Update on the ALL-RISE Trial:
FFR_{angio} vs. Wire-Based Physiology

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Disclosures

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

| Affiliation/Financial Relationship	Company
Grant/Research Support	Abbott, Medtronic NIH R61 HL139929-01A1 (PI)
Consulting Fees/Honoraria	CathWorks (previous), HeartFlow
Major Stock Shareholder/Equity	
Royalty Income	
Ownership/Founder	
Intellectual Property Rights	
Other Financial Benefit	

Angiography-Derived Physiology

Measurement of FFR without the need of a pressure wire or adenosine
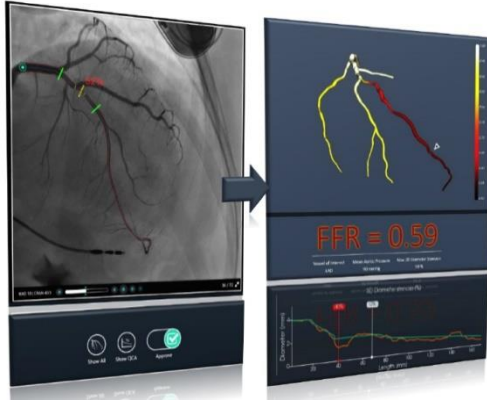
FFR$_{angio}$
CathWorks
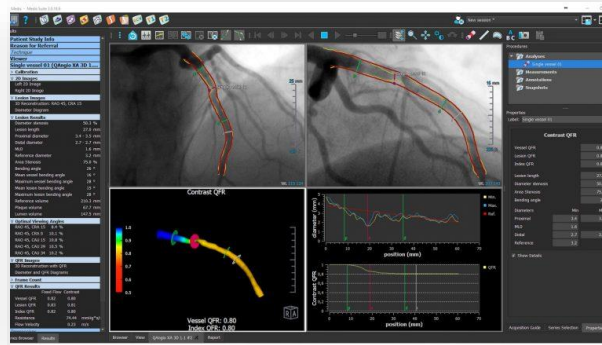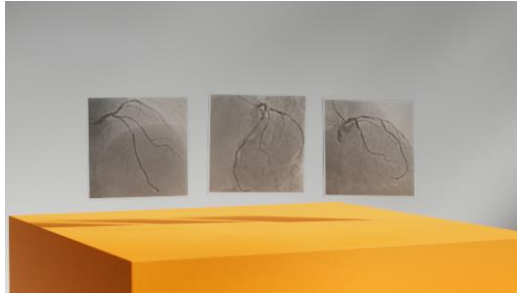
QFR
Medis Medical
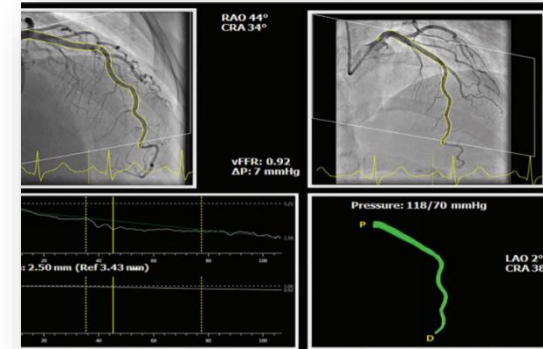
vFFR
Pie Medical

Drug-free, Wire-free Coronary Physiology

1 — Optimal 2D Angiography
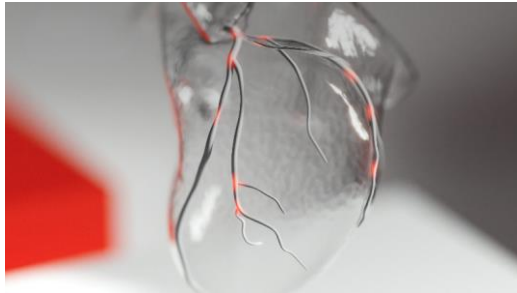

2 — 3D Model Reconstruction

3 — Resistance Analysis

4 — Comprehensive Physiological Assessment

Optimal 2D Angiography

The analysis begins with **three angiograms** that best demonstrate the coronary anatomy:

