Breakthroughs in Peripherally Inserted Central Catheter Technology

Combining Practice and Product to Strive for ***ZERO*** Complications

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Disclosure

Author: Cheryl Kelley RN BSN, VA-BC

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Learning Objectives

- Discuss the incidence of PICC-associated infection and thrombotic complications
- Explain the differences between the two existing antimicrobial PICC technologies
- Differentiate the two existing antithrombogenic PICC technologies

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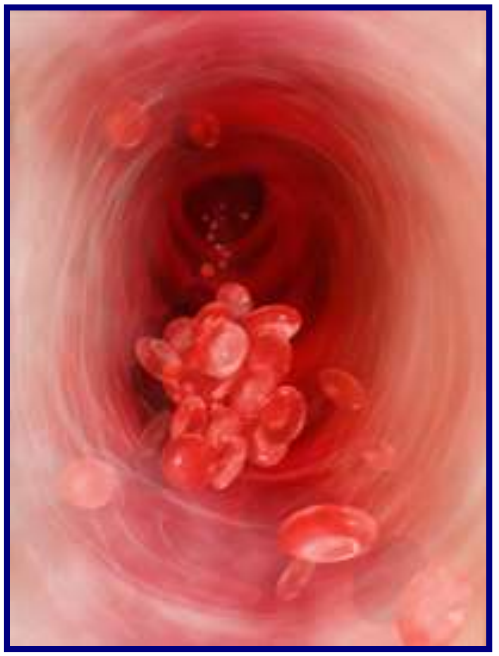
Introduction

- Two most common complications of central venous catheters (Raad 1994)
  - Catheter-related bloodstream infection (CRBSI)
  - Catheter-related thrombosis (CRT)
- Large focus on *CRBSI*
  - In the forefront of news
  - Educated consumers
  - Unacceptable risk
- Limited focus on *CRT*
  - Is it an avoidable risk?
  - Are consequences limited?



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Is It Real? PICC-Related Infection

PICC: Rates of Infection (Maki 2006)	
In-patient	**2.1**/1000 days
Out-patient	**1.0**/1000 days
CVC: Rates of Infection	
Antimicrobial	**1.6**/1000 days
Non-antimicrobial	**2.7**/ 1000 days

PICC rate higher than antimicrobial CVC

Similar rates of infection

Ajenjo 2011 revealed overall PICC infection rate: 3.13/1000 catheter days

- ICU: 4.79/1000 catheter days
- Acute care: 2.79/1000 catheter days

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PICC Related Infection)

Bloodstream Infection, Venous Thrombosis, and Peripherally Inserted Central Catheters: Reappraising the Evidence

Vineet Chopra, MD, MSc,[a] Sarah Anand, MD,[a] Sarah L. Krein, RN, PhD,[a,b] Carol Chenoweth, MD,[c] Sanjay Saint, MD, MPH[a,b]

[a]Division of General Internal Medicine, [b]Hospital Outcomes Program of Excellence of the Ann Arbor Veterans Affairs Medical Center, [c]The Division of Infectious Diseases, University of Michigan Health System, Ann Arbor, Mich.

Chopra 2012

INFECTION	Patients without Cancer	Patients with Cancer
Incidence	1.0 to 2.1/1000 catheter days	1.8 to 7.7/1000 catheter days
Mortality	Estimated 12-25%	Estimated 31-36%

