

Drug Eluting Balloon for Stenotic Arterial Venous Fistulas

Clinical Data from a Single Center Case Series

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Potential conflicts of interest

Speaker's name: Domenico Patanè

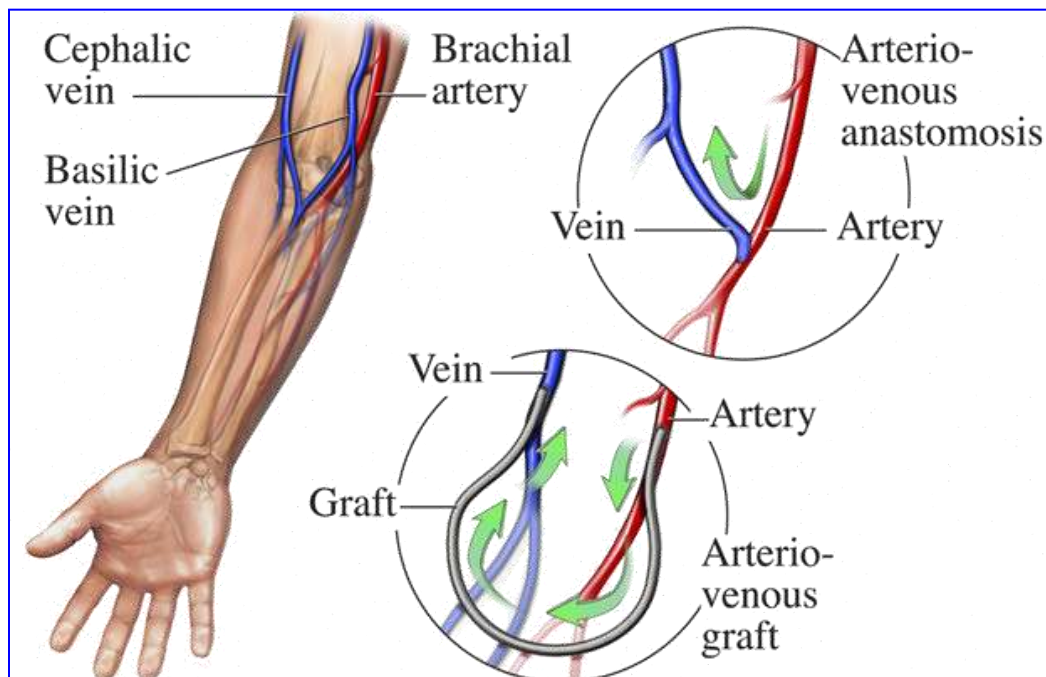
☐ **I have the following** potential conflicts of interest to report:

- ☐ Research contracts
- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

☒ **I do not have any potential conflict of interest**



Introduction: SRD and AV Fistulas



- ESRD prevalence in Europe = 65.000 new p/y
- Hemodialysis with AV = 70%
- ArerioVenous bridge:
 - AV Fistulas uses a segment of an autogenous vein
 - AV Graft uses a segment of prosthetic graft
- AVF viewed as a better option due to its superior long term clinical outcome

Giovanni Lipari et al., "Outcomes of surgical revision of stenosed and thrombosed forearm arteriovenous fistulae for haemodialysis", Nephrol Dial Transplant (2007) 22: 2605–2612

Background

End Stage Renal Disease and Hemodialysis



Hematomas, aneurisms and stenosis are typical recurrent complications from repeated access

- **Major unmet and urgent needs:**
 - 1) Preserve the Vascular Access; 2) Increase Patency

Increase patency to prolong the lifespan of the Vascular Access

- Maintenance of the access site is one of the most challenging concerns in the care of hemodialysis-dependent patients ¹
- Hemodialysis access failure has become the most frequent cause of hospitalization among ESRD patients

1. Yasumitsu Mori, et al., "Stenotic Lesions in Vascular Access: Treatment with Transluminal Angioplasty Using High-Pressure Balloons", Internal Medicine Vol. 33, No. 5, May 1994

Background

AV Fistula PTA and Patency Rates

- The Dialysis Outcomes Quality Initiative Guidelines of the National Kidney Foundation ^[1] recommend PTA for the treatment of hemodialysis access stenosis, BUT....:

	Nr AV Fistulas	Type of AV Fistula	Succ Rate	12m Prim. Patency	12m Sec. Patency
Asif et al (2006) ²	73	Forearm + arm	97%	51%	90%
Maeda et al (2005) ³	60	Forearm	92%	53%	84%
Manninen et al (2001) ⁴	53	Forearm	91%	44%	85%
Clark et al (2002) ⁵	53	Forearm + arm	94%	26%	82%
Lay et al (1998) ⁶	31	Forearm	90%	64%	81%
Turmel-Rodrigues et al (2000) ⁷	155 65	Forearm + arm	95% 97%	51% 35%	85% 82%

Primary patency rates remain too low (<< 50%) and the clinical burden of repeated interventions and reduced lifespan of the access site too high

1. NKF-K/DOQI American Journal of Kidney Diseases 2001
2. Asif A, Kidney International 2006
3. Maeda K, European Journal of Radiology 2005
4. Manninen H, Radiology 2001
5. Clark TW, J Vasc Interv Radiol 2002
6. Lay JP, Clin Radiol 1998
7. Turmel-Rodrigues L, Nephrol Dial Transplant 2000

