Drug-Eluting Balloons will Have an Important Role in Coronary and Peripheral Interventional Therapy!

Juan F. Granada, MD

Executive Director and Chief Scientific Officer
Skirball Center for Cardiovascular Research
Cardiovascular Research Foundation
Columbia University Medical Center, New York

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization's listed below.

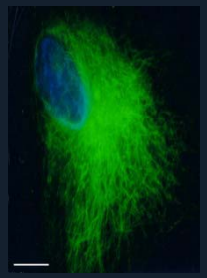
Affiliation/Financial Relationship	Company
• Grant/Research Support	• Abbott, BSCI, Medrad, Medtronic.
• Consulting Fees/Honoraria	• Medrad.
• Major Stock Shareholder/Equity	
• Royalty Income	
• Ownership/Founder	
• Intellectual Property Rights	
• Other Financial Benefit	

Drug Coated Balloon Technologies

A Viable Technological Concept?

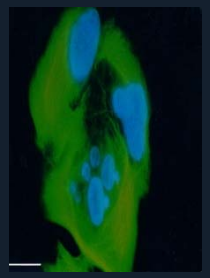
Control (hSMC)

(+) anti–ß-tubulin

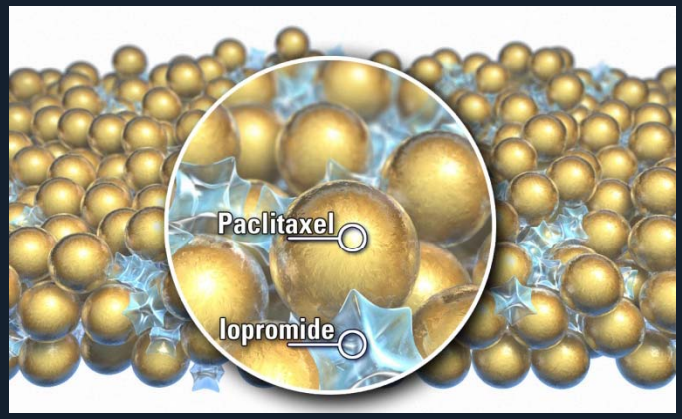


Paclitaxel (hSMC)

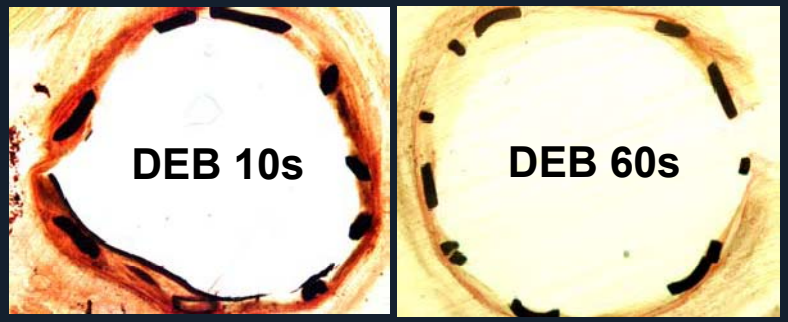
(+) anti–ß-tubulin



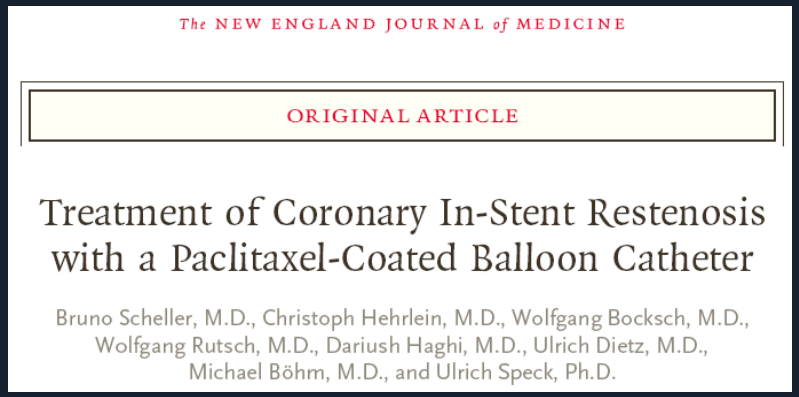
Axel DI. Circulation. 1997;96:636-645



Scheller J Am Coll Cardiol 2003



Cremers B. Thromb Haemost. 2009 Jan;101(1):201-6



The NEW ENGLAND JOURNAL of MEDICINE

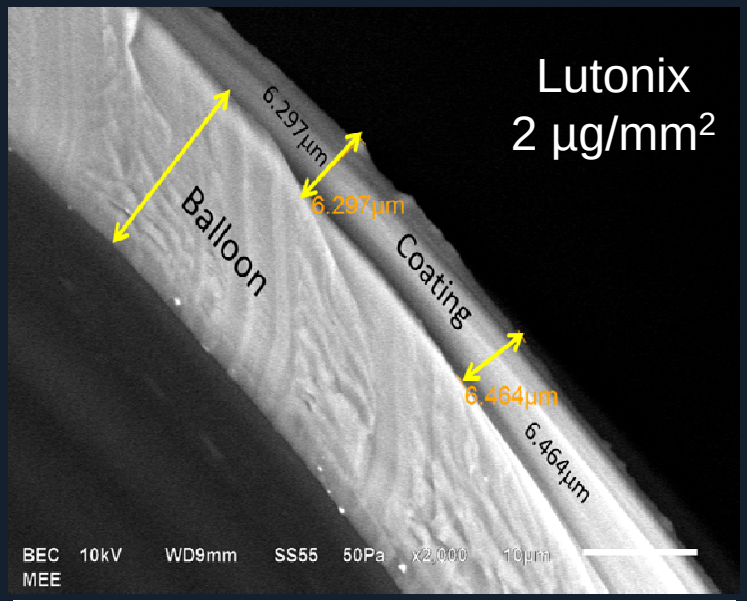
ORIGINAL ARTICLE

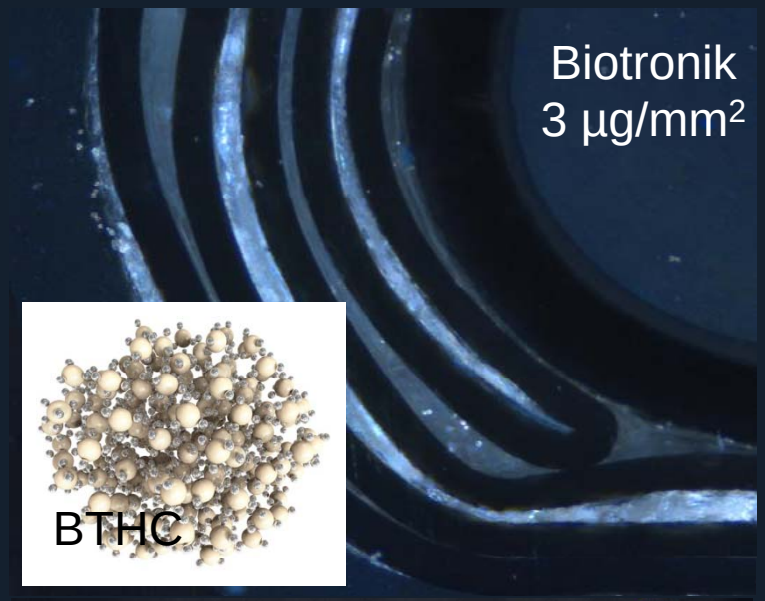
Treatment of Coronary In-Stent Restenosis with a Paclitaxel-Coated Balloon Catheter