- **30° apart** (avoid all cranial or all caudal views)

- **End diastolic frame** (capture at least two cardiac cycles)

- **Good opacification of the full tree** (avoid zooming and limit panning)

- **Good view of the lesion and target vessel** (avoid overlap and foreshortening)
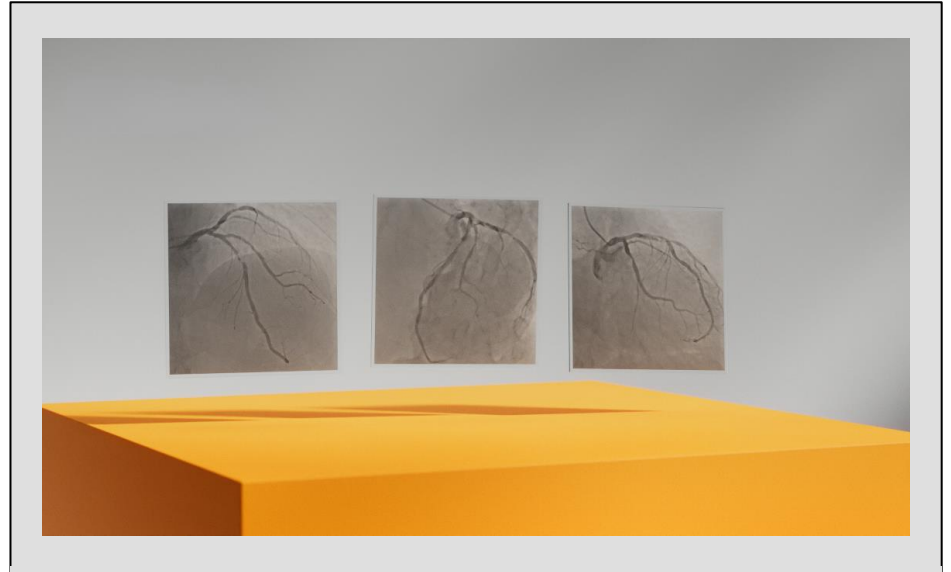
3D Model Reconstruction

The system generates an **3D volumetric model** of the coronary tree from the angiograms.

- The system **compensates for small motions** during image acquisition

- The system **carefully evaluates each image** for adequacy using AI

- By using information from three image planes, the **3D model represents the true 3D volumetric geometry**, including eccentricity

Resistance Analysis

The system analyzes every branch and bifurcation.

- The system **calculates resistance to blood flow along each segment of the coronary tree based on diameter and length**

- The system **arranges the segments like resistors** in an electrical circuit
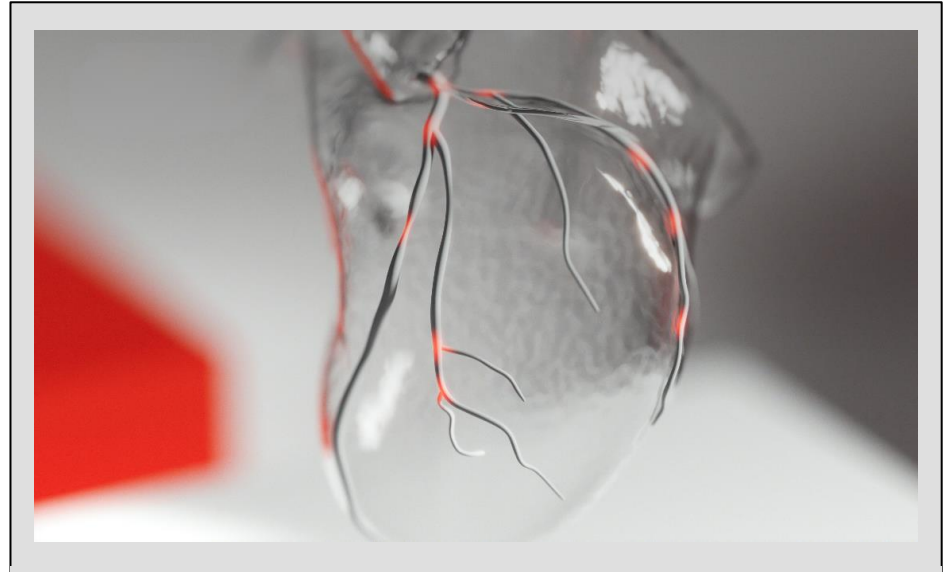
Comprehensive Physiological Assessment

