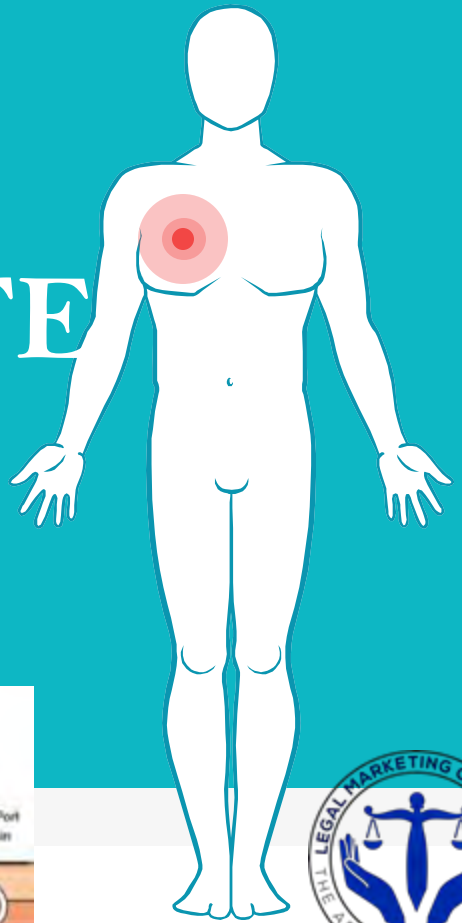
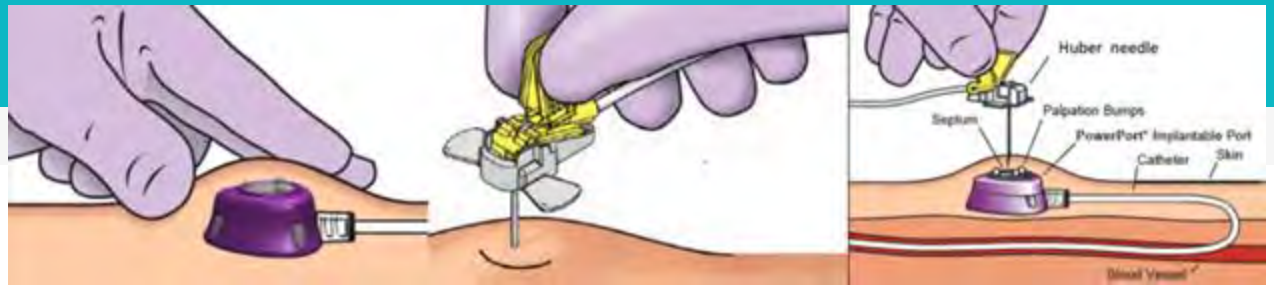
IMPLANTED PORT CATHETER LITIGATION UPDATE



December 4, 2024



LEGAL MARKETING CONCEPTS
THE APOGEE OF INTEGRITY

MDL #3081: Bard Implanted Port Catheters

Transfer Date: August 8, 2023 - District of Arizona

Sr. Judge David G. Campbell

Appointed by George W. Bush (2003)

Previously oversaw Bard IVC Filters MDL #2641

MDL # 3125: AngioDynamics Port Catheters

Transfer Date: October 3, 2024 - Southern District of California

Judge Jinsook Ohta

Appointed by Joe Biden (2021)

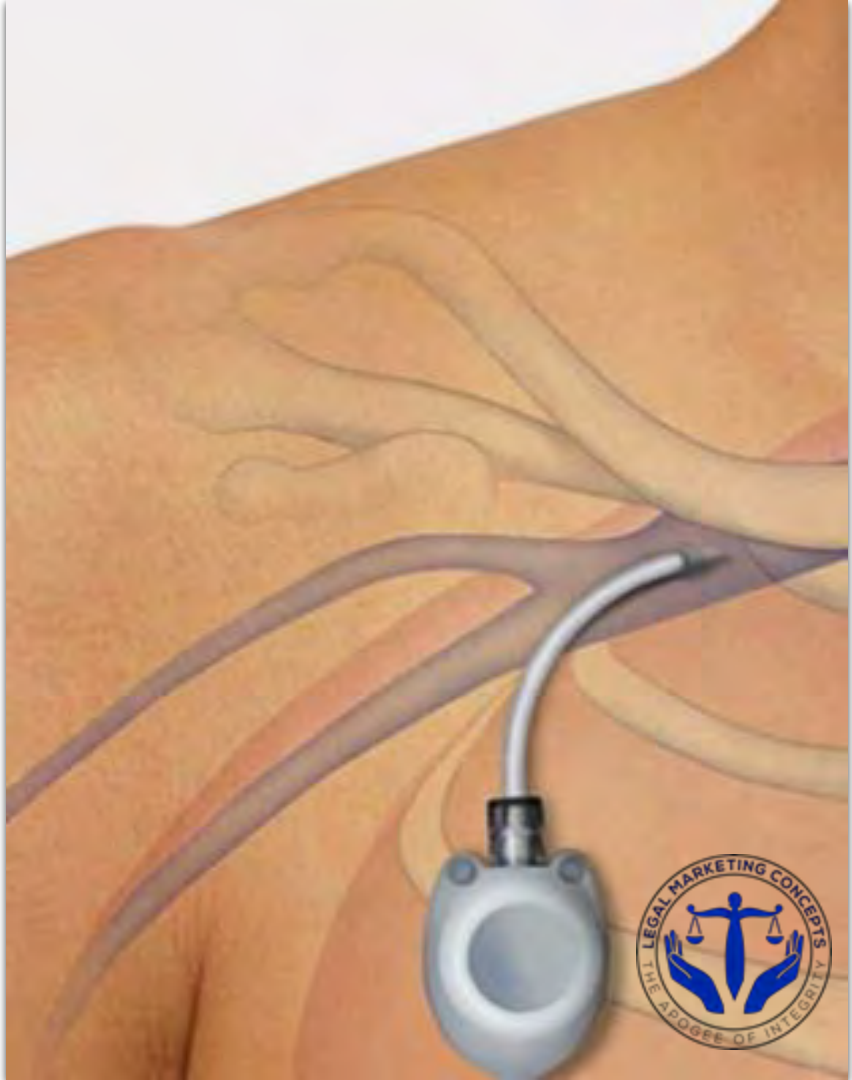
Previously worked in consumer protection in California Attorney General's office 2011-2020

NJ MCL: Bard Implanted Port Catheters

Transfer Date: October 15, 2024 - Bergen County, NJ

Judge Gregg A. Padovano

Appointed by Gov. Chris Christie (2015)



MDL #3081 Bard Port Catheter Products Litigation Leadership

Adam Evans - Partner
Dickerson Oxton - Kansas City

Rebecca Phillips - Director
Mass Torts - The Lanier Firm - Houston

Michael Sacchet - Partner
Ciresi Conlin - Minneapolis

Plaintiff Executive Committee:

Tom Pirtle (Laminack Pirtle Martines) - Tom Cartmell (Wagstaff & Cartmell) - Alex Barlow (Scott + Scott) - Shanon Carson (Berger Montague) - Stuart Ratzan (Ratzan Weissman & Boldt) - Danielle Rogers (Langdon & Emison) - Anne Schiavone (Holman Schiavone) - Larry Taylor (The Cochran Firm) - Roman Balaban (Balaban Law)

MDL #3125 AngioDynamics Port Catheter Products

Adam Evans
Dickerson Oxton

*Mr. Evans filed motion to transfer in July 2024

Anne Schiavone
Holman Schiavone

*Ms. Schiavone successfully argued for centralization in October 2024

Judge Jinsook Ohta
Southern District of California

*Appointed to oversee MDL #3125

- On October 3, 2024 the JPML panel issued a transfer order creating AngioDynamics Port Catheter Products MDL #3125 and transferred the cases to the Southern District of California assigning them to District Court Judge Jinsook Ohta.

- Judge Ohta has requested that all submissions for leadership appointments for MDL #3125 be submitted by the next status conference on December 13, 2024.

Current Status of Litigation

MDL #3081 Bard Implanted Port Products - District of Arizona
Senior District Judge David G. Campbell

- Corporate Depos ongoing
- 48 Bellwether submissions were made on April 1, 2024
- Pool to be narrowed to 15 cases December 13, 2024
- March 3, 2025 Bellwether Group #1 (six cases) will be selected

Some Important Developments:

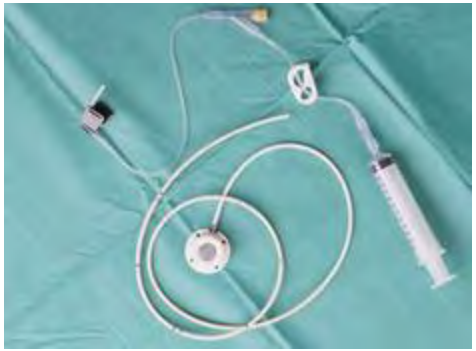
1. Joint Stipulation re Becton Dickinson Successor Liability, Bankruptcy Protection
2. Development of top experts, fact witnesses in support of powerful liability theories
3. Discovery Schedule extended by one month
4. Robust Third-Party Discovery ongoing

Current Status of Litigation

MDL #3125 AngioDynamics Port-a-Cath - District of Southern California
District Court Judge Jinsook Ohta
Biden Appointee (September 2021)
Formed October 3, 2024
Next Status Conference: December 13, 2024. Judge Ohta has requested plaintiffs submit applications for leadership prior to this status conference.

State Court MCL Bard Implanted Port Products - Bergen County, NJ
Superior Court Judge Gregg A. Padovano
Formed October 15, 2024

Products in Question



A Port-A-Cath is a small medical device which is the main form of a central venous access device. Central venous access devices are small, flexible tubes placed in large veins for people who require frequent access to the bloodstream to administer medication, intravenous fluid or parenteral nutrition.

The Port-A-Cath is made of two parts:

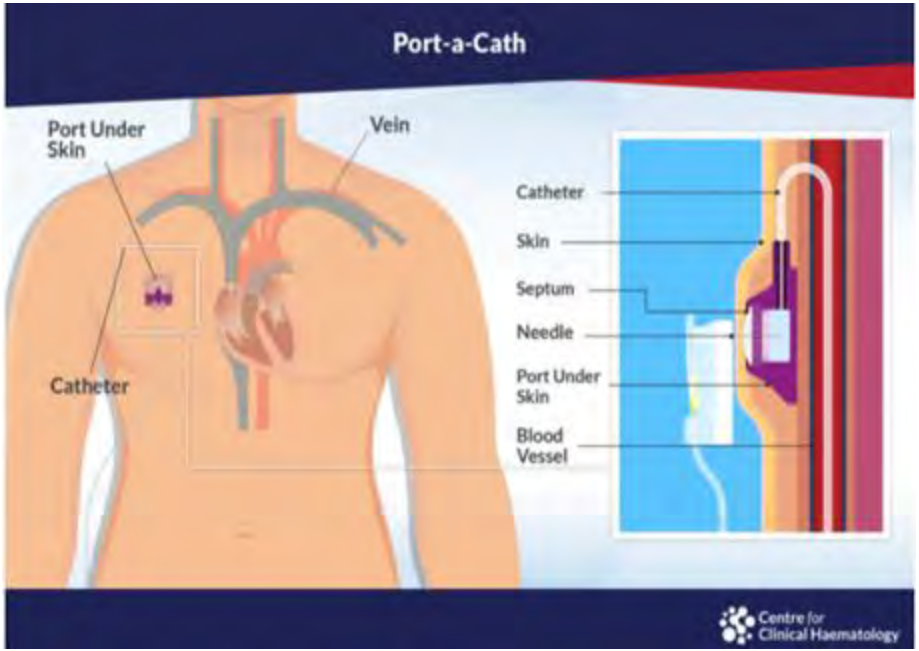
1. A soft, thin hollow plastic tube known as a catheter, which is made of either silicone or polyurethane. The tube is tunnelled under the skin with the tip sitting just outside the heart.
2. A port or disc (Approximately 2.5- 4cm in diameter) which is constructed of either a plastic or titanium reservoir and implanted in the chest and connected to the tube/catheter.

