# Diagnostic Accuracy of Fractional Flow Reserve from Anatomic Computed TOmographic Angiography: The DeFACTO Study

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# Disclosures

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- No study investigator had any financial interest related to the study sponsor

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# Background

- Coronary CT Angiography:
  - High diagnostic accuracy for anatomic stenosis
  - Cannot determine physiologic significance of lesions[1]
- Fractional Flow Reserve (FFR):
  - Gold standard for diagnosis of lesion-specific ischemia[2]
  - Use improves event-free survival and cost effectiveness[3,4]
- FFR Computed from CT ($FFR_{CT}$):
  - Novel non-invasive method for determining lesion-specific ischemia[5]

[1]Min et al. J Am Coll Cardiol 2010; 55: 957-65; [2]Piljs et al. Cath Cardiovasc Interv 2000; 49: 1-16; [3]Tonino et al. N Engl J Med 2009; 360: 213-24; [4]Berger et al. J Am Coll Cardiol 2005; 46: 438-42; [5]Kim et al. Ann Biomed Eng 2010; 38: 3195-209

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# Overall Objective

- To determine the diagnostic performance of $FFR_{CT}$ for detection and exclusion of hemodynamically significant CAD

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# Study Endpoints

- **Primary Endpoint**: Per-patient diagnostic accuracy of $FFR_{CT}$ plus CT to diagnose hemodynamically significant CAD, compared to invasive FFR reference standard
  - Null hypothesis rejected if lower bound of 95% CI > 0.70
    - 0.70 represents 15% increase in diagnostic accuracy over myocardial perfusion imaging and stress echocardiography, as compared to FFR[1,2]
  - 252 patients: >95% power
- **Secondary Endpoint**:
  - Diagnostic performance for intermediate stenoses (30-70%)

[1]Mellikan N et al. JACC: Cardiovasc Inter 2010, 3: 307-314; [2]Jung PH et al. Eur Heart J 2008; 29: 2536-43

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# Study Criteria

## Inclusion Criteria:

- Underwent ≥64-row CT
- Scheduled for ICA within 60 days of CT
- No intervening cardiac event

## Exclusion Criteria:

- Prior CABG
- Suspected in-stent restenosis
- Suspected ACS
- Recent MI within 40 days of CT

ICA = Invasive coronary angiography; CABG = coronary artery bypass surgery; ACS = acute coronary syndrome; MI = myocardial infarction

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# Study Procedures

- Intention-to-Diagnose Analysis
  - Independent blinded core laboratories for CT, QCA, FFR and $FFR_{CT}$
  - $FFR_{CT}$ for all CTs received from CT Core Laboratory
- CT: Stenosis severity range[1]
  - 0%, 1-29%, 30-49%, 50-69%, 70-89%, ≥90%
- QCA: Stenosis severity (%)
- FFR: At maximum hyperemia during ICA
  - Definition: (Mean distal coronary pressure) / (Mean aortic pressure)
- Obstructive CAD: ≥50%stenosis (CT and QCA)
- Lesion-Specific Ischemia: ≤0.80 (FFR and $FFR_{CT}$)[2]

[1]Raff GL et al. J Cardiovasc Comp Tomogr 2009; 3: 122-36; [2]Tonino PA et al. N Engl J Med 2009; 360: 213-24; FFR, subtotal / total occlusions assigned value of 0.50; $FFR_{CT}$, subtotal / total occlusions assigned value of 0.50, <30% stenosis assigned value of 0.90

