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
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
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?
# Is It Real? PICC-Related Infection

<table>
<thead>
<tr>
<th></th>
<th>Rates of Infection</th>
<th>(Maki 2006)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PICC:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-patient</td>
<td>2.1/1000 days</td>
<td></td>
</tr>
<tr>
<td>Out-patient</td>
<td>1.0/1000 days</td>
<td></td>
</tr>
<tr>
<td><strong>CVC:</strong></td>
<td>Rates of Infection</td>
<td></td>
</tr>
<tr>
<td>Antimicrobial</td>
<td>1.6/1000 days</td>
<td></td>
</tr>
<tr>
<td>Non-antimicrobial</td>
<td>2.7/1000 days</td>
<td></td>
</tr>
</tbody>
</table>

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
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

aDivision of General Internal Medicine, bHospital Outcomes Program of Excellence of the Ann Arbor Veterans Affairs Medical Center, cThe Division of Infectious Diseases, University of Michigan Health System, Ann Arbor, Mich.

<table>
<thead>
<tr>
<th>INFECTION</th>
<th>Patients without Cancer</th>
<th>Patients with Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>1.0 to 2.1/1000 catheter days</td>
<td>1.8 to 7.7/1000 catheter days</td>
</tr>
<tr>
<td>Mortality</td>
<td>Estimated 12-25%</td>
<td>Estimated 31-36%</td>
</tr>
</tbody>
</table>

Chopra 2012
Four Sources of CRI

- **INTRALUMINAL**
  - Access sites (26%)

- **EXTRALUMINAL**
  - Insertion site (45%)

- **HEMATOGEOUS SEEDING**
  - Distant site

- **INFUSATE**
  - Rare

Safdar & Maki, 2004
# PICC Related Thrombosis

<table>
<thead>
<tr>
<th>THROMBOSIS</th>
<th>Patients without Cancer</th>
<th>Patients with Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>2.0 to 5.5% (symptomatic thrombosis)</td>
<td>3.4 to 7.8% (symptomatic thrombosis)</td>
</tr>
<tr>
<td>Mortality</td>
<td>1-2%</td>
<td>2-4% (50% higher for cancer patient)</td>
</tr>
</tbody>
</table>

“…measures for preventing arm DVT in cancer patients should be a first-line aim for oncologists.”  

(Munoz 2008)
### Risk Factors: PICC-Related Thrombosis

<table>
<thead>
<tr>
<th>Hypercoagulability</th>
<th>Endothelial Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormalities in clotting factors</td>
<td>Solutions with high or low pH or high osmolality</td>
</tr>
<tr>
<td>Previous DVT</td>
<td>Traumatic vessel cannulation</td>
</tr>
<tr>
<td>Ethnicity; Age</td>
<td>Multiple insertion attempts</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Large bore introducer</td>
</tr>
<tr>
<td>Trauma</td>
<td>Repetitive passes thru subclavian</td>
</tr>
<tr>
<td>Inflammatory process</td>
<td>Placement in area of friction</td>
</tr>
<tr>
<td>Pregnancy, hormone replacement</td>
<td>Large catheter size (dialysis, PICC)</td>
</tr>
<tr>
<td></td>
<td>Left sided insertion site</td>
</tr>
<tr>
<td></td>
<td>Previous central venous catheter</td>
</tr>
<tr>
<td></td>
<td>Location site (femoral, IJ, subclavian)</td>
</tr>
<tr>
<td></td>
<td>Suboptimal tip location</td>
</tr>
<tr>
<td></td>
<td>Length of dwell</td>
</tr>
</tbody>
</table>

- **Venous Stasis**
  - Dehydration, leukocytosis
  - Multi-lumen catheters
  - Immobility of blood flow
  - Inappropriate catheter vessel ratio
  - Vessel compression (tumor)
  - Small vein size
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
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**
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
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)
Cook Spectrum®
Turbo-ject® PICC
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.
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)

