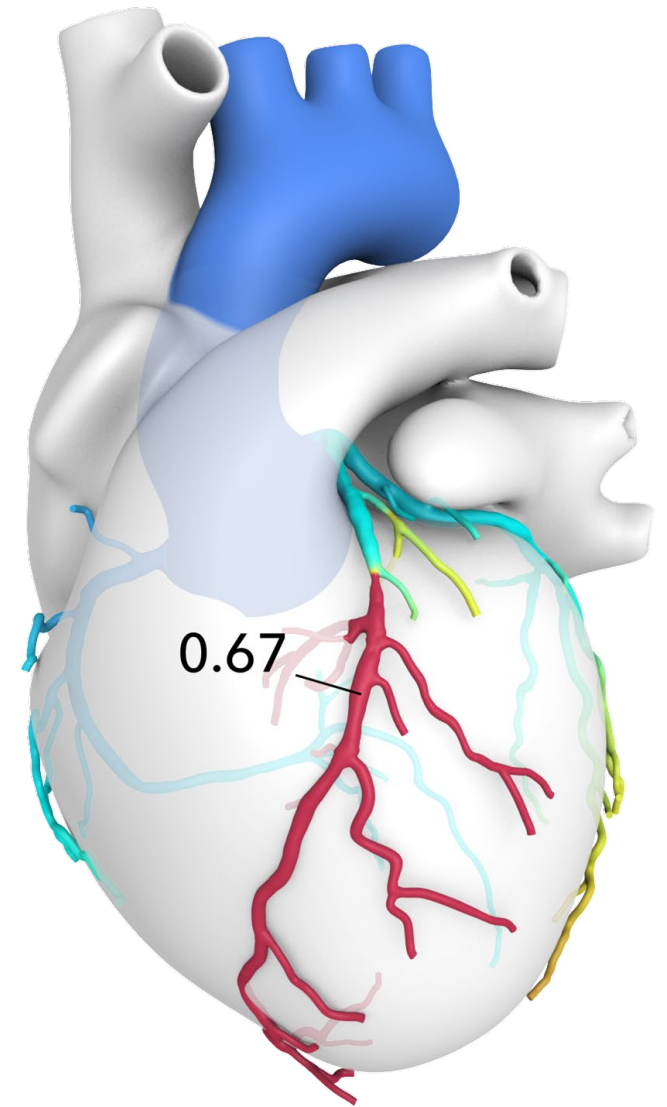


Cardiac Digital Twins: From the Academy to the Clinic

Charles A. Taylor, Ph.D.

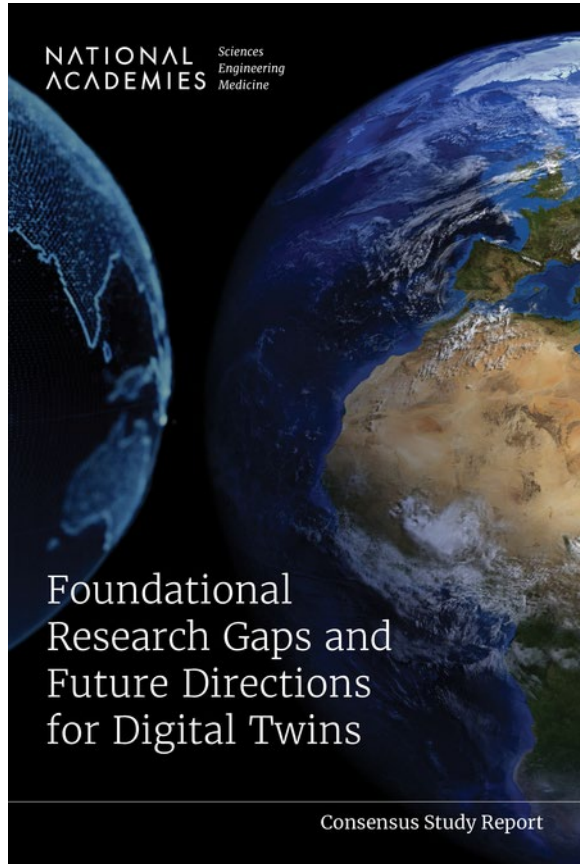
*W.A. “Tex” Moncrief, Jr., Chair in Computational Medicine
Professor, Department of Internal Medicine and the Oden
Institute for Computational Engineering and Sciences
Director of the Center for Computational Medicine
University of Texas at Austin*



Disclosures

- Founder, Board Member, and Shareholder, HeartFlow, Inc., Mountain View, California, U.S.A.

Recent National Academies report on Digital Twins to “inform clinical decisions regarding interventions including treatments and clinical assessments ...”



Biomedical Digital Twins (my synopsis)

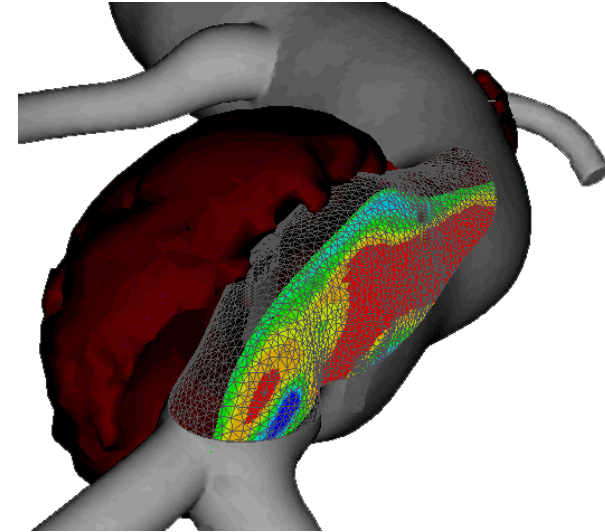
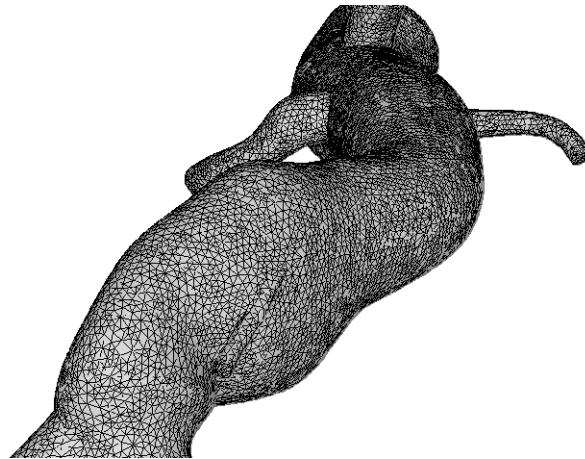
Virtual model of biological system that ...

1. mimics the biological system
2. is fit for purpose
3. is created & updated with data from its biological twin
4. has a predictive capability to inform decisions for the biological twin

Chapter 1 – The Academy



Patient-specific Modeling of Blood Flow started at Stanford University in 1995

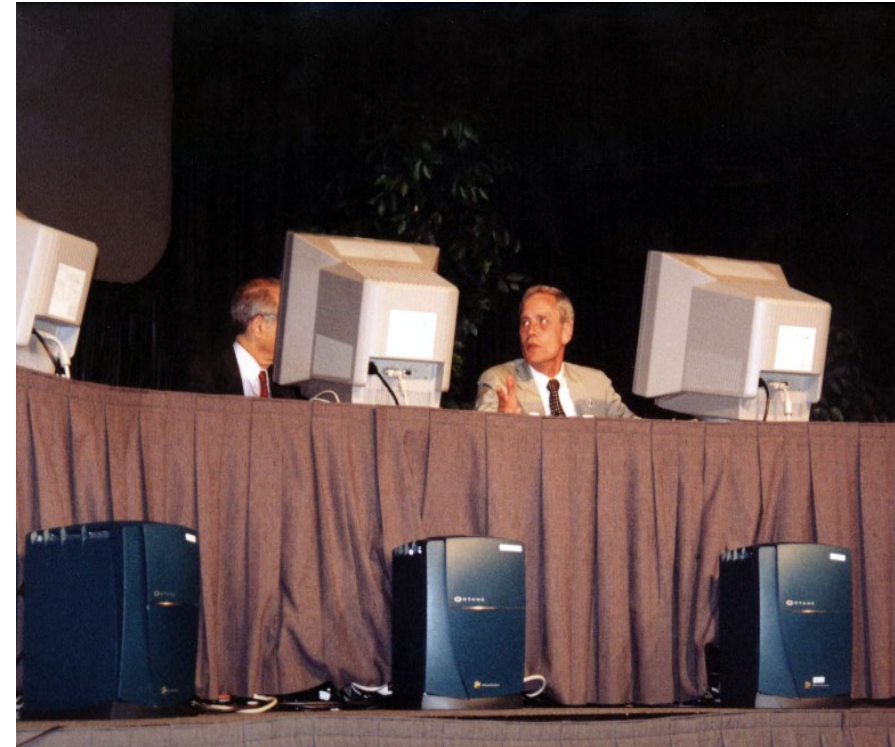


1. C.A. Taylor, T.J.R. Hughes, and C.K. Zarins, (1996) Computers in Physics, Vol. 10, No. 3, pp. 224-232.
2. C.A. Taylor, T.J.R. Hughes, and C.K. Zarins, (1998) Finite Element Modeling of Blood Flow in Arteries. Computer Methods in Applied Mechanics and Engineering. Vol. 158, Nos. 1-2, pp. 155-196.

Predictive Medicine circa 1998



ASPIRE System



Live Demo at 1998 Society for Vascular Surgeons

Taylor et al., Predictive Medicine: Computational Techniques in Therapeutic Decision-Making, *Computer Aided Surgery*, Vol. 4, No. 5, pp. 231-247, 1999.

Predictive Medicine paper published 25 years ago ...

Computer Aided Surgery 4:231-247 (1999)

Biomedical Paper

Predictive Medicine: Computational Techniques in Therapeutic Decision-Making

Charles A. Taylor, Ph.D., Mary T. Draney, M.S., Joy P. Ku, M.S., David Parker, B.S., Brooke N. Steele, M.S., Ken Wang, M.S., and Christopher K. Zarins, M.D.

Division of Vascular Surgery, Department of Surgery (C.A.T., C.K.Z.), Department of Mechanical Engineering (C.A.T., M.T.D., D.P., B.N.S.), and Department of Electrical Engineering (J.P.K., K.W.), Stanford University, Stanford, California, USA

ABSTRACT The current paradigm for surgery planning for the treatment of cardiovascular disease relies exclusively on diagnostic imaging data to define the present state of the patient, empirical data to evaluate the efficacy of prior treatments for similar patients, and the judgement of the surgeon to decide on a preferred treatment. The individual variability and inherent complexity of human biological systems is such that diagnostic imaging and empirical data alone are insufficient to predict the outcome of a given treatment for an individual patient. We propose a new paradigm of *predictive medicine* in which the physician utilizes computational tools to construct and evaluate a combined anatomic/physiologic model to predict the outcome of alternative treatment plans for an individual patient. The predictive medicine paradigm is implemented in a software system developed for Simulation-Based Medical Planning. This system provides an integrated set of tools to test hypotheses regarding the effect of alternate treatment plans on blood flow in the cardiovascular system of an individual patient. It combines an internet-based user interface developed using Java and VRML, image segmentation, geometric solid modeling, automatic finite element mesh generation, computational fluid dynamics, and scientific visualization techniques. This system is applied to the evaluation of alternate, patient-specific treatments for a case of lower extremity occlusive cardiovascular disease. *Comp Aid Surg* 4:231-247 (1999). ©1999 Wiley-Liss, Inc.

INTRODUCTION

Significant advances have been made in the diagnosis and treatment of cardiovascular disease since the introduction of modern medical imaging technology and surgical and pharmacologic therapeutic options. In recent years, three-dimensional (3D) cardiovascular imaging techniques and medical visualization software have enabled physicians to interactively view the cardiovascular anatomy externally and even to "fly through" blood vessels in order to examine sites of disease.^{27,30,37-40} In addition to obtaining anatomic data, physicians can

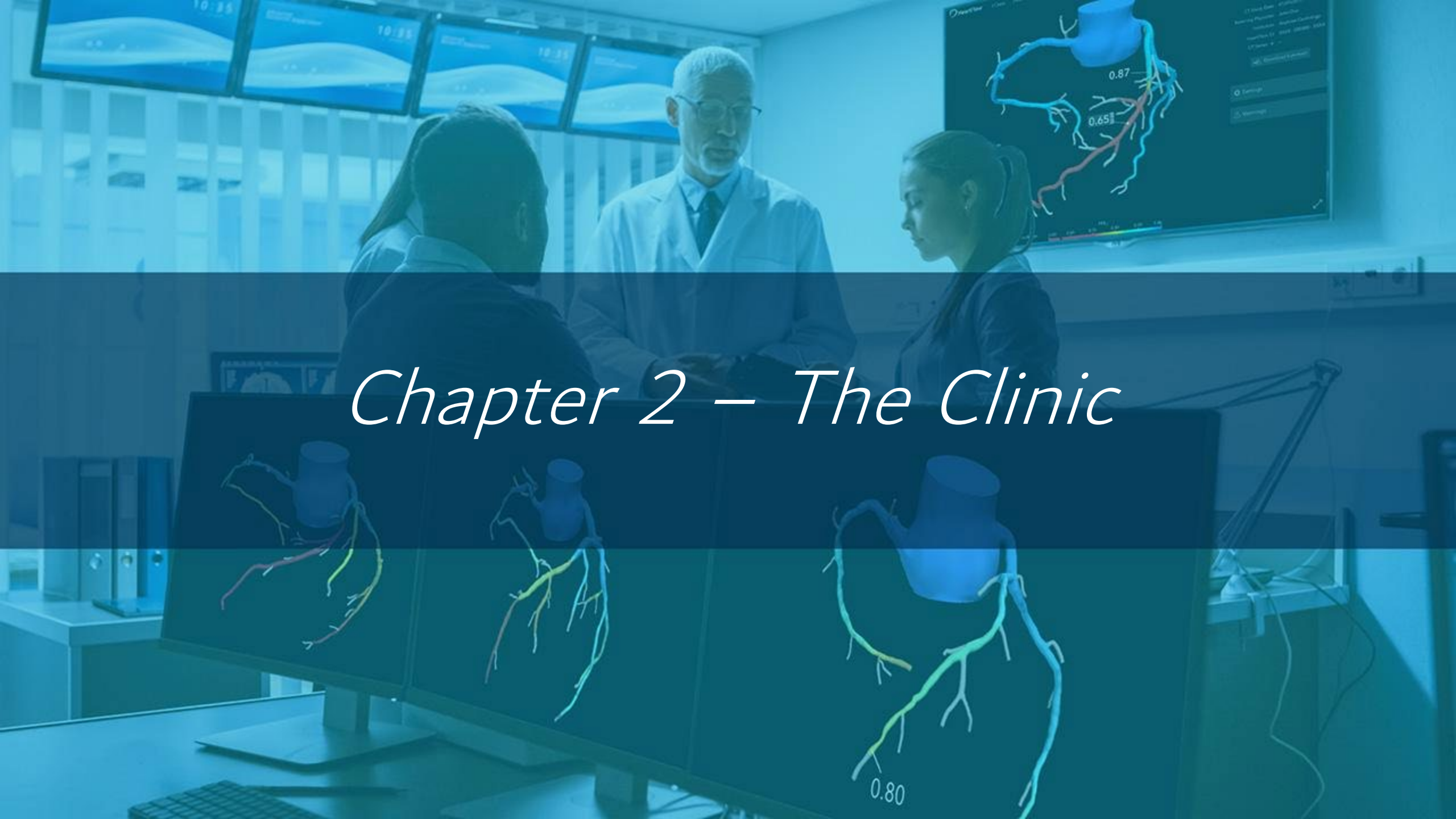
obtain physiologic data from a variety of sources, including Doppler ultrasound and magnetic resonance imaging. It is now possible to obtain time-resolved 3D flow fields in the cardiovascular system using magnetic resonance imaging (MRI) techniques in a matter of minutes.¹⁴ In parallel with these developments in diagnostic methods, therapeutic options including conventional surgical repair, minimally invasive endoluminal approaches, and drug and gene therapy have emerged. Within these different classes of therapeutic options lie many more subclasses. The physician must choose

The predictive medicine paradigm, whereby a physician would use diagnostic data to reconstruct a model of an individual's anatomy and physiology, and then use simulation techniques, implemented in a simulation-based medical planning software system, will have important applications in medicine of the future. This approach could allow physicians to "design" improved, patient-specific treatment plans.

Received March 5, 1999; accepted August 20, 1999.

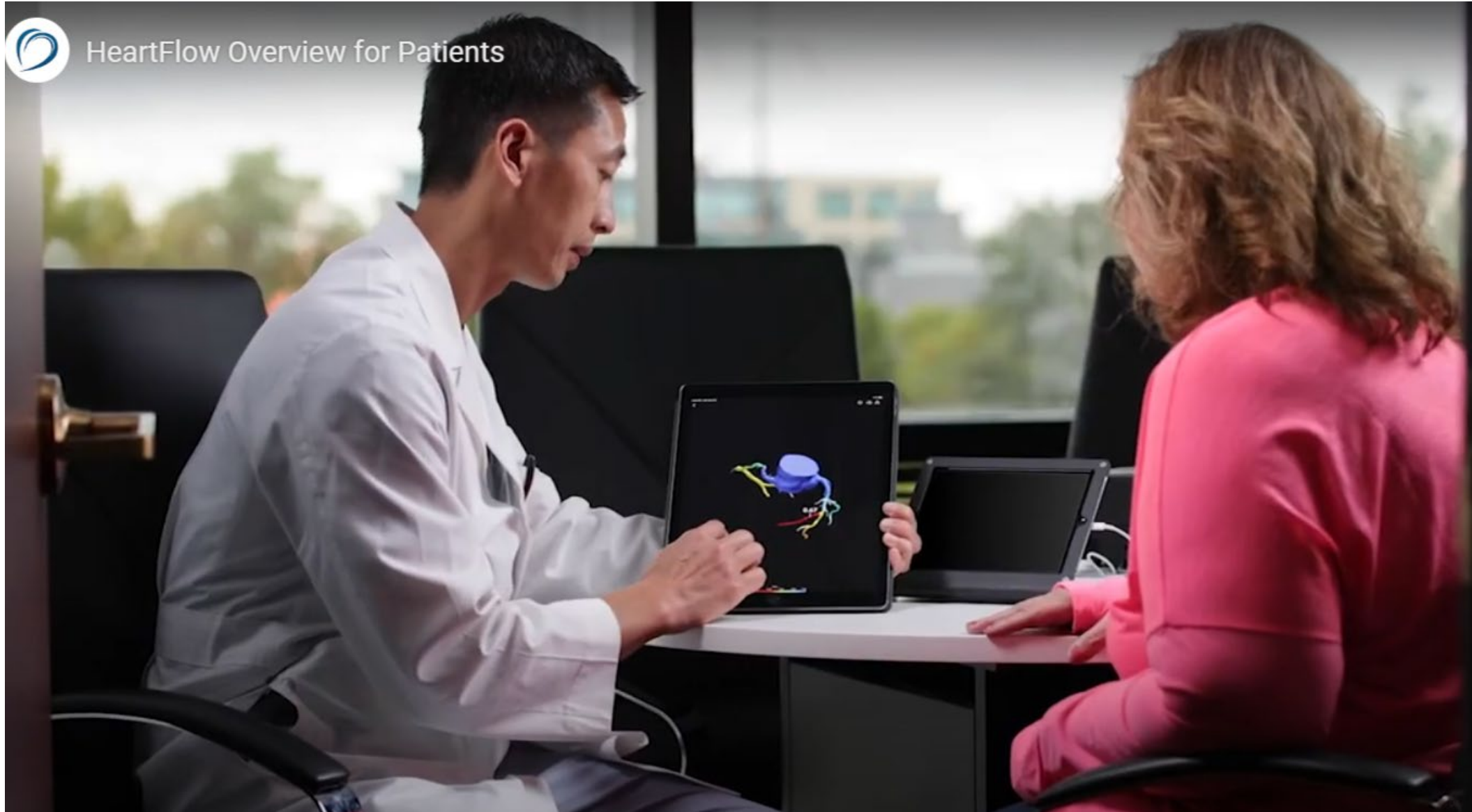
Address correspondence/reprint requests to: Charles A. Taylor, Ph.D., Division of Vascular Surgery, Department of Surgery, Stanford University, Stanford, CA 94305, U.S.A. Telephone: (650) 723-3487; Fax: (650) 723-3521. E-mail: taylorca@leland.stanford.edu.
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Taylor et al., Predictive Medicine: Computational Techniques in Therapeutic Decision-Making, *Computer Aided Surgery*, Vol. 4, No. 5, pp. 231-247, 1999.