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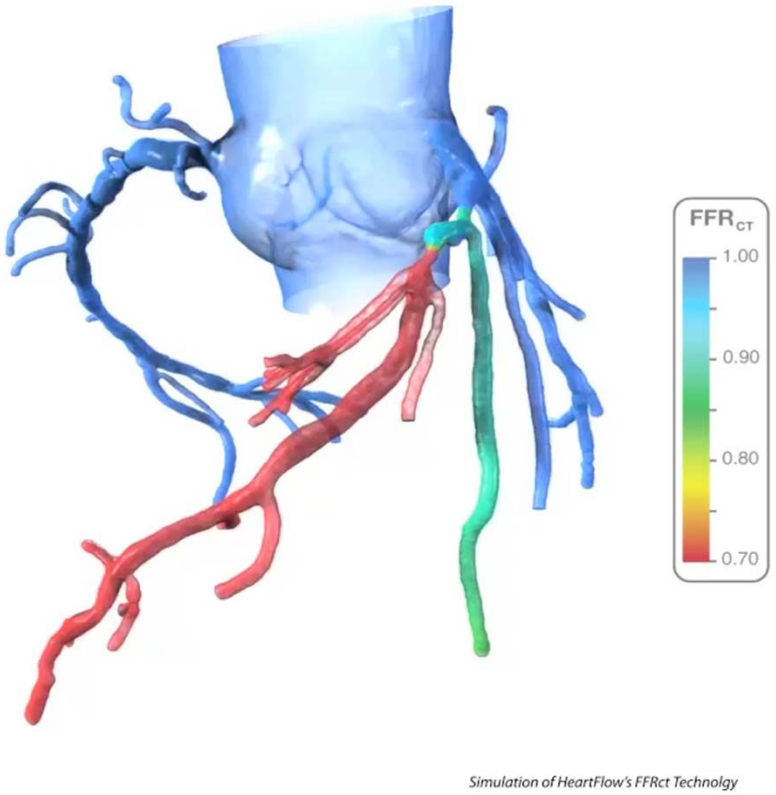
# Study Procedures: $FFR_{CT}$

**$FFR_{CT}$: Derived from typical CT**

- No modification to imaging protocols
- No additional image acquisition
- No additional radiation
- No administration of adenosine
- Selectable at any point of coronary tree

**Patient-Specific Coronary Pressure:**

- Image-based modeling
- Heart-Vessel Interactions
- Physiologic conditions, incl. Hyperemia
- Fluid dynamics to calculate $FFR_{CT}$




*Simulation of coronary pressure and flow*

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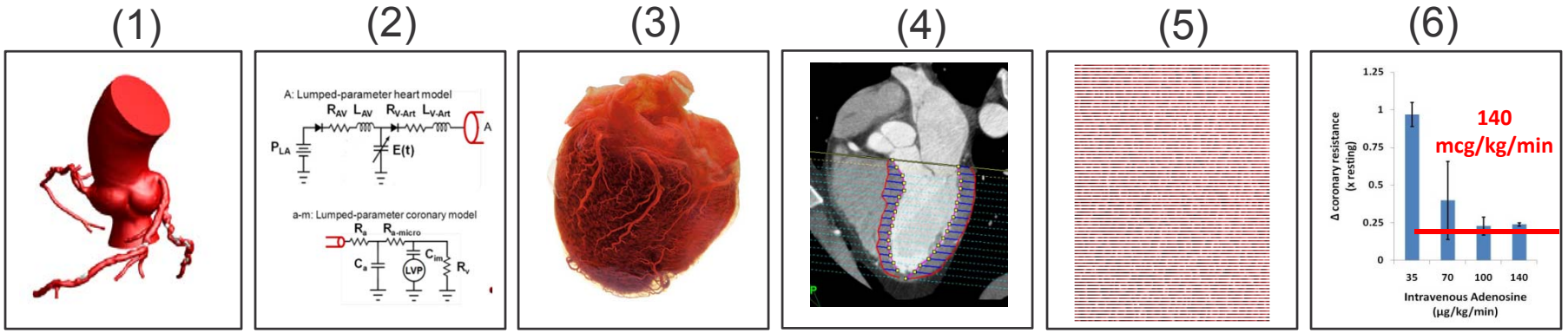
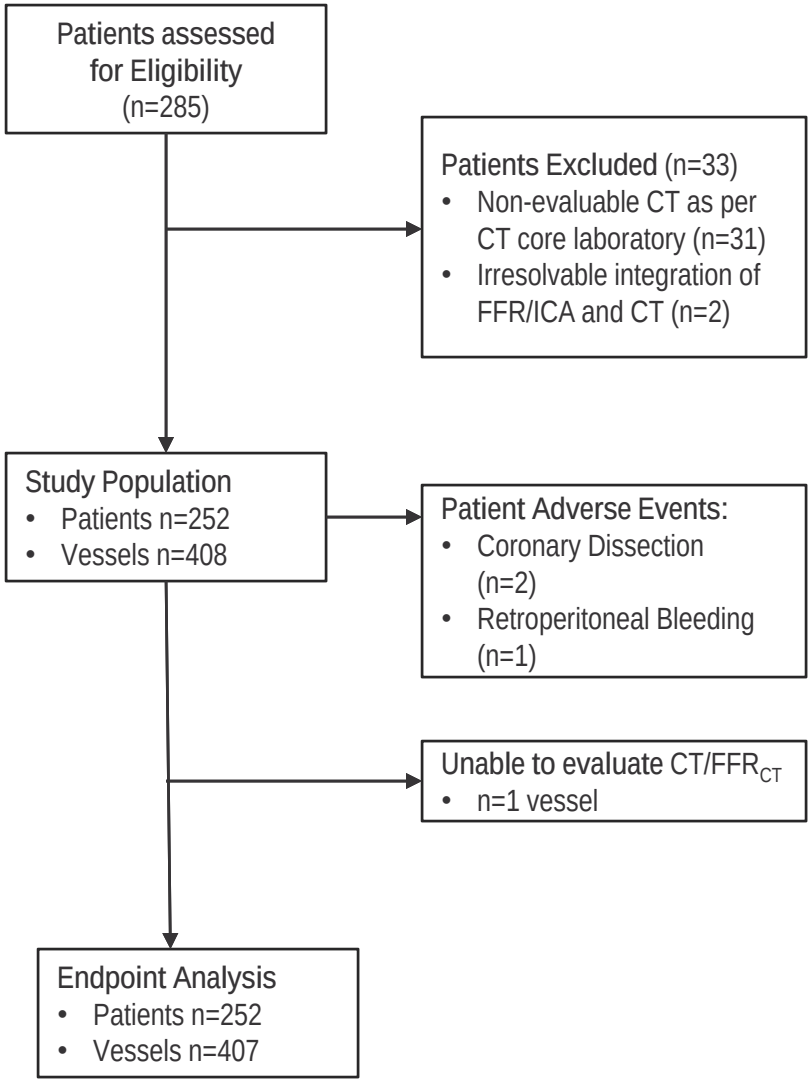
# Patient-Specific Computation of $FFR_{CT}$