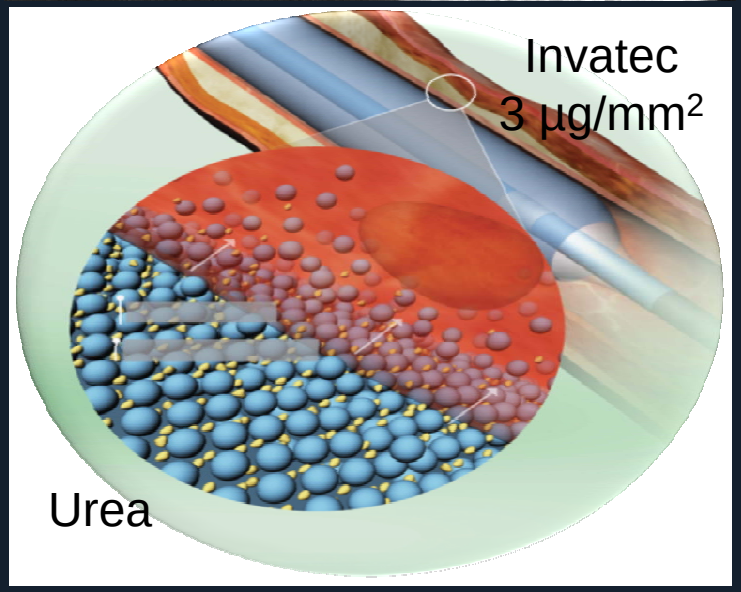
Bruno Scheller, M.D., Christoph Hehrlein, M.D., Wolfgang Bocksch, M.D., Wolfgang Rutsch, M.D., Dariush Haghi, M.D., Ulrich Dietz, M.D., Michael Böhm, M.D., and Ulrich Speck, Ph.D.

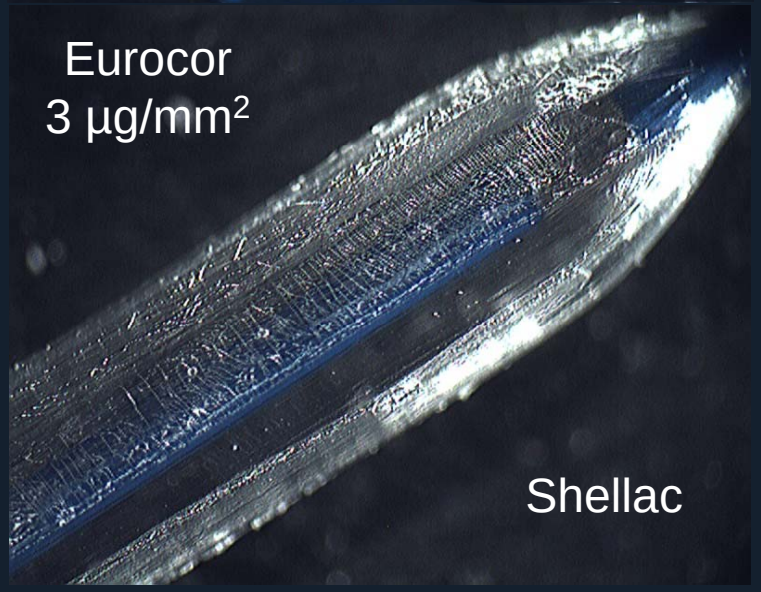
Scheller et al., N Engl J Med 2006;355: 2113

New DCB Programs Under Development



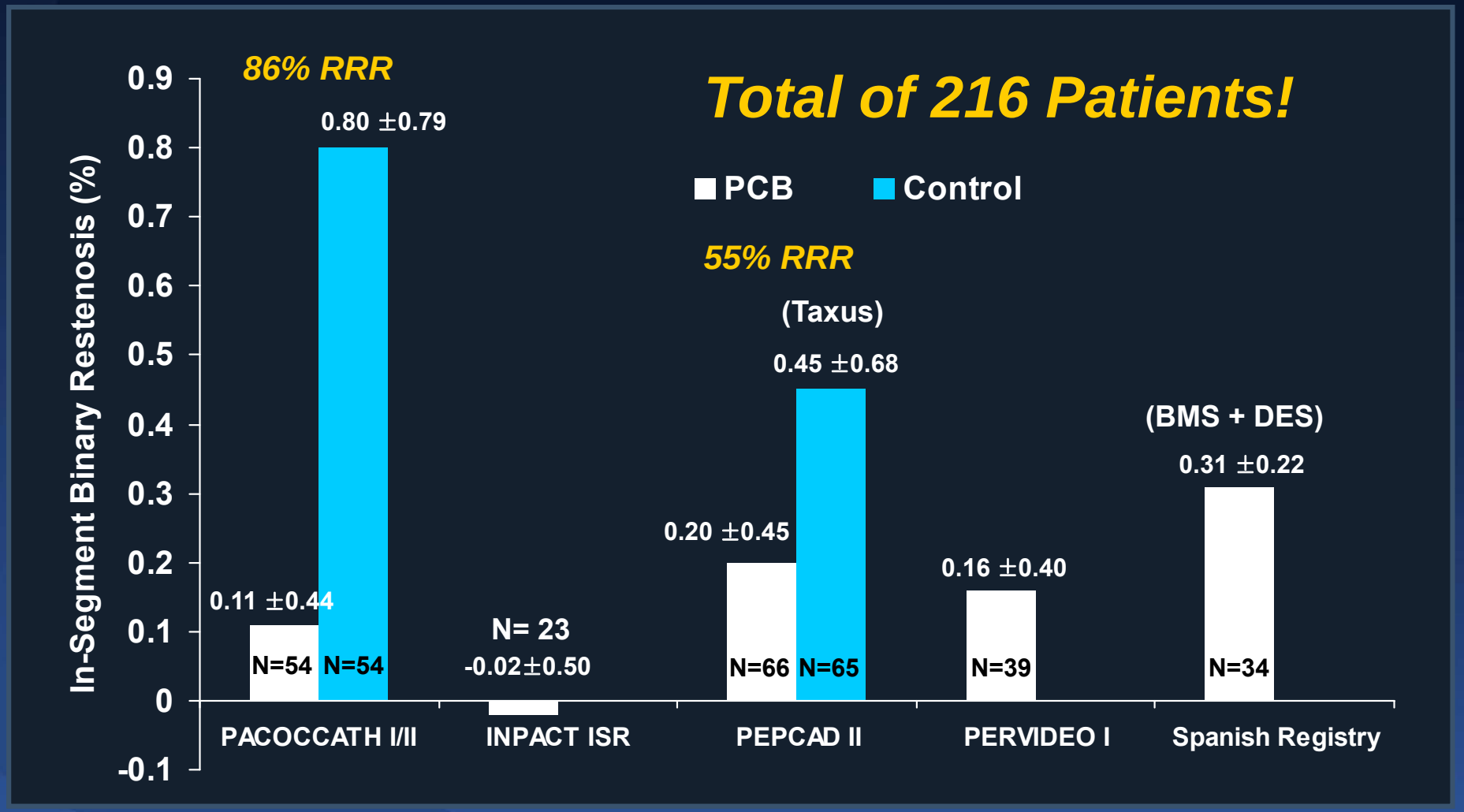






PCB for the Treatment of ISR

Angiographic Outcomes (Absence of Stent)



