

Anatomical and Functional Approaches for Bifurcation Lesions **“CROSS and PERFECT” Trials**

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On behalf of CROSS and PERFECT investigators.

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Current RCTs for Bifurcation Lesions

Evaluation of the Benefit of Complex Stenting

Trials

Comparison

NORDIC,

Single branch stenting

BBK,

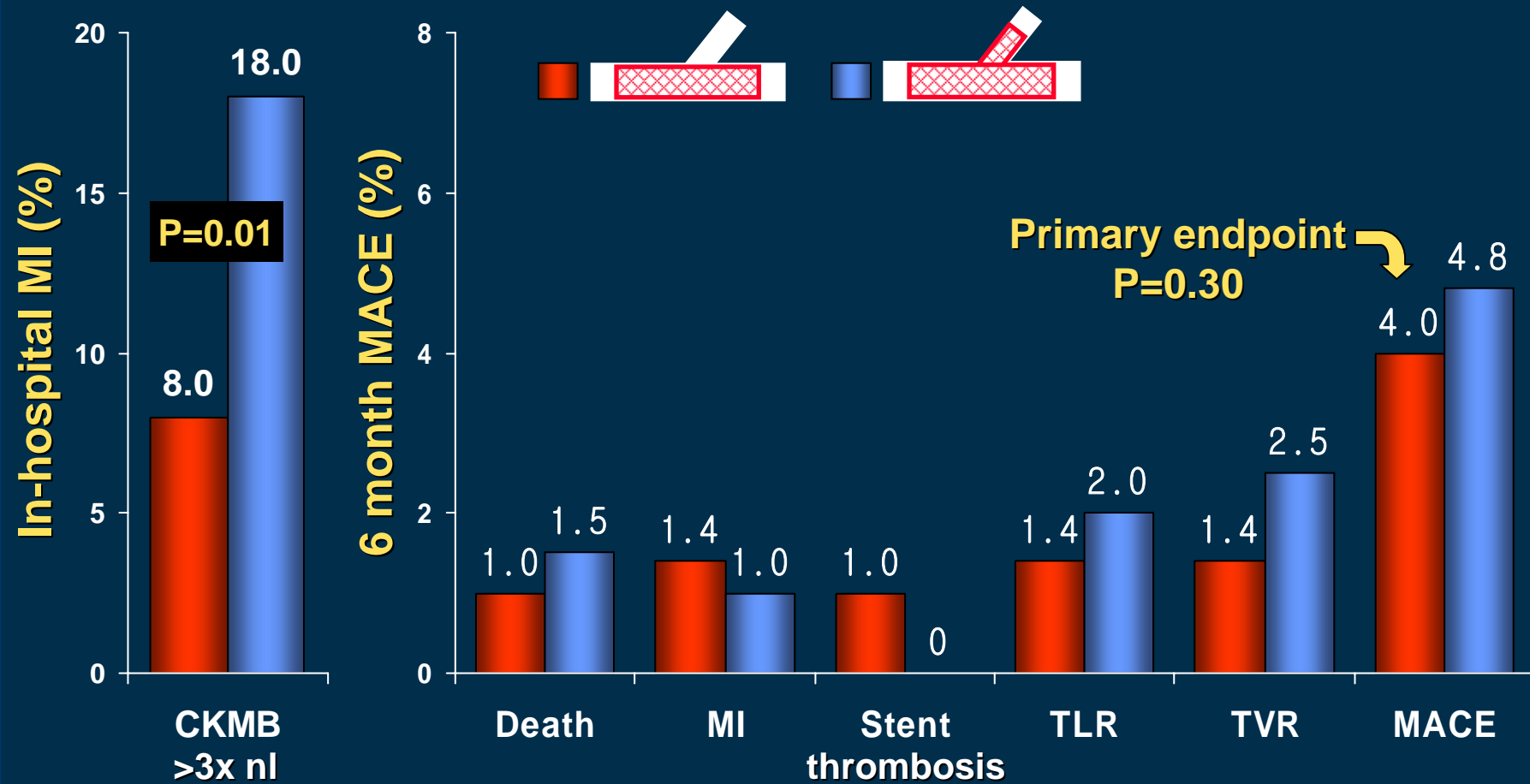
Vs.

Double branch stenting

CACTUS

Nordic Bifurcation Study (413 pts)

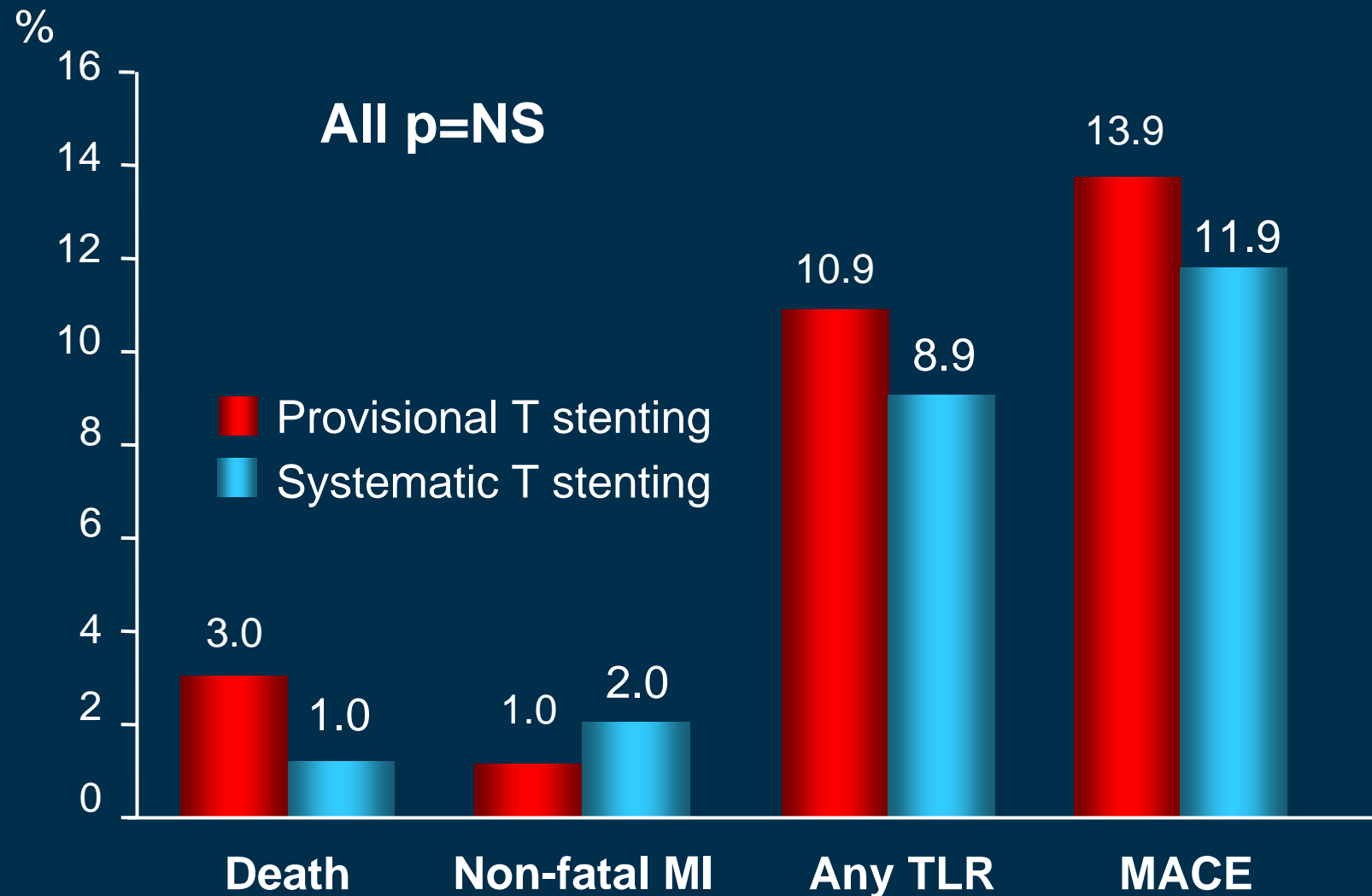
Single vs. Two



Steigen T. et al; Circulation 2006;114:1955-61

BBK trial (202 pts)

Provisional T vs. Systemic T

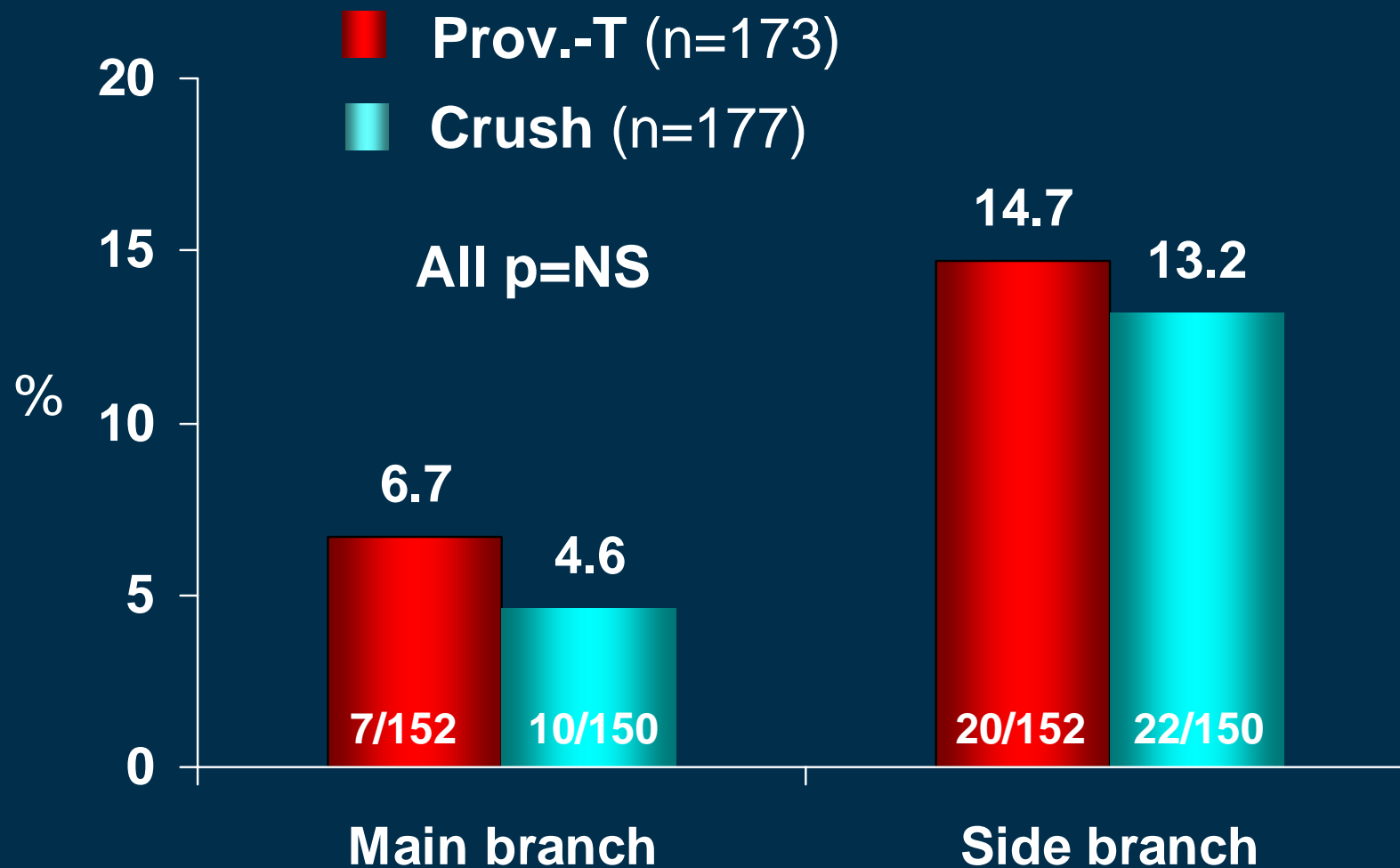


Ferenc M. et al, *Eur Heart J.* 2008;29:2859

CACTUS trial (350 pts)

