PLACE

PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

Intelligenza Artificiale

ARTIFICIAL INTELLIGENCE IN ADVANCED CORONARY PLAQUE ANALYSIS

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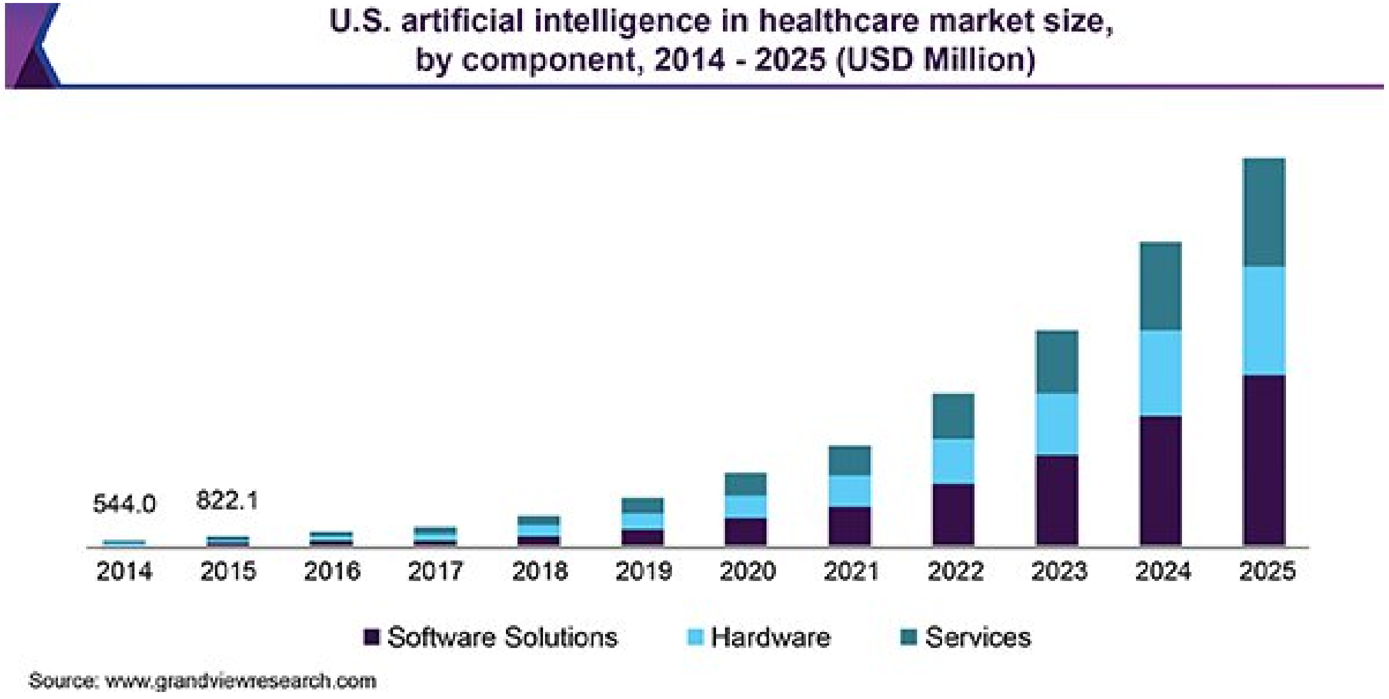
Disclosures

Consultant for / Research support from / Stock Options:

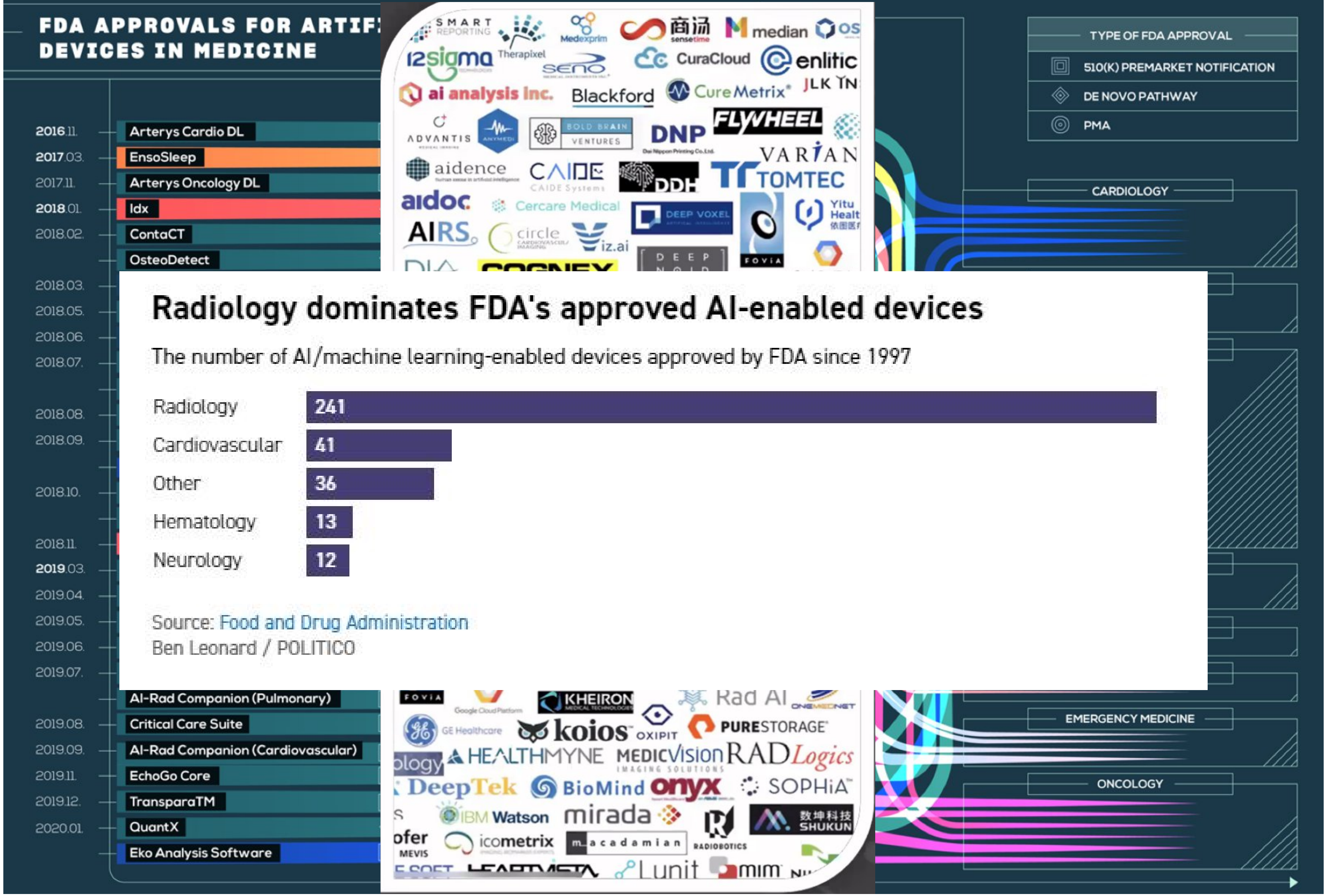
- Siemens Healthineers
- Covanos Inc.
- Elucid
- Cleerly
- NIH Grants

AI in Healthcare



- The AI in healthcare market estimated to be valued USD 4.9 billion in 2020
- Expected to reach USD 45.2 billion by 2026
- Big Data availability and demand to reduce healthcare cost drive the growth

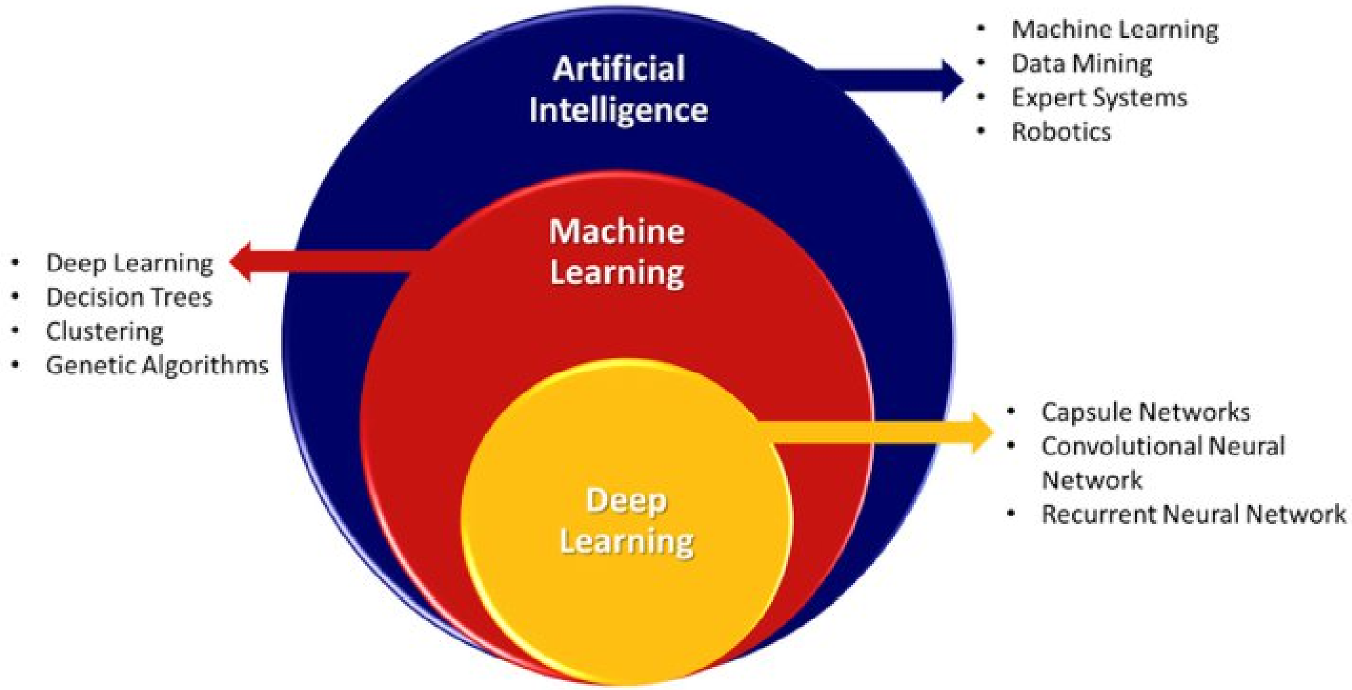
Accenture; ARTIFICIAL INTELLIGENCE (AI): HEALTHCARE'S NEW NERVOUS SYSTEM



Benjamens S et al., npj Digital Medicine 2020

Artificial Intelligence

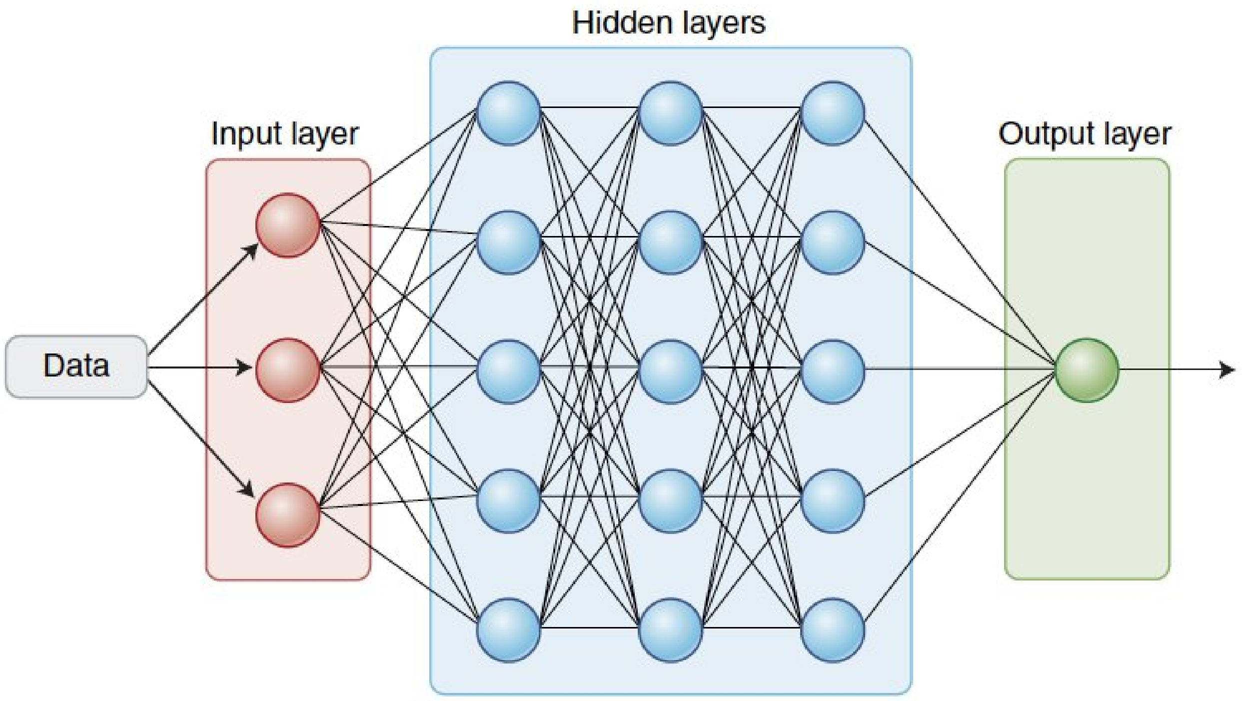
The ability for a program to perceive its environment and take actions that maximize its chance of successfully achieving its goal



Singh G, De Cecco CN, Min J JCCT 2018

Deep Neural Networks

Pattern Recognition



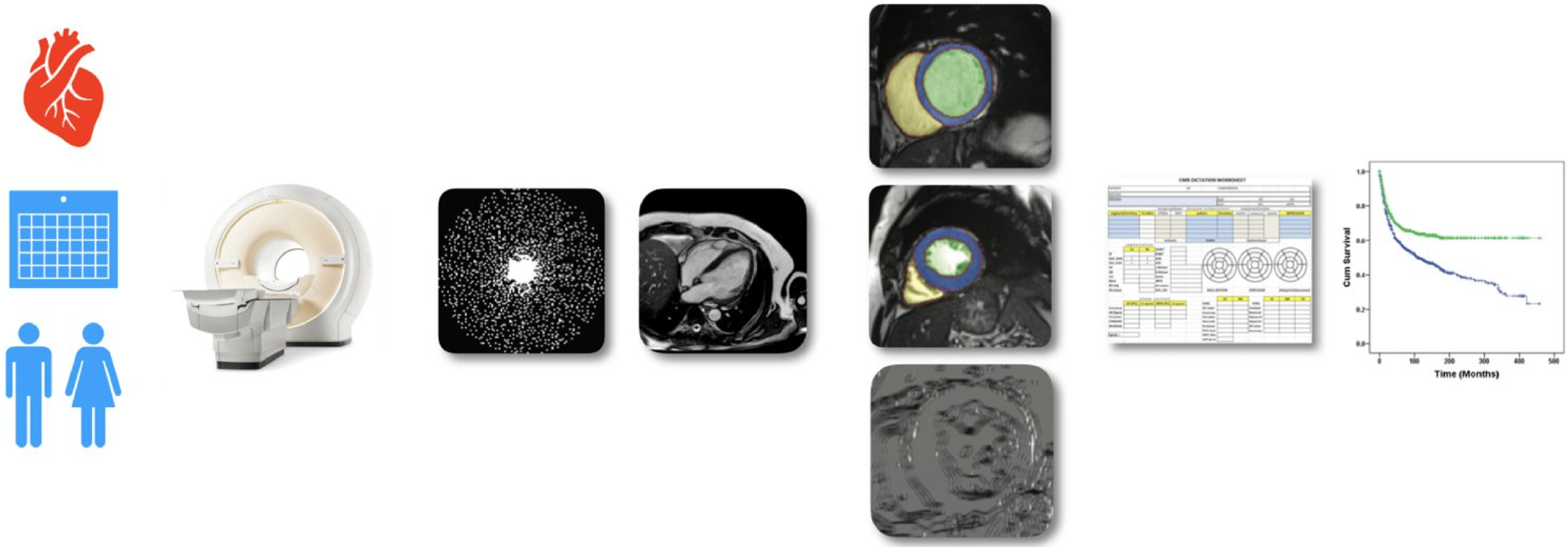
DNNS Type

1. Convolutional
2. Recurrent
3. Generative Adversarial
4. Transfer
5. Reinforcement
6. Representation

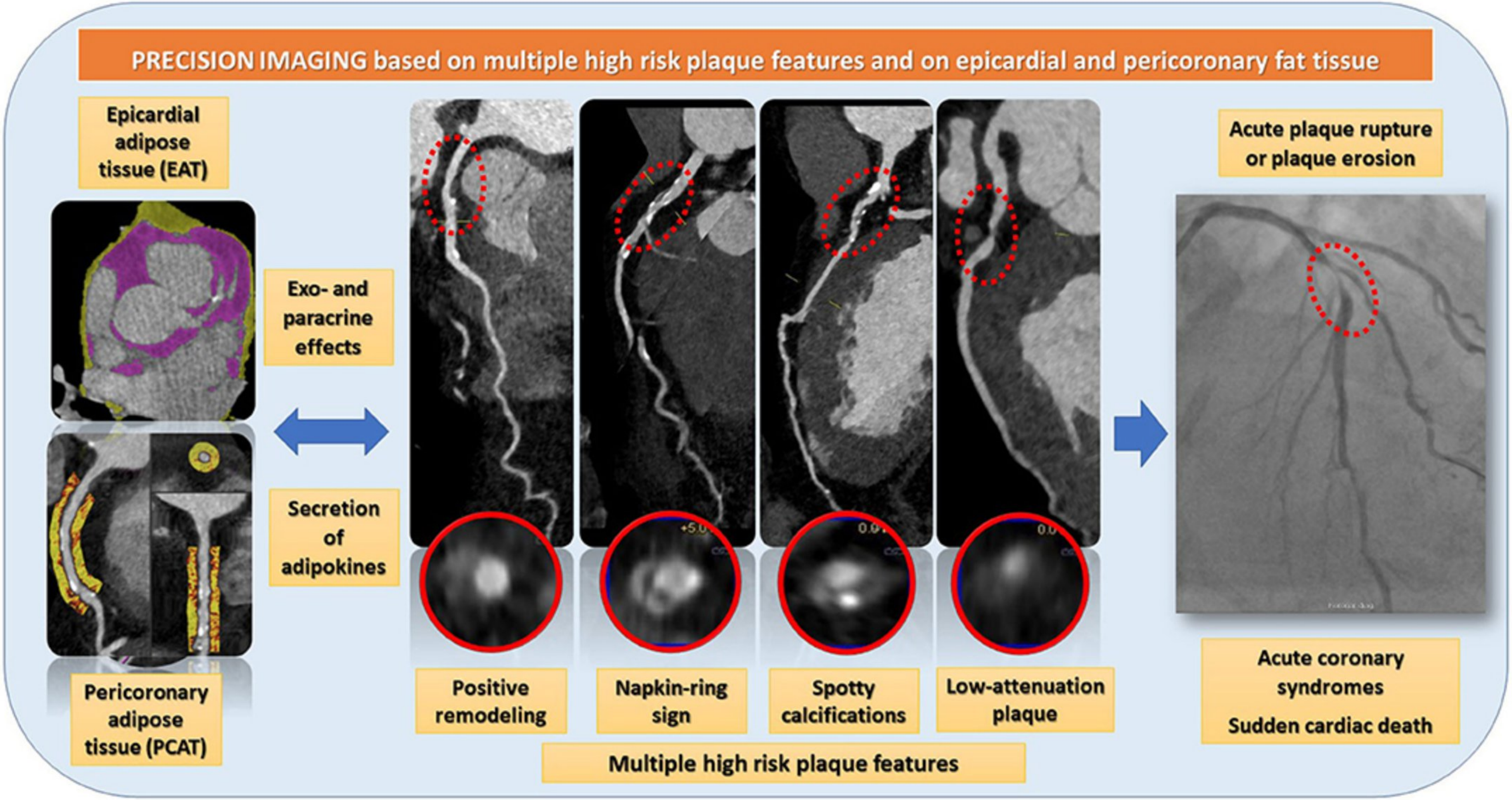
1. *Autodidactic Quality*
2. *Neural network is not designed by humans, but rather the number of layers is determined by the data itself*

