DEFER 15-Year Follow-up
Stenting a non-ischemic stenosis has no benefit compared to medical therapy.

FAMOUS NSTEMI
Angio-guided management showed higher rates of revascularization compared with FFR-guided management.

CONTRAST
Contrast FFR is superior to resting Pd/Pa and iFR™ assessment for predicting FFR.

PRIMULTI
FFR-guided revascularization of MVD in STEMI patients resulted in lower risk of primary composite endpoint vs. standard care.

FAME 3
Compare FFR-guided PCI of MVD with angio-guided CABG.

Future

Compare-ACUTE FFR
FFR-guided PCI in MVD STEMI

FAMOUS STEMI
Compare FFR to angio in non-culprit lesions in STEMI patients

POST-IT/R3F
FFR guided Dx vs. angio-guided Dx

FFR/ACS Registry

Resting Indices Registry
Pd/Pa, cFFR, and Pd/Pa Min
CLINICAL HIGHLIGHTS FROM THE CONTRAST STUDY\(^1\)

#1

Hyperemic FFR remains the reference standard for diagnostic accuracy.

#2

Contrast FFR is superior to resting Pd/Pa and iFR™ assessment for predicting FFR.

#3

Resting Pd/Pa and iFR™ assessment provide equivalent diagnostic accuracy.

---

**Binary Approach\(^1\)**

- No Adenosine Used

**Hybrid Approach\(^1\)**

- Selective Adenosine Used

---

**Accuracy Compared to FFR (%)**

- RESOLVE\(^2\)
- ADVISE II\(^1\)
- VERIFY 2\(^1\)
- CONTRAST\(^1\)

---

Prior to using hyperemic agents, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions.
**KEY DATA**

- Age 65 ± 10 years, 72% male.
- Average 8 ± 2 mL of IC contrast, 8 different agents: iomeron = 29%, iodoxanol = 25%, iohexol = 14%, ioversol = 8%, iopromide = 9%.

**STUDY DESIGN AND ENROLLMENT**

- 750 patients (prospective) with 1 lesion/patient.
- Age 18 years or older.
- Any lesion fulfilling a clinical indication for FFR were assessed.
- 3 variations of hyperemic drugs were examined.
- Referral FFR will be measured using standard adenosine. Reference FFR  will offer superior diagnostic agreement compared to resting conditions.

**INCLUSION CRITERIA:**

- Undergoing FFR assessment for standard clinical indications.
- Ability to understand and willingness to sign a written informed consent.

**EXCLUSION CRITERIA:**

- Prior coronary artery bypass grafting (CABG).
- Extremely tortuous or calcified coronary arteries precluding intracoronary physiologic measurements.
- Known severe LVH (septal wall thickness at echo of > 13 mm).
- Inability to receive adenosine.
- Recent (within 3 weeks prior to cardiac catheterization) STEMI.

**OVERVIEW**

- To determine the diagnostic performances of iodine contrast medium and resting conditions to predict fractional flow reserve (FFR). Reference FFR will be measured using standard adenosine. We hypothesize that contrast FFR will offer superior diagnostic agreement compared to resting conditions.

**SECONDARY OBJECTIVES:**

- To describe the diagnostic performance of resting conditions and contrast medium injection using sensitivity and specificity, positive and negative predictive value, and area under the receiver operating characteristic (ROC) curve, compared to adenosine-derived FFR ≤ 0.8 as the reference standard.

**SUMMARY AND CONCLUSIONS**

- Contrast FFR is superior to resting Pd/Pa and iFR™ assessment for predicting FFR (using binary or hybrid approach).
- iFR™ assessment and resting Pd/Pa provide equivalent diagnostic accuracy.
- Hyperemic FFR remains the reference standard for diagnostic accuracy.

- In healthcare systems in which adenosine is prohibitively expensive or in the rare cases when adenosine is contraindicated, contrast FFR:
  - Is easy, inexpensive, and safe;
  - Displays excellent test/retest stability;
  - Does not depend on a specific software platform (available on all pressure-wire systems) or ECG gating (core lab excluded 14% of ECG tracings).

