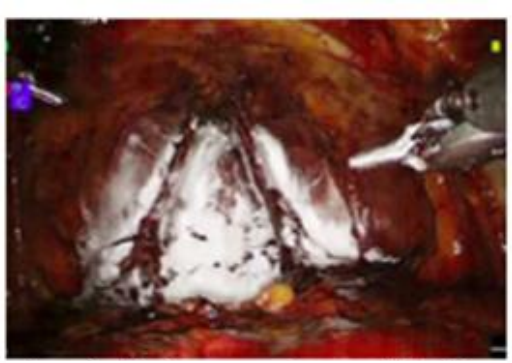
- **Absorbable Powdered Hemostats** provide **broad surface coverage** to address diffuse bleeding on rough or hard-to-reach surfaces.† [5]
- They are typically **ready-to-use out of the package**, and require no preparation, mixing, or special storage conditions.[51]
- Absorbable Powdered Hemostats may offer an extended ***shelf-life of 5 years***.



Absorbable Powdered Hemostat in Robotic-Assisted Radical Prostatectomy

Absorbable Powdered Hemostat in Robotic-Assisted Total Laparoscopic Hysterectomy

† C.R. BARD Preclinical Data on File. Preclinical data may not correlate to clinical performance in humans.

Arista™ Ease of Use

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Proven Safety and Efficacy in a Variety of Surgical Areas and Procedure Types[3,4]

Examples include:

- Cardiothoracic and Cardiovascular
- Gynecological
- Urology
- General Surgery
- Plastic Surgery
- Orthopedics

Use of ARISTA™ AH in neurological or ophthalmic surgical procedures is excluded from its approved indication.

SIMPLE

- No mixing and no refrigeration
- Simply pop the cap and apply powder directly to the bleeding site[5]

SAFE

- 100% plant-based and thrombin-free
- Typically absorbed and cleared within 24-48 hours[2] by amylases
- FDA approved Cell Saver Safe Hemostat with 40µ transfusion filter

EFFECTIVE

- Accelerates the clotting process, regardless of the patient's coagulation status[1]
- Dehydrates and gels the blood on contact
- Provides broad area coverage on rough surfaces and in hard-to-reach areas
- Attach the FlexiTip™ applicator for a controlled delivery of ARISTA™AH

1. ARISTA™ AH Instructions for Use
2. Safety and effectiveness of Arista™ AH have not been clinically evaluated in children and pregnant women. Because there have been reports of decreased amylase activity in newborns up to 10 months, absorption rates of ARISTA™ AH in this population may be longer than 48 hours.
3. Preclinical data on file. Preclinical data may not correlate to outcome in humans.
4. ARISTA™ AH PMA P050038 Clinical Study
5. See full Instructions for Use for detailed application instructions.

Absorbable Hemostatic Particles

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The Clinical Value of MPH™:

- In an unpublished pivotal trial of 288 patients, MPH™ was associated with improved outcomes when compared with an absorbable gelatin sponge:[54]
  - **90.3% vs. 80.4% of patient achieved hemostasis within 5 minutes**
  - **50.3% vs. 32.9% of patients hemostasis within 1 minute**
  - **1.0 minute vs. 2.0 minutes for median time to hemostasis**
- A retrospective study of 240 patients found that MPH™ improved clinical outcomes vs. a historical control that included a gelatin thrombin matrix, an absorbable gelatin sponge with thrombin, or an oxidized cellulose polymer.

Improved Outcomes with MPH™ vs. Control[55]

Outcome	MPH™	Control	P Value
Protamine to skin closure	93.4 minutes	107.6 minutes	0.02
Units of red blood cells	2.4	4.0	<0.001
Chest tube output	1594 mL	2112 mL	<0.001
ICU length of stay	8	9	0.08

- **In a preclinical study, animals treated with MPH™ exhibited fewer adhesions when compared with controls, including surgical adhesive (P<0.05). †[57]**

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† C.R. BARD Preclinical Data on File. Preclinical data may not correlate to clinical performance in humans. Absorption rates in infants up to 10 months may be longer than 48 hours. Safety and effectiveness of Arista™ AH have not been clinically evaluated in children and pregnant women. Because there have been reports of decreased amylase activity in newborns up to 10 months, absorption rates of Arista™ AH in this population may be longer than 48 hours.

