MULTİVESSEL DİSEASE,CORONARY REVASCULARIZATION DECISION-HEMODYNAMIC ASSESSMENT

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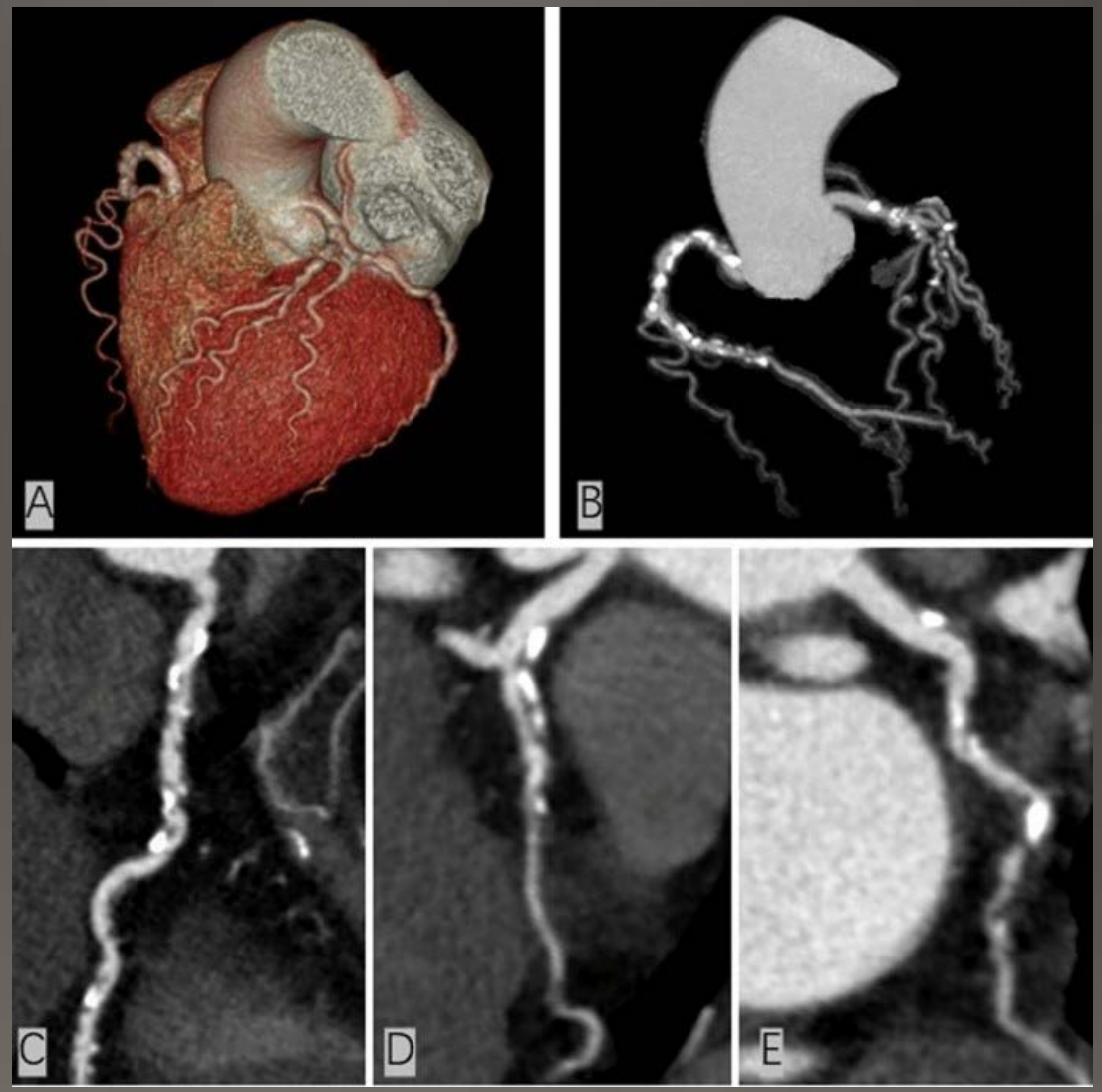
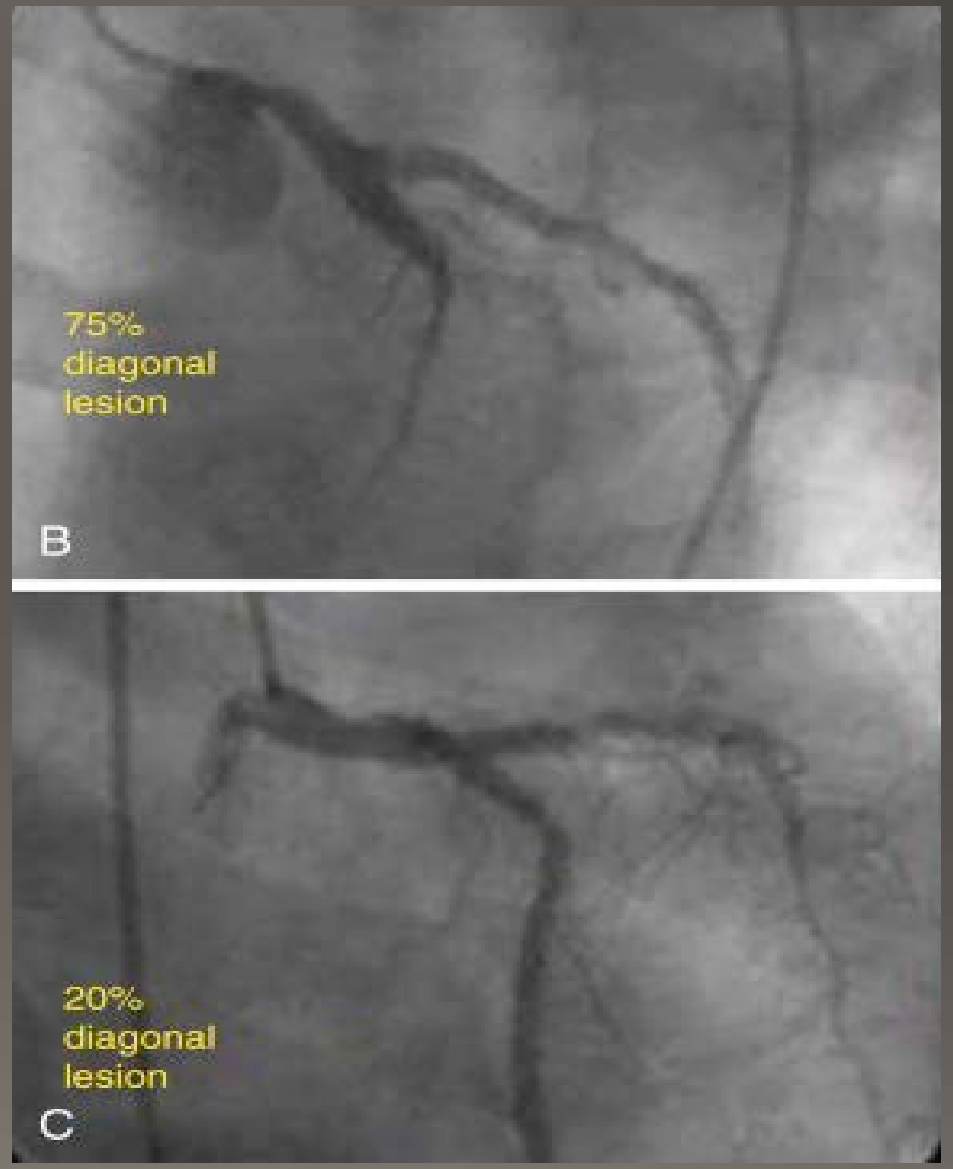
Multivessel coronary artery disease, defined as significant stenosis in two or more major coronary arteries

The diagnosis and treatment of multivessel disease have evolved in the PCI era from solely a visual estimation of ischemic risk to a functional evaluation during angiography.