**REFERENCES**

1. Prior to using hyperemic agents, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions.
CLINICAL HIGHLIGHTS FROM THE DEFER STUDY 15-YEAR FOLLOW-UP

#1
Performing PCI of a non-ischemic stenosis *still has no prognostic or symptomatic long-term benefits* as compared to medical treatment.

#2
Rates of MI showed a significant advantage in the Defer Group versus the Perform and Reference Groups and most infarctions were related to the target vessel.

#3
There was a significant difference in MI between the Defer Group and Perform Group.

### DEFER STUDY 15-YEAR FOLLOW-UP: RATES OF MI

![Graph showing myocardial infarction rates over 15 years for Defer, Perform, and Reference groups. Defer vs. Perform, log-rank p = 0.03.]

### MOST INFRINGEMENTS WERE RELATED TO THE TARGET VESSEL

<table>
<thead>
<tr>
<th>Event</th>
<th>Defer Group (n = 91)</th>
<th>Perform Group (n = 90)</th>
<th>Reference Group (n = 144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Death</td>
<td>30</td>
<td>28</td>
<td>53</td>
</tr>
<tr>
<td>Any Myocardial Infarction</td>
<td>2 → 13</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Any Revascularization</td>
<td>60</td>
<td>53</td>
<td>86</td>
</tr>
</tbody>
</table>

*All Cumulative Events*
The DEFER Study – 15 Year Follow-up

**Title**: The DEFER Study – 15 Year Follow-up

**Sponsor**: Catharina Hospital, Eindhoven, The Netherlands

**Purpose**: The purpose of this study was to investigate the appropriateness of stenting a functionally non-significant stenosis (≥ 0.75).

**Publication**: EuroPCR 2015 Session presented by Nico Pijls, MD, PhD, Catharina Hospital Eindhoven, Eindhoven, the Netherlands

**Primary Endpoint**: Freedom from major adverse cardiac events (MACE).

**Secondary Endpoint**: MACE at 5 years, individual components of MACE at 2 and 5 years, and functional class at 2 and 5 years.

**Study Design and Enrollment**

- International, multi-center, prospective and randomized study performed in 12 hospitals in Europe and 2 hospitals in Asia between June 1997 and December 1998.

- Out of 325 patients, 167 were randomly assigned to deferral and 158 to performance of PCI.

**Inclusion Criteria**:

- Referral for elective PCI of a single angiographically significant de novo stenosis (more than 50% diameter stenosis by visual assessment) in a native coronary artery with a reference diameter of more than 2.5 mm.

- No evidence of reversible ischemia documented by noninvasive testing within the last 2 months.

**Exclusion Criteria**:

- Patients with a total occlusion of the target artery, acute Q-wave infarction, or unstable angina documented by transient ST-segment abnormality were excluded.

- Patients with small-sized target arteries (reference diameter < 2.5 mm) were excluded because these patients have less benefit from PCI and their inclusion could bias the outcome in favor of deferral of PCI.

