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“FLAVOUR”

Physiology or Imaging for Revascularization Strategy

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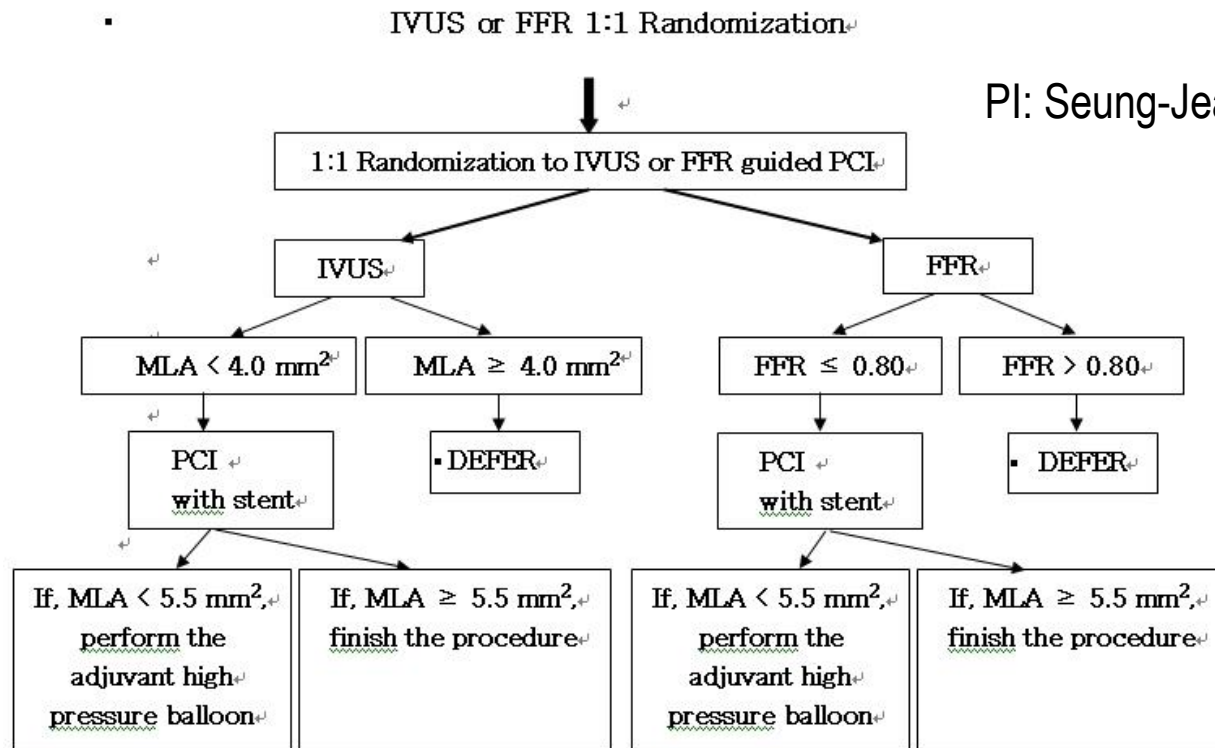
***Fractional FLow Reserve And IntraVascular Ultrasound for
Clinical OUTcomes in Patients with InteRmediate Stenosis***

Where dose the “FLAVOUR” come from?



- FAVOR study (2010)

Comparison the Clinical Outcomes between FFR Guided PCI and IVUS Guided PCI
with DES in Stable Angina Patients with Intermediate Coronary Artery Lesion



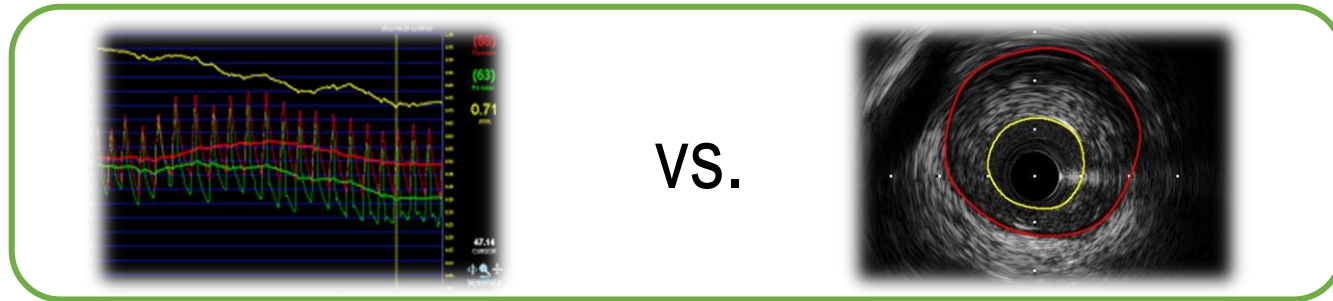


- Principal Investigators

Name	Center	Position
Seung-Jea Tahk	Ajou University Hospital	Professor
Jianan Wang	Second affiliated hospital of Zhejiang university	Professor
Bon-Kwon Koo	Seoul National University Hospital	Professor