Provisional T vs. Crush

6-Month In-segment Restenosis



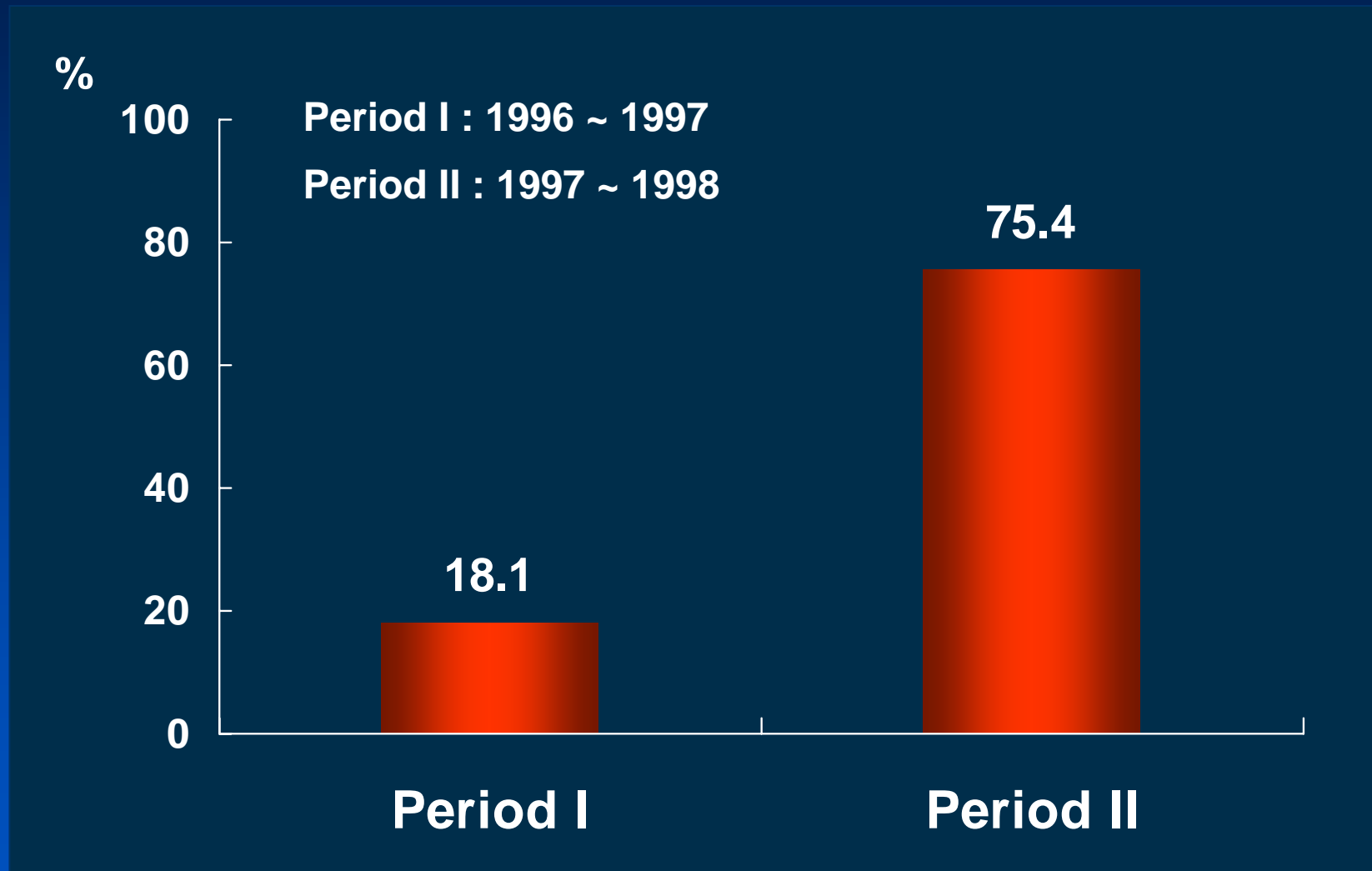
Simple Message From Trials

- Single-DES is good when good TIMI flow in the side branch is maintained.
- Two-DESs is also good with optimal stenting technique.

However, several issues remain uncertain.

- ✓ Need for kissing balloon inflation
- ✓ Impact of current DES design on the SB occlusion
- ✓ Role of IVUS guidance
- ✓ Limitation of angiographic assessment
- ✓ Benefit of functional assessment
- ✓ Need of complex stenting strategy according to the lesion classification
- ✓ Clinical implication of dedicated bifurcation QCA software

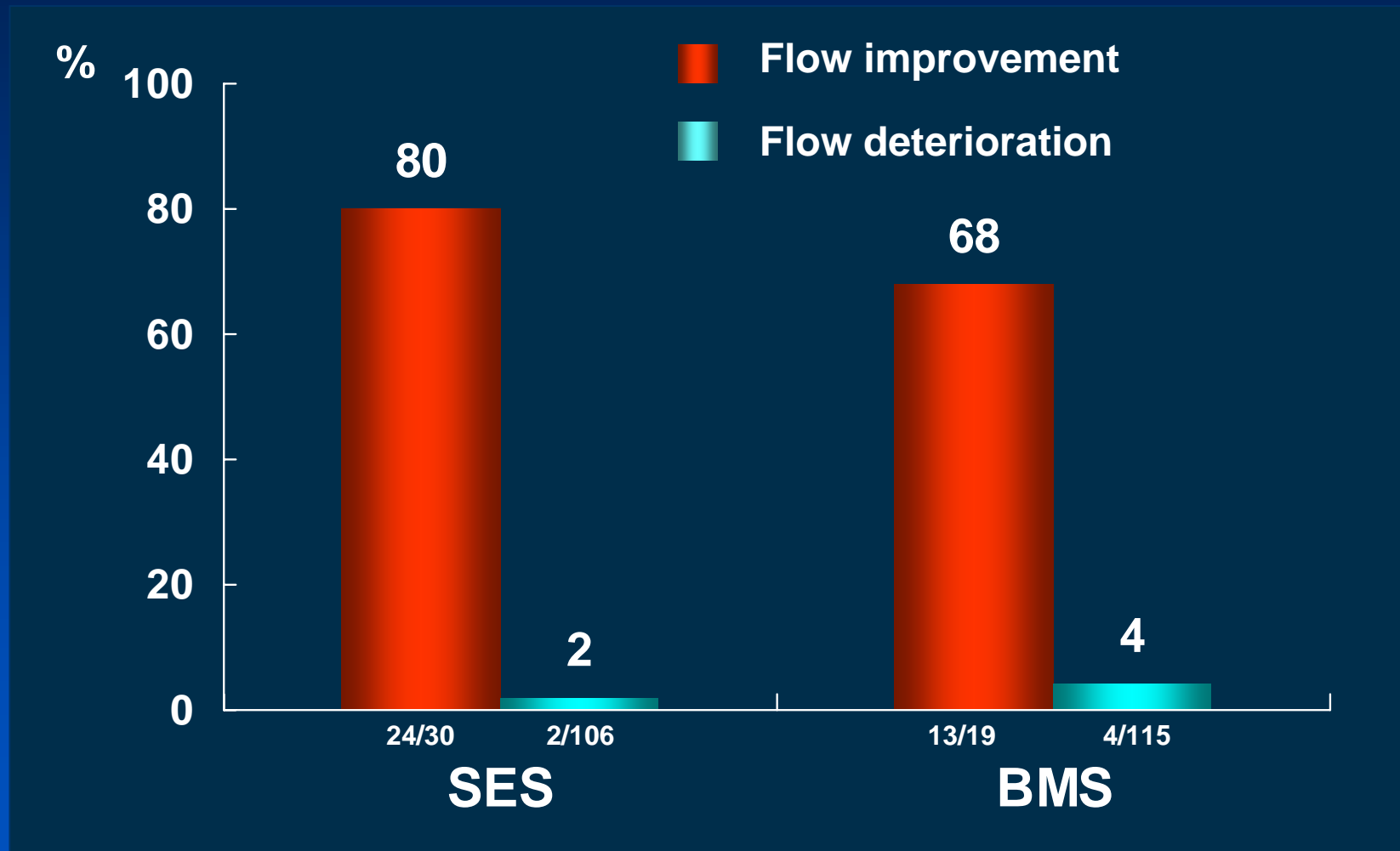
Increase of Kissing Balloon Inflation



Lefevre et al. Catheter Cardiovasc Intervent 2000;49:274

SB flow is improving over time.

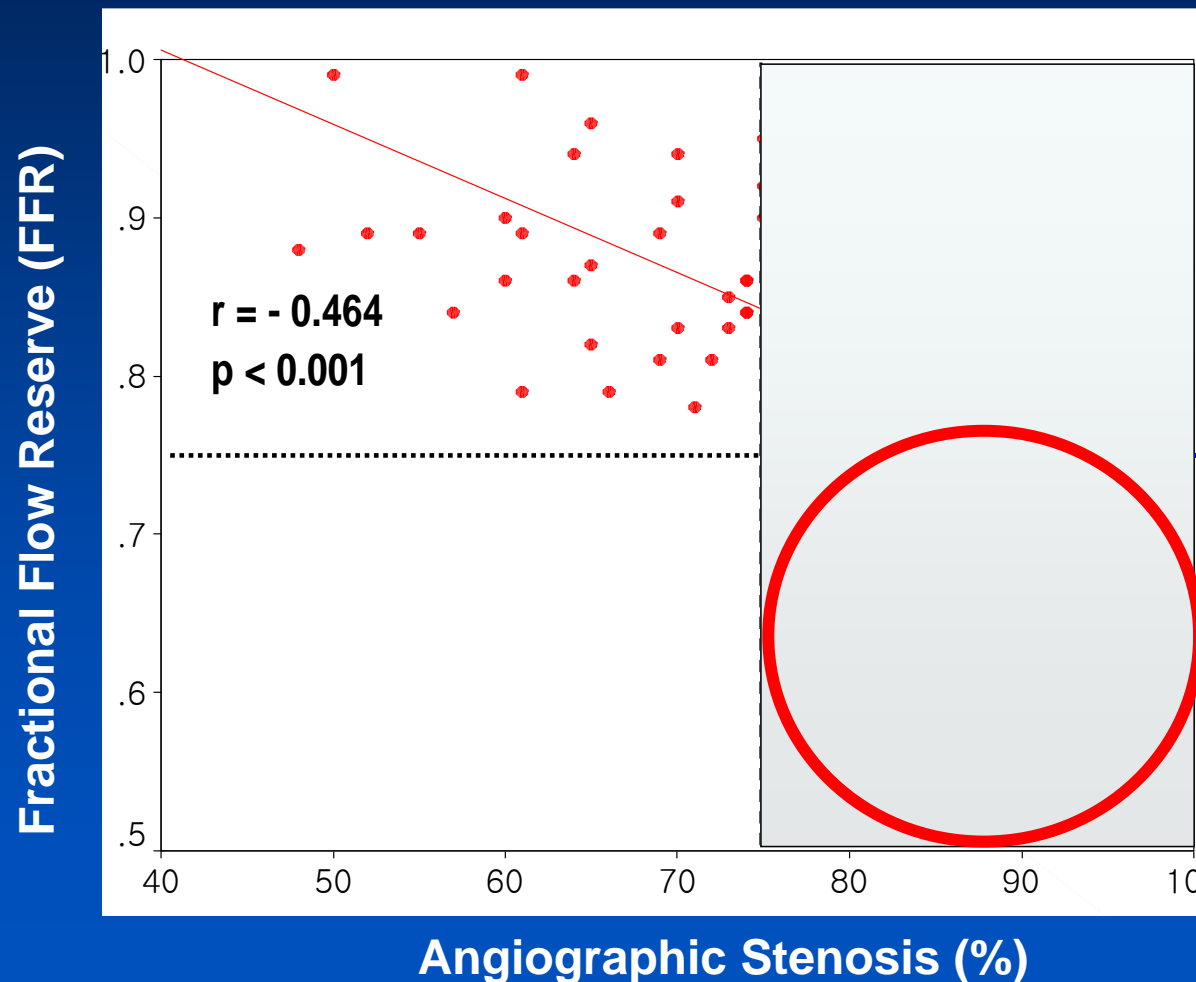
SB TIMI Flow at Follow-up in RAVEL Substudy



Tanabe T et al. Am J Cardiol 2002;90:937

Angiography has limitation to assess the functional SB flow.