1. **Image-Based Modeling** – Segmentation of patient-specific arterial geometry
2. **Heart-Vessel Interactions** – Allometric scaling laws relate caliber to pressure and flow
3. **Microcirculatory resistance** – Mophometry laws relate coronary dimension to resistance
4. **Left Ventricular Mass** – Lumped-parameter model couples pulsatile coronary flow to time-varying myocardial pressure
5. **Physiologic Conditions** – Blood as Newtonian fluid adjusted to patient-specific viscosity
6. **Induction of Hyperemia** – Compute maximal coronary vasodilation
7. **Fluid Dynamics** – Navier-Stokes equations applied for coronary pressure

# Patient Enrollment




- Study Period
  - October 2010 – 2011
- Study Sites
  - 17 centers from 5 countries
- Study Enrollment (n=285)
  - n=33 excluded
- Final study population
  - Patients (n=252)
  - Vessels (n=407)

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# Patient and Lesion Characteristics

| Variable | Mean ± SD or % |
|---|---|
| Age (years) | 63 ± 9 |
| Prior MI | 6 |
| Prior PCI | 6 |
| Male gender | 71 |
| Race / Ethnicity | |
| White | 67 |
| Asian | 31 |
| Other | 2 |
| Diabetes mellitus | 21 |
| Hypertension | 71 |
| Hyperlipidemia | 80 |
| Family history | 20 |
| Current smoker | 18 |

- ICA
  - Stenosis ≥50% — 47%
  - Mean Stenosis — 47%
- FFR
  - FFR ≤ 0.80 — 37%
- CT
  - Stenosis ≥50% — 53%
  - Calcium Score — 381
  - Location
    - LAD — 55%
    - LCx — 22%
    - RCA — 23%

Abbreviations: MI = myocardial infarction; PCI = percutaneous intervention; FH = family history; CAD = coronary artery disease; FFR = fractional flow reserve; CACS = coronary artery calcium score; LAD = left anterior descending artery; LCx = left circumflex artery; RCA = right coronary artery