The catheter tip will be fished into either the subclavian or jugular vein just above the heart and the other end connects to the port just underneath the skin on the chest.

THE HISTORY OF PORT-A-CATHS

OVERVIEW:

- Totally Implantable Venous Access Devices (TIVADs), more commonly referred to as Port-a-Caths, which are a type of Central Venous Catheters (CVC), first came into use in 1981. The first power injection port received 510(k) clearance by the FDA in 2006.
- Port-a-Catheters are a small central venous access port implanted under the skin of the chest area. It is attached to a catheter (thin, flexible tube) that is threaded along a large vein into a place near the heart.
- Acceptance of these devices has grown rapidly, with well over 300,000 TIVADs implanted into patients in the US annually.
- Intravascular catheter market in the US is a **$10 Billion** with a ~5% annual growth rate



COMMON USES OF SUBCUTANEOUS INJECTION PORT CATHETERS

- Chemotherapy Administration
- Medication Administration
- Parenteral Nutrition
- Intravenous Infusions
- Contrast for CT & MRI

The usage of the TIVADs continues to increase year-over-year due their instrumental value in convenience and ease of access for the administration of long-term treatment. Advances in chemotherapy, the need for repeated and continuous intravenous blood transfusions, chronic diseases, parenteral nutrition for ailments such as terminal cancer or short bowel syndrome are readily initiated eliminating the need for long-term hospitalization.

Manufacturers and Products

Bard Access (BD)

- Bard MRI Ports
- BardPort
- Bard PowerPort
- Bard SlimPort
- ClearVue
- Titanium Low-Profile
- Vaccess CT
- X-Port ISP
- *Numerous Others

Angiodynamics

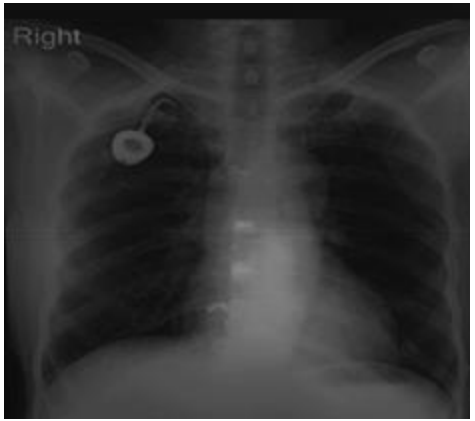
- BioFlo
- SmartPort
- Vaxcel
- Vortex
- Xcela
- *Numerous Others

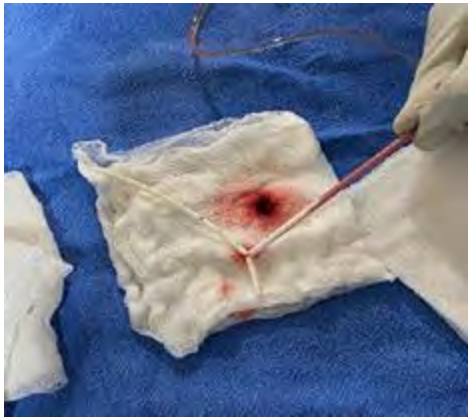
Injuries

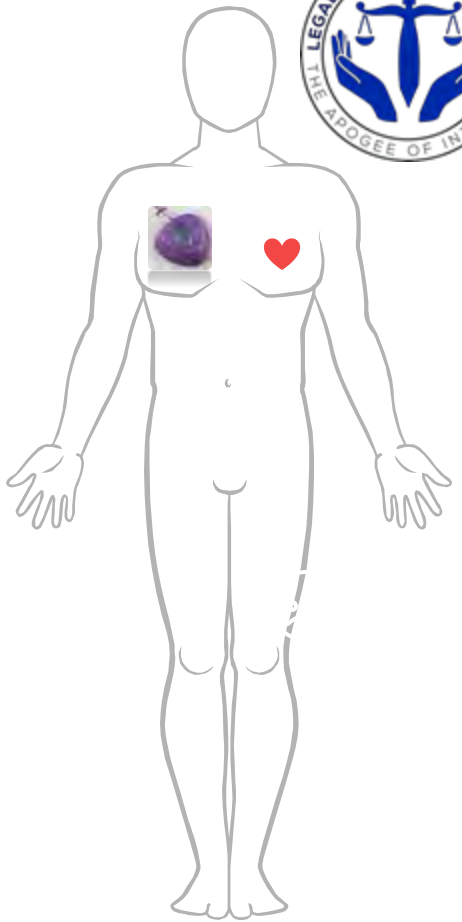
- Fracture of catheter tube
- Dislodgement of catheter from port ↟
- Port site erosion*
- Infection/Sepsis
- Thrombovascular complications

↟ Specific to Angiodynamics SmartPort

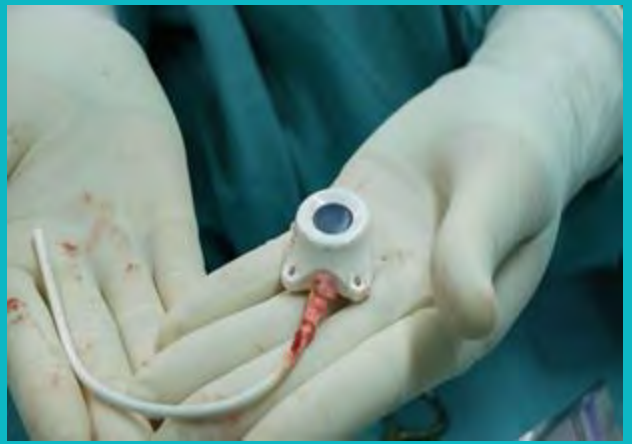
*Specific to Bard models with palpation bumps on the port septum







Design & Mechanism of Complications



While expert reports and testimony will further elucidate how the shoddy manufacturing practices create a rough surface of the catheter tube, creating the injury environment, numerous peer-reviewed studies over the past four decades have shown how issues with the design and manufacturing correlate to the injuries.

Mechanism of fracture

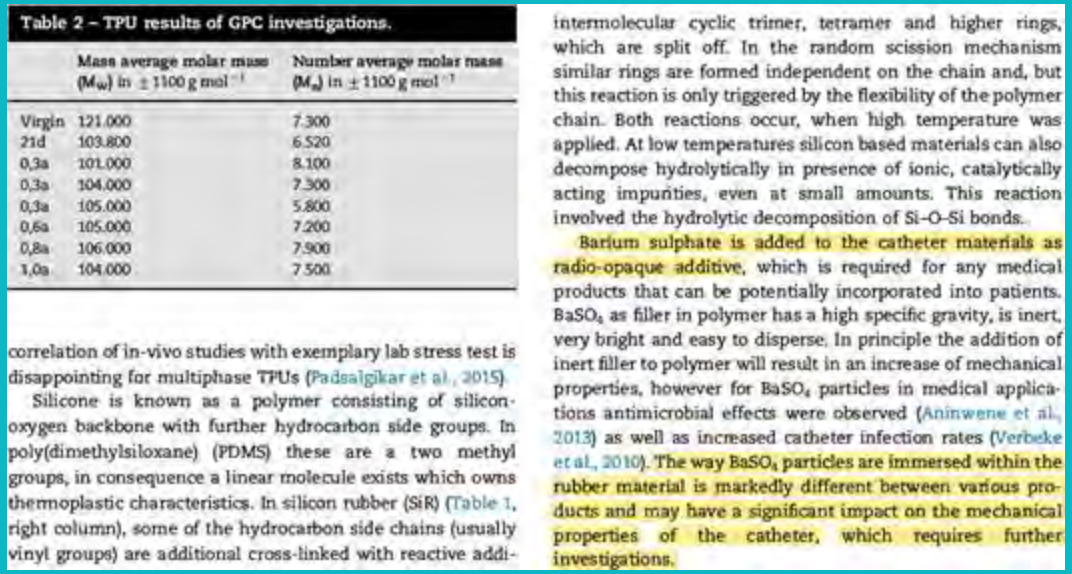


Table 2 – TPU results of GPC investigations.

	Mass average molar mass (M_w) in ±1100 g mol^{-1}	Number average molar mass (M_n) in ±1100 g mol^{-1}
Virgin	121.000	7.300
21d	103.800	6.520
0,3a	101.000	8.100
0,3a	104.000	7.300
0,3a	105.000	5.800
0,6a	105.000	7.200
0,8a	106.000	7.900
1,0a	104.000	7.500

correlation of in-vivo studies with exemplary lab stress test is disappointing for multiphase TPUs (Padsalgikar et al., 2015).

Silicone is known as a polymer consisting of silicon-oxygen backbone with further hydrocarbon side groups. In poly(dimethylsiloxane) (PDMS) these are a two methyl groups, in consequence a linear molecule exists which owns thermoplastic characteristics. In silicon rubber (SiR) (Table 1, right column), some of the hydrocarbon side chains (usually vinyl groups) are additional cross-linked with reactive addi-

intermolecular cyclic trimer, tetramer and higher rings, which are split off. In the random scission mechanism similar rings are formed independent on the chain and, but this reaction is only triggered by the flexibility of the polymer chain. Both reactions occur, when high temperature was applied. At low temperatures silicon based materials can also decompose hydrolytically in presence of ionic, catalytically acting impurities, even at small amounts. This reaction involved the hydrolytic decomposition of Si–O–Si bonds.

Barium sulphate is added to the catheter materials as radio-opaque additive, which is required for any medical products that can be potentially incorporated into patients. $BaSO_4$ as filler in polymer has a high specific gravity, is inert, very bright and easy to disperse. In principle the addition of inert filler to polymer will result in an increase of mechanical properties, however for $BaSO_4$ particles in medical applications antimicrobial effects were observed (Aninwene et al., 2013) as well as increased catheter infection rates (Verbeke et al., 2010). The way $BaSO_4$ particles are immersed within the rubber material is markedly different between various products and may have a significant impact on the mechanical properties of the catheter, which requires further investigations.