AI Implementation

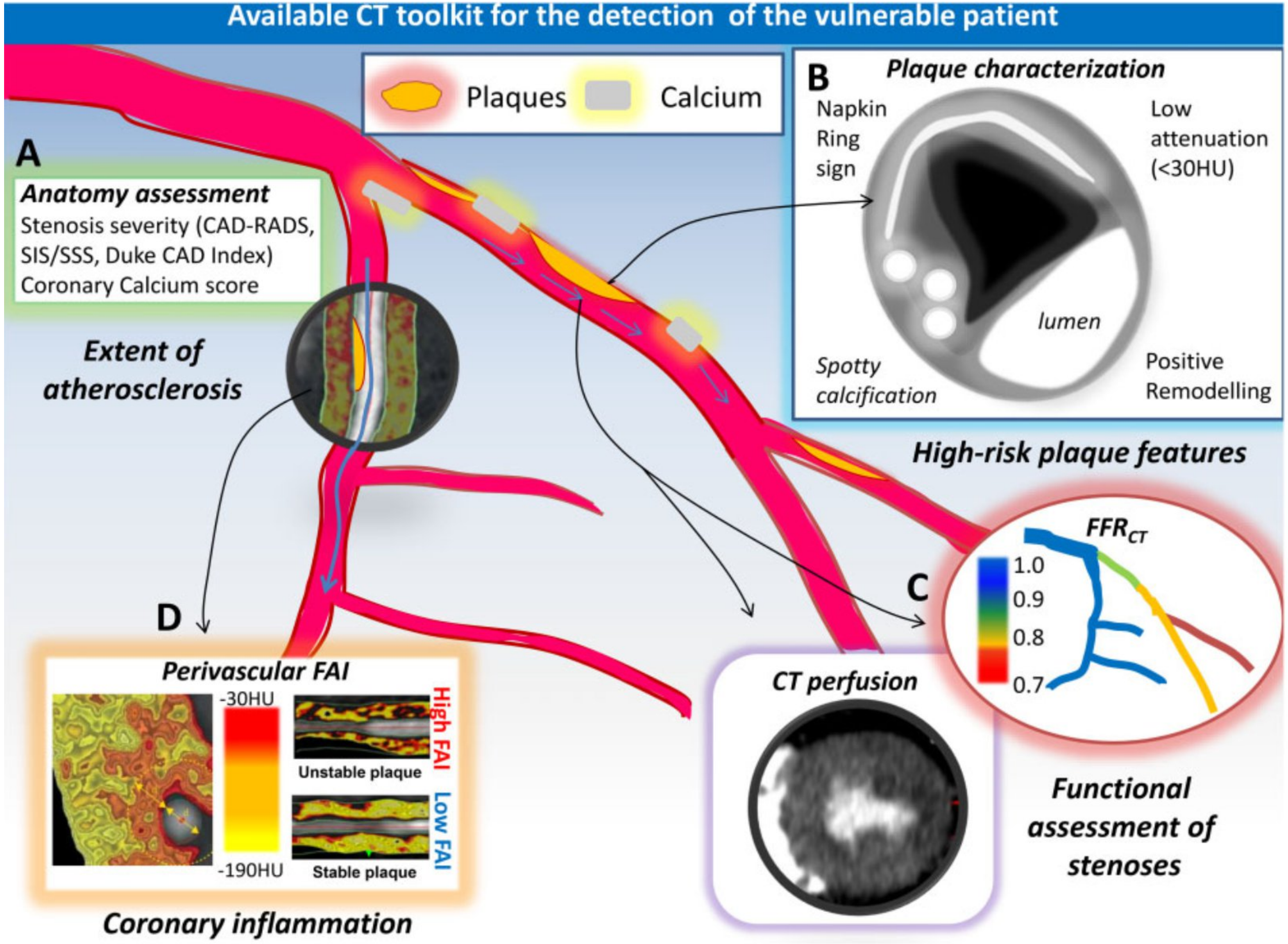
Indication & Patient Scheduling | Acquisition | Image Reconstruction & Image Quality | Segmentation, Quantification & Radiomics | Classification & Reporting | Prognosis



Leiner *et al. Journal of Cardiovascular Magnetic Resonance* (2019) 21:61

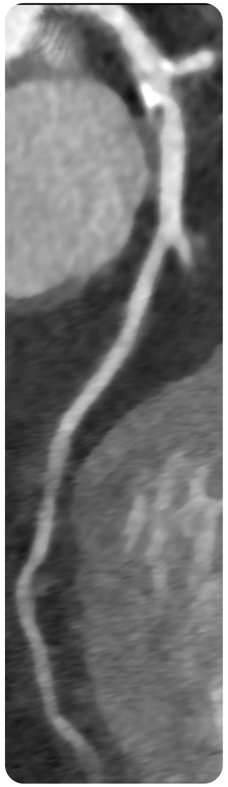


Tesche C. et al., Front Cardiovasc Med 2022



Antonopoulos A. et al., Eur J Preventive Cardiology 2021

Quantitative Coronary Features



- Stenosis (High vs Low Grade)
- Plaque Location (ostium, bifurcation)
- Plaque Length
- Plaque Concentricity / Direction
- Plaque Composition
- Plaque Burden
- High-Risk Plaques (Napkin ring, spotty calc, etc.)
- Vascular Remodeling and Morphology
- Myocardium at Risk

CAD-RADS^{TM} 2.0

2022 Coronary Artery Disease – Reporting and Data System

An Expert Consensus Document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Cardiology (ACC), the American College of Radiology (ACR) and the North America Society of Cardiovascular Imaging (NASCI)

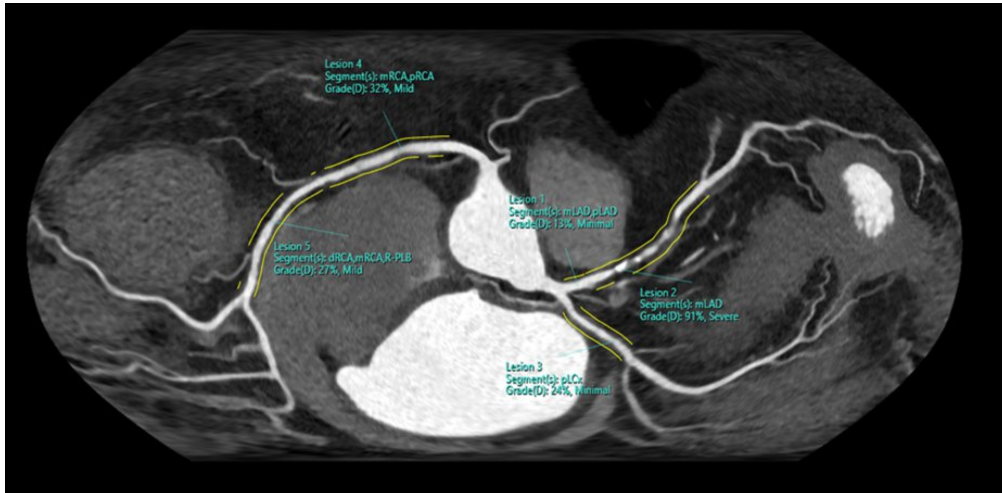
	2016 CAD-RADS	**2022 CAD-RADS**
Stenosis grading	CAD-RADS 0, 1, 2, 3, 4A, 4B and 5	No change
Plaque burden grading	No systematic classification	New CAD-RADS category grading scale for Plaque Burden ranging from P1 to P4
Modifiers	Four modifiers were introduced to complement the CAD-RADS classification First: modifier N (non-diagnostic) Second: modifier S (stent) Third: modifier G (graft) Fourth: modifier V (vulnerability)	Addition of two new modifiers: modifier I (ischemia) and modifier E (exceptions) and replacement of modifier V (vulnerable) with HRP (high-risk plaque) First: modifier N (non-diagnostic) **Second: modifier HRP** (replaces V) **Third: modifier I+ (ischemia), I- and I+/-** Fourth: modifier S (stent)

Grading Scale for plaque burden:

Terminology	**Overall plaque burden**
P1	Mild amount of plaque
P2	Moderate amount of plaque
P3	Severe amount of plaque
P4	Extensive amount of plaque

AI in Cardiac Imaging

- Automatic Calcium Score
- Automatic Coronary Analysis and Quantification (CAD-RADS)
- Coronary Plaque Burden & Vulnerability Features
- ML-based CT-Fractional Flow Reserve (CT-FFR)
- Radiomics
- Prognostication



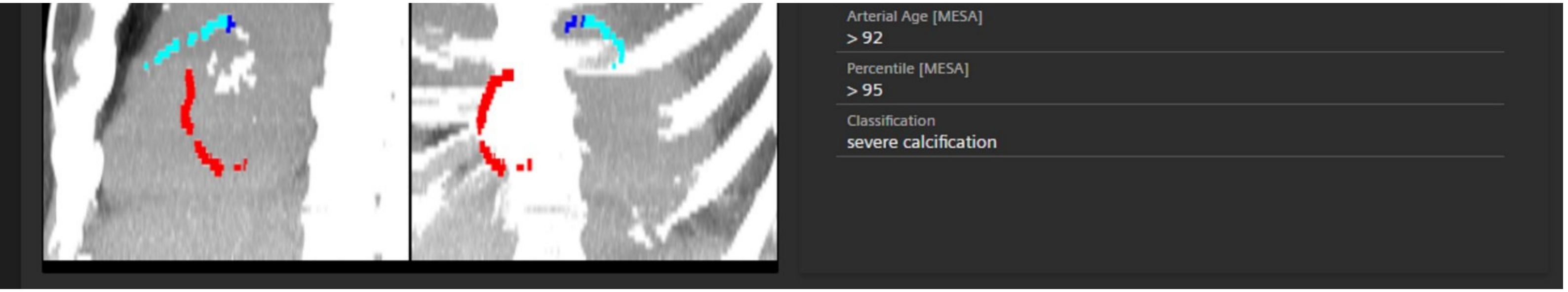
Calcium Score

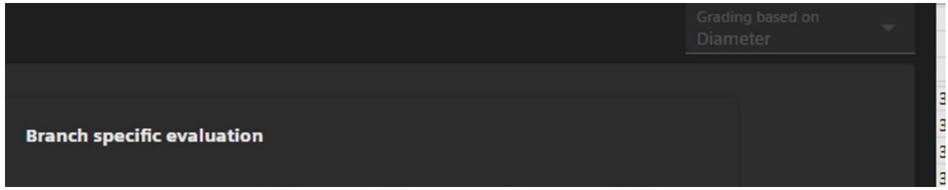
ESC
European Society of Cardiology

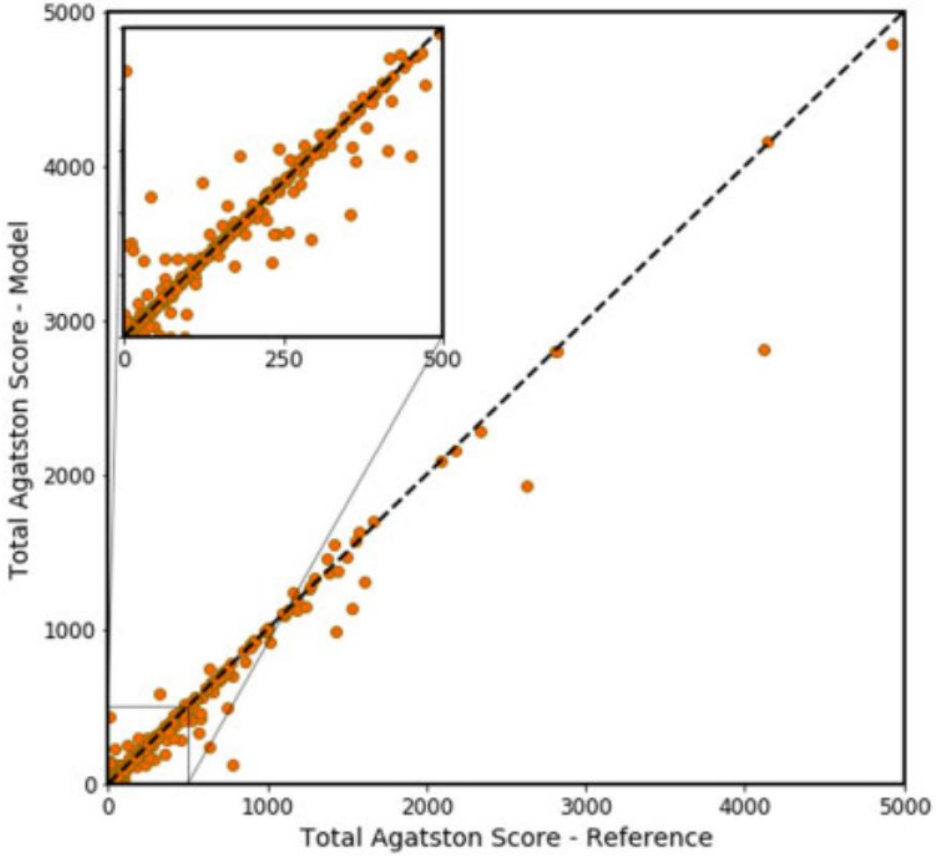
European Heart Journal - Cardiovascular Imaging (2021) **00**, 1–9
doi:10.1093/ehjci/jeab119

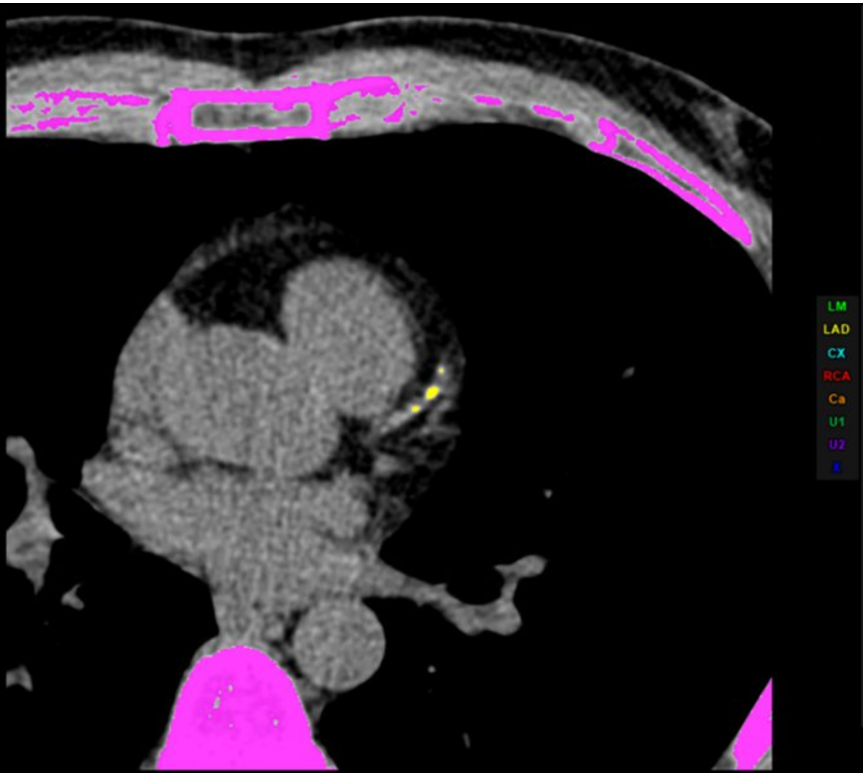
Deep learning for vessel-specific coronary artery calcium scoring: validation on a multi-centre dataset

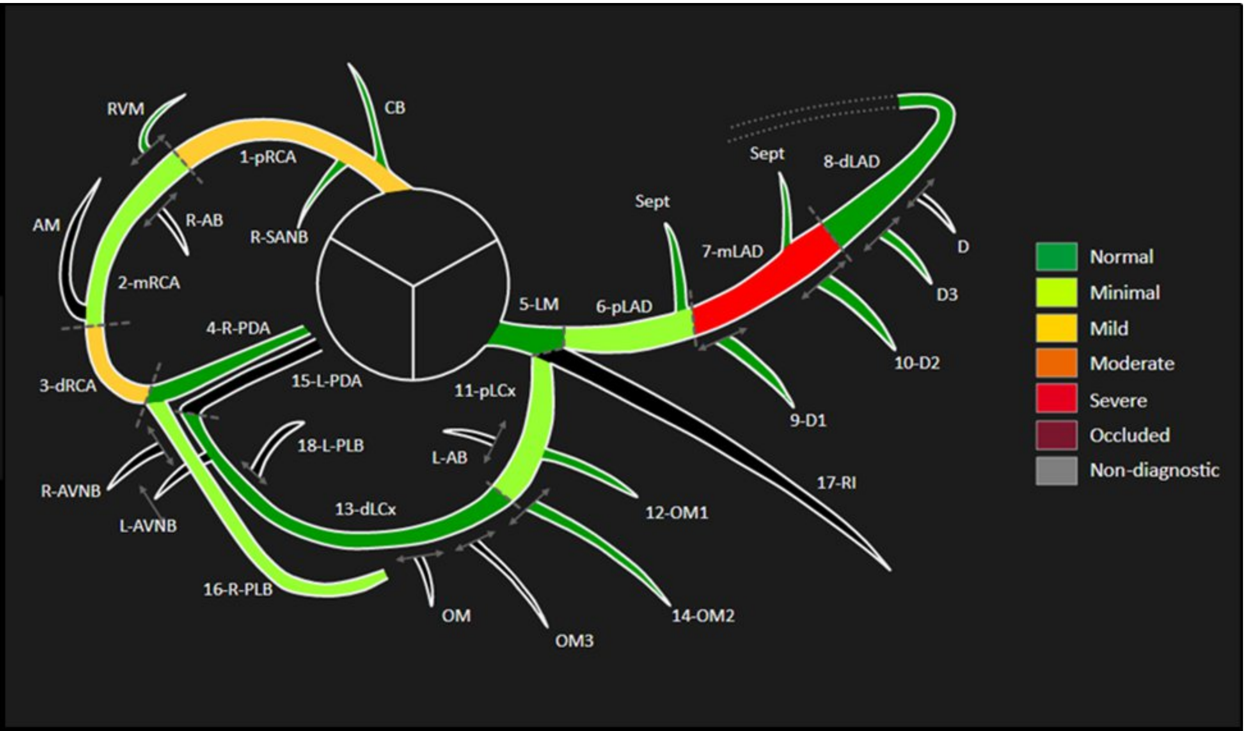
David J. Winkel [1,2]*, V. Reddappagari Suryanarayana[3], A. Mohamed Ali[3], Johannes Görich[4], Sebastian Johannes Buß[4], Axel Mendoza[2], Chris Schwemmer[5], Puneet Sharma[2], U. Joseph Schoepf[6], and Saikiran Rapaka[2]



