

2019 GAVeCeLT

Verona, December 2nd-3rd-4th



La guaina fibroblastica, questa sconosciuta

Antonio La Greca
Chirurgia d'Urgenza e Trauma

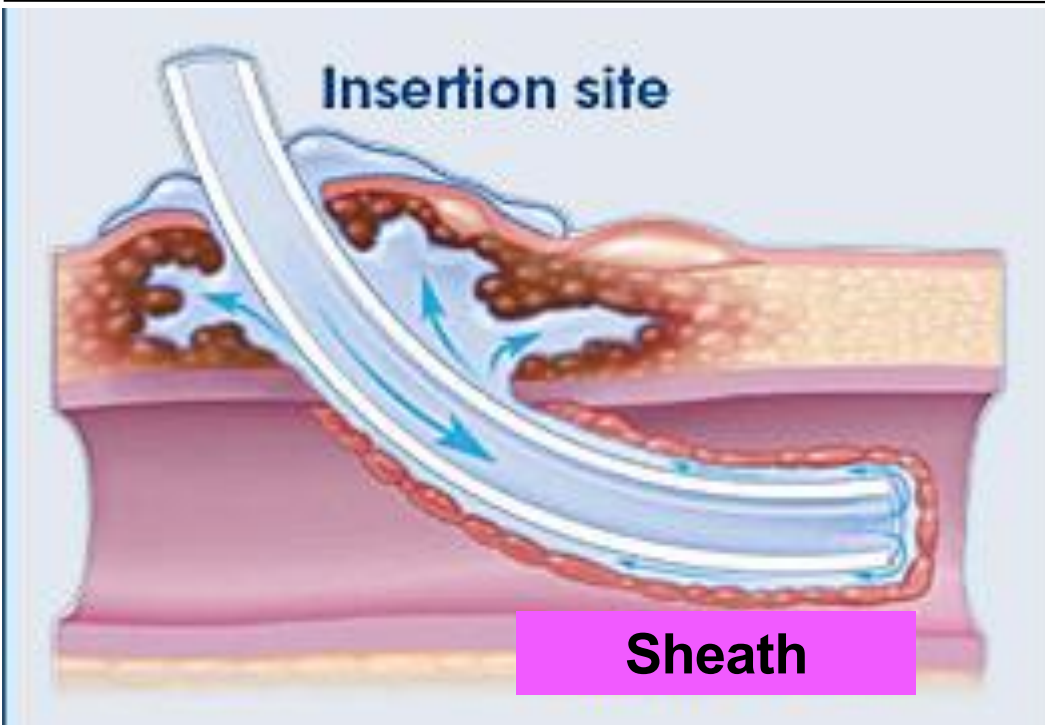


Gemelli

Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore



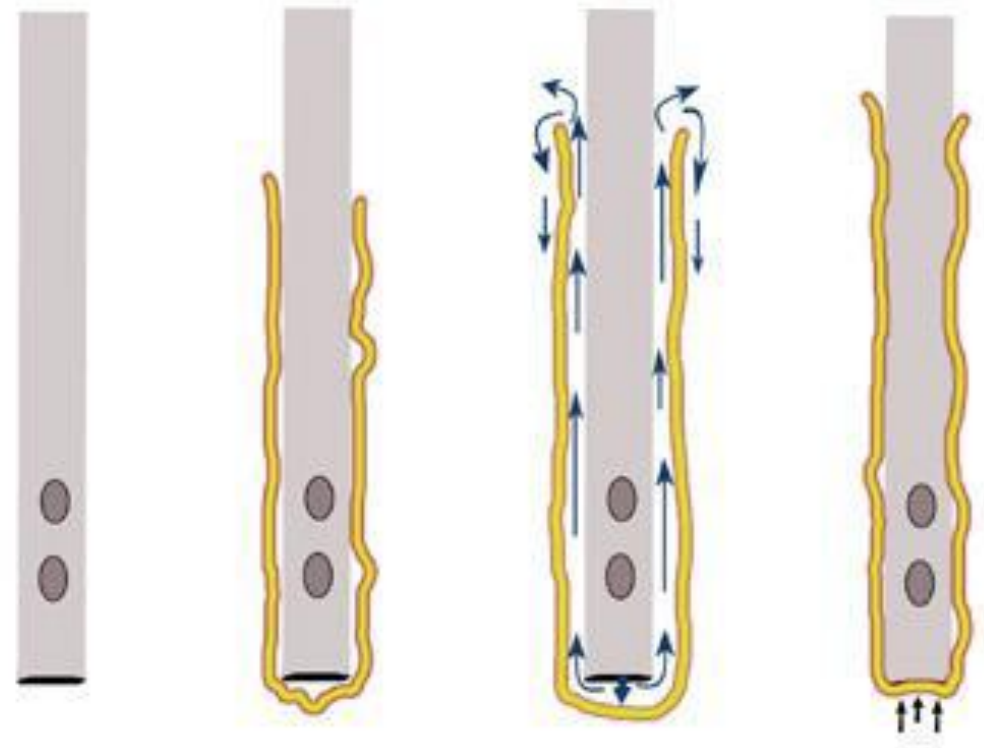
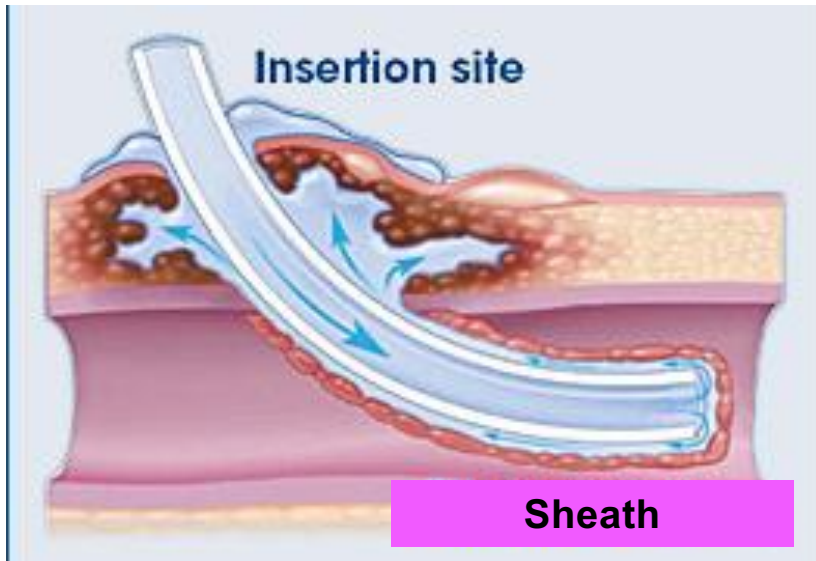
The sleeve



Collagenic (not «fibrin») sleeve, lined with endothelial cells, enveloping the catheter in its endovascular route but even extending to the subcutaneous tract / pocket



Pericatheter sleeve



- Clinically relevant as a potential reason for VAD malfunction (**withdrawal occlusion, extravasation**)
- Association with infection or venous thrombosis?

“Fibrin” sleeve

Motin J, Fischer G, Evreux J. Interet de la voie sous-claviculaire en reanimation prolongee. Lyon Med 1964;40 583–593.

Lyon Med. 1964 Oct 4;212:583-93.

IMPORTANCE OF THE SUBCLAVICULAR ROUTE IN PROLONGED RESUSCITATION (APROPOS OF 154 CASES)].

MOTIN J, FISCHER G, EVREUX J.

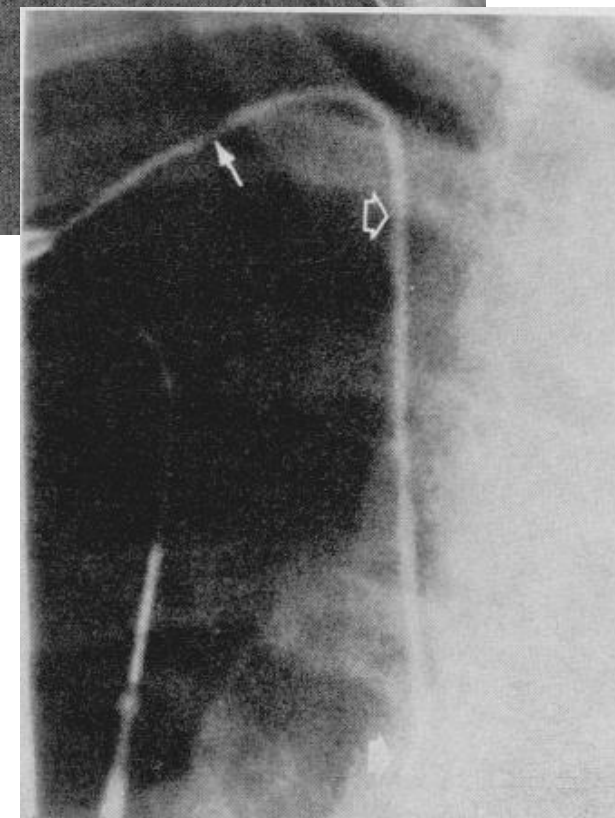


Fibrin Sleeve Formation on Indwelling Subclavian Central Venous Catheters

Verne L. Hoshal, Jr., MD;
Robert G. Ause, MD; and
Phillip A. Hoskins, MD,
Ann Arbor, Mich

Fifty-five subclavian veins with previous indwelling catheters were dissected at autopsy. Two groups of subclavian catheters injected with contrast material during removal were studied by cinefluoroscopy. Group 1 consisted of 25 patients with indwelling Teflon and polyethylene catheters. Group 2 comprised six patients with indwelling graphite-benzakonium chloride-heparin sodium (GBH) bonded polyethylene catheters. The vein dissections and the cinefluoroscopic studies in group 1 revealed that totally circumferential fibrin sleeves consistently and extensively formed on indwelling subclavian catheters. They developed on polyethylene, Teflon, nylon, and siliconized rubber catheters. These fibrin sleeves were noted at dissection on catheters within 24 hours after insertion. Two associated thrombi were discovered. Cinefluoroscopy detected one additional thrombus. These findings are an undesirable potential hazard and concern of thromboembolism is certainly warranted. Methods to eliminate fibrin sleeves seem justified. Evidence suggests that GBH-bonded catheters significantly inhibit fibrin sleeve formation.

Accepted for publication Dec 15, 1970.
From St. Joseph Mercy Hospital, Ann Arbor, Mich.
Read before the 78th annual meeting of the Western Surgical Association, Colorado Springs, Colo, Nov 20, 1970.
Reprint requests to St. Joseph Mercy Hospital, 326 N Ingalls St, Ann Arbor, Mich 48104 (Dr. Hoshal).



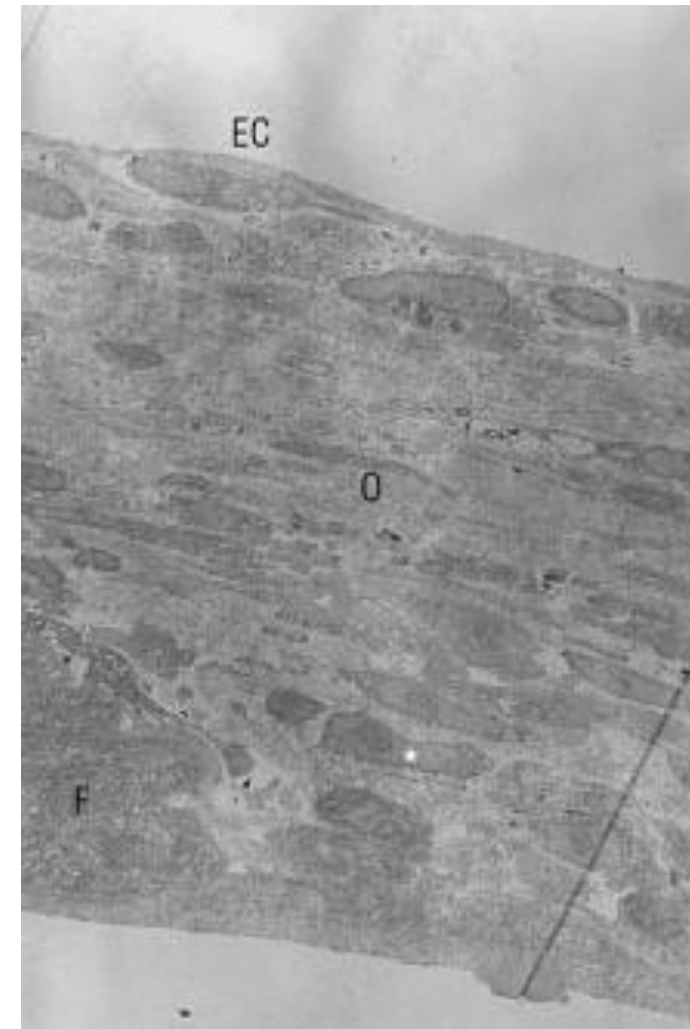
Composition and formation of the sleeve enveloping a central venous catheter

JOURNAL OF VASCULAR SURGERY
Volume 28, Number 2 1998

D.Z. Xiang, MD, E.K. Verbeken, MD, PhD, A.T.L. Van Lommel, PhD, M. Stas, MD, and I. De Wever, MD, PhD, *Leuven, Belgium*

The tissue around the catheter is a thrombus in the early stage, but a cellular-collagen tissue covered by endothelium after 1 week. Migration and proliferation of activated SMCs from the vein wall to the PCT is an important step in its transformation.

Motin introduced the term “fibrin sleeve” to describe a visible sheath around the catheter seen at autopsy. Although fibrin coating occurs, the visible sleeve is not composed of fibrin. Therefore it is appropriate to distinguish fibrin coating and catheter sleeve.



Brief Communication

Histologic Development of the Sheath That Forms Around Long-Term Implanted Central Venous Catheters

LAURA O'FARRELL, DVM, PhD; JAMES W. GRIFFITH, DVM; AND C. MAX LANG, DVM

Department of Comparative Medicine, The Milton S. Hershey Medical Center of Pennsylvania State University, Hershey, Pennsylvania

Radiology

Radiology: Volume 240: Number 2—August 2006

Andrew R. Forauer, MD
Constantine G. A. Theoharis, MD
Narasimham L. Dasika, MD

Jugular Vein Catheter Placement: Histologic Features and Development of Catheter-related (Fibrin) Sheaths in a Swine Model¹

Purpose:

To evaluate the development and histologic features of jugular vein catheter-related (fibrin) sheaths in a swine model.

Pathogenesis

INSERTION

**TIP/SHAFT
MOVEMENTS**

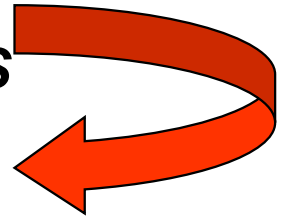
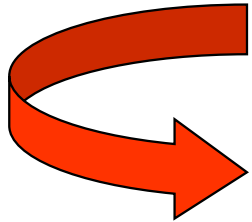
*Endothelial damage - Thromboplastin
SMCs activation and thrombogenesis
(24 hrs)*

FIBRIN

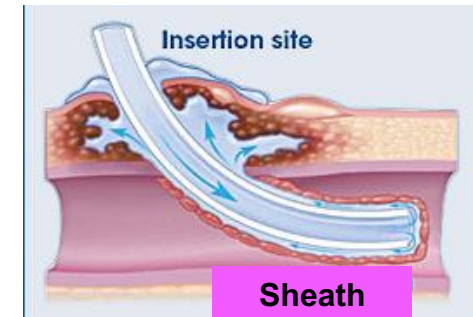
COLLAGEN

**SMOOTH MUSCLE
CELLS**

ENDOTHELIUM



Sleeve: pathogenesis



Day 1: pericatheter thrombus (PT)