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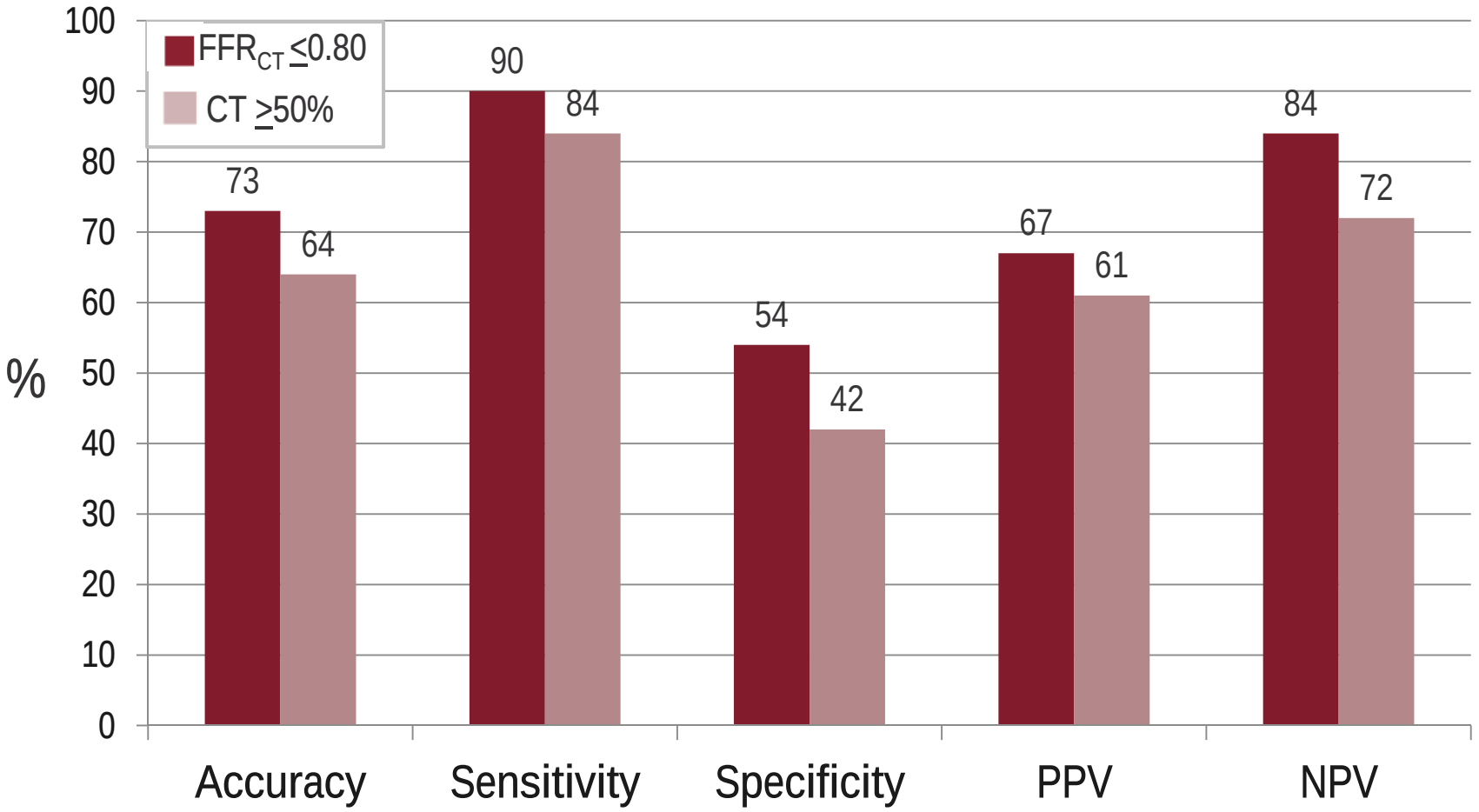
# Per-Patient Diagnostic Performance




| N=252 | | | | | |
|---|---|---|---|---|---|
| FFR$_{CT}$ | 95% CI | 95% CI | 95% CI | 95% CI | 95% CI |
| | 67-78 | 84-95 | 46-83 | 60-74 | 74-90 |
| CT | 58-70 | 77-90 | 34-51 | 53-67 | 61-81 |

