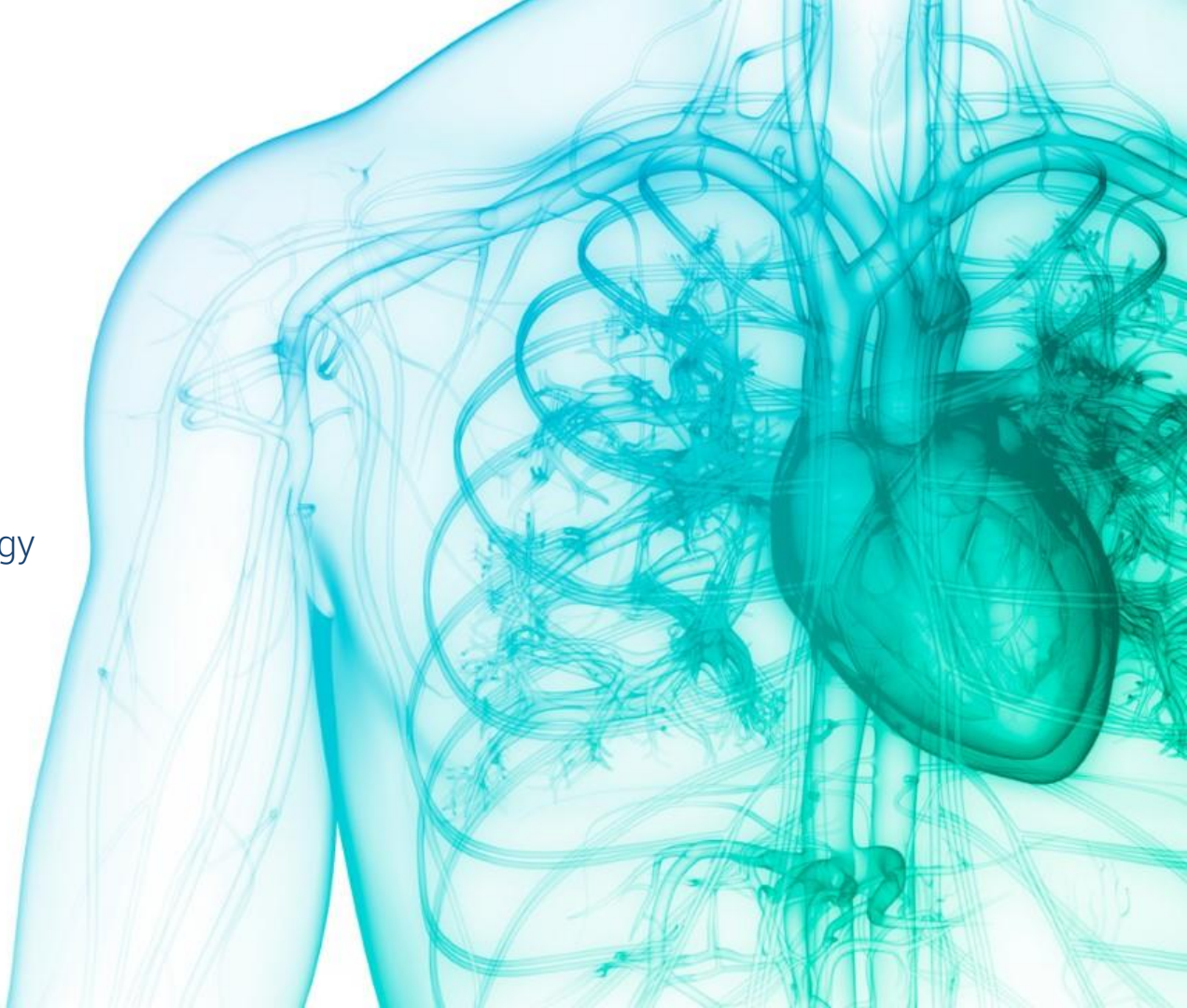




Coronary CT Imaging and Physiology for Multivessel Disease

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Founder & CEO, Cleerly



Computed tomographic angiography in coronary artery disease

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P.W. Seurrys and N. Kotoku contributed equally to this work.

This paper also includes supplementary data published online at: <https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-22-00776>

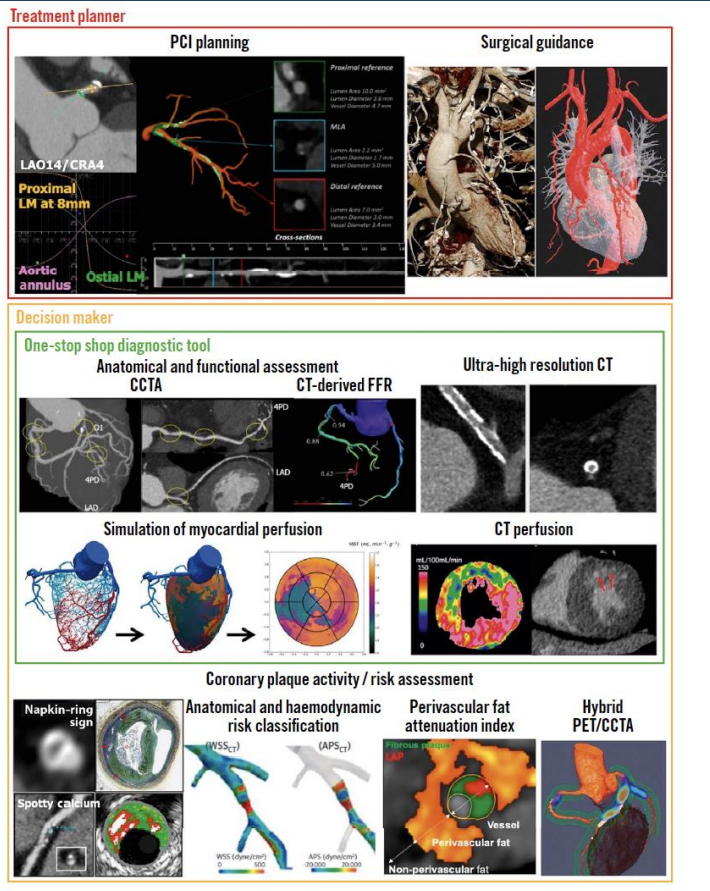
KEYWORDS

- fractional flow reserve
- MSCT
- non-invasive imaging

Abstract

Coronary computed tomographic angiography (CCTA) is becoming the first-line investigation for establishing the presence of coronary artery disease and, with fractional flow reserve (FFR_{CT}), its haemodynamic significance. In patients without significant epicardial obstruction, its role is either to rule out atherosclerosis or to detect subclinical plaque that should be monitored for plaque progression/regression following prevention therapy and provide risk classification. Ischaemic non-obstructive coronary arteries are also expected to be assessed by non-invasive imaging, including CCTA. In patients with significant epicardial obstruction, CCTA can assist in planning revascularisation by determining the disease complexity, vessel size, lesion length and tissue composition of the atherosclerotic plaque, as well as the best fluoroscopic viewing angle; it may also help in selecting adjunctive percutaneous devices (e.g., rotational atherectomy) and in determining the best landing zone for stents or bypass grafts.

