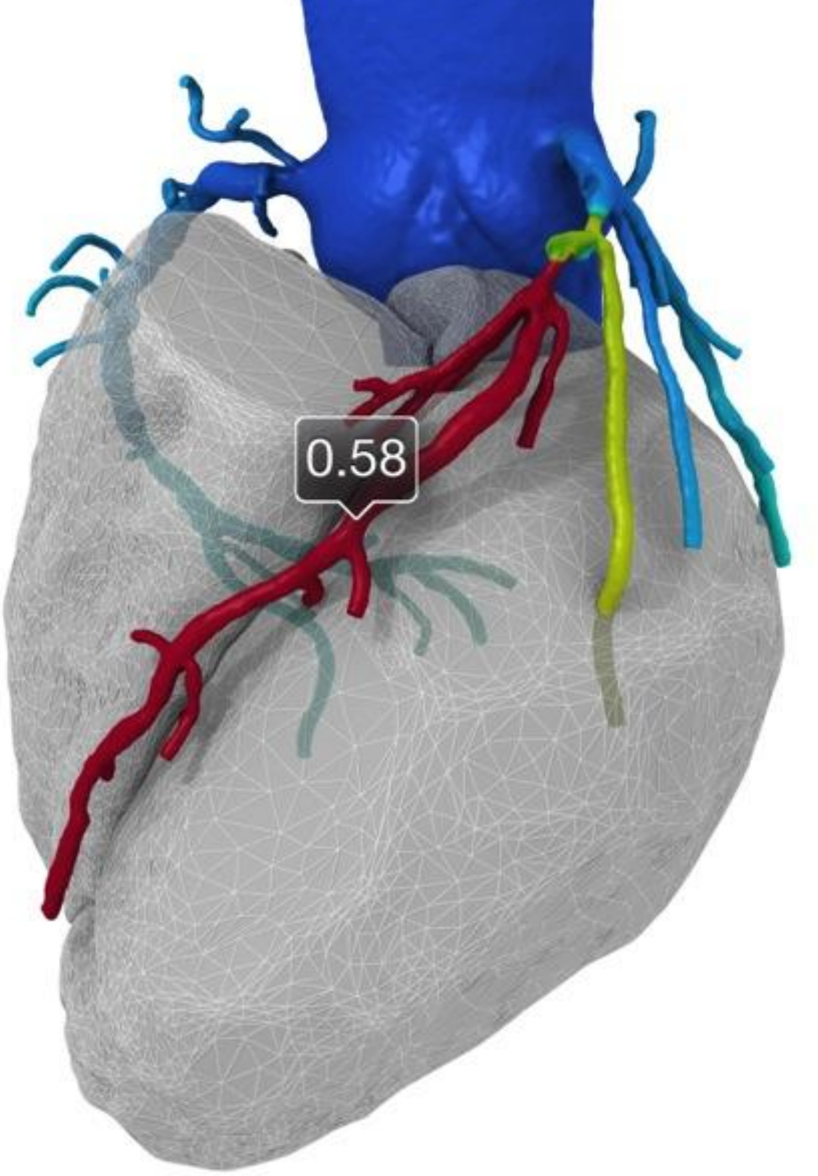
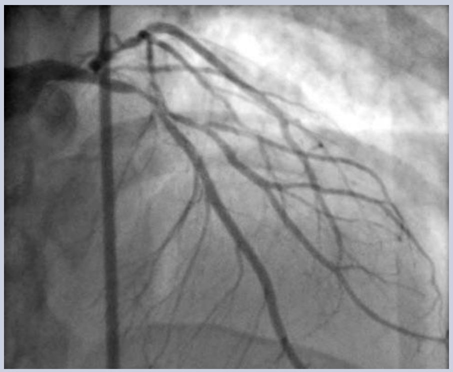
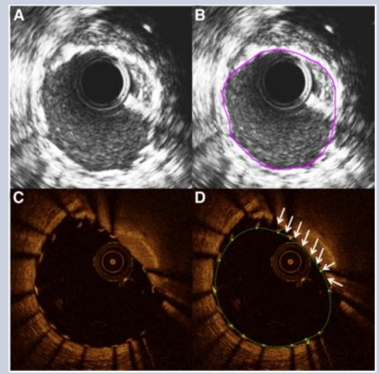
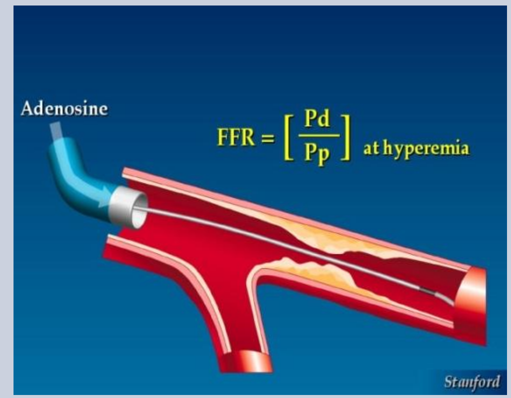
FFR_{CT}
The Basics

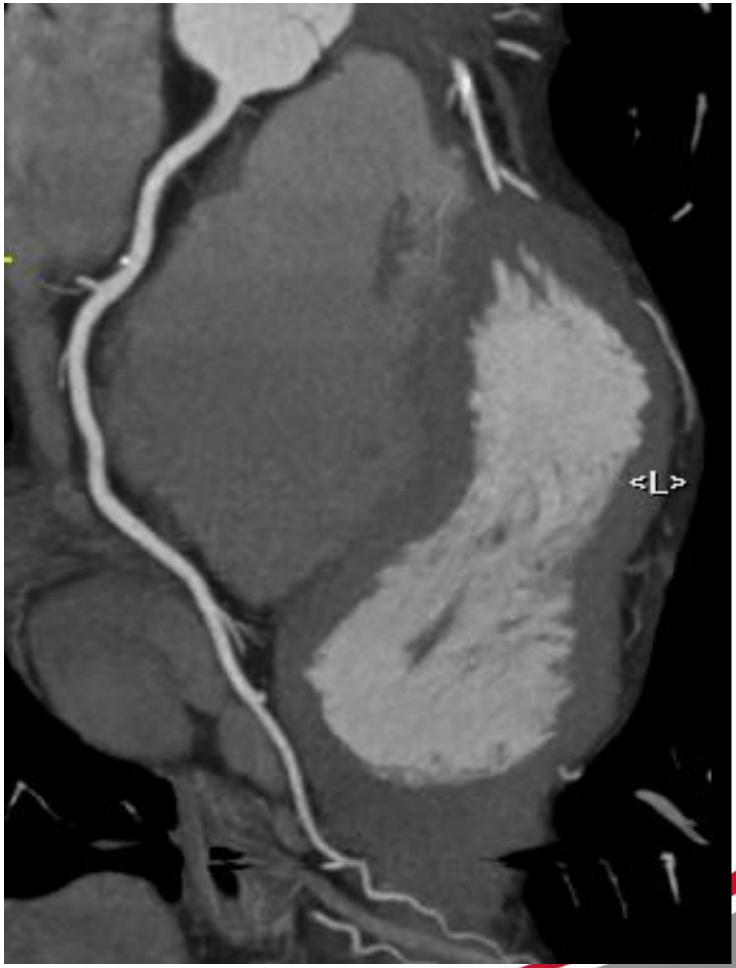
Campbell Rogers MD, FACC
Chief Medical Officer
HeartFlow, Inc.



Diagnosing anatomic and functionally-significant CAD

	ANATOMY ***Identify obstructive CAD***	***FUNCTION*** ***Identify lesion-specific ischemia that may benefit from PCI***
Invasive	 	
Non-invasive		

Cardiac CT has emerged as a superb noninvasive method for imaging coronary anatomy, but does not provide functional data



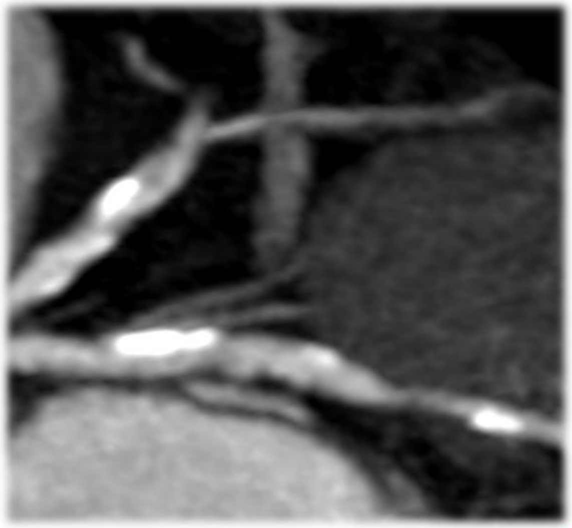
Images provided by J. Leipsic

Coronary CT angiography

- Coronary CTA has a high sensitivity and high negative predictive value for diagnosis of obstructive CAD

- However, coronary CTA cannot define the hemodynamic significance of coronary lesions

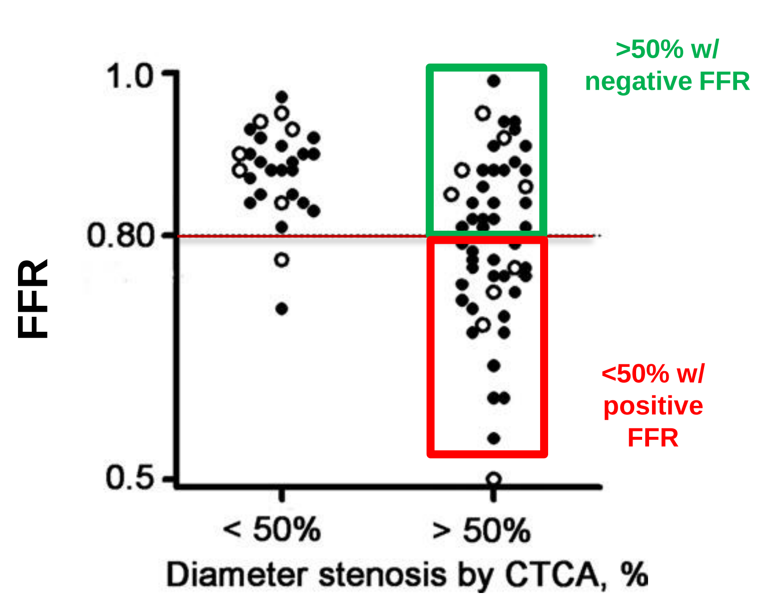
>50% diameter stenosis



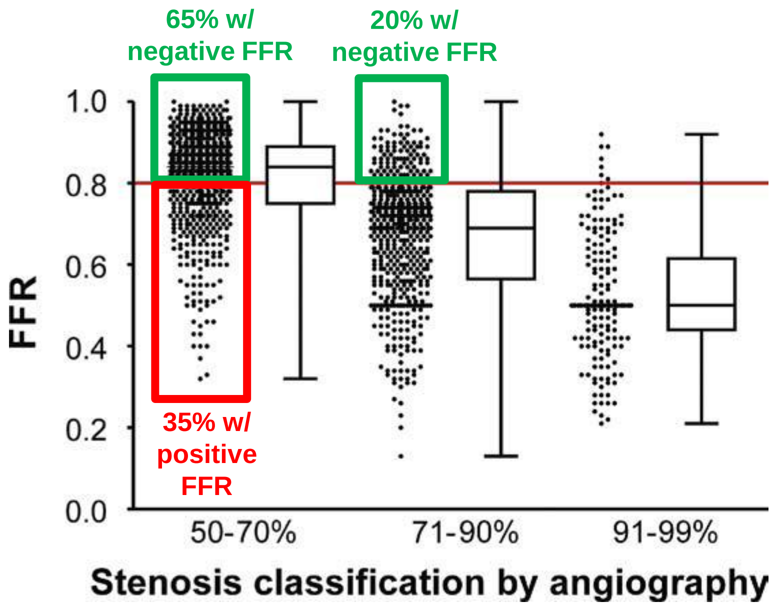
>50% diameter stenosis

Obstructive CAD identified by coronary CTA or by Coronary Angiography correlates poorly with FFR

>50% of lesions with greater than 50% diameter stenosis by CCTA have FFR>0.8[1]

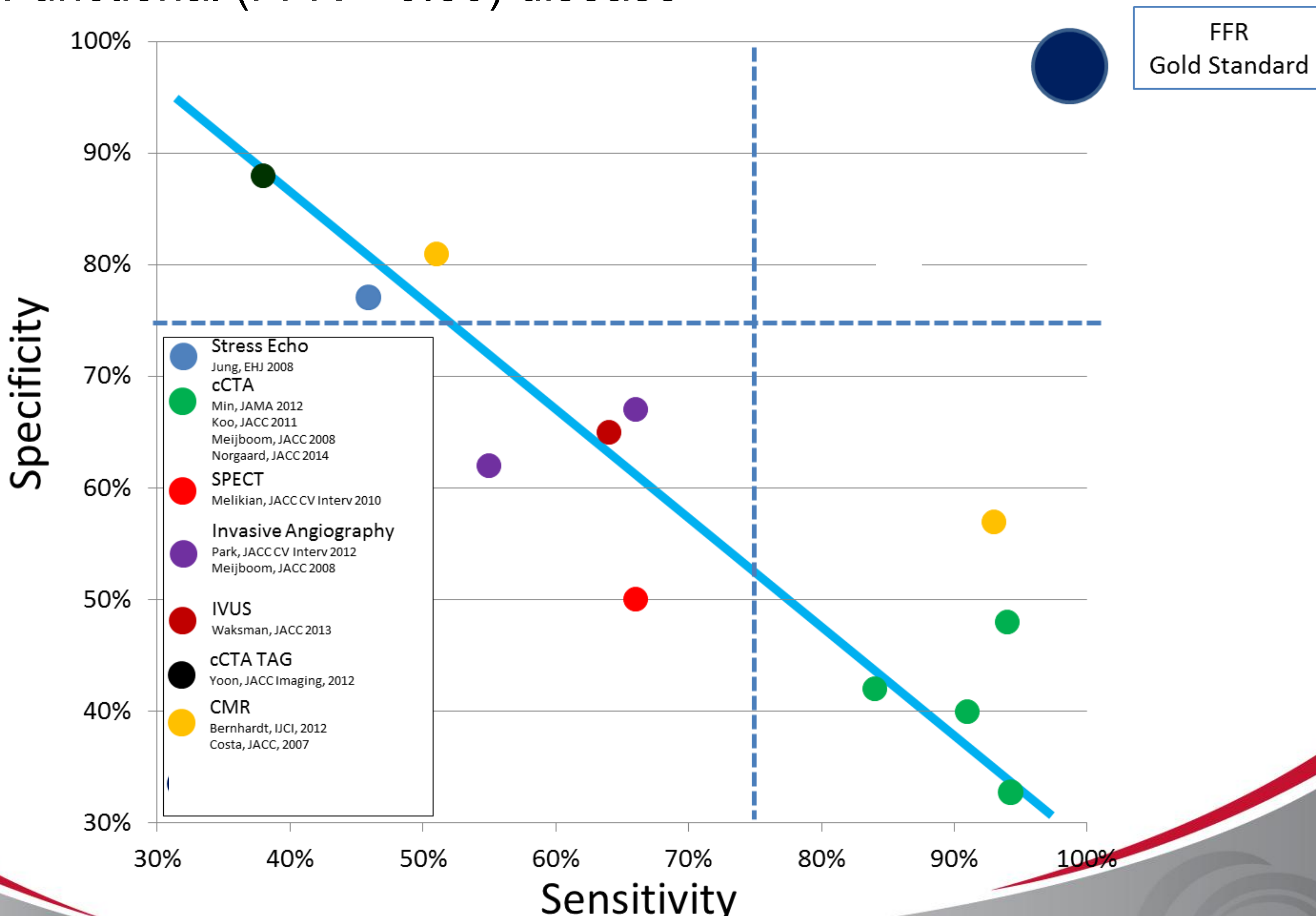


65% of intermediate lesions are incorrectly identified for stent placement by Angiograms[2]

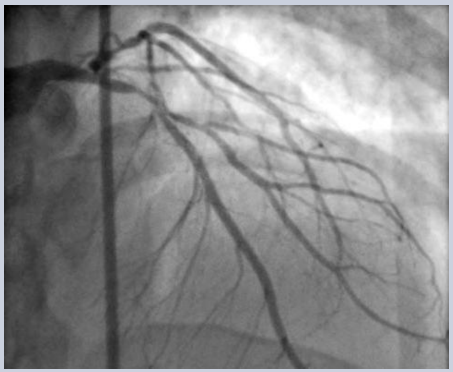
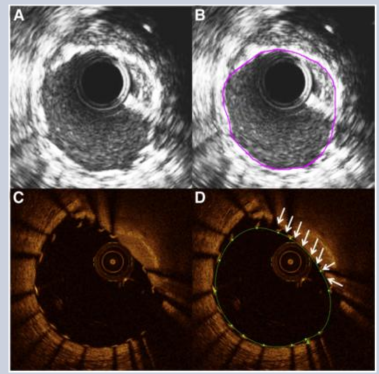
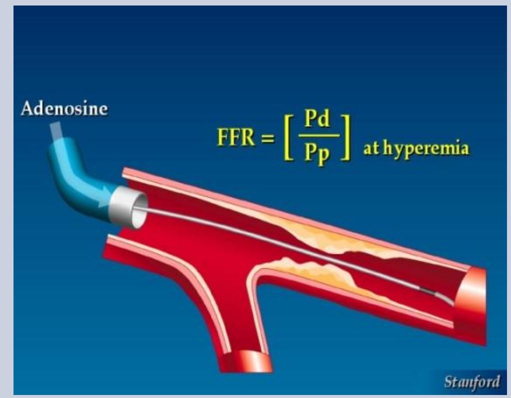
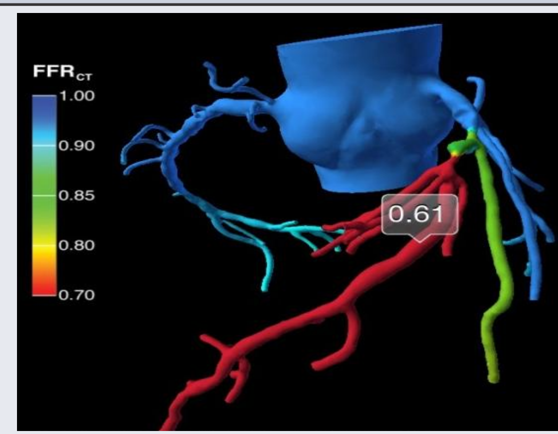


1. Meijboom et al. J Am CollCardiol 2008;52:636–43
2. Tonino et al. JACC 2010;55:2816-21

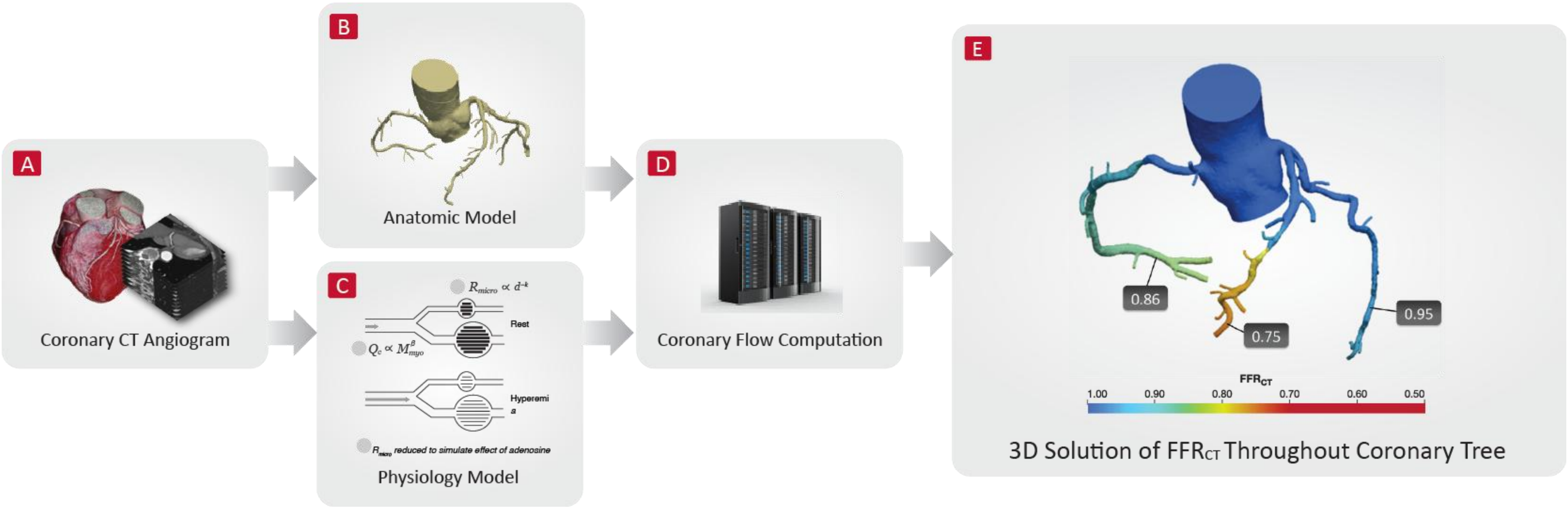
Diagnostic performance of Coronary diagnostic tests for Functional (FFR ≤ 0.80) disease



Diagnosing anatomic and functionally-significant CAD

	<u>ANATOMY</u> ***Identify obstructive CAD***	***<u>FUNCTION</u>*** ***Identify lesion-specific ischemia that may benefit from PCI***
Invasive	 	
Non-invasive		

FFR_{CT} Technology



Patient-Specific Coronary Flow and Pressure:

- Using a standard CT dataset a quantitative model is built
- A physiological model is developed using LV and coronary anatomy and established form-function principles
- A fluid model calculates flow and pressure under simulated hyperemic conditions

Taylor et al, JACC 2013; 61: 2233-41

FFR_{CT} Analysis Process

Geometry: 3D Model Creation from CT

Uploaded DICOM CT data

HeartFlow builds highly accurate 3D model of coronary tree

Physiological Boundary Conditions

Blood pressure

1. <u>Resting coronary flow</u> calculated from myocardial mass

2. Coronary <u>microcirculatory resistance</u> determined from size of feeding vessel

3. Effect of <u>hyperemia</u> on microcirculation

Fluid Properties

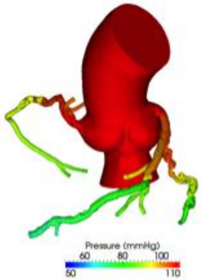
Viscosity and density of blood

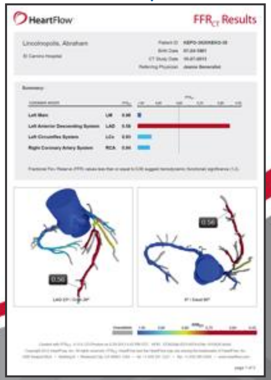
Supercomputer solves Equations of Blood Flow

$$\rho \vec{v}_{,t} + \rho \vec{v} \bullet \nabla \vec{v} = -\nabla p + \nabla \bullet \underset{\sim}{\tau}$$

$$\nabla \bullet \vec{v} = 0$$

Calculated Hyperemic Blood Flow & Pressure





HeartFlow — FFR_{CT} Results

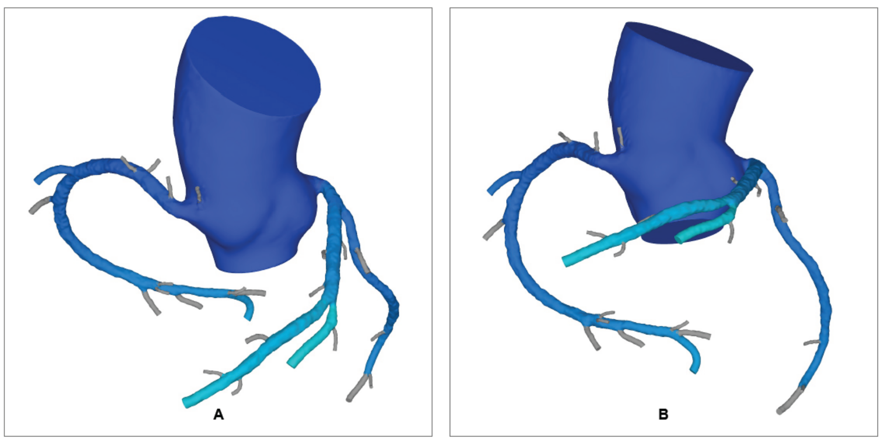
[redacted]

Patient ID 19-0062-S-L
Birth Date 4/23/1959
CT Study Date 1/21/2014

Summary

CORONARY ARTERY		FFR_{CT}
Left Main	LM	0.97
Left Anterior Descending System	LAD	0.91
Left Circumflex System	LCx	0.96
Right Coronary Artery System	RCA	0.94

Measured Fractional Flow Reserve (FFR) values ≤ 0.80 suggest hemodynamic (functional) significance (1,2,3).



FFR_{CT}: Unavailable | 1.00 | 0.90 | 0.80 | 0.70 | 0.60 | 0.50

Created with FFR_{CT} HeartFlow_v1.5.0.823 on 1/22/2014 10:44:24 PM UTC. HFID: 3aa905ef-4f87-4cde-9f3a-d8ecab6ee7f2

1400 Seaport Blvd • Building B • Redwood City, CA 94063 USA • tel: +1.650.241.1221 • fax: +1.650.368.2564 • www.heartflow.com

HeartFlow — FFR_{CT} Results

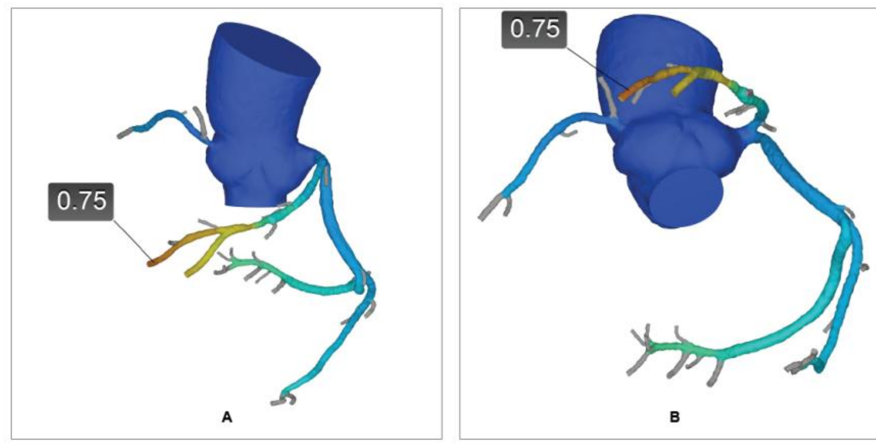
[redacted]

Patient ID 29-0070-G-C
Birth Date *Not provided*
CT Study Date 1/14/2014

Summary

CORONARY ARTERY		FFR_{CT}
Left Main	LM	0.98
Left Anterior Descending System	LAD	0.75
Left Circumflex System	LCx	0.86
Right Coronary Artery System	RCA	0.94

Measured Fractional Flow Reserve (FFR) values ≤ 0.80 suggest hemodynamic (functional) significance (1,2,3).



FFR_{CT}: Unavailable | 1.00 | 0.90 | 0.80 | 0.70 | 0.60 | 0.50

Created with FFR_{CT} HeartFlow_v1.5.0.823 on 1/15/2014 2:17:44 AM UTC. HFID: 3b5e974c-48f7-4cd6-82d3-d7bad4c1d582

1400 Seaport Blvd • Building B • Redwood City, CA 94063 USA • tel: +1.650.241.1221 • fax: +1.650.368.2564 • www.heartflow.com

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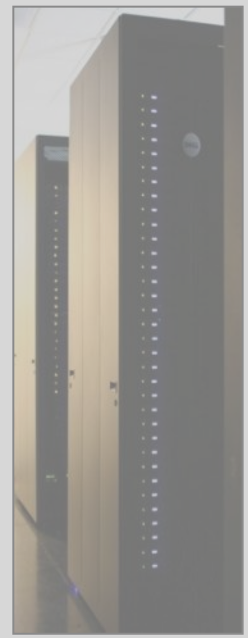
$$\nabla \bullet \vec{v} = 0$$

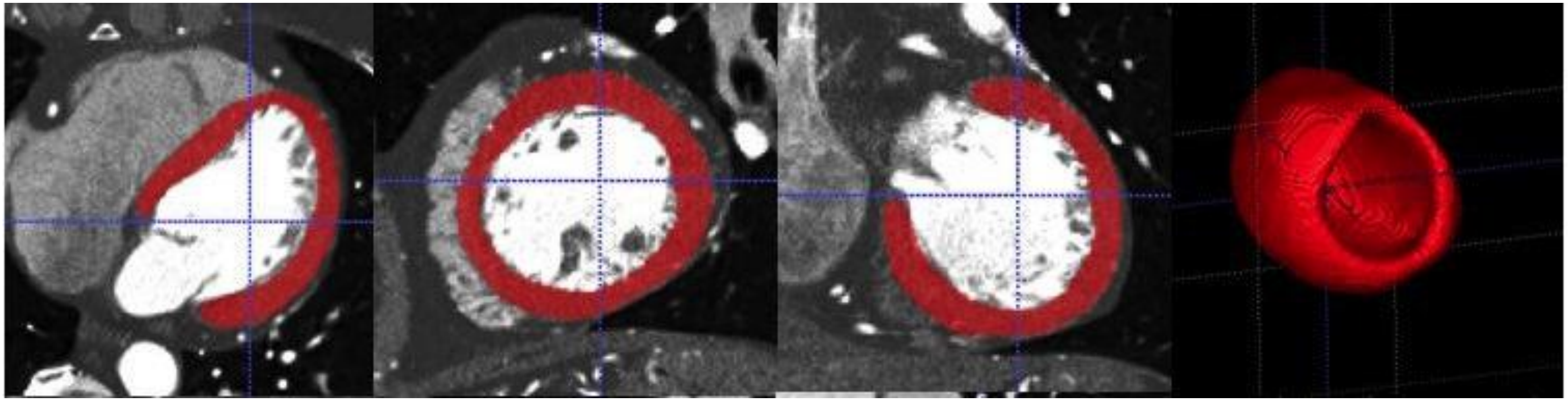


Calculated Hyperemic Blood Flow & Pressure

Physiological Boundary Conditions: Resting Coronary Flow

Scientific Principle #1:

Resting coronary blood flow proportional to myocardial mass



Measuring the size of the organ to determine total coronary flow

Physiological Boundary Conditions: Coronary Microcirculatory Resistance

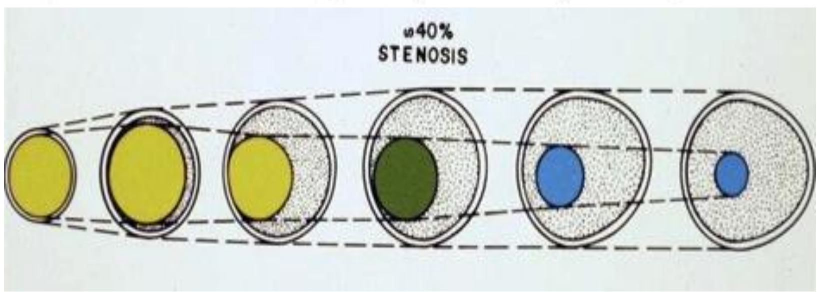
Scientific Principle #2

Resistance of microcirculatory vascular bed at rest is inversely proportional to size of feeding vessel

HeartFlow technology leverages 30 years of research on hemodynamics, vascular wall biology and atherosclerosis

COMPENSATORY ENLARGEMENT OF HUMAN ATHEROSCLEROTIC CORONARY ARTERIES

SEYMOUR GLAGOV, M.D., ELLIOT WEISENBERG, B.A., CHRISTOPHER K. ZARINS, M.D., REGINA STANKUNAVICIUS, M.P.H., AND GEORGE J. KOLETTIS, B.A.



- Atherosclerotic plaque evolution
- Artery wall adaptive responses

Small coronary artery branches have a higher resistance to flow than larger branches

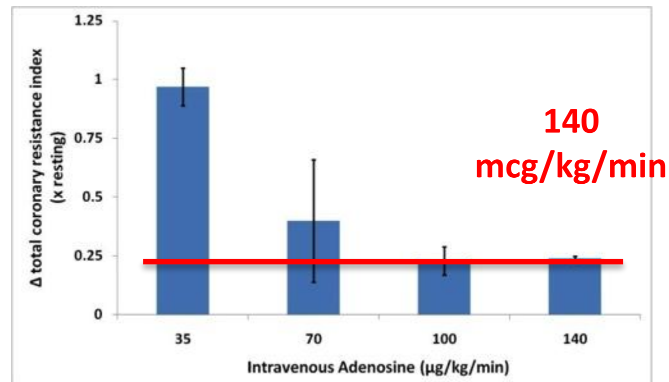
The ability to calculate microcirculatory resistance

Physiological Boundary Conditions: Effect of Adenosine

Scientific Principle #3

Microcirculation has a predictable response to adenosine

Adenosine relaxes smooth muscle cells lining arterioles resulting in vasodilation



Intravenous administration of adenosine elicits remarkably consistent vasodilatory response at sufficient doses

The ability to model the effect of adenosine

HeartFlow Clinical Trial Data

- **DISCOVER-FLOW**
  - Completed 2011
  - N=104 patients

Journal of the American College of Cardiology
Published by Elsevier Inc.
Vol. 58, No. 19, 2011
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.06.066

Cardiac Imaging

Diagnosis of Ischemia-Causing Coronary Stenoses by Noninvasive Fractional Flow Reserve Computed From Coronary Computed Tomographic Angiograms

Results From the Prospective Multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) Study

Bon-Kwon Koo, MD, PhD,* Andrejs Erglis, MD, PhD,† Joon-Hyung Doh, MD, PhD,‡ David V. Daniels, MD,§ Sanda Jegere, MD,‖ Hyo-Soo Kim, MD, PhD,* Allison Dunning, MD,¶ Tony DeFrance, MD,# Alexandra Lansky, MD,** Jonathan Leipsic, BSc, MD,†† James K. Min, MD‡‡

Seoul and Goyang, South Korea; Riga, Latvia; Palo Alto, San Francisco, and Los Angeles, California; New York, New York; New Haven, Connecticut; and Vancouver, British Columbia, Canada

- **DeFACTO**
  - Completed 2012
  - N=252 patients

ONLINE FIRST

Diagnostic Accuracy of Fractional Flow Reserve From Anatomic CT Angiography

JAMA. 2012;308(12):doi:10.1001/2012.jama.11274

- **NXT**
  - Completed 2013
  - N=254 patients
  - 10 Worldwide Sites
    - EU
    - Australia
    - Japan
    - Korea

Journal of the American College of Cardiology
Published by Elsevier Inc.
Vol. 63, No. 12, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.11.043

CLINICAL RESEARCH — Clinical Trials

(J Am Coll Cardiol 2014;63:1145–55) © 2014 by the American College of Cardiology Foundation

Diagnostic Performance of Noninvasive Fractional Flow Reserve Derived From Coronary Computed Tomography Angiography in Suspected Coronary Artery Disease

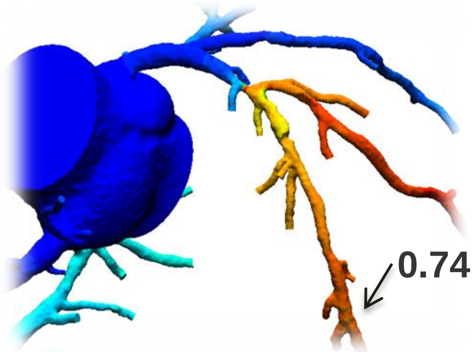
The NXT Trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps)

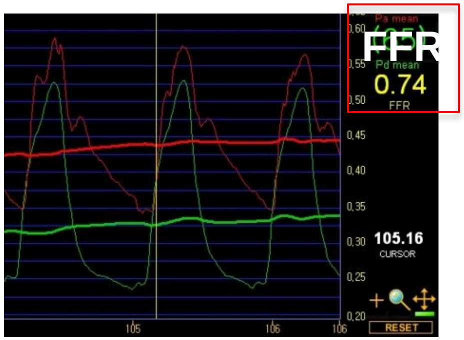
Bjarne L. Nørgaard, MD, PhD,* Jonathon Leipsic, MD, PhD,† Sara Gaur, MD,* Sujith Seneviratne, MBBS,‡ Brian S. Ko, MBBS, PhD,‡ Hiroshi Ito, MD, PhD,§ Jesper M. Jensen, MD, PhD,* Laura Mauri, MD, PhD,‖ Bernard De Bruyne, MD, PhD,¶ Hiram Bezerra, MD, PhD,# Kazuhiro Osawa, MD,§ Mohamed Marwan, MD, PhD,** Christoph Naber, MD, PhD,†† Andrejs Erglis, MD, PhD,‡‡ Seung-Jung Park, MD, PhD,§§ Evald H. Christiansen, MD, PhD,* Anne Kaltoft, MD, PhD,* Jens F. Lassen, MD, PhD,* Hans Erik Bøtker, MD, DMSci,* Stephan Achenbach, MD, PhD,** on behalf of the NXT Trial Study Group

Aarhus, Denmark; Vancouver, British Columbia, Canada; Victoria, Australia; Okayama, Japan; Boston, Massachusetts; Aalst, Belgium; Cleveland, Ohio; Erlangen and Essen, Germany; Riga, Latvia; and Seoul, South Korea

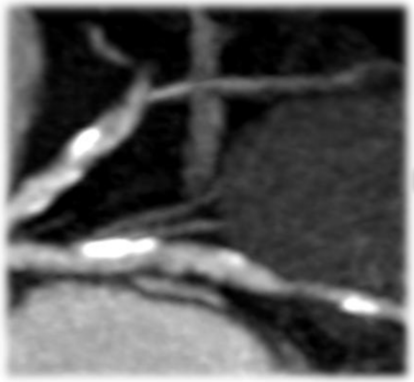
HeartFlow Clinical Trial Case Examples

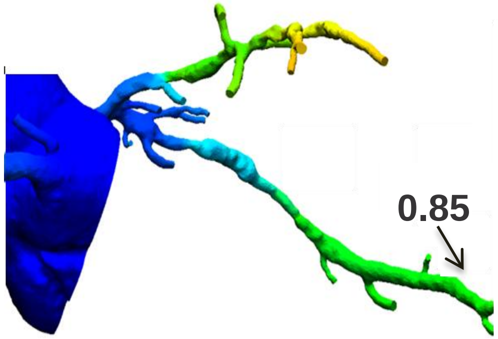
Coronary CTA	FFR_{CT}	Invasive angiography	FFR

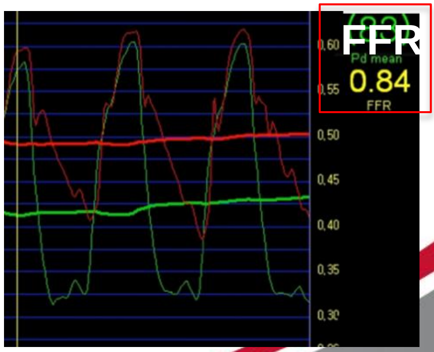




>50% diameter stenosis | FFR_{CT} 0.74 → ischemia | >50% diameter stenosis | FFR 0.74 → ischemia



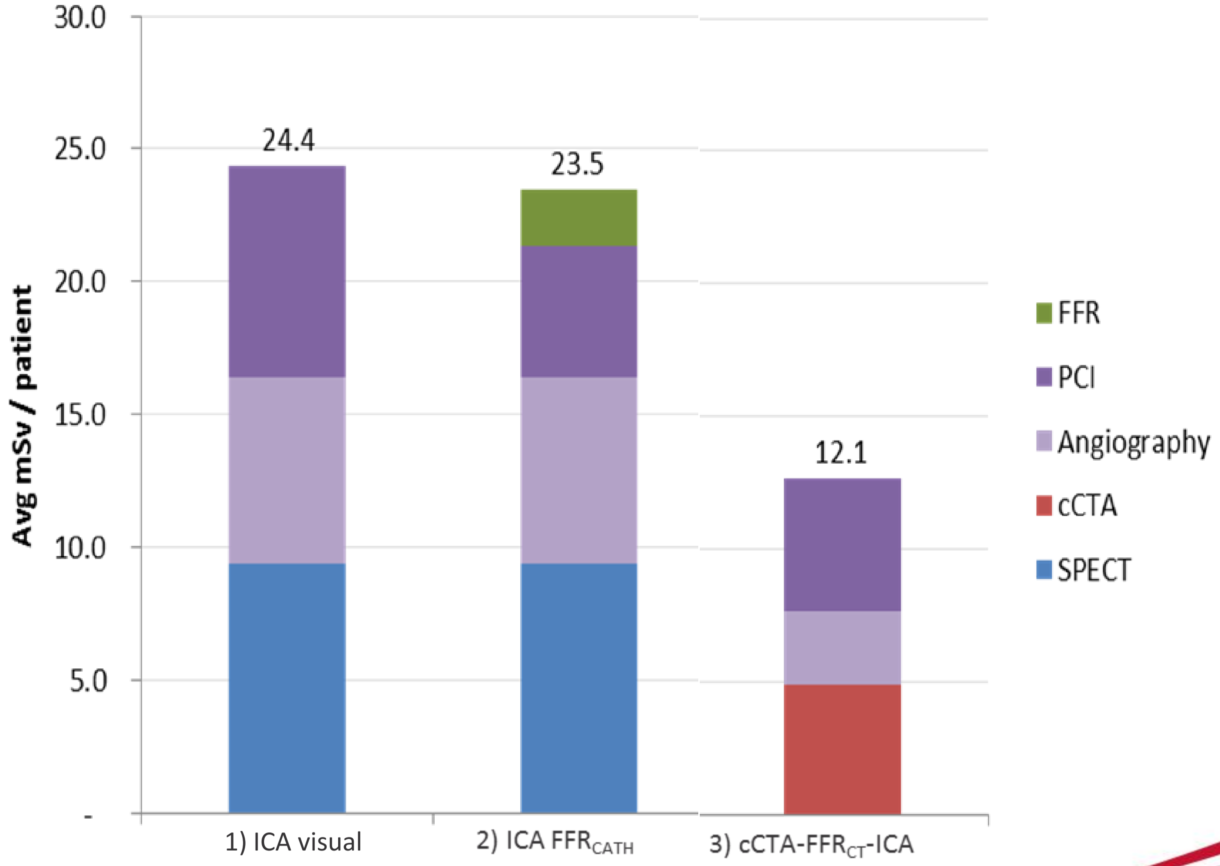




>50% diameter stenosis | FFR_{CT} 0.85 → no ischemia | >50% diameter stenosis | FFR 0.84 → no ischemia

Source: Koo et al. J Am Coll Cardiol 2011

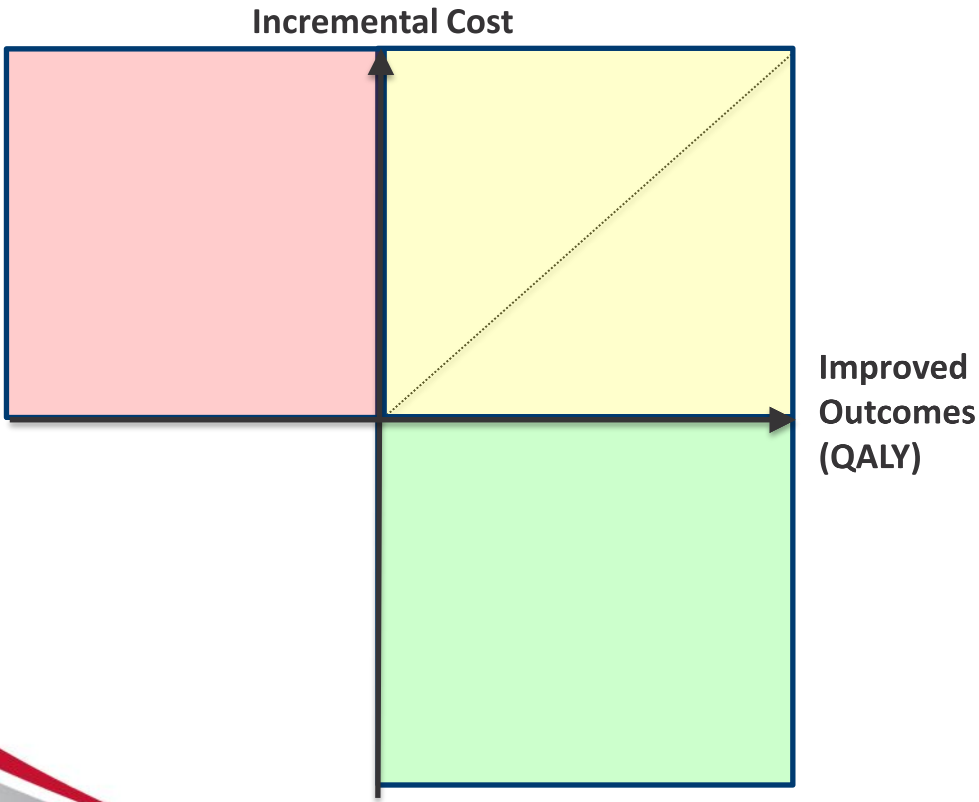
Estimated Patient Radiation Exposure Based on CAD Dx Pathway



Data on file, HeartFlow Inc.

What are the health economic tradeoffs associated with FFR use in patients with known CAD?

Economic Evaluation of Fractional Flow Reserve Guided Percutaneous Coronary Intervention in Patients With Multivessel Disease
William F. Fearon, Bernhard Bornschein, Pim A.L. Tonino, Raffaella M. Gothe, Bernard De Bruyne, Nico H.J. Pijls, Uwe Siebert and for the Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) Study Investigators
Circulation 2010;122;2545-2550; originally published online Nov 29, 2010;



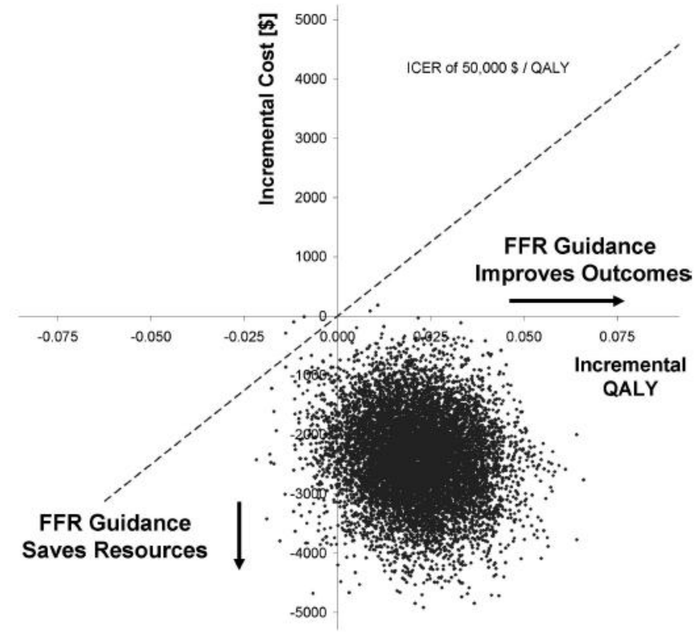


Figure 1. Bootstrap simulation of incremental costs and effects. Numbers on axes represent differences between FFR-guided and angiography-guided strategies. Positive incremental quality-adjusted life-years (QALYs) indicate higher effectiveness for FFR-guided treatment. Negative incremental costs indicate lower costs for FFR-guided treatment compared with angiography-guided strategy. Data are from 5000 bootstrap replications.

CLINICAL CARDIOLOGY

Clinical Investigations

Projected Costs and Consequences of Computed Tomography-Determined Fractional Flow Reserve

Mark A . Hlatky, MD; Akshay Saxena, MD; Bon-Kwon Koo, MD; Andrejs Erglis, MD; Christopher K. Zarins, MD; James K. Min, MD

	Diagnostic Strategy		
	ICA/Visual	ICA/FFR_{ICA}	cCTA/ICA/Visual
No. of ICAs (per 100 patients)	100	100	84
No. of patients undergoing PCI (per 100 patients)	81	48	72
No. of vessels treated by PCI (per 100 patients)	98	51	88
No. of vessels treated per patient undergoing PCI	1.21	1.07	1.22
Death/MI rate at 1 year	2.63%	1.96%	2.56%
Initial treatment costsper patient	$10702	$8499	$9635

Hlatky et al, Clin Cardiol 2013; DOI:10.1002/clc.22205

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	Diagnostic Strategy			
	ICA/Visual	ICA/FFR_{ICA}	cCTA/ICA/Visual	cCTA/ FFR_{CT}/ICA
No. of ICAs (per 100 patients)	100	100	84	51
No. of patients undergoing PCI (per 100 patients)	81	48	72	49
No. of vessels treated by PCI (per 100 patients)	98	51	88	59
No. of vessels treated per patient undergoing PCI	1.21	1.07	1.22	1.21
Death/MI rate at 1 year	2.63%	1.96%	2.56%	2.31%
Initial treatment costsper patient	$10702	$8499	$9635	$7674

- **Use of FFR_{CT} to select patients for ICA and PCI may result in 30% lower costs and 12% fewer events at one year compared to the most common strategy of ICA and visual guidance for PCI**

Hlatky et al, Clin Cardiol 2013; DOI:10.1002/clc.22205

Primary Peer-reviewed Publications

1.	DISCOVER-FLOW study results	Koo	JACC 2011; 58: 1989
2.	DISCOVER-FLOW intermediate stenosis	Min	Am J Cardiol 2012; 971
3.	DISCOVER-FLOW image quality	Min	JCCT 2012; 6: 191
4.	DeFACTO rationale and design	Min	JCCT 2011; 5: 3011
5.	DeFACTO study results	Min	JAMA 2012; 308(12): 1237
6.	DeFACTO intermediate stenosis	Nakazato	Circulation: CV Imaging 2013 ; 6: 881
7.	DeFACTO image quality, patient prep	Leipsic	Am J Radiology 2013, in press
8.	Non-invasive FFR: scientific basis	Serruys	EuroIntervention 2012; 8: 511
9.	Scientific basis of FFR_{CT}	Taylor	JACC 2013, 61: 2233-41
10.	FFR_{CT} derived from cCTA	Zarins	J Cardiovasc Transl Res 2013
11.	Non-inv dx of ischemia-causing stenosis	Yoon	JACC Imaging 2012; 5: 1088
12.	CT-FFR next level in cardiac imaging	Meijs	Neth Heart J 2012; 20: 410
13.	Noninvasive FFR using CT	Yoon	Cardiovasc Dx and Rx 2012; 2: 105
14.	Integrating physiology and anatomy	Arsanjani	Curr Cardiovasc Imaging Rep 2012; 5: 301
15.	Modeling of FFR based on cCTA	Grunau	Curr Cardio Rep 2013; 15: 336
16.	ABSORB trial 5 year follow up	Serruys	JACC Interventions 2013, 6: 999
17.	FFR_{CT} anatomic-functional integration	Al-Hassan	Future Cardiol 2013; 9: 243
18.	New frontiers in CTA	Min	Heart 2013; 99: 661
19.	Virtual FFR by CT	Rajani	Eurointervention 2013; 9:277
20.	Physiologic assessment of CAD by CT	Kochar	Korean Circ J 2013; 43: 435
21.	Virtual coronary stenting and FFR_{CT}	Kim	JACC Interventions 2013
22.	Cost-consequences of FFR_{CT}	Hlatky	Clinical Cardiology 2013, 36: 743
23.	HeartFlowNXT rationale and design	Gaur	JCCT 2013, 7: 279
24.	HeartFlowNXT study results	Norgaard	JACC 2014 (on line January 29, 2014)