MANAGEMENT OF AORTIC INFECTIONS

The newest polyester grafts are the current best option

Elixène JEAN-BAPTISTE, MD, PhD
(Nice University Hospital)

Centre Hospitalier Universitaire de Nice

Instituts thématiques Inserm Institut national de la santé et de la recherche médicale

Lille 2 U1008

CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE
CONTROVERSIES & UPDATES IN VASCULAR SURGERY
JANUARY 22-24 2015
MARRIOTT RIVE GAUCHE & CONFERENCE CENTER, PARIS, FRANCE

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Disclosure

Speaker name: Elixène JEAN-BAPTISTE

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- ☐ **No potential conflicts of interest to report with respect to that topic!**

INTRODUCTION

- Controversies: options for peripheral perfusion

Extra-anatomic bypass (----)

In-situ reconstruction (++++)

- **Allografts**
- **Autogenous**
- **Synthetic**

Conservative

O'Connor et al. J Vasc Surg 2006;44:38-45

Batt M, Jean-Baptiste E et al., Vascular 2012; 20:129-137

In-situ Revascularisation for Patients with Aortic Graft Infection: A Single Centre Experience with Silver Coated Polyester Grafts

M. Batt [a,*], E. Jean-Baptiste [a], S. O'Connor [b], P.-J. Bouillanne [a], P. Haudebourg [a], R. Hassen-Khodja [a], S. Declemy [a], R. Farhad [c]

[a] *Department of Vascular Surgery, Hôpital Saint-Roch, Université de Nice Sophia-Antipolis, Nice, France*
[b] *4, The Green, Bromham, Bedfordshire, MK43 8JR, UK*
[c] *Department of Infectiology, Hôpital Archet I, Université de Nice Sophia Antipolis, Nice, France*

Submitted 27 September 2007; accepted 26 February 2008
Available online 25 April 2008

- ❑ **Off label use**
- ❑ **Operative mortality: 21% (5/24)**
- ❑ **Recurrent Infections: 16% (3/19 survivors)**

Peri-operative morbidity and mortality were 46% and 21% respectively. Early infections occurred in 6 (25%) patients and late secondary intervention were required in 3 (15.7%), caused by silver graft reinfection. The late mortality was 26%.

Conclusion: In-situ reconstruction with the silver graft confirms similarity with other modalities. The greatest advantage for the silver graft is its ease of use but the risk of reinfection remains significant.

Aortic Graft Infection
Silver coated prostheses (contemporary clinical studies)

Author (year)	*N (Mo)*	*30d mort. (%)*	*RI(%)*
Zegelman M. (2009)	44 (11)	6.5	**6.5**
Batt M. (2008)	24 (32)	21.0	**16**
Pupka A. (2011)	27 (23)	11.0	**4.0**
Bisdas T. (2011)	11(18)	18.0	**22.0**

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Seminars in VASCULAR SURGERY

Antimicrobial Silver Grafts for Prevention and Treatment of Vascular Graft Infection

Jean-Baptiste Ricco, MD, PhD,* and Ojan Assadian, MD, DTMH†

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Seminars in VASCULAR SURGERY

Antibiotic-Impregnated Grafts for Aortic Reconstruction

Wesley Lew, MD and Wesley Moore, MD

Aortic Graft Infection
Rifampicin bonded prostheses (contemporary clinical studies)

Author (year)	*N (Mo)*	*30d mort. (%)*	*RI(%)*
Hayes P.D. (1999)	11 (31)	18.2	22
Bandyk D.F. (2001)	27 (17)	8.0	8.0
Oderich G.S. (2001)	52 (40)	9.0	10.0
Torsello G. & Sandmann W. (1997)	12 (33)	0.0	8.3

Allograft vs Synthetic material resistant to bacterial infection

- Allografts not always available
- Impact on procedural time
- The Results aren’t so GOOD

Fresh / CP Allografts (contemporary clinical studies)

Author (year)	*N (Mo)*	Biomat.	*30d mort. (%)*	*RI(%)*	Fate (%)
Chiesa R (1998)	44 (15)	31CP–11F	13,6	NA	Occlusion: 21
Locati P (1998)	18 (22)	10CP–8F	16,6	13,3	Occlusion: 6
Kieffer E (2004)	179 (46)	38CP+62F	20,0	7,0	Rupture: 5,3 Occlusion:31,4 Dilatation: 4,1
Verhelst R. (2000)	90 (36)	CP	17,0	4,0	Rupture: 12,2 Dilatation: 9,5 Sténoses: 5,4 Occlusion: 8,1

Cryopreserved Allografts (contemporary clinical studies)

Author (year)	*N (Mo)*	*30d mort. (%)*	*RI(%)*	Fate (%)
Vogt P.R. (2002)	49 (27)	6,0	NA	Rupture: 10, Occlusion: 2 Stenose: 2 , Dilatation:2
Lesèche (2001)	28 (35)	17,8	0,0	Dilatation: 17
Lavigne (2003)	22 (18)	14,0	5,0	Dilatation: 5
Gabriel (2004)	43 (NA)	15,0	12,8	Rupture: 10 ; Occlusion: 5 Stenose 25,6
Teebken (2004)	42 (20)	14,0	NA	Rupture: 10 ; Stenose: 9,3 Occlusion: 3
Noel A.A. (2002)	56 (5)	13,0	9,0	Rupture: 9 ; Dilatation: 2
Zhou W (2006	42 (13)	17,0	NA	Occlusion: 6
Bisdas T (2010)	57 (36)	9,0	0,0	Dilatation 1,7; Rupture:1,7 Occlusion: 1,7