Linograms (dynamic fluoroscopic imaging with contrast injection), Barium Sulphate, and the degradation of structural integrity

BARIUM SULFATE INFUSION AND THE DEGRADING INTEGRITY OF CATHER

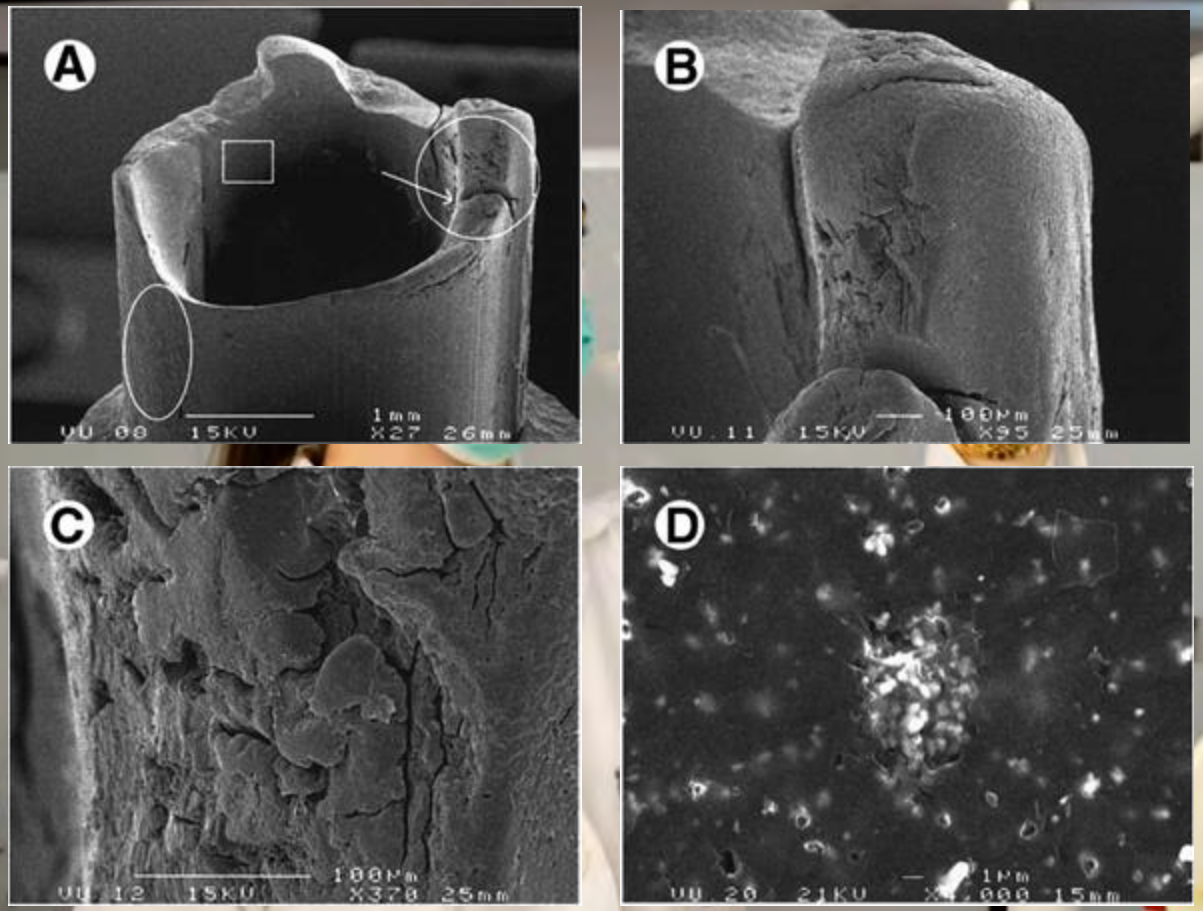
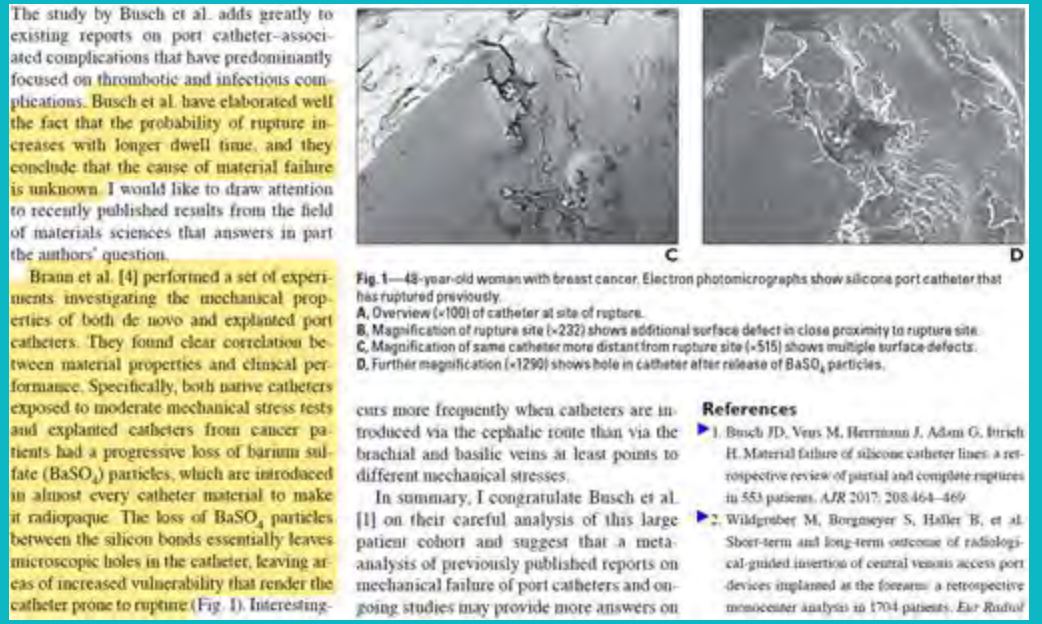


Fig 3. Scanning electron microscopy analysis. Overview of the fracture. (A) In the circle, the abnormal surface and structure are visible, including a tear (arrow) where the fracture started. The oval shows a part of the catheter with a very irregular surface. In the rectangle, the normal surface structure is apparent. (B) Detail from the white circle in A. (C) Further magnification of B, showing a lumpy texture full of voids lacking internal cohesion and beginning ruptures. (D) A barium sulfate lump with backscatter technique clearly shows entrapped air, causing a weak zone in the silicone matrix. (E) Normal smooth inner surface of the catheter. (F) Porous surface in the rupture

How does the use of barium sulphate correlate with fracture of the catheter tube?



The study by Busch et al. adds greatly to existing reports on port catheter–associated complications that have predominantly focused on thrombotic and infectious complications. Busch et al. have elaborated well the fact that the probability of rupture increases with longer dwell time, and they conclude that the cause of material failure is unknown. I would like to draw attention to recently published results from the field of materials sciences that answers in part the authors' question.

Braun et al. [4] performed a set of experiments investigating the mechanical properties of both de novo and explanted port catheters. They found clear correlation between material properties and clinical performance. Specifically, both native catheters exposed to moderate mechanical stress tests and explanted catheters from cancer patients had a progressive loss of barium sulfate ($BaSO_4$) particles, which are introduced in almost every catheter material to make it radiopaque. The loss of $BaSO_4$ particles between the silicon bonds essentially leaves microscopic holes in the catheter, leaving areas of increased vulnerability that render the catheter prone to rupture (Fig. 1). Interestingly, rupture occurs more frequently when catheters are introduced via the cephalic route than via the brachial and basilic veins at least points to different mechanical stresses.

In summary, I congratulate Busch et al. [1] on their careful analysis of this large patient cohort and suggest that a meta-analysis of previously published reports on mechanical failure of port catheters and ongoing studies may provide more answers on

C D

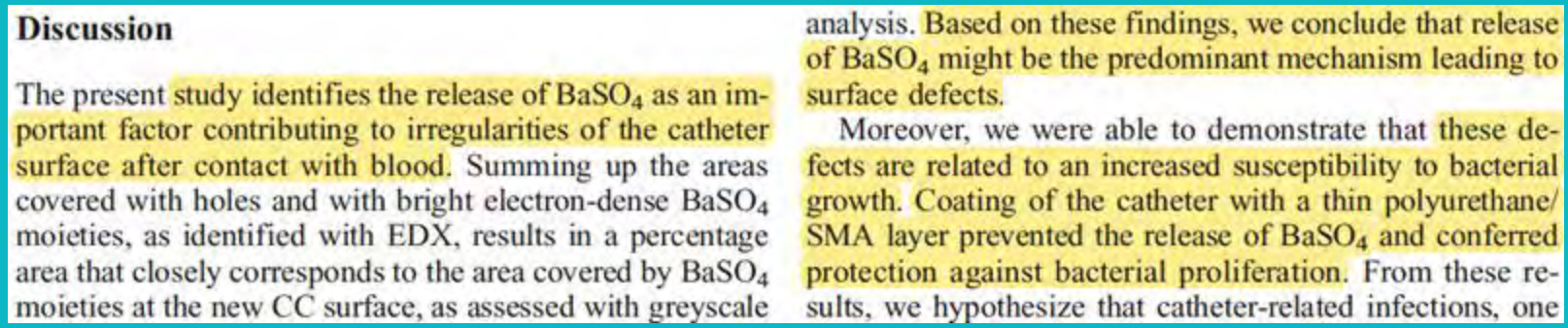
Fig. 1—48-year-old woman with breast cancer. Electron photomicrographs show silicone port catheter that has ruptured previously.
A, Overview (×100) of catheter at site of rupture.
B, Magnification of rupture site (×232) shows additional surface defect in close proximity to rupture site.
C, Magnification of same catheter more distant from rupture site (×515) shows multiple surface defects.
D, Further magnification (×1290) shows hole in catheter after release of $BaSO_4$ particles.

References

1. Busch JD, Veus M, Herrmann J, Adam G, Ittrich H. Material failure of silicone catheter lines: a retrospective review of partial and complete ruptures in 553 patients. *AJR* 2017; 208:464–469
2. Wildgruber M, Borgmeyer S, Haller B, et al. Short-term and long-term outcome of radiological-guided insertion of central venous access port devices implanted at the forearm: a retrospective monocenter analysis in 1704 patients. *Eur Radiol*

Researcher's letter to the editor in scientific journal encapsulates the studies that define the issue and its mechanism for causation of a fracture injury

How is the use of barium sulphate an issue?



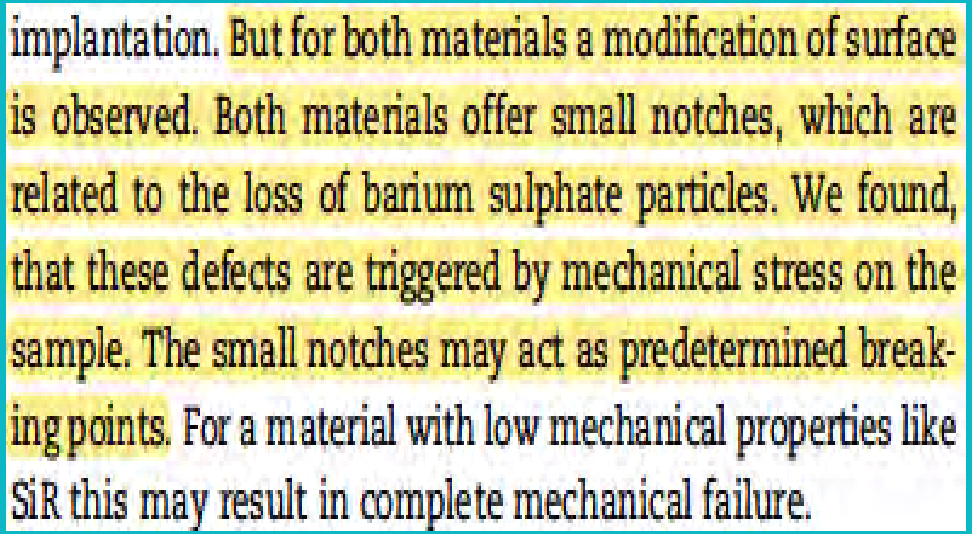
Discussion

The present study identifies the release of $BaSO_4$ as an important factor contributing to irregularities of the catheter surface after contact with blood. Summing up the areas covered with holes and with bright electron-dense $BaSO_4$ moieties, as identified with EDX, results in a percentage area that closely corresponds to the area covered by $BaSO_4$ moieties at the new CC surface, as assessed with greyscale analysis. Based on these findings, we conclude that release of $BaSO_4$ might be the predominant mechanism leading to surface defects.