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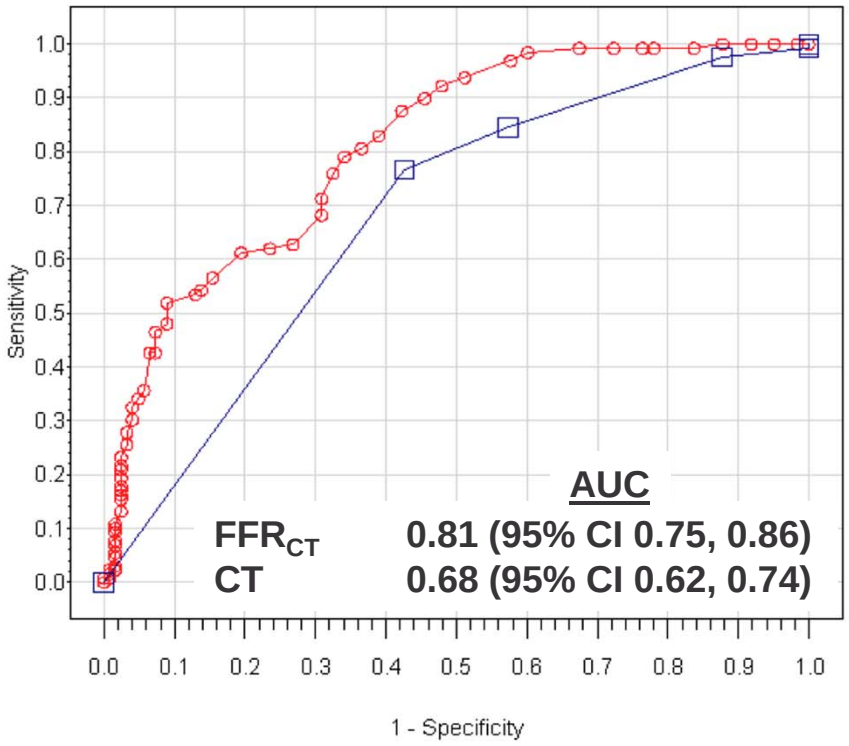
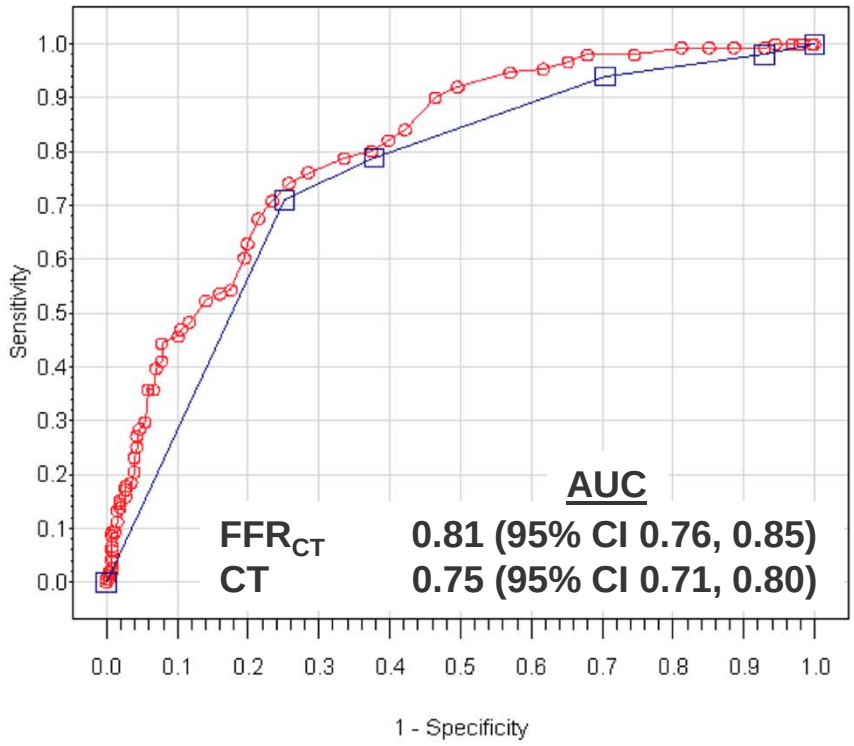
# Discrimination

## Per-Patient




## Per-Vessel




- Greater discriminatory power for FFR$_{CT}$ versus CT stenosis
  - Per-patient (Δ 0.13, p<0.001)
  - Per-vessel (Δ 0.06, p<0.001)

*AUC = Area under the receiver operating characteristics curve

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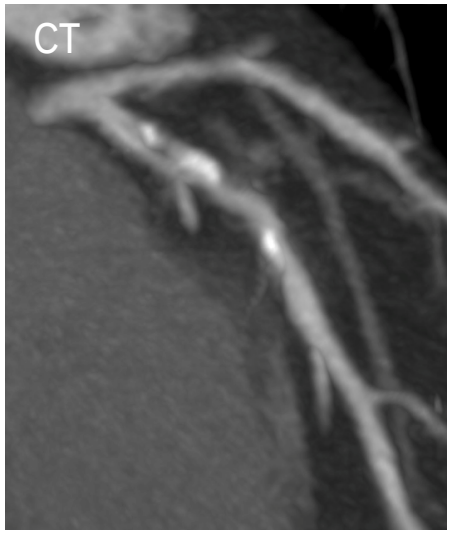
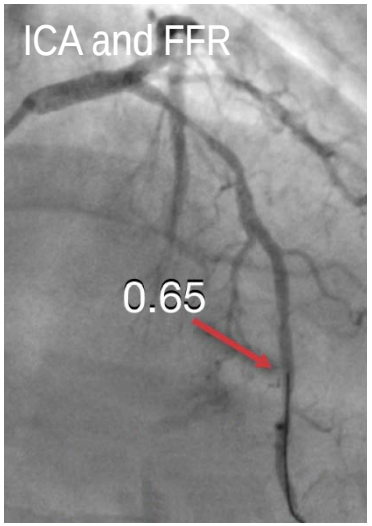
# Case Examples: Obstructive CAD