LIMITATIONS OF CORONARY ANGIOGRAPHY

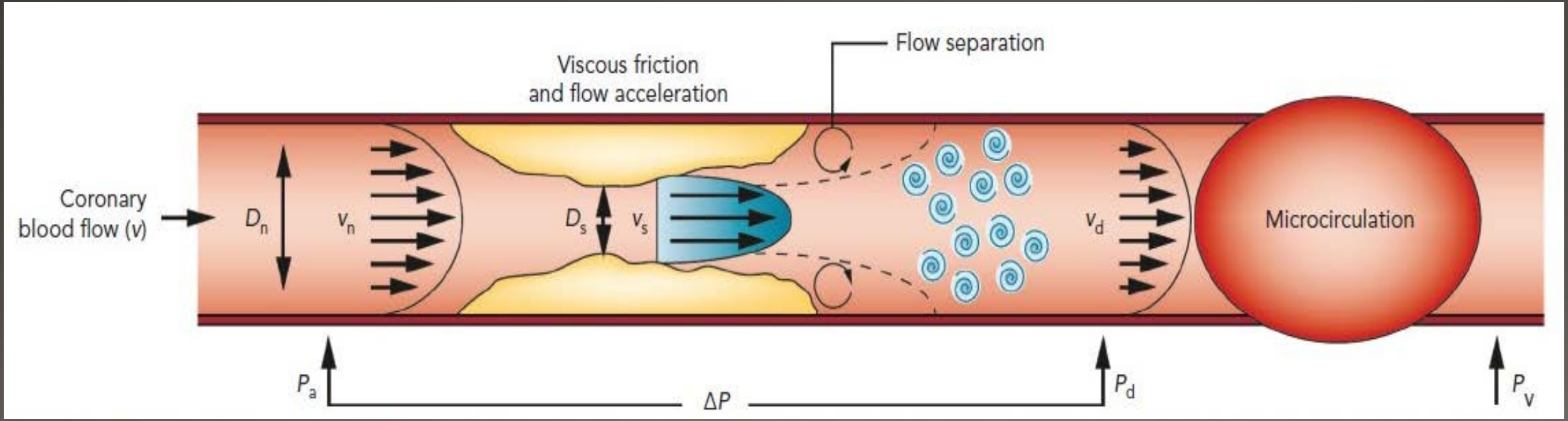
- *İnterpretation is highly subjective*
- *Cannot accurately predict physiologic significance, especially for intermediate lesions (40-70%)*
- *İdentification of normal and diseased segments is complicated by diffuse disease*
- *Artifacts of contrast streaming*
- *İmage foreshortening*
- *Overlapping vessels*



FRACTİONAL FLOW RESERVE (FFR)= Pd/Pa

The resistance to flow through a stenosis result in energy loss

Energy loss produces pressure loss distal to the stenosis and thus a pressure gradient across the narrowed segment



FRACTİONAL FLOW RESERVE (FFR)= Pd/Pa

- *Normal value 1*
- *An FFR value 0.6 means the maximum myocardial flow across the stenosis is only 60% of what it should be without stenosis*
- ***An FFR value <0.75 is associated with inducible ischemia (specifity 100%)***

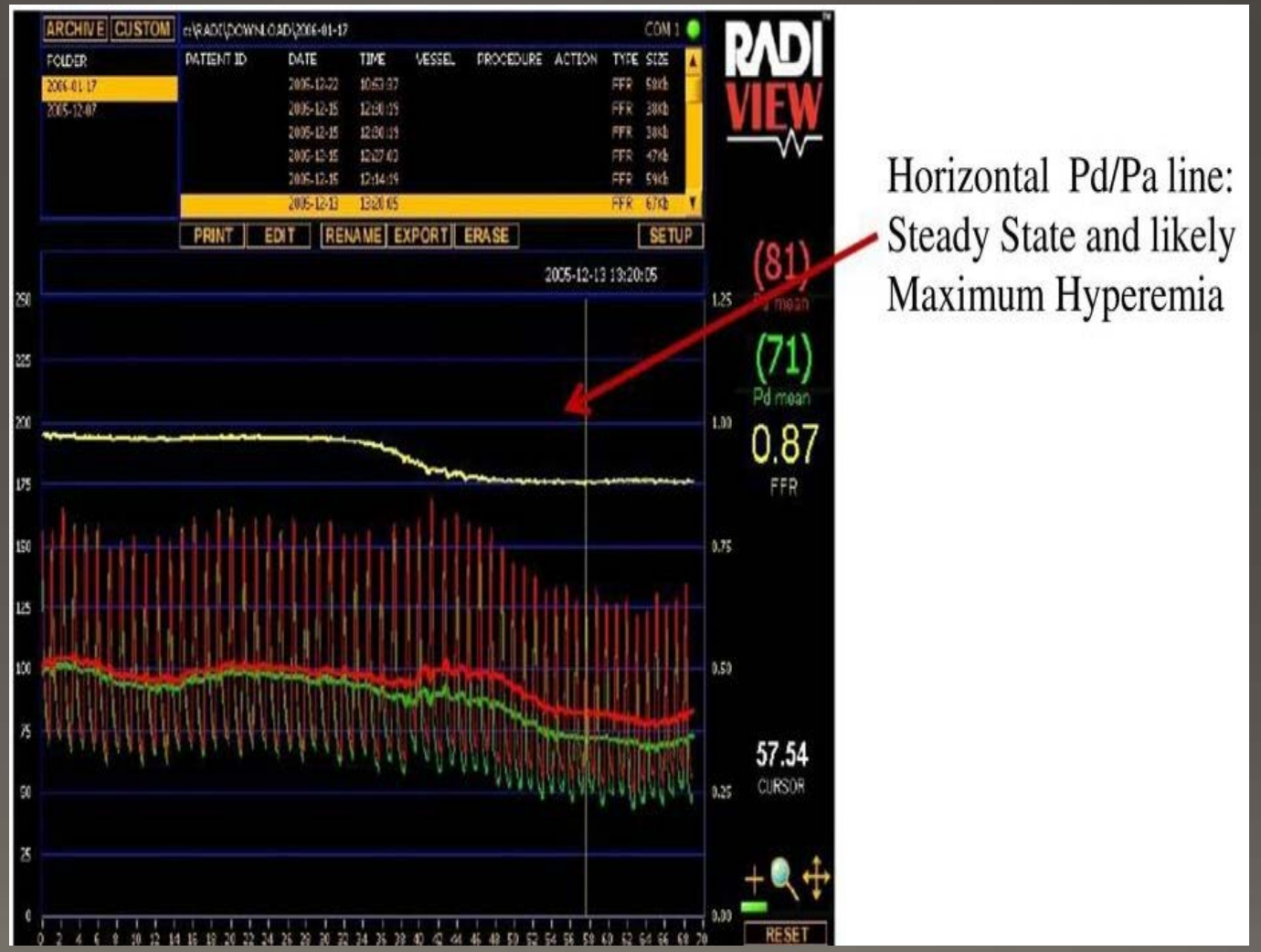
➡ *Positive assessment indicates a significant functional stenosis, suggesting the need for coronary revascularization to improve blood flow and reduce the risk of adverse cardiac events*.

