Prospective Longitudinal Trial of \( FFR_{CT} \) Outcome and Resource Impacts

Clinical outcomes of \( FFR_{CT} \)-guided diagnostic strategies versus usual care in patients with suspected coronary artery disease

Pamela S. Douglas, Gianluca Pontone, Mark A. Hlatky, Manesh R. Patel, Campbell Rogers, Bernard De Bruyne

On behalf of the PLATFORM Investigators

Supported by HeartFlow Inc, Redwood, CA, USA
Background and Aim

- The optimal evaluation of new onset stable chest pain is uncertain. Ideally, testing will clarify the diagnosis and direct subsequent care while maximizing efficiency and safety.

- The recent PROMISE and SCOT-HEART trials compared anatomic and functional strategies, finding that CTA improved processes of care. However, CTA also increased rates of invasive catheterization and revascularization with no significant reduction in events.

- Fractional Flow Reserve derived from CTA ($\text{FFR}_{\text{CT}}$) may address these limitations by providing both functional and anatomic data.

- **STUDY AIM:** To determine whether use of a CTA/$\text{FFR}_{\text{CT}}$ guided strategy, as compared to standard practice, will reduce the rate of invasive angiograms that show no obstructive CAD, without increasing the occurrence of major cardiac events.
Fractional Flow Reserve by CTA (FFR\textsubscript{CT})

- Routine CTA images are segmented and analysed quantitatively
- 3D coronary blood flow is modelled using computational fluid dynamics
- Maximal hyperemia is simulated to derive pressure and flow data, expressed as numeric values similar to invasive FFR evaluation
- FFR\textsubscript{CT} has been validated against invasively measured FFR

Hemodynamically significant LAD lesion by FFR\textsubscript{CT}
PLATFORd Trial Design

Stable CAD symptoms; Planned non-emergent NI test or catheterization
Age ≥ 18y; No prior CAD hx; Intermediate pretest probability of CAD

Planned NI test

Sequential cohorts

Standard NI test
Exercise ECG
Stress nuclear
Stress echo
Stress MRI
CTA

CTA + FFR<sub>CT</sub>

FFR<sub>CT</sub>
No FFR<sub>CT</sub>

Cath w/o obstructive CAD (QCA or FFR ≤ 0.80) at 90 days

1° — MACE: death, MI, UA; Radiation (Costs; QOL)

Planned ICA

Sequential cohorts

Standard ICA

CTA + FFR<sub>CT</sub>

FFR<sub>CT</sub>
No FFR<sub>CT</sub>

Testing/cath performed and interpreted locally; FFR<sub>CT</sub> results w/in 24–48 hrs
All F/U testing and management decisions by care team following best practices
Endpoints and Statistical Analyses

For the primary endpoint of the rate of ICA without finding obstructive CAD, a sample size was used which provided 90% power to detect a 50% reduction with $\text{FFR}_{\text{CT}}$ guided care, using a one-sided Wald test for a risk difference $< 0$ with an $\alpha$ error $= 0.025$

- Absence of obstructive CAD was determined by a blinded central laboratory
- Three sensitivity analyses performed: Propensity-matched, Best practices, Analyzable images; Primary endpoint also assessed using site read data

Safety endpoints: MACE adjudicated by blinded CEC

All treatment comparisons were performed as allocated (ITT)

All statistical assessments were independently confirmed by Duke Clinical Research Institute
Cohort Assignment and Follow-up

Enrolled and consented; N=584
Sept 13, 2013 – Nov 26, 2014

Planned NI test (N=204)

- Standard NI test N=100
- Received NI test N=100 pts
- Invasive cath N=12
- Revascularization N=5
- 90-day follow-up complete (N=97; 97.0%)
- Analysis (N=100; 100%)

Planned ICA (N=380)

- Standard ICA N=187
- FFR<sub>CT</sub> guided N=193
- Invasive cath N=187
- Revascularization N=59
- 90-day follow-up complete (N=179; 95.7%)
- Analysis (N=187; 100%)

- CTA / FFR<sub>CT</sub> N=104
- Invasive cath N=19
- Revascularization N=10
- 90-day follow-up complete (N=101; 97.1%)
- Analysis (N=104; 100%)