Std. PTA in AV-Fistulas: Personal Experience

170 Patients

Fore-arm (Radio-cephalic Fistulas) = 125

Arm (Brachio-cephalic Fistulas) = 45

luxta-anastomotic stenosis = 70%

Technical and Clinical Success = 95.8%

1 year Primary Patency = 71.7%

GIORNALE ITALIANO DI NEFROLOGIA / ANNO 26 N. 2, 2009 / PP. 236-245

RICERCA

TRATTAMENTO ENDOVASCOLARE DELLE COMPLICANZE STENO-
OSTRUTTIVE DELLE FISTOLE ARTERO-VENOSE EMODIALITICHE: NUOVI
ASPETTI DI INTERVENTO CON RADIOLOGIA INTERVENTISTICA

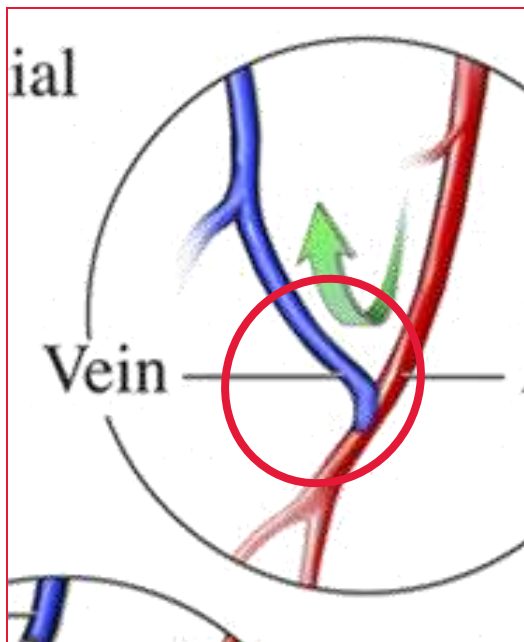
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luxta-anastomotic Region



Stenosis are most prevalent within 3cm of the arteriovenous anastomosis (64%, *Rajan, Radiology 2004*)

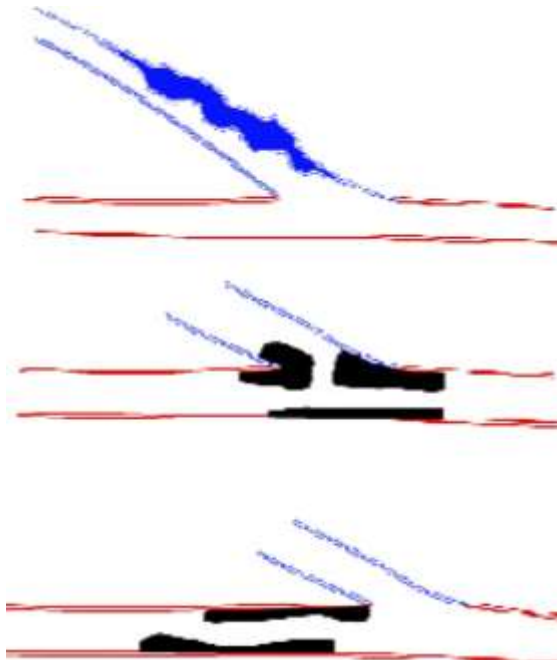
luxta anastomotic stenosis are the most common lesion observed (98/112, *Asif, Kidney Int 2006*)

luxta anastomosis is a critical area for poor angiographic results and lower patency rates vs. non-anastomotic stenosis, although the difference is not statistically significant (*Manninen, 2001*)

1-year primary patency rates after PTA of perianastomotic stenoses in nonthrombosed RCFs

Author	Primary patency rates (%)
Tessitore et al, 2006	54
Asif et al, 2006	47
Manninen et al, 2001	20
Cohen et al, 2009	56
Long et al, 2011	41