In Situ Reconstruction in Native and Prosthetic Aortic Infections Using Cryopreserved Arterial Allografts

J. Touma [a], F. Cochennec [a], J. Parisot [b], A. Fialaire Legendre [c], J.-P. Becquemin [a], P. Desgranges [a,*]

[a] Department of Vascular Surgery, Henri Mondor University Hospital, 51 Avenue Mal de Lattre de Tassigny, 94000 Créteil, France
[b] Public Health Department, Henri Mondor University Hospital, Créteil, France
[c] EFS Saint Antoine Tissue Bank, Paris, France

WHAT THIS PAPER ADDS

This study reports the outcome of in situ aortic reconstruction using cryopreserved allografts. It emphasizes the need for close postoperative surveillance because of the substantial early graft-related complication rate. It studies the influence on allograft behavior of two cryopreservation protocols generally reported and used in this series. It also identifies five independent predictors of early mortality: age, chronic kidney disease, coronary disease, prosthetic infection, and urgent procedures.

Objectives: To evaluate overall survival and complications of cryopreserved arterial allografts in aortic graft infections and infected aortic aneurysms.

Methods: A retrospective review of consecutive patients was conducted with native or prosthetic aortic infections, who underwent local debridement and in situ implantation of a cryopreserved aortic allograft from

- ❑ **N = 54 patients**
- ❑ **Early significant postoperative complications occurred in 28 (52%) patients.**
- ❑ **Graft-related complication : 19%**

30-day survival rate, as well as a substantial early graft-related complication rate. Longer follow-up is needed in order to support the preferential use of cryopreserved allografts based on their long-term behavior.

Article history: Received 4 September 2013, Accepted 15 April 2014, Available online 10 June 2014

Keywords: Allograft, Infected aneurysm, Prosthesis-related infection

In Situ Reconstruction in Native and Prosthetic Aortic Infections Using Cryopreserved Arterial Allografts

J. Touma [a], F. Cochennec [a], J. Parisot [b], A. Fialaire Legendre [c], J.-P. Becquemin [a], P. Desgranges [a,*]

[a] Department of Vascular Surgery, Henri Mondor University Hospital, 51 Avenue Mal de Lattre de Tassigny, 94000 Créteil, France
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This study reports the outcome of in situ aortic reconstruction using cryopreserved allografts. It emphasizes the need for close postoperative surveillance because of the substantial early graft-related complication rate. It studies the influence on allograft behavior of two cryopreservation protocols generally reported and used in this series. It also identifies five independent predictors of early mortality: age, chronic kidney disease, coronary disease, prosthetic infection, and urgent procedures.

Objectives: To evaluate overall survival and complications of cryopreserved arterial allografts in aortic graft infections and infected aortic aneurysms.

- ❑ **Graft-related complication (19%)**
- ✓ **Anastomotic disruption (2 cases)**
- ✓ **Allograft body disruption (4 cases)**
- ✓ **Allograft leg thrombosis or dissection (4)**
- ❑ **Graft-related mortality : 7%**

Keywords: Allograft, Infected aneurysm, Prosthesis-related infection

Abdominal aortic reconstruction in infected fields: Early results of the United States Cryopreserved Aortic Allograft Registry

Audra A. Noel, MD,[a] Peter Gloviczki, MD,[a] Kenneth J. Cherry, Jr, MD,[a] Hazim Safi, MD,[b] Jerry Goldstone, MD,[c] Mark D. Morasch, MD,[d] Kaj H. Johansen, MD,[e] and Members of the United States Cryopreserved Aortic Allograft Registry, *Rochester, Minn; Houston, Tex; Cleveland, Ohio; Chicago, Ill; and Seattle, Wash*

Objective: Aortic reconstructions for primary graft infection (PGI), mycotic aneurysm (MA), and aortic graft-enteric erosion (AEE) bear high morbidity and mortality rates, and current treatment options are not ideal. Cryopreserved grafts have been implanted successfully in infected fields and may be suitable for abdominal aortic reconstructions. Registry data from several institutions were compiled to examine results of cryopreserved aortic allograft (CAA) placement.
Methods: The experience of 31 institutions was reviewed for CAAs inserted from March 4, 1999, to August 23, 2001. Indications for CAA, organisms, mortality, and complications were identified.
Results: Fifty-six patients, 43 men and 13 women, with a mean age of 66 years (range, 44 to 90 years) had in situ aortic replacement with CAA. Indications for CAA placement were PGI in 43 patients (77%), MA in seven (14%), AEE in four (7%), and aortic reconstruction with concomitant bowel resection in two (4%). Infectious organisms were identified in 33 patients (59%); the most frequent organism was *Staphylococcus aureus* in 17 (52%). Thirty-one patients (55%) needed an additional cryopreserved segment for reconstruction. The mean follow-up period was 5.3 months (range, 1 to 22 months). One patient died in the operating room, and the 30-day surgical mortality rate was 13% (7/56). Seven additional patients died during the follow-up period, yielding an overall mortality rate of 25% (14 patients). Two patients (4%) had graft-related mortality as the result of hemorrhage from the CAA and persistent infection. Graft-related complications included persistent infection with perianastomotic hemorrhage in five patients (9%), graft limb occlusion in five (9%), and pseudoaneurysm in one (2%). Three patients (5%) needed amputation.
Conclusion: In situ aortic reconstruction with CAA in infected fields carries a high mortality rate, but most deaths are not the result of allograft failure. However, CAA infection and lethal hemorrhage caused by graft rupture occurs and is concerning. Early reinfection was not reported. Late graft-related complications, such as reinfection, thrombosis, or aneurysmal changes, are unknown. Preliminary data from this registry fail to justify the preferential use of CAA for PGI, MA, or AEE. A multicenter, randomized study is needed to compare results with established techniques. (J Vasc Surg 2002;35:847-52.)