- ***An FFR value >0.80 indicates absence of inducible ischemia (sensitivity 90%)***

➡ *Negative assessment indicates a non-significant functional stenosis, implying that revascularization may not be necessary, and medical management or observation may be appropriate.*

FFR İS MEASURED DURİNG A MAXİMALLY İNDUCED HYPEREMİA

- *Epicardial and resistance arteries have to be vasodilated*
- *Epicardial vessels are dilated using a bolus of 100-200mcg of intracoronary nitroglycerine at least 30 seconds before the first measurement*
- *Hyperemia is induced in the resistance vessels using adenosine (İC or İV) or papaverine (İC)*



HYPEREMİC AGENTS FOR FFR

	Adenosine	Adenosine	Papaverine	NTP	Regadenoson
Route	IV	IC	IC	IC	IV
Dosage	140 mcg/kg/min	200 mcg LCA 100 mcg RCA	15 mcg LCA 10 mcg RCA	50-100 mcg	0.4 mg
Half Life	1-2 min	30-60 sec	2 min	1-2 min	2-4 min (up to 30 min)
Time to Max Hyperemia	< 1-2 min	5-10 sec	20-60 sec	10-20 sec	1-4 min
Advantage	GOLD STANDARD	Short action	Short action	Short action	IV bolus
Disadvantage	↓BP, chest burning	AV Block, ↓BP	Torsades, ↓BP	↓BP	↑HR, ?redose, long action

FFR TECNİQUE-CATHETERS

- **Diagnostic catheters cannot be used to measure FFR:**

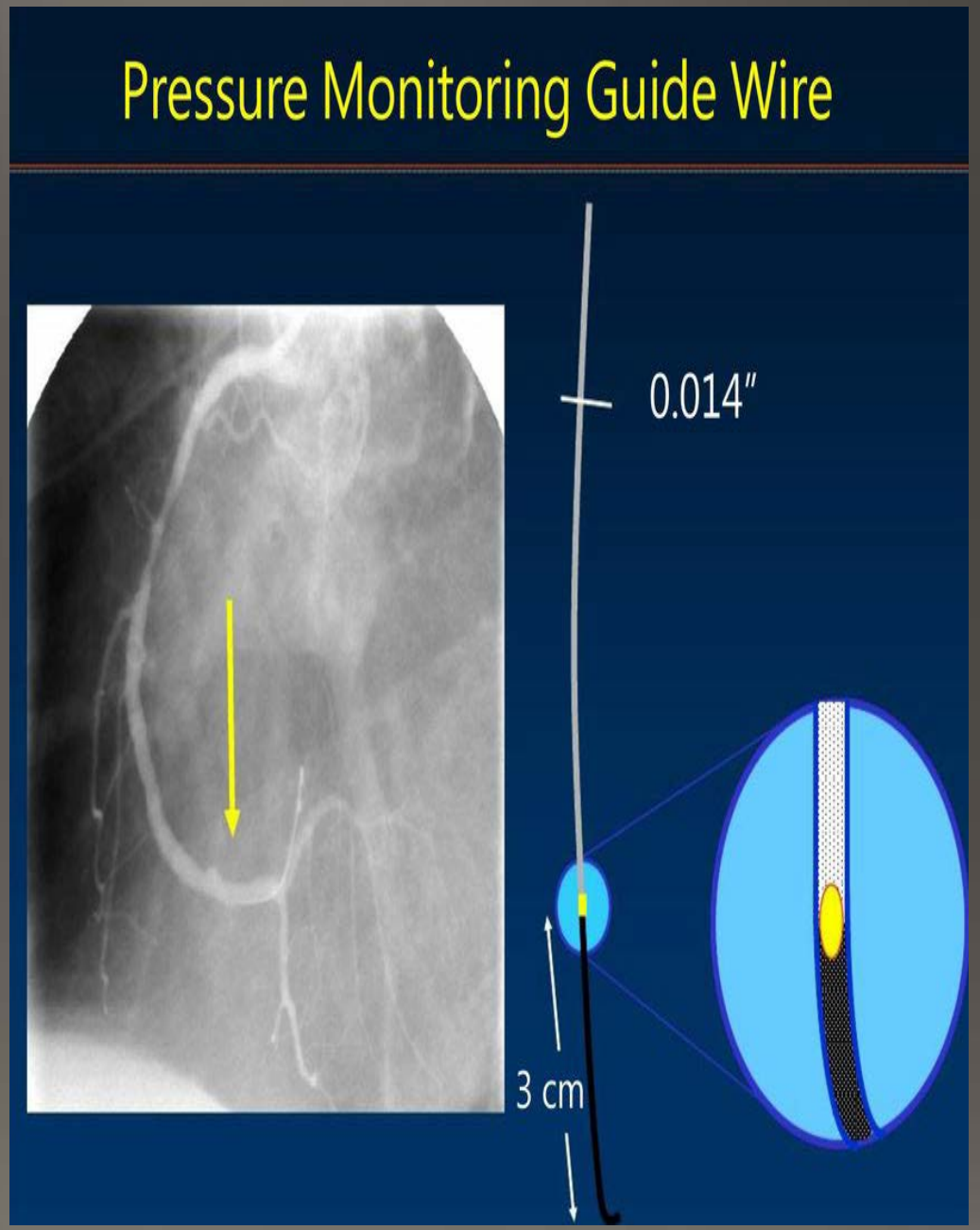
✓ *pressure measurement can be inaccurate*

✓ *the wire manipulationis met with friction due to smaller internal diameters compared to guide catheters*