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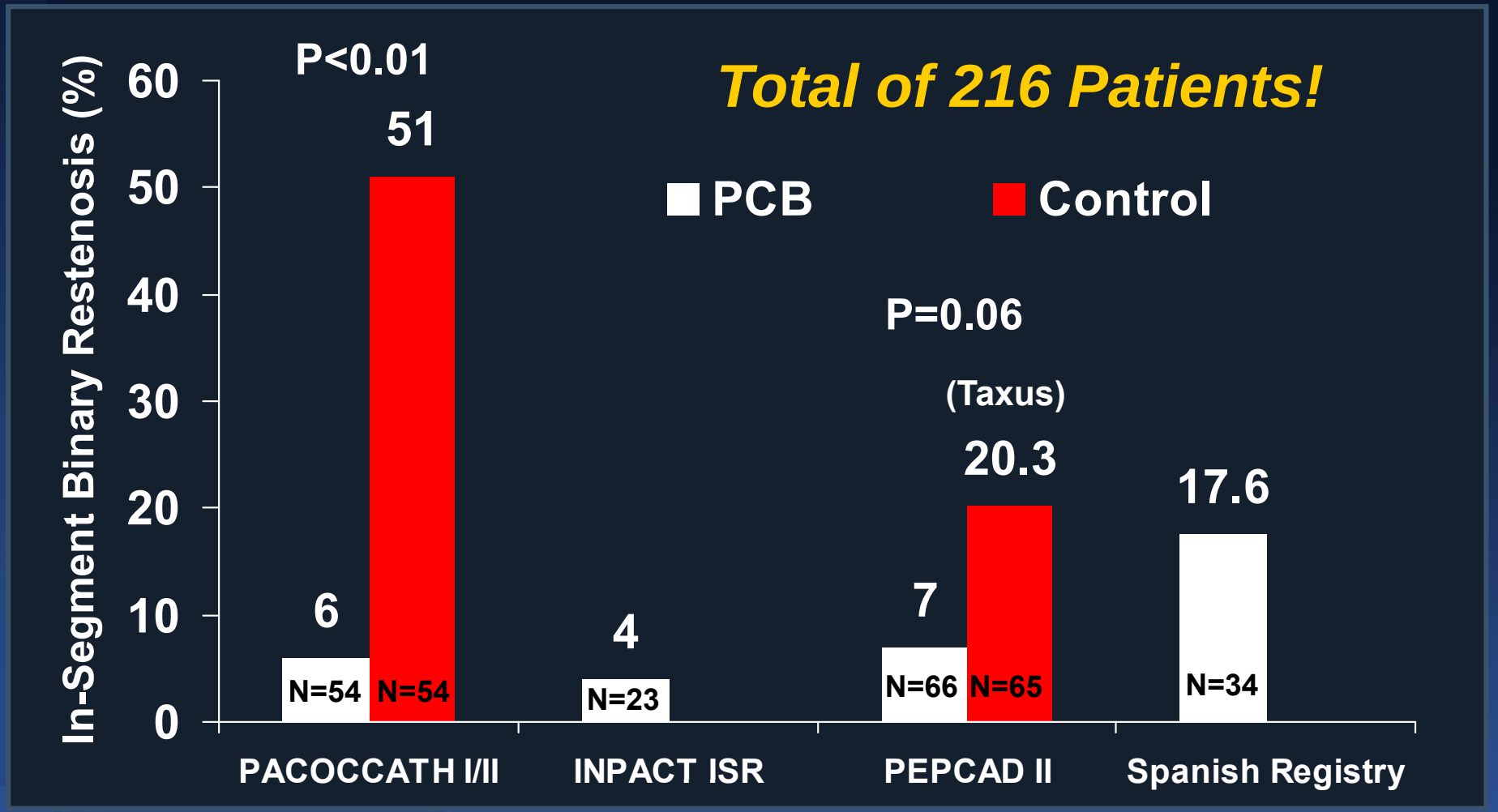

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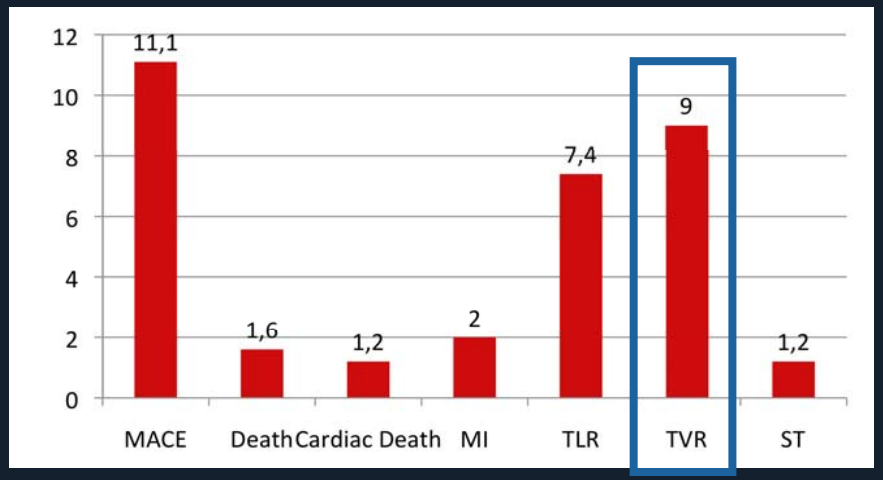
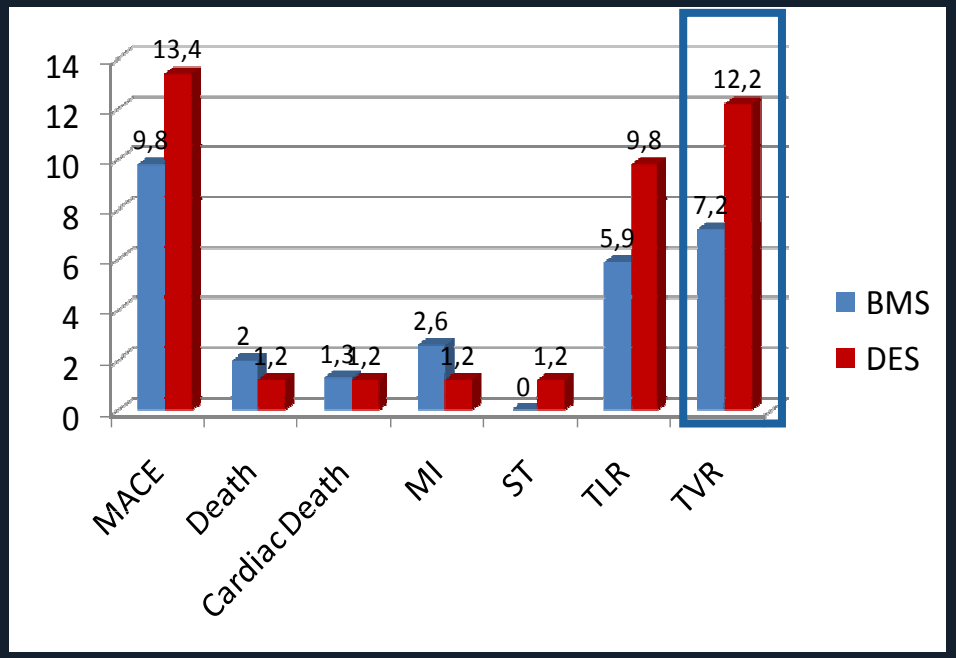
Clinical Outcomes Among 250 Patients Presenting with ISR (DES and BMS)

The Valentines Trial

Frequency of Stent Implantation 4.9%

- **DIOR II PCB Technology (3 µg/mm²)**
- **40.6% Diffuse ISR**
- **Length Covered by PCB 24±9.1 mm**





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Silber S, Presented at CRT 2011.