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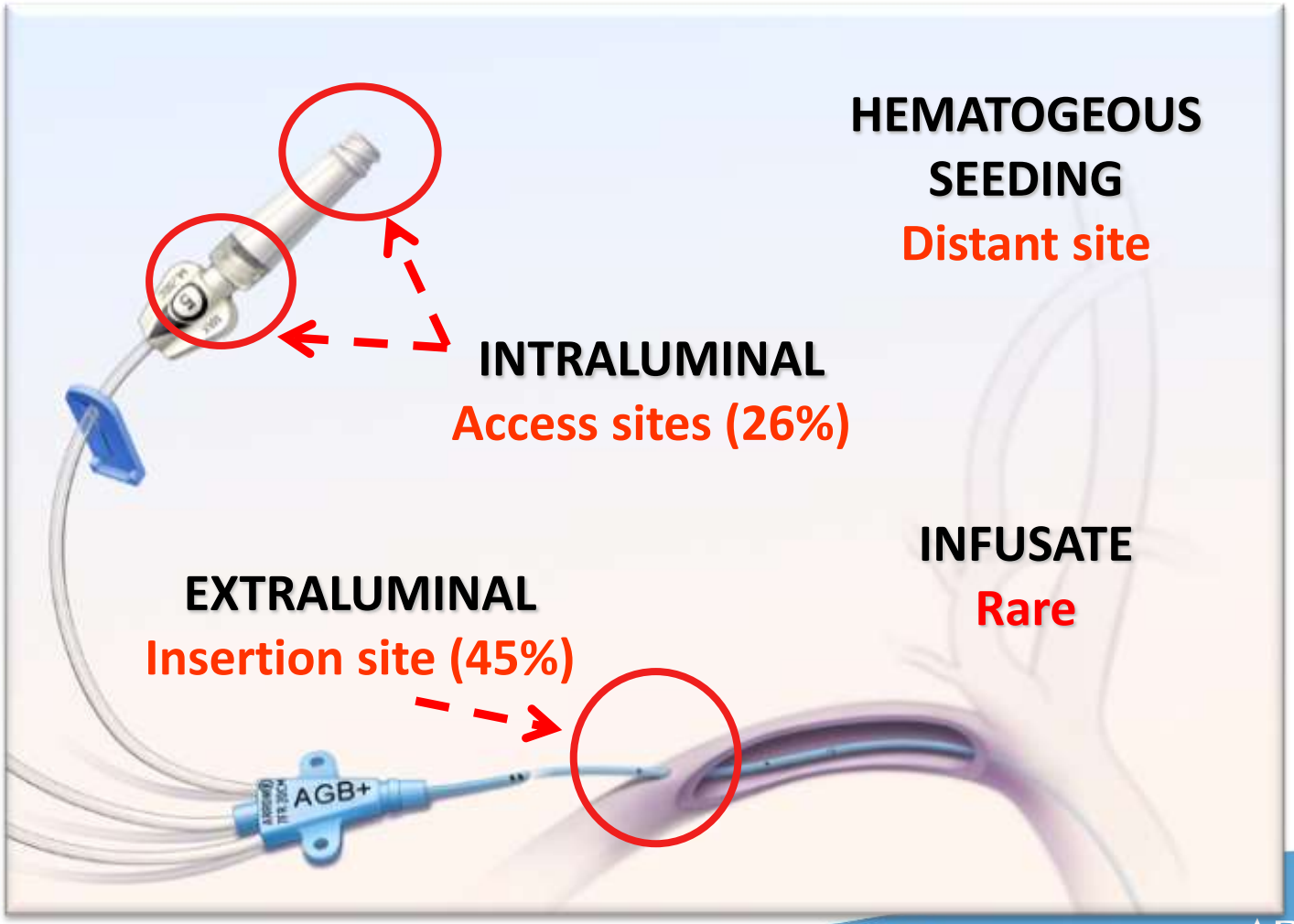
Four Sources of CRI



Safdar & Maki, 2004

PICC Related Thrombosis

THROMBOSIS	Patients without Cancer	Patients with Cancer
Incidence	**2.0 to 5.5 %** (symptomatic thrombosis)	**3.4 to 7.8%** (symptomatic thrombosis)
Mortality	**1-2%**	**2-4%** (50% higher for cancer patient)

Chopra 2012

"….measures for preventing arm DVT in cancer patients should be a first-line aim for oncologists." (Munoz 2008)

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Risk Factors: PICC-Related Thrombosis

Hypercoagulability

- Abnormalities is clotting factors
- Previous DVT
- Ethnicity; Age
- Malignancy
- Trauma
- Inflammatory process
- Pregnancy, hormone replacement

Venous Stasis

- Dehydration, leukocytosis
- Multi-lumen catheters
- Immobility of blood flow
- Inappropriate catheter vessel ratio
- Vessel compression (tumor)
- Small vein size

Endothelial Damage

- Solutions with high or low pH or high osmolality
- Traumatic vessel cannulation
- Multiple insertion attempts
- Large bore introducer
- Repetitive passes thru subclavian
- Placement in area of friction
- Large catheter size (dialysis, PICC)
- Left sided insertion site
- Previous central venous catheter
- Location site (femoral, IJ, subclavian)
- Suboptimal tip location
- Length of dwell

Relationship between infection and thrombosis

Raad 1994

- Post mortem exam 72 cancer patients
- Findings:
  - Fibrin layer on all
  - Mural thrombus on 38% veins
  - CR sepsis in 7 patients
  - Sepsis only in patients with thrombosis

Timsit 1998

- Critical Care Study
- 208 catheters
- Findings:
  - 10 of 139 (7.2%) with CR sepsis without CRT
  - 13 of 69 (18.8%) with CR sepsis with CRT
  - When CRT present, risk of CRI increases **2.6** fold

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So….where from here?