QCA vs FFR

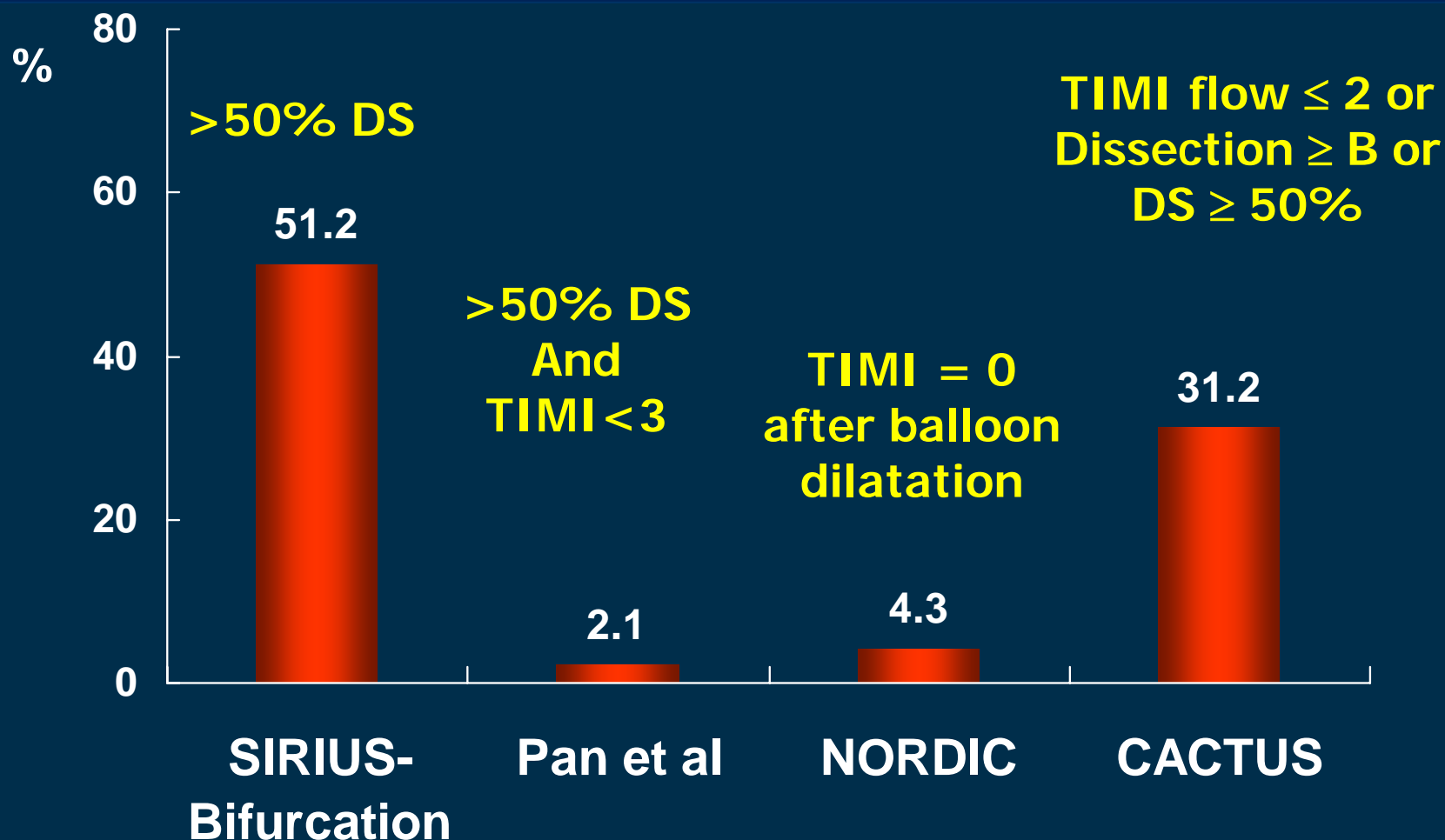


*Only 27% among
SB with > 75%
has FFR < 0.75*

Koo BK et al JACC 2005; 46: 633

When do we need two stents ?

% Cross-over to 2 stents in provisional group

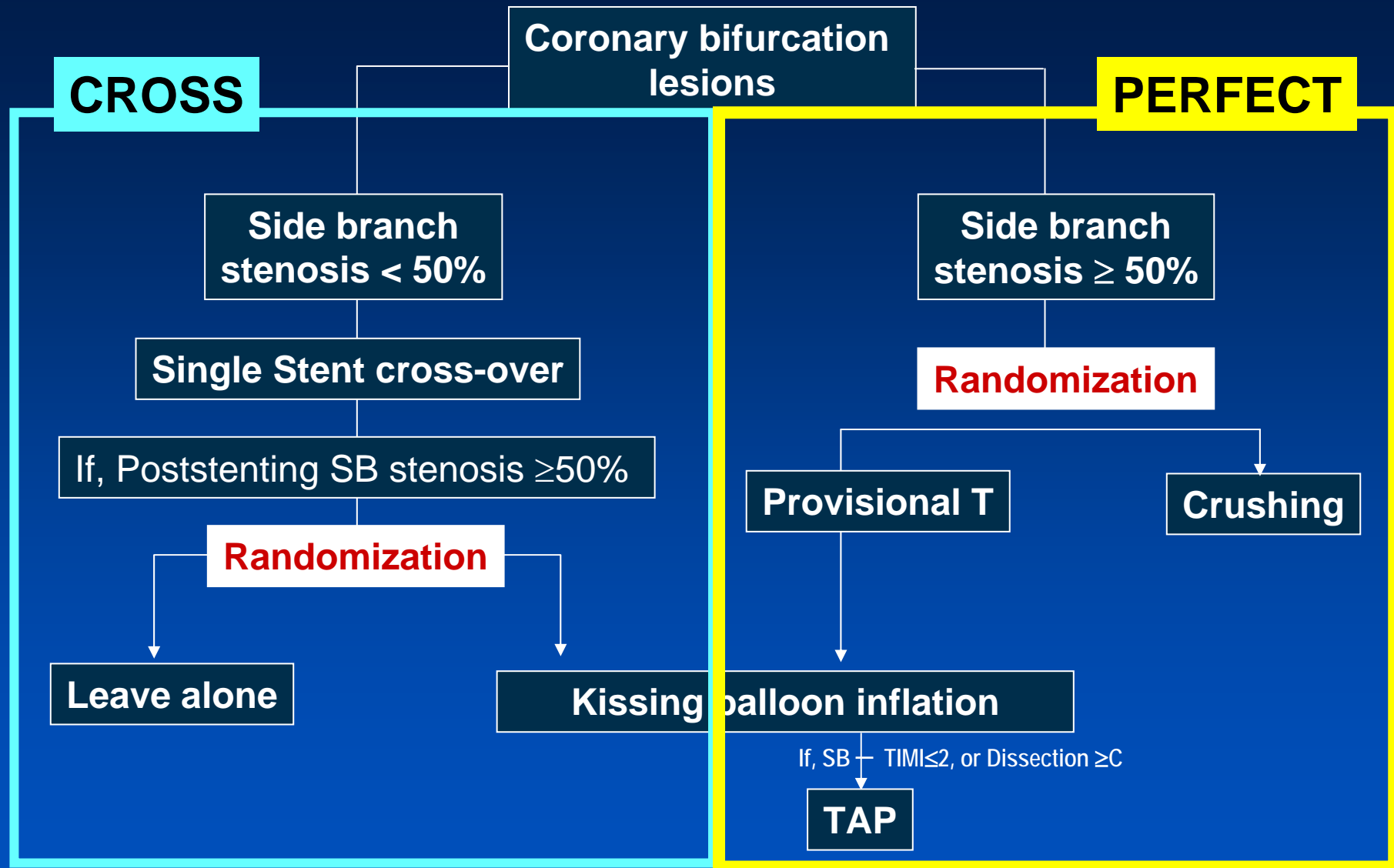


- Colombo A, et al. SIRIUS Bifurcation Study, Circulation 2004;109:1244-9
- Pan M, et al. Am Heart J 2004;148:857-64.
- Steigen TK, et al. NORDIC Study, Circulation 2006;114:1955-61.

What is CROSS and PERFECT trials ?

Study Design

CROSS & PERFECT Trials



PI: Seung-Jung Park, MD

Administration and Sites

Sites (15 in Korea)

Asan Medical Center
Aju University Hospital
Busan Saint Mary's Hospital
Busan University Hospital
Catholic University, Kangnam St. Mary's Hospital
Chungju Saint Mary's Hospital
Chungnam National University Hospital
Hallym University Sacred Heart Hospital
Kangwon University Hospital
Korea Veterans Hospital
Kyungsang University Hospital
Soonchunhyang University Seoul Hospital
Soonchunhyang University Bucheon Hospital
Soonchunhyang University Cheonan Hospital
Ulsan University Hospital

