FFR$_{angio}$ Accuracy vs. Standard FFR (FAST-FFR) Trial

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Disclosure Statement of Financial Interest

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

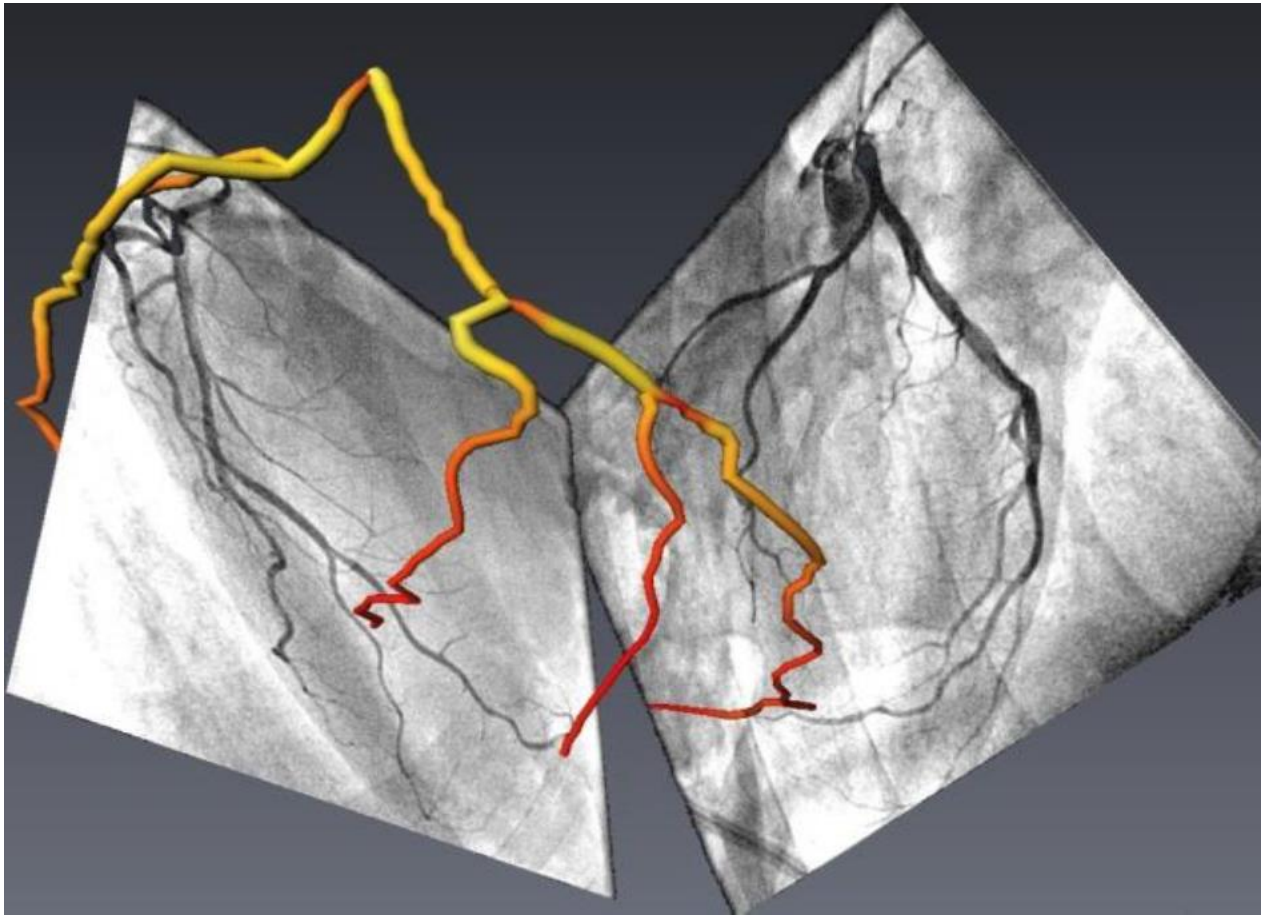
Affiliation/Financial Relationship	Company
Grant/ Research Support:	**Abbott, Medtronic, CathWorks,**
Consulting Fees/Honoraria:	
Major Stock Shareholder/Equity Interest:	
Royalty Income:	
Ownership/Founder:	
Salary:	**NIH R61 HL139929-01A1 (PI)**
Intellectual Property Rights:	
Other Financial Benefit: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

Why We Don't Perform FFR

- $$$
- It takes time…
- Wire handling characteristics…
- Pressure drift is frustrating…
- Side effects of adenosine…
- It is expensive…
- There is a small risk…