Rationale for Drug Therapy in AV Shunts



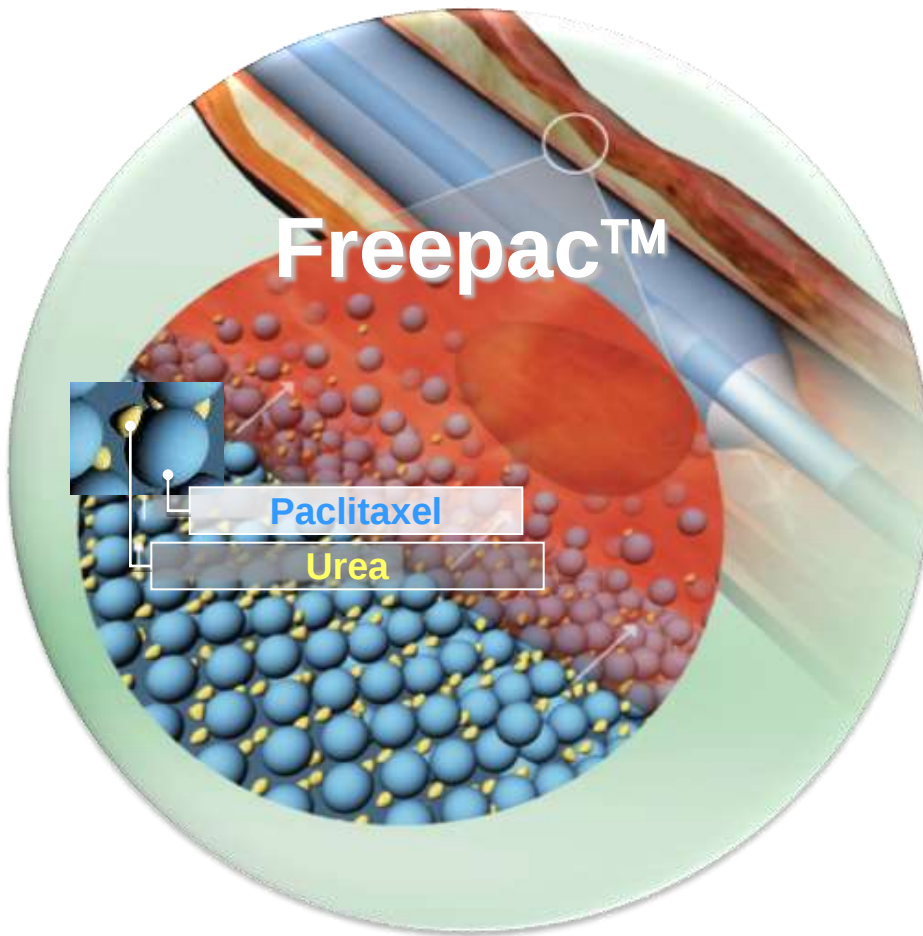
- **luxta-anastomotic lesions of native AV fistulas are usually related to intimal hyperplasia especially for anastomotic and venous stenosis [1]**
- **Animal data support the benefit of local antiproliferative drugs such as sirolimus and paclitaxel to decrease neointimal hyperplasia at the venous side of hemodialysis access [2,3,4]**

1. Bertrand Long et al, *Perianastomotic stenosis of direct wrist autogenous radial-cephalic arteriovenous accesses for dialysis: Transluminal angioplasty or surgery?* J Vasc Surg Vol. 53, Issue 1, Pages 108-114, January 2011
2. Rotmans J, Pattynama PM, Verhagen HJ, et al. *Sirolimus-eluting stents to abolish intimal hyperplasia and improve flow in porcine arteriovenous grafts: a 4-week follow-up study.* Circulation 2005; 111:1537-1542
3. Lee BH, Nam HY, Kwon T, et al. *Paclitaxel-coated expanded polytetrafluoroethylene haemodialysis grafts inhibit neointimal hyperplasia in porcine model of graft stenosis.* Nephrol Dial Transplant 2006; 21:2432-2438
4. Kohler TR, Toleikis PM, Gravett DM, Avelar RL. *Inhibition of neointimal hyperplasia in a sheep model of dialysis access failure with the bioabsorbable Vascular Wrap paclitaxel-eluting mesh.* J Vasc Surg 2007; 45:1029-1037

- We aimed to evaluate the efficacy of DEB to address the most common and unmet need of luxta-anastomotic stenosis
- From June 2009, 25 consecutive patients undergoing routine hemodialysis due to ESRD and presenting with stenosis (ex novo and recurrent) of the iuxta-anastomotic region were treated with In.Pact™ DEB (Medtronic) within our standard practice
- Main objective was the assessment of Primary Patency defined as absence of hemodialysis access malfunctioning according to the NKF-DOQI-protocol criteria (1996) confirmed by <50% DS without clinically driven TLR (reintervention of the target lesion due to insufficient dialysis flow)
- Results were compared to benchmark data from a matched population treated with standard PTA from our historical series



In.Pact™ DEB and FreePac™ Coating Technology



In.Pact™

- Medtronic-Invatec DEB balloon line

Freepac™

- Medtronic proprietary hydrophilic drug coating formulation
 - separates Paclitaxel molecules
 - balances hydrophilic and lipophilic properties
 - facilitates Paclitaxel elution into the vessel wall

In.Pact™ DEB Treatment Protocol

1. Detailed Echo Colour Doppler evaluation (performed by the same operating interventional radiologist)
2. Ultrasound guided retrograde needling of the vein most of the times or transbrachial arterial approach only when necessary
3. Diagnostic angiographic evaluation
4. Stenosis and anastomosis crossed and guide-wire is advanced retrogradely into the proximal radial artery
5. 0.014" guidewires and low profile PTA balloons for predilatation of the luxta-anastomotic stenosis
6. DEB sizing: + 0.5 mm vs. the PTA balloon used for the anastomosis
7. High pressure PTA performed at the venous site in case of outflow lesions



In.Pact™ DEB in AV Fistulas luxta-anastomotic stenosis

- 25 AV Fistulas in 25 patients treated with DEB due to de-novo (72.0%) or recurrent (28.0%) stenosis

Baseline Demographics

Nr of Patients	25
Mean age	71 ± 13 years
Male Gender	20 (80.0%)
Hypertension	13 (52.0%)
Hyperlipidemia	11 (44.0%)
Diabetes mellitus	14 (56.0%)
AV Fistulas mean age	31 ± 36 months
Stenosis type	
de-novo	18 (72.0%)
recurrent	7 (28.0%)