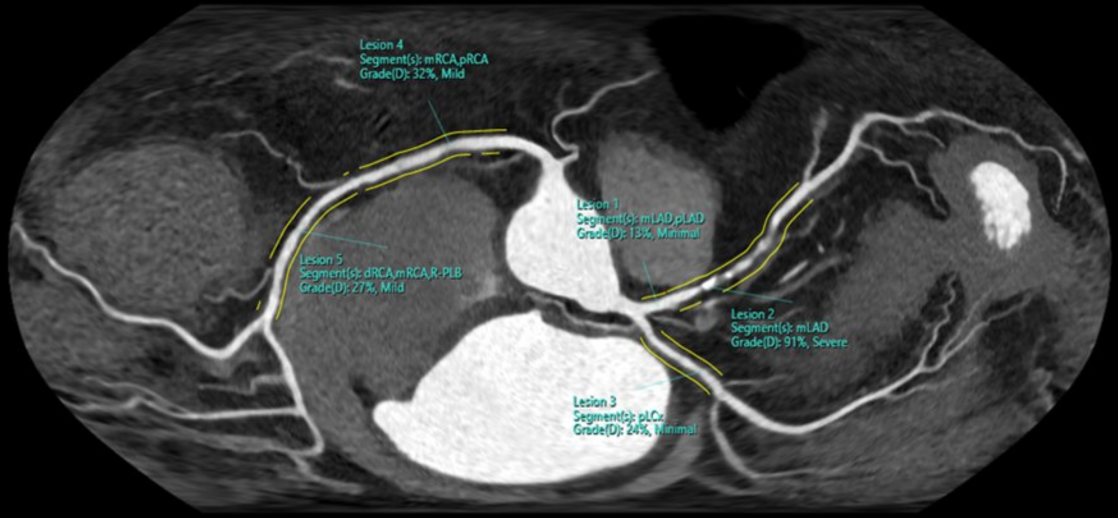








Artery	Lesions	Volume / mm³	Equiv. Mass / mg	Score
LM	0	0.0	0.00	0.0
LAD	3	78.9	13.31	91.7
CX	0	0.0	0.00	0.0
RCA	0	0.0	0.00	0.0
Ca	0	0.0	0.00	0.0
Total	3	78.9	13.31	91.7



Siemens AI-Heart - Emory

CAD-RADS

Siemens AI-Heart - Emory

Segment Analysis

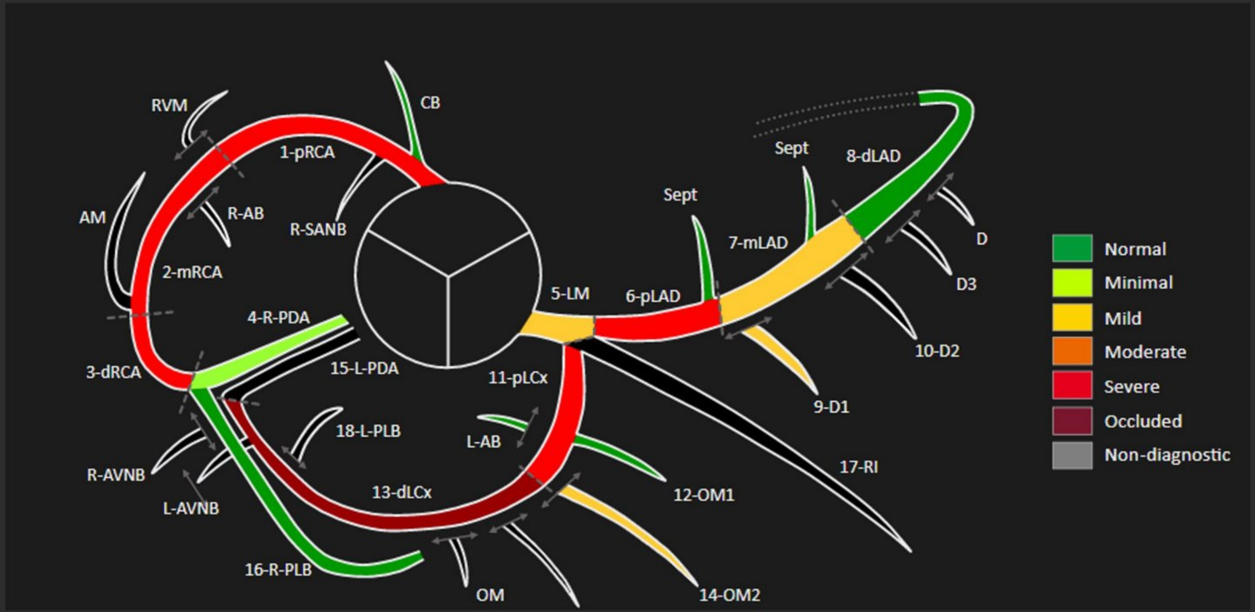
CCTA - Overview | **CCTA - Segments** | CCTA - Lesions | CaScoring

Grading based on
Diameter

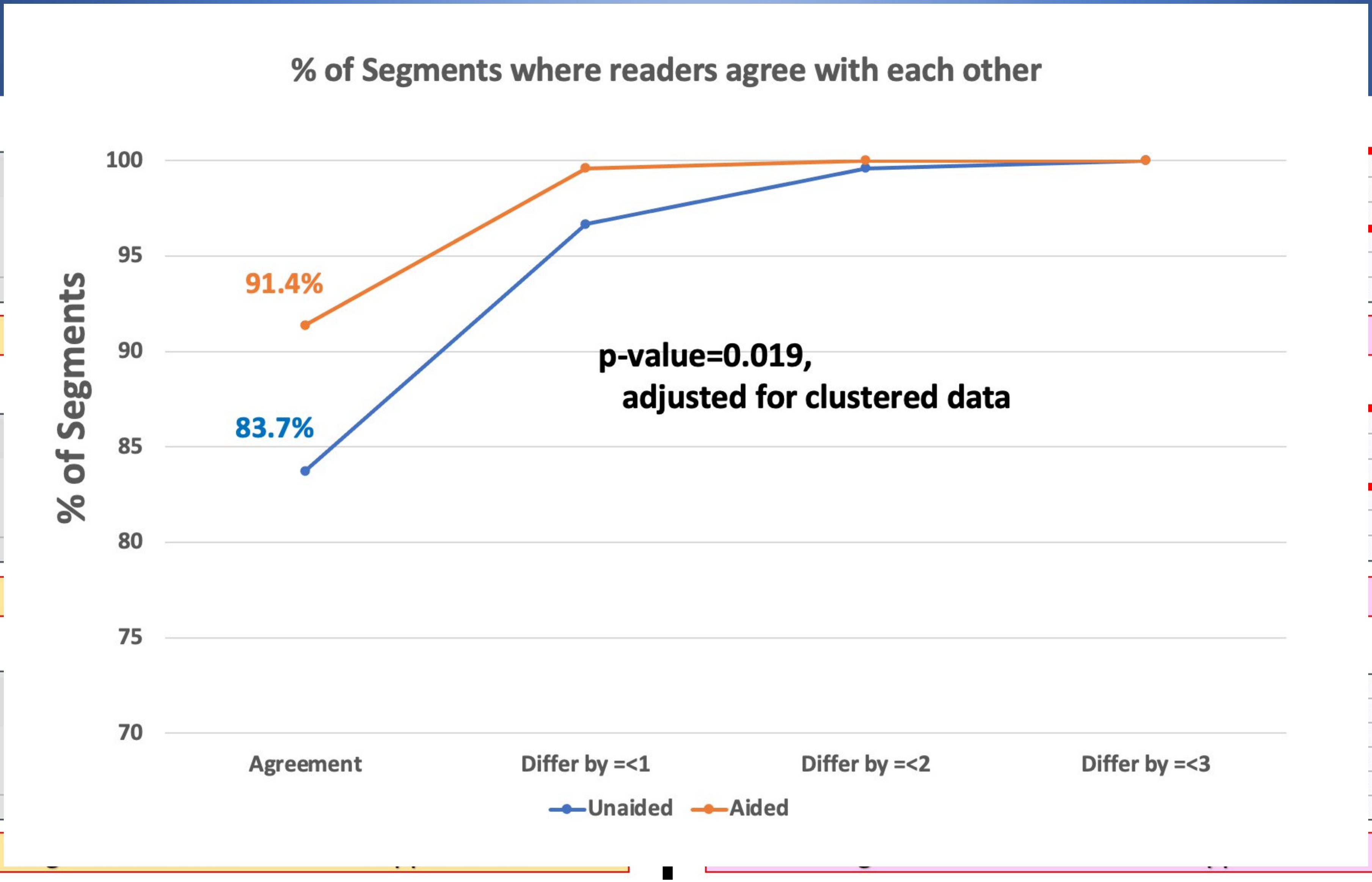
Segment	Available	Diseased Sections	Max. Stenosis Grade	Max. Stenosis Severity	Plaque composition	Non-diagnostic
LM	☑	1	Diam Mild	Diam [%] 34	Calcified	☐
pLAD	☑	1	Diam Severe	Diam [%] 95	Calcified	☐
mLAD	☑	1	Diam Mild	Diam [%] 38	Calcified	☐
dLAD	☑	0	Diam Normal	Diam [%] 0	NA	☐
D1	☑	1	Diam Mild	Diam [%] 34	Calcified	☐
D2	☐	0	Diam Normal	Diam [%] 0	NA	☐
pLCx	☑	1	Diam Severe	Diam [%] 73	Mixed	☐
dLCx	☑	1	Diam Occluded	Diam [%] 100	Mixed	☐
OM1	☑	0	Diam Normal	Diam [%] 0	NA	☐

Summary
CAD-RADs 5
3 (70%) vessel, no LM involvement

Schematic | Unfolded



AI Integration & Inter-Reader Variability



C

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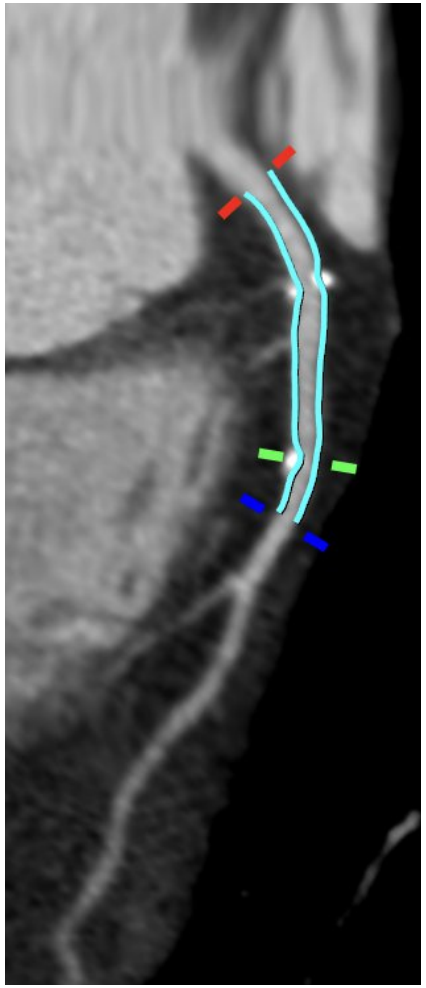
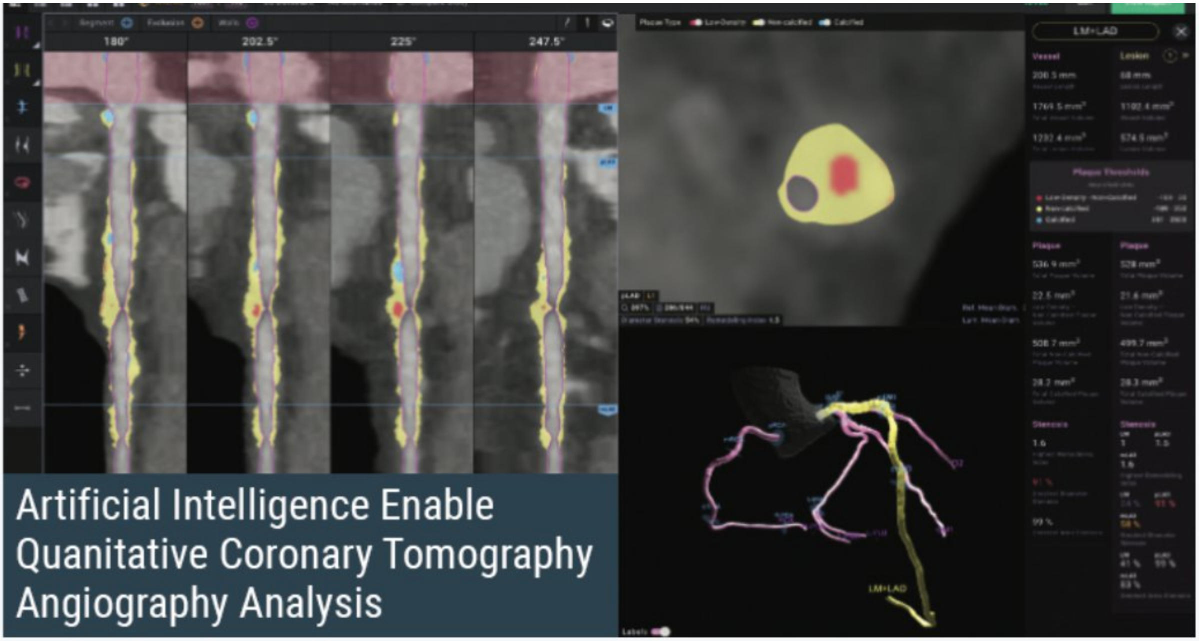


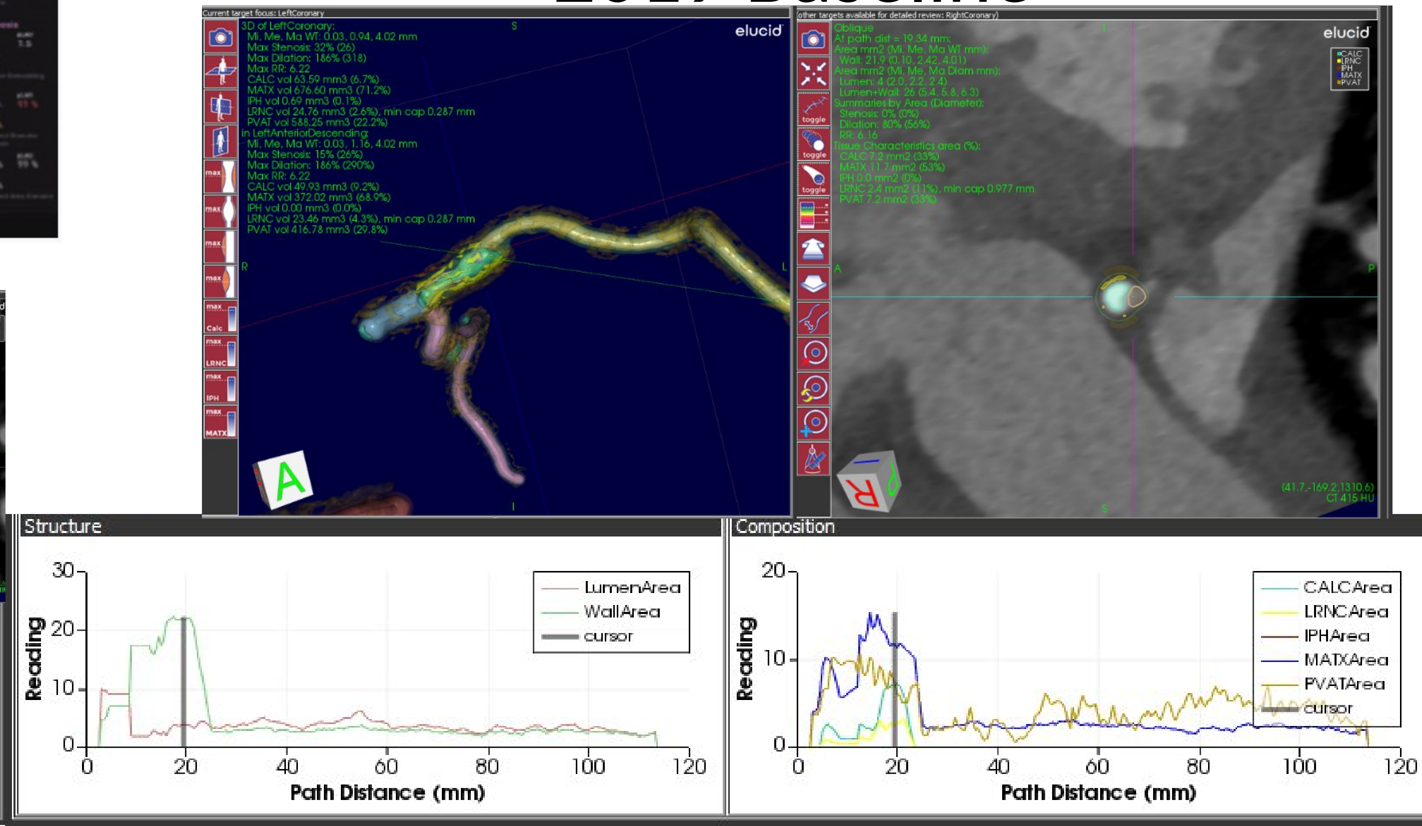
Plaque Burden AI Solution



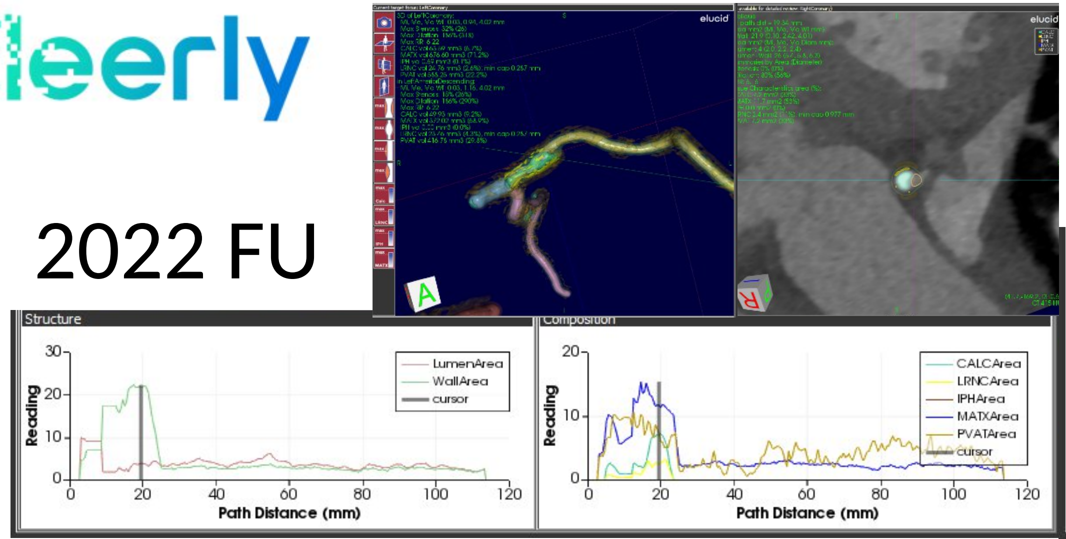
cleerly

ELUCID

2019 Baseline



2022 FU



JACC: CARDIOVASCULAR IMAGING VOL. ■, NO. ■, 2022

NEW RESEARCH PAPER

AI Evaluation of Stenosis on Coronary CT Angiography, Comparison With Quantitative Coronary Angiography and Fractional Flow Reserve