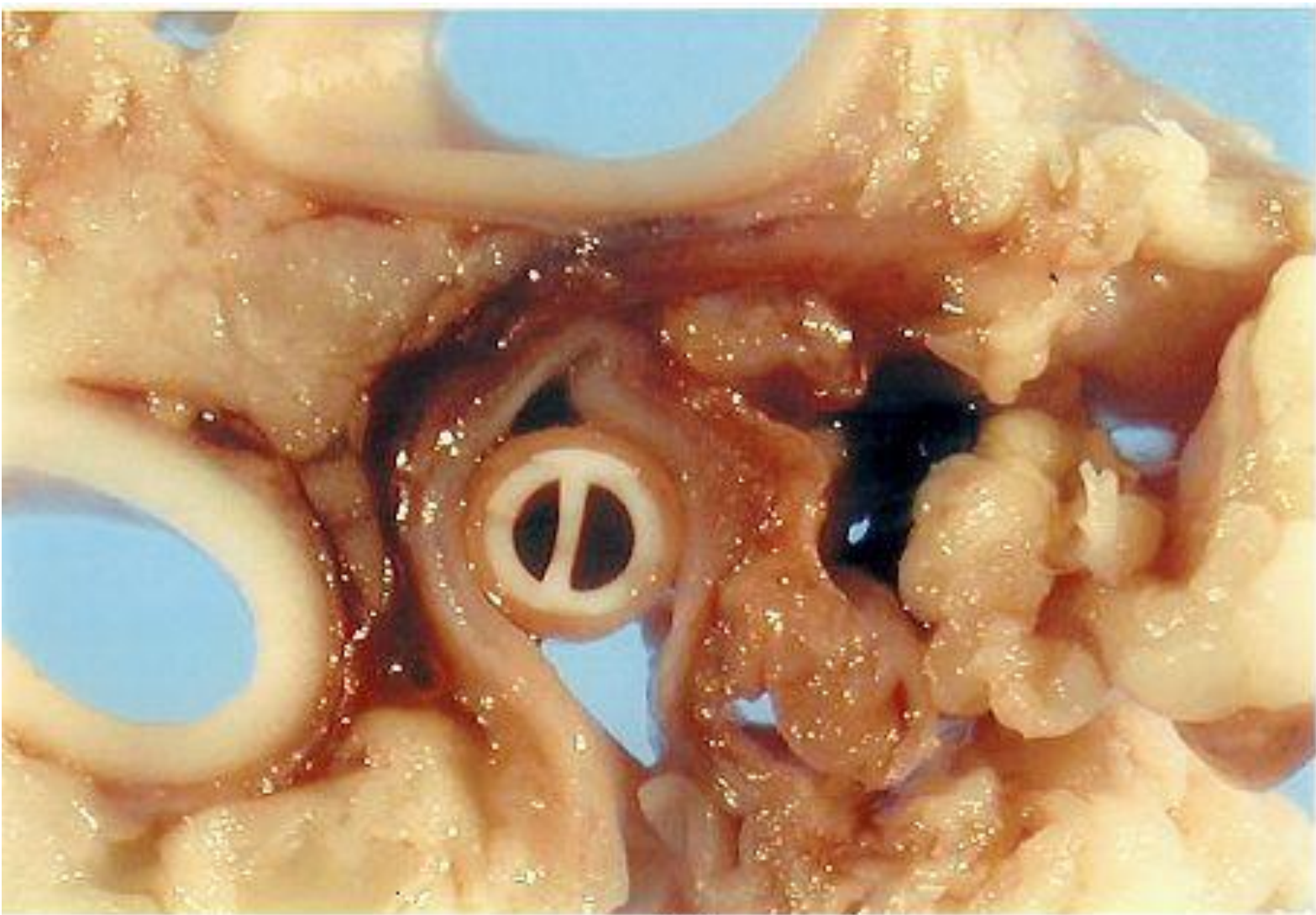
- Fibrin and platelet network
- RBC and WBC entrapped in the network all over the catheter surface

Days 3-7: thickening and protrusion

- Fibrin bridging pericatheter network / vein wall, near areas with endothelial erosion and SMC exposure
- Vein wall SMC phenotype shift from contractile to synthetic (fibroblasts)

Days 7-28: maturation of cell-collagen sleeve

- Fibrin-platelet-RGC-WBC network invaded by activated SMC
- Scarce extracellular matrix and fibrin
- Collagen fibrils, gradually dominant over cells
- Dominant collagen structure with few cells; inner endothelial lining – flow direction



Fibrin Sheaths and Central Venous Catheter Occlusions: Diagnosis and Management

Techniques in Vascular and Interventional Radiology, Vol 5, No 2 (June), 2002: pp 89-94

John Santilli, MD

Pericatheter thrombus (!!!) will persist at areas where there is repeated contact with the vein with subsequent vessel wall injury. Chronic venous injury can occur where the catheter enters the vein, where the tip contacts vascular endothelium, and at normal anatomic turning points



***Bridging close to areas of
endothelial damage / erosion /
intimal thickening***

***Proximal (insertion site)
Distal (tip)
Intermediate (shaft)***

***Pathogenetic subtypes with
clinical meaning***



Sleeve: pathogenesis

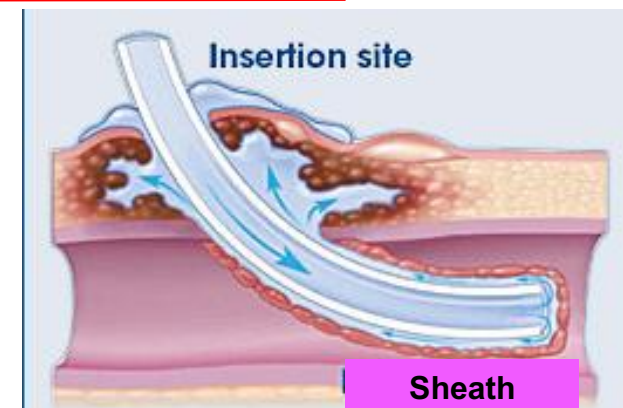
Central Venous Catheter Tip Position: A Continuing Controversy

Thomas M. Vesely, MD J Vasc Interv Radiol 2003; 14:527–534

A catheter inserted into a vein will be recognized as a foreign object and quickly covered with fibrin and plasma proteins (29). This is often fol-

Vascular injury is considered a primary initiating event for catheter-related thrombosis (30). Vascular damage may occur early at the time of catheter insertion, or the injury may be progressive, as in the setting of a malpositioned catheter tip.

eter. Although the deposition of plasma proteins and platelets onto the surface of a catheter is an expected event, in certain situations, this process may further evolve into catheter thrombosis or fibrin sheath formation.

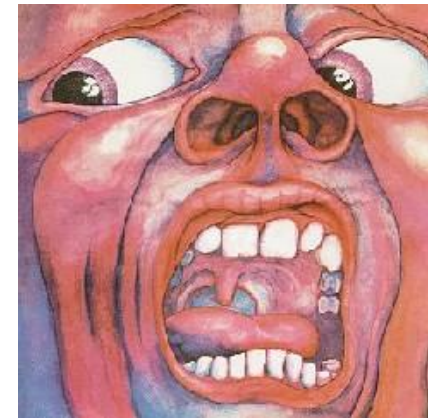


Sleeve: pathogenesis

- Dynamic response of the vein wall and plasma to the foreign body and associated insertional thrombus
- Pathogenetic steps similar in humans and animals: endothelial cells, inflammatory cells, activated SMCs are biologically active elements
- Almost «physiological»: 40%100% in the Literature
- Different from venous mural thrombus: the catheter as a physical support allows progression well beyond the focal device/wall contact (non-mural progression)

(Percarpio, 2013)

Confusion will be my epitaph ... (The King Crimson, 1969)



| NEW PARADIGMS IN ANTICOAGULATION AND THROMBOLYSIS |

Hematology 2014



Central venous catheter-related thrombosis

William Geerts¹ American Society of Hematology

¹Thromboembolism Program, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada



Pathophysiology of CRT

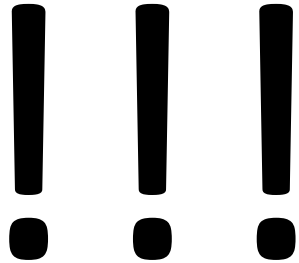
Thrombosis associated with a CVC can be classified into 3 types: pericatheter sheath ("fibrin sleeve"), thrombotic occlusion of the catheter lumen, and mural thrombosis, either superficial (SVT) or deep vein thrombosis (DVT). Insertion of a CVC produces local venous injury at the access site. Deposition of fibrin on the thrombogenic catheter surface and the subsequent in-growth of smooth muscle and endothelial cells are universal and begin within hours of insertion.² This pericatheter sheath grows along the catheter from the venotomy site. Blood flow is reduced up to 60% around the CVC, which leads to further cellular adhesion to the catheter and vein walls.³ Ongoing movement of the catheter within

Fibrin Sheaths and Central Venous Catheter Occlusions: Diagnosis and Management

Techniques in Vascular and Interventional Radiology, Vol 5, No 2 (June), 2002: pp 89-94

John Santilli, M

Thrombus formation associated with central venous catheters occurs in 2 very distinct forms. First, soft thrombus often forms at or within the tip of a catheter. However, clot can form anywhere along the entire intravascular catheter. Thrombus also forms at the site of venous entry. Clot formation here can remain relatively unnoticed for some time, thus allowing transformation into a sheath-like structure enveloping a catheter. Both types of thrombus have the potential to, and often do, propagate. Each of these types of thrombus requires their own specific treatments. The management of catheter-induced venous thrombosis is discussed elsewhere in this issue.





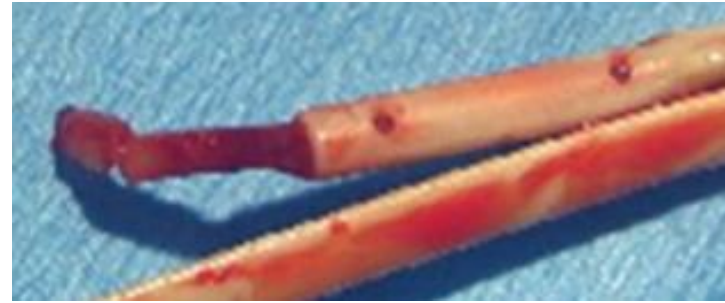
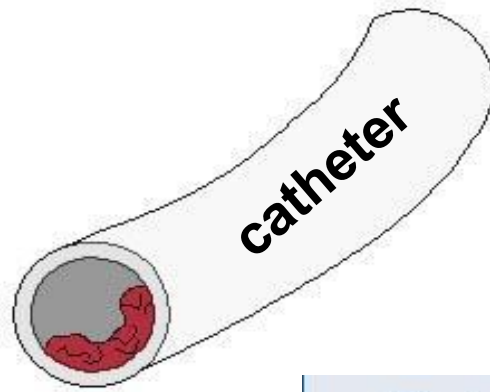
Journal of Infectious Diseases Advance Access published June 7, 2014

MAJOR ART

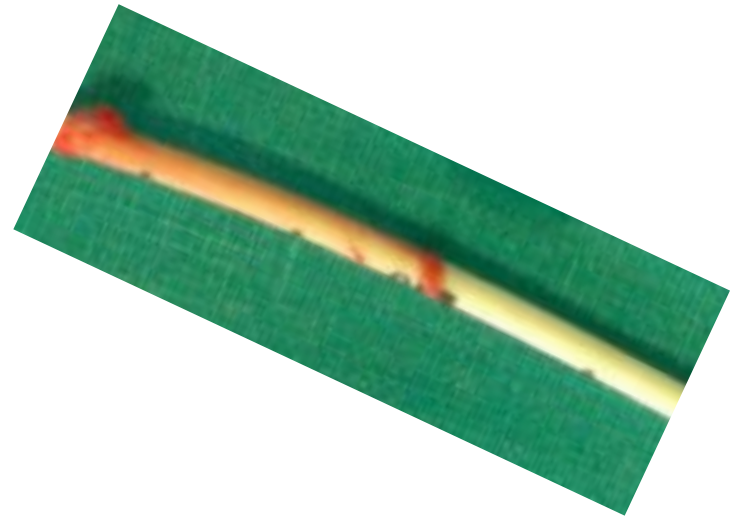
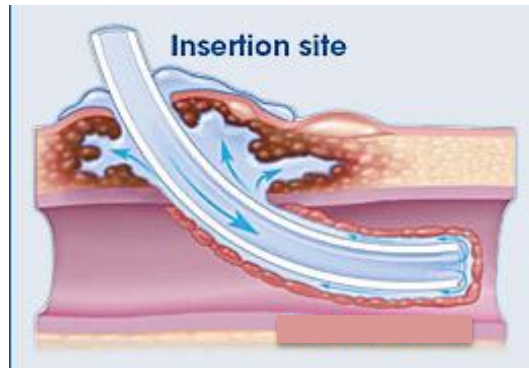
The use of catheters and other implanted devices is constantly increasing in modern medicine. Although catheters improve patients' healthcare, the hydrophobic nature of their surface material promotes protein adsorption and cell adhesion. Catheters are therefore prone to complications, such as colonization by bacterial and fungal biofilms, associated infections, and **thrombosis**. Here we describe the in vivo efficacy of biologically inspired glycocalyxlike antiadhesive coatings to inhibit *Staphylococcus aureus* and *Pseudomonas aeruginosa* colonization on commercial totally implantable venous access ports (TIVAPs) in a clinically relevant rat model of biofilm infection. Although noncoated TIVAPs implanted in rats were heavily colonized by the 2 biofilm-forming pathogens with a high percentage of occlusion, coating TIVAPs reduced their initial adherence and subsequently led to 4-log reduction in biofilm formation and reduced occlusion. Our antiadhesive approach is a simple and generalizable strategy that could be used to minimize clinical complications associated with the use of implantable medical devices.

Christophe Beloin,^{1,a} and Vincent Semetey^{2,4,a}

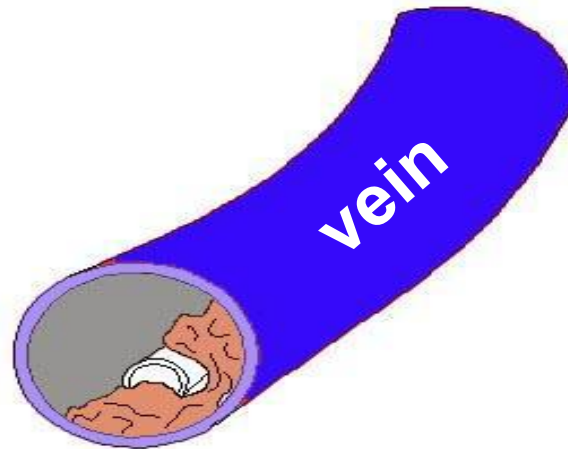
- Occlusion



- Fibroblastic sleeve



- Parietal thrombus



Sleeve: incidence

Genoa Cancer Institute (IT) 1990/2001 – 1680 pts

<i>SLEEVE</i>	62	(3.69 %)
<i>Deep Venous Thrombosis</i>	29	(1.72 %)
<i>Malposition</i>	15	(0.89 %)
<i>Extravasation</i>	14	(0.83 %)
<i>Skin erosion / decubitus</i>	13	(0.77 %)
<i>Occlusion / Fracture</i>	12	(0.71 %)
<i>TOTAL</i>	142	(8.53 %)

The most frequent late complication in LT-CVCs

Sleeve: incidence

Genoa Cancer Institute (IT) 1990/2001 – 1680 pts

	Incidenza
Ports	58/1522 (3.8%)
Tunneled/cuffed CVCs	4/ 158 (2.5%)
Total for LT-CVCs	62/1680 (3.7%)

74% symptoms within first 6 months



- **EARLY EVENT**
- **LATE CLINICAL PRESENTATION**

Sleeve: incidence

Genoa Cancer Institute (IT) 1990/2001 – 1680 pts

	Incidenza
Tip – Atrium distance <3 cm	20/62 (32.2%)
Tip – Atrium distance >3 cm	42/62 (67,8%)
	<i>p<0.05</i>



RISK FACTOR: «short» catheters are at higher risk

Sleeve: risk factors

Genoa Cancer Institute (IT) 1990/2001 – 1680 pts

Univariate analysis:

<i><u>Continuous</u> vs. intermitten infusion</i>	<i>($p < .005$)</i>
<i><u>Peristaltic</u> pumps vs elastomers</i>	<i>($p < 0.05$)</i>
<i><u>5FU</u> vs Adri/Ifosfamide/Taxani</i>	<i>($p < 0.005$)</i>

Multivariate analysis:

???

Sleeve: risk factors

Something more specific?

Sleeve: incidence and clinical features

European Journal of
Haematology



European Journal of Haematology 95 (472–479)

ORIGINAL ARTICLE

Incidence of ultrasound-detected asymptomatic long-term central vein catheter-related thrombosis and fibrin sheath in cancer patients

Maria Boddi¹, Gianluca Villa², Marco Chiostrì¹, Francesco De Antoniis¹, Ilaria De Fanti²,
Alessandra Spinelli¹, Andrea Savino¹, Gian Franco Gensini^{1,3}, Cecilia Pelagatti²

¹Department of Experimental and Clinical Medicine, Careggi Teaching Hospital, Florence; ²Section of Anesthesia and Intensive Care, Department of Human Health Science, Careggi Teaching Hospital, Florence; ³Don Carlo Gnocchi Foundation, IRCCS, Florence, Italy

400 consecutive patients candidate to CHT and referred to CVC service for insertion of a LT-CVC

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innominate, and axillary veins). Features suggestive of fibrin sheaths were considered echogenic signal longer than 20 mm and thicker than 10 mm around CVC in the tract directly explorable at the junction between jugular and sub-clavian vein, without venous wall involvement(17, 18). A



ORIGINAL ARTICLE

Incidence of ultrasound-detected asymptomatic long-term central vein catheter-related thrombosis and fibrin sheath in cancer patients

Maria Boddi¹, Gianluca Villa², Marco Chiostrì¹, Francesco De Antoniis¹, Ilaria De Fanti², Alessandra Spinelli¹, Andrea Savino¹, Gian Franco Gensini^{1,3}, Cecilia Pelagatti²

¹Department of Experimental and Clinical Medicine, Careggi Teaching Hospital, Florence; ²Section of Anesthesia and Intensive Care, Department of Human Health Science, Careggi Teaching Hospital, Florence; ³Don Carlo Gnocchi Foundation, IRCCS, Florence, Italy

- Global incidence:
 - 11.3% (45/395)
 - 0.71/1000 cath days
- 44 at 1st month
- 42 repeated US at 6 months
 - 25 LMWH: 11 persistent, 13 disappeared
 - 17 no therapy: 5 persistent, 12 disappeared
- No cateter disfunction

Table 3 Characteristics of patients with or without CVC-related fibrin sheath (RFS) at 1st-month ultrasound check-up

	CVC-RFS <i>n</i> = 45	No CVC-RFS <i>n</i> = 350	<i>P</i>
Age (yr)	63 (55–68)	60 (48–68)	0.088
Male gender (%)	23 (51.1)	101 (28.9)	0.002
Body mass index (kg/m ²)	23.4 (22.4–26.7)	24.2 (21.6–27.5)	0.453
Previous implantation (%)	2 (4.4)	24 (6.9)	0.539
No- sinus rithm at basal ECG (%)	1 (2.2)	2 (0.6)	0.230
Left side of implantation (%)	7 (15.6)	71 (20.3)	0.453
Vein area (mm ²)	126 (86–162)	99 (69–140)	0.029
Number of venipuncture			
<i>N</i> = 1	44 (97.8)	331 (94.6)	0.356
<i>N</i> > 1	1 (2.2)	19 (5.4)	
Platelet count (10 ³ /μL)	274 (201–341)	251 (199–313)	0.308

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Incidence of ultrasound-detected asymptomatic long-term central vein catheter-related thrombosis and fibrin sheath in cancer patients

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- Sheaths showed a high incidence (about 12%) and early onset (1st month)
- Sheaths and thrombotic events were not linked (only one patient had both)
- Sheaths never caused CVC dysfunction
- Resolution of sheaths occurred independently of LMWH therapy.