Arista™ Preclinical Procedures**

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- Arista™ AH provides broad area coverage on raw tissue surfaces and in hard-to-reach areas**
- Arista™ AH is **cell saver compatible** when used with a 40µ transfusion filter**
- Arista™ AH is a plant based hemostat that is typically absorbed from the body in 24-48 hours*,**
- Arista™ AH did not enhance infection of the wound site, as demonstrated in a preclinical model inoculated with E. Coli.**
- Arista™ AH does not promote adhesion formation[29]

* Because there have been reports of decreased amylase activity in newborns up to 10 months, absorption rates of ARISTA™AH Absorbable Hemostatic Particles in this population may be longer than 48 hours.
**Data generated in a preclinical model. Data may not correlate to performance in humans.
29. Hoffman et al: **Choice of Hemostatic Agent Influences Adhesion Formation in a Rat Cecal Adhesion Model**. *J Surg Res* 2009, 155: 77-81.
As demonstrated in preclinical abdominal adhesion model. Preclinical testing may not correlate to clinical outcomes.

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Value Proposition

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- **What would be the advantages of using an all natural, 100% plant based hemostat?**

- **How could the use of a product that required no preparation have a beneficial impact on cost?**

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Orthopedic Fit

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Surgical Considerations: Minimize Bleeding

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Total Joints

- Knee
- Hip
- Shoulder

Fractures

Fasciotomies/Soft Tissue Surgery

- Compartment fasciotomies
- Distal Biceps Repairs

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Surgical Considerations: Minimize Bleeding

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Intra-Op Goals:

- Maintain Visualization

  **decreased surgical time*

- Minimize Blood Loss

Post-Op Goals:

- Minimize Transfusion Needs
- Maintain stable post-op blood pressure

  ** early ambulation*

- Minimize Hematoma Formation

  ** earlier return of motion*

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Possible Arista™ AH Use?

- Posterior capsule – **medial/lateral** branches of the geniculates and surrounding areas of soft tissue
- Periphery where the meniscus has been removed from the bone and surrounding tissue
- The skin envelope and supra-patella pouch
- 14cm tip can be helpful in reaching the posterior portions of the *joint*
- ***** AVOID INTERACTION WITH BONE CEMENT!***

Schreiber MA[1], Neveleff DJ. Achieving hemostasis with topical hemostats: making clinically and economically appropriate decisions in the surgical and trauma settings. AORN J. 2011 Nov;94(5):S1-20. doi: 10.1016/j.aorn.2011.09.018.

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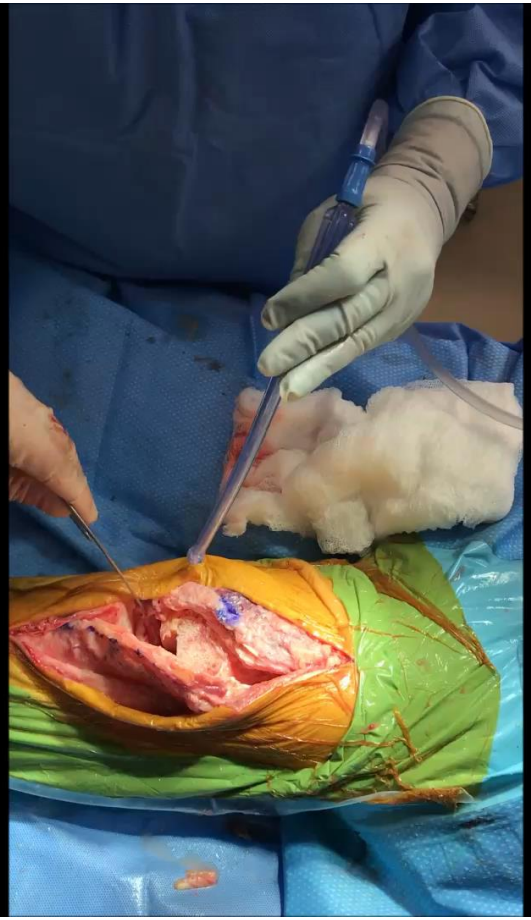