A CREDENCE Trial Substudy

William F. Griffin, MD,[a] Andrew D. Choi, MD,[a] Joanna S. Riess, MD,[a] Hugo Marques, MD,[b] Hyuk-Jae Chang, MD, PhD,[c]

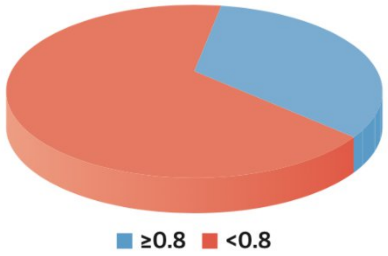
Artificial Intelligence-Enabled Coronary Computed Tomography Angiography vs Quantitative Coronary Angiography for Detection of Stenosis, Per Patient

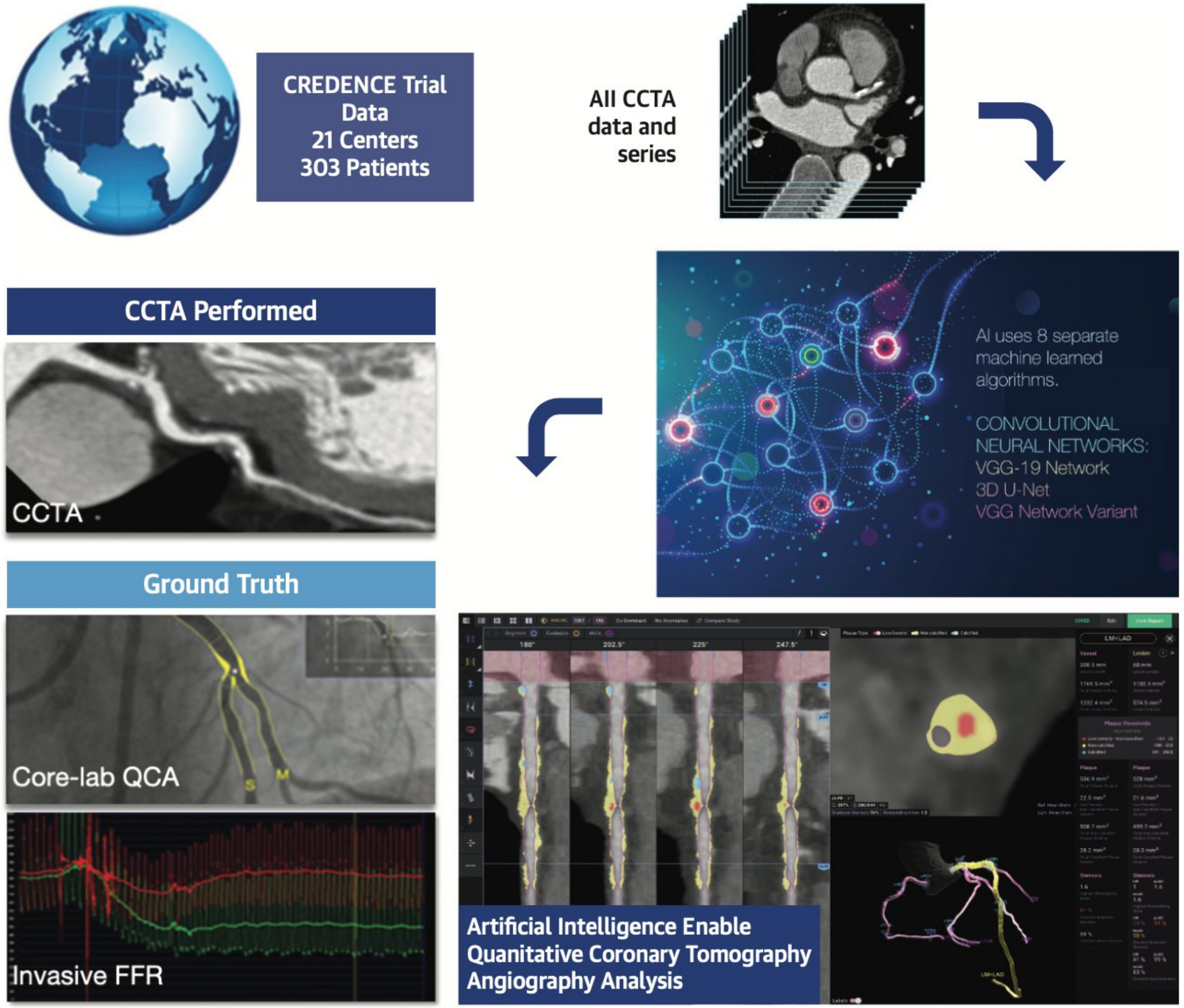
Artificial Intelligence-Enabled Coronary Computed Tomography Angiography vs Quantitative Coronary Angiography	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy	Area Under the Receiver-Operating Characteristic Curve
≥50% Stenosis	94%	68%	81%	90%	84%	0.88
≥70% Stenosis	94%	82%	69%	97%	86%	0.92

Fractional Flow Reserve

Discordant Cases:

When artificial intelligence-enabled coronary computed tomography angiography ≥70% and quantitative coronary angiography <70% fractional flow reserve is <0.8 in 67%





JACC: CARDIOVASCULAR IMAGING, VOL. 14, NO. 3, 2021

CT Angiographic and Plaque Predictors of Functionally Significant Coronary Disease and Outcome Using Machine Learning

Seokhun Yang, MD,[a] Bon-Kwon Koo, MD,[a,b] Masahiro Hoshino, MD,[c] Joo Myung Lee, MD,[d] Tadashi Murai,

METHODS A total of 1,013 vessels with fractional flow reserve (FFR) measurement and available coronary computed tomography angiography were analyzed. Stenosis and plaque features of the target lesion and vessel were evaluated by an independent core laboratory. Relevant features associated with low FFR (≤0.80) were identified by using machine learning, and their predictability of 5-year risk of vessel-oriented composite outcome, including cardiac death, target vessel myocardial infarction, or target vessel revascularization, were evaluated.

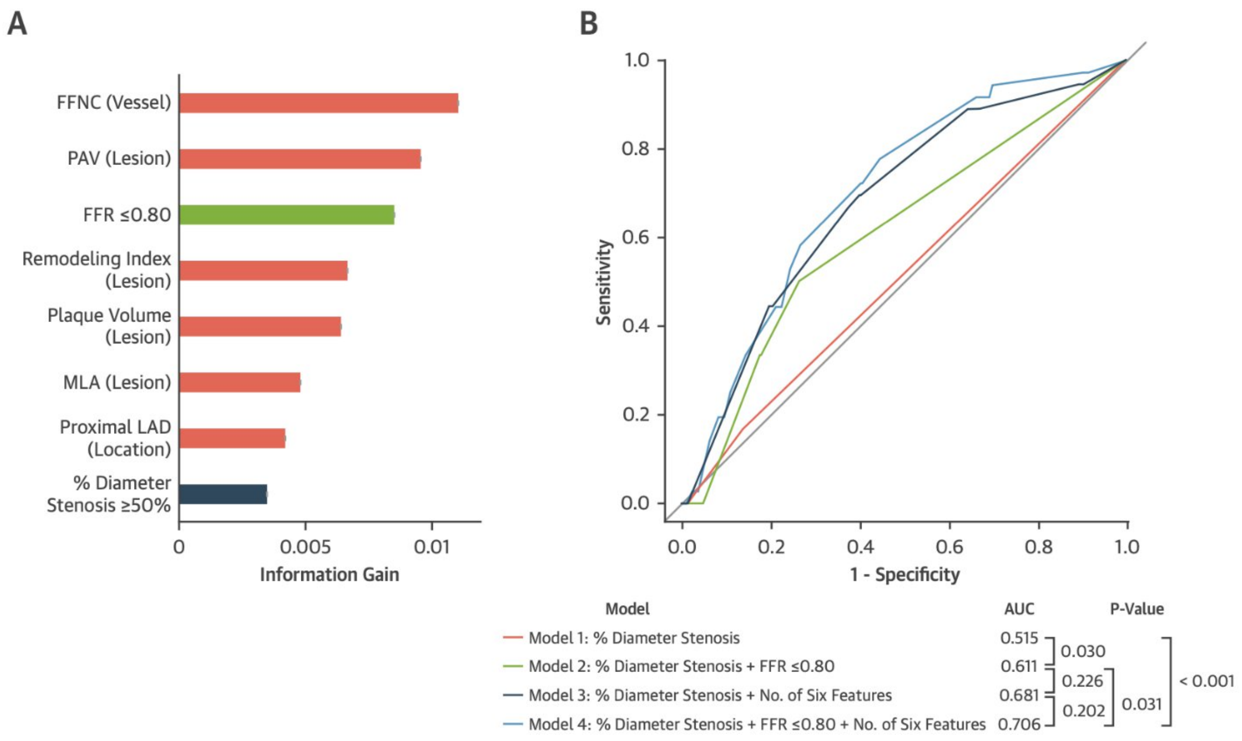
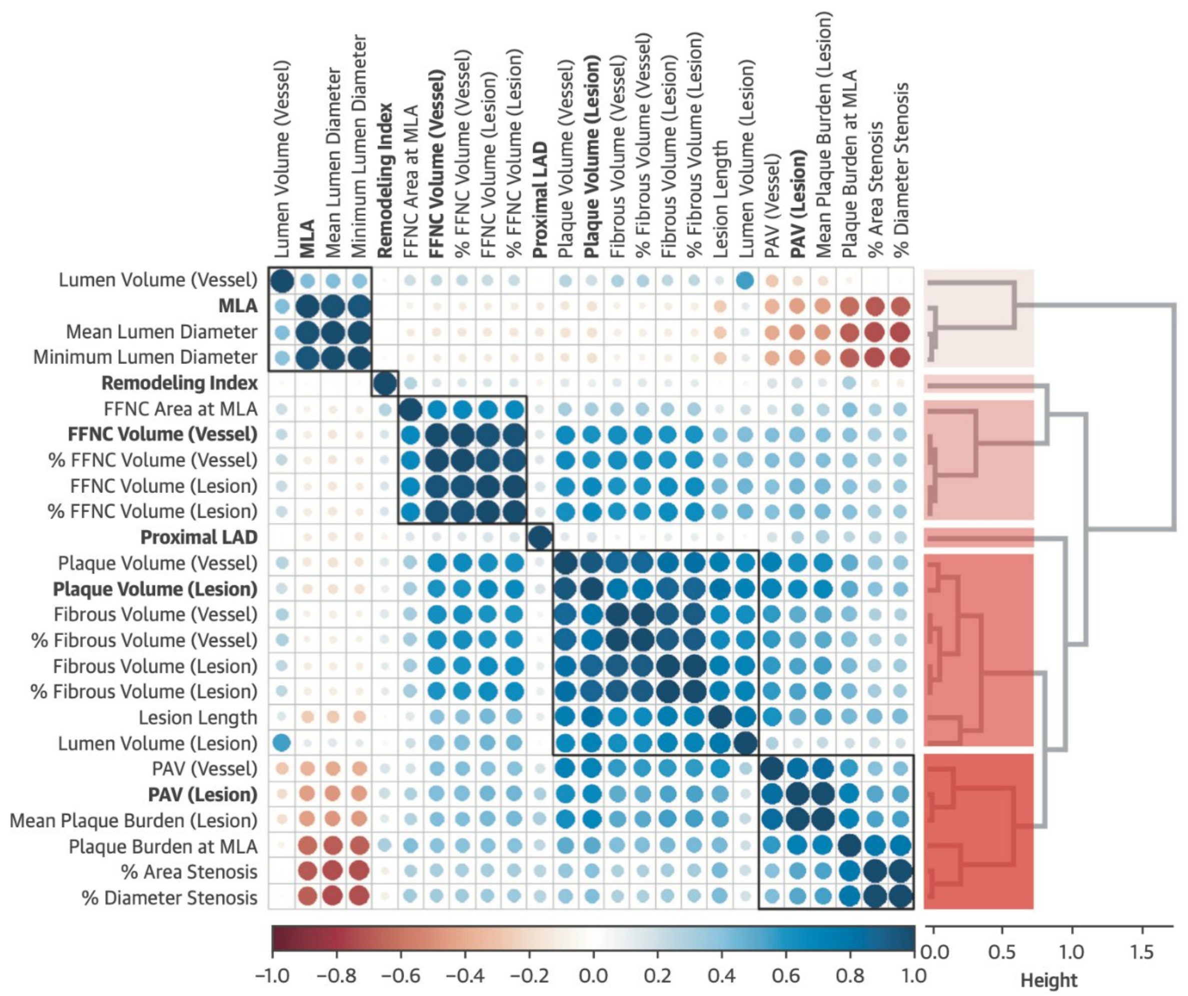
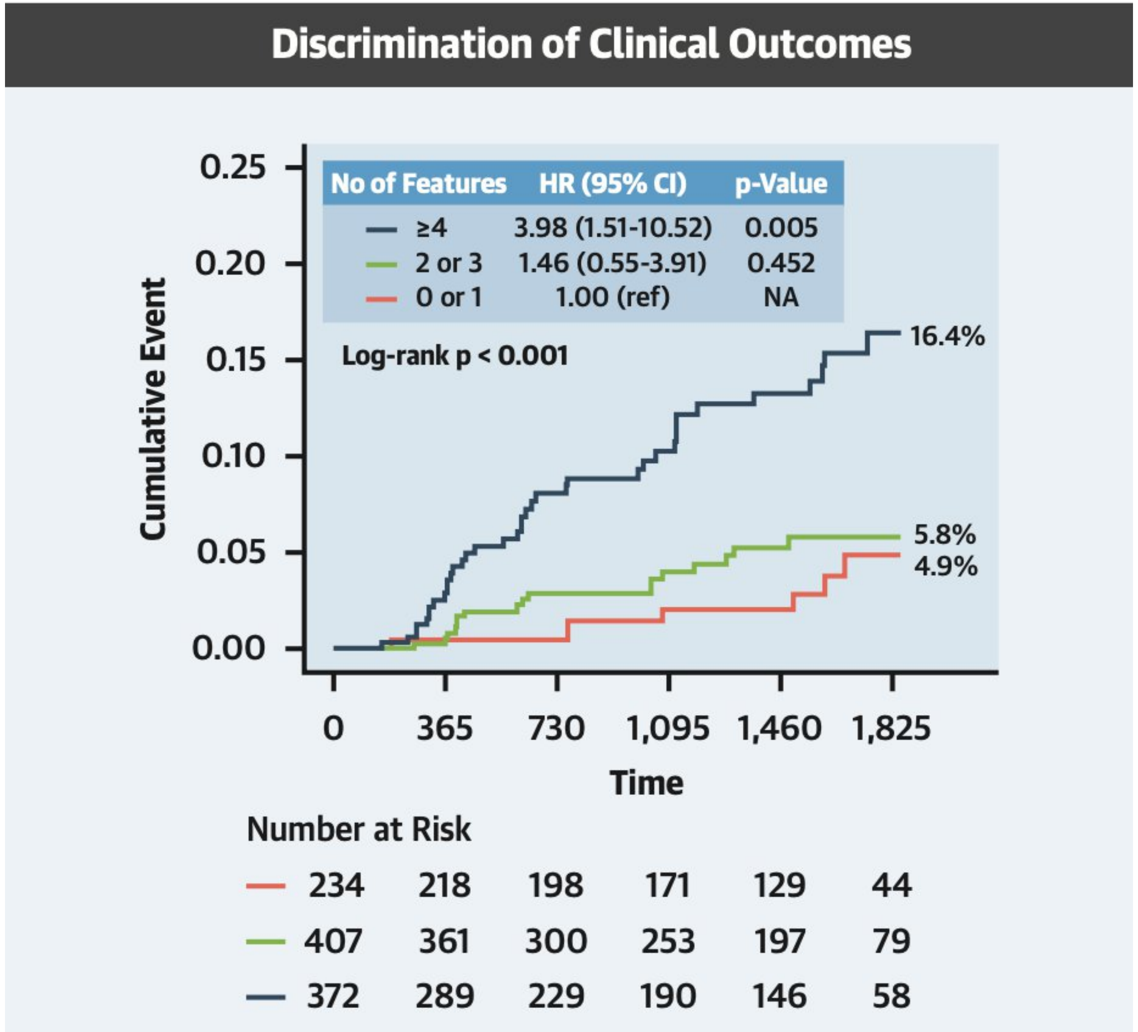
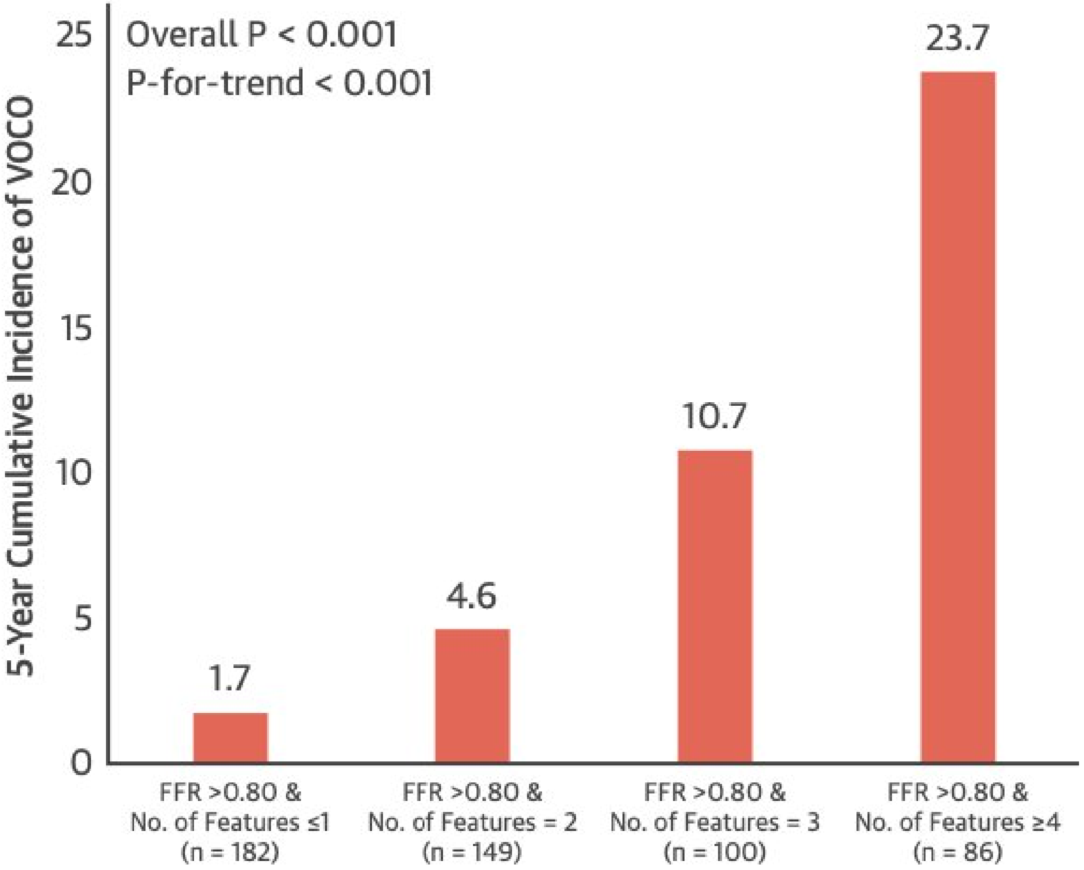