Comments

ORIGINAL ARTICLE

Incidence of ultrasound-detected asymptomatic long-term central vein catheter-related thrombosis and fibrin sheath in cancer patients

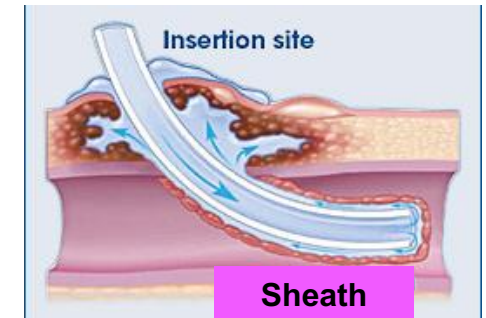
Maria Boddi¹, Gianluca Villa², Marco Chiostrì¹, Francesco De Antoniis¹, Ilaria De Fanti², Alessandra Spinelli¹, Andrea Savino¹, Gian Franco Gensini^{1,3}, Cecilia Pelagatti²

¹Department of Experimental and Clinical Medicine, Careggi Teaching Hospital, Florence; ²Section of Anesthesia and Intensive Care, Department of Human Health Science, Careggi Teaching Hospital, Florence; ³Don Carlo Gnocchi Foundation, IRCCS, Florence, Italy

- Diagnosis and definition: the so called «**pericatheter thrombus**» usually seen on radiological reports is the **ultrasound counterpart of the sleeve**
- «Pericatheter thrombus» is not a mural thrombotic event and seemengly does not represent a precursor of nor a risk factor for mural thrombosis
- Response to anticoagulation is at least not demonstrated
- As shown by its clinical evolution, maybe we should not treat it when asyptomatic (might disappear)
- The case of very thick sleeves (sporadic association with arm edema in PICC lines – unpublished data): is there any risk of vein flow reduction thus introducing a new risk factor (CATHETER TO VEIN RATIO) for venous thrombosis?



Sleeve: clinical features



1. Loss of catheter patency: Partial (withdrawal occlusion) or complete
2. Extravasation (usually associated with loss of patency):
 - at the exit site
 - within the tunnel
 - within the reservoir pocket
3. INCIDENTAL FINDING

Sleeve: clinical relevance

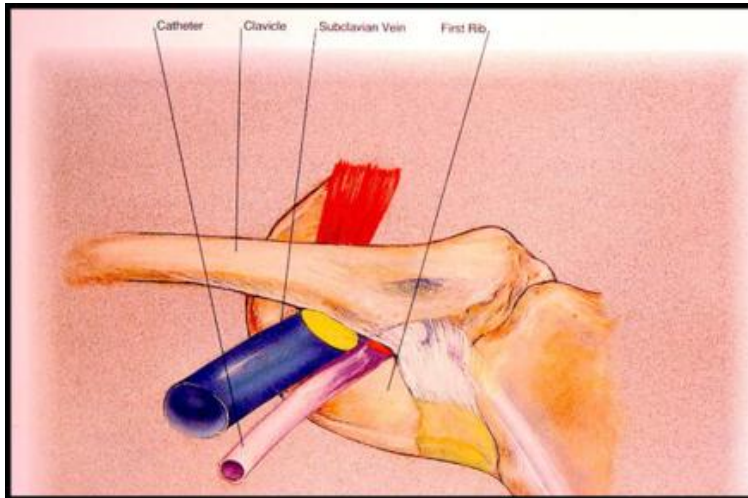
- Catheter dysfunction secondary to fibrin sheath formation can be seen in 13% to 57% of all hemodialysis patients

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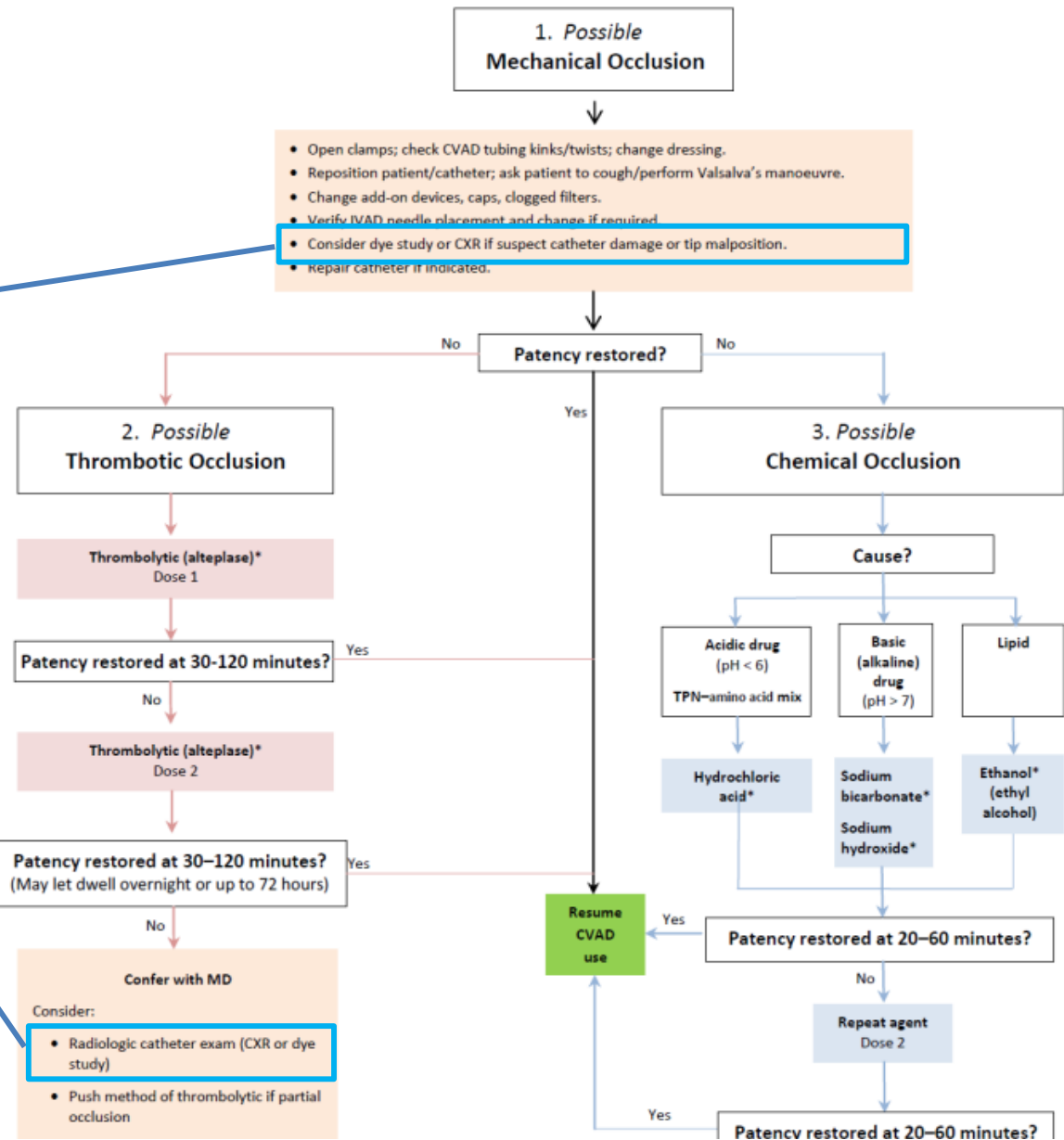
John Santilli, MD

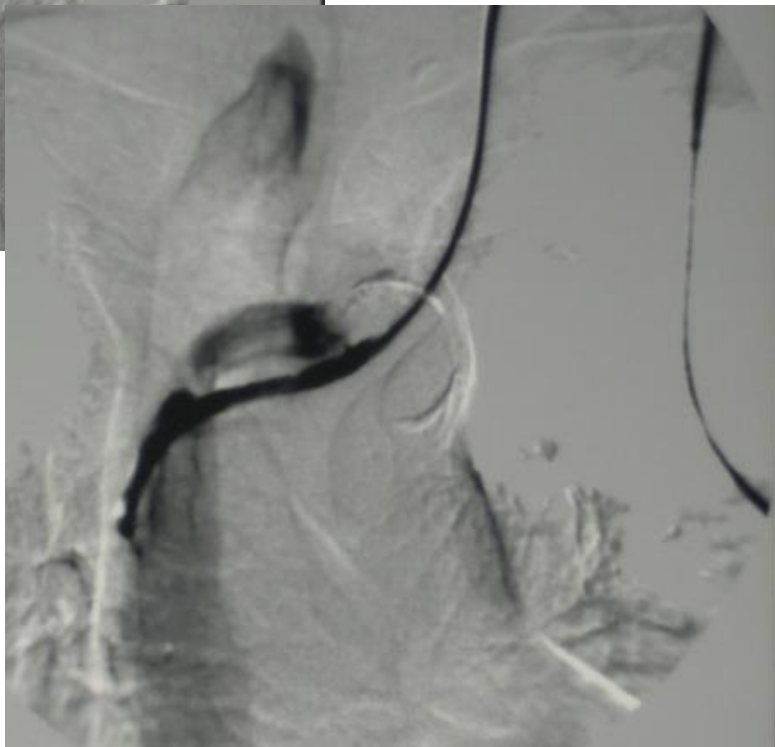
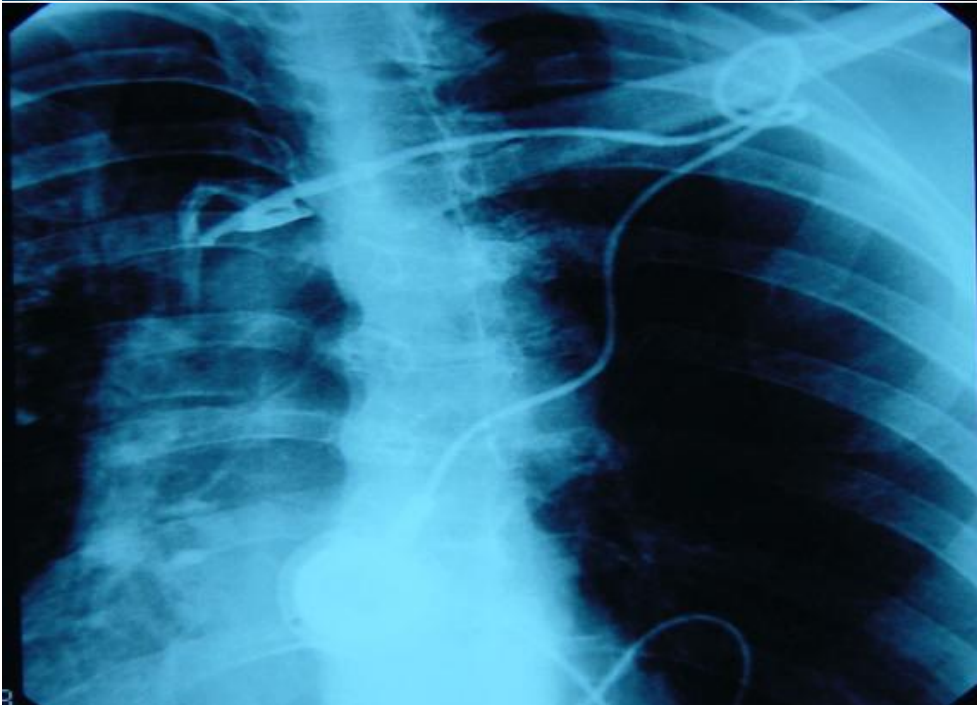
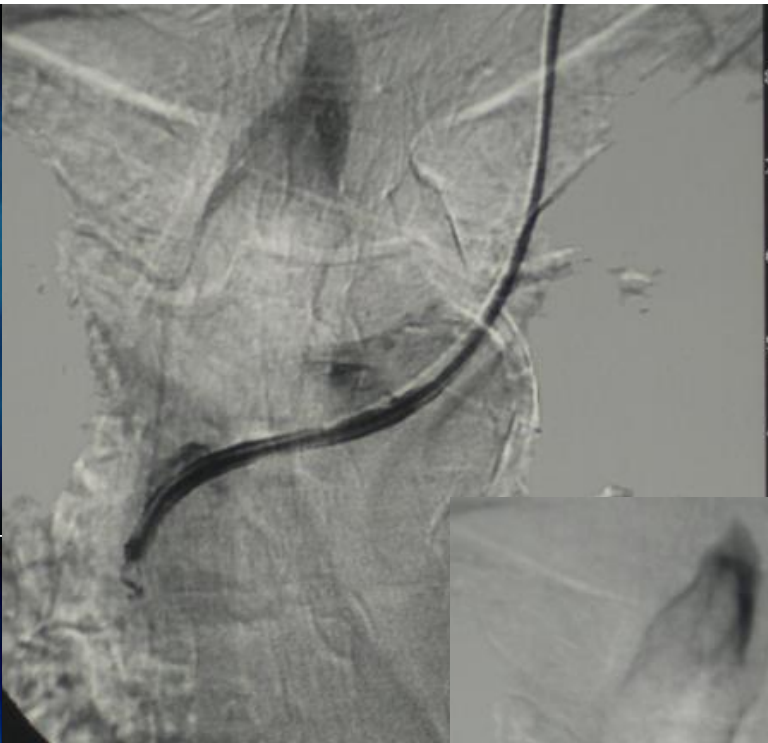
Sleeve: diagnosis



Consider chest X-Ray and/or line-o-gram (expecially if catheter placed via subclavear access):

- PINCH OFF ?
- KINKING ?
- TIP MALPOSITION ?
- **SLEEVE ?**





Symptomatic sleeve: treatment

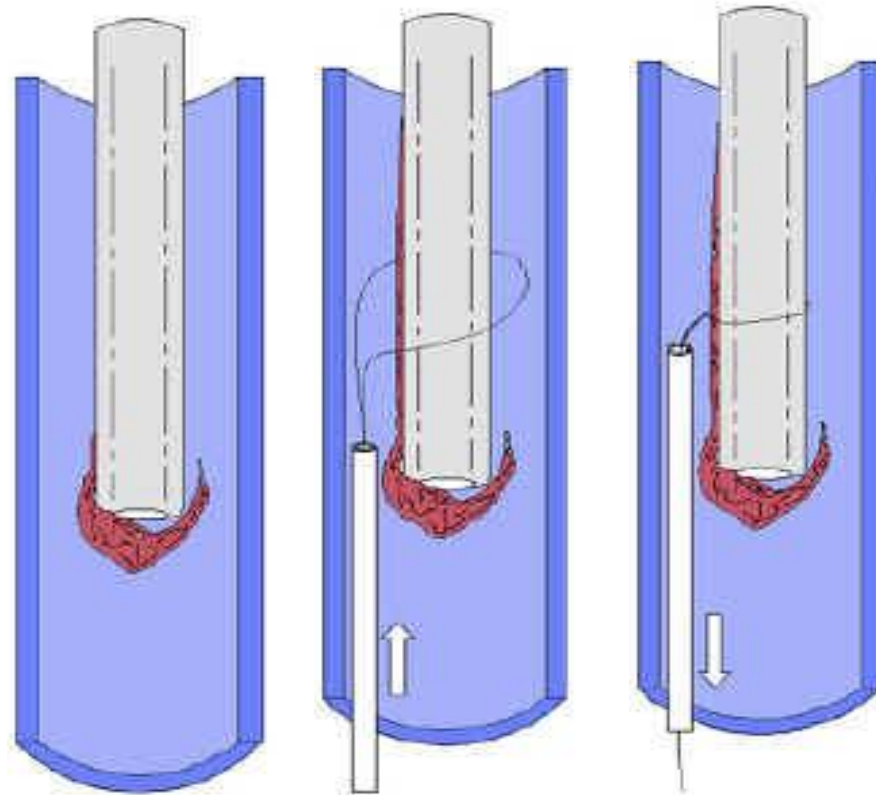
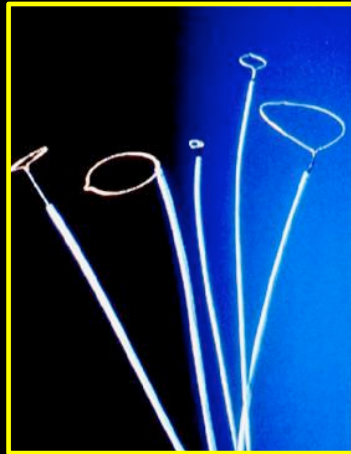
- Angiographic “peeling” or “stripping”
- Balloon dilatation
- Fibrinolytic agents
- Over-guidewire exchange (with reservoir preservation for ports)
- REMOVAL AND NEW INSERTION