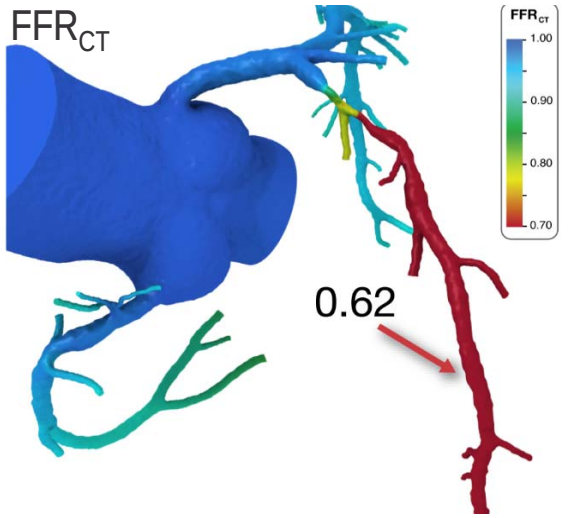
Case 1




LAD stenosis

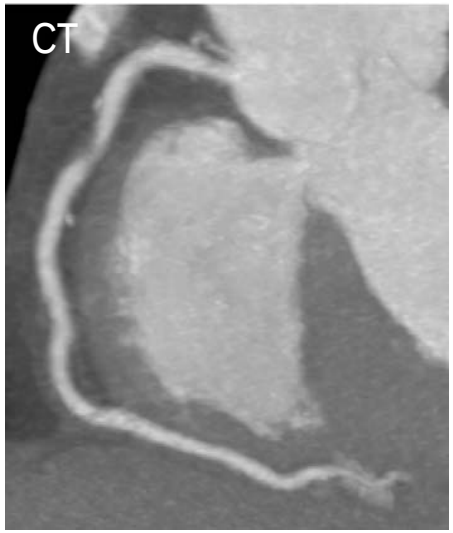



FFR 0.65
= Lesion-specific ischemia

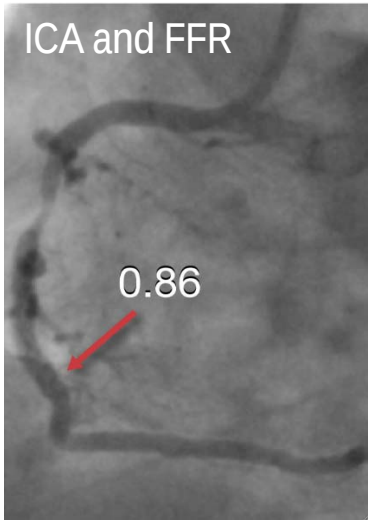



FFR$_{CT}$ 0.62
= Lesion-specific ischemia

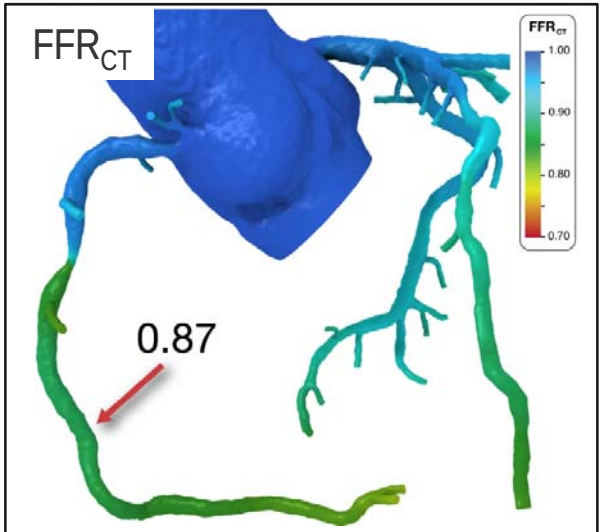
Case 2




RCA stenosis

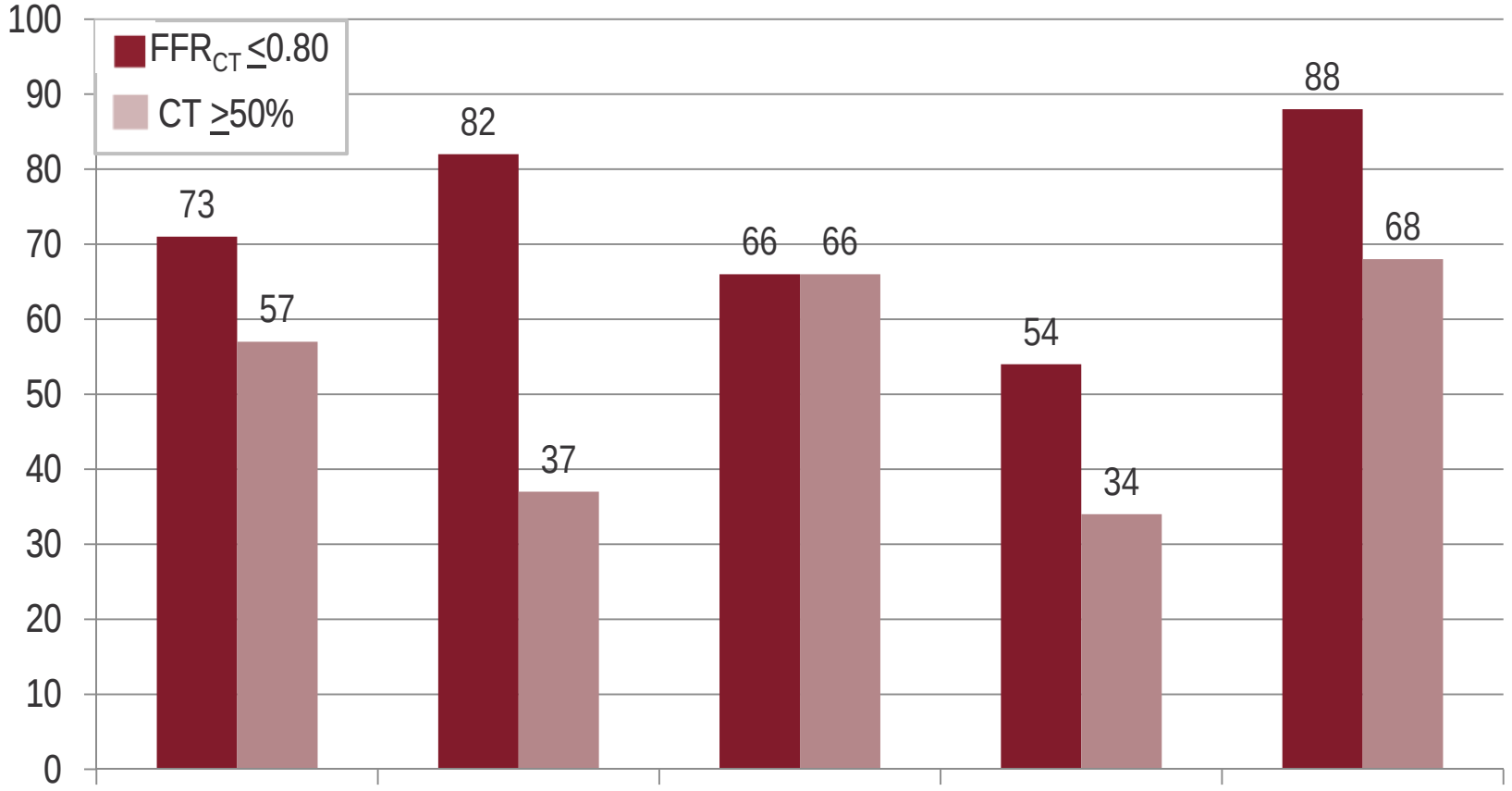



FFR 0.86
= No ischemia




FFR$_{CT}$ 0.87
= No ischemia

# Per-Patient Diagnostic Performance for Intermediate Stenoses by CT (30-70%)




| N=83 | Accuracy | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|
| FFR$_{CT}$ | 95% CI<br>61-80 | 95% CI<br>63-92 | 95% CI<br>53-77 | 95% CI<br>39-68 | 95% CI<br>75-95 |
| CT | 46-67 | 22-56 | 53-77 | 20-53 | 55-79 |