FIGURE 2 Correlation Matrix of 25 Relevant Features for Prediction of FFR ≤0.80 and Dendrogram Created by Hierarchical Clustering





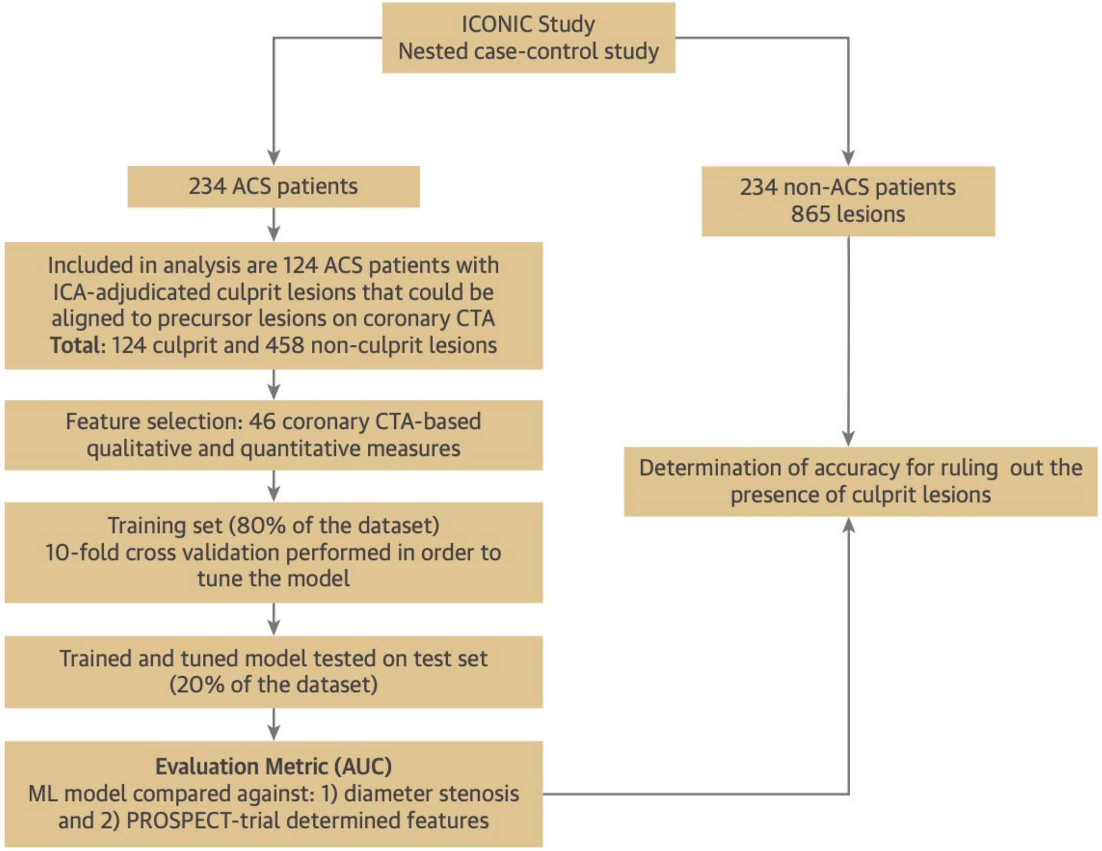


CONCLUSIONS Six functionally relevant features, including minimum lumen area, percent atheroma volume, fibrofatty and necrotic core volume, plaque volume, proximal left anterior descending coronary artery lesion, and remodeling index, help define the presence of myocardial ischemia and provide better prognostication in patients with CAD. (CCTA-FFR

A Boosted Ensemble Algorithm for Determination of Plaque Stability in High-Risk Patients on Coronary CTA

JACC: CARDIOVASCULAR IMAGING, VOL. 13, NO. 10, 2020

Subhi J. Al'Aref, MD,[a] Gurpreet Singh, PhD,[b] Jeong W. Choi, MD,[c] Zhuoran Xu, MD,[c] Gabriel Maliakal, MSc,[d]



	Culprit Lesions (n = 124)	Nonculprit Lesions (n = 458)	p Value
Reference vessel area, mm^2	8.93 (6.71-14.3)	6.77 (4.61-10.74)	<0.001
Ostium to MLD lesion distance, mm	35.300 (21.380-46.510)	40.860 (26.300-71.760)	0.0016
Atherosclerotic plaque characteristics, %			
Positive remodeling	79.84	80.79	0.813
Spotty calcification	18.54	13.10	0.124
Low-attenuation plaque	25.00	14.63	0.006
Napkin-ring sign	3.23	0.66	0.040
Lesion length, mm^2	28.76 (19.64-47.81)	18.3 (13.35-28.2)	<0.001
Vessel volume (of the lesion), mm^3	253.24 (136.80-546.17)	135.36 (70.38-255.65)	<0.001
Lumen volume (of the lesion), mm^3	173.72 (96.49-318.35)	98.04 (57.86-181.87)	<0.001
Plaque volume (of the lesion), mm^3	90.75 (26.51-193.66)	24.71 (9.64-67.2)	<0.001
Plaque burden, %	63.25 (43.38-79.34)	50.14 (35.79-64.78)	<0.001
Fibrous volume (of the lesion), mm^3	34.30 (12.190-91.70)	11.27 (4.59-30.69)	<0.001
Fibrofatty volume (of the lesion), mm^3	8.36 (1.08-30.05)	1.75 (0.13-9.16)	<0.001
Necrotic core volume (of the lesion), mm^3	0.15 (0.00-2.36)	0.00 (0.00-0.34)	<0.001
Dense calcium volume (of the lesion), mm^3	17.89 (2.25-73.52)	5.73 (1.38-20.03)	0.001

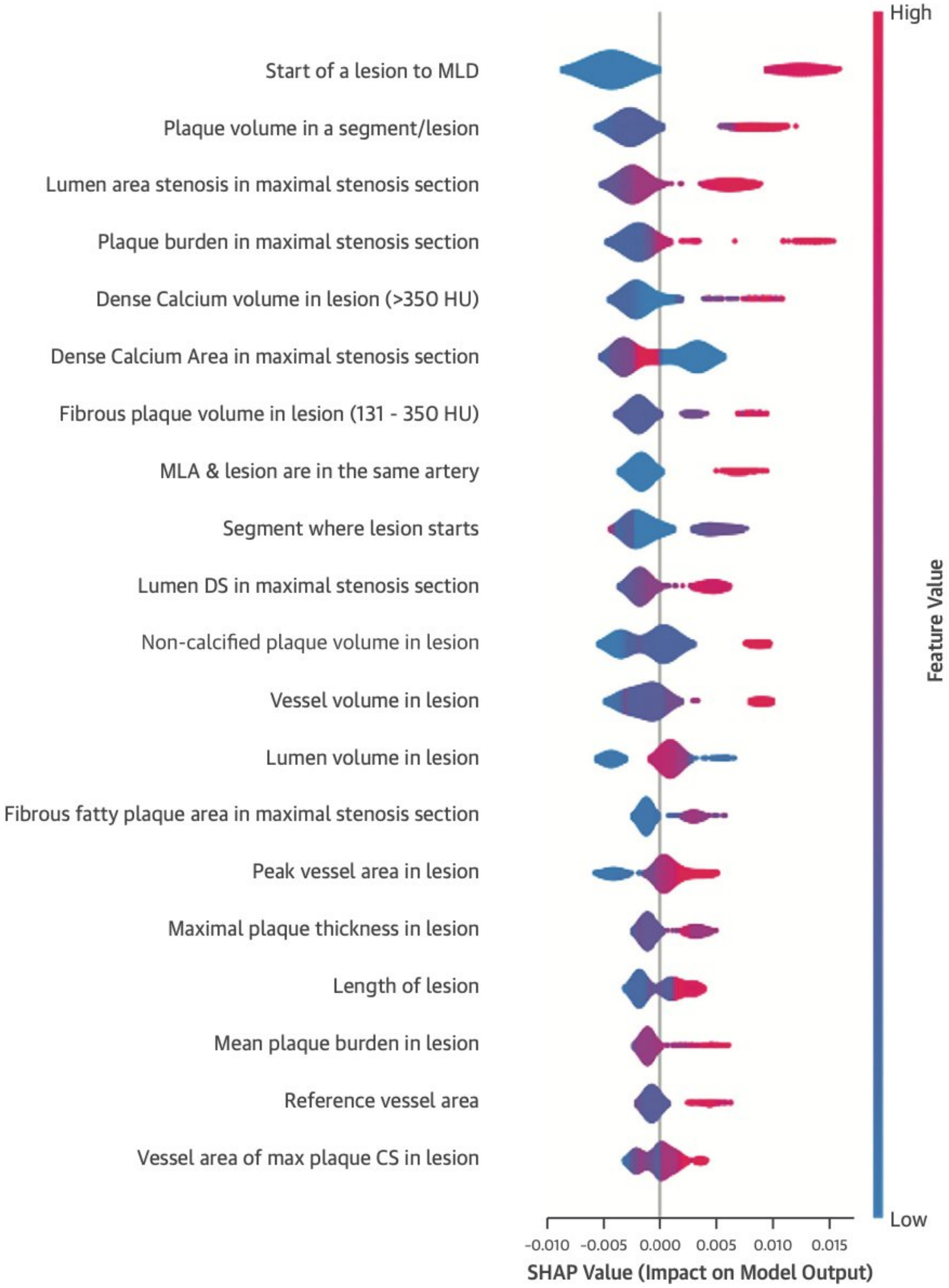
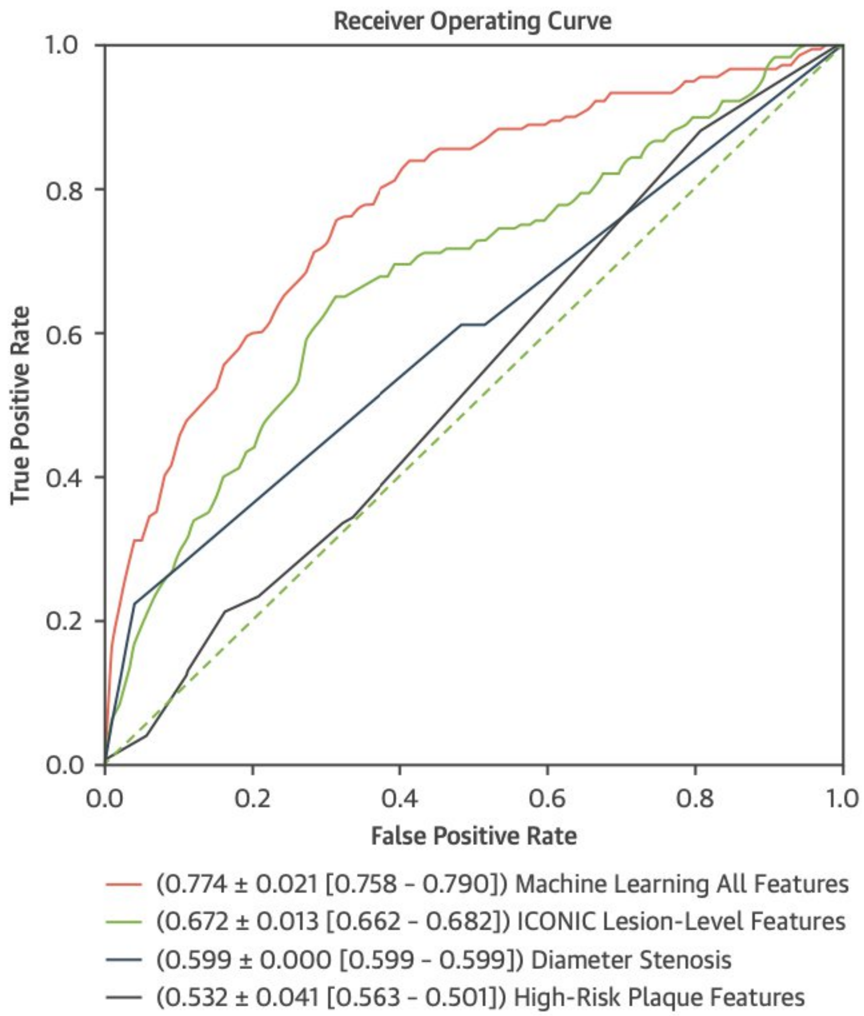
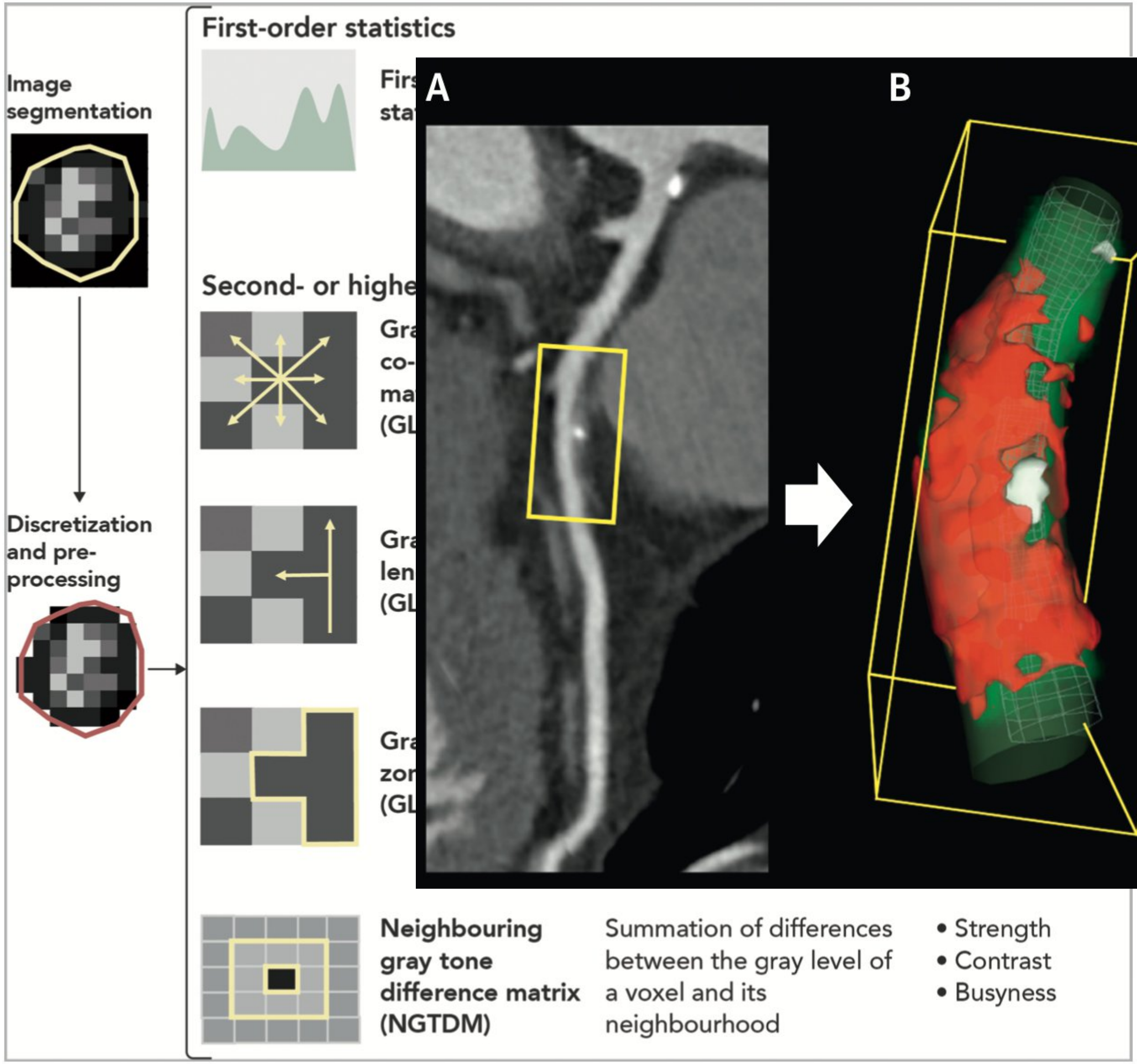
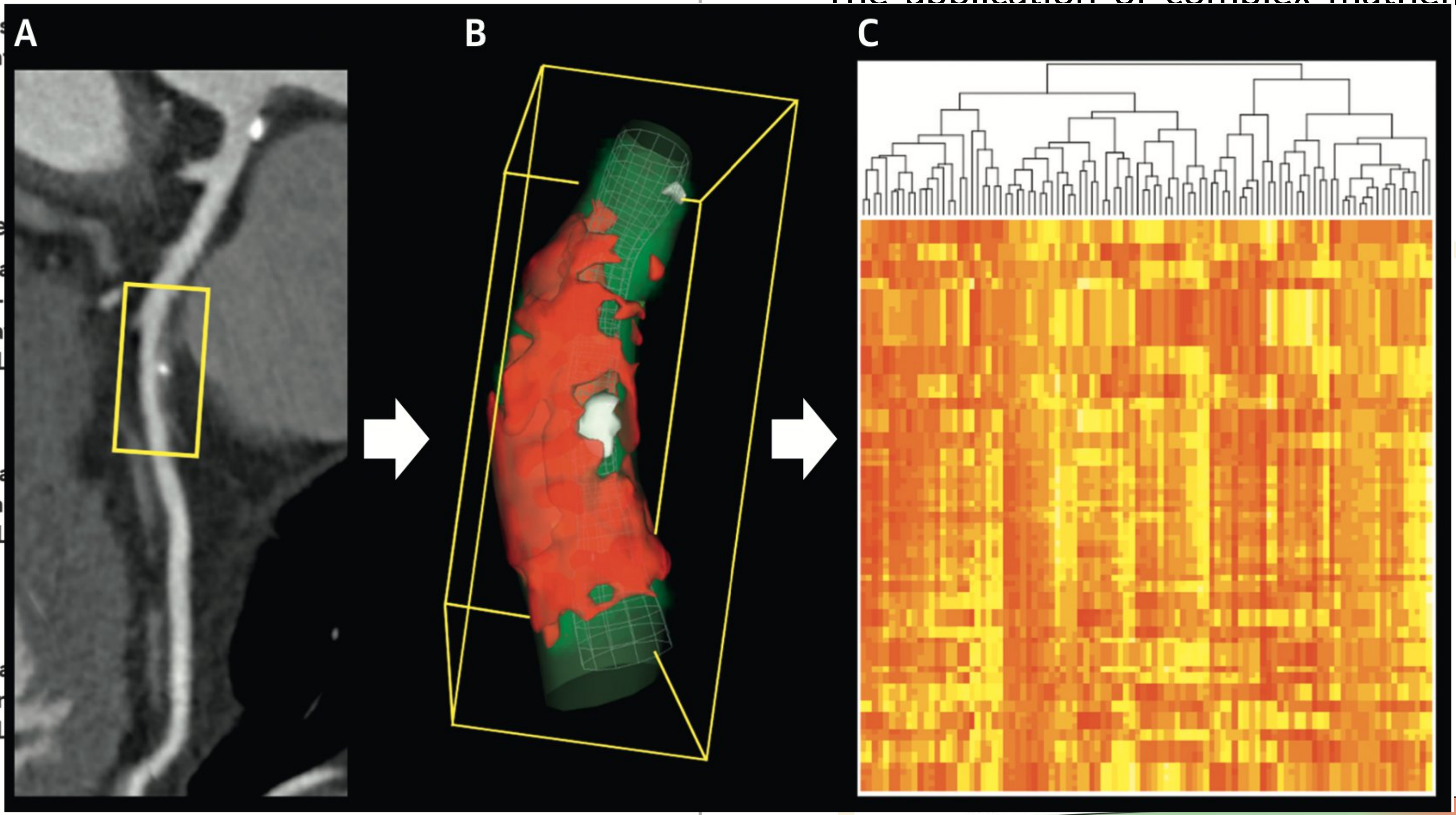


FIGURE 2 **Prediction of Culprit Lesion Precursors Across Four Different Models**



Radiomics





The application of complex mathematic formulae to a ... the calculation of a ... ng to the shape, ... volume of interest.