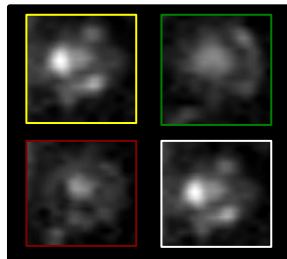
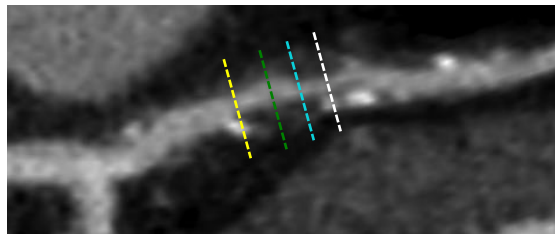
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Outline

- Whole-Heart Evaluation to Identify All Important CAD Features
- AI-Enabled Tools to Better Understand Angiographic Stenosis
- AI-Enabled Tools to Better Understand Atherosclerosis
- AI-Enabled Tools to Better Understand Ischemia
- Validation of Whole-Heart Evaluation

Comprehensive Coronary CT Evaluation to Optimize MVD Treatment



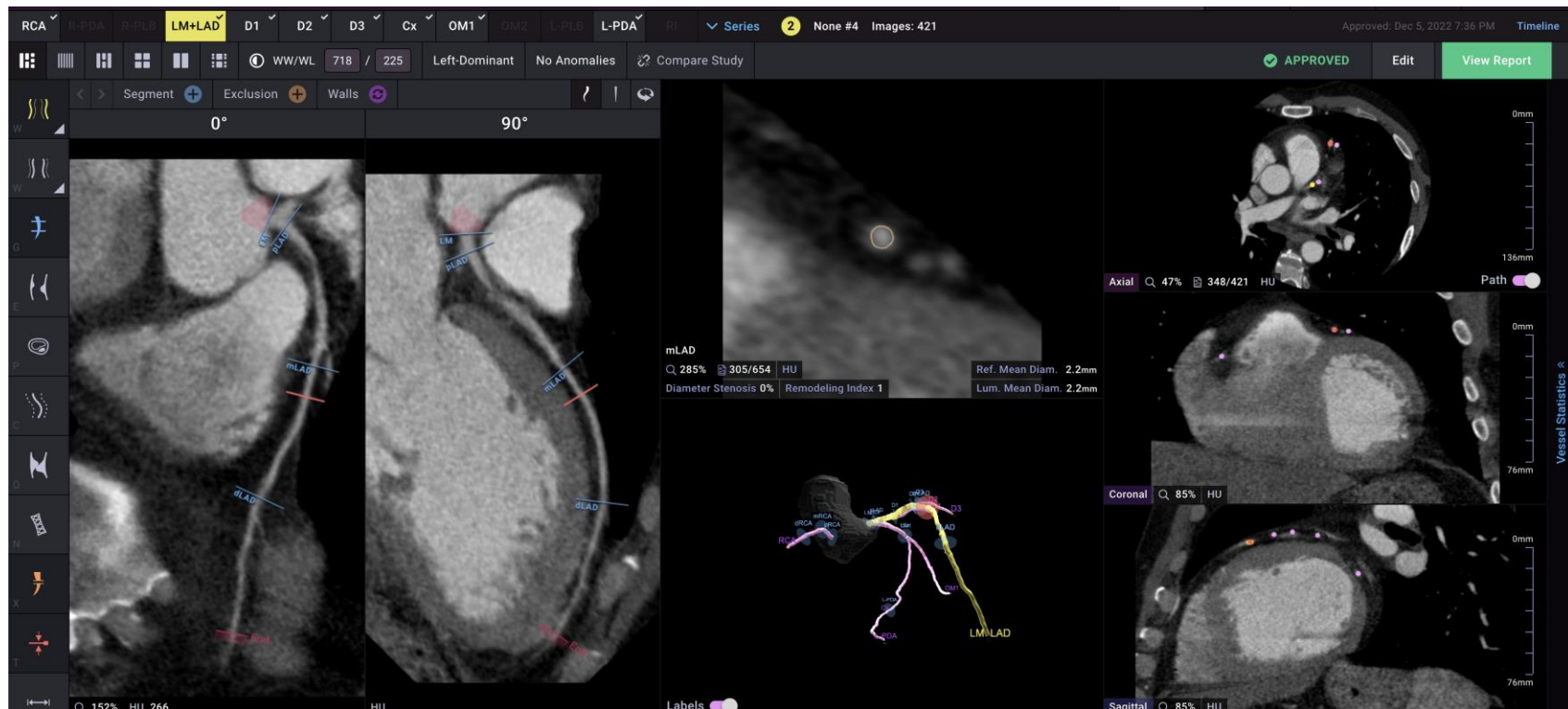
Each CAD feature associated with adverse patient outcomes (e.g., MACE, Ischemia, Rapid Disease Progression, Statin Non-Response)

Atherosclerotic plaque characteristics

1. **High-Grade Stenosis** (%DS, %AS, MLD, MLA)
2. **Plaque Burden** (volume; length, PAV; TAVnorm)
3. **Plaque Location** (artery, bifurcation, trifurcation)
4. **Plaque Composition** (non-calcified, calcified)
5. **“Lipid dense” Necrotic Core** (low attenuation plaque)
6. **High-Risk Plaques** (e.g., napkin ring sign)
7. **Plaque Concentricity** vs. Eccentricity
8. **Plaque Direction** (myocardial- vs. pericardial-facing)
9. **Plaque Diffuseness**
10. **Vascular Remodeling** (positive, negative, intermediate)
11. **Vascular Morphology** (lumen / vessel volume)
12. **Ischemia**
13. **% Myocardium at Risk** (subtended myocardium)
14. **Inflammation**