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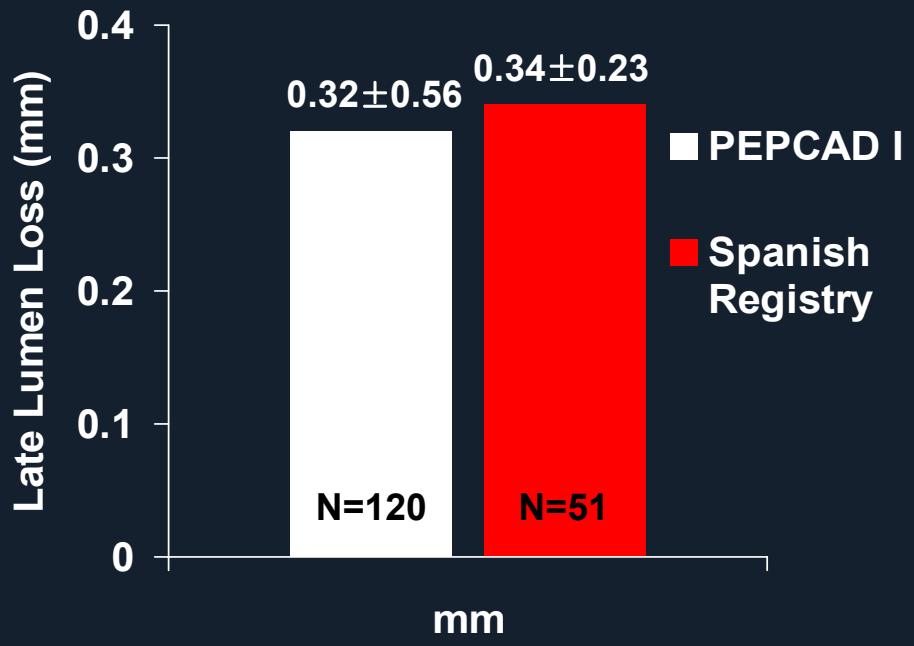
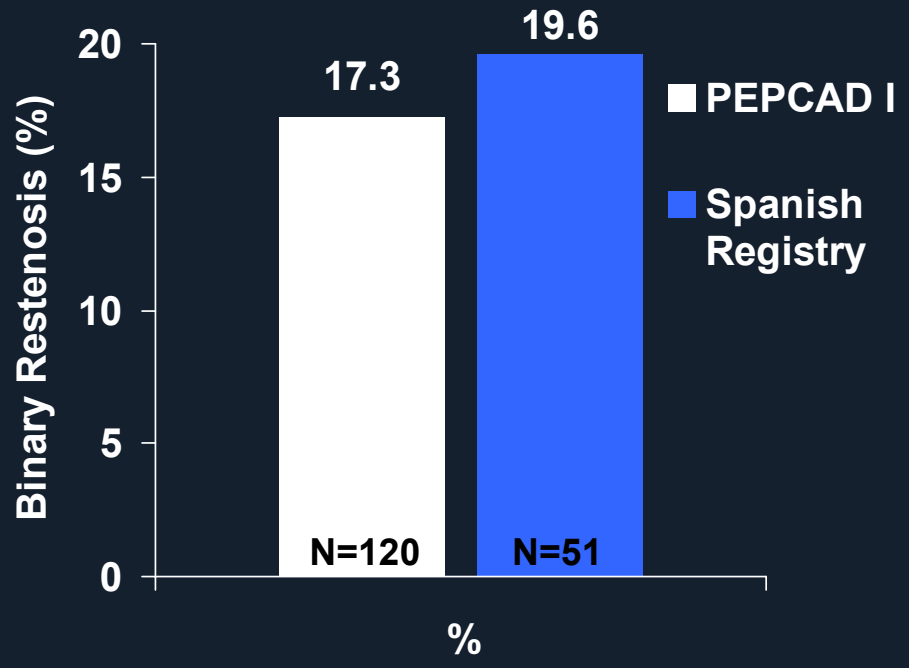
PCB for the Treatment of SVD

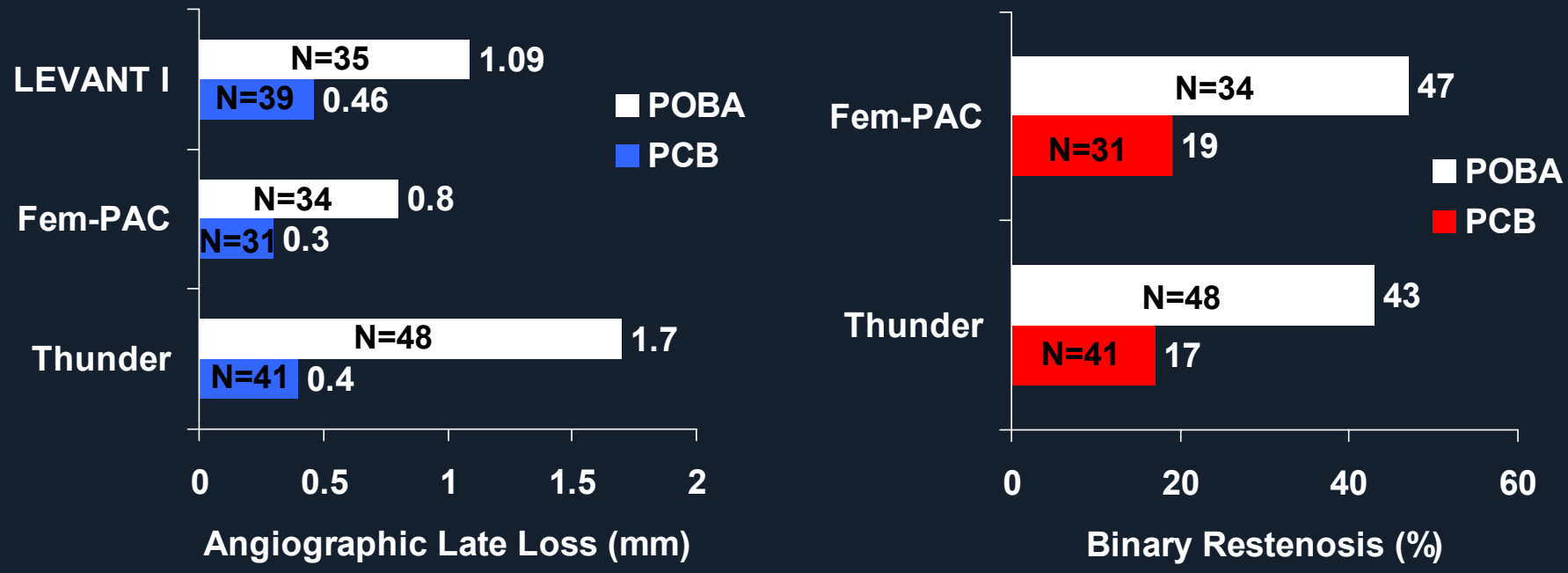
Angiographic Outcomes (Absence of Stent)

- **PEPCAD I:** De-novo lesions, RVD: 2.25 - 2.8 mm; SeQuent Please
- **Spanish Registry:** De-novo lesions, RVD: <2.5 mm; Dior I (87%)





PCB for the Treatment of De Novo SFA Disease (ITT= PTA Only)

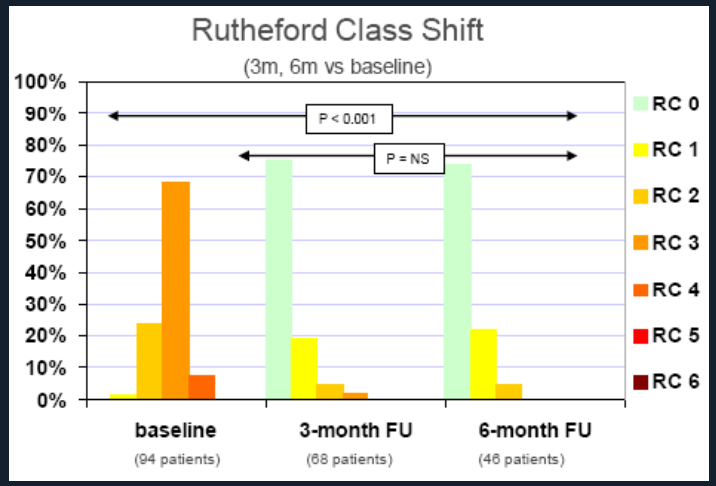


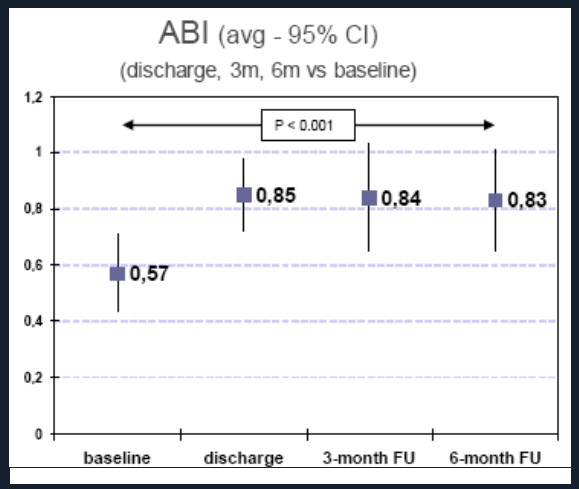
- **FAST Trial** (Luminexx, LL ~4.5 cms)
  - *Binary Restenosis by DU: PTA 36.6% versus Stent 23.8% (p=0.073)*
- **Absolute Trial** (LL ~13 cms)
  - *Binary Restenosis by DU: PTA 45% versus Stent 25% (p=0.06)*

