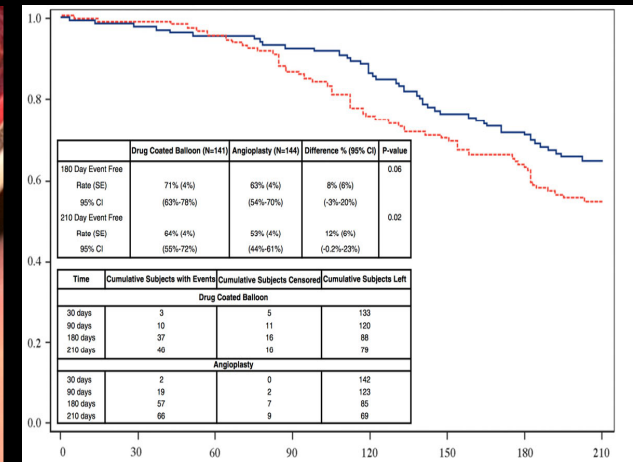
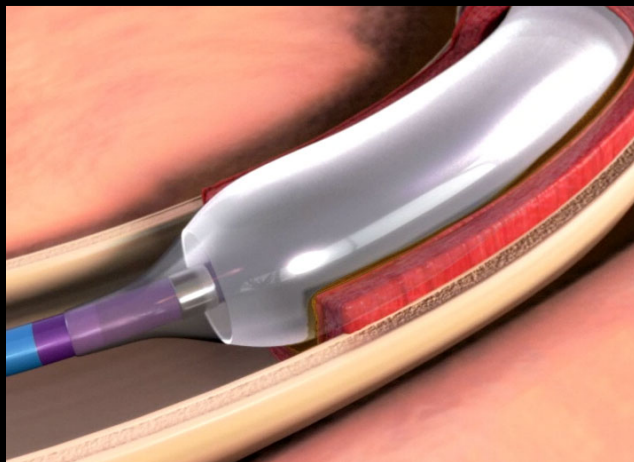
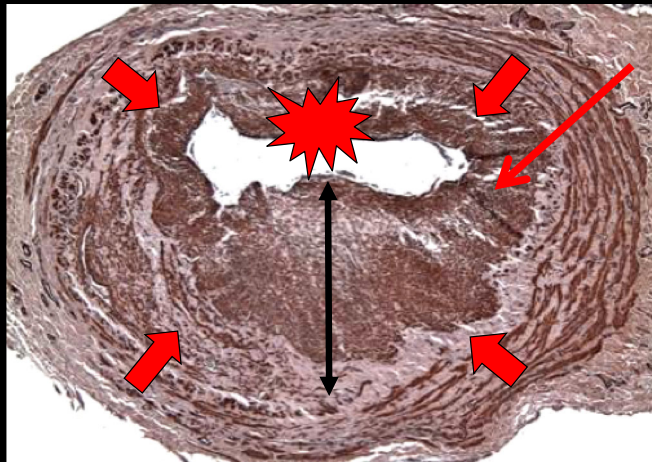


# Drug Eluting Balloons for Dialysis Vascular Access

***Prabir Roy-Chaudhury, MD, PhD, FRCP (Edin)***  
***University of North Carolina Kidney Center***



# Disclosures

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- Consultant/Advisory Board: **WL Gore, Medtronic, Bard-BD, Humacyte, Cormedix, Akebia, Vifor-Relypsa, Bayer, Reata**
- Founder and Chief Scientific Officer: **Inovasc**
- Grant/Research Support: **NIH, VA, NSF**
- Foundation: **ASN Councilor at Large**

