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# FAME 3 Trial:

## *FFR-Guided PCI vs. CABG*

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Associate Professor of Medicine

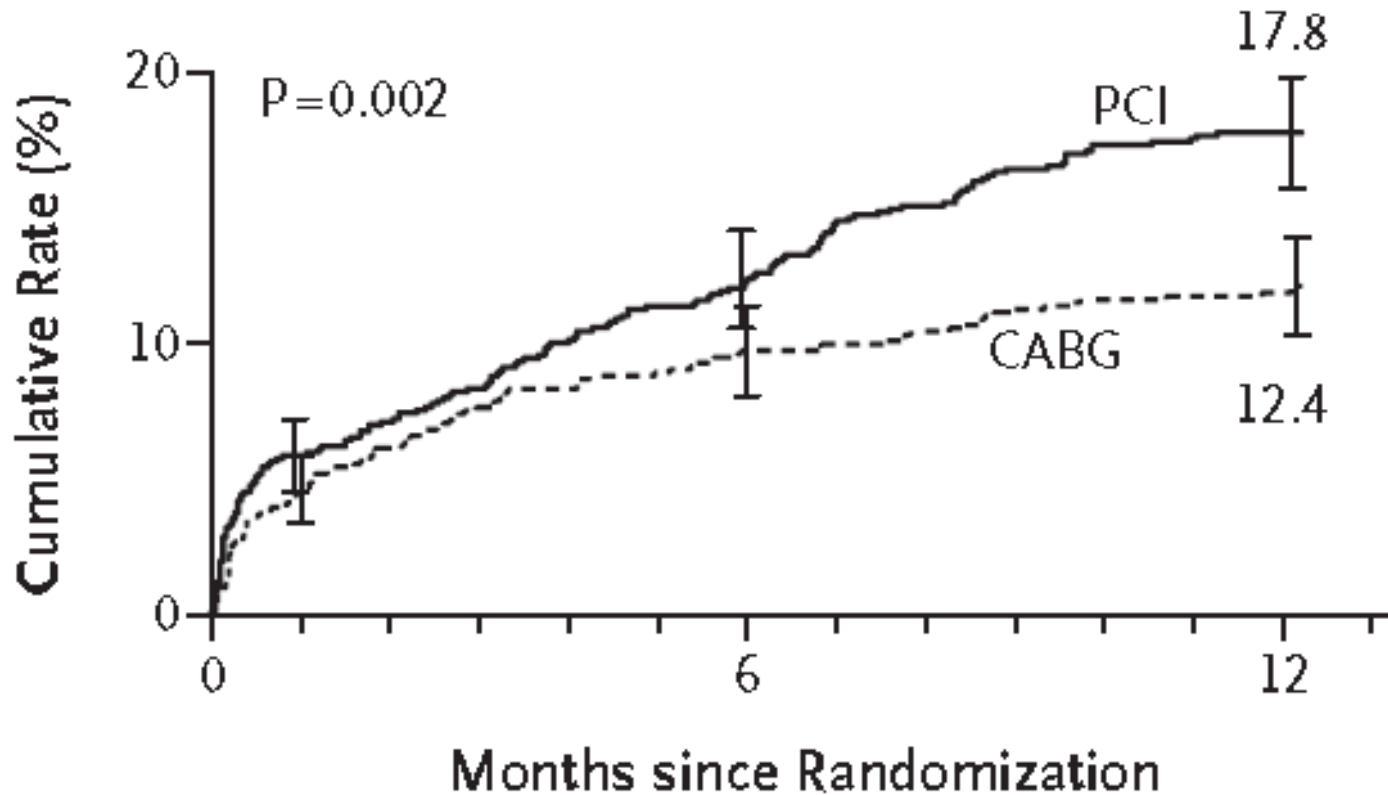
Director, Interventional Cardiology

Stanford University Medical Center



# Background:

## *SYNTAX Trial One Year MACCE Results*



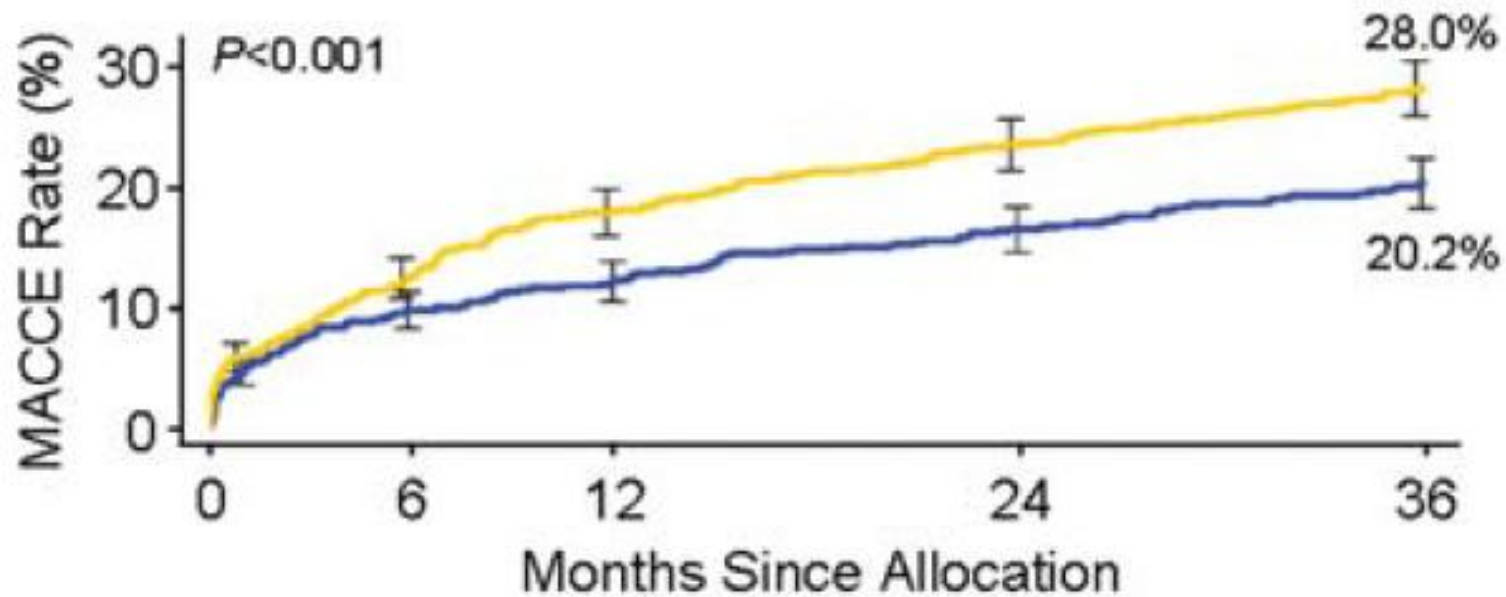
# Background:

- At one year in the SYNTAX trial:
  - Cardiac death was higher in PCI arm vs. CABG (3.7 vs. 2.1%,  $p=0.05$ )
  - MI was higher in PCI arm vs. CABG (4.8 vs. 3.3%,  $p=0.11$ )
  - Stroke was higher in CABG arm vs. PCI (2.2 vs. 0.6%,  $p=0.003$ )
  - Repeat revascularization was higher with PCI (13.5 vs. 5.9%,  $p<0.001$ )



# Background:

## *SYNTAX Trial Three Year MACCE Results*



# Background:

- At three years in the SYNTAX trial:
  - Cardiac death was higher in PCI arm vs. CABG (6.0 vs. 3.6%,  $p=0.02$ )
  - MI was higher in PCI arm vs. CABG (7.1 vs. 2.6%,  $p=0.002$ )
  - Stroke was higher in CABG arm vs. PCI (3.4 vs. 2.0%,  $p=0.07$ )
  - Repeat revascularization was higher with PCI (21 vs. 11%,  $p<0.001$ )



# Background:

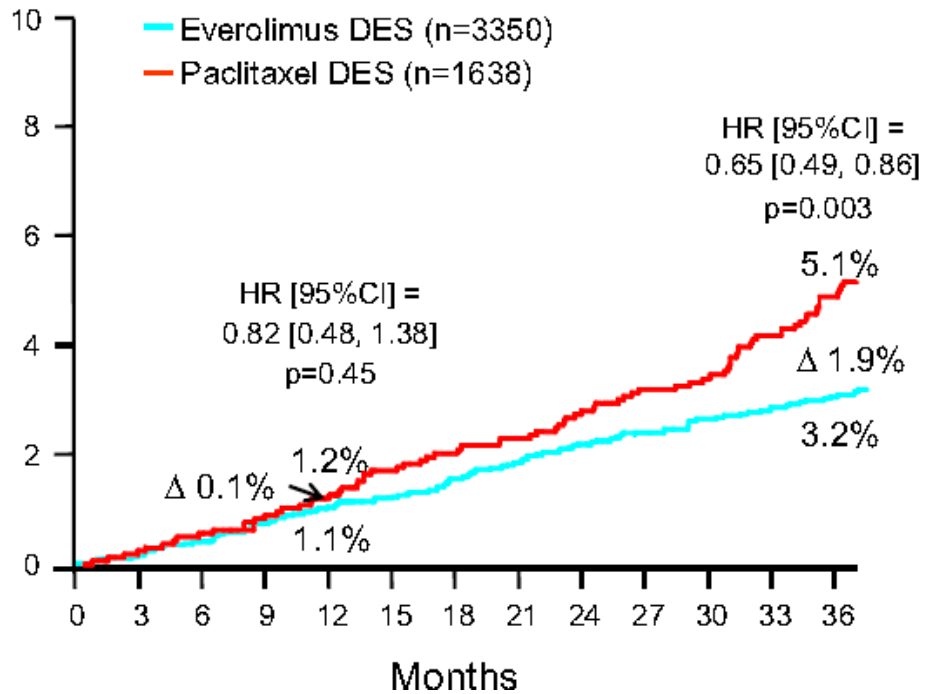
- Why should we expect a different result with FAME 3?
  - 2<sup>nd</sup> Generation DES outperform 1<sup>st</sup> Generation.
  - Fractional Flow Reserve-guided PCI outperforms angiography-guided PCI.