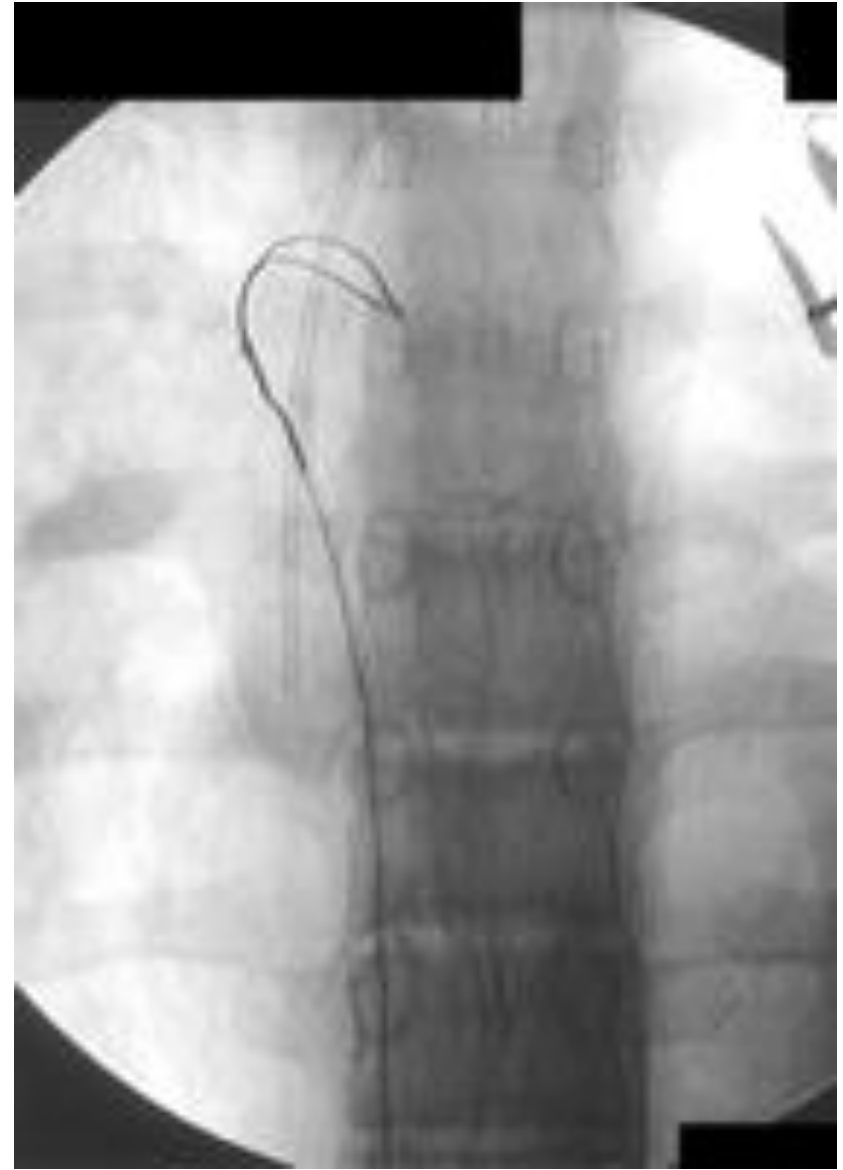


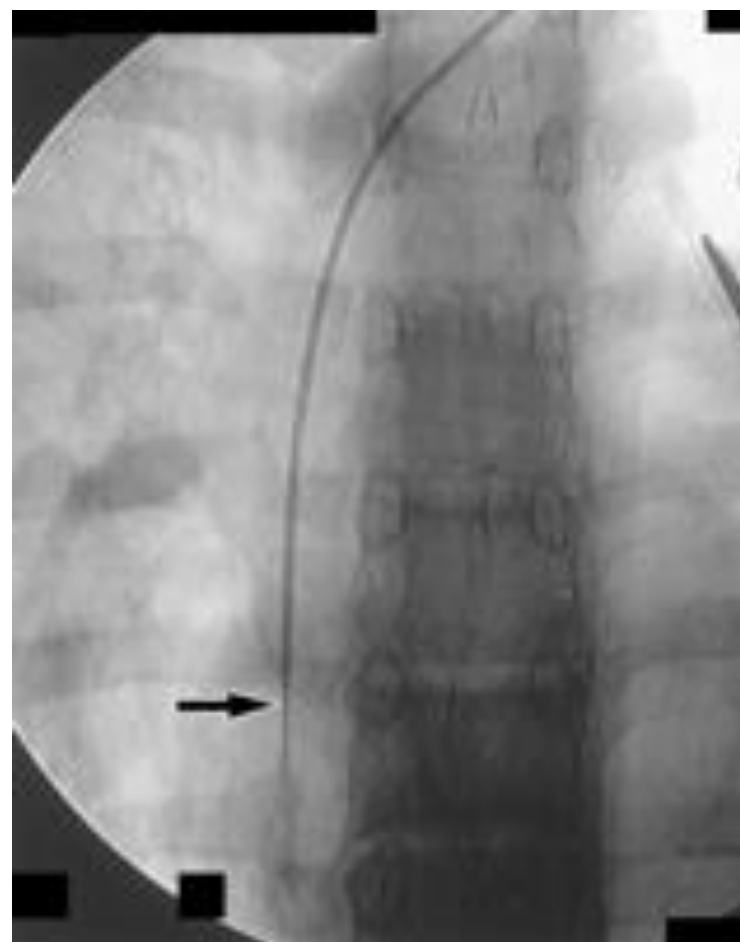
**Papers from the
hemodialysis
setting**

Angiographic “peeling” or “stripping”

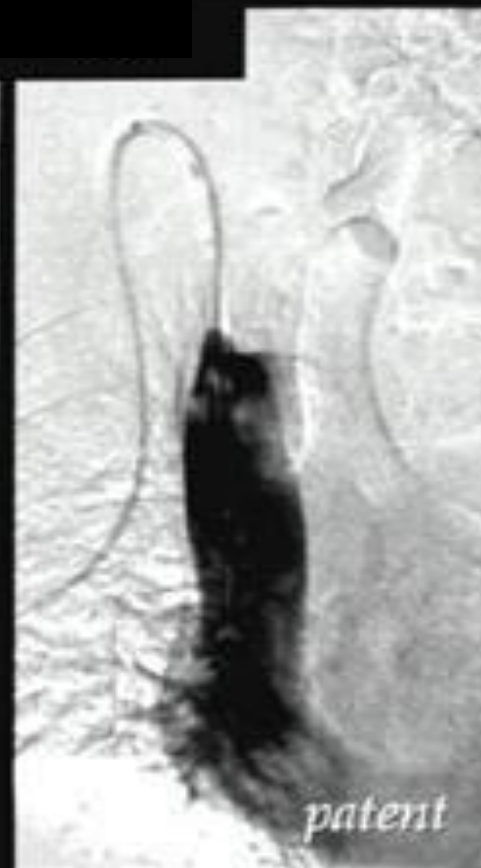
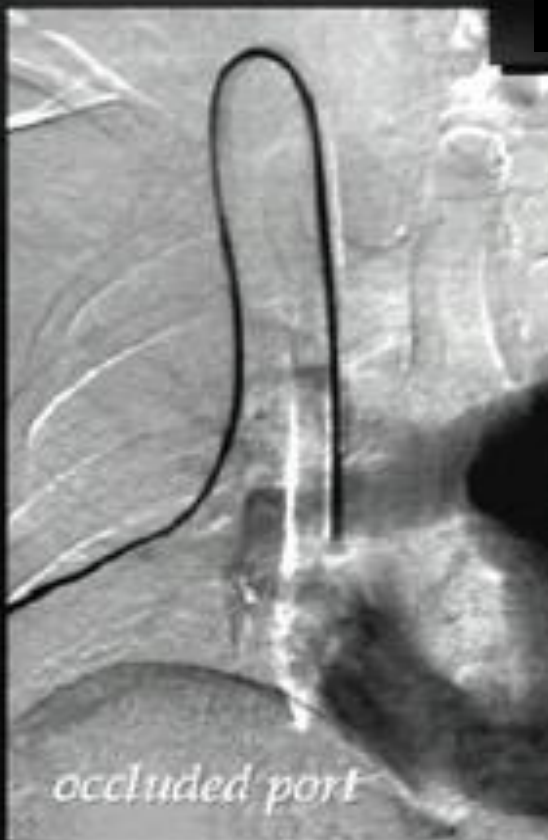
Snare catheters used for removing fragmented catheters and fibrin sheath







STRIPPING

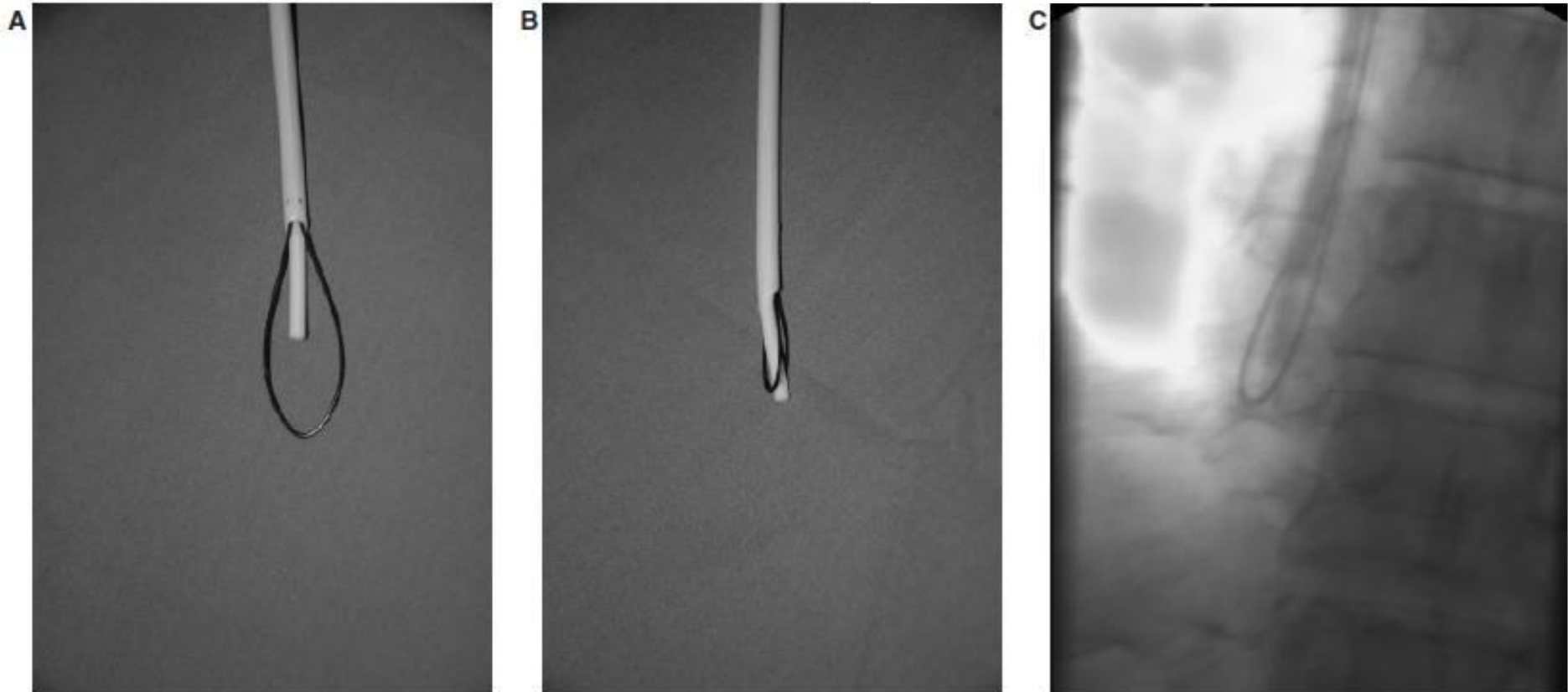


Technical Note

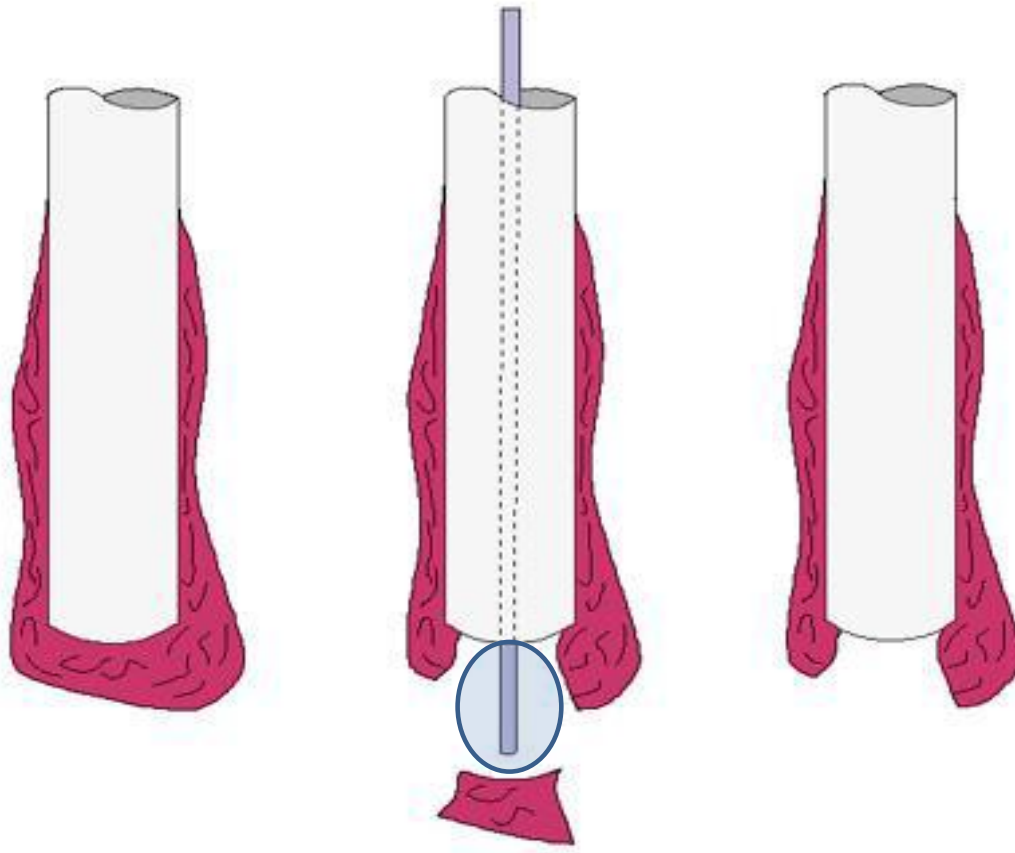
Fibrin sheath removal from central venous catheters: an internal snare manoeuvre

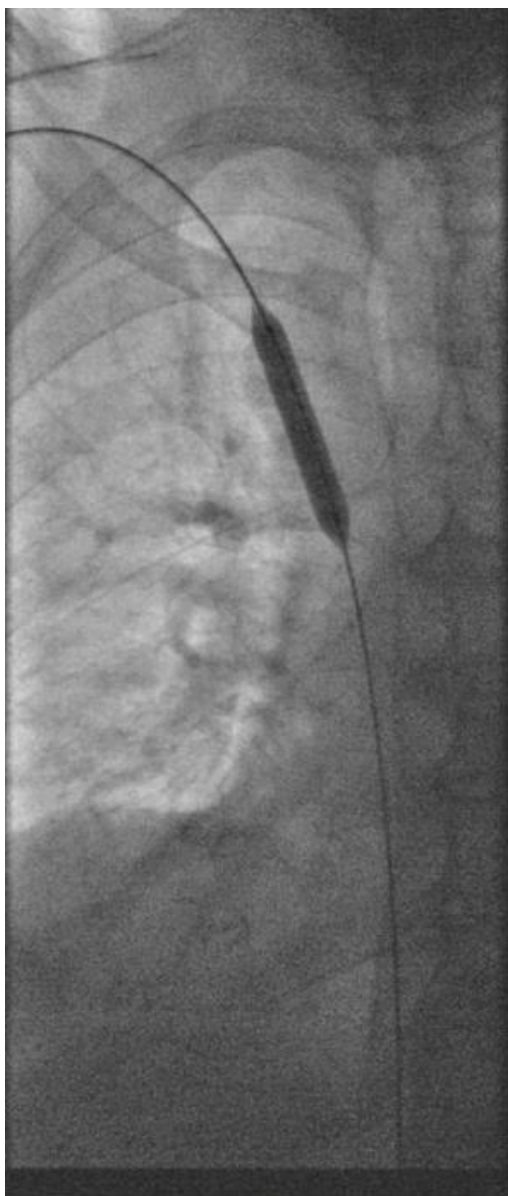
Arra S. Reddy, Elvira V. Lang, Jennifer Cutts, Shaun Loh and Max P. Rosen

Internal snare peeling

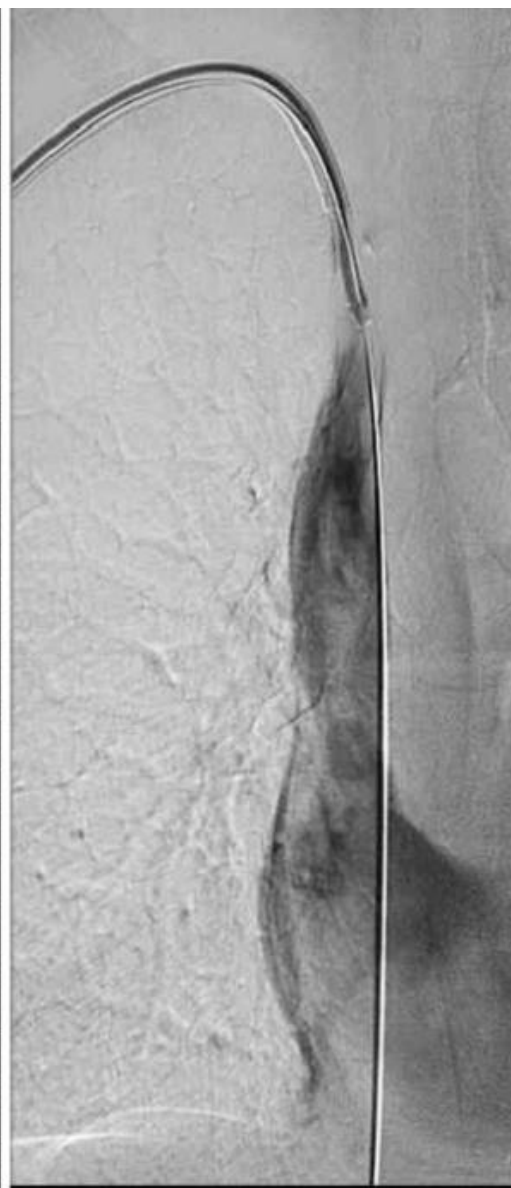


Balloon dilatation





(a)



(b)

Fibrin Sleeve Stripping for Salvage of Failing Hemodialysis Catheters: Technique and Initial Results¹

Martin R. Crain, MD • Mark W. Mewissen, MD • Gregory J. Ostrowski, DO
Ricardo Paz-Fumagalli, MD • Robert A. Beres, MD² • Richard A. Wertz, MD

Radiology 1996; 198:41–44

CONCLUSION: Multiple PFSS procedures can prolong patency in hemodialysis catheters with a fibrin sleeve.