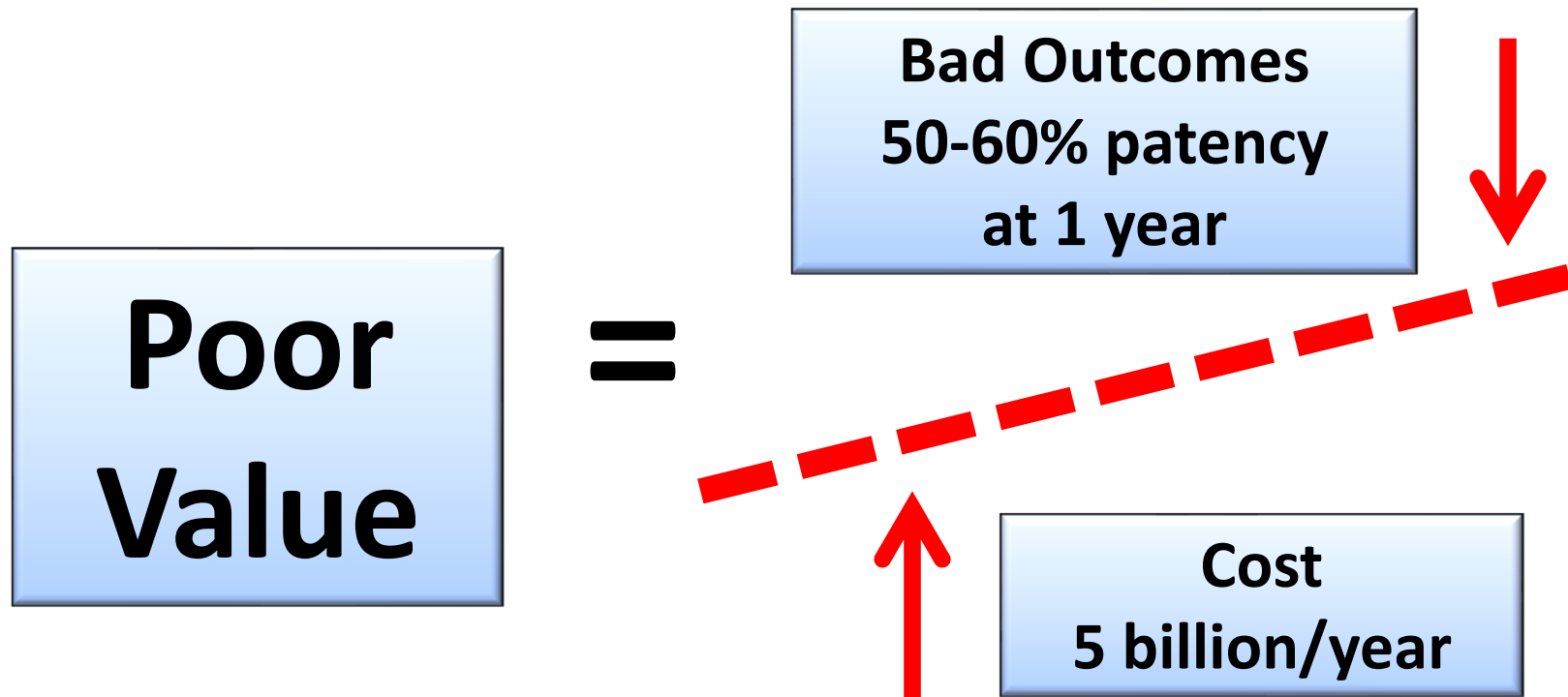
# Outline

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- **Describe to you the current state of the data for drug eluting balloons**
- **Make a case for a future precision medicine approach to vascular access care**

# Message for the present: **poor value in vascular access care**

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**Without any mention of quality of life**

# Interventions for dialysis access stenosis have terrible results!

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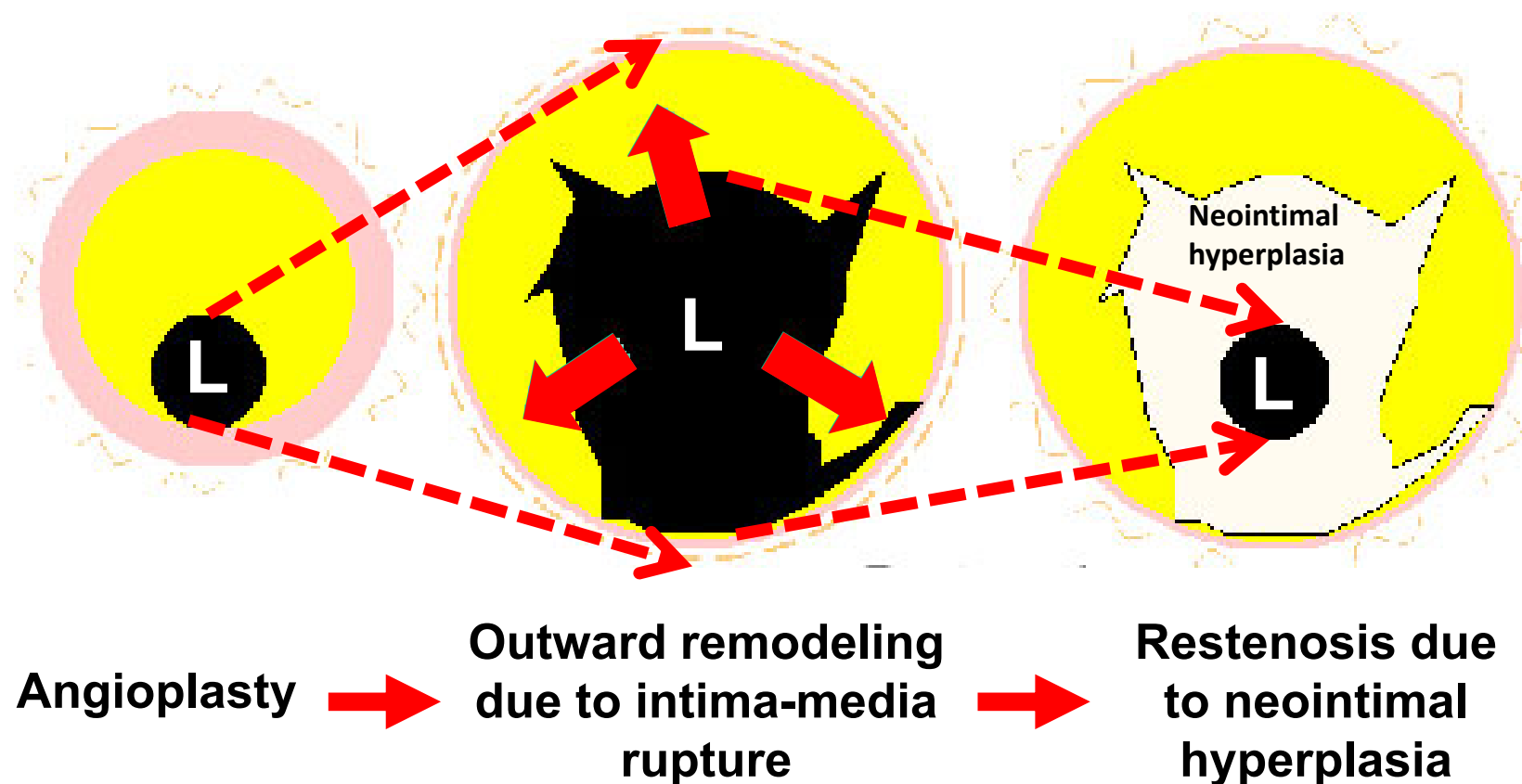
## Procedure

## Result

- |                                    |                                          |
|------------------------------------|------------------------------------------|
| ● Coronary Angioplasty             | 90% @ 9 months                           |
| ● Carotid Angioplasty              | 90% @ 1 year                             |
| ● Iliac Angioplasty                | 70% @ 5 years                            |
| ● Femoral Angioplasty              | 50% @ 2 years                            |
| ● Peri-anastomotic AVF angioplasty | 50% @ 1 year                             |
| ● PTFE graft angioplasty           | 50% @ 6 months (p)<br>40% @ 3 months (t) |