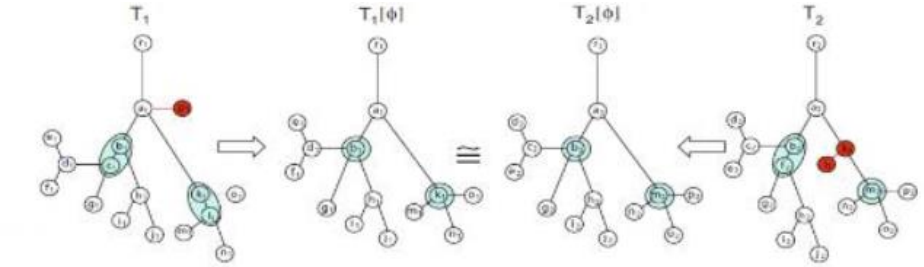
Coronary Pressure Wire

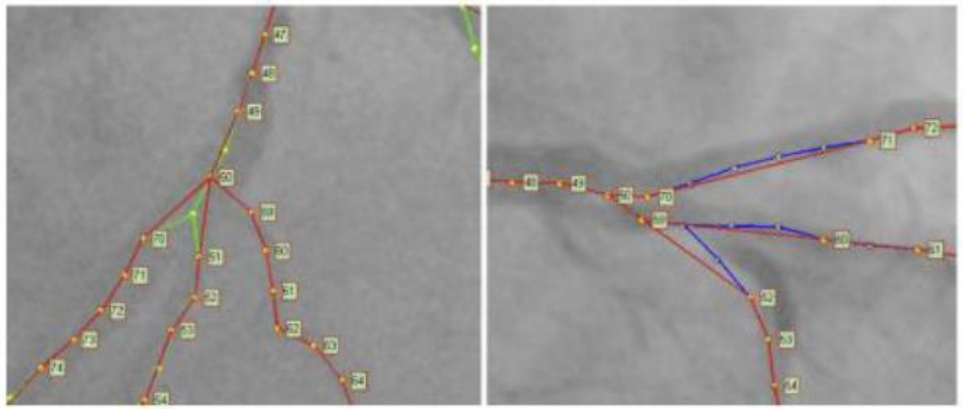
FFR_{angio}

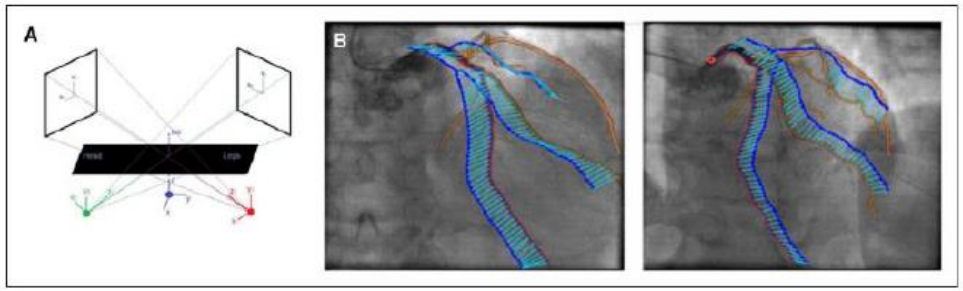


Courtesy of CathWorks

FFR_{angio}





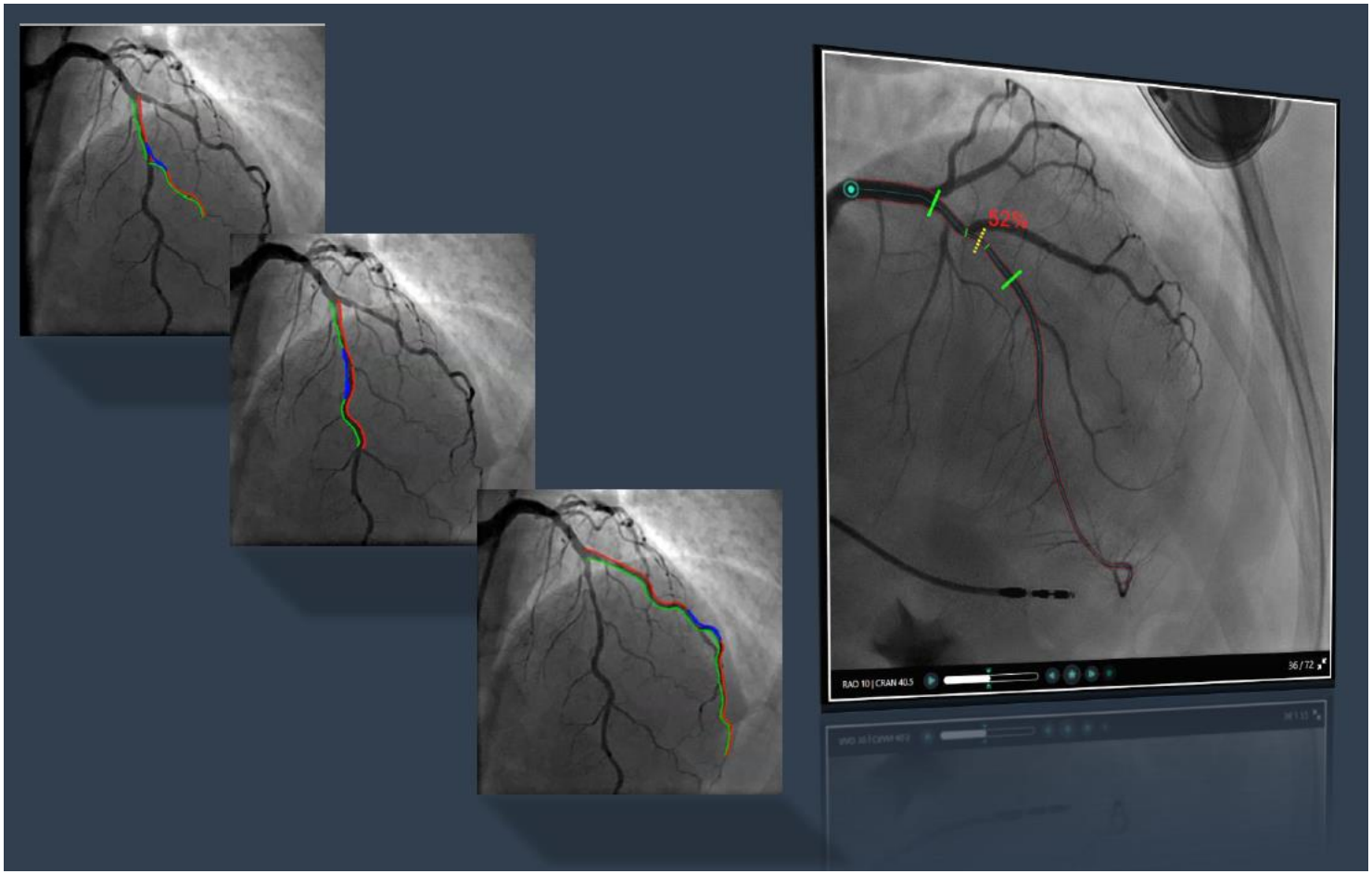


The 3D engine contains a compensation mechanism which uses all available projections to account for respiratory and cardiac motion and optimizes the 3D reconstruction.

Courtesy of CathWorks

FFR_{angio}

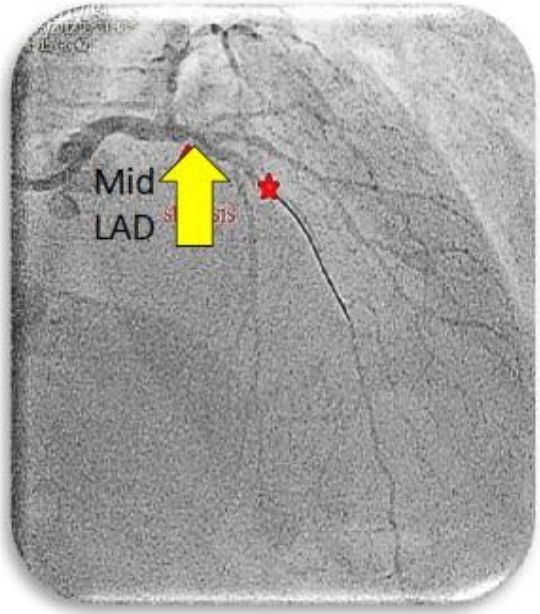
Automatic stenosis detection by scanning the entire 3D reconstruction