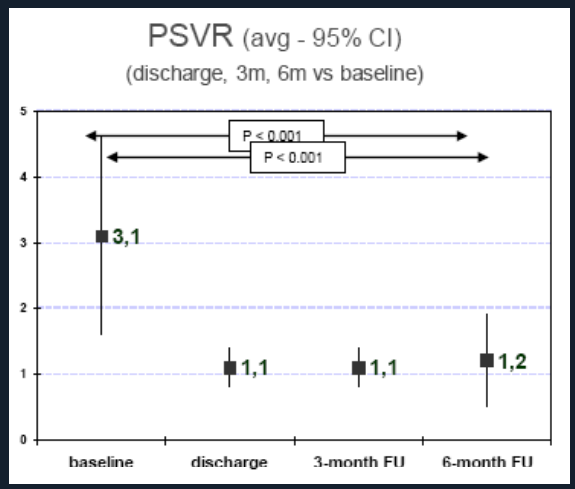
DEB SFA Italian Registry

De-Novo SFA Disease

- **Multicenter SFA Observational Registry**
- **94 patients / 103 lesions**
- **Lesion length 77.0 ± 38.6 mm**
- **Ruth Class 2: 23.4 %; 3: 68.1 %; 4: 7.4 %**
- **PTA alone: 86.4% / + Stent: 13.6%**







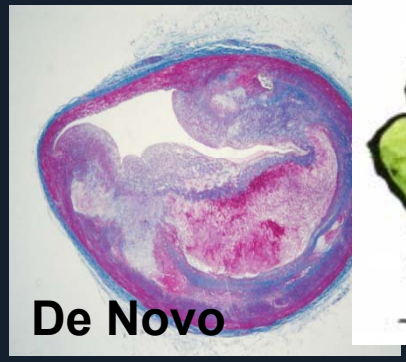
Vascular Healing Following PCB Use

De Novo vs. ISR Applications

Can we extrapolate the data gat
development of DCB technolog

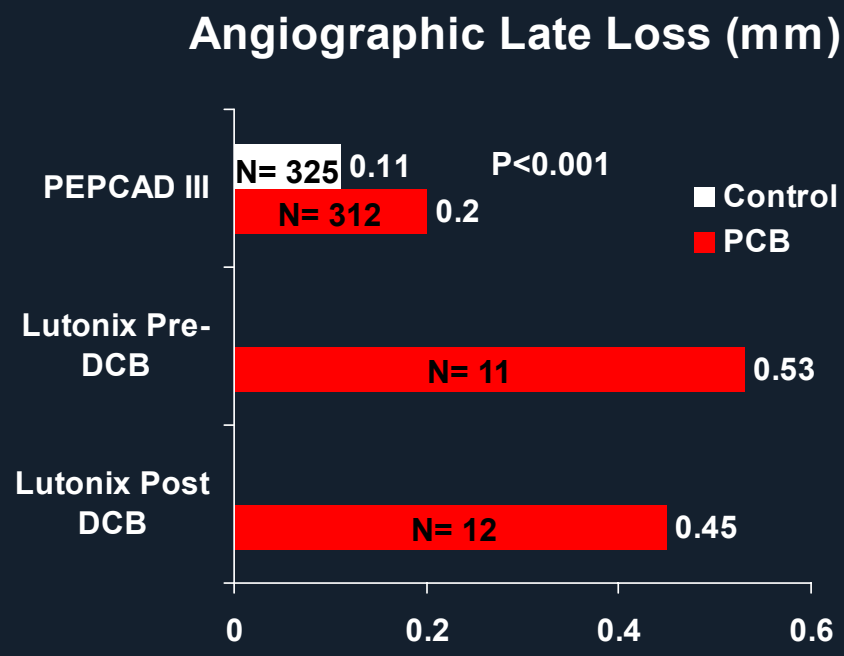
In-Stent Restenosis

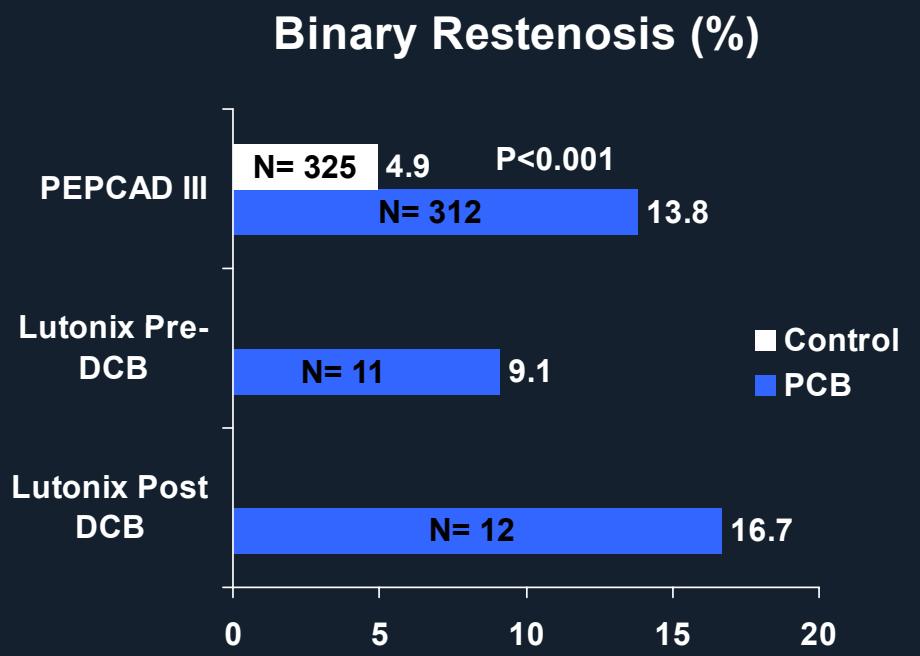
- Ballooning inside of a stent.
- Quiescent disease state.
- Mature neointima.
- Smaller degree of injury induc
- No additional material left behi



Angiographic Outcomes: PCB Trials for "De Novo" Applications

- **PEPCAD III:** BMS Crimped on PCB (3 µg/mm^2) versus Cypher Stent
- **Lutonix** De Novo Registry: Pre or Post Dilatation Using PCB (2 µg/mm^2)