## Back to Basics: Angioplasty causes forceful outward remodeling followed by aggressive neointimal hyperplasia

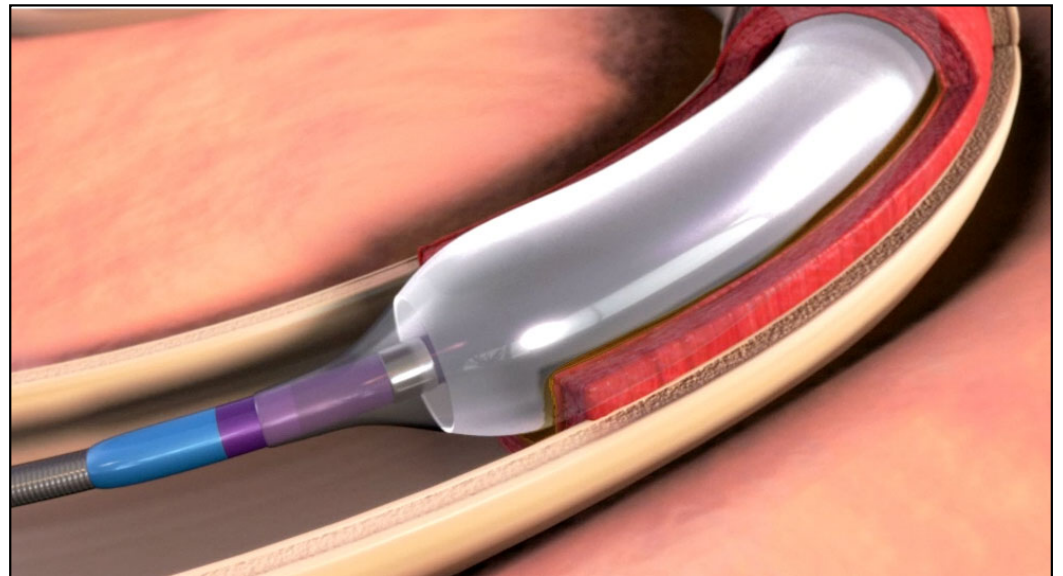
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## **Drug eluting balloons coated with an anti-proliferative agent**

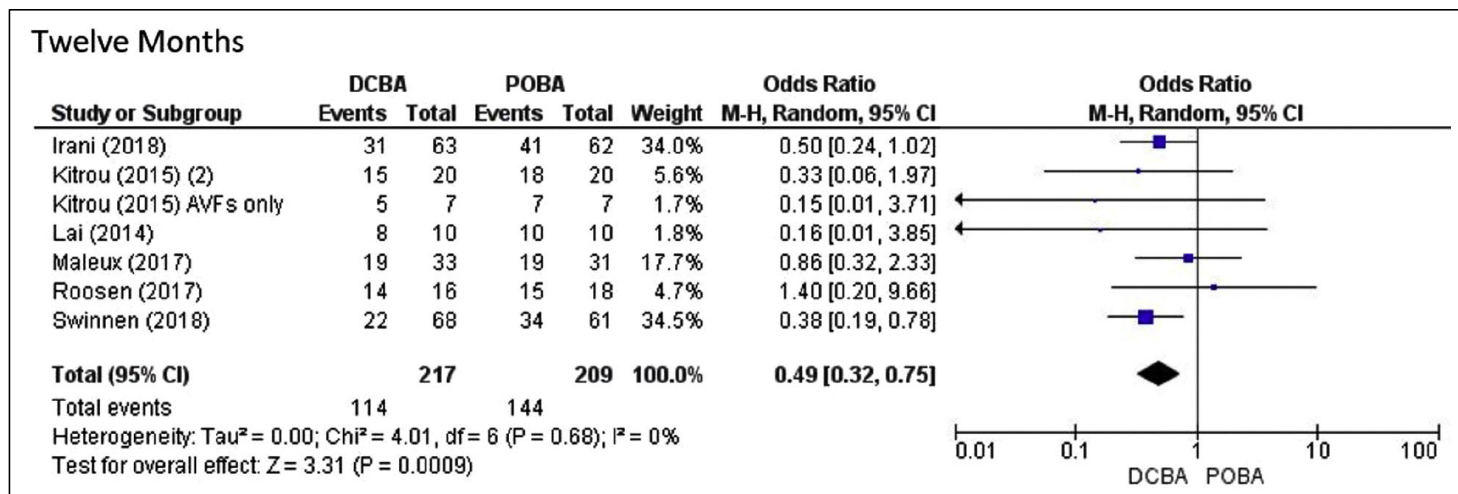
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- **Placement of a DEB coated with a lipophilic anti-proliferative agent over the site of angioplasty injury**
- **Result in high local levels of anti-proliferative agent**
- **Prevent restenosis due to neointimal hyperplasia**



# What's the data for DEBs in dialysis access?

- Large number of small usually non randomized studies using DEB
  - *AVF stenosis*
  - *In-stent restenosis*
  - *Central vein stenosis*



1yr data for RCTs in AVFs shows an OR of 0.49

Kennedy et al. JVIR 2019

# RCT of a paclitaxel DEB

## Drug Coated Balloon Angioplasty in Failing AV Fistulas A Randomized Controlled Trial

Scott O. Trerotola,<sup>1</sup> Jeffrey Lawson,<sup>2,3</sup> Prabir Roy-Chaudhury,<sup>4</sup> and Theodore F. Saad,<sup>5</sup> for the Lutonix AV Clinical Trial Investigators