A blue-tinted photograph of three medical professionals in a clinic. A male doctor in a white lab coat stands in the center, gesturing towards a large monitor on the right. Two other professionals, a man and a woman, are looking at the monitor. The room is filled with multiple computer monitors displaying medical data, including 3D vascular models and numerical values. The overall atmosphere is professional and high-tech.

Chapter 2 – The Clinic

HeartFlow Founded in 2010 to improve diagnosis of Heart Disease



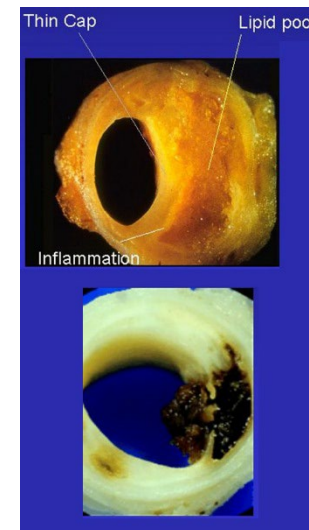
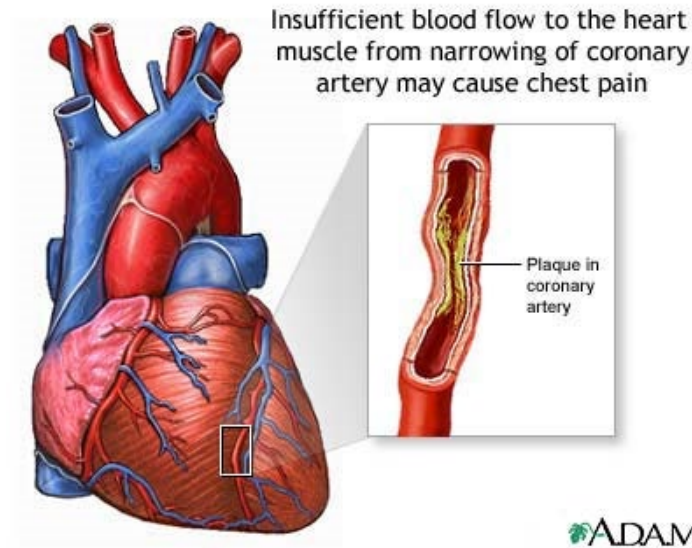
Coronary Artery Disease (CAD) one of primary heart diseases

Can elicit symptoms - Angina (chest pain)

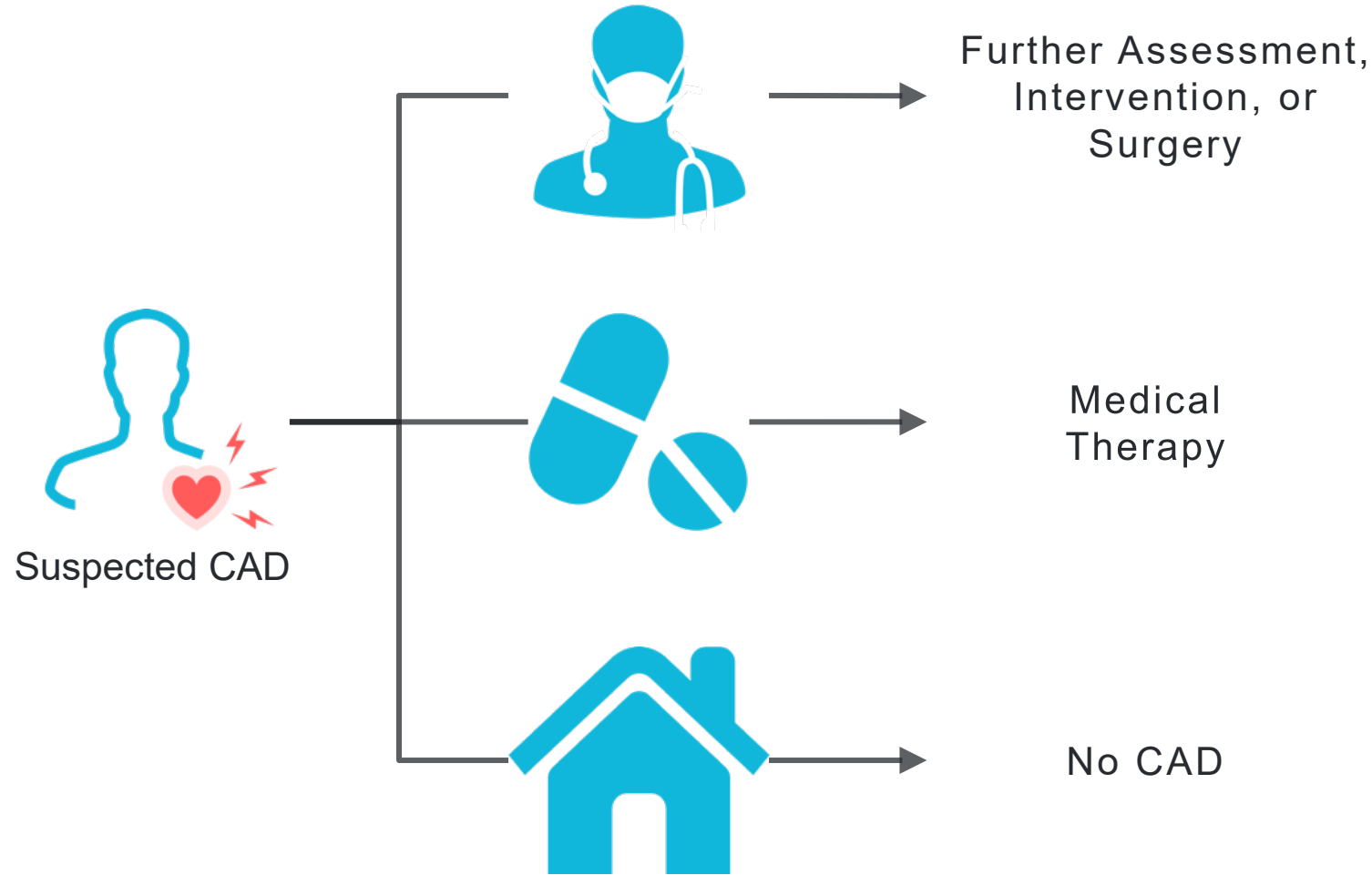
- Atherosclerotic plaque build-up in artery
- Reduced blood flow → pain
- Typically first noticed during exertion

Can increase risk of a myocardial infarction, e.g. heart attack

- Plaque rupture results in embolization of contents and/or triggers clot formation which obstructs artery
- Reduced blood flow triggers tissue necrosis and interferes with electrical and/or contractile function

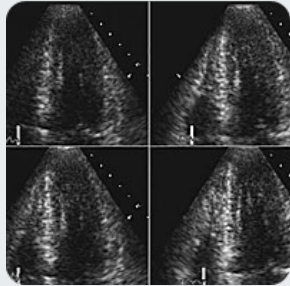


Cardiac Testing Should Help Physicians Determine the Right Treatment Pathway for Each Patient with Suspected Coronary Artery Disease (CAD)

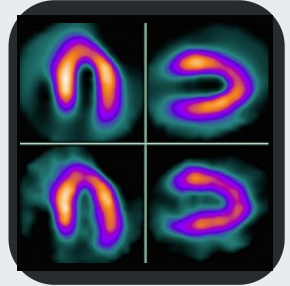


A finding of No CAD does not diminish the role of initiating or continuing primary prevention efforts

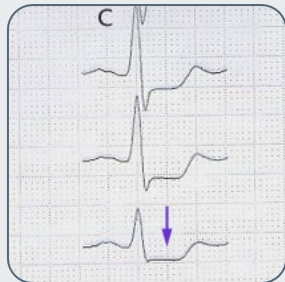
Patients with suspected Heart Disease are often referred to Non-invasive Functional Testing, but these tests are limited in detecting Coronary Artery Disease (CAD)



Stress Echo

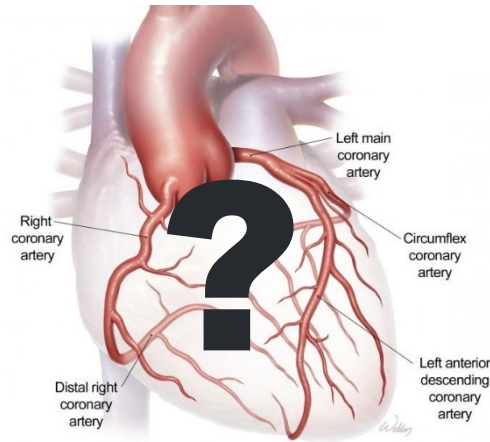


SPECT



Treadmill

No direct information on disease in the coronary arteries



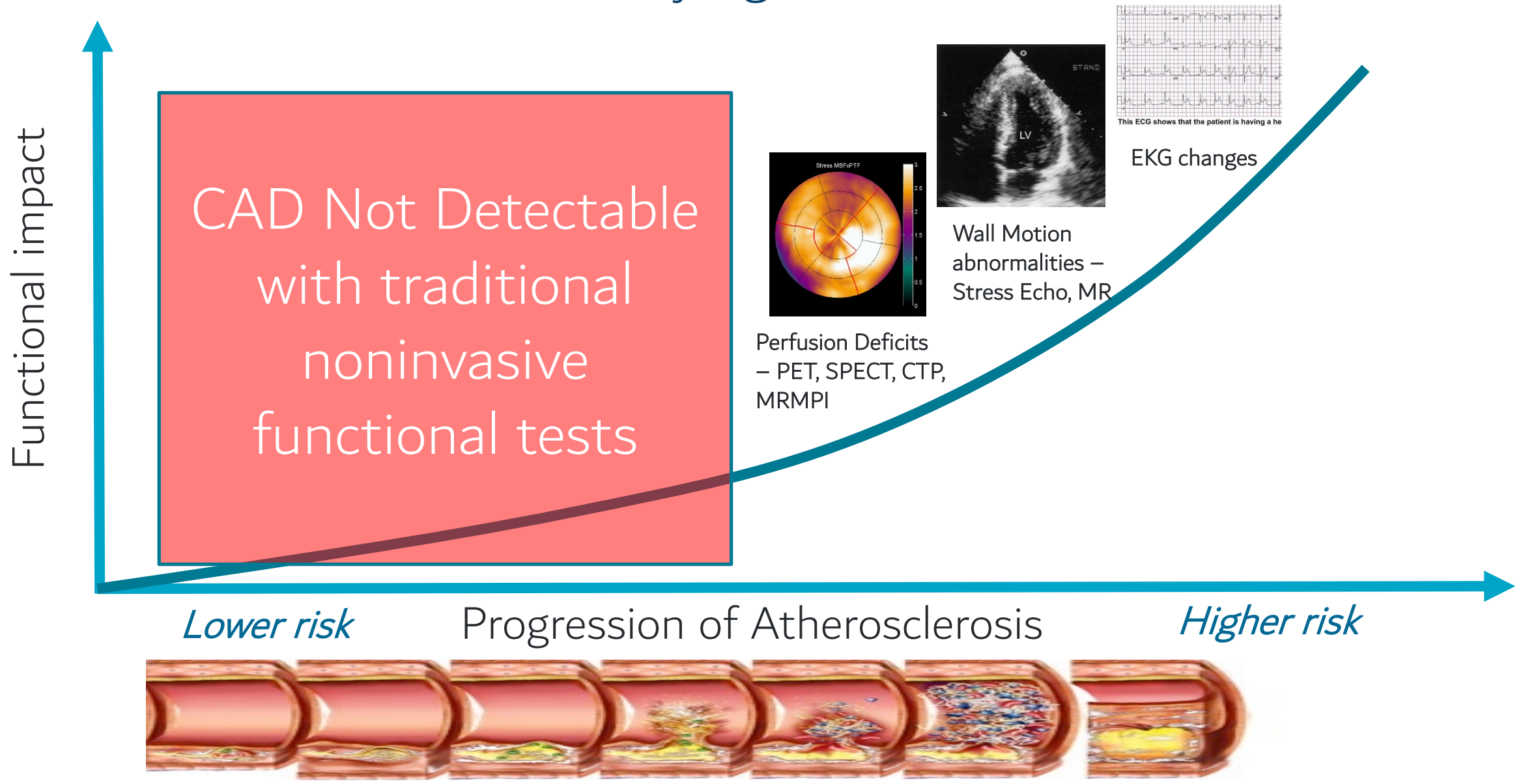
High rate of
**unnecessary
downstream testing**

More than 50% of patients sent for an invasive angiogram have **no obstructive CAD¹**

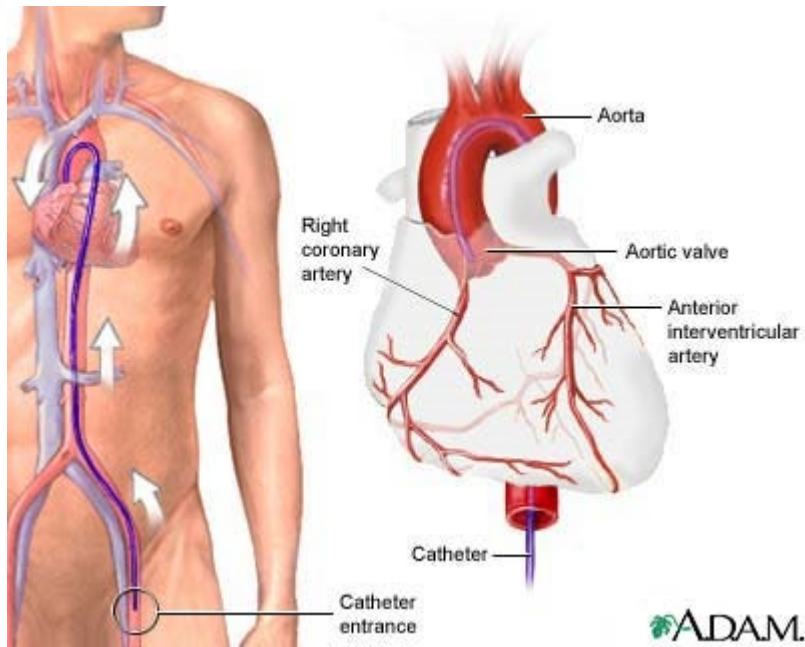
High rate of
missing CAD

20-30% of patients are sent home with their coronary disease **undetected²**

Ischemic Cascade Explains Lower Sensitivity of Noninvasive functional tests for identifying Obstructive CAD

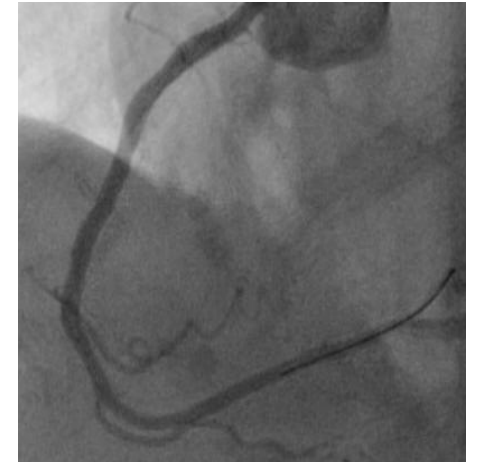


Due to Limitations in Noninvasive Cardiac Stress Testing, many patients are referred for Invasive Diagnostic Tests

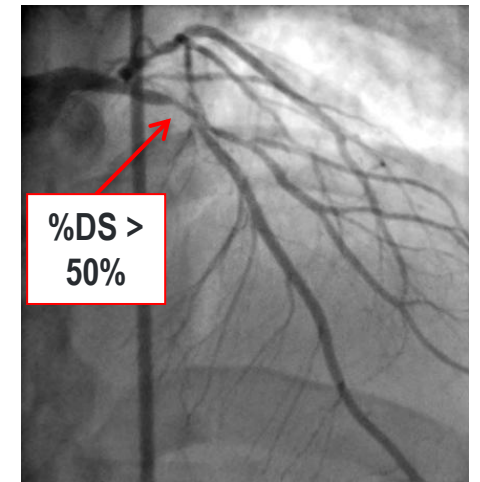


Courtesy of Paul Yock, M.D.

Normal right coronary artery



Diseased left coronary artery

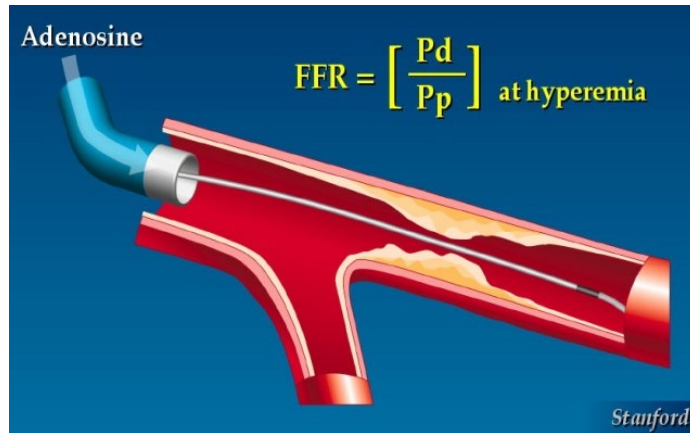


Invasive Coronary Physiology Tests are gold standard

Invasive coronary physiology measurements have emerged as the gold-standard test to identify whether disease is limiting blood supply to the heart and consequently whether a patient may benefit from Percutaneous Coronary Intervention (PCI)

- **Fractional Flow Reserve (FFR)**

- Defines the functional significance of coronary lesions*
- Measured with pressure wire during coronary angiography

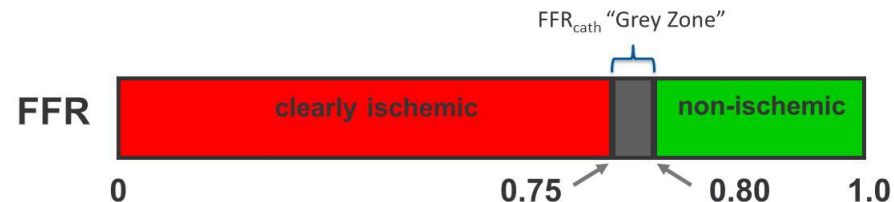
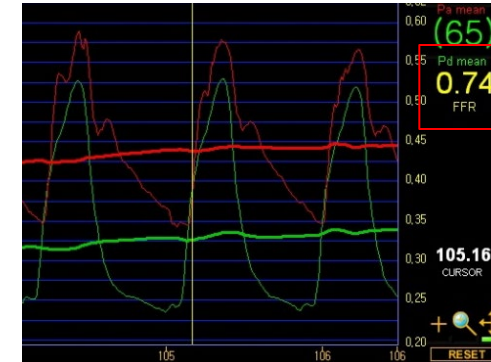


*Pijls NH et al. J Am Coll Cardiol. 2007
Pijls NH et al. J. Am. Coll. Cardiol. 2010

Angiography



FFR



Robust clinical evidence has established FFR as the gold-standard test to identify flow-limiting coronary artery disease

FAME

Defer PCI for lesions with $FFR > 0.8$

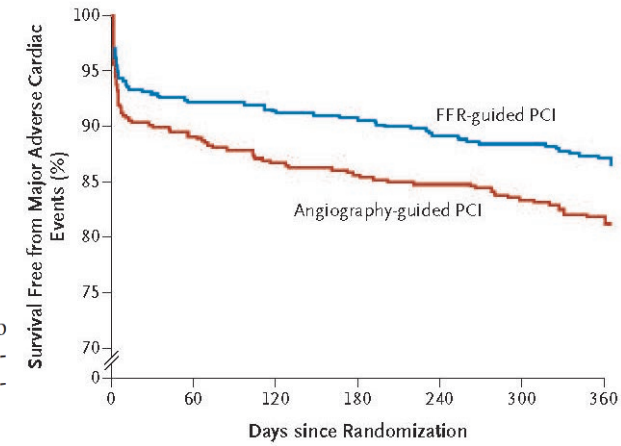


Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

CONCLUSIONS

Routine measurement of FFR in patients with multivessel coronary artery disease who are undergoing PCI with drug-eluting stents significantly reduces the rate of the composite end point of death, nonfatal myocardial infarction, and repeat revascularization at 1 year. (ClinicalTrials.gov number, NCT00267774.)