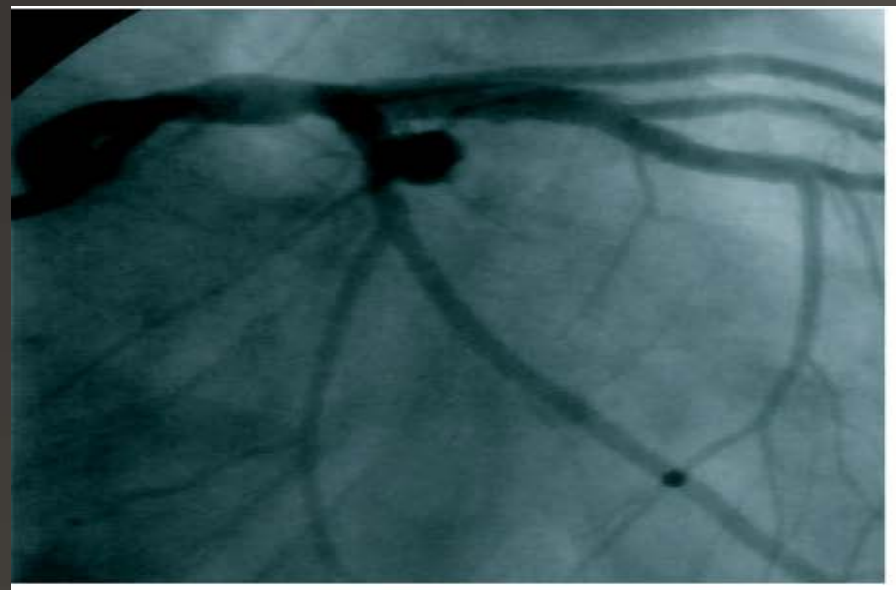
- **The main advantage of guide catheters is that PCI is immediately possible if required**
- **Guide catheters with side holes should not be used:**

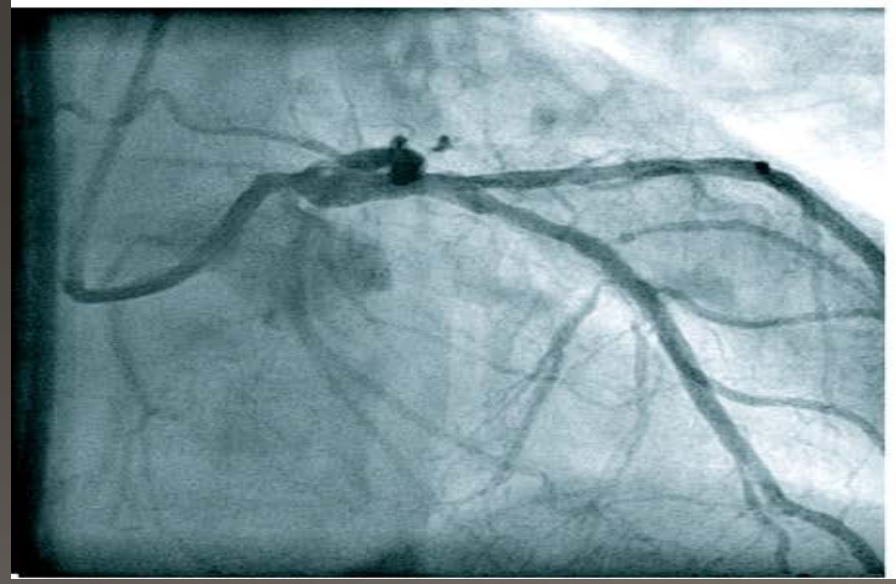
✓ *it can create a false gradient between the side holes and the tip of catheter creating a false positive FFR*

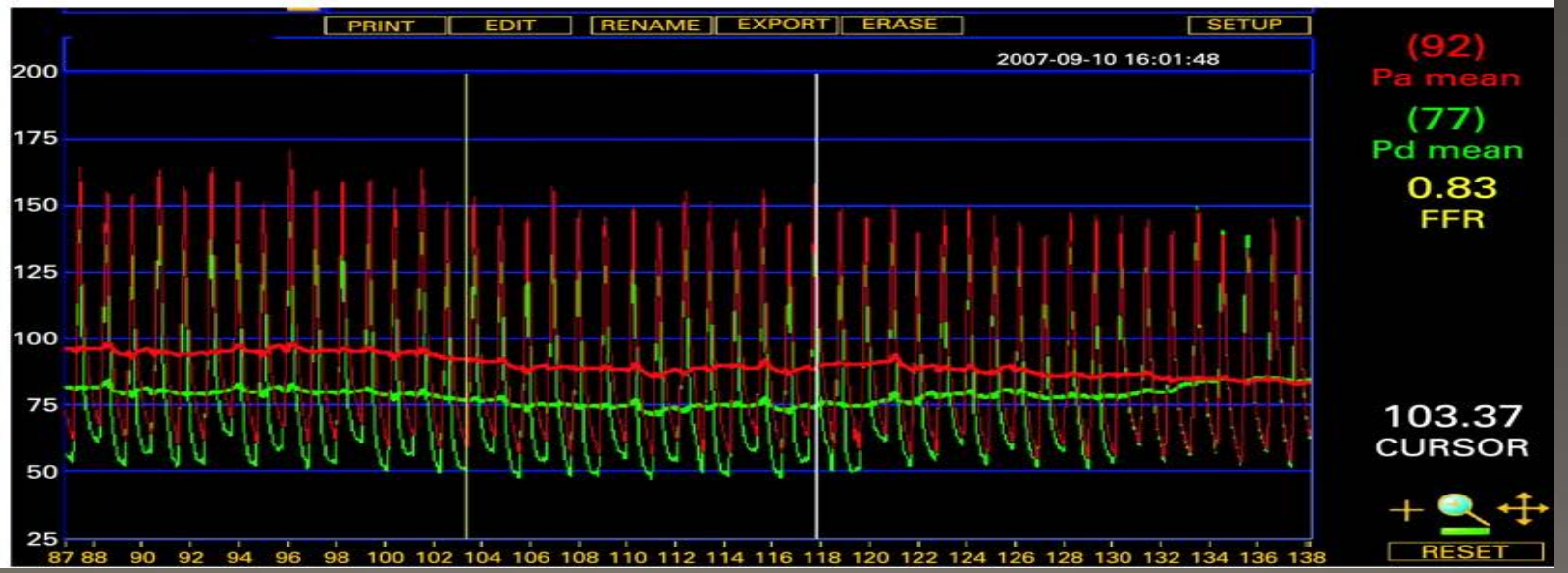
✓ *vasodilatory agent may be flushed into the aorta instead of the coronary arthery*



FRACTİONAL FLOW RESERVE (FFR)







RELATION BETWEEN FFR AND VIABLE MYOCARDIUM

If a stenotic vessel supplies a larger viable myocardial mass, there will be a larger hyperemic flow during maximal vasodilation resulting in a greater gradient between Pd and Pa, and thus, a lower value of FFR

Haemodynamic significance of a lesion is dependent on its perfusion territory

Rationale for Physiologic Assessment of Coronary Stenosis

1. Defining ischemia-causing stenosis

↓

2. Change in clinical management

↓

3. Improved outcomes

DEFER study (Deferral vs Performance of PCI of functionally non-signifacant coronary stenosis)

The purpose of this study was to investigate the appropriateness of stenting a functionally nonsignificant intermediate stenosis.