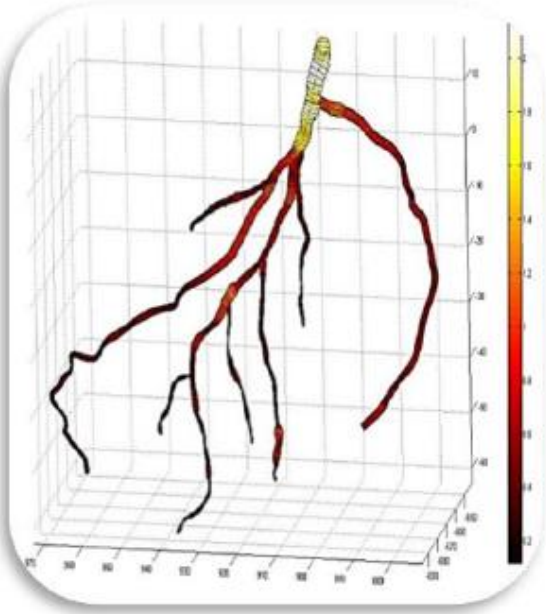


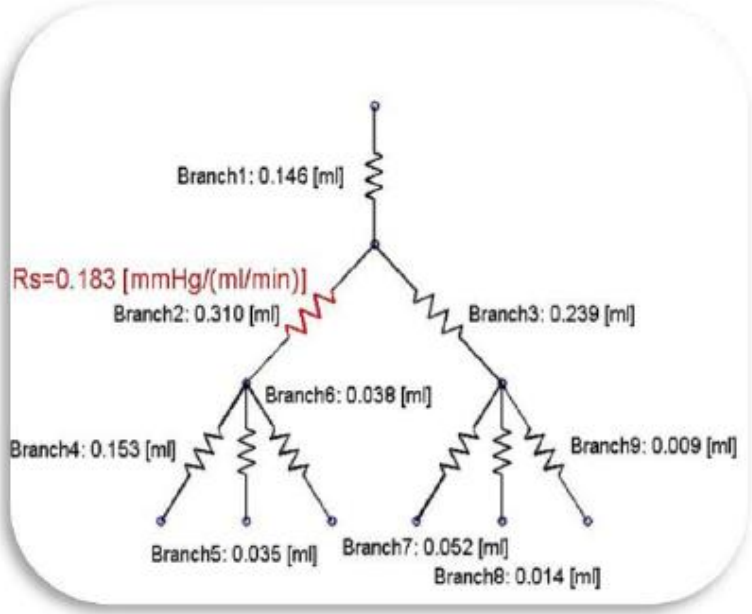
Courtesy of CathWorks

FFR_{angio}

The coronary arterial network is modeled as an electrical circuit with each segment acting as a resistor. The vessel resistance is estimated based on its length and diameter. Each vessel's contribution to flow is based on its impact on overall resistance depending on the arrangement.