Synergistic Use of PCB and BMS

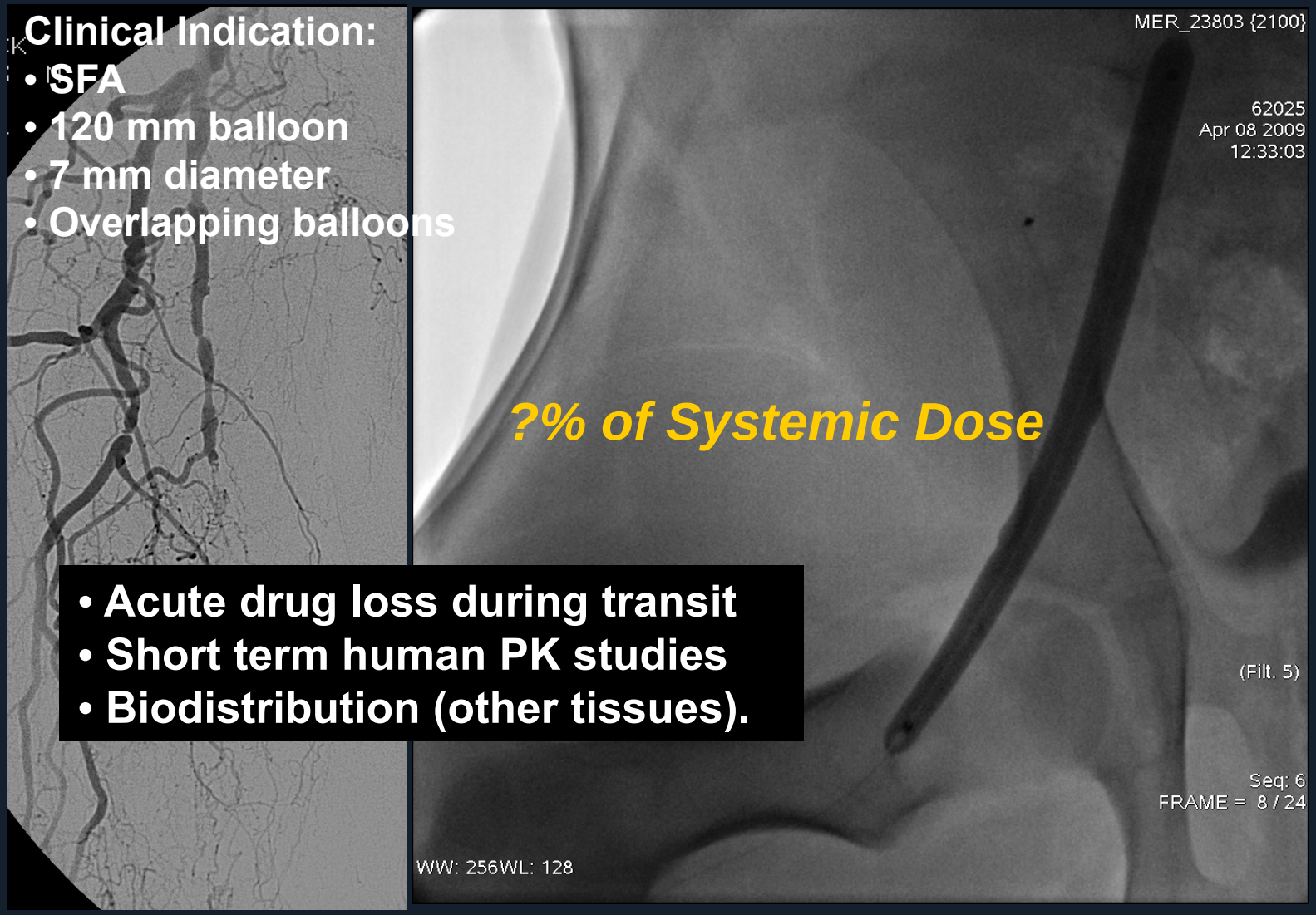
Lessons Learned From the PEPCAD Trials

- **PEPCAD I (SVD):**
  - Binary Restenosis: DEB Only (5.5%) *versus* DEB+BMS (41.3%)
  - Stent Thrombosis: DEB Only (0%) versus DEB+BMS (1.7%)
- **PEPCAD III (De Novo + BMS):**
  - Definite Stent Thrombosis: DEB+BMS (1.3%) *versus* Cypher (0.3%)
- **PEPCAD V (28 Patients Bifurcation Study)**
  - Late Stent Thrombosis Rate (7.1%)

Now, Where Are We in 2011?

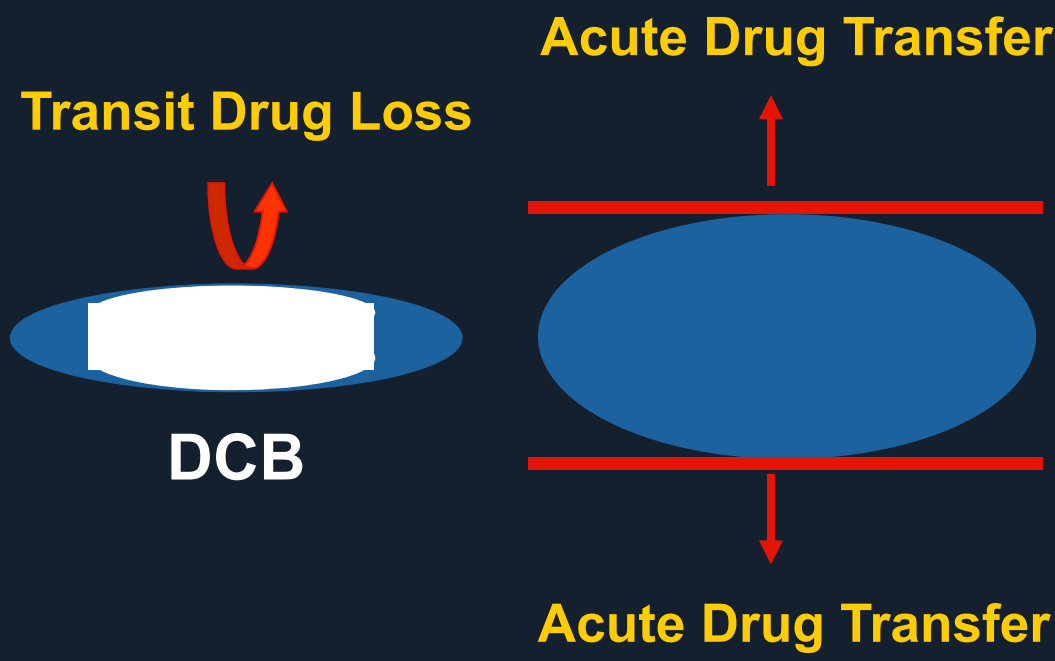
What do DCB need to prove to become mainstream therapy?

(1) Systemic Release of Paclitaxel



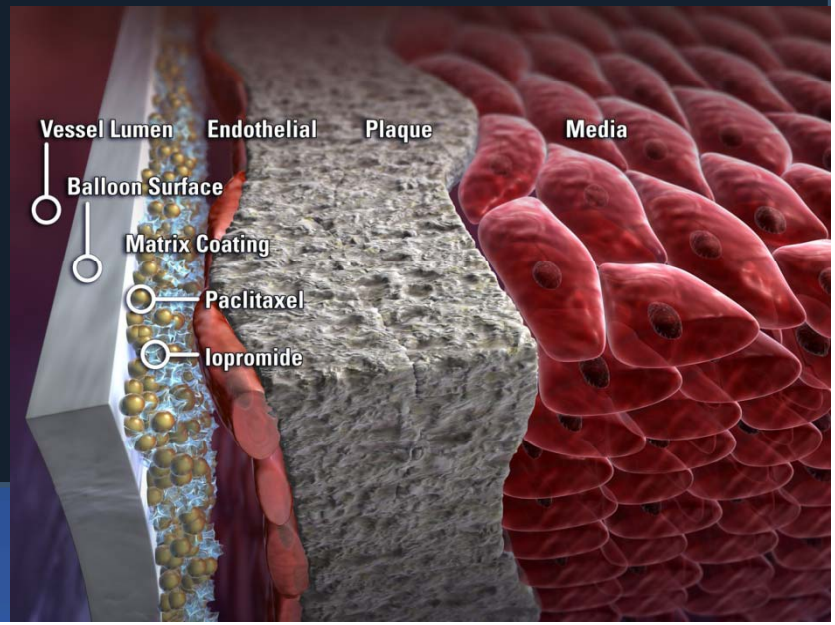
(2) Mechanism of Action of DCB

Sustained Tissue Retention of Paclitaxel



TISSUE LEVEL ENDPOINTS

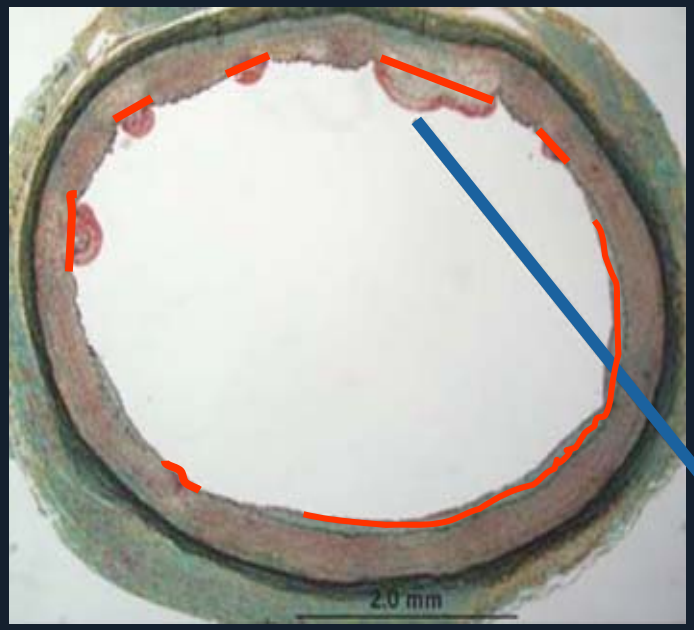
- ***Below toxic threshold***
- ***Homogeneous distribution***
- ***Sustained therapeutic levels***