BD

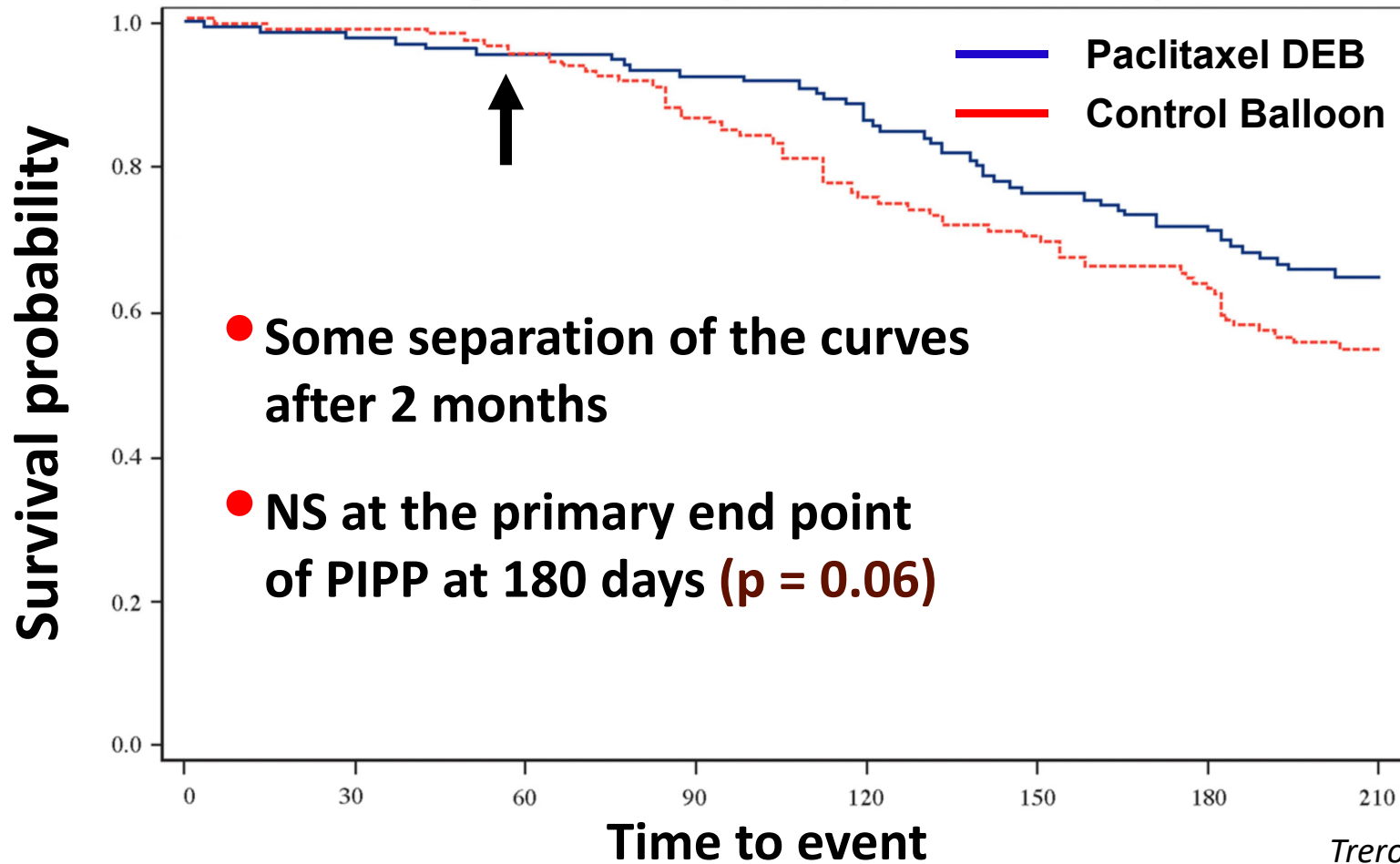
BAIRD

has joined BD

- Multi-center RCT
- Dysfunctional AVFs
- 285 patients in 23 centers
- Conventional pre-angioplasty
- < 30% residual stenosis
- Randomized 1:1 to DEB/Control balloon
- Primary efficacy end point was post intervention primary patency at 6 months
- Followed for 24 months
- Efficacy and Safety data at 24 months

Trerotola et al. CJASN 2018

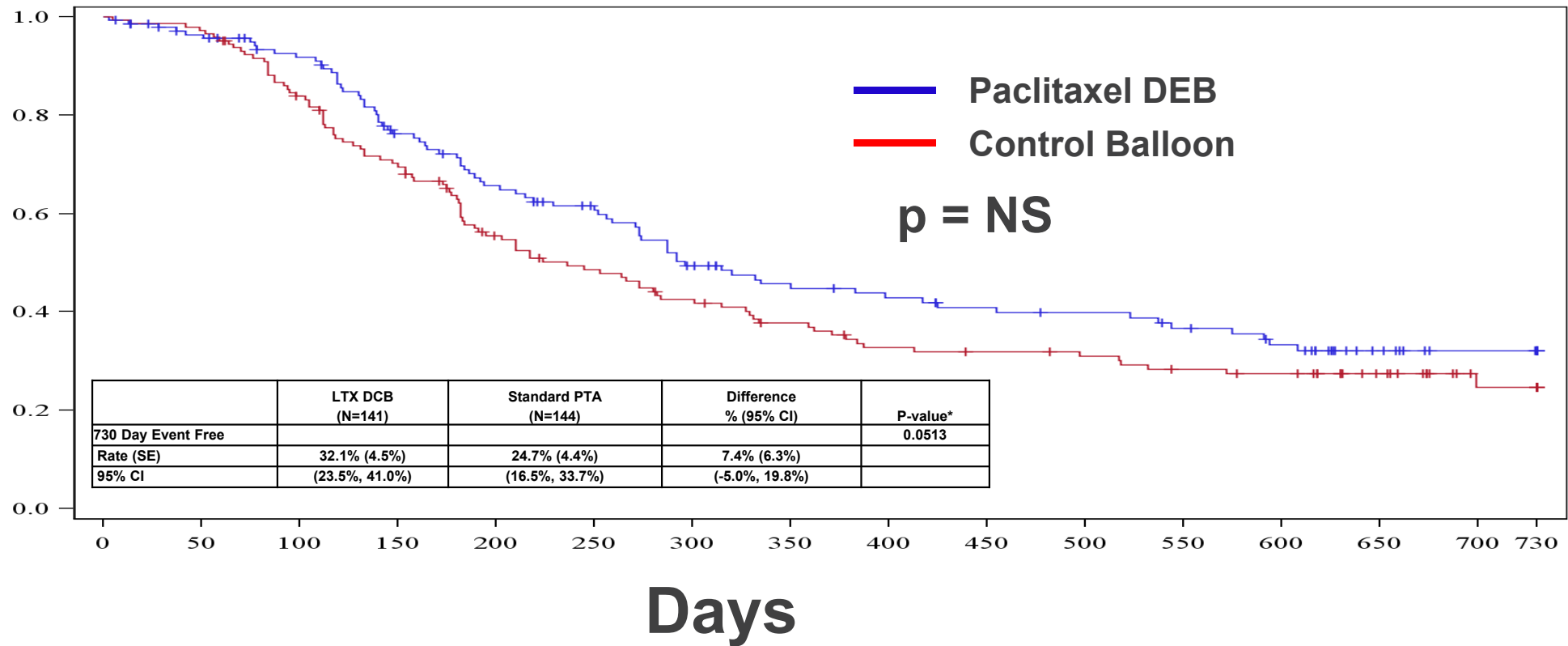
# Efficacy of DEB (Paclitaxel)