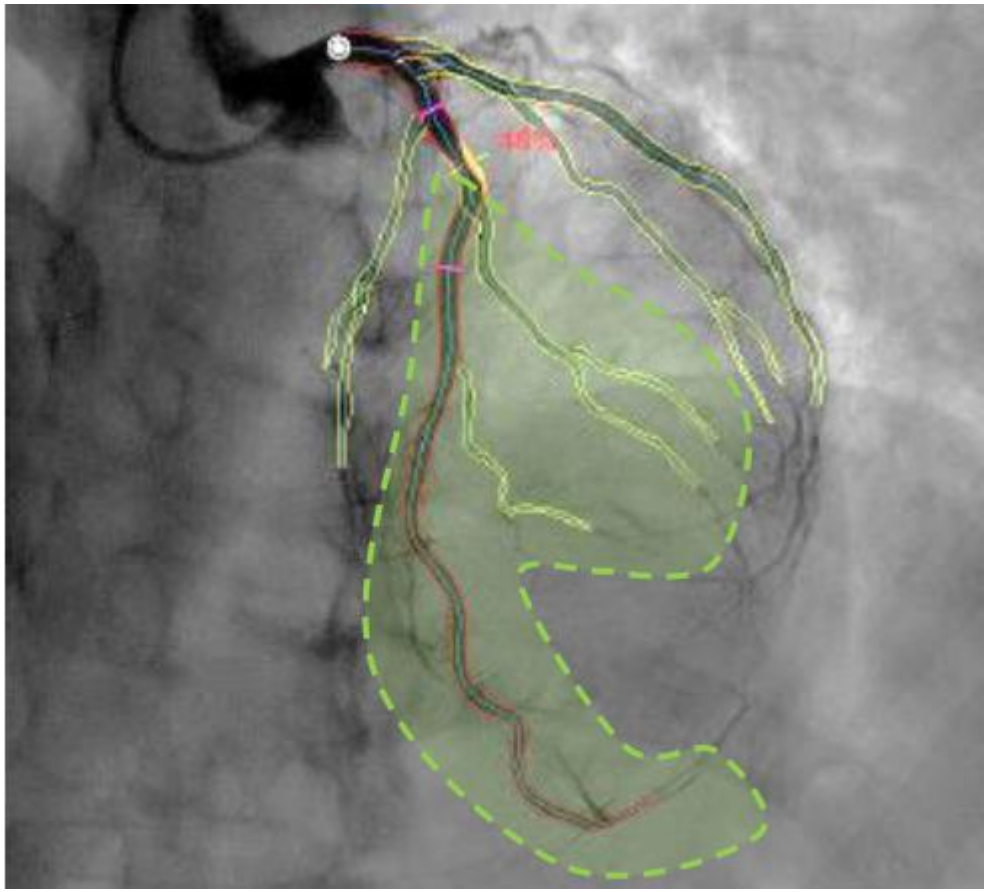




Courtesy of CathWorks

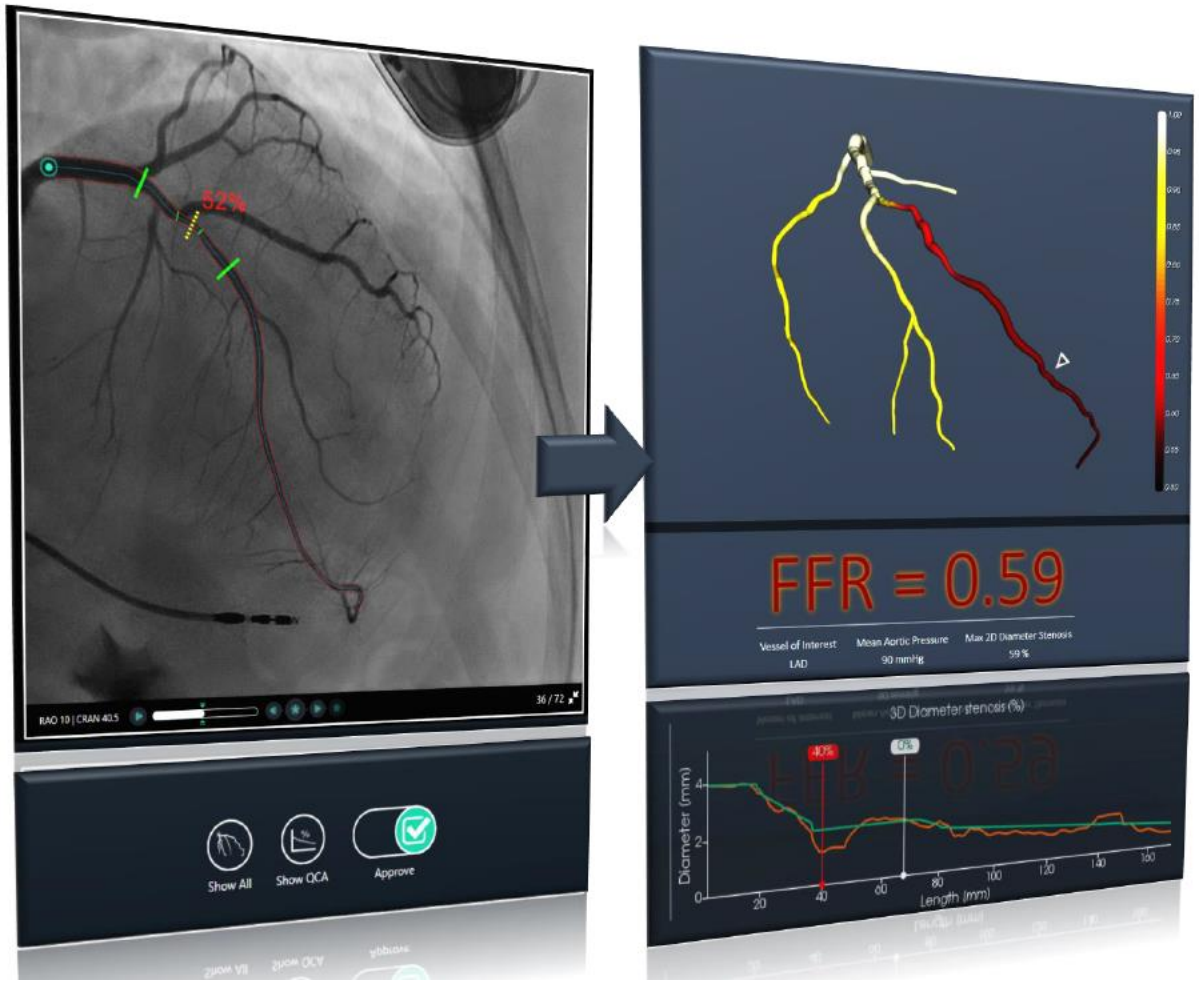
FFR_{angio}

Normal maximal flow is estimated based on the volume of coronary vessels and total coronary length.



Courtesy of CathWorks

FFR_{angio}



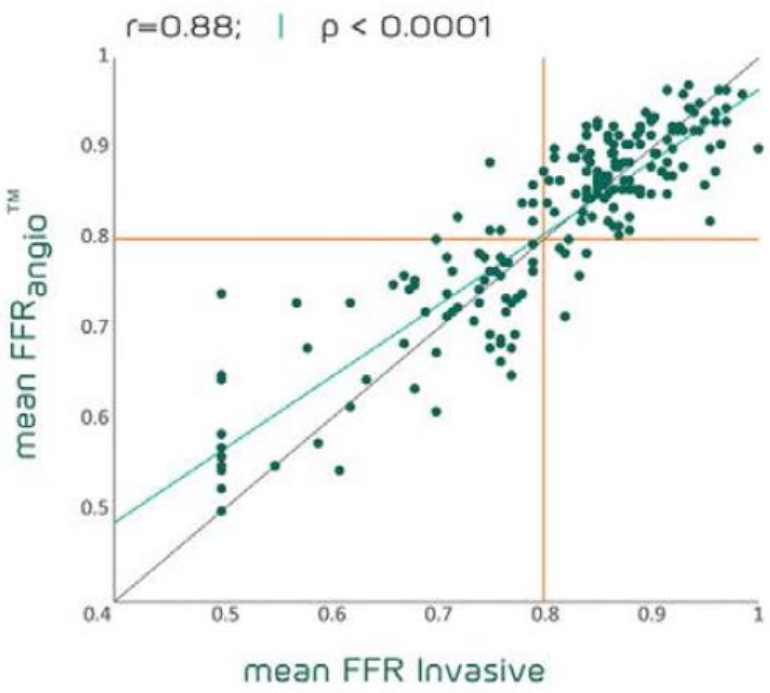
FFR_{angio} is then calculated as the ratio of the maximal flow rate in the stenosed artery compared with the flow rate in the absence of the stenosis:

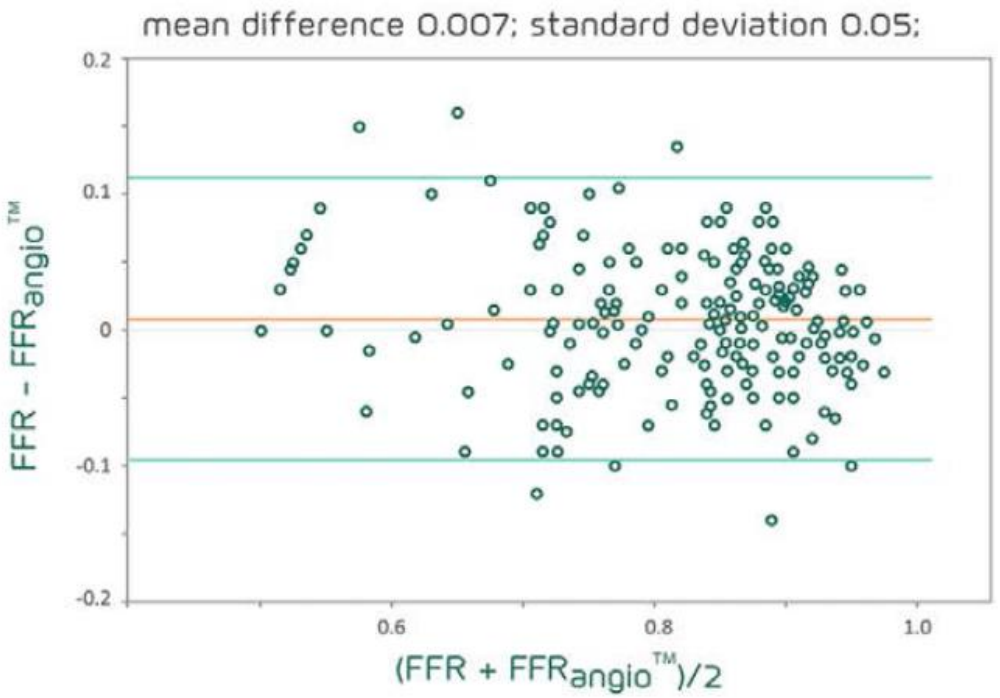
$$FFR_{angio} = Q_S / Q_N$$

Courtesy of CathWorks

FFR_{angio} Data

FFR_{angio} compared with invasive FFR in 203 lesions (184 patients)





Sensitivity, specificity and accuracy of FFR_{angio} was 88%, 95% and 93%

Pellicano, et al. Circ Cardiovasc Interv 2017;10:e005259.