- We have established that PICC infection and PICC thrombosis is a serious concern
- There is a relationship between infection and thrombosis
- How have medical device companies stepped up to the challenge?

Antimicrobial (AM) and Antithrombogenic (AT) combination PICC Technology

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Protected PICC Technology

Antibiotic Impregnated PICC:

Cook Spectrum® Turbo-ject® PICC

Antimicrobial Impregnated PICC:

Arrow® PICC with Chlorag+ard® Technology

Technology that damages cell wall and inhibits growth of bacterial and/or fungal pathogens

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Protected PICC Technology

Antibiotic Technology

"Bacteriostatic or bactericidal"

- Against gram positive organisms
- Very weak against gram negative
- Ineffective against fungal pathogens

Stops bacterial from multiplying

Antimicrobial Technology

"Bactericidal"

- Effective against gram positive, gram negative

"Fungicidal"

- Effective against fungal pathogens

Damages cell wall inhibiting cell function

Disinfectant

(used on solid surfaces)

Antiseptic

(used on human skin surfaces)

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Cook Spectrum®
Turbo-ject® PICC

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Cook Spectrum® Turbo-ject® PICC

Product Overview:

- Polyurethane: 60cm, trimable, reverse tapered; short or long term use therapy

Antibiotic impregnation:

- Minocycline and Rifampin
- Two drugs work synergistically together to provide protection against the most common bacteria that cause CRBSI.

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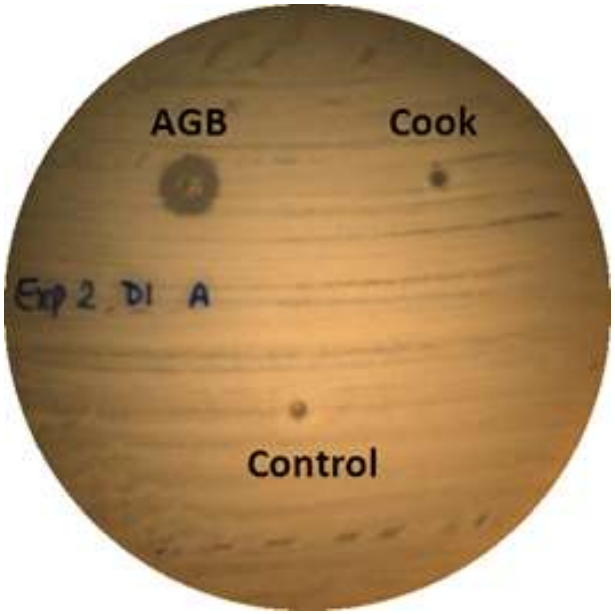
Cook Spectrum® Turbo-ject® PICC

- Provides protection against gram positive and gram negative organisms
  - Questions have risen addressing resistant gram negatives, e.g. *pseudomonas* and fungus (Hanna 2006)



Zones of inhibition in petry dish

Zone of inhibition testing: AKA Kirby-Bauer

- Used to test the ability of an antibiotic to suppress bacteria growth
- Size of zone and rate of antibiotic diffusion determine with a visual quanitative antibiotic the bacteria is sensitive to

Log reduction:

- Used to show the relative number of live microbes eliminated from a surface
- Only method accepted by FDA today when testing antimicrobial properties

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Cook Spectrum® Turbo-ject® PICC

- Impregnation:
  - Internal catheter lumen surfaces
  - External catheter lumen surface
  - Combination of minocycline and rifampin make it appear orange

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Cook Spectrum® Turbo-ject® PICC

Contraindications	• Allergy to minocycline or rifampin • Pregnancy
Resistance	• Questions raised about development of resistance • Literature both supports and questions this
Supporting Literature	• *In vitro* study showing 15 mm zone of inhibition > 30 days (Sheretz 1993)

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Arrow® PICC with Chlorag+ard® Technology

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Review of Chlorhexidine in General

- Chlorhexidine (CH) is:
  - Bactericidal: Capable of destroying *pathogens*
    - Fast acting, damaging cell wall
    - Broad spectrum: Bacteria, fungus, some viruses
  - CH very effective when combined with alcohol (Adams 2005)
- CH binds strongly to proteins in skin and mucosa
  - Thus antimicrobial effects are persistent, long-lasting
  - Hand washing, skin preparation, IV placement, etc.
- Antimicrobial activity of CH is not affected by presence of blood as can occur with povidone iodine