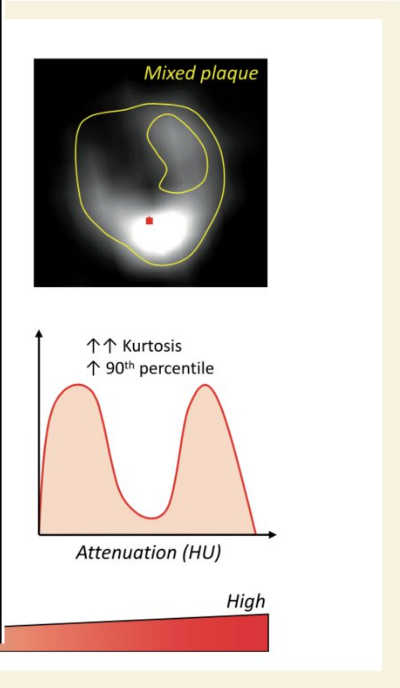


Figure 3 Radiomic phenotyping of coronary lesions. Differences in coronary plaque composition will manifest as different radiomic texture patterns on computed tomography analysis, which can then be quantified using first- and higher-order radiomic features. Changes in these metrics can be used in an automated way to not only detect plaques but also provide a deep characterization of the histology and biology of a given lesion.

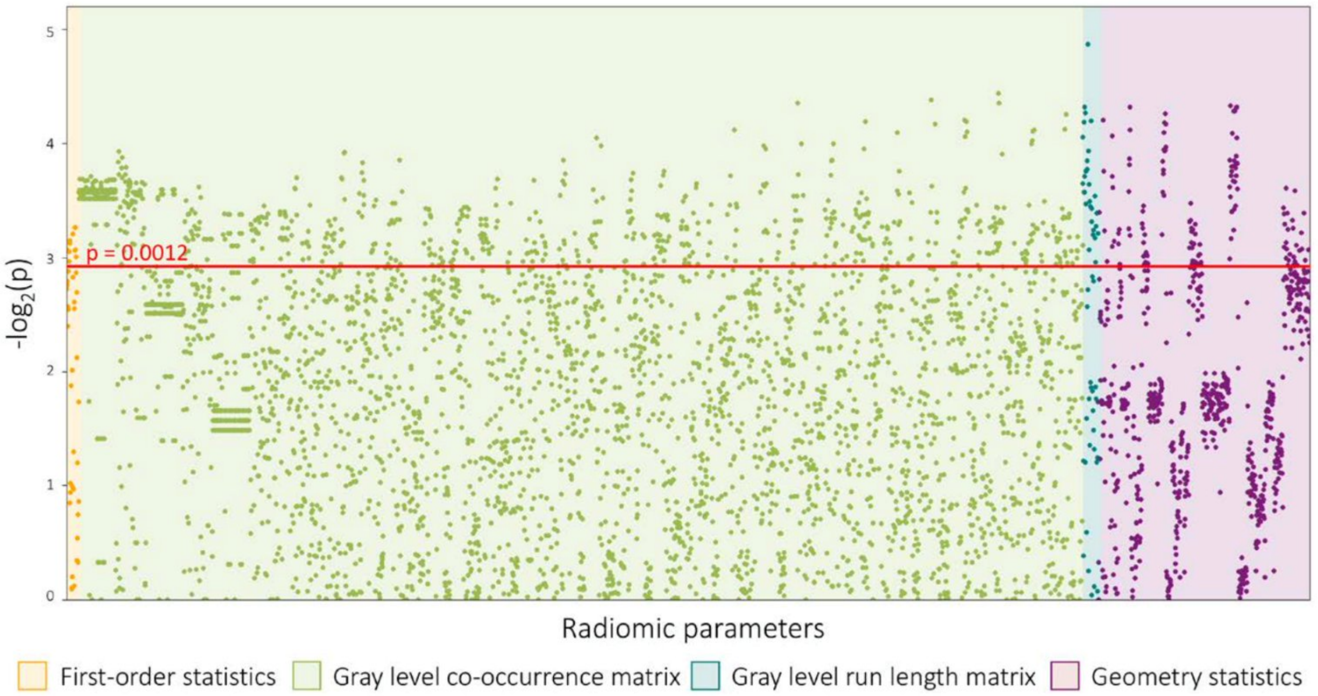
Oikonomou E, at al. Cardiovascular Research (2020) **116**, 2040–2054

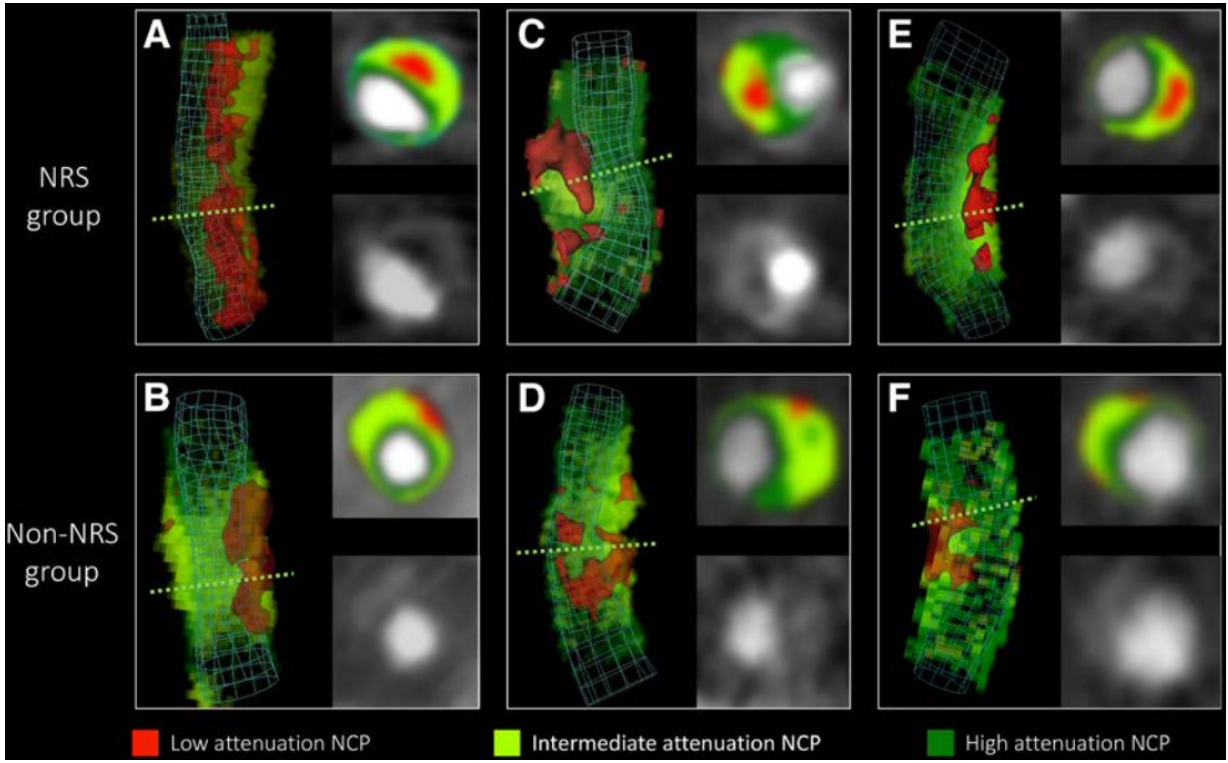
Radiomic Features Are Superior to Conventional Quantitative Computed Tomographic Metrics to Identify Coronary Plaques With Napkin-Ring Sign

Circ Cardiovasc Imaging. 2017;10:e006843.

Márton Kolossváry, MD; Júlia Karády, MD; Bálint Szilveszter, MD; Pieter Kitslaar, MSc;

Methods and Results—From 2674 patients referred to coronary computed tomographic angiography caused by stable chest pain, expert readers identified 30 patients with NRS plaques and matched these with 30 non-NRS plaques with similar degree of calcification, luminal obstruction, localization, and imaging parameters. All plaques were segmented manually, and image data information was analyzed using Radiomics Image Analysis package for the presence of 8 conventional and 4440 radiomic parameters. We used the permutation test of symmetry to assess differences between NRS and non-





Conclusions—A large number of radiomic features are different between NRS and non-NRS plaques and exhibit excellent discriminatory value. (*Circ Cardiovasc Imaging*. 2017;10:e006843. DOI: 10.1161/CIRCIMAGING.117.006843.)

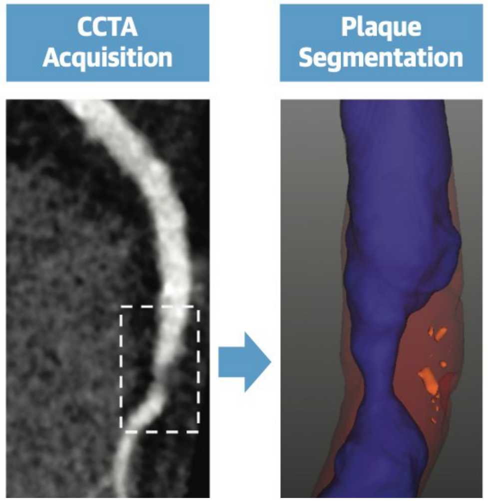
JACC: CARDIOVASCULAR IMAGING

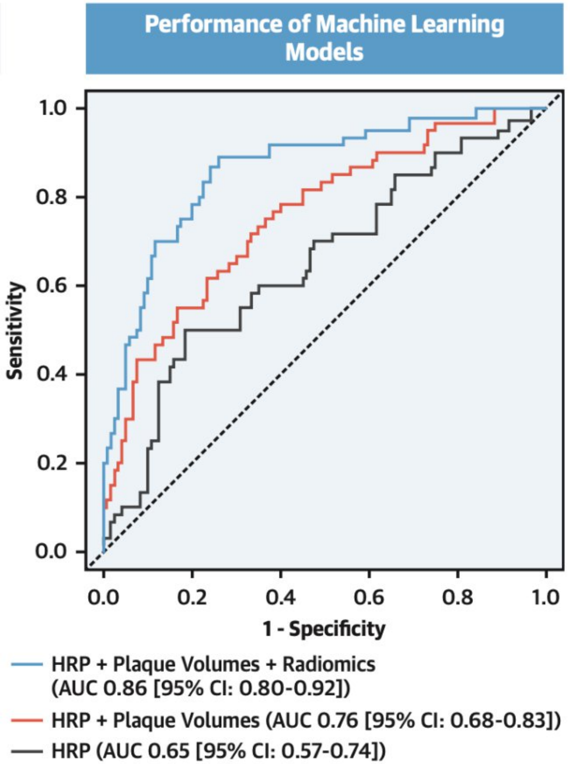
PUBLISHED BY ELSEVIER

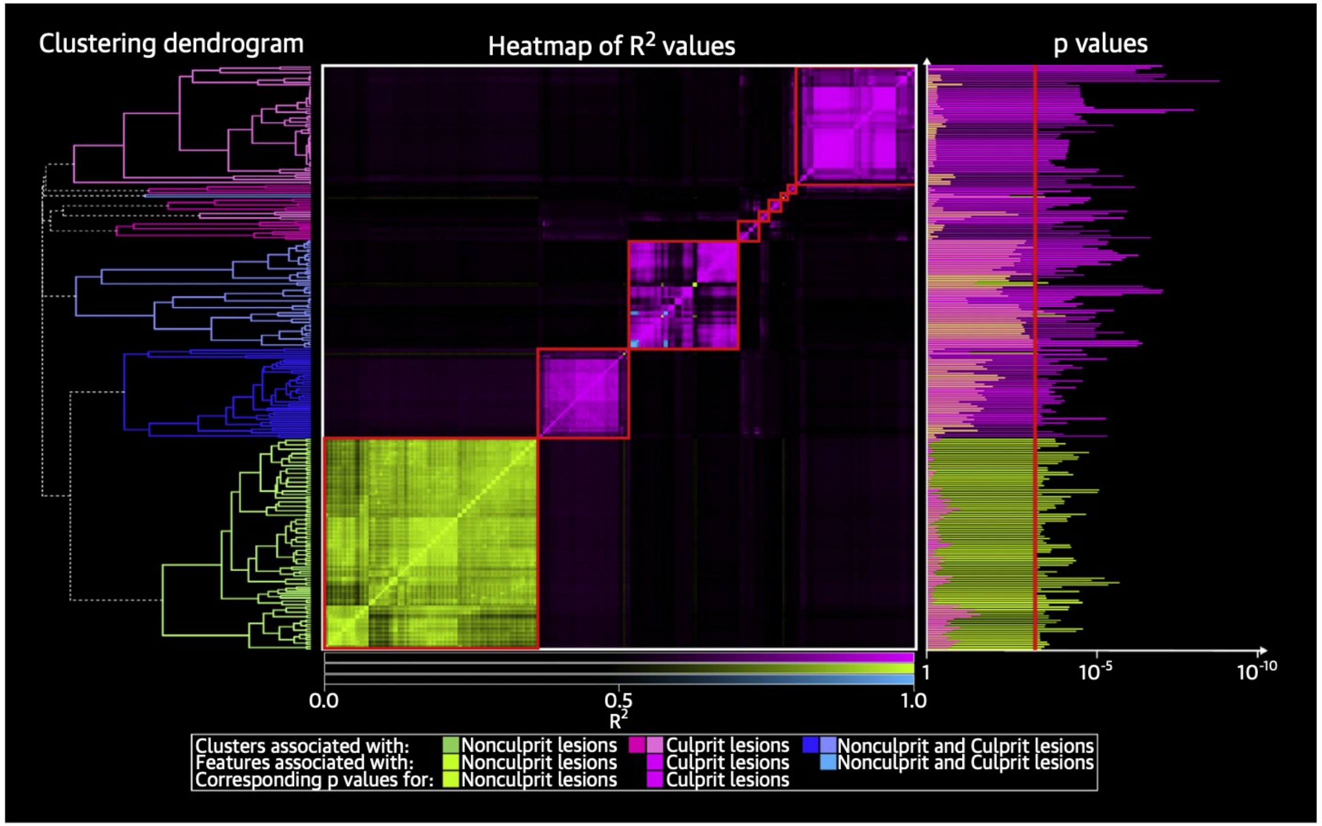
ORIGINAL RESEARCH

Radiomics-Based Precision Phenotyping Identifies Unstable Coronary Plaques From Computed Tomography Angiography

Andrew Lin, MBBS, BMedSci, PhD,[a,b,*] Márton Kolossváry, MD, PhD,[c,*] Sebastien Cadet, MSc,[d]



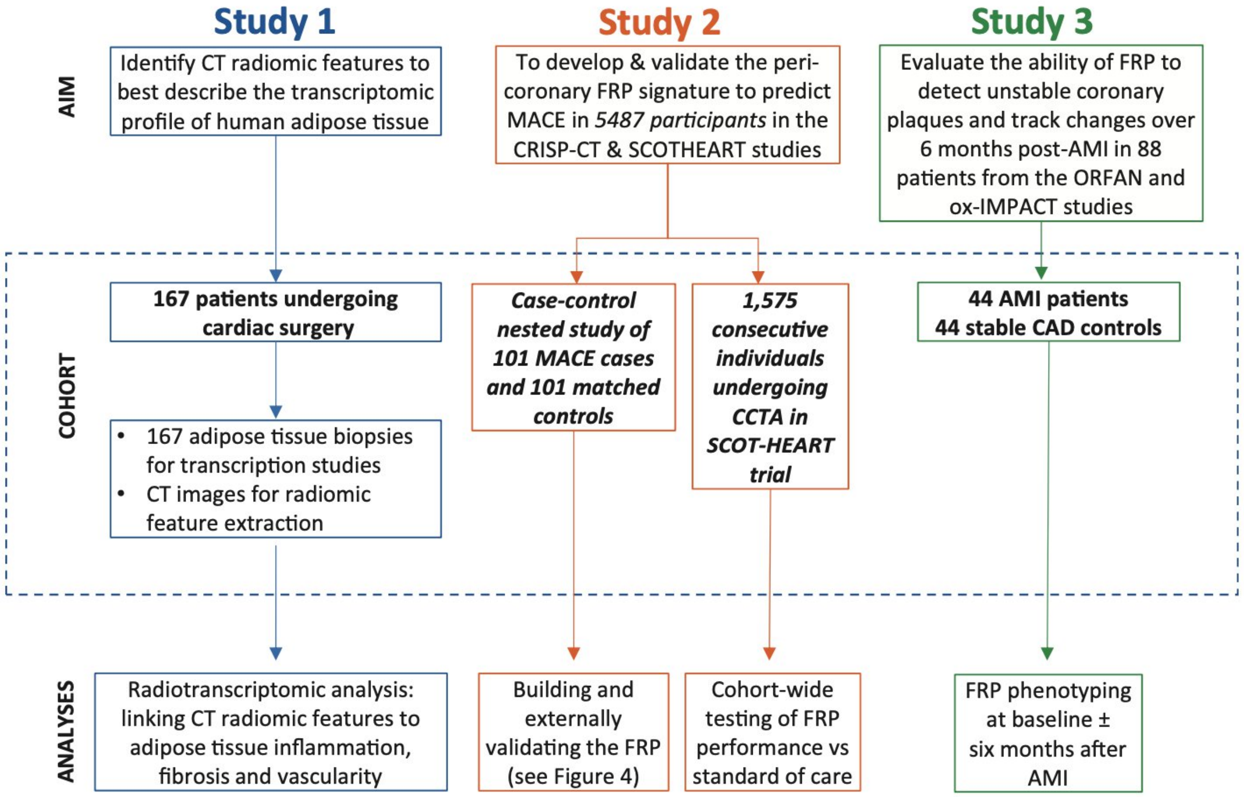




A novel machine learning-derived radiotranscriptomic signature of perivascular fat improves cardiac risk prediction using coronary CT angiography