Percutaneous Fibrin Sheath Stripping versus Transcatheter Urokinase Infusion for Malfunctioning Well- positioned Tunneled Central Venous Dialysis Catheters: A Prospective, Randomized Trial¹

Richard J. Gray, MD
Abraham Levitin, MD²
David Buck, MD
Lisa C. Brown, RN
Yvonne H. Sparling, MS
Kathleen A. Jablonski, PhD
Amanuel Fessahaye, MD³
Atul K. Gupta, MD

JVIR 2000; 11:1121-1129

CONCLUSION: There is no significant difference in time to primary patency between the two methods. Both allow temporary catheter salvage in most patients.

Fibrin Sheath Stripping versus Catheter Exchange for the Treatment of Failed Tunneled Hemodialysis Catheters: Randomized Clinical Trial¹

Michael Merport, MD
Timothy P. Murphy, MD
Thomas K. Eggin, MD
Gregory J. Dubel, MD

JVIR 2000; 11:1115–1120

CONCLUSIONS: Malfunctioning tunneled hemodialysis catheters treated by means of EX are significantly more likely to remain patent for up to 4 months than are those treated by means of PFSS. According to the results of this trial, PFSS should not be performed as a routine therapy for catheter malfunction.

Symptomatic sleeve: thrombolysis

1. Systemic (higher dose, less technical issues)
2. Local (lower dose, technical issues may be important)
3. Lock

Gray et al (2000):

- No outcome difference between urokinase (250.000 U / 4 hrs) and stripping
- Low dose (5000 to 9000 U) lock: disomogeneous results (success rate 14 – 95%)
- High dose (25,000 to 100000 IU) lock: success up to 100% (Donati et al, 2011)
- Hypotesis: active over fibrin quote (early treatment)

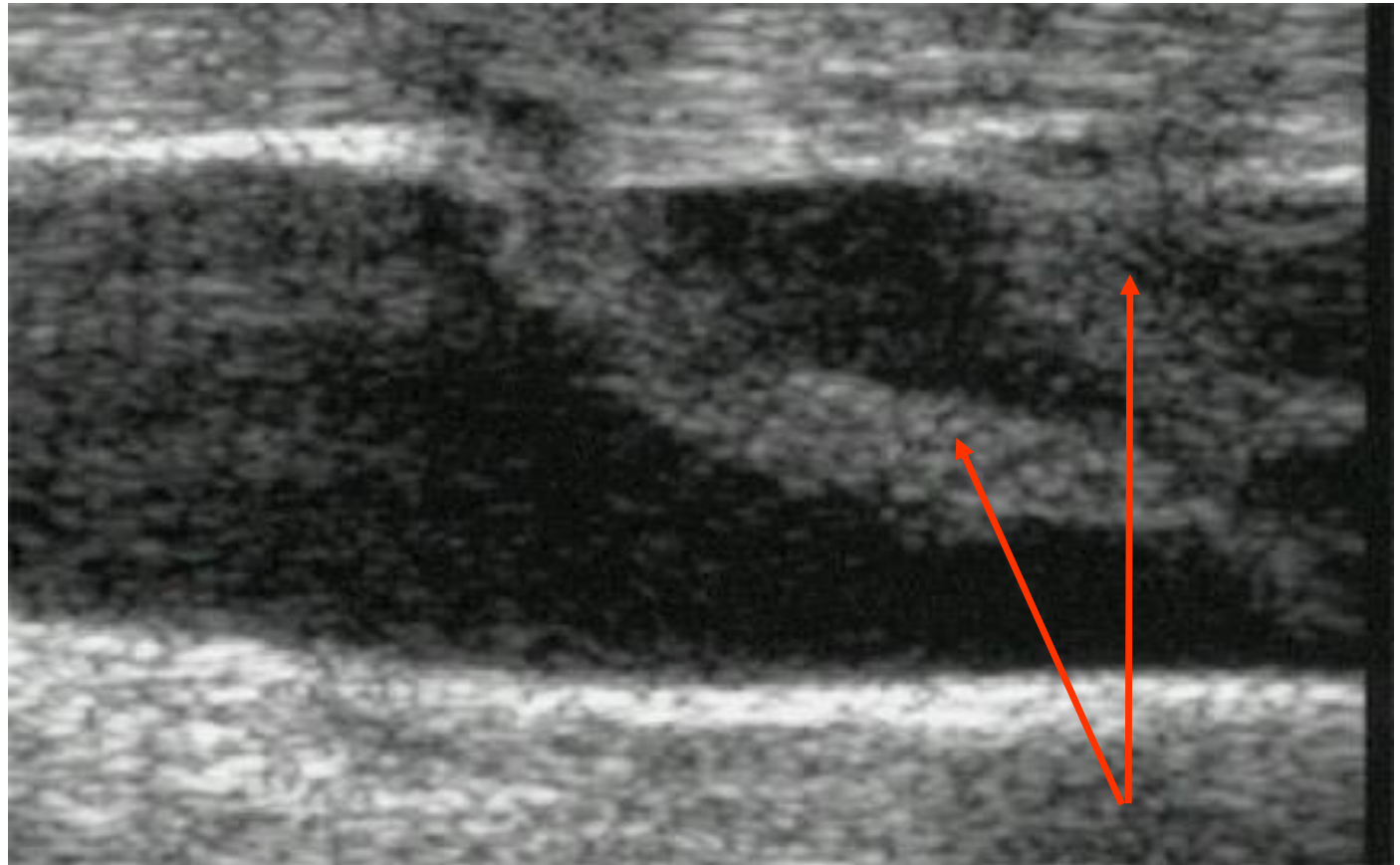
Symptomatic sleeve: treatment by removal and new insertion ...

- Anticoagulation: no significant effect, significant side effects
- Thrombolysis: high costs, high risks, effective only in heavily selected patients
- Over guidewire removal and re-insertion: risk factors still there
- REMOVAL AND NEW SITE RE-INSERTION SEEMS THE MOST REASONABLE OPTION ***FOR PATIENTS WITH SUITABLE VASCULAR RESIDUAL ANATOMY***, REMOVING ANY POTENTIALLY REMOVABLE RISK FACTOR

Symptomatic sleeve: treatment by removal and new insertion ...

Fear of embolysm?

- The sleeve remains on site, attached to its vein wall origin
- Blood flow pushes it towards the vein wall
- Later embedded in the vein wall (intimal hyperplasia)
- Possible vein stenosis: a reason to attempt at treating?



If it looks like a catheter and winds like a catheter . . . fibroblastic sheath mimicking a central venous catheter fragment: A case report

Marco Baciarello¹ , Giada Maspero² ,

The Journal of Vascular Access
1–4

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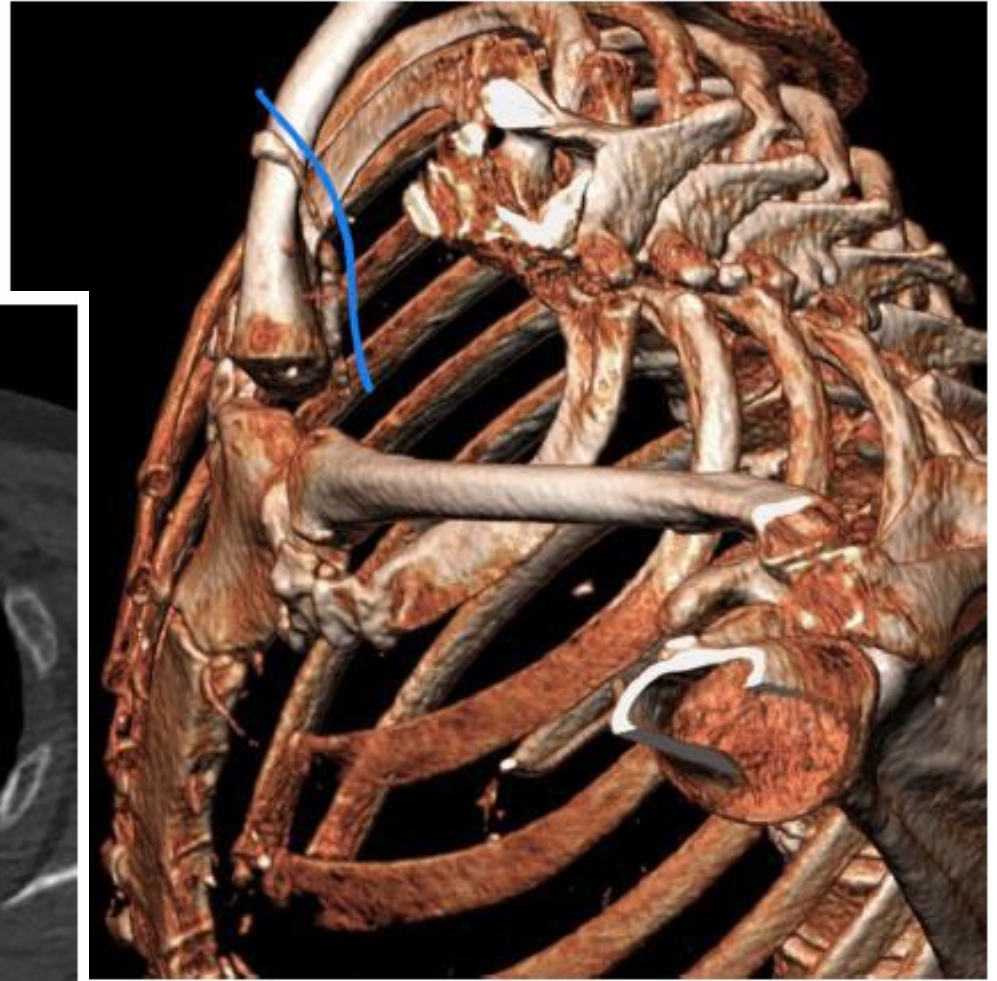
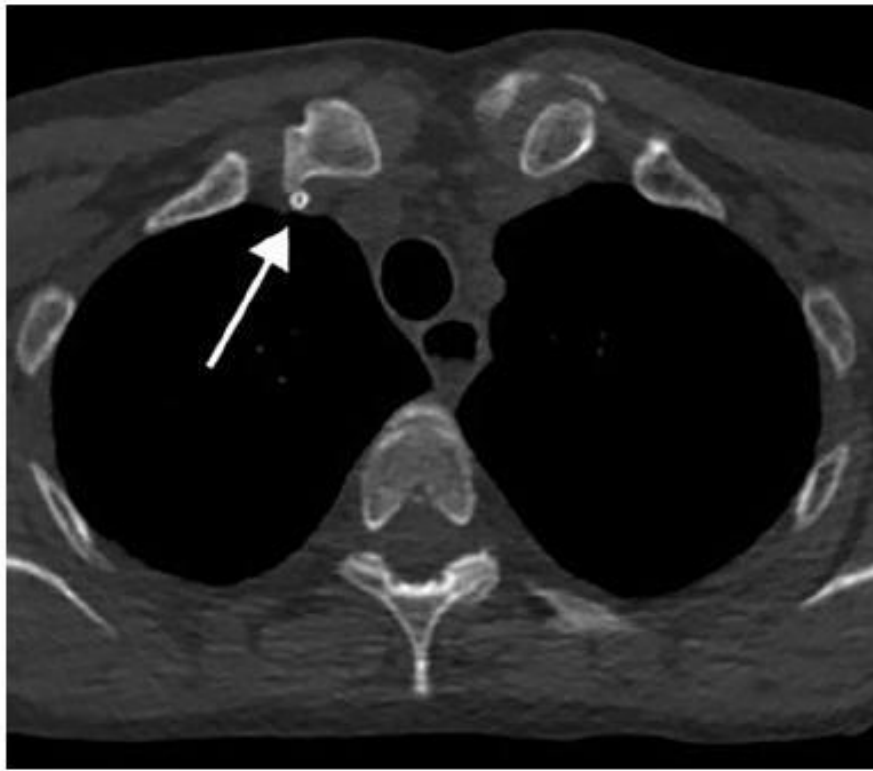
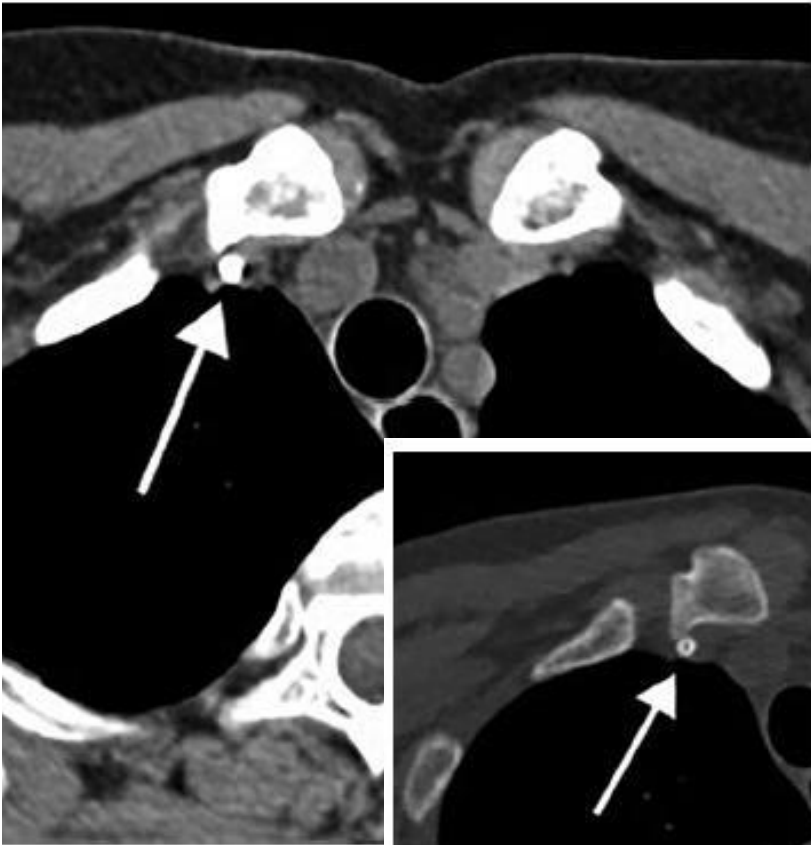
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Asymptomatic sleeve

- All treatment options have at least questionable effectiveness and not negligible side effects
- Most sleeves are asymptomatic and do not show significant trends towards catheter malfunction, venous thrombosis, infection
- IT SEEMS REASONABLE NOT TO TREAT ASYMPTOMATIC SLEEVE
- BY THE WAY, THE SLEEVE MAY BE CONSIDERED AN ALERT TO INVESTIGATE A POSSIBLE REMOVABLE PROBLEM:
 - Tip malposition ?
 - Endothelial disruption ?