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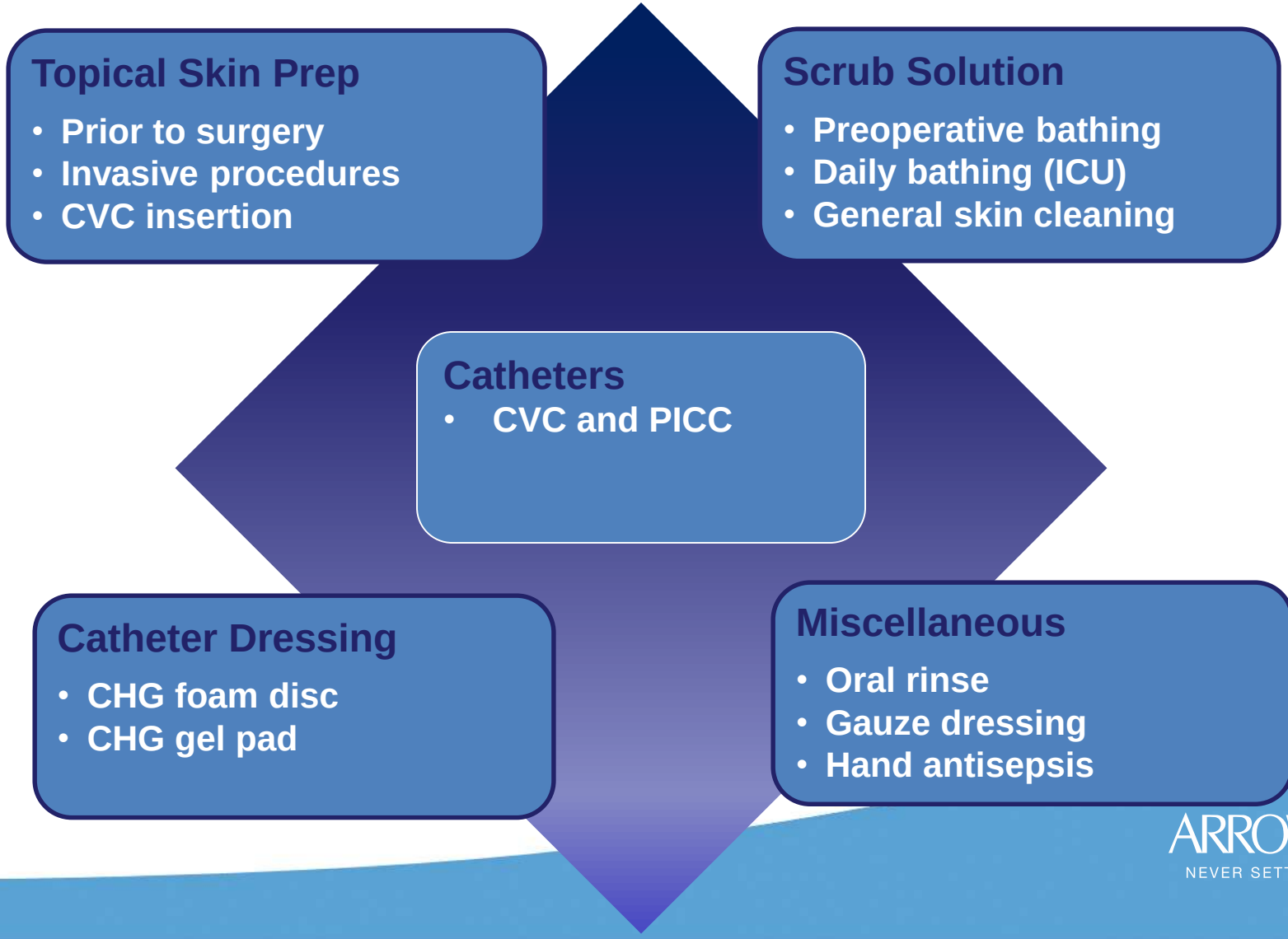
Chlorhexidine Usage in Healthcare



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Chlorhexidine on Catheter Surfaces

- Treated/chemically bonded onto catheter
- Immediately after insertion:
  - CH is designed for initial “burst” in order to “prep” the subcutaneous track.
- After 24 hours, CH slowly elutes out of catheter surface into surrounding environment/tissue
  - Designed to provide long-lasting protection for at least 30 days
- This action limits microbial colonization at entry site, through subcutaneous tract and on catheter surface

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Arrow® PICC with Chlorag+ard® Technology