PI Seung-Jung Park, MD

Sponsor

KSCVI, CVRF

Angiographic core lab

CVRF

IVUS core lab

CVRF

Data management

CVRF, Center for Biostatistics

Clinical Event Committee

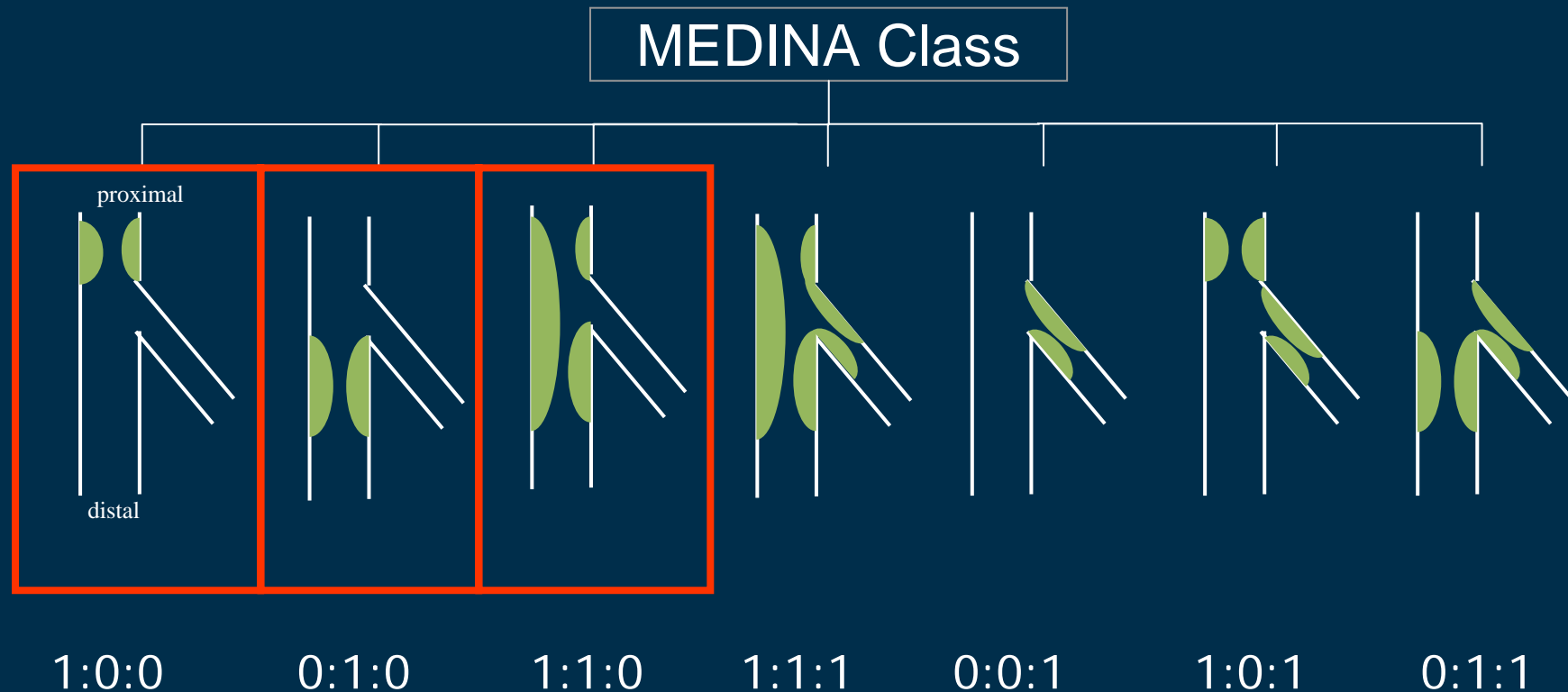
CVRF



Choice of optimal strategy for bifurcation lesions
with normal side branch

CROSS Trial

Bifurcations without SB Stenosis



CROSS Trial Study Design

- Primary end points : angiographic FU outcomes
 - Frequency of post-procedural stent jail according to the DES type
 - 8-month diameter stenosis in SB between the kissing balloon vs. leave alone
- Design and hypothesis : Two-step randomization
 - H_a for 'stent jail study' :
SES > PES, ZES > PES, SES = ZES
 - H_a for 'kissing balloon study' :
Leave alone \geq Kissing balloon

Inclusion Criteria

1. Clinical

- Patients with angina and documented ischemia or patients with documented silent ischemia
- Patients who are eligible for intracoronary stenting
- Age >18 years, <75 ages

2. Angiographic

- **De novo lesion** located in a major bifurcation point with the MEDINA classification type 1.1.0, 1.0.0, or 0.1.0
- **Main vessel** : ≥ 2.5 mm in vessel size, $\geq 50\%$ in diameter stenosis and ≤ 50 mm in lesion length by visual estimation, in which the lesion is **covered with ≤ 2 stents**
- **Side branch** : ≥ 2.0 mm in vessel size and $< 50\%$ diameter stenosis by visual estimation

CROSS Trial

Bifurcation without SB stenosis by angiography

1st Randomization: type of stent

• Stratified by sites

SES
(N=200)

PES
(N=200)

ZES
(N=200)

After MV stenting

SB DS \geq 50% & TIMI 3 flow

TIMI \leq 2 flow

SB DS < 50% & TIMI 3 flow

2nd Randomization

• Stratified by sites

Registry

1. Treatment at the operator's discretion

Registry

1. IVUS exam in MV
2. FFR in SB (selected sites)

Kissing balloon group
(estimated N=90)

1. FFR in SB before kissing balloon
2. Rewire into SB
3. Kissing balloon inflation

Leave it alone group
(estimated N=90)

1. IVUS exam in MV
2. FFR in SB (selected sites)

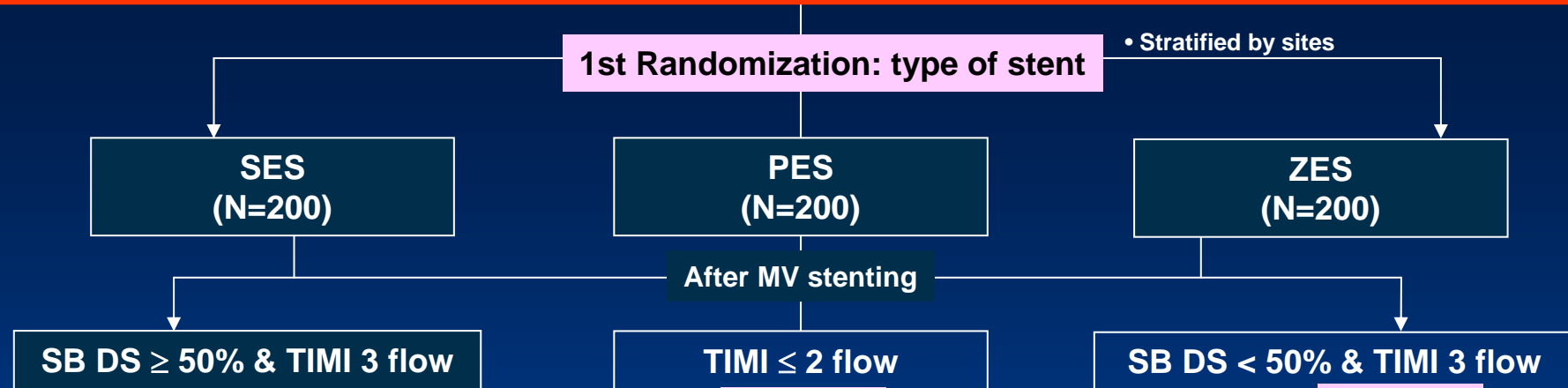
SB DS < 70% & TIMI 3
Dissection none or \leq class B

1. IVUS in MV
2. FFR in SB (selected sites)

SB DS \geq 70% or TIMI \leq 2 or
Dissection \geq class C

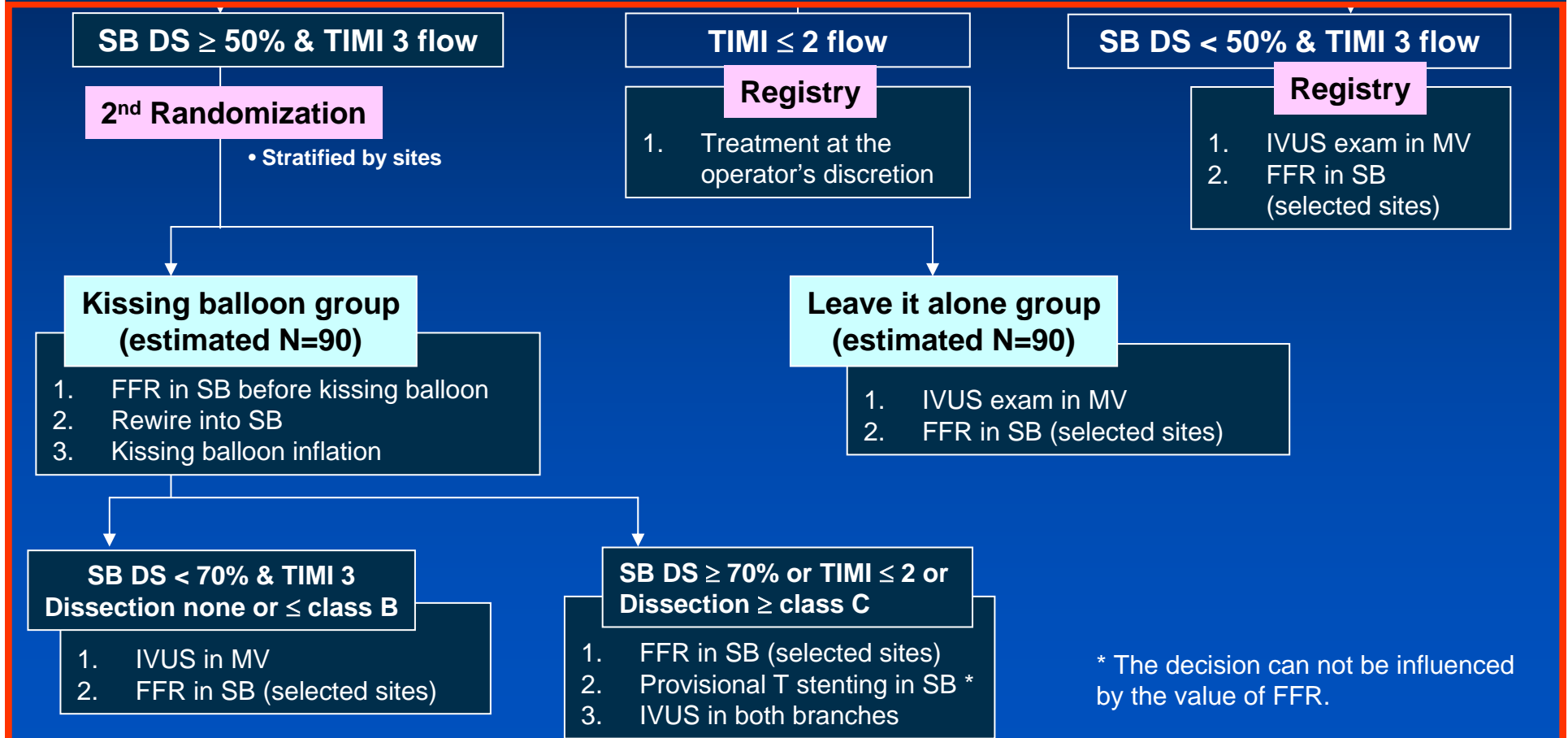
1. FFR in SB (selected sites)
2. Provisional T stenting in SB *
3. IVUS in both branches

* The decision can not be influenced by the value of FFR.