Sleeve: the future

Primary prevention on removable risk factors:

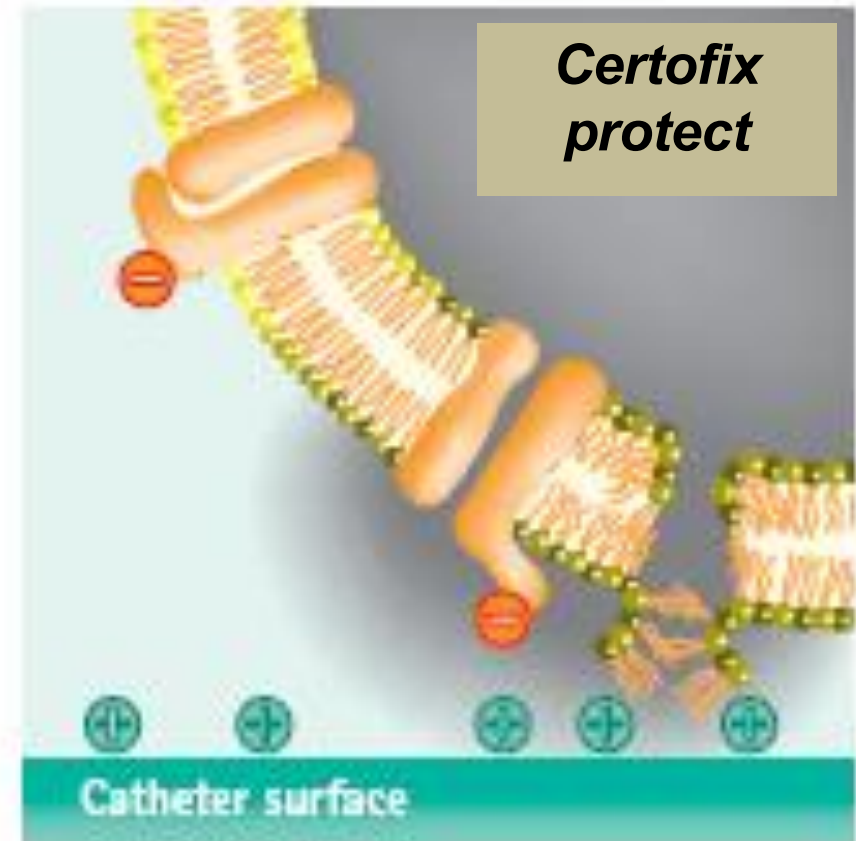
- Tip position (IC-ECG !!!): do not tolerate «acceptable» tip position ***as for DVT prevention***
- Endothelial damage (ULTRASOUND!!!): pay attention to catheter to vein ratio and technical issues (delicate venepuncture, first time pass, micro-introducers ...) ***as for DVT prevention***
- Choose insertion pathways (possibly straight) and devices (good quality materials) that prevent «rubbing» against curvilinear venous segments

Secondary prevention, as for cardiac stents: modified surface devices?

Sleeve prevention: modified catheter surfaces

Poliexanide metacrilate (PM)

- Biguanide groups give the catheter surface a negative charge and thus an idrohilic surface
- Bacterial membrane destabilization and disruption
- Activity against protein adhesion and biofim creation
- Acitivity against sleeve / thrombosis ?



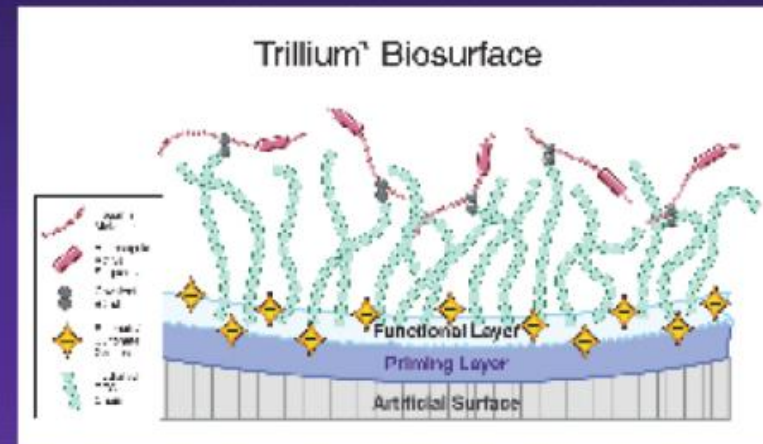
Sleeve prevention: modified catheter surfaces

which incorporates both non-thrombogenic and anti-thrombogenic properties on the same polymer backbone that provides endothelial-like action, preventing protein adsorption and inhibiting thrombin at the same time.

- Activity against protein adhesion and biofilm creation
- Activity against sleeve / thrombosis ?

Trillium™ Biosurface: Triple endothelial-like action for biocompatibility

- **Heparin**
 - Covalently-bonded
 - Non-leaching
- **Negative charge**
 - Sulphate and sulfonate groups
 - Heparin
- **Hydrophilicity**
 - Polyethylene oxide (PEO) chains
 - Hydrophilic priming layer



Sleeve prevention: modified catheter surfaces

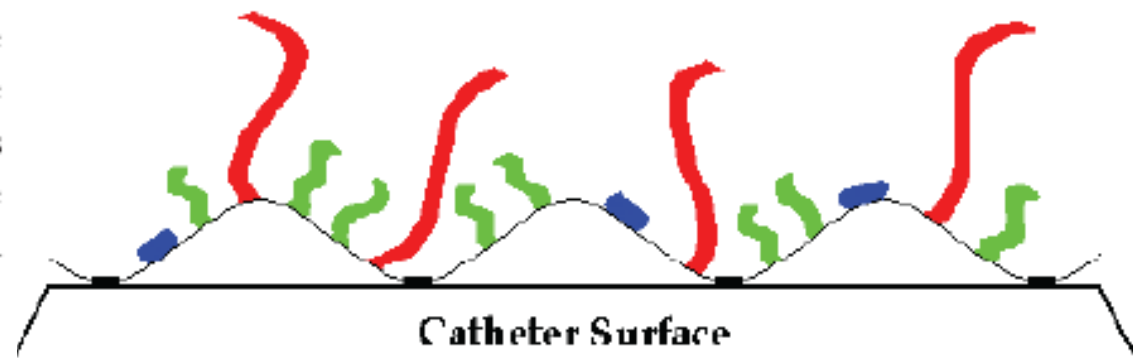
polymer consists of polyhexanide pendant to a polymer chain chemically linked to a non-thrombogenic polymer (see *Figure 2*). This is prepared by functionalising the polyhexanide with a methacrylate group, which is co-polymerised with PEG monomers that have non-thrombogenic properties.

The polyhexanide structure comprises biguanide groups, which bind to the cell membrane. The proposed mechanism^{18,19} has been described as being the binding of the biguanide to the phospholipids in the cell wall, causing separation and then, finally, cell disruption.

This unique polymer formulation of Polycil gives a coating that is biocompatible, lubricous and antimicrobial. The coating can be applied to medical

Polycil ***Antimicrobial/antithrombogenic polymer***

Idrophilic and so anti thrombogenic



polyethylene glycol/oxide

- MPEG2000MA
- MPEG350MA
- POLYHEXANIDE
- BUTYL METHACRYLATE

Cytolytic by physical (non chemical) mechanism

Sleeve prevention: modified catheter surfaces



RYDER SCIENCE
—medical biofilm research

The Effect of Chlorhexidine Catheter Coating Compared to a Biomimetic Catheter on the Reduction of Fibrin Sheath Formation in the presence of *Staphylococcus aureus* colonization in an *in vivo* Clinically Simulated Ovine Model

Ryder M.¹, Gunther RA.², Sylvia CJ.³, Breznock EM.³, Griffey S⁴., James G.⁵, Pulcini E.⁵ Parker A

¹ Ryder Science, Escondido, CA, ² University of California-Davis, Davis, CA, ³ BioSurg Inc., Winters, CA, ⁴ Winters, CA, ⁵ Center for Biofilm Engineering, Bozeman, MT.

BioSurg
Consulting
Biomedical Product Evaluation
Research & Development



- Ten sheep
- Randomly assigned to CH catheter, Biomimetic Catheter and Control Catheter
- Inoculation of Staph Aureus
- Euthanasia and pathology of the cannulated vein

Sleeve prevention: modified catheter surfaces

TEST CATHETER



Fig. 1 Chlorhexidine coated test catheter (CH). Fibrin sheath formation at 3 days. Vessel wall unremarkable

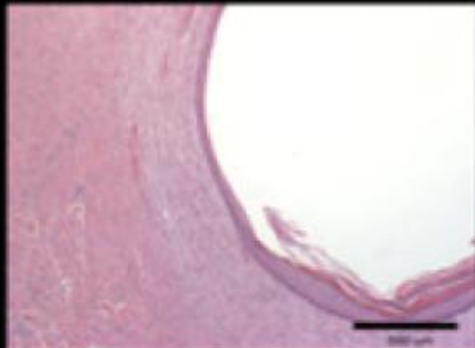


Fig. 1a Subcutaneous tract

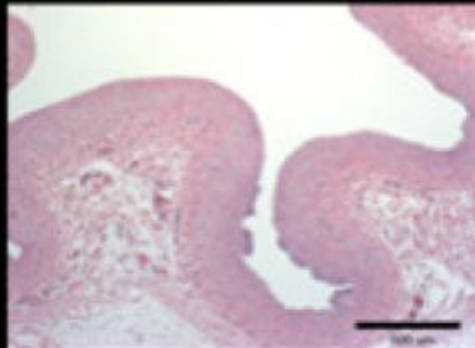


Fig. 2c Vein wall midway

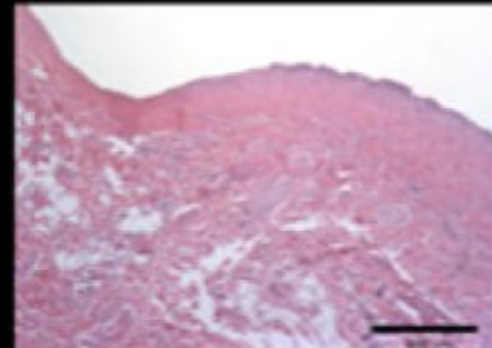


Fig. 2d Vein wall tip

Sleeve prevention: modified catheter surfaces



Fig. 2 Uncoated control catheter (C1). Fibrin sheath formation at 5 day. Marked phlebitis of the vessel wall and cellulitis of the surrounding tissue

Fig. 2a
Subcutaneous
tract

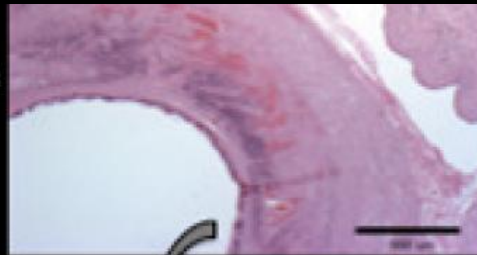


Fig. 2b
Subcutaneous
tract

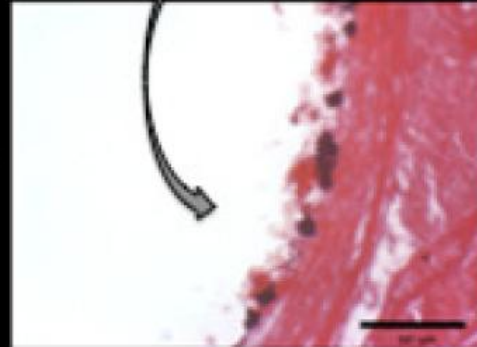


Fig. 2c Vein
wall midway

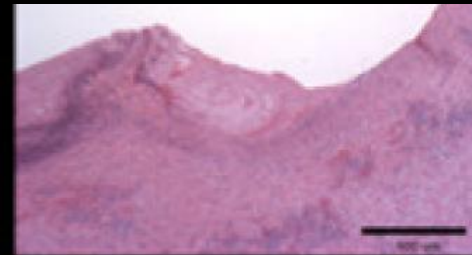
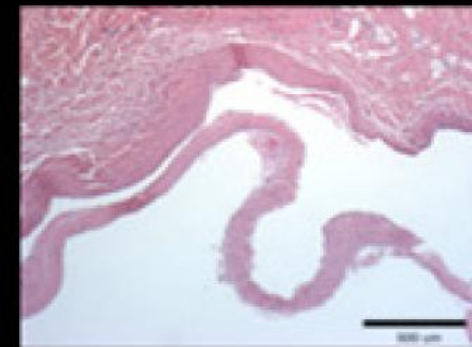
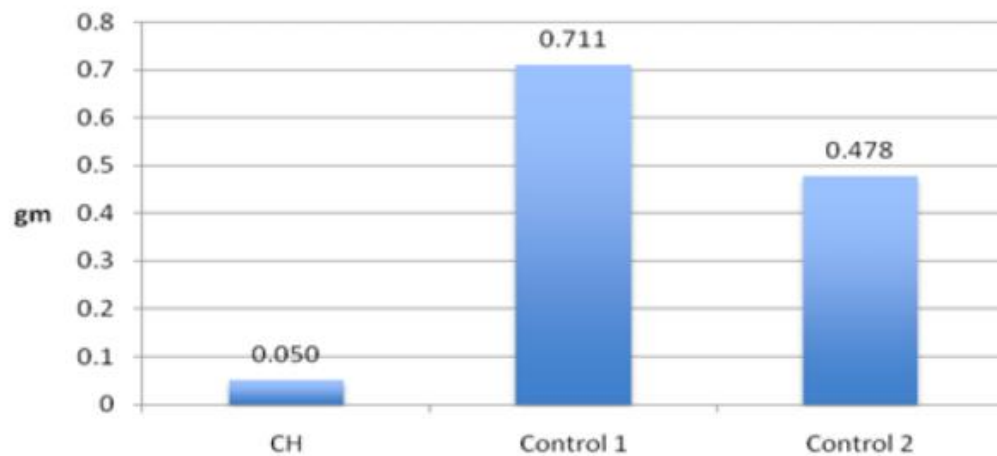


Fig. 2d Vein
wall tip

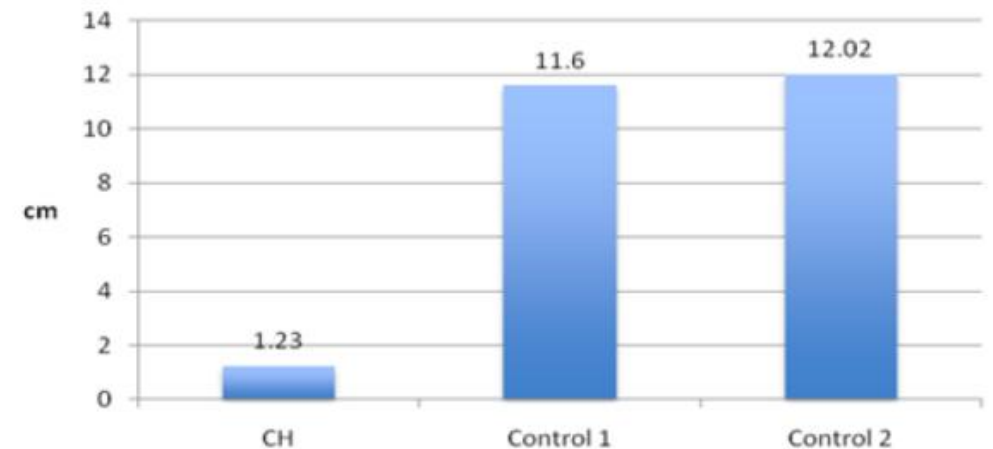


Sleeve prevention: modified catheter surfaces

Median Fibrin Sheath Weights



Median Fibrin Sheath Lengths



Sleeve prevention: modified catheter surfaces

Original research article

JVA | The Journal of
Vascular Access

Chlorhexidine-coated peripherally inserted central catheters reduce fibroblastic sleeve formation in an in vivo ovine model

**Charles J Sylvia Jr¹, Molly A Wagel², Kamna Giare-Patel²,
Taylor A Spangler³, Eugene M Breznock¹ and Nisha Gupta²**

The Journal of Vascular Access
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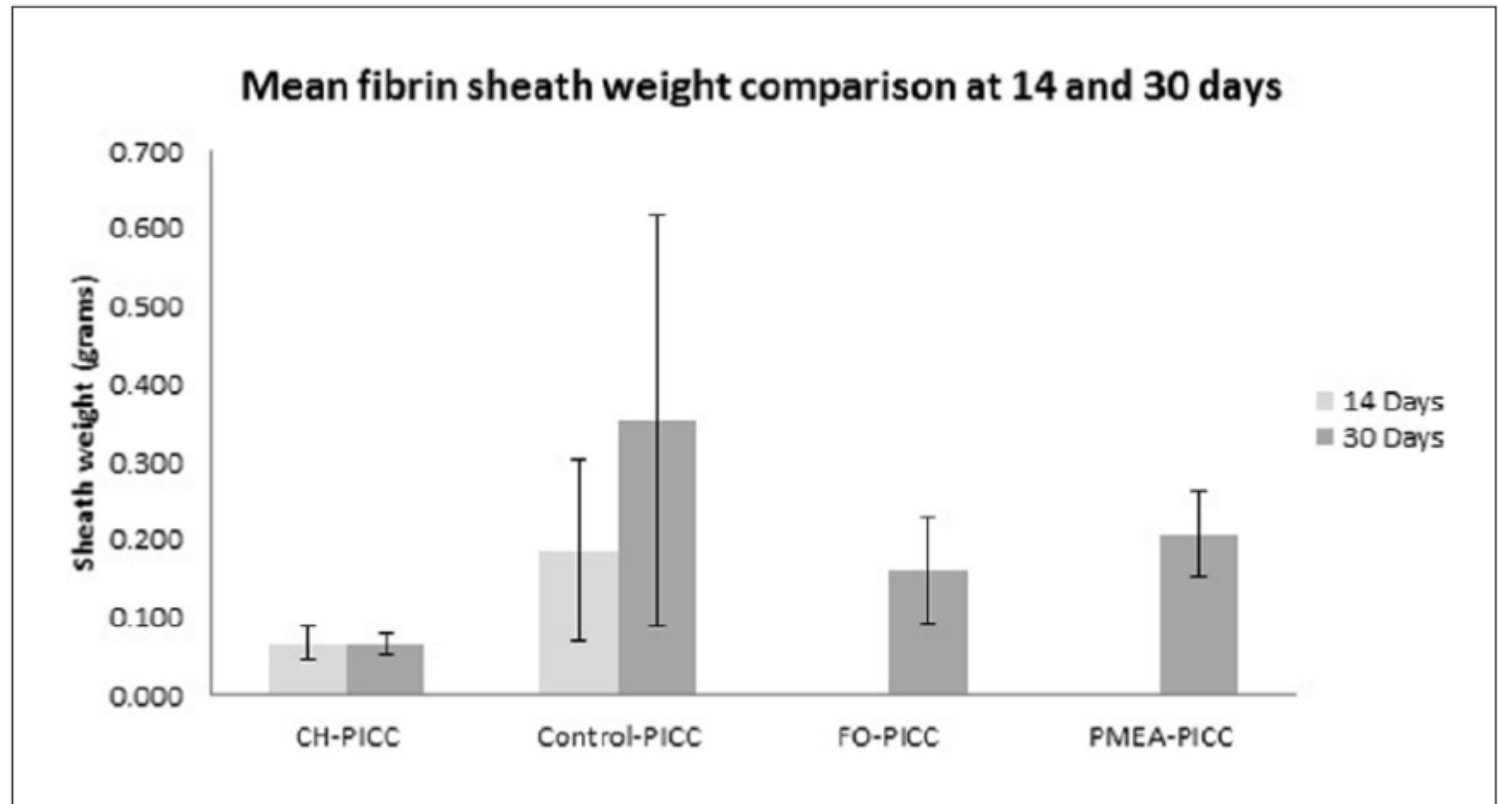