FAST FFR Trial

FFR$_{angio}$ Accuracy versus STandard FFR

- Rationale:
  - FFR$_{angio}$ has not been well validated when performed on-site by independent, local operators blinded to pressure wire-derived FFR and compared with core laboratory analyzed FFR values in a large, prospective, multicenter fashion.

Circulation 2019;139:477-84

FAST FFR Trial

Exclusion Criteria

- STEMI within the last 12 months
- Prior CABG, valve surgery or heart transplant
- Severe aortic stenosis
- Known LVEF ≤45%

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FAST FFR Trial Endpoints

Co-Primary Endpoints

- Lower bound of the 95% CI of the sensitivity and specificity for dichotomously scored FFR_{angio} measured index per vessel as compared with wire-derived FFR.
  - Performance goal for sensitivity = 0.70
  - Performance goal for specificity = 0.75

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FAST FFR Trial Endpoints

Secondary Endpoints

- Diagnostic accuracy of FFR_{angio}
- Correlation between FFR_{angio} and FFR
- FFR_{angio} device success

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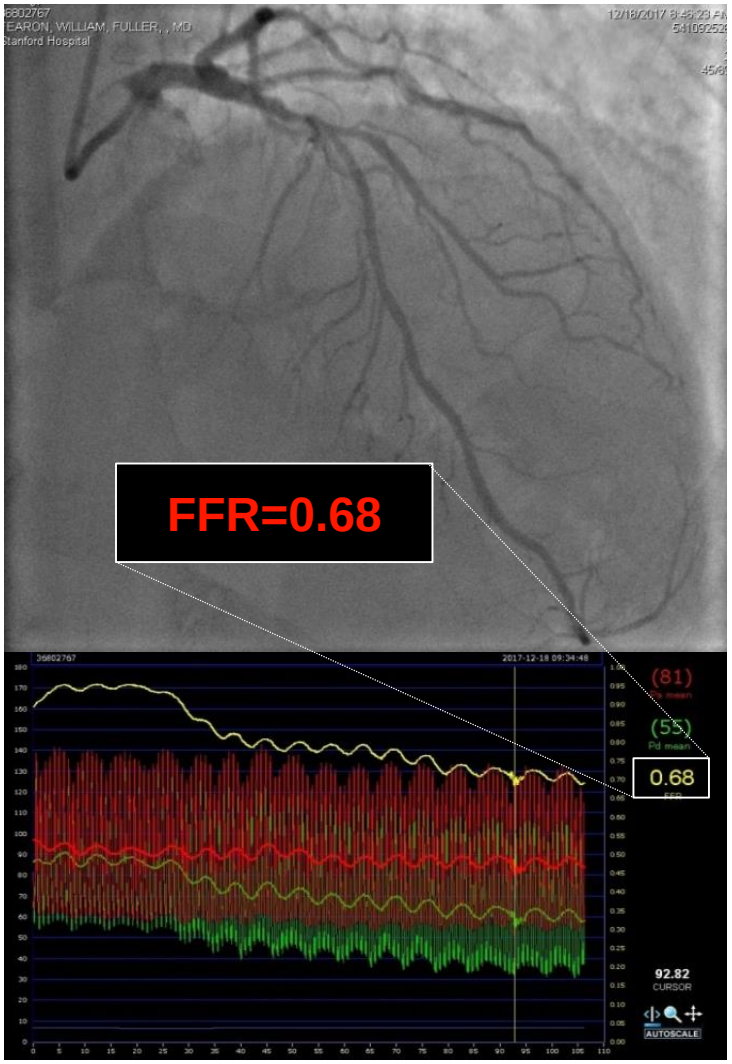
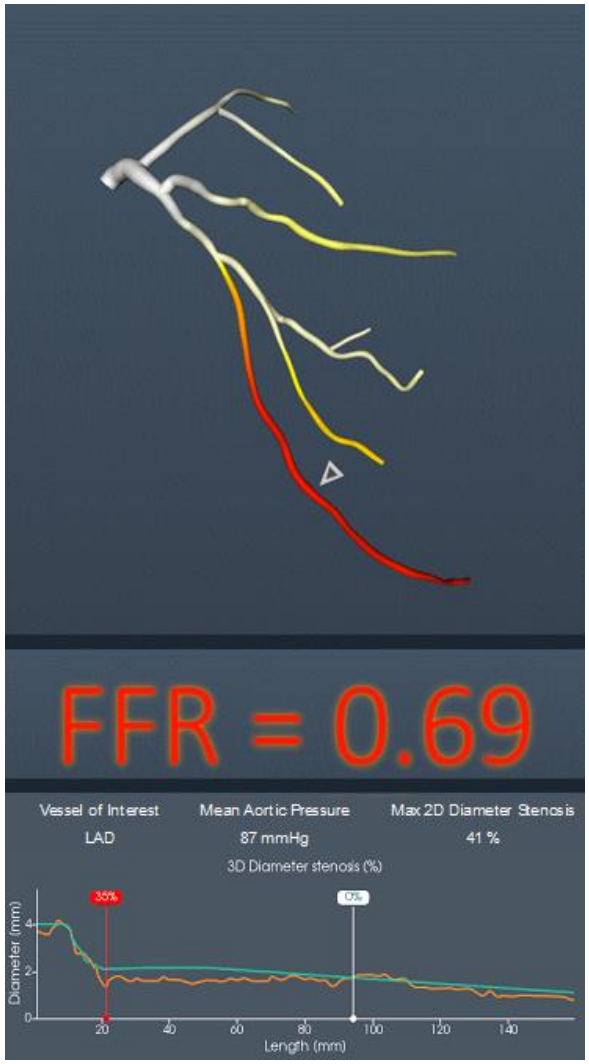
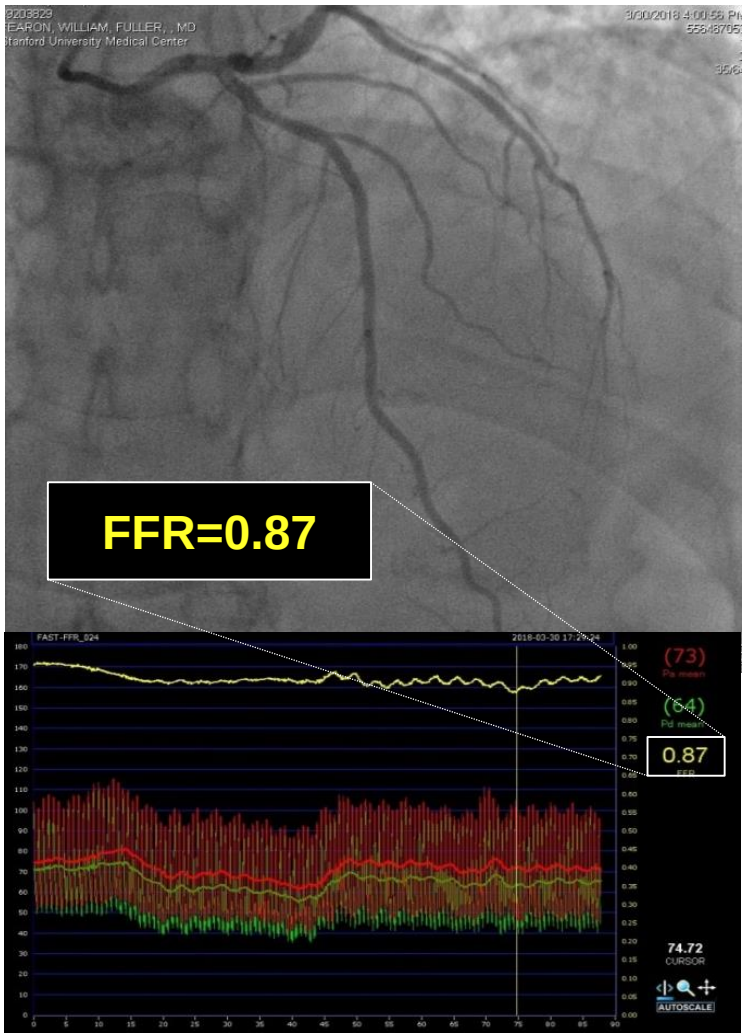
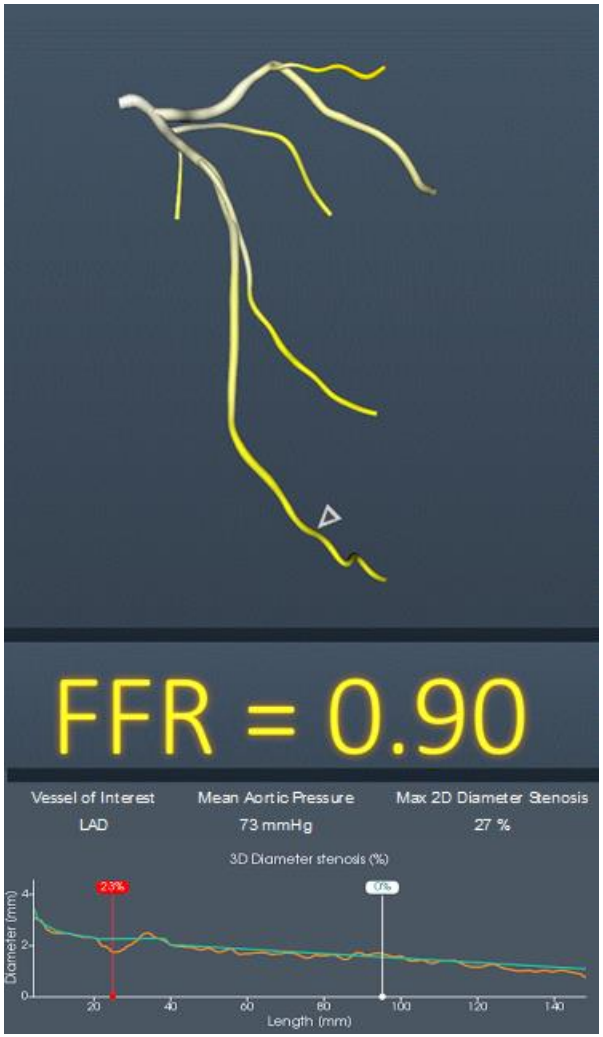
FFR_{angio} Case Examples