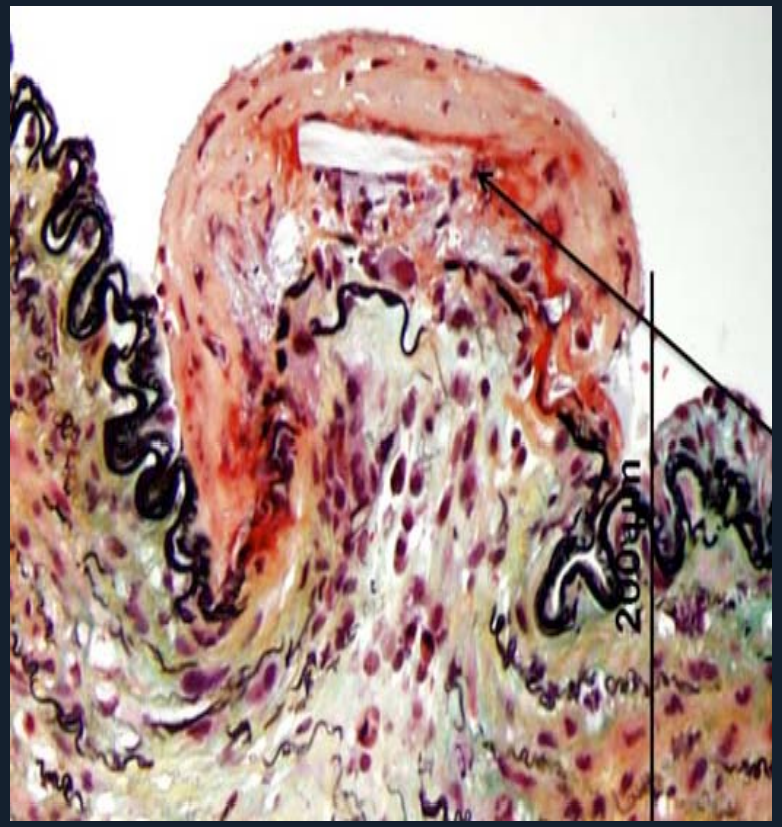
Drug Transfer Technology

Deposition of a Drug Delivery Biofilm

Proposed Mechanism of Action

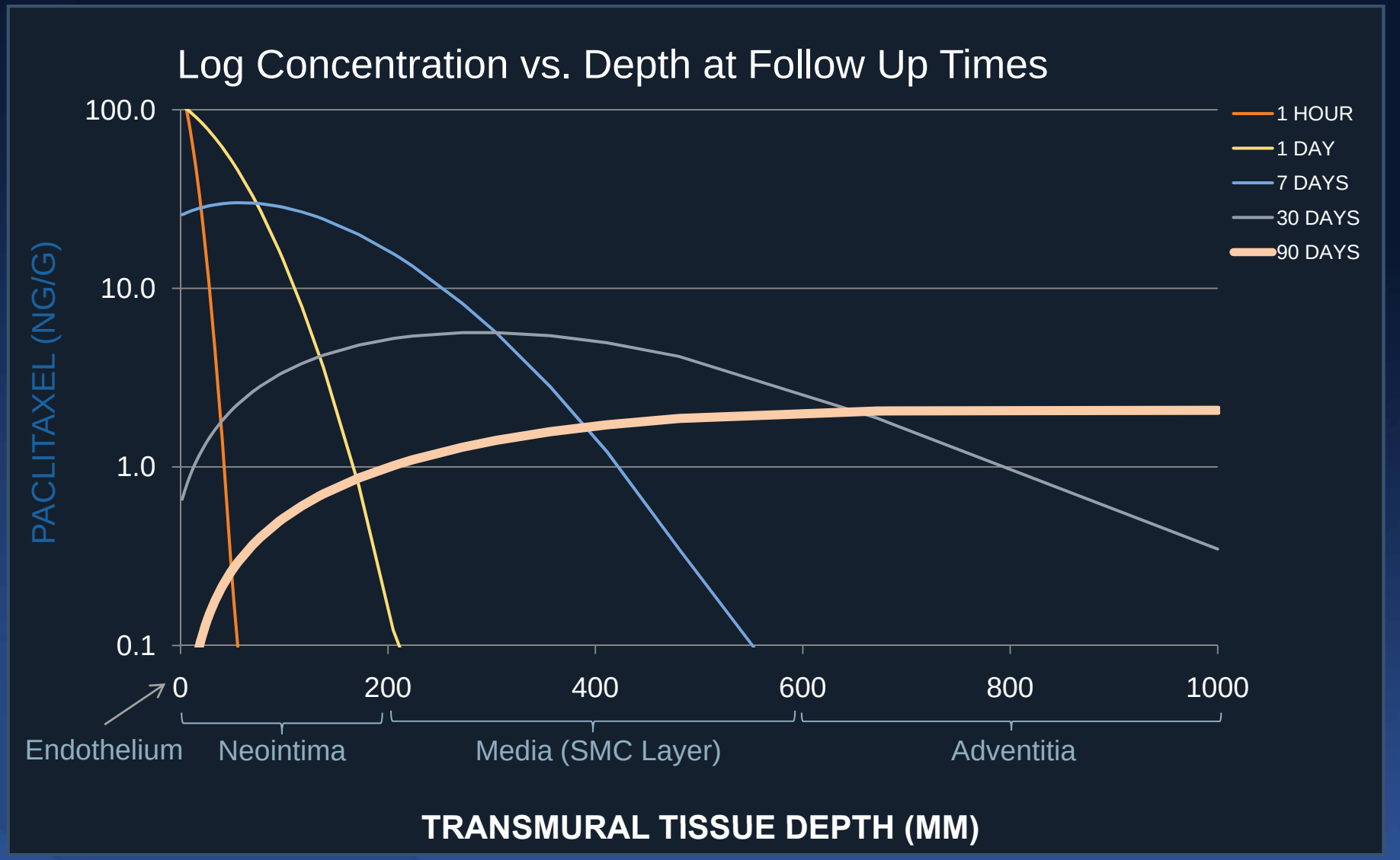


Cotavance™ DCB Technology



Localized endovascular retention of paclitaxel particles serving as a reservoir for sustained drug delivery

Concentration vs. Depth at 90 Days



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Slide courtesy of Lutonix Inc

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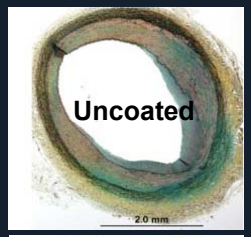
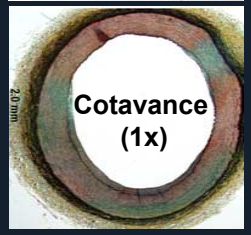
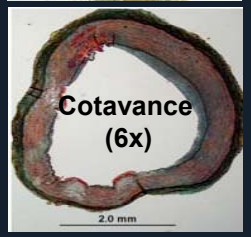
(3) Local Tissue Effects (Safety)

