## Morphology is overestimated - FFR makes simple! -

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No conflicts to declare

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### Morphology is overestimated - FFR makes simple! -



- Why do we perform PCI?
  - To improve symptoms
  - To improve prognosis
- What causes symptoms, influences prognosis?
  - Ischemia

So: find ischemic lesions and treat them!

## Stenting of ischemia-related stenoses improves symptoms and outcome





## But ...., minority of patients have proof of ischemia pre-PCI !



 Only 44.5% (20.1% - 70.6%) of Medicare patients undergoing elective PCI, underwent stress-testing < 90 days before PCI



## Which lesions cause ischemia?





Morphology is overestimated - FFR makes simple! -



## What test to use?

- Angiography, QCAIVUS
- FFR

## Morphology

versus

Physiology





#### Angiography, QCA under- and overestimate a lesion's severity







#### IVUS

 Most accurate method for morphologic imaging of coronary arteries and stenoses



Gold standard to evaluate stent deployment

•Poor instrument for physiologic stenosis assessment (i.e. whether a particular stenosis is responsible for myocardial ischemia)

CATHARINA-ZIEKENHUIS



(LM: 6 mm2)







#### **IVUS versus FFR**



Takagi, et al. Circulation 1999;100:250-5

	Sensitivity	Specificity	
AS >70%	100%	68%	
MLD <1.8mm	100%	66%	
MLA <4.0mm <sup>2</sup>	82%	56%	

Briguori, et al. AJC 2001;87:136-41



IVUS doesn't account for cumulative effect of serial stenosis or diffuse disease in a long segment





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No evidence of ischemia, because IVUS CSA is >4.0mm2 everywhere





## IVUS doesn't account for cumulative effect of serial stenosis or diffuse disease in a long segment







## **Either small, non-randomized, or non-conclusieve** IVUS-guided PCI in BMS era: 12 studies

Study	Angio Better	IVUS Better	IVUS Also Cheaper
Choi et al (AHJ 2001;142:112-8)		X	
CENIC (JACC 2002;39:54A)		X	
CRUISE (Circulation 2000;102:523-30)		X	
SIPS ( <i>Circulation</i> 2000;102:2497-502 and AJC 2003;91:143-7)		x	X
AVID (Circulation Intervent, in press)		X	
Gaster et al ( <i>Scan Cardiovasc J 2001;35:80-5 &amp; Heart</i> 2003;89:1043-9)		x	X
RESIST (JACC 1998;32:320-8 & Int J Cardiovasc Intervent 2000;3:207-13)		x	
TULIP (Circulation 2003;107:62-7)		X	
BEST (Circulation2003;107:545-551)		X	
OPTICUS (Circulation. 2001;104:1343-9)	X		
PRESTO (Am Heart J. 2004;148:501-6)	X		
DIPOL (Am Heart J 2007;154:669-75)		X	



#### **IVUS-guided PCI in DES era: 1 study**

Matched controll study in 884 patients: (Roy et al. Eur Heart J 2008;29:1851-7)

	IVUS- guided	Angio- guided	р
30 day			
MACE	2.8%	5.2%	0.01
Stent thrombosis	0.5%	1.4%	0.045
TLR	0.7%	1.7%	0.045
1 year			
MACE	14.5%	16.2%	0.3
Definite stent thrombosis	0.7%	2 0%	<del>0.014</del>
Probably stent thrombosis	4.0%	5.8%	0.08
TLR	5.1%	7.2%	0.06
Late definite stent thrombosis	0.2%	0.7%	0.3



## Threshold value of FFR to detect significant stenosis





FFR is the *only* functional index which has ever been validated versus a true gold standard.

(Prospective multi-testing Bayesian methodology)

Sensitivity : 90% Specificity : 100%

N Engl J Med 1996; 334:1703-1708

## FFR makes simple!



#### **KEYNOTE**

In patients with coronary artery disease, the most important factor with respect to <u>both</u>

- functional class (symptoms)
- and prognosis (outcome)

Is the presence and extent of inducible ischemia

## FFR makes simple!



In Single Vessel Disease

Death and myocardial infarction at 5 year follow-up



## FFR makes simple!



#### In Multivessel Disease

In multivessel coronary disease (MVD), identifying which stenoses cause ischemia is difficult:

Non-invasive tests are often unreliable in MVD and coronary angiography often results in both underor overestimation of functional stenosis severity

Fractional Flow Reserve (FFR), is the most accurate and selective index to indicate whether a particular stenosis is responsible for inducible ischemia

FFR guidance may improve outcome?