Moreover, we were able to demonstrate that these defects are related to an increased susceptibility to bacterial growth. Coating of the catheter with a thin polyurethane/SMA layer prevented the release of $BaSO_4$ and conferred protection against bacterial proliferation. From these results, we hypothesize that catheter-related infections, one

Study after study continue to identify barium sulphate distribution throughout the catheter as one of the mechanisms for catheter integrity failure and a source of thrombosis and infection…

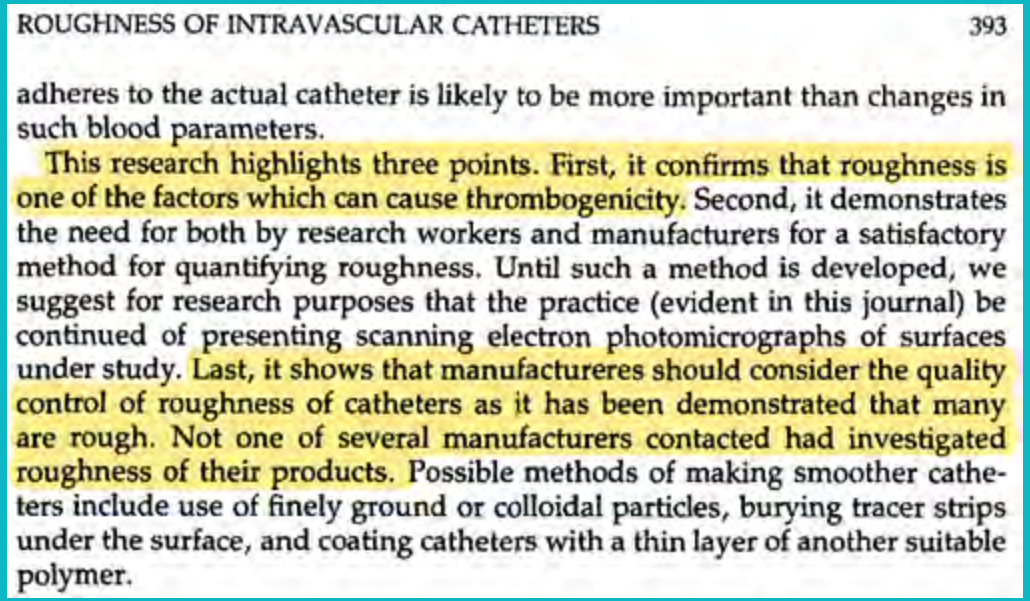
Studies confirm issues for both silicon and polyurethane catheters



implantation. But for both materials a modification of surface is observed. Both materials offer small notches, which are related to the loss of barium sulphate particles. We found, that these defects are triggered by mechanical stress on the sample. The small notches may act as predetermined breaking points. For a material with low mechanical properties like SiR this may result in complete mechanical failure.

Numerous studies draw congruent conclusions as to material morphology of the catheter surface of both silicon and polyurethane based catheters. Noting that Thermoplastic Polyurethanes (TPU) had a higher correlation with infections and thrombogenicity, whereas silicone-based catheters a higher propensity to fracture.

These issues have been documented for over 30 years



ROUGHNESS OF INTRAVASCULAR CATHETERS 393

adheres to the actual catheter is likely to be more important than changes in such blood parameters.

This research highlights three points. First, it confirms that roughness is one of the factors which can cause thrombogenicity. Second, it demonstrates the need for both by research workers and manufacturers for a satisfactory method for quantifying roughness. Until such a method is developed, we suggest for research purposes that the practice (evident in this journal) be continued of presenting scanning electron photomicrographs of surfaces under study. Last, it shows that manufactureres should consider the quality control of roughness of catheters as it has been demonstrated that many are rough. Not one of several manufacturers contacted had investigated roughness of their products. Possible methods of making smoother catheters include use of finely ground or colloidal particles, burying tracer strips under the surface, and coating catheters with a thin layer of another suitable polymer.

A 1985 study noted connection between roughness of catheter surface causing complications. Researchers contacted all Port-a-cath manufacturers about the issue and offered an easy solution… but nothing was ever done..

Material Degradation

(Information obtained from non-confidential sources)

Bard (and essentially all other port manufacturers) use a polymer called Chronoflex in their polyurethane catheters.

Original formulation of Chronoflex was biodurable and resistant to degradation *in vivo.*

A key material required to manufacture Chronoflex was discontinued in 2008. Using anything else in its place creates a totally different polymer with different physical properties.

Bard and Angiodynamics began to manufacture PU catheters with poor-performing substitute materials

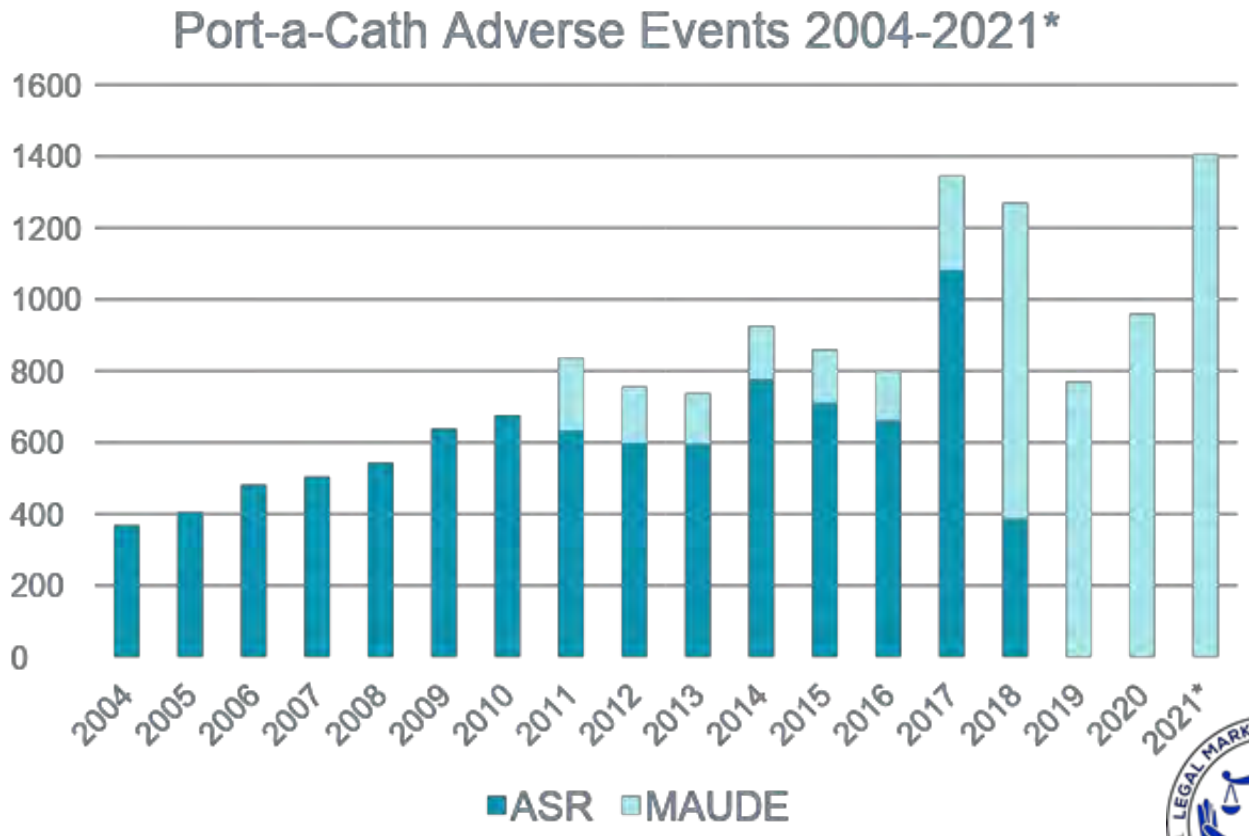
- Never notified the FDA, sought 510(k)
- Continue to sell adulterated products branded as “Chronoflex”

From **2004-2010 there were *0* MDR reports in MAUDE**, while there were over 3,600 filed in the ASR.

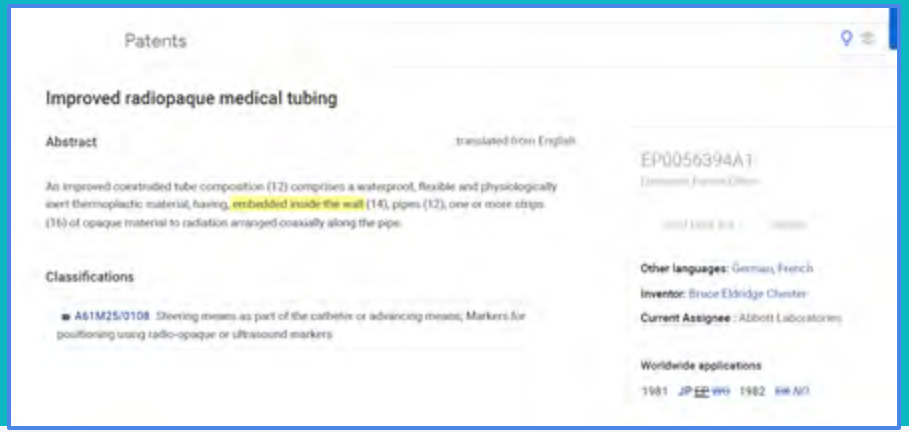
From 2004-17, there were more than 9,000 DENs submitted, while only 1,200 MDRs showed up in MAUDE.

In total there were more than 14,000 issues reported 2004-21*.

***77% uptick** in estimated AEs for 2021



Safer Alternatives in use



Patents

Improved radiopaque medical tubing

Abstract

translated from English

An improved coextruded tube composition (12) comprises a waterproof, flexible and physiologically inert thermoplastic material, having, embedded inside the wall (14), pipes (12), one or more strips (16) of opaque material to radiation arranged coaxially along the pipe.