**Incidence of SB occlusion
according to DES type**

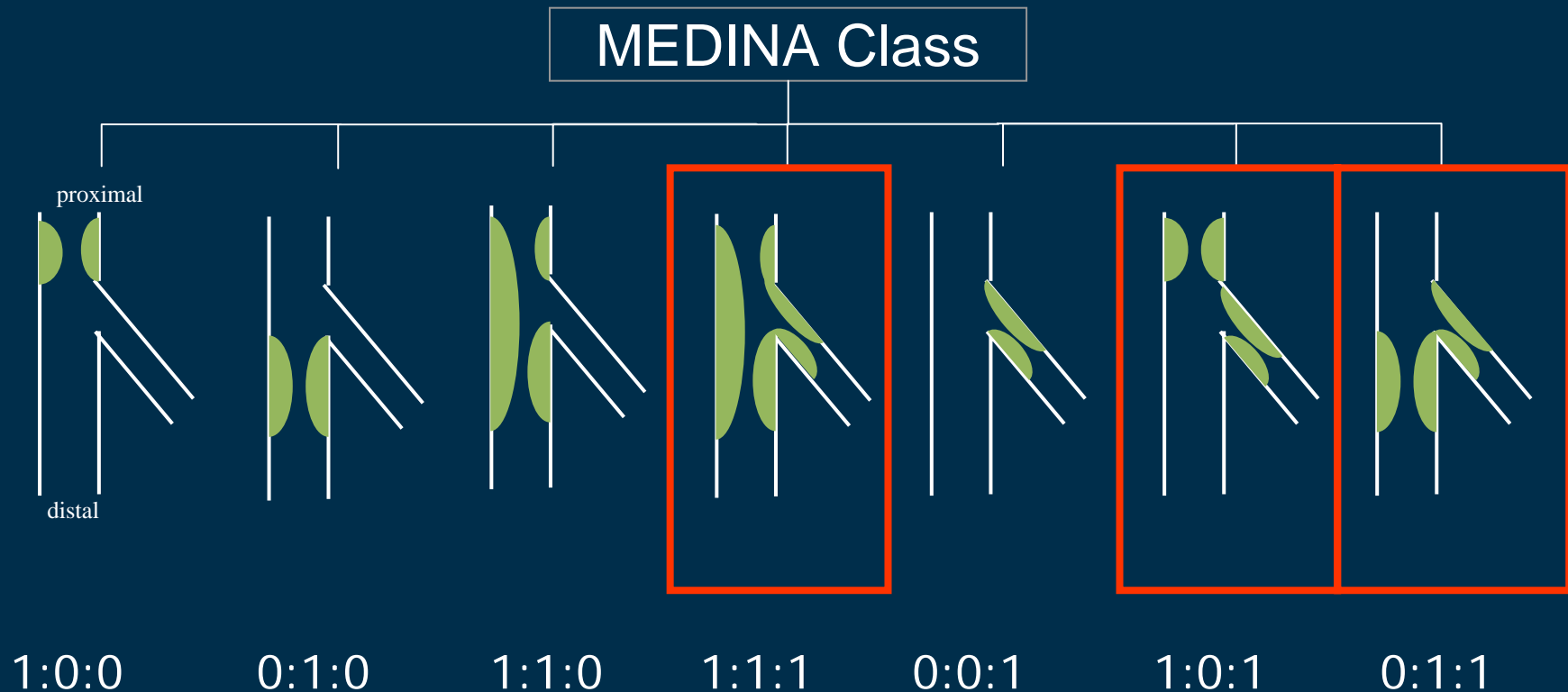
- Influence of Kissing Balloon Inflation
- Morphologic Evaluation by IVUS
- Functional Assessment by FFR



OPTimal StEnting StRategy For TruE BifurCaTion

PERFECT Trial

Bifurcations with SB Stenosis



PERFECT Trial Study Design

- Primary end point : angiographic FU outcome
 - 8-month overall restenosis rate in MB or SB
- Hypothesis for sample size estimation
 - H_a :
Provisional T \geq Crush technique

Inclusion Criteria

1. Clinical

- Patients with angina and documented ischemia or patients with documented silent ischemia
- Patients who are eligible for intracoronary stenting
- Age >18 years, <75 ages

2. Angiographic (MEDINA classification 1.1.1, 1.0.1, 0.1.1)

- **De novo lesion** located in a major bifurcation point with the MEDINA classification type 1.1.0, 1.0.0, or 0.1.0
- **Main vessel** : ≥ 2.5 mm in vessel size, $\geq 50\%$ in diameter stenosis and ≤ 50 mm in lesion length by visual estimation, in which the lesion seems to be **covered with ≤ 2 stents**
- **Side branch** : ≥ 2.0 mm in vessel size, $\geq 50\%$ in diameter stenosis, and < 20 mm in lesion length by visual estimation, in which the lesion seems to be **covered with 1 stent**

PERFECT Trial

True bifurcation by angiography

Wire insertion into both branches

Randomization

**Crush group
(N=240)**

1. Preprocedural IVUS in both branches
2. Predilation in the MV and SB
3. SB stenting while keeping MB stent
4. Removal of SB stent and wire
5. MV stenting
6. Rewire into the SB stent
7. Sequential high pressure balloon dilatation in both in-stent areas
8. Kissing balloon inflation
9. Postprocedural IVUS in both branches

**Crossover to
crush**

Serious dissection
necessitating urgent
stenting in SB after
predilation*

**Provisional T stenting group
(N=240)**

1. Preprocedural IVUS in both branches
2. Predilation in the MV
3. MV stenting while keeping jailed wire in the SB
4. Rewire into the SB
5. Kissing balloon inflation with low pressure at SB

Indication of SB Stenting

Angiography at SB

1.

- $\text{TIMI} \leq 2$ flow or
- $\text{DS} \geq 70\%$ or
- $\text{Dissection} \geq \text{NHLBI class C}$

* Predilation in SB is strongly discouraged.

4. Kissing balloon inflation
5. Postprocedural IVUS in both branches



Current Status

From May 2008

CROSS Trial

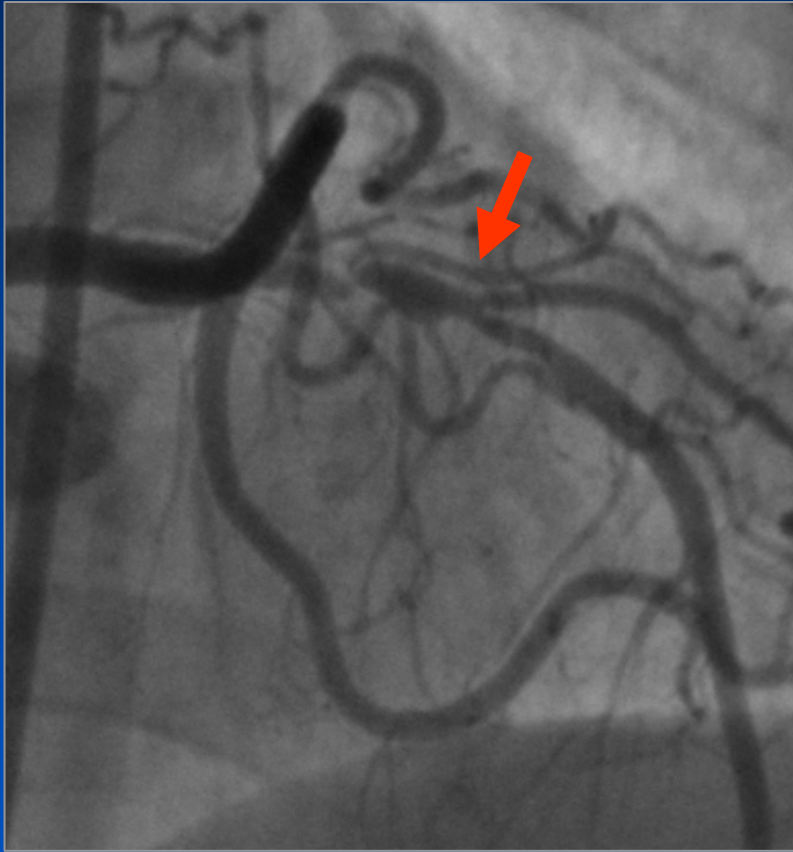
- ~ 400 enrolled
- ~ 250 randomization to kissing vs. leave alone