- Primary objective
 - To compare the efficacy of FFR-guided PCI strategy with IVUS-guided PCI strategy in patients with intermediate coronary stenosis.



- Working hypothesis
 - FFR-guided PCI strategy will show non-inferior rate of patients-oriented composite outcomes (POCO) at 24 months after randomization, compared with IVUS-guided PCI strategy



• Study Design

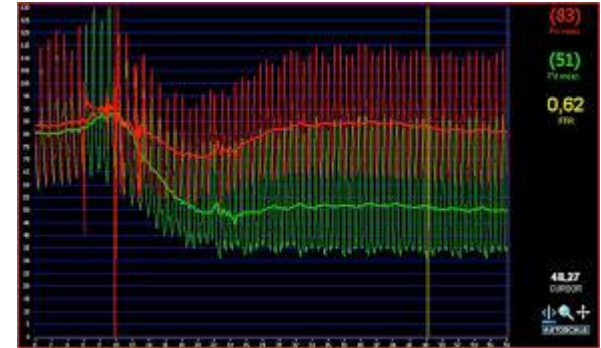
- ✓ Prospective, randomized, international, multicenter trial
(Registration: [http:// clinicaltrials.gov](http://clinicaltrials.gov) [NCT02673424])
- ✓ Patients with intermediate stenosis (40-70% by visual estimation) at proximal and mid part of major epicardial coronary artery
- ✓ Randomization: 1:1 to FFR-guided vs. IVUS-guided strategy
- ✓ Blinding of study arm during f/u: FLAVOUR-defer, FLAVOUR-PCI



- **PCI criteria**

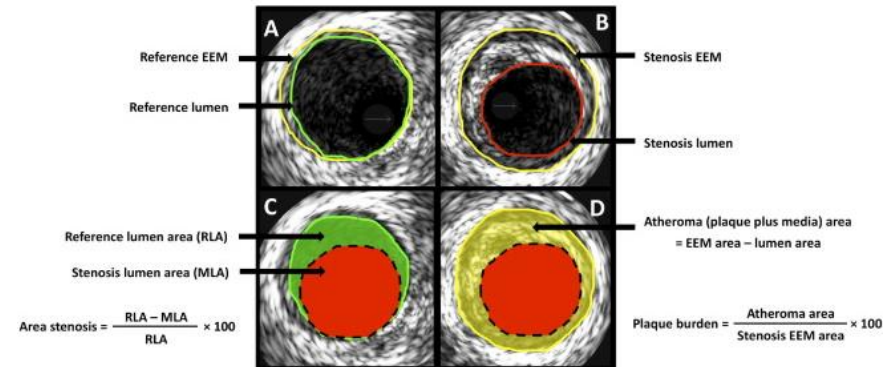
- **FFR-guided strategy**

Criteria for revascularization: $\text{FFR} \leq 0.80$



- **IVUS-guided strategy**

Criteria for revascularization: Minimum lumen area (MLA) $\leq 3\text{mm}^2$ or
MLA $3\sim 4\text{mm}^2$ AND Plaque burden $>70\%$



- **PCI optimization**



- PCI criteria
- **PCI optimization**
 - **FFR-guided strategy**
 - Post PCI FFR ≥ 0.88 , or
Post PCI delta FFR < 0.05
([FFR at stent distal] – [FFR at stent proximal edge])
 - **IVUS-guided strategy**
 - Plaque burden at stent edge $\leq 55\%$
 - MSA $\geq 5.5\text{mm}^2$, or MSA \geq distal reference lumen area