# Background:

## *3 Year Benefit of 2<sup>nd</sup> Generation DES in SPIRIT meta-analysis*

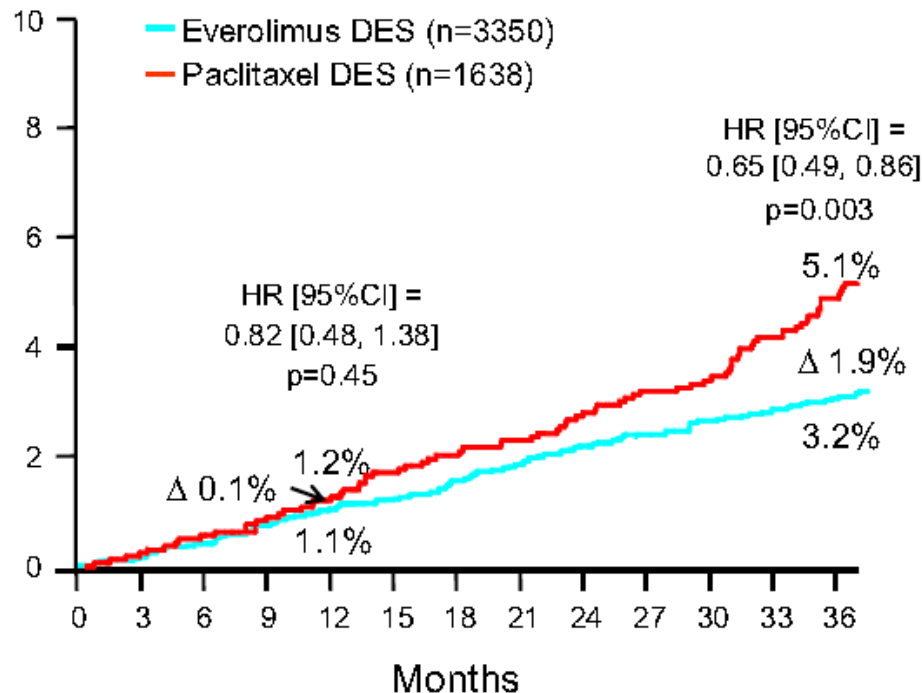
### All-cause Death



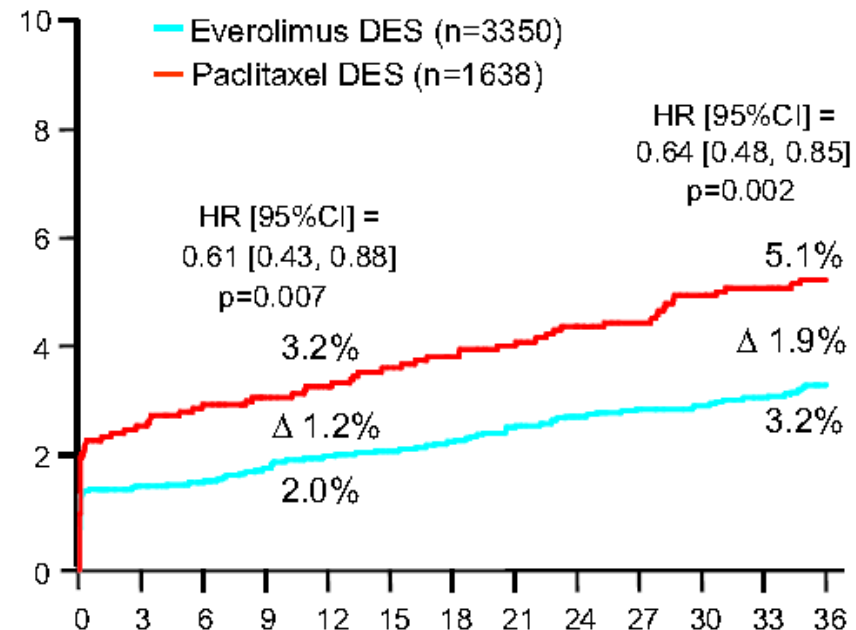
# Background:

## 3 Year Benefit of 2<sup>nd</sup> Generation DES in SPIRIT meta-analysis

All-cause Death



Myocardial Infarction



**Ischemia-driven TLR reduced from 8.2 to 6.0%, p=0.004**



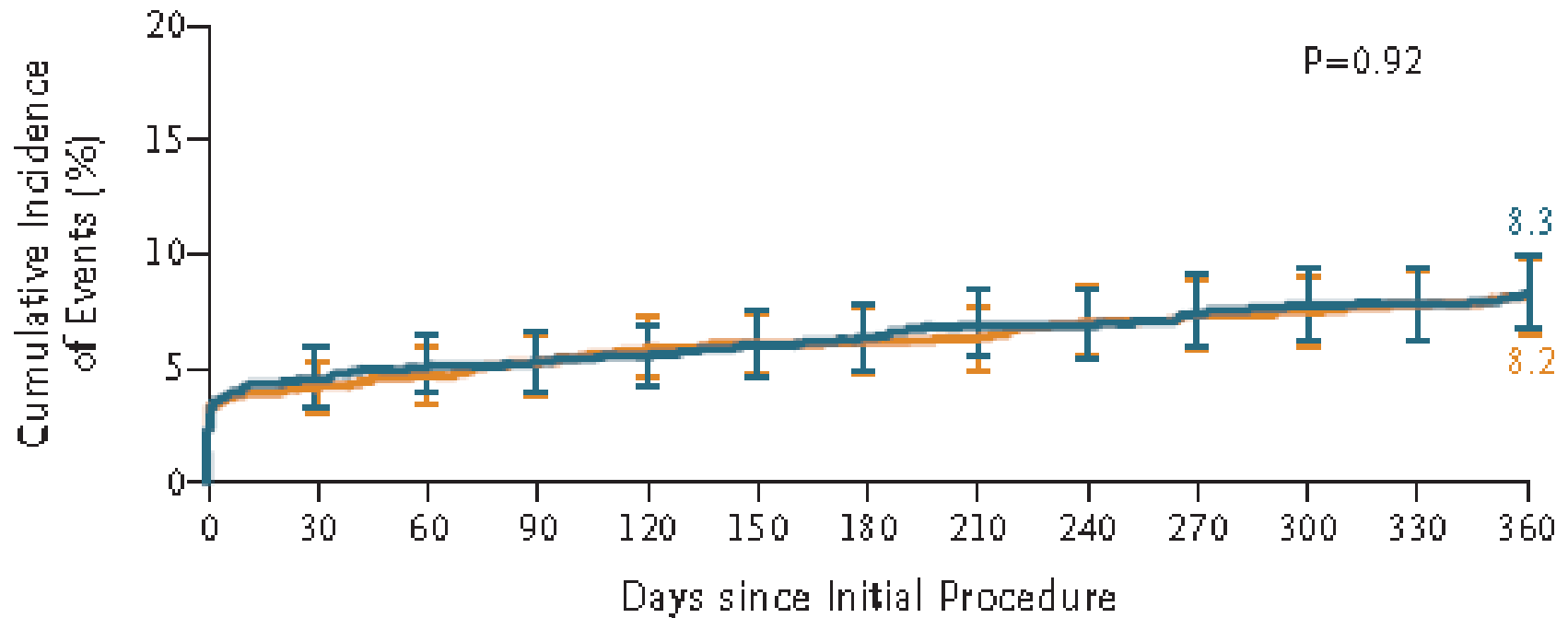


# Background:

## *Randomized comparison of two 2<sup>nd</sup> generation DES (Resolute and Xience stents)*

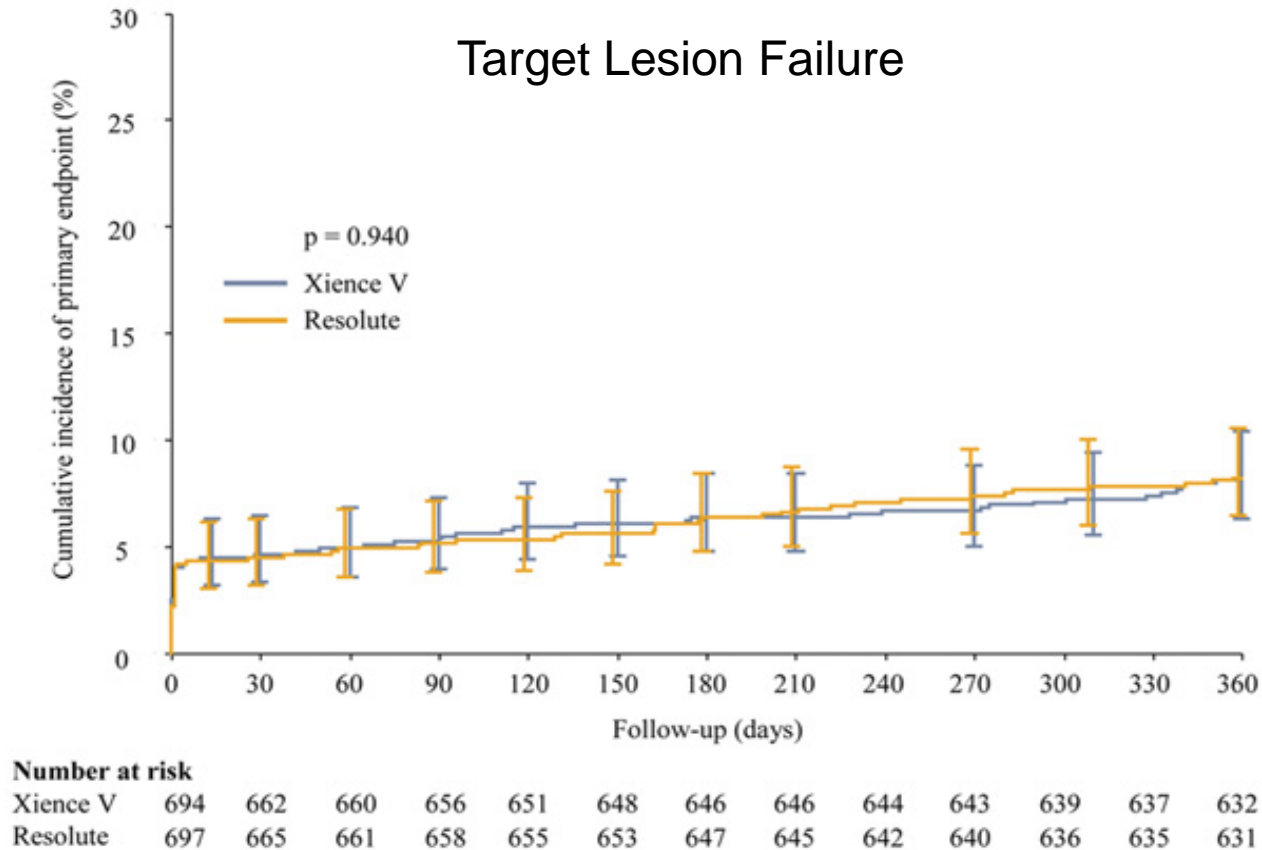
Target Lesion Failure

Target Lesion Failure



# Background:

## *Randomized comparison of 2<sup>nd</sup> generation Resolute and Xience stents in the TWENTE trial*



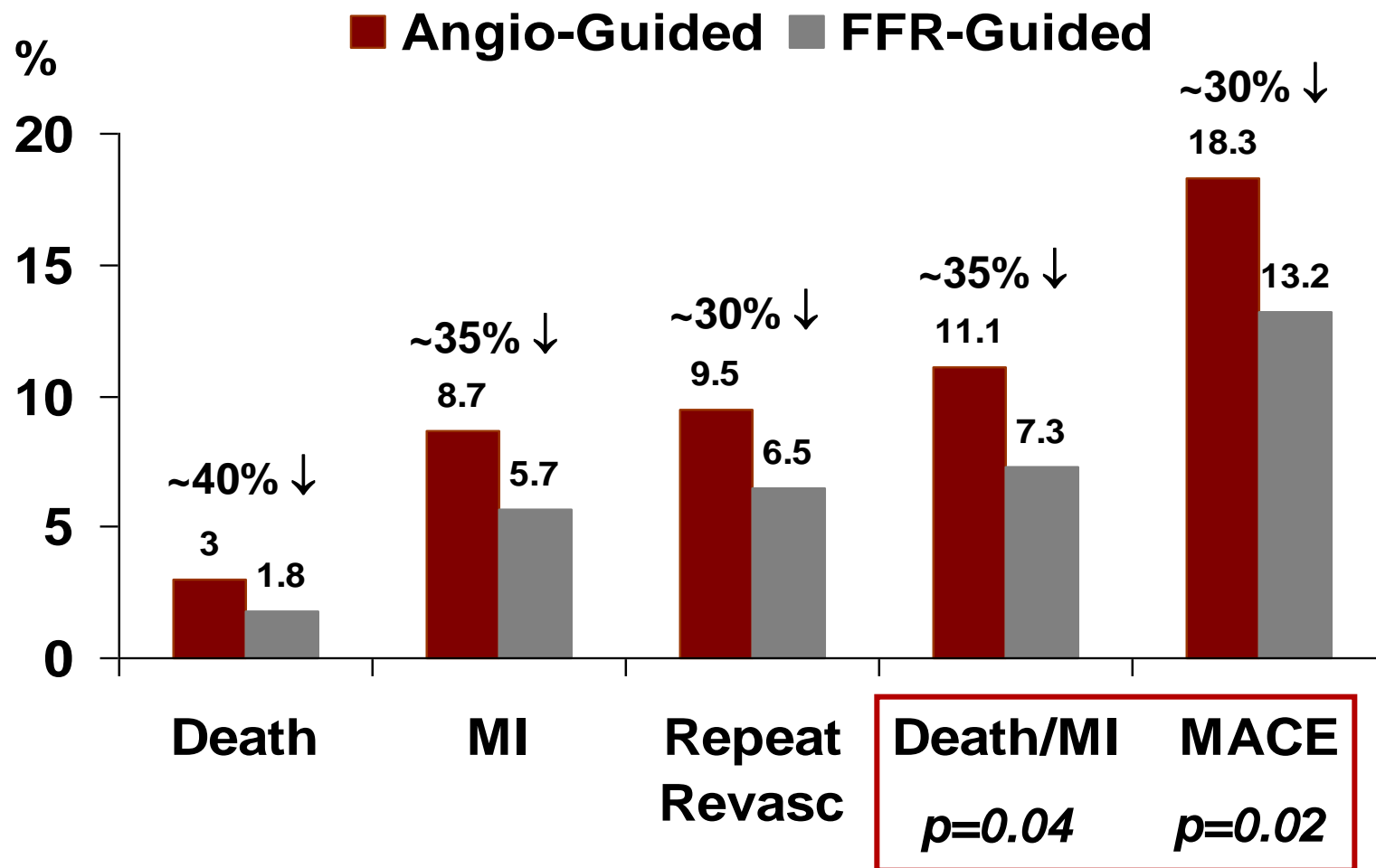
# Background:

- Why should we expect a different result with FAME 3?
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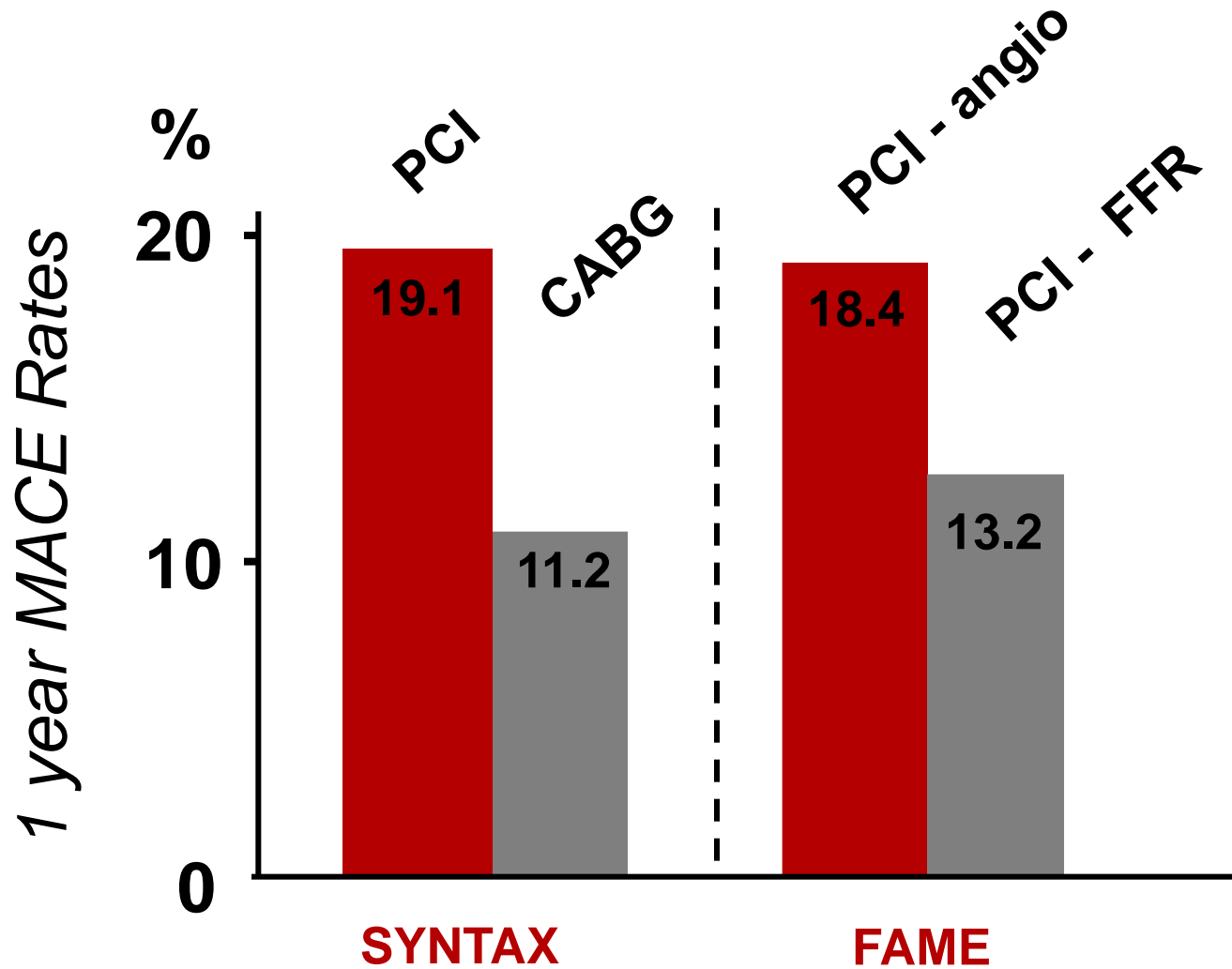