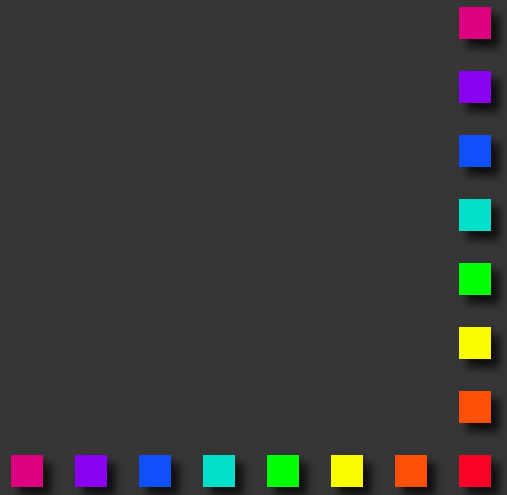
- **In situ CAA infection and lethal hemorrhage caused by graft rupture occurs and is concerning.**
- **Preliminary data from this registry fail to justify the preferential use of CAA for PGI, MA, or AEE.**

Rochester, MN 55905 (e-mail: noel.audra@mayo.edu).

0741-5214/2002/$35.00 + 0 24/6/123755
doi:10.1067/mva.2002.123755

primary graft infection (PGI) placed for abdominal aortic aneurysm or occlusive disease, MA, aortoenteric erosion/fistula (AEE), or aortic reconstruction with concomitant bowel resection. The data were collected on data sheets for

No prospective randomized controlled trial
Low incidence of aortic infections



Cryopreserved arterial homografts vs silver-coated Dacron grafts for abdominal aortic infections with intraoperative evidence of microorganisms

Theodosios Bisdas, MD, Mathias Wilhelmi, MD, Axel Haverich, MD, and Omke E. Teebken, MD, *Hannover, Germany*

22 CP Allografts & 11 Silver

Operative mortality: 14% vs 18% (P>0.99)

2-yr Survival: 82% vs 73% (P=0.79)

- **Median cost:**

CP Allograft: $41,697 ($28,347 - $53,362)

Silver: $15,531 ($11,310-$22,209) P = 0.02

53:1274-81.)

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European Journal of Cardio-thoracic Surgery 15 (1999) 639–645

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

Explanted cryopreserved allografts: a morphological and immunohistochemical comparison between arterial allografts and allograft heart valves from infants and adults[☆]

Paul R. Vogt[a,*], Thomas Stallmach[b], Urs Niederhäuser[a], Jakob Schneider[b], Gregor Zünd[a], Mario Lachat[a], Andreas Künzli[a], Marko I. Turina[a]

[a]*Clinic for Cardiovascular Surgery, University Hospital Zurich, Rämistr. 100, CH-8091 Zurich, Switzerland*
[b]*Department of Pathology, University Hospital Zurich, Rämistr. 100, CH-8091 Zurich, Switzerland*

Received 21 September 1998; received in revised form 13 January 1999; accepted 27 January 1999

Abstract

Objective: Life expectancy of cryopreserved allografts implanted in infants is different from those implanted in adults. A morphological study of explanted allograft heart valves was performed to determine the mechanism of deterioration and to compare cryopreserved arterial and heart valve allografts from adult patients with those explanted from infants. **Method**: Between 1987 and 1996, 209 cryopreserved allografts were implanted: 125 valved conduits or monocusps to reconstruct the right ventricular outflow tract in congenital heart disease, 50 allograft heart valves to treat native aortic and prosthetic aortic valve endocarditis and 34 cryopreserved arterial allografts to replace mycotic aortic aneurysms or infected aortic prosthetic grafts. Two months to 8 years after implantation, 23 heart valve allografts, 11 right-sided and 12 left-sided, and four arterial allografts had to be explanted for reasons such as degeneration, recurrent infection, aneurysm formation or rupture. Besides conventional staining, immunohistochemical detection of cell populations was performed as follows: CD45RO, CD3 and CD43 for T lymphocytes, CD20 for B lymphocytes, CD68 for macrophages, protein S100 for Langerhans-cells, vimentin for fibroblasts, α-actin for smooth muscle cells and factor VIII for endothelial cells. **Results**: Explanted cryopreserved allografts were all fibrotic, acellular, non-vital and without endothelial cells. The fibrous tissue was preserved. T lymphocytes, indicating rejection, were found in all right-sided allografts from the paediatric population, but only in 9% of left-sid of the four of arterial allografts. Macrophages and Langerhans-cells were found only in righ **Conclusion**: Right-sided cryopreserved allografts from a paediatric population showed ongoin only a weak T-cell mediated rejection to adult heart valve and arterial allografts. Therefore, si adult arterial and heart valve allografts, whereas longevity of right-sided heart valve allograft in by cellular rejection. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Explant studies; Cryopreserved allografts; Infants; Adults