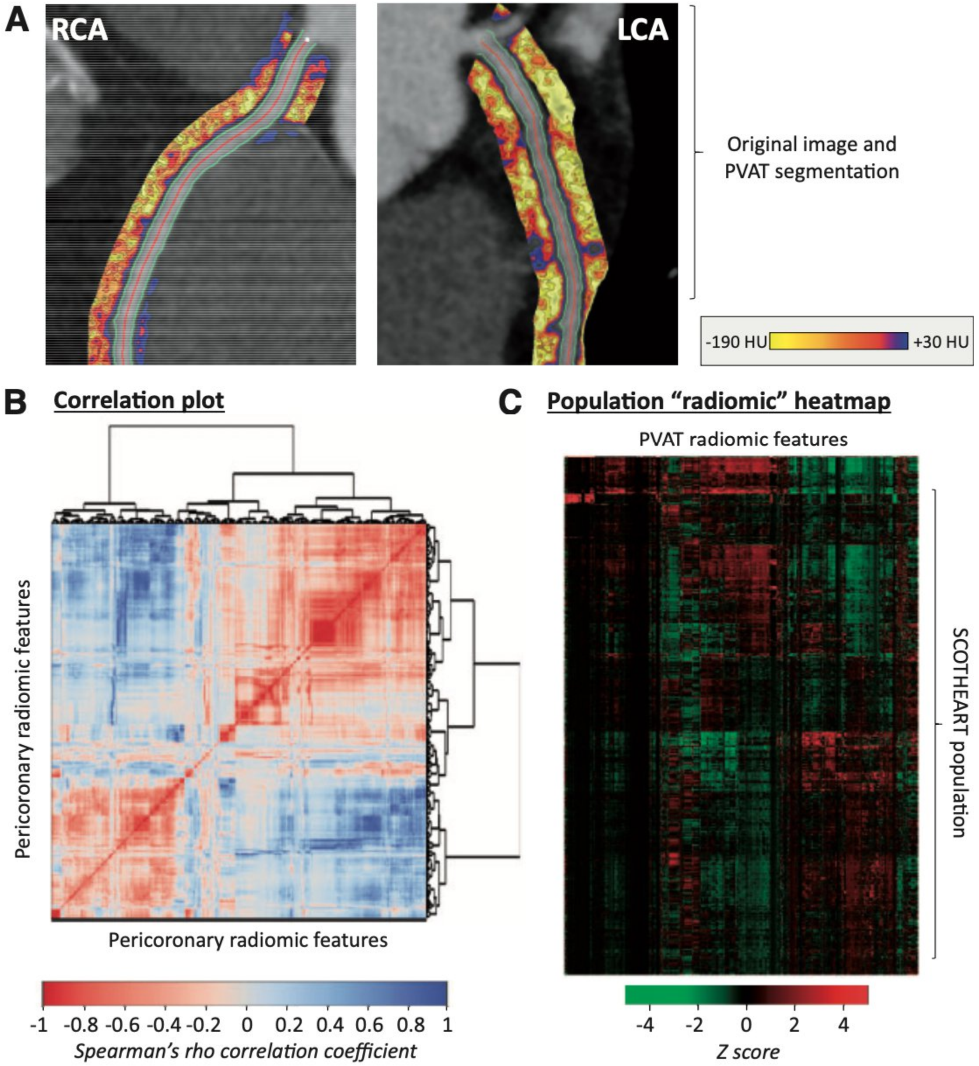
European Heart Journal (2019) **40**, 3529–3543
doi:10.1093/eurheartj/ehz592

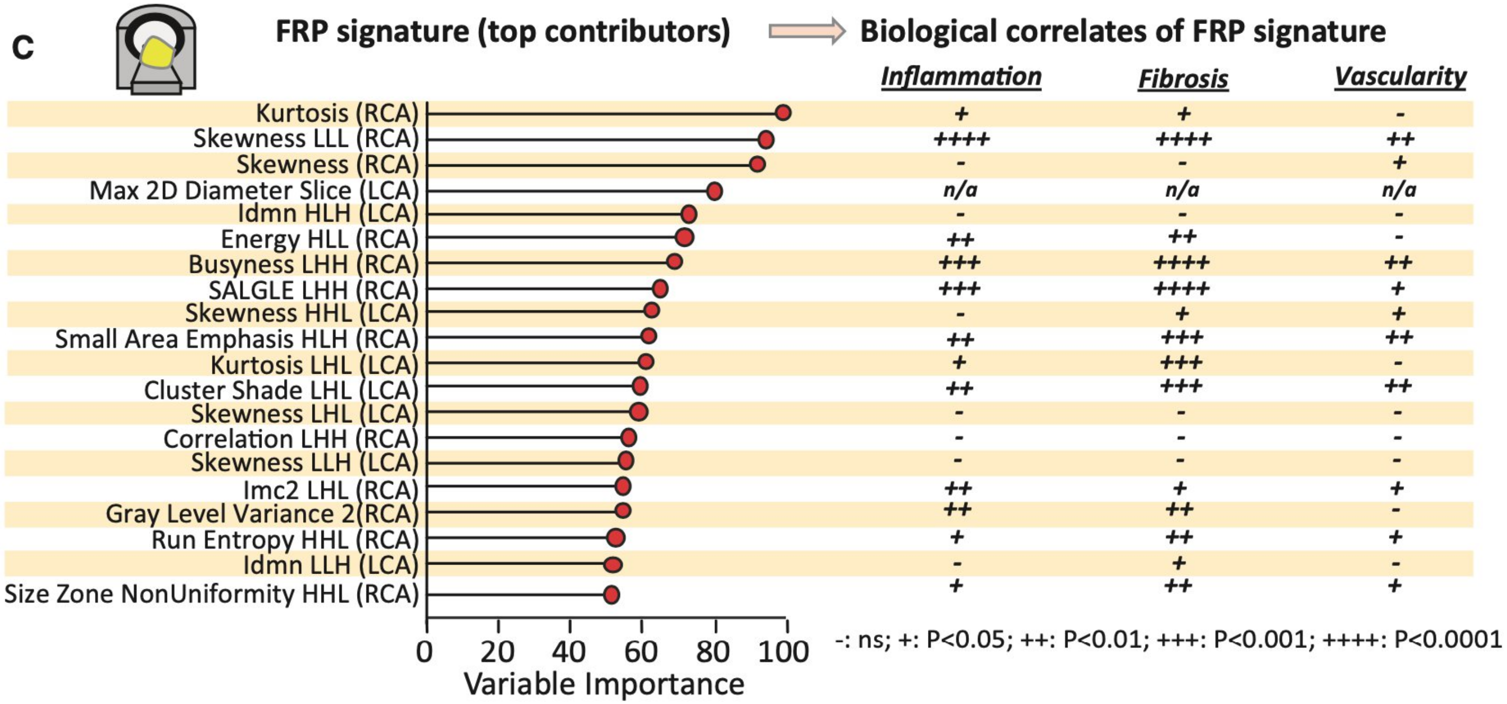
Evangelos K. Oikonomou [1,2], Michelle C. Williams [3,4], Christos P. Kotanidis [1,2], Milind Y. Desai[5], Mohamed Marwan[6],



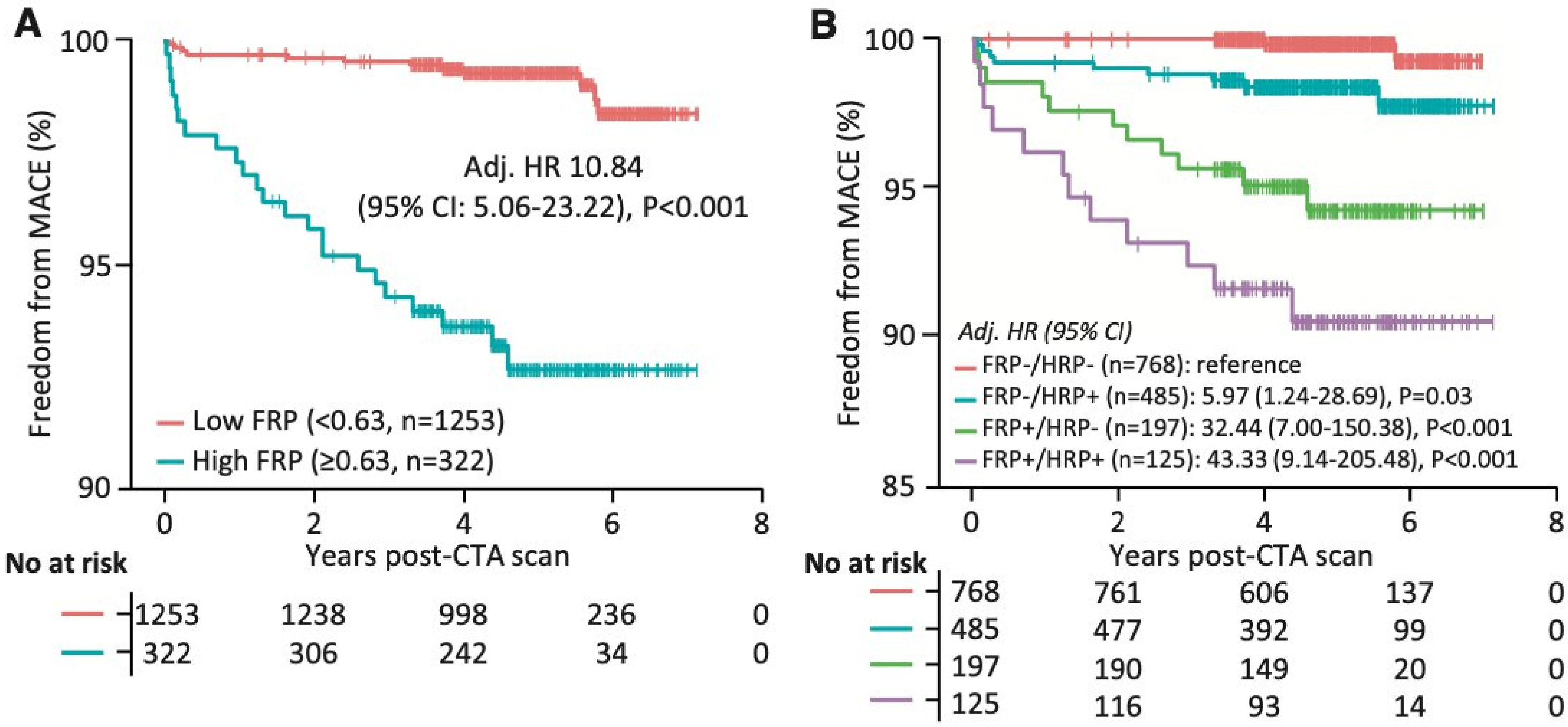
A new artificial intelligence-powered method to predict cardiac risk by analysing the radiomic profile and results of coronary PVAT, developed and validated in patient cohorts acquired in three different studies