# FAME Study: One Year Outcomes

1,005 patients with MVD randomized to FFR or Angio-guided PCI

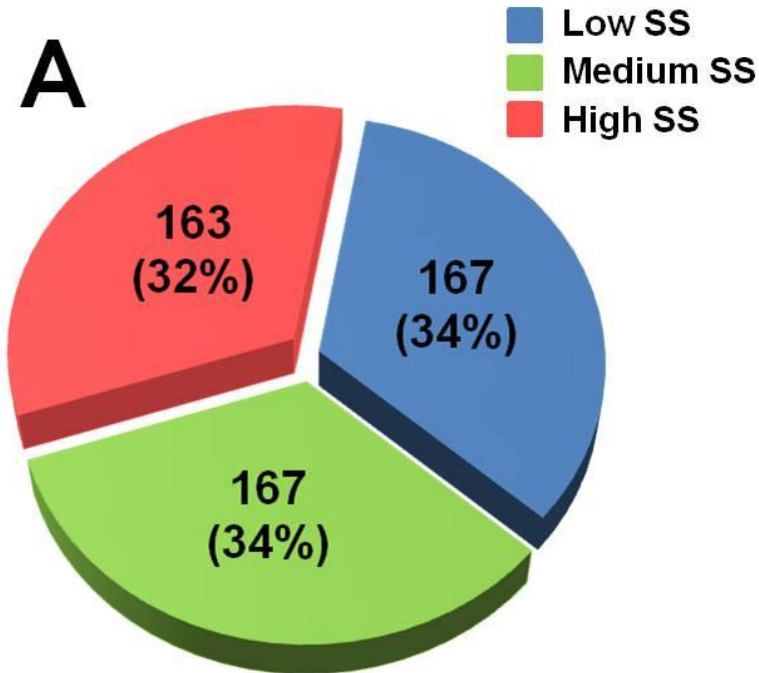


# Implications of FAME



# Functional SYNTAX Score

*Reclassifies > 30% of Cases*

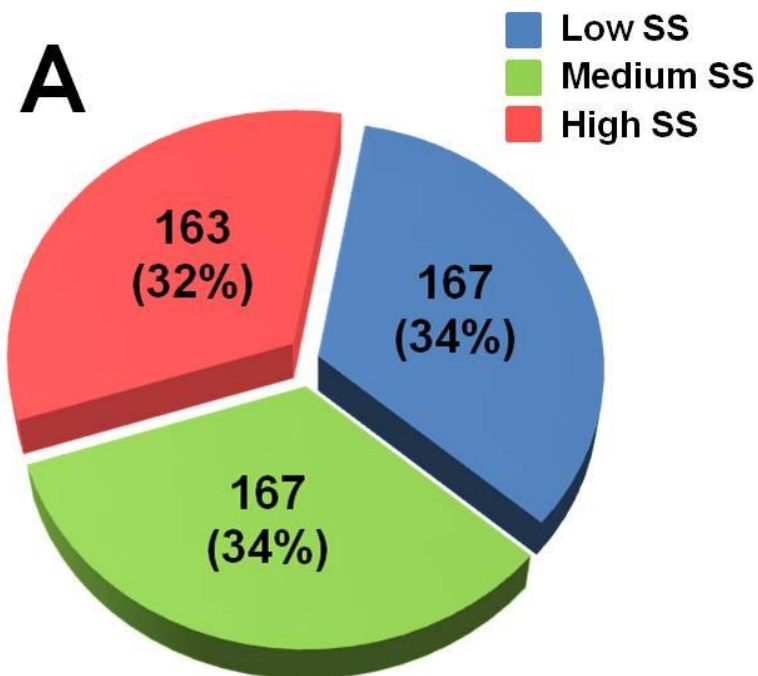


*Without FFR*

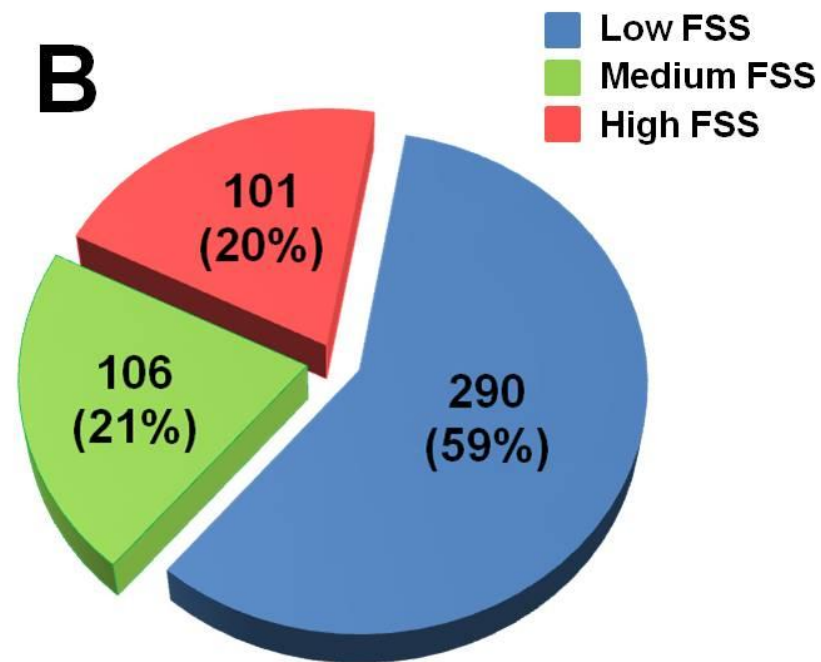


# Functional SYNTAX Score

*Reclassifies > 30% of Cases*



*Without FFR*

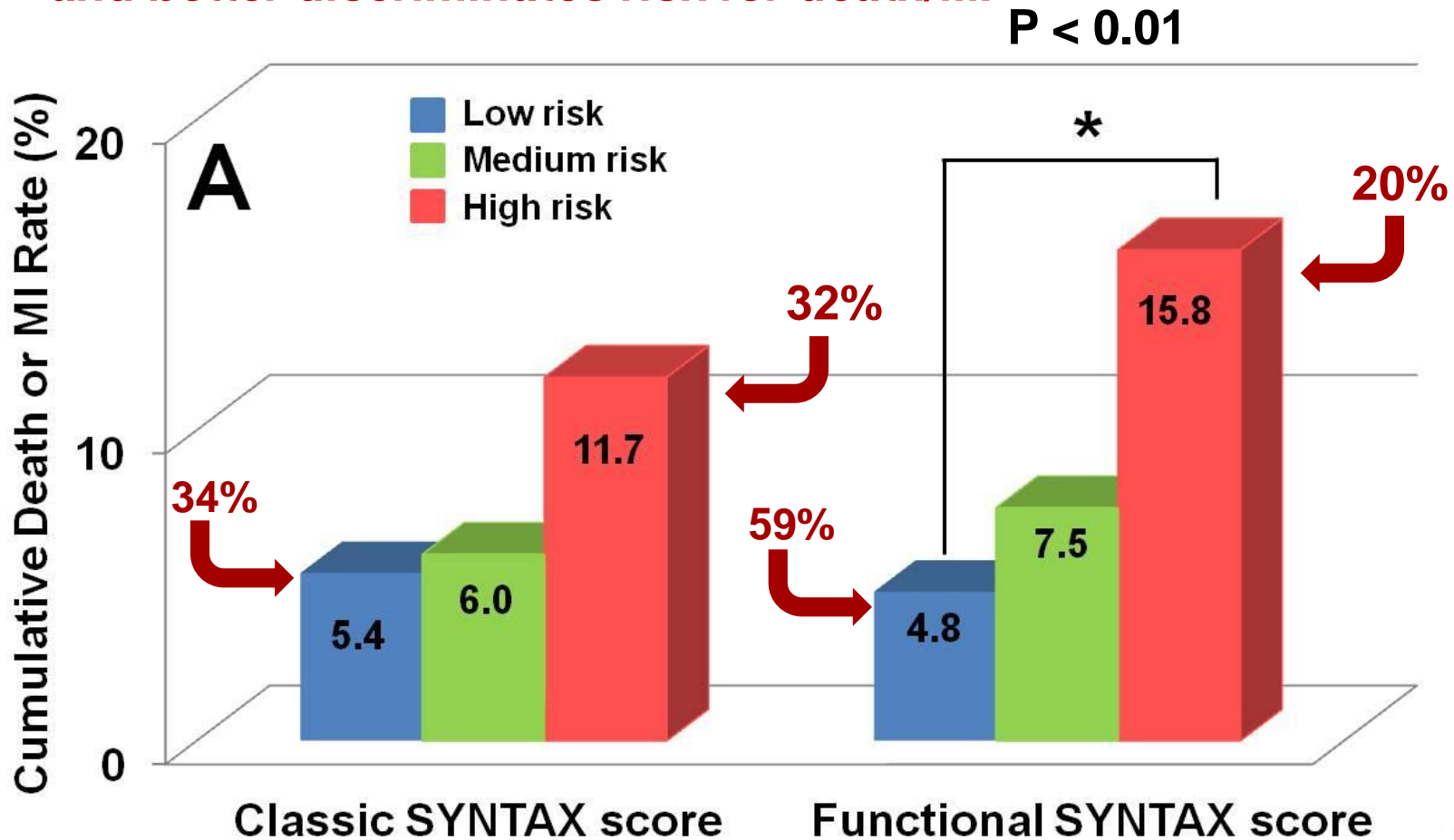


*With FFR*



# Functional SYNTAX Score (FSS)

*FSS converts patients from higher to lower risk and better discriminates risk for death/MI*

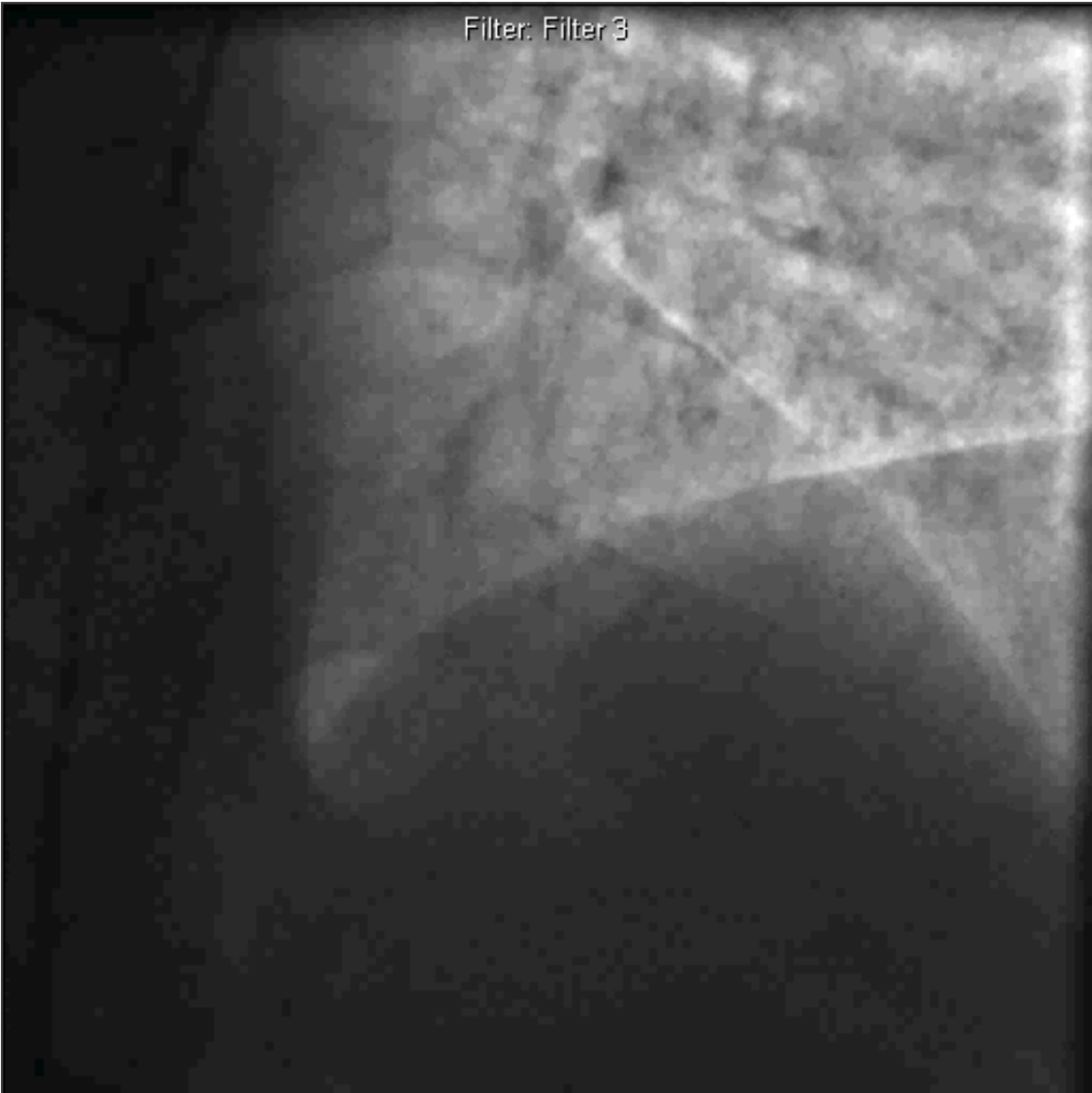




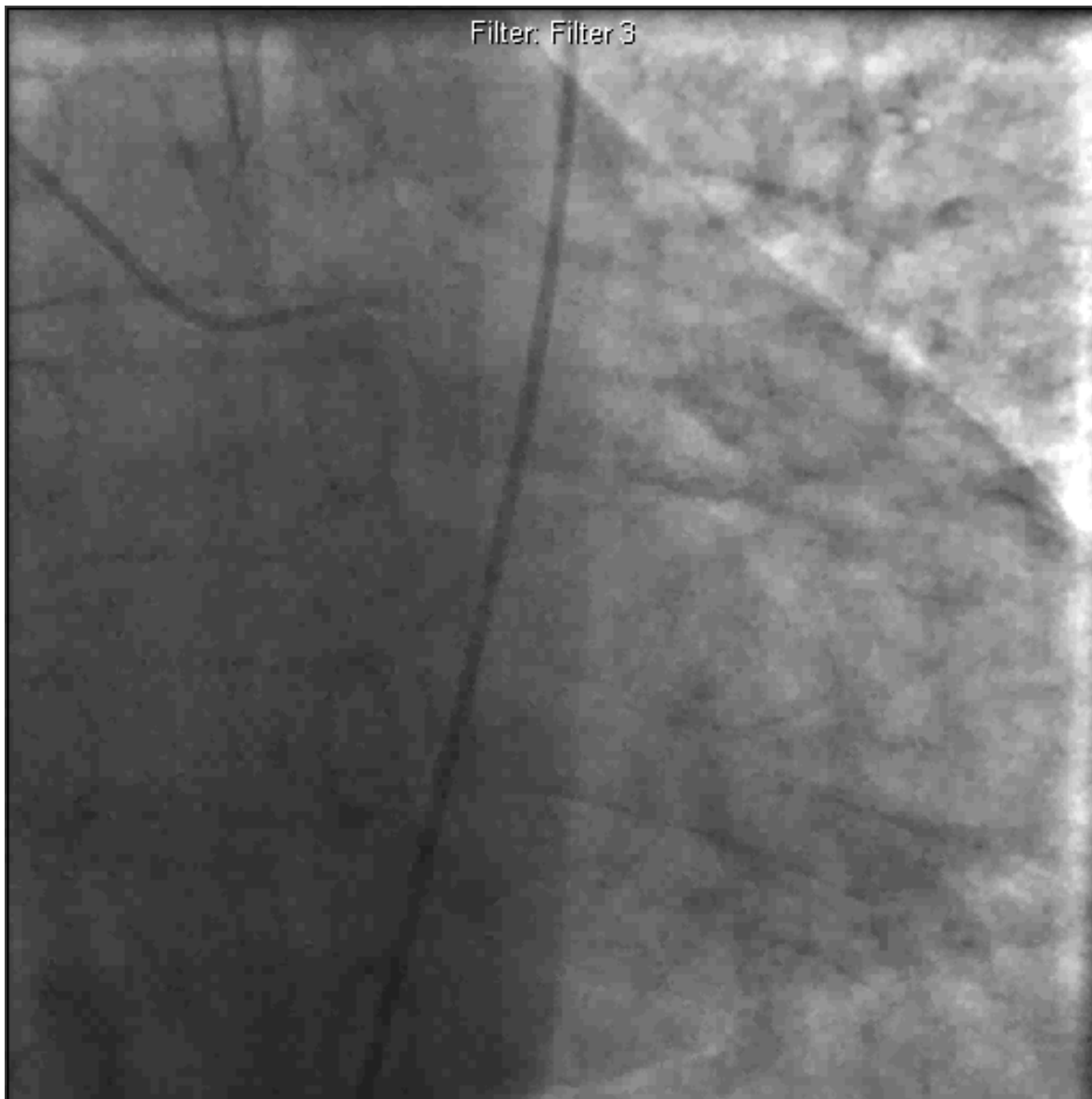
***55 year old man with dyslipidemia, tobacco use and chest pain***