FFR_{angio} Case Examples





FAST FFR Trial

Patient Characteristics

Baseline Characteristic	n=301 patients
Age	64.7 ± (9.7)
Male	74.1%
Body Mass Index (kg/m^2)	28.9 ± (4.8)
Hypertension	69.1%
Hypercholesterolemia	76.4%
Diabetes Mellitus	31.9%
Smoking (current or former)	52.8%
Left Ventricular Ejection Fraction (LVEF)	58 ± (6)%
Family history of coronary artery disease	39.3%
Prior STEMI	3.3%
Prior PCI with stent	29.2%
Presentation	
Acute coronary syndrome (UA or NSTEMI)	41.9%
Stable patients	57.2%

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FAST FFR Trial

Lesion Characteristics

Angiographic Result	n=319 vessels
Lesions per patient	1.1 ±0.3
Target Vessel	
LAD	54.2%
RCA	24.1%
LCX	19.1%
Ramus	2.5%
% Diameter Stenosis (Visual)	63 ±17%
% Diameter Stenosis (QCA)	51 ±10%
Lesion and Vessel Characteristics	
Bifurcation	17.3%
Moderate/Severe Tortuosity	5.5%
Moderate/Severe Calcification	19.9%
Lesion Class B or C	88.8%

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FAST FFR Trial

FFR and FFR_{angio} Results

Physiologic Result	FFR	FFR_{angio}
Mean	0.81 ± (0.13)	0.80 ± (0.12)
Median	0.83 (0.74, 0.90)	0.82 (0.73, 0.89)
% of positive lesions (≤ 0.80)	43.3%	45.5%
% within 0.70-0.90	58.9%	63.6%
% within 0.75-0.85	31.3%	31.0%