The system compares resistance to blood flow in diseased versus simulated healthy vessels and **provides FFRangio values at every point along the coronary tree.**

FAST-FFR Trial

FFR$_{angio}$ compared with pressure wire-based FFR in 319 vessels at 10 centers
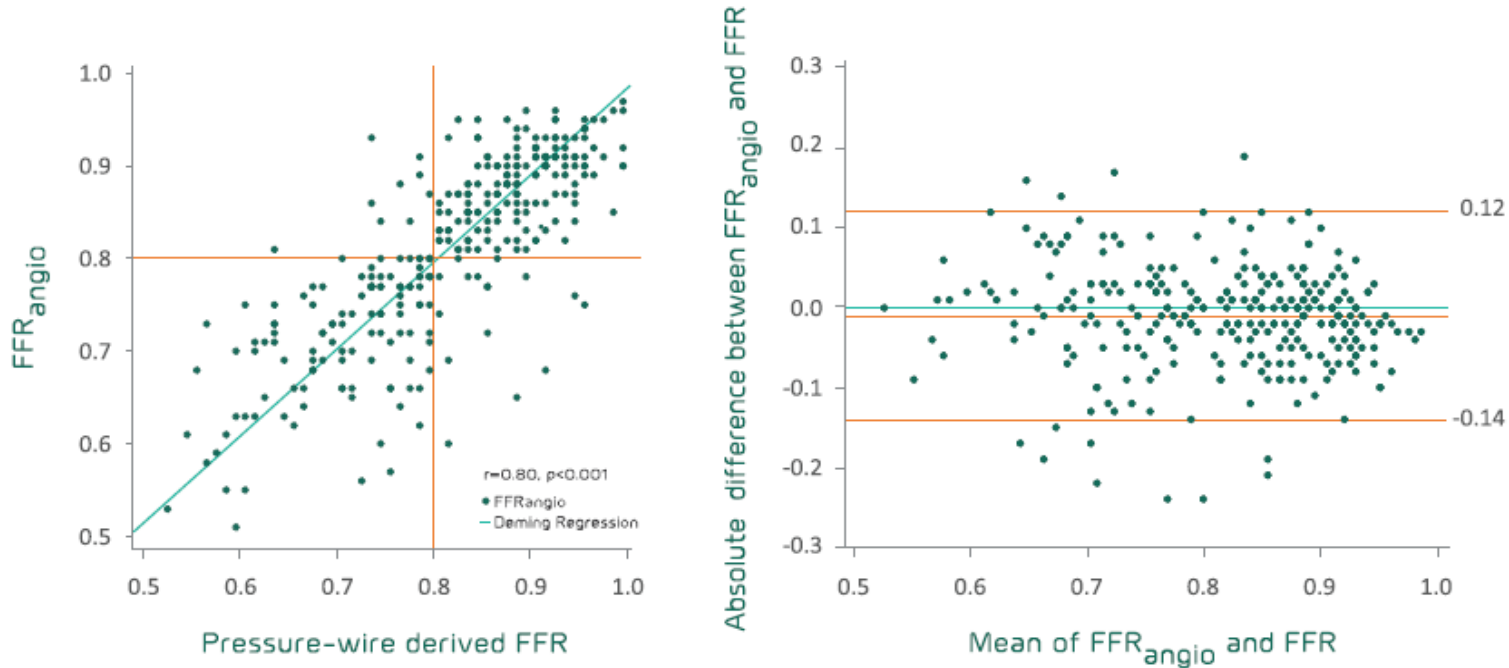

Sensitivity, specificity and accuracy of FFRangio was 94%, 91% and 92%

Circulation 2019;139:477-84.