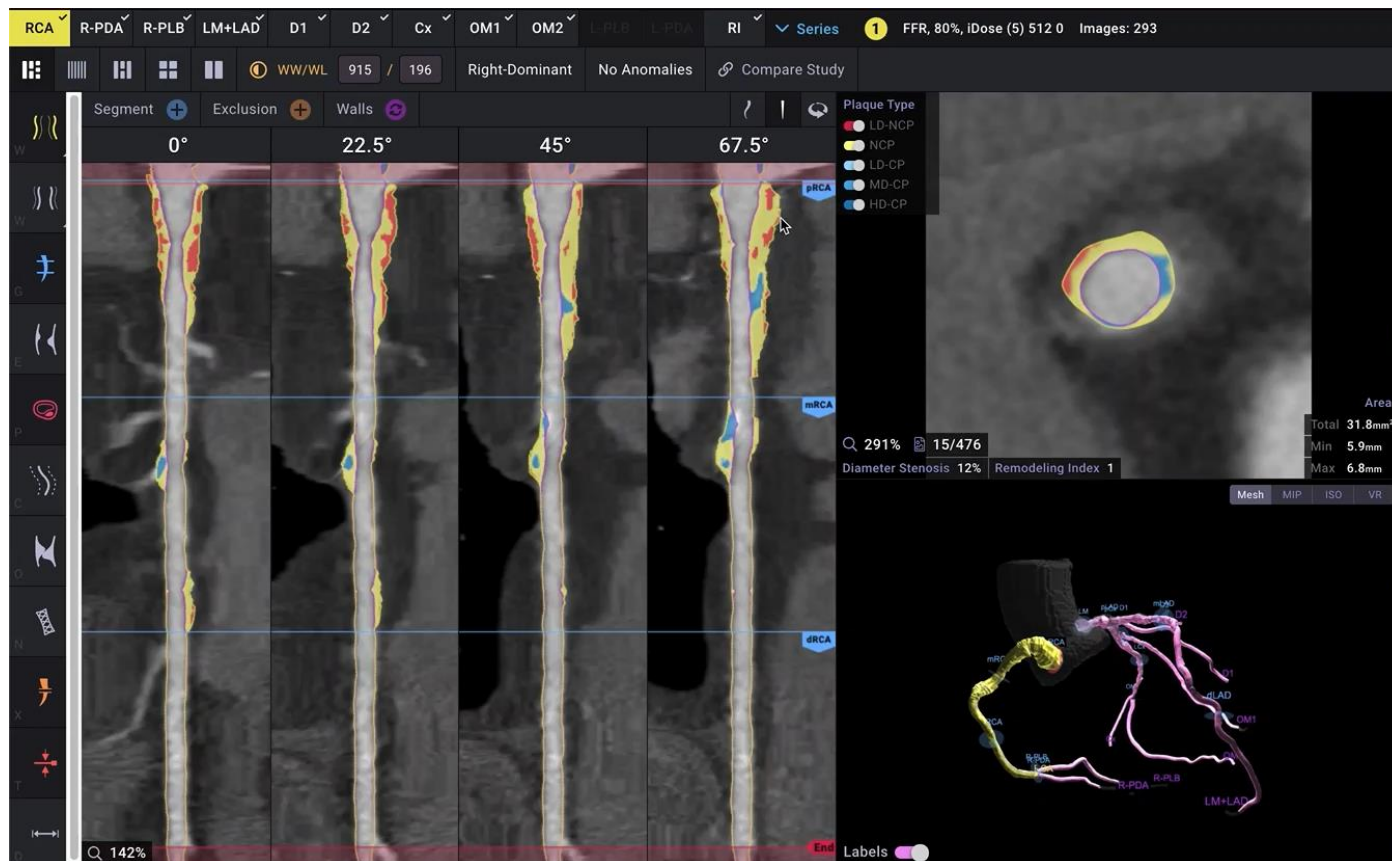
AI-Enabled Tools Now Allow for Comprehensive Whole Heart Evaluation

Atherosclerosis, Vascular Morphology, Ischemia in Minutes-Long Evaluation



AI-Enabled Tools Now Allow for Comprehensive Whole Heart Evaluation

Atherosclerosis, Vascular Morphology, Ischemia in Minutes-Long Evaluation



AI-Enabled Tools Now Allow for Comprehensive Whole Heart Evaluation Per-Patient, -Vessel, -Segment and -Lesion Quantification

Comprehensive Coronary Artery Evaluation

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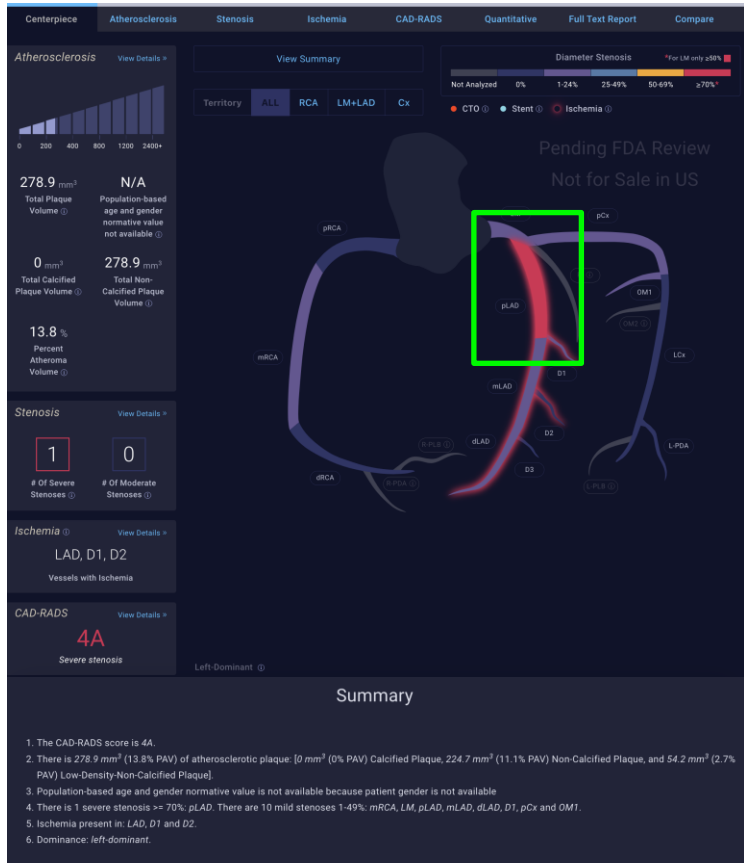
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Artery	Segment	Length (mm)	Vessel Volume (mm ³)	Lumen Volume (mm ³)	Total Plaque Volume (mm ³)	Greatest Diameter Stenosis (%)	Greatest Area Stenosis (%)	Highest Remodeling Index
LM	LM	6.3	87.2	72.4	14.8	16	28	1
Total		6.3	87.2	72.4	14.8	-	-	-
LAD	pLAD	51	494.3	279.8	214.5	88	98	1.2
	mLAD	48	190.7	184.8	5.8	4	5	1.1
	dLAD	47.3	159.7	158.5	1.1	4	12	1.1
	D1	29.5	75.6	75	0.6	6	13	1.2
	D2	13.3	25.7	25.7	0	N/A	N/A	1
	D3	30	61	61	0	N/A	N/A	1
	RI	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total		219	1007	784.8	222	-	-	-
RCA	pRCA	12.5	55.1	55.1	0	N/A	N/A	1
	mRCA	13.3	45.7	44.5	1.1	5	0	1.1
	dRCA	12	33.9	33.9	0	N/A	N/A	1
	R-PDA	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	R-PLB	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total		37.8	134.7	133.5	1.1	-	-	-
Cx	pCx	26	232.4	195.7	36.6	23	39	1.2
	LCx	63.5	247.8	247.8	0	N/A	N/A	1
	L-PLB	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	L-PDA	49.3	113.1	113.1	0	N/A	N/A	1
	OM1	60.5	200	195.6	4.4	5	3	1.2
	OM2	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total		199.3	793.3	752.2	41	-	-	-
Sum Total		462.3	2022.2	1742.9	278.9	-	-	-