Procedure

outflow lesions	25 (100.0%)
successfully treated (PTA)	25 (100.0%)
Pre-dilatation (std PTA)	25 (100.0%)
Cutting Balloon	1 (4.0%)
Tech Success ¹	25 (100.0%)
Clinical Success ²	25 (100.0%)

Follow up (8.7 ± 4.3 months)

Freedom from TLR	23 (92.0%)
Primary Patency	23 (92.0%)
Recurrency rate (>1 TLR)	0 (0.0%)
Mean time of 1st occurrence	9.0 ± 2.8 months
TSR (outflow lesions)	5 (20.0%)

- Obtainment of <30% DS by visual estimate
- Successful re-establishment dialysis flow flow as measured during subsequent dialysis

standard PTA in AV Fistulas Iuxta-anastomotic stenosis retrospective analysis

- 86 AV Fistulas in 86 patients treated with standard PTA dilatation from SEP-2002 to JUL-2009 due to de-novo (69.8%) or recurrent stenosis (30.2%)

Baseline Demographics

Nr of Patients	86
Mean age	69 ± 12 years
Male Gender	72 (83.7%)
Hypertension	51 (59.3%)
Hyperlipidemia	23 (26.7%)
Diabetes mellitus	60 (69.8%)
AV Fistulas mean age	11 (2–36) months
Stenosis type	
<i>de-novo</i>	60 (69.8%)
<i>recurrent</i>	26 (30.2%)

Procedure

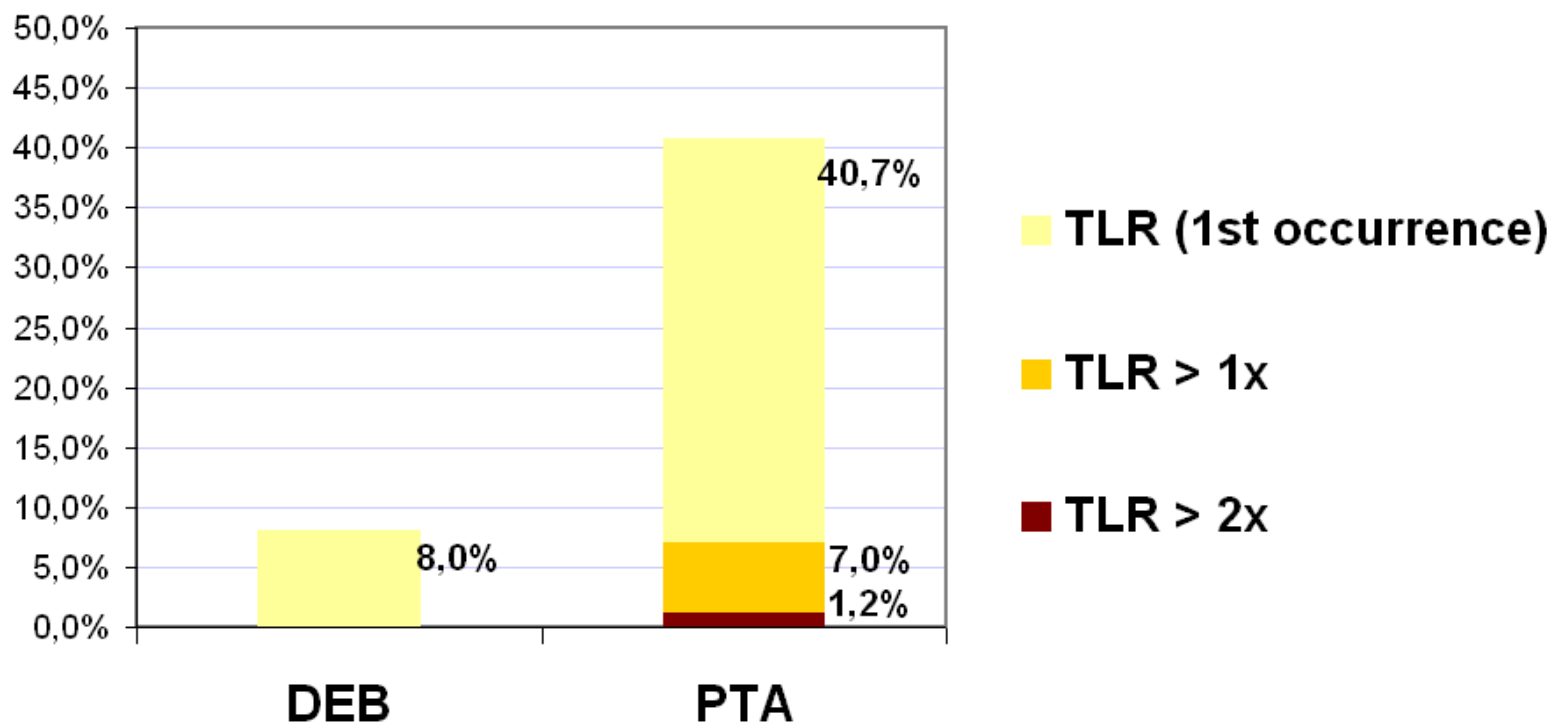
outflow lesions	86 (100.0%)
successfully treated (PTA)	86 (100.0%)
Tech Success ¹	82 (95%)
Clinical Success ²	100%