FFR_{angio} Clinical Data

Multiple studies showing excellent concordance with wire-base FFR

Publication	Study Overview	Accuracy	Sensitivity	Specificity	AUC	Conclusions
Witberg G, et al. Diagnostic Performance of Angiogram Derived Fractional Flow Reserve[1]	**Pooled analysis of five prospective studies assessing FFRangio diagnostic performance** 588 patients, 700 lesions	**93%**	91%	94%	0.95	The pooled analysis demonstrated that FFRangio had excellent diagnostic performance and a strong correlation with invasive FFR. The results were robust across a wide spectrum of patients and lesions.
Fearon W, et al. Accuracy of Fractional Flow Reserve Derived from Coronary Angiography[2]	**FAST-FFR pivotal trial assessing FFRangio diagnostic performance in 10 centers** 301 patients, 319 vessels	**92%**	94%	91%	0.94	The study demonstrated that FFRangio had excellent diagnostic performance versus invasive FFR, including in the grey zone between 0.75 and 0.85.
Omori H, et al. Angiogram Based Fractional Flow Reserve in Patients with Dual/Triple Vessel Coronary Artery Disease[3]	**Prospective study assessing FFRangio diagnostic performance in patients with multivessel disease** 50 patients, 118 lesions	**92%**	92%	92%	0.92	The study demonstrated that FFRangio had excellent diagnostic performance versus invasive FFR, with high per-vessel accuracy, sensitivity and specificity.
Skalidis I, et al. Diagnostic Performance of Angiography-derived Fractional Flow Reserve in Patients with NSTEMI[4]	**Prospective study assessing FFRangio diagnostic performance in patients with NSTEMI** 46 patients, 60 vessels	**97%**	96%	97%	0.97	The study demonstrated that FFRangio had excellent diagnostic performance in NSTEMI patients with values for sensitivity, specificity, PPV, NPV and accuracy all being greater than 95% compared to invasive FFR.

1. Witberg G, et al. Diagnostic performance of angiogram derived fractional flow reserve. J Am Coll Cardiol Intv. 2020 Feb, 13 (4)
2. Fearon W, et al. Accuracy of fractional flow reserve derived from coronary angiography. Circ. 2019; 139: 477-484
3. Omori H, et al. Angiogram based fractional flow reserve in patients with dual/triple vessel coronary artery disease. Int. J. Cardiol. 2019; 283: 17-22
4. Skalidis I, et al. Diagnostic performance of angiography-derived fractional flow reserve in patients with NSTEMI. Catheter Cardiovasc Interv. 2022; 1-8