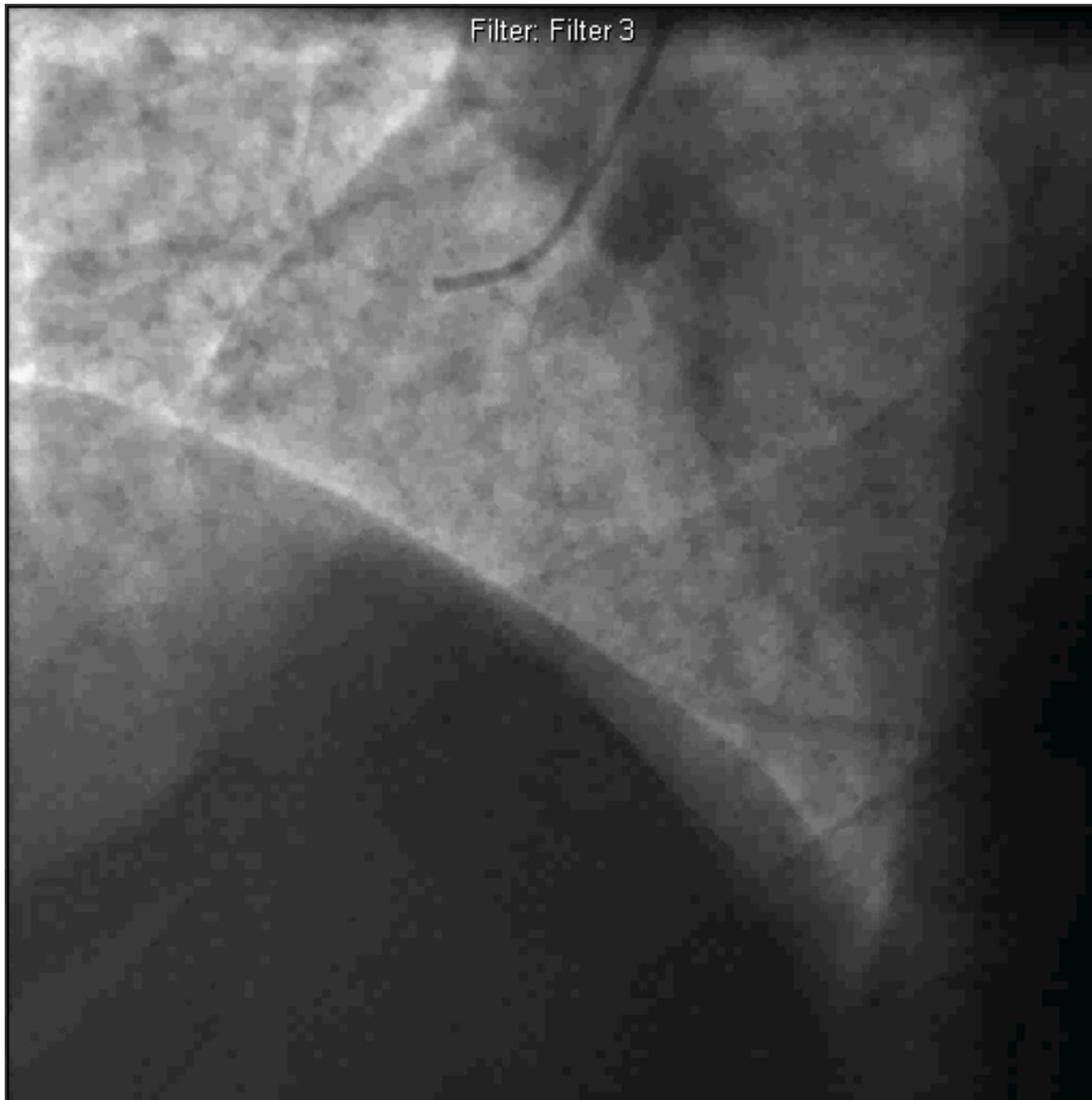
Filter: Filter 3



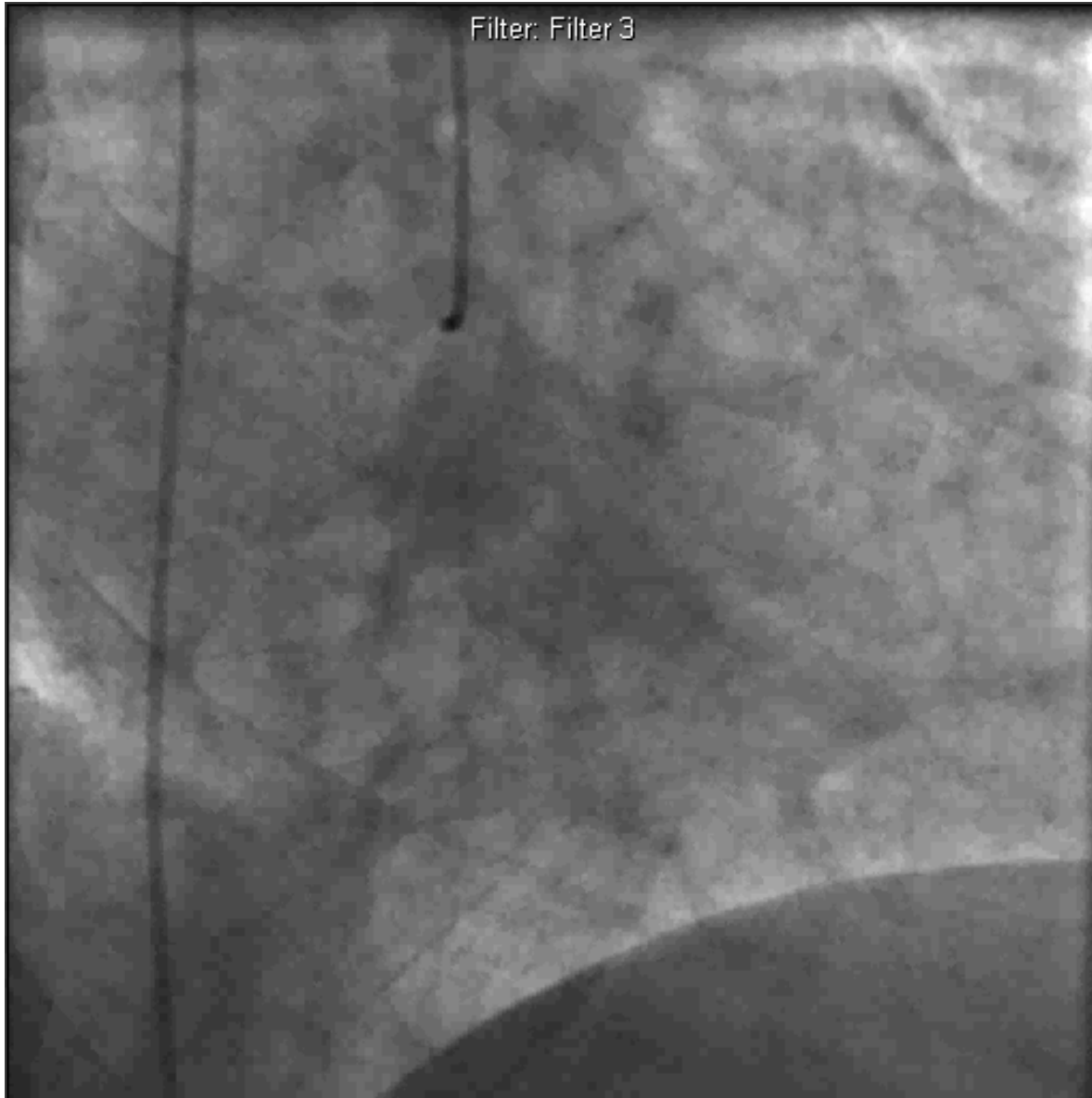
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Filter: Filter 3