- Patients with single vessel stenosis and FFR > 0.75 who did not undergo PCI had excellent outcomes
- The risk of cardiac death or MI related to the stenosis was <1% per year and was not reduced with PCI
- In contrast patient with single vessel stenosis and FFR < 0,75 are 5x more likely to experience cardiac death or MI within 5 years, despite undergoing revascularization

FAME Study(Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention)

- ✓ *1005 patients (all with multivessel disease)*
- ✓ *At least 2 stenoses >50% in 2 or 3 major coronary artery disease, amenable for stenting*
- ✓ *Exclusion criteria: left main disease or previous bypass surgery, STEMI with CK>1000 U/L within last 5 days, extremely tortuous or calcified coronary arteries*

Routine measurement of FFR in patients with MVD who are undergoing PCI with drug-eluting stents significantly reduces the rate of the composite end point of death, nonfatal myocardial infarction, and repeat revascularization at 1 year.

FAME 2 Trial (stable coronary artery disease)

- *A total of 888 patients underwent randomization (447 patients in the PCI group and 441 in the medical-therapy group)*
- *All patients with stabil coronary artery disease (multivessel disease consisting of 26% and 22% of patients)*

FFR-guided PCI vs optimal medical therapy alone

Trial stopped prematurely due to a significantly lower rate of death, myocardial infarction, or urgent revascularization in the FFR-guided PCI group of the study at 2 years.

NON-HYPEREMIC PRESSURE RATIOS (NHPR)

Although FFR is the gold standart in invasive physiologic assessment, its clinical and economical benefits have been proven , it remais underutilized (~6% of patients undergoing PCI for intermediate lesions)

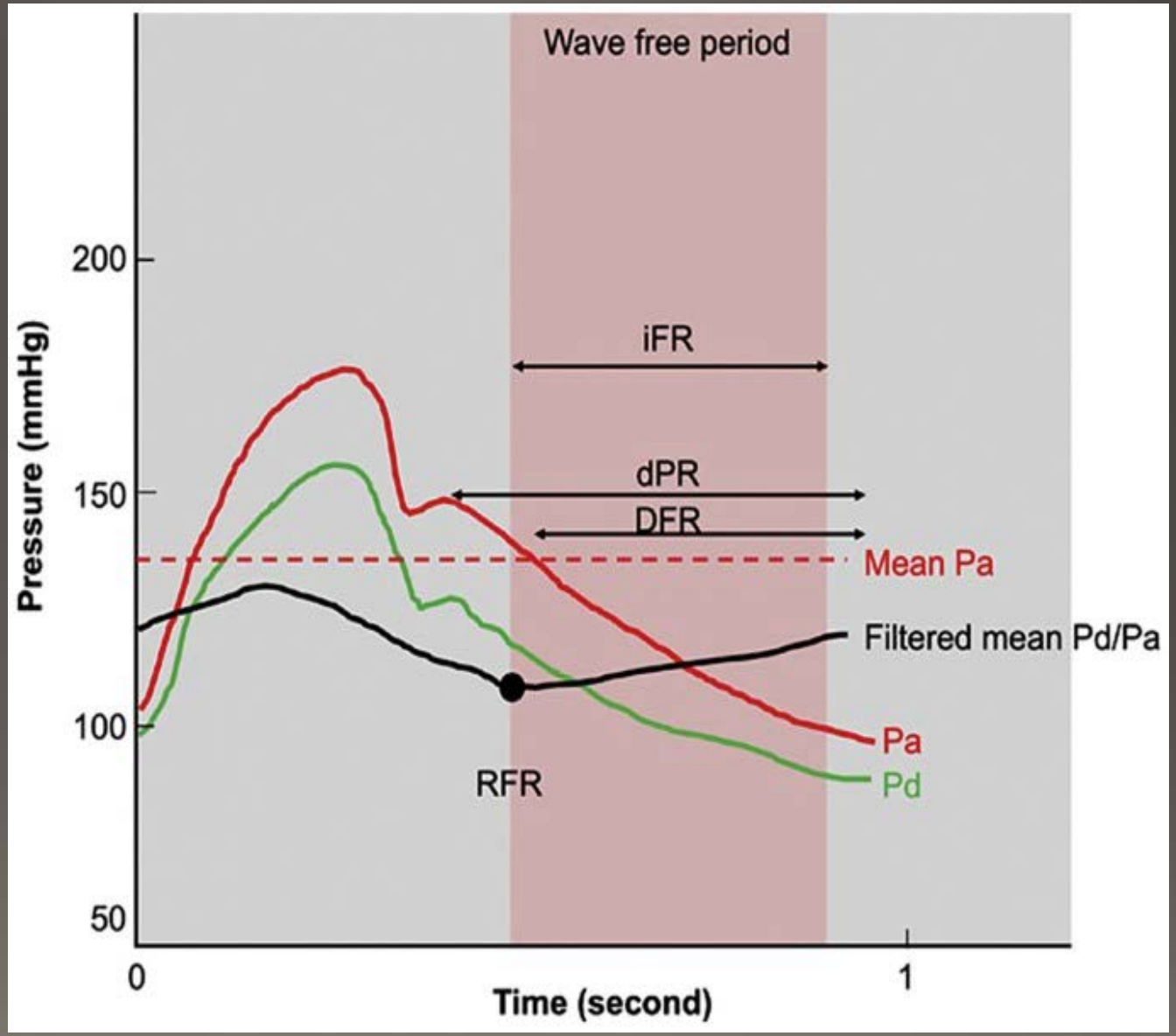
- ✓ *Operator reluctance to delay procedures (especially in vessels with multiple lesions)*
- ✓ *Hospital costs (high price for single FFR-wire: 600-800 euro)*
- ✓ *Conceptual scepticism*
- ✓ *Side effects of hyperemic pharmacologic agents*

NYPR were developed as an alternative to FFR

NON-HYPEREMIC PRESSURE RATIOS (NHPR)

*The **resting** distal/aortic pressure over either the whole cardiac cycle or confined to diastole only*

- *iFR (average Pd/Pa during the wave-free period)*
- *dPR (diastolic pressure ratio)*
- *DFR (diastolic hyperemia-free ratio)*
- *RFR (resting full-cycle ratio)*