**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 quantitative 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

Zones of inhibition in petry dish
Cook Spectrum® Turbo-ject® PICC

- **Impregnation:**
  - Internal catheter lumen surfaces
  - External catheter lumen surface
  - Combination of minocycline and rifampin make it appear orange
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)
Arrow® PICC with Chlorag+ard® Technology
• 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
**Chlorhexidine Usage in Healthcare**

- **Topical Skin Prep**
  - Prior to surgery
  - Invasive procedures
  - CVC insertion

- **Scrub Solution**
  - Preoperative bathing
  - Daily bathing (ICU)
  - General skin cleaning

- **Catheters**
  - CVC and PICC

- **Catheter Dressing**
  - CHG foam disc
  - CHG gel pad

- **Miscellaneous**
  - Oral rinse
  - Gauze dressing
  - Hand antisepsis
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
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
Arrow® PICC with Chlorag+ard® Technology

Continuous protection for at least 30 days**

**In vitro data on file, Teleflex Incorporated

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

**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
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
## Antimicrobial PICC Summary Table

<table>
<thead>
<tr>
<th></th>
<th>Arrow® PICC w/ Chlorag+ard® Technology</th>
<th>Cook Spectrum® Turbo-ject®</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organisms Covered</strong></td>
<td>Gram positive, Gram negative, Fungal</td>
<td>Gram positive, Gram negative</td>
</tr>
<tr>
<td><strong>Testing methods</strong></td>
<td>Log reduction focusing on colonization reduction</td>
<td>Zone of inhibition focusing on attachment</td>
</tr>
<tr>
<td><strong>Length of protection</strong></td>
<td>Up to 30 days</td>
<td>&gt; 30 days</td>
</tr>
<tr>
<td><strong>Surface area</strong></td>
<td>Internal and external catheter surface, extension lines, catheter hub</td>
<td>Internal and external catheter surface</td>
</tr>
</tbody>
</table>
Antithrombogenic PICC Technologies

Angiodynamics® Bioflo with Endexo™ Technology

(Formerly Navilyst)

Arrow® PICC with Chlorag+ard® Technology

Endexo is trademark or registered trademark of Interface Biologics Inc.
Angiodynamics®
Bioflo with Endexo™
Technology
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
Bioflo PICC with Endexo™ Technology Claims

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

• Catheter Occlusion
  No mention
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
**Bioflow PICC with Endexo™ Technology**

<table>
<thead>
<tr>
<th>Section</th>
<th>Details</th>
</tr>
</thead>
</table>
| **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                                         |
Arrow® PICC with Chlorag+ard® Technology
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
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
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

*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*
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
Antithrombogenic Summary Table

<table>
<thead>
<tr>
<th>Extraluminal Catheter Surface Thrombus Reduction</th>
<th>Arrow® PICC with ChloraG+ard® Technology</th>
<th>Angiodynamics® Bioflow PICC with Endexo™ Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>For 30 days with live biological system data</td>
<td>For 30 days with live biological system data</td>
<td>Up to 2 hours in bench top testing:</td>
</tr>
<tr>
<td>• 61% in ovine model</td>
<td>• 92% when challenged by infection</td>
<td>• 87% reduction in vitro bloodflow loop model</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thrombus resistance does not outperform control catheter in ovine model at days 14 and 31</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intraluminal Catheter Occlusion Reduction</th>
<th>For 30 days:</th>
<th>None demonstrated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• 51% reduction in flush pressure</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Vessel Protection</th>
<th>For 30 days:</th>
<th>None demonstrated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Reduction in phlebitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 72% less intimal hyperplasia</td>
<td></td>
</tr>
</tbody>
</table>

| Areas of Protection | Entire fluid pathway | Catheter body only |
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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Lareau, R. Fachini, F. A New Option for Short or Long Term Peripheral Access to the Central Venous System. AVA 2012 Scientific Meeting.


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