**Chlorhexidine
Polimethoxyethyl
acrylate
Fluoro Oligomers**

**Chlorhexidine-coated peripherally inserted
central catheters reduce fibroblastic sleeve
formation in an in vivo ovine model**

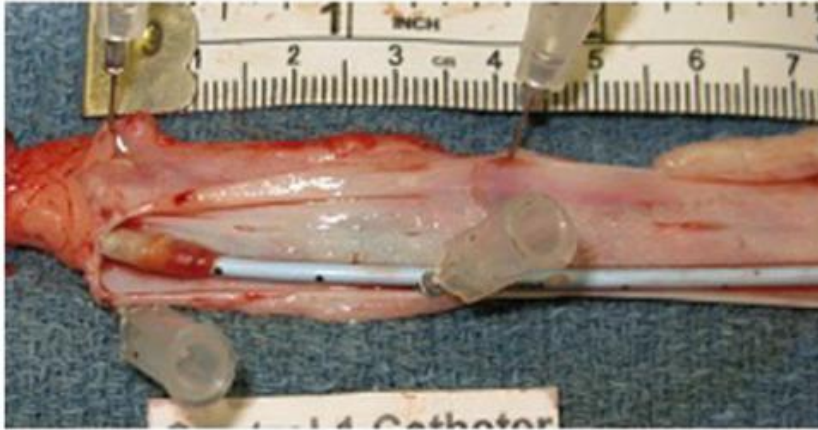
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18 sheep randomized

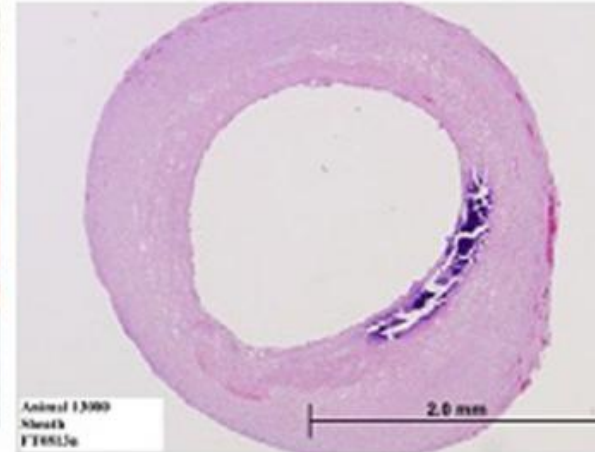
- CH 14 days
- CH 30 days
- FO 14 days
- FO 30 days
- PMEA 14 days
- PMEA 30 days
- Control 14 days
- Control 30 Days



Sleeve prevention: modified catheter surfaces



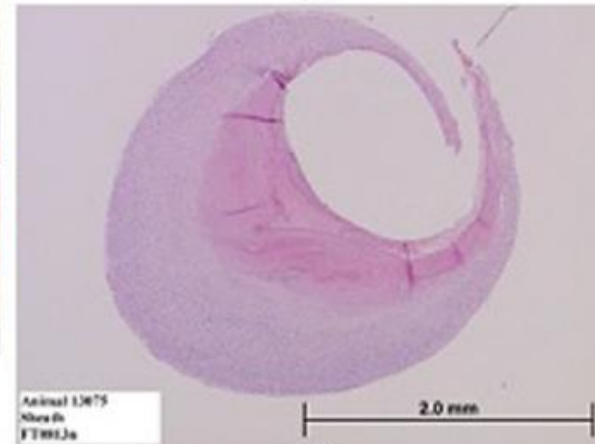
(a)



(b)



(c)



(d)

European Journal of Haematology

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Volume 98, Issue 4

April 2017

Pages 318–319

Editorial



Central venous catheter thrombosis and the fibrin sleeve: unraveling the mystery

[Katherine A. Hajjar](#)

So mysterious that the word «sleeve» appears once only at the end of the editorial

Original research article

JVA | The Journal of
Vascular Access

Vascular endothelium damage from catheter-induced mechanical stimulation causes catheter sleeve formation in a rabbit model

Hidenori Tanabe^{1,2} , Naoto Takemura², Hisako Terao²,

The Journal of Vascular Access

1–8

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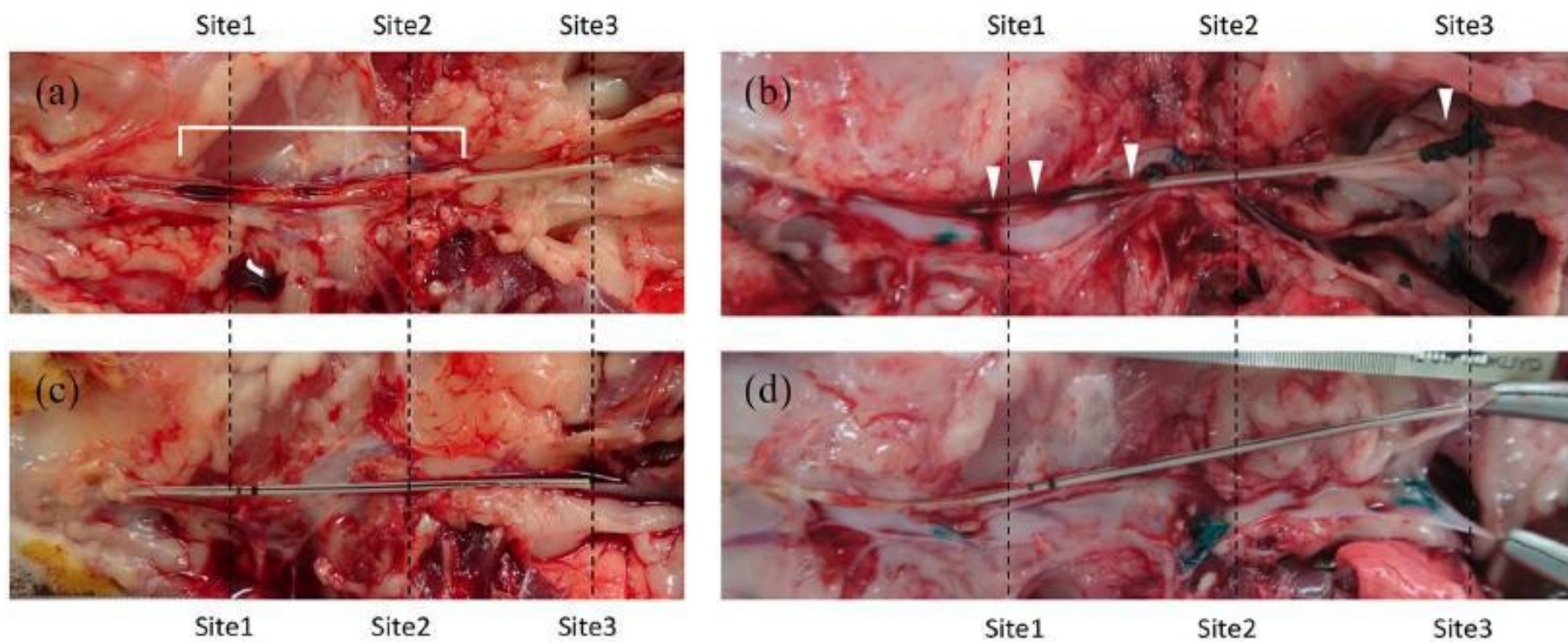


Figure 3. Photographs of the catheters: (a) uncoated catheter with stylet, (b) uncoated catheter without stylet, (c) PMEA-coated catheter with stylet, and (d) PMEA-coated catheter without stylet.

Bracket indicates a catheter sleeve, and arrowheads indicate thrombus sites. Dashed lines indicate the sites at which tissue was collected for histological analysis.

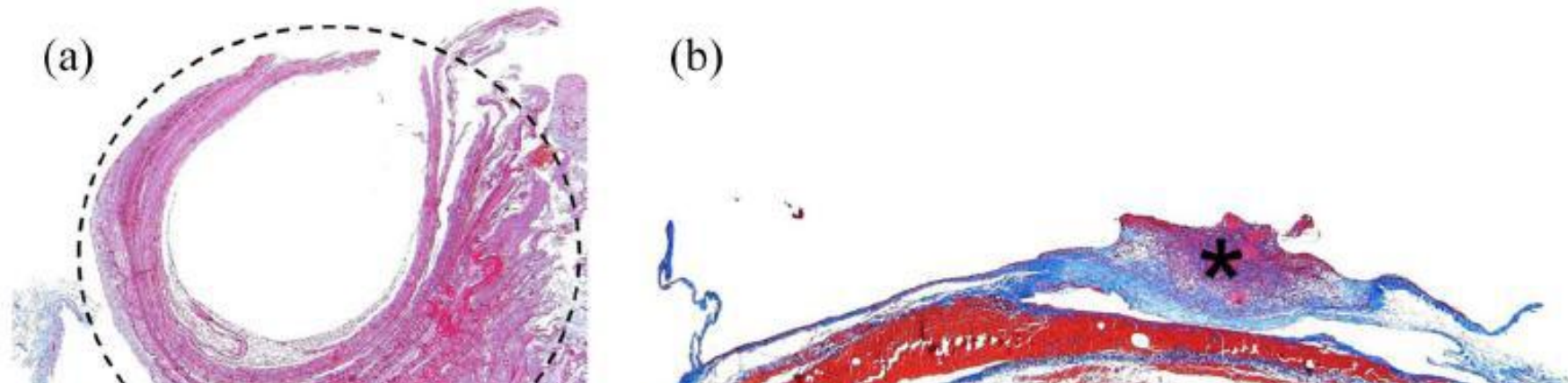
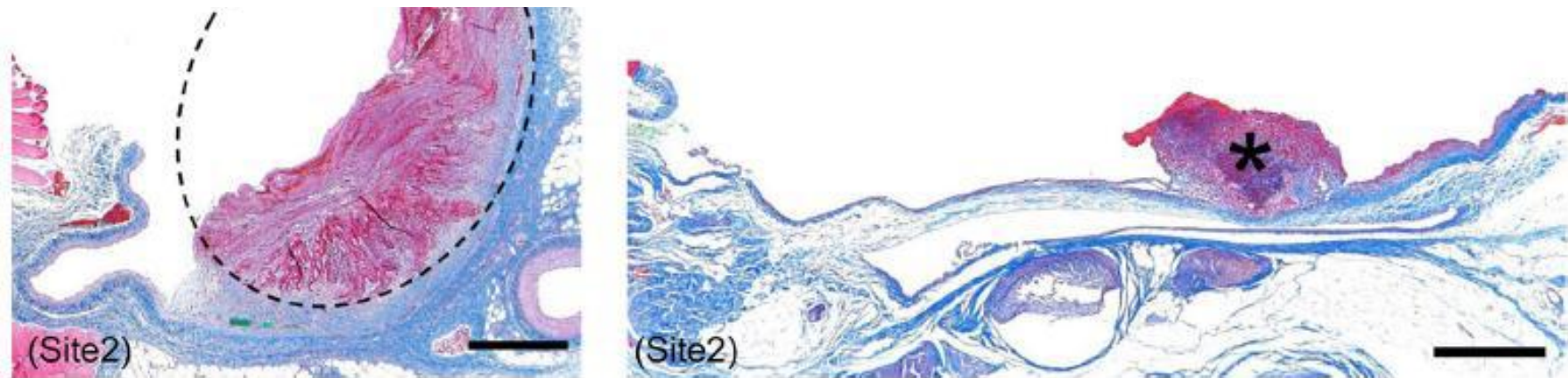


Figure 4. Histological analysis of cross-sections of veins obtained from site 2: Masson's trichrome (MT) staining of veins that contained the (a) uncoated catheter with stilet, (b) uncoated catheter without stilet, (c) PMEA-coated catheter with stilet, and (d) PMEA-coated catheter without stilet.

MT staining indicates thrombus deposits (red) separated from the vein wall (blue). Circular regions enclosed by dotted lines show a catheter sleeve partially surrounding the catheter mold (a) and thrombus deposits on the vessel wall (c). The asterisk marks a mural thrombus in (b) and (d). All scale bars are 500 μm .



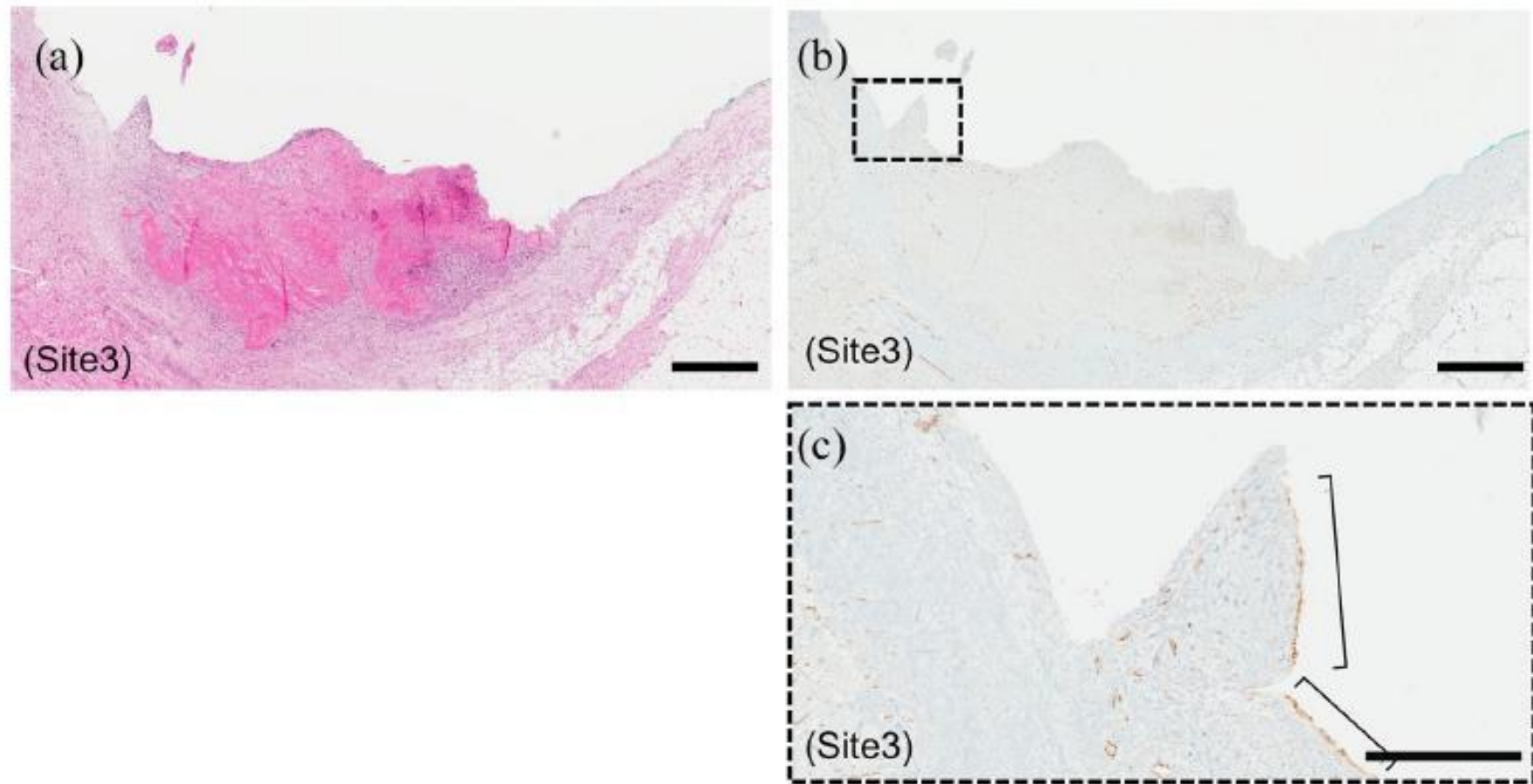
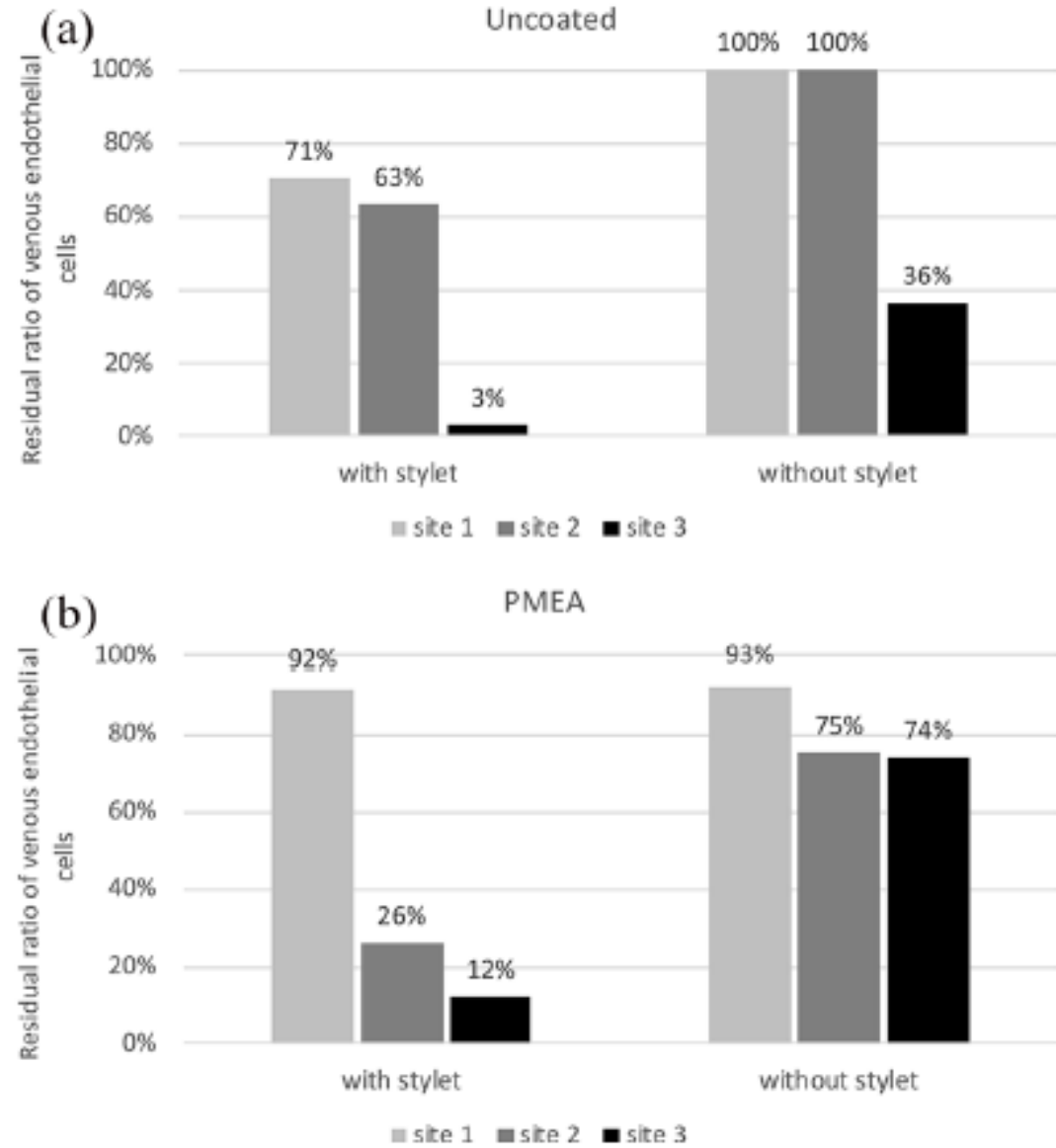