Artery	Segment	Total Plaque Volume (mm ³)	Non-Calcified Plaque				Calcified Plaque	Percent Atheroma Volume (%)
			Non-Calcified Plaque Volume (mm ³)	Low-Density - Non-Calcified Plaque Volume (mm ³)	Total Non-Calcified Plaque Volume (mm ³)			
LM	LM	14.8	14.8	0		14.8	0	17
Total		14.8	14.8	0		14.8	0	17
LAD	pLAD	214.5	160.3	54.2		214.5	0	43.4
	mLAD	5.8	5.8	0		5.8	0	3
	dLAD	1.1	1.1	0		1.1	0	0.7
	D1	0.6	0.6	0		0.6	0	0.8
	D2	0	0	0		0	0	0
	D3	0	0	0		0	0	0
	RI	N/A	N/A	N/A		N/A	N/A	N/A
Total		222	167.8	54.2		222	0	22
RCA	pRCA	0	0	0		0	0	0
	mRCA	1.1	1.1	0		1.1	0	2.4
	dRCA	0	0	0		0	0	0
	R-PDA	N/A	N/A	N/A		N/A	N/A	N/A
	R-PLB	N/A	N/A	N/A		N/A	N/A	N/A
Total		1.1	1.1	0		1.1	0	0.8
Cx	pCx	36.6	36.6	0		36.6	0	15.7
	LCx	0	0	0		0	0	0
	L-PLB	N/A	N/A	N/A		N/A	N/A	N/A
	L-PDA	0	0	0		0	0	0
	OM1	4.4	4.4	0		4.4	0	2.2
	OM2	N/A	N/A	N/A		N/A	N/A	N/A
Total		41	41	0		41	0	5.2
Sum Total		278.9	224.7	54.2		278.9	0	13.8

AI-Enabled Tools Now Allow for Effortless Visualization

Translating Advanced Image-Based Disease Phenotyping into Actionable Clinical Insights



- Fully Interactive Web-Based Platform
- Deep Dive Visualization
- Patient-, Segment-, Vessel-, Vessel-territory Interrogation

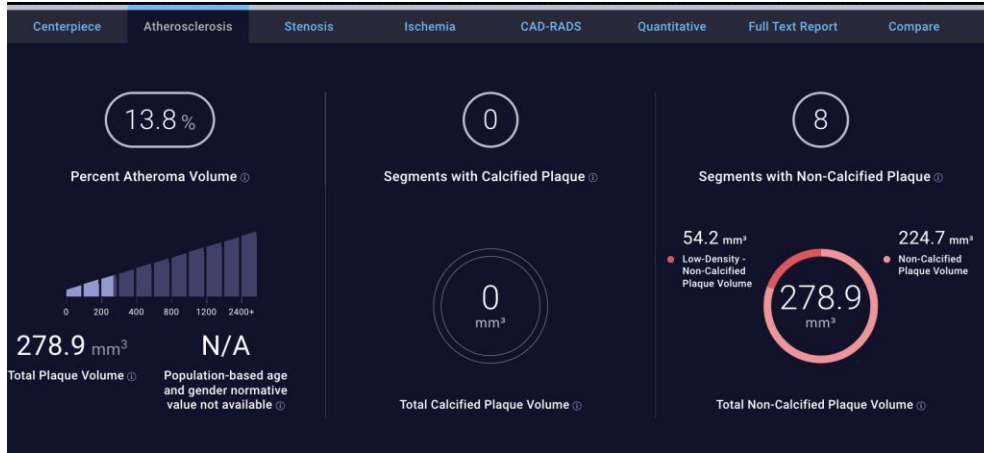
AI-Enabled Tools to Better Understand Angiographic Stenosis