FDA clearance in August 2010 as antimicrobial PICC

- Chlorhexidine solution
  - 1990 chlorhexidine/silver sulfadiazine on CVC
  - Why was chlorhexidine diacetate used as active ingredient on PICC?
    - Slower release of the chlorhexidine
    - Allow for longer duration on catheter surfaces

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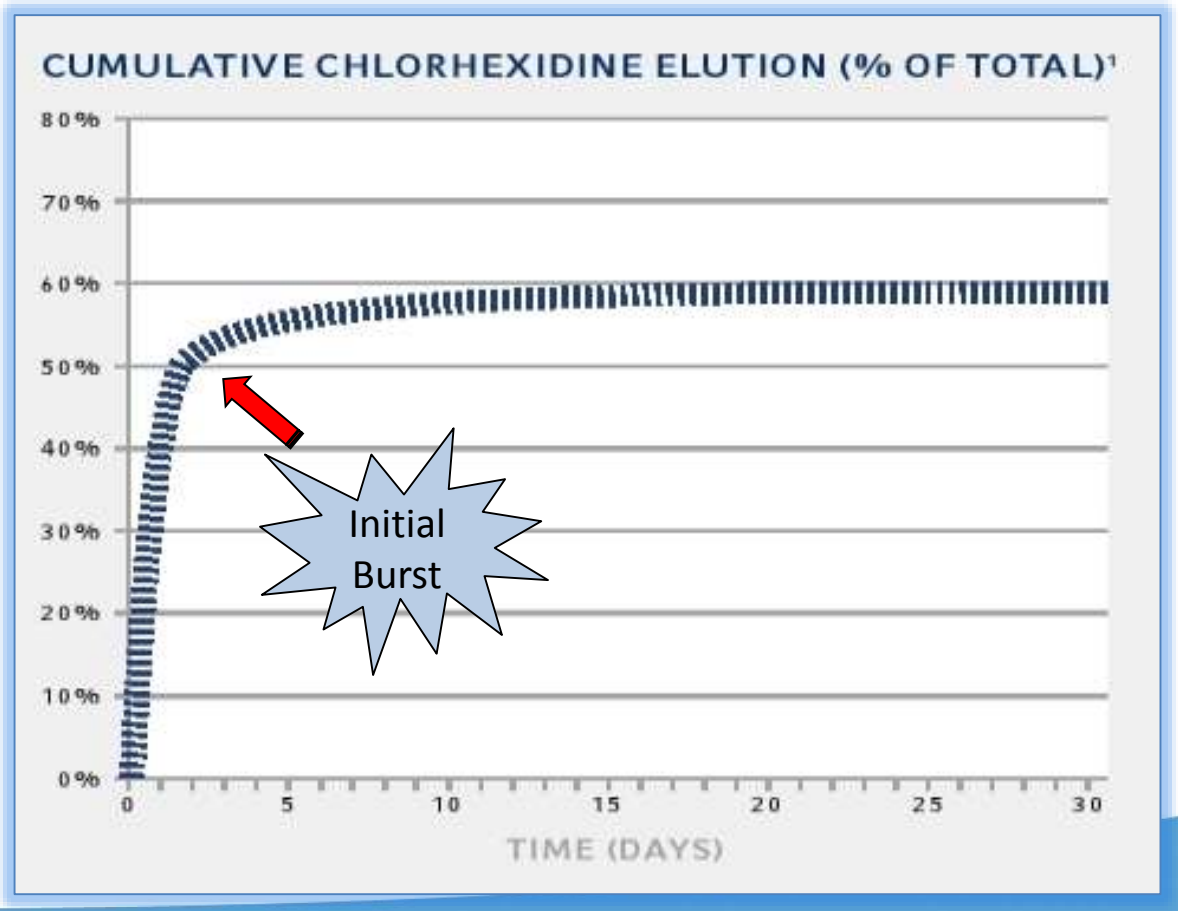
Continuous protection for at least 30 days**



As one can see, the elution of Chlorag+ard® Technology is consistent to 30 days

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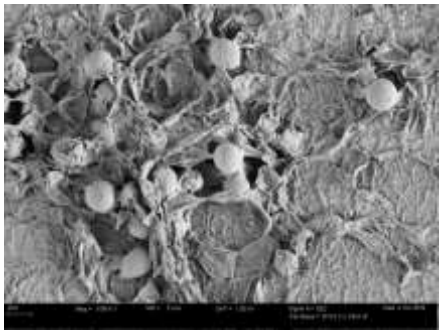
***In vitro* data on file, Teleflex Incorporated**