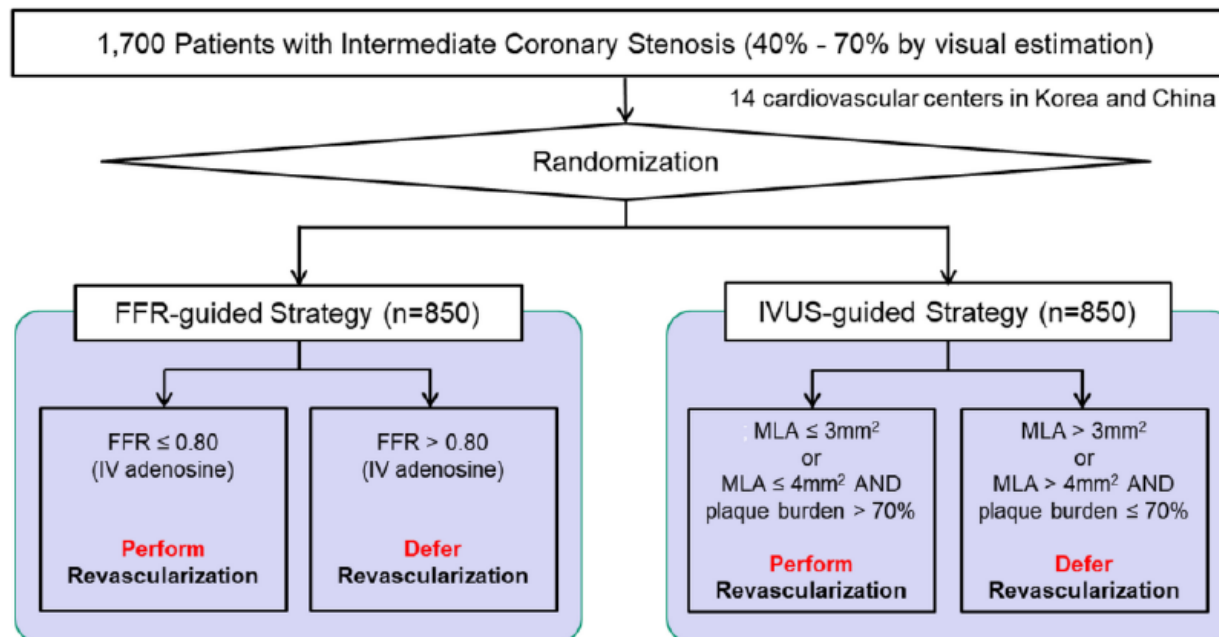
Kang SJ et al. Am J Cardiol 2013;111(10):1408-14.
Song HG et al. Catheter Cardiovasc Interv 2014;83(6):873-8.
Li SJ et al. JACC interv 2017;10(10):986-995.

FLAVOUR study: Rationale of the non-inferiority design

• Sample size calculation

- Estimated 24m POCO rate in the FFR-guided PCI strategy group: 10%
- Estimated 24m POCO rate in the IVUS-guided PCI strategy group: 12%
- Non-inferiority margin for the difference in event rates: 2.5% points
- Type I error rate: 5%, Study power: 90%

➔ ***A total of 1,700 patients needed***



- 1. What is the Rationale for 'IVUS vs. FFR'?***
- 2. What is the theoretical background of non-inferior comparison?***

1. What is the rationale for 'IVUS vs. FFR'?



Anatomy vs. Function

FFR and IVUS are not 'Antagonistic' (対立), but rather 'Cooperative' (協同) tools. Why these TWO should be compared?

1. What is the Rationale for 'IVUS vs. FFR'?

- We still need comparison of these two methods, because...
 - ✓ These two strategies are commonly used methods to select the patients for revascularization and to optimize PCI.
 - ✓ We cannot use both for all patients due to limited resources.
 - ✓ We need to determine which is more important, '*Whom to treat*' vs. '*How to treat*'

2. What is the theoretical background of non-inferior comparison?

The general form of a non-inferior trial:

- Comparing a 'comparator' vs. 'the gold standard', and proving non-inferiority of the 'comparator'
- The comparator usually has a higher event rate, but with no significance.

2. What is the theoretical background of non-inferior comparison?

- General form

*Proving non-inferiority of the **comparator**, compared to the **standard**.*

- In the FLAVOUR trial,

*Proving non-inferiority of the **FFR**, compared to **IVUS***

???? FFR as the comparator and IVUS as the Standard ????