Whole-Heart Segment-by-Segment Stenosis Analysis for Pre-Procedural Planning



AI-Enabled Tools to Better Understand Atherosclerosis

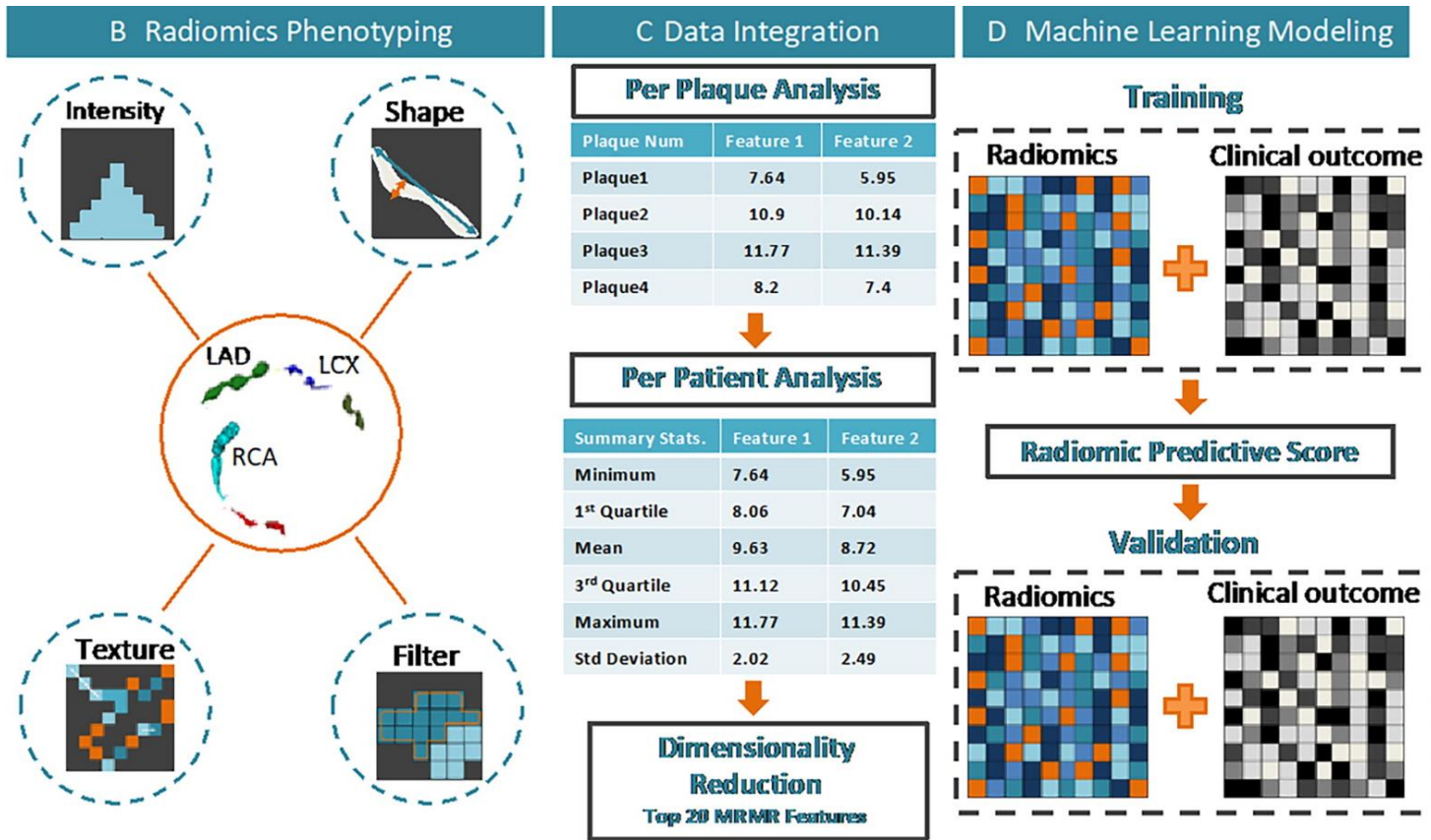
Extending Knowledge Beyond Traditional Measures of Angiographic Stenosis Alone



Interactive Emphasis on Atherosclerosis Supports Pre-Procedural Decision Making

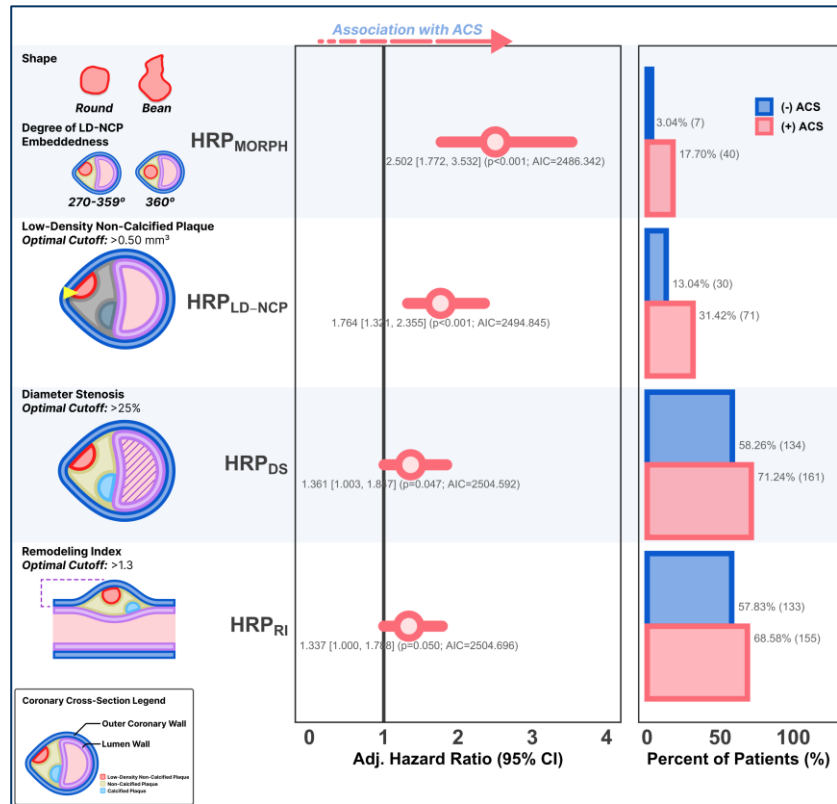
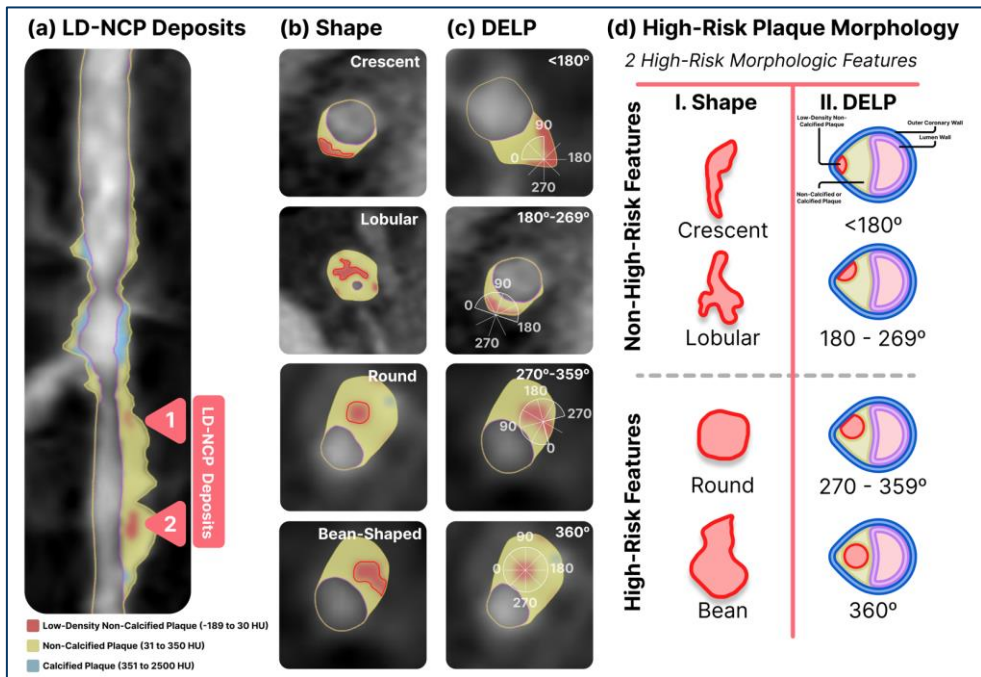
AI-Enabled Tools to Better Understand Atherosclerosis