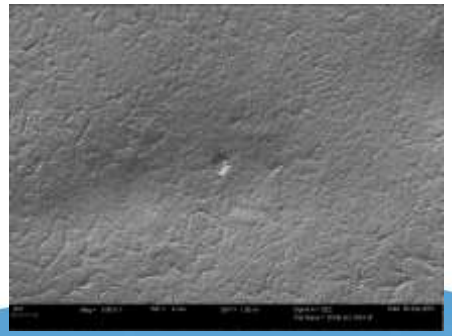
Arrow® PICC with Chlorag+ard® Technology

- Protection along entire fluid path:
  - External indwelling catheter surface
  - Internal indwelling catheter surface
    - 71% of infections occur after 5 days many via intraluminal contamination (Davis 2011)
  - Hubs and extension lines

Microscopy Results**



SEM of a Control Catheter Tip showing S. aureus attached to the intraluminal catheter surface.



SEM of ARROW PICC with Chlorag+ard technology with no attached bacteria apparent in the image.

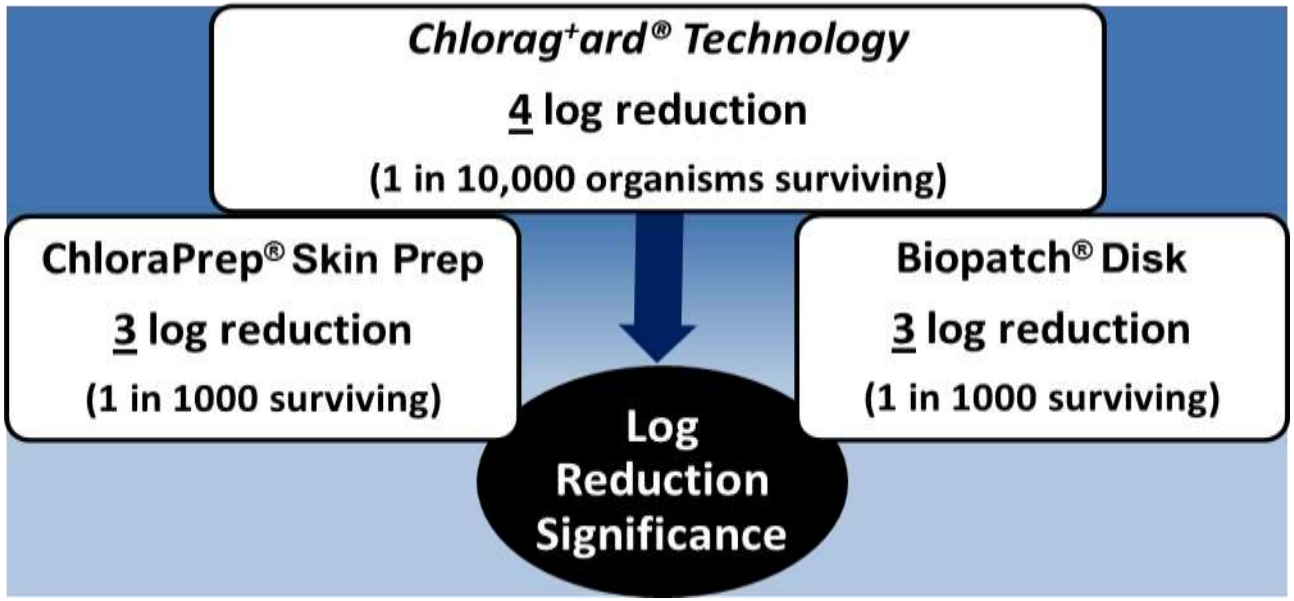
SEM = Scanning Electron Microscope

**As compared to uncoated PICCs, *in vitro* model demonstrated 51% less pressure to clear thrombus (TFX data on file)

Colonization Reduction Testing

99.99% (4 log) reduction in colonization**

***In vitro* data on file, Teleflex Incorporated



2011 CDC Guidelines: (O'Grady 2011)

1A: Antimicrobial catheters

1A: CH skin prep prior to CVC insertion

1B: Chlorhexidine sponge

2011 INS Standards of Practice: (2011)

Level 1: Antimicrobial catheters

Level 1: CH skin prep prior to CVC insertion

Level 1: CH sponge

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Arrow® PICC with Chlorag+ard® Technology

Contraindications	• Allergy to chlorhexidine
Resistance	• Unlikely due to quick “kill” properties of CH
Supporting Literature	• Animal studies • Log reduction claim supported by FDA clearance

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Antimicrobial PICC Summary Table