Medical Engineering & Physics 31 (2009) 825–832

Contents lists available at ScienceDirect

Medical Engineering & Physics

journal homepage: www.elsevier.com/locate/medengphy

Mechanical properties of arteries cryopreserved at −80 °C and −150 °C

Ingrid Masson[a], Anne Fialaire-Legendre[b], Caroline Godin[c], Pierre Boutouyrie[d,e], Philippe Bierling[b], Mustapha Zidi[a,*]

[a] *CNRS UMR 7054, Faculté de Médecine, Université Paris 12, Créteil F-94010, France*
[b] *Etablissement Français du Sang Ile de France, Hôpital Henri Mondor, Créteil F-94010, France*
[c] *Institut Supérieur des BioSciences, Faculté de Médecine, Université Paris 12, Créteil F-94010, France*
[d] *INSERM UMR S 872, Centre de Recherche des Cordeliers, Université Pierre et Marie Curie, Université Paris Descartes, Paris F-75006, France*
[e] *Service de Pharmacologie, Assistance Publique Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Paris F-75015, France*

ARTICLE INFO

Article history:
Received 22 April 2008
Received in revised form 14 February 2009
Accepted 24 March 2009

Keywords:
Cryopreservation
Artery
Dynamics pressure device
Mechanical properties

ABSTRACT

A new protocol for cryopreservation of arteries frozen at −80 °C was compared to the reference protocol for cryopreservation at −150 °C and to freshly harvested arteries. The aim of the study is to evaluate both protocols as global procedures to freeze and thaw arteries commonly used in tissue banks. Changes in mechanical properties of rabbit common carotid arteries were studied. Vascular segments were tested in vitro under dynamics loading conditions. Pressure and diameter were recorded simultaneously by a high fidelity transducer and an echotracking device, respectively. The pressure–diameter relationship was fitted by the arctangent Langewouters' model and the arterial thickness was derived from histological measurements. Histological sections showed that the fresh and −80 °C groups were less damaged by hemodynamic load and histological preparation than the −150 °C group ($p < 0.05$). No differences between fresh and cryopreserved arteries regarding the structural (diameter, intimal-media thickness) and mechanical parameters (distensibility, circumferential stress, elastic modulus) were found. The isobaric circumferential stress was reduced in frozen arteries. These results demonstrate that the cryopreservation at −80 °C preserves the histological structure and mechanical properties better than the cryopreservation at −150 °C, suggesting that the new cryopreservation protocol at −80 °C is a method of choice for storing vessel replacement in vascular surgery.

In vitro evaluation of the antimicrobial efficacy of a new silver-triclosan vs a silver collagen-coated polyester vascular graft against methicillin-resistant *Staphylococcus aureus*

Jean-Baptiste Ricco, MD, PhD,[a] Afshin Assadian, MD,[b] Fabrice Schneider, MD,[a] and Ojan Assadian, MD,[c] *Poitiers, France; and Vienna, Austria*

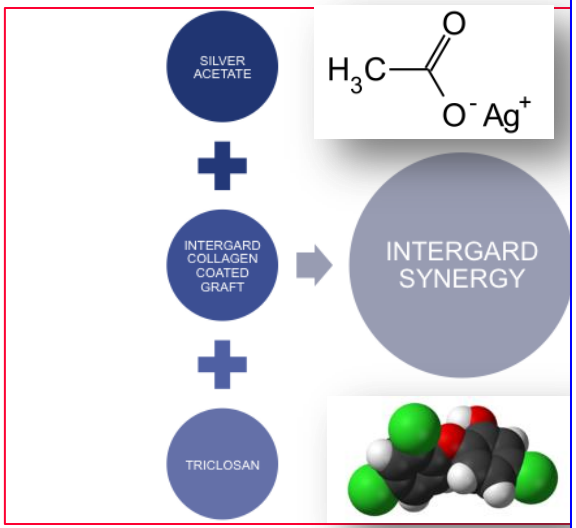
Objectives: Vascular graft infection is a rare but serious complication of vascular reconstructive surgery. This in vitro study investigated the antimicrobial efficacy of a new, silver-triclosan collagen-coated polyester vascular graft compared with a silver collagen-coated polyester vascular graft alone during the first 24 hours.