EP0056394A1

Classifications

A61M25/0108 Steering means as part of the catheter or advancing means; Markers for positioning using radio-opaque or ultrasound markers

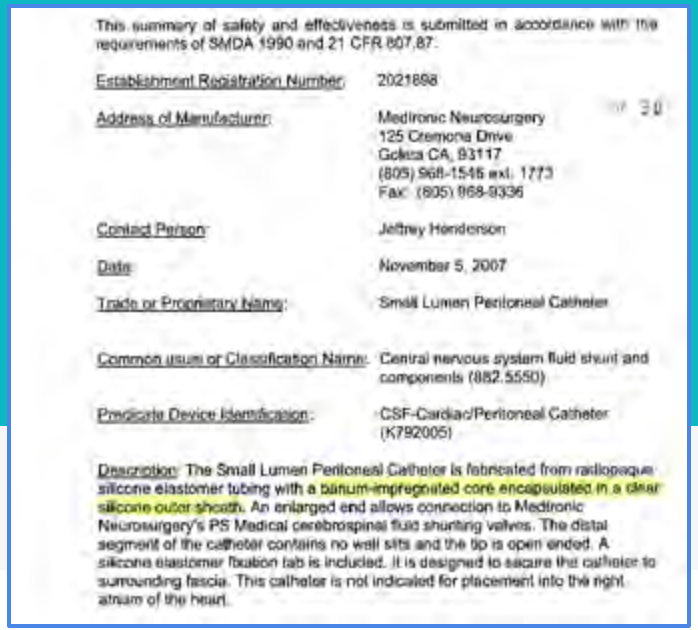
Other languages: German, French

Inventor: Bruce Eldridge Chester

Current Assignee : Abbott Laboratories

Worldwide applications

1981 JP EP WO 1982 DE NO



This summary of safety and effectiveness is submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.87.

Establishment Registration Number: 2021898

Address of Manufacturer: Medtronic Neurosurgery
125 Cremona Drive
Goleta CA, 93117
(805) 968-1545 ext. 1773
Fax: (805) 968-9336

Contact Person: Jeffrey Henderson

Date: November 5, 2007

Trade or Proprietary Name: Small Lumen Peritoneal Catheter

Common usual or Classification Name: Central nervous system fluid shunt and components (882.5550)

Predicate Device Identification: CSF-Cardiac/Peritoneal Catheter (K792005)

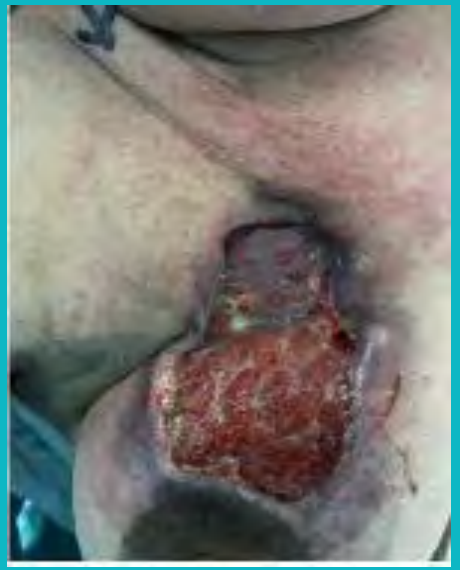
Description: The Small Lumen Peritoneal Catheter is fabricated from radiopaque silicone elastomer tubing with a barium-impregnated core encapsulated in a clear silicone outer sheath. An enlarged end allows connection to Medtronic Neurosurgery's PS Medical cerebrospinal fluid shunting valves. The distal segment of the catheter contains no wall slits and the tip is open ended. A silicone elastomer fixation tab is included. It is designed to secure the catheter to surrounding fascia. This catheter is not indicated for placement into the right atrium of the heart.

1. Coated catheters
2. Properly compounded polymers
3. Use of 'original recipe' Chronoflex

Injury Profile

1. Mechanical Failure/Fracture
2. Infection and Sepsis
3. Thrombogenesis
4. Port Body Erosion

Within 5 years of implant of port-a-cath



While the signature injury associated with the rough surface of a non-SMA coated catheter is the fracturing of the tube, infection, thrombosis and post op arrhythmia are far more prevalent. Sepsis, a common evolution of CRBSI's, is the #1 hospital related expense in the United States.

Common Injury Profile: Catheter Fracture

Reason For Exam
(IR Removal Port a Cath) port removal

Report
History: Patient with history of left subclavian Port-A-Cath placed 5 years ago. Presented to the hospital with syncopal episode and found to have a fractured catheter extending from the SVC into the right ventricle. Port chamber remains over the left chest.

Procedure:
1. Fluoroscopic guided retrieval of fractured Port-A-Cath.
2. Ultrasound-guided access to the right internal jugular vein
3. Removal of left chest Port-A-Cath
4. Conscious sedation for a total 60 minutes.

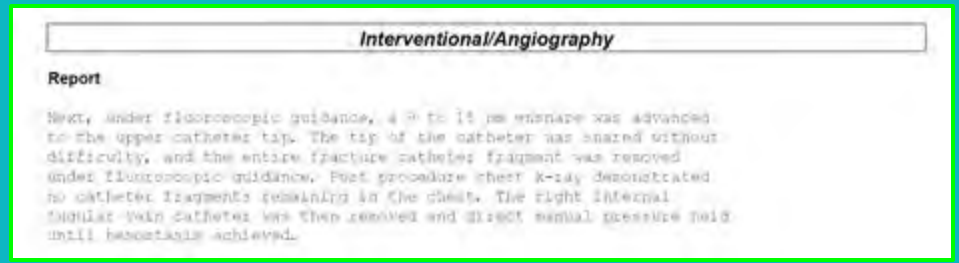
Interventional/Angiography

Report

Next, under fluoroscopic guidance, a 5 to 15 mm snare was advanced to the upper catheter tip. The tip of the catheter was snared without difficulty, and the entire fracture catheter fragment was removed under fluoroscopic guidance. Post procedure chest x-ray demonstrated no catheter fragments remaining in the chest. The right internal jugular vein catheter was then removed and direct manual pressure held until hemostasis achieved.

Catheter Fracture: Common Treatment

Standard Percutaneous Retrieval

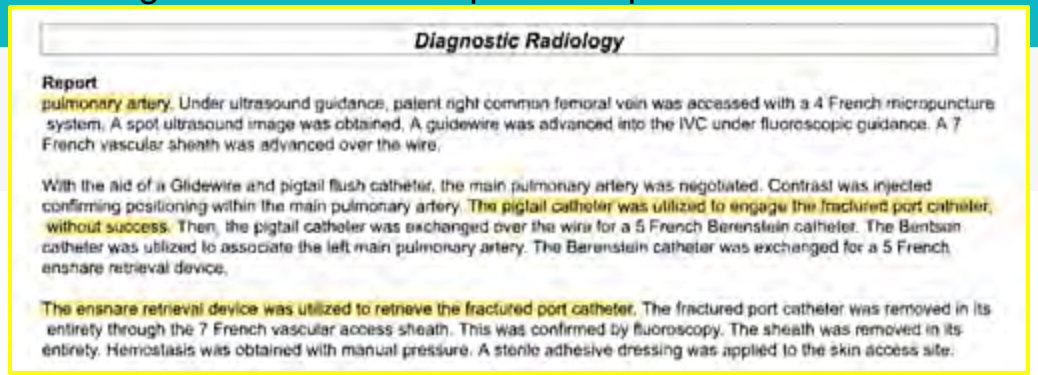


Interventional/Angiography

Report

Next, under fluoroscopic guidance, a [illegible] ensnare was advanced to the upper catheter tip. The tip of the catheter was snared without difficulty, and the entire fracture catheter fragment was removed under fluoroscopic guidance. Post procedure chest X-ray demonstrated no catheter fragments remaining in the chest. The right internal jugular vein catheter was then removed and direct manual pressure held until hemostasis achieved.

Prolonged Retrieval - Multiple Attempts*



Diagnostic Radiology

Report

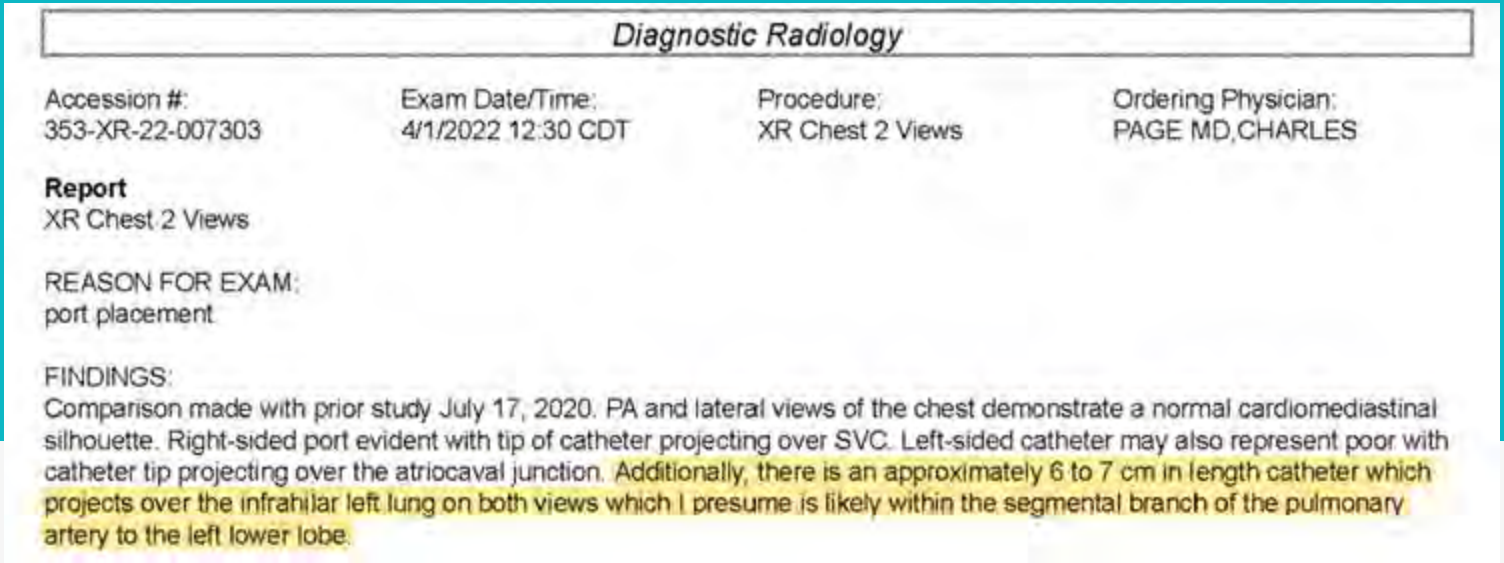
pulmonary artery. Under ultrasound guidance, patent right common femoral vein was accessed with a 4 French micropuncture system. A spot ultrasound image was obtained. A guidewire was advanced into the IVC under fluoroscopic guidance. A 7 French vascular sheath was advanced over the wire.

With the aid of a Glidewire and pigtail flush catheter, the main pulmonary artery was negotiated. Contrast was injected confirming positioning within the main pulmonary artery. The pigtail catheter was utilized to engage the fractured port catheter, without success. Then, the pigtail catheter was exchanged over the wire for a 5 French Berenstein catheter. The Berenstein catheter was utilized to associate the left main pulmonary artery. The Berenstein catheter was exchanged for a 5 French ensnare retrieval device.

The ensnare retrieval device was utilized to retrieve the fractured port catheter. The fractured port catheter was removed in its entirety through the 7 French vascular access sheath. This was confirmed by fluoroscopy. The sheath was removed in its entirety. Hemostasis was obtained with manual pressure. A sterile adhesive dressing was applied to the skin access site.