	Arrow® PICC w/ Chlorag+ard® Technology	Cook Spectrum® Turbo-ject®
Organisms Covered	Gram positive, Gram negative, Fungal	Gram positive, Gram negative
Testing methods	Log reduction focusing on colonization reduction	Zone of inhibition focusing on attachment
Length of protection	Up to 30 days	> 30 days
Surface area	Internal and external catheter surface, extension lines, catheter hub	Internal and external catheter surface

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Antithrombogenic PICC Technologies

Angiodynamics® Bioflo with Endexo™ Technology

(Formerly Navilyst)

Arrow® PICC with Chlorag+ard® Technology

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Angiodynamics® Bioflo with Endexo™ Technology

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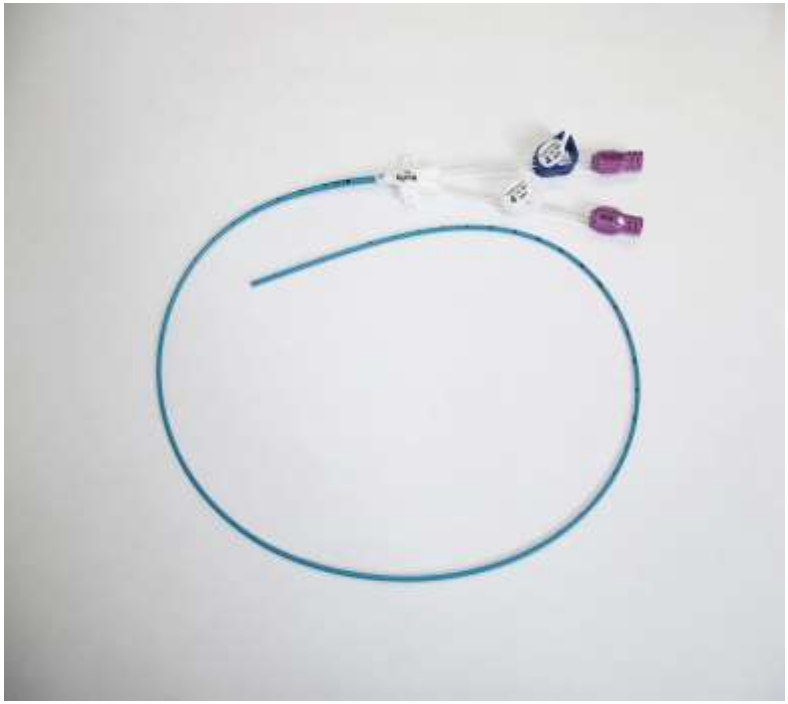
Angiodynamics® Bioflo PICC with Endexo™ Technology



- Goals for non-eluting technology:
  - Resists accumulation of platelets and thrombus
  - Added into polyurethane during catheter manufacture
  - Designed to passivate the catheter surface
  - Permanent surface modification

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Bioflo PICC with Endexo™ Technology Claims

- **Catheter surface**

  87% less thrombus accumulation on catheter surfaces over 2 hours (Larue, 2012)

- **Catheter Occlusion**

  No mention

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Bioflo PICC with Endexo™ Technology Testing

Catheter Testing: (Larue, 2012 AVA)

- Flow loop model showed average of 87% less thrombus accumulation at two hours than a standard catheter
  - Based on platelet count
  - Total amount of thrombus accumulation not disclosed
- Animal study: compared to heparin coated dialysis catheter and was “generally comparable” at day 14 and 31

Catheter design:

- Present only on intraluminal and extraluminal catheter surfaces

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Bioflow PICC with Endexo™ Technology

Contraindications	• Hypercoagulopathy unless patient is on anticoagulation therapy • Patients with known tape or adhesive allergies
Flushing/ Pressure Injection	• Requires heparinized saline • Single lumen: 3.5 cc/sec • Dual lumen: 4 cc/sec
Length of anti-thrombogenic properties	• Not mentioned

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Arrow® PICC with Chlorag+ard® Technology

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Antithrombogenic Properties

Chlorag+ard® Technology:

- Impregnated onto catheter surface
- Specially formulated for controlled release of chlorhexidine diacetate over specific time

Mechanism of Action

- Reduces thrombus accumulation on catheter surfaces by inhibiting thrombin formation
- Significance of inhibition of thrombin:
  - Does not allow the final step of the common pathway of blood coagulation—the conversion of fibrinogen to fibrin **clot**