POSTERIOR CAPSULE

ARISTA: CAPSULE AND GUTTERS: TKA

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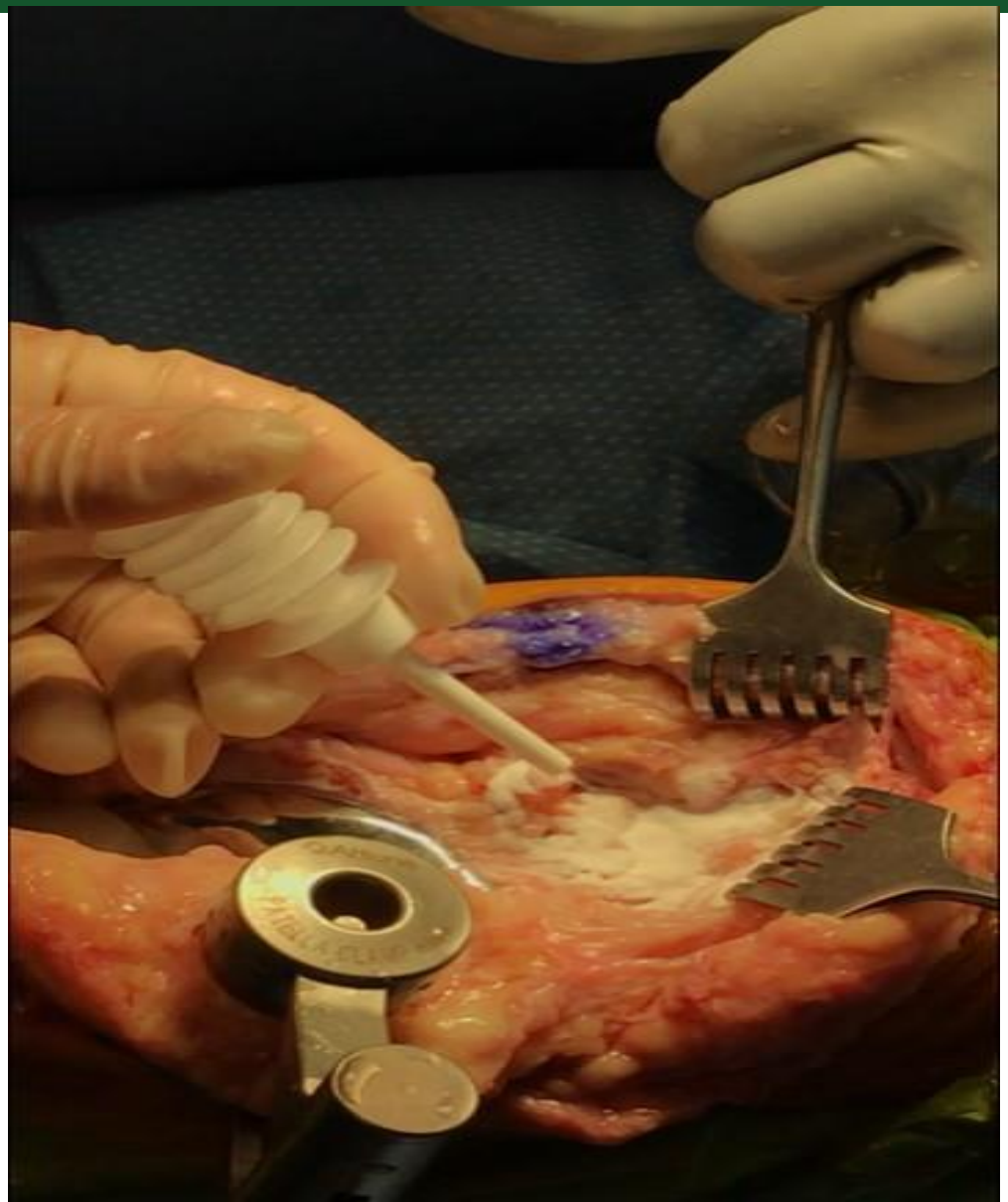

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Total Hip Replacement

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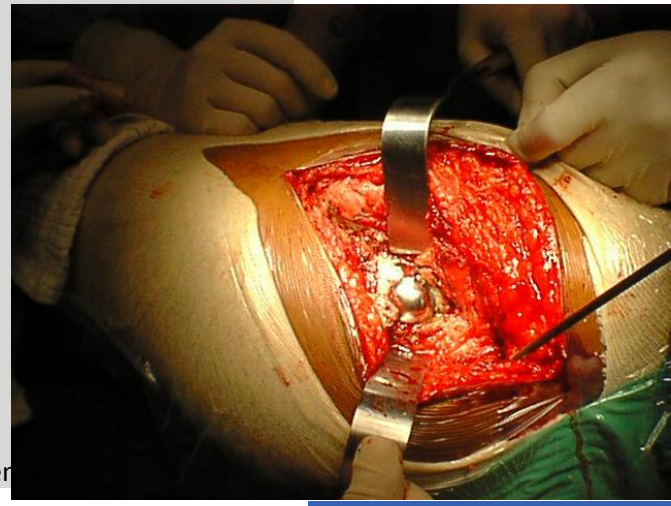
Potential Arista™ AH Use?