Extending Knowledge Beyond Traditional Measures of Angiographic Stenosis Alone



AI-Enabled Tools Now Allow for Lesion-Level Understanding of Atherosclerosis

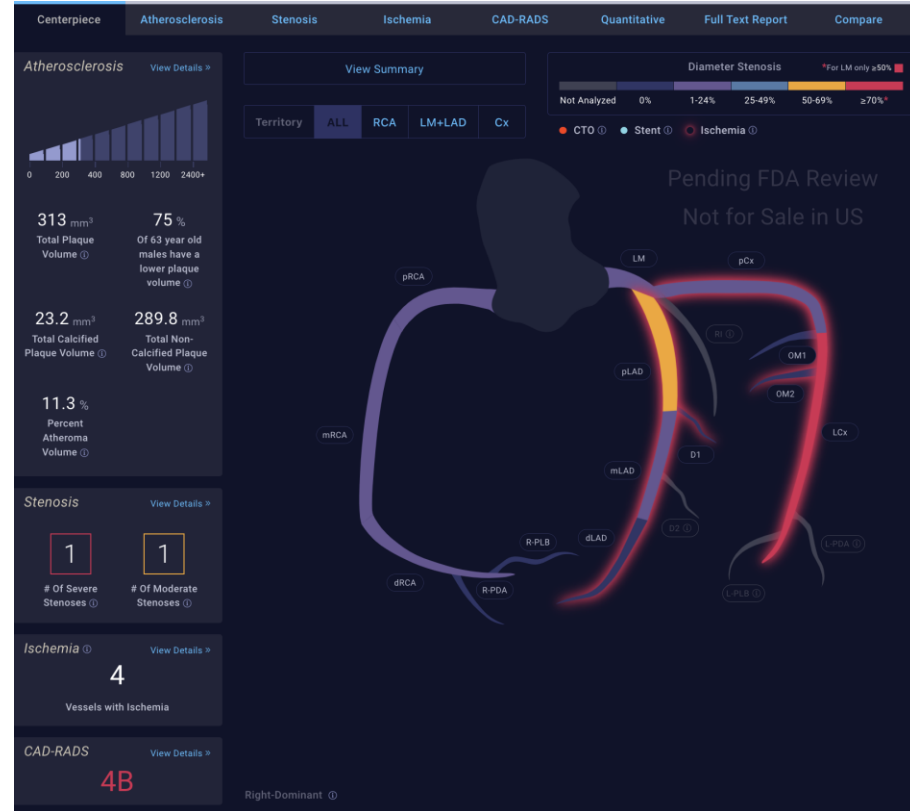
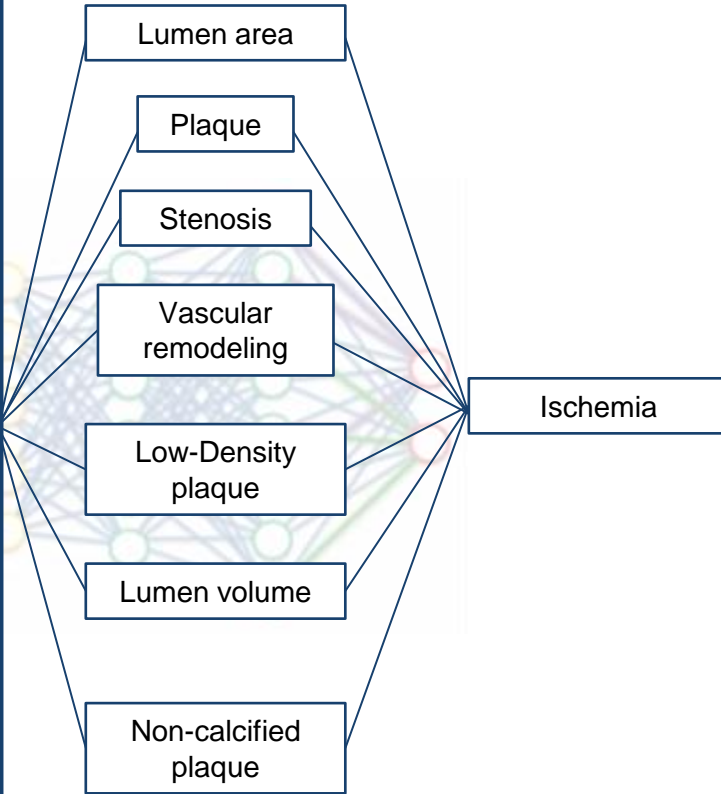
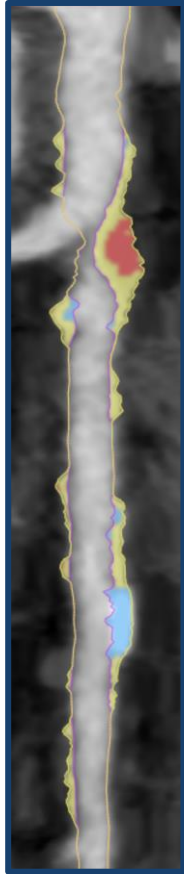
Standardizing Definitions of Plaque Type (e.g., High-Risk Plaque as a Use Case)