Methods: The antimicrobial efficacy of the investigated vascular grafts was assessed by performing a time-kill kinetic assay following Clinical and Laboratory Institute Standards-approved guidelines M26-A. For the purpose of the experimental study, the ATCC 33591 strain of methicillin-resistant *Staphylococcus aureus* (American Type Culture Collection, Manassas, Va) was used. All assays were repeated sixfold. Bacterial survival numbers were obtained at 1, 4, 8, 12, and 24 hours using a standard plate count procedure. Bactericidal activity was defined as a 3 $\log_{10}$ reduction factor (logRF), according to the approved guideline M26-A.

Results: Both antimicrobial vascular grafts achieved >3 logRF and fulfilled the efficacy criterion for bactericidal activity but performed differently in their speed of antimicrobial action. The silver-triclosan vascular graft achieved 3.37 logRF after 8 hours, and the silver vascular graft showed a 4.19 logRF after 24 hours. The silver-triclosan graft yielded significantly lower colony-forming units/mL counts after 4 hours compared with the silver graft (4.29×10^4 vs 1.03×10^6; $P = .031$).

Conclusions: Both antimicrobial collagen-coated polymer vascular grafts showed bactericidal activity against methicillin-resistant *Staphylococcus aureus* in vitro. Although the silver-triclosan vascular graft showed a faster antimicrobial efficacy, the silver graft exhibited its antimicrobial properties after 24 hours. Which concept will protect an implanted vascular prosthetic graft better from bacterial contamination and subsequent infection needs to be investigated further in in vivo animal and clinical studies. (J Vasc Surg 2012;55:823-9.)

Clinical Relevance: Vascular graft infection is a rare but one of the most serious complications of vascular reconstructive surgery. Conservative treatment of prosthetic graft infections is rarely successful and is used only in patients with a high operative risk or apparently limited infection. The most pre-eminent strategy against this severe complication therefore is primary prevention of vascular graft infection. The use of antimicrobial vascular grafts might support prevention of vascular graft infection. Results of a standardized experimental study on the antimicrobial efficacy of the silver-triclosan collagen polyester vascular graft with an identical collagen polyester vascular graft containing silver alone are presented.



Prevention of *Staphylococcus aureus* graft infection by a new gelatin-sealed vascular graft prebonded with antibiotics

Isabelle Javerliat, MD,[a] Olivier Goëau-Brissonnière, MD, PhD,[a] Valérie Sivadon-Tardy, MD,[b] Marc Coggia, MD,[a] Jean-Louis Gaillard, MD,[b] *Boulogne-Billancourt and Versailles, France*

Objective: The aim of this study was to evaluate the efficacy of a new gelatin-sealed graft prebonded with two antibiotics in resisting infection with *Staphylococcus aureus (S aureus)* A980142 after direct bacterial application in a dog model.

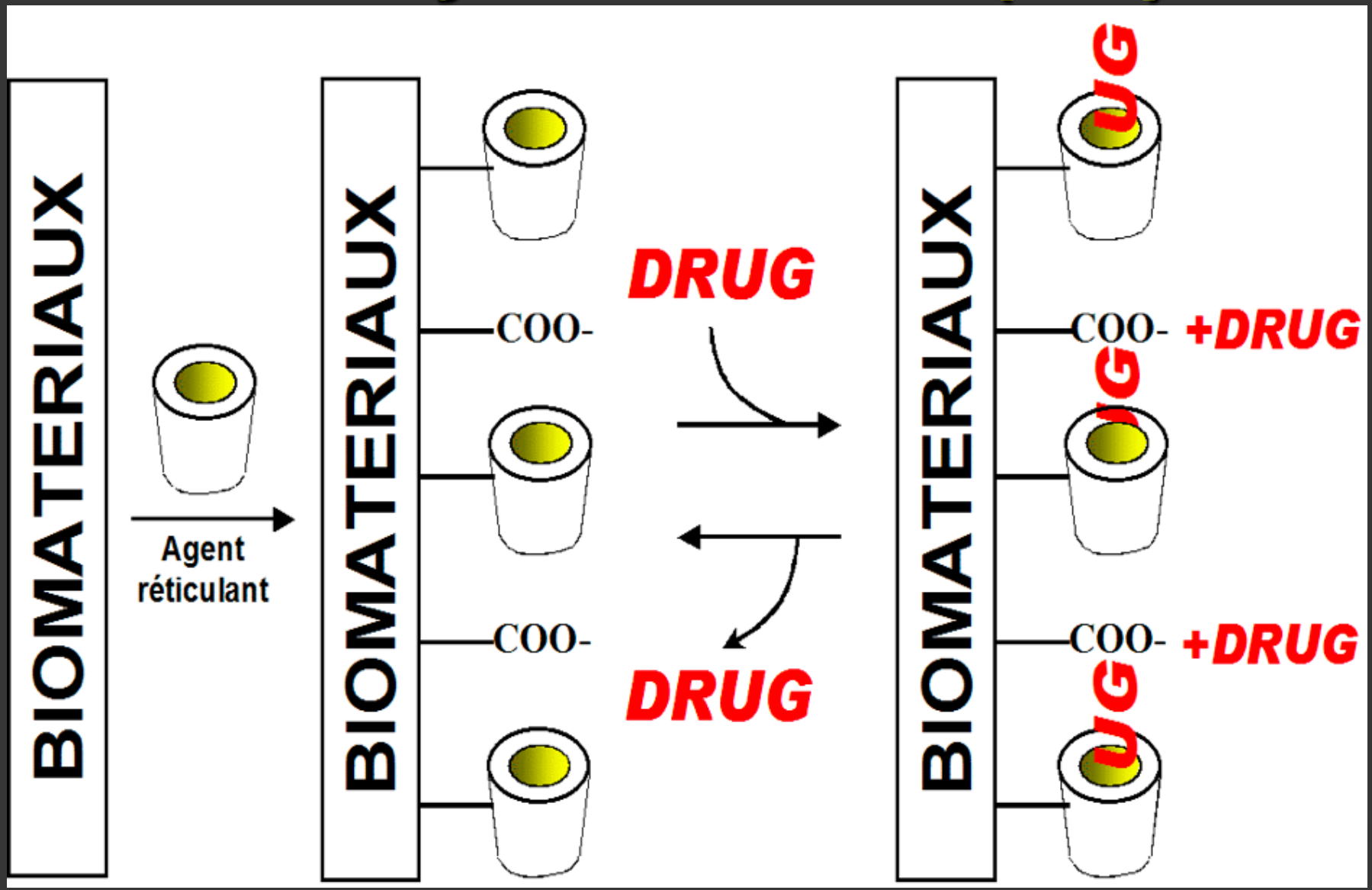
Methods: Twelve 6.0-mm polyester grafts were implanted in dogs end-to-end into the infrarenal aorta. The dogs were divided into two groups. A test group (n = 6) received experimental antibiotic-bonded gelatin-sealed knitted polyester grafts, loaded with two antibiotics, rifampin and tobramycin. A control group (n = 6) received commercial gelatin-sealed knitted polyester grafts. At the end of graft implantation, 50 µl of a 1.8×10^4 CFU/mL *S aureus* solution were instilled directly over the graft. One week after implantation, grafts were harvested with sterile technique. Quantitative cultures were obtained from all the harvested grafts. The results were expressed as colony-forming units per cm^2 of surface of the graft. Bacteriological study was also performed on various tissue samples. The χ^2 test was used to compare the culture proven infection of control and antibiotics-bonded grafts.