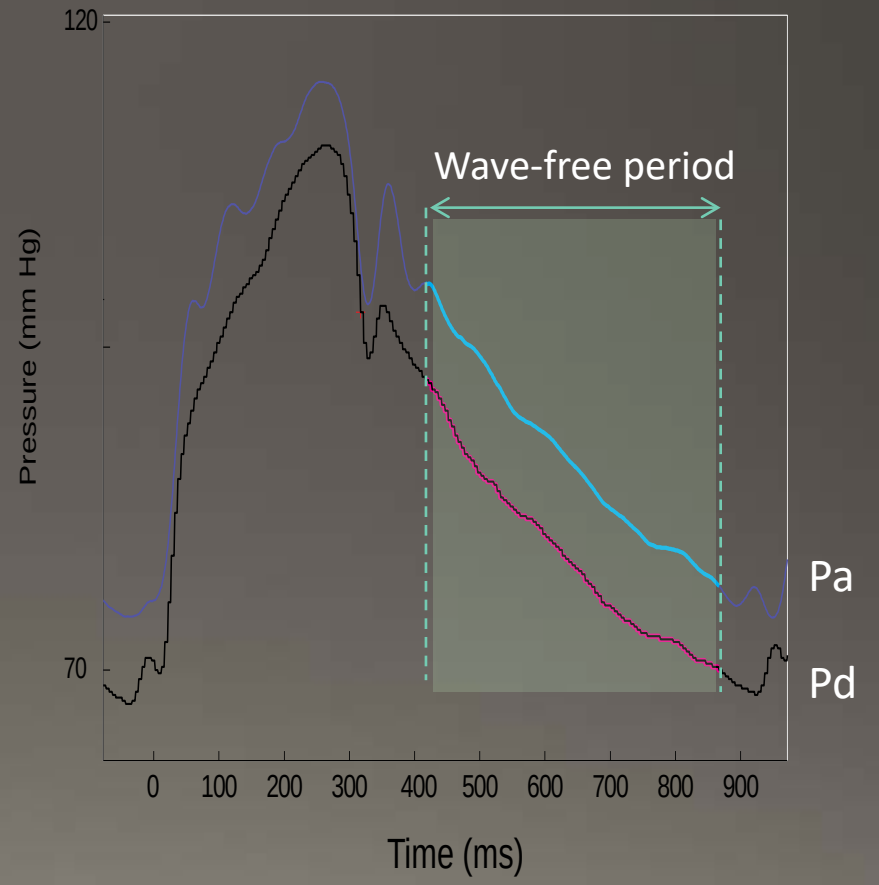


Instantaneous Wave-Free Ratio (iFR)

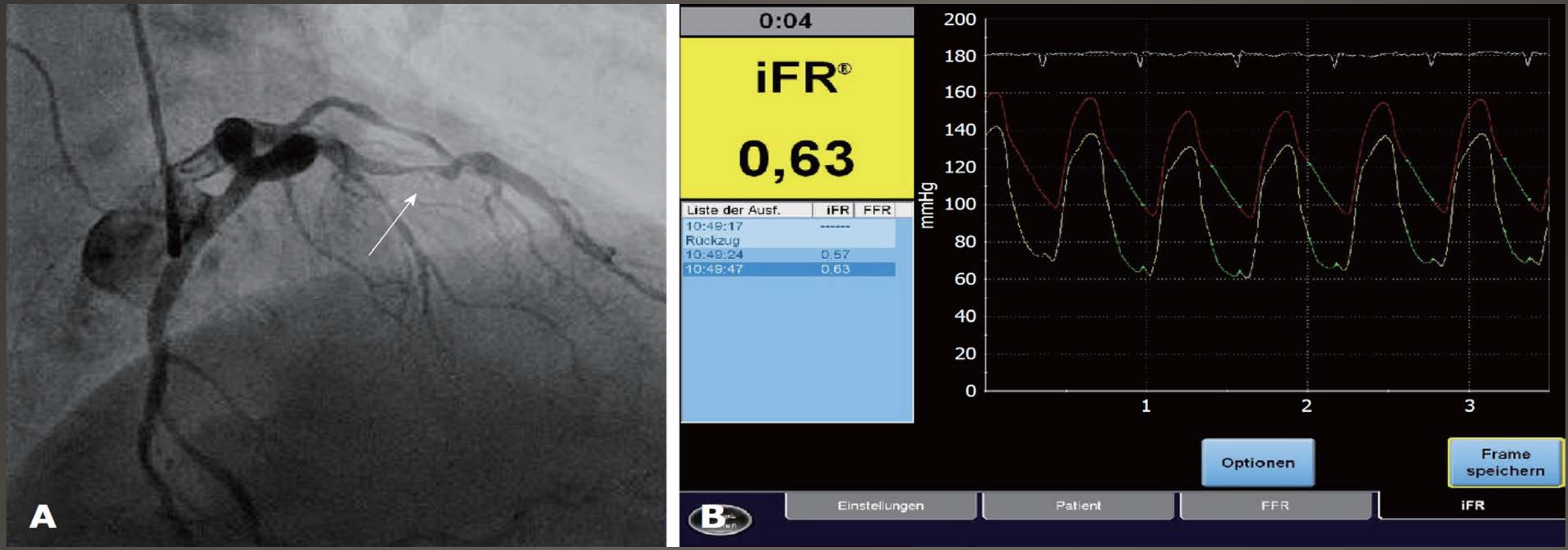
iFR- measures the ratio of the average distal coronary pressure to the average aortic pressure during a specific period of the cardiac cycle, known as the diastolic "wave-free period" (beginning 25% of the way into diastole and ending 5ms before the end of diastole). In this period microvascular resistance is naturally minimized without the need of hyperemia induced by the administration of a vasodilator.

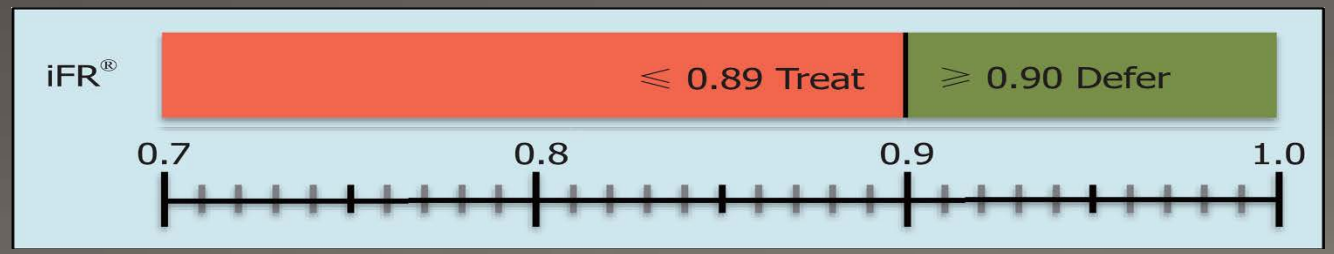
$$iFR = \frac{Pd_{wave\ free\ period}}{Pa_{wave\ free\ period}}$$

ISHEMIC THRESHOLD 0.89



Instantaneous Wave-Free Ratio (iFR)