*Difficult retrievals = more time under anesthesia/fluoroscopy; greater thromboembolic risk

Catheter Fracture: Severe Presentations



Diagnostic Radiology

Accession #:	Exam Date/Time:	Procedure:	Ordering Physician:
353-XR-22-007303	4/1/2022 12:30 CDT	XR Chest 2 Views	PAGE MD,CHARLES

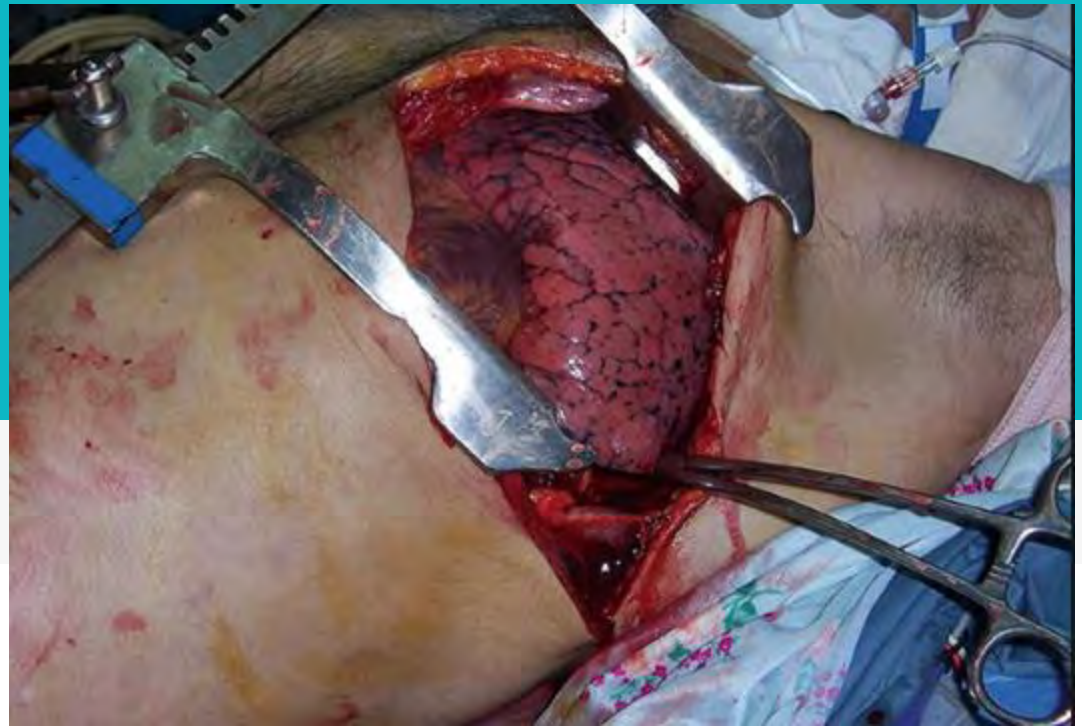
Report
XR Chest 2 Views

REASON FOR EXAM:
port placement

FINDINGS:
Comparison made with prior study July 17, 2020. PA and lateral views of the chest demonstrate a normal cardiomediastinal silhouette. Right-sided port evident with tip of catheter projecting over SVC. Left-sided catheter may also represent poor with catheter tip projecting over the atriocaval junction. Additionally, there is an approximately 6 to 7 cm in length catheter which projects over the infrahilar left lung on both views which I presume is likely within the segmental branch of the pulmonary artery to the left lower lobe.

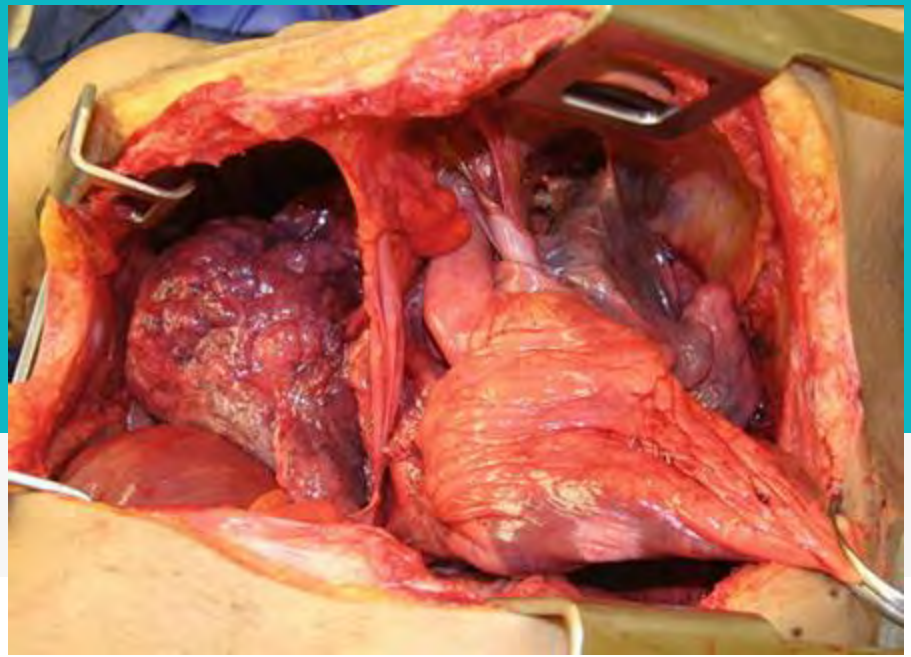
*Difficult retrievals = more time under anesthesia/fluoroscopy; greater thromboembolic risk

Catheter Fracture: Severe Presentations



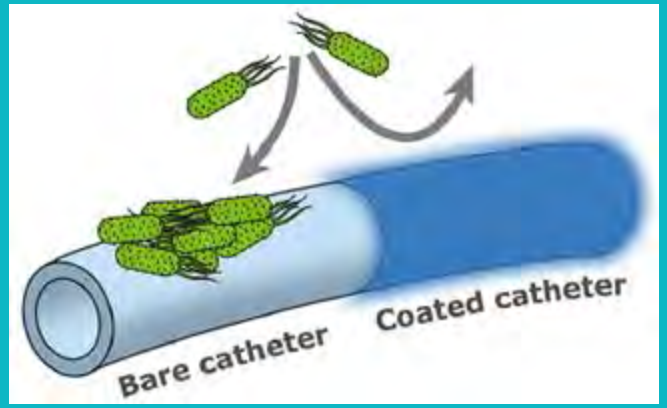
Anterolateral Thoracotomy

Catheter Fracture: Severe Presentations

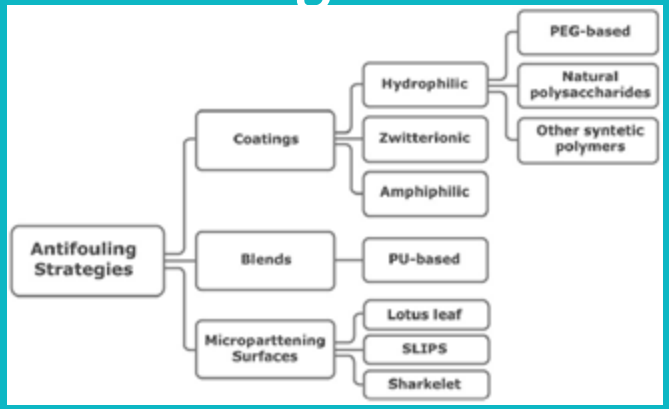


Clamshell surgery used to remove catheter fragments from the lungs

The prevalence of easily mitigated bacterial infections via Surface Modifying Adhesive Coatings



formed biofilms.[9,10] Surface modification is emerging as a promising strategy for preventing biofilm formation on abiotic surfaces. There is increasing evidence that bacterial attachment and subsequent biofilm formation are significantly impacted by surface topography.[11–13] For surfaces with topographic features at



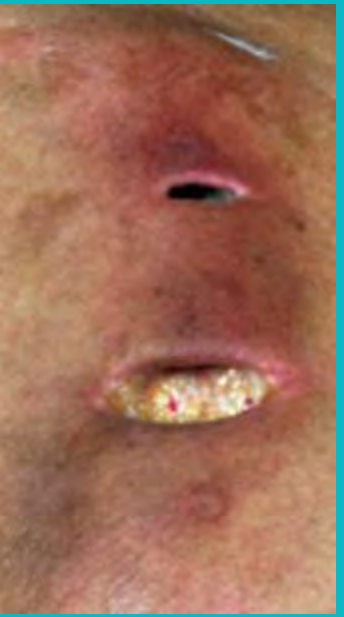
Catheter-related bloodstream infection (CRBSI) is the commonest cause of nosocomial bacteraemia.

The incidence of CRBSI arising from central venous catheters may exceed 10%.

CRBSI has a mortality rate of up to 25% and significantly increases hospital length of stay and overall treatment costs.

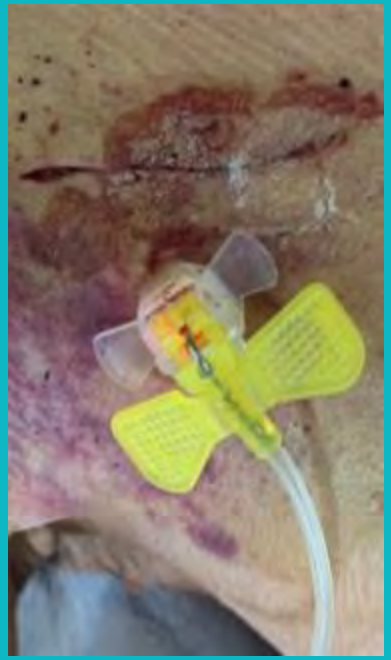
Catheter-related bloodstream infections (CRBSI's) are one of the most common sources of hospitalization and the highest morbidity related complication associated with TIVADs

Causation - Infection



- *Sepsis caused by colonization of the catheter*
  - *Transient bacteremia happen all the time*
  - *Catheter defect creates a surface more amenable to adhesion of biofilm exponentially increasing infection risk*
- *Refer to Hernia Mesh infection claims successfully resolved*
- *'Failure to warn' claim*
  - *Infection listed on IFU*
  - *Inadequate as its listing pertains to surgical site infection*
- *IFU Failed to Warn of high potential for late onset infection*
  - **Longer insitu time, exponential increase in infection risk*
  - *IFU failed to advise interval medical monitoring for immunocompromised patients who have higher risk of infection*

Notably, *A scope at antifouling strategies to prevent catheter-associated infections* (Faustino et al., 2020) found 80% - 90% reduction in infection and thrombogenic events after the application of an antimicrobial SMA coatings.