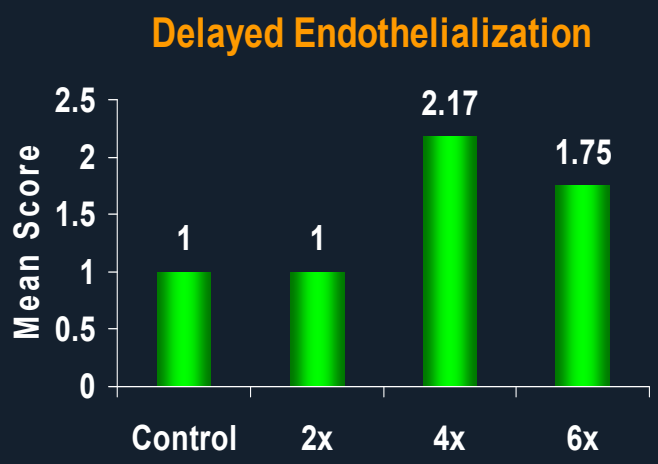
Vascular Healing According to Dose

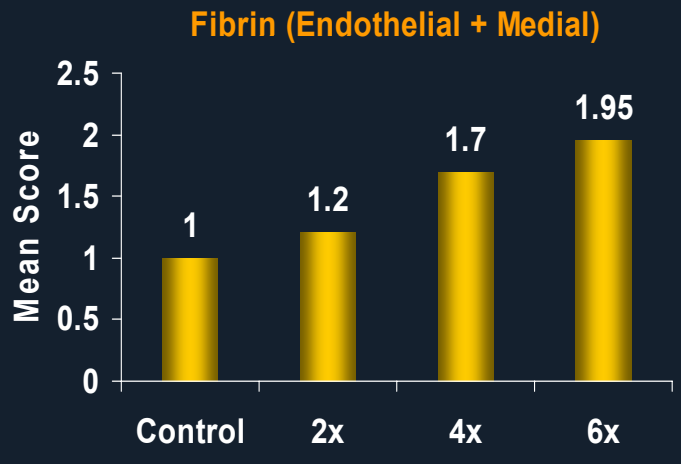
1= Minimal
2= Slight
3= Moderate
4= Marked
5= Massive

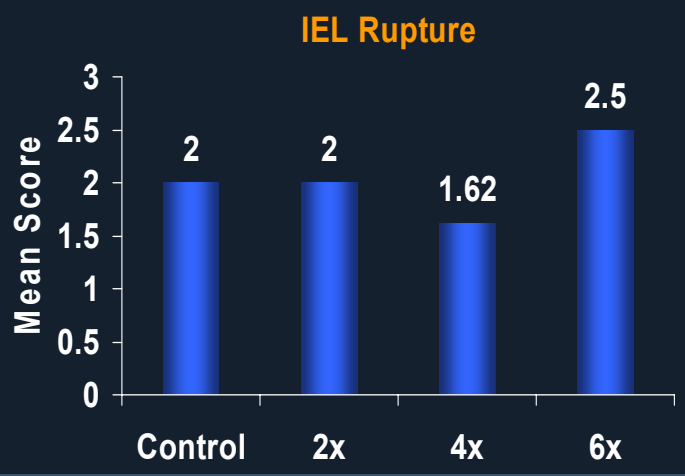


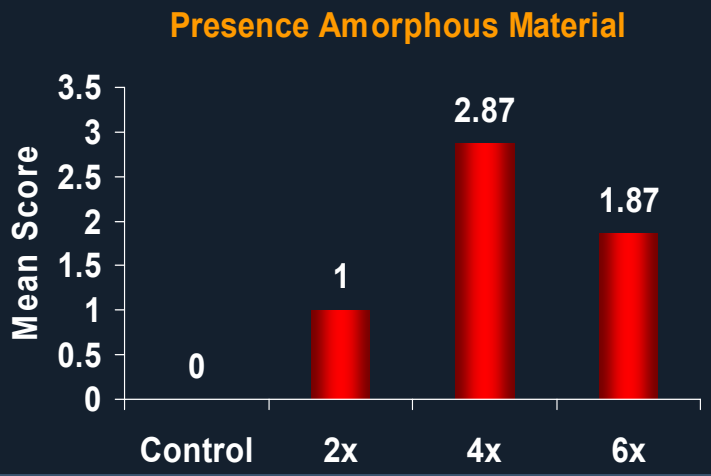












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Histology picture obtained from CVPath

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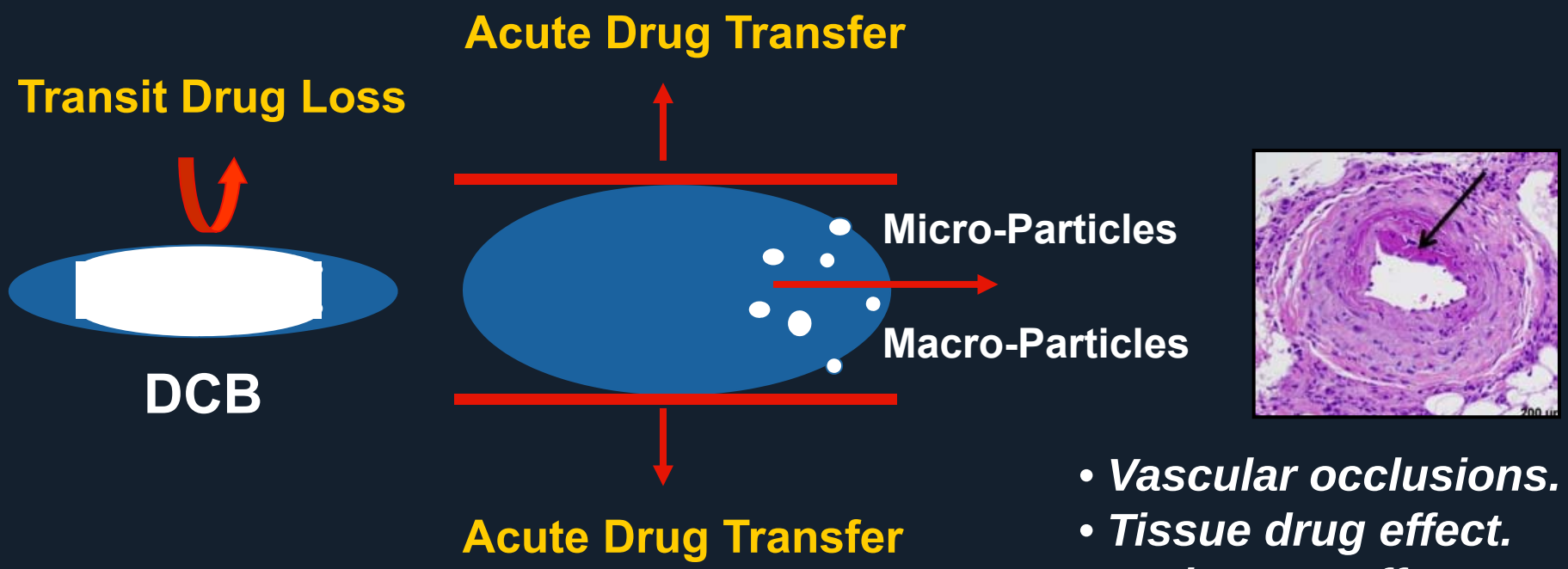
(4) Particulate Coating Formation

Local Tissue Effects



- *Vascular occlusions.*
- *Tissue drug effect.*
- *End-organ effects.*

Conclusions: PCB Technologies

- PCB technologies continue to show efficacy in reducing restenosis in specific clinical scenarios (i.e., ISR).
- However, the synergistic use of stents must be carefully studied in a prospective manner in a larger population.
- Newer generations of PCB appear to offer improved coating platforms providing more precise drug transfer to the tissue.
- Preliminary data suggests that specific features of the coating regulates the long-term transfer and retention of the drug.
- The real clinical effect of micro-particle drug release into distal tissues needs to be carefully evaluated against the potential therapeutic benefit of this technology.
- If proper technical balance is achieved (acute transfer-tissue levels-particulate formation), PCB have the potential to become a strong competitor in the PCI arena.