2. What is the theoretical background of non-inferior comparison?

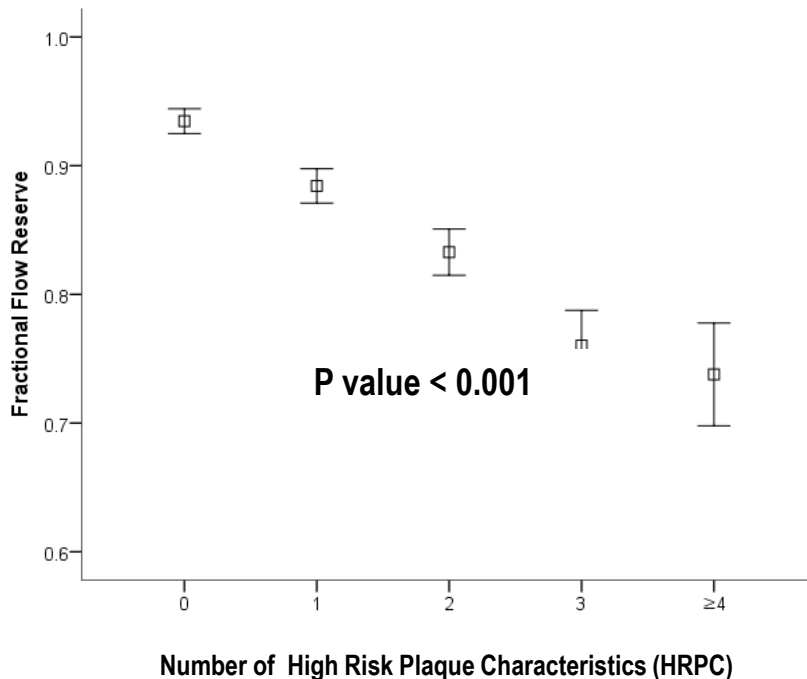
- *No evidence that FFR is better than IVUS.*
- *FFR is the gold standard in evaluating ischemia, not in improving outcomes after PCI.*
- *IVUS-guided DES implantation reduced event rate (including hard endpoints) compared with angiography-guided DES implantation.*
- *IVUS can assess the plaque vulnerability (indirectly). However, FFR also contains the concept of vulnerability.*

FLAVOUR study: Rationale of the non-inferiority design



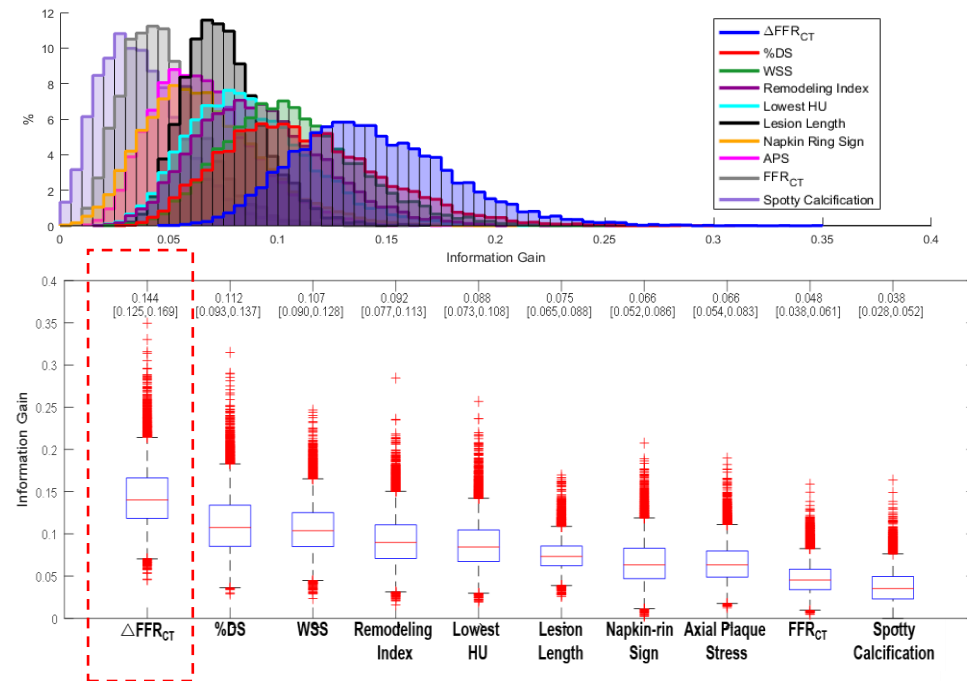
FFR vs. Plaque and patient vulnerability