FFR$_{angio}$ Clinical Outcome Data
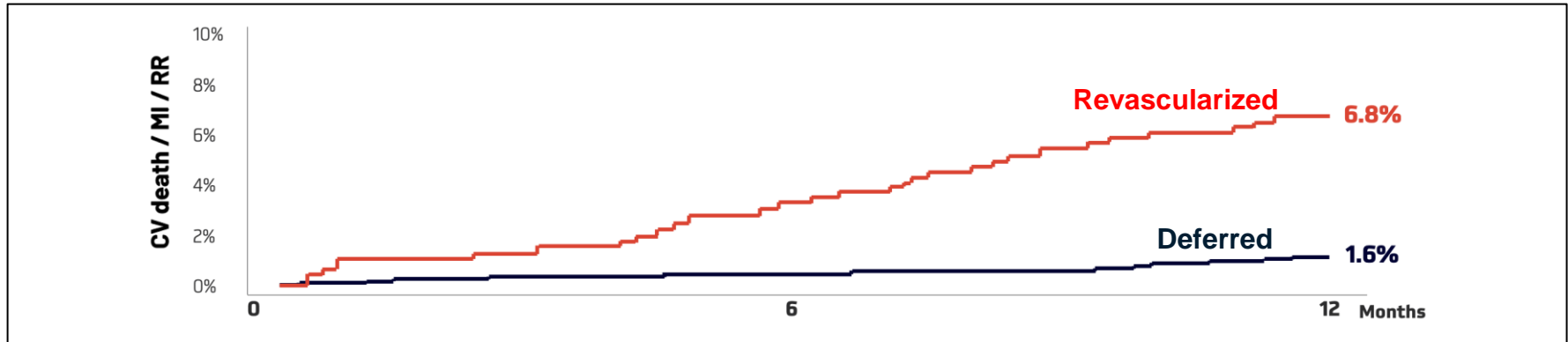
	Deferred (n=888)	Revascularized (n=547)
CV death / MI / RR	1.6%	6.8%
CV death	0.4%	0%
Myocardial infraction	0.1%	1.0%
Repeat revascularization	1.2%	6.8%
Target vessel MI	0%	0.4%
Target vessel revascularization	0.3%	2.3%
Target lesion revascularization	0.3%	0.9%

Witberg G, et al. One-year clinical outcomes of FFR angio-guided treatment of coronary artery disease, as presented at EuroPCR 2023

ALL-RISE Trial

Objective

- The primary objective is to test whether FFR_{angio}-guided treatment is noninferior to conventional pressure wire-guided treatment in patients with coronary artery disease being evaluated for percutaneous coronary intervention with respect to major adverse cardiac events at one year.

ALL-RISE Trial

Inclusion Criteria

- Subjects with chronic coronary syndromes (CCS) or non-ST elevation acute coronary syndromes (NSTEACS) undergoing coronary angiography who have a coronary lesion(s) deemed appropriate for physiology-based assessment.

ALL-RISE Trial

Major Exclusion Criteria

- Recent STEMI
- LVEF ≤ 30%
- Severe valvular heart disease
- Patent bypass graft to study vessel
- Study vessel supplies nonviable myocardium

ALL-RISE Trial

1924 Patients
Patients presenting w/ coronary lesion(s) with clinical indication for physiology-based assessment

Declare angio-based treatment plan, in detail

ALL-RISE Trial

1924 Patients
Patients presenting w/ coronary lesion(s) with clinical indication for physiology-based assessment

Declare angio-based treatment plan, in detail

1:1 Randomization
Stratified by FFR/NHPR and presentation (ACS/SAP)

962 FFRangio-guided treatment

FFRangio ≤0.80

FFRangio >0.80

PCI

Defer

962 Pressure wire-guided Treatment

FFR ≤0.80 NHPR ≤0.89

FFR >0.80 NHPR >0.89

PCI

Defer

ALL-RISE Trial

1924 Patients
Patients presenting w/ coronary lesion(s) with clinical indication for physiology-based assessment

Declare angio-based treatment plan, in detail

1:1 Randomization
Stratified by FFR/NHPR and presentation (ACS/SAP)