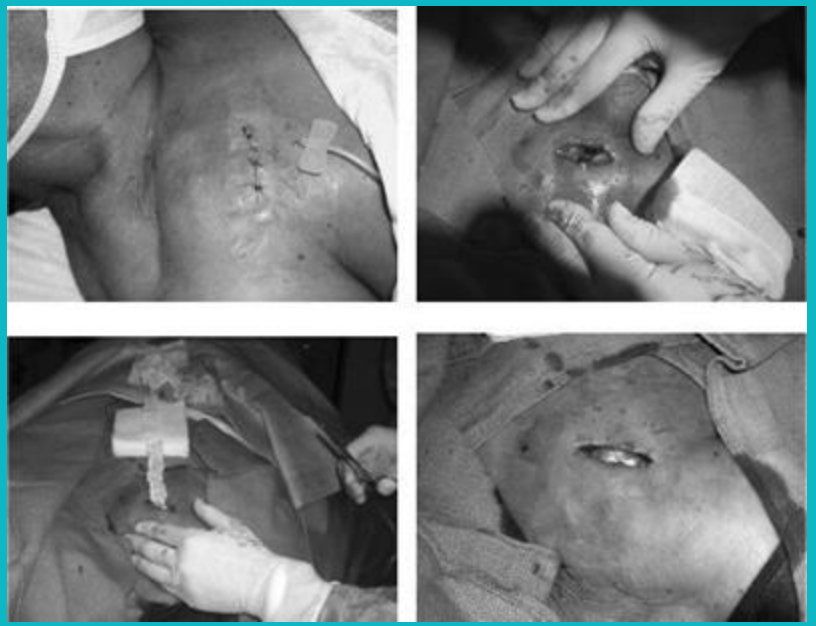
Specific Causation - Infection

- ***Bellwether Infection - Immunocompromised***
- ***Cases must have blood cultures, labs, and port studies***
- ***Have to look at microbe client tested positive for***
- ***May be compromised for one type of immune cell, but not others (e.g. compromised for T-Cells, but not Leukocytes or Neutrophils)***
- ***Patient may be predisposed to infection, but no patient is predisposed to a 'port-related infection'***
- ***Infectious disease expert rules out other contributing factors***
- ***Studies show that the rough exterior of the catheter tube, and the cracks created by the degradation of the catheter tube create a medium***
- ***Confirms port infection, rules out other causes***

When a port-related infection is suspected, cultures are taken from the port, the catheter tip, and blood from the arm on the opposite side of the body as the port implant.

The cost of sepsis management in U.S. hospitals ranks highest among admissions for all disease states. For example, in 2013, sepsis accounted for more than $24 billion in hospital expenses, representing 13% of total U.S. hospital costs, but accounted for only 3.6% of hospital stays. The $24 billion (~$18,244 per hospitalization) attributed to sepsis far surpassed the next most costly conditions: second most costly being osteoarthritis at $17

have been rising year over year (1). A 2-decade study of U.S. hospitalizations identified an increase in the incidence of sepsis among hospitalized patients by 8.7% per year (2). Additionally, sepsis accounts for more than 50% of hospital deaths (3), and mortality increases dramatically with greater disease severity: 10–20% for sepsis, 20–40% for severe sepsis, and 40–80% for septic shock (4).



Infections are one of the most common complications associated with port-a-caths. A cohort analysis reviewing more than 93,000 patients found that infections had been reported in 18% of patients within five years of implant. Sepsis is a common evolution in the infections. The 2018 study highlighted above, points to sepsis infections being the largest single hospital expense, accounting for over $24 billion in 2013 alone.

Since the 1980's hundreds of studies have been conducted on Surface Modifying Coatings that thwart bacterial growth..

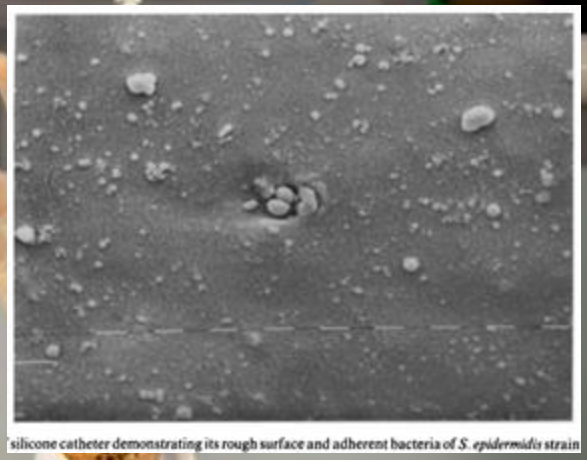
Catheter-related bacteraemia

This is the most serious type of infection. This occurs with 7–33% of catheters.[21 90] The larger value relates to patients receiving parenteral nutrition. The mortality is estimated at between 14 and 24%.[80] The usual presentation is a bacteraemia with no other obvious source of sepsis. This may be secondary to chronic colonization of the intravascular portion of the catheter from the exit site or external portions of the catheter. There is a strong correlation between thrombus formation and infection. The thrombus probably serves as a culture medium for bacteria. It is likely

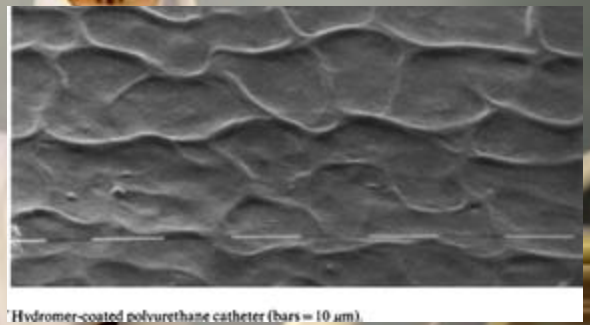
formed biofilms.[9,10] Surface modification is emerging as a promising strategy for preventing biofilm formation on abiotic surfaces. There is increasing evidence that bacterial attachment and subsequent biofilm formation are significantly impacted by surface topography.[11–13] For surfaces with topographic features at

The cost of treating catheter-related sepsis is such that the saving made by the introduction of antibiotic-coated catheters would be of the order of $100 million in the USA, with 7000–12 000 deaths prevented.[78] However, to date no long-term devices have been marketed with such coatings or impregnation.

Since the 1980's hundreds of studies have been conducted on Surface Modifying Coatings that thwart bacterial growth..



silicone catheter demonstrating its rough surface and adherent bacteria of *S. epidermidis* strain



Hydromer-coated polyurethane catheter (bars = 10 μm)

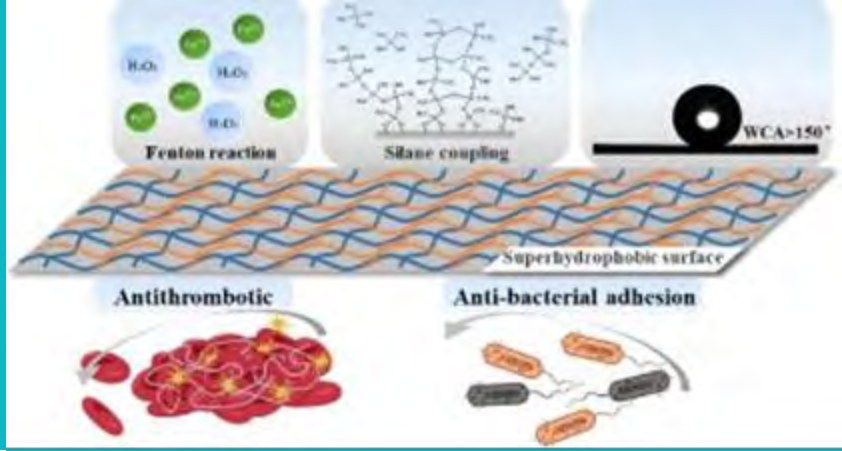
the effect of surface topography is similar for all microorganisms, even if the magnitude of F_{max} varies among the different strains. This is extremely meaningful from a practical perspective, because it indicates that further decreasing the pore size and increasing the surface porosity will improve the anti-attachment ability of anodic surfaces.

The findings of this study are of high importance, as they demonstrate a science based, yet relatively simple and practical way to prevent attachment and subsequent biofilm formation by diverse pathogenic, as well as non-pathogenic bacteria.

Introduction

Staphylococcus epidermidis is an important cause of infection of implanted medical devices such as intravascular catheters, prosthetic heart valves, pacemakers, chronic ambulatory peritoneal dialysis catheters, and orthopaedic devices [1–3]. Infection associated with central venous catheters (CVC) is a significant cause of mortality and morbidity and is a major source of bacteraemia and septicaemia in hospitalised patients [4, 5]. Intravascular catheter-related sepsis is a principle cause of sepsis in the western world with over 5000 cases of associated bacteraemias occurring annually in England and Wales (6). Microorganisms gain access to catheters over varying time periods after insertion resulting in colonisation or catheter-related sepsis following extralu-

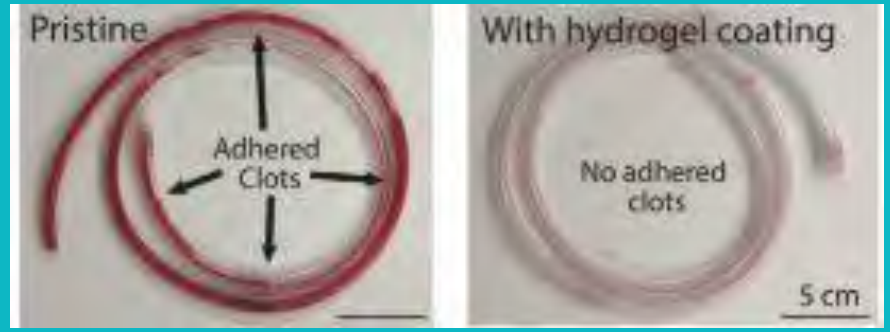
SMA coatings prevent platelet adhesion and biofilm adhesion, while providing a protective barrier between…

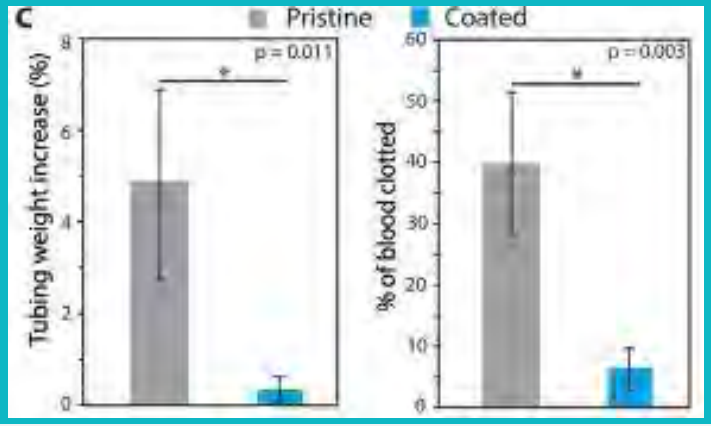


ings were prepared on a variety of substrates via a simple method. *In vitro* experiments demonstrated that the coating could effectively resist non-specific adsorption of proteins and platelet adhesion, and showed excellent anti-adhesion effects against *S. aureus* and *E. coli*. Meanwhile, the coating was not cytotoxic. *Ex vivo* experiments demonstrated that the coating exhibited anti-thrombotic properties and no tendency to exacerbate inflammatory responses. Particularly, the nanofiber coatings were proved to be stable and superhydrophobicity was retained after 28

… barium sulfate and the bloodstream

The mean tubing weight increase for the pristine tubing is 5.03% while that of coated tubing is 0.19%. This statistically significant increase ($p < 0.05$) indicates that blood clots adhered more readily to the pristine than to the coated tubing. Next, the fraction of the original blood that had formed a blood clot was assessed (clots adhered to the tubing and those in the petri dish). Approximately 40% of the blood in contact with the pristine tubing clotted, as compared to the 6.2% of that in contact with the coated tubing.





Studies of minocycline and rifampicin coatings have shown lower rates of infection than for antiseptic impregnated catheters.[23 85] The rate of colonization decreased from 22.8–26 to 7.9–8%. More importantly, the rate of catheter-related sepsis fell from 3.4–5 to 0–0.3%. It must be stated

Study after study show extraordinary statistically significant reduction of thrombogenic and bacterial infection rates when catheter tubes have an SMA coating. Further studies have also concluded that such coating would prevent barium sulfate oxidation, preventing tube fracture.