Follow up (9.9 ± 3.4 months)

Freedom from TLR	51 (59.2%)
Primary Patency	51 (59.2%)
Recurrency rate (>1 TLR)	6 (7.0%)
Mean time of 1st occurrence	5.3 months
TSR (outflow lesions)	6 (6.9%)

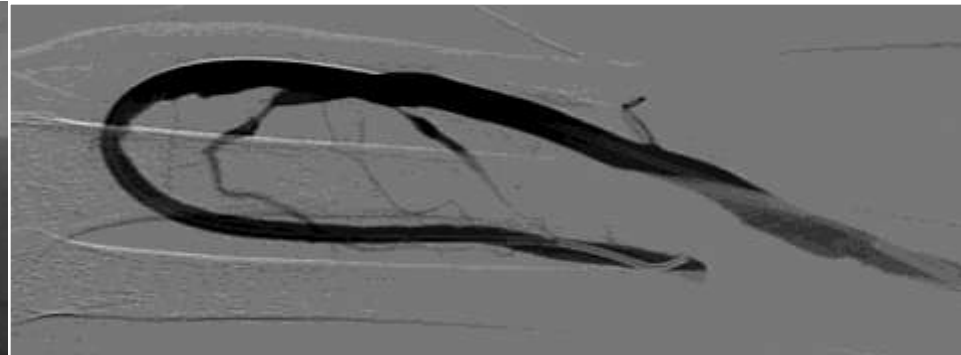
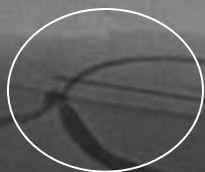
- Obtainment of <30% DS by visual estimate
- Successful re-establishment dialysis flow flow as measured during subsequent dialysis

TLR ~ 9m outcome



mean re-occurrence time = ~ 9m (DEB) vs. ~5m (PTA)

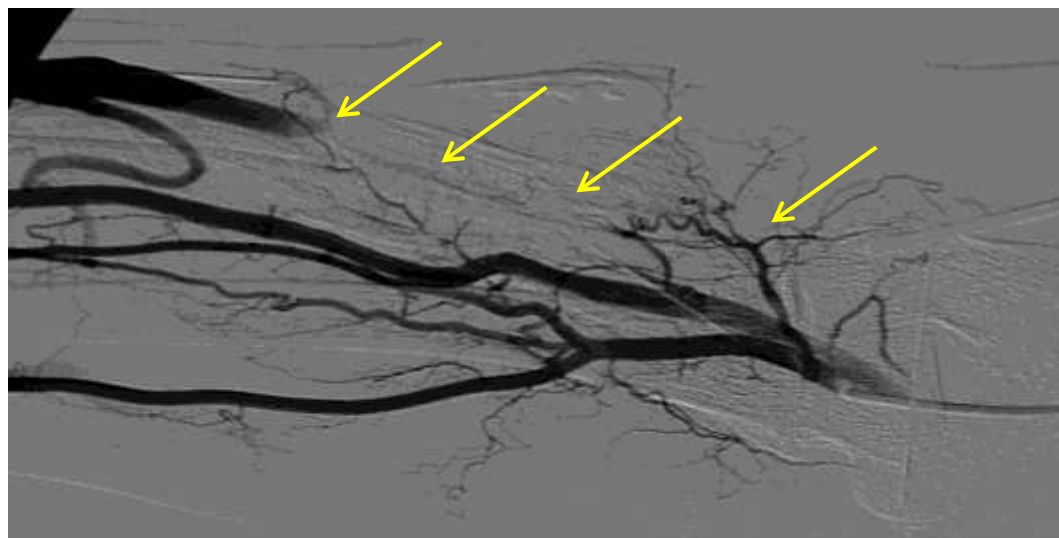
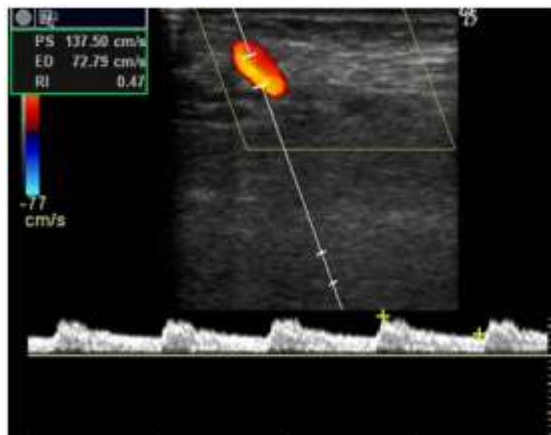
case example # 1