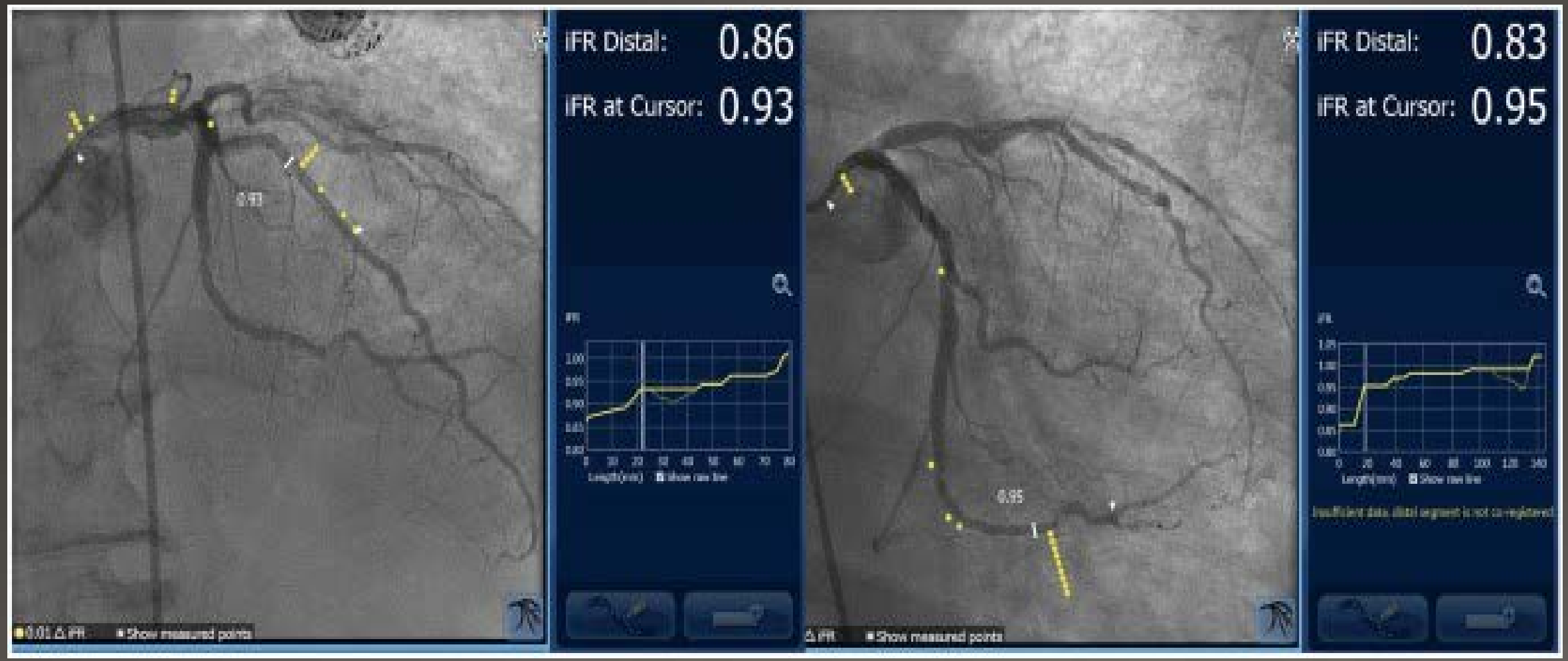




iFR ADVANTAGES

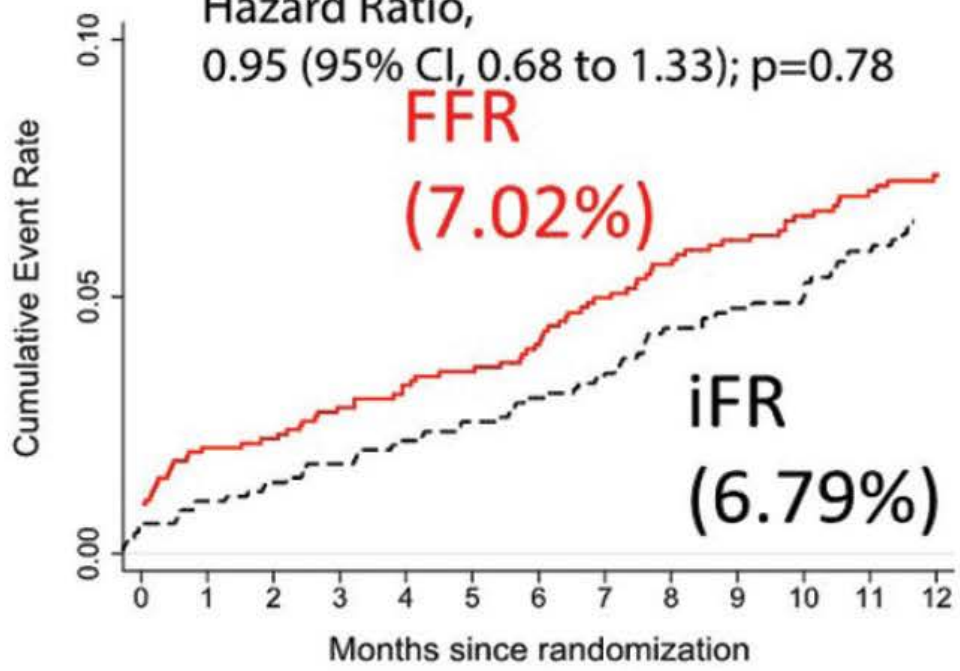
- ✓ *iFR offers a more convenient and cost-effective alternative to FFR*
- ✓ *iFR does not require the administration of a pharmacological vasodilator to induce hyperemia. It eliminates the hyperemia-induced discomfort for the patient*
- ✓ *iFR can be enhanced by iFR-pullback. It is especially useful in diffuse disease and serial lesions, which provides the possibility to display iFR changes over the course of the vessel to create a hemodynamic map (individual estimation of each stenosis)*
- ✓ *Angiography co-registration available*