Radiomic phenotyping of coronary perivascular adipose tissue



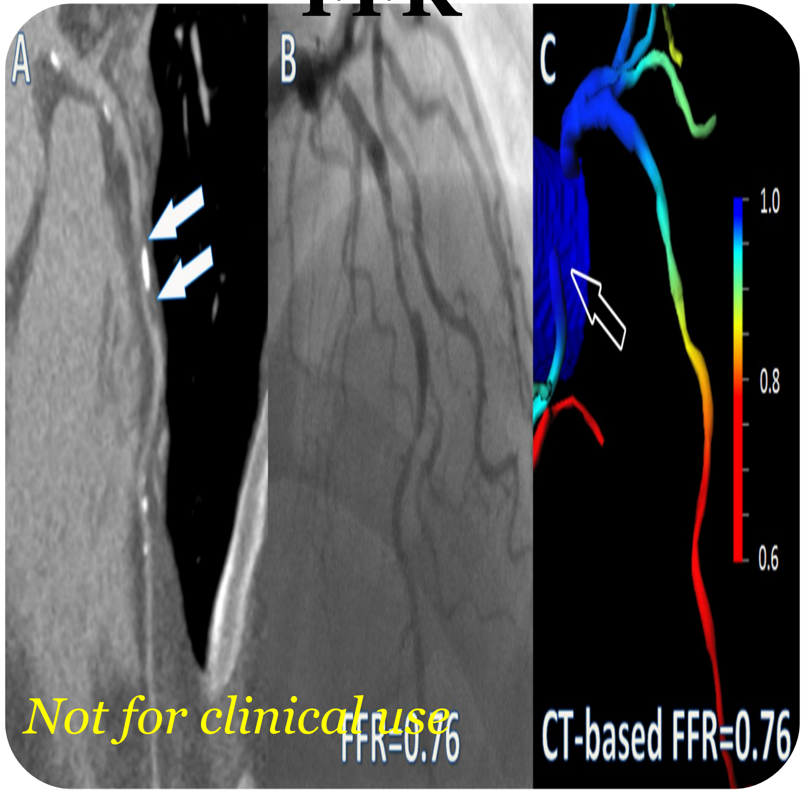


Prognostic value of the pericoronary fat radiomic profile

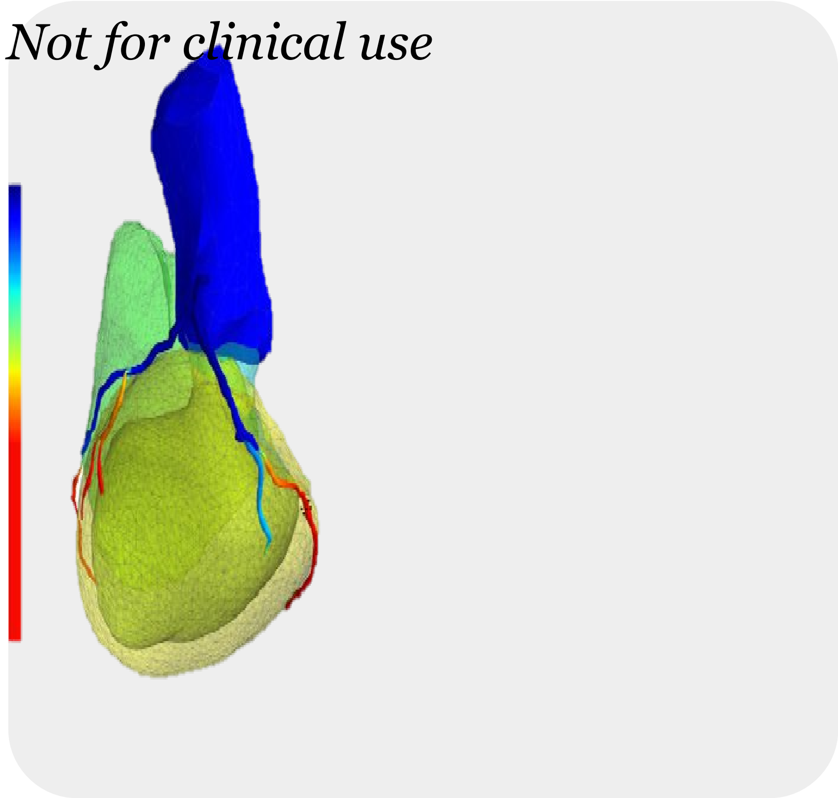


Machine Learning-based CT-FFR

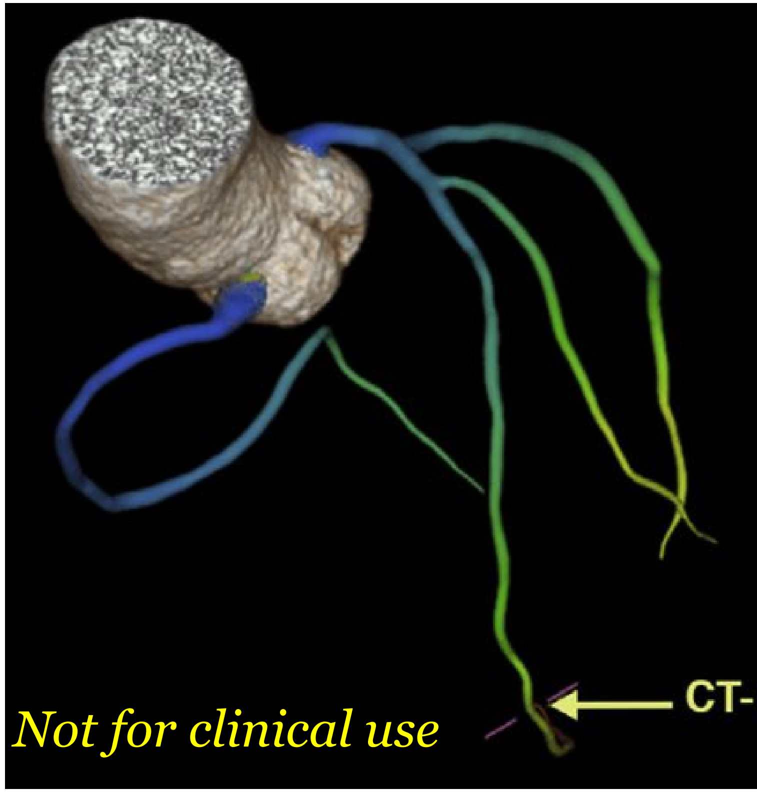
Siemens CT-FFR®



Philips®



Toshiba®

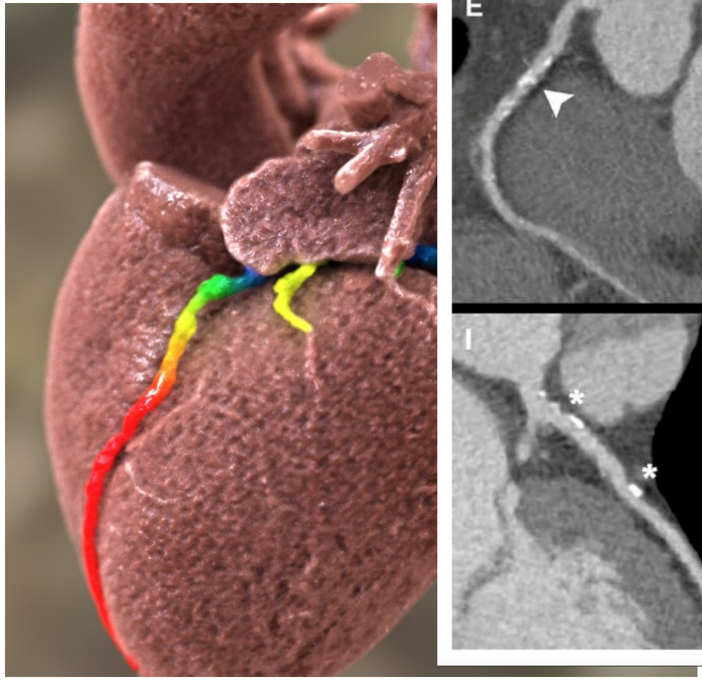


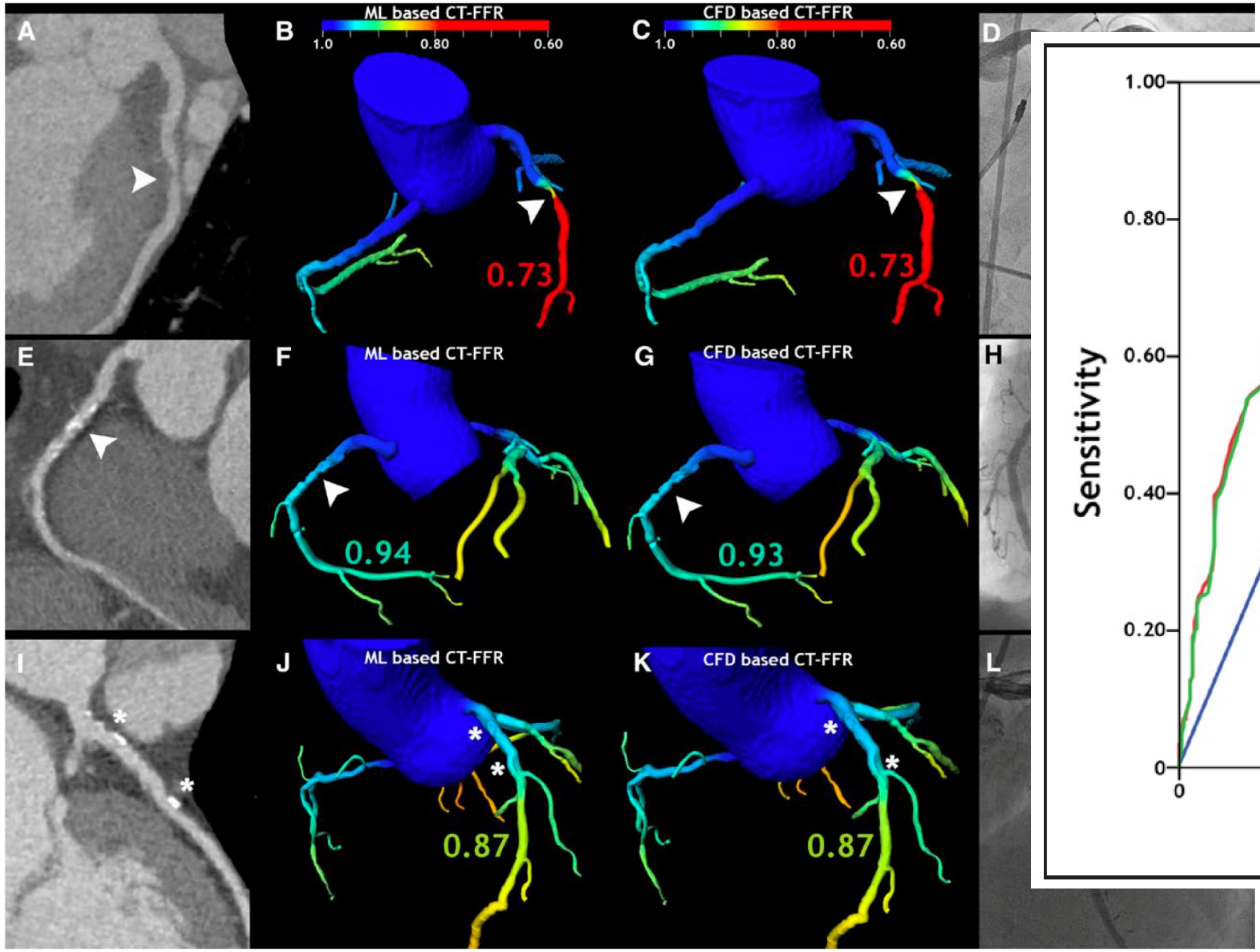
Itu L. et al., Journal of Applied Physiology 2016
Freiman M et al., Medical Physics 2017
Ko BS et al., JACC Cardiovasc Img 2017

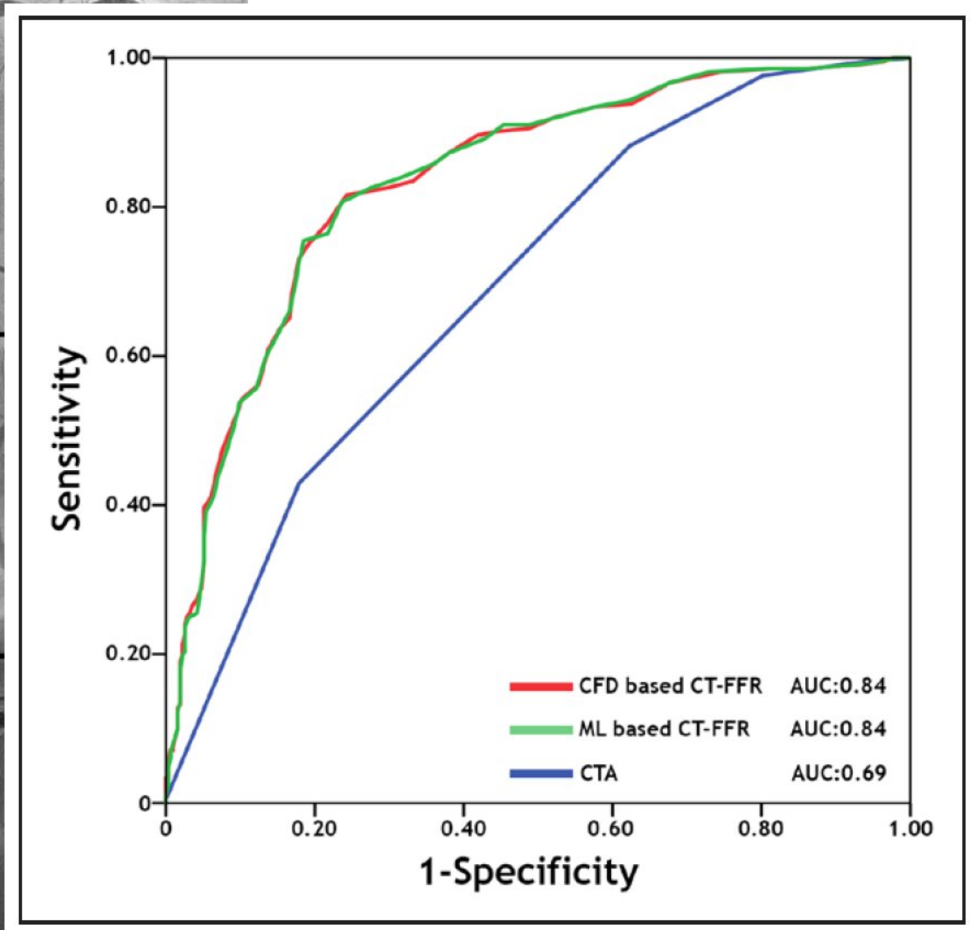
ML CT-FFR: Evidence

Diagnostic Ac
Approach to
Angiography

Result From the M

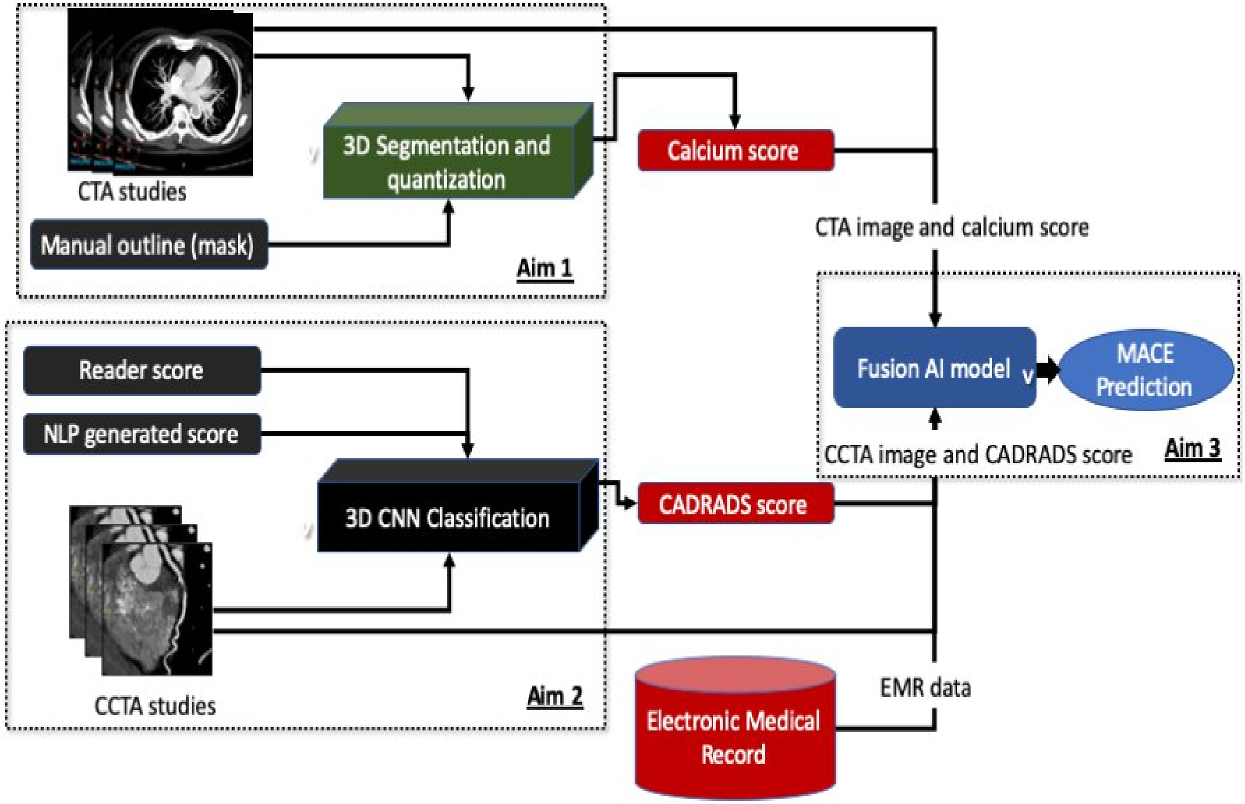


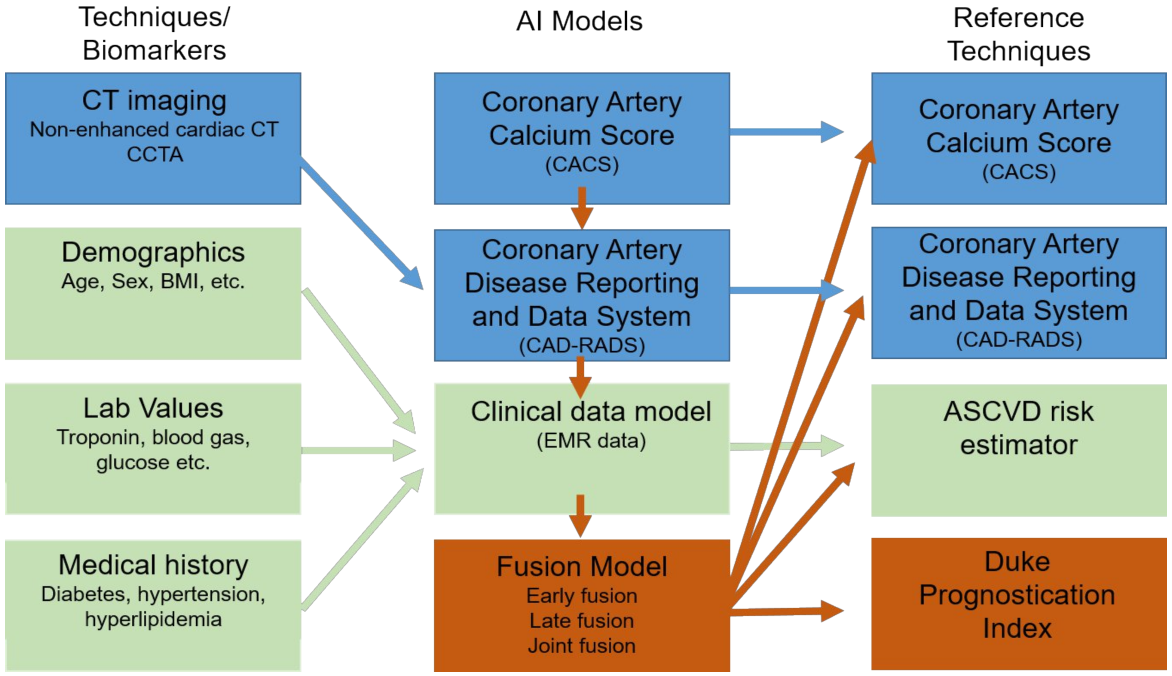




Coenen A. et al., Circ Cardiovasc Imaging 2018

Automated Imaging and EMR Data Integration





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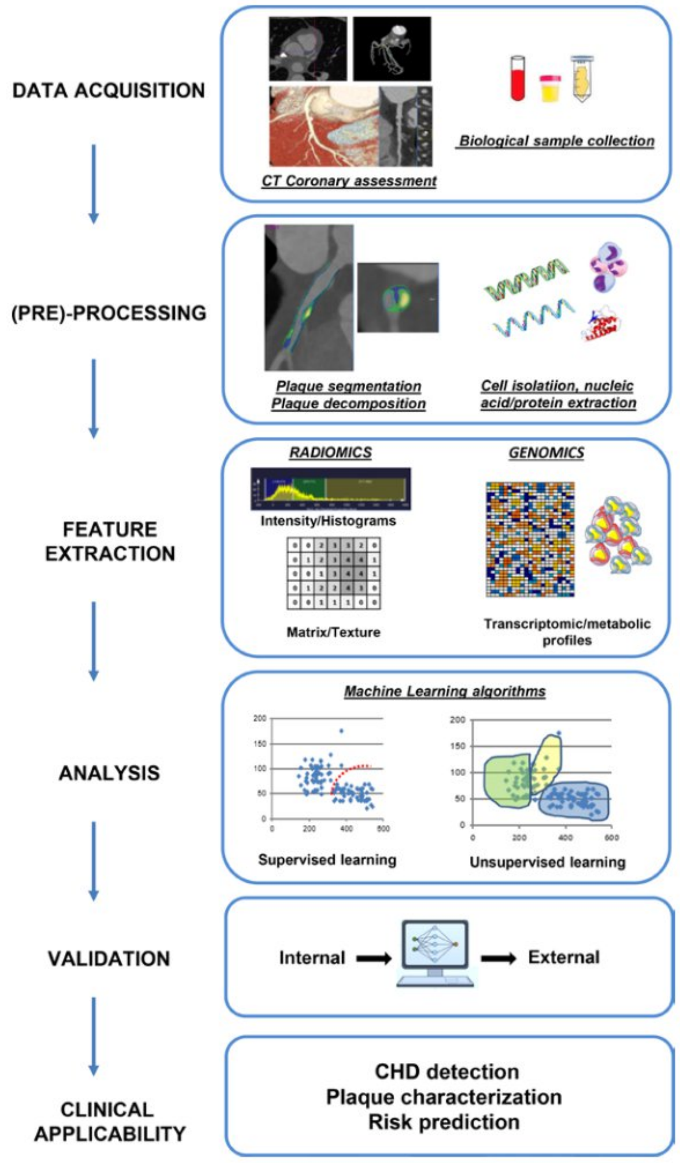
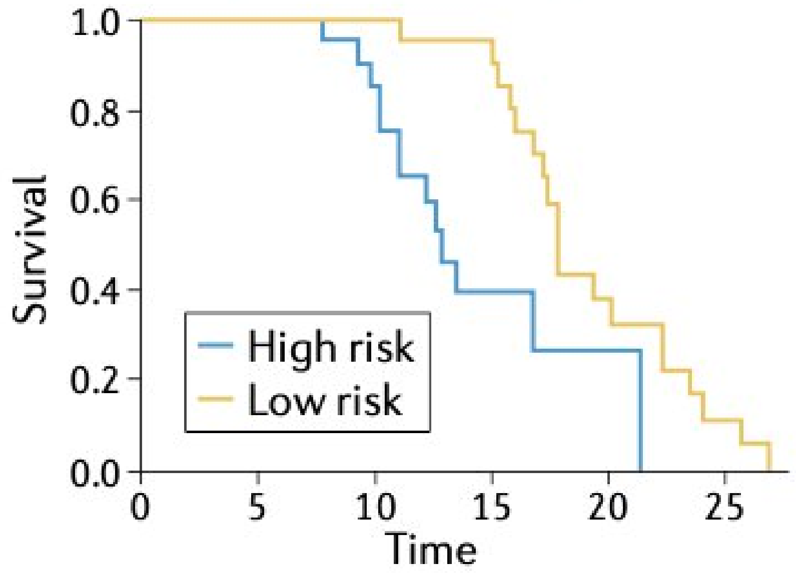
Multi-Omics Integration



- Integrating different and composite data derived from multi-omics approaches to cardiology patients.

- Managing the big amount of data from different types of analysis, including information derived from DNA and RNA sequencing, and imaging.



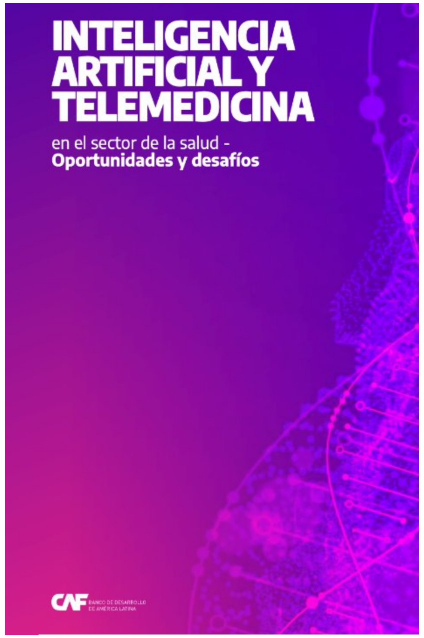
Infante T et al, Circulation Cardiovasc Imag 2021

AI Challenges

- Data **Accessibility**, **Quality**, **Sufficiency** and **Representativeness**
- Results **Reproducibility**, ensuring that insights withstand known challenges with replication
- Algorithms **Transparency**, moving beyond black-box algorithms to ensure results are understood and trusted
- Algorithms **Credibility**, results should be consistent with established science
- Demonstrate and quantify the **Gain** from the use of an algorithm compared with other approaches
- Avoid data **Biases,** data reflect the clinical and social context in which healthcare is delivered

AI Barriers

1. Infrastructure
2. Regulations
3. Funding and Reimbursement
4. Healthcare Personnel training
5. Patient Education and Relationship
6. Data Protection & Cybersecurity



BANCO DE DESARROLLO DE AMÉRICA LATINA

Strategic Use of Data and Artificial Intelligence in the Public Sector.
C. De Cecco, M. van Assen. CAF - Latin America Development Bank 2021

Conclusions

- Machine Learning and Radiomics can play a significant role in the identification and clinical application of novel imaging biomarkers and workflow optimization in cardiac CT and coronary plaque analysis

- AI can rapidly and accurately provide physicians with better data and intel allowing for better decision making and, ultimately, better patient outcomes

- **Results Reproducibility, Outcome Prediction** and **Workflow Integration** are the main challenges

Conclusions

"Artificial Intelligence is changing the medical sector. We need to embrace and guide this revolution to improve the quality of healthcare, reducing disparities in the access to medical services and the cost of medical treatments, to achieve health equity and democratize healthcare."

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