Trerotola et al. CJASN 2018

# 24 month target lesion primary patency

Survival Probability



Data shown are interim, site reported and subject to change

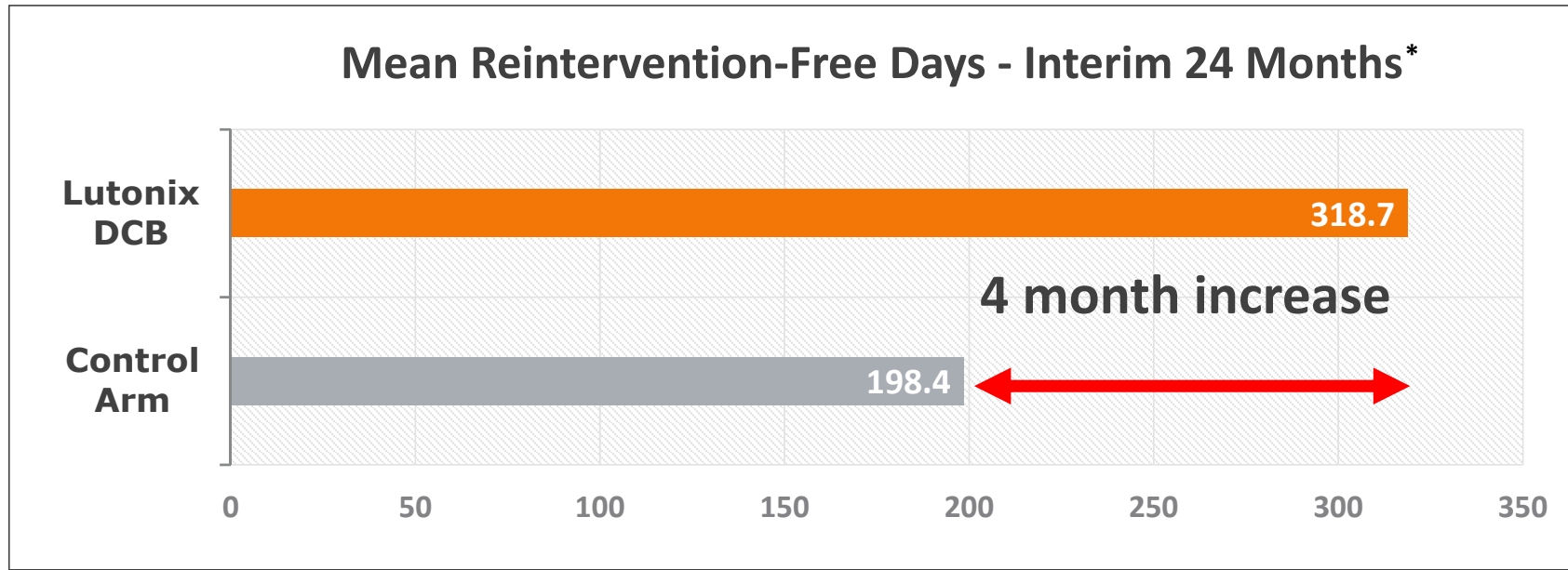
# DEB needed fewer interventions to maintain patency

## 31.3% Fewer interventions to maintain TLP at 6 months

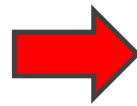
|                                    | LTX DCB<br>(n=141) | Standard<br>PTA<br>(n=144) | P-value* | % Fewer<br>Interventions<br>than PTA |
|------------------------------------|--------------------|----------------------------|----------|--------------------------------------|
| Number of interventions, 6 Months  | 44                 | 64                         | 0.034    | 31.3% Fewer                          |
| Number of interventions, 9 Months  | 76                 | 103                        | 0.023    | 26.2% Fewer                          |
| Number of interventions, 12 Months | 114                | 138                        | 0.086    | 17.4% Fewer                          |
| Number of interventions, 18 Months | 161                | 185                        | 0.106    | 13.0% Fewer                          |
| Number of interventions, 24 Months | 195                | 211                        | 0.131    | 7.6% Fewer                           |

Data shown are interim, site reported and subject to change  
Patients may have required more than one intervention