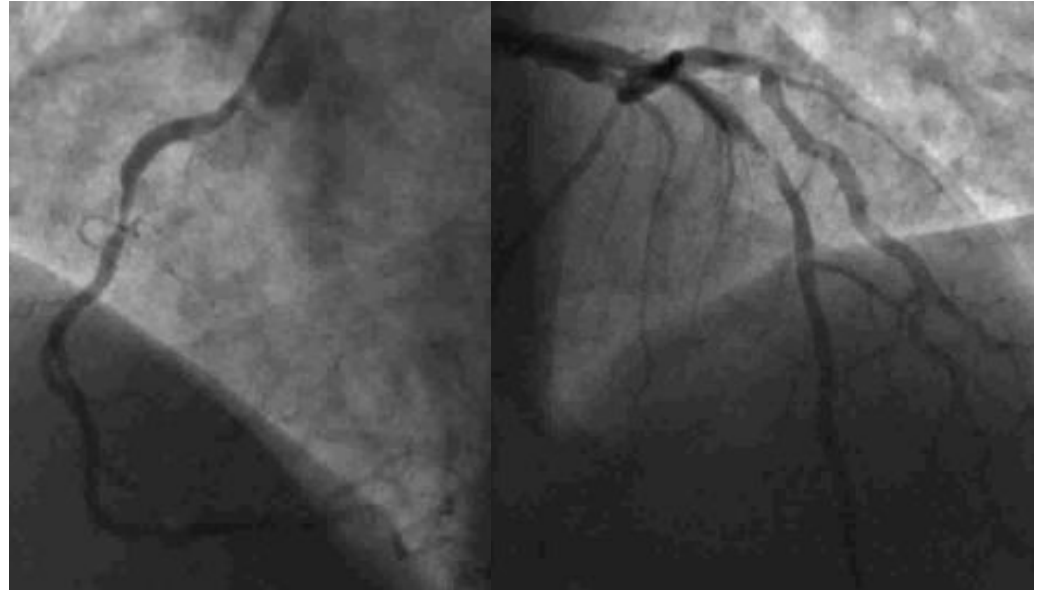


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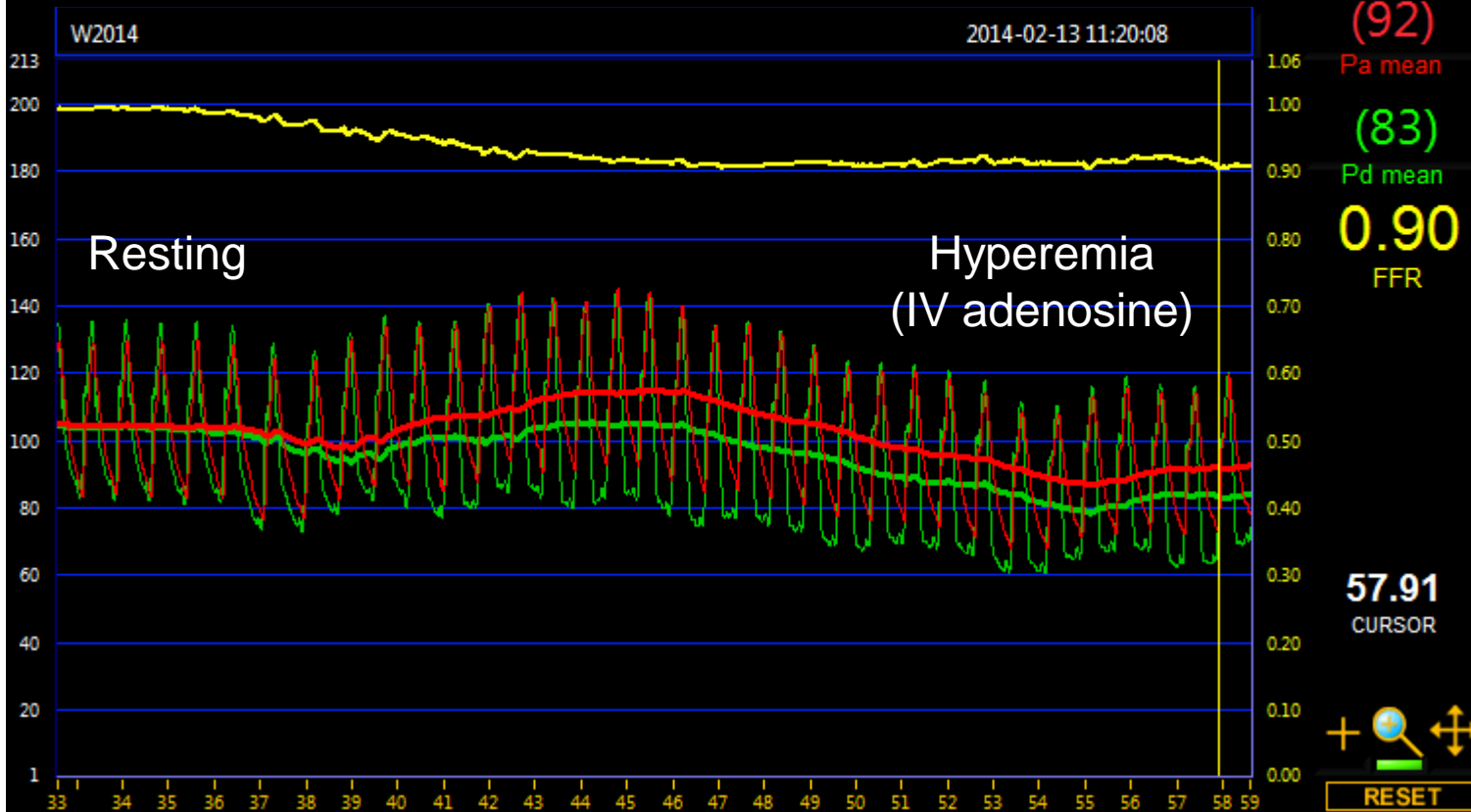


# What should we do now?

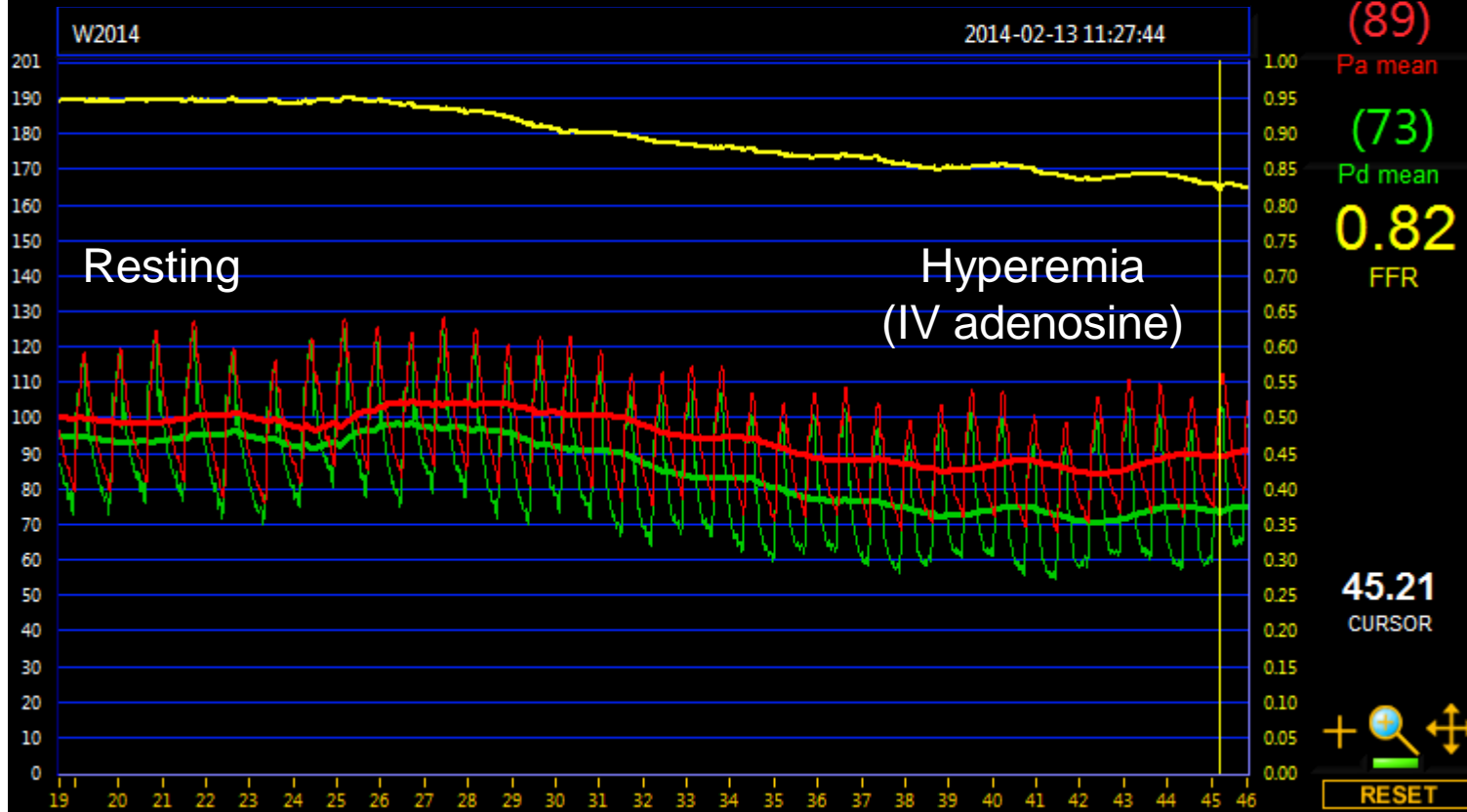
- Med Rx alone
- PCI
  - Which vessels?
- CABG