- There are several potential bleeding sites in a total hip replacement:
  - Posterolateral - Anatomical
  - Cut down:
    - Glutials (Gluteus Maximus/Medius) - superior gluteal artery and vein
    - External rotators and quadratus - gluteal artery and medial circumflex artery
    - Capsule exposure
    - Acetabulum - obturator bleeding
    - Labrum
    - All exposed soft tissue and fat



*ARISTA™ AH should not be used at the interface of the prosthetic implant and bone and/or bone cemen

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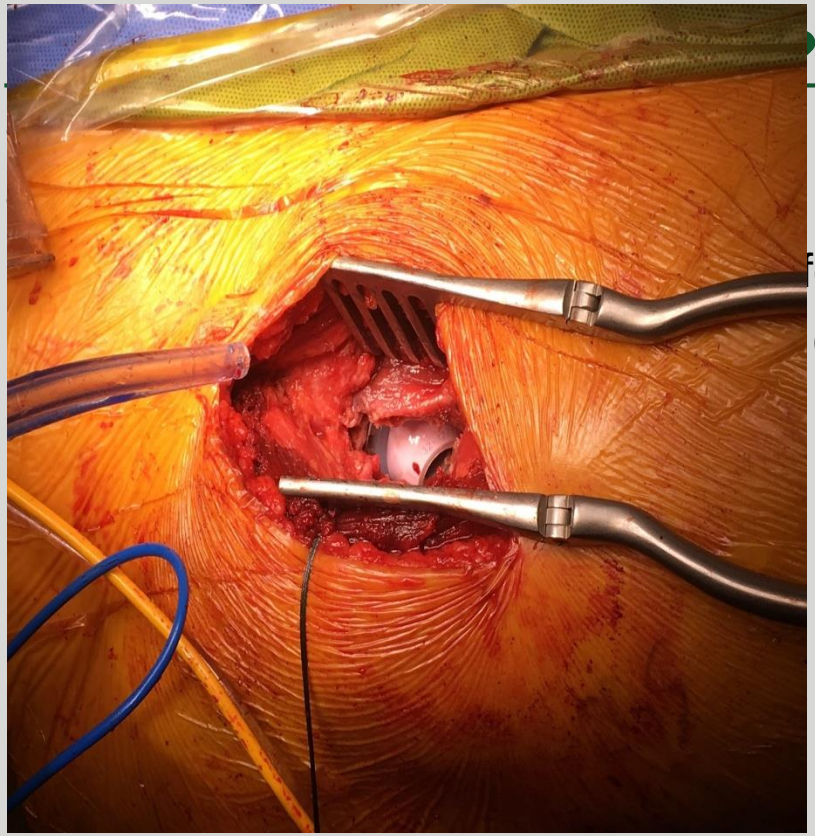
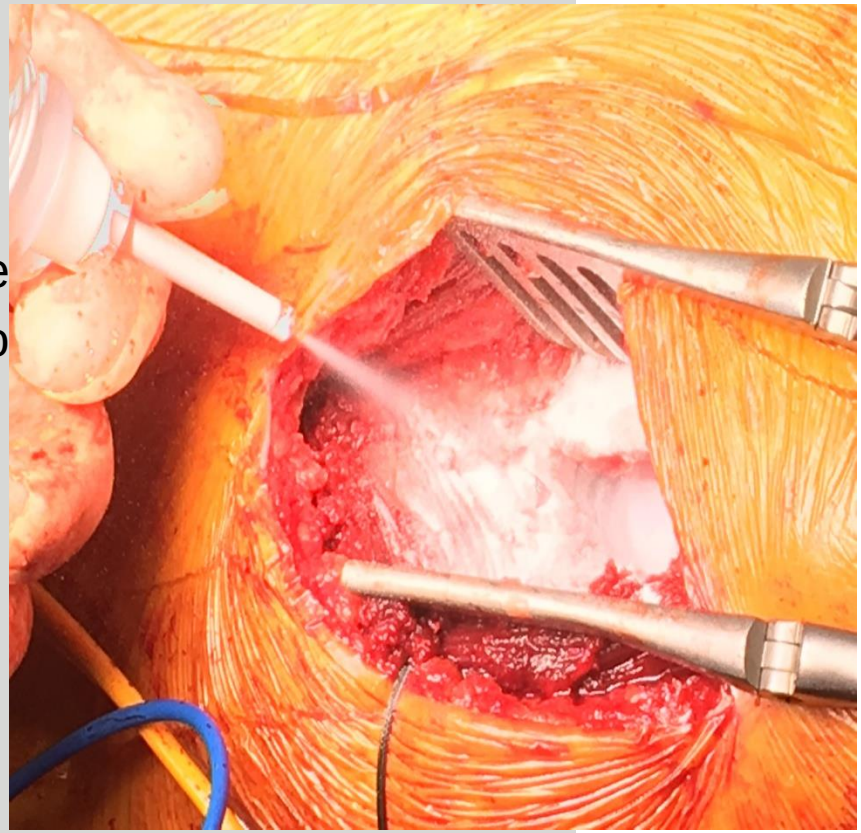
Professional opinion of Dr. Bishai