An Example:
Traditional criteria for high-risk plaque are overly simplistic

AI-Enabled Tools to Better Understand Ischemia

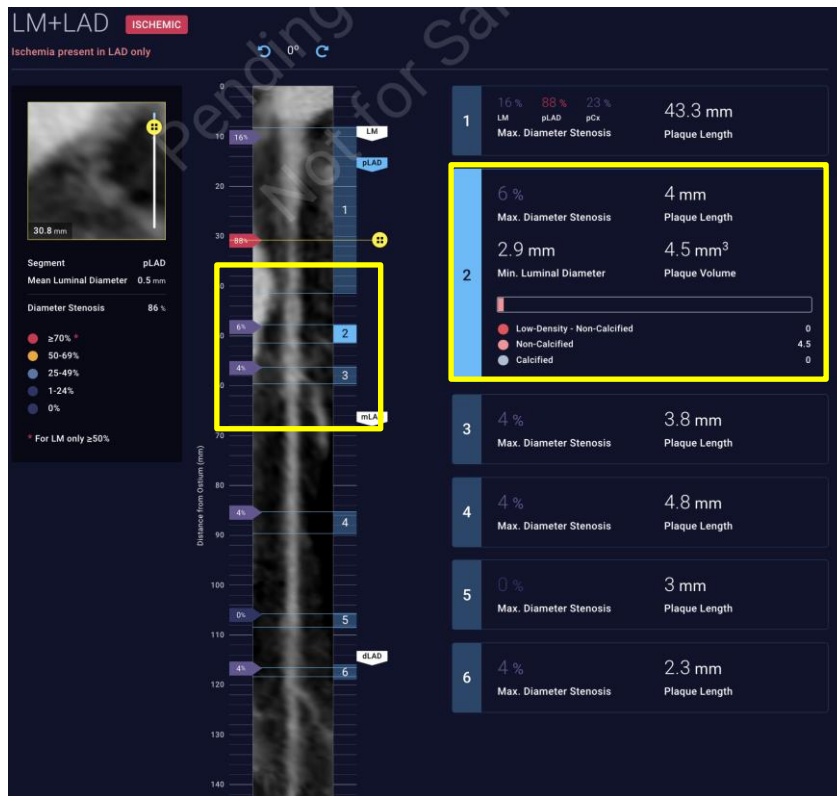
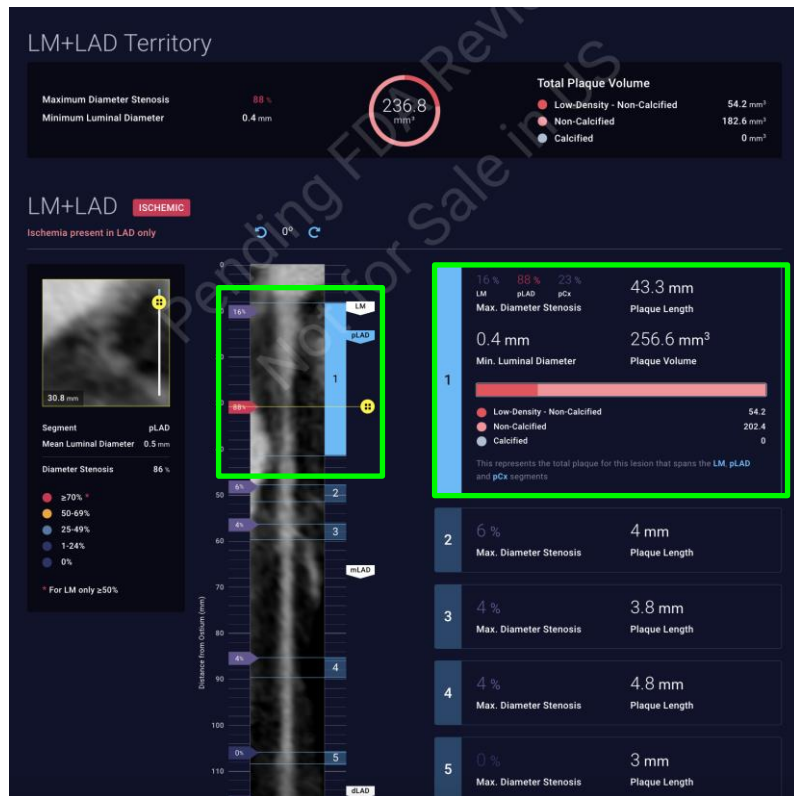
Integrating atherosclerosis and vascular morphology to diagnose coronary ischemia



Cleerly ISCHEMIA for investigational use only.

Coupling Ischemia with All CAD Features Explains Why Ischemia is Present

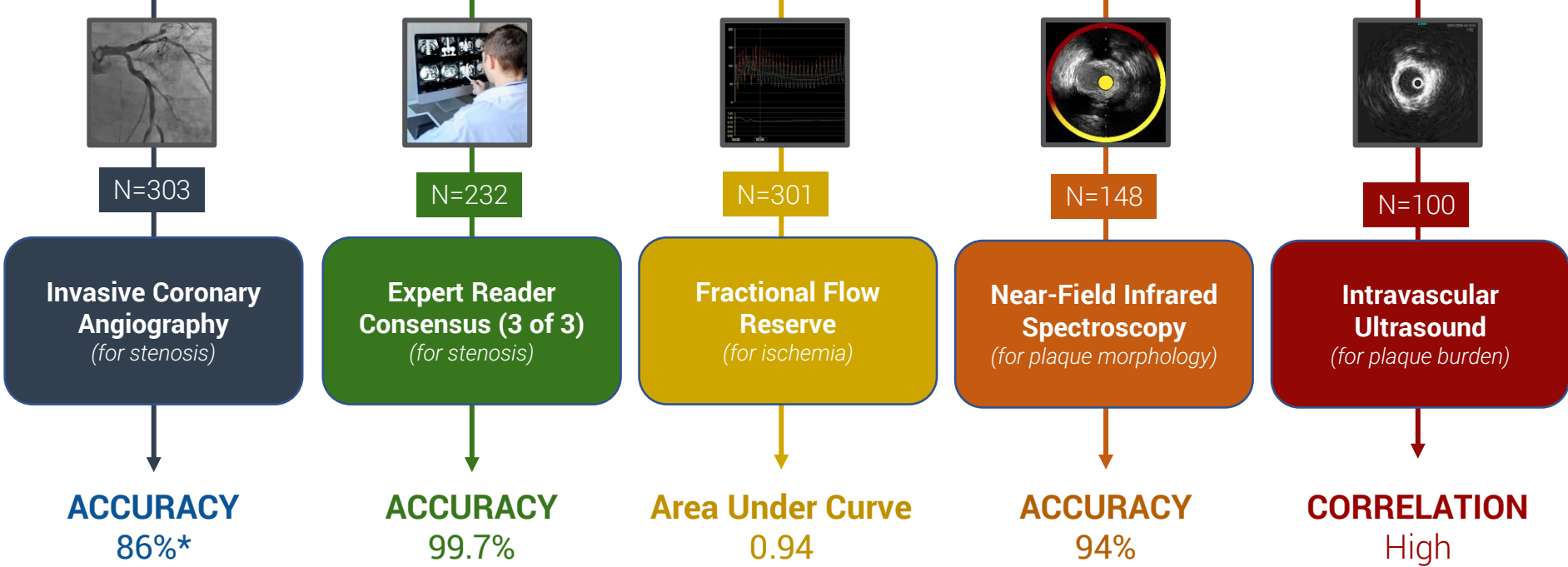
Ischemia is a Function of Every Lesion Across Length of Vessel