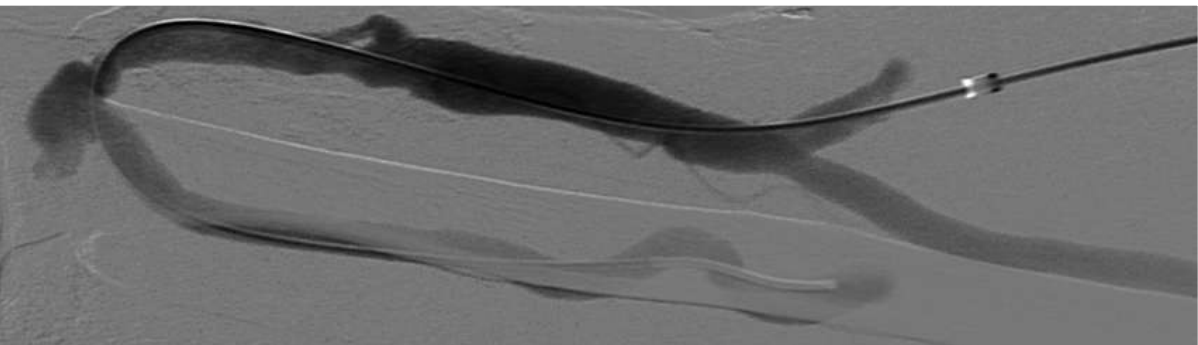
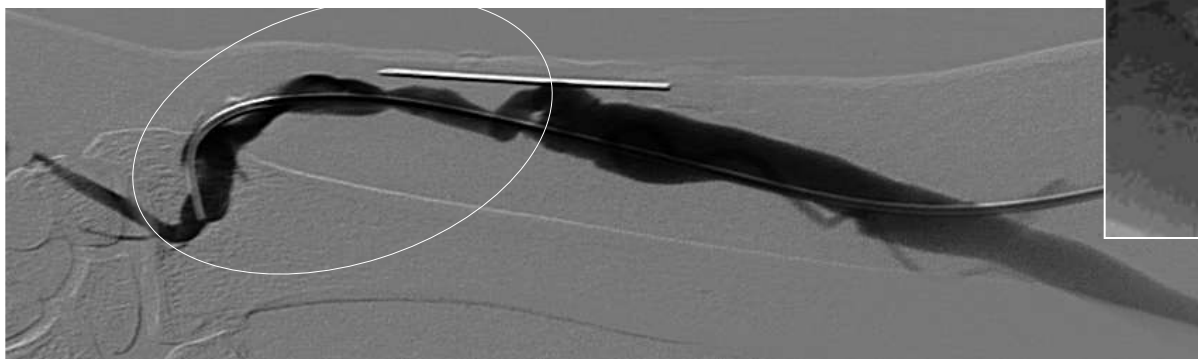
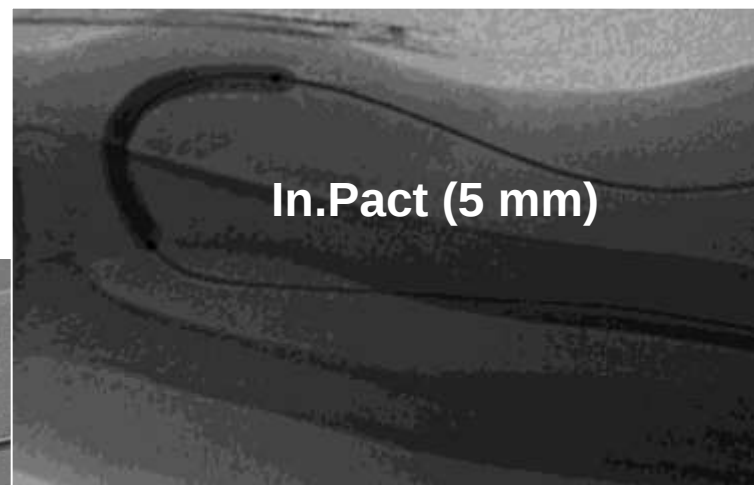
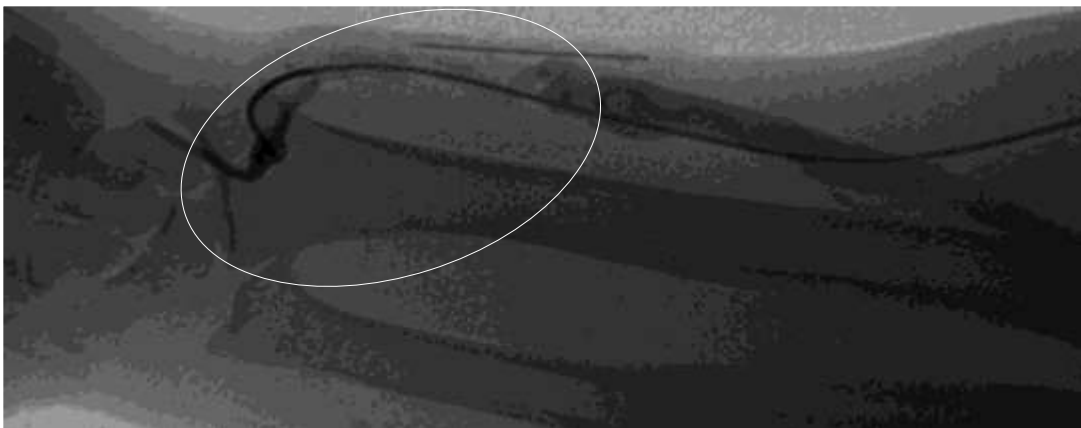
In.Pact (4mm)