Association between FFR and HRPC



Lee JM, Koo BK, et al. JACC, in press

Information gain in prediction of ACS risk



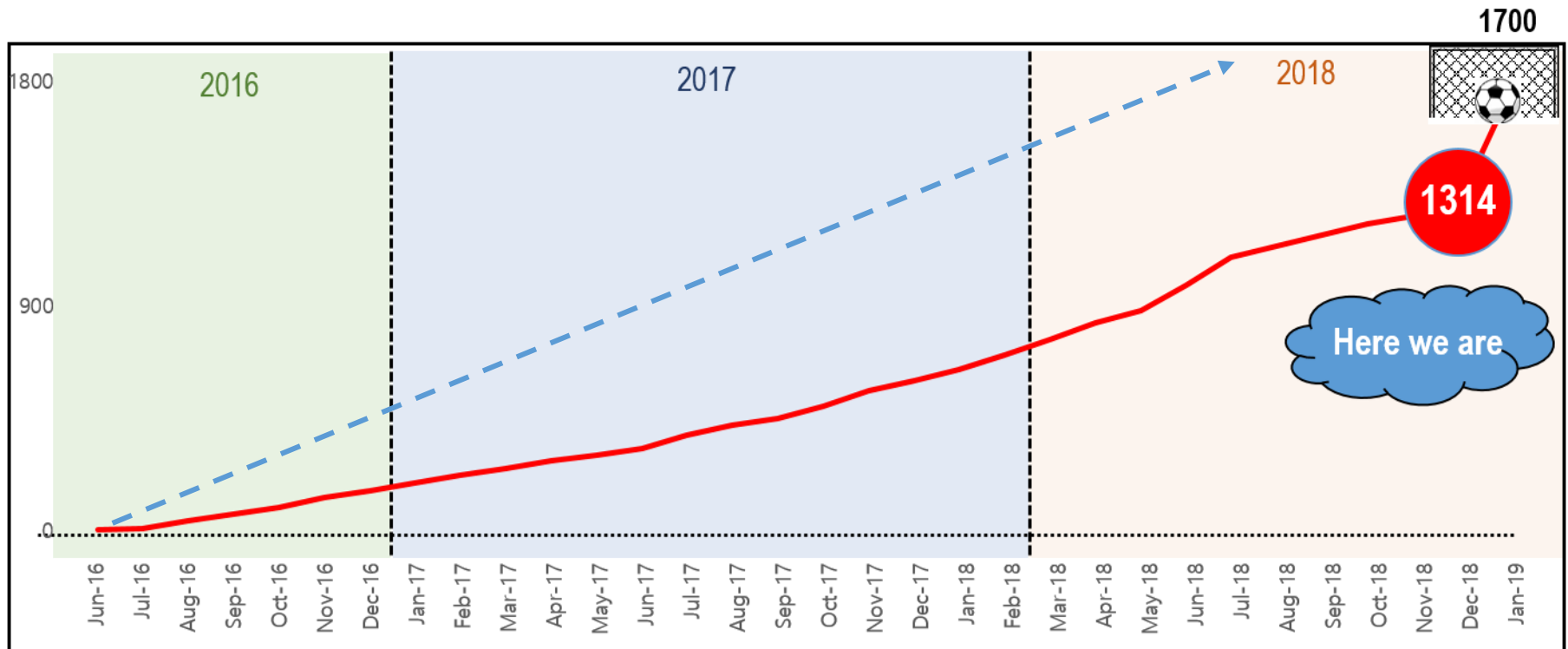
Lee JM, Koo BK, et al. JACC imaging, in press

2. What is the theoretical background of non-inferior comparison?

- *After proving the non-inferiority of FFR, we will focus on the ‘number of stents used per patient and per lesion’.*
- *Using minimal medial resource and achieving maximal efficacy is a very important issue in daily clinical practice.*
- *In the end, we will be able to prove superiority of FFR-guided PCI; ‘consuming less medial resource and achieving non-inferior efficacy’.*

FLAVOUR study: enrollment status

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Summary



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- “FLAVOUR” is the first randomized prospective trial to compare FFR and IVUS head to head as adjunctive strategies for the management of intermediate lesions.
- Through this study, we will be able to assess the safety and efficacy of the two most commonly used adjunctive procedures to assess the angiographic intermediate stenosis and to optimize PCI.



*Let's Enjoy This "FLAVOUR"
Together!*