FFR_{angio} was successfully measured in 98.7% of cases

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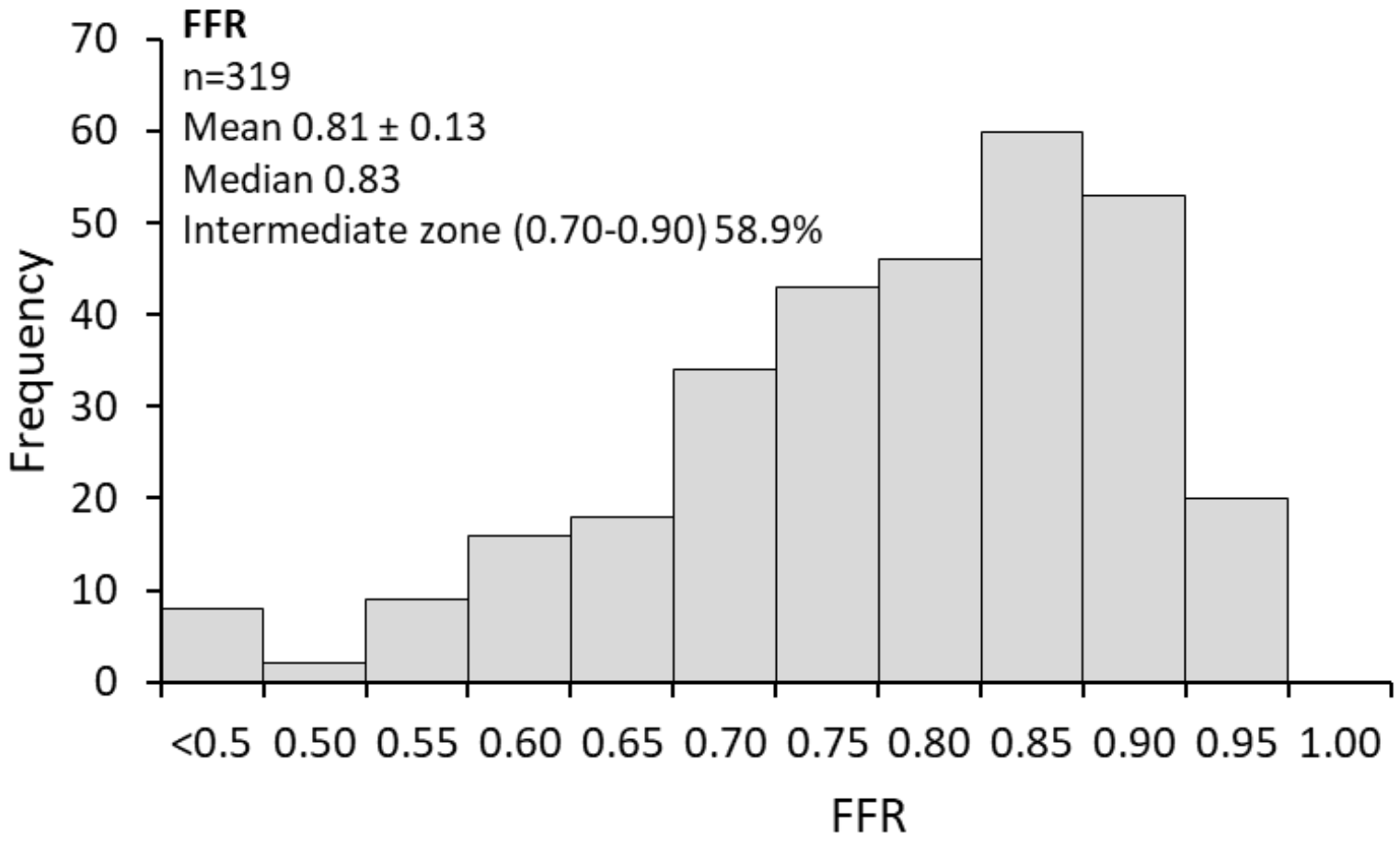
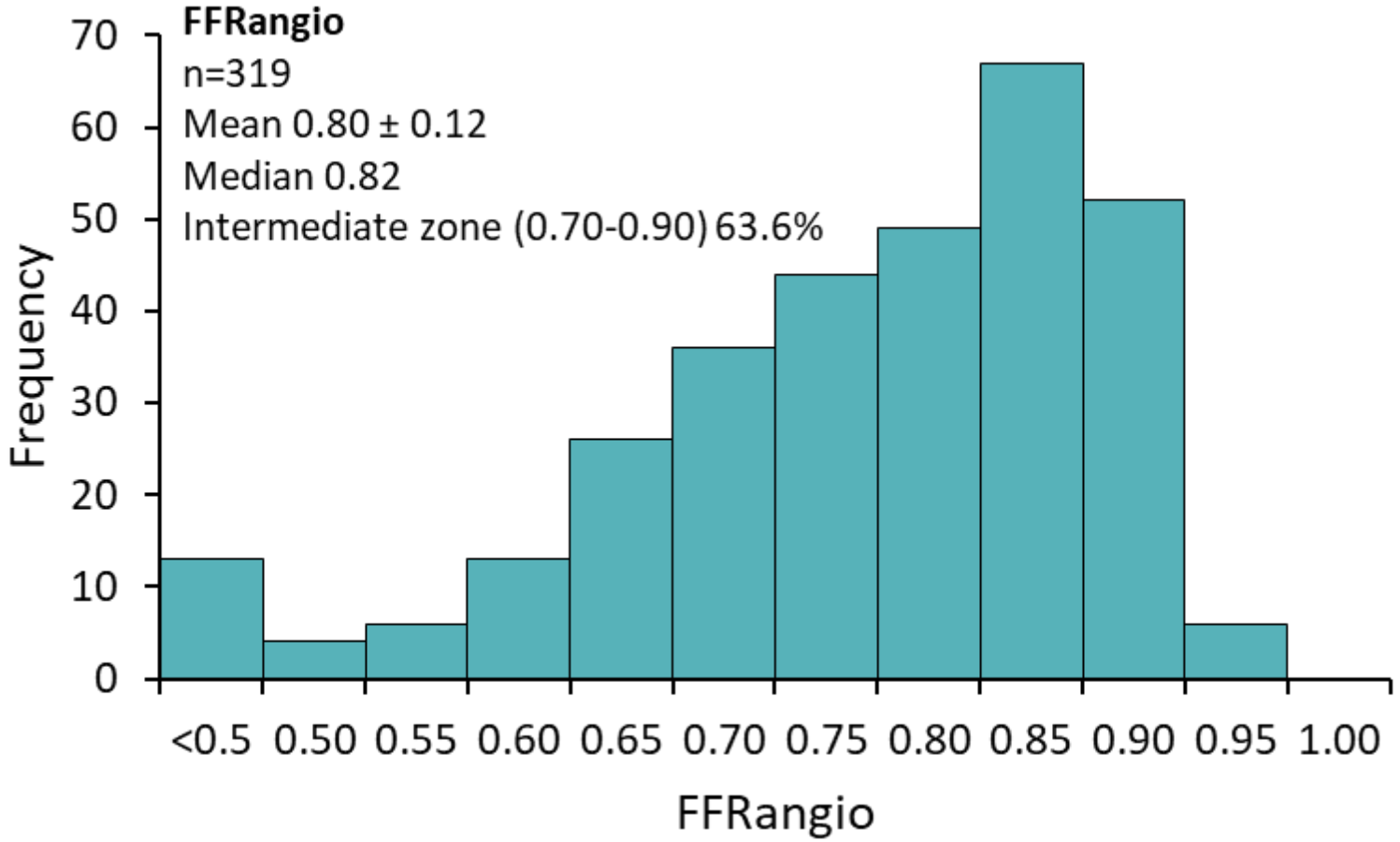
FAST FFR Trial

FFR and FFR_{angio} Results



FAST FFR Trial

FFR and FFR_{angio} Results



FAST FFR Trial

Co-Primary and Secondary Endpoints

Diagnostic Characteristic	
Sensitivity	**93.5% (87.8, 96.6)**
Specificity	**91.2% (86.0, 94.6)**
Diagnostic accuracy	92.2% (88.7, 94.8)
Positive Predictive Value	89.0% (82.6, 93.2)
Negative Predictive Value	94.8% (90.3, 97.3)