Results: Mean inoculum size was similar in the two groups of dogs. Five of the six control grafts grew *S aureus* A980142 at the time of graft removal, whereas none of the six antibiotic-bonded gelatin-sealed grafts were infected ($P = .0192$). None of the organ samples were infected in the group implanted with antibiotic-bonded grafts, whereas 15/34 samples grew *S. aureus* in the control group.

Conclusion: These results indicate that this gelatin sealed graft prebonded with two antibiotics resists infection caused by *S aureus* graft contamination in a dog model. (J Vasc Surg 2007;46:1026-31.)

Clinical relevance. Graft infection remains a crucial problem in vascular surgery, even if its occurrence is rare. Several authors have proposed the use of antibiotic-bonded grafts to prevent or to treat graft infections. Development of grafts that are resistant to infection has considerable appeal, but, until now, none is commercially available. We used a dog model to evaluate the resistance to infection of a new gelatin-sealed graft manufactured prebonded with two antibiotics, rifampin and tobramycin. In this study, we demonstrate that this prebonded graft resists to infection caused by local contamination with *Staphylococcus aureus*. Further studies are required to confirm our experimental findings.

Polyester grafts functionnalised with cyclodextrins (CD)



European Journal of Vascular and Endovascular Surgery 43 (2012) 188–197

Contents lists available at SciVerse ScienceDirect

European Journal of Vascular and Endovascular Surgery

journal homepage: www.ejves.com

Safety, Healing, and Efficacy of Vascular Prostheses Coated with Hydroxypropyl-β-cyclodextrin Polymer: Experimental *In Vitro* and Animal Studies

E. Jean-Baptiste [a,b,c,d], N. Blanchemain [a,b], B. Martel [a,e], C. Neut [a,f], H.F. Hildebrand [a,b], S. Haulon [a,b,c,*]

[a] *L'Université Lille Nord de France, 59000 Lille, France*
[b] *INSERM U 1008, Controlled Drug Delivery Systems and Biomaterials, Université Lille 2, Lille, France*
[c] *Service de Chirurgie Vasculaire, Hôpital Cardiologique, CHRU de Lille, Lille, France*
[d] *Service de Chirurgie Vasculaire, Hôpital Saint Roch, CHU de Nice, Nice, France*
[e] *UMET, Unité des Matériaux Et Transformations, CNRS, UMR 8009, Université Lille 1, Lille, France*
[f] *INSERM U 995, Laboratoire de Bactériologie, Université Lille 2, Lille, France*

WHAT THIS PAPER ADDS

- This study is a significant milestone in the development of drug-eluting polyester vascular prosthesis using a polymer of cyclodextrins. It addresses experimentally the safety and the efficacy of these prostheses before this innovative concept could be applied in clinical medicine. For that reason, this study is unique. The influence of this concept could be tremendous in the near future since one might be able to load specific bioactive molecules, especially antibiotics, onto a graft or stent graft according to therapeutic goals.