Over the past few decades mediports have become more pervasive in intravenous treatment as they are heralded for low infection risk, low profile appearance, and the long duration for use… but studies and <u>hidden</u> Adverse Event Reports paint a more troubling picture…

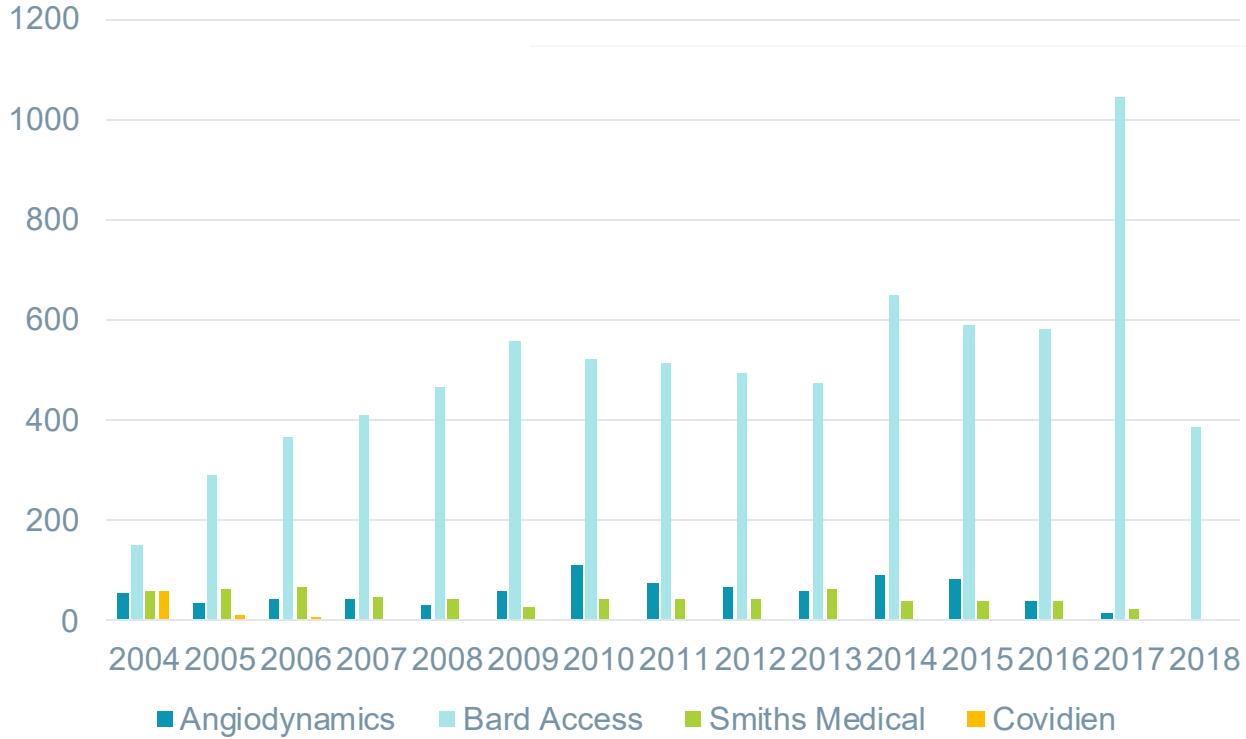

Kaiser Health News exposé in 2019 shed light on all of the hidden adverse event reports manufacturers submitted to the Alternative Summary Reporting program that was not accessible by medical professionals or the public. ***Roughly two-thirds*** of the AEs from 2004-2018 regarding Port-a-cath complications were hidden here. Although the ASR officially ended in 2019, manufacturers are still able to file for exemptions under 21 CFR 803.19

ALTERNATIVE SUMMARY REPORTING PROGRAM

DEVICE EXPERIENCE NETWORK REPORT

From 1999-2018 there were more than ***11,000*** Medical Device Reports (called Device Experience Network or DENs) reported through the Alternative Summary Reporting program.

From 2011-2018, Bard Access Systems filed 87% of all DENs, followed by Angiodynamics 8%, and Smiths Medical 5%

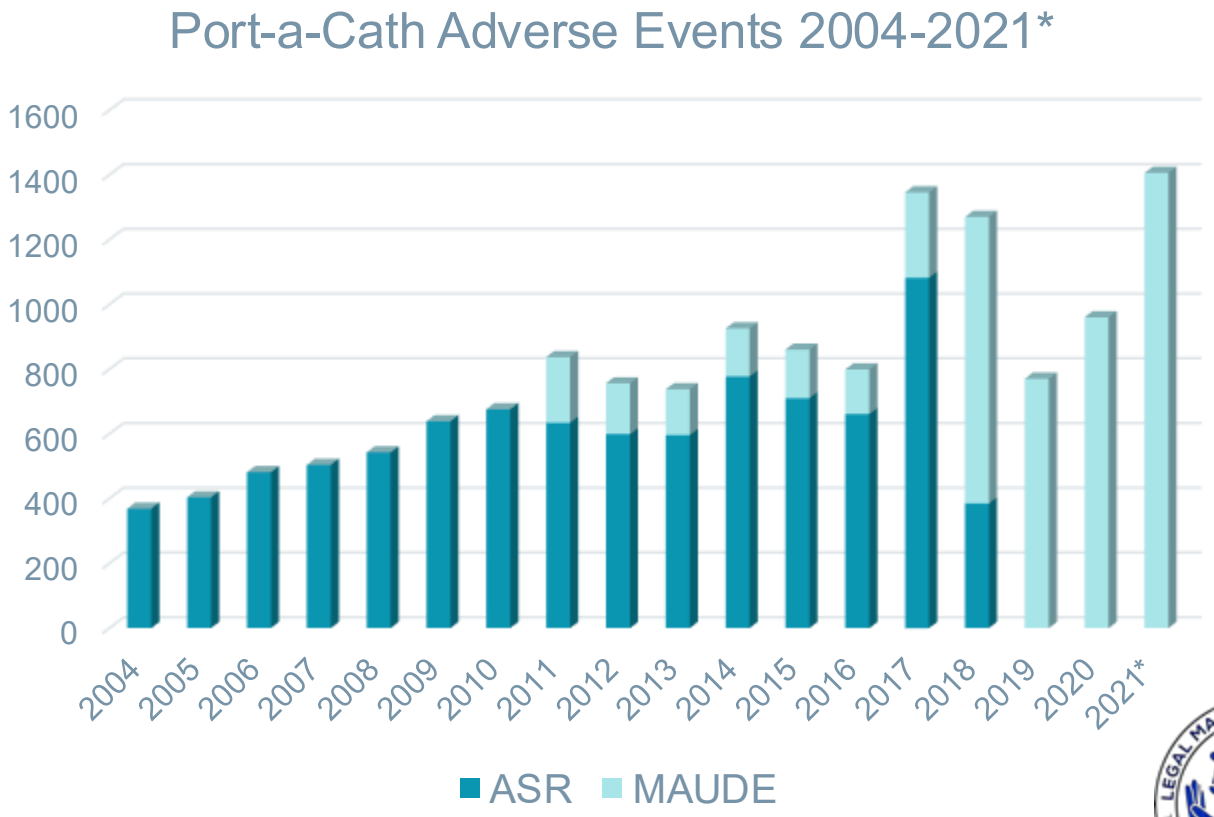


From **2004-2010 there were *0* MDR reports in MAUDE**, while there were over 3,600 filed in the ASR.

From 2004-17, there were more than 9,000 DENs submitted, while only 1,200 MDRs showed up in MAUDE.

In total there were more than 14,000 issues reported 2004-21*.

***77% uptick** in estimated AEs for 2021



MAUDE ADVERSE EVENT REPORTS 2011-2021* BREAKDOWN AS A PERCENTAGE BY COMPANY

Angiodynamics 11% Telexflex 0.25% B. Braun Medical SAS 6% **Bard Access Systems 75%**
Cook Vascular 2% Medcomp 2.25% Smiths Medical 3.5% All Others Combine >1%

Complications with respect to subcutaneous implantable ports are a pervasive issue

Caths. This study suggests that catheter fracture may be more common (8.7%) and must be considered in patients with malfunctioning low-profile Port-a-Caths. Embolized catheters can be removed by interventi

Of 2,270 patients meeting the inclusion criteria, 538 had an SI catheter, and 1,732 had a PUR catheter. Total dwell time was 584,853 catheter days. Mean total complication rate was 12.25% (SI, 14.87%; PUR,

11.43%; $P = .040$). Subanalysis revealed significant differences for material failures (eg, catheter fracture [SI,

Overwhelming evidence from studies confirming significant complication rates in both silicon and polyurethane catheters

Complication rates increase exponentially in correlation with insitu duration

Table 2
Complication rates occurring within 5 years postoperatively

Complications	*Total* n *(%)*
Any complication	55,353 (59.0%)
Infection	16,745 (17.9%)
Thrombovascular	34,499 (36.8%)
Mechanical complication	9,670 (10.3%)
Arrhythmogenic	30,625 (32.7%)

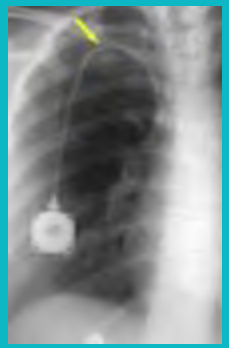
2020 Khalid et al., “Outcomes Following Port-a-Cath Placement in Medicare Patients,” cohort study reviewing more than 90,000 TIVADs over five year placement period found that **more than half** of all port-a-cath implants reported complications. Thus providing further substantiation of conclusions of Braun et al. study and greater context and supportive data for the duration exponentiality of complication conclusion.

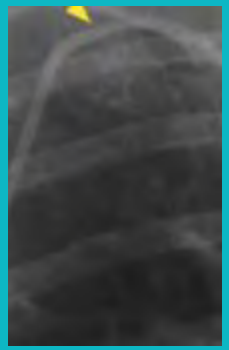
*Study identified history of atrial fibrillation as a major risk factor for development of any complication

Where we are, Where we're going

A. Bard Bellwether Protocol has been forward-thinking, deliberate and thorough
B. Evidence uncovered in discovery and via independent investigation has created compelling punitives case, new liability sources
C. Privilege and confidentiality challenges have been aggressive and has turned up valuable evidence

LITIGATION & MARKETING METRICS





- ✓ 42% of AEs reported were mechanical failure related
- ✓ ~15% Complication rate > 9 months implanted
- ✓ **59%+** Complication rate ≤ 5 years implanted
- ✓ ~80,000 devices implanted in USA in 2013
- ✓ ~300,000 devices implanted in USA in 2020
- ✓ 77% Estimated increase in AE reports for 2021*

Potential Claimant Pool: 80,000+ fracture/embolism incidents, 450,000+ compensable incidents

* Assumptions: 1,800,000 implanted ports since 2006, 4.5% fracture rate, 25% Complication Rate

Injury metrics from first 1,500 retained claimants:

- 39% of retained claimants primary injury: fracture
- 54% of retained claimants primary injury: infection
- 7% of retained claimants primary injury: thrombosis

PRESENTED BY:

This Implantable Venous Access Port litigation overview is the work product of Ethan Heck and Legal Marketing Concepts. Data and information was derived from PACER, FDA website databases (e.g. MAUDE), and exhaustive review of scientific journals prior to quantitative and qualitative analysis of said information. Data and research interpretations in addition to the corresponding hypothesis presented here are solely those of Mr. Heck.