High-pressure PTA

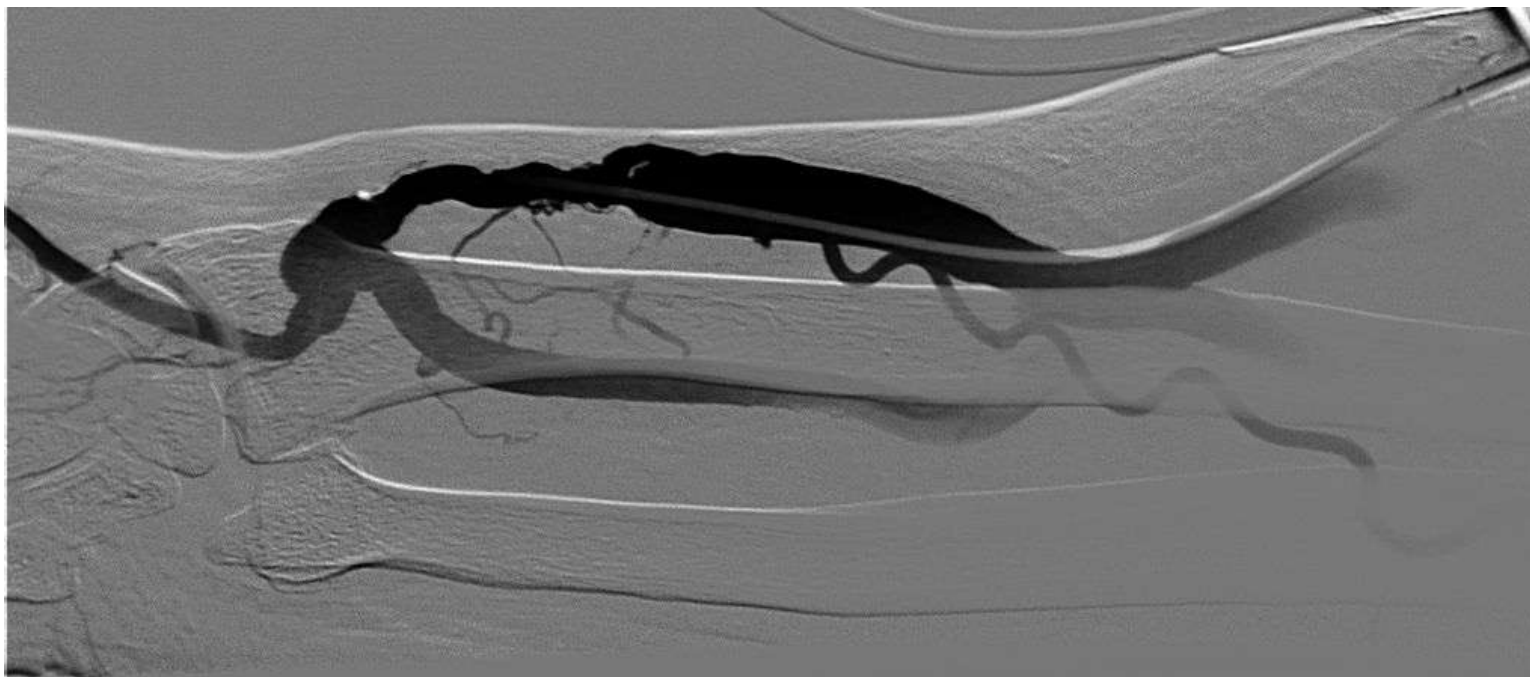
case example # 1 (4 month FU)



case example # 2



case example # 2 (*12 month FU*)



Additional Data of DEB in AV-Fistulas

Konstantinos Katsanos – Charing Cross 2011

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Drug Eluting Balloon Angioplasty for Dialysis Access Treatment

This study is ongoing, but not recruiting participants.

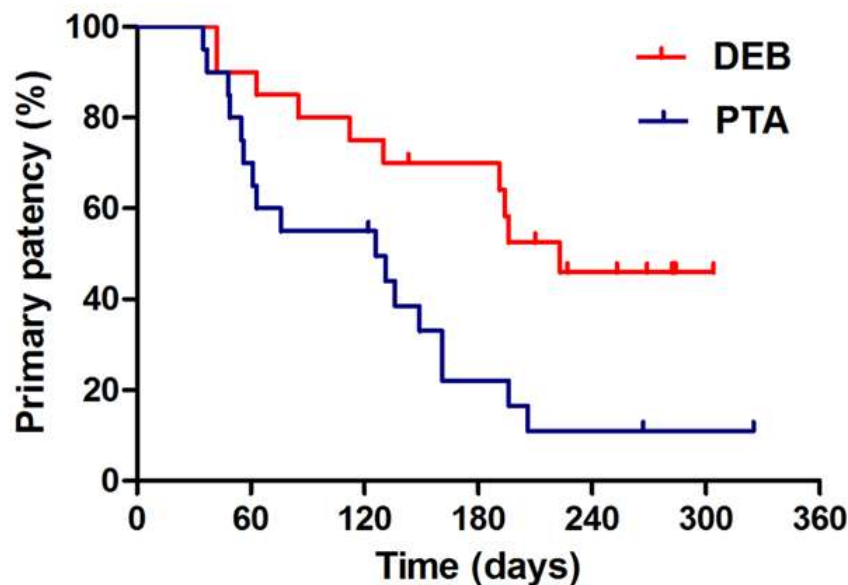
First Received on July 21, 2010. Last Updated on February 10, 2011 [History of Changes](#)