IFR-pullback. Angiography co-registration

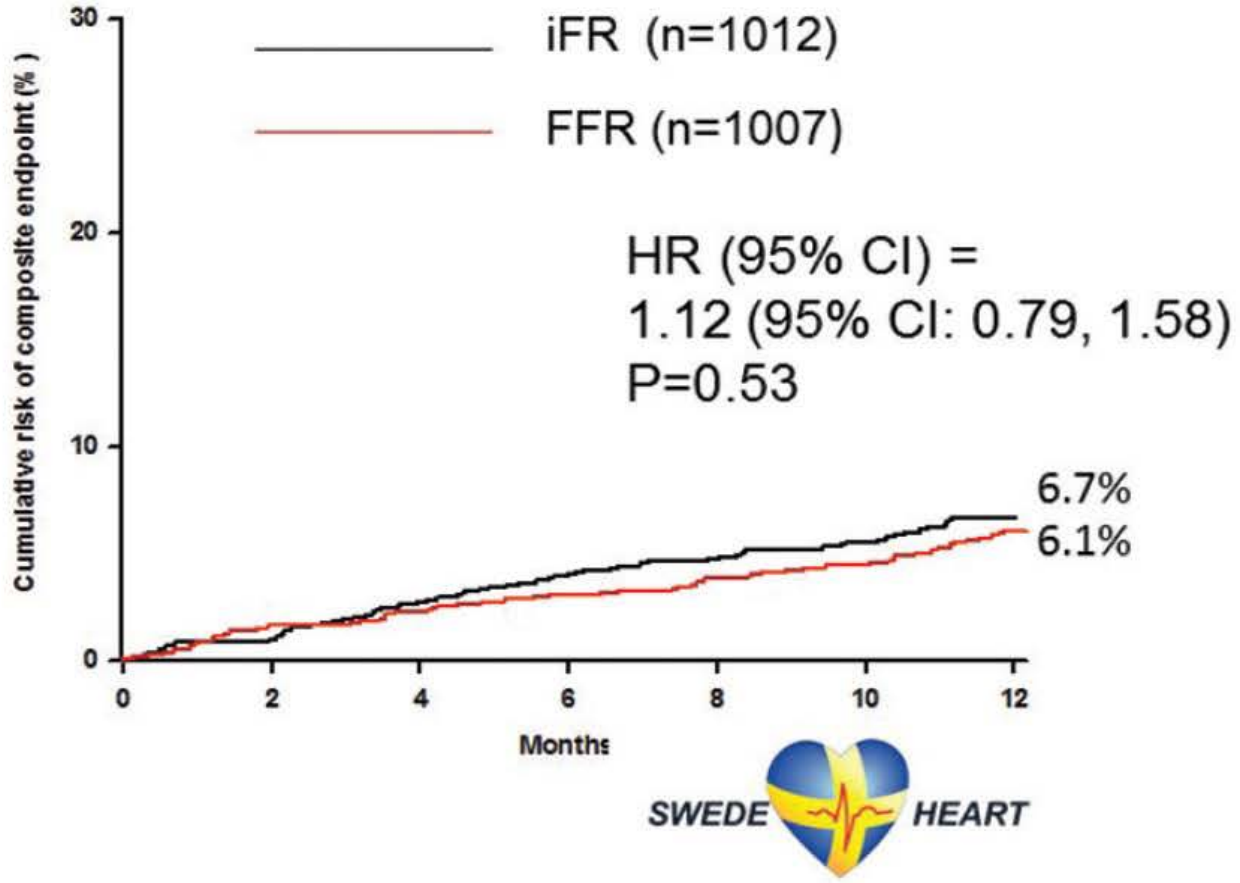


Pull back pressure recordings. (Left), difuse disease. (Right), focal step up in distal vessel with no gradient across circumfex ostium

Two large multicenter studies (DEFINE-FLAIR and SWEDEHEART) proved the non-inferiority of iFR towards FFR



DEFINE FLAIR



SWEDE HEART

DEFINE-FLAIR STUDY

- ✓ *Multicenter, international, randomized, blinded study*
- ✓ ***Primary endpoint:*** *1-year risk for MACE (cardiovascular death, nonfatal myocardial infarction, unplanned revascularization)*
- ✓ *2492 patients were included, 1242 in the iFR and 1250 in the FFR-group*.

The 1-year analysis showed comparable results regarding the endpoints, confirming the non-inferiority of iFR towards FFR.

- ✓ The length of the procedure time was significantly shorter in the iFR-group (iFR 40.5 min, FFR: 45.0 min; P < 0.001)
- ✓ Less patients suffered from adverse effects like angina pectoris and dyspnea (3.1% vs 30.8%, P < 0.001)
- ✓ When compared to FFR, iFR was identified as more economically advantageous.

SWEDEHEART STUDY

- ✓ *Multicenter, randomized, clinical study*
- ✓ ***Primary endpoint:*** *1-year risk for MACE (cardiovascular death, nonfatal myocardial infarction, unplanned revascularization*
- ✓ *2037 patients, 1019 received iFR and 1018 received FFR.*
- ✓ ***Major inclusion criteria:*** *Patients with suspected stable angina pectoris or unstable angina pectoris/NSTEMI with a clinical indication for physiology-guided assessment of coronary lesions (30-80% stenosis grade)*
- ✓ ***Major exclusion criteria:***
- ❑ *Known terminal disease with a life expectancy <1 year*
- ❑ *Unstable hemodynamics (Killip class III-IV)*
- ❑ *Inability to tolerate adenosine*
- ❑ *Previous CABG with patent graft to the interrogated vessel*
- ❑ *Heavily calcified or tortuous vessel where inability to cross the lesion with a pressure wire was expected*

SWEDEHEART STUDY

The 1-year analysis of endpoints confirmed the non-inferiority of the iFR-method.

- ✓ *Especially in uncertain cases, where iFR and FFR results differ, the data indicate that iFR provides more accurate results.*
- ✓ *iFR was superior to FFR regarding procedural discomfort*

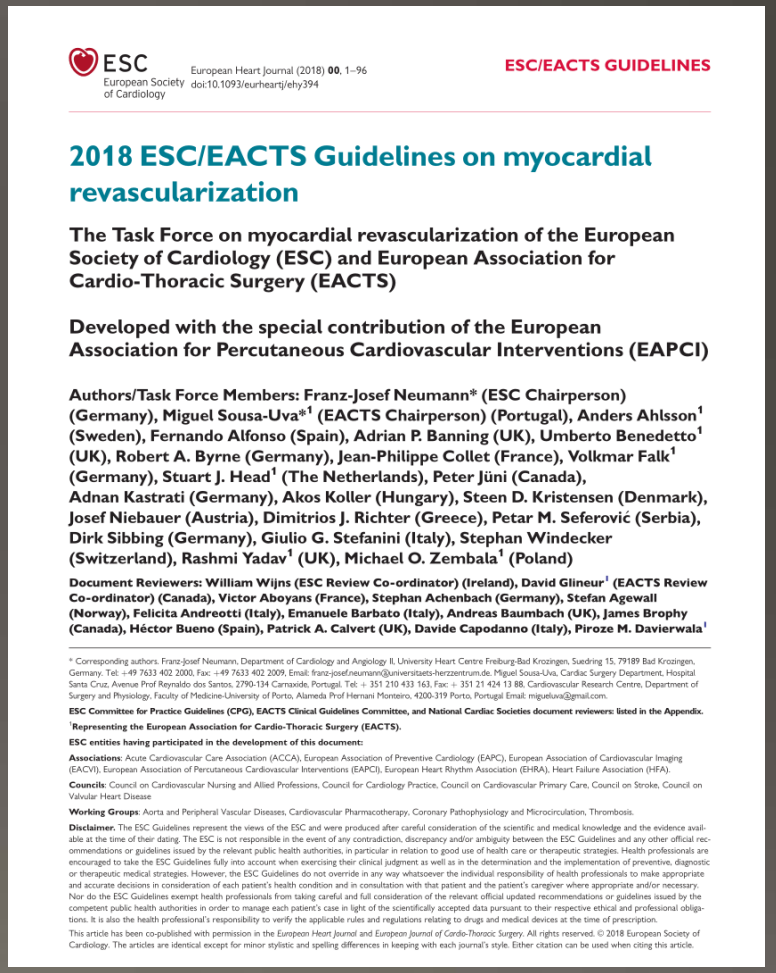
SAFETY OF INTRACORONARY SENSOR-WIRE MEASUREMENTS

TRANSIENT BRADYCARDIA	*CORONARY SPASM*	*VENTRICULAR FIBRILLATION*
1.7 %	*2%*	*0.2%*

ESC/EACTS MYOCARDIAL REVASCULARIZTION GUIDELINES

- *FFR initially adopted as a ClassIA recommendation in the ESC/ECTS guidelines of 2014 on myocardial revascularization*

- *Besides FFR, iFR adopted as a **CLASS IA** recommendation in the ESC/EACTS guidelines of 2018.*



ESC European Society of Cardiology

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ESC/EACTS GUIDELINES

2018 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)

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Councils: Council on Cardiovascular Nursing and Allied Professions, Council for Cardiology Practice, Council on Cardiovascular Primary Care, Council on Stroke, Council on Valvular Heart Disease

Working Groups: Aorta and Peripheral Vascular Diseases, Cardiovascular Pharmacotherapy, Coronary Pathophysiology and Microcirculation, Thrombosis.

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