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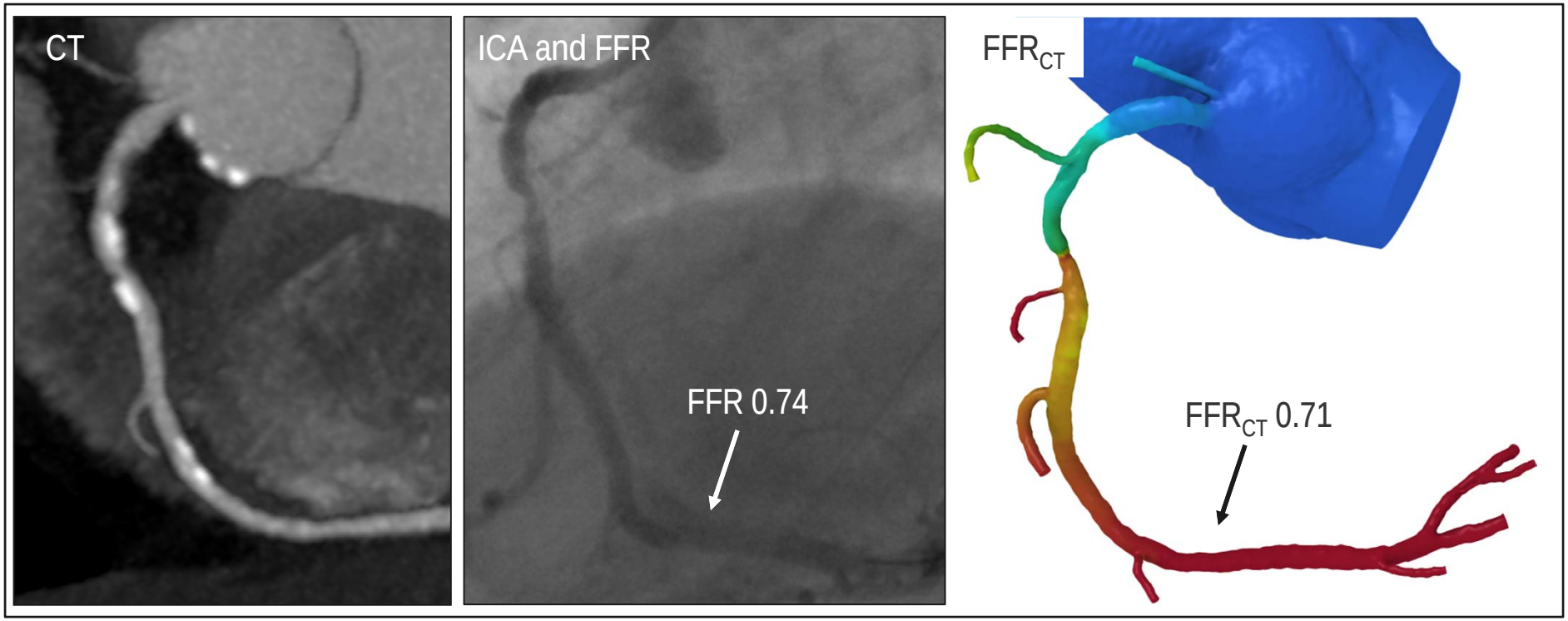
# Case Example: Intermediate Stenosis




31-49% stenosis
CT Core Lab

50-69% stenosis
QCA Core Lab

FFR 0.74
= Lesion-specific ischemia

FFR$_{CT}$ 0.71
= Lesion-specific ischemia

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# Limitations

- Did not interrogate every vessel with invasive FFR
- Did not solely enroll patients with intermediate stenosis[1,2]
- Did not test whether $FFR_{CT}$-based revascularization reduces ischemia[3]
- Did not enroll prior CABG / In-Stent Restenosis / Recent MI

[1]Koo BK et al. 2012 EuroPCR Scientific Sessions, [2]Fearon et al. Am J Cardiol 2000: 86: 1013-4; [2]Melikian N et al. JACC Cardiovasc Interv 2010; 3: 307-14

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# Conclusions

- $FFR_{CT}$ demonstrated **improved accuracy** over CT for diagnosis of patients and vessels with ischemia
  - $FFR_{CT}$ diagnostic accuracy 73% (95% CI 67-78%)
    - Pre-specified primary endpoint >70% lower bound of 95% CI
  - Increased discriminatory power

- $FFR_{CT}$ superior to CT for **intermediate stenoses**

- $FFR_{CT}$ computed **without additional radiation** or imaging

- First large-scale demonstration of **patient-specific computational models to calculate physiologic pressure and velocity fields** from CT images

- **Proof of feasibility of $FFR_{CT}$ for diagnosis of lesion-specific ischemia**

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Thank you.