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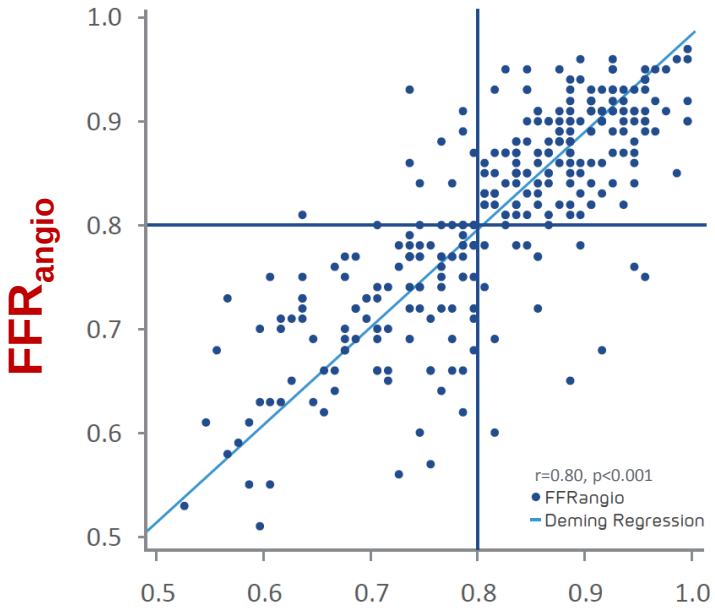
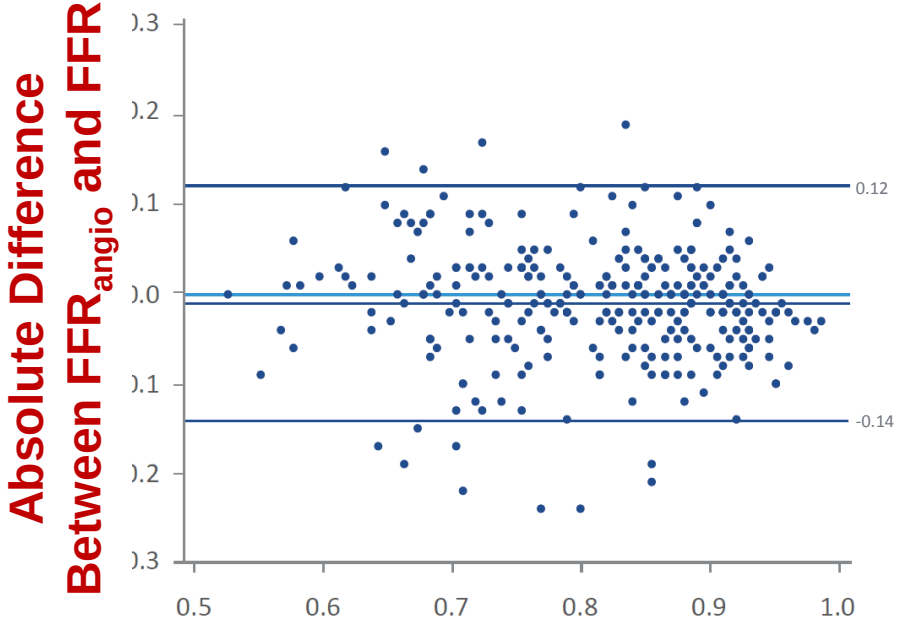
FAST FFR Trial

Correlation and Bland-Altman



FFR_{angio}

Pressure Wire-Derived FFR



Absolute Difference Between FFR_{angio} and FFR

Mean of FFR_{angio} and FFR

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FAST FFR Trial

Features of Discordant Results

Characteristic	Concordant (N = 277)	Discordant (N = 24)	P value
Age	64.7 ± (9.7)	64.6 ± (9.8)	0.52
Male	74.1%	73.3%	0.28
Body Mass Index (kg/m^2)	28.9 ± (4.8)	28.8 ± (4.9)	0.07
Hypertension	69.1%	69.0%	0.85
Hypercholesterolemia	76.4%	76.5%	0.87
Diabetes Mellitus	31.9%	32.1%	0.77
Smoking (current or former)	52.8%	53.4%	0.48
Left Ventricular Ejection Fraction (LVEF)	58 ± (6)%	58 ± (6)%	0.99
Family history of coronary artery disease	39.3%	39.9%	0.53
Presentation			
Acute coronary syndrome (UA or NSTEMI)	41.5%	45.8%	0.68
Stable patients	44.8%	33.3%	0.28

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FAST FFR Trial

Features of Discordant Results

Characteristic	Concordant (N = 297)	Discordant (N = 25)	P value
Target vessel			
LAD	55.9%	32.0%	0.03
RCA	22.6%	40.0%	0.04
LCX	19.5%	20.0%	0.14
Ramus	2.0%	8.0%	0.09
% Diameter Stenosis (Visual estimation)	63 ± (17)	63 ± (9.8)	0.88
Mean FFR	0.80 ± (0.13)	0.83 ± (0.07)	0.16
FFR ≤ 0.80	43.9%	36.0%	0.42
Mean FFRangio	0.80 ± (0.12)	0.79 ± (0.08)	0.52
FFRangio ≤ 0.80	43.9%	64.0%	0.05

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FAST FFR Trial

Substudy

Which correlates better with wire-based FFR: a non-hyperemic pressure ratio (e.g., iFR, dPR, or Pd/Pa) or FFR_{angio}?

Diagnostic Accuracy
iFR or dPR = 82.7%
Pd/Pa = 85.3%
FFR_{angio} = 92.4%

Johnson, et al. J Am Coll Cardiol 2019;in press.

FAST FFR Trial

Substudy

- Physiologically, these results imply that “simulated hyperemia” outperforms “assumed hyperemia” even when disadvantaged by an indirect computation of coronary pressure.

- Practically, these findings suggest that centers wishing to avoid wire-based FFR for whatever logistical or clinical reasons would be better served by abandoning pressure wires completely and instead by employing FFR derived from the angiogram.

Johnson, et al. J Am Coll Cardiol 2019;in press.

Summary

- FFR derived from routine coronary angiography (FFR_{angio}) had very high sensitivity, specificity and diagnostic accuracy, all of which were greater than 90% for predicting the reference standard, coronary pressure wire-derived FFR.

- FFR_{angio} and FFR remained highly correlated over the entire range of FFR values.

- FFR_{angio} was successfully measured in almost all cases included.

Conclusion

- FFR_{angio} may provide an easier and potentially faster method for performing physiology guided assessment of the overall coronary angiogram with similar accuracy to the reference standard, coronary pressure wire-based FFR.

- This may translate into a greater percentage of patients undergoing physiologic guidance for revascularization decisions and ultimately improve long-term outcomes.