- FFR<sub>CT</sub> guided N=193
- 69% CTAs sent for FFR<sub>CT</sub>
- FFR<sub>CT</sub> calculated in 87%
- ICA cancelled in 61%
- Analysis (N=193; 100%)
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Planned NI Test</th>
<th>Planned ICA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age — mean ± SD, yr</strong></td>
<td>Usual care strategy N=100</td>
<td>FFR&lt;sub&gt;CT&lt;/sub&gt; strategy N=104</td>
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<tr>
<td></td>
<td>57.9±10.7</td>
<td>59.5±9.3</td>
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<tr>
<td><strong>Female sex — no. (%)</strong></td>
<td>34 (34.0)</td>
<td>44 (42.3)</td>
</tr>
<tr>
<td><strong>Racial/ethnic minority — no. (%)</strong></td>
<td>5 (5.0)</td>
<td>0 (0.0)</td>
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<thead>
<tr>
<th>Cardiac risk factors</th>
<th>Planned NI Test</th>
<th>Planned ICA</th>
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<tbody>
<tr>
<td><strong>Hypertension — no. (%)</strong></td>
<td>Usual care strategy N=100</td>
<td>FFR&lt;sub&gt;CT&lt;/sub&gt; strategy N=104</td>
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<tr>
<td></td>
<td>38 (38.0)</td>
<td>57 (54.8)</td>
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<tr>
<td><strong>Diabetes — no. (%)</strong></td>
<td>8 (8.0)</td>
<td>6 (5.8)</td>
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<td><strong>Dyslipidemia — no. (%)</strong></td>
<td>22 (22.0)</td>
<td>28 (26.9)</td>
</tr>
<tr>
<td><strong>Tobacco use — no. (%)</strong></td>
<td>52 (52.0)</td>
<td>59 (56.7)</td>
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<thead>
<tr>
<th>Pre-test probability CAD — ±SD, % (Updated Diamond and Forrester)</th>
<th>Planned NI Test</th>
<th>Planned ICA</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Usual care strategy N=100</td>
<td>FFR&lt;sub&gt;CT&lt;/sub&gt; strategy N=104</td>
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<tr>
<td></td>
<td>44.5±15.3</td>
<td>45.3±16.8</td>
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<thead>
<tr>
<th>Statin use — no. (%)</th>
<th>Planned NI Test</th>
<th>Planned ICA</th>
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<tbody>
<tr>
<td></td>
<td>Usual care strategy N=100</td>
<td>FFR&lt;sub&gt;CT&lt;/sub&gt; strategy N=104</td>
</tr>
<tr>
<td></td>
<td>24 (24.0)</td>
<td>29 (27.9)</td>
</tr>
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<thead>
<tr>
<th>Angina — no. (% typical / atypical)</th>
<th>Planned NI Test</th>
<th>Planned ICA</th>
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<tr>
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<td>FFR&lt;sub&gt;CT&lt;/sub&gt; strategy N=104</td>
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<tr>
<td></td>
<td>99 (99.0)</td>
<td>98 (94.2)</td>
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</tbody>
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Primary Endpoint
Invasive Catheterization w/o Obstructive CAD

Similar results in all pre-specified subgroups and cohorts

- Site-read ICA w/o obstructive CAD
  57% usual care; 9% FFR\textsubscript{CT}
- Age, sex, race, diabetes, pretest probability of CAD, country
- Propensity matched cohort
- Best practices cohort
- Adequate image cohort

![Planned ICA Chart]

<table>
<thead>
<tr>
<th>Planned ICA</th>
<th>Usual Care</th>
<th>FFRCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>No-Obs CAD</td>
<td>N (%): 137 (73.3)</td>
<td>24 (12.4)</td>
</tr>
<tr>
<td>Obs CAD</td>
<td>P &lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>No ICA</td>
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Primary Endpoint
Invasive Catheterization w/o Obstructive CAD

Planned NI Test

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<tbody>
<tr>
<td>No-Obs CAD</td>
<td>6 (6.0)</td>
<td>13 (12.5)</td>
</tr>
<tr>
<td>Obs CAD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No ICA</td>
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</table>

N (%): 6 (6.0) 13 (12.5)  P = 0.95

Planned ICA

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N (%): 137 (73.3) 24 (12.4)  P < 0.0001
## Safety Endpoints and Data at Revascularization

<table>
<thead>
<tr>
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<th>Planned NI Test N=204</th>
<th>Planned ICA N=380</th>
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<tr>
<td></td>
<td>Usual care strategy N=100</td>
<td>FFR&lt;sub&gt;CT&lt;/sub&gt; strategy N=104</td>
</tr>
<tr>
<td><strong>SAFETY: MACE — no. (%)</strong></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>FFR&lt;sub&gt;CT&lt;/sub&gt; strategy N=187</td>
<td>FFR&lt;sub&gt;CT&lt;/sub&gt; strategy N=193</td>
</tr>
<tr>
<td><strong>SAFETY: RADIATION EXPOSURE (enrolment to 90 days)</strong></td>
<td>0.0002</td>
<td>0.20</td>
</tr>
<tr>
<td>Mean ± SD, mSv</td>
<td>5.8 ± 7.1</td>
<td>9.4 ± 4.9</td>
</tr>
<tr>
<td></td>
<td>8.8 ± 9.9</td>
<td>9.9 ± 8.7</td>
</tr>
<tr>
<td><strong>FUNCTIONAL DATA AT REVASCULARIZATION</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI or CABG — no.</td>
<td>5</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>55</td>
</tr>
<tr>
<td>Functional data available</td>
<td>100%</td>
<td>51%</td>
</tr>
<tr>
<td></td>
<td>90%</td>
<td>96%</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>&lt;0.0001</td>
</tr>
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*P* values indicate statistical significance.
Summary

- PLATFORM enrolled a symptomatic, intermediate risk population for whom testing is currently recommended.

- Use of CT/FFR$_{CT}$ in patients with planned invasive catheterization was associated with a reduction in the rate of finding no obstructive CAD at ICA, from 73% to 12%.
  - Similar results in all subgroups.
  - No differences in MACE or radiation exposure.
  - No differences in revascularization rates.

- Use of FFR$_{CT}$ resulted in cancellation of 61% of ICAs and doubled the availability of functional data at PCI/CABG.
Conclusion

Among patients with planned ICA, use of a combined anatomic AND functional strategy employing CTA/FFR$_{CT}$ was safe and improved patient selection for invasive catheterization.
Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs. usual care in patients with suspected coronary artery disease: the prospective longitudinal trial of FFRct: outcome and resource impacts study

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...and to the PLATFORM Team

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