PERFECT Trial

- ~ 300 randomization

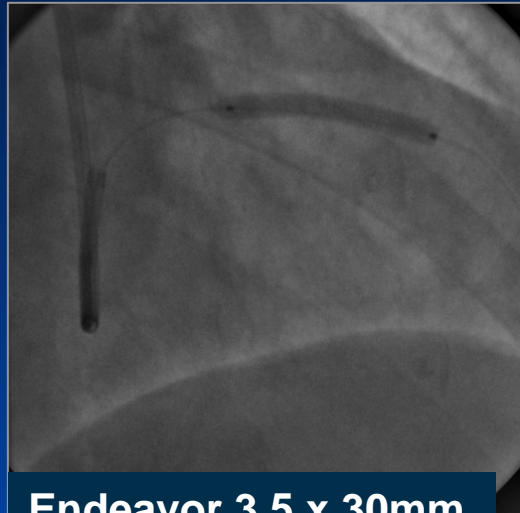
Intermediate Stenosis at SB

CROSS Patient

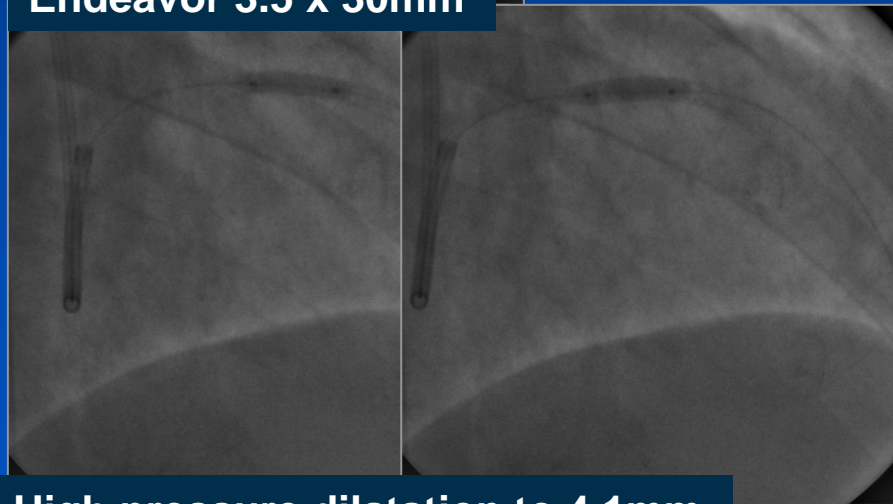


Main Branch Stenting

Randomized to Endeavor Stent



Endeavor 3.5 x 30mm



High pressure dilatation to 4.1mm



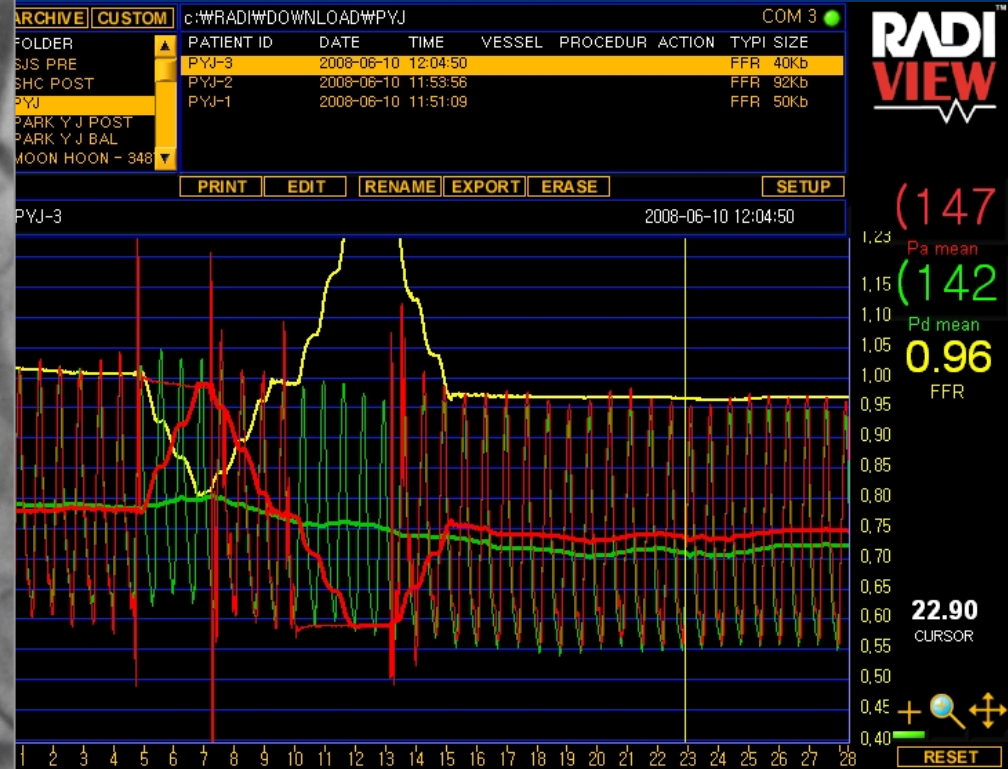
Significant SB jail with TIMI 3 flow

- FFR before kissing
- Randomization to kissing balloon



Final FFR after Kissing

- Post-procedure FFR



Final Angiogram

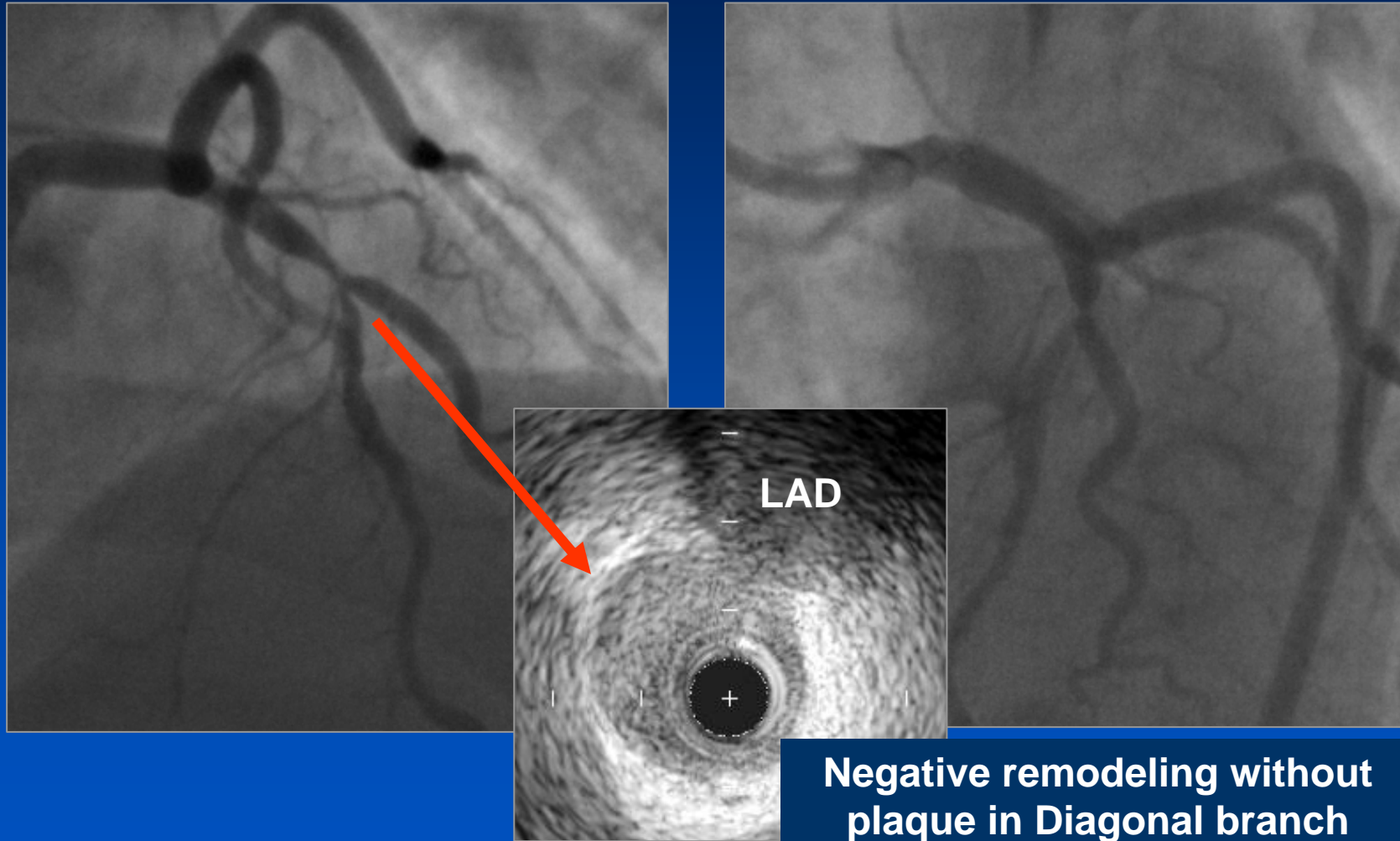


CROSS with FFR Evaluation in AMC

- 90 lesions were enrolled in AMC.
- 42 (48%) lesions were randomized to kissing B vs. leave alone due to significant stent jail ($> 50\%$) in the SB by visual estimate.
- Only 2 lesions (2%) received provisional SB stenting.
- 77 lesions (78%) received final FFR evaluation in the SB.
- Only 7 lesions (10%) showing stenosis $> 90\%$ in the SB after stenting had $\text{FFR} < 0.80$ after hyperemia.
- Negative remodeling is very often in the ostial side branch.