Total Hip Replacement





*ARISTA™ AH should not be used at the interface of the prosthetic implant and bone and/or bone cement.

Picture coursesy of Dr. Corey Solmani

FRACTURE WORK: Soft Tissue

FASCIOTOMIES

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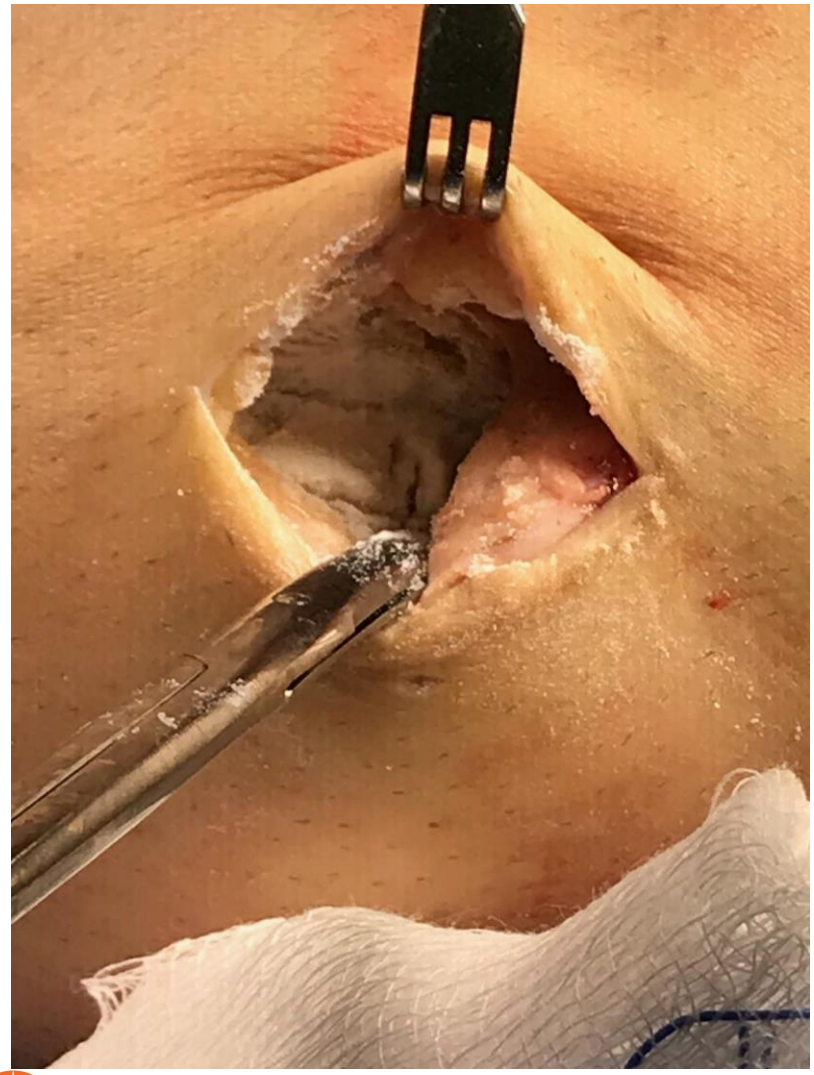