# FFR L Cx = 0.90

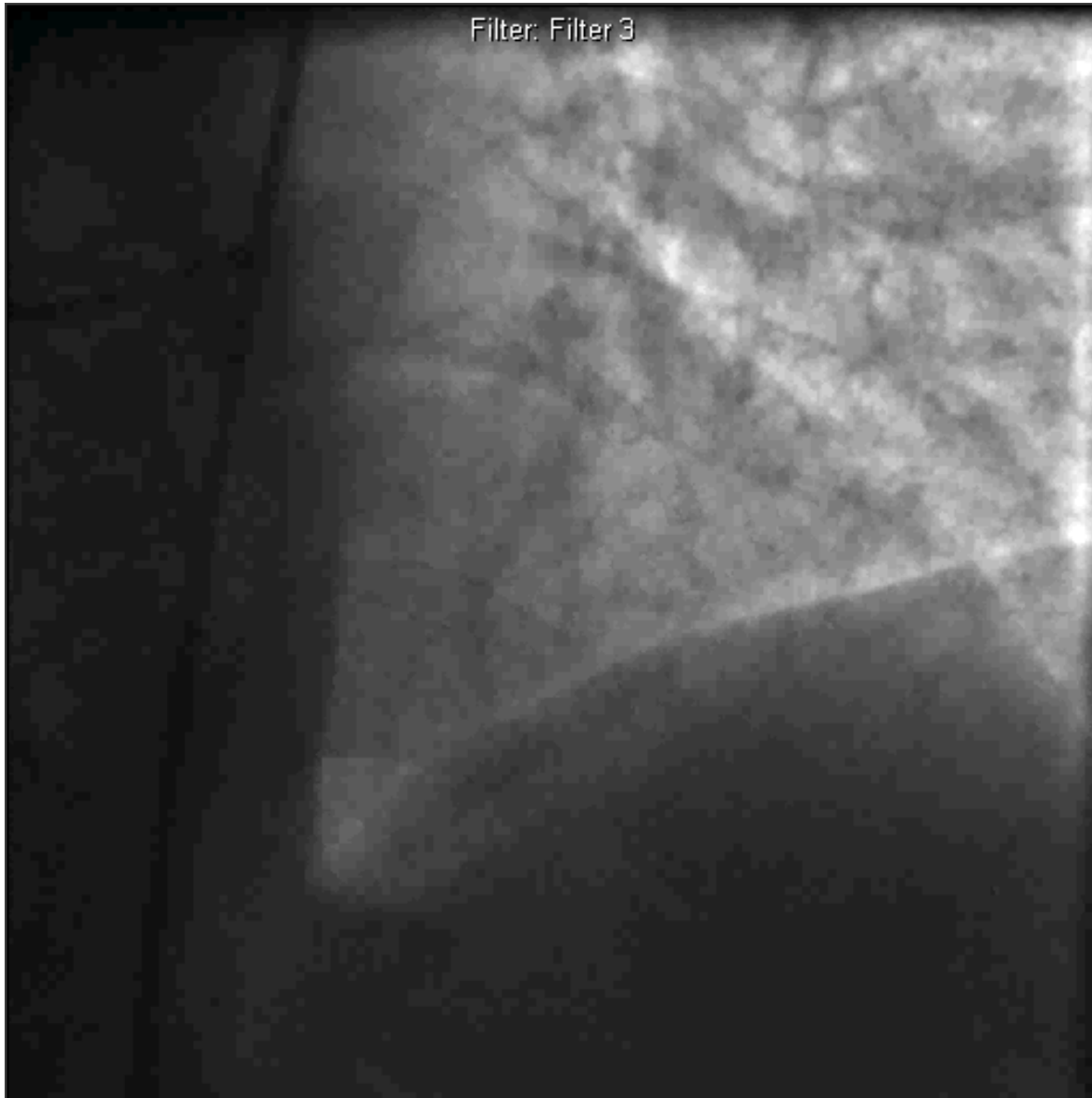


# FFR RCA = 0.82





Filter: Filter 3



# Summary of Case

- Anatomic 3V CAD, functional 1V CAD
- Successfully treated with single stent
- <150 cc contrast, < 1 hour procedure
- Angina free at 1 month



# FAME 3:

## Hypothesis

- Fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) using the 2<sup>nd</sup> generation Resolute DES in patients with multivessel coronary artery disease (CAD) will result in similar outcomes to coronary artery bypass graft surgery (CABG).



# FAME 3:

## Objective

- The primary objective of the FAME 3 Trial is to demonstrate that FFR-guided PCI with the 2<sup>nd</sup> generation Resolute DES is non-inferior to CABG in patients with multivessel CAD.



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# FAME 3:

## *Design*

- Multicenter, worldwide, prospective, randomized trial
- Non-inferiority design
- 1500 patients from 50 sites
- Plan for 2 years enrolment and up to 5 year follow-up



# Study Flow:

**All Comers with 3 V CAD  
(not involving LM)**



**Heart team identifies lesions for PCI/CABG  
and then patient is randomized**

**FFR-Guided PCI with Resolute DES  
Stent all lesions with  $FFR \leq 0.80$   
(n=750)**

**Perform CABG based on  
coronary angiogram  
(n=750)**

**Primary: One Year follow-up for Death, MI, CVA, Revascularization  
Key Secondary: Three Year follow-up for Death/MI/CVA**

**Non-inferior Design**



# FAME 3:

## *Inclusion Criteria*

- Age  $\geq$  21 years
- Three vessel CAD, defined as  $\geq$  50% diameter stenosis by visual estimation in each of the three major epicardial vessels, but not involving left main coronary artery, and amenable to revascularization by both PCI and CABG as determined by the Heart Team
- Willing and able to provide informed, written consent



# FAME 3:

## *Key Exclusion Criteria*

- Requirement for other cardiac or non-cardiac surgical procedure (e.g., valve replacement)
- Previous CABG
- Left main disease requiring revascularization
- Cardiogenic shock and/or need for mechanical/pharmacologic hemodynamic support
- Recent STEMI (<5 days)
- Ongoing Non STEMI with biomarkers (e.g., cardiac troponin) still rising
- Known left ventricular ejection fraction <30%





# FAME 3:

## Major Endpoints

- Primary Endpoint:
  - One year rate of Death, MI, Stroke and Revascularization
- Key Secondary Endpoint:
  - Three year rate of Death, MI and Stroke



# FAME 3:

## *Secondary Endpoints*

- MACCE rate at 1 and 6 months, 3 years and 5 years
- Stent thrombosis (ARC definition) and graft occlusion at each time point
- Bleeding complication
- Significant arrhythmia
- Development of acute renal failure
- Length of hospitalization
- Rehospitalization
- Quality of life and cost-effectiveness
- Utility of Functional SYNTAX Score



# FAME 3

## *Study Organization*

- Investigator initiated trial
- Coordinated by Stanford with support of a CRO
- Funded by research grants from Medtronic and St. Jude Medical
- Independent DSMB and CEC



# Conclusion:

- By incorporating FFR-guided PCI and utilizing the 2<sup>nd</sup> generation Resolute Integrity stent, FAME 3 aims to demonstrate that FFR-guided PCI is non-inferior to CABG in patients with 3-vessel coronary disease not involving the left main coronary artery.