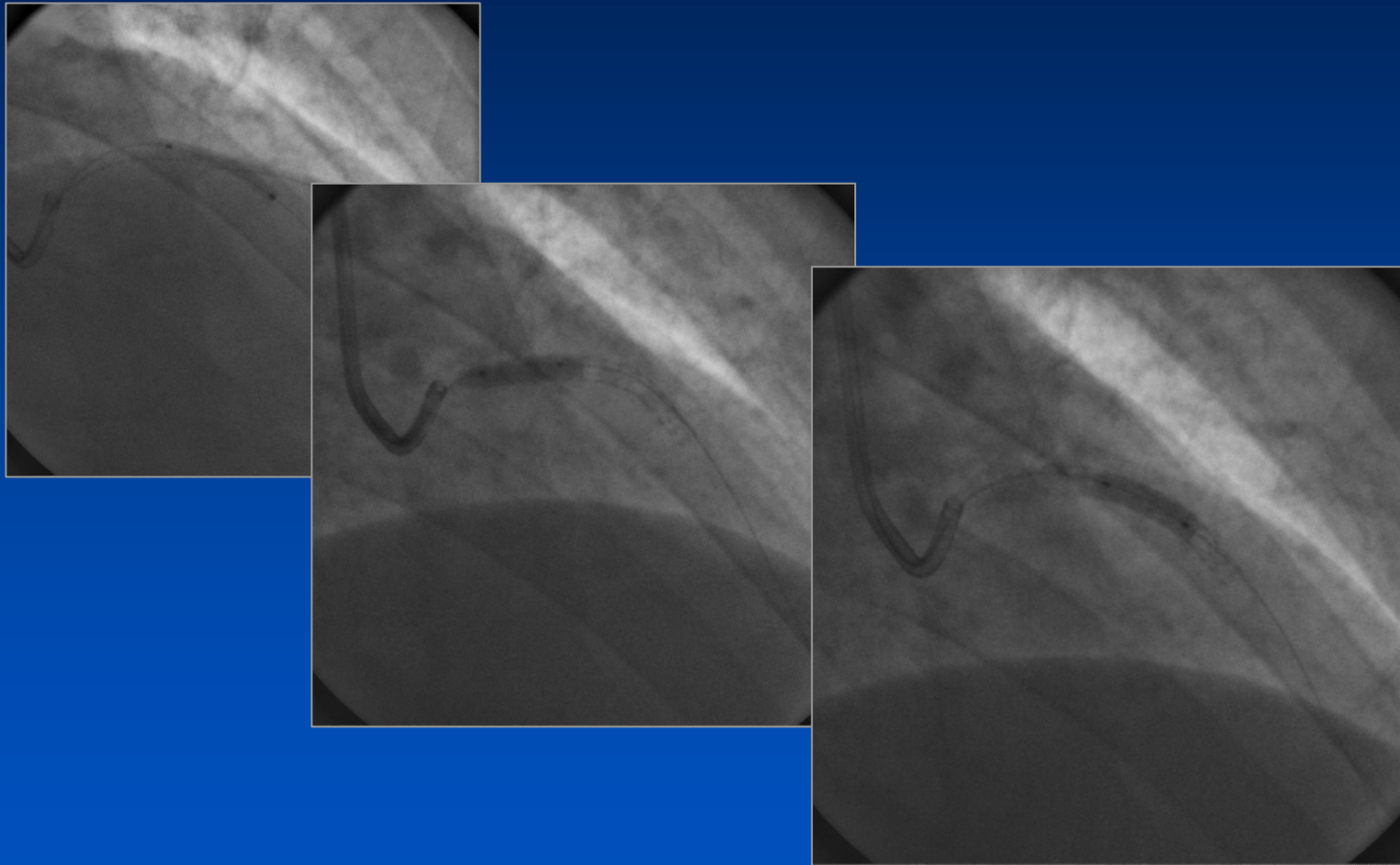
Significant Stenosis at SB

PERFECT Patient



Randomized to 1 Stent Implantation

Stenting with Cypher (3.5x33mm) and Post-dilation

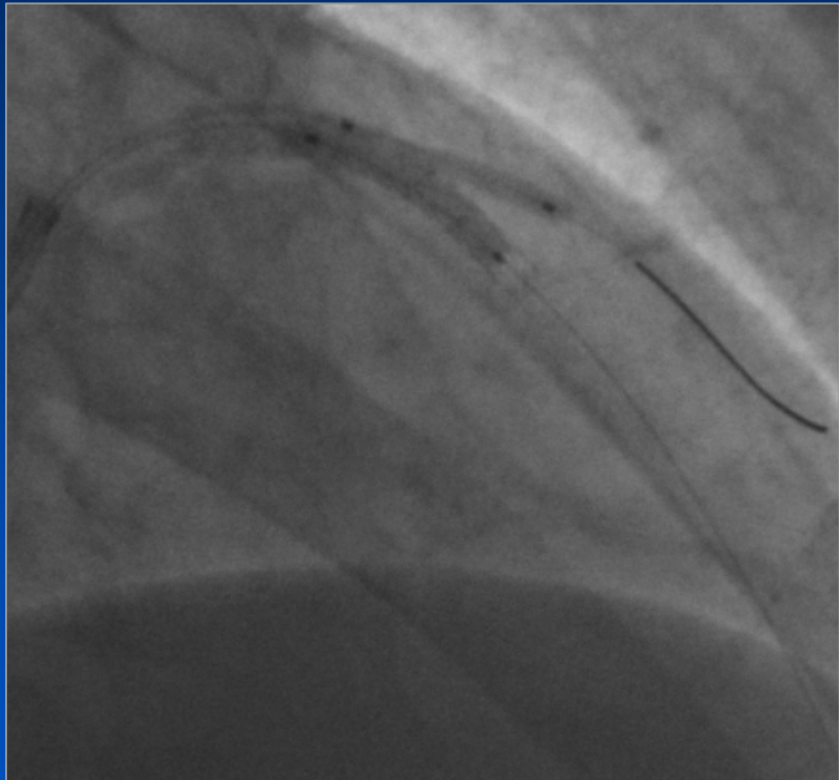


FFR Assessment

Due to TIMI 3 flow and no dissection



Kissing Balloon Inflation

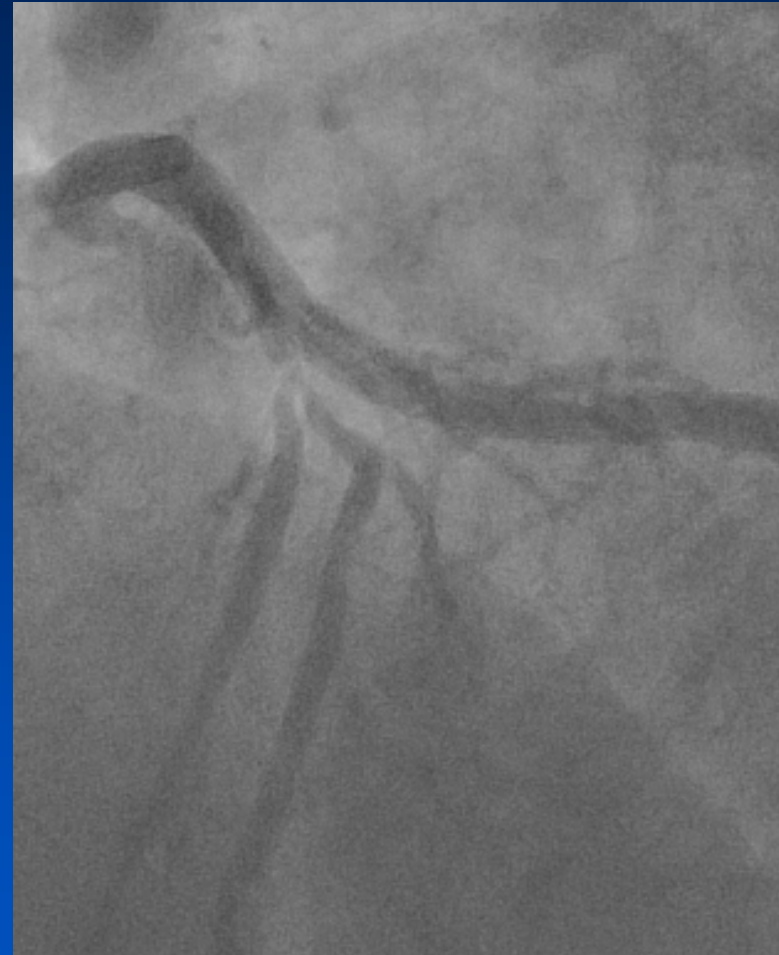


Final Result with FFR

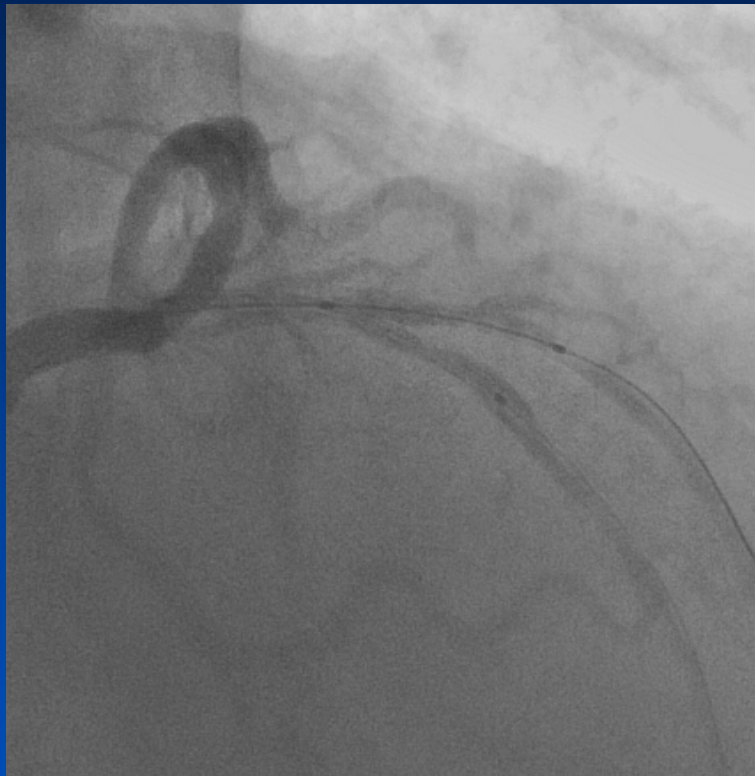


Significant Stenosis at SB

PERFECT Patient



Randomized to Crush

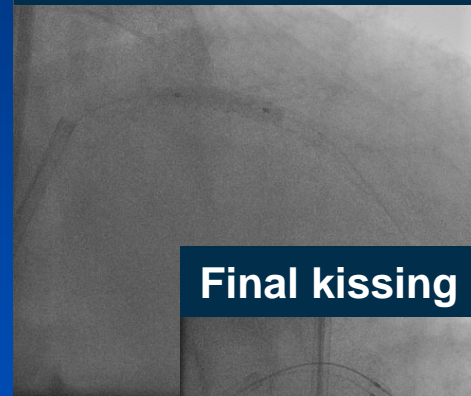


Cypher 3.5 x 28 & 3.0 x 18mm

SB stenting at 14atm



MB non-compliant
balloon to 4.1mm



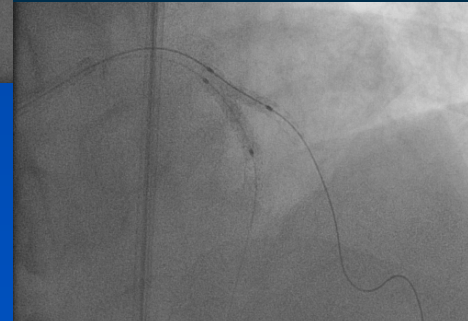
MB stenting at 8atm



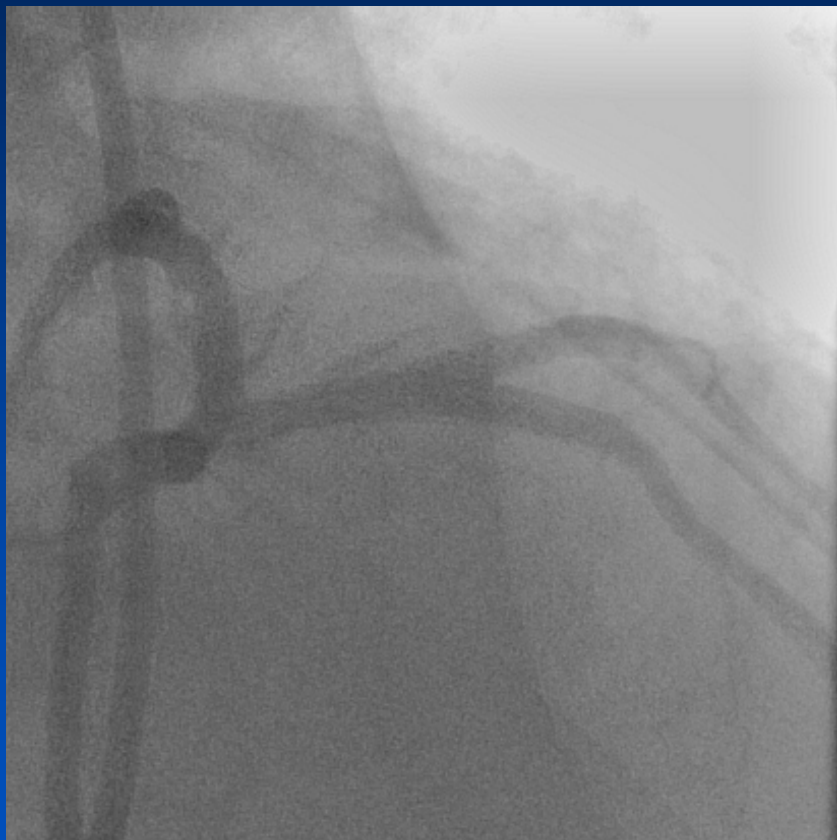