# Increased time to intervention



**Decreased number of procedures  
Increased time to intervention**

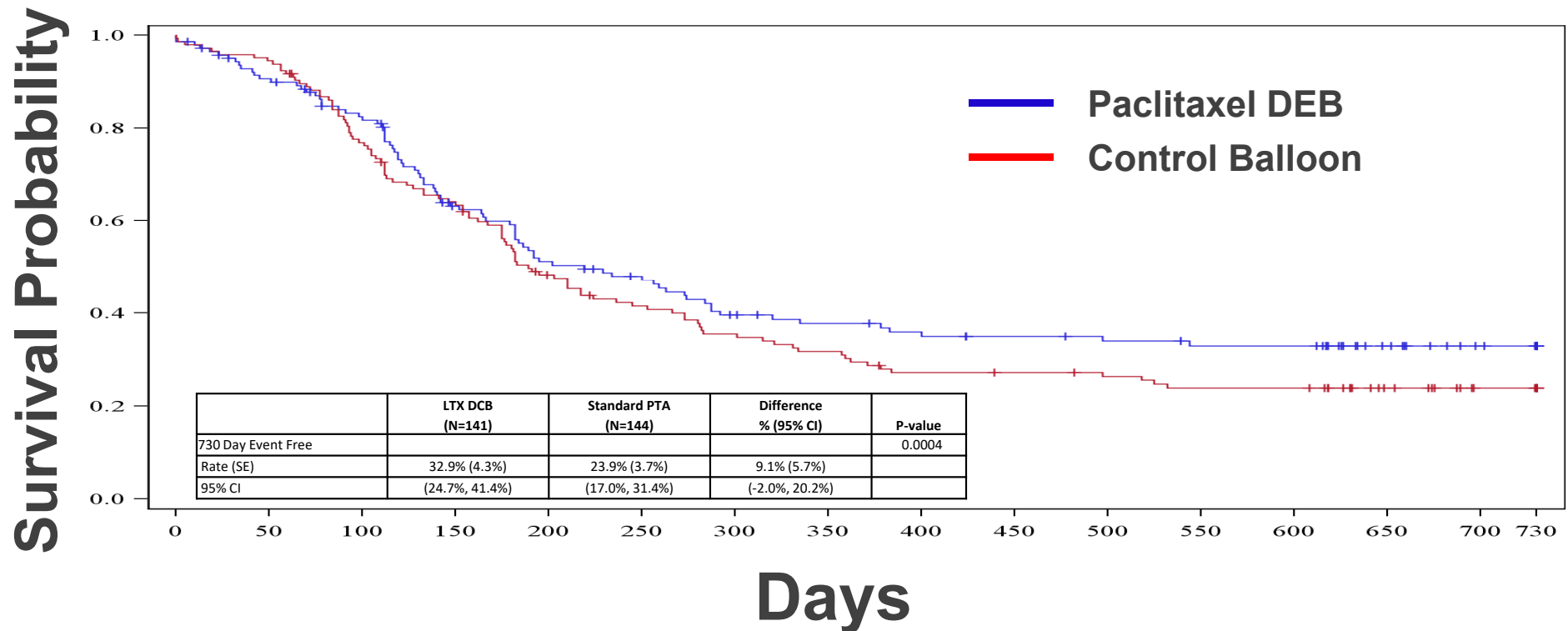


**Marked impact on quality of life  
50% 3 year survival on HD**

\*Data presented is interim, site reported, and subject to change

\* Control arm includes successful predilatation in addition to control balloon

# Safety: paclitaxel DEB non-inferior to PTA



Data shown are interim, site reported and subject to change

Primary Safety Endpoint- 30 Days Freedom from any serious adverse event(s) involving the AV access circuit

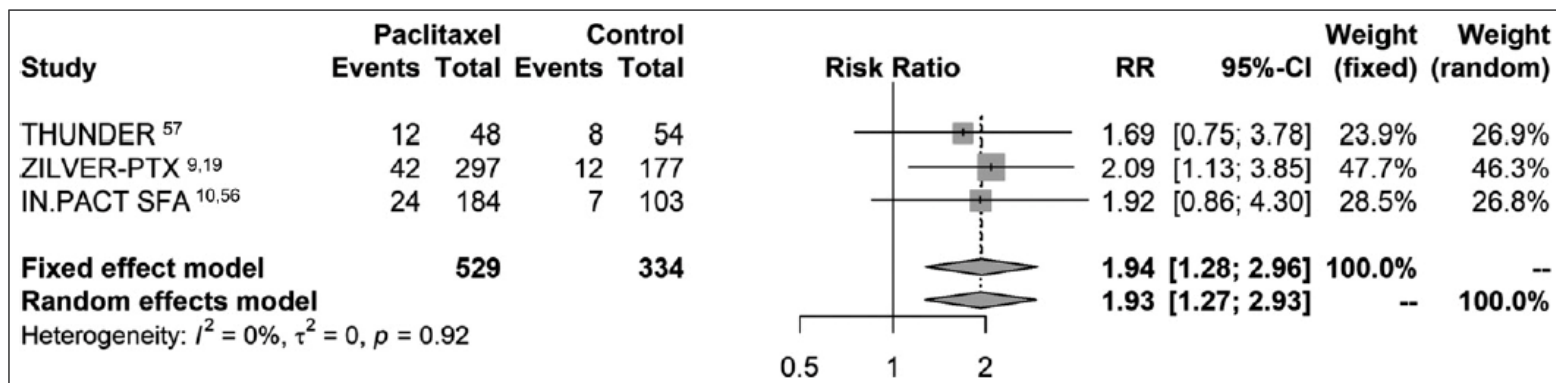
# Safety: paclitaxel DEB increases mortality in PVD

## SYSTEMATIC REVIEW AND META-ANALYSIS



### Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Konstantinos Katsanos, MD, PhD, MSc, EBIR; Stavros Spiliopoulos, MD, PhD; Panagiotis Kitrou, MD, PhD; Miltiadis Krokidis, MD, PhD; Dimitrios Karnabatidis, MD, PhD



Katsanos et al. JAMA 2018

## **Safety: paclitaxel DEB increases mortality**

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**Treatment of Peripheral Arterial Disease with  
Paclitaxel-Coated Balloons and Paclitaxel-  
Eluting Stents Potentially Associated with  
Increased Mortality - Letter to Health Care  
Providers**

# Safety: paclitaxel DEB does not increase mortality

## Journal of the American College of Cardiology

January 2019

DOI: 10.1016/j.jacc.2019.01.013

Just Accepted

 PDF Article

### Mortality Not Correlated with Paclitaxel Exposure: An Independent Patient-level Meta-Analysis

Peter A. Schneider, John R. Laird, Gheorghe Doros, Qi Gao, Gary Ansel, Marianne Brodmann, Antonio Micari, Mehdi H. Shishehbor, Gunnar Tepe and Thomas Zeller