Figure 5. Histological images obtained from site 3 of the uncoated catheter with stylet: (a) HE-stained section, (b) CD31-stained section, and (c) close-up of boxed region in (b). Scale bars in (a), (b), and (c) indicate 600, 600, and 200 μm , respectively. Brackets indicate remaining venous endothelial cells.

Figure 6. Graphs showing residual ratios of venous endothelial cells using catheters with and without a stylet: (a) uncoated catheters and (b) PMEA-coated catheters.



Conclusion

High levels of mechanical stimulation induced by catheters with a stylet reduced the ratio of residual venous endothelial cells and promoted the formation of an extensive CS. In contrast, PMEA coating reduced thrombus formation on the surface of catheters, and prevented CS formation when using stiffened catheters, which induce high mechanical force. These findings indicate that CS formation is exacerbated by vascular endothelium damage due to catheter-induced mechanical stimulation and can be prevented by using soft catheters and/or anti-thrombogenic technology such as PMEA coating. Further studies are needed to determine the maximum acceptable degree of venous endothelial damage before CS formation using catheters of varying stiffness and to compare other catheter technologies with PMEA coating for preventing CS formation in this model.

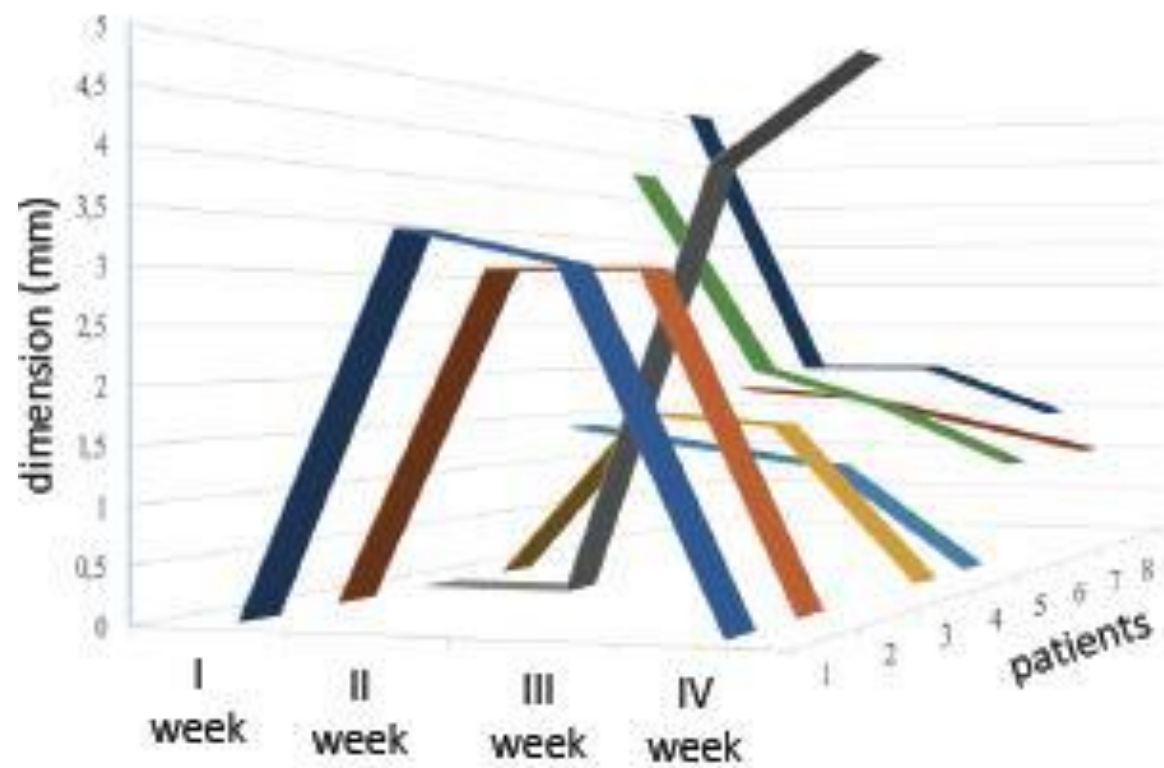
- Timing: early event
- Pathogenesis: endothelial damage at insertion site + catheter stiffness

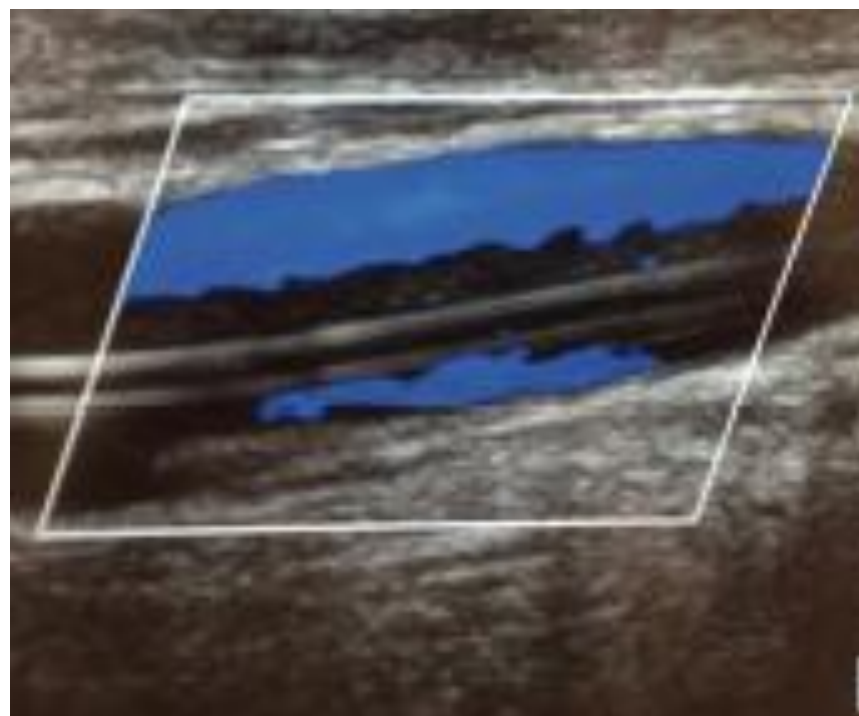
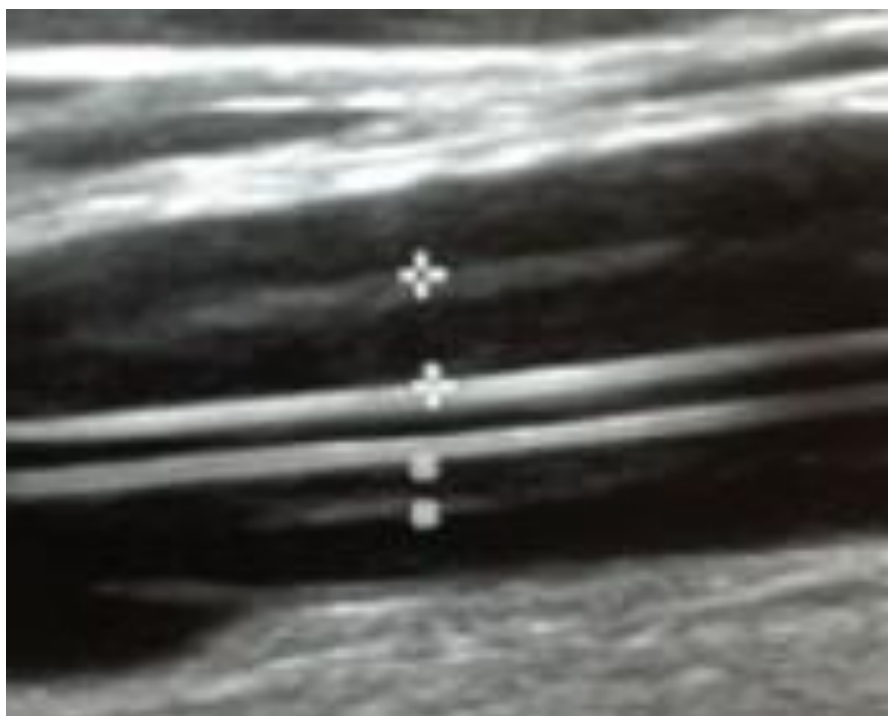
PROSPECTIVE STUDY OF ULTRASOUND-DETECTED FIBROBLASTIC SLEEVE IN CANCER PATIENTS WITH PICC OR PICC-PORT: FIRST PRELIMINARY RESULTS

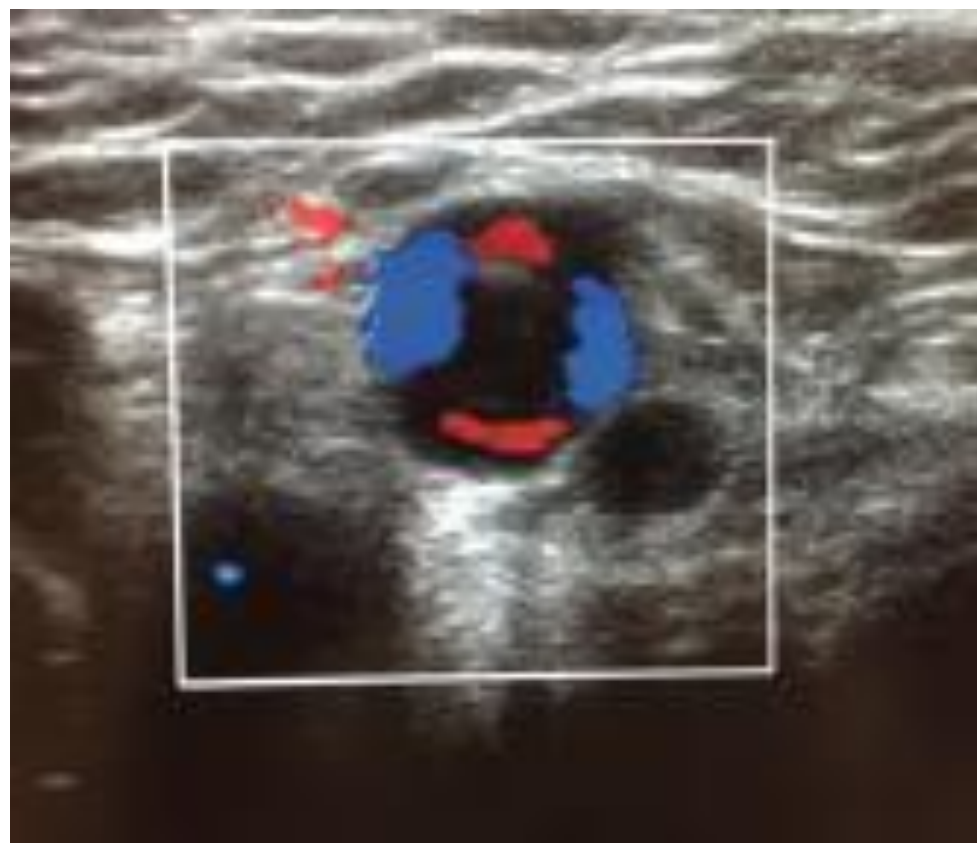
G. Passaro, A. La Greca, A. Emoli, B. Marche, M. Pittiruti
 Fondazione Policlinico "A. Gemelli" IRCCS, Rome, Italy

	Fibroblastic sleeve N (%)	Asymptomatic thrombosis N(%)	None N(%)
Overall (n=16)	8 (50)	1 (6)	7 (44)
PICC (n= 10)	8 (80)	1 (10)	1 (10)
PICC-Port (n= 6)	0	0	6 (100)

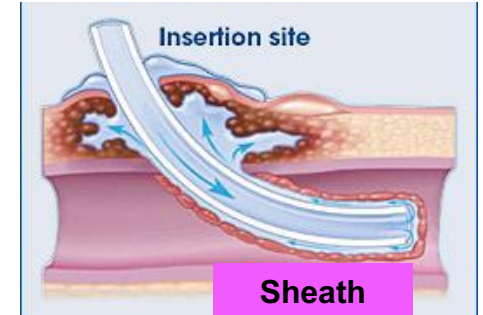
PROSPECTIVE STUDY OF ULTRASOUND-DETECTED FIBROBLASTIC SLEEVE IN CANCER PATIENTS WITH PICC OR PICC-PORT: FIRST PRELIMINARY RESULTS





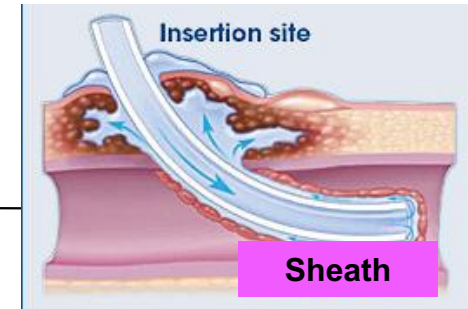


Conclusions (1)



- Pathogenesis: some pathways are similar to CR-VT
- Early event with late clinical signs
- Why some endothelial traumas evolve into sleeve instead of thrombosis? More data on thrombosis/sleeve relationships?
- Thrombosis and sleeve seemingly are not linked to each other
- Please use correct terminology: **pericatheter thrombus is a sleeve**
- Clinical relevance:
 - Low incidence in general population, high in selected populations (dialysis)
 - Important in chronically cannulated patients (dialysis, TPN): SAVE THE CATHETER
 - No clear correlation with VENOUS THROMBOSIS, PULMONARY EMBOLISM, INFECTION

Conclusions (2)



- No data available on real clinical impact: often confused with venous thrombosis (RIGOROUS DEFINITION NEEDED)
- No drugs available for treatment
- Operative treatments effective but recurrence rate high
- Prevention: insertion-related risk factors
 - Tip position
 - Device length
- Research on anti-sleeve materials: promising but no clinical data available yet