**DEFER 15-YEAR FOLLOW-UP STUDY OVERVIEW**

**Key Data**

- As presented at EuroPCR 2015, Paris, May 19, 2015

**Table 1. Baseline Characteristics of Patients in the Three Groups**

<table>
<thead>
<tr>
<th></th>
<th>Defer Group (n = 91)</th>
<th>Perform Group (n = 90)</th>
<th>Reference Group (n = 144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>61 ± 9</td>
<td>61 ± 11</td>
<td>60 ± 9</td>
</tr>
<tr>
<td>Gender, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>65</td>
<td>63</td>
<td>80</td>
</tr>
<tr>
<td>Female</td>
<td>35</td>
<td>37</td>
<td>20</td>
</tr>
<tr>
<td>Risk Factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>15</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36</td>
<td>34</td>
<td>42</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>43</td>
<td>48</td>
<td>49</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>27</td>
<td>23</td>
<td>29</td>
</tr>
<tr>
<td>Family History of CAD</td>
<td>56</td>
<td>46</td>
<td>45</td>
</tr>
<tr>
<td>Ejection Fraction, %</td>
<td>67 ± 9</td>
<td>67 ± 10</td>
<td>68 ± 9</td>
</tr>
<tr>
<td>Angiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference Diameter, mm</td>
<td>3.00 ± 0.64</td>
<td>2.94 ± 0.57</td>
<td>2.97 ± 0.58</td>
</tr>
<tr>
<td>DS, %</td>
<td>48 ± 9</td>
<td>48 ± 10</td>
<td>57 ± 12</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>1.55 ± 0.37</td>
<td>1.50 ± 0.36</td>
<td>1.28 ± 0.39</td>
</tr>
<tr>
<td>Lesion Length, mm</td>
<td>9.8 ± 5.4</td>
<td>10.2 ± 4.3</td>
<td>9.5 ± 3.9</td>
</tr>
<tr>
<td>FFR</td>
<td>0.87 ± 0.07</td>
<td>0.87 ± 0.06</td>
<td>0.56 ± 0.16</td>
</tr>
</tbody>
</table>

- Complete follow-up occurred in 91% of patients. Follow-up relative to mortality was 97% of all patients. Median follow-up was 16.8 years.

**Table 2. Performing PCI of a Non-ischemic Stenosis Still has No Prognostic or Symptomatic Long-term Benefits as Compared to Medical Treatment**

<table>
<thead>
<tr>
<th></th>
<th>Defer Group (n = 91)</th>
<th>Perform Group (n = 90)</th>
<th>Reference Group (n = 144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>4 (4)</td>
<td>4 (4)</td>
<td>15 (10)</td>
</tr>
<tr>
<td>Unknown</td>
<td>16 (16)</td>
<td>11 (12)</td>
<td>18 (13)</td>
</tr>
<tr>
<td>Non-cardiac</td>
<td>11 (12)</td>
<td>13 (14)</td>
<td>27 (19)</td>
</tr>
<tr>
<td>Total</td>
<td>30 (33)</td>
<td>28 (31)</td>
<td>52 (36)</td>
</tr>
</tbody>
</table>

- No statistical differences between Defer/Perform/Reference Groups.

**Table 3. All Cumulative Events**

<table>
<thead>
<tr>
<th></th>
<th>Defer Group (n = 91)</th>
<th>Perform Group (n = 90)</th>
<th>Reference Group (n = 144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Death</td>
<td>30</td>
<td>28</td>
<td>53</td>
</tr>
<tr>
<td>Any MI</td>
<td>2</td>
<td>13</td>
<td>19</td>
</tr>
<tr>
<td>Any Revascularization</td>
<td>60</td>
<td>53</td>
<td>88</td>
</tr>
</tbody>
</table>

- No difference in mortality;

- Myocardial infarction significantly favored the Defer Group;

- There were no differences in repeated PCI and CABG.

**Summary and Conclusions**

Deferral vs. performance of PCI in non-ischemic stenosis (based upon FFR ≥ 0.75) at 15 years showed:

- No difference in mortality;

- Myocardial infarction significantly favored the Defer Group;

- There were no differences in repeated PCI and CABG.

**Figures**

- Figure 2. Rates of MI Showed a Significant Advantage in the Defer Group vs. the Perform and Reference Groups.

- Figure 3. Most Infarctions Were Related to the Target Vessel.


Brief Summary: Prior to using these devices, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use.

iFR is a trademark of Volcano Corporation and Adobe Acrobat Reader is a trademark of Adobe Systems Incorporated. Unless otherwise noted, ™ indicates that the name is a trademark of, or licensed to, St. Jude Medical or one of its subsidiaries. ST. JUDE MEDICAL and the nine-squares symbol are trademarks and service marks of St. Jude Medical, Inc. and its related companies. © 2015 St. Jude Medical, Inc. All Rights Reserved.