## The windtunnel for every standpoint is a prospective randomized controlled trial

## -----> FAME STUDY



#### FAME study: HYPOTHESIS



## FFR – guided PCI in multivessel disease is superior to current angiography – guided PCI FAME

#### FAME study: DESIGN



Randomized multicenter study in 1005 patients undergoing DES-stenting for multivessel disease in 20 US and European centers

- independent core-lab
- independent data analysis
- blinded adverse event committee

#### **Multivessel disease:**

Stenoses of > 50% in at least 2 of the 3 <u>major</u> coronary arteries



## FAME study: Baseline Characteristics (1)



	ANGIO-group N=496	FFR-group N=509	P- value
Age, mean±SD	64±10	65±10	0.47
Male, %	73	75	0.30
Diabetes, %	25	24	0.65
Hypertension, %	66	61	0.10
Current smoker, %	32	27	0.12
Hyperlipidemia, %	74	72	0.62
Previous MI, %	36	37	0.84
Unstable angina, %	36	29	0.11
Previous PCI , %	26	29	0.34
LVEF, mean±SD	57±12	57±11	0.92
LVEF < 50% , %	27	29	0.47

FAME study: Baseline Characteristics (2)			
	ANGIO-group N=496	FFR-group N=509	P- value
Indicated lesions/patient (n=)	2.7±0.9	2.8±1.0	0.34
Pts. with ≥1 total occlusion (%)	7.5	10.6	80.0
Prox. LAD involved, No (%) Lesions in prox.or mid	186 (38)	210 (41)	0.39
segment, No (%)	960 (71)	1032 (73)	0.42

FAME study: Procedural results (1)			
	ANGIO-group N=496	FFR-group N=509	P- value
Indicated lesions/patient (n=)	2.7±0.9	2.8±1.0	0.34
FFR results			
Lesions succesfully measured, No (%)	-	1329 (98%)	-
Lesions with FFR $\leq$ 0.80 ,No (%)	-	874 (63%)	-
Lesions with FFR > 0.80 ,No (%)	-	513 (37%)	-
Stents per patient	2.7 ± 1.2	1.9 ± 1.3	<0.001
Lesions succesfully stented (%)	92%	94%	-
DES, total, No	1359	980	-

### FAME study: Event-free Survival









## "measuring FFR takes too much time"

## FAME study: Procedural results



	ANGIO-group	FFR-group	P- value
Procedure time (min)	70 ± 44	71 ± 43	0.51
Contrast agent used (ml)	302 ± 127	272 ± 133	<0.001
Procedural materials (US \$)	6007	5332	<0.001
Length of hospital stay (days)	3.7 ± 3.5	3.4 ± 3.3	0.05



# *"I seal every plaque because it can rupture in the future ......"*

*"I seal every plaque because it can rupture in the future ......"* 



not every plaque ruptures

- not every rupture leads to infarction
- chance to die or have AMI from non-ischemic plaque < 1% / year</li>

 chance to die or have AMI from unnecessary stent ~ 3 % / y



1329 lesions measured by FFR









#### 7 out of 513 (1.4%) were stented











7 out of 513 (1.4%) were stented

0 out of 513 were related to AMI: 0%

• A very low event rate for deferred lesions in the FFR-guided arm at 1 year

 Deferring PCI of lesions with FFR > 0.80 in MVD patients is safe



## Why is outcome of FFR guided procedures so good?



Physiologic Lesion Assessment in MVD



Routine measurement of FFR in multivessel PCI is superior to angiography guided treatment.

It improves outcome of PCI significantly

It makes PCI a better and safer treatment

It supports the evolving paradigm of

"Functionally Complete Revascularization", i.e. stenting of ischemic lesions and medical treatment of non-ischemic ones





 Morphology in guiding PCI is overestimated FFR-guidance of PCI: Improves outcome of PCI! Is cost-saving! Makes simple!