**TABLE 2** Safety Outcomes Using Kaplan-Meier Estimates Through 5 Years

|                              | DCB<br>(n = 1,837 Patients) | 95% CI of DCB | PTA<br>(n = 143 Patients) | 95% CI of PTA | Hazard Ratio<br>(95% CI)* | p<br>Value* |
|------------------------------|-----------------------------|---------------|---------------------------|---------------|---------------------------|-------------|
| MAE composite†               | 35.21 (541)                 | (29.98–41.05) | 45.39 (59)                | (31.87–61.46) | 0.71 (0.51–0.98)          | 0.036       |
| Death (all-cause)            | 9.29 (140)                  | (6.45–13.30)  | 11.15 (12)                | (4.86–24.47)  | 1.32 (0.69–2.50)          | 0.399       |
| CD-TVR‡                      | 27.72 (407)                 | (22.67–33.62) | 37.17 (49)                | (23.81–54.82) | 0.60 (0.41–0.86)          | 0.005       |
| Major target limb amputation | 0.94 (12)                   | (0.27–3.25)   | 0.00 (0)                  | (0.00–0.00)   | —                         | —           |
| Thrombosis                   | 4.85 (79)                   | (2.82–8.28)   | 3.59 (5)                  | (0.70–17.30)  | 0.74 (0.25–2.16)          | 0.581       |
| CD-TLR§                      | 26.54 (389)                 | (21.58–32.39) | 32.56 (43)                | (19.59–50.94) | 0.61 (0.42–0.90)          | 0.012       |
| Any TVR                      | 28.41 (418)                 | (23.31–34.35) | 36.78 (49)                | (23.44–54.49) | 0.61 (0.43–0.87)          | 0.007       |
| Any TLR                      | 27.19 (399)                 | (22.16–33.09) | 34.50 (46)                | (21.33–52.58) | 0.59 (0.41–0.85)          | 0.005       |

Schneider et al. JACC 2019

# Summary of the dialysis access studies

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- **Number of small DEB studies which suggest benefit**
- **Large randomized pivotal study which did not meet the efficacy end point**
- **Documents a decrease in interventions and an increase in time to intervention**

# Precision Medicine!!

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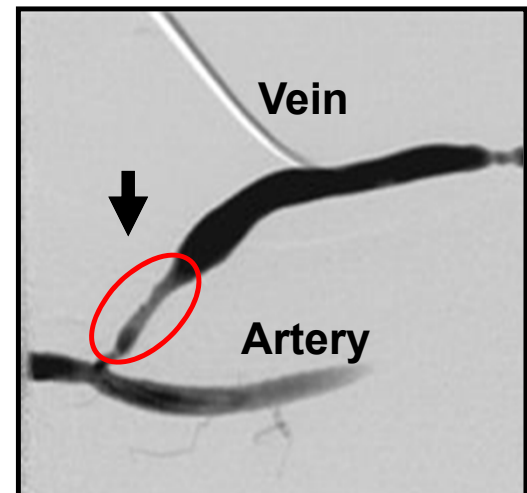
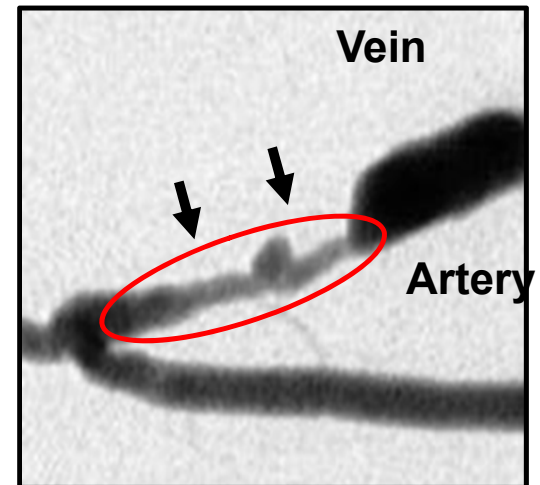


- Get away from the “one size fits all” construct
- Patients as unique individuals

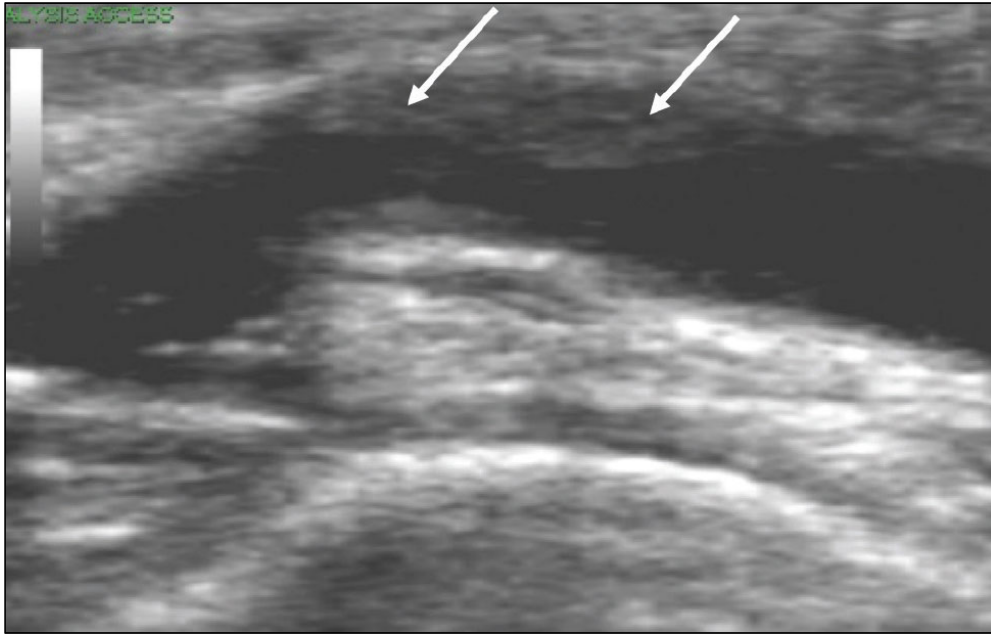
# This is just the beginning...