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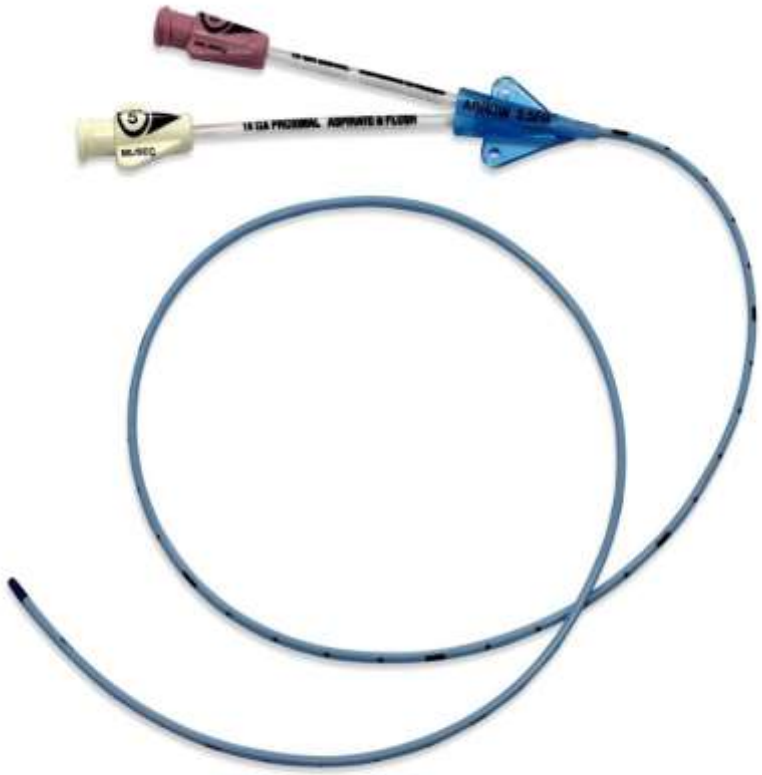
Arrow® PICC with Chlorag+ard® Technology

Catheter Testing

- Animal Studies: Marcia Ryder
- Thrombus measurement (weight and microscopically) and vessel analysis after 30 days

Catheter Surfaces Protected

- Intraluminal, extraluminal catheter surfaces, extension lines, hub



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Arrow® PICC with Chlorag+ard® Technology

Catheter Surface Protection

- Extraluminal:
  - 61% reduction in thrombus after 30 days*
  - When challenged with infection, 92% reduction after 30 days*
- Intraluminal:
  - 51% reduction in flush pressure**

Vessel Protection

- 72% reduction in intimal hyperplasia after 30 days*
- Reduction in phlebitis

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*As compared to an uncoated PICC , *in vivo* model

**As compared to uncoated PICCs, *in vitro* model demonstrated 51% less pressure to clear thrombus

Animal Study Images

In an *in vivo* intravascular animal model, three different catheters were challenged with *Staphylococcus aureus*

ARROW® PICC with CHLORAG+ARD® Technology: Day 31

Absence of infection; minimal thrombus formation

Unprotected Control PICC #2: Day 31

Highly infected tissue and significant thrombus formation

Unprotected Control PICC #1: Day 7

Infection present in tissue with significant thrombus formation

Arrow® PICC with Chlorag+ard® Technology

Contraindications	• Allergy to chlorhexidine
Flushing/ Pressure Injection	• Saline or heparinized saline • Single and dual lumen: max of 5 cc/sec
Length of anti-thrombogenic properties	• 30 days

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Antithrombogenic Summary Table

	Arrow® PICC with ChloraG+ard ® Technology	Angiodynamics® Bioflow PICC with Endexo™ Technology
Extraluminal Catheter Surface Thrombus Reduction	**For 30 days with live biological system data** • 61% in ovine model • 92% when challenged by infection	**Up to 2 hours in bench top testing:** • 87% reduction *in vitro* bloodflow loop model Thrombus resistance does not outperform control catheter in ovine model at days 14 and 31
Intraluminal Catheter Occlusion Reduction	**For 30 days**: • 51% reduction in flush pressure	None demonstrated
Vessel Protection	**For 30 days:** • Reduction in phlebitis • 72% less intimal hyperplasia	None demonstrated
Areas of Protection	Entire fluid pathway	Catheter body only

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Summary

- Antimicrobial (AM) Technology
  - Cook® Spectrum® Turbo-ject® PICC
  - Arrow® PICC with Chlorag+ard® Technology
- Antithrombogenic (AT) Technology
  - Angiodynamics® Bioflow PICC with Endexo™ Technology
  - Arrow® PICC with Chlorag+ard® Technology
- Combination AM and AT Technology
  - Arrow® PICC with Chlorag+ard® Technology

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