ARTICLE INFO

Article history:
Received 31 July 2011
Accepted 21 October 2011
Available online 29 November 2011

Keywords:
Cyclodextrins
Blood vessel prosthesis
Prosthesis-related infections
Drug delivery systems

ABSTRACT

Objectives: Polyester vascular prostheses (PVPs) coated with a polymer of hydroxypropyl-β-cyclodextrin (HPβCD) have been designed to provide an *in situ* reservoir for the sustained delivery of one or more bioactive molecules. The goal of this study was to assess the efficacy, the safety and the healing properties of these prostheses.

Methods: Collagen-sealed PVPs were coated with the HPβCD-based-polymer (PVP-CD) using the pad–dry–cure textile finishing method and loaded with one or two antibiotics. Appropriate control and PVP-CD samples were tested in several *in vitro* and animal model conditions. The study end points included haemolysis, platelet aggregation, antibacterial efficacy, polymer biodegradation, acute toxicity and chronic tolerance.

Results: PVP-CD proved to be compatible with human blood, since it did not induce haemolysis nor influenced ADP-mediated platelet aggregation. Sustained antimicrobial efficacy was achieved up to 7 days against susceptible bacteria when PVP-CDs were loaded with the appropriate drugs. Analysis of harvested PVP-CD from the animal model revealed that the HPβCD-based coating was still present at 1 month but had completely disappeared 6 months after implantation. All grafts were patent, well encapsulated without healing abnormalities. Clinical data, blood-sample analysis and histological examination did not evidence any signs of acute or chronic, local or systemic toxicity in the animal models.

Conclusion: PVP-CD was proved safe and demonstrated excellent biocompatibility, healing and degradation properties. Effective antimicrobial activity was achieved with PVP-CD in conditions consistent with a sustained-release mechanism.

Journal of Infection (2014) 68, 116–124

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BIAM British Infection Association

www.elsevierhealth.com/journals/jinf

Evaluation of the anti-infectious properties of polyester vascular prostheses functionalised with cyclodextrin

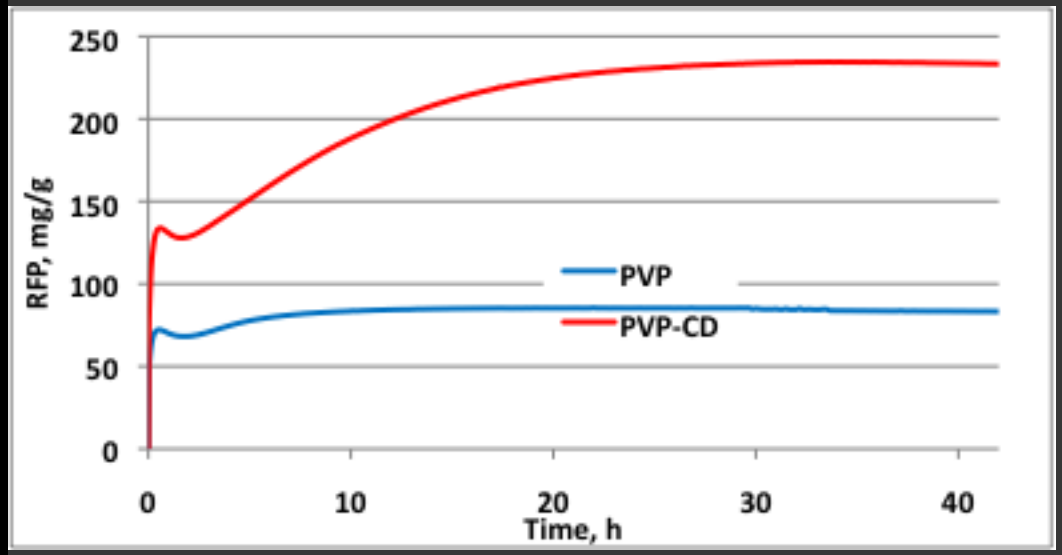
Elixène Jean-Baptiste [a,b,c,d,*], Nicolas Blanchemain [a,b], Christel Neut [a,e], Feng Chai [a,b], Mickael Maton [a,b], Bernard Martel [a,f], Hartmut Hildebrand [a,b], Stéphan Haulon [a,b,c]

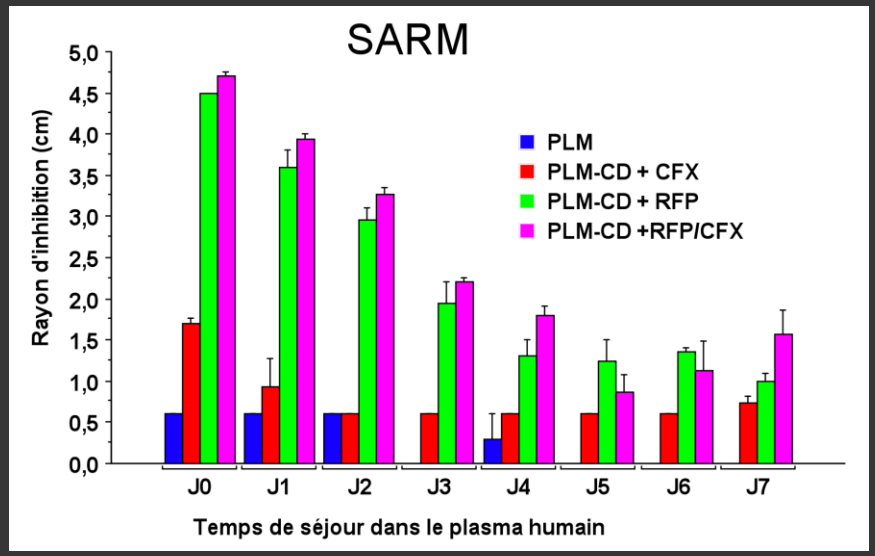
[a] Université Lille Nord de France, 59000 Lille, France
[b] INSERM U 1008, Controlled Drug Delivery Systems and Biomaterials, Université Lille 2, 59000 Lille, France
[c] Service de Chirurgie Vasculaire, Hôpital Cardiologique, CHRU de Lille, 59000 Lille, France