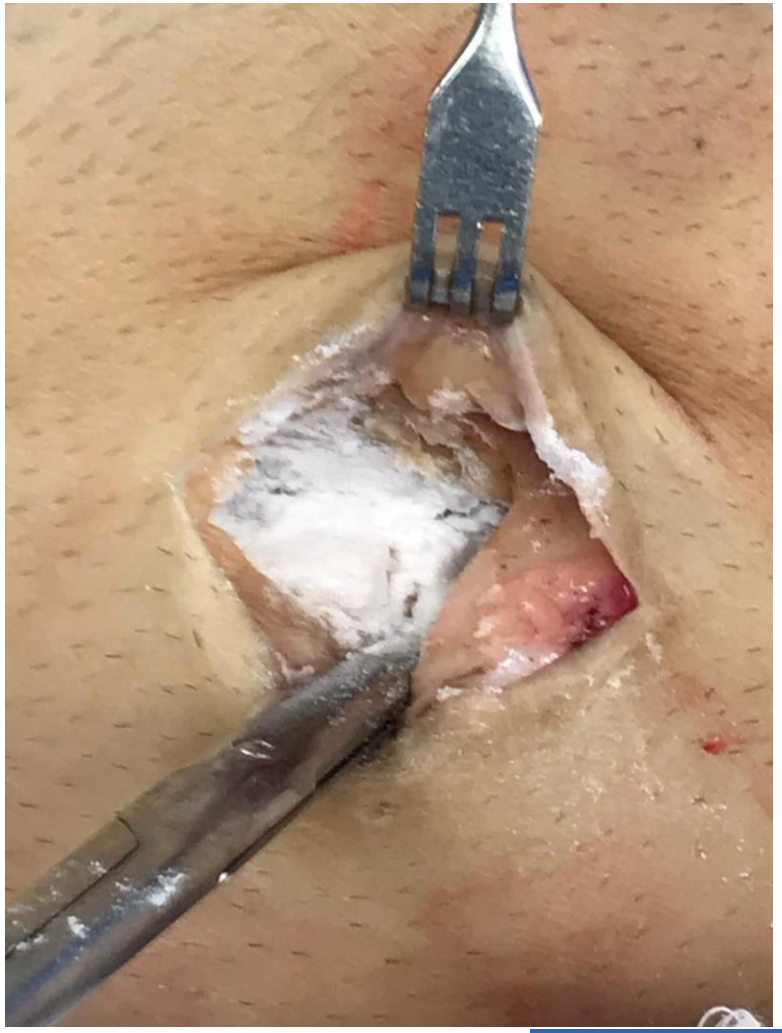

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NOT ALL POWDERS ARE CREATED EQUAL!

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- **Compared to SURGICEL® Hemostatic Power:**
  - **Not Dependent Upon Patient's Coagulopathic State**
  - **Absorbs in 24-48 hours VS 10-14 Days**
  - **Comes in 1 gram, 3 gram & 5 Gram options vs 3 gram SURGICEL POWDER**
    - Cost Savings Options

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Preference Card

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- Soft Tissue/ Small Fractures: 1Gram
- Total Joints: 3Gram
- Revisions: 5Gram

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MY EXPERIENCE

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- 24 Months of Use : >250 cases
- Transfusions For Elective Cases : 0
- Infections / Hematomas Post-Op: 1
- Post-Operative Drains: 1

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Arista™: Ortho Highlights

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Arista™ AH is a great option for orthopedic surgeons

- ***Its Safe!*** *– (#1 concern for doctors)*[3]
  - Not a known source for infection*
- ***Absorbs in 24-28 Hours***
- ***Doesn't cause adhesions****
- ***It works!***
  - Molecular sieve: dehydrates the blood of nonessential fluids
  - RBCs, platelets and proteins can form a clot naturally[3]
- ***Its cost effective!***
  - Compared to other hemostats or a PRP[1]
- ***Its simple to use - No mixing, no fiddle factor*** [4]

1. LIT-0191 REV A - Competitive Product ASP, Storage and Handling.
2. *As demonstarted in preclinical testing. Preclinical testing may not correlate to clinical outcomes. LIT-0177 REV A 11/13 – Clinical Infection in a Rat Abdominal Wound Model.
3. Arista Summary of Safety and Effctiveness. FDA Approval.
4. Arista AH IFU

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Thank You!!

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References

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