962 FFRangio-guided treatment

962 Pressure wire-guided Treatment

FFRangio ≤0.80 — PCI
FFRangio >0.80 — Defer

FFR ≤0.80 NHPR ≤0.89 — PCI
FFR >0.80 NHPR >0.89 — Defer

Primary Endpoint: MACE
(death, MI, clinically indicated revascularization)
Non-inferiority Design
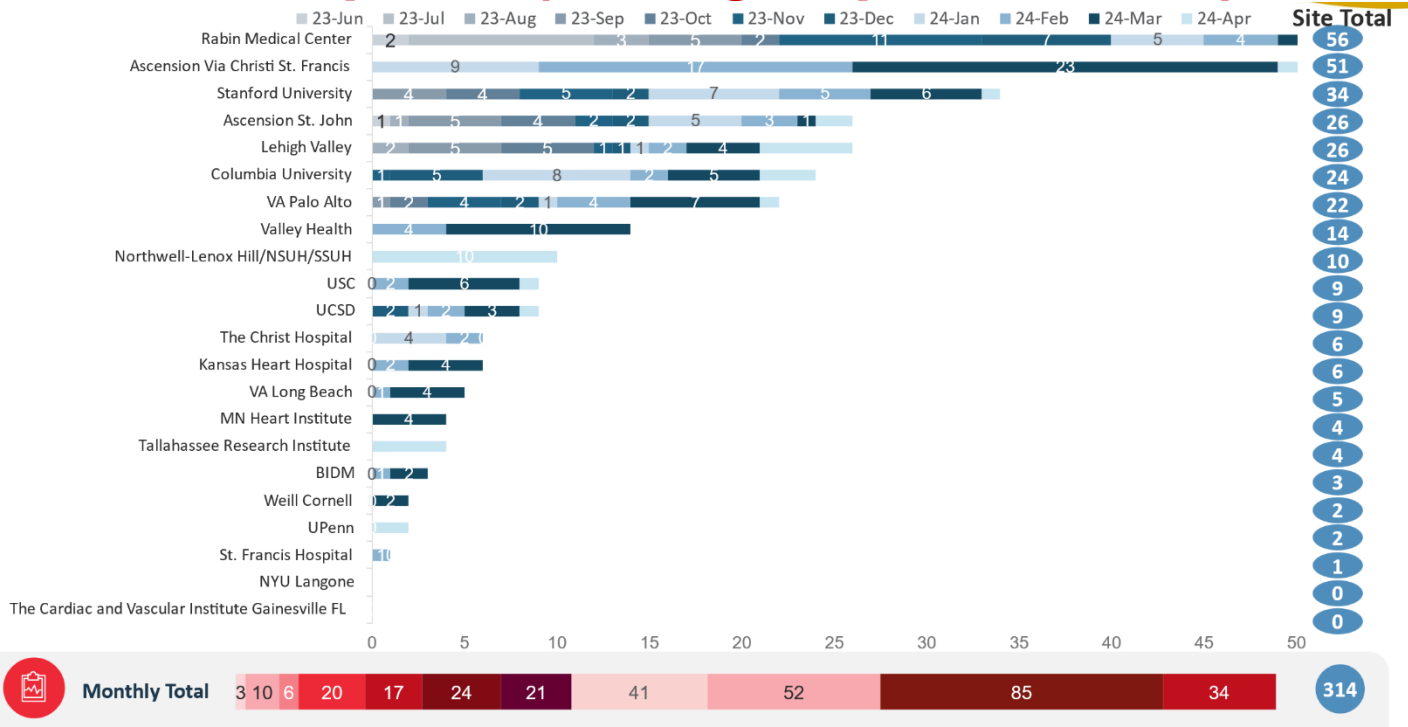Secondary Endpoints: Cost-effectiveness, QOL, procedure time, complications

1924 patient to be enrolled in up to 60 sites globally, with a limit of up to 200 patients per site.

ALL-RISE Trial

Enrolment Update (through April 16, 2024)

ALL-RISE Trial

Summary

- We expect the ALL-RISE trial will demonstrate that FFR_{angio}-guided PCI is non-inferior to wire based physiology-guided PCI.

- We anticipate it will be quicker, reduce contrast usage and ultimately be a cost-effective strategy.

- If this is the case, angiography-derived physiology should become an important tool for guiding PCI decisions.

Thank You!