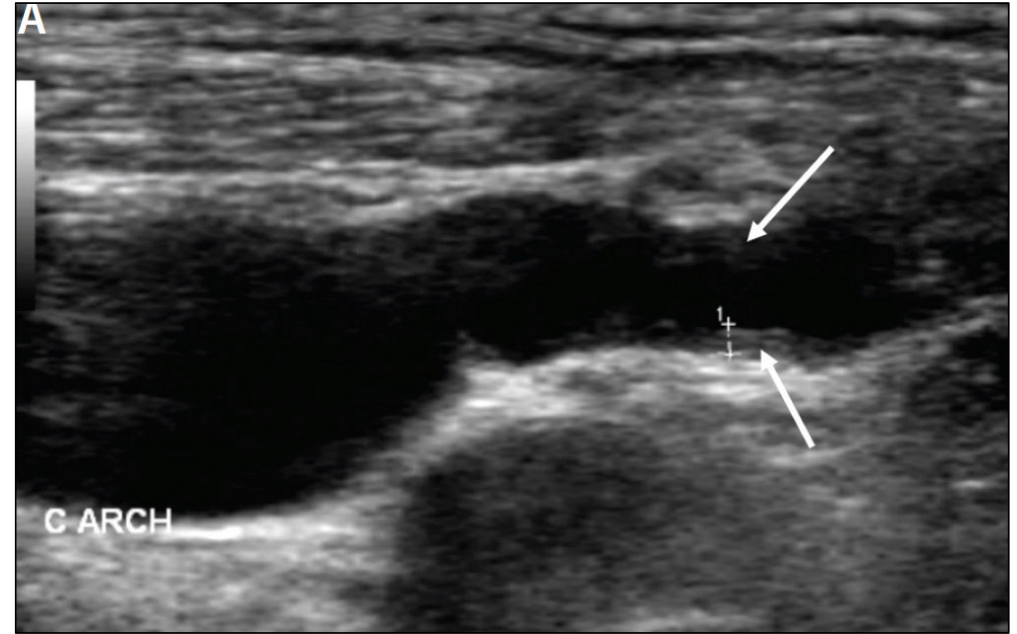
- Just as people are different
- Vascular access stenoses are different



# Vascular access stenoses are different



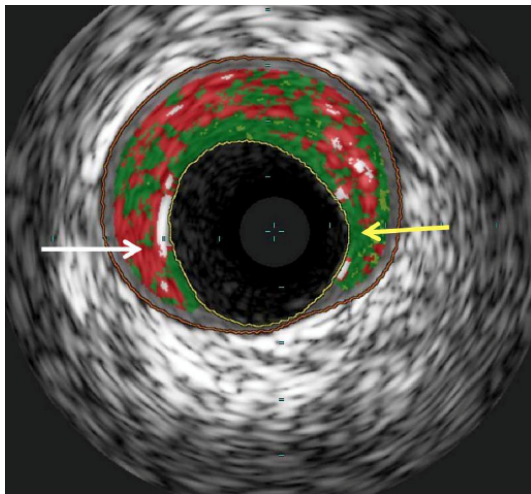
Stenosis due to neointimal hyperplasia = **DEB**



Stenosis due to vascular constriction = **DES**

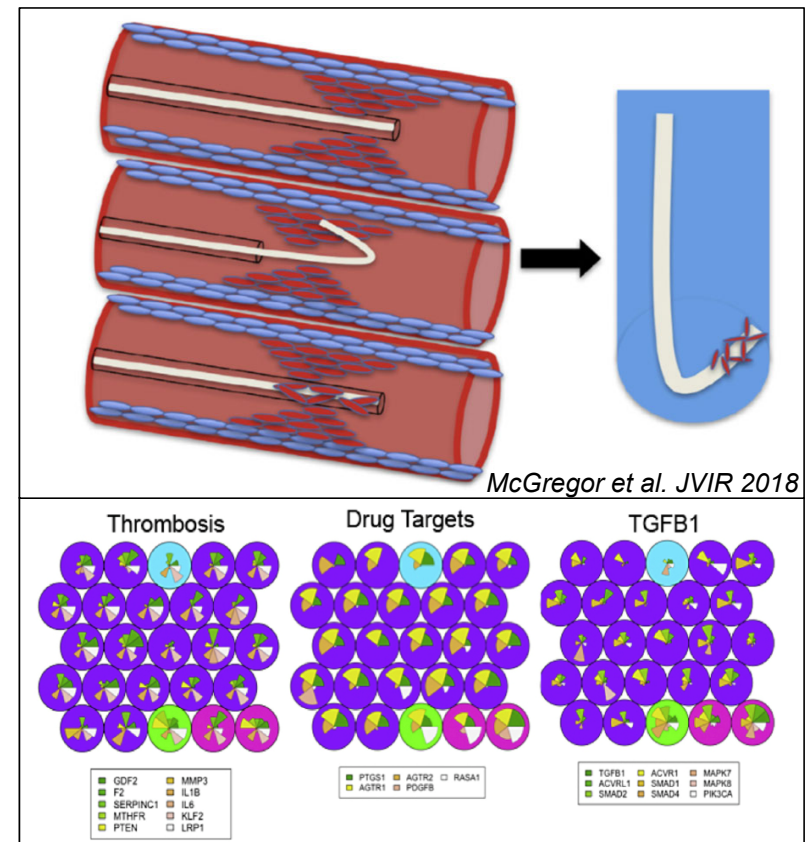
# Stratify both patients *and* their stenotic lesions!

## Advanced imaging (IVUS histology)



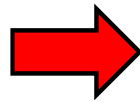
- Lesion A needs **DEB Z**
- Lesion B needs **DEB Y**
- Lesion C needs a new access
- Lesion D does **NOT** need a DEB

## Direct sampling and single cell RNA analysis



# A different FUTURE!

Precision  
Medicine  
Approach



Vascular  
Access Care



ADD VALUE  
to Vascular Access  
Care and take  
better care of our  
patients