Diagnostic Validation of AI-Enabled Tools for Stenosis and Atherosclerosis

'Gold Standard' Validation Determined by Blinded, Expert Core Laboratory Measurements

Proven Accuracy in Multicenter Clinical Trials



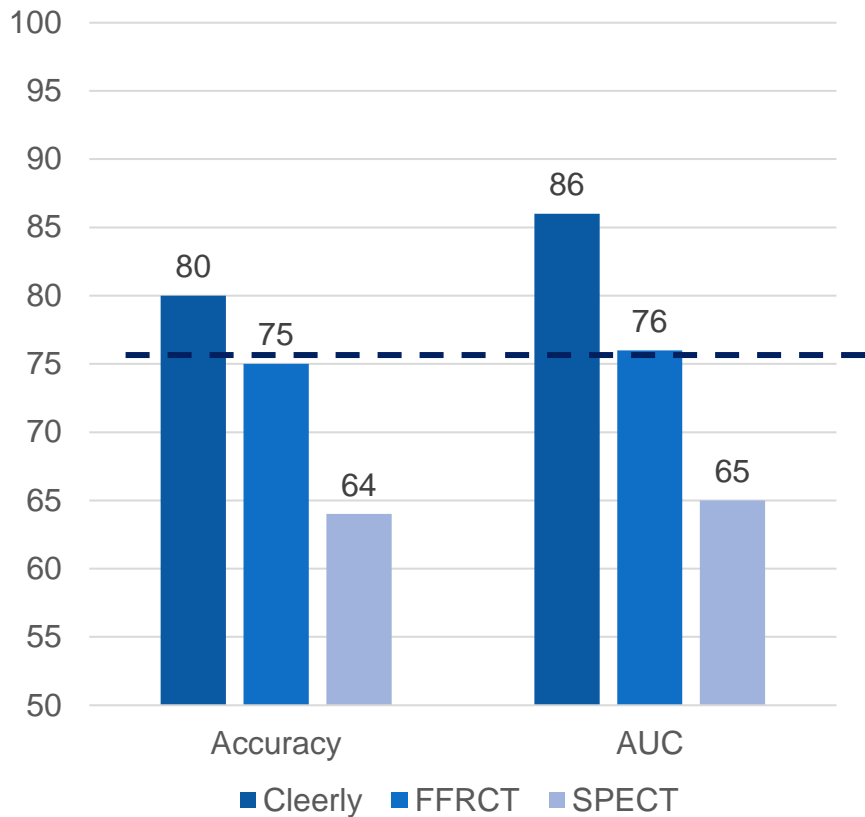
*Clearly demonstrates **higher agreement with invasive fractional flow** discordant cases than invasive coronary angiography (~2/3 cases)

Clearly vs. OCT trial in progress

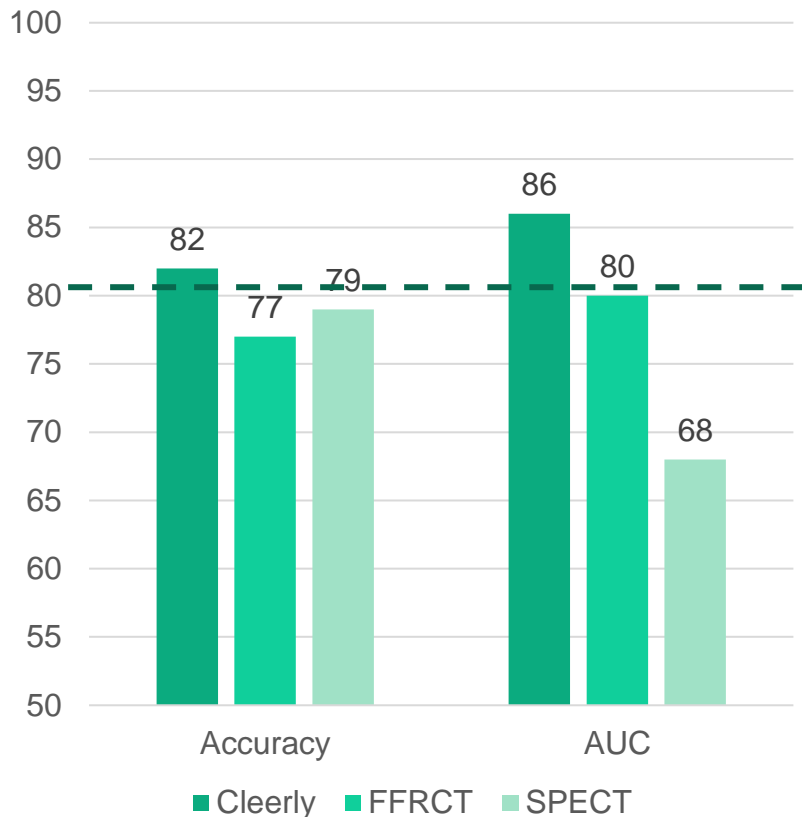
Diagnostic Validation of AI-Enabled Tools for Ischemia

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Comparison to SPECT and FFRCT in CREDESCENCE and PACIFIC



CREDESCENCE Trial (n=868 vessels)



PACIFIC Trial (n=612 vessels)

Conclusions

- AI-Enabled Tools Now Allow for Quantitative Evaluation of All CAD Features
- Platform technology facilitates ease of clinical review, and helps to explain the *why*
- Performance Similar to All Invasive Gold Standards
- Performance Superior to Other Non-Invasive Methods
- Entering New Era That Extends CAD Evaluation Beyond Binary (e.g., 50% stenosis, 0.8 FFR)