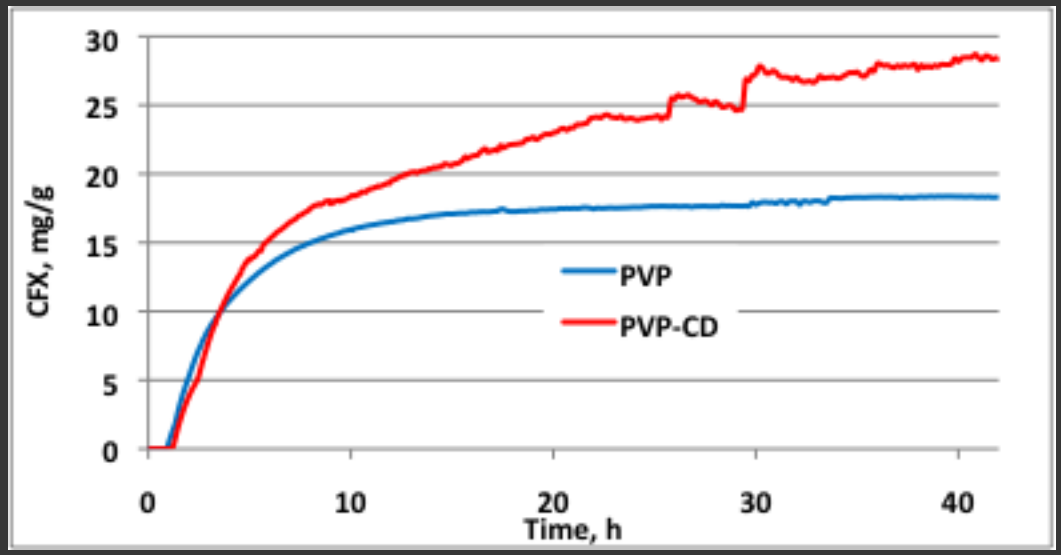
- **Proved efficacy against 6 bacteria commonly encountered in vascular graft infections: 3 Gram positive and 3 Gram negative.**

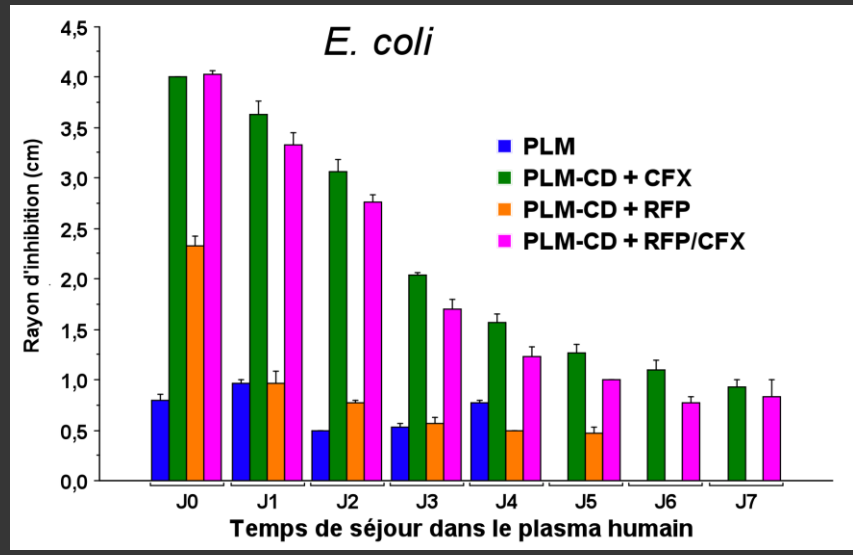
negative (*Escherichia coli*, *En. cloacae* and *Pseudomonas aeruginosa*) bacteria were tested. *Results:* PVP-CD loaded with rifampin showed significant bacterial adhesion reduction and growth inhibition against Gram-positive bacteria. Similar results were obtained against Gram-negative bacteria with PVP-CD loaded with ciprofloxacin. In the mouse model, Gram-positive and Gram-negative bacterial proliferations were significantly prevented by PVP-CD loaded with rifampin or with ciprofloxacin respectively. A decrease in macroscopic infections

Co-delivery of dual antibiotics from CD-functionnalised polyester









CONCLUSIONS

- Allografts: Intuition vs Facts
- Rate of recurrent infections vs Rate of degenerative complications
- Availaibility and Cost
- Only the newest polyester grafts hold the promise of better outcomes