Sponsor:	University of Patras
Information provided by:	University of Patras
ClinicalTrials.gov Identifier:	NCT01174472

Baseline variables

	Group DEB	Group PTA
Subjects (n)	20 lesions	20 lesions
Gender (M/F)	15M / 5F	14M / 6F
Age (years)	65.7 ± 13.2	62.5 ± 15.4
Dialysis access	13AVG / 7AVF	13AVG / 7AVF
AV age (years)	2.5 ± 2.0	2.5 ± 3.2

Preliminary analysis (AV primary patency)

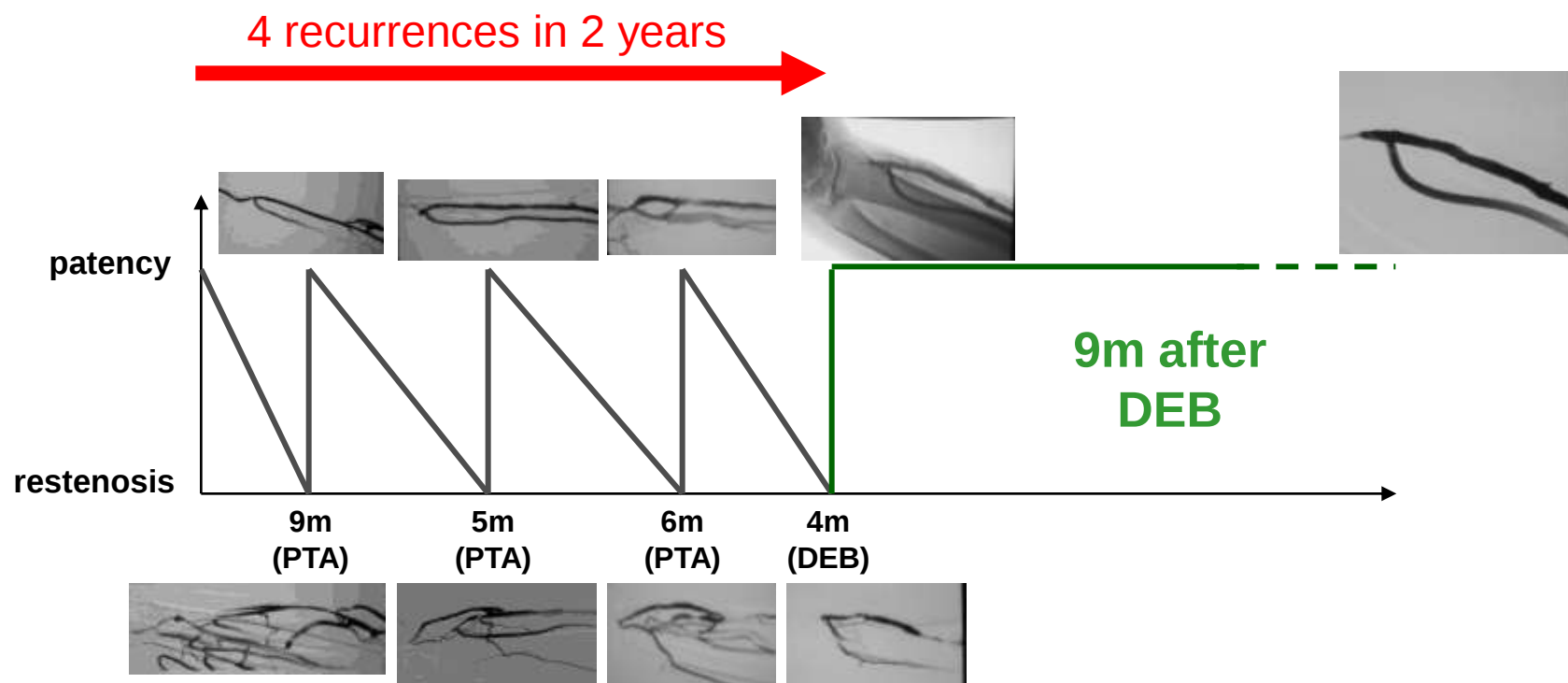


Median patency: 223 vs 126 days

HR=0.35 (CI: 0.16-0.76); P=0.008 Log rank test

DEB for recurrent Av-Fistulas stenosis

- Refractory, relapsing restenosis



- **This initial experience indicates the safety and effectiveness of In.Pact™ DEB for the treatment of stenotic AV Fistulas**
- **92% Primary Patency rate at 9m looks very promising and remarkably better vs. literature derived data as well as our previous experience with standard PTA**
- **Lower reintervention rates and associated reduced hospital stay suggests a potential cost-effectiveness benefit of DEB vs. PTA**
- **The benefit of DEB for AV-Fistulas seems confirmed by other clinical experiences (Katsanos – Charing Cross 2011)**
- **Further Randomized studies are awaited to further explore and confirm such promising results**