SB non-compliant
balloon to 3.3mm



Final kissing balloon

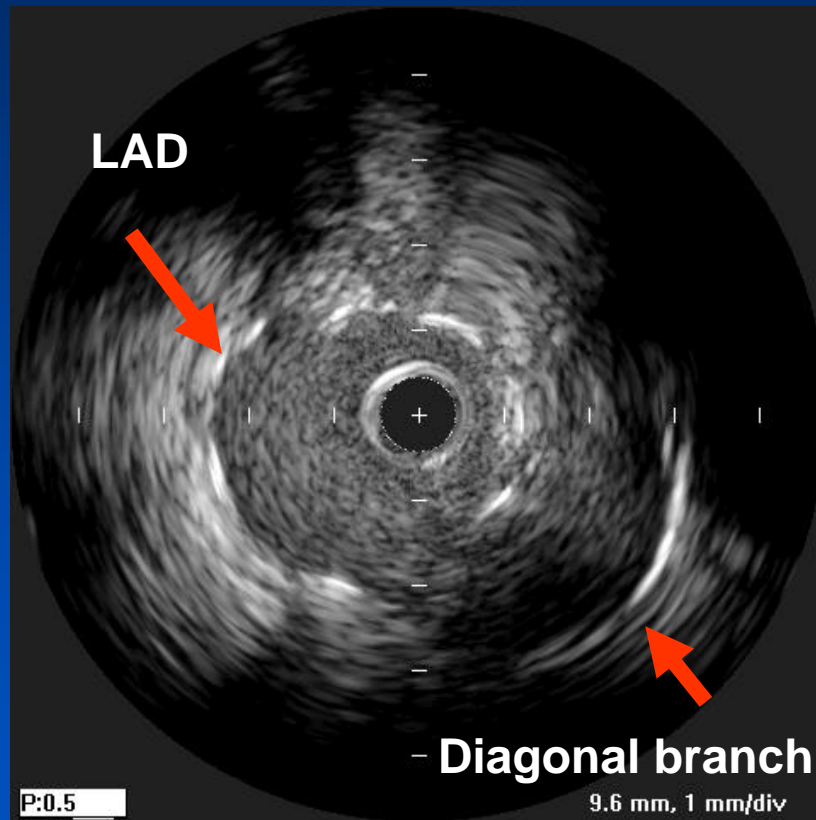


Final Angiogram

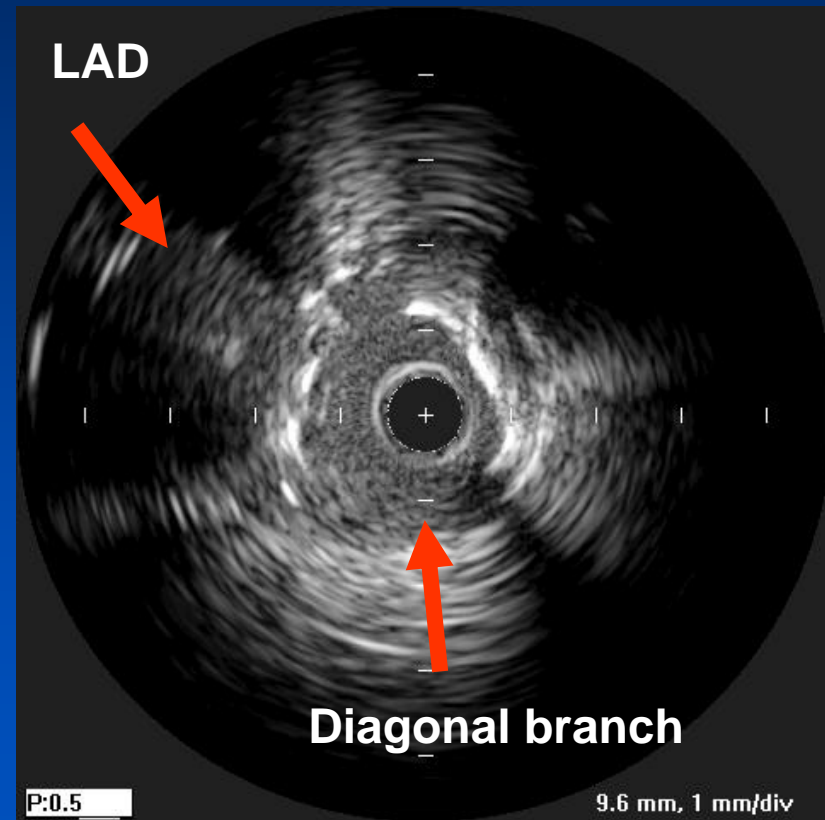


IVUS Finding

From LAD
CAS 7.49 mm²

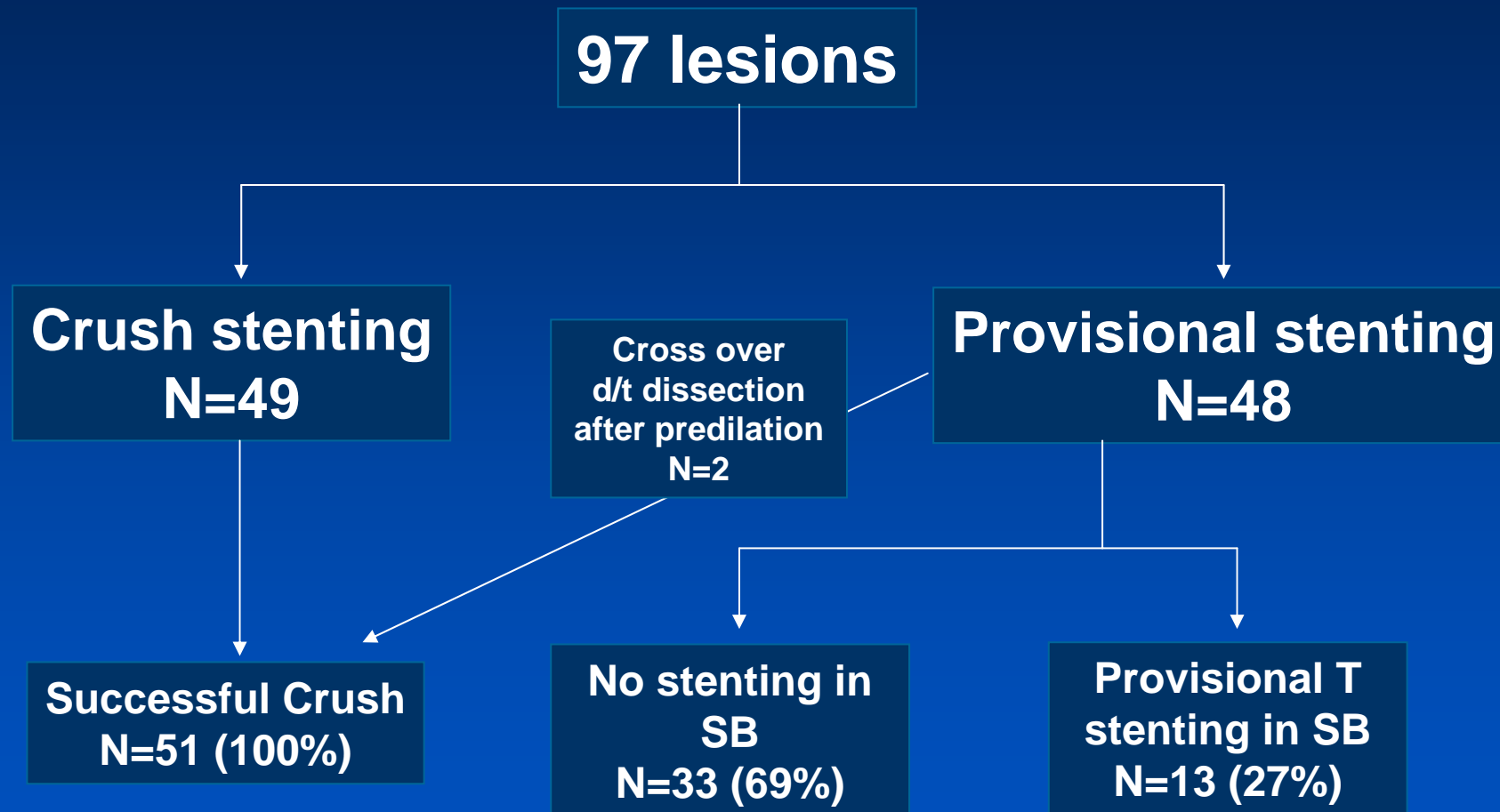


From Diag.
4.62 mm²

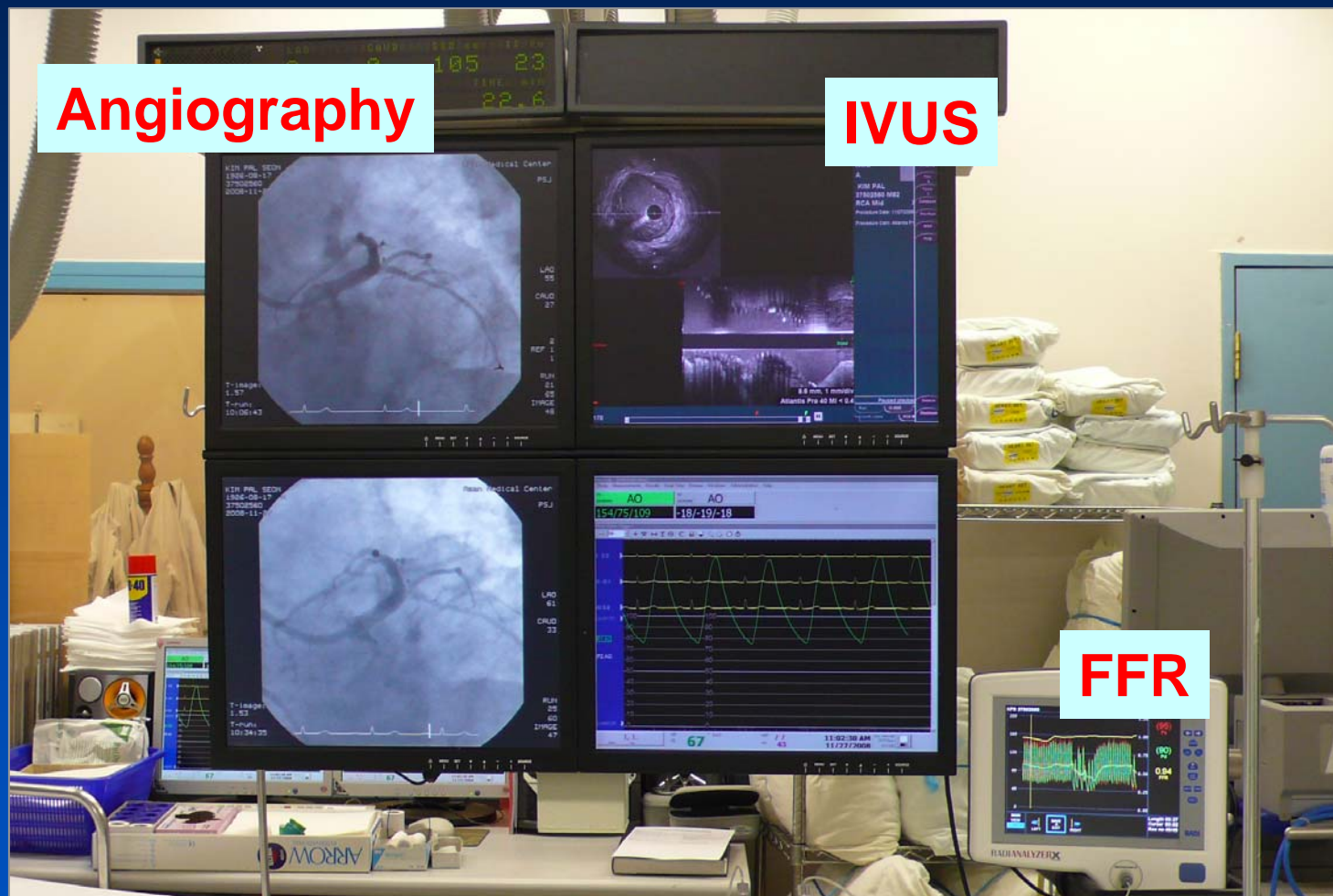


PERFECT Preliminary in AMC

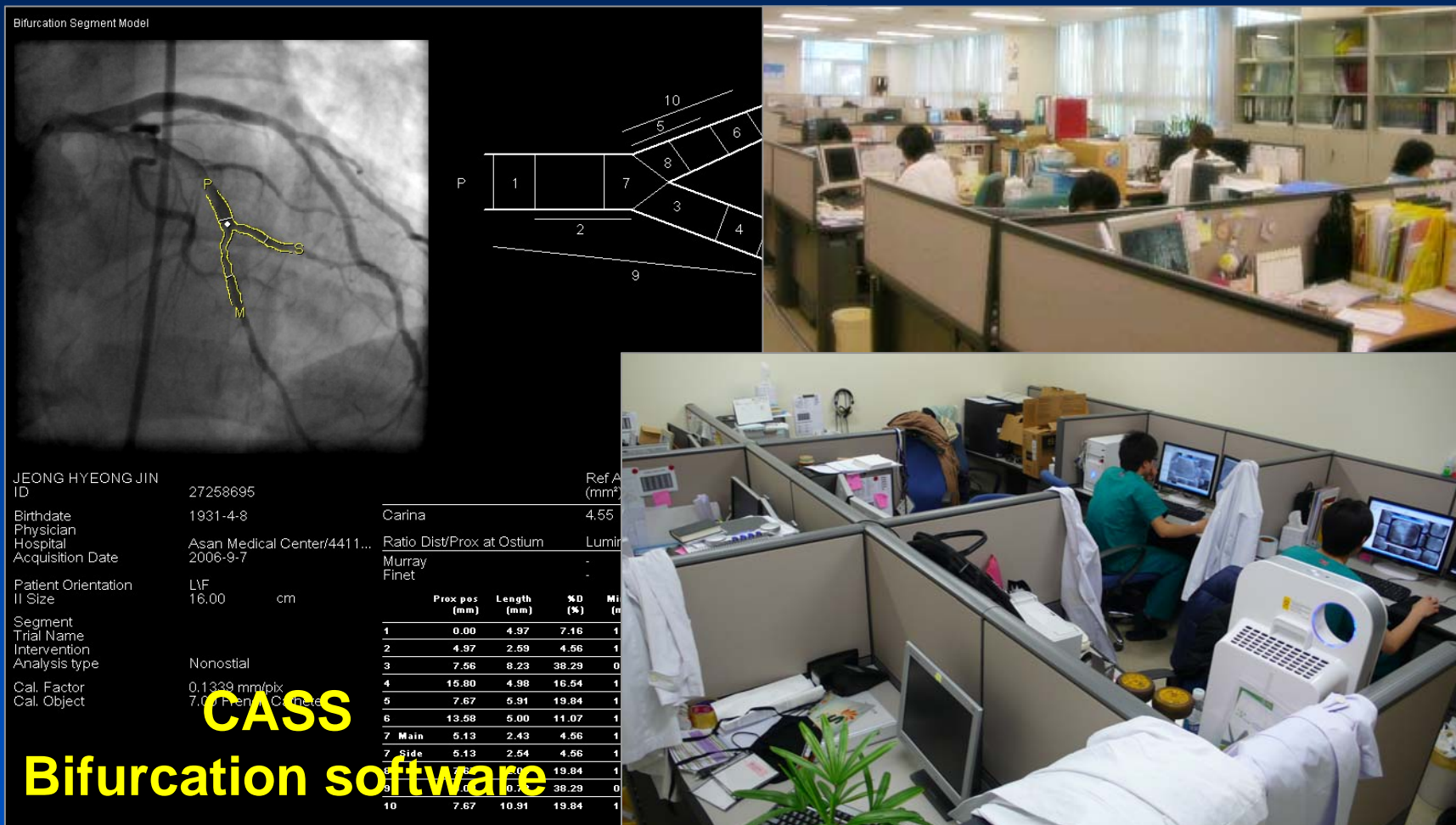
Cases in 2008



Morphological & Functional Approach



Dedicated Bifurcation QCA Software in Our Core Lab



From CROSS and PERFECT

We hope that a careful anatomical & functional evaluation by our study will provide very useful information improving the outcomes of PCI with DES for bifurcation coronary lesions.