Tonino et al. NEJM 2009, 360: 213



FAME-2

Perform PCI for lesions with $FFR \leq 0.8$

THE NEW ENGLAND JOURNAL of MEDICINE

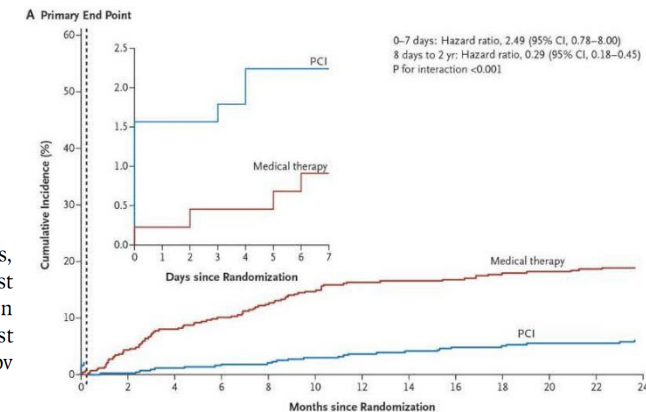
ORIGINAL ARTICLE

Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease

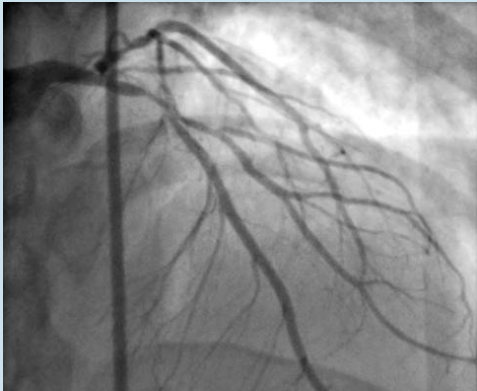
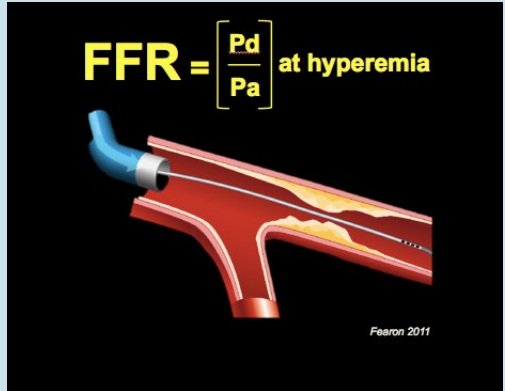
CONCLUSIONS

In patients with stable coronary artery disease and functionally significant stenoses, FFR-guided PCI plus the best available medical therapy, as compared with the best available medical therapy alone, decreased the need for urgent revascularization. In patients without ischemia, the outcome appeared to be favorable with the best available medical therapy alone. (Funded by St. Jude Medical; ClinicalTrials.gov number, NCT01132495.)

De Bruyne et al. NEJM 2012, 367: 991



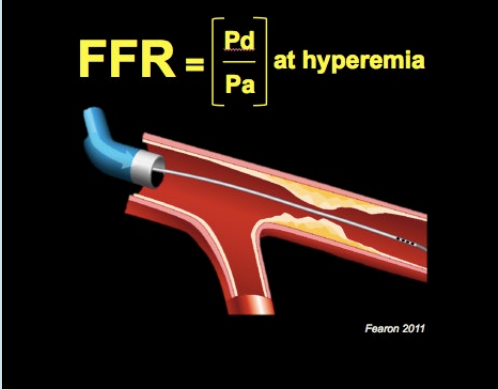
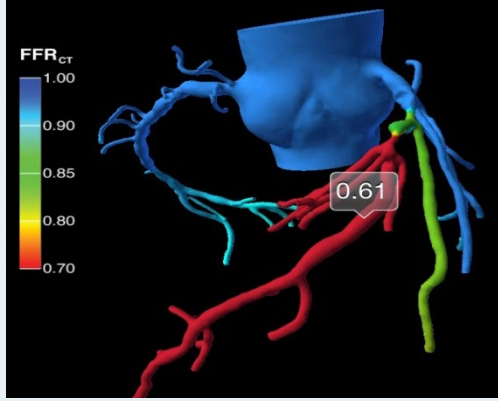
Diagnosing Anatomic and Functionally-Significant CAD Invasively

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

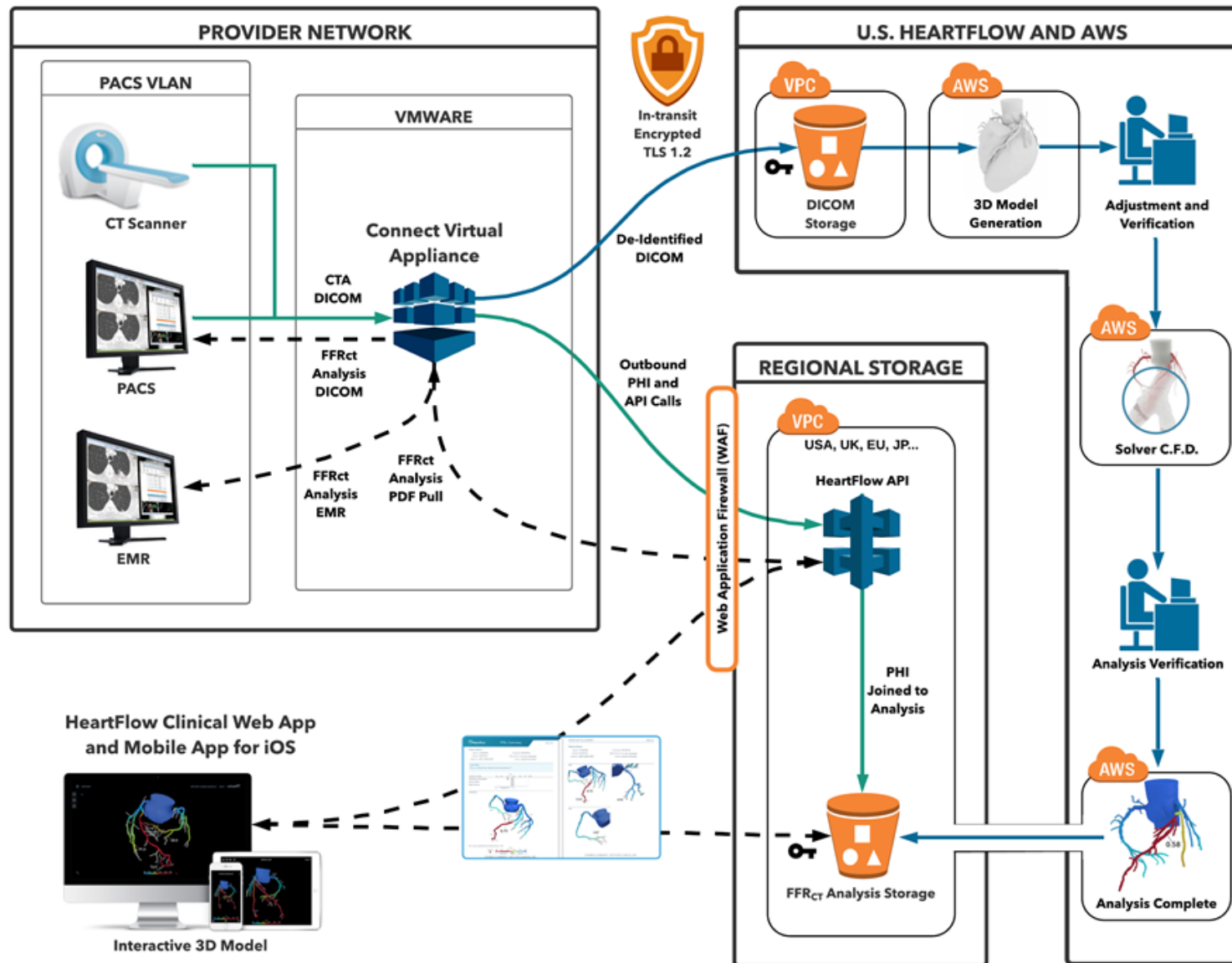
- Angiography and FFR require invasive cardiac catheterization
 - ≈40% of patients that enter the cath lab have obstructive CAD¹
 - ≈40% of patients with obstructive CAD on angiography have +’ve FFR²
- Only 16% of patients in cath lab have both obstructive CAD and +’ve FFR

*Can we identify obstructive CAD and quantify FFR **before** cardiac cath?*

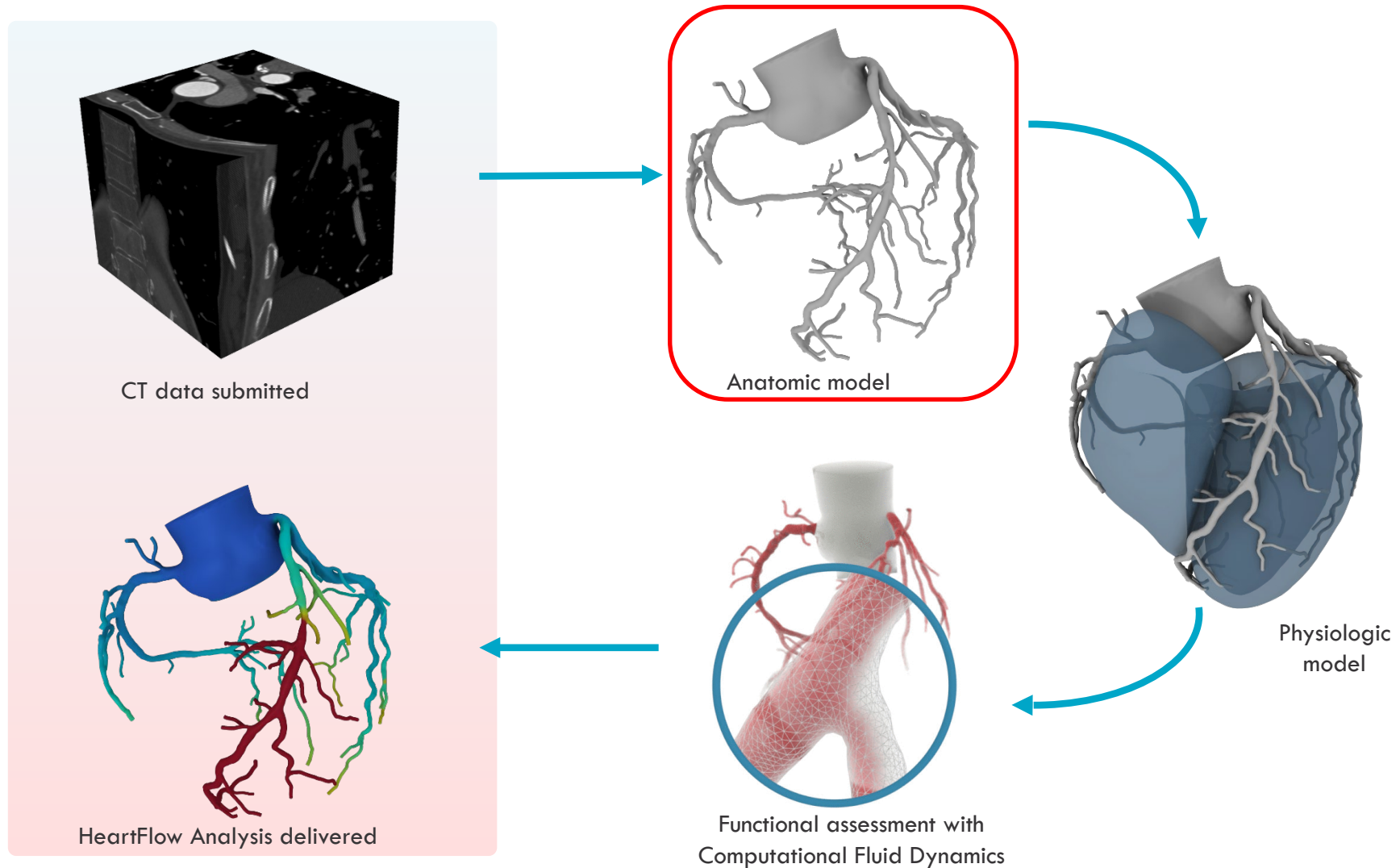
Diagnosing Anatomic and Functionally-Significant CAD

	<u><i>ANATOMY</i></u> <i>Identify obstructive CAD</i>	<u><i>FUNCTION</i></u> <i>Identify lesion-specific ischemia that may benefit from PCI</i>
<i>Invasive</i>		$FFR = \frac{P_d}{P_a} \text{ at hyperemia}$ 
<i>Noninvasive</i>		

HeartFlow's Cloud-based AI-Enabled Clinical Service



FFR_{CT} Analysis Process



Accurate Image Analysis in Complex CAD is Challenging

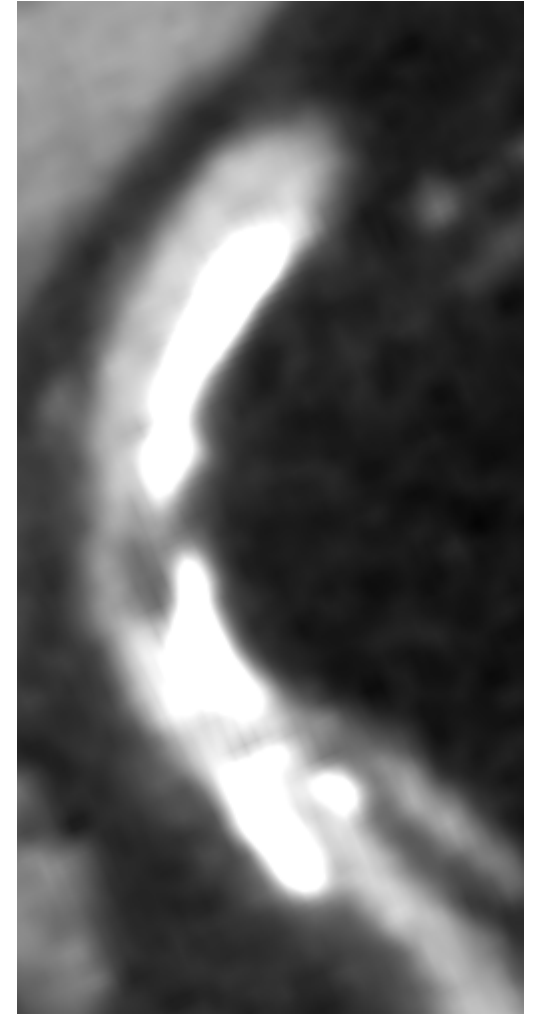
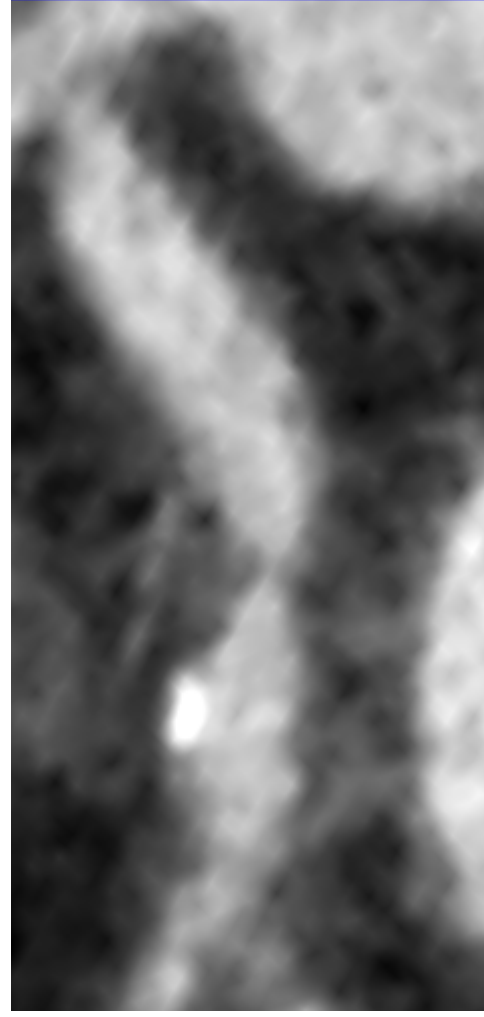
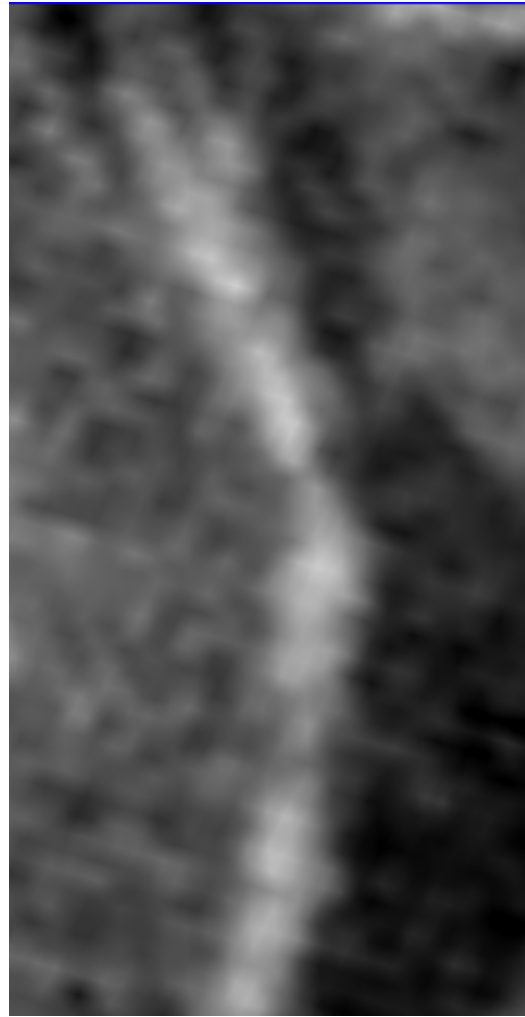
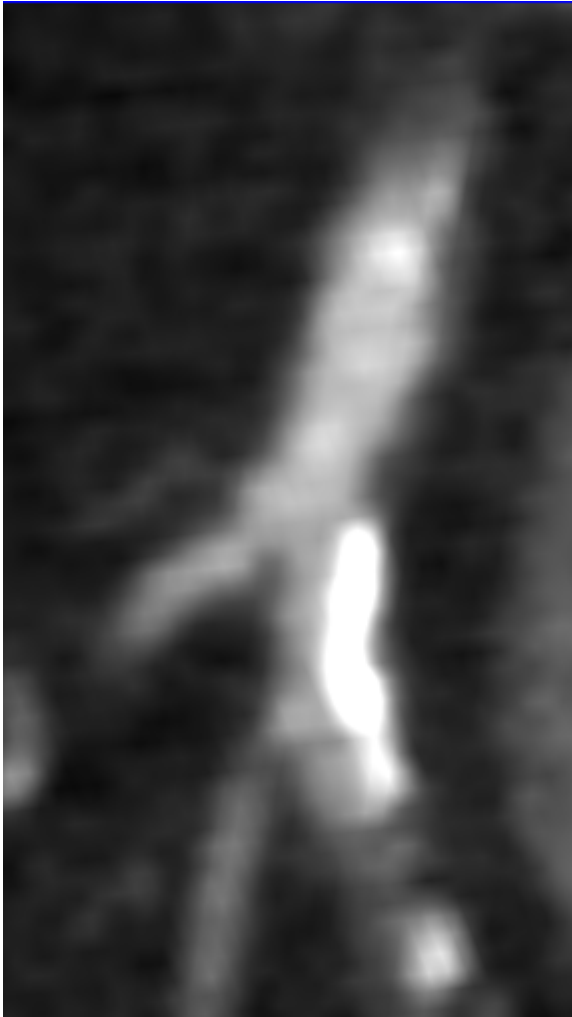
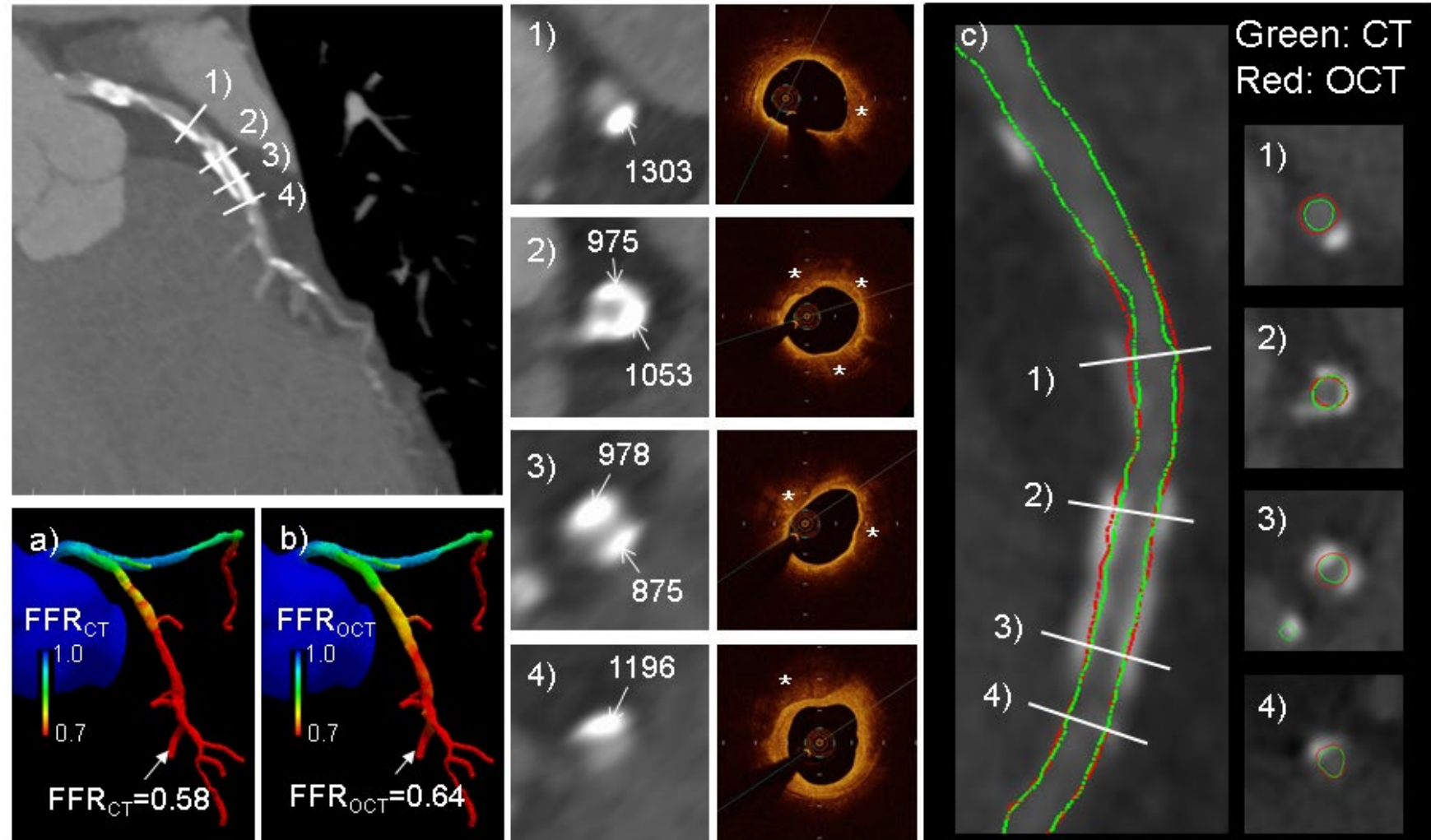
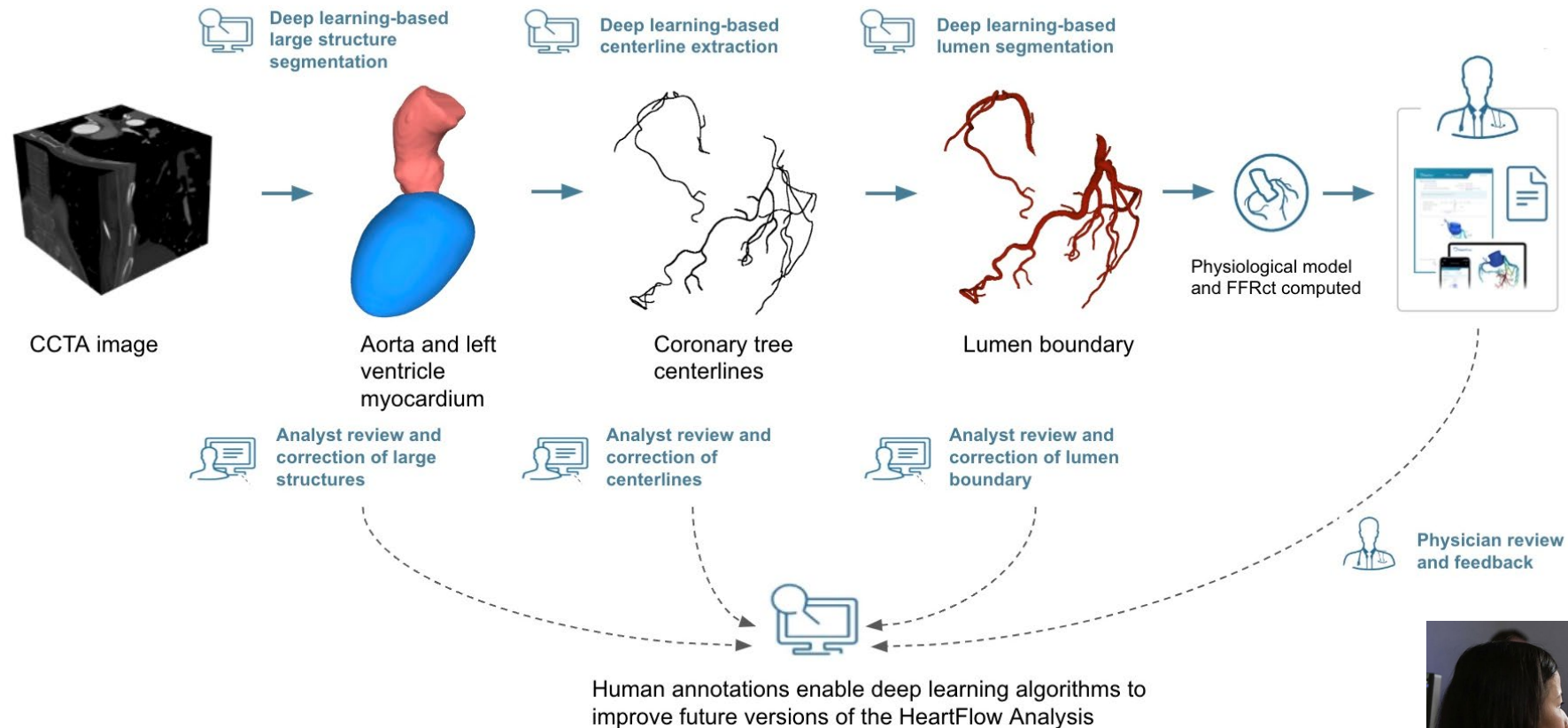


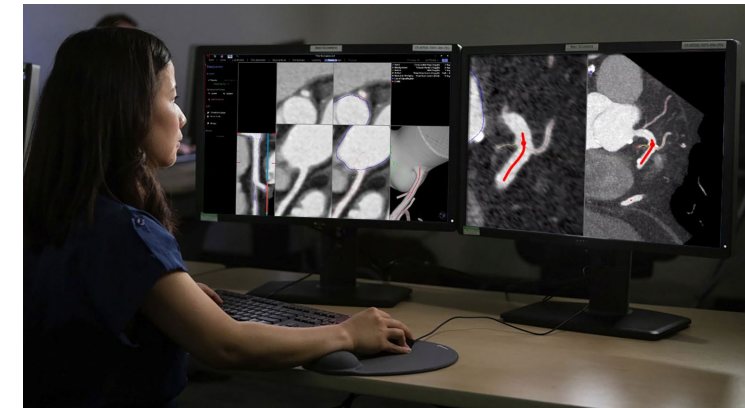
Image segmentation methods developed and validated using invasive imaging data



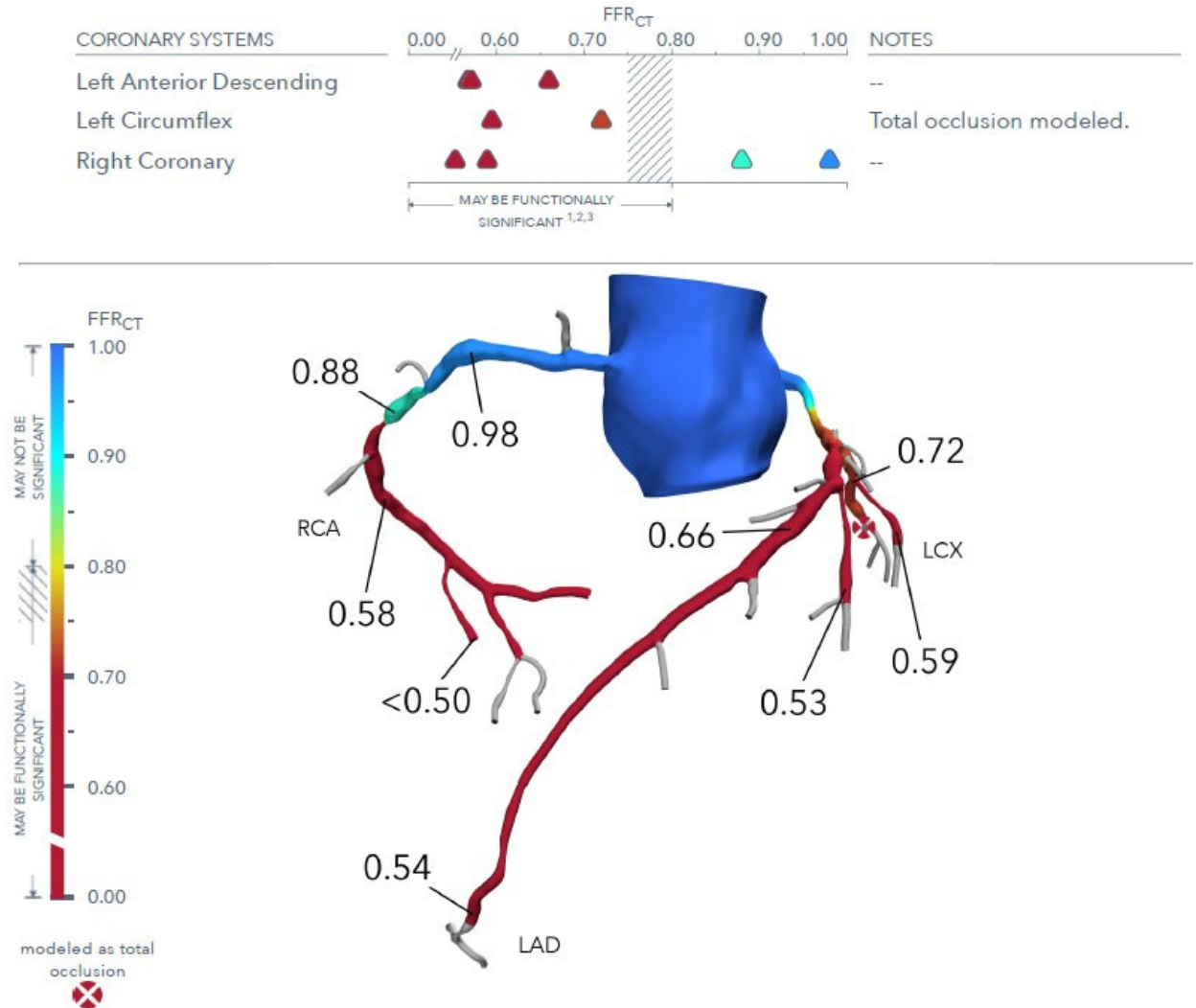
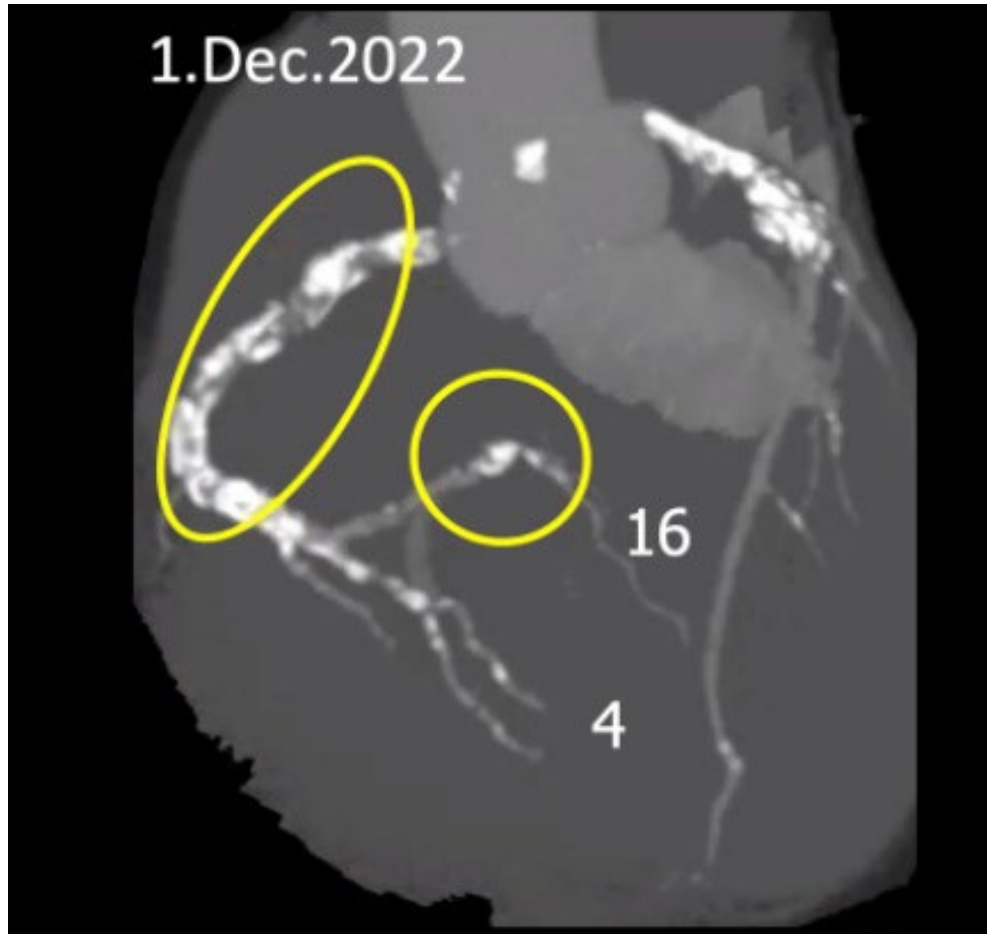
HeartFlow built a Human-in-the-loop AI Foundation for FFR_{CT}



Taylor et. al. Computer Methods in Applied Mechanics and Engineering, 2023



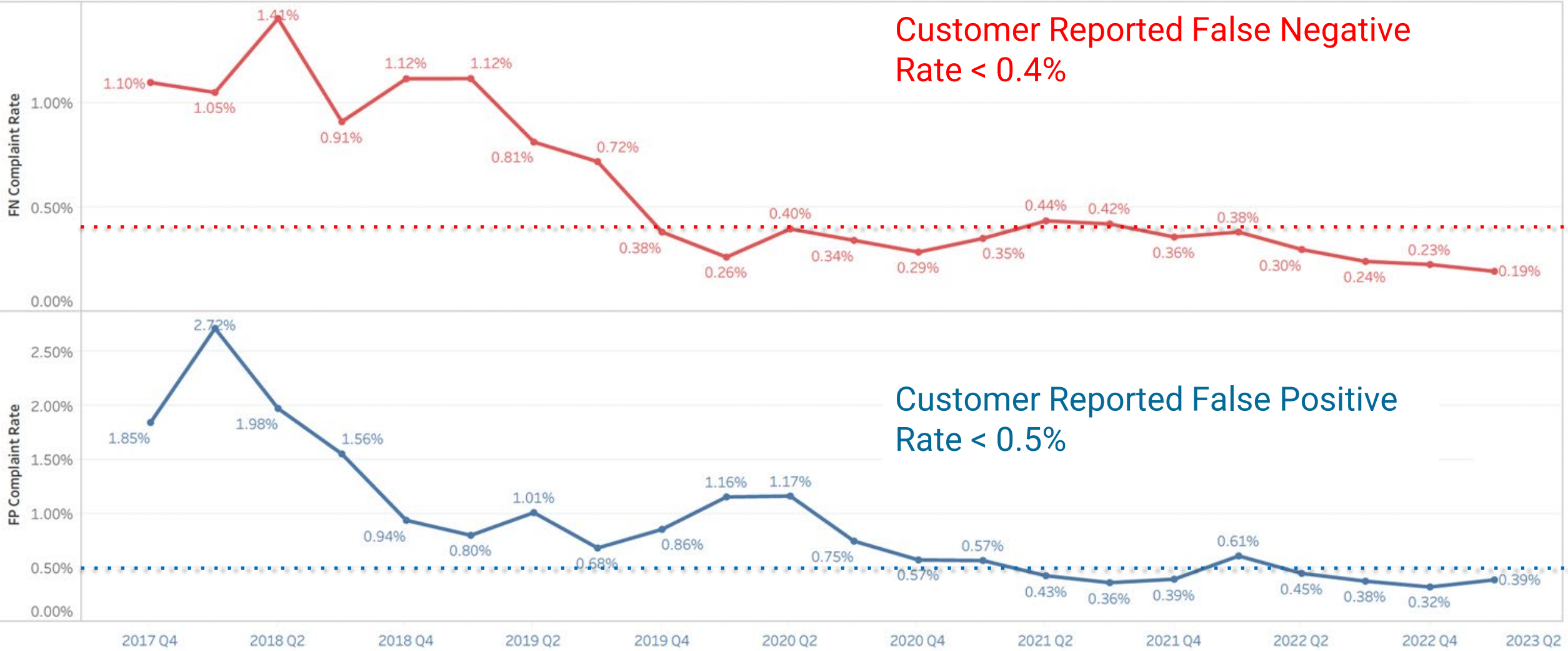
HeartFlow routinely processes cases with high calcium score



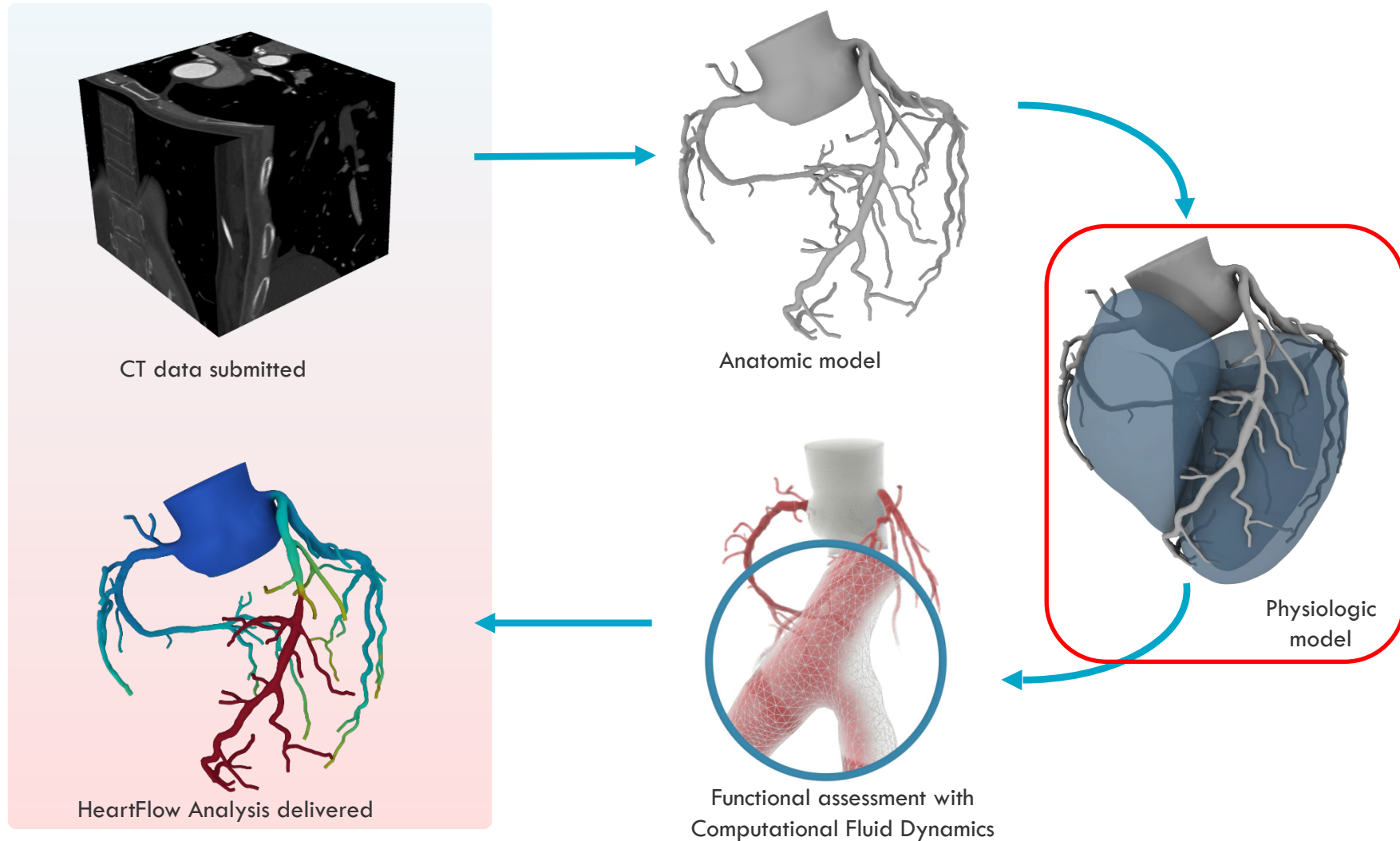
Customer-reported False Negative, False Positive Rates

2018 - Present

FN & FP Complaint Rates



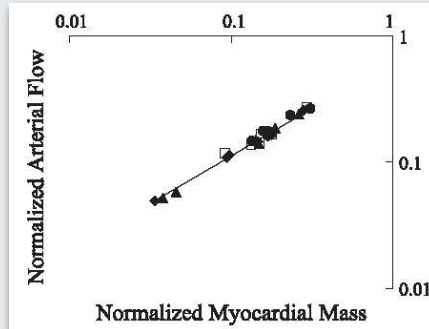
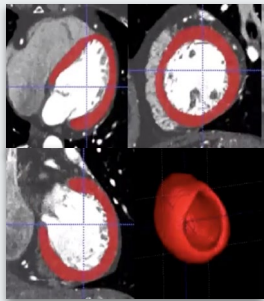
FFR_{CT} Analysis Process



Physiologic Model of FFR_{CT} – 3rd Generation (Released 2021)

Principle #1

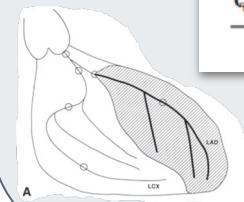
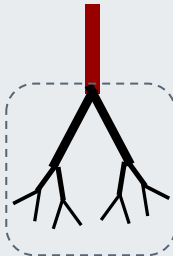
The demand: resting coronary blood flow is proportional to myocardial mass



Choy et. al., Scaling of myocardial mass to flow and morphometry of coronary arteries. J Appl Physiol, 2008.

Principle #2

The supply: local flow is related to vessel size

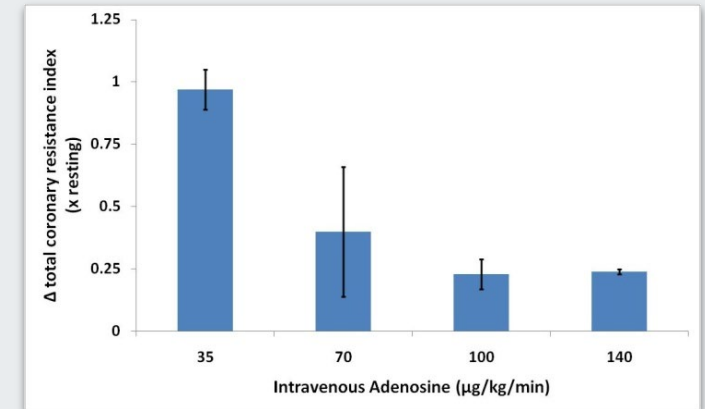


scaling relations	anatomical data
$V_c \propto D^X$	3.38 ± 0.63
$Q_s \propto L_c^X$	0.94 ± 0.28
$D_s \propto L_c^X$	0.37 ± 0.08
$Q_s \propto D_s^X$	2.62 ± 0.65
$Q_s \propto V_c^X$	0.79 ± 0.055

Huo and Kassab. Intraspecific scaling laws of vascular trees. J R Soc Interface (2012) 9 190:200

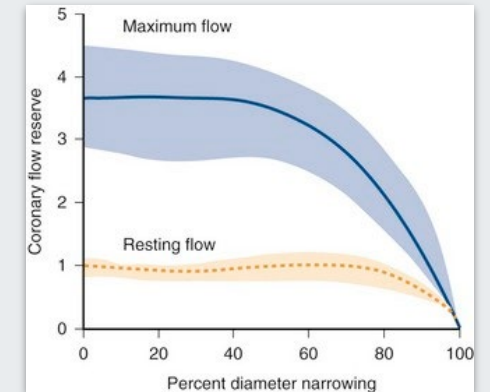
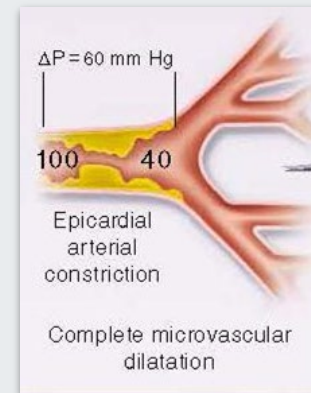
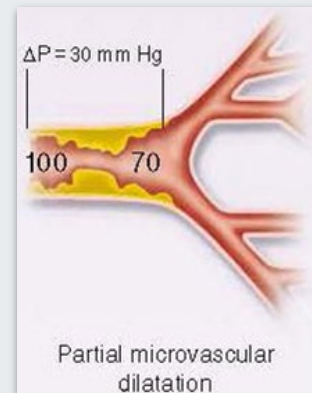
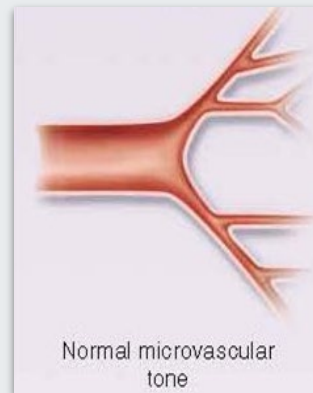
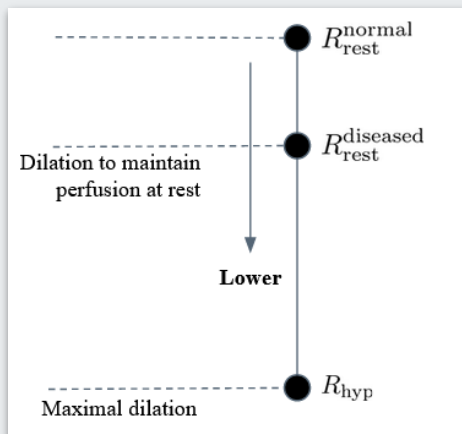
Principle #3

Maximal hyperemia: predictable response to adenosine



Adapted from Wilson, et. al. Effect of Adenosine on human coronary arterial circulation. Circulation 1990

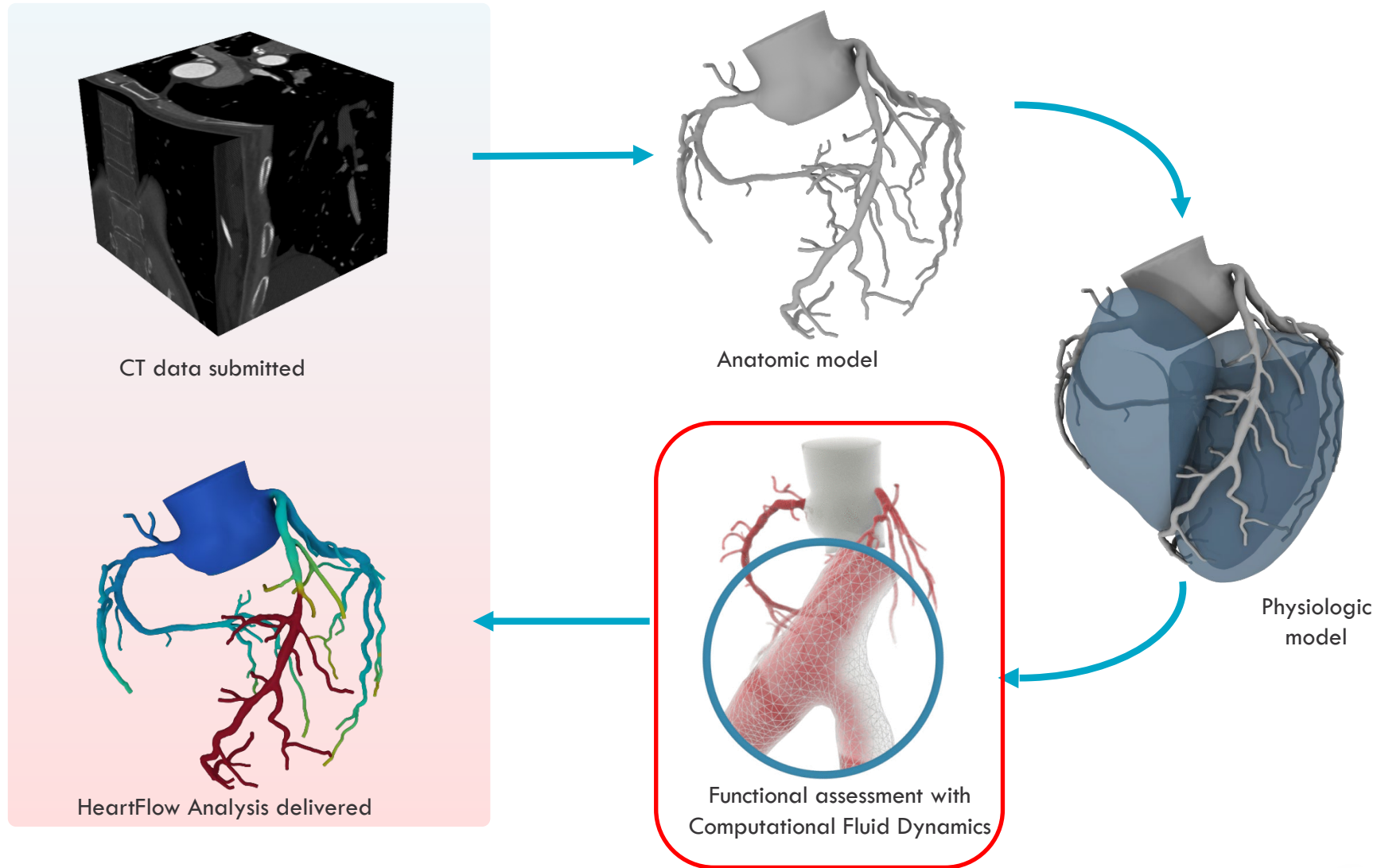
Principle #4 Resting flow demand is maintained in the presence of epicardial disease by using dilatory reserve



Adapted from Wilson, R.F., Assessing the Severity of Coronary Artery Stenoses, NEJM 1996

Adapted from Gould et al. Physiologic basis for assessing critical coronary stenosis... Am J Cardiol. 1974.

FFR_{CT} Analysis Process



Computational fluid dynamic analysis used to quantify blood flow and pressure

3D Modeling of Blood Flow Requires Solving the Governing Partial Differential Equations

Mass Conservation (1 equation):

$$\frac{\partial v_x}{\partial x} + \frac{\partial v_y}{\partial y} + \frac{\partial v_z}{\partial z} = 0$$

This law states that blood is an incompressible fluid

Momentum Balance (3 equations):

$$\rho \frac{\partial v_x}{\partial t} + \rho \left(v_x \frac{\partial v_x}{\partial x} + v_y \frac{\partial v_x}{\partial y} + v_z \frac{\partial v_x}{\partial z} \right) = -\frac{\partial p}{\partial x} + \mu \left(\frac{\partial^2 v_x}{\partial x^2} + \frac{\partial^2 v_y}{\partial y^2} + \frac{\partial^2 v_z}{\partial z^2} \right)$$

$$\rho \frac{\partial v_y}{\partial t} + \rho \left(v_x \frac{\partial v_y}{\partial x} + v_y \frac{\partial v_y}{\partial y} + v_z \frac{\partial v_y}{\partial z} \right) = -\frac{\partial p}{\partial y} + \mu \left(\frac{\partial^2 v_x}{\partial x^2} + \frac{\partial^2 v_y}{\partial y^2} + \frac{\partial^2 v_z}{\partial z^2} \right)$$

$$\rho \frac{\partial v_z}{\partial t} + \rho \left(v_x \frac{\partial v_z}{\partial x} + v_y \frac{\partial v_z}{\partial y} + v_z \frac{\partial v_z}{\partial z} \right) = -\frac{\partial p}{\partial z} + \mu \left(\frac{\partial^2 v_x}{\partial x^2} + \frac{\partial^2 v_y}{\partial y^2} + \frac{\partial^2 v_z}{\partial z^2} \right)$$

These equations come from the application of Newton's 2nd law, F=ma to a fluid

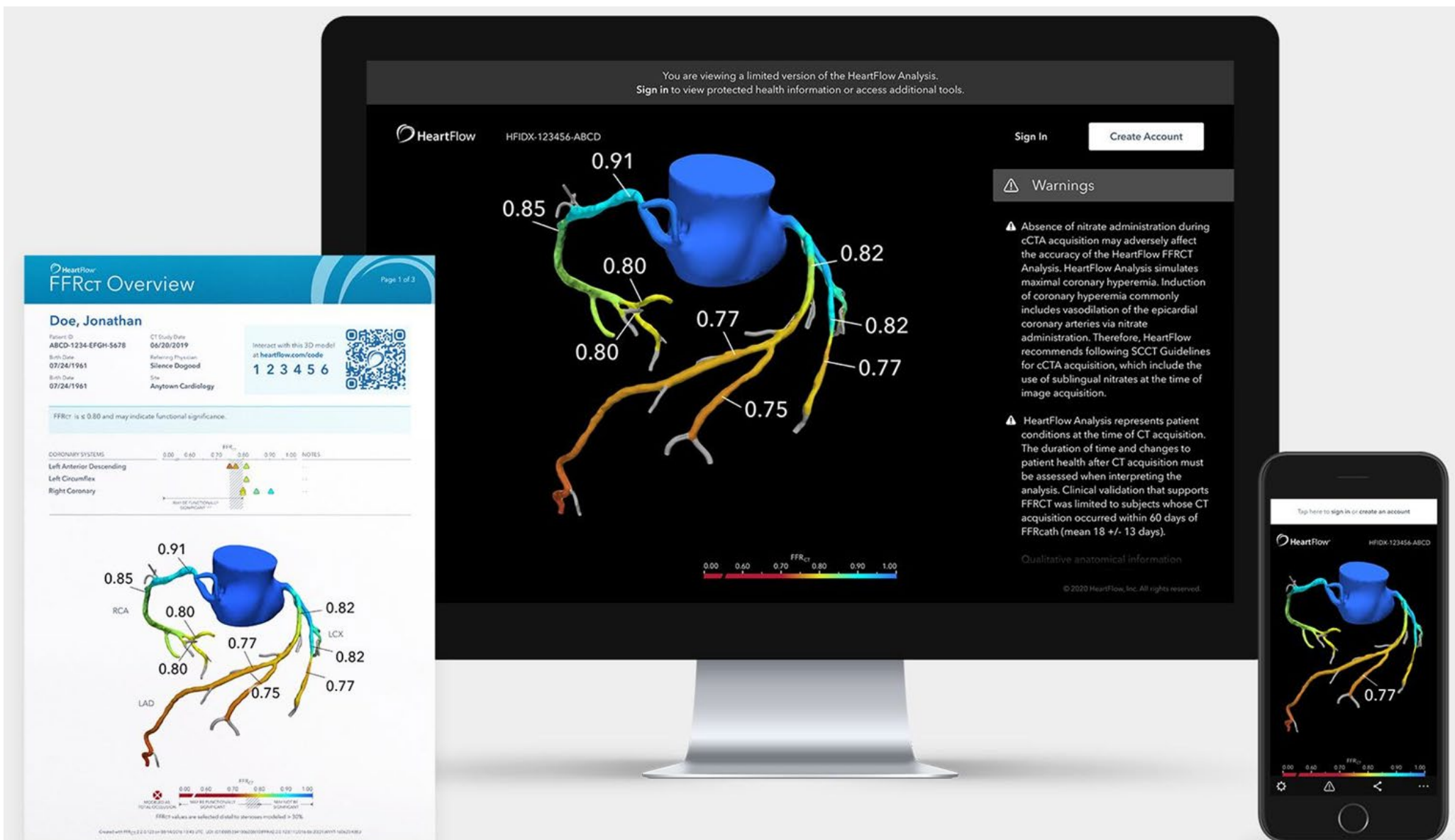
where ρ is the fluid density, and μ is the fluid viscosity (both assumed known).

We solve these for $v_x(x, y, z, t)$, $v_y(x, y, z, t)$, $v_z(x, y, z, t)$, $p(x, y, z, t)$

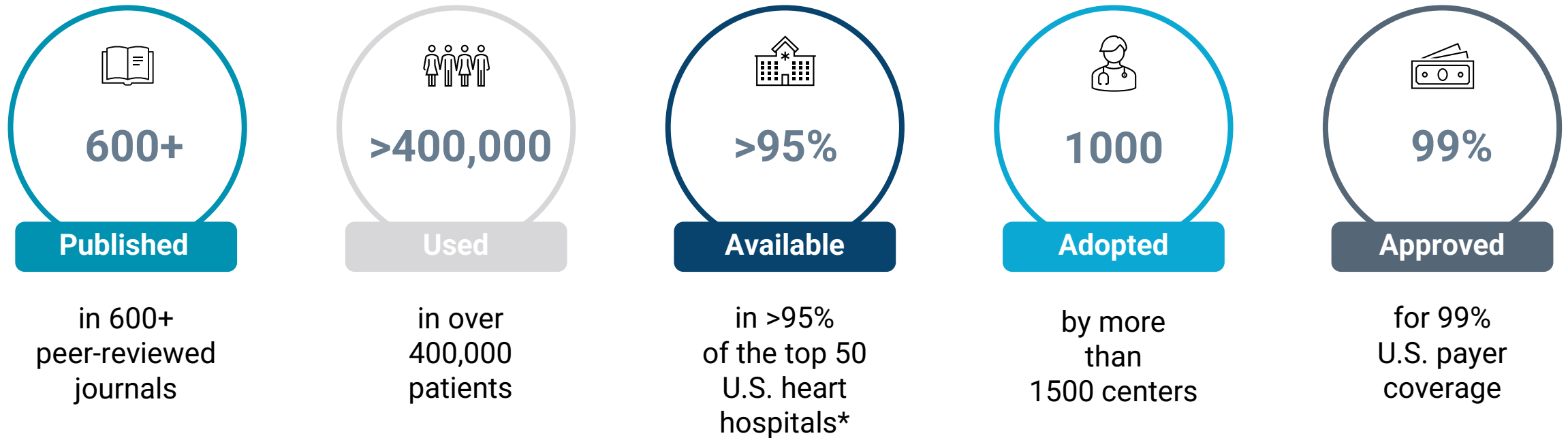
for every point in the 3D model and over whatever time interval we are interested in.



FFR_{CT} data available for entire coronary tree



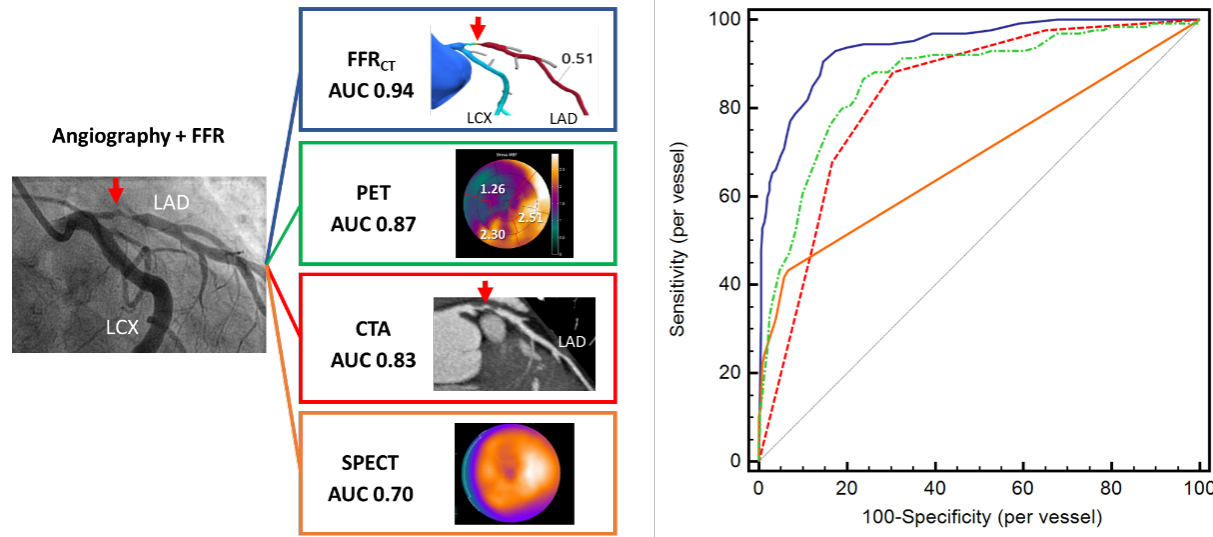
HeartFlow FFR_{CT}



*As designated by US News & World Report. Jan 2022

FFR_{CT} diagnostic accuracy evaluated in multiple studies involving more than 1000 patients

Discriminative ability for the detection of per-vessel FFR-defined ischemia



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VOL. 73, NO. 2, 2019

Comparison of Coronary Computed Tomography Angiography, Fractional Flow Reserve, and Perfusion Imaging for Ischemia Diagnosis

Roel S. Driessen, MD,^a Ibrahim Danad, MD,^a Wijnand J. Stuijzand, MD,^a Pieter G. Raijmakers, MD, PhD,^b Stefan P. Schumacher, MD,^a Pepijn A. van Diemen, MD,^a Jonathon A. Leipsic, MD,^c Juhani Knuuti, MD, PhD,^d S. Richard Underwood, MD, PhD,^e Peter M. van de Ven, PhD,^f Albert C. van Rossum, MD, PhD,^a Charles A. Taylor, PhD,^{g,h} Paul Knaapen, MD, PhD^a

“FFR_{CT} has highest accuracy among noninvasive tests to predict FFR”

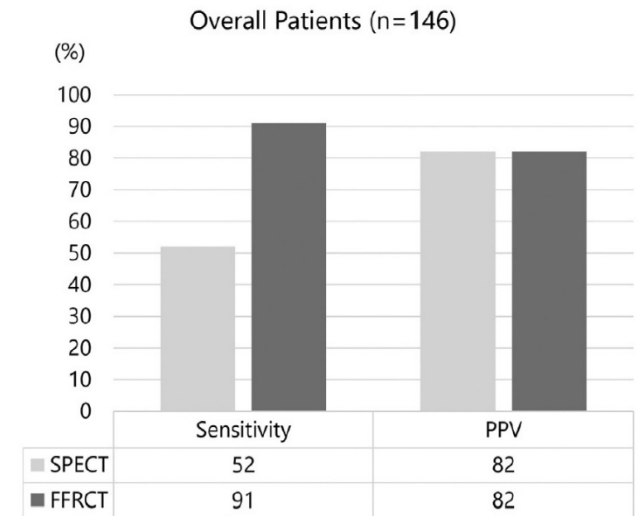
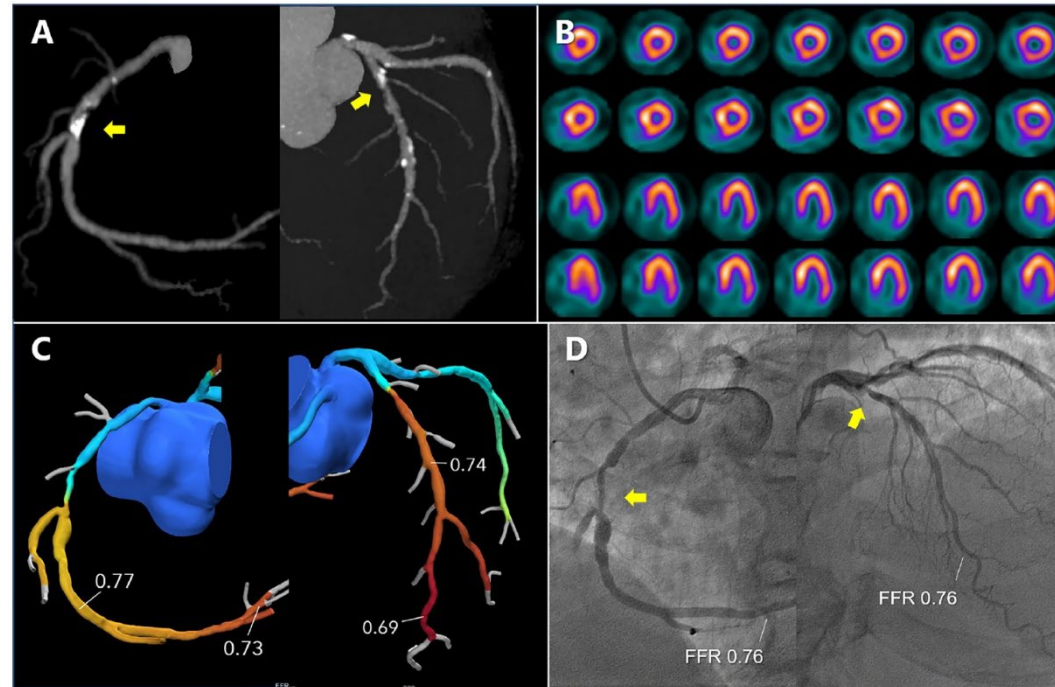
Driessen et. al. JACC 2019

FFR_{CT} diagnostic accuracy evaluated in multiple studies involving more than 1000 patients

Comparison of Diagnostic Performance of Fractional Flow Reserve Derived from Coronary Computed Tomographic Angiography Versus Single-Photon Emission Computed Tomographic Myocardial Perfusion Imaging

Taichi Okonogi, Tomohiro Kawasaki*, Hisashi Koga, Yoshiya Orita, Kyoko Umeji, Ryota Fukuoka, Keisuke Hirai, Kazuki Haraguchi, Kimihiro Kajiyama, Yurie Fukami, Toshiya Soejima, Hiroshige Yamabe, and Nobuhiko Koga

Fraction flow reserve (FFR) derived from computed tomography (FFR_{CT}) has been proposed to be an effective gatekeeper for invasive angiographic referral. The purpose of the present study is to examine the real-world diagnostic performance of FFR_{CT} and myocardial perfusion imaging as well as to assess the utility of FFR_{CT} as a gatekeeper for invasive coronary angiography in patients suspected of having obstructive coronary artery disease. Total of 146 consecutive patients underwent both single-photon emission computed tomography (SPECT) and invasive FFR were evaluated. An FFR_{CT} value 1 to 2 cm distal to a stenosis ≤ 0.80 was defined as positive for ischemia and a summed stress score ≥ 2 or transient ischemic dilatation ≥ 1.2 were positive for ischemia with the invasive FFR value of < 0.80 serving as the gold standard. The patient-based sensitivity of FFR_{CT} was significantly higher than SPECT (91 vs 52%, $p < 0.001$) and exhibited similar positive predictive value (82 vs 82%, $p = 0.91$). These trends were observed even in patients with multivessel and left main trunk disease and those with severe coronary calcification. In conclusion, our data suggest that FFR_{CT} has higher diagnostic performance characteristics than SPECT and details the superior FFR_{CT} analysis in detecting patients with hemodynamically significant coronary artery disease. Our results support the clinical utility of FFR_{CT} analysis as a gatekeeper for invasive coronary angiography in clinical practice. © 2021 Elsevier Inc. All rights reserved. (Am J Cardiol 2021;300:1–8)



Asymptomatic male of 60s with diabetes, hypertension, and past smoking. CCTA showed intermediate calcified lesion in the mid RCA and proximal LAD (arrow, A). Adenosine stress SPECT showed no ischemia in both area (B), while FFR_{CT} showed the FFR_{CT} values 1-2cm distal to the lesions were 0.77 in RCA and 0.74 in LAD, indicating positive ischemia of both lesions (C). Invasive coronary angiography confirmed intermediate lesions at the corresponding site with CCTA, and invasive FFR was 0.76 in RCA and 0.76 in LAD (D). In this case, elective PCI was performed on both lesions later.

Okonogi, Kawasaki et. al.
American Journal of
Cardiology 2021

PRECISE Randomized Control Trial



CLINICAL OVERVIEW



Research

JAMA Cardiology | Original Investigation

Comparison of an Initial Risk-Based Testing Strategy vs Usual Testing in Stable Symptomatic Patients With Suspected Coronary Artery Disease The PRECISE Randomized Clinical Trial

Pamela S. Douglas, MD; Michael G. Nanna, MD, MHS; Michelle D. Kelsey, MD; Eric Yow, MS; Daniel B. Mark, MD, MPH; Manesh R. Patel, MD; Campbell Rogers, MD; James E. Udelson, MD; Christopher B. Fordyce, MD, MHS, MSc; Nick Curzen, BM(Hons), PhD; Gianluca Pontone, MD, PhD; Pál Maurovich-Horvat, MD, PhD, MPH; Bernard De Bruyne, MD, PhD; John P. Greenwood, MBChB, PhD; Victor Marinescu, MD, PhD, MHCAM; Jonathon Leipsic, MD; Gregg W. Stone, MD; Ori Ben-Yehuda, MD; Colin Berry, MBChB, PhD; Shea E. Hogan, MD; Bjorn Redfors, MD, PhD; Ziad A. Ali, MD, DPhil; Robert A. Byrne, MBBCh, PhD; Christopher M. Kramer, MD; Robert W. Yeh, MD, MSc; Beth Martinez, BS, PMP; Sarah Mullen, MBT; Whitney Huey, CCRP; Kevin J. Anstrom, PhD; Hussein R. Al-Khalidi, PhD; Sreekanth Vemulapalli, MD; for the PRECISE Investigators

Study Design

N=2103 Patients

Usual Care

SPECT, Stress Echo
Direct-to-Cath, etc

Precision Strategy

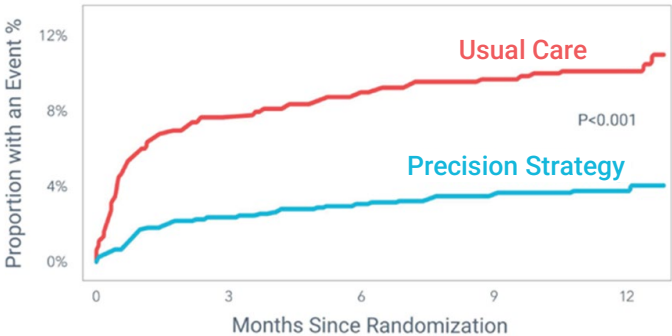
Low-Risk: Defer Testing
All others: CT +/- FFRCT

Composite at 1 Year

- MACE (death/ non-fatal MI)
- Cath finding no obstructive CAD

Results

70% Reduction in unnecessary procedures



> 2X Increase in Cath Lab Efficiency

Usual Care

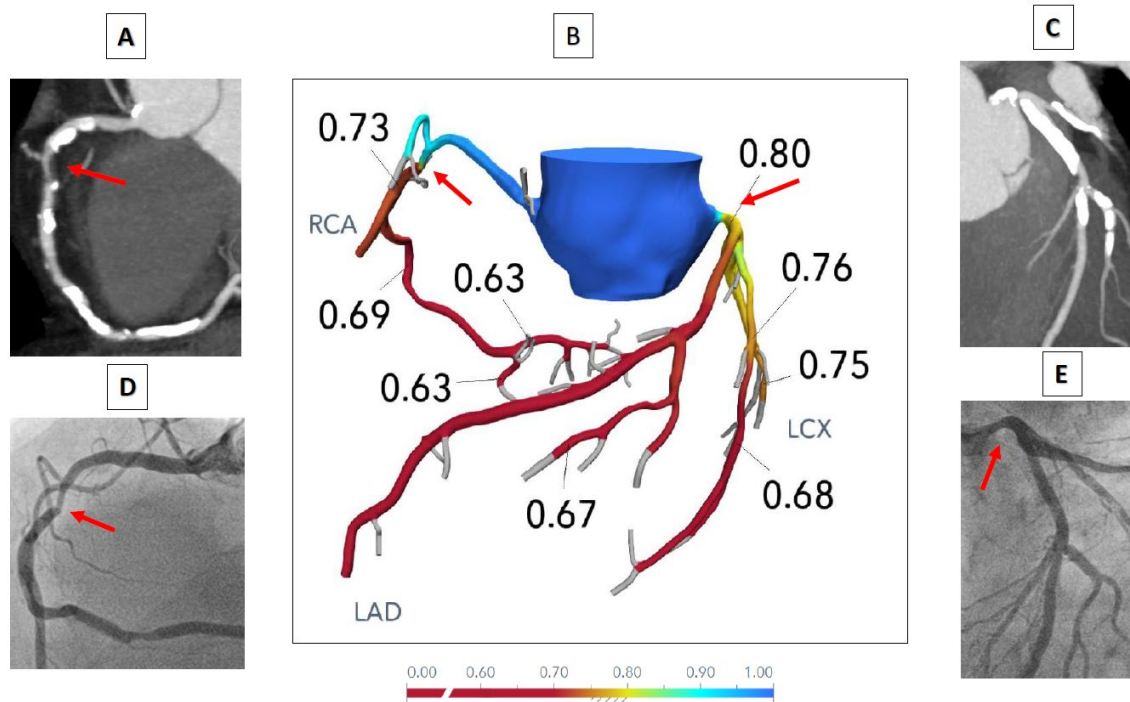
54
(~31%)

Precision Strategy

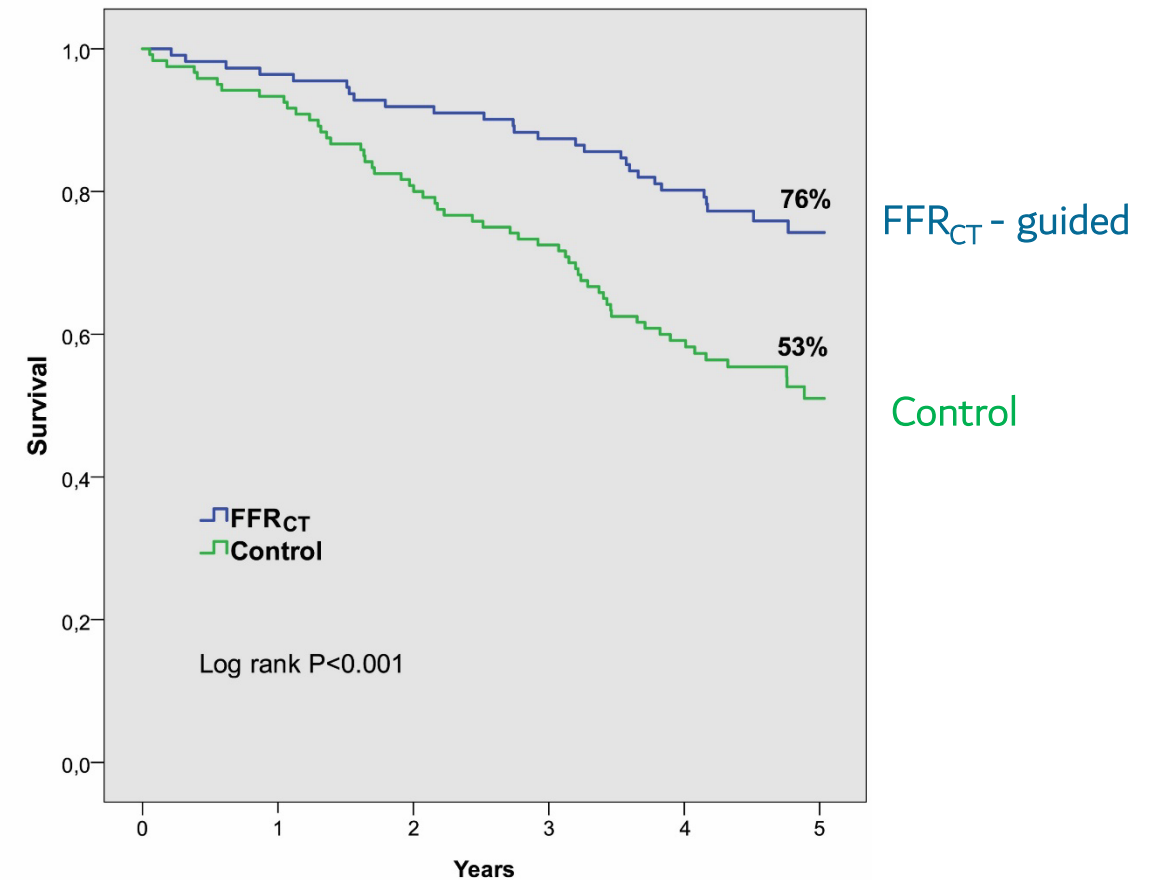
97
(~72%)

Total
Revascularizations
(% of ICA)

FFR_{CT} identifies Coronary Artery Disease and improves survival



67 year old man with no cardiac history or symptoms admitted to the hospital for treatment of ischemic rest pain of the left foot with an ankle-brachial index of 0.44.



Use of HeartFlow FFR_{CT} Analysis to inform cardiac treatment improved survival in patients with no CAD history or symptoms that were treated for chronic limb threatening ischemia

Krievens et. al. Journal of Vascular Surgery, 2021., Zellens et. al. J. Critical Limb Ischemia, 2021, Latkovskis et.al. EJVES, 2024.

NHS mandates AI-powered analysis to treat coronary heart disease

1 FEBRUARY 2021 08:49

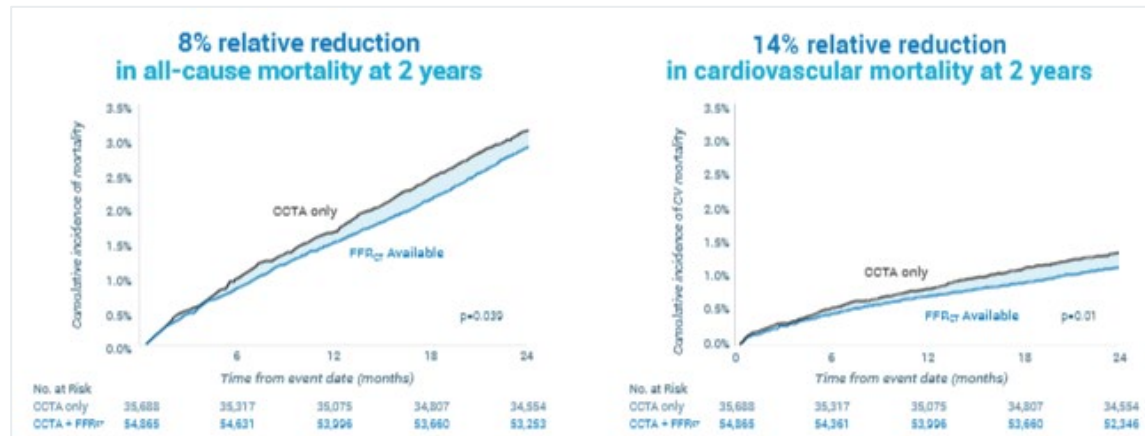
HeartFlow has announced that the National Health Service England (NHSE) and NHS Improvement have mandated that English hospitals adopt the AI-powered HeartFlow FFRct Analysis to fight coronary heart disease (CHD).



FISH&Chips study in NHS hospitals reveals FFR_{CT} significantly reduces all-cause death and death due to cardiovascular causes

FISH&CHIPS is a real world, multi-center, retrospective study including **more than 90,000 patients** assessing at a national level the incremental impact of adding FFR_{CT} to a CCTA-first diagnostic paradigm for evaluating and managing coronary artery disease (CAD).

Primary Endpoints*



After 2 years of follow up, FFR_{CT} availability was associated with:

- 8% relative reduction in all-cause mortality
- 14% relative reduction in CV mortality

Secondary Endpoints

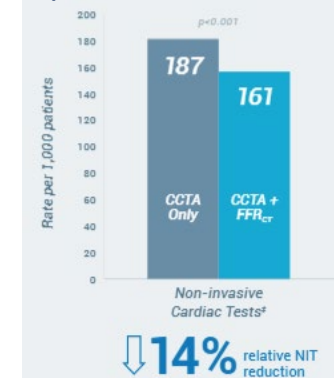
- A 14% relative reduction in additional cardiac testing following CCTA.
- An increase in cath lab efficiency, driven by a 5% relative reduction in ICA

*p<0.01

†Cardiac testing AFTER the initial CCTA.

‡Includes cardiac MRI, echo, nuclear medicine, repeat CCTA, and invasive physiology or imaging

Impact on downstream testing†



Cath Lab Impact

Increase in cath lab efficiency, driven by a



High Prognostic Value

Patients with severely abnormal FFR_{CT} values (≤ 0.50) had





American
Heart
Association.



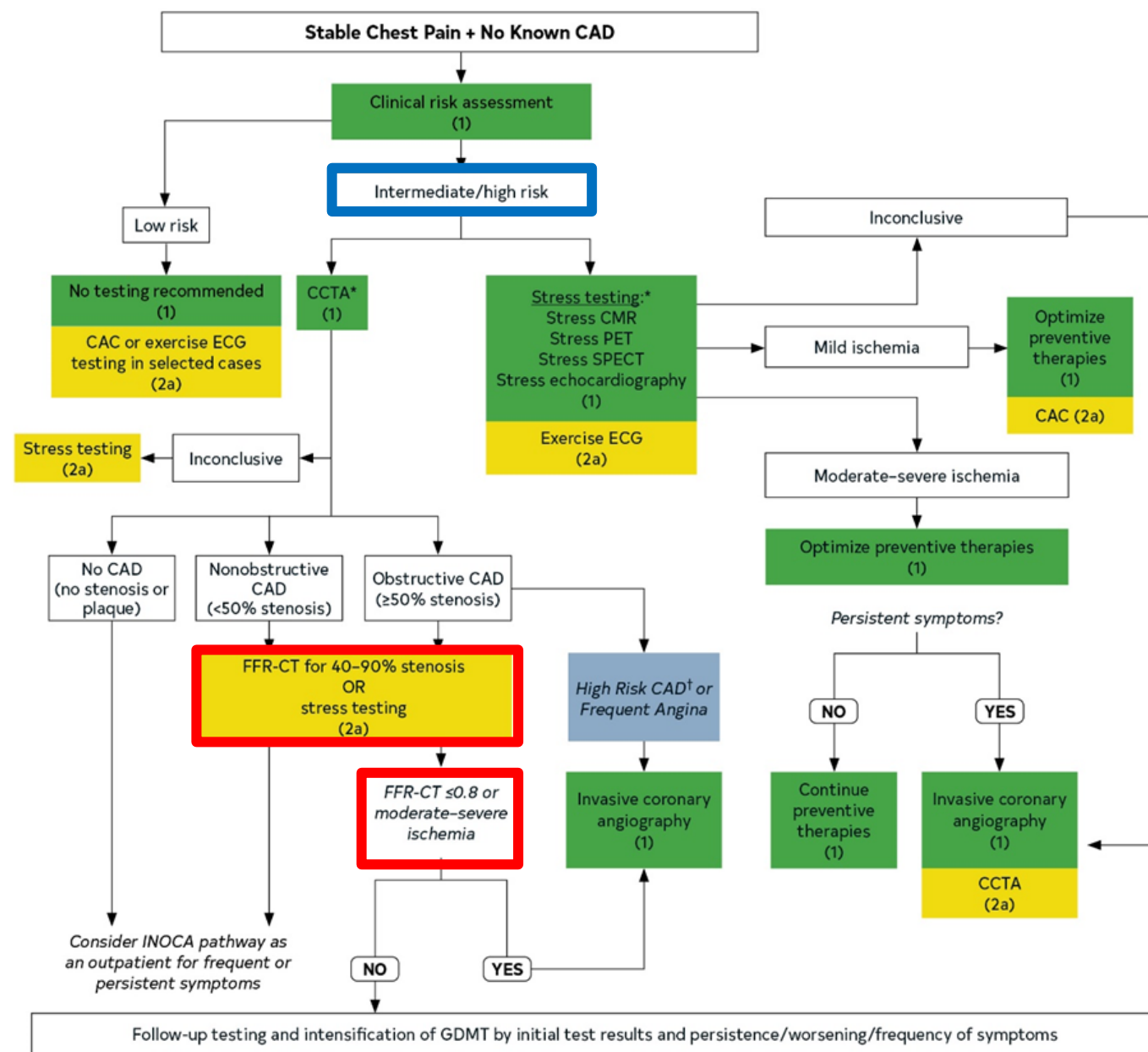
AMERICAN
COLLEGE *of*
CARDIOLOGY
FOUNDATION

2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain

Endorsed by the American Society of Echocardiography, American College of Chest Physicians, Society for Academic Emergency Medicine, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance

Figure 12. Clinical Decision Pathway for Patients With Stable Chest Pain and No Known CAD

Colors correspond to the Class of Recommendation in Table 1.



HeartFlow has become standard for software as a medical device

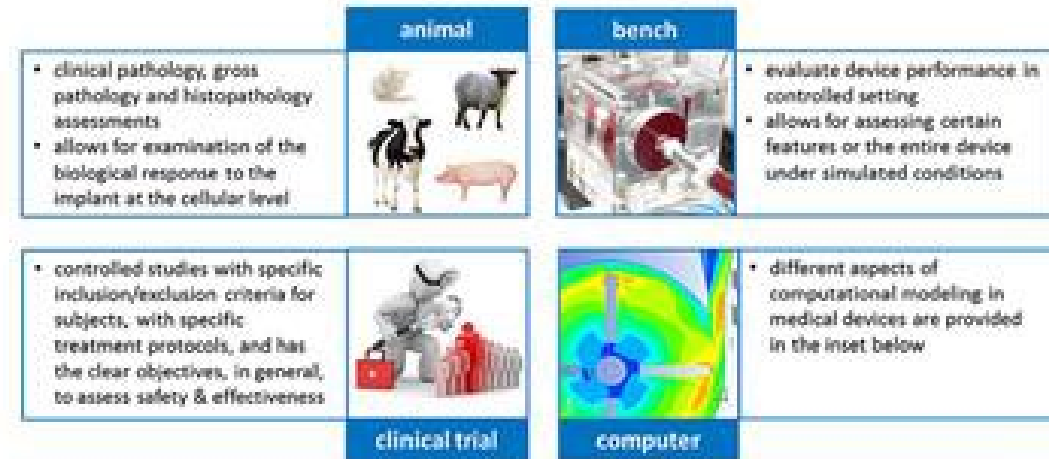


Advancing Regulatory Science With Computational Modeling for Medical Devices at the FDA's Office of Science and Engineering Laboratories

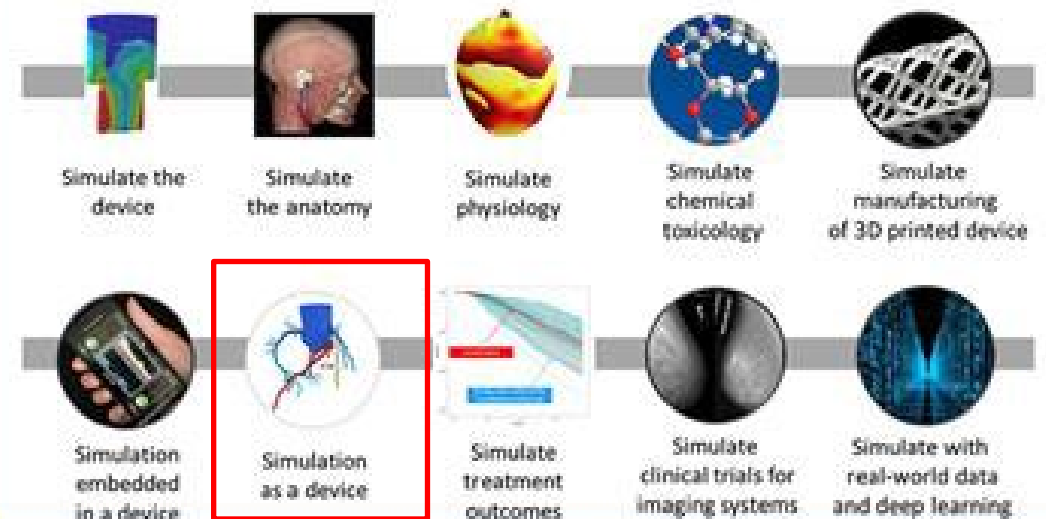
Tina M. Morrison*, Pras Pathmanathan, Mariam Adwan and Edward Margerrison

Office of Science and Engineering Laboratories, Center for Devices and Radiological Health, U.S. Food and Drug Administration, Silver Spring, MD, United States

A Scientific evidence for medical device regulatory decision-making comes from four different types of models.



B Simulation opportunities for medical devices



HeartFlow among mostly widely adopted Clinical A.I.



DOI: 10.1056/Aloa2300030

ORIGINAL ARTICLE

Characterizing the Clinical Adoption of Medical AI Devices through U.S. Insurance Claims

Kevin Wu , M.S.,¹ Eric Wu , M.S.,² Brandon Theodorou ,³ Weixin Liang , M.S.,⁴ Christina Mack , Ph.D.,⁵ Lucas Glass , Ph.D.,⁵ Jimeng Sun , Ph.D.,^{3,6} and James Zou , Ph.D.^{1,2,4}

Received: July 9, 2023; Revised: September 15, 2023; Accepted: September 29, 2023; Published: November 9, 2023

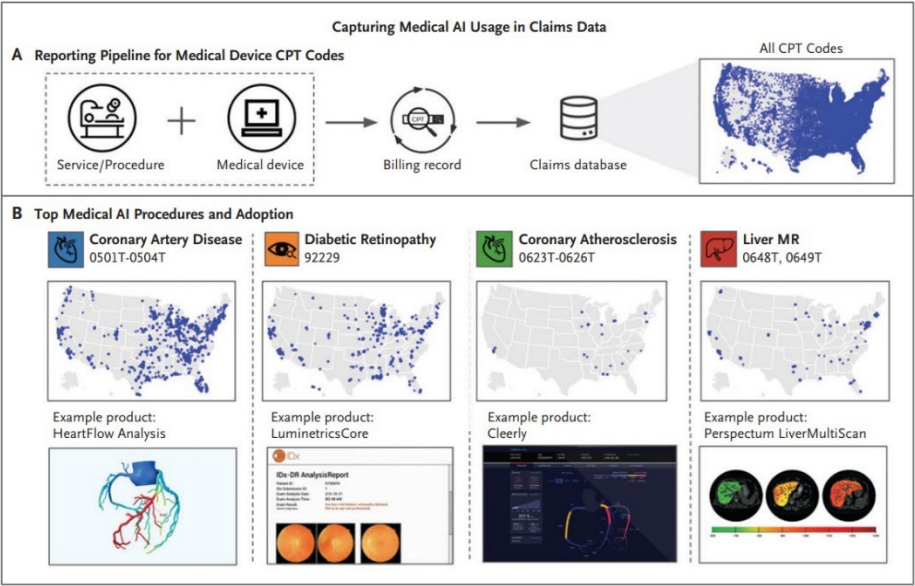
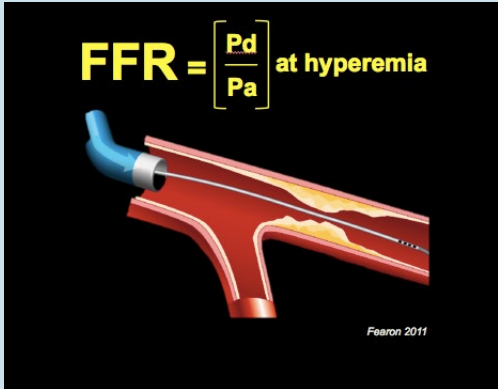
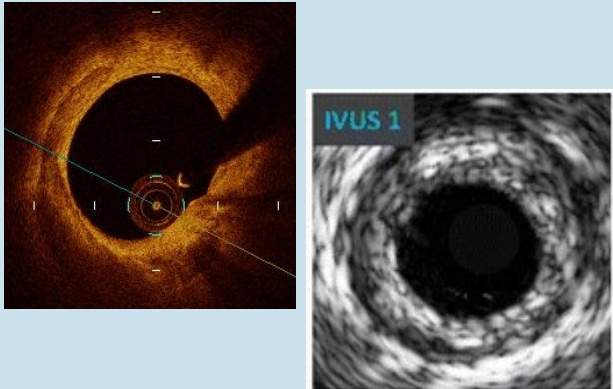
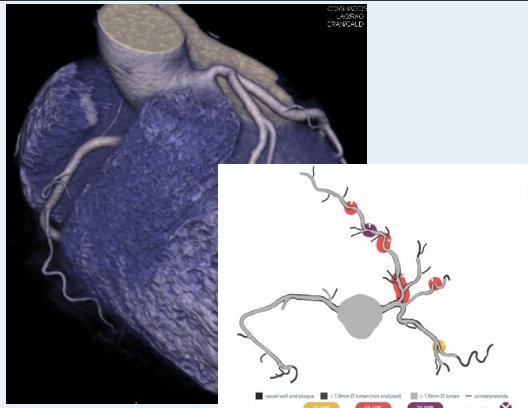
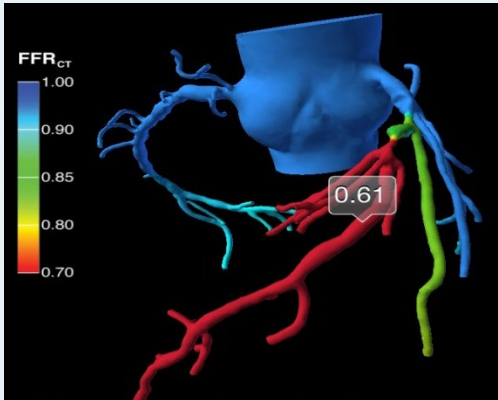
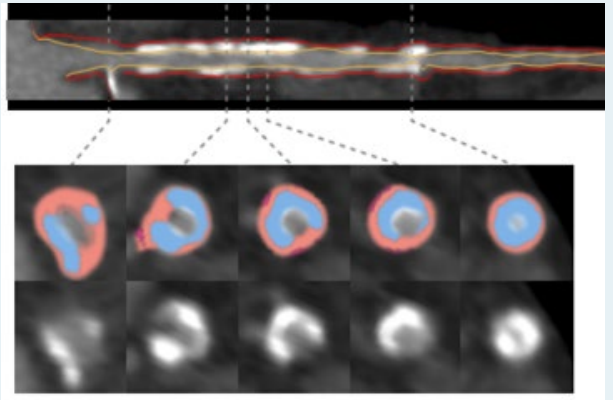


Figure 1. Capturing Medical AI Usage in Claims Data.

Table 1. Summary of AI CPT Codes.*

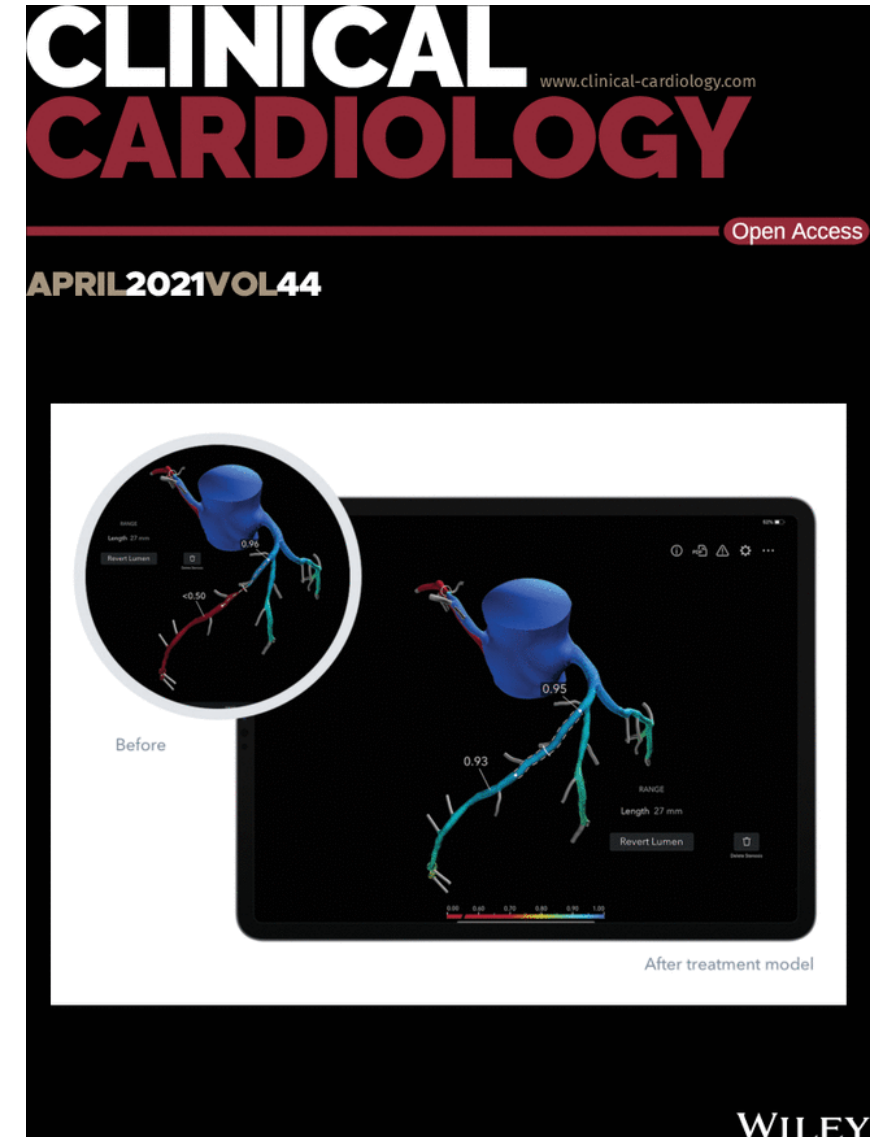
Total Claims	Condition or Medical AI Procedure	CPT Code(s)	Example Product Name	Effective Date
67,306	Coronary artery disease	0501T–0504T	HeartFlow Analysis ⁴⁸	June 1, 2018
15,097	Diabetic retinopathy	92229	LumineticsCore ⁴⁹	January 1, 2021
4,459	Coronary atherosclerosis	0623T–0626T	Cleerly ⁵⁰	January 1, 2021
2,428	Liver MR	0648T–0649T	Perspectum LiverMultiScan ⁵¹	January 1, 2021
591	Multiorgan MRI	0697T–0698T	Perspectum CoverScan ⁵²	January 1, 2022
552	Breast ultrasound	0689T–0690T	Koios DS ⁵³	January 1, 2022

Methods to assess coronary anatomy, physiology and plaque

	<u>ANATOMY</u> Identify obstructive CAD	<u>PHYSIOLOGY</u> Identify lesion-specific ischemia that may benefit from PCI	<u>PLAQUE</u> Characterize and Quantify atherosclerosis
Invasive		 $FFR = \frac{P_d}{P_a}$ at hyperemia Febron 2011	
Noninvasive			

HeartFlow Planner for CT-guided Coronary Stenting

- Noninvasive interactive tool that leverages the information within the HeartFlow Analysis
- Explore different clinical scenarios by virtually modifying the vessel and assess the FFR_{CT} value(s) resulting from each scenario





Post-PCI FFR can be predicted using HeartFlow Planner



JACC: CARDIOVASCULAR IMAGING
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THE CC BY LICENSE (<http://creativecommons.org/licenses/by/4.0/>).

NEW RESEARCH PAPER

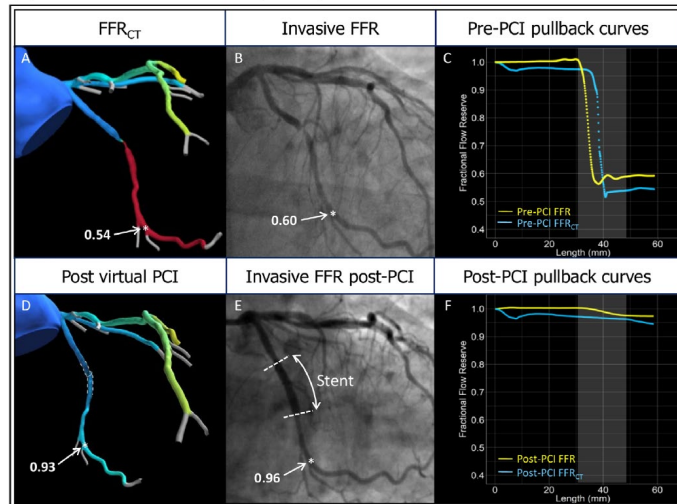
Clinical Validation of a Virtual Planner for Coronary Interventions Based on Coronary CT Angiography

Jeroen Sonck, MD,^{a,b} Sakura Nagumo, MD, PhD,^{a,c} Bjarne L. Norgaard, MD, PhD,^d Hiromasa Otake, MD, PhD,^e
Brian Ko, MD, PhD,^f Jinlong Zhang, MD,^g Takuya Mizukami, MD, PhD,^{a,h} Michael Maeng, MD, PhD,ⁱ
Daniele Andreini, MD, PhD,^{j,k} Yu Takahashi, MD, PhD,^e Jesper Møller Jensen, MD, PhD,^l Abdul Ikhdayhid, MD, PhD,^f
Ward Heggermont, MD, PhD,^g Emanuele Barbato, MD, PhD,^{a,b} Niya Mileva, MD,^g Daniel Munhoz, MD,^{a,b,k}
Jozef Bartunek, MD, PhD,^g Adam Updegrave, PhD,^l Amy Collinsworth, MS,^l Martin Penicka, MD, PhD,^g
Lieven Van Hoe, MD,^m Jonathon Leipsic, MD, PhD,ⁿ Bwon-Kon Koo, MD, PhD,^g Bernard De Bruyne, MD, PhD,^{a,o}
Carlos Collet, MD, PhD^g

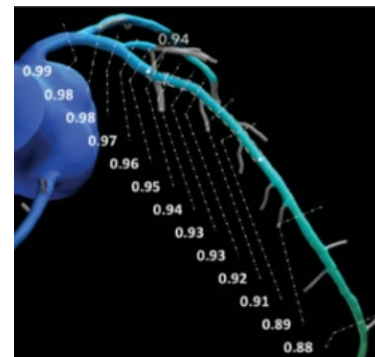
*“HeartFlow technology is accurate and
precise for predicting FFR after PCI”*

Mean Difference between FFRCT Planner and
Invasive Post-PCI FFR Pullback Curves

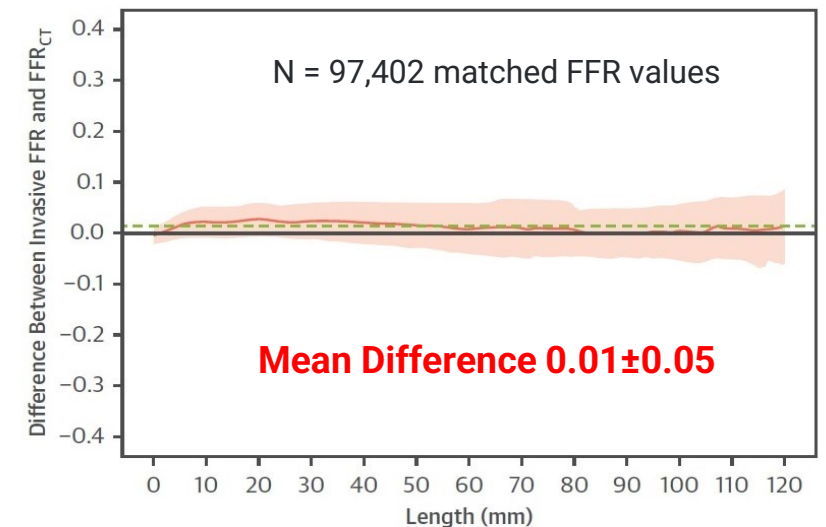
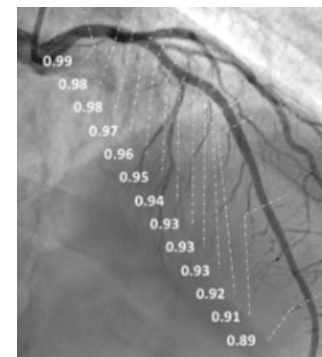
(A) Focal functional coronary artery disease



HeartFlow Predicted Post-PCI
FFR



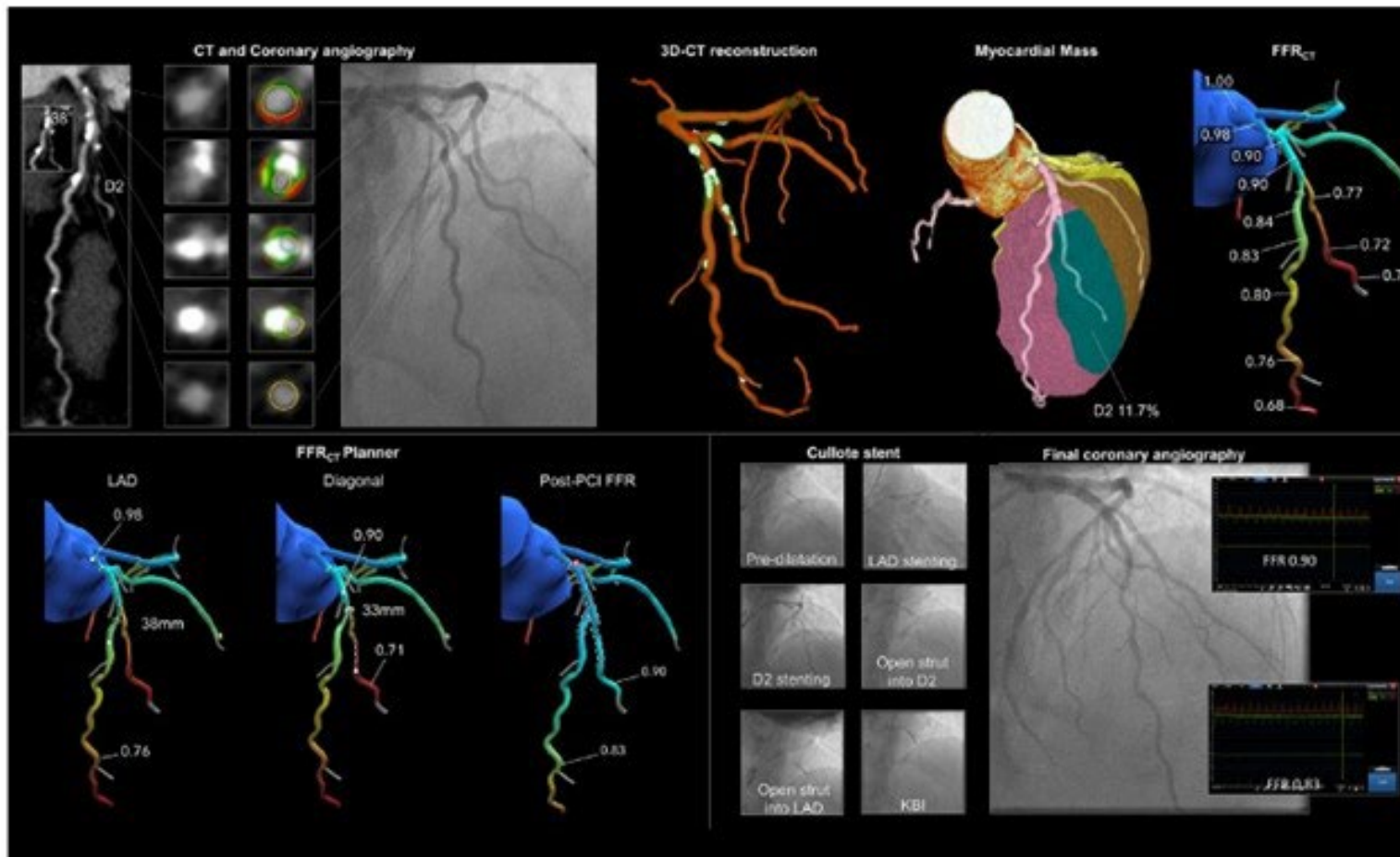
Post-PCI Invasive
FFR



Nagumo et. al., Clinical Cardiology, 2021.

Sonck et. al., JACC Imaging, 2023.

Precise Procedural and PCI Planning Using Coronary CT Angiography (P4)



Objective: Test the hypothesis that a CT-guided PCI strategy (including HeartFlow Planner) is non-inferior to IVUS guided PCI with respect to MACE

Study Design:

- Randomized Controlled Trial
- 14 sites, 1000 patients (Stable CAD patients with stenosis >70% and FFR_{CT} ≤0.80)
- Endpoint: Death, MI, Ischemia-driven TVR at 1 Year

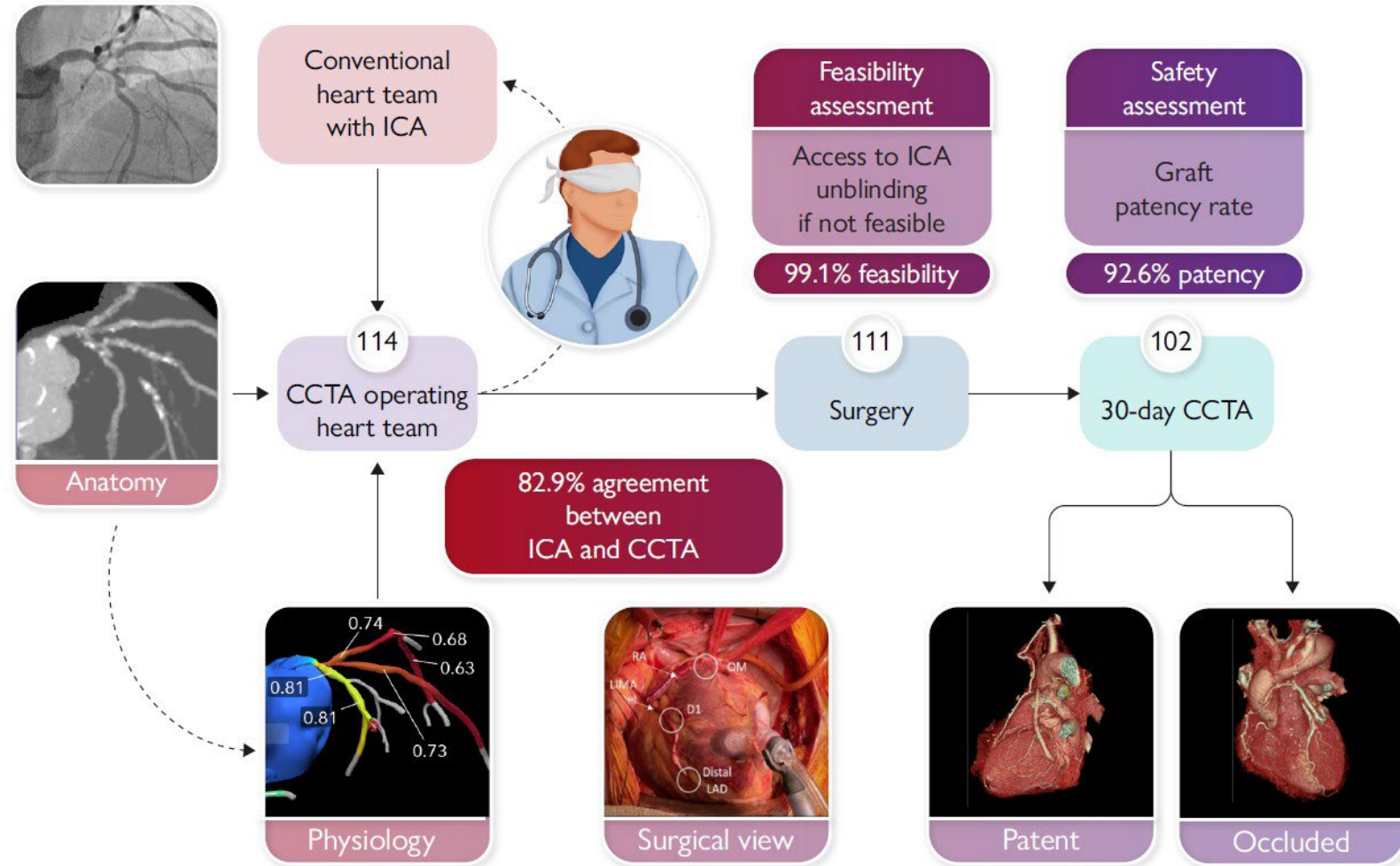
CURRENTLY ENROLLING

FAST-TRACK CABG showed that cCTA and FFR_{CT} can be used to plan CABG Procedures

Coronary bypass surgery guided by computed tomography in a low-risk population

Patrick W. Serruys ^{1*}, Shigetaka Kageyama ¹, Giulio Pompilio ^{2,3},
Daniele Andreini ^{4,5}, Gianluca Pontone ², Saima Mushtaq², Mark La Meir ⁶,
Johan De Mey ⁷, Kaoru Tanaka ⁸, Torsten Doent ⁹, Ulf Teichgräber ¹⁰,
Ulrich Schneider⁹, John D. Puskas ¹¹, Jagat Narula ¹², Himanshu Gupta¹³,
Vikram Agarwal¹¹, Jonathon Leipisch¹⁴, Shinichiro Masuda ¹, Nozomi Kotoku ¹,
Tsung-Ying Tsai¹, Scot Garg ¹⁵, Marie-Angele Morel¹, and Yoshinobu Onuma ¹

“CABG guided by CCTA is feasible and has an acceptable safety profile in a selected population of complex coronary artery disease.”



Concluding Remarks

- Patient-specific models (Digital Twins) of blood flow have now moved from the academy to the clinic
- ACC/AHA Guidelines recommend FFR_{CT} for patients with at least one stenosis in the 40-90% range
- FFR_{CT} can be used to explain chest pain, safely defer cardiac catheterization when negative and when positive can identify patients most likely to benefit from stenting
- Patient-specific models of blood flow can be used by interventional cardiologists to plan PCI prior to entering the cardiac catheterization lab and by cardiac surgeons to plan bypass surgery

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VOL. 78, NO. 7, 2021

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Coronary Computed Tomographic Angiography for Complete Assessment of Coronary Artery Disease



JACC State-of-the-Art Review

Patrick W. Serruys, MD, PhD,^{a,b,*} Hironori Hara, MD,^{a,c,*} Scot Garg, MD, PhD,^d Hideyuki Kawashima, MD,^{a,c} Bjarne L. Nørgaard, MD, PhD,^e Marc R. Dweck, MD, PhD,^f Jeroen J. Bax, MD, PhD,^g Juhani Knuuti, MD, PhD,^h Koen Nieman, MD, PhD,ⁱ Jonathon A. Leipsic, MD,^j Saima Mushtaq, MD,^k Daniele Andreini, MD, PhD,^{k,l} Yoshinobu Onuma, MD, PhD^a

CENTRAL ILLUSTRATION The Pyramid of Coronary Artery Disease and the Diagnostic Role of Multislice Computed Tomography

Pyramid